Supporting Information

Combination of the structural components of amino acids with fatty acids: Access to an unknown class of "fatty" α-amino acids by palladium-catalyzed amidocarbonylation

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Abstract: Applying the palladium-catalyzed amidocarbonylation a new class of amino acid derivatives, so-called fatty amino acids, are synthesized in one step in 100% atom-efficient manner. Utilizing 0.5 mol% of $Pd(OAc)_2$ simple diverse new N-acyl fatty amino acids can be synthesized in good to high yields in up to multi-g-scale. The shown products represent a combination of two essential classes of natural products.

Summary

General Remarks

All commercial reagents were obtained from the following chemical companies: Aldrich, Fisher Scientific, BLDpharm, TCI, ABCR and Strem. Unless otherwise noted, the commercial reagents were used without purification. The reactions with air- and moisture-sensitive reagents were carried out under argon atmosphere using standard Schlenk technique or in a M. Braun glovebox. Anhydrous and oxygen-free solvents (THF, DCM, diethyl ether, toluene, benzene, *n*-pentane, *n*-hexane and *n*-heptane) were received from an Innovative Technology PS-MD-6 solvent purification system or they were prepared by freeze-pump-thaw technique. All anhydrous solvent were stored over 3 Å molecular sieves under argon atmosphere.

Analytical thin-layer chromatography (TLC) was performed on Machery-Nagel pre-coated ALUGRAM Xtra SIL G/UV254 TLC sheets. Visualization was achieved by irradiation with UV-light, or by staining with potassium permanganate, *p*-anisaldehyde or phosphomolybdic acid solution. Flash Column chromatography was performed with a Combi Flash Rf + from Teledyne ISCO using HPLC grade solvents.

NMR spectra were recorded on Bruker Avance 300 (300 MHz) or 400 (400 MHz) NMR spectrometers. The chemical shifts (δ) are reported in parts per million (ppm) and coupling constants (J) in hertz (Hz). All chemical shifts (δ) are given relative to solvent: references for $CDCl_3$ 7.26 ppm (^1H) and 77.16 ppm (^{13}C). MeOD refers to CD_3OD. Multiplets of NMR were assigned as s (singlet), br s (broad singlet) d (doublet), t (triplet), q (quartet), ps-qui (pseudo-quintet), ps-h (pseudo-hextet), hept (heptet), ps-n (pseudo-nonet), dd (doublet of doublet), dt (doublet of triplet), dq (doublet of quartet), dh (doublet of heptet), ddd (doublet of doublet of doublet), td (triplet of doublet), and m (multiplet). All NMR measurements were carried out at room temperature.

GC measurements were performed on an Agilent HP 6890 with a HP5 column. GC-MS spectra were recorded on a GC-MS Agilent 5973 Network. HRMS measurements were performed using a Waters Xevo G2XS TOF MS. ATR-IR spectra were recorded on a Nicolet iS5 FT-IR equipped with a PIKE Technologies GladiATR (Thermo Fisher).

Data were collected on a Bruker Kappa APEX II Duo diffractometer. The structure was solved by intrinsic phasing (SHELXT: Sheldrick, G. M. *Acta Cryst.* **2015**, *A71*, 3.) and refined by full-matrix least-squares procedures on F^2 (SHELXL-2019: Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3.). XP (Bruker AXS) was used for graphical representation. CCDC 2332462 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

General procedure for amidocarbonylation of aldehyde

A 8 mL vial equipped with a stir bar was charged with $Pd(OAc)_2$ (0.5 mol%), aldehyde (0.5 mmol, 1 equiv), amide (0.5 mmol, 1 equiv), LiBr (35 mol%) and H_2SO_4 (1 mol%) in NMP (1 mL). The reactional mixture was stirred under 60 bar CO at 100°C for 16 h. After this time, the crude was filtered through a small pad of Celite® with EtOAc and it was concentrated under reduced pressure. Then, NMP was removed from the crude with distillation (1 mbar, 68°C) and proceeded to one of the following extraction methods or column chromatography.

Extraction method A: After distillation of NMP, the crude was dissolved in EtOAc (50 mL) and washed with saturated aqueous $NaHCO_3$ solution (3 x 30 mL), resulting in organic phase A and aqueous phase A. The combined aqueous phase A were acidified with HCl until pH 2, and then, extracted with EtOAc (3 x 30 mL), resulting in organic phase B and aqueous phase B. Both organic phases (A and B) were combined and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was washed with n-pentane and the desired product was precipitated as a white solid.

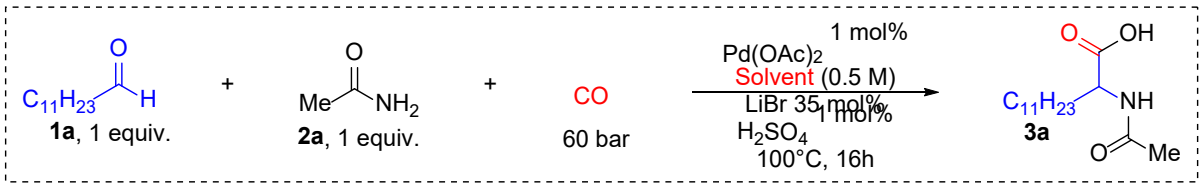
Extraction method B: After distillation of NMP, the crude was dissolved in EtOAc (50 mL) and washed with aqueous solution of NaOH 1,0 mol/L (1 x 50 mL). Aqueous phase was acidified with HCl until pH 2, and then, extracted with EtOAc (3 x 30 mL). Organic phases were combined and dried over Na_2SO_4 and concentrated under reduced pressure. The residue was washed with n-pentane and the desired product was precipitated as a white solid.

Screening of the reaction conditions

Table 1. Evaluation of palladium sources

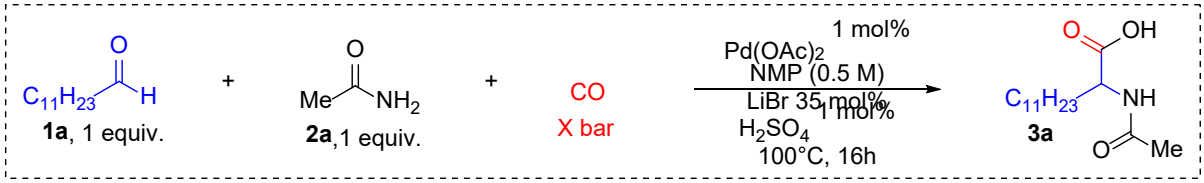
Entry	[Pd]	Yield (%)
1	**$Pd(OAc)_2$**	**Quantitative**
2	$PdBr_2$	74
3	Pd/C	65
4	$Pd(acac)_2$	Quantitative
5	$Pd_2(dba)_3$	61

Table 2. Evaluation of solvents



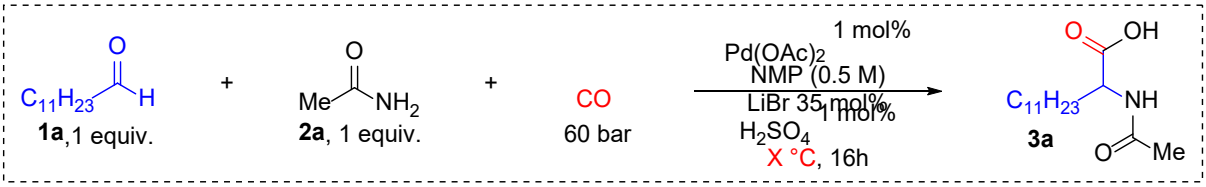
Entry	Solvent	Yield (%)
1	**NMP**	**98**
2	DMA	78
3	MeCN	Traces
4	DMF	Traces
5	Ethyl acetate	34

Table 3. Evaluation of CO pressure



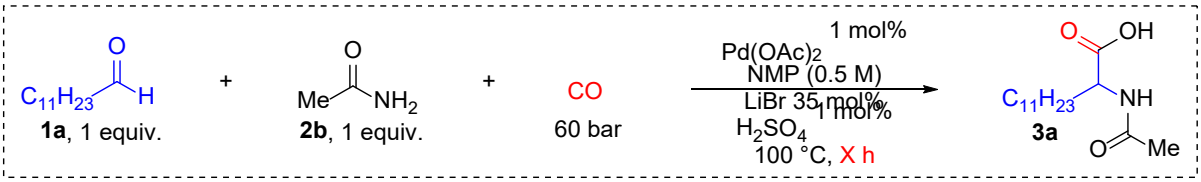
Entry	CO pressure	Yield (%)
1	**60 bar**	**98**
2	40 bar	95
3	20 bar	91

Table 4. Evaluation of temperature



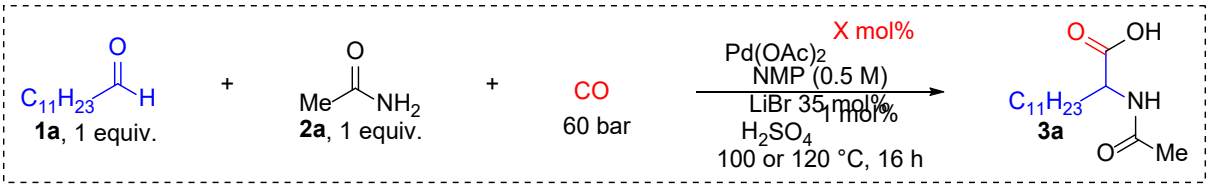
Entry	Temperature	Yield (%)
1	**100 °C**	**98**
2	80 °C	89
3	60 °C	73

Table 5. Evaluation of reaction time



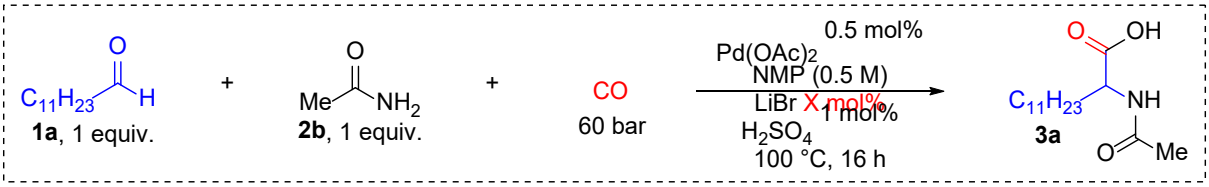
Entry	Time (h)	Yield (%)
1	**16 (16h to 8h)**	**98**
2	12 (20h to 8h)	73

Table 6. Evaluation of palladium amount at different temperatures



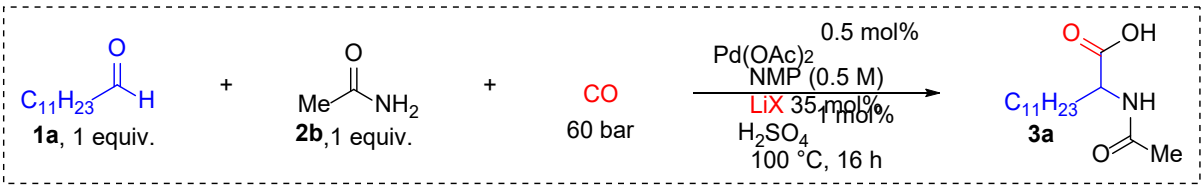
Entry	$Pd(OAc)_2$ (mol%)	100 °C Yield (%)	120 °C Yield (%)
1	1.0	>99	-
2	**0.5**	**>99**	-
3	0.1	80	72
4	0.05	62	49
5	0.01	23	-

Table 7. Evaluation of LiBr amount



Entry	LiBr (mol%)	Yield (%)
1	**35**	**<99**
2	25	73
3	15	52
4	5	32

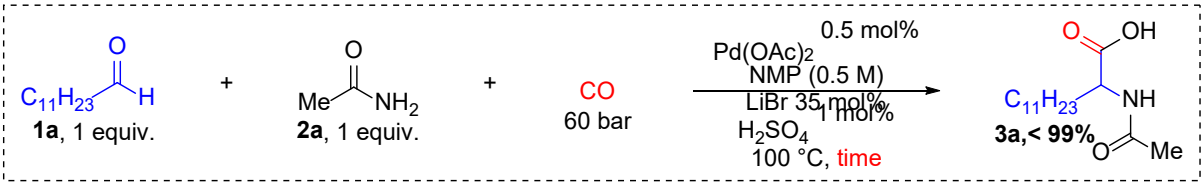
Table 8. Evaluation of lithium salt source



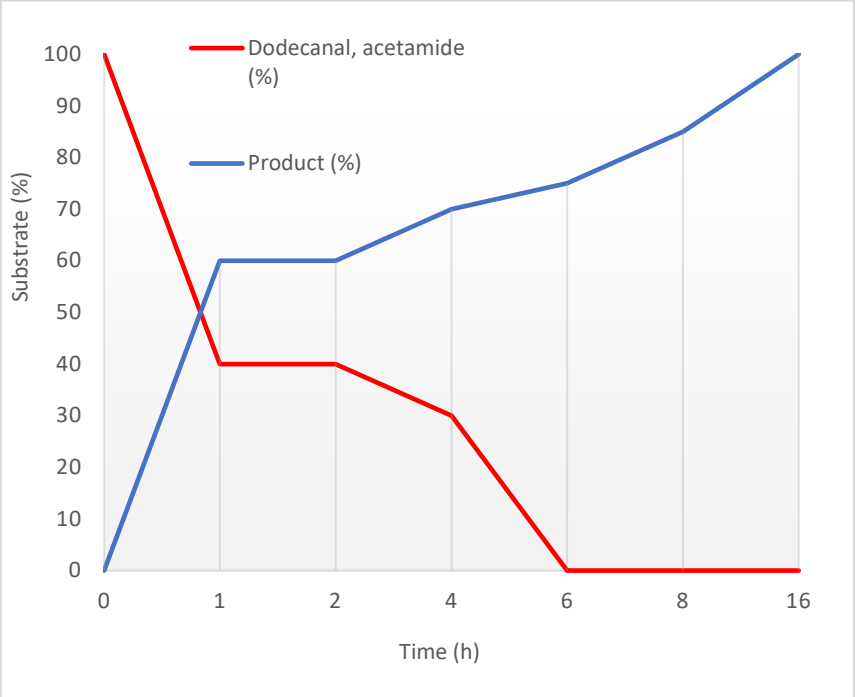
Entry	LiX (mol%)	Yield (%)
1	LiCl	27
2	**LiBr**	**>99**

Optimized condition:

Table 9. Kinetics studies

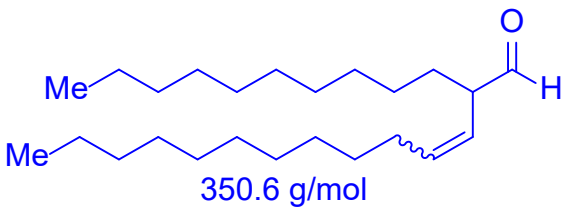


Entry	Time (h)	Aldehyde (%)	Amide (%)	Product (%)
1	0	100	100	0
2	1	40	40	60
3	2	40	40	60
4	4	30	30	70
5	6	0	0	75
6	8	0	0	85
7	16	0	0	100
8	16+24	40	60	140
9	16 / without CO	50	60	0



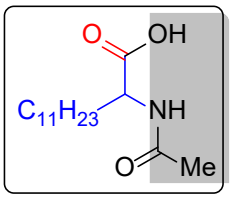
Entry 8: the same as entry 7, and after 16h, it was added all chemicals (NMP, LiBr, H_2SO_4, aldehyde, amide, CO) to reaction but $Pd(OAc)_2$ to see if the catalyst was still "alive" after 16h. It was observed formation of additional 40% of product after 24h, indicating the catalyst was alive, but a little bit "weak".

Entry 9: the reaction was performed without CO, and after 16h there was 50% of aldehyde, 60% of amide and 0% of product. The main byproduct observed by GC-MS was from aldol reaction:



Characterization of the compounds

2-Acetamidotridecanoic acid (3a)



84% (109.3 mg, 0.423 mmol), white solid, MP = 104-105 °C.

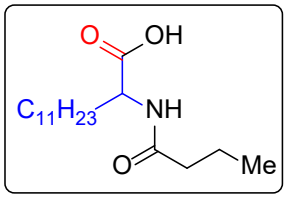
Multi-gram scale: 72% (7.4611 g, 36.38 mmol).

^{1}H NMR (300 MHz, MeOD) δ 4.34 (dd, J = 8.8, 5.0 Hz, 1H), 1.98 (s, 3H), 1.81 (ddd, J = 15.4, 7.3, 5.0 Hz, 1H), 1.74 – 1.59 (m, 1H), 1.30 (d, J = 3.4 Hz, 19H), 0.95 – 0.84 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 175.8, 173.3, 53.8, 33.1, 32.7, 30.7, 30.7, 30.5, 30.5, 30.2, 26.9, 23.7, 22.3, 14.4.

HRMS (ESI+) calculated for $[C_{15}H_{29}NO_3H]^+$: 272.2226, found: 272.2228.

2-Butyramidotridecanoic acid (3b)



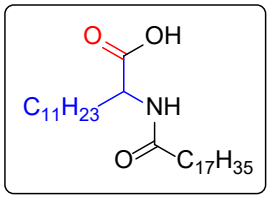
90% (134.7 mg, 0.45 mmol), white solid, MP = 82-83 °C.

^{1}H NMR (300 MHz, MeOD) δ 4.36 (dd, J = 9.0, 4.9 Hz, 1H), 2.22 (dd, J = 7.8, 6.9 Hz, 2H), 1.83 (ddd, J = 15.3, 7.5, 4.9 Hz, 1H), 1.76 – 1.57 (m, 3H), 1.30 (d, J = 4.3 Hz, 18H), 1.00 – 0.85 (m, 6H).

^{13}C NMR (75 MHz, MeOD) δ 176.2, 175.8, 53.5, 38.7, 33.1, 32.6, 30.7, 30.6, 30.5, 30.5, 30.2, 26.9, 23.7, 20.4, 14.4, 14.0.

HRMS (ESI+) calculated for $[C_{17}H_{33}NO_3Na]^+$: 322.2352, found: 322.2351.

2-Stearamidotridecanoic acid (3c)



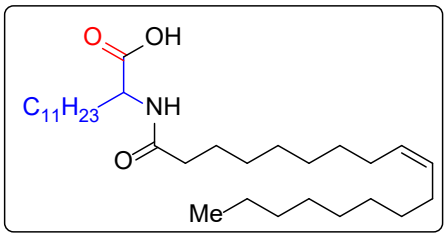
78% (193.9 mg, 0.39 mmol), white solid, MP = 84-85 °C.

^{1}H NMR (300 MHz, MeOD) δ 4.37 (dd, J = 9.2, 4.7 Hz, 1H), 2.30 – 2.19 (m, 2H), 1.93 – 1.74 (m, 1H), 1.74 – 1.55 (m, 3H), 1.29 (d, J = 1.3 Hz, 47H), 0.95 – 0.85 (m, 6H).

^{13}C NMR (75 MHz, MeOD) δ 176.4, 175.7, 53.5, 36.8, 33.1, 32.6, 30.8, 30.8, 30.5, 30.2, 26.9, 23.7, 14.5.

HRMS (ESI+) calculated for $[C_{31}H_{61}NO_3H]^+$: 496.4724, found: 496.4720.

2-Oleamidotridecanoic acid (3d)



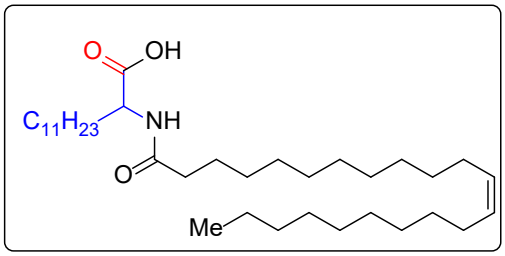
68% (167.9 mg, 0.34 mmol), colorless oil.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.02 (s, 1H), 5.44 – 5.27 (m, 2H), 4.59 (s, 1H), 2.23 (d, J = 7.8 Hz, 2H), 2.07 – 1.95 (m, 3H), 1.64 (s, 3H), 1.39 – 1.19 (m, 40H), 0.91 – 0.84 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.0, 130.2, 129.9, 52.5, 36.7, 32.1, 29.9, 29.8, 29.7, 29.6, 29.5, 29.4, 27.4, 25.8, 25.4, 22.8, 14.3.

HRMS (ESI+) calculated for $[C_{31}H_{59}NO_3H]^+$: 494.4568, found: 494.4565.

(*Z*)-2-(Docos-12-enamido)tridecanoic acid (3e)



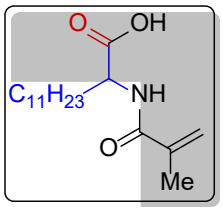
71% (196.1 mg, 0.36 mmol), white solid, MP = 63-64 °C.

1H NMR (300 MHz, $CDCl_3$) δ 7.54 (s, 1H), 6.13 (d, J = 7.7 Hz, 1H), 5.36 – 5.32 (m, 2H), 4.59 (td, J = 7.5, 5.1 Hz, 1H), 2.24 (dd, J = 8.4, 6.7 Hz, 2H), 2.01 (q, J = 6.3 Hz, 3H), 1.87 (dd, J = 9.6, 5.0 Hz, 1H), 1.65 (dt, J = 15.1, 7.7 Hz, 3H), 1.38 – 1.21 (m, 47H), 0.92 – 0.84 (m, 6H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.3, 174.1, 130.0, 130.0, 52.4, 36.7, 32.2, 32.1, 29.9, 29.9, 29.8, 29.7, 29.7, 29.7, 29.6, 29.5, 29.5, 29.4, 27.4, 25.8, 25.4, 22.8, 14.2.

HRMS (ESI+) calculated for $[C_{35}H_{67}NO_3H]^+$: 550.5194, found: 550.5204.

2-Methacrylamidotridecanoic acid (3f)



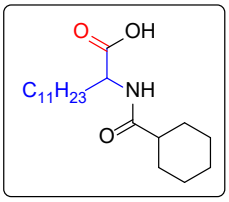
55% (81.5 mg, 0.27 mmol), white solid, MP = 81-82 °C.

^{1}H NMR (300 MHz, $CDCl_3$) δ 6.30 (d, J = 7.6 Hz, 1H), 5.81 – 5.73 (m, 1H), 5.45 – 5.37 (m, 1H), 4.64 (td, J = 7.4, 5.3 Hz, 1H), 1.99 (d, J = 1.3 Hz, 3H), 1.95 – 1.86 (m, 1H), 1.80 – 1.69 (m, 1H), 1.25 (s, 18H), 0.90 – 0.85 (m, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2, 168.7, 139.3, 121.0, 52.6, 32.2, 32.0, 29.7, 29.7, 29.5, 29.5, 29.4, 25.4, 22.8, 18.6, 14.3.

HRMS (ESI+) calculated for $[C_{17}H_{31}NO_3Na]^+$: 320.2196, found: 320.2202.

2-(Cyclohexanecarboxamido)tridecanoic acid (3g)



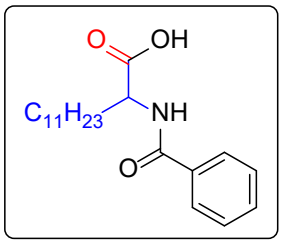
75% (150,5 mg, 0.38 mmol), white solid, MP = 118-119 °C.

^{1}H NMR (300 MHz, MeOD) δ 4.32 (dd, J = 8.7, 4.9 Hz, 1H), 2.33 – 2.20 (m, 1H), 1.88 – 1.74 (m, 5H), 1.73 – 1.62 (m, 2H), 1.47-1-19 (m, 24H), 0.95 – 0.86 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 178.9, 53.9, 46.2, 33.1, 33.0, 30.9, 30.8, 30.7, 30.6, 30.6, 30.5, 30.4, 30.2, 26.9, 26.8, 26.8, 26.7, 23.7, 14.4.

HRMS (ESI+) calculated for $[C_{20}H_{37}NO_3H]^+$: 340.2852, found: 340.2852.

2-Benzamidotridecanoic acid (3h)



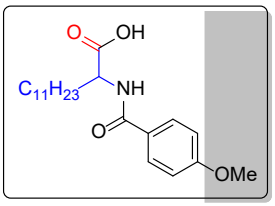
75% (125.0 mg, 0.37 mmol), white solid, MP = 69-70 °C.

