Electronic Supplementary Material (ESI) for Organic Chemistry Frontiers.

Palladium catalyzed remote-*meta* C–H functionalization of aniline scaffolds

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Supporting Information

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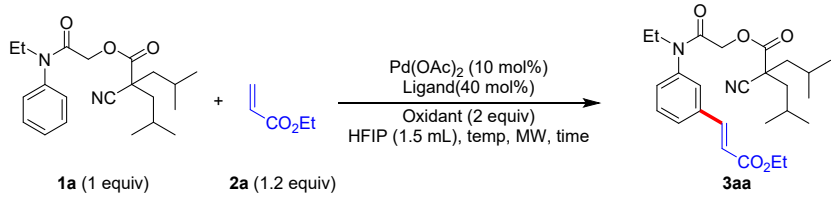
Experimental:

General: IR spectra were recorded on a Bruker Tensor 37 (FTIR) spectrophotometer. ^{1}H NMR spectra were recorded on Bruker Avance (400 or 600 MHz) spectrometer at 295 K in $CDCl_3$; chemical shifts (δ ppm) and coupling constants (Hz) are reported in standard fashion concerning either internal standard tetramethylsilane (TMS) (δ_H = 0.00 ppm) or $CDCl_3$ (δ_H = 7.26 ppm). $^{13}C\{^{1}H\}$ NMR spectra were recorded on Bruker Advance (100 or 150 MHz) spectrometer at RT in $CDCl_3$. Chemical shifts (δ ppm) are reported relative to $CDCl_3$ [δ_C = 77.00 ppm (central line of the triplet)]. In the ^{1}H-NMR, the following abbreviations were used throughout: s = singlet, d = doublet, t = triplet, q = quartet, qui = quintet, sept = septet, dd = doublet of doublet, m = multiplet and br. s = broad singlet. The assignment of signals was confirmed by ^{1}H, $^{13}C\{^{1}H\}$ CPD, and DEPT spectra. In the $^{13}C\{^{1}H\}$ NMR, the nature of carbons (C, CH, CH_2, and CH_3) was determined by recording the DEPT-135 spectra. High-resolution mass spectra (HR-MS) were recorded on an Agilent 6538 UHD Q-TOF electron spray ionization (ESI) mode and atmospheric pressure chemical ionization (APCI) modes. Melting points are recorded using Tempo and Mettler FP1 melting point apparatus in capillary tubes and are uncorrected. A single crystal of **3fa** was selected and mounted on an Oxford SuperNova, Dual, Cu at zero, Eos diffractometer. The crystal was kept at 298 K during data collection. Using Olex2, the structure was solved with the olex2.solve structure solution program using direct methods and refined with the olex2. refinement package using Gauss−Newton minimization. All small-scale reactions were carried out by using a Schlenk tube. Reactions were monitored by TLC on silica gel using a combination of hexane and ethyl acetate as eluents. Solvents were distilled before use; petroleum ether the boiling range of 60−80 °C was used. $Pd(OAc)_2$, Ac-Gly-OH, AgOAc and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) were purchased from Sigma-Aldrich and used as received. Olefin coupling partners, DMF, DCM, K_2CO_3, and HCl were purchased from Sigma-Aldrich/TCI/local sources and used as received. Acme's silica gel (60–120 mesh) was used for column chromatography (approximately 20 g per one gram of crude material).

With the best template system ($\mathbf{T_2}$) toward the formation of *meta*-olefination product **3aa**, the conditions of the reactions were varied to elevate the yields of **3aa** by taking substrate **1a** and coupling partner **2a**, and the details are as presented in Table S1. Firstly, the reaction was carried out by using $Pd(OAc)_2$ (10 mol%), *N*-Ac-Gly-OH (40 mol%), AgOAc (2 equiv), in HFIP (1.5 mL) under microwave irradiation at 85 °C for 30 minutes (entry 1, Table S1). Encouragingly, the product **3aa** was isolated in 25% of yield with 92:08 *meta*-selectivity. When the irradiation temperature has been increased to 100 °C for 30 minutes, consequently, the product **3aa** yield was enhanced to 40% (entry 2, Table S1). When the reaction time was increased to 45 minutes, the yield of the product was further improved to 55% (entry 3, Table S1). Only a trace amount of product **3aa** was afforded when the ligand *N*-Ac-Gly-OH was replaced with *N*-Boc-Gly-OH (entry 4, Table S1). While 30% yield of the product **3aa** was obtained in the presence of the ligand *N*-Boc-L-valine (entry 5, Table S1). Next, employing CF_3CO_2Ag as the oxidant instead of AgOAc, furnished **3aa** in a poor 37% of yield (entry 6, Table S1). There was no much improvement in the yield of **3aa** when AgO was used as an oxidant (entry 7, Table S1). To our delight, the reaction with 2.4 equiv of ethyl acrylate **2a**, afforded the product **3aa** in 78% of isolated yield with 92:08 regio-selectivity (entry 8, Table S1). On the other hand, the reaction in solvent mixture, such as DCE and HFIP (in 1:1 ratio) as the reaction medium, delivered the product **3aa** in moderate 45% of yield (entry 9, Table S1). Later the solvent HFIP was replaced with trifluoroethanol; unfortunately, the product **3aa** was not formed (entry 10, Table S1). Overall, based on the above screening study, the conditions from entry 8 of Table S1 determined to be the best to provide the requisite product **3aa**.

Table S1. Optimization studies.



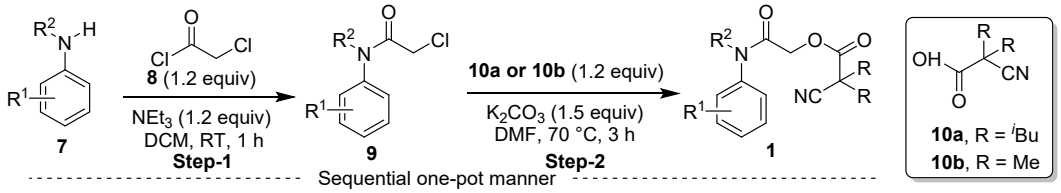
1a (1 equiv) **2a** (1.2 equiv) **3aa**

S. No	Oxidant	Ligand	Irradiation temperature (°C)	Time	Yield (*m*:o)[a]
1	AgOAc	*N*-Ac-Gly-OH	85	30 min	25% (93:08)
2	AgOAc	*N*-Ac-Gly-OH	100	30 min	40% (93:08)
3	AgOAc	*N*-Ac-Gly-OH	100	45 min	55% (93:08)
4	AgOAc	*N*-Boc-Gly-OH	100	45 min	Trace
5	AgOAc	*N*-Boc-L-valine	100	45 min	30% (90:10)

6	Ag(TFA)	*N*-Ac-Gly-OH	100	45 min	37% (93:08)
7	AgO	*N*-Ac-Gly-OH	100	45 min	35% (93:08)
8[b]	**AgOAc**	***N*-Ac-Gly-OH**	100	45 min	**78% (93:08)**
9[c]	AgOAc	*N*-Ac-Gly-OH	100	45 min	45% (93:08)
10[d]	AgOAc	*N*-Ac-Gly-OH	100	45 min	NR

[a]Isolated yields of **3aa**. [b]**2a** (2.4 equiv). [c]DCE and HFIP in 1:1 ratio. [d] TFE as solvent.

The required precursor **1** have been prepared according to the synthetic sequence, as depicted in Scheme S1.



Scheme S1. Synthesis of precursor **1**.

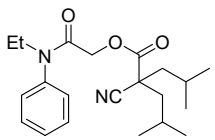
General Procedure-1 (GP-1) Preparation of Template Precursor (1):

Step 1: To an oven 25 mL round bottom flask charged with a magnetic stirring bar, were added aniline **7** (1 equiv), and chloroacetyl chloride **8** (1.1 equiv) in dichloromethane (15 mL) as the solvent. Then to the resulted solution, was added triethylamine (1.5 equiv) dropwise and stirred at the room temperature for 1 h. The reaction was monitored by TLC. Then, the reaction mixture was quenched by the addition of an aqueous NH_4Cl solution and extracted with dichloromethane (3×30 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and filtered. After evaporating the solvent under reduced pressure, the crude product **9** was directly subjected to the next step as follows.

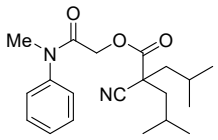
Step 2: To an oven dried 25 mL round bottom flask charged with magnetic stirring bar, were added above crude compound **9** (1 equiv), K_2CO_3 (1.5 equiv), *N*,*N*-dimethyl formamide (DMF) solvent (15 mL), and 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** or 2-cyano-2-methylpropanoic acid **10b** (1.2 equiv) under nitrogen atmosphere. The resultant reaction mixture was stirred at room temperature for 6 h. The reaction conversion was monitored by TLC. Then, the reaction mixture was quenched by the addition of an aqueous NH_4Cl solution and extracted with ethyl acetate (3×30 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and filtered. Evaporation of the solvent under reduced pressure

and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **1** (77 to 93%), as a colourless/brown liquid or solid.

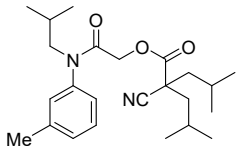
General Procedure-2 (GP-2) for Microwave Assisted *meta*-Selective C–H Olefination (3): An oven-dried 10 mL glass vial equipped with a magnetic stirring bar, was charged with template bearing substrate **1** (0.2 mmol), olefin **2** (0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol%), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (67 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL). The resultant reaction mixture was subjected to microwave irradiation 100 °C for 45 minutes. The reaction mixture was cooled to room temperature. The reaction mixture was diluted with ethyl acetate (15 mL) and filtered through a short pad of celite with an additional amount of ethyl acetate (15 mL). Evaporation of the solvent(s) under reduced pressure and purification of the residue by silica gel column chromatography using petroleum ether/ethyl acetate as the eluent furnished the *meta*-olefinated product **3** (20 to 80%), as viscous colourless/yellowish/brown liquid or solid.



2-(Ethyl(phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1a): GP-1 was carried out with compound **7a** (73 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h; followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72 mmol), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of the crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1a** (197 mg, 92%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7a**) = 0.70, *Rf*(**1a**) = 0.30, UV detection]. Melting point: 80-82 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2958, 1748, 1679, 1455, 1212, 762 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.37 (m, 3H), 7.28 – 7.20 (m, 2H), 4.41 (s, 2H), 3.76 (q, *J* = 7.2 Hz, 2H), 1.98 – 1.87 (m, 4H), 1.71 (dd, *J* = 16.3, 8.9 Hz, 2H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.07 – 1.01 (m, 6H), 0.93 – 0.88 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.5, 139.9, 130.1 (2C), 128.8, 128.3 (2C), 119.5, 62.8, 47.6, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{21}H_{31}N_2O_3$ 359.2329 Found 359.2342.

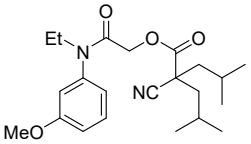


2-(Methyl(phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1b): GP-1 was carried out with compound **7b** (64 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1b** (192 mg, 93%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7b**) = 0.70, *Rf*(**1b**) = 0.30, UV detection]. Melting point: 105-107 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2956, 1747, 1679, 1432, 1213, 768 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.38 (m, 3H), 7.30 – 7.24 (m, 2H), 4.48 (s, 2H), 3.29 (s, 3H), 1.94 (ddd, *J* = 12.9, 9.5, 6.4 Hz, 4H), 1.75 – 1.66 (m, 2H), 1.05 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.3 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.6, 165.0, 141.7, 130.2 (2C), 128.7, 127.2 (2C), 119.5, 62.7, 47.5, 46.7 (2C), 37.4, 25.8 (2C), 23.3 (2C), 22.9 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{20}H_{29}N_2O_3$ 345.2173 Found 345.2170.

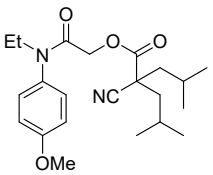


2-(Isobutyl(m-tolyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1c): GP-1 was carried out with compound **7c** (98 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1c** (211 mg, 88%) as a brown liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7c**) = 0.70, *Rf*(**1c**) = 0.3, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2960, 1748, 1683, 1455, 1214, 755 ν_{max} = cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.2 Hz, 1H), 7.21 (d, *J* = 7.6 Hz, 1H), 7.08 – 7.03 (m, 2H), 4.43 (s, 2H), 3.55 (d, *J* = 7.5 Hz, 2H), 2.40 (s,

3H), 1.96 – 1.85 (m, 4H), 1.77 – 1.66 (m, 3H), 1.04 (d, *J* = 6.4 Hz, 6H), 0.91 (dd, *J* = 6.5, 4.2 Hz, 12H) ppm. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 165.1, 140.5, 140.3, 129.8, 129.5, 128.6, 125.1, 119.6, 62.9, 56.3, 47.7, 46.7 (2C), 26.5, 25.8 (2C), 23.4 (2C), 23.0 (2C), 21.3 (2C), 19.9 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{24}H_{37}N_2O_3$ 401.2799 Found 401.2792.

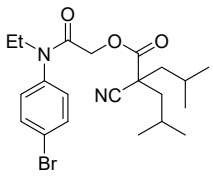


2-(Ethyl(3-methoxyphenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1d): GP-1 was carried out with compound **7d** (90 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1d** (207 mg, 89%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7d**) = 0.60, *Rf*(**1d**) = 0.20, UV detection]. Melting point: 71-73 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2956, 1748, 1679, 1595, 1446, 1280, 1213, 760 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.37 (t, *J* = 8.1 Hz, 1H), 6.95 (dd, *J* = 8.3, 2.3 Hz, 1H), 6.84 – 6.80 (m, 1H), 6.77 (dd, *J* = 2.2, 2.2 Hz, 1H), 4.46 (s, 2H), 3.84 (s, 3H), 3.75 (q, *J* = 7.2 Hz, 2H), 1.97 – 1.88 (m, 4H), 1.70 (t, *J* = 6.2 Hz, 2H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.05 (d, *J* = 6.3 Hz, 6H), 0.91 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.4, 160.7, 141.0, 130.7, 120.4, 119.5, 114.2, 114.0, 62.7, 55.4, 47.6, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{22}H_{33}N_2O_4$ 389.2435 Found 389.2448.

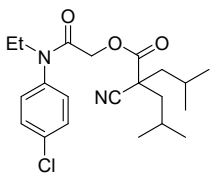


2-(Ethyl(4-methoxyphenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1e): GP-1 was carried out with compound **7e** (90 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude

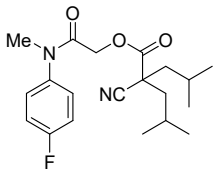
product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1e** (212 mg, 91%) as a brown liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7e**) = 0.60, *Rf*(**1e**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2957, 1748, 1678, 1435, 1213, 1128, 738 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.14 (d, *J* = 8.9 Hz, 2H), 6.95 (d, *J* = 8.9 Hz, 2H), 4.39 (s, 2H), 3.83 (s, 3H), 3.70 (q, *J* = 7.2 Hz, 2H), 1.95 – 1.82 (m, 4H), 1.70 (t, *J* = 8.1 Hz, 2H), 1.09 (t, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.8, 159.6, 132.3, 129.4 (2C), 119.5, 115.2 (2C), 62.8, 55.5, 47.6, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 22.9 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+Na)]^+$ Calcd for $C_{22}H_{32}N_2NaO_4$ 411.2254 Found 389.2269.



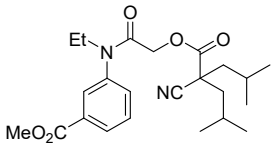
2-((4-Bromophenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1f): GP-1 was carried out with compound **7f** (119 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1f** (235 mg, 90%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7f**) = 0.50, *Rf*(**1f**) = 0.30, UV detection]. Melting point: 89-91 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2957, 1746, 1678, 1481, 1423, 1211, 1138, 834 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.5 Hz, 2H), 7.13 (d, *J* = 8.6 Hz, 2H), 4.38 (s, 2H), 3.72 (q, *J* = 7.2 Hz, 2H), 1.90 (ddd, *J* = 14.0, 10.9, 6.5 Hz, 4H), 1.72 – 1.65 (m, 2H), 1.09 (t, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 6H), 0.88 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.2, 138.9, 133.3 (2C), 130.0 (2C), 122.8, 119.4, 62.7, 47.5, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 22.9 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{21}H_{30}{}^{79}BrN_2O_3$ 437.1434 Found 437.1453; Calcd for $C_{21}H_{30}{}^{81}BrN_2O_3$ 439.1414 Found 439.1435.



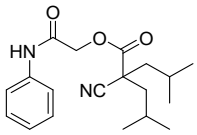
2-((4-Chlorophenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1g): GP-1 was carried out with compound **7g** (93 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1g** (207 mg, 88%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7g**) = 0.50, *Rf*(**1g**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2957, 1747, 1678, 1486, 1420, 1211, 838, 751 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.5 Hz, 2H), 7.14 (d, *J* = 8.6 Hz, 2H), 4.33 (s, 2H), 3.66 (q, *J* = 7.2 Hz, 2H), 1.91 – 1.76 (m, 4H), 1.73 – 1.57 (m, 2H), 1.04 (t, *J* = 7.2 Hz, 3H), 0.97 (d, *J* = 6.3 Hz, 6H), 0.83 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.5, 164.3, 138.4, 134.7, 130.3 (2C), 129.6 (2C), 119.4, 62.7, 47.5, 46.7 (2C), 44.2, 25.7 (2C), 23.2 (2C), 22.9 (2C), 12.7 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{21}H_{30}ClN_2O_3$ 393.1939 Found 393.1953.



2-((4-Fluorophenyl)(methyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1h): GP-1 was carried out with compound **7h** (83 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1h** (184 mg, 85%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7h**) = 0.50, *Rf*(**1h**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2956, 1736, 1681, 1464, 1277, 1215, 756 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.23 (m, 2H), 7.16 (dd, *J* = 8.4, 8.4 Hz, 2H), 4.45 (s, 2H), 3.27 (s, 3H), 1.98 – 1.88 (m, 4H), 1.76 – 1.70 (m, 2H), 1.05 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.3 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 165.1, 162.2 (d, $J_{C\text{-}F}$ = 249.9 Hz), 137.7 (d, $J_{C\text{-}F}$ = 2.9 Hz), 129.14 (2C, d, $J_{C\text{-}F}$ = 8.7 Hz), 119.4, 117.23 (d, $J_{C\text{-}F}$ = 22.8 Hz, 2C), 62.6, 47.5, 46.8 (2C), 37.6, 25.8 (2C), 23.3 (2C), 23.0 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{20}H_{28}FN_2O_3$ 363.2078 Found 363.2091.

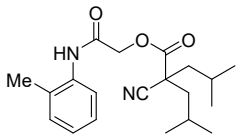


Methyl 3-(2-((2-cyano-2-isobutyl-4-methylpentanoyl)oxy)-*N*-ethylacetamido)benzoate (1i): GP-1 was carried out with compound **7i** (107 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1i** (224 mg, 90%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7i**) = 0.40, *Rf*(**1i**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 1729, 1680, 1440, 1286, 1211, 1146, 759 ν_{max} = cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 1H), 7.89 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.57 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.49 – 7.42 (m, 1H), 4.38 (s, 2H), 3.94 (s, 3H), 3.77 (q, *J* = 7.1 Hz, 2H), 1.94 – 1.87 (m, 4H), 1.71 (dd, *J* = 10.6, 5.8 Hz, 2H), 1.11 (t, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 6H), 0.88 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 165.7, 164.3, 140.2, 132.8, 132.3, 130.3, 129.9, 129.3, 119.4, 62.7, 52.5, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{23}H_{33}N_2O_5$ 417.2384 Found 417.2395.

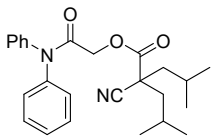


2-Oxo-2-(phenylamino)ethyl 2-cyano-2-isobutyl-4-methylpentanoate (1j): GP-1 was carried out with compound **7j** (59 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1j** (188 mg, 90%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7j**) = 0.50, *Rf*(**1j**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 3312, 2959, 1751,

1685, 1604, 1543, 1210, 1151, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.66 – 7.56 (m, 2H), 7.40 – 7.29 (m, 2H), 7.16 (dd, *J* = 10.7, 4.2 Hz, 1H), 4.76 (s, 2H), 1.95 – 1.87 (m, 4H), 1.80 (dd, *J* = 10.5, 6.2 Hz, 2H), 1.07 (d, *J* = 6.4 Hz, 6H), 0.91 (d, *J* = 6.3 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.1, 163.5, 136.7, 129.1 (2C), 125.0, 119.8, 119.7 (2C), 64.2, 47.6, 46.9 (2C), 26.0 (2C), 23.3 (2C), 22.5 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{19}H_{27}N_2O_3$ 331.2016 Found 331.2027.

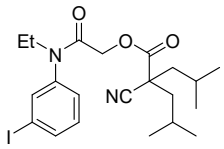


2-Oxo-2-(*o*-tolylamino)ethyl 2-cyano-2-isobutyl-4-methylpentanoate (1k): GP-1 was carried out with compound **7k** (64 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1k** (159 mg, 77%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7k**) = 0.50, *Rf*(**1k**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2958, 1751, 1683, 1530, 1456, 1207, 1149, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.97 – 7.73 (m, 2H), 7.20 – 7.12 (m, 2H), 7.04 (dd, *J* = 7.4, 7.4 Hz, 1H), 4.73 (s, 2H), 2.27 (s, 3H), 1.84 (ddd, *J* = 10.3, 9.6, 6.1 Hz, 4H), 1.71 (t, *J* = 6.0 Hz, 2H), 0.99 (d, *J* = 6.3 Hz, 6H), 0.84 (d, *J* = 6.3 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 168.4, 163.5, 134.4, 130.6, 128.9, 126.7, 125.6, 122.5, 119.3, 64.5, 47.30, 47.29 (2C), 26.0 (2C), 23.3 (2C), 22.5 (2C), 17.7 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{20}H_{29}N_2O_3$ 345.2173 Found 345.2184.

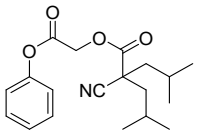


2-(Diphenylamino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1l): GP-1 was carried out with compound **7l** (101 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product

1l (204 mg, 84%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7l**) = 0.40, *Rf*(**1l**) = 0.20, UV detection]. Melting point: 110-112 °C. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2957, 1747, 1691, 1389, 1213, 1150, 755, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 5H), 4.62 (s, 1H), 1.99 – 1.87 (m, 2H), 1.72 (d, *J* = 7.4 Hz, 1H), 1.05 (d, *J* = 6.4 Hz, 3H), 0.91 (d, *J* = 6.3 Hz, 3H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.56, 164.87, 119.46, 77.00, 63.20, 47.51, 46.59, 25.73, 23.29, 22.96. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{25}H_{31}N_2O_3$ 407.2329 Found 407.2342.

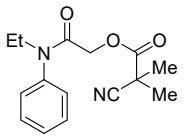


2-(Ethyl(3-iodophenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (1m): GP-1 was carried out with compound **7l** (147 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1m** (241 mg, 83%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7m**) = 0.50, *Rf*(**1m**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): ν_{max} = 2957, 1748, 1681, 1507, 1216, 1130, 846, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 7.4 Hz, 1H), 7.55 (d, *J* = 1.6 Hz, 1H), 7.21 – 7.10 (m, 2H), 4.35 (s, 2H), 3.67 (q, *J* = 7.2 Hz, 2H), 1.85 (dt, *J* = 12.6, 5.0 Hz, 4H), 1.75 – 1.55 (m, 2H), 1.05 (t, *J* = 7.2 Hz, 3H), 0.98 (d, *J* = 6.3 Hz, 6H), 0.84 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.3, 141.2, 138.0, 137.2, 131.5, 127.9, 119.5, 94.8, 62.8, 47.6, 46.7 (2C), 44.5, 25.8 (2C), 23.4 (2C), 23.1 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{21}H_{30}IN_2O_3$ 485.1296 Found 485.1311.

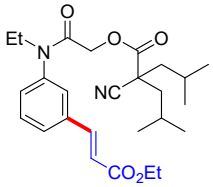


2-Oxo-2-phenoxyethyl 2-cyano-2-isobutyl-4-methylpentanoate (1n): GP-1 was carried out with compound **7n** (58 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h followed by 2-cyano-

2-isobutyl-4-methylpentanoic acid **10a** (145 mg, 0.72), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1n** (174 mg, 88%) as a colourless liquid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7n**) = 0.50, *Rf*(**1n**) = 0.30, UV detection]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 7.34 (m, 2H), 7.31 – 7.21 (m, 1H), 7.15 – 7.07 (m, 2H), 4.95 (s, 2H), 1.99 – 1.84 (m, 4H), 1.75 (t, *J* = 8.2 Hz, 2H), 1.06 (d, *J* = 6.4 Hz, 6H), 0.92 (d, *J* = 6.3 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 169.6, 165.2, 149.8, 129.6, 126.4, 121.1, 119.2, 61.7, 47.4, 47.1, 25.8, 23.2, 22.9 ppm.

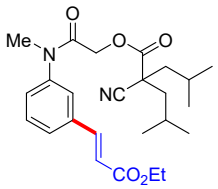


2-(Ethyl(phenyl)amino)-2-oxoethyl 2-cyano-2-methylpropanoate (1o): GP-1 was carried out with compound **7a** (73 mg, 0.6 mmol), chloroacetyl chloride **9** (80 mg, 0.72 mmol), NEt_3 (72 mg, 0.72 mmol), dichloromethane (10 mL) at room temperature for 1 h; followed by 2-cyano-2-methylpropanoic acid **10b** (81 mg, 0.72 mmol), K_2CO_3 (124 mg, 0.9 mmol), *N*,*N*-Dimethyl formamide (DMF) (5 mL) at 70 °C for 4 h. Purification of the crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 85/10), furnished the product **1o** (154 mg, 94%) as a white solid. [TLC (petroleum ether/ethyl acetate 90:10, *Rf*(**7a**) = 0.70, *Rf*(**1o**) = 0.30, UV detection]. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.39 (m, 3H), 7.23 (dd, *J* = 6.8, 1.6 Hz, 2H), 4.41 (s, 2H), 3.73 (q, *J* = 7.2 Hz, 2H), 1.66 (s, 6H), 1.11 (t, *J* = 7.2 Hz, 3H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 169.4, 164.6, 139.6, 130.1 (2C), 129.9, 128.9, 128.7, 128.2 (2C), 128.1, 120.5, 62.9, 44.2, 38.5, 24.7 (2C), 12.7 ppm.

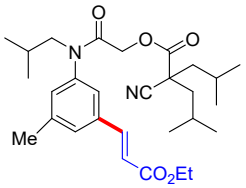


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3aa): GP-2 was carried out with the substrate **1a** (71 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of the crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3aa**

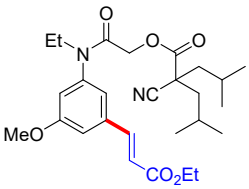
(68 mg, 75%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1a**) = 0.50, *Rf*(**3aa**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 1682, 1439, 1265, 1169, 758 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.38 (dd, *J* = 1.7, 1.7 Hz, 1H), 7.28 – 7.24 (m, 1H), 6.47 (d, *J* = 16.0 Hz, 1H), 4.40 (s, 2H), 4.27 (q, *J* = 7.1 Hz, 2H), 3.76 (q, *J* = 7.2 Hz, 2H), 1.94 – 1.87 (m, 4H), 1.72 – 1.68 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.4, 164.3, 142.6, 140.7, 136.7, 130.7, 129.8, 128.1, 127.6, 120.2, 119.5, 62.7, 60.7, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.2, 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{26}H_{37}N_2O_5$ 457.2697 Found 457.2713.



(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)(methyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ba): GP-2 was carried out with the substrate **1b** (69 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ba** (69 mg, 78%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1b**) = 0.50, *Rf*(**3ba**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 1744, 1683, 1441, 1271, 1168, 1030, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 16.0 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.49 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.42 (dd, *J* = 1.8, 1.8 Hz, 1H), 7.31 – 7.26 (m, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 4.47 (s, 2H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.29 (s, 3H), 1.92 (dt, *J* = 12.6, 5.0 Hz, 4H), 1.71 (td, *J* = 8.8, 5.3 Hz, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.4 Hz, 6H), 0.90 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.6, 166.4, 165.0, 142.5, 130.8, 128.7, 128.7, 128.1, 126.5, 120.3, 120.3, 119.5, 62.6, 60.8, 47.6, 46.8 (2C), 37.5, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.2 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{25}H_{35}N_2O_5$ 443.2540 Found 443.2535.

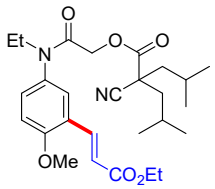


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)-5-methylphenyl)(isobutyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ca): GP-2 was carried out with the substrate **1c** (80 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ca** (75 mg, 76%), as a yellowish solid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1c**) = 0.50, *Rf*(**3ca**) = 0.30, UV detection]. Melting point: 98-100 °C. IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 1688, 1450, 1270, 1164, 1037, 755 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 1H), 7.36 (s, 1H), 7.19 (s, 1H), 7.07 (s, 1H), 6.44 (d, *J* = 16.0 Hz, 1H), 4.42 (s, 2H), 4.28 (t, *J* = 7.1 Hz, 2H), 3.54 (d, *J* = 7.5 Hz, 2H), 2.41 (s, 3H), 1.93 – 1.87 (m, 4H), 1.75 – 1.64 (m, 4H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.03 (d, *J* = 6.4 Hz, 6H), 0.90 (dd, *J* = 8.0, 6.5 Hz, 12H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.5, 164.9, 142.9, 141.2, 140.9, 136.4, 130.2, 128.8, 124.6, 119.9, 119.5, 62.8, 60.7, 56.3, 47.6, 46.7 (2C), 26.5, 25.8 (2C), 23.3 (2C), 23.0 (2C), 21.2, 19.9 (2C), 14.2 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{29}H_{43}N_2O_5$ 499.3166 Found 499.3184.

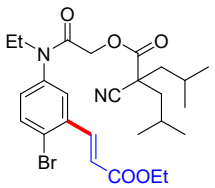


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)-5-methoxyphenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3da): GP-2 was carried out with the substrate **1d** (78 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3da** (68 mg, 70%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1d**) = 0.40, *Rf*(**3da**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1745, 1680, 1592, 1452, 1213, 1168, 699 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 1H), 7.36 (t, *J* = 8.1

Hz, 1H), 7.08 (s, 1H), 6.99 – 6.95 (m, 51H), 6.82 – 6.74 (m, 2H), 6.46 (d, J = 16.0 Hz, 1H), 4.46 (s, 2H), 4.28 (q, J = 7.2 Hz, 2H), 3.87 (d, J = 3.8 Hz, 3H), 3.84 (s, 2H), 3.75 (dd, J = 7.2, 1.1 Hz, 3H), 1.92 (dt, J = 11.2, 5.2 Hz, 4H), 1.71 (dd, J = 16.3, 8.8 Hz, 2H), 1.35 (t, J = 7.1 Hz, 3H), 1.05 (d, J = 6.4 Hz, 6H), 0.91 (d, J = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.3, 164.3, 161.0, 142.7, 141.6, 137.4, 120.4, 120.0, 119.5, 115.6, 113.2, 62.7, 60.8, 55.6, 47.6, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.2, 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{27}H_{39}N_2O_6$ 487.2803 Found 487.2821.

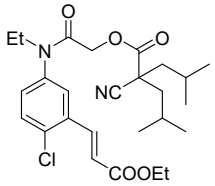


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)-4-methoxyphenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ea): GP-2 was carried out with the substrate **1e** (78 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ea** (74 mg, 76%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ea**) = 0.20, UV detection]. ^1H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, J = 16.2 Hz, 1H), 7.35 (d, J = 2.6 Hz, 1H), 7.24 – 7.17 (m, 1H), 6.98 (d, J = 8.7 Hz, 1H), 6.54 (d, J = 16.2 Hz, 1H), 4.41 (s, 2H), 4.27 (q, J = 7.1 Hz, 2H), 3.93 (s, 3H), 3.72 (q, J = 7.2 Hz, 2H), 1.96 – 1.87 (m, 4H), 1.74 – 1.67 (m, 2H), 1.34 (t, J = 7.1 Hz, 3H), 1.11 (t, J = 7.2 Hz, 3H), 1.04 (d, J = 6.3 Hz, 6H), 0.90 (d, J = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.9, 164.7, 158.1, 138.3, 132.5, 130.9, 128.4, 125.1, 120.6, 119.5, 112.4, 62.7, 60.6, 55.8, 47.6, 46.7 (2C), 44.2, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.3, 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{27}H_{39}N_2O_6$ 487.2803 Found 487.2819.



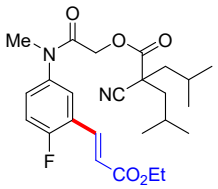
(*E*)-2-((4-bromo-3-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3fa): GP-2 was carried out with the substrate **1f** (87

mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol%), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3fa** (69 mg, 65%), as a white crystallin solid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1f**) = 0.50, *Rf*(**3fa**) = 0.30, UV detection]. Melting point: 121-123 °C. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1684, 1463, 1270, 1270, 1279 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 16.0 Hz, 1H), 7.71 (d, *J* = 8.4 Hz, 1H), 7.47 (d, *J* = 2.5 Hz, 1H), 7.13 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.41 (d, *J* = 15.9 Hz, 1H), 4.41 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.74 (q, *J* = 7.1 Hz, 2H), 1.90 (dt, *J* = 11.4, 5.0 Hz, 4H), 1.75 – 1.68 (m, 2H), 1.34 (t, *J* = 7.1 Hz, 3H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.2 Hz, 6H), 0.89 (d, *J* = 6.1 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 165.8, 164.2, 141.4, 139.8, 136.7, 135.2, 130.7, 127.4, 125.2, 122.9, 119.4, 62.7, 60.9, 47.5, 46.8 (2C), 44.4, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.2, 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{26}H_{36}{}^{79}BrN_2O_5$ 535.1802 Found 535.1795; Calcd for $C_{26}H_{36}{}^{81}BrN_2O_5$ 537.1782 Found 537.1782.

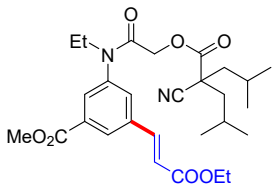


(*E*)-2-((4-chloro-3-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ga): GP-2 was carried out with the substrate **1g** (78 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol%), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ga** (60 mg, 61%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1g**) = 0.50, *Rf*(**3ga**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2960, 1720, 1683, 1465, 1263, 1173, 1030, 733 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (d, *J* = 16.1 Hz, 1H), 7.46 (d, *J* = 8.4 Hz, 1H), 7.43 (d, *J* = 2.5 Hz, 1H), 7.15 (dd, *J* = 8.4, 2.5 Hz, 1H), 6.39 (d, *J* = 16.0 Hz, 1H), 4.34 (s, 2H), 4.23 (q, *J* = 7.1 Hz, 2H), 3.68 (q, *J* = 7.2 Hz, 2H), 1.89 – 1.81 (m, 4H), 1.64 (dd, *J* = 16.3, 8.9 Hz, 2H), 1.28 (t, *J* = 7.1 Hz, 3H), 1.06 (t, *J* = 7.1 Hz, 3H), 0.98 (d, *J* = 6.3 Hz, 6H), 0.83 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.6, 165.9, 164.3, 139.1, 138.8, 131.9, 130.5, 129.7, 127.3, 122.7, 119.4, 62.7, 60.9, 47.5, 46.8 (2C), 44.4, 25.8

(2C), 23.3 (2C), 23.0 (2C), 14.2, 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{26}H_{36}ClN_2O_5$ 491.2307 Found 491.2299.

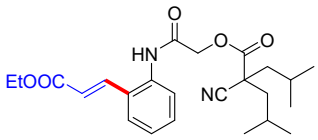


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)-4-fluorophenyl)(methyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ha): GP-2 was carried out with the substrate **1h** (72 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ha** (57 mg, 62%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1h**) = 0.50, *Rf*(**3ha**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1687, 1493, 1493, 1272, 1213, 1172, 756 cm^{-1}. ^1H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, *J* = 16.2 Hz, 1H), 7.46 (dd, *J* = 6.0, 2.3 Hz, 1H), 7.28 (dd, *J* = 7.1, 4.2 Hz, 1H), 7.21 (t, *J* = 9.0 Hz, 1H), 6.57 (d, *J* = 16.2 Hz, 1H), 4.46 (s, 2H), 4.31 – 4.27 (m, 2H), 3.27 (s, 3H), 1.92 (dd, *J* = 15.6, 6.4 Hz, 4H), 1.73 – 1.69 (m, 2H), 1.35 (d, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.4 Hz, 6H), 0.90 (d, *J* = 6.2 Hz, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.7, 166.2, 165.0, 160.6 (d, *J* = 258.4 Hz), 138.2, 135.4, 130.3 (d, *J* = 8.4 Hz), 127.8, 124.5 (d, *J* = 13.1 Hz), 122.8 (d, *J* = 5.8 Hz), 119.4, 118.2 (d, *J* = 23.9 Hz), 62.5, 60.9, 47.5, 46.8 (2C), 37.6, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.2 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{25}H_{34}FN_2O_5$ 461.2446 Found 461.2461.

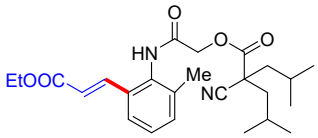


Methyl (*E*)-3-(2-((2-cyano-2-isobutyl-4-methylpentanoyl)oxy)-*N*-ethylacetamido)-5-(3-ethoxy-3-oxoprop-1-en-1-yl)benzoate (3ia): GP-2 was carried out with the substrate **1i** (83 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under

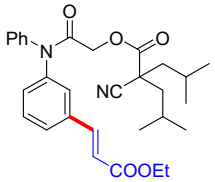
microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ia** (59 mg, 57%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1i**) = 0.40, *Rf*(**3ia**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 1746, 1668, 1254, 1214, 749 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (s, 1H), 7.91 – 7.87 (m, 1H), 7.69 (d, *J* = 16.1 Hz, 1H), 7.57 (t, *J* = 1.7 Hz, 1H), 6.56 (d, *J* = 16.0 Hz, 1H), 4.40 (s, 2H), 4.29 (q, *J* = 7.1 Hz, 2H), 3.97 (s, 3H), 3.78 (d, *J* = 7.3 Hz, 2H), 1.91 (dd, *J* = 7.8, 4.4 Hz, 4H), 1.70 (d, *J* = 7.4 Hz, 2H), 1.35 (t, *J* = 7.1 Hz, 3H), 1.13 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.3 Hz, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$) δ 169.6, 166.1, 165.2, 164.2, 141.5, 141.1, 137.2, 132.8, 131.7, 130.3, 128.9, 121.6, 119.4, 62.6, 60.9, 52.7, 47.6, 46.8, 44.5, 25.8, 23.3, 23.0, 14.2, 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{28}H_{39}N_2O_7$ 515.2752 Found 515.2742.



(*E*)-2-((2-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ja): GP-2 was carried out with the substrate **1j** (66 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ja** (24 mg, 28%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1j**) = 0.50, *Rf*(**3ja**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2960, 1749, 1703, 1308, 1264, 1158, 758 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (s, 1H), 7.71 (d, *J* = 15.8 Hz, 1H), 7.65 – 7.59 (m, 1H), 7.51 (d, *J* = 7.9 Hz, 1H), 7.34 (ddd, *J* = 7.9, 7.9, 1.4 Hz, 1H), 7.25 – 7.14 (m, 1H), 6.34 (d, *J* = 15.8 Hz, 1H), 4.77 (s, 2H), 4.27 – 4.16 (m, 2H), 1.92 – 1.82 (m, 4H), 1.72 (s, 2H), 1.26 (t, *J* = 7.1 Hz, 4H), 1.00 (dd, *J* = 7.4, 4.3 Hz, 7H), 0.85 (dd, *J* = 6.2, 2.3 Hz, 7H) ppm. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) δ 168.7, 166.8, 166.3, 164.5, 143.8, 143.6, 138.6, 137.3, 134.2, 130.6, 129.6, 129.0, 128.7, 127.4, 126.7, 125.3, 124.5, 121.5, 119.8, 119.3, 119.1, 117.5, 64.3, 64.1, 60.6, 60.5, 47.6, 47.0, 46.8, 26.0, 26.0, 23.3, 22.6, 14.2 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{24}H_{33}N_2O_5$ 429.2384 Found 429.2381.

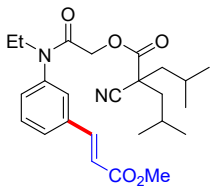


(*E*)-2-((2-(3-ethoxy-3-oxoprop-1-en-1-yl)-6-methylphenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ka): GP-2 was carried out with the substrate **1k** (69 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ka** (17 mg, 20%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1k**) = 0.50, *Rf*(**3ka**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2960, 1748, 1704, 1528, 1308, 1156, 1033, 761 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, *J* = 15.9 Hz, 1H), 7.62 (s, 1H), 7.49 – 7.42 (m, 1H), 7.26 – 7.20 (m, 2H), 6.35 (d, *J* = 15.9 Hz, 1H), 4.81 (s, 2H), 4.17 (q, *J* = 7.1 Hz, 2H), 2.22 (s, 3H), 1.88 – 1.80 (m, 4H), 1.71 (dt, *J* = 8.2, 4.1 Hz, 2H), 1.25 (t, *J* = 7.1 Hz, 4H), 1.01 (d, *J* = 6.4 Hz, 6H), 0.88 (d, *J* = 6.3 Hz, 6H) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{25}H_{35}N_2O_5$ 443.2540 Found 443.2539.

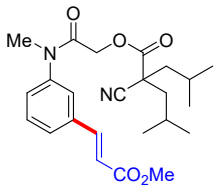


(*E*)-2-((3-(3-ethoxy-3-oxoprop-1-en-1-yl)phenyl)(phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3la): GP-2 was carried out with the substrate **1l** (81 mg, 0.2 mmol), olefin **2a** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3la** (73 mg, 73%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1l**) = 0.50, *Rf*(**3la**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2959, 1747, 1698, 1384, 1209, 1170, 756 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.82 – 7.27 (m, 10H), 6.46 – 6.36 (m, 1H), 4.62 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 2H), 1.94 (ddd, *J* = 12.0, 9.2, 6.4 Hz, 4H), 1.73 (td, *J* = 8.8, 4.4 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H), 1.05 (d, *J* = 6.3 Hz, 6H), 0.91 (d, *J* = 6.3 Hz, 6H). $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.7, 166.6, 165.1, 119.5, 63.3, 60.7, 47.6, 46.7 (2C), 25.9 (2C),

23.4 (2C), 23.1 (2C), 14.3 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{30}H_{37}N_2O_5$ 505.2697 Found 505.2685.

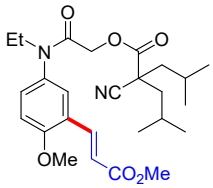


(*E*)-2-(ethyl(3-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ab): GP-2 was carried out with the substrate **1a** (69 mg, 0.2 mmol), olefin **2b** (41 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ab** (71 mg, 80%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1a**) = 0.50, *Rf*(**3ab**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 1679, 1434, 1267, 1168, 987, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 16.1 Hz, 1H), 7.57 (d, *J* = 7.8 Hz, 1H), 7.50 (dd, *J* = 7.8 Hz, 1H), 7.38 (t, *J* = 1.7 Hz, 1H), 7.30 – 7.25 (m, 1H), 6.48 (d, *J* = 16.1 Hz, 1H), 4.41 (s, 2H), 3.82 (s, 3H), 3.75 (dd, *J* = 8.8, 5.3 Hz, 2H), 1.95 – 1.86 (m, 4H), 1.69 (dd, *J* = 10.1, 6.2 Hz, 2H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.06 – 1.01 (m, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.8, 164.4, 142.9, 140.7, 136.7, 130.7, 129.9, 129.7, 128.2, 127.6, 119.5, 62.7, 51.9, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{25}H_{35}N_2O_5$ 443.2540 Found 443.2555.

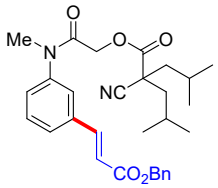


(*E*)-2-((3-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)(methyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3bb): GP-2 was carried out with the substrate **1b** (69 mg, 0.2 mmol), olefin **2b** (41 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3bb** (68

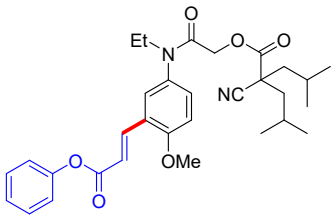
mg, 79%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1b**) = 0.50, *Rf*(**3bb**) = 0.30, UV detection]. Melting point: 85-87 °C. IR (MIR-ATR, 4000–600 cm^{-1}): 2954, 1682, 1437, 1272, 1168, 1026, 989, 698 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, *J* = 16.1 Hz, 1H), 7.56 (d, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.7 Hz, 1H), 7.42 (s, 1H), 7.32 – 7.27 (m, 1H), 6.48 (d, *J* = 16.0 Hz, 1H), 4.47 (s, 2H), 3.82 (s, 3H), 3.29 (s, 3H), 1.96 – 1.88 (m, 4H), 1.74 – 1.67 (m, 2H), 1.04 (d, *J* = 6.3 Hz, 6H), 0.90 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.8, 165.0, 142.8, 142.5, 136.7, 130.8, 128.7, 128.1, 126.5, 119.8, 119.5, 62.6, 51.9, 47.5, 46.8 (2C), 37.5, 25.8 (2C), 23.3 (2C), 23.0 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{24}H_{33}N_2O_5$ 429.2384 Found 429.2399.



(*E*)-2-(ethyl(4-methoxy-3-(3-methoxy-3-oxoprop-1-en-1-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3eb): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2b** (41 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3eb** (73 mg, 77%), as a white solid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3eb**) = 0.20, UV detection]. Melting point: 125-127 °C. IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 1678, 1495, 1436, 1263, 1210, 1166, 1027, 749 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.92 (d, *J* = 16.2 Hz, 1H), 7.35 (d, *J* = 2.6 Hz, 1H), 7.22 (dd, *J* = 8.7, 2.6 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 1H), 6.54 (d, *J* = 16.2 Hz, 1H), 4.40 (s, 2H), 3.93 (s, 3H), 3.81 (s, 3H), 3.71 (q, *J* = 7.2 Hz, 2H), 1.94 – 1.86 (m, 4H), 1.73 – 1.66 (m, 2H), 1.10 (t, *J* = 7.2 Hz, 3H), 1.03 (d, *J* = 6.3 Hz, 6H), 0.88 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 167.4, 164.8, 158.1, 138.6, 132.5, 131.0, 128.4, 125.0, 120.1, 119.5, 112.4, 62.7, 55.8, 51.7, 47.5, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{26}H_{37}N_2O_6$ 473.2646 Found 473.2660.

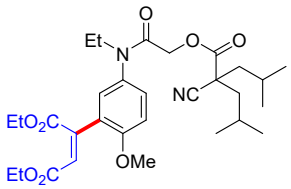


(*E*)-2-((3-(3-(benzyloxy)-3-oxoprop-1-en-1-yl)phenyl)(methyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3bc): GP-2 was carried out with the substrate **1b** (69 mg, 0.2 mmol), olefin **2c** (77 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3bc** (69 mg, 69%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1b**) = 0.50, *Rf*(**3bc**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 1682, 1590, 1440, 1385, 1268, 1211, 1159, 987, 697 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, *J* = 16.1 Hz, 1H), 7.55 (d, *J* = 7.7 Hz, 1H), 7.49 (t, *J* = 7.8 Hz, 1H), 7.43 – 7.38 (m, 5H), 7.38 – 7.34 (m, 1H), 7.31 – 7.27 (m, 1H), 6.53 (d, *J* = 16.0 Hz, 1H), 5.26 (s, 2H), 4.47 (s, 2H), 3.29 (s, 3H), 1.92 (dt, *J* = 12.7, 5.0 Hz, 4H), 1.73 – 1.68 (m, 2H), 1.04 (d, *J* = 6.3 Hz, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 166.1, 164.9, 143.1, 142.4, 136.7, 135.7, 130.8, 128.8, 128.6 (2C), 128.3, 128.3 (2C), 128.1, 119.9, 119.4, 66.6, 62.6, 47.5, 46.8 (2C), 37.5, 25.8 (2C), 23.3 (2C), 23.0 (2C) ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{30}H_{37}N_2O_5$ 505.2697 Found 505.2713.

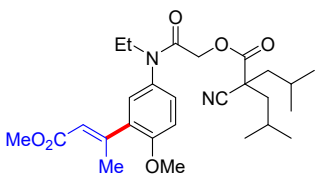


(*E*)-2-(ethyl(4-methoxy-3-(3-oxo-3-phenoxyprop-1-en-1-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ed): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2d** (71 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ed** (65 mg, 61%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ed**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1734, 1677, 1492, 1452, 1259, 1200, 1135, 749 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 16.2 Hz, 2H), 7.45 –

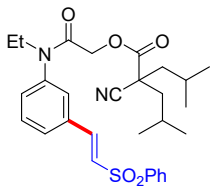
7.37 (m, 6H), 7.31 – 7.21 (m, 6H), 7.20 – 7.14 (m, 4H), 7.02 (d, J = 8.8 Hz, 2H), 6.76 (d, J = 16.2 Hz, 2H), 4.43 (s, 4H), 3.97 (s, 6H), 3.74 (q, J = 7.2 Hz, 4H), 1.98 – 1.86 (m, 8H), 1.75 – 1.67 (m, 4H), 1.13 (t, J = 7.2 Hz, 5H), 1.05 (d, J = 6.3 Hz, 12H), 0.90 (d, J = 6.2 Hz, 12H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.7, 165.4, 164.7, 158.4, 150.7, 140.3, 132.6, 131.4, 129.4, 128.8, 125.8, 124.8, 121.6, 119.7, 119.5, 112.5, 62.8, 55.9, 47.6, 46.8 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{31}H_{39}N_2O_6$ 535.2803 Found 535.2787.



Diethyl 2-(5-(2-((2-cyano-2-isobutyl-4-methylpentanoyl)oxy)-N-ethylacetamido)-2-methoxyphenyl)maleate (3ee): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2e** (82 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ee** (87 mg, 78%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.30, *Rf*(**3ee**) = 0.10, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1728, 1678, 1497, 1447, 1261, 1176, 1028, 752 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.24 (d, J = 2.6 Hz, 1H), 7.20 (d, J = 2.6 Hz, 1H), 6.98 (d, J = 8.7 Hz, 1H), 6.44 (s, 1H), 4.39 (s, 2H), 4.38 – 4.32 (m, 2H), 4.25 (q, J = 7.1 Hz, 2H), 3.87 (s, 3H), 3.72 – 3.67 (m, 2H), 1.92 (dt, J = 11.2, 5.0 Hz, 4H), 1.74 – 1.68 (m, 2H), 1.33 (dt, J = 12.2, 7.1 Hz, 6H), 1.10 (t, J = 7.2 Hz, 3H), 1.05 (d, J = 6.3 Hz, 6H), 0.90 (d, J = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 167.2, 164.8, 164.7, 157.5, 143.0, 132.7, 131.1, 129.6, 125.5, 123.5, 119.5, 112.7, 62.7, 61.7, 61.1, 56.0, 47.6, 46.8 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 14.1, 14.0, 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{30}H_{43}N_2O_8$ 559.3014 Found 559.3007.

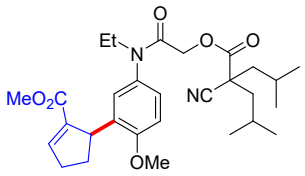


(*E*)-2-(ethyl(4-methoxy-3-(4-methoxy-4-oxobut-2-en-2-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ef): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2f** (48 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ef** (77 mg, 79%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ef**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 1719, 1677, 1433, 1218, 1162, 1028, 649 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.18 (dd, *J* = 8.6, 2.7 Hz, 1H), 7.02 (d, *J* = 2.6 Hz, 1H), 6.95 (d, *J* = 8.7 Hz, 1H), 5.89 (d, *J* = 1.3 Hz, 1H), 4.42 (s, 2H), 3.87 (s, 3H), 3.76 (s, 5H), 2.49 (d, *J* = 1.2 Hz, 3H), 1.97 – 1.90 (m, 4H), 1.71 (dd, *J* = 16.3, 8.9 Hz, 3H), 1.11 (t, *J* = 7.2 Hz, 3H), 1.08 – 1.04 (m, 6H), 0.91 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.6, 166.7, 164.7, 156.4, 154.8, 134.5, 132.3, 129.3, 128.4, 119.7, 119.5, 112.0, 62.76, 55.7, 51.1, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 19.6, 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{27}H_{39}N_2O_6$ 487.2803 Found 487.2785.

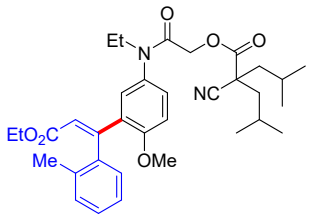


(*E*)-2-(ethyl(3-(2-(phenylsulfonyl)vinyl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ag): GP-2 was carried out with the substrate **1a** (71 mg, 0.2 mmol), olefin **2g** (80 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ag** (74 mg, 71%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 80:20, *Rf*(**1a**) = 0.40, *Rf*(**3ag**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1746, 1676, 1440, 1305, 1214, 1143, 832, 692 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.96 (dd, *J* = 5.3, 3.4 Hz, 2H), 7.70 – 7.63 (m, 2H), 7.61 – 7.55 (m, 2H), 7.52 (d, *J* = 7.4 Hz, 2H), 7.38 (s, 1H), 7.32 – 7.27 (m, 1H), 6.94 (d, *J* = 15.4 Hz, 1H), 4.37 (s, 2H), 3.74 (q, *J* = 7.2 Hz, 2H), 1.93 – 1.85 (m, 4H), 1.71 – 1.66 (m, 2H), 1.10 (t, *J* = 7.1 Hz, 3H), 1.02 (d, *J* = 6.3 Hz, 6H), 0.89 – 0.84 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.7, 164.3, 140.4, 140.2, 134.7, 133.7, 131.0, 130.9, 130.8, 129.5 (2C), 128.9, 128.1, 128.0 (2C), 127.9, 119.5, 62.8, 47.6, 46.8 (2C), 44.4, 36.6, 25.8 (2C), 23.3 (2C),

23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{29}H_{37}N_2O_5S$ 525.2418 Found 525.2421.

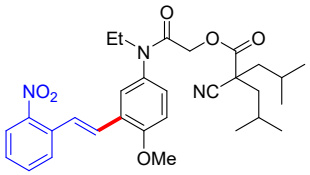


Methyl (R)-5-(5-(2-((2-cyano-2-isobutyl-4-methylpentanoyl)oxy)-N-ethylacetamido)-2-methoxyphenyl)cyclopent-1-ene-1-carboxylate (3eh): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2h** (60 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3eh** (57 mg, 56%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.50, *Rf*(**3eh**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2954, 1717, 1675, 1496, 1436, 1213, 1139, 1029, 747 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.05 (d, *J* = 1.9 Hz, 1H), 7.02 (dd, *J* = 8.5, 2.6 Hz, 1H), 6.89 (d, *J* = 8.6 Hz, 1H), 6.73 (d, *J* = 2.6 Hz, 1H), 4.52 – 4.43 (m, 1H), 4.33 (d, *J* = 4.3 Hz, 2H), 3.87 (s, 3H), 3.62 (s, 5H), 2.55 – 2.50 (m, 2H), 1.94 – 1.86 (m, 4H), 1.72 – 1.66 (m, 2H), 1.03 (d, *J* = 6.3 Hz, 9H), 0.89 (d, *J* = 5.9 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.47, 165.0, 164.9, 156.9, 146.4, 137.3, 134.9, 131.8, 126.8, 126.7, 119.6, 111.4, 62.7, 55.6, 51.3, 47.6, 46.7 (2C), 44.0, 43.3, 32.6, 31.9, 25.7 (2C), 23.3 (2C), 23.0 (2C), 12.7. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{29}H_{41}N_2O_6$ 513.2959 Found 513.2976.

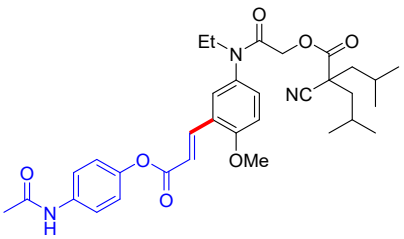


(*E*)-2-((3-(3-ethoxy-3-oxo-1-(*o*-tolyl)prop-1-en-1-yl)-4-methoxyphenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ei): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2i** (91 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product

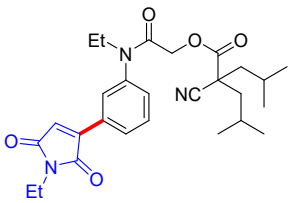
using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ei** (69 mg, 60%), as a colourless liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ei**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 1681, 1493, 1447, 1262, 1217, 1155, 1030, 754 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 1H), 7.20 – 7.13 (m, 3H), 7.04 (d, *J* = 7..5 Hz, 1H), 6.98 (d, *J* = 8.7 Hz, 1H), 6.77 (d, *J* = 2.7 Hz, 1H), 6.66 (s, 1H), 4.27 (s, 2H), 4.01 (q, *J* = 7.1 Hz, 2H), 3.85 (s, 3H), 3.61 (q, *J* = 7.2 Hz, 2H), 2.10 (s, 3H), 1.91 (dt, *J* = 12.9, 5.1 Hz, 4H), 1.69 (d, *J* = 7.4 Hz, 2H), 1.05 (dd, *J* = 7.6, 6.8 Hz, 9H), 0.98 (t, *J* = 7.2 Hz, 3H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 169.5, 166.1, 164.6, 157.5, 150.6, 139.0, 135.2, 132.0, 130.8, 130.6, 129.8, 129.4, 128.4, 127.9, 125.3, 123.0, 119.5, 112.7, 62.6, 60.0, 55.9, 47.6, 46.7 (2C), 44.1, 25.8 (2C), 23.3 (2C), 22.9 (2C), 19.4, 13.9, 12.7 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{34}H_{45}N_2O_6$ 577.3272 Found 577.3292.



(*E*)-2-(ethyl(4-methoxy-3-(2-nitrostyryl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ej): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2j** (71 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ej** (75 mg, 70%), as a yellow-coloured liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ej**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 1746, 1675, 1521, 1346, 1250, 1213, 1027, 742 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (dd, *J* = 8.1, 1.0 Hz, 1H), 7.78 (d, *J* = 7.8 Hz, 1H), 7.66 (d, *J* = 16.3 Hz, 1H), 7.61 (d, *J* = 7.9 Hz, 1H), 7.46 – 7.39 (m, 2H), 7.33 (d, *J* = 16.3 Hz, 1H), 7.15 (dd, *J* = 8.6, 2.6 Hz, 1H), 6.97 (d, *J* = 8.7 Hz, 1H), 4.46 (s, 2H), 3.94 (s, 3H), 3.75 (q, *J* = 7.1 Hz, 2H), 1.92 (dt, *J* = 11.2, 6.6 Hz, 5H), 1.76 – 1.65 (m, 4H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.3 Hz, 6H), 0.90 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ 169.6, 164.8, 157.2, 148.0, 133.1, 132.7, 129.2, 128.4, 128.2, 127.5, 127.3, 127.1, 125.9, 124.8, 119.6, 112.1, 62.8, 55.8, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{30}H_{38}N_3O_6$ 536.2755 Found 536.2742.

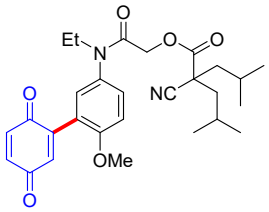


(*E*)-2-((3-(3-(4-acetamidophenoxy)-3-oxoprop-1-en-1-yl)-4-methoxyphenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3ek): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2k** (98 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3ek** (65 mg, 55%), as a yellow-coloured liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3ek**) = 0.10, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 1955, 1733, 1671, 1501, 1259, 1201, 1137, 1024, 736 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J* = 16.2 Hz, 1H), 7.61 – 7.50 (m, 3H), 7.41 (d, *J* = 2.3 Hz, 1H), 7.11 (d, *J* = 8.8 Hz, 2H), 7.01 (d, *J* = 8.8 Hz, 1H), 6.74 (d, *J* = 16.2 Hz, 1H), 4.42 (s, 2H), 3.96 (s, 3H), 3.73 (q, *J* = 7.1 Hz, 2H), 2.18 (s, 3H), 1.92 (d, *J* = 9.5 Hz, 4H), 1.71 (d, *J* = 7.5 Hz, 2H), 1.12 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.2 Hz, 6H), 0.90 (d, *J* = 6.1 Hz, 6H) ppm. ^{13}C{^{1}H} NMR (151 MHz, $CDCl_3$) δ 169.6, 168.5, 165.6, 164.7, 158.4, 146.8, 140.5, 135.7, 131.5, 128.8, 124.7, 121.9 (2C), 120.8 (2C), 119.5, 119.5, 112.6, 62.8, 55.9, 47.6, 46.7 (2C), 44.3, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{33}H_{42}N_3O_7$ 592.3017 Found 592.3041.

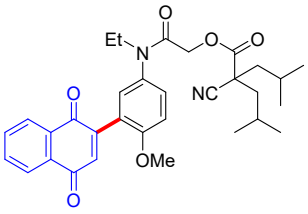


2-(ethyl(3-(1-ethyl-2,5-dioxo-2,5-dihydro-1H-pyrrol-3-yl)phenyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3al): GP-2 was carried out with the substrate **1a** (71 mg, 0.2 mmol), olefin **2l** (60 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3al** (52 mg, 51%), as a yellow-coloured liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1a**) =

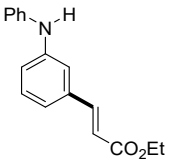
0.50, *Rf*(**3al**) = 0.30, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 1747, 1698, 1443, 1405, 1214, 753 cm^{-1}.^{1}H NMR (600 MHz, $CDCl_3$) δ 7.92 (d, *J* = 7.8 Hz, 1H), 7.87 (s, 1H), 7.58 (dd, *J* = 7.9 Hz, 1H), 7.37 (dd, *J* = 7.9, 1.1 Hz, 1H), 6.80 (s, 1H), 4.44 (s, 2H), 3.82 – 3.78 (m, 2H), 3.68 – 3.64 (m, 2H), 1.93 – 1.90 (m, 4H), 1.71 (d, *J* = 7.5 Hz, 2H), 1.24 (d, *J* = 7.2 Hz, 4H), 1.15 (t, *J* = 7.1 Hz, 3H), 1.04 (d, *J* = 6.4 Hz, 6H), 0.89 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 170.1, 169.6 (2C), 164.4, 142.1, 140.7, 130.8, 130.7, 130.6, 128.7, 128.4, 125.3, 119.5, 62.8, 47.6, 46.7 (2C), 44.4, 33.1, 25.8 (2C), 23.3 (2C), 23.0 (2C), 13.9, 12.9. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{27}H_{36}N_3O_5$ 482.2649 Found 482.2667.



2-(Ethyl(6-methoxy-2',5'-dioxo-2',5'-dihydro-[1,1'-biphenyl]-3-yl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3em): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2m** (52 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3em** (67 mg, 68%), as a yellow-coloured liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3em**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 1746, 1662, 1497, 1436, 1274, 1212, 1140, 735 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.06 (d, *J* = 2.6 Hz, 1H), 7.02 (d, *J* = 8.8 Hz, 1H), 6.93 – 6.79 (m, 3H), 4.46 (s, 2H), 3.83 (s, 3H), 3.72 (q, *J* = 7.1 Hz, 2H), 1.95 – 1.87 (m, 4H), 1.72 – 1.69 (m, 2H), 1.12 (t, *J* = 7.2 Hz, 3H), 1.04 (d, *J* = 6.3 Hz, 6H), 0.90 (d, *J* = 6.2 Hz, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 187.4, 185.3, 169.6, 164.8, 157.2, 143.5, 136.9, 136.2, 135.0, 132.2, 130.8, 130.7, 123.6, 119.5, 112.4, 62.8, 56.0, 47.6, 46.7 (2C), 44.4, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.8 ppm. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{28}H_{35}N_2O_6$ 495.2490 Found 495.2477.

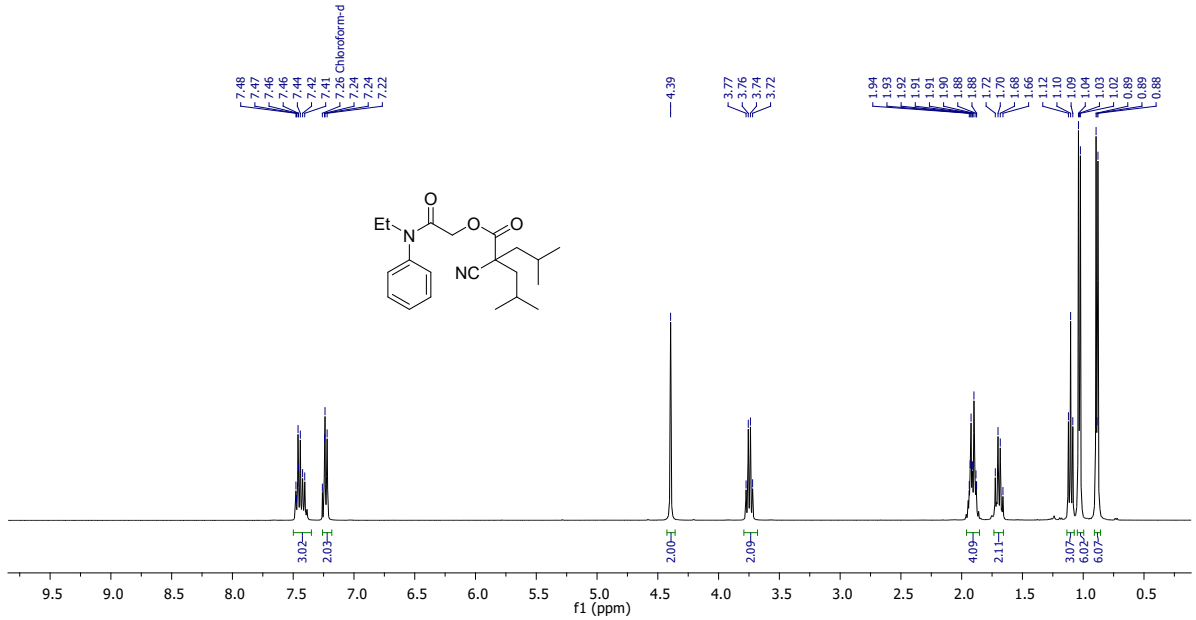


2-((3-(1,4-dioxo-1,4-dihydronaphthalen-2-yl)-4-methoxyphenyl)(ethyl)amino)-2-oxoethyl 2-cyano-2-isobutyl-4-methylpentanoate (3en): GP-2 was carried out with the substrate **1e** (77 mg, 0.2 mmol), olefin **2n** (76 mg, 0.48 mmol), $Pd(OAc)_2$ (5 mg, 10 mol %), Ac-Gly-OH (10 mg, 40 mol%), AgOAc (66 mg, 0.4 mmol), and hexafluoroisopropanol (HFIP) (1.5 mL) under microwave irradiation at 100 °C for 45 minutes. Purification of crude product using silica gel column chromatography (hexane/ethyl acetate, 100/0 to 75/25), furnished the product **3en** (76 mg, 70%), as a yellow-coloured liquid. [TLC (petroleum ether/ethyl acetate 85:15, *Rf*(**1e**) = 0.40, *Rf*(**3en**) = 0.20, UV detection]. IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 1746, 1667, 1495, 1435, 1252, 1142, 1025, 732 cm^{-1}.^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (td, *J* = 5.8, 3.3 Hz, 2H), 7.82 – 7.72 (m, 2H), 7.31 (dd, *J* = 8.7, 2.7 Hz, 1H), 7.15 (d, *J* = 2.6 Hz, 1H), 7.07 (s, 1H), 7.05 (d, *J* = 8.8 Hz, 1H), 4.50 (s, 2H), 3.84 (s, 3H), 3.74 (q, *J* = 7.2 Hz, 2H), 1.97 – 1.88 (m, 4H), 1.71 (dd, *J* = 14.4, 7.0 Hz, 2H), 1.14 (t, *J* = 7.2 Hz, 3H), 1.07 – 1.03 (m, 6H), 0.94 – 0.89 (m, 6H) ppm. $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 184.9, 183.3, 169.7, 164.9, 157.3, 145.6, 137.4, 133.9, 133.9, 132.2, 132.2, 132.0, 130.8, 130.6, 127.0, 126.1, 124.4, 119.6, 112.4, 62.9, 56.1, 47.6, 46.7 (2C), 44.4, 25.8 (2C), 23.3 (2C), 23.0 (2C), 12.9 ppm. HRMS (ESI) m/z: $[(M+NH_4)]^+$ Calcd for $C_{32}H_{40}N_3O_6$ 562.2912 Found 562.2898.

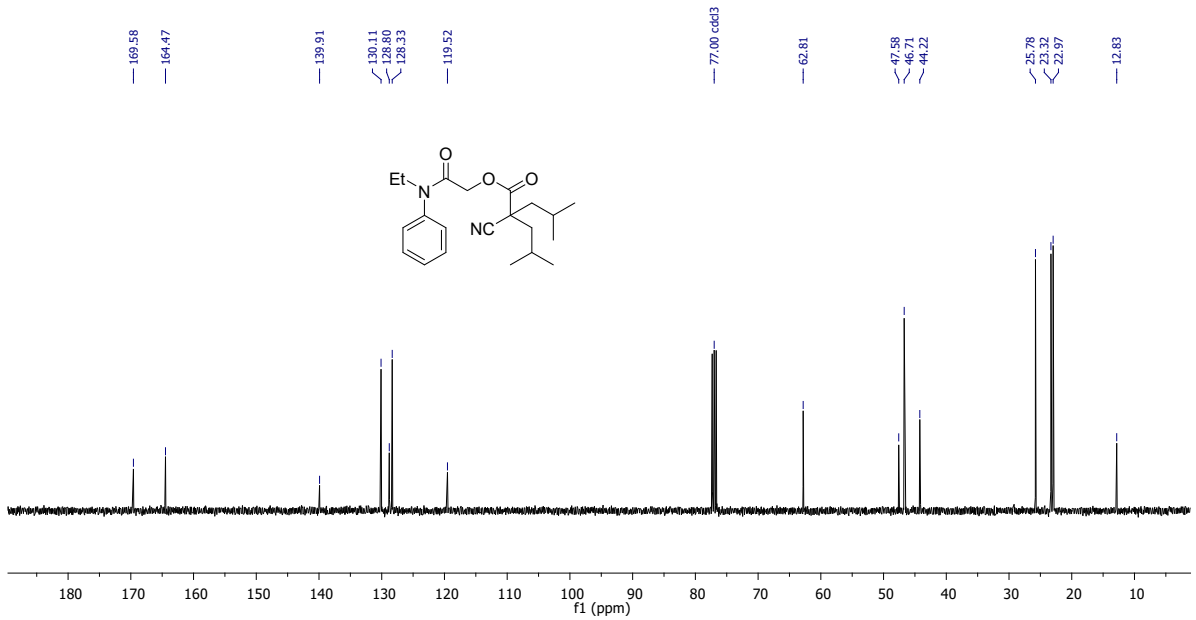


Ethyl (*E*)-3-(3-(phenylamino)phenyl)acrylate (5): To an oven dried 25 mL round bottom flask charged with a magnetic stirring bar, were added substrate **3la** (100 mg, 0.2 mmol), MeOH (1 mL) and H_2O (1 mL) followed by potassium hydroxide (4 equiv) at 70 °C for 12 h. The reaction progress was monitored by TLC, then MeOH was removed under reduced pressure, resulted mixture was acidified with 2M HCl and extracted with ethyl acetate (3×10 mL), then dried with Na_2SO_4 and filtered. The crude material was obtained after evaporating the solvent under reduced pressure, which was then subjected for the esterification step by adding ethyl bromide (1.5 equiv), potassium carbonate (4 equiv) in DMF (10 mL) for 6 h at room temperature. The conversion was monitored by TLC. Then, the mixture was quenched

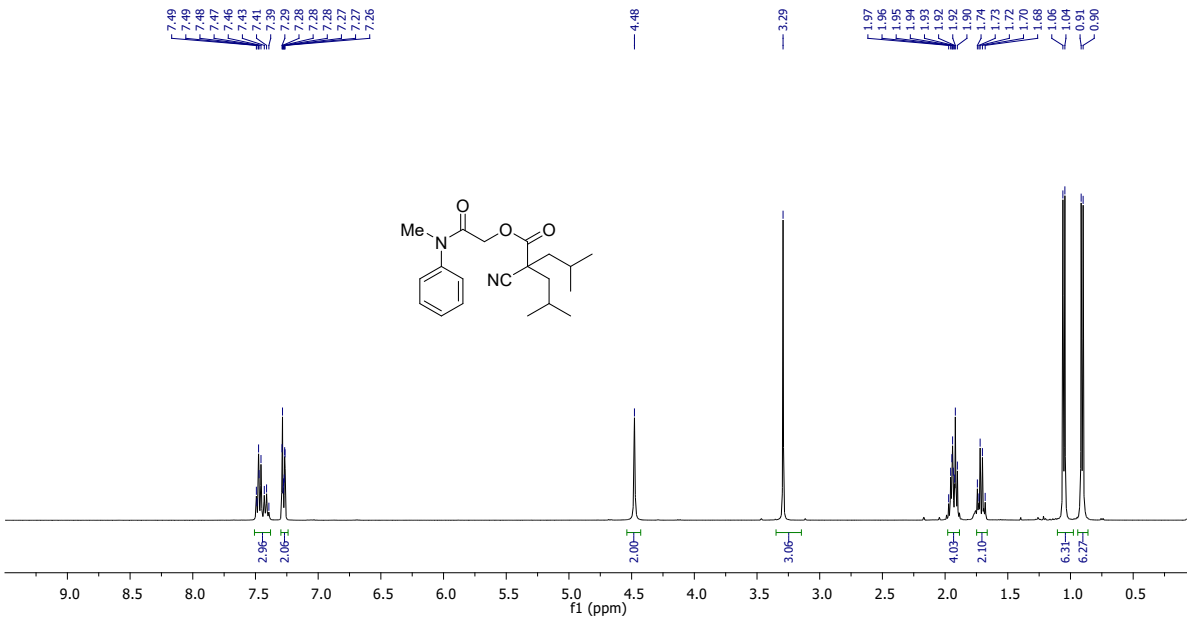
by the addition of an aqueous NH_4Cl solution and extracted with dichloromethane (3×10 mL). The organic layers were washed with saturated NaCl solution, dried (Na_2SO_4), and filtered. Evaporation of the solvent under reduced pressure and purification of the crude material by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **5** (48 mg, 90%). IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 1725, 1591, 1512, 1335, 1243, 1102, 751 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 16.0 Hz, 2H), 7.33 – 7.24 (m, 7H), 7.21 (t, *J* = 1.9 Hz, 2H), 7.13 – 7.03 (m, 8H), 7.01 – 6.94 (m, 2H), 6.39 (d, *J* = 16.0 Hz, 2H), 5.76 (s, 2H), 4.26 (q, *J* = 7.1 Hz, 4H), 1.33 (t, *J* = 7.1 Hz, 6H). $^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$) δ 167.0, 144.6, 143.9, 142.4, 135.6, 129.8, 129.5 (2C), 121.7, 120.5, 119.2, 118.5 (2C), 118.3, 116.3, 60.5, 14.3. HRMS (ESI) m/z: $[(M+H)]^+$ Calcd for $C_{17}H_{18}NO_2$ 268.1332 Found 268.1323.



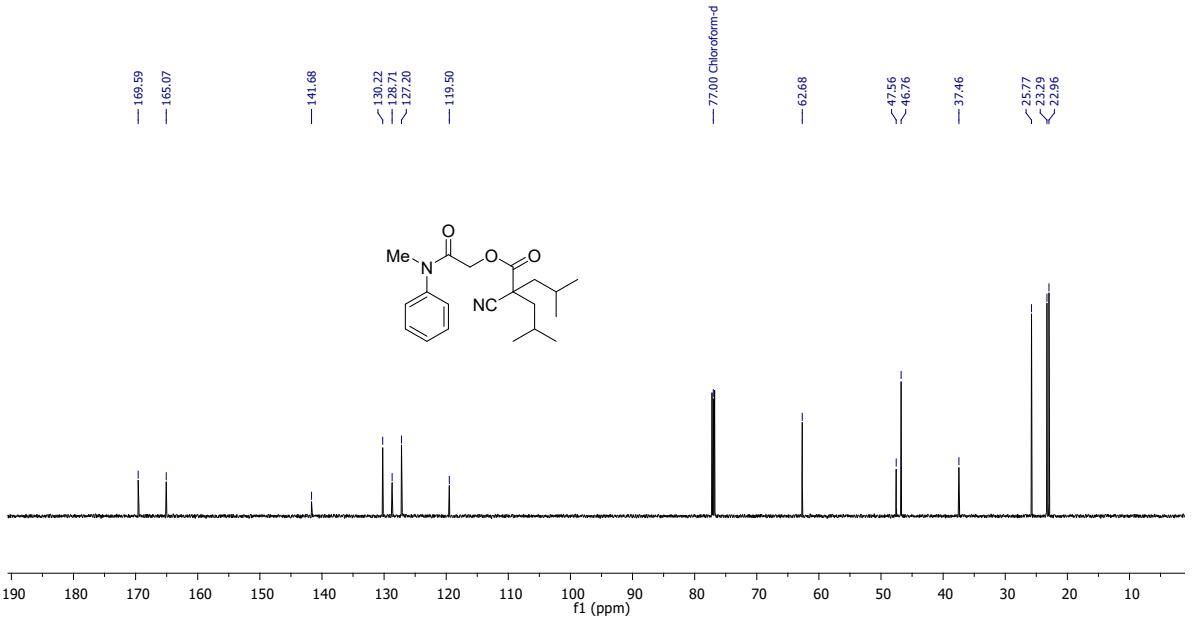
^{1}H NMR (400 MHz) spectrum of **1a** in $CDCl_3$



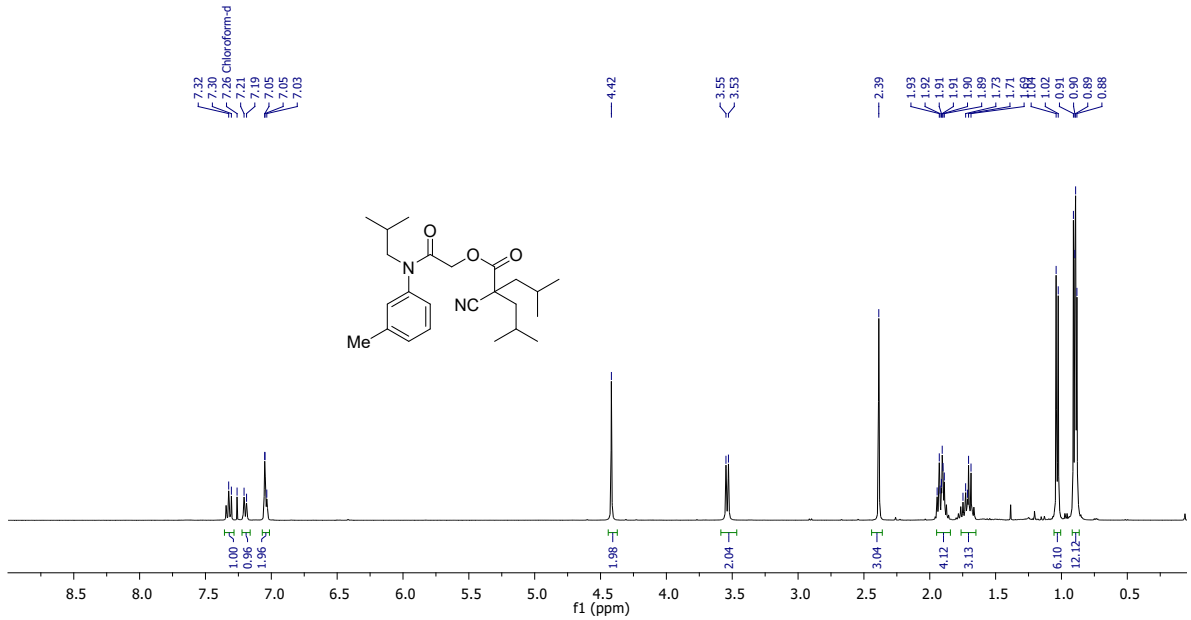
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1a** in $CDCl_3$



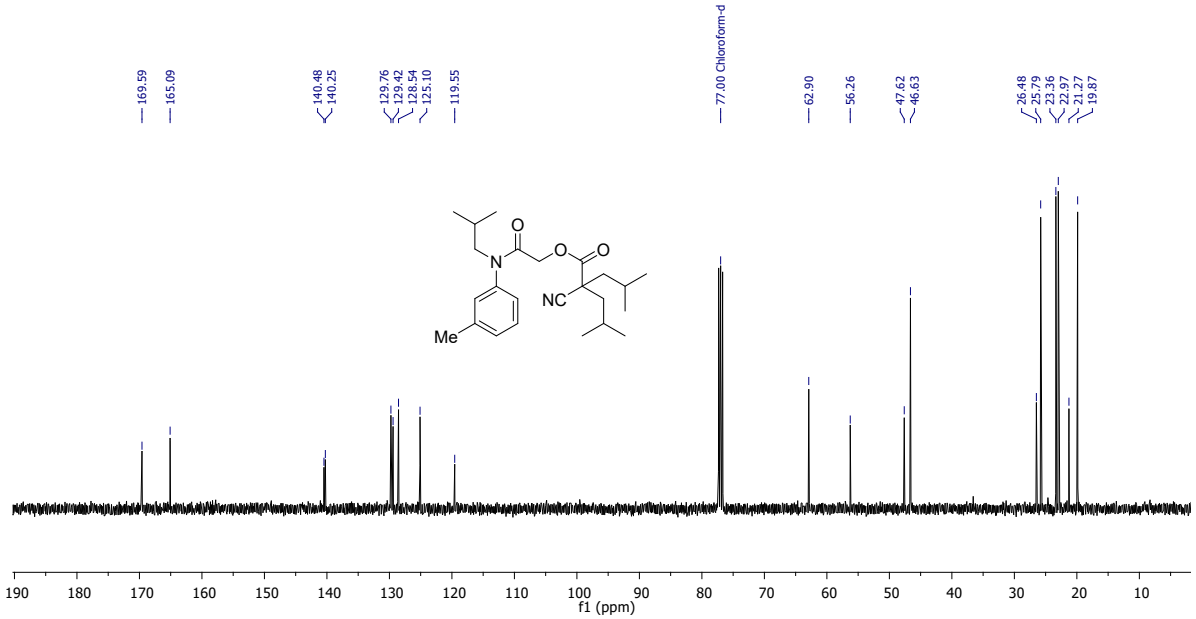
^{1}H NMR (400 MHz) spectrum of **1b** in $CDCl_3$



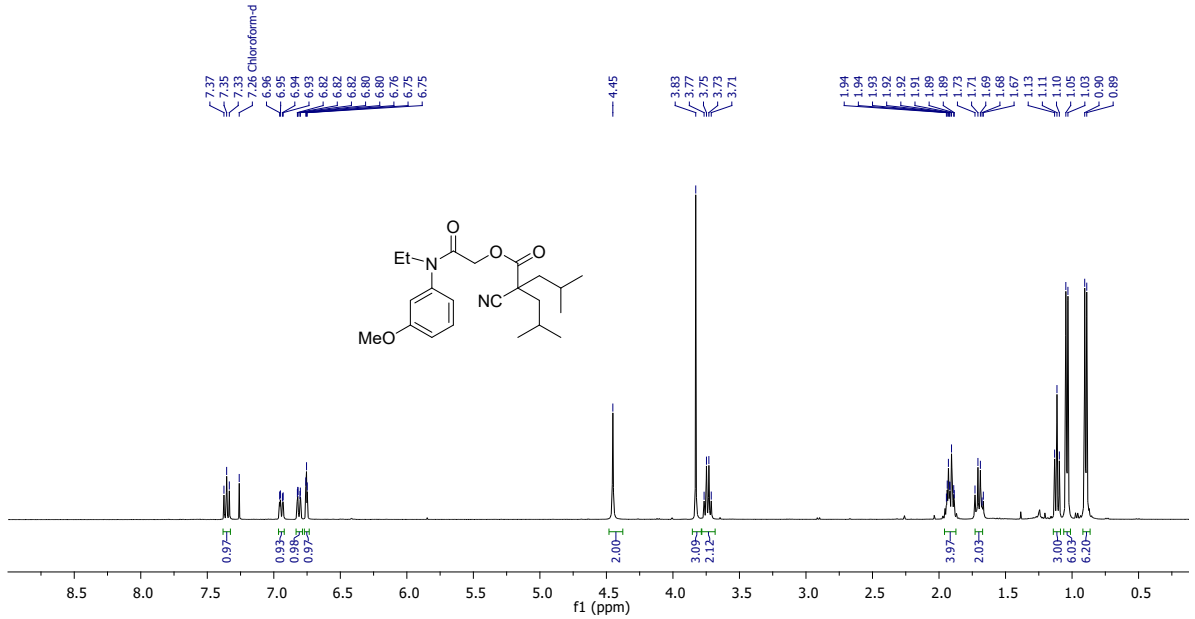
^{13}C {^{1}H} NMR (150 MHz) spectrum of **1b** in $CDCl_3$



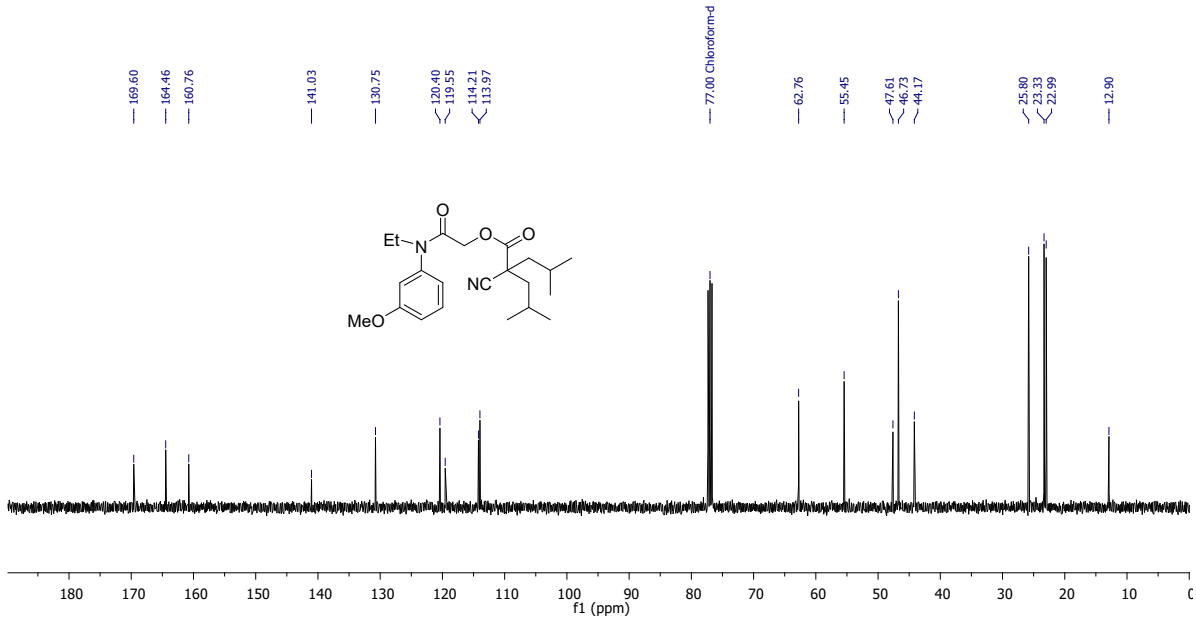
^{1}H NMR (400 MHz) spectrum of **1c** in $CDCl_3$



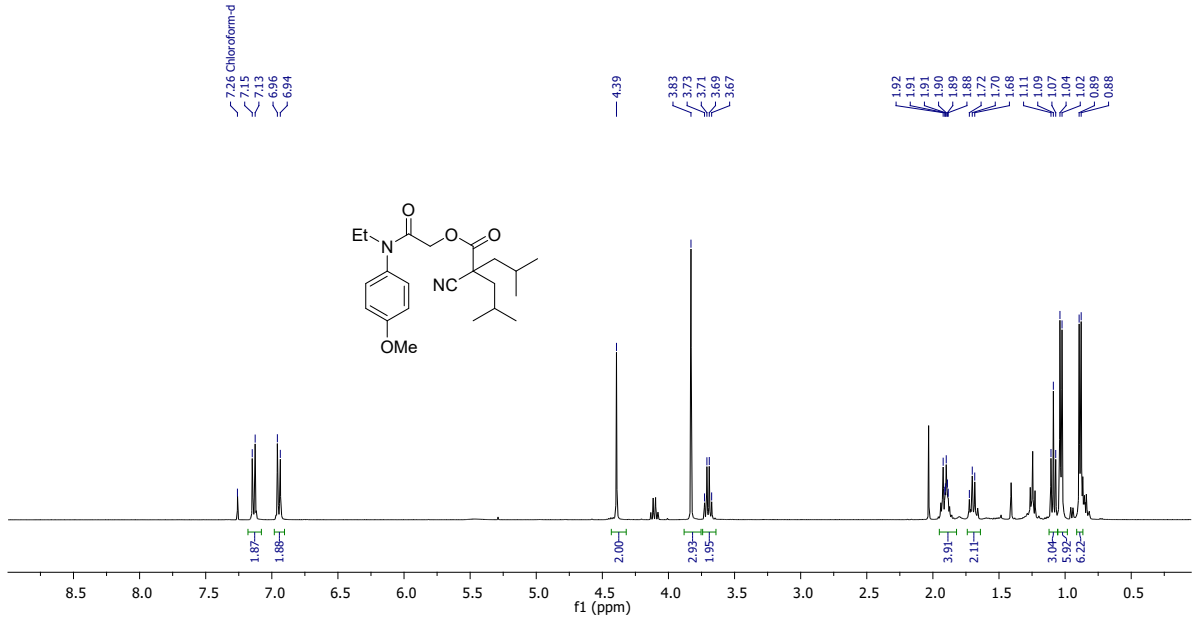
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1c** in $CDCl_3$



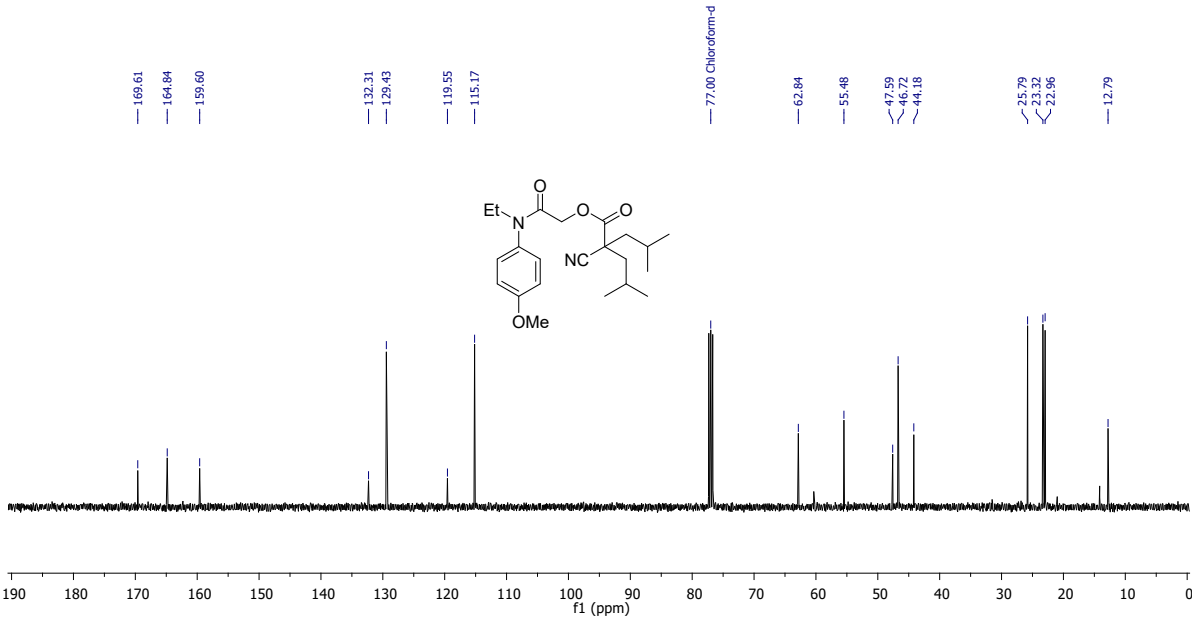
^{1}H NMR (400 MHz) spectrum of **1d** in $CDCl_3$



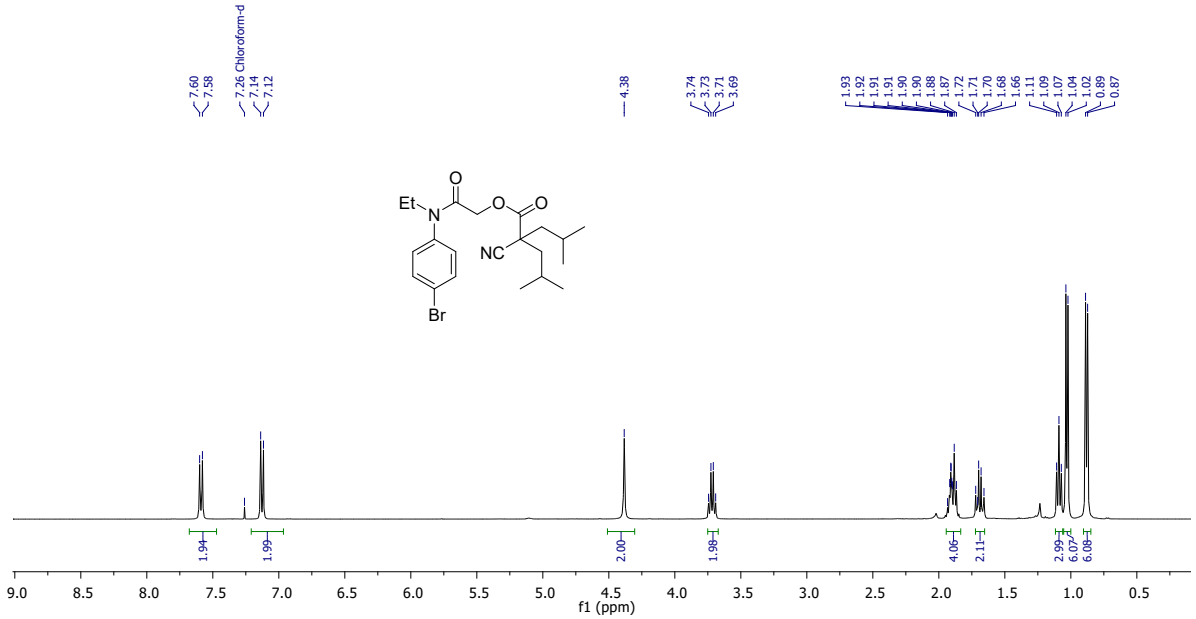
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1d** in $CDCl_3$



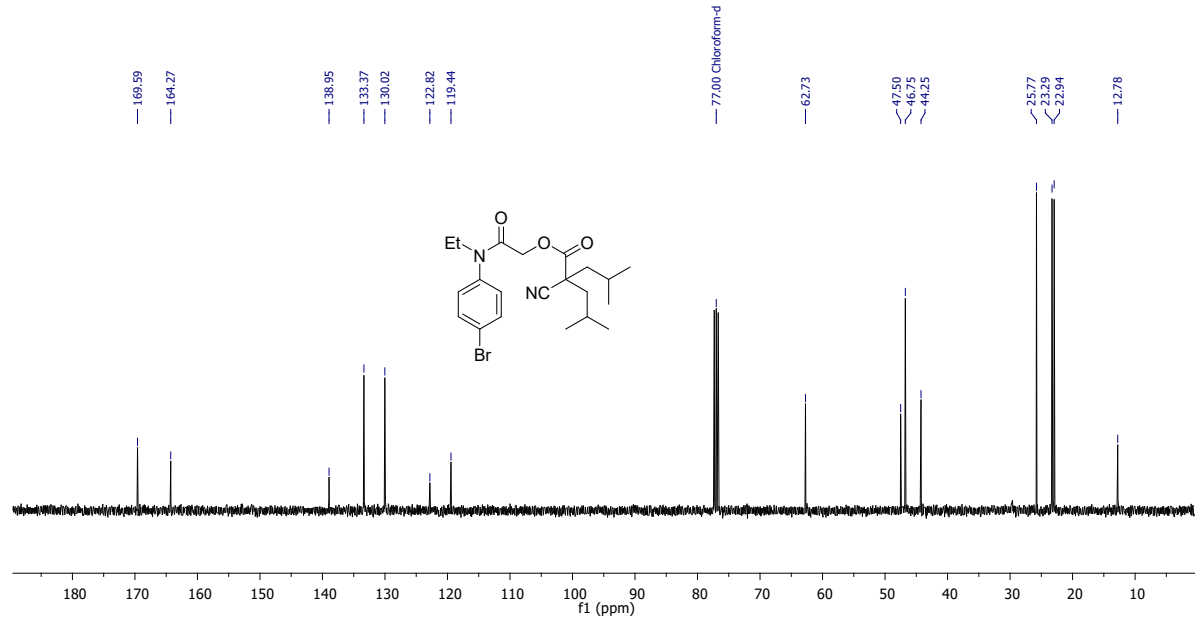
^{1}H NMR (400 MHz) spectrum of **1e** in $CDCl_3$



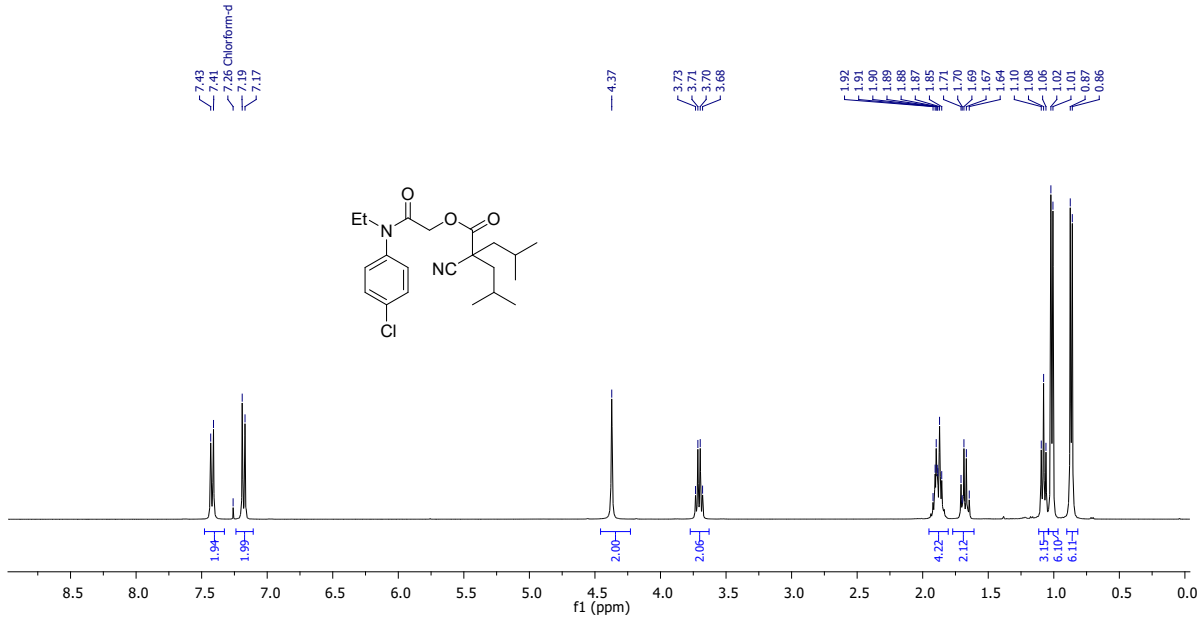
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1e** in $CDCl_3$



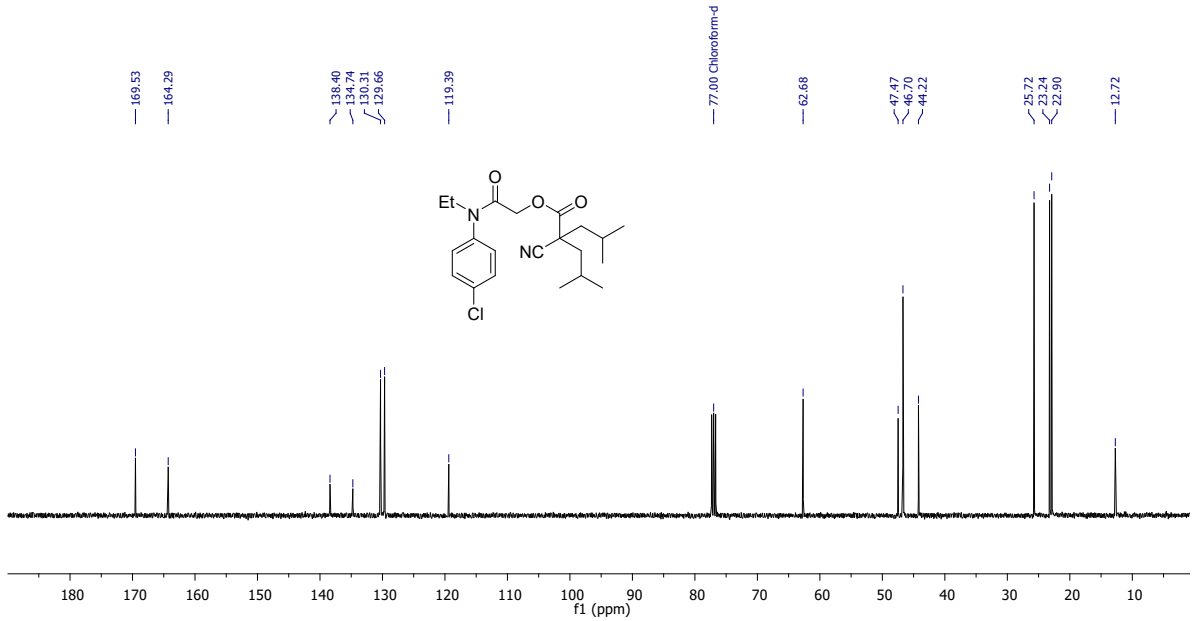
^{1}H NMR (400 MHz) spectrum of **1f** in $CDCl_3$



^{13}C {^{1}H} NMR (100 MHz) spectrum of **1f** in $CDCl_3$



^{1}H NMR (400 MHz) spectrum of **1g** in $CDCl_3$



^{13}C {^{1}H} NMR (100 MHz) spectrum of **1g** in $CDCl_3$

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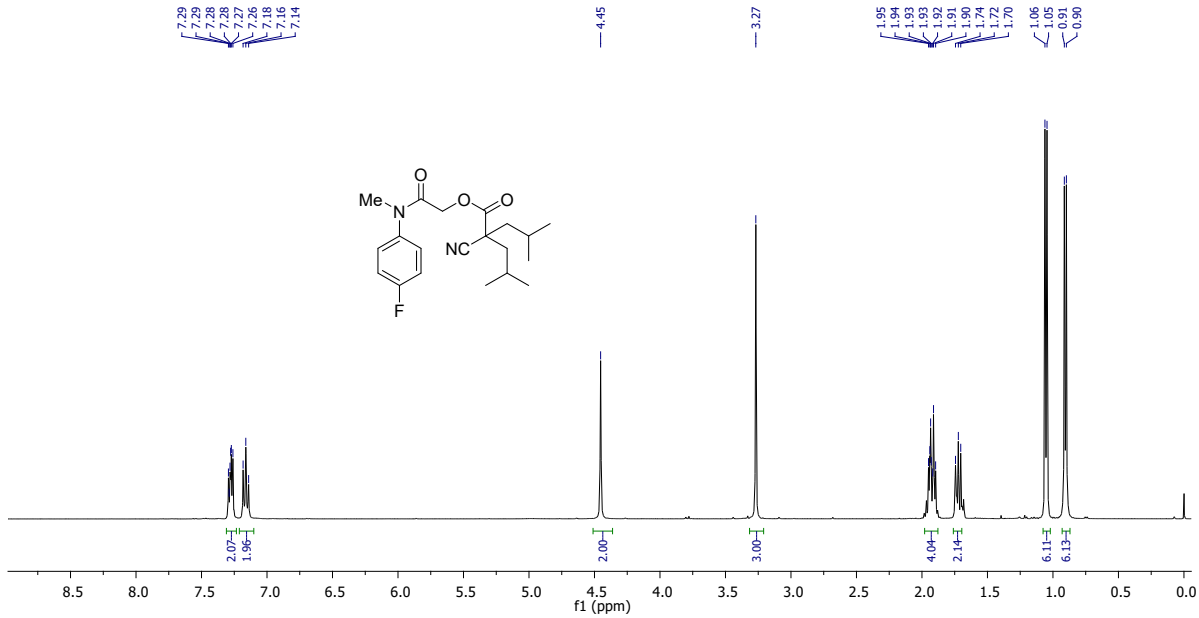
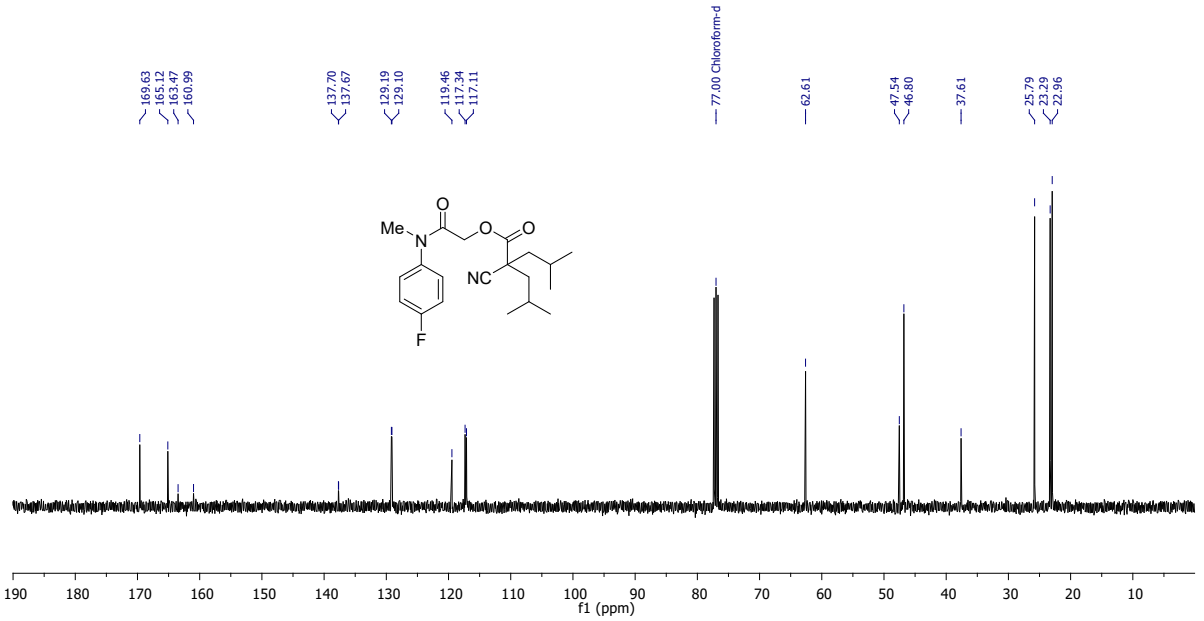
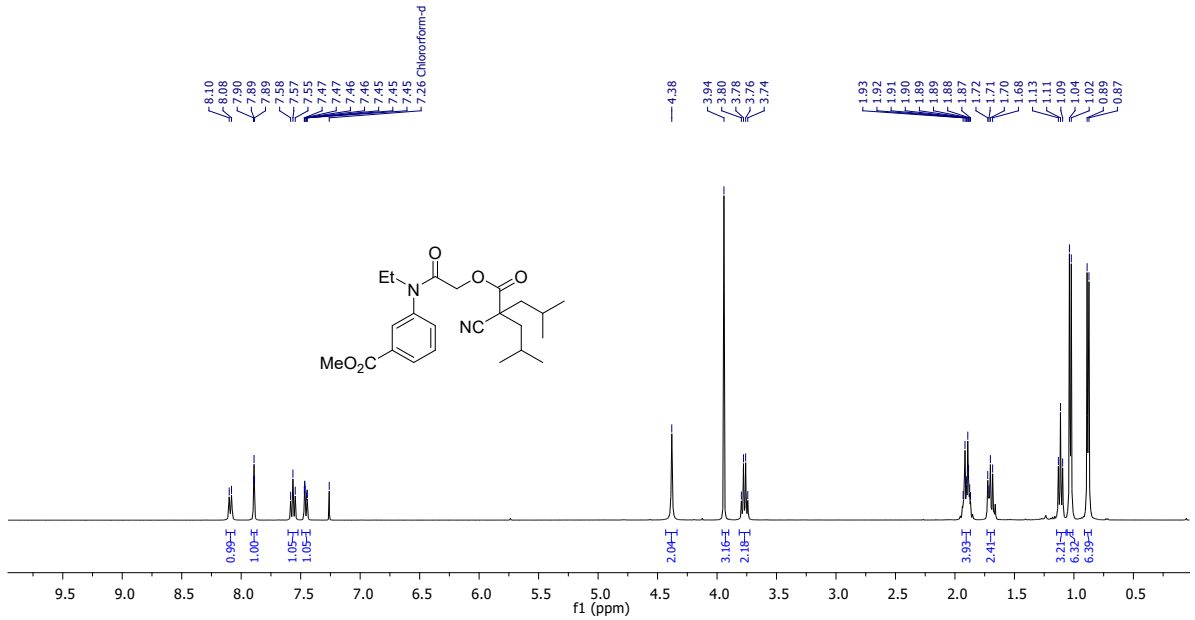


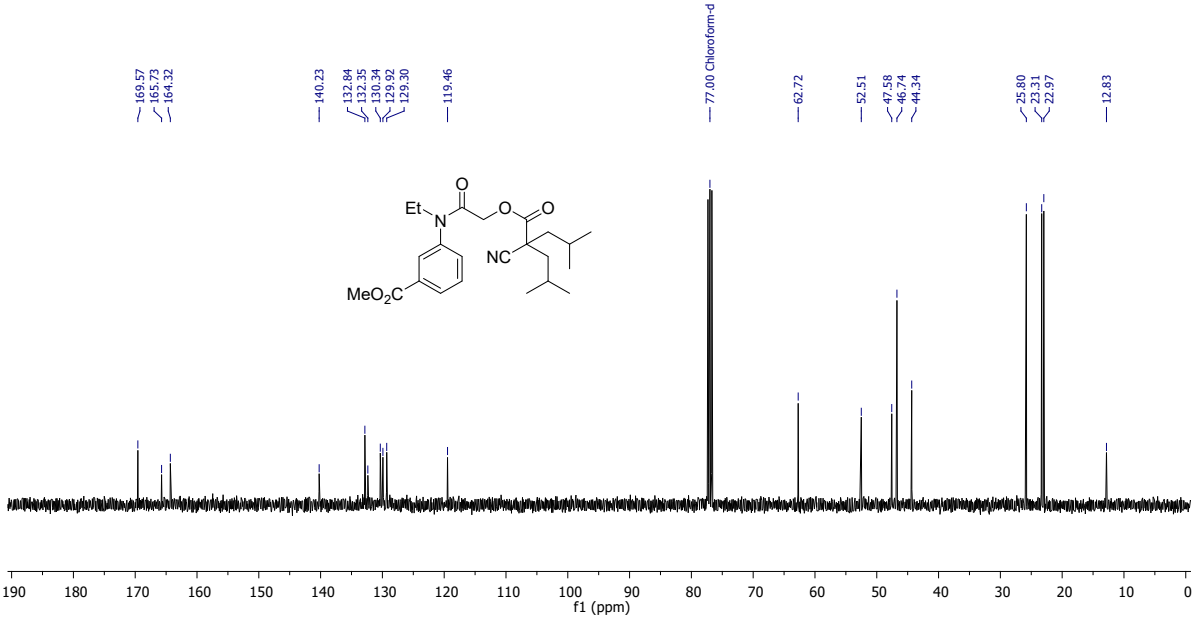
^{1}H NMR (400 MHz) spectrum of **1h** in $CDCl_3$



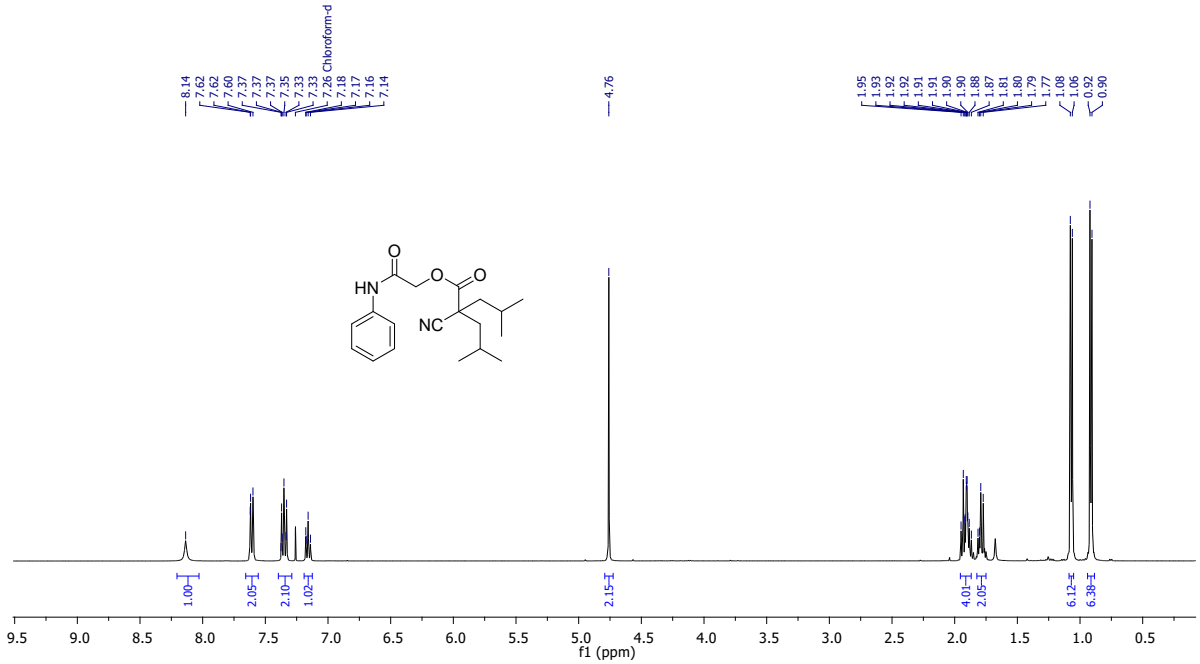
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1h** in $CDCl_3$



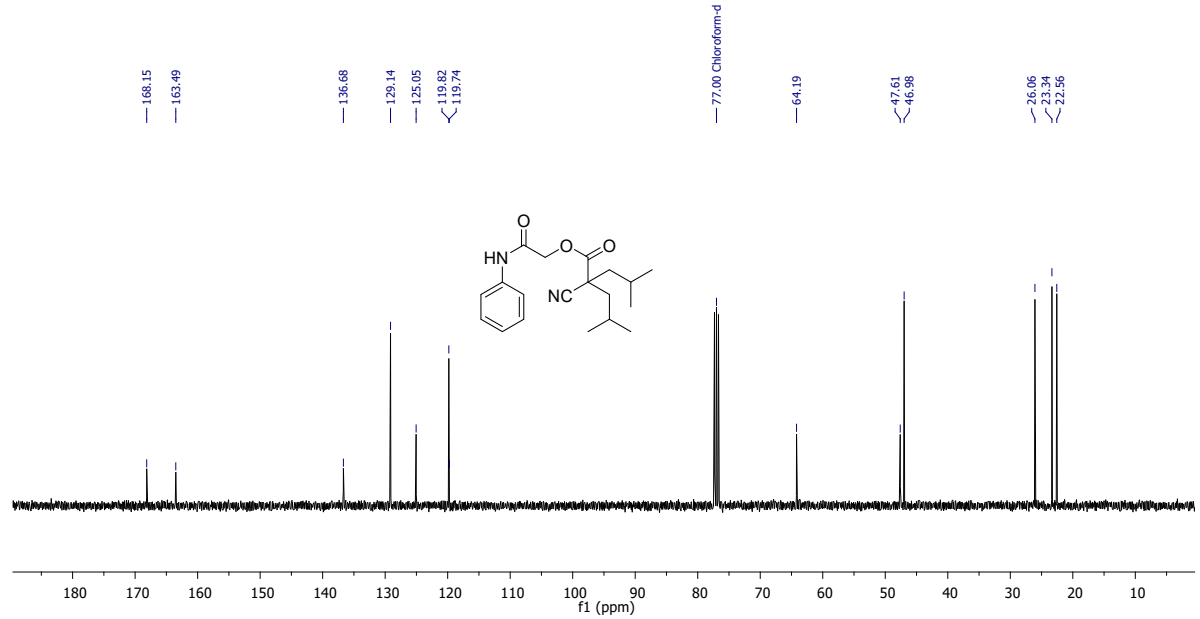
^{1}H NMR (400 MHz) spectrum of **1i** in $CDCl_3$



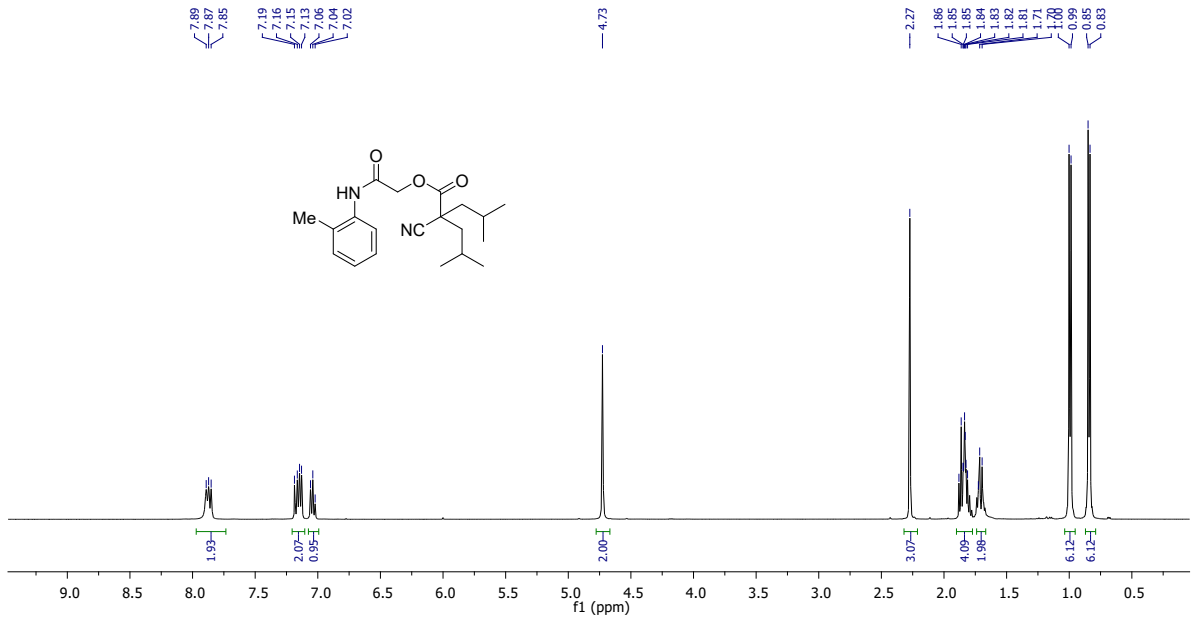
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1i** in $CDCl_3$



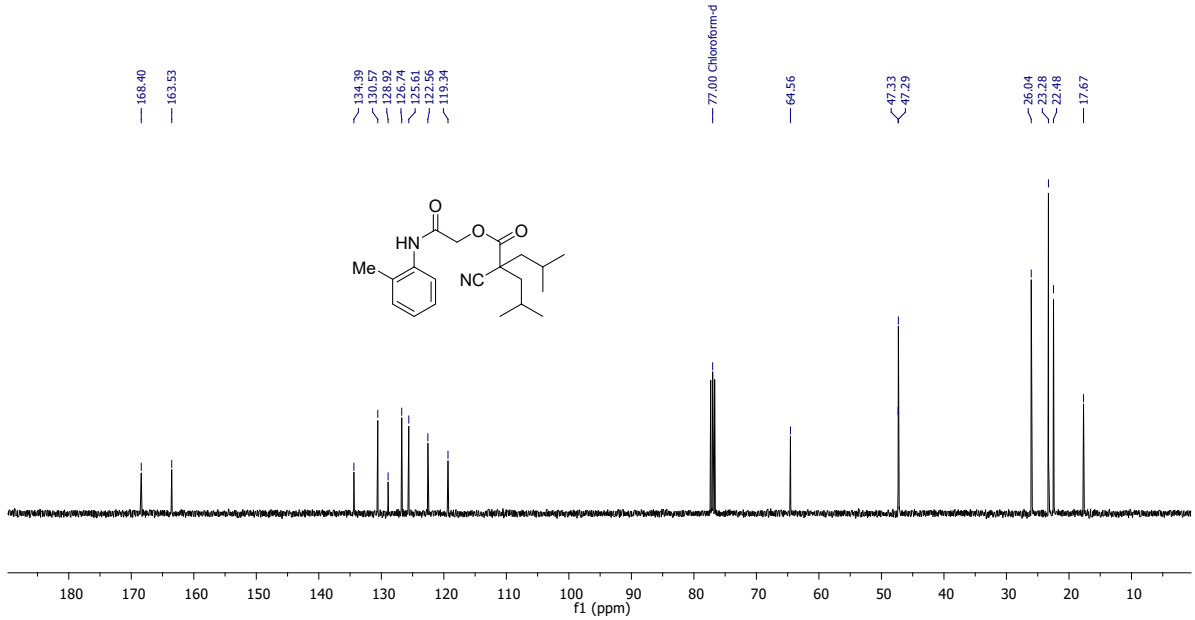
^{1}H NMR (400 MHz) spectrum of **1j** in $CDCl_3$



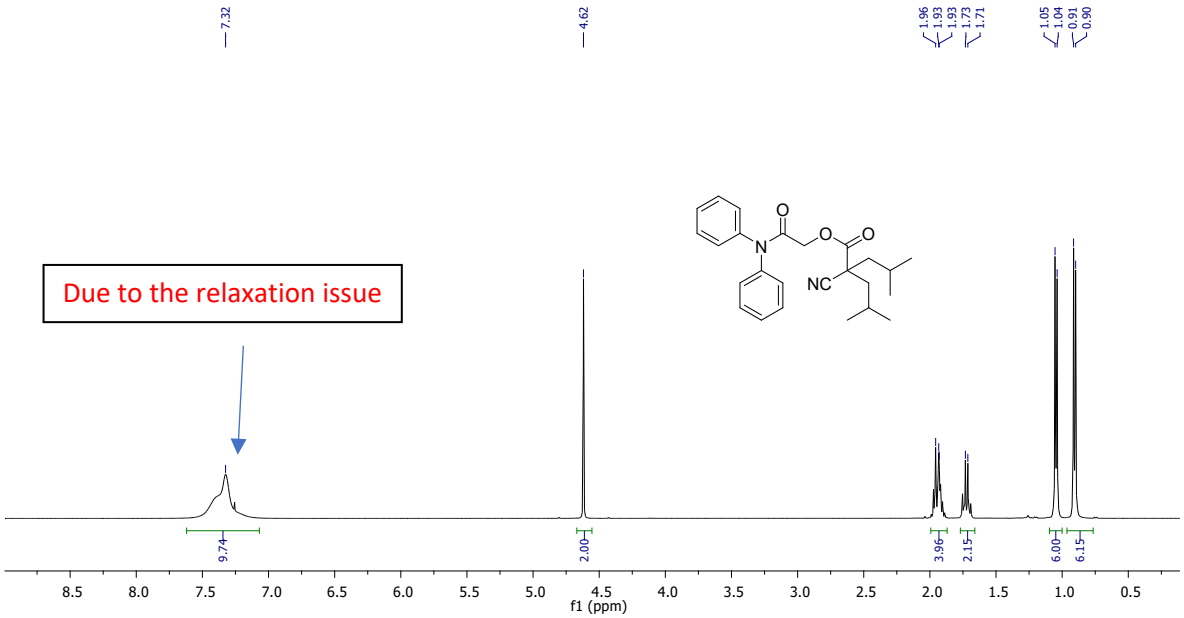
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1j** in $CDCl_3$



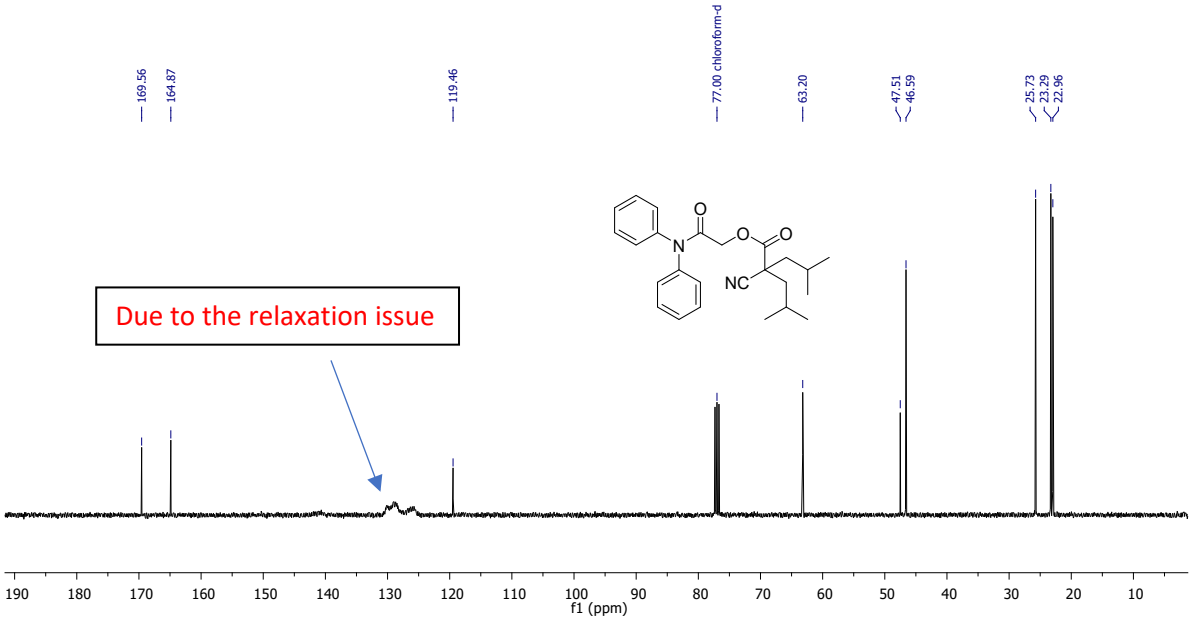
^{1}H NMR (400 MHz) spectrum of **1k** in $CDCl_3$



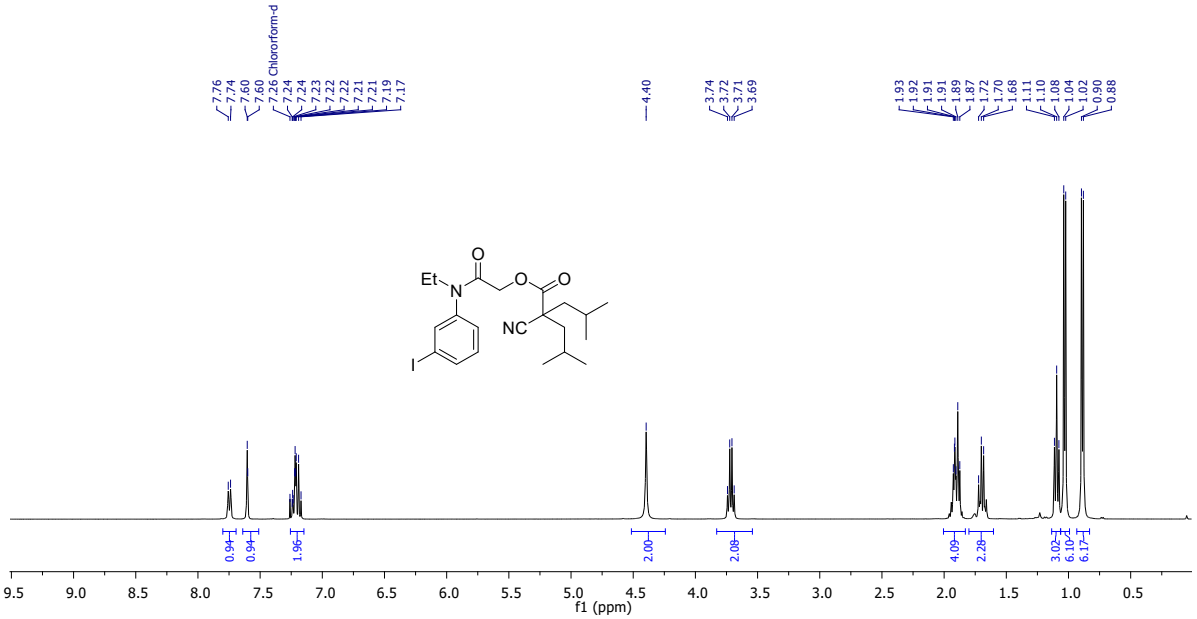
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1k** in $CDCl_3$



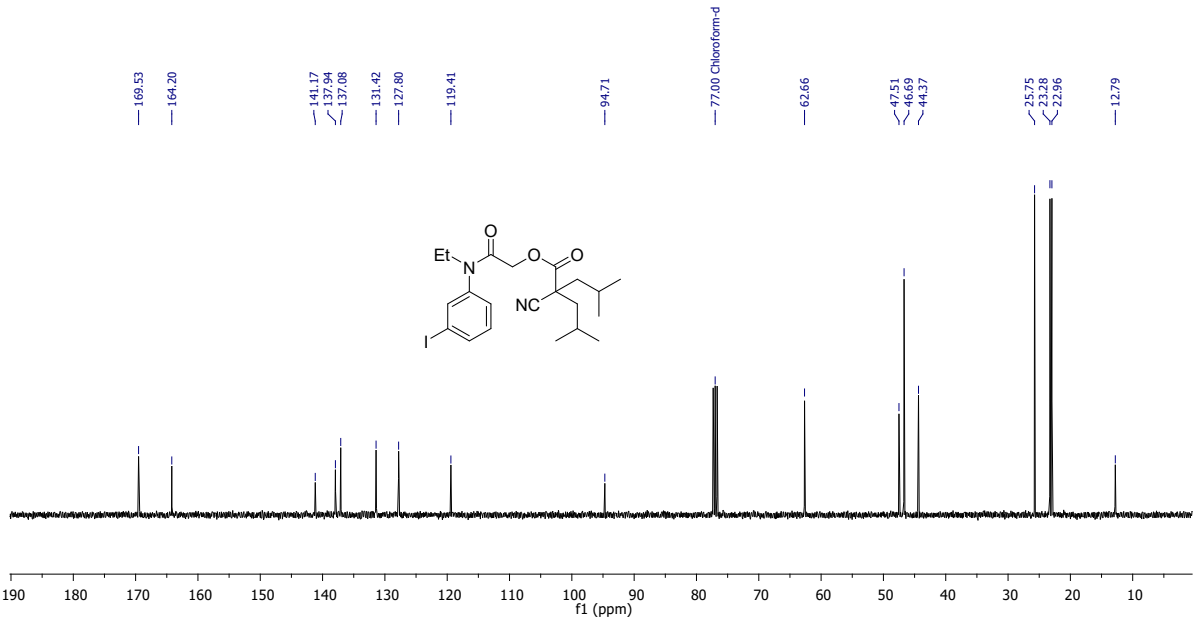
^{1}H NMR (400 MHz) spectrum of **1l** in $CDCl_3$



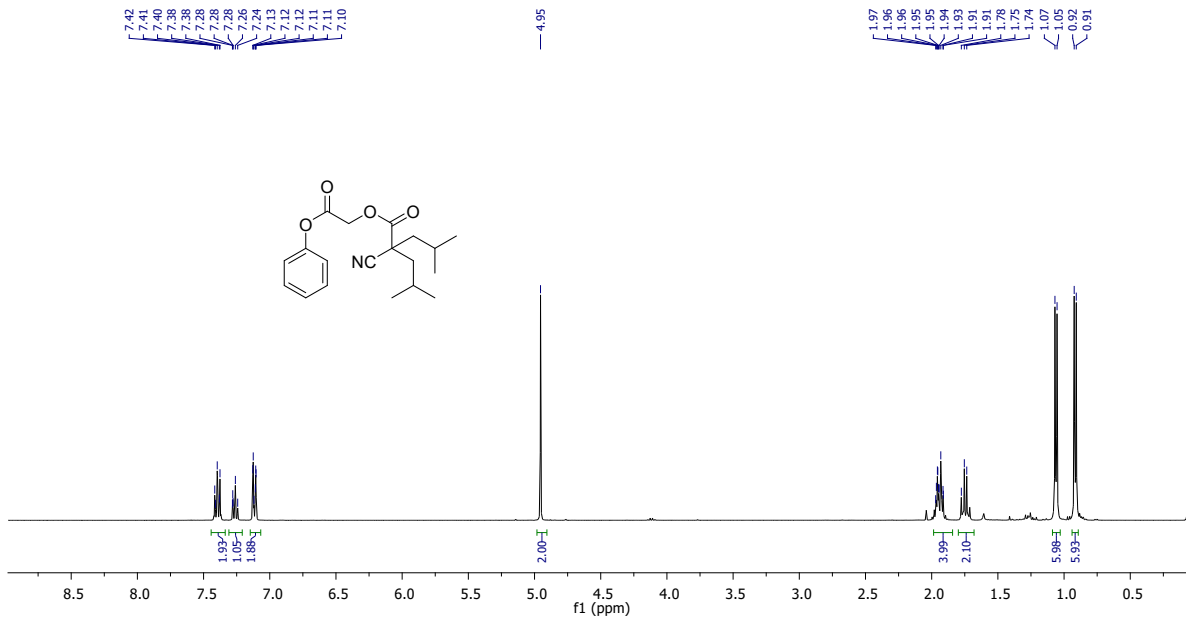
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1l** in $CDCl_3$



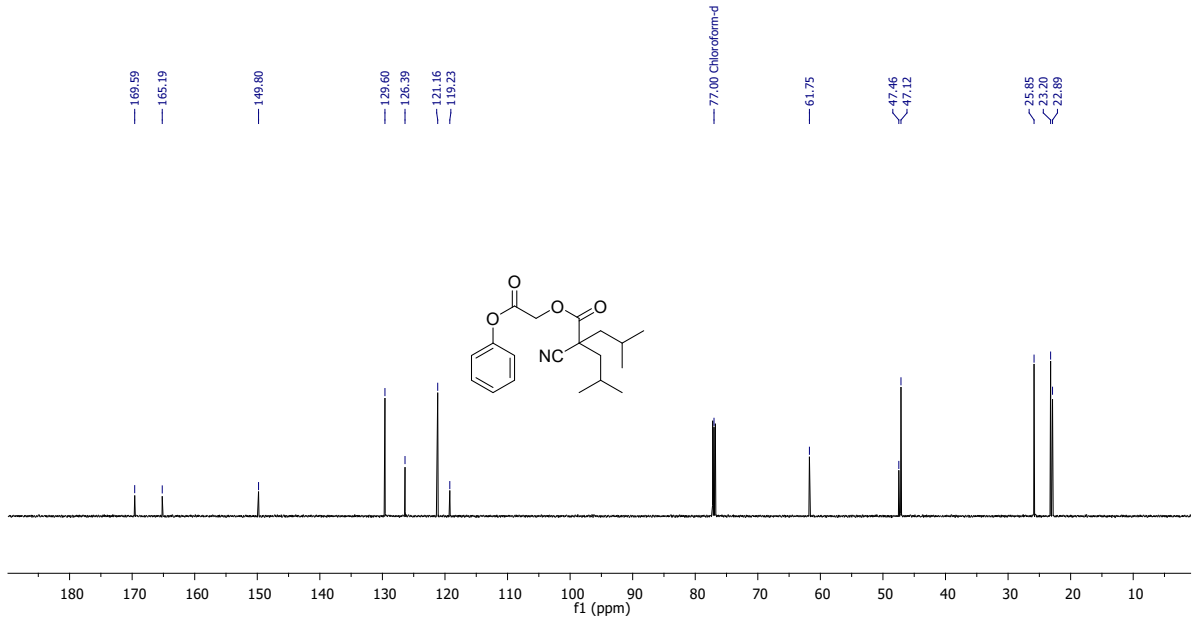
^{1}H NMR (400 MHz) spectrum of **1m** in $CDCl_3$



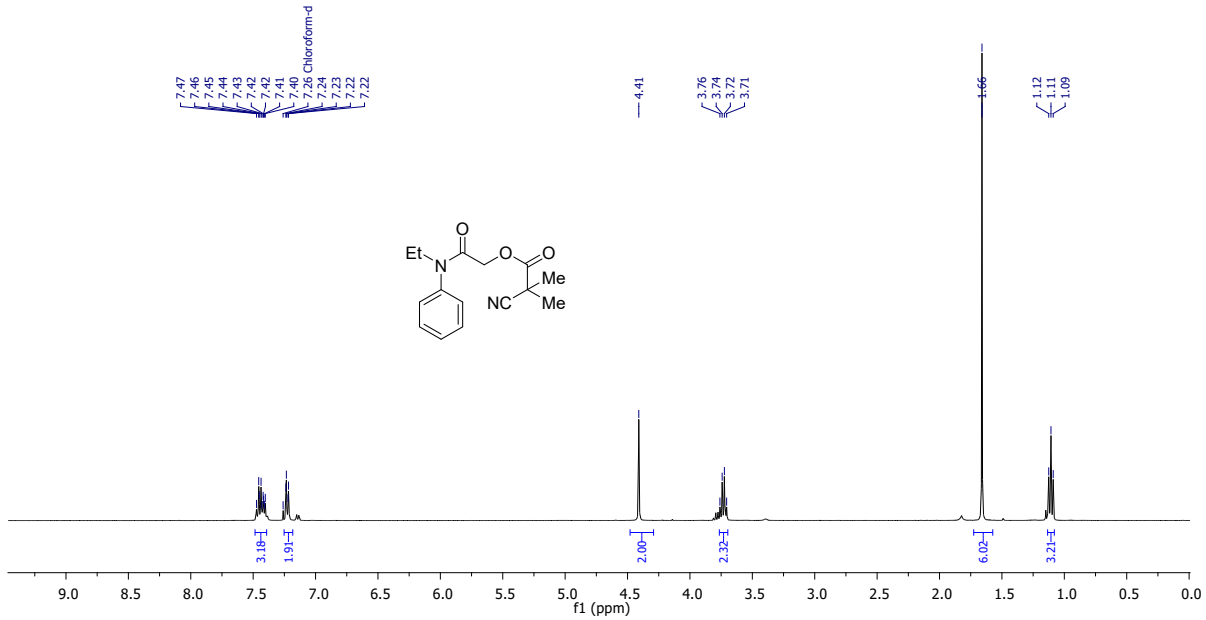
^{13}C {^{1}H} NMR (100 MHz) spectrum of **1m** in $CDCl_3$



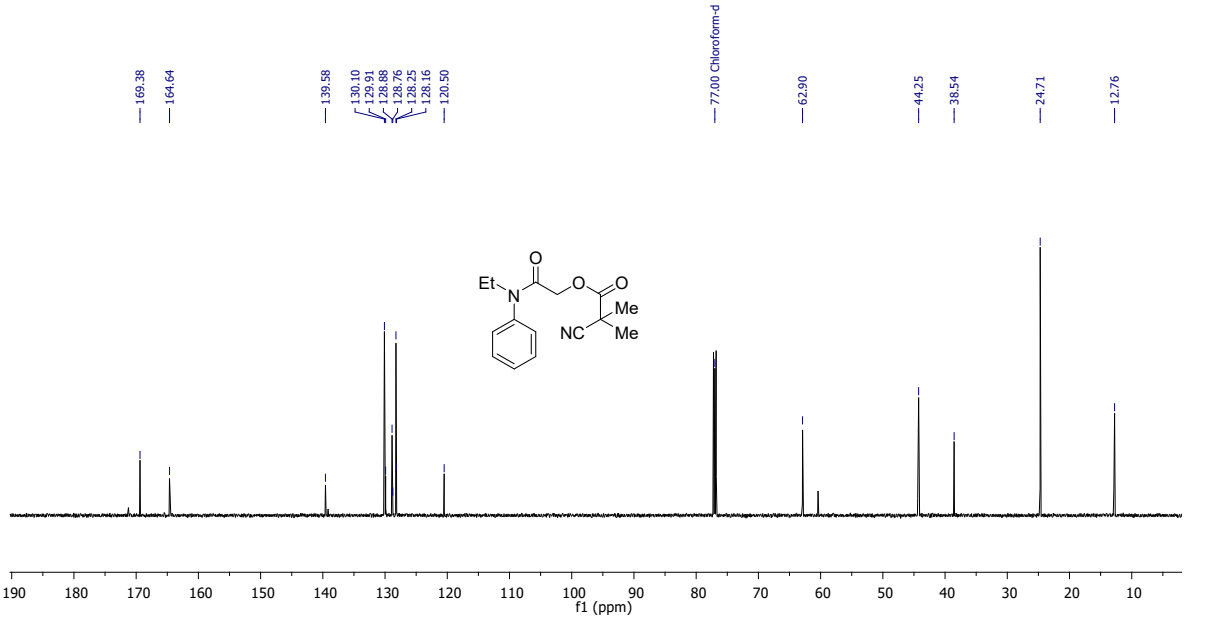
^{1}H NMR (400 MHz) spectrum of **1n** in $CDCl_3$



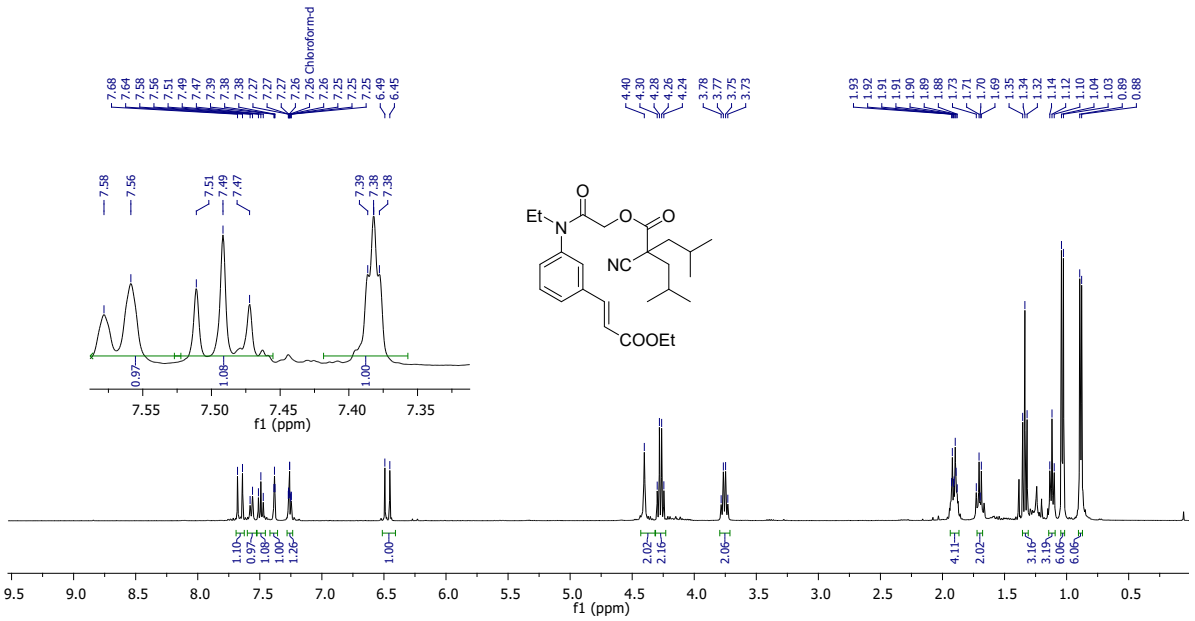
^{13}C {^{1}H} NMR (150 MHz) spectrum of **1n** in $CDCl_3$



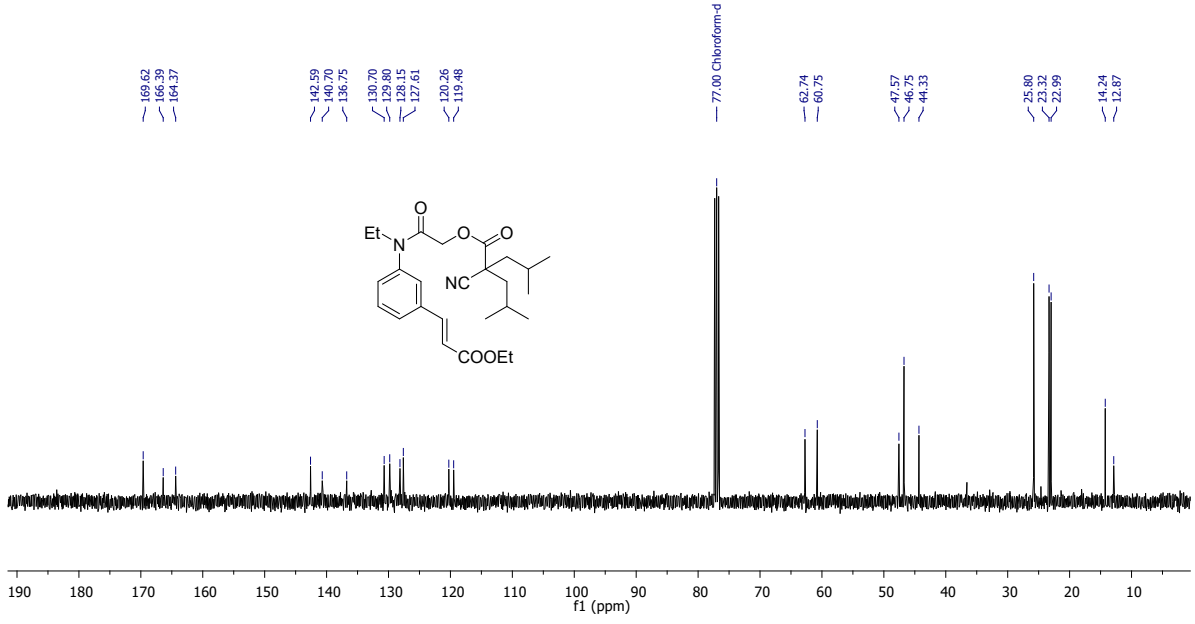
^{1}H NMR (400 MHz) spectrum of **1o** in $CDCl_3$



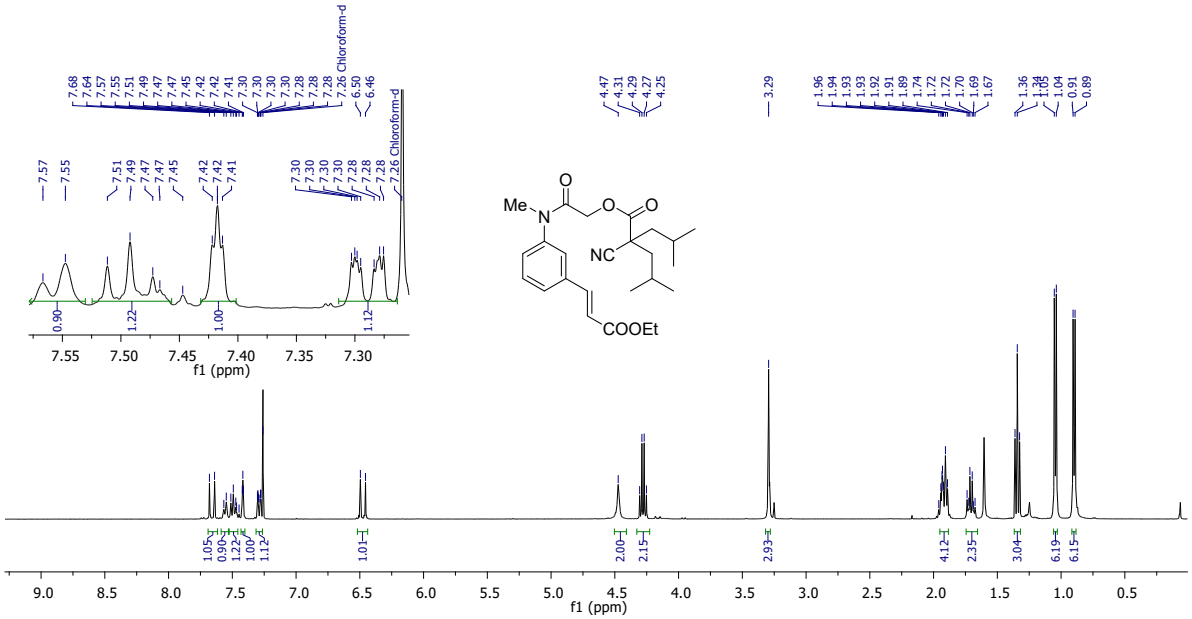
^{13}C {^{1}H} NMR (150 MHz) spectrum of **1o** in $CDCl_3$



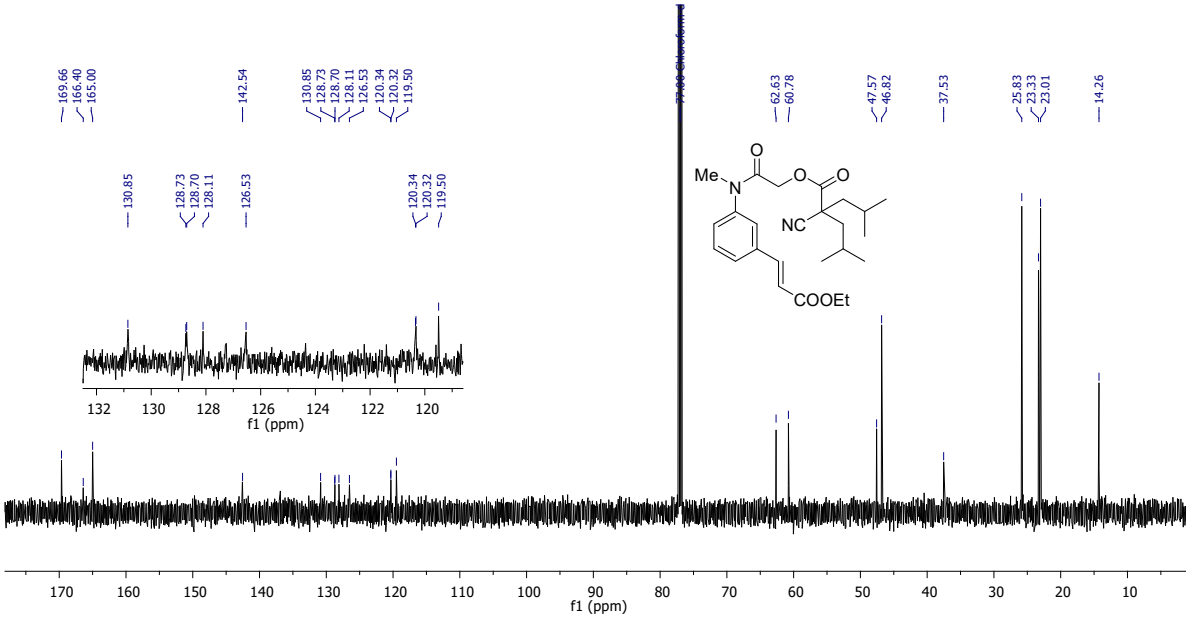
^{1}H NMR (400 MHz) spectrum of **3aa** in $CDCl_3$



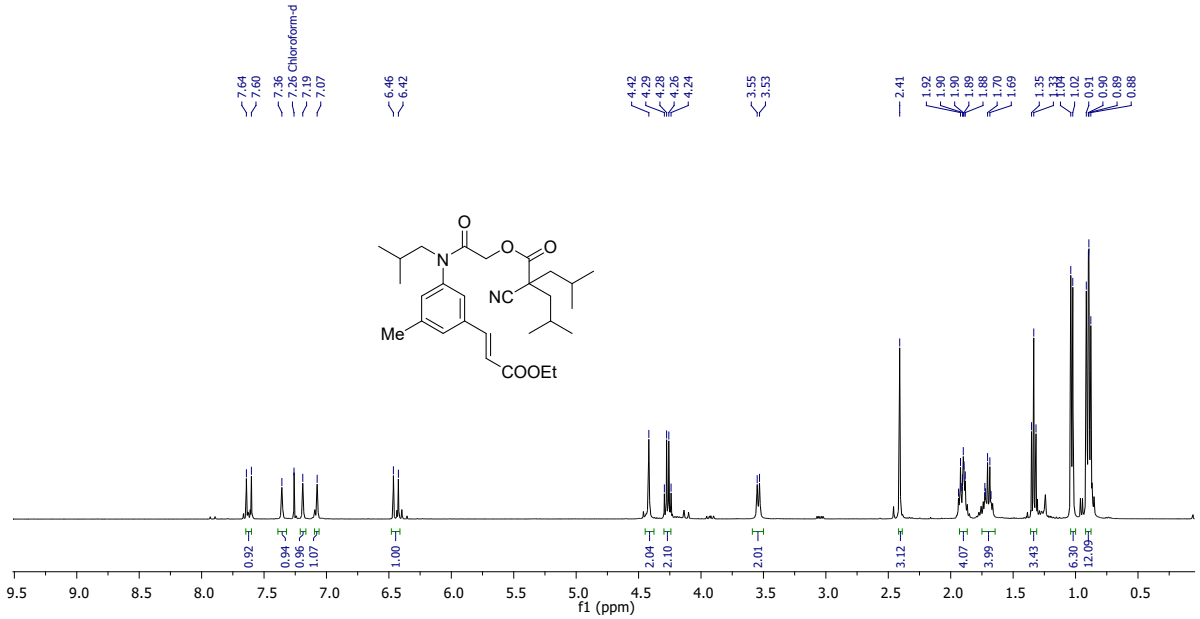
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3aa** in $CDCl_3$



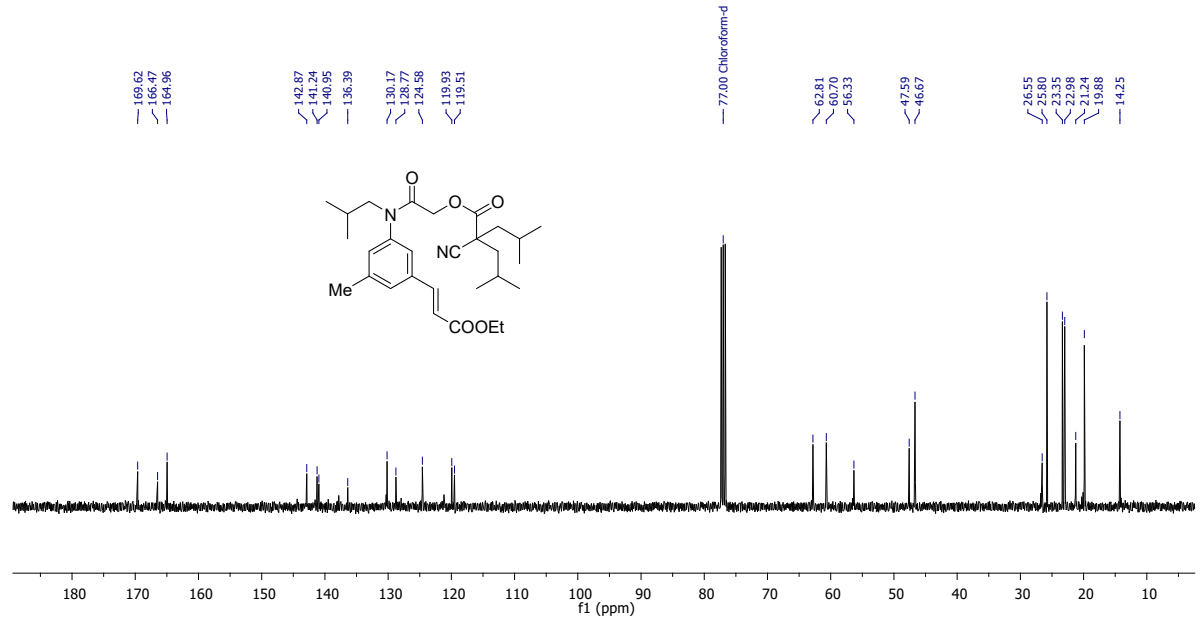
^{1}H NMR (400 MHz) spectrum of **3ba** in $CDCl_3$



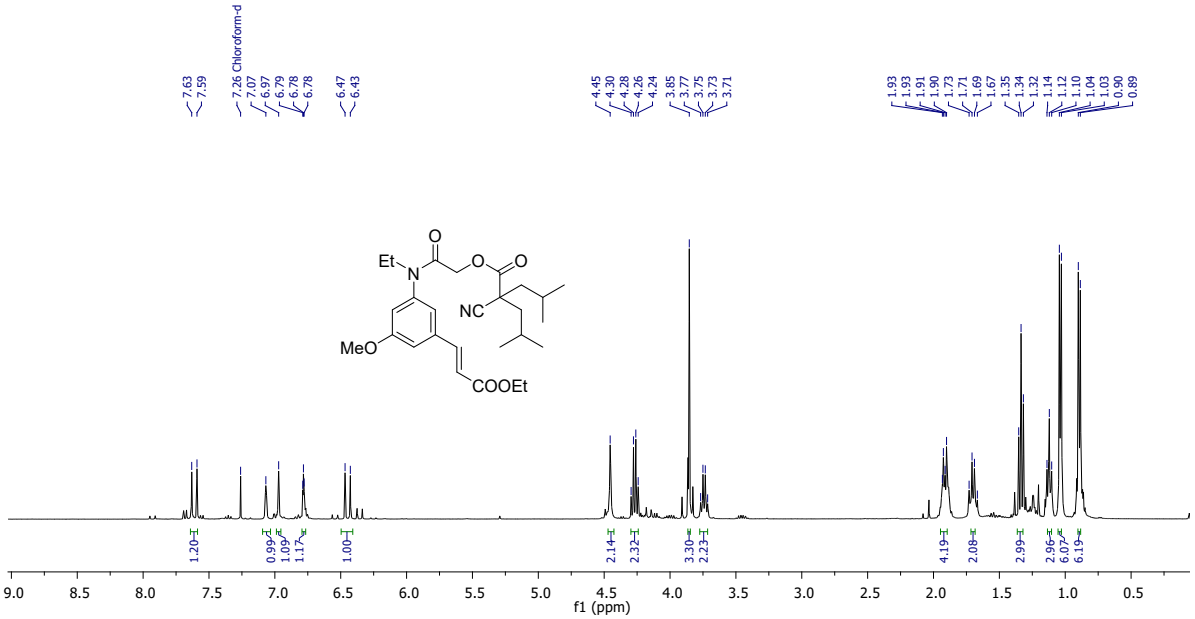
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ba** in $CDCl_3$



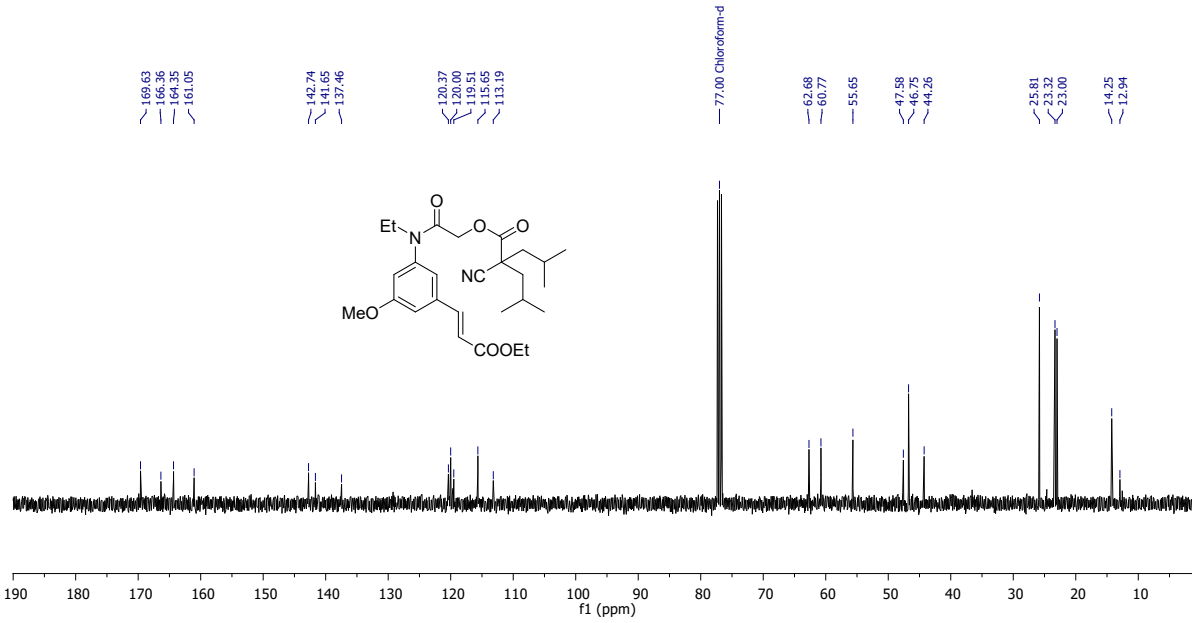
^{1}H NMR (400 MHz) spectrum of **3ca** in $CDCl_3$



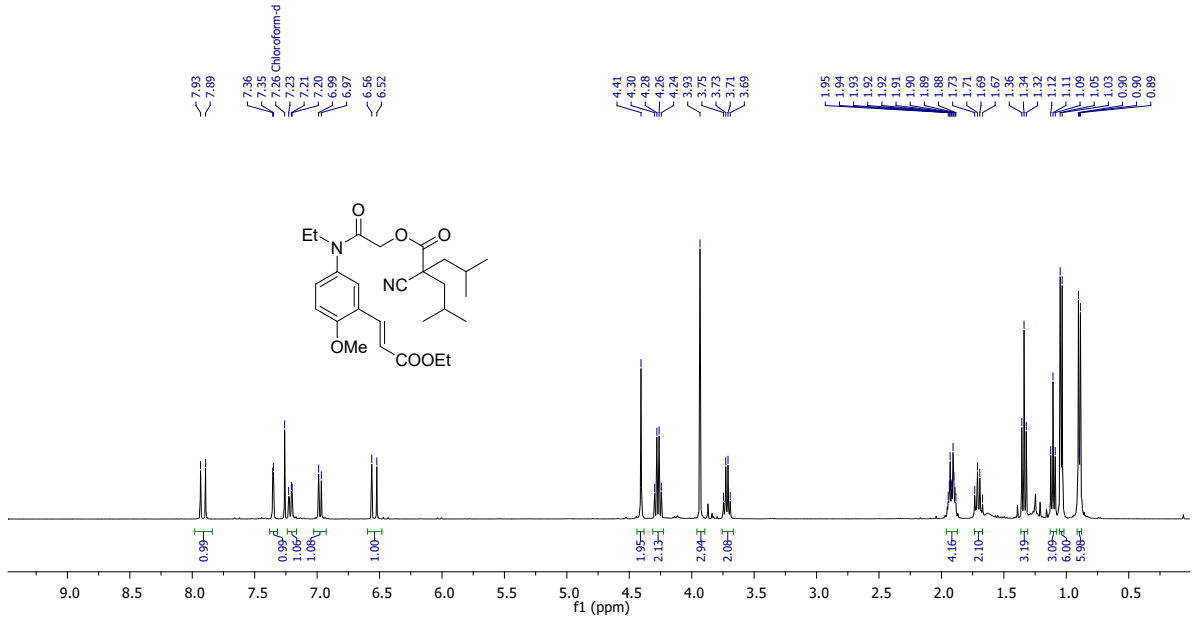
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ca** in $CDCl_3$



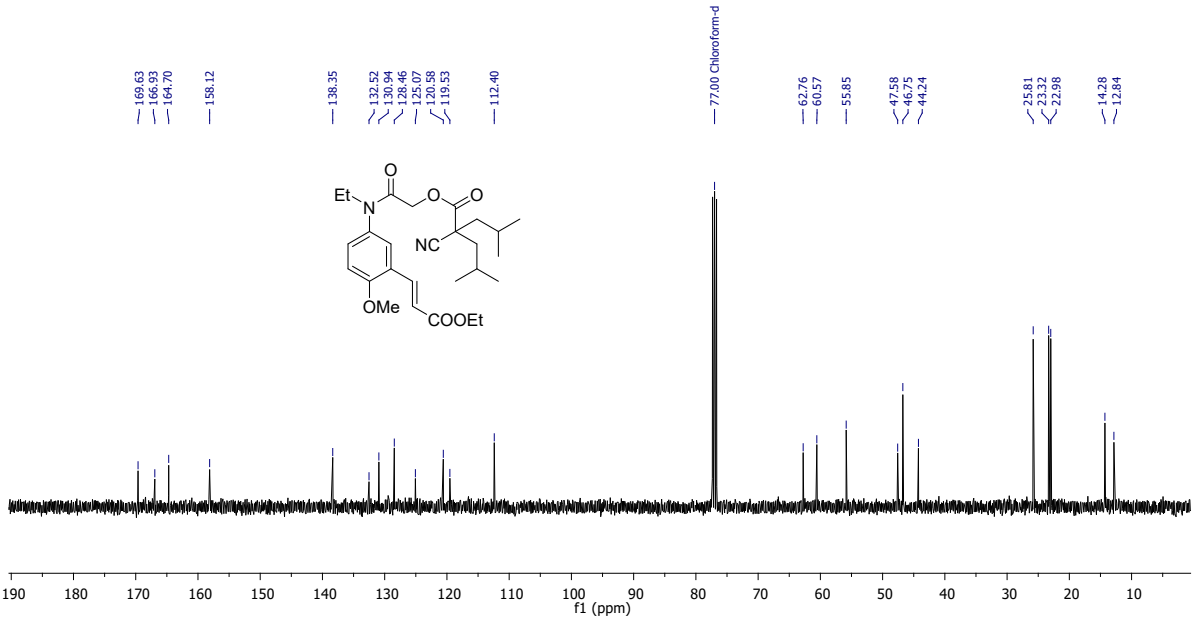
^{1}H NMR (400 MHz) spectrum of **3da** in $CDCl_3$



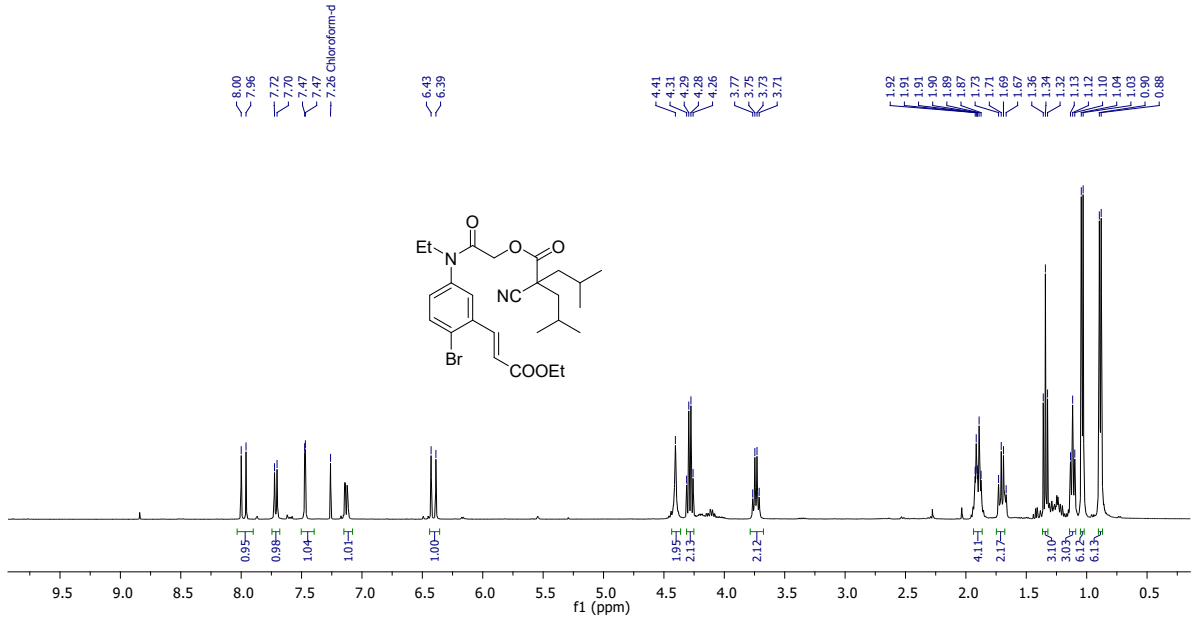
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3da** in $CDCl_3$



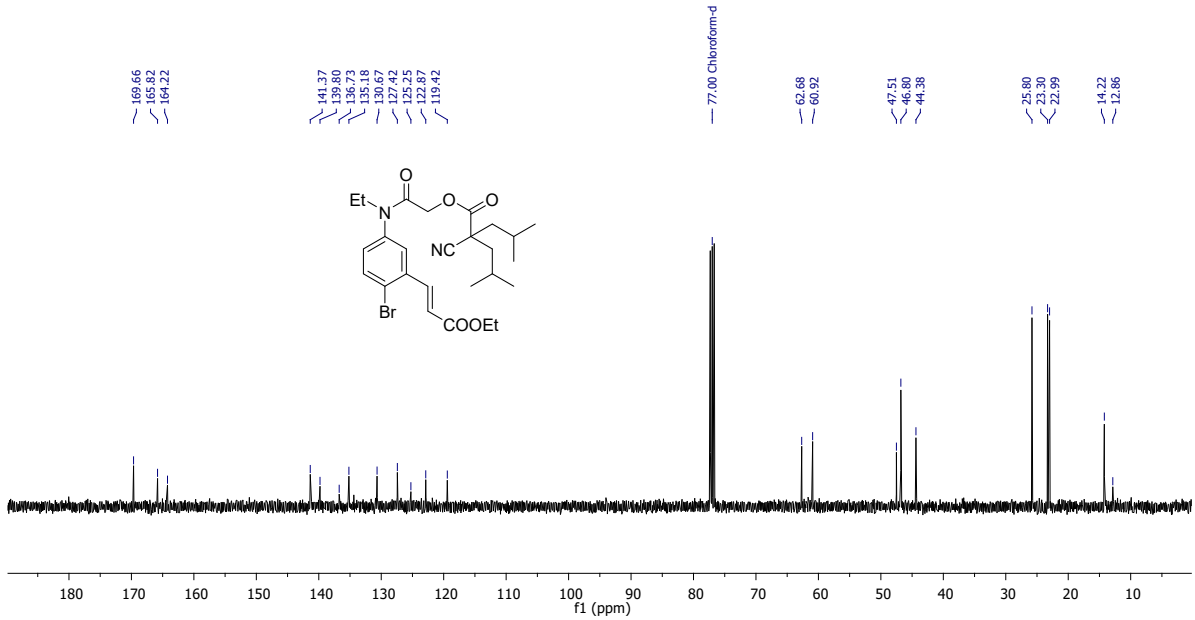
^{1}H NMR (400 MHz) spectrum of **3ea** in $CDCl_3$



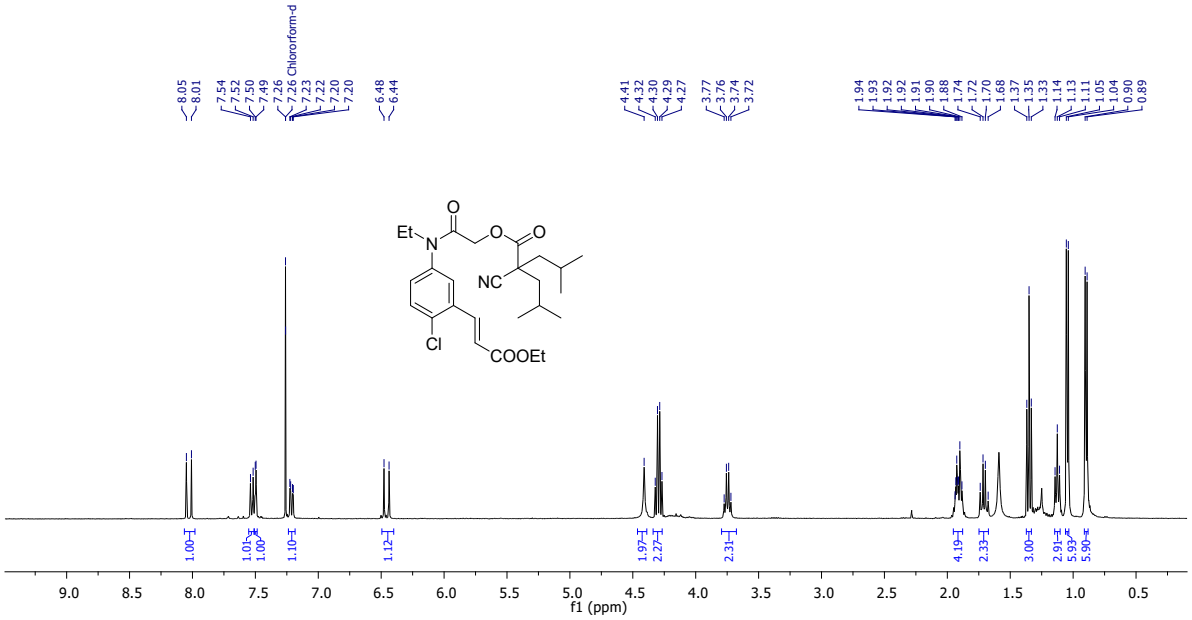
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ea** in $CDCl_3$



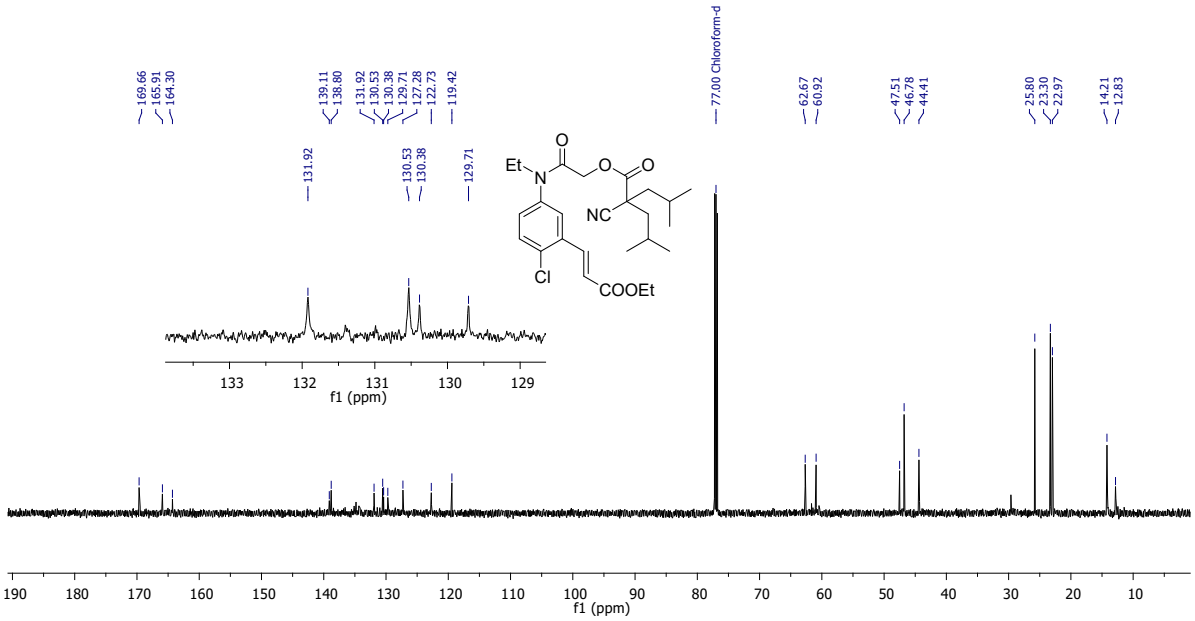
^{1}H NMR (400 MHz) spectrum of **3fa** in $CDCl_3$



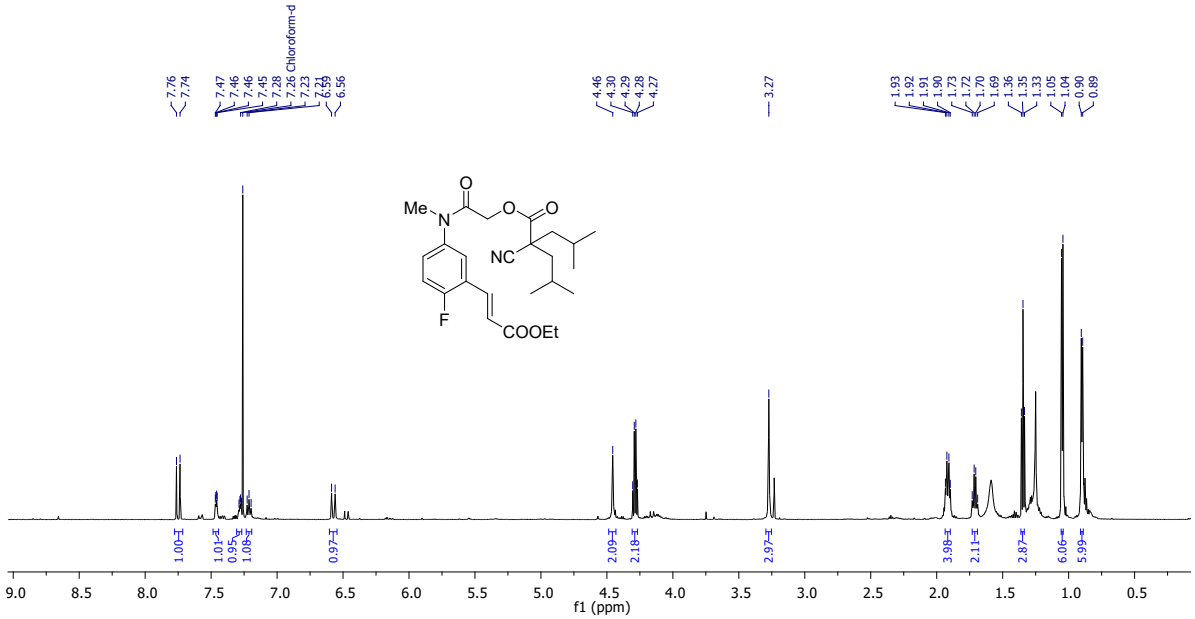
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3fa** in $CDCl_3$



