Supplementary Information (SI) for Organic & Biomolecular Chemistry.

Dual Strategy Approach for an Aliphatic Nitrile Directing Group Assisted Palladium-Catalyzed *meta*-C–H Arylation/Acetoxylation of Arenes

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Supporting Information

Experimental:

General: IR spectra were recorded on a Bruker Tensor 37 (FTIR) spectrophotometer. ^{1}H NMR spectra were recorded on Bruker Avance 400 (400 MHz) and 600 (600 MHz) spectrometers 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). $^{13}C\{^1H\}$ NMR spectra were recorded on Bruker Advance 400 (101 MHz) and 600 (151 MHz) spectrometers at RT in $CDCl_3$. Chemical shifts (δ ppm) are reported relative to $CDCl_3$ [δ_C = 77.16 ppm (central line of the triplet)]. In ^{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. In $^{13}C\{^1H\}$ NMR, the nature of carbons (C, CH, CH_2, and CH_3) was determined by recording the DEPT-135 spectra. The assignment of signals was confirmed by ^{1}H, $^{13}C\{^1H\}$ CPD, and DEPT spectra. High-resolution mass spectra (HR-MS) were recorded using an Agilent 6538 UHD Q-TOF instrument in electron spray ionization (ESI) mode and atmospheric pressure chemical ionization (APCI) mode. Melting points are recorded using the Tempo and Mettler FP1 melting point apparatus in capillary tubes and are uncorrected. Using Olex$_2$, the structure was solved with olex$_2$. Solve the structure solution program using direct methods, and refine with the olex$_2$. Refinement package using Gauss−Newton minimization. All small-scale reactions were carried out using a Schlenk tube and a round-bottomed flask. 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 in the boiling range of 60−80 °C was used. $Pd(OAc)_2$, *N*-Ac-Gly-OH, AgOAc, and 1,1,1,3,3,3-hexafluoro-2-propanol (HFIP) were purchased from Sigma-Aldrich and used as received. Iodo-benzoic acids, K_2CO_3, DPEPhos, TEBAC, Diphenylacetylene, Dialkylacetylene, ligands, and Solvents were purchased from Sigma Aldrich/TCI/BLD/AVRA/local sources used as received. All the final reactions were conducted in a microwave using a CEM instrument (Model No.: 908010) in sealed reaction vessels at 100 watts, and reaction temperatures were monitored by an equipped IR sensor. All the temperature reactions were conducted using a Heidolph magnetic stirrer in an oil bath. Acme's silica gel (60−120 mesh) was used for column chromatography (approximately 20 g per 1 g of crude material.

General Procedure for functionalisation:

All the precursors (**1a-1h**) were prepared according to the reported procedure.[1-2]

General Procedure for mono *meta*-selective C–H Arylation: GP-1

An oven-dried 10 mL glass vial equipped with a magnetic stir-bar was charged with substrates **1/5** (0.2 mmol), iodoarenes **2** (60-97 mg, 0.3 mmol), Pd(OAc)$_2$ (10 mol%), *N*-Ac-gly-OH (20 mol%), AgOAc (0.4 mmol), and hexafluoroisopropanol (HFIP) (1 mL). The resulting mixture was heated in a microwave (100 W) at 100 °C and in a conventional oil bath at 60 °C. The reaction mixture was diluted with ethyl acetate and filtered through a short pad of Celite. Evaporation of organic solvent under reduced pressure and purification of the residue by silica gel column chromatography using petroleum ether/ethyl acetate as the eluent provided the desired *meta*-arylated coupled products **3aa-3al** (45-75%) & **3bb** (75%) and **6ba-6bi** (60-86%) & **6ad-6ed** (40-85%), colorless liquid and white solid.

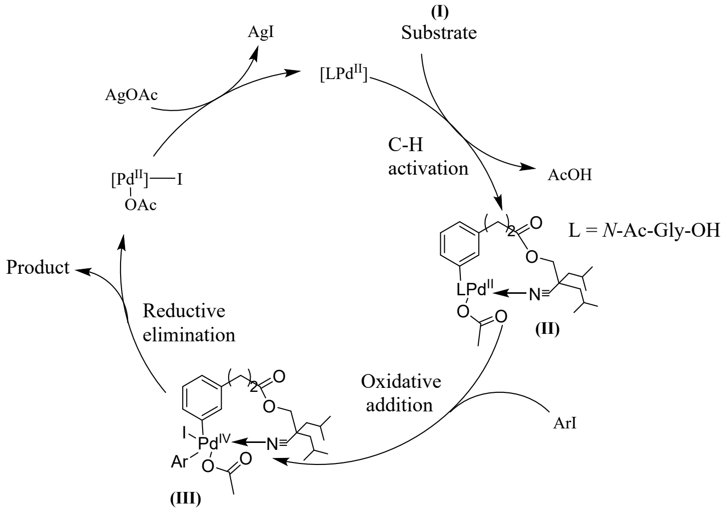
General Procedure for mono *meta*-selective C–H Acetoxylation: GP-2

An oven-dried 10 mL glass vial equipped with a magnetic stir-bar was charged with substrates **1/5** (0.2 mmol), Pd(OAc)$_2$ (10 mol%), *N*-Ac-gly-OH (20 mol%), (diacetoxyiodo)benzene (154 mg, 0.48 mmol), and hexafluoroisopropanol (HFIP) (1 mL). The resulting mixture was kept in a microwave (100 W) at a temperature of 100 °C for 25 min. The reaction mixture was diluted with ethyl acetate and filtered through a short pad of Celite. Evaporation of organic solvent under reduced pressure and purification of the residue by silica gel column chromatography using petroleum ether/ethyl acetate as the eluent provided the desired *meta*-acetoxylated coupled products **8b** & **8c** (55 & 31%) and **9c** & **9f** (61 & 63%) yellow liquids.

Plausible Mechanistic Pathways:

Plausible catalytic path for *meta*-C−H arylation:

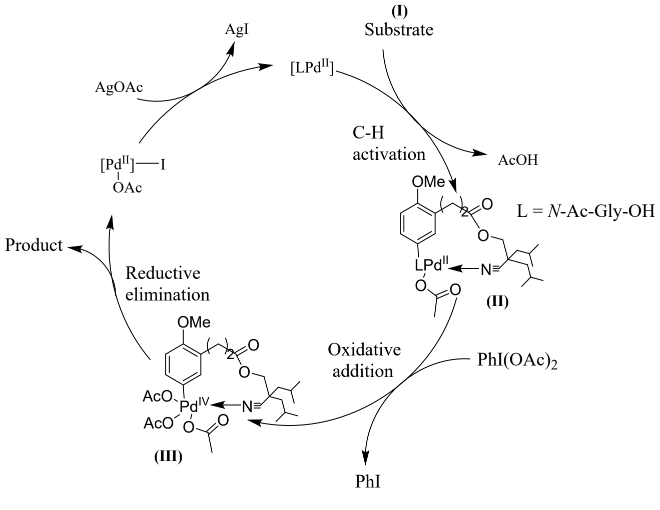
The plausible catalytic cycle for *meta*-arylation has been proposed based on the previous report,[3–5], and identification of mass spectral analysis macrocyclic palladacycle intermediate **(II)**, as described in Scheme S2. Essentially, the weak coordination of the nitrile group with Pd$^{(II)}$ leads the metal-center to the close vicinity of the *meta*-C–H bond and facilitate to form 12 membered palladacycle **II** by cleaving the *meta*-C–H bond. Then iodoarene undergoes oxidative addition with the Pd-centre of **(II)**, resulting in the formation of the Pd$^{(IV)}$ intermediate **(III)**. Subsequently, reductive elimination occasioned *meta*-arylated product **6ad** by leaving the I-Pd-OAc. Subsequently, the active pre-catalyst will be regenerated using AgOAc to restart the catalytic cycle.



Scheme S1: Catalytic cycle for *meta*-arylation to furnish **6ad**

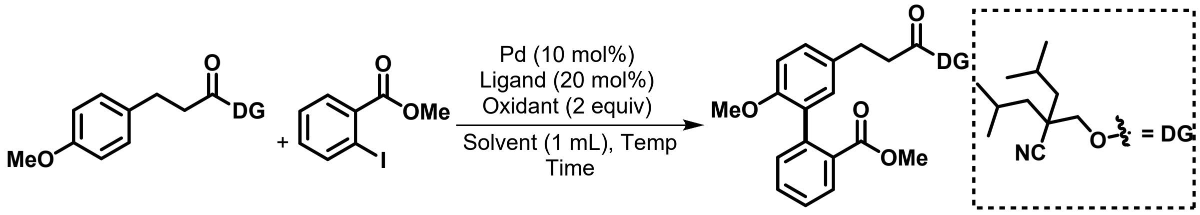
Plausible catalytic path for *meta*-C-H acetoxylation:

The plausible catalytic cycle for the *meta*- acetoxylation has been proposed based on a previous report.[6,7] Essentially, the weak coordination of the nitrile group with Pd^{II} leads the metal-center to the close vicinity of the *meta*-C-H bond and to facilitate to form 12 membered palladacycle **II** by cleaving the *meta*-C-H bond. Then (diacetoxyiodo)benzene undergoes oxidative addition with the Pd-centre of **II**, resulting in the formation of Pd intermediate **III**. Subsequently, reductive elimination occasioned the *meta*-acetoxylated product **9f** by regenerating the active Pd^{II} catalyst to restart the catalytic cycle.



Scheme S2: Catalytic cycle for *meta*-acetoxylation to furnish **9f.**

Table S1: Screening conditions for the *meta*-selective arylation of **5b**.



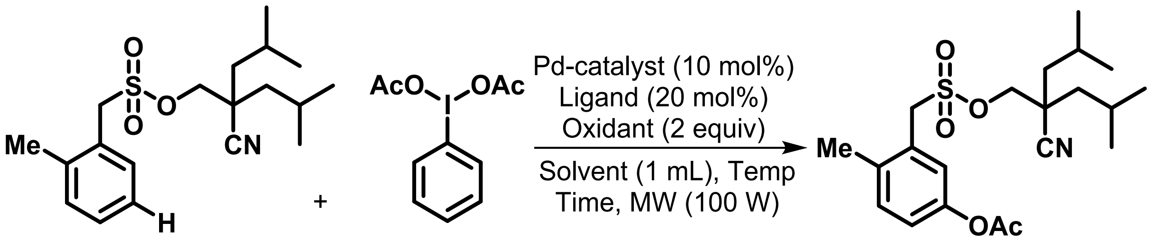
5b (1 equiv) **2a** (1.5 equiv) **6ba**

Sr. No	Catalyst (10 mol%)	Oxidant (2 equiv)	Ligand (20 mol%)	Solvent (1 mL)	Temp (°C)	Time	Yield%[b] (*m*: *others*)[c]
1[d]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	100	25 min	55 (90:10)
2	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	rt	18 h	45 (92:08)
3	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	40	18 h	42 (92:08)
4	**Pd(OAc)$_2$**	**AgOAc**	***N*-Ac-gly-OH**	**HFIP**	**60**	**18 h**	**86 (96:04)**
5	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	80	18 h	80 (89:11)
6	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	60	24 h	84 (95:05)
7	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DMF	60	18 h	10 (86:14)
8	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DCE	60	18 h	40 (92:08)
9	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	CH_3CN	60	18 h	Trace
10	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DMA	60	18 h	Trace
11	Pd(OAc)$_2$	Ag_2CO_3	*N*-Ac-gly-OH	HFIP	60	18 h	65 (90:10)
12	Pd(OAc)$_2$	Oxone	*N*-Ac-gly-OH	HFIP	60	18 h	20 (85:15)
13[e]	Pd(OAc)$_2$	O_2 gas	*N*-Ac-gly-OH	HFIP	60	18 h	NR
14	Pd(OAc)$_2$	AgOAc	*N*-Boc-alanine	HFIP	60	18 h	35 (88:12)
15	Pd(OAc)$_2$	AgOAc	*N*-Boc-L-phenylglycine	HFIP	60	18 h	Trace
16	Pd(OAc)$_2$	AgOAc	*N*-Boc-Glycine	HFIP	60	18 h	45 (85:15)
17[e]	$PdCl_2$	AgOAc	*N*-Ac-gly-OH	HFIP	60	18 h	NR

[a] **Conditions:** Reaction was carried out using **5b** (69 mg, 0.20 mmol), **2a** (58 mg, 0.30 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.40 mmol), HFIP (1 mL), 60 °C. [b] Yields of isolated product **6ba**. [c] Regioselectivity was determined by ^{1}H NMR analysis. [d] Microwave (100 W) condition. [e] NR = No reaction.

Initially, the reaction was carried out between substrate 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** and methyl iodoester **2a** under standard conditions "$Pd(OAc)_2$ (10 mol%), *N*-Ac-Gly-OH (20 mol%), AgOAc (2 equiv), in HFIP (1 mL) for 25 min in microwave irradiation condition (100 W) at 100 °C which leads to the formation of product **6ba** in moderate yield 55% and regioselectivity *meta*: *others* = 90:10(entry 1, Table S1). Hence, to further improve the yields of **6ba**, we decided to conducted the reaction in conventional thermal conditions. $Pd(OAc)_2$ (10 mol%), *N*-Ac-Gly-OH (20 mol%), AgOAc (2 equiv), in HFIP (1 mL) for 18 hours at room temperature; delightedly, the desired product **6ba** was observed 45% yield "*meta*: *others* = 92:08" (entry 2, Table S1). Subsequently, temperature optimization was carried out at 40 °C (entry 3, Table S1), 60 °C (entry 4, Table S1), and 80 °C (entry 5, Table S1), The optimal temperature was found to be 60 °C, affording an 86% yield with excellent *meta* selectivity (*meta*: *others* = 96:04; entry 4, Table S1), Increasing the temperature led to the formation of byproducts, resulting in diminished yields. Extending the reaction time to 24 h at 60 °C did not lead to any significant improvement (entry 6, Table S1), To optimize these parameters, various conditions—including ligands, oxidants, temperature, and reaction time—were evaluated (Table S1 In DMF, product formation was also observed; however, the yield dropped to 10% with reduced selectivity 86:14 (entry 7, Table S1), Changing the solvent to DCE gratifyingly afforded **6ba**, albeit in a moderate yield of 40% with a *meta*: *others* selectivity of 92:08 (entry 8, Table S1), On the other hand, the reactions with other solvents such as CH_3CN and DMA (entries 9-10, Table S1) gave **6ba** in trace amounts. Subsequently, different oxidants were screened. The use of Ag_2CO_3 afforded the desired product in 65% yield with a *meta*: *others* ratio of 90:10 (entry 11, Table S1), which was encouraging. Other oxidants, such as Oxone and O_2 gas, were also evaluated; however, only Oxone resulted in product formation, delivering a low yield of 20% with reduced selectivity (*meta*: *others* = 85:15; entry 12, Table S1). These results further confirmed AgOAc as the most suitable oxidant for the reaction. Next, the effect of ligands was examined using *N*-Boc-alanine, *N*-Boc-L-phenylglycine, and *N*-Boc-glycine, which afforded moderate but unsatisfactory yields of 35% (*meta*: *others* = 88:12) (entry 14, Table S1), traces (entry 15, Table 3), and 45% (*meta*: *others* = 85:15) (entry 16, Table S1). The $PdCl_2$ delivered the product in 25% yield with a *meta*: *others* ratio of 90:10 (entry 17, Table S1).

Table S2: Screening conditions for the *meta*-selective acetoxylation **8b**.



1b (1 equiv) **7** (1.5 equiv) **8b**

Sr. No	Pd-catalyst (10 mol%)	Oxidant (2 equiv)	Ligand (20 mol%)	Solvent (1 mL)	Temp (°C)	Time	Yield%[b] (*m: others*)[c]
1[a]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	rt	24 h	25 (93:07)
2[a]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	60	24 h	35 (90:10)
3[a]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	90	24 h	49 (88:12)
4	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	80	25 min	45 (93:07)
5	**Pd(OAc)$_2$**	**AgOAc**	***N*-Ac-gly-OH**	**HFIP**	**100**	**25 min**	**65 (94:06)**
6	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	100	35 min	62 (92:08)
7	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	120	25 min	60 (90:10)
8	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DCE	100	25 min	30 (85:15)
9[e]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DMF	100	25 min	NR
10[e]	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	DMA	100	25 min	NR
11	Pd(OAc)$_2$	AgOAc	*N*-Ac-gly-OH	CH$_3$CN	100	25 min	15 (91:09)
12	Pd(OAc)$_2$	Ag$_2$CO$_3$	*N*-Ac-gly-OH	HFIP	100	25 min	45 (90:10)
13	Pd(OAc)$_2$	Oxone	*N*-Ac-gly-OH	HFIP	100	30 min	20 (86:14)
14	Pd(OAc)$_2$	PIDA	*N*-Ac-gly-OH	HFIP	100	25 min	50 (88:12)

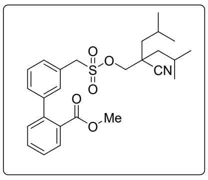
15[e]	Pd(OAc)$_2$	AgOAc	*N*-Boc-Valine	HFIP	100	25 min	NR
16	Pd(OAc)$_2$	AgOAc	*N*-Boc-Glycine	HFIP	100	25 min	35 (88:12)
17	Pd(OAc)$_2$	AgOAc	*N*-Boc-Phenylglycine	HFIP	100	25 min	40 (85:15)
18[e]	PdCl$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	100	25 min	NR
19	Pd(acac)$_2$	AgOAc	*N*-Ac-gly-OH	HFIP	100	25 min	55 (90:10)
20[e]	Pd(PPh$_3$)$_4$	AgOAc	*N*-Ac-gly-OH	HFIP	100	25 min	NR

Conditions: Reaction was carried out with [a]**1b** (67 mg, 0.20 mmol) and **7** (96.6 mg, 0.30 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.40 mmol), HFIP (1 mL), 100 °C, MW (100 W). [b]Yields of isolated product **8b**. [c]Regioselectivity was determined by ^{1}H NMR analysis. [e]NR= No reaction.

Initially, the reaction was carried out between substrate 2-phenylmethanesulfonic ester **1b** and PIDA **7** under the reaction conditions "Pd(OAc)$_2$ (10 mol%), *N*-Ac-Gly-OH (20 mol%), AgOAc (2 equiv), in HFIP (1 mL) for 18 hours at room temperature"; Unfortunately, only **8b** 25% *meta* selectivity of 93:07 product was observed (entry 1, Table S2). Further, we elevated the temperature to 60 °C and 90 °C, but we observed **8b** with minimal yield (entries 2-3, Table S2). Subsequently, the microwave conditions were optimized at 80 °C (entry 4, Table S2) and 100 °C (entry 5, Table S2) for 25 min. The optimal conditions were identified as microwave irradiation at 100 W and 100 °C, affording **8b** in 65% yield with a *meta* selectivity of 94:06 (entry 5, Table S2). To optimise the reaction condition, the reaction time increased to 35 min (entry 6, Table S2). To optimize these parameters, various conditions—including ligands, oxidants, and temperature were evaluated (Table S2). The reaction was also carried out at 120 °C, resulting in decreased yields (entry 7, Table S2). However, under microwave irradiation in solvents such as DCE, only 30% of **8b** were observed (entry 8, Table S2). On the other hand, reactions with other solvents, such as CH$_3$CN, DMA, and DMF (entries 9-11, Table S2), yielded **8b** in trace amounts or no reaction. Subsequently, different oxidants were evaluated. The use of Ag$_2$CO$_3$ afforded **8b** in 45% yield (entry 12, Table S2), which was promising; however, Oxone and PIDA have provided product formation, albeit in low to moderate yields (entries 13 & 14, Table S2). These results confirmed AgOAc as the most effective oxidant for this reaction. Next, the effect of ligands was investigated using *N*-Boc-valine, *N*-Boc-glycine, and *N*-Boc-phenylglycine, which delivered product in moderate but unsatisfactory yields (entries 15–17, Table S2). Finally, different palladium catalysts were screened. Among Pd$^{(II)}$ catalysts, whereas $PdCl_2$ resulted in no detectable product formation (entry 18, Table S2), $Pd(acac)_2$ provided **3aa** in 55% yield (entry 19, Table S2). The Pd$^{(0)}$ catalyst $Pd(PPh_3)_4$ failed to afford any product (entry 20, Table S2).

NMR data:

Methyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-Carboxylate (3aa):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), methyl iodo-ester **2a** (78 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3aa** (69 mg, 73%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$ (**1a**) = 0.70, R$_f$(**2a**) = 0.50, R$_f$(**3aa**) = 0.40 UV detection].

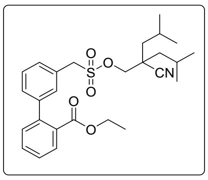
IR (MIR-ATR, 4000–600 cm^{-1}): 2959, 2345, 1717, 1362, 1051, 760 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 7.87 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.54 (ddd, *J* = 7.7, 7.6, 1.4 Hz, 1H), 7.49 – 7.41 (m, 3H), 7.39 (d, *J* = 2 Hz, 1H), 7.37 – 7.33 (m, 2H), 4.48 (s, 2H), 4.02 (s, 2H), 3.68 (s, 3H), 1.80 – 1.76 (m, 2H), 1.47 (d, *J* = 6.2 Hz, 4H), 0.98 (d, *J* = 6.6 Hz, 6H), 0.95 (d, *J* = 6.6 Hz, 6H).

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): *δ* 168.5, 142.5, 141.7, 131.6, 130.9, 130.8, 130.7, 130.2, 129.7, 129.5, 128.8, 127.7, 127.1, 121.4, 71.9, 57.4, 52.2, 43.2 (2C), 39.6, 24.8 (2C), 24.0 (2C), 23.9 (2C).

HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for C$_{26}$H$_{33}$NNaO$_5$S$^+$ 494.1972; Found: 494.1944.

Ethyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ab):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), ethyl iodo-ester **2b** (83 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100 °C. Purification of the crude mixture by silica gel column chromatography (petroleum ether/ethyl acetate) furnished the product **3ab** (69 mg, 71%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1a**) = 0.70, R_f(**2b**) = 0.50, R_f(**3ab**) = 0.35, UV detection].

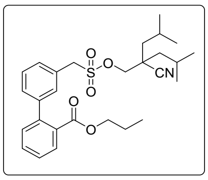
IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 2348, 1716, 1462, 985 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.87 (dd, J = 7.8, 1.2 Hz, 1H), 7.53 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.46 – 7.41 (m, 3H), 7.39 (d, J = 0.9 Hz, 1H), 7.38 – 7.33 (m, 2H), 4.47 (s, 2H), 4.12 (q, J = 7.1 Hz, 2H), 4.04 (s, 2H), 1.82 – 1.74 (m, 2H), 1.48 (d, J = 6.2, 4H), 1.07 (t, J = 7.1 Hz, 3H), 0.98 (d, J = 6.6 Hz, 6H), 0.95 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 168.2, 142.7, 141.6, 131.4, 131.1, 130.8, 130.8, 130.1, 129.6, 129.5, 128.8, 127.7, 127.0, 121.4, 71.8, 61.1, 57.3, 43.2 (2C), 39.6, 24.8 (2C), 24.0 (2C), 23.9 (2C), 13.9 ppm.

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{27}H_{39}N_2O_5S^+$ 503.2574; Found: 503.2598.

Propyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ac):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), propyl iodo-ester **2c** (87 mg, 0.30 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3ac** (68.5 mg, 68%) as a colourless liquid. [TLC control (petroleum ether/ethyl acetate 90:10), R_f(**1a**) = 0.70, R_f(**2c**) = 0.50, R_f(**3ac**) = 0.40 UV detection].

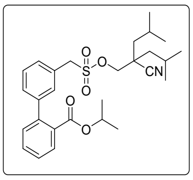
IR (MIR-ATR, 4000–600 cm^{-1}): 2959, 2346, 1716, 1465, 982 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.87 (dd, J = 7.8, 1.3 Hz, 1H), 7.54 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.49 – 7.41 (m, 3H), 7.39 (d, J = 0.9 Hz, 1H), 7.37 – 7.34 (m, 2H), 4.47 (s, 2H), 4.10 – 3.98 (m, 4H), 1.84 – 1.71 (m, 2H), 1.50 – 1.42 (m, 6H), 0.98 (d, J = 6.6 Hz, 6H), 0.95 (d, J = 6.6 Hz, 6H), 0.78 (t, J = 7.4 Hz, 3H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 168.2, 142.5, 141.5, 131.3, 131.0, 130.7, 130.7, 130.0, 129.5, 129.4, 128.7, 127.6, 127.0, 121.3, 71.7, 66.7, 57.2, 43.1 (2C), 39.4, 24.7 (2C), 23.9 (2C), 23.8 (2C), 21.7, 10.3 ppm.

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{28}H_{41}N_2O_5S^+$ 517.2731; Found: 517.2717.

Isopropyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ad):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), isopropyl iodo-ester **2d** (87 mg, 0.30 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100 °C. Purification of the crude mixture by silica gel column chromatography (petroleum ether/ethyl acetate, 100:0 to 88:12) furnished the product **3ad** (68.4 mg, 68%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 87:13), R_f(**1a**) = 0.70, R_f(**2d**) = 0.50, R_f(**3ad**) = 0.40 UV detection].

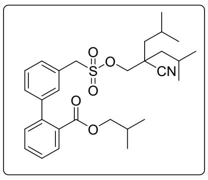
IR (MIR-ATR, 4000–600 cm^{-1}): 2956, 2343, 1720, 1461, 984 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.84 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.52 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H) , 7.45 – 7.41 (m, 3H), 7.39 (d, *J* = 1.2, 1H), 7.37 – 7.32 (m, 2H), 4.99 (dt, *J* = 12.5, 6.2 Hz, 1H), 4.47 (s, 2H), 4.05 (s, 2H), 1.82 – 1.74 (m, 2H), 1.49 (d, *J* = 6.2 Hz, 4H), 1.08 (d, *J* = 6.3 Hz, 6H), 0.98 (d, *J* = 6.6 Hz, 6H), 0.95 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$): δ 167.7, 142.6, 141.3, 131.6, 131.1, 130.8, 130.6, 129.8, 129.6, 129.5, 128.7, 127.6, 126.9, 121.3, 71.6, 68.6, 57.2, 43.1 (2C), 39.5, 24.7 (2C), 23.9 (2C), 23.8 (2C), 21.5 (2C) ppm.

HRMS (ESI) *m/z*: $[M + NH_4]^+$ Calcd for $C_{28}H_{41}N_2O_5S^+$ 517.2731; Found: 517.2708.

Isobutyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ae):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (60 mg, 0.2 mmol), isobutyl iodo-ester **2e** (91.2 mg, 0.30 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave condition for 100°C. Purification of the crude mixture by silica gel column chromatography (petroleum ether/ethyl acetate, 100:0 to 88:12) furnished the product **3ae** (66 mg, 65%) as a colourless liquid. [TLC control (petroleum ether/ethyl acetate 87:13), R_f(**1a**) = 0.70, R_f(**2e**) = 0.50, R_f(**3ae**) = 0.45 UV detection].

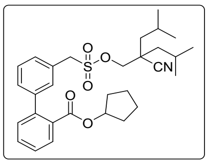
IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 2421, 1717, 1463, 909 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.88 (dd, J = 7.8, 1.1 Hz, 1H), 7.54 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.46 – 7.42 (m, 3H), 7.40 (d, J = 0.8 Hz, 1H), 7.35 – 7.33 (m, 2H), 4.47 (s, 2H), 4.04 (s, 2H), 3.87 (d, J = 6.7 Hz, 2H), 1.82 – 1.72 (m, 3H), 1.49 (d, J = 6.5, 4H), 0.98 (d, J = 6.6 Hz, 6H), 0.95 (d, J = 6.6 Hz, 6H), 0.78 (t, J = 5.1 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 168.2, 142.4, 141.4, 131.3, 130.9, 130.7, 130.7, 130.0, 129.6, 129.3, 128.7, 127.5, 126.9, 121.3, 71.7, 71.2, 57.1, 43.0 (2C), 39.4, 27.4, 24.7 (2C), 23.8 (2C), 23.8 (2C), 18.9 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{29}H_{43}N_2O_5S^+$ 531.2887; Found: 531.2864.

Cyclopentyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3af):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), cyclopentyl 2-iodobenzoate **2f** (95 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave condition at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3af** (29 mg, 45%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R_f(**1a**) = 0.70, R_f(**2f**) = 0.50, R_f(**3af**) = 0.55 UV detection].

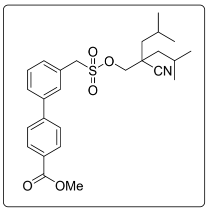
IR (MIR-ATR, 4000–600 cm^{-1}): 2959, 2377, 1710, 1466, 983, 702 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.84 (dd, J = 7.8, 1.2 Hz, 1H), 7.52 (ddd, J = 7.5, 1.4 Hz, 1H), 7.45 – 7.43 (m, 2H), 7.42 (dd, J = 7.6, 1.2 Hz, 1H), 7.38 (d, J = 2.0 Hz, 1H), 7.36 – 7.34 (m, 1H), 7.33 (dd, J = 7.6, 0.9 Hz, 1H), 5.19 – 5.15 (m, 1H), 4.47 (s, 2H), 4.05 (s, 2H), 1.81 – 1.75 (m, 2H), 1.51 – 1.42 (m, 1H), 0.99 (d, J = 6.6 Hz, 6H), 0.99 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 167.9, 142.6, 141.3, 131.4, 131.2, 130.7, 130.7, 130.0, 129.5, 129.5, 128.7, 127.6, 126.9, 121.3, 71.5, 57.1, 43.1 (2C), 39.4, 32.3 (2C), 24.7 (2C), 23.9 (2C), 23.8 (2C), 23.6 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{30}H_{43}N_2O_5S^+$ 543.2887; Found: 543.2897.

Methyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-4-carboxylate(3ag):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), methyl 4-iodo-ester **2g** (78 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3ag** (69 mg, 73%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$ (**1a**) = 0.70, R$_f$(**2g**) = 0.50, R$_f$(**3ag**) = 0.40 UV detection].

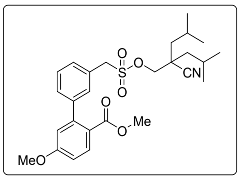
IR (MIR-ATR, 4000–600 cm^{-1}): 2940, 2310, 1712, 1350, 1051, 760 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.13 – 8.11 (m, 2H), 7.70 (t, *J* = 1.5 Hz, 1H), 7.69 – 7.66 (m, 3H), 7.53 (dd, *J* = 7.6,1.2 Hz, 1H), 7.49 (dd, *J* = 5.3, 3.8 Hz, 1H), 4.53 (s, 2H), 4.05 (s, 2H), 3.95 (s, 3H), 1.75 (dt, *J* = 13.0, 6.5 Hz, 2H), 1.45 (dd, *J* = 6.2, 5.1 Hz, 4H), 0.96 (d, *J* = 6.6 Hz, 6H), 0.93 (d, *J* = 6.6 Hz, 6H).

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 167.0, 144.4, 141.0, 130.5, 130.3 (2C), 129.8, 129.7, 129.5, 128.3, 128.2, 127.2(2C), 121.4, 71.3, 57.3, 52.3, 43.2(2C), 24.8(2C), 23.9(2C), 23.9(2C).

HRMS (ESI) *m*/*z*: [M]$^+$ Calcd for $C_{26}H_{33}NO_5S^+$ 471.2074; Found: 471.2058.

ethyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-5-methoxy-[1,1'-biphenyl]-2-carboxylate (3ah):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), methyl 2-iodo-5-methoxybenzoate **2h** (88 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the **3ah** (73 mg, 73%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$(**1a**) = 0.70, R$_f$(**2h**) = 0.50, R$_f$(**3ah**) = 0.40 UV detection].

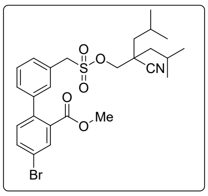
IR (MIR-ATR, 4000–600 cm^{-1}): 2968, 2360, 1722, 1410, 981, 735 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.40 (d, J = 7.5 Hz, 1H), 7.39 (t, J = 1.7 Hz, 1H), 7.35 (d, J = 2.7 Hz, 1H), 7.33 (d, J = 1.2 Hz, 1H), 7.32-7.28 (m, 1H), 7.24 (d, J = 5.0 Hz, 1H), 7.05 (dd, J = 8.5, 2.8 Hz, 1H), 4.44 (s, 2H), 3.99 (s, 2H), 3.85 (s,3H), 3.65 (s, 3H), 1.75 (m, 2H), 1.45 (d, J = 6.2 Hz, 4H), 0.96 (d, J = 6.6 Hz, 6H), 0.93 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 168.4, 159.0, 142.2, 134.1, 132.1, 131.6, 130.9, 129.6, 129.4, 128.8, 127.0, 121.4, 117.7, 114.9, 71.9, 57.4, 55.7, 52.3, 43.2 (2C), 39.6, 24.8 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + K]$^+$ Calcd for $C_{27}H_{35}NKO_6S^+$ 540.1817; Found: 540.1791.

Methyl-4-bromo-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ai):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), methyl 4-bromo-2-iodobenzoate **2i** (102 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3ai** (70 mg, 64%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 88:12 R$_f$(**1a**) = 0.70, R$_f$(**2i**) = 0.50, R$_f$(**3ai**) = 0.40 UV detection].

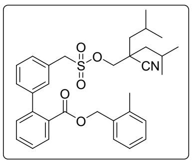
IR (MIR-ATR, 4000–600 cm^{-1}): 2959, 2346, 1717, 1465, 1087, 734 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 8.01 (d, J = 2.1 Hz, 1H), 7.67 (dd, J = 8.2, 2.1 Hz, 1H), 7.47 – 7.44 (m, 2H), 7.36 (d, J = 2.0 Hz, 1H), 7.34 – 7.30 (m, 1H), 7.24 (d, J = 8.2 Hz, 1H), 4.47 (s, 2H), 4.03 (s, 2H), 3.69 (s, 3H), 1.82-1.76 (m, 2H), 1.48 (d, J = 6.2 Hz, 4H), 0.99 (d, J = 6.6 Hz, 6H), 0.96 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 166.7, 140.9, 140.3, 134.2, 132.7, 132.1, 131.9, 130.4, 129.7, 129.0, 128.6, 126.9, 121.4, 121.1, 71.7, 57.0, 52.2, 42.9 (2C), 39.2, 24.5 (2C), 23.6 (2C), 23.6 (2C) ppm.

HRMS (ESI) *m/z*: $[M + NH_4]^+$ Calcd for $C_{26}H_{36}Br^{79}N_2O_5S^+$ 567.1523; Found: 567.1528; Calcd for $C_{26}H_{36}Br^{81}N_2O_5S^+$ 569.1502; Found: 569.1513.

2-Methylbenzyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3aj):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), 2-methylbenzyl 2-iodobenzoate **2j** (116 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3aj** (72 mg, 66%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 84:16 R*f*(**1a**) = 0.70, R*f*(**2j**) = 0.50, R*f*(**3aj**) = 0.25 UV detection].

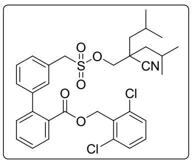
IR (MIR-ATR, 4000–600 cm^{-1}): 2922, 2341, 1741, 1461, 883, 669 cm^{-1}.

^1H NMR (600 MHz, $CDCl_3$): δ 7.89 (dd, J = 7.8, 1.2 Hz, 1H), 7.54 (ddd, J = 7.5, 7.5, 1.4 Hz, 1H), 7.43 (ddd, J = 7.6, 7.6, 1.3 Hz, 1H), 7.37 – 7.29 (m, 6H), 7.23 – 7.20 (m, 1H), 7.15 – 7.13 (m, 2H), 5.16 (s, 2H), 4.31 (s, 2H), 3.99 (s, 2H), 2.18 (s, 3H), 1.80 – 1.72 (m, 2H), 1.44 (d, J = 6.2 Hz, 4H), 0.97 (d, J = 6.6 Hz, 6H), 0.94 (d, J = 6.6 Hz, 6H) ppm.