^{1}H NMR (300 MHz, MeOD) δ 7.91 – 7.82 (m, 2H), 7.57 – 7.41 (m, 3H), 4.47 (dd, J = 7.4, 4.9 Hz, 1H), 2.03 – 1.91 (m, 1H), 1.86 – 1.72 (m, 1H), 1.47 – 1.18 (m, 20H), 0.92 – 0.85 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 179.3, 169.1, 136.0, 132.5, 129.5, 128.2, 56.9, 34.1, 33.1, 30.7, 30.7, 30.6, 30.4, 26.8, 24.2, 23.7, 14.4.

HRMS (ESI+) calculated for $[C_{20}H_{31}NO_3H]^+$: 334.2377, found: 334.2382.

2-(4-Methoxybenzamido)tridecanoic acid (3i)



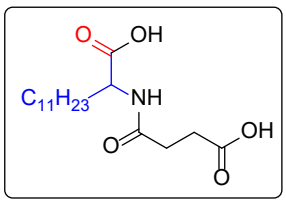
63% (115.1 mg, 0.32 mmol), white solid, MP = 85-86 °C.

^{1}H NMR (300 MHz, MeOD) δ 7.88 – 7.78 (m, 2H), 7.03 – 6.93 (m, 2H), 4.56 (dd, J = 9.2, 5.1 Hz, 1H), 3.85 (s, 3H), 2.03 – 1.89 (m, 1H), 1.81 (ddd, J = 14.1, 9.2, 5.9 Hz, 1H), 1.54 – 0.96 (m, 19H), 0.92 – 0.84 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 176.0, 169.9, 164.0, 130.4, 127.4, 114.7, 55.9, 54.2, 33.1, 32.5, 30.7, 30.7, 30.6, 30.5, 30.5, 30.2, 27.1, 23.7, 14.4.

HRMS (ESI+) calculated for $[C_{21}H_{33}NO_4Na]^+$: 386.2302, found: 386.2298.

2-(3-Carboxypropanamido)tridecanoic acid (3j)



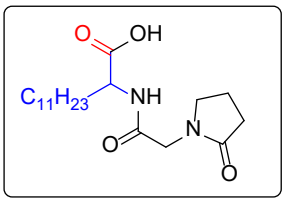
34% (56.8 mg, 0.17 mmol), white solid, MP = 103-104 °C.

^{1}H NMR (300 MHz, MeOD) δ 4.36 (dd, J = 8.7, 5.0 Hz, 1H), 2.65 – 2.51 (m, 4H), 1.82 (qd, J = 7.5, 5.1 Hz, 1H), 1.66 (ddd, J = 14.2, 8.7, 5.7 Hz, 1H), 1.30 (d, J = 4.6 Hz, 21H), 0.92 – 0.87 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 176.2, 174.5, 53.7, 33.1, 32.7, 31.4, 30.7, 30.7, 30.5, 30.5, 30.3, 26.8, 23.7, 14.4.

HRMS (ESI+) calculated for $[C_{17}H_{31}NO_5H]^+$: 330.2275, found: 330.2280.

2-(2-(2-Oxopyrrolidin-1-yl)acetamido)tridecanoic acid (3k)



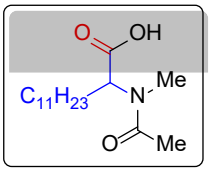
77% (135.8 mg, 0.38 mmol), white solid, MP = 90-91 °C.

^{1}H NMR (300 MHz, CDCl$_3$) δ 6.85 (d, J = 7.8 Hz, 1H), 4.53 (td, J = 7.6, 5.3 Hz, 1H), 4.05 (dd, J = 66.2, 15.1 Hz, 2H), 3.61 – 3.48 (m, 2H), 2.46 (dd, J = 8.8, 6.6 Hz, 2H), 2.14 – 2.06 (m, 2H), 1.85 (dq, J = 10.6, 5.4 Hz, 1H), 1.67 (dt, J = 14.6, 7.5 Hz, 1H), 1.25 (s, 18H), 0.89 (d, J = 6.5 Hz, 3H).

^{13}C NMR (75 MHz, CDCl$_3$) δ 177.0, 174.6, 168.1, 52.4, 48.9, 32.1, 32.1, 30.7, 29.8, 29.7, 29.6, 29.5, 29.4, 25.5, 22.8, 18.1, 14.3.

HRMS (ESI+) calculated for $[C_{19}H_{34}N_2O_4Na]^+$: 377.2411, found: 377.2415.

2-(*N*-Methylacetamido)tridecanoic acid (3l)



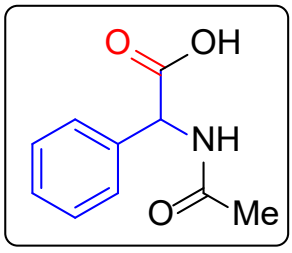
9% (12.7 mg, 0.044 mmol), white solid.

^{1}H NMR (400 MHz, CDCl$_3$) δ 5.02 (dd, J = 10.2, 5.5 Hz, 1H), 2.96 (s, 3H), 2.16 (s, 3H), 2.04 – 1.96 (m, 1H), 1.73 (dt, J = 13.7, 9.4 Hz, 1H), 1.25 (d, J = 2.5 Hz, 19H), 0.89 (d, J = 6.7 Hz, 3H).

^{13}C NMR (101 MHz, CDCl$_3$) δ 174.5, 172.9, 57.5, 33.1, 32.1, 29.9, 29.8, 29.7, 29.5, 29.5, 29.3, 28.4, 26.3, 22.8, 22.1, 14.3.

HRMS (ESI+) calculated for $[C_{16}H_{31}NO_3Na]^+$: 308.2196, found: 308.2199.

2-Acetamido-2-phenylacetic acid (3m)



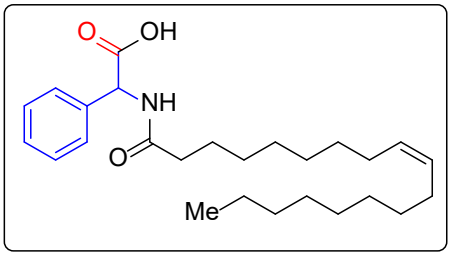
83% (80.0 mg, 0.41 mmol), pale yellow solid, MP = 199-200 °C.

^{1}H NMR (300 MHz, MeOD) δ 7.43 – 7.33 (m, 5H), 5.44 (s, 1H), 2.01 (s, 3H).

^{13}C NMR (75 MHz, MeOD) δ 173.7, 172.9, 138.0, 129.8, 129.4, 128.8, 58.2, 22.3.

HRMS (ESI+) calculated for $[C_{10}H_{11}NO_3Na]^+$: 216.0631, found: 216.0634.

2-Oleamido-2-phenylacetic acid (3n)



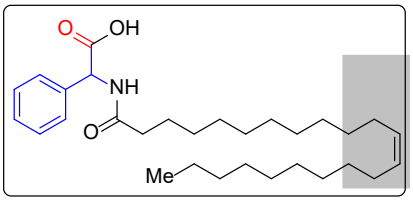
31% (66.1 mg, 0.16 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 7.50 – 7.19 (m, 5H), 5.45 (s, 1H), 5.34 (td, J = 4.5, 2.2 Hz, 2H), 2.27 (td, J = 7.3, 1.0 Hz, 2H), 2.09 – 1.92 (m, 3H), 1.61 (t, J = 7.2 Hz, 2H), 1.47 – 1.17 (m, 21H), 0.95 – 0.85 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 175.9, 173.8, 138.3, 130.8, 130.8, 129.8, 129.3, 128.8, 58.2, 36.6, 33.1, 30.8, 30.8, 30.7, 30.6, 30.5, 30.4, 30.3, 30.2, 30.2, 28.1, 28.1, 26.9, 23.7, 14.4.

HRMS (ESI+) calculated for $[C_{26}H_{41}NO_3Na]^+$: 438.2979, found: 438.2984.

(*Z*)-2-(Docos-12-enamido)-2-phenylacetic acid (3o)



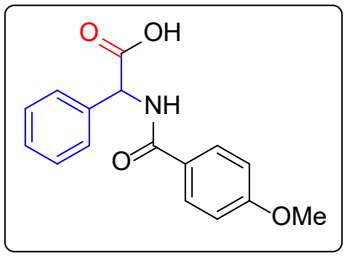
65% (153.9 mg, 0.33 mmol), pale yellow oil.

^{1}H NMR (300 MHz, MeOD) δ 7.46 – 7.28 (m, 5H), 5.46 (s, 1H), 5.42 – 5.27 (m, 2H), 2.27 (td, J = 7.3, 1.0 Hz, 2H), 2.09 – 1.98 (m, 3H), 1.61 (dd, J = 10.3, 4.7 Hz, 3H), 1.44 – 1.22 (m, 30H), 0.92 – 0.88 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 180.4, 175.8, 173.7, 138.2, 130.8, 129.7, 129.3, 128.8, 58.0, 47.0, 36.6, 33.6, 33.1, 33.0, 30.9, 30.8, 30.7, 30.6, 30.5, 30.4, 30.3, 30.2, 28.5, 28.2, 26.9, 23.7, 23.7, 14.5, 14.5.

HRMS (ESI+) calculated for $[C_{30}H_{49}NO_3H]^+$: 472.3785, found: 472.3789.

2-(4-Methoxybenzamido)-2-phenylacetic acid (3p)



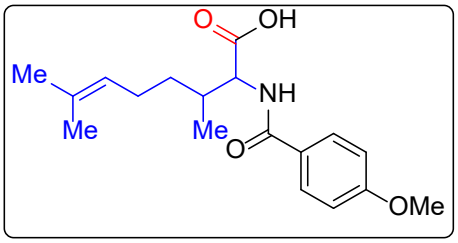
38% (54.3 mg, 0.19 mmol), white solid, MP = 186-188 °C.

^{1}H NMR (300 MHz, MeOD) δ 7.89 – 7.81 (m, 2H), 7.54 – 7.46 (m, 2H), 7.42 – 7.28 (m, 3H), 7.01 – 6.94 (m, 2H), 5.64 (s, 1H), 3.84 (s, 3H), 2.15 (s, 1H).

^{13}C NMR (75 MHz, MeOD) δ 174.2, 169.3, 164.1, 138.6, 130.5, 129.7, 129.2, 128.9, 127.2, 114.7, 58.8, 55.9.

HRMS (ESI+) calculated for $[C_{16}H_{15}NO_4Na]^+$: 308.0893, found: 308.0894.

2-(4-Methoxybenzamido)-3,7-dimethyloct-6-enoic acid (3q)



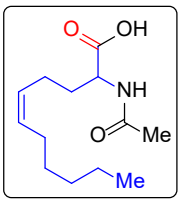
35% (55.1 mg, 0.17 mmol), white solid. MP: 146-147°C

^{1}H NMR (300 MHz, $CDCl_3$) δ 7.68 – 7.63 (m, 2H), 6.86 – 6.82 (m, 2H), 5.86 (d, J = 7.8 Hz, 1H), 4.48 (s, 1H), 3.77 (s, 3H), 2.32 – 2.20 (m, 2H), 2.06 – 1.97 (m, 1H), 1.84 – 1.74 (m, 1H), 1.60 (d, J = 1.3 Hz, 6H), 1.36 – 1.23 (m, 1H), 0.98 (d, J = 6.9 Hz, 3H).

^{13}C NMR (75 MHz, $CDCl_3$) δ 166.2, 162.1, 135.6, 129.1, 128.7, 127.3, 124.5, 113.8, 58.9, 55.5, 43.0, 31.3, 29.0, 21.9, 20.9, 18.1.

HRMS (ESI+) calculated for $[C_{18}H_{25}NO_4Na]^+$: 342.1676 found: 342.1689.

(*Z*)-2-Acetamidoundec-5-enoic acid (3r)



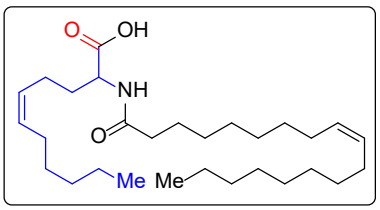
85% (102.7 mg, 0.426 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 5.51 – 5.28 (m, 2H), 4.35 (dd, J = 9.0, 4.8 Hz, 1H), 2.23 – 1.99 (m, 4H), 1.99 (s, 3H), 1.91 – 1.80 (m, 1H), 1.78 – 1.66 (m, 1H), 1.39 – 1.25 (m, 8H), 0.92 – 0.88 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 175.6, 173.3, 132.5, 128.8, 53.3, 32.7, 32.6, 30.5, 28.1, 24.5, 23.6, 22.3, 14.4.

HRMS (ESI+) calculated for $[C_{13}H_{23}NO_3H]^+$: 242.1751, found: 242.1753.

(*Z*)-2-Oleamidoundec-5-enoic acid (3s)



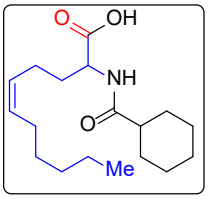
57% (133.0 mg, 0.29 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 5.42 – 5.31 (m, 4H), 4.26 (dd, J = 7.9, 4.4 Hz, 1H), 2.24 (dt, J = 7.2, 3.4 Hz, 2H), 2.03 (q, J = 6.3 Hz, 6H), 1.72 – 1.56 (m, 4H), 1.36 – 1.28 (m, 30H), 0.90 (q, J = 2.5 Hz, 6H).

^{13}C NMR (75 MHz, MeOD) δ 179.3, 175.3, 131.3, 130.8, 130.8, 130.0, 56.0, 37.4, 34.1, 33.1, 32.7, 30.9, 30.8, 30.8, 30.8, 30.6, 30.6, 30.5, 30.4, 30.4, 30.3, 30.3, 28.2, 28.1, 27.1, 24.7, 23.7, 23.7, 14.5.

HRMS (ESI+) calculated for $[C_{29}H_{53}NO_3Na]^+$: 486.3918, found: 486.3924.

(*Z*)-2-(Cyclohexanecarboxamido)undec-5-enoic acid (3t)



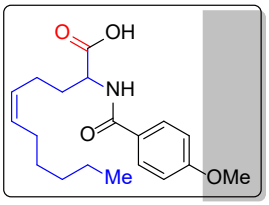
69% (106.6 mg, 0.343 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 5.50 – 5.28 (m, 2H), 4.34 (dd, J = 9.3, 4.6 Hz, 1H), 2.32 – 2.01 (m, 5H), 1.93 – 1.55 (m, 10H), 1.36 – 1.29 (m, 10H), 0.90 (d, J = 2.0 Hz, 3H).

^{13}C NMR (75 MHz, MeOD) δ 179.3, 175.8, 132.4, 128.9, 52.9, 46.1, 32.7, 32.6, 30.9, 30.5, 30.4, 28.2, 26.9, 26.8, 26.7, 24.6, 23.6, 14.4.

HRMS (ESI+) calculated for $[C_{18}H_{31}NO_3H]^+$: 310.2377, found: 310.2383.

(*Z*)-2-(4-Methoxybenzamido)undec-5-enoic acid (3u)



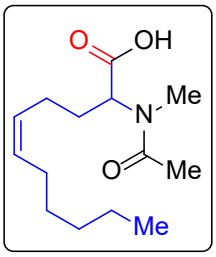
85% (142.4 mg, 0.427 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 7.90 – 7.79 (m, 2H), 7.03 – 6.94 (m, 2H), 5.51 – 5.31 (m, 2H), 4.55 (dd, J = 9.4, 4.9 Hz, 1H), 3.85 (d, J = 0.7 Hz, 3H), 2.42 – 2.15 (m, 2H), 2.07 – 1.84 (m, 2H), 1.63 – 1.43 (m, 3H), 1.32 – 1.22 (m, 7H), 0.90 – 0.81 (m, 3H).

^{13}C NMR (75 MHz, MeOD) δ 176.0, 169.9, 164.0, 132.6, 130.4, 128.9, 127.4, 114.7, 55.9, 32.8, 32.7, 32.4, 30.5, 28.2, 24.7, 23.5, 14.4.

HRMS (ESI+) calculated for $[C_{19}H_{27}NO_4H]^+$: 334.2013 found: 334.2020.

(*Z*)-2-(*N*-Methylacetamido)undec-5-enoic acid (3v)



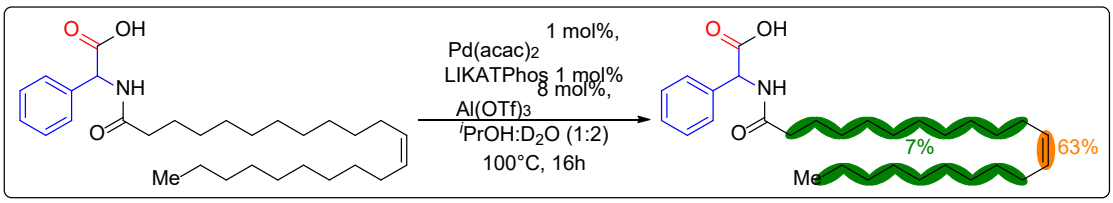
23% (29.5 mg, 0.11 mmol), colorless oil.

^{1}H NMR (300 MHz, MeOD) δ 5.46 – 5.37 (m, 2H), 5.06 – 5.00 (m, 1H), 3.00 (s, 3H), 2.81 (s, 1H), 2.14 (s, 3H), 2.06 – 2.01 (m, 4H), 1.35 – 1.29 (m, 8H), 0.90 (d, J = 0.7 Hz, 3H).

^{13}C NMR (75 MHz, MeOD) δ 174.5, 174.4, 132.3, 129.0, 61.2, 57.4, 35.3, 33.1, 32.7, 30.5, 29.7, 23.6, 23.4, 14.4.

HRMS (ESI+) calculated for $[C_{14}H_{25}NO_3Na]^+$: 278.1726 found: 278.1733.

Deuteration reaction



X-Ray Diffraction

X-ray crystal structure analysis of **3f**

Data were collected on a Bruker Kappa APEX II Duo diffractometer. The structure was solved by intrinsic phasing (SHELXT: Sheldrick, G. M. *Acta Cryst.* **2015**, *A71*, 3.) and refined by full-matrix least-squares procedures on F^2 (SHELXL-2019: Sheldrick, G. M. *Acta Cryst.* **2015**, *C71*, 3.). XP (Bruker AXS) was used for graphical representation. CCDC 2332462 contains the supplementary crystallographic data for this paper. These data are provided free of charge by the joint Cambridge Crystallographic Data Centre and Fachinformationszentrum Karlsruhe Access Structures service www.ccdc.cam.ac.uk/structures.

Crystal data of **3f**: $C_{17}H_{31}NO_3$, M = 297.43, triclinic, space group $P\bar{1}$, a = 5.0699(3), b = 9.3359(5), c = 19.6712(11) Å, α = 92.250(3), β = 96.251(3), γ = 103.900(3)°, V = 896.37(9) Å^3, T = 150(2) K, Z = 2, 13069 reflections measured, 3133 independent reflections (R_{int} = 0.0242), final R values ($I > 2\sigma(I)$): R_1 = 0.0508, wR_2 = 0.1414, final R values (all data): R_1 = 0.0567, wR_2 = 0.1477, 199 parameters.

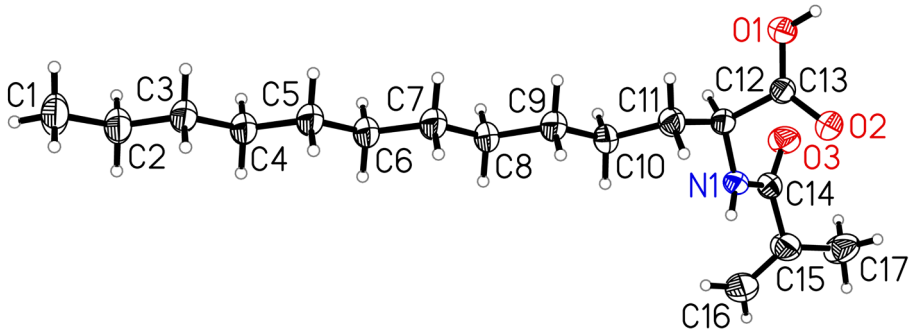


Figure S1. Molecular structure of **3f**. Displacement ellipsoids correspond to 50% probability. The distances C13-O1 (1.2582(19) Å) and C13-O2 (1.2655(19) Å) are between a single and a double bond due to unresolved disorder.

NMR Spectra

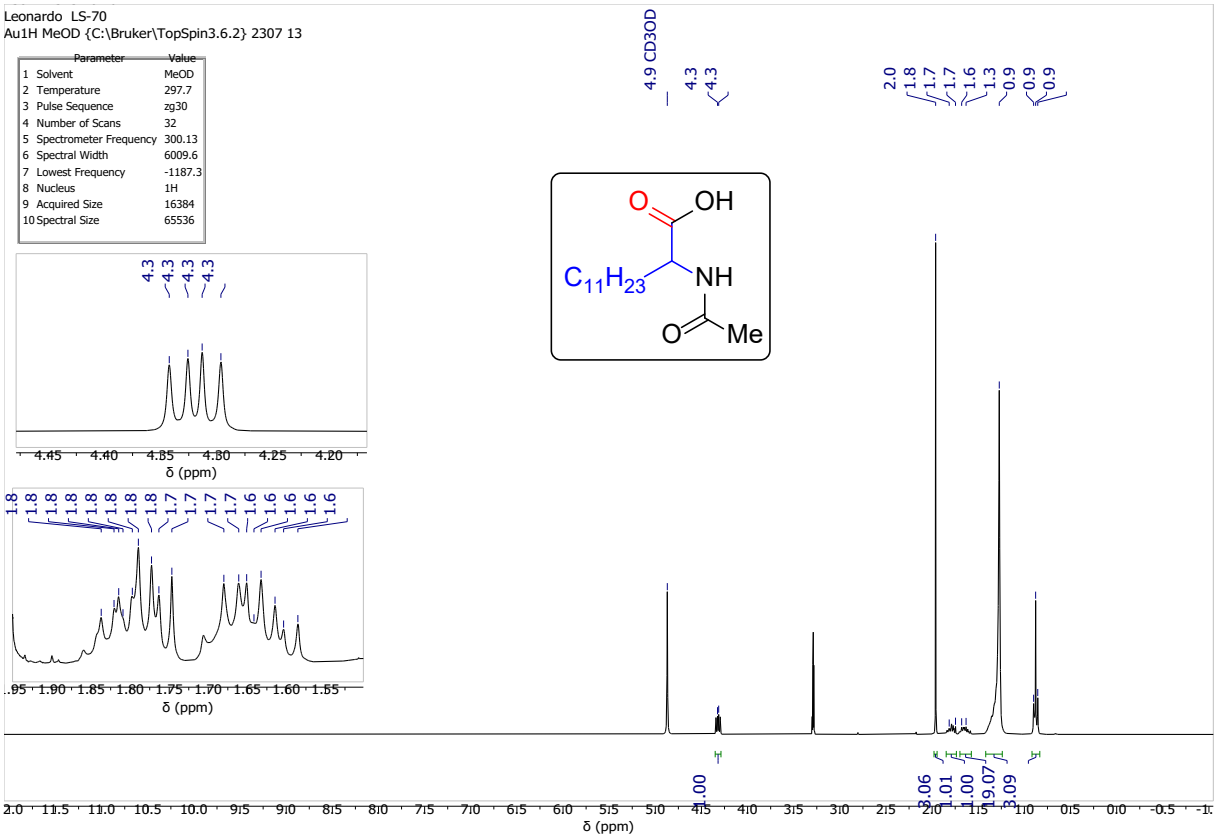


Figure S2: ^{1}H NMR of compound **(3a)**.

