Selective C–N Bond Cleavage in Unstrained Pyrrolidines Enabled by Lewis Acid and Photoredox Catalysis

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Table of Contents

1. General

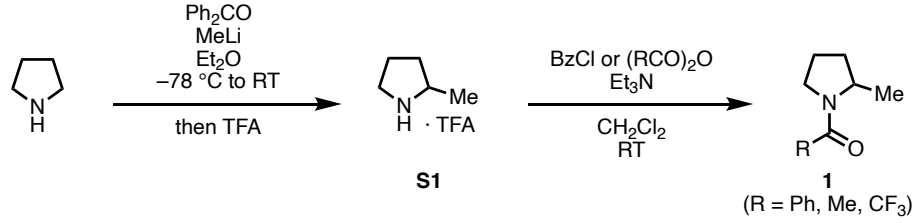
Unless otherwise noted, all reactants or reagents including dry solvents were obtained from commercial suppliers and used as received. Benzophenone, trifluoroacetic anhydride (TFAA), L-proline *tert*-butyl ester hydrochloride, L-proline methyl ester hydrochloride, L-proline benzyl ester hydrochloride, (*S*)-pyrrolidine-2-carboxamide, (*S*)-2-(methoxymethyl)pyrrolidine, 3-chloropropylamine hydrochloride, 4,4′-di-*tert*-butylbiphenyl (DTBB), nitrocyclohexane, (*S*)-2-methylpyrrolidine-2-carboxylic acid, L-proline, benzyl (*S*,*S*,*S*)-2-azabicyclo[3.3.0]octane-3-carboxylate hydrochloride, L-prolinol, L-methionine methyl ester hydrochloride, L-serine methyl ester hydrochloride, L-tyrosine methyl ester hydrochloride, L-proline methyl ester hydrochloride, Raney Ni, (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptane dihydrobromide, lithium hydroxide anhydrous (LiOH), *p*-toluenesulfonyl chloride (TsCl), sodium hydride (NaH: 60%, dispersion in paraffin liquid), 4-ethynyltoluene, azetidine-2-carboxylic acid, (trimethylsilyl)diazomethane, hexane solution (abt. 10%), *N*-(triphenylmethyl)-L-serine methyl ester, azepane, methyl chloroformate, methyl pipecolinate hydrochloride, lithium chloride anhydrous (LiCl), *p*-anisic acid, *p*-toluic acid, 4-chlorobenzoic acid, 4-(trifluoromethyl)benzoic acid, 4-cyanobenzoic acid, and *o*-toluic acid were obtained from Tokyo Chemical Industry (TCI). Pyrrolidine, methyl lithium (MeLi), trifluoroacetic acid (TFA), benzoyl chloride (BzCl), triethylamine (Et_3N), acetic anhydride (Ac_2O), *N*,*N*-dimethylaminopyridine (DMAP), benzyl bromide (BnBr), lithium, lump, in paraffin liquid, methyl acrylate, potassium hydroxide, thionyl chloride ($SOCl_2$), ethylamine hydrochloride, di-*tert*-butyl dicarbonate (Boc_2O), picolinic acid, pivaloyl chloride (PivCl), methanesulfonyl chloride (MsCl), and sodium borohydride ($NaBH_4$) were obtained from KANTO Chemical. Zinc(II) trifluoromethanesulfonate ($Zn(OTf)_2$), L-phenylalanine methyl ester hydrochloride, and sodium carbonate were obtained from FUJIFILM Wako Pure Chemical Corporation. 1,4-Cyclohexadiene (1,4-CHD) was obtained from ACROS Chemical and purified by distillation before use. Lithium aluminum hydride ($LiAlH_4$) was obtained from Sigma-Aldrich. EDC·HCl was obtained from Peptide Institute. CH_2Cl_2 was purified by a Glass Contour Ultimate Solvent System. Tris[5-fluoro-2-(2-pyridinyl-*κN*)phenyl-*κC*]iridium(III) (Ir(4-Fppy)$_3$),[1] methyl (*S*)-1-benzoylpiperidine-2-carboxylate (**S13**),[2] and 2-methyl-1-phenylpyrrolidine (**1ai**)[3] were synthesized according to procedures and the spectra matched with those of compounds reported in the literature. Unless otherwise noted, all reactions were performed with dry solvents under an atmosphere of N_2 in dried glassware using standard vacuum-line techniques. All work-up and purification procedures were carried out with reagent-grade solvents in the air.

Analytical thin-layer chromatography (TLC) was performed using Silica-gel 70 TLC Plate-Wako (0.25 mm). The developed chromatogram was analyzed by UV lamp (254 nm). Flash column chromatography was performed with Biotage Isolera® equipped with Biotage Sfär Silica (HC) D Duo columns. Preparative thin-layer chromatography (PTLC) was performed using Wakogel B5-F silica coated plates (0.75 mm) prepared in our laboratory. Preparative recycling gel permeation chromatography (GPC) was performed with a JAI LaboACE LC-5060 instrument equipped with

JAIGEL-2HR columns using $CHCl_3$ as an eluent. High-resolution mass spectra (HRMS) were conducted on Thermo Fisher Scientific ExactivePlus Orbitrap (ESI) and Bruker Compact QTOF (APCI). Nuclear magnetic resonance (NMR) spectra were recorded on a JEOL JNM-ECS-400 and JNM-ECZ-400S (^{1}H 400 MHz, $^{13}C\{^1H\}$ 101 MHz, ^{19}F 376 MHz) spectrometer. Chemical shifts for ^{1}H NMR are expressed in parts per million (ppm) relative to tetramethylsilane (δ 0.00 ppm) in $CDCl_3$, $(CD_3)_2SO$, and benzene-d_6, and CHD_2CN (δ 1.94 ppm) in CD_3CN. Chemical shifts for $^{13}C\{^1H\}$ NMR are expressed in ppm relative to $CDCl_3$ (δ 77.0 ppm), C_6D_6 (δ 128.0 ppm), C_4D_8O (δ 67.0 ppm), $(CD_3)_2SO$ (δ 40.0 ppm), and CD_3CN (δ 118.0 ppm). Chemical shifts for ^{19}F NMR are expressed in ppm relative to PhF (δ –113.15 ppm) or C_6F_6 (δ –164.90 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplets, td = triplet of doublets, q = quartet, qd = quartet of doublets, ddd = doublet of doublets of doublets, tdd = triplet of doublets of doublets, dtd = doublet of doublets of doublets, m = multiplet, br s = broad singlet), coupling constant (Hz), and integration.

2. Preparation of the Starting Materials

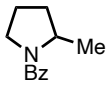
2-1. Synthesis of 1a, 1ab, and 1ac



General Procedure A

2-Methylpyrrolidine TFA salt (**S1**) was synthesized according to the reported procedure.[4] To a solution of pyrrolidine (821 μL, 10 mmol, 1.0 equiv) and benzophenone (2.19 g, 12 mmol, 1.2 equiv) in Et_2O (20 mL, 0.50 M) was added MeLi (1.0 M in Et_2O, 25 mL, 25 mmol, 2.5 equiv) dropwise at –78 °C under an atmosphere of N_2. After being stirred at the same temperature for 10 min, the reaction mixture was allowed to warm to room temperature and stirred for 7 h. The reaction was quenched with MeOH at 0 °C, and the mixture was diluted with water and extracted with 6.0 M HCl aq. (pH = 1). The aqueous layer was basified to pH = 13 with 6.0 M NaOH aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was acidified to pH = 1 with TFA, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

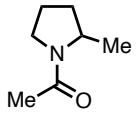
To a solution of the crude product obtained above (1.0 equiv) and Et_3N (3.0 equiv) in CH_2Cl_2 (25 mL, 0.40 M) was added BzCl (1.2 equiv), Ac_2O (1.5 equiv), or TFAA (1.5 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 1 h, which was then quenched with a saturated $NaHCO_3$ aqueous solution and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® to afford *N*-acyl pyrrolidine **1**.



1a

(2-Methylpyrrolidin-1-yl)(phenyl)methanone (1a)

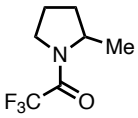
According to **General Procedure A**, **1a** was prepared using BzCl (1.4 mL, 12 mmol, 1.2 equiv). Purification by Isolera® (9:1 to 4:1 hexane/EtOAc) afforded **1a** (986.5 mg, 52% over 2 steps) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53–7.34 (m, 5H), 4.40–4.28 (m, 0.7H), 4.05–3.95 (m, 0.3H), 3.80–3.60 (m, 0.6H), 3.52–3.34 (m, 1.4H), 2.20–1.85 (m, 2H), 1.80–1.69 (m, 0.7H), 1.66–1.56 (m, 1.3H), 1.36 (d, *J* = 6.0 Hz, 2.2H), 0.91 (br s, 0.8H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 169.7, 137.8, 129.5, 128.2, 127.0, 53.3, 49.8, 32.9, 24.8, 19.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{16}ON$ 190.1226; found 190.1227.



1ab

1-(2-Methylpyrrolidin-1-yl)ethan-1-one (1ab)

According to **General Procedure A**, **1ab** was prepared using Ac_2O (1.4 mL, 15 mmol, 1.5 equiv). Purification by Isolera® (19:1 $CHCl_3$/MeOH) afforded **1y** (461.8 mg, 36% over 2 steps) as a light-yellow oil. The spectra are in accordance with those reported in the literature.[5]

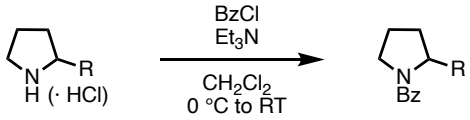


1ac

2,2,2-Trifluoro-1-(2-methylpyrrolidin-1-yl)ethan-1-one (1ac)

According to **General Procedure A**, **1ac** was prepared using TFAA (2.1 mL, 15 mmol, 1.5 equiv). Purification by Isolera® (19:1 to 5:1 hexane/EtOAc) afforded **1z** (697.4 mg, 39% yield over 2 steps) as a brown oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 4.38–4.21 (m, 1H), 3.70–3.53 (m, 2H), 2.11–1.88 (m, 3H), 1.68–1.58 (m, 1H), 1.28–1.21 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 155.5 (q, $J_{C–F}$ = 36.7 Hz), 116.4 (q, $J_{C–F}$ = 289.9 Hz), 55.1, 54.0 (m), 46.5 (m), 33.1, 31.3, 24.1, 20.7, 20.4, 18.5 (four excess peaks are observed due to rotamer); **^{19}F NMR** (376 MHz, $CDCl_3$, 323 K) δ –70.9, –72.6; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_7H_{10}ONF_3Na$ 204.0607; found 204.0608.

2-2. Synthesis of 1b, 1g–1j, and 1m

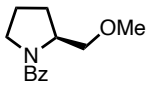


1

General Procedure B

To a solution of pyrrolidine (1.0 equiv) and Et_3N (3.0 equiv–4.0 equiv, see ***Note***) in CH_2Cl_2 (0.40 M) was added benzoyl chloride (BzCl: 1.2 equiv) dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 30 min, which was then quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® to afford pyrrolidine **1**.

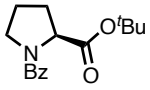
(***Note***: Et_3N (3.0 equiv) was used for **1b** and **1j**; Et_3N (4.0 equiv) was used for **1g**, **1h**, **1i**, and **1m**.)



1b

(*S*)-(2-(Methoxymethyl)pyrrolidin-1-yl)(phenyl)methanone (1b)

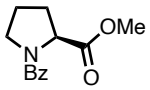
According to **General Procedure B**, **1b** was prepared from (*S*)-2-(methoxymethyl)pyrrolidine (517.1 mg, 4.5 mmol). Purification by Isolera® (19:1 to 2:1 hexane/EtOAc) afforded **1b** (899.2 mg, 91% yield) as a colorless oil. **^{1}H NMR** (400 MHz, C_6D_6, 338 K) δ 7.52–7.48 (m, 2H), 7.13–7.08 (m, 3H), 4.41 (br s, 1H), 3.50 (br s, 2H), 3.25–3.00 (m, 5H), 1.83–1.75 (m, 1H), 1.74–1.62 (m, 1H), 1.54–1.44 (m, 1H), 1.28–1.21 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, CD_3CN, 338 K) δ 170.5, 139.3, 130.5, 129.35, 129.26, 129.2, 128.0, 74.0, 59.4, 58.0, 50.4, 29.0, 25.1; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{18}O_2N$ 220.1332; found 220.1333.



1g

***tert*-Butyl benzoyl-L-prolinate (1g)**

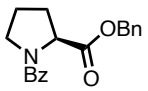
According to **General Procedure B**, **1g** was prepared from L-proline *tert*-butyl ester hydrochloride (1.66 g, 8.0 mmol). Purification by Isolera® (9:1 to 3:2 hexane/EtOAc) afforded **1g** (1.47 g, 67% yield) as a white solid. The spectra are in accordance with those reported in the literature.[6]



1h

Methyl benzoyl-L-prolinate (1h)

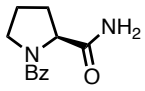
According to **General Procedure B**, **1h** was prepared from L-proline methyl ester hydrochloride (1.35 g, 8.1 mmol). Purification by Isolera® (9:1 to 3:2 hexane/EtOAc) afforded **1h** (1.46 g, 77% yield) as a white solid. The spectra are in accordance with those reported in the literature.[7]



1i

Benzyl benzoyl-L-prolinate (1i)

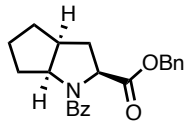
According to **General Procedure B**, **1i** was prepared from L-proline benzyl ester hydrochloride (482.9 mg, 2.0 mmol). Purification by Isolera® (4:1 to 1:1 hexane/EtOAc) afforded **1i** (613.4 mg, 99% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[8]



1j

(*S*)-1-Benzoylpyrrolidine-2-carboxamide (1j)

According to **General Procedure B**, **1j** was prepared from (*S*)-pyrrolidine-2-carboxamide (456.6 mg, 4.0 mmol). Purification by Isolera® (19:1 $CHCl_3$/MeOH) afforded **1j** (805.9 mg, 92% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.54–7.48 (m, 2H), 7.40–7.35 (m, 3H), 6.93 (br s, 1H), 5.40 (br s, 1H), 4.80 (br s, 1H), 3.60–3.40 (m, 2H), 2.47 (br s, 1H), 2.12–1.95 (m, 2H), 1.85 (br s, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 174.1, 170.1, 136.1, 129.7, 127.9, 126.8, 59.6, 50.0, 28.4, 24.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{15}O_2N_2$ 219.1128; found 219.1129.

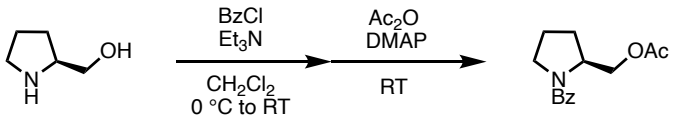


1m

Benzyl (2*S*)-1-benzoyloctahydrocyclopenta[*b*]pyrrole-2-carboxylate (1m)

According to **General Procedure B**, **1m** was prepared from benzyl (*S*,*S*,*S*)-2-azabicyclo[3.3.0]octane-3-carboxylate hydrochloride (229.6 mg, 0.8 mmol). Purification by Isolera® (9:1 to 1:1 hexane/EtOAc) afforded **1m** (261.5 mg, 92% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.51–7.26 (m, 10H), 5.16 (br s, 2H), 4.81 (br s, 1H), 4.23 (br s, 1H), 2.74–2.65 (m, 1H), 2.48–2.40 (m, 1H), 1.93–1.65 (m, 5H), 1.49–1.27 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 172.3, 170.2, 137.1, 135.6, 129.4, 128.5, 128.2, 128.1, 126.7, 66.9, 65.5, 61.1, 43.6, 33.7, 31.1, 24.9 (two peaks are missing due to overlapping); **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{22}H_{24}O_3N$ 350.1751; found 350.1751.

2-3. Synthesis of (*S*)-(1-benzoylpyrrolidin-2-yl)methyl acetate (1c)

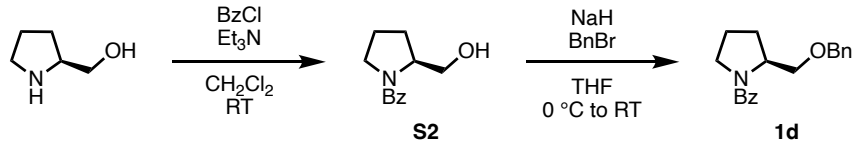


1c

To a solution of L-prolinol (210.9 mg, 2.1 mmol, 1.0 equiv) and Et_3N (872 μL, 6.3 mmol, 3.0 equiv) in CH_2Cl_2 (4.2 mL, 0.50 M) was added BzCl (291 μL, 2.5 mmol, 1.2 equiv) dropwise at 0 °C. After the mixture had been allowed to warm to room temperature and stirred for 30 min, to the mixture were added Ac_2O (296 μL, 3.1 mmol, 1.5 equiv) and DMAP (26.2 mg, 0.21 mmol, 10 mol%). After being stirred at room temperature for 3.5 h, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:1 hexane/EtOAc) to afford **1c** (400.8 mg, 78% yield over 2 steps) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.52–7.46 (m, 2H), 7.43–7.35 (m, 3H), 4.54 (br s, 1H), 4.37–4.12 (m, 2H), 3.52–3.37

(m, 2H), 2.14–2.02 (m, 4H), 2.00–1.90 (m, 1H), 1.89–1.76 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 170.7, 170.2, 137.1, 129.8, 128.2, 127.0, 64.4, 55.8, 50.0, 27.7, 24.7, 20.7; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}O_3N$ 248.1281; found 248.1281.

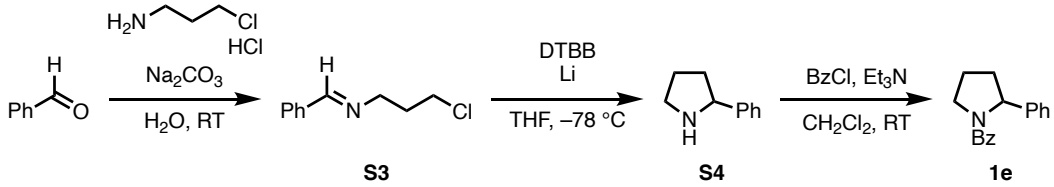
2-4. Synthesis of (*S*)-(2-((benzyloxy)methyl)pyrrolidin-1-yl)(phenyl)methanone (1d)



To a solution of L-prolinol (820.8 mg, 8.1 mmol, 1.0 equiv) and Et_3N (3.4 mL, 24 mmol, 3.0 equiv) in CH_2Cl_2 (20 mL, 0.40 M) was added BzCl (1.0 mL, 8.9 mmol, 1.1 equiv) dropwise at 0 °C. After being stirred at room temperature for 30 min, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:2 hexane/EtOAc) to afford (*S*)-(2-(hydroxymethyl)pyrrolidin-1-yl)(phenyl)methanone (**S2**) (1.43 g, 86% yield) as a colorless oil.

To a solution of **S2** (515.5 mg, 2.5 mmol, 1.0 equiv) in THF (6.3 mL, 0.40 M) was slowly added sodium hydride (NaH: 60% dispersion in paraffin liquid, 150.1 mg, 3.8 mmol, 1.5 equiv). To the mixture was added benzyl bromide (BnBr: 358 μL, 3.0 mmol, 1.2 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 30 min, the reaction was quenched with water. The mixture was extracted three times with Et_2O. The combined organic layer was dried over $MgSO_4$, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 3:2 hexane/EtOAc) to afford **1d** (666.3 mg, 90% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.55–7.26 (m, 10H), 4.65–4.30 (m, 3H), 3.90–3.31 (m, 4H), 2.12–1.88 (m, 3H), 1.85–1.65 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 169.8, 138.5, 137.4, 129.5, 128.1, 128.0, 127.4, 127.3, 127.0, 73.1, 70.5, 56.8, 50.3, 27.8, 24.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}O_2N$ 296.1645; found 296.1645.

2-5. Synthesis of phenyl(2-phenylpyrrolidin-1-yl)methanone (1e)



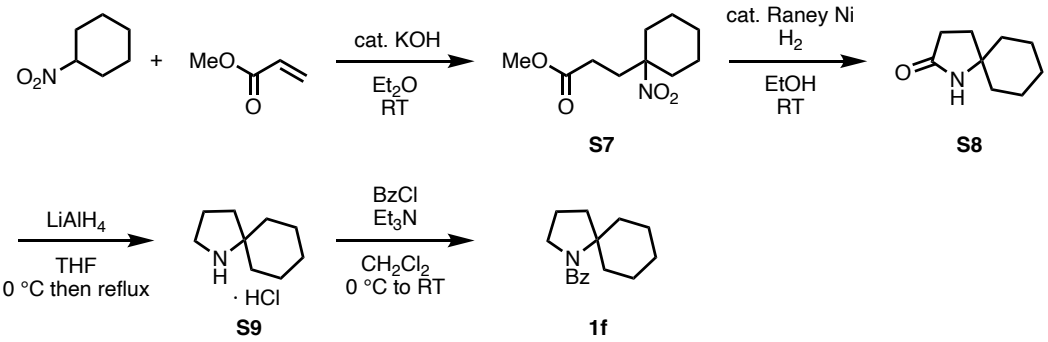
To a solution of 3-chloropropan-1-amine hydrochloride (715.1 mg, 5.5 mmol, 1.0 equiv) and Na_2CO_3 (529.9 mg, 5.0 mmol, 1.0 equiv) in H_2O (25 mL, 0.20 M) was added benzaldehyde (530.6 mg, 5.0 mmol, 1.0 equiv). After being stirred at room temperature for 18 h, the reaction was diluted with EtOAc. The mixture was extracted three times with EtOAc. The combined organic layer was washed with brine,

dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of 4,4'-di-*tert*-butylbiphenyl (66.6 mg, 0.25 mmol, 5.0 mol%) in THF (25 mL, 0.20 M) was added lithium (*ca.* 347 mg, 50 mmol, 10 equiv). After the mixture was stirred for 1 h at –78 °C, the crude product obtained above was added to the mixture. After being stirred for 5 h, the reaction was quenched with water. The mixture was allowed to warm to room temperature and extracted three times with EtOAc. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above and Et_3N (2.09 mL, 15 mmol, 3.0 equiv) in CH_2Cl_2 (12.5 mL, 0.40 M) was added BzCl (871 µL, 7.5 mmol, 1.5 equiv). After being stirred for 3 h, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1e** (1.04 g, 83% yield in 3 steps) as a yellow oil. The spectra are in accordance with those reported in the literature.[9]

2-6. Synthesis of phenyl(1-azaspiro[4.5]decan-1-yl)methanone (1f)



To a solution of nitrocyclohexane (609 µL, 5.0 mmol, 1.0 equiv) and KOH (8.0 mg, 0.15 mmol, 3.0 mol%) in Et_2O (1.0 mL, 4.8 M) was added methyl acrylate (673 µL, 7.5 mmol, 1.5 equiv). After the mixture had been stirred at room temperature for 17 h, the mixture was acidified to ca. pH = 5 with acetic acid. The mixture was concentrated *in vacuo* and the residue was purified by Isolera® (49:1 to 19:1 hexane/EtOAc) to afford methyl 3-(1-nitrocyclohexyl)propanoate (**S7**) (956.7 mg, 89% yield) as a colorless oil.

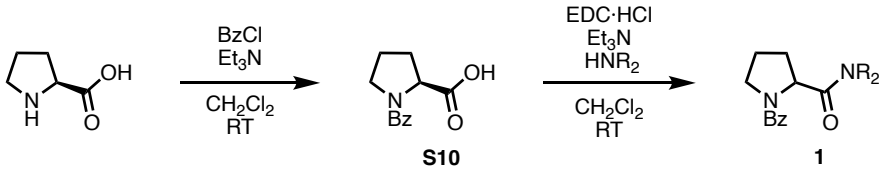
To a 50 mL round-bottom flask containing a magnetic stirring bar were added **S7** (162.7 mg, 0.76 mmol, 1.0 equiv), Raney Ni (a suitable amount, a spatula), and EtOH (7.5 mL, 0.10 M). The flask was subjected to H_2 gas with a balloon (1 atm). After being stirred at room temperature for 12 h, the mixture was passed through a pad of Celite® with EtOAc as an eluent. The filtrate was concentrated *in vacuo* and recrystallized (hot MeOH/Et_2O) to afford 1-azaspiro[4.5]decan-2-one (**S8**) (93.1 mg, 80% yield) as a white solid.

To a solution of lithium aluminum hydride ($LiAlH_4$: 57.0 mg, 1.5 mmol, 2.5 equiv) in THF (0.60 mL, 1.0 M) was added **S8** (90.9 mg, 0.60 mmol, 1.0 equiv) at 0 °C. The reaction mixture was refluxed for

22 h. After being cooled to room temperature, the mixture was diluted with Et_2O (1.0 mL) and quenched with water (60 μL), 3.0 M NaOH aq. (60 μL), and water (180 μL). The precipitates were removed by passing through a pad of Celite® with EtOAc as an eluent. To the filtrate was added 1.0 M HCl aq. and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above and Et_3N (330 μL, 2.4 mmol, 4.0 equiv) in CH_2Cl_2 (1.5 mL, 0.40 M) was added BzCl (83 μL, 0.71 mmol, 1.2 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 30 min, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The residue was purified by Isolera® (19:1 to 4:1 hexane/EtOAc) to afford **1f** (66.9 mg, 46% yield over 2 steps) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.48–7.33 (m, 5H), 3.35 (t, J = 6.8 Hz, 2H), 2.94–2.87 (m, 2H), 1.95 (t, J = 6.8 Hz, 2H), 1.77–1.73 (m, 4H), 1.62 (br s, 1H), 1.48–1.42 (m, 2H), 1.38–1.29 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 169.5, 139.8, 128.8, 128.1, 126.1, 66.4, 51.5, 36.3, 32.9, 25.0, 24.2, 23.2; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{22}ON$ 244.1696; found 244.1694.

2-7. Synthesis of 1k and 1n–1r

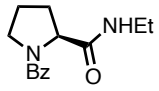


S10 **1**

General Procedure C

To a solution of L-proline (1.0 equiv) and Et_3N (3.0 equiv) in CH_2Cl_2 (0.50 M) was added BzCl (1.2 equiv) dropwise and stirred at room temperature for 30 min, which was then quenched with water. The mixture was extracted with 6.0 M NaOH aq. The aqueous layer was acidified to pH = 1 with 6.0 M HCl aq. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The crude product was used for the next step without further purification.

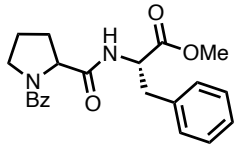
To a solution of the crude product obtained above (1.0 equiv) in CH_2Cl_2 (0.50 M) was added EDC·HCl (1.2 equiv). After the mixture had been stirred at room temperature for 30 min, to a mixture were added Et_3N (1.5 equiv) and amine (1.2 equiv). The solution was stirred for several hours while the reaction progress was being monitored by TLC. After the starting material had been completely consumed, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The residue was purified by Isolera® to afford pyrrolidine **1**.



1k

(*S*)-1-Benzoyl-*N*-ethylpyrrolidine-2-carboxamide (1k)

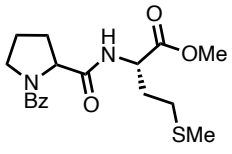
According to **General Procedure C** (3.0 mmol scale), **1k** was prepared with ethylamine hydrochloride (293.7 mg, 3.6 mmol). Purification by Isolera® (9:1 to 2:3 hexane/EtOAc) afforded **1k** (263.3 mg, 36% yield over 2 steps) as a colorless oil. **^{1}H NMR** (400 MHz, C_6D_6, 338 K) δ 7.42–7.37 (m, 2H), 7.11–7.02 (m, 3H), 4.64 (br s, 1H), 3.22–2.84 (m, 4H), 2.45 (br s, 1H), 1.75–1.65 (m, 1H), 1.56–1.46 (m, 1H), 1.28–1.17 (m, 1H), 0.90 (t, J = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, C_6D_6, 338 K) δ 171.3, 170.5, 137.6, 129.9, 78.1, 60.5, 50.2, 34.6, 28.2, 25.3, 14.9 (one peak is missing due to overlapping); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{18}O_2N_2Na$ 269.1261; found 269.1259.



1n

Methyl benzoylprolyl-L-phenylalaninate (1n)

According to **General Procedure C** (2.0 mmol scale), **1n** was prepared with L-phenylalanine methyl ester hydrochloride (517.4 mg, 2.4 mmol). Purification by Isolera® (4:1 to 1:5 hexane/EtOAc) afforded **1n** (316.5 mg, 42% yield over 2 steps, as a mixture of diastereomers) as a white solid. **^{1}H NMR** of the mixture of the diastereomers (400 MHz, $CDCl_3$, 323 K) δ 7.47–7.35 (m, 5H), 7.24–7.10 (m, 5H), 4.89–4.70 (m, 2H), 3.75–3.67 (m, 3H), 3.54–3.36 (m, 2H), 3.23–3.13 (m, 1H), 3.10–3.00 (m, 1H), 2.36 (br s, 1H), 2.06–1.73 (m, 3H); **^{13}C{^{1}H} NMR** of the mixture of the diastereomers (101 MHz, $CDCl_3$, 323 K) δ 171.4, 170.7, 170.6, 136.0, 129.8, 128.9, 128.2, 128.1, 127.9, 126.8, 126.5, 59.5, 53.1, 51.8, 49.8, 37.5, 27.2, 24.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}O_4N_2$ 381.1809; found 381.1808.

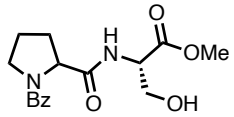


1o

Methyl benzoylprolyl-L-methioninate (1o)

According to **General Procedure C** (3.0 mmol scale), **1o** was prepared with L-methionine methyl ester hydrochloride (718.4 mg, 3.6 mmol). Purification by Isolera® (4:1 to 1:2 hexane/EtOAc) afforded **1o** (476.7 mg, 44% yield over 2 steps, as a mixture of diastereomers) as a light-yellow solid. **^{1}H NMR** of the mixture of the diastereomers (400 MHz, $CDCl_3$, 323 K) δ 7.56–7.48 (m, 2H), 7.46–7.34 (m, 3H), 4.90–4.65 (m, 2H), 3.77–3.70 (m, 3H), 3.62–3.42 (m, 2H), 2.60–2.30 (m, 3H), 2.25–1.95 (m, 7H), 1.91–1.78 (m, 1H); **^{13}C{^{1}H} NMR** of the mixture of the diastereomers (101 MHz, $CDCl_3$, 323 K) δ 171.6,

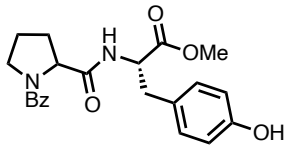
170.9, 170.5, 170.2, 136.0, 129.7, 127.8, 126.6, 59.5, 51.8, 51.19, 51.17, 49.9, 31.1, 30.9, 29.7, 29.6, 27.4, 24.9, 14.9 (four excess peaks are observed due to diastereomers); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{25}O_4N_2S$ 365.1530; found 365.1530.



1p

Methyl benzoylprolyl-L-serinate (1p)

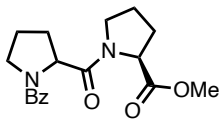
According to **General Procedure C** (3.0 mmol scale), **1p** was prepared with L-serine methyl ester hydrochloride (559.8 mg, 3.6 mmol). Purification by Isolera® (19:1 to 9:1 $CHCl_3$/MeOH) afforded **1p** (556.7 mg, 59% yield over 2 steps, as a mixture of diastereomers) as a white solid. **^{1}H NMR** of the mixture of the diastereomers (400 MHz, $CDCl_3$, 323 K) δ 7.56–7.50 (m, 2H), 7.45–7.36 (m, 3H), 7.20 (br s, 1H), 4.85–4.50 (m, 2H), 4.10–3.88 (m, 2H), 3.80–3.74 (m, 3H), 3.68–3.46 (m, 2H), 2.36–1.98 (m, 3H), 1.94–1.80 (m, 1H); **^{13}C{^{1}H} NMR** of the mixture of the diastereomers (101 MHz, CD_3OD, 328 K) δ 174.4, 172.2, 172.1, 137.6, 131.4, 129.4, 128.1, 62.8, 61.7, 56.3, 52.8, 51.6, 30.7, 26.1; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{21}O_5N_2$ 321.1445; found 321.1444.



1q

Methyl benzoylprolyl-L-tyrosinate (1q)

According to **General Procedure C** (3.0 mmol scale), **1q** was prepared with L-tyrosine methyl ester hydrochloride (834.0 mg, 3.6 mmol). Purification by Isolera® (4:1 to 1:9 hexane/EtOAc) afforded **1q** (807.0 mg, 68% yield over 2 steps, as a mixture of diastereomers) as a colorless oil. **^{1}H NMR** of the mixture of the diastereomers (400 MHz, $CDCl_3$, 323 K) δ 7.46–7.33 (m, 5H), 7.20–7.15 (m, 1H), 6.98–6.93 (m, 2H), 6.66–6.57 (m, 2H), 6.36 (br s, 1H), 4.85–4.66 (m, 2H), 3.73–3.67 (m, 3H), 3.55–3.35 (m, 2H), 3.13–3.04 (m, 1H), 2.96 (dd, J = 14.4, 6.8 Hz, 1H), 2.30 (br s, 1H), 2.10–1.90 (m, 2H), 1.85–1.75 (m, 1H); **^{13}C{^{1}H} NMR** of the mixture of the diastereomers (101 MHz, $CDCl_3$, 323 K) δ 171.6, 171.3, 171.0, 170.8, 155.8, 135.6, 130.0, 129.9, 128.1, 126.8, 126.4, 115.3, 59.9, 53.4, 51.9, 50.0, 36.7, 28.0, 24.9 (one excess peak is observed due to diastereomers); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{25}O_5N_2$ 397.1758; found 397.1758.

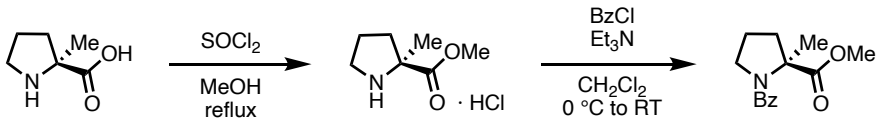


1r

Methyl benzoylprolyl-L-prolinate (1r)

According to **General Procedure C** (3.0 mmol scale), **1r** was prepared with L-proline methyl ester hydrochloride (596.8 mg, 3.6 mmol). Purification by Isolera® (99:1 to 19:1 $CHCl_3$/MeOH) afforded **1r** (538.0 mg, 54% yield over 2 steps, as a mixture of diastereomers) as a colorless oil. **^{1}H NMR** of the mixture of the diastereomers (400 MHz, $(CD_3)_2SO$, 413 K) δ 7.43–7.35 (m, 5H), 4.75–4.50 (m, 1H), 4.31 (br s, 1H), 3.67–3.59 (m, 3H), 3.57–3.26 (m, 2H), 2.83–2.76 (m, 2H), 2.30–1.75 (m, 8H); **^{13}C{^{1}H} NMR** of the mixture of the diastereomers (101 MHz, $(CD_3)_2SO$, 413 K) δ 171.8, 170.2, 168.3, 137.3, 137.1, 129.2, 129.0, 127.83, 127.77, 126.5, 126.4, 58.7, 58.3, 51.2, 48.3, 46.0, 28.6, 28.2, 24.1, 23.6 (four excess peaks are observed due to diastereomers); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{23}O_4N_2$ 331.1652; found 331.1652.

2-8. Synthesis of methyl (*S*)-1-benzoyl-2-methylpyrrolidine-2-carboxylate (1l)

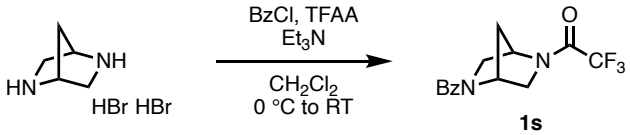


S11 **1l**

To a solution of (*S*)-2-methylpyrrolidine-2-carboxylic acid (258.5 mg, 2.0 mmol, 1.0 equiv) in MeOH (4.0 mL, 0.50 M) was added thionyl chloride ($SOCl_2$: 92 μL, 4.0 mmol, 2.0 equiv) dropwise at 0 °C. The reaction mixture was refluxed for 3 h. After the reaction mixture had been cooled to room temperature, the mixture was concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above (1.0 equiv) and Et_3N (836 μL, 6.0 mmol, 3.0 equiv) in CH_2Cl_2 (5.0 mL, 0.40 M) was added BzCl (279 μL, 2.4 mmol, 1.2 equiv) dropwise at 0 °C. After the mixture was allwed to warm to room temperature and stirred for 1 h, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:1 hexane/EtOAc) to afford **1l** (438.7 mg, 89% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.62–7.40 (m, 2H), 7.42–7.35 (m, 3H), 3.77 (s, 3H), 3.65–3.52 (m, 2H), 2.27–2.17 (m, 1H), 2.07–1.85 (m, 3H), 1.73 (s, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 174.0, 168.8, 136.8, 129.5, 127.9, 126.5, 65.8, 51.9, 50.6, 38.7, 23.9, 21.7; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{18}O_3N$ 248.1281; found 248.1281.

2-9. Synthesis of 1-((1*S*,4*S*)-5-benzoyl-2,5-diazabicyclo[2.2.1]heptan-2-yl)-2,2,2-trifluoroethan-1-one (1s)

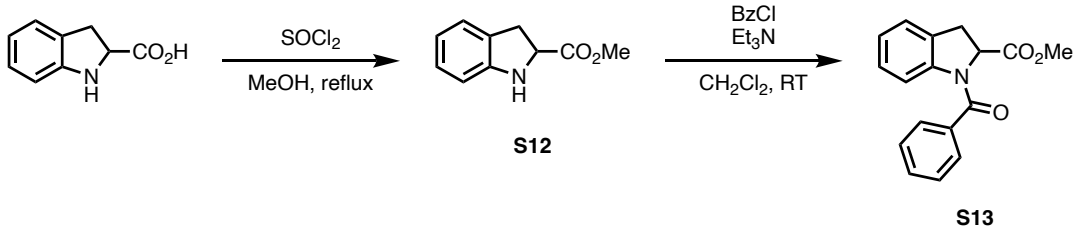


1s

To a solution of (1*S*,4*S*)-2,5-diazabicyclo[2.2.1]heptane dihydrobromide (434.4 mg, 1.7 mmol, 1.0 equiv) in CH_2Cl_2 (4.0 mL, 0.40 M) were added Et_3N (1.16 mL, 8.4 mmol, 5.0 equiv), BzCl (194 µL, 1.7 mL, 1.0 equiv), and TFAA (232 µL, 1.7 mmol, 1.0 equiv) at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 8 h, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1s** (89.4 mg, 11% yield) as a light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53–7.39 (m, 5H), 5.15–4.54 (m, 2H), 3.99 (d, *J* = 10.4 Hz, 0.2H), 3.87–3.57 (m, 3.3H), 3.51–3.40 (m, 0.5H), 2.14–1.97 (m, 1.8H), 1.91–1.85 (m, 0.2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.5, 170.2, 169.3, 155.8–154.2 (m), 135.4, 134.9, 130.9, 130.6, 128.7, 128.5, 127.3, 127.2, 127.0, 116.0 (q, *J* = 289 Hz), 59.6 , 58.8, 58.1, 58.0, 57.6, 57.1, 56.9, 56.4, 56.3, 55.3, 55.1, 54.8, 54.3, 53.8, 53.4, 52.8, 38.5, 36.9, 36.3, 34.8 (21 excess peaks are observed due to rotamer); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –71.6, –71.7, –72.8, –73.0 (three excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{13}O_2F_3N_2Na$ 321.0821; found 321.0820.

2-10. Synthesis of other aza-heterocycles

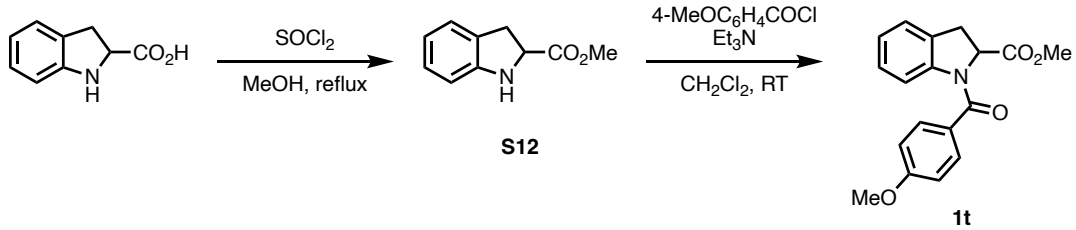
Methyl 1-(4-methoxybenzoyl)indoline-2-carboxylate (1t)



S12 **S13**

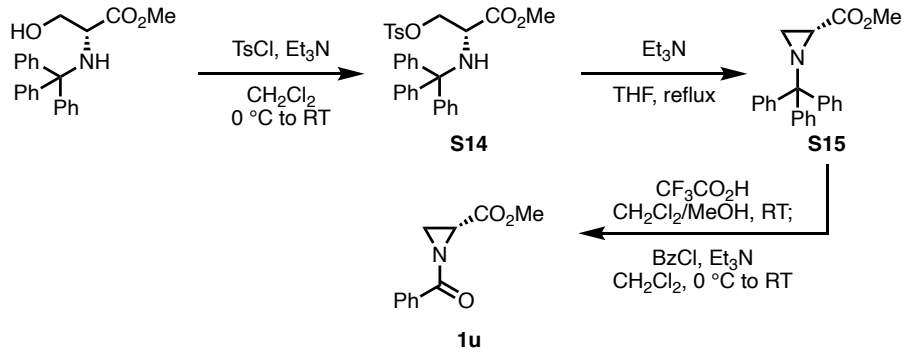
To a solution of indoline-2-carboxylic acid (244.8 mg, 1.5 mmol, 1.0 equiv) in MeOH (3.0 mL, 0.50 M) was added $SOCl_2$ (219 µL, 3.0 mmol, 2.0 equiv). After being heated at 70 °C for 3 h, the reaction mixture was concentrated *in vacuo*. To the residue were added CH_2Cl_2 (5.0 mL, 0.40 M), Et_3N (1.1 mL, 8.0 mmol, 4.0 equiv), and BzCl (406 µL, 3.0 mmol, 1.5 equiv). After being stirred for 2 h, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (19:1 to 3:1 hexane/EtOAc) to afford **S13** (350.0 mg, 83% yield) as an orange oil. The spectra are in accordance with those reported in the literature.[10]

Methyl 1-(4-methoxybenzoyl)indoline-2-carboxylate (1t)



To a solution of indoline-2-carboxylic acid (336.5 mg, 2.0 mmol, 1.0 equiv) in MeOH (4.0 mL, 0.50 M) was added $SOCl_2$ (292 µL, 4.0 mmol, 2.0 equiv). After being heated at 70 °C for 3 h, the reaction mixture was concentrated *in vacuo*. To the residue were added CH_2Cl_2 (5.0 mL, 0.40 M), Et_3N (1.1 mL, 8.0 mmol, 4.0 equiv), and 4-methoxybenzoyl chloride (406 µL, 3.0 mmol, 1.5 equiv). After being stirred for 20 min, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 3:1 hexane/EtOAc) to afford **1t** (304.2 mg, 49% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.4 Hz, 2H), 7.18–7.16 (m, 1H), 7.00–6.93 (m, 4H), 5.13 (dd, *J* = 10.8, 4.4 Hz, 1H), 3.87 (s, 3H), 3.73 (s, 3H), 3.55 (dd, *J* = 16.0, 10.8 Hz, 1H), 3.17 (dd, *J* = 16.0, 4.4 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.8, 168.9, 161.6, 142.3, 129.8, 129.6, 128.0, 127.3, 125.0, 123.4, 115.3, 113.9, 61.8, 55.3, 52.5, 32.3; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{18}O_4N$ 312.1230; found 312.1225.

Methyl (*R*)-1-benzoylaziridine-2-carboxylate (1u)



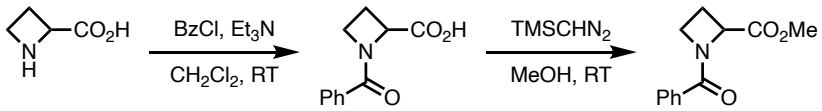
To a solution of *N*-(triphenylmethyl)-L-serine methyl ester (1.03 g, 2.9 mmol, 1.0 equiv) and Et_3N (797 µL, 5.7 mmol, 2.0 equiv) in CH_2Cl_2 (8.7 mL, 0.30 M) was added TsCl (599.9 mg, 3.2 mmol, 1.1 equiv) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 21 h. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2, and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above in THF (1.7 mL, 1.7 M) was added Et_3N (797 µL, 5.7 mmol, 2.0 equiv). The reaction was heated at 70 °C for 11 h and concentrated *in vacuo*. The residue was

purified by Isolera® (97:3 to 4:1 hexane/EtOAc) to afford **S15** (790.5 mg, 80% yield in 2 steps) as a colorless oil.

To a solution of **S15** (790.5 mg, 2.3 mmol, 1.0 equiv) in CH_2Cl_2/MeOH (3.0 mL/ 4.0 mL, 0.30 M) was added TFA (881 µL, 11.5 mmol, 5.0 equiv). After the reaction was stirred for 1 h at room temperature and cooled to 0 °C, to the mixture were added Et_3N (2.57 mL, 18.4 mmol, 8.0 equiv) and BzCl (539 µL, 4.6 mmol, 2.0 equiv) at 0 °C. After the reaction was allowed to warm to room temperature and stirred for 2 h, to the mixture were added Et_3N (856 µL, 6.1 mmol, 2.3 equiv) and BzCl (539 µL, 4.6 mmol, 2.0 equiv). After being stirred for 7 h, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1u** (282.4 mg, 36% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.03–8.00 (m, 2H), 7.59–7.55 (m, 1H), 7.48–7.44 (m, 2H), 3.74 (s, 3H), 3.28 (dd, *J* = 5.6, 2.8 Hz, 1H), 2.77 (dd, *J* = 2.8, 1.2 Hz, 1H), 2.69 (dd, *J* = 5.6, 1.2 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.7, 168.6, 133.1, 132.3, 128.9, 128.5, 52.6, 35.3, 31.3; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{11}H_{11}O_3NNa$ 228.0631; found 228.0632.

Methyl 1-benzoylazetidine-2-carboxylate (1v)

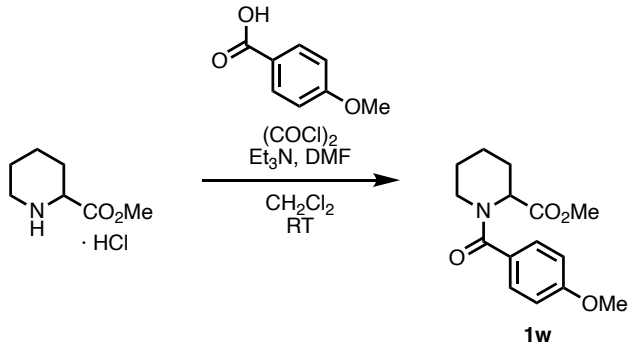


S16 **1v**

To a solution of azetidine-2-carboxylic acid (198.3 mg, 2.0 mmol, 1.0 equiv) in CH_2Cl_2 (5.0 mL, 0.40 M) were added Et_3N (820 µL, 5.9 mmol, 3.0 equiv) and BzCl (250 µL, 2.2 mmol, 1.1 equiv). After being stirred for 3 h, the reaction was quenched with 1.0 M HCl aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above in MeOH (5.0 mL, 0.40 M) was added $TMSCHN_2$ (in *ca.* 0.60 M hexane, 6.0 mL, 3.6 mmol, 1.8 equiv) slowly. After being stirred for 15 min, the reaction mixture was concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1v** (90.3 mg, 14% yield) as a light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74–7.62 (m, 2H), 7.50–7.37 (m, 3H), 4.96 (dd, *J* = 9.2, 5.2 Hz, 1H), 4.51–4.38 (m, 1H), 4.25–4.13 (m, 1H), 3.88–3.47 (m, 3H), 2.77–2.59 (m, 1H), 2.43–2.22 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.4, 169.9, 132.5, 131.3, 128.4, 128.0, 59.7, 52.3, 51.7, 20.6; **HRMS** (APCI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}O_3N$ 220.0968; found 220.0962.

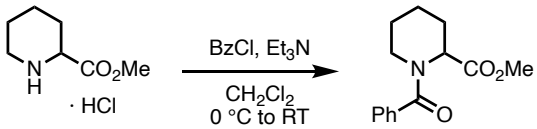
Methyl 1-(4-methoxybenzoyl)piperidine-2-carboxylate (1w)



1w

To a solution of 4-methoxybenzoic acid (286.9 mg, 1.9 mmol, 3.6 equiv) in CH_2Cl_2 (4.0 mL, 0.10 M) were added $(COCl)_2$ (171 µL, 2.0 mmol, 4.0 equiv) and DMF (5 drops). After the reaction was stirred for 20 min, to the solution were added Et_3N (1.3 mL, 9.2 mmol, 23.8 equiv) and methyl pipecolinate hydrochloride (92.1 mg, 0.39 mmol, 1.0 equiv) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1w** (100.8 mg, 94% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[11]

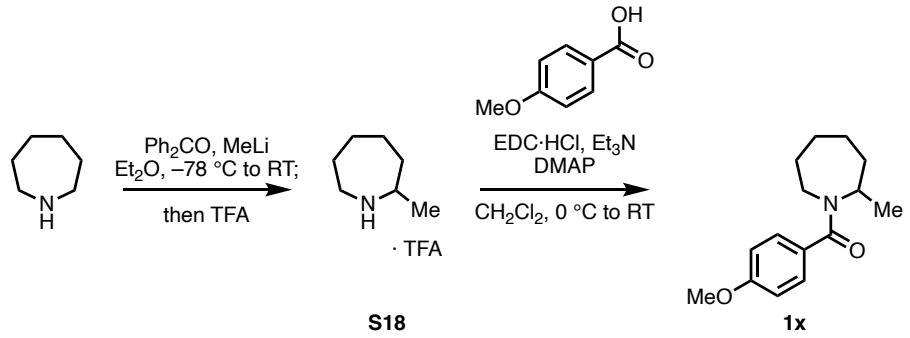
Methyl 1-benzoylpiperidine-2-carboxylate (S17)



S17

To a solution of methyl pipecolinate hydrochloride (409.0 mg, 2.3 mmol, 1.0 equiv) and Et_3N (793 µL, 5.7 mmol, 2.5 equiv) in CH_2Cl_2 was added BzCl (317 µL, 2.7 mmol, 1.2 equiv) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 5 h. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **S17** (560 mg, 99% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[12]

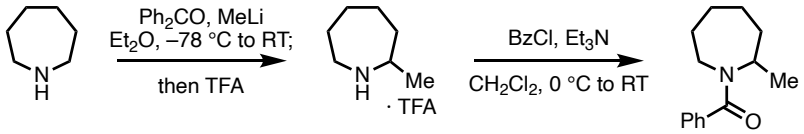
(4-Methoxyphenyl)(2-methylazepan-1-yl)methanone (1x)



To a solution of azepane (313.2 mg, 3.0 mmol, 1.0 equiv) and benzophenone (656.0 mg, 3.6 mmol, 1.2 equiv) in Et_2O (6.0 mL, 0.50 M) was added MeLi (1.1 M in Et_2O, 7.1 mL, 7.5 mmol, 2.5 equiv) at –78 °C. After being stirred for 30 min, the reaction was allowed to warm to room temperature and stirred for 14 h. The reaction was quenched with 1.0 M HCl aq. and acidified to pH = 1 with 6.0 M HCl aq. The mixture was extracted with Et_2O and the aqueous layer was basified to pH = 14 with 6.0 M NaOH aq. The mixture was extracted three times with CH_2Cl_2 and the combined organic layer was acidified to pH = 1 with TFA. The mixture was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above in CH_2Cl_2 (7.5 mL, 0.40 M) were added Et_3N (2.1 mL, 15.0 mmol, 5.0 equiv), EDC·HCl (632.6 mg, 3.3 mmol, 1.1 equiv), DMAP (110.0 mg, 0.90 mmol, 30 mol%) and 4-methoxybenzoic acid (547.7 mg, 3.6 mmol, 1.2 equiv). After being stirred for 3.5 h, the reaction was quenched with 1.0 M HCl aq. The mixture was extracted three times with CH_2Cl_2 and the combined organic layer was washed with a saturated $NaHCO_3$ aq. dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (97:3 to 9:1 $CHCl_3$/MeOH) and GPC to afford **1x** (122.0 mg, 16% yield in 2 steps) as a colorless oil. **^{1}H NMR** (400 MHz, C_6D_6) δ 7.30 (d, J = 8.4 Hz, 2H), 6.69 (d, J = 8.4 Hz, 2H), 4.98–4.78 (m, 0.2H), 4.50–4.31 (m, 0.8H), 3.75–3.57 (m, 0.8H), 3.44–3.28 (m, 0.2H), 3.24 (s, 3H), 2.68–2.32 (m, 1H), 2.14–1.93 (m, 0.8H), 1.81–0.66 (m, 10.2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.9, 171.1, 159.7, 130.2, 127.7, 127.5, 113.8, 113.6, 55.2, 53.5, 50.1, 43.4, 39.9, 36.4, 35.4, 30.7, 30.1, 29.1, 27.6, 25.2, 24.9, 20.9, 19.6 (10 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{22}O_2N$ 248.1645; found 248.1650.

(2-Methylazepan-1-yl)(phenyl)methanone (S19)

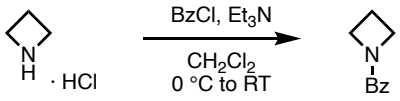


S18 **S19**

To a solution of azepane (308.5 mg, 3.1 mmol, 1.0 equiv) and benzophenone (680.2 mg, 3.7 mmol, 1.2 equiv) in Et_2O (6.2 mL, 0.50 M) was added MeLi (1.1 M in Et_2O, 6.9 mL, 7.8 mmol, 2.5 equiv) at –78 °C. After being stirred for 5 min, the reaction was allowed to warm to room temperature and stirred for 10 h. The reaction was quenched with 1.0 M HCl aq. and acidified to pH = 1 with 6.0 M HCl aq. The mixture was extracted with Et_2O and the aqueous layer was basified to pH = 14 with 6.0 M NaOH aq. The mixture was extracted three times with CH_2Cl_2 and the combined organic layer was acidified to pH = 1 with TFA. The mixture was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product above in CH_2Cl_2 were added Et_3N (2.2 mL, 15.6 mmol, 5.0 equiv) and BzCl (434 μL, 3.7 mmol, 1.2 equiv) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 1 h. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 hexane/EtOAc to EtOAc) to afford **S17** (128.3 mg, 13% yield in 2 steps) as a light yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42–7.37 (m, 2H), 7.34–7.30 (m, 3H), 4.72–4.66 (m, 0.4H), 4.29–4.22 (m, 0.6H), 3.72–3.64 (m, 0.6H), 3.47–3.40 (m, 0.4H), 3.03–2.97 (m, 0.4H), 2.82–2.75 (m, 0.6H), 2.14–2.06 (m, 0.4H), 1.98–1.87 (m, 1.4H), 1.84–1.72 (m, 2.6H), 1.40–1.24 (m, 3.6H), 1.20 (d, J = 6.4 Hz, 1.2H), 1.05 (d, J = 6.4 Hz, 1.8H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.9, 171.1, 137.9, 137.7, 128.5, 128.44, 128.40, 128.3, 125.8, 125.7, 53.4, 50.0, 43.2, 39.7, 36.2, 35.3, 30.6, 30.0, 29.0, 27.6, 25.1, 24.8, 20.8, 19.5 (twelve excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{20}ON$ 218.1539; found 218.1540.

Azetidin-1-yl(phenyl)methanone (1y)

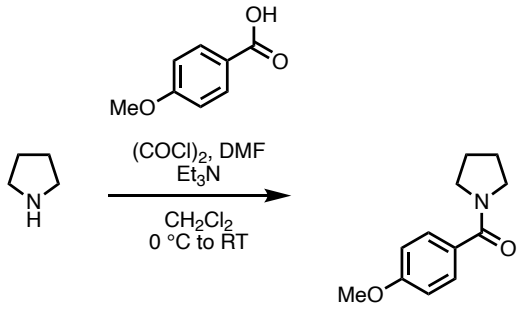


1y

To a solution of azetidine hydrochloride (280.7 mg, 3.0 mmol, 1.0 equiv) and Et_3N (627 μL, 4.5 mmol, 1.5 equiv) in CH_2Cl_2 (10 mL, 0.30 M) was added BzCl (418 μL, 3.6 mmol, 1.2 equiv) at 0 °C. The mixture was allowed to warm to room temperature and stirred for 3 h. The reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was washed with brine, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera®

(92:8 to 2:1 hexane/EtOAc) to afford a mixture of **1y** and BzOH. The mixture was diluted with CH_2Cl_2 and to the mixture was added 1.0 M NaOH aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (97:3 to 9:1 $CHCl_3$/MeOH) to afford **1y** (60.8 mg, 9% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[6]

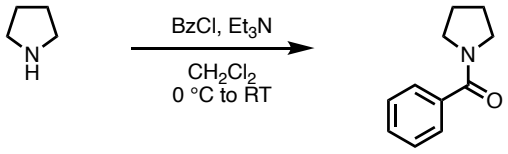
(4-Methoxyphenyl)(pyrrolidin-1-yl)methanone (1z)



1z

To a solution of 4-methoxybenzoic acid (284.5 mg, 1.9 mmol, 1.1 equiv) in CH_2Cl_2 (4.0 mL, 0.40 M) were added $(COCl)_2$ (190 µL, 2.2 mmol, 1.3 equiv) and DMF (5 drops). After the mixture was stirred for 30 min, the reaction was cooled to 0 °C. To the mixture were added Et_3N (1.04 mL, 7.5 mmol, 4.4 equiv) and pyrrolidine (139.6 µL, 1.7 mmol, 1.0 equiv) at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 3 h, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (92:8 to 1:2 hexane/EtOAc) to afford **1z** (373.9 mg, quant.) as a white solid. The spectra are in accordance with those reported in the literature.[13]

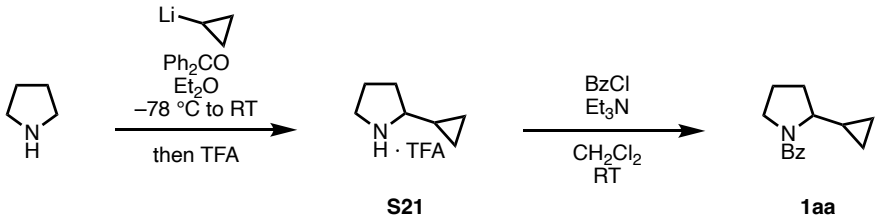
Phenyl(pyrrolidin-1-yl)methanone (S20)



S20

To a solution of pyrrolidine (145.1 mg, 2.0 mmol, 1.0 equiv) and Et_3N (853 µL, 6.1 mmol, 3.0 equiv) in CH_2Cl_2 (8.0 mL, 0.25 M) was added BzCl (284 µL, 2.5 mmol, 1.2 equiv). After being stirred for 30 min, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (19:1 to 4:1 hexane/EtOAc) to afford **S20** (342.5 mg, 96% yield) as a yellow oil. The spectra are in accordance with those reported in the literature.[13]

2-11. Synthesis of (2-cyclopropylpyrrolidin-1-yl)(phenyl)methanone (1aa)

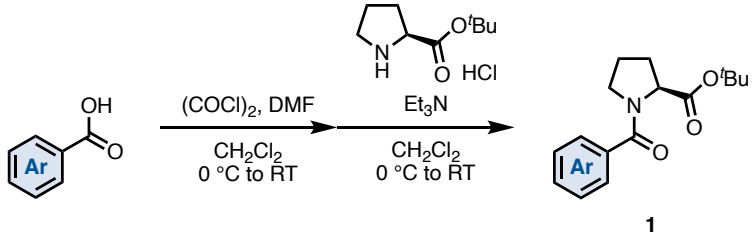


S21 **1aa**

Cyclopropyl lithium[14] and 2-cyclopropylpyrrolidine TFA salt (**S17**)[4] were synthesized according to the reported procedures. To a solution of cyclopropyl lithium (9.0 mmol, 3.0 equiv) in Et_2O (5.0 mL, 1.8 M) were added pyrrolidine (246 μL, 3.0 mmol, 1.0 equiv), benzophenone (655 mg, 3.6 mmol, 1.2 equiv), and Et_2O (1.0 mL) at –78 °C under an atmosphere of N_2. After being stirred at the same temperature for 10 min, the reaction mixture was allowed to warm to room temperature and stirred for 7 h, which was then quenched with MeOH at 0 °C. The mixture was diluted with water and extracted with 6.0 M HCl aq. (pH = 1). The aqueous layer was basified to pH = 13 with 6.0 M NaOH aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was acidified to pH = 1 with TFA, dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above and Et_3N (1.67 mL, 12.0 mmol, 4.0 equiv) in CH_2Cl_2 (7.5 mL, 0.40 M) was added BzCl（523 μL, 3.6 mmol, 1.2 equiv) dropwise. The reaction mixture was stirred at room temperature for 1 h, which was then quenched with a saturated $NaHCO_3$ aqueous solution. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (19:1 to 1:1 hexane/EtOAc) and GPC ($CHCl_3$) to afford **1aa** (57.1 mg, 9% yield over 2 steps) as a colorless oil. **^{1}H NMR** (400 MHz, C_6D_6, 348 K) δ 7.50–7.45 (m, 2H), 7.11–7.07 (m, 3H), 4.25 (br s, 0.1H), 3.94 (br s, 0.9H), 3.30–3.10 (m, 2H), 1.75–1.15 (m, 4H), 0.87–0.77 (m, 1H), 0.60–0.43 (m, 1H), 0.40–0.31 (m, 1H), 0.30–0.21 (m,1H), 0.16–0.04 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 170.4, 169.9, 137.9, 137.3, 129.8, 129.5, 128.1, 127.1, 60.1, 49.8, 30.2, 24.6, 22.7, 15.5, 4.2, 1.7 (four excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{17}ONNa$ 238.1202; found 238.1202.

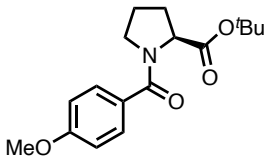
2-12. Synthesis of *N*-aroyl prolines



1

General Procedure D

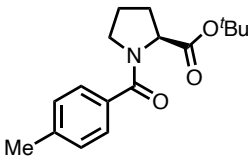
To a solution of benzoic acid (2.0 mmol, 1.1 equiv) in CH_2Cl_2 (5.0 mL, 0.40 M) were added $(COCl)_2$ (223 μL, 2.6 mmol, 1.3 equiv) and DMF (5 drops) at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 30 min, the reaction was cooled to 0 °C. To the mixture were added Et_3N (1.12 mL, 8.0 mmol, 4.4 equiv) and L-proline *tert*-butyl ester hydrochloride (374.2 mg, 1.8 mmol, 1.0 equiv) at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 1 h, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by Isolera® to afford the corresponding *N*-aroyl pyrrolidines.



1ad

***tert*-Butyl (4-methoxybenzoyl)-L-prolinate (1ad)**

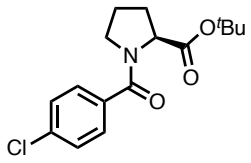
According to **Gereral Procedure D**, **1ad** was prepared using 4-methoxybenzoic acid (304.3 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera (9:1 to 2:1 hexane/EtOAc) afforded **1ad** (362.3 mg, 66% yield) as a white solid. The spectra are in accordance with those reported in the literature.[15]



1ae

***tert*-Butyl (4-methylbenzoyl)-L-prolinate (1ae)**

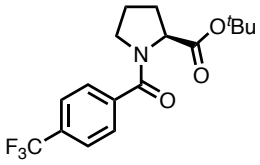
According to **Gereral Procedure D**, **1ae** was prepared using 4-toluic acid (272.3 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera (9:1 to 2:1 hexane/EtOAc) afforded **1ae** (348.2 mg, 67% yield) as a white solid. The spectra are in accordance with those reported in the literature.[16]



1af

***tert*-Butyl (4-chlorobenzoyl)-L-prolinate (1af)**

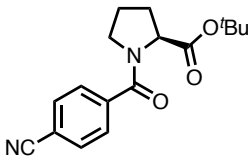
According to **Gereral Procedure D**, **1af** was prepared using 4-chlorobenzoic acid (313.1 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera (9:1 to 1:1 hexane/EtOAc) afforded **1af** (395.9 mg, 71% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53–7.50 (m, 1.4H), 7.39–7.32 (m, 2.6H), 4.54 (dd, *J* = 8.4, 5.2 Hz, 0.7H), 4.23–4.17 (m, 0.3H), 3.77 (t, *J* = 7.2 Hz, 0.6H), 3.64–3.58 (m, 0.7H), 3.51–3.45 (m, 0.7H), 2.36–2.17 (m, 1H), 2.06–1.82 (m, 3H), 1.49 (s, 6.3H), 1.33 (s, 2.7H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.2, 169.3, 168.4, 136.1, 135.7, 135.5, 134.8, 128.7, 128.5, 128.3, 81.9, 81.3, 61.9, 60.0, 49.9, 46.7, 31.6, 29.3, 28.0, 27.7, 25.3, 22.5 (10 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{21}O_3NCl$ 310.1205; found 310.1203.



1ag

***tert*-Butyl (4-(trifluoromethyl)benzoyl)-L-prolinate (1ag)**

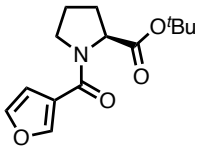
According to **Gereral Procedure D**, **1ag** was prepared using 4-trifluoromethylbenzoic acid (380.2 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera (9:1 to 1:1 hexane/EtOAc) afforded **1ag** (390.6 mg, 63% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.70–7.62 (m, 3.4H), 7.54 (d, *J* = 8.0 Hz, 0.6H), 4.56 (dd, *J* = 8.4, 5.2 Hz, 0.7H), 4.18 (dd, *J* = 8.4, 2.8 Hz, 0.3H), 3.82–3.77 (m, 0.6H), 3.62–3.56 (m, 0.7H), 3.47–3.42 (m, 0.7H), 2.38–2.18 (m, 1H), 2.06–1.84 (m, 3H), 1.50 (s, 6.3H), 1.30 (s, 2.7H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.1, 169.0, 168.1, 140.5, 139.9, 131.9 (q, *J* = 32.5 Hz), 127.5, 127.2, 125.3, 123.7 (q, *J* = 274 Hz), 82.0, 81.5, 61.8, 59.9, 49.8, 46.8, 31.6, 29.3, 28.0, 27.6, 25.2, 22.5 (9 excess peaks are observed due to rotamer); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –62.96, –63.02 (one excess peak is observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{21}O_3NF_3$ 344.1468; found 344.1469.



1ah

***tert*-Butyl (4-cyanobenzoyl)-L-prolinate (1ah)**

According to **Gereral Procedure D**, **1ah** was prepared using 4-cyanobenzoic acid (294.3 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera® (9:1 to 1:1 hexane/EtOAc) afforded a mixture of **1ah** and 4-cyanomethylbenzoic acid. The residue was diluted with CH_2Cl_2 and a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo* to afford **1ah** (439.6 mg, 81% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73–7.64 (m, 3.4H), 7.53 (d, *J* = 8.0 Hz, 0.6H), 4.55 (dd, *J* = 8.8, 5.2 Hz, 0.7H), 4.14 (dd, *J* = 8.4, 2.8 Hz, 0.3H), 3.81–3.72 (m, 0.6H), 3.60–3.54 (m, 0.7H), 3.45–3.40 (m, 0.7H), 2.35–2.21 (m, 1H), 2.08–1.97 (m, 2.3H), 1.94–1.85 (m, 0.7H), 1.50 (s, 6.3H), 1.31 (s, 2.7H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 170.9, 168.4, 167.5, 141.3, 140.6, 132.21, 132.17, 127.8, 127.6, 118.1, 113.8, 113.4, 82.2, 81.6, 61.7, 59.9, 49.8, 46.8, 31.6, 29.3, 28.0, 27.7, 25.2, 22.5 (11 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{20}O_3N_2Na$ 323.1366; found 323.1360.

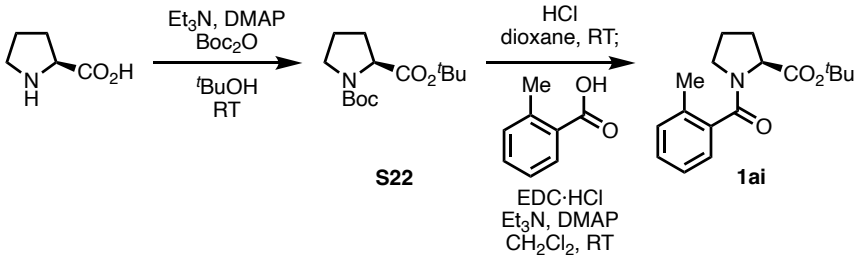


1ak

***tert*-Butyl (furan-3-carbonyl)-L-prolinate (1ak)**

According to **General Procedure D**, **1ak** was prepared using 3-furoic acid (224.2 mg, 2.0 mmol, 1.1 equiv). Purification by Isolera® (19:1 to 2:3 hexane/EtOAc) afforded **1ak** (252.1 mg, 57% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84 (br s, 0.7H), 7.71 (br s, 0.3H), 7.42–7.39 (m, 1H), 6.76 (d, *J* = 0.8 Hz, 0.7H), 6.65 (br s, 0.3H), 4.53 (dd, *J* = 8.4, 4.8 Hz, 0.7H), 4.45 (d, *J* = 8.4 Hz, 0.3H), 3.83–3.70 (m, 2H), 2.30–2.04 (m, 2H), 2.02–1.92 (m, 2H), 1.48 (s, 6.3H), 1.40 (s, 2.7H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.4, 162.3, 144.5, 143.4, 142.7, 122.2, 110.6, 110.2, 82.1, 81.2, 61.2, 60.3, 48.5, 47.0, 31.7, 28.9, 27.9, 27.7, 25.1, 22.2 (8 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{20}O_4N$ 266.1387; found 266.1382.

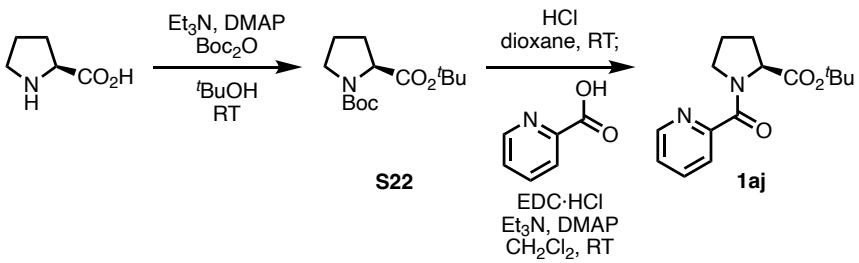
***tert*-Butyl (2-methylbenzoyl)-L-prolinate (1ai)**



To a solution of L-proline (345.3 mg, 3.0 mmol, 1.0 equiv) and Et_3N (125 µL, 0.90 mmol, 30 mol%) in ^{t}BuOH (6.0 mL, 0.50 M) were added Boc_2O (1.86 mL, 8.1 mmol, 2.7 equiv) and DMAP (110.0 mg, 0.90 mmol, 30 mol%). After being stirred for 3 h, the mixture was diluted with Et_2O. The mixture was washed with 1.0 M HCl aq. a saturated $NaHCO_3$ aq. and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above was added HCl (4.0 M in dioxane, 750 µL, 3.0 mmol, 1.0 equiv). After being stirred for 1 h, the mixture was concentrated *in vacuo*. To the residue were added CH_2Cl_2 (7.5 mL, 0.40 M), *o*-toluic acid (490.1 mg, 3.6 mmol, 1.2 equiv), Et_3N (2.1 mL, 15 mmol, 5.0 equiv), DMAP (144.2 mg, 1.2 mmol, 40 mol%), and EDC·HCl (632.6 mg, 3.3 mmol, 1.1 equiv). After being stirred for 12 h, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (88:12 hexane/EtOAc to EtOAc) and GPC to afford **1ai** (291.1 mg, 34% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26–7.14 (m 4H), 4.55 (dd, J = 8.4, 4.0 Hz, 0.7H), 4.04–3.99 (m, 0.3H), 3.86–3.76 (m, 0.6H), 3.39–3.31 (m, 0.7H), 3.25–3.18 (m, 0.7H), 2.39 (s, 2.1 H), 2.33–1.80 (m, 4.9H), 1.51 (s, 6.3H), 1.29 (s, 2.7H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.4, 171.2, 170.2, 169.8, 137.0, 134.5, 134.4, 130.5, 130.4, 128.9, 126.0, 125.73, 125.67, 125.5, 81.6, 81.4, 61.3, 59.2, 48.8, 46.0, 31.4, 29.6, 28.0, 27.7, 24.8, 22.7, 19.1, 18.9 (13 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}O_3N$ 290.1751; found 290.1748.

***tert*-Butyl picolinoyl-L-prolinate (1aj)**

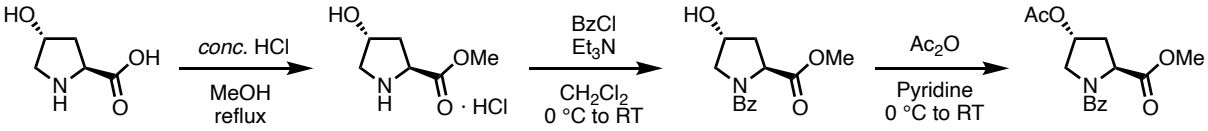


To a solution of L-proline (345.3 mg, 3.0 mmol, 1.0 equiv) and Et_3N (125 µL, 0.90 mmol, 30 mol%) in ^{t}BuOH (6.0 mL, 0.50 M) were added Boc_2O (1.86 mL, 8.1 mmol, 2.7 equiv) and DMAP (110.0 mg, 0.90 mmol, 30 mol%). After being stirred for 3 h, the mixture was diluted with Et_2O. The mixture was

washed with 1.0 M HCl aq. a saturated $NaHCO_3$ aq. and brine. The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above was added HCl (4.0 M in dioxane, 750 µL, 3.0 mmol, 1.0 equiv). After being stirred for 1 h, the mixture was concentrated *in vacuo*. To the residue were added CH_2Cl_2 (7.5 mL, 0.40 M), picolinic acid (443.2 mg, 3.6 mmol, 1.2 equiv), Et_3N (2.1 mL, 15 mmol, 5.0 equiv), DMAP (144.2 mg, 1.2 mmol, 40 mol%), and EDC·HCl (632.6 mg, 3.3 mmol, 1.1 equiv). After being stirred for 12 h, the reaction was quenched with water. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (88:12 hexane/EtOAc to EtOAc) and Isolera® (97:3 to 9:1 $CHCl_3$/MeOH) to afford **1aj** (240.7 mg, 29% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.59 (ddd, *J* = 4.8, 2.0, 0.8 Hz, 0.3H), 8.50 (ddd, *J* = 4.8, 2.0, 0.8 Hz, 0.7H), 8.03 (dt, *J* = 8.0, 0.8 Hz, 0.7H), 7.89 (dt, *J* = 8.0, 0.8 Hz, 0.3H), 7.78 (td, *J* = 8.0, 2.0 Hz, 1H), 7.36–7.30 (m, 1H), 5.08 (dd, *J* = 8.8, 3.6 Hz, 0.7H), 4.57 (dd, *J* = 8.4, 4.0 Hz, 0.3H), 4.00–3.77 (m, 2H), 2.34–2.22 (m, 1H), 2.16–1.91 (m, 3H), 1.50 (s, 2.7H), 1.33 (s, 6.3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.9, 171.3, 166.2, 165.8, 153.8, 153.3, 147.9, 147.2, 136.8, 136.7, 124.9, 124.6, 124.2, 81.1, 80.8, 62.1, 60.8, 49.6, 48.2, 31.9, 28.9, 28.0, 27.9, 27.8, 25.3, 22.0 (13 excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{15}H_{20}O_3N_2Na$ 299.1366; found 299.1369.

2-13. Synthesis of methyl (2*S*,4*R*)-1-benzoyl-4-hydroxypyrrolidine-2-carboxylate (1al) and methyl (2*S*,4*R*)-4-acetoxy-1-benzoylpyrrolidine-2-carboxylate (1am)

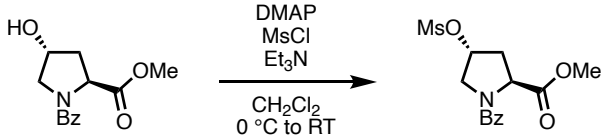


To a solution of *trans*-4-hydroxy-L-proline (1.31 g, 10 mmol, 1.0 equiv) in MeOH (20 mL, 0.50 M) was added *conc.* HCl (1.1 mL, 12 mmol, 1.2 equiv). After being refluxed for 20 h, the mixture was concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above and Et_3N (5.6 mL, 40 mmol, 4.0 equiv) in CH_2Cl_2 (25 mL, 0.40 M) was added BzCl (1.16 mL, 10 mmol, 1.0 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature and stirred for 30 min, the reaction was quenched with a saturated $NaHCO_3$ aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:4 hexane/EtOAc) to afford **1al** (2.05 g, 82% yield over 2 steps) as a white solid. The spectra are in accordance with those reported in the literature.[17]

To a solution of **1al** (249.6 mg, 1.0 mmol, 1.0 equiv) in pyridine (2.0 mL, 0.50 M) was added Ac_2O (142 μL, 1.5 mmol, 1.5 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature, stirred for 4 h, and then diluted with EtOAc, the reaction was quenched with a 3.0 M HCl aq. The mixture was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:4 hexane/EtOAc) to afford **1am** (303.8 mg, quant.) as a colorless oil. **^{1}H NMR** (400 MHz, CD_3CN, 348 K) δ 7.54–7.42 (m, 5H), 5.25 (br s, 1H), 4.69 (br s, 1H), 3.86 (dd, *J* = 12.4, 4.4 Hz, 1H), 3.80–3.45 (m, 4H), 2.50–2.41 (m, 1H), 2.32–2.23 (m, 1H), 1.99 (s, 3 H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 171.7, 169.7, 169.5, 135.2, 130.2, 128.0, 127.0, 72.5, 57.4, 54.7, 51.9, 34.5, 20.4; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{18}O_5N$ 292.1180; found 292.1188.

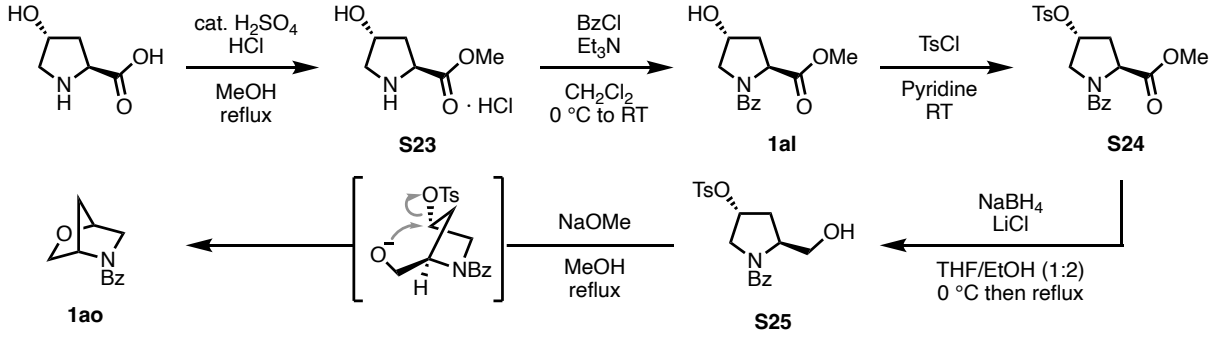
2-14. Synthesis of methyl (2*S*,4*R*)-1-benzoyl-4-((methylsulfonyl)oxy)pyrrolidine-2-carboxylate (1an)



1al **1an**

To a solution of **1al** (see section **2-13**, 201.5 mg, 0.81 mmol, 1.0 equiv), methanesulfonyl chloride (MsCl: 94 μL, 1.2 mmol, 1.5 equiv), and DMAP (19.4 mg, 0.16 mmol, 10 mol%) in CH_2Cl_2 (4.0 mL, 0.20 M) was added Et_3N (203 μL, 1.5 mmol, 1.8 equiv) dropwise at 0 °C. After the mixture was allowed to warm to room temperature, the reaction mixture was quenched with water. The mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. The residue was purified by Isolera® (4:1 to 1:4 hexane/EtOAc) and recrystallization (CH_2Cl_2/hexane) to afford **1an** (159.4 mg, 60% yield) as a white solid. The spectra are in accordance with those reported in the literature.[9]

2-15. Synthesis of ((1*S*,4*S*)-2-oxa-5-azabicyclo[2.2.1]heptan-5-yl)(phenyl)methanone (1ao)



S23 **1al** **S24**

1ao **S25**

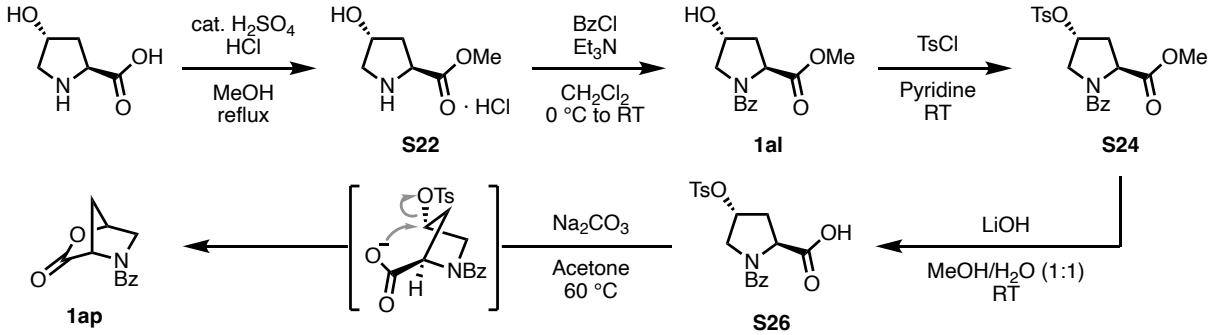
To a solution of **1al** (see section **2-13**, 1.37 g, 5.5 mmol, 1.0 equiv) and *p*-toluenesulfonyl chloride (TsCl: 2.10 g, 11 mmol, 2.0 equiv) was added pyridine (11 mL, 0.50 M). After being stirred at room temperature for 23 h, the reaction mixture was diluted with EtOAc and the reaction was quenched with

a 3.0 M HCl aq. The mixture was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 1:4 hexane/EtOAc) to afford **S24** (2.03 g, 91% yield) as a white solid.

To a solution of **S24** (806.9 mg, 2.0 mmol, 1.0 equiv) and lithium chloride (LiCl: 166.3 mg, 4.0 mmol, 2.0 equiv) in THF/EtOH (2.7 mL/5.4 mL, 0.25 M) was added sodium borohydride ($NaBH_4$: 151.6 mg, 4.0 mmol, 2.0 equiv) at 0 °C. After being stirred at 0 °C for 1 h, the reaction was refluxed for 3 h while the reaction progress was being monitored by LC/MS and quenched with a saturated NH_4Cl aq. The mixture was extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 to 0:100 hexane/EtOAc) to afford **S25** (590.3 mg, 79% yield) as a white solid.

To a solution of **S25** (590.3 mg, 1.57 mmol, 1.0 equiv) in MeOH (24 mL, 0.065 M) was added sodium methoxide (NaOMe: 170.0 mg, 3.14 mmol, 2.0 equiv). The reaction was refluxed for 3.5 h while the reaction progress was being monitored by LC/MS and quenched with water. The solvent was removed under reduced pressure, and the residue was extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (9:1 hexane/EtOAc to EtOAc) to afford **1ao** (297.8 mg, 93% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.55–7.37 (m, 5H), 5.06 (s, 0.4H), 4.73 (s, 0.6H), 4.58 (s, 0.4H), 4.43 (d, J = 1.2 Hz, 0.6H), 4.06 (d, J = 7.6 Hz, 0.4H), 3.99 (d, J = 7.6 Hz, 0.6H), 3.88 (dd, J = 7.6, 1.2 Hz, 0.4H), 3.82 (dd, J = 7.6, 1.2 Hz, 0.6H), 3.70–3.57 (m, 1H), 3.44 (s, 1H), 1.99–1.85 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 169.6, 168.3, 135.6, 135.2, 129.9, 129.7, 128.0, 127.8, 126.8, 126.7, 75.6, 75.3, 73.7, 73.4, 59.6, 57.5, 56.0, 53.8, 36.6, 35.1 (ten excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}O_2N$: 204.1019; found 204.1019.

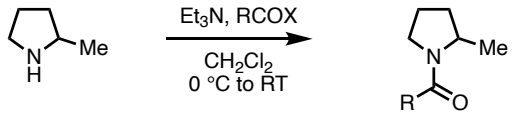
2-16. Synthesis of (1*S*,4*S*)-5-benzoyl-2-oxa-5-azabicyclo[2.2.1]heptan-3-one (1ap)



To a solution of **S24** (see section **2-15**, 671.4 mg, 1.7 mmol, 1.0 equiv) in MeOH/H_2O (3.3 mL/3.3 mL, 0.25 M) was added lithium hydroxide anhydrous (LiOH: 120.0 mg, 5.0 mmol, 3.0 equiv). After being stirred at room temperature for 5 min, the reaction was quenched with a 3.0 M HCl aq. (pH = 1) and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude product was used for the next step without further purification.

To a solution of the crude product obtained above in acetone (8.1 mL, 0.10 M) was added sodium carbonate (Na_2CO_3: 129.1 mg, 1.22 mmol, 1.5 equiv). The mixture was stirred at 60 °C for 7 h while the reaction progress was being monitored by LC/MS. The solvent was removed under reduced pressure. The residue was diluted with water and extracted three times with EtOAc. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® (hexane/EtOAc = 9:1 to 1:4) to afford **1ap** (123.3 mg, 70% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.65–7.60 (m, 2H), 7.52–7.42 (m, 3H), 5.19 (s, 1H), 4.69 (br s, 1H), 3.85 (d, J = 11.6 Hz, 1H), 3.67 (d, J = 11.6 Hz, 1H), 2.27 (d, J = 11.2 Hz, 1H), 2.08 (dd, J = 11.2, 2.0 Hz, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 170.6, 169.2, 134.5, 131.0, 128.5, 127.6, 78.2, 59.5, 50.5, 39.3; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{12}O_3N$ 218.0812; found 218.0815.

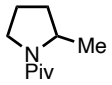
2-17. Synthesis of *N*-substituted 2-methylpyrrolidines



S1 **1**

General Procedure E

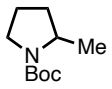
To a solution of 2-methyl pyrrolidine (68.1 mg, 0.80 mmol, 1.0 equiv) in CH_2Cl_2 (2.0 mL, 0.40 M) were added Et_3N (167 µL, 1.2 mmol, 1.5 equiv) and RCOX (1.2 equiv) at 0 °C. The reaction was allowed to warm to room temperature and stirred for 8 h. The reaction was quenched with water and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The residue was purified by Isolera® to afford **1**.



S26

2,2-Dimethyl-1-(2-methylpyrrolidin-1-yl)propan-1-one (S26)

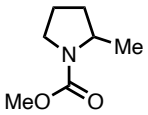
According to **Gereneal Procedure E**, **S26** was prepared using PivCl (118 µL, 0.96 mmol, 1.2 equiv). Purification by Isolera® (94:6 to 1:1 hexane/EtOAc) afforded **S26** (74.5 mg, 55% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[18]



S27

***tert*-Butyl 2-methylpyrrolidine-1-carboxylate (S27)**

According to **Gereral Procedure E**, **S27** was prepared using Boc_2O (221 μL, 0.96 mmol, 1.2 equiv) without Et_3N. Purification by Isolera® (99:1 to 9:1 hexane/EtOAc) without extraction afforded **S27** (93.4 mg, 63% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[19]



S28

Methyl 2-methylpyrrolidine-1-carboxylate (S28)

According to **Gereral Procedure E**, **S28** was prepared using $ClCO_2Me$ (74 μL, 0.96 mmol, 1.2 equiv). Purification by Isolera (88:12 hexane/EtOAc to EtOAc) afforded **S28** (44.3 mg, 39% yield) as a colorless oil. The spectra are in accordance with those reported in the literature.[20]

3. Ring-Opening Reactions

3-1. Photochemical Reaction Setup

The blue LED lamps (PR160L-456 nm Kessil® LED lamp, λ_{max} = 456 nm) were used with the intensity dial set to 100. The reaction tubes were placed 4.0 cm away from the LED lamps (**Figure S1**). During the reaction, an overhead fan was turned on to keep the external temperature at approximately 35 °C. On the other hand, when the fan is off, the reaction temperature was approximately 40 °C.

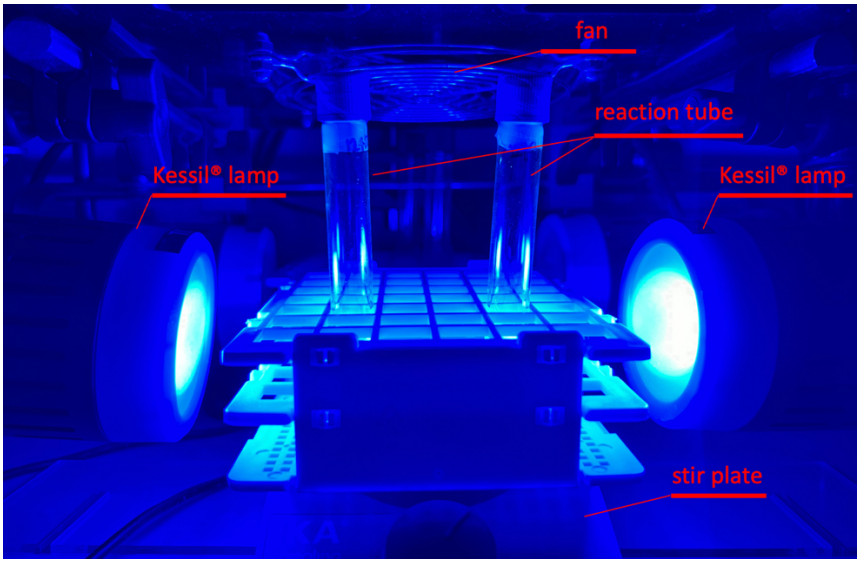
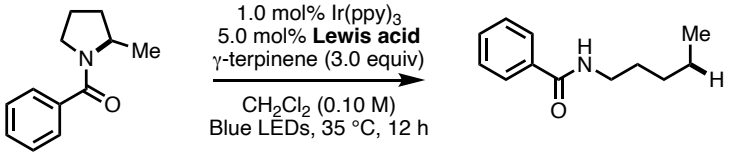


Figure S1. Photochemical reaction setup

3-2. Condition screening

To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1** (0.10 mmol, 1.0 equiv), photocatalyst (1.0 μmol, 1.0 mol%), and Lewis acid (5.0 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled three times with N_2 gas. To this tube were added CH_2Cl_2 (1.0 mL, 0.10 M) and γ-terpinene (48 μL, 0.30 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 12 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. Yields were determined by ^{1}H NMR of the crude product using CH_2Br_2 as an internal standard.

3-2-1. Lewis acid



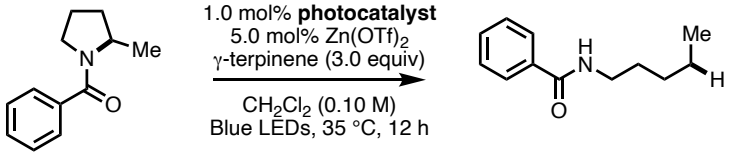
1a (0.10 mmol) **2a**

Entry	**Lewis acid**	Yield of **2a** /%	Recovery of **1a** /%
1	none	0	88
2	$Sc(OTf)_3$	1	quant.
3	$Mg(OTf)_2$	2	quant.
4	$Zn(OTf)_2$	30	82
5	$BF_3{\cdot}Et_2O$	5	72
6	TMSOTf	6	94
7	$Zn(OAc)_2$	trace	92
8	TfOH	13	84

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

Table S1. Lewis acid screening

3-2-2. Photocatalyst



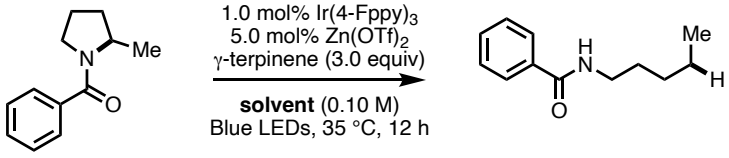
1a (0.10 mmol) **2a**

Entry	**photocatalyst**	Yield of **2a** /%	Recovery of **1a** /%
1	$Ir(ppy)_3$	30	82
2	$Ir(4\text{-}^t\text{Buppy})_3$	trace	86
3	$Ir(4\text{-Fppy})_3$	92	5
4	$Ir(dFppy)_3$	0	quant.
5	$[Ir(dFCF_3ppy)_2{\cdot}dtbbpy]{\cdot}PF_6$	3	98

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

Table S2. Photocatalyst screening

3-2-3. Solvent



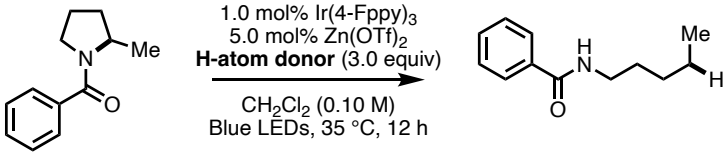
1a (0.10 mmol) **2a**

Entry	**solvent**	Yield of **2a** /%	Recovery of **1a** /%
1	CH_2Cl_2	92	5
2	THF	2	96
3	DMF	0	74

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

Table S3. Solvent screening

3-2-4. H-atom donor



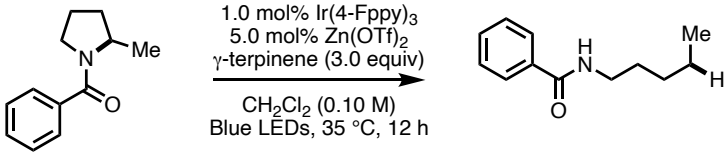
1a (0.10 mmol) **2a**

Entry	**H-atom donor**	Yield of **2a** /%	Recovery of **1a** /%
1	γ-terpinene	92	5
2	1,4-CHD	84	25
3	Hantzsch ester	0	quant.
4	Et_3SiH	4	93
5	TTMSS	12	90[a]

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.
[a] Isolated yield.