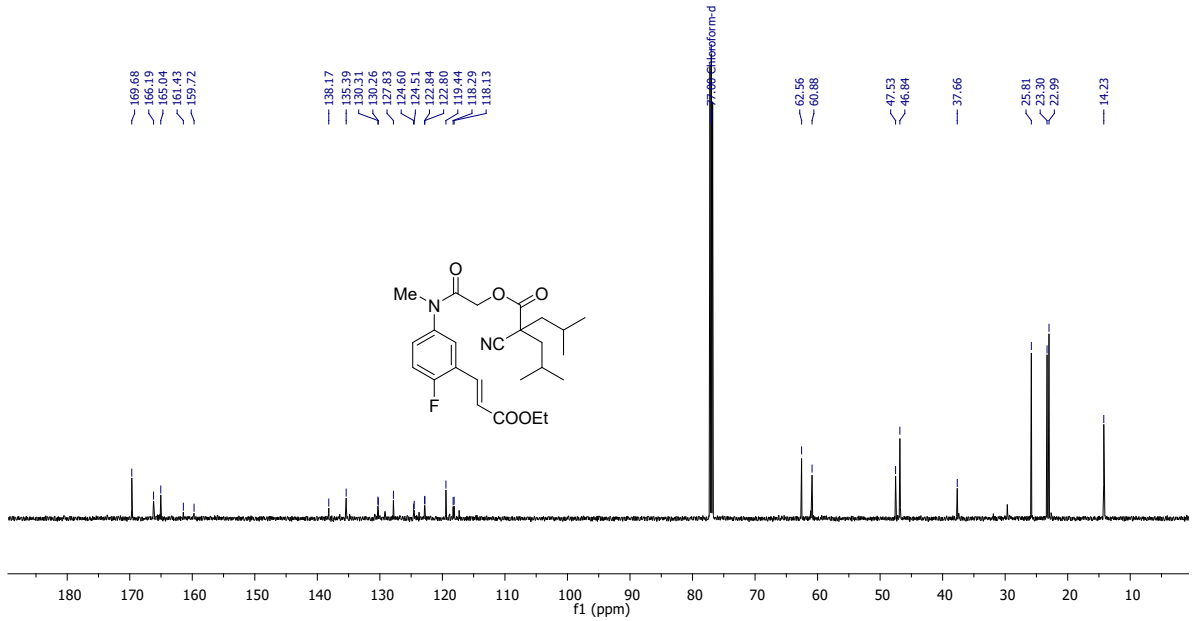
^{1}H NMR (400 MHz) spectrum of **3ga** in $CDCl_3$



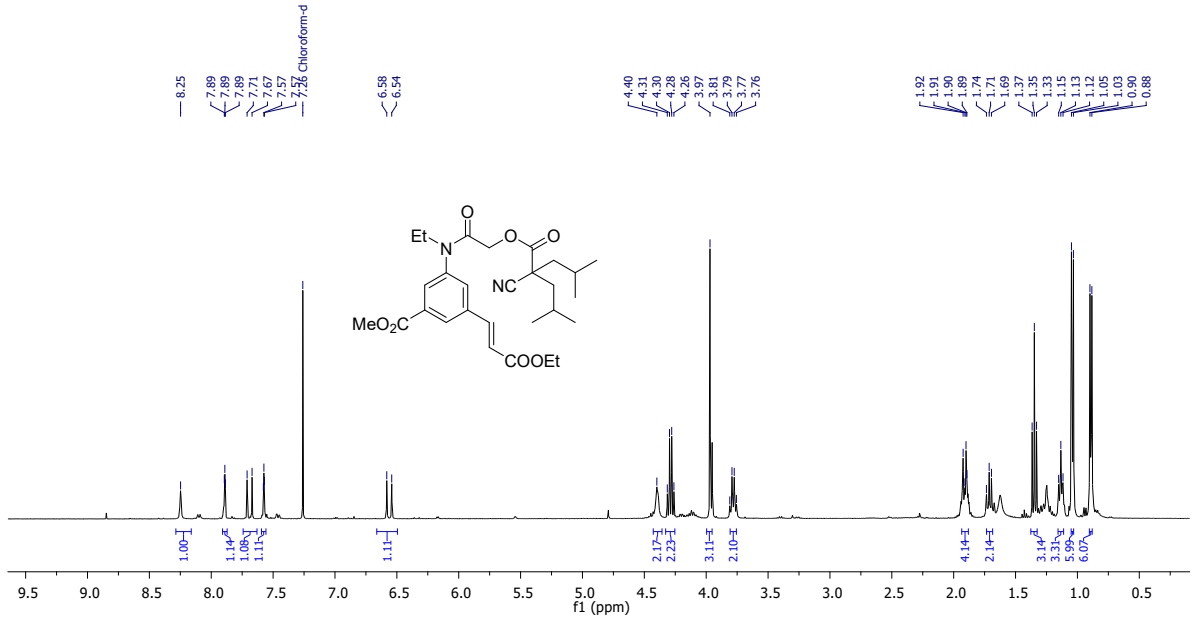
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ga** in $CDCl_3$



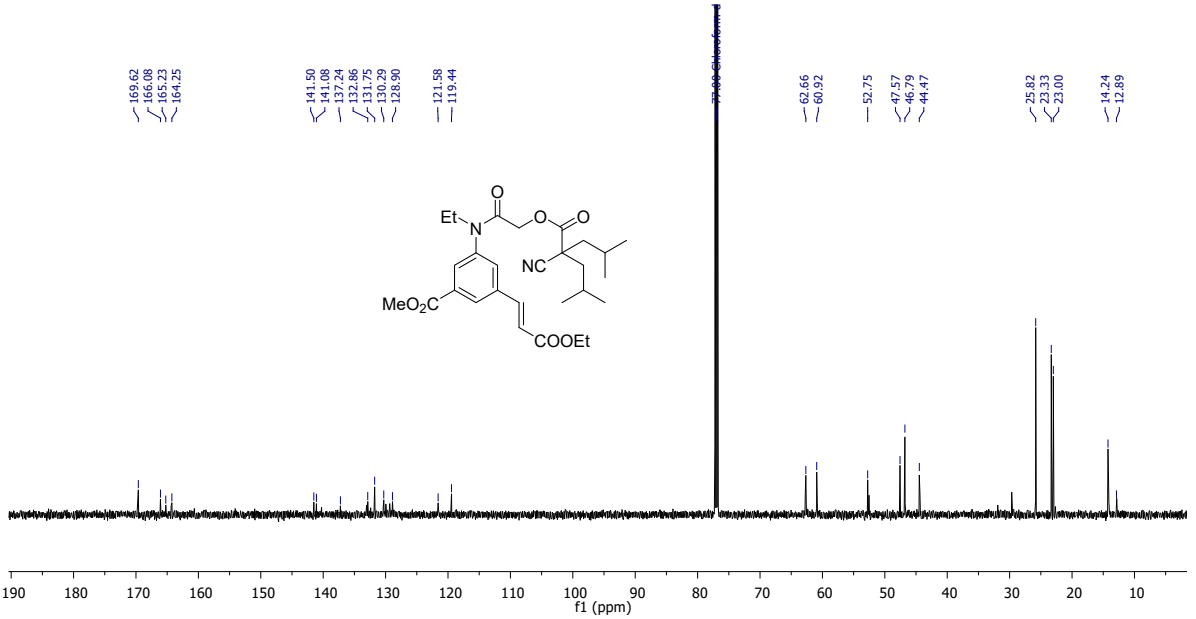
^{1}H NMR (600 MHz) spectrum of **3ha** in $CDCl_3$



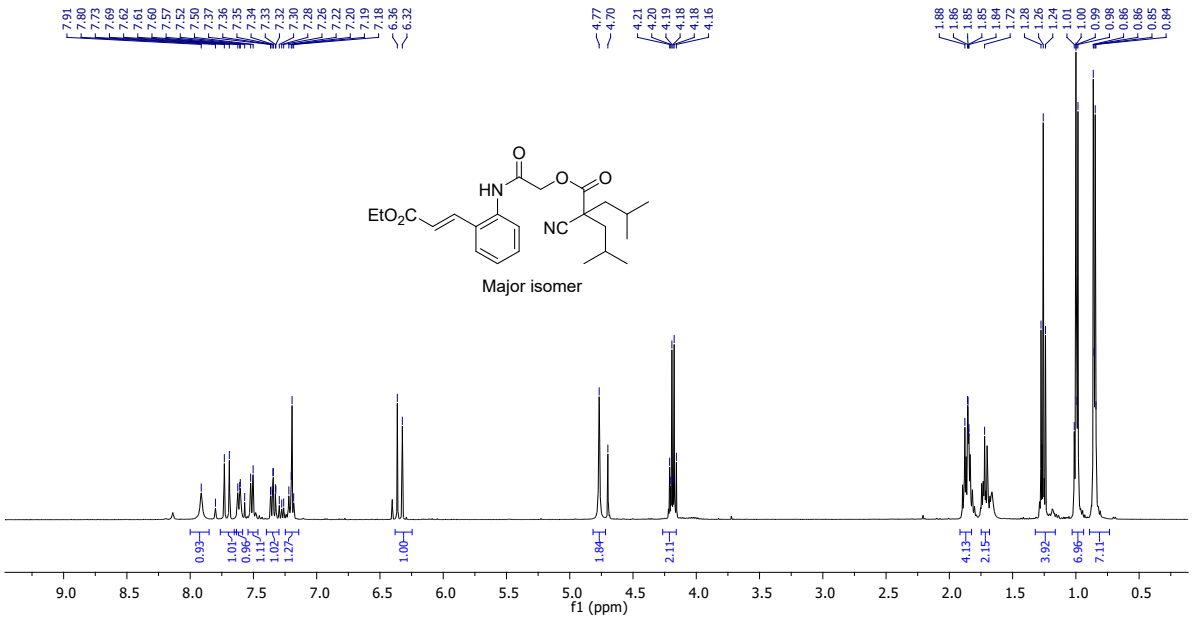
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ha** in $CDCl_3$



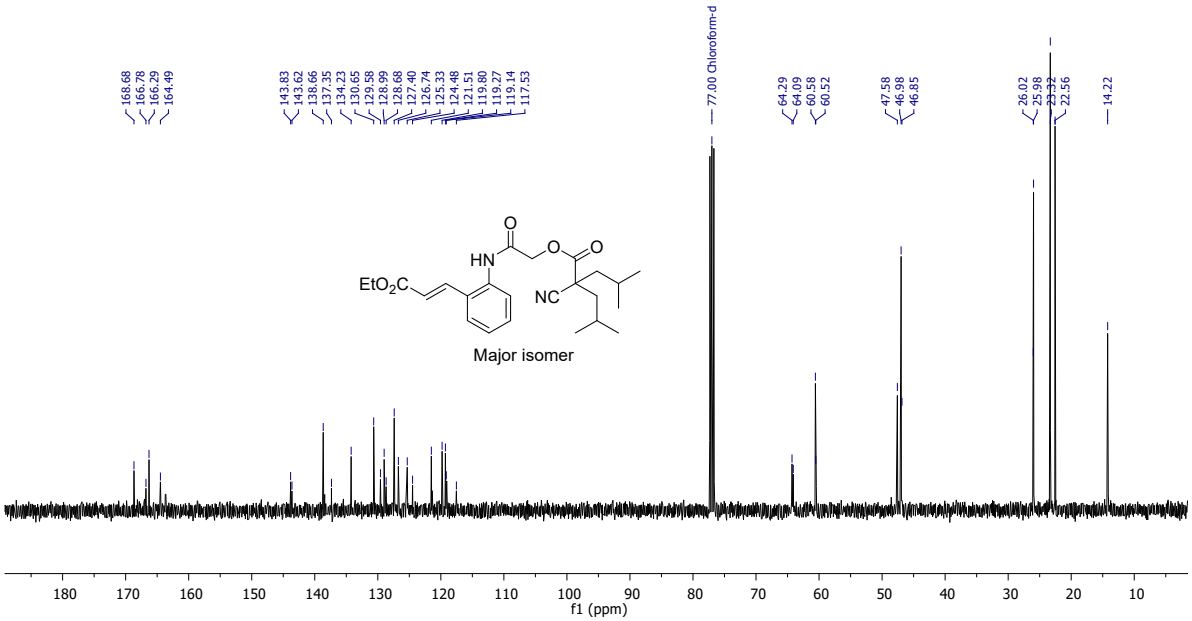
^{1}H NMR (400 MHz) spectrum of **3ia** in $CDCl_3$



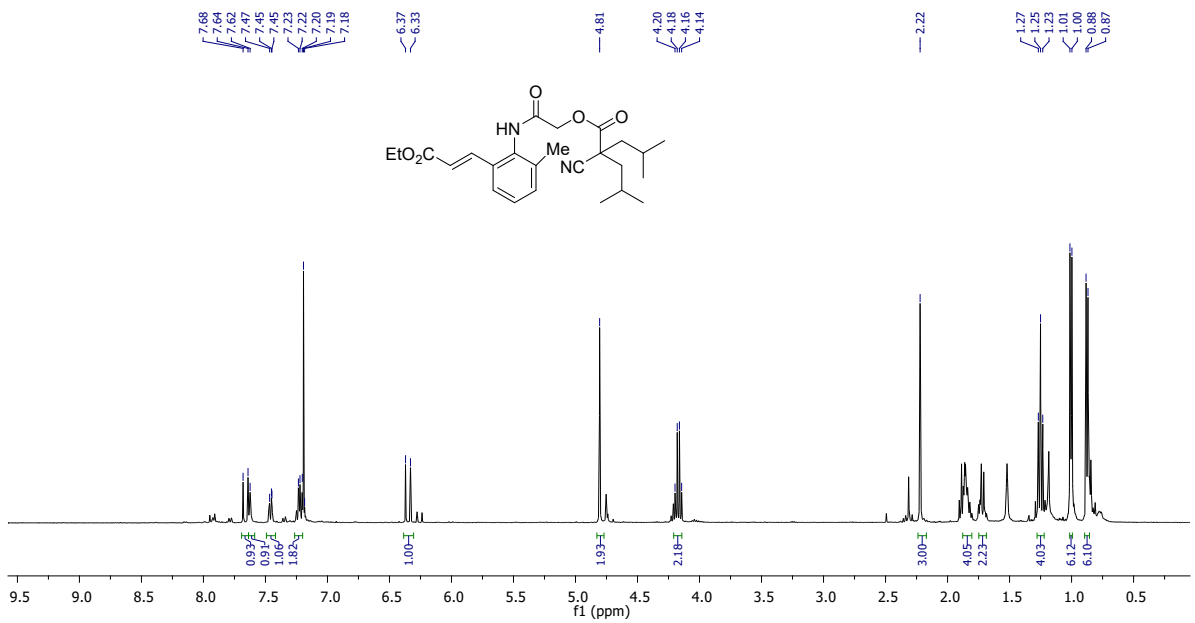
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ia** in $CDCl_3$



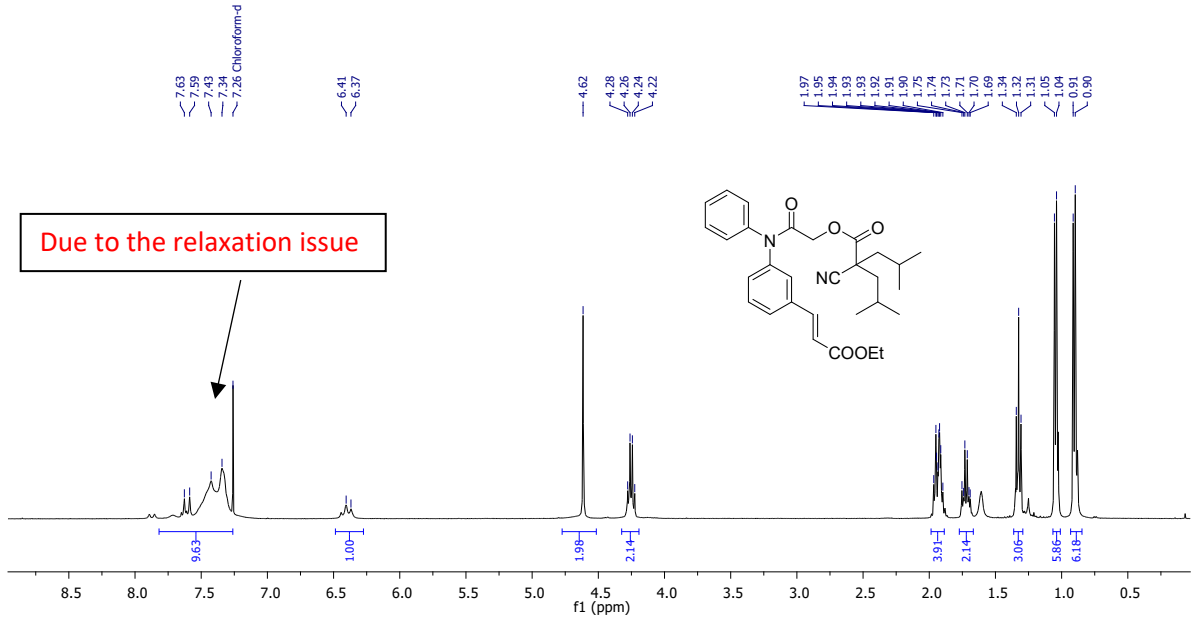
^{1}H NMR (400 MHz) spectrum of **3ja** in $CDCl_3$



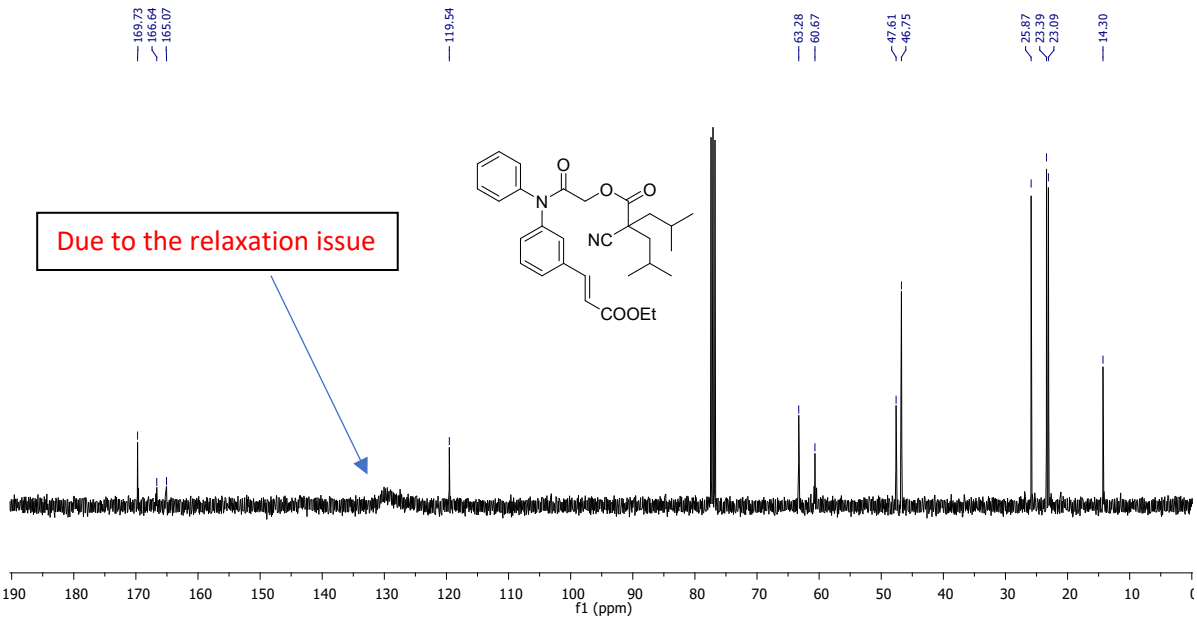
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ja** in $CDCl_3$



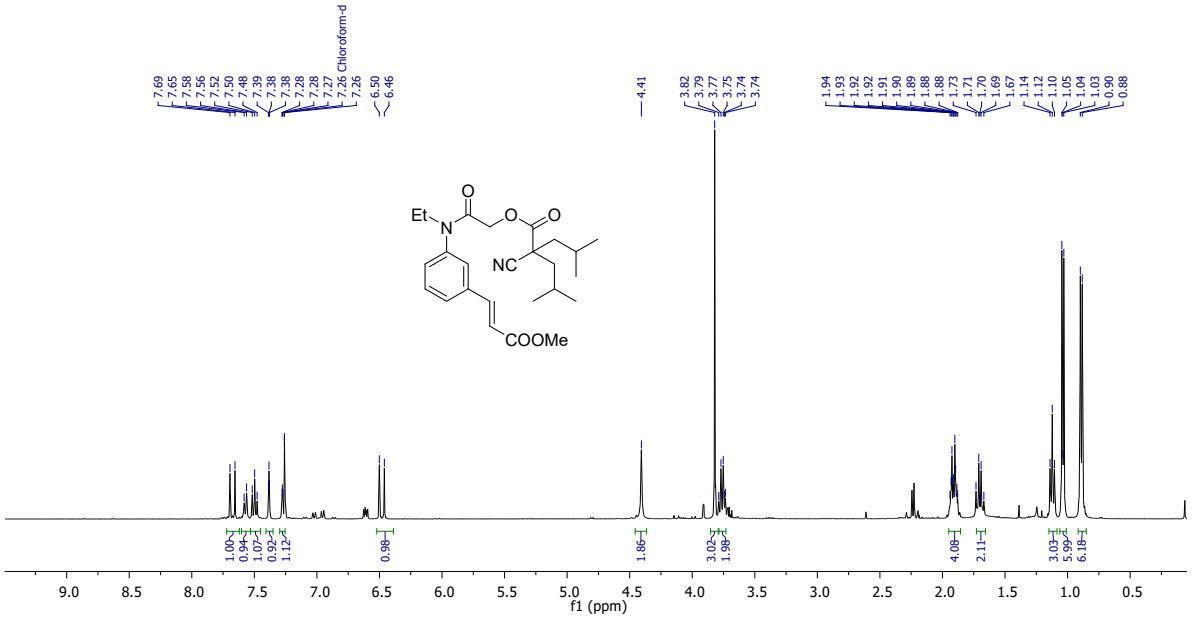
^{1}H NMR (400 MHz) spectrum of **3ka** in $CDCl_3$



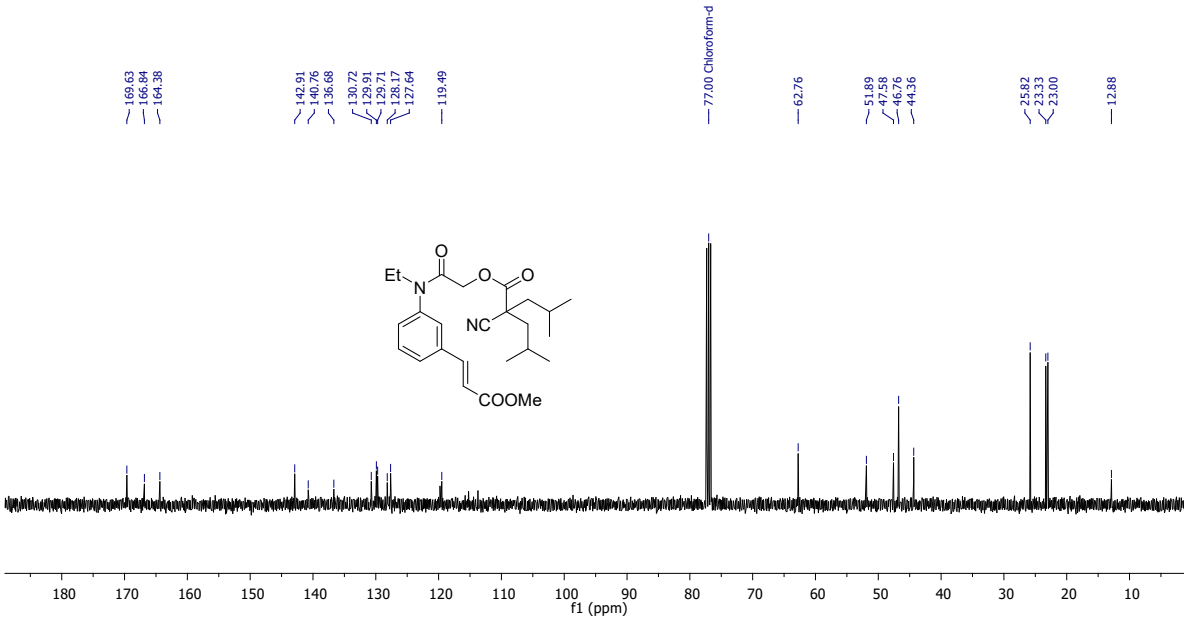
^{1}H NMR (400 MHz) spectrum of **3la** in $CDCl_3$



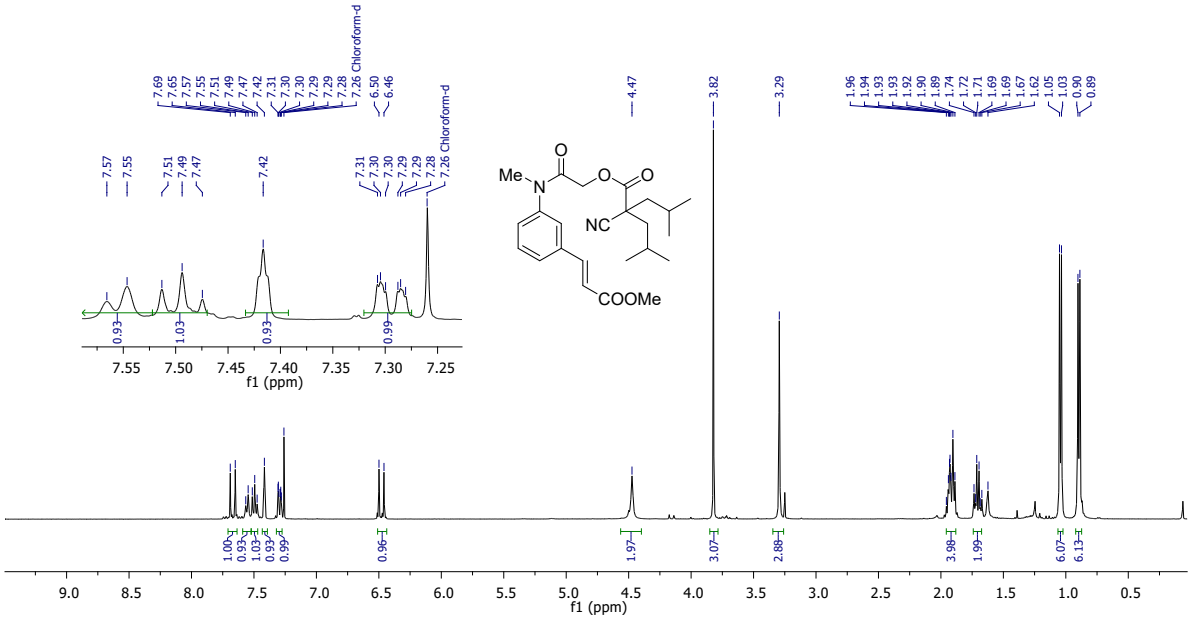
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3la** in $CDCl_3$



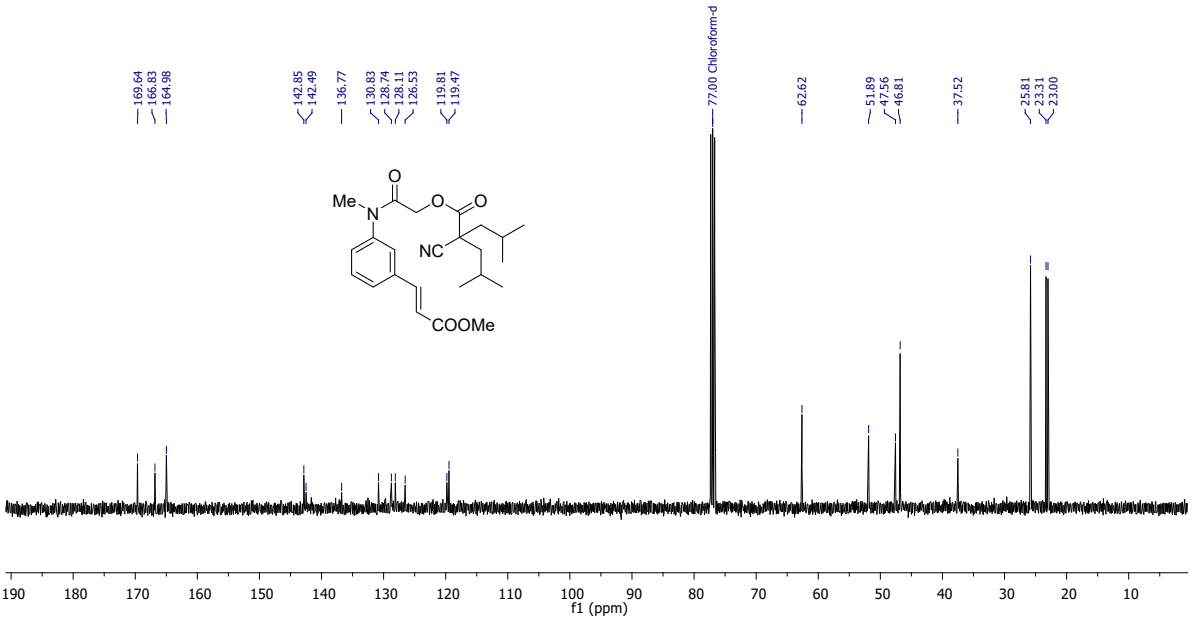
^{1}H NMR (400 MHz) spectrum of **3ab** in $CDCl_3$



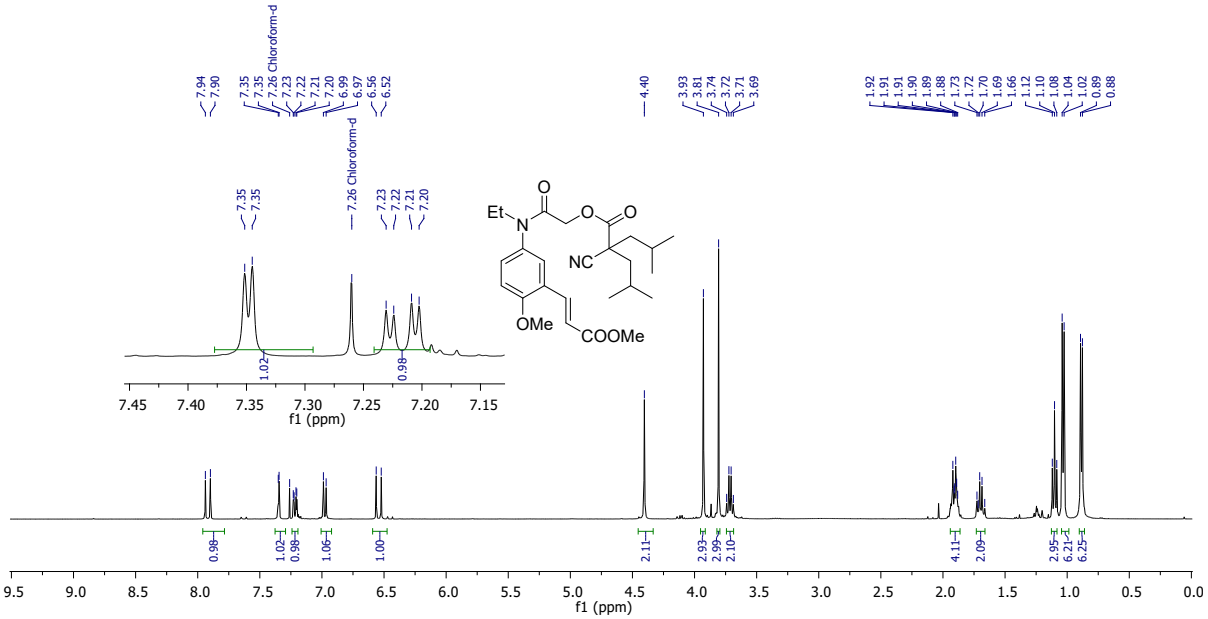
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ab** in $CDCl_3$



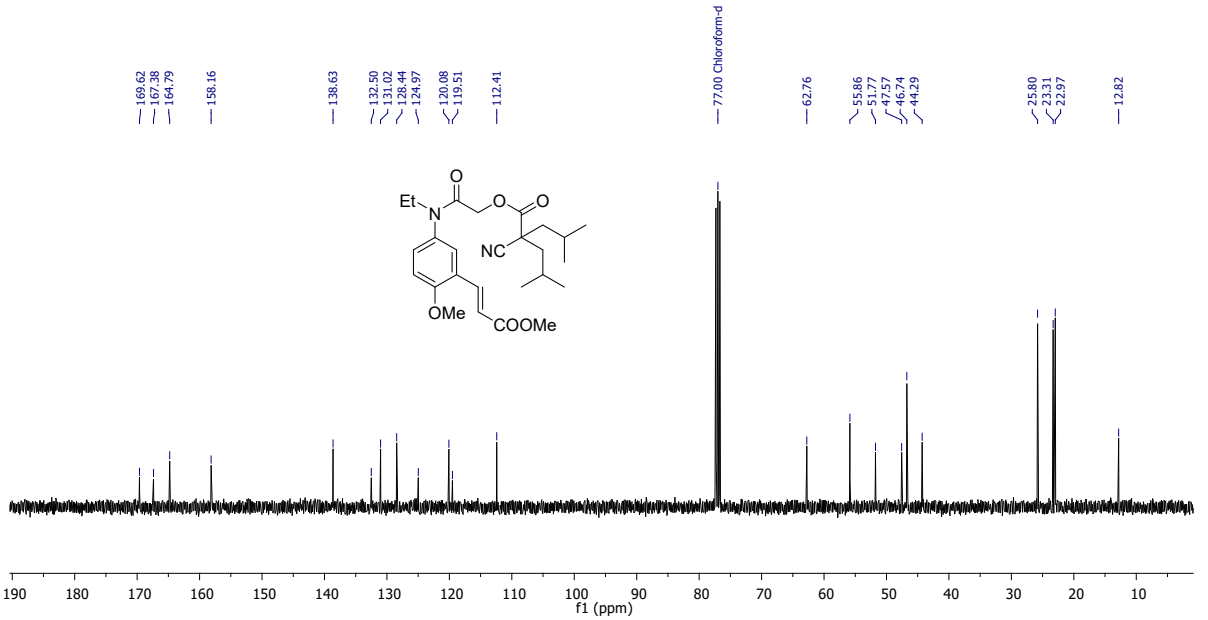
^{1}H NMR (400 MHz) spectrum of **3bb** in $CDCl_3$



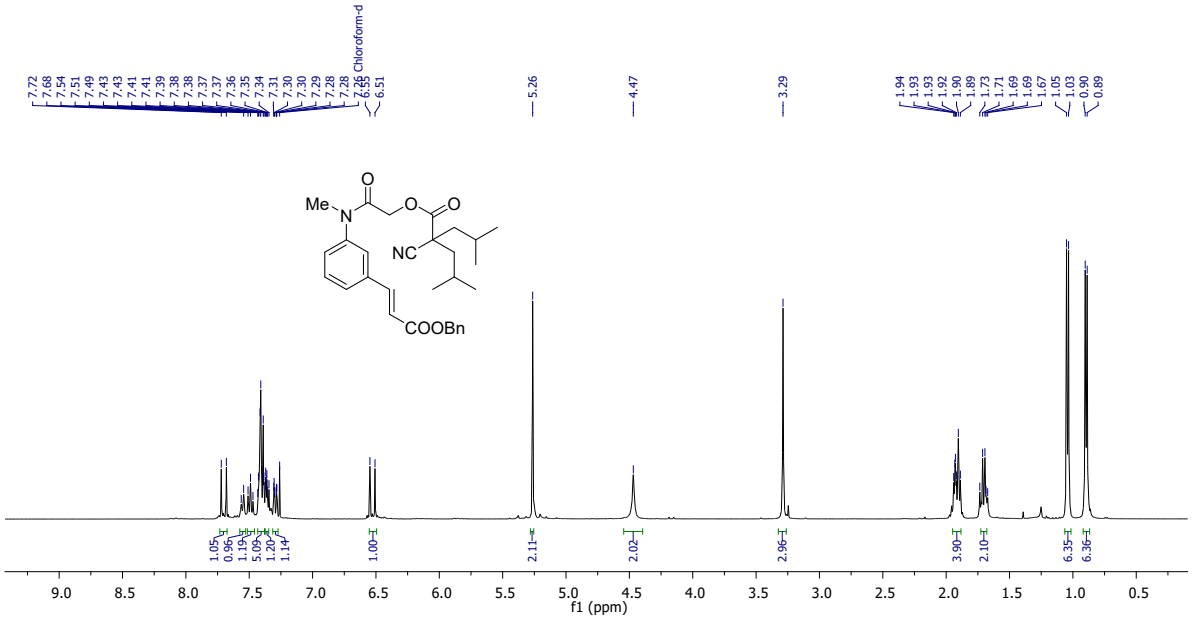
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3bb** in $CDCl_3$



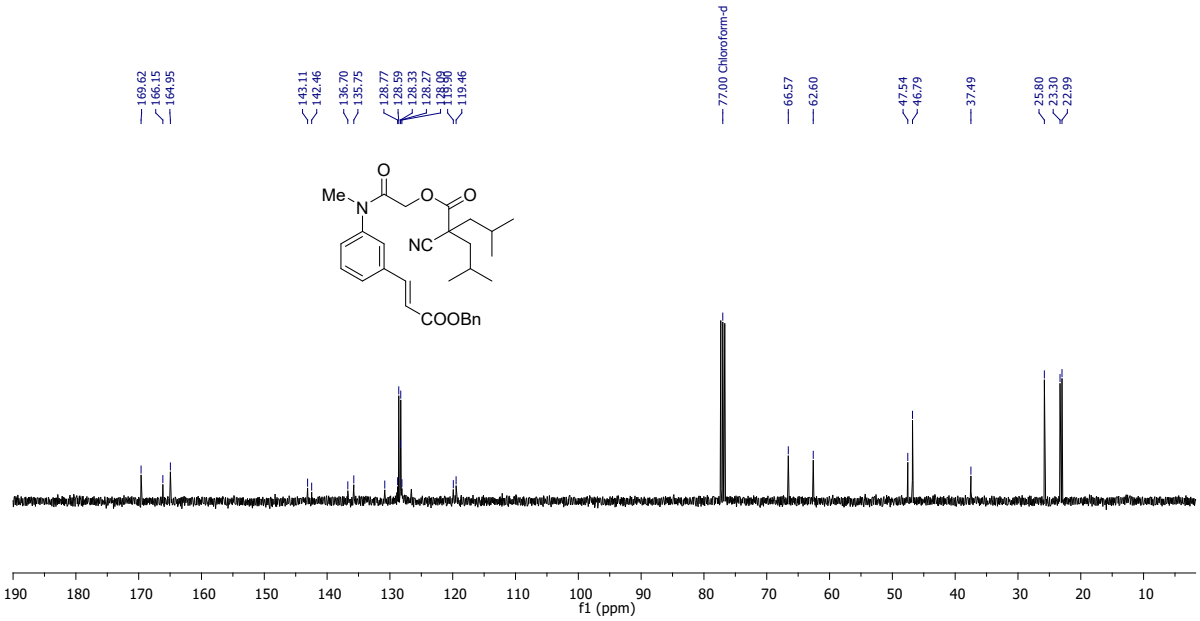
^{1}H NMR (400 MHz) spectrum of **3eb** in $CDCl_3$



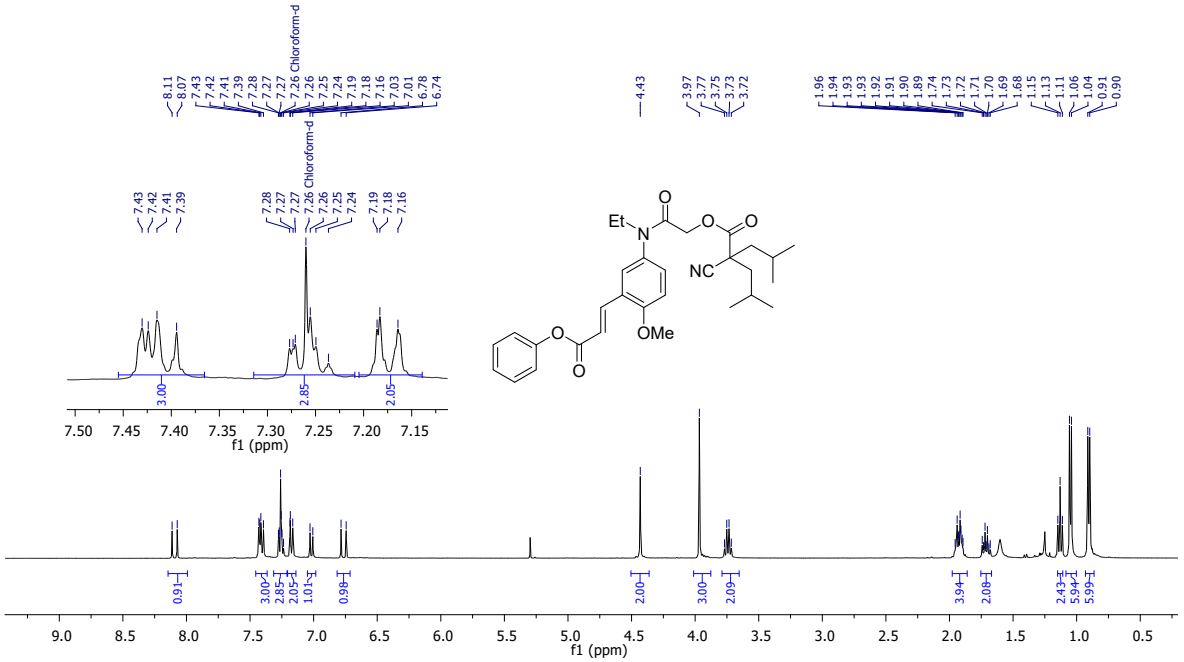
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3eb** in $CDCl_3$



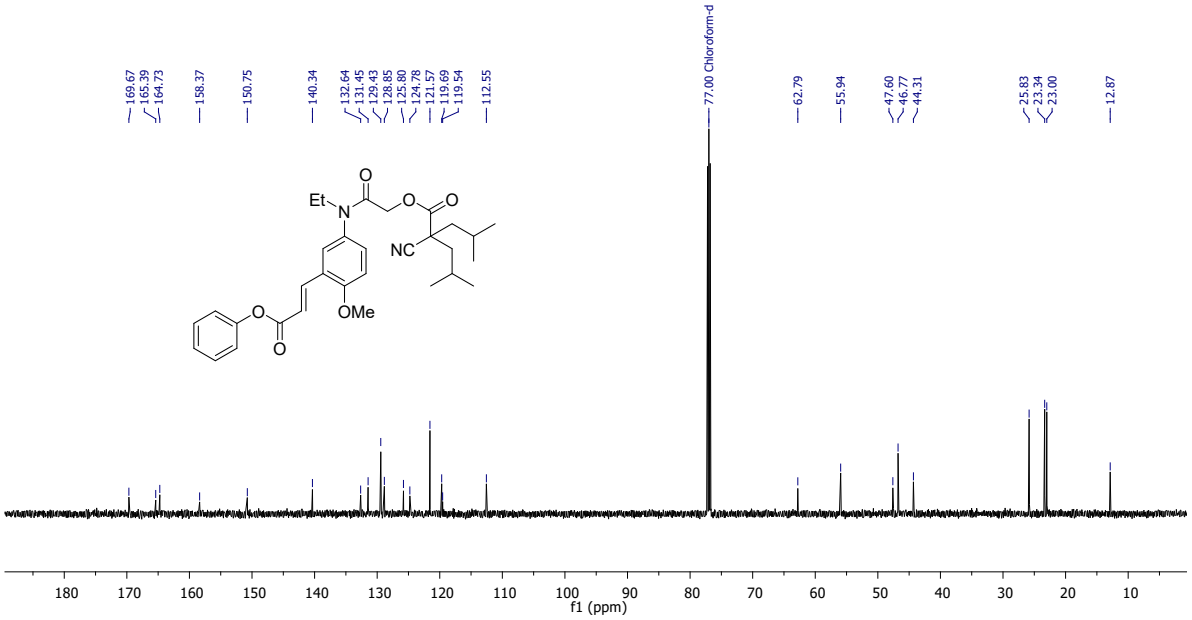
^{1}H NMR (400 MHz) spectrum of **3bc** in $CDCl_3$



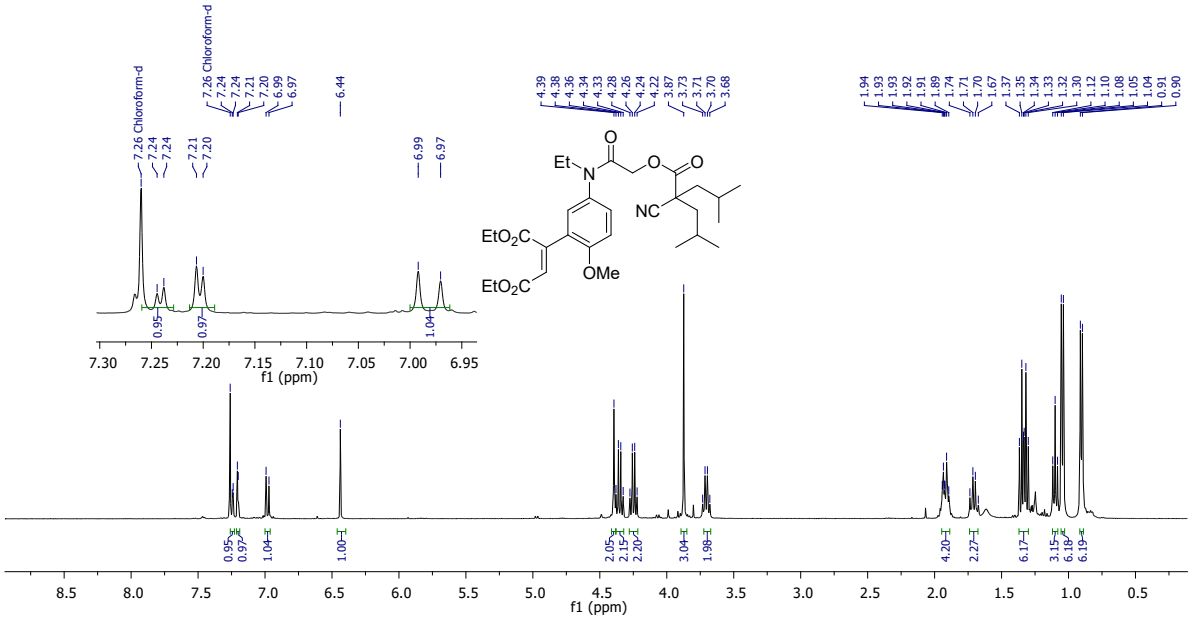
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3bc** in $CDCl_3$



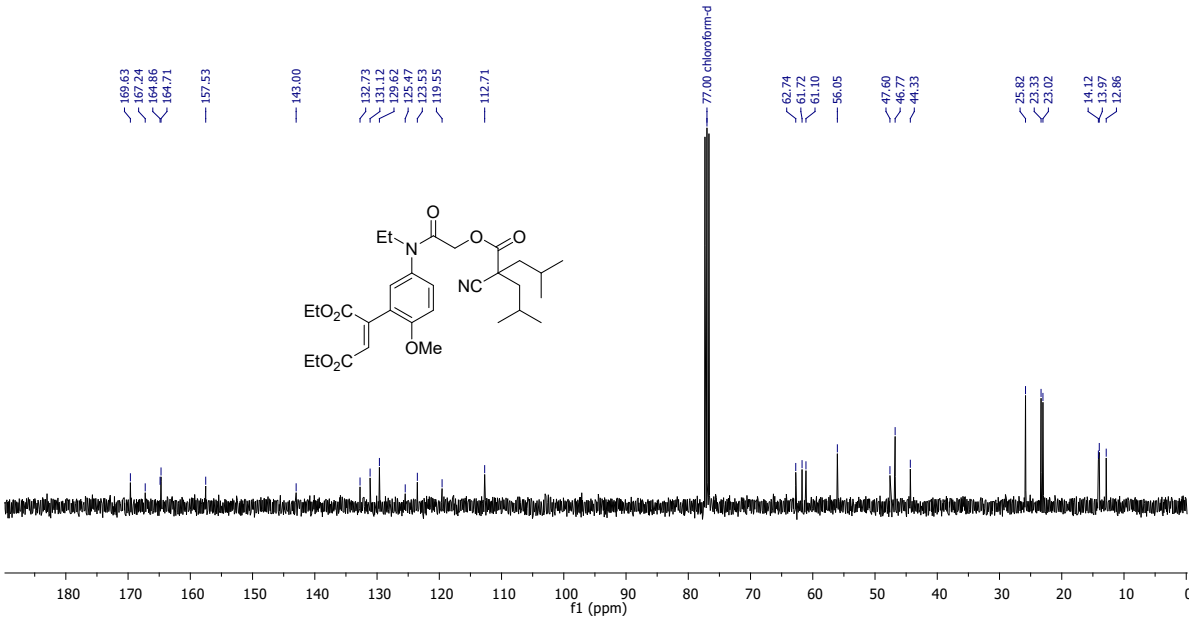
^{1}H NMR (400 MHz) spectrum of **3ed** in $CDCl_3$



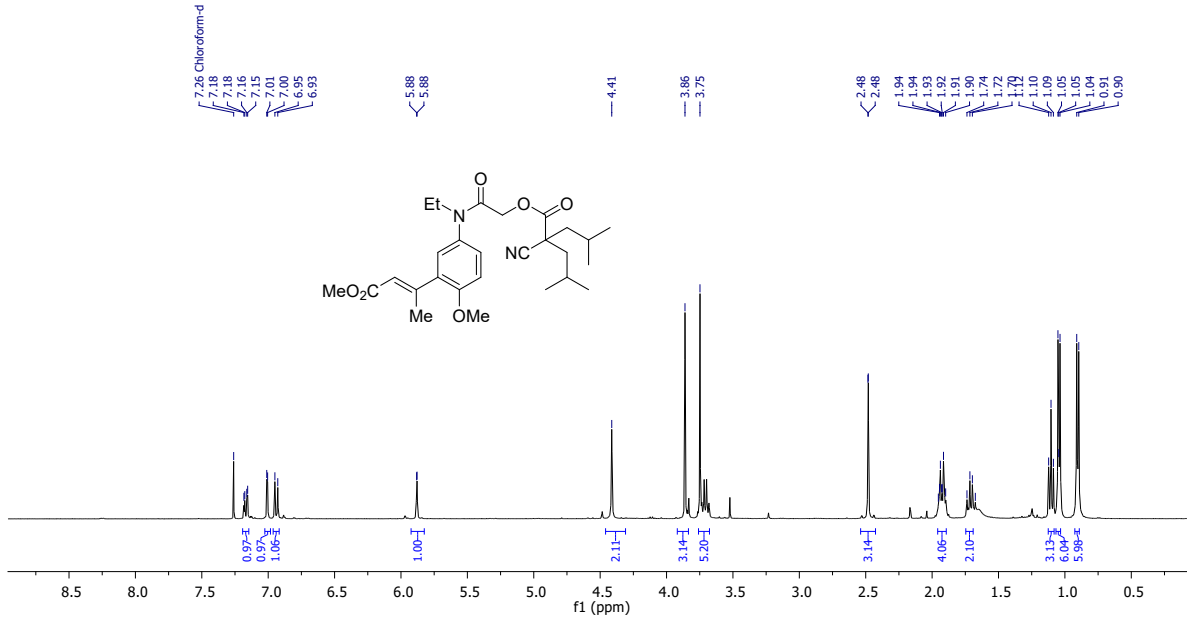
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ed** in $CDCl_3$



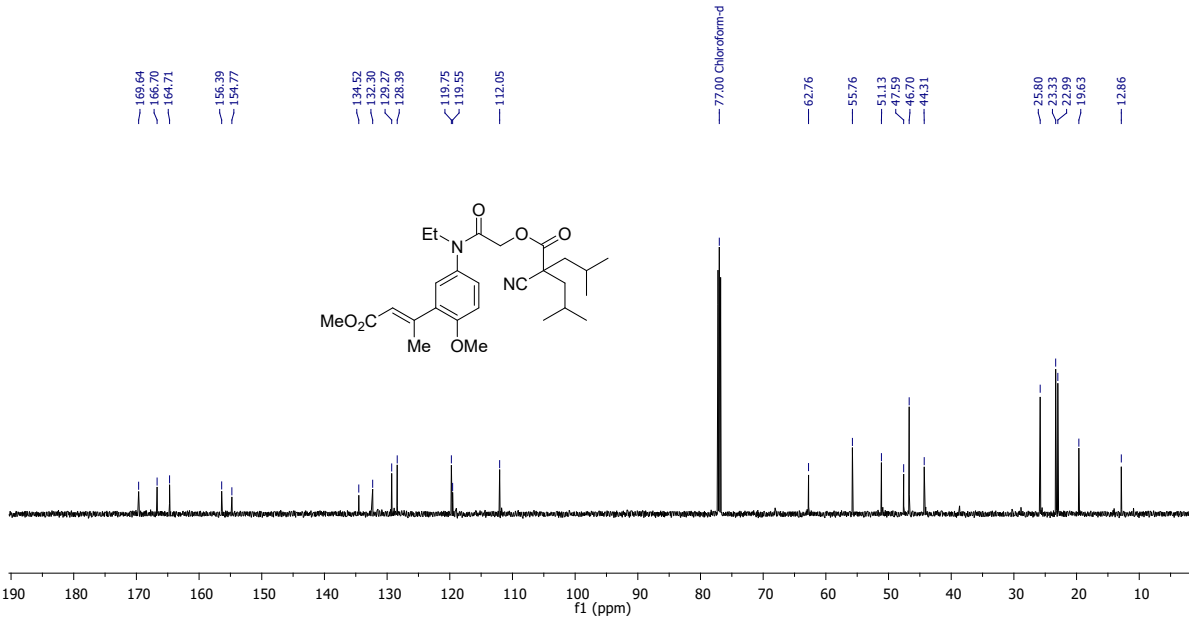
^{1}H NMR (400 MHz) spectrum of **3ee** in $CDCl_3$



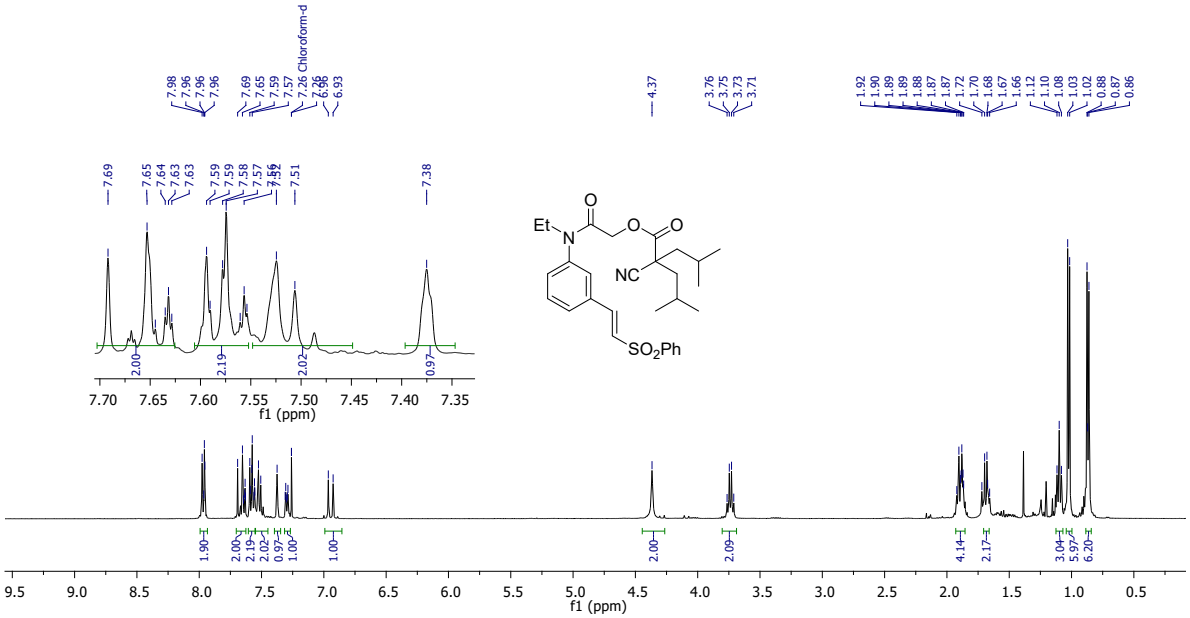
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ee** in $CDCl_3$



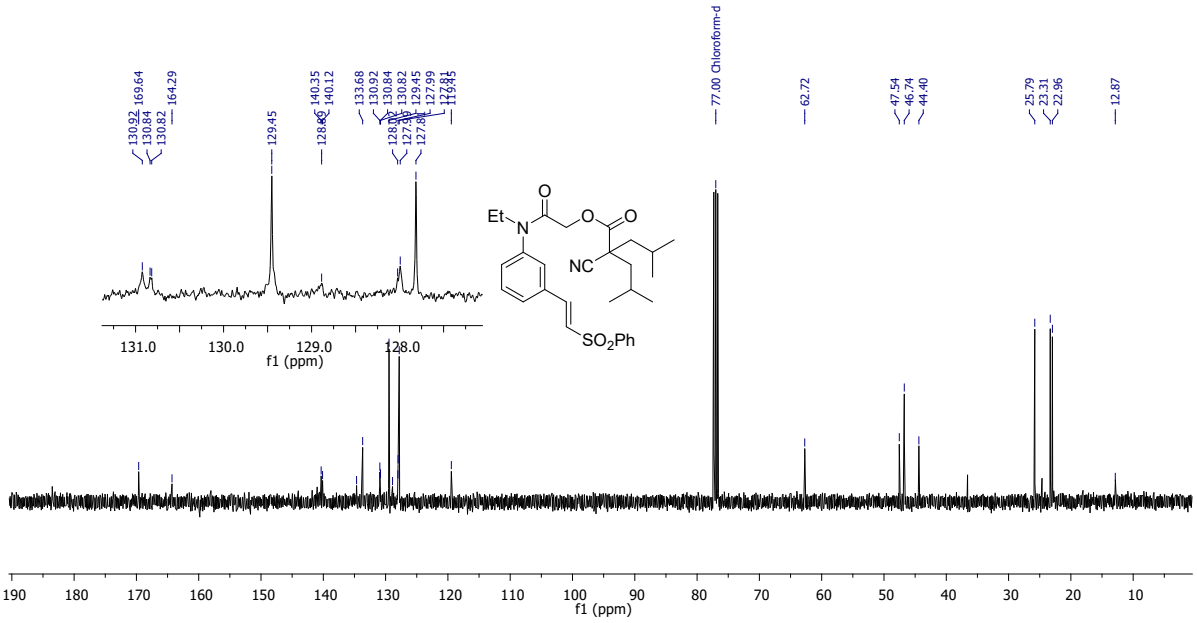
^{1}H NMR (400 MHz) spectrum of **3ef** in $CDCl_3$



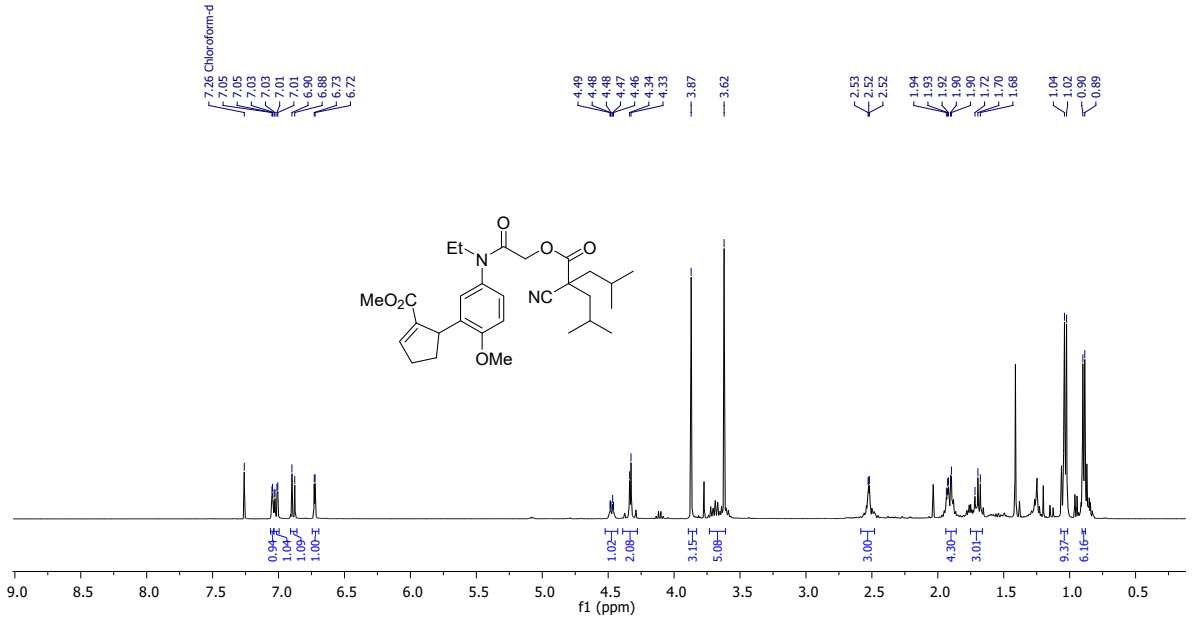
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ef** in $CDCl_3$



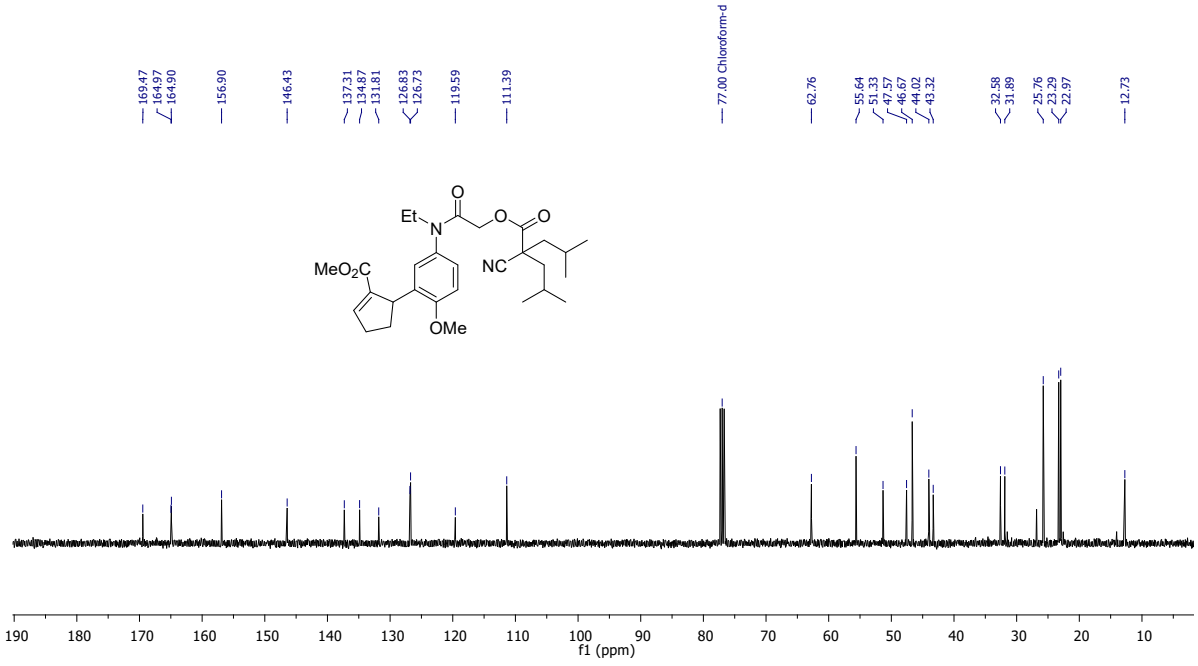
^{1}H NMR (400 MHz) spectrum of **3ag** in $CDCl_3$



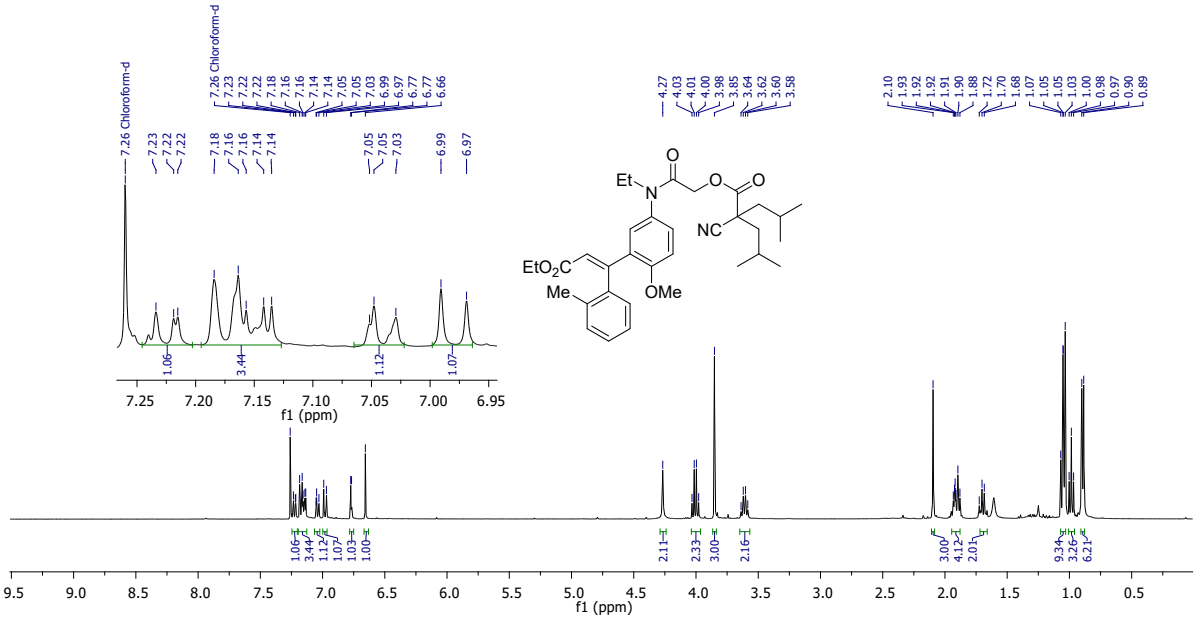
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ag** in $CDCl_3$



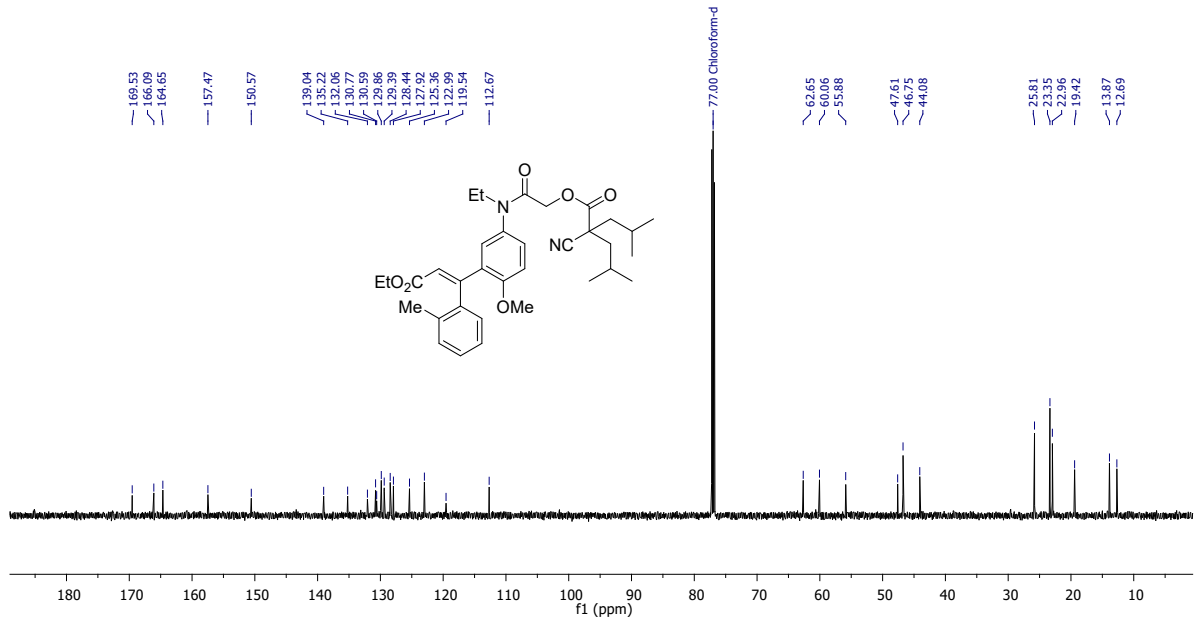
^{1}H NMR (400 MHz) spectrum of **3eh** in $CDCl_3$



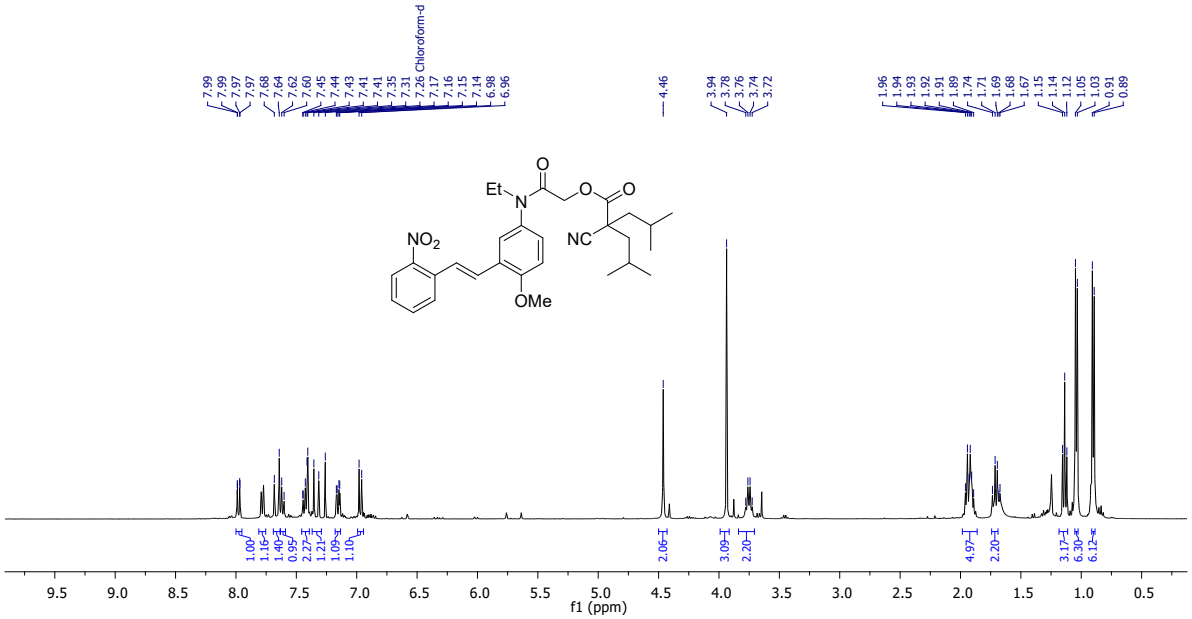
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3eh** in $CDCl_3$



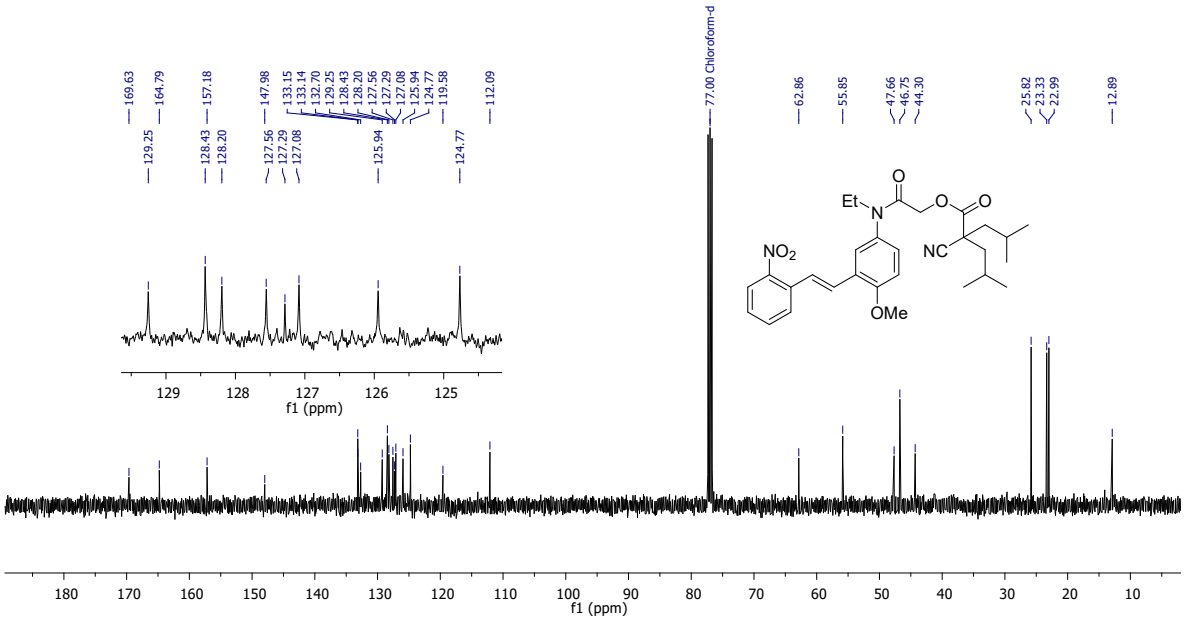
^{1}H NMR (400 MHz) spectrum of **3ei** in $CDCl_3$



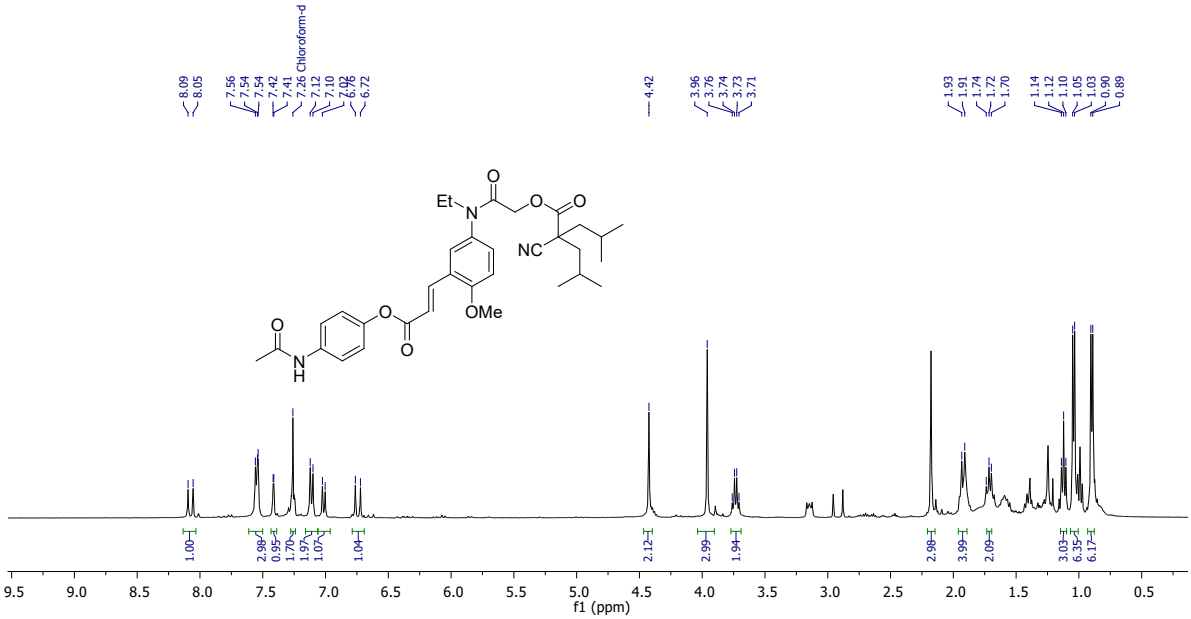
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ei** in $CDCl_3$



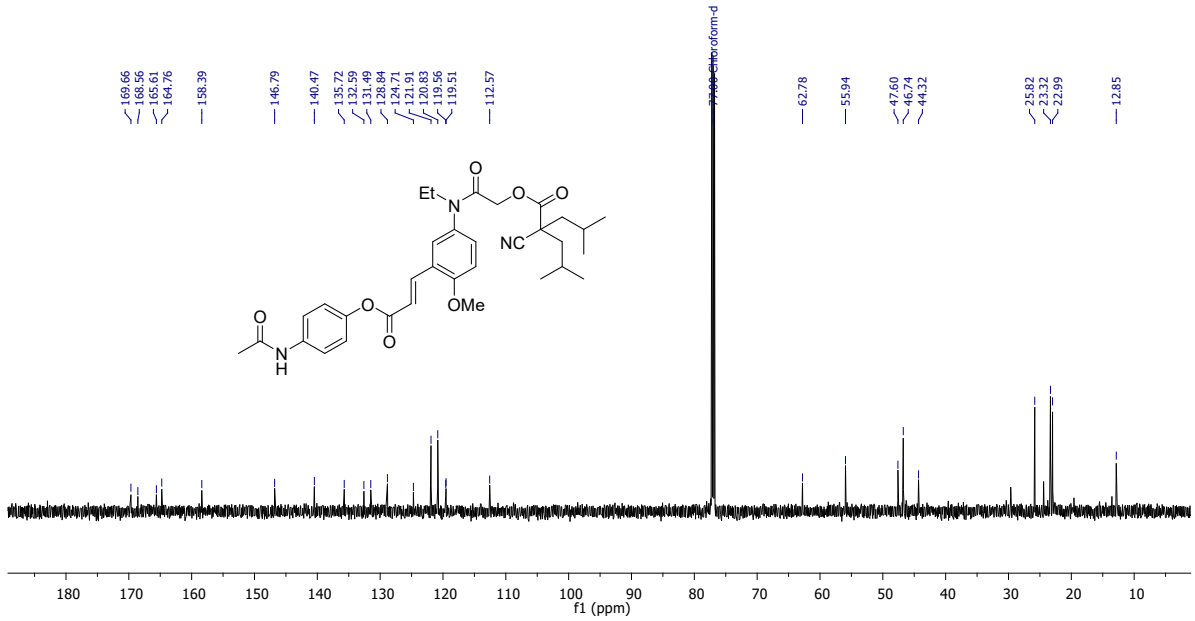
^{1}H NMR (400 MHz) spectrum of **3ej** in $CDCl_3$



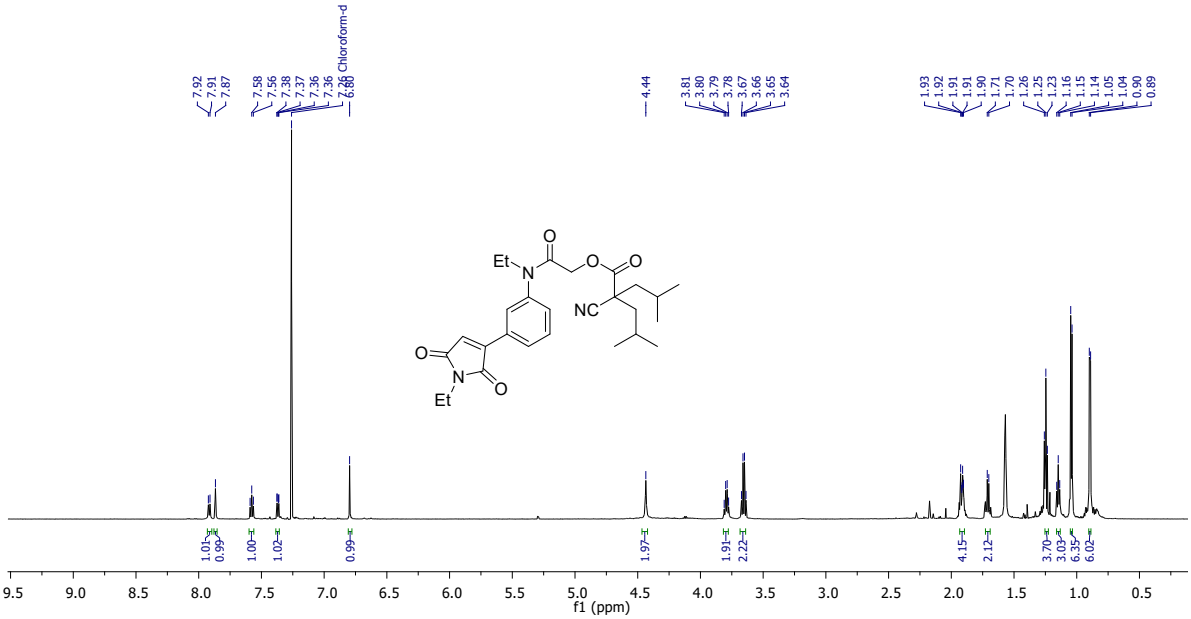
^{13}C {^{1}H} NMR (100 MHz) spectrum of **3ej** in $CDCl_3$



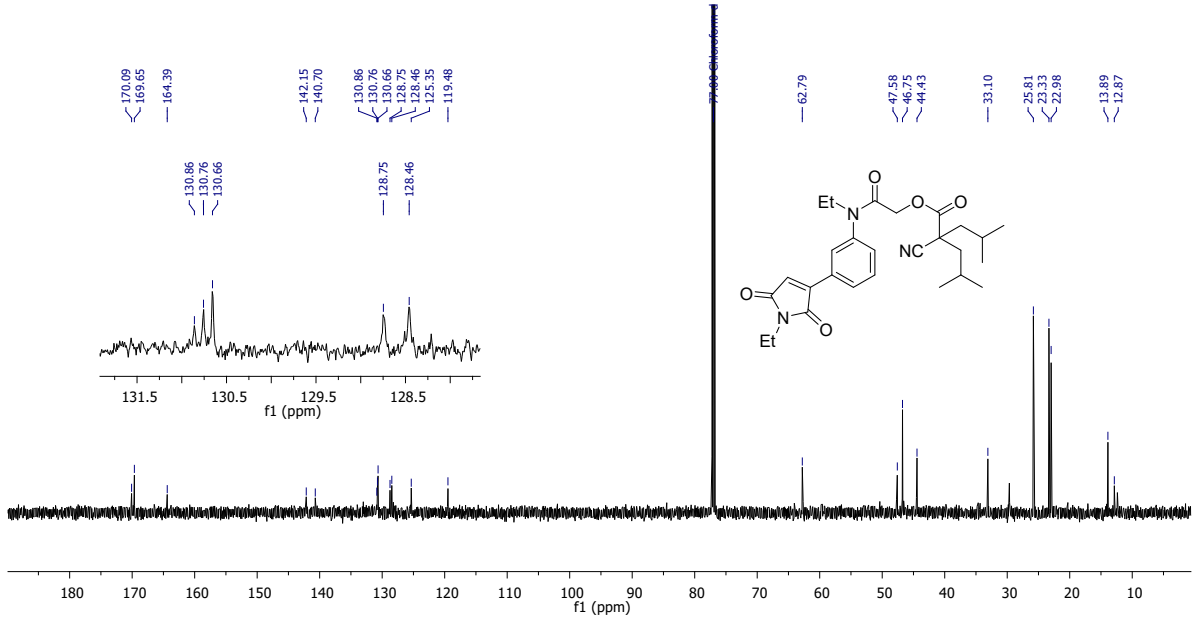
^{1}H NMR (400 MHz) spectrum of **3ek** in $CDCl_3$



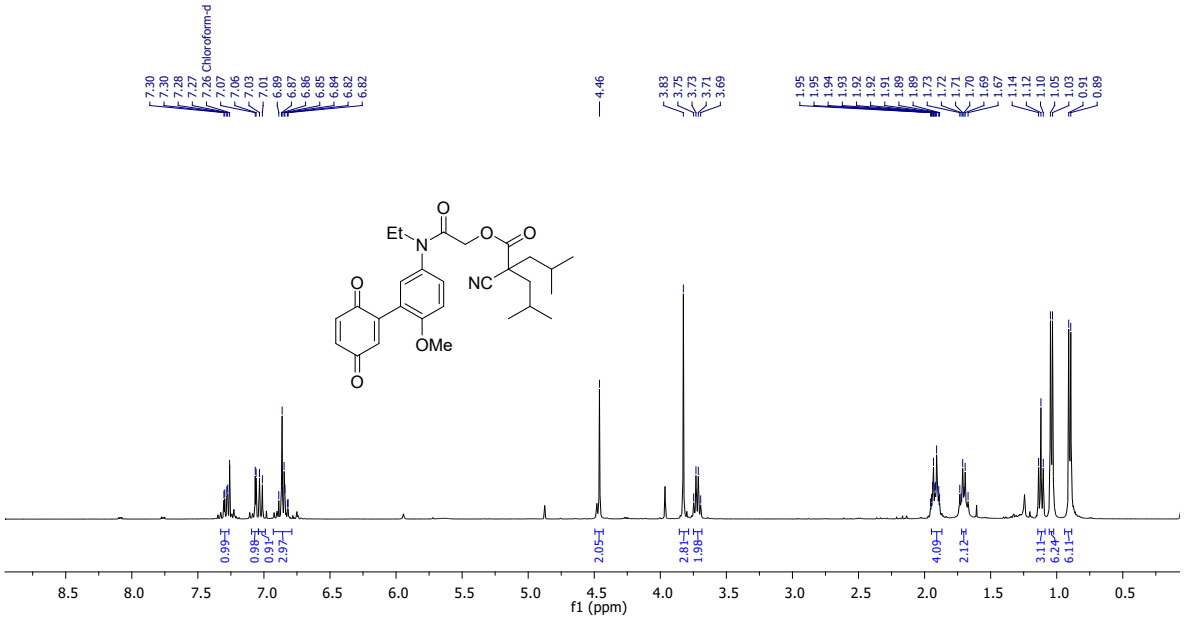
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3ek** in $CDCl_3$



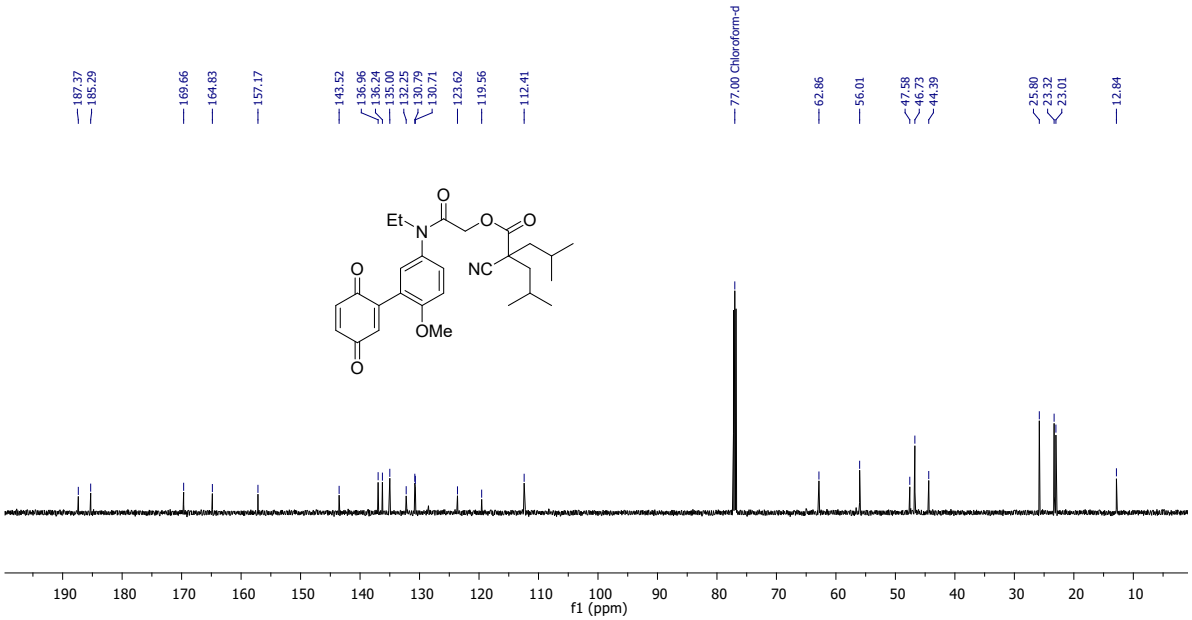
^{1}H NMR (400 MHz) spectrum of **3al** in $CDCl_3$



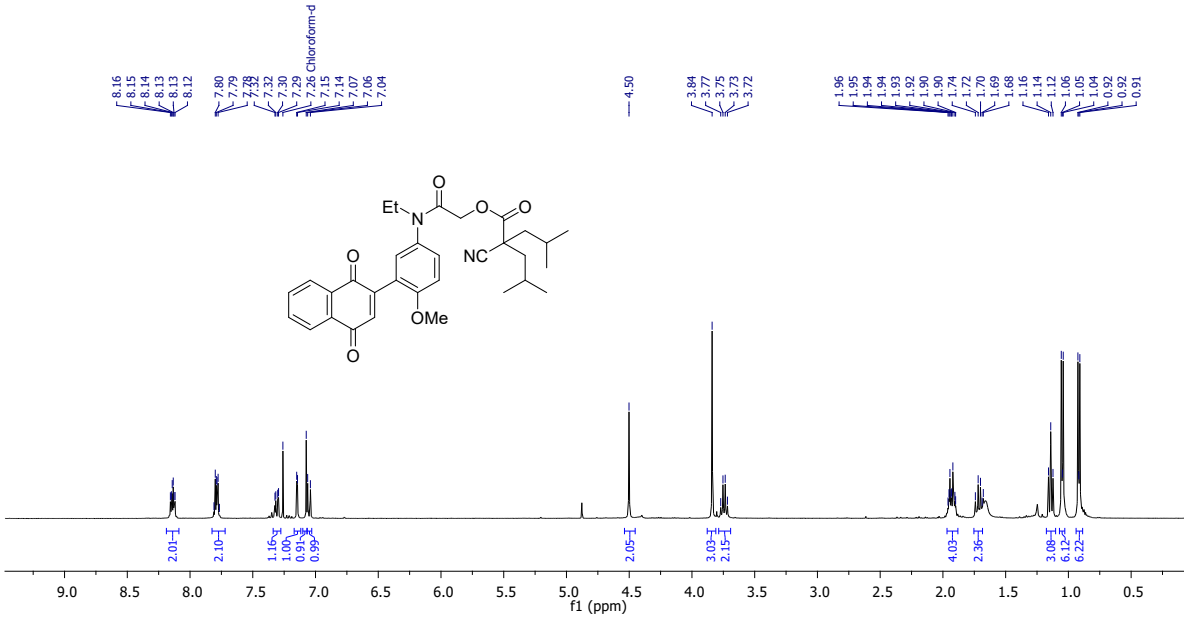
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3al** in $CDCl_3$



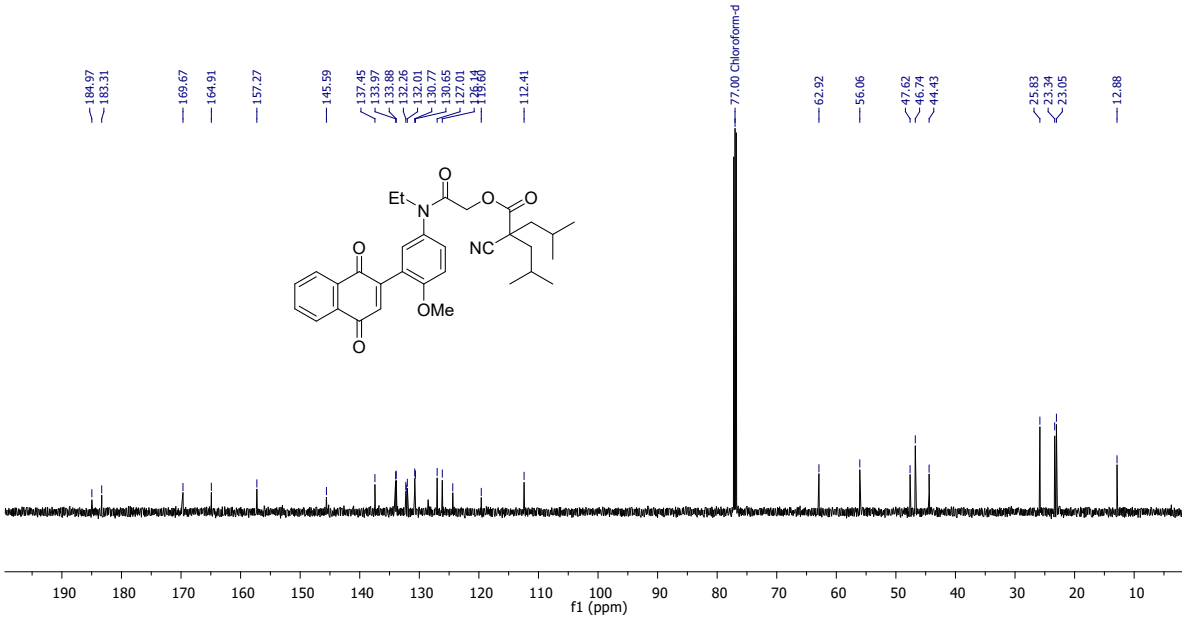
^{1}H NMR (400 MHz) spectrum of **3em** in $CDCl_3$



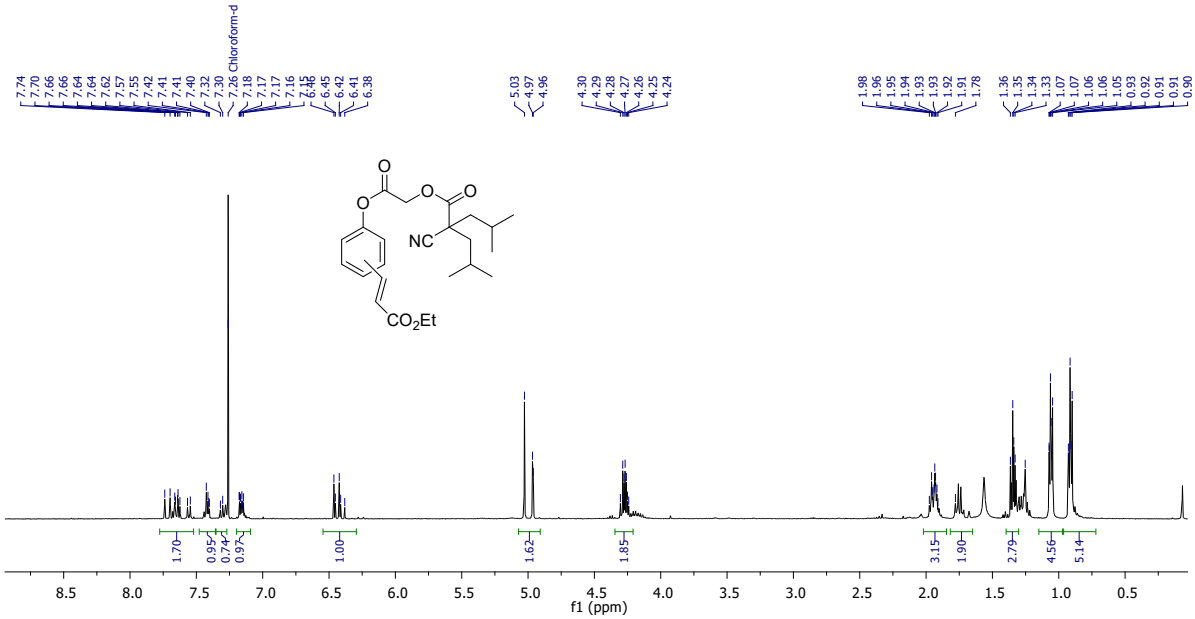
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3em** in $CDCl_3$



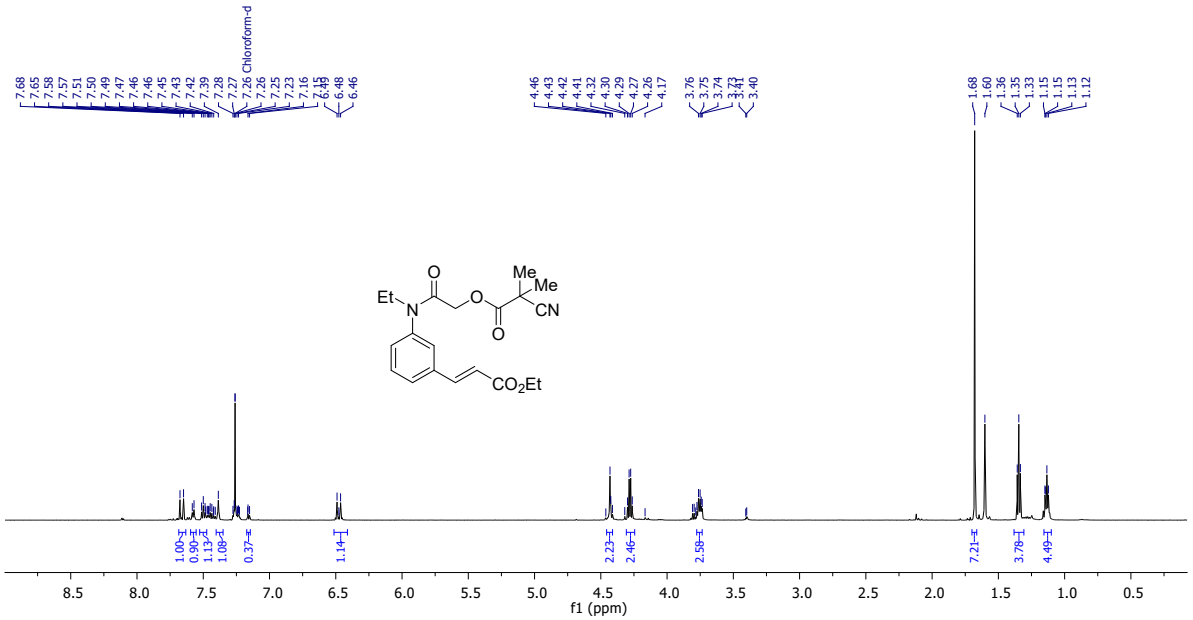
^{1}H NMR (400 MHz) spectrum of **3en** in $CDCl_3$



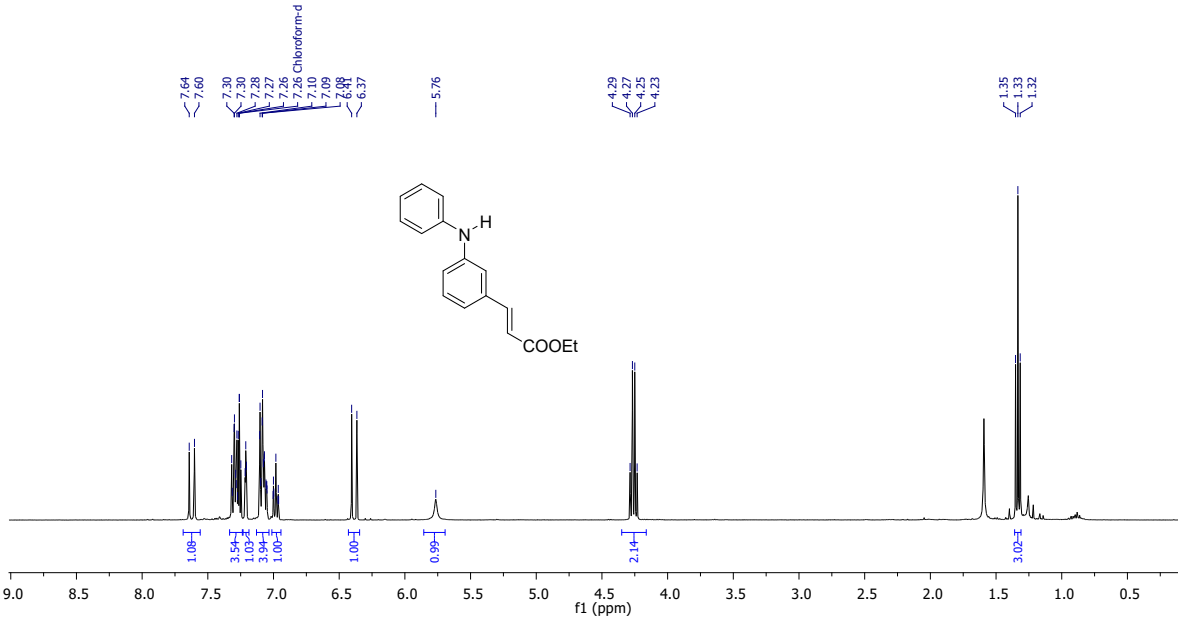
^{13}C {^{1}H} NMR (150 MHz) spectrum of **3en** in $CDCl_3$



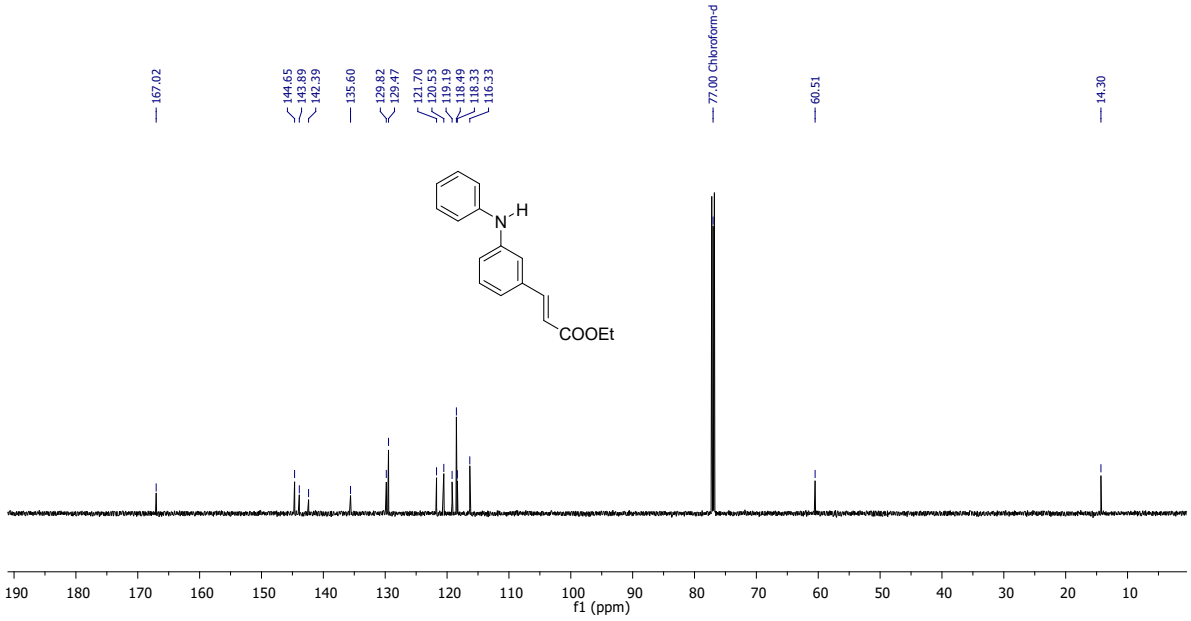
^{1}H NMR (400 MHz) spectrum of **4a** in $CDCl_3$



^{1}H NMR (400 MHz) spectrum of **3oa** in $CDCl_3$



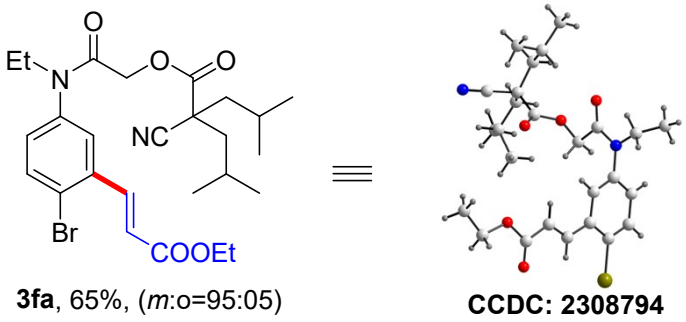
^{1}H NMR (400 MHz) spectrum of **5** in $CDCl_3$



^{13}C {^{1}H} NMR (150 MHz) spectrum of **5** in $CDCl_3$

X-ray Diffraction Analysis of Compound 3fa:

Crystal of compound **3fa** was obtained by dissolving product in mixture of DCM and hexane in 3:1 ratio, allowing the solvent to slowly evaporate at room temperature. The crystal structure information for this compound has been deposited at the Cambridge Crystallographic Data Centre. **CCDC No: 2308794** contains the crystal structure information of this compound and can be obtained free of charge *via* http://www.ccdc.cam.ac.uk



3fa, 65%, (*m*:o=95:05) **CCDC: 2308794**

Figure S1. X-ray structure of the product **3fa** with the ellipsoids drawn at the 50% probability level.

Crystal data and structure refinement for mo_GS_DS_2_527_1_0m.

Identification code	mo_GS_DS_2_527_1_0m
Empirical formula	$C_{26}H_{35}BrN_2O_5$
Formula weight	535.47
Temperature/K	299
Crystal system	triclinic
Space group	P-1
a/Å	10.1993(10)
b/Å	10.9217(9)
c/Å	12.8849(12)
α/°	74.979(3)
β/°	88.847(4)
γ/°	83.562(3)
Volume/Å^3	1377.5(2)
Z	2
ρ_{calc}g/cm^3	1.291
μ/mm^{-1}	1.528
F(000)	560.0
Crystal size/mm^3	0.053 × 0.045 × 0.023
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	4.018 to 54.296
Index ranges	-13 ≤ h ≤ 13, -13 ≤ k ≤ 13, -16 ≤ l ≤ 16
Reflections collected	44428
Independent reflections	6083 [R_{int} = 0.0858, R_{sigma} = 0.0544]
Data/restraints/parameters	6083/0/314

Goodness-of-fit on F^2	1.015
Final R indexes [I>=2σ (I)]	$R_1 = 0.0517$, $wR_2 = 0.1142$
Final R indexes [all data]	$R_1 = 0.1196$, $wR_2 = 0.1408$
Largest diff. peak/hole / e $Å^{-3}$	0.44/-0.48