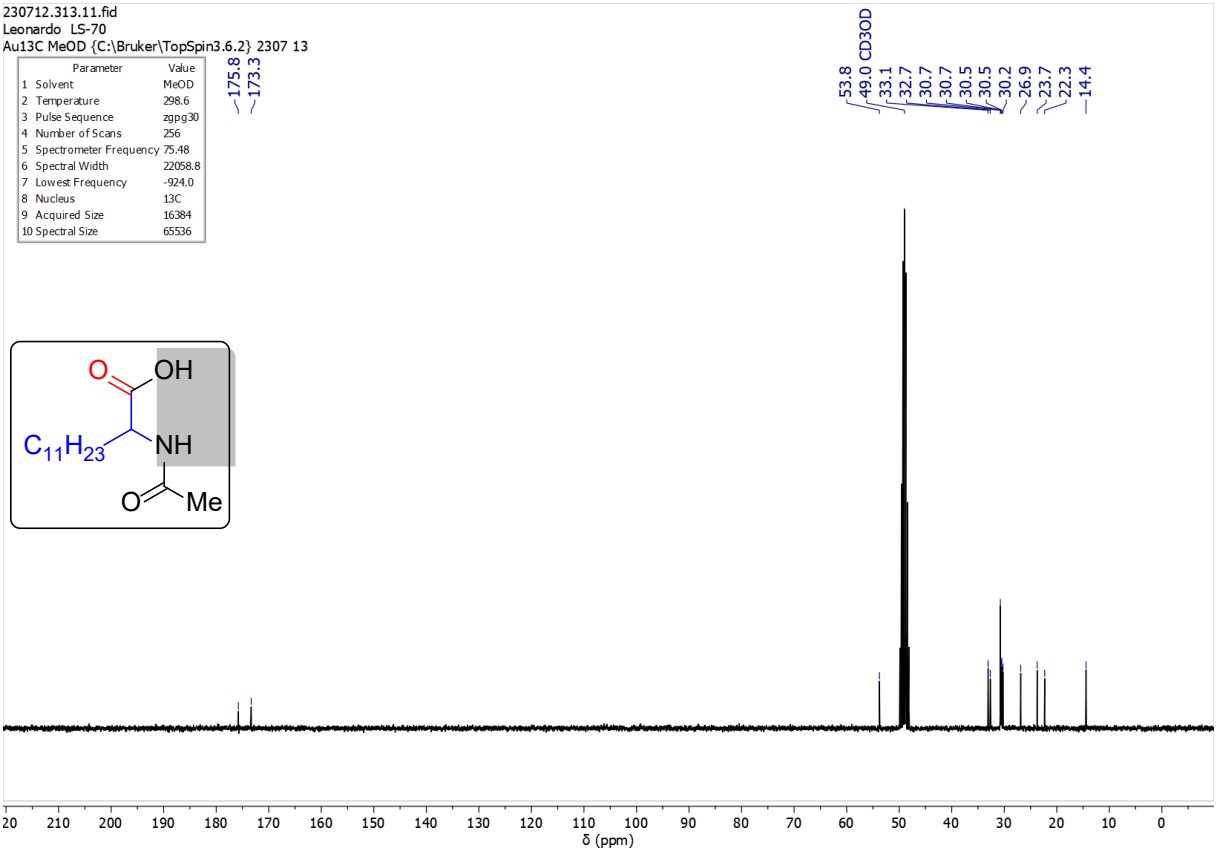


Figure S3: ^{13}C NMR of compound **(3a)**.

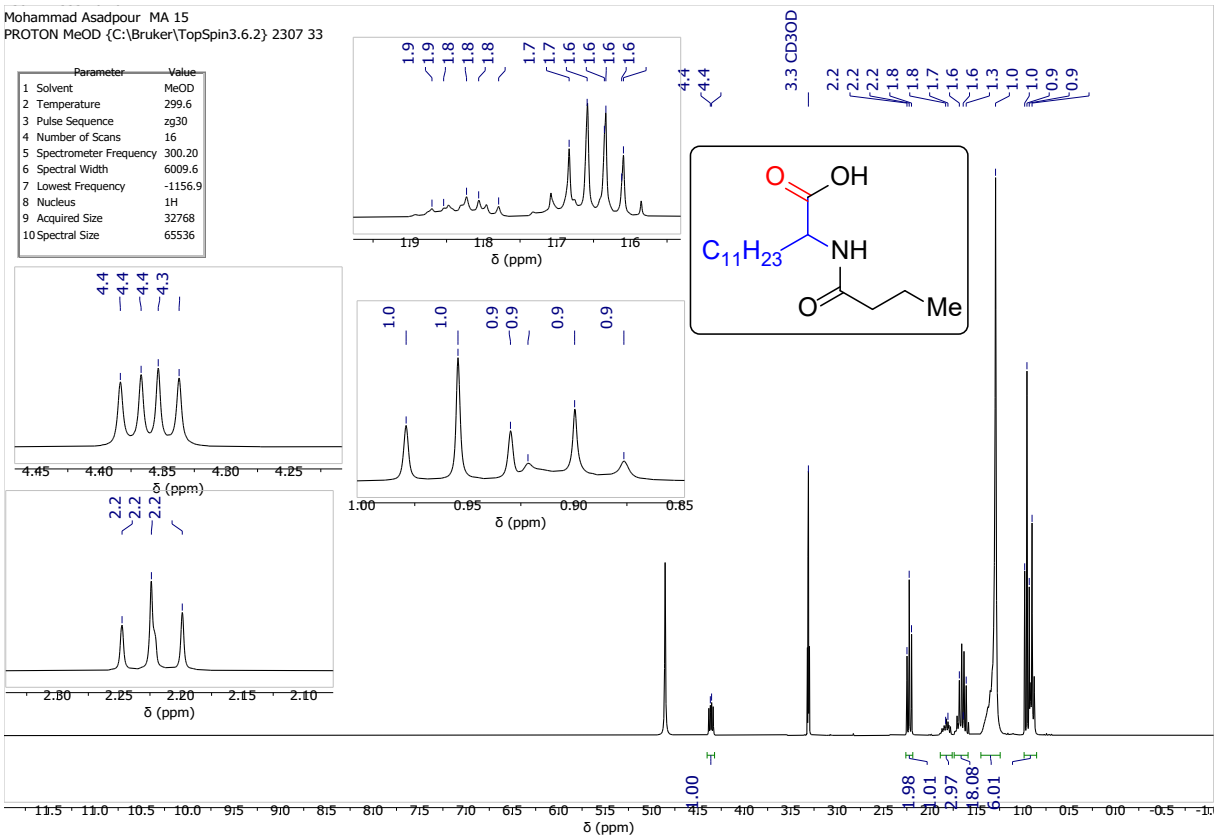


Figure S4: ^{1}H NMR of compound **(3b)**.

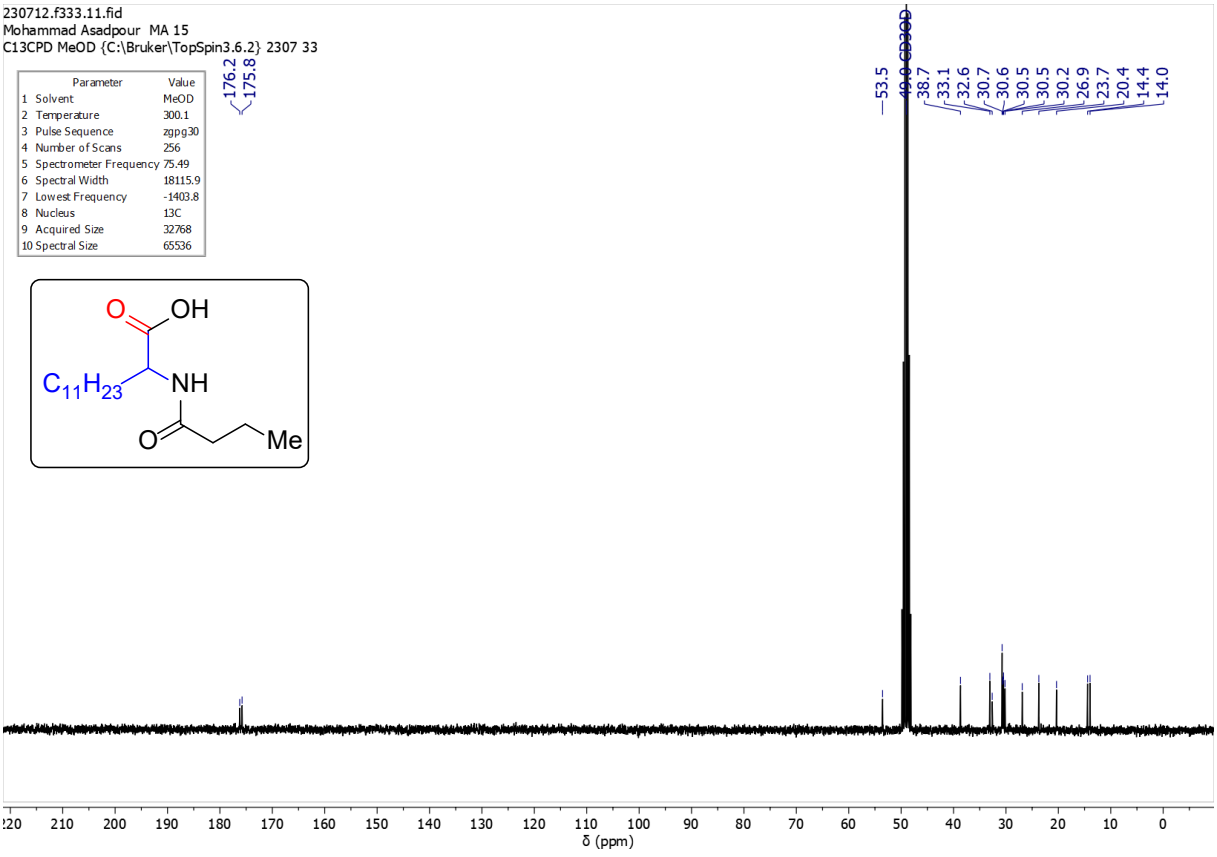


Figure S5: ^{13}C NMR of compound **(3b)**.

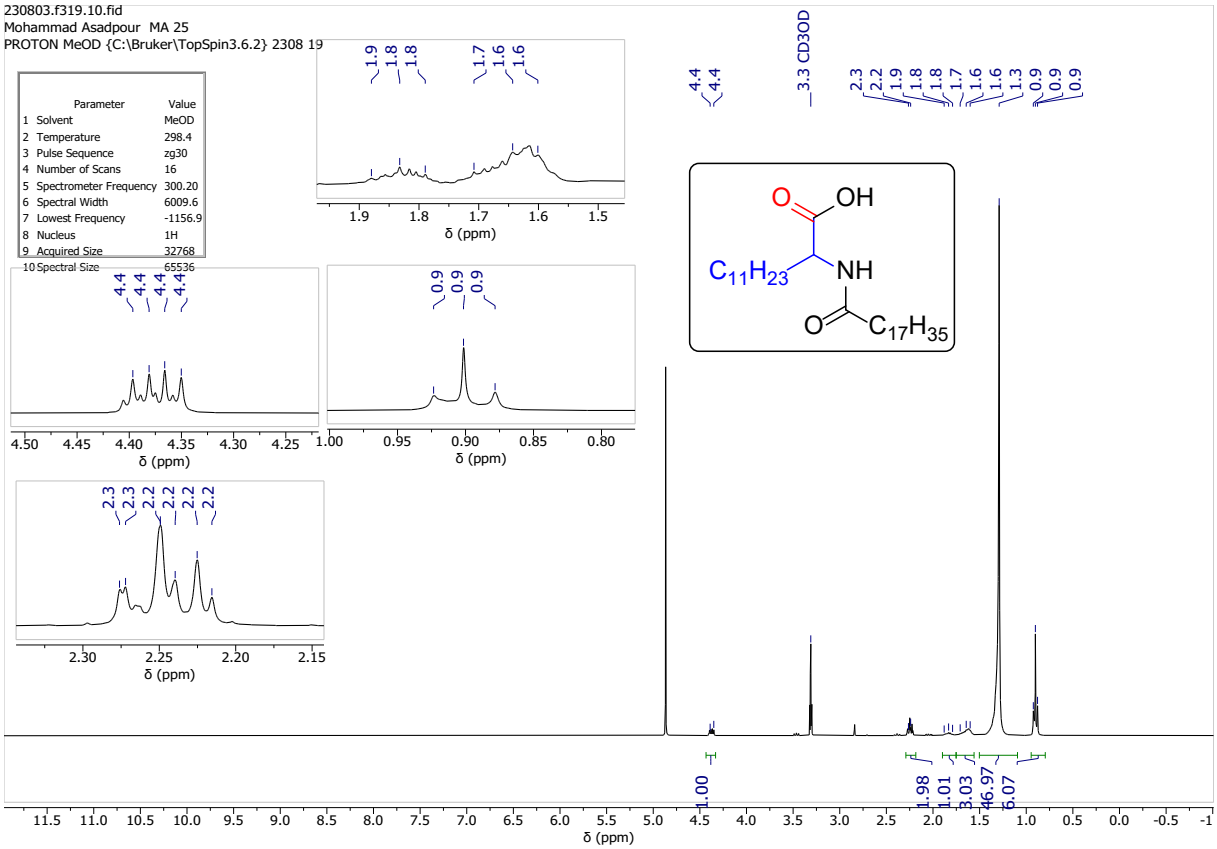


Figure S6: ^{1}H NMR of compound **(3c)**.

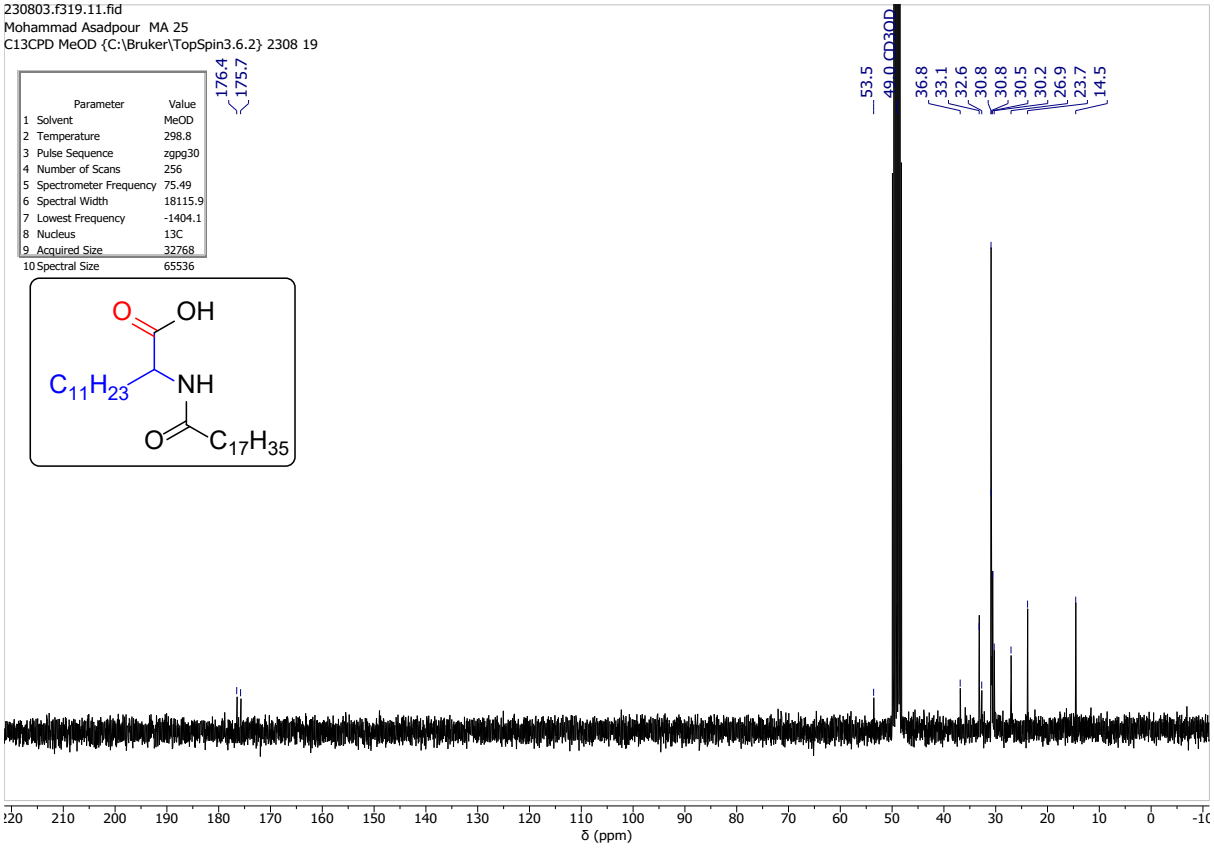


Figure S7: ^{13}C NMR of compound **(3c)**.

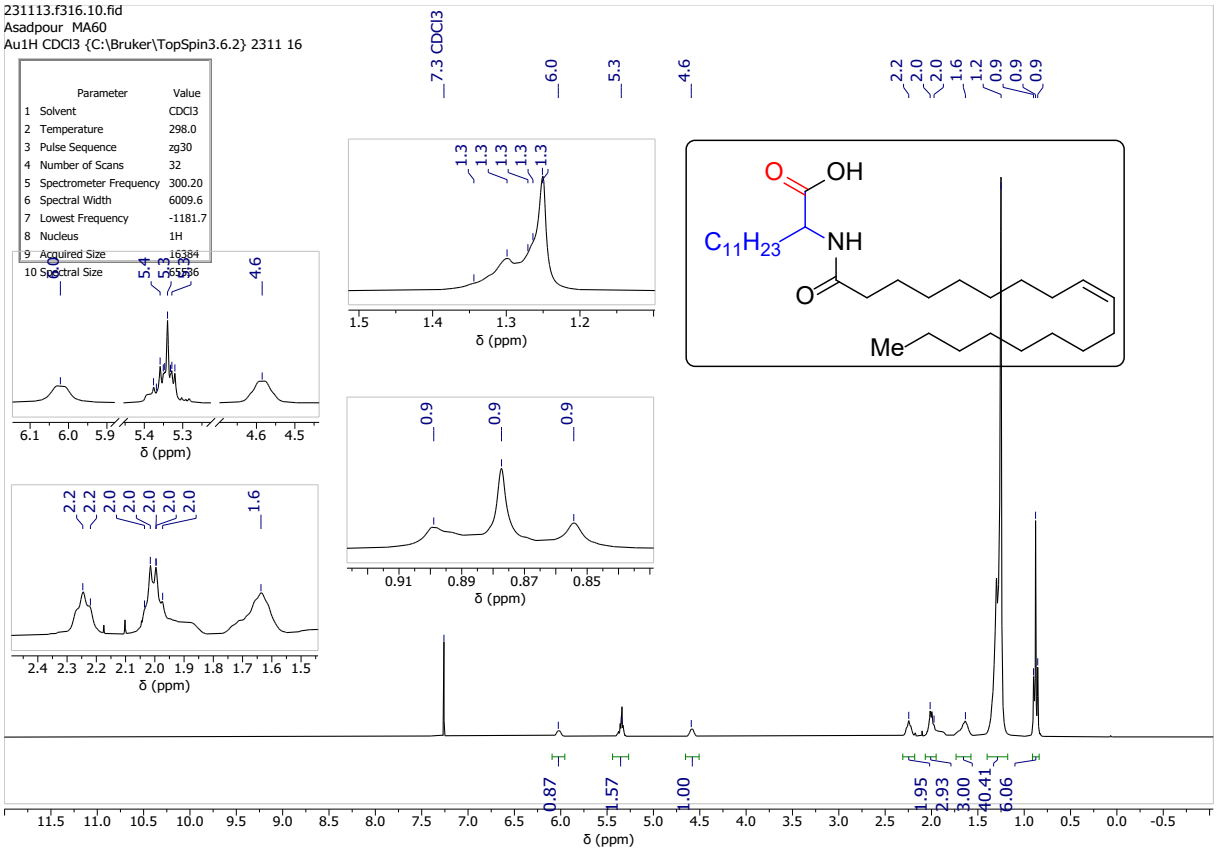


Figure S8: ^{1}H NMR of compound **(3d)**.

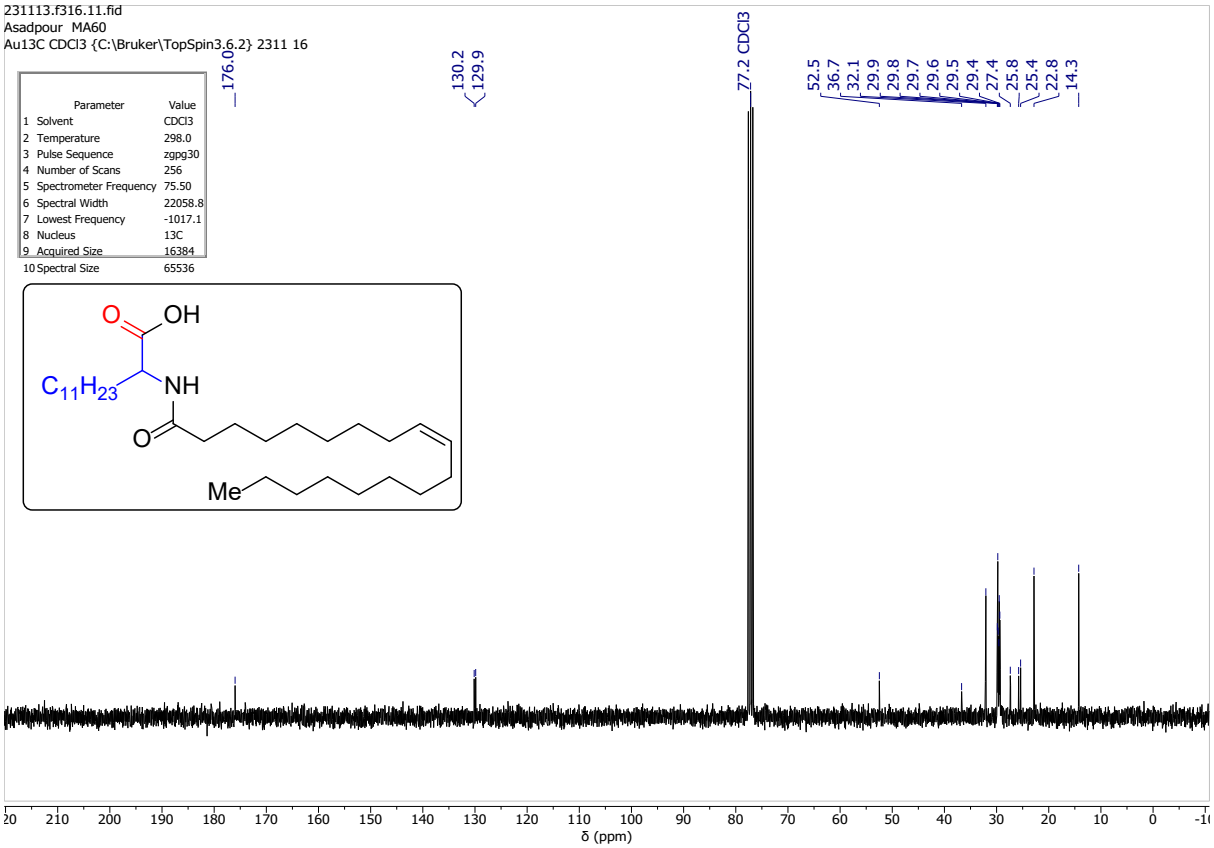


Figure S9: ^{13}C NMR of compound **(3d)**.