$^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$): δ 168.0, 142.3, 141.6, 140.5, 133.6, 131.6, 130.9, 130.9, 130.7, 130.4, 130.3, 129.7, 129.6, 129.4, 128.9, 128.6, 127.7, 127.1, 126.0, 121.4, 71.7, 65.2, 57.2, 43.2 (2C), 39.5, 24.8 (2C), 24.0 (2C), 23.9 (2C), 18.9 ppm.

HRMS (ESI) m/z: $[M + NH_4]^+$ Calcd for $C_{33}H_{43}N_2O_5S^+$ 579.2887; Found: 579.2884.

2,6-Dichlorobenzyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3ak):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), 2,6-dichlorobenzyl 2-iodobenzoate **2k** (121 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C temperature. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **3ak** (81 mg, 68%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 84:16 R*f*(**1a**) = 0.70, R*f*(**2k**) = 0.50, R*f*(**3ak**) = 0.20 UV detection.

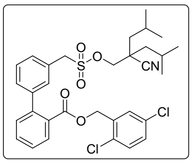
IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 2310, 1721, 1444, 980, 768 cm^{-1}.

^{1}H NM R (600 MHz, CDCl$_3$): δ 7.93 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1H), 7.43 (ddd, *J* = 7.7, 7.7, 1.2 Hz, 1H), 7.34 – 7.28 (m, 6H), 7.23 (dd, *J* = 8.7, 7.3 Hz, 2H), 5.40 (s, 2H), 4.39 (s, 2H), 4.00 (s, 2H), 1.81 – 1.73 (m, 2H), 1.46 (d, *J* = 6.2, 4H), 0.97 (d, *J* = 6.6 Hz, 6H), 0.94 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 167.3, 142.4, 142.0, 137.1, 131.8, 131.4, 131.3, 131.2, 131.0, 130.7, 130.6, 130.5, 130.0, 129.5, 129.4, 128.6, 128.4 (2C), 127.8, 126.8, 71.8, 61.7, 57.3, 43.2 (2C), 39.6, 24.8 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) m/z: [M + NH$_4$]$^+$ Calcd for $C_{32}H_{39}Cl_2N_2O_5S^+$ 633.1951; Found: 633.1945.

2,5-Dichlorobenzyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-[1,1'-biphenyl]-2-carboxylate (3al):



GP-1 was carried out with compound 2-phenylmethanesulfonic ester **1a** (67 mg, 0.2 mmol), 2,5-dichlorobenzyl 2-iodobenzoate **2l** (121 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography (petroleum ether/ethyl acetate, 100:0 to 84:16) furnished the *meta*-aryl-coupling product **3al** (72 mg, 60%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 84:16 R*f*(**1a**) = 0.70, R*f*(**2l**) = 0.50, R*f*(**3al)** = 0.20 UV detection].

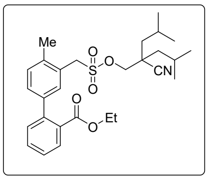
IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 2333, 1715, 1453, 963, 798 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.94 (dd, *J* = 7.8, 1.3 Hz, 1H), 7.58 (ddd, *J* = 7.5, 7.5, 1.4 Hz, 1H), 7.47 (ddd, *J* = 7.6, 7.6 ,1.3 Hz, 1H), 7.42 – 7.36 (m, 5H), 7.27 – 7.25 (m, 1H), 7.21 (d, *J* = 2.4 Hz, 1H), 6.96 (d, *J* = 2.4 Hz, 1H), 5.18 (s, 2H), 4.43 (s, 2H), 4.02 (s, 2H), 1.82 – 1.72 (m, 2H), 1.47 (d, *J* = 6.2 Hz, 4H), 0.98 (d, *J* = 6.6 Hz, 6H), 0.95 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 167.7, 141.8, 135.0, 132.7, 131.9, 131.5, 131.0, 130.9, 130.8, 130.6, 130.5, 129.9, 129.4, 129.4, 129.3, 129.1, 129.0, 127.9, 127.2, 121.4, 71.7, 63.6, 57.3, 43.2 (2C), 39.5, 24.8 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m/z*: [M + NH$_4$]$^+$ Calcd for $C_{32}H_{39}Cl_2N_2O_5S^+$ 633.1951; Found: 633.1943.

Ethyl-3'-((((2-cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-4'-methyl-[1,1'-biphenyl]-2-carboxylate (3bb):



GP-1 was carried out with compound 2-(2-methylphenyl)methanesulfonic ester **1b** (67 mg, 0.2 mmol), ethyl iodo-ester **2b** (81 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the product **3bb** (69 mg, 73%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$(**1b**) = 0.70, R$_f$(**2b**) = 0.50, R$_f$(**3bb**) = 0.40 UV detection].

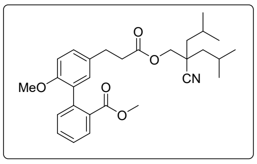
IR (MIR-ATR, 4000–600 cm^{-1}): 2955, 2345, 1720, 1350, 1050, 760 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 7.85 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.52 (dd, *J* = 7.5, 1.4 Hz, 1H), 7.43 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.34 (dd, *J* = 5.5, 1.6 Hz, 2H), 7.28 (t, *J* = 6.0 Hz, 1H), 7.26 – 7.22 (m, 1H), 4.53 (s, 2H), 4.15 (q, *J* = 7.1 Hz, 2H), 4.04 (s, 2H), 2.51 (s, 3H), 1.77 (dt, *J* = 13.0, 6.5 Hz, 2H), 1.47 (d, *J* = 6.2 Hz, 4H), 1.11 (t, *J* = 7.1 Hz, 3H), 0.95 (2 x d, *J* = 6.6 Hz, 12H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): *δ* 168.4, 143.9, 141.5, 139.9, 137.2, 131.6, 131.3, 130.7, 129.9, 129.6, 127.4, 125.4, 124.4, 121.3, 71.6, 61.0, 54.7, 43.1(2C), 39.4, 24.7(2C), 23.86(2C), 23.8(2C), 19.4, 13.9 ppm.

HRMS (ESI) *m/z*: [M + NH4]$^+$ Calcd for $C_{28}H_{37}NO_5S^+$ 517.2731; Found: 517.2697.

Methyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6ba):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), **2a** (87 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6ba** (75 mg, 77%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 88:12 R_f(**5b**) = 0.70, R_f(**2a**) = 0.50, R_f(**6ba**) = 0.40 UV detection].

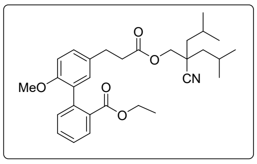
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2348, 1727, 1604, 1087, 769 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.85 (dd, J = 7.8, 1.2 Hz, 1H), 7.54 (ddd, J = 7.6, 7.6, 1.4 Hz, 1H), 7.39 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.32 (dd, J = 7.6, 1.1 Hz, 1H), 7.17 (dd, J = 8.4, 2.3 Hz, 1H), 7.09 (d, J = 2.3 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 4.13 (s, 2H), 3.69 (s, 3H), 3.66 (s, 3H), 2.97 (t, J = 7.9 Hz, 2H), 2.73 (t, J = 7.9 Hz, 2H), 1.90 – 1.76 (m, 2H), 1.51 (d, J = 6.2 Hz, 4H), 1.02 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.2, 168.5, 154.5, 138.5, 132.0, 131.5, 131.2, 130.4, 129.7, 129.2, 128.2, 127.1, 122.1, 110.1, 77.1, 66.6, 55.2, 51.6, 43.7 (2C), 39.0, 35.7, 29.8, 24.8 (2C), 23.9 (2C), 23.8 (2C) ppm.

HRMS (ESI) *m/z*: [M + H]$^+$ Calcd for $C_{29}H_{38}NO_5^+$ 480.2744; Found: 480.2735.

Ethyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6bb):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), ethyl iodo-ester **2b** (81 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bb** (80.6 mg, 80%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R_f(**5b**) = 0.70, R_f(**2b**) = 0.50, R_f(**6bb**) = 0.35 UV detection].

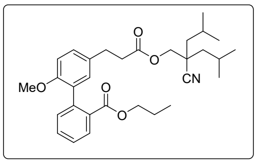
IR (MIR-ATR, 4000–600 cm^{-1}): 2954, 2355, 1729, 1607, 1249, 1021 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.86 (dd, J = 7.8, 1.2 Hz, 1H), 7.53 (ddd, J = 7.6, 1.4, 1.4 Hz, 1H), 7.39 (ddd, J = 7.6, 7.6, 1.3 Hz, 1H), 7.31 (dd, J = 7.6, 1.0 Hz, 1H), 7.16 (dd, J = 8.3, 2.3 Hz, 1H), 7.08 (d, J = 2.3 Hz, 1H), 6.81 (d, J = 8.4 Hz, 1H), 4.13 (s, 2H), 4.09 (q, J = 7.1 Hz, 2H), 3.68 (s, 3H), 2.99 – 2.94 (m, 2H), 2.74 – 2.69 (m, 2H), 1.86-1.82 (m, 2H), 1.53 – 1.50 (m, 4H), 1.04 (t, J = 7.2 Hz, 3H), 1.02 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 172.2, 168.1, 154.6, 138.4, 132.0, 131.8, 131.3, 131.1, 130.7, 129.7, 129.2, 128.1, 127.1, 122.1, 110.1, 77.1, 66.5, 60.4, 55.2, 43.6 (2C), 39.0, 35.8, 29.8, 24.7 (2C), 23.9 (2C), 23.8 (2C), 13.7 ppm.

HRMS (ESI) *m*/*z*: $[M + Na]^+$ Calcd for $C_{30}H_{39}NNaO_5^+$ 516.2720; Found: 516.2699.

Propyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6bc):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), n-propyl iodo-ester **2c** (96 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bc** (75.6 mg, 73%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R_f(**5b**) = 0.70, R_f(**2c**) = 0.50, R_f(**6bc**) = 0.40 UV detection].

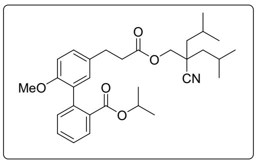
IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 2345, 1718, 1603, 1282, 964 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): *δ* 7.87 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (ddd, *J* = 7.5, 1.4, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.6, 1.3 Hz, 1H), 7.31 (dd, *J* = 7.6, 0.9 Hz, 1H), 7.16 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.09 (d, *J* = 2.3 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.13 (s, 2H), 4.00 (t, *J* = 5.9 Hz, 2H), 3.68 (s, 3H), 3.00 – 2.92 (m, 2H), 2.73 – 2.68 (m, 2H), 1.86-1.82 (m, 2H), 1.53 – 1.50 (m, 4H), 1.44 (dd, *J* = 14.1, 6.9 Hz, 2H), 1.02 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H), 0.75 (t, *J* = 7.4 Hz, 3H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): *δ* 172.2, 168.3, 154.7, 138.5, 132.1, 131.9, 131.3, 131.2, 130.8, 129.8, 129.3, 128.2, 127.1, 122.2, 110.2, 66.6, 66.3, 55.3, 43.7 (2C), 39.1, 35.8, 29.9, 24.8 (2C), 24.0 (2C), 23.9 (2C), 21.6, 10.3 ppm.

HRMS (ESI) *m*/*z*: $[M + NH_4]^+$ Calcd for $C_{31}H_{45}N_2O_5^+$ 525.3323; Found: 525.3333.

Isopropyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6be):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), isopropyl iodo-ester **2e** (96 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6be** (77.7 mg, 75%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$(**5b**) = 0.70, R$_f$(**2e**) = 0.50, R$_f$(**6be**) = 0.35 UV detection].

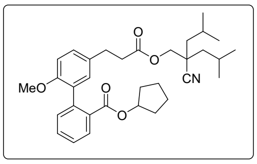
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2350, 1742, 1604, 1248, 1042 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.86 (dd, *J* = 7.7, 1.2 Hz, 1H), 7.51 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.3 Hz, 1H), 7.29 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.17 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.06 (d, *J* = 2.3 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.96 (dt, *J* = 12.5, 6.3 Hz, 1H), 4.13 (s, 2H), 3.69 (s, 3H), 2.99 – 2.93 (m, 2H), 2.73 – 2.69 (m, 2H), 1.84 (m, 2H), 1.52 (d, *J* = 6.2 Hz, 4H), 1.06 (d, *J* = 6.2 Hz, 6H), 1.03 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 172.4, 167.8, 154.9, 138.6, 132.5, 132.1, 131.4, 131.3, 131.1, 129.9, 129.4, 128.3, 127.3, 122.3, 110.3, 77.1, 68.1, 66.8, 55.4 (2C), 43.9 (2C), 39.2, 36.0, 30.0, 24.9 (2C), 24.1 (2C), 24.1 (2C) ppm.

HRMS (ESI) *m/z*: [M + NH$_4$]$^+$ Calcd for $C_{31}H_{45}N_2O_5^+$ 525.3323; Found: 525.3315.

Cyclopentyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6bf):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), cyclopentyl iodo-ester **2f** (106 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bf** (63.6 mg, 60%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R$_f$(**5b**) = 0.70, R$_f$(**2f**) = 0.50, R$_f$ (**6bf**) = 0.40 UV detection].

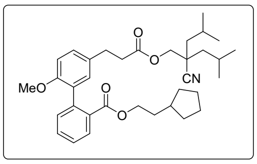
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2340, 1741, 1603, 1284, 898 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): *δ* 7.85 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.52 (ddd, *J* = 7.5, 1.4, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.28 (d, *J* = 0.9 Hz, 1H), 7.16 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.06 (d, *J* = 2.2 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 5.17-5.13 (m, 1H), 4.13 (s, 2H), 3.69 (s, 3H), 2.98 – 2.93 (m, 2H), 2.73 – 2.68 (m, 2H), 1.87-1.83 (m, 2H), 1.72-1.68 (m, 2H), 1.53 – 1.50 (m, 4H), 1.45-1.41 (m, 6H), 1.03 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): *δ* 172.2, 167.9, 154.6, 138.3, 132.2, 132.0, 131.1, 131.1, 130.9, 129.7, 129.4, 128.1, 127.1, 122.1, 110.1, 66.6, 55.2, 43.7 (2C), 39.0, 35.9 (2C), 29.8, 24.8 (2C), 23.9 (2C), 23.8 (2C), 23.5 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + Na]$^+$ Calcd for $C_{33}H_{43}NNaO_5^+$ 556.3033; Found: 556.3041.

2-Cyclopentylethyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6bg):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), **2g** (116 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bg** (70 mg, 63%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R$_f$(**5b**) = 0.70, R$_f$(**2g**) = 0.50, R$_f$(**6bg**) = 0.40 UV detection].

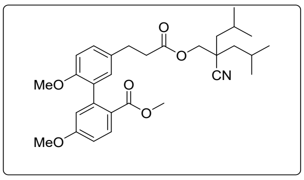
IR (MIR-ATR, 4000–600 cm^{-1}): 2954, 2347, 1718, 1604, 1284, 885 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 7.86 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.52 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.40 (dd, *J* = 7.6, 1.1 Hz, 1H), 7.30 (d, *J* = 7.6 Hz, 1H), 7.16 (dd, *J* = 8.3, 2.2 Hz, 1H), 7.08 (d, *J* = 2.2 Hz, 1H), 6.81 (d, *J* = 8.4 Hz, 1H), 4.13 (s, 2H), 4.05 (t, *J* = 6.6 Hz, 2H), 3.68 (s, 3H), 3.00 – 2.93 (m, 2H), 2.75 – 2.67 (m, 2H), 1.90 – 1.80 (m, 2H), 1.65-1.61 (m, 3H), 1.60-1.52 (m, 8H), 1.52 (d, *J* = 6.1 Hz, 4H), 1.50 – 1.44 (m, 2H), 1.42-1.38 (m, 2H), 1.02 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm .

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): *δ* 172.3, 168.4, 154.7, 138.5, 132.1, 132.0, 131.4, 131.2, 130.9, 129.8, 129.4, 128.2, 127.2, 122.2, 110.2, 66.6, 64.3, 55.3, 43.8 (2C), 39.1, 36.5, 35.9 (2C), 34.4, 32.5, 29.9, 25.0 (2C), 24.8 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m*/*z*: $[M + H]^+$ Calcd for $C_{35}H_{48}NO_5^+$ 562.3527; Found: 562.3517.

Methyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2',5-dimethoxy-[1,1'-biphenyl]-2-carboxylate (6bh):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), **2h** (59 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bh** (86 mg, 83%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 88:12 R_f(**5b**) = 0.70, R_f(**2h**) = 0.50, R_f(**6bh**) = 0.30 UV detection].

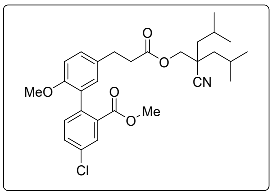
IR (MIR-ATR, 4000–600 cm^{-1}): 2952, 2349, 1733, 1653, 1018 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.38 (d, *J* = 2.8 Hz, 1H), 7.24 (d, *J* = 8.5 Hz, 1H), 7.14 (dd, *J* = 8.3, 2.3 Hz, 1H), 7.08 (dd, *J* = 8.6, 2.7 Hz, 2H), 6.80 (d, *J* = 8.4 Hz, 1H), 4.13 (s, 2H), 3.88 (d, *J* = 5.5 Hz, 3H), 3.69 (s, 3H), 3.66 (d, *J* = 8.4 Hz, 3H), 2.99 – 2.94 (m, 2H), 2.75 – 2.70 (m, 2H), 1.87 – 1.80 (m, 2H), 1.52 (d, *J* = 6.2 Hz, 4H), 1.02 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.4, 168.4, 158.5, 154.7, 132.5, 132.1, 130.8, 130.3, 129.9, 128.0, 122.2, 117.6, 114.2, 110.1, 66.6, 55.5, 55.3, 51.8, 43.7 (2C), 39.1, 35.8, 29.9, 24.7 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m*/*z*: $[M + K]^+$ Calcd for $C_{30}H_{39}KNO_6^+$ 548.2409; Found: 548.2419.

Methyl-4-chloro-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylate (6bi):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5b** (69 mg, 0.2 mmol), **2i** (97 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at

60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6bi** (84mg, 81%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 88:12 R$_f$(**5b**) = 0.70, R$_f$(**2i**) = 0.50, R$_f$(**6bi**) = 0.40 UV detection].

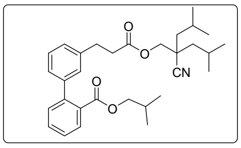
IR (MIR-ATR, 4000–600 cm^{-1}): 2952, 2349, 1733, 1653, 1018 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): .δ 7.80 (d, J = 8.3 Hz, 1H), 7.36 (dd, J = 8.3, 2.2 Hz, 1H), 7.30 (d, J = 2.1 Hz, 1H), 7.18 (dd, J = 8.4, 2.3 Hz, 1H), 7.07 (d, J = 2.3 Hz, 1H), 6.82 (d, J = 8.4 Hz, 1H), 4.13 (s, 2H), 3.69 (s, 3H), 3.65 (s, 3H), 3.00 – 2.94 (m, 2H), 2.76 – 2.70 (m, 2H), 1.84 (m, 2H), 1.53 – 1.51 (m, 4H), 1.02 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H) ppm .

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.2, 167.6, 154.6, 140.5, 137.4, 132.2, 131.3, 130.8, 129.9, 129.6, 129.2, 128.9, 127.2, 122.4, 110.3, 66.7, 55.3, 51.8, 43.7 (2C), 39.1, 35.8, 29.9, 24.8 (2C), 24.0 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + H]$^+$ Calcd for $C_{29}H_{37}ClNO_5^+$ 514.2355; Found: 514.2325.

Isobutyl-3'-chloro-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-[1,1'-biphenyl]-2-carboxylate (6ad):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-phenylpropanoate **5a** (63 mg, 0.2 mmol), isobutyl benzoate **2d** (91 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6ad** (85 mg, 81%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R$_f$(**5a**) = 0.70, R$_f$(**2d**) = 0.50, R$_f$(**6ad**) = 0.30 UV detection].

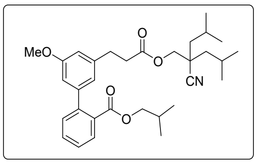
IR (MIR-ATR, 4000–600 cm^{-1}): 2943, 2188, 1662, 1497, 1412, 643 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.82 (dd, J = 7.7, 1.2 Hz, 1H), 7.51 (ddd, J = 7.5, 1.4, 1.4 Hz, 1H), 7.41 (ddd, J = 7.6, 7.6, 1.3 Hz, 1H), 7.35 (dd, J = 7.6, 0.9 Hz, 1H), 7.31 (dd, J = 7.8, 0.9 Hz, 1H), 7.20 – 7.16 (m, 3H), 4.14 (s, 2H), 3.83 (d, J = 6.6 Hz, 2H), 3.04 – 2.97 (m, 2H), 2.75 – 2.70 (m, 2H), 1.85 (m, 2H), 1.66 (tq, J = 13.4, 6.7 Hz, 1H), 1.52 (dd, J = 6.2, 1.2 Hz, 4H), 1.03 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H), 0.71 (d, J = 6.7 Hz, 6H).

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.0, 168.8, 142.0, 141.7, 139.8, 131.2, 130.9, 130.5, 129.6, 128.2, 128.1, 127.0, 126.9, 126., 122.07, 71.1, 66.6, 43.6 (2C), 39.0, 35.4, 30.6, 27.3, 24.7 (2C), 23.9 (2C), 23.8 (2C), 18.8 (2C).

HRMS (ESI) *m*/*z*: [M]$^+$ Calcd for $C_{31}H_{41}NO_4^+$ 491.3030; Found: 491.3011.

Isobutyl 5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-3'-methoxy-[1,1'-biphenyl]-2-carboxylate (6cd):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(3-methoxyphenyl)propanoate **5c** (69 mg, 0.2 mmol), isobutyl benzoate **2d** (91 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6cd** (84 mg, 81%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R_f (**5c**) = 0.70, R_f (**2d**) = 0.50, R_f (**6cd**) = 0.40 UV detection].

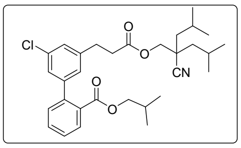
IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 2344, 1725, 1595, 1458, 733 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.81 – 7.77 (m, 1H), 7.51 (ddd, *J* = 7.6, 1.2, 1.2 Hz, 1H), 7.41 (ddd, *J* = 7.6, 7.6, 1.0 Hz, 1H), 7.37 – 7.34 (m, 1H), 6.76 (d, *J* = 1.2 Hz, 1H), 6.74 - 6.70 (m, 2H), 4.13 (s, 2H), 3.83 (d, *J* = 6.6 Hz, 2H), 3.80 (s, 3H), 2.99 – 2.94 (m, 2H), 2.73 – 2.69 (m, 2H), 1.86-1.82 (m, 2H), 1.72 – 1.64 (m, 1H), 1.53-1.50 (m, 4H), 1.02 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H), 0.72 (d, *J* = 6.7 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 172.2, 169.1, 159.6, 143.0, 141.9, 141.4, 131.5, 131.0, 130.5, 129.6, 127.2, 122.2, 120.8, 113.1, 111.9, 71.3, 66.7, 55.3, 43.7 (2C), 39.1, 35.4, 30.7, 27.4, 24.8 (2C), 24.0 (2C), 23.9 (2C), 18.9 (2C) ppm.

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{32}H_{47}N_2O_5^+$ 539.3479; Found: 539.3491.

Isobutyl-3'-chloro-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-[1,1'-biphenyl]-2-carboxylate (6dd):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(3-chlorophenyl)propanoate **5d** (70 mg, 0.2 mmol), isobutyl benzoate **2d** (91 mg, 0.3 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6dd** (85 mg, 81%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R_f (**5d**) = 0.70, R_f (**2d**) = 0.50, R_f (**6dd**) = 0.40 UV detection].

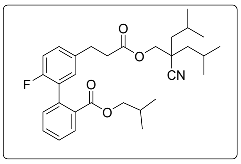
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2344, 1723, 1497, 1458, 760 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.85 (dd, J = 7.8, 1.1 Hz, 1H), 7.52 (dd, J = 7.6, 1.4 Hz, 1H), 7.45 (dd, J = 7.6, 1.2 Hz, 1H), 7.32 (dd, J = 7.6, 0.9 Hz, 1H), 7.19-7.17 (m, 2H), 7.05 (d, J = 1.5 Hz, 1H), 4.14 (s, 2H), 3.86 (d, J = 6.6 Hz, 2H), 2.98 (t, J = 7.8 Hz, 2H), 2.72 (t, J = 7.8 Hz, 2H), 1.86-1.82 (m, 2H), 1.74-1.69 (m, 1H), 1.52 (d, J = 6.2, 4H), 1.03 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H), 0.76 (d, J = 6.7 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 171.8, 168.3, 143.4, 141.7, 140.7, 131.2, 131.0, 130.5, 130.0, 127.7, 127.0, 126.7(2C), 122.1, 105.5, 71.4, 66.8, 43.7 (2C), 39.1, 35.1, 30.3, 27.5, 24.8 (2C), 24.0 (2C), 23.9 (2C), 18.9 (2C) ppm.

HRMS (ESI) *m/z*: [M + H]$^+$ Calcd for $C_{31}H_{41}ClNO_4^+$ 526.2719; Found: 526.2689.

Isobutyl-5'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-2'-fluoro-[1,1'-biphenyl]-2-carboxylate (6ed):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-fluorophenyl)propanoate **5e** (66 mg, 0.2 mmol), isobutyl benzoate **2d** (91 mg, 0.3 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6ed** (75.4 mg, 74%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 90:10 R_f(**5e**) = 0.70, R_f(**2d**) = 0.50, R_f(**6ed**) = 0.30 UV detection].

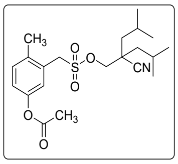
IR (MIR-ATR, 4000–600 cm^{-1}): 2923, 2355, 1723, 1602, 1252, 718 cm^{-1}.

^{1}H NMR (600 MHz, CDCl$_3$): δ 7.98 (dd, J = 7.8, 1.1 Hz, 1H), 7.57 (ddd, J = 7.6, 1.4, 1.4 Hz, 1H), 7.46 (ddd, J = 7.7, 7.7, 1.3 Hz, 1H), 7.33 (dd, J = 7.6, 1.0 Hz, 1H), 7.19 – 7.13 (m, 2H), 7.00 (dd, J = 9.6, 8.4 Hz, 1H), 4.13 (s, 4H), 3.90 (d, J = 6.7 Hz, 3H), 2.99 (t, J = 7.9 Hz, 2H), 2.72 (t, J = 7.9 Hz, , 2H), 1.88 – 1.82 (m, 2H), 1.78 – 1.72 (m, 2H), 1.51 (d, J = 6.2 Hz, 4H), 1.03 (d, J = 6.6 Hz, 6H), 1.00 (d, J = 6.6 Hz, 6H), 0.79 (d, J = 6.7 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.0 (d, J = 231.6 Hz, 1H), 167.4(2C), 143.3, 135.8 (d, J = 3.6 Hz), 131.4, 130.3 (d, J = 31.6 Hz),129.9 (d, J = 9.7 Hz),129.8 (d, J = 7.7 Hz), 127.2 (2C), 122.3, 119.7,115.4 (d, J = 21.5 Hz),115.3 (d, J = 20.9 Hz), 71.1, 47.4 (2C), 43.7, 27.4, 26.0, 24.8, 24.0 (2C), 23.95 (2C), 23.42(2C), 22.40, 19.01 (2C) ppm.

HRMS (ESI) *m/z*: [M + NH$_4$]$^+$ Calcd for $C_{31}H_{44}FN_2O_4^+$ 527.3280; Found: 527.3294.

3-((((2-Cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-4-methylphenylacetate (8b):



GP-2 was carried out with compound **1b** (70 mg, 0.2 mmol), **7** (193.26 mg, 0.6 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-acetoxy-coupling product **8b** (57 mg, 70%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R$_f$(**1b**) = 0.70, R$_f$(**7**) = 0.50, R$_f$(**8b**) = 0.45 UV detection].

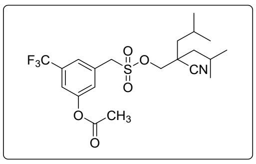
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2345, 1722, 1497, 983, 701 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 7.28 – 7.25 (m, 1H), 7.16 (d, J = 2.4 Hz, 1H), 7.04 (dd, J = 8.3, 2.4 Hz, 1H), 4.48 (s, 2H), 4.00 (s, 2H), 2.44 (s, 3H), 2.28 (s, 13H), 1.80-1.76 (m, 2H), 1.47 (d, J = 6.0 Hz, 4H), 1.00 (d, J = 6.6 Hz, 6H), 0.98 (d, J = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): δ 169.4, 148.9, 135.8, 131.9, 126.9, 124.7, 122.7, 121.3, 71.6, 54.5, 43.0 (2C), 39.4, 31.5, 24.7 (2C), 23.8 (2C), 21.0 (2C), 19.1 ppm.

HRMS (ESI) *m/z*: [M + Na]$^+$ Calcd for $C_{21}H_{31}NNaO_5S^+$ 432.1815; Found: 432.1801.

3-((((2-Cyano-2-isobutyl-4-methylpentyl)oxy)sulfonyl)methyl)-5-(trifluoromethyl)phenyl acetate (8c):



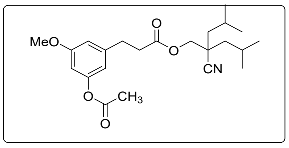
GP-2 was carried out with compound **1c** (80 mg, 0.2 mmol), **7** (193.26 mg, 0.6 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-acetoxy-coupling product **8c** (50 mg, 55%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R*f* (**1c**) = 0.70, R*f* (**7**) = 0.60, R*f* (**8c**) = 0.40 UV detection].

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 7.57 (d, *J* = 1.6 Hz, 1H), 7.49 – 7.42 (m, 2H), 4.50 (s, 2H), 4.08 (s, 2H), 2.33 (s, 3H), 1.80 – 1.76 (m, 2H), 1.47 (d, *J* = 6.2 Hz, 4H), 1.00 (d, *J* = 6.6 Hz, 6H), 0.98 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (101 MHz, CDCl$_3$): *δ* 168.5, 151.0, 132.54 (d, *J* = 33.5 Hz), 130.1, 127.7, 126.4, 124.9(d, *J* = 3.6 Hz), 121.4, 119.8(d, *J* = 3.9 Hz), 71.6, 56.4, 43.1 (2C), 39.6, 24.8 (2C), 23.9 (2C), 23.9 (2C), 21.1 ppm.

HRMS (ESI) *m*/*z*: $[M + NH_4]^+$ Calcd for $C_{21}H_{32}F_3N_2O_5S^+$ 481.1979; Found: 481.1978.

2-Acetate-2-isobutyl-4-methylpentyl 3-(3-methoxy-3-cyanophenyl)propanoate (9c):



GP-2 was carried out with compound **5c** (69 mg, 0.2 mmol), **7** (193.26 mg, 0.6 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-acetoxy-coupling product **9c** (55 mg, 63%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R*f* (**5c**) = 0.70, R*f* (**7**) = 0.50, R*f* (**9c**) = 0.40 UV detection].

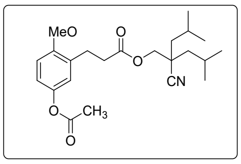
IR (MIR-ATR, 4000–600 cm^{-1}): 2958, 2319, 1741, 1204, 1133 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): *δ* 6.64 – 6.62 (dd, *J* = 2.2, 1.6 Hz,1H), 6.54 (dd, *J* = 2.2, 1.6 Hz, 1H), 6.49 (dd, *J* = 2.2,1.6 Hz, 1H), 4.12 (s, 2H), 3.78 (s, 3H), 2.94 (t, *J* = 7.7 Hz, 2H), 2.70 (t, *J* = 7.7 Hz, 2H), 2.28 (s, 3H), 1.85-1.81 (m, 2H), 1.49 (d, 4H), 1.02 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 171.5, 159.8, 143.0, 124.2, 122.1, 119.5, 118.6, 114.8, 113.2, 77.0, 66.9, 55.5, 43.6 (2C), 39.0, 34.8, 30.2, 24.8 (2C), 23.9 (2C), 23.9 (2C) ppm.

HRMS (ESI) *m*/*z*: $[M + NH_4]^+$ Calcd for $C_{23}H_{37}N_2O_5^+$ 421.2697; Found: 421.2701.

2-Acetate-2-isobutyl-4-methylpentyl 3-(2-methoxy-3-cyanophenyl)propanoate (9f):



GP-2 was carried out with compound **5f** (69 mg, 0.2 mmol), **7** (193.26 mg, 0.6 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%) in HFIP (1 mL), microwave conditions at 100°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-acetoxy-coupling product **9f** (53 mg, 61%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R_f(**5f**) = 0.70, R$_f$(**7**) = 0.50, R$_f$(**9f**) = 0.40 UV detection].

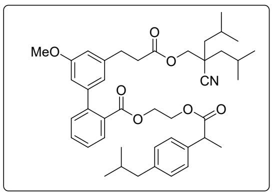
IR (MIR-ATR, 4000–600 cm^{-1}): 2926, 2238, 1741, 1599, 1197 cm^{-1}.

^{1}H NMR (400 MHz, CDCl$_3$): δ 6.93 – 6.88 (m, 2H), 6.81 (d, *J* = 8.6 Hz, 1H), 4.10 (s, 3H), 3.82 (s, 3H), 2.93 (t, *J* = 7.7 Hz, 2H), 2.69 (t, *J* = 7.7 Hz, 2H), 2.26 (s, 3H), 1.86 – 1.82 (m, 2H), 1.52 – 1.49 (m, 4H), 1.03 (d, *J* = 6.6 Hz, 6H), 1.00 (d, *J* = 6.6 Hz, 6H) ppm.

^{13}C{^{1}H} NMR (151 MHz, CDCl$_3$): δ 172.6, 170.1, 155.2, 143.9, 129.5, 123.1, 122.4, 120.2, 110.6, 77.1, 66.7, 55.7, 43.9 (2C), 39.1, 33.6, 26.0, 24.9 (2C), 24.1 (2C), 24.0 (2C), 21.1 ppm**.**

HRMS (ESI) *m*/*z*: [M + NH$_4$]$^+$ Calcd for $C_{23}H_{37}N_2O_5^+$ 421.2697; Found: 421.2717.

2-((2-(4-isobutylphenyl)propanoyl)oxy)ethyl-3'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-5'-methoxy-[1,1'-biphenyl]-2-carboxylate(6cp):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5c** (69 mg, 0.2 mmol), **2p** (97 mg, 0.2 mmol), Pd(OAc)$_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6cp** (97 mg, 70%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R$_f$(**5c**) = 0.70, R$_f$(**2p**) = 0.40, R$_f$(**6cp**) = 0.20 UV detection].

IR (MIR-ATR, 4000–600 cm^{-1}): 2943, 2354, 1658, 1113, 1019 cm^{-1}

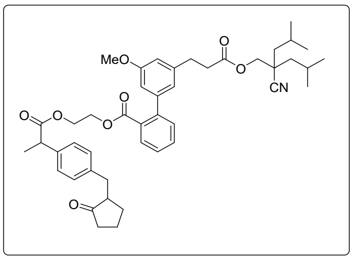
^{1}H NMR (600 MHz, CDCl$_3$): δ 7.74 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.53 (ddd, *J* = 7.6, 1.4, 1.4 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.6, 1.2 Hz, 1H), 7.35 (dd, *J* = 7.7, 0.8 Hz, 1H), 7.16 (d, *J* = 8.0 Hz, 2H), 7.02 (d, *J* = 8.1 Hz, 2H), 6.76 – 6.73 (m, 1H), 6.68 (dd, *J* = 5.5, 3.2 Hz, 2H), 4.24 (ddd, *J* = 18.7, 6.1, 3.6 Hz, 2H), 4.13 (s, 2H), 4.10 – 4.02 (m, 2H), 3.87 (d, *J* = 18.6 Hz, 1H), 3.80 –

3.75 (m, 3H), 3.66 (d, *J* = 7.2 Hz, 1H), 2.95 (d, *J* = 8.1 Hz, 2H), 2.74 – 2.66 (m, 2H), 2.40 (d, *J* = 7.2 Hz, 2H), 1.82 (ddd, *J* = 19.5, 13.1, 6.6 Hz, 4H), 1.51 (dd, *J* = 6.2, 1.1 Hz, 2H), 1.46 (d, *J* = 7.2 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 6H), 0.99 (d, *J* = 6.6 Hz, 6H), 0.87 (d, *J* = 6.6 Hz, 6H) ppm.

$^{13}C\{^{1}H\}$ NMR (151 MHz, $CDCl_3$): *δ* 174.5, 172.2, 168.1, 159.6, 143.0, 141.4, 140.7, 131.4, 130.7, 130.5, 129.9, 129.4, 127.4, 127.2, 120.9, 120.9, 112.9, 112.2, 66.8, 62.2, 55.3, 45.1, 45.0, 43.9 (2C), 35.5, 30.8, 30.2, 24.9 (2C), 24.1 (2C), 24.0 (2C), 22.5, 18.6 ppm.

HRMS (ESI) *m/z*: $[M + N]^+$ Calcd for $C_{43}H_{55}N_2O_7^+$ 711.4004; Found: 711.4010.

2-((2-(4-((2-oxocyclopentyl)methyl)phenyl)propanoyl)oxy)ethyl-3'-(3-((2-cyano-2-isobutyl-4-methylpentyl)oxy)-3-oxopropyl)-5'-methoxy-[1,1'-biphenyl]-2-carboxylate (6cq):



GP-1 was carried out with compound 2-cyano-2-isobutyl-4-methylpentyl 3-(4-methoxyphenyl)propanoate **5c** (69 mg, 0.2 mmol), **2q** (105 mg, 0.2 mmol), $Pd(OAc)_2$ (4.5 mg, 10 mol%), *N*-Ac-Gly-OH (4.7 mg, 20 mol%), AgOAc (66.4 mg, 0.4 mmol) in HFIP (1 mL) at 60°C. Purification of the crude mixture by silica gel column chromatography furnished the *meta*-aryl-coupling product **6cq** (113 mg, 77%) as a colorless liquid. [TLC control (petroleum ether/ethyl acetate 91:09 R_f(**5c**) = 0.70, R_f(**2q**) = 0.40, R_f(**6cq**) = 0.20 UV detection].

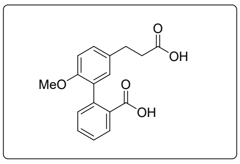
IR (MIR-ATR, 4000–600 cm^{-1}): 2957, 2334, 1733, 1207, 763 cm^{-1}

^{1}H NMR (600 MHz, $CDCl_3$): *δ* 7.74 – 7.71 (m, 1H), 7.53 (ddd, *J* = 7.5, 1.3, 1.3 Hz, 1H), 7.39 (ddd, *J* = 7.6, 7.6, 1.1 Hz, 1H), 7.35 (dd, *J* = 7.7, 0.9 Hz, 1H), 7.17 (d, *J* = 8.1 Hz, 2H), 7.06 – 7.03 (m, 2H), 6.74 (d, *J* = 1.7 Hz, 1H), 6.67 (dd, *J* = 6.4, 1.3 Hz, 2H), 4.28 – 4.19 (m, 2H), 4.13 (s, 2H), 4.10 – 4.04 (m, 2H), 3.77 (s, 3H), 3.66 (d, *J* = 7.2 Hz, 1H), 3.08 (dd, *J* = 13.9, 4.1 Hz, 1H), 2.95 (t, *J* = 7.9 Hz, 2H), 2.75 – 2.68 (m, 2H), 2.47 – 2.42 (m, 1H), 2.35 – 2.29 (m, 2H), 2.10 (ddd, *J* = 19.0, 10.4, 8.9 Hz, 1H), 1.96 – 1.90 (m, 2H), 1.83 (ddd, *J* = 13.0, 6.5, 6.5 Hz, 2H), 1.71 – 1.67 (m, 2H), 1.51 (dd, *J* = 6.2, 1.1 Hz, 4H), 1.45 (d, *J* = 7.2 Hz, 3H), 1.02 (d, *J* = 6.6 Hz, 6H), 0.99 (d, *J* = 6.6 Hz, 6H) ppm.

$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 220.3, 174.3, 172.2, 172.1, 168.1, 159.6, 142.9, 141.4, 139.1, 131.5, 130.7, 130.4, 129.9, 129.2, 127.6, 127.4, 122.3, 120.9, 112.9, 112.2, 66.9, 62.5, 62.2, 55.3, 51.1, 44.9, 43.8 (2C), 39.2, 38.3, 35.5, 35.3, 30.8, 29.3, 25.7, 24.9 (2C), 24.1 (2C), 24.0 (2C), 20.6, 18.5 ppm.

HRMS (ESI) ***m*/*z***: $[M + K]^+$ Calcd for $C_{45}H_{55}KNO_8^+$ 776.3559; Found: 776.3582.

5'-(2-carboxyethyl)-2'-methoxy-[1,1'-biphenyl]-2-carboxylic acid (7):



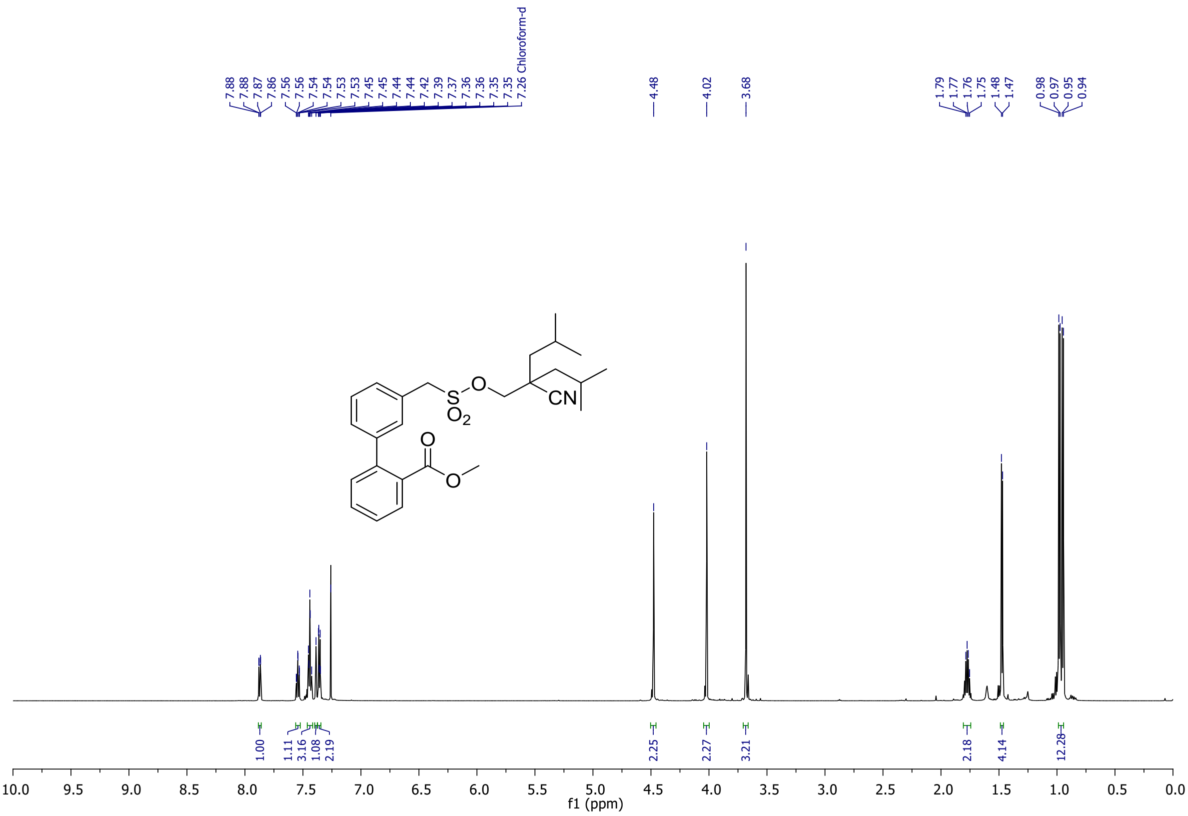
To the solution of compound **6ba** (60 mg, 0.15 mmol) in MeOH (1.2 mL), THF (0.6 mL), and H_2O (0.3 mL) was added $LiOH\cdot H_2O$ (38 mg, 0.90 mmol) at 60 °C reflux temperature for 12h. The organic solvents were removed under reduced pressure, and the resulting residue was diluted with H_2O (15 mL). The aqueous phase was acidified with 2 M HCl (2 mL) and extracted with DCM (3 × 10 mL). The combined organic extract was dried over Na_2SO_4, concentrated in a rotavapour, and purified by flash column chromatography to get the diacid product **7** (35 mg, 85%) as a white amorphous solid, along with recovered template **4** in 85% yield, mp 190–193 °C.

^1H NMR (600 MHz, $CDCl_3$): δ 9.27 (s, 2H), 7.93 (dd, *J* = 7.8, 1.1 Hz, 1H), 7.56 (ddd, *J* = 7.6, 1.4, 1.2 Hz, 1H), 7.40 (ddd, *J* = 7.6, 1.4, 1.2 Hz, 1H), 7.32 (dd, *J* = 7.6, 0.8 Hz, 1H), 7.14 (dd, *J* = 8.4, 2.2 Hz, 1H), 7.10 (d, *J* = 1.8 Hz, 1H), 6.77 (d, *J* = 8.4 Hz, 1H), 3.65 (s, 3H), 2.93 (t, *J* = 7.5 Hz, 2H), 2.68 (t, *J* = 7.6 Hz, 2H) ppm.

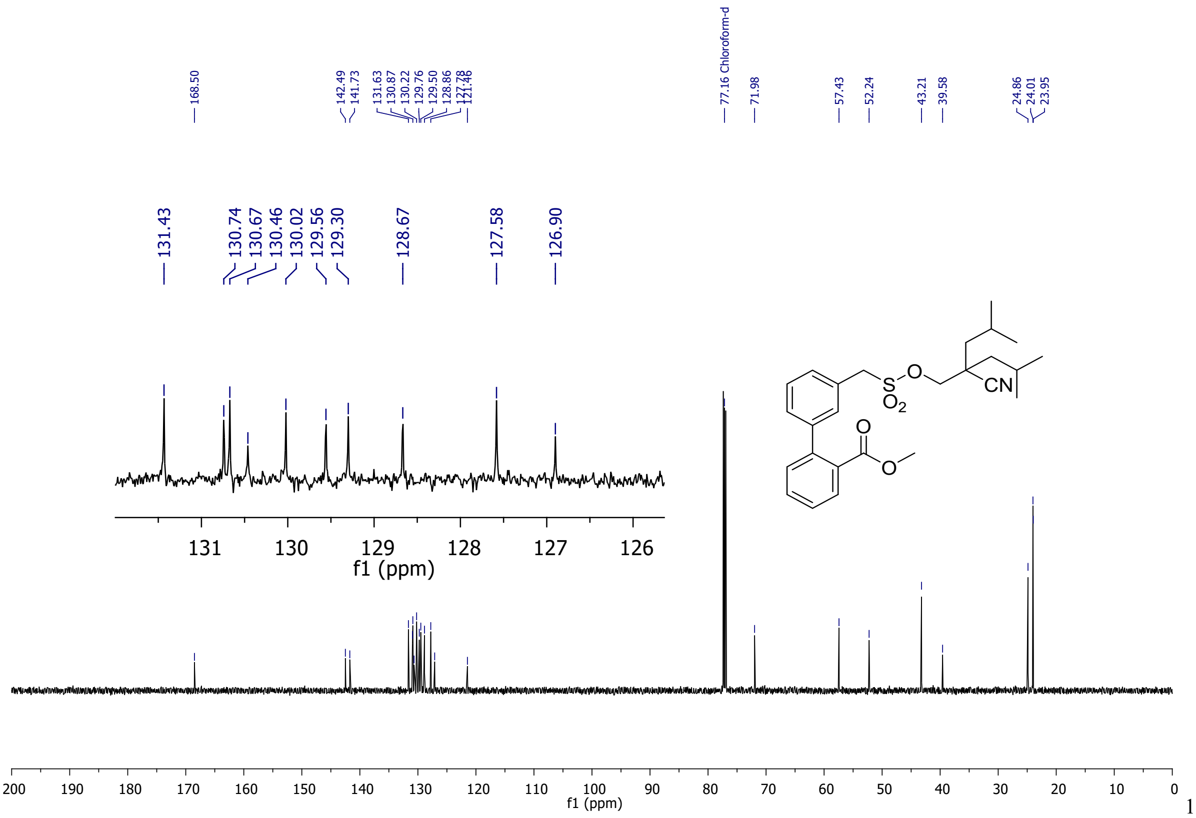
$^{13}C\{^1H\}$ NMR (151 MHz, $CDCl_3$): δ 179.2, 173.7, 154.7, 138.9, 132.3, 132.2, 131.5, 130.6, 130.0, 129.8(2C), 128.7, 127.2, 110.5, 55.1, 35.7, 29.8 ppm.

HRMS (ESI) ***m*/*z***: $[M + K]^+$ Calcd for $C_{17}H_{16}KO_5^+$ 339.0629; Found: 339.0659.

NMR Spectra:

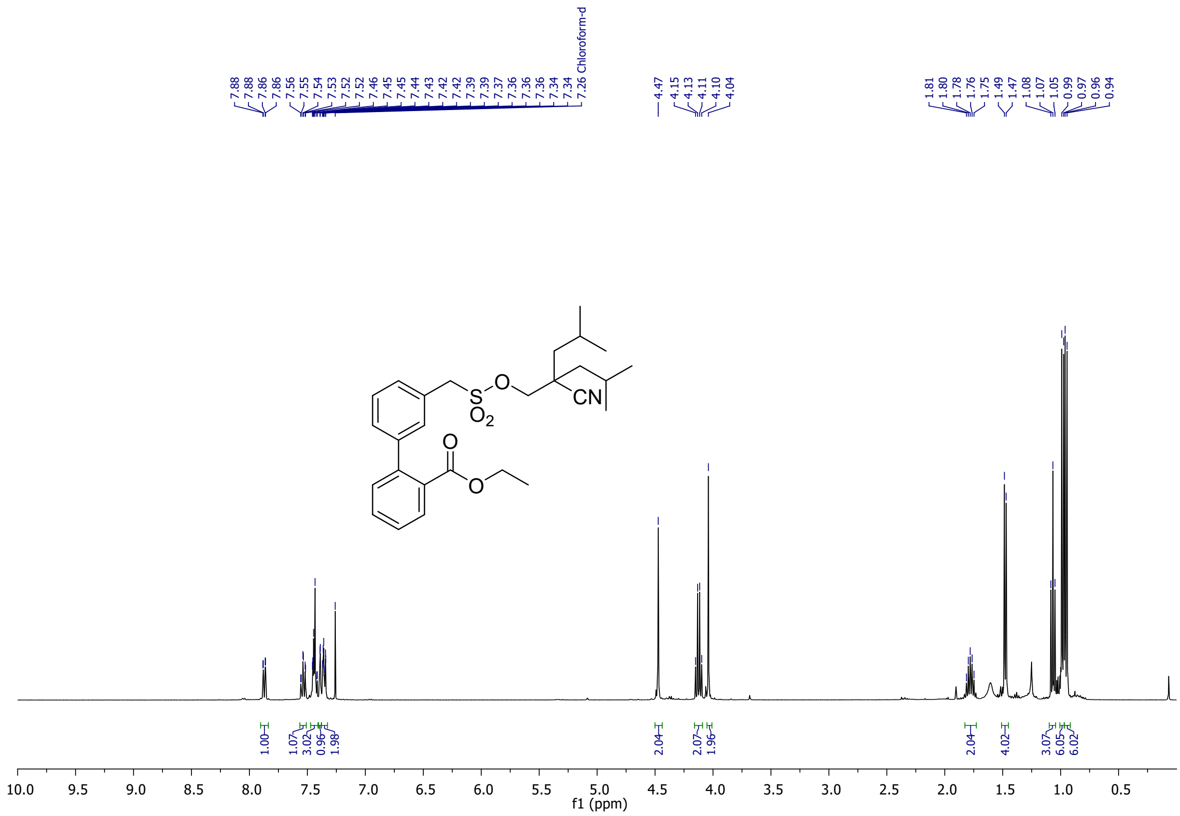


^{1}H NMR (400 MHz) spectrum of **3aa** in $CDCl_3$.



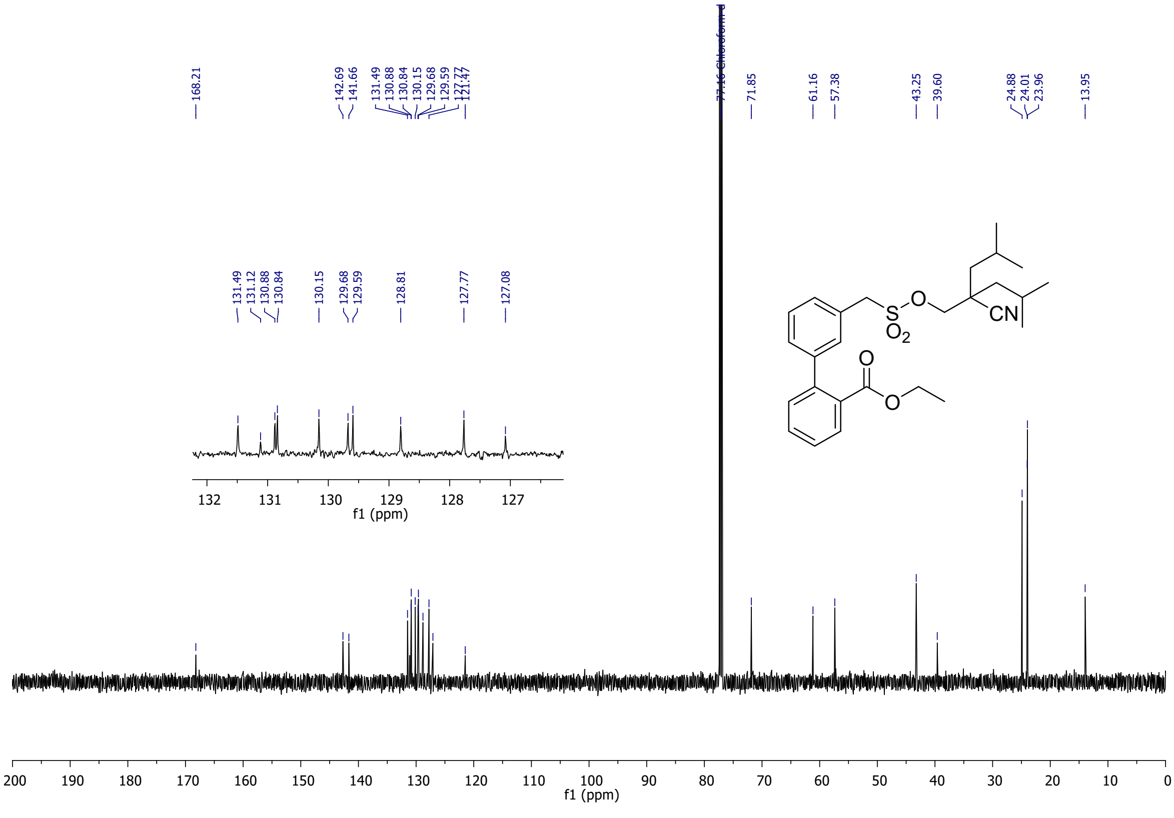
1

^{3}C{^{1}H} NMR (151 MHz) spectrum of **3aa** in $CDCl_3$.



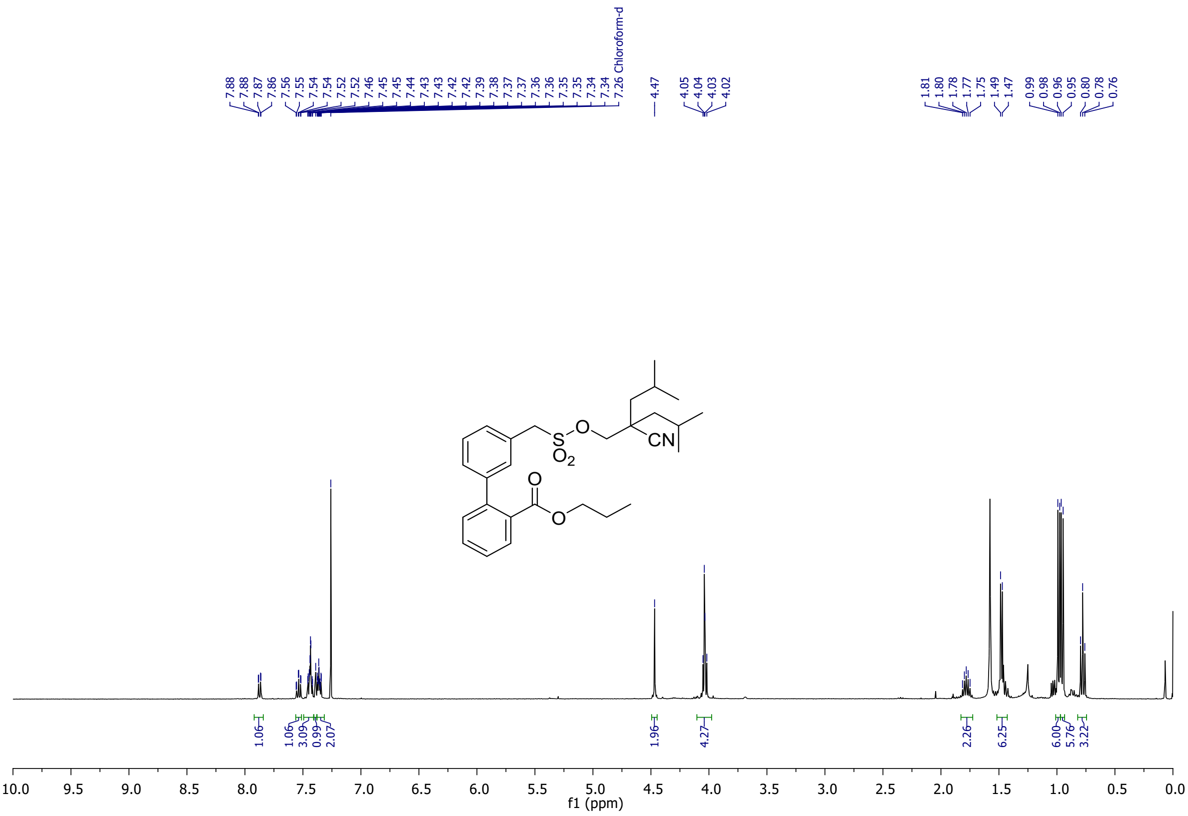
1

H NMR (400 MHz) spectrum of **3ab** in $CDCl_3$.

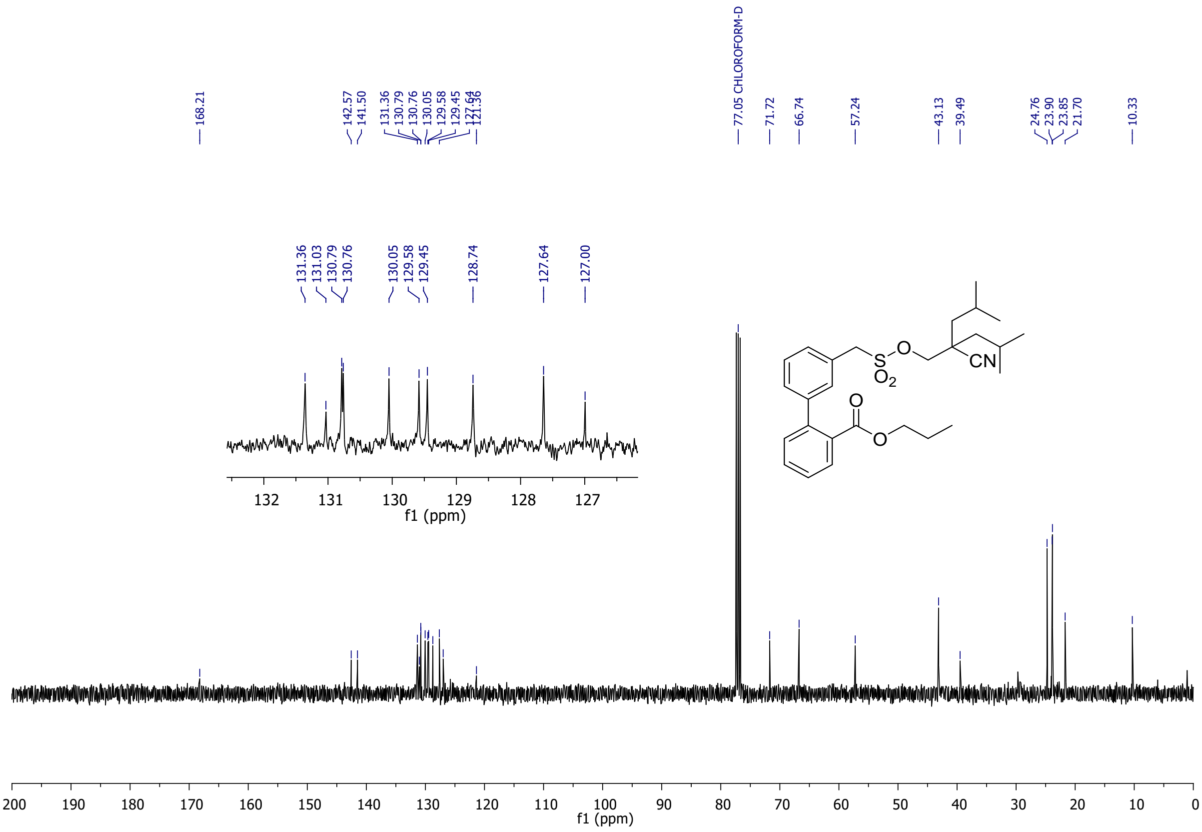


13

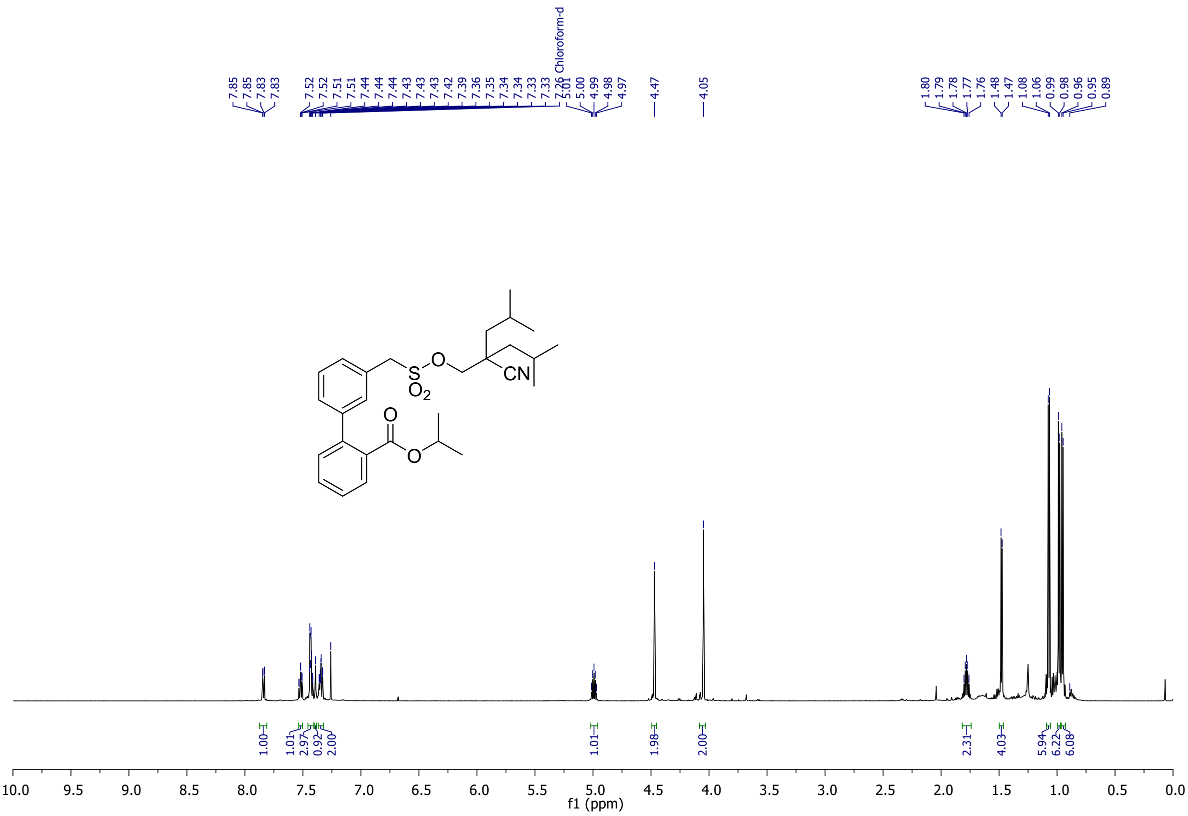
C{^{1}H} NMR (151 MHz) spectrum of **3ab** in $CDCl_3$.



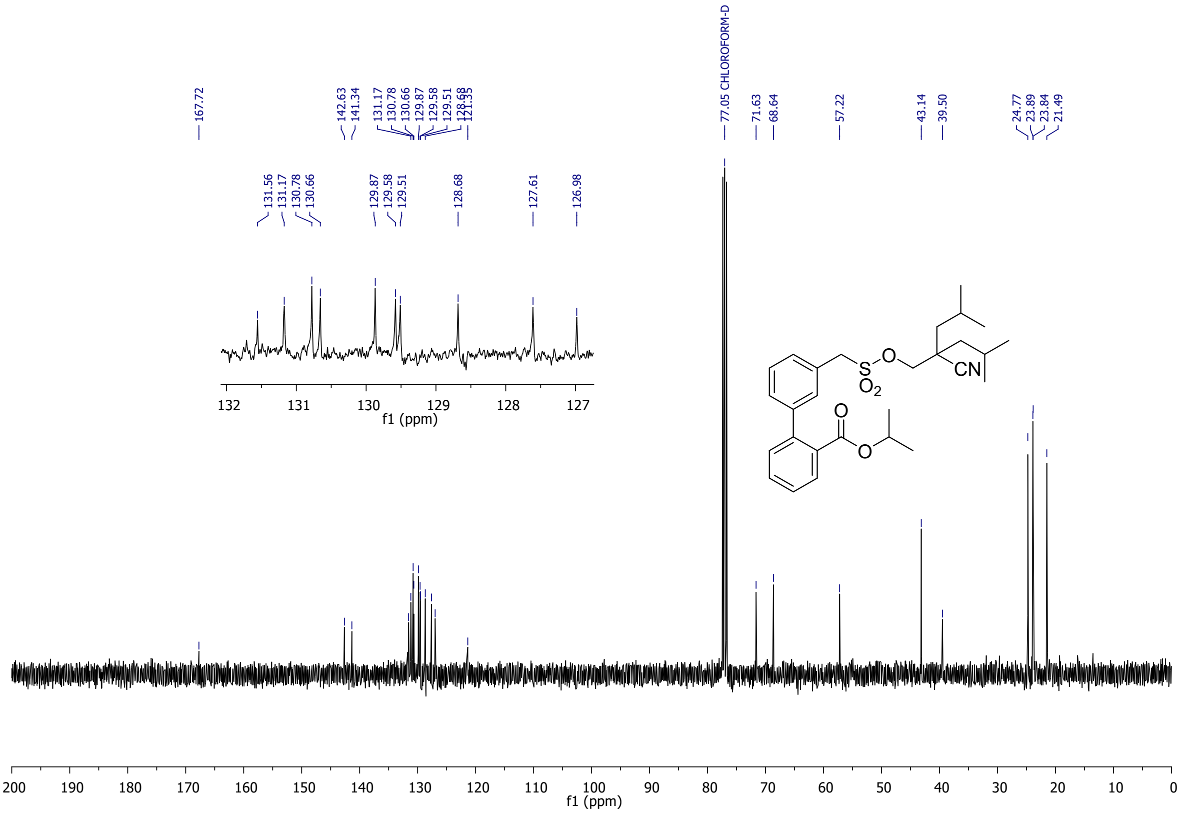
^{1}H NMR (400 MHz) spectrum of **3ac** in $CDCl_3$.



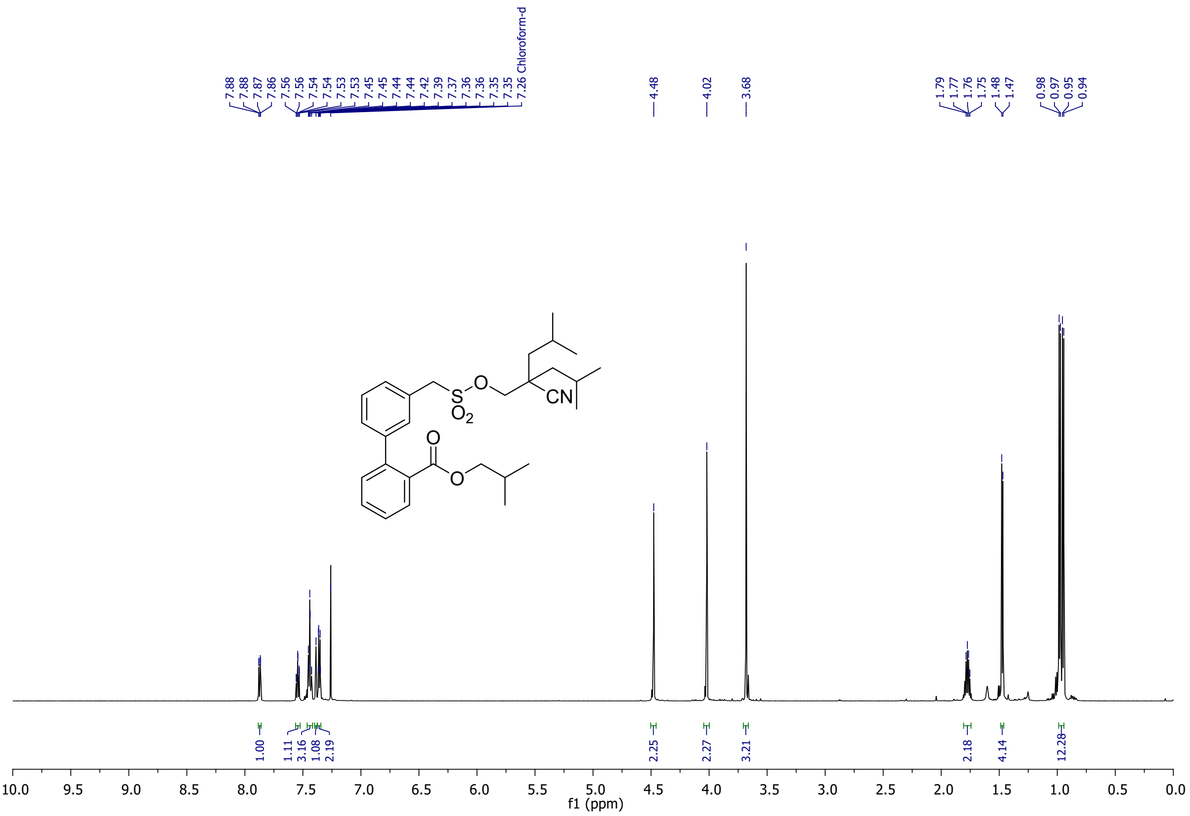
$^{13}C\{^{1}H\}$ NMR (101 MHz) spectrum of **3ac** in $CDCl_3$.



