Electronic Supplementary Material (ESI) for ChemComm.

Palladium-Catalyzed Site-Selective Functionalization of Unactivated Alkenes with Vinylcyclopropanes Aided by Weakly Coordinating Native Amides

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Electronic Supporting Information (ESI)

Table of Contents

Experimental Section

General information: All reactions were carried out under the N_2 atmosphere in flame-dried glassware. Syringes which were used to transfer anhydrous solvents or reagents were purged with nitrogen prior to use (three times). Dry solvents are used for the reaction. Column chromatographical purifications were performed using SiO_2 (120- 200 mesh ASTM) from Merck if not indicated otherwise. Abbrevations for signal coupling are as follows: s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet. Commercially available metal salts and acids were purchased from Sigma-Aldrich and Spectrochem. Pvt. Ltd., India and used without further purification. Starting materials **1a-1j**[1], **2a-2p**[2] and ligands **L1-L5**[3], **L10**[4], **L9** and **L14**[5] were prepared according to known literature procedures.[1-6]

1. General Procedure for the *β*-selective allylation of amide 1 with 2:

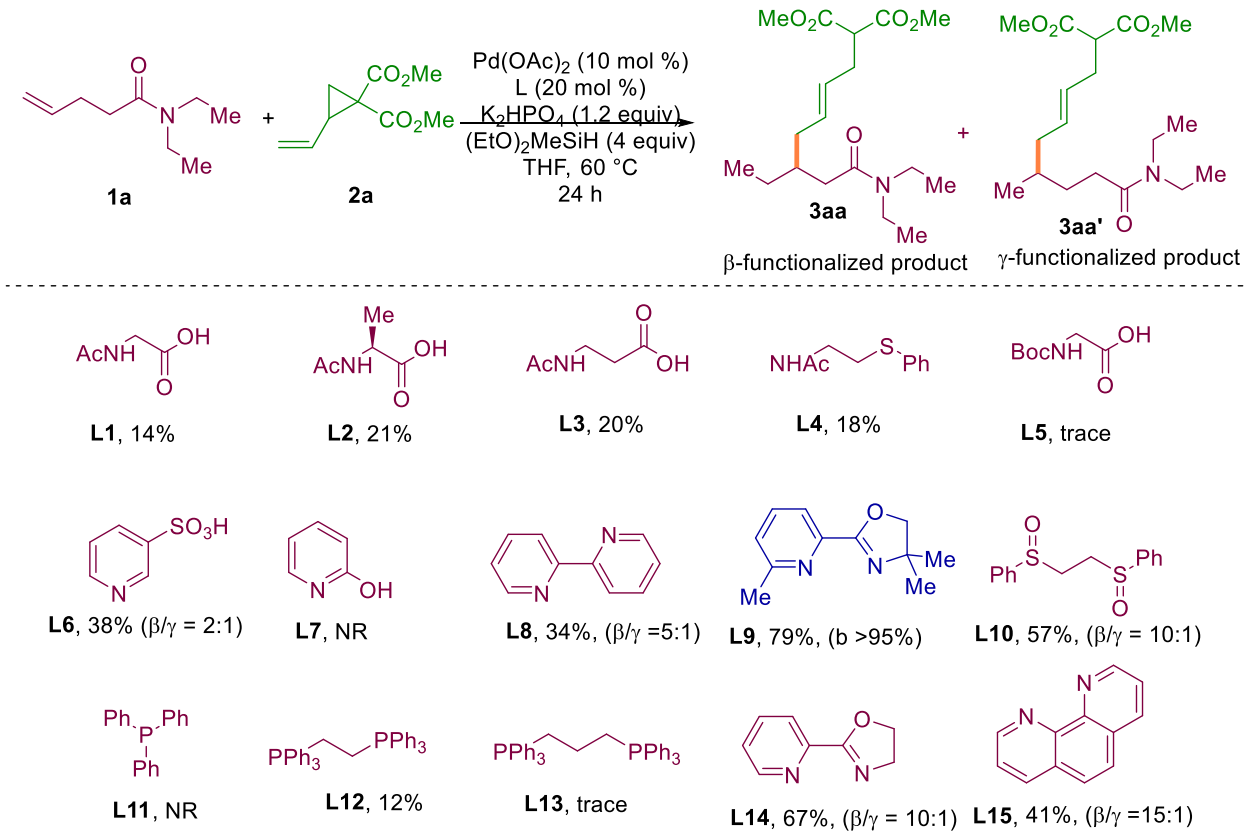
A 15ml Schlenk tube with septum containing $Pd(OAc)_2$ (10 mol %), **L9** (20 mol %) and K_2HPO_4 (1.2 equiv) were evacuated and purged with nitrogen gas three times. Followed by, amide **1** (50 mg, 1.0 equiv) and vinylcyclopropane **2** (5.0 equiv) was dissolved in THF (1.0 mL each) and was added to the Schlenk tube *via* syringe. Further, $(EtO)_2MeSiH$ (4.0 equiv) was added to the reaction mixture dropwise and the reaction mixture was evacuated and purged with nitrogen gas three times. The rubber septum was taken out and the reaction mixture was covered with screw cap. The reaction mixture was allowed to stir at 60 ^oC for 24 h. Then, the reaction mixture was allowed to cool to ambient temperature and diluted with CH_2Cl_2, followed by filtration through celite and the filtrate was concentrated. The crude residue was purified through a silica gel column using hexane and ethyl acetate as eluent to give pure **3**.

Optimization Studies:

The effect of ligands was judiciously evaluated for the reaction (**Scheme S1**). The best results were obtained when **L9** was used as a ligand to provide the desired product **3aa** in 79% yield with good β-selectivity (>95%). However, when the reaction was screened with various monoprotected amino acid ligands such as **L1-L5**, the yield of the product **3aa** was drastically reduced. Mono and diphosphine ligands **L11-L13** were also ineffective for the reaction. However, when ligand **L6** was utilized the allylated product was observed in 38% yield. In this case, low β-selectivity was observed with a β/γ ratio of 2:1. The bipryidyl ligand **L8** gave the

desired product in 34% yield with regioisomers **3aa** and **3aa'** in the ratio of 5:1. Further, when 1,2-bis(phenylsulfinyl)ethane **L10** was probed for the reaction, a drastic improvement of 57% in the yield of the product was observed with a β/γ ratio of 10:1. Low β–selectivity was observed for ligand **L14** which does not poses any substitution at either pyridine or oxazoline ring.

Scheme S1. Ligand Optimization.



Next, the effect of catalyst loading on the allylation reaction was examined. Decreasing the catalyst loading to 5 mol % reduced the yield of the product **3aa** in to 65%. Increasing the catalyst loading shows only slight increase in the product yield. Further, the product formation was completely inhibited in the absence of ligand and base (**Table 1**, entries 1-2). Reducing the base concentration to 50 mol % reduced the yield of the product **3aa** to 51% (entry 3). In the presence of alternate bases such as KOPiv and K_2CO_3 the reaction yield was reduced to 52% and 48% respectively. Other bases were ineffective for the reaction (entries 5-9). Further, when the reaction was screened with PivOH instead of base the product formation was not observed (entry

10). Various hydride sources such as Et_3SiH, Diphenyl silane and PMHS were also screened for the reaction. In these cases, Et_3SiH gave the corresponding product **3aa** in 32% yield. Other reductants were ineffective for the reaction (entries 11-13). The reaction was also examined with various solvents. Acetonitrile, 1, 4-dioxane and DMSO delivered the product **3aa** in 69%, 38% and 42% respectively. Other solvents such as toluene, DCE and TFE were ineffective for the reaction (entries 14-19). Varying the reaction temperature to 80 ^oC and 45 ^oC reduced the yield of the product to 71% and 64% respectively (entries 20-21). Further, restricting the reaction time to 12 h reduced the yield of the product to 66% (entry 22).

Scheme S2. *β*-selective allylation of amide 1a

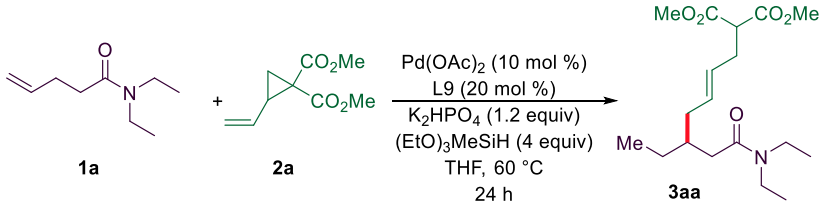


Table S1

Entry	Ligand (mol %)	Base (equiv.)	Additive	Solvent (mL)	Yield (%)
1	-	K_2HPO_4	$(EtO)_2MeSiH$	THF	NR
2	L9	-	$(EtO)_2MeSiH$	THF	NR
3	L9	K_2HPO_4 (50 mol %)	$(EtO)_2MeSiH$	THF	51
4	**L9**	**K_2HPO_4**	$(EtO)_2MeSiH$	**THF**	**79**
5	L9	KOPiv	$(EtO)_2MeSiH$	THF	52
6	L9	CsOAc	$(EtO)_2MeSiH$	THF	NR
7	L9	K_2CO_3	$(EtO)_2MeSiH$	THF	48
8	L9	NaOAc	$(EtO)_2MeSiH$	THF	NR
9	L9	$LiOAc{\cdot}2H_2O$	$(EtO)_2MeSiH$	THF	NR
10	L9	PivOH	$(EtO)_2MeSiH$	THF	NR
11	L9	K_2HPO_4	Et_3SiH	THF	32
12	L9	K_2HPO_4	Diphenyl silane	THF	NR
13	L9	K_2HPO_4	PMHS	THF	NR
14	L9	K_2HPO_4	$(EtO)_2MeSiH$	Acetonitrile	69

15	L9	K_2HPO_4	$(EtO)_2MeSiH$	Toluene	NR
16	L9	K_2HPO_4	$(EtO)_2MeSiH$	TFE	trace
17	L9	K_2HPO_4	$(EtO)_2MeSiH$	Dioxane	38
18	L9	K_2HPO_4	Et_3SiH	DCE	NR
19	L9	K_2HPO_4	$(EtO)_2MeSiH$	DMSO	42
20[a]	L9	K_2HPO_4	$(EtO)_2MeSiH$	THF	71
21[b]	L9	K_2HPO_4	$(EtO)_2MeSiH$	THF	64
22[c]	L9	K_2HPO_4	$(EtO)_2MeSiH$	THF	66

[a]reaction was carried out at 80 ^oC, [b]reaction was carried out at 45 ^oC, [c]reaction time was restricted to 12 h.

2. General Procedure for the synthesis of Vinyl Cyclopropanes:

The VCPs were prepared according to the reported literature procedures.[2] To a mixture of NaH (20 mmol) and THF (40 mL) was added corresponding malonate (10 mmol) dropwise under ice bath. After 1 hour, a solution of dibromo-2-butene (10 mmol) in THF (40 mL) was added slowly over 1 hour. Then the reaction was warmed to room temperature. After the reaction was complete (monitored by TLC), it was quenched with water. The mixture was extracted with EtOAc (50 mL x 3). The organic layer was washed with brine, dried over Na2SO4, filtered and concentrated by rotary evaporation. Then the residue was purified by silica gel column chromatography (PE/EtOAc = 20/1) to afford the desired product **2**.

3. General Procedure for synthetic transformations:

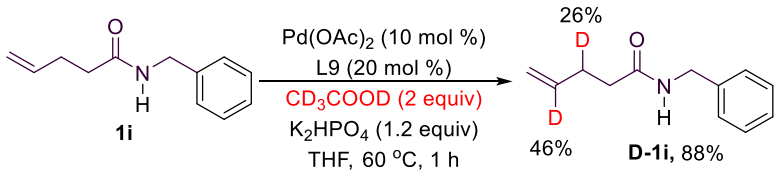
(a) General procedure for synthesis of 4: To a solution of **3ha** (0.25 mmol) in THF (0.4 mL), NaH (1.5 equiv.) was added portion wise at 0 ^oC. This solution was allowed to stir for 30 minutes and allyl bromide (1.5 equiv.) was added to the solution dropwise. The reaction mixture was allowed to stir under rt for next 12 h. The progress of the reaction was monitored by the TLC analysis. After completion of the reaction, the mixture was filtered through the celite and washed with ethyl acetate. The organic layer was extracted with ethyl acetate, concentrated under reduced pressure and subjected to column chromatographic purification, gave pure product **4** as yellow liquid in 40% yield.

(b) General procedure for synthesis of 5[6]: A 10 mL Schlenk tube equipped with a stir bar was evacuated and filled with argon. **3ea** (1.00 equiv) was dissolved in CH_3OH. NaOH (5 equiv) was

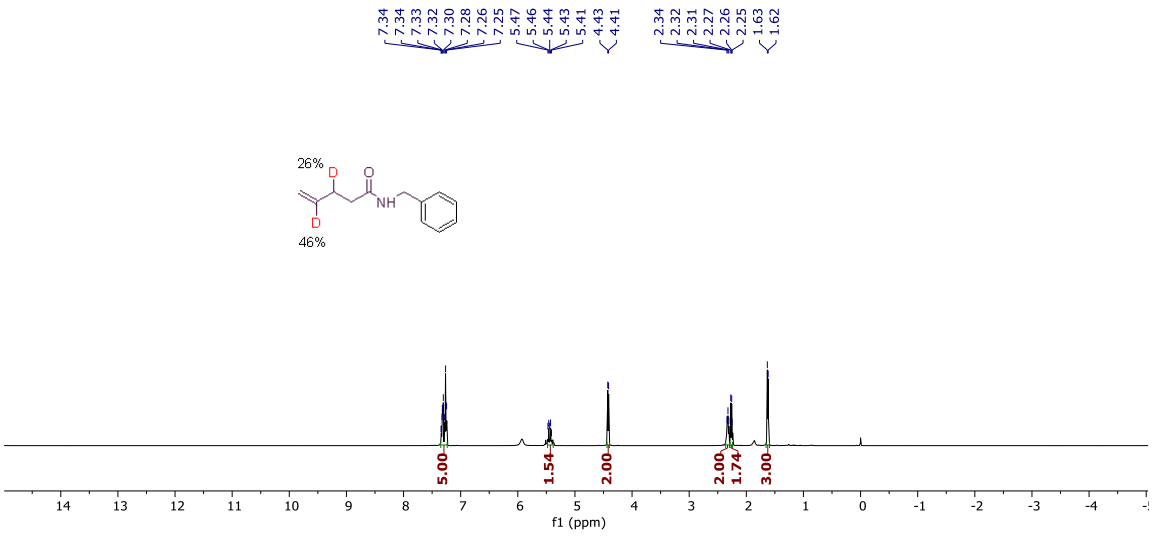
added to the reaction mixture. The reaction mixture was refluxed at 75 ^{o}C for 8 h. The resulting mixture was diluted with DI water and then extracted with EtOAc. The combined organic layers were dried (anhyd. Na_2SO_4) and concentrated under reduced pressure to afford **5**.

3. Mechanistic investigation

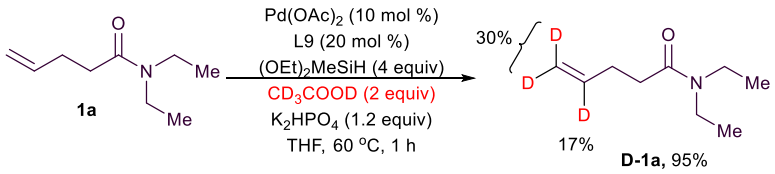
a) Deuterium labeling studies for *β*-selective allylation in absence of hydride source.



A 15ml Schlenk tube with septum containing $Pd(OAc)_2$ (10 mol %), **L9** (20 mol %) and K_2HPO_4 (1.2 equiv) were evacuated and purged with nitrogen gas three times. Amide **1i** (20 mg,) was dissolved in THF (1.0 mL each) and was added to the Schlenk tube *via* syringe. Then, CD_3COOD (2 equiv.) was added to the reaction mixture. The tube was sealed using screw cap and the reaction mixture was allowed to stir at 60 °C for 1 h in an oil bath. After cooling to the ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and the filtrate was concentrated to produce **D-1i** in 88% yield. 26% deuterium incorporation was obtained at allylic carbon and 46% deuterium incorporation was observed at the terminal carbon of alkene.

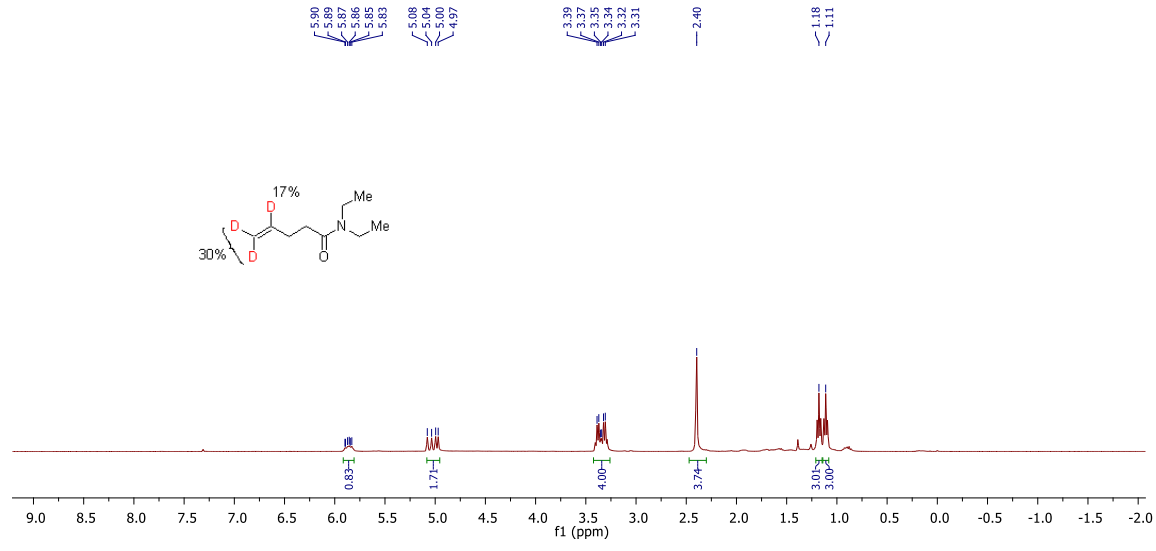


b) Deuterium labeling studies for *β*-selective allylation in presence of hydride source.

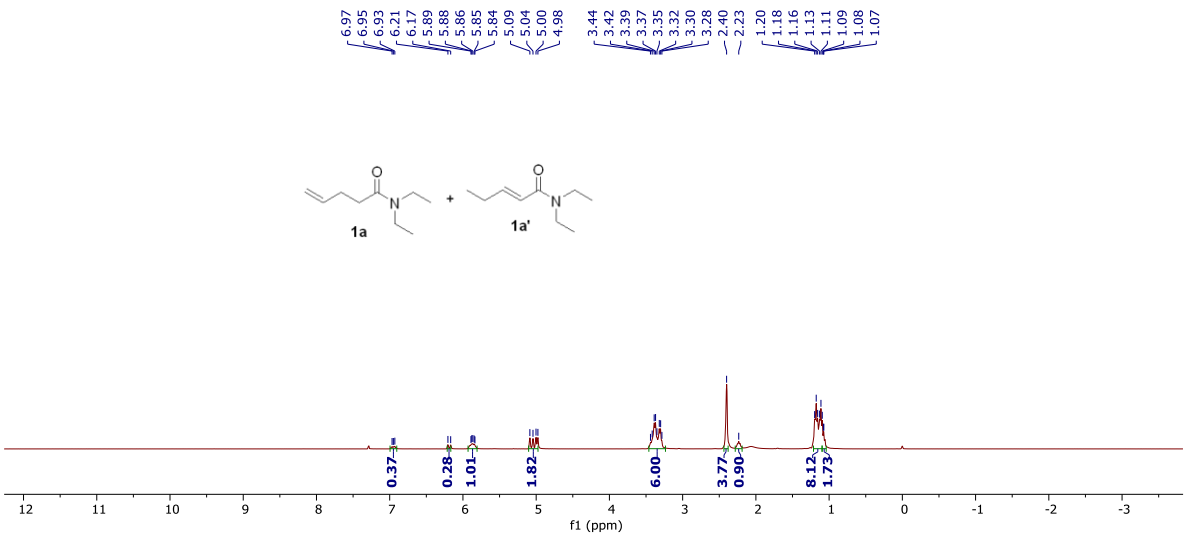


A 15ml Schlenk tube with septum containing $Pd(OAc)_2$ (10 mol %), **L9** (20 mol %) and K_2HPO_4 (1.2 equiv) were evacuated and purged with nitrogen gas three times. Amide **1a** (20 mg,) was dissolved in THF (1.0 mL each) and was added to the Schlenk tube *via* syringe. $(OEt)_2MeSiH$ (4.0 equiv) was then added dropwise to the reaction mixture. Further, CD_3COOD (2.0 equiv) was added to the reaction mixture. The tube was sealed using screw cap and the reaction mixture was allowed to stir at 60 °C for 1 h in an oil bath. After cooling to the ambient temperature, the reaction mixture was diluted with CH_2Cl_2, filtered through Celite and the filtrate was concentrated to produce **D-1a** in 95% yield. 17% deuterium incorporation was obtained at γ position and 30% deuterium incorporation was observed at the terminal carbon of alkene. Further, H/D exchange between CD_3COOD and Si–H was confirmed by HRMS. The mass corresponding to $(OEt)_2MeSiD$ was detected in the HRMS.

$(OEt)_2MeSiD$: **HRMS (ESI-TOF) m/z:** $[M + K]^+$ Calcd for $C_5H_{13}DKO_2Si$ 174.0463 ; Found 174.0480.



c) Alkene Isomerization



Reference:

1. T. Itoh, T. Matsueda, Y. Shimizu, M. Kanai, *Chem. Eur. J*., **2015**, *21*, 15955–15959.
2. H. Li, Y. Liu, S. Chiba, *Chem. Commun*., **2021**, *57*, 6264-626.
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4. G. Naturale, M. Lamblin, C Commandeur, F. X Felpin, J. Dessolin, *Eur. J. Org. Chem.* .**2012**, 5774–5788.
5. A. J. Young, M. C. White, *J. Am. Chem. Soc.* **2008**, *43*, 14090–14091.
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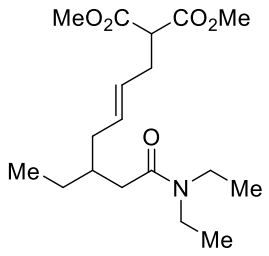
Spectral Data of Compounds

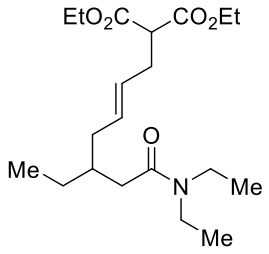
Dimethyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3aa):



Prepared according to general procedure **1**; yellow oil; eluent (18% ethyl acetate:hexane); yield is 79%.

^{1}H NMR (400 MHz, $CDCl_3$): 6.99 – 6.82 (m, 1H), 6.14 (dd, J = 14.8, 2.8 Hz, 1H), 5.80 – 5.64 (m, 1H), 4.98 (m, 2H), 3.69 (s, 6H), 3.35 (m, 6.9 Hz, 4H), 2.18 (m, J = 7.5 Hz, 2H), 2.05 (m, 2H), 1.96 (d, J = 7.7 Hz, 3H), 1.12 (m, 6H), 1.09 – 0.75 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.8, 166.1, 147.6, 136.7, 119.4, 77.4, 77.1, 76.8, 52.5, 50.8, 42.1, 40.8, 31.2, 27.9, 25.5, 14.8, 13.1, 12.7.**HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{18}H_{32}NO_5$ 342.2280 ; Found 342.2294.

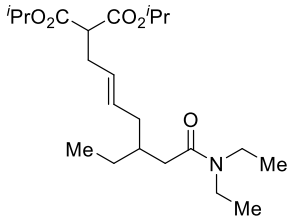
Diethyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ab):



Prepared according to general procedure **1**; yellow oil; eluent (18% ethyl acetate:hexane); yield is 78%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (m, J = 14.9, 1H), 6.19 (dd, J = 14.8, 1H), 5.77 (m, 1H), 5.01 (m, 1H), 4.27 – 3.95 (m, 4H), 3.51 – 3.36 (m, 5H), 3.36 (m, 2H), 2.24 (m, J = 7.4 Hz, 2H), 2.10 (t, J = 7.4 Hz, 2H), 2.05 – 1.92 (m, 1H), 1.27 (m, 6H), 1.23 – 1.13 (m, 6H), 1.10 – 1.01 (t, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.5, 166.1, 147.6, 136.9, 119.5, 116.0, 77.4, 77.3, 76.7, 61.3, 51.2, 42.1, 40.8, 31.3, 27.8, 25.6, 14.8, 14.1, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{20}H_{36}NO_5$ 370.2593; Found 370.2599

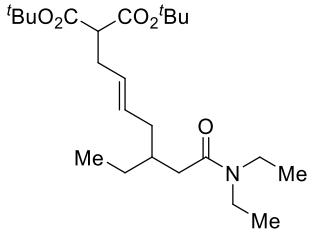
Diisopropyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ac):



Prepared according to general procedure **1**; yellow oil; eluent (19% ethyl acetate:hexane); yield is 71%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 – 6.91 (m, 1H), 5.88 – 5.71 (dd, 1H), 5.05 (m, 3H), 4.97 (m, J = 18.2 Hz, 1H), 3.41 (m, 4H), 3.34 – 3.20 (m, 1H), 2.24 (m, 2H), 2.09 (m, J = 7.5 Hz, 2H), 1.97 (m, 3H), 1.25 (t, J = 6.5 Hz, 12H), 1.18 (d, J = 21.9 Hz, 6H), 1.13 – 1.01 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 171.0, 169.0, 166.1, 147.6, 137.7, 119.5, 115.9, 77.4, 76.8, 68.7, 56.9, 51.5, 42.1, 40.8, 31.4, 31.3, 28.3, 27.7, 25.6, 21.6,14.8, 13.1, 12.7. **HRMS (ESI-TOF) m/z:** [M + H]$^+$ Calcd for $C_{22}H_{40}NO_5$ 398.2906; Found 398.2918.

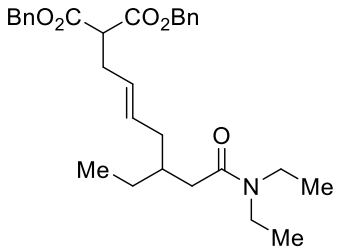
Di-*tert*-butyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ad):



Prepared according to general procedure **1**; yellow oil; eluent (18% ethyl acetate: hexane); yield is 74%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.06 – 6.80 (m, 1H), 5.88 – 5.60 (m, 1H), 5.25 – 4.65 (m, 2H), 3.65 – 3.30 (m, 4H), 3.14 (t, J = 9.7 Hz, 1H), 2.41 – 1.78 (m, 4H), 1.89 (m, 3H), 1.44 (s, J = 3.8 Hz, 18H), 1.15 (m, J = 21.5 Hz, 6H), 1.09 – 0.94 (m, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 13C NMR (101 MHz, CDCl3) δ 170.8, 168.9, 166.1, 147.6, 137.9, 119.5, 115.7, 114.8, 81.3, 77.4, 76.7, 57.9, 53.1, 44.4, 42.2, 40.8, 31.3, 28.3, 27.9, 27.8, 25.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** [M + H]$^+$ Calcd for $C_{24}H_{44}NO_5$ 426.3219; Found 426.3211.

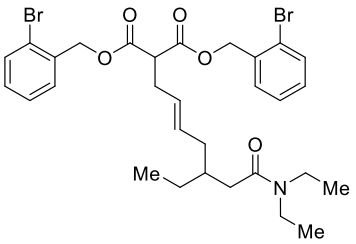
Dibenzyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ae):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate: hexane); yield is 68%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 – 6.90 (m, 10H), 7.01 – 6.64 (m, 1H), 6.18 (m, J = 15.0 Hz, 1H), 5.79 – 5.53 (m, 1H), 5.15 (m, J = 3.0 Hz, 4H), 4.98 (m, J = 14.6 Hz, 2H), 3.42 (m, J = 22.6, 15.8, 7.5 Hz, 5H), 2.23 (m, 2H), 2.05 (m, 4H), 1.32 – 0.97 (m, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.1, 166.1, 147.6, 136.7, 135.4, 128.6, 128.3, 128.2, 119.5, 116.1, 77.4, 77.1, 77.0, 76.8, 67.1, 60.4, 51.2, 42.2, 40.8, 31.2, 27.9, 25.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** [M + H]$^+$ Calcd for $C_{30}H_{40}NO_5$ 494.2906; Found 494.2901.

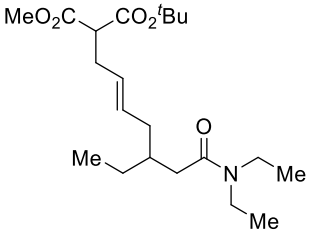
Bis(2-bromobenzyl) (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3af):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate: hexane); yield is 58%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.00 – 6.90 (m, 8H), 7.01 – 6.64 (m, 1H), 6.18 (d, J = 15.0 Hz, 1H), 5.79 – 5.53 (m, 1H), 5.15 (m, 4H), 4.98 (m, 2H), 3.42 (m, 5H), 2.23 (t, J = 7.6 Hz, 2H), 2.05 (m, J = 9.4, 4.7 Hz, 3H), 1.32 – 0.97 (m, 9H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.11, 166.07, 147.57, 136.72, 135.37, 128.57, 128.35, 128.18, 119.52, 116.13, 77.41, 77.09, 77.05, 76.77, 67.10, 60.43, 51.16, 42.15, 40.81, 31.23, 27.86, 25.60, 14.84, 13.19, 12.72. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{30}H_{38}Br_2NO_5$ 650.1117; Found 650.1124.