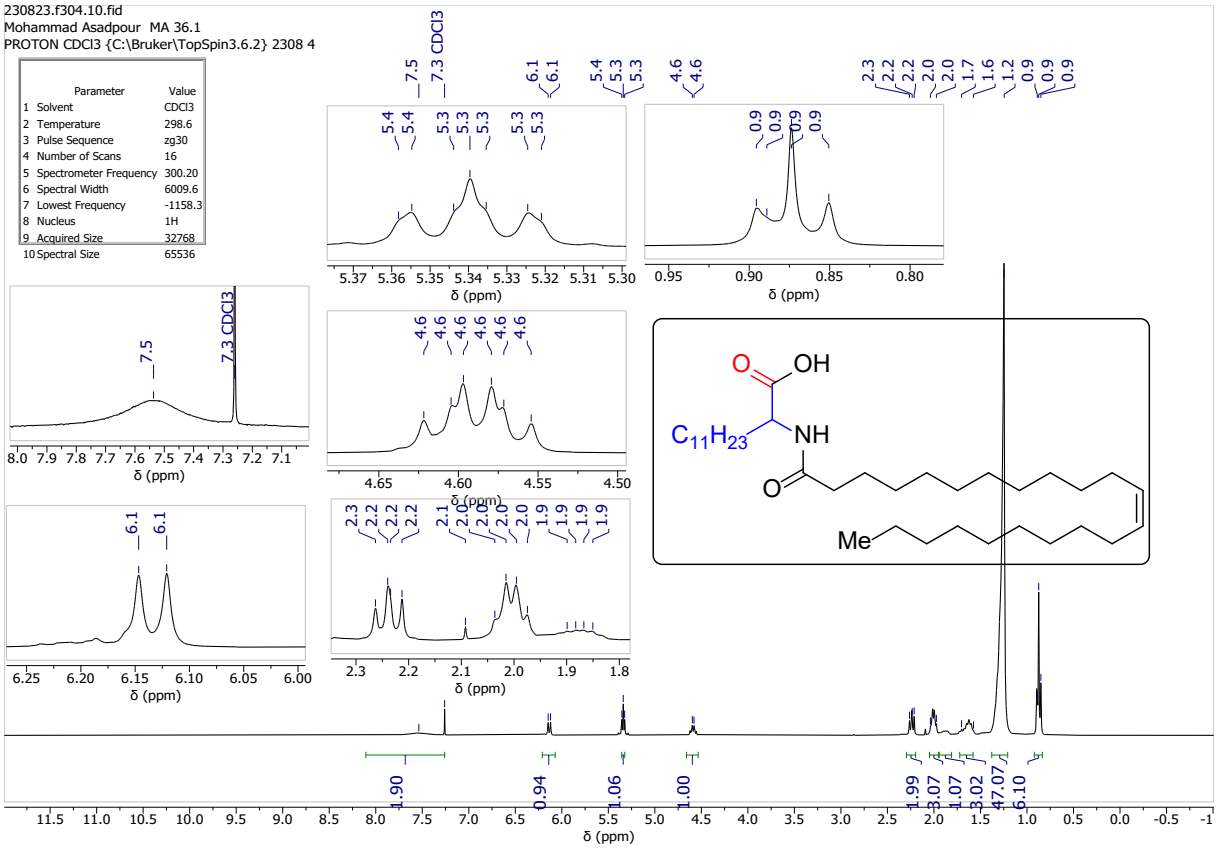


Figure S10: ^{1}H NMR of compound **(3e)**.

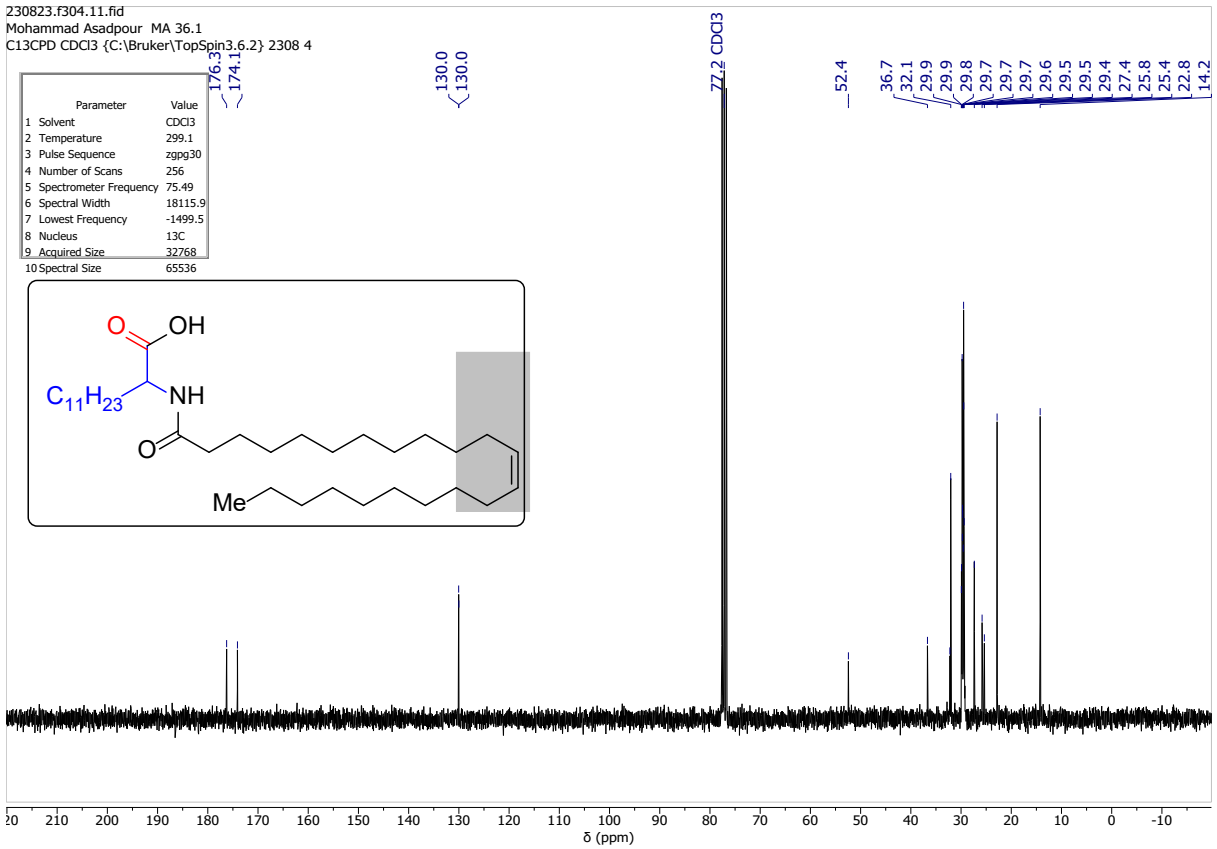


Figure S11: ^{13}C NMR of compound **(3e)**.

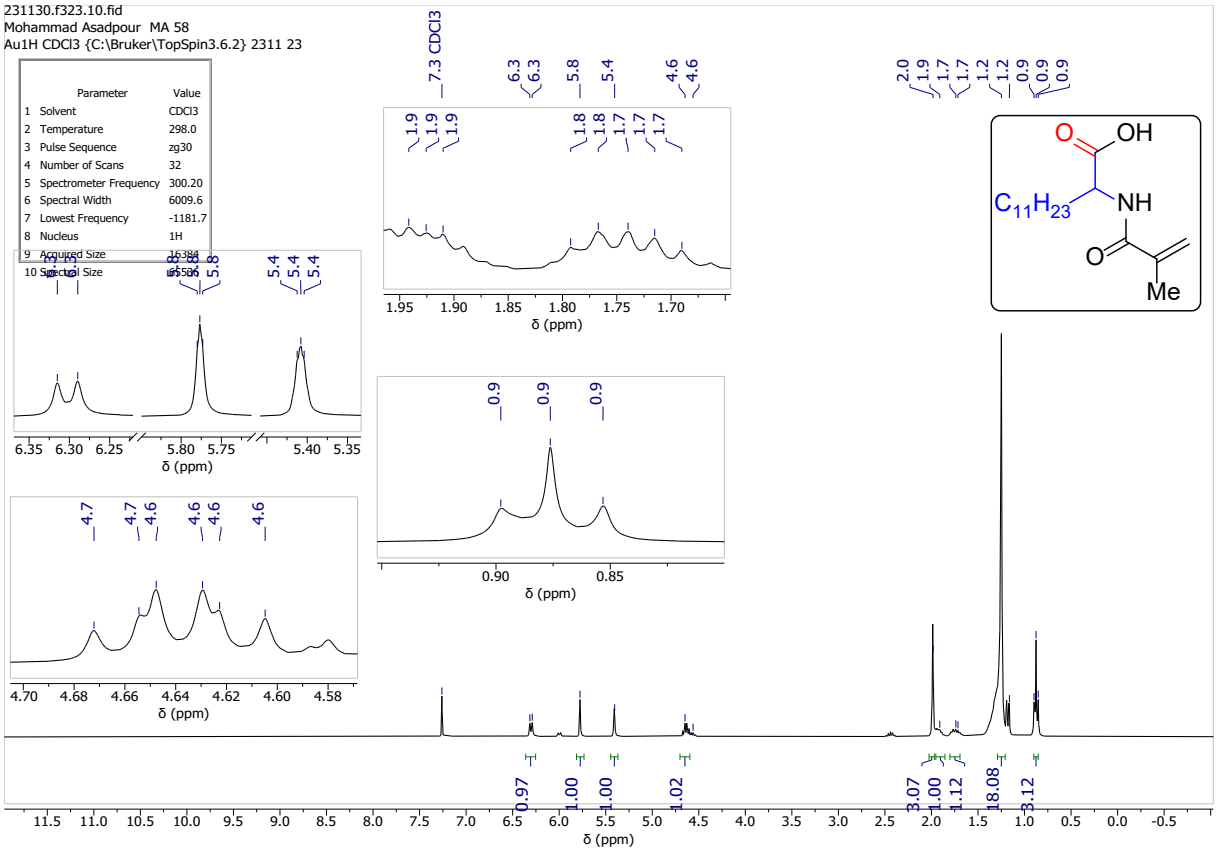


Figure S12: ^{1}H NMR of compound **(3f)**.

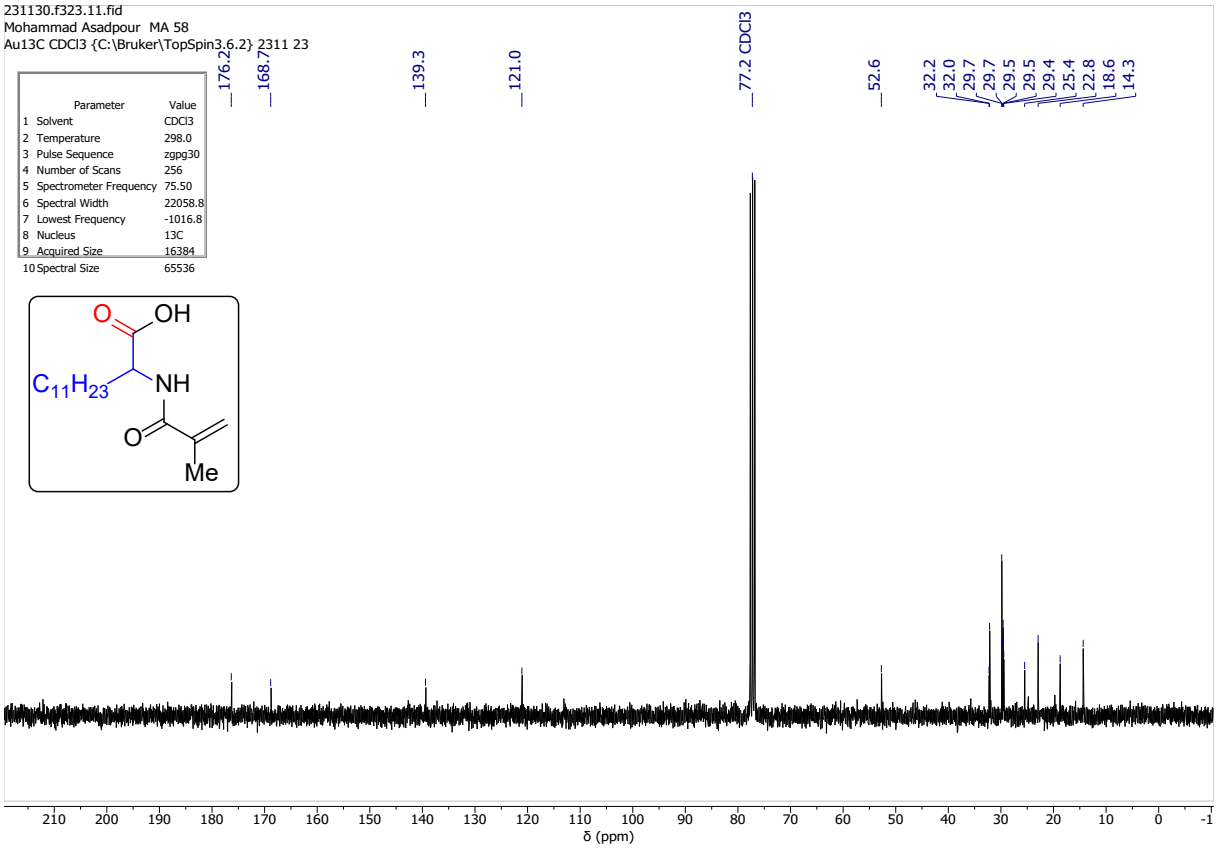


Figure S13: ^{13}C NMR of compound **(3f)**.

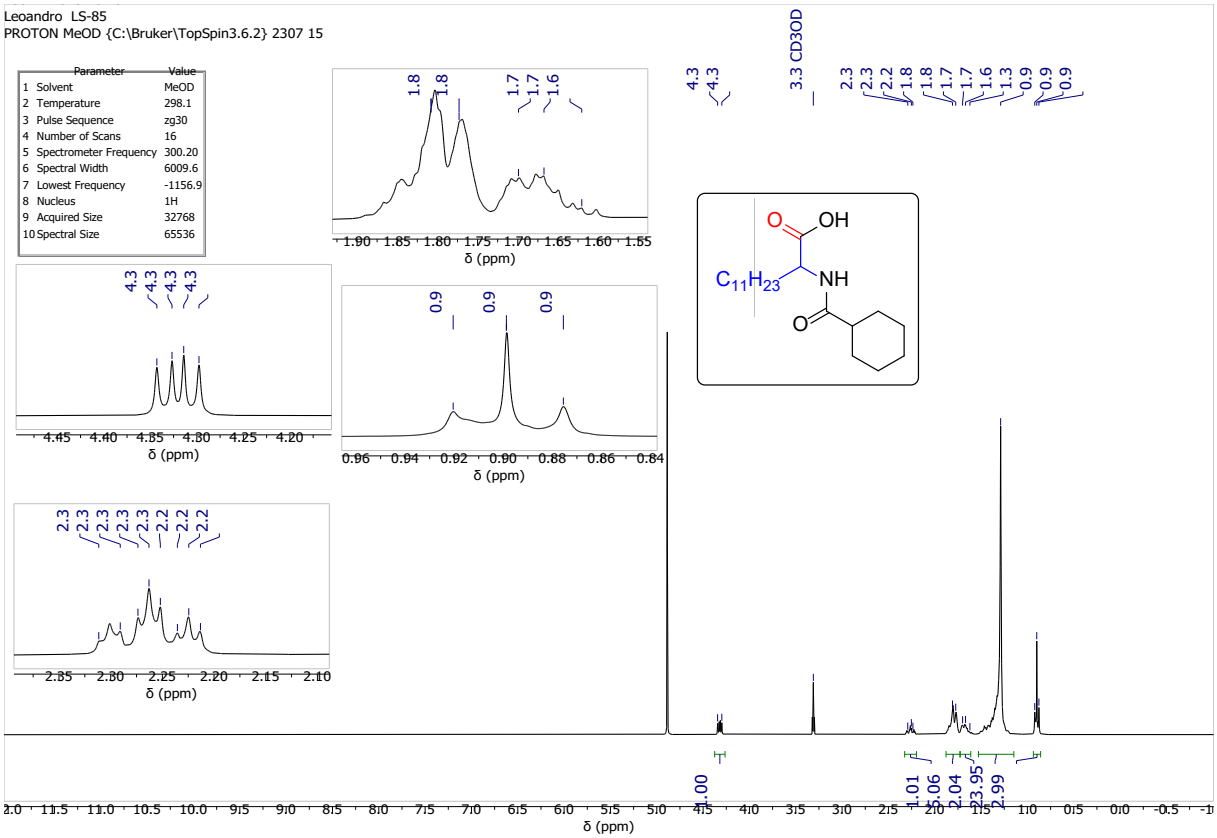


Figure S14: ^{1}H NMR of compound **(3g)**.

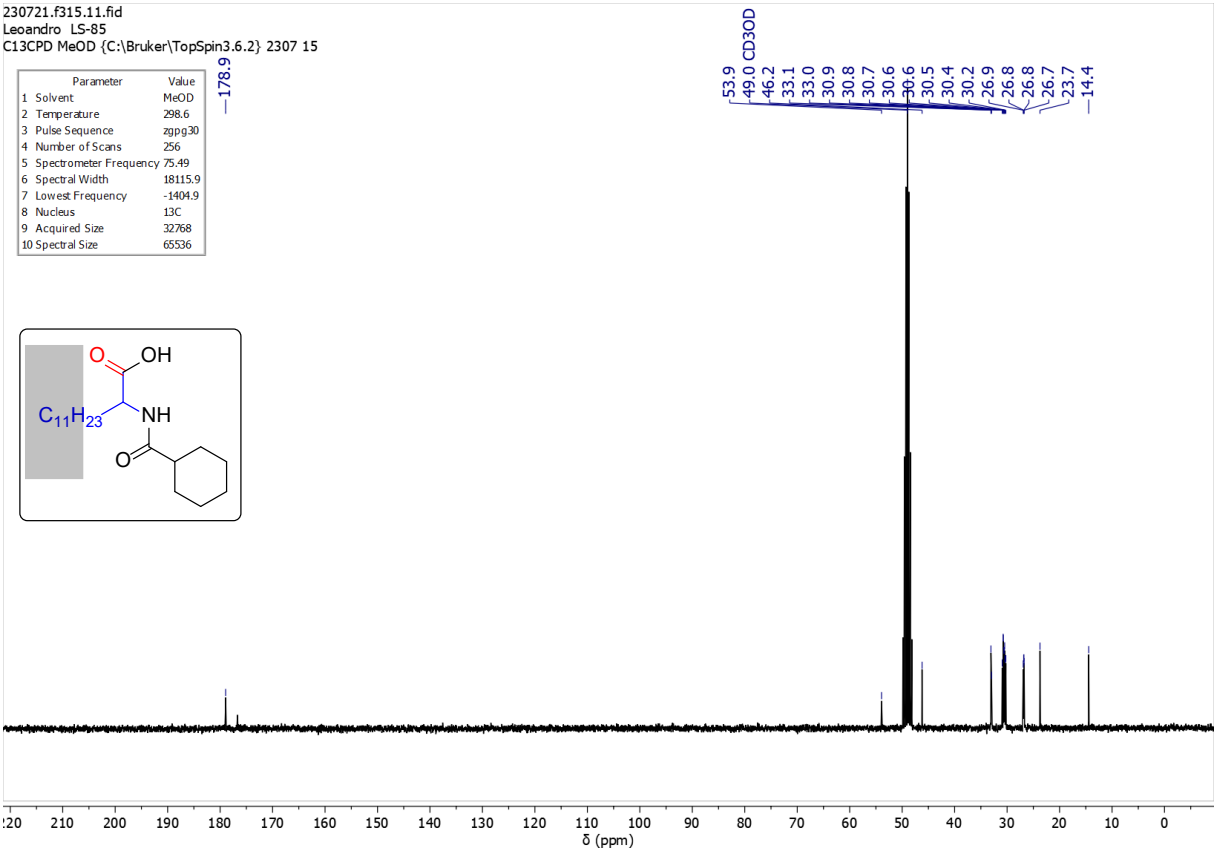


Figure S15: ^{13}C NMR of compound **(3g)**.

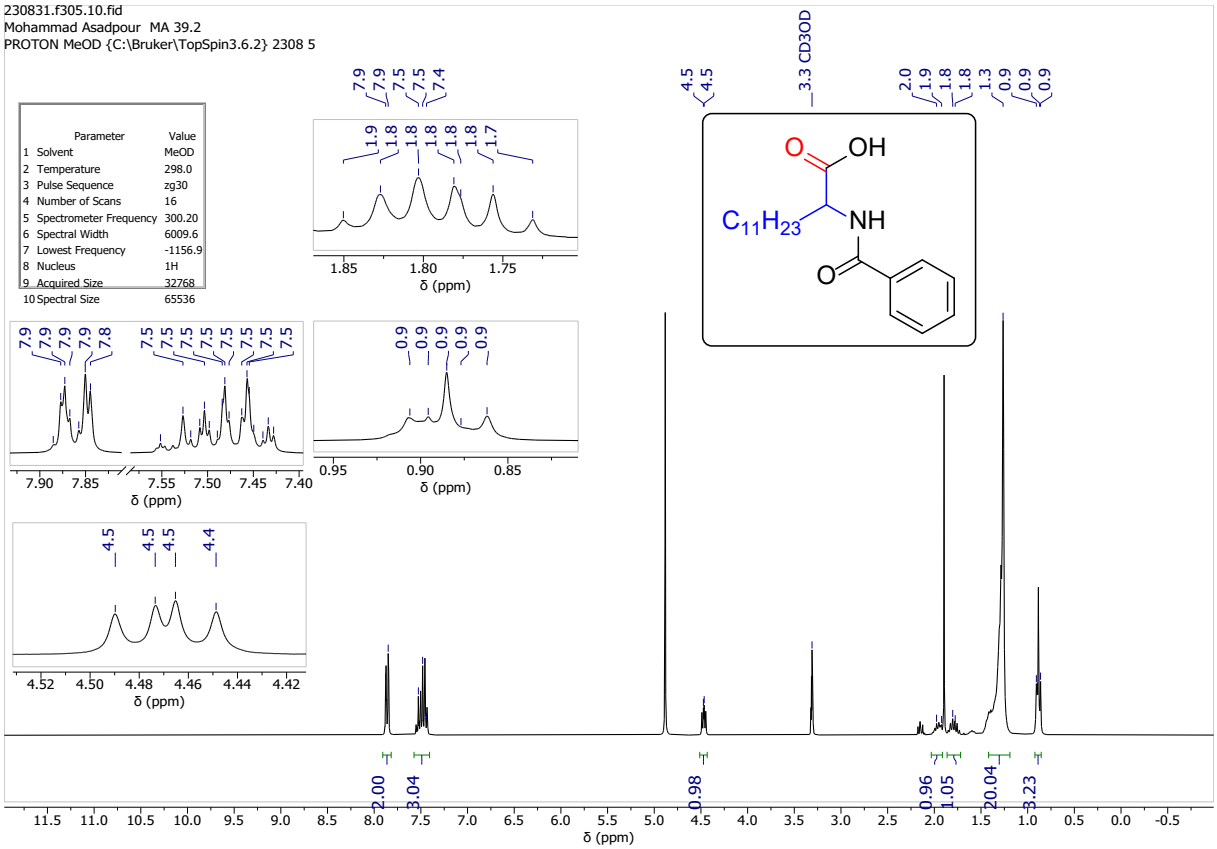


Figure S16: ^{1}H NMR of compound **(3h)**.

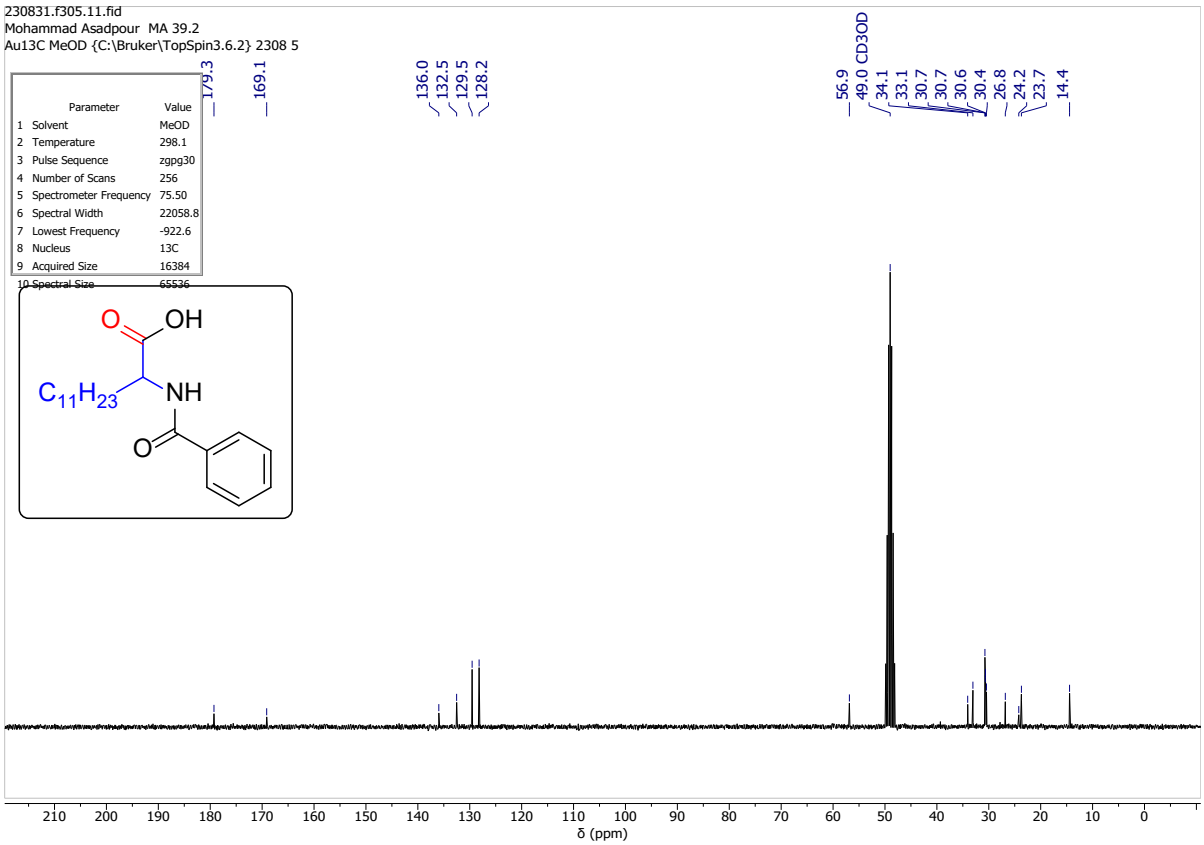


Figure S17: ^{13}C NMR of compound **(3h)**.

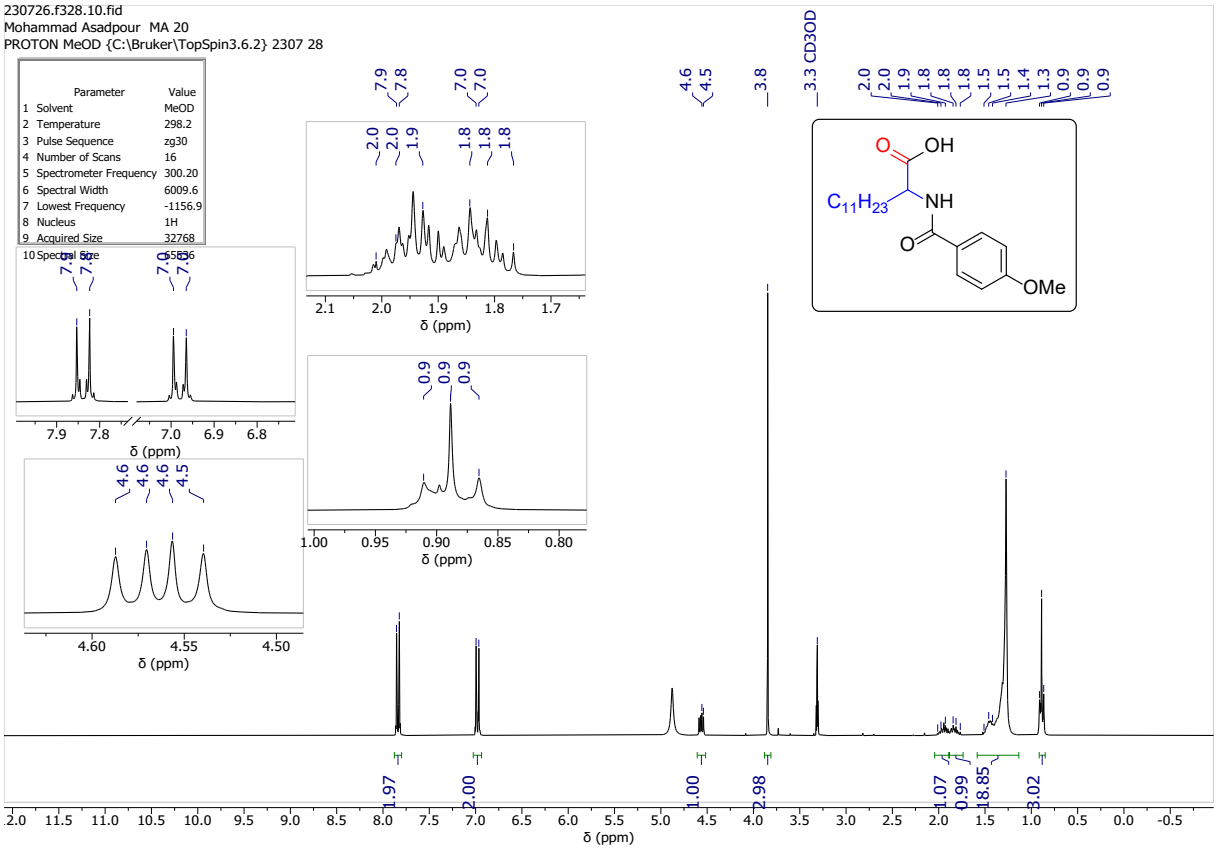


Figure S18: ^{1}H NMR of compound **(3i)**.

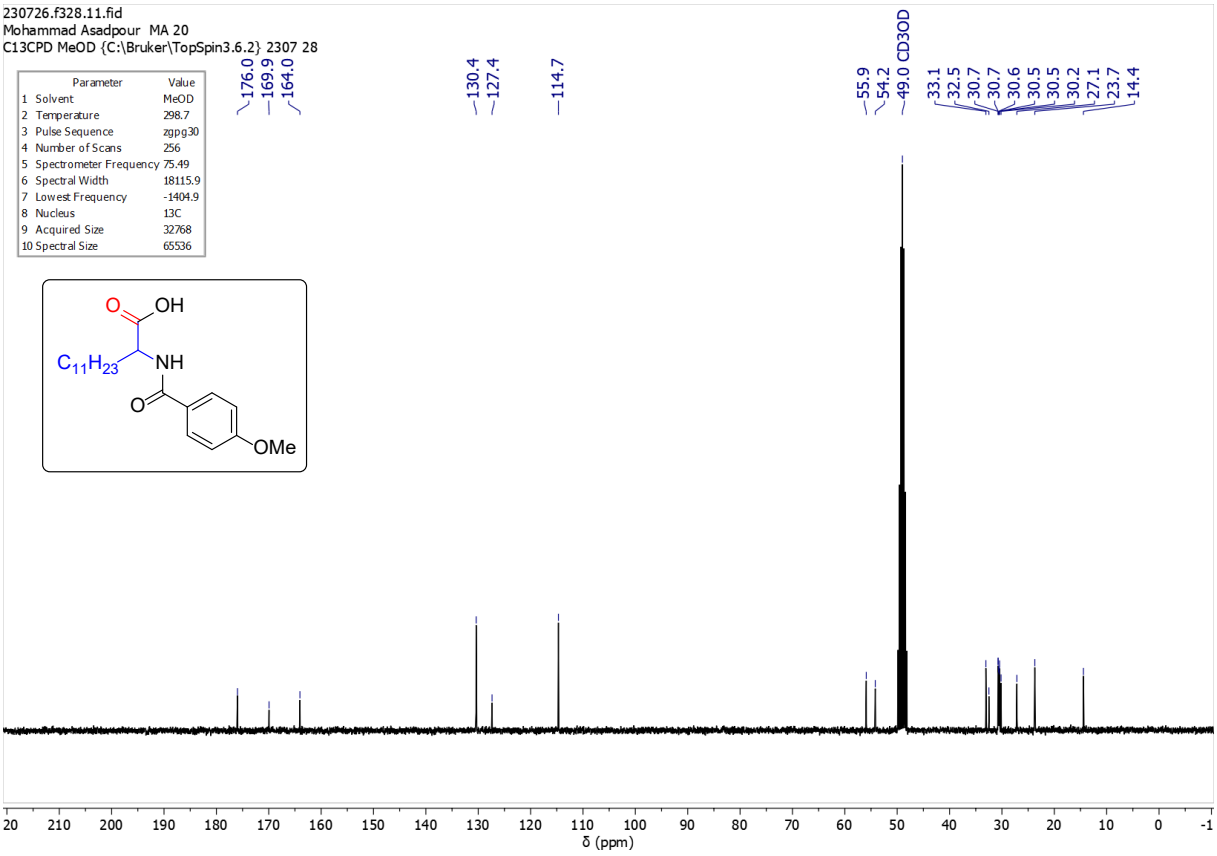


Figure S19: ^{13}C NMR of compound **(3i)**.

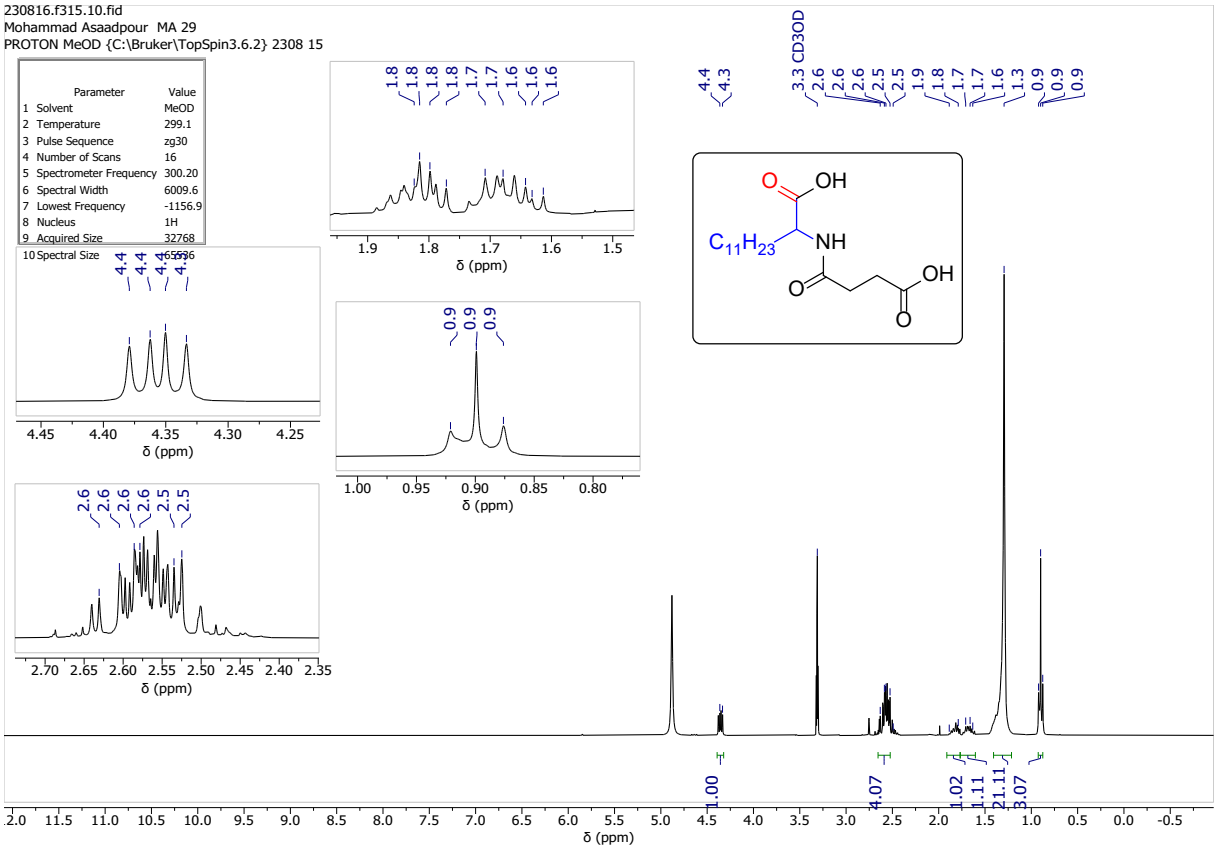


Figure S20: ^{1}H NMR of compound **(3j)**.

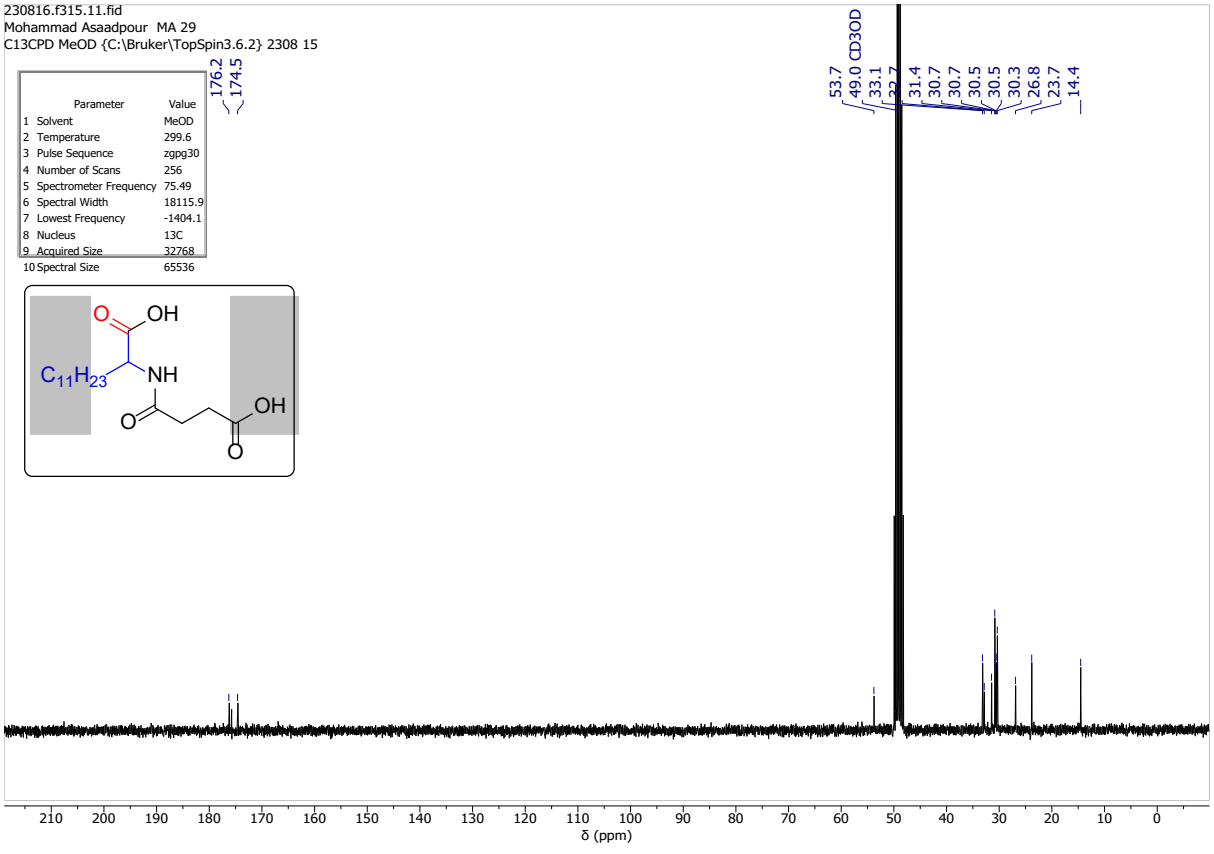


Figure S21: ^{13}C NMR of compound **(3j)**.

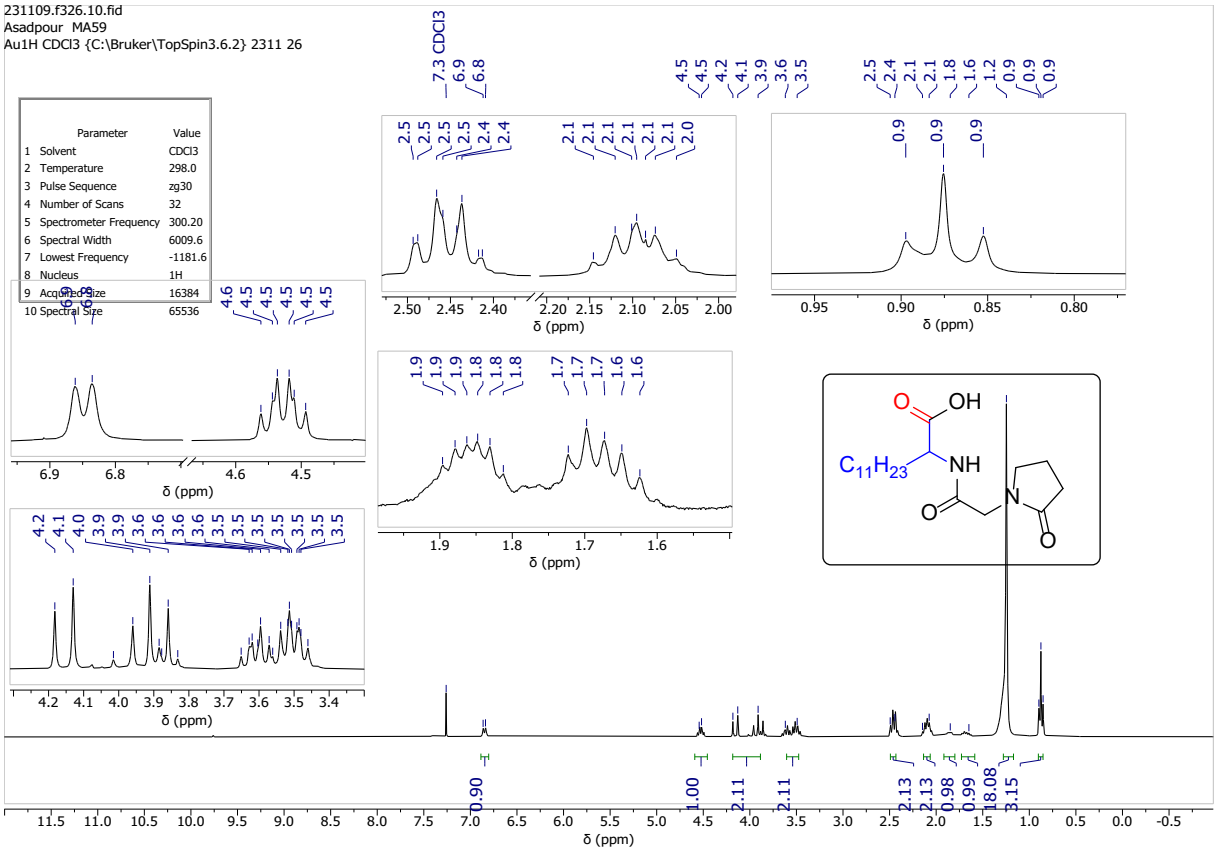


Figure S22: ^{1}H NMR of compound **(3k)**.

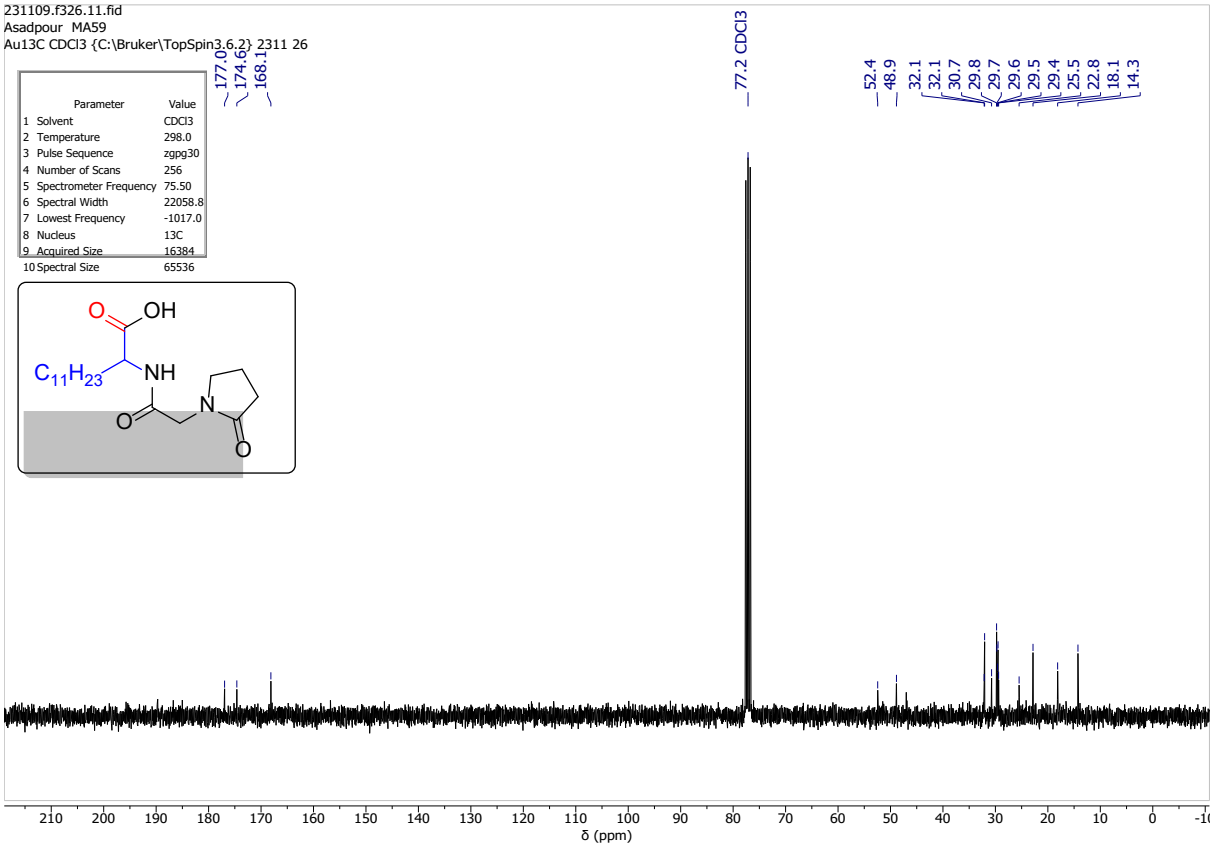


Figure S23: ^{13}C NMR of compound **(3k)**.

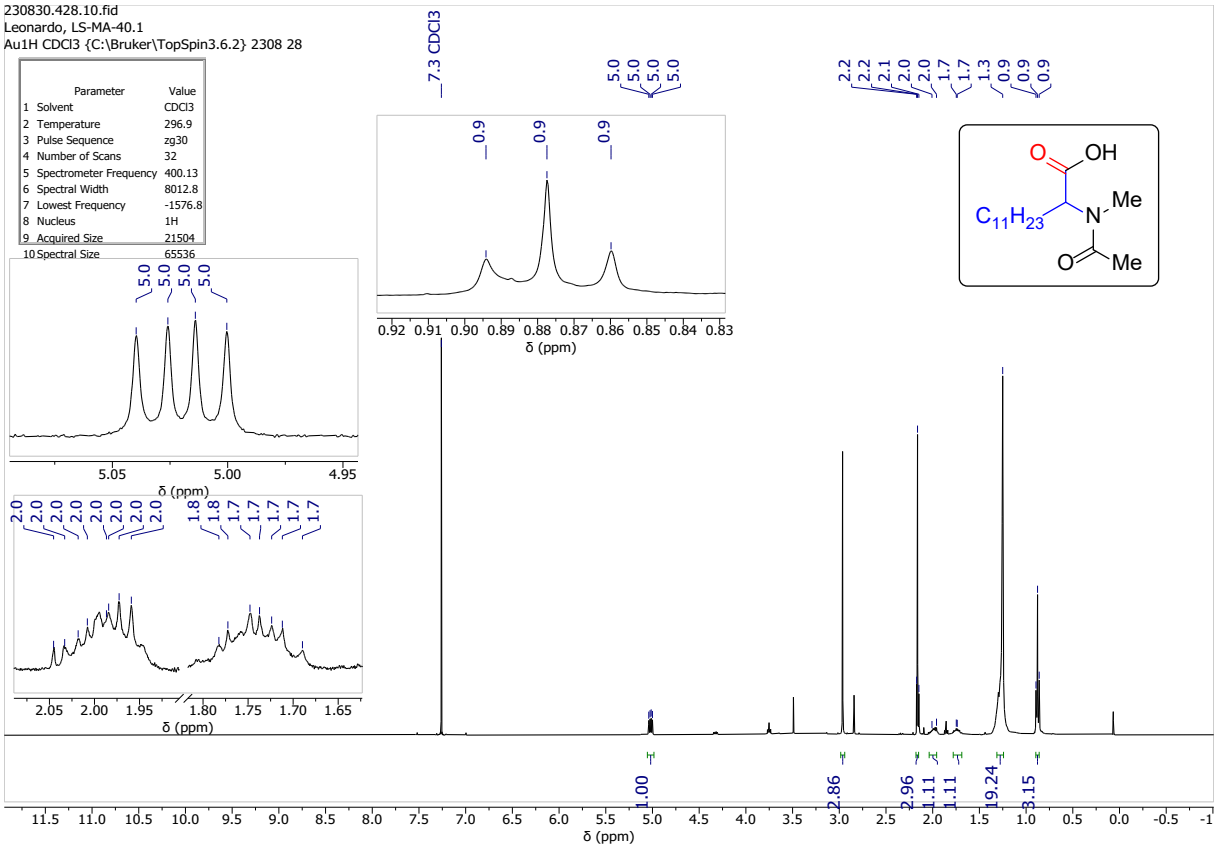


Figure S24: ^{1}H NMR of compound **(3l)**.

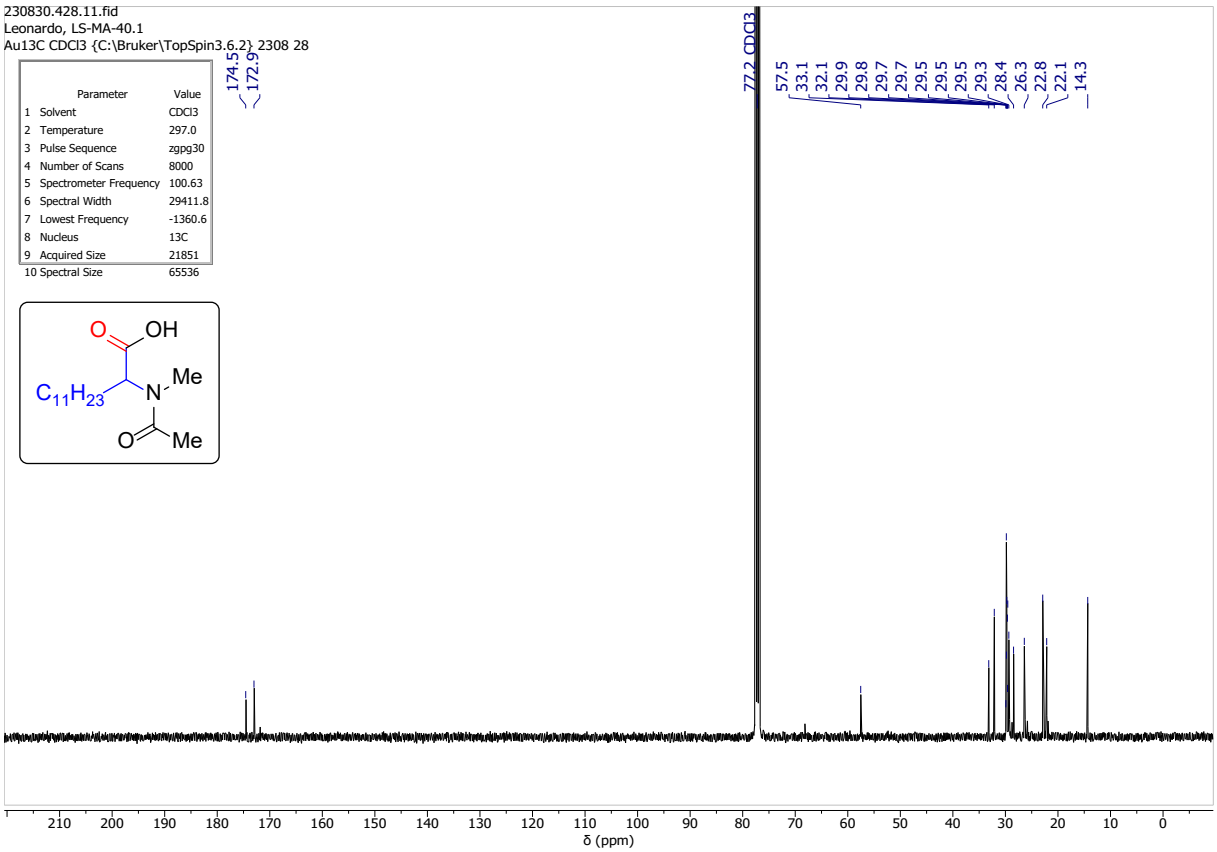


Figure S25: ^{13}C NMR of compound **(3l)**.

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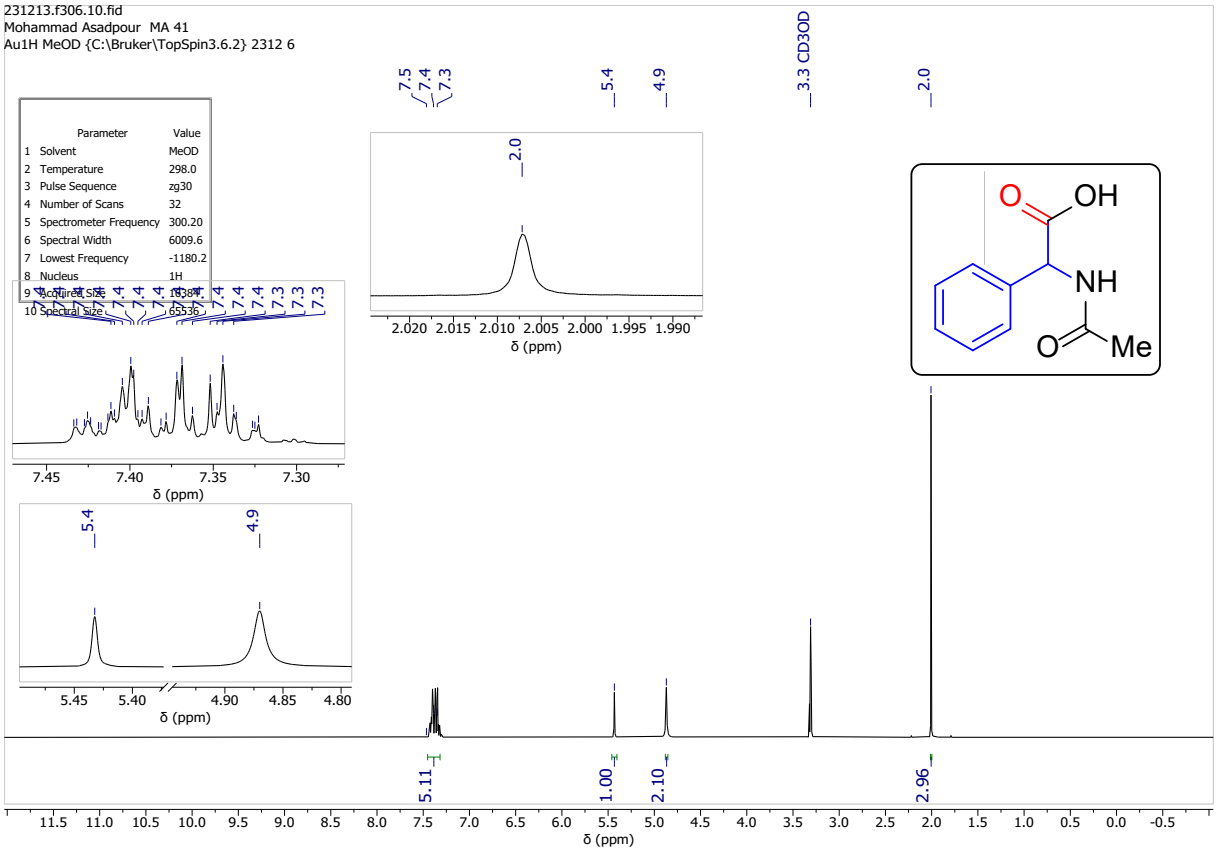

Figure S26: ^{1}H NMR of compound **(3m)**.

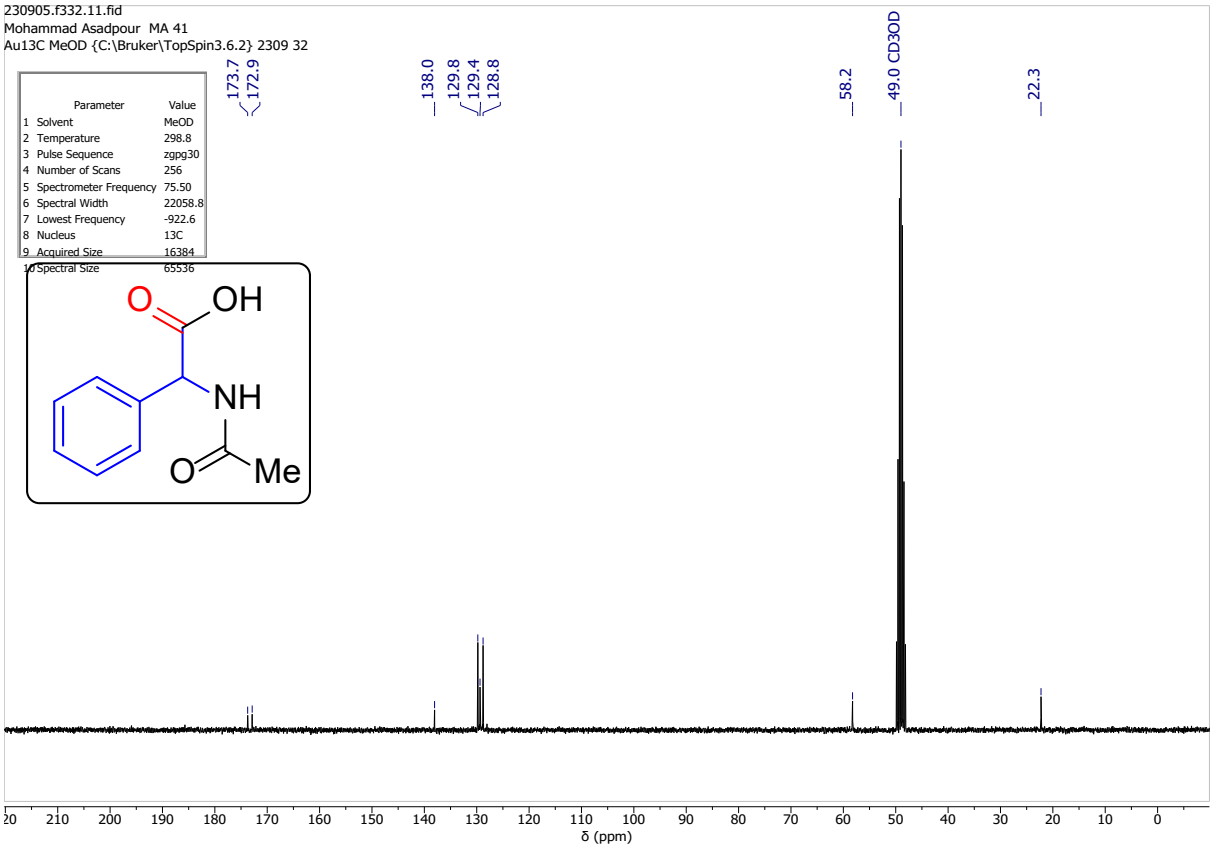

Figure S27: ^{13}C NMR of compound **(3m)**.

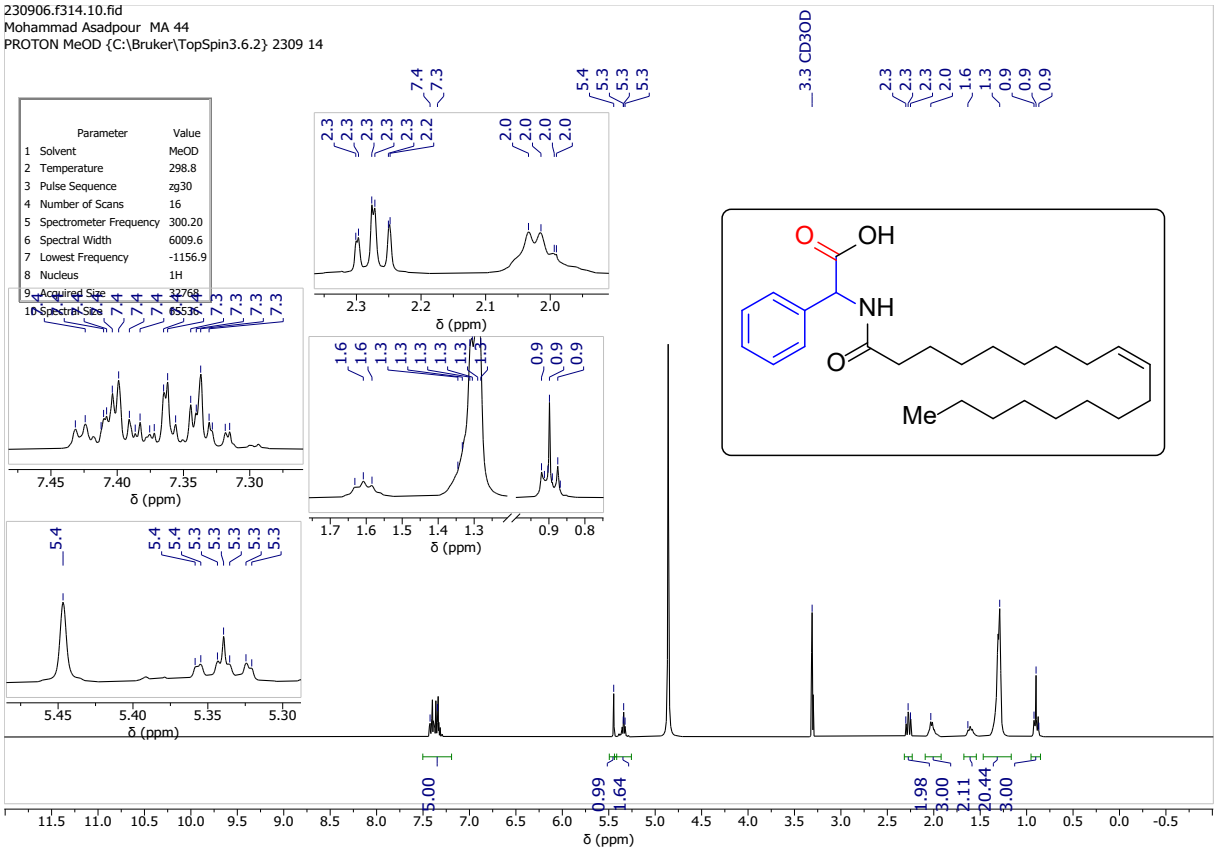

Figure S28: ^{1}H NMR of compound **(3n)**.

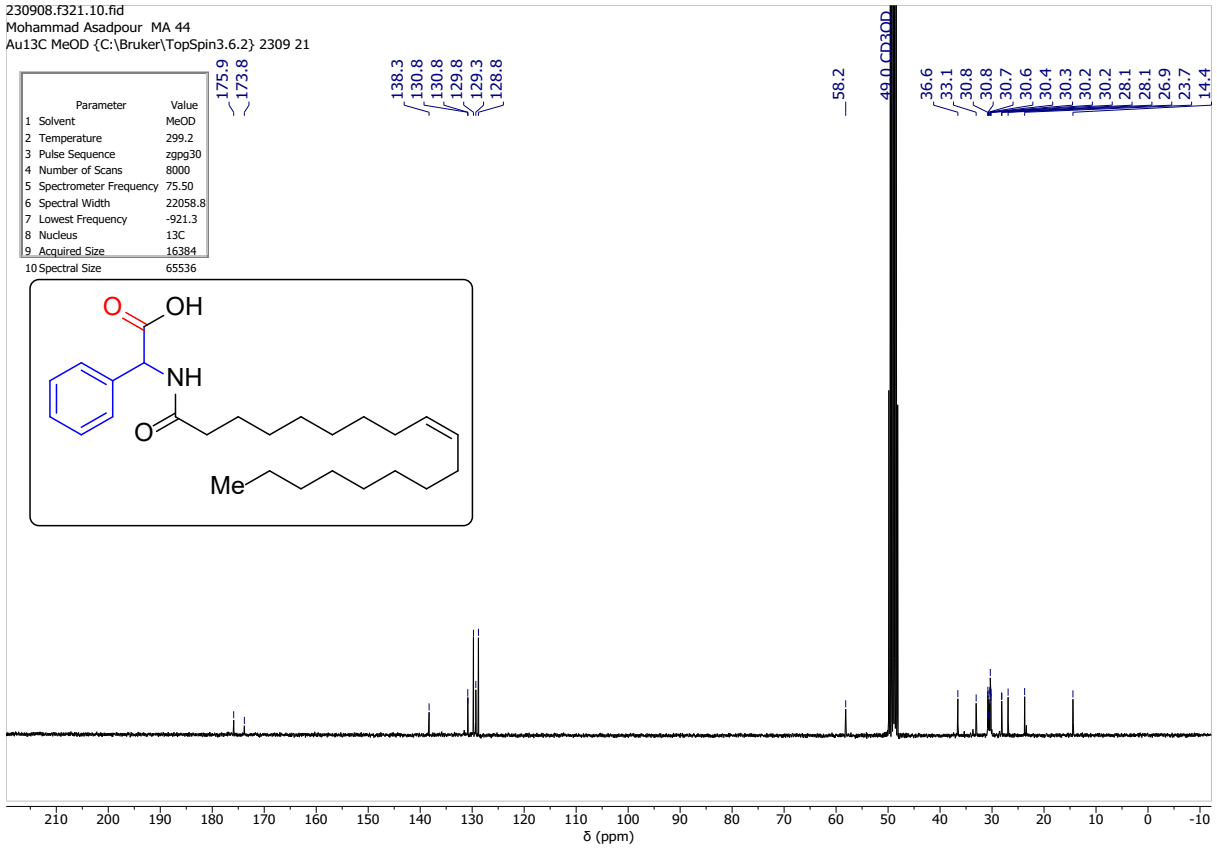

Figure S29: ^{1}H NMR of compound **(3n)**.

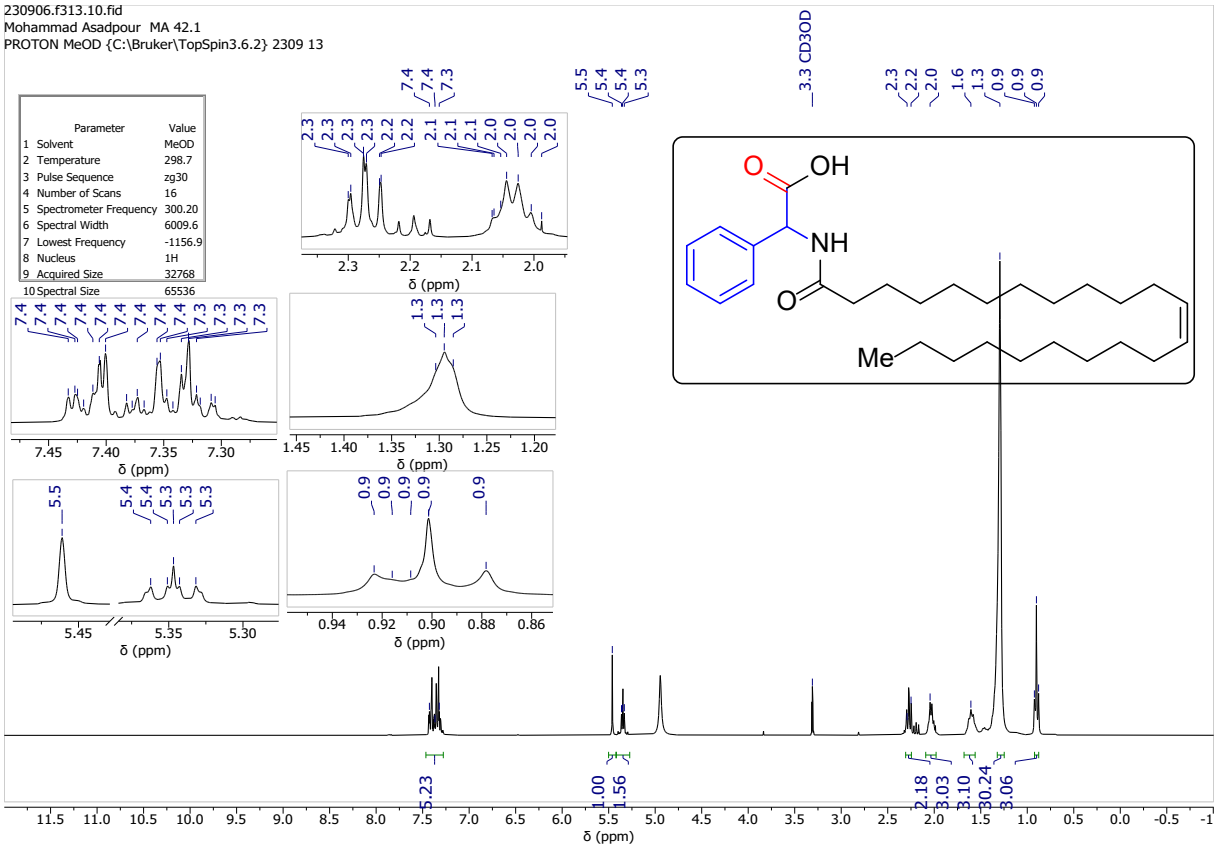

Figure S30: ^{1}H NMR of compound **(3o)**.

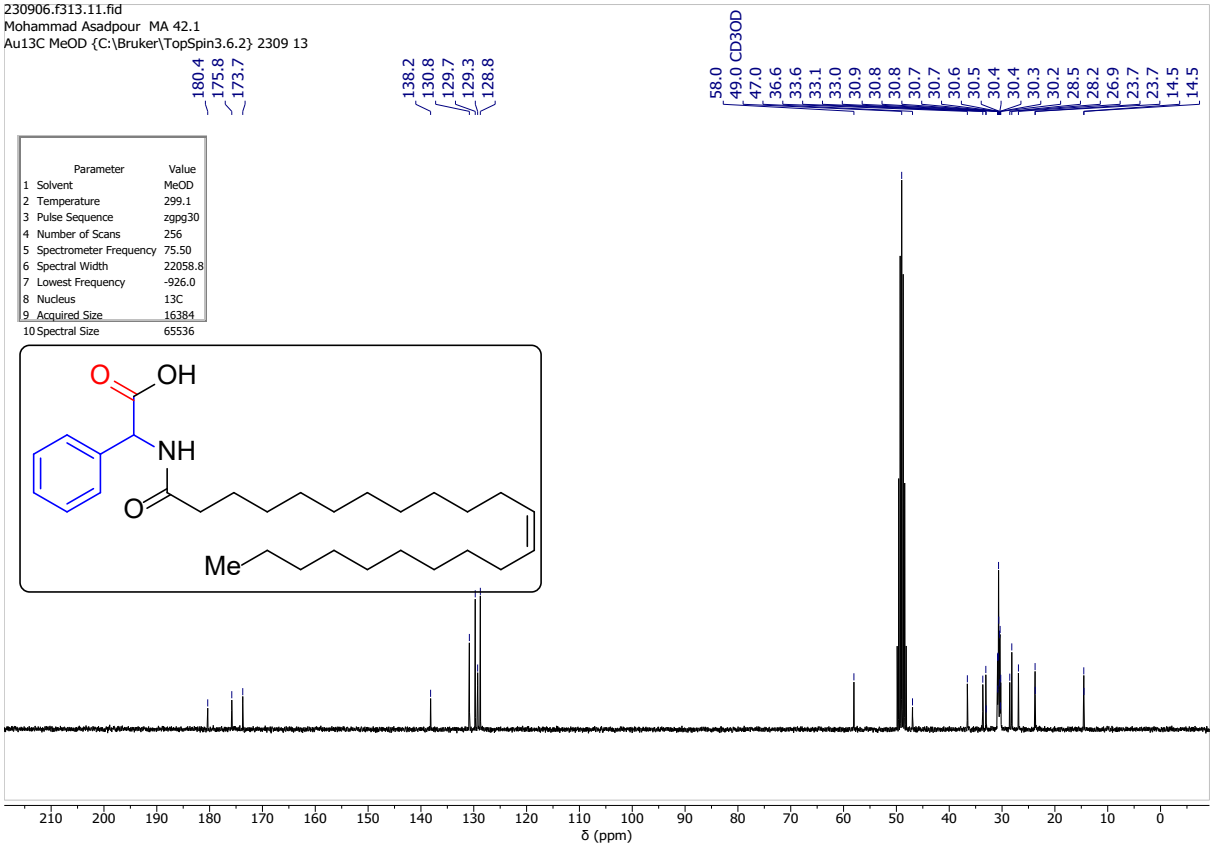

Figure S31: ^{13}C NMR of compound **(3o)**.

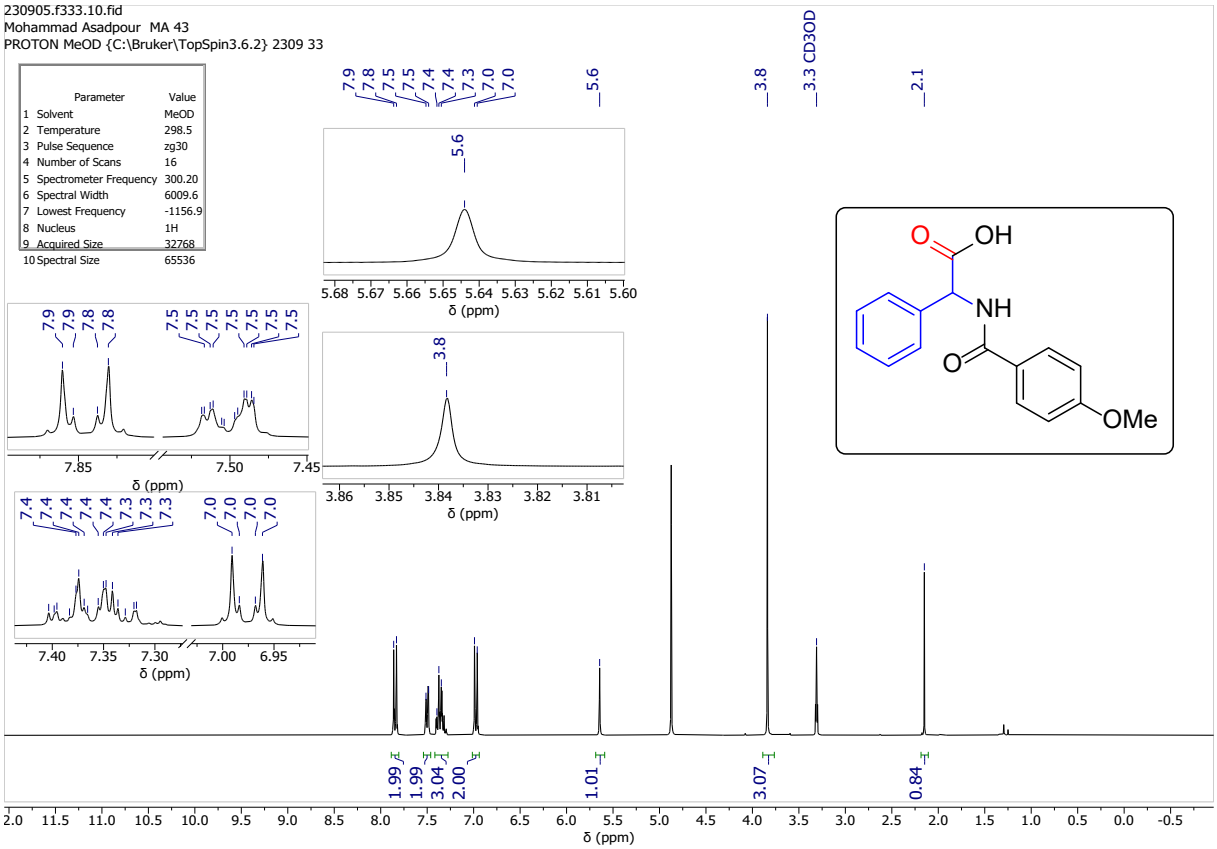

Figure S32: ^{1}H NMR of compound **(3p)**.

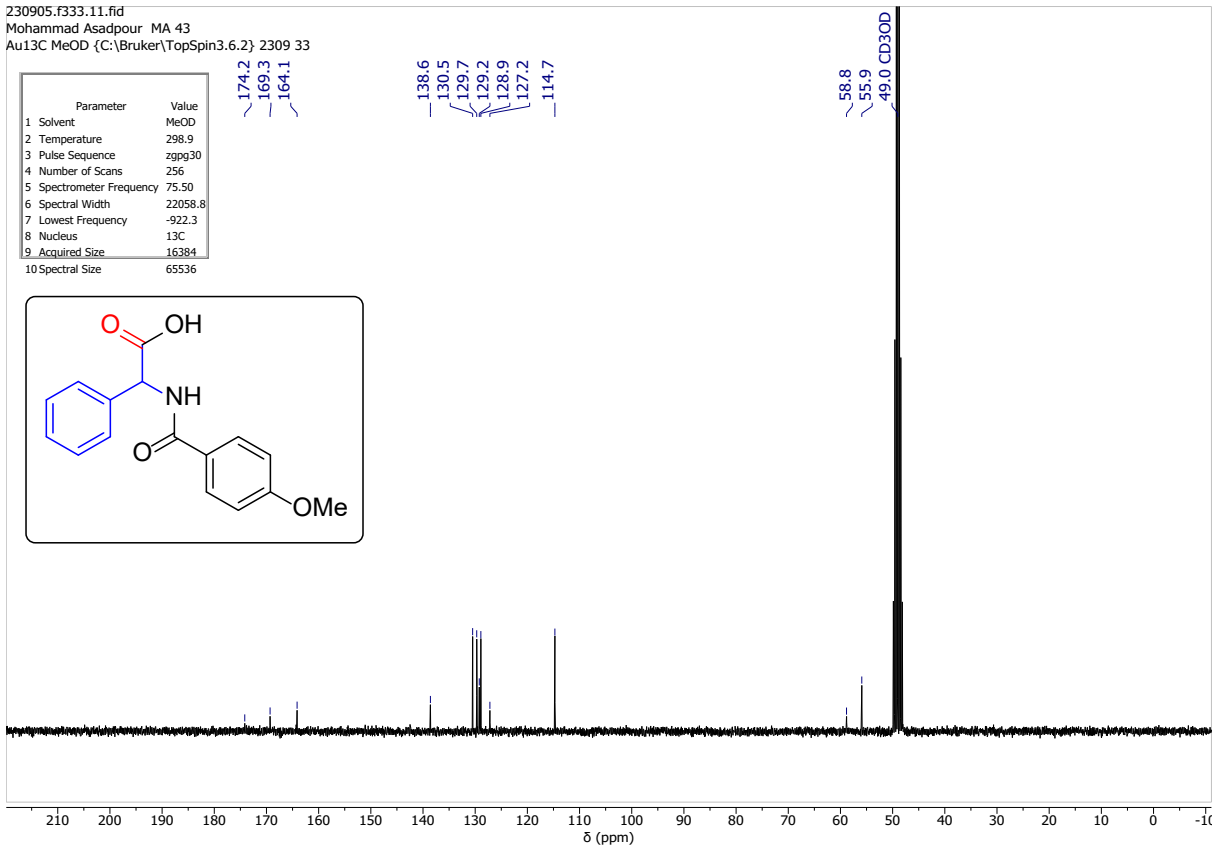

Figure S33: ^{13}C NMR of compound **(3p)**.

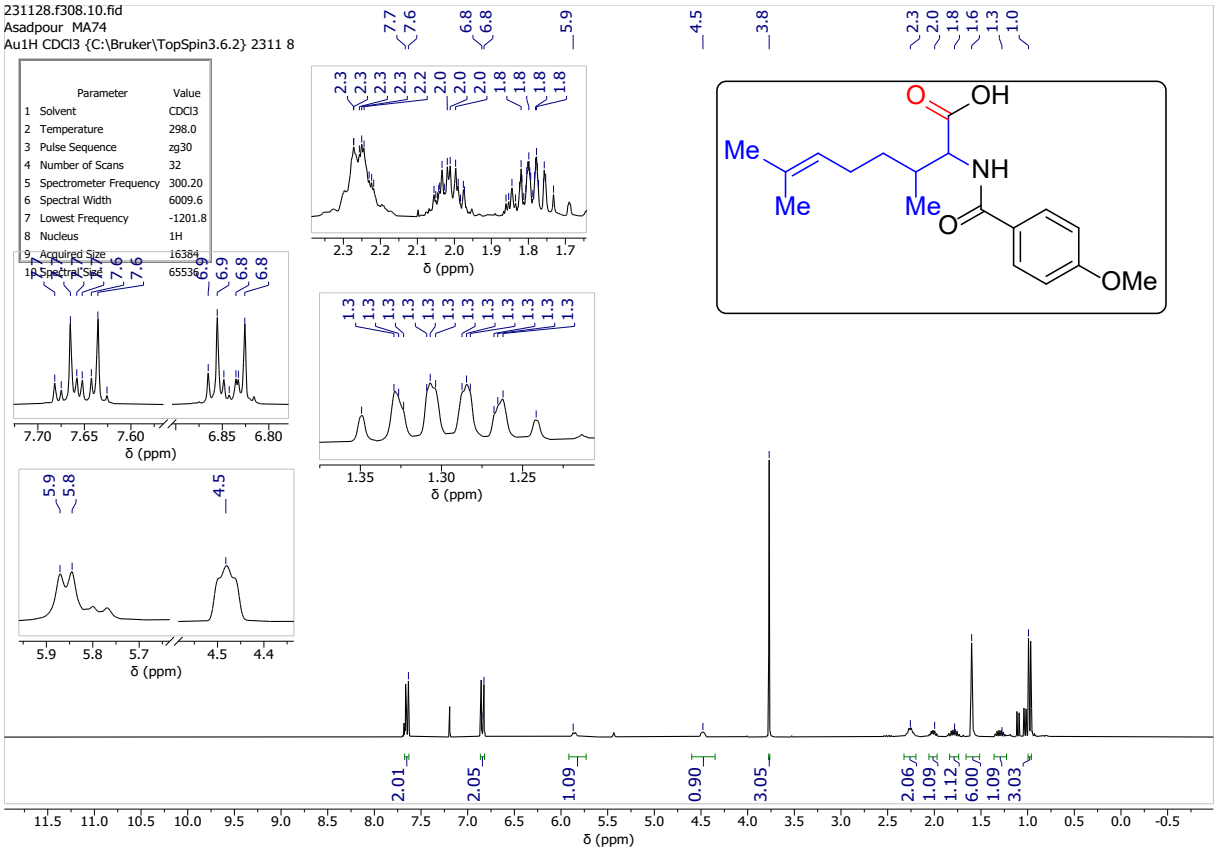

Figure S34: ^{1}H NMR of compound **(3q)**.

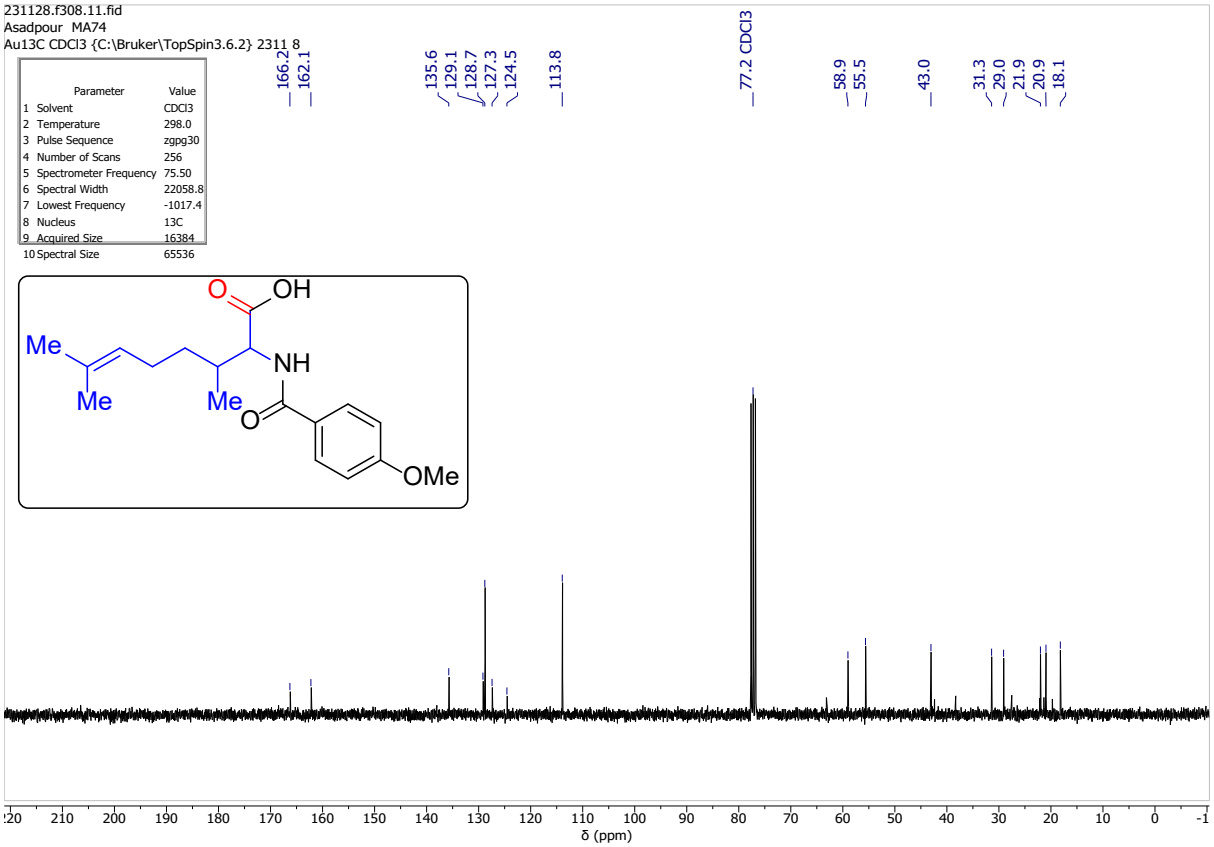

Figure S35: ^{13}C NMR of compound **(3q)**

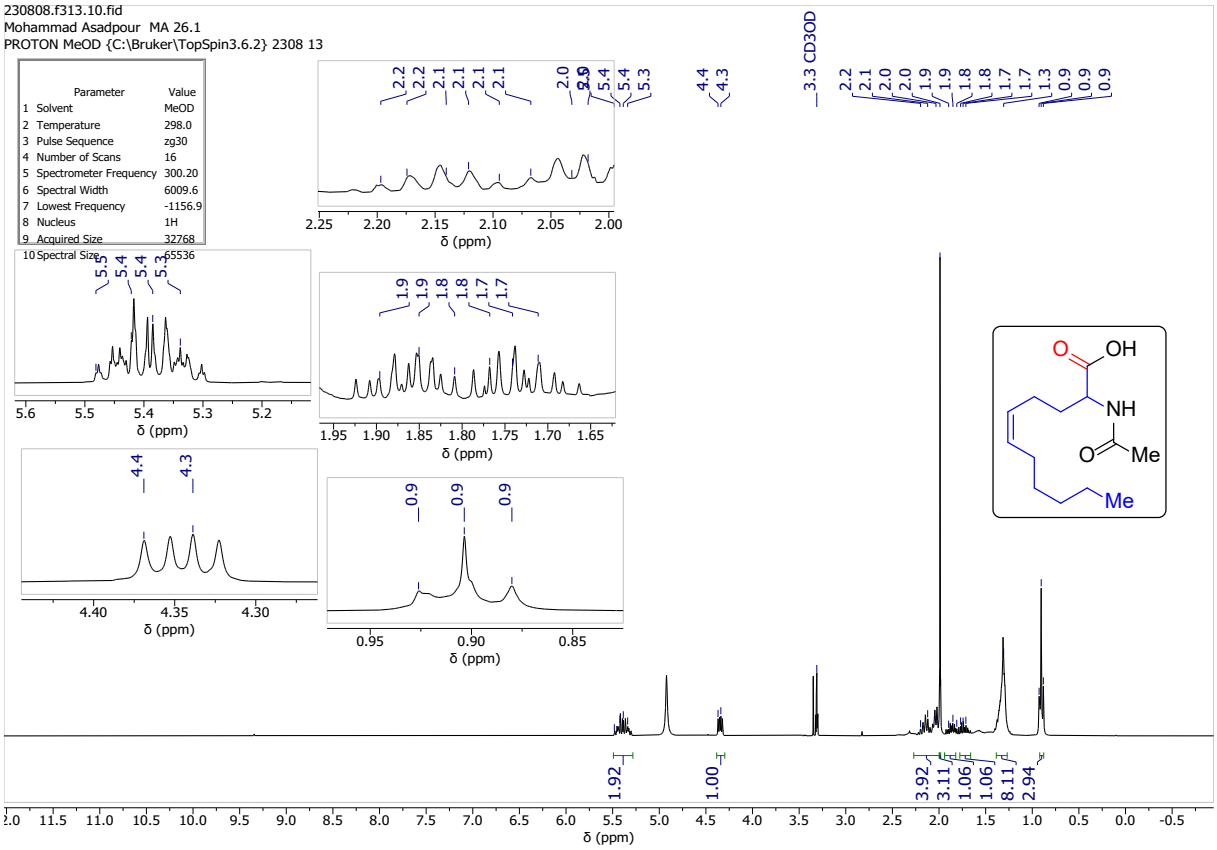

Figure S36: ^{1}H NMR of compound **(3r)**.

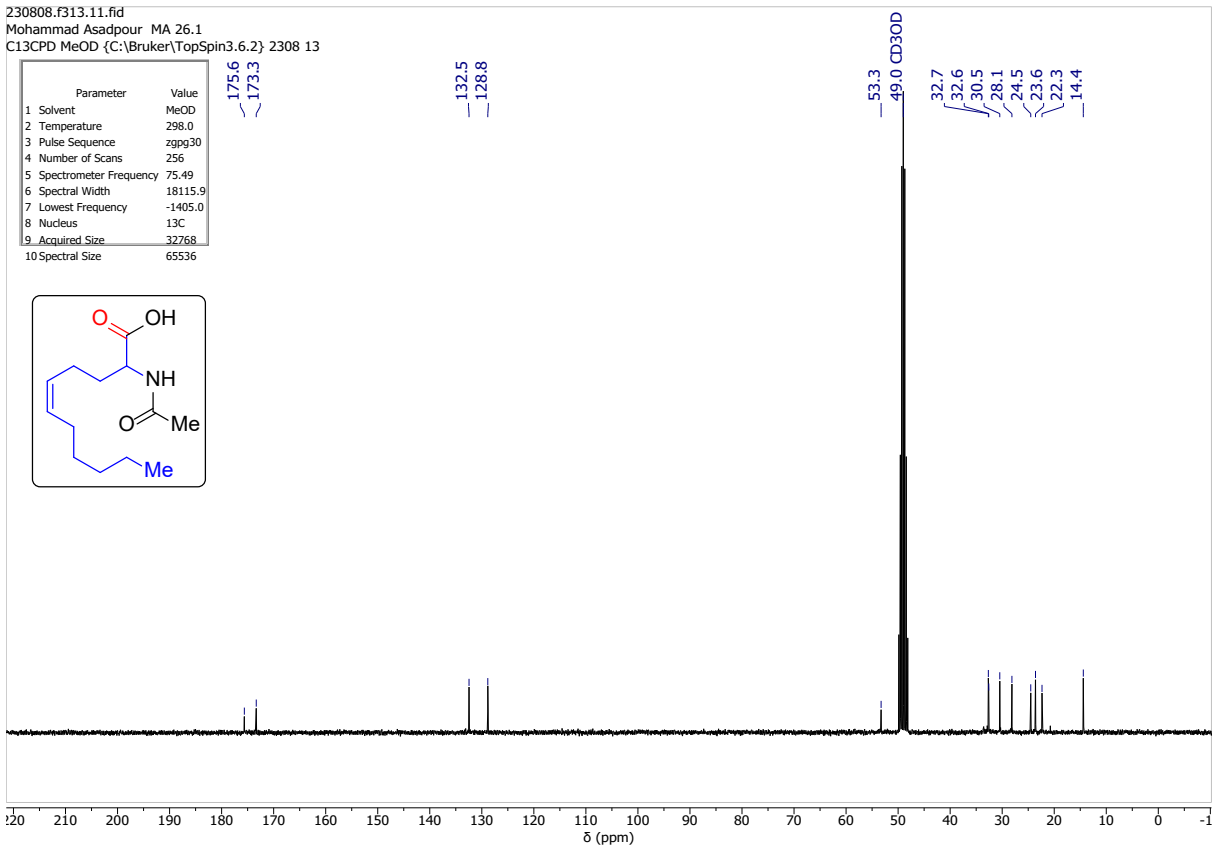

Figure S37: ^{13}C NMR of compound **(3r)**.

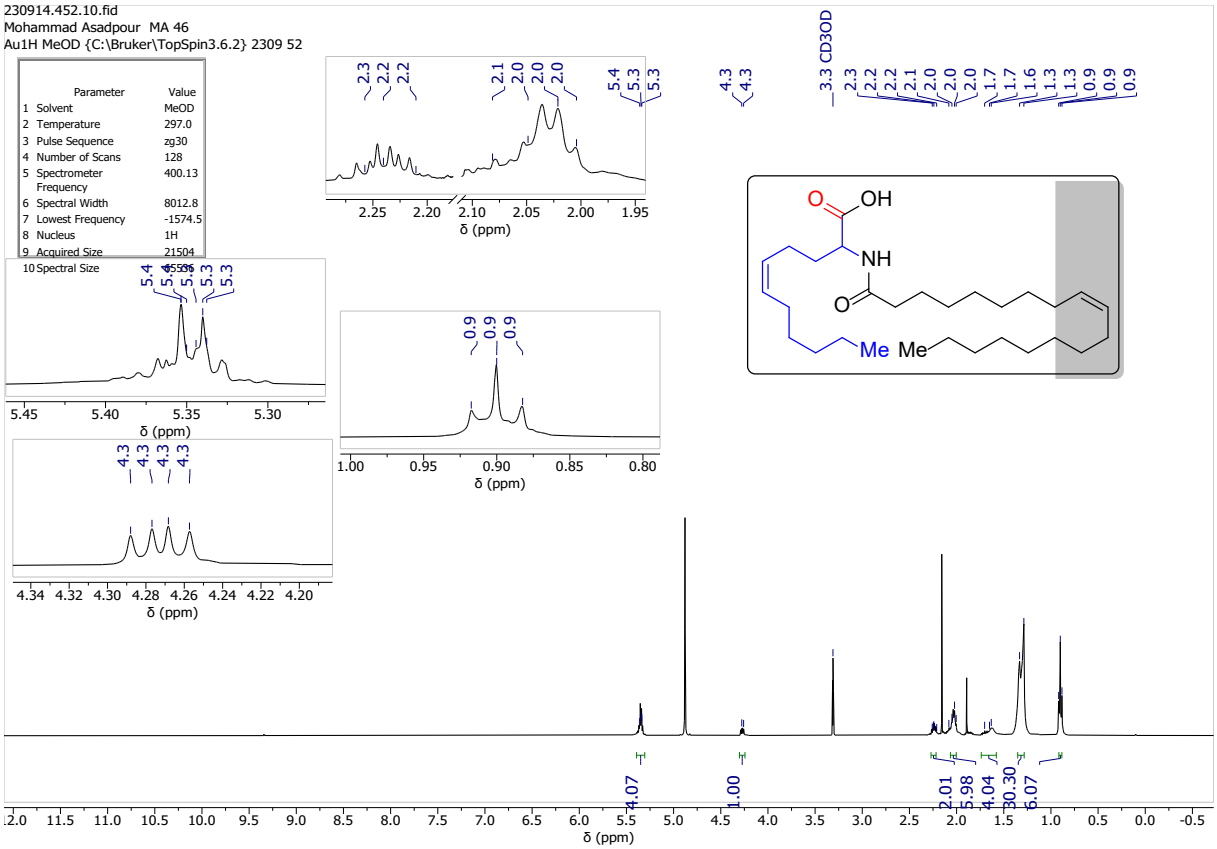

Figure S38: ^{1}H NMR of compound **(3s)**.

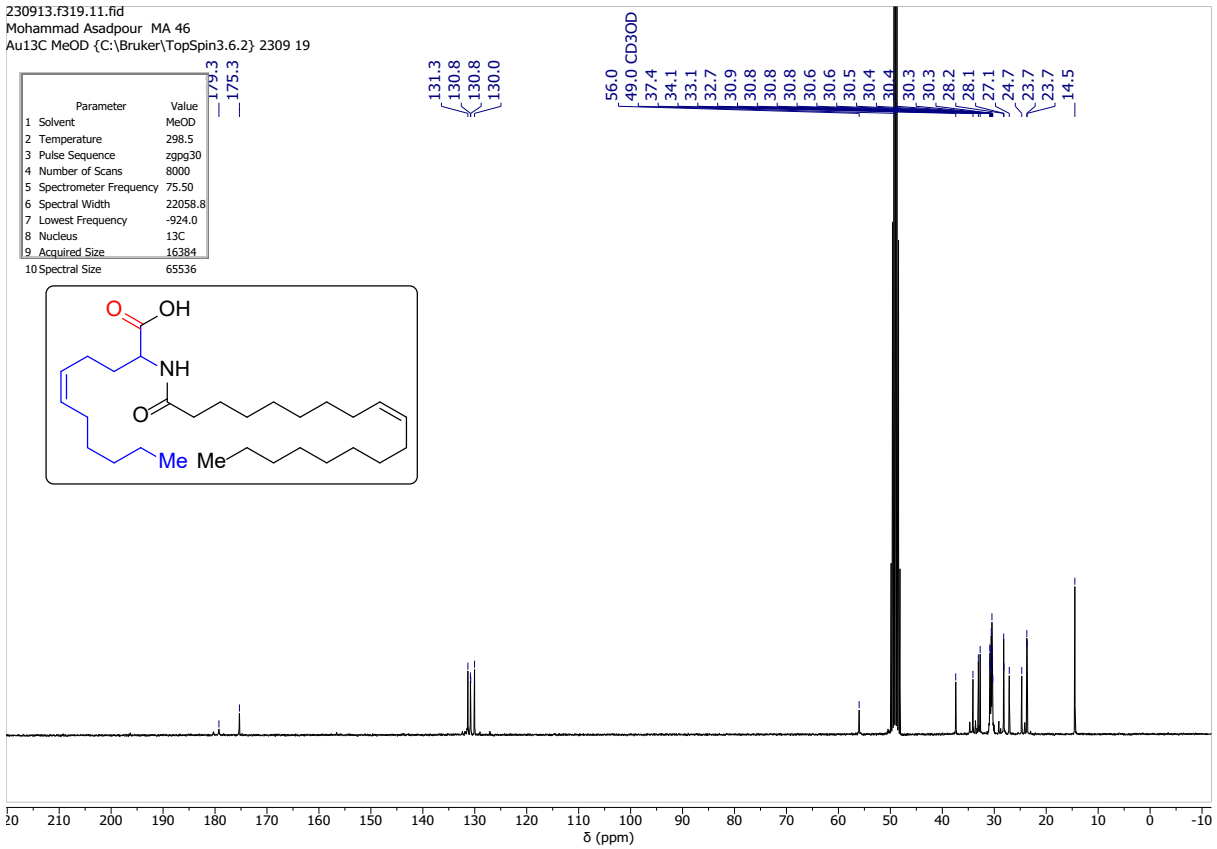

Figure S39: ^{13}C NMR of compound **(3s)**.

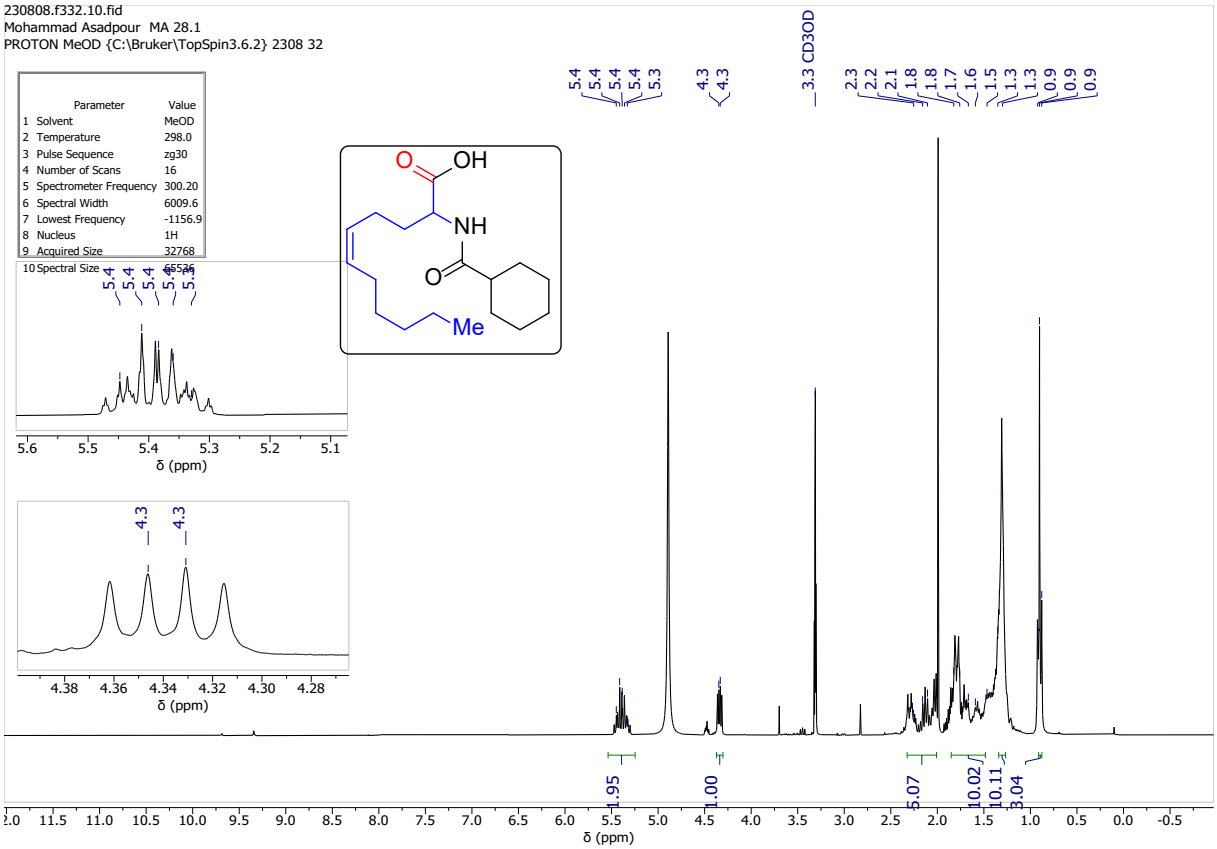

Figure S40: ^{1}H NMR of compound **(3t)**.

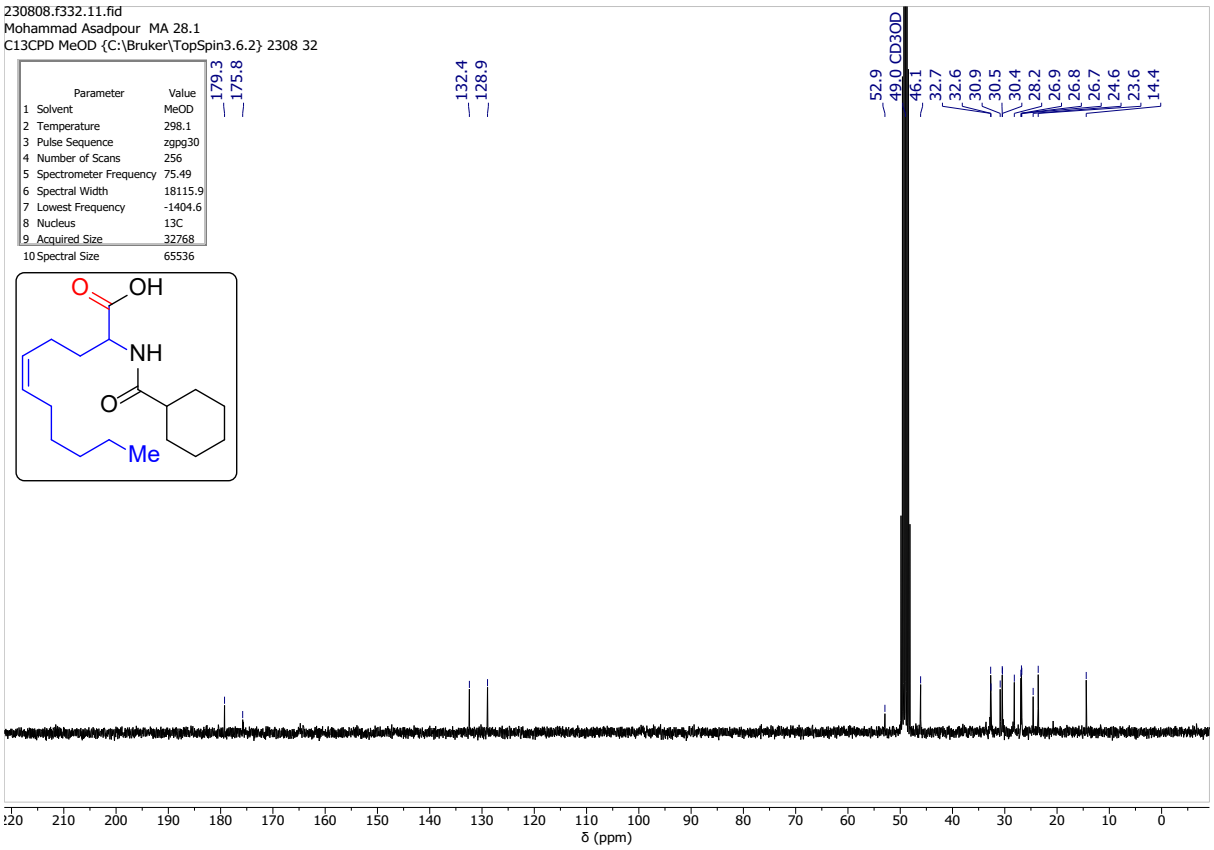

Figure S41: ^{13}C NMR of compound **(3t)**.

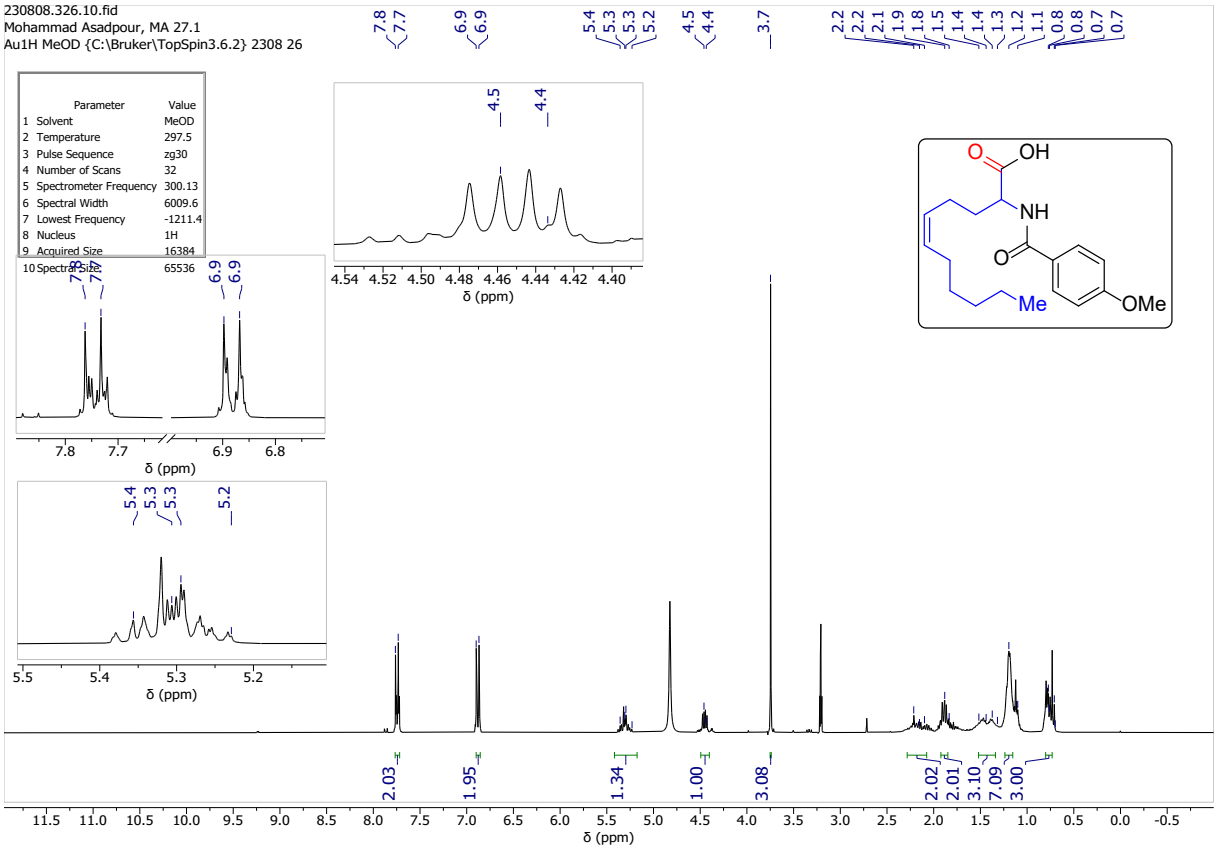

Figure S42: ^{1}H NMR of compound **(3u)**.

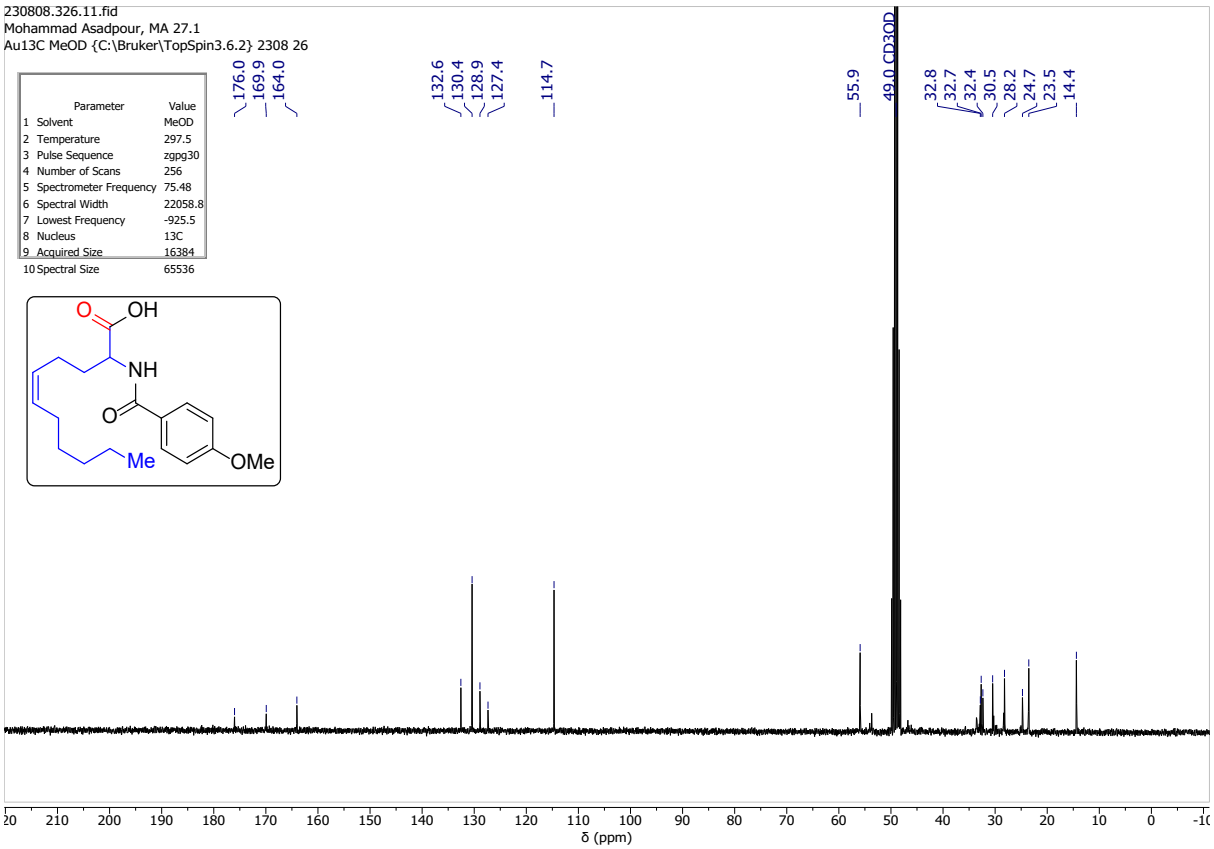

Figure S43: ^{13}C NMR of compound **(3u)**.

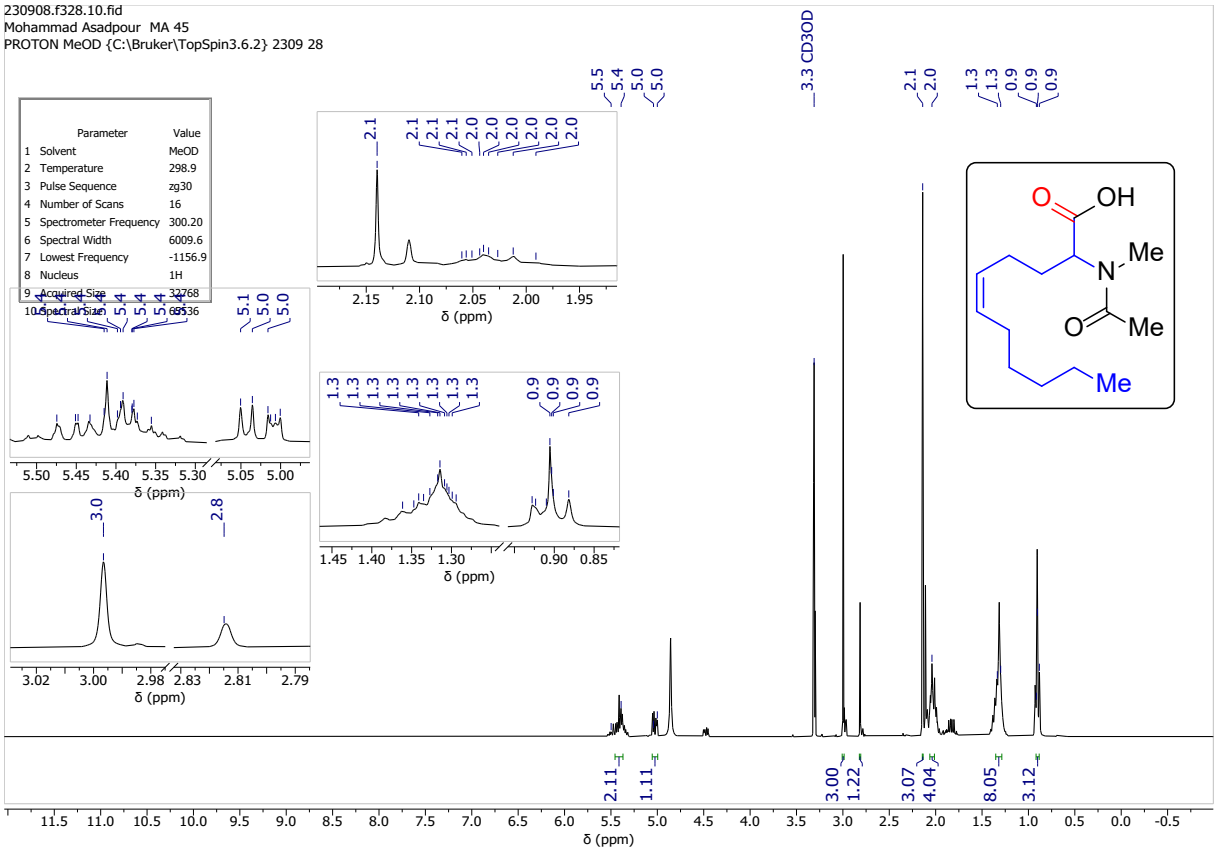

Figure S44: ^{1}H NMR of compound **(3v)**.

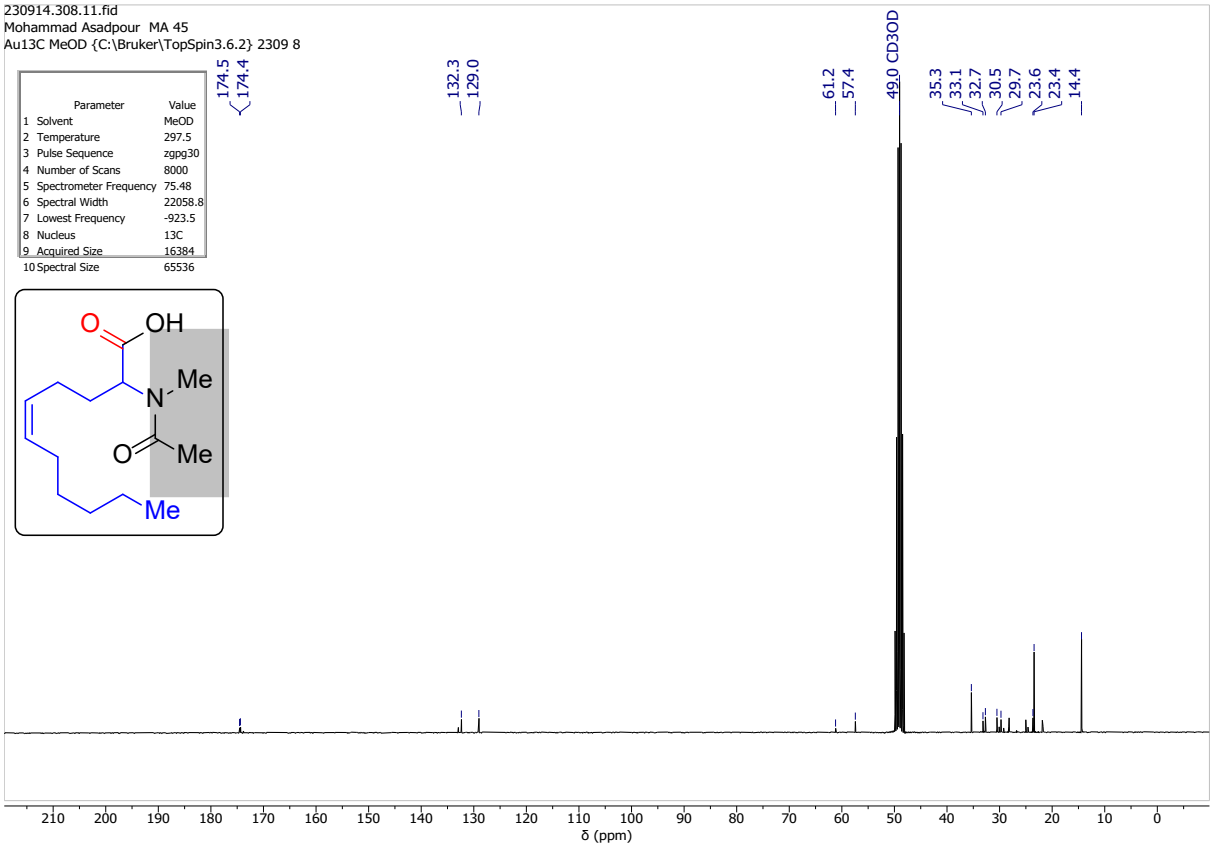

Figure S45: ^{13}C NMR of compound **(3v)**.