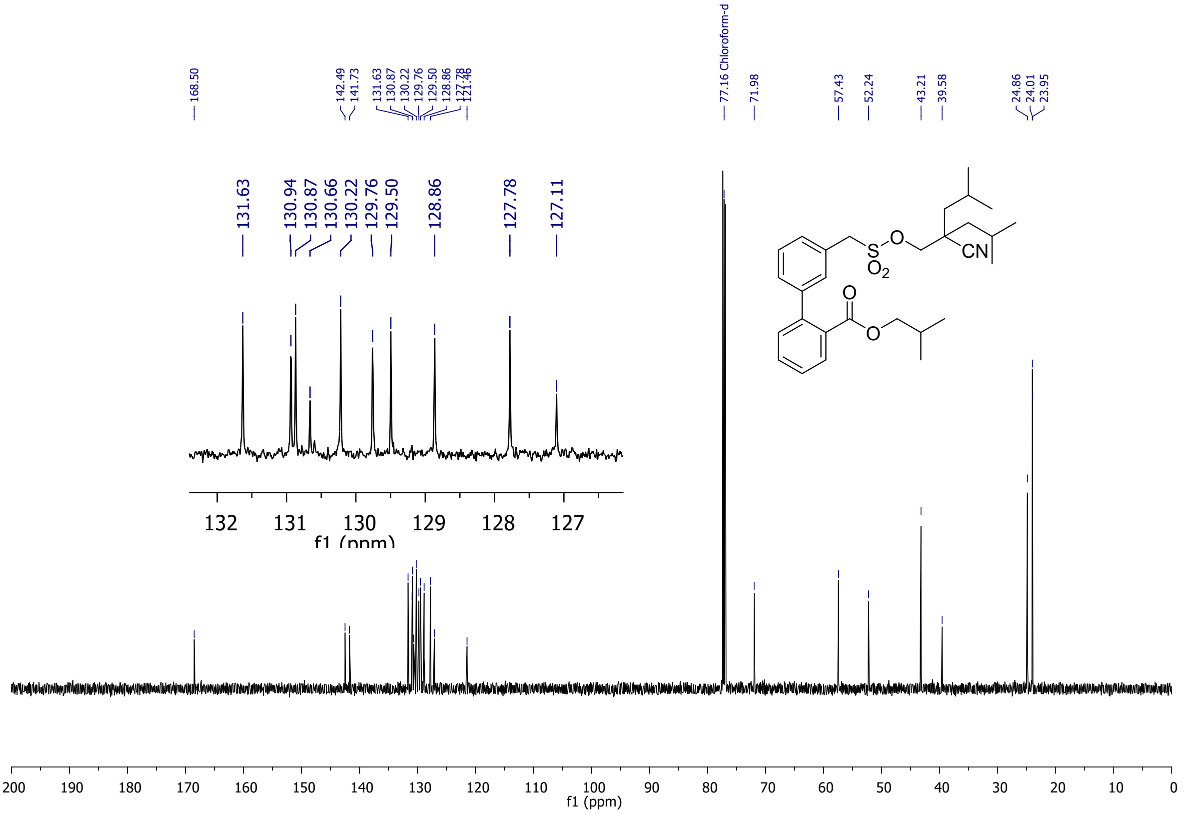
^{1}H NMR (400 MHz) spectrum of **3ad** in CDCl$_3$.



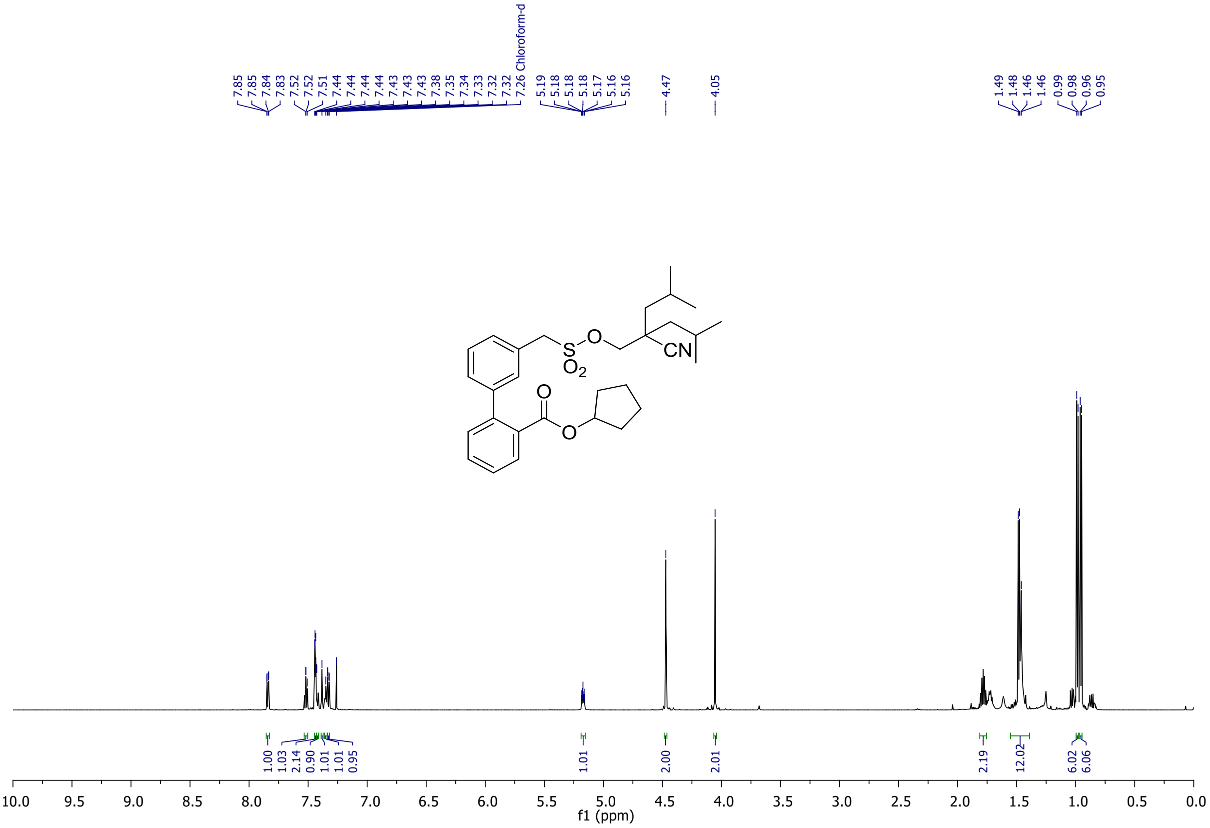
^{13}C{^{1}H} NMR (101 MHz) spectrum of **3ad** in CDCl$_3$.



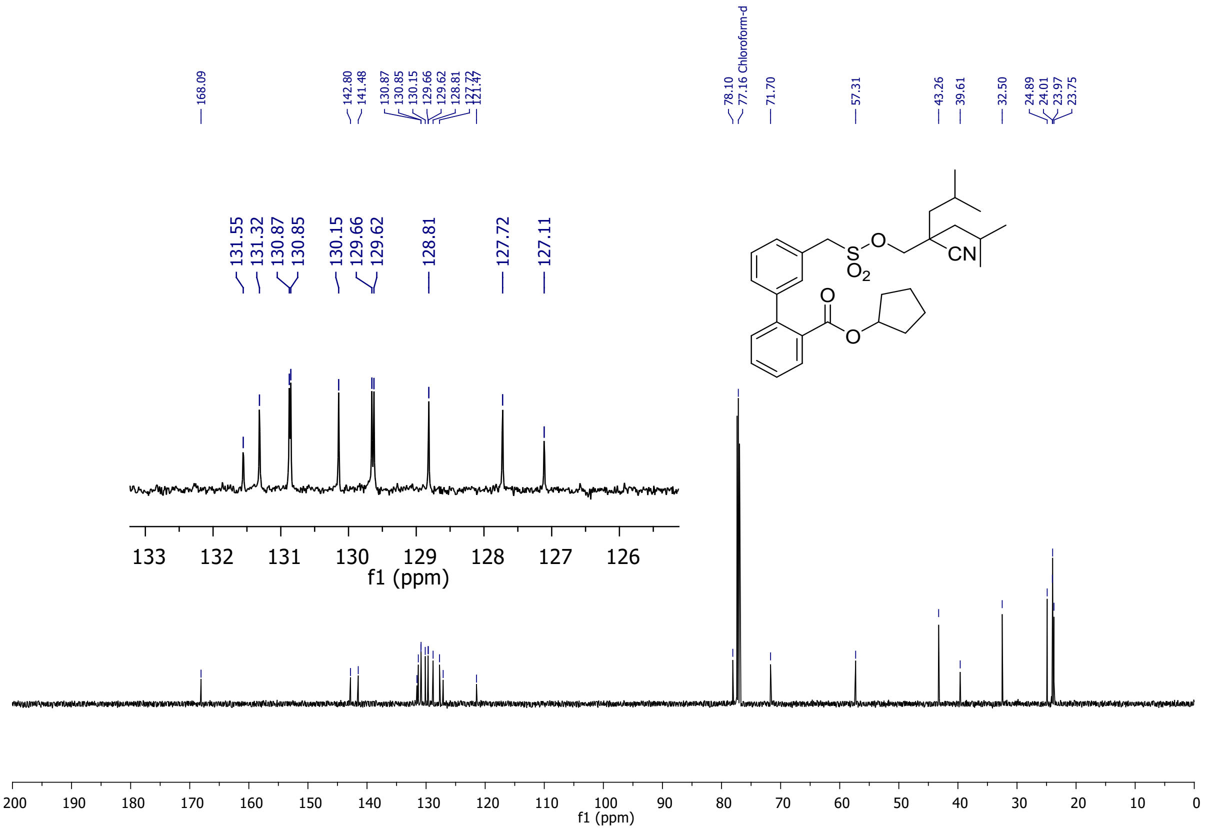
^{1}H NMR (600 MHz) spectrum of **3ae** in $CDCl_3$.



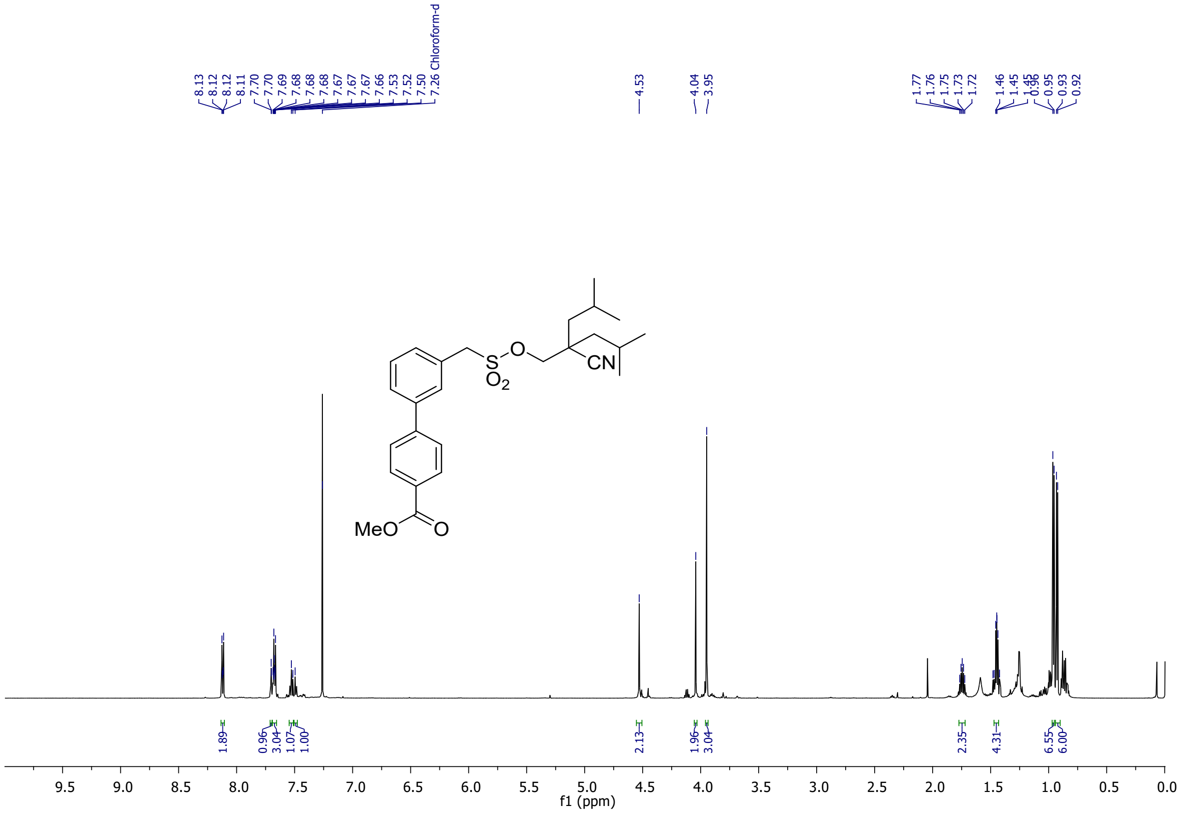
$^{13}C\{^1H\}$ NMR (101 MHz) spectrum of **3ae** in $CDCl_3$.



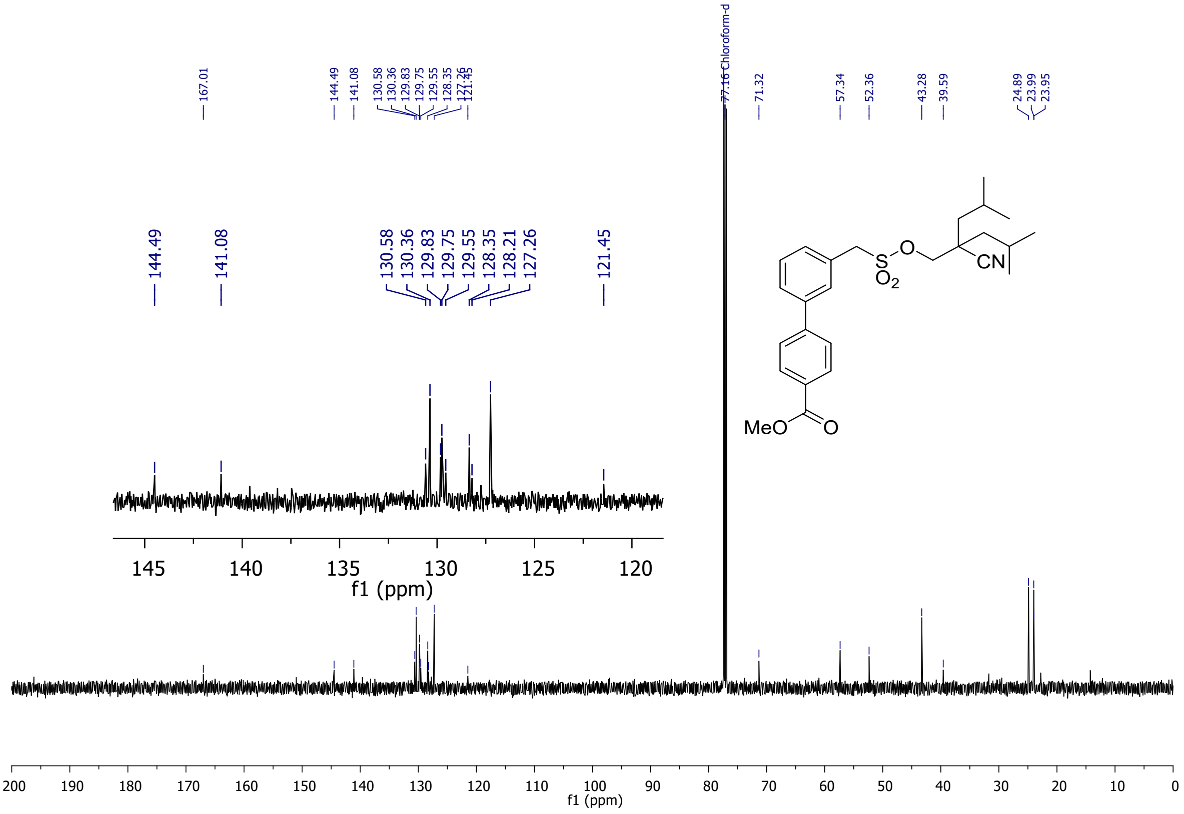
^{1}H NMR (600 MHz) spectrum of **3af** in CDCl$_3$.



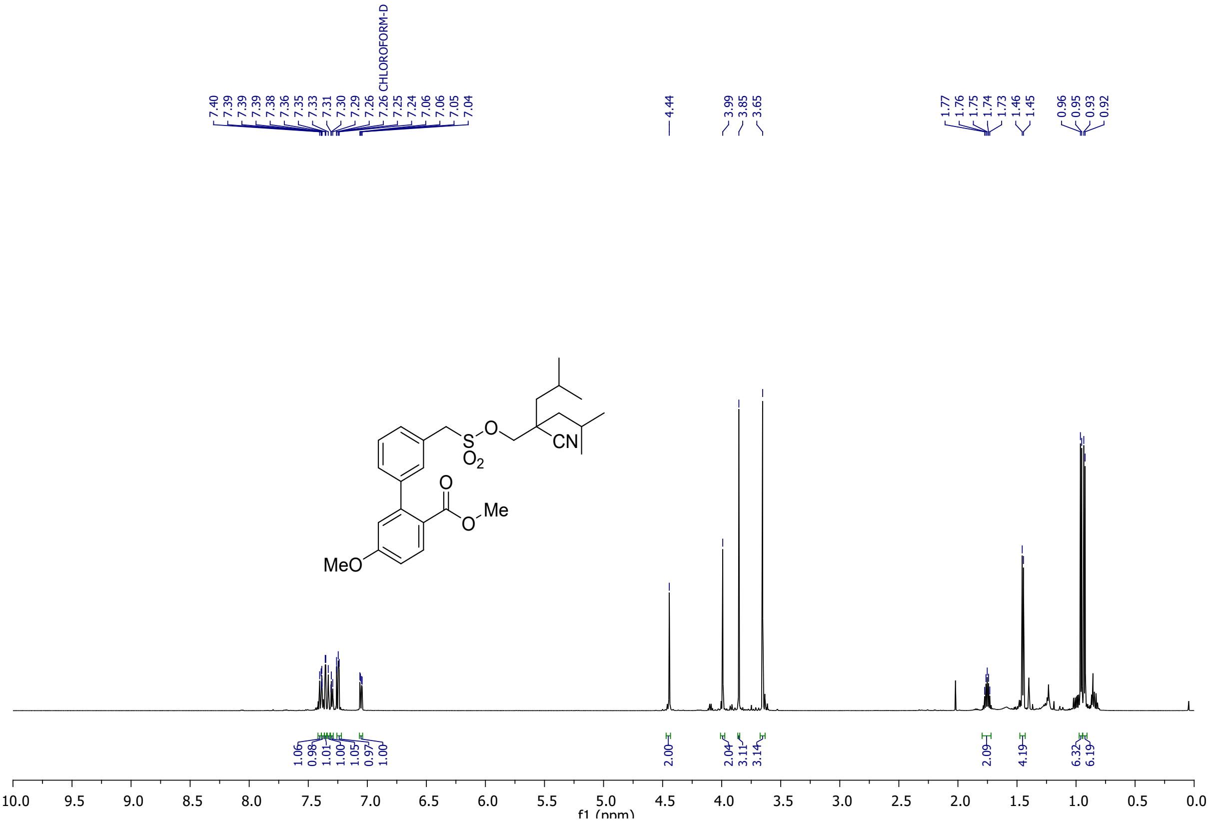
^{13}C{^{1}H} NMR (151 MHz) spectrum of **3af** in CDCl$_3$.



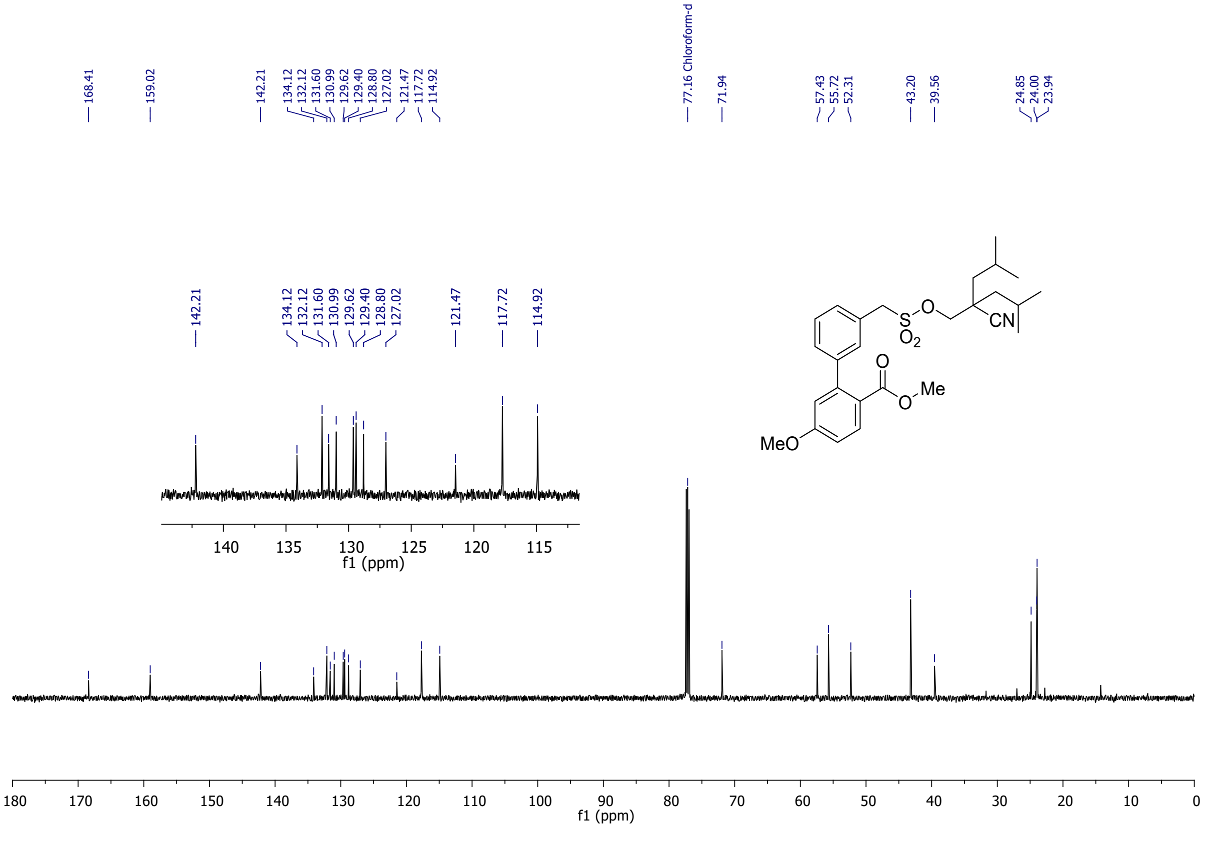
^{1}H NMR (600 MHz) spectrum of **3ag** in CDCl$_3$.



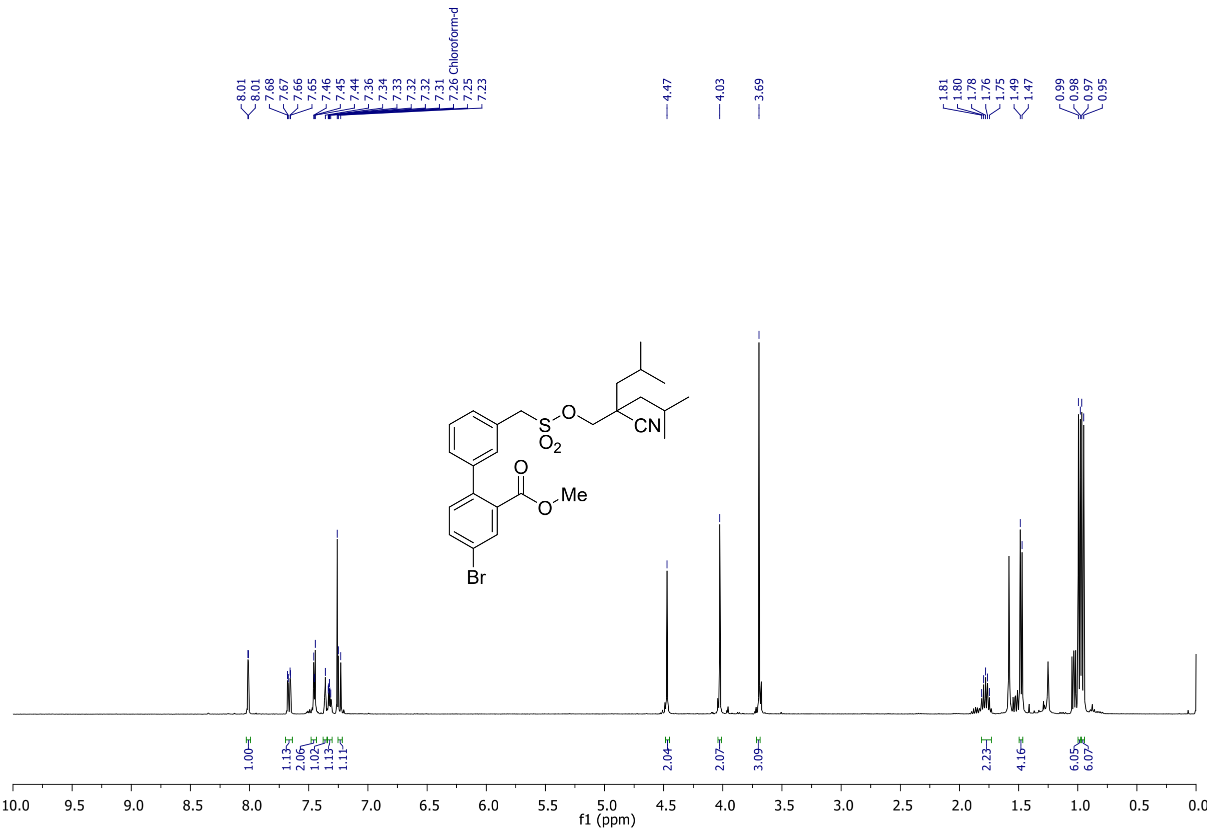
^{13}C{^{1}H} NMR (151 MHz) spectrum of **3ag** in CDCl$_3$.



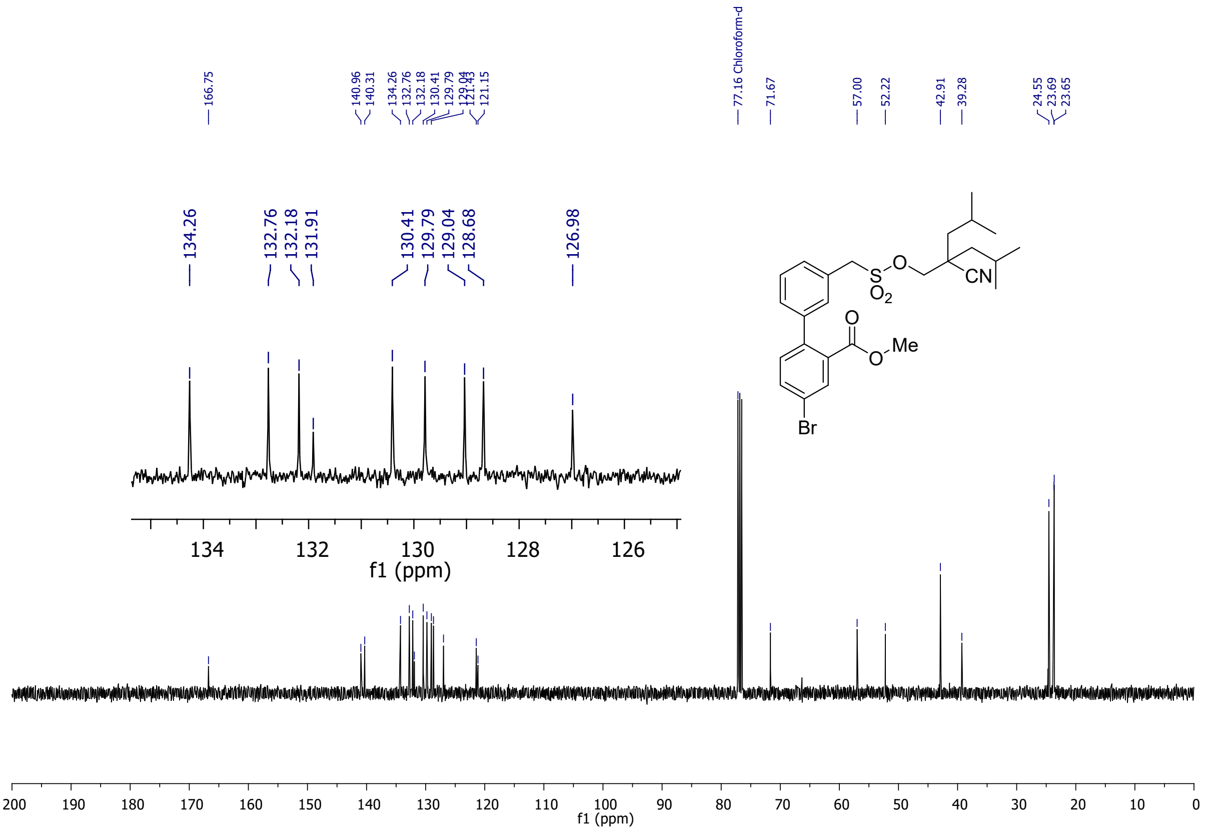
^{1}H NMR (600 MHz) spectrum of **3ah** in CDCl$_3$.



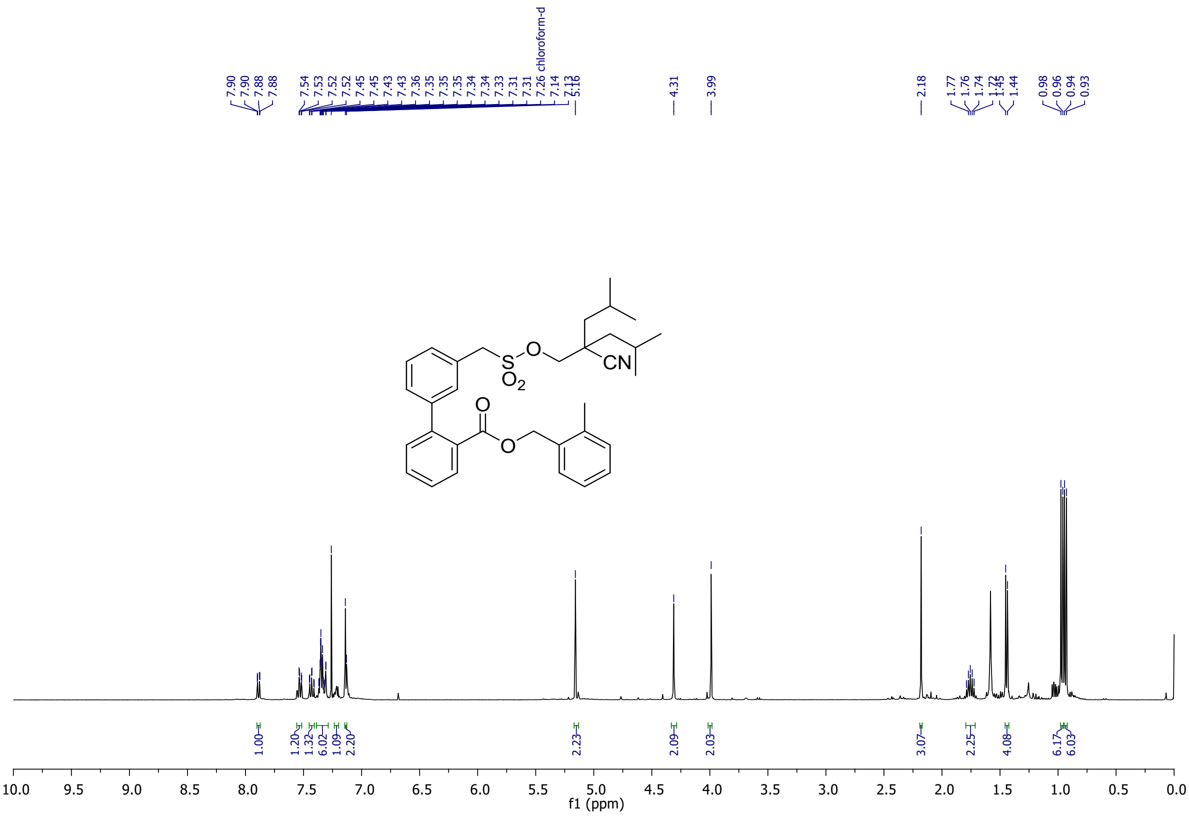
^{13}C{^{1}H} NMR (151 MHz) spectrum of **3ah** in CDCl$_3$.



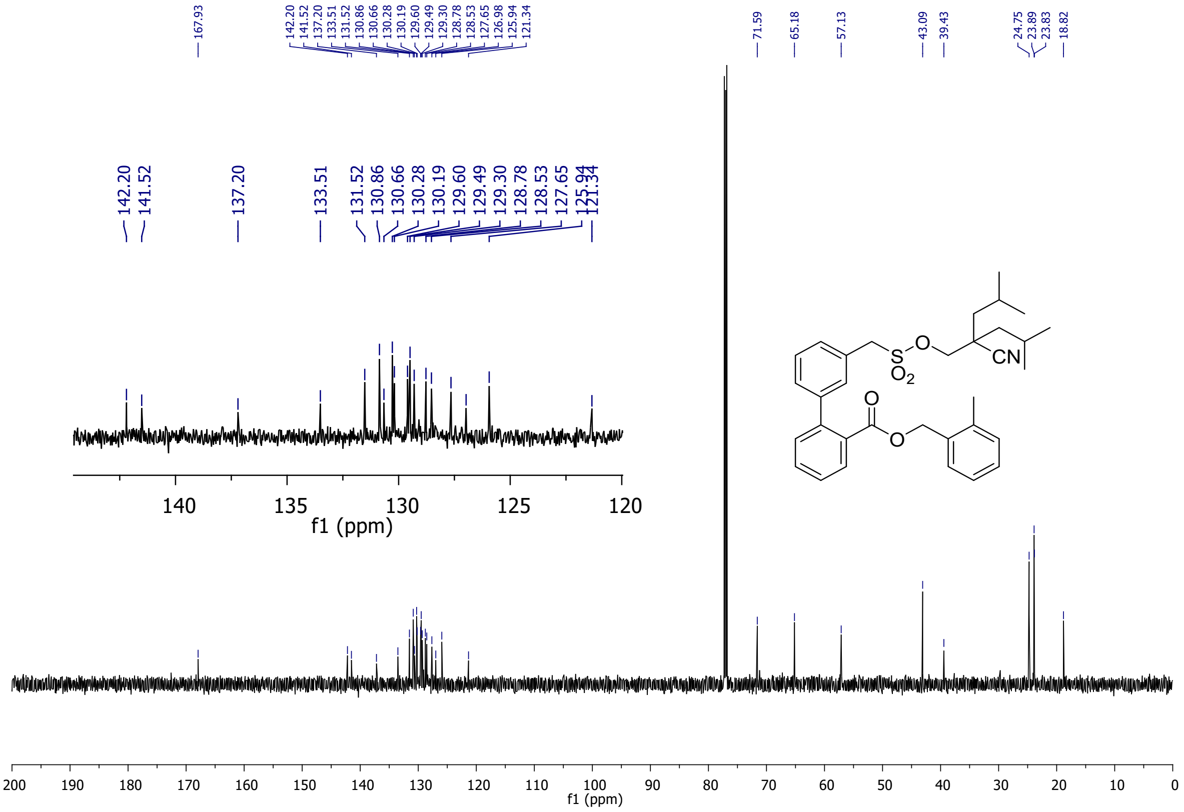
^{1}H NMR (400 MHz) spectrum of **3ai** in CDCl$_3$.



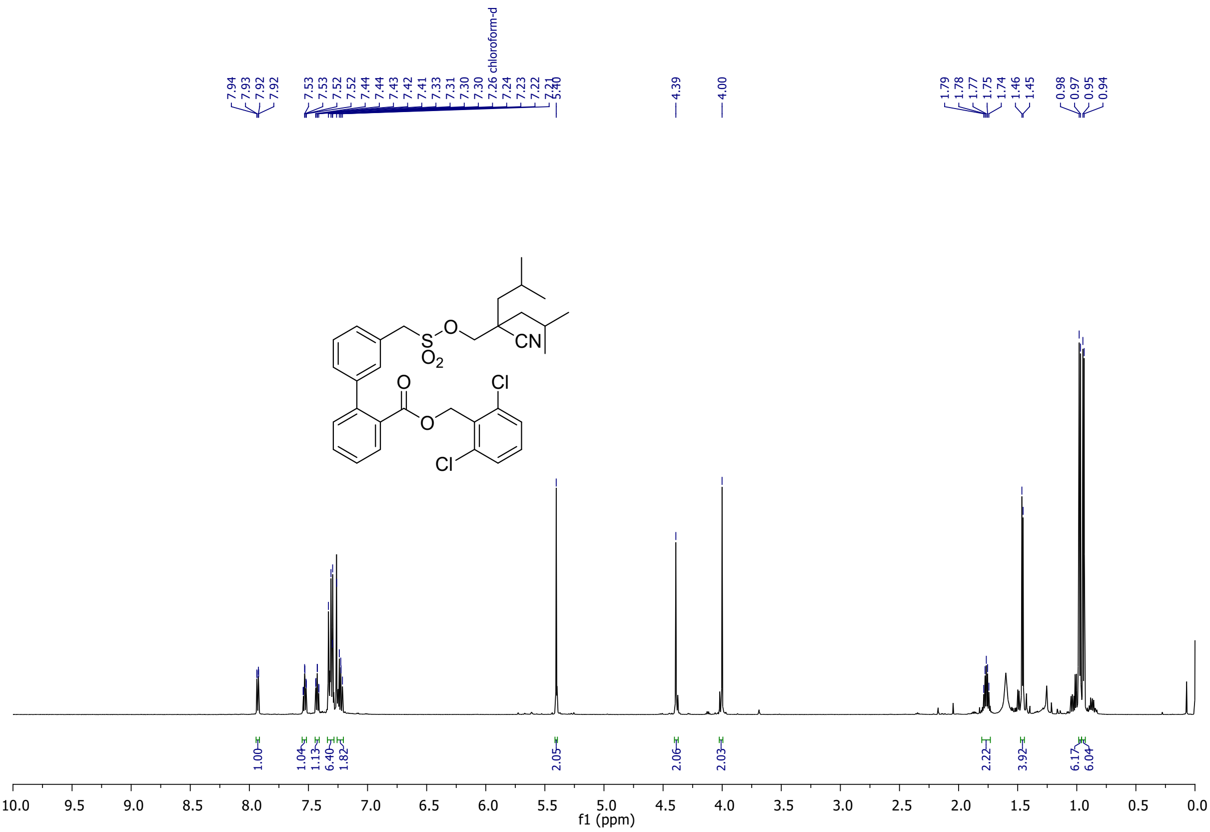
^{13}C{^{1}H} NMR (101 MHz) spectrum of **3ai** in CDCl$_3$.



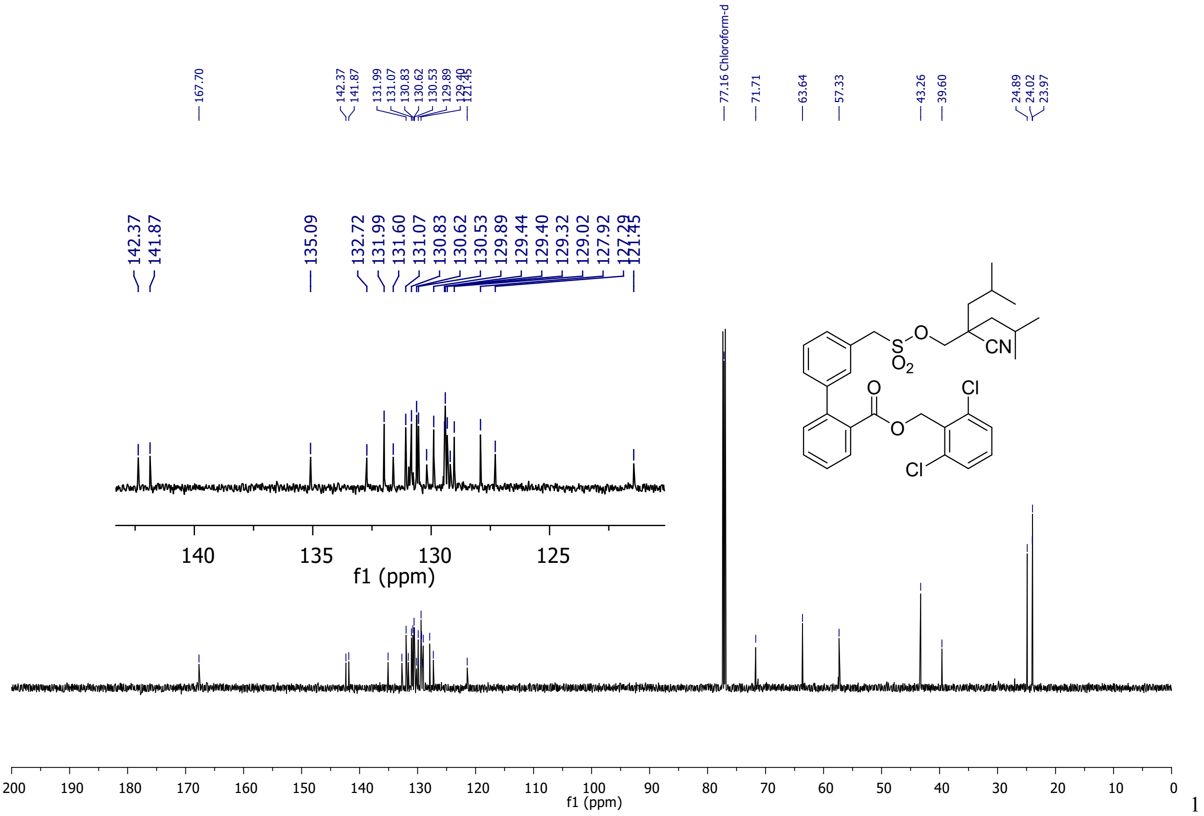
^{1}H NMR (600 MHz) spectrum of **3aj** in CDCl$_3$.



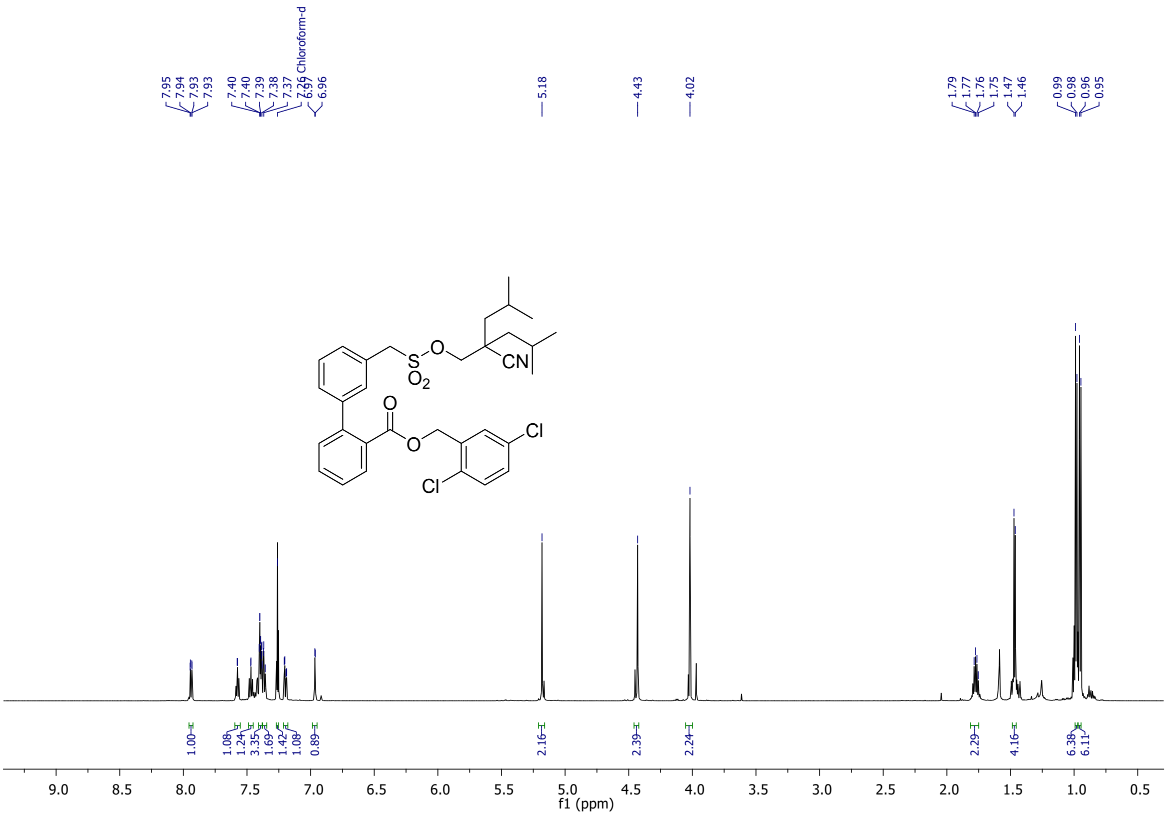
^{13}C{^{1}H} NMR (101 MHz) spectrum of **3aj** in CDCl$_3$.



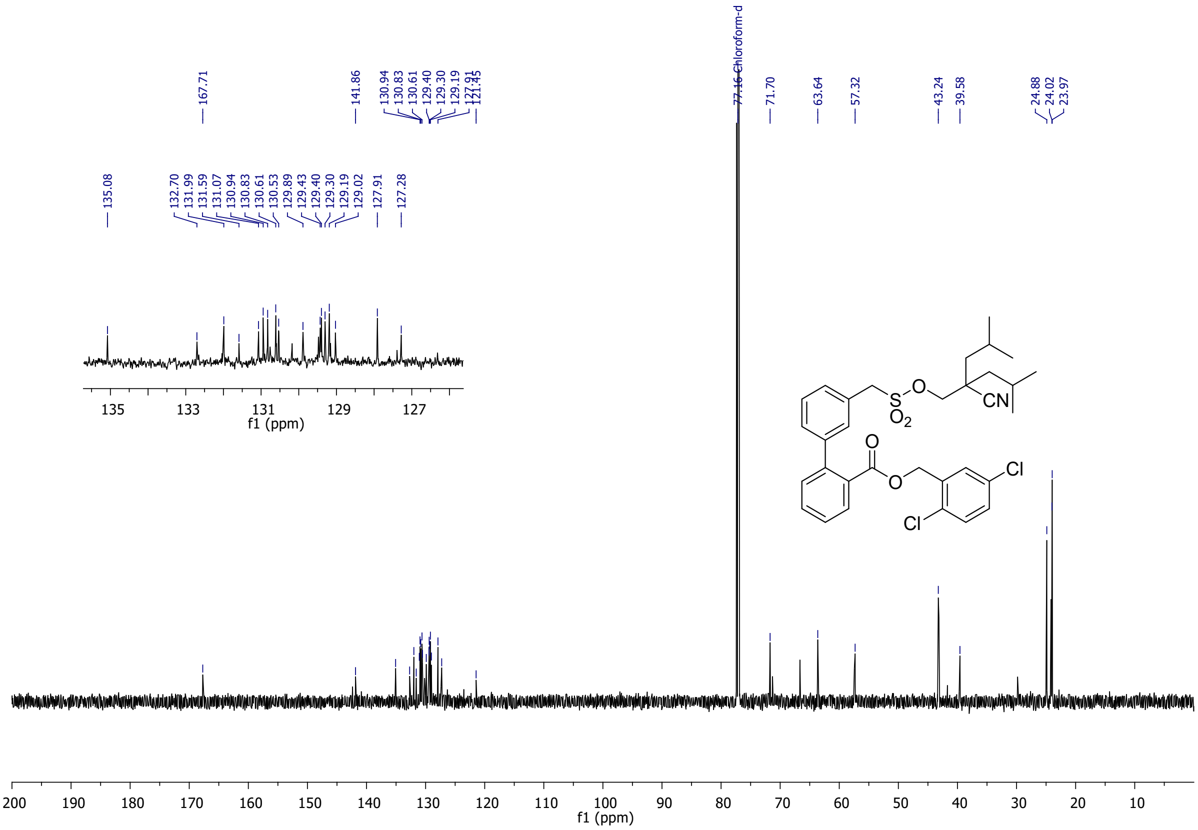
^{1}H NMR (600 MHz) spectrum of **3ak** in CDCl$_3$.



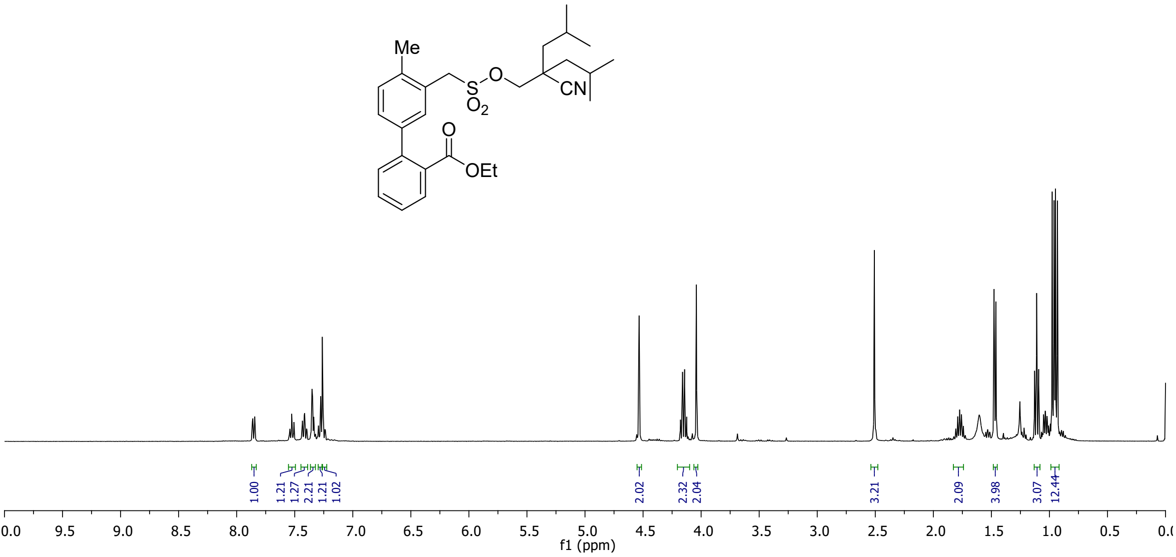
^{3}C{^{1}H} NMR (101 MHz) spectrum of **3ak** in CDCl$_3$.



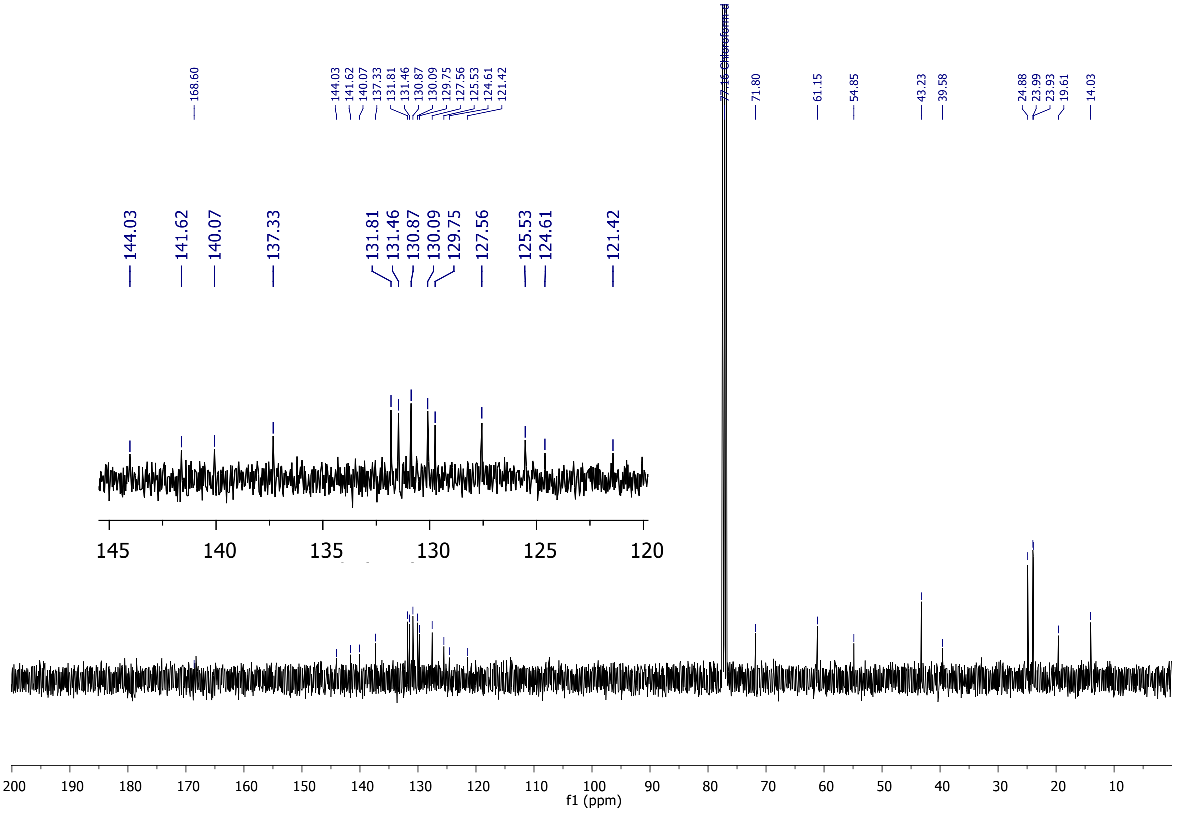
^{1}H NMR (400 MHz) spectrum of **3al** in $CDCl_3$.



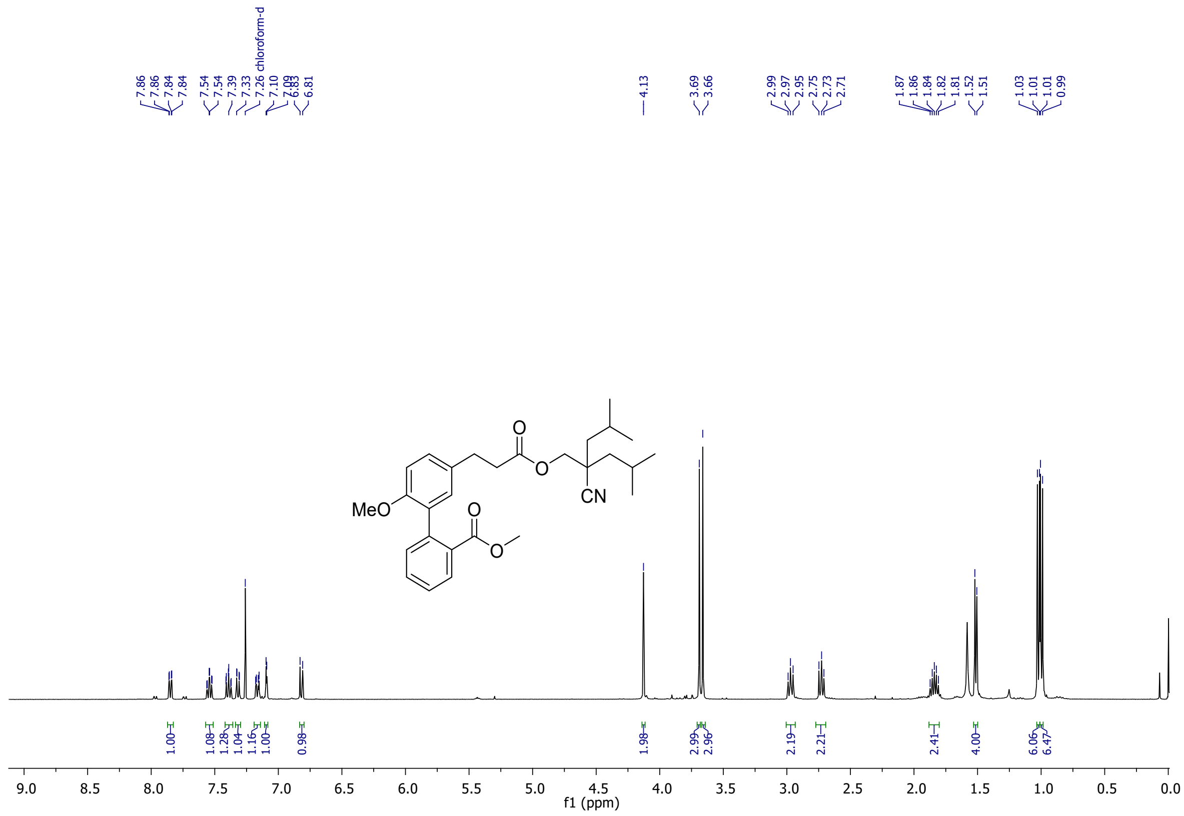
$^{13}C\{^{1}H\}$ NMR (151 MHz) spectrum of **3al** in $CDCl_3$



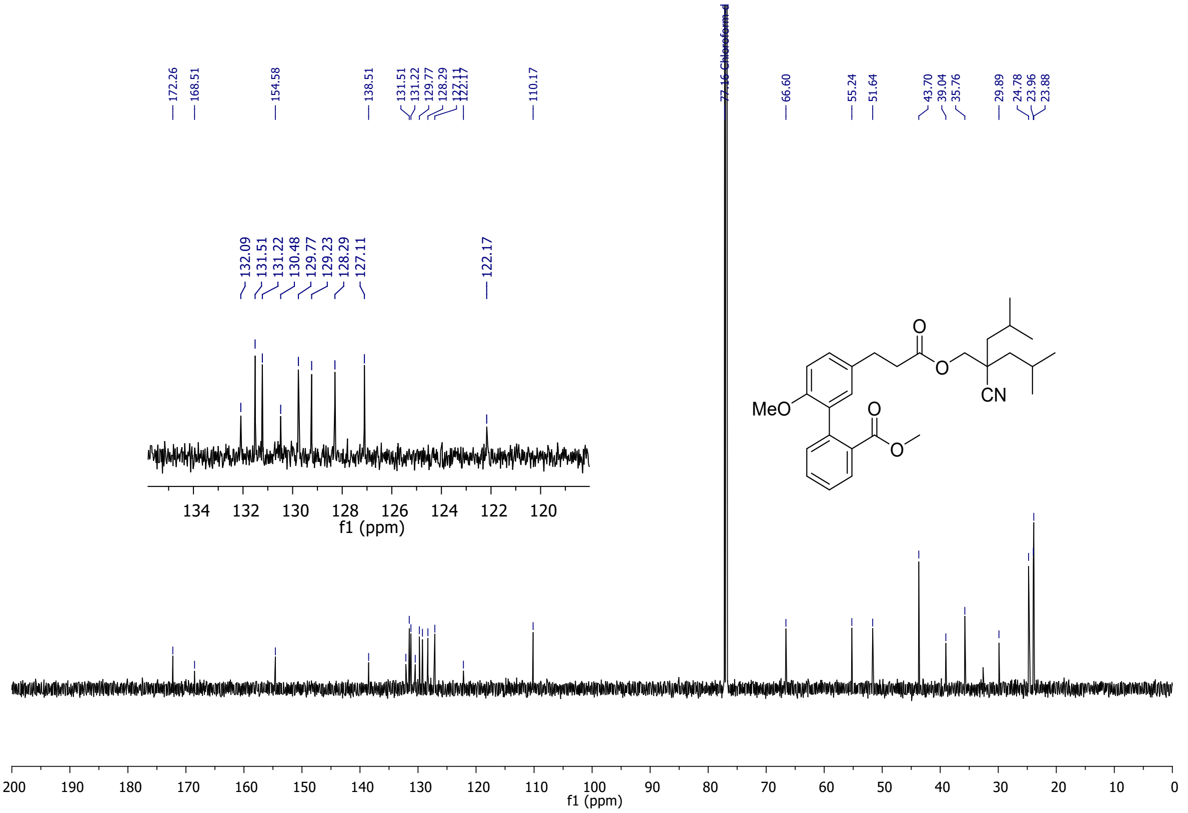
^{1}H NMR (600 MHz) spectrum of **3bb** in CDCl$_3$.



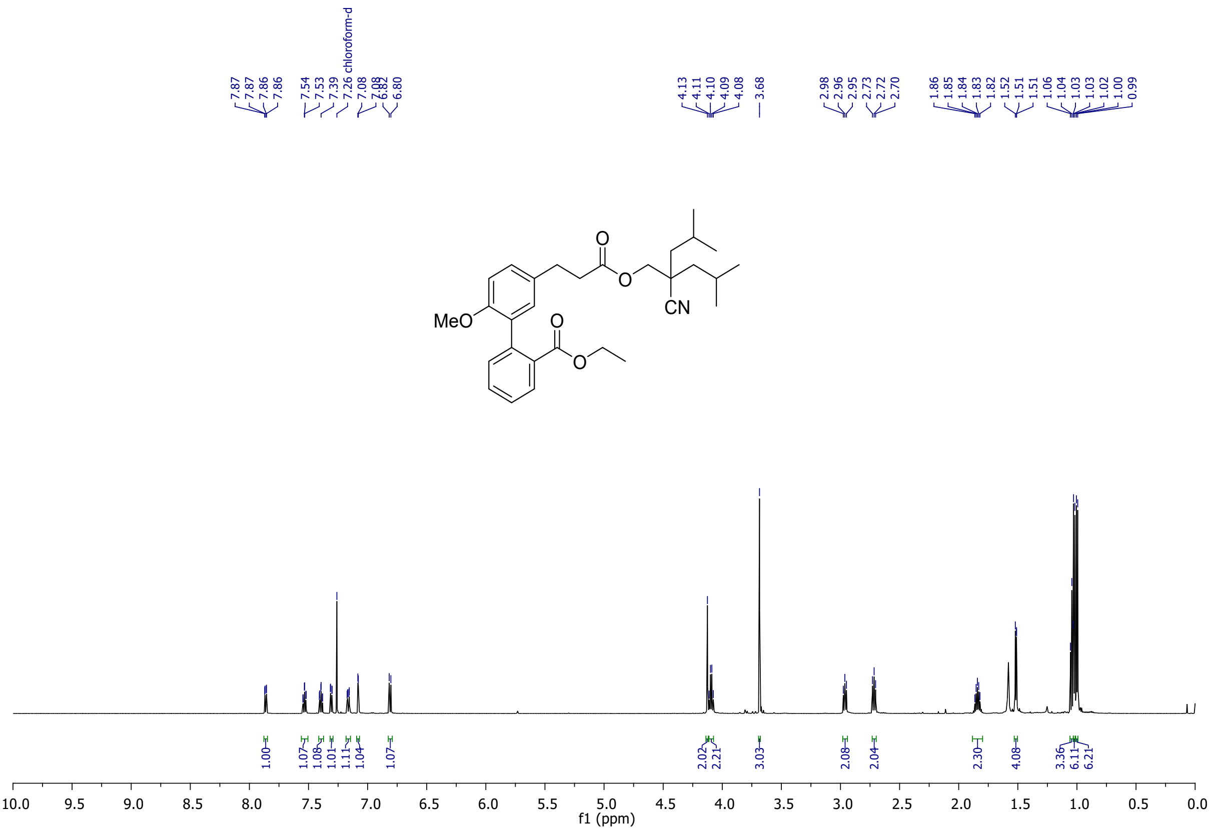
^{13}C{^{1}H} NMR (151 MHz) spectrum of **3bb** in CDCl$_3$



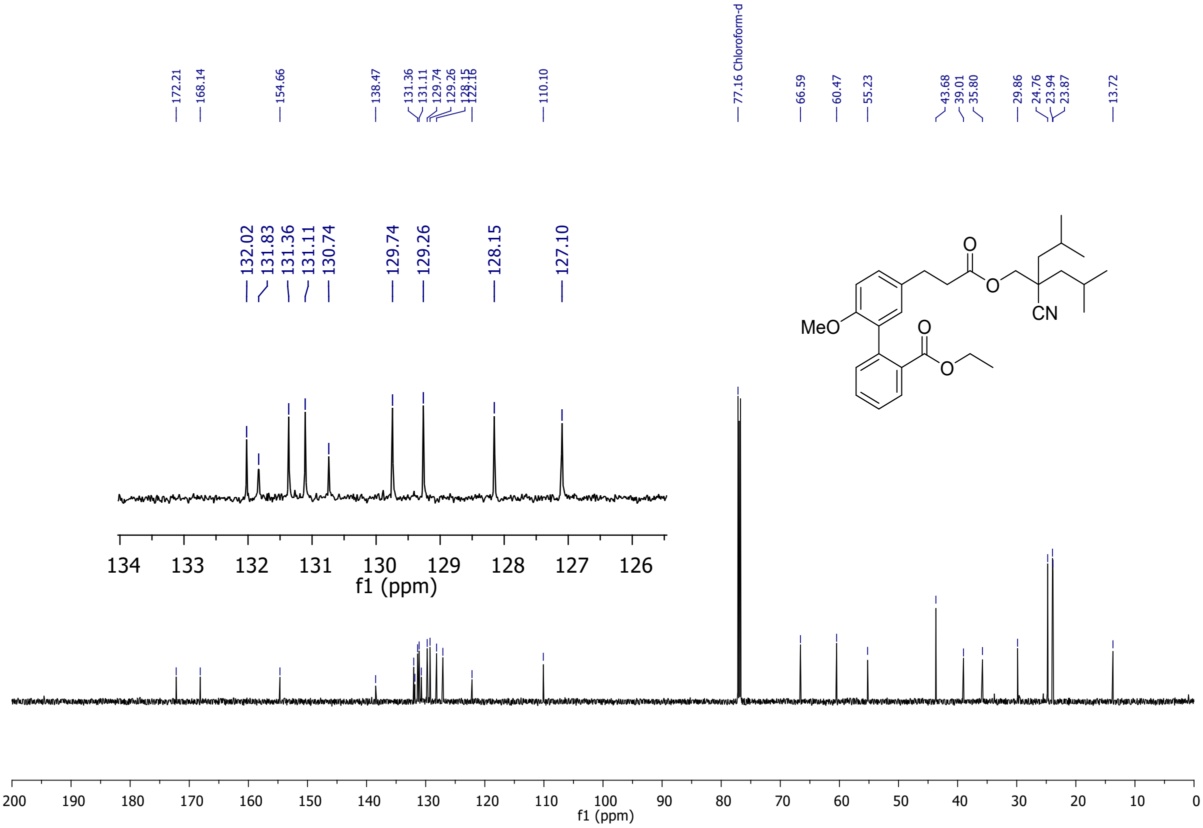
^{1}H NMR (600 MHz) spectrum of **6ba** in CDCl$_3$.



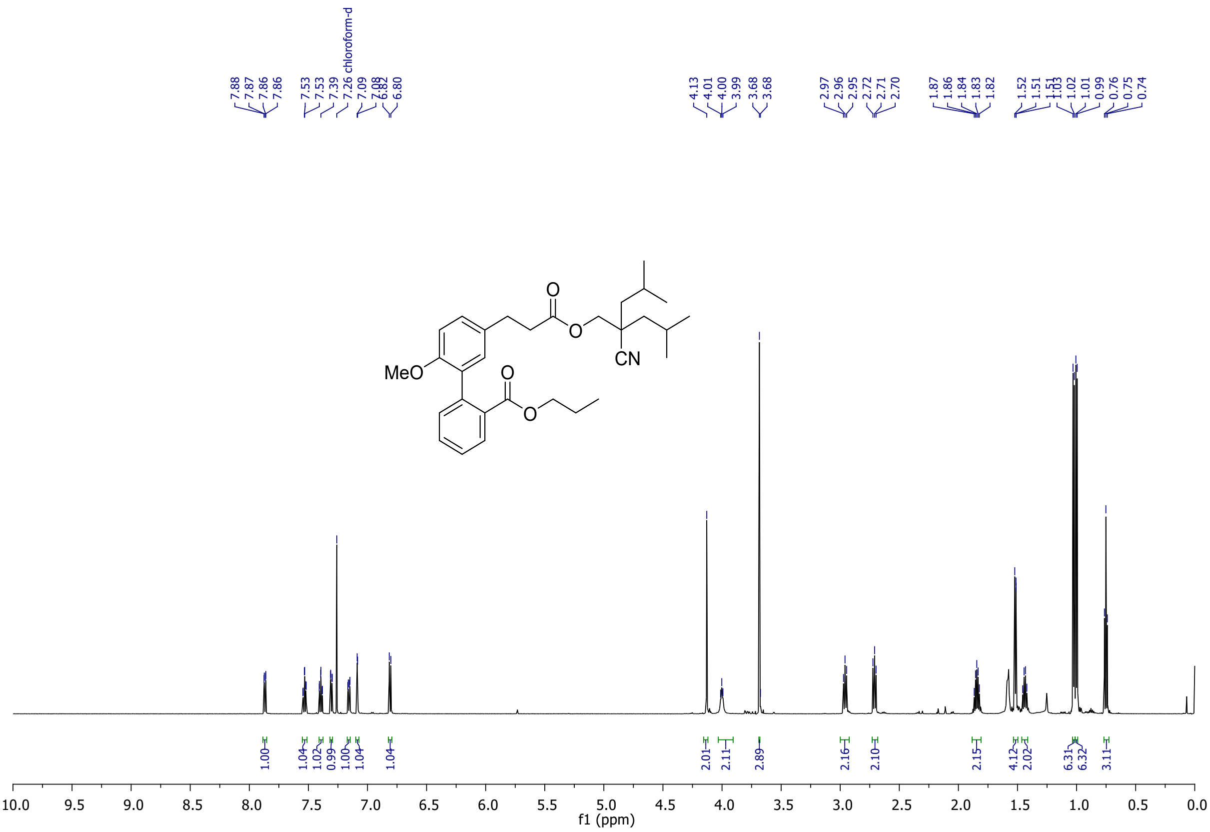
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6ba** in CDCl$_3$.



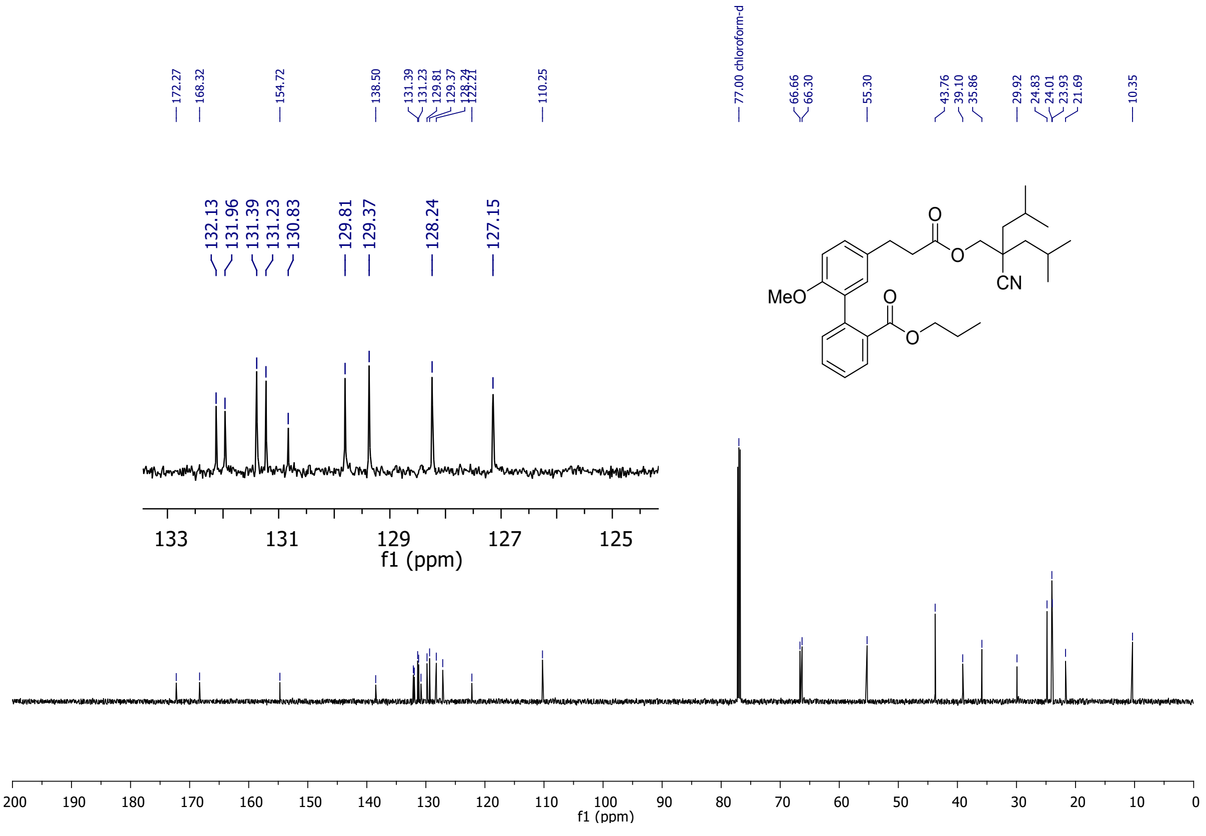
^{1}H NMR (600 MHz) spectrum of **6bb** in CDCl$_3$.



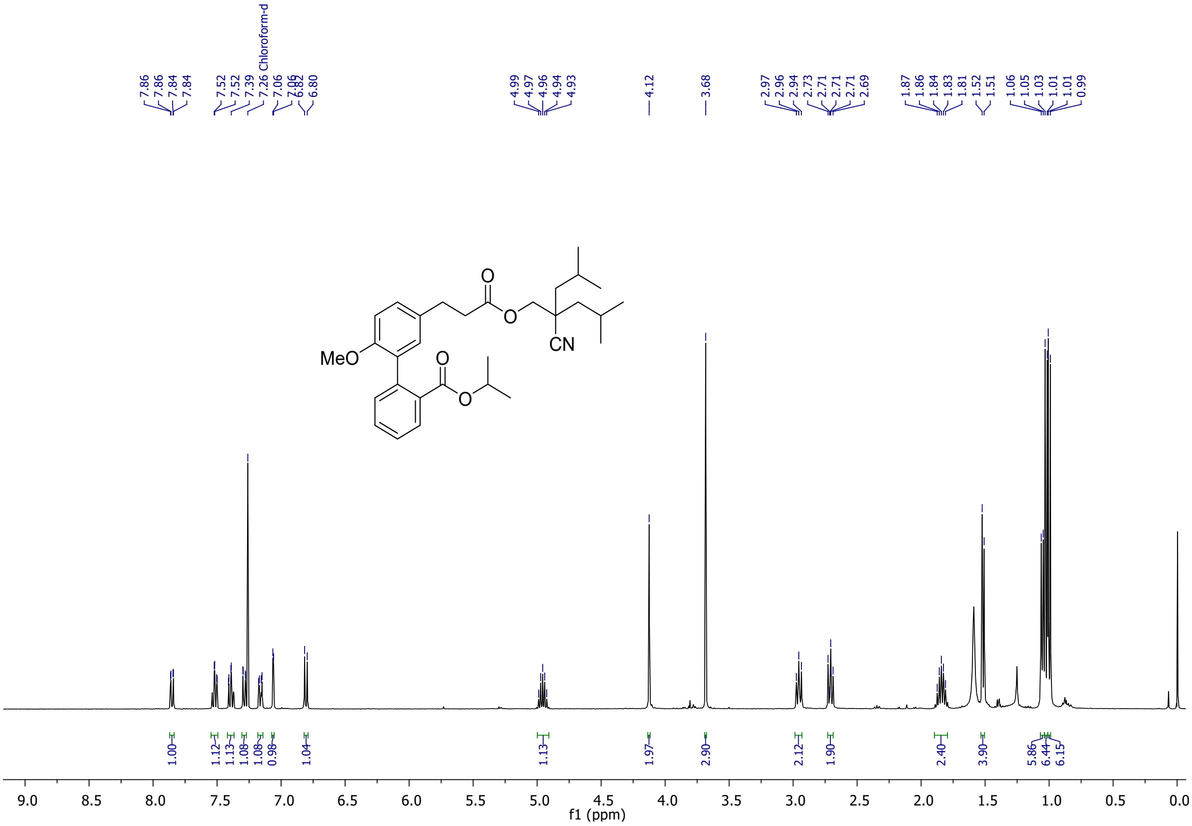
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6bb** in CDCl$_3$.



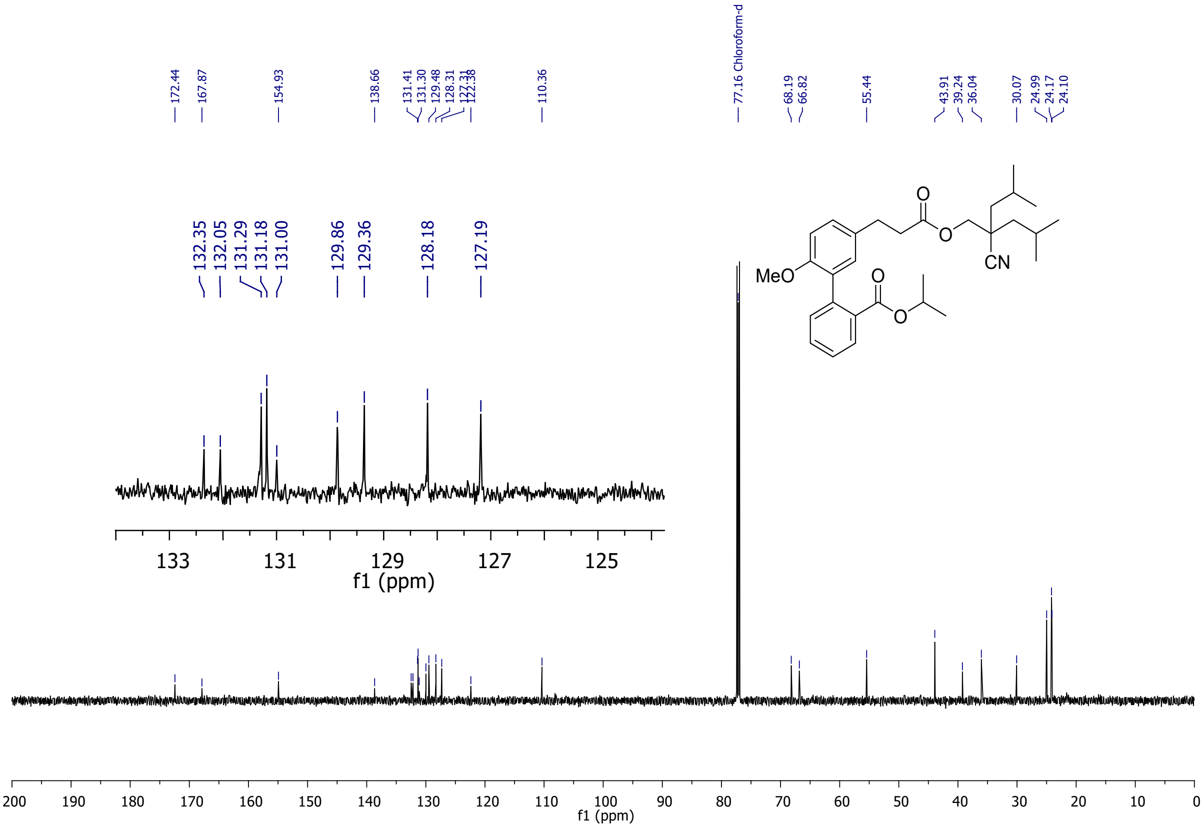
^{1}H NMR (400 MHz) spectrum of **6bc** in CDCl$_3$.



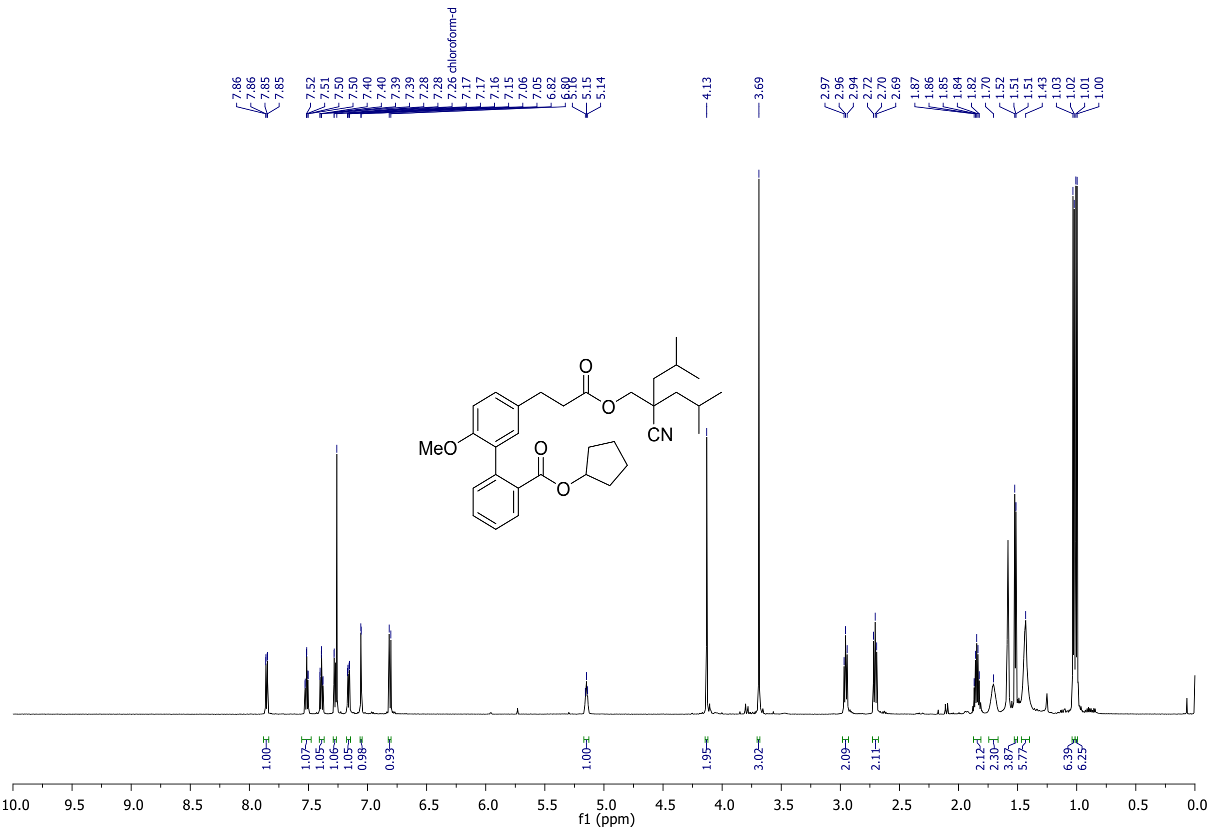
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6bc** in CDCl$_3$.



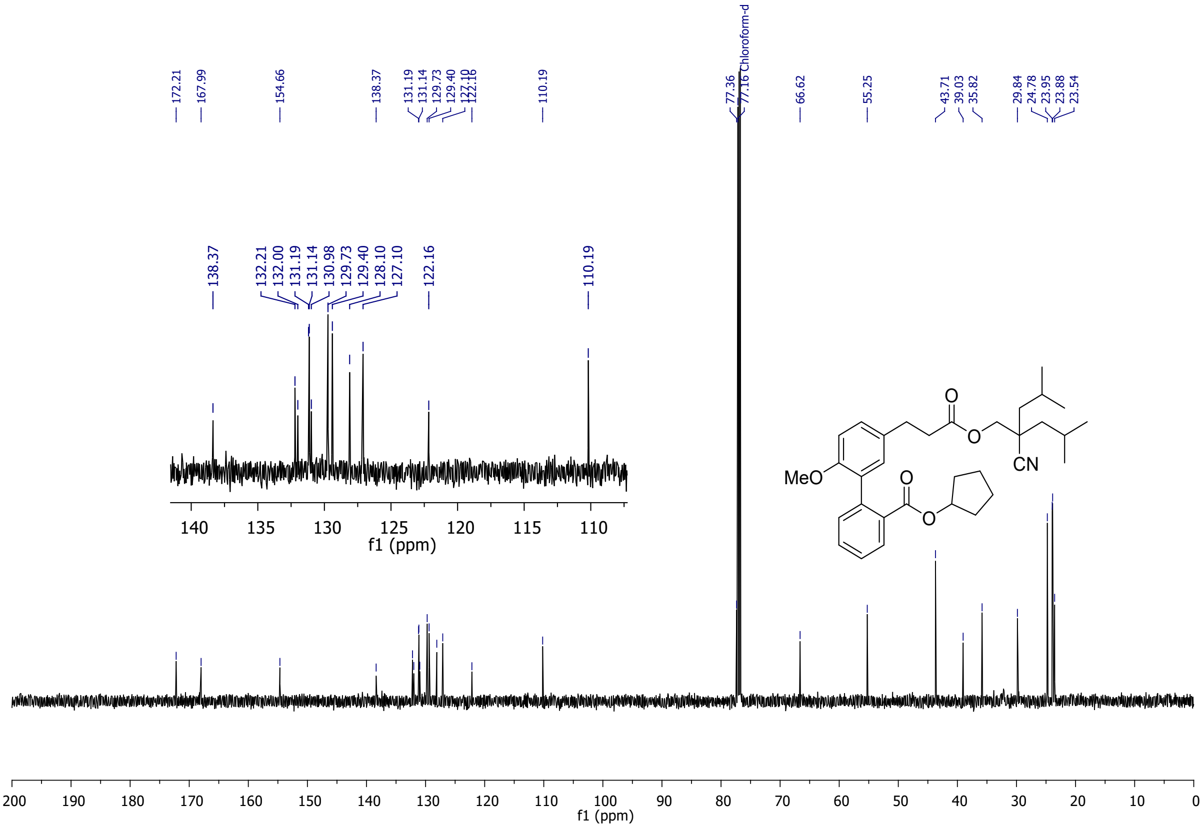
^{1}H NMR (400 MHz) spectrum of **6be** in CDCl$_3$.



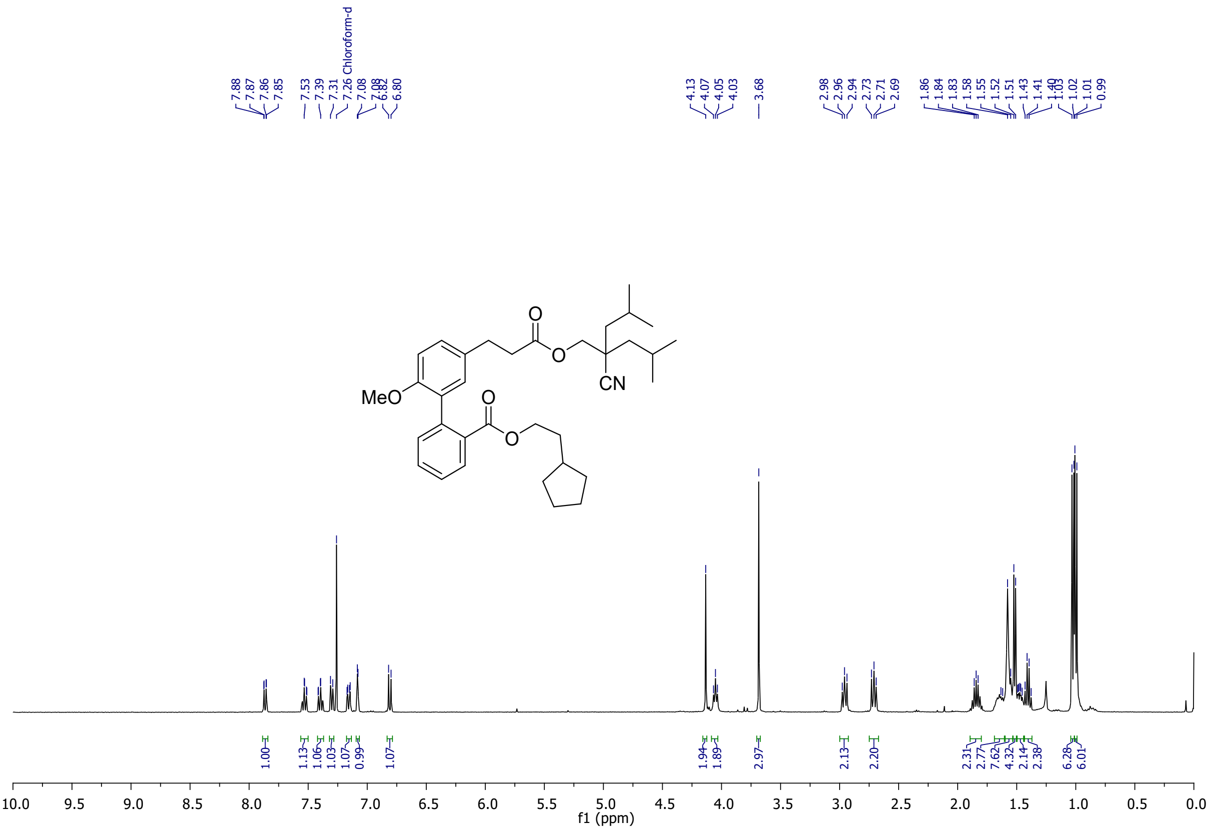
^{13}C{^{1}H} NMR (101 MHz) spectrum of **6be** in CDCl$_3$.



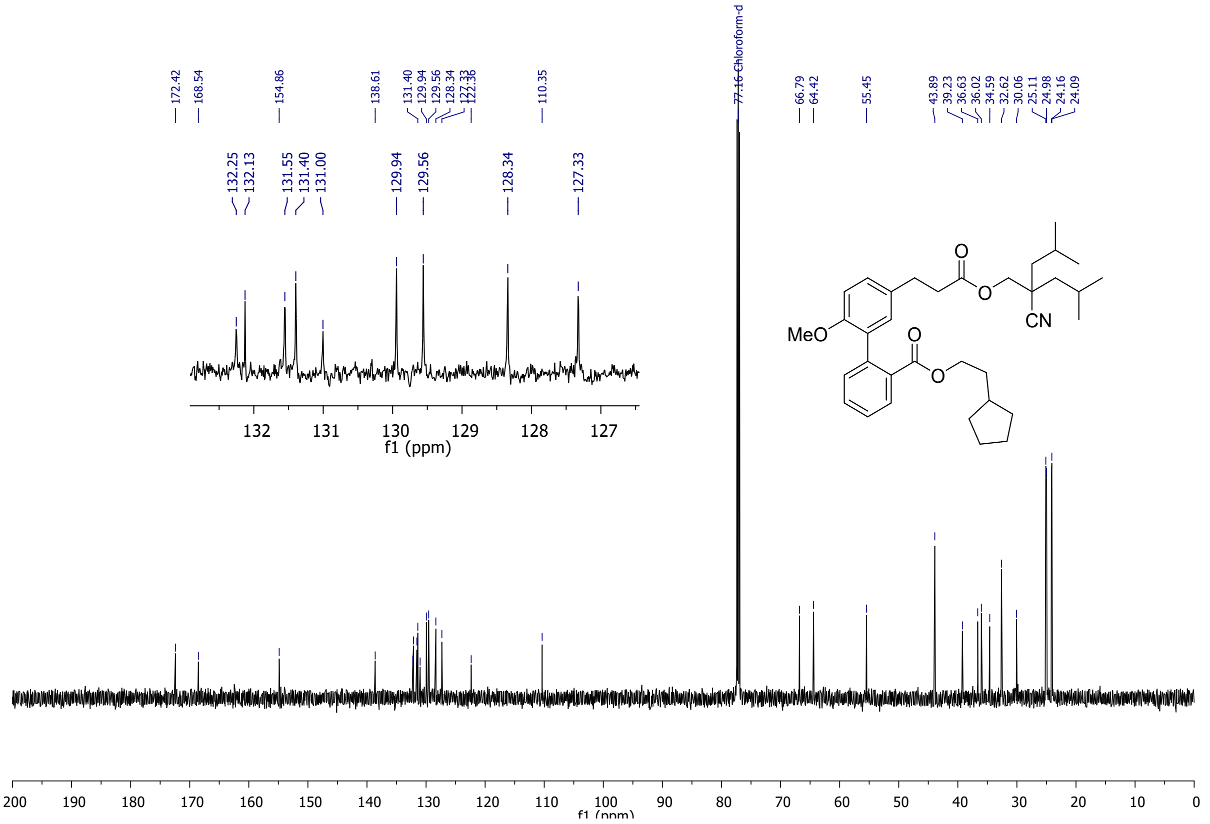
^{1}H NMR (600 MHz) spectrum of **6bf** in CDCl$_3$.



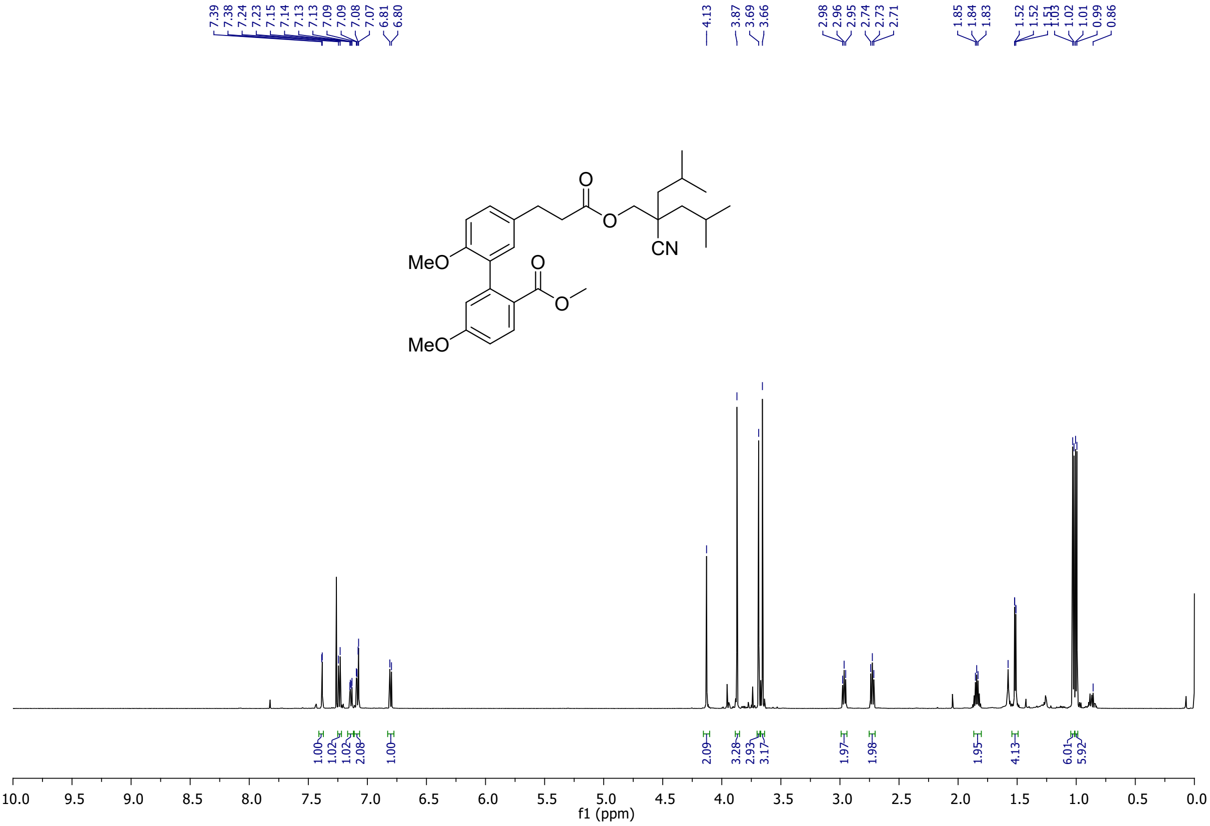
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6bf** in CDCl$_3$.



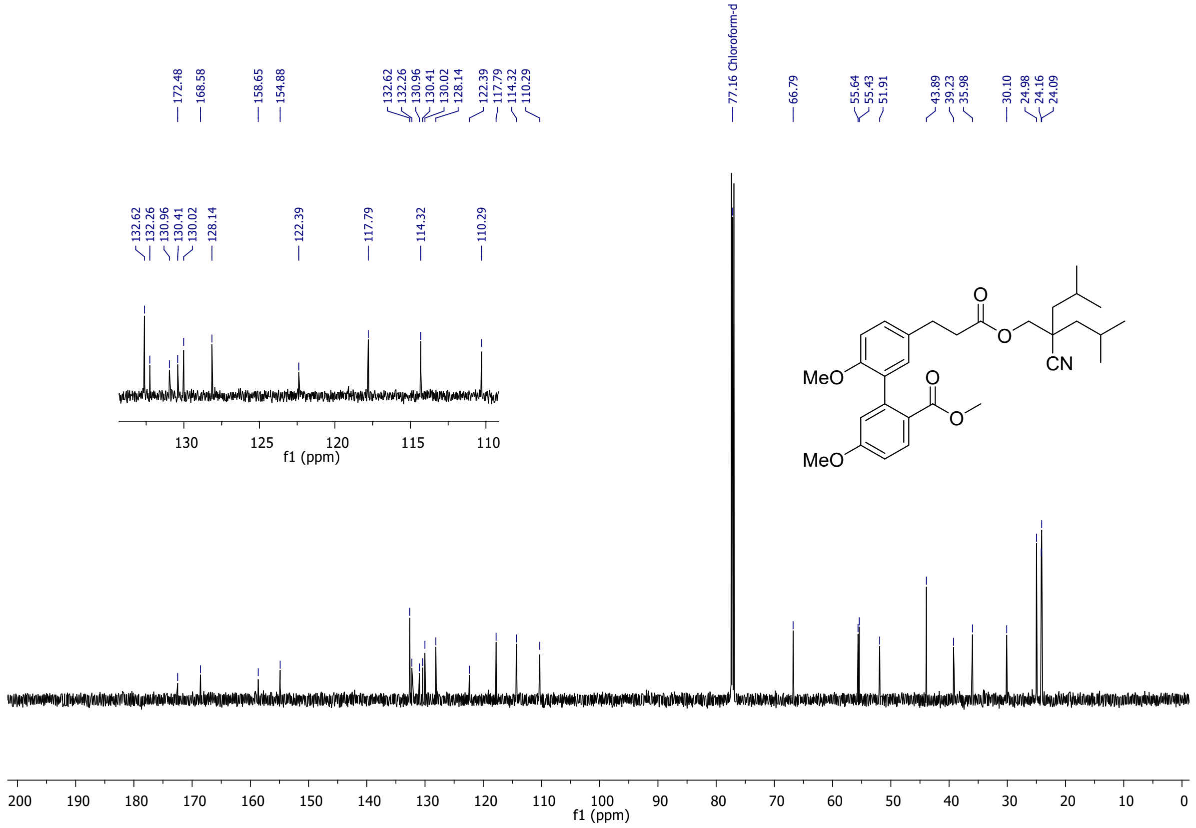
^{1}H NMR (400 MHz) spectrum of **6bg** in $CDCl_3$.



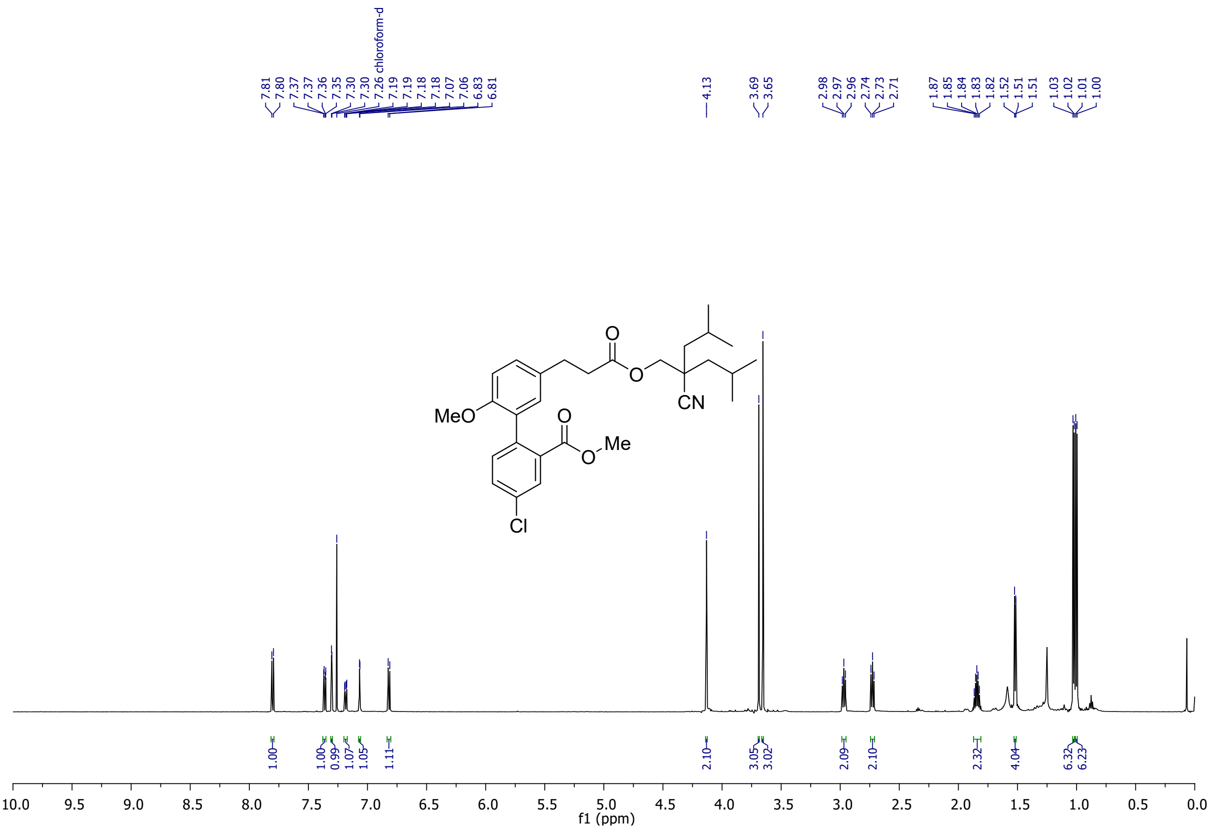
$^{13}C\{^{1}H\}$ NMR (151 MHz) spectrum of **6bg** in $CDCl_3$.



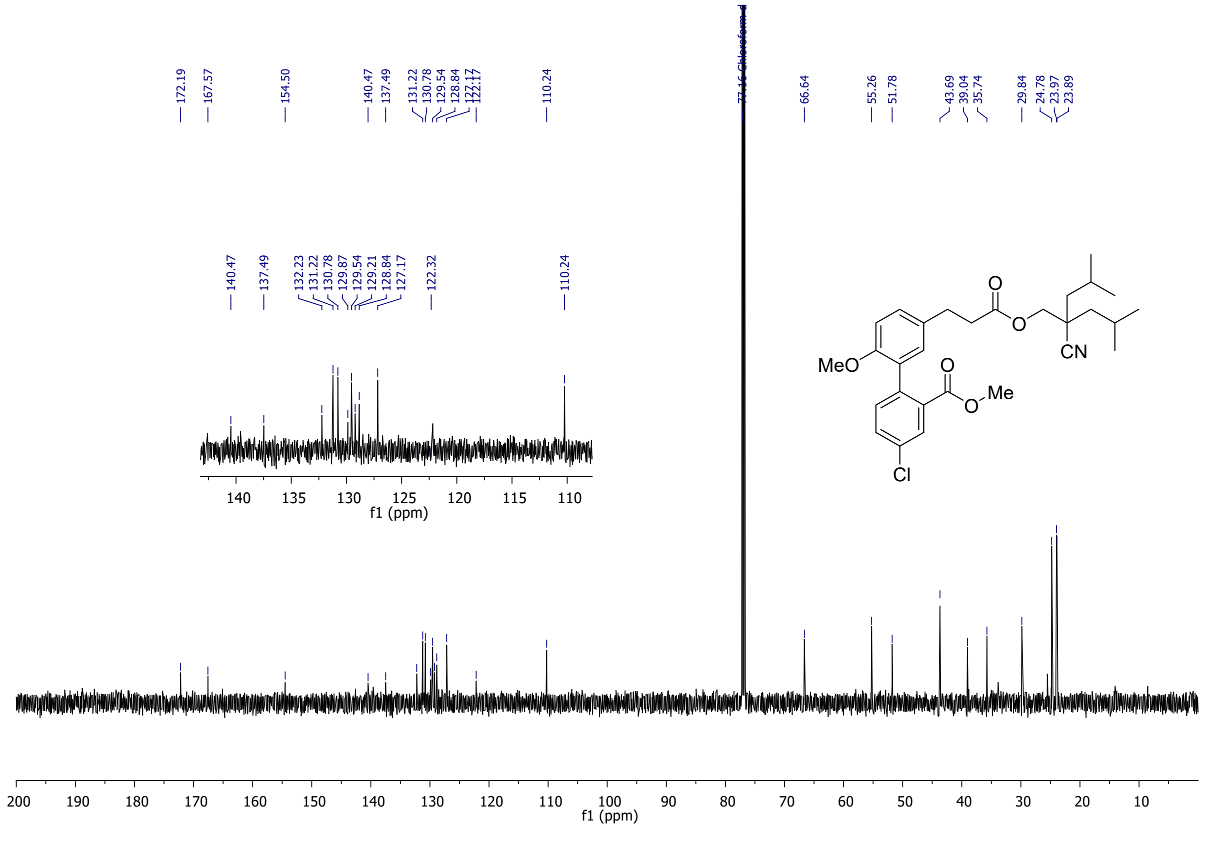
^{1}H NMR (400 MHz) spectrum of **6bh** in $CDCl_3$.



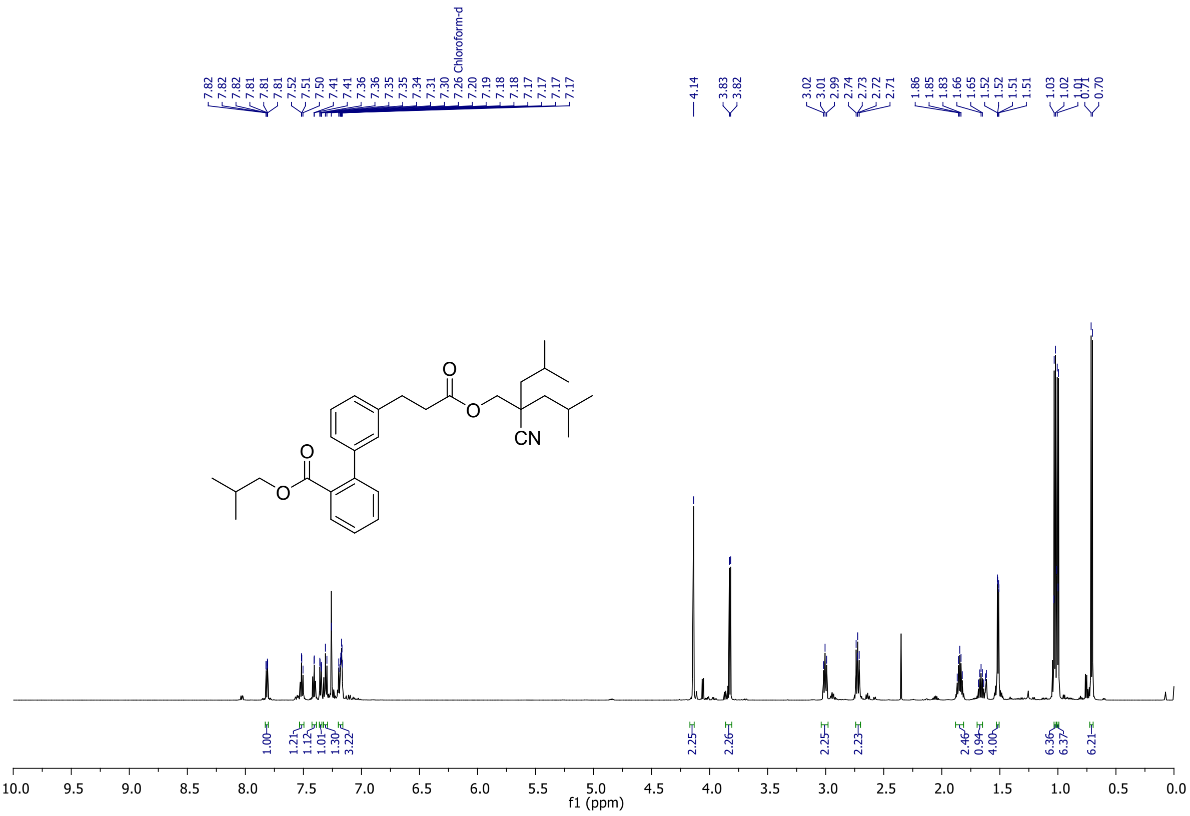
$^{13}C\{^1H\}$ NMR (151 MHz) spectrum of **6bh** in $CDCl_3$.



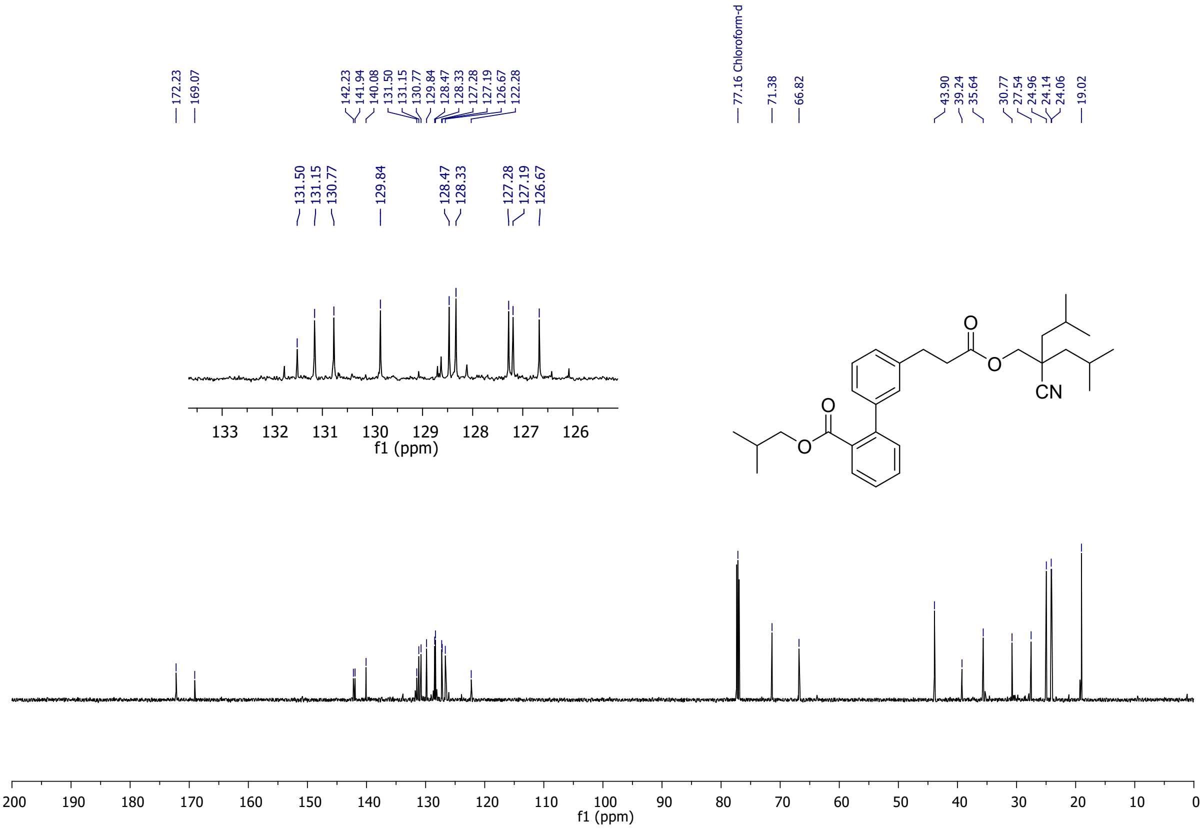
^{1}H NMR (600 MHz) spectrum of **6bi** in CDCl$_3$.



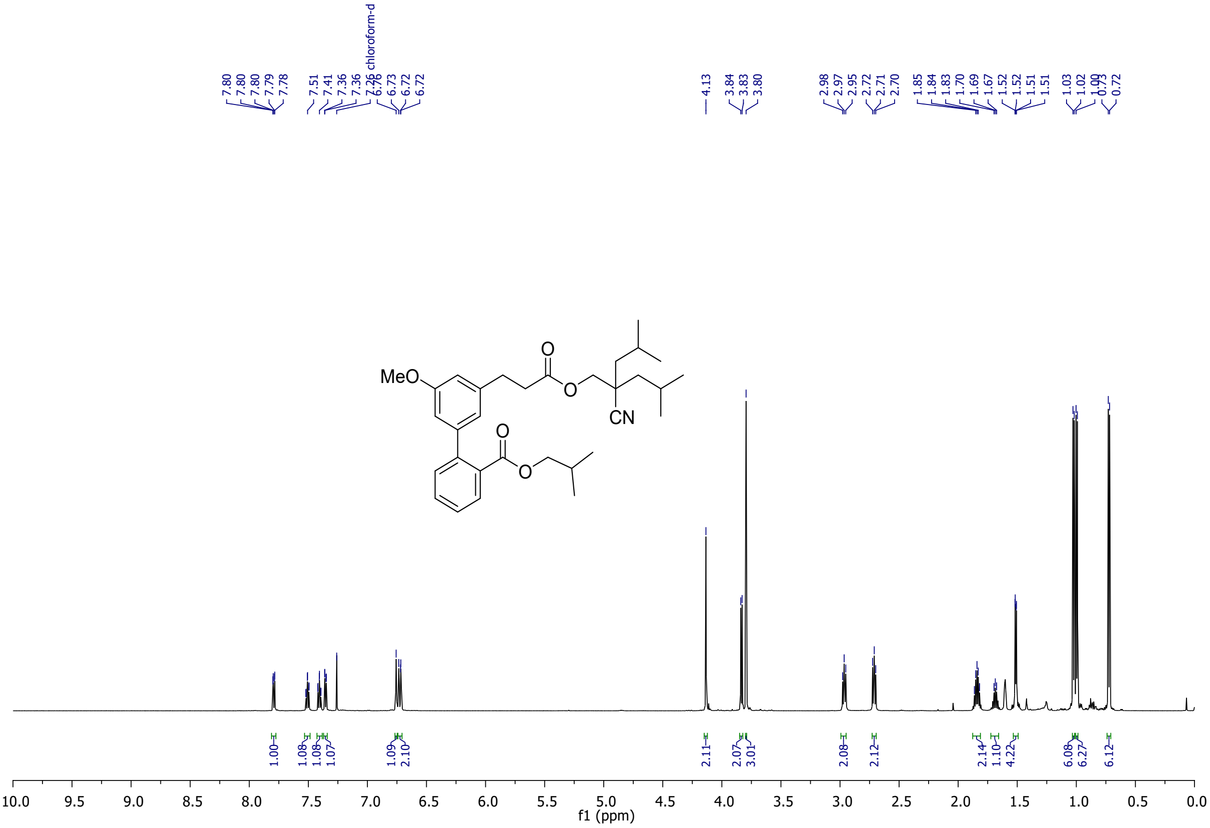
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6bi** in CDCl$_3$



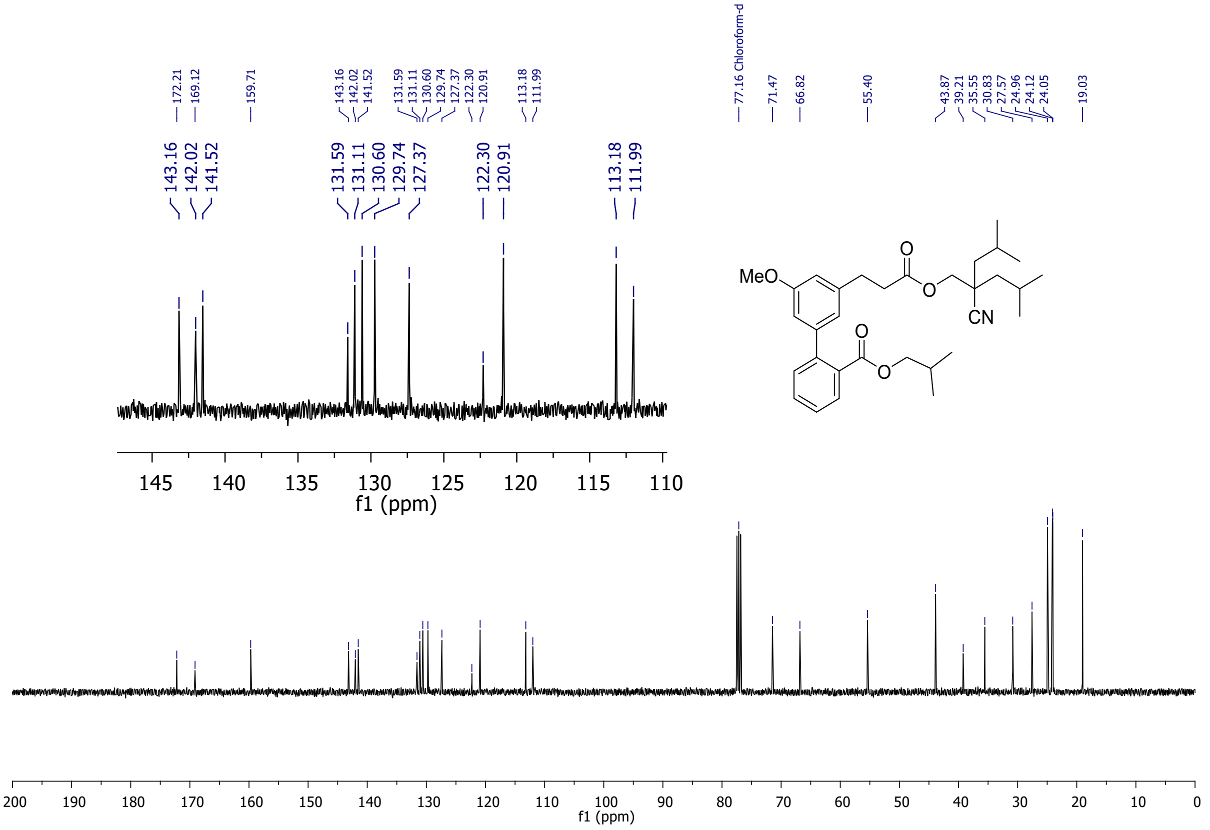
^{1}H NMR (600 MHz) spectrum of **6ad** in CDCl$_3$.



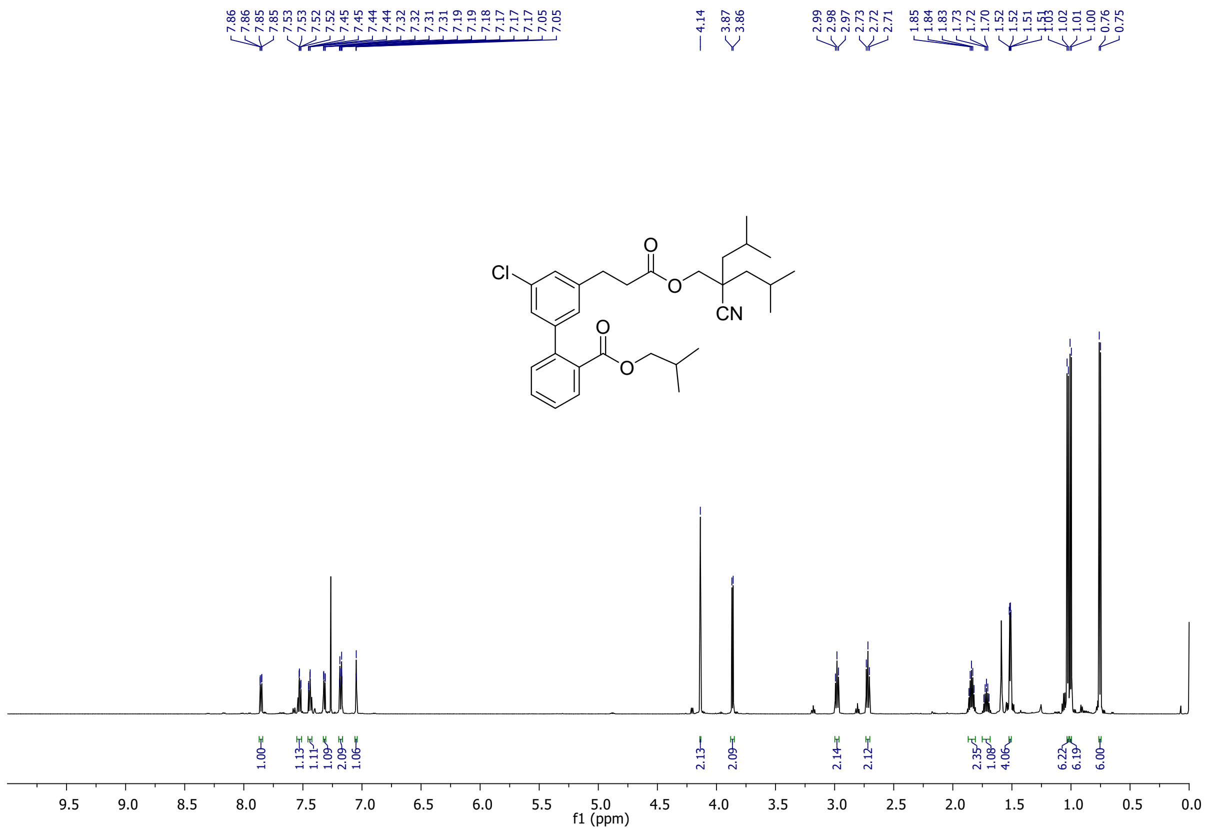
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6ad** in CDCl$_3$.



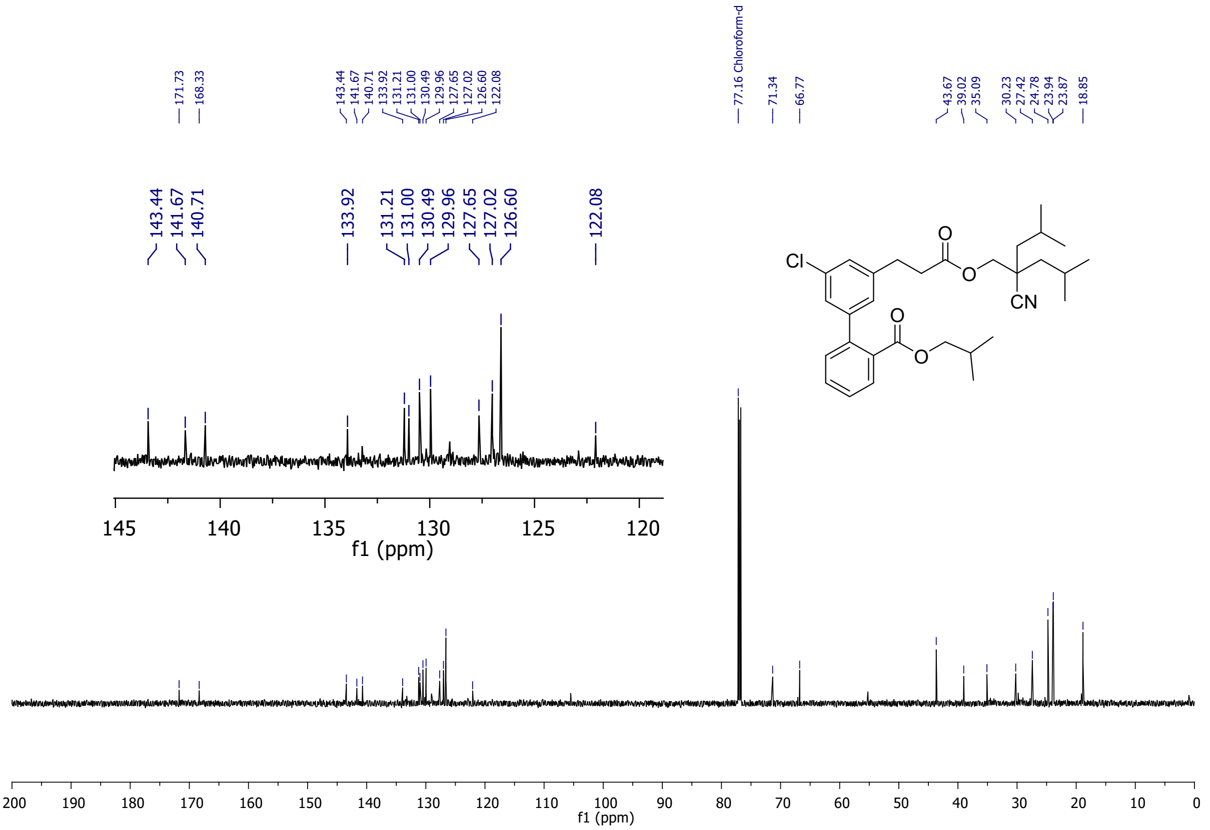
^{1}H NMR (600 MHz) spectrum of **6cd** in $CDCl_3$.



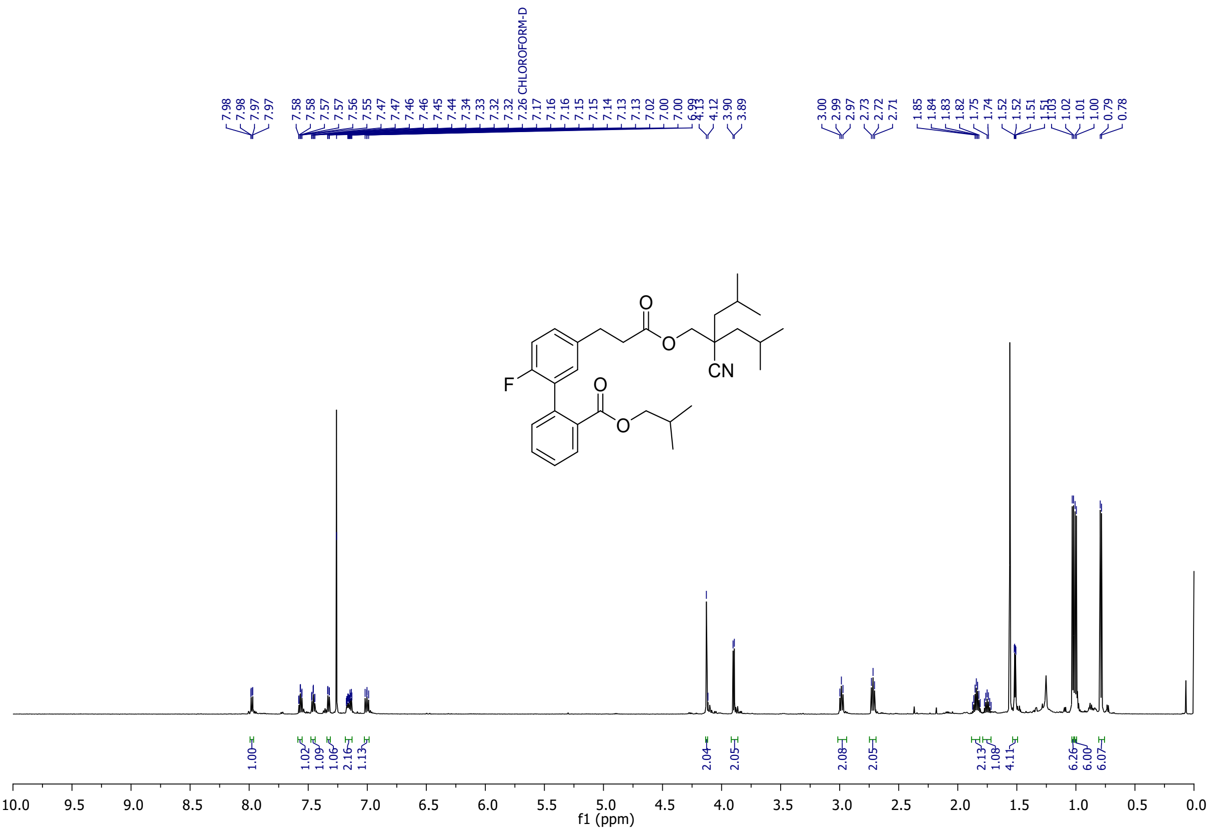
$^{13}C\{^{1}H\}$ NMR (101 MHz) spectrum of **6cd** in $CDCl_3$.



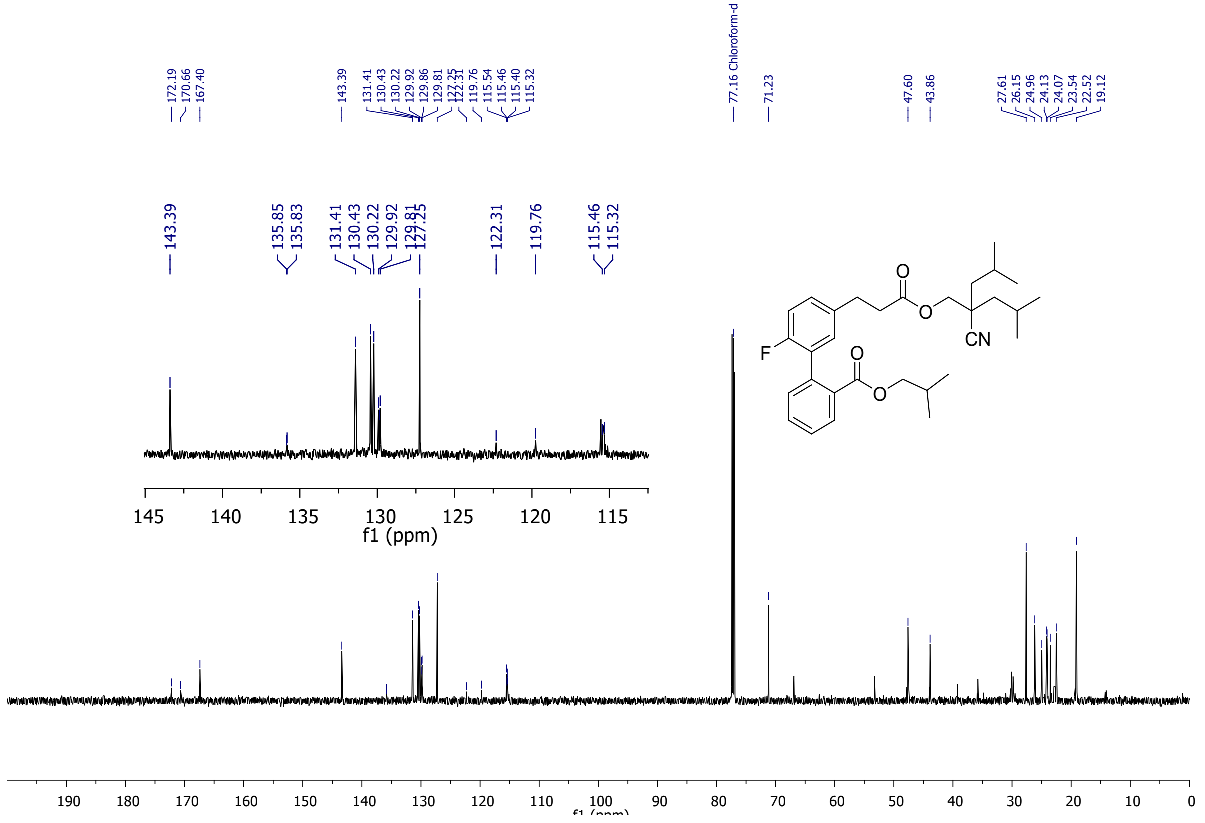
^{1}H NMR (600 MHz) spectrum of **6dd** in $CDCl_3$.



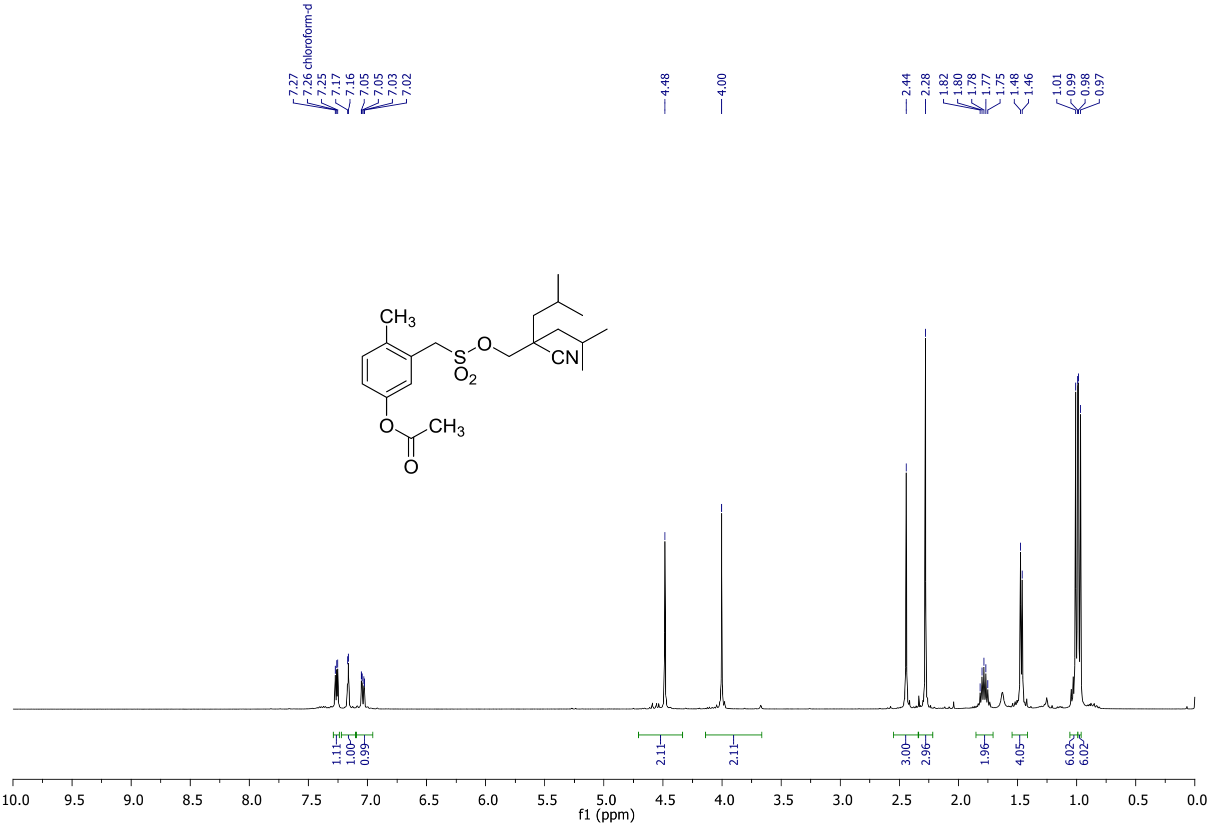
$^{13}C\{^1H\}$ NMR (101 MHz) spectrum of **6dd** in $CDCl_3$.



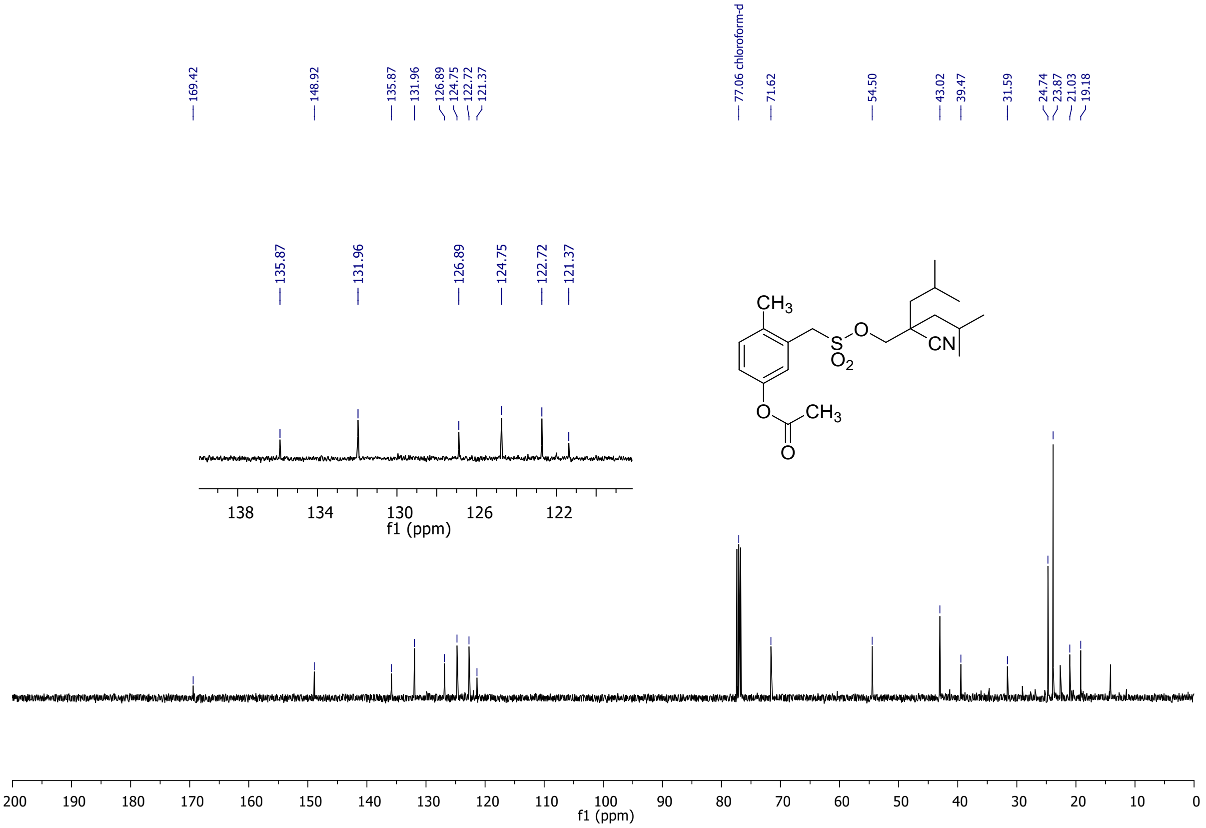
^{1}H NMR (600 MHz) spectrum of **6ed** in CDCl$_3$.



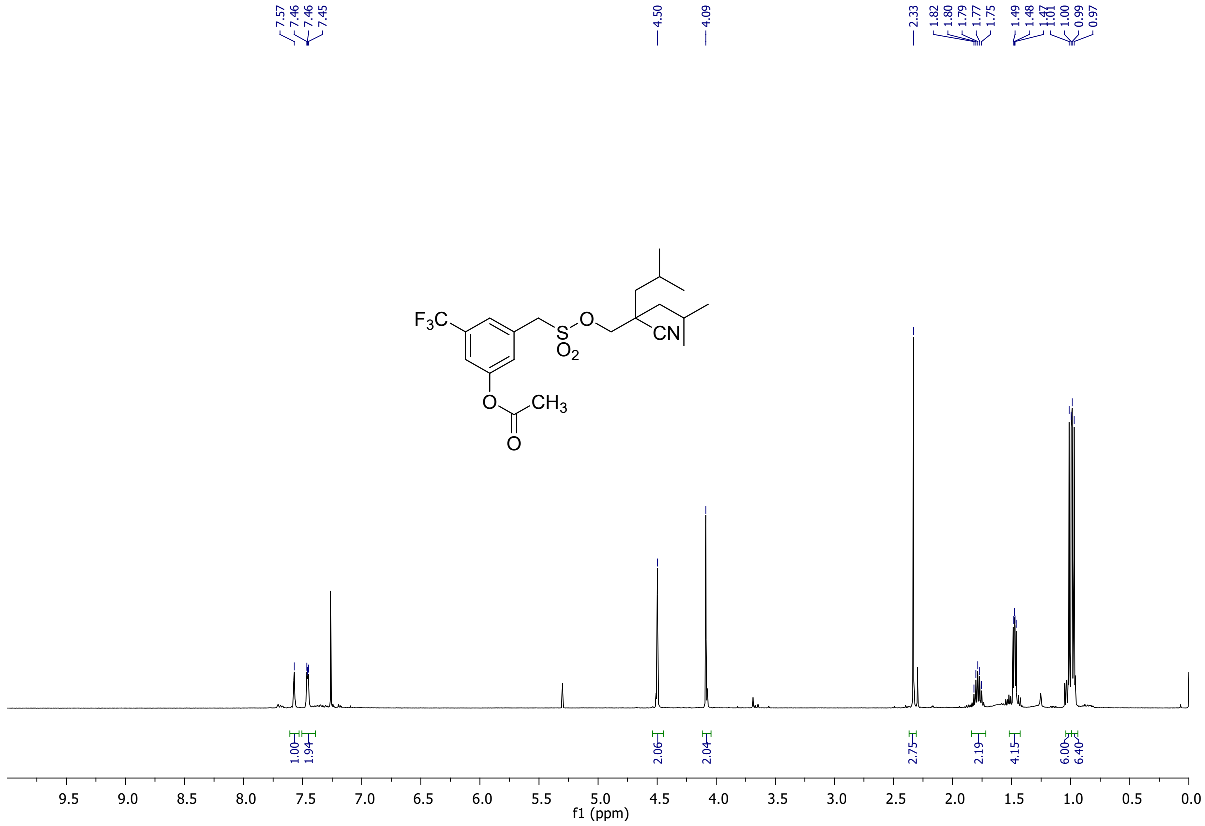
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6ed** in CDCl$_3$.



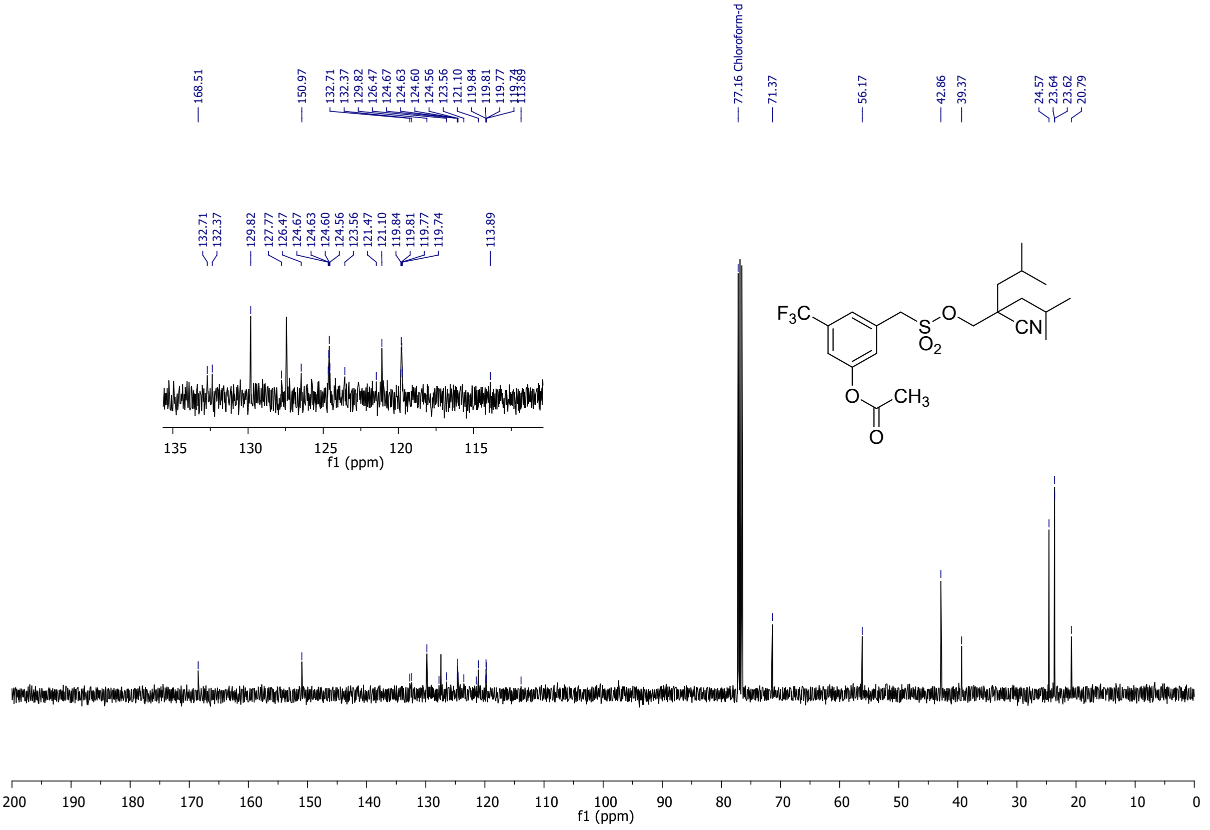
^{1}H NMR (400 MHz) spectrum of **8b** in CDCl$_3$.



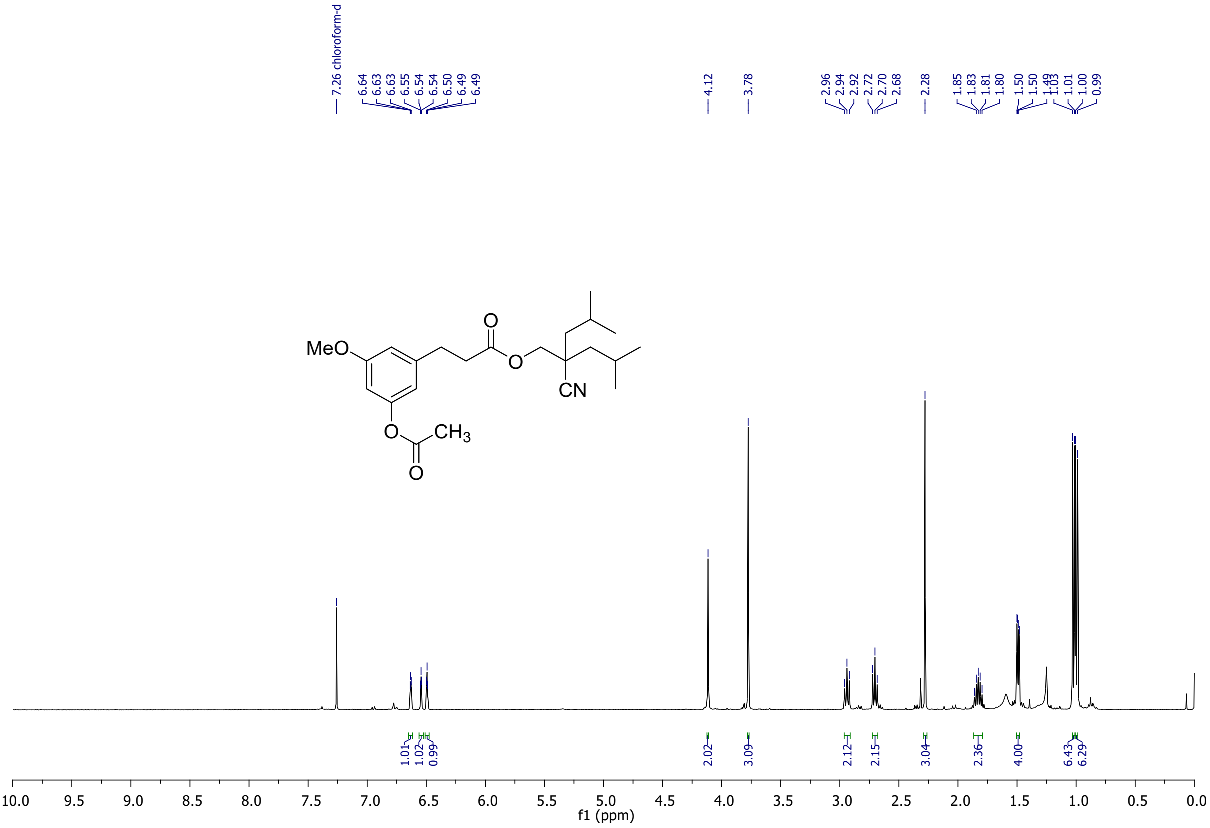
^{13}C{^{1}H} NMR (101 MHz) spectrum of **8b** in CDCl$_3$.



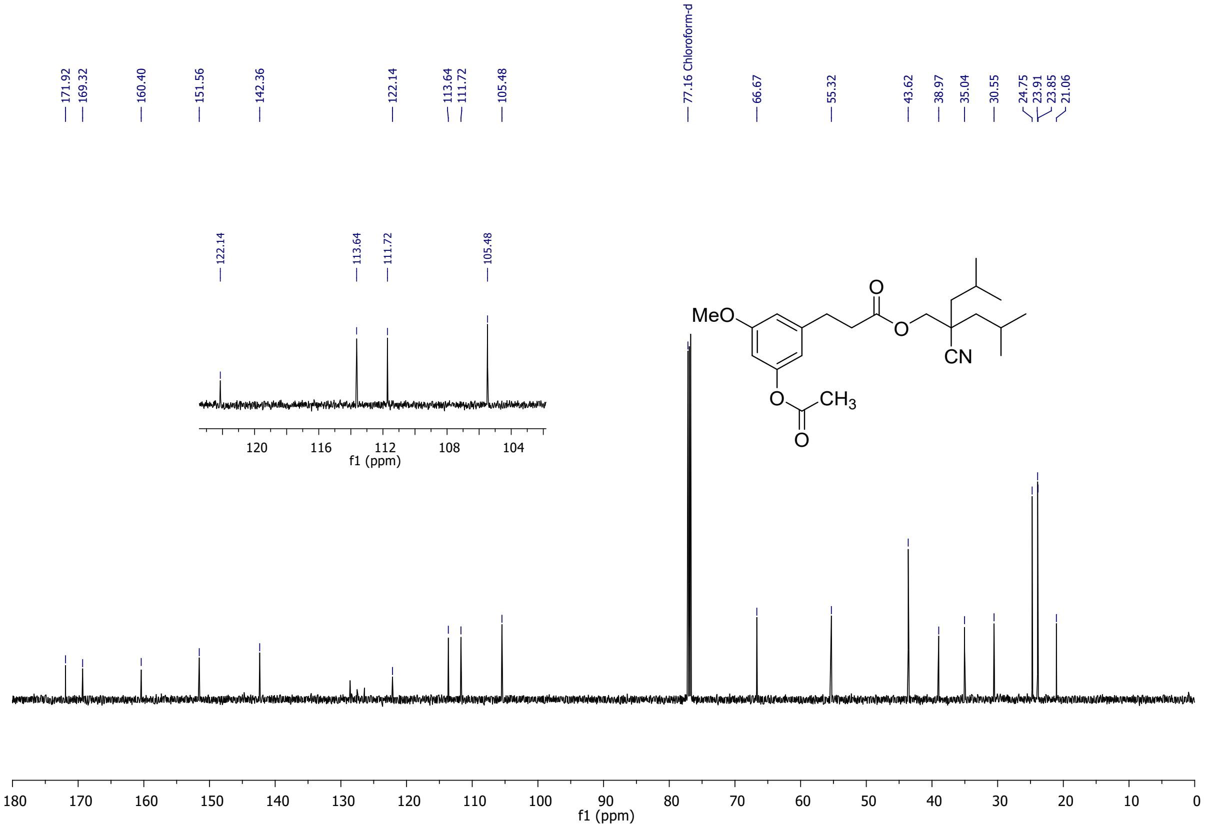
^{1}H NMR (400 MHz) spectrum of **8c** in CDCl$_3$.



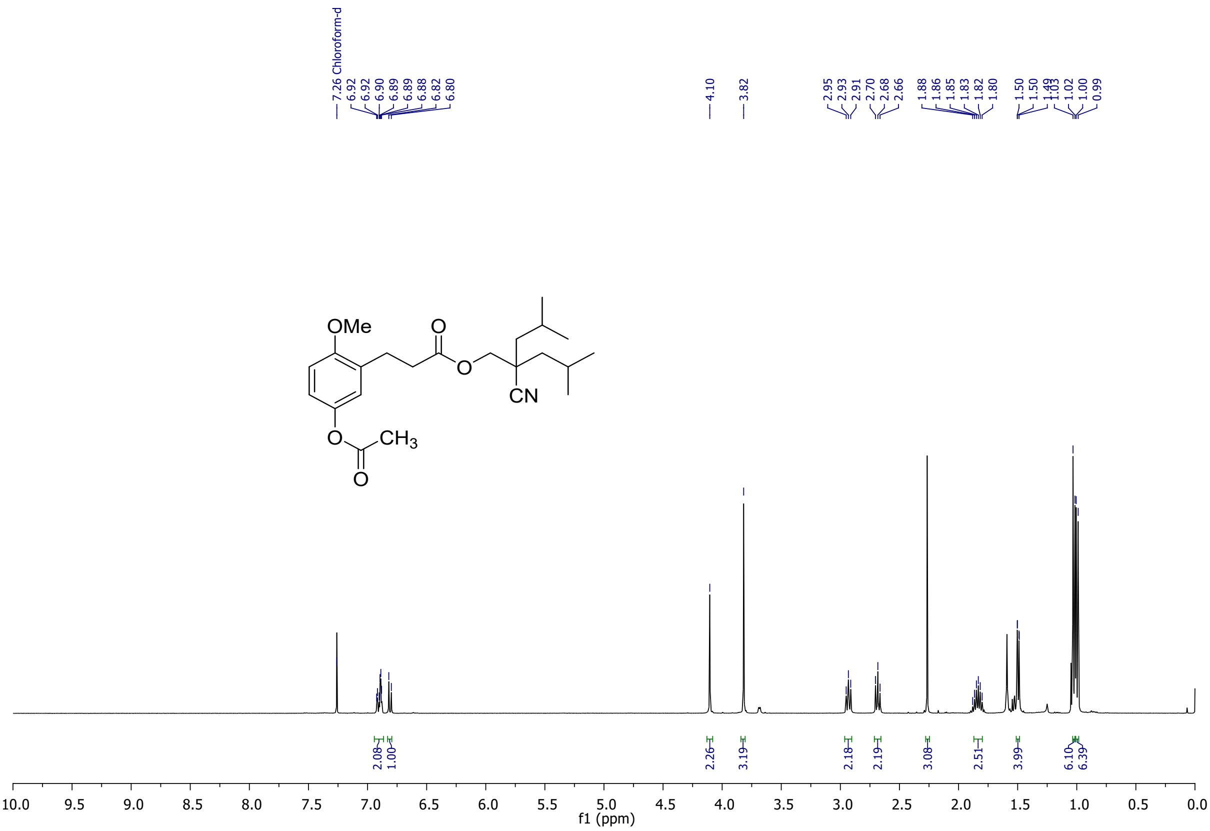
^{13}C{^{1}H} NMR (101 MHz) spectrum of **8c** in CDCl$_3$.



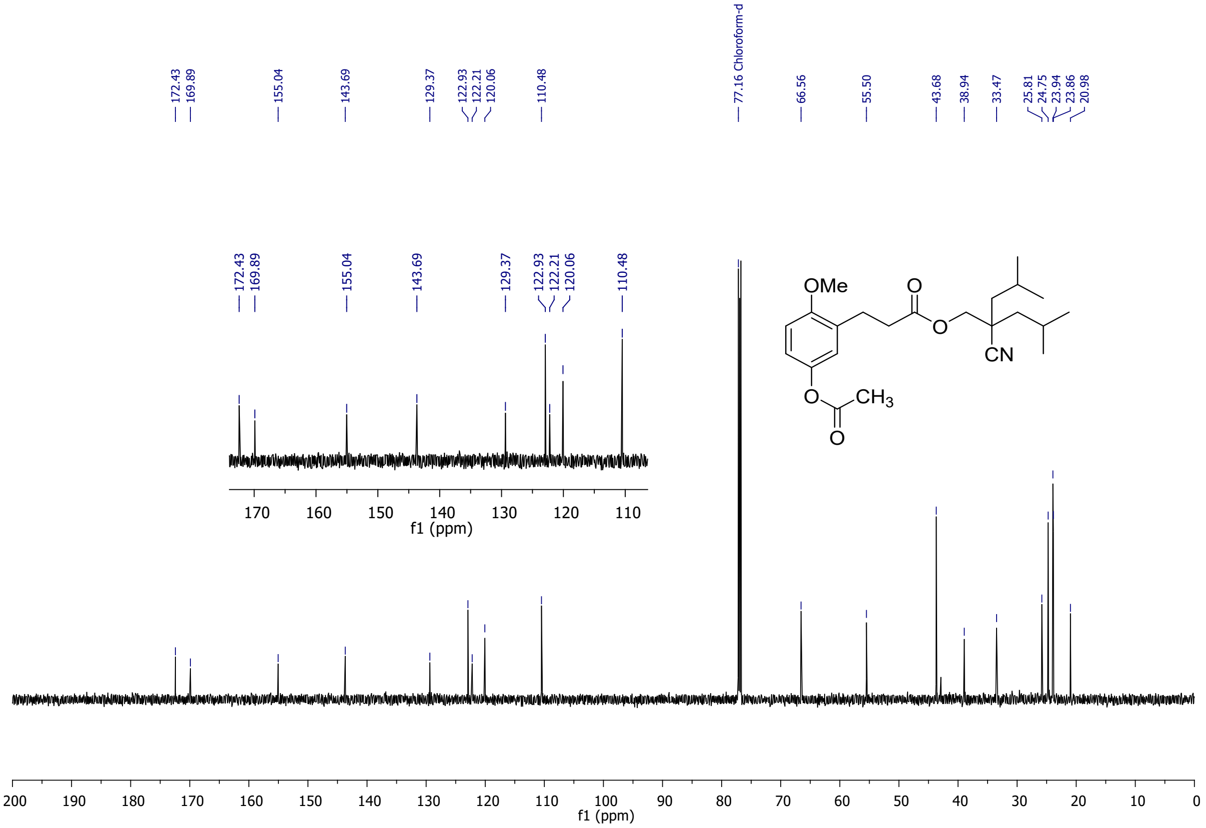
^{1}H NMR (400 MHz) spectrum of **9c** in $CDCl_3$.



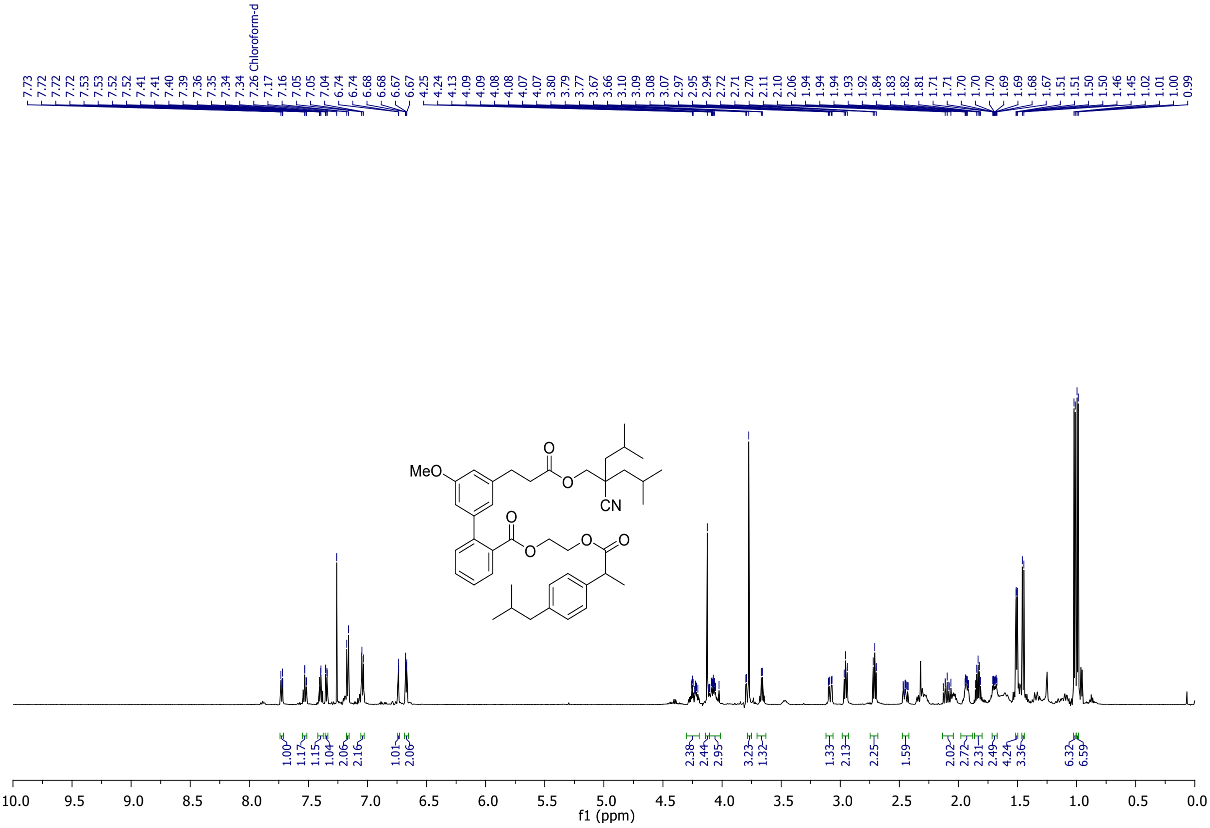
$^{13}C\{^1H\}$ NMR (151 MHz) spectrum of **9c** in $CDCl_3$.



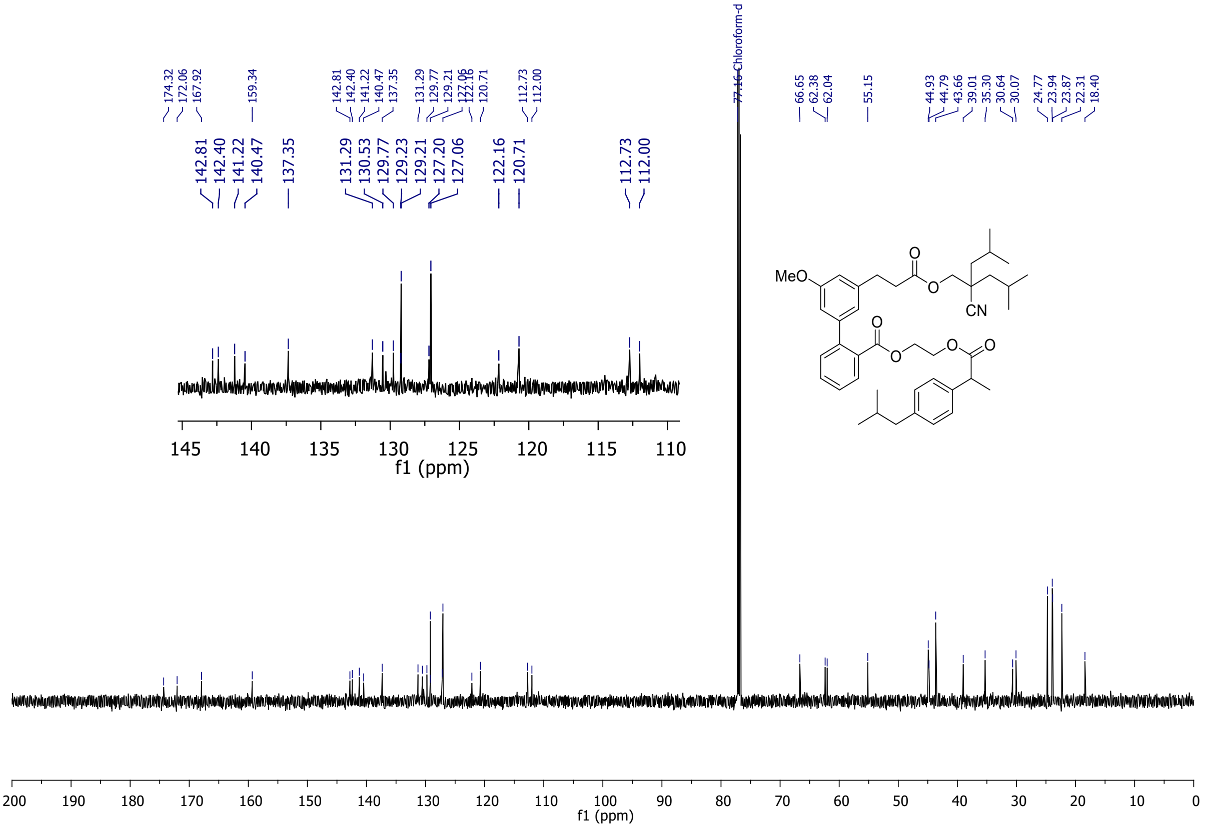
^{1}H NMR (400 MHz) spectrum of **9f** in CDCl$_3$.



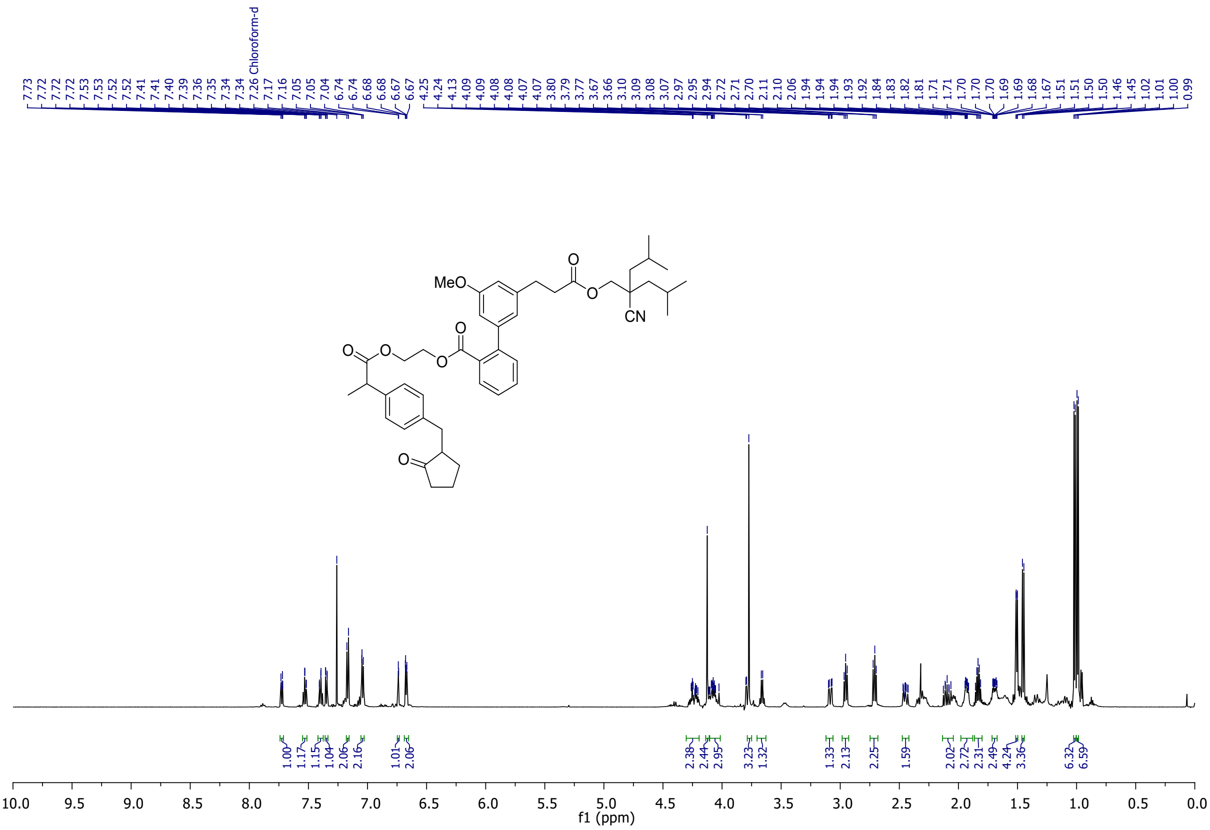
^{13}C{^{1}H} NMR (151 MHz) spectrum of **9f** in CDCl$_3$.



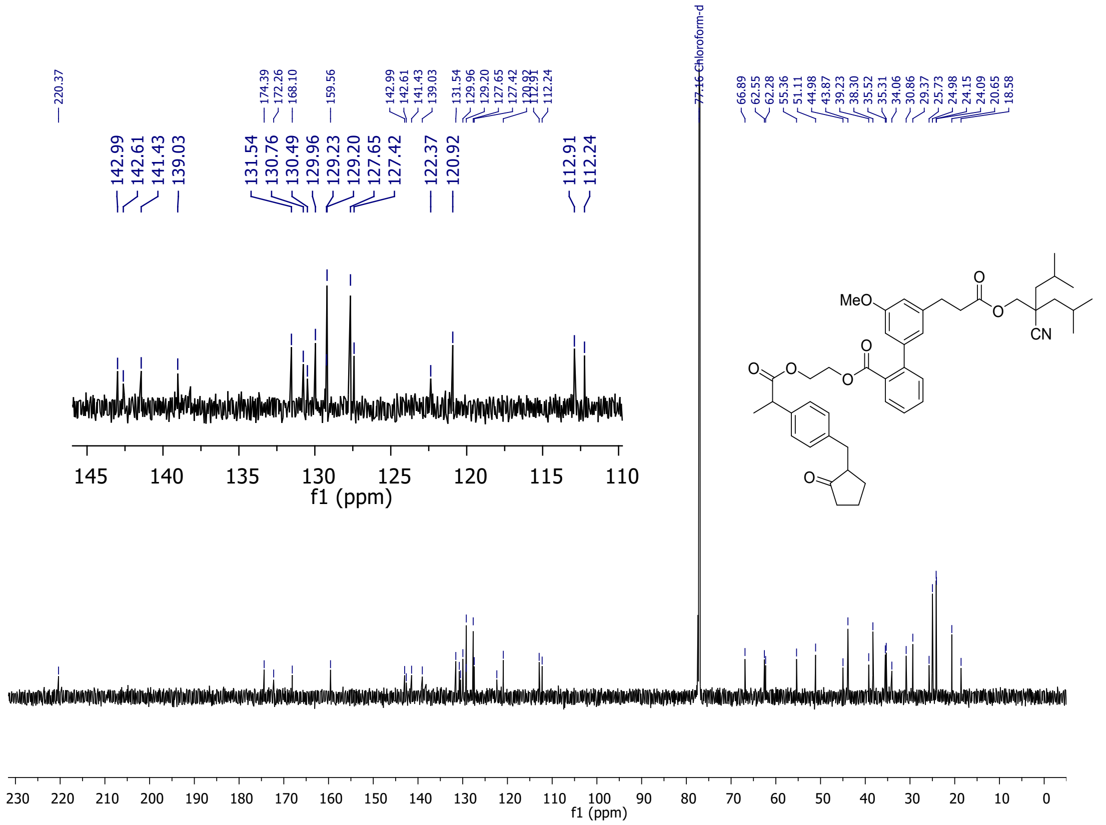
^{1}H NMR (600 MHz) spectrum of **6cp** in CDCl$_3$.



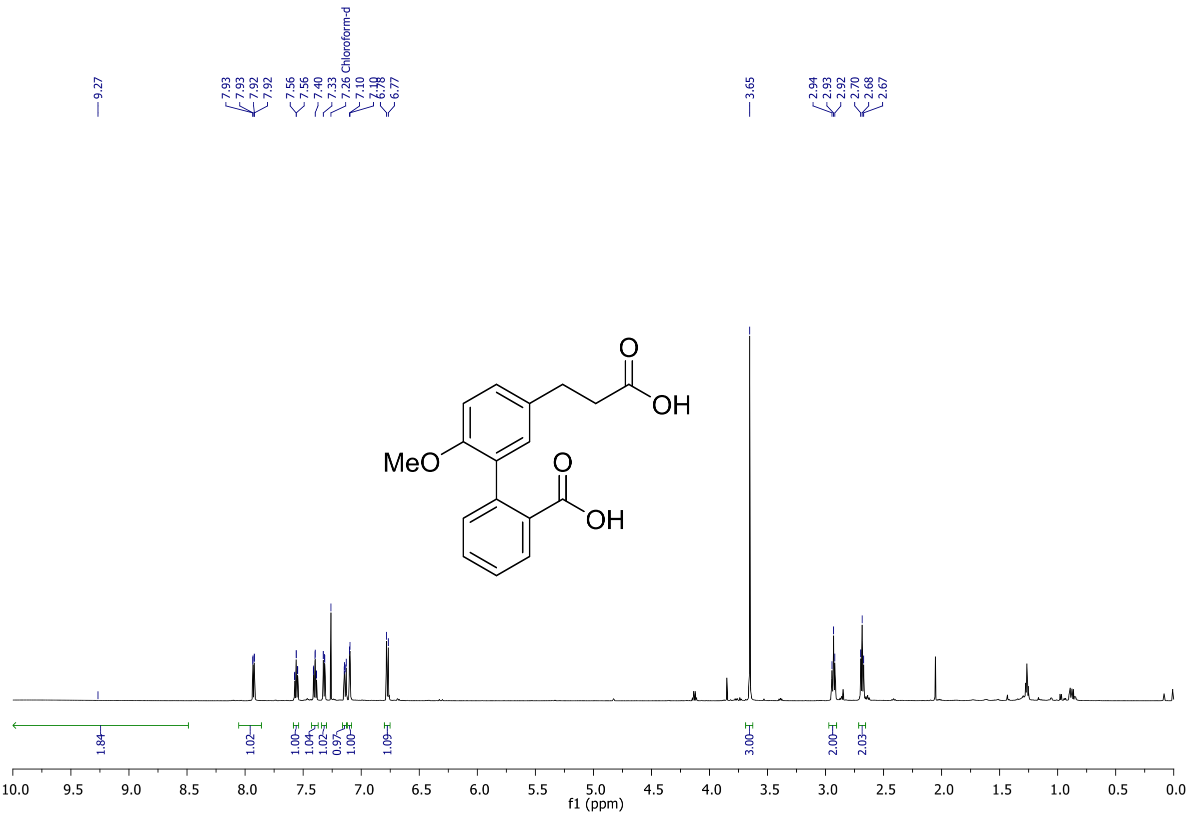
^{13}C{^{1}H} NMR (151 MHz) spectrum of **6cp** in CDCl$_3$.



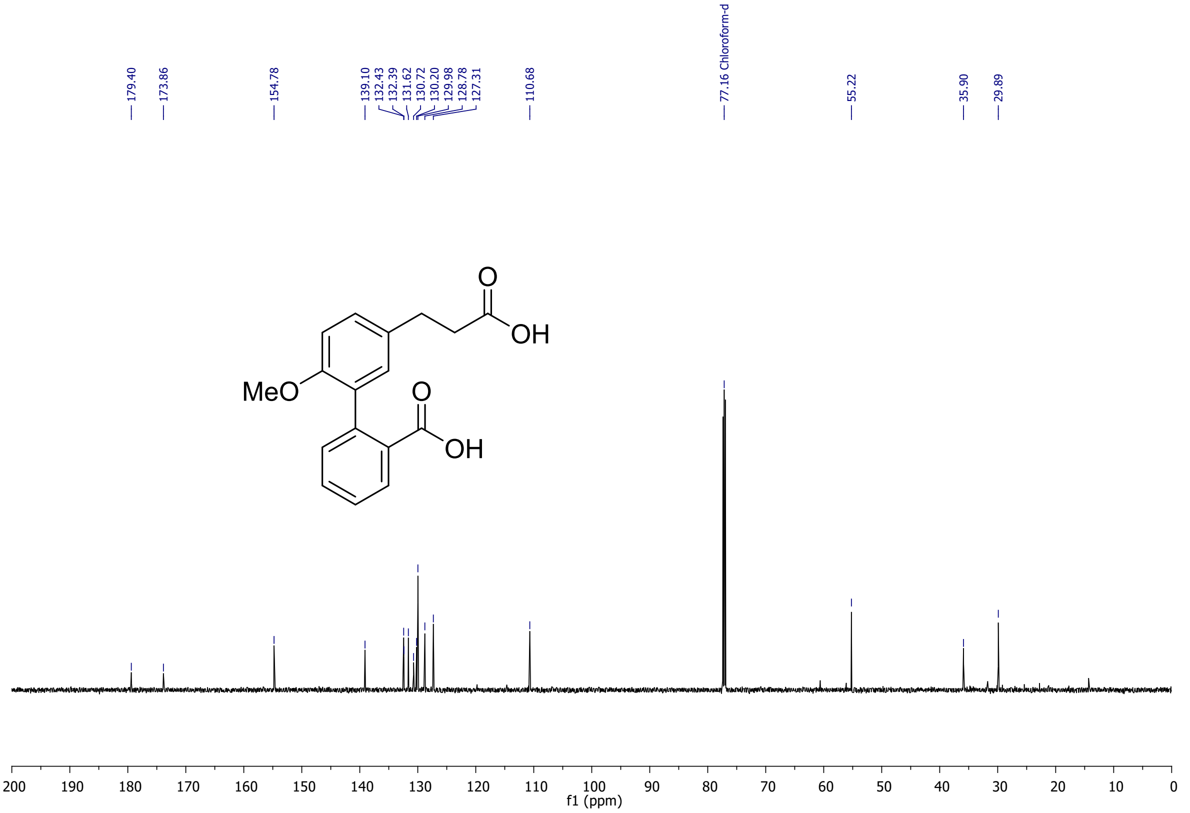
^{1}H NMR (600 MHz) spectrum of **6cq** in CDCl$_3$.



^{13}C{^{1}H} NMR (151 MHz) spectrum of **6cq** in CDCl$_3$.



^{1}H NMR (600 MHz) spectrum of **7** in $CDCl_3$.



$^{13}C\{^1H\}$ NMR (151 MHz) spectrum of **7** in $CDCl_3$.

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