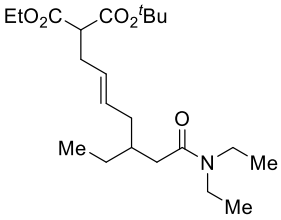
1-(*Tert*-butyl) 3-methyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ag):



Prepared according to general procedure **1**; yellow oil; eluent (20% ethyl acetate:hexane); yield is 71%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.10 – 6.83 (m, 1H), 6.18 (m, J = 15.0 Hz, 1H), 5.77 (m, J = 9.1 Hz, 1H), 5.03 (m, 2H), 3.73 (m, J = 4.3 Hz, 3H), 3.48 – 3.32 (m, 4H), 3.43 – 3.09 (m, 1H), 2.22 (m, J = 7.6 Hz, 4H), 2.07 (m, 2H), 1.58 – 1.41 (m, 9H), 1.17 (m, J = 21.3 Hz, 6H), 1.07 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 170.3, 168.5, 166.1, 147.6, 137.7, 137.1, 119.5, 115.9, 114.9, 81.8, 52.3, 52.0, 42.1, 40.8, 31.5, 31.3, 28.4, 27.9, 27.9, 25.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{21}H_{38}NO_5$ 384.2750; Found 384.2744.

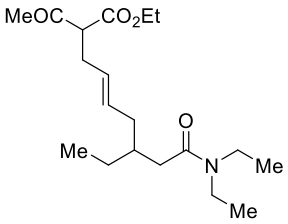
1-(*Tert*-butyl) 3-ethyl (*E*)-2-(7-(diethylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (**3ah**):



Prepared according to general procedure **1.** yellow oil; eluent (20% ethyl acetate:hexane); yield is 70%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 – 6.86 (m, 1H), 5.85 – 5.70 (m, 1H), 5.03 (m, J = 14.1 Hz, 2H), 4.19 (m, 2H), 3.40 (m, 4H), 3.26 (m, 1H), 2.23 (m, J = 7.5 Hz, 2H), 2.11 (m, 2H), 1.95 (d, J = 6.7 Hz, 3H), 1.46 (d, J = 2.8 Hz, 9H), 1.36 – 1.26 (m, 3H), 1.17 (d, 6H), 1.13 – 0.96 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 171.8, 170.5, 169.8, 168.6, 147.6, 137.7, 119.5, 115.8, 114.9, 81.7, 81.4, 77.4, 77.1, 61.1, 57.5, 52.2, 40.8, 31.4, 28.3, 27.8, 25.6, 14.8, 14.1, 13.1, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{22}H_{40}NO_5$ 398.2906; Found 398.2911.

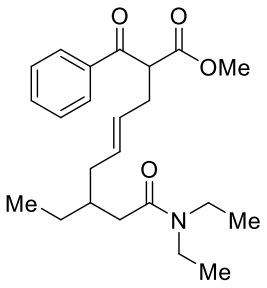
Ethyl (*E*)-2-acetyl-9-(diethylamino)-7-ethyl-9-oxonon-4-enoate (3ai):



Prepared according to general procedure **1** yellow oil; eluent (15% ethyl acetate: hexane); yield is 54%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (m, J = 14.9, 6.9 Hz, 1H), 6.19 (m, J = 15.0 Hz, 1H), 5.91 – 5.74 (m, 1H), 5.11 – 4.72 (m, 2H), 4.20 (m, J = 7.5 Hz, 2H), 4.11 (m, 1H), 3.41 (m, 4H), 2.24 (d, J = 2.8 Hz, 3H), 2.10 – 2.01 (m, 4H), 2.03 – 1.89 (m, 2H), 1.28 (t, J = 7.1 Hz, 3H), 1.17 (d, J = 21.6 Hz, 6H), 1.14 – 0.89 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)** δ 203.1, 169.7, 166.1, 147.5, 137.5, 137.0, 119.5, 116.0, 61.4, 58.8, 42.2, 40.8, 31.4, 29.0, 27.1, 25.6, 14.8, 14.1, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ Calcd for $C_{19}H_{33}NNaO_4$ 362.2307; Found 362.2318.

Methyl (*E*)-2-benzoyl-9-(diethylamino)-7-ethyl-9-oxonon-4-enoate (3aj):

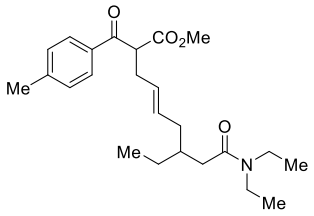


Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate:hexane); yield is 46%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (m, J = 7.8 Hz, 2H), 7.78 (m, J = 7.5 Hz, 1H), 7.61 (m, 1H), 7.49 (m, 3H), 7.17 – 6.71 (m, 1H), 6.19 (d, J = 15.1 Hz, 1H), 3.76 (m, J = 2.6 Hz, 3H), 3.40 (m,4H), 2.46 – 2.07 (m, 4H), 1.17 (m, J = 21.1 Hz, 10H), 1.20 – 0.92 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: 192.4, 168.0, 166.1, 147.6, 133.8, 128.8, 128.5, 119.5, 52.5, 45.7, 42.1, 40.8,

25.5, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{23}H_{34}NO_4$ 388.2488; Found 388.2496.

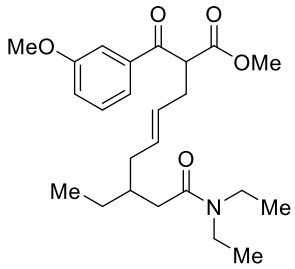
Methyl (*E*)-9-(diethylamino)-7-ethyl-2-(4-methylbenzoyl)-9-oxonon-4-enoate (3ak):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate:hexane); yield is 41%.

^{1}H NMR (400 MHz, $CDCl_3$): 7.88 (m, J = 7.7 Hz, 2H), 7.53 – 7.03 (m, 2H), 7.06 – 6.81 (m, 1H), 6.19 (d, J = 15.0 Hz, 1H), 5.95 – 5.69 (m, 1H), 5.01 (m, 2H), 4.36 (m, 1H), 3.68 (m, J = 3.1 Hz, 3H), 3.40 (m, J = 21.4, 7.3 Hz, 4H), 2.42 (s, 3H), 2.08 (m, J = 27.4 Hz, 4H), 1.26 – 0.76 (m, 10H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 194.7, 170.5, 166.1, 147.5, 144.6, 137.1, 129.3, 128.8, 119.5, 116.1, 77.4, 76.7, 52.8, 52.5, 42.2, 40.8, 31.5, 28.1, 25.6, 21.7, 14.8, 14.2, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{24}H_{36}NO_4$ 402.2644; Found 402.2641.

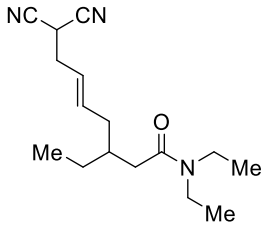
Methyl (*E*)-9-(diethylamino)-7-ethyl-2-(3-methoxybenzoyl)-9-oxonon-4-enoate (3al):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate:hexane); yield is 38%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.64 – 7.43 (m, 4H), 7.46 – 7.22 (m, 1H), 7.15 (m 1H), 6.95 (m, J = 14.6, 4.0 Hz, 1H), 6.19 (d, J = 14.6 Hz, 1H), 3.86 (m, 3H), 3.76 (s, 3H), 3.40 (m, 4H), 2.23 (m, 4H), 1.32 – 1.12 (m, 10H), 1.08 (t, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 192.3, 168.0, 166.1, 159.9, 147.6, 137.2, 129.8, 129.6, 121.2, 120.4, 119.5, 118.5, 117.3, 112.5, 111.2, 55.5, 52.5, 51.5, 45.8, 42.1, 40.8, 25.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{24}H_{36}NO_5$ 418.2593; Found 418.2581

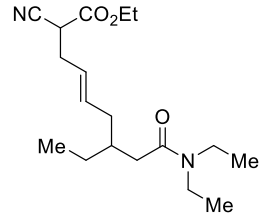
(*E*)-8,8-Dicyano-*N*, *N*,3-triethyloct-5-enamide (3am):



Prepared according to general procedure **1**; yellow oil; eluent (25% ethyl acetate:hexane); yield is 64%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.92 (m, J = 14.8, 5.8 Hz, 1H), 6.16 (d, J = 15.1 Hz, 1H), 5.87 – 5.57 (m, 1H), 5.28 – 5.11 (m, 2H), 3.78 (s, 1H), 3.57 – 3.31 (m, 4H), 2.38 (q, J = 7.7, 7.2 Hz, 2H), 2.33 – 2.01 (m, 4H), 1.27 – 0.87 (m, 9H).**^{13}C NMR (101 MHz, $CDCl_3$):** δ 166.1, 147.6, 133.8, 119.5, 118.8, 112.5, 77.4, 77.1, 42.2, 30.3, 29.9, 25.6, 21.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ Calcd for $C_{16}H_{25}N_3NaO$ 298.1895; Found 298.1889.

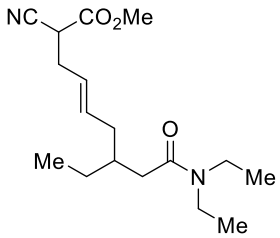
Ethyl (*E*)-2-cyano-9-(diethylamino)-7-ethyl-9-oxonon-4-enoate (3an):



Prepared according to general procedure **1**; yellow oil; eluent (10% ethyl acetate:hexane); yield is 78%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.03 – 6.71 (m, 1H), 6.12 (m, J = 15.1 Hz, 1H), 5.68 (m, J = 10.4, 5.2 Hz, 1H), 5.05 (m, 4H), 4.20 (dd, J = 7.5, 2.7 Hz, 4H), 3.45 (d, J = 7.4 Hz, 2H), 3.42 – 3.16 (m, 4H), 2.20 (m, J = 21.9, 7.2 Hz, 3H), 1.99 (d, J = 7.7 Hz, 2H), 1.28 – 1.09 (m, 7H), 1.08 – 0.86 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 166.1, 166.1, 147.6, 135.3, 119.5, 116.4, 76.7, 62.8, 42.1, 36.7, 30.6, 29.7, 28.9, 25.6, 21.1, 14.8, 14.2, 14.0, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ Calcd for $C_{18}H_{31}N_2O_3$ 323.2335; Found 323.2348.

Methyl (*E*)-2-cyano-9-(diethylamino)-7-ethyl-9-oxonon-4-enoate (3ao):

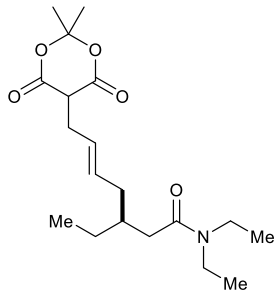


Prepared according to general procedure **1**; yellow oil; eluent (20% ethyl acetate: hexane); yield is 76%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.01 – 6.71 (m, 1H), 6.11 (m, J = 15.0 Hz, 1H), 5.78 – 5.59 (m, 1H), 5.12 – 4.98 (m, 2H), 3.75 (m, J = 2.8 Hz, 3H), 3.47 (m, 1H), 3.40 – 3.25 (m, 4H), 2.20 (m, J

= 22.3, 7.2 Hz, 4H), 1.99 (q, J = 5.6, 3.2 Hz, 2H), 1.10 (m, J = 21.8, 7.4 Hz, 6H), 1.03 – 0.97 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 166.61, 166.1, 147.6, 135.3, 119.5, 117.4, 77.4, 77.1, 76.7, 13.2, 12.7. **HRMS (ESI-TOF) m/z**: $[M + H]^+$ Calcd for $C_{17}H_{29}N_2O_3$ 309.2178; Found 309.2184.

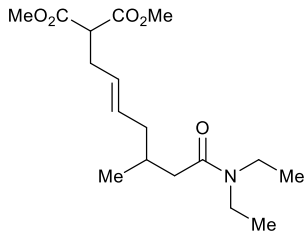
(*E*)-7-(2,2-dimethyl-4,6-dioxo-1,3-dioxan-5-yl)-*N*,*N*,3-triethylhept-5-enamide (3ap):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate: hexane); yield is 26%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.04 – 6.85 (m, 1H), 6.18 (m, 2H), 5.79 (m, *J* = 16.9, 10.1, 6.7 Hz, 1H), 5.07 (t, *J* = 13.8 Hz, 2H), 3.54 (t, 1H), 3.48 – 3.24 (m, 4H), 2.29 (m, 2H), 2.24 (dd, 4H), 1.77 (s, 3H), 1.76 (s, 3H), 1.19 (m, 2H), 1.15 (m, 3H), 1.07 (t, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 166.3, 166.1, 165.5, 155.0, 147.8, 136.7, 119.4, 116.6, 104.9, 77.3, 77.0, 76.7, 44.9, 42.2, 40.9, 30.6, 28.5, 26.7, 25.6, 25.4, 14.7, 13.1, 12.6. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{19}H_{32}NO_5$ 354.2280; Found 354.2270.

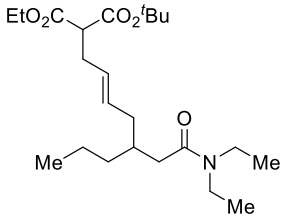
Dimethyl (*E*)-2-(7-(diethylamino)-5-methyl-7-oxohept-2-en-1-yl)malonate (3ba):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate: hexane); yield is 78%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21 – 7.08 (m, 1H), 5.90 (dd, J = 14.7, 6.2 Hz, 1H), 5.76 (m, J = 16.9, 2H), 5.01 (d, 1H), 3.74 (s, 6H), 3.39 (m, J = 14.5, 7.2 Hz, 4H), 3.07 (t, 1H), 2.10 (m, 2H), 2.02 (t, J = 7.2 Hz, 3H), 1.96 (t, 3H), 1.89 (t, J = 7.2 Hz, 1H), 1.83 – 1.76 (m, 1H), 1.15 (m, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.8, 150.6, 149.3, 148.4, 141.2, 136.8, 122.0, 116.0, 52.5, 50.8, 46.6 41.8, 31.3, 27.9, 25.9, 18.1.**HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{17}H_{30}NO_5$ 328.2124; Found 328.2112.

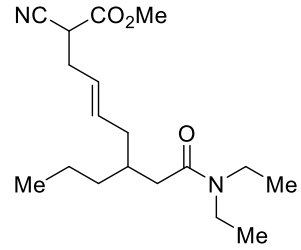
1-(*Tert*-butyl) 3-ethyl (*E*)-2-(5-(2-(diethylamino)-2-oxoethyl)oct-2-en-1-yl)malonate (3ch):



Prepared according to general procedure **1.** yellow oil; eluent (20% ethyl acetate:hexane); yield is 66%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.08 – 6.86 (m, 1H), 5.85 – 5.70 (m, 2H), 5.03 (m, J = 14.1 Hz, 2H), 4.19 (m, 2H), 3.40 (m, 4H), 3.26 (m, 1H), 2.23 (m, J = 7.5 Hz, 3H), 2.11 (m, 2H), 1.95 (d, J = 6.7 Hz, 3H), 1.46 (d, J = 2.8 Hz, 9H), 1.36 – 1.26 (m, 3H), 1.17 (d, 6H), 1.13 – 0.96 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 171.8, 170.5, 169.8, 168.6, 147.6, 137.7, 119.5, 115.8, 114.9, 81.7, 81.4, 77.4, 77.1, 61.1, 57.5, 52.2, 40.8, 31.4, 28.3, 27.8, 25.6, 14.8, 14.1, 13.1, 12.7. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{23}H_{42}NO_5$ 412.3063; Found 412.3060.

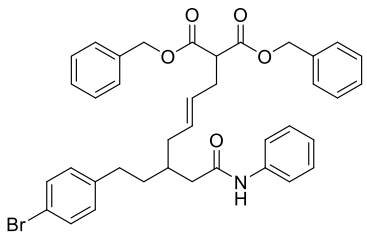
Ethyl (*E*)-2-cyano-7-(2-(diethylamino)-2-oxoethyl)dec-4-enoate (3co):



Prepared according to general procedure **1**; yellow oil; eluent (10% ethyl acetate:hexane); yield is 62%.

^{1}H NMR (400 MHz, $CDCl_3$): **^{1}H NMR (400 MHz, $CDCl_3$)**: δ 7.03 – 6.71 (m, 1H), 6.12 (m, J = 15.1 Hz, 1H), 5.68 (m, J = 10.4, 5.2 Hz, 1H), 5.05 (m, 4H), 4.20 (dd, J = 7.5, 2.7 Hz, 4H), 3.45 (d, J = 7.4 Hz, 2H), 3.42 – 3.16 (m, 4H), 2.20 (m, J = 21.9, 7.2 Hz, 3H), 1.99 (d, J = 7.7 Hz, 2H), 1.28 – 1.09 (m, 7H), 1.08 – 0.86 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 166.1, 166.1, 147.6, 135.3, 119.5, 116.4, 76.7, 62.8, 42.1, 36.7, 30.6, 29.7, 28.9, 25.6, 21.1, 14.8, 14.2, 14.0, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ Calcd for $C_{18}H_{30}N_2NaO_3$ 345.2154; Found 345.2168.

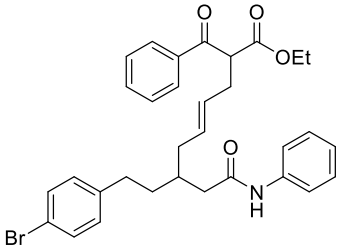
Dibenzyl (*E*)-2-(5-(4-bromophenethyl)-7-oxo-7-(phenylamino)hept-2-en-1-yl)malonate (3de):



Prepared according to general procedure **1**; yellow oil; eluent (20% ethyl acetate: hexane); yield is 58%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.14 (d, J = 8.3 Hz, 1H), 7.54 – 7.28 (m, 4H), 7.24 (m, 14H), 5.76 – 5.61 (m, 1H), 5.14 (s, 4H), 4.96 (m, 2H), 3.48 (m, 1H), 2.76 (m, 2H), 2.57 (m, 2H), 2.55 – 1.46 (m, 7H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 171.5, 169.1, 148.1, 141.5, 138.4, 136.7, 136.4, 135.4, 134.5, 128.6, 128.6, 128.5, 128.4, 128.2, 128.0, 127.5, 126.0, 121.6, 121.5, 116.5, 116.2, 77.4, 77.1, 76.8, 67.1, 51.2, 37.3, 35.2, 31.3, 27.9, 27.1. **HRMS (ESI-TOF) m/z**: [M + H]+ Calcd for $C_{39}H_{39}BrNO_5$ 668.2012; Found 668.2001.

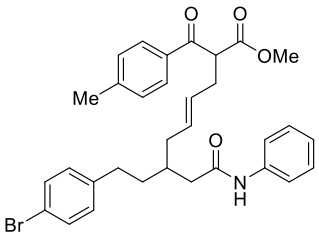
Ethyl (*E*)-2-benzoyl-7-(4-bromophenethyl)-9-oxo-9-(phenylamino)non-4-enoate (3dp):



Prepared according to general procedure **1**; yellow oil; eluent (20% ethyl acetate: hexane); yield is 36%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.15 (m, J = 8.3 Hz, 1H), 7.63 – 7.27 (m, 5H), 7.25 (m, J = 15.7, 8H), 5.88 – 5.47 (m, 1H), 5.35 – 4.57 (m, 1H), 4.26 (m, 2H), 3.51 (t, 1H), 2.77 (m, J = 7.9 Hz, 2H), 2.57 (m, 2H), 2.41 – 2.15 (m, 2H), 2.27 – 2.14 (m, 3H), 2.05 (d, 2H), 1.32 (t, 3H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 171.5, 166.1, 148.1, 141.5, 138.3, 136.4, 135.4, 134.5, 128.6, 128.4, 128.0, 127.5, 126.0, 121.6, 121.4, 117.4, 116.5, 62.9, 37.3, 36.7, 35.2, 30.7, 28.9, 27.1, 14.0. **HRMS (ESI-TOF) m/z**: [M + H]+ Calcd for $C_{32}H_{35}BrNO_4$ 576.1749; Found 576.1751.

Methyl (*E*)-7-(4-bromophenethyl)-2-(4-methylbenzoyl)-9-oxo-9-(phenylamino)non-4-enoate (3dk):

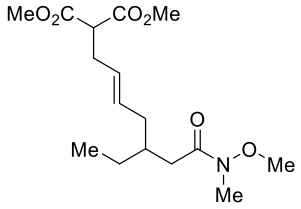


Prepared according to general procedure **1**; yellow oil; eluent (20% ethyl acetate: hexane); yield is 29%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 9.79 (s, 1H), 8.14 (m, J = 8.3 Hz, 1H), 7.88 (m, 1H), 7.60 – 7.36 (m, 4H), 7.24 (m, 7H), 5.96 – 5.60 (m, 1H), 5.21 – 4.74 (m, 1H), 4.36 (m, 1H), 3.67 (s, 3H), 2.77 (m, 2H), 2.57 (t, 2H), 2.40 (s, 3H), 2.41 – 1.91 (m, 7H). **^{13}C NMR (101 MHz, $CDCl_3$)**: δ 194.8,

171.5, 170.5, 148.1, 144.6, 141.5, 138.3, 137.2, 136.4, 134.5, 133.7, 129.5, 128.8, 128.6, 128.5, 128.0, 127.4, 126.0, 121.6, 121.4, 116.5, 116.1, 52.8, 52.5, 37.3, 35.2, 31.5, 28.1, 27.1, 21.7. **HRMS (ESI-TOF) m/z**: $[M + Na]^+$ Calcd for $C_{32}H_{34}BrNNaO_4$ 598.1569; Found 598.1558.

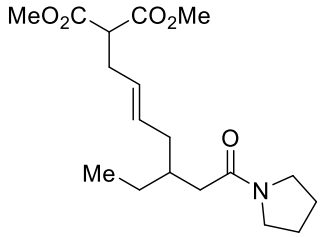
Dimethyl (*E*)-2-(5-ethyl-7-(methoxy(methyl)amino)-7-oxohept-2-en-1-yl)malonate (3ea):



Prepared according to general procedure **1**; yellow oil; eluent (15% ethyl acetate:hexane); yield is 78%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.22 – 6.96 (m, 1H), 5.98 – 5.69 (m, 1H), 5.13 – 4.89 (m, 2H), 3.75 (s, J = 3.2 Hz, 6H), 3.72 (s, J = 10.9 Hz, 3H), 3.45 – 3.34 (m, 2H), 3.25 (m, J = 3.0 Hz, 1H), 2.26 (m, J = 7.5 Hz, 2H), 2.20 – 2.05 (s, 3H), 2.02 (t, J = 7.6 Hz, 2H), 1.09 (t, J = 7.3 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: 169.9, 153.4, 149.5, 136.7, 119.7, 117.6, 116.1, 61.7, 52.5, 50.8, 31.3, 27.9, 25.6, 25.4, 12.5, 12.0. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{16}H_{27}NO_6$ 329.1838; Found 329.1841.

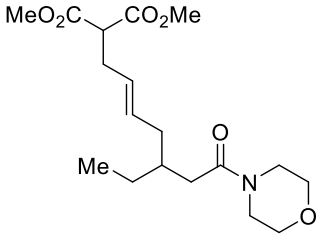
Dimethyl (*E*)-2-(5-ethyl-7-oxo-7-(pyrrolidin-1-yl)hept-2-en-1-yl)malonate (3fa):



Prepared according to general procedure **1**; yellow oil; eluent (25% ethyl acetate: hexane); yield is 66%.

^{1}H NMR (500 MHz, $CDCl_3$): 7.03 – 6.87 (m, 1H), 6.09 (m, J = 15.2 Hz, 1H), 5.75 (m, J = 8.7 Hz, 1H), 5.03 (m, 3H), 3.74 (s, J = 2.7 Hz, 6H), 3.52 (m, 2H), 3.41 (m, J = 2.6 Hz, 3H), 2.18 – 1.71 (m, 9H)1.07 (t, J = 7.7 Hz, 3H).**^{13}C NMR (126 MHz, $CDCl_3$)**: δ 169.8, 147.2, 136.7, 120.7, 116.1, 77.4, 53.9, 50.8, 46.8, 43.9, 32.2, 27.9, 26.1, 25.5, 24.4, 24.3, 12.6, 12.1. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{18}H_{30}NO_5$ 340.2124; Found 340.2119.

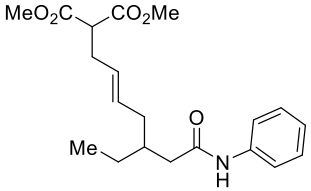
Dimethyl (*E*)-2-(5-ethyl-7-morpholino-7-oxohept-2-en-1-yl)malonate (3ga):



Prepared according to general procedure **1**; yellow oil; eluent (28% ethyl acetate:hexane); yield is 64%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.98 (m, 1H), 5.86 – 5.59 (m, 1H), 5.03 (m, 3H), 3.70 (m, 6H), 3.57 (m, J = 8.5 Hz, 3H), 3.41 (m, 1H), 3.05 (m, J = 16.4, 8.1 Hz, 1H), 2.78 (dt, J = 15.9, 3.7 Hz, 1H). 2.23 (m, 2H), 2.49 – 1.97 (m, 2H), 2.18 – 2.01 (m, 2H), 2.06 – 1.97 (m, 3H), 1.07 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.8, 168.5, 148.6, 136.7, 118.5, 116.1, 77.4, 76.7, 66.8, 53.6, 52.5, 50.8, 46.7, 42.2, 41.7, 32.2, 31.3, 27.9, 12.5, 12.1. $[M + H]^+$ Calcd for $C_{18}H_{30}NO_6$ 356.2073; Found 356.2085.

Dimethyl (*E*)-2-(5-ethyl-7-oxo-7-(phenylamino)hept-2-en-1-yl)malonate (3ha):

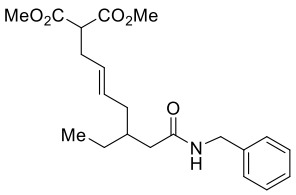


Prepared according to general procedure **1**; yellow oil; eluent (8% ethyl acetate:hexane); yield is 58%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.62 – 7.52 (m, 5H), 7.10 (m, J = 7.5 Hz, 1H), 5.76 (m, 1H), 5.17 – 4.96 (m, 2H), 3.74 (m, J = 3.1 Hz, 6H), 3.41 (m, J = 2.8 Hz, 1H), 2.30 – 2.03 (m, 2H), 2.02 (m, 2H), 1.98 (m, 3H), 1.08 (t, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.9, 141.3, 136.7, 128.9, 128.6, 124.4, 124.2, 120.0, 119.9 116.1, 77.4, 77.1, 76.8, 52.5, 50.8, 31.3, 27.9, 25.2, 12.4.

HRMS (ESI-TOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{27}NNaO_5$ 384.1787; Found 384.1781.

Dimethyl (*E*)-2-(7-(benzylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ia):

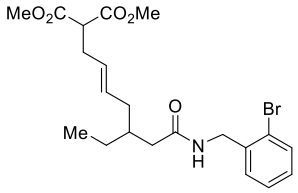


Prepared according to general procedure **1** yellow oil; eluent (16% ethyl acetate:hexane); yield is 50%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, J = 5.8, 4.8 Hz, 5H), 6.88 (s, 1H), 5.94 – 5.58 (m, 1H), 5.14 – 4.91 (m, 2H), 4.53 – 4.34 (d, 2H), 3.72 (s, J = 6.1, 4.3 Hz, 6H), 3.40 (t, J = 2.8 Hz, 1H), 2.20 (m, 2H), 2.08 (m, 2H), 2.00 (m, J = 3.3 Hz, 3H), 1.04 (t, J = 7.5, 6.4, 3.8 Hz, 3H). **^{13}C NMR**

(101 MHz, $CDCl_3$): δ 170.2, 169.9, 166.2, 146.5, 138.4, 128.6, 128.1, 1278.0, 127.4, 126.5, 122.5, 116.1, 77.4, 77.1, 76.8, 52.5, 50.8, 43.5, 31.3, 27.9, 25.1, 23.2, 12.4. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{21}H_{29}NNaO_5$ 398.1943; Found 398.1945.

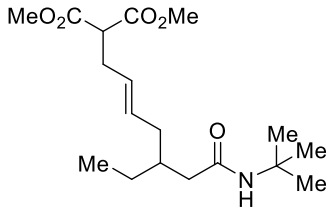
Dimethyl (*E*)-2-(7-((2-bromobenzyl)amino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ja):



Prepared according to general procedure **1** yellow oil; eluent (20% Ethylacetate: hexane yield is 38%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.28 (m, J = 5.8, 4.8 Hz, 5H), 6.88 (s, 1H), 5.94 – 5.58 (m, 1H), 5.14 – 4.91 (m, 2H), 4.53 – 4.34 (d, 2H), 3.72 (s, J = 6.1, 4.3 Hz, 6H), 3.40 (t, J = 2.8 Hz, 1H), 2.20 (m, 2H), 2.08 (m, 2H), 2.00 (m, J = 3.3 Hz, 3H), 1.04 (t, J = 7.5, 6.4, 3.8 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 170.2, 169.9, 166.2, 146.5, 138.4, 138.3, 136.7, 128.6, 128.1, 127.8, 127.4, 126.5, 122.5, 116.1, 77.4, 77.1, 76.8, 52.5, 50.8, 43.7, 43.5, 31.3, 27.9, 25.1, 23.2, 12.4. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{21}H_{29}BrNO_5$ 454.1229; Found 454.1237.