Table S4. H-atom donor screening

3-2-5. Control experiments



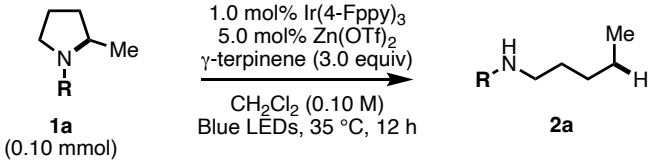
1a (0.10 mmol) **2a**

Entry	**Deviations**	Yield of **2a** /%	Recovery of **1a** /%
1	none	92	5
2	without irradiation	0	88
3	without $Zn(OTf)_2$	0	88

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

Table S5. Control experiments

3-2-6. Effect of *N*-substituent



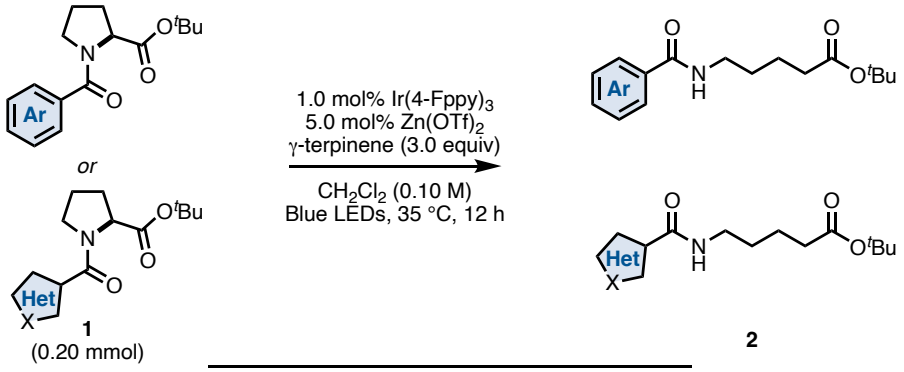
1a (0.10 mmol) **2a**

Entry	**R**	Yield of **2a** /%	Recovery of **1a** /%
1	Bz	92	0
2	Ac	0	quant.
3	CF_3CO	0	72
4	Ts	0	quant.
5	Piv	0	95
6	Boc	0	81
7	CO_2Me	0	92
8	Ph	0	quant.

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

Table S6. Effect of *N*-substituent

3-2-7. Effect of substituent on the aroyl group



Entry	**Ar** or **Het**	Yield of **2** /%	Recovery of **1** /%[a]
1	**1ad**	92	0
2	**1ae**	99	0
3	**1g**	88	0
4	**1af**	94	0
5	**1ag**	59	20
6	**1ah**	trace	88
7	**1ai**	39	57
8	**1aj**	0	79
9[b]	**1ak**	0	100

[a] Yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard.
[b] 0.10 mmol.

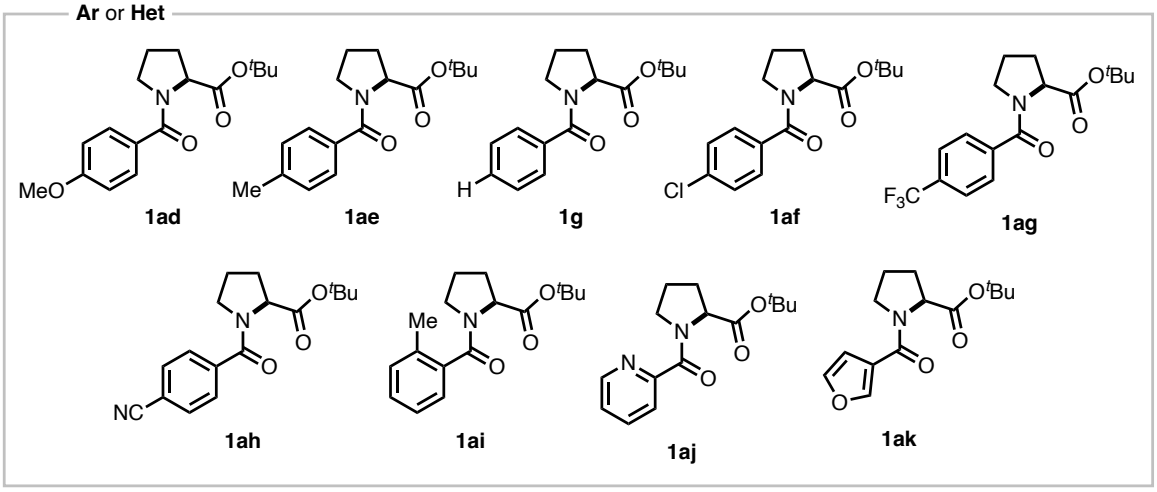
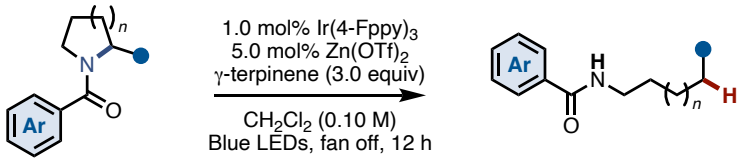
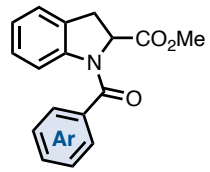
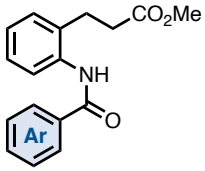
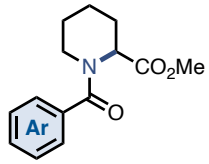
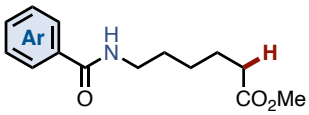
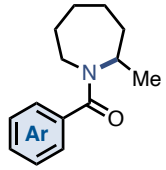
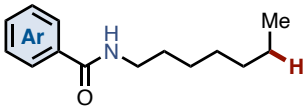
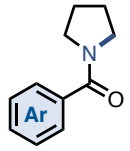
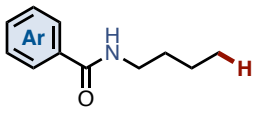


Table S7. Effect of substituent on the aroyl group

3-2-8. Effect of substituent on the aroyl group for other substrates

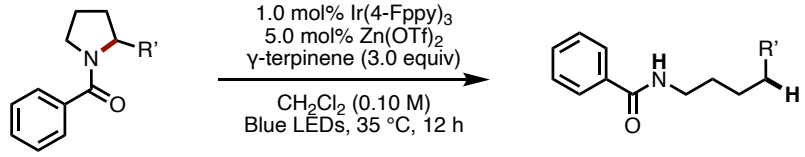


 **S13** (Ar = Ph) **1t** (Ar = 4-MeOC$_6$H$_4$)	PC Zn	 **S29** (Ar = Ph) **2t** (Ar = 4-MeOC$_6$H$_4$)	**S13** → **S29** 6% yield **1t** → **2t** 87% yield
 **S17** (Ar = Ph) **1w** (Ar = 4-MeOC$_6$H$_4$)	PC Zn	 **S30** (Ar = Ph) **2w** (Ar = 4-MeOC$_6$H$_4$)	**S17** → **S30** 24% yield[a] **1w** → **2w** 47% yield
 **S19** (Ar = Ph) **1x** (Ar = 4-MeOC$_6$H$_4$)	PC Zn	 **S31** (Ar = Ph) **2x** (Ar = 4-MeOC$_6$H$_4$)	**S19** → **S31** 4% yield[b,c] **1x** → **2x** 11% yield
 **S20** (Ar = Ph) **1z** (Ar = 4-MeOC$_6$H$_4$)	PC Zn	 **S32** (Ar = Ph) **2z** (Ar = 4-MeOC$_6$H$_4$)	**S20** → **S32** 0% yield[c,d,e] **1z** → **2z** 24% yield

[a] 72 h. [b] 120 h. [c] Yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard. [d] fan on. [e] 0.10 mmol.

Table S8. Effect of substituent on the aroyl group for other substrates

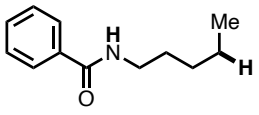
3-3. Ring opening of Pyrrolidines



1: 0.20 mmol **2**

General Procedure F

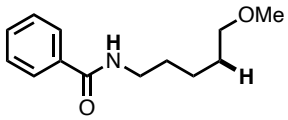
To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1** (0.20 mmol, 1.0 equiv), $Ir(4\text{-}Fppy)_3$ (1.4 mg, 2.0 μmol, 1.0 mol%), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 3.6 mg, 10 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled three times with N_2 gas. To this tube were added CH_2Cl_2 (2.0 mL, 0.10 M) and γ-terpinene (96 μL, 0.60 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 12 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*, and the residue was purified to afford the corresponding product **2**.



2a

***N*-Pentylbenzamide (2a)**

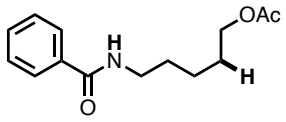
Purification by PTLC (2:1 hexane/EtOAc) afforded **2a** (33.7 mg, 88% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.52–7.40 (m, 3H), 6.10 (br s, 1H), 3.46 (td, J = 7.2, 5.6 Hz, 2H), 1.66–1.58 (m, 2H), 1.42–1.32 (m, 4H), 0.95–0.89 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 134.8, 131.2, 128.4, 126.8, 40.0, 29.3, 29.1, 22.3, 13.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{18}ON$ 192.1383; found 192.1384. The spectra are in accordance with those reported in the literature.[21]



2b

***N*-(5-Methoxypentyl)benzamide (2b)**

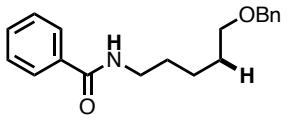
Purification by PTLC (19:1 $CHCl_3$/MeOH) afforded **2b** (34.7mg, 78% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.52–7.40 (m, 3H), 6.20 (br s, 1H), 3.47 (td, J = 7.2, 5.6 Hz, 2H), 3.39 (t, J = 6.4 Hz, 2H), 3.33 (s, 3H), 1.70–1.57 (m, 4H), 1.52–1.45 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 134.7, 131.2, 128.4, 126.8, 72.5, 58.5, 39.9, 29.3, 29.2, 23.6; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{20}O_2N$ 222.1489; found 222.1488.



2c

5-Benzamidopentyl acetate (2c)

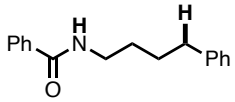
Purification by PTLC (1:1 hexane/EtOAc) afforded **2c** (40.3 mg, 81% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.53–7.41 (m, 3H), 6.14 (br s, 1H), 4.08 (t, *J* = 6.8 Hz, 2H), 3.47 (td, *J* = 7.2, 6.0 Hz, 2H), 2.04 (s, 3H), 1.74–1.63 (m, 4H), 1.51–1.42 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 171.2, 167.5, 134.6, 131.3, 128.4, 126.8, 64.1, 39.8, 29.2, 28.2, 23.3, 20.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{20}O_3N$ 250.1438; found 250.1438.



2d

***N*-(5-(Benzyloxy)pentyl)benzamide (2d)**

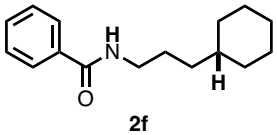
Purification by PTLC (3:1 hexane/EtOAc) and GPC ($CHCl_3$) afforded **2d** (40.3 mg, 68% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77–7.73 (m, 2H), 7.52–7.46 (m, 3H), 7.45–7.27 (m, 5H), 6.14 (br s, 1H), 4.50 (s, 2H), 3.52–3.43 (m, 4H), 1.72–1.61 (m, 4H), 1.54–1.45 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 138.5, 134.8, 131.2, 128.5, 128.3, 127.6, 127.5, 126.8, 72.9, 70.1, 39.9, 29.33, 29.29, 23.7; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{24}O_2N$ 298.1802; found 298.1800.



2e

***N*-(4-Phenylbutyl)benzamide (2e)**

Purification by PTLC (2:1 hexane/EtOAc) afforded **2e** (21.3 mg, 43% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75–7.72 (m, 2H), 7.51–7.47 (m, 1H), 7.45–7.40 (m, 2H), 7.31–7.26 (m, 2H), 7.21–7.17 (m, 3H), 6.06 (br s, 1H), 3.48 (td, *J* = 7.2, 5.6 Hz, 2H), 2.68 (t, *J* = 7.2 Hz, 2H), 1.77–1.62 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 142.0, 134.7, 131.3, 128.5, 128.4, 128.3, 126.8, 125.8, 39.9, 35.5, 29.2, 28.7. The spectra are in accordance with those reported in the literature.[22]

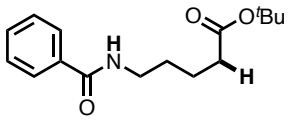


2f

***N*-(3-Cyclohexylpropyl)benzamide (2f)**

Purification by PTLC (4:1 hexane/EtOAc) afforded a mixture of **2f** and inseparable olefin as a byproduct (43.8 mg, ca. 14:1 (determined by ^{1}H NMR analysis)). To the solution of this mixture (43.8 mg, 0.18

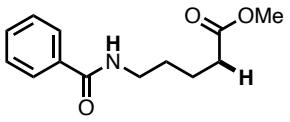
mmol (calculated as **2f**), 1.0 equiv) in CH_2Cl_2 (450 μL, 0.40 M) was added 3-chlorobenzoperoxoic acid (*m*CPBA: 77% purity, 3.8 mg, 17 μmol, 0.094 equiv). After being stirred for 7 h, the reaction was quenched with a saturated $NaHCO_3$ aqueous solution and a saturated $Na_2S_2O_3$ aqueous solution. The reaction mixture was extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo,* and the residue was purified by PTLC (2:1 hexane/EtOAc) to afford **2f** (39.2 mg, 80% yield over 2 steps) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77–7.73 (m, 2H), 7.52–7.40 (m, 3H), 6.09 (br s, 1H), 3.43 (td, *J* = 7.2, 6.0 Hz, 2H), 1.75–1.57 (m, 7H), 1.30–1.07 (m, 6H), 0.95–0.85 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 134.9, 131.2, 128.5, 126.8, 40.4, 37.4, 34.7, 33.3, 27.0, 26.6, 26.3; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{24}ON$ 246.1852; found 246.1853.



2g

***tert*-Butyl 5-benzamidopentanoate (2g)**

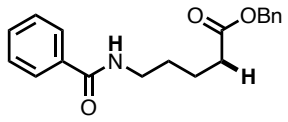
Purification by PTLC (2:1 hexane/EtOAc) afforded **2g** (55.1 mg, 82% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82–7.76 (m, 2H), 7.52–7.38 (m, 3H), 6.36 (br s, 1H), 3.47 (td, *J* = 6.0, 5.6 Hz, 2H), 2.29 (t, *J* = 6.8 Hz, 2H), 1.76–1.63 (m, 4H), 1.45 (s, 9H); **^{13}C{1H} NMR** (101 MHz, $CDCl_3$) δ 173.1, 167.5, 134.7, 131.3, 128.5, 126.9, 80.4, 39.5, 34.9, 28.9, 28.1, 22.1; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{16}H_{23}O_3NNa$ 300.1570; found 300.1569.



2h

Methyl 5-benzamidopentanoate (2h)

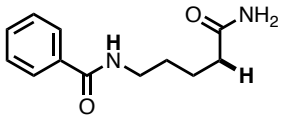
Purification by PTLC (2:1 hexane/EtOAc) afforded **2h** (42.6 mg, 90% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.52–7.40 (m, 3H), 6.35 (br s, 1H), 3.68 (s, 3H), 3.47 (td, *J* = 6.4, 6.0 Hz, 2H), 2.38 (t, *J* = 6.8 Hz, 2H), 1.78–1.63 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 174.0, 167.6, 134.5, 131.3, 128.4, 126.8, 51.5, 39.4, 33.4, 28.9, 21.9; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{13}H_{17}O_3NNa$ 258.1101; found 258.1102. The spectra are in accordance with those reported in the literature.[23]



2i

Benzyl 5-benzamidopentanoate (2i)

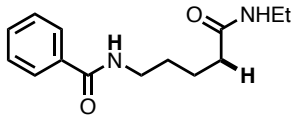
Purification by PTLC (2:1 hexane/EtOAc) afforded **2d** (49.4 mg, 80% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.52–7.30 (m, 8H), 6.26 (br s, 1H), 5.13 (s, 2H), 3.46 (td, *J* = 6.4, 6.0 Hz, 2H), 2.43 (t, *J* = 6.8 Hz, 2H), 1.79–1.62 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.4, 167.5, 135.9, 134.7, 131.4, 128.6, 128.5, 128.3, 128.2, 126.9, 66.3, 39.5, 33.7, 28.9, 22.0; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{19}H_{22}O_3N$ 312.1594; found 312.1593.



2j

***N*-(5-Amino-5-oxopentyl)benzamide (2j)**

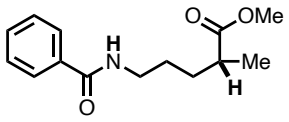
The reaction was conducted with CH_2Cl_2/DMF (0.10 M, 9:1) due to the low solubility of **2j** in CH_2Cl_2. After the reaction, the solvent was removed under reduced pressure, and the residue was purified by Isolera® (19:1 to 9:1 $CHCl_3$/MeOH) to afford **2e** (24.2 mg, 55% yield) as a white solid. **^{1}H NMR** (400 MHz, CD_3OD) δ 7.83–7.79 (m, 2H), 7.55–7.42 (m, 3H), 3.40 (t, *J* = 6.8 Hz, 2H), 2.27 (t, *J* = 7.2 Hz, 2H), 1.75–1.61 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, CD_3OD, 323 K) δ 178.9, 170.3, 136.0, 132.5, 129.5, 128.2, 40.6, 36.0, 30.0, 24.2; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{17}O_2N_2$ 221.1285; found 221.1286.



2k

***N*-(5-(Ethylamino)-5-oxopentyl)benzamide (2k)**

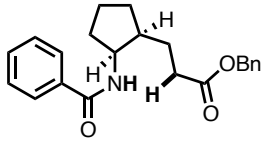
Purification by PTLC (19:1 $CHCl_3$/MeOH) afforded **2k** (39.2 mg, 78% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.84–7.79 (m, 2H), 7.53–7.40 (m, 3H), 6.62 (br s, 1H), 5.61 (br s, 1H), 3.47 (td, *J* = 6.4, 6.0 Hz, 2H), 3.29 (qd, *J* = 7.2, 5.6 Hz, 2H), 2.25 (t, *J* = 6.8 Hz, 2H), 1.80–1.63 (m, 4H), 1.14 (t, *J* = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 172.9, 167.6, 134.5, 131.3, 128.4, 126.9, 39.2, 35.6, 34.3, 28.8, 22.5, 14.7; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{20}O_2N_2Na$ 271.1417; found 271.1418.



2l

Methyl 5-benzamido-2-methylpentanoate (2l)

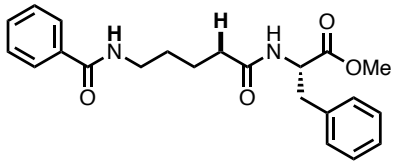
When the reaction time was 12 h, purification by PTLC (1:1 hexane/EtOAc) and GPC ($CHCl_3$) afforded **2j** (29.9 mg, 59% yield) as a colorless oil. When the reaction time was 24 h, purification by PTLC (1:1 hexane/EtOAc) afforded **2j** (45.2 mg, 90% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.52–7.40 (m, 3H), 6.25 (br s, 1H), 3.68 (s, 3H), 3.53–3.38 (m, 2H), 2.56–2.46 (m, 1H), 1.81–1.48 (m, 4H), 1.18 (d, *J* = 6.8 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 177.0, 167.5, 134.6, 131.3, 128.5, 126.8, 51.6, 39.7, 39.1, 30.8, 27.2, 17.2; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{14}H_{20}O_3N$ 250.1438; found 250.1438.



2m

Benzyl 3-((1*S*,2*S*)-2-benzamidocyclopentyl)propanoate (2m)

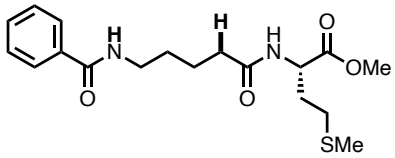
Purification by PTLC (2:1 hexane/EtOAc) afforded **2m** (53.2 mg, 76% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75–7.71 (m, 2H), 7.52–7.47 (m, 1H), 7.45–7.40 (m, 2H), 7.36–7.29 (m, 5H), 5.95 (d, *J* = 8.8 Hz, 1H), 5.08 (s, 2H), 4.59–4.52 (m, 1H), 2.44 (t, *J* = 7.6 Hz, 2H), 2.09–1.99 (m, 2H), 1.95–1.55 (m, 6H), 1.37–1.26 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.5, 167.2, 135.9, 134.9, 131.3, 128.5, 128.4, 128.1, 126.8, 66.1, 52.8, 42.5, 33.1, 32.2, 29.4, 24.9, 21.6 (one peak is missing due to overlapping); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{26}O_3N$ 352.1907; found 352.1907.



2n

Methyl (5-benzamidopentanoyl)-L-phenylalaninate (2n)

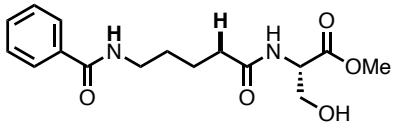
Purification by PTLC (1:5 hexane/EtOAc) afforded **2n** (49.2 mg, 64% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81–7.78 (m, 2H), 7.52–7.41 (m, 3H), 7.30–7.27 (m, 1H), 7.26–7.20 (m, 2H), 7.11–7.08 (m, 2H), 6.53 (br s, 1H), 5.99 (d, *J* = 7.6 Hz, 1H), 4.90 (dt, *J* = 7.6, 6.4 Hz, 1H), 3.72 (s, 3H), 3.48–3.38 (m, 2H), 3.16 (dd, *J* = 14.0, 5.6 Hz, 1H), 3.06 (dd, *J* = 14.0, 6.4 Hz, 1H), 2.32–2.19 (m, 2H), 1.75–1.66 (m, 2H), 1.62–1.56 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 172.6, 172.1, 167.5, 135.9, 134.5, 131.2, 129.1, 128.5, 128.4, 127.0, 126.9, 53.0, 52.2, 39.1, 37.7, 35.3, 28.5, 22.2; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{27}O_4N_2$ 383.1965; found 383.1966.



2o

Methyl (5-benzamidopentanoyl)-L-methioninate (2o)

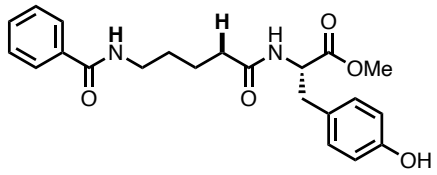
Purification by PTLC (19:1 $CHCl_3$/MeOH) afforded **2o** (60.9 mg, 83% yield) as a light yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82–7.78 (m, 2H), 7.52–7.40 (m, 3H), 6.60 (br s, 1H), 6.37 (d, *J* = 7.6 Hz, 1H), 4.72 (td, *J* = 7.6, 5.2 Hz, 1H), 3.74 (s, 3H), 3.48 (td, *J* = 6.4, 6.4 Hz, 2H), 2.51 (t, *J* = 7.2 Hz, 2H), 2.33 (t, *J* = 7.2 Hz, 2H), 2.20–2.11 (m, 1H), 2.08 (s, 3H), 2.04–1.94 (m, 1H), 1.80–1.72 (m, 2H), 1.71–1.64 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.0, 172.5, 167.6, 134.5, 131.3, 128.4, 126.9, 52.4, 51.4, 39.1, 35.3, 31.4, 30.0, 28.7, 22.3, 15.4; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{26}O_4N_2NaS$ 389.1506; found 389.1506.



2p

Methyl (5-benzamidopentanoyl)-L-serinate (2p)

Purification by PTLC (9:1 $CHCl_3$/MeOH) afforded **2p** (34.1 mg, 53% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.52–7.40 (m, 3H), 6.84 (d, *J* = 7.6 Hz, 1H), 6.73–6.67 (m, 1H), 4.68 (dt, *J* = 7.6, 3.6 Hz, 1H), 4.00 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.91 (dd, *J* = 11.4, 3.6 Hz, 1H), 3.77 (s, 3H), 3.70 (br s, 1H), 3.55–3.35 (m, 2H), 2.42–2.30 (m, 2H), 1.85–1.65 (m, 4H); **^{13}C{1H} NMR** (101 MHz, $CDCl_3$) δ 173.5, 171.1, 168.1, 134.2, 131.5, 128.5, 126.9, 62.9, 54.8, 52.5, 39.2, 35.2, 28.4, 22.3; **HRMS** (ESI) *m/z*: $[M+H]^+$ calcd for $C_{16}H_{23}O_5N_2$ 323.1602; found 323.1603.

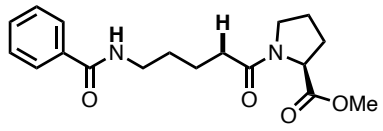


2q

Methyl (5-benzamidopentanoyl)-L-tyrosinate (2q)

Purification by PTLC (9:1 $CHCl_3$/MeOH) afforded **2q** (57.6 mg, 72% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.82–7.78 (m, 2H), 7.52–7.39 (m, 3H), 7.32 (br s, 1H), 6.93 (d, *J* = 8.8 Hz, 2H), 6.74 (d, *J* = 8.8 Hz, 3H), 6.13 (d, *J* = 8.0 Hz, 1H), 4.88 (td, *J* = 8.0, 5.2 Hz, 1H), 3.73 (s, 3H), 3.34 (q, *J* = 6.4 Hz, 2H), 3.13 (dd, *J* = 14.0, 5.2 Hz, 1H), 2.87 (dd, *J* = 14.0, 8.0 Hz, 1H), 2.26–2.11 (m, 2H), 1.66–1.38 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.3, 172.3, 168.1, 155.8, 134.2, 131.5, 130.1, 128.5,

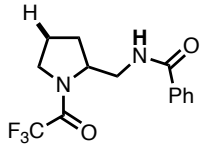
127.0, 126.9, 115.7, 53.2, 52.3, 39.3, 37.0, 35.3, 28.4, 22.4; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{22}H_{27}O_5N_2$ 399.1915; found 399.1915.



2r

Methyl (5-benzamidopentanoyl)-L-prolinate (2r)

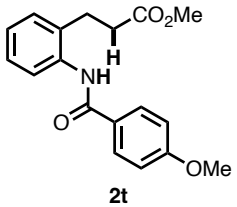
Purification by PTLC (1:5 hexane/EtOAc) afforded **2r** (63.8 mg, 95% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$, 323 K) δ 7.84–7.80 (m, 2H), 7.48–7.37 (m, 3H), 6.85–6.70 (m, 1H), 4.49 (dd, *J* = 8.4, 4.0 Hz, 0.8H), 4.40 (dd, *J* = 8.4, 2.4 Hz, 0.2H), 3.75 (s, 0.5H), 3.69 (s, 2.5H), 3.66–3.59 (m, 1H), 3.55–3.37 (m, 3H), 2.46–1.85 (m, 6H), 1.84–1.63 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, 323 K) δ 172.8, 172.6, 171.9, 167.5, 134.8, 131.0, 128.3, 127.0, 59.3, 58.7, 52.0, 47.0, 46.4, 39.3, 33.5, 33.4, 31.3, 29.1, 28.6, 24.7, 22.5, 21.3 (six excess peaks are observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{18}H_{25}O_4N_2$ 333.1809; found 333.1809.



2s

***N*-((1-(2,2,2-Trifluoroacetyl)pyrrolidin-2-yl)methyl)benzamide (2s)**

The reaction was conducted for 24 h without fan cooling. Purification by PTLC (3:2 hexane/EtOAc) afforded **2s** (19.6 mg, 33% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81–7.78 (m, 2H), 7.51–7.41 (m, 4H), 4.46–4.41 (m, 1H), 3.83–3.68 (m, 3H), 3.50 (ddd, *J* = 14.0, 8.8, 4.0 Hz, 1H), 2.20–2.09 (m, 2H), 2.05–1.97 (m, 1H), 1.93–1.86 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.6, 157.5 (q, *J* = 33.7 Hz), 133.8, 131.5, 128.6, 126.9, 116.3 (q, *J* = 289 Hz), 59.5, 47.3 (q, *J* = 3.9 Hz), 44.3, 28.6, 24.3; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –70.3, –72.2 (one excess peak was observed due to rotamer); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{15}F_3O_2N_2Na$ 323.0978; found 323.0991.

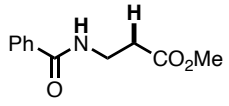


2t

Methyl 3-(2-(4-methoxybenzamido)phenyl)propanoate (2t)

The reaction was conducted without fan cooling. Purification by PTLC (2:1 hexane/EtOAc) afforded **2t** (53.9 mg, 87% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.49 (br s, 1H), 8.10–8.06 (m, 2H), 7.83 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.29–7.25 (m, 1H), 7.21–7.13 (m, 2H), 7.03–6.99 (m, 2H), 3.89 (s,

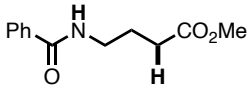
3H), 3.68 (s, 3H), 2.93 (dd, *J* = 8.0, 4.4 Hz, 2H), 2.79 (dd, *J* = 8.0, 4.4 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 175.3, 165.4, 162.3, 135.8, 133.0, 129.8, 129.3, 127.1, 127.0, 125.6, 125.4, 113.8, 55.4, 52.2, 35.5, 25.0; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{18}H_{19}O_4NNa$ 336.1206; found 336.1220.



2u

Methyl 3-benzamidopropanoate (2u)

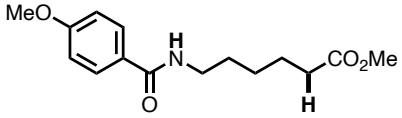
The reaction was conducted using 3.0 mol% Ir(4-Fppy)$_3$. Purification by PTLC (2:1 hexane/EtOAc) afforded **2u** (19.4 mg, 47% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.52–7.48 (m, 1H), 7.46–7.41 (m, 2H), 6.83 (br s, 1H), 3.74 (q, *J* = 6.0 Hz, 2H), 3.72 (s, 3H), 2.67 (t, *J* = 6.0 Hz, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.4, 167.3, 134.3, 131.5, 128.5, 126.9, 51.8, 35.2, 33.7. The spectra are in accordance with those reported in the literature.[24]



2v

Methyl 4-benzamidobutanoate (2v)

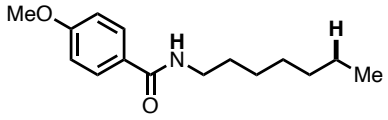
Purification by PTLC (2:1 hexane/EtOAc) afforded **2v** (34.8 mg, 72% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79–7.77 (m, 2H), 7.52–7.48 (m, 1H), 7.46–7.41 (m, 2H), 6.52 (br s, 1H), 3.67 (s, 3H), 3.52 (q, *J* = 6.8 Hz, 2H), 2.46 (t, *J* = 6.8 Hz, 2H), 2.01–1.94 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 174.2, 167.6, 134.4, 131.3, 128.4, 126.8, 51.7, 39.6, 31.6, 24.4; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{15}O_3NNa$ 244.0944; found 244.0944.



2w

Methyl 6-benzamidohexanoate (2w)

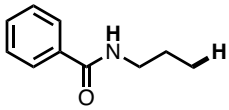
The reaction was conducted without fan cooling. Purification by PTLC (3:2 hexane/EtOAc) afforded **2w** (26.2 mg, 47% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74–7.72 (m, 2H), 6.93–6.91 (m, 2H), 6.08 (br s, 1H), 3.85 (s, 3H), 3.67 (s, 3H), 3.46–3.43 (m, 2H), 2.34 (t, *J* = 7.6 Hz, 2H), 1.72–1.60 (m, 4H), 1.46–1.38 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 174.1, 167.0, 162.0, 128.6, 127.0, 113.6, 55.3, 51.5, 39.6, 33.8, 29.3, 26.3, 24.4. The spectra are in accordance with those reported in the literature.[25]



2x

***N*-Heptyl-4-methoxybenzamide (2x)**

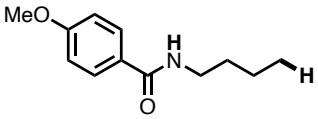
The reaction was conducted without fan cooling. Purification by PTLC (3:2 hexane/EtOAc) and followed by PTLC (39:1 $CHCl_3$/MeOH) afforded **2x** (5.6 mg, 11% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75–7.70 (m, 2H), 7.00–6.90 (m, 2H), 6.04 (br s, 1H), 3.85 (s, 3H), 3.43 (q, *J* = 6.8 Hz, 2H), 1.64–1.58 (m, 2H), 1.40–1.20 (m, 8H), 0.88 (t, *J* = 6.8 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.0, 162.0, 128.6, 127.1, 113.7, 55.4, 40.0, 31.7, 29.7, 29.0, 27.0, 22.6, 14.1. The spectra are in accordance with those reported in the literature.[26]



2y

***N*-Propylbenzamide (2y)**

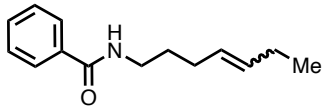
Purification by PTLC (2:3 hexane/EtOAc) afforded **2y** (22.7 mg, 66% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.52–7.48 (m, 1H), 7.46–7.41 (m, 2H), 6.10 (br s, 1H), 3.46–3.41 (m, 2H), 1.68–1.60 (m, 2H), 1.00 (t, *J* = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.6, 134.8, 131.2, 128.5, 126.8, 41.7, 22.9, 11.4. The spectra are in accordance with those reported in the literature.[27]



2z

***N*-Butyl-4-methoxybenzamide (2z)**

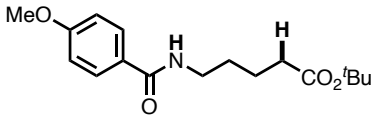
The reaction was conducted without fan cooling. Purification by PTLC (3:2 hexane/EtOAc) afforded **2z** (6.2 mg, 15% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 8.8 Hz, 2H), 6.92 (d, *J* = 8.8 Hz, 2H), 6.02 (br s, 1H), 3.85 (s, 3H), 3.44 (q, *J* = 7.2 Hz, 2H), 1.63–1.55 (m, 2H), 1.46–1.37 (m, 2H), 0.96 (t, *J* = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.0, 162.0, 128.6, 127.1, 113.7, 55.4, 39.7, 31.8, 20.2, 13.8. The spectra are in accordance with those reported in the literature.[28]



2aa

***N*-(Hept-4-en-1-yl)benzamide (2aa)**

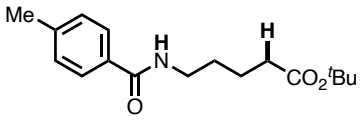
The reaction was conducted on 0.15 mmol scale. Purification by PTLC (1:1 hexane/EtOAc) afforded **2aa** (27.6 mg, 85% yield, as an *E*/*Z* mixture ; the ratio could not be determined by ^{1}H NMR analysis) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77–7.72 (m, 2H), 7.52–7.40 (m, 3H), 6.15 (br s, 1H), 5.56–5.32 (m, 2H), 3.47 (dt, *J* = 8.4, 7.2 Hz, 2H), 2.18–1.97 (m, 4H), 1.74–1.65 (m, 2H), 0.97 (t, *J* = 7.2 Hz, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 134.8, 133.0, 132.6, 131.2, 128.5, 128.0, 127.9, 126.8, 39.8, 39.7, 30.0, 29.5, 29.3, 25.5, 24.6, 20.5, 14.2, 13.8 (seven excess peaks are observed due to *E*/*Z* isomers); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{14}H_{19}ONNa$ 240.1359; found 240.1358.



2ad

***tert*-Butyl 5-(4-methoxybenzamido)pentanoate (2ad)**

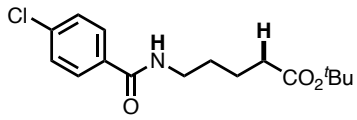
Purification by PTLC (2:1 hexane/EtOAc) afforded **2ad** (56.6 mg, 92% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75 (d, *J* = 8.4 Hz, 2H), 6.92 (d, *J* = 8.4 Hz, 2H), 6.28 (br s, 1H), 3.85 (s, 3H), 3.45 (q, *J* = 6.0 Hz, 2H), 2.28 (t, *J* = 6.8 Hz, 2H), 1.72–1.62 (m, 4H), 1.45 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.1, 167.0, 161.9, 128.6, 126.9, 113.5, 80.2, 55.3, 39.4, 34.8, 28.8, 28.0, 22.1; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{26}O_4N$ 308.1856; found 308.1857.



2ae

***tert*-Butyl 5-(4-methylbenzamido)pentanoate (2ae)**

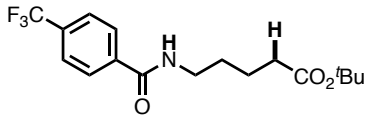
Purification by PTLC (2:1 hexane/EtOAc) afforded **2ae** (58.2 mg, 99% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 2H), 7.27–7.22 (m, 2H), 6.31 (br s, 1H), 3.45 (q, *J* = 6.0 Hz, 2H), 2.39 (s, 3H), 2.28 (t, *J* = 7.2 Hz, 2H), 1.73–1.61 (m, 4H), 1.45 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.1, 167.4, 141.7, 131.9, 129.2, 126.8, 80.4, 39.5, 34.9, 28.9, 28.1, 22.1, 21.4; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{26}O_3N$ 292.1907; found 292.1907.



2af

***tert*-Butyl 5-(4-chlorobenzamido)pentanoate (2af)**

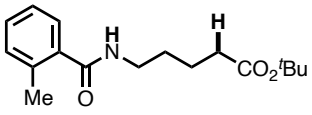
Purification by PTLC (2:1 hexane/EtOAc) afforded **2af** (58.4 mg, 94% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.75–7.73 (m, 2H), 7.42–7.39 (m, 2H), 6.43 (br s, 1H), 3.47–3.43 (m, 2H), 2.29 (t, *J* = 6.8 Hz, 2H), 1.72–1.62 (m, 4H), 1.45 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.2, 166.4, 137.5, 133.1, 128.7, 128.4, 80.5, 39.6, 34.8, 28.7, 28.1, 21.9; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{16}H_{23}O_3NCl$ 312.1361; found 312.1359.



2ag

***tert*-Butyl 5-(4-(trifluoromethyl)benzamido)pentanoate (2ag)**

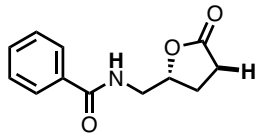
Purification by PTLC (2:1 hexane/EtOAc, three times) afforded **2ag** (40.5 mg, 59% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 8.0 Hz, 2H), 7.70 (d, *J* = 8.0 Hz, 2H), 6.55 (br s, 1H), 3.48 (q, *J* = 6.4 Hz, 2H), 2.30 (t, *J* = 6.8 Hz, 2H), 1.74–1.65 (m, 4H), 1.46 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.2, 166.2, 137.9, 133.0 (q, *J* = 32.7 Hz), 127.4, 125.5 (q, *J* = 3.8 Hz), 123.7 (q, *J* = 274 Hz), 80.5, 39.7, 34.7, 28.6, 28.0, 21.9; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –63.0; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{22}O_3F_3NNa$ 368.1444; found 368.1444.



2ai

***tert*-Butyl 5-(2-methylbenzamido)pentanoate (2ai)**

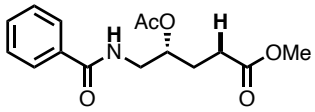
Purification by PTLC (2:1 hexane/EtOAc) afforded **2ai** (22.6 mg, 39% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36–7.27 (m, 2H), 7.22–7.16 (m, 2H), 5.92 (br s, 1H), 3.44 (q, *J* = 6.0 Hz, 2H), 2.44 (s, 3H), 2.27 (t, *J* = 6.8 Hz, 2H), 1.73–1.59 (m, 4H), 1.44 (s, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 172.9, 170.1, 136.6, 135.9, 130.9, 129.7, 126.6, 125.7, 80.3, 39.3, 34.9, 29.0, 28.1, 22.2, 19.7; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{17}H_{25}O_3NNa$ 314.1727; found 314.1728.



2al

(*R*)-*N*-((5-Oxotetrahydrofuran-2-yl)methyl)benzamide (2al)

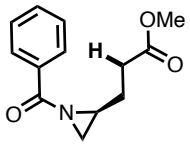
Purification by PTLC (19:1 $CHCl_3$/MeOH) afforded **2al** (42.6 mg, 97% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.56–7.43 (m, 3H), 6.53 (br s, 1H), 4.74 (tdd, *J* = 7.6, 7.2, 3.2 Hz, 1H), 3.99 (ddd, *J* = 14.0, 7.2, 3.2 Hz, 1H), 3.54 (ddd, *J* = 14.0, 7.2, 5.6 Hz, 1H), 2.62–2.56 (m, 2H), 2.43–2.34 (m, 1H), 2.09–1.98 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.9, 167.9, 133.7, 131.8, 128.5, 127.0, 79.6, 43.3, 28.5, 24.7; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}O_3N$ 220.0968; found 220.0969.



2am

Methyl (*R*)-4-acetoxy-5-benzamidopentanoate (2am)

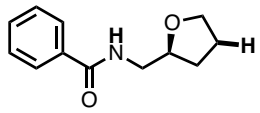
Purification by PTLC (1:2 hexane/EtOAc) afforded **2am** (52.3 mg, 88% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.53–7.41 (m, 3H), 6.63 (br s, 1H), 5.11–5.04 (m, 1H), 3.69 (s, 3H), 3.67–3.63 (m, 2H), 2.44 (t, *J* = 7.2 Hz, 2H), 2.09 (s, 3H), 2.07–1.95 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.2, 171.4, 167.5, 134.1, 131.5, 128.5, 126.9, 72.4, 51.7, 43.2, 29.7, 26.8, 21.0; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{15}H_{20}O_5N$ 294.1336; found 294.1343.



2an

Methyl (*S*)-3-(1-benzoylaziridin-2-yl)propanoate (2an)

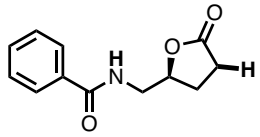
The reaction was conducted with Ir(4-Fppy)$_3$ (5.2 mg, 6.0 μmol, 3.0 mol%) for 24 h. Purification by PTLC (2:1 hexane/EtOAc) afforded **2an** (19.2 mg, 41% yield) as a yellow solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.95–7.91 (m, 2H), 7.50–7.45 (m, 1H), 7.43–7.38 (m, 2H), 4.81–4.73 (m, 1H), 4.16 (dd, *J* = 14.8, 9.6 Hz, 1H), 3.688 (dd, *J* = 14.8, 7.2 Hz), 3.685 (s, 3H), 2.60–2.47 (m, 2H), 2.09–1.95 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.3, 163.7, 131.3, 128.3, 128.1, 127.7, 78.7, 59.9, 51.7, 30.6, 29.8; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{16}O_3N$ 234.1125; found 234.1126.



2ao

(*S*)-*N*-((Tetrahydrofuran-2-yl)methyl)benzamide (2ao)

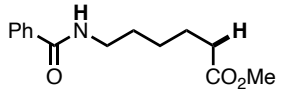
Purification by PTLC (20:1 $CHCl_3$/MeOH) afforded **2ao** (34.6 mg, 84% yield) as a yellow oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.77 (m, 2H), 7.52–7.47 (m, 1H), 7.46–7.41 (m, 2H), 6.52 (br s, 1H), 4.11–4.04 (m, 1H), 3.90 (dt, *J* = 8.0, 6.8 Hz, 1H), 3.83–3.75 (m, 2H), 3.35 (ddd, *J* = 13.6, 7.2, 4.8 Hz, 1H), 2.08–1.99 (m, 1H), 1.97–1.89 (m, 2H), 1.67–1.57 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 167.5, 134.4, 131.3, 128.4, 126.9, 77.8, 68.1, 43.5, 28.6, 25.8; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{16}O_2N$ 206.1176; found 206.1177. The spectra are in accordance with those reported in the literature.[29]



2ap

(*S*)-*N*-((5-Oxotetrahydrofuran-2-yl)methyl)benzamide (2ap)

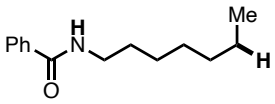
Purification by PTLC (20:1 $CHCl_3$/MeOH) afforded **2ap** (38.5 mg, 88% yield) as a white solid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.56–7.51 (m, 1H), 7.48–7.43 (m, 2H), 6.56 (br s, 1H), 4.74 (dtd, *J* = 8.0, 7.2, 3.2 Hz, 1H), 3.98 (ddd, *J* = 14.8, 7.2, 3.2 Hz, 1H), 3.54 (ddd, *J* = 14.8, 7.2, 5.6 Hz, 1H), 2.62–2.56 (m, 2H), 2.43–2.34 (m, 1H), 2.09–1.98 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.9, 167.9, 133.7, 131.8, 128.5, 127.0, 79.6, 43.3, 28.5, 24.7; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{14}O_3N$ 220.0968; found 220.0972.



S30

Methyl 6-benzamidohexanoate (S30)

The reaction was irradiated with blue LEDs for 72 h without fan cooling. Purification by PTLC (3:2 hexane/EtOAc) afforded **S30** (13.3 mg, 24% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.52–7.48 (m, 1H), 7.46–7.41 (m, 2H), 6.18 (br s, 1H), 3.67 (s, 3H), 3.47 (td, *J* = 7.2, 6.0 Hz, 2H), 2.34 (t, *J* = 7.2 Hz, 2H), 1.71–1.61 (m, 4H), 1.47–1.39 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 174.1, 167.5, 134.7, 131.3, 128.5, 126.8, 51.5, 39.7, 33.8, 29.2, 26.3, 24.4. The spectra are in accordance with those reported in the literature.[25]



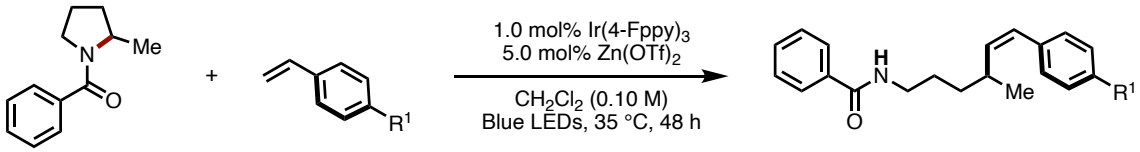
S31

***N*-Heptylbenzamide (S31)**

The reaction was irradiated with blue LEDs for 120 h without fan cooling. Yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard. In the case of **General Procedure F**, purification by PTLC (2:1 hexane/EtOAc) afforded **S31** (1.1 mg, 3% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.77–7.74 (m, 2H), 7.52–7.46 (m, 1H), 7.45–7.41 (m, 2H), 6.08 (br s, 1H), 3.46 (td, J = 7.2, 6.4 Hz, 2H), 1.66–1.56 (m, 2H), 1.39–1.24 (m, 8H), 0.89 (t, J = 6.8 Hz, 3H). The spectrum is in accordance with those reported in the literature.[30]

3-4. Intermolecular Radical Addition

3-4-1. Ring-Opening/Alkenylation

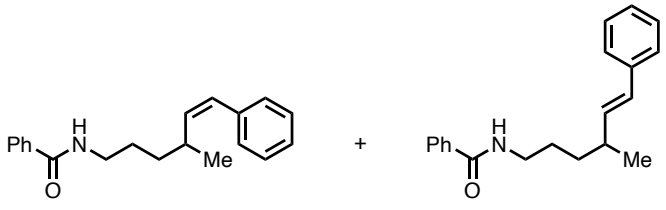


1a: 0.20 mmol **3a–c**: 3.0 equiv **4a–c**

General Procedure G

To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1a** (38.0 mg, 0.20 mmol, 1.0 equiv), Ir(4-Fppy)$_3$ (1.4 mg, 2.0 μmol, 1.0 mol%), and zinc trifluoromethanesulfonate (Zn(OTf)$_2$: 3.6 mg, 10 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (2.0 mL, 0.10 M) and alkene **3** (0.60 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 48 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2. The combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by PTLC or PTLC and GPC afforded the corresponding styrene **4**.

***N*-(4-Methyl-6-phenylhex-5-en-1-yl)benzamide (4a)**

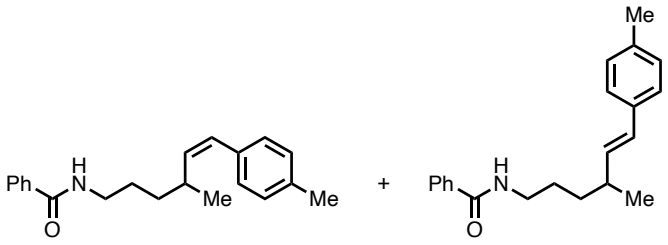


(*Z*)-**4a** (*E*)-**4a**

Purification by PTLC (2:1 hexane/EtOAc) followed by GPC afforded **4a** (18.7 mg, 32% yield, a mixture of diasteromers, *E*/*Z* = 19:81) as a colorless oil. Characterization of **4a** as a mixture of *E*/*Z* isomers was done as follows; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.71 (m, 2H), 7.52–7.47 (m, 1H), 7.45–7.40 (m,

2H), 7.34–7.29 (m, 2H), 7.26–7.19 (m, 3H), 6.41 (*Z* isomer, d, *J* = 11.6 Hz, 0.81H), 6.36 (*E* isomer: d, *J* = 15.6 Hz, 0.19H), 6.11–5.98 (m, 1.19H), 5.43 (*Z* isomer, dd, *J* = 11.6, 10.4 Hz, 0.81H), 3.49–3.30 (m, 2H), 2.83–2.72 (m, 1H), 1.67–1.58 (m, 1H), 1.55–1.32 (m, 3H), 1.11 (*E* isomer, d, *J* = 6.8 Hz, 0.57H), 1.08 (*Z* isomer, d, *J* = 6.4 Hz, 2.43H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, for *Z* isomer) δ 167.5, 138.7, 137.7, 134.8, 131.3, 128.5, 128.2, 128.0, 126.8, 126.5, 126.0, 40.1, 34.8, 31.9, 27.6, 21.1; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{20}H_{23}ONNa$ 316.1672; found 316.1682.

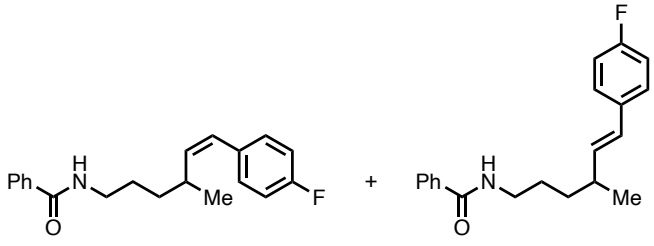
N-(4-Methyl-6-(*p*-tolyl)hex-5-en-1-yl)benzamide (4b)



(*Z*)-4b (*E*)-4b

Purification by PTLC (2:1 hexane/EtOAc), GPC, and followed by PTLC (4:1 hexane/acetone) afforded **4b** (a mixture of diasteromers, 19.1 mg, 31% yield, *E*/*Z* = 12:88) as a colorless oil. Characterization of **4b** as a mixture of *E*/*Z* isomers was done as follows; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.71 (m, 2H), 7.51–7.46 (m, 1H), 7.44–7.40 (m, 2H), 7.25–7.05 (m, 4H), 6.38–6.31 (m, 1H), 6.07–5.98 (m, 1.17H), 5.38 (*Z* isomer, dd, *J* = 11.6, 10.4 Hz, 0.83H), 3.49–3.30 (m, 2H), 2.85–2.74 (m, 1H), 2.33–2.32 (m, 3H), 1.66–1.59 (m, 1H), 1.55–1.32 (m, 3H), 1.10–1.06 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, for *Z* isomer) δ 167.4, 138.1, 136.2, 134.80, 134.77, 131.3, 128.9, 128.5, 128.4, 127.9, 126.8, 40.1, 34.8, 31.9, 27.6, 21.11, 21.08; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{21}H_{25}ONNa$ 330.1828; found 330.1830.

N-(6-(4-Fluorophenyl)-4-methylhex-5-en-1-yl)benzamide (4c)

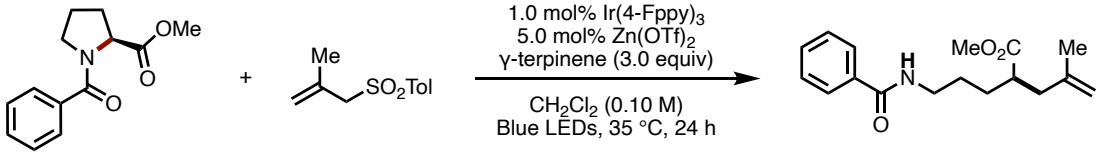


(*Z*)-4c (*E*)-4c

Purification by PTLC (2:1 hexane/EtOAc) followed by GPC afforded *N*-(6-(4-fluorophenyl)-4-methylhex-5-en-1-yl)benzamide (a mixture of diasteromers, 18.7 mg, 32% yield, *E*/*Z* = 8:92) as a colorless oil. Characterization of **4c** as a mixture of *E*/*Z* isomers was done as follows; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76–7.71 (m, 2H), 7.51–7.47 (m, 1H), 7.44–7.40 (m, 2H), 7.21–7.18 (m, 2H), 7.03–6.98 (m, 2H), 6.37–6.30 (m, 1H), 6.11–5.95 (m, 1.08H), 5.41 (*Z* isomer, dd, *J* = 11.6, 10.4 Hz, 0.92H), 3.49–3.32 (m, 2H), 2.76–2.68 (m, 1H), 1.66–1.58 (m, 1H), 1.55–1.32 (m, 3H), 1.11 (*E* isomer, d, *J* =

6.8 Hz, 0.24H), 1.07 (*Z* isomer, d, *J* = 6.8 Hz, 2.76H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$, for *Z* isomer) δ 167.4, 161.5 (d, *J* = 247 Hz), 138.7, 134.7, 133.7 (d, *J* = 3.6 Hz), 131.3, 130.0 (d, *J* = 8.2 Hz), 128.5, 126.9, 126.8, 115.1 (d, *J* = 21.4 Hz), 40.1, 34.8, 31.9, 27.7, 21.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –118.9; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{20}H_{22}OFNNa$ 334.1578; found 334.1575.

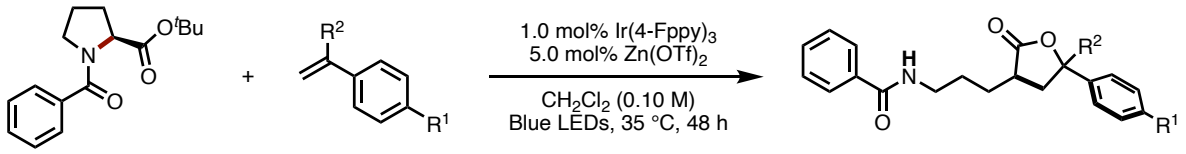
3-4-2. Synthesis of methyl 2-(3-benzamidopropyl)-4-methylpent-4-enoate (5)



1h: 0.20 mmol **3d**: 2.0 equiv **5**: 45%

To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1h** (46.6 mg, 0.20 mmol, 1.0 equiv), alkene **3d** (84.0 mg, 0.40 mmol, 2.0 equiv), $Ir(4\text{-Fppy})_3$ (1.4 mg, 2.0 μmol, 1.0 mol%), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 3.6 mg, 10 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (2.0 mL, 0.10 M) and γ-terpinene (96 μL, 0.60 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 24 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. Purification by PTLC (2:1 hexane/EtOAc) afforded 5 (26.0 mg, 45% yield) as a colorless oil. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.79–7.74 (m, 2H), 7.52–7.40 (m, 3H), 6.24 (br s, 1H), 4.77–4.75 (m, 1H), 4.71–4.68 (m, 1H), 3.67 (s, 3H), 3.52–3.38 (m, 2H), 2.68–2.59 (m, 1H), 2.37 (dd, *J* = 14.0, 8.4 Hz, 1H), 2.15 (dd, *J* = 14.0, 6.4 Hz, 1H), 1.71 (s, 3H), 1.70–1.53 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 176.2, 167.5, 142.6, 134.7, 131.4, 128.5, 126.8, 112.4, 51.6, 43.5, 40.7, 39.7, 29.2, 27.4, 22.1; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{17}H_{24}O_3N$ 290.1751; found 290.1751.

3-4-3. Radical Addition to Alkenes 3a–c and 3e

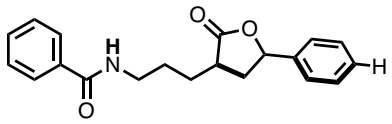


1g: 0.20 mmol **3**: 3.0 equiv **6**

General Procedure H

To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1g** (55.1 mg, 0.20 mmol, 1.0 equiv), $Ir(4\text{-Fppy})_3$ (1.4 mg, 2.0 μmol, 1.0 mol%), and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 3.6 mg, 10 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (2.0 mL, 0.10 M) and alkene **3** (0.60 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 48 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 using

ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. Purification by PTLC or Isolera® afforded the corresponding lactone **6**.



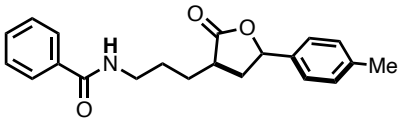
6a

***N*-(3-(2-Oxo-5-phenyltetrahydrofuran-3-yl)propyl)benzamide (6a)**

Purification by PTLC (7:1 Et_2O/EtOAc) afforded separable two diastereomers of **6a** (35.5 mg, 55% yield, *dr* = 1.9:1): major diastereomer (23.3 mg, 36%) as a white solid and minor diastereomer (12.2 mg, 19%) as a colorless oil.

For a major diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.52–7.31 (m, 8H), 6.43 (br s, 1H), 5.38 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.57–3.44 (m, 2H), 2.89–2.75 (m, 2H), 2.05–1.64 (m, 5H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.6, 167.6, 138.8, 134.5, 131.4, 128.7, 128.6, 126.9, 125.4, 79.5, 41.0, 39.4, 37.8, 27.1, 27.0 (one peak is missing due to overlapping); **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}O_3N$ 346.1414; found 346.1412.

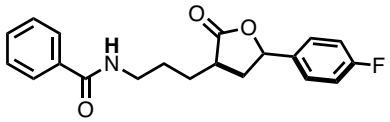
For a minor diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.53–7.27 (m, 8H), 6.41 (br s, 1H), 5.58 (t, *J* = 6.4 Hz, 1H), 3.57–3.45 (m, 2H), 2.76–2.68 (m, 1H), 2.43 (dd, *J* = 8.4, 6.4 Hz, 2H), 2.01–1.92 (m, 1H), 1.88–1.64 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 179.2, 167.6, 139.6, 134.4, 131.5, 128.8, 128.6, 128.3, 126.9, 124.9, 78.7, 39.6, 38.4, 36.5, 27.7, 27.1.



6b

***N*-(3-(2-Oxo-5-(*p*-tolyl)tetrahydrofuran-3-yl)propyl)benzamide (6b)**

Purification by Isolera® (4:1 to 0:100 hexane/EtOAc) afforded an inseparable diastereomeric mixture of **6b** (55.9 mg, 83% yield, *dr* = 2.2:1) as a yellow solid. Characterization of **6b** as a mixture of diastereomers was done as follows; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.52–7.41 (m, 3H), 7.25–7.17 (m, 4H), 6.04 (br s, 1H), 5.55 (dd, *J* = 6.8, 5.6 Hz, 0.31H), 5.35 (dd, *J* = 6.8, 5.6 Hz, 0.69H), 3.56–3.46 (m, 2H), 2.88–2.68 (m, 1.38H), 2.43–2.38 (m, 0.62H), 2.36 (s, 3H), 2.05–1.62 (m, 5H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 179.2, 178.7, 167.6, 138.4, 138.0, 136.4, 135.6, 134.4, 131.3, 129.34, 129.30, 128.4, 126.9, 125.5, 124.9, 79.6, 78.8, 41.0, 39.5, 39.4, 38.5, 37.6, 36.3, 27.7, 27.05, 27.02, 21.1, 21.0 (four peaks are missing due to overlapping); **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{23}O_3NNa$ 360.1570; found 360.1569.



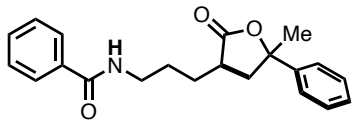
6c

***N*-(3-(5-(4-Fluorophenyl)-2-oxotetrahydrofuran-3-yl)propyl)benzamide (6c)**

Purification by PTLC (7:1 Et_2O/EtOAc) afforded separable two diastereomers of **6c** (40.4 mg, 59% yield, *dr* = 2.0:1): major diastereomer (26.9 mg, 39%) as a white solid and minor diastereomer (13.5 mg, 20%) as a white solid.

For a major diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.76 (m, 2H), 7.53–7.48 (m, 1H), 7.46–7.41 (m, 2H), 7.35–7.30 (m, 2H), 7.11–7.05 (m, 2H), 6.36 (br s, 1H), 5.36 (dd, *J* = 10.8, 5.6 Hz, 1H), 3.58–3.45 (m, 2H), 2.90–2.75 (m, 2H), 2.06–1.97 (m, 1H), 1.93–1.61 (m, 4H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.3, 167.6, 162.7 (d, $J_{C–F}$ = 249.0 Hz), 134.5 (d, $J_{C–F}$ = 3.2 Hz), 134.4, 131.5, 128.6, 127.4 (d, $J_{C–F}$ = 8.3 Hz), 126.8, 115.7 (d, $J_{C–F}$ = 22.0 Hz), 78.9, 41.0, 39.4, 37.8, 27.1, 27.0; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –116.3; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{21}H_{23}O_3NFNa$ 364.1319; found 364.1317.

For a minor diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80–7.75 (m, 2H), 7.53–7.41 (m, 3H), 7.30–7.25 (m, 2H), 7.10–7.04 (m, 2H), 6.41 (br s, 1H), 5.55 (t, *J* = 6.4 Hz, 1H), 3.58–3.44 (m, 2H), 2.76–2.68 (m, 1H), 2.47–2.35 (m, 2H), 2.01–1.91 (m, 1H), 1.88–1.66 (m, 3H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.9, 167.6, 162.5 (d, $J_{C–F}$ = 248.7 Hz), 135.3 (d, $J_{C–F}$ = 3.3 Hz), 134.4, 131.5, 128.6, 126.85 (d, $J_{C–F}$ = 8.3 Hz), 126.84, 115.8 (d, $J_{C–F}$ = 21.8 Hz), 78.2, 39.6, 38.5, 36.5, 27.7, 27.1; **^{19}F NMR** (376 MHz, $CDCl_3$) δ –116.8.



6e

***N*-(3-(5-Methyl-2-oxo-5-phenyltetrahydrofuran-3-yl)propyl)benzamide (6e)**

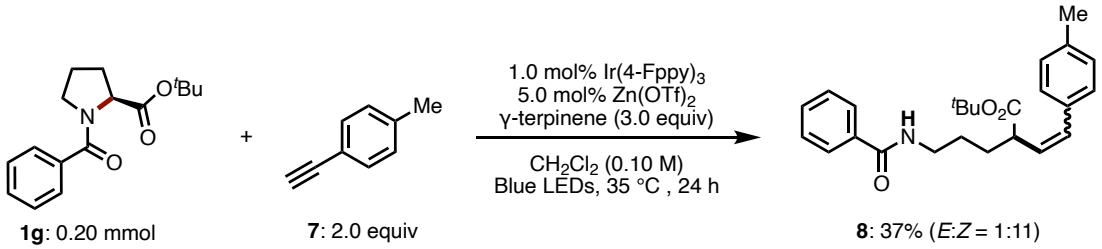
Purification by PTLC (1:1 hexane/EtOAc) afforded separable two diastereomers of **6e** (56.7 mg, 84% yield, *dr* = 3.5:1): major diastereomer (44.1 mg, 65%) as a yellow solid and minor diastereomer (12.6 mg, 19%) as a yellow oil.

For a major diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.74 (m, 2H), 7.51–7.46 (m, 1H), 7.45–7.39 (m, 2H), 7.38–7.33 (m, 4H), 7.31–7.26 (m, 1H), 6.50–6.30 (m, 1H), 3.52–3.38 (m, 2H), 2.98–2.87 (m, 1H), 2.68 (dd, *J* = 12.8, 8.8 Hz, 1H), 2.13 (dd, *J* = 12.8, 11.2 Hz, 1H), 1.95–1.86 (m, 1H), 1.84–1.64 (m, 5H), 1.60–1.48 (m, 1H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.2, 167.6, 145.1, 134.4, 131.4, 128.6, 128.5, 127.6, 126.8, 123.8, 84.9, 41.8, 40.0, 39.4, 28.8, 27.5, 27.0; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd for $C_{21}H_{24}O_3N$ 338.1751; found 338.1750.

For a minor diastereomer: **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.52–7.47 (m, 1H), 7.45–7.40 (m, 2H), 7.39–7.34 (m, 4H), 7.33–7.27 (m, 1H), 6.41 (m, 1H), 3.52–3.39 (m, 2H), 2.75 (dd,

J = 12.0, 8.4 Hz, 1H), 2.54–2.45 (m, 1H), 2.09 (t, J = 12.0 Hz, 1H), 1.97–1.88 (m, 1H), 1.81–1.67 (m, 5H), 1.66–1.55 (m, 2H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 178.7, 167.5, 143.6, 134.5, 131.4, 128.6, 128.5, 127.7, 126.8, 124.1, 84.9, 42.8, 39.8, 39.6, 30.3, 27.1, 26.9.

3-4-4. Synthesis of *N*-(6,6-dimethyl-4-(4-methylstyryl)-5-oxoheptyl)benzamide (8)

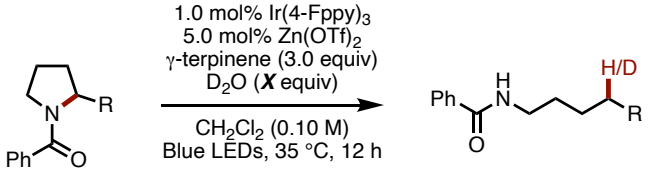


1g: 0.20 mmol　　**7**: 2.0 equiv　　**8**: 37% (*E*:*Z* = 1:11)

To an 8-mL glass tube equipped with a magnetic stirring bar were added pyrrolidine **1g** (55.1 mg, 0.20 mmol, 1.0 equiv), Ir(4-Fppy)$_3$ (1.4 mg, 2.0 μmol, 1.0 mol%), and zinc trifluoromethanesulfonate (Zn(OTf)$_2$: 3.6 mg, 10 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (2.0 mL, 0.10 M), alkyne **7** (51 μL, 0.40 mmol, 2.0 equiv), and γ-terpinene (96 μL, 0.60 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 24 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 using ISOLUTE® phase separator. The combined organic layer was concentrated *in vacuo*. Purification by PTLC (20:1 $CHCl_3$/EtOAc) afforded **8** (29.1 mg, 37% yield, as a mixture of *E*/*Z* isomers; *E*:*Z* = 1:11) as a yellow oil. Characterization of **8** as a mixture of *E*/*Z* isomers was done as follows; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.78–7.72 (m, 2H), 7.51–7.46 (m, 1H), 7.45–7.39 (m, 2H), 7.27–7.23 (m, 2H), 7.16–7.10 (m, 2H), 6.55 (*Z* isomer: d, J = 11.2 Hz, 0.91H), 6.44 (*E* isomer: d, J = 16.4 Hz, 0.09H), 6.25–6.14 (m, 1H), 6.13–6.07 (m, 0.09H), 5.54 (t, J = 11.2 Hz, 0.91H), 3.55–3.43 (m, 1.09H), 3.39 (*Z* isomer: q, J = 6.4 Hz, 1.82H), 3.07 (*E* isomer: q, J = 6.4 Hz, 0.09H), 2.34 (s, 3H), 1.94–1.80 (m, 1H), 1.74–1.52 (m, 3H), 1.51–1.42 (m, 9H); **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 173.4, 167.4, 136.9, 134.7, 133.8, 131.34, 131.28, 129.1, 129.0, 128.6, 128.5, 126.8, 81.0, 45.4, 39.7, 30.3, 28.0, 26.9, 21.1; **HRMS** (ESI) *m/z*: $[M+Na]^+$ Calcd for $C_{25}H_{31}O_3NNa$ 416.2196; found 416.2196.

3-5. Control experiments for the detection of carbanion intermediate

When the reaction affords carbanion intermediates, the addition of D_2O would deuterate the product. However, the addition of D_2O in the reaction did not afford any deuterated products. Then, we concluded that the reaction proceeds in radical mechanism without any carbanion intermediates.



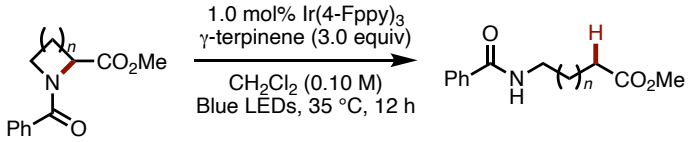
1 (0.10 mmol) **2**

Entry	R	***X***	Yield of **2** /%	Deuterated ratio /% D	Recovery of **1** /%
1	Me	1	72	<5[a]	22
2	Me	3	36	<5[a]	40
3	Me	5	21	<5[a]	71
4	Me	10	14	<5[a]	75
5	Me	20	11	<5[a]	80
6	CO_2Bn	1	48	<5[a]	50

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.
[a] Deuterated ratio was determined after isolation.

To an 8-mL glass tube equipped with a magnetic stirring bar were added $Ir(4\text{-}Fppy)_3$ (0.7 mg, 1.0 μmol, 1.0 mol%) and zinc trifluoromethanesulfonate ($Zn(OTf)_2$: 1.8 mg, 5.0 μmol, 5.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (1.0 mL, 0.10 M), pyrrolidine (0.10 mmol, 1.0 equiv), D_2O, and γ-terpinene (48 μL, 0.30 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 12 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Purification by PTLC (2:1 hexane/EtOAc) to afford the corresponding ring-opening product and the deuterated ratio was determined by ^1H NMR.

3-6. Control experiments for the ring opening of *N*-Bz aziridine and azetidine



1 (0.10 mmol) **2**

Entry	*n*	Yield of **2** /%	Recovery of **1** /%	Total /%
1	0 (**1u**)	28	59	87
2	1 (**1v**)	21	38	59

Yields were determined by ^1H NMR using CH_2Br_2 as an internal standard.

To a 3 mL glass tube equipped with a magnetic stirring bar was added Ir(4-Fppy)$_3$ (0.7 mg, 1.0 μmol, 1.0 mol%). After being sealed with a screw cap, the tube was evacuated and backfilled with N_2 gas three times. To this tube were added CH_2Cl_2 (1.0 mL, 0.10 M), aziridine or azetidine (0.10 mmol, 1.0 equiv), and γ-terpinene (48 μL, 0.30 mmol, 3.0 equiv). After being stirred under the irradiation with blue LEDs (Kessil®, 456 nm) for 12 h, the reaction mixture was diluted with water and extracted three times with CH_2Cl_2 and the combined organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. Yields were determined by ^{1}H NMR using CH_2Br_2 as an internal standard.

4. Cyclic Voltammetry

Cyclic voltammograms were collected with an HSV-110 (Hokuto Denko). Each sample was prepared by dissolving appropriate substrates in 3 mL of 0.1 M [nBu_4N][BF_4] in dry, degassed acetonitrile. Measurements employed a glassy carbon as a working electrode (electrode surface = 7.07 mm^2), platinum wire as a counter electrode, Ag/Ag^+ (in 0.1 M [nBu_4N][ClO_4]/0.01 M $AgNO_3$ in MeCN) as a reference electrode, and a scan rate of 100 mV/s. Reductions were measured by scanning potentials in the negative direction; the glassy carbon electrode was polished between each scan.

(2-Methylpyrrolidin-1-yl)(phenyl)methanone (1a)

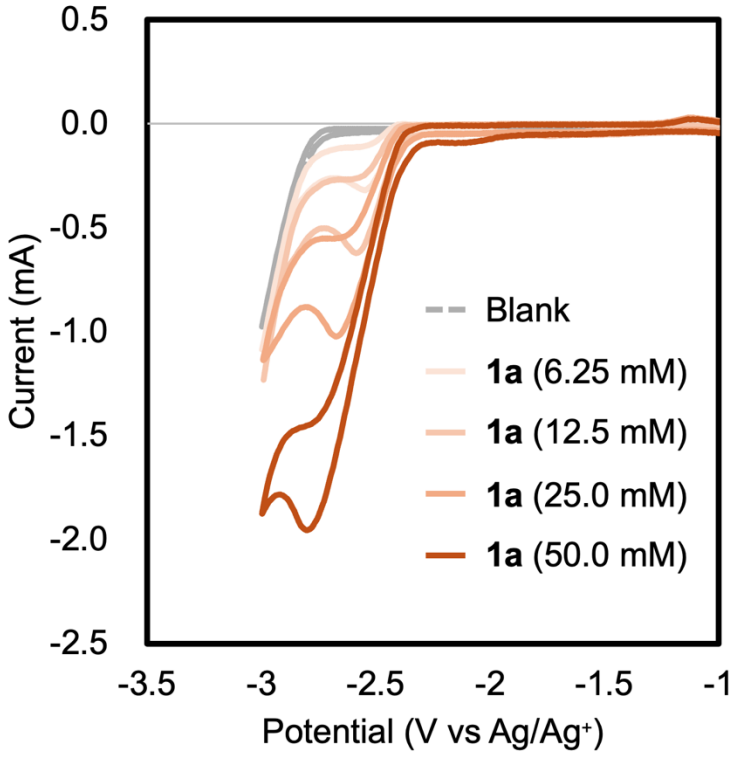


Figure S2. Cyclic Voltammogram of **1a**

1-(2-Methylpyrrolidin-1-yl)ethan-1-one (1ab)

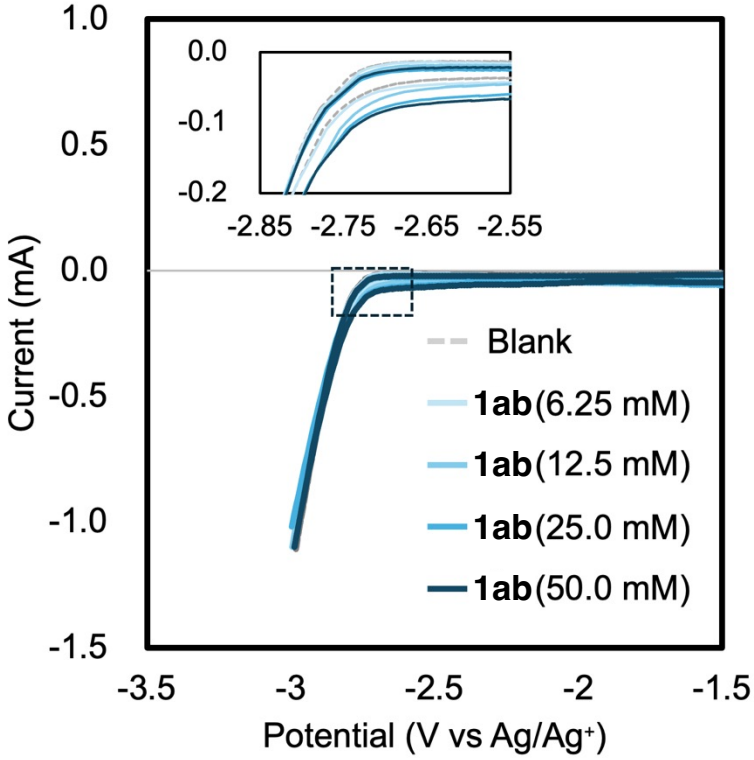


Figure S3. Cyclic Voltammogram of **1ab**

2,2,2-Trifluoro-1-(2-methylpyrrolidin-1-yl)ethan-1-one (1ac)

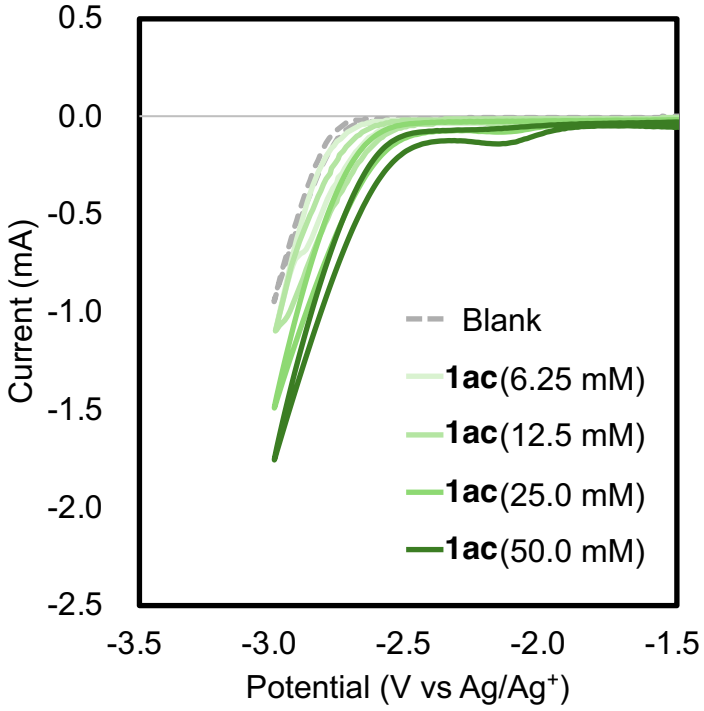


Figure S4. Cyclic Voltammogram of **1ac**

5. NMR Studies

$^{13}C\{^{1}H\}$ NMR spectra of *N*-acyl pyrrolidines **1** (0.40 mmol for **1a** (*N*-COPh), 0.60 mmol for **1s** (*N*-COMe) and **1t** (*N*-$COCF_3$), 1.0 equiv) in the presence of $Zn(OTf)_2$ (5.0 mol%, 10 mol%, and 30 mol%) were measured in tetrahydrofuran-d_8 (550 μL) at 338 K. $CHCl_3$ (1.0 equiv, δ 79.0 ppm) was added as a reference standard. Although CH_2Cl_2 was used in the optimal conditions of the ring opening of pyrrolidines, in NMR studies, tetrahydrofuran-d_8 was used due to the low solubility of $Zn(OTf)_2$ in CD_2Cl_2.

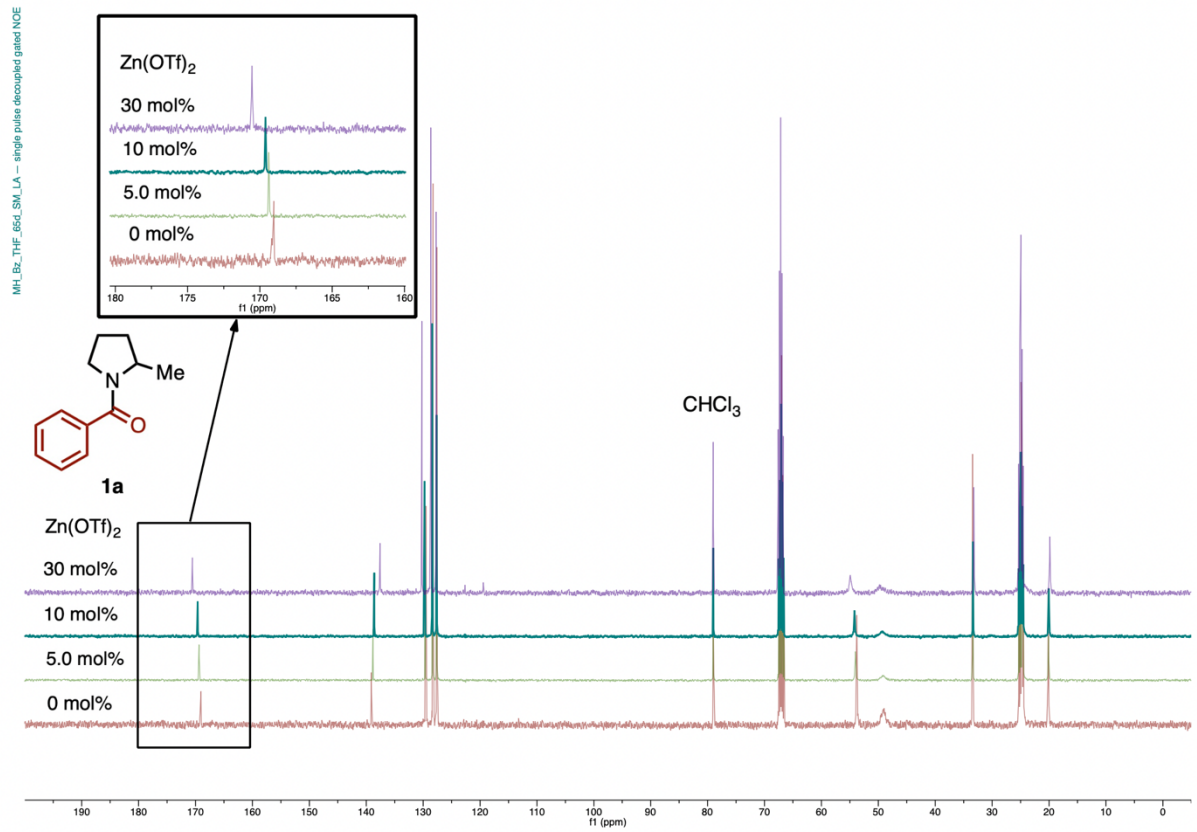


Figure S4. $^{13}C\{^{1}H\}$ NMR spectra of pyrrolidine **1a** with different equivalents of $Zn(OTf)_2$ in THF-d_8

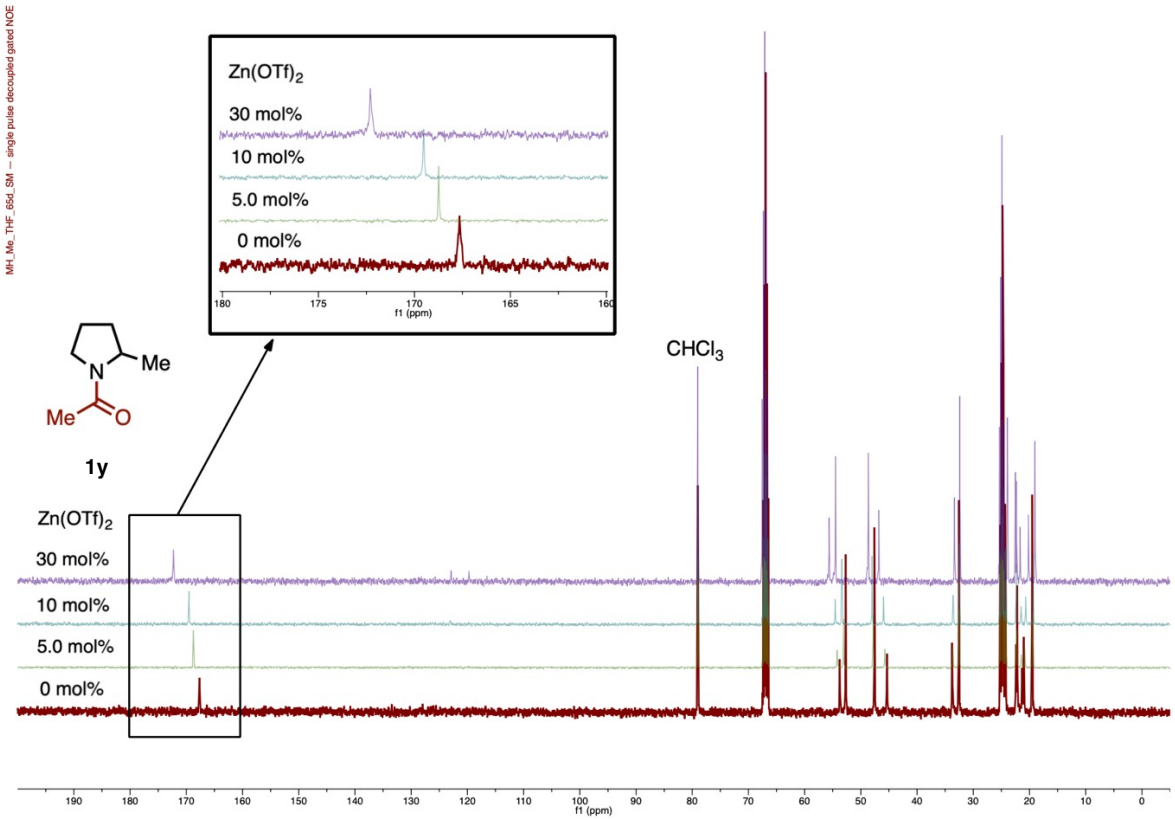


Figure S5. $^{13}C\{^{1}H\}$ NMR spectra of pyrrolidine **1y** with different equivalents of $Zn(OTf)_2$ in THF-d_8

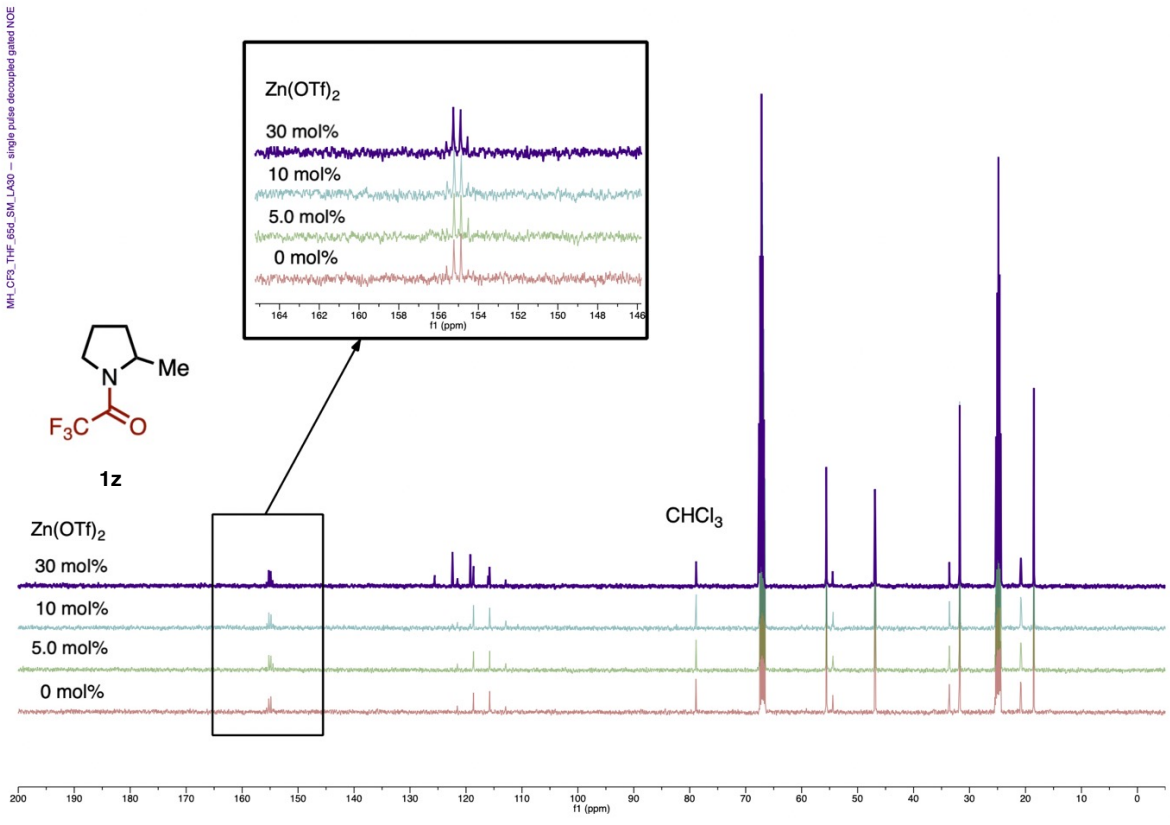


Figure S6. $^{13}C\{^{1}H\}$ NMR spectra of pyrrolidine **1z** with different equivalents of $Zn(OTf)_2$ in THF-d_8

6. References

[1] Pfund, B.; Steffen, D. M.; Schreier, M. R.; Bertrams, M.-S.; Ye, C.; Börjesson, K.; Wenger, O. S.; Kerzig, C. UV Light Generation and Challenging Photoreactions Enabled by Upconversion in Water. *J. Am. Chem. Soc*. **2020**, *142*, 10468–10476.

[2] Li, T.; Hammond, G. B.; Xu, B. Cobalt-Catalyzed Aerobic Oxidative Cleavage of Alkyl Aldehydes: Synthesis of Ketones, Esters, Amides, and α-Ketoamides. *Chem. Eur. J.* **2021**, *27*, 9737–9741.

[3] Ruffoni, A.; Juliá, F.; Svejstrup, T. D.; McMillan, A. J.; Douglas, J. J.; Leonori, D. Practical and Regioselective Amination of Arenes Using Alkyl Amines. *Nat. Chem.* **2019**, *11*, 426–433.

[4] Chen, W.; Ma, L.; Paul, A.; Seidel, D. Direct α-C–H Bond Functionalization of Unprotected Cyclic Amines. *Nat. Chem.* **2017**, *10*, 165–169.

[5] Nguyen, S. T.; Zhu, Q.; Knowles, R. R. PCET-Enabled Olefin Hydroamidation Reactions with *N*-Alkyl Amides. *ACS Catal*. **2019**, *9*, 4502–4507.

[6] Xu, Z.; Yang, T.; Tang, N.; Ou, Y.; Yin, S.-F.; Kambe, N.; Qiu, R. UV-Light-Induced *N*-Acylation of Amines with α-Diketones. *Org. Lett.* **2021**, *23*, 5329–5333.

[7] Ghosh, S. C.; Ngiam, J. S. Y.; Seayad, A. M.; Tuan, D. T.; Johannes, C. W.; Chen, A. Tandem Oxidative Amidation of Benzyl Alcohols with Amine Hydrochloride Salts Catalysed by Iron Nitrate. *Tetrahedron Lett.* **2013**, *54*, 4922–4925.

[8] Das, S.; Li, Y.; Bornschein, C.; Pisiewicz, S.; Kiersch, K.; Michalik, D.; Gallou, F.; Junge, K.; Beller, M. Selective Rhodium-Catalyzed Reduction of Tertiary Amides in Amino Acid Esters and Peptides. *Angew. Chem., Int. Ed.* **2015**, *54*, 12389–12393.

[9] Hu, X.; Zhang, G.; Bu, F.; Nie, L.; Lei, A. Electrochemical-Oxidation-Induced Site-Selective Intramolecular C(sp^3)–H Amination. *ACS Catal.* **2018**, *8*, 9370–9375.

[10] Xu, Y.; Liu, D.; Zhou, Y.; Zhang, W. Rhodium-Catalyzed Asymmetric Hydrogenation of 3-Benzoylaminocoumarins for the Synthesis of Chiral 3-Amino Dihydrocoumarins. *Angew. Chem., Int. Ed.* **2021**, *60*, 23602–23607.

[11] Onomura, O.; Izumi, Y.; Yamamoto, H. Method for Producing Optically Active Amino Acid Ester Derivative, and Optically Active Amino Acetal Derivative. JP2009227594A 2008, March, 21.

[12] Minato, D.; Arimoto, H.; Nagasue, Y.; Demizu, Y.; Onomura, O. Asymmetric Electrochemical Oxidation of 1,2-Diols, Aminoalcohols, and Aminoaldehydes in the Presence of Chiral Copper Catalyst. *Tetrahedron* **2008**, *64*, 6675–6683.

[13] Ghinato, S.; Meazzo, C.; De Nardi, F.; Maranzana, A.; Blangetti, M.; Prandi, C. One-Pot, Telescoped Alkenylation of Amides via Stable Tetrahedral Intermediates as Lithium Enolate Precursors. *Org. Lett.* **2023**, *25*, 3904–3909.

[14] Giannerini, M.; Vila, C.; Hornillos, V.; Feringa, B. L. One-Pot Sequential 1,2-Addition, Pd-Catalysed Cross-Coupling of Organolithium Reagents with Weinreb Amides. *Chem. Commun.* **2016**, *52*,

1206–1209.

[15] Rathod, G. K.; Jain, R. Palladium-Catalyzed Aminocarbonylation of (Hetero)aryl Iodides with α-Amino Acid Esters as Nucleophiles. *J. Org. Chem.* **2022**, *87*, 8005–8016.

[16] Ekoue-Kovi, K.; Wolf, C. Metal-Free One-Pot Oxidative Amination of Aldehydes to Amides. *Org. Lett.* **2007**, *9*, 3429–3432.

[17] Nacsa, E. D.; Lambert, T. H. Cyclopropenone Catalyzed Substitution of Alcohols with Mesylate Ion. *Org. Lett*. **2012**, *15*, 38–41.

[18] Kuroda, Y.; Park, K.; Shimazaki, Y.; Zhong, R.-L.; Sakaki, S.; Nakao, Y. An Iridium/Aluminum Cooperative Strategy for the β-C(sp^3)–H Borylation of Saturated Cyclic Amines. *Angew. Chem., Int. Ed.* **2023**, *62*, e202300704.

[19] Zhao, D.; Kuethe, J. T.; Journet, M.; Peng, Z.; Humphrey, G. R. Efficient and Practical Synthesis of (*R*)-2-Methylpyrrolidine. *J. Org. Chem.* **2006**, *71*, 4336–4338.

[20] Pichette, S.; Aubert-Nicol, S.; Lessard, J.; Spino, C. Photochemical and Thermal Ring-Contraction of Cyclic Hydroxamic Acid Derivatives. *J. Org. Chem.* **2012**, *77*, 11216–11226.

[21] O'Brien, M.; Hall, A.; Schrauwen, J.; van der Made, J. An Open-Source Approach to Automation in Organic Synthesis: The Flow Chemical Formation of Benzamides Using an Inline Liquid-Liquid Extraction System and a Homemade 3-Axis Autosampling/Product-Collection Device. *Tetrahedron* **2018**, *74*, 3152–3157.

[22] Häring, A. P.; Biallas, P.; Kirsch, S. F. An Unconventional Reaction of 2,2-Diazido Acylacetates with Amines. *Eur. J. Org. Chem.* **2017**, *2017*, 1526–1539.

[23] Johnson, D. A.; Gribble, G. W. Synthetic Studies towards *N*-Substituted 3-Vinyl-4-piperidineacetic Acid Derivatives. *Arkivoc* **2019**, *5*, 178–195.

[24] Zheng, Y.; Zhao, Y.; Tao, S.; Li, X.; Cheng, X.; Jiang, G.; Wan, X. Green Esterification of Carboxylic Acids Promoted by *tert*-Butyl Nitrite. *Eur. J. Org. Chem.* **2021**, *2021*, 2713–2718.

[25] Jung, M.; Brosch, G.; Kölle, D.; Scherf, H.; Herhäuser, C.; Loidl, P. Amide Analogues of Trichostatin A as Inhibitors of Histone Deacetylase and Inducers of Terminal Cell Differentiation. *J. Med. Chem.* **1999**, *42*, 4669–4679.

[26] Pilo, M.; Porcheddu, A.; De Luca, L. A Copper-Catalysed Amidation of Aldehydes via *N*-Hydroxysuccinimide Ester Formation. *Org. Biomol. Chem.* **2013**, *11*, 8241–8246.

[27] Mohanty, A.; Sadhukhan, S.; Nayak, M. K.; Roy, S. Aminocarbonylation Reaction Using a Pd–Sn Heterobimetallic Catalyst: Three-Component Coupling for Direct Access of the Amide Functionality. *J. Org. Chem.* **2024**, *89*, 1010–1017.

[28] Thurow, S.; Lenardão, E. J.; Just-Baringo, X.; Procter, D. J. Reduction of Selenoamides to Amines Using SmI_2–H_2O. *Org. Lett.* **2017**, *19*, 50–53.

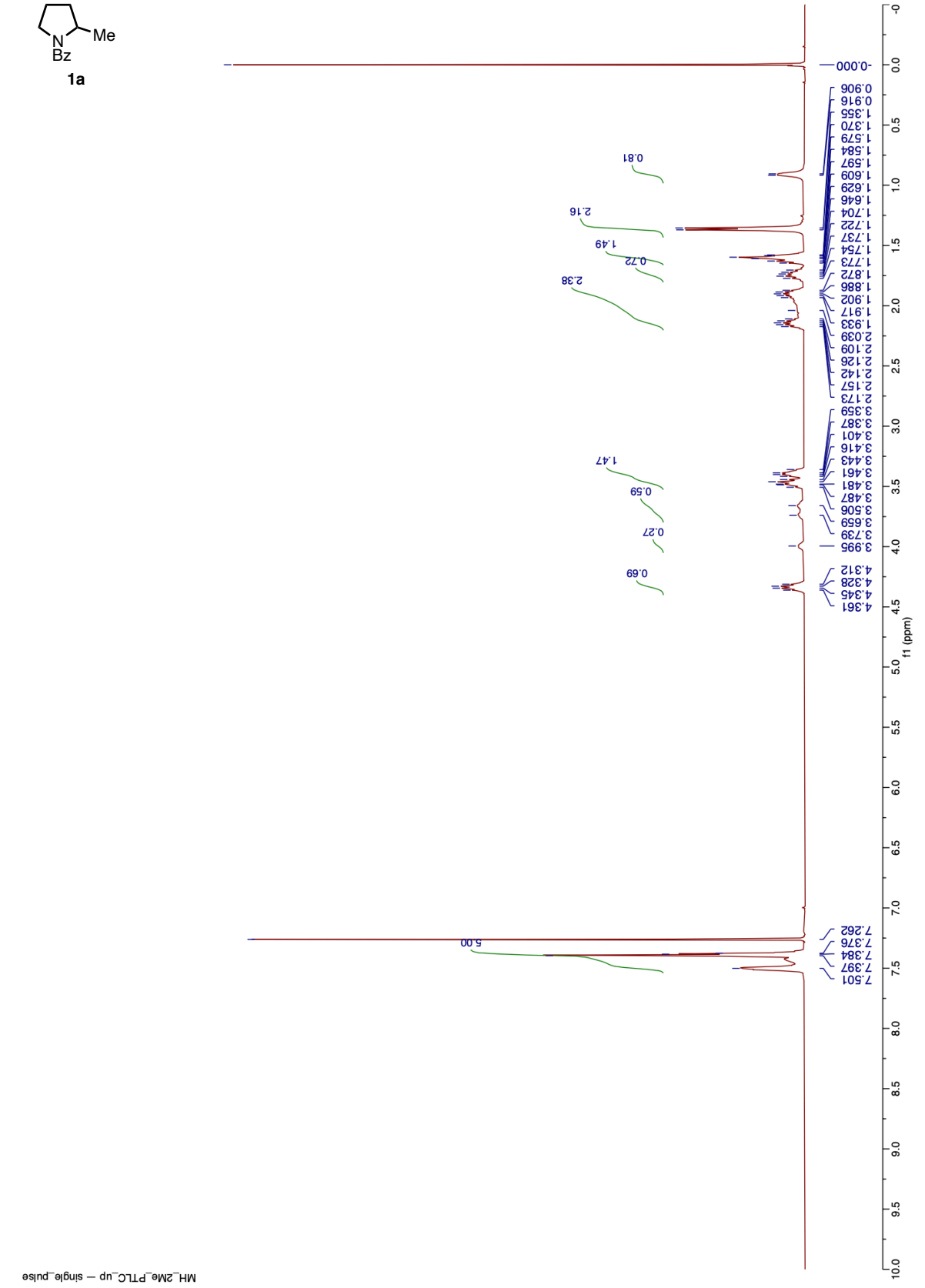
[29] Halima, T. B.; Masson-Makdissi, J.; Newman, S. G. Nickel-Catalyzed Amide Bond Formation from

Methyl Esters. *Angew. Chem., Int. Ed.* **2018**, *57*, 12925–12929.

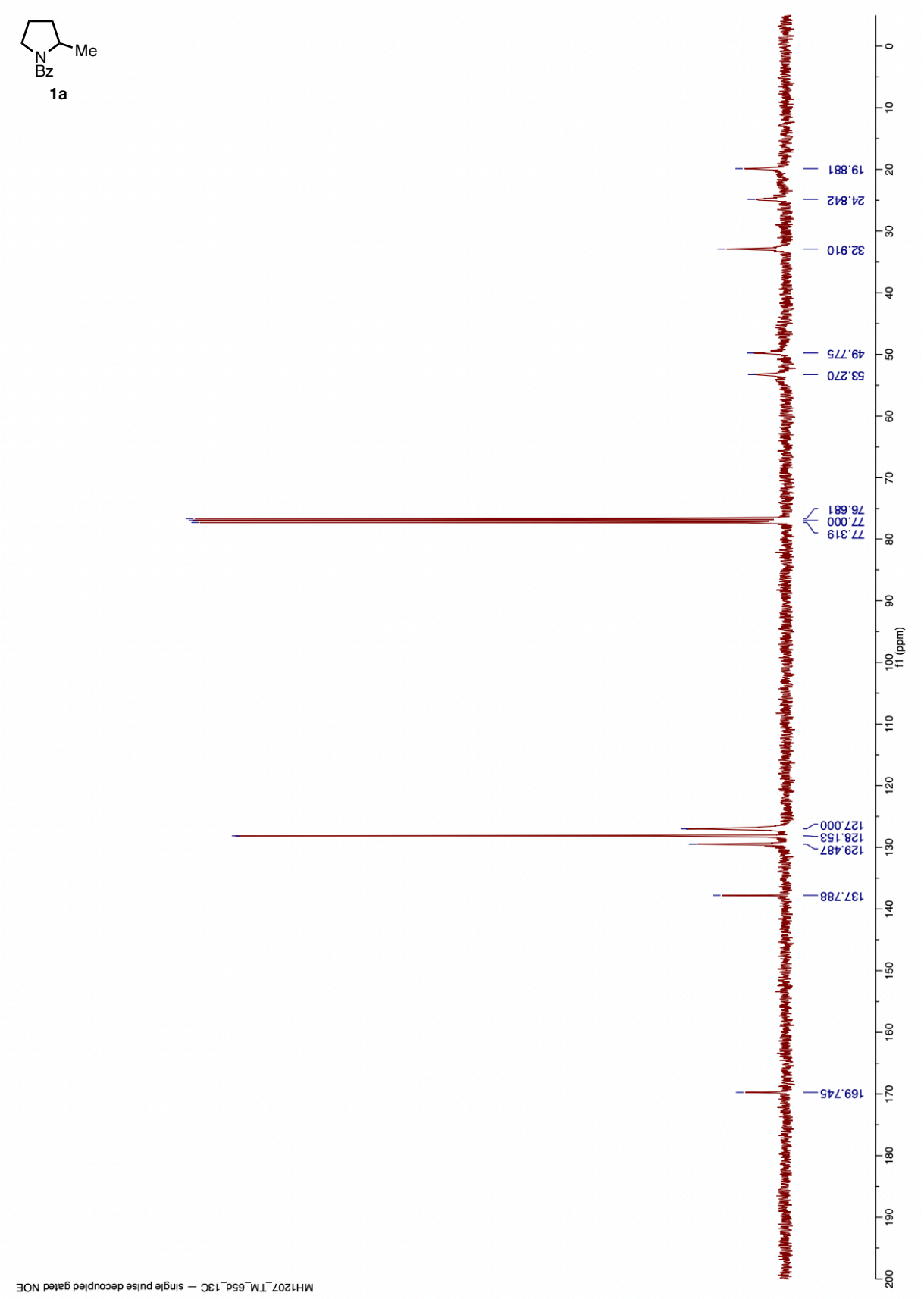
[30] Yu, C.-J.; Li, R.; Gu, P. Intermolecular Schmidt Reaction of Alkyl Azides with Acyl Silanes. *Tetrahedron Lett.* **2016**, *57*, 3568–3570.

7. NMR Spectral Data

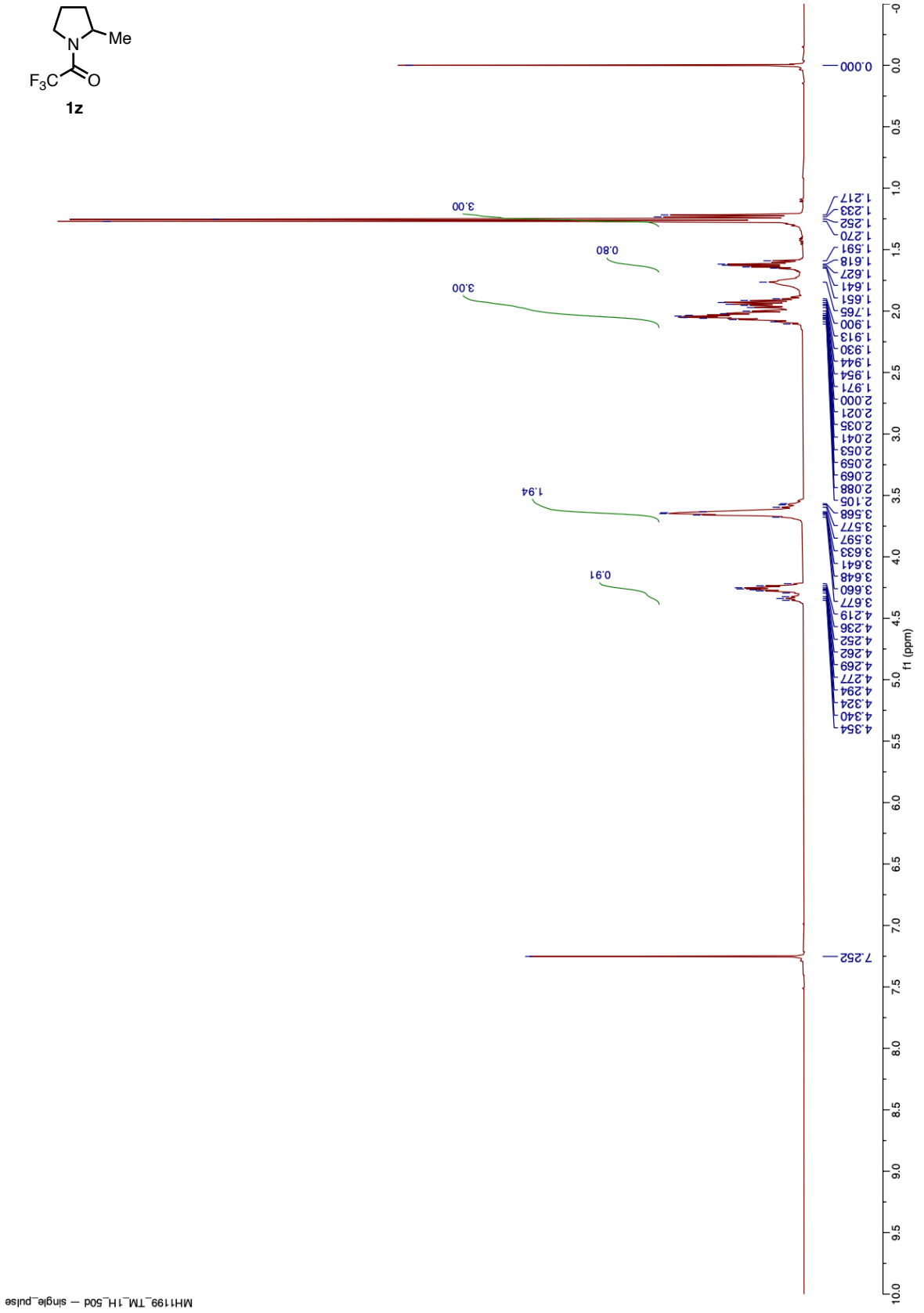
^{1}H NMR of 1a (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 1a (101 MHz, $CDCl_3$, 323 K)



^{1}H NMR of 1z (400 MHz, $CDCl_3$, 323 K)



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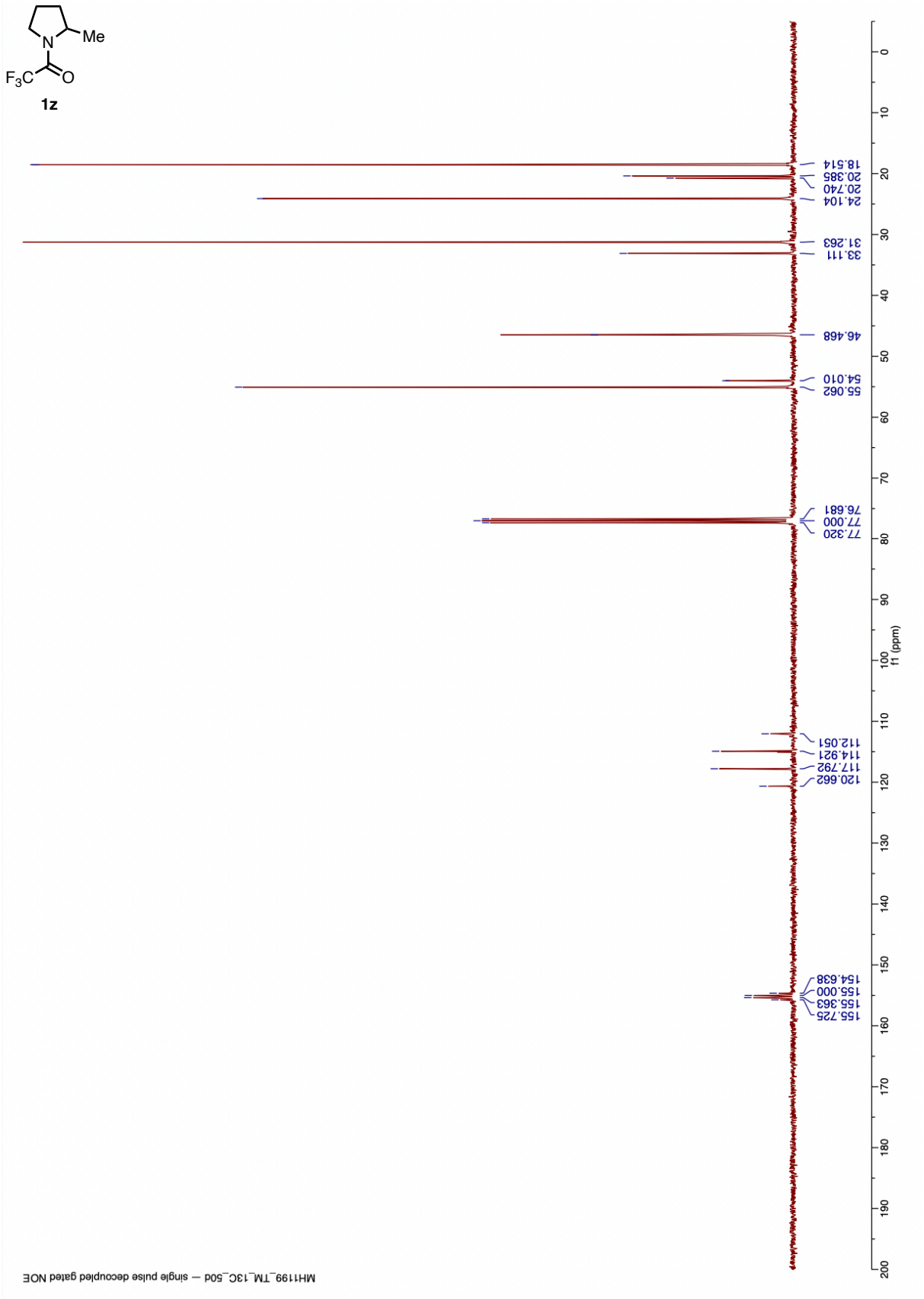
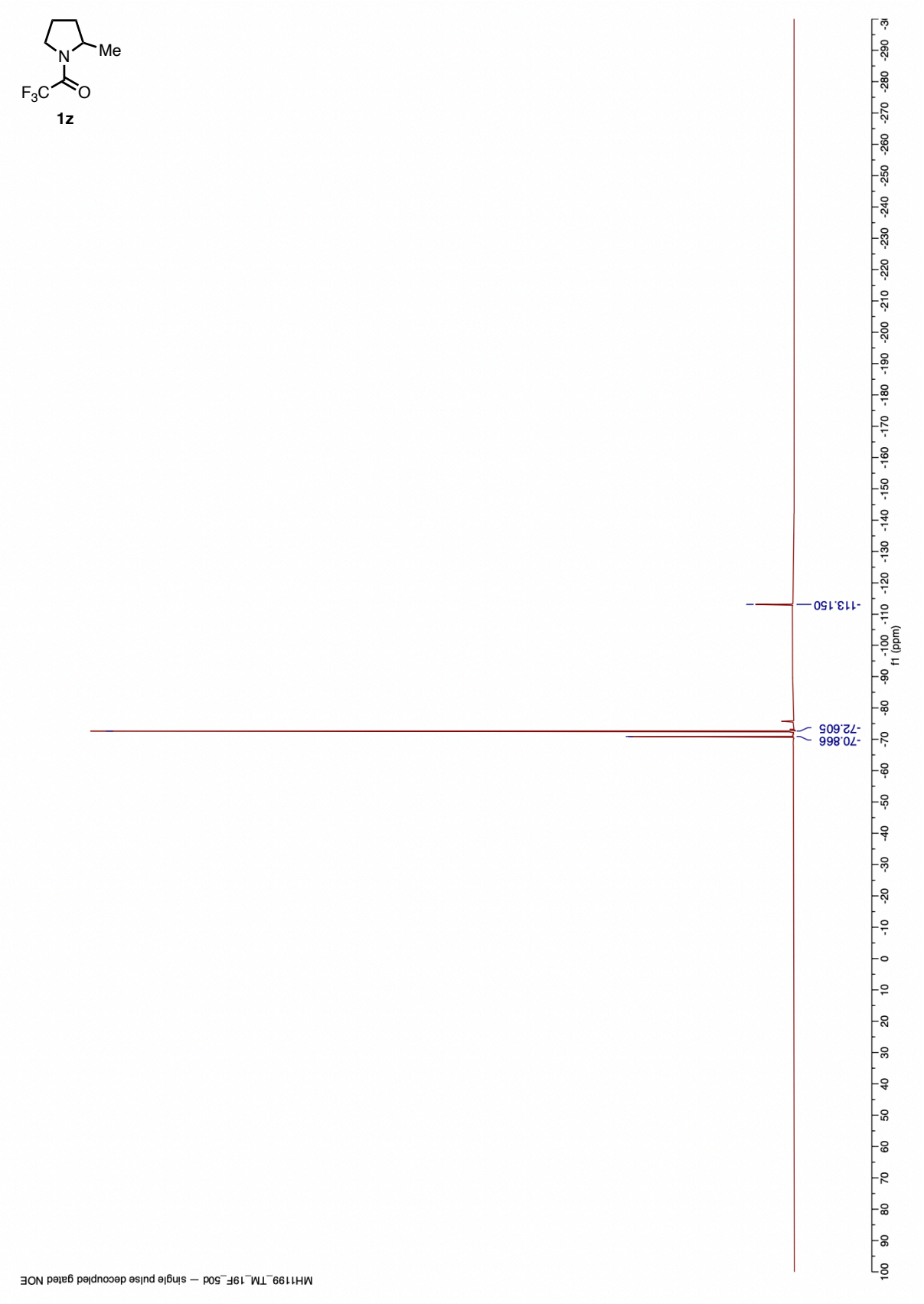
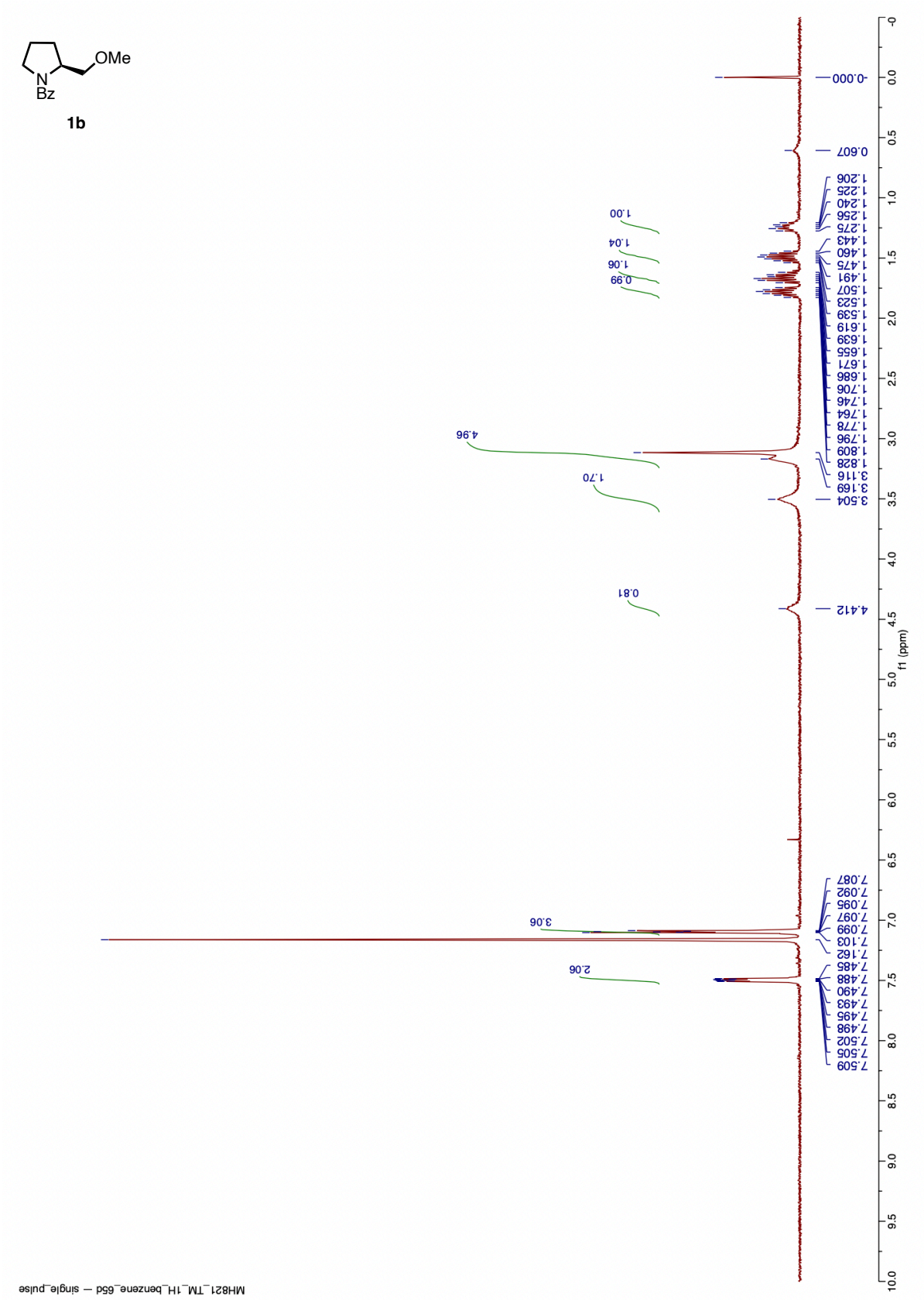


^{19}F NMR of 1t (376 MHz, $CDCl_3$, 323 K)



^{1}H NMR of 1b (400 MHz, C_6D_6, 338 K)



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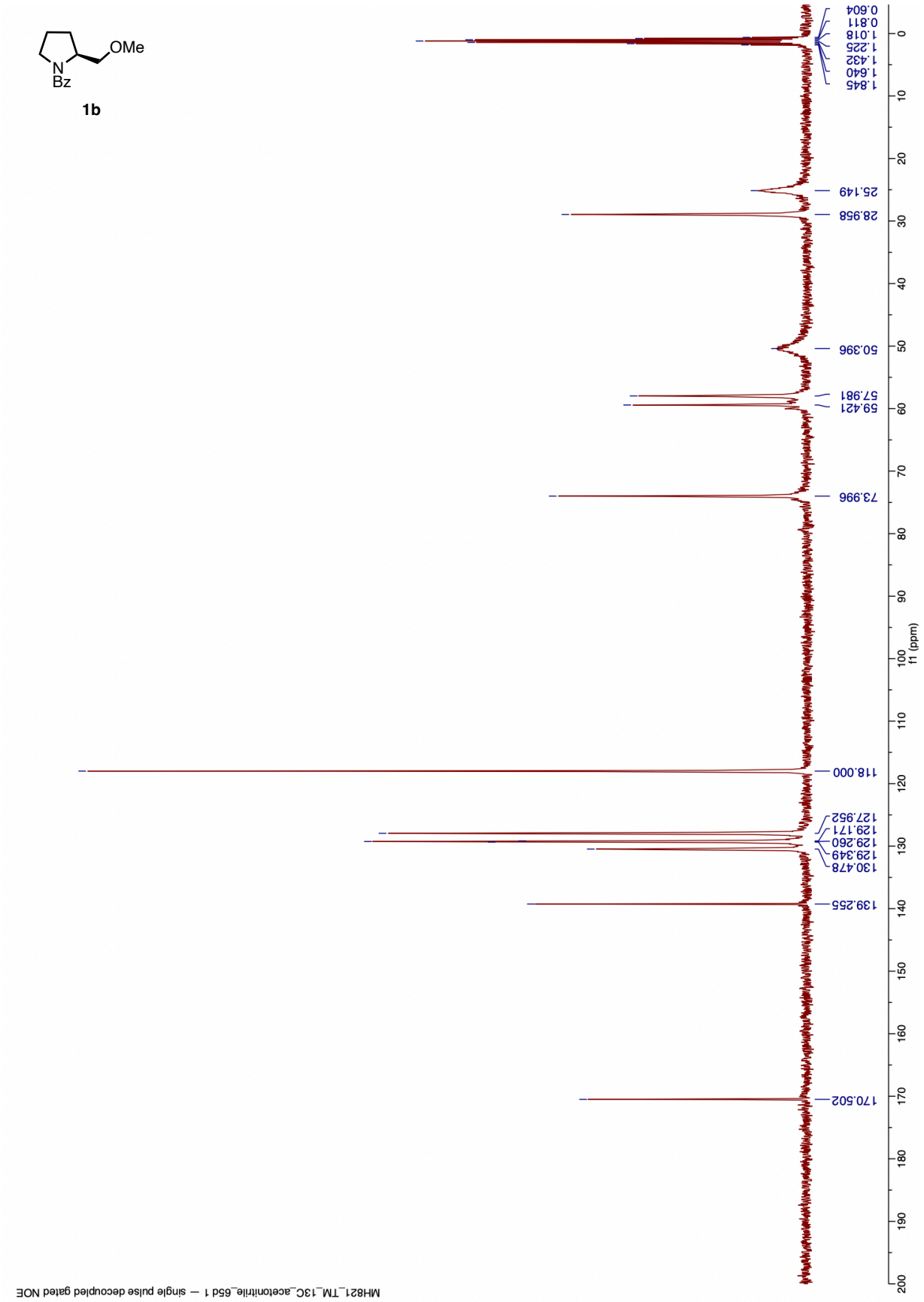
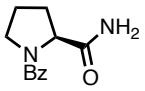


^{1}H NMR of 1j (400 MHz, $CDCl_3$, 323 K)



1j

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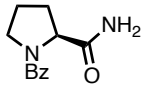

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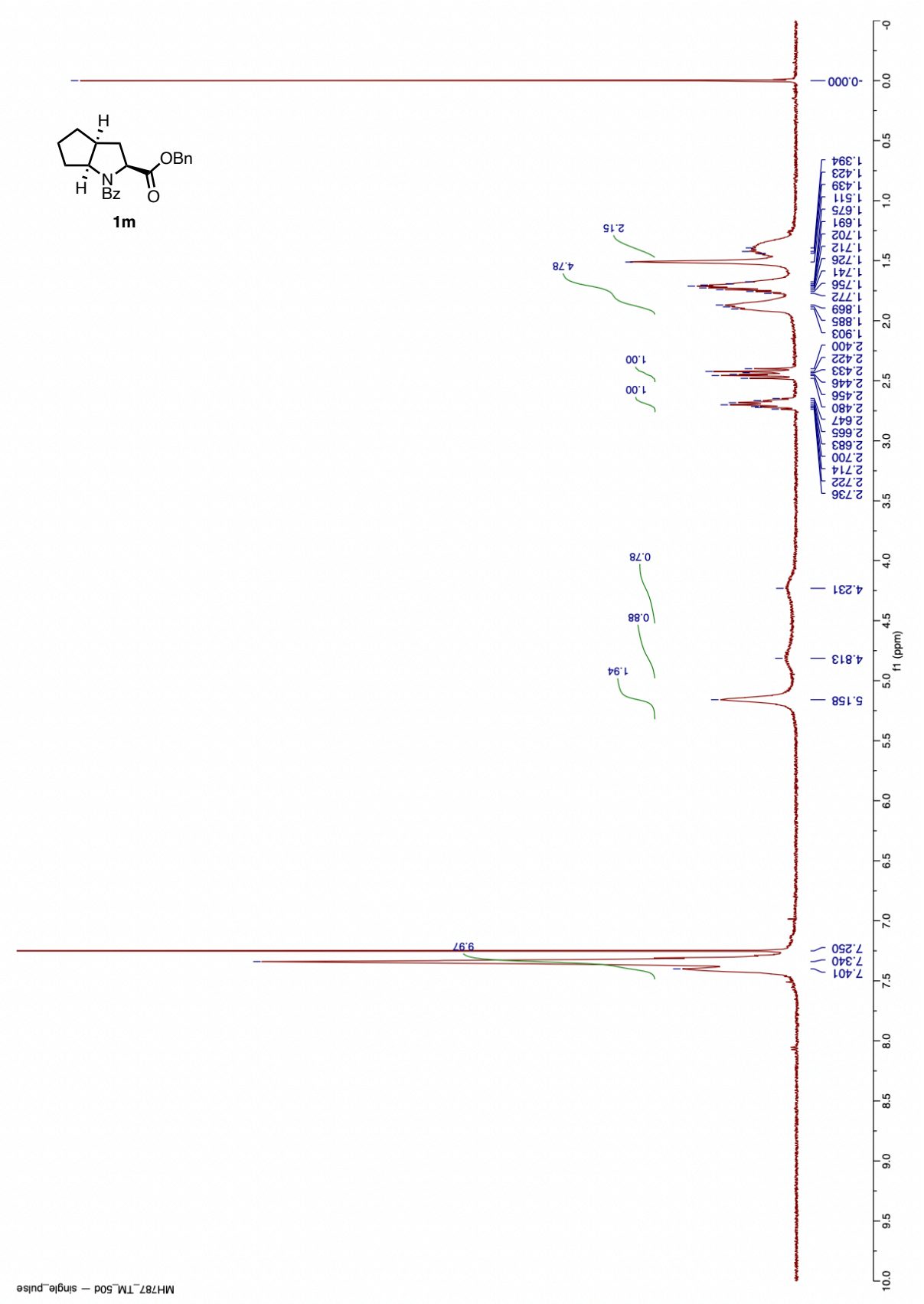
^{1}H NMR of 1m (400 MHz, $CDCl_3$, 323 K)



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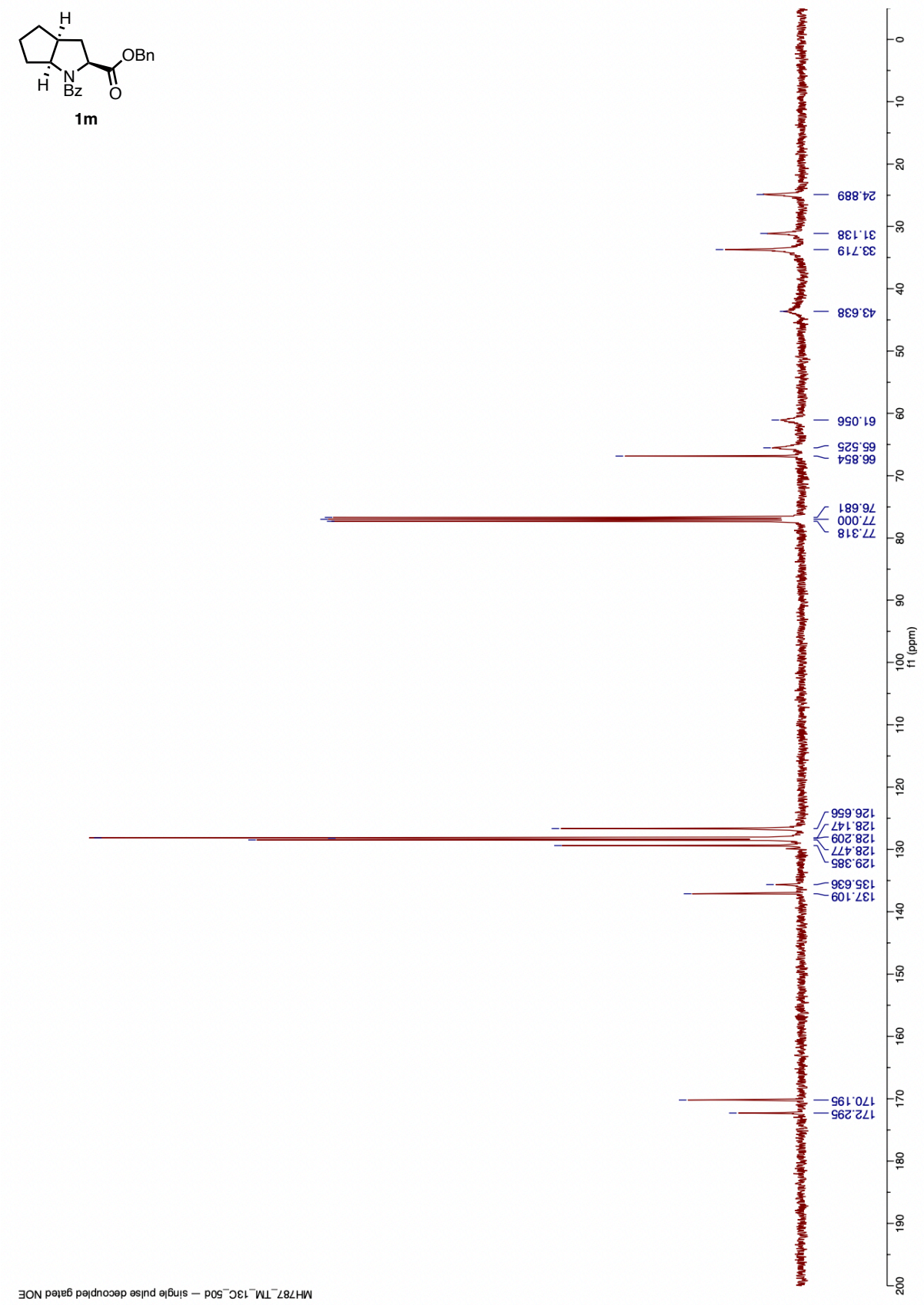
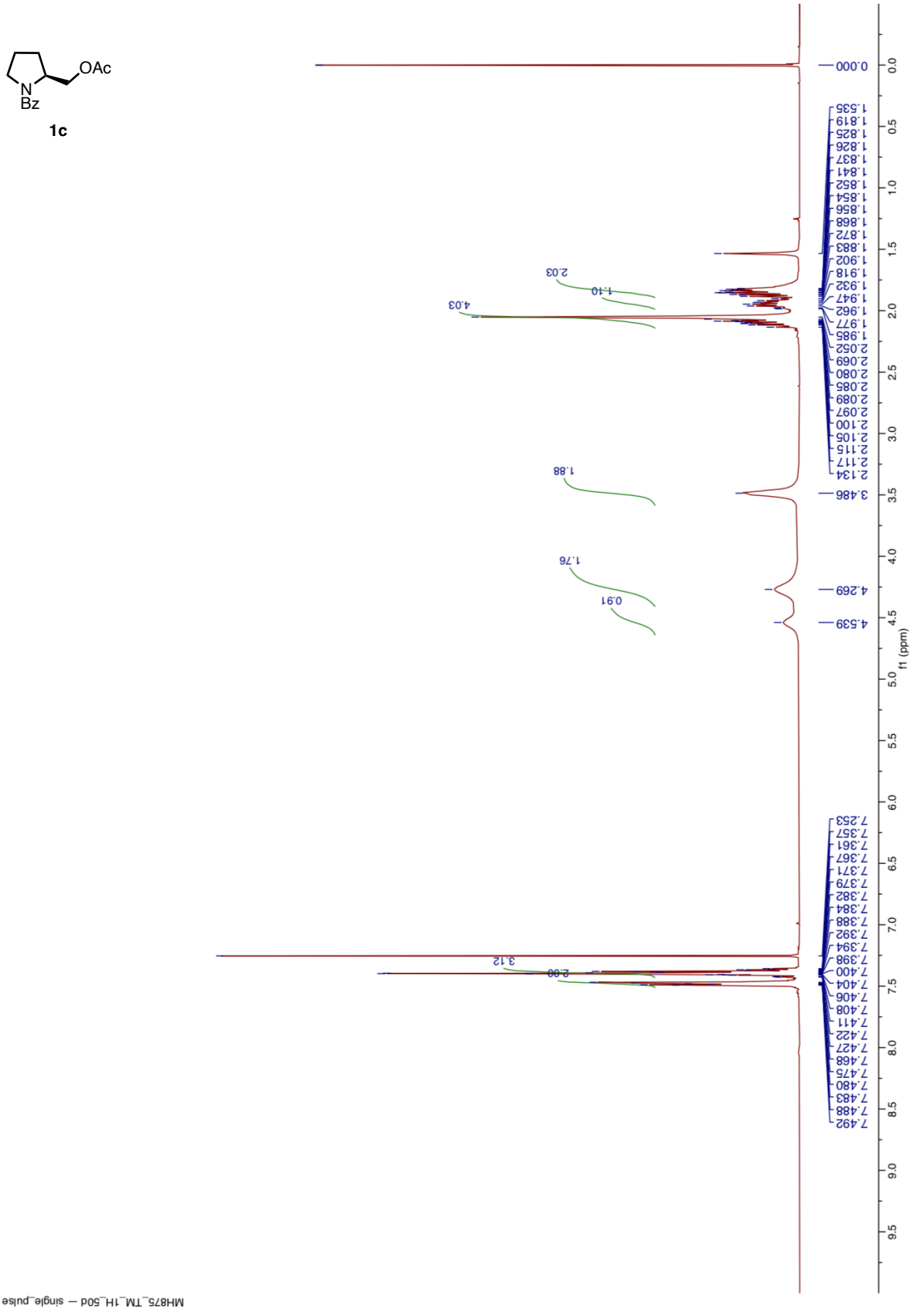
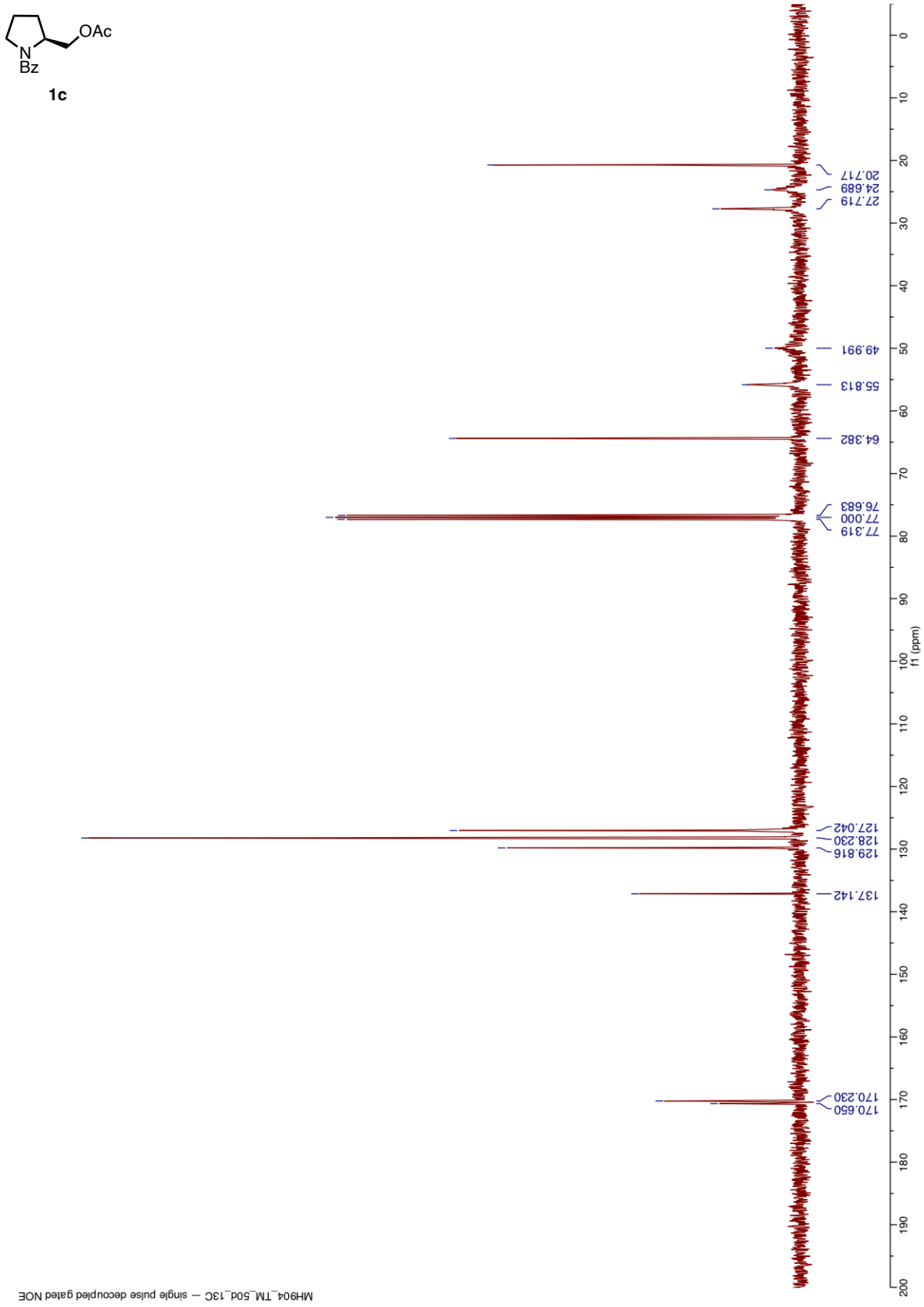


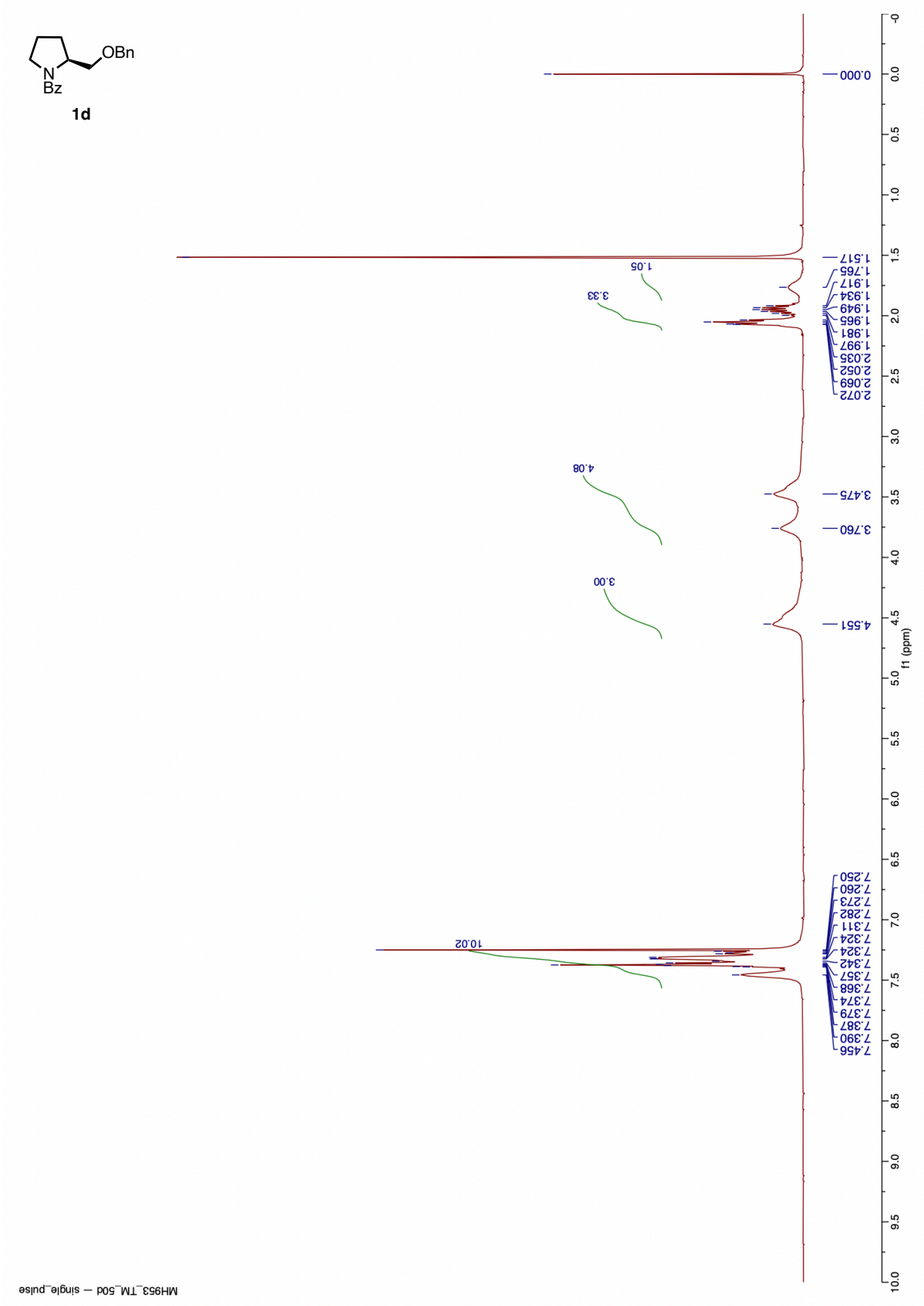
^{1}H NMR of 1c (400 MHz, $CDCl_3$, 323 K)



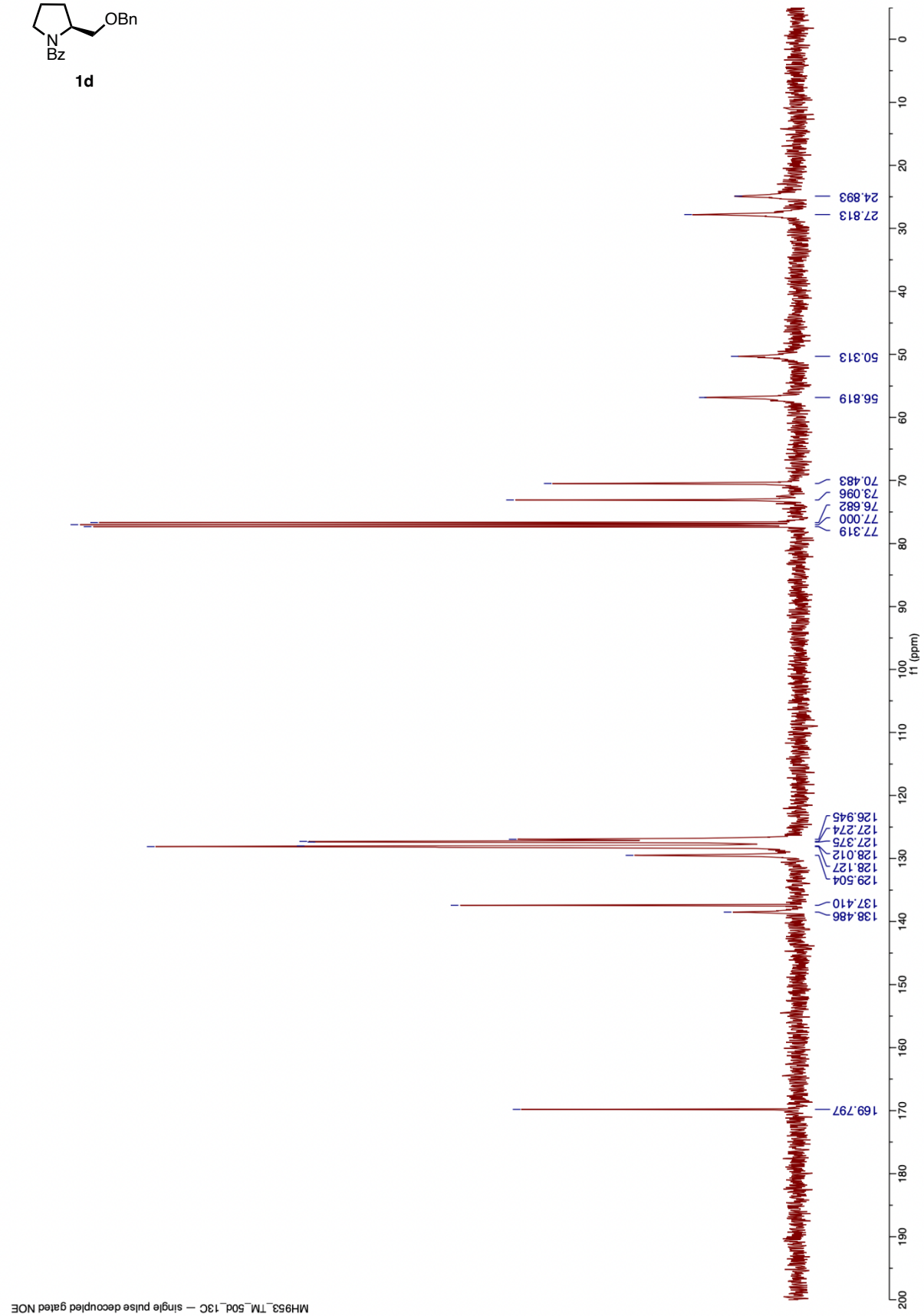
$^{13}C\{^{1}H\}$ NMR of 1c (101 MHz, $CDCl_3$, 323 K)



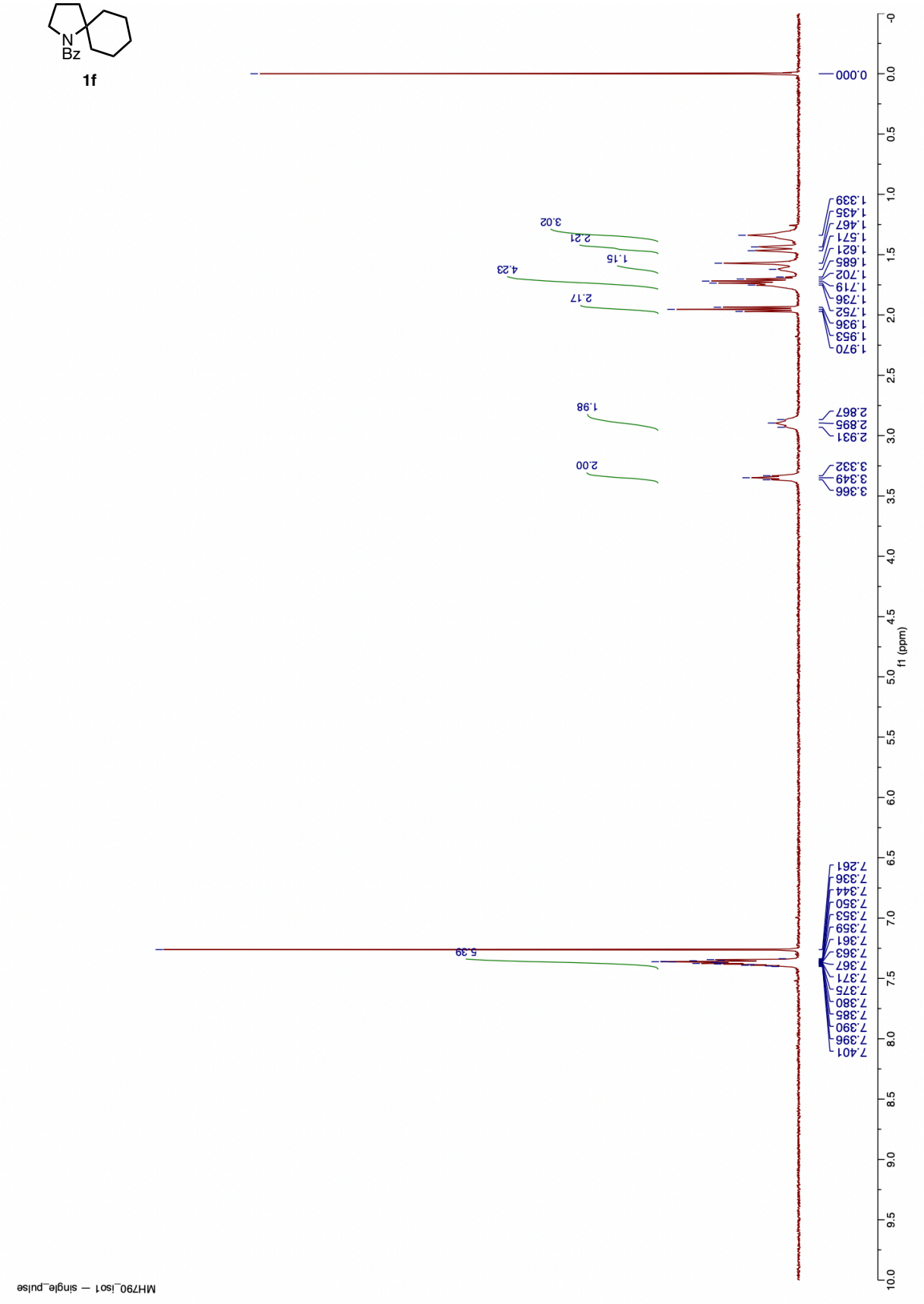
^{1}H NMR of 1d (400 MHz, $CDCl_3$, 323 K)



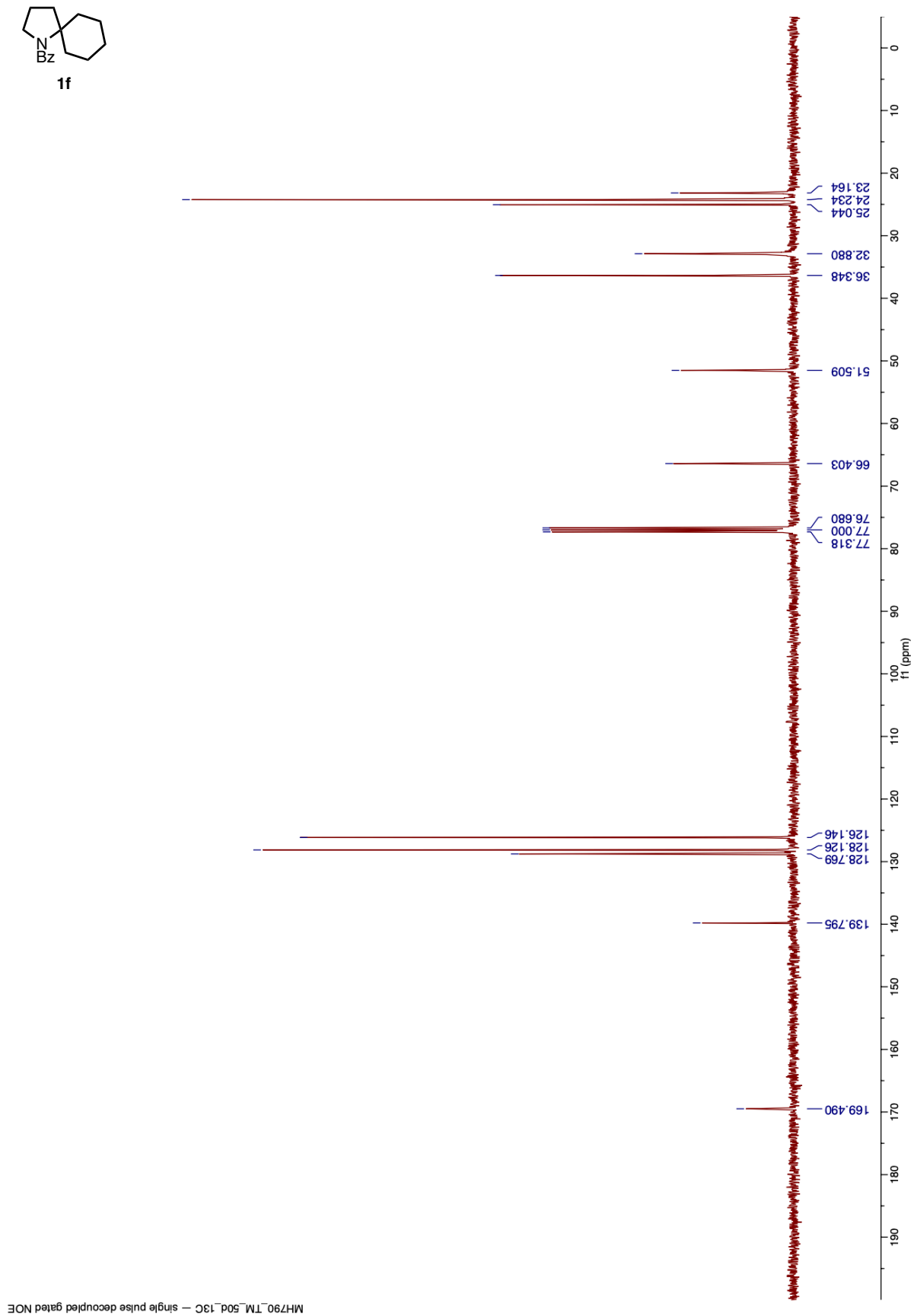
$^{13}C\{^{1}H\}$ NMR of 1d (101 MHz, $CDCl_3$, 323 K)



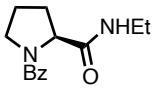
^{1}H NMR of 1f (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 1f (101 MHz, $CDCl_3$, 323 K)

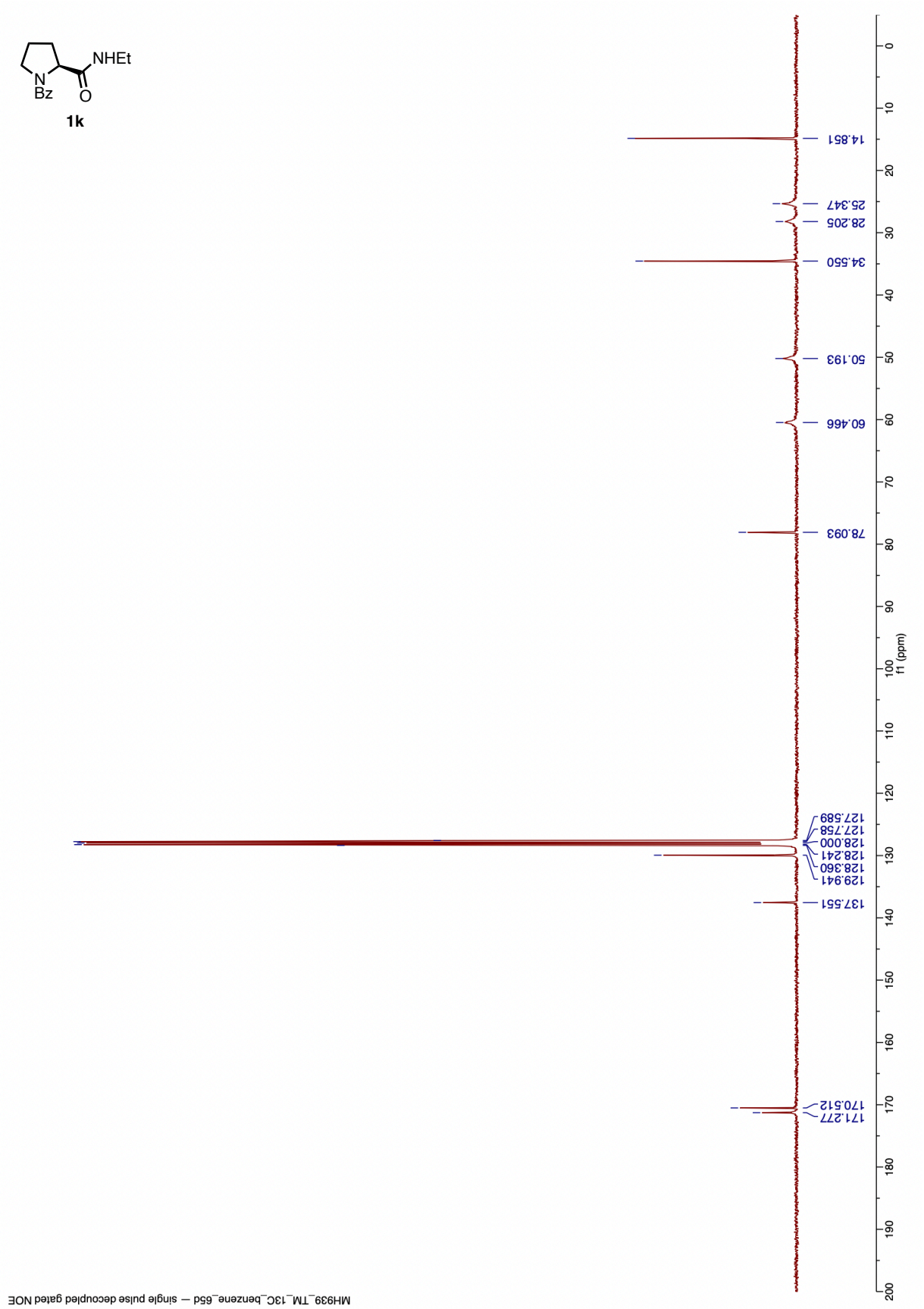


^{1}H NMR of 1k (400 MHz, C_6D_6, 338 K)

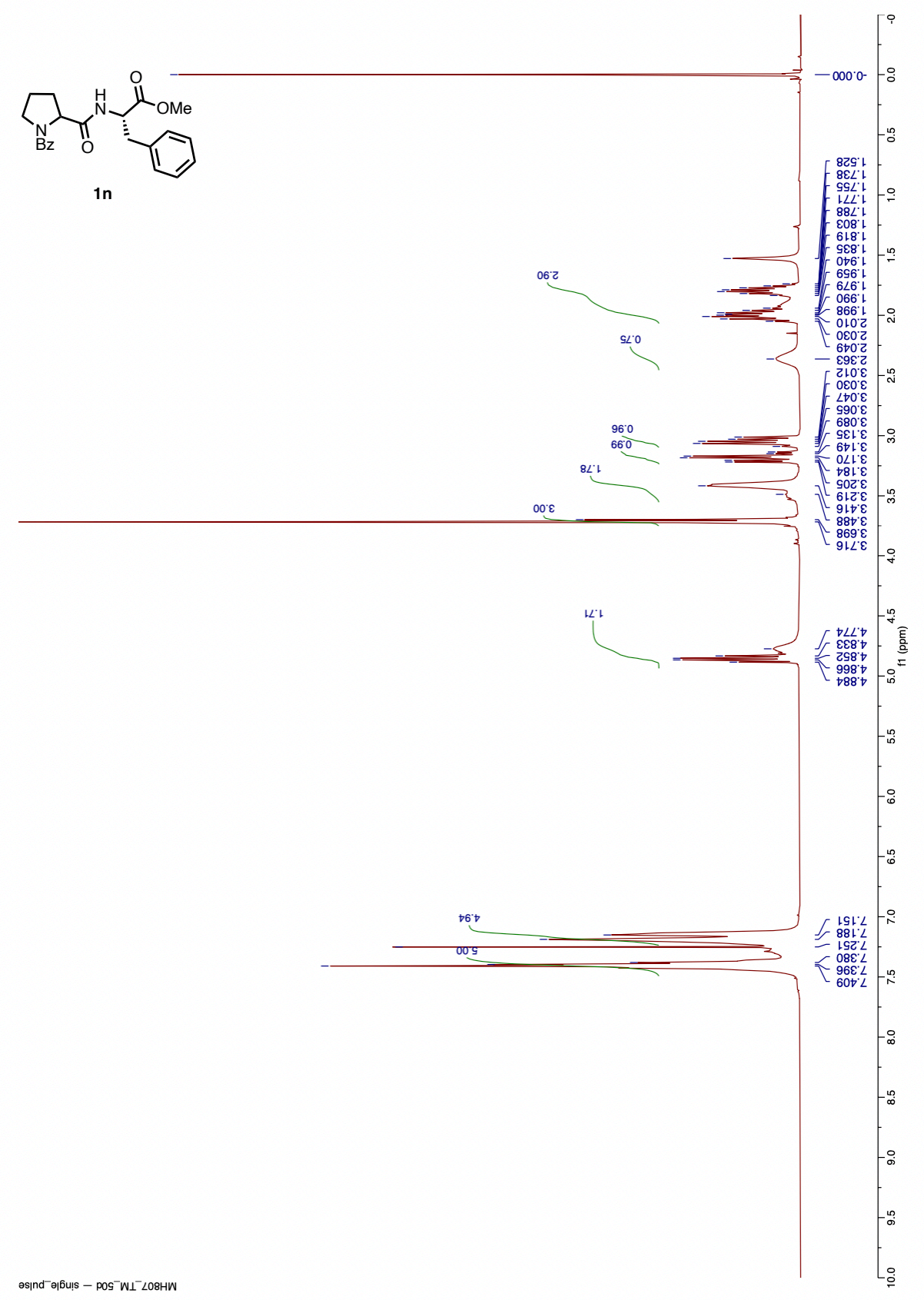


1k

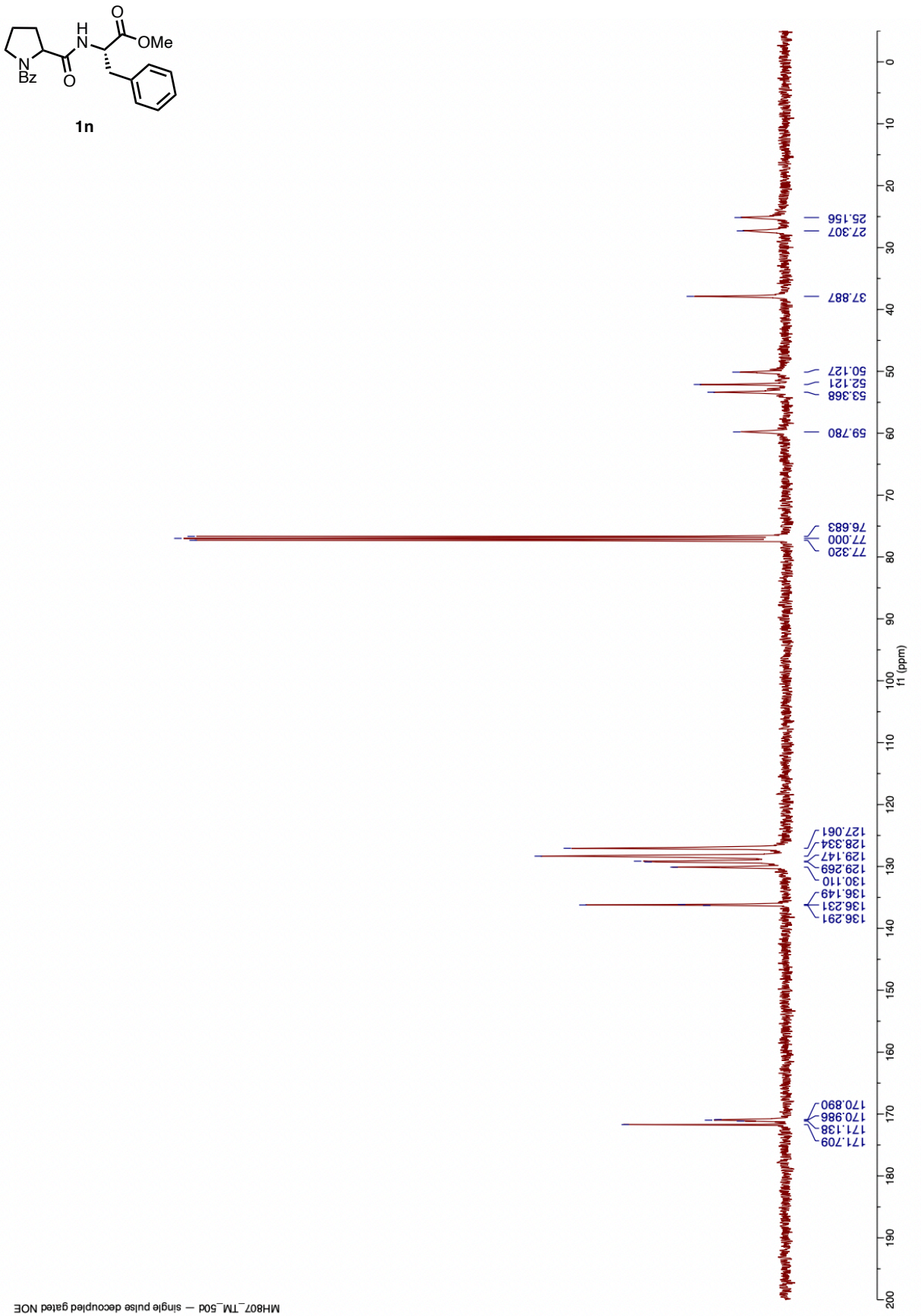
$^{13}C\{^{1}H\}$ NMR of 1k (101 MHz, C_6D_6, 338 K)



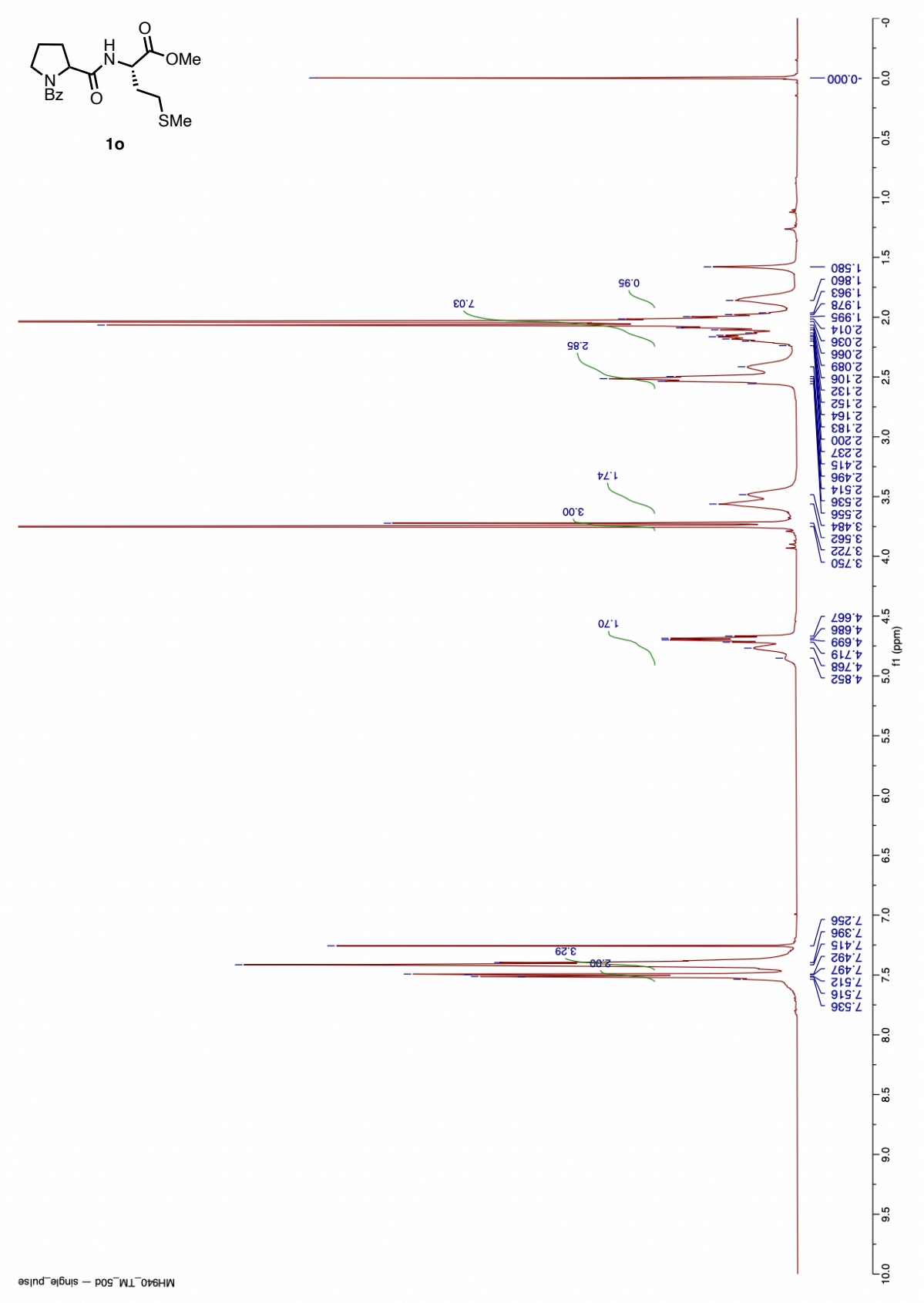
^{1}H NMR of 1n (400 MHz, $CDCl_3$, 323 K)



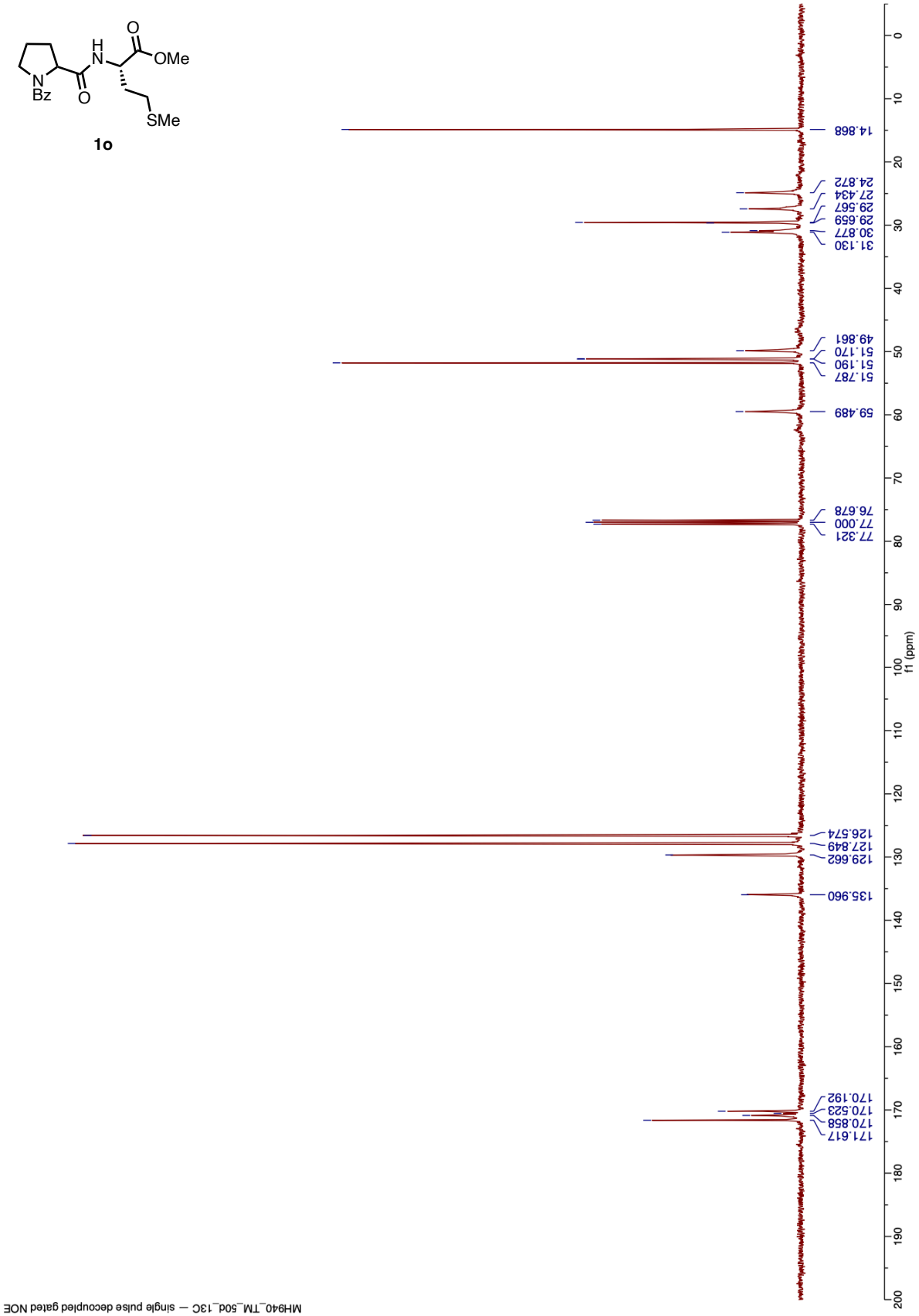
$^{13}C\{^{1}H\}$ NMR of 1n (101 MHz, $CDCl_3$, 323 K)



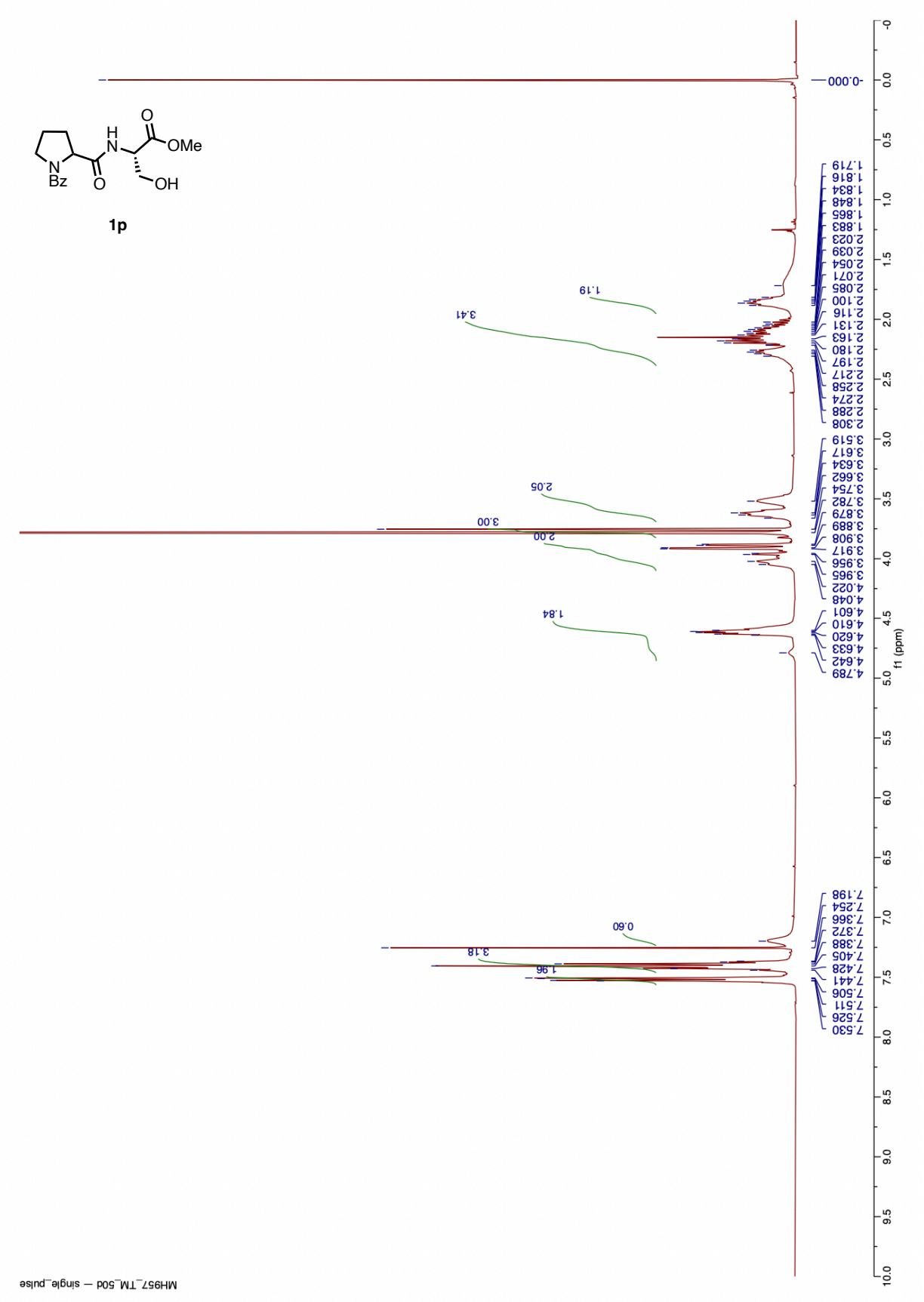
^{1}H NMR of 1o (400 MHz, $CDCl_3$, 323 K)



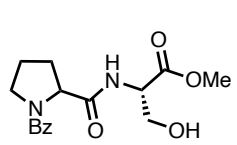
$^{13}C\{^{1}H\}$ NMR of 1o (101 MHz, $CDCl_3$, 323 K)



^{1}H NMR of 1p (400 MHz, $CDCl_3$, 323 K)

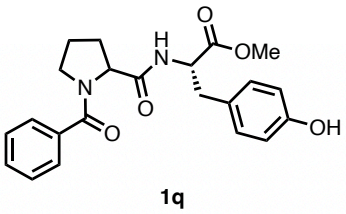


$^{13}C\{^{1}H\}$ NMR of 1p (101 MHz, CD_3OD, 328 K)



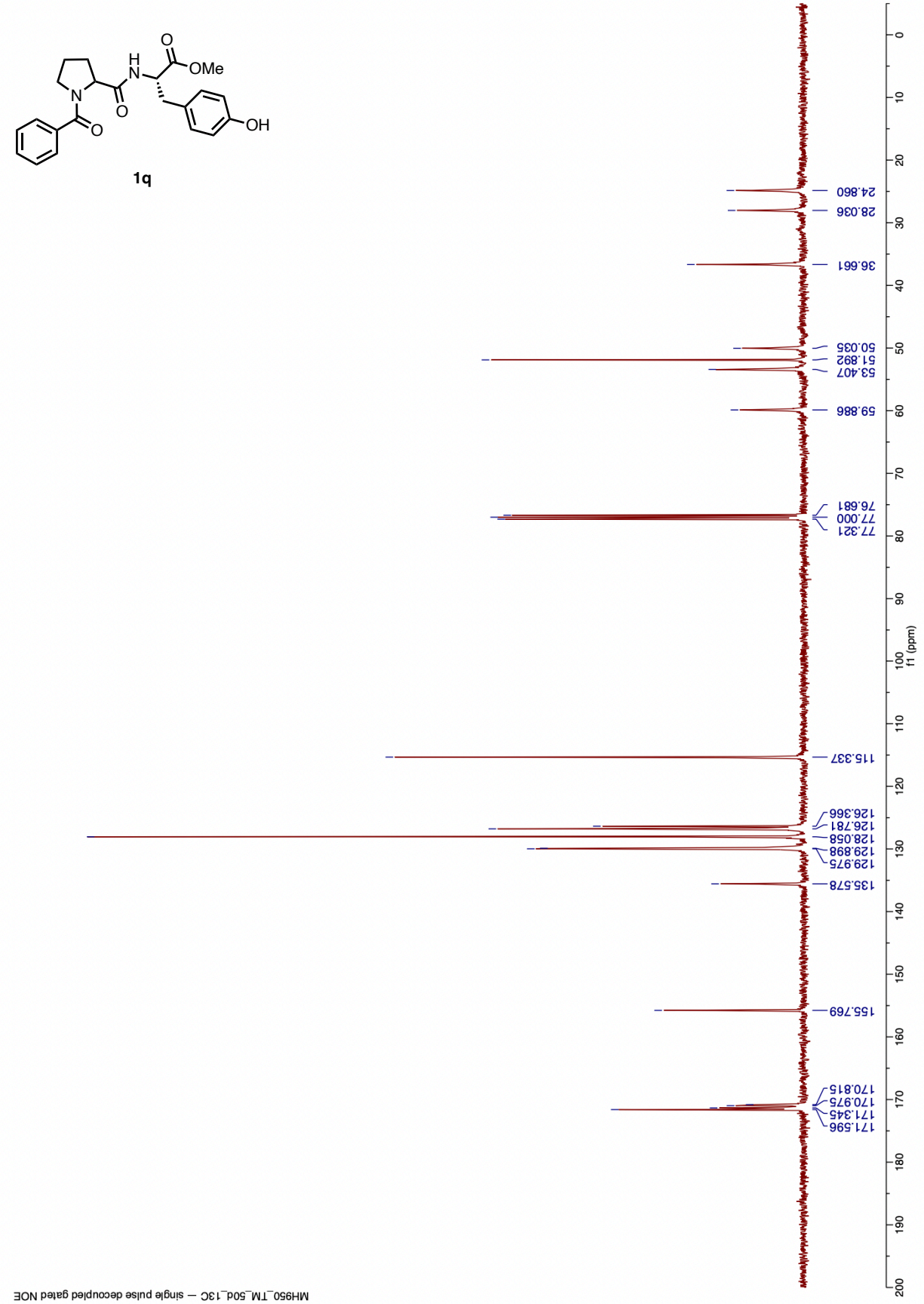
1p

^{1}H NMR of 1q (400 MHz, $CDCl_3$, 323 K)

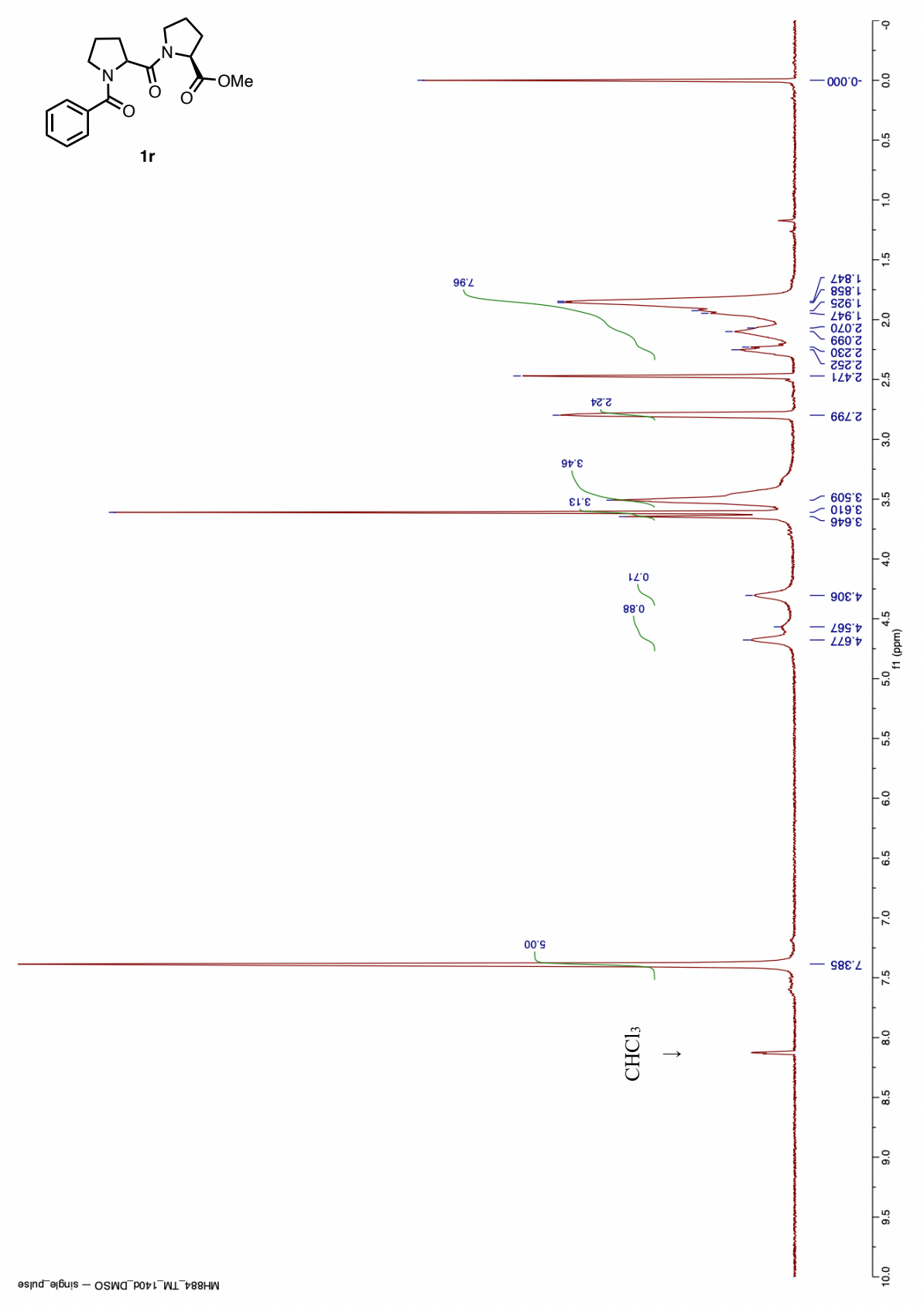


1q

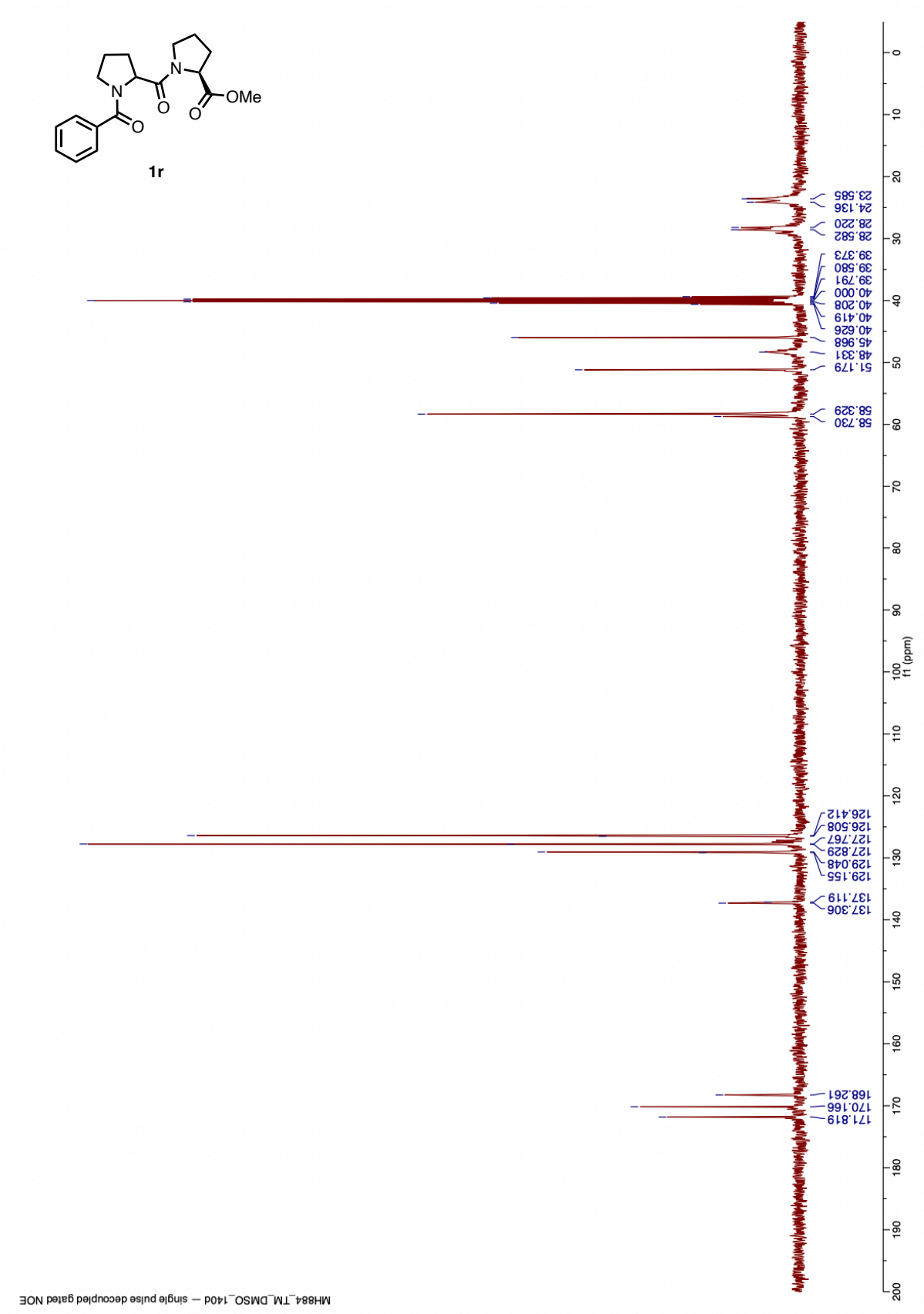
$^{13}C\{^{1}H\}$ NMR of 1q (101 MHz, $CDCl_3$, 323 K)



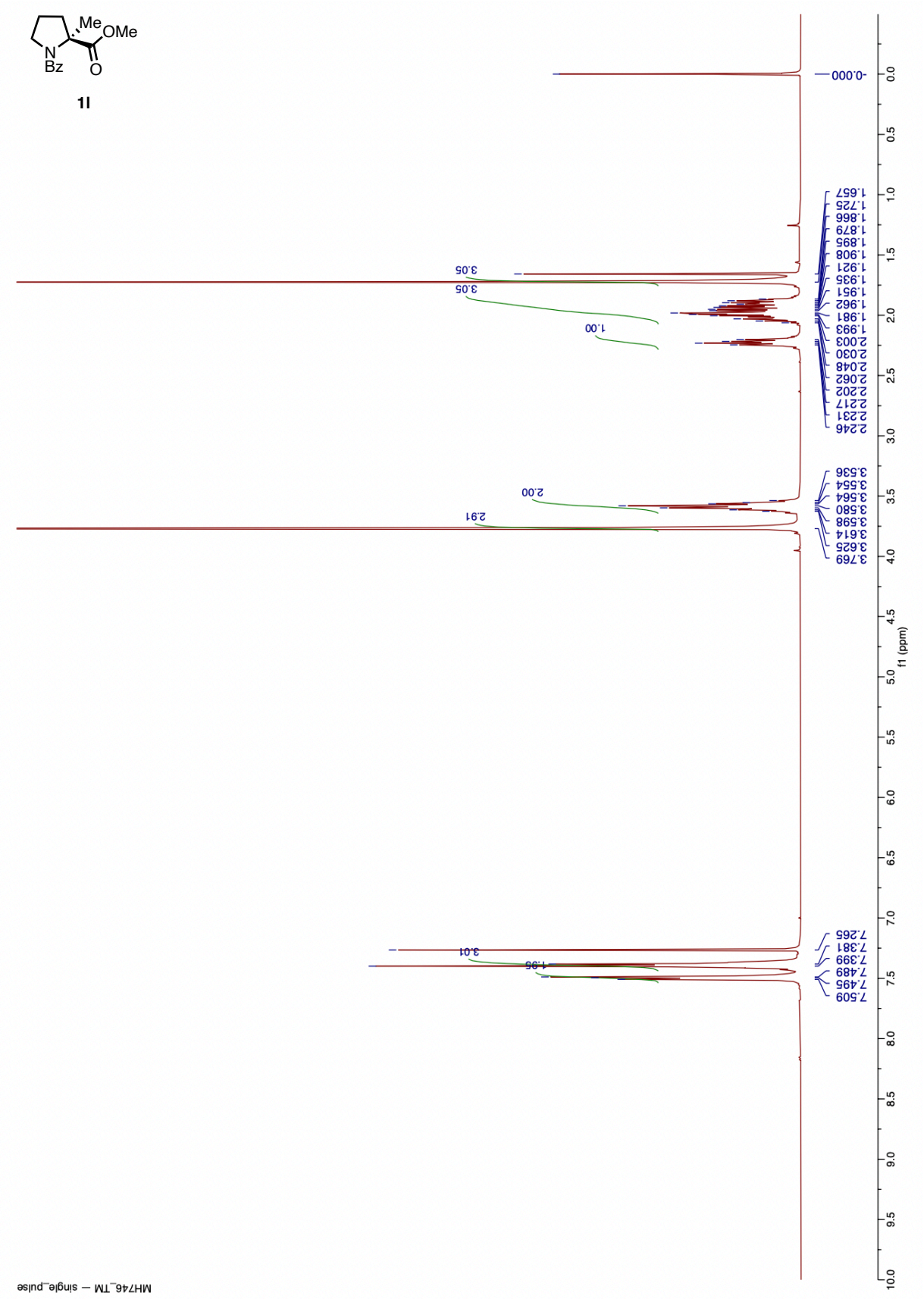
^{1}H NMR of 1r (400 MHz, $(CD_3)_2SO$, 413 K)



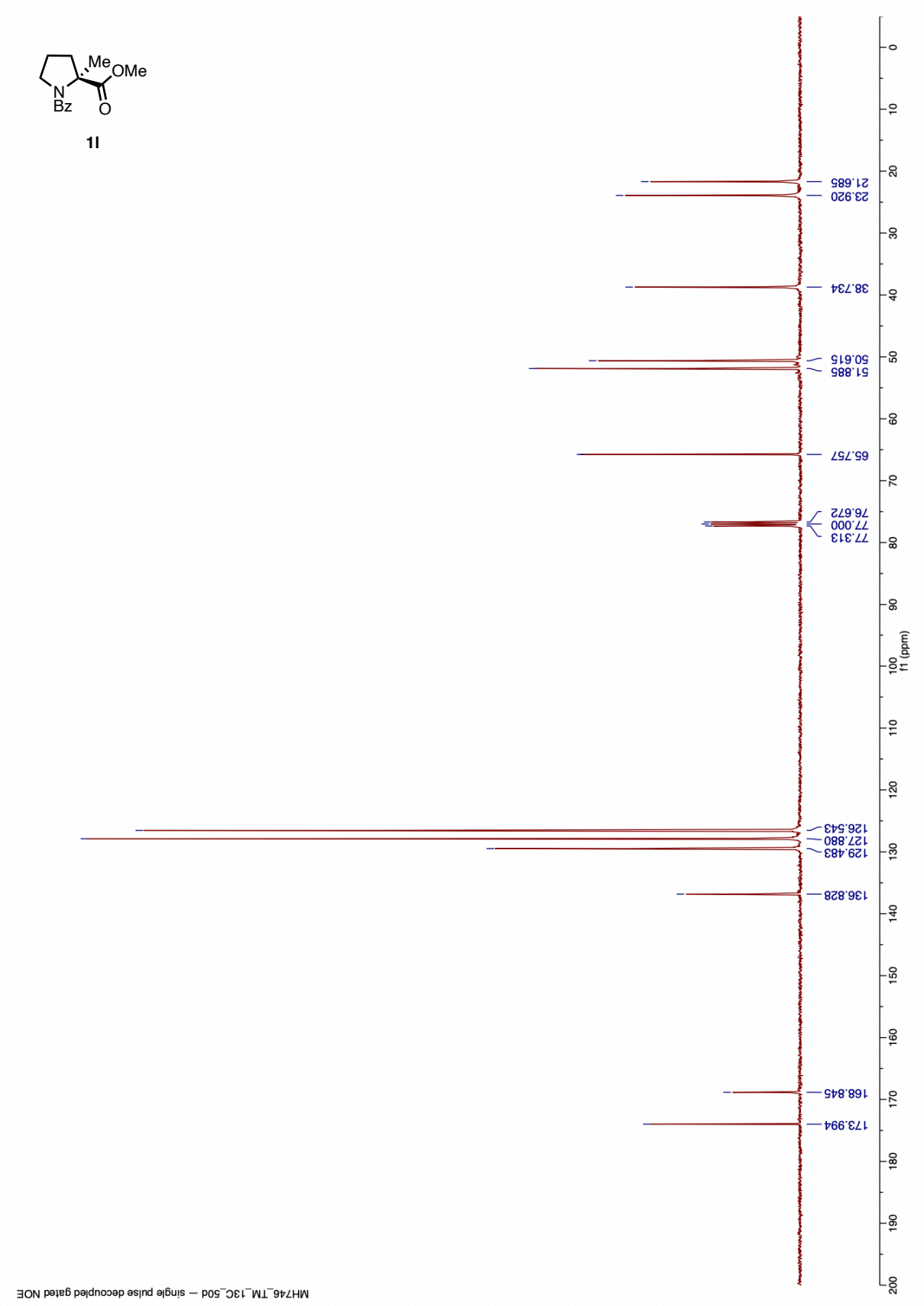
$^{13}C\{^{1}H\}$ NMR of 1r (101 MHz, $(CD_3)_2SO$, 413 K)



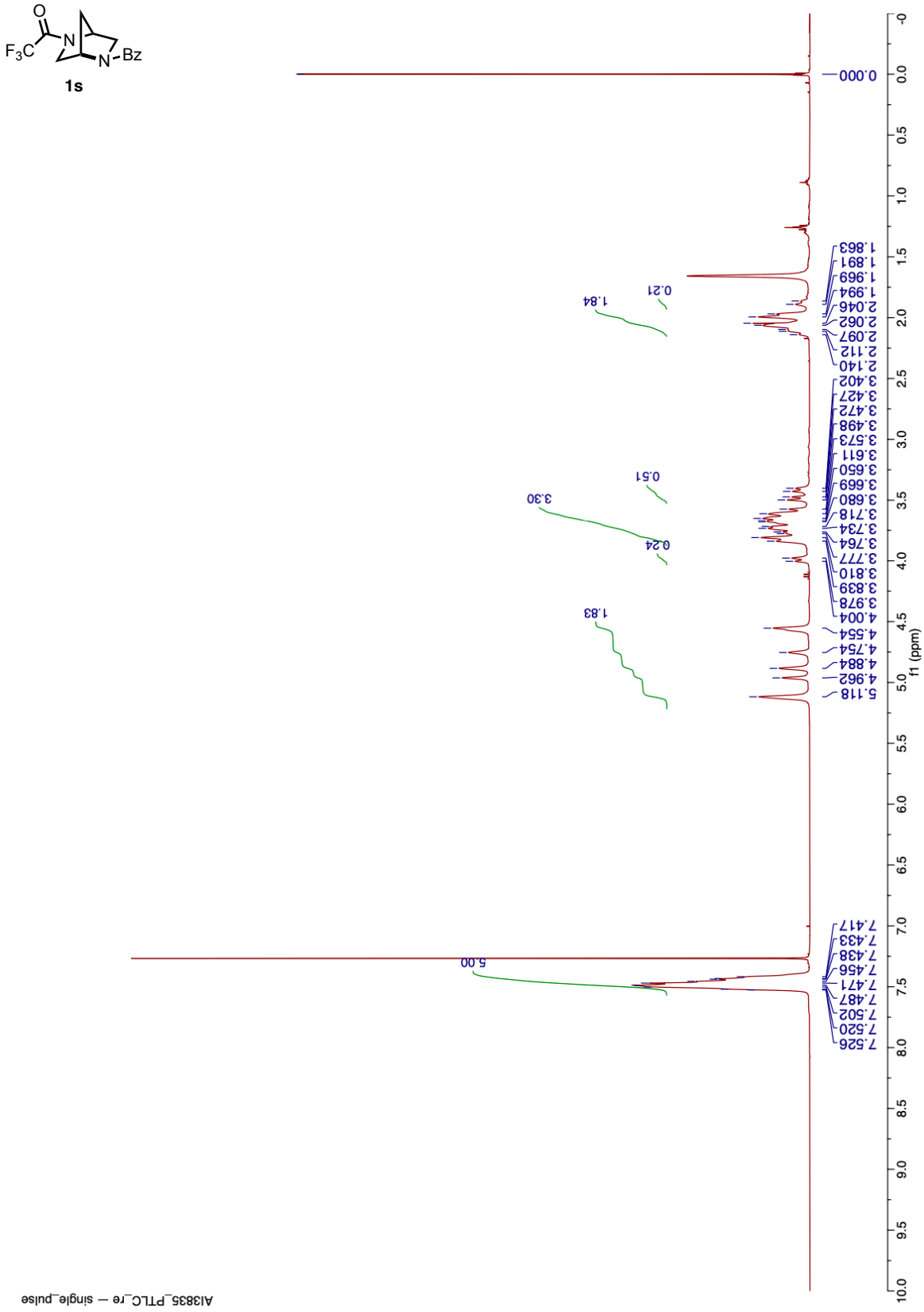
^{1}H NMR of 1l (400 MHz, $CDCl_3$)



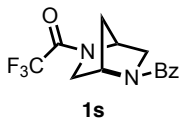
$^{13}C\{^{1}H\}$ NMR of 1l (101 MHz, $CDCl_3$, 323 K)



^{1}H NMR of 1s (400 MHz, $CDCl_3$)

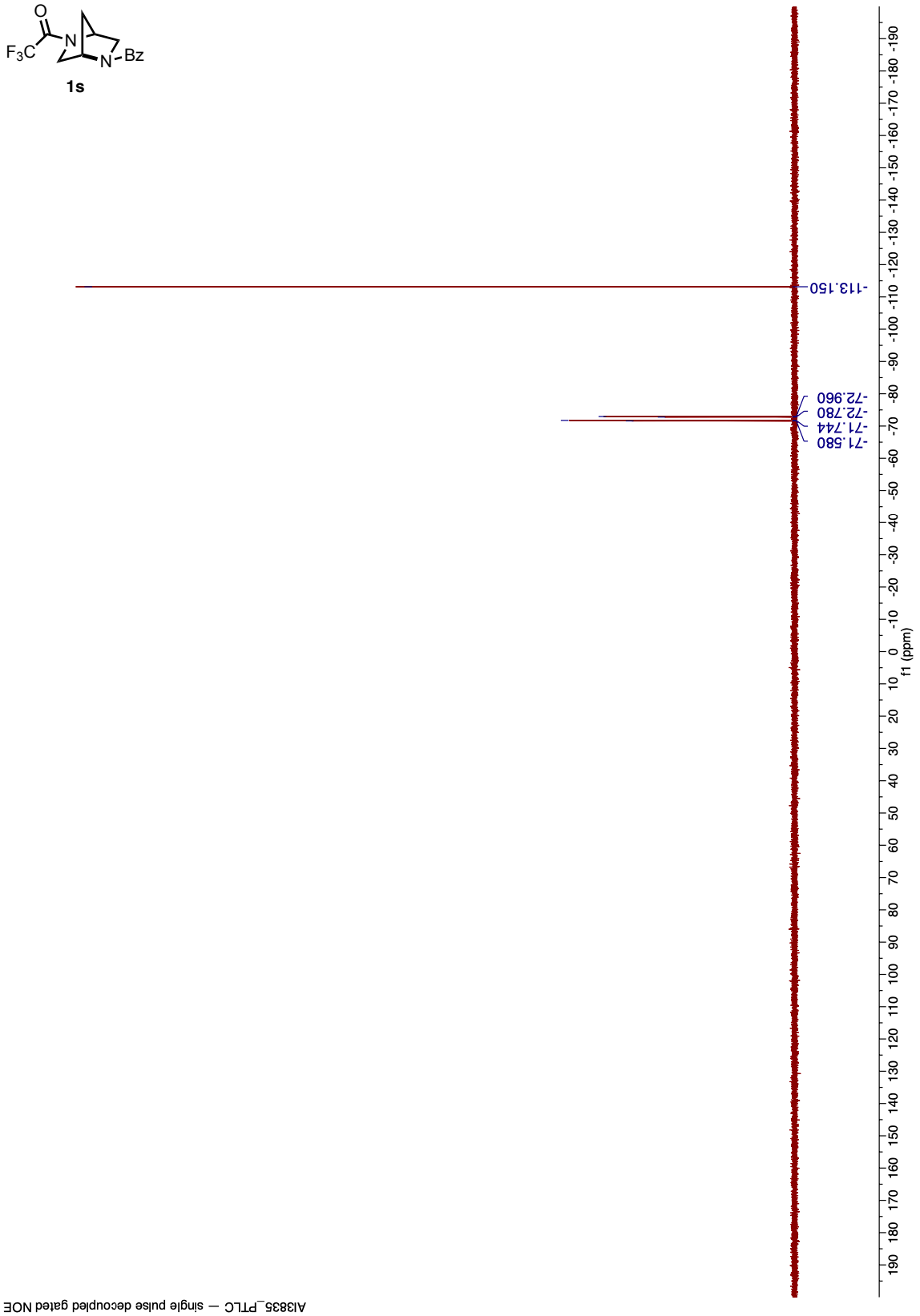


$^{13}C\{^{1}H\}$ NMR of 1s (101 MHz, $CDCl_3$)

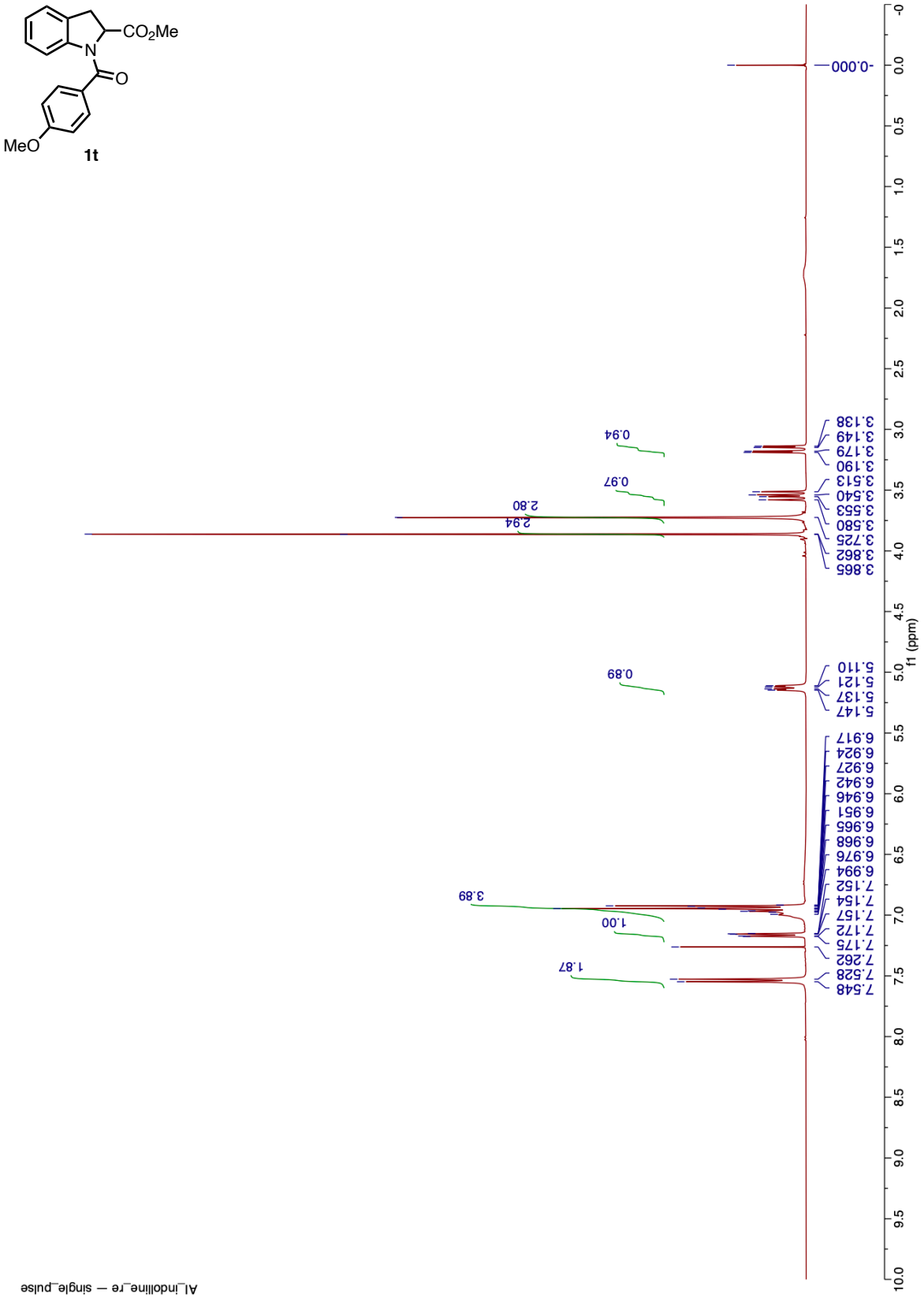


1s

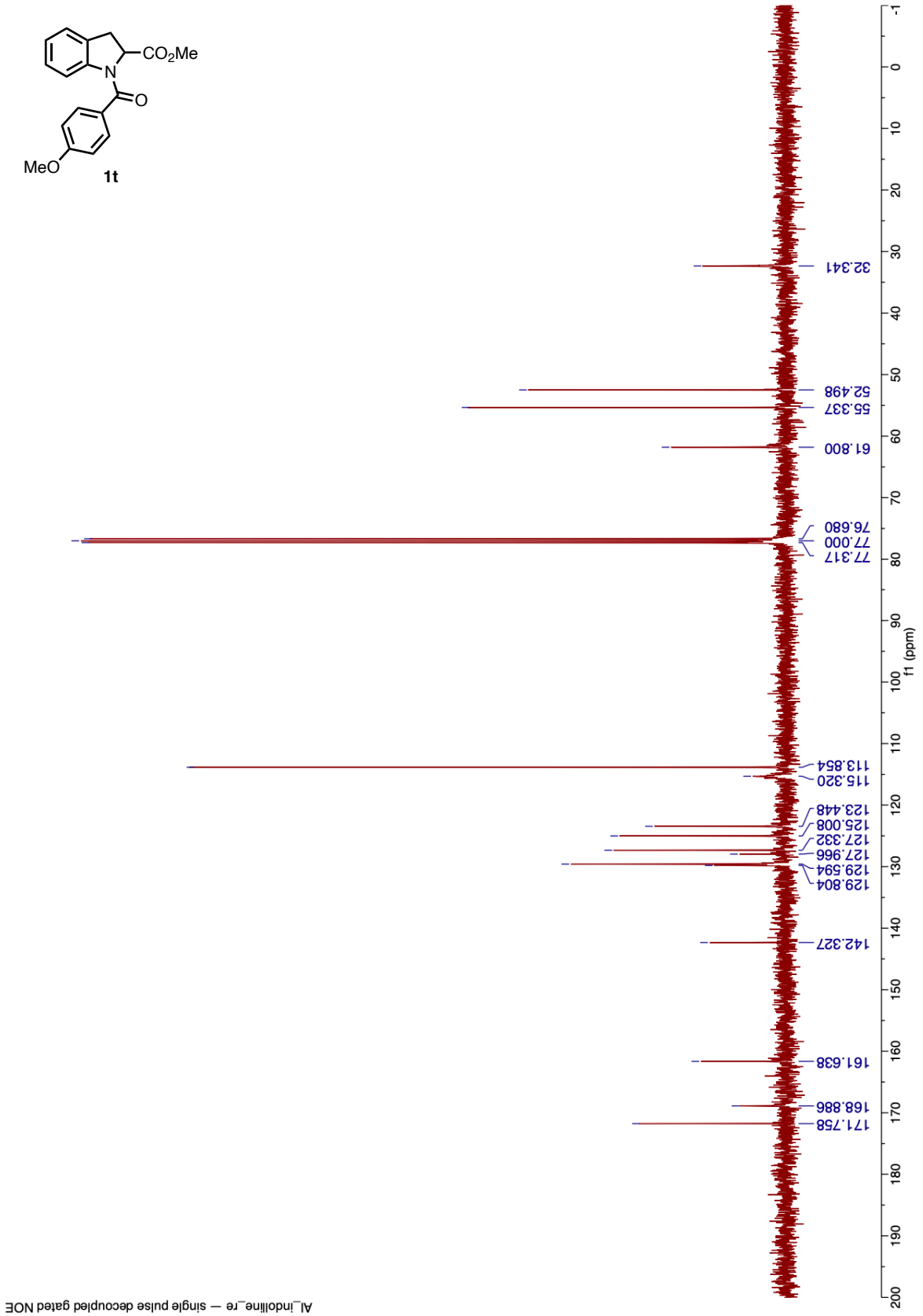
^{19}F NMR of 1s (376 MHz ,$CDCl_3$)



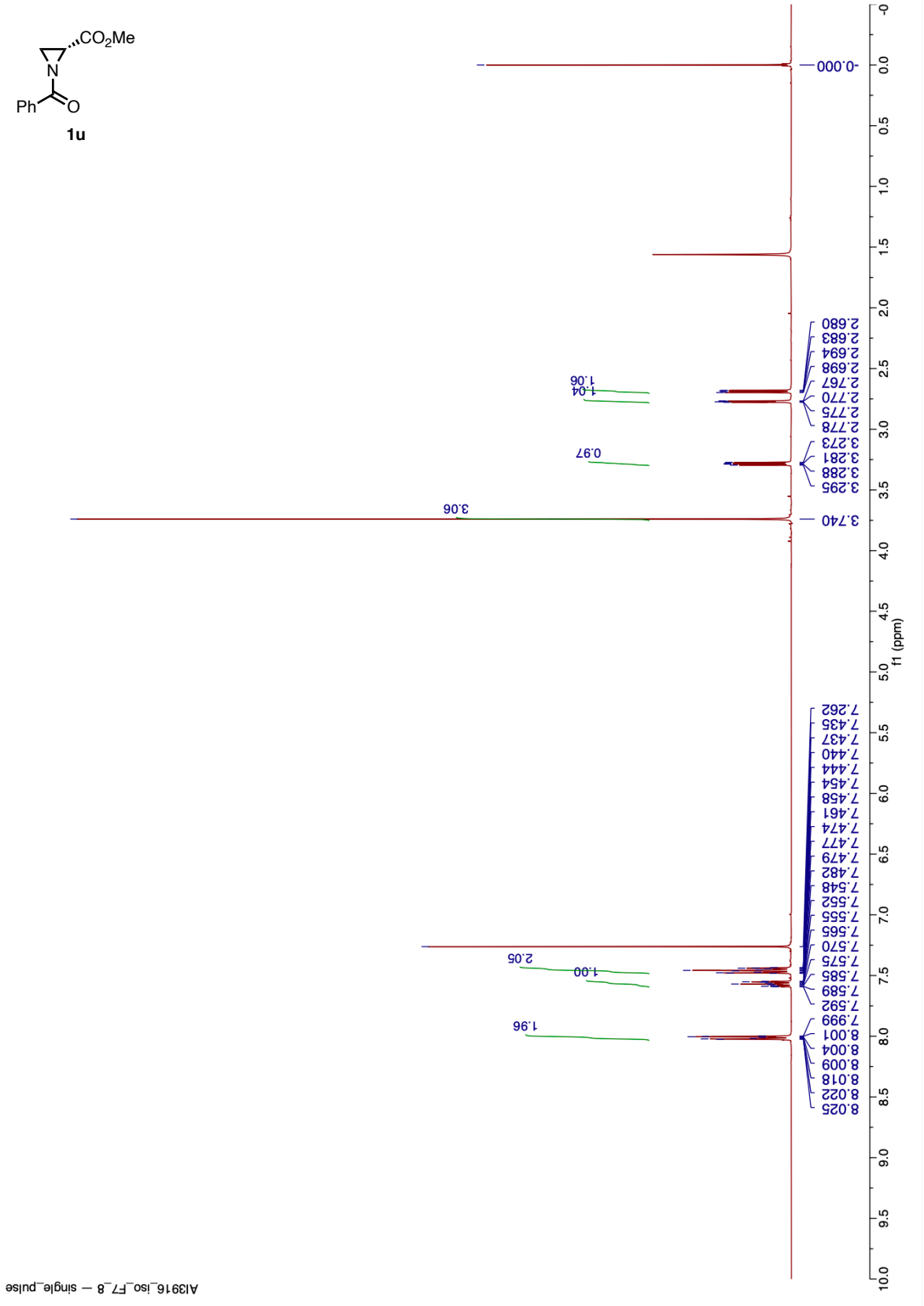
^{1}H NMR of 1t (400 MHz, $CDCl_3$)



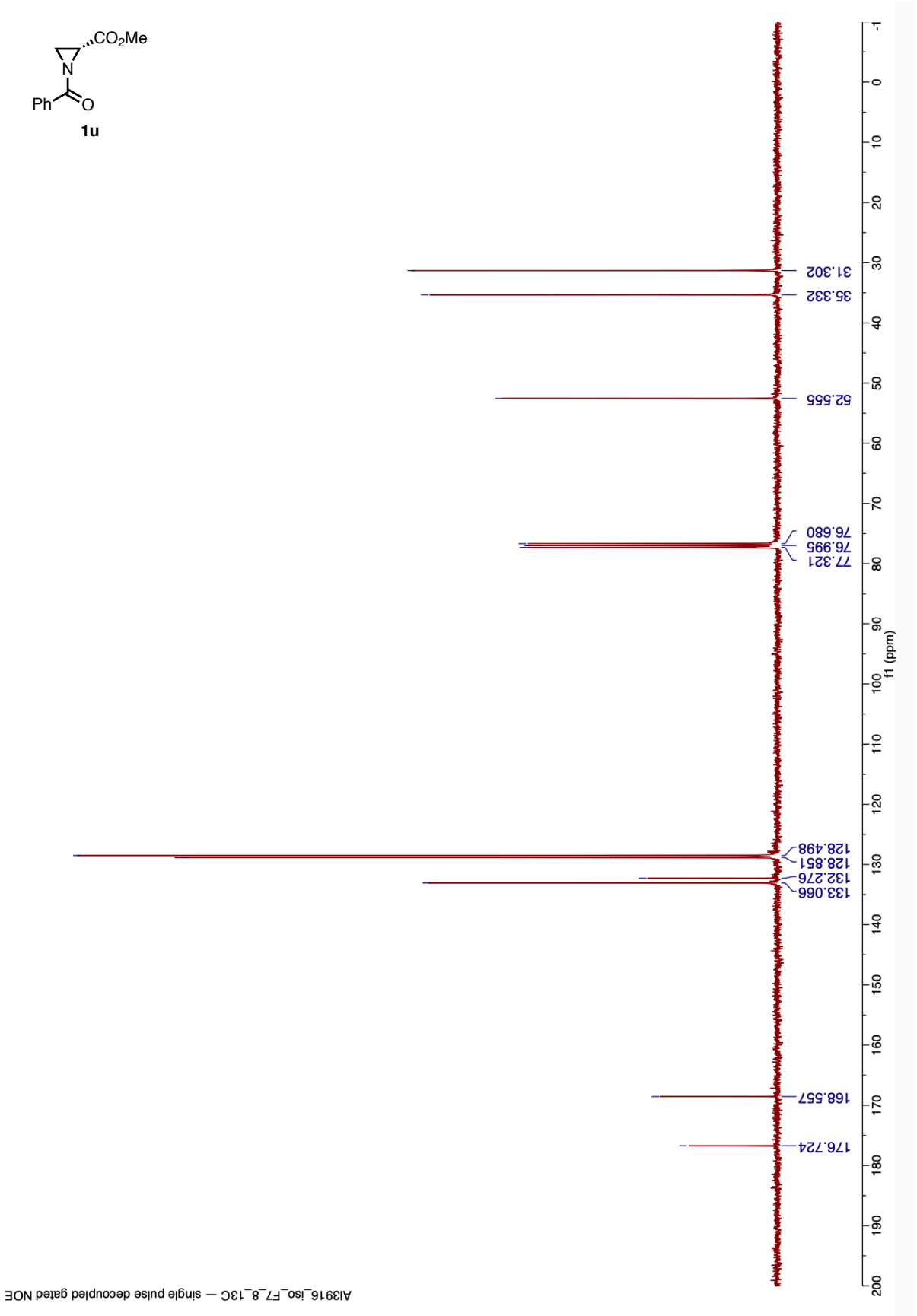
$^{13}C\{^{1}H\}$ NMR of 1t (101 MHz, $CDCl_3$)



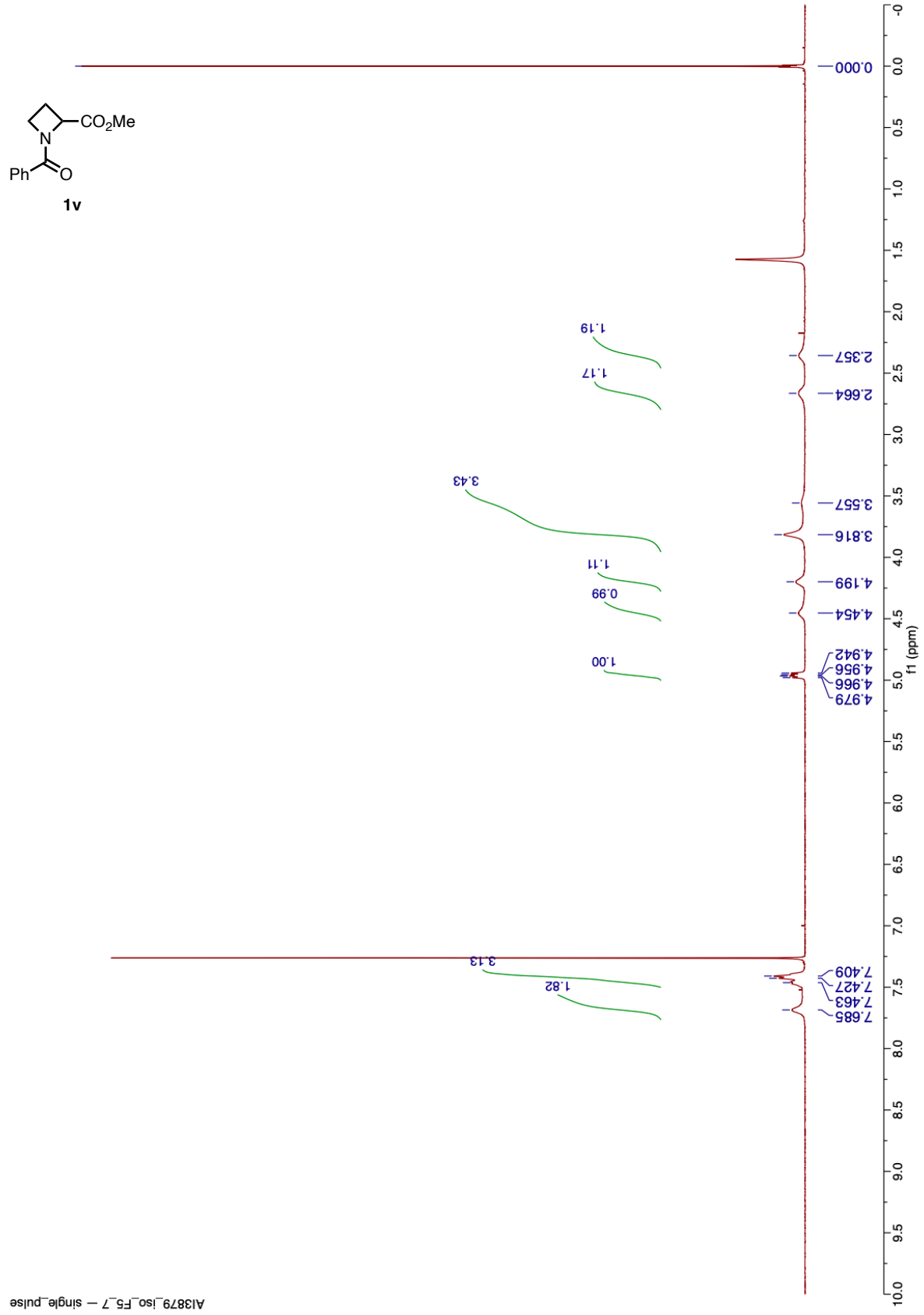
^{1}H NMR of 1u (400 MHz, $CDCl_3$)



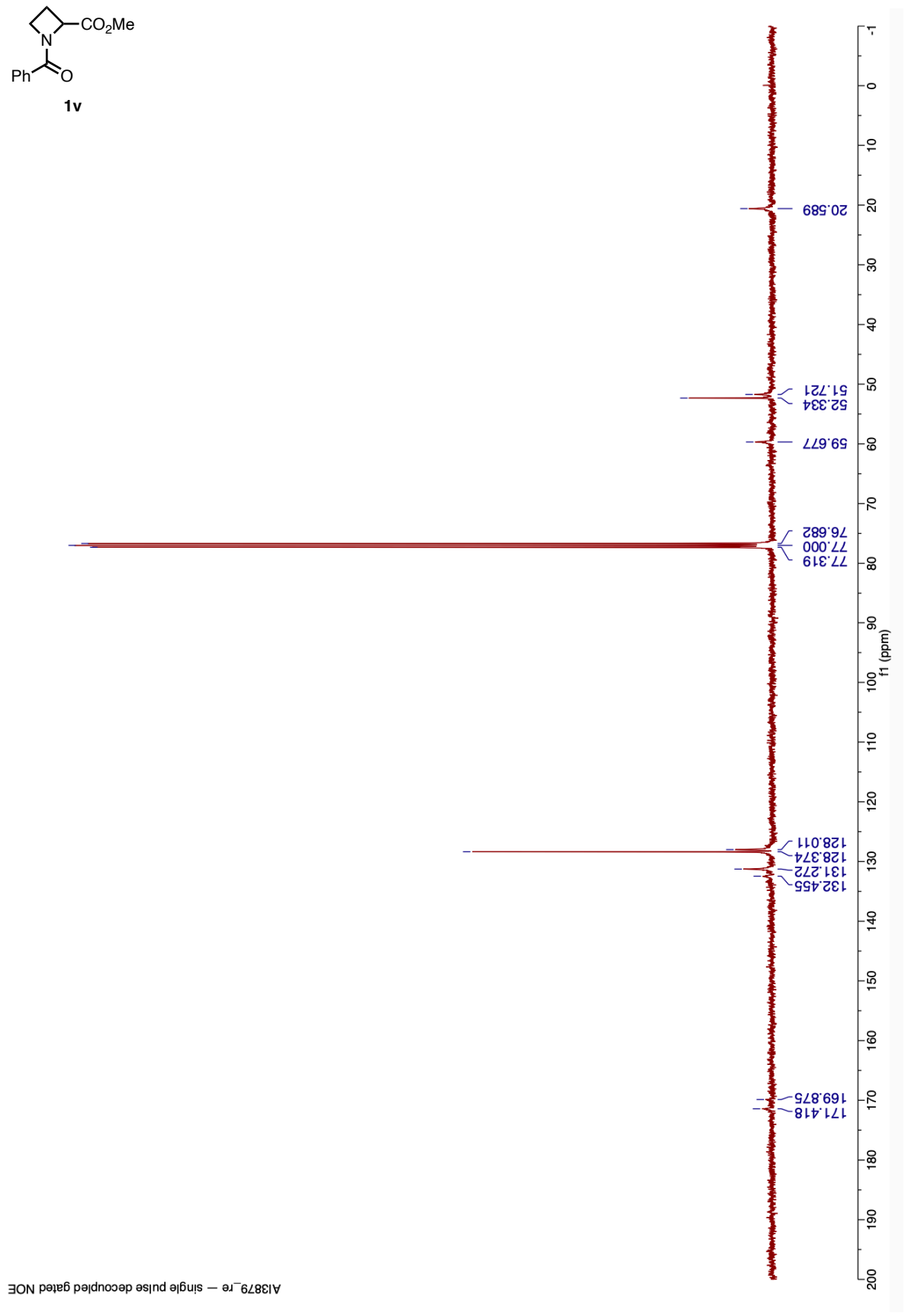
$^{13}C\{^{1}H\}$ NMR of 1u (101 MHz, $CDCl_3$)



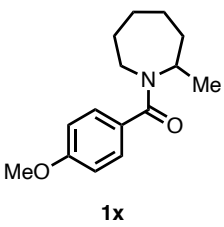
^{1}H NMR of 1v (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 1v (101 MHz, $CDCl_3$)

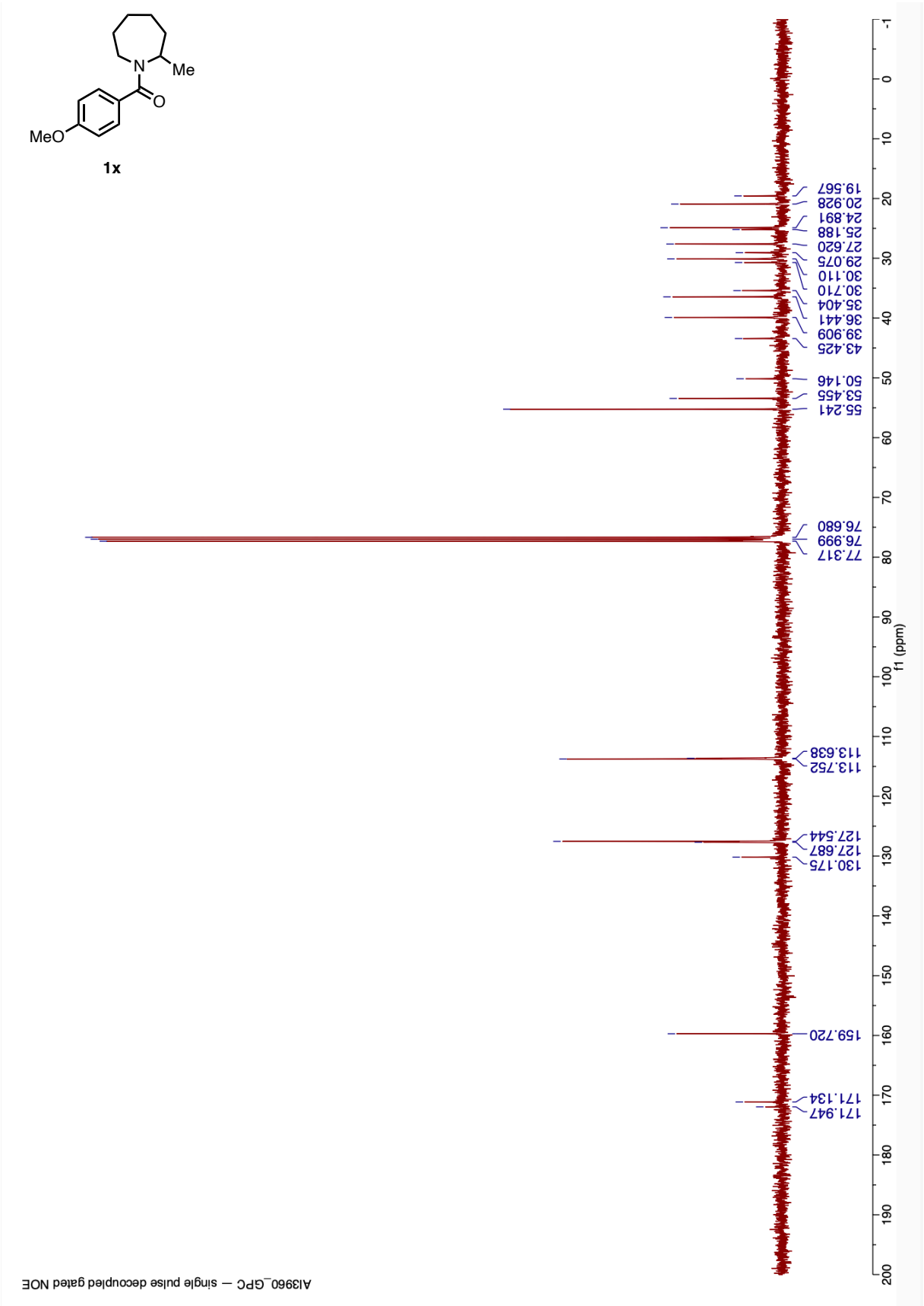


^{1}H NMR of 1x (400 MHz, C_6D_6)

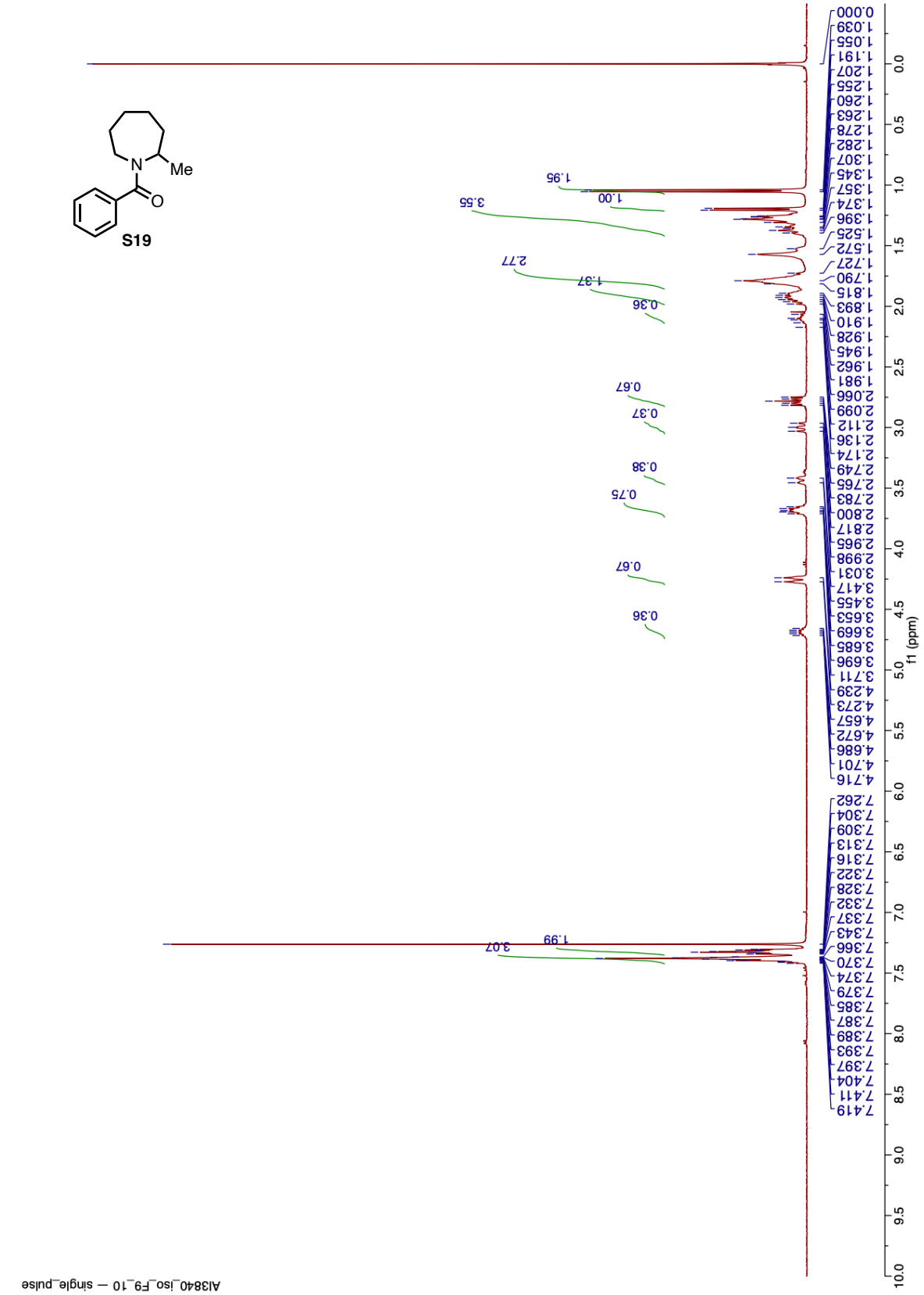


1x

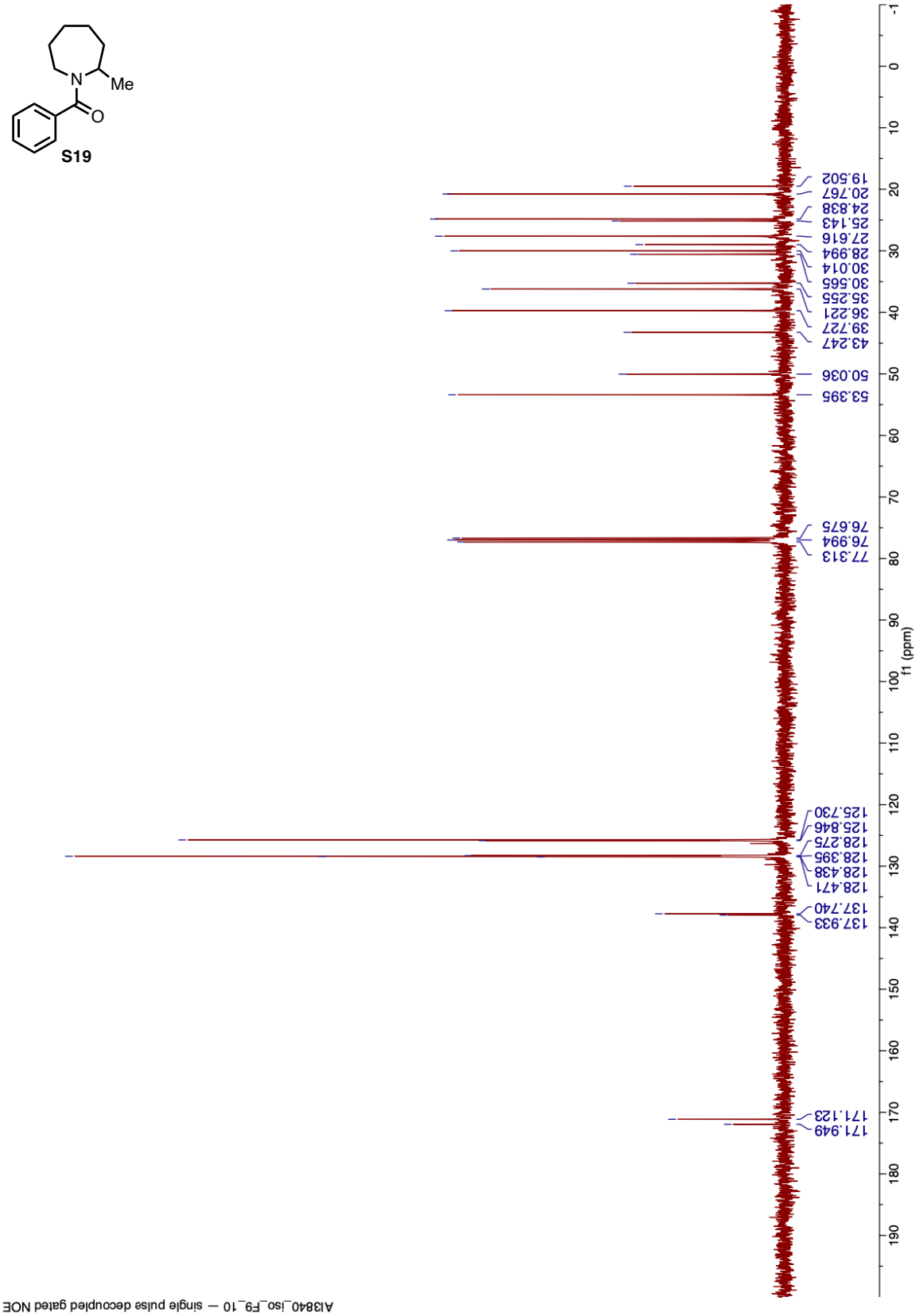
$^{13}C\{^{1}H\}$ NMR of 1x (101 MHz, $CDCl_3$)



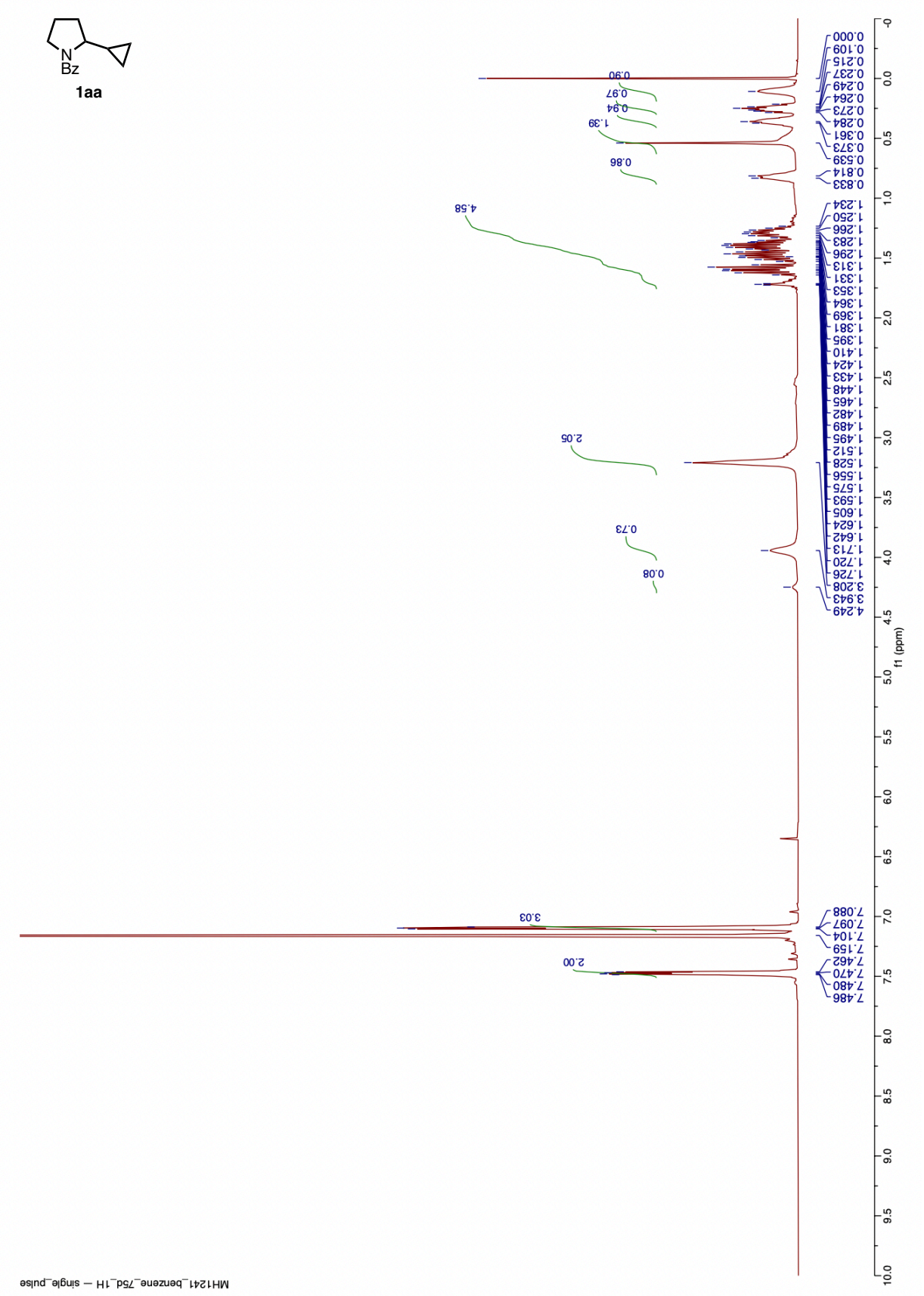
^{1}H NMR of S19 (400 MHz, $CDCl_3$)



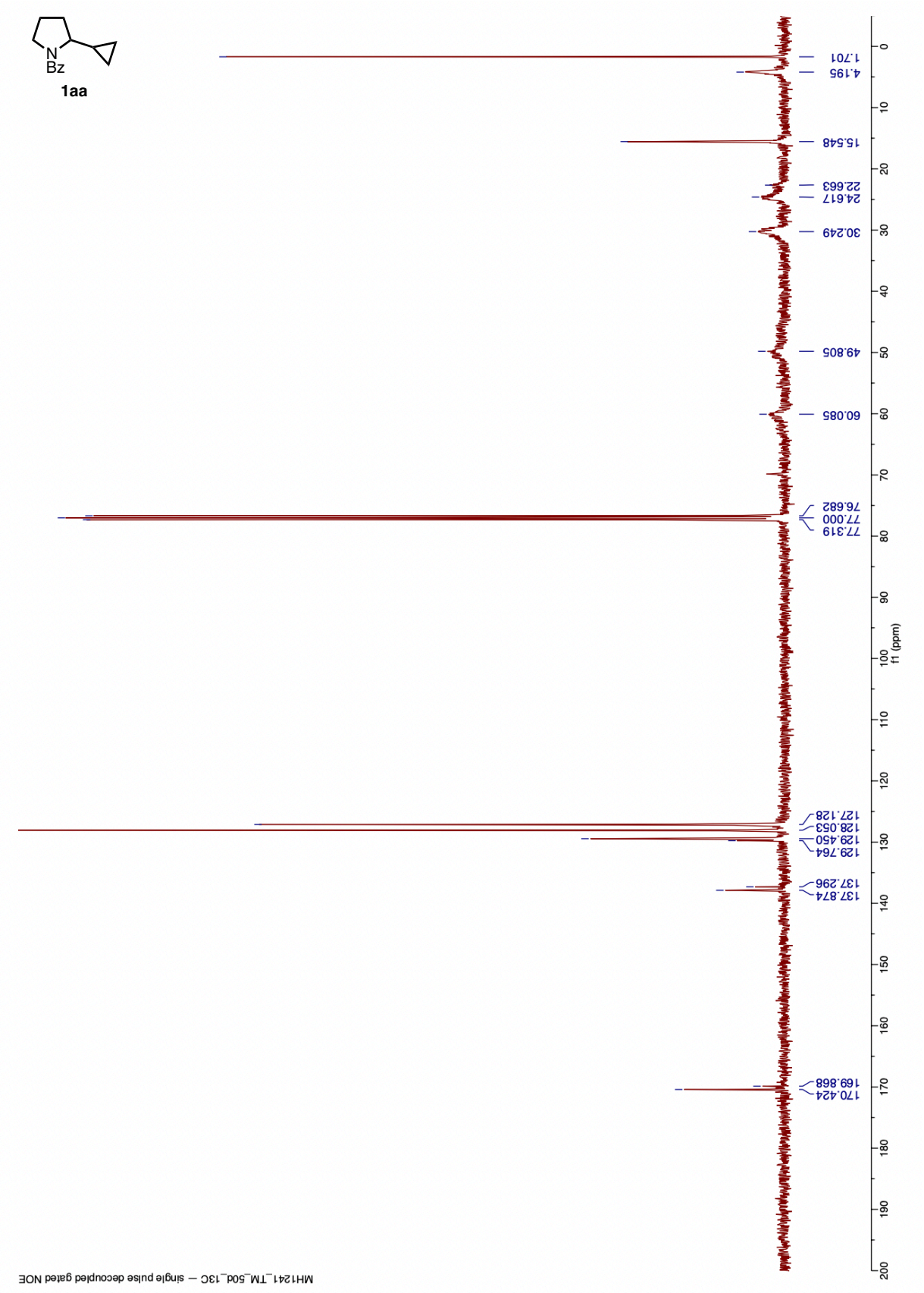
$^{13}C\{^{1}H\}$ NMR of S19 (101 MHz, $CDCl_3$)



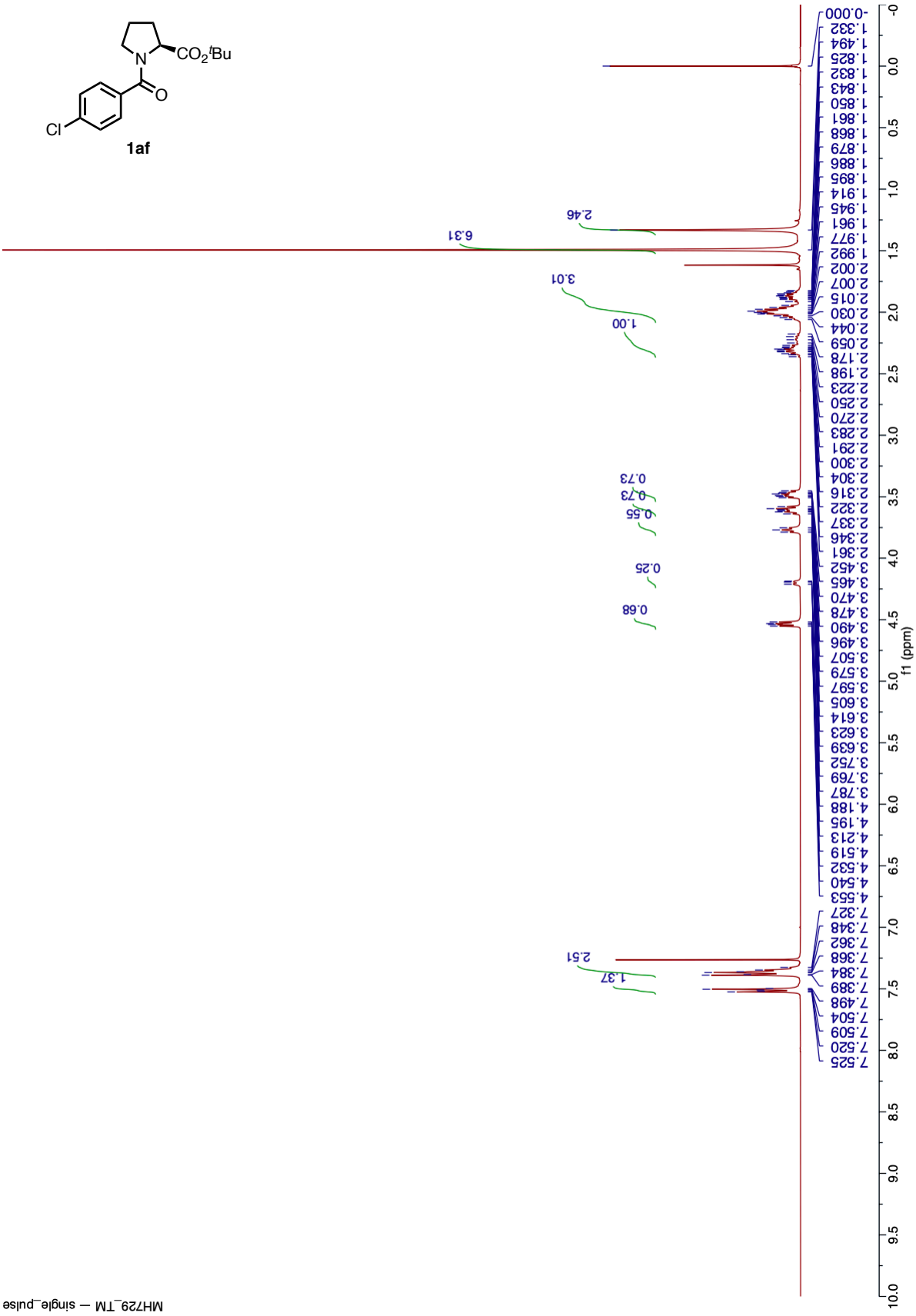
^{1}H NMR of 1aa (400 MHz, C_6D_6, 348 K)



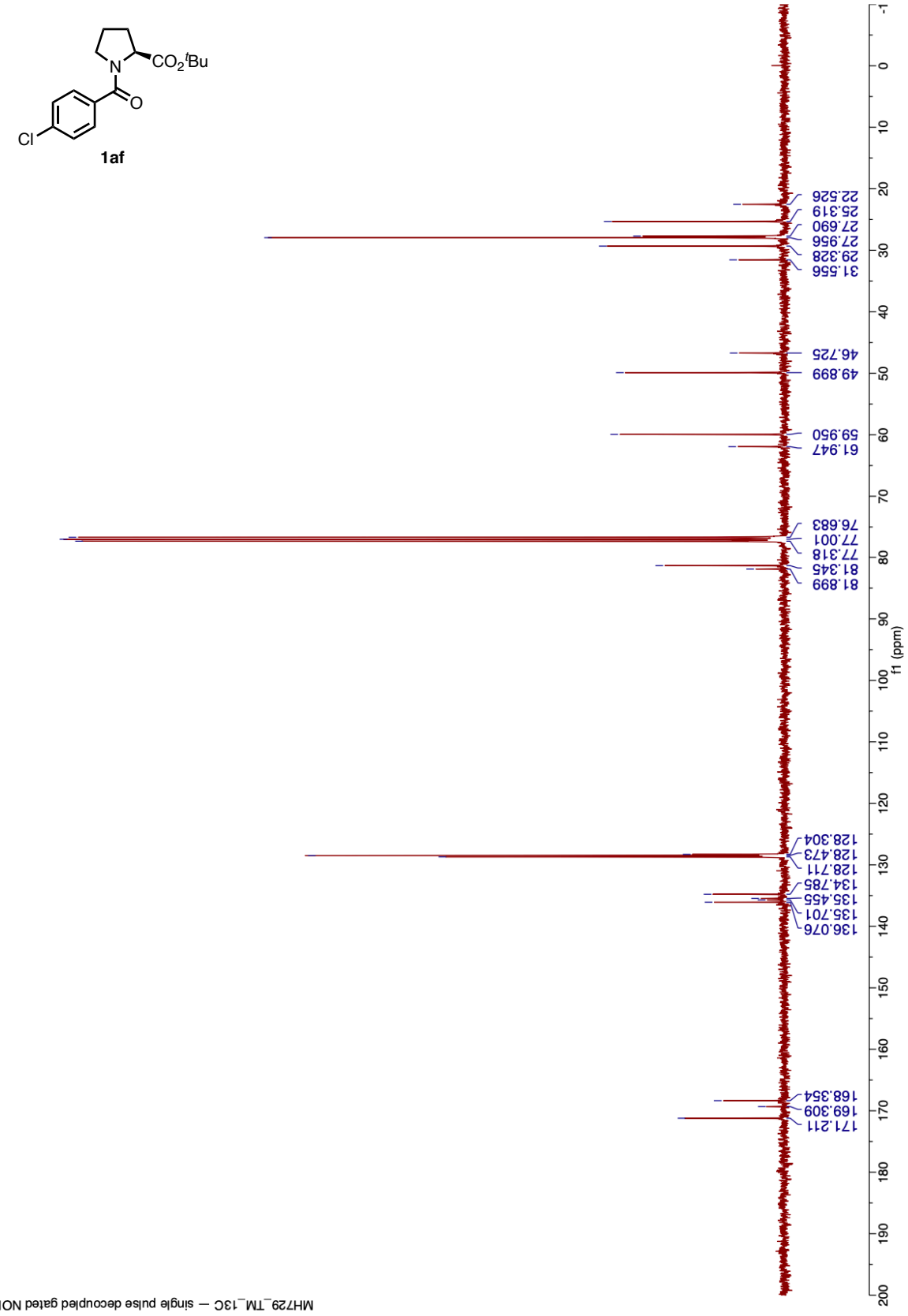
$^{13}C\{^{1}H\}$ NMR of 1aa (101 MHz, $CDCl_3$, 323 K)



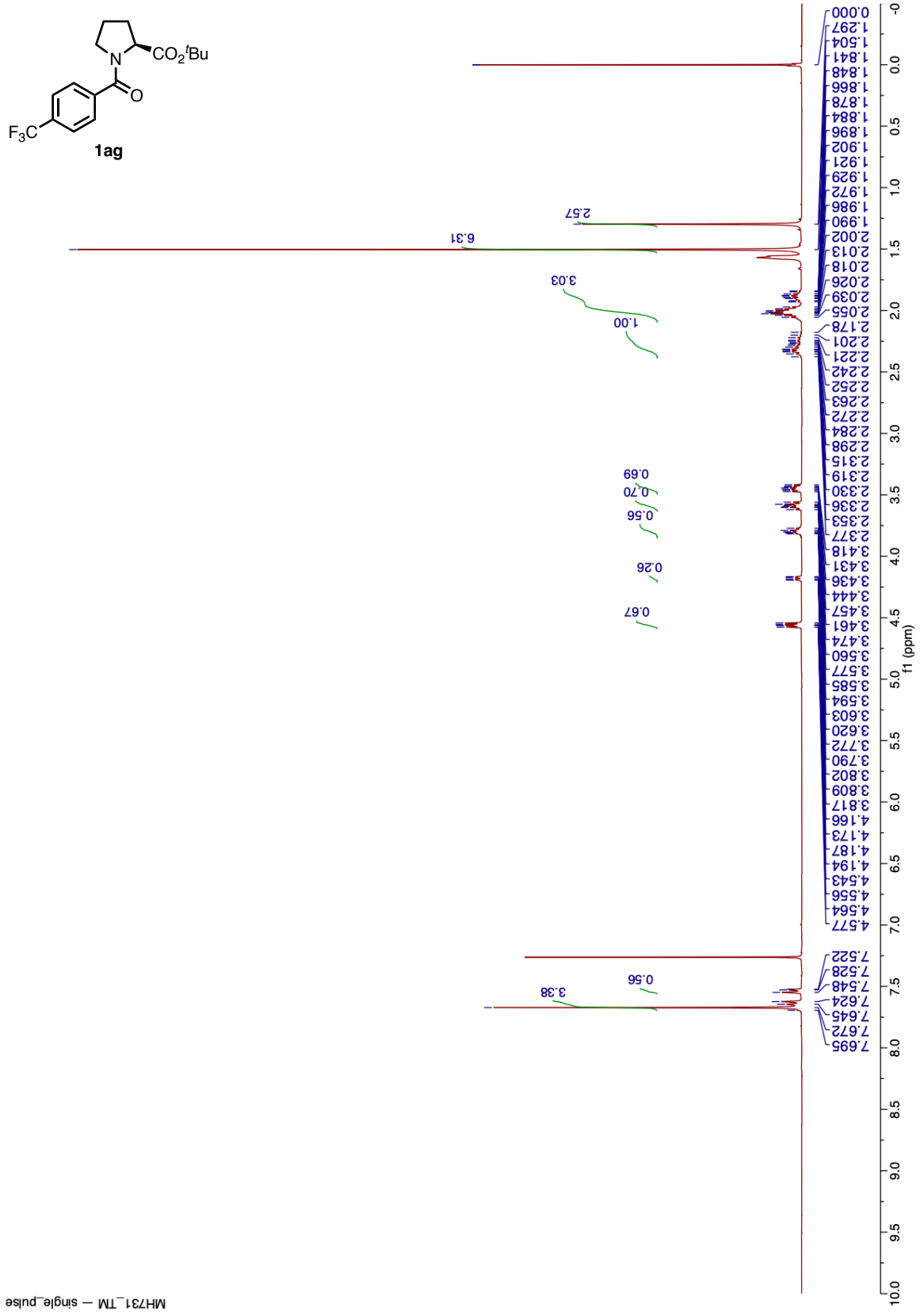
^{1}H NMR of 1af (400 MHz, $CDCl_3$)



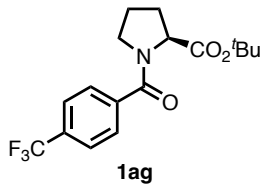
$^{13}C\{^{1}H\}$ NMR of 1af (101 MHz, $CDCl_3$)



^{1}H NMR of 1ag (400 MHz, $CDCl_3$)

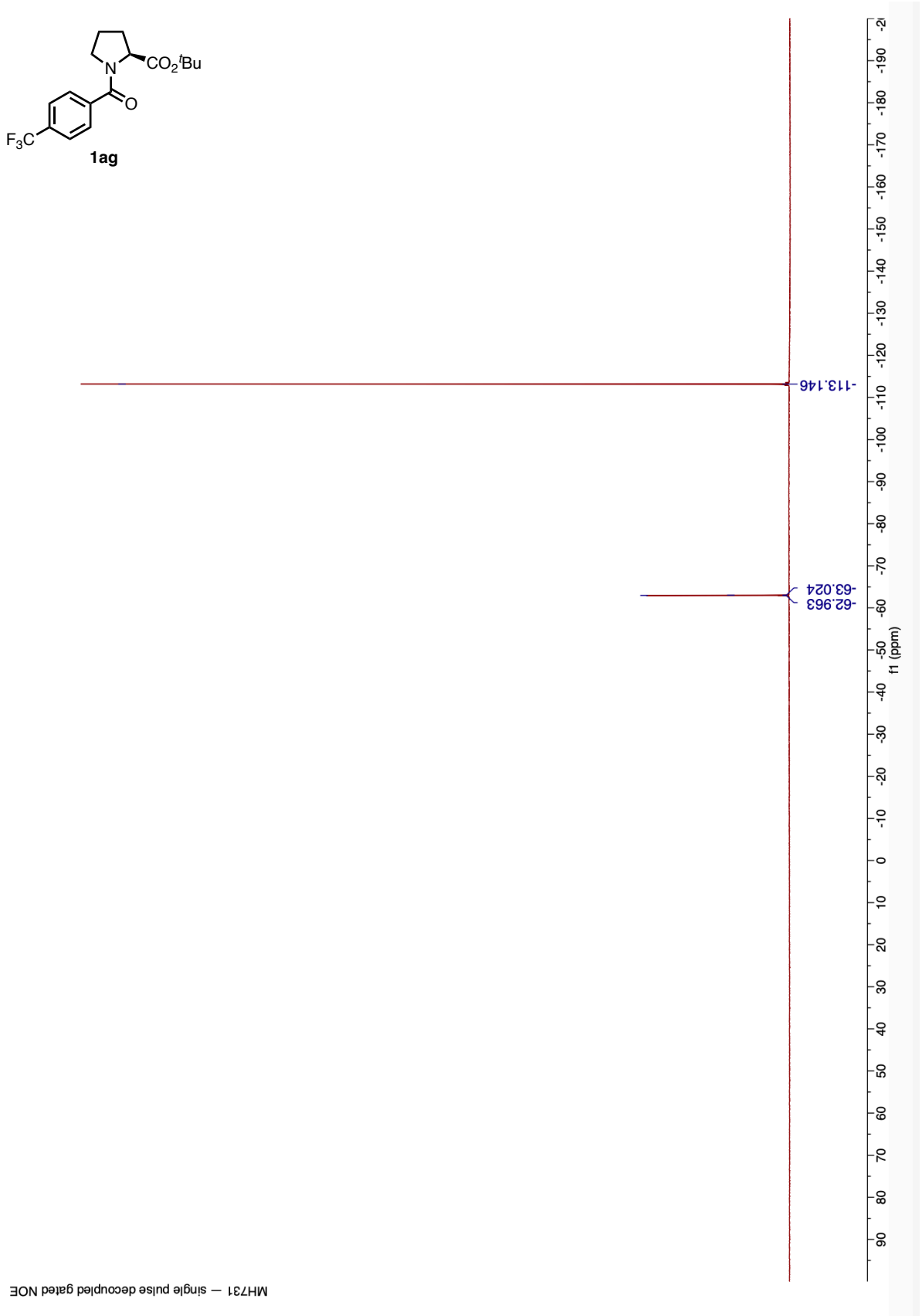


$^{13}C\{^{1}H\}$ NMR of 1ag (101 MHz, $CDCl_3$)

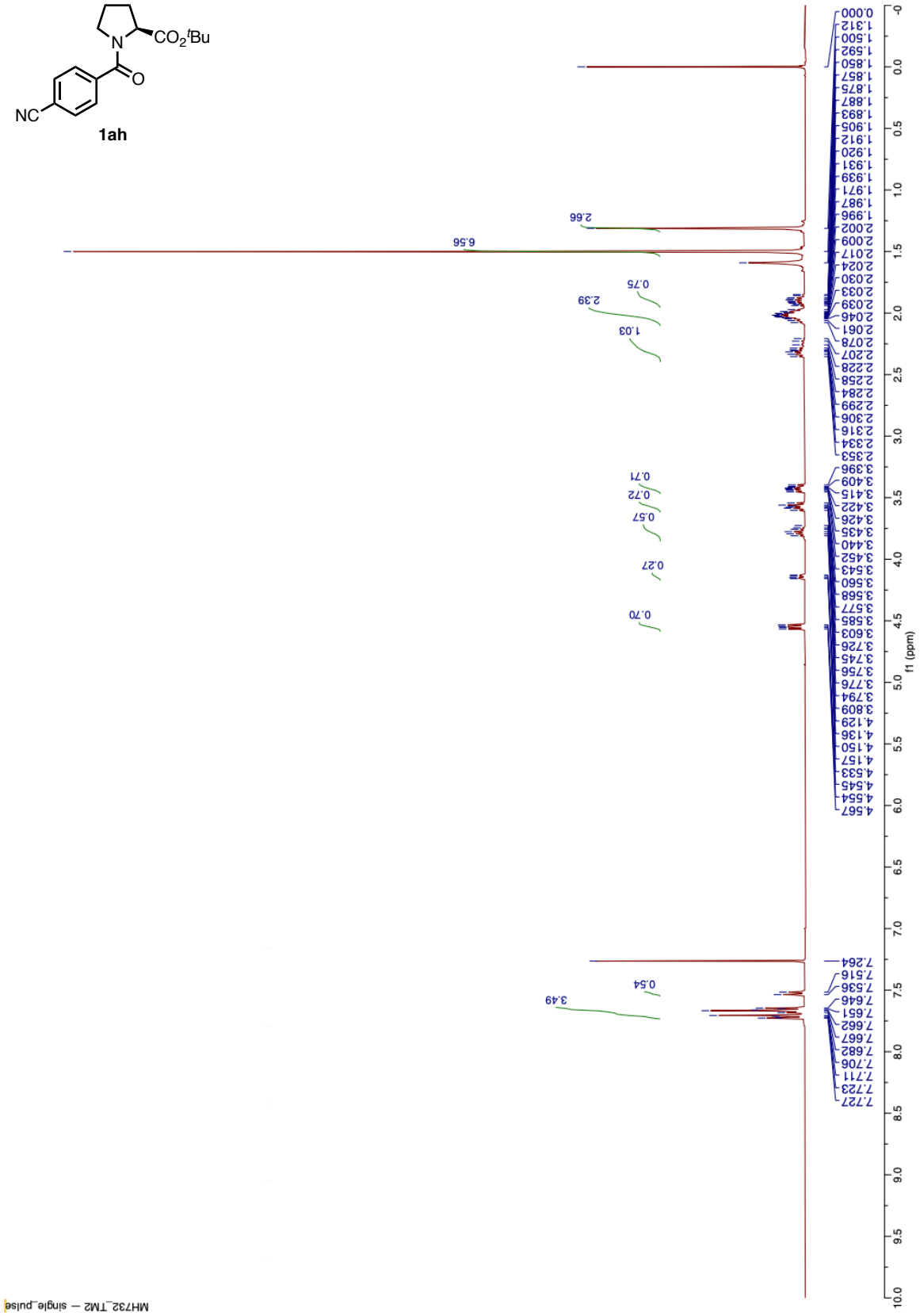


1ag

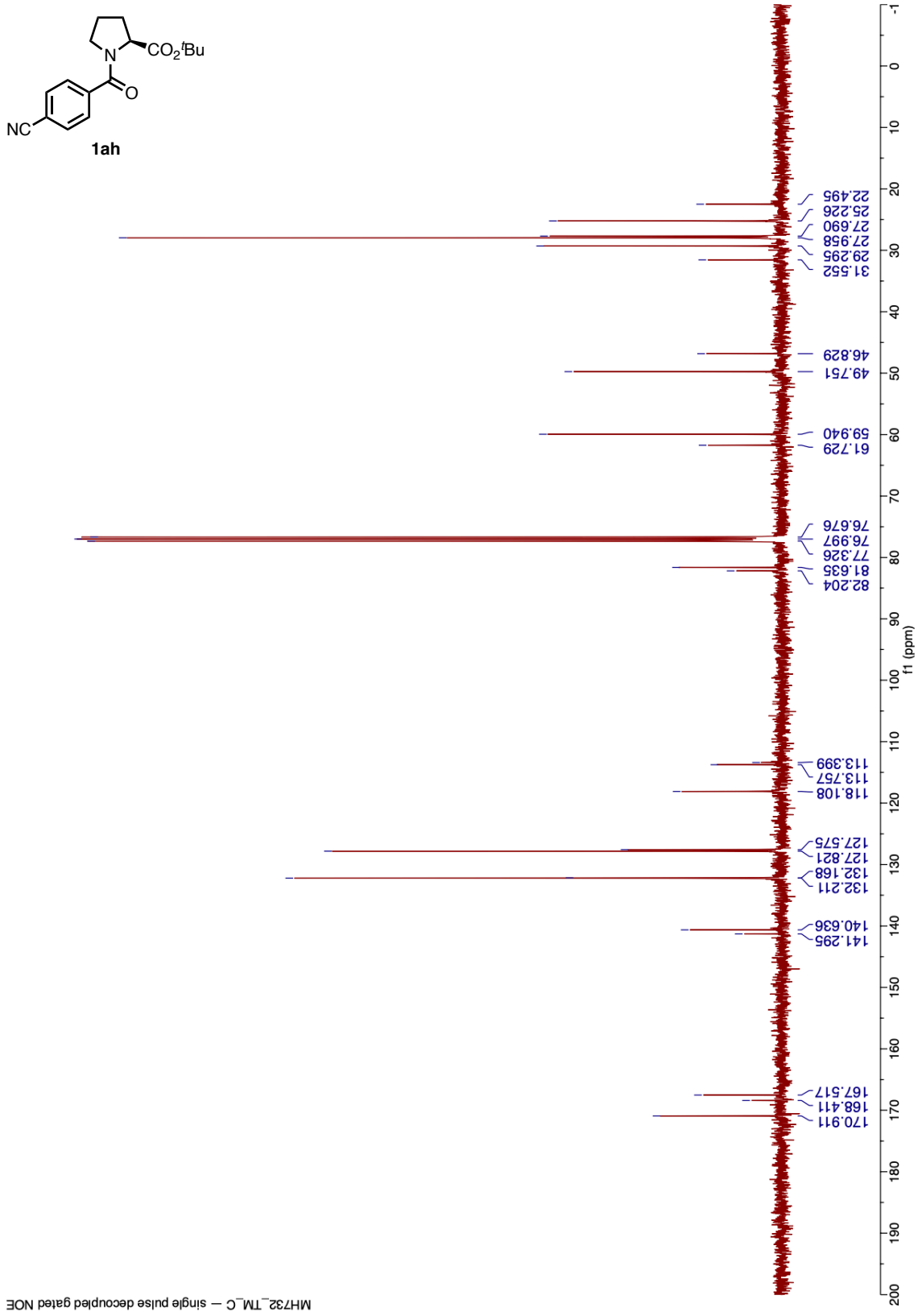
^{19}F NMR of 1ag (376 MHz ,$CDCl_3$)



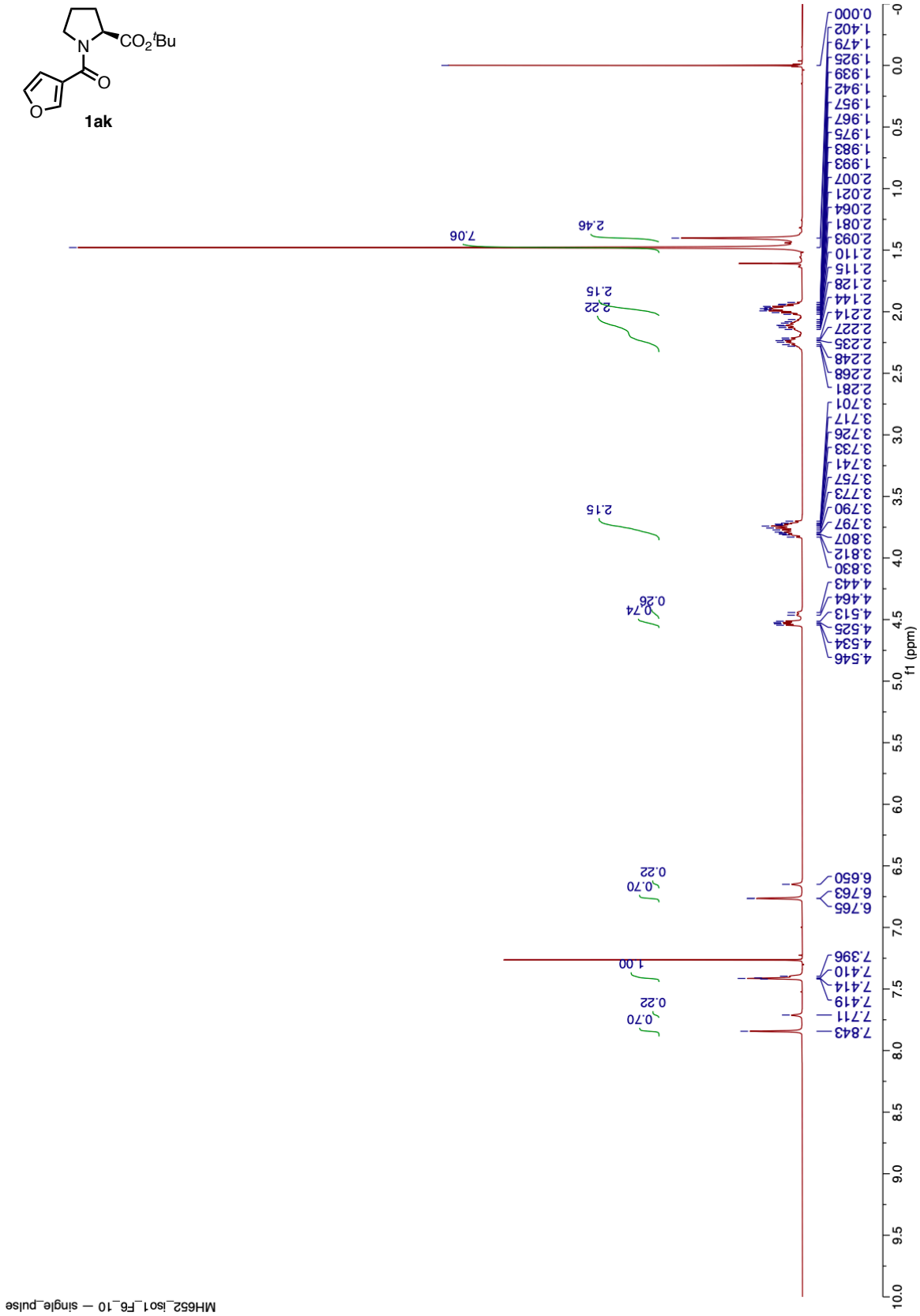
^{1}H NMR of 1ah (400 MHz, $CDCl_3$)



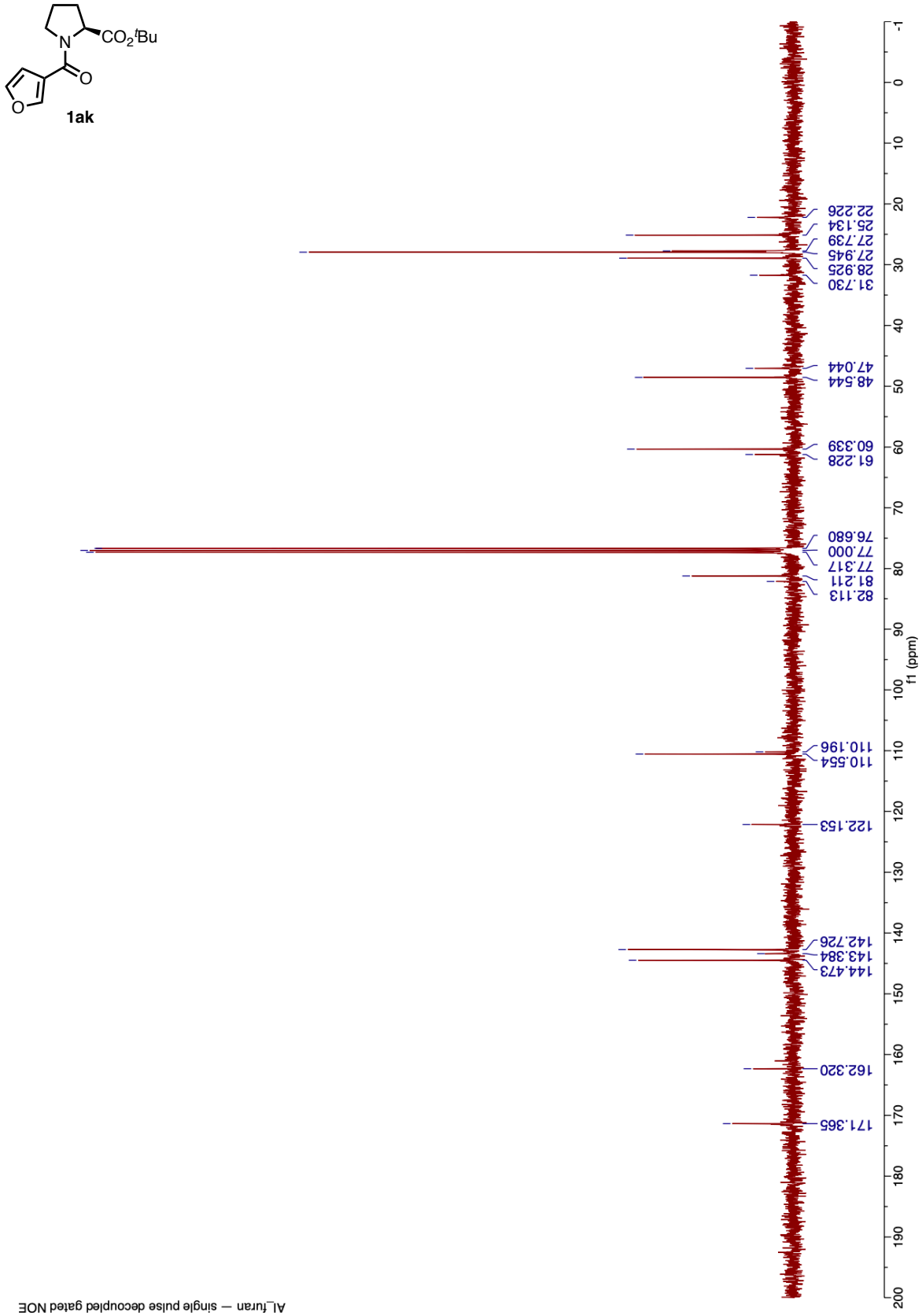
$^{13}C\{^{1}H\}$ NMR of 1ah (101 MHz, $CDCl_3$)



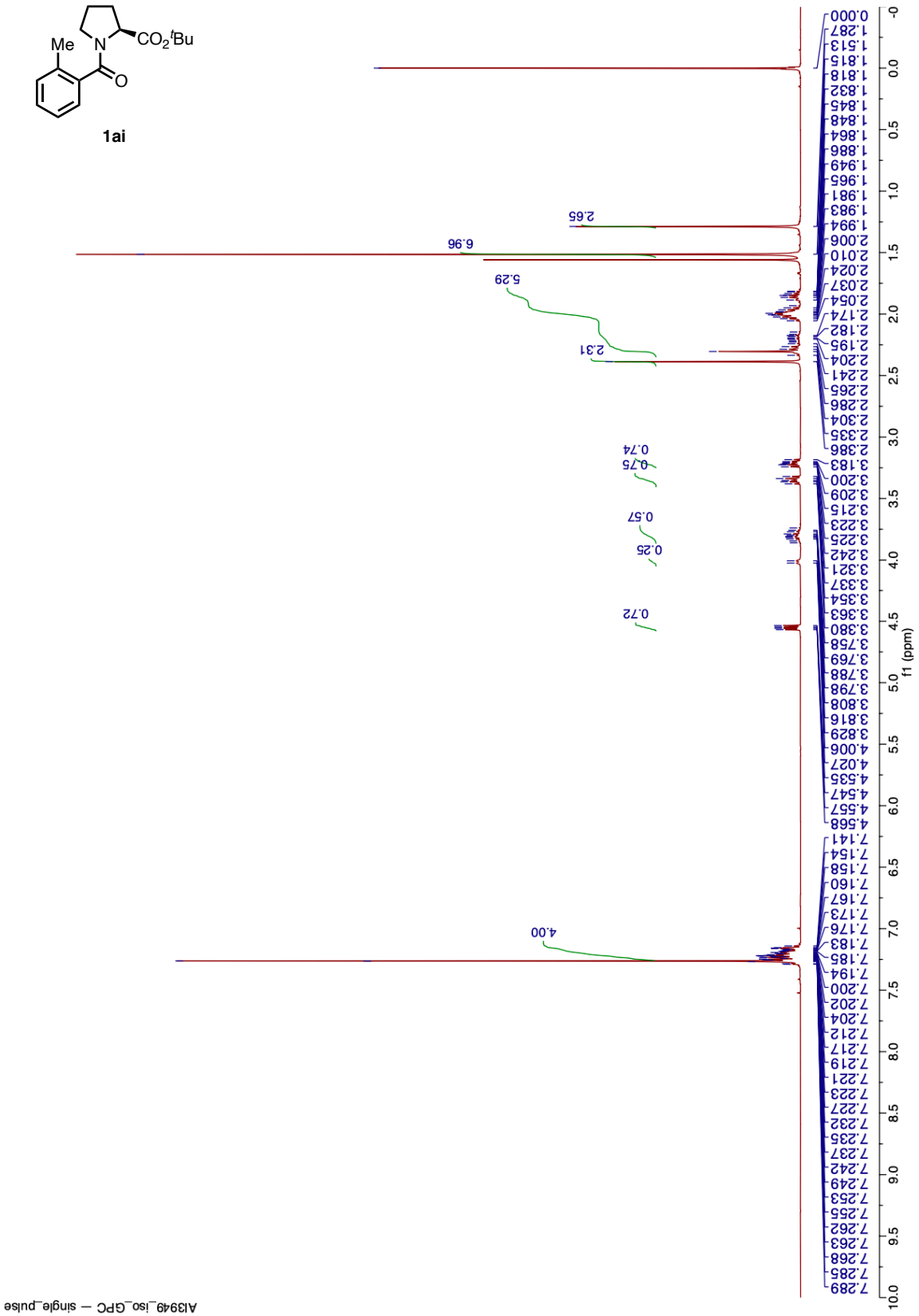
^{1}H NMR of 1ak (400 MHz, $CDCl_3$)



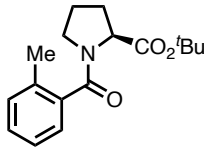
$^{13}C\{^{1}H\}$ NMR of 1ak (101 MHz, $CDCl_3$)



^{1}H NMR of 1ai (400 MHz, $CDCl_3$)

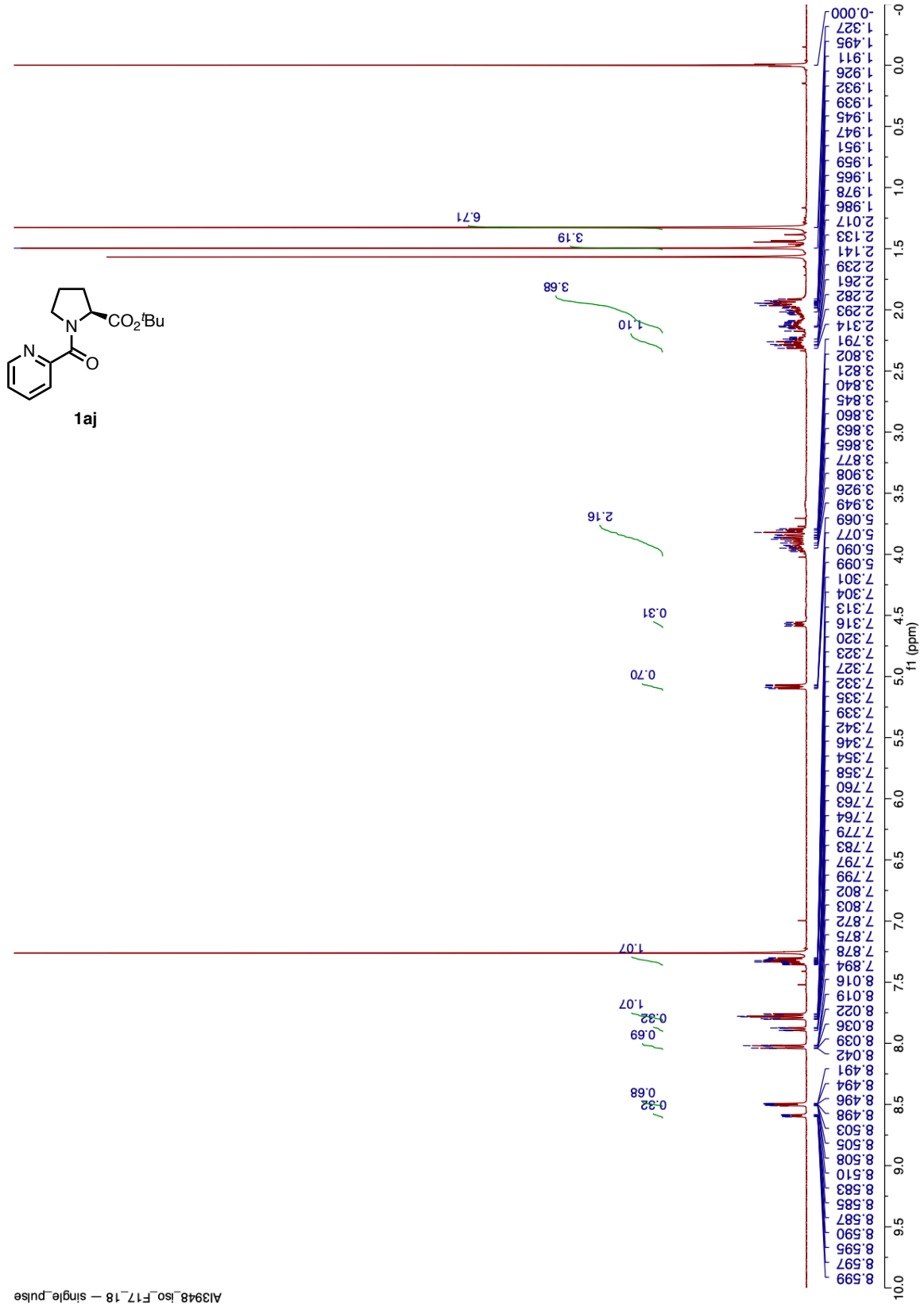


$^{13}C\{^{1}H\}$ NMR of 1ai (101 MHz, $CDCl_3$)

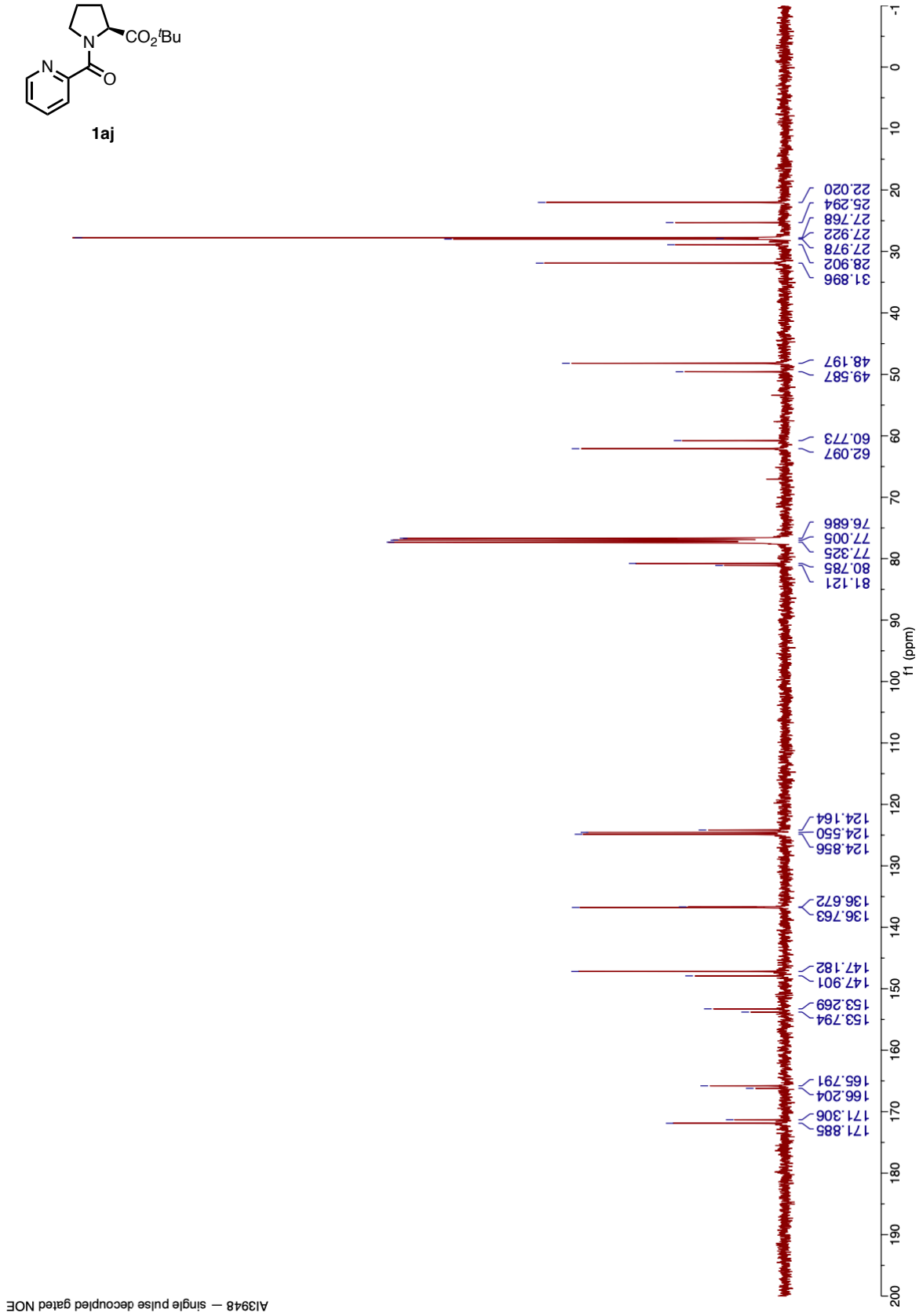


1ai

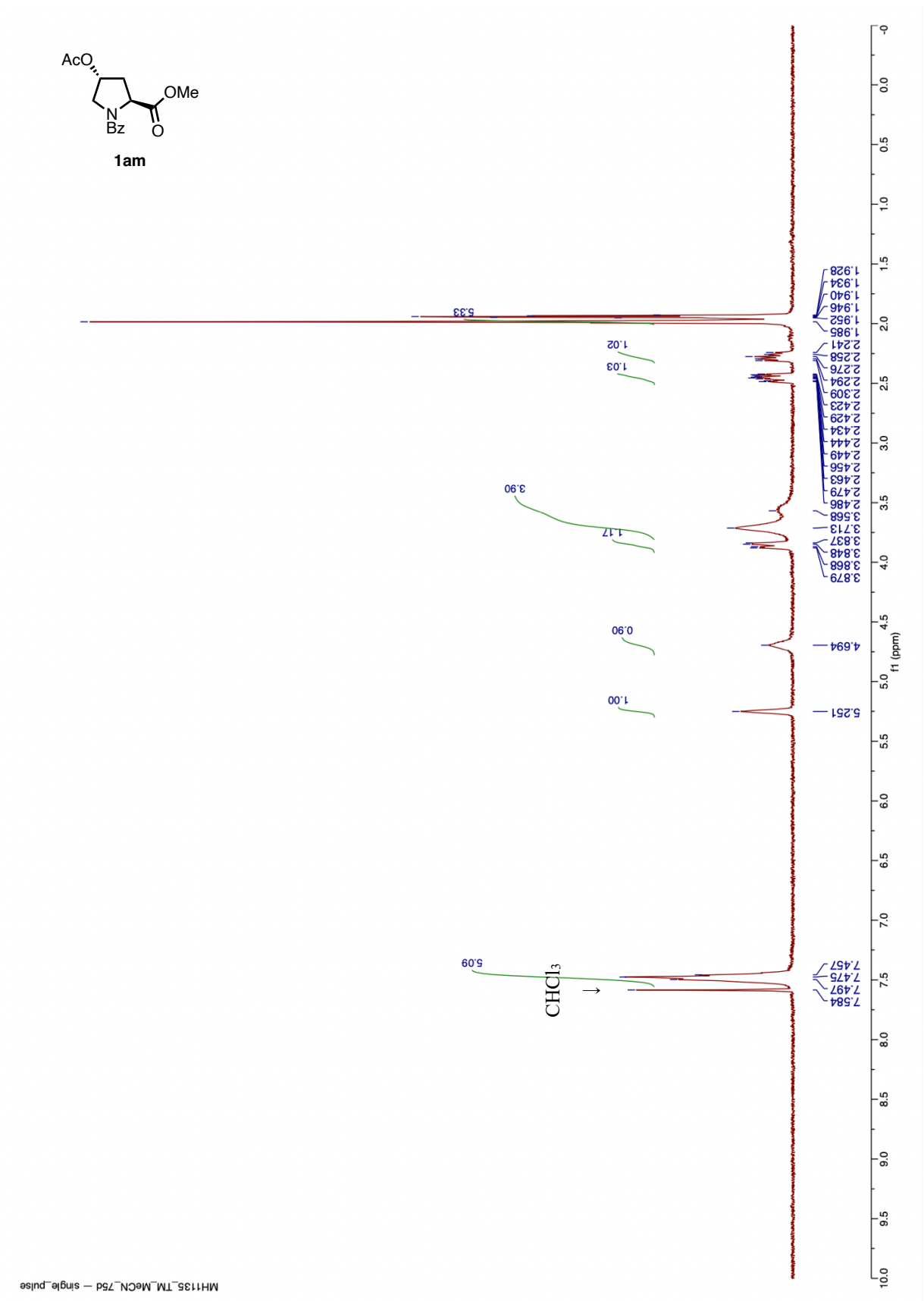
^{1}H NMR of 1aj (400 MHz, $CDCl_3$)



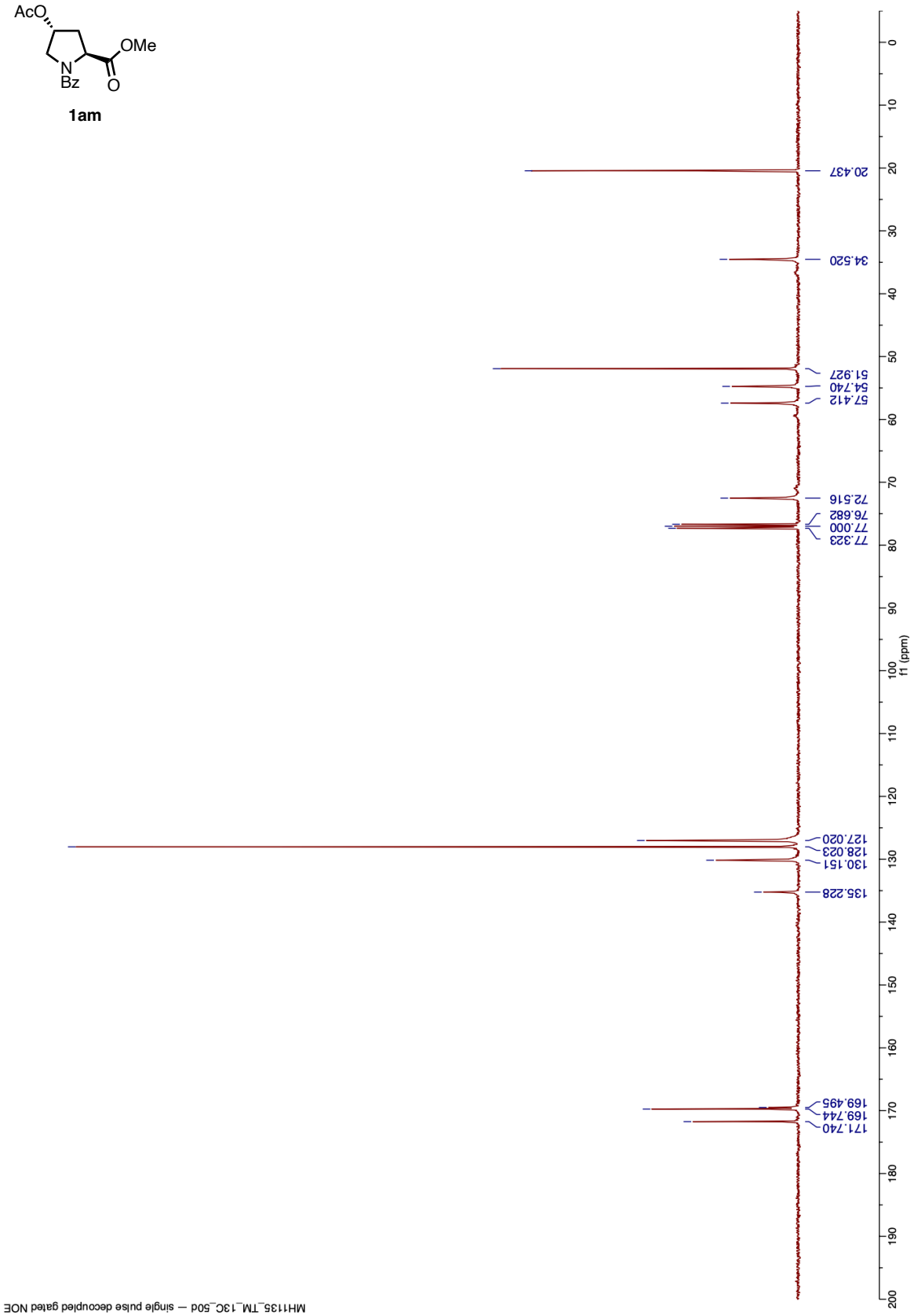
$^{13}C\{^{1}H\}$ NMR of 1aj (101 MHz, $CDCl_3$)



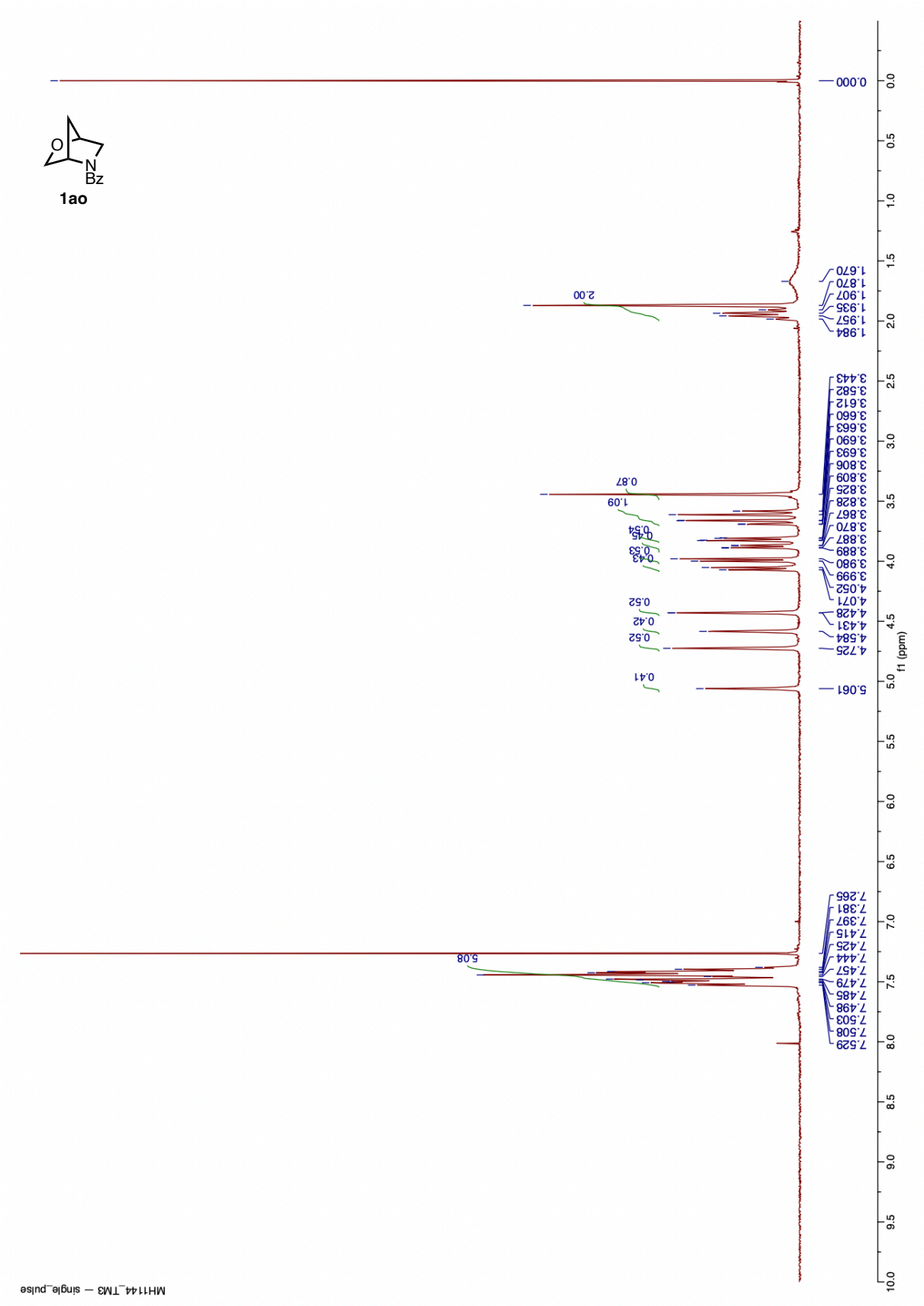
^{1}H NMR of 1am (400 MHz, CD_3CN, 348 K)



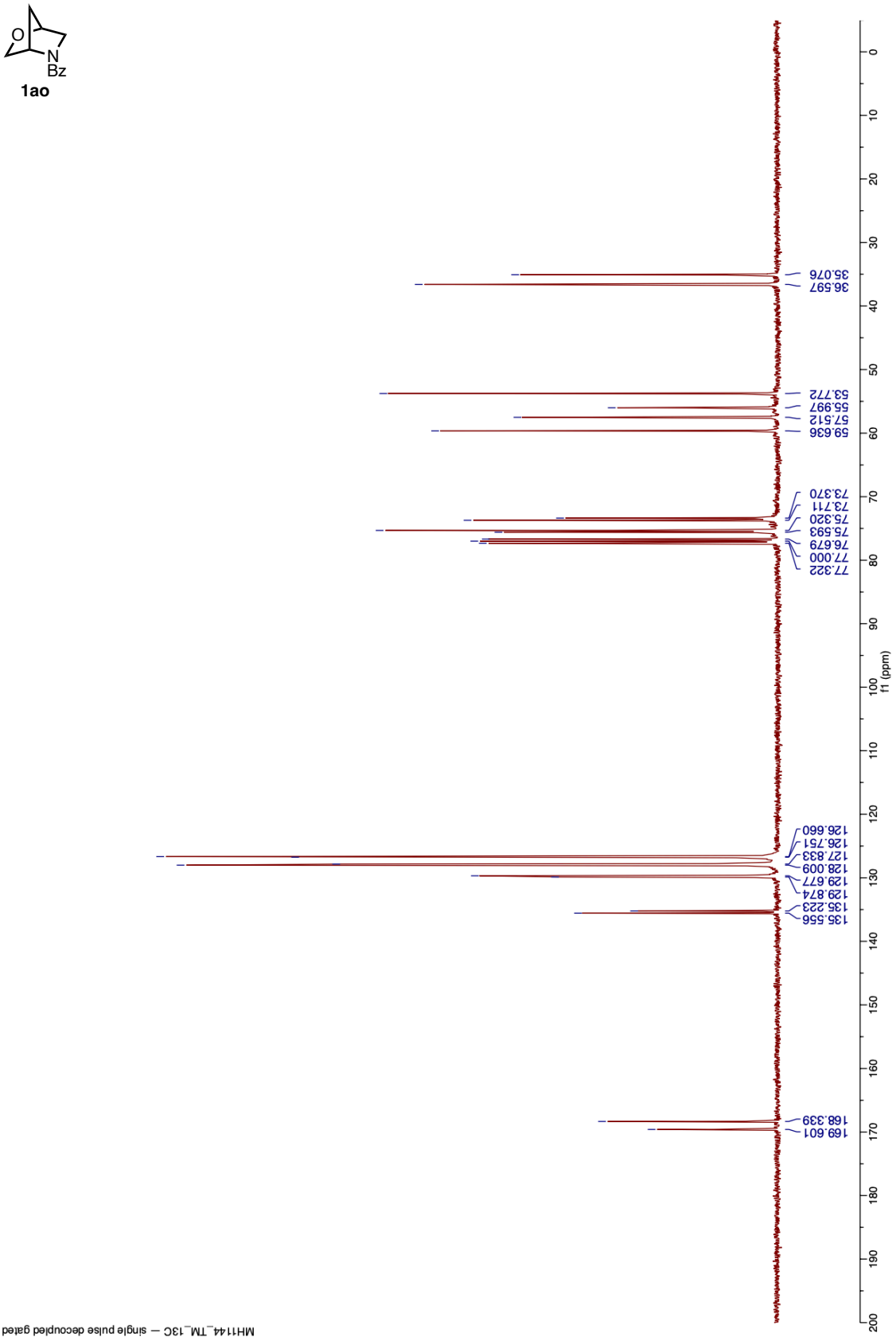
$^{13}C\{^{1}H\}$ NMR of 1am (101 MHz, $CDCl_3$, 323 K)



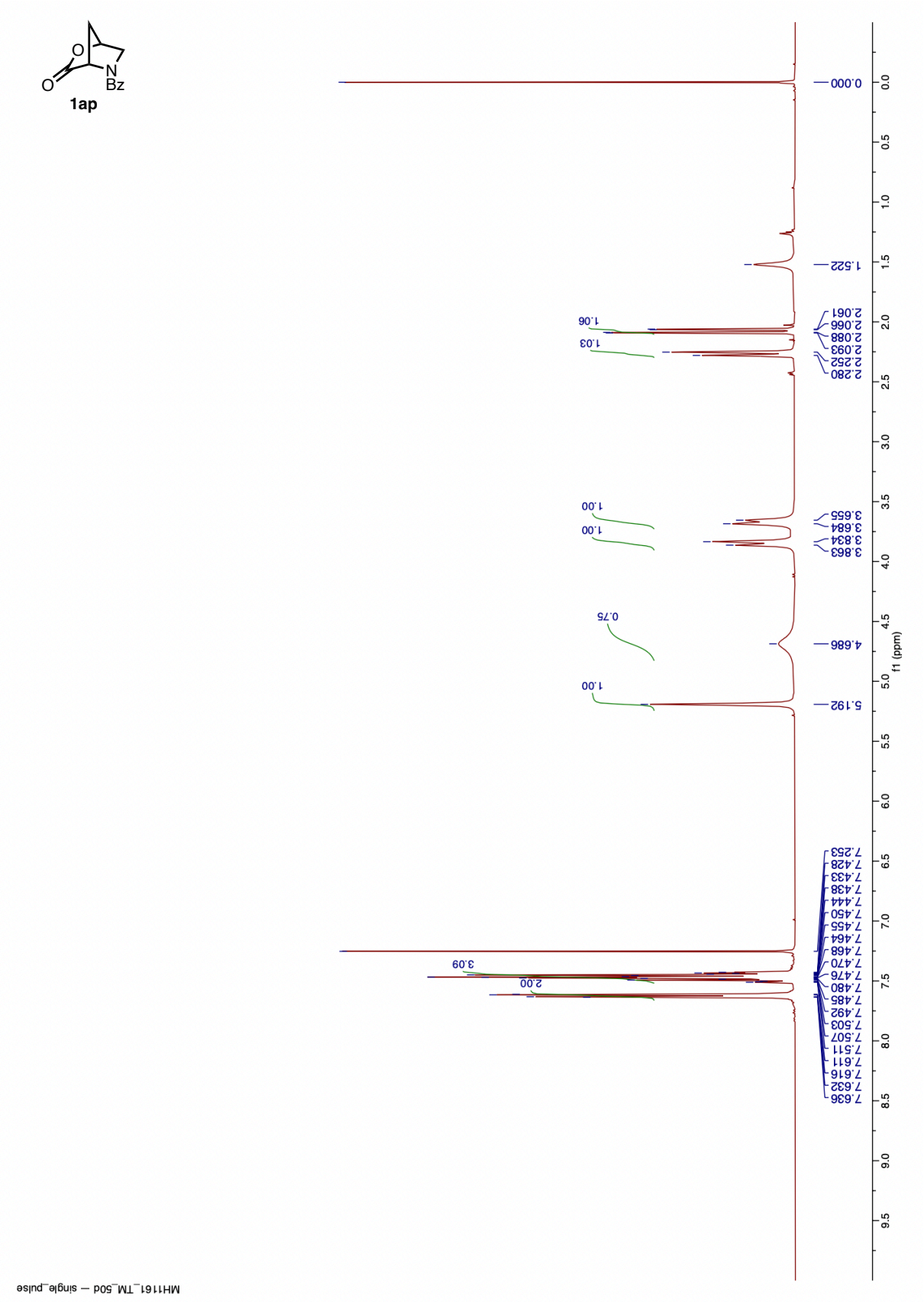
^{1}H NMR of 1ao (400 MHz, $CDCl_3$)



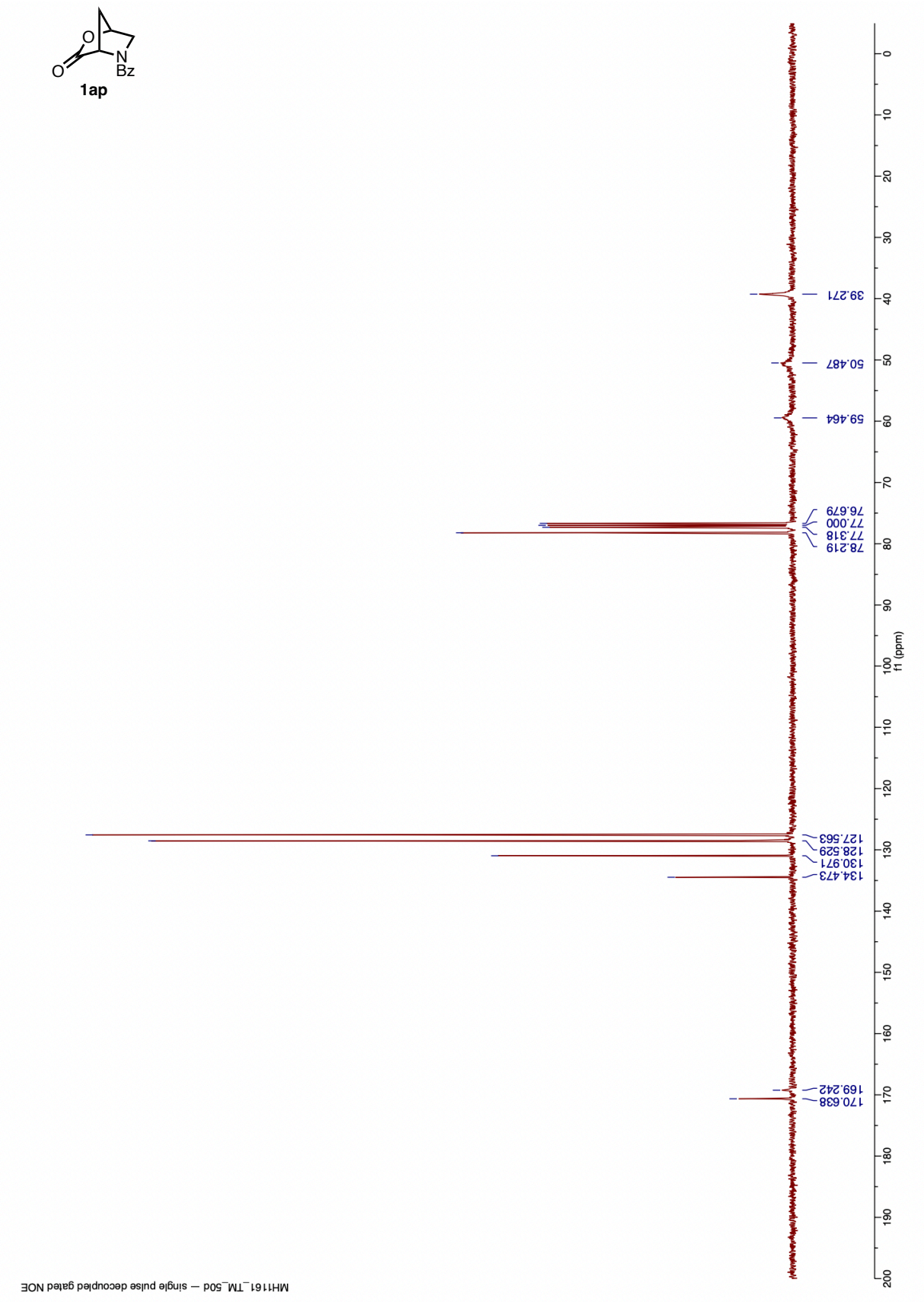
$^{13}C\{^{1}H\}$ NMR of 1ao (101 MHz, $CDCl_3$)



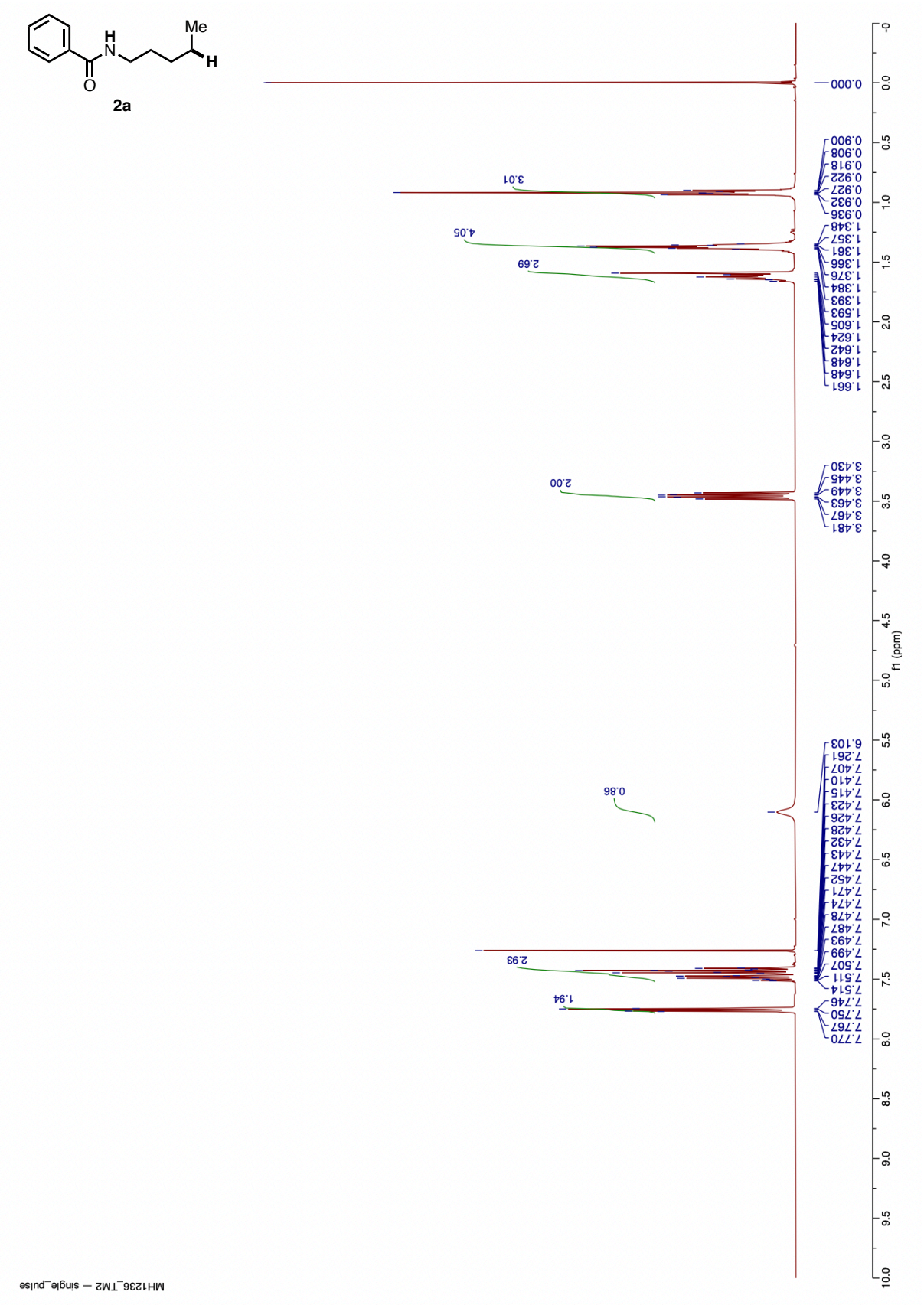
^{1}H NMR of 1ap (400 MHz, $CDCl_3$, 323 K)



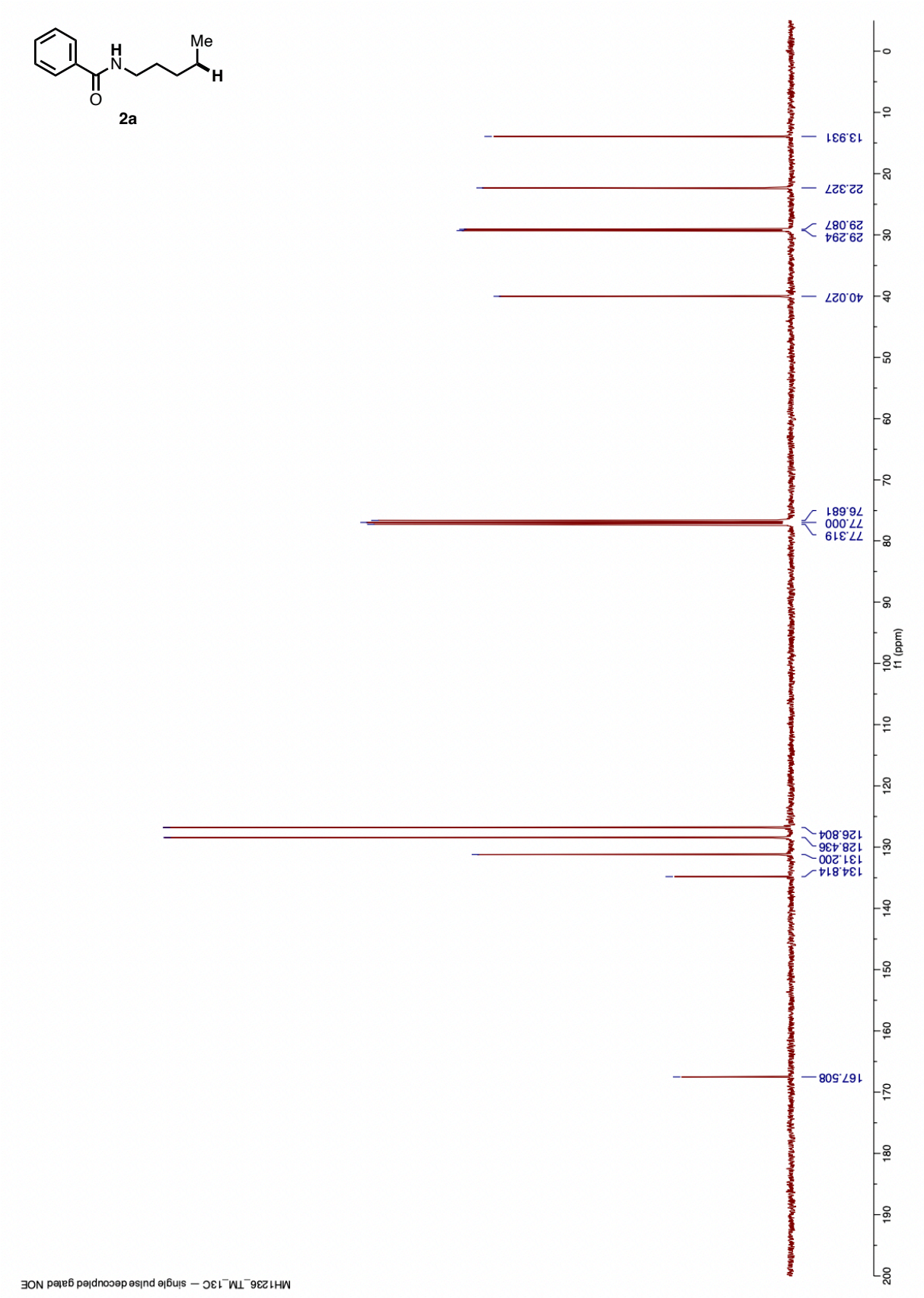
$^{13}C\{^{1}H\}$ NMR of 1ap (101 MHz, $CDCl_3$, 323 K)



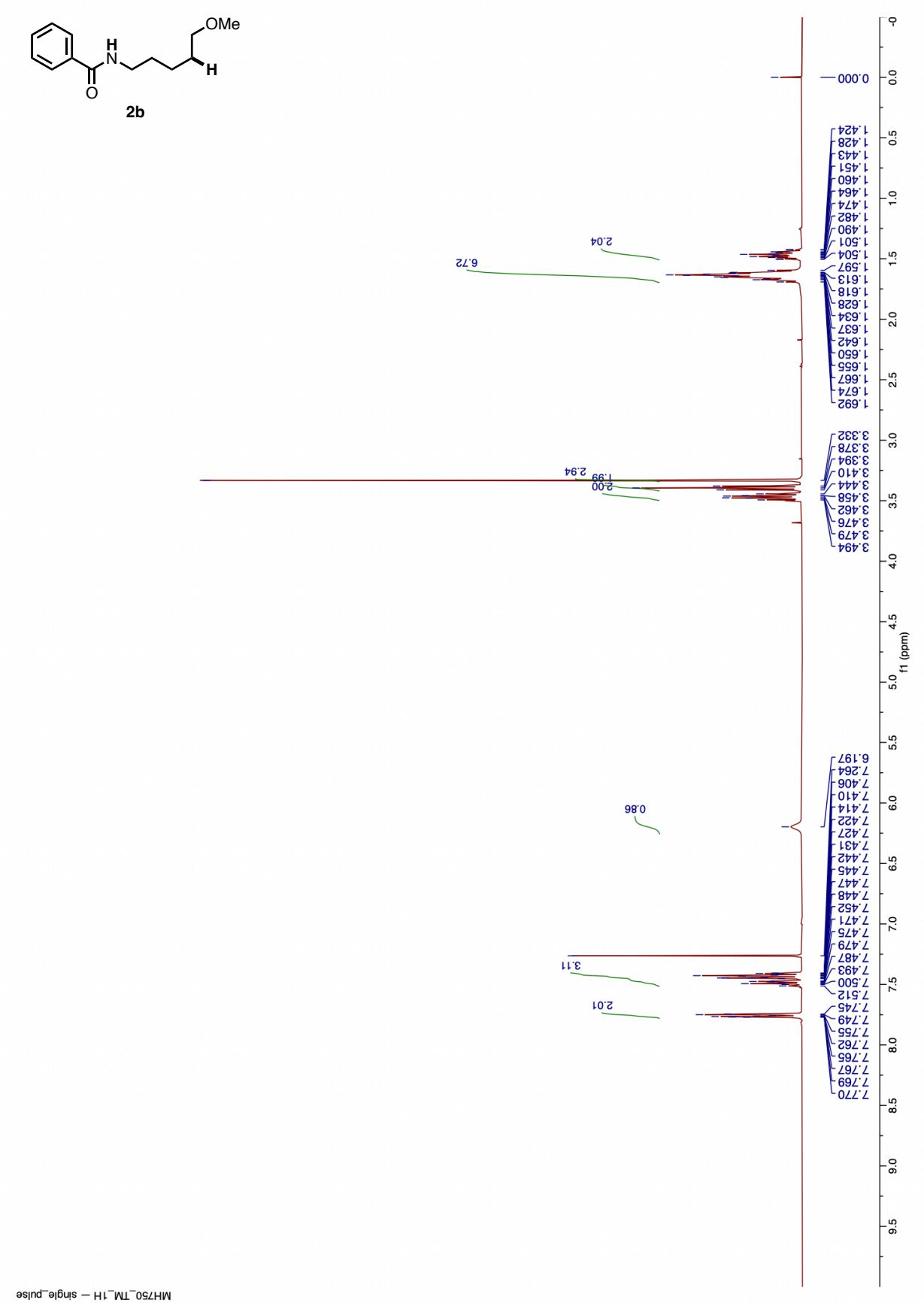
^{1}H NMR of 2a (400 MHz, $CDCl_3$)



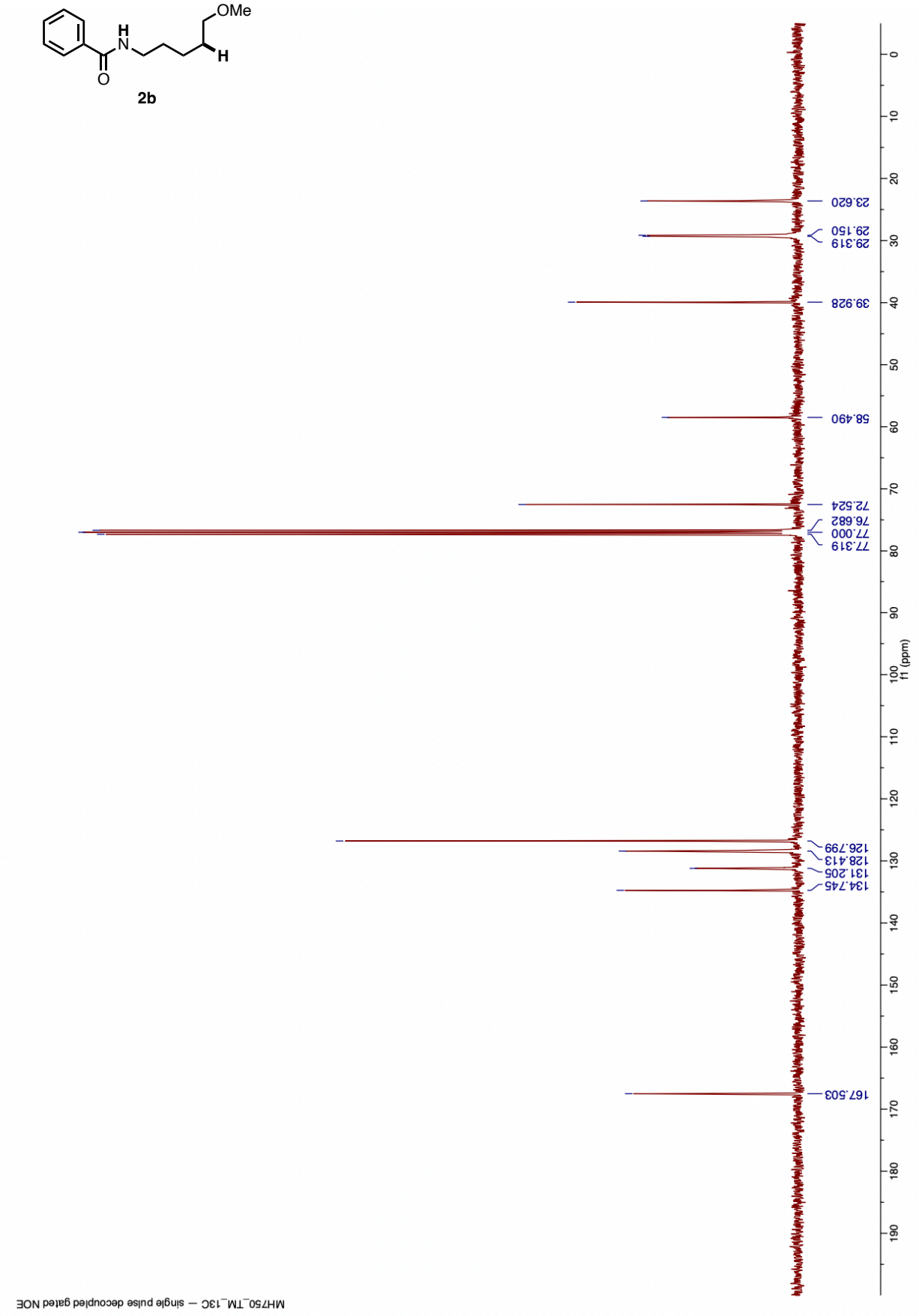
$^{13}C\{^{1}H\}$ NMR of 2a (101 MHz, $CDCl_3$)



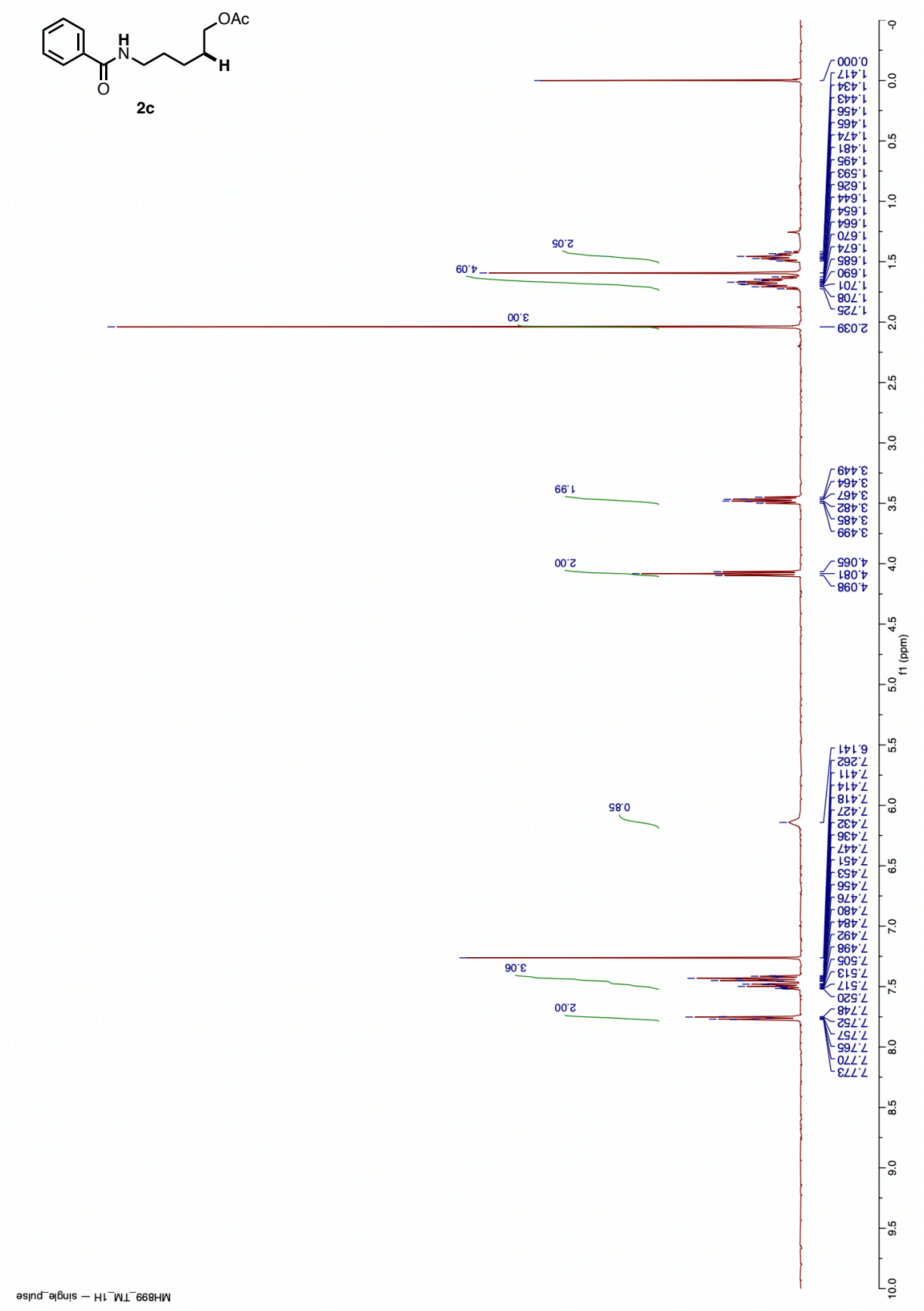
^{1}H NMR of 2b (400 MHz, $CDCl_3$)



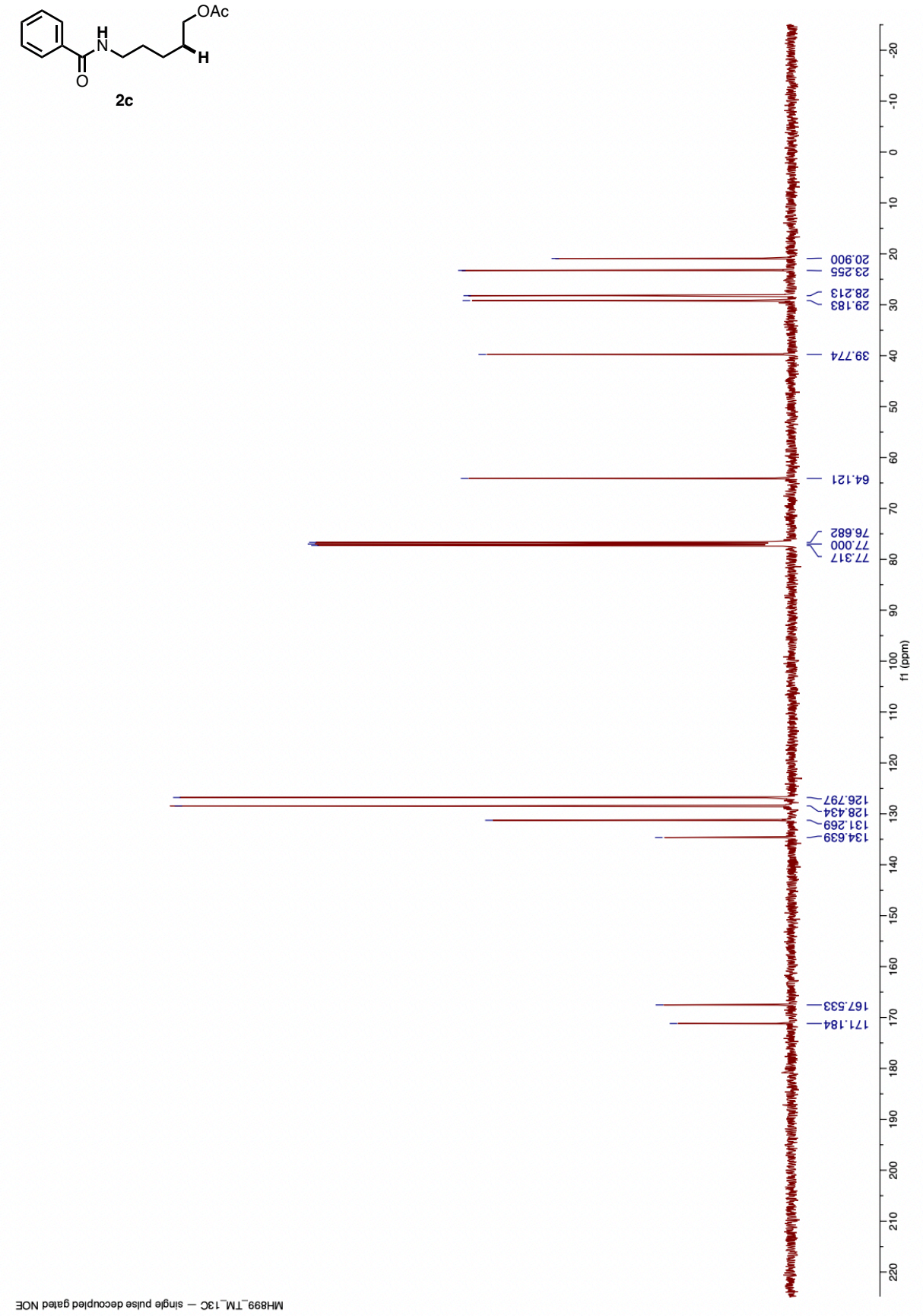
$^{13}C\{^{1}H\}$ NMR of 2b (101 MHz, $CDCl_3$)



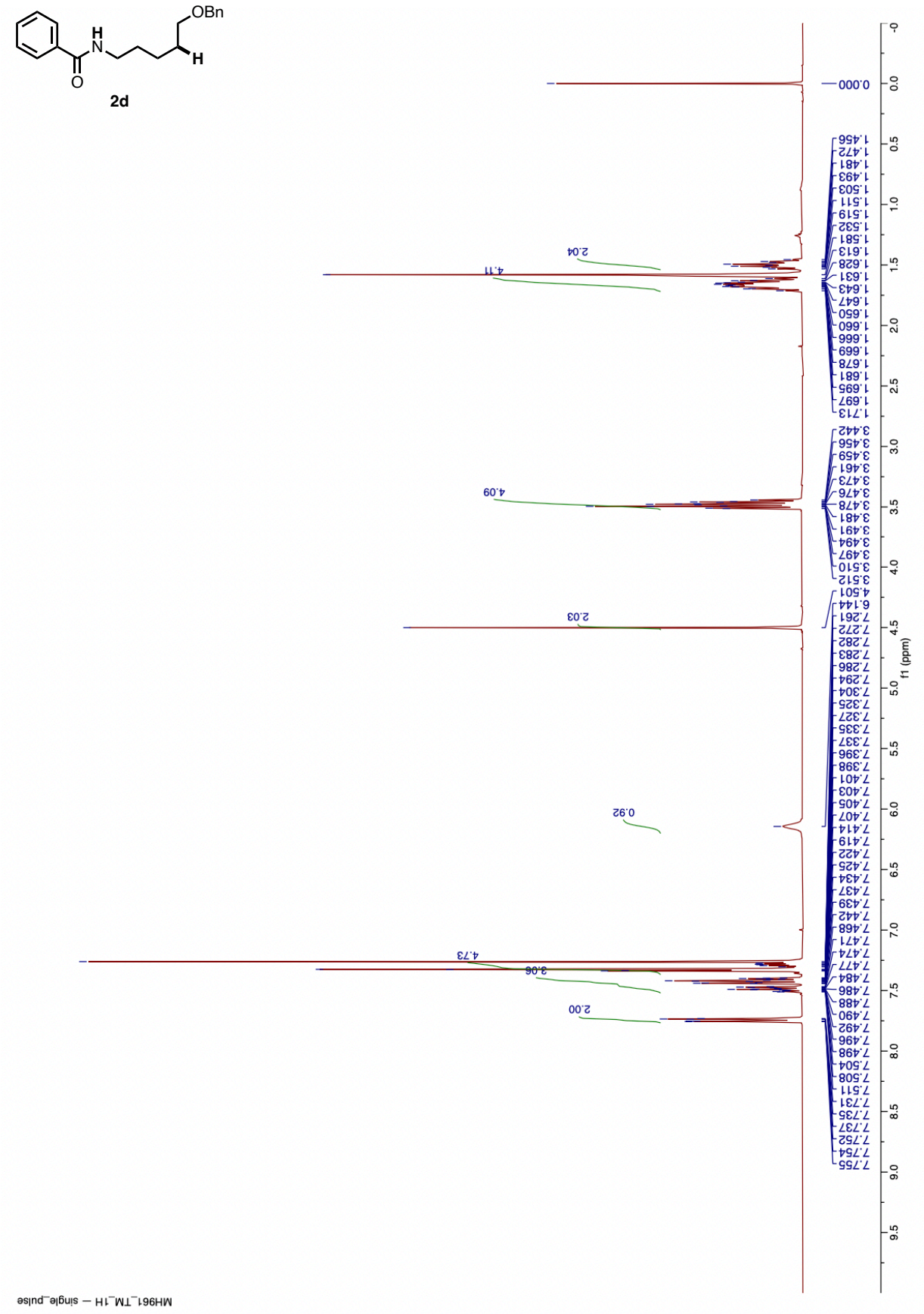
^{1}H NMR of 2c (400 MHz, $CDCl_3$)



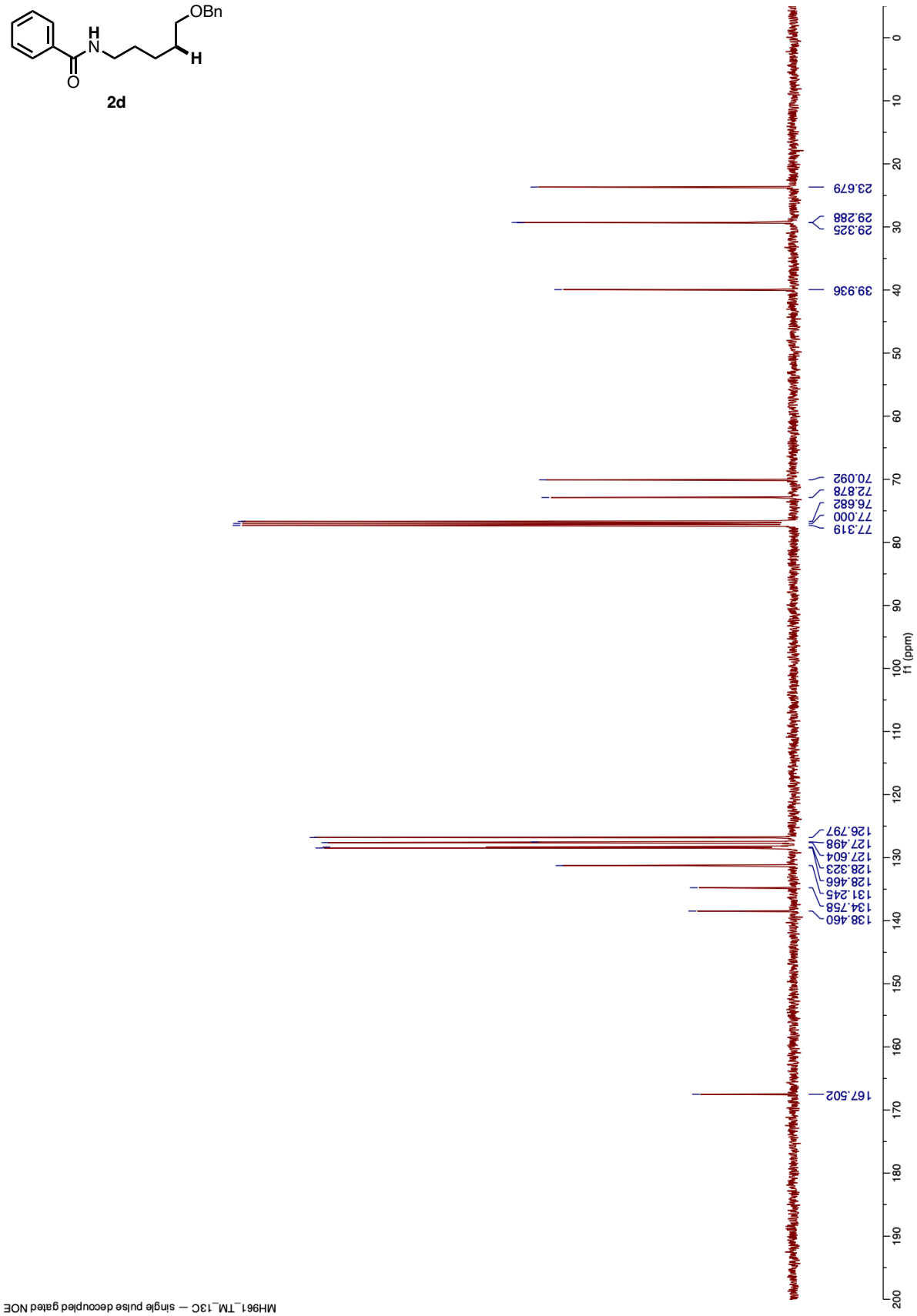
$^{13}C\{^{1}H\}$ NMR of 2c (101 MHz, $CDCl_3$)



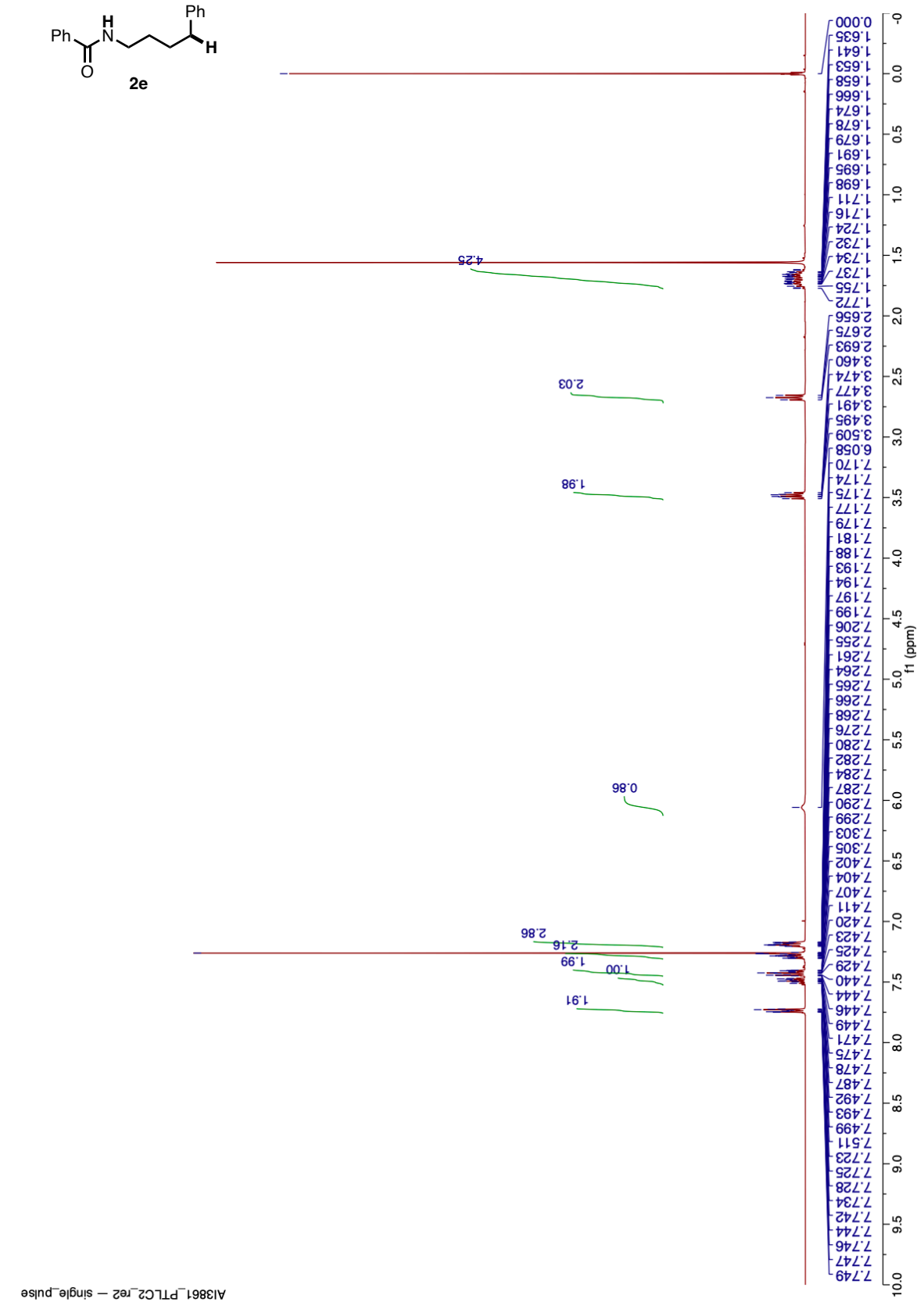
^{1}H NMR of 2d (400 MHz, $CDCl_3$)



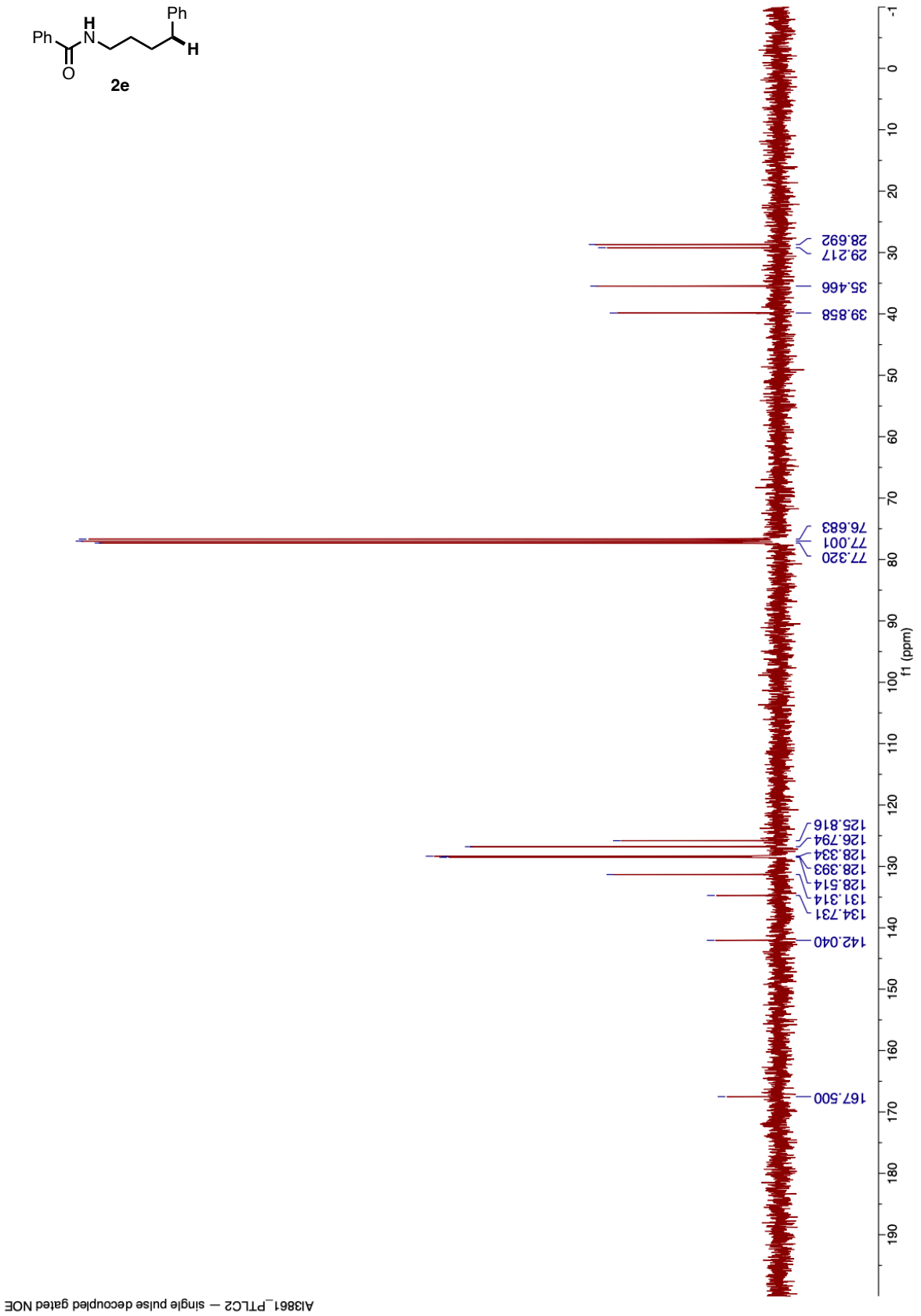
$^{13}C\{^{1}H\}$ NMR of 2d (101 MHz, $CDCl_3$)



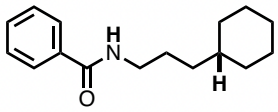
^{1}H NMR of 2e (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 2e (101 MHz, $CDCl_3$)

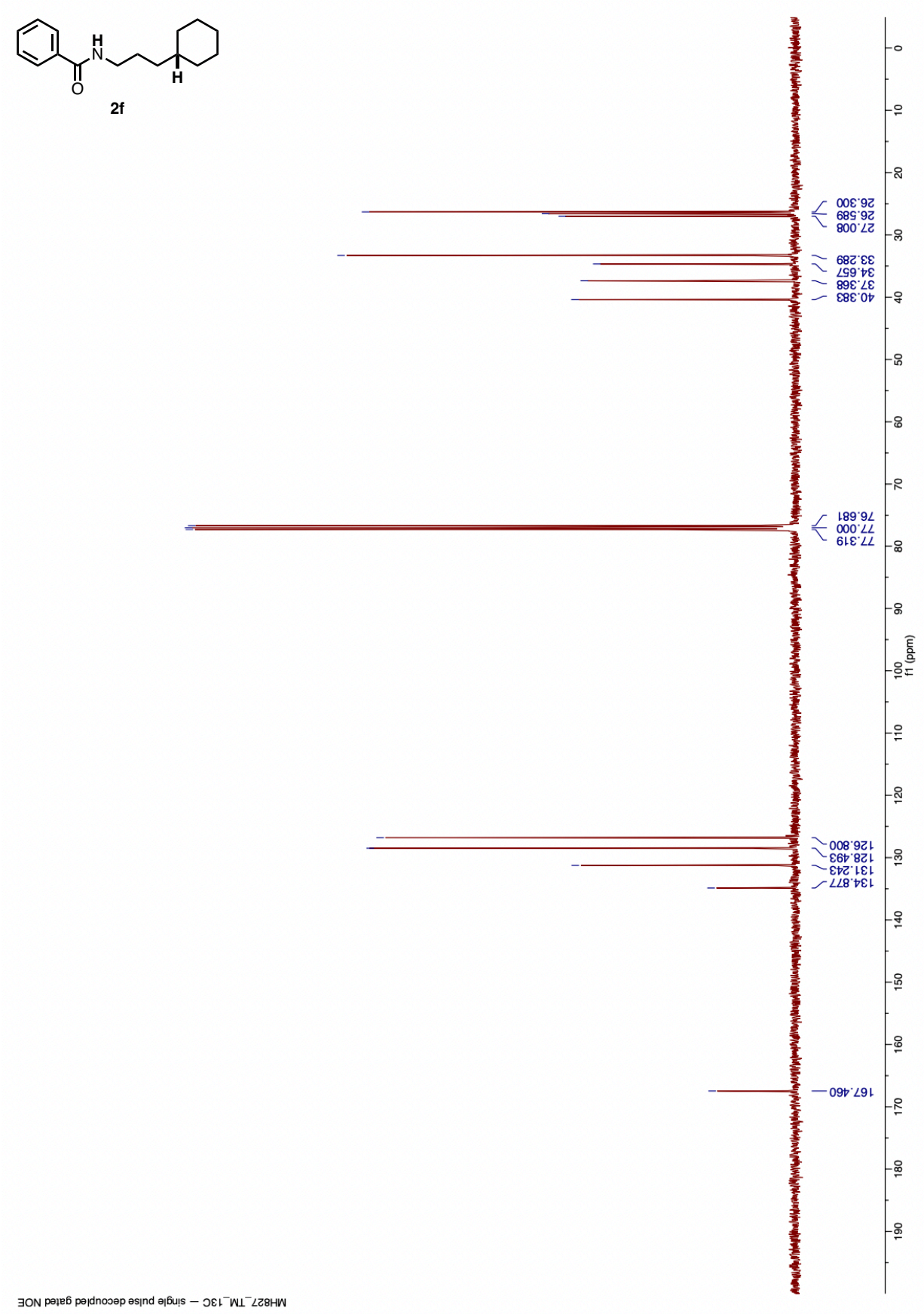


^{1}H NMR of 2f (400 MHz, $CDCl_3$)

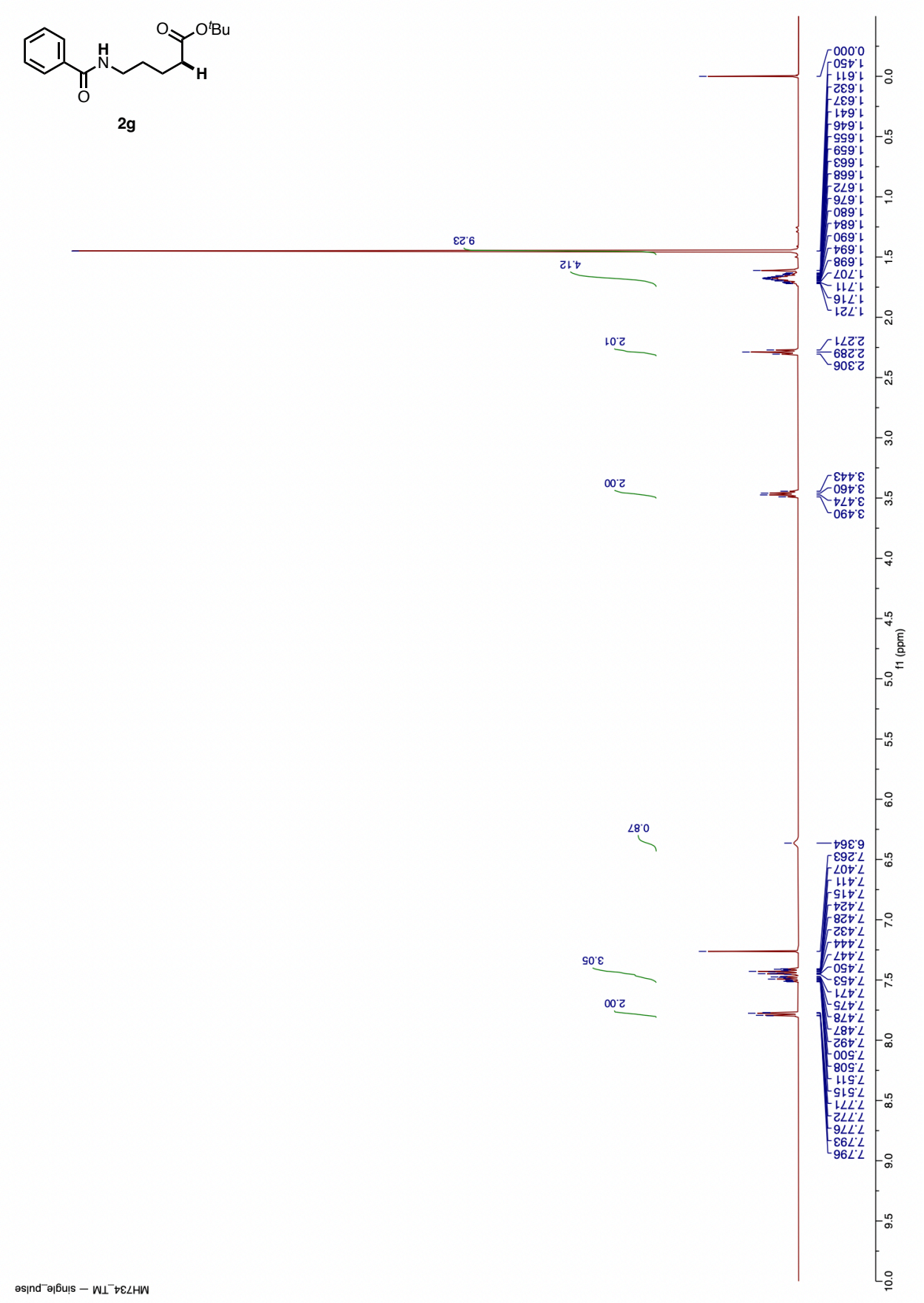


2f

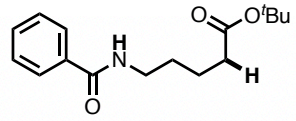
$^{13}C\{^{1}H\}$ NMR of 2f (101 MHz, $CDCl_3$)



^{1}H NMR of 2g (400 MHz, $CDCl_3$)

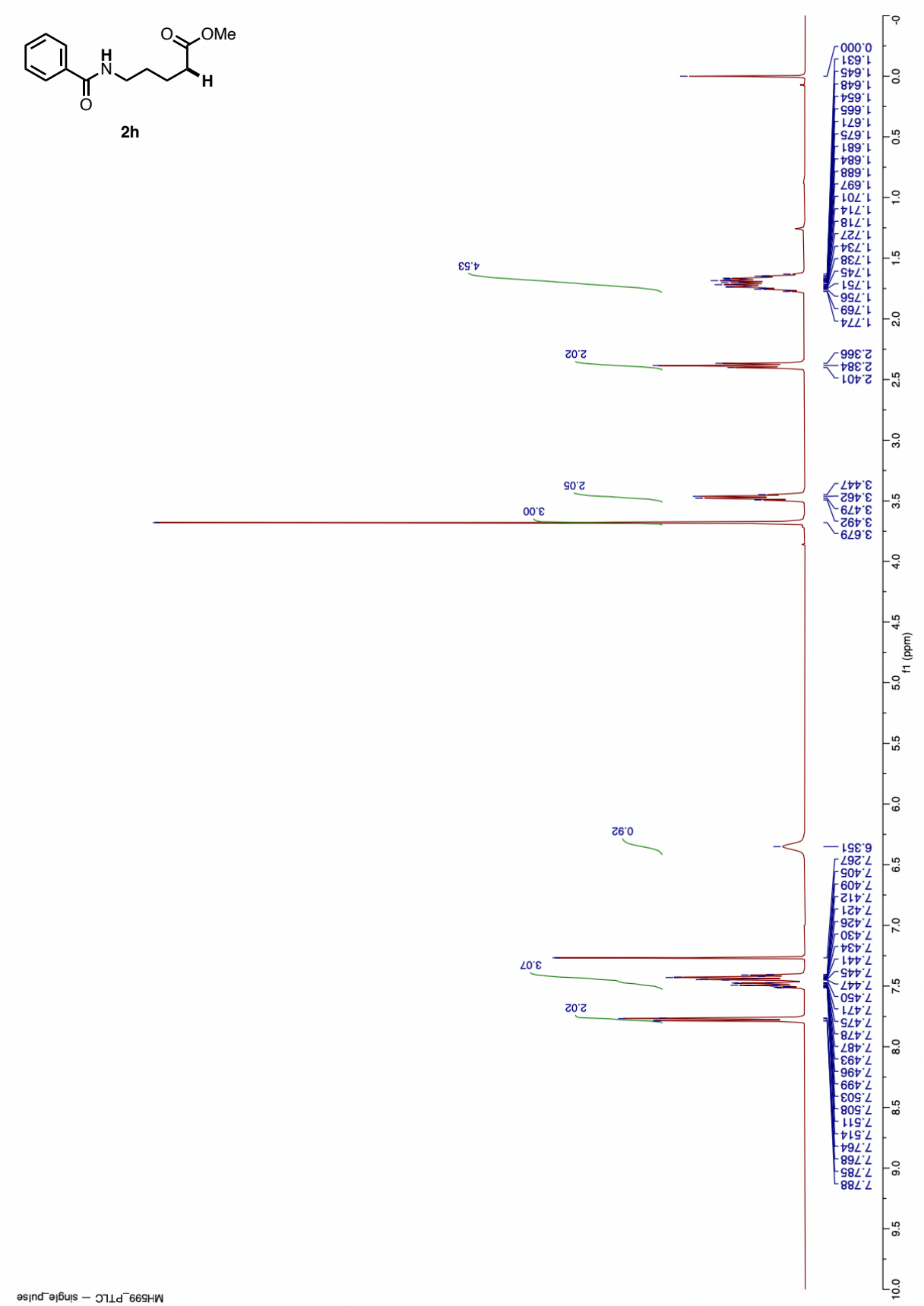


$^{13}C\{^{1}H\}$ NMR of 2g (101 MHz, $CDCl_3$)

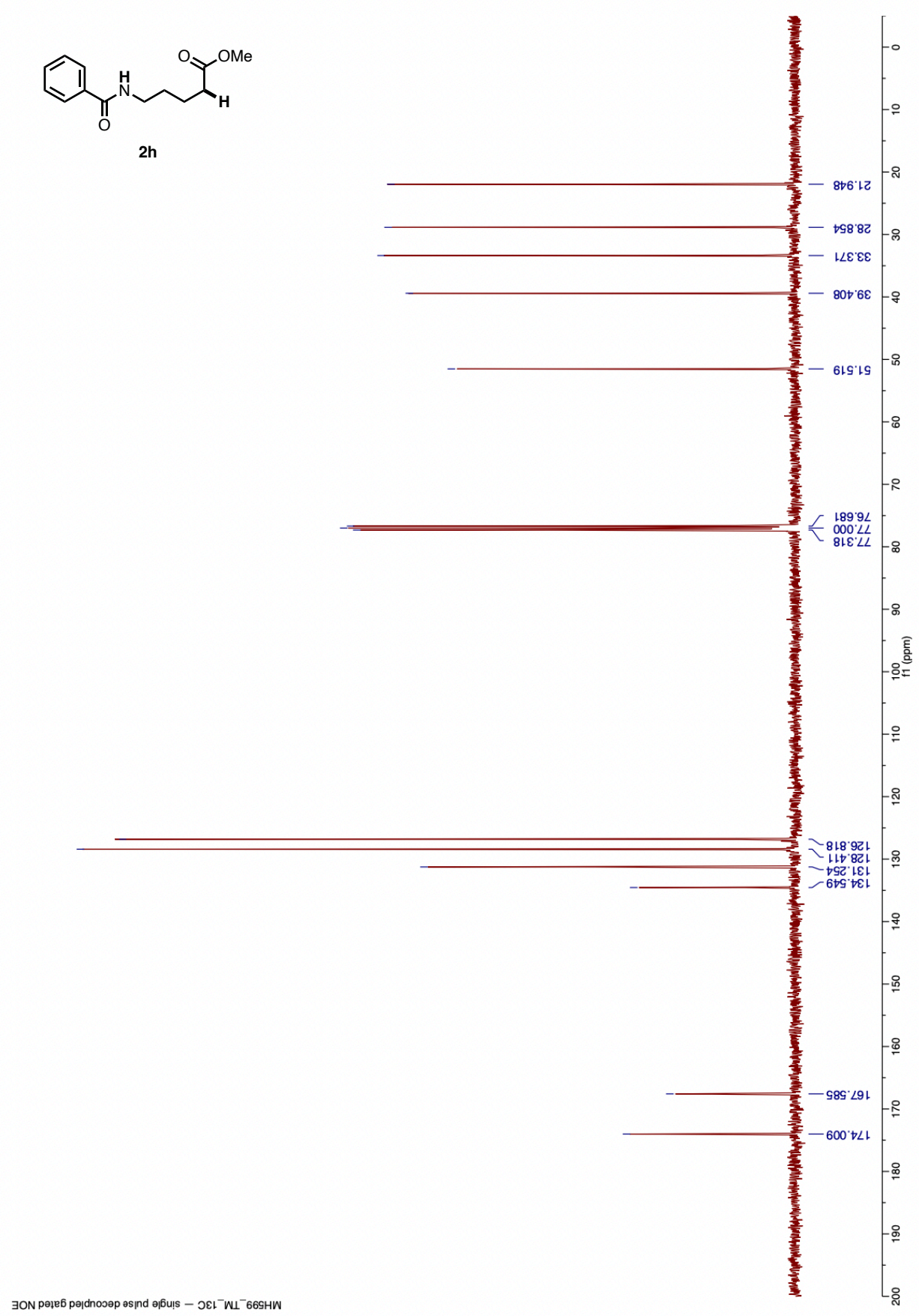


2g

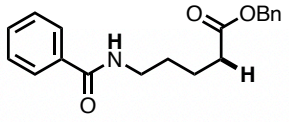
^{1}H NMR of 2h (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 2h (101 MHz, $CDCl_3$)

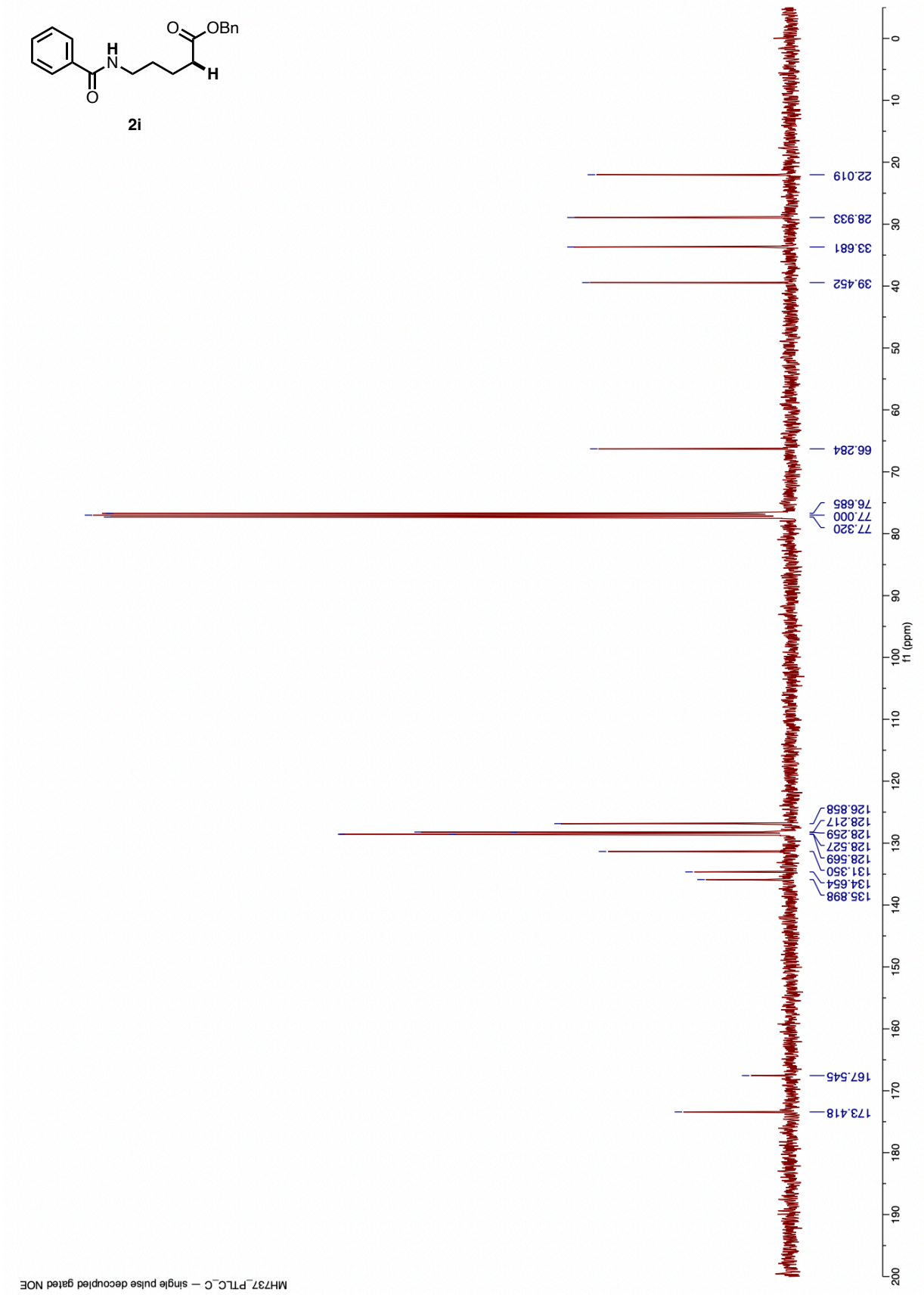


^{1}H NMR of 2i (400 MHz, $CDCl_3$)

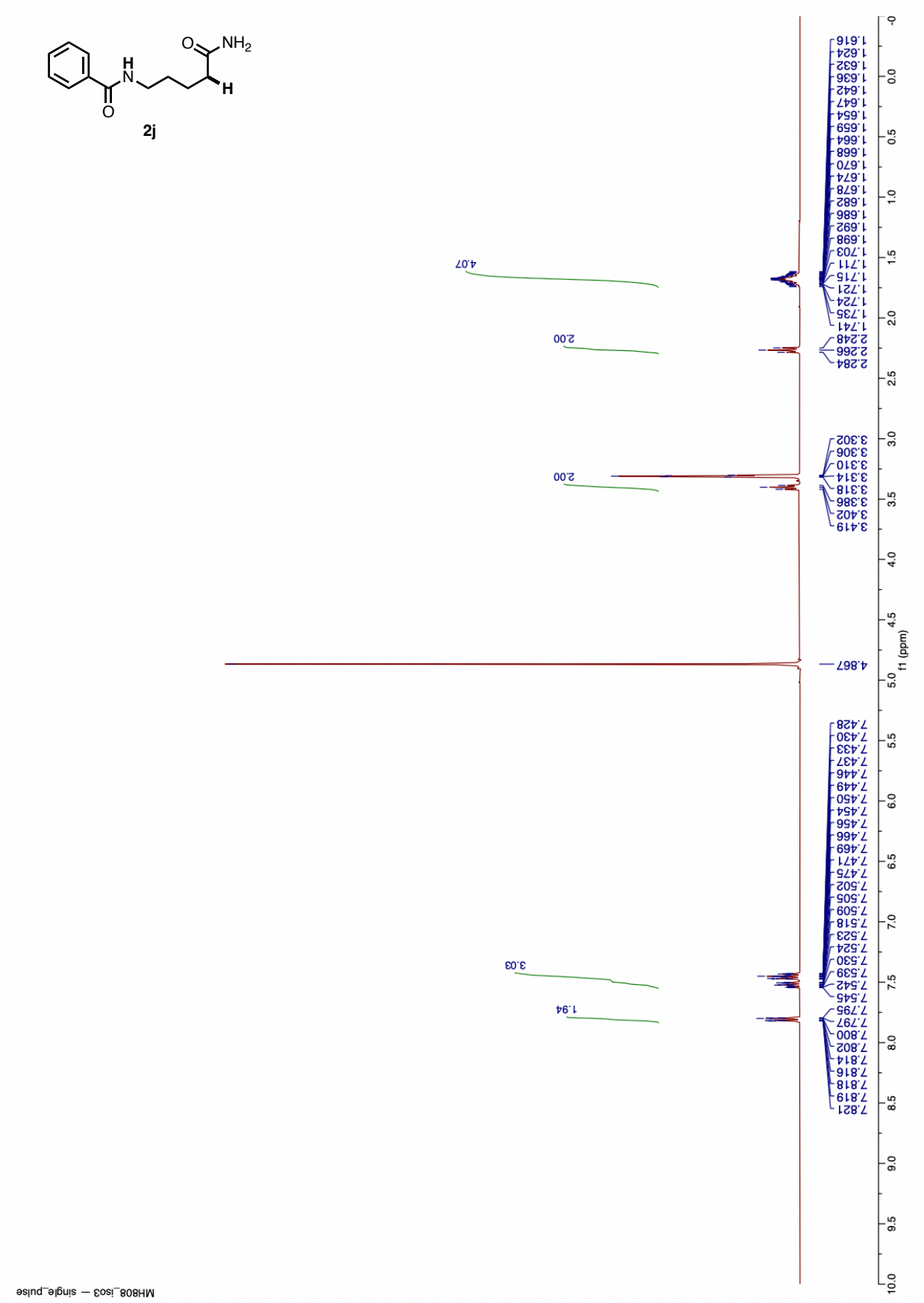


2i

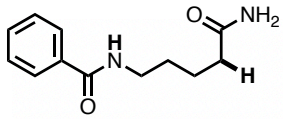
$^{13}C\{^{1}H\}$ NMR of 2i (101 MHz, $CDCl_3$)



^{1}H NMR of 2j (400 MHz, CD_3OD)

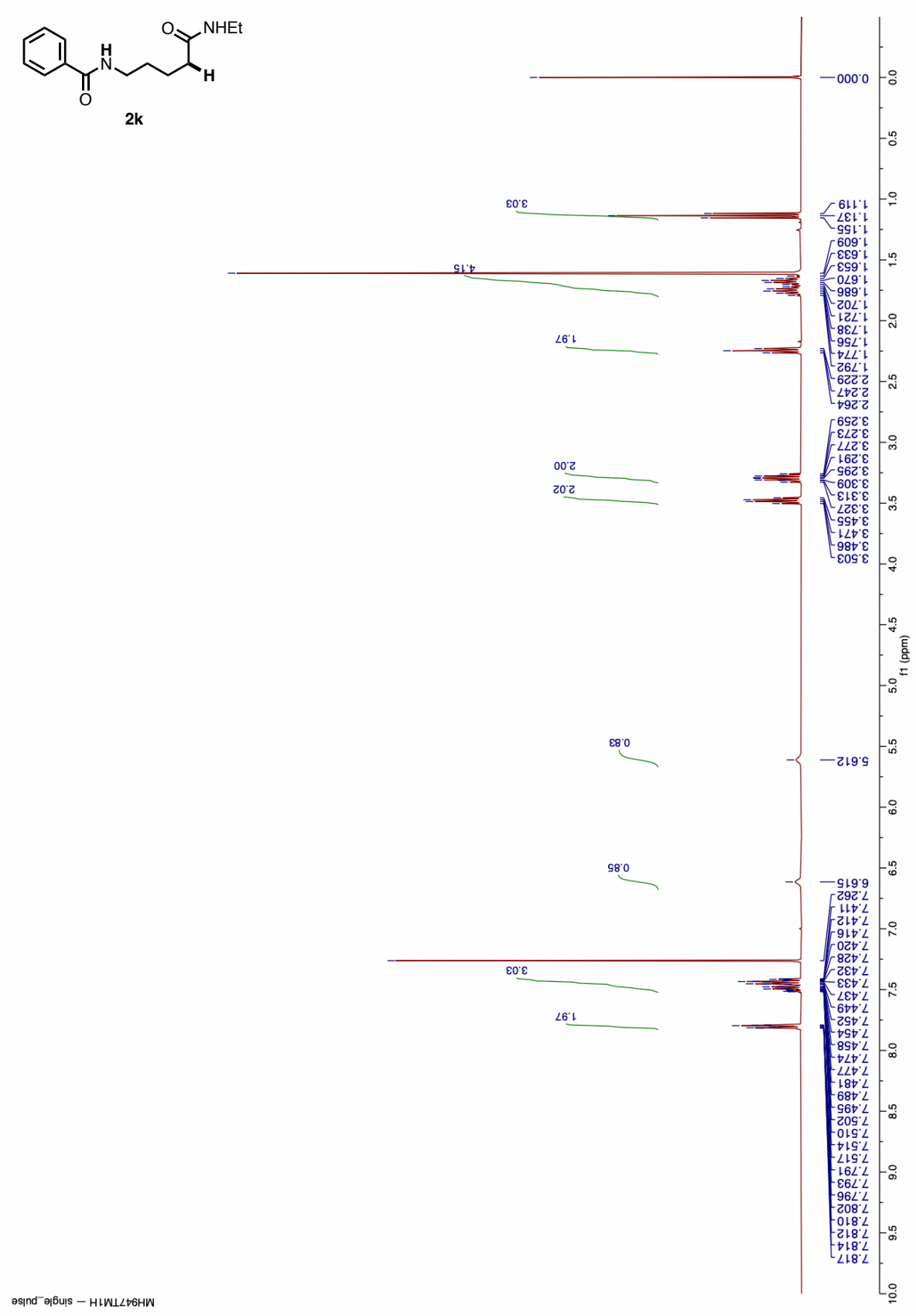


$^{13}C\{^{1}H\}$ NMR of 2j (101 MHz, CD_3OD, 323 K)

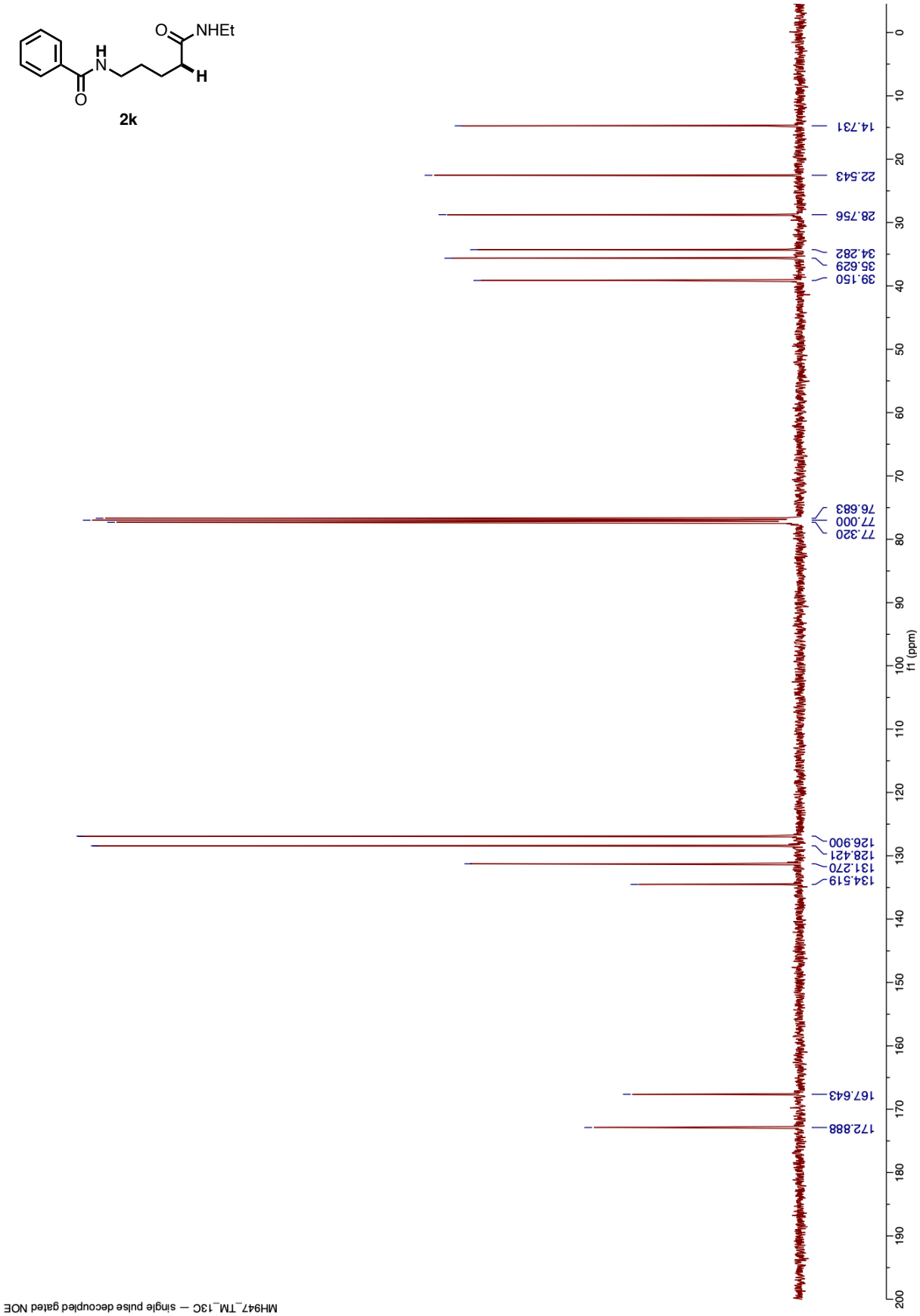


2j

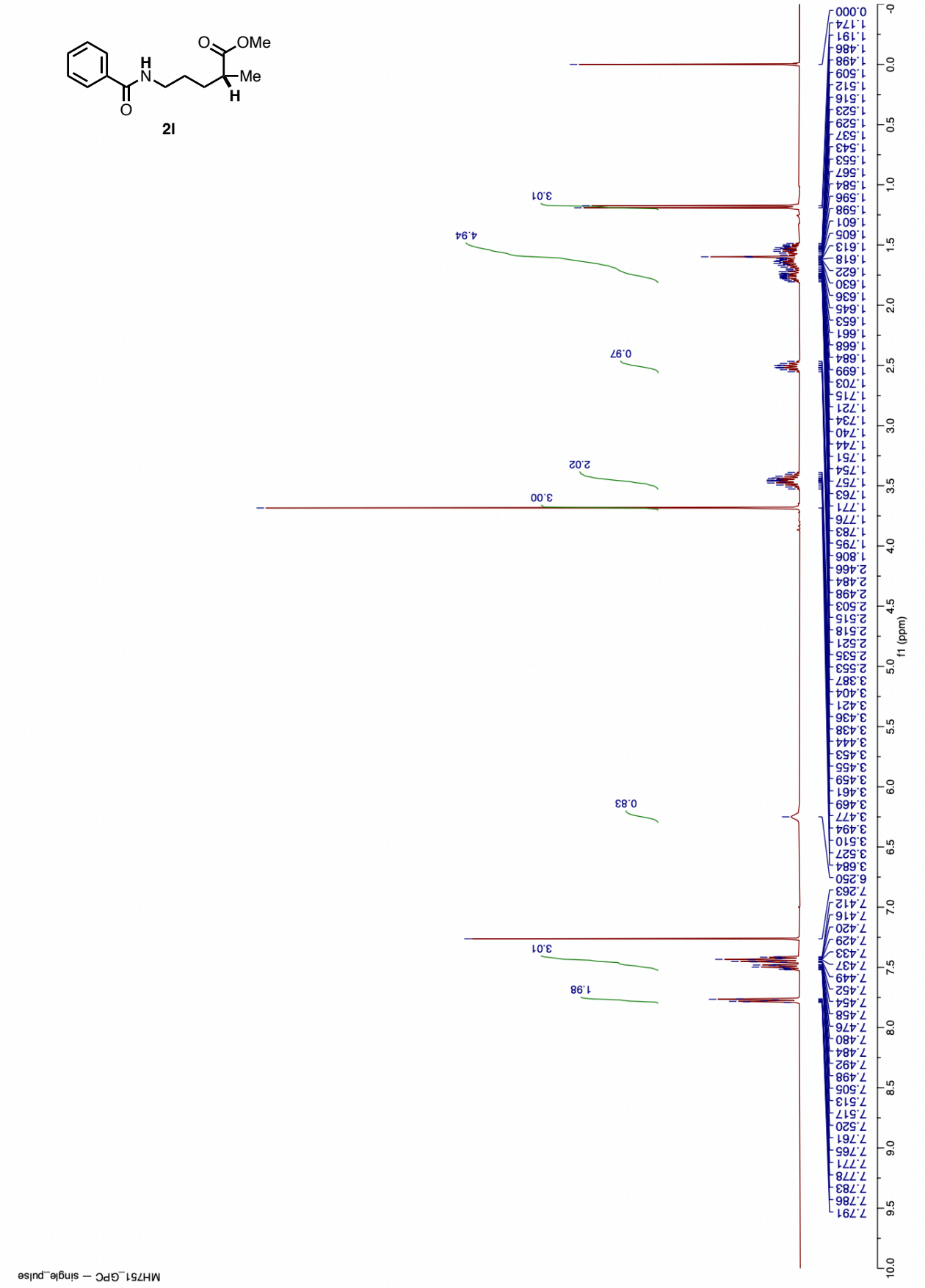
^{1}H NMR of 2k (400 MHz, $CDCl_3$)



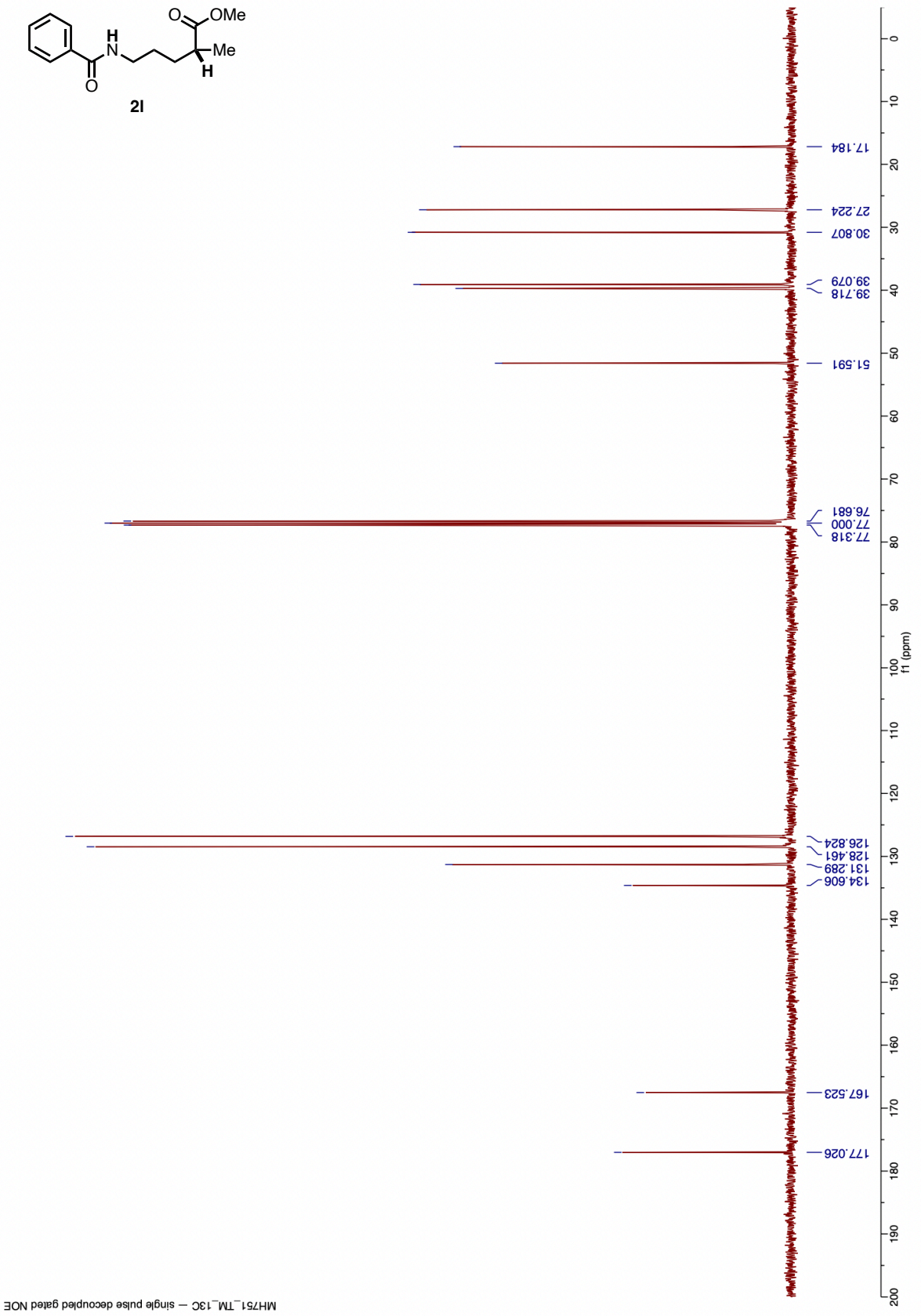
$^{13}C\{^{1}H\}$ NMR of 2k (101 MHz, $CDCl_3$)



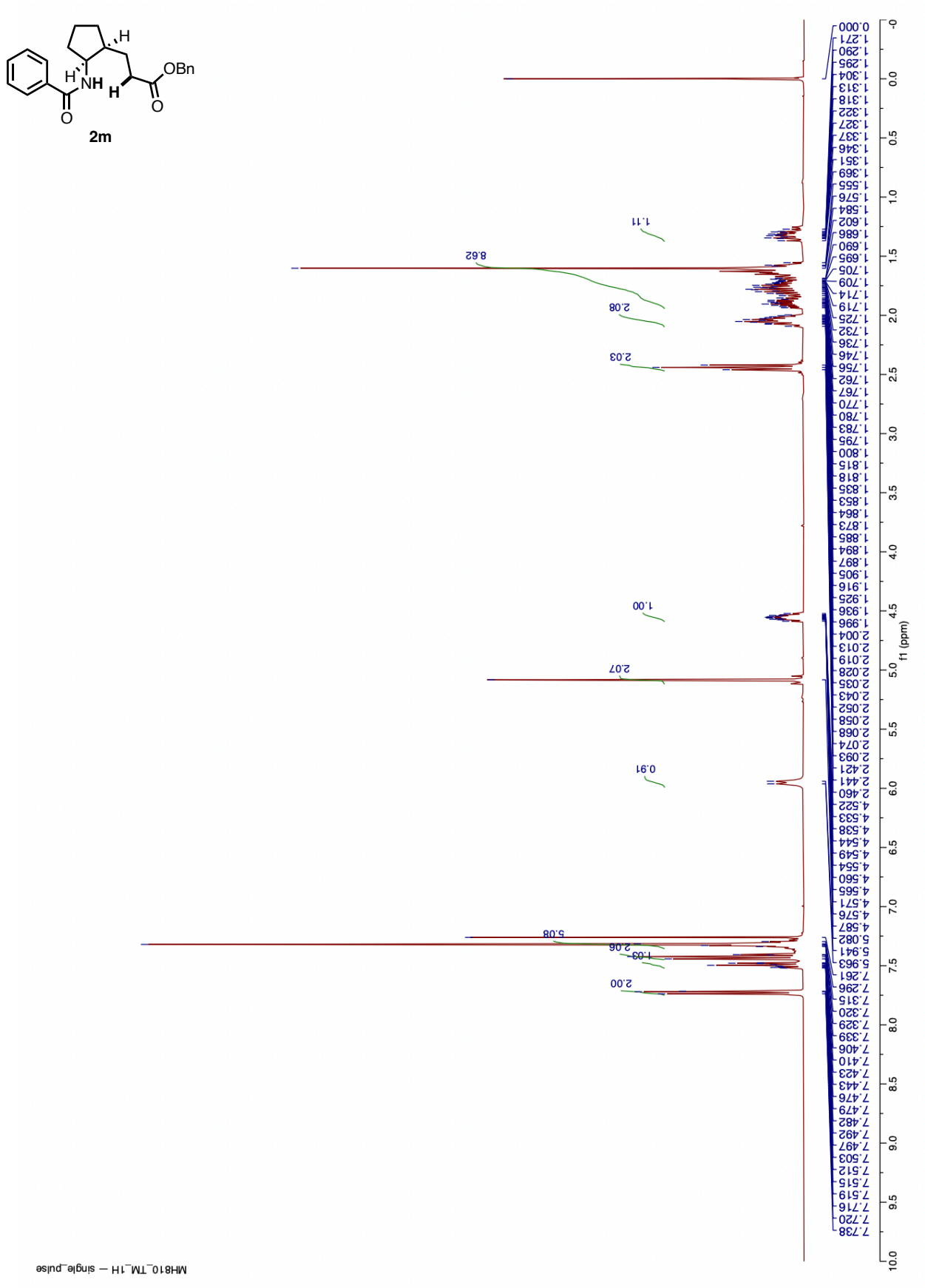
^{1}H NMR of 2l (400 MHz, $CDCl_3$)



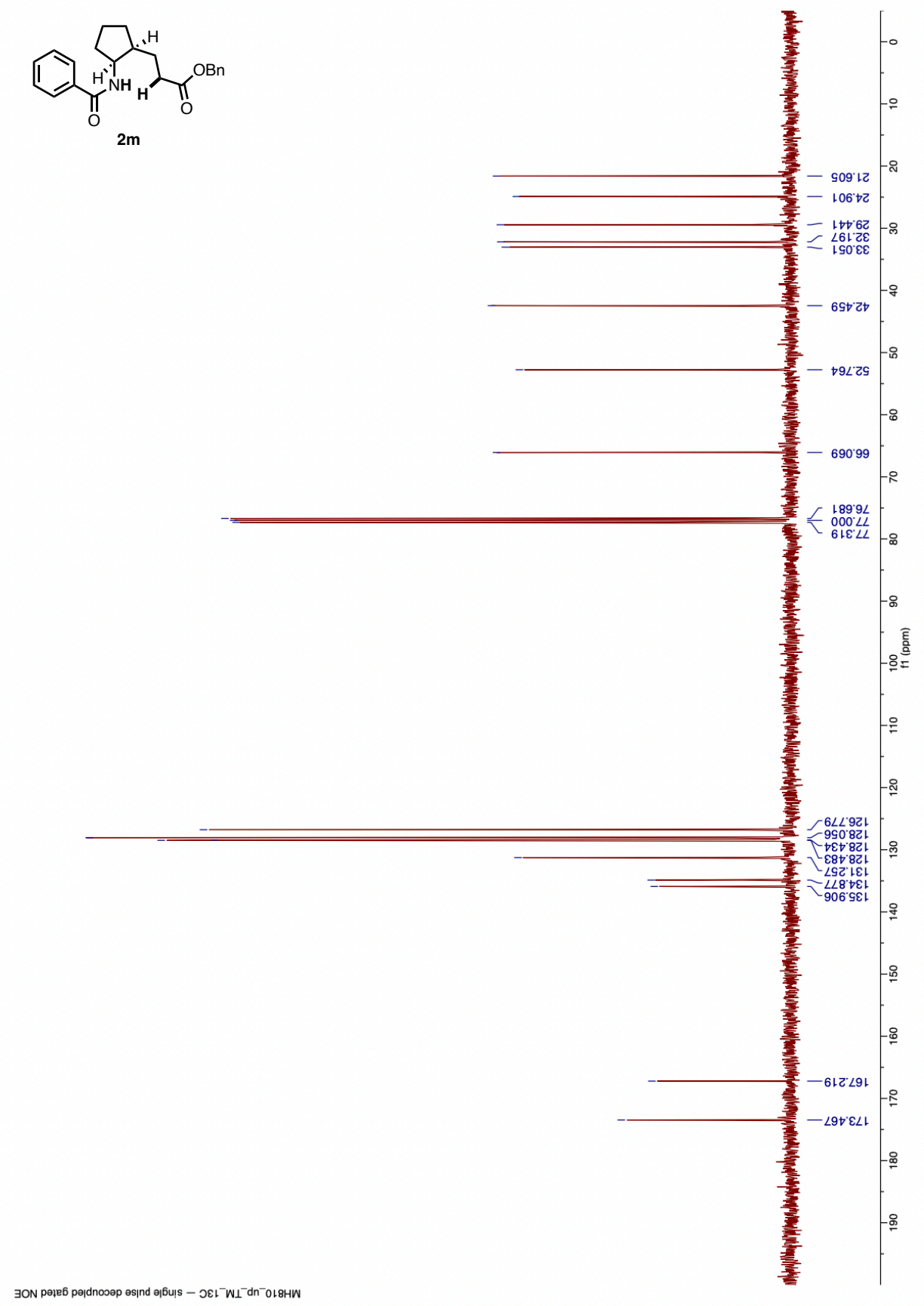
$^{13}C\{^{1}H\}$ NMR of 2l (101 MHz, $CDCl_3$)



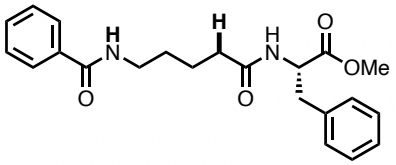
^{1}H NMR of 2m (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 2m (101 MHz, $CDCl_3$)

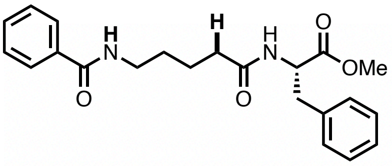


^{1}H NMR of 2n (400 MHz, $CDCl_3$)

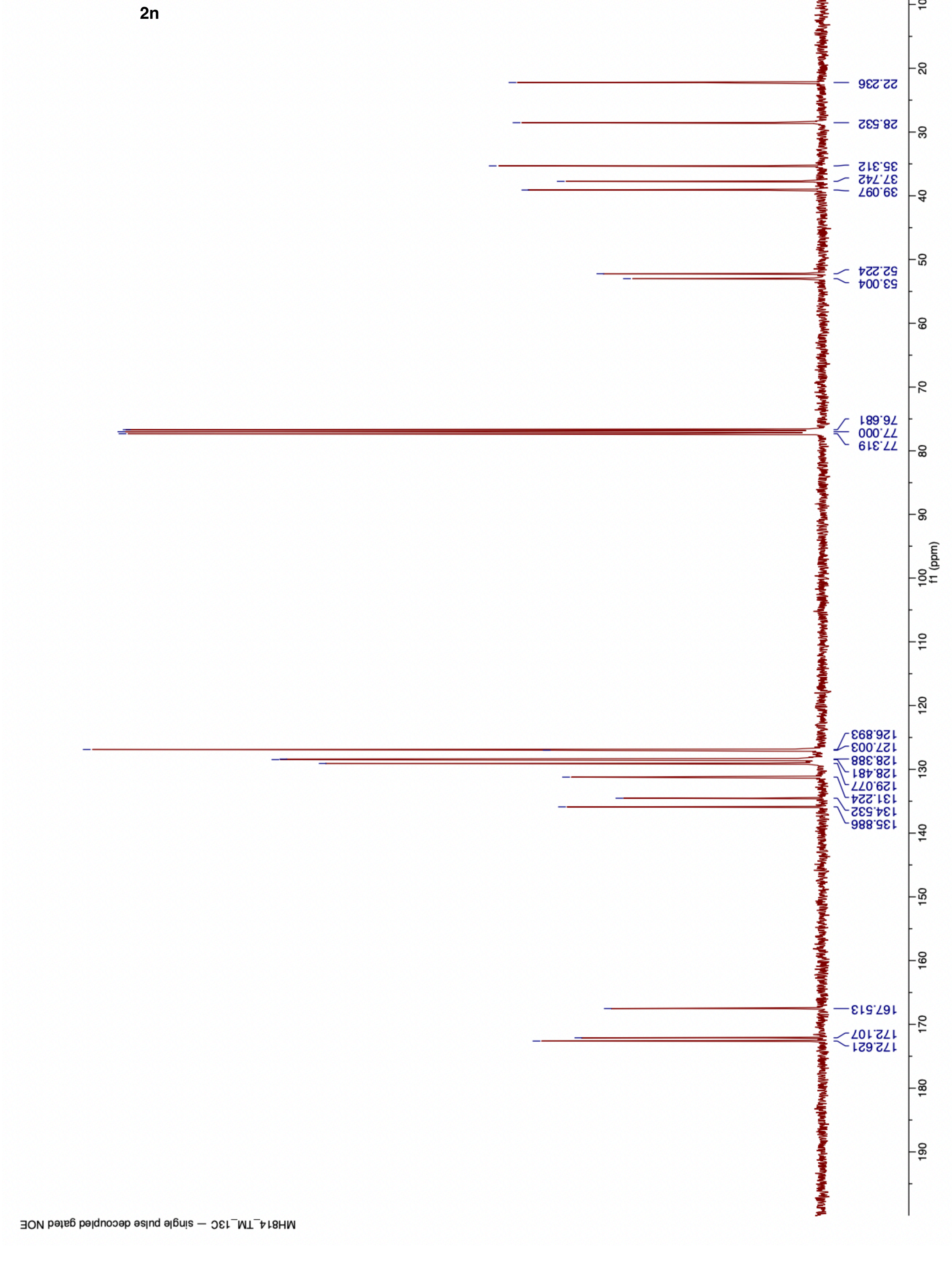


2n

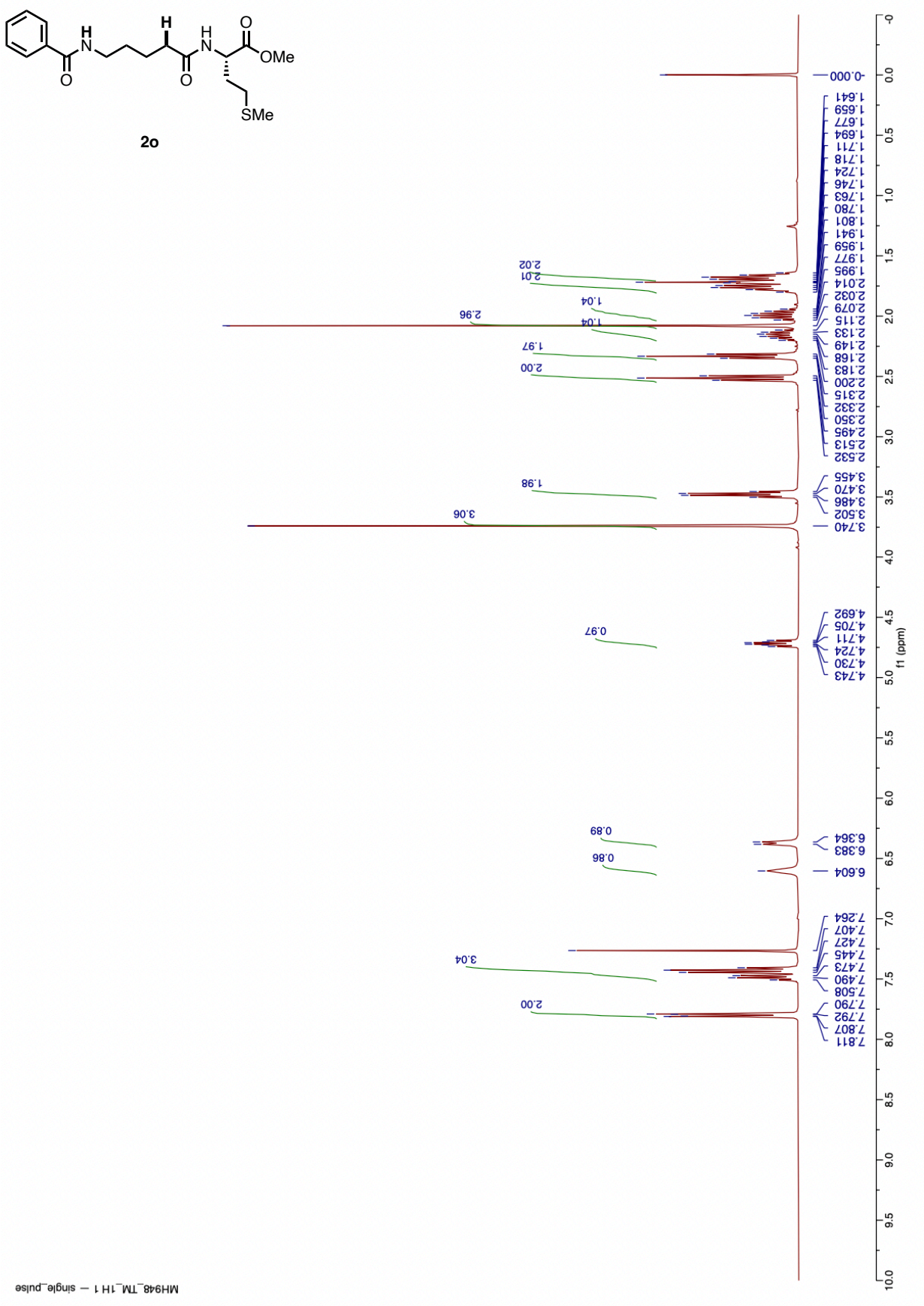
$^{13}C\{^1H\}$ NMR of 2n (101 MHz, $CDCl_3$)



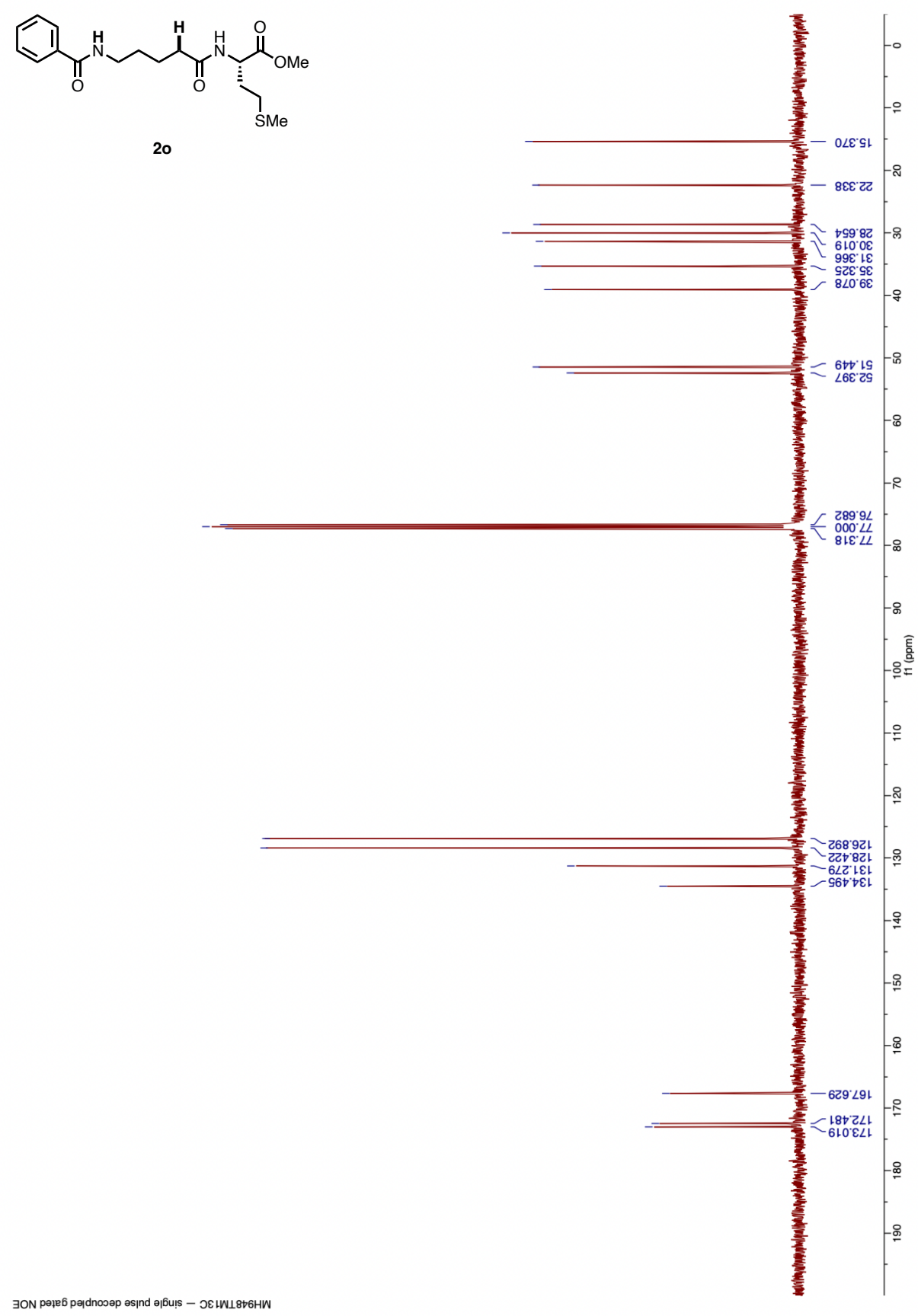
2n



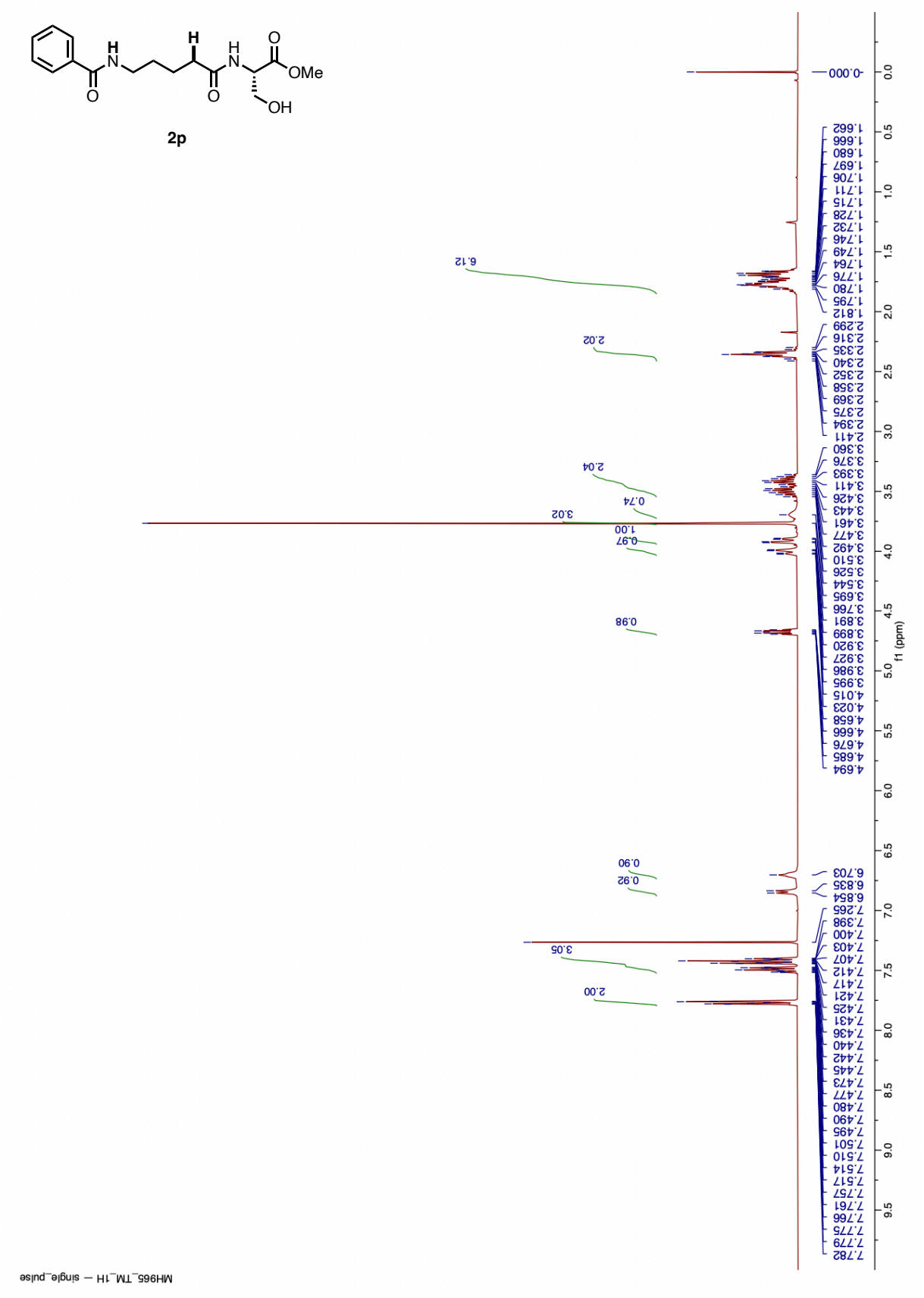
^{1}H NMR of 2o (400 MHz, $CDCl_3$)



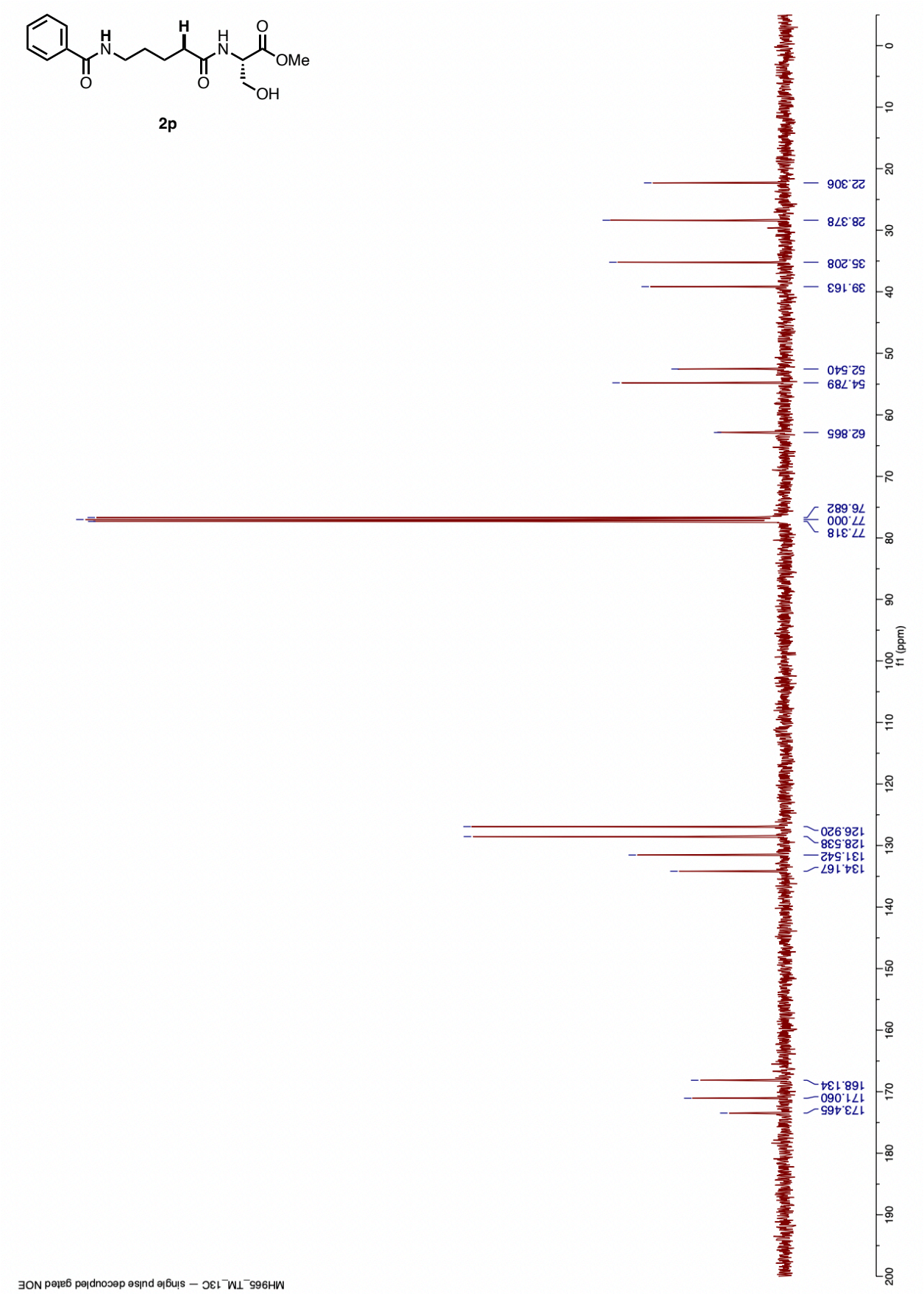
$^{13}C\{^{1}H\}$ NMR of 2o (101 MHz, $CDCl_3$)



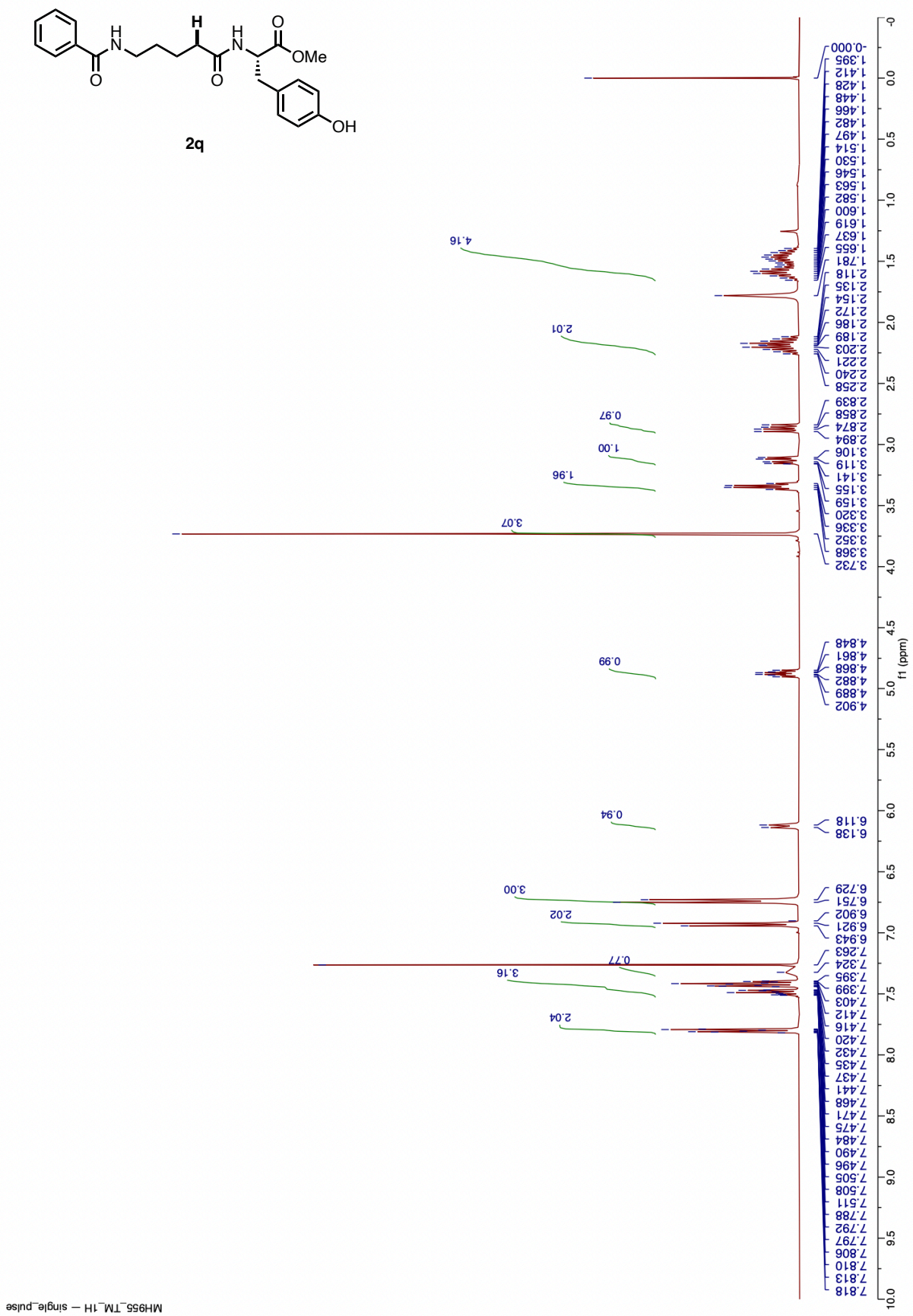
^{1}H NMR of 2p (400 MHz, $CDCl_3$)



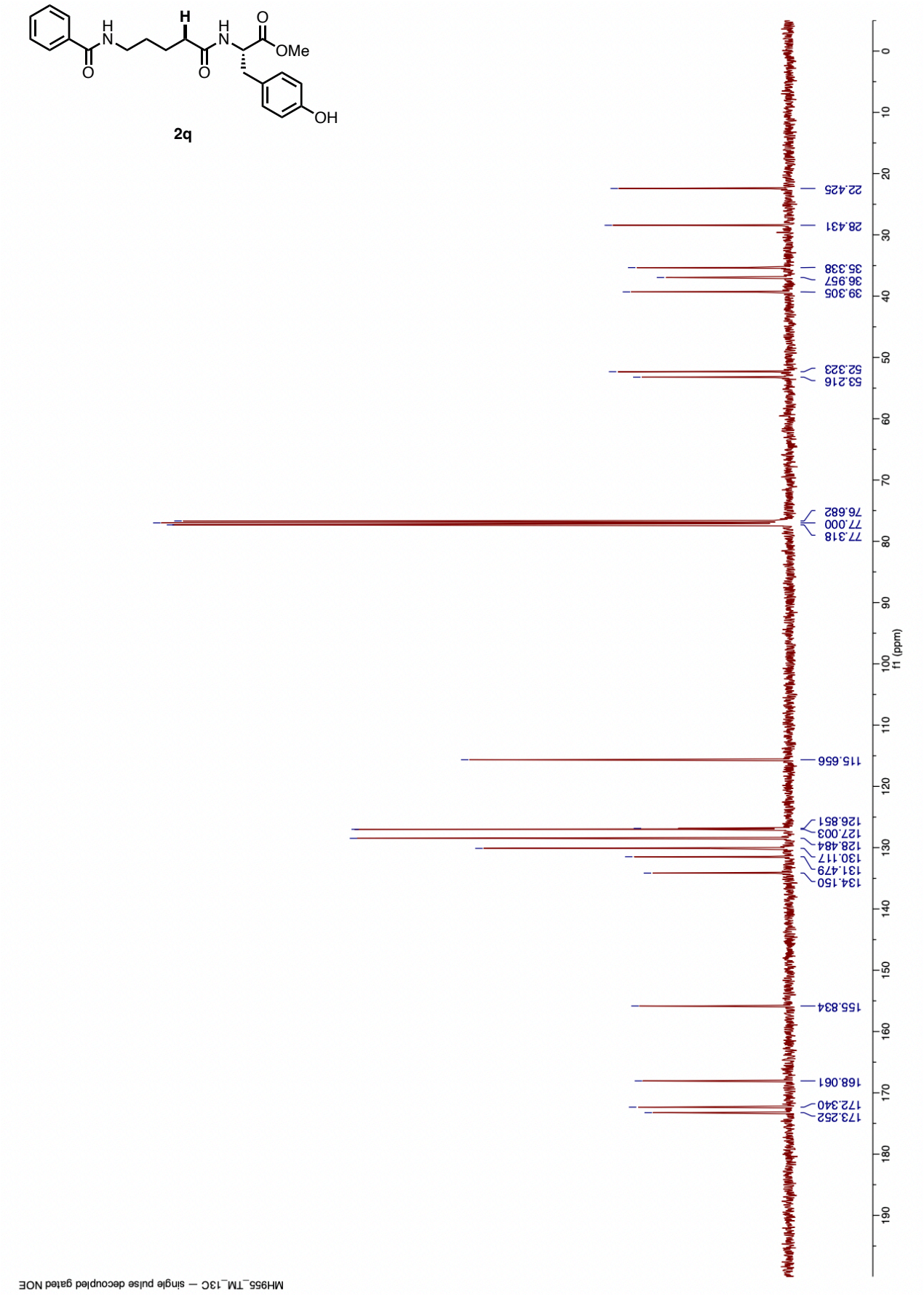
$^{13}C\{^{1}H\}$ NMR of 2p (101 MHz, $CDCl_3$)



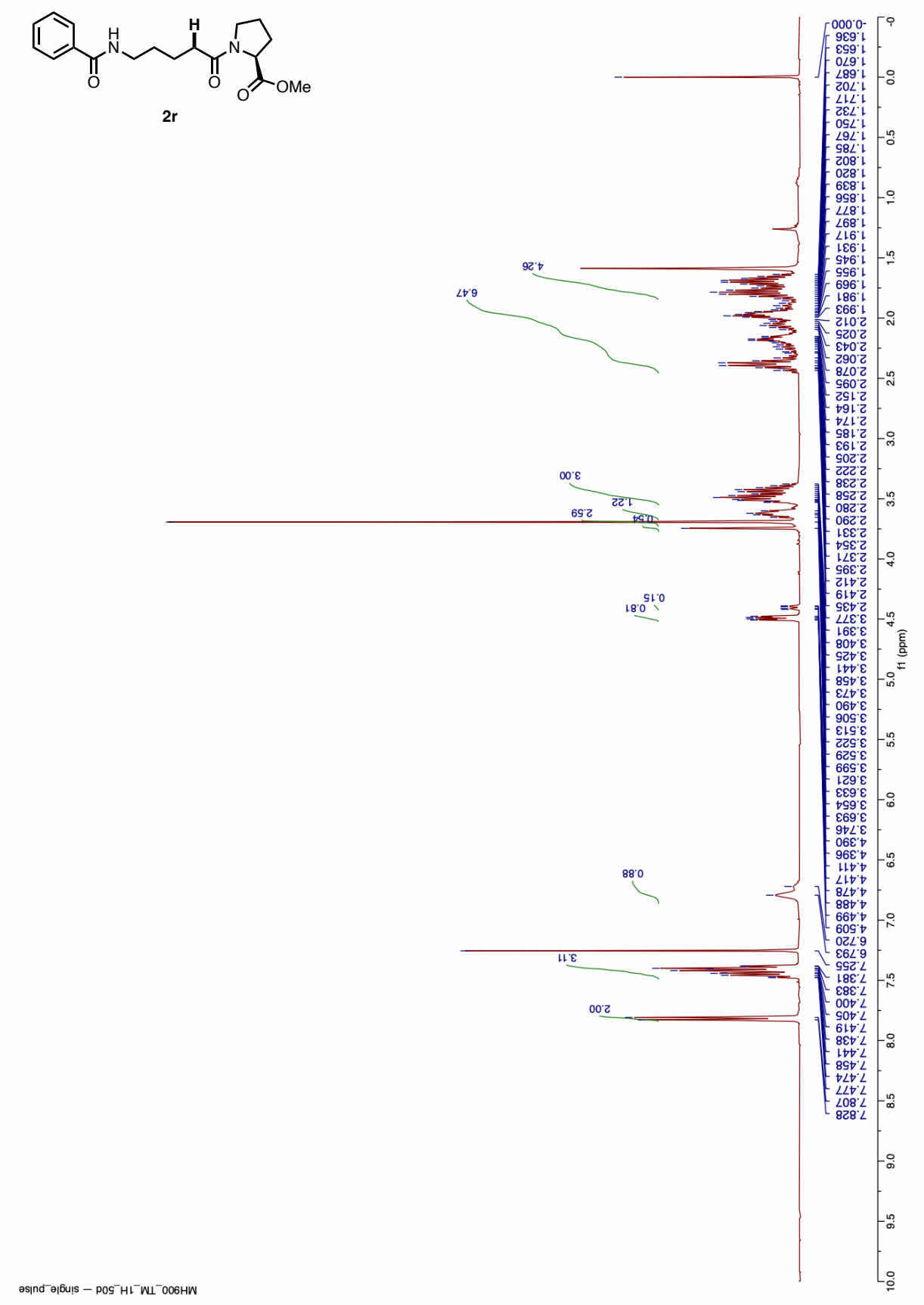
^{1}H NMR of 2q (400 MHz, $CDCl_3$)



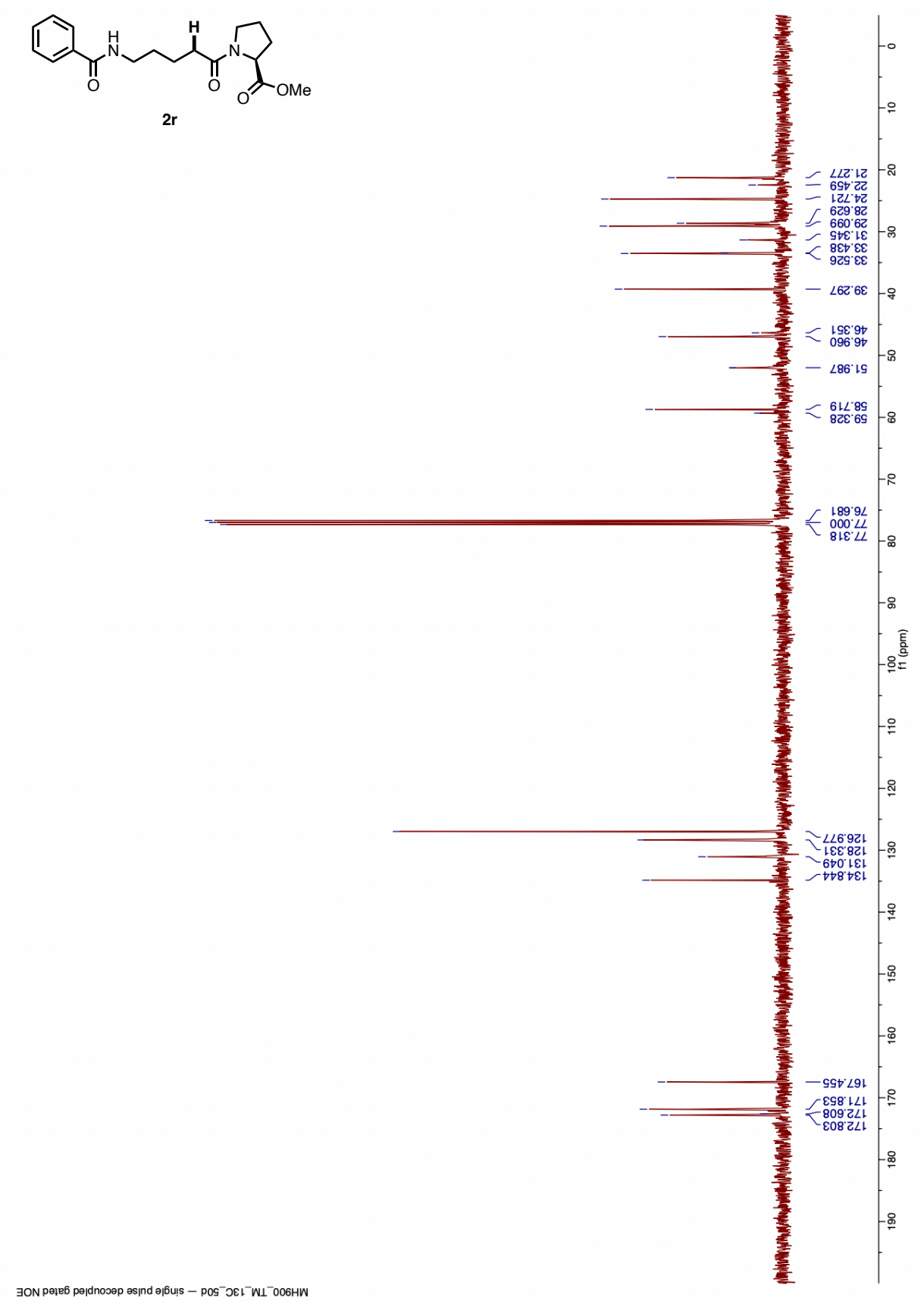
$^{13}C\{^{1}H\}$ NMR of 2q (101 MHz, $CDCl_3$)



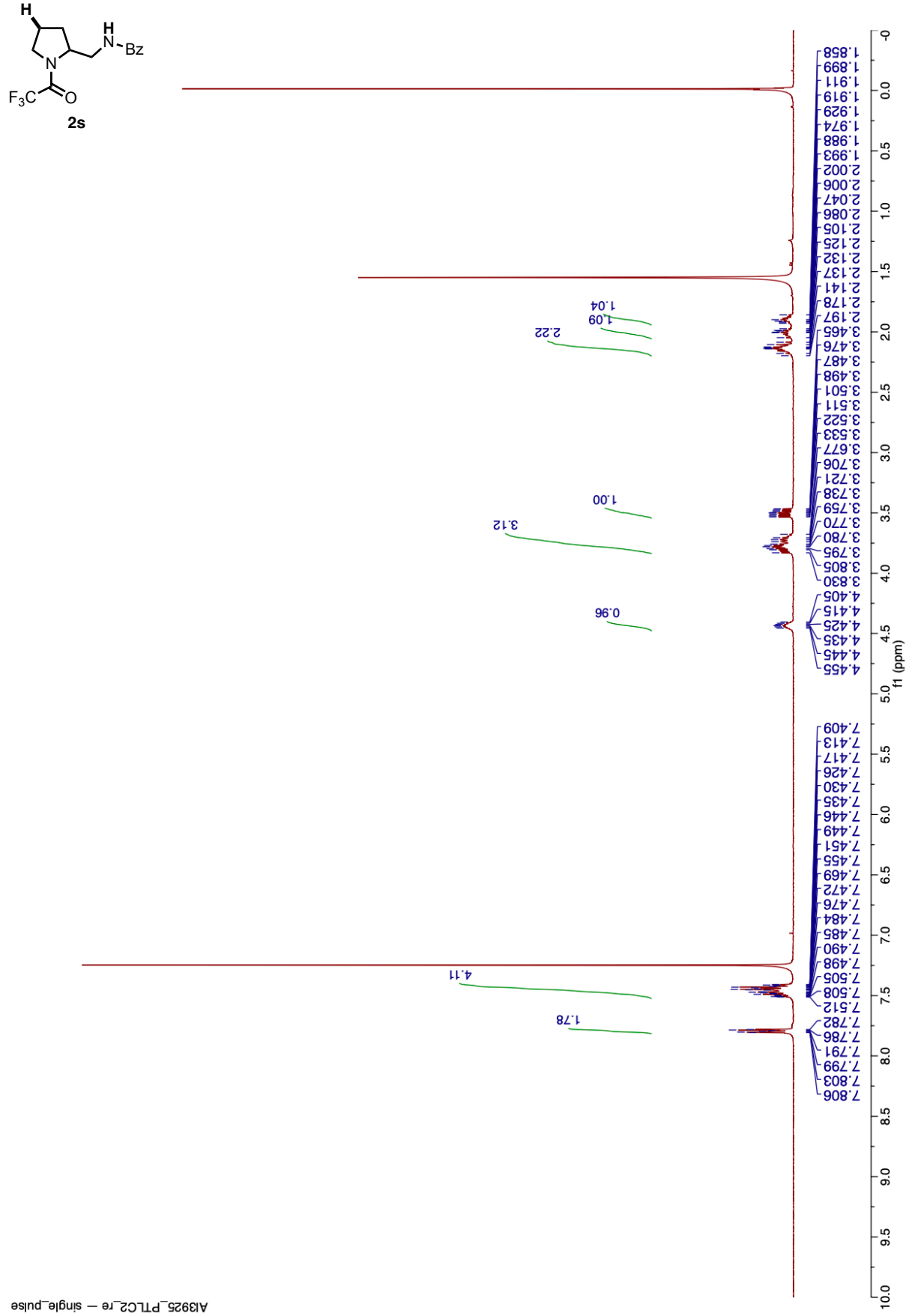
^{1}H NMR of 2r (400 MHz, $CDCl_3$, 323 K)



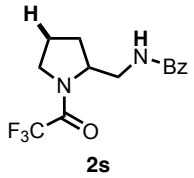
$^{13}C\{^{1}H\}$ NMR of 2r (101 MHz, $CDCl_3$, 323 K)



^{1}H NMR of 2s (400 MHz, $CDCl_3$)

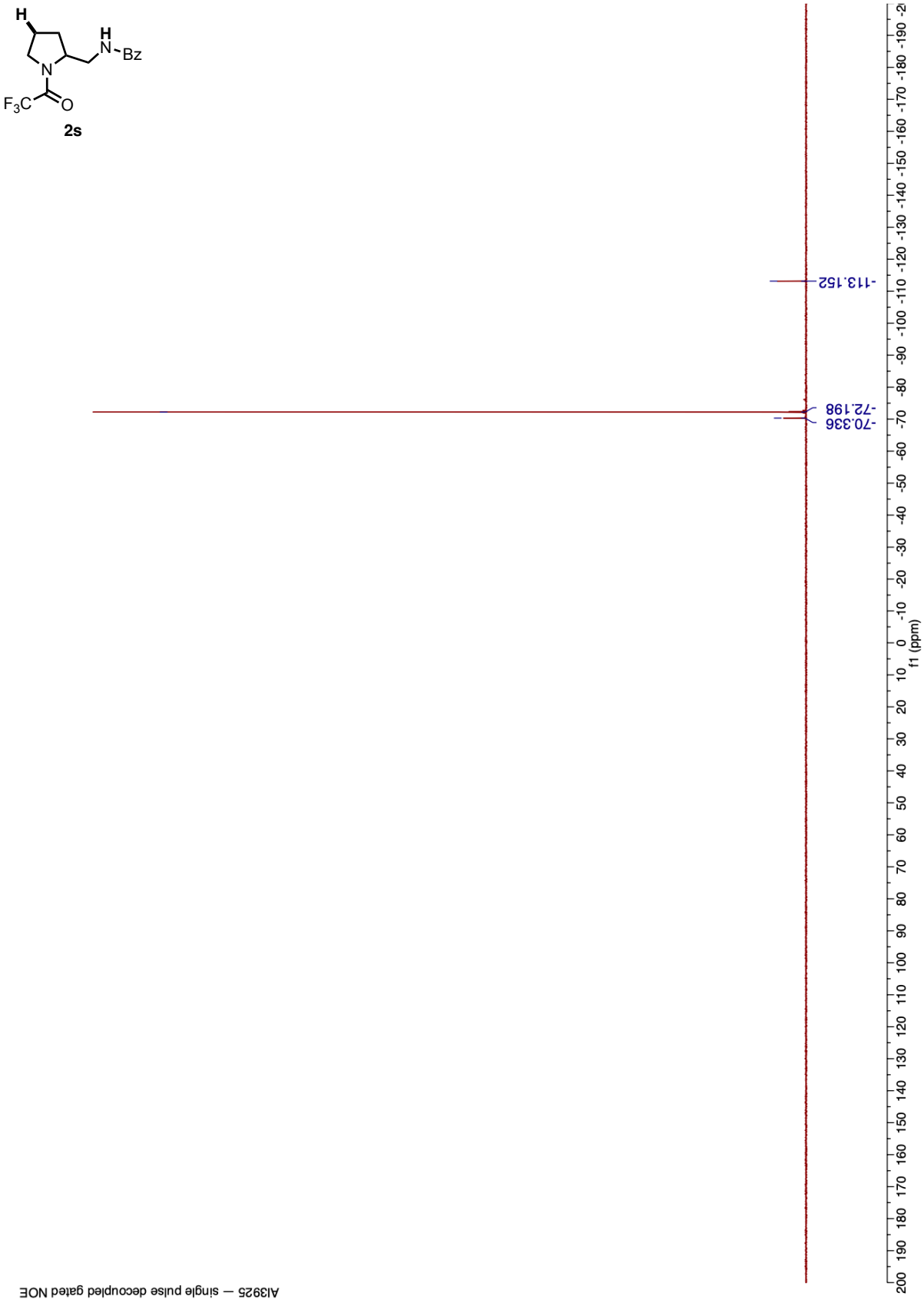


$^{13}C\{^{1}H\}$ NMR of 2s (101 MHz, $CDCl_3$)

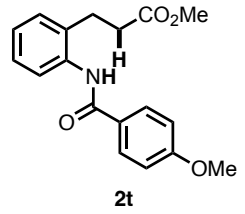


2s

^{19}F NMR of 2s (376 MHz, $CDCl_3$)

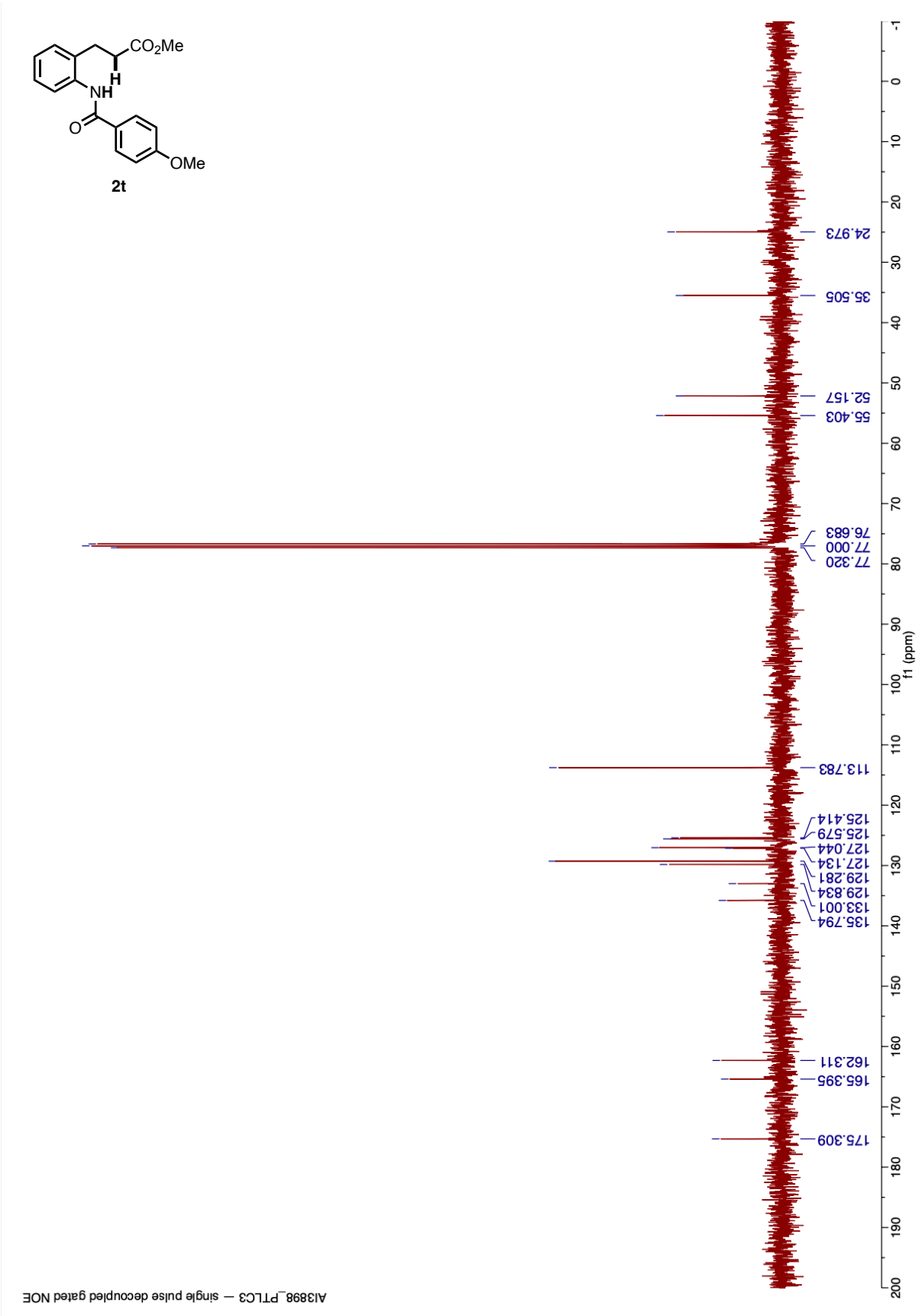


^{1}H NMR of 2t (400 MHz, $CDCl_3$)

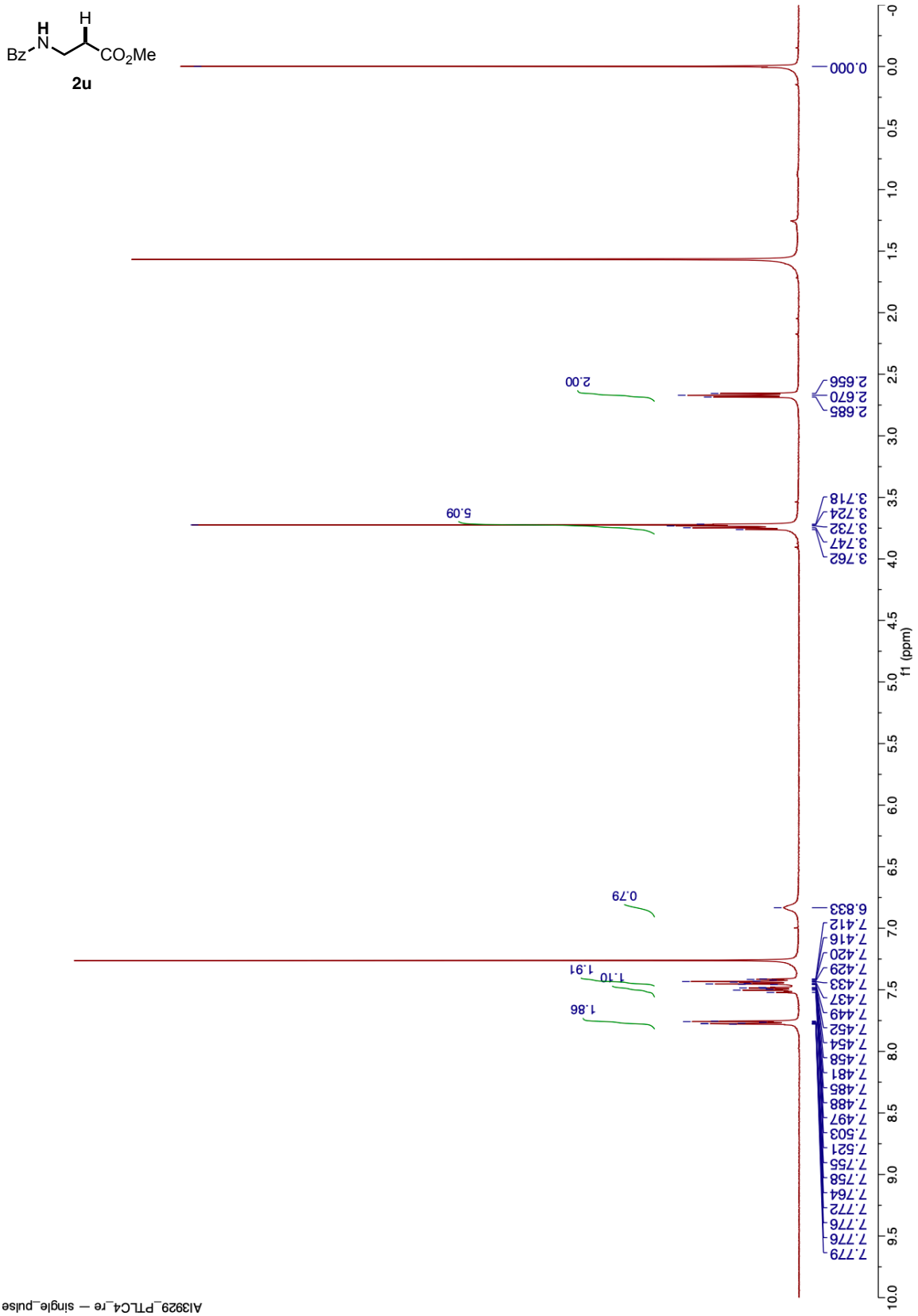


2t

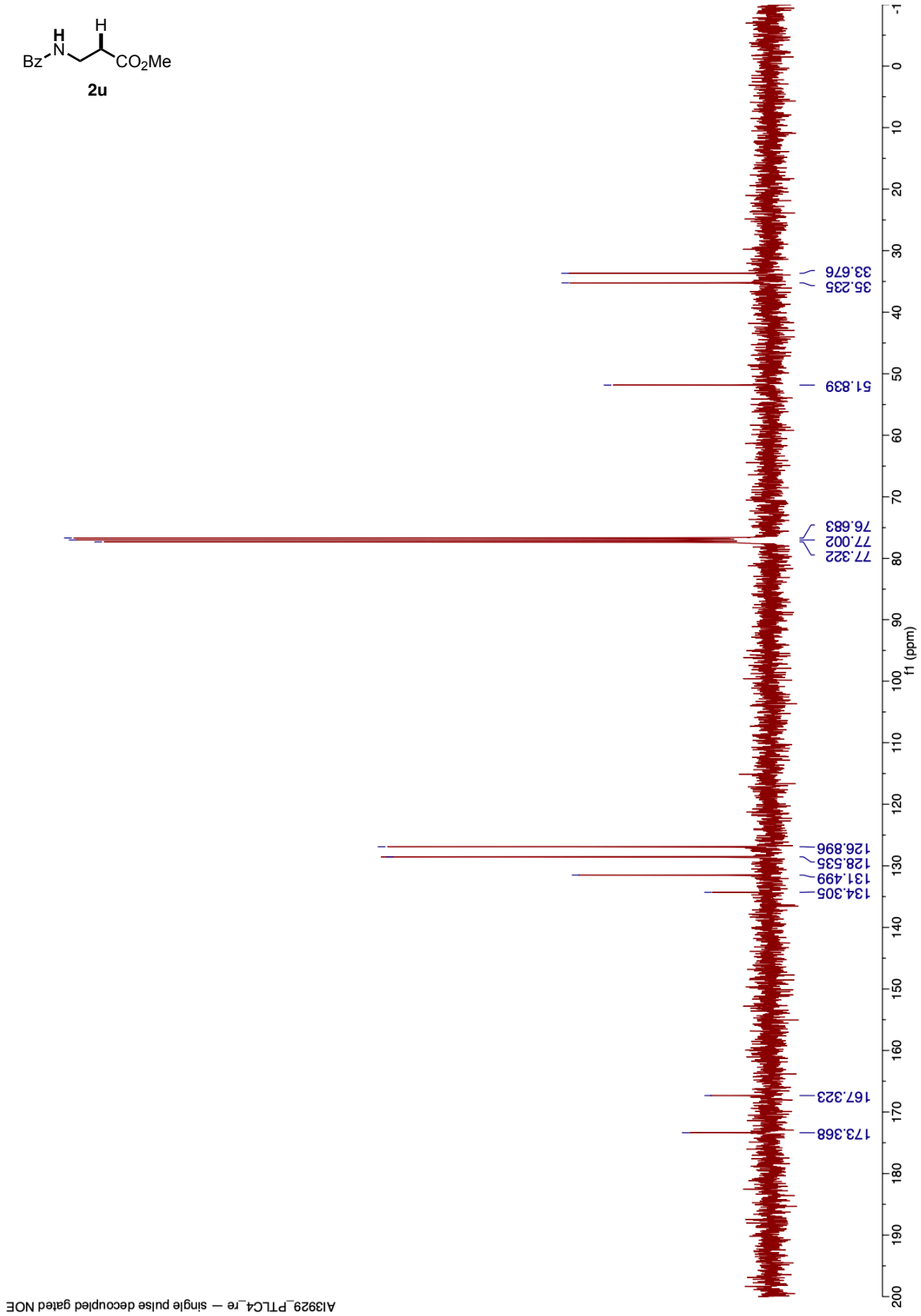
$^{13}C\{^{1}H\}$ NMR of 2t (101 MHz, $CDCl_3$)



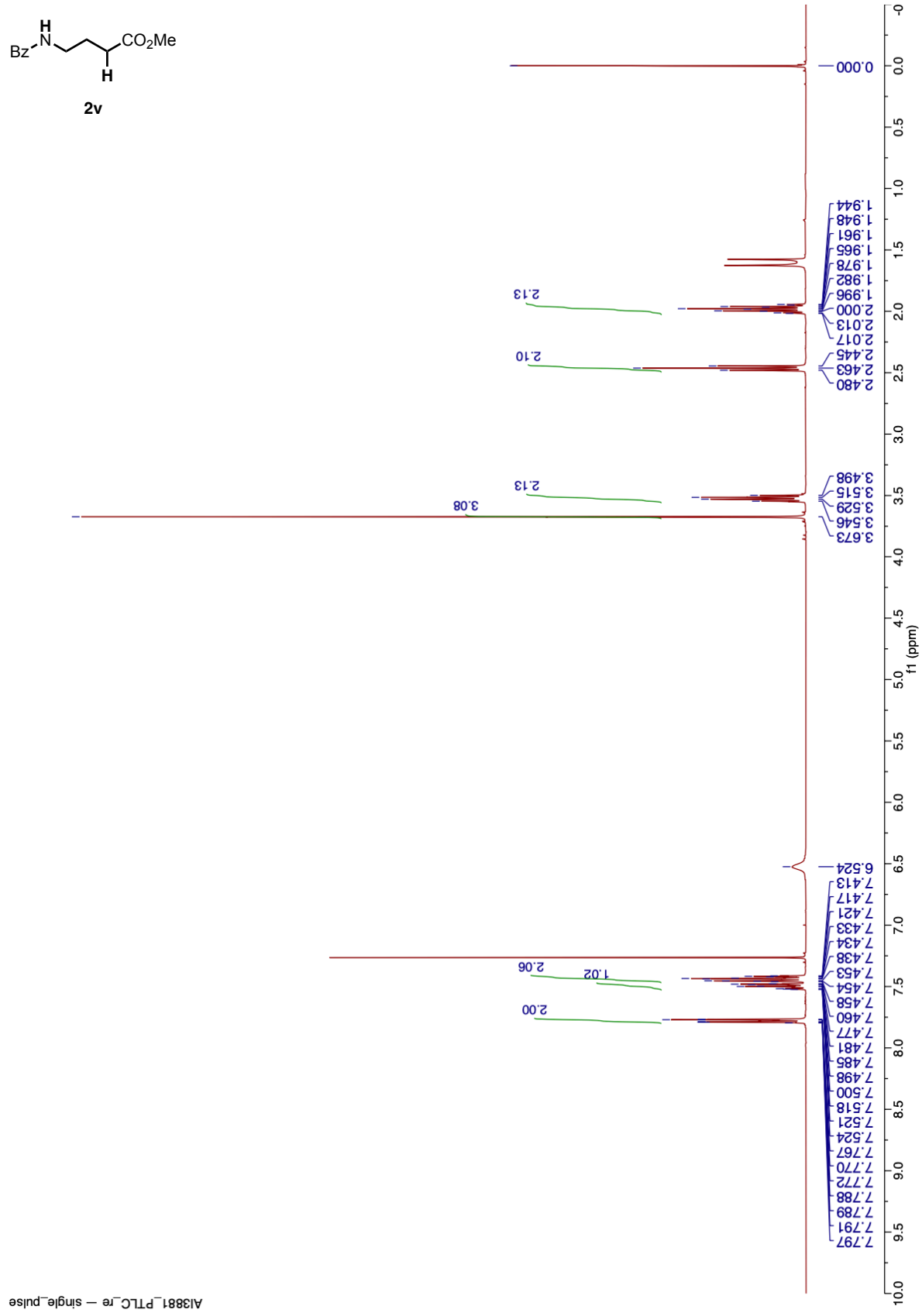
^{1}H NMR of 2u (400 MHz, $CDCl_3$)



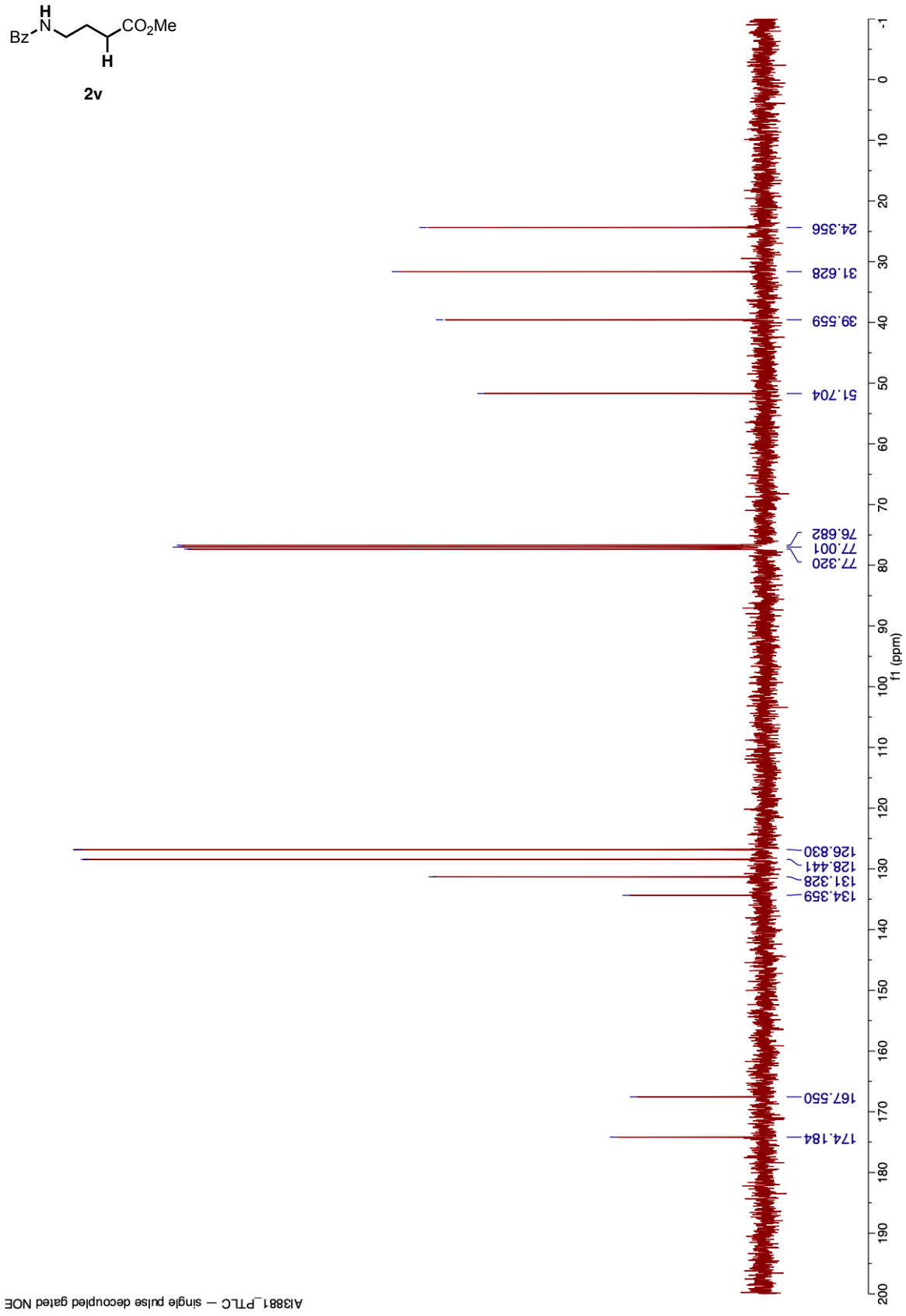
$^{13}C\{^{1}H\}$ NMR of 2u (101 MHz, $CDCl_3$)



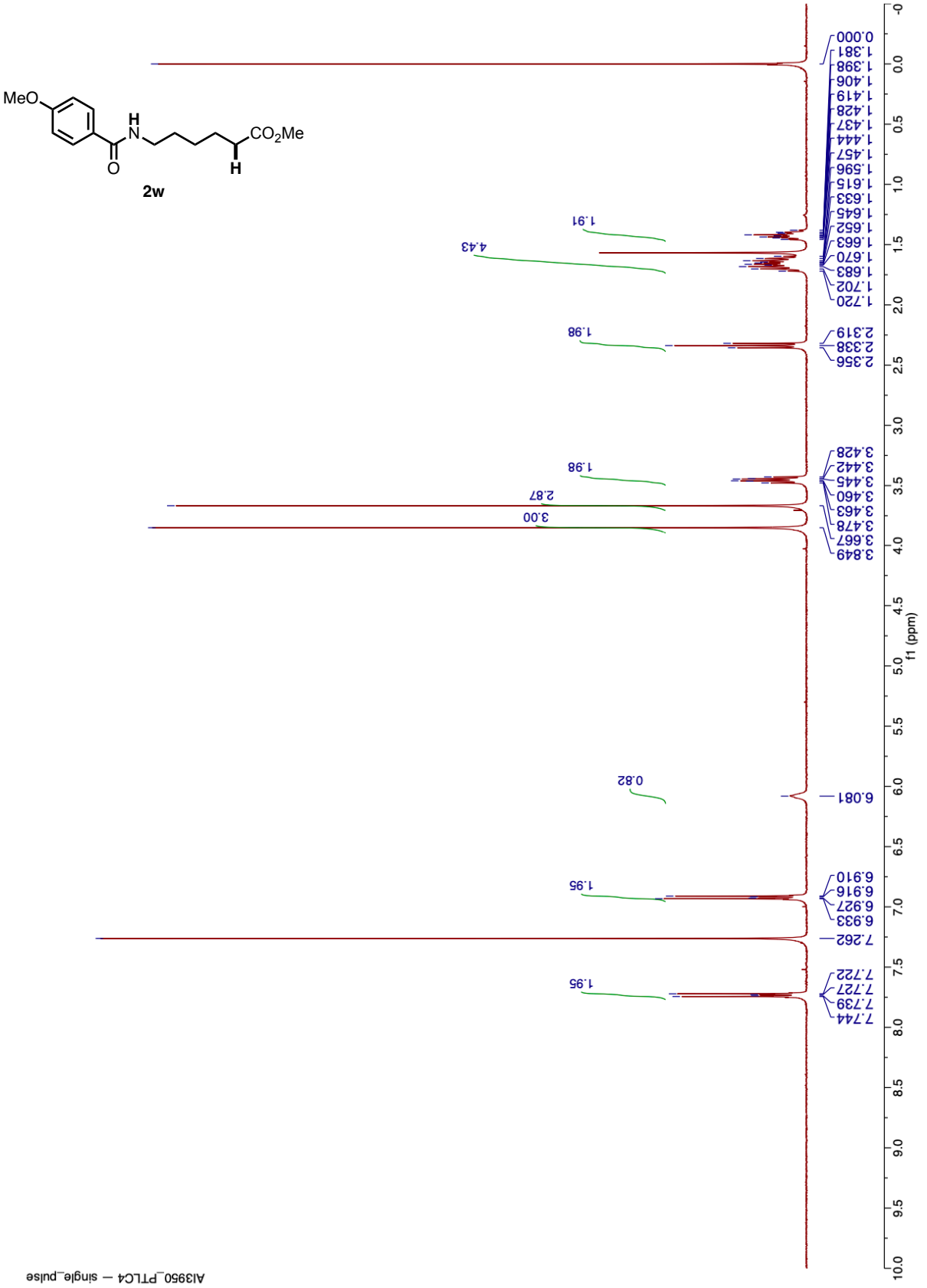
^{1}H NMR of 2v (400 MHz, $CDCl_3$)



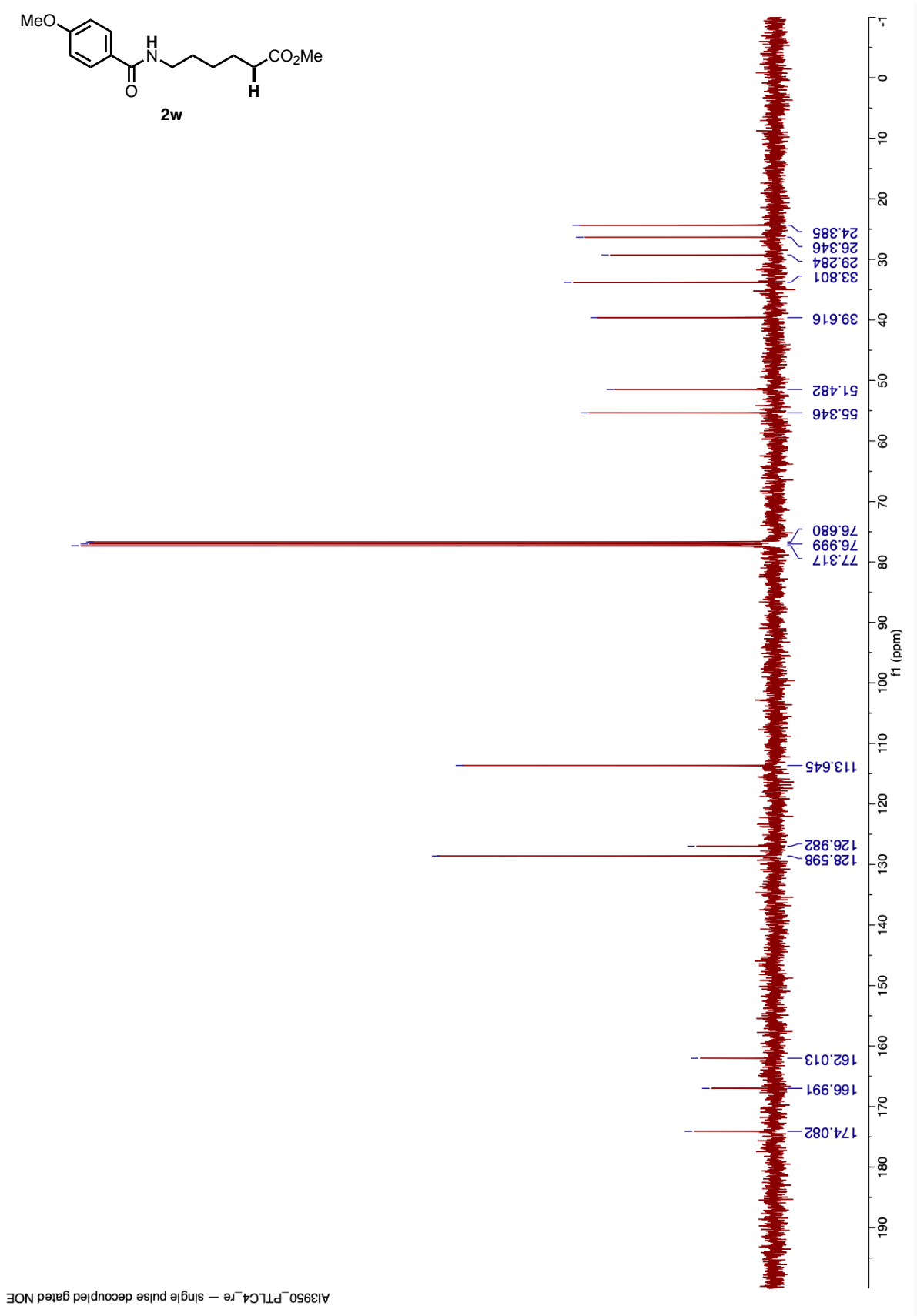
$^{13}C\{^{1}H\}$ NMR of 2v (101 MHz, $CDCl_3$)



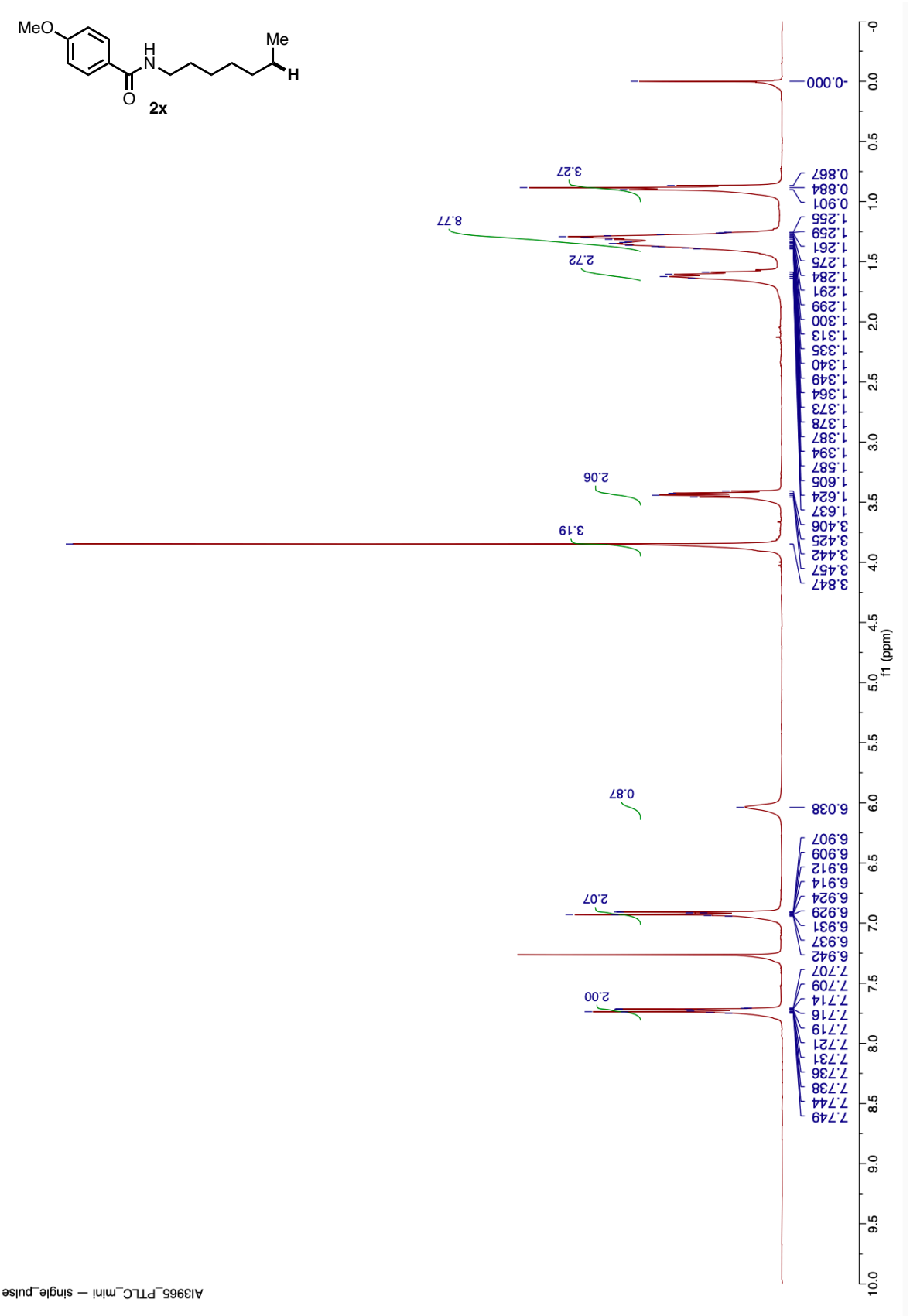
^{1}H NMR of 2w (400 MHz, $CDCl_3$)



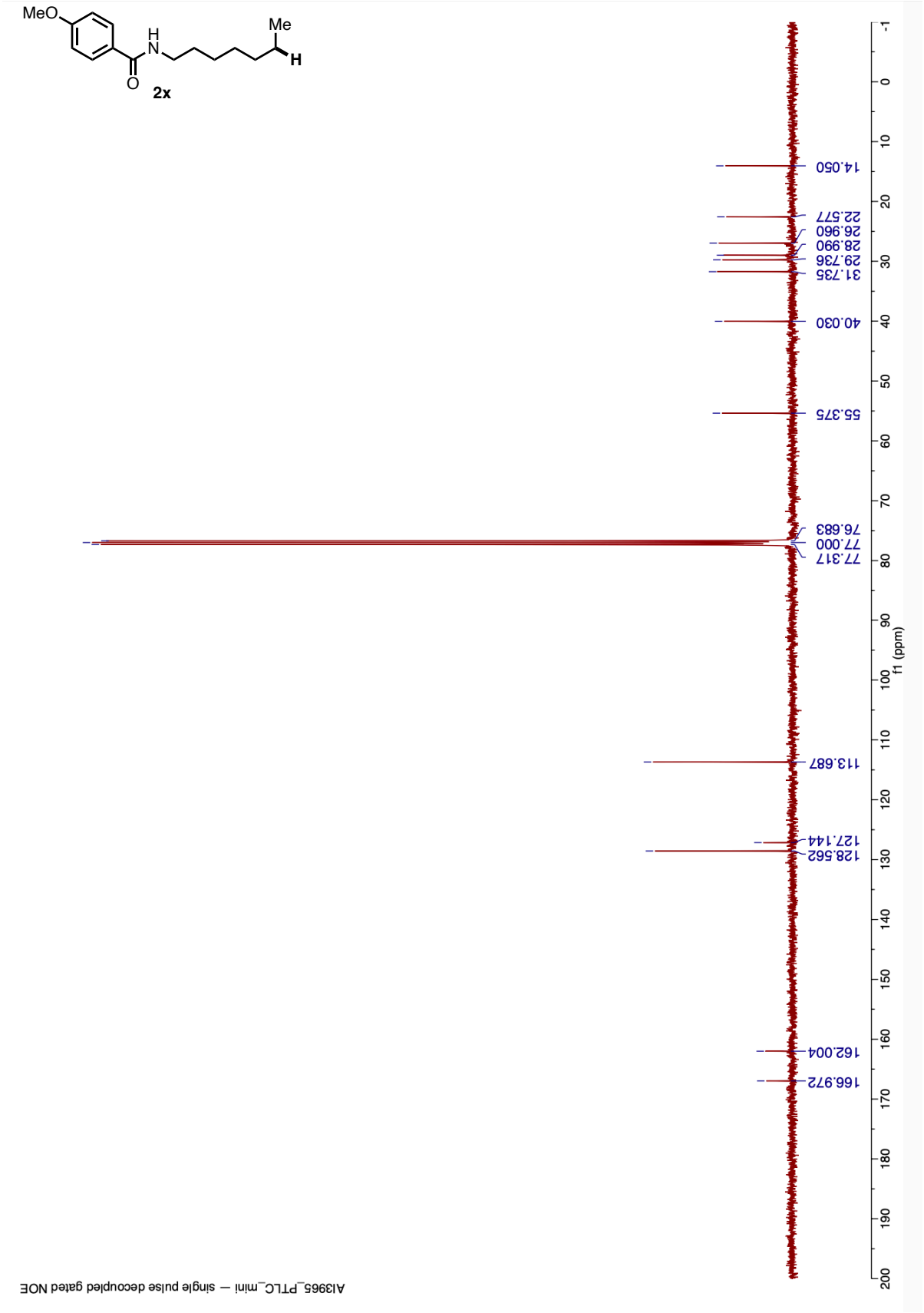
$^{13}C\{^{1}H\}$ NMR of 2w (101 MHz, $CDCl_3$)



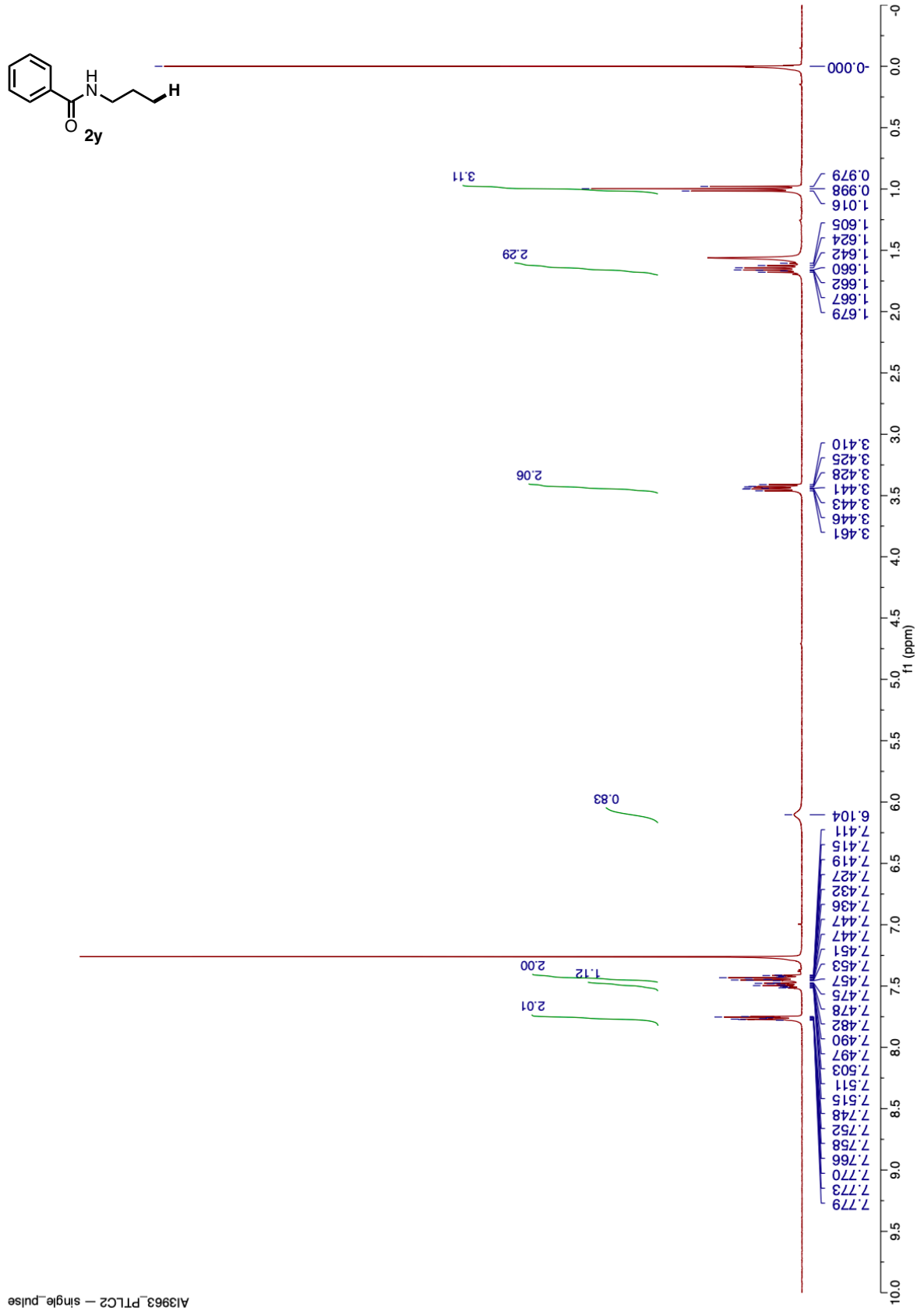
^{1}H NMR of 2x (400 MHz, $CDCl_3$)



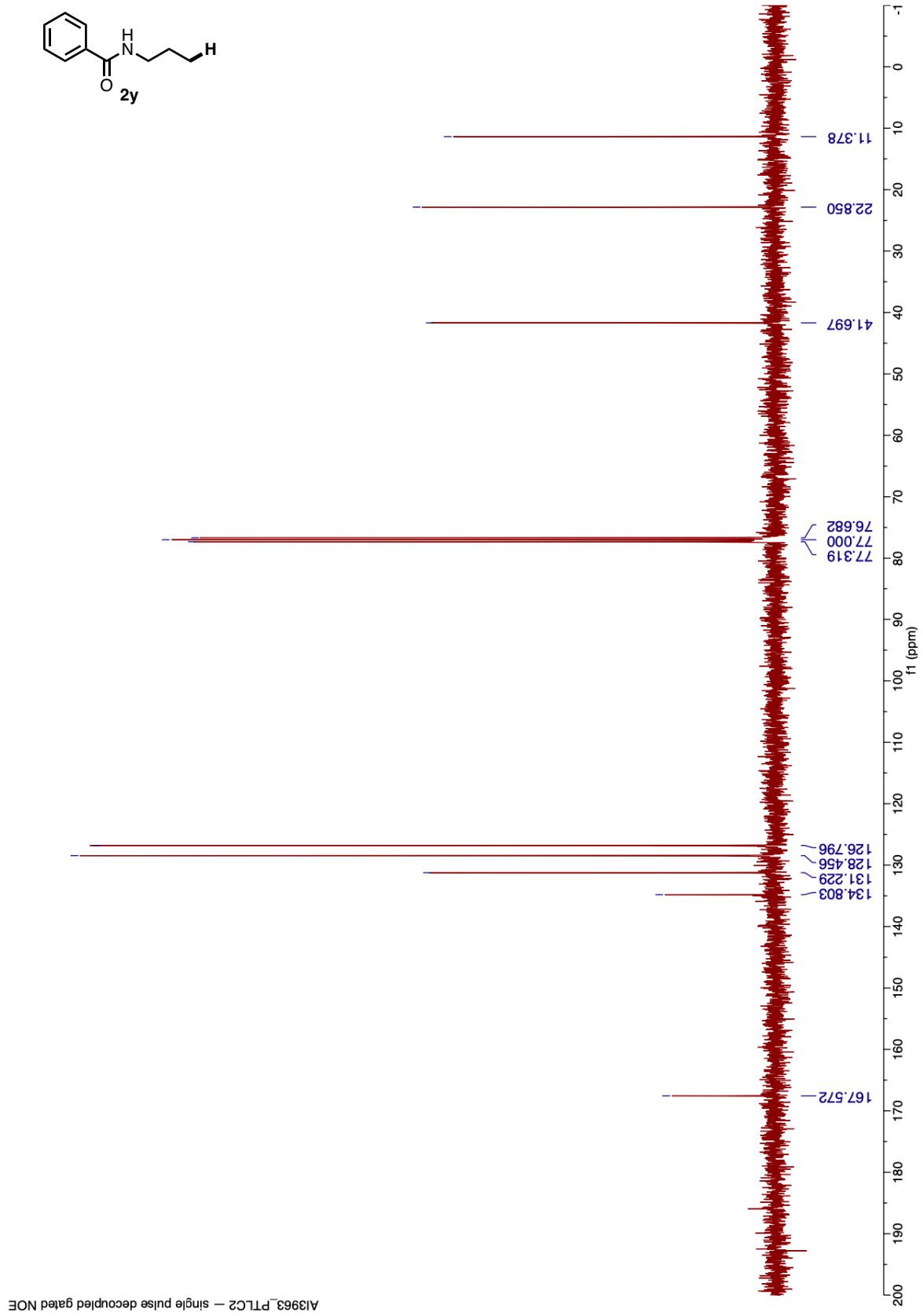
$^{13}C\{^{1}H\}$ NMR of 2x (101 MHz, $CDCl_3$



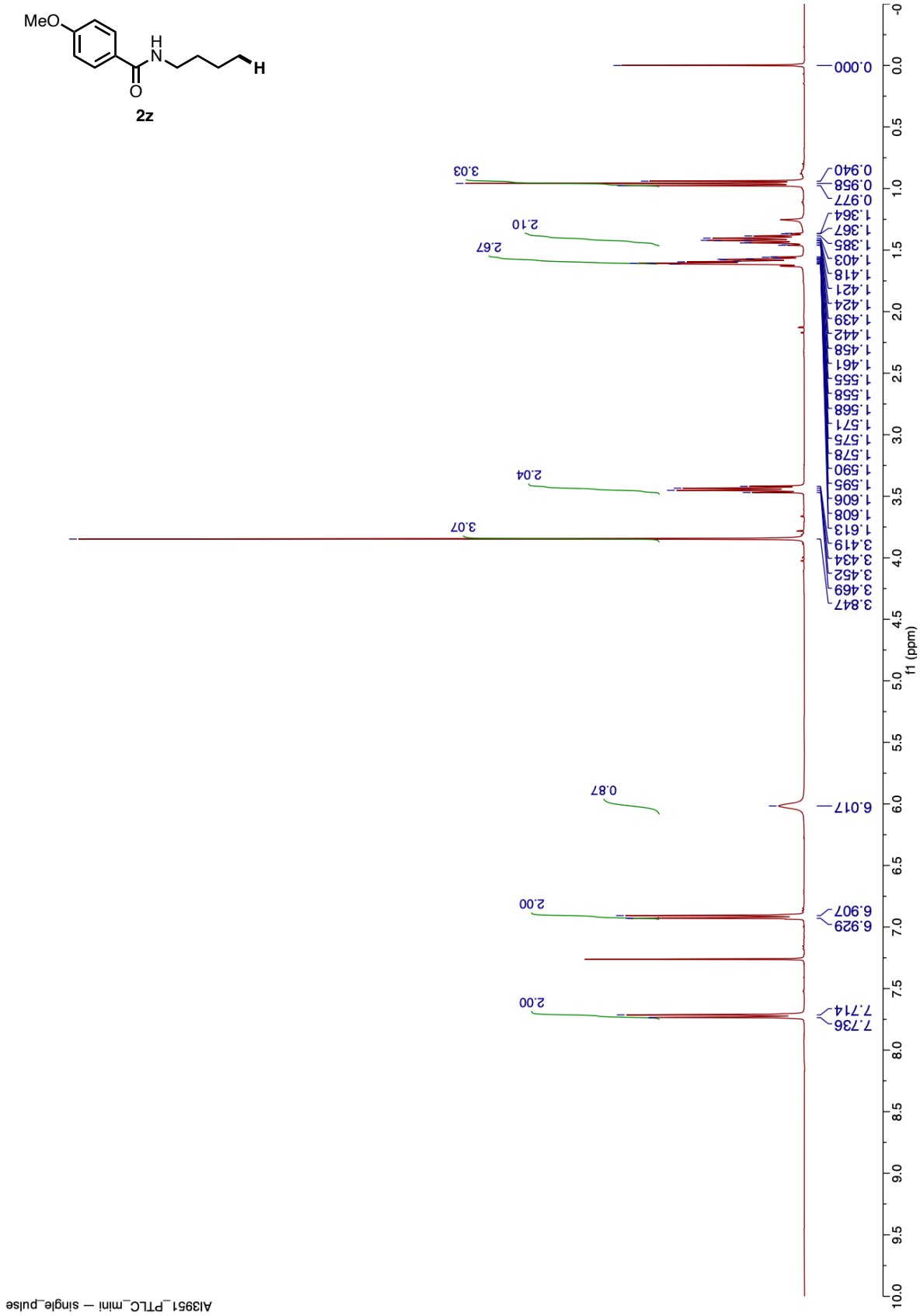
^{1}H NMR of 2y (400 MHz, $CDCl_3$)



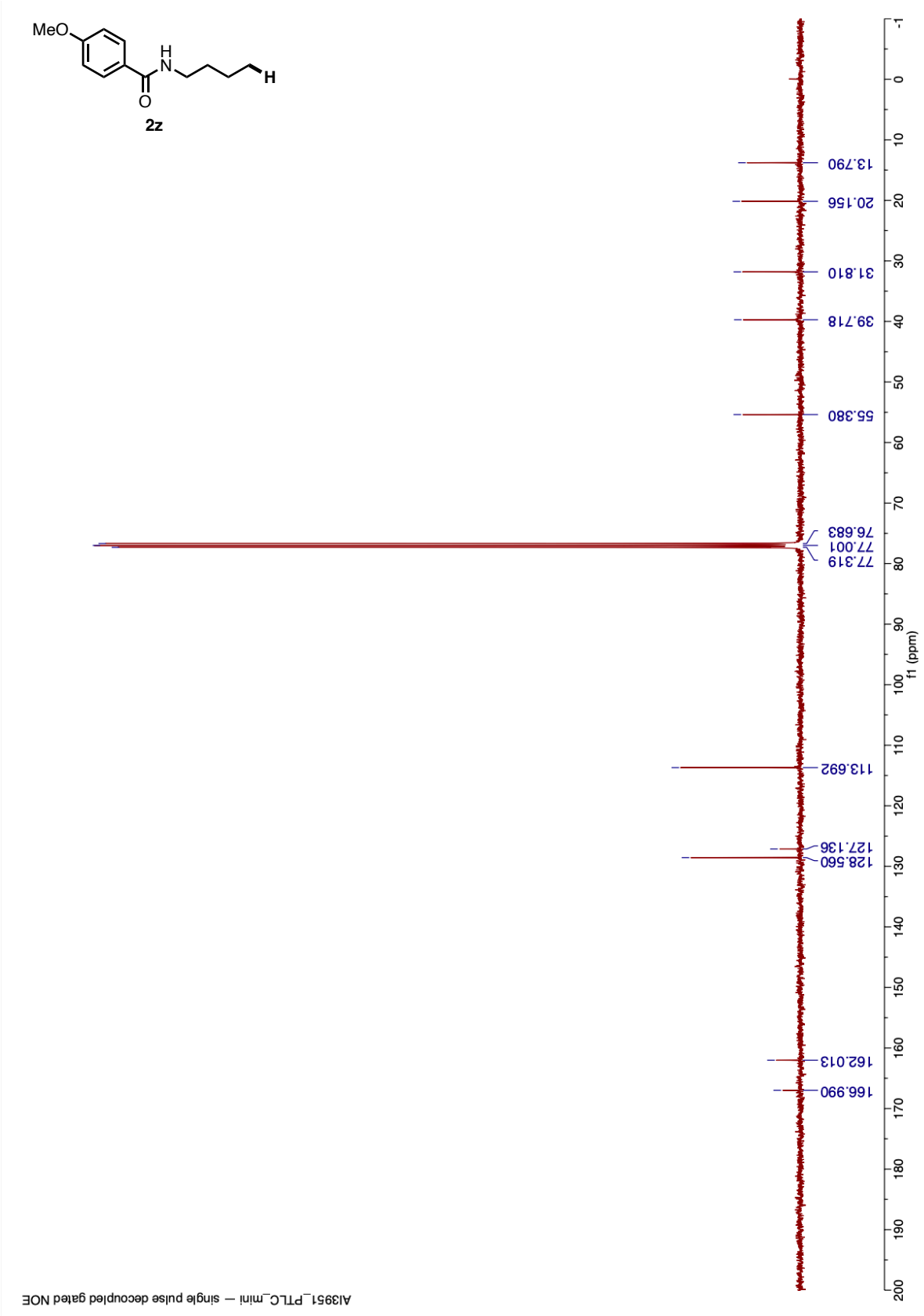
$^{13}C\{^{1}H\}$ NMR of 2y (101 MHz, $CDCl_3$)



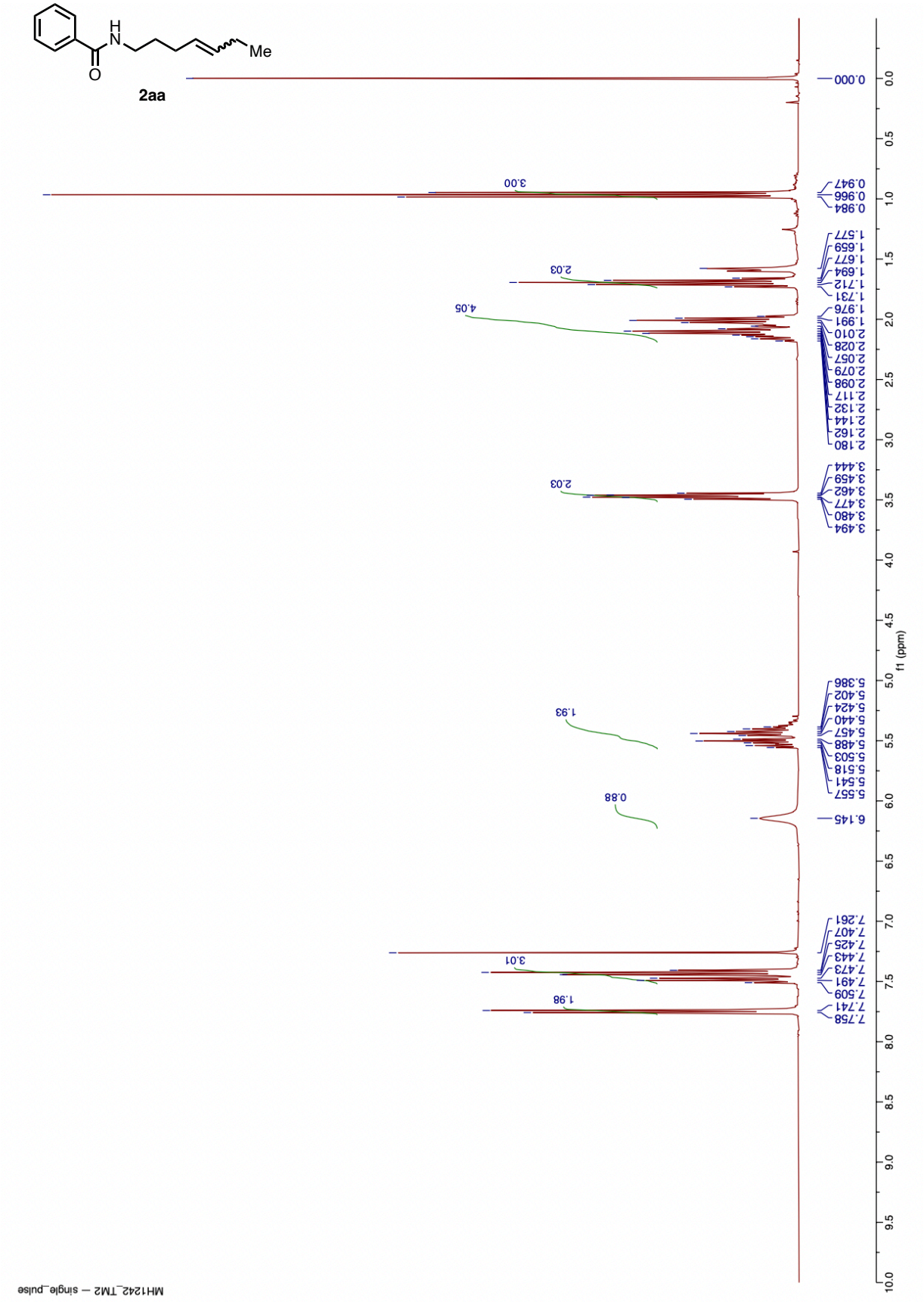
^{1}H NMR of 2z (400 MHz, $CDCl_3$)



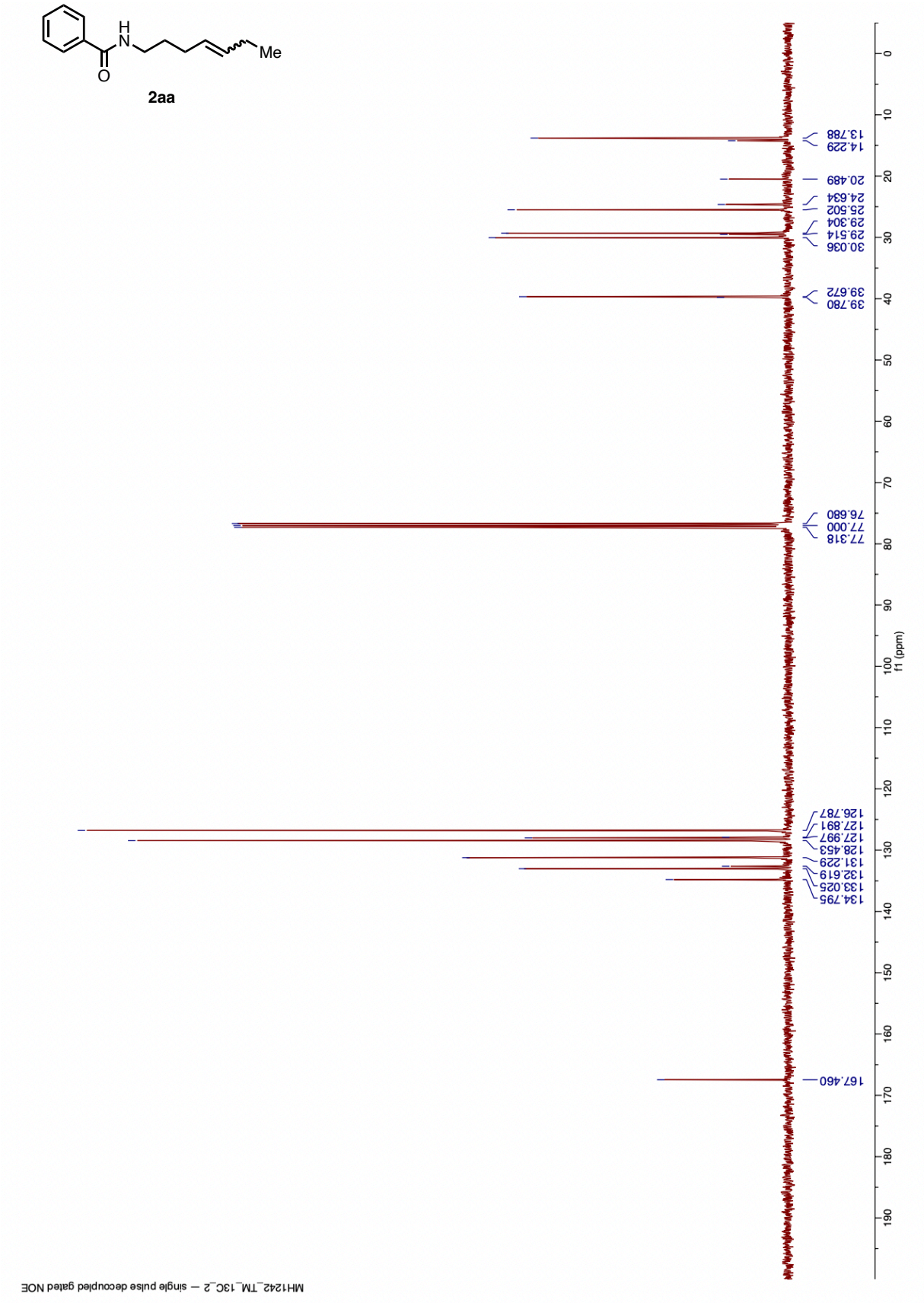
$^{13}C\{^{1}H\}$ NMR of 2z (101 MHz, $CDCl_3$)



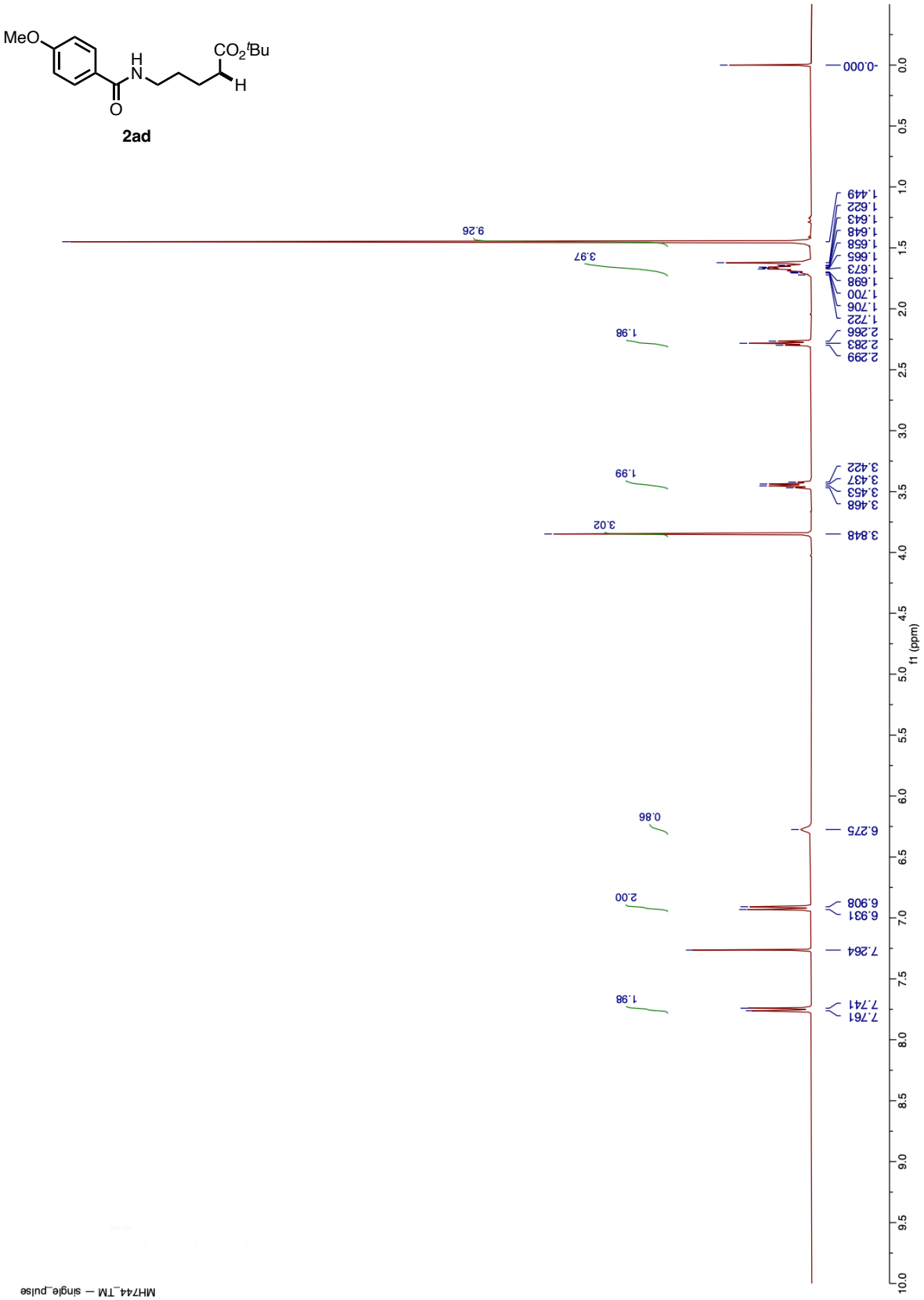
^{1}H NMR of 2aa (400 MHz, $CDCl_3$)



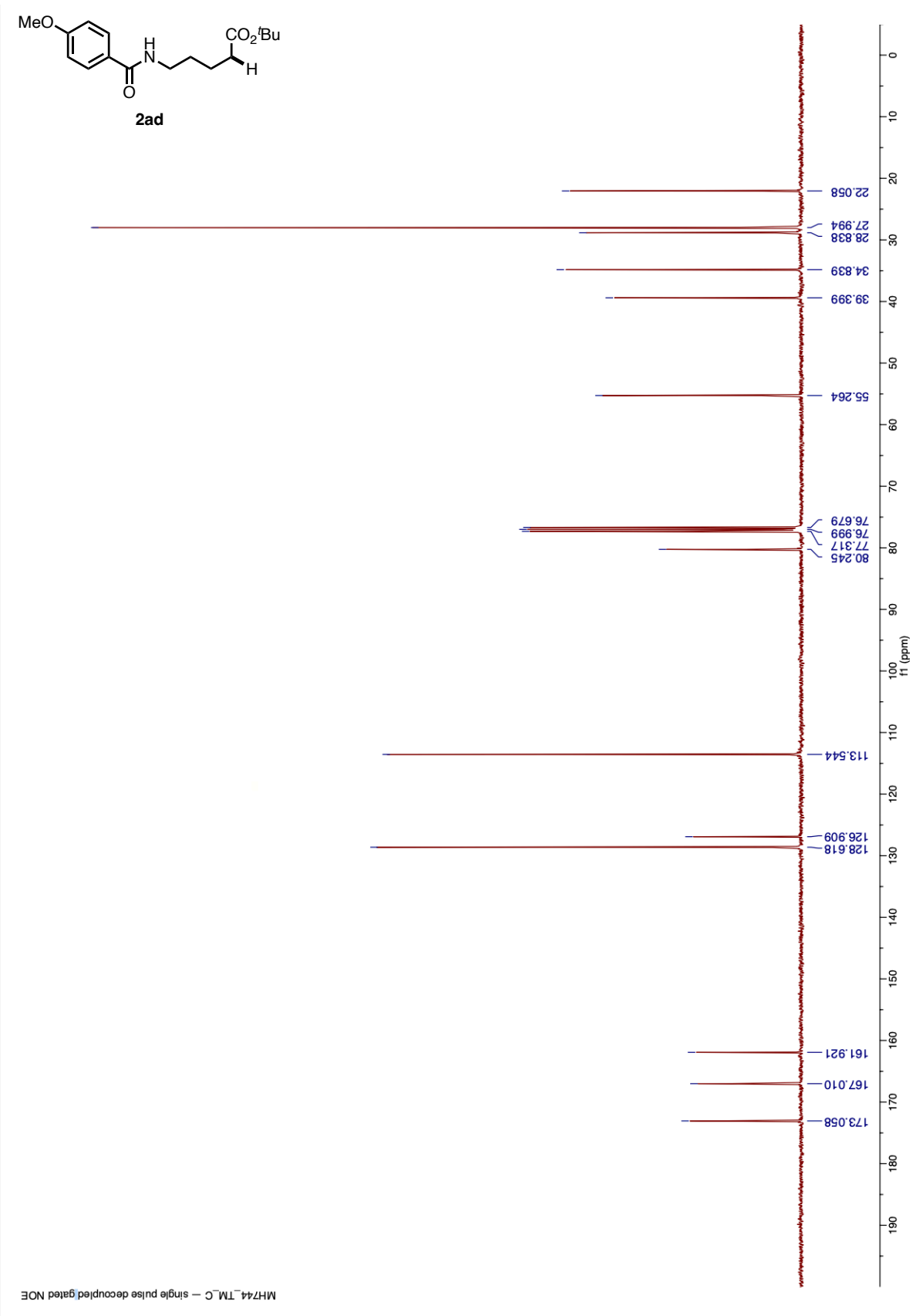
$^{13}C\{^{1}H\}$ NMR of 2aa (101 MHz, $CDCl_3$)



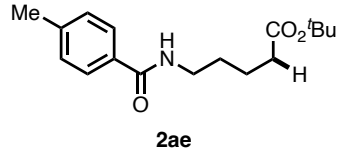
^{1}H NMR of 2ad (400 MHz, $CDCl_3$)



$^{13}C\{^{1}H\}$ NMR of 2ad (101 MHz, $CDCl_3$)

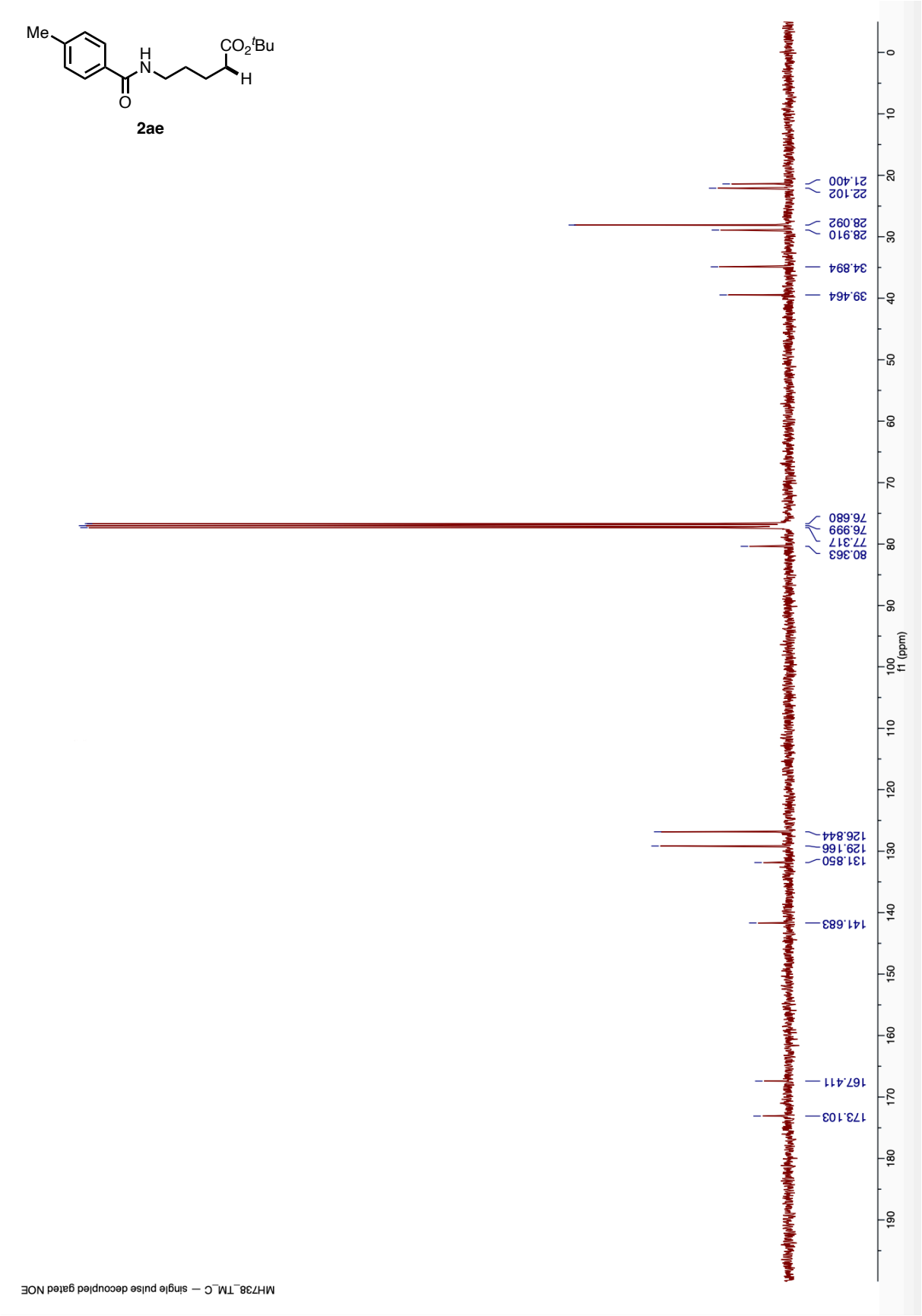


^{1}H NMR of 2ae (400 MHz, $CDCl_3$)

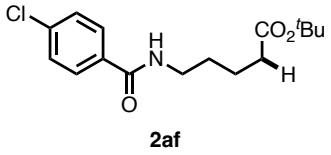


2ae

$^{13}C\{^{1}H\}$ NMR of 2ae (101 MHz, $CDCl_3$)

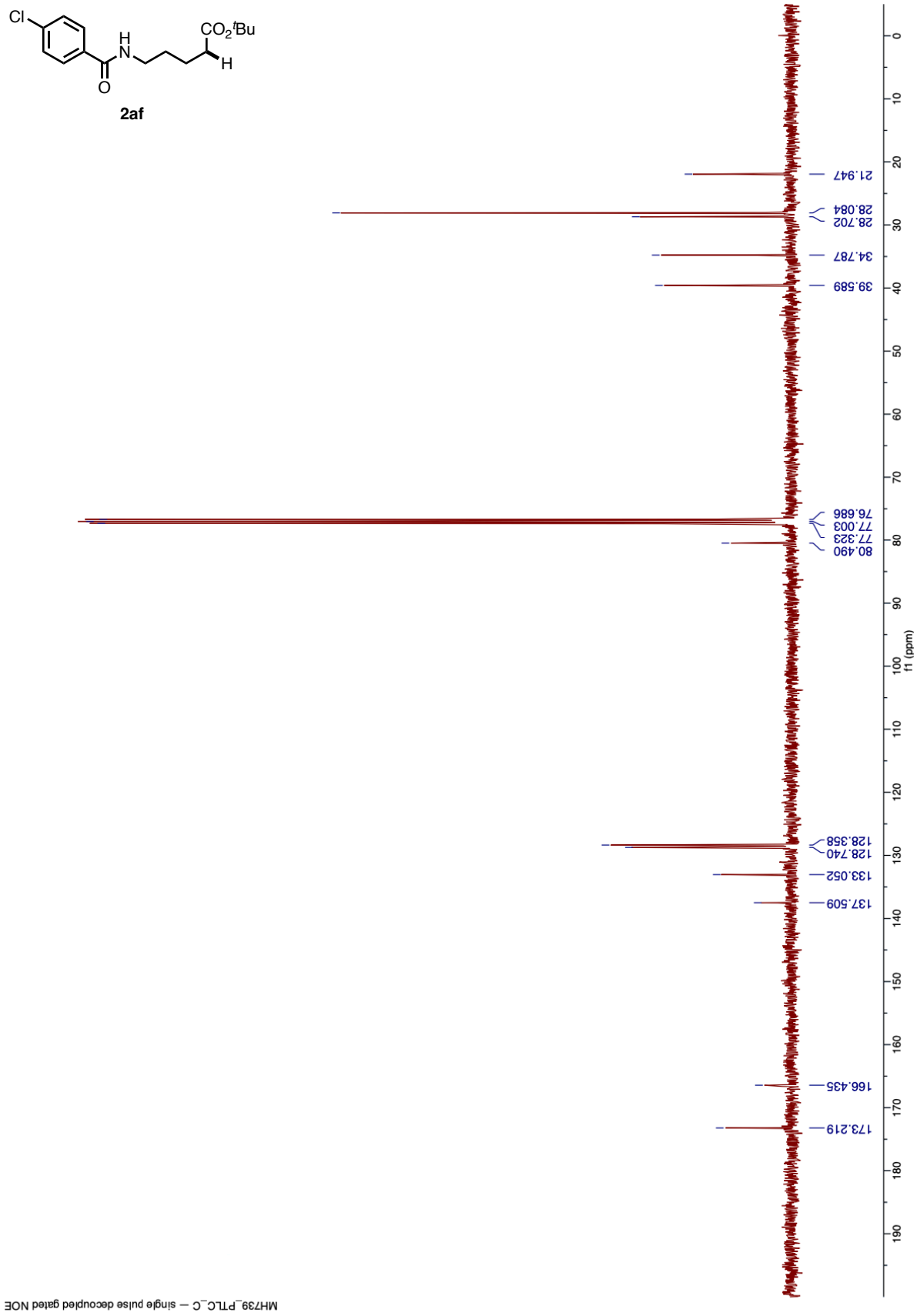


^{1}H NMR of 2af (400 MHz, $CDCl_3$)

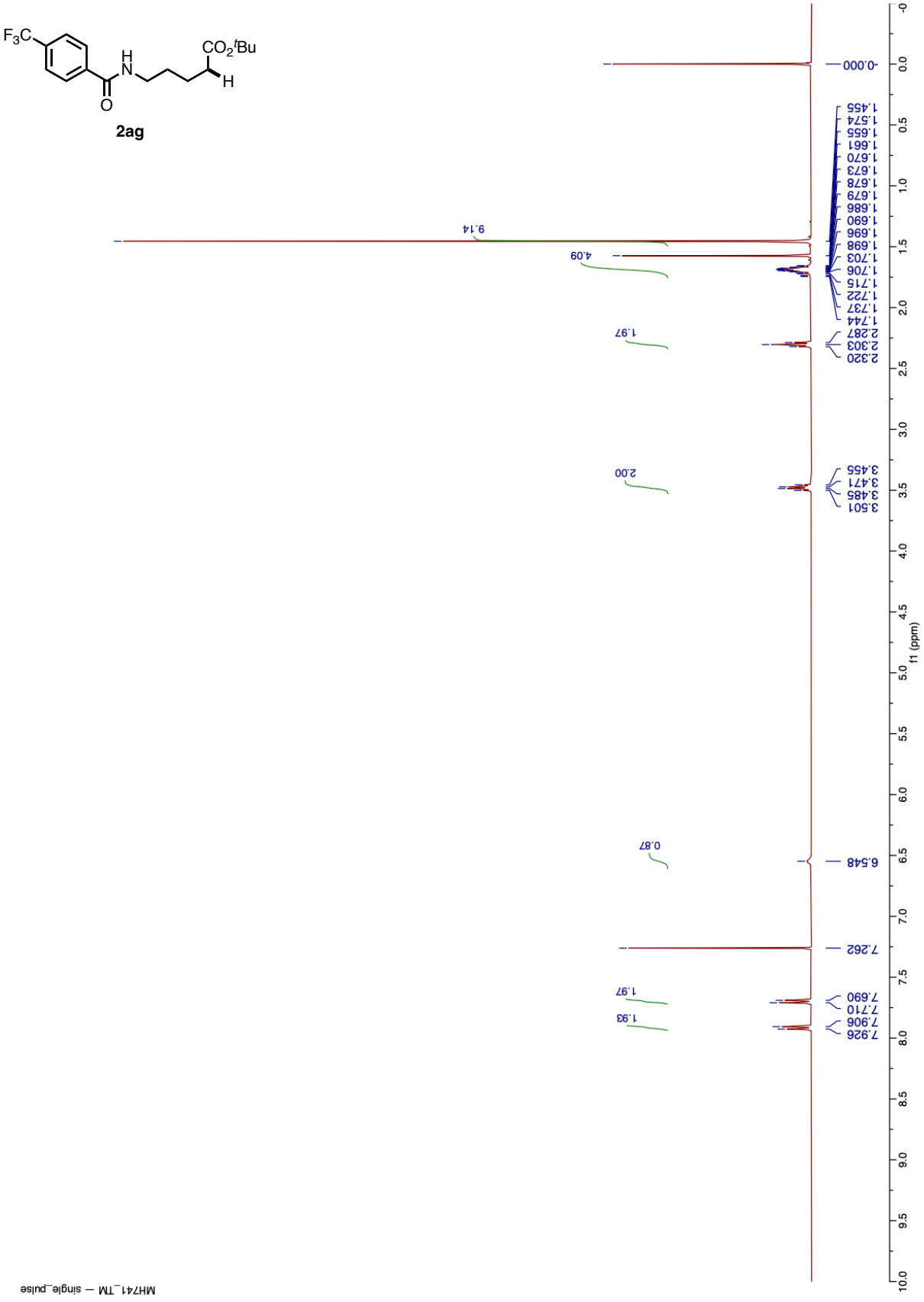


2af

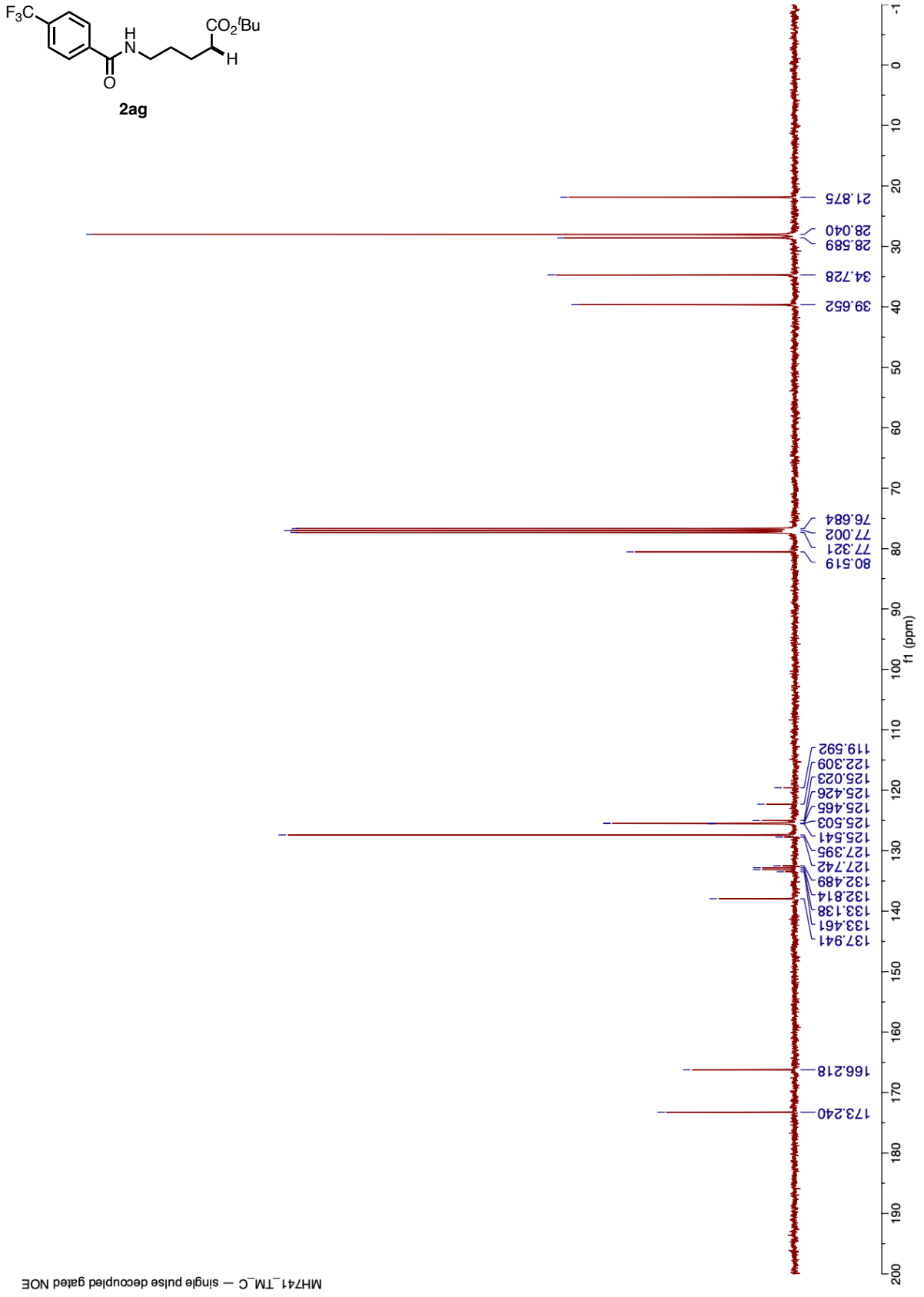
$^{13}C\{^{1}H\}$ NMR of 2af (101 MHz, $CDCl_3$)



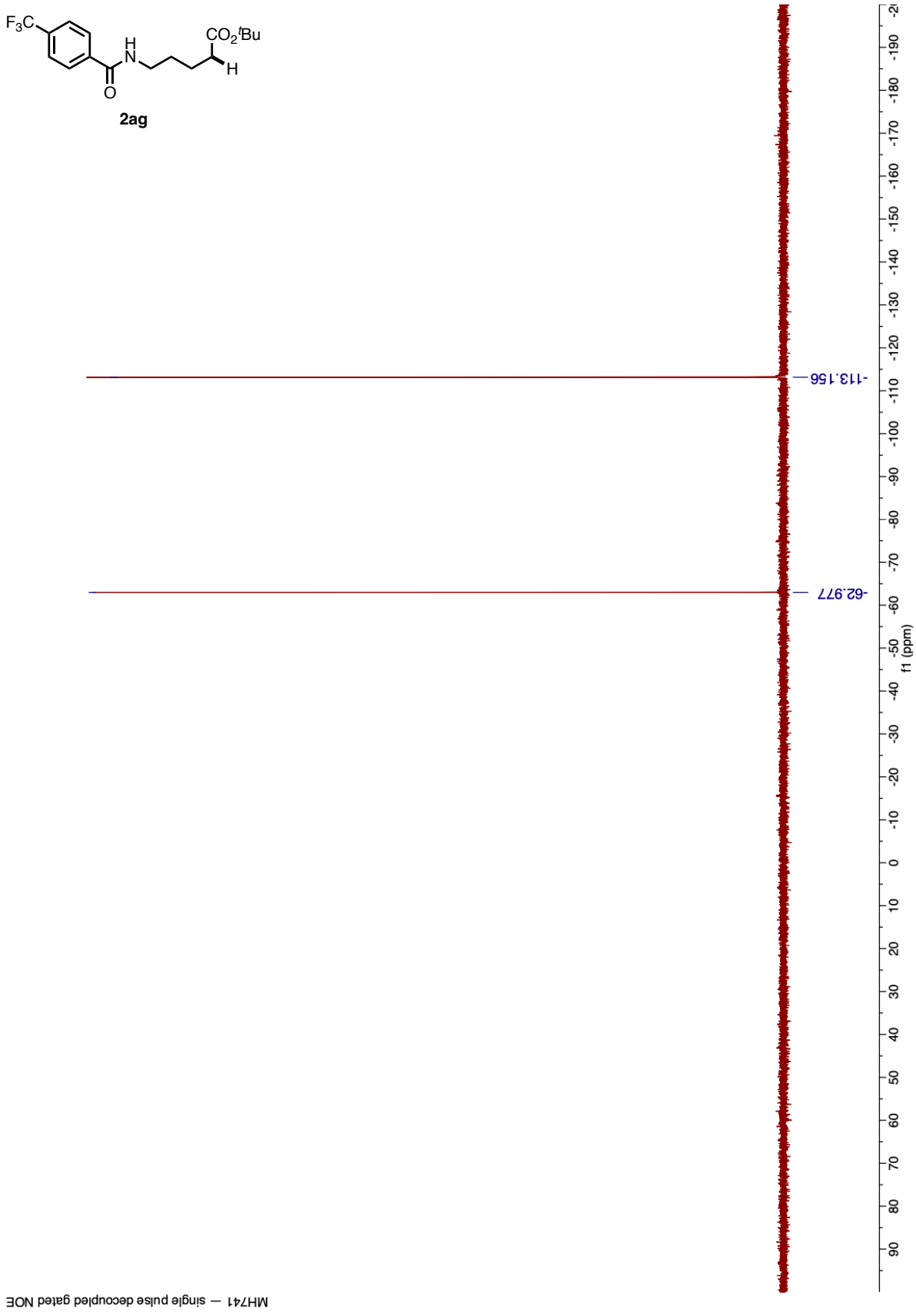
^{1}H NMR of 2ag (400 MHz, $CDCl_3$)



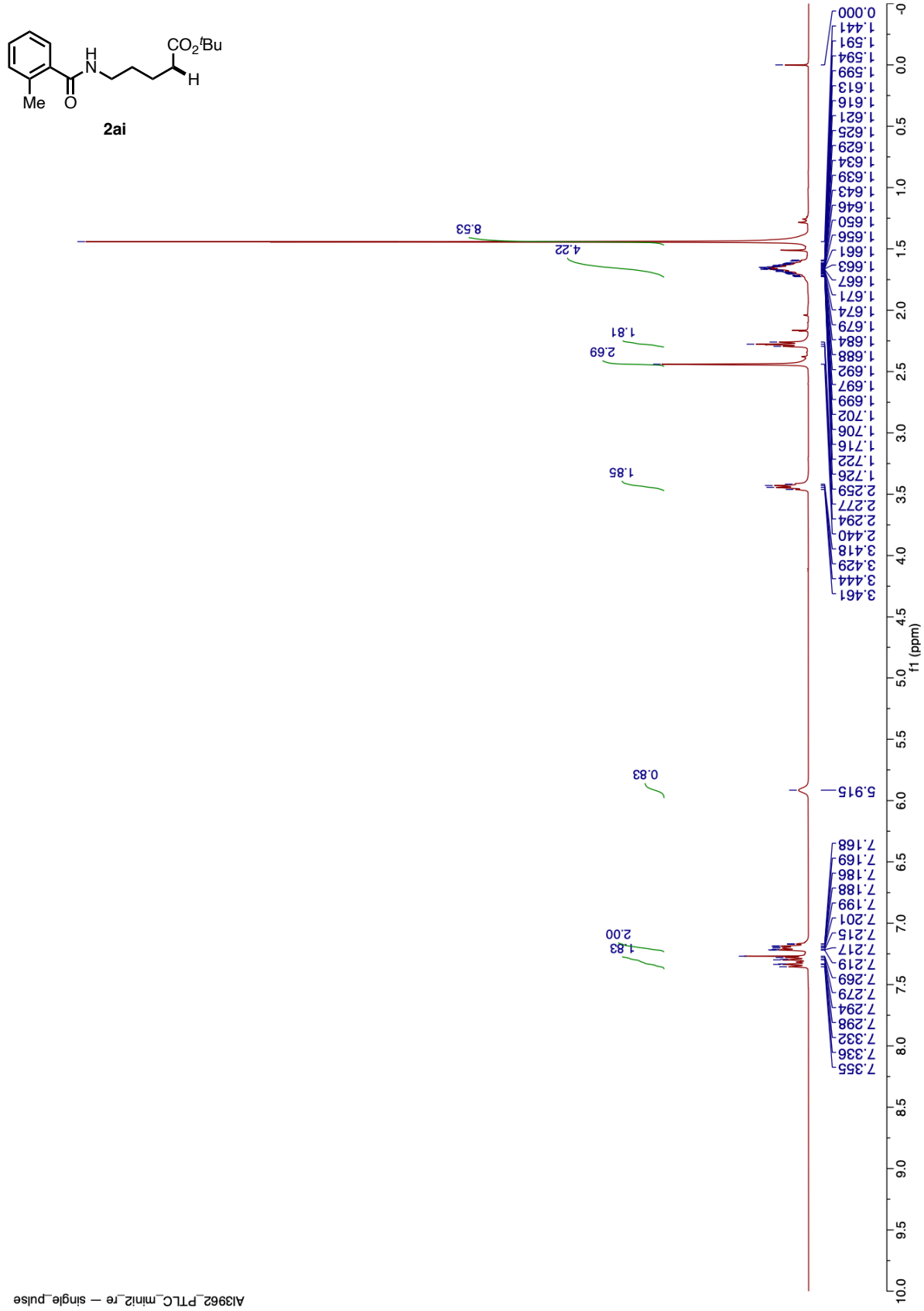
$^{13}C\{^{1}H\}$ NMR of 2ag (101 MHz, $CDCl_3$)



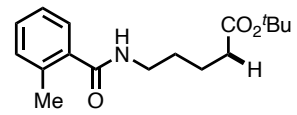
^{19}F NMR of 2ag (376 MHz, $CDCl_3$)



^{1}H NMR of 2ai (400 MHz, $CDCl_3$)

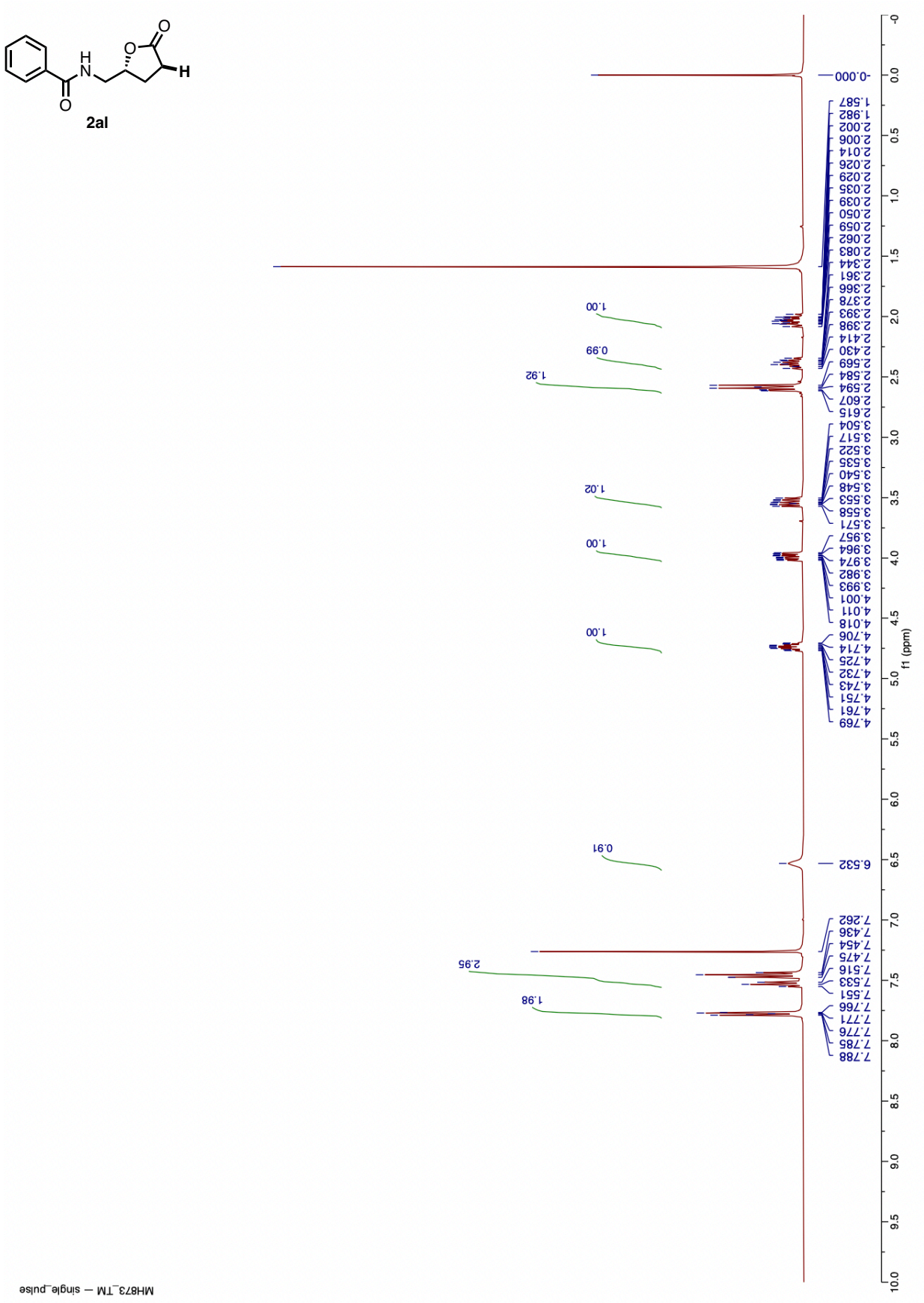


$^{13}C\{^{1}H\}$ NMR of 2ai (101 MHz, $CDCl_3$)

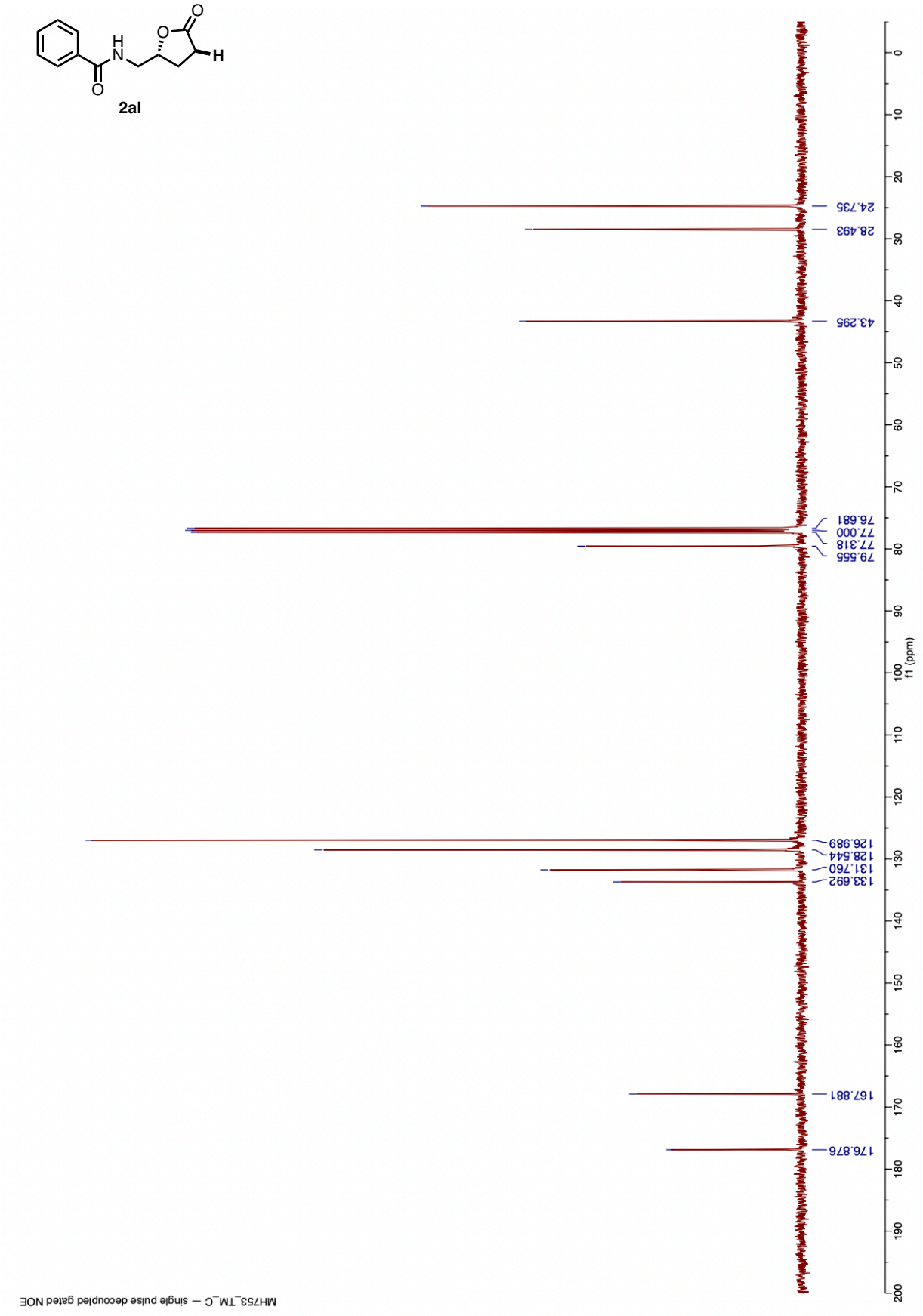


2ai

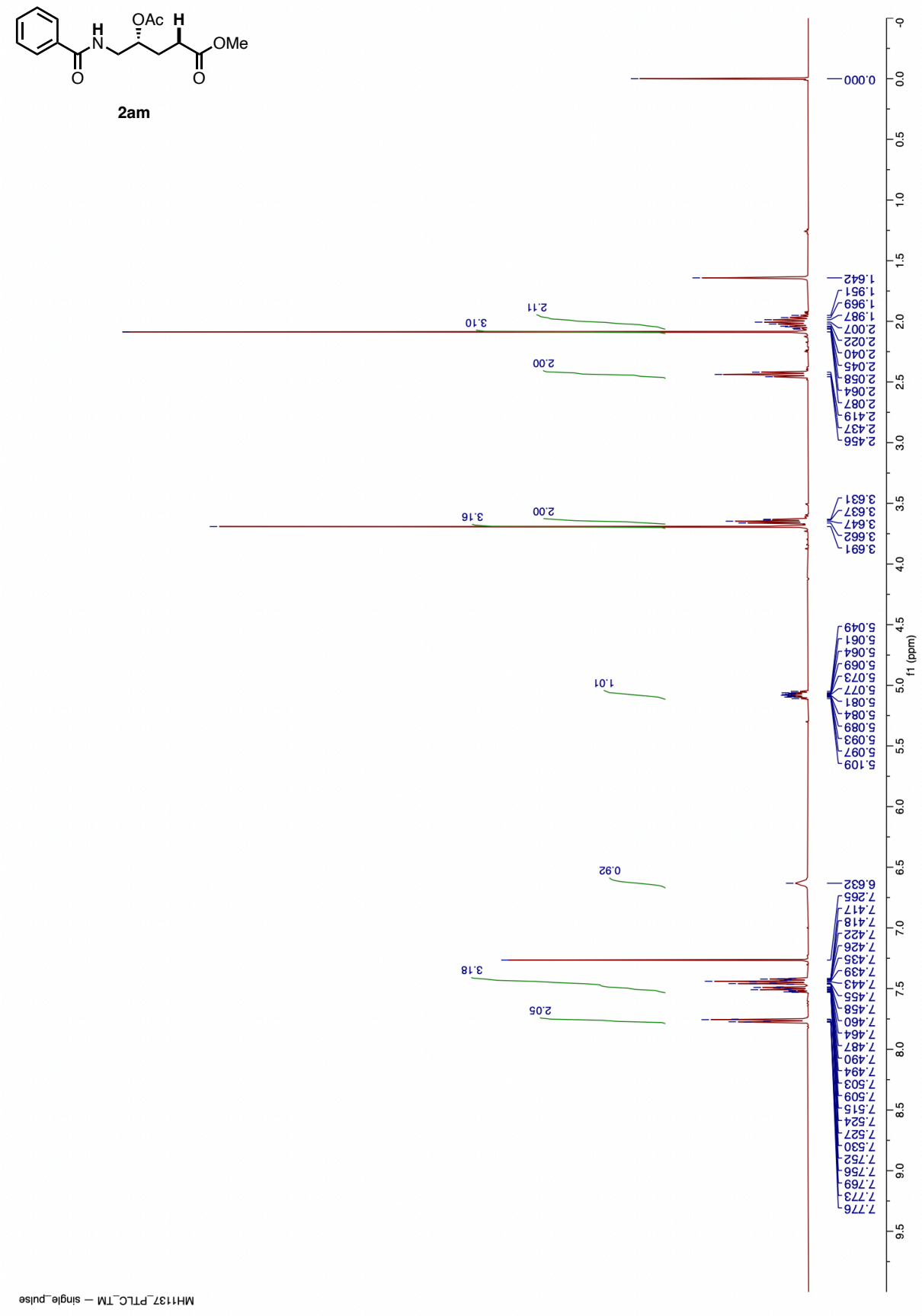
^{1}H NMR of 2al (400 MHz, $CDCl_3$)



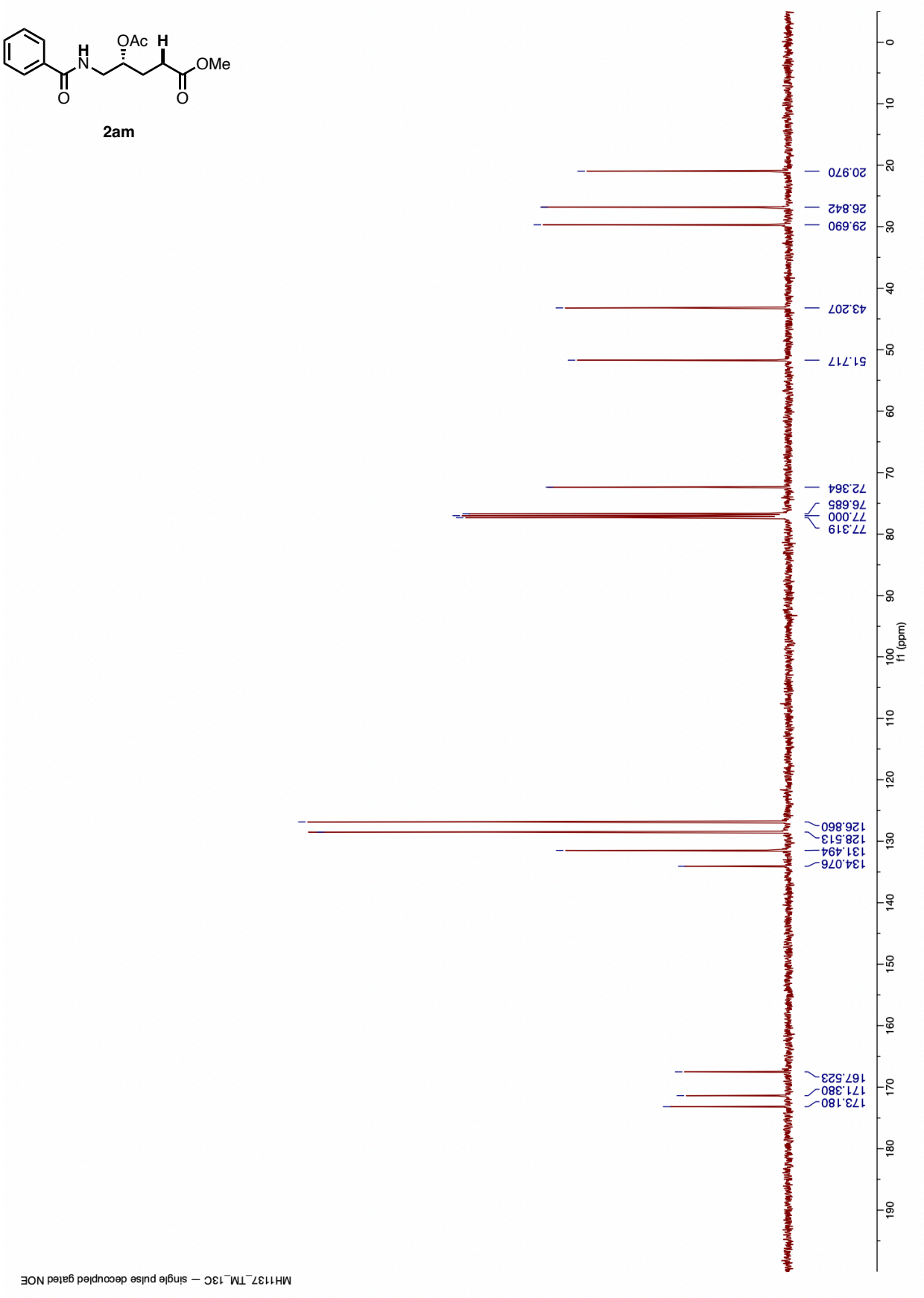
$^{13}C\{^{1}H\}$ NMR of 2al (101 MHz, $CDCl_3$)



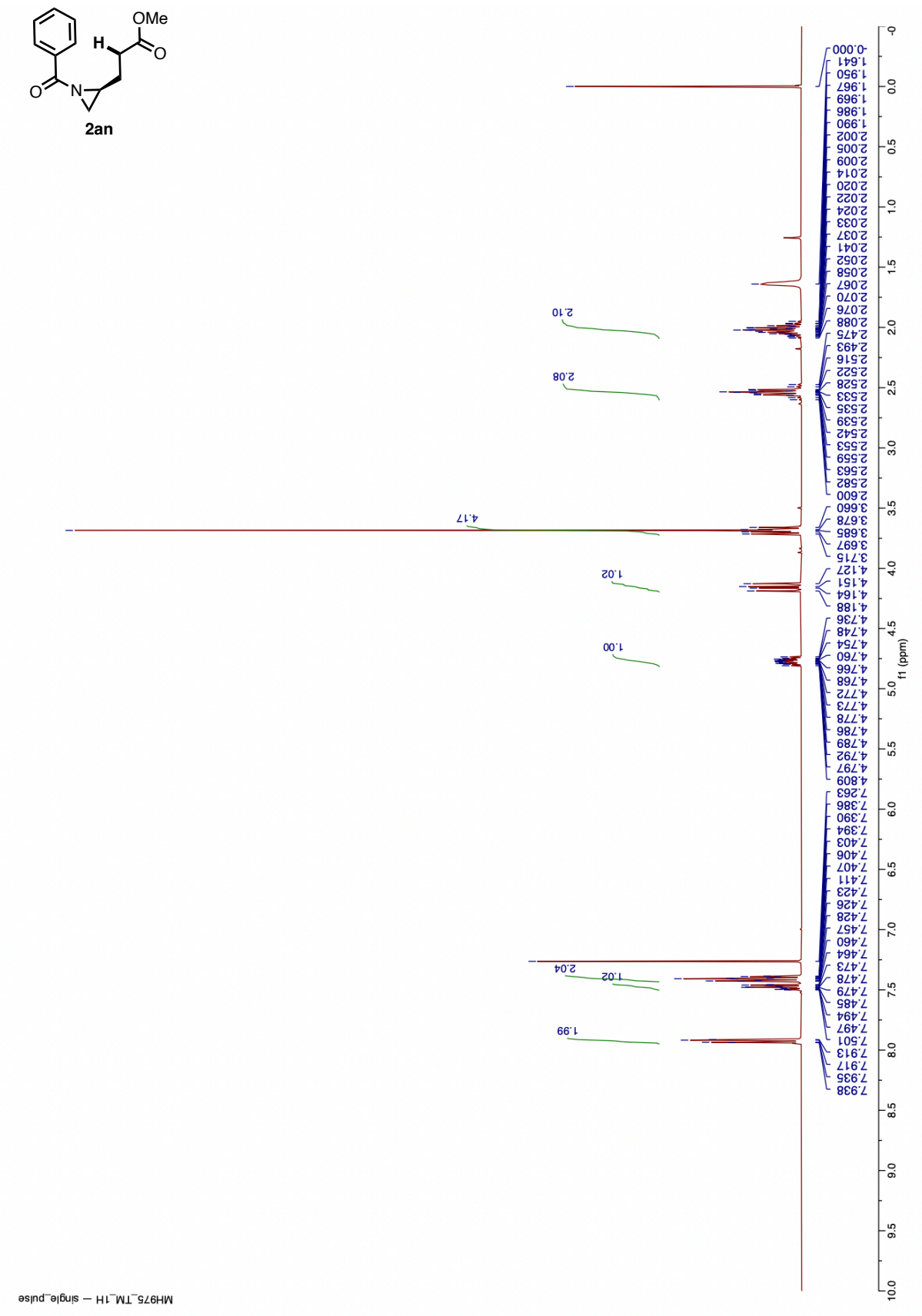
^{1}H NMR of 2abm (400 MHz, $CDCl_3$)



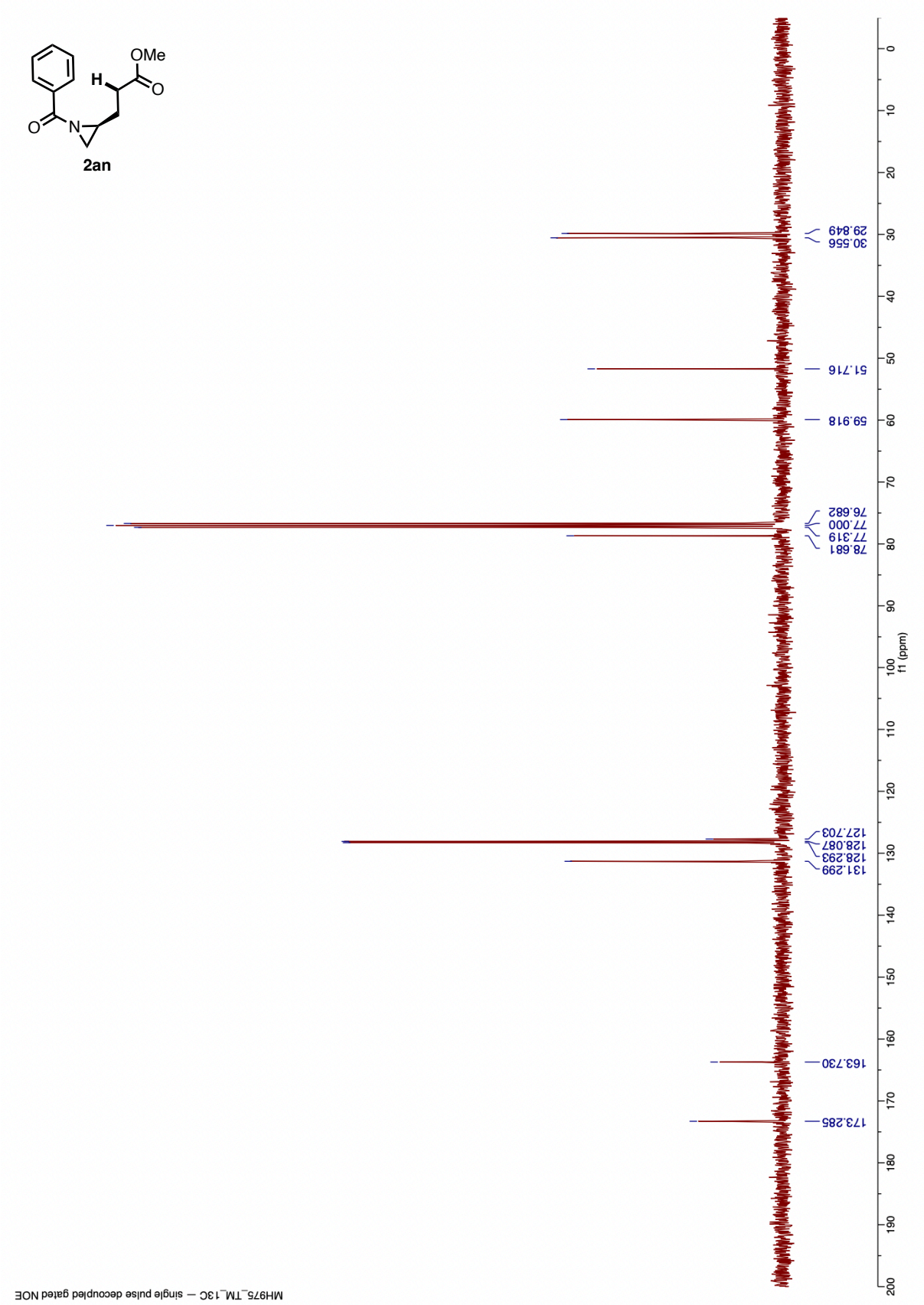
$^{13}C\{^{1}H\}$ NMR of 2am (101 MHz, $CDCl_3$)



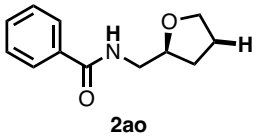
^{1}H NMR of 2an (400 MHz, $CDCl_3$)



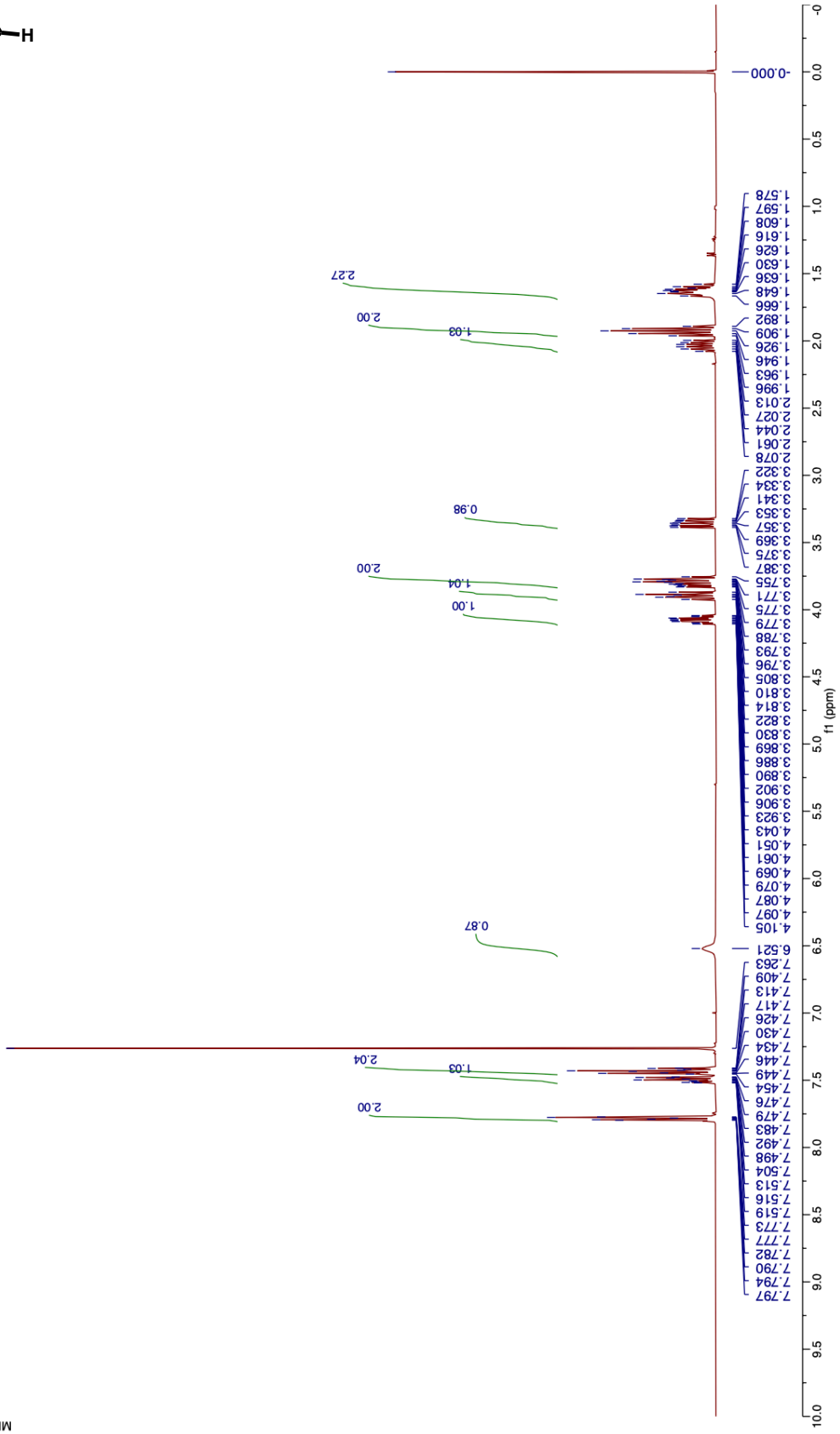
$^{13}C\{^{1}H\}$ NMR of 2an (101 MHz, $CDCl_3$)



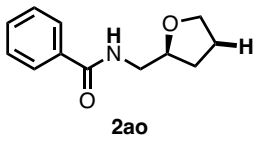
^{1}H NMR of 2ao (400 MHz, $CDCl_3$)



2ao

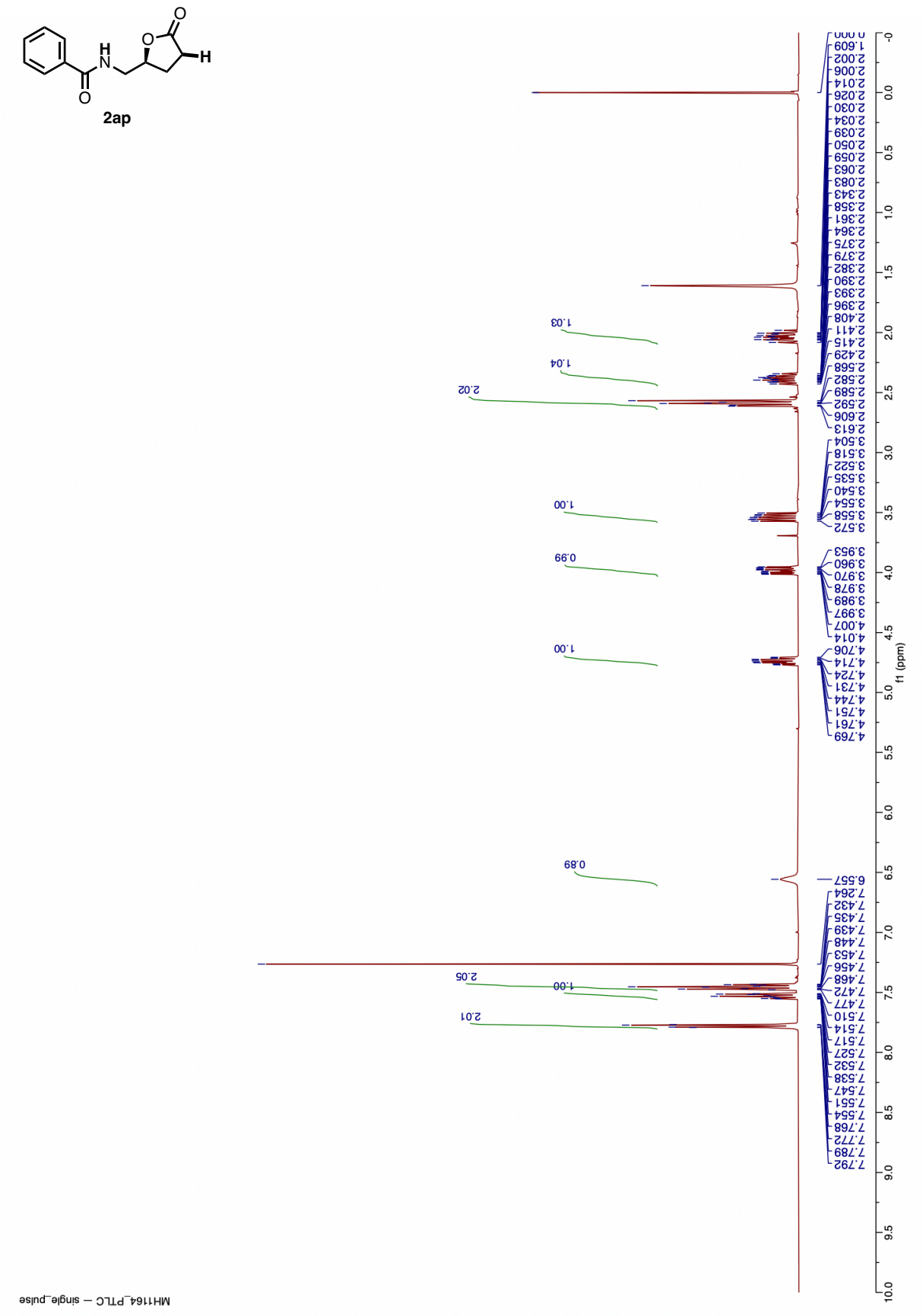


$^{13}C\{^{1}H\}$ NMR of 2ao (101 MHz, $CDCl_3$)

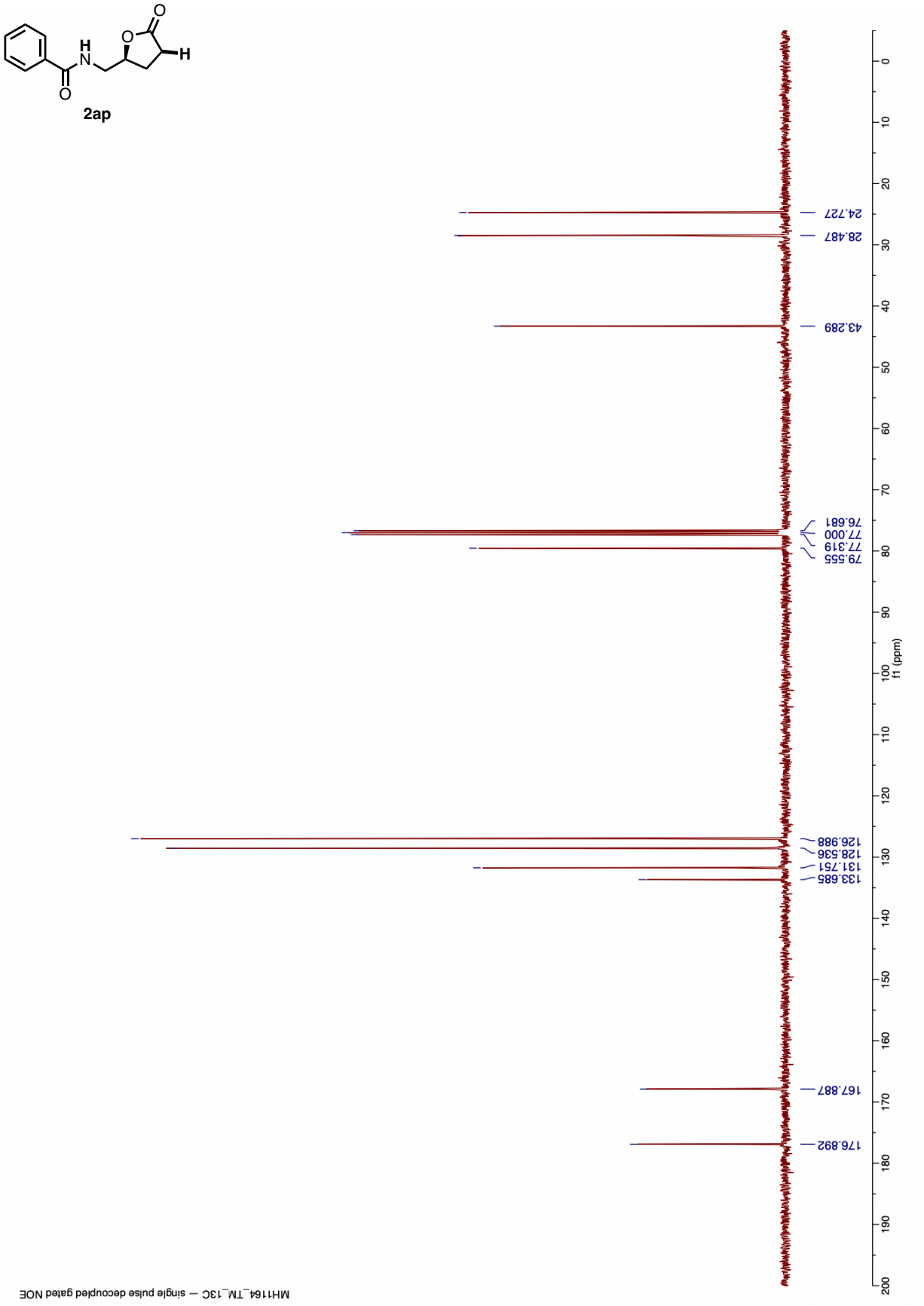


2ao

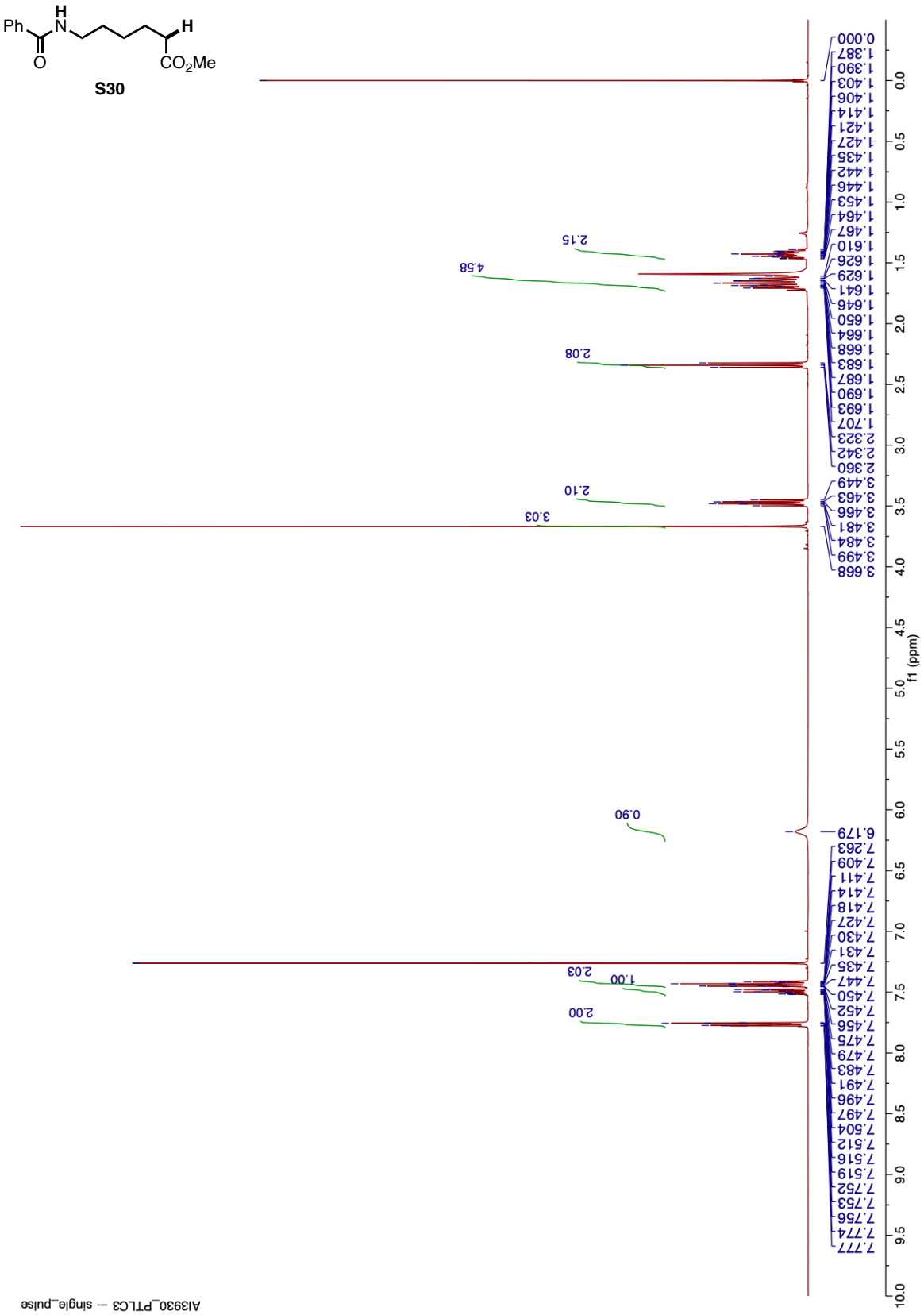
^{1}H NMR of 2ap (400 MHz, $CDCl_3$)



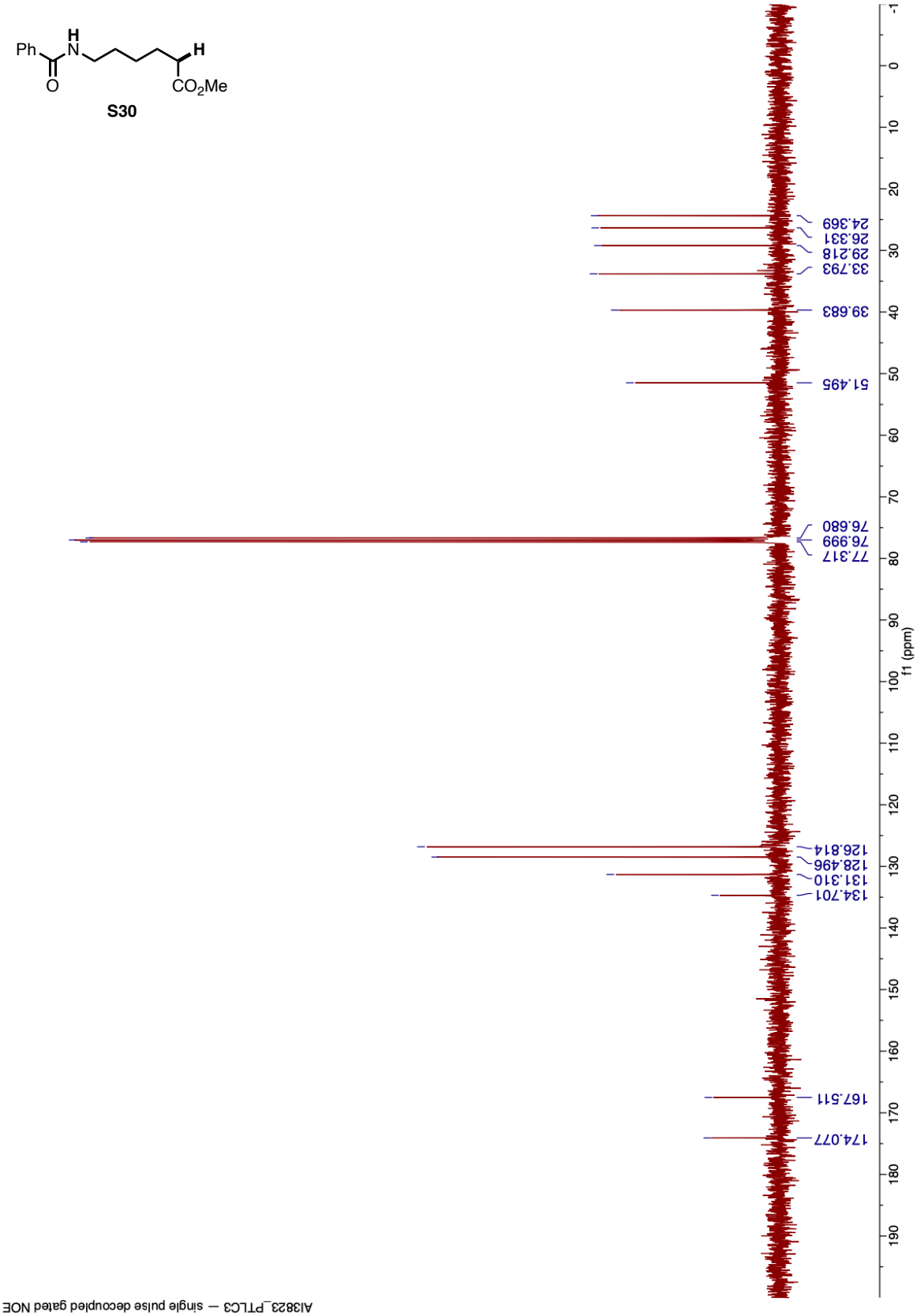
$^{13}C\{^{1}H\}$ NMR of 2ap (101 MHz, $CDCl_3$)



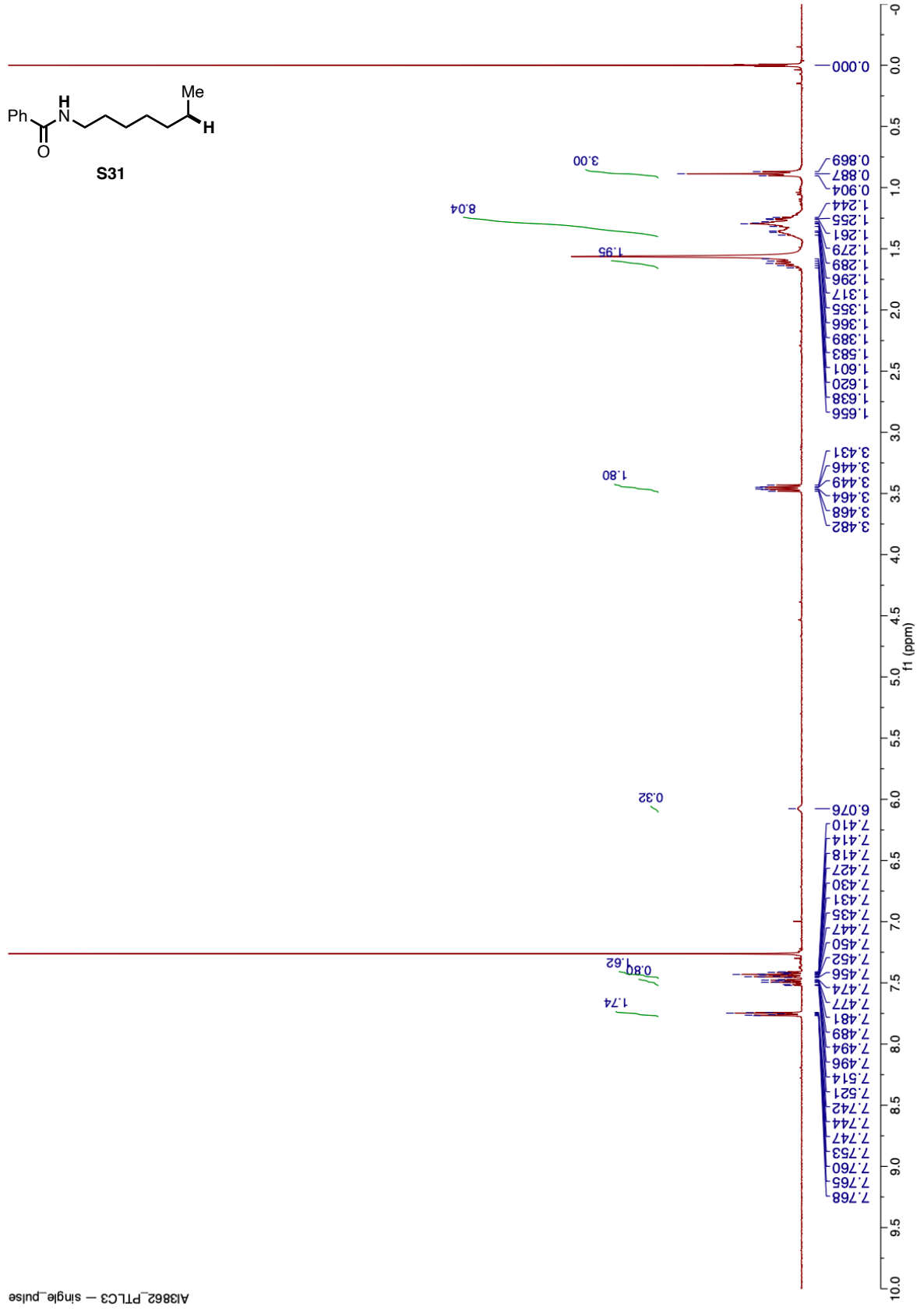
^{1}H NMR of S30 (400 MHz, $CDCl_3$)



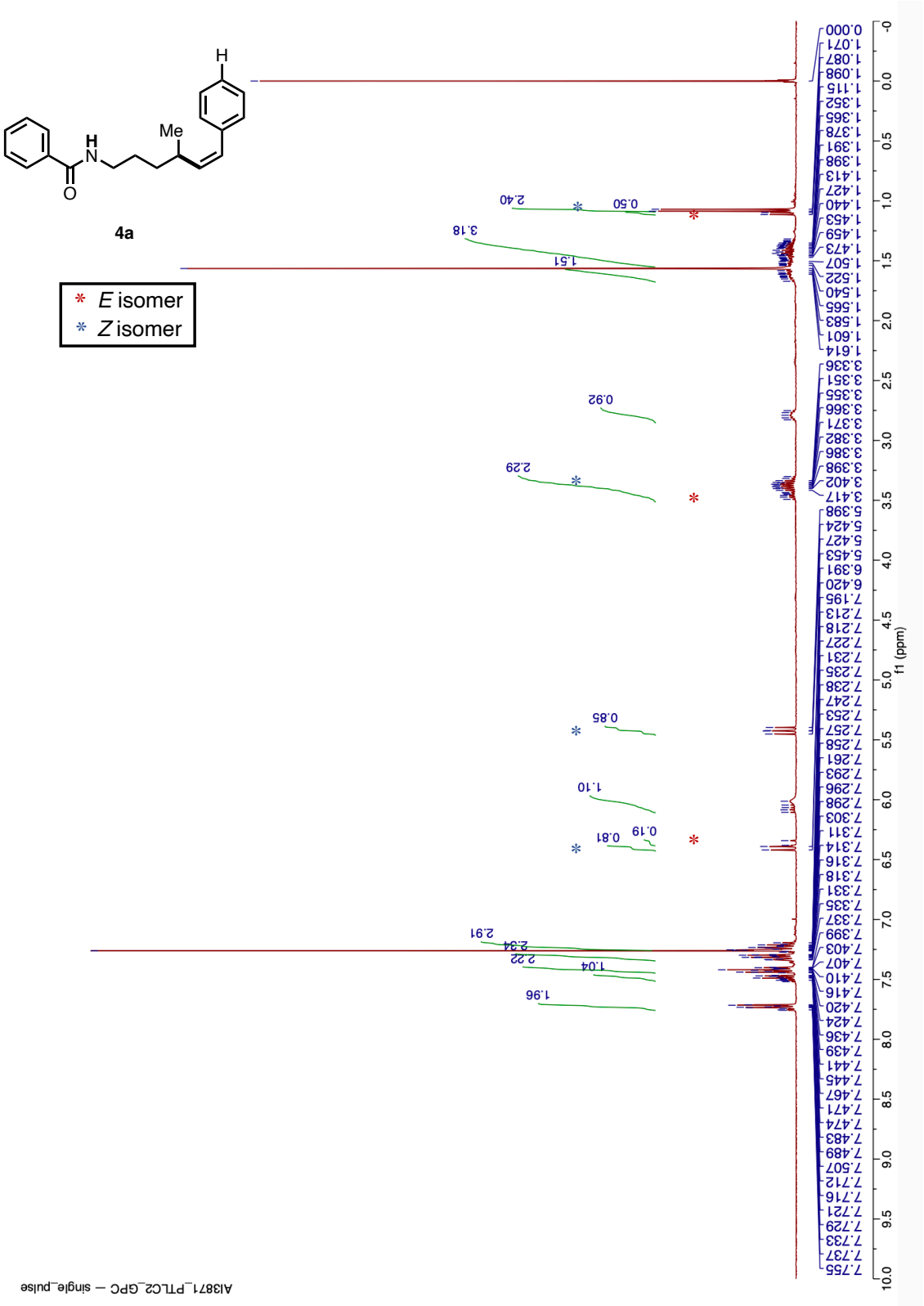
$^{13}C\{^{1}H\}$ NMR of S30 (101 MHz, $CDCl_3$)



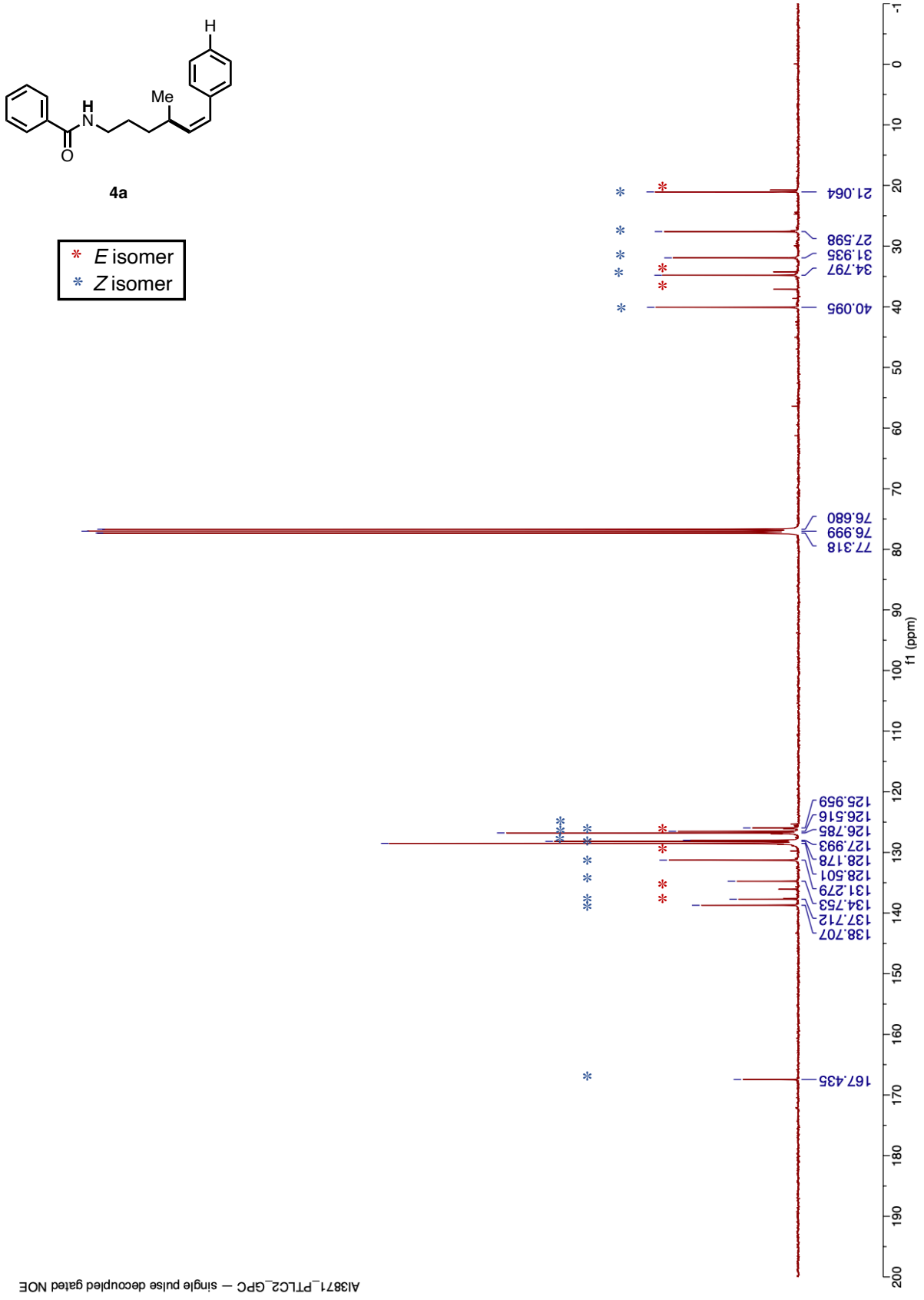
^{1}H NMR of S31 (400 MHz, $CDCl_3$)



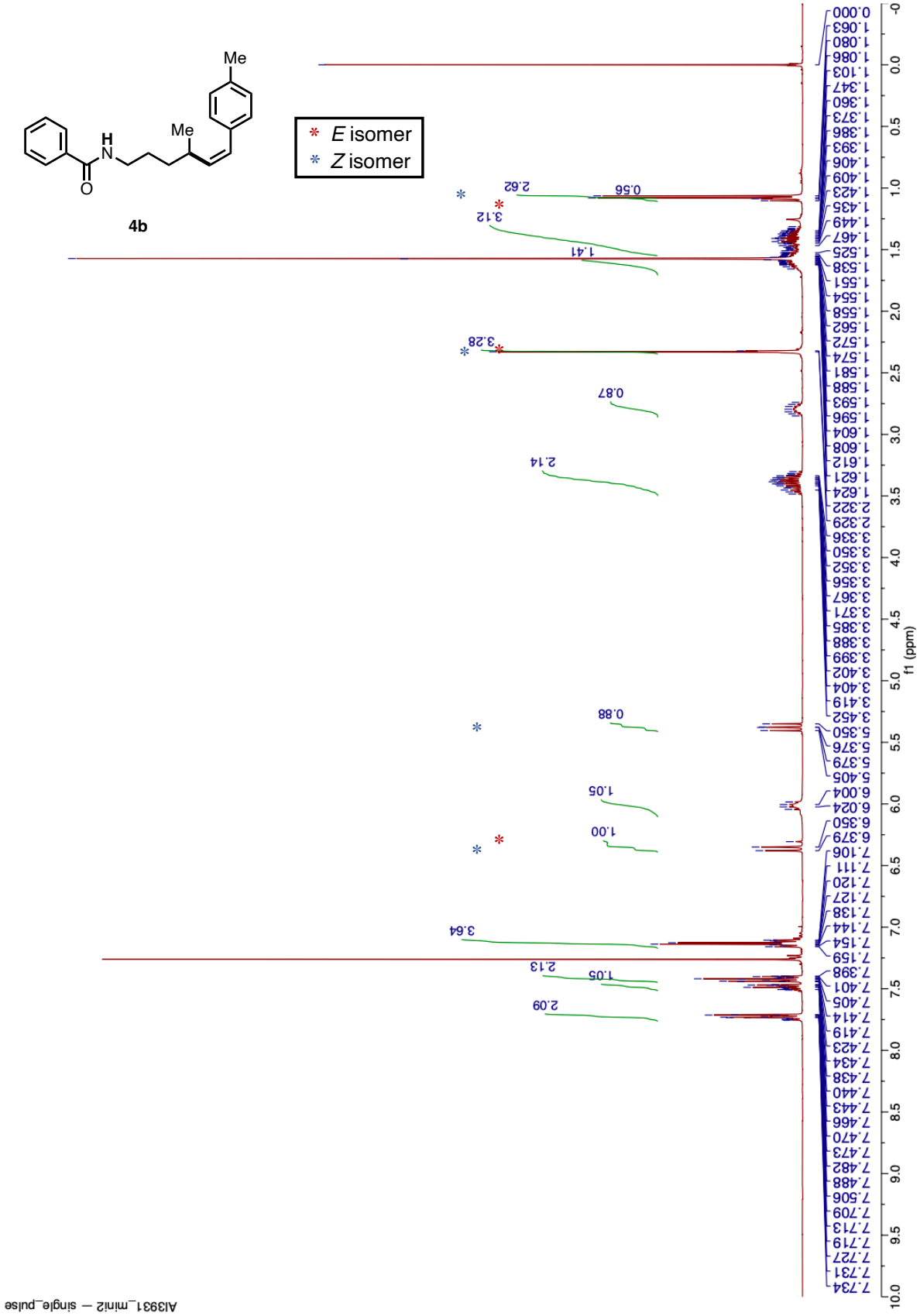
^{1}H NMR of 4a (400 MHz, $CDCl_3$)



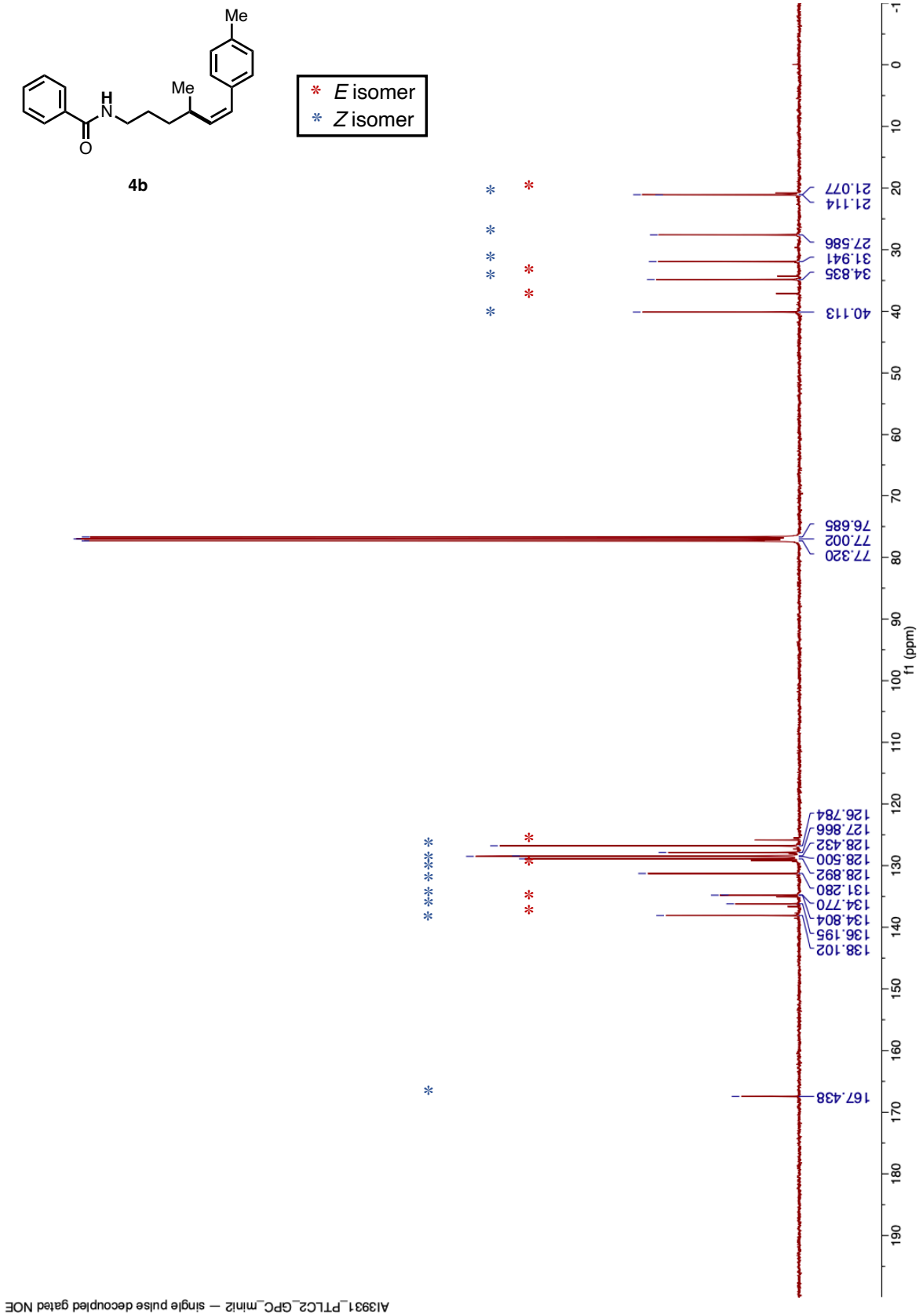
$^{13}C\{^{1}H\}$ NMR of 4a (101 MHz, $CDCl_3$)



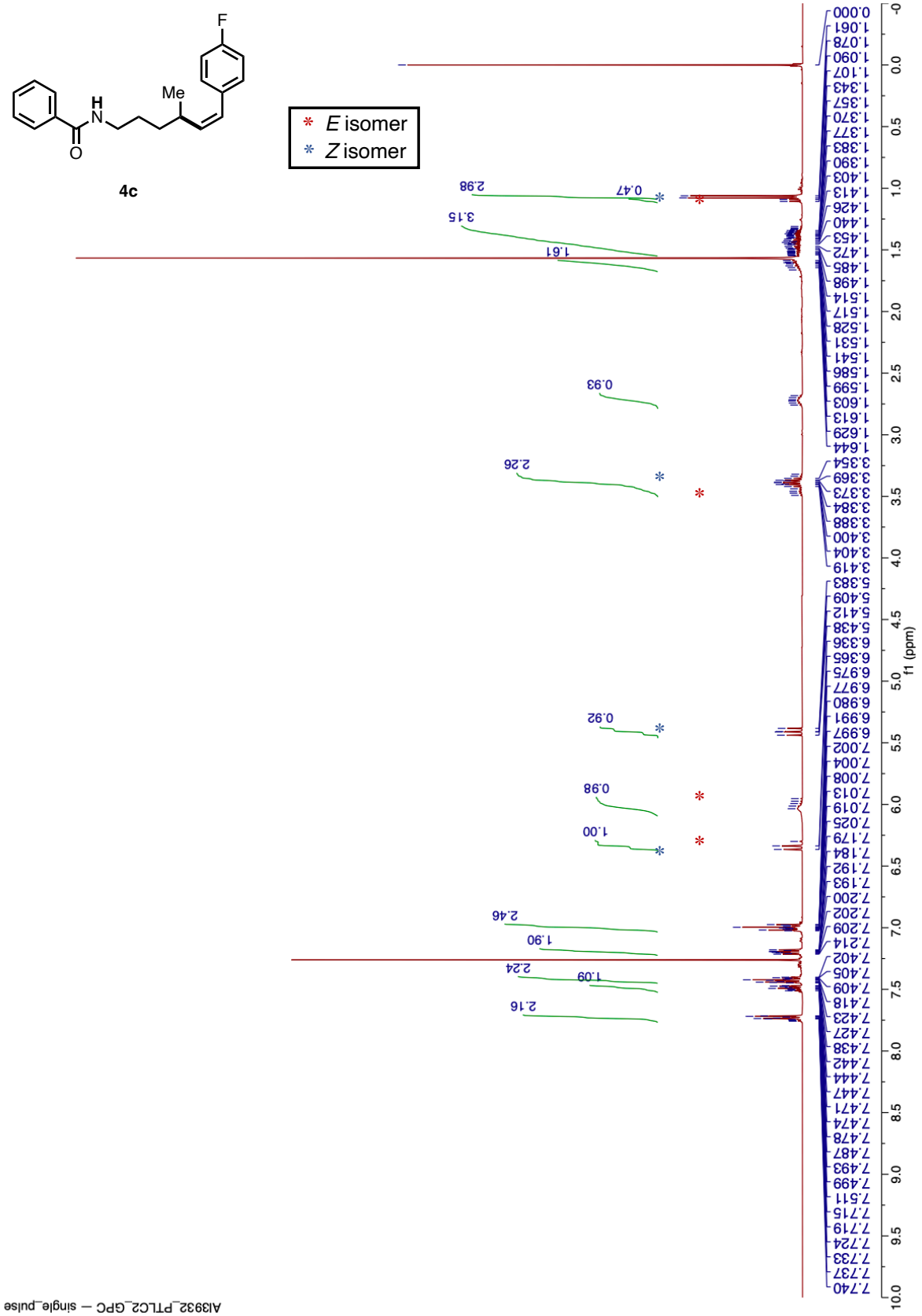
^{1}H NMR of 4b (400 MHz, $CDCl_3$)



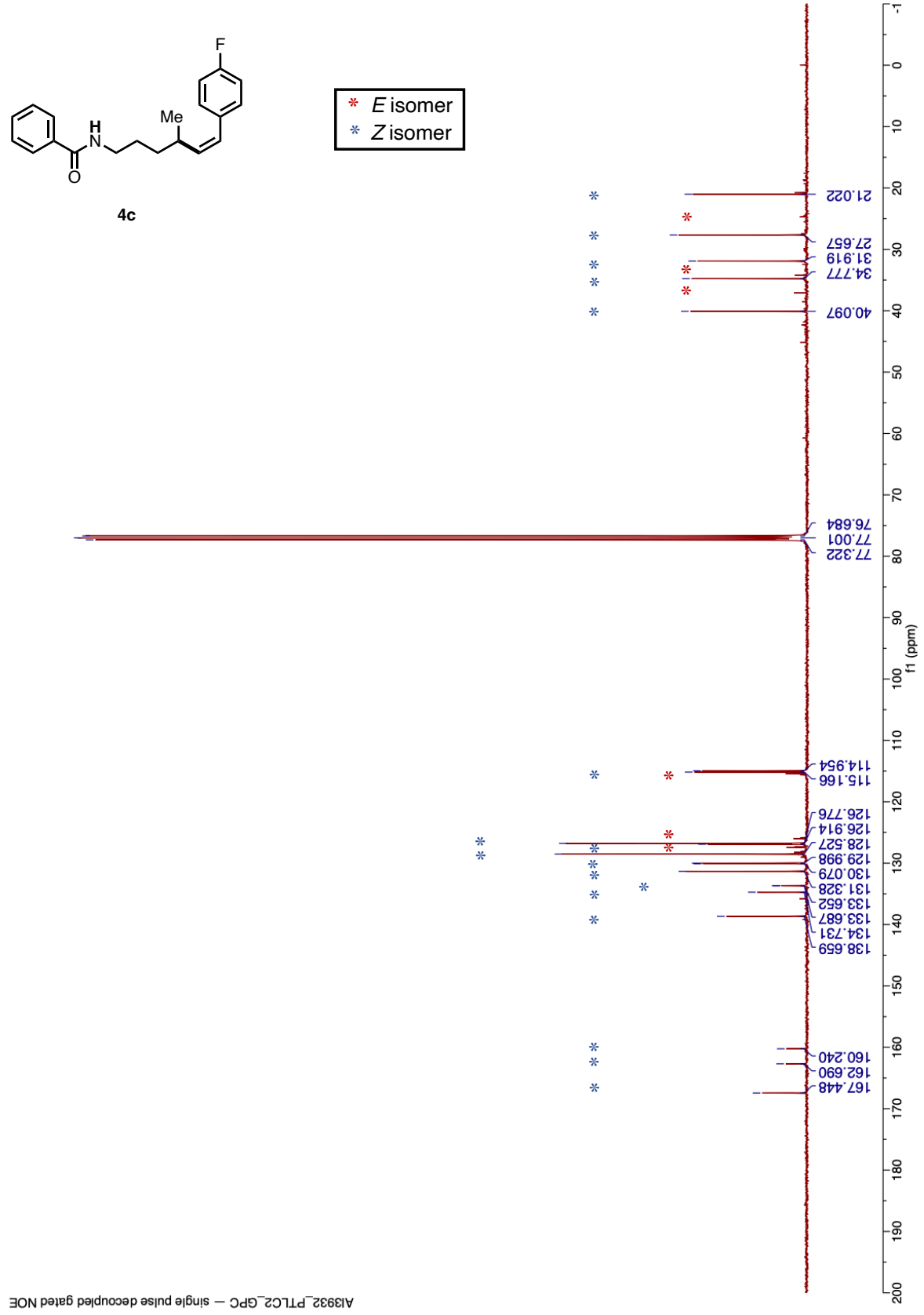
$^{13}C\{^{1}H\}$ NMR of 4b (101 MHz, $CDCl_3$)



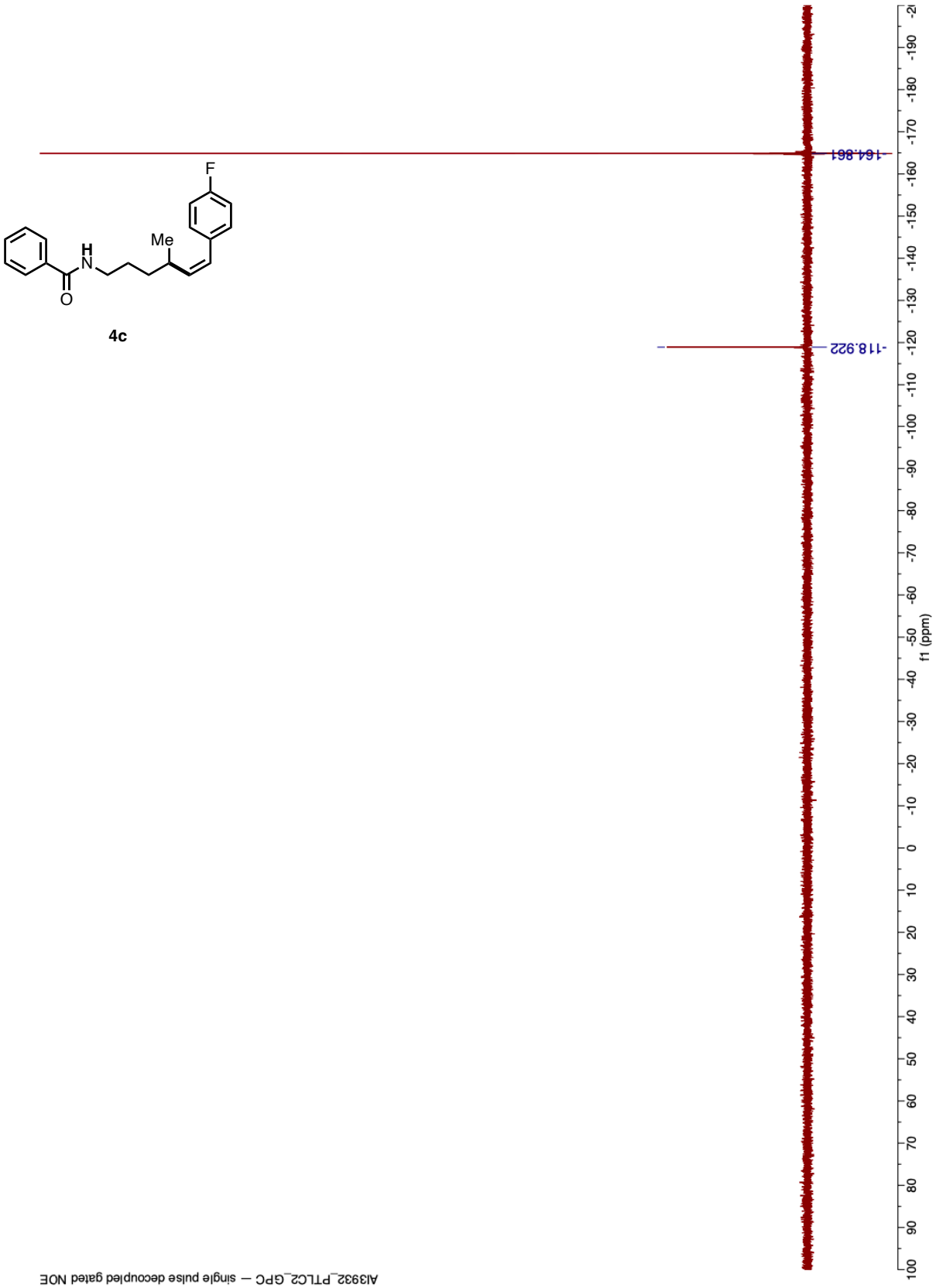
^{1}H NMR of 4c (400 MHz, $CDCl_3$)



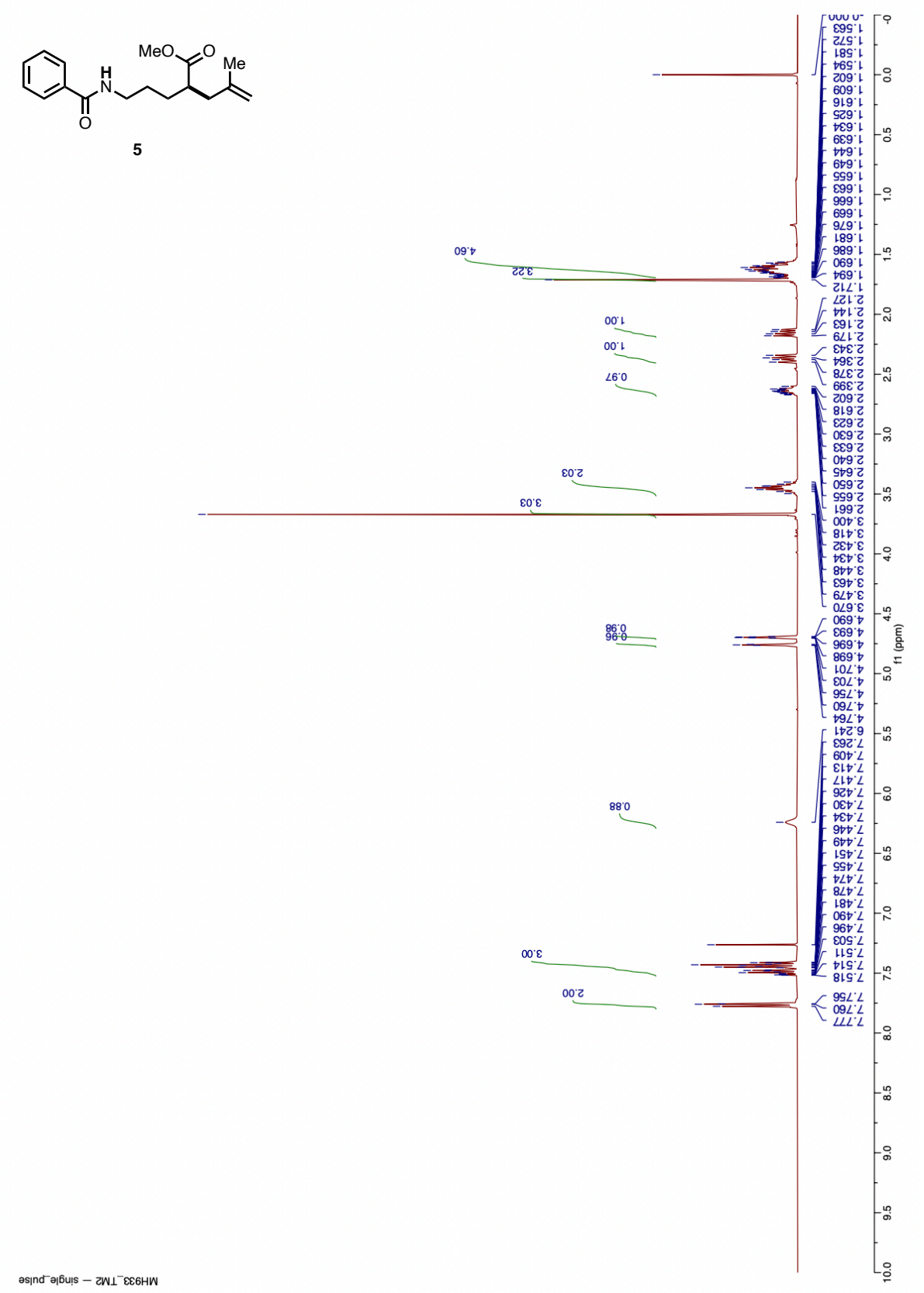
$^{13}C\{^{1}H\}$ NMR of 4c (101 MHz, $CDCl_3$)



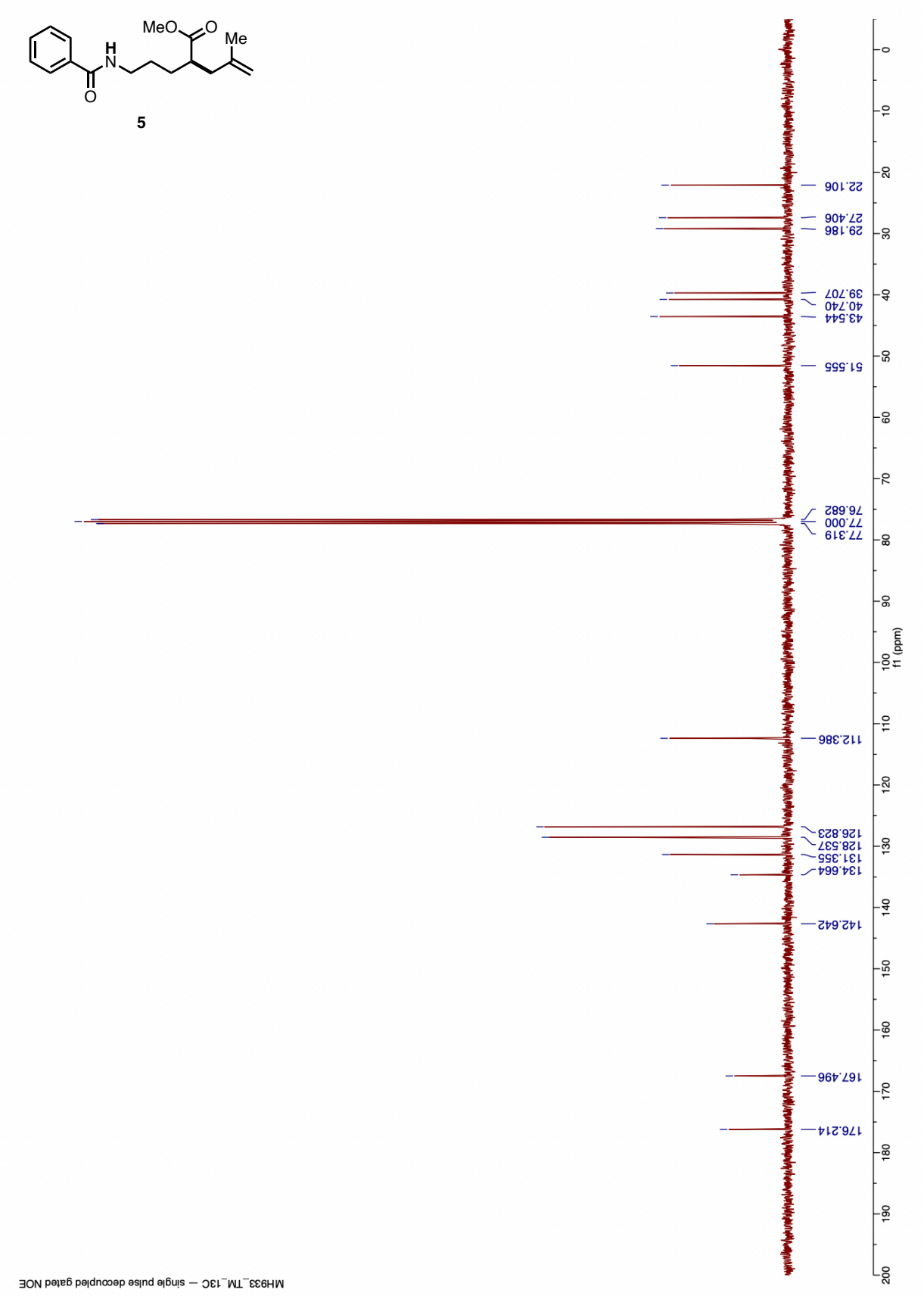
^{19}F NMR of 4c (376 MHz, $CDCl_3$)



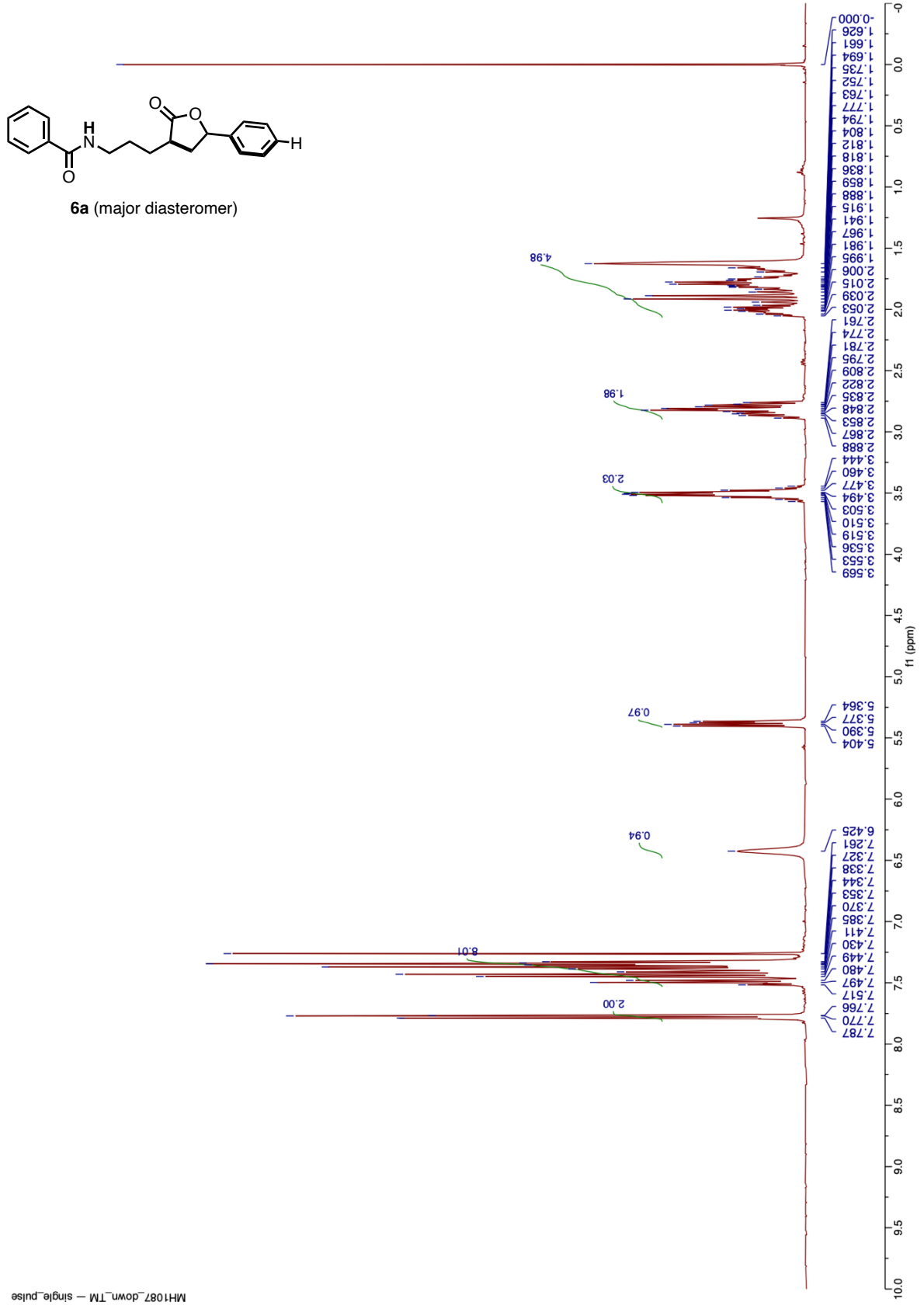
^{1}H NMR of 5 (400 MHz, $CDCl_3$)



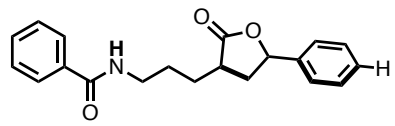
$^{13}C\{^{1}H\}$ NMR of 5 (101 MHz, $CDCl_3$)



^{1}H NMR of 6a (400 MHz, $CDCl_3$): major diastereomer

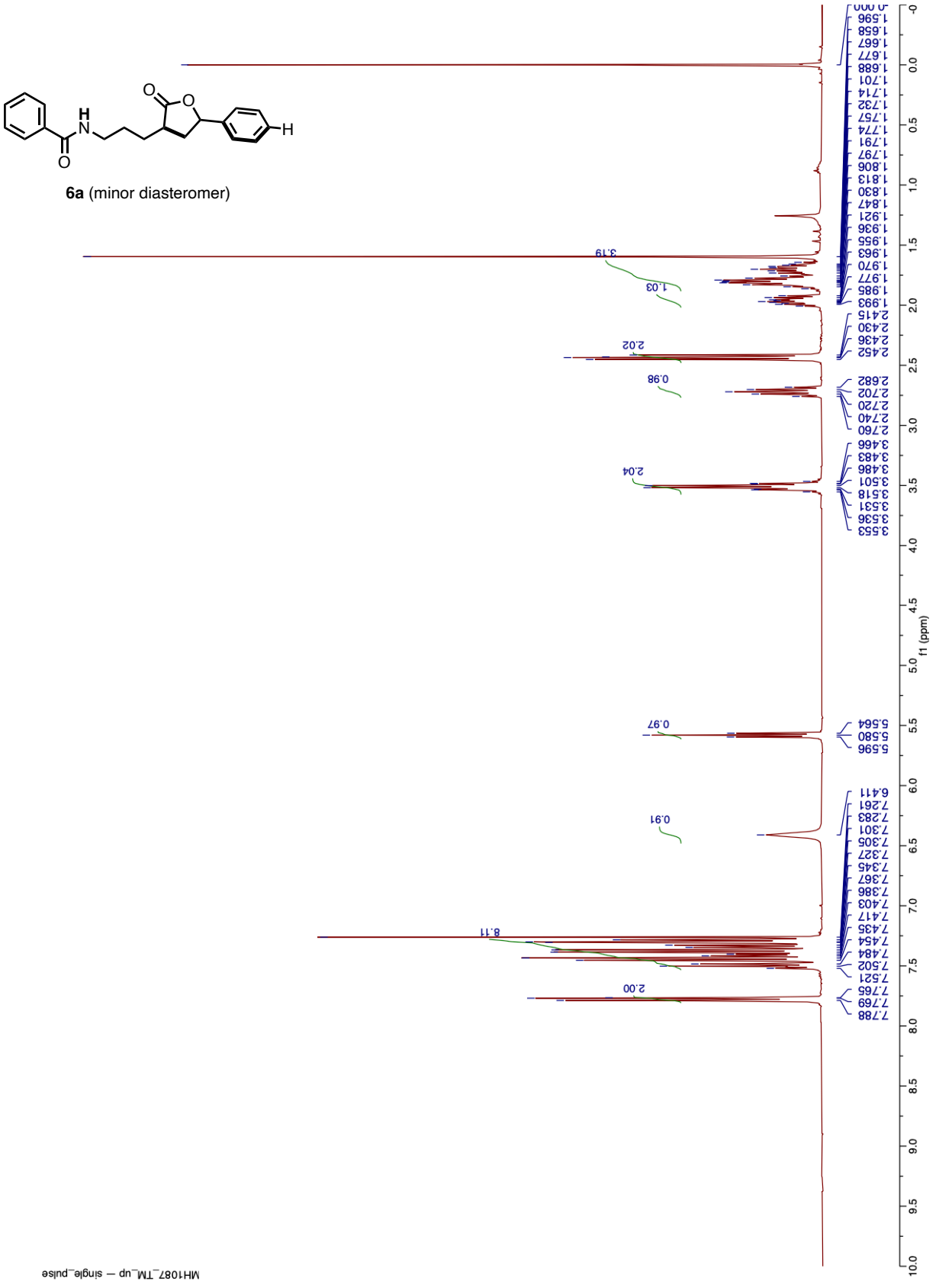


$^{13}C\{^{1}H\}$ NMR of 6a (101 MHz, $CDCl_3$): major diastereomer

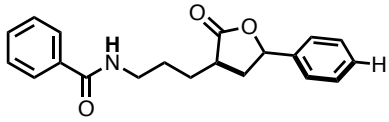


6a (major diasteromer)

^{1}H NMR of 6a (400 MHz, $CDCl_3$): minor diastereomer

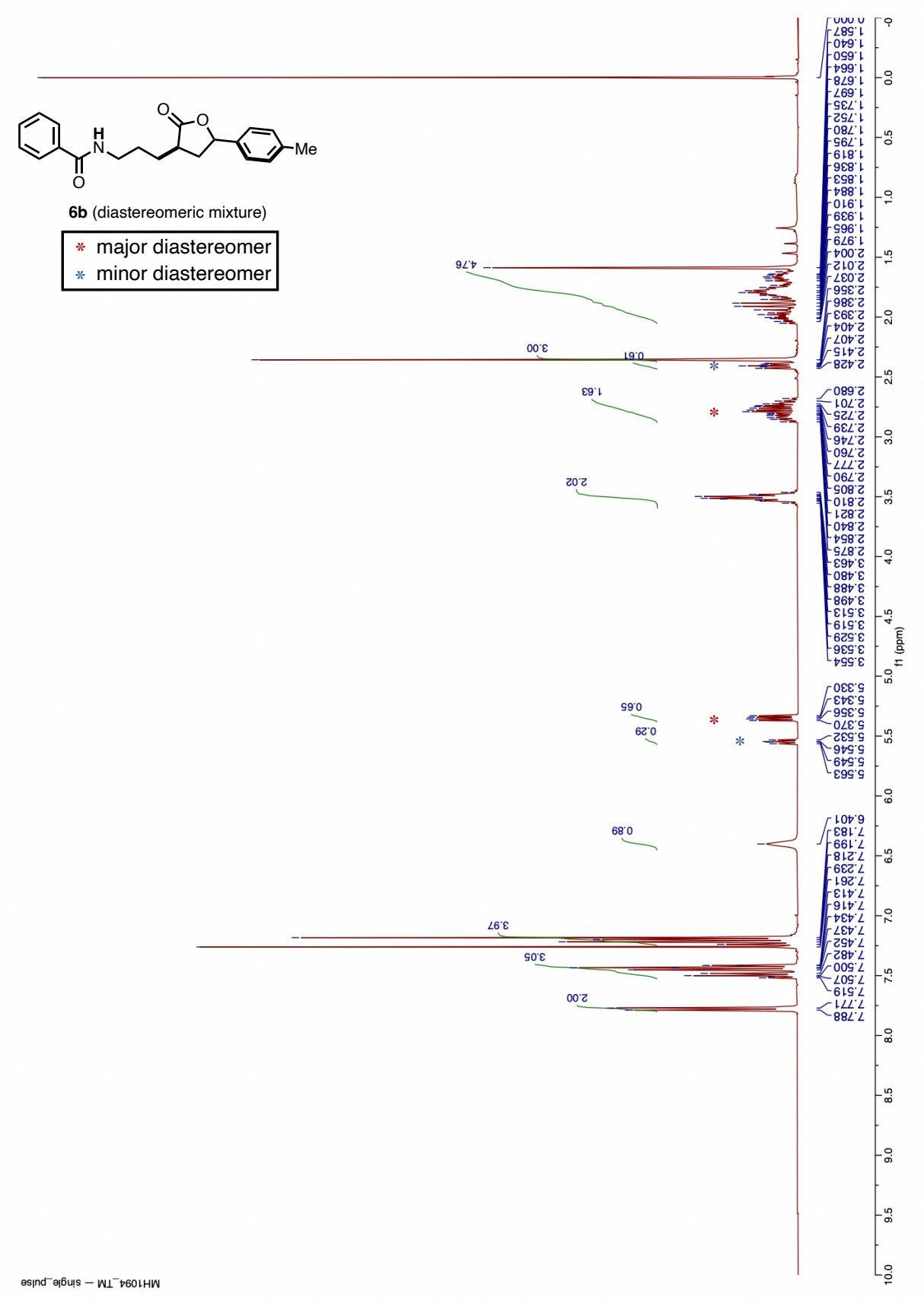


$^{13}C\{^{1}H\}$ NMR of 6a (101 MHz, $CDCl_3$): minor diastereomer

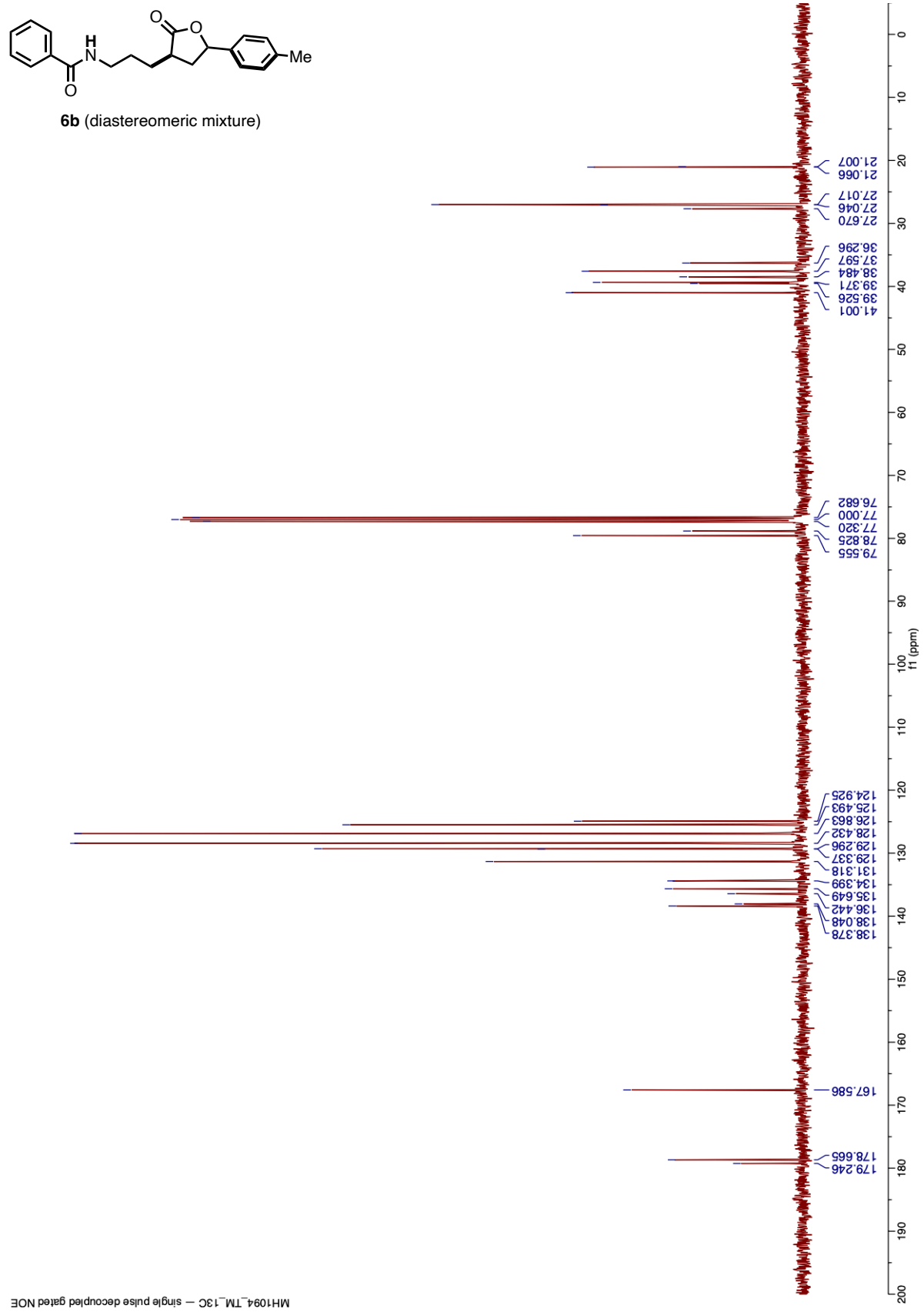


6a (minor diasteromer)

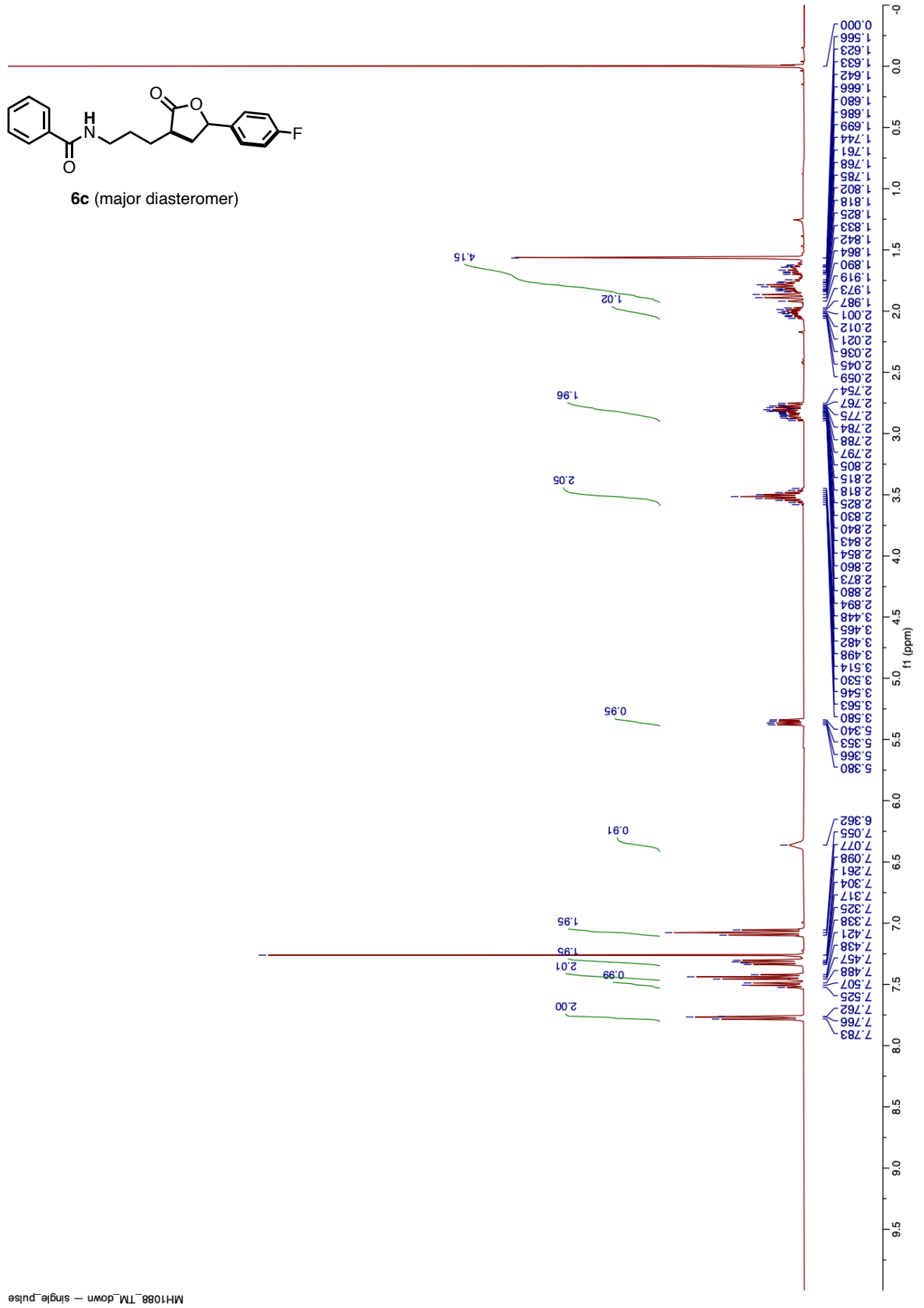
^{1}H NMR of 6b (400 MHz, $CDCl_3$): diastereomeric mixture



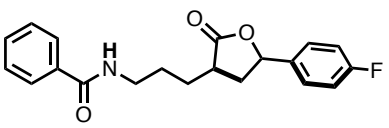
$^{13}C\{^{1}H\}$ NMR of 6b (101 MHz, $CDCl_3$): diastereomeric mixture



^{1}H NMR of 6c (400 MHz, $CDCl_3$): major diastereomer

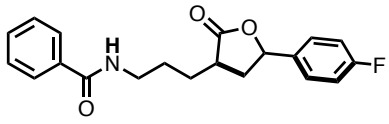


$^{13}C\{^{1}H\}$ NMR of 4c (101 MHz, $CDCl_3$): major diastereomer



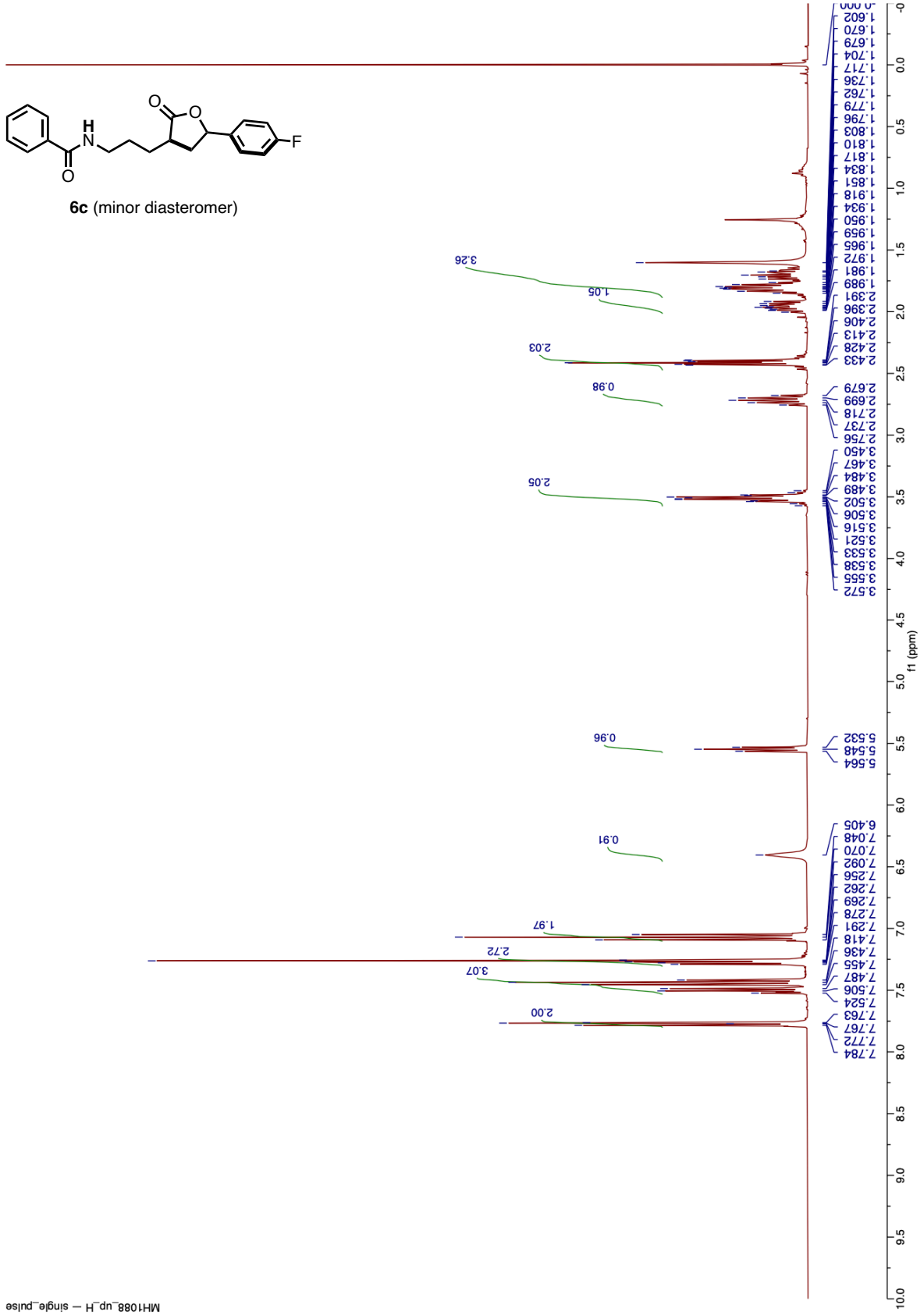
6c (major diasteromer)

^{19}F NMR of 6c (376 MHz, $CDCl_3$): major diastereomer

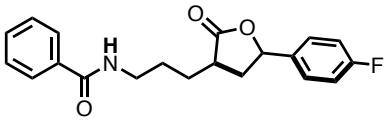


6c (major diasteromer)

^{1}H NMR of 6c (400 MHz, $CDCl_3$): minor diastereomer

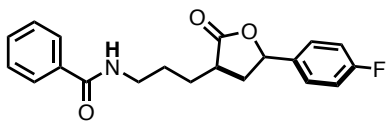


$^{13}C\{^{1}H\}$ NMR of 6c (101 MHz, $CDCl_3$): minor diastereomer



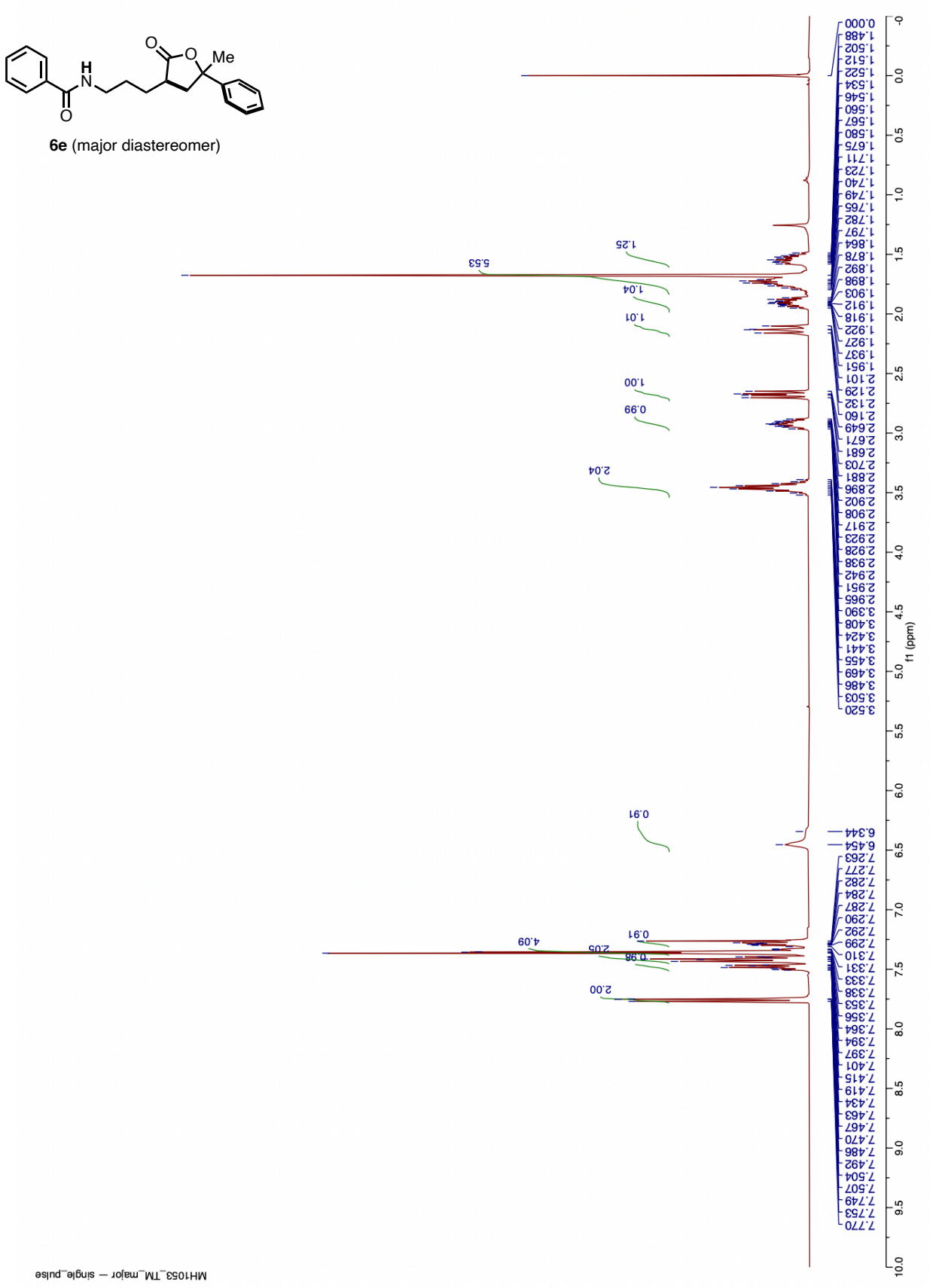
6c (minor diasteromer)

^{19}F NMR of 6c (376 MHz, $CDCl_3$): minor diastereomer

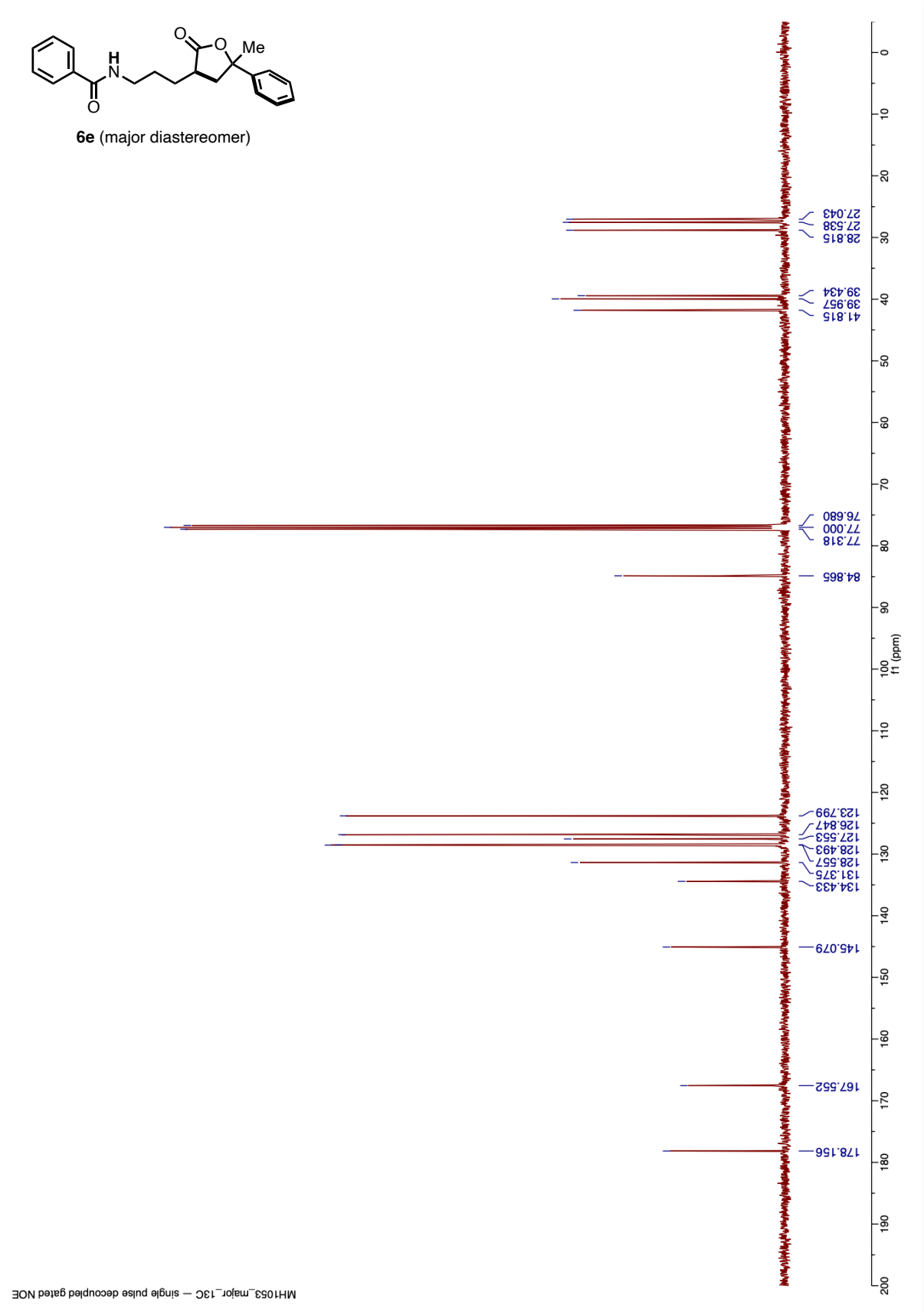


6c (minor diasteromer)

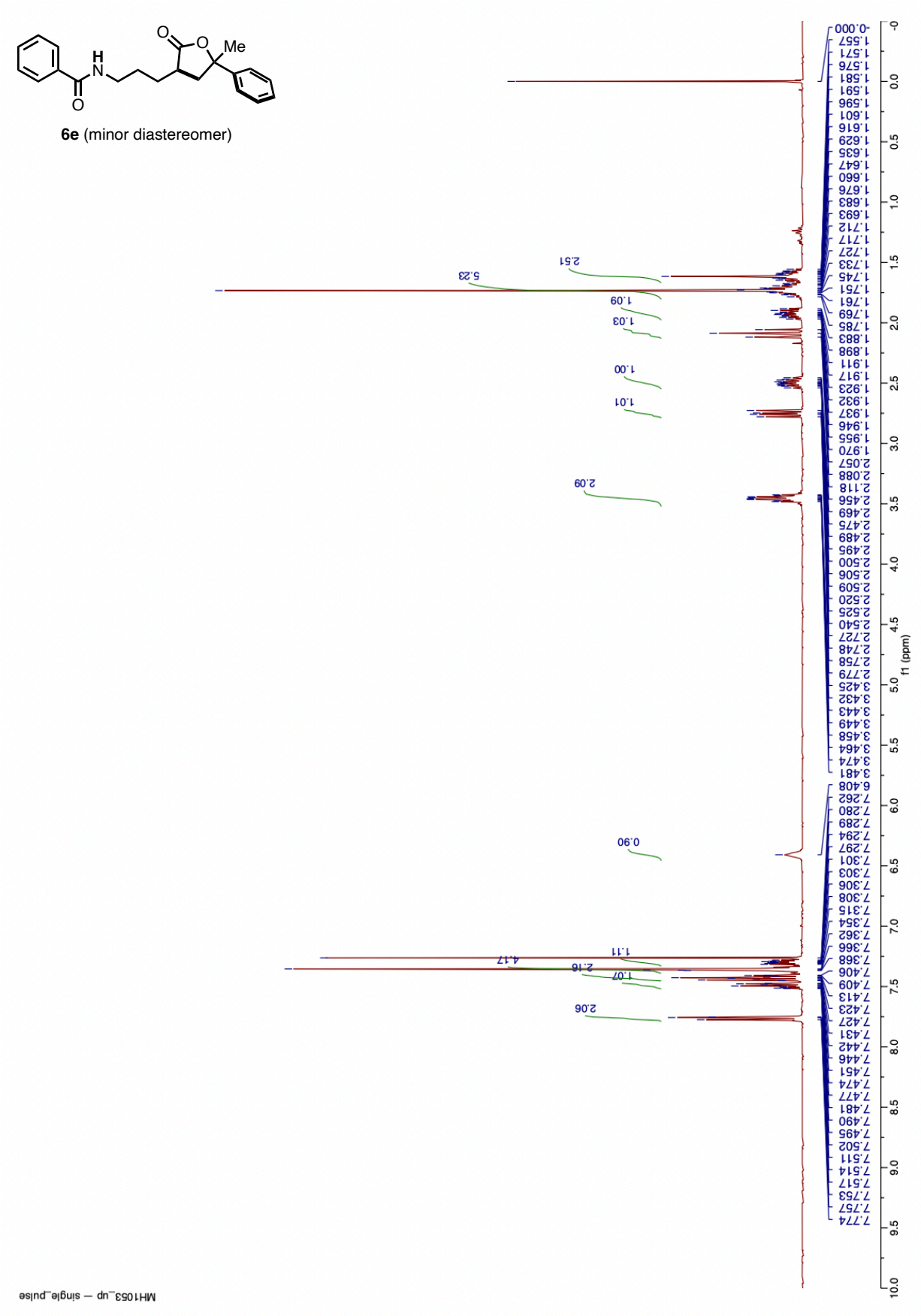
^{1}H NMR of 6e (400 MHz, $CDCl_3$): major diastereomer



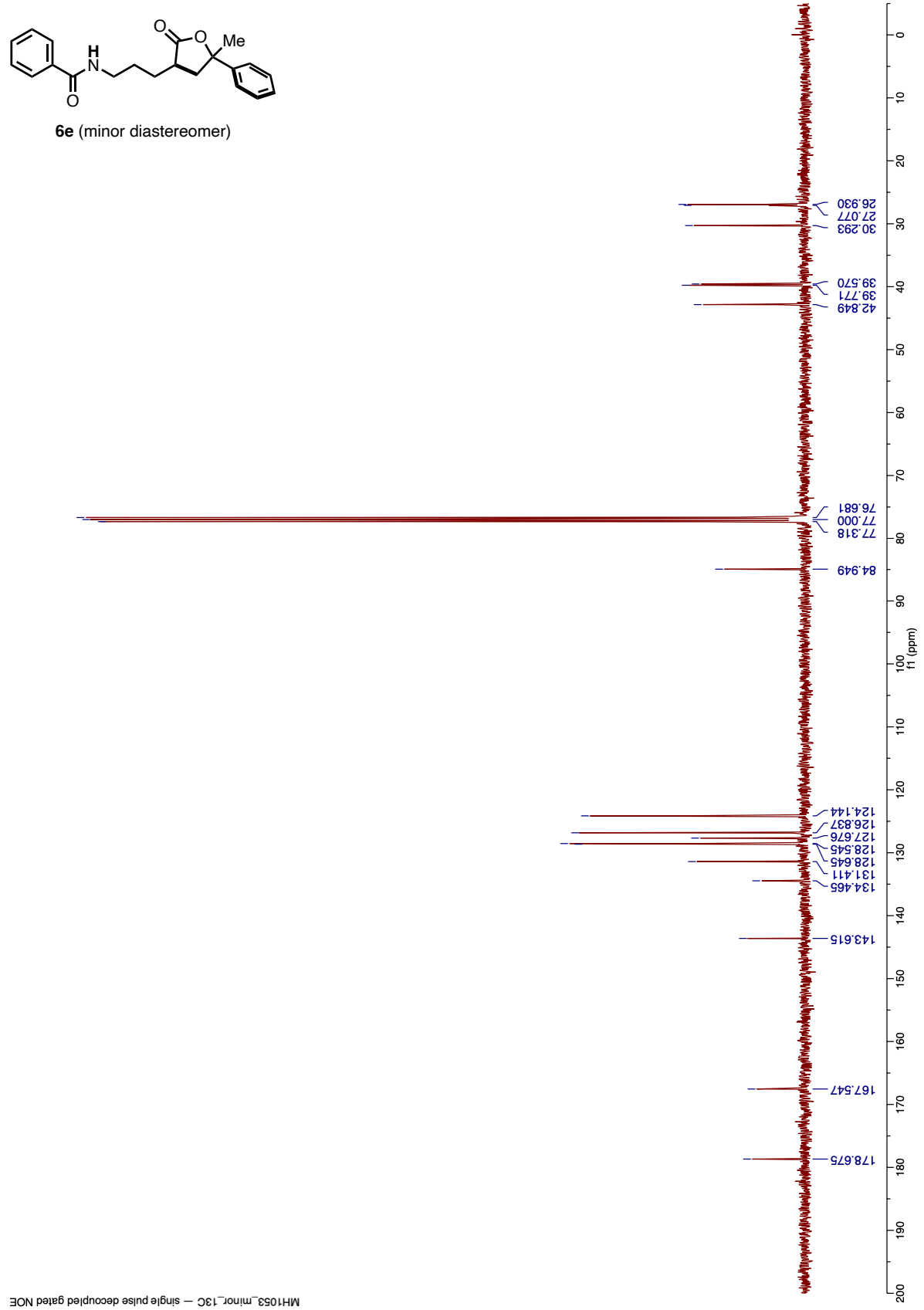
$^{13}C\{^{1}H\}$ NMR of 6e (101 MHz, $CDCl_3$): major diastereomer



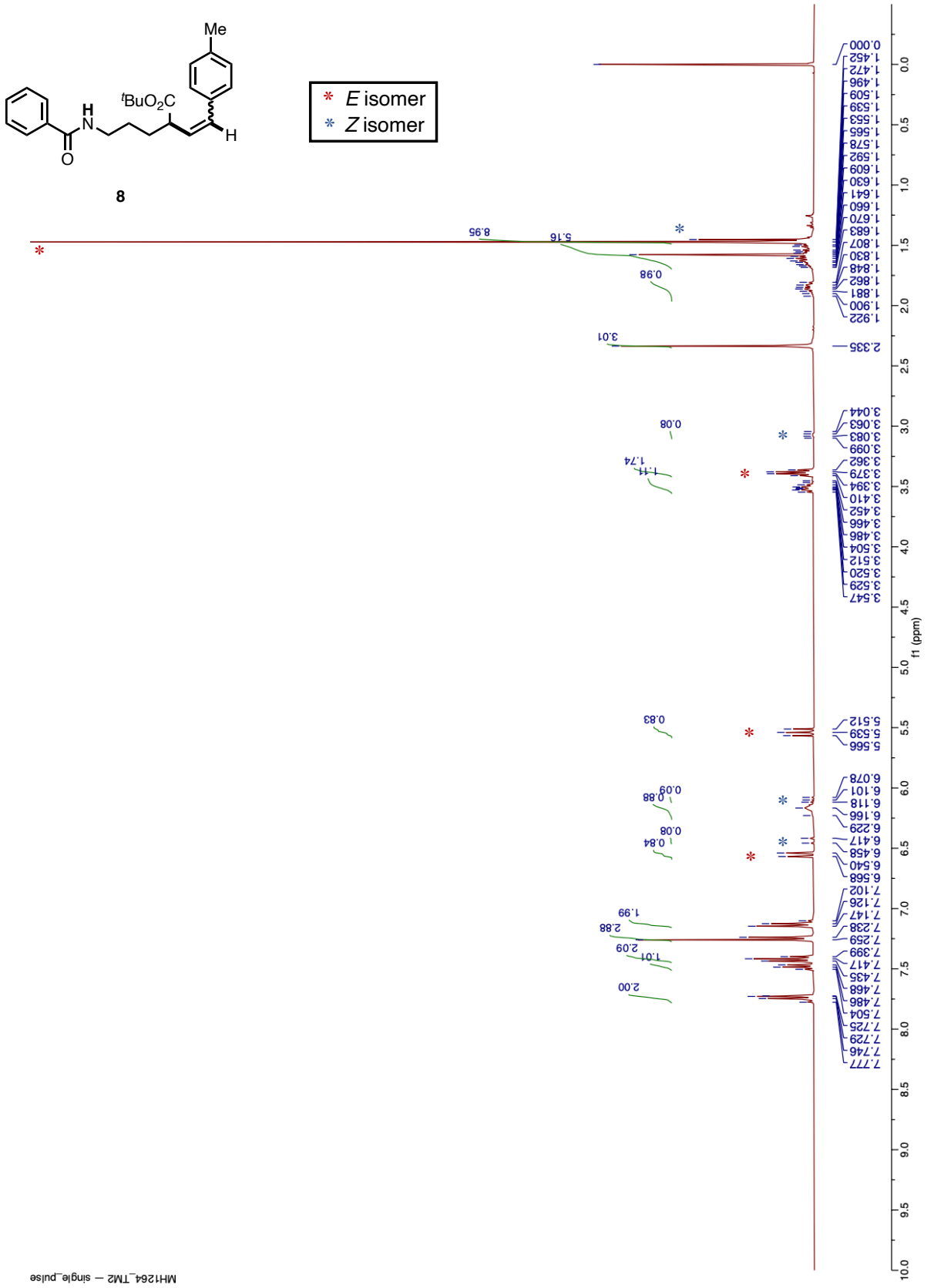
^{1}H NMR of 6e (400 MHz, $CDCl_3$): minor diastereomer



$^{13}C\{^{1}H\}$ NMR of 6e (101 MHz, $CDCl_3$): minor diastereomer



^{1}H NMR of 8 (400 MHz, $CDCl_3$): diastereomeric mixture



$^{13}C\{^{1}H\}$ NMR of 8 (101 MHz, $CDCl_3$): diastereomeric mixture