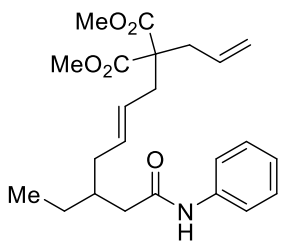
Dimethyl (*E*)-2-(7-(*tert*-butylamino)-5-ethyl-7-oxohept-2-en-1-yl)malonate (3ka)



Prepared according to general procedure **1**; yellow oil; eluent (6% ethyl acetate:hexane); yield is 59%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 – 6.69 (m, 1H), 5.74 (m, J = 22.9, 15.9, 10.7 Hz, 1H), 5.03 (m, J = 11.9 Hz, 2H), 3.74 (s, J = 2.4 Hz, 6H), 3.40 (m, J = 6.8 Hz, 1H), 2.26 – 2.09 (m, 2H), 2.06 (m, J = 26.5 Hz, 2H), 1.91 (m, J = 2.2 Hz, 3H), 1.36 (s, J = 15.9, 2.4 Hz, 9H), 1.05 (t, J = 7.2 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 169.83, 165.55, 145.22, 136.72, 123.74, 116.06, 77.38, 77.06, 76.75, 52.51, 51.16, 50.83, 31.28, 28.84, 28.76, 27.88, 24.95, 24.54, 12.50. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{18}H_{31}NNaO_5$ 364.2100; Found 364.2110.

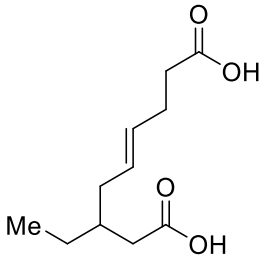
Dimethyl (*E*)-2-allyl-2-(5-ethyl-7-oxo-7-(phenylamino)hept-2-en-1-yl)malonate (4):



Prepared according to general procedure 3; yellow oil; eluent (3% ethyl acetate:hexane); yield is 40%.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.37 – 7.25 (m, 4H), 7.20 (dd, *J* = 16.0, 9.0 Hz, 1H), 6.44 (m, *J* = 15.8 Hz, 1H), 6.01 (m, *J* = 15.8, 9.6 Hz, 1H), 3.74 (s, 3H), 3.65 (s, 3H), 3.46 (d, *J* = 8.8 Hz, 1H), 2.93 (ddd, *J* = 18.8, 9.4, 3.6 Hz, 1H), 1.57 – 1.32 (m, 4H), 0.86 (t, *J* = 6.6 Hz, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 168.8, 168.6, 137.1, 132.5, 129.7, 128.5, 127.4, 126.3, 57.1, 52.4, 52.3, 43.6, 32.8, 31.6, 26.8, 22.5, 14.0. **HRMS (ESI-TOF) m/z:** $[M + H]^+$ Calcd for $C_{23}H_{32}NO_5$ 402.2280; Found 402.2284.

(*E*)-7-Ethylnon-4-enedioic acid (5):

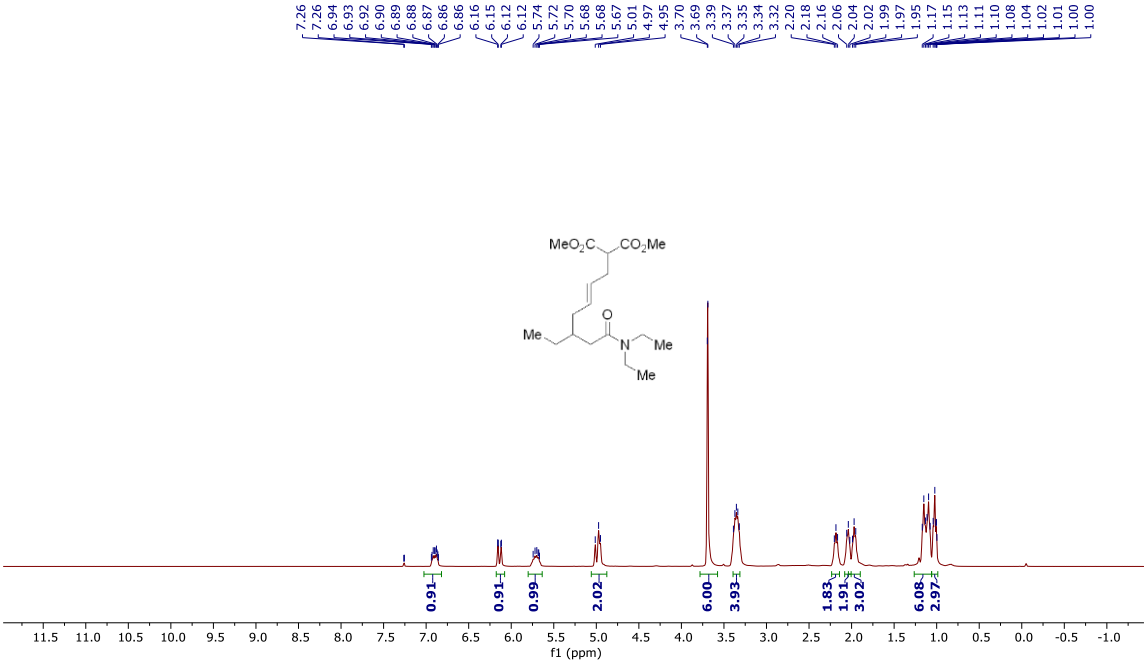


Prepared according to general procedure 3; colorless oil; eluent (30% ethyl acetate:hexane); yield is 60%.

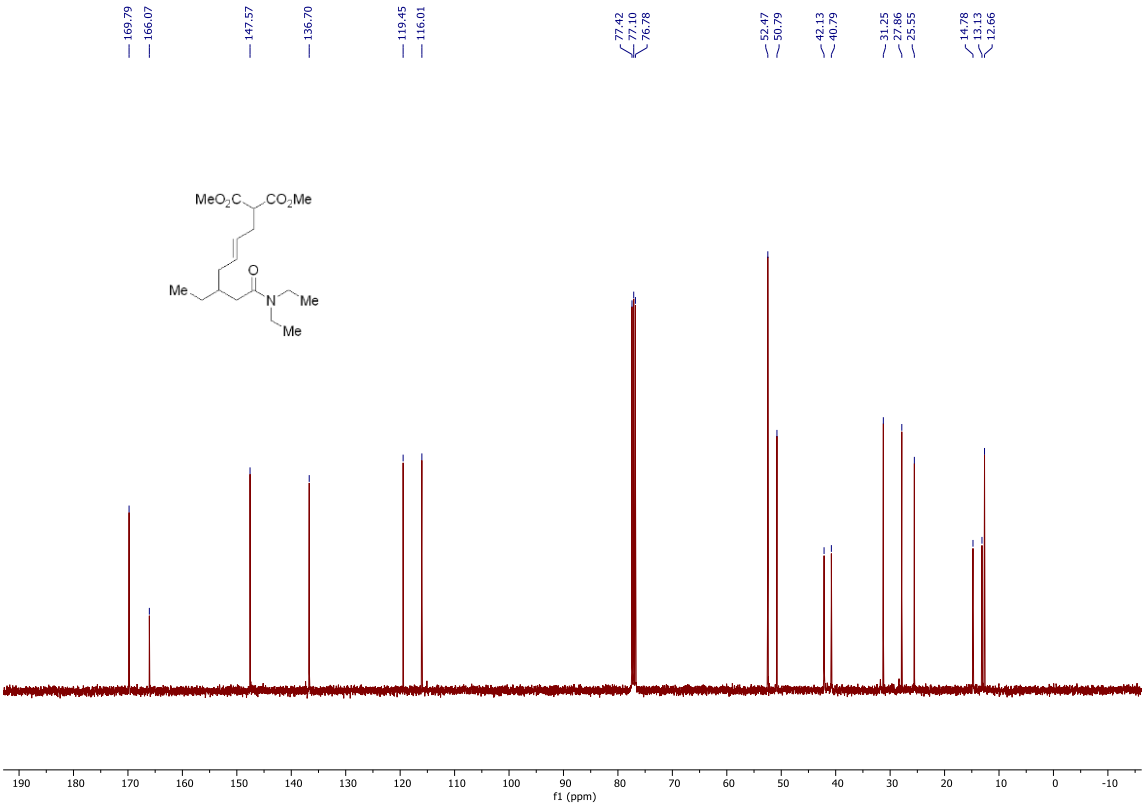
^{1}H NMR (400 MHz, $CDCl_3$): δ 6.95 (m, J = 14.6, 1H), 6.18 (m, J = 15.0 Hz, 1H), 5.93 – 5.70 (m, 1H), 5.21 – 4.99 (m, 2H), 3.40 (m, 5H), 2.62 (d, 2H), 2.23 (t, J = 7.4 Hz, 2H), 1.18 (m, 8H), 1.10 – 0.98 (m, 3H).**^{13}C NMR (101 MHz, $CDCl_3$)**: δ 166.0, 147.6, 135.1, 119.5, 117.5, 42.1, 40.8, 36.9, 32.0, 25.6, 14.8, 13.2, 12.7. **HRMS (ESI-TOF) m/z:** $[M + Na]^+$ Calcd for $C_{11}H_{18}NaO_4$ 237.1103; Found 237.1119.

Copies of ^{1}H and ^{13}C of the compounds:

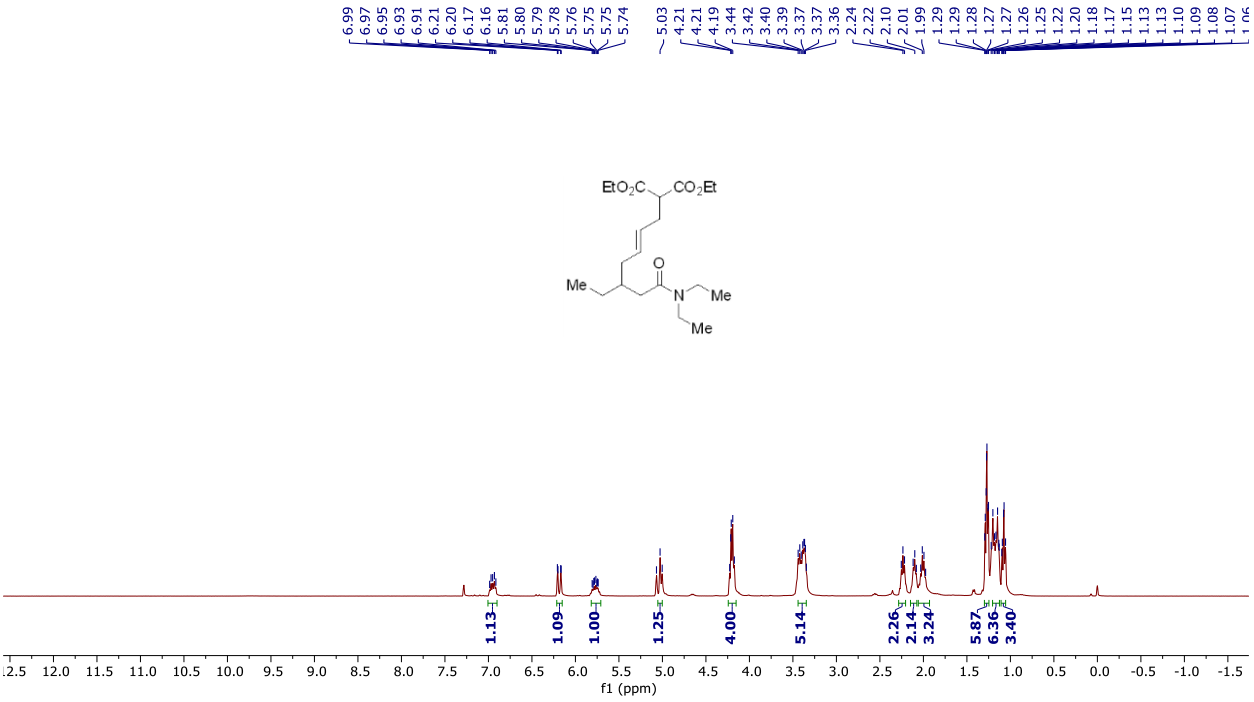
^{1}H NMR of compound **3aa** in $CDCl_3$ at 400 MHz:



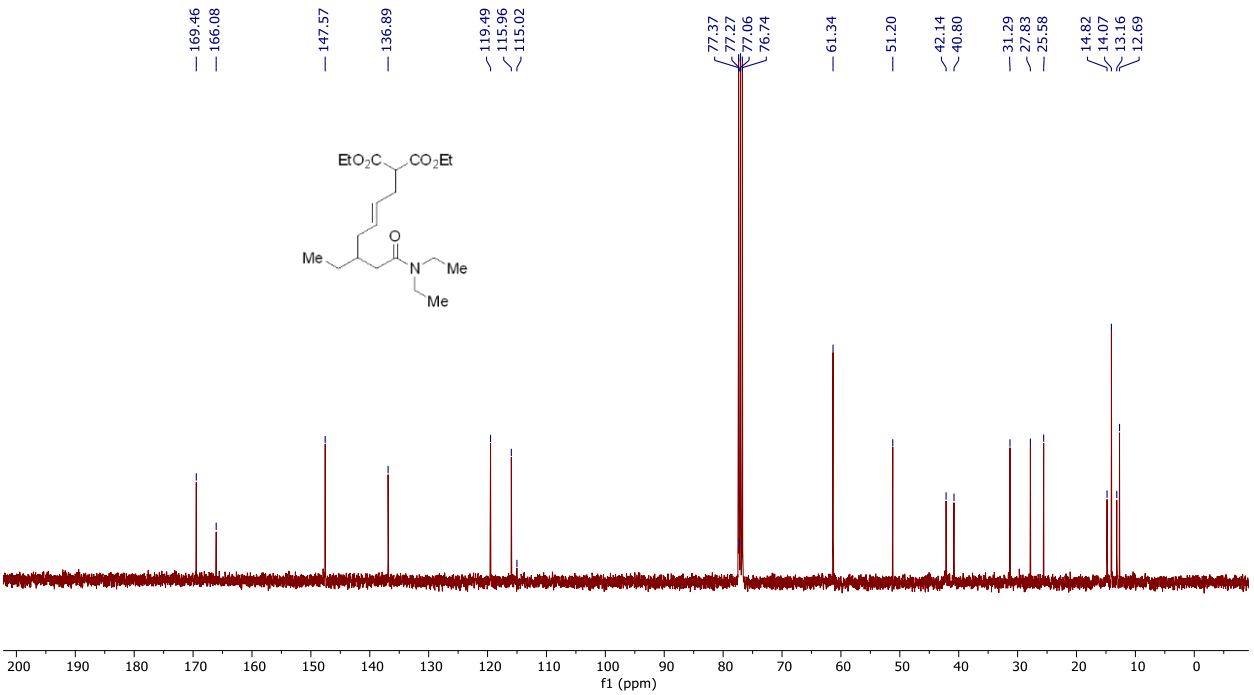
$^{13}C\{H\}$ NMR of compound **3aa** in $CDCl_3$ at 101 MHz:



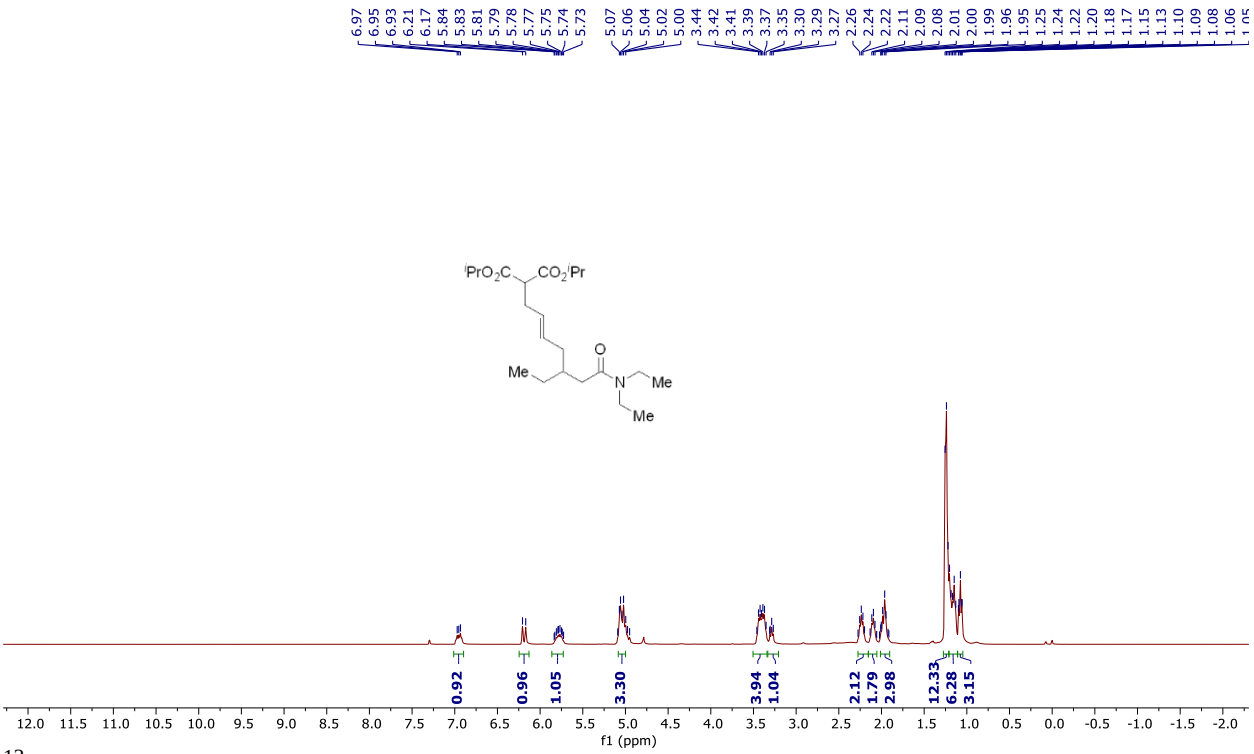
^{1}H NMR of compound **3ab** in $CDCl_3$ at 400 MHz:



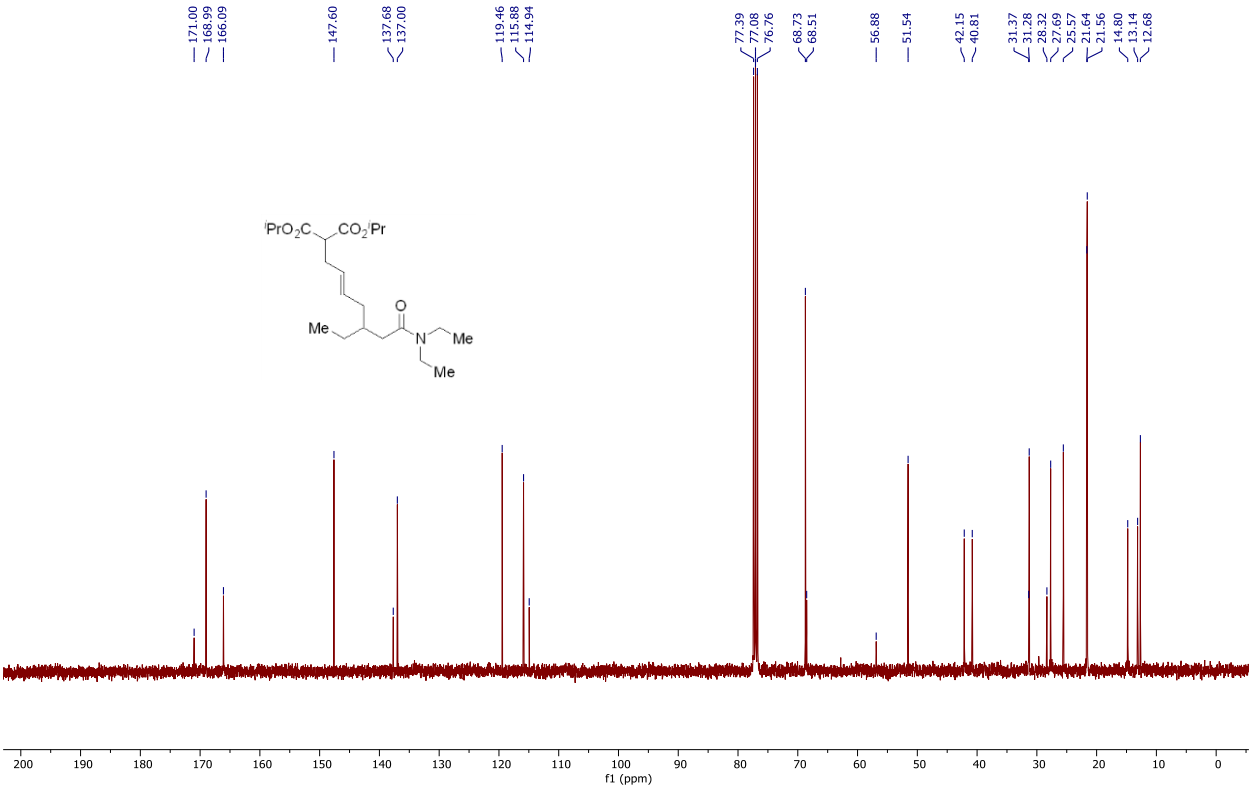
^{13}C{H} NMR of compound **3ab** in $CDCl_3$ at 101 MHz:



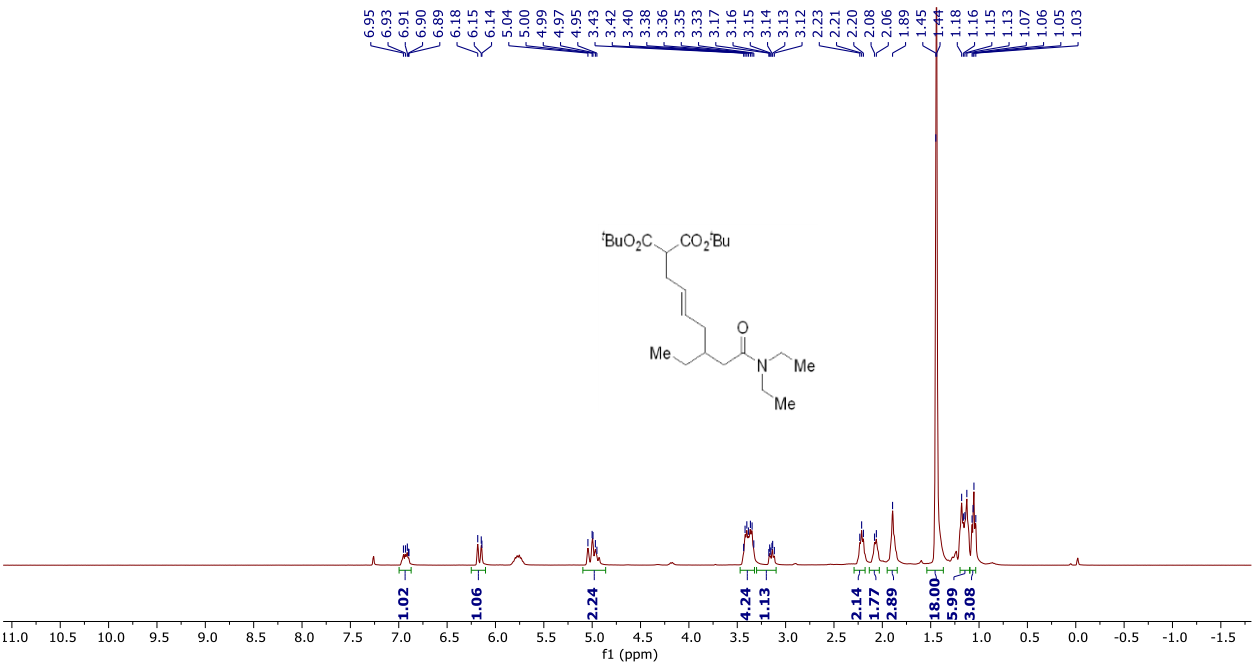
^{1}H NMR of compound **3ac** in $CDCl_3$ at 400 MHz:



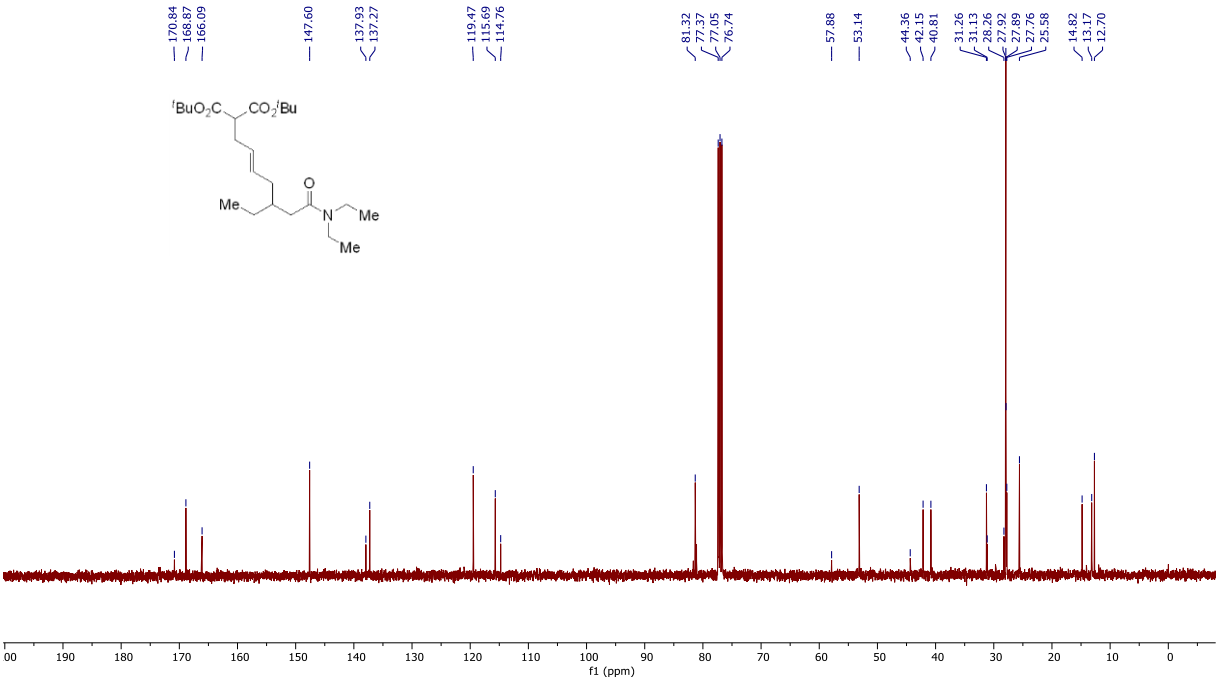
^{13}C{H} NMR of compound **3ac** in $CDCl_3$ at 101 MHz:



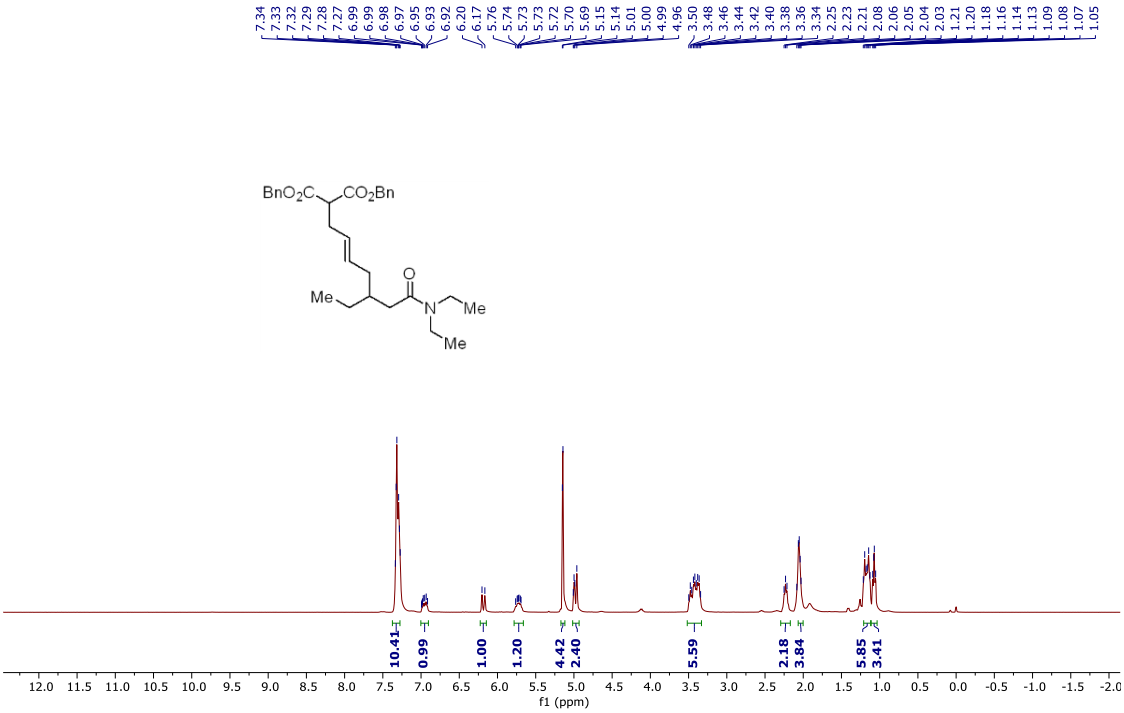
^{1}H NMR of compound **3ad** in $CDCl_3$ at 400 MHz:



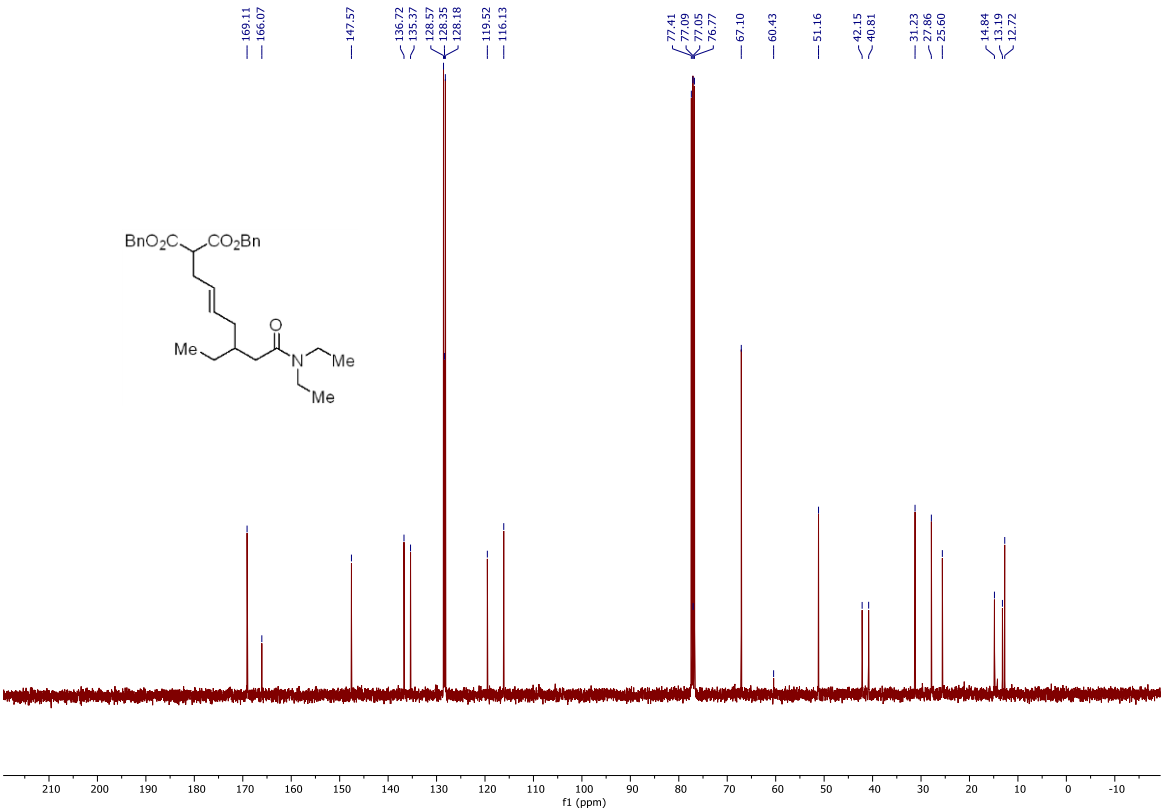
^{13}C{H} NMR of compound **3ad** in $CDCl_3$ at 101 MHz:



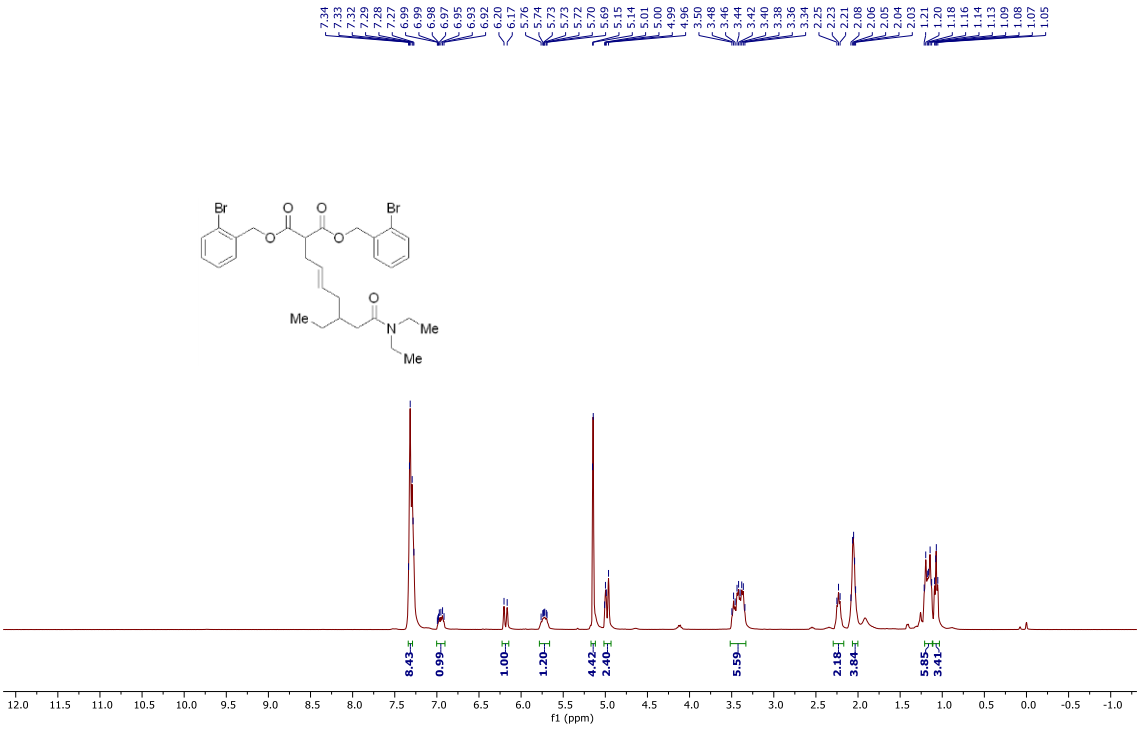
^{1}H NMR of compound **3ae** in $CDCl_3$ at 400 MHz:



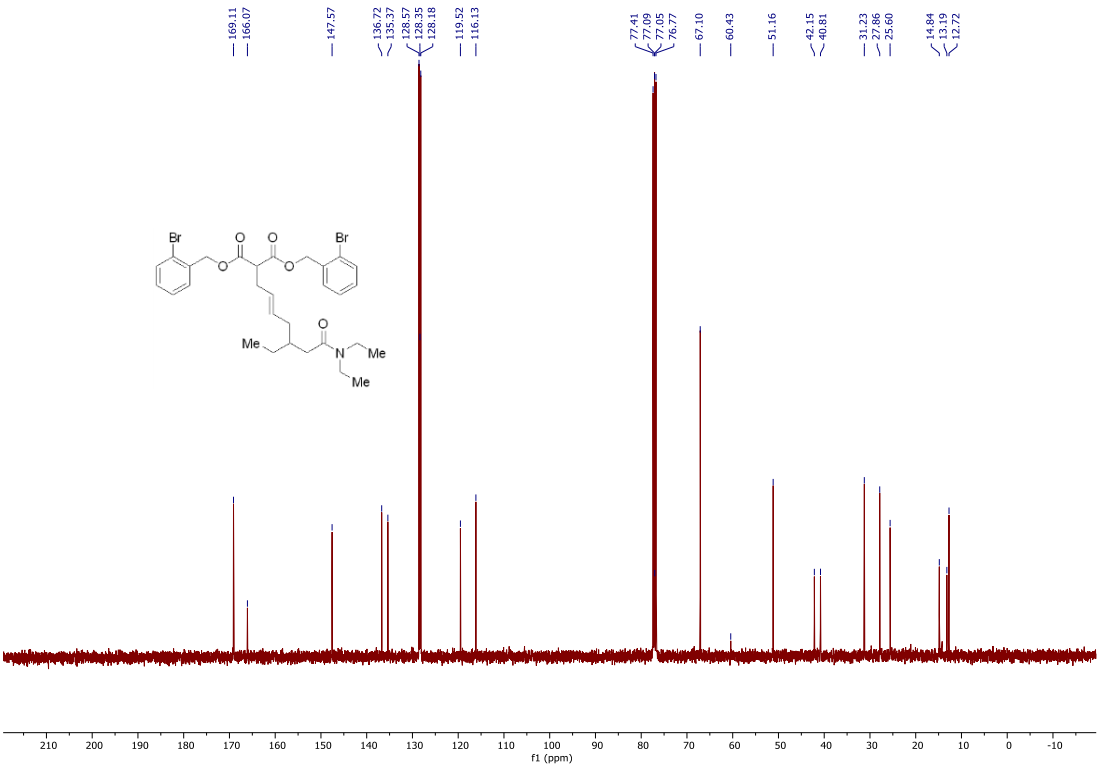
^{13}C{H} NMR of compound **3ae** in $CDCl_3$ at 101 MHz:



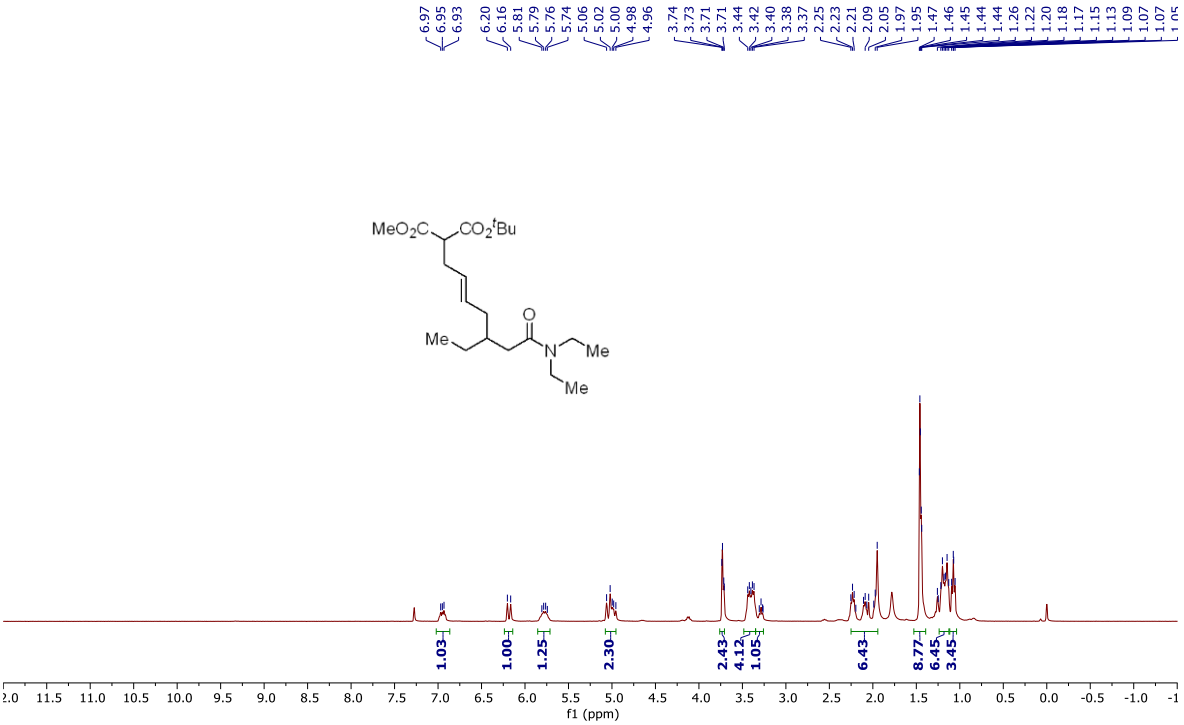
^{1}H NMR of compound **3af** in $CDCl_3$ at 400 MHz:



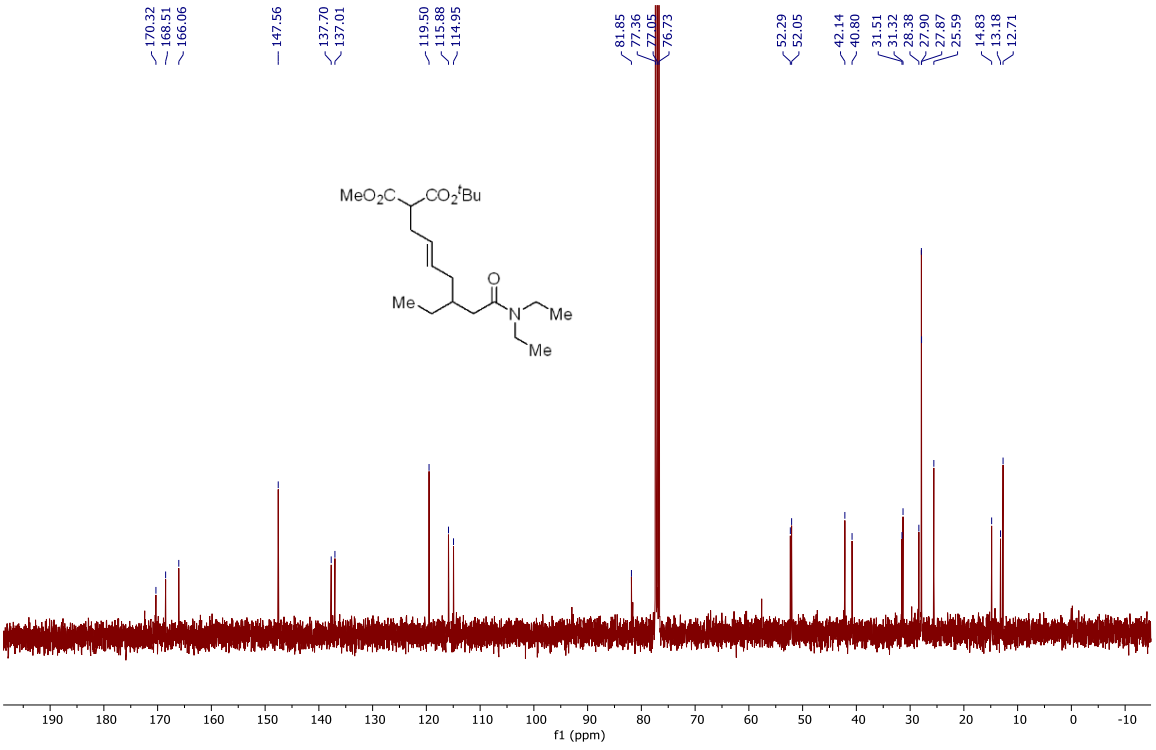
^{13}C{H} NMR of compound **3af** in $CDCl_3$ at 101 MHz:



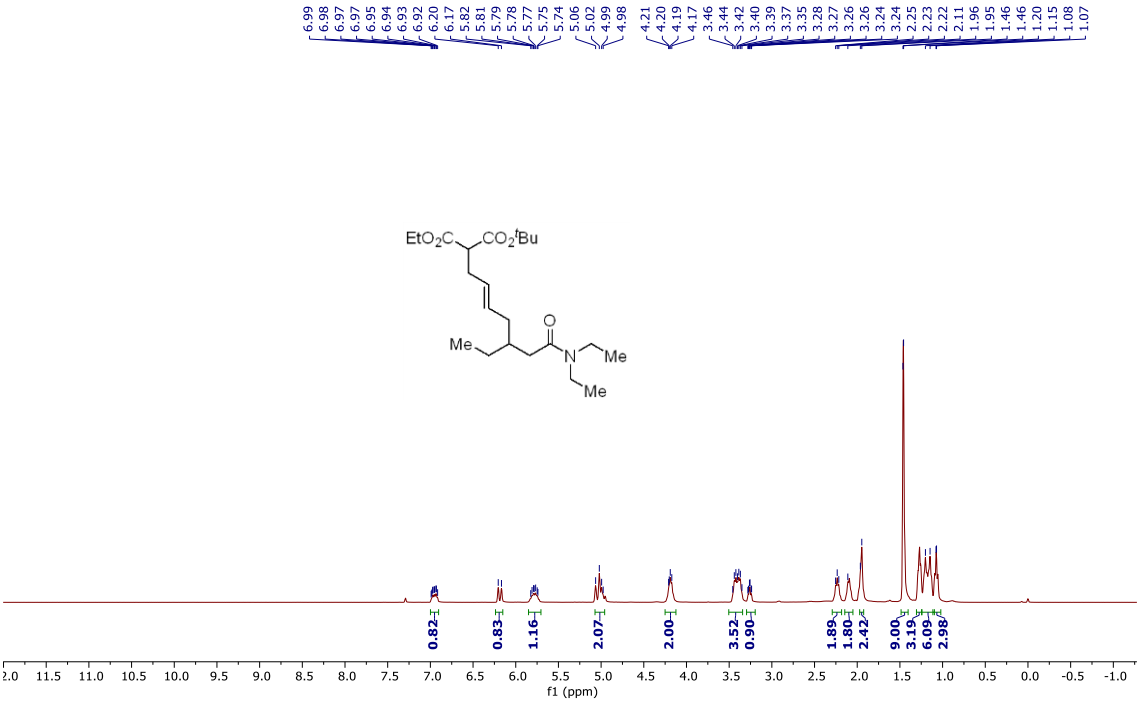
^{1}H NMR of compound **3ag** in $CDCl_3$ at 400 MHz:



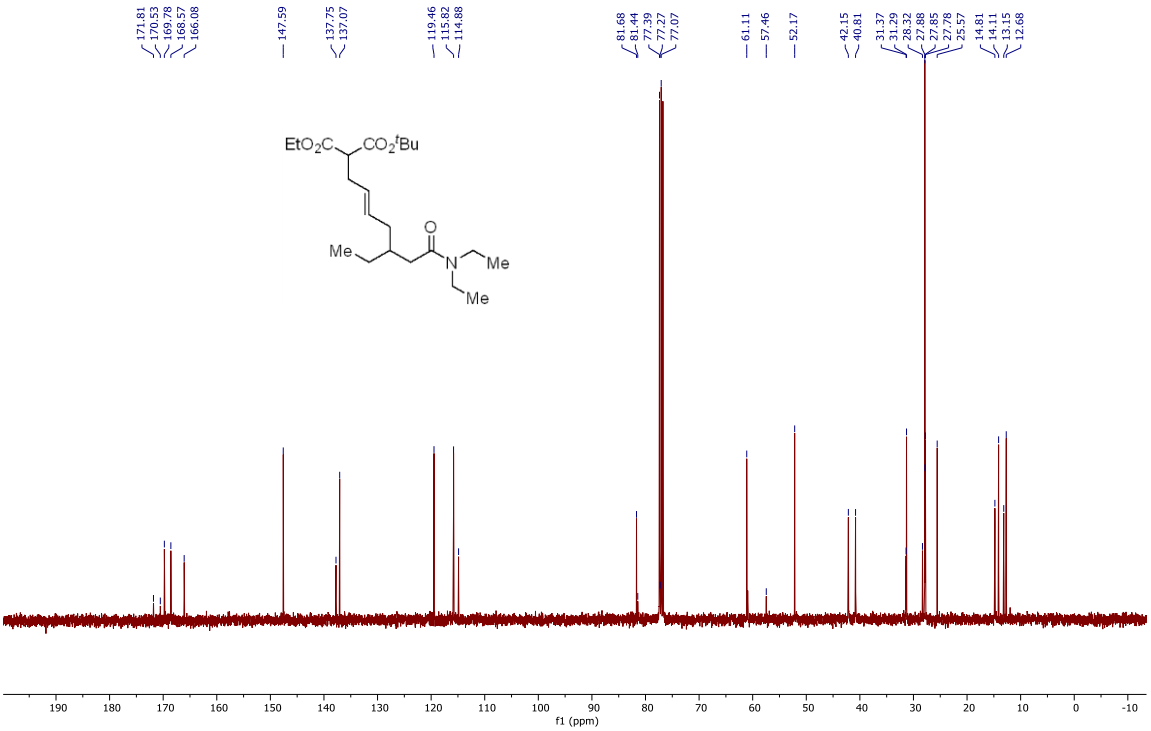
^{13}C{H} NMR of compound **3ag** in $CDCl_3$ at 101 MHz:



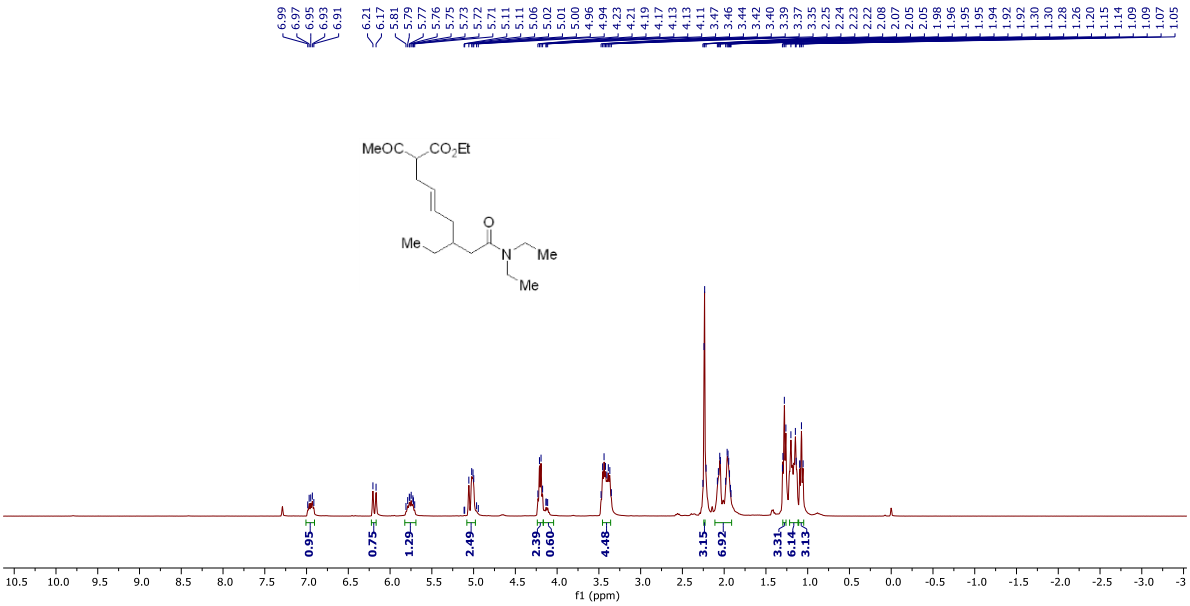
^{1}H NMR of compound **3ah** in $CDCl_3$ at 400 MHz:



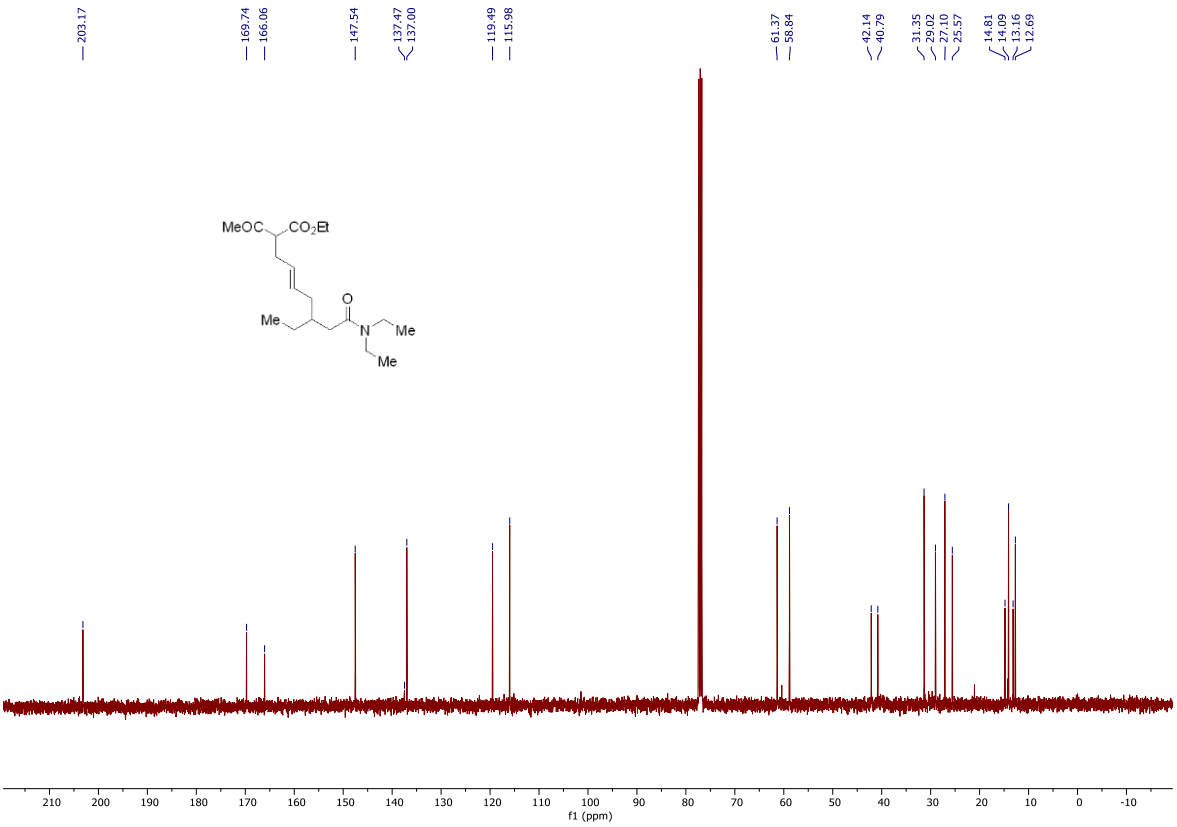
^{13}C{H} NMR of compound **3ah** in $CDCl_3$ at 101 MHz:



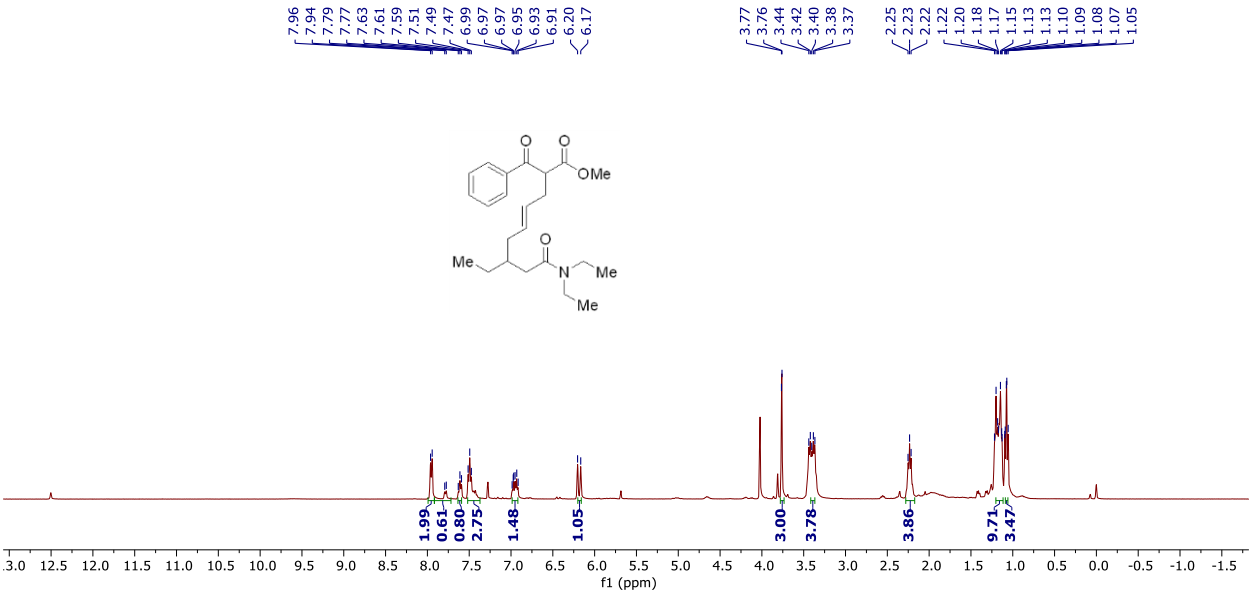
^{1}H NMR of compound **3ai** in $CDCl_3$ at 101 MHz:



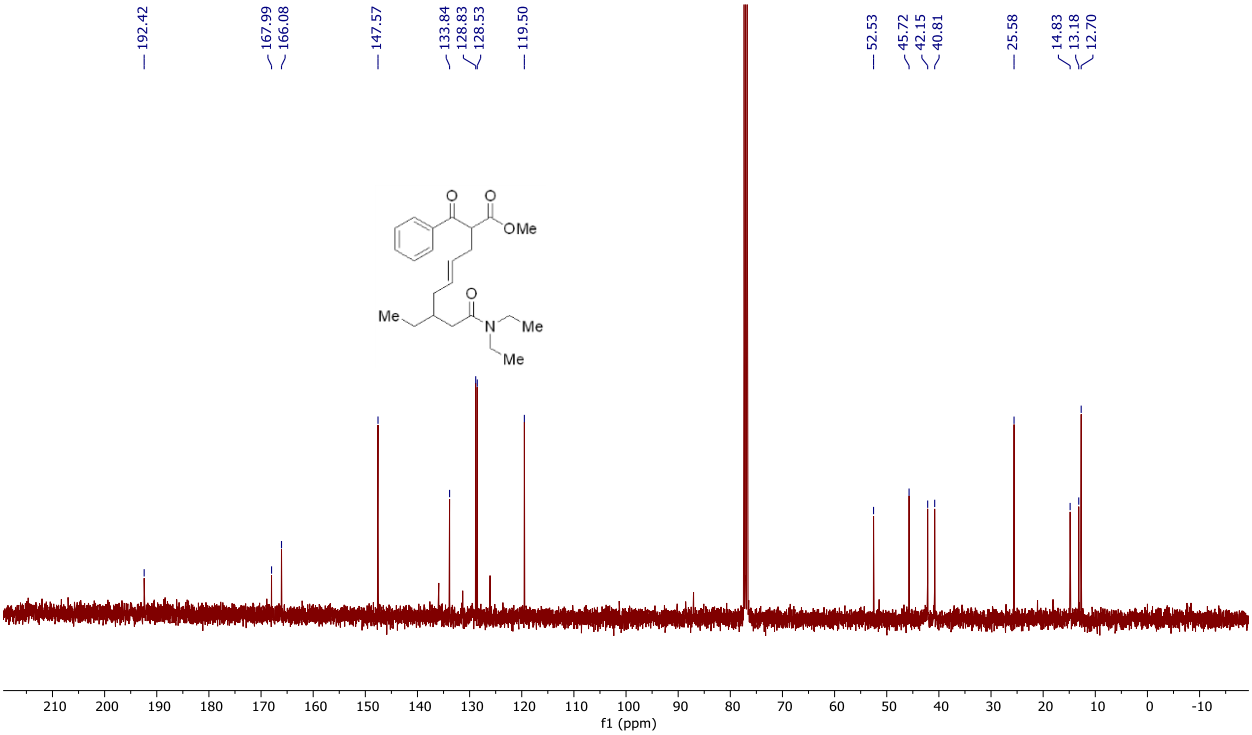
^{13}C{H} NMR of compound **3ai** in $CDCl_3$ at 101 MHz:



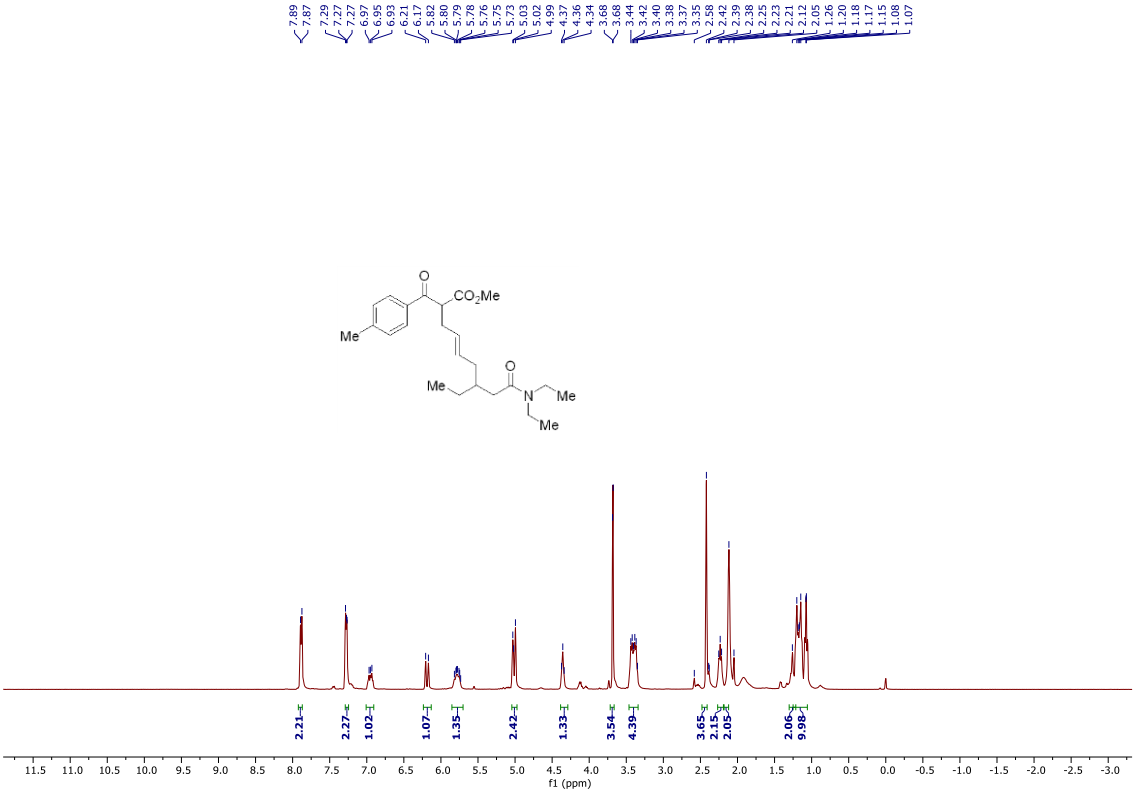
^{1}H NMR of compound **3aj** in $CDCl_3$ at 101 MHz:



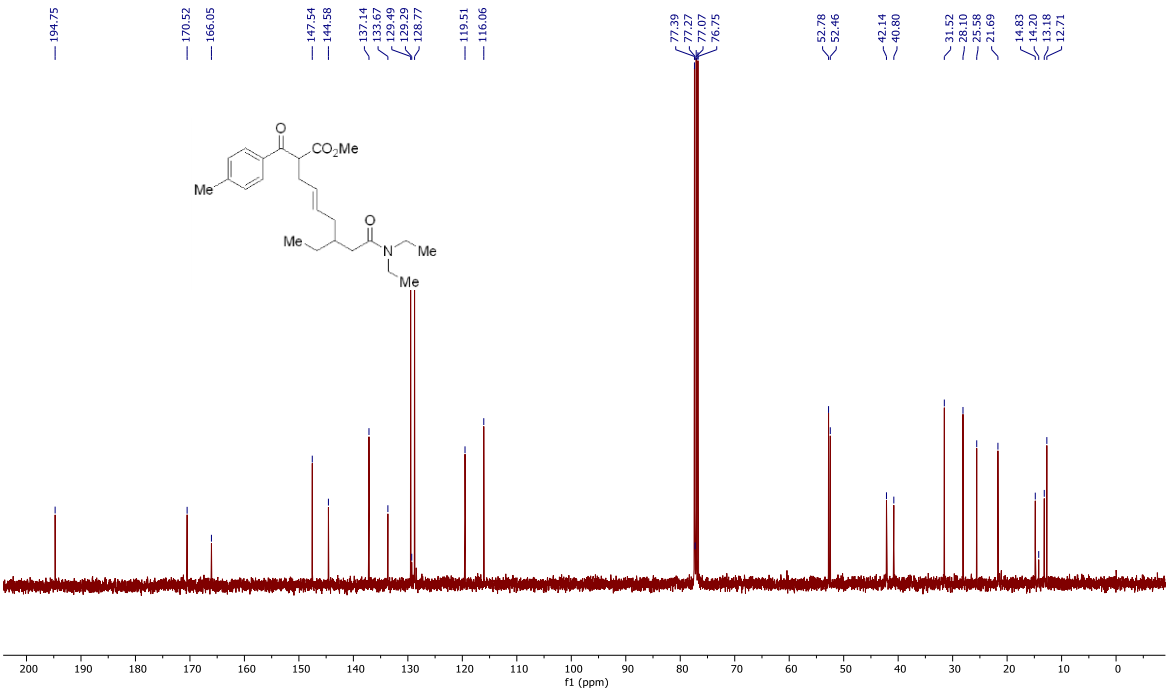
^{13}C{H} NMR of compound **3aj** in $CDCl_3$ at 101 MHz:



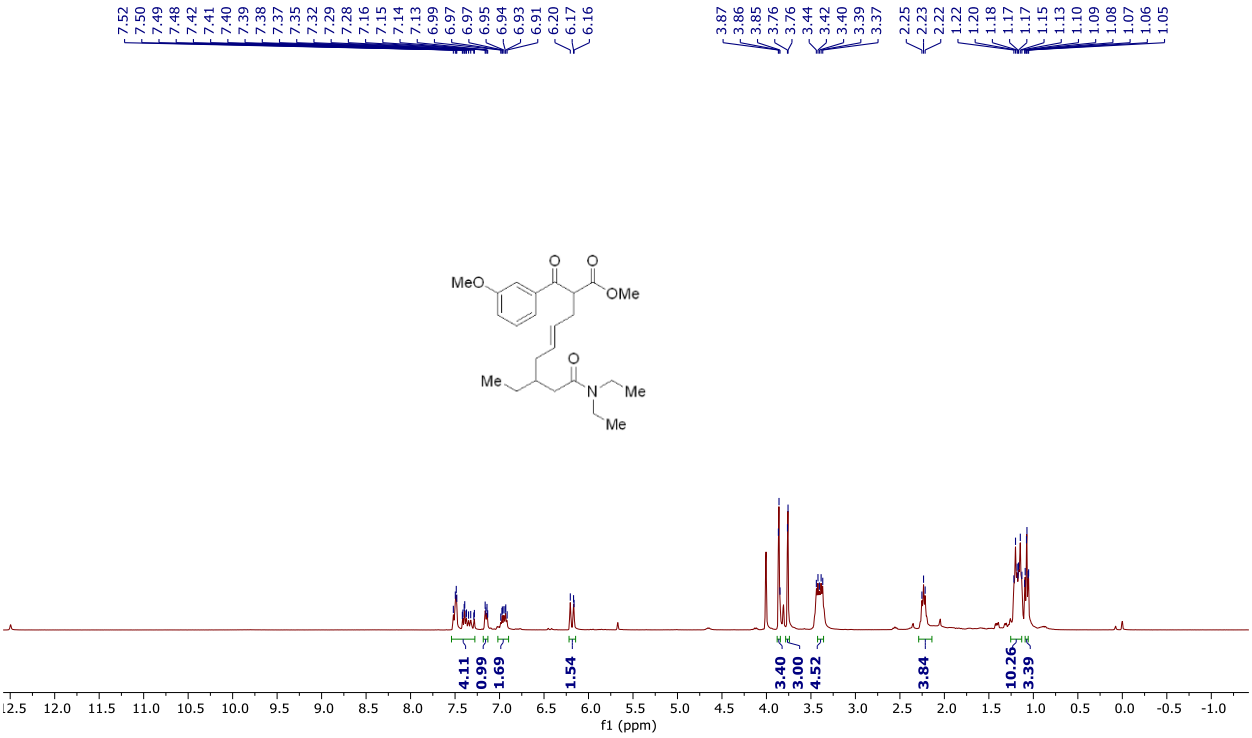
^{1}H NMR of compound **3ak** in $CDCl_3$ at 400 MHz:



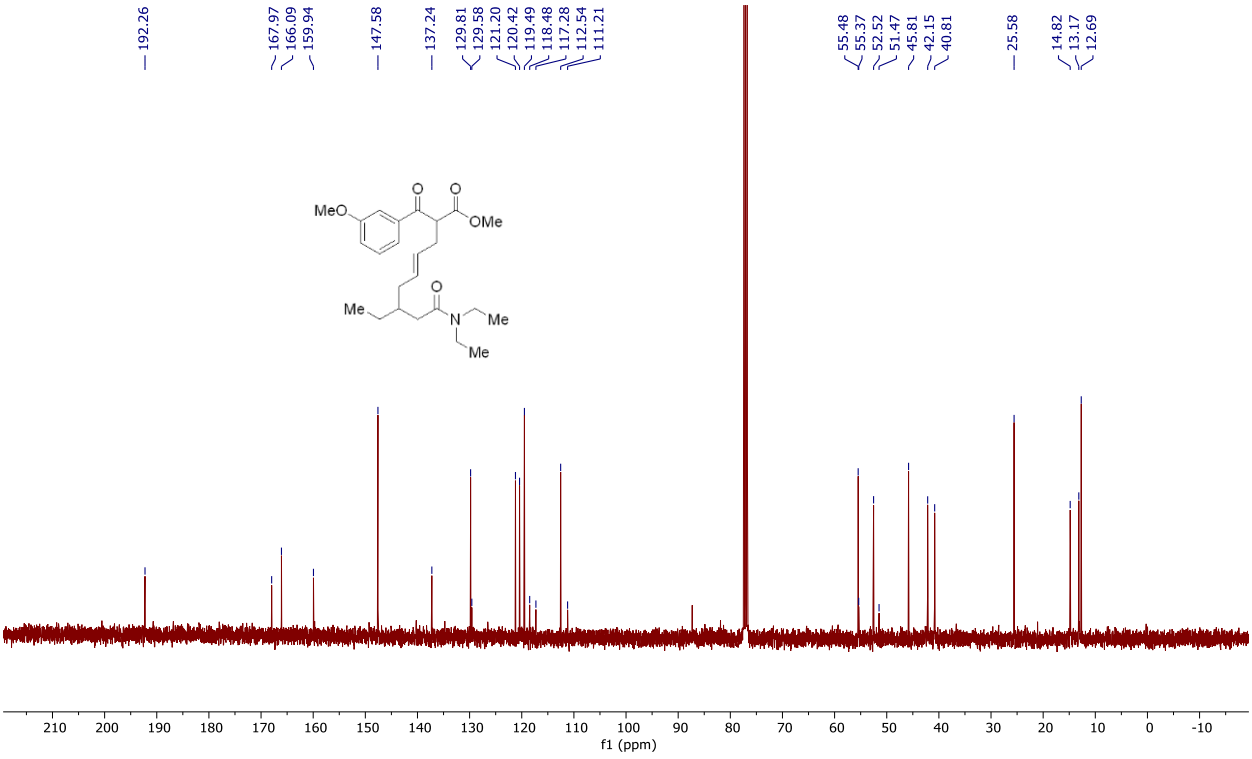
^{13}C{H} NMR of compound **3ak** in $CDCl_3$ at 101 MHz:



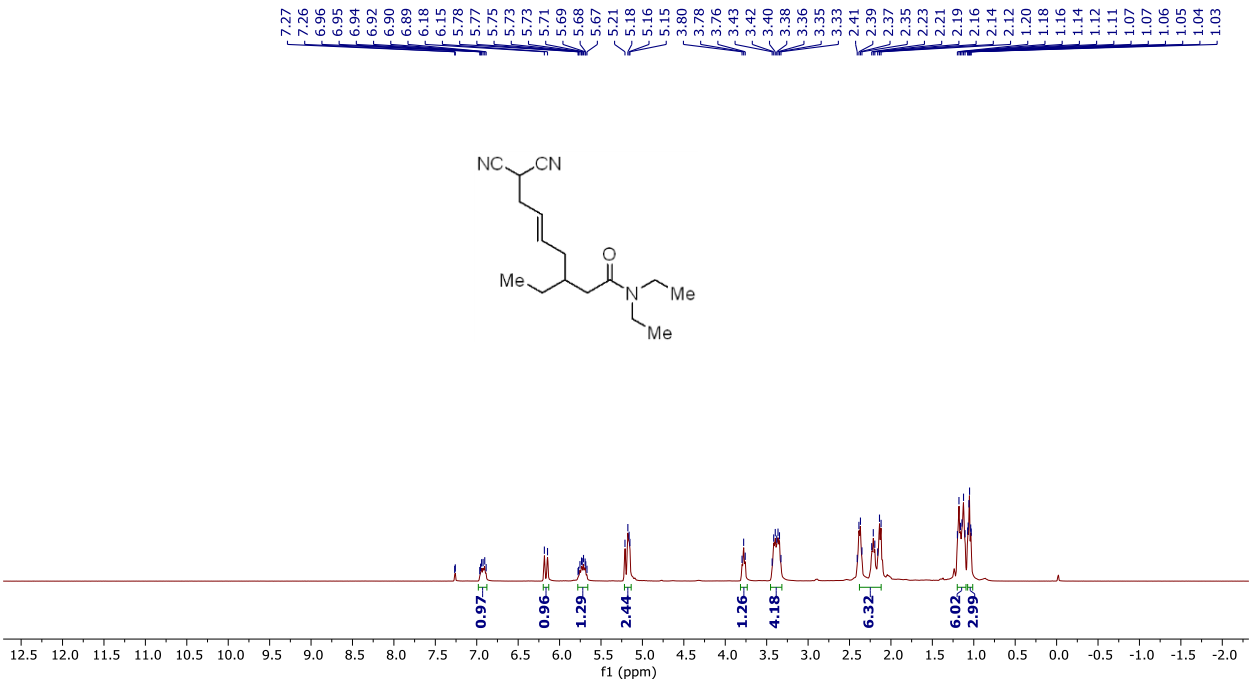
^{1}H NMR of compound **3al** in $CDCl_3$ at 400 MHz:



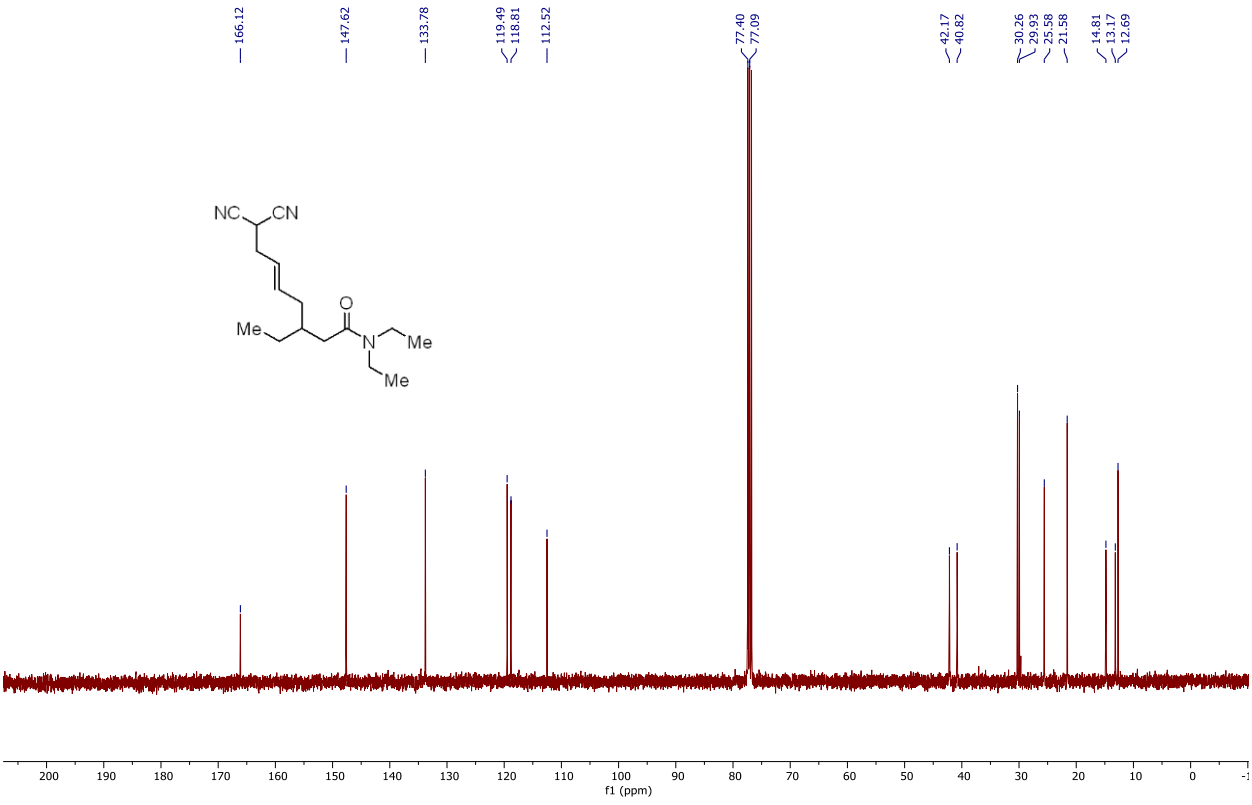
^{13}C{H} NMR of compound **3al** in $CDCl_3$ at 101 MHz:



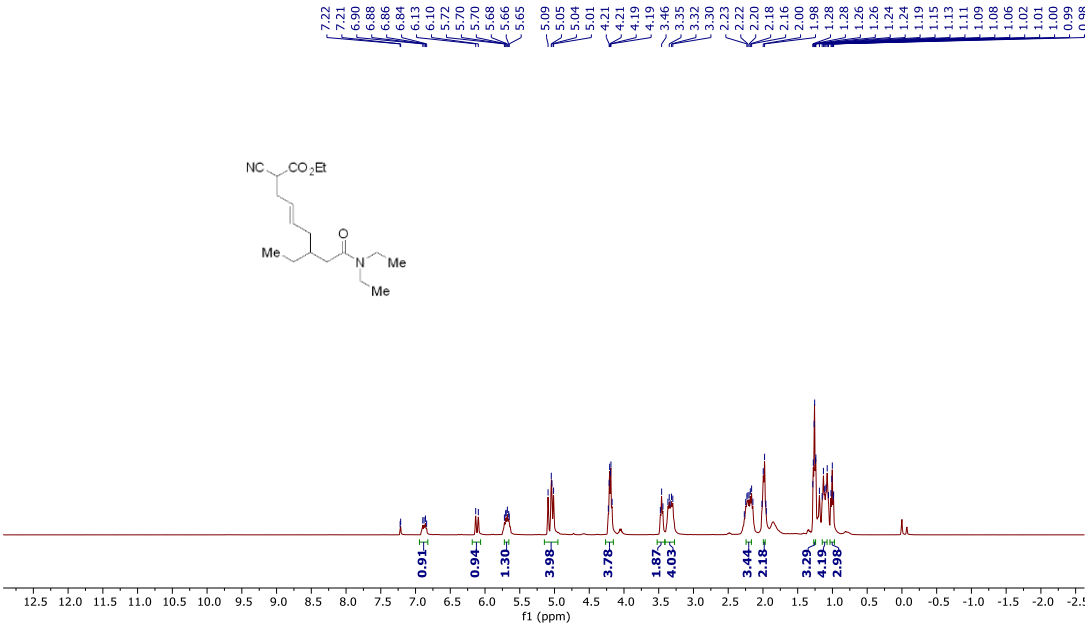
^{1}H NMR of compound **3am** in $CDCl_3$ at 400 MHz:



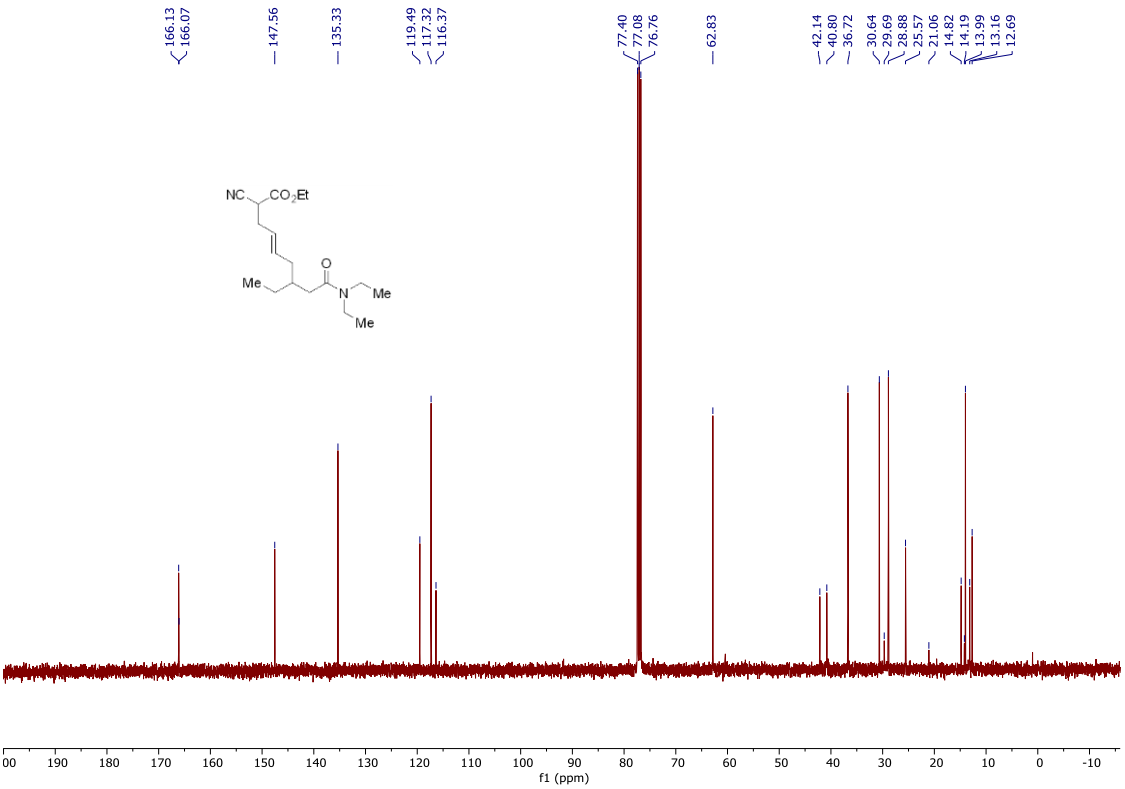
^{13}C{H} NMR of compound **3am** in $CDCl_3$ at 101 MHz:



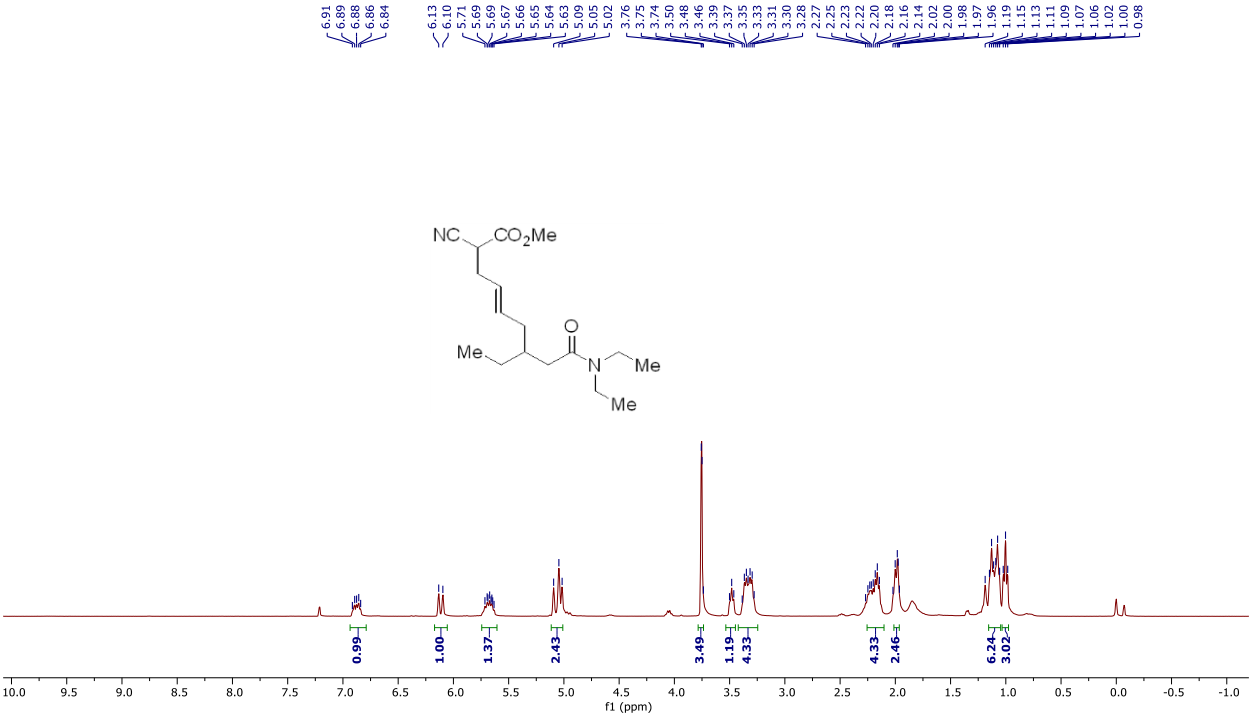
^{1}H NMR of compound **3an** in $CDCl_3$ at 101 MHz:



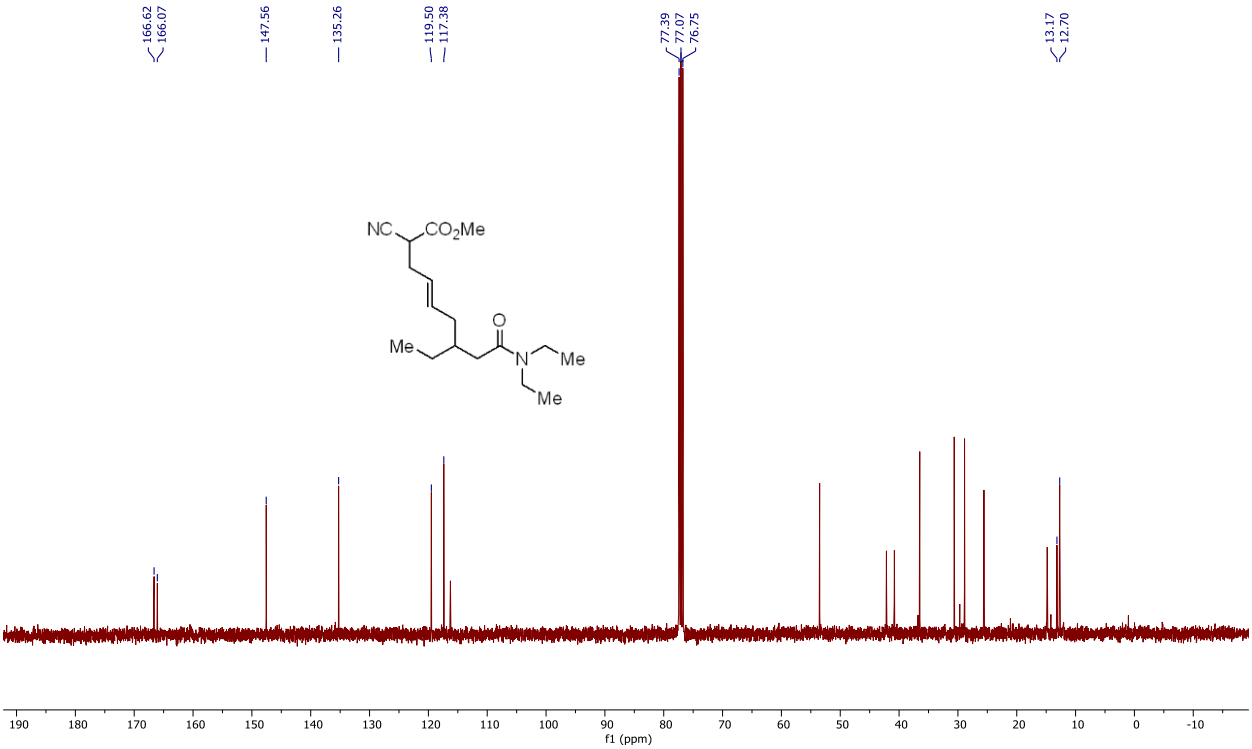
^{13}C{H} NMR of compound **3an** in $CDCl_3$ at 101 MHz:



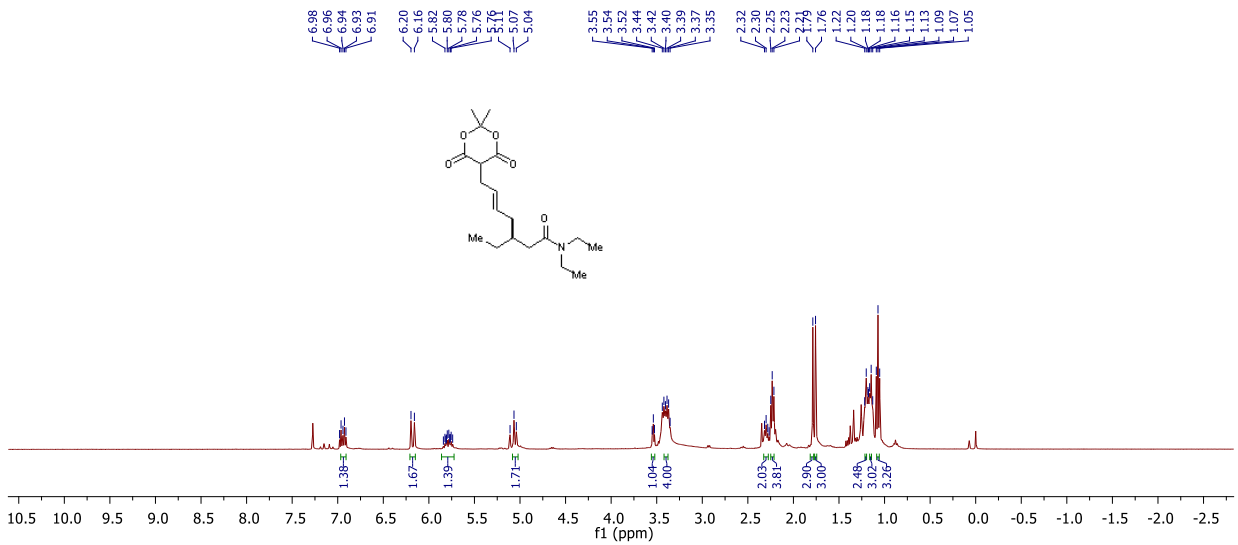
^{1}H NMR of compound **3ao** in $CDCl_3$ at 400 MHz:



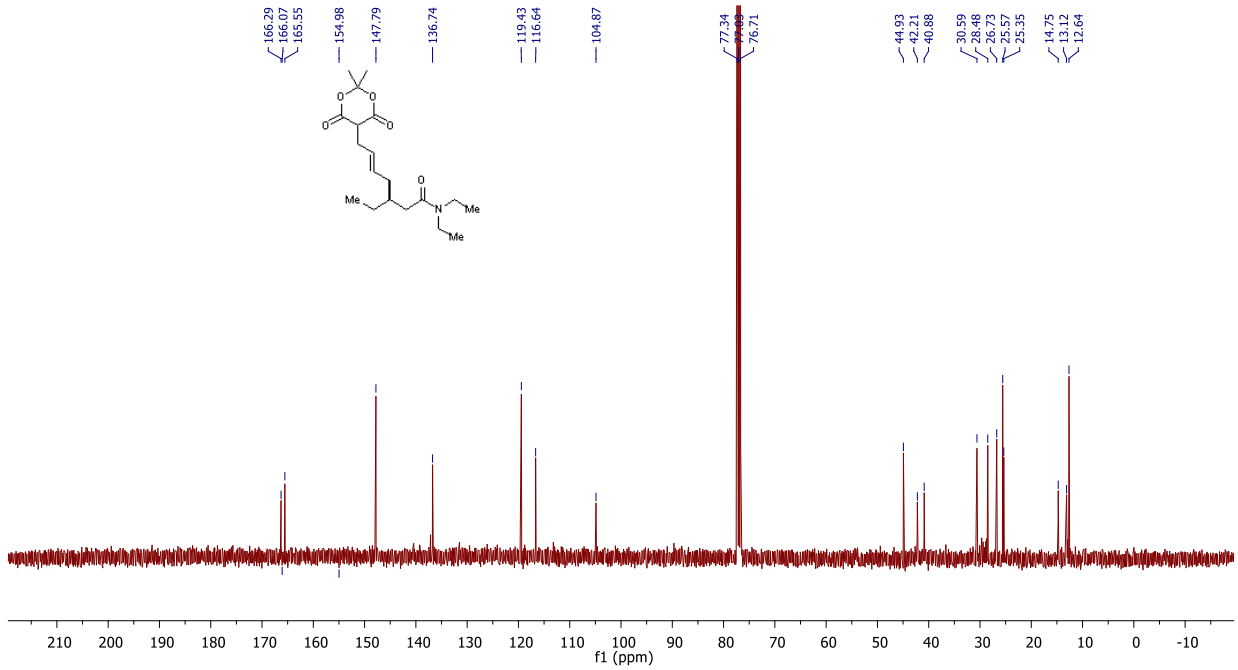
^{13}C{H} NMR of compound **3ao** in $CDCl_3$ at 101 MHz:



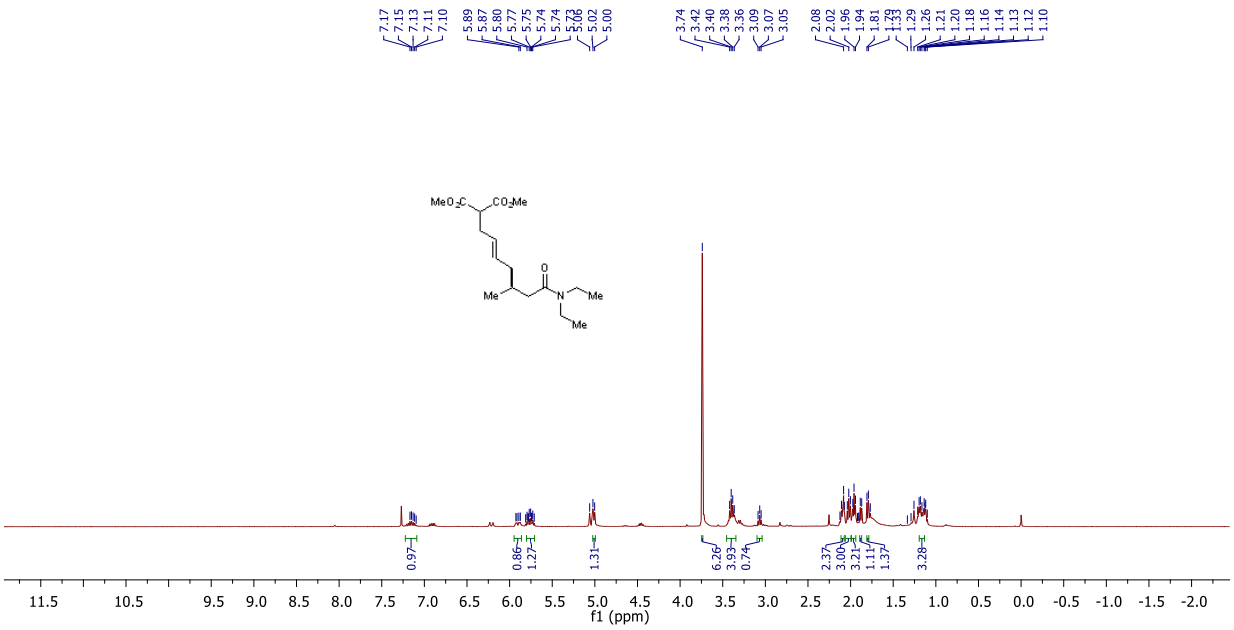
^{1}H NMR of compound **3ap** in $CDCl_3$ at 400 MHz:



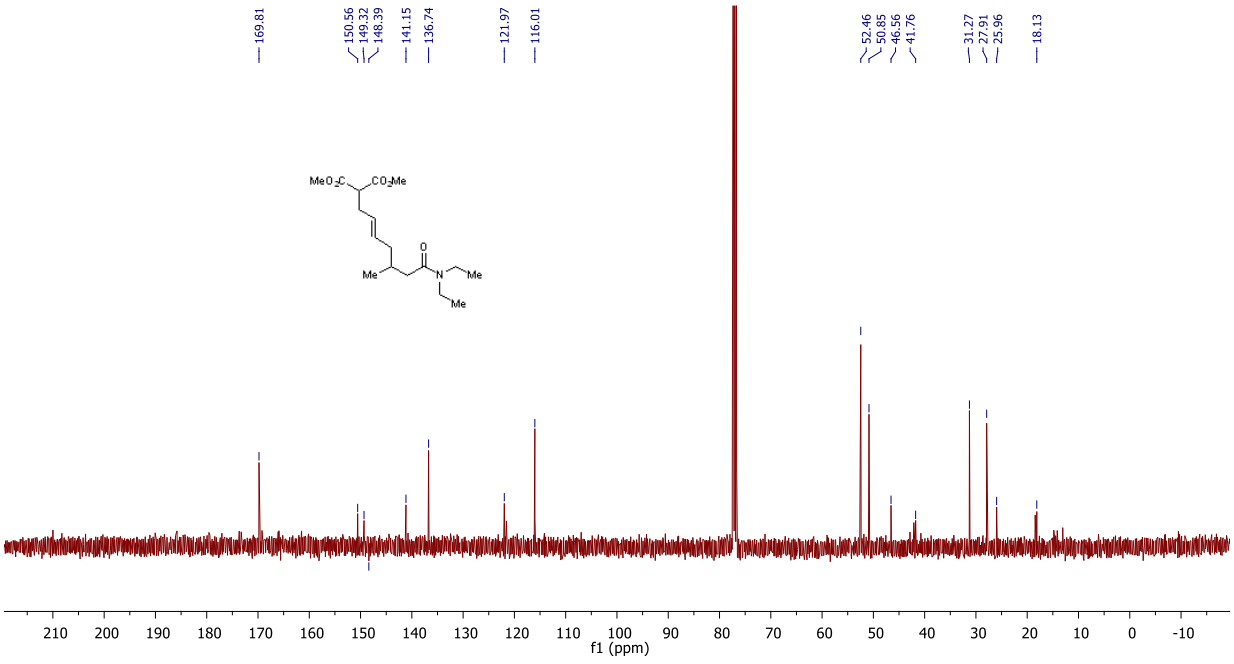
^{13}C{H} NMR of compound **3ap** in $CDCl_3$ at 101 MHz:



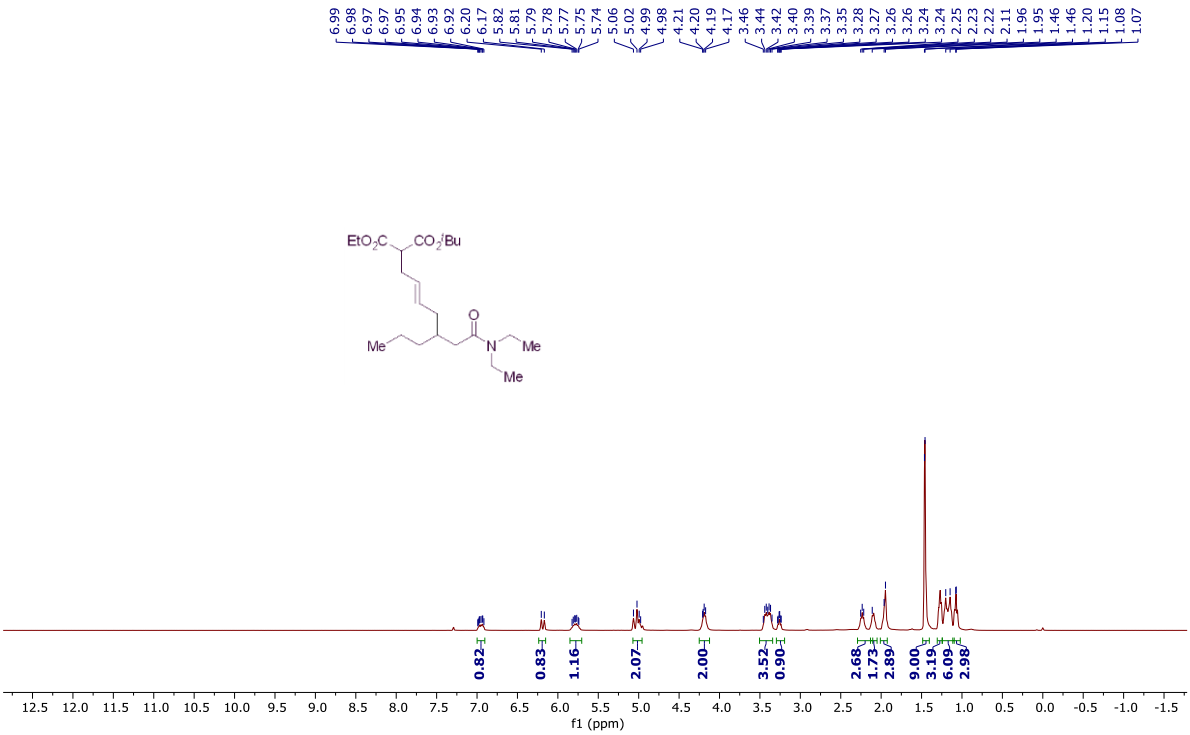
^{1}H NMR of compound **3ba** in $CDCl_3$ at 400 MHz:



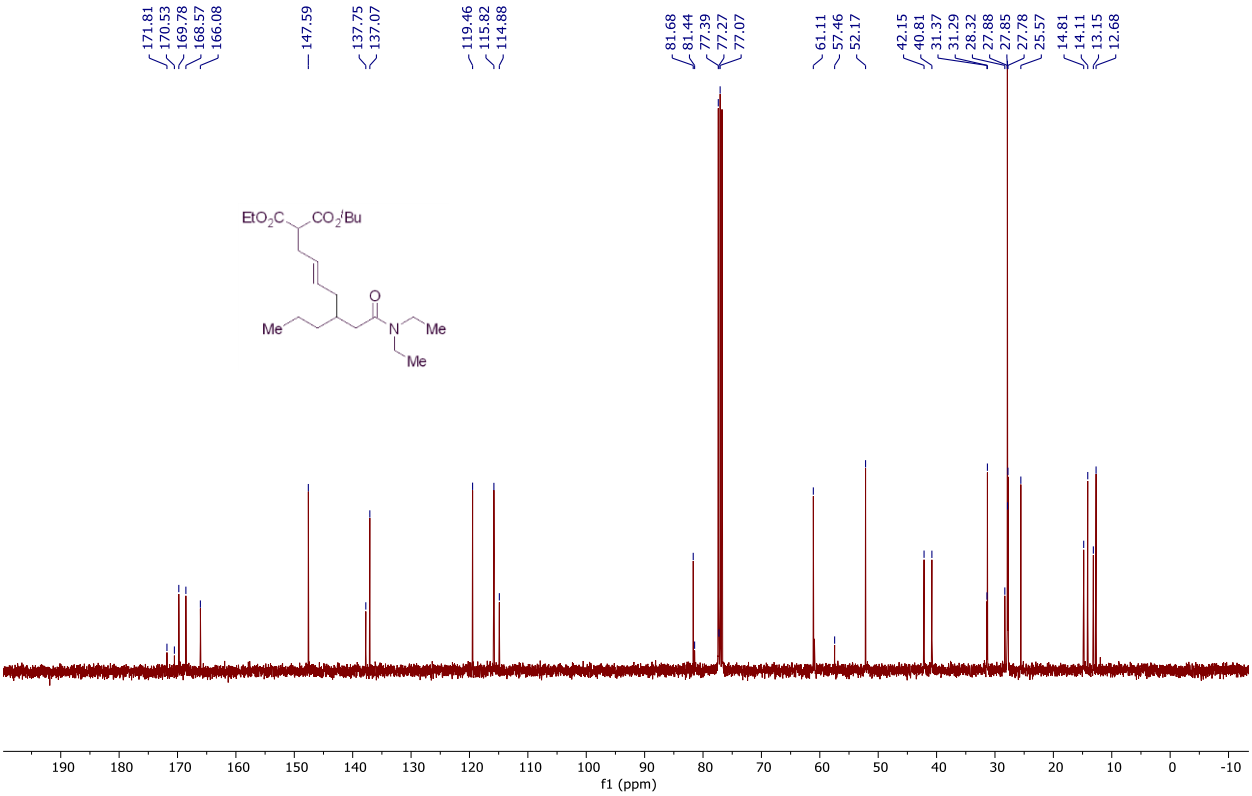
^{13}C{H} NMR of compound **3ba** in $CDCl_3$ at 101 MHz:



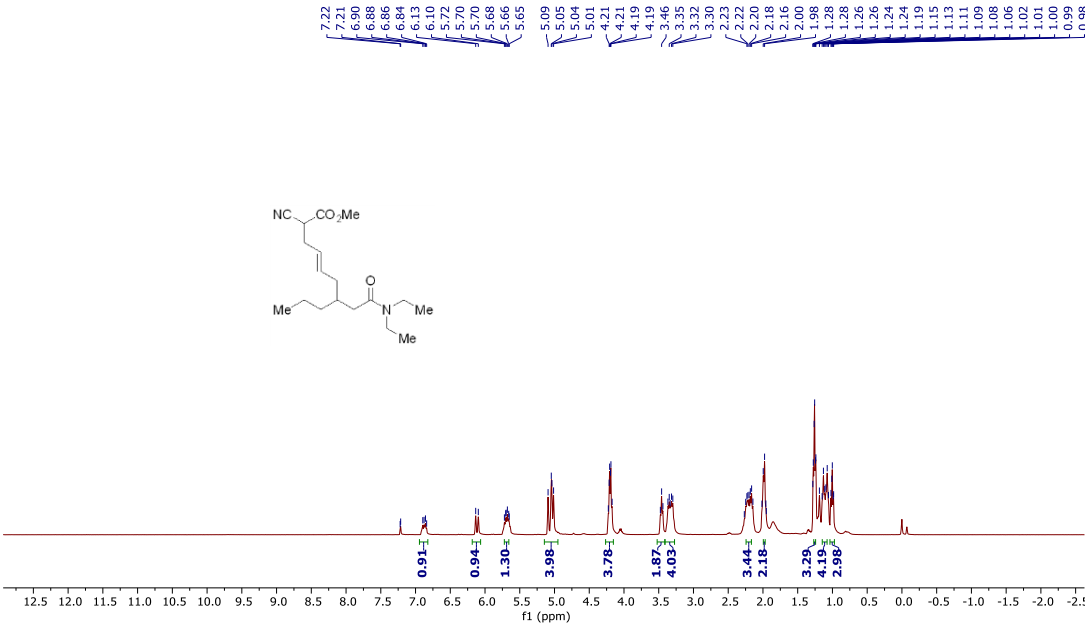
^{1}H NMR of compound **3ch** in $CDCl_3$ at 400 MHz:



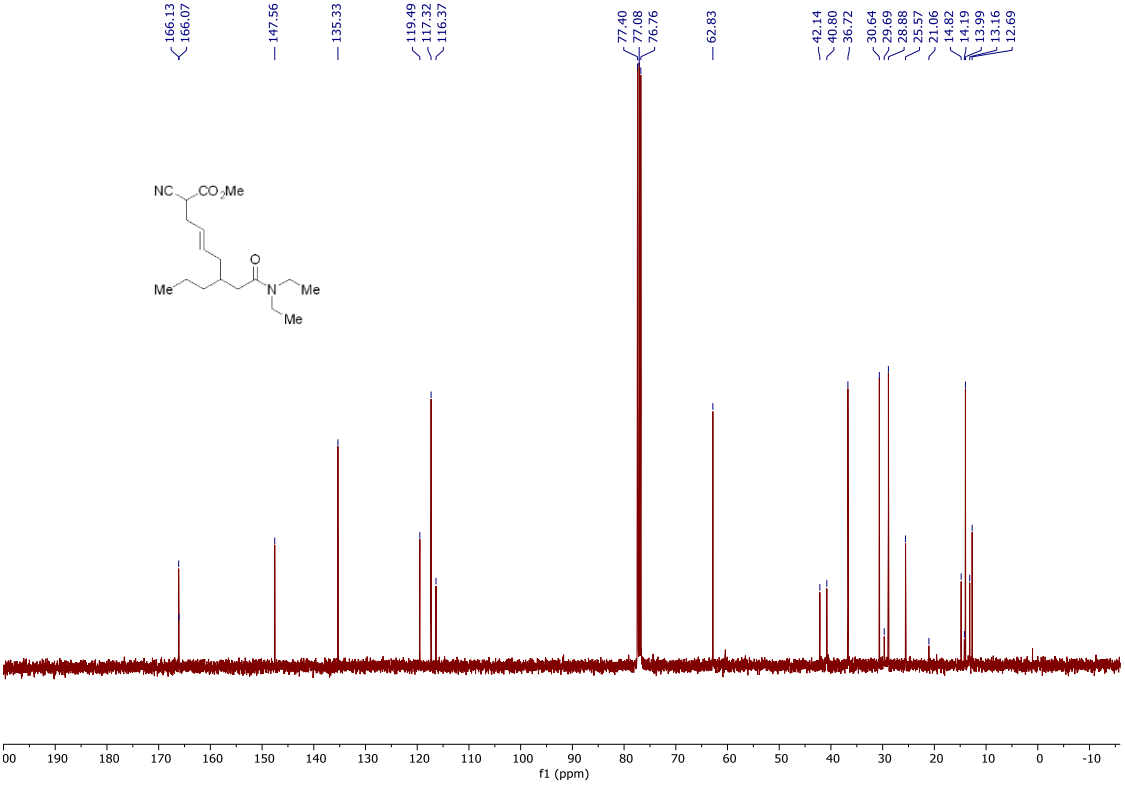
^{13}C{H} NMR of compound **3ch** in $CDCl_3$ at 101 MHz:



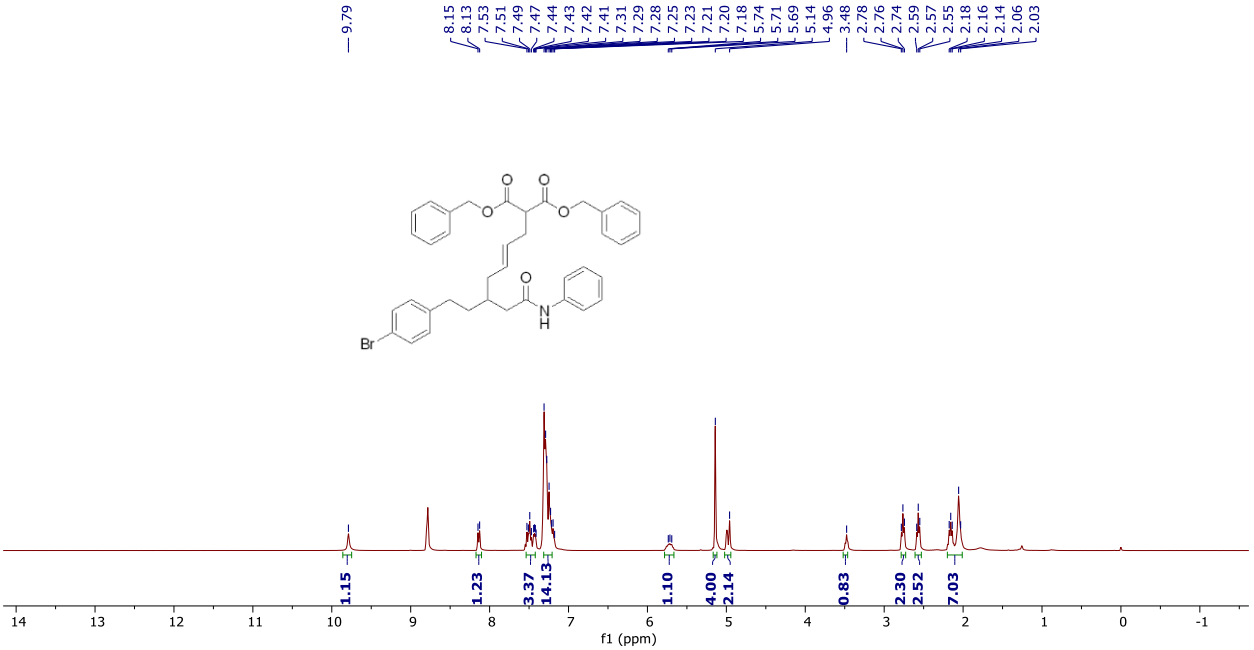
^{1}H NMR of compound **3co** in $CDCl_3$ at 101 MHz:



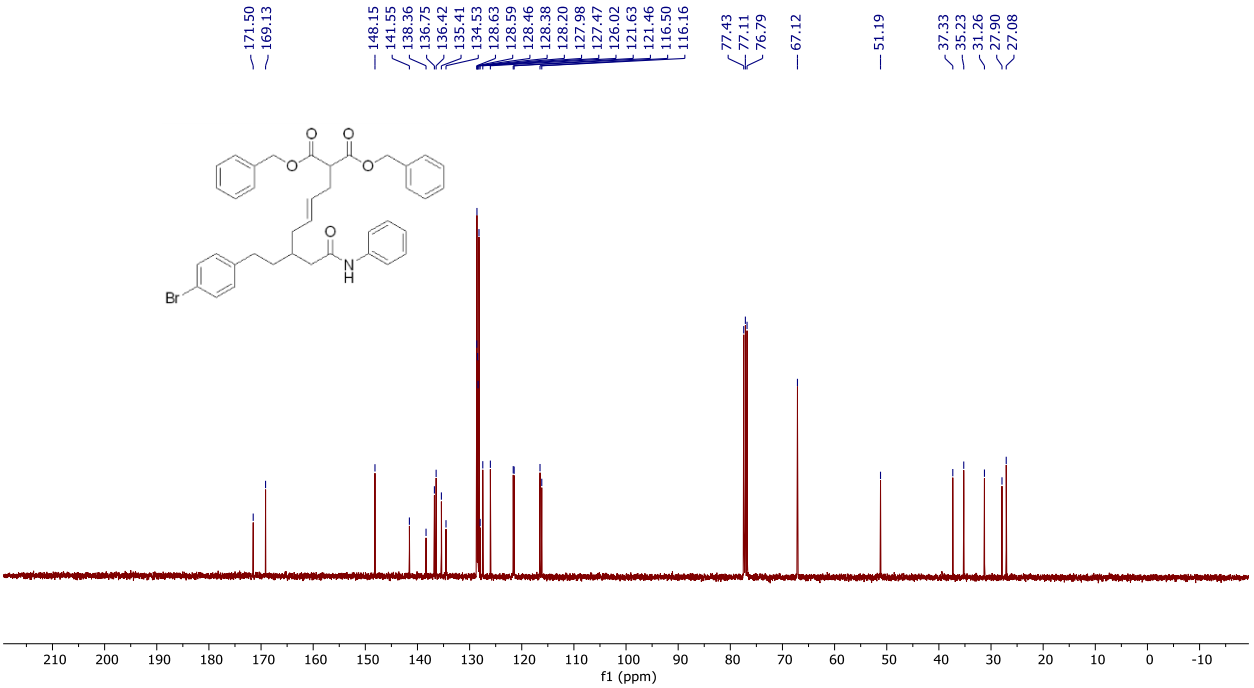
^{13}C{H} NMR of compound **3co** in $CDCl_3$ at 101 MHz:



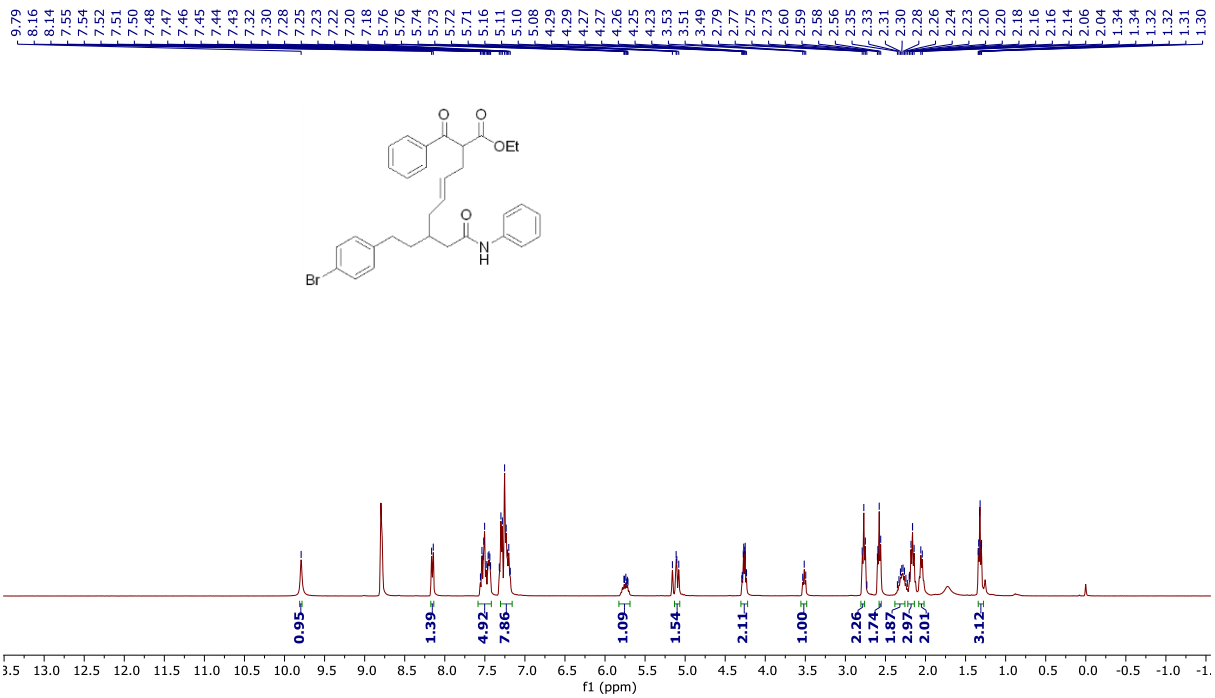
^{1}H NMR of compound **3de** in $CDCl_3$ at 400 MHz:



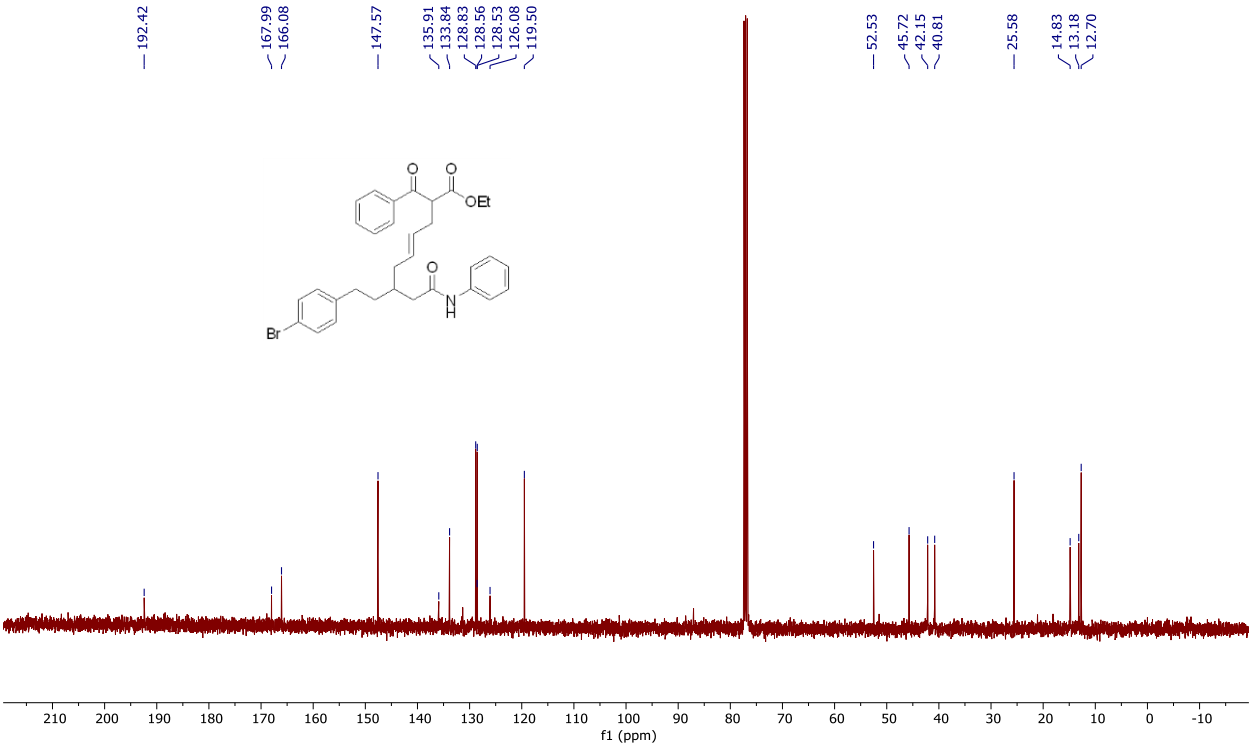
^{13}C{H} NMR of compound **3de** in $CDCl_3$ at 101 MHz:



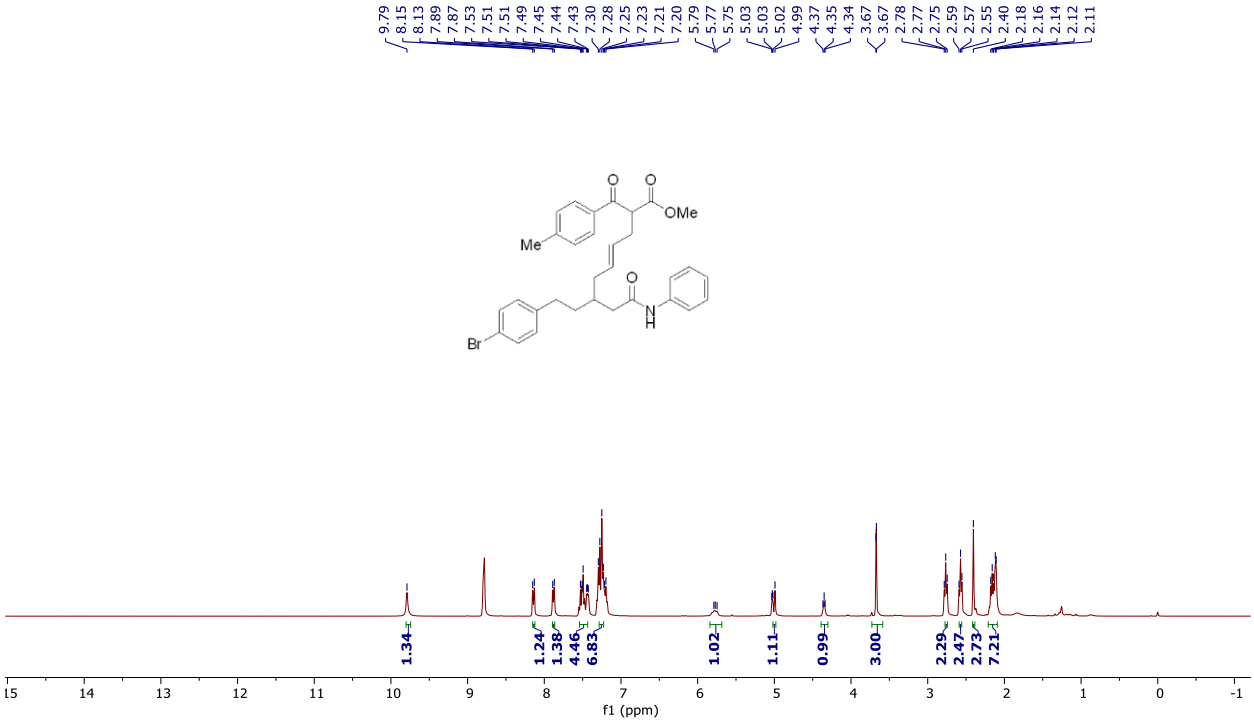
^{1}H NMR of compound **3dp** in $CDCl_3$ at 400 MHz:



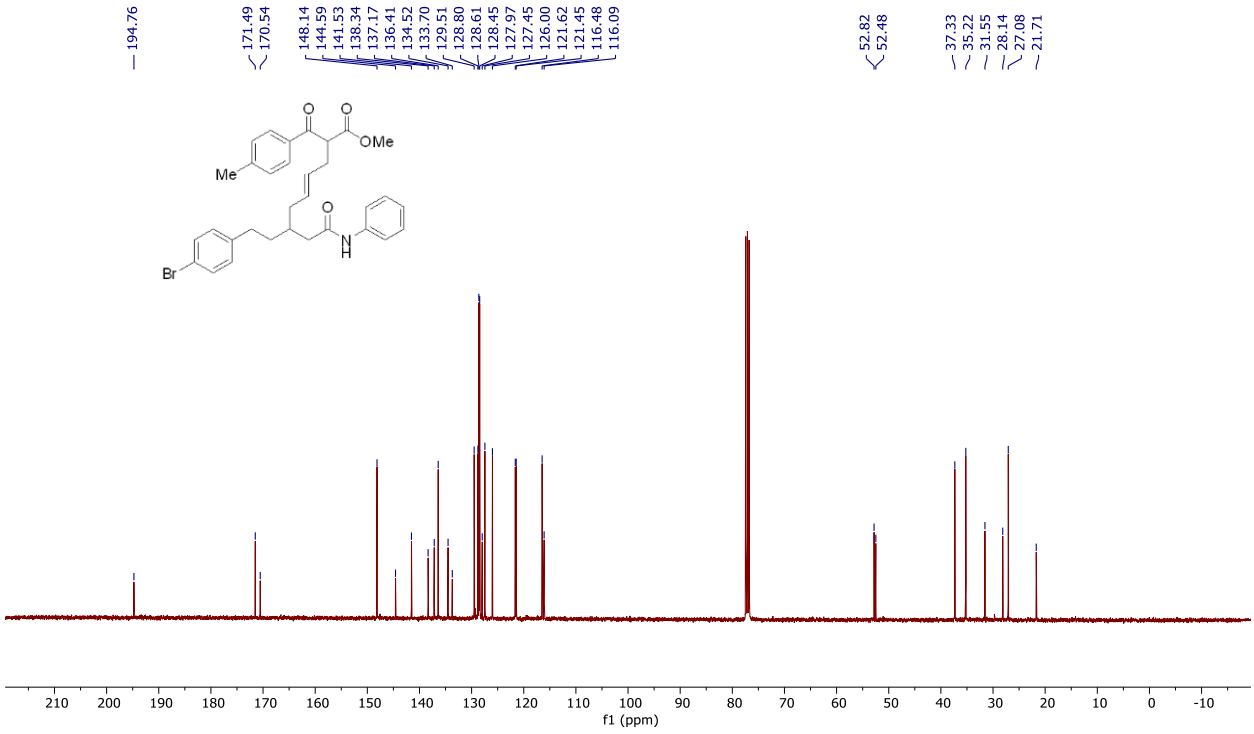
^{13}C{H} NMR of compound **3dp** in $CDCl_3$ at 101 MHz:



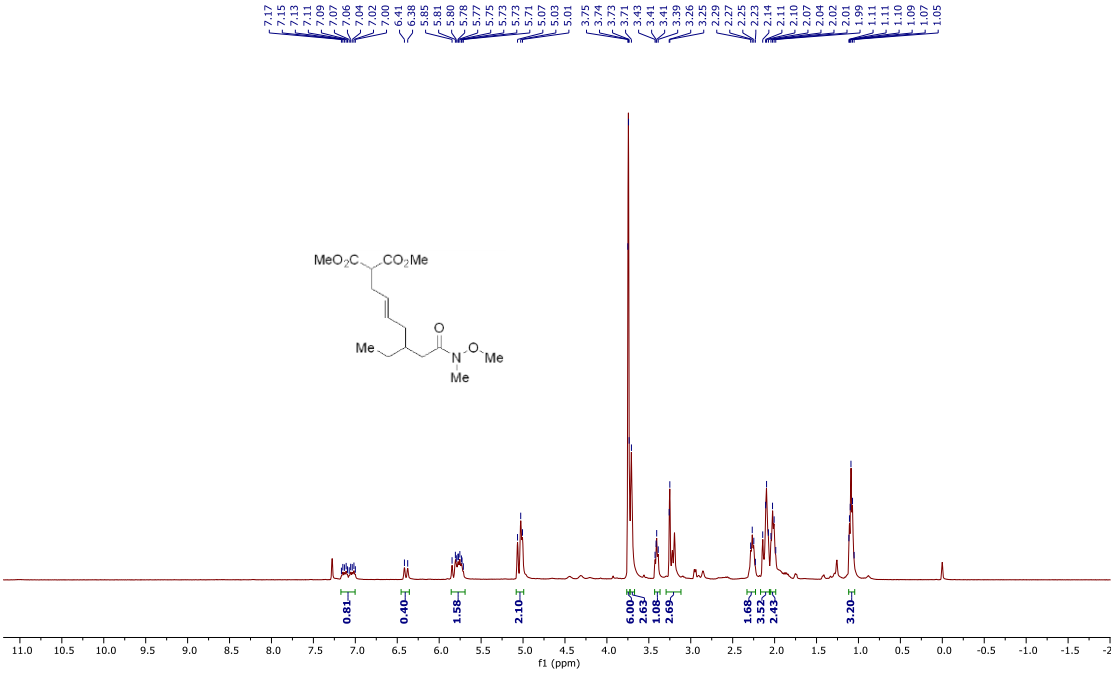
^{1}H NMR of compound **3dk** in $CDCl_3$ at 400 MHz:



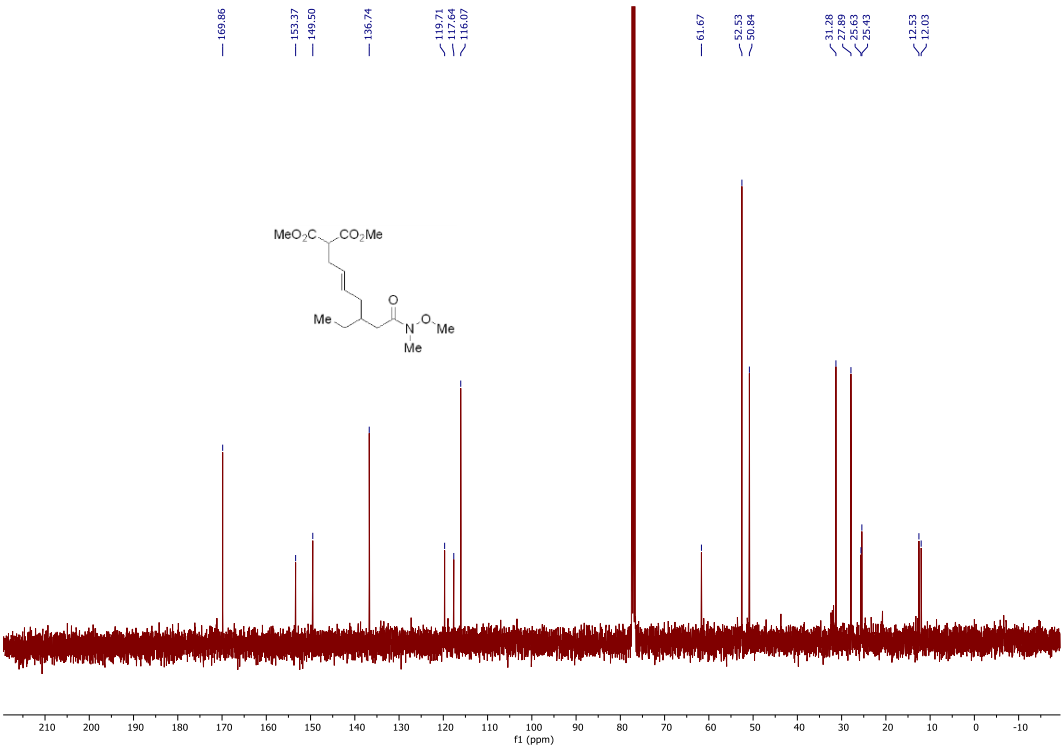
^{13}C{H} NMR of compound **3dk** in $CDCl_3$ at 101 MHz:



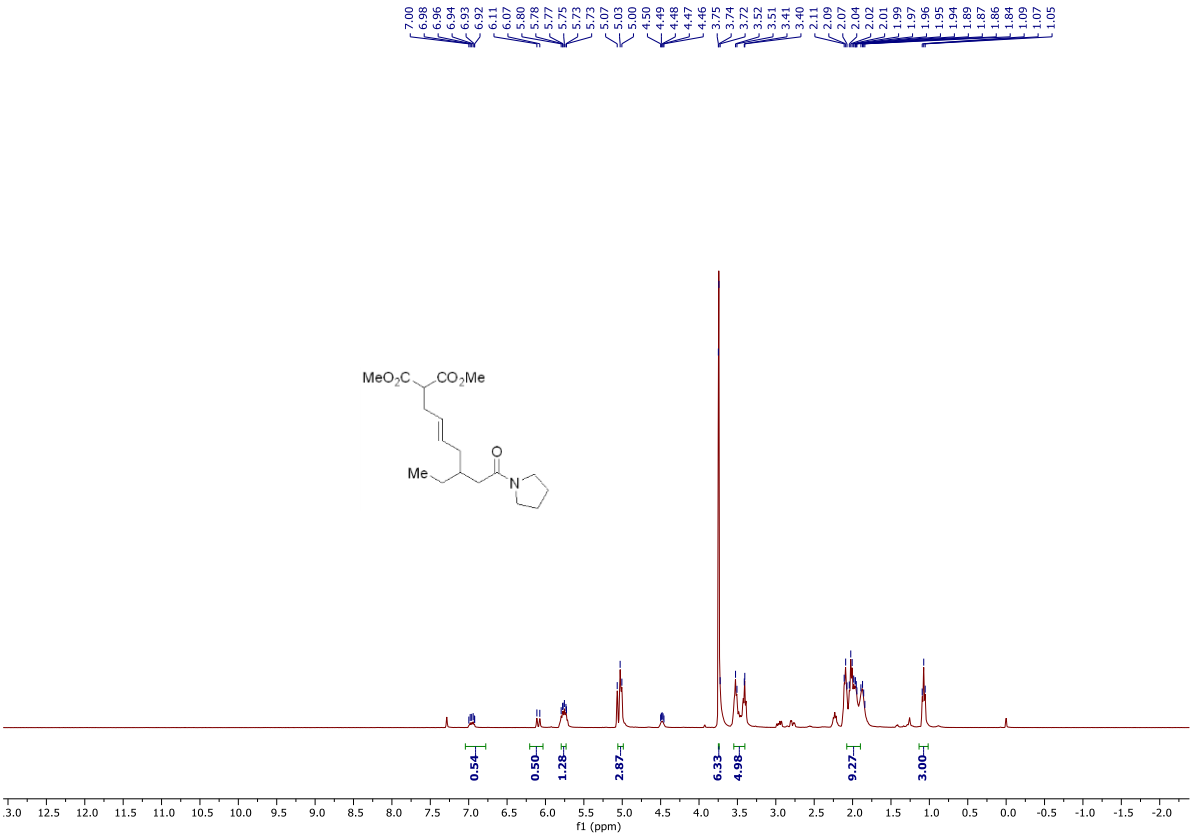
^{1}H NMR of compound **3ea** in $CDCl_3$ at 400 MHz:



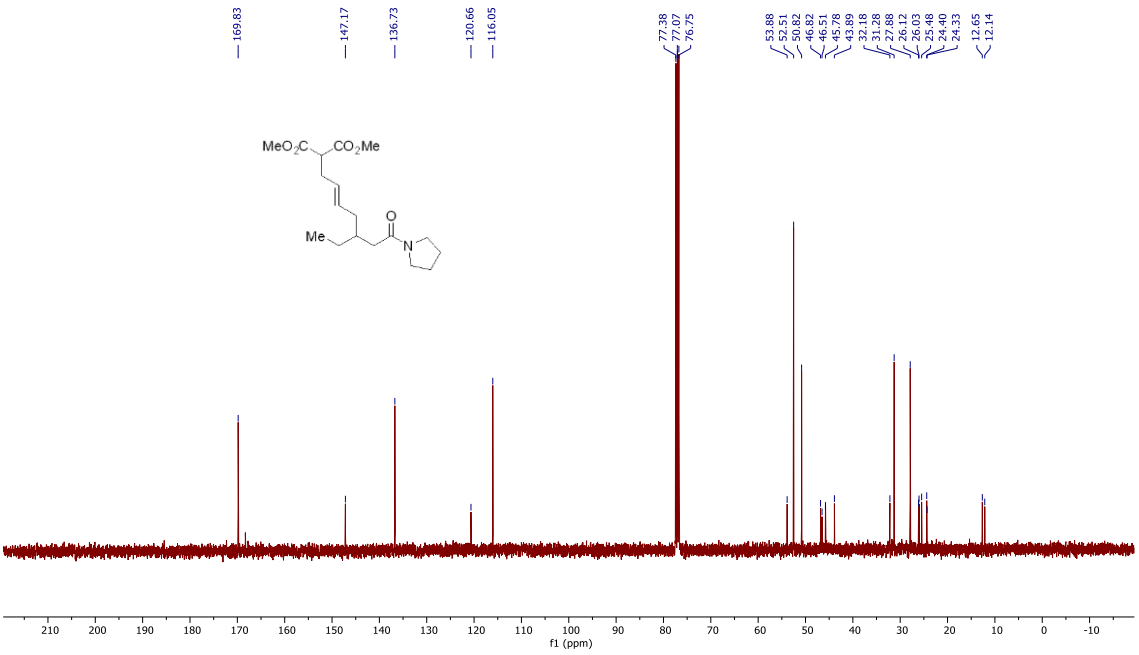
^{13}C{H} NMR of compound **3ea** in $CDCl_3$ at 101 MHz:



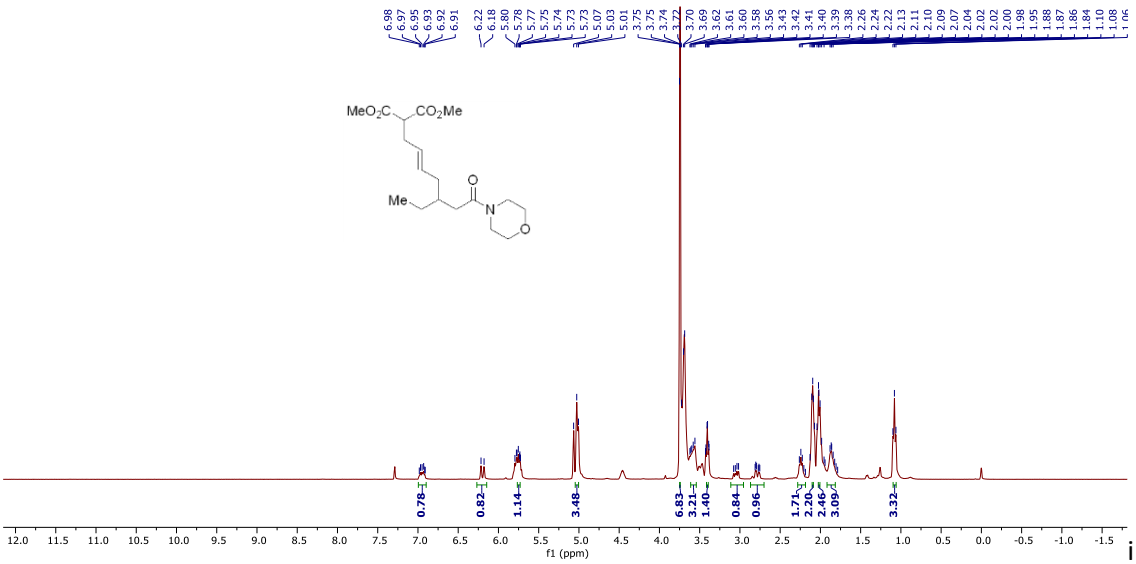
^{1}H NMR of compound **3fa** in $CDCl_3$ at 400 MHz:



^{13}C{H} NMR of compound **3fa** in $CDCl_3$ at 101 MHz:



^{1}H NMR of compound **3ga** in $CDCl_3$ at 400 MHz:



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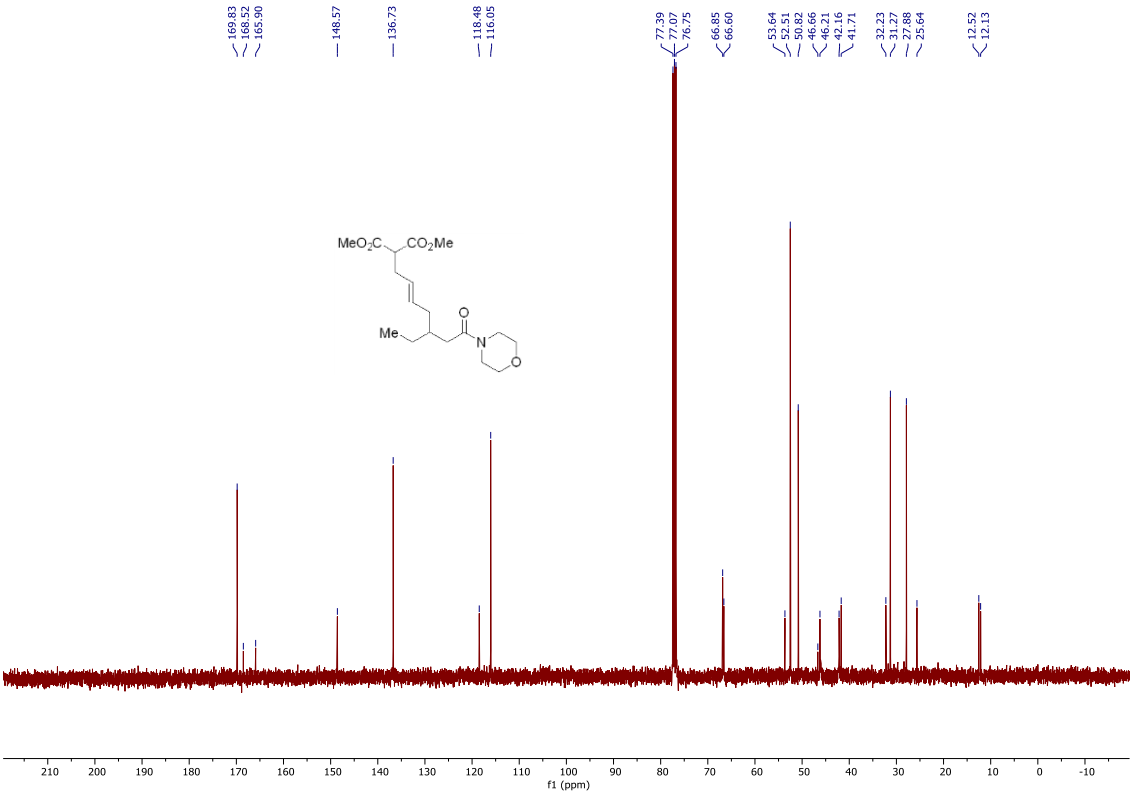
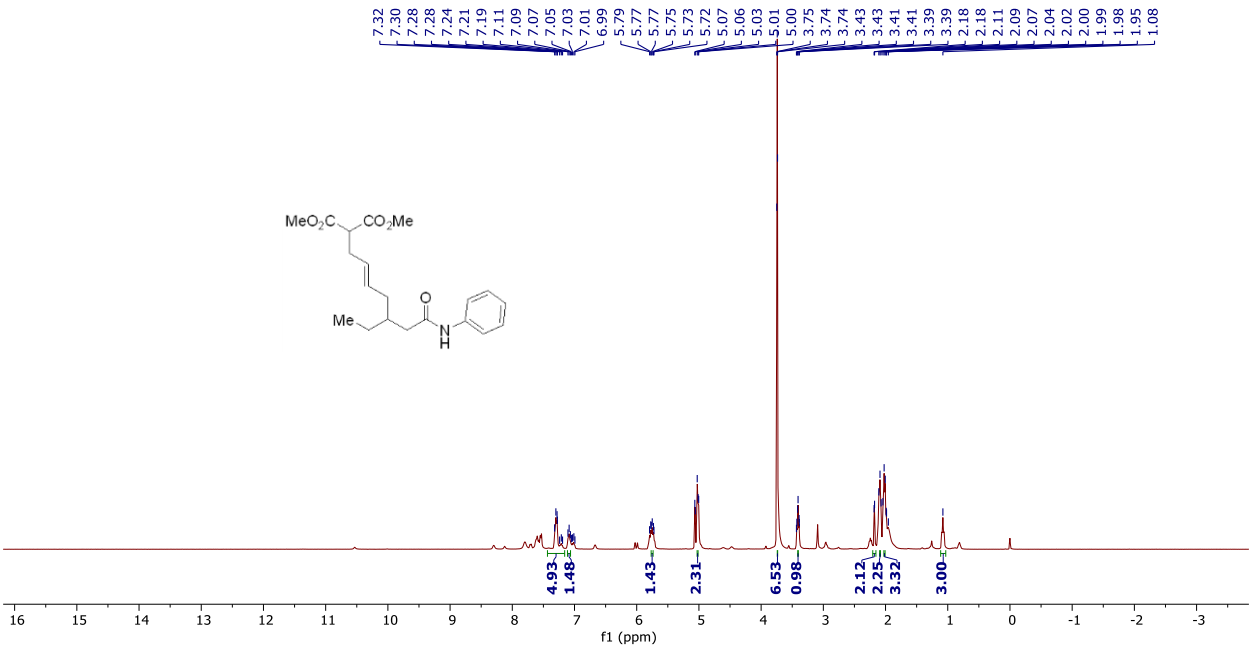
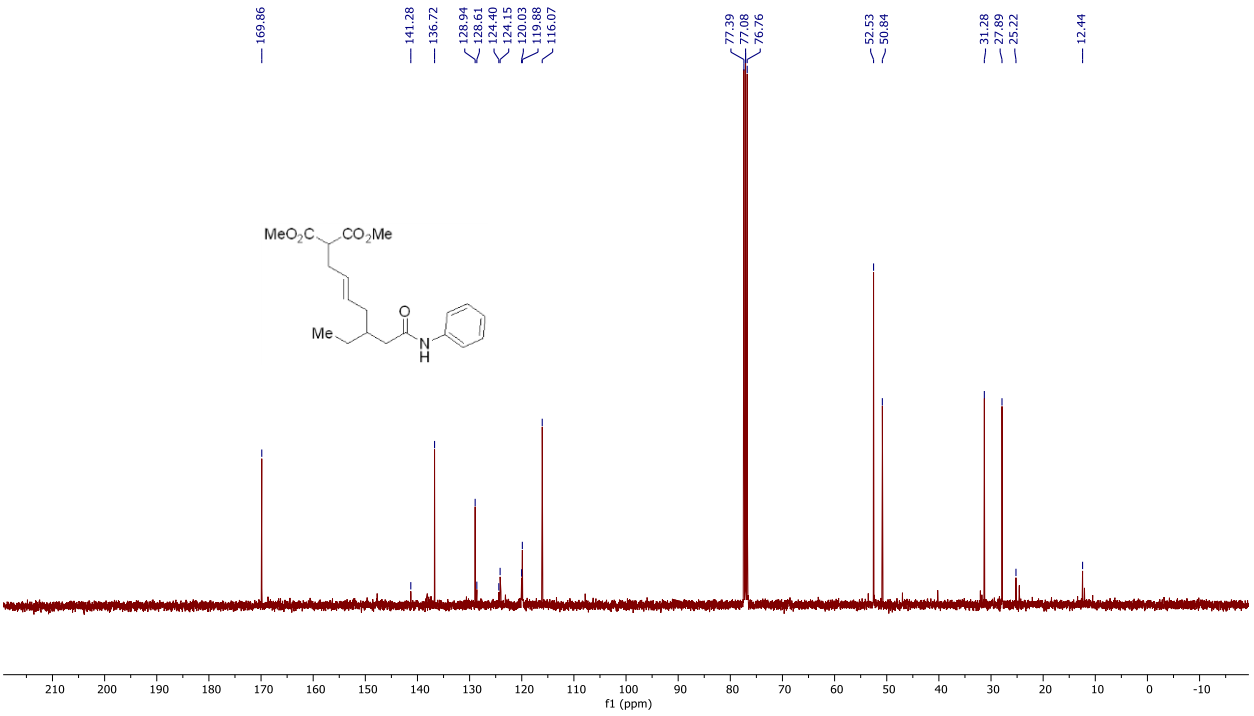
^{13}C{H} NMR of compound **3ga** in $CDCl_3$ at 101 MHz:



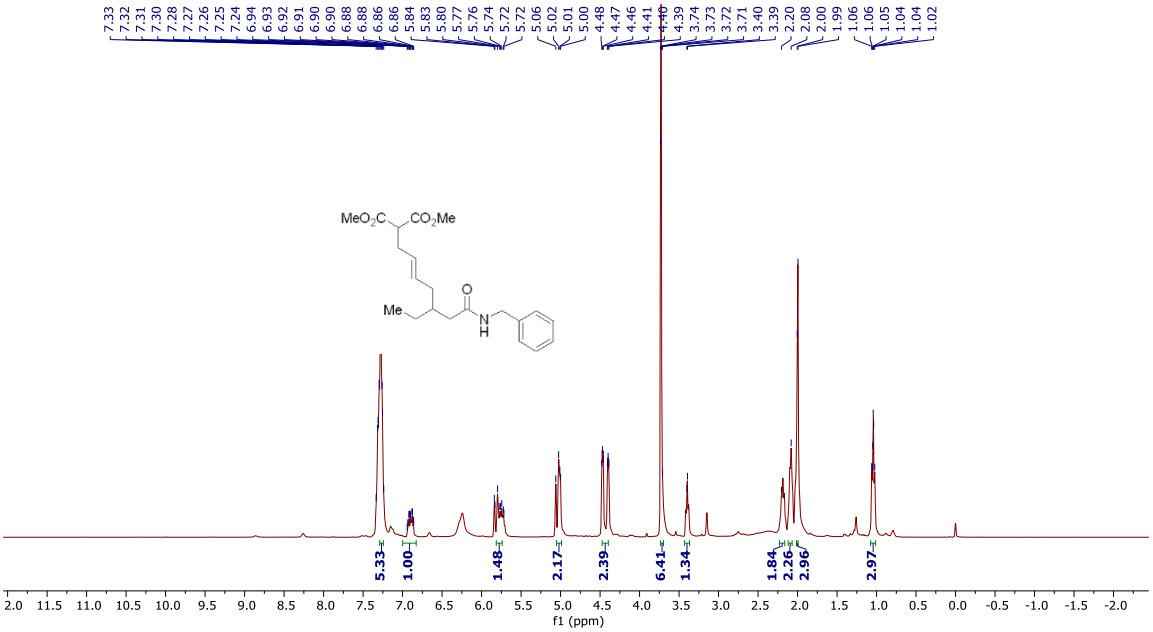
^{1}H NMR of compound **3ha** in $CDCl_3$ at 400 MHz:



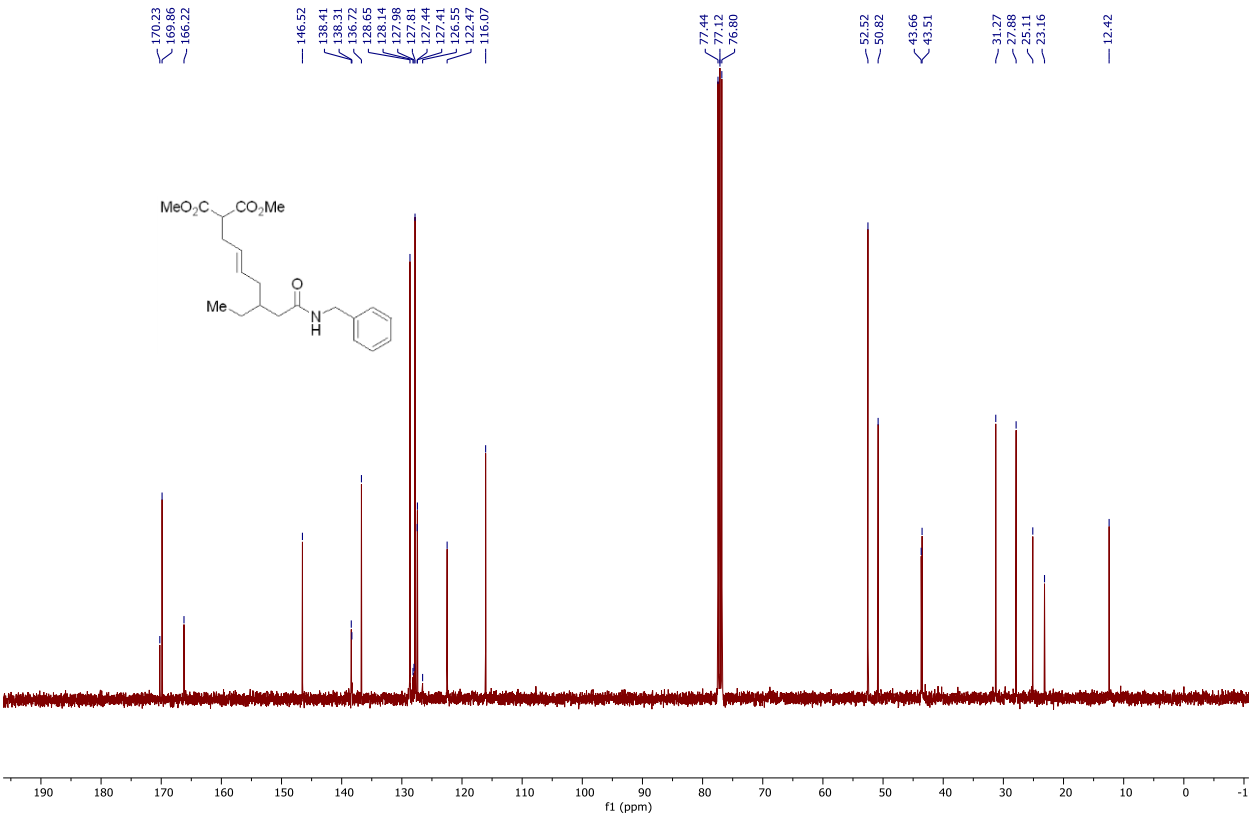
^{13}C{H} NMR of compound **3ha** in $CDCl_3$ at 400 MHz:



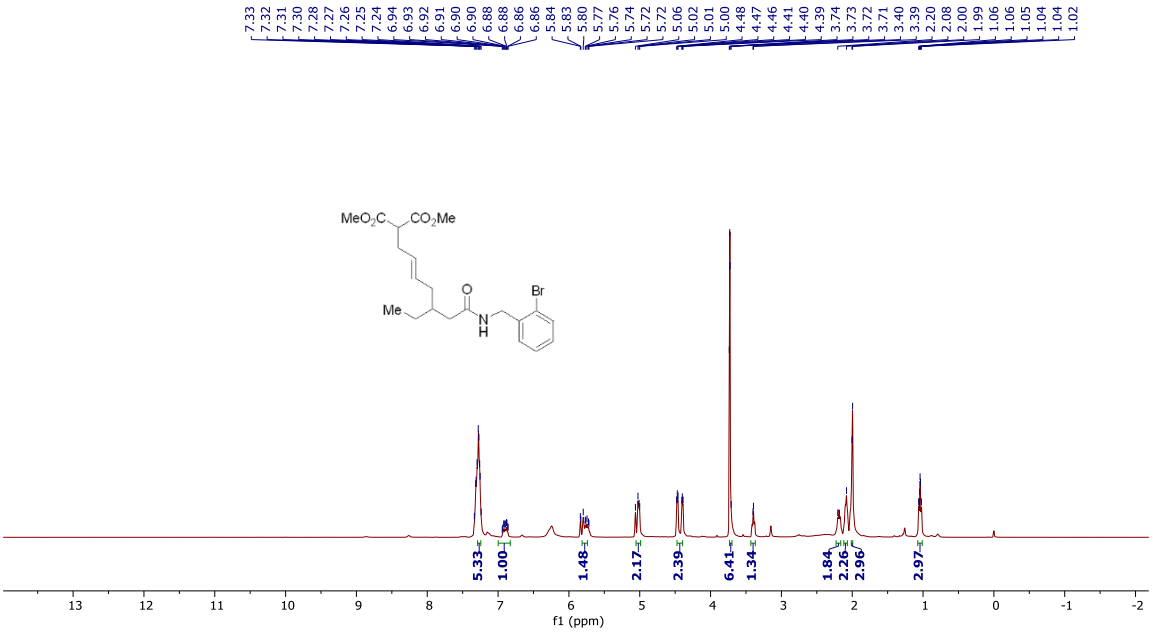
^{1}H NMR of compound **3ia** in $CDCl_3$ at 400 MHz



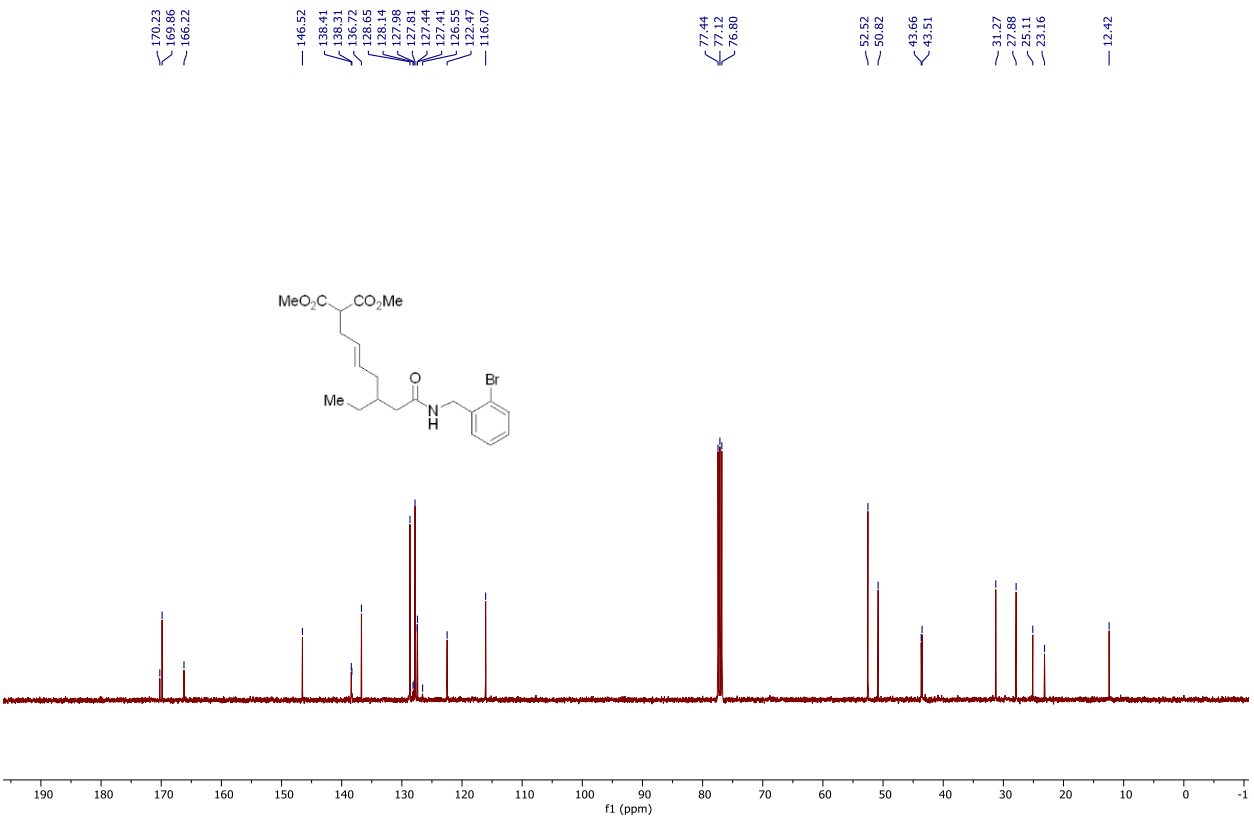
^{13}C{H} NMR of compound **3ia** in $CDCl_3$ at 400 MHz:



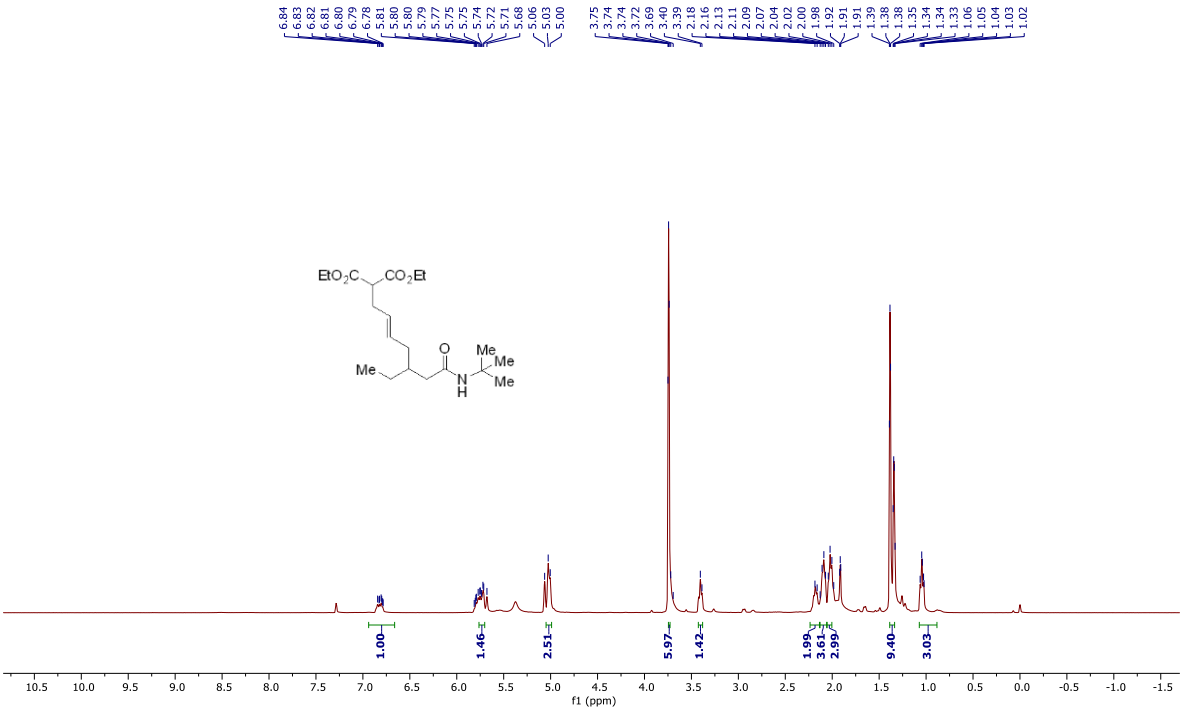
^{1}H NMR of compound **3ja** in $CDCl_3$ at 400 MHz



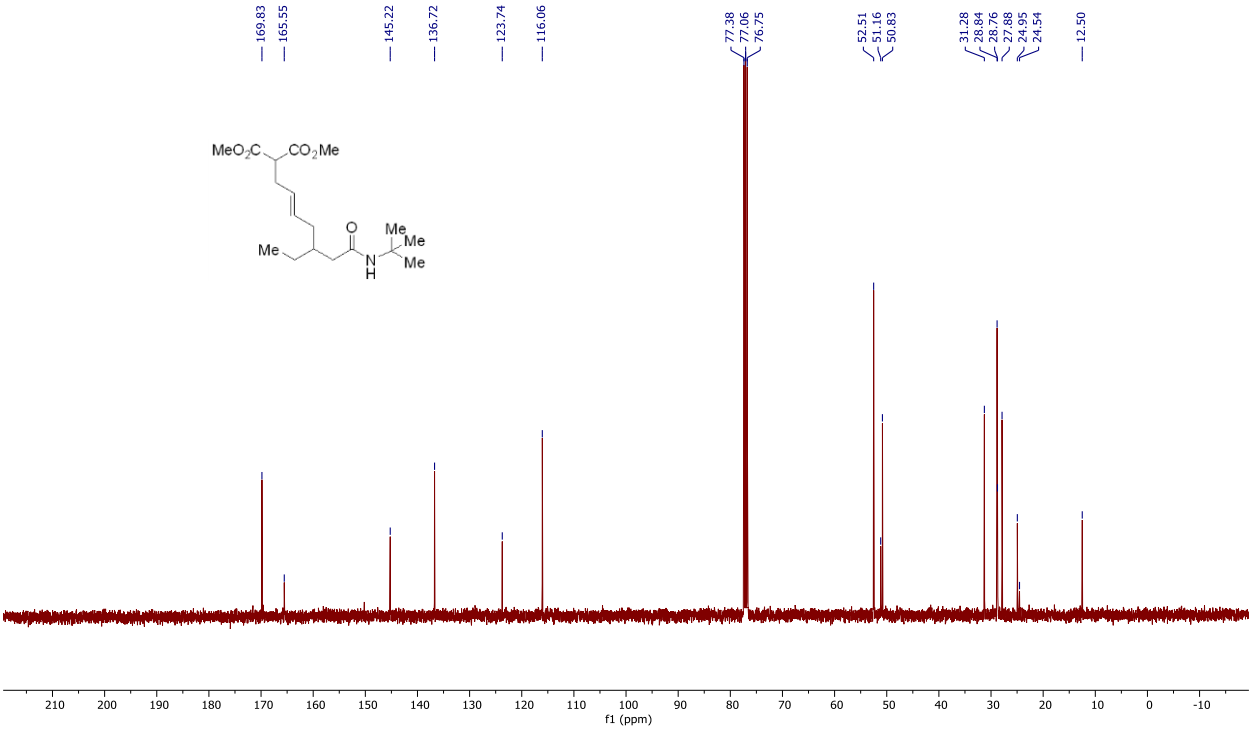
^{13}C{H} NMR of compound **3ja** in $CDCl_3$ at 400 MHz:



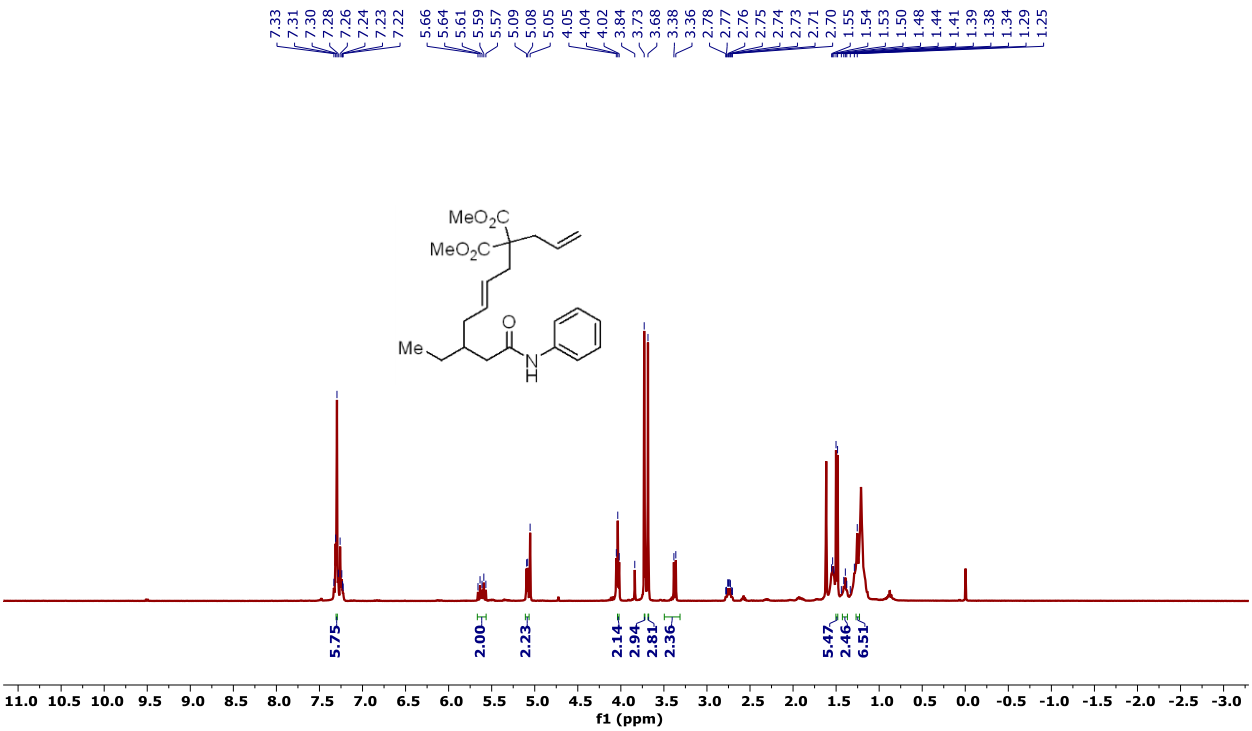
^{1}H NMR of compound **3ka** in $CDCl_3$ at 400 MHz



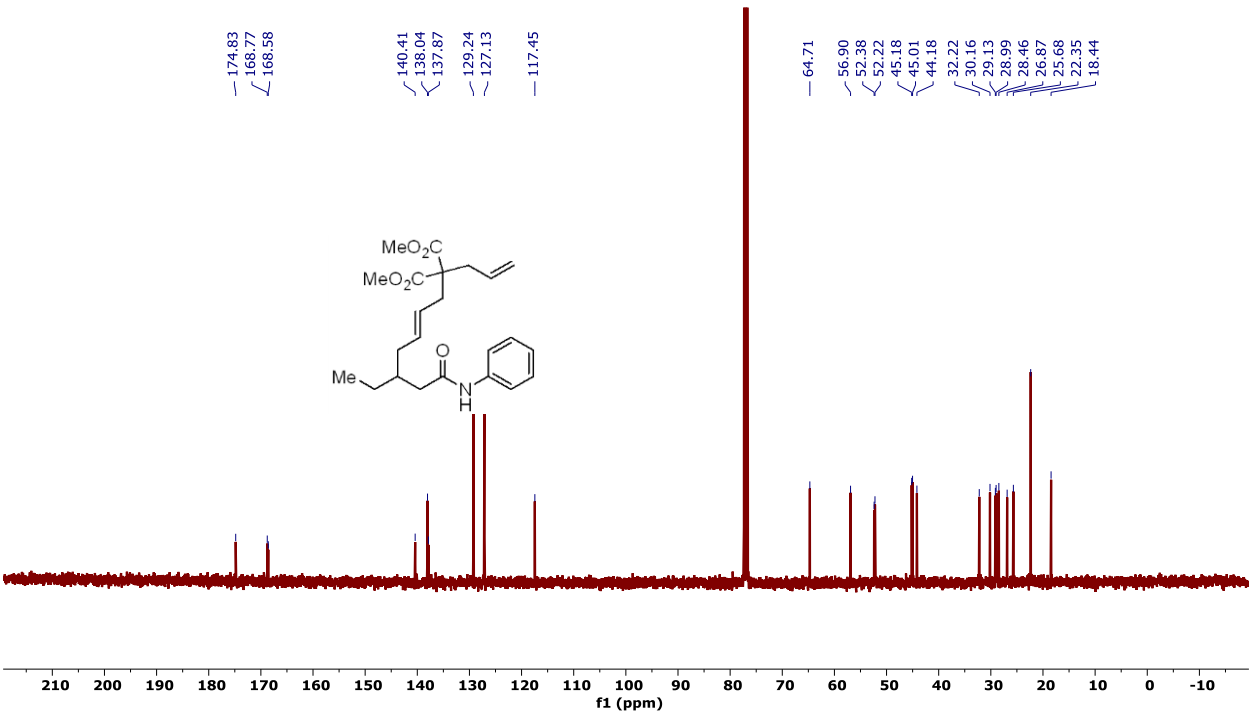
^{13}C{H} NMR of compound **3ja** in $CDCl_3$ at 400 MHz:



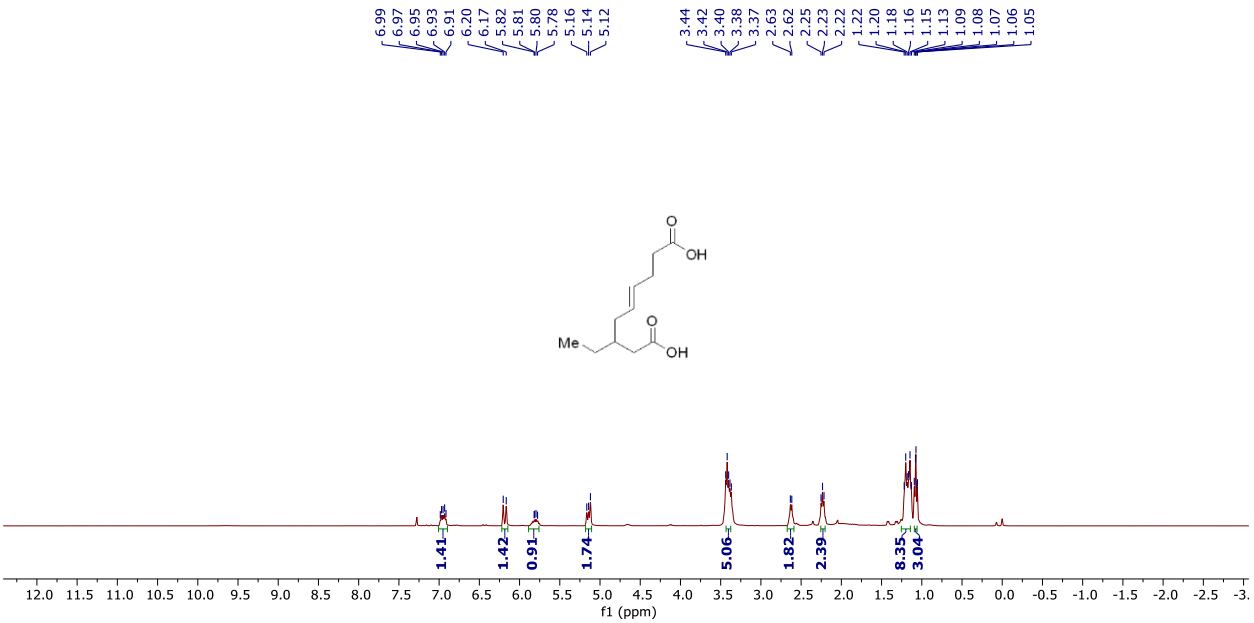
^{1}H NMR of compound **4** in $CDCl_3$ at 400 MHz:



^{13}C{H} NMR of compound **4** in $CDCl_3$ at 101 MHz:



^{1}H NMR of compound **5** in $CDCl_3$ at 400 MHz:



^{13}C{H} NMR of compound **5** in $CDCl_3$ at 400 MHz: