Supporting Information

Decarboxylative Alkyl Coupling Promoted by NADH and Blue Light

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1. General Information

Materials: All reactions were carried out using oven-dried glassware under an atmosphere of argon unless otherwise specified. Carboxylic acids were purchased from Sigma Aldrich, Fluorochem and TCI Chemicals. Dry solvents were obtained by passing them through activated alumina columns. Anhydrous dimethyl sulfoxide was purchased from Sigma Aldrich. The solvents used in column chromatography, petroleum ether, pentane, dichloromethane, methanol and ethyl acetate, were obtained from commercial suppliers in HPLC grade and used without further purification. Dihydropyridine was synthesized using the literature procedure reported by Hollmann and co-workers.[12] **S2-DNA headpiece** (5'd Phos-GAGTCA-Spacer 9-Amino C7-Spacer 9-TGACTCCC 3') was purchased from LGC Biosearch Technologies.

Chromatography: Thin layer chromatography (TLC) was carried out on 0.25 mm E. Merck silica plates ($60F_{254}$) using UV light (λ = 254 nm) as visualizing agent and a vanillin, phosphomolybdic acid (PMA) or $KMnO_4$ solution and heat as developing agents, as specified. Flash column chromatography on SiO_2 was performed using E. Merck silica gel (60 Å, particle size 0.043-0.063 mm).

Spectroscopy: NMR spectra for the characterization of compounds were recorded at room temperature on a Bruker instrument 400 MHz (^{1}H) and at 101 MHz (^{13}C) and 376 MHz (^{19}F), or 500 MHz (^{1}H) and at 126 MHz (^{13}C). Chemical shifts (δ) are reported in ppm, using the residual solvent peak in $CDCl_3$ (δ_H = 7.26 and δ_C = 77.16 ppm), coupling constants (*J*) are given in hertz (Hz). Data are reported as follows: chemical shift, multiplicity (s: singlet, d: doublet, t: triplet, q: quartet, br: broad, m: multiplet), coupling constants and integration. High-resolution mass spectra (HRMS) were determined with a Bruker Daltonics microTOF Mass Spectrometer using an ESI ion source. UV-visible experiments were done using a Cary-50 spectrometer in advanced mode (settings: average time (sec): 0.250; data interval (nm): 1.00; scan rate (nm/min): 240.00) at wavelengths 300 – 800 nm.

Experimental details: Starting materials were synthesized using common Pyrex® round bottom flasks. Photo-induced reactions were carried out in 5 mL flat bottomed vials crimped on top with 20 mm Sil/PTFE Septa (Cronus, SMI-LabHut Ltd.). Reactions were illuminated at 1 cm distance from the bottom of the reaction vial with a single Osram OSLON SSL 80 LED operating at 700 mA current. Reaction temperature was maintained using an aluminium block connected to a cooling Huber Minichiller 300 OLÉ®.

***Figure S1**: Experimental set up.*

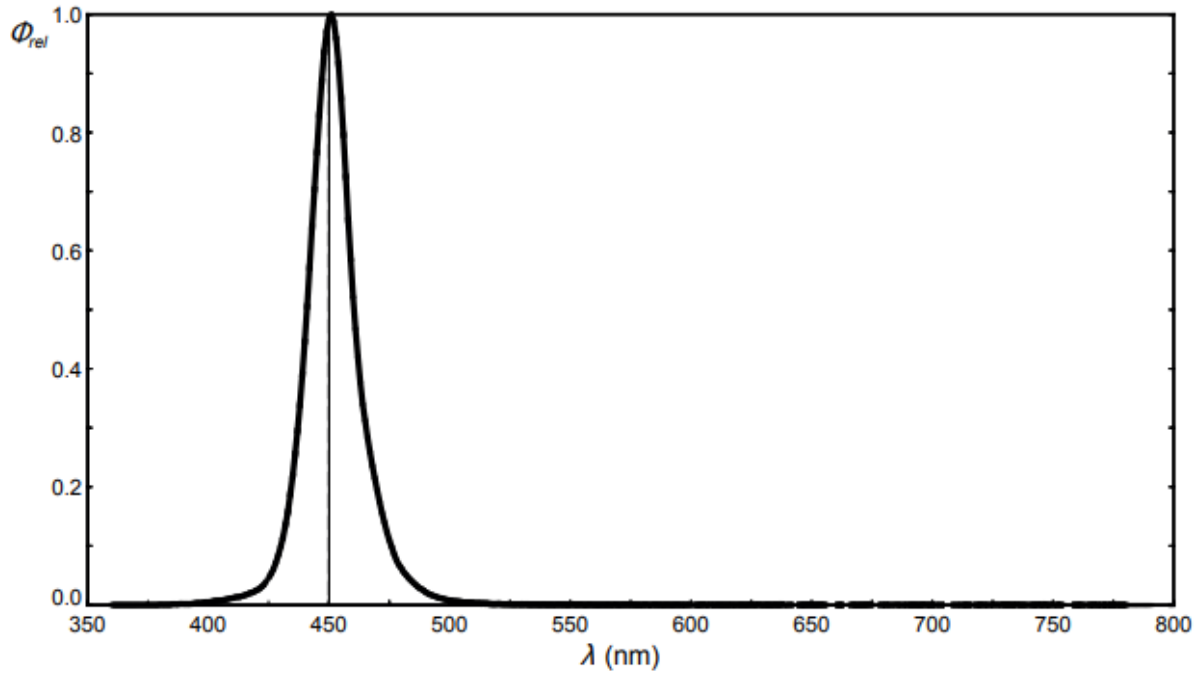
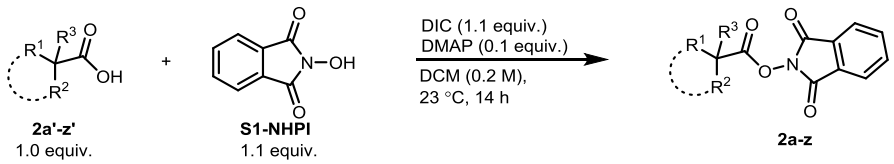


***Figure S2**: Normalized emission spectrum of the light source used in this study.*

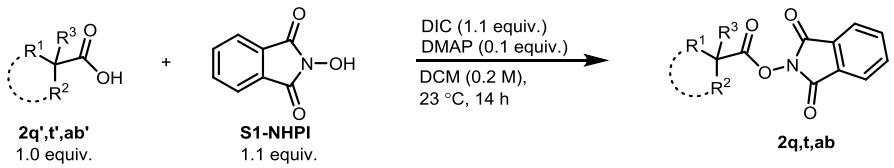
2. Synthesis of starting materials

General procedure (A1): Synthesis of redox-active esters from solid carboxylic acids



N-hydroxyphthalimide (**S1**; 1.1 equiv.), DMAP (0.1 equiv.) and carboxylic acid (solid) (1.0 equiv.) were charged in a round bottomed flask. DCM (0.2 M) was added followed by dropwise addition of *N,N'*-diisopropylcarbodiimide (1.1 equiv.). The resulted mixture was stirred overnight at room temperature. After completion of the reaction (as monitored by TLC) the reaction mixture was filtered through a Celite pad (1.5 – 2.0 cm) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on SiO_2 using a mixture of petroleum ether and EtOAc or DCM as the eluent.

General procedure (A2): Synthesis of redox-active esters from liquid carboxylic acids



N-hydroxyphthalimide (**S1**; 1.1 equiv.) and DMAP (0.1 equiv.) were charged in a round bottomed flask. Carboxylic acid (1.0 equiv.) dissolved in DCM (0.2 M) was added followed by dropwise addition of *N,N'*-diisopropylcarbodiimide (1.1 equiv.). The resulting mixture was stirred overnight at room temperature. After completion of the reaction (as monitored by TLC) the reaction mixture was filtered through a Celite pad (1.5 – 2.0 cm) and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on SiO_2 using a mixture of petroleum ether and EtOAc or DCM as the eluent.

The following redox-active esters were synthesized according to the literature procedures. All the data are in accordance with the literature.[1-7]

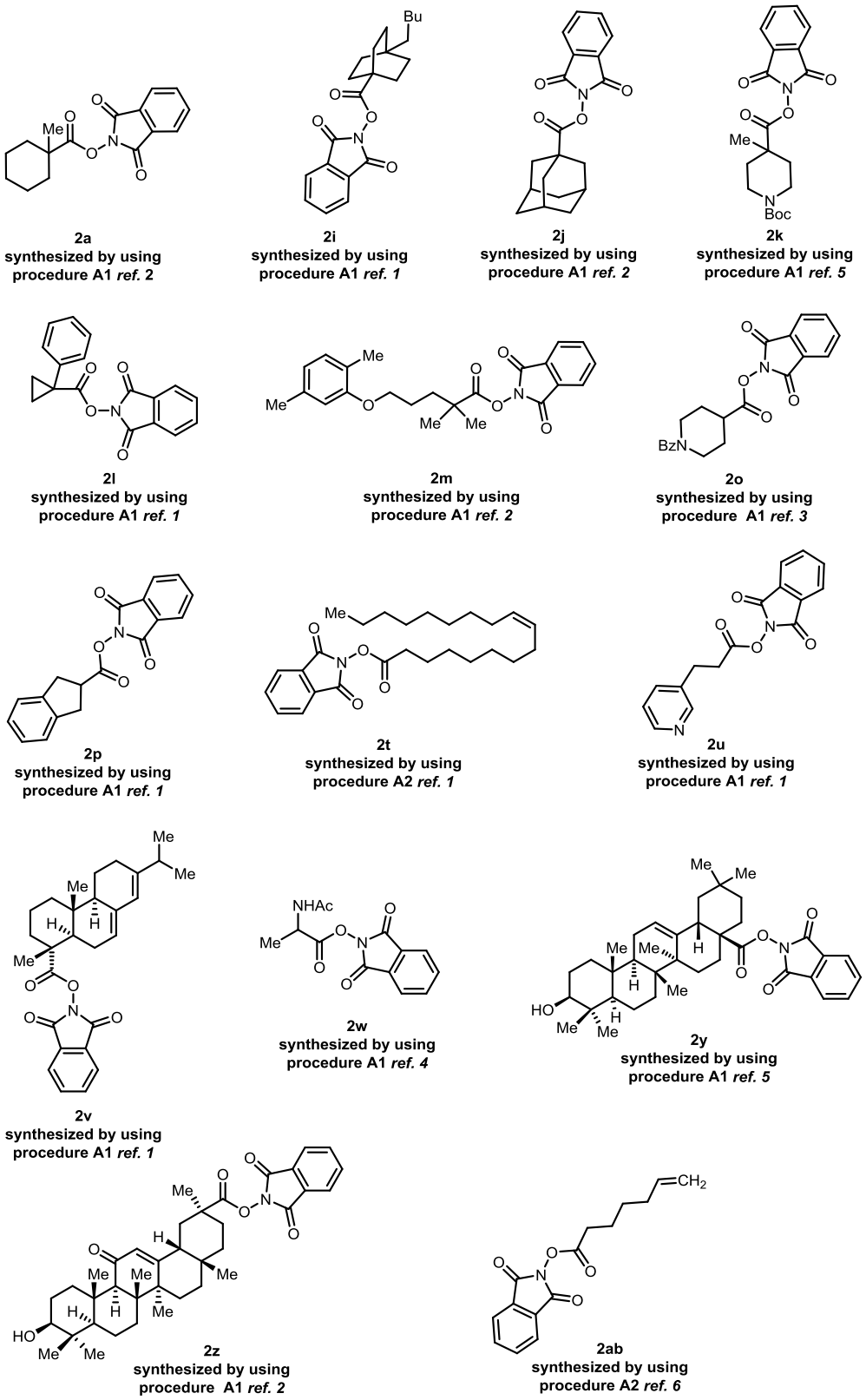
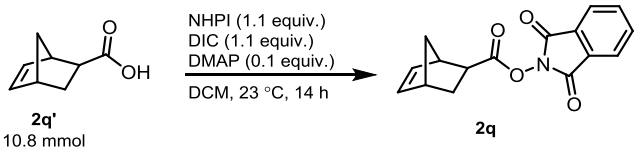


***Figure S3**: Reported NHPI-esters.*

*Synthesis of 1,3-dioxoisoindolin-2-yl (1R,4R)-bicyclo[2.2.1]hept-5-ene-2-carboxylate (**2q**)*



General procedure A2 was applied using (1*R*,4*R*)-bicyclo[2.2.1]hept-5-ene-2-carboxylic acid (98% endo) (**2q'**; 1.5 g, 10.8 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (**S1**; 1.9 g, 11.9 mmol, 1.1 equiv.), *N,N'*-diisopropylcarbodiimide (1.5 g, 11.9 mmol, 1.1 equiv.) and DMAP (133 mg, 1.1 mmol, 0.1 equiv.) in 50 mL DCM for 14 h. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 1:1) to afford pure **2q** (2.3 g, 8.12 mmol, 75%).

Appearance: white solid.

TLC: R_f = 0.55 (petroleum ether/EtOAc = 85:15, UV-active and stains in permanganate).

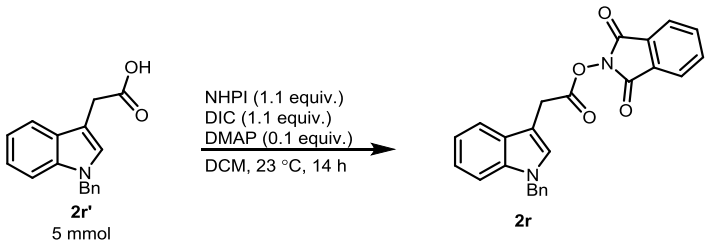
m.pt. = 105.8 – 110.6 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.90 – 7.84 (m, 2H), 7.81 – 7.75 (m, 2H), 6.28 – 6.18 (m, 2H), 3.49 – 3.46 (m, 1H), 3.31 (dt, *J* = 9.2, 3.8 Hz, 1H), 3.05 – 2.98 (m, 1H), 2.13 – 2.01 (m, 1H), 1.60 – 1.52 (m, 2H), 1.41 – 1.34 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 170.9, 162.1, 138.2, 134.7, 134.6, 132.2, 129.0, 123.9, 123.9, 49.7, 46.5, 42.6, 40.7, 29.6.

HRMS: could not be obtained due to poor ionization.

*Synthesis of 1,3-dioxoisoindolin-2-yl 2-(1-benzyl-1H-indol-3-yl)acetate (**2r**)*



General procedure A1 was applied using 2-(1-benzyl-1*H*-indol-3-yl)acetic acid (**2r'**; 1.325 g, 5.0 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (**S1**; 0.896 g, 5.5 mmol, 1.1 equiv.), *N,N'*-diisopropylcarbodiimide (0.694 g, 5.5 mmol, 1.1 equiv.) and DMAP (61 mg, 0.5 mmol, 0.1 equiv.) in 30 mL DCM for 14 h. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 1:1) to afford pure **2r** (1.8 g, 4.38 mmol, 88%).

Appearance: white solid.

TLC: R_f = 0.4 (petroleum ether/EtOAc = 7:3, UV-active and stains violet in vanillin).

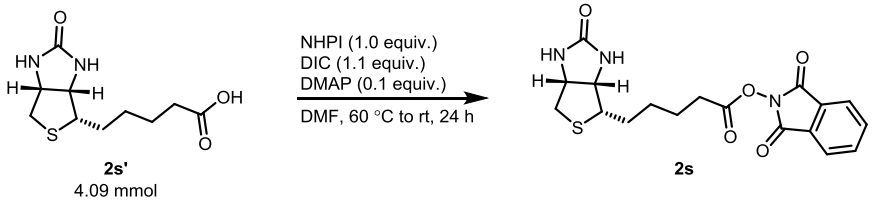
m.pt. = 142.8 – 146.1 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.89 – 7.87 (m, 2H), 7.79 – 7.77 (m, 2H), 7.69 (dd, *J* = 7.1, 2.0 Hz, 1H), 7.33 – 7.22 (m, 5H), 7.21 – 7.13 (m, 4H), 5.32 (s, 2H), 4.16 (s, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 167.9, 161.9, 137.3, 136.5, 134.7, 129.0, 128.8, 127.7, 127.5, 126.9, 124.0, 122.3, 119.8, 118.9, 109.9, 105.0, 50.2, 28.1.

HRMS (ESI-TOF) calc'd for $C_{25}H_{18}N_2O_4Na$ $[M+Na]^+$: 433.1159, found: 433.1155.

*Synthesis of NHPI-ester of D-biotin (**2s**)*



2s'
4.09 mmol

2s

D-biotin (**2s'**; 1.0 g, 4.09 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (**S1**; 0.67 g, 4.09 mmol, 1.0 equiv.) and DMAP (50 mg, 0.04 mmol, 0.1 equiv.) were dissolved in hot DMF (60 °C) (0.13 M) in a round bottomed flask. *N,N'*-diisopropylcarbodiimide (0.93 g, 4.502 mmol, 1.1 equiv.) was added and the solution was stirred for 24 h during which time a white precipitate was formed. The reaction mixture was filtered, the solvent was evaporated (70 °C water bath, 13 mbar), and the residue was triturated with diethyl ether. The white precipitate was filtered and washed with diethyl ether to give **2s** (1.35 g, 3.46 mmol, 85%).

Appearance: white powder.

TLC: R_f = 0.55 (DCM/ methanol = 9:1, UV-active and stains in permanganate).

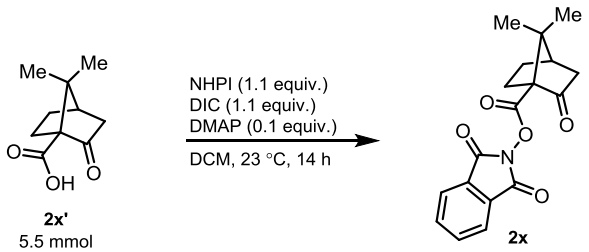
m.pt. = 180.2 – 185.5 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.89 – 7.86 (m, 2H), 7.81 – 7.77 (m, 2H), 6.08 (s, 1H), 5.26 (s, 1H), 4.55 – 4.51 (m, 1H), 4.37 – 4.33 (m, 1H), 3.20 (ddd, *J* = 8.2, 6.7, 4.6 Hz, 1H), 2.95 – 2.88 (m, 2H), 2.77 – 2.70 (m, 2H), 1.86 (p, *J* = 7.4 Hz, 2H), 1.80 – 1.71 (m, 2H), 1.61 – 1.53 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 169.8, 163.8, 162.2, 135.0, 129.0, 123.7, 62.0, 60.3, 55.6, 40.7, 30.8, 28.3, 28.1, 24.7.

HRMS: could not be obtained due to poor ionization.

*Synthesis of 1,3-dioxoisoindolin-2-yl (1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxylate (**2x**)*



2x'
5.5 mmol

2x

General procedure A1 was applied using (1*R*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxylic acid (**2x'**; 1.0 g, 5.5 mmol, 1.0 equiv.), *N*-hydroxyphthalimide (**S1**; 1.0 g, 6.0 mmol, 1.1 equiv.), *N,N'*-diisopropylcarbodiimide (0.8 g, 6.0 mmol, 1.1 equiv.) and DMAP (67 mg, 0.55 mmol, 0.1 equiv.) in 50 mL DCM for 14 h. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 1:1) to afford pure **2x** (1.6 g, 4.89 mmol, 89%).

Appearance: white solid.

TLC: R_f = 0.55 (petroleum ether/EtOAc = 6:4, UV-active).

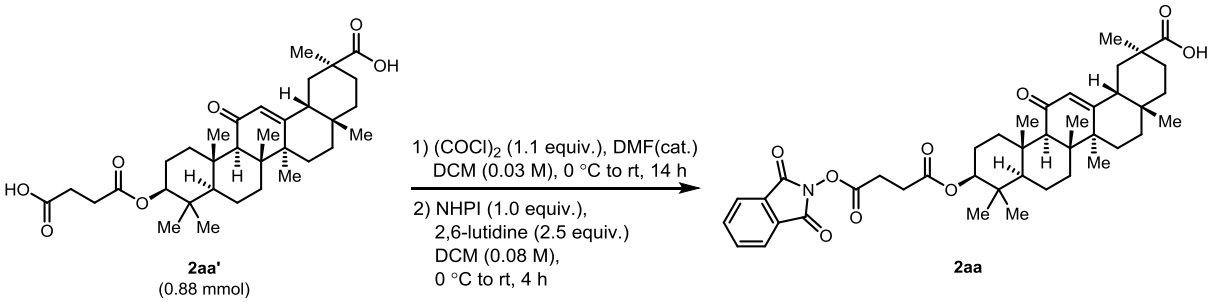
m.pt. = 128.2 – 133.8 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.90 – 7.87 (m, 2H), 7.81 – 7.77 (m, 2H), 2.69 – 2.56 (m, 2H), 2.23 (t, *J* = 4.4 Hz, 1H), 2.20 – 2.11 (m, 1H), 2.09 (d, *J* = 18.4 Hz, 1H), 2.03 – 1.97 (m, 1H), 1.55 (td, *J* = 9.1, 4.7 Hz, 1H), 1.27 (d, *J* = 9.5 Hz, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 207.7, 166.2, 161.7, 134.7, 129.0, 123.9, 66.8, 51.0, 44.5, 43.9, 26.7, 26.3, 20.9, 19.6.

HRMS (ESI-TOF) calc'd for $C_{18}H_{17}NO_5Na$ $[M+Na]^+$: 350.0999, found: 350.0995.

*Synthesis of NHPI ester of derivative of 18β-Glycyrrhetinic acid (**2aa**)*



2aa' (0.88 mmol)

2aa

To a suspension of (3β,18β,20β)-3-(3-Carboxy-1-oxopropoxy)-11-oxo-olean-12-en-29-oic acid (**2aa'**, 500 mg, 0.88 mmol, 1.0 equiv.) in dry DCM (25 mL), DMF (3 µL, 0.04 mmol, 0.04 equiv.) was added under argon. The suspension was placed in an ice-water bath and stirred for 10 min. Then, oxalyl chloride (83 µL, 0.96 mmol, 1.1 equiv.) was added dropwise over 30 min (Note: gas evolution was observed and this step should be performed in a well-ventilated fume hood). After the addition, the mixture was stirred at 0 °C for 20 min before the ice-bath was removed. The mixture was stirred at room temperature overnight. Volatiles were removed under reduced pressure and fresh dry DCM (15 mL) was added. The resulting solution was placed in an ice-bath under argon. Then, a briefly sonicated solution of *N*-hydroxyphthalimide **S1** (143 mg, 0.88 mmol, 1.0 equiv.) and 2,6-lutidine (254 µL, 2.2 mmol, 2.5 equiv.) in dry DCM (10 mL) was added slowly. The reaction was allowed to reach room temperature over 30 min and further stirred for 4 h at this temperature. Then the volume of DCM was reduced to approx. 20% under reduced pressure and the crude yellow oil was purified by column chromatography on SiO_2 (DCM/EtOAc = 10:1 to 5:1) to obtain the title compound **2aa** (200 mg, 0.28 mmol, 32%).

Appearance: white solid.

TLC: R_f = 0.45 (DCM/ MeOH = 10:1, UV-active).

m.pt. = 248.9 – 251.3 °C.

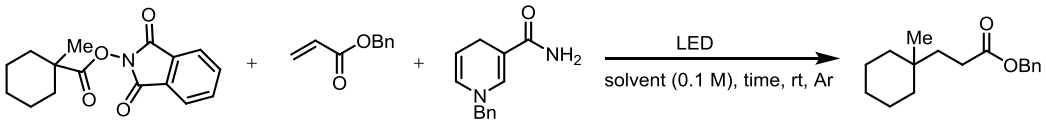
^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.90 – 7.85 (m, 2H), 7.81 – 7.75 (m, 2H), 5.71 (s, 1H), 4.58 (dd, *J* = 11.8, 4.7 Hz, 1H), 3.09 – 2.96 (m, 2H), 2.84 – 2.71 (m, 3H), 2.36 (s, 1H), 2.25 – 2.11 (m, 1H), 2.09 – 1.53 (m, 9H), 1.48 – 1.29 (m, 8H), 1.25 – 0.97 (m, 13H), 0.92 – 0.75 (m, 10H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 200.5, 182.1, 170.9, 169.7, 168.8, 161.8, 134.9, 129.0, 128.5, 124.1, 81.7, 61.8, 55.1, 48.4, 45.6, 43.9, 43.3, 40.9, 38.9, 38.2, 37.8, 37.0, 32.8, 32.0, 31.0, 29.3, 28.7, 28.6, 28.2, 26.6, 26.5, 23.6, 23.5, 18.8, 17.5, 16.9, 16.5.

HRMS (ESI-TOF) calc'd for $C_{42}H_{53}NO_9Na$ $[M+Na]^+$: 738.3613, found: 738.3617.

3. Optimization studies and control experiments

***Table S1**: Initial exploration of the reaction parameters*



2a 0.1 mmol + **3a** 1.5 equiv. + **5** 1.5 equiv. → **4a**

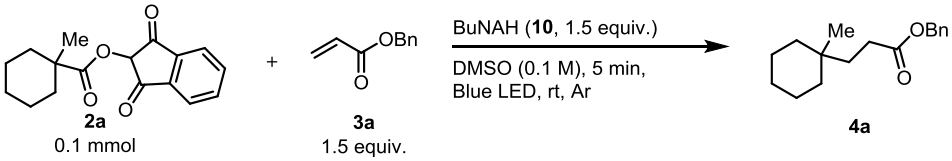
Entry	Solvent	Type of LED	Time (h)	NMR yield **(4a)** (%)
1	DMF	Blue LED	17	81
2	Toluene	Blue LED	40	38
3	CH_3CN	Blue LED	18	65
4	DCM	Blue LED	40	36
5	THF	Blue LED	40	45
6	DMA	Blue LED	19	75
7	DMSO	Blue LED	19	92
8	Acetone	Blue LED	19	58
9	^{i}PrOH	Blue LED	18	51
10	$CF_3C_6H_5$	Blue LED	18	44
11	EtOAc	Blue LED	18	38
12	1,4-dioxane	Blue LED	24	36
13	HFIP	Blue LED	18	15
14	DMSO (0.5 mL)	Blue LED	24	89
15	DMSO (1 mL)	Blue LED	24	89
16	DMSO (2 mL)	Blue LED	24	91
17	DMSO[a]	Blue LED	20	89
18	THF/H_2O = 7/3	Blue LED	24	61
19[b]	DMSO (40 ^{o}C)	Blue LED	24	89
20	DMSO	Blue LED	16	99
21[c]	DMSO	Green LED	16	99
22[c]	DMSO	White LED	16	92
23[c]	DMSO	UV LED	16	98
24[d]	DMSO	White LED	2.5	95
25[d]	DMSO	UV LED	2.5	80
26[d]	DMSO	Green LED	2.5	90
27[d]	DMSO	Blue LED	2.5	93
28[d]	DMSO	White LED	0.5	50 (50)[e]
29[d]	DMSO	UV LED	0.5	14 (15)[e]
30[d]	DMSO	Green LED	0.5	32 (32)[e]
31[d]	DMSO	Blue LED	0.5	70 (70)[e]
32[c]	DMSO	No irradiation[f]	16	No reaction

a) not degassed via sonication; b) $[Ru(bpy)_3]Cl_2$ (2 mol%); c) I = 0.3 A; d) I = 0.1 A;
e) conversion f) reaction was covered in aluminium foil

***Table S2**: Study of control experiments*

Entry	Deviation from standard condition	NMR yield (**4a**) (%)
1	no	99
2	no light	0
3	no BuNAH	0
4	DMSO (1 mM), 20 min	87
5	DMSO:H_2O = 1:1 (1 mM), 60 min	72
6	BuNAH (3.0 equiv.), DMSO:H_2O = 1:1 (1 mM), 60 min, Air	79
7	DMSO (10 mM), NADH was used instead of BuNAH	63
8	DMSO (10 mM), NADH (10.0 equiv.) was used instead of BuNAH	69

***Table S3**: Stability of the BuNAH (**10**) as a solution in DMSO*

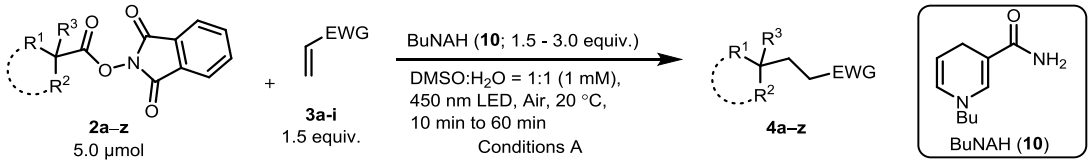


Entry	BuNAH (**10**) solution storage time (days)	NMR yield (**4a**) (%)
1	0	99
2	1	99
3	2	99
4	4	99
5	6	99
6	8	92
7	14	92

BuNAH **10** was dissolved in DMSO (0.1 M) and stored in the freezer at -20 °C

4. Scope studies

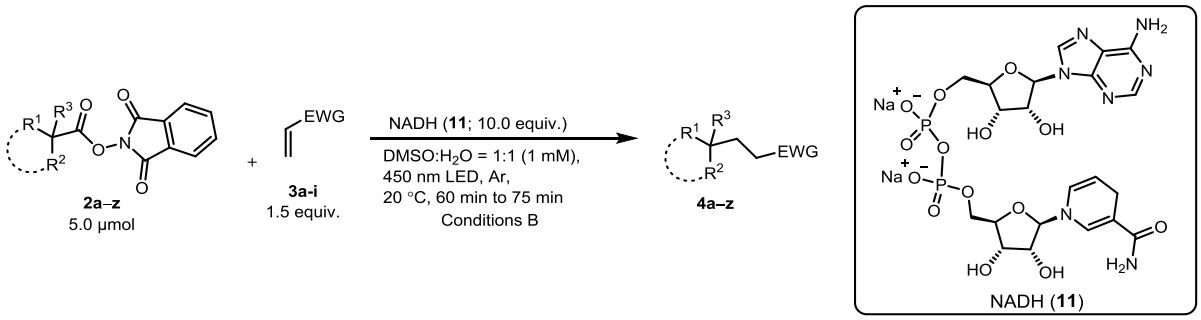
General Procedure (B1): Decarboxylative coupling of redox-active carboxylates with electron-poor olefins using BuNAH (10) and blue light



The stock solution of the redox-active ester **2a-z** (5.0 µmol, 1.0 equiv.), Michael acceptor **3a-i** (7.5 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 16.2 mg, 15.0

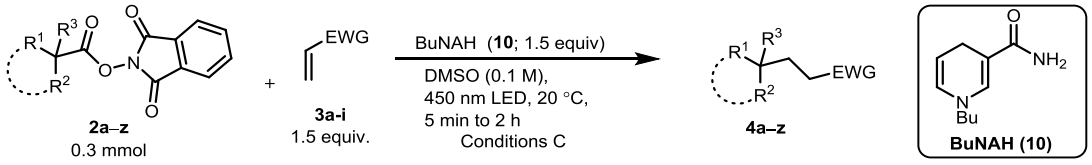
µmol, 3.0 equiv.) were prepared in DMSO (1.2 mL) in three different 2 mL vials. Next, an aliquot (0.2 mL, unless otherwise specified) of each stock solution was injected in a 7 mL vial equipped with a stirring bar. DMSO (1.9 mL) was added to the mixture, followed by the addition of ice-cold water (2.5 mL). The vial was closed with a sure seal septum, the mixture was stirred, and illuminated under blue light for the specified time at 20 °C. After completion, the reaction mixture was diluted with water (10 mL) and EtOAc (15 mL) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (2x15 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude **4a-z**. ^{1}H-NMR was measured in the presence of 1,1,2,2-tetrachloroethane as an internal standard to determine the yield of the crude product.

General Procedure (B2): Decarboxylative coupling of redox-active carboxylates with electron-poor olefins using BuNAH (10) and blue light NADH (11) and blue



A 7 mL vial equipped with a stirring bar was evacuated and refilled with argon (three cycles). Redox-active ester **2a-2z** (5.0 µmol, 1.0 equiv.) and Michael acceptor **3a-i** (7.5 µmol, 1.5 equiv.) were added in form of a stock solution (0.2 mL in DMSO). NADH (**11**; 35.0 mg, 50.0 µmol, 10.0 equiv.) dissolved in DMSO (2.1 mL) was added to the mixture, followed by the addition of ice-cold water (2.5 mL). The resulting mixture was stirred and illuminated under blue light for the specified time at 20 °C. The reaction mixture was diluted with water (10 mL) and EtOAc (15 mL) was added. The organic layer was separated and the aqueous layer was extracted with EtOAc (2x15 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure to afford the crude **4a-z**. ^{1}H-NMR was measured in the presence of 1,1,2,2-tetrachloroethane as an internal standard to determine the yield of the crude product.

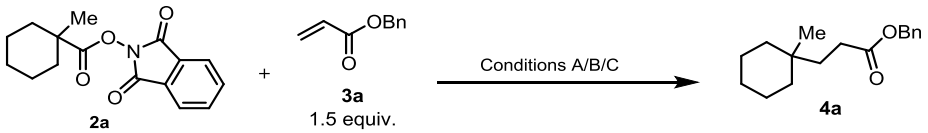
General procedure (B3): Preparative decarboxylative coupling of redox-active carboxylates with electron-poor olefins BuNAH (10) and blue light.



Redox-active ester **2a-2z** (0.30 mmol, 1.0 equiv.) and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81.0 mg, 0.45 mmol, 1.5 equiv.) were weighed in a 7 mL oven-dried vial equipped with a magnetic stirring bar. The vial was closed with a sure seal septum, followed by evacuation and refilling with argon (three times). Then anhydrous DMSO (3 mL) was added

followed by addition of Michael acceptor **3a-i** (0.45 mmol, 1.5 equiv.). The mixture was then irradiated with blue LEDs for 5 min to 2 h at 20 ˚C. The reaction mixture was diluted with DCM (15 mL), then water (15 mL) and brine (10 mL) were added to it. The organic layer was separated and the aqueous layer was extracted with DCM (2x15 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude was purified by column chromatography on SiO_2 to afford **4a–4aa**.

*Synthesis of benzyl 3-(1-methylcyclohexyl)propanoate (**4a**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4a** in 79%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4a** in 69%.

Preparative procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 5:1 to 2:1) to afford **4a** (68.0 mg, 0.26 mmol, 87%).

Appearance: colorless oil.

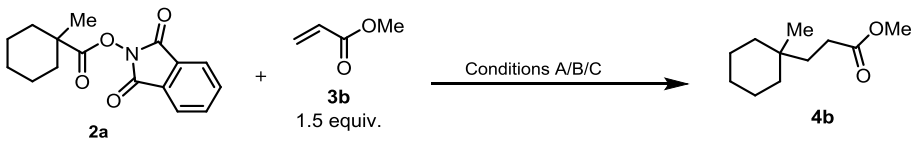
TLC: R_f = 0.22 (pentane/DCM = 2:1, UV-active and stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.30 (m, 5H), 5.12 (s, 2H), 2.35 – 2.27 (m, 2H), 1.64 – 1.58 (m, 2H), 1.48 – 1.37 (m, 5H), 1.36 – 1.28 (m, 1H), 1.26 – 1.21 (m, 4H), 0.85 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.4, 136.1, 128.5, 128.2, 128.2, 66.2, 37.5, 36.7, 32.3, 29.0, 26.4, 24.4, 22.0.

All the data are in accordance with the literature.[2]

*Synthesis of methyl 3-(1-methylcyclohexyl)propanoate (**4b**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), methyl acrylate (**3b**; 0.65 mg, 7.5 µmol, 1.5

equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4b** in 72%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylat (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), methyl acrylate (**3b**; 0.65 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4b** in 51%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), methyl acrylate (**3b**; 39 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/DCM = 5:1 to 2:1) to afford **4b** (42.0 mg, 0.23 mmol, 76%).

Appearance: colorless oil.

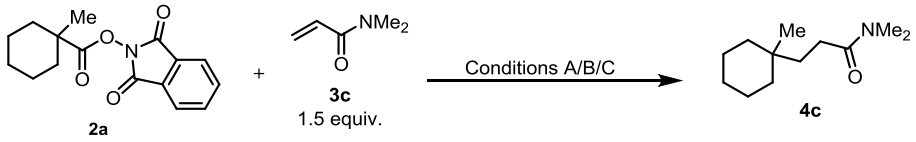
TLC: R_f = 0.65 (pentane/EtOAc = 20:1, stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 3.66 (s, 3H), 2.31 – 2.21 (m, 2H), 1.60 – 1.55 (m, 2H), 1.48 – 1.38 (m, 5H), 1.35 – 1.27 (m, 1H), 1.25 – 1.20 (m, 4H), 0.85 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 175.1, 51.5, 37.5, 36.7, 32.3, 28.8, 26.4, 24.4, 21.9.

All the data are in accordance with the literature.[9]

*Synthesis of N,N-dimethyl-3-(1-methylcyclohexyl)propanamide (**4c**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), *N,N*-dimethylacrylamide (**3c**; 0.75 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4c** in 86%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), *N,N*-dimethylacrylamide (**3c**; 0.75 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4c** in 85%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), *N,N*-dimethylacrylamide (**3c**; 45 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 10 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 1:1 to 1:2) to afford **4c** (44 mg, 0.22 mmol, 74%).

Appearance: colorless oil.

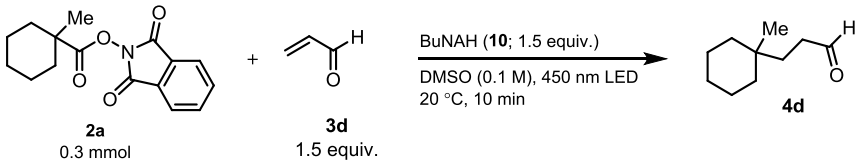
TLC: R_f = 0.50 (pentane/EtOAc = 1:2, stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 3.01 (s, 3H), 2.93 (s, 3H), 2.29 – 2.21 (m, 2H), 1.59 – 1.53 (m, 2H), 1.48 – 1.37 (m, 5H), 1.34 – 1.28 (m, 1H), 1.25 (m, 4H), 0.87 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.0, 37.6, 37.4, 36.9, 35.4, 32.4, 27.9, 26.4, 24.6, 22.0.

All the data are in accordance with the literature.[13]

*Synthesis of 3-(1-methylcyclohexyl)propanal (**4d**)*



General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), acrylaldehyde (**3d**; 25 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 10 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 2:1) to afford **4d** (19 mg, 0.123 mmol, 41%).

Appearance: colorless oil.

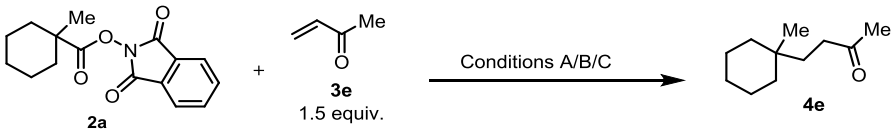
TLC: R_f = 0.33 (pentane/EtOAc = 20:1, stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 9.79 (t, *J* = 1.9 Hz, 1H), 2.38 (ddd, *J* = 10.0, 6.3, 2.0 Hz, 2H), 1.57 – 1.53 (m, 2H), 1.44 (m, 5H), 1.30 (m, 1H), 1.27 – 1.20 (m, 4H), 0.85 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 203.3, 38.7, 37.6, 33.7, 32.2, 26.4, 24.5, 21.9.

All the data are in accordance with the literature.[9]

*Synthesis of 4-(1-methylcyclohexyl)butan-2-one (**4e**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), methyl vinyl ketone (**3e**; 0.53 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4e** in 68%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), methyl vinyl ketone (**3e**; 0.53 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4e** in 68%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), methyl vinyl ketone (**3e**; 32 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in

DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 5:1 to 2:1) to afford **4e** (43.9 mg, 0.26 mmol, 87%).

Appearance: colorless oil.

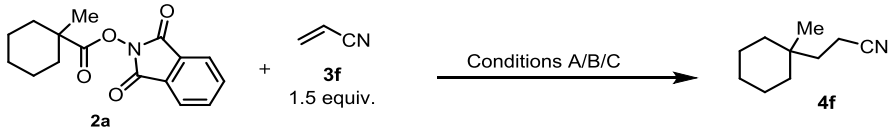
TLC: R_f = 0.33 (pentane/EtOAc = 10:1, stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.39 – 2.33 (m, 2H), 2.15 (s, 3H), 1.52 – 1.47 (m, 2H), 1.43 (m, 5H), 1.30 (m, *J* = 8.1, 4.6, 2.5 Hz, 1H), 1.22 (m, 4H), 0.83 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 209.9, 38.3, 37.6, 35.5, 32.2, 29.9, 26.4, 24.6, 22.0.

All the data are in accordance with the literature.[2]

*Synthesis of 3-(1-methylcyclohexyl)propanenitrile (**4f**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), acrylonitrile (**3f**; 0.39 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4f** in 66%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), acrylonitrile (**3f**; 0.39 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4f** in 68%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), acrylonitrile (**3f**; 24 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/DCM = 5:1 to 2:1) to afford **4f** (43.1 mg, 0.29 mmol, 95%).

Appearance: colorless oil.

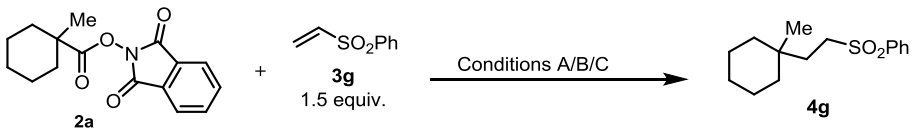
TLC: R_f = 0.33 (pentane/EtOAc = 10:1, stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 2.30 – 2.22 (m, 2H), 1.68 – 1.61 (m, 2H), 1.53 – 1.40 (m, 5H), 1.37 – 1.18 (m, 5H), 0.88 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 120.7, 37.4, 37.1, 32.6, 26.2, 24.1, 21.8, 11.7.

All the data are in accordance with the literature.[2]

*Synthesis of ((2-(1-methylcyclohexyl)ethyl)sulfonyl)benzene (**4g**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4g** in 70%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4g** in 96%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 75 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 10:1 to 5:1) to afford **4g** (66.2 mg, 0.25 mmol, 83%).

Appearance: colorless oil.

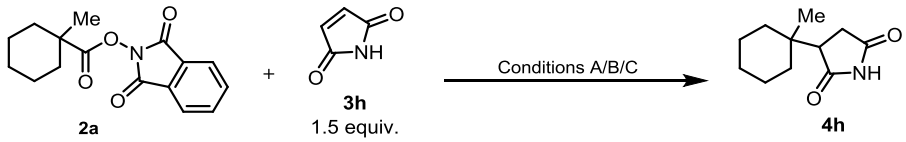
TLC: R_f = 0.51 (pentane/EtOAc = 5:1, UV-active).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.94 – 7.86 (m, 2H), 7.69 – 7.61 (m, 1H), 7.60 – 7.54 (m, 2H), 3.08 – 2.98 (m, 2H), 1.64 – 1.60 (m, 2H), 1.41 – 1.33 (m, 5H), 1.29 – 1.23 (m, 1H), 1.23 – 1.13 (m, 4H), 0.80 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 139.3, 133.6, 129.2, 128.0, 52.0, 37.4, 33.6, 32.3, 26.1, 24.4, 21.7.

All the data are in accordance with the literature.[13]

*Synthesis of 3-(2-(1-methylcyclohexyl)ethyl)pyrrolidine-2,5-dione (**4h**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), 1*H*-pyrrole-2,5-dione (**3h**; 0.73 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in DMSO (20 mM) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4h** in 82%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 1.43 mg, 5.0 µmol, 1.0 equiv.), 1*H*-pyrrole-2,5-dione (**3h**; 0.73 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in DMSO (20 mM) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4h** in 71%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 86 mg, 0.30 mmol, 1.0 equiv.), 1*H*-pyrrole-2,5-dione (**3h**; 44 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in

DMSO (3 mL) for 10 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 5:1 to 2:1) to afford **4h** (43.1 mg, 0.22 mmol, 74%).

Appearance: white solid.

TLC: R_f = 0.42 (Pentane/EtOAc = 2:1, stains in PMA).

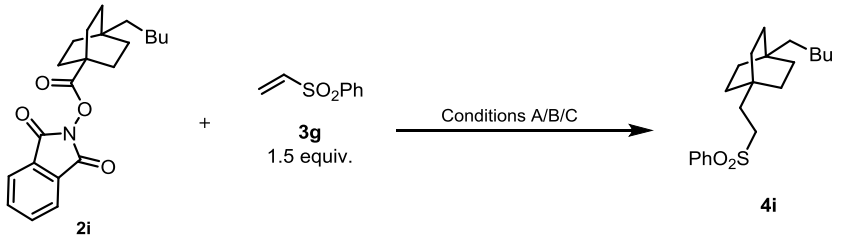
m.pt. = 132.2 – 135.6 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.30 (s, 1H), 2.90 (dd, *J* = 9.0, 5.3 Hz, 1H), 2.71 (dd, *J* = 18.0, 9.0 Hz, 1H), 2.60 (dd, *J* = 18.5, 5.3 Hz, 1H), 1.69 – 1.40 (m, 8H), 1.32 (m, 2H), 0.98 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 178.9, 176.8, 36.0, 35.7, 35.4, 32.0, 25.9, 21.7, 21.4.

HRMS (ESI-TOF) calc'd for $C_{11}H_{17}NO_2$ $[M-H]^-$: 194.1187, found: 194.1185.

*Synthesis of 1-pentyl-4-(2-(phenylsulfonyl)ethyl)bicyclo[2.2.2]octane (**4i**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 4-pentylbicyclo[2.2.2]octane-1-carboxylate (**2i**; 1.84 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4i** in 47%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 4-pentylbicyclo[2.2.2]octane-1-carboxylate (**2i**; 1.84 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4i** in 58%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 4-pentylbicyclo[2.2.2]octane-1-carboxylate (**2i**; 110.8 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 75 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 15 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 19:1 to 9:1) to afford **4i** (77 mg, 0.22 mmol, 73%).

Appearance: white solid.

TLC: R_f = 0.65 (pentane/EtOAc = 5:1, UV-active).

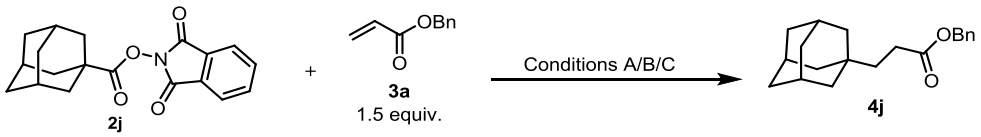
m.p.: 85.7 – 87.7 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.91 – 7.86 (m, 2H), 7.67 – 7.62 (m, 1H), 7.59 – 7.53 (m, 2H), 3.03 – 2.95 (m, 2H), 1.52 – 1.45 (m, 2H), 1.33 – 1.23 (m, 14H), 1.22 – 1.07 (m, 5H), 1.06 – 0.97 (m, 2H), 0.85 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 139.3, 133.5, 129.2, 128.0, 52.2, 41.5, 33.3, 32.8, 31.0, 30.9, 30.4, 30.4, 23.3, 22.7, 14.1.

HRMS (ESI-TOF) calc'd for $C_{21}H_{32}O_2SNa$ $[M+Na]^+$: 371.2015, found: 371.2010.

*Synthesis of benzyl 3-adamantan-1-yl propanoate (**4j**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl (3r,5r,7r)-adamantane-1-carboxylate (**2j**; 1.62 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4j** in 50%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl (3r,5r,7r)-adamantane-1-carboxylate (**2j**; 1.62 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4j** in 46%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl (3r,5r,7r)-adamantane-1-carboxylate (**2j**; 97.6 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 99:1) to afford **4j** (71 mg, 0.23 mmol, 79%).

Appearance: colorless oil.

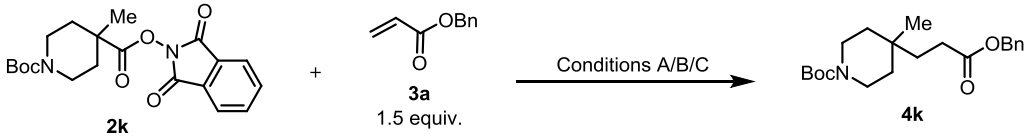
TLC: R_f = 0.7 (pentane/EtOAc = 19:1, UV-active and stains blue in PMA or in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.29 (m, 5H), 5.11 (s, 2H), 2.35 – 2.28 (m, 2H), 1.94 (p, *J* = 3.0 Hz, 3H), 1.73 – 1.66 (m, 3H), 1.64 – 1.58 (m, 3H), 1.49 – 1.41 (m, 8H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.5, 136.1, 128.5, 128.2, 128.1, 66.1, 42.0, 38.9, 37.1, 31.9, 28.6, 28.2.

HRMS (ESI-TOF) calc'd for $C_{20}H_{26}O_2Na$ $[M+Na]^+$: 321.1825, found: 321.1826.

*Synthesis of tert-butyl 4-(3-(benzyloxy)-3-oxopropyl)-4-methylpiperidine-1-carboxylate (**4k**)*



General procedure B1 was applied using 1-(*tert*-butyl) 4-(1,3-dioxoisoindolin-2-yl) 4-methylpiperidine-1,4-dicarboxylate (**2k**; 1.94 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under

argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4k** in 99%.

General procedure B2 was applied using 1-(*tert*-butyl) 4-(1,3-dioxoisoindolin-2-yl) 4-methylpiperidine-1,4-dicarboxylate (**2k**; 1.94 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4k** in 64%.

General procedure B3 was applied using 1-(*tert*-butyl) 4-(1,3-dioxoisoindolin-2-yl) 4-methylpiperidine-1,4-dicarboxylate (**2k**; 58.3 mg, 0.15 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 36.5 mg, 0.26 mmol, 1.5 equiv.), and NADH (**11**; 159 mg, 0.26 mmol, 1.5 equiv.) in anhydrous DMSO (1.5 mL) for 30 min at 20 ˚C under argon. The crude was purified by column chromatography on SiO_2 (pentane/EtOAc = 19:1 to 10:1) to afford **4k** (29 mg, 80 µmol, 53%).

Appearance: colorless oil.

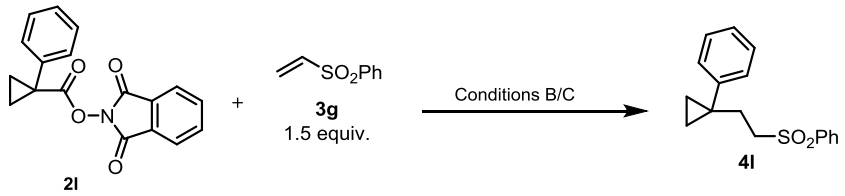
TLC: R_f = 0.3 (pentane/EtOAc = 10:1, UV-active and stains blue in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.30 (m, 5H), 5.11 (s, 2H), 3.56 (d, *J* = 14.4 Hz, 2H), 3.17 (ddd, *J* = 13.4, 9.1, 4.0 Hz, 2H), 2.36 – 2.30 (m, 2H), 1.67 – 1.62 (m, 2H), 1.45 (s, 9H), 1.38 – 1.26 (m, 4H), 0.91 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.9, 154.9, 135.9, 128.6, 128.3, 128.3, 79.3, 66.3, 39.7, 36.5, 36.3, 31.1, 28.8, 28.5, 22.8.

HRMS (ESI-TOF) calc'd for $C_{21}H_{31}NO_4Na$ $[M+Na]^+$: 384.2147; found: 384.2145.

*Synthesis of ((2-(1-phenylcyclopropyl)ethyl)sulfonyl)benzene (**4l**)*



General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-phenylcyclopropane-1-carboxylate (**2l**; 1.53 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4l** in 64%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-phenylcyclopropane-1-carboxylate (**2l**; 92.8 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 75 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 19:1 to 9:1) to afford **4l** (73 mg, 0.25 mmol, 85%).

Appearance: colorless oil.

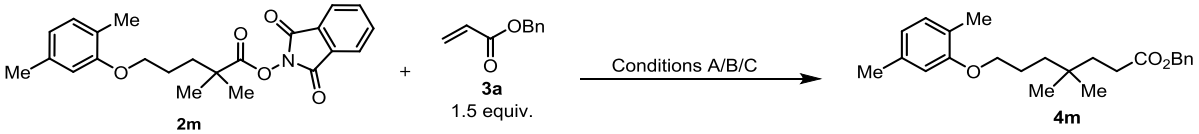
TLC: R_f = 0.5 (pentane/EtOAc = 6:1, UV-active).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.86 – 7.79 (m, 2H), 7.67 – 7.60 (m, 1H), 7.58 – 7.50 (m, 2H), 7.27 – 7.22 (m, 2H), 7.20 – 7.13 (m, 3H), 3.09 – 3.01 (m, 2H), 2.00 – 1.93 (m, 2H), 0.87 – 0.82 (m, 2H), 0.73 – 0.68 (m, 2H).

^{13}C-NMR (100 MHz, $CDCl_3$) δ (ppm) = 142.8, 139.2, 133.6, 129.2, 128.6, 128.5, 127.9, 126.6, 54.4, 33.0, 24.4, 13.3.

HRMS (ESI-TOF) calc'd for $C_{17}H_{18}O_2SNa$ $[M+Na]^+$: 309.0920, found: 309.0927.

*Synthesis of benzyl 7-(2,5-dimethylphenoxy)-4,4-dimethylheptanoate (**4m**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 1.97 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4m** in 95%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 1.97 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4m** in 81%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 118.6 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane to pentane/EtOAc = 20:1) to afford **4m** (103 mg, 0.28 mmol, 93%).

Appearance: colorless oil.

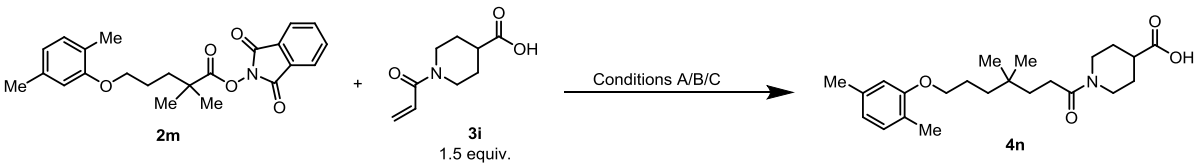
TLC: R_f = 0.55 (pentane/EtOAc = 20:1, UV-active and stains red in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.30 (m, 5H), 7.01 (d, *J* = 8.0 Hz, 1H), 6.67 (d, *J* = 8.0 Hz, 1H), 6.62 (s, 1H), 5.12 (s, 2H), 3.91 (t, *J* = 6.4 Hz, 2H), 2.39 – 2.33 (m, 2H), 2.31 (s, 3H), 2.17 (s, 3H), 1.79 – 1.70 (m, 2H), 1.65 – 1.59 (m, 2H), 1.40 – 1.32 (m, 2H), 0.91 (s, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.1, 157.0, 136.4, 136.1, 130.3, 128.6, 128.2, 128.2, 123.6, 120.6, 112.0, 68.4, 66.2, 37.9, 36.3, 32.3, 29.6, 26.8, 24.2, 21.4, 15.8.

All the data are in accordance with the literature.[10]

*Synthesis of 1-(7-(2,5-dimethylphenoxy)-4,4-dimethylheptanoyl)piperidine-4-carboxylic acid (**4n**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 1.97 mg, 5.0 µmol, 1.0 equiv.), 1-acryloylpiperidine-4-carboxylic acid (**3i**; 1.37 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4n** in 88%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 1.97 mg, 5.0 µmol, 1.0 equiv.), 1-acryloylpiperidine-4-carboxylic acid (**3i**; 1.37 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4n** in 50%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 5-(2,5-dimethylphenoxy)-2,2-dimethylpentanoate (**2m**; 59.0 mg, 0.15 mmol, 1.0 equiv.), 1-acryloylpiperidine-4-carboxylic acid (**3i**; 41.0 mg, 0.23 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 41.0 mg, 0.23 mmol, 1.5 equiv.) in DMSO (1.5 mL) for 1 h. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 3:2 to 3:7 + 1% AcOH) to afford **4n** (45 mg, 0.12 mmol, 77%).

Appearance: colorless oil.

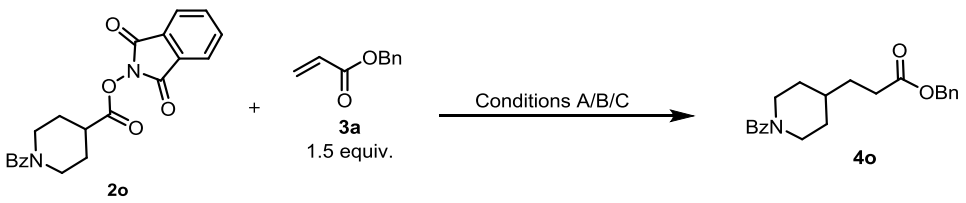
TLC: Rf = 0.27 (Pentane/EtOAc = 1:1 + 1% AcOH, UV-active and stains in PMA).

^{1}H MR (400 MHz, $CDCl_3$) δ (ppm) = 7.00 (d, *J* = 7.4 Hz, 1H), 6.65 (d, *J* = 7.6 Hz, 1H), 6.62 (s, 1H), 4.47 – 4.34 (m, 1H), 3.93 (t, *J* = 6.3 Hz, 2H), 3.82 (d, *J* = 13.7 Hz, 1H), 3.12 (ddd, *J* = 14.0, 11.1, 2.9 Hz, 1H), 2.84 (ddd, *J* = 13.9, 11.0, 3.0 Hz, 1H), 2.57 (tt, *J* = 10.6, 4.0 Hz, 1H), 2.36 – 2.26 (m, 5H), 2.17 (s, 3H), 2.02 – 1.90 (m, 2H), 1.84 – 1.62 (m, 4H), 1.60 – 1.52 (m, 2H), 1.43 – 1.34 (m, 2H), 0.92 (s, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 179.2, 172.6, 157.1, 136.6, 130.4, 123.6, 120.8, 112.1, 68.5, 45.1, 41.2, 40.8, 38.0, 37.1, 32.5, 28.6, 28.5, 27.8, 27.0, 24.4, 21.5, 15.9.

HRMS (ESI-TOF) calc'd for $C_{23}H_{34}NO_4$ $[M-H]^-$: 388.2482, found: 388.2489.

*Synthesis of benzyl 3-(1-benzoylpiperidin-4-yl)propanoate (**4o**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2o**; 1.89 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4o** in 90%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2o**; 1.89 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4o** in 72%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2o**; 98.2 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 8:2 to 6:4) to afford **4o** (77 mg, 0.22 mmol, 73%).[10, 11]

Appearance: colorless oil.

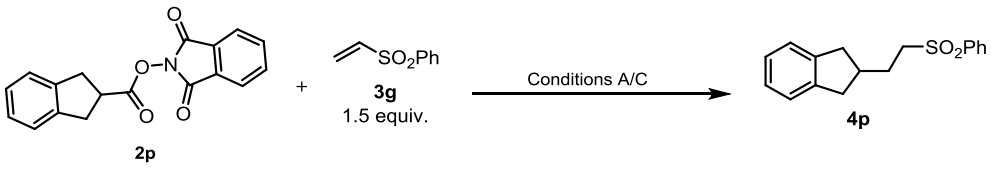
TLC: R_f = 0.45 (pentane/EtOAc = 6:4, UV-active).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.41 – 7.30 (m, 10H), 5.12 (s, 2H), 4.69 (br.s., 1H), 3.72 (br.s., 1H), 3.01 – 2.63 (m, 2H), 2.39 (t, *J* = 7.6 Hz, 2H), 1.86 – 1.46 (m, 5H), 1.32 – 1.05 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.3, 170.3, 136.4, 135.9, 129.4, 128.6, 128.6, 128.4, 128.3, 126.8, 66.3, 47.9, 42.3, 35.6, 31.5, 31.2.

HRMS (ESI-TOF) calc'd for $C_{22}H_{25}NO_3Na$ $[M+Na]^+$: 374.1727; found: 374.1724.

*Synthesis of 2-(2-(phenylsulfonyl)ethyl)-2,3-dihydro-1H-indene (**4p**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 2,3-dihydro-1H-indene-2-carboxylate (**2p**; 1.53 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4p** in 61%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 2,3-dihydro-1H-indene-2-carboxylate (**2p**; 92 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 76 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in 3 mL DMSO for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 5:1) to afford **4p** (45.0 mg, 0.16 mmol, 52%).

Appearance: white solid.

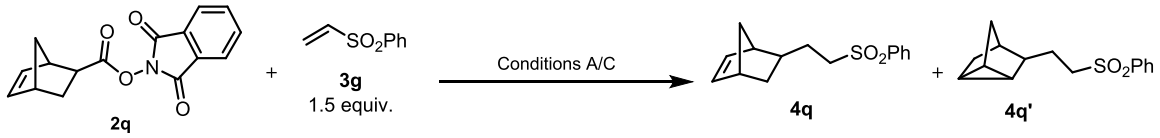
TLC: R_f = 0.50 (petroleum ether/EtOAc = 5:1, UV-active).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.99 – 7.91 (m, 2H), 7.74 – 7.66 (m, 1H), 7.65 – 7.56 (m, 2H), 7.21 – 7.10 (m, 4H), 3.23 – 3.15 (m, 2H), 3.06 (dd, *J* = 14.6, 7.2 Hz, 2H), 2.63 – 2.46 (m, 3H), 2.02 – 1.90 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 142.3, 139.1, 133.6, 129.2, 128.0, 126.3, 124.3, 55.2, 38.7, 38.6, 28.2.

All the data are in accordance with the literature.[10]

*Synthesis of (1S,4S)-5-(2-(phenylsulfonyl)ethyl)bicyclo[2.2.1]hept-2-ene (**4q**) and 3-(2-(phenylsulfonyl)ethyl)tricyclo[2.2.1.02,6]heptane (**4q'**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl (1*R*,4*R*)-bicyclo[2.2.1]hept-5-ene-2-carboxylate (**2q**; 1.41 mg, 5.0 µmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 1.26 mg, 7.5 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4q,q'** in 78% as a mixture (1.2:1).

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl (1*R*,4*R*)-bicyclo[2.2.1]hept-5-ene-2-carboxylate (**2q**; 85 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 75 mg, 0.45 mmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 15 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 19:1 to 9:1) to afford **4q**,**q'** (43 mg, 0.16 mmol, 57%) as inseparable mixture (1.2:1).

Appearance: colorless oil.

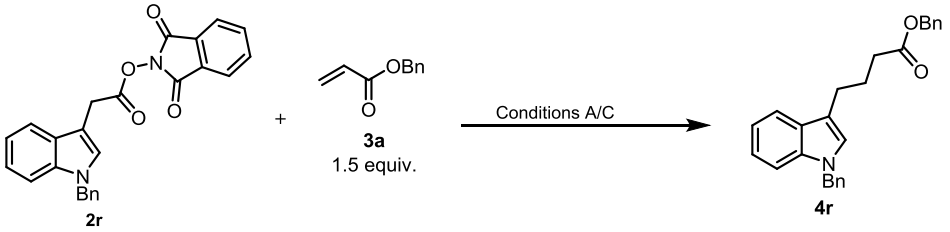
TLC: R_f = 0.55 (pentane/EtOAc = 6:1, UV-active and stains in permanganate).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.94 – 7.87 (m, 4H), 7.69 – 7.62 (m, 2H), 7.61 – 7.54 (m, 4H), 6.02 (dt, *J* = 2.5, 1.1 Hz, 2H; **4q**), 3.17 – 3.00 (m, 4H), 2.79 (dq, *J* = 3.5, 1.6 Hz, 1H; **4q**), 2.47 (dt, *J* = 3.0, 1.4 Hz, 1H; **4q**), 1.87 – 1.70 (m, 2H), 1.67 – 1.64 (m, 1H; **4q'**), 1.63 – 1.50 (m, 2H), 1.46 (qt, *J* = 7.5, 1.8 Hz, 1H; **4q'**), 1.37 – 1.18 (m, 7H), 1.12 – 0.98 (m, 4H), 0.86 (tt, *J* = 5.2, 1.2 Hz, 1H; **4q'**).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 139.3, 139.2, 136.6, 136.3, 133.6, 133.6, 129.3, 129.2, 128.0, 128.0, 55.8, 55.3, 46.1, 45.1, 43.8, 41.9, 37.8, 34.0, 32.7, 32.6, 28.9, 28.9, 22.7, 14.5, 11.5, 9.6.

HRMS (ESI-TOF) calc'd for $C_{15}H_{18}O_2SNa$ $[M+Na]^+$: 285.0920; found: 285.0929.

*Synthesis of benzyl 4-(1-benzyl-1H-indol-3-yl)butanoate (**4r**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 2-(1-benzyl-1*H*-indol-3-yl)acetate (**2r**; 2.05 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4r** in 50%. The reaction was also performed in water (1 mM), which gave rise to 51% ^{1}H-NMR yield of **4r**.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 2-(1-benzyl-1H-indol-3-yl)acetate (**2r**; 123.1 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 2 h. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 99:1 to 98:2) to afford **4r** (35 mg, 0.09 mmol, 30%).

Appearance: white solid.

TLC: R_f = 0.47 (pentane/EtOAc = 19:1, UV-active and stains violet in vanillin).

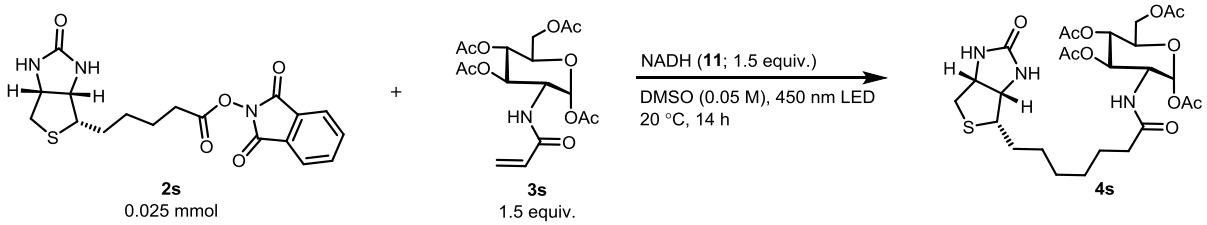
m.p.: 40.1 – 43.1 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.59 (dd, *J* = 7.8, 1.0 Hz, 1H), 7.39 – 7.30 (m, 5H), 7.30 – 7.22 (m, 4H), 7.16 (ddd, *J* = 8.3, 7.0, 1.3 Hz, 1H), 7.13 – 7.06 (m, 3H), 6.88 (s, 1H), 5.26 (s, 2H), 5.11 (s, 2H), 2.81 (td, *J* = 7.5, 0.9 Hz, 2H), 2.44 (t, *J* = 7.4 Hz, 2H), 2.07 (p, *J* = 7.5 Hz, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.5, 137.7, 136.7, 136.1, 128.7, 128.5, 128.2, 128.2, 128.1, 127.5, 126.8, 125.7, 121.7, 119.1, 118.9, 114.8, 109.6, 66.1, 49.9, 33.9, 25.5, 24.4.

HRMS (ESI-TOF) calc'd for $C_{26}H_{25}NO_2Na$ $[M+Na]^+$: 406.1778; found: 406.1772.

*Synthesis of biotin-glucosamine conjugate (**4s**)*



Biotin NHPI-ester (**2s**; 9.7 mg, 25.0 µmol, 1.0 equiv.), *N*-acroloyl glucosamine derivative (**3s**; 15.1 mg, 38.0 µmol, 1.5 equiv.), and NADH (**11**; 26.6 mg, 38.0 µmol, 1.5 equiv.) were carefully added in a vial. The vial was then evacuated and refilled with argon (three cycles). DMSO (0.5 mL) was added to the vial. The mixture was irradiated with blue light for 14 h. Upon completion, water (10 mL) and $CHCl_3$ (10 mL) were added to the reaction mixture. The organic layer was separated and the aqueous layer was extracted with $CHCl_3$ (2x10 mL). The combined organic layer was washed with brine (10 mL), dried over Na_2SO_4, and concentrated under

reduced pressure. The crude was purified by column chromatography on SiO_2 (DCM/methanol = 99:1 to 9:1) followed by recrystallization with DCM/petroleum ether to afford **4s**.

^{1}H-NMR yield: 49%

Appearance: white solid.

TLC: R_f = 0.5 (DCM/methanol = 9:1, stains in permanganate).

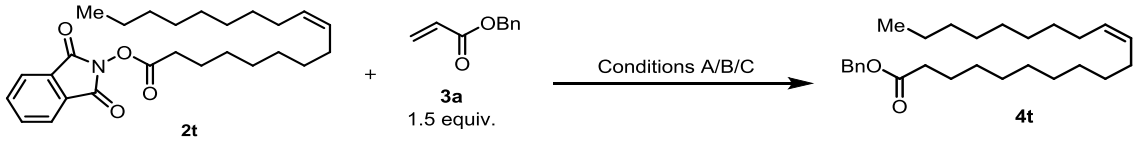
m.p.: 133.4 – 137.6 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 6.60 (d, *J* = 9.6 Hz, 1H), 5.99 (s, 1H), 5.73 (d, *J* = 8.8 Hz, 1H), 5.31 – 5.09 (m, 3H), 4.54 (dd, *J* = 7.8, 5.0 Hz, 1H), 4.41 – 4.24 (m, 3H), 4.11 (dd, *J* = 12.5, 2.2 Hz, 1H), 3.82 (ddd, *J* = 9.5, 4.6, 2.2 Hz, 1H), 3.16 (q, *J* = 7.1, 6.2 Hz, 1H), 2.94 (dd, *J* = 12.8, 5.0 Hz, 1H), 2.74 (d, *J* = 12.6 Hz, 1H), 2.19 – 1.97 (m, 14H), 1.76 – 1.68 (m, 1H), 1.45 – 1.19 (m, 7H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.5, 171.3, 170.7, 169.6, 169.3, 163.6, 92.7, 73.0, 72.7, 67.9, 62.0, 61.7, 60.2, 55.6, 52.6, 40.4, 36.6, 28.9, 28.8, 28.6, 28.4, 25.6, 21.0, 20.8, 20.8, 20.6.

HRMS (ESI-TOF) calc'd for $C_{26}H_{39}N_3O_{11}SNa$ $[M+Na]^+$: 624.2198; found: 624.2199.

*Synthesis of benzyl (Z)-icos-11-enoate (**4t**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2t**; 2.13 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in DMSO (5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4t** in 61%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2t**; 2.13 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in DMSO (0.25 mL) for 75 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4t** in 64%.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl oleate (**2t**; 128 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 20:1) to afford **4t** (85.0 mg, 0.21 mmol, 71%).

Appearance: colorless oil.

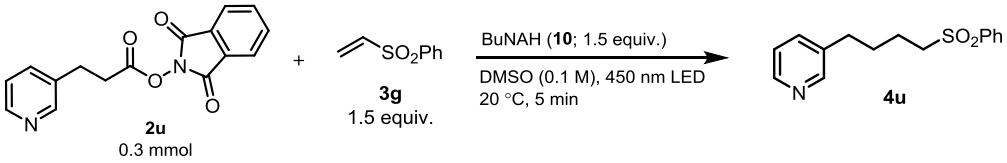
TLC: R_f = 0.41 (petroleum ether/EtOAc = 10:1, UV-active and stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.39 – 7.30 (m, 5H), 5.39 – 5.30 (m, 2H), 5.14 (s, 2H), 2.38 (t, *J* = 7.5 Hz, 2H), 2.12 – 1.97 (m, 4H), 1.64 (q, *J* = 7.3 Hz, 1H), 1.40 – 1.24 (m, 24H), 0.94 – 0.87 (m, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.6, 136.1, 129.9, 129.8, 128.5, 128.1, 128.1, 66.0, 34.3, 31.9, 29.7, 29.7, 29.5, 29.4, 29.4, 29.3, 29.2, 29.2, 29.1, 27.2, 24.9, 22.6, 14.0.

All the data are in accordance with the literature.[10]

*Synthesis of 3-(4-(phenylsulfonyl)butyl)pyridine (**4u**)*



General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl 3-(pyridin-3-yl)propanoate (**2u**; 89 mg, 0.30 mmol, 1.0 equiv.), phenyl vinyl sulfone (**3g**; 76 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 0.45 mmol, 81 mg, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (petroleum ether/EtOAc = 1:1) to afford **4u** (44.0 mg, 0.16 mmol, 53%).

Appearance: yellow oil.

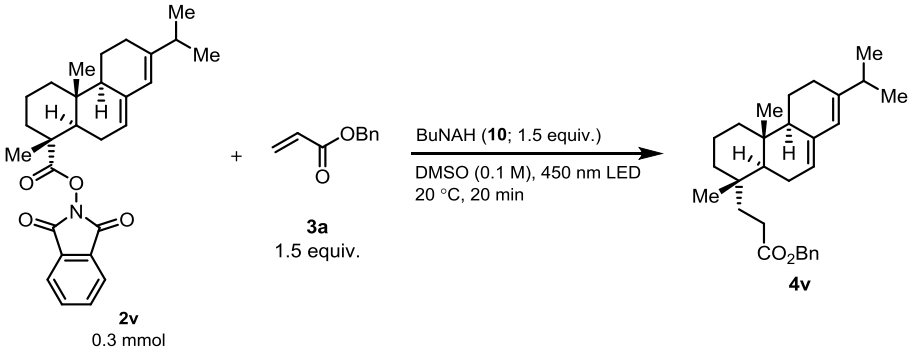
TLC: R_f = 0.15 (petroleum ether/EtOAc = 1:1, UV-active).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 8.44 (dd, J = 4.8, 1.7 Hz, 1H), 8.39 (d, J = 2.3 Hz, 1H), 7.97 – 7.83 (m, 2H), 7.71 – 7.63 (m, 1H), 7.61 – 7.53 (m, 2H), 7.45 (dt, J = 7.8, 2.0 Hz, 1H), 7.21 (ddd, J = 7.8, 4.8, 0.9 Hz, 1H), 3.20 – 2.98 (m, 2H), 2.61 (t, J = 7.3 Hz, 2H), 1.87 – 1.64 (m, 4H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 149.7, 147.6, 139.2, 136.6, 135.9, 133.8, 129.4, 128.1, 123.5, 56.0, 32.5, 29.7, 22.3.

HRMS (ESI-TOF) calc'd for $C_{15}H_{17}NO_2SH$ $[M+H]^+$: 276.1053; found: 276.1055.

*Synthesis of derivative of abietic acid (**4v**)*



General procedure B3 was applied using redox-active ester of abietic acid (**2v**; 134.3 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 20 min. The crude product was purified by column chromatography on SiO_2 (pentane to pentane/EtOAc = 99:1) to afford **4v** (87 mg, 0.20 mmol, 69%) with d.r. > 20:1.

Appearance: colorless oil.

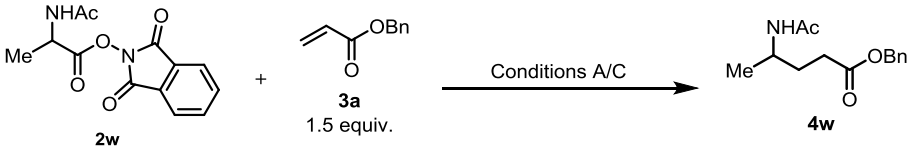
TLC: R_f = 0.64 (pentane/EtOAc = 98:2, UV-active and stains green in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.29 (m, 5H), 5.78 (s, 1H), 5.40 (dt, *J* = 5.2, 2.4 Hz, 1H), 5.09 (s, 2H), 2.30 – 2.19 (m, 3H), 2.13 – 2.04 (m, 3H), 2.01 – 1.94 (m, 1H), 1.88 – 1.76 (m, 3H), 1.66 – 1.45 (m, 5H), 1.36 (dtd, *J* = 12.8, 3.2, 1.6 Hz, 1H), 1.31 – 1.25 (m, 1H), 1.24 – 1.14 (m, 2H), 1.01 (ddd, *J* = 7.2, 3.7, 1.8 Hz, 6H), 0.93 (s, 3H), 0.82 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.3, 145.2, 136.1, 135.4, 128.5, 128.2, 128.2, 122.4, 121.1, 66.2, 51.1, 47.9, 39.0, 38.6, 37.6, 35.1, 34.9, 34.9, 28.9, 27.5, 23.7, 22.7, 21.4, 20.8, 20.6, 18.5, 14.1.

HRMS (ESI-TOF) calc'd for $C_{29}H_{40}O_2Na$ $[M+Na]^+$: 443.2931; found: 443.2930.

*Synthesis of benzyl 4-acetamidopentanoate (**4w**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 2-(1-benzyl-1H-indol-3-yl)acetate (**2w**; 1.38 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in a mixture of DMSO (2.5 mL) and water (2.5 mL) for 60 min under air. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4w** in 75%. The reaction was also performed in water (1 mM), which gave rise to 60% ^{1}H-NMR yield of **4w**.

General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl acetylalaninate (**2w**; 83 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by preparative TLC (DCM/MeOH/Et_3N = 50:1:1) to afford **4w** (27.0 mg, 0.11 mmol, 36%).

Appearance: white solid.

TLC: R_f = 0.20 (petroleum ether/EtOAc = 1:1, UV-active and stains in iodine).

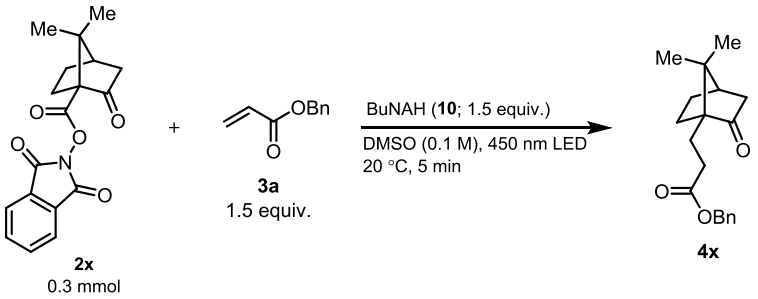
m.p.: 64.3 – 66.5 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.45 – 7.29 (m, 5H), 5.48 – 5.36 (m, 1H), 5.19 – 5.09 (m, 2H), 4.11 – 3.94 (m, 1H), 2.54 – 2.33 (m, 2H), 1.92 (s, 3H), 1.87 – 1.73 (m, 2H), 1.17 (d, *J* = 6.6 Hz, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.6, 169.6, 136.0, 128.7, 128.4, 128.3, 66.5, 45.3, 31.6, 31.3, 23.5, 21.2.

HRMS (ESI-TOF) calc'd for $C_{14}H_{19}NO_3Na$ $[M+Na]^+$: 272.1257; found: 272.1250.

*Synthesis of benzyl 3-((1R,4R)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptan-1-yl)propanoate (**4x**)*



General procedure B3 was applied using 1,3-dioxoisoindolin-2-yl (1*R*,4*R*)-7,7-dimethyl-2-oxobicyclo[2.2.1]heptane-1-carboxylate (**2x**; 98.2 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 98:2 to 19:1) to afford **4x** (51 mg, 0.17 mmol, 56%).

Appearance: white solid.

TLC: R_f = 0.45 (Pentane/EtOAc = 12:1, UV-active and stains blue in vanillin).

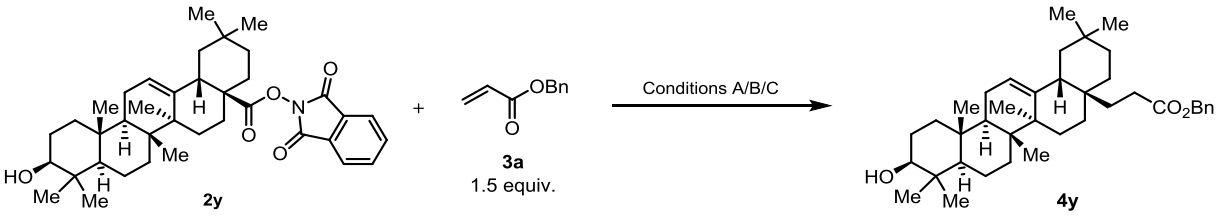
m.p.: 45.7 – 49.4 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.29 (m, 5H), 5.12 (s, 2H), 2.88 (ddd, *J* = 16.6, 11.5, 5.2 Hz, 1H), 2.39 – 2.27 (m, 2H), 2.05 (t, *J* = 4.5 Hz, 1H), 2.00 – 1.92 (m, 1H), 1.92 – 1.85 (m, 1H), 1.81 (d, *J* = 18.3 Hz, 1H), 1.75 – 1.67 (td, *J* = 16.0, 4.0 Hz, 1H), 1.64 – 1.55 (m, 1H), 1.45 (ddd, *J* = 13.3, 9.3, 4.4 Hz, 1H), 1.35 (ddd, *J* = 12.9, 9.3, 3.7 Hz, 1H), 0.96 (s, 3H), 0.88 (s, 3H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 218.9, 173.9, 136.1, 128.5, 128.3, 128.2, 66.2, 59.2, 47.5, 43.4, 43.3, 29.8, 26.9, 26.7, 20.9, 20.2, 19.5.

HRMS (ESI-TOF) calc'd for $C_{19}H_{24}O_3Na$ $[M+Na]^+$: 323.1618; found: 323.1620.

*Synthesis of derivative of oleanolic acid (**4y**)*



General procedure B1 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2y**; 3.0 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 2.71 mg, 0.015 mmol, 3.0 equiv.) in DMSO (5 mL) for 60 min under argon. The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4y** in 74%.

General procedure B2 was applied using 1,3-dioxoisoindolin-2-yl 1-benzoylpiperidine-4-carboxylate (**2y**; 2.13 mg, 5.0 µmol, 1.0 equiv.), benzyl acrylate (**3a**; 1.21 mg, 7.5 µmol, 1.5 equiv.), NADH (**11**; 35.0 mg, 0.05 mmol, 10.0 equiv.) in DMSO (0.02 M) for 75 min under argon.

The crude yield was measured by ^{1}H-NMR in presence of 1,1,2,2-tetrachloroethane to obtain **4y** in 71%.

General procedure B3 was applied using redox-active ester of oleanolic acid (**2y**; 180.5 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 25 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 19:1 to 9:1) to afford **4y** (138 mg, 0.24 mmol, 80%) with d.r. > 20:1.

Appearance: white solid.

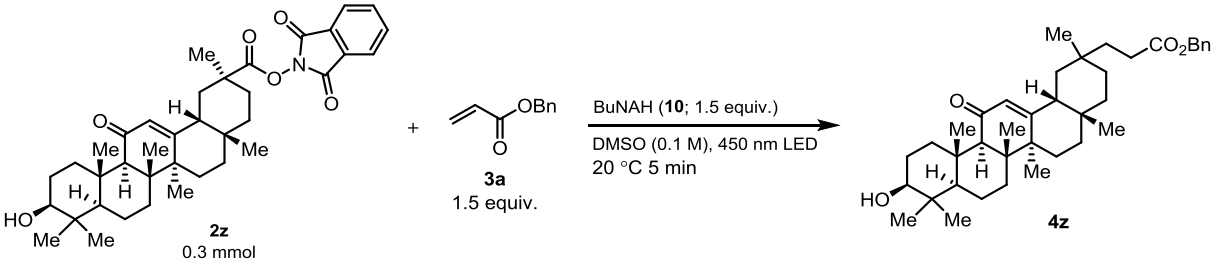
TLC: R_f = 0.53 (pentane/EtOAc = 8:2, UV-active and stains blue in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.39 – 7.29 (m, 5H), 5.19 (t, *J* = 3.6 Hz, 1H), 5.09 (d, *J* = 0.9 Hz, 2H), 3.22 (d, *J* = 9.2 Hz, 1H), 2.33 – 2.18 (m, 2H), 2.00 – 1.79 (m, 5H), 1.71 (t, *J* = 13.6 Hz, 1H), 1.67 – 1.53 (m, 4H), 1.56 – 1.52 (m, 2H), 1.52 – 1.33 (m, 2H), 1.33 – 1.22 (m, 6H), 1.14 (s, 3H), 1.13 – 1.08 (m, 1H), 1.07 – 1.01 (m, 1H), 1.00 (s, 3H), 0.97 – 0.88 (m, 9H), 0.87 (s, 3H), 0.85 (s, 3H), 0.80 (s, 3H), 0.73 (dd, J = 11.5, 1.9 Hz, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 174.3, 144.3, 136.1, 128.5, 128.2, 128.1, 122.5, 79.0, 66.1, 55.2, 47.7, 47.0, 46.6, 41.6, 39.8, 38.8, 38.6, 36.9, 34.8, 34.4, 33.2, 32.8, 32.5, 30.9, 28.4, 28.1, 27.3, 26.1, 25.7, 23.6, 23.0, 22.3, 18.3, 16.7, 15.6, 15.5, 14.0.

All the data are in accordance with the literature.[5]

*Synthesis of derivative of 18β-Glycyrrhetinic acid (**4z**)*



General procedure B3 was applied using redox-active ester of 18 β-Glycyrrhetinic acid (**2z**; 184.7 mg, 0.30 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 73 mg, 0.45 mmol, 1.5 equiv.), 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 81 mg, 0.45 mmol, 1.5 equiv.) in DMSO (3 mL) for 5 min. The crude product was purified by column chromatography on SiO_2 (pentane/EtOAc = 9:1 to 8:2) to afford **4z** (140 mg, 0.23 mmol, 79%) with d.r. = 1.3:1.

Appearance: white foam.

TLC: R_f = 0.68 (pentane/EtOAc = 7:3, UV-active and stains blue in vanillin).

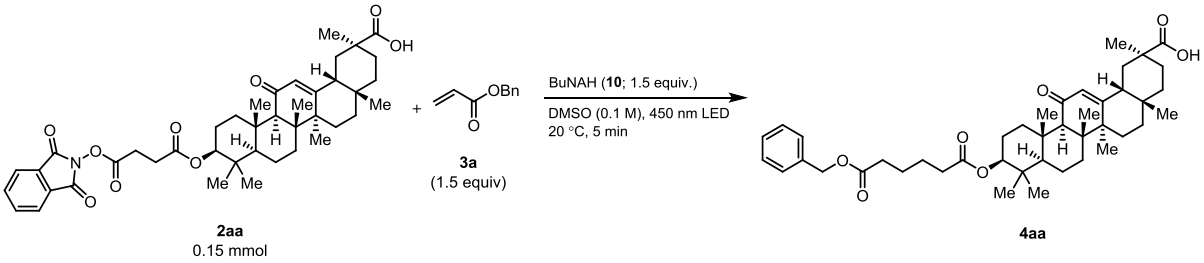
^{1}H-NMR (400 MHz, $CDCl_3$; mixture of diastereomers) δ (ppm) = 7.39 – 7.29 (m, 5H), 5.57 (s, 1H), 5.11 (dd, *J* = 8.0, 1.3 Hz, 2H), 3.25 – 3.19 (m, 1H), 2.79 (dq, *J* = 13.5, 3.4 Hz, 1H), 2.37 – 2.29 (m, 2H), 2.24 (t, *J* = 8.4 Hz, 1H), 2.15 – 1.96 (m, 2H), 1.81 (tt, *J* = 13.6, 4.2 Hz, 1H), 1.71 – 1.55 (m, 7H), 1.49 – 1.39 (m, 3H), 1.36 – 1.25 (m, 6H), 1.22 – 1.04 (m, 9H), 1.00 (s, 3H), 0.99 – 0.92 (m ,2H), 0.85 (m, 6H), 0.80 (m, 3H), 0.73 – 0.65 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$; mixture of diastereomers) δ (ppm) = 200.2, 200.1, 174.1, 174.0, 170.1, 169.9, 136.0, 128.6, 128.3, 128.2, 128.2, 78.8, 77.2, 66.3, 66.3, 61.8, 55.0, 54.9, 47.1,

46.8, 45.4, 45.4, 43.4, 43.4, 43.2, 43.1, 40.4, 39.1, 37.1, 37.1, 36.0, 35.8, 33.3, 33.0, 32.8, 32.8, 32.7, 32.6, 32.3, 32.2, 29.7, 29.0, 28.9, 28.8, 28.7, 28.6, 28.1, 27.3, 26.7, 26.4, 26.4, 26.4, 23.5, 23.4, 20.5, 18.7, 17.5, 16.4, 15.6.

HRMS (ESI-TOF) calc'd for $C_{39}H_{56}O_4Na$ $[M+Na]^+$: 611.4071; found: 611.4085.

*Synthesis of derivative of 18β-Glycyrrhetinic acid (**4aa**)*



General procedure B3 was applied using (3β,18β,20β)-3-((4-((1,3-dioxoisoindolin-2-yl)oxy)-4-oxobutanoyl)oxy)-11-oxo-olean-12-en-29-oic acid (**2aa**; 110 mg, 0.15 mmol, 1.0 equiv.), benzyl acrylate (**3a**; 37.4 mg, 0.23 mmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 41.5 mg, 0.23 mmol, 1.5 equiv.) in DMSO (1.5 mL) for 5 min. The crude product was purified by preparative TLC (DCM/EtOAc = 1:1) to afford **4aa** (48.0 mg, 0.07 mmol, 45%).

Appearance: white solid.

TLC: R_f = 0.34 (DCM/MeOH = 20:1, UV-active).

M.pt. = 229.5 – 230.6 °C.

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.40 – 7.29 (m, 5H), 5.71 (s, 1H), 5.11 (s, 2H), 4.52 (dd, *J* = 11.6, 4.9 Hz, 1H), 2.79 (dt, *J* = 13.6, 3.7 Hz, 1H), 2.44 – 2.26 (m, 5H), 2.23 – 2.13 (m, 1H), 2.08 – 1.91 (m, 3H), 1.88 – 1.77 (m, 1 H), 1.75 – 1.52 (m, 8H), 1.51 – 1.33 (m, 8H), 1.31 (d, *J* = 6.1 Hz, 1H), 1.28 – 1.19 (m, 5H), 1.16 (s, 3H), 1.13 (s, 3H), 1.08 – 1.01 (m, 2H), 0.86 (d, *J* = 2.9 Hz, 6H), 0.84 (s, 3H), 0.82 – 0.77 (m, 1H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 200.5, 181.6, 173.3, 173.2, 169.6, 136.1, 128.7, 128.6, 128.4, 128.3, 80.7, 66.4, 61.8, 55.2, 48.4, 45.6, 43.9, 43.4, 41.0, 38.9, 38.2, 37.9, 37.1, 34.5, 34.1, 32.8, 32.0, 31.1, 28.7, 28.6, 28.2, 26.6, 26.6, 24.7, 24.6, 23.7, 23.5, 18.8, 17.5, 16.9, 16.5.

HRMS (ESI-TOF) calc'd for $C_{43}H_{60}NO_7Na$ $[M+Na]^+$: 711.4231; found: 711.4222.

5. Alkyl photo-coupling on DNA.

LCMS Analysis

Liquid chromatography-mass spectrometry (HPLC-MS) analyses were performed on Agilent 1260 Infinity II system using an Electrospray ionization (ESI) ion source.

Column: Reverse phase (YMC-Triart C18, 5 µm particle size, 4.6 mm x 150 mm); column temperature: 40 °C; flow rate: 0.8 mL/min.

Mobile phase: (A). 0.038% v/v Et_3N, 0.75% v/v HFIP in H_2O; (B). 0.038% v/v Et_3N, 0.75% v/v HFIP in 9:1 MeOH/H_2O.

Gradient: 5 to 95% B over 10 min.

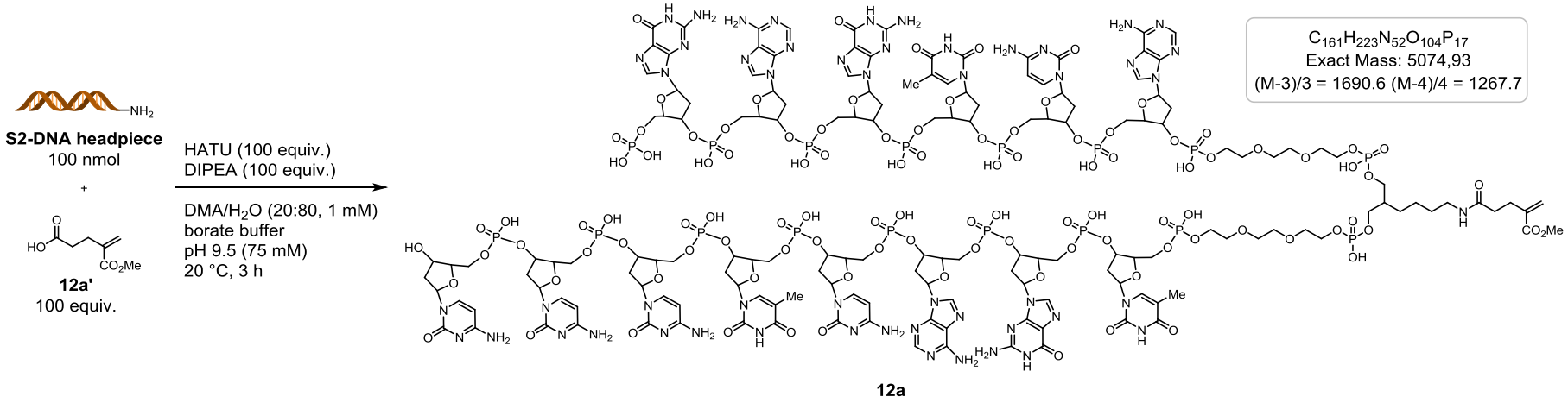
UV detection: 260 nm.

MS data: range: 500-2000 *m/z*; ionization polarity: negative, triply charged mass was observed (M–3)/3.

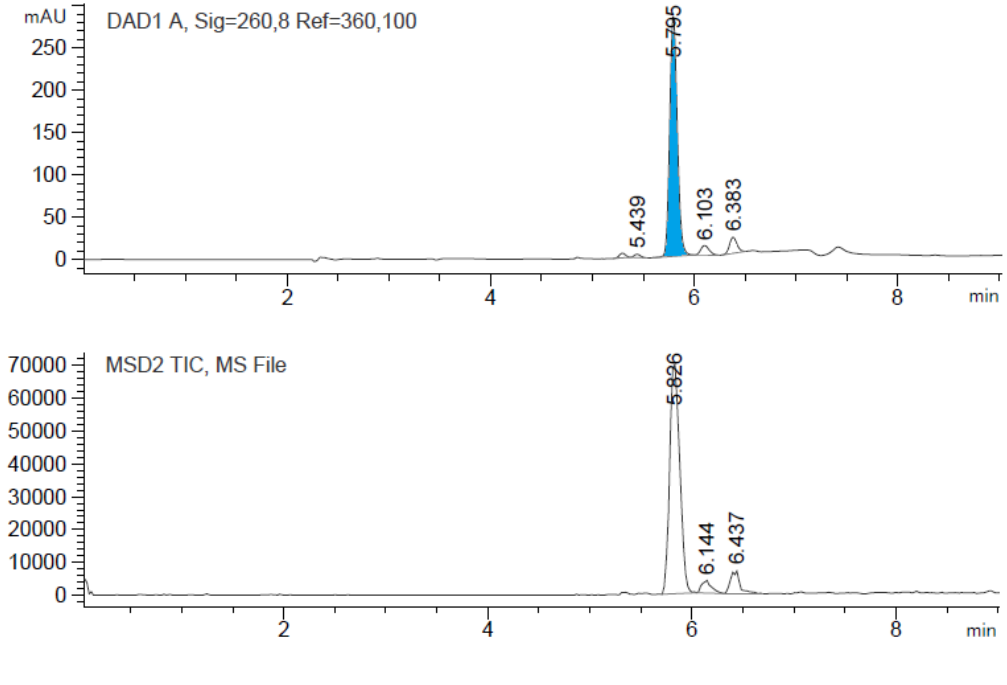
Sample preparation: 10–20 µL of DNA stock solution (0.1 mM) in a mixture of 0.038% v/v Et_3N, 0.75% v/v HFIP in H_2O/MeOH (95.5:4.5) (130 µL)

Injection amount: 20 µL.

*Synthesis of DNA acrylate **12a***



The DNA acrylate **12a** was synthesized according to the literature procedure.[17] A 1.0 M solution of 4-(methoxycarbonyl)pent-4-enoic acid (**12a'**; 10 µL, 10 µmol, 100 equiv.) in H_2O and *N,N*-diisopropylethylamine (DIPEA; 10 µL, 10 µmol, 1.0 M in DMA, 100 equiv.) were added in an Eppendorf tube containing 1-[bis(dimethylamino)methylene]-1*H*-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU; 3.8 mg, 10 µmol, 100 equiv.). The reaction mixture was vortexed and allowed to stand at room temperature for 1 h, followed by the addition to a solution of the DNA headpiece (**S2**; 5 µL, 20 mM in H_2O, 0.1 µmol, 1.0 equiv.) in borate buffer (75 µL, 100 mM, pH 9.5). The mixture was vortexed and allowed to stand at room temperature for 2 h. Sodium chloride (10 µL, 5.0 M in H_2O) and cold ethanol (0.3 mL) were added. The resulting mixture was vortexed and allowed to stand at –20 °C for 30 min. The suspension was centrifuged at 12000 RPM for 3 min. After discarding the supernatant, the pellet was dried under reduced pressure and redissolved in H_2O (200 µL) to afford a stock solution of DNA acrylate **12a** (0.5 mM).



Signal 1: DAD1 A, Sig=260,8 Ref=360,100

Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.295	BB	0.0692	23.59167	5.48505	1.4234
2	5.439	BB	0.0667	16.15655	3.87164	0.9748
3	5.795	BB	0.0800	1457.12097	283.31946	87.9148
4	6.103	BB	0.0887	64.36923	11.25957	3.8837
5	6.383	BB	0.0792	96.18471	18.96378	5.8033
Totals :				1657.42313	322.89949	

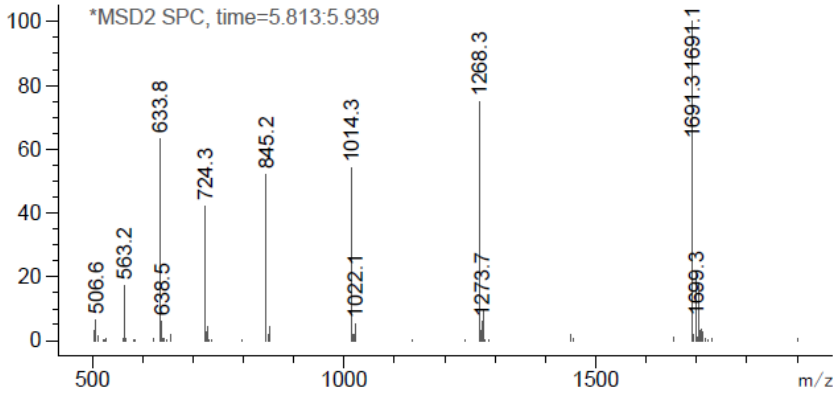
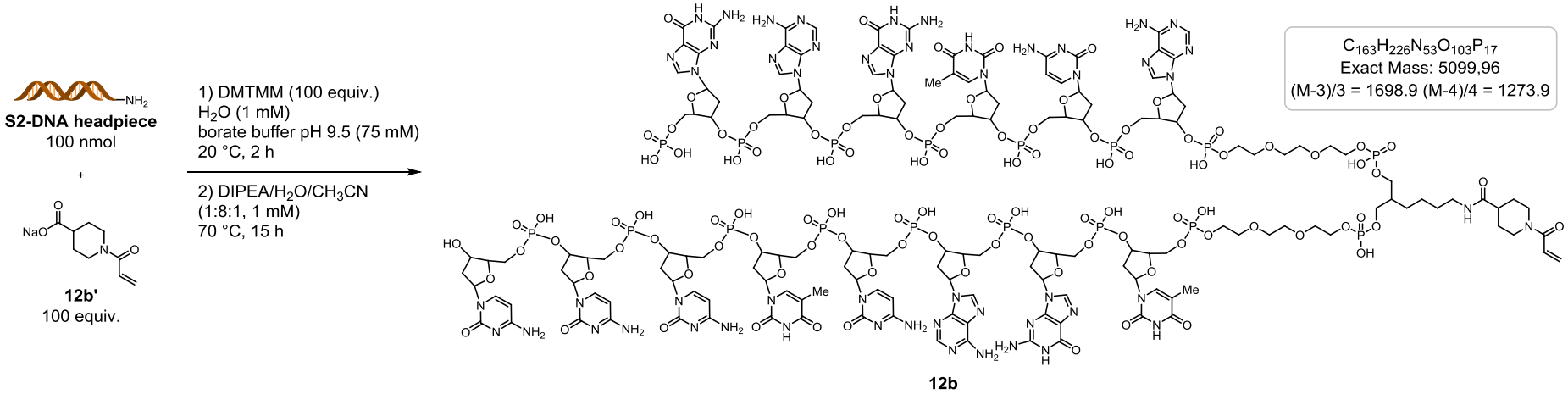


***Figure S4**: LCMS traces of DNA acrylate **12a**.*

The by-products formed in the synthesis of DNA acrylates were not taken into account for the yield determination of the following photo-ligated coupling reactions.

*Synthesis of DNA acrylamide **12b***



The DNA amide **12b** was synthesized according to the literature procedure.[17] Sodium 1-acryloylpiperidine-4-carboxylate (**12b'**) was prepared as a 1.0 M solution in H_2O using 1-acryloylpiperidine-4-carboxylic acid (1.8 mg, 10 µmol, 100 equiv.) and sodium hydroxide (0.40 mg, 10 µmol, 100 equiv.). Sodium 1-acryloylpiperidine-4-carboxylate (**12b'**, 10 µL, 10 µmol, 1.0 M in H_2O, 100 equiv.), 4-(4,6-dimethoxy-1,3,5-triazin-2-yl)-4-methylmorpholinium chloride (DMTMM; 10 µL, 10 µmol, 1.0 M in H_2O, 100 equiv.), borate buffer (75 µL, 100 mM, pH 9.5), and DNA headpiece (**S2**; 5 µL, 20 mM in H_2O, 0.1 µmol, 1.0 equiv.) were added in a 1.5 mL Eppendorf tube. The reaction mixture was vortexed and allowed to stand at room temperature for 2 h. Sodium chloride (10 µL, 5.0 M in H_2O) and cold ethanol (0.3 mL) were added to the mixture. The suspension was mixed by vortex and allowed to stand at –20 °C for 30 min. Then, the mixture was centrifuged at 12000 RPM for 3 min and the supernatant was discarded. The pellet obtained was dried under reduced pressure and dissolved in a mixture of H_2O (80 µL), MeCN (10 µL), and *N,N*-diisopropylethylamine (DIPEA ;10 µL). The resulting mixture was heated at 70 °C for 15 h. After cooling to room temperature, sodium chloride (10 µL, 5.0 M in H_2O) and cold ethanol (0.3 mL) were added. The mixture was vortexed and allowed to stand at –20 °C for 30 min. The suspension was centrifuged at 12000 RPM for 3 min and after discarding the supernatant, the pellet was dried under reduced pressure and redissolved in H_2O (200 µL) to afford a stock solution of DNA acrylamide **12b** (0.5 mM).

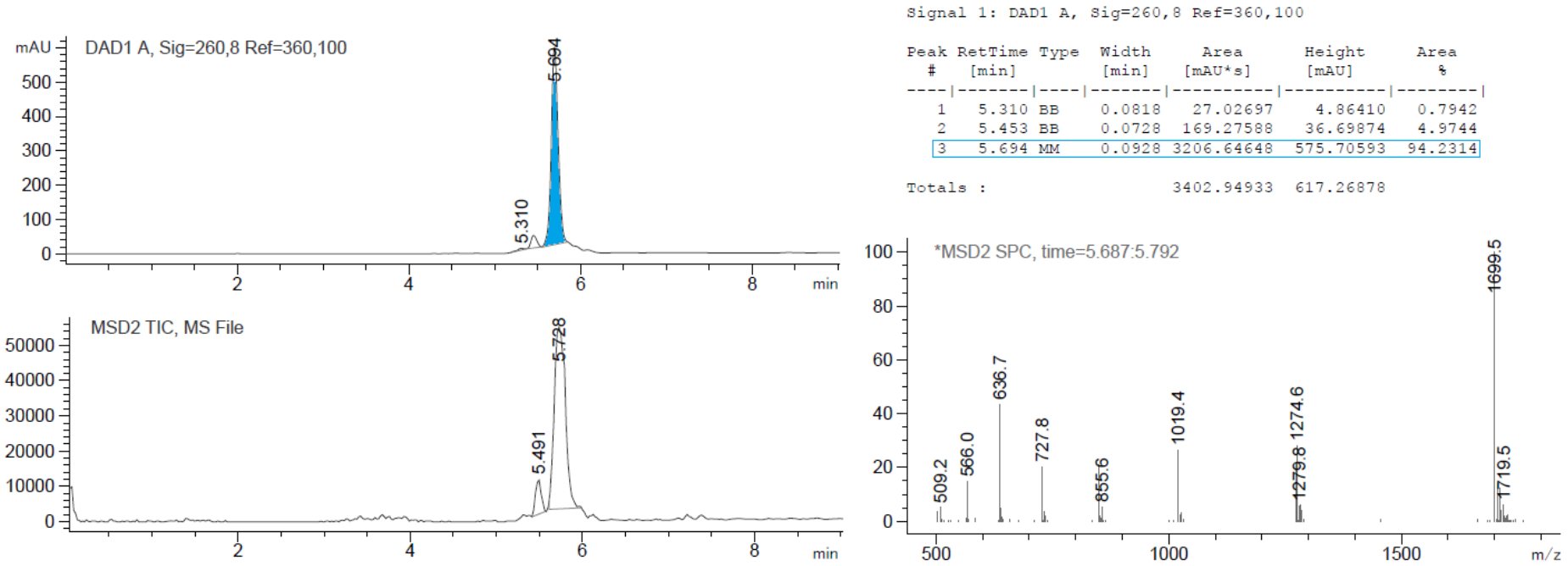
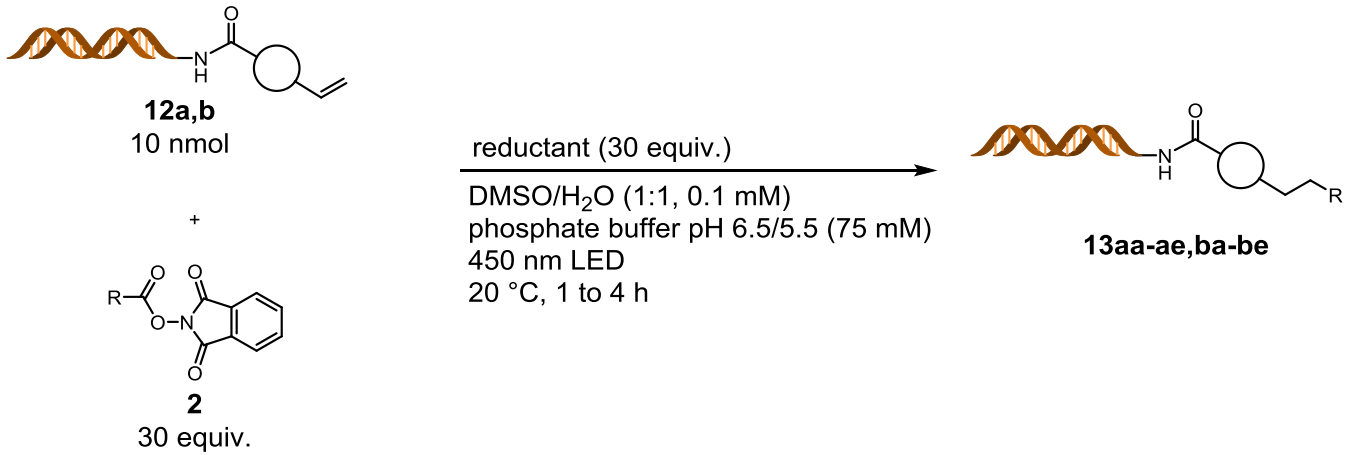


***Figure S5**: LCMS traces of DNA acrylamide **12b**.*

General procedure (C): Photo-mediated decarboxylative coupling of redox-active esters with DNA Michael acceptors.



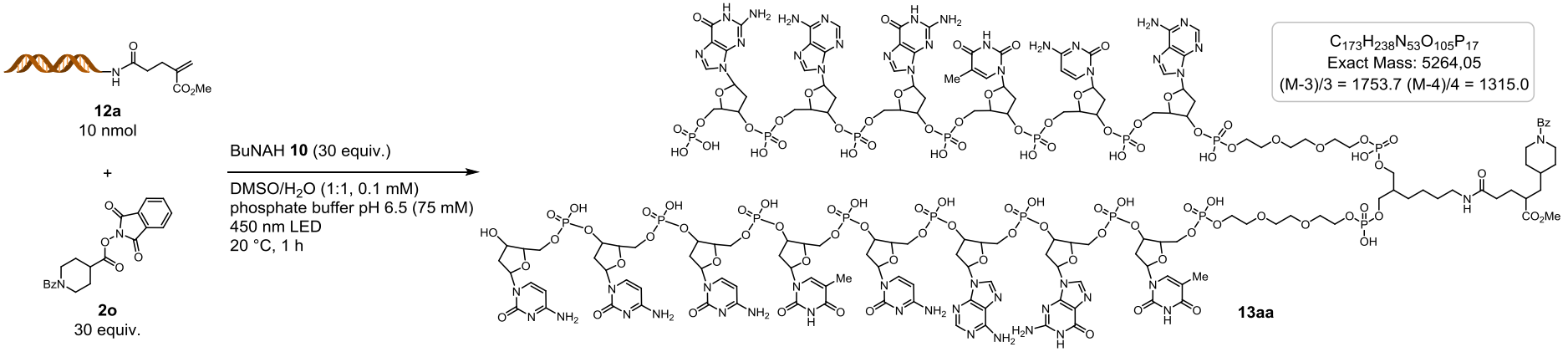
DNA containing electron poor olefin **12a,b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1 equiv.), redox-active ester **2** (3 mM in DMSO, 300 nmol, 30 equiv.), BuNAH (**10**; 3 mM in DMSO, 300 nmol, 30 equiv.) or NADH (**11**; 3 mM in DMSO, 300 nmol, 30 equiv.), DMSO (30 µL), and phosphate buffer (30 µL 250 mM, pH 6.5) were added to a screw top vial. The vial was closed with a septum, evacuated for 2 s and refilled with argon (six times). The mixture was then irradiated with blue LEDs for 1 to 4 h at room temperature (using a fan from the top for cooling the reaction mixture). Sodium chloride (10 µL, 5.0 M in H_2O) and cold ethanol (0.3 mL) were added. The mixture was vortexed and allowed to stand at –20 °C for 30 min. The suspension was centrifuged at 12000 RPM for 3 min, and after discarding the supernatant, the pellet was dried under reduced pressure and redissolved in H_2O (100 µL) to give a stock solution of DNA product **13aa-ae,ba-be** (0.1 mM).

Yield determination of the photo mediated decarboxylative coupling reaction of DNA acrylates

The yield of the photo-mediated decarboxylative coupling reaction of DNA acrylates was determined by LC-MS as reported in the literature for DEL synthesis[17-20] by integration of the UV absorbance at 260 nm, assuming total DNA recovery and that all DNA compounds have similar UV absorbance. To calculate the yield the area of the product was divided by the summed up area of all DNA containing compounds. Non-DNA impurities (molecular weight < 1000 g/mol) were not included in the yield calculation.

$$\text{Yield (\%)} = \frac{Area\ (peak\ of\ the\ DNA\ product)}{Area\ (all\ DNA\ containing\ compounds)}$$

*Synthesis of DNA functionalized product **13aa** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2o** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 78% (4% s.m.)

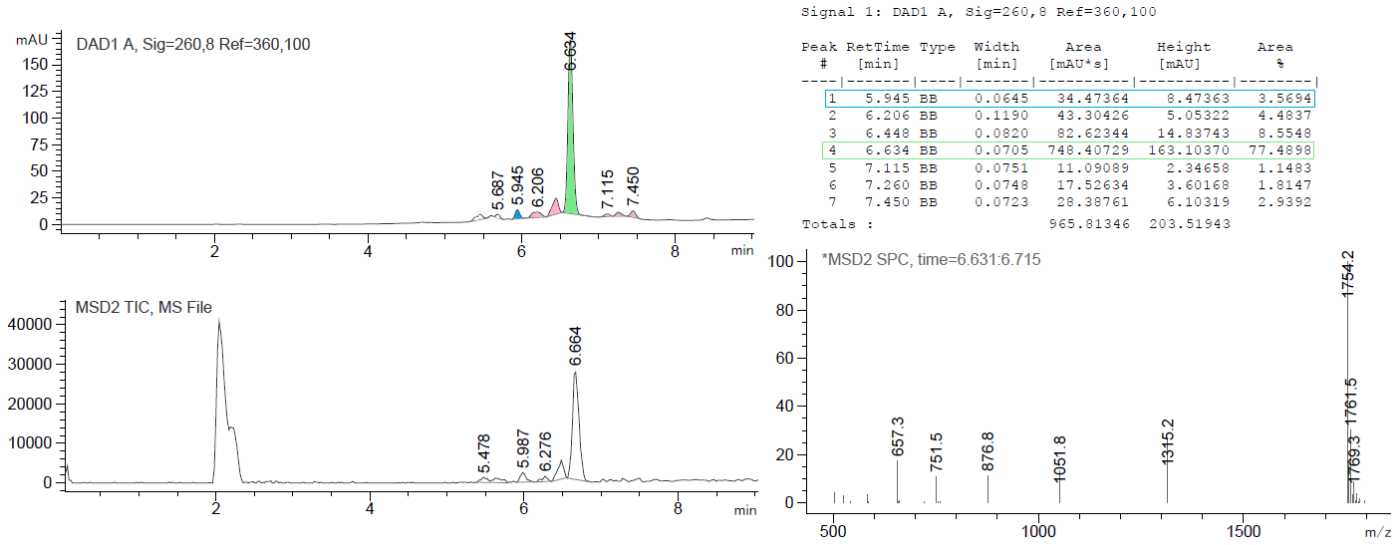
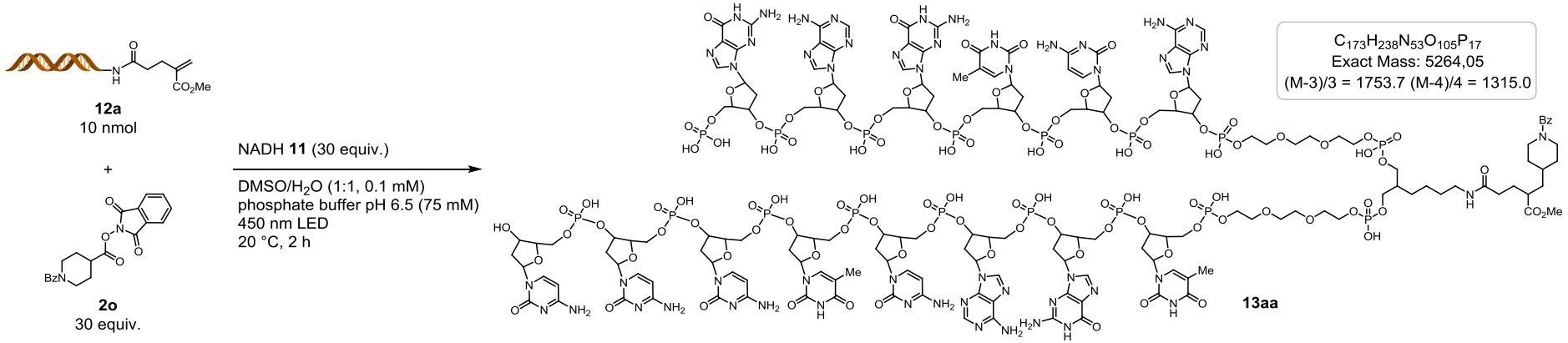


***Figure S6**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13aa** (green)*

*Synthesis of DNA functionalized product **13aa** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2o** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 2 h. **Yield:** 88% (2% s.m.)

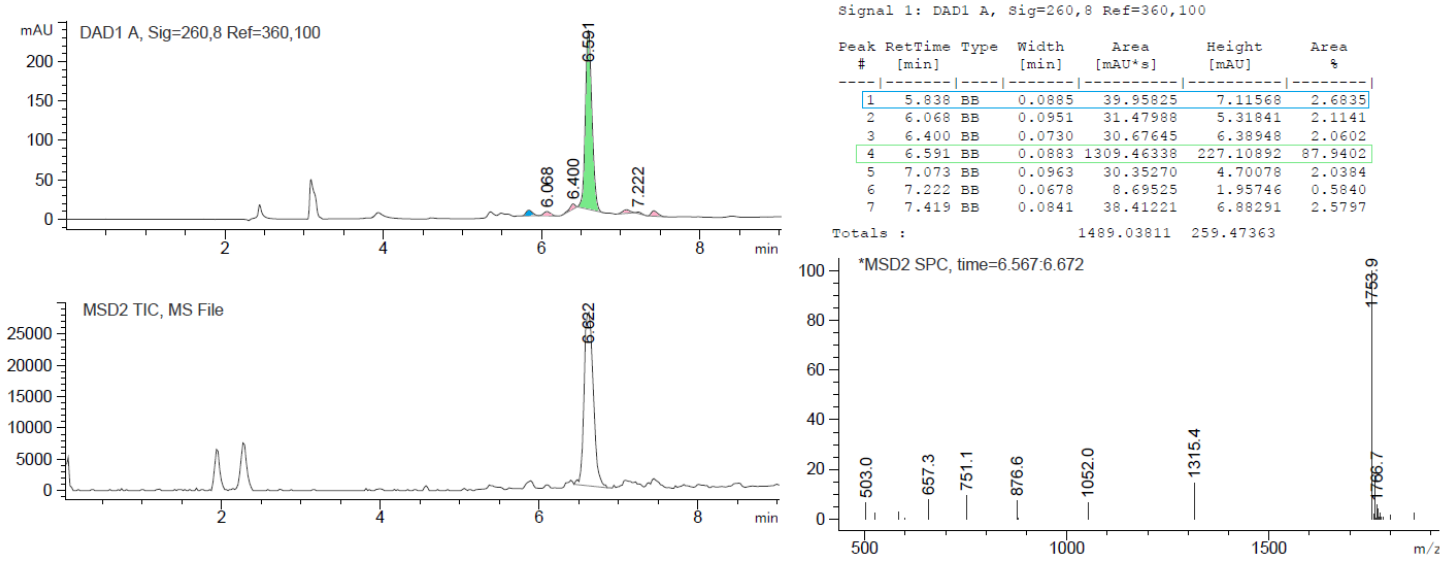
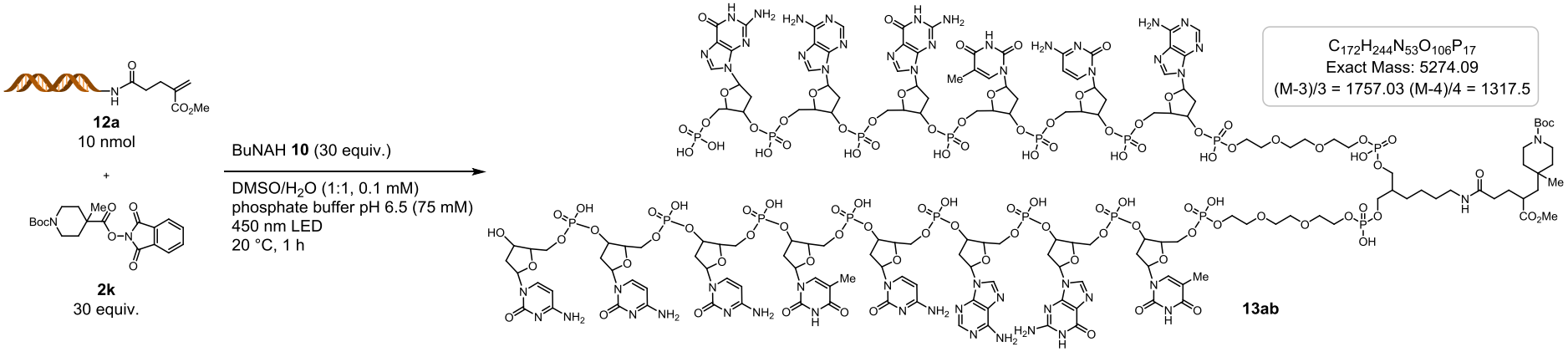


***Figure S7**: LCMS trace of NADH (**11**) promoted DNA coupled product **13aa** (green)*

*Synthesis of DNA functionalized product **13ab** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2k** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 81% (0% s.m.)

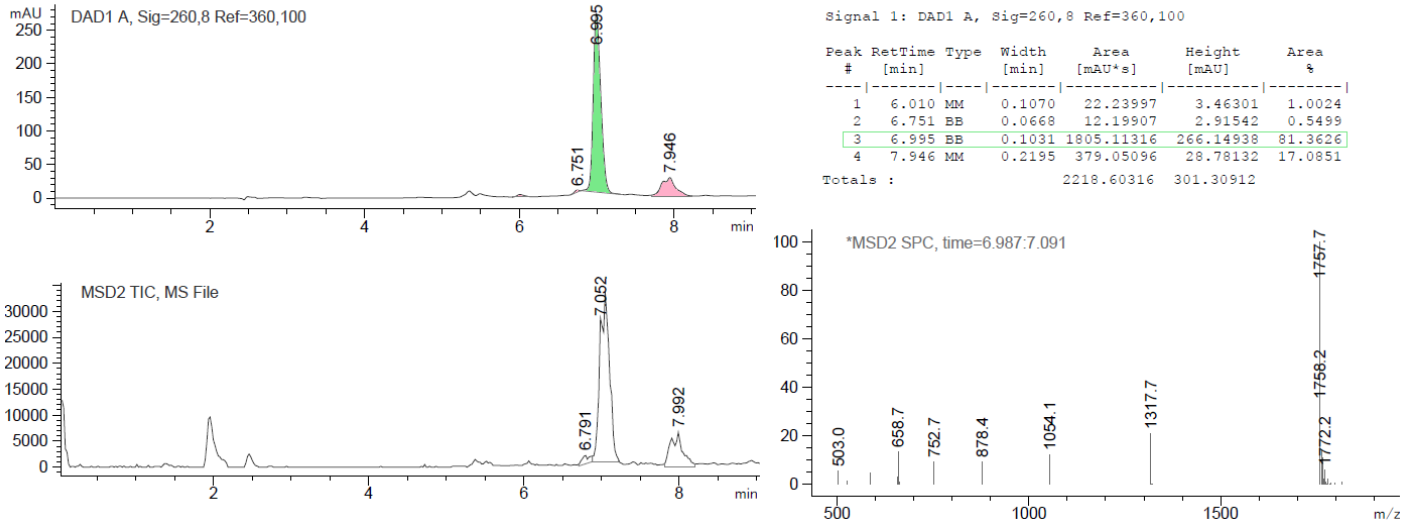
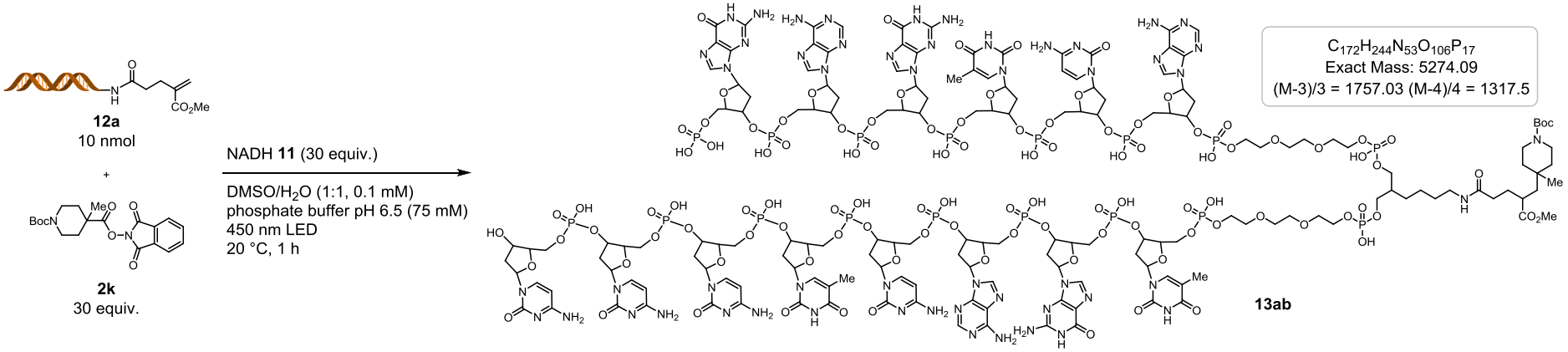


***Figure S8**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13ab** (green)*

*Synthesis of DNA functionalized product **13ab** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2k** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 77% (0% s.m.)

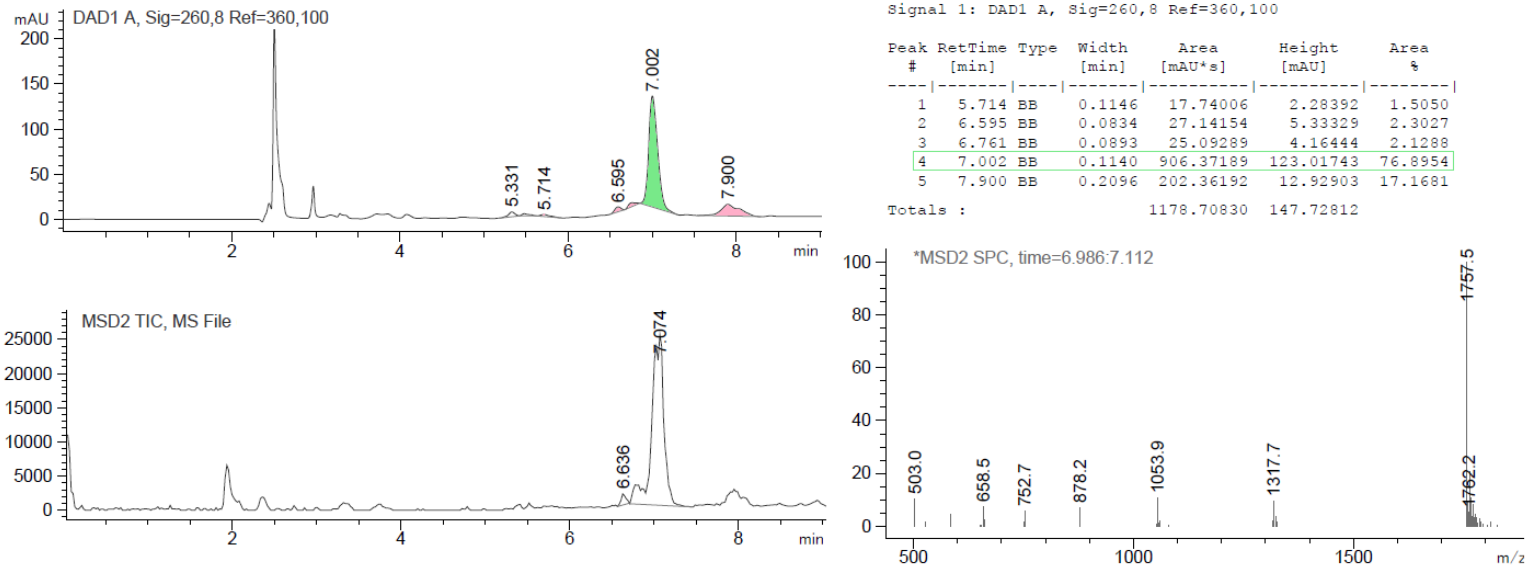
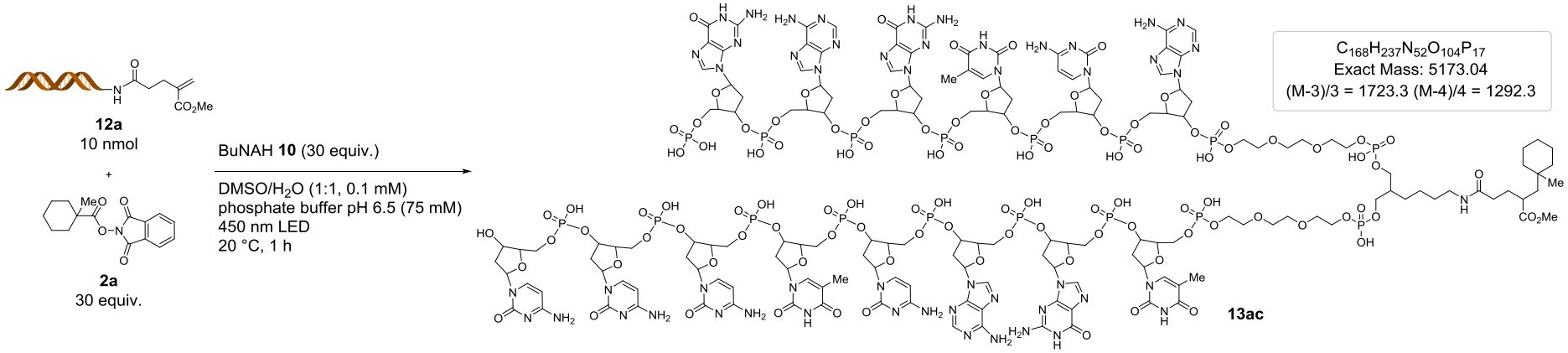


***Figure S9:** LCMS trace of NADH (**11**) promoted DNA coupled product **13ab** (green)*

*Synthesis of DNA functionalized product **13ac** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2a** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.) and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL), for 1 h. **Yield:** 91% (0% s.m.)

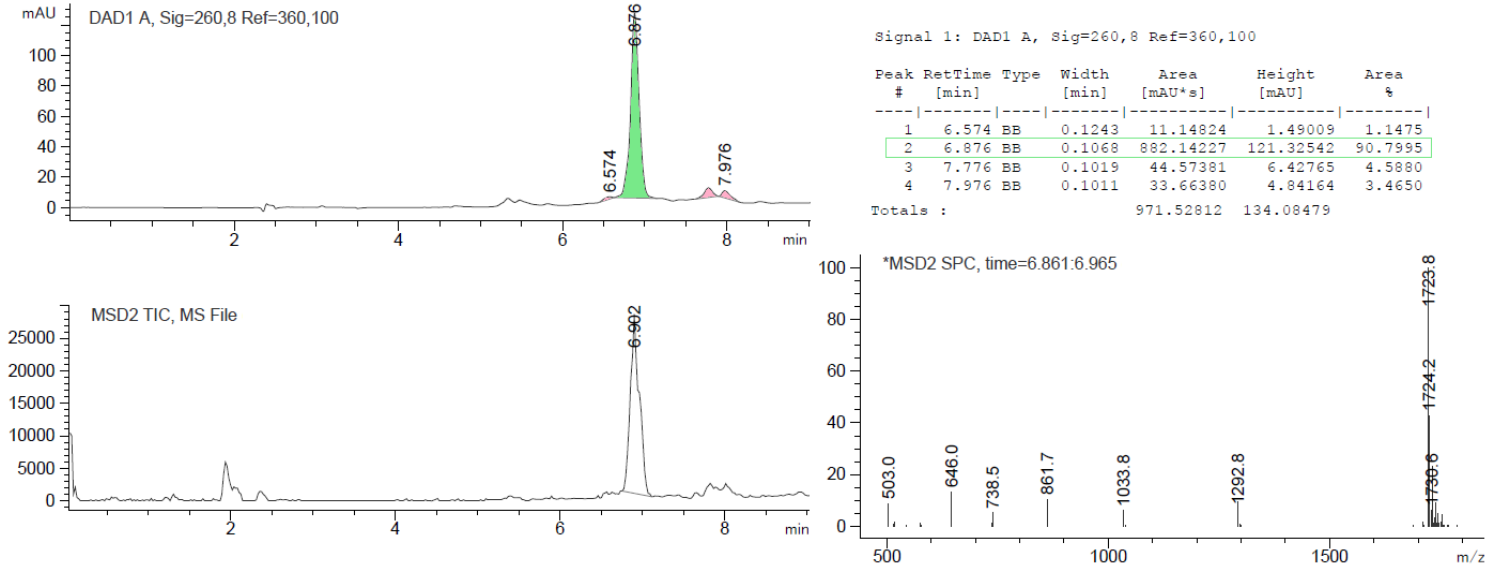
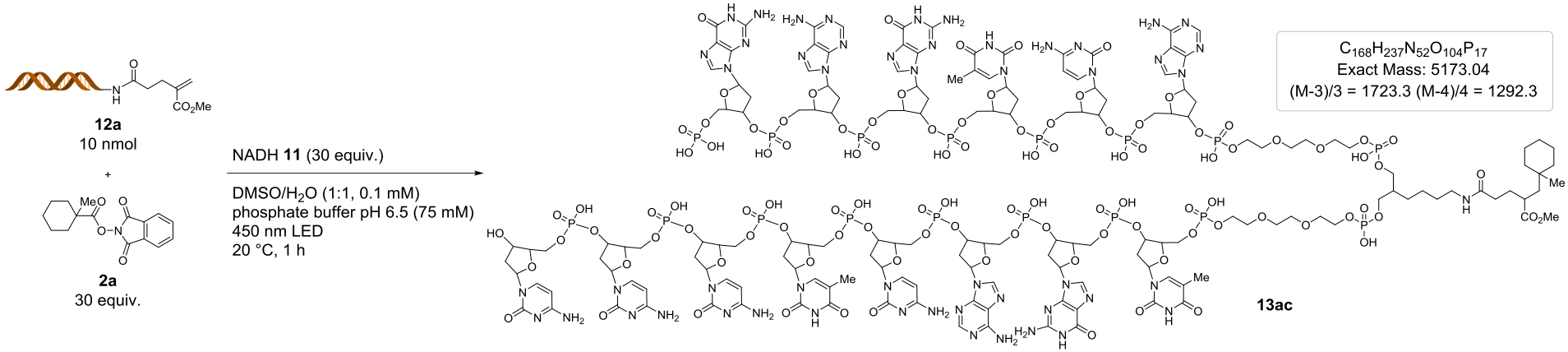


***Figure S10**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13ac** (green)*

*Synthesis of DNA functionalized product **13ac** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2a** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 83% (0% s.m.)

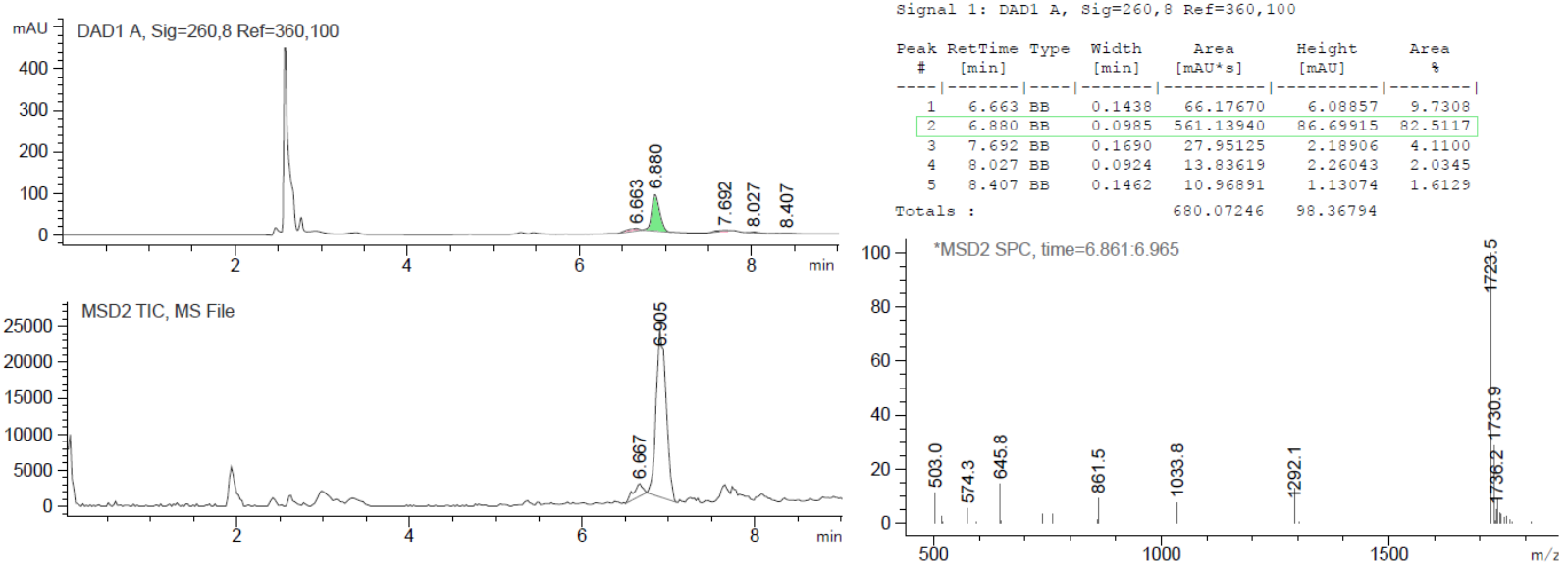
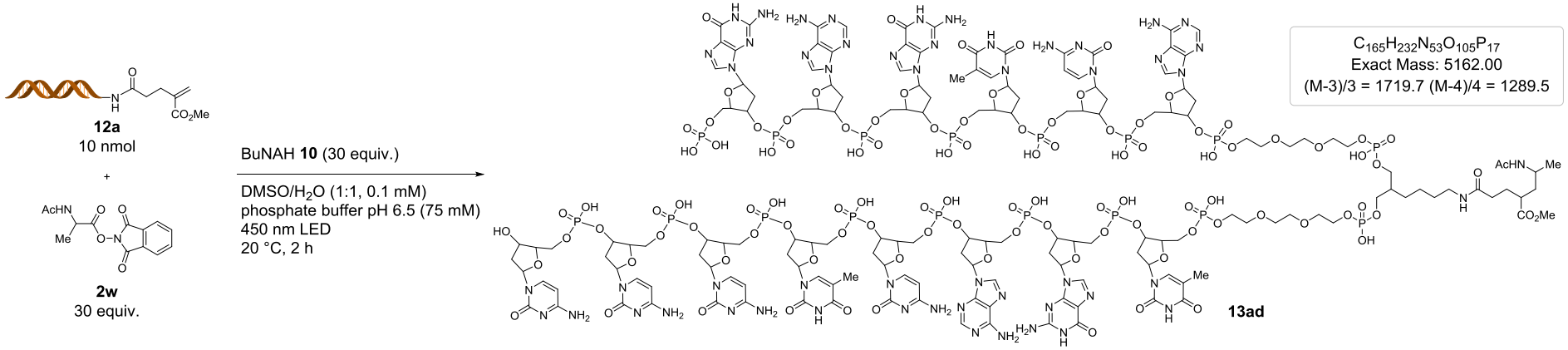


***Figure S11**: LCMS trace of NADH (**11**) promoted DNA coupled product **13ac** (green)*

*Synthesis of DNA functionalized product **13ad** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2w** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 2 h. **Yield:** 92% (0% s.m.)

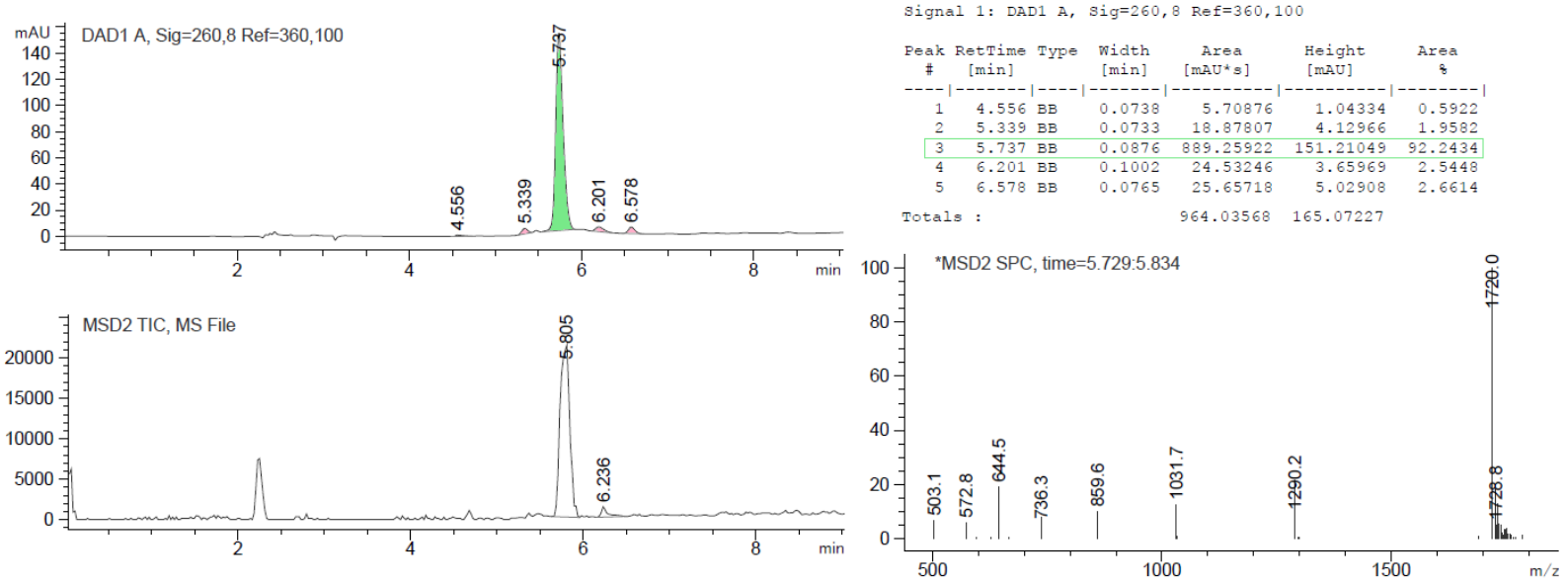
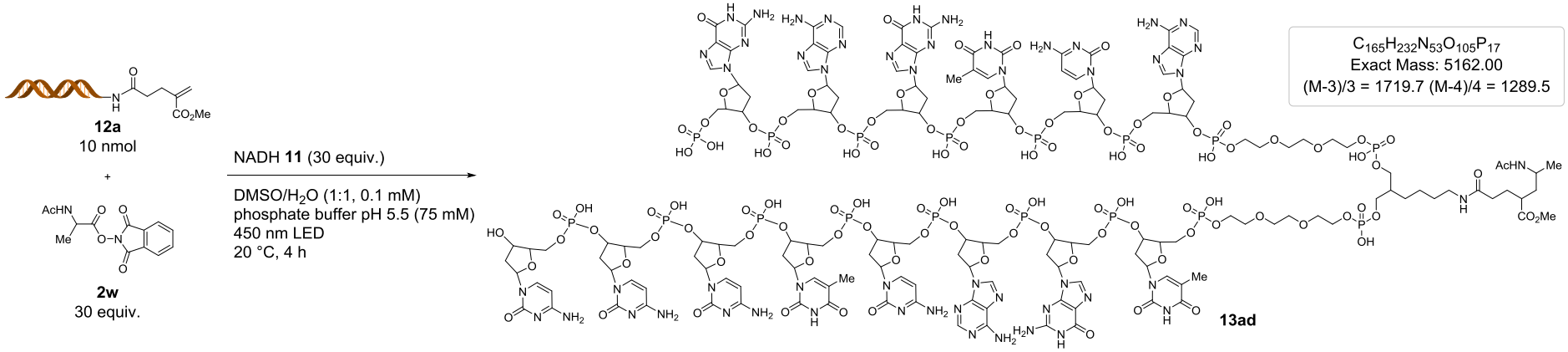


***Figure S12**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13ad** (green)*

*Synthesis of DNA functionalized product **13ad** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2w** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 4 h. **Yield:** 92% (0% s.m.)

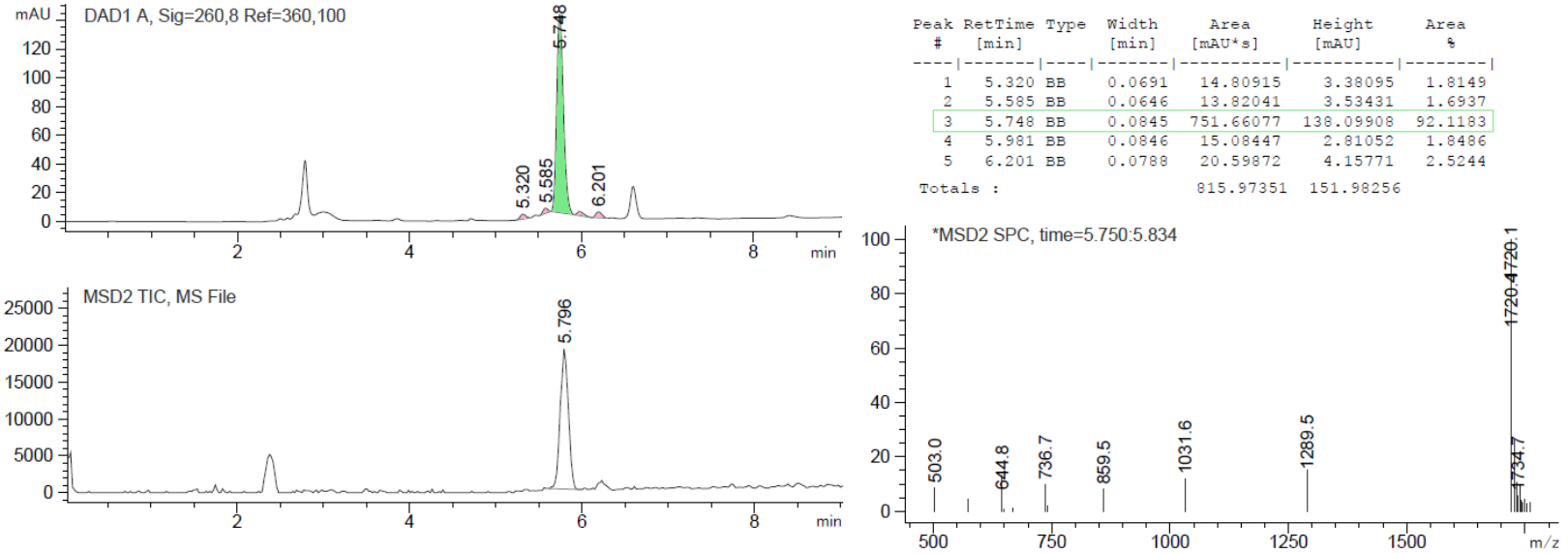
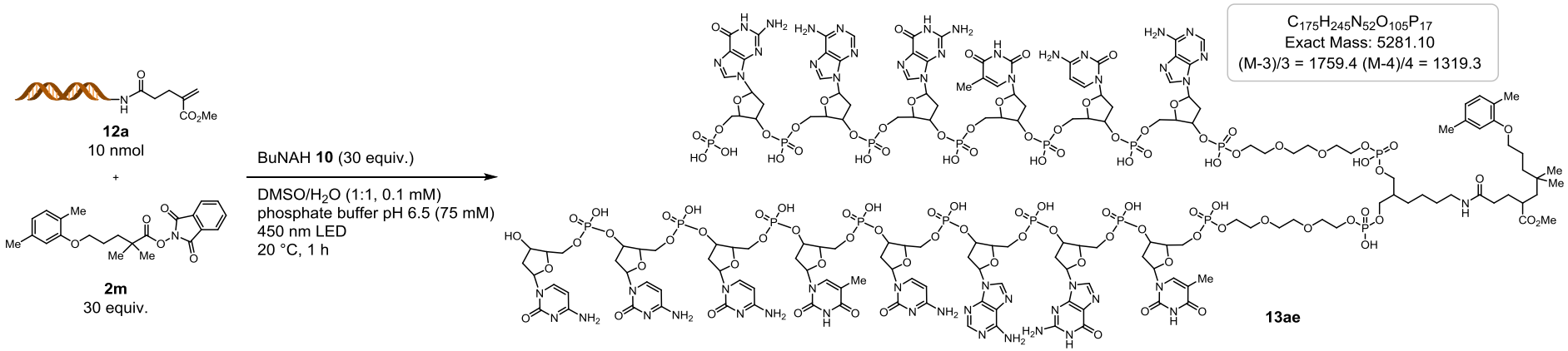


***Figure S13**: LCMS trace of NADH (**11**) promoted DNA coupled product **13ad** (green)*

*Synthesis of DNA functionalized product **13ae** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2m** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 86% (14% s.m.)

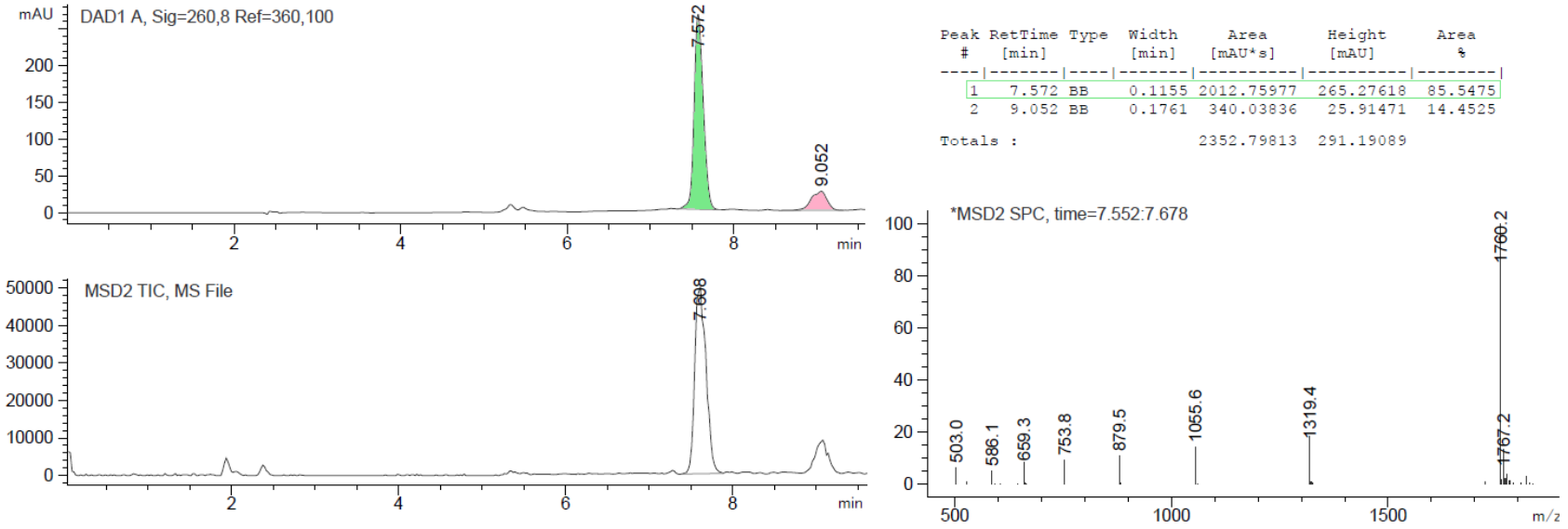
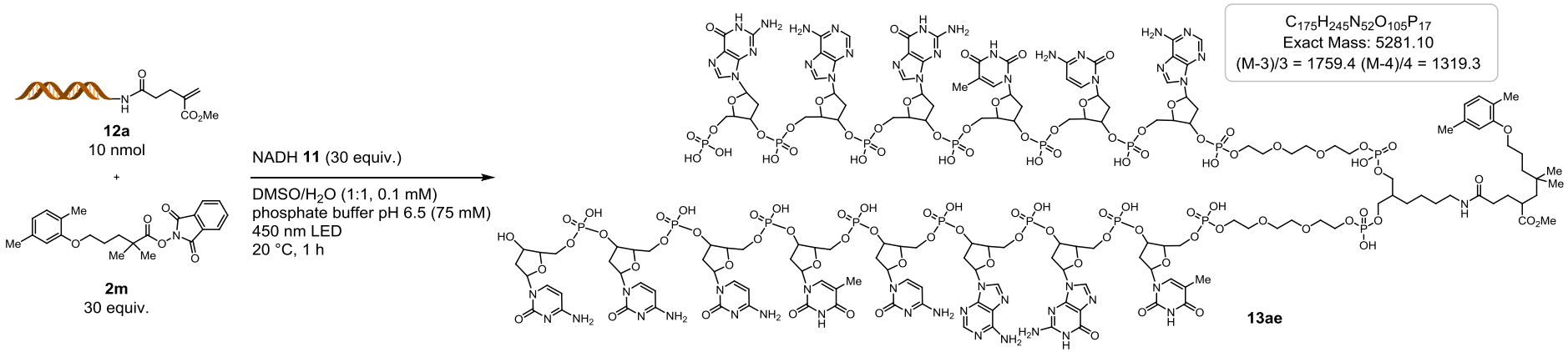


***Figure S14**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13ae** (green)*

*Synthesis of DNA functionalized product **13ad** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12a** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2m** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 59% (4% s.m.)

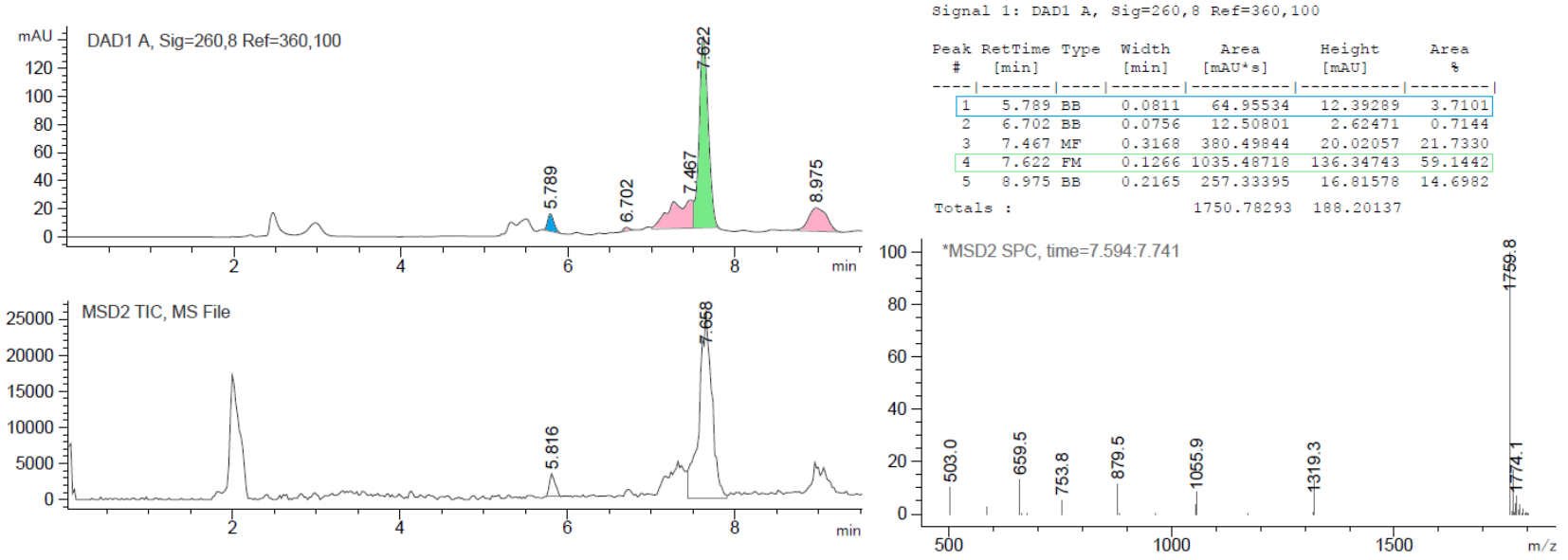
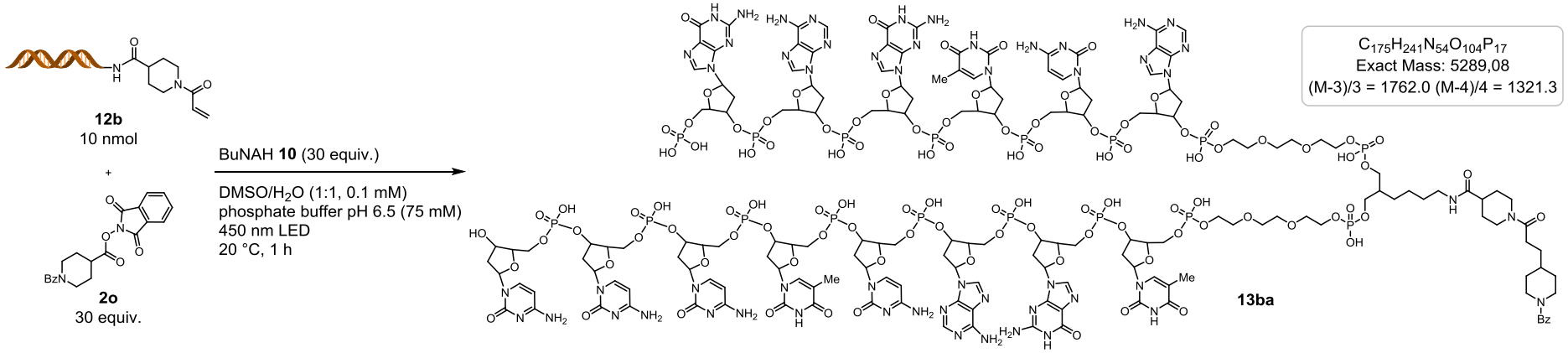


***Figure S15**: LCMS trace of NADH (**11**) promoted DNA coupled product **13ae** (green)*

*Synthesis of DNA functionalized product **13ba** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2o** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 83% (10% s.m.)

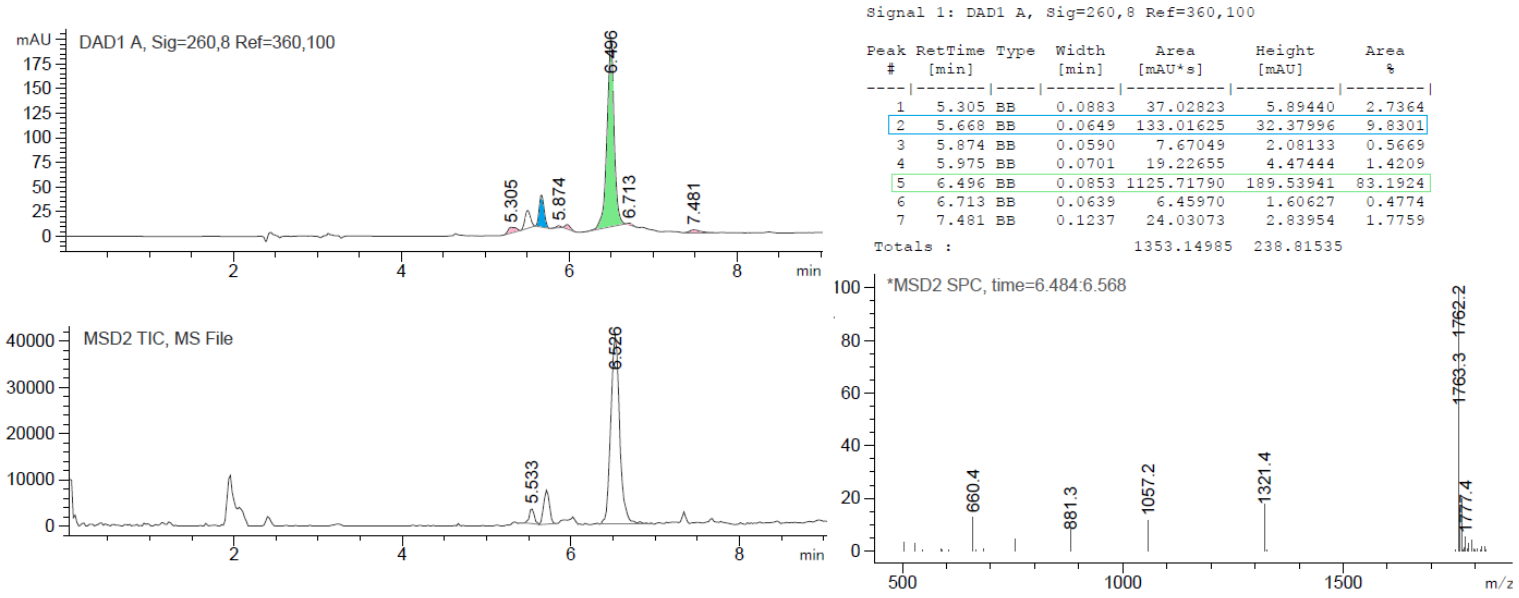
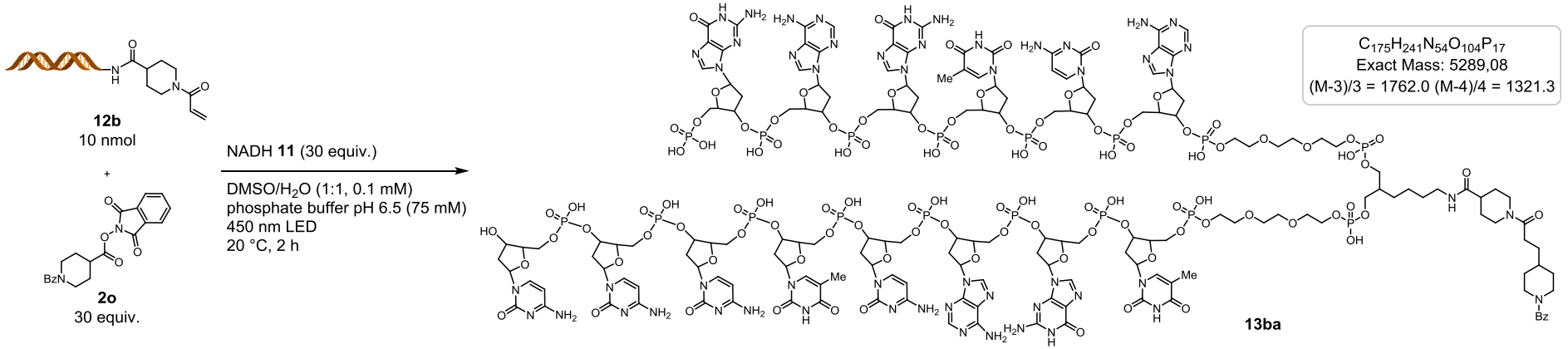


***Figure S16**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13ba** (green)*

*Synthesis of DNA functionalized product **13ba** using NADH (**11**) as a reductant*



General procedure **C** was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2o** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 2 h. **Yield:** 90% (6% s.m.)

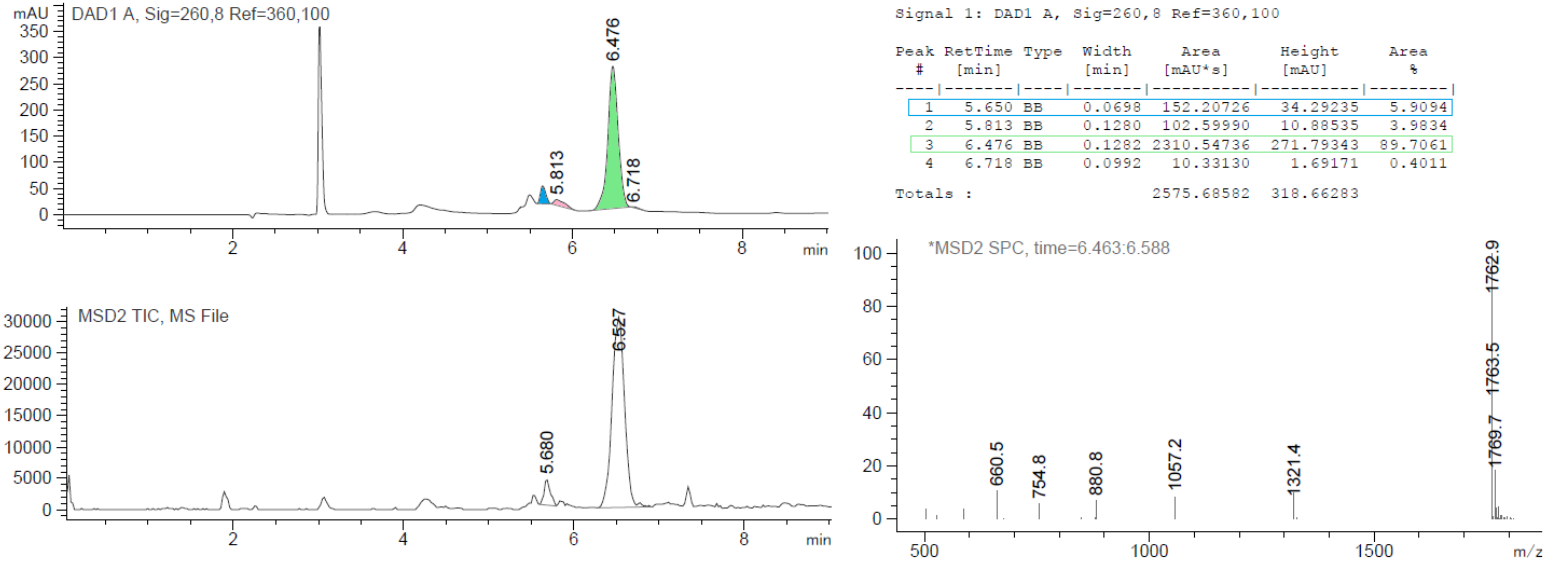
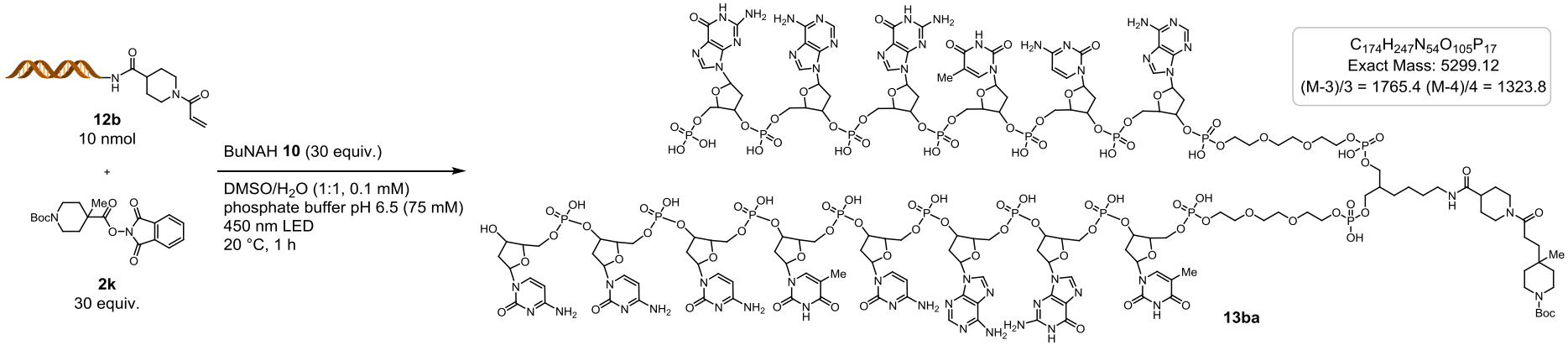


***Figure S17**: LCMS trace of NADH (**11**) promoted DNA coupled product **13ba** (green)*

*Synthesis of DNA functionalized product **13bb** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2k** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 96% (0% s.m.)

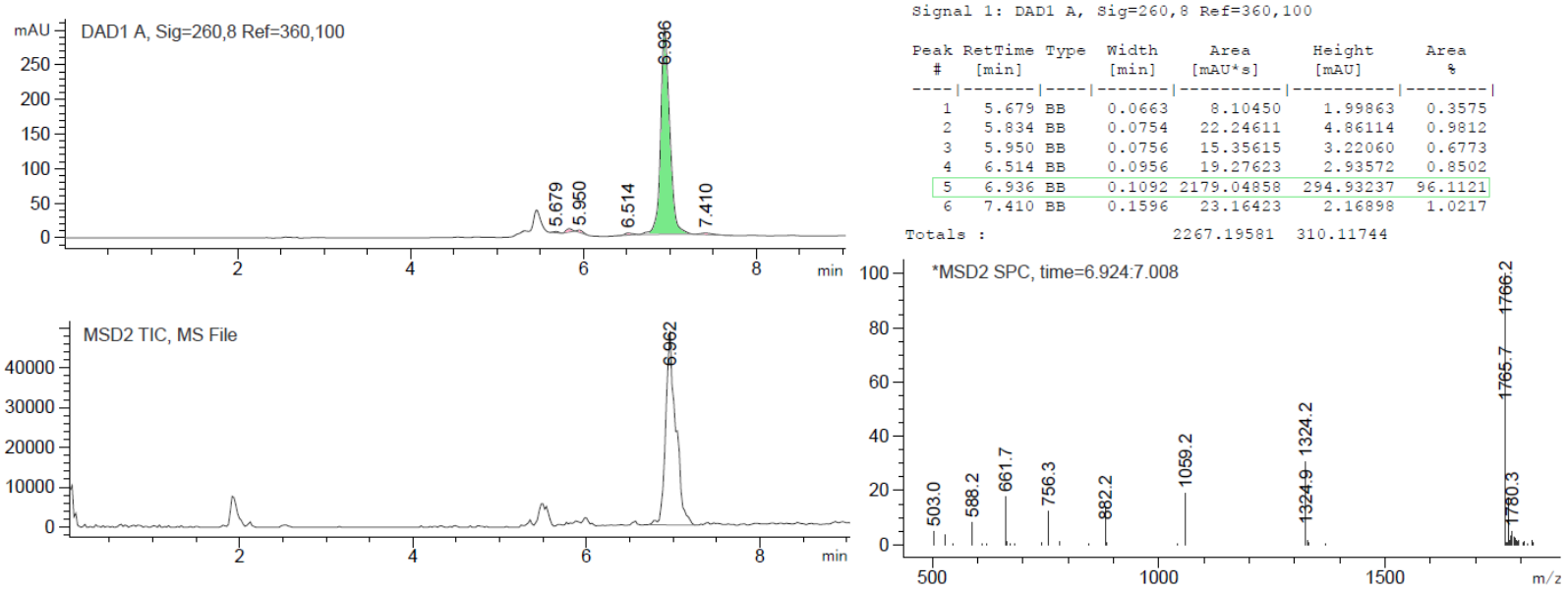
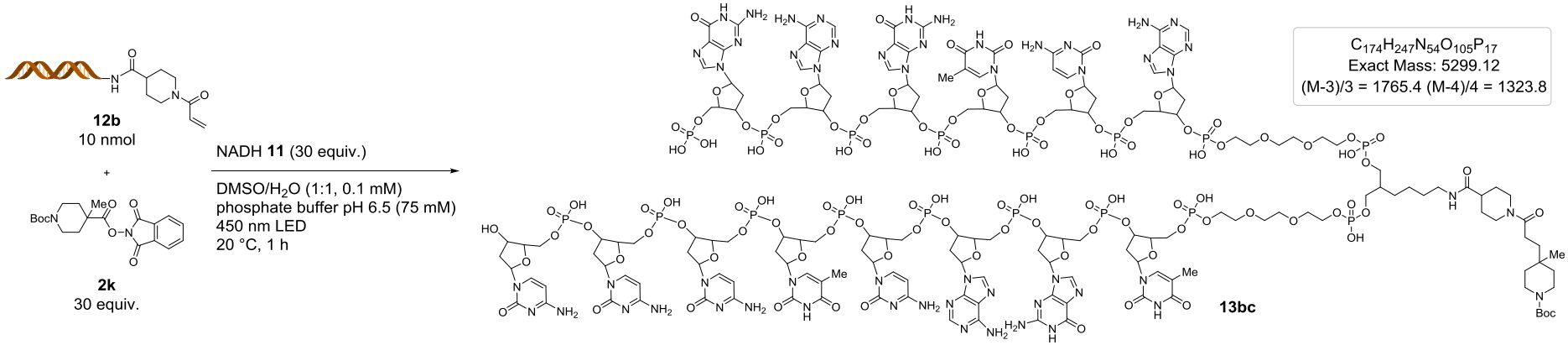


***Figure S18**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13bb** (green)*

*Synthesis of DNA functionalized product **13bb** using NADH (**11**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2k** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 93% (2% s.m.)

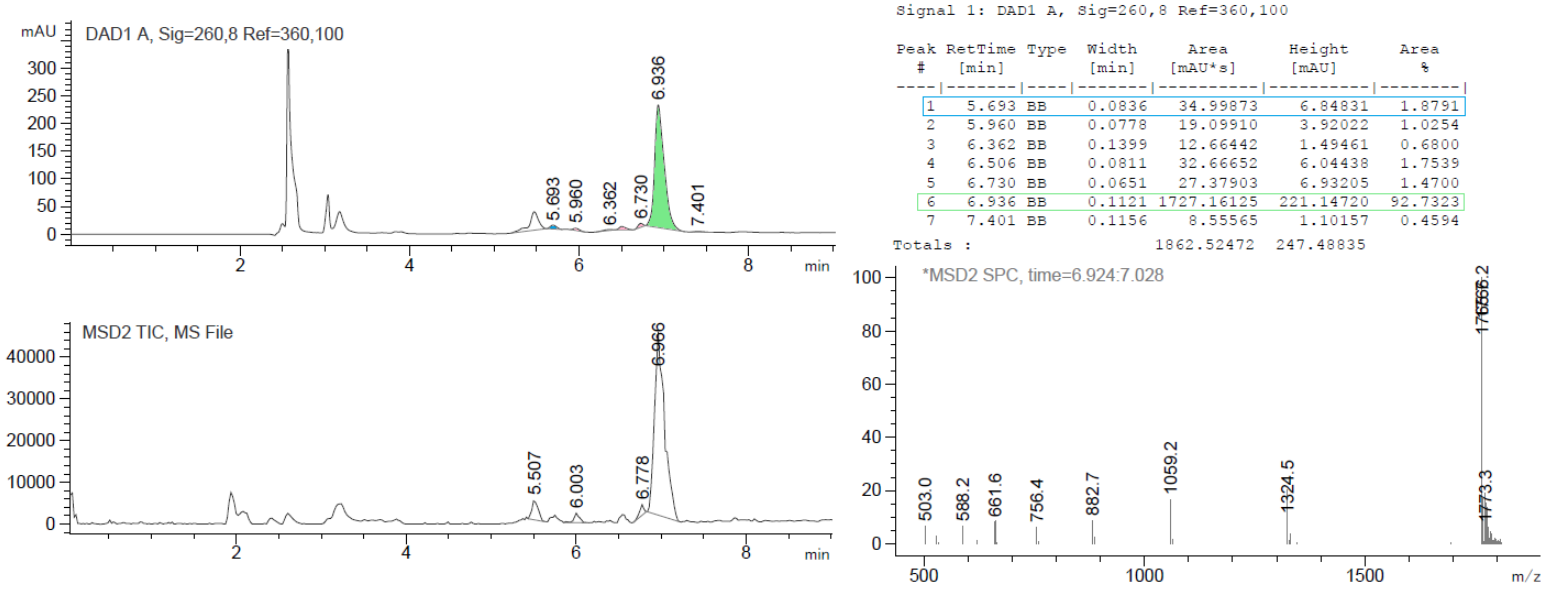
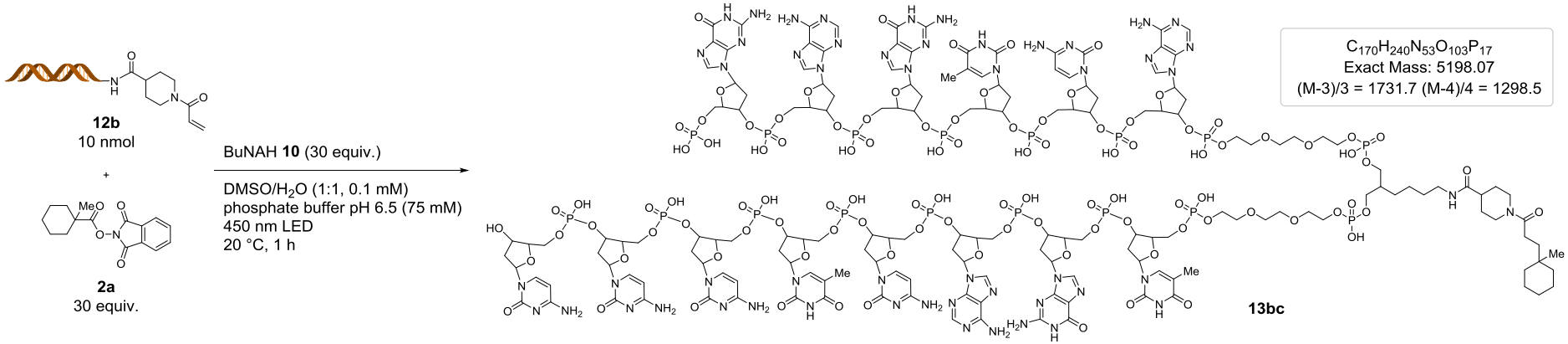


***Figure S19**: LCMS trace of NADH (**11**) promoted DNA coupled product **13bb** (green)*

*Synthesis of DNA functionalized product **13bc** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2a** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 97% (0% s.m.)

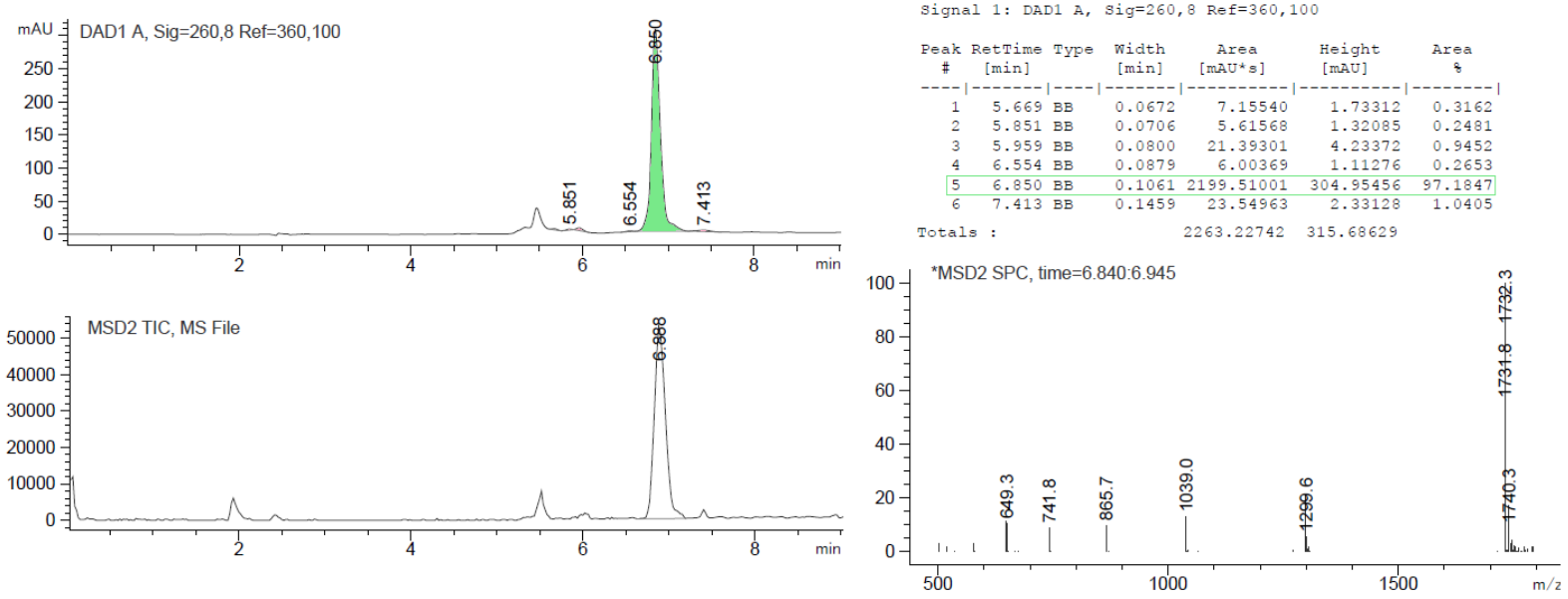
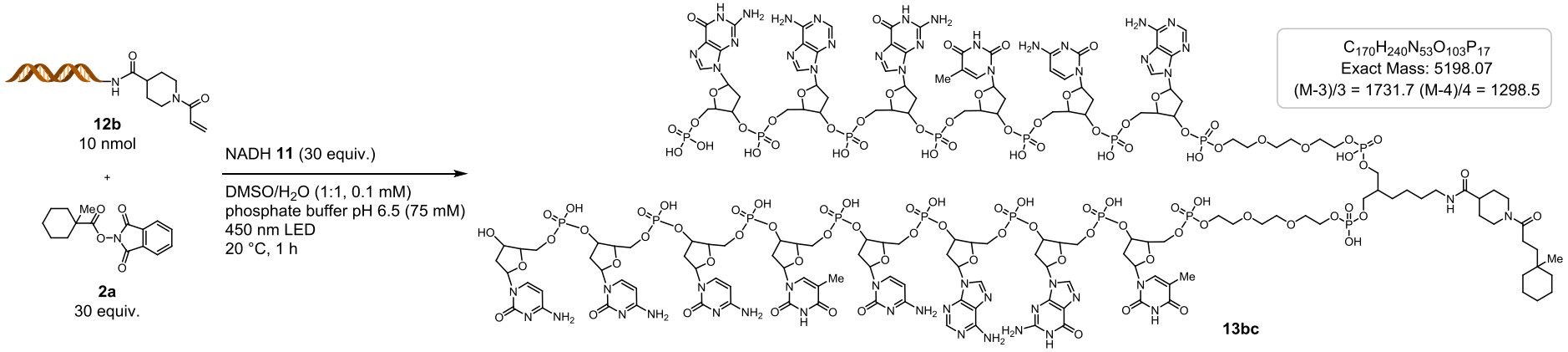
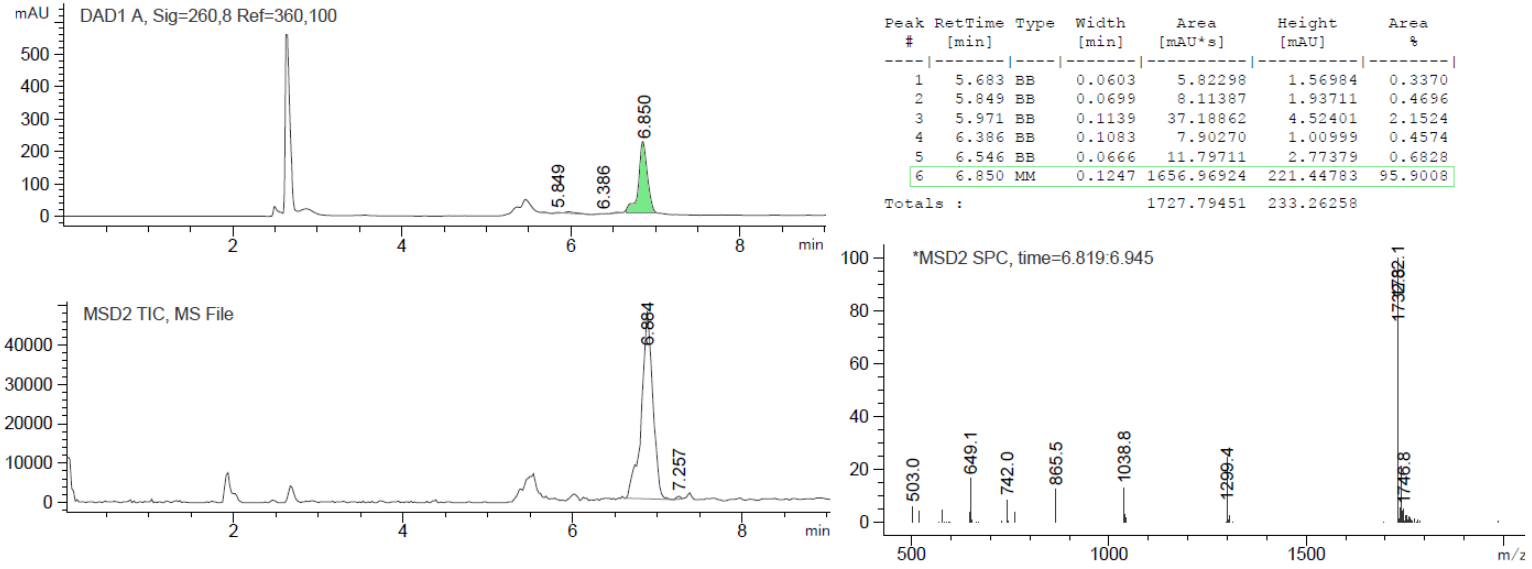


***Figure S20**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13bc** (green)*

*Synthesis of DNA functionalized product **13bc** using NADH (**11**) as a reductant*



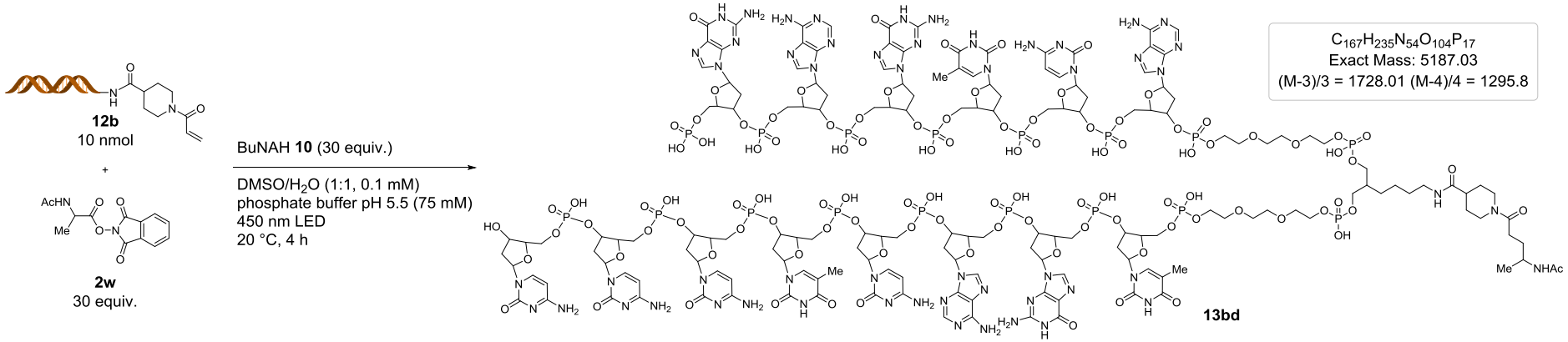
General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2a** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 96% (0% s.m.)



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.683	BB	0.0603	5.82298	1.56984	0.3370
2	5.849	BB	0.0699	8.11387	1.93711	0.4696
3	5.971	BB	0.1139	37.18862	4.52401	2.1524
4	6.386	BB	0.1083	7.90270	1.00999	0.4574
5	6.546	BB	0.0666	11.79711	2.77379	0.6828
6	6.850	MM	0.1247	1656.96924	221.44783	95.9008
Totals :				1727.79451	233.26258	

***Figure S21**: LCMS trace of NADH (**11**) promoted DNA coupled product **13bc** (green)*

*Synthesis of DNA functionalized product **13bd** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2w** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.) in DMSO (30 µL), and phosphate buffer (30 µL, 250 mM, pH 5.5) for 4 hours. **Yield:** n.d.

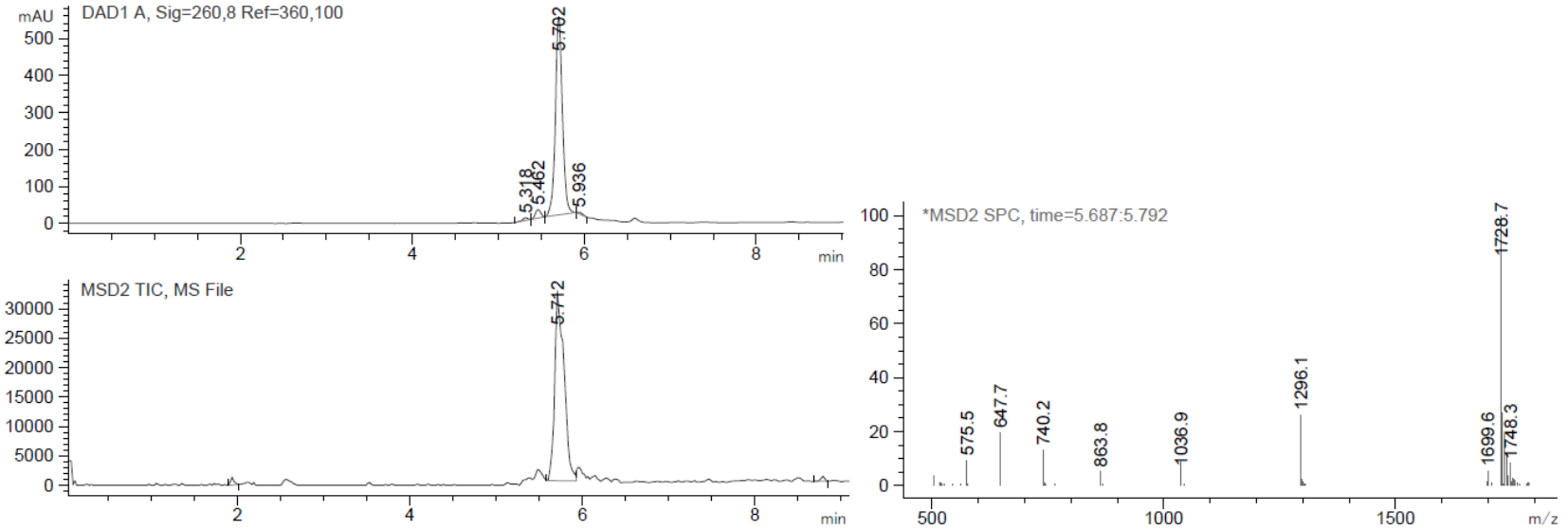
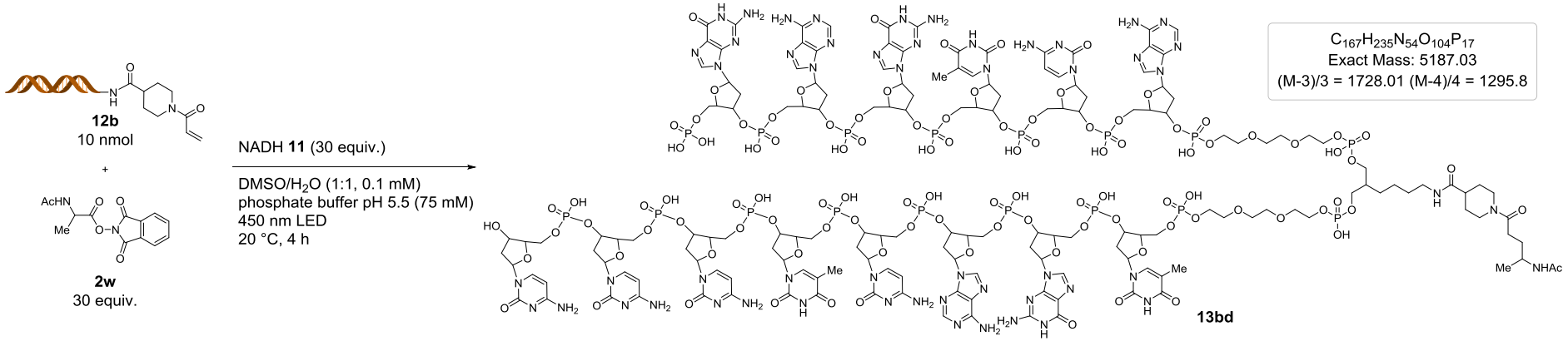


***Figure S22**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13bd**.*

*Synthesis of DNA functionalized product **13bd** using NADH (**11**) as a reductant*



General procedure C was applied using DNA acrylate **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester (**2v**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.) in DMSO (30 µL), and phosphate buffer (30 µL, 250 mM, pH 6.5) for 4 hours. **Yield:** n.d.

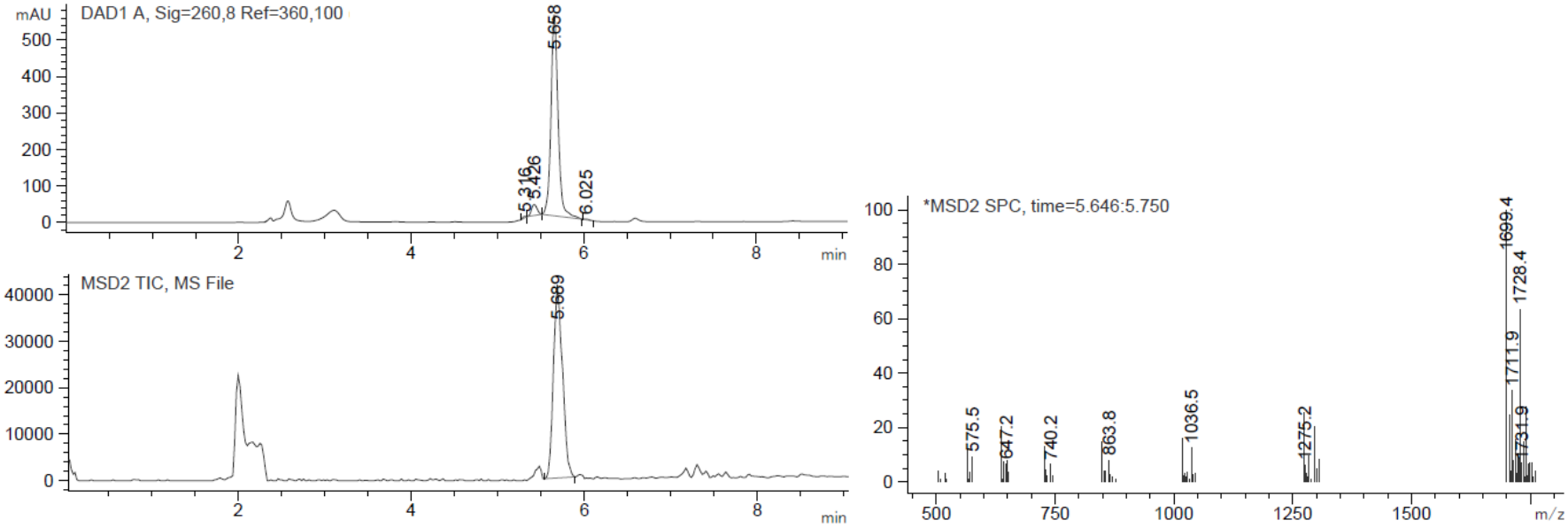
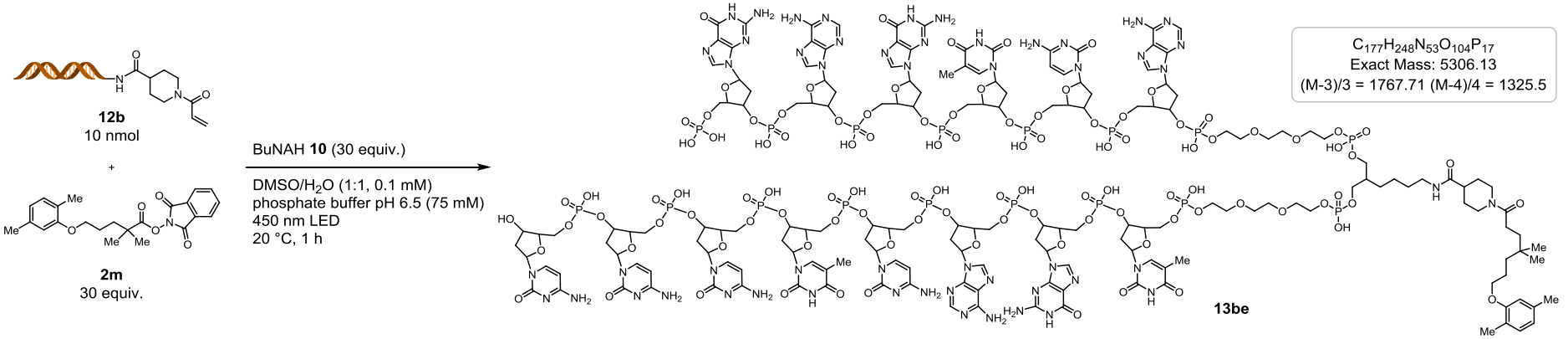


***Figure S23**: LCMS trace of NADH (**10**) promoted DNA coupled product **13bd**.*

*Synthesis of DNA functionalized product **13be** using BuNAH (**10**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2m** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), BuNAH (**10**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 97% (0% s.m.)

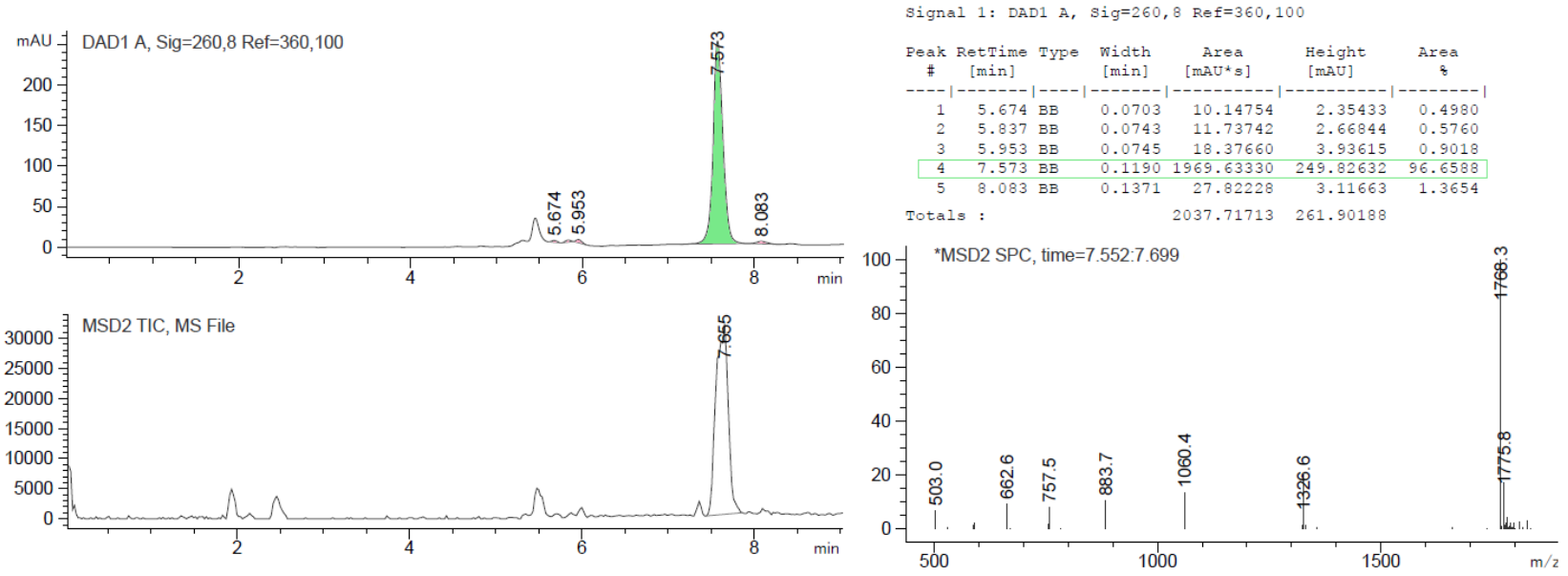
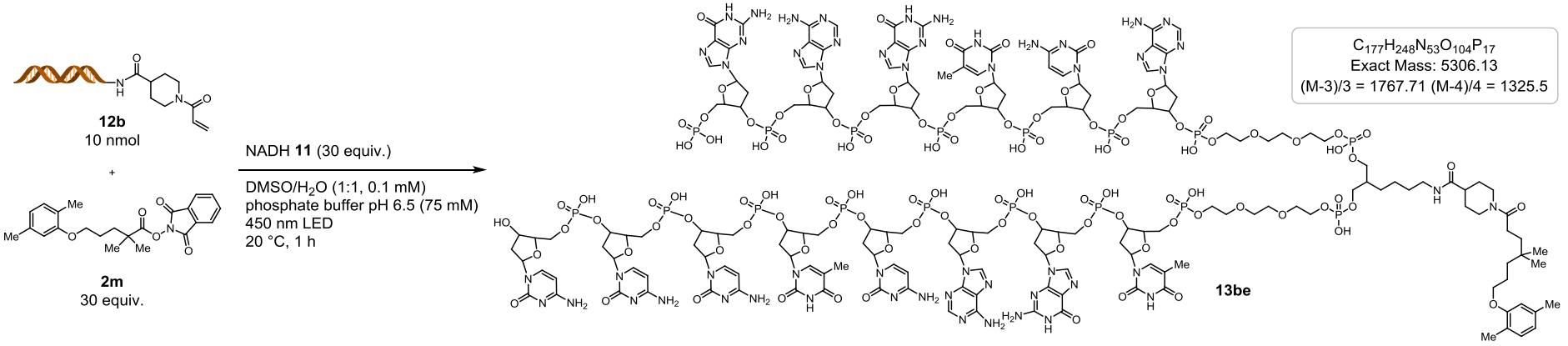


***Figure S24**: LCMS trace of BuNAH (**10**) promoted DNA coupled product **13be** (green)*

*Synthesis of DNA functionalized product **13be** using NADH (**11**) as a reductant*



General procedure C was applied using DNA amide **12b** (20 µL, 0.5 mM in H_2O, 10 nmol, 1.0 equiv.), redox-active ester **2o** (10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), NADH (**11**; 10 µL, 30 mM in DMSO, 0.30 µmol, 30 equiv.), and phosphate buffer (30 µL, 250 mM, pH 6.5) in DMSO (30 µL) for 1 h. **Yield:** 74% (20% s.m.)

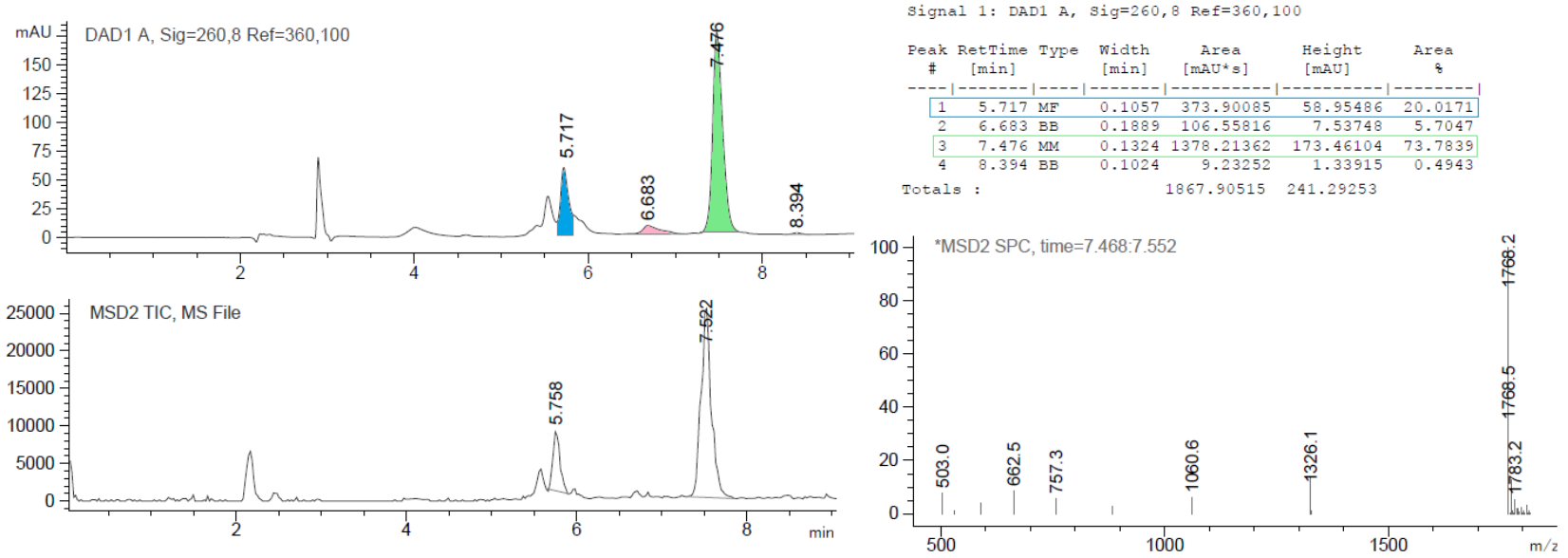
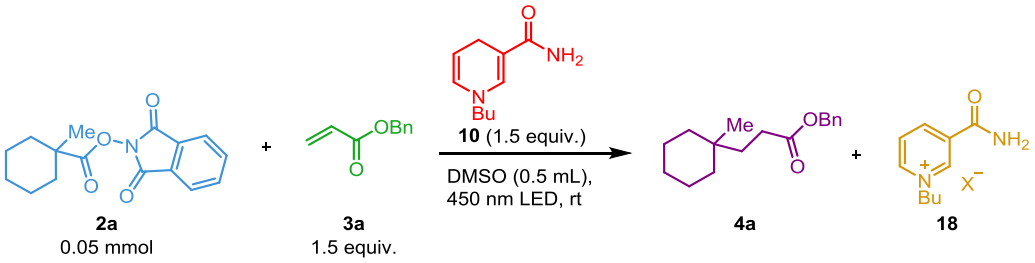


***Figure S25**: LCMS trace of NADH (**11**) promoted DNA coupled product **3be** (green)*

6. Kinetic profiling by in situ NMR experiments

Procedure for the in situ NMR experiment under standard reaction conditions (no-D NMR)



The reaction sample was prepared in a NMR tube under inert gas atmosphere in the dark. 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 14 mg, 50 µmol, 1.0 equiv.) was dissolved in DMSO (0.1 mL), and benzyl acrylate (**3a**; 11 µL, 75 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 0.4 mL in DMSO, 0.2 M, 75 µmol, 1.5 equiv.) were subsequently added. The reaction mixture was illuminated with blue LED at 20–22 °C, and progress of the reaction was followed by *no-D* NMR.

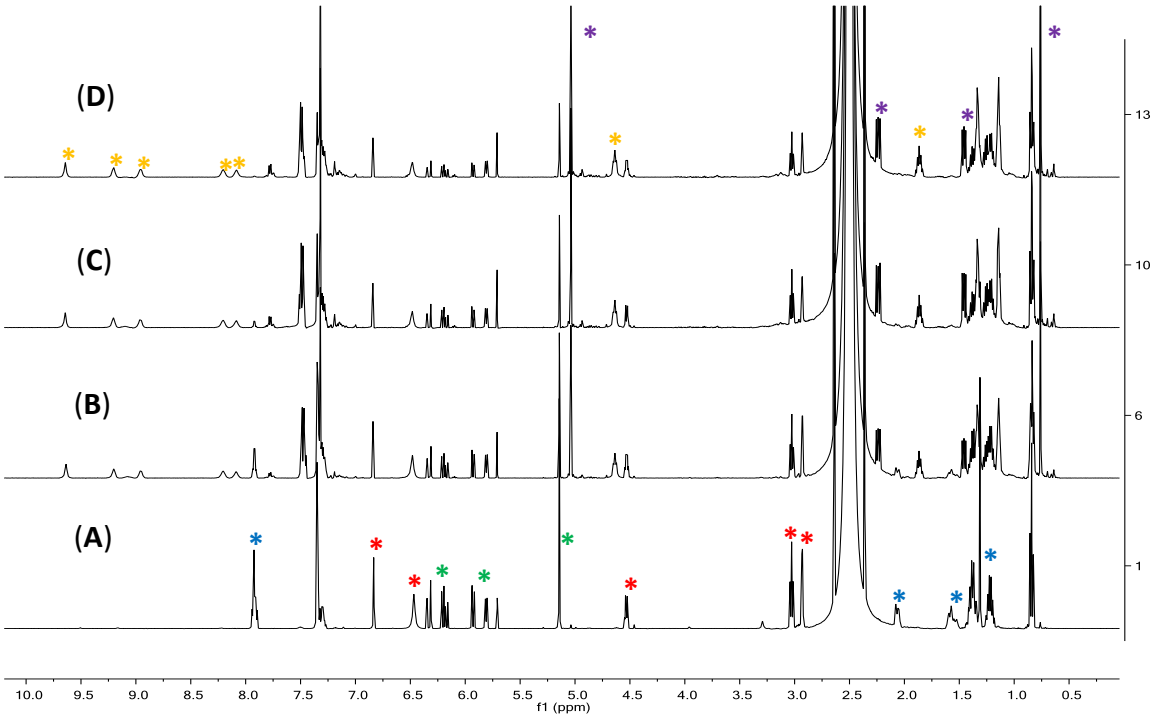


***Figure S26**: [1]H-NMR spectra after (A) 0 s, (B) 100 s, (C) 180 s; (D) 240 s irradiation in DMSO.*

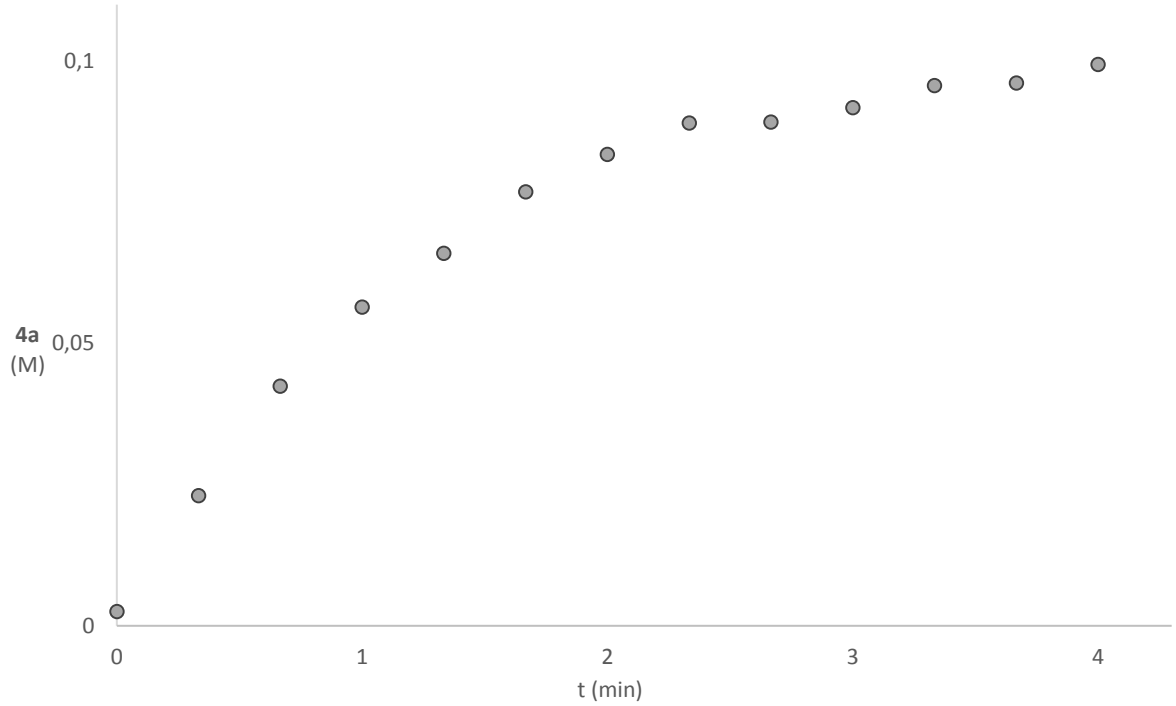


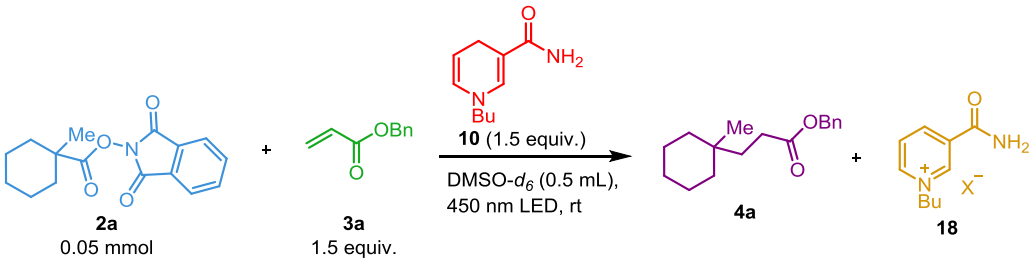
Figure S27*: Kinetic profiling of photo-ligation under standard reaction conditions. (see.* ***Table S4****)*

Table S4*: Data of progress of photo-ligation reaction under standard reaction condition. (see.* ***Figure S27***

Entry	Time (s)	Conversion **2a** (%)	[**4a**] (M)
1	0	0	0.002
2	20	22	0.023
3	40	46	0.042
4	60	59	0.056
5	80	70	0.066
6	100	77	0.077
7	120	83	0.083
8	140	88	0.089
9	160	93	0.089
10	180	94	0.092
11	200	97	0.096
12	220	97	0.096
13	240	97	0.099

Reaction conditions: **2a** (0.1 M), BuNAH (**10**; 0.15 M) and benzyl acrylate (**3a**; 0.15 M) in DMSO (0.5 mL), irradiation with blue LEDs at 20−22 °C.

Procedure for the in situ NMR experiment in DMSO-d_6



To a solution of 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 14 mg, 50 µmol, 1.0 equiv.) in DMSO-d_6 (0.1 mL), in a NMR tube was added benzyl acrylate (**3a**; 11 µL, 75 µmol, 1.5 equiv.) and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 0.4 mL in DMSO-d_6, 0.2 M, 75 µmol, 1.5 equiv.). Preparation of the reaction sample was done in the dark under argon. The sample was illuminated with blue LED at 20−22 °C and the progress of the reaction was followed by ^{1}H-NMR.

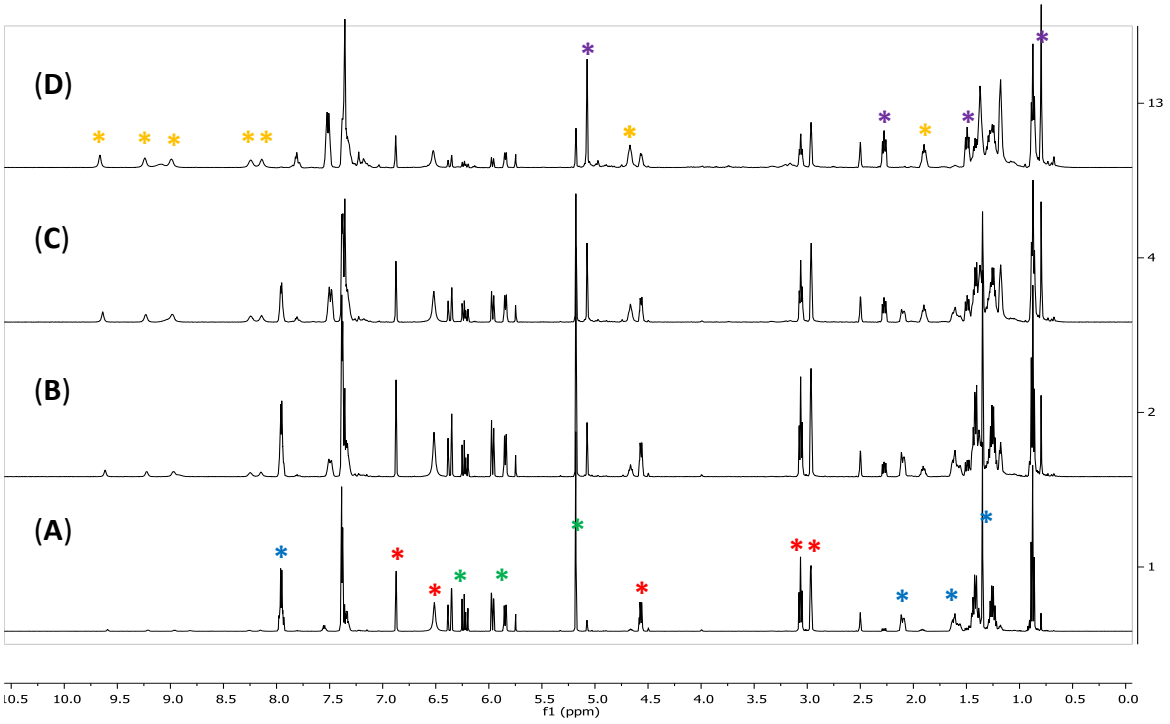


***Figure S28**: ^{1}H-NMR spectra after (A) 0 s, (B) 20 s, C) 60 s, (D) 240 s irradiation in DMSO-d_6*

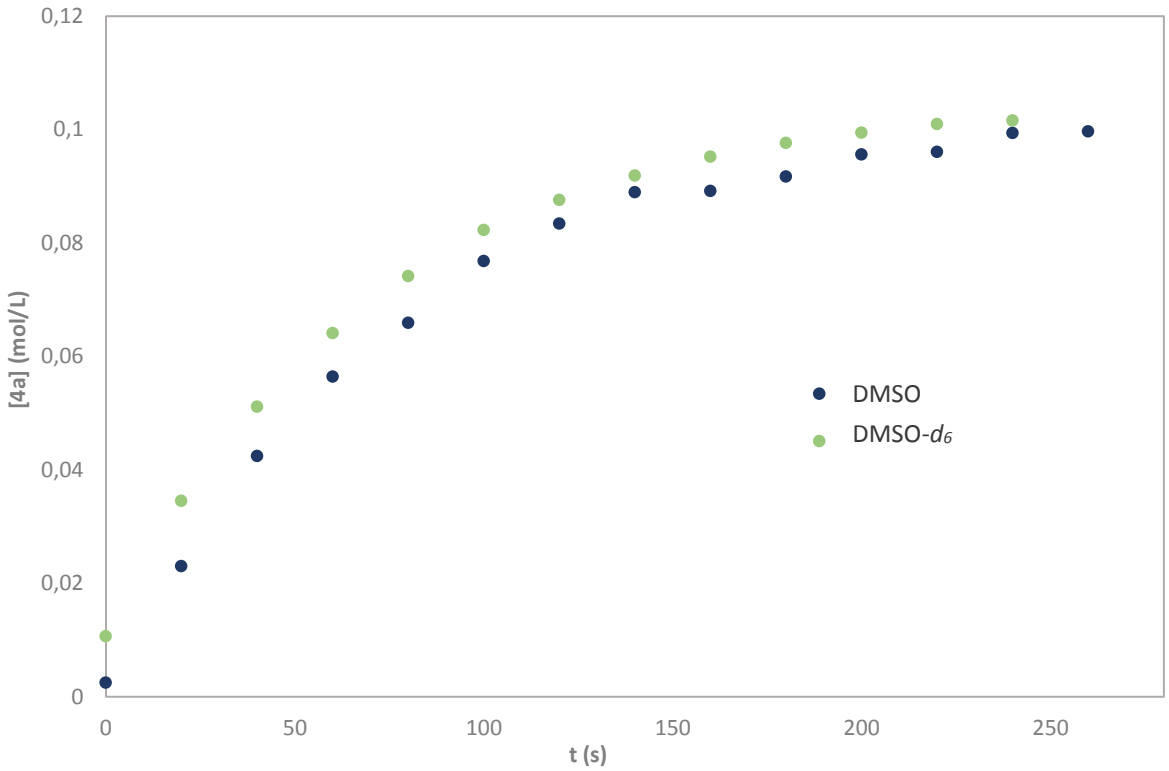


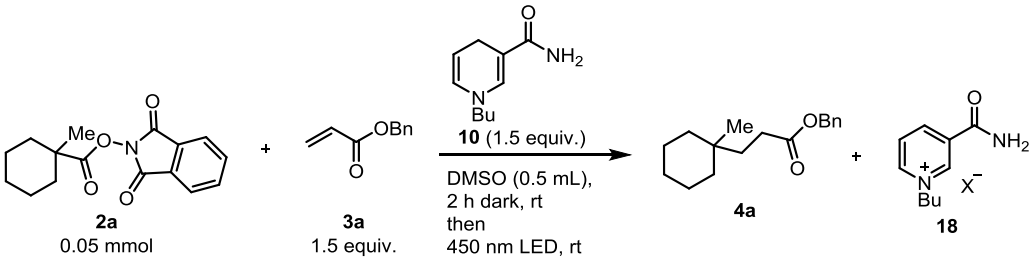
***Figure S29**: Overlay of the standard reaction in DMSO (see. **Figure S27**) and DMSO-d_6 (see. **Table S5**)*

***Table S5**: Data of the reaction progress in DMSO and in DMSO-d_6 (see **Figure S29**).*

Entry	**DMSO**		**DMSO-d_6**	
	Time (s)	[**4a**] (M)	Time (s)	[**4a**] (M)
1	0	0.002	0	0.010
2	20	0.023	20	0.035
3	40	0.042	40	0.051
4	60	0.056	60	0.064
5	80	0.066	80	0.074
6	100	0.077	100	0.082
7	120	0.083	120	0.088
8	140	0.089	140	0.092
9	160	0.089	160	0.095
10	180	0.092	180	0.098
11	200	0.096	200	0.100
12	220	0.096	220	0.100
13	240	0.099	240	0.101

Reaction conditions: **2a** (0.1 M), BuNAH (**10**; 0.15 M) and benzyl acrylate (**3a**; 0.15 M) in solvent (0.5 mL), irradiation with blue LEDs at 20−22 °C.

Procedure for the in situ NMR experiment to profile the background and deactivation of the system



To a solution of 1,3-dioxoisoindolin-2-yl 1-methylcyclohexane-1-carboxylate (**2a**; 14 mg, 50 µmol, 1.0 equiv.) in DMSO (0.1 mL), benzyl acrylate (**3a**; 11 µL, 75 µmol, 1.5 equiv.), and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**; 0.4 mL in DMSO, 0.2 M, 75 µmol, 1.5 equiv.) were added in the dark under argon. The sample was kept at 20 °C for 2 h during which it was monitored by ^{1}H-NMR under strict exclusion of light. Then, the sample was illuminated at 20−22 °C with blue LEDs, and the progress of the reaction was followed by no-D ^{1}H-NMR.

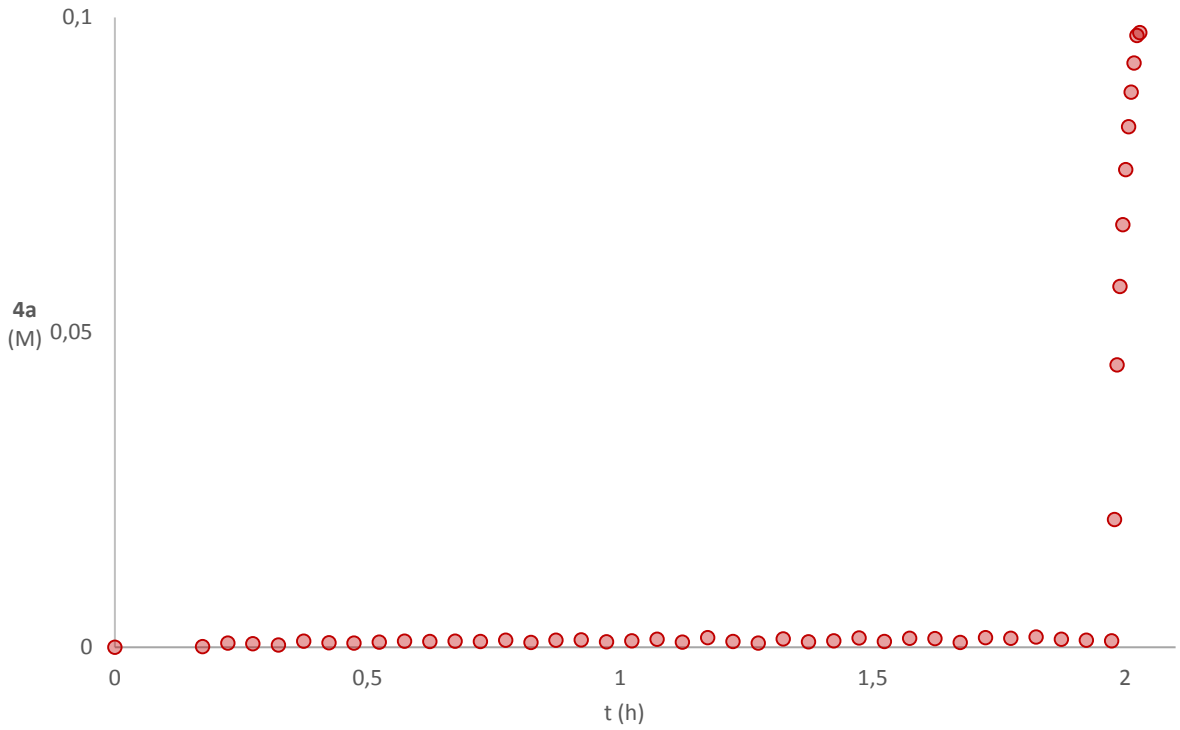


Figure S30: *Reaction profile of the formation of* ***4a*** *in the absence of light and during the illumination period after 2 h of dark pre-treatment (see* ***Table S6****).*

Table S6: *Data of the formation of* ***4a*** *in the absence of light and during the illumination period after 2 h of dark pre-treatment.(see.* ***Figure S30****)*

Entry	Time (s)	[**4a**] (M)		Entry	Time (s)	[**4a**] (M)
1	0	0.000		28	4764	0.001
2	85	0.000		29	4944	0.001
3	265	0.000		30	5124	0.001
4	445	0.000		31	5304	0.001
5	624	0.000		32	5485	0.001
6	804	0.001		33	5665	0.001
7	984	0.001		34	5845	0.001
8	1165	0.000		35	6025	0.001
9	1345	0.001		36	6205	0.002
10	1525	0.001		37	6385	0.001
11	1705	0.001		38	6565	0.001
12	1885	0.001		39	6745	0.001
13	2065	0.001		40	6925	0.001
14	2245	0.001		41	7104	0.001
15	2425	0.001		42	7124	0.020
16	2605	0.001		43	7144	0.045
17	2785	0.001		44	7164	0.057
18	2965	0.001		45	7184	0.067
19	3144	0.001		46	7204	0.076
20	3324	0.001		47	7224	0.083
21	3504	0.001		48	7244	0.088
22	3684	0.001		49	7264	0.093
23	3865	0.001		50	7284	0.097
24	4045	0.001		51	7304	0.098
25	4225	0.002		52	7324	0.100
26	4405	0.001		53	7344	0.101
27	4585	0.001		54	7364	0.101

Conditions: **2a** (0.1 M), BuNAH (**10**; 0.15 M) and benzyl acrylate (**3a**; 0.15 M) in DMSO (0.5 mL).

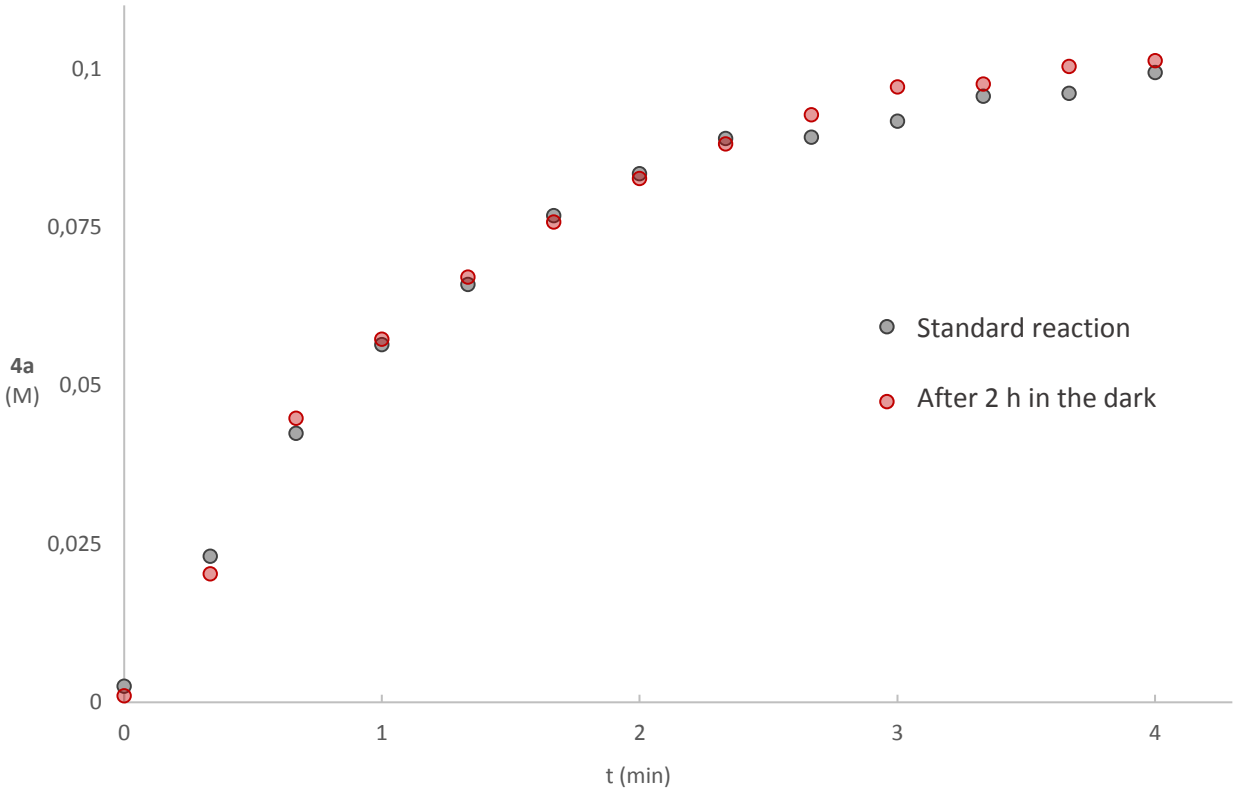


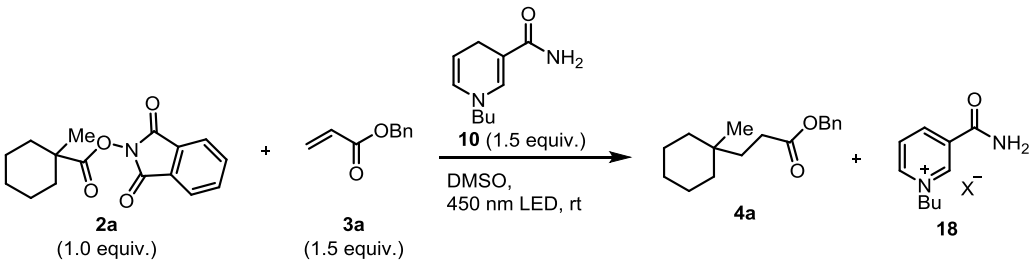
***Figure S31**: Overlay of the reaction profiles of the standard reaction (see. **Figure S27**) and the reaction after 2 h in the dark (see. **Figure S30**). Time has been normalized to the period of illumination. (see. **Table S7**)*

Table S7**: Time normalized data of the illumination periods in the standard reaction (See: **Table S4**) and after 2h dark pre-treatment (see **Table S6**). See **Figure S31

	Standard condition		After 2 h in dark	
Entry	Time (s)	[**4a**] (M)	Time (s)	[**4a**] (M)
1	0	0.002	0	0.001
2	20	0.023	20	0.020
3	40	0.042	40	0.045
4	60	0.056	60	0.057
5	80	0.066	80	0.067
6	100	0.077	100	0.076
7	120	0.083	120	0.083
8	140	0.089	140	0.088
9	160	0.089	160	0.093
10	180	0.092	180	0.097
11	200	0.096	200	0.098
12	220	0.096	220	0.100
13	240	0.099	240	0.101

Standard condition: **2a** (0.1 M), BuNAH (**10**; 0.15 M) and benzyl acrylate (**3a**; 0.15 M) in DMSO (0.5 mL), irradiation with blue LEDs at 20−22 °C.

Procedure for the in situ NMR experiment to study the kinetic effect of the initial concentration of 2a



An oven-dried NMR tube was charged with the appropriate amount of stock solutions of **2a** (1.0 equiv.), BuNAH (**10**; 1.5 equiv.) and benzyl acrylate (**3a**; 1.5 equiv.) in DMSO under argon and exclusion of light. The mixture was diluted with DMSO up to a total volume of 0.5 mL, and irradiated with blue LEDs at 20−22 °C. The progress of the reaction was monitored by ^{1}H-NMR spectroscopy.

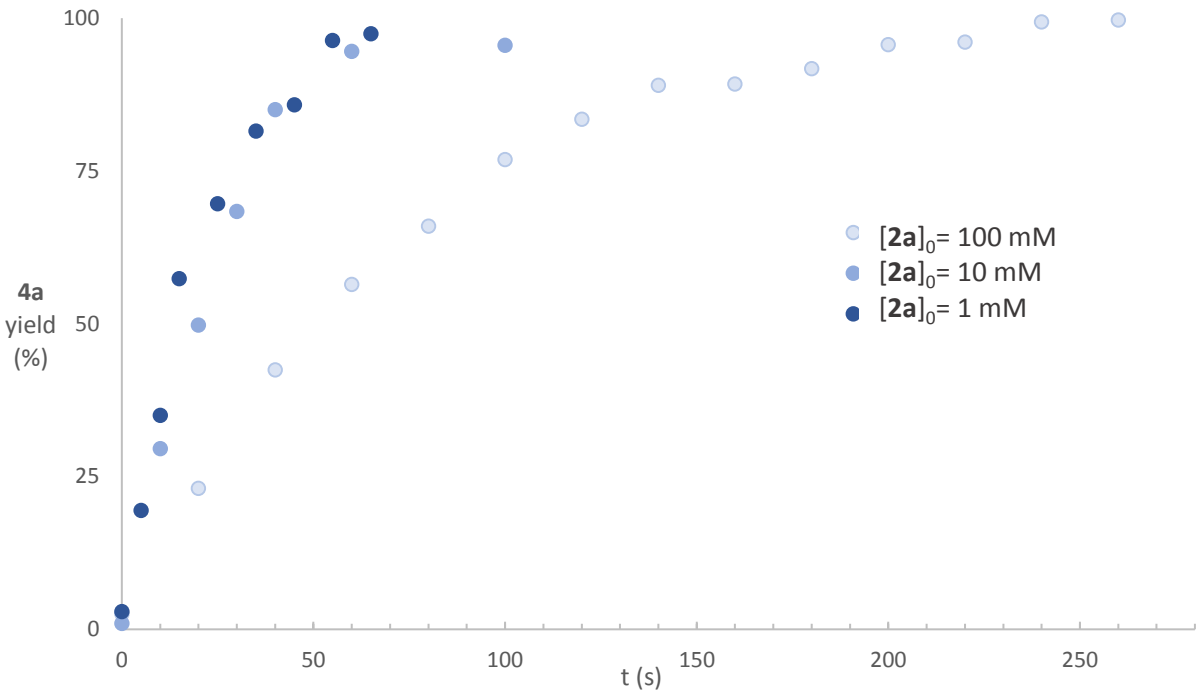


***Figure S32**: Reaction profile of the production of 4a with different initial concentrations of **2a** (see. **Table S8**)*

***Table S8**: Data of the formation of **4a** with **3a** at different initial concentrations of **2a** (**see. Figure S32**).*

Entry	$[\mathbf{2a}]_0$ = 100 mM[a]		$[\mathbf{2a}]_0$ = 10 mM		$[\mathbf{2a}]_0$ = 1 mM[b]	
	Time (s)	Yield **4a** (%)	Time (s)	Yield **4a** (%)	Time (s)	Yield **4a** (%)
1	0	2.52	0	0	0	2.92
2	20	23.07	10	29.57	5	19.43
3	40	42.45	20	49.79	10	35.02
4	60	56.45	30	68.399	15	57.37
5	80	65.94	40	85.01	25	69.65
6	100	76.84	60	94.54	35	81.52
7	120	83.46	100	95.54	45	85.80
8	140	89.01	-	-	55	96.37
9	160	89.21	-	-	65	97.44
10	180	91.73	-	-	-	-
11	200	95.66	-	-	-	-
12	220	96.11	-	-	-	-
13	240	99.40	-	-	-	-
14	260	99.72	-	-	-	-

Conditions: **2a** (1.0 equiv.), **10** (1.5 equiv.), and **3a** (1.5 equiv.) in DMSO (0.5 mL) irradiation with blue LEDs at 20−22 °C; a) standard reaction conditions (see.

Table S4); b) DMSO-d_6 was used as solvent.

Procedure for the control reaction for the inner filter effect

A standard reaction mixture with **2a** (14 mg, 50 µmol, 0.1 M), **10** (0.4 mL in DMSO-d_6, 0.2 M, 75 µmol, 1.5 equiv.), and **3a** (11 µL, 75 µmol, 1.5 equiv.) were pre-mixed under inert atmosphere using a screw-neck vial that was wrapped in aluminum foil. All reactants were dissolved in additional DMSO-d_6 (0.1 mL) under strict exclusion of light. Then 60 µL of the reaction mixture was filled into a thin NMR reactor (d = 1.25 mm). The reactor was closed under inert gas, placed in an empty NMR tube, and illuminated with blue LEDs at 20−22 °C. The progress of the reaction was followed by ^{1}H-NMR.

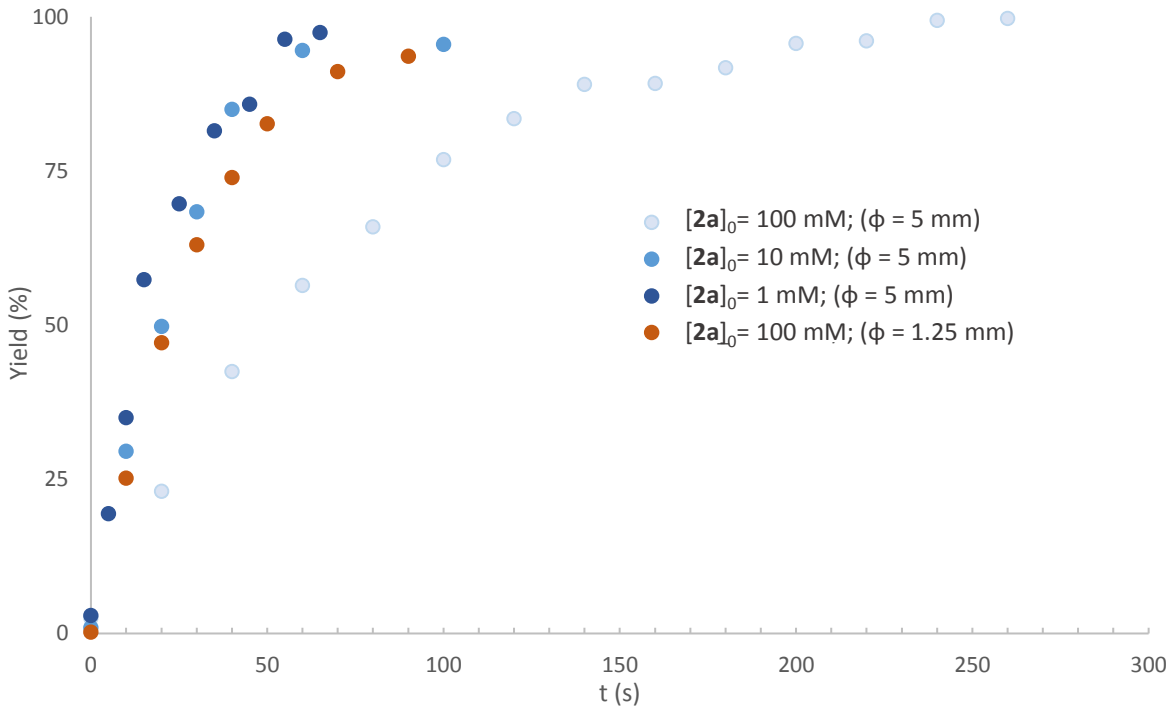


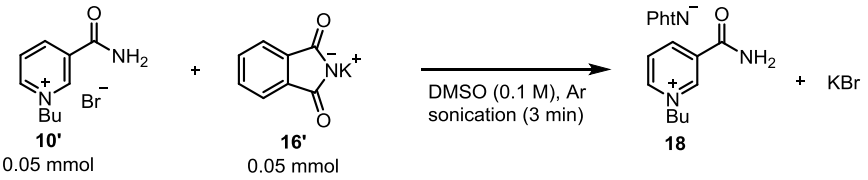
***Figure S33**. Inner filter effect. Overlay of the different initial concentration profiles (see. **Table S8**) with standard initial concentration in a thin NMR tube (ϕ = 1.25 mm) (see. **Table S9**).*

***Table S9**: Data for the inner filter effect experiment.*

Entry	Time (s)	[**4a**] (M)	Yield **4a** (%)
1	0	0.000203	0.20
2	10	0.02519	25.19
3	20	0.047124	47.12
4	30	0.063005	63.00
5	40	0.073932	73.93
6	50	0.08265	82.65
7	70	0.091137	91.14
8	90	0.0936	93.60

Conditions: **2a** (0.1 M), BuNAH (**10**; 0.15 M) and benzyl acrylate (**3a**; 0.15 M) in DMSO-d_6, irradiation with blue LEDs at 20−22 °C.

In situ detection of pyridinium salt (18) by ^{1}H-NMR



An oven-dried NMR tube was charged with 1-butyl-3-carbamoylpyridin-1-ium bromide (**10'**; 12.95 mg, 0.05 mmol) and potassium phthalimide (**16'**; 9.24 mg, 0.05 mmol). The tube was evacuated and refilled with argon (three cycles), followed by addition of anhydrous DMSO (0.5 mL). The mixture was then sonicated for 3 min and the colourless mixture turned into yellow. A ^{1}H-NMR spectrum of the mixture was recorded.

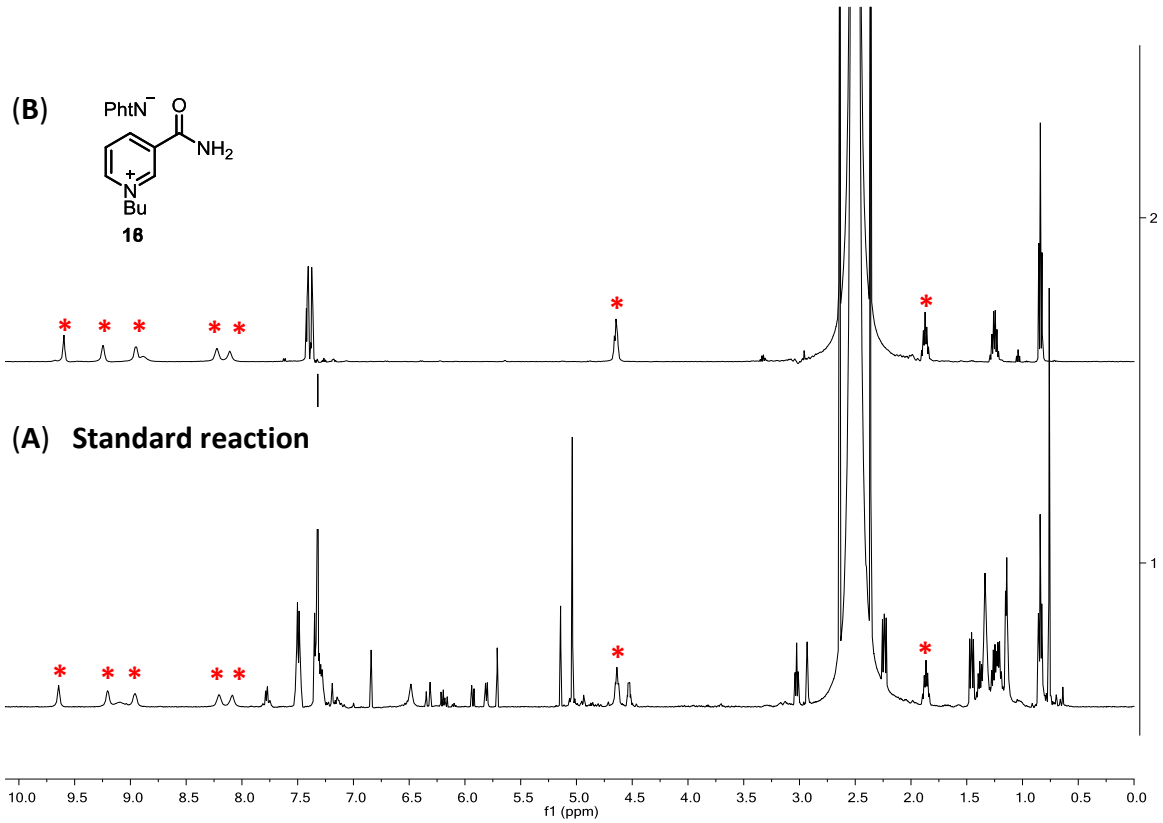


***Figure S34**: ^{1}H-NMR of (A) the standard reaction after complete conversion of **2a** (see. **Figure S27**); (B) **18** in DMSO; signals for **18** are highlighted in red.*

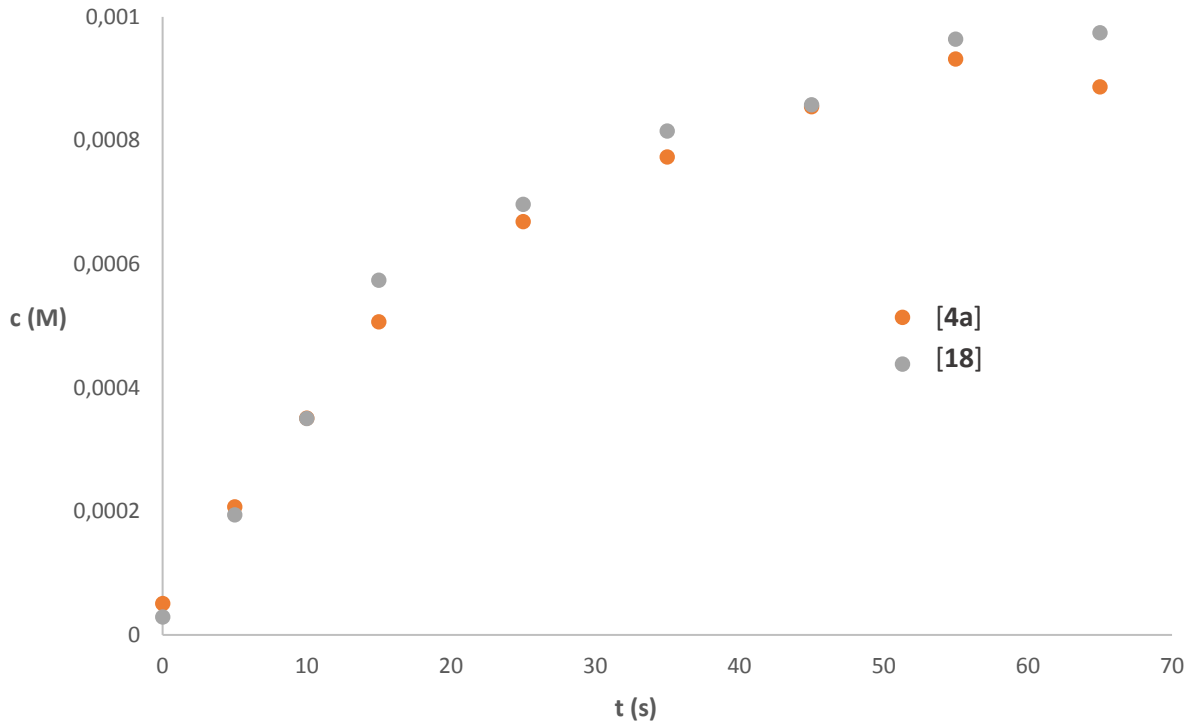


***Figure S35**: Formation of photo-ligated product **4a** and pyridinium salt **18** ([**2a**]0 = 1 mM) in DMSO-d6 (see. Table S10).*

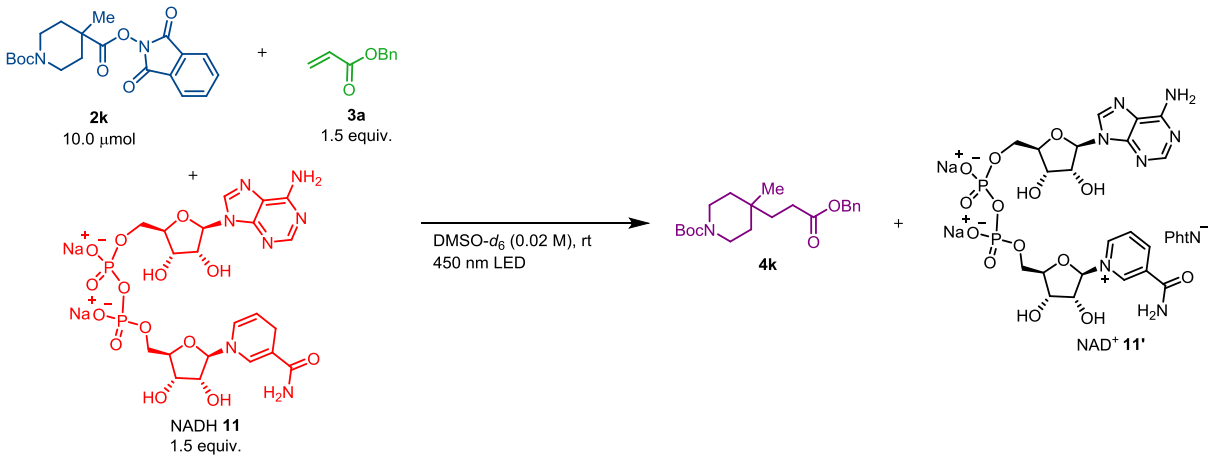
***Table S10**: Formation of **4a** and pyridinium salt **18** ([**2a**]$_0$ = 1 mM). (see. Figure S35)*

Entry	Time (s)	[**4a**] (mM)	[**18**] (mM)
1	0	0	0
2	20	0.136	0.139
3	40	0.274	0.275
4	60	0.396	0.406
5	80	0.594	0.625
6	100	0.707	0.748
7	120	0.784	0. 818
8	140	0.824	0. 879
9	160	0.854	0. 912

Reaction conditions: **2a** (50 µmol), **3a** (1.5 equiv.), **10** (1.5 equiv.) in DMSO-d_6 irradiation with blue LEDs at 20-22 °C.

7. Preliminary evaluation of the photo-coupling with NADH (11)

Profiling of photo-ligation using NADH (11) as reductant by ^{1}H-NMR



The reaction was performed under strict exclusion of light. Redox-active ester **2k** (3.9 mg, 10.0 µmol, 1.0 equiv.) and NADH (**11**; 10.6 mg, 15.0 µmol, 1.5 equiv.) were weighed carefully in a NMR tube. After closing with a rubber septum, the vial was evacuated, refilled with argon (three times) and dry degassed DMSO-d_6 (0.5 mL) containing benzyl acrylate (**3a**; 2.4 mg, 15 µmol, 1.5 equiv.) was added. The mixture was then irradiated with 450 nm LED at 20–22°C. The progress of the reaction was monitored by ^{1}H-NMR.

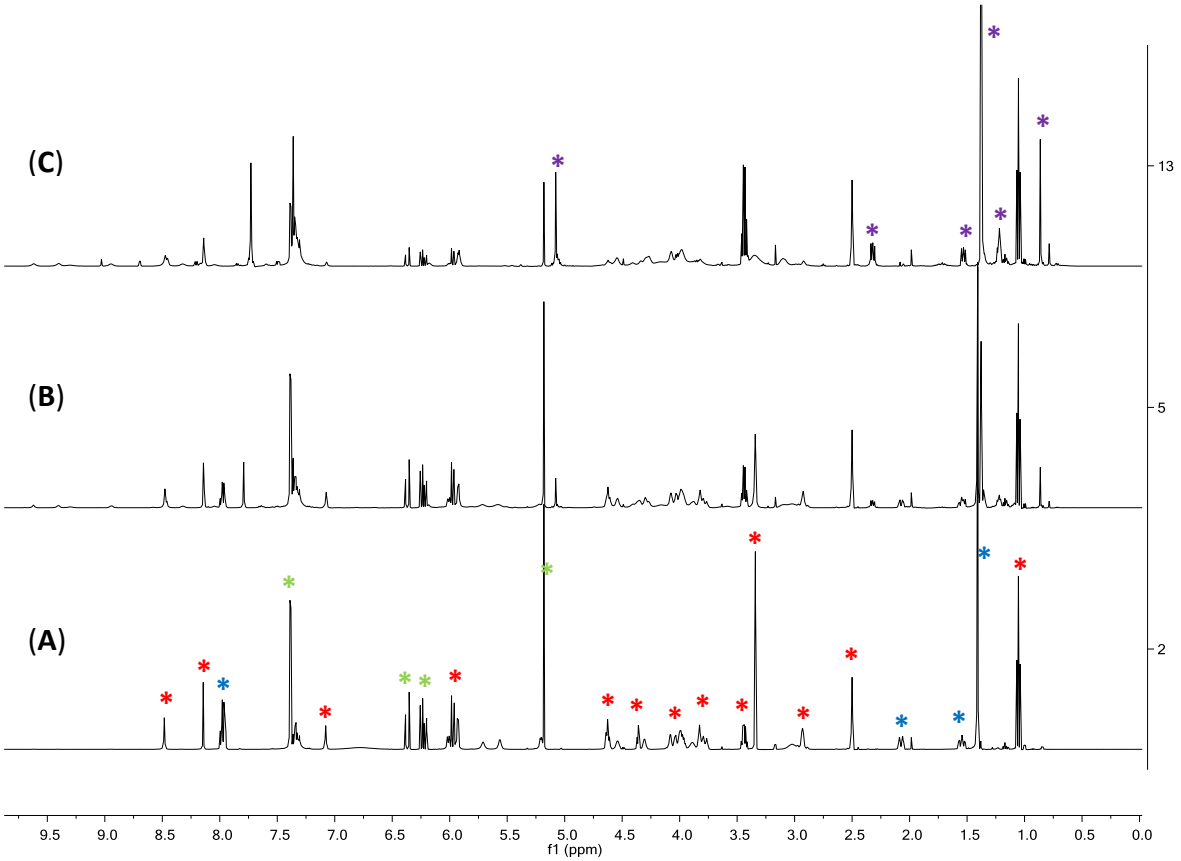


Figure S36: ^{1}H-*NMR spectra of the conversion of **2k** to **4k** using NADH (**11**) as reductant after (A) 0 min; (B) 6 min; (C) 73 min of irradiation.*

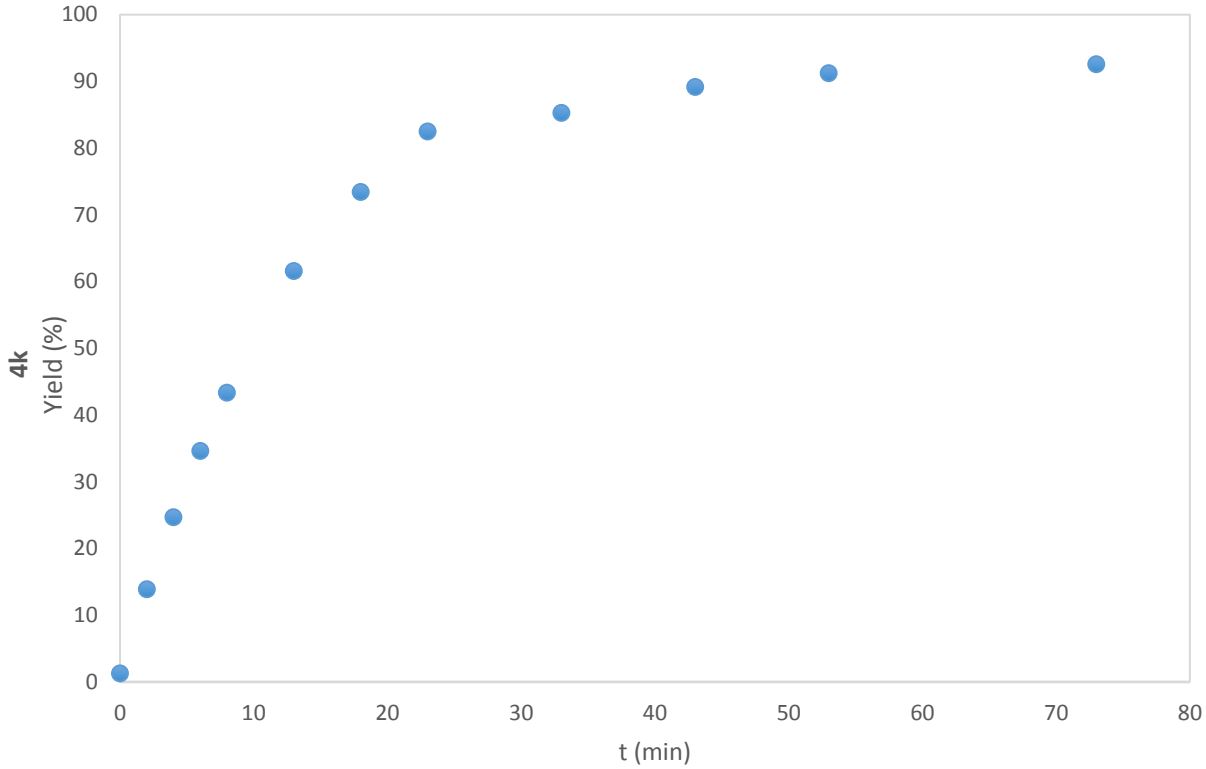


***Figure S37**: Progress of photo-ligation reaction using NADH (**11**) as reductant monitored by ^{1}H-NMR (see. **Table S11**).*

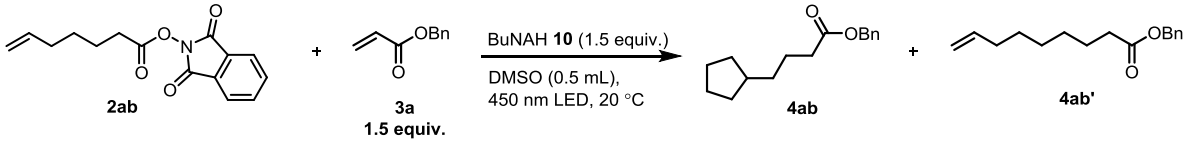
***Table S11**: Data of photo-ligation promoted by NADH (**11**) (see. **Figure S37**).*

Entry	Time (min)	[**4k**] (M)	Yield **4k (%)**
1	0	0.0002	1
2	2	0.002	13
3	4	0.004	24
4	6	0.006	34
5	8	0.008	43
6	13	0.012	61
7	18	0.014	73
8	23	0.016	82
9	33	0.017	85
10	43	0.017	89
11	53	0.018	91
12	73	0.018	92

8. Mechanistic studies

Radical clock experiments

*Syntheses of benzyl 4-cyclopentylbutanoate (**4ab**) and benzyl non-8-enoate (**4ab'**)*



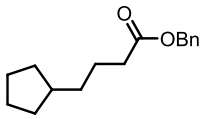
Following General procedure B3, 1,3-dioxoisoindolin-2-yl hept-6-enoate (**2ab**, 1.0 equiv.), benzyl acrylate (**3a**, 1.5 equiv.) and 1-butyl-1,4-dihydropyridine-3-carboxamide (**10**, 1.5 equiv.) in DMSO were illuminated for 5 min. The product was obtained as a mixture of **4ab** and **4ab'**. The yield was determined by ^{1}H-NMR using 1,1,2,2-tetrachloroethane as internal standard.

***Table S12**: Data of radical clock experiment.*

Entry	[**2ab**]$_0$ (M)	Conversion **2ab** (%)	Ratio (**4ab/4ab'**)	Yield (**4ab+4ab'**) (%)[a]
1[b]	0.01	>99	94:6	78
2[b]	0.05	>99	80:20	66
3[c]	0.1	>99	51:49	96
4[c]	0.2	>99	40:60	82

a) The yield was determined by ^{1}H-NMR with 1,1,2,2-tetrachloroethane as an internal standard; b) 50 µmol of **2ab**; c) 100 µmol of **2ab**.

*Characterization of benzyl 4-cyclopentylbutanoate **(4ab)***



Appearance: colorless oil.

TLC: R_f = 0.38 (petroleum ether/EtOAc = 10:1, UV-active and stains in permanganate).

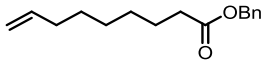
^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.42 – 7.29 (m, 5H), 5.12 (s, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 1.79 – 1.70 (m, 3H), 1.70 – 1.61 (m, 2H), 1.61 – 1.54 (m, 2H), 1.52 – 1.44 (m, 2H), 1.35 – 1.25 (m, 2H), 1.13 – 0.98 (m, 2H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.9, 136.3, 128.7, 128.3, 128.3, 66.2, 40.0, 35.8, 34.7, 32.7, 25.3, 24.3.

HRMS (ESI-TOF) calc'd for $C_{16}H_{22}O_2Na$ $[M+Na]^+$: 269.1512; found: 269.1517.

All the data are in accordance with the literature.[7]

*Characterization of benzyl non-8-enoate **(4ab')***



Appearance: colorless oil.

TLC: R_f = 0.36 (petrol ether/EtOAc = 10:1, UV-active and stains blue in vanillin).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.44 – 7.30 (m, 5H), 5.79 (ddt, *J* = 16.9, 10.2, 6.6 Hz, 1H), 5.11 (s, 2H), 5.07 – 4.82 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 2.08 – 1.94 (m, 2H), 1.75 – 1.57 (m, 2H), 1.43 – 1.27 (m, 6H).

^{13}C-NMR (101 MHz, $CDCl_3$) δ (ppm) = 173.7, 139.0, 136.1, 128.5, 128.2, 128.2, 114.3, 66.1, 34.3, 33.7, 29.0, 28.7, 28.7, 24.9.

HRMS (ESI-TOF) calc'd for $C_{16}H_{22}O_2Na$ $[M+Na]^+$: 269.1512; found: 269.1517.

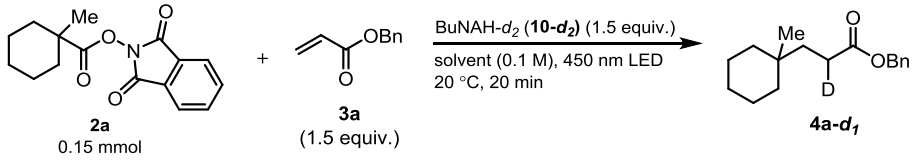
Deuterium labelling experiment

*Synthesis of 1-Butyl-4,4-dideuterio-1,4-dihydronicotinamide (**10**-d_2)*

1-Butyl-4,4-dideuterio-1,4-dihydronicotinamide (**10**-d_2) was prepared from **10'** by sequential reduction and oxidation following literature known procedure.[14] The product was obtained after four reduction and oxidation cycles with 94% D-incorporation as a yellow oil.

The spectroscopic data was found consistent with the literature.[14]

*Synthesis of benzyl 3-(1-methylcyclohexyl)propanoate-d_1 (**4a**-d_1)*



General procedure B3 was applied using redox-active ester **2a** (43.1 mg, 0.15 mmol, 1.0 equiv.), BuNAH-d_2 (**10**-d_2; 41.0 mg, 0.26 mmol, 1.5 equiv., 94% D; determined by ^{1}H-NMR), and benzyl acrylate (**3a**; 36.5 mg, 0.26 mmol, 1.5 equiv.) under illumination with blue LEDs at 20 °C for 20 min in the appropriate solvent (0.1 M) to yield **4a**-d_1. Yields and D% were determined by ^{1}H-NMR using 1,1,2,2-tetrachloroethane as internal standard.

Entry	Solvent	Yield **4a**-d_1 (%)	Ratio (**4a**/**4a**-d_1)
1	DMSO-d_6	57	31:69
2	DMSO	50	32:68
3	DMSO/H_2O 1:1	35[a]	30:70

a) 85% conversion after 30 min illumination.

Appearance: colorless oil.

TLC: Rf = 0.22 (pentane/DCM = 2:1, UV-active stains in PMA).

^{1}H-NMR (400 MHz, $CDCl_3$) δ (ppm) = 7.41 – 7.29 (m, 5H), 5.11 (s, 2H), 2.35 – 2.26 (m, 1.2 H), 1.65 – 1.56 (m, 2H), 1.49 – 1.37 (m, 5H), 1.36 – 1.26 (m, 1H), 1.30 – 1.17 (m, 4H), 0.85 (s, 3H).

^{13}C-NMR (126 MHz, $CDCl_3$) δ (ppm) = 174.6, 136.3, 128.7, 128.4, 128.3, 66.3, 37.6, 36.8, 32.5, 29.1, 29.0, 28.9, 28.7, 26.5, 24.6, 22.1.

HRMS (ESI-TOF) calc'd for $C_{17}H_{23}DO_2Na$ $[M+Na]^+$: 284.1731, found: 284.1730.

Determination of the quantum yield of the photo–ligation

The photon flux of the spectrophotometer was determined by standard potassium ferrioxalate actinometry.[15]

Preparation of buffered phenanthroline solution (Solution A)

A buffered solution was made by dissolving phenanthroline (25 mg, 138.0 µmol) and anhydrous sodium acetate (5.63 g, 0.07 mol) in 0.5 M H_2SO_4 (25 mL).

Preparation of potassium ferrioxalate solution (Solution B)

The solution of potassium ferrioxalate trihydrate in 0.05 M H_2SO_4 was prepared in a dark laboratory illuminated with red light. Potassium ferrioxalate trihydrate (736 mg, 1.5 mmol) was dissolved in 0.05 M H_2SO_4 (10 mL) in a volumetric flask to yield a 0.15 M solution.

Four cuvettes were charged with solution B (2 mL). The cuvettes were irradiated at λ = 450 nm with an excitation slit width of 5.0 nm for the time as indicated in table S1. After irradiation, phenanthroline solution (0.35 mL solution A) was added to every cuvette (irradiated and non-irradiated). The solutions were then allowed to rest for 1 h in the dark to complete the chelation of ferrous ions to the phenanthroline. After 1 h, absorbance was measured for all four solutions (and a 0.05 M H_2SO_4 blank) solution at λ = 510 nm.
For the calculation of photon flux the following equations were used:

$$\text{mol of } Fe^{2+} = \frac{V * \Delta A}{l * \varepsilon}$$

$$Photon\ flux = \frac{mol\ of\ Fe^{2+}}{\Phi * t * f}$$

Where V is the total volume of the solution (2.35 mL), ΔA is the difference in absorption between the irradiated and non-irradiated samples, l is the path length (1 cm), and Ɛ is the molar absorptivity at λ = 510 nm (11110 L mol^{-1} cm^{-1}),[15] ϕ is the quantum yield for the potassium ferrioxalate actinometer (1.01),[15] t is the time of irradiation (s), and f is the fraction of light absorbed at λ = 450 nm by potassium ferrioxalate (0.99833).[15]

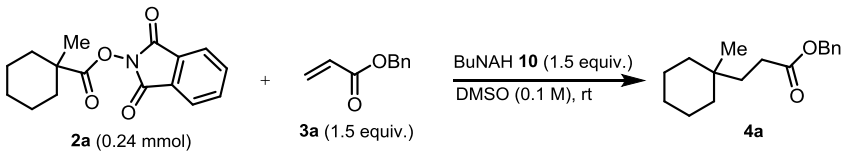
Determination of photon flux

Table S13: *Determination of photon flux using ferrioxalate actinometry*

	Irradiation time (s)	Abs (A)	ΔA	V ($Lx10^{-3}$)	Fe^{2+} ($molx10^{-8}$)	Photon flux ($einstein.s^{-1}x10^{-9}$)
1	0	0.40	0	2.35	-	-
2	11.40	0.69	0.29	2.35	6.08	5.28
3	20.90	0.81	0.41	2.35	8.72	4.14
4	30.90	1.02	0.61	2.35	12.99	4.17
						Average: 4.53
						Std. dev.: 0.65

Considering 95% confidence interval: average photon flux of the spectrofluorometer is (4.53 ± 0.74) $x10^{-9}$ $einstein.s^{-1}$.

Determination of the quantum yield



The reactions were set up inside the glove box. A cuvette was charged with redox-active ester **2a** (68.9 mg, 0.24 mmol, 1.0 equiv.) and BuNAH (**10**; 64.9 mg, 0.36, 1.5 equiv.). Anhydrous DMSO (2.4 mL) was added to the mixture, followed by the addition of benzyl acrylate (**3a**; 58.4 mg, 0.36 mmol, 1.5 equiv.). The cuvette was wrapped in an aluminium foil and was brought outside of the glove box. The absorption was measured at λ = 450 nm. The sample was irradiated in the spectrofluorometer for the indicated period of time (table S2) at λ = 450 nm with an excitation slit width of 5.0 nm. Internal standard, 1,3,5-trimethoxybenzene (40.36 mg, 0.24 mmol) was added to the cuvette. The mixture was shaken and 0.5 mL aliquot was used to measure the NMR yield by using no-*D* ^{1}H-NMR.

$$Quantum\ yield, \Phi = \frac{mol\ of\ \mathbf{4a}}{\text{photon flux} * \text{t} * \text{f}}$$

Where t is the time of the reaction and f is the fraction of the light absorbed at 450 nm by the reaction mixture = $1–10^{–A}$. Absorbance (A) of the reaction mixture at λ = 450 nm is 1.99. So, f = $1–10^{–1.99}$ = 0.9897.

Additionally, the absorbance (A) of the reaction mixture after 90 min irradiation at λ = 450 nm was controlled. The corresponding fraction of the light absorbed was determined to be f = $1–10^{–2.79}$ = 0.9984, which is approximately equal to the starting value.

Table S14: *Determination of the quantum yield of the photo-ligation reaction*

	Irradiation time (s)	*NMR yield **4a** (%)*	***4a** (molx10^{-5})*	*Quantum yield (ϕ)*	*Error (Δϕ)*
1	3720	21	5.04	3.02	0.87
2	3720	19.5	4.68	2.80	0.85
3	4500	24	5.76	2.85	0.75

Considering 5% error in measuring the NMR yield, the error in determining the mol of **4a** is 1.20x10^{-5}.

The following equations were used to calculate the error in determining the quantum yield.

$$\Phi = \frac{mol\ of\ 4a}{photon\ flux * t * f}$$

The error in measuring the quantum yield (ϕ) is

$$\Delta\Phi = \sqrt{[\frac{\delta\Phi}{\delta(mol\ of\ 4a)} * \Delta(mol\ of\ 4a)]^2 + [\frac{\delta\Phi}{\delta(photon\ flux)} * \Delta(photon\ flux)]^2}$$

Or, $\Delta\Phi = \sqrt{\left[\frac{\partial}{\partial(mol\ of\ 4a)}(\frac{mol\ of\ 4a}{photon\ flux*t*f}) * \Delta(mol\ of\ 4a)\right]^2 + \left[\frac{\partial}{\partial(photon\ flux)}(\frac{mol\ of\ 4a}{photon\ flux*t*f}) * \Delta(photon\ flux)\right]^2}$

Or, $\Delta\Phi = \sqrt{\left[\frac{1}{photon\ flux*t*f} * \Delta(mol\ of\ 4a)\right]^2 + \left[(-)\frac{mol\ of\ 4a}{(photon\ flux)^2*t*f} * \Delta(photon\ flux)\right]^2}$

Or, $\Delta\Phi = \sqrt{\left[\frac{1}{photon\ flux*t*f} * \Delta(mol\ of\ 4a)\right]^2 + \left[\frac{mol\ of\ 4a}{(photon\ flux)^2*t*f} * \Delta(photon\ flux)\right]^2}$

$$Thus, \Delta\Phi_1 = \sqrt{\left[\frac{1.20 * 10^{-6}}{4.53 * 10^{-9} * 3720 * 0.9984}\right]^2 + \left[\frac{5.04 * 10^{-5} * 7.38 * 10^{-10}}{(4.53 * 10^{-9})^2 * 3720 * 0.9984}\right]^2} = 0.871$$

$$\Delta\Phi_2 = \sqrt{\left[\frac{1.20 * 10^{-6}}{4.53 * 10^{-9} * 3720 * 0.9984}\right]^2 + \left[\frac{4.68 * 10^{-5} * 7.38 * 10^{-10}}{(4.53 * 10^{-9})^2 * 3720 * 0.9984}\right]^2} = 0.852$$

$$\Delta\Phi_3 = \sqrt{\left[\frac{1.20 * 10^{-6}}{4.53 * 10^{-9} * 4500 * 0.9984}\right]^2 + \left[\frac{5.76 * 10^{-5} * 7.38 * 10^{-10}}{(4.53 * 10^{-9})^2 * 4500 * 0.9984}\right]^2} = 0.754$$

Average quantum yield of the photo-ligation reaction was calculated to be

$$\bar{\Phi} = \frac{\Phi_1 + \Phi_2 + \Phi_3}{3} = 2.89.$$

The error in measuring the average quantum yield of the photo-ligation reaction is

$$\Delta\bar{\Phi} = \sqrt{(\frac{\delta\bar{\Phi}}{\delta\Phi_1} * \Delta\Phi_1)^2 + (\frac{\delta\bar{\Phi}}{\delta\Phi_2} * \Delta\Phi_2)^2 + (\frac{\delta\bar{\Phi}}{\delta\Phi_3} * \Delta\Phi_3)^2}$$

$$\text{Or, } \Delta\bar{\Phi} = \sqrt{(\tfrac{1}{3} * \Delta\Phi_1)^2 + (\tfrac{1}{3} * \Delta\Phi_2)^2 + (\tfrac{1}{3} * \Delta\Phi_3)^2} = 0.48$$

After taking into account all these errors, the average quantum yield of the photo-ligation reaction, $\bar{\Phi} = 2.9 \pm 0.5$.

UV-Vis study

UV-Vis absorption spectra of the BuNAH (**10**), redox-active ester **2a**, and the mixture of **10** and **2a** at different concentration were measured to provide information on the formation of EDA complex. From the study it is evident that there is no such difference in absorption on addition of **2a**, which defies the formation of EDA complex (see **Figure S38**). An EDA complex may be formed but absorption enhancement is only marginal at the wavelength of irradiation (450 nm) (see **Figure S40**).

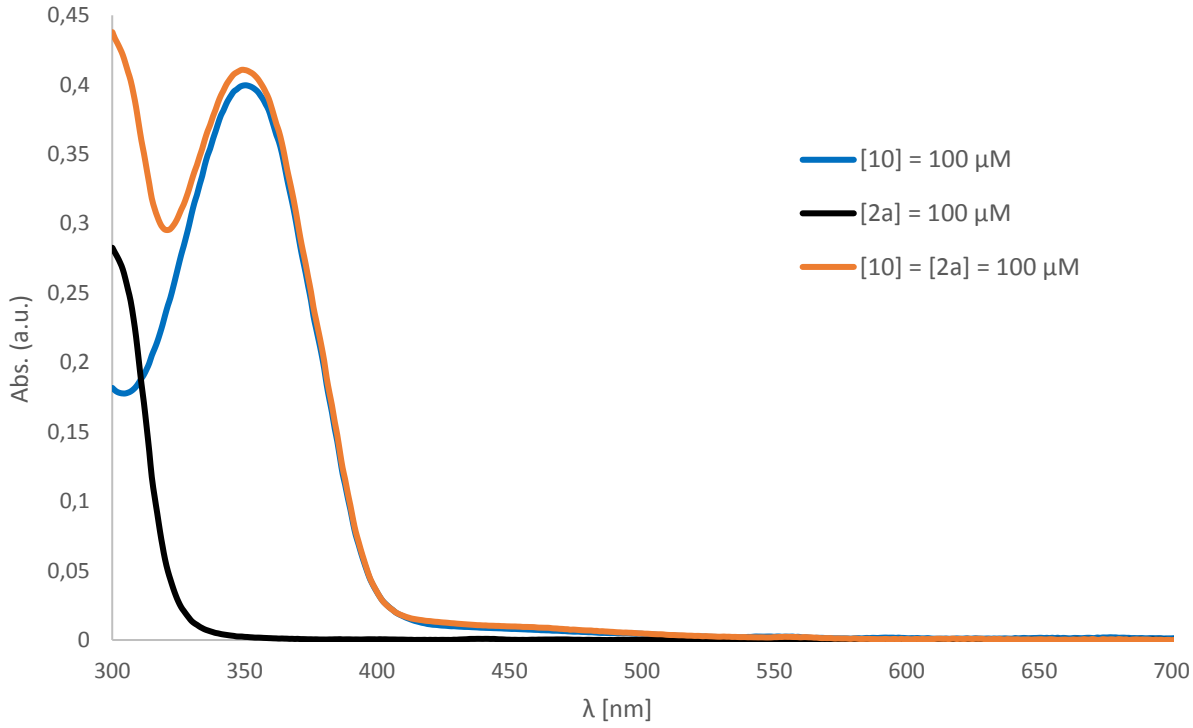


Figure S38*: UV-Vis spectra of* ***2a****,* ***10*** *and their 1:1 mixture at 100 uM concentration. Complete spectrum cannot be acquired due to detector saturation.*

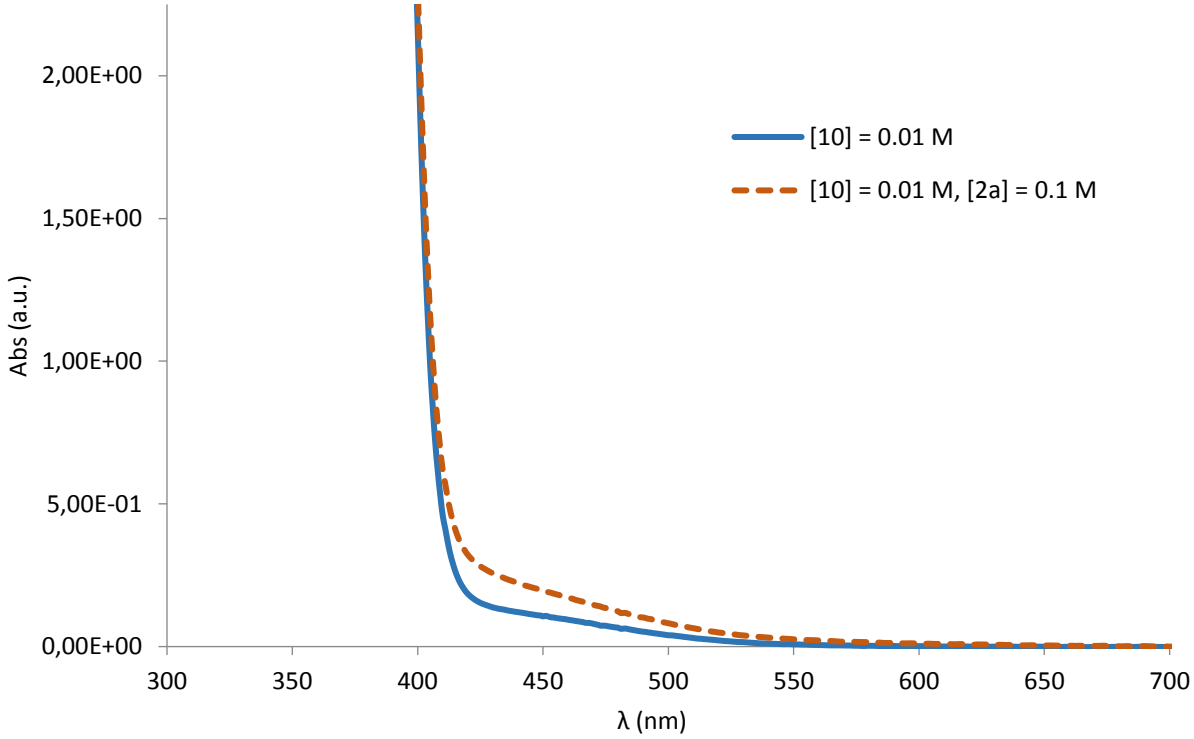


Figure S39: *Absorbance of BuNAH (**10**) before and after quenching with 10 equiv. of redox-active ester **2a**.*

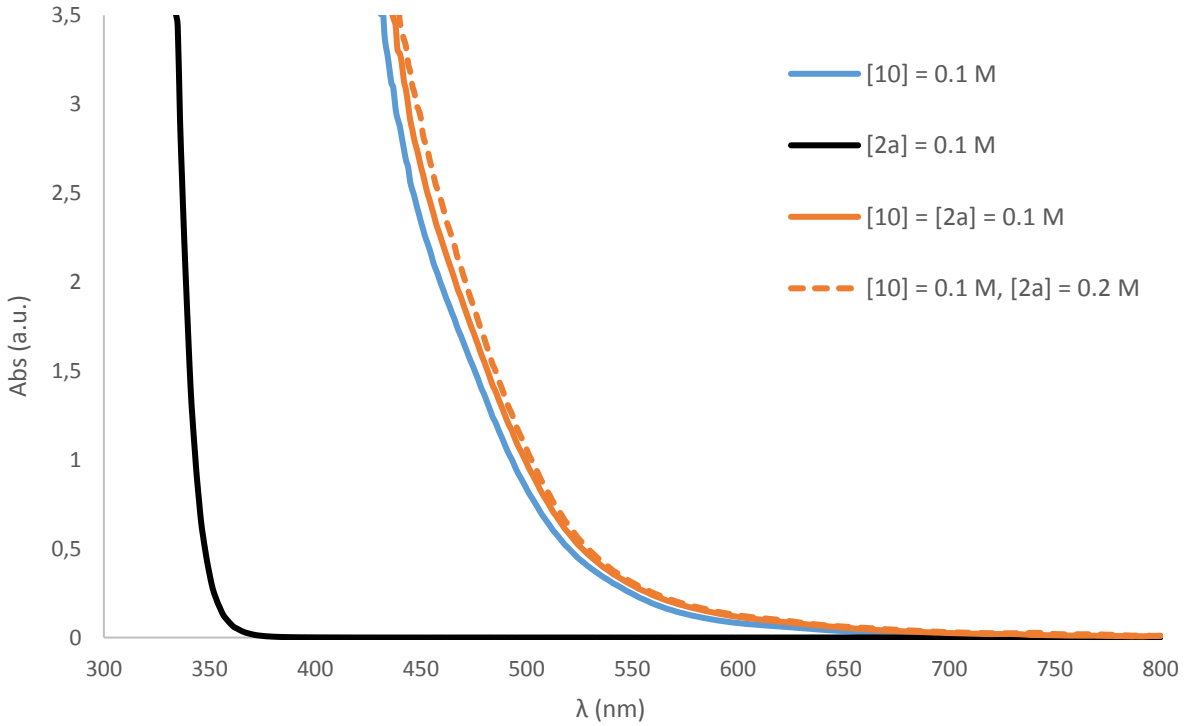


Figure S40*:* UV-Vis *spectra of **2a**, **10** and their 1:1 mixture at 0.1 M (standard preparative reaction concentration)*. Marginal enhancement of absorption may indicate the presence of an EDA complex. *The spectrometer data may be affected by the high concentration of the sample.*

Steady-state fluorescence

*Emission spectrum of BuNAH (**10**) and BuNAH (**10**) - redox-active ester **2a** mixture*

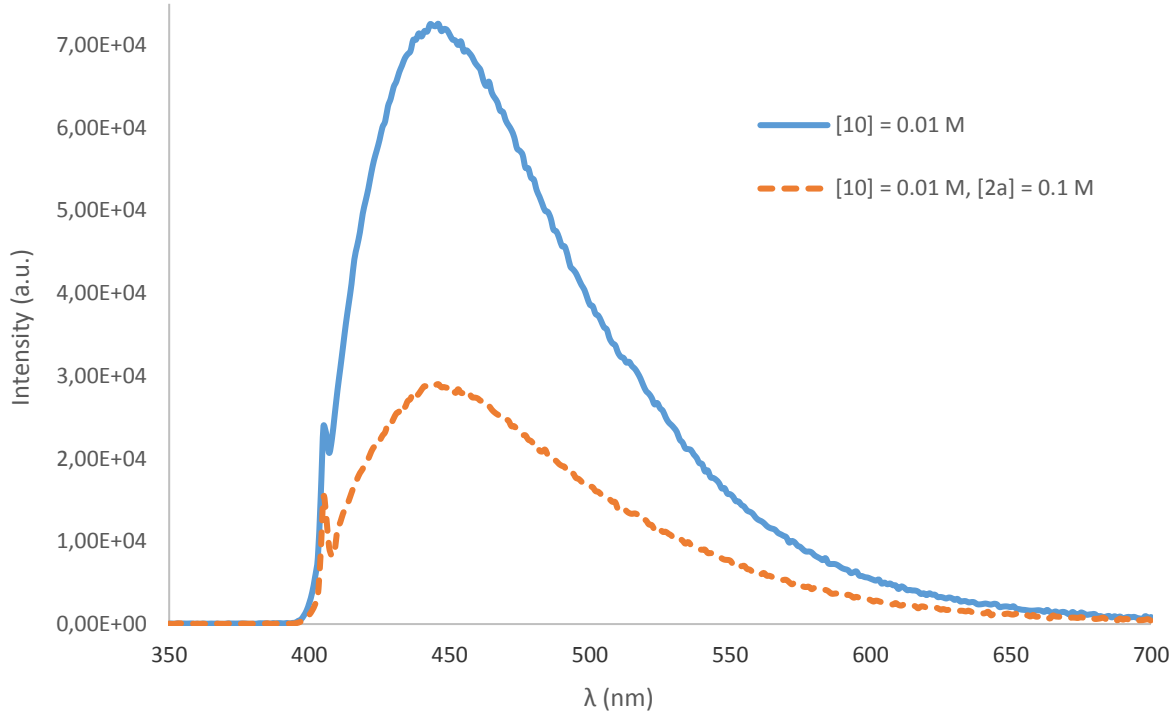


Figure S41: *Emission spectra of BuNAH (**10**) with excitation at 405 nm in absence or presence of redox-active ester **2a**.*

*Excitation spectrum of BuNAH (**10**) and BuNAH (**10**) - redox-active ester **2a** mixture*

Excitation spectra was recorded to confirm that no modifications on the excitation profile of the sample were observed in the range of concentrations used in the quenching experiments.

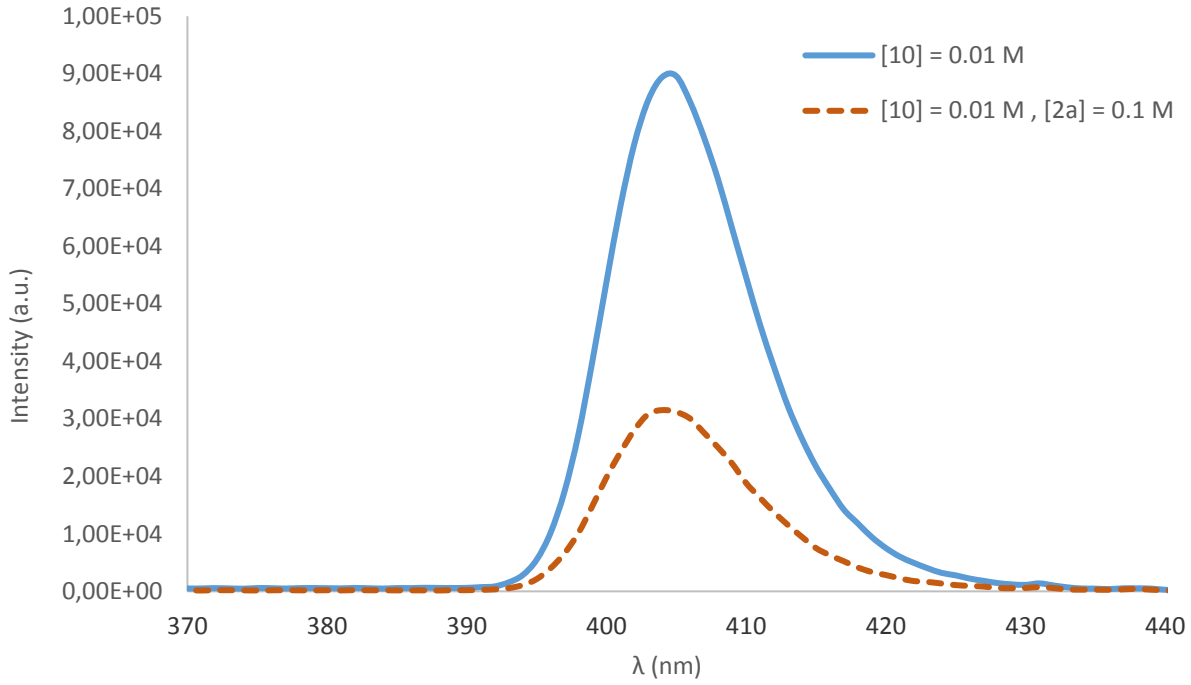


***Figure S42:** Excitation scan of BuNAH (**10**) before and after quenching with 10 equiv. of redox-active ester **2a**. The excitation profile does not reveal a new species upon mixing **10** and **2a**.*

Stern-Volmer quenching experiment

Emission scans were measured at an excitation wavelength, λ = 405 nm with bandwidth of 1.0 nm

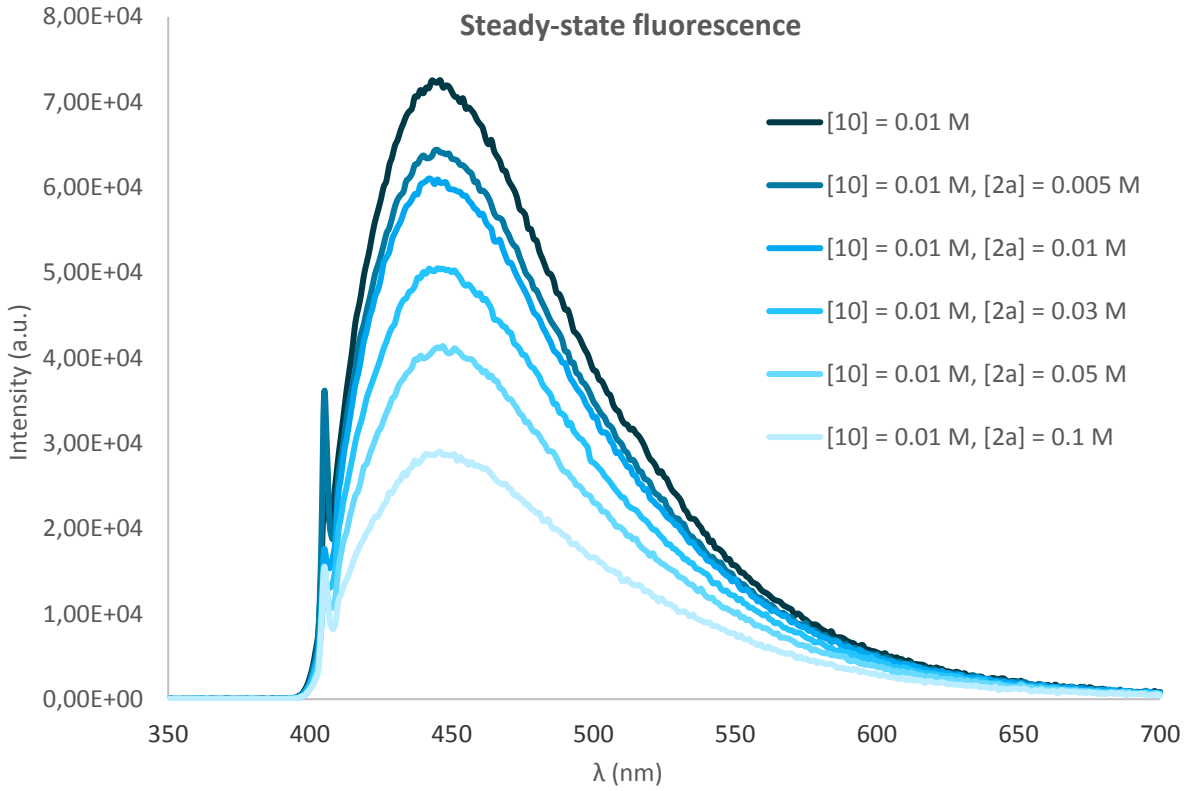


Figure S43: *Luminescence of the BuNAH (**10**) in presence of different amount of redox-active ester **2a**.*

Table S15*: Data of the Stern–Volmer quenching experiment of BuNAH (**10**) and redox-active ester **2a**.*

	2a (mmol)	**10** (mmol)	V (mL)	[**2a**] (Mx10^{-2})	[**10**] (M)	I	I_0/I
0	0.00	0.02	2.00	0	0.01	7.26	1.00
1	0.01	0.02	2.00	0.50	0.01	6.41	1.13
2	0.02	0.02	2.00	1.00	0.01	6.05	1.20
3	0.06	0.02	2.00	3.00	0.01	5.04	1.44
5	0.10	0.02	2.00	5.00	0.01	4.12	1.76
5	0.20	0.02	2.00	10.00	0.01	2.90	2.50

Fluorescence lifetime

Stern–Volmer quenching experiment

Inside the glove box, a dry cuvette was charged with freshly synthesized BuNAH (**10**; 0.02 mmol, 0.01 M) and DMSO (dry, degassed, spectroscopy grade) was added to adjust the total volume to 2 mL. The cuvette was closed with a rubber septum. Every time the quenching of the BuNAH (**10**) by redox-active ester **2a** was performed in a new cuvette. The redox-active ester **2a** was added as indicated in table S3 and the excited state lifetime was measured by TCSPC using a 375 nm laser at 20 MHz pulsing frequency with stop condition 10000 counts per channel (with emission at λ = 450 nm at a bandwidth of 5.0 nm). The time domain decay was fitted using the exponential decay (τ, table S3). LUDOX® SM colloidal silica (30 wt. % suspension in H_2O) was used to measure the instrument response function (IRF).

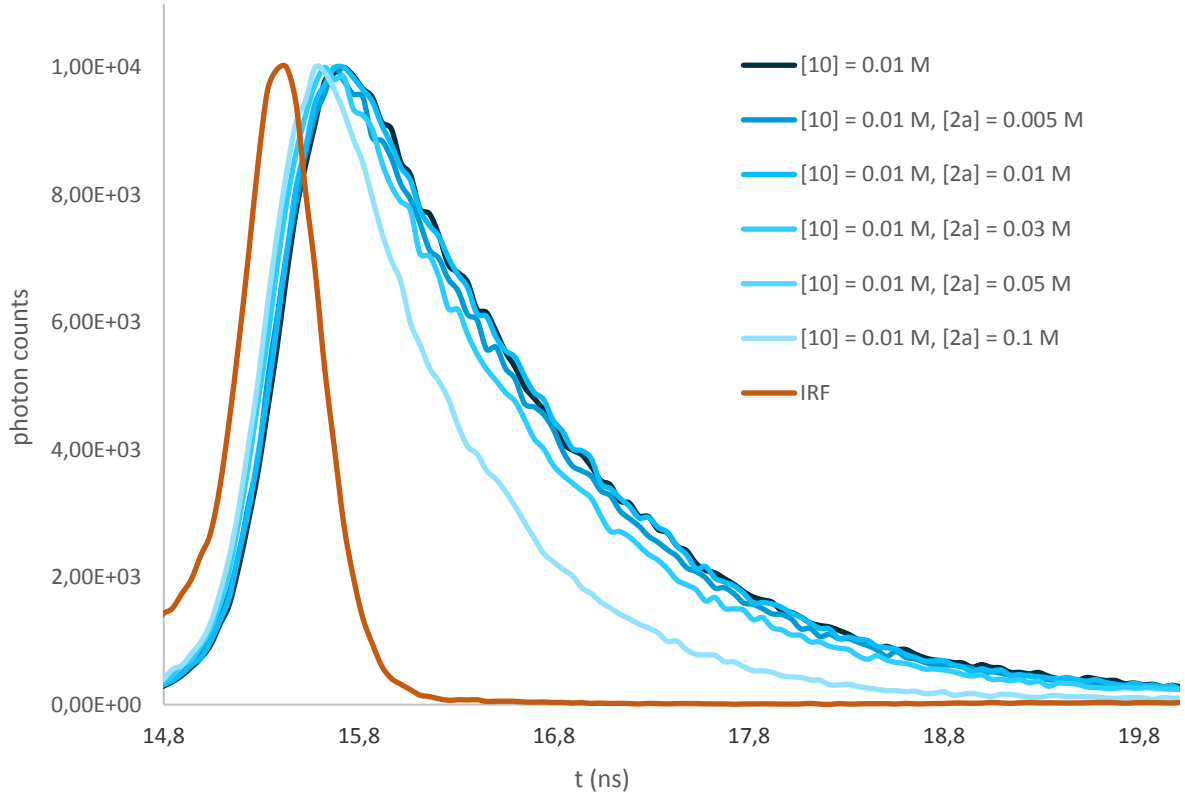


Figure S44: Lifetime measurement of BuNAH (**10**) in presence of different amount of the redox-active ester **2a**.

Table S16**: Data of the Stern–Volmer quenching experiment of BuNAH (**10**) and redox-active ester **2a

	2a (mmol)	**10** (mmol)	V (mL)	[**2a**] (Mx10^{-2})	[**10**] (M)	τ (ns)	χ^2	τ_0/τ
0	0.00	0.02	2.00	0	0.01	1.08	1.28	1.00
1	0.01	0.02	2.00	0.50	0.01	1.05	1.64	1.03
2	0.02	0.02	2.00	1.00	0.01	1.06	1.80	1.02
3	0.06	0.02	2.00	3.00	0.01	0.98	1.36	1.10
4	0.10	0.02	2.00	5.00	0.01	0.86	1.49	1.26
5	0.20	0.02	2.00	10.00	0.01	0.70	1.59	1.54

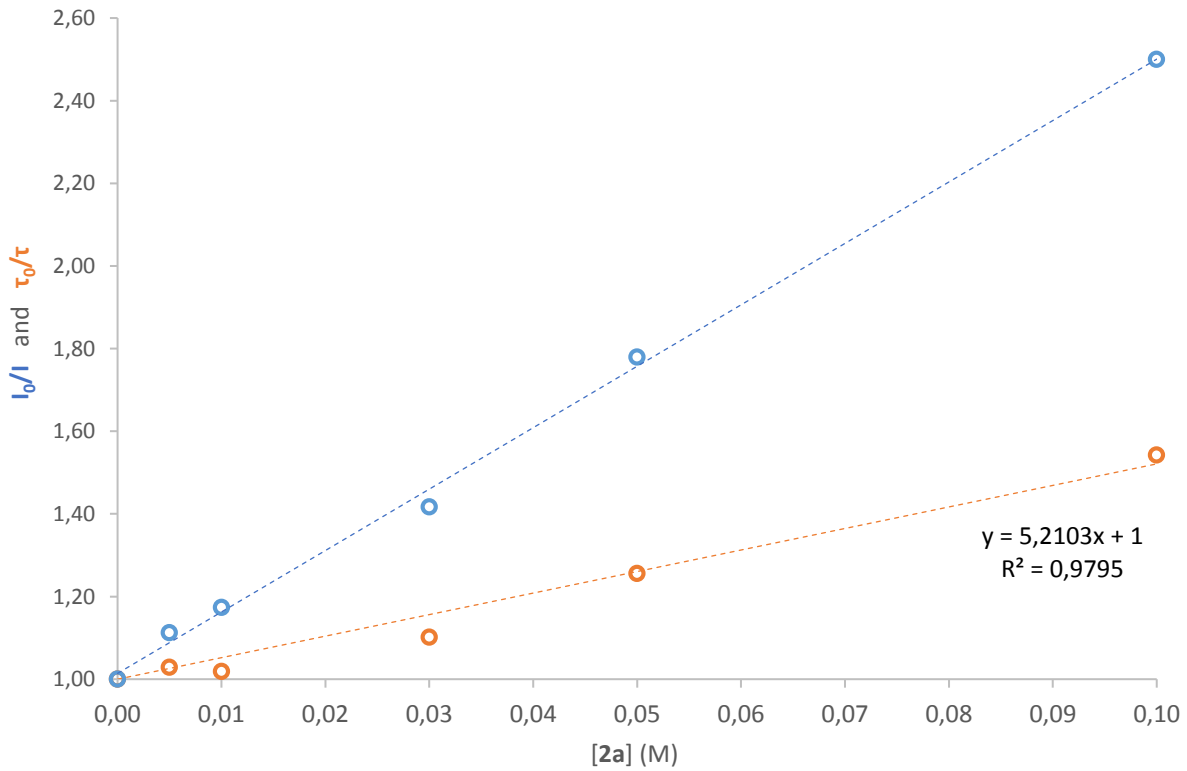


***Figure S45:** Stern-Volmer quenching of BuNAH (**10**) and redox-active ester **2a**: steady-state data (blue; see Table S15) and time-resolved data (orange; see **Table S16**). The different slopes of steady-state and time-resolved data is clearly not consistent with either dynamic or static quenching mechanisms.*

Mixed static and dynamic quenching model

From the above figure, different slopes of lifetime measurement and steady state quenching experiment suggest the occurrence of both dynamic and static quenching with quenching constant k_q and K_{eq} respectively. The reason behind the static quenching can be attributed to the formation of a non-emissive EDA complex (see **Figure S40** for UV-Vis enhanced absorption) between BuNAH (**10**) and redox-active ester **2a**.

The following figure can be considered to explain the dynamic and static quenching of BuNAH (**10**) by **2a**.[16]

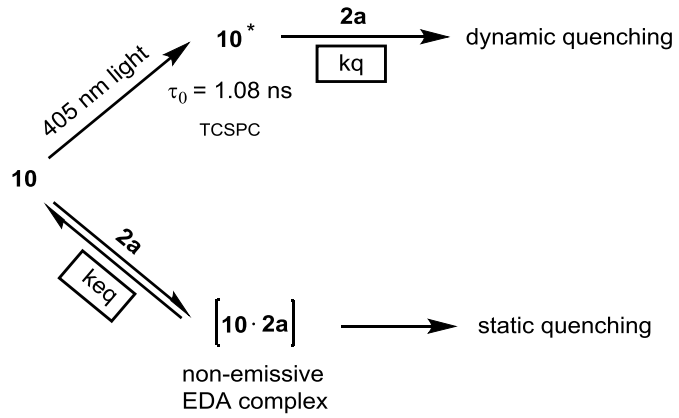


Figure S46**: Model of dynamic and static quenching of BuNAH (**10**) in presence of redox-active ester **2a.

Considering this model, the steady state quenching intensities correspond to dynamic and static components, as follows:

$$\frac{I_0}{I} = \left(1 + k_q \tau_0 [\mathbf{2a}]\right) * (1 + K_{eq}[\mathbf{2a}])$$

Rate of dynamic quenching

Using the lifetime data (see **Figure S22**), we can determine the kinetics of the dynamic quenching component, using the Stern-Volmer expression:

$$\frac{\tau_0}{\tau} = 1 + k_q \tau_0 [\mathbf{2a}]$$

Where k_q is the quenching constant and τ_0 is the lifetime of BuNAH (**10**) without the quencher. The fluorescence lifetime of the pure BuNAH (**10**) was measured, τ_0 = 1.08 ns (see **Table S16**, entry 0). From the linear regression of the time-resolved data (see **Figure S45**), we obtain 5.21 = $k_q\tau_0$.

Thus, the quenching constant of the dynamic component is

$$k_q = \frac{5.21}{\tau_0} = \frac{5.21}{1.08 * 10^{-9} s} = 4.82 * 10^9 \, M^{-1} s^{-1}$$

Fitting of the non-emissive EDA complex association constant:

With this information in hand, the steady-state data was fitted using a mixed dynamic/static quenching model, where the equilibrium constant (K_{eq}) for the formation of the dark complex can be optimized to best fit the data from the equation below. This way, a value of K_{eq} = 6.75 was estimated (see **Figure S47**). This value should only be considered as a rough estimation of the equilibrium constant.

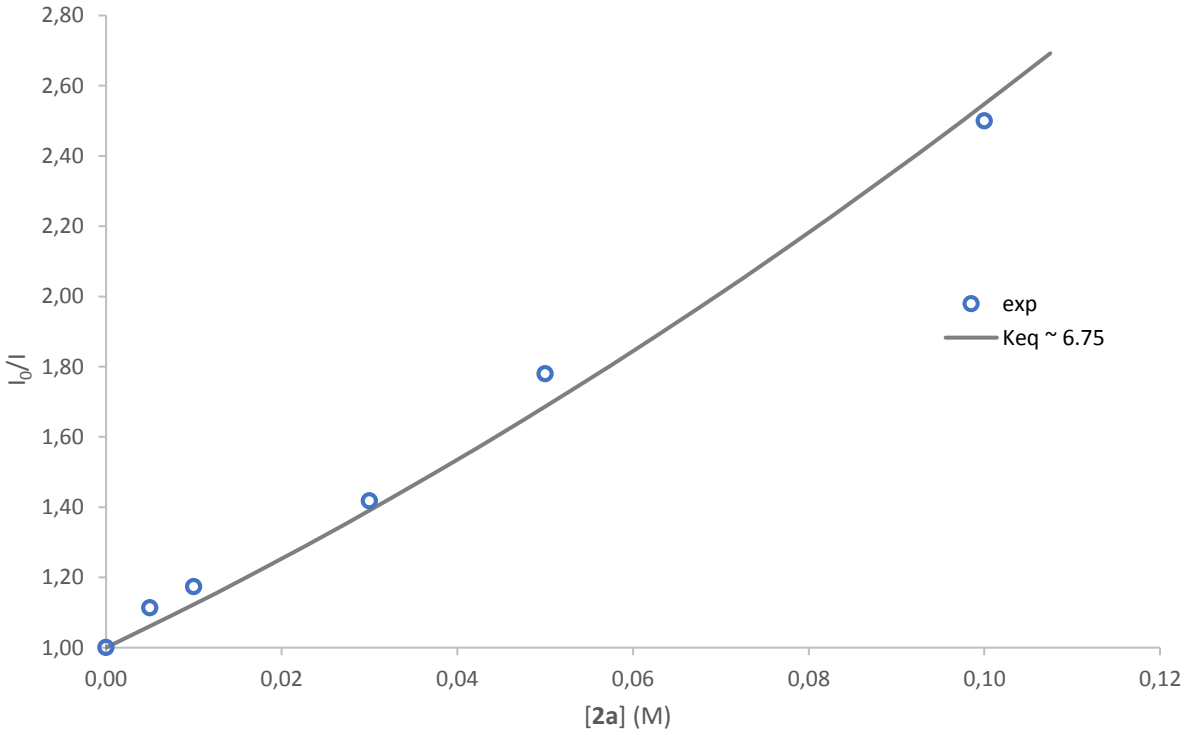


Figure S47: *Fitting of the steady-state luminescence quenching data of BuNAH (**10**) with a model including static and dynamic quenching.*

9. References

1. Fawcett, A.; Pradeilles, J.; Wang, Y.; Mutsuga, T.; Myers, E. L.; Aggarwal, V. K. *Science*, **2017**, *357*, 283–286.

2. Pratsch, G.; Lackner, G. L.; Overman, L. E.; *J. Org. Chem.* **2015**, *80*, 6025 – 6036.

3. Lu, X.; Xiao, B.; Liu, L.; Fu, Y. *Chem. Eur. J.* **2016**, *22*, 11161–11164.

4. Shen, M, L.; Shen, Y.; Wang, P. S. *Org. Lett.* **2019**, *21*, 2993-2997.

5. Qin, T.; Malins, L. R.; Edwards, J. T.; Merchant, R. R.; Novak, A. J. E.; Zhong, J. Z.; Mills, R. B.; Yan, M.; Yuan, C.; Eastgate, M. D.; Baran, P. S. *Angew. Chem. Int. Ed.* **2017**, *56*, 260 – 265.

6. Xue, W.; Oestreich, M. *Angew. Chem. Int. Ed.* **2017**, *56*, 11649–11652.

7. Gao, L.; Wang, G.; Cao, J.; Yuan, D.; Cheng, X.; Guo, X.; Lia, S. *Chem. Commun.* **2018**, *54*, 11534-11537.

8. Nawrat, C. C.; Jamison, C. R.; Slutskyy, Y.; MacMillan, D. W. C.; Overman, L. E. *J. Am. Chem. Soc.* **2015**, *137*, 11270−11273.

9. Lackner, G. L.; Quasdorf, K. W.; Overman, L. E. *J. Am. Chem. Soc.* **2013**, 1*35*, 15342−15345.

10. Zheng, C.; Wang, G. Z.; Shang, R. *Adv. Synth. Catal.* **2019**, *361*, 4500 – 4505.

11. ElMarrouni, A.; Ritts. C. B.; Balsells. J. *Chem. Sci.*, **2018**, *9*, 6639–6646.

12. Paul, C. E.; Gargiulo, S.; Opperman, D. J.; Lavandera, I.; Gotor-Fernandez, V.; Gotor, V.; Taglieber, A.; Arends, I. W. C. E.; Hollmann, F. *Org. Lett.* **2013**, *15*, 180-183.

13. Lackner, G. L.; Quasdorf, K. W.; Pratsch, G.; Overman, L. E. *J. Org. Chem.* **2015**, *80*, 6012−6024.

14. Geddes, A.; Paul, C. E.; Hay, S.; Hollmann, F.; Scrutton, N. S. *J. Am. Chem. Soc.* **2016,** *138*, 11089-11092.

15. Cismesiaa, M. A.; Yoon, T. P. *Chem. Sci.*, **2015**, *6*, 5426-5434.

16. Fraiji, L. K.; Hayes, D. M.;1 Werner, T. C.; *J. Chem. Educ.* **1992**, *69,* 424-428.

17. Wang, J.; Lundberg, H.; Asai, S.; Martín-Acosta, P.; Chen, J. S.; Brown, S.; Farrell, W.; Dushin, R. G.; O'Donnell, C. J.; Ratnayake, A. S.; Richardson, P.; Liu, Z.; Qin, T.; Blackmond, D. G.; Baran, P. S., *Proc. Natl. Acad. Sci.* **2018**, *115(28)*, E6404−E6410.

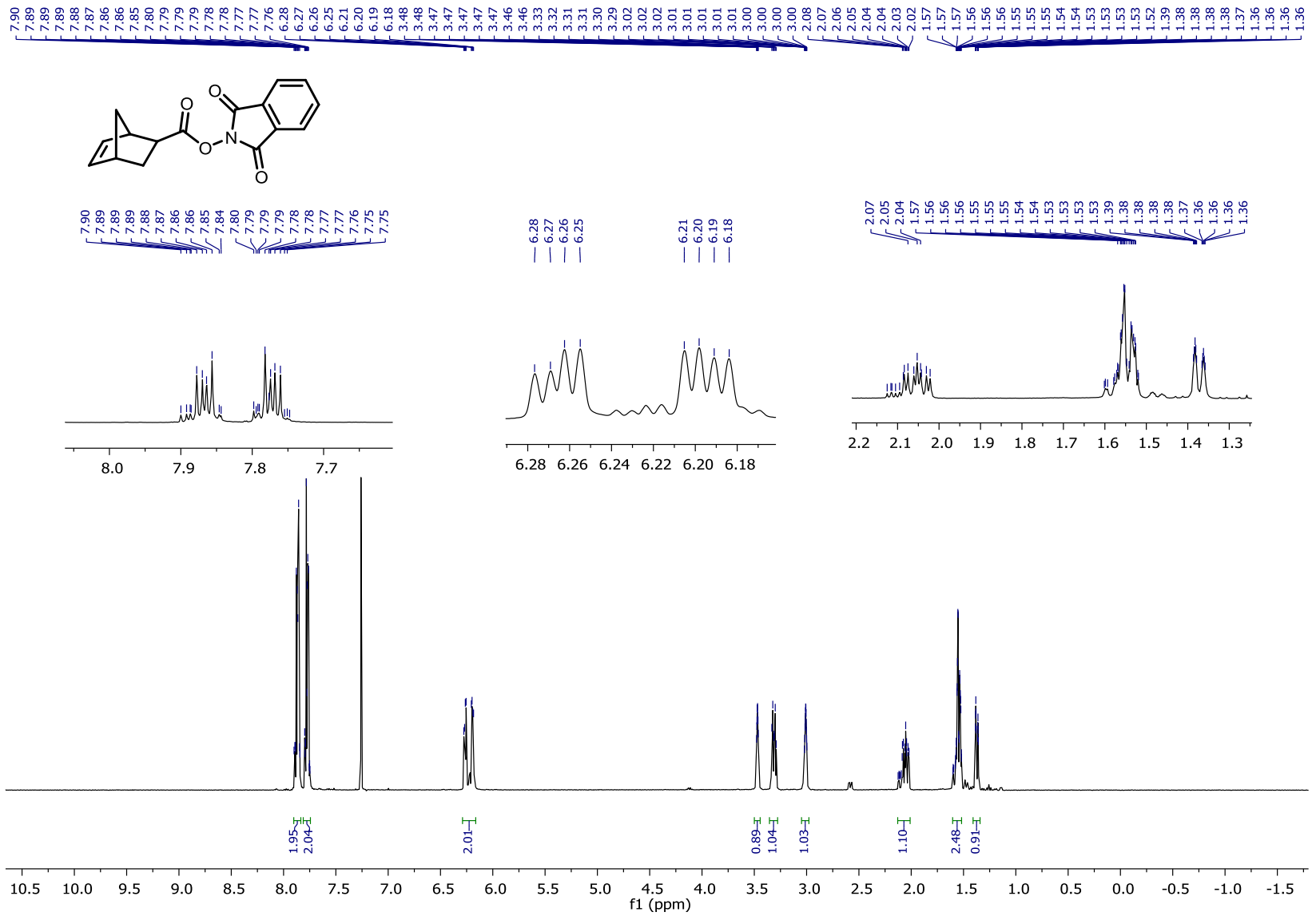
18 Kölmel, D. K.; Loach, R. P.; Knauber, T.; Flanagan, M. E., *ChemMedChem* **2018**, *13*, 2159−2165.

19 Ding, Y.; Franklin, G. J.; DeLorey, J. L.; Centrella, P. A.; Mataruse, S.; Clark, M. A.; Skinner, S. R.; Belyanskaya, S., *ACS Comb. Sci.* **2016**, *18*, 625−629.

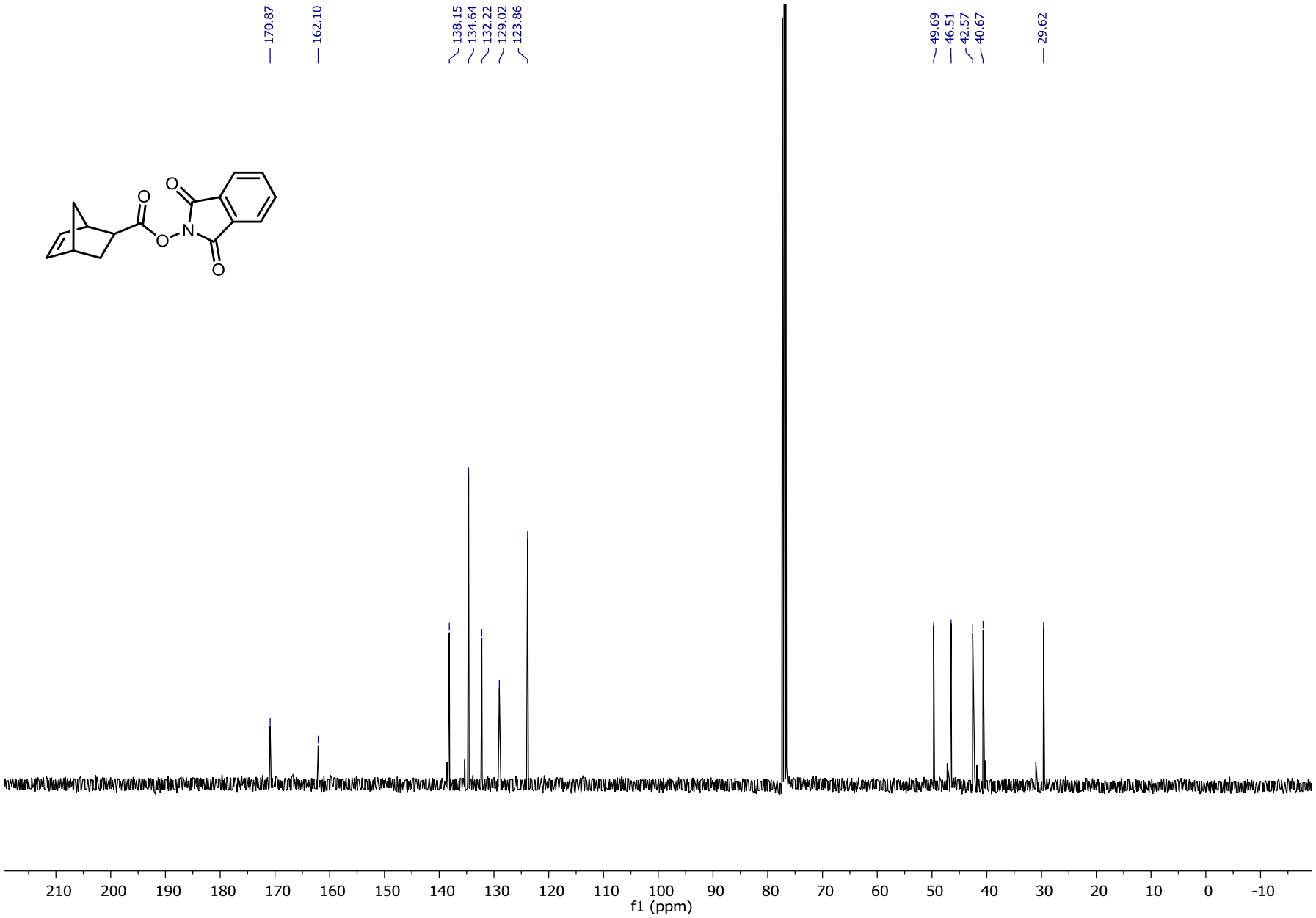
20 Satz, A. L.; Cai, J.; Chen, Y.; Goodnow, R.; Gruber, F.; Kowalczyk, A.; Petersen, A.; Naderi-Oboodi, G.; Orzechowski, L.; Strebel, Q., *Bioconjugate Chem.* **2015**, *26*, 1623−1632.

10. NMR spectra of synthesised compounds

*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **2q***



*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **2q***



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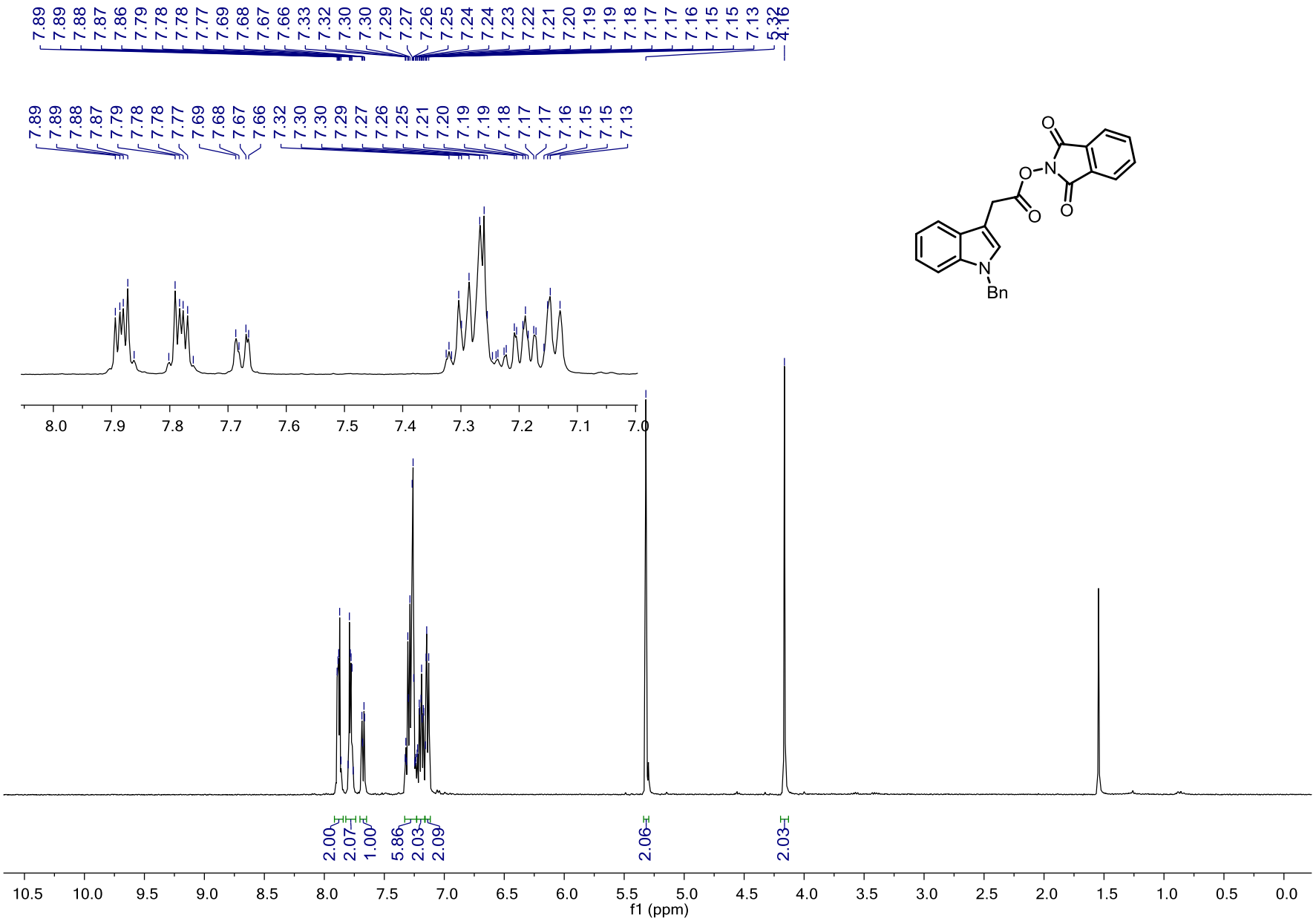

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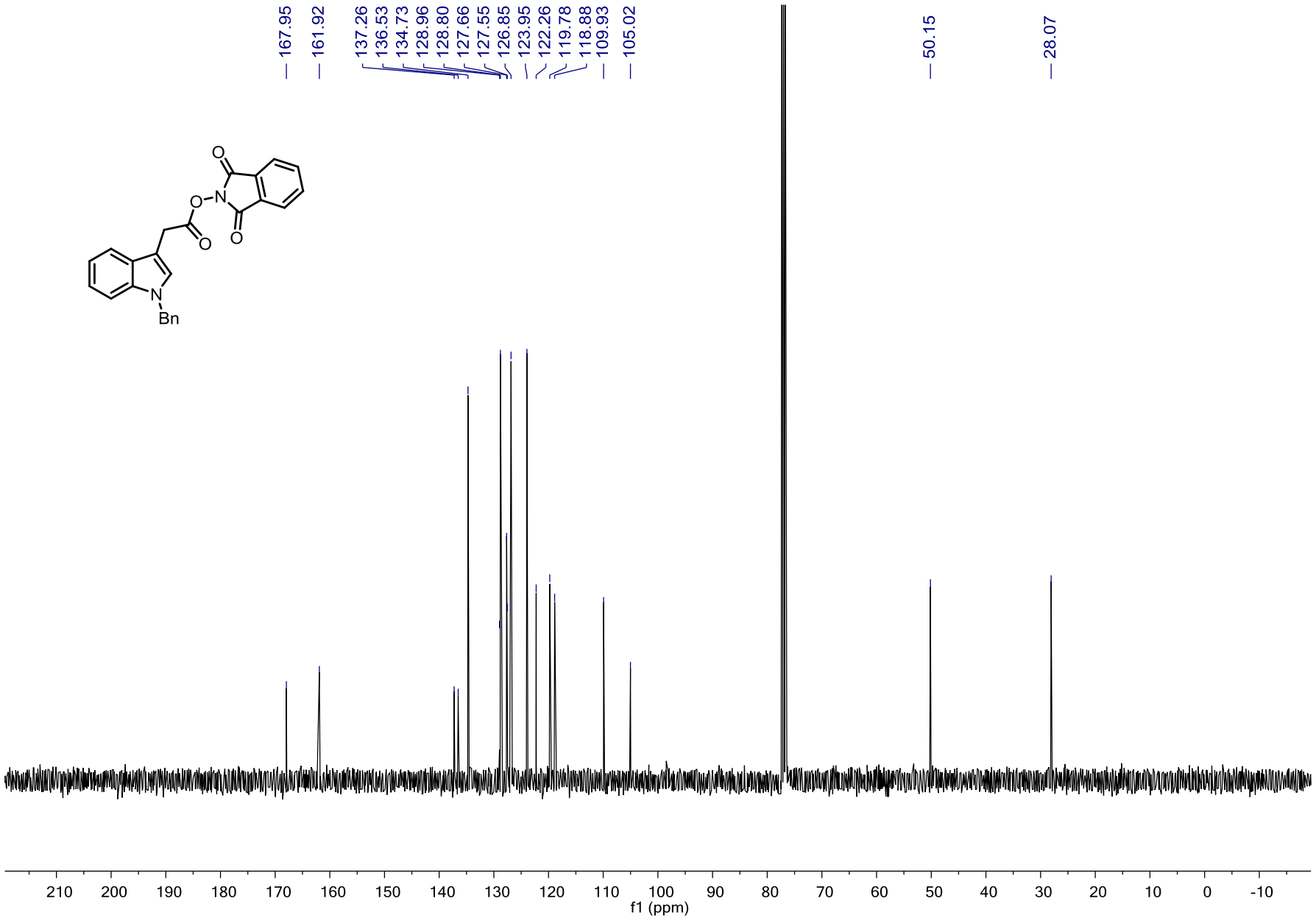
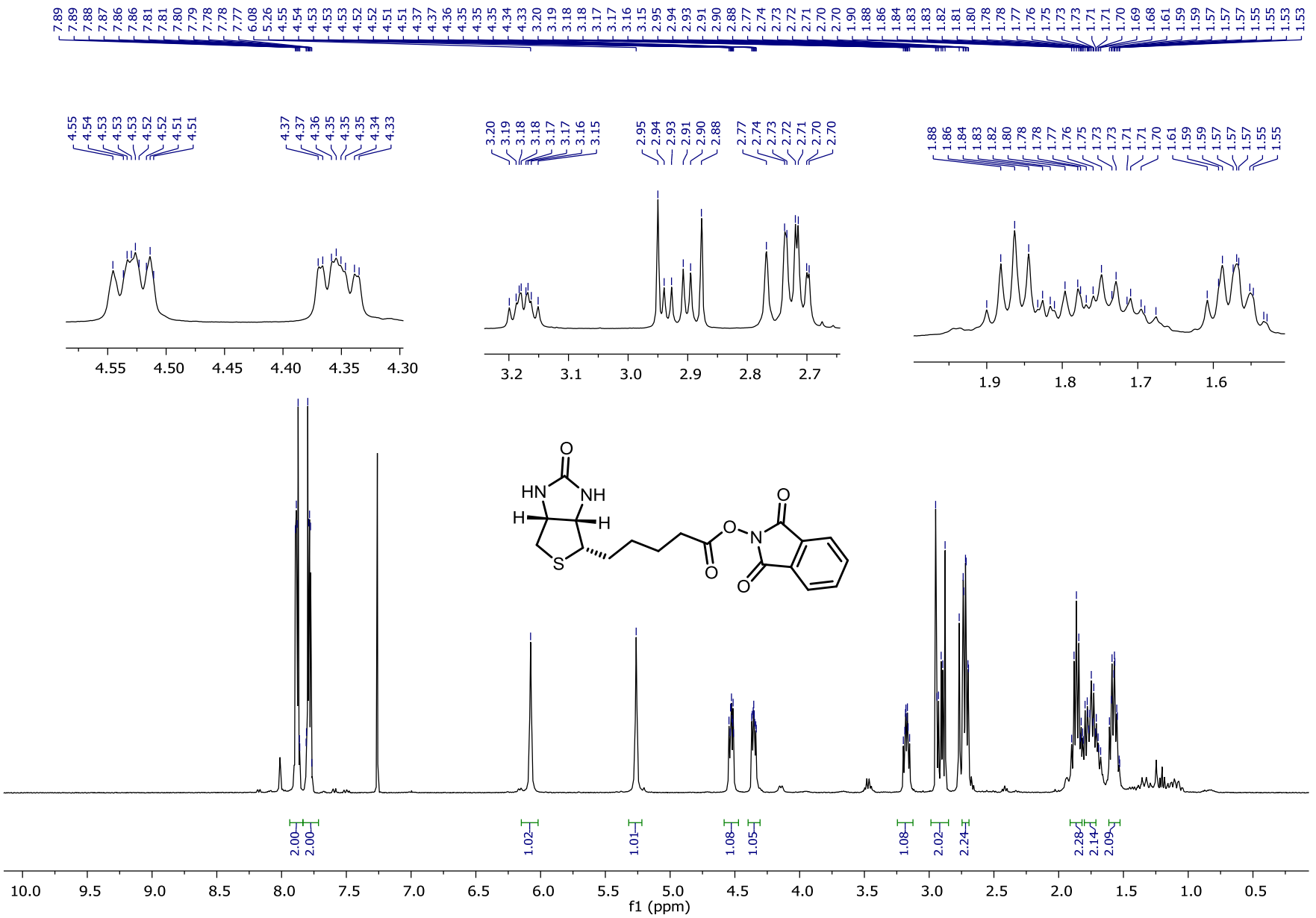


*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **2s***



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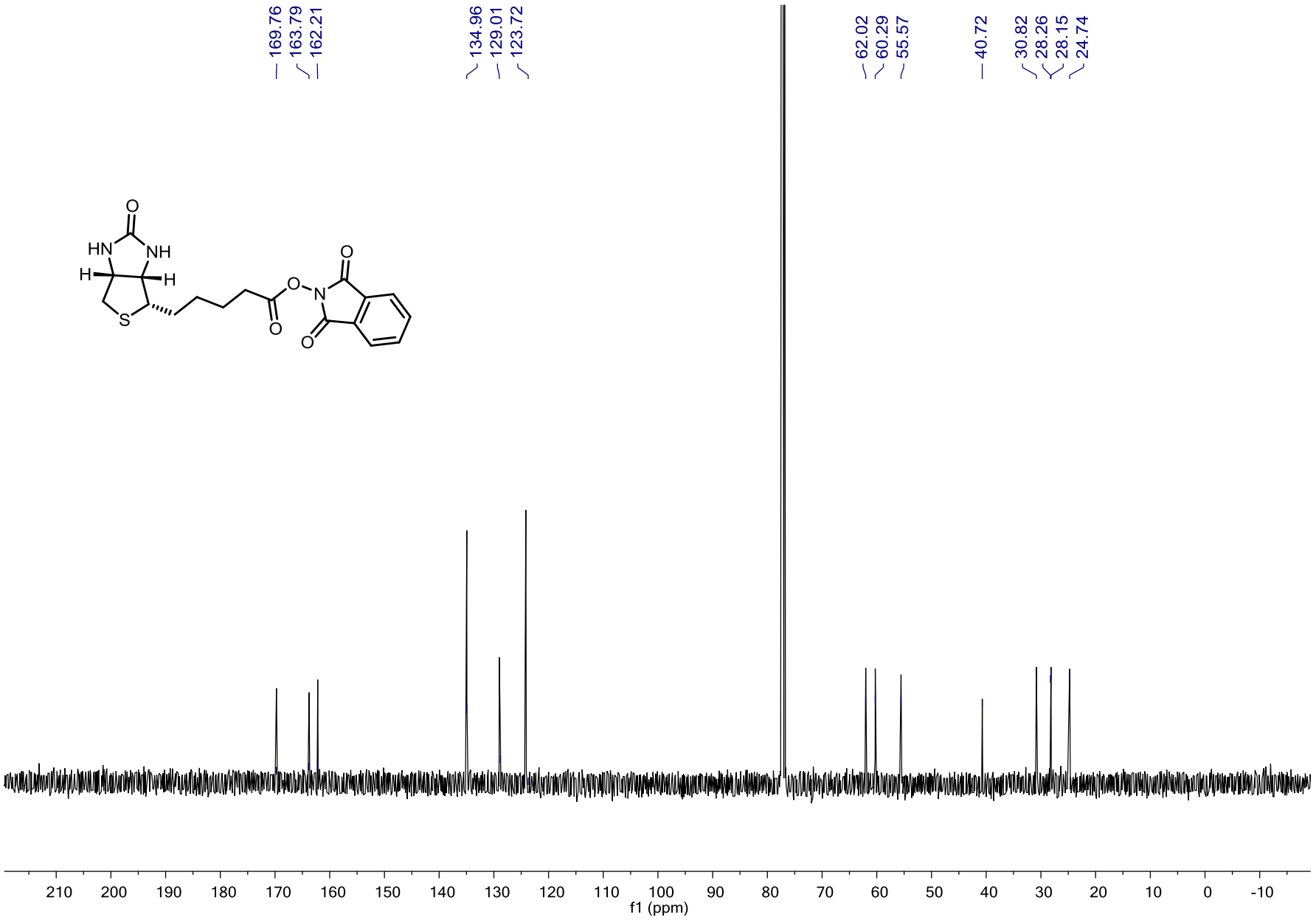
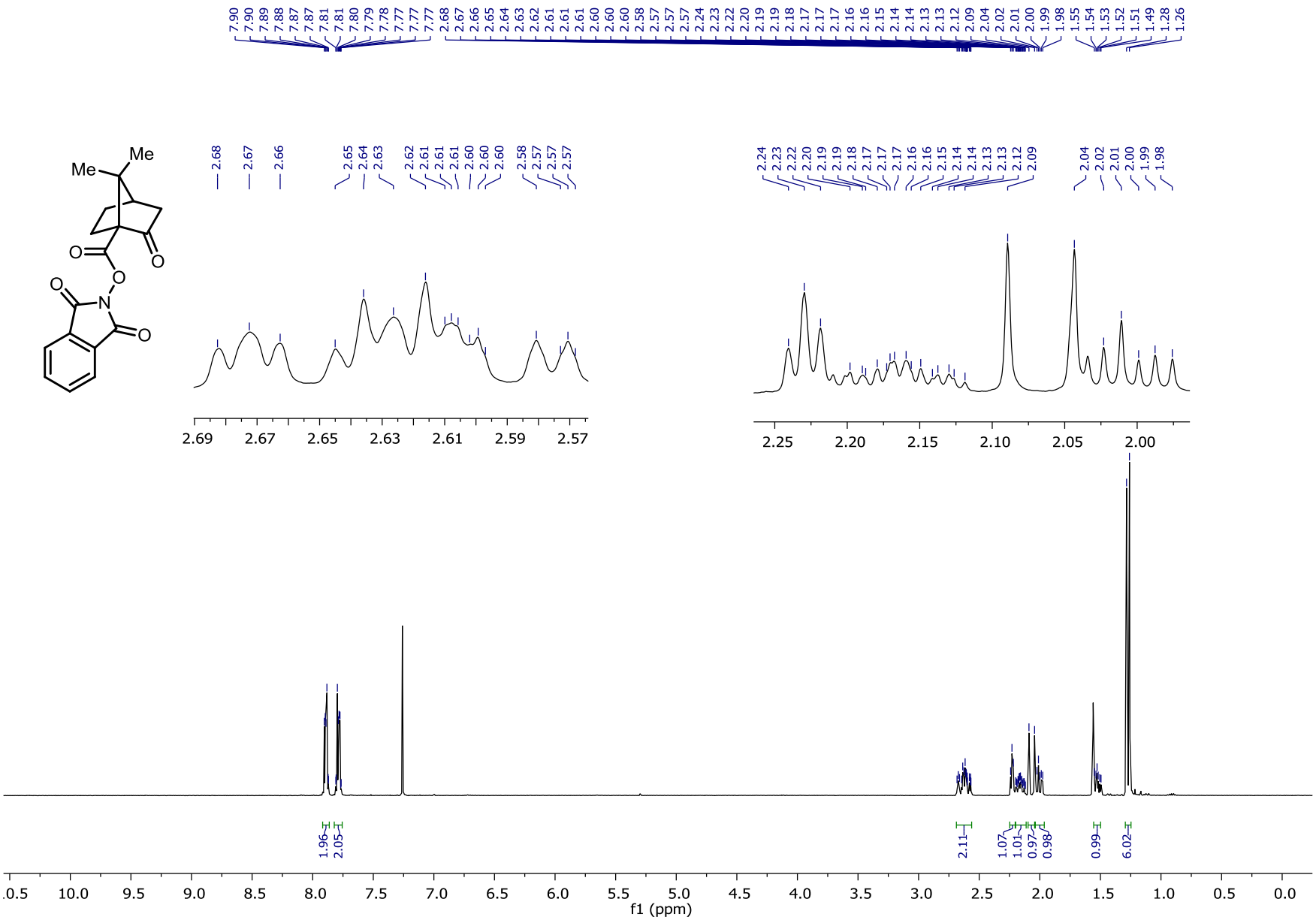
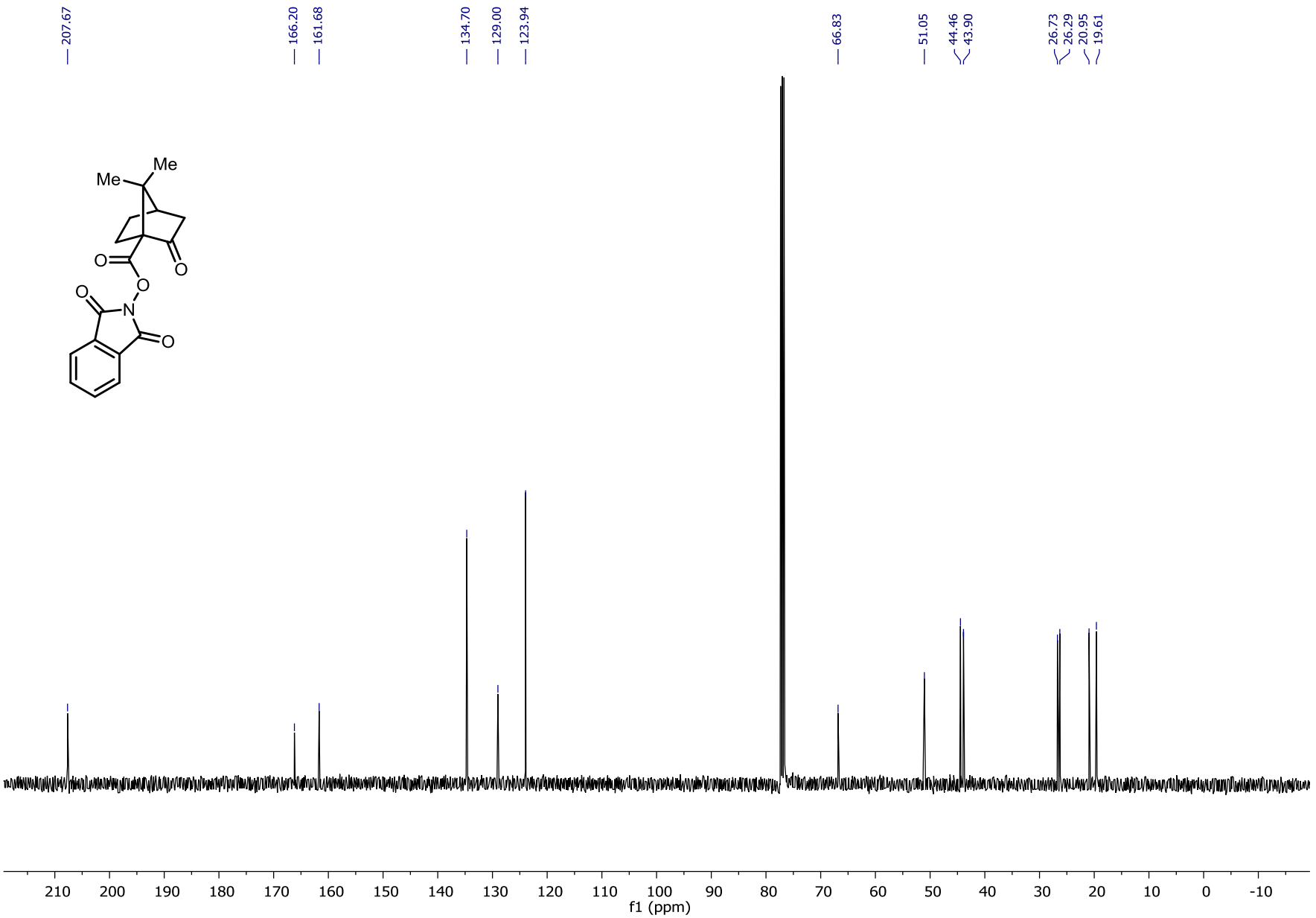


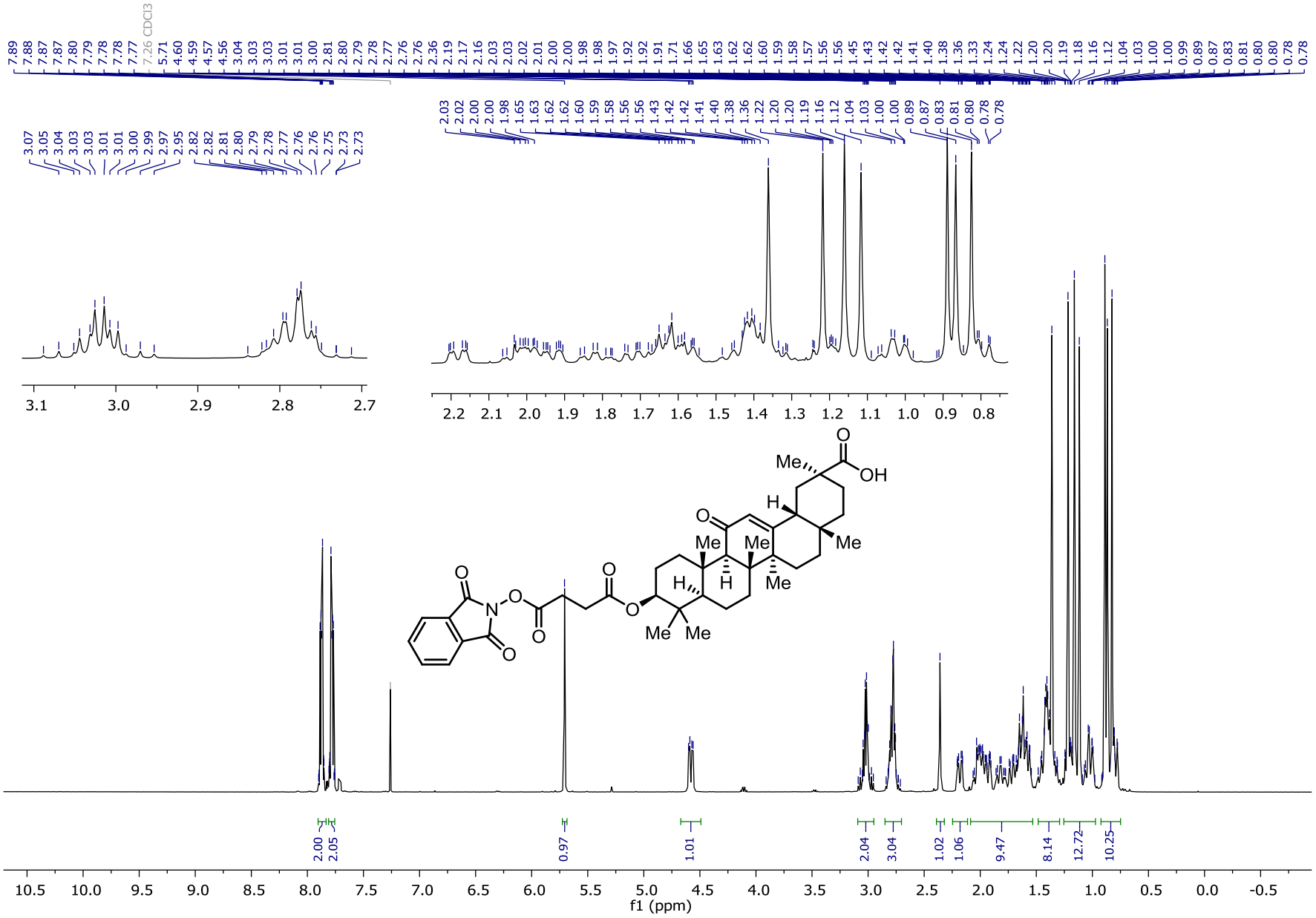
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **2x***



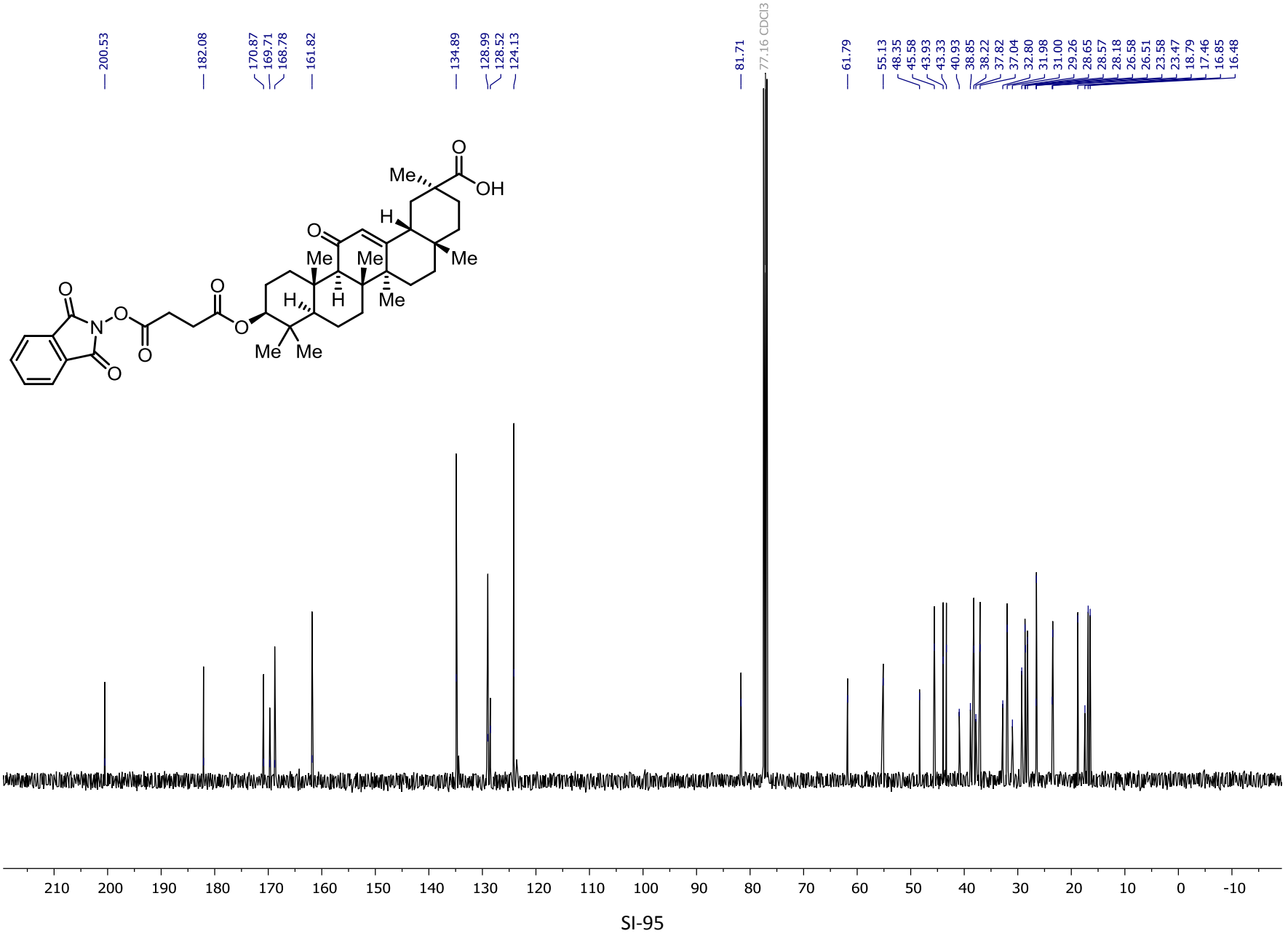
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **2x***



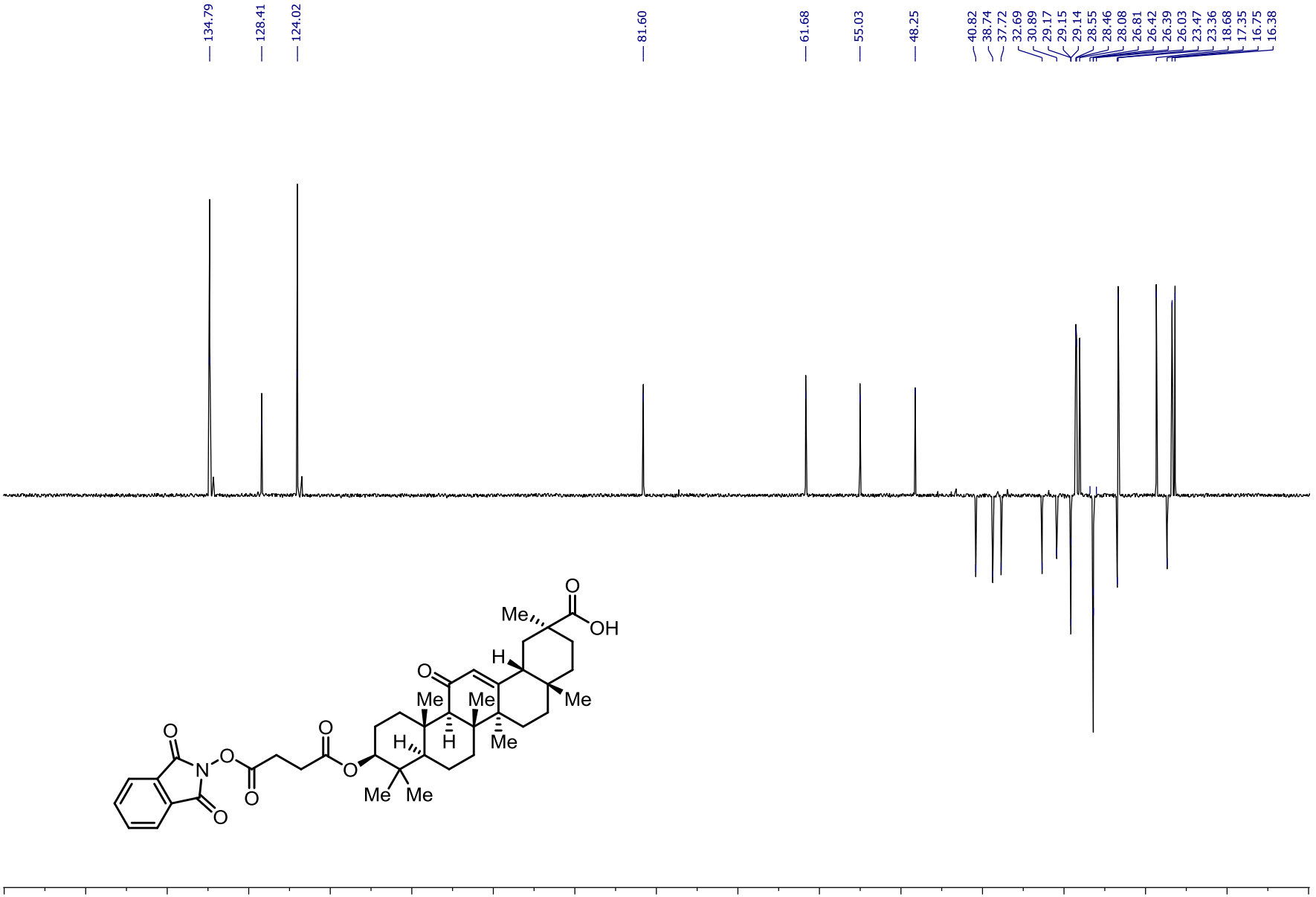
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **2aa***



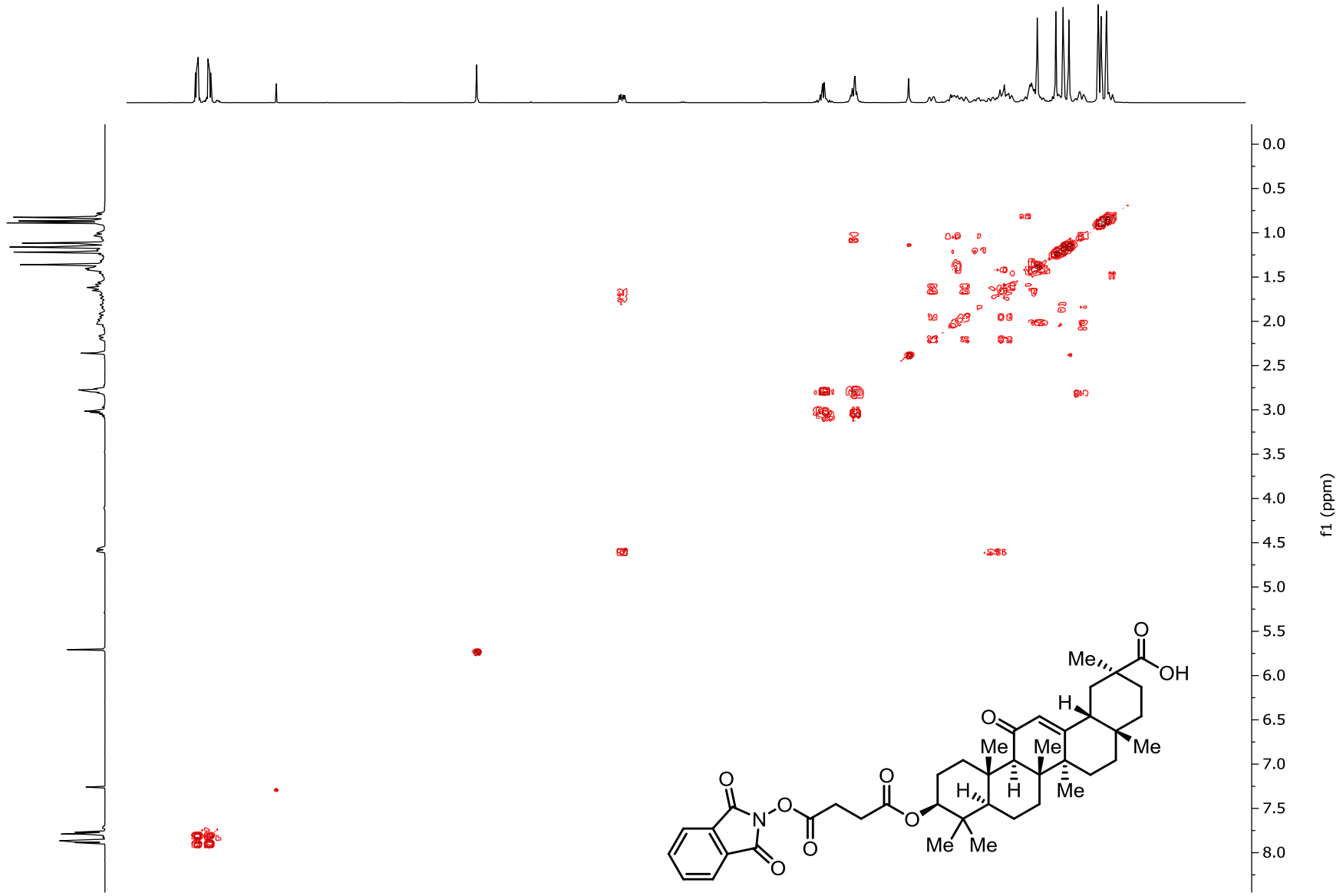
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **2aa***



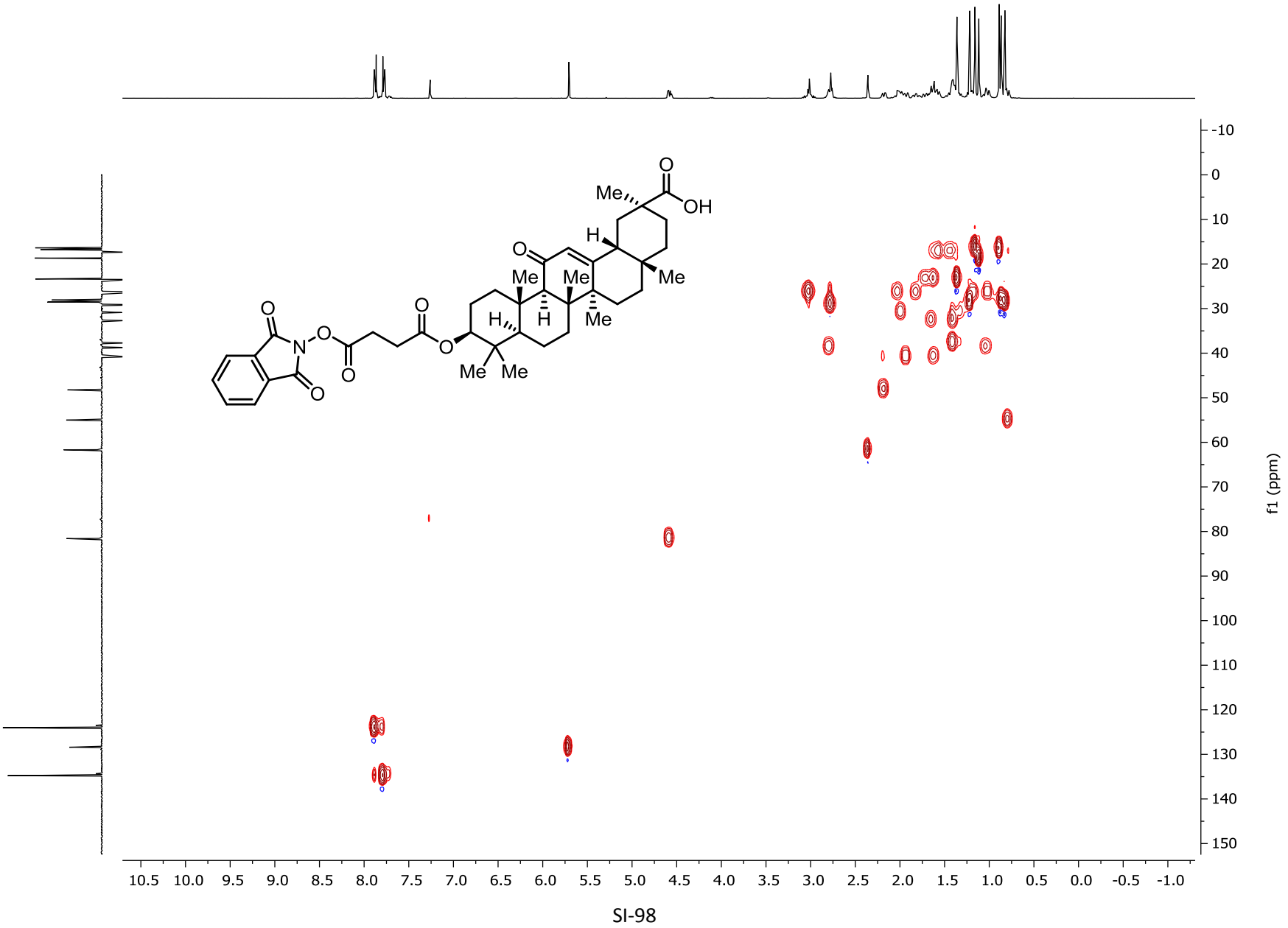
*DEPT 135 (101 MHz, $CDCl_3$) for compound **2aa***



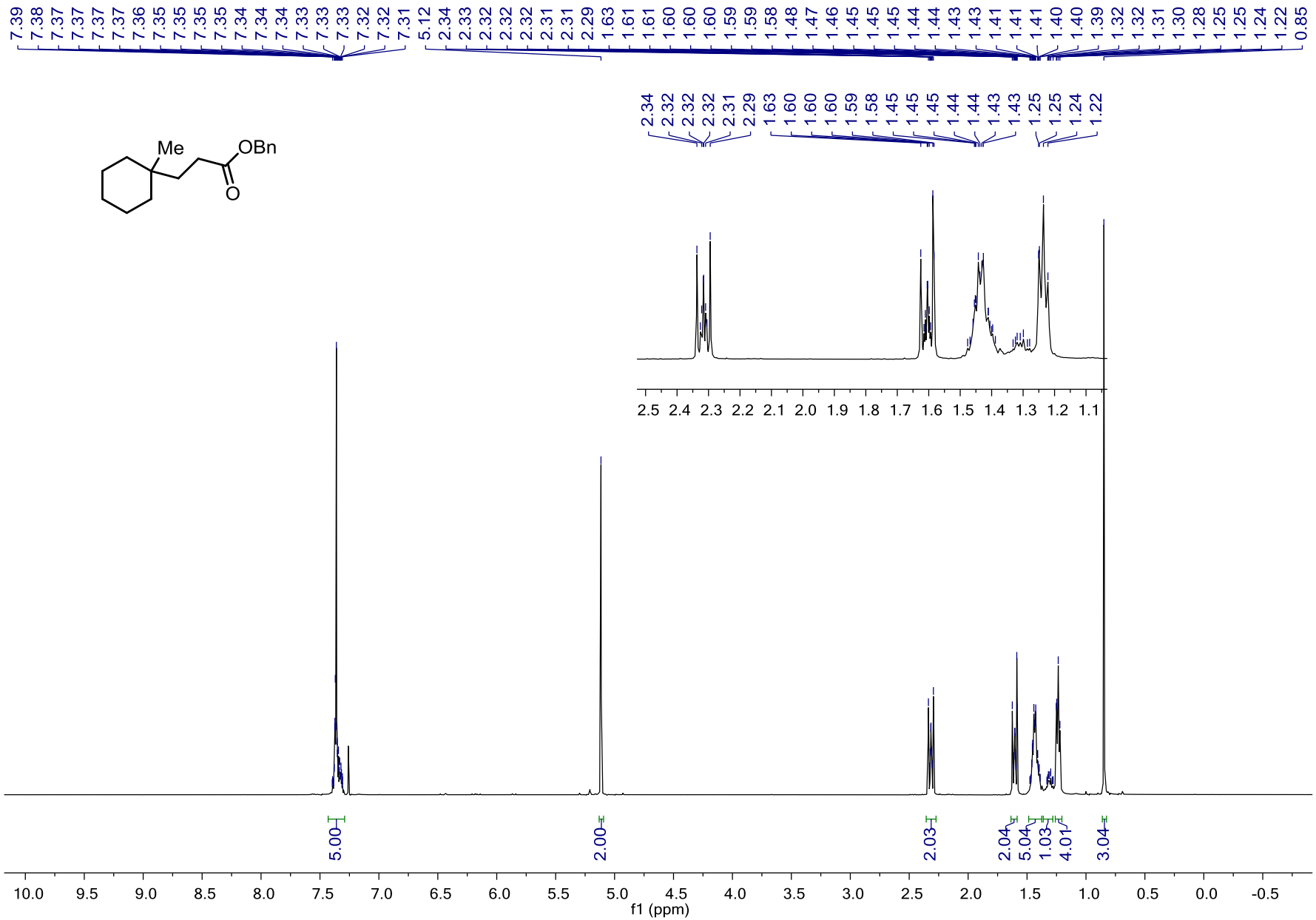
*COSY (400 MHz, $CDCl_3$) for compound **2aa***



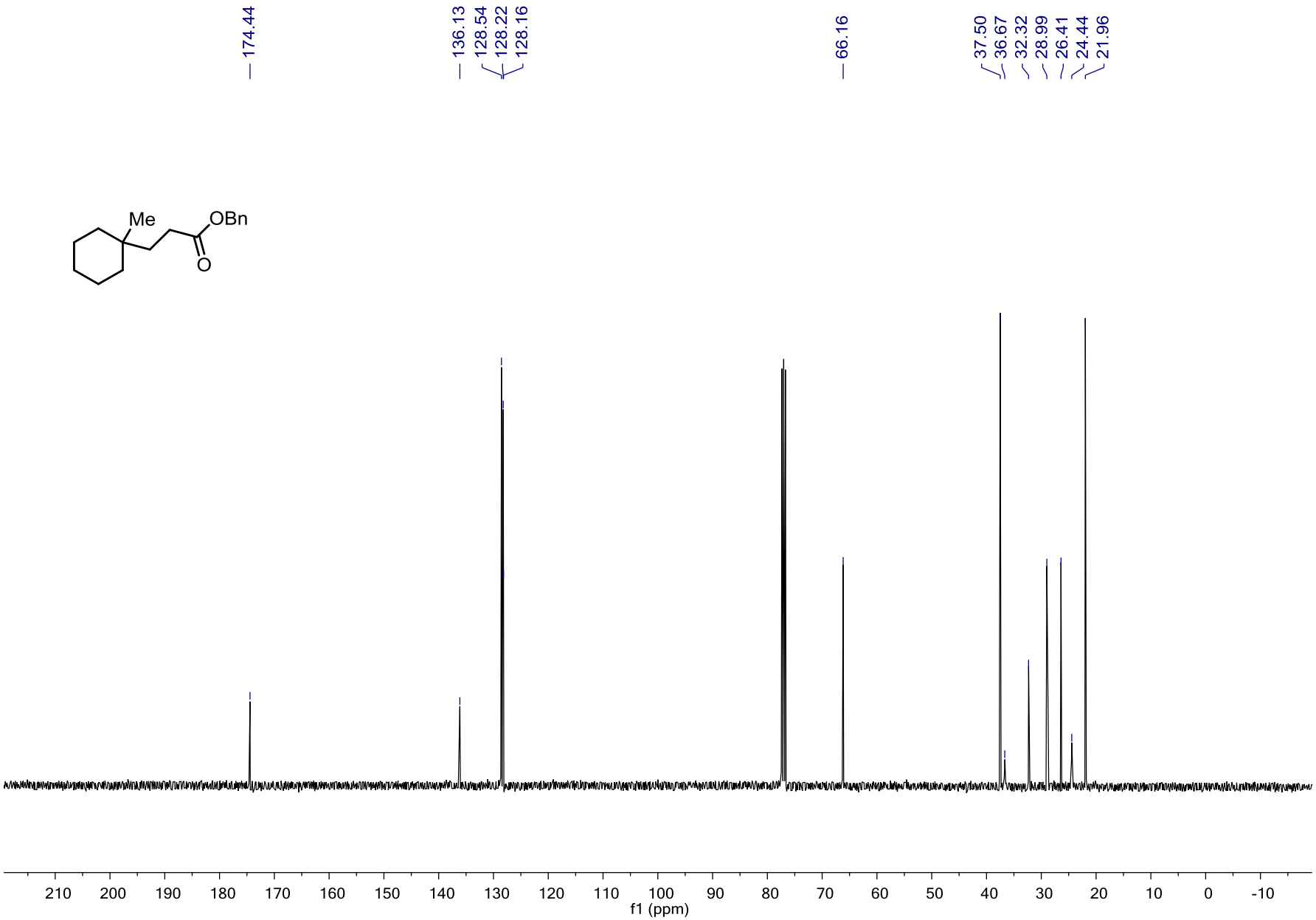
*HSQC NMR ($CDCl_3$) for compound **2aa***



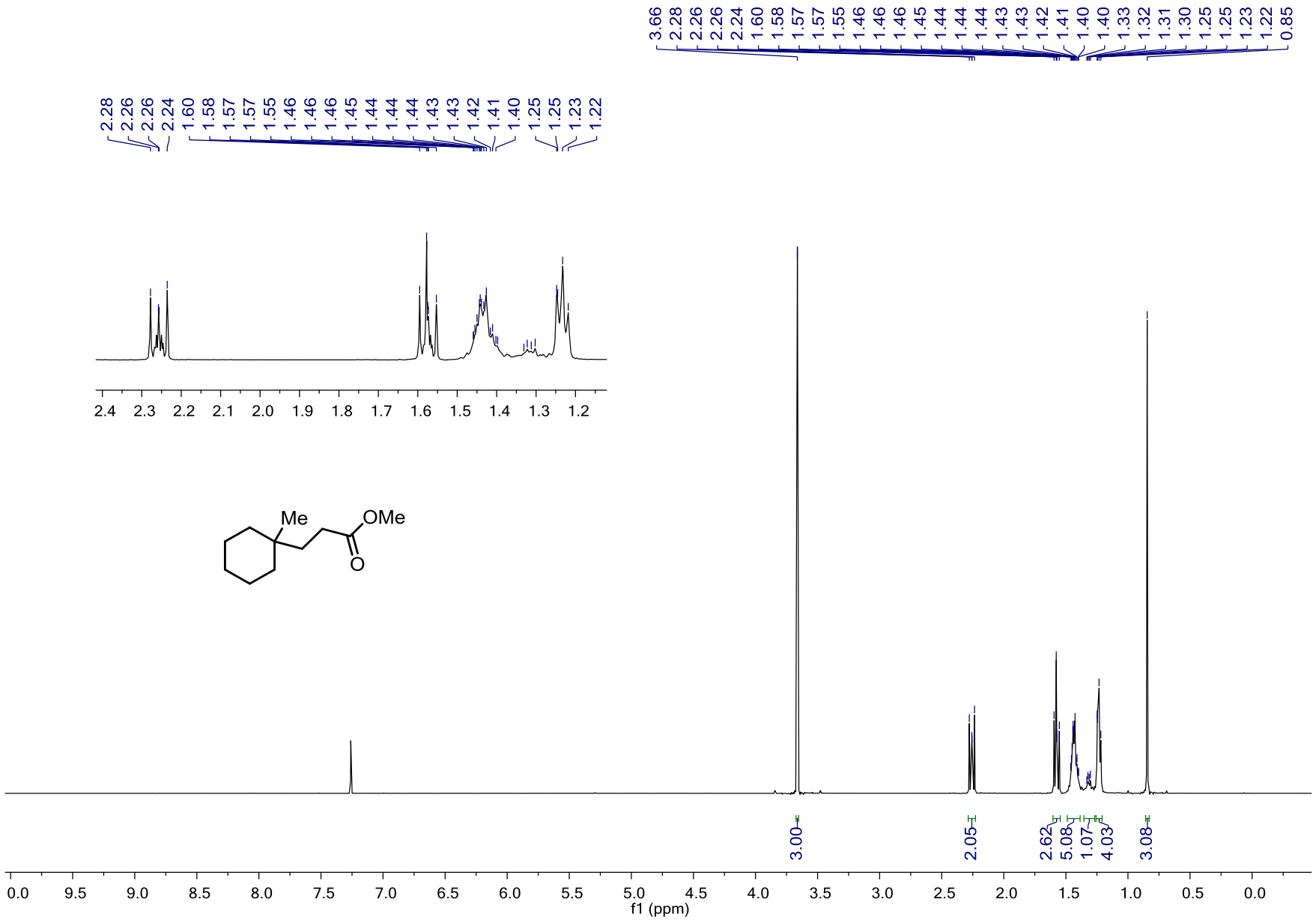
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4a***



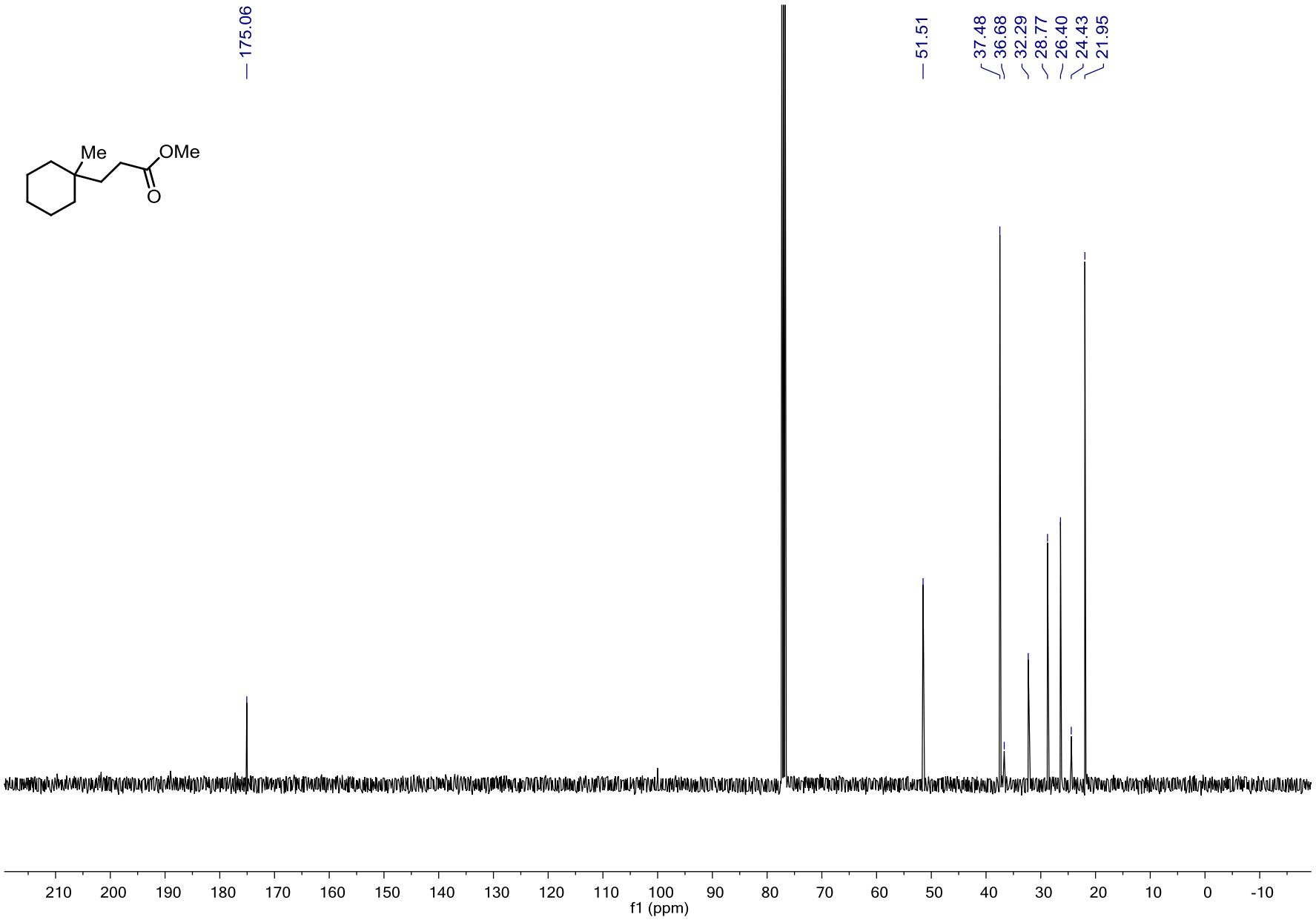
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4a***



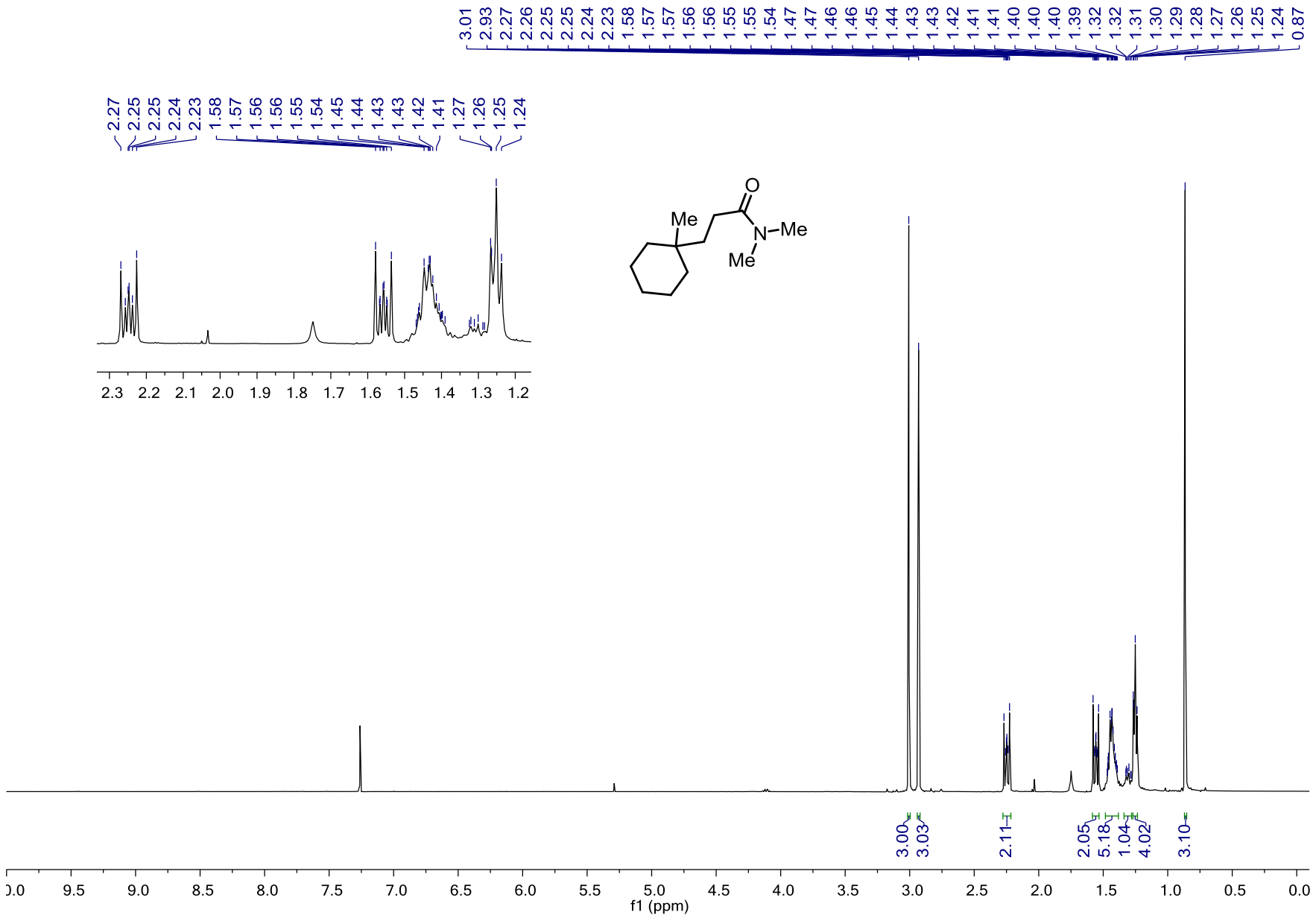
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4b***



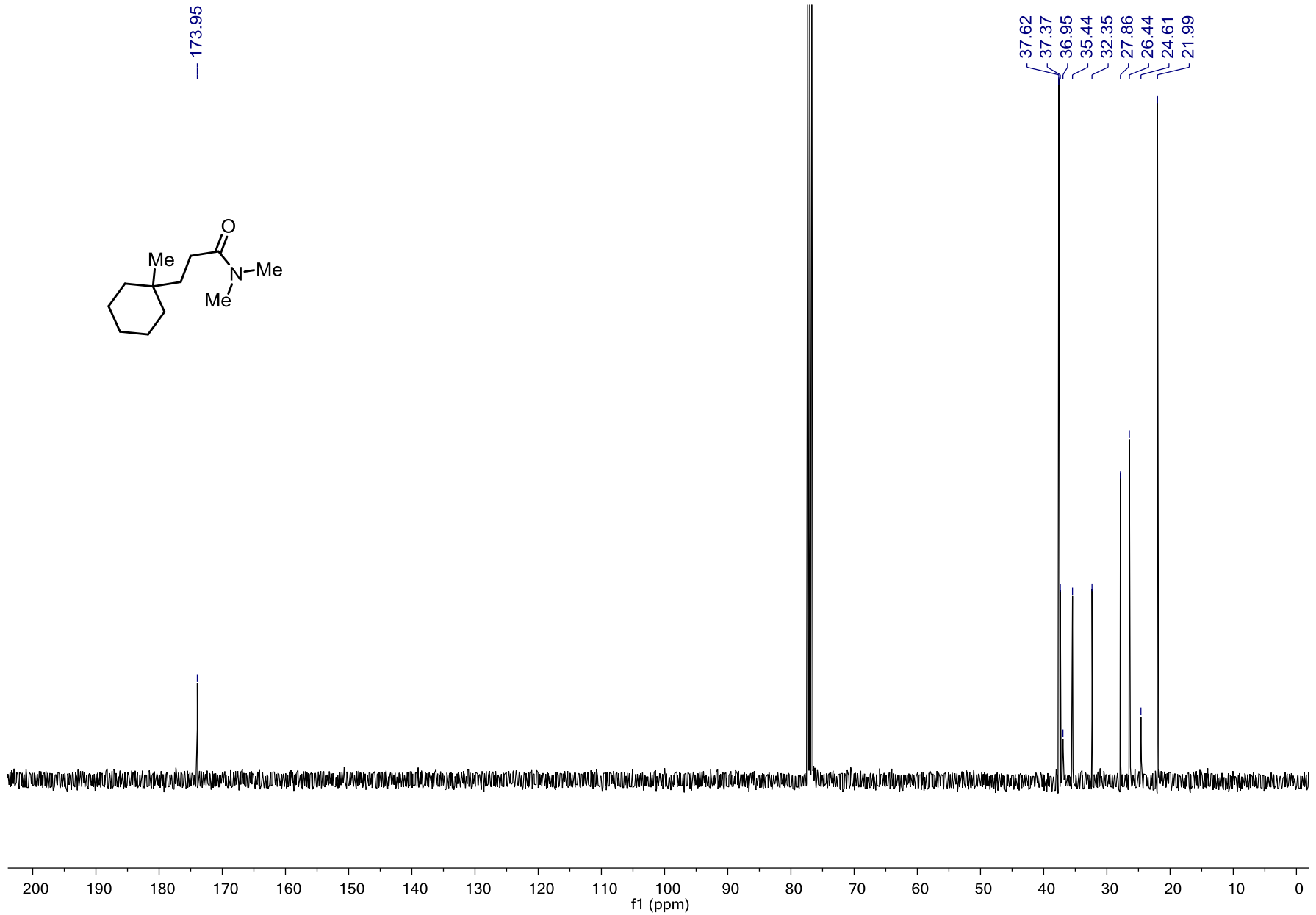
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4b***



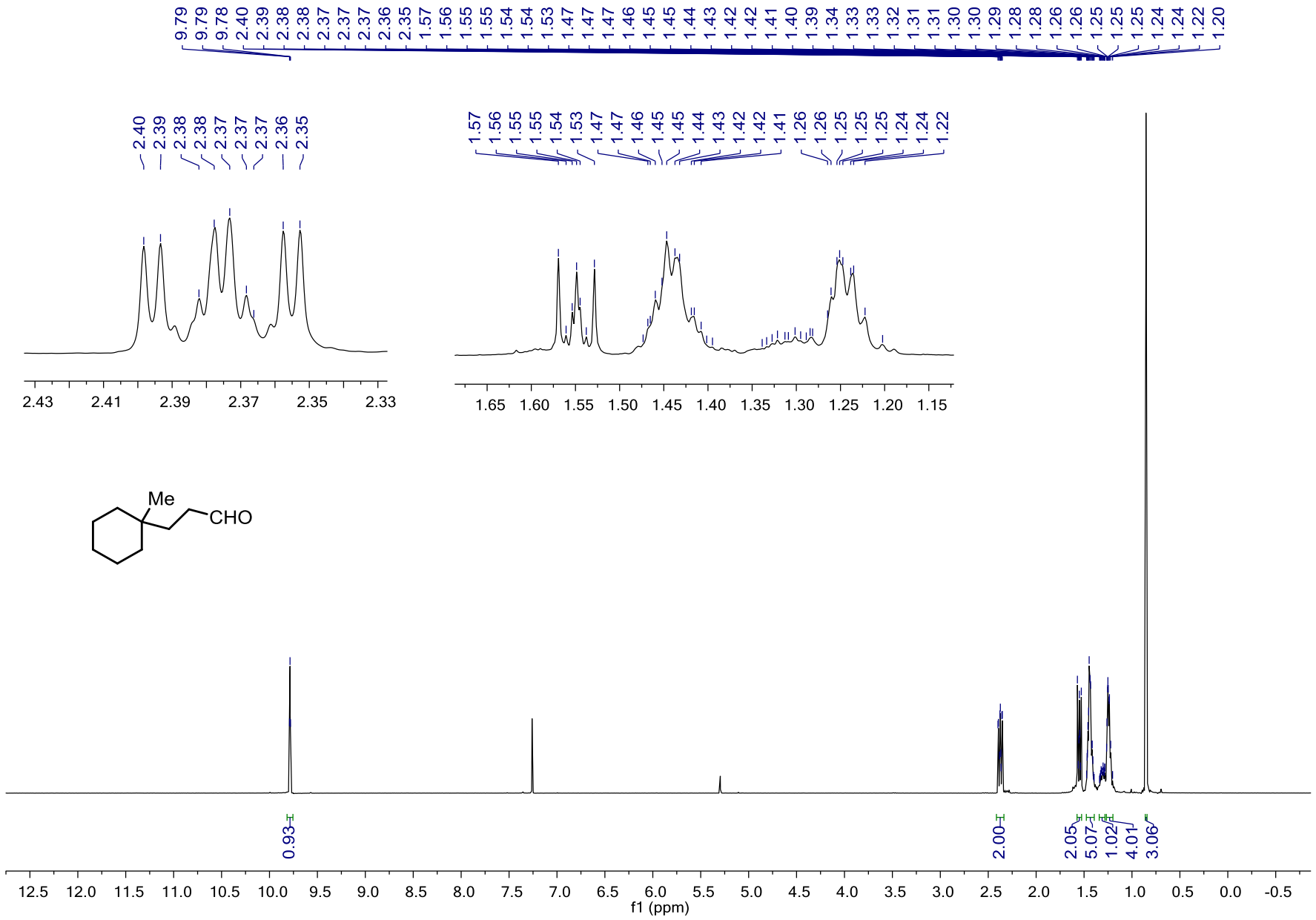
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4c***



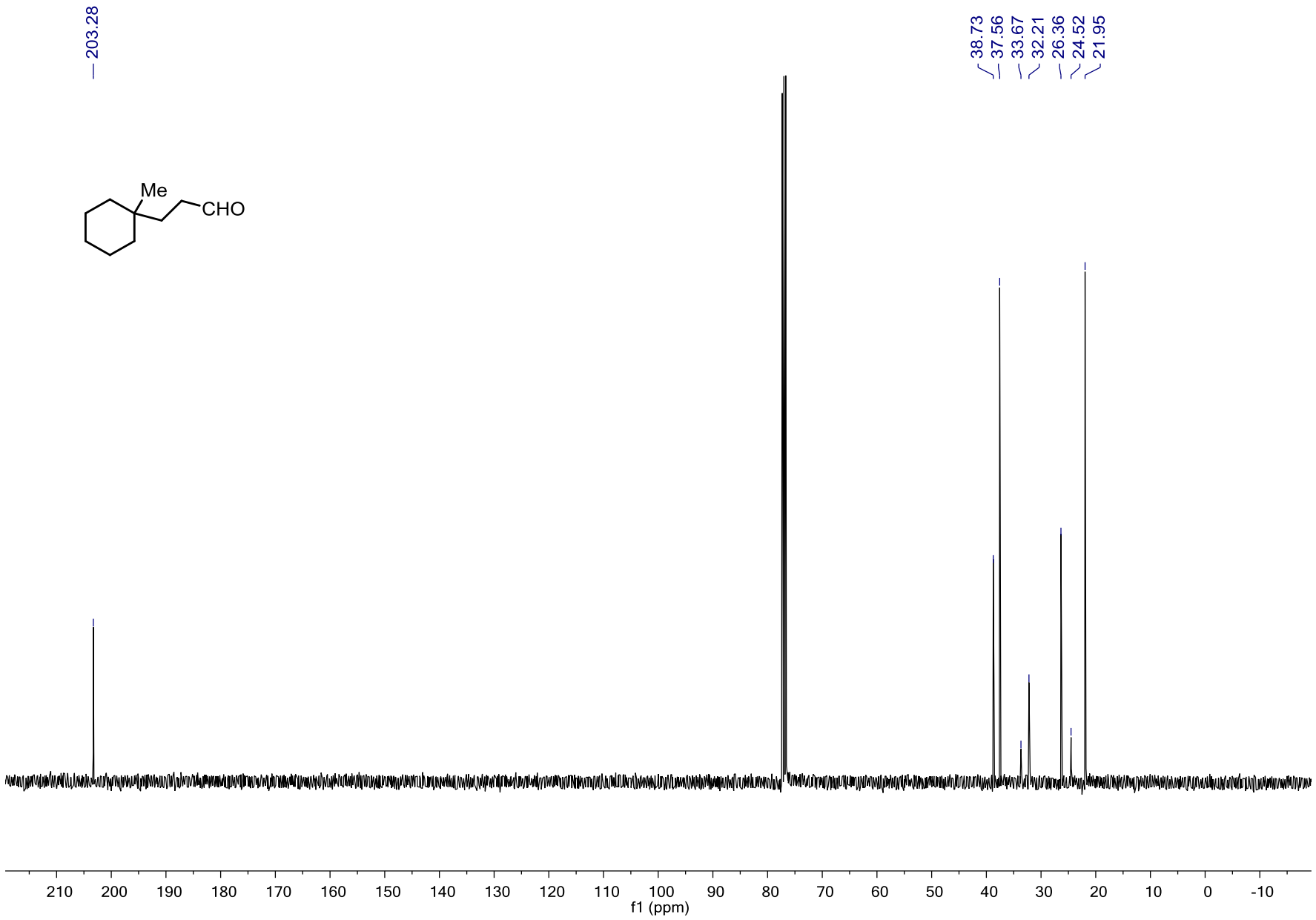
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4c***



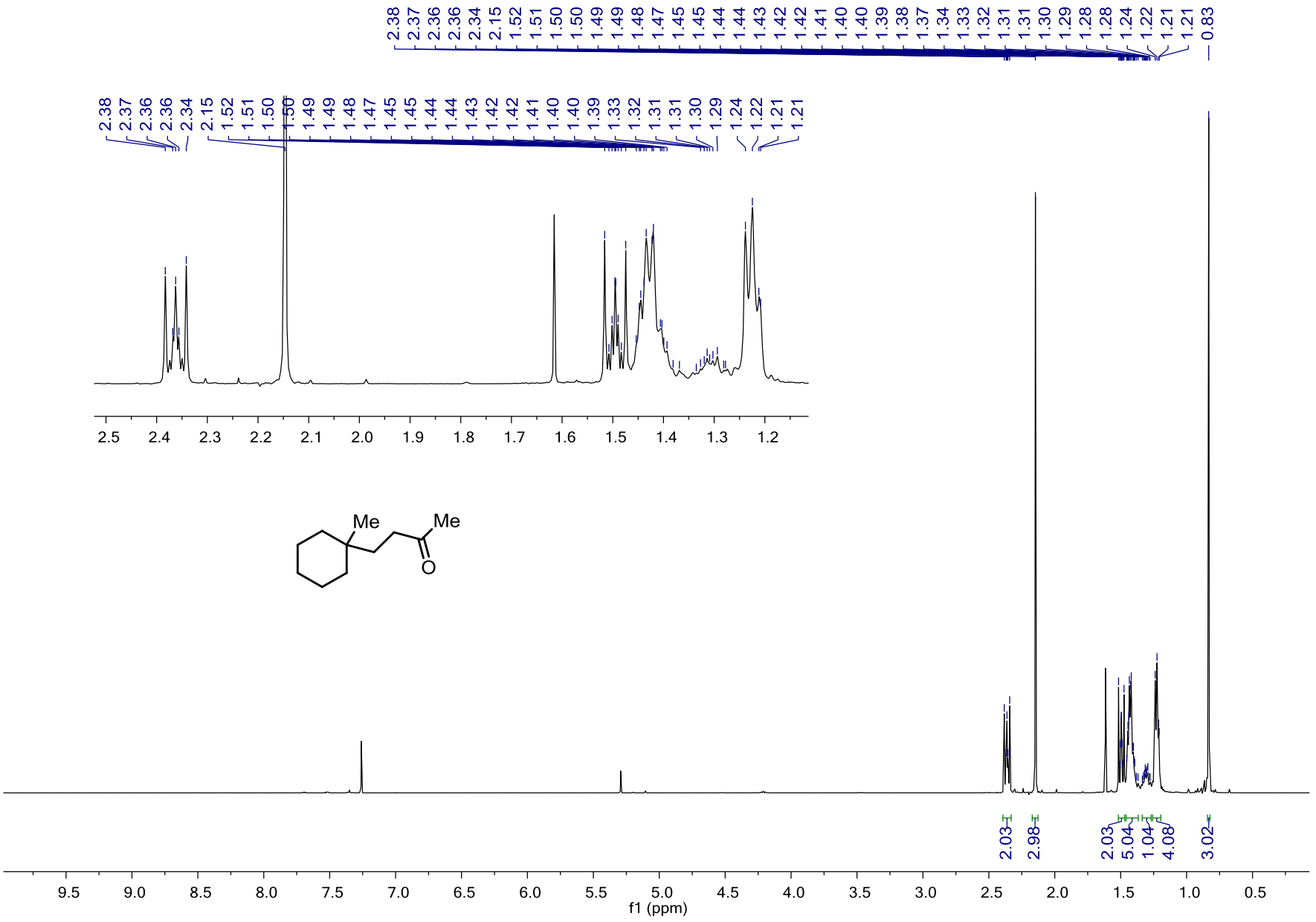
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4d***



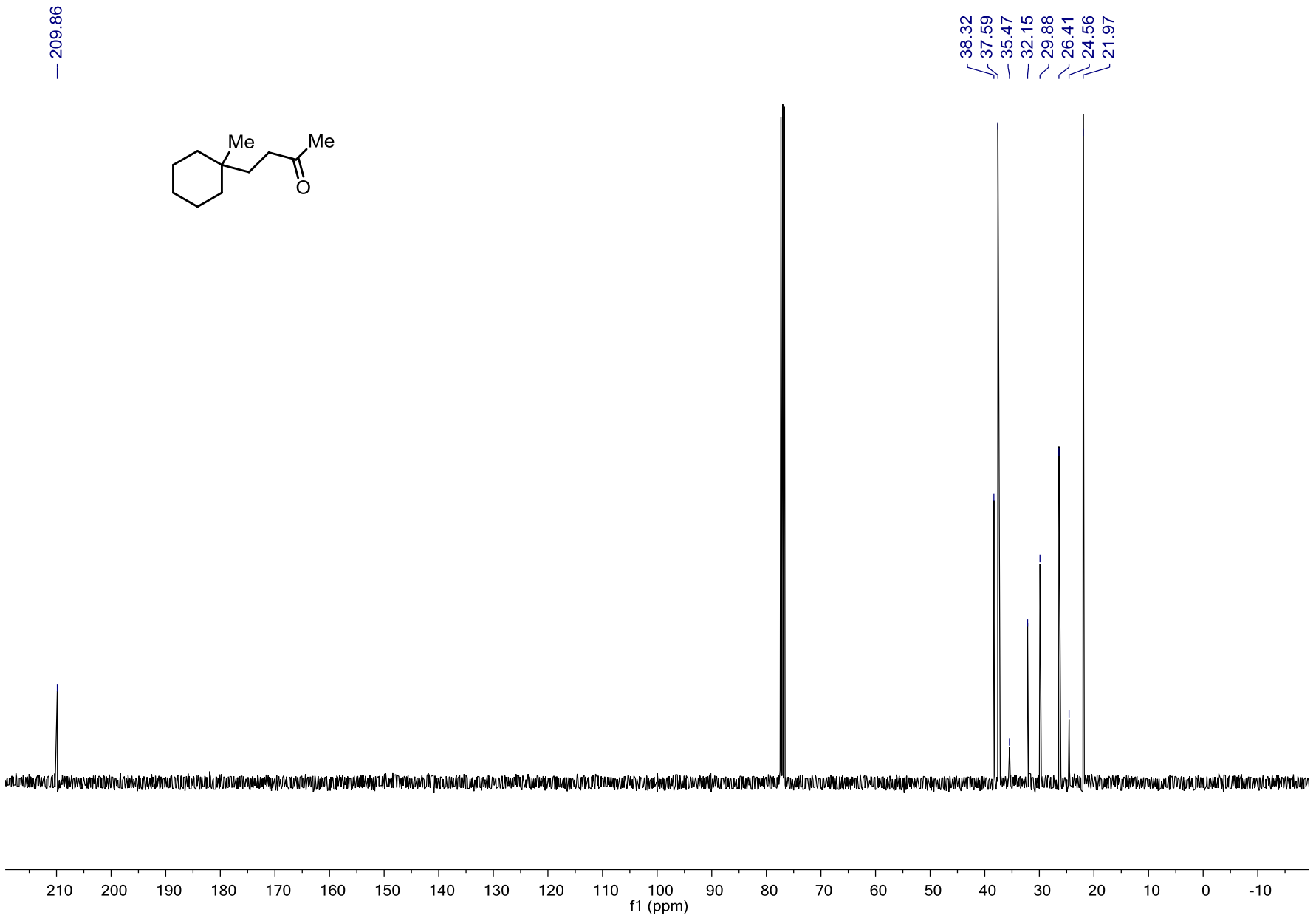
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4d***



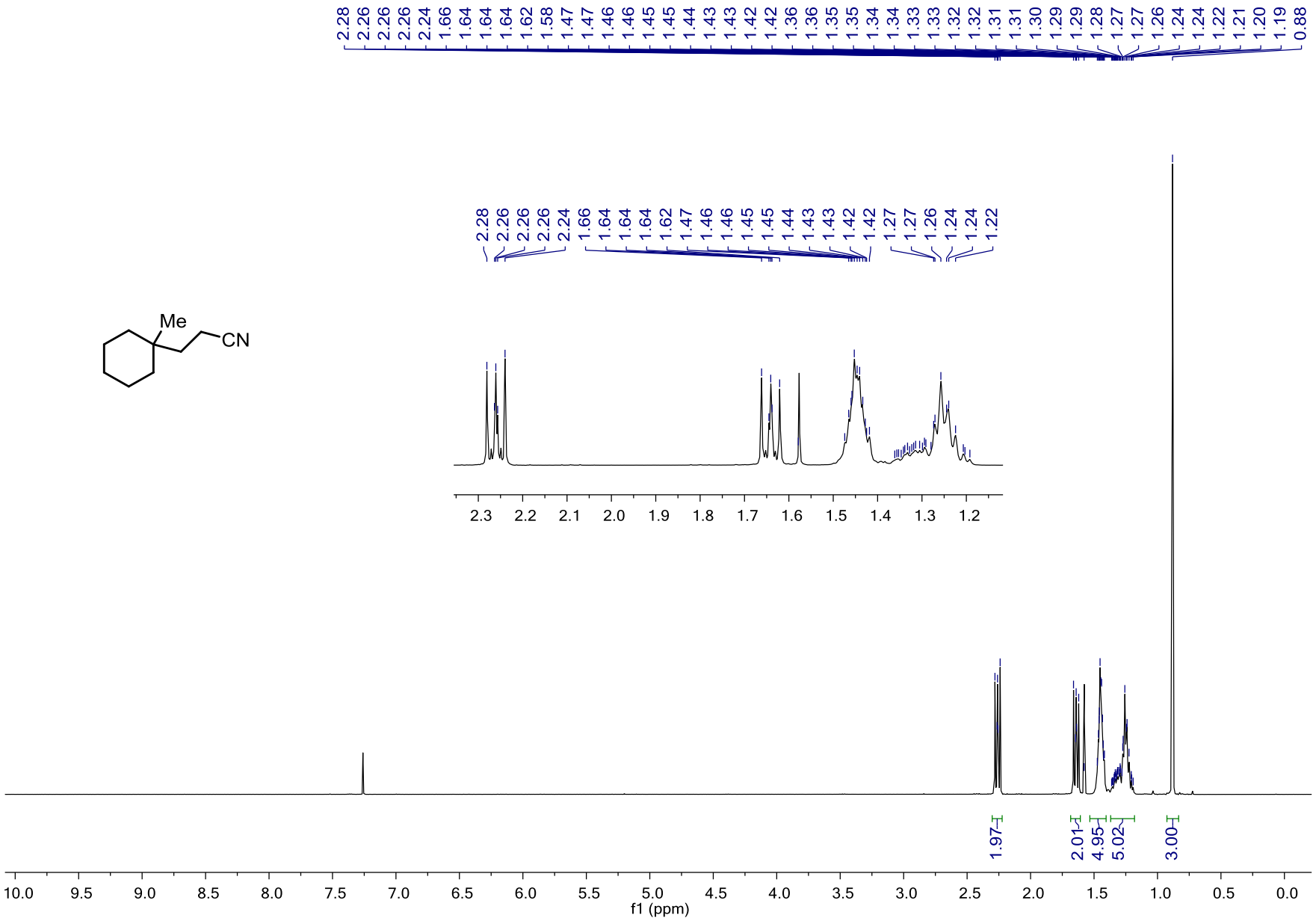
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4e***



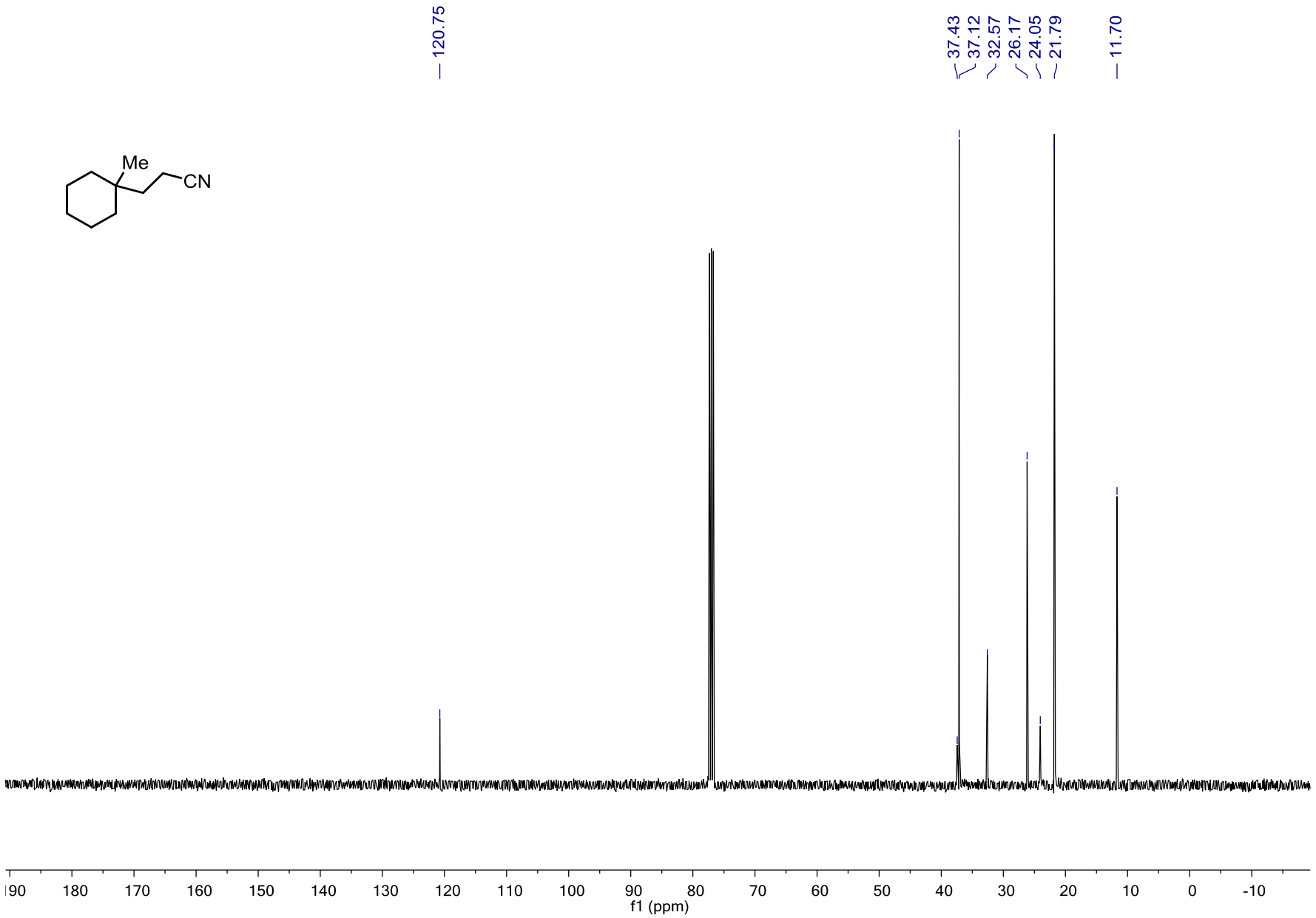
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4e***



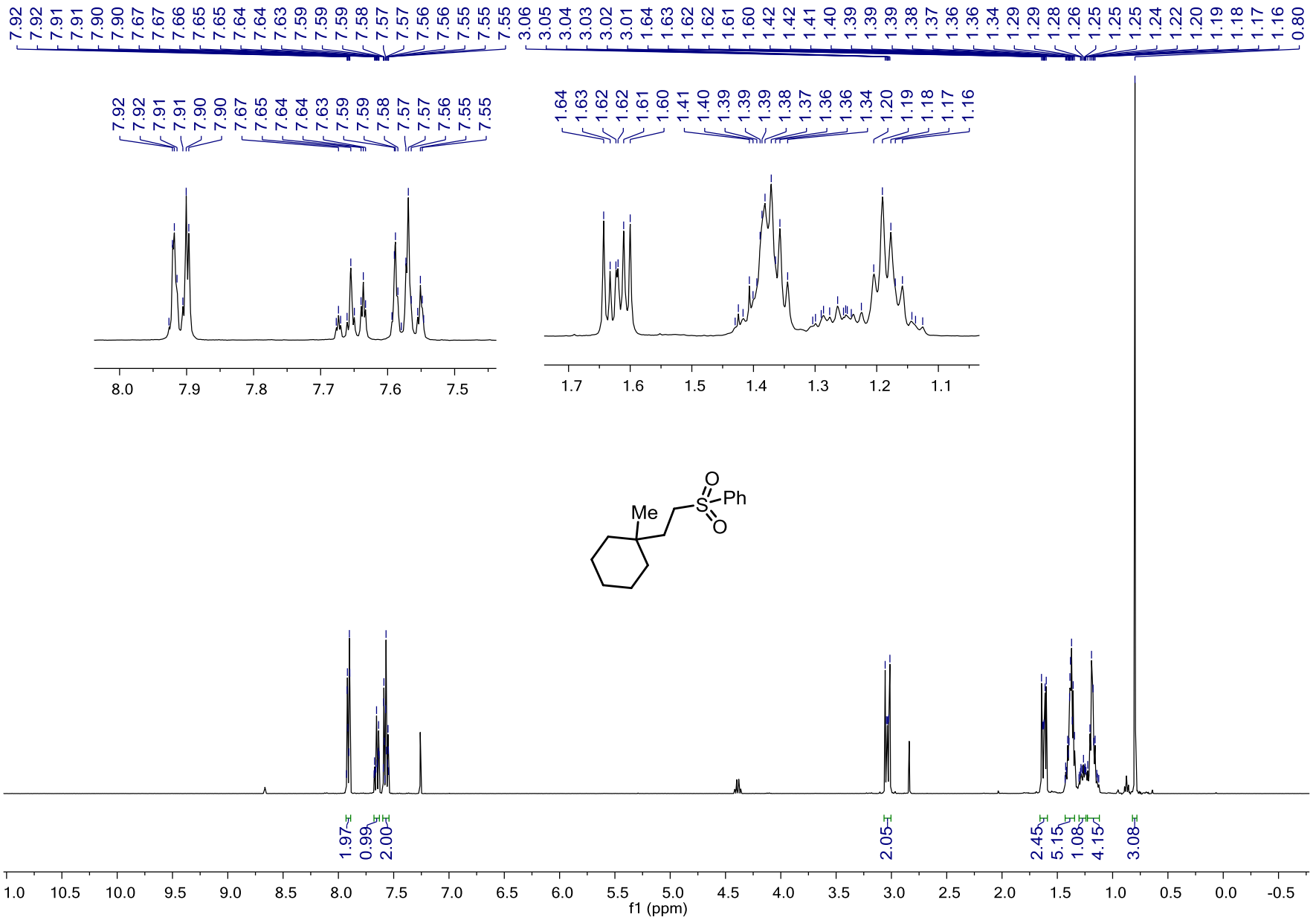
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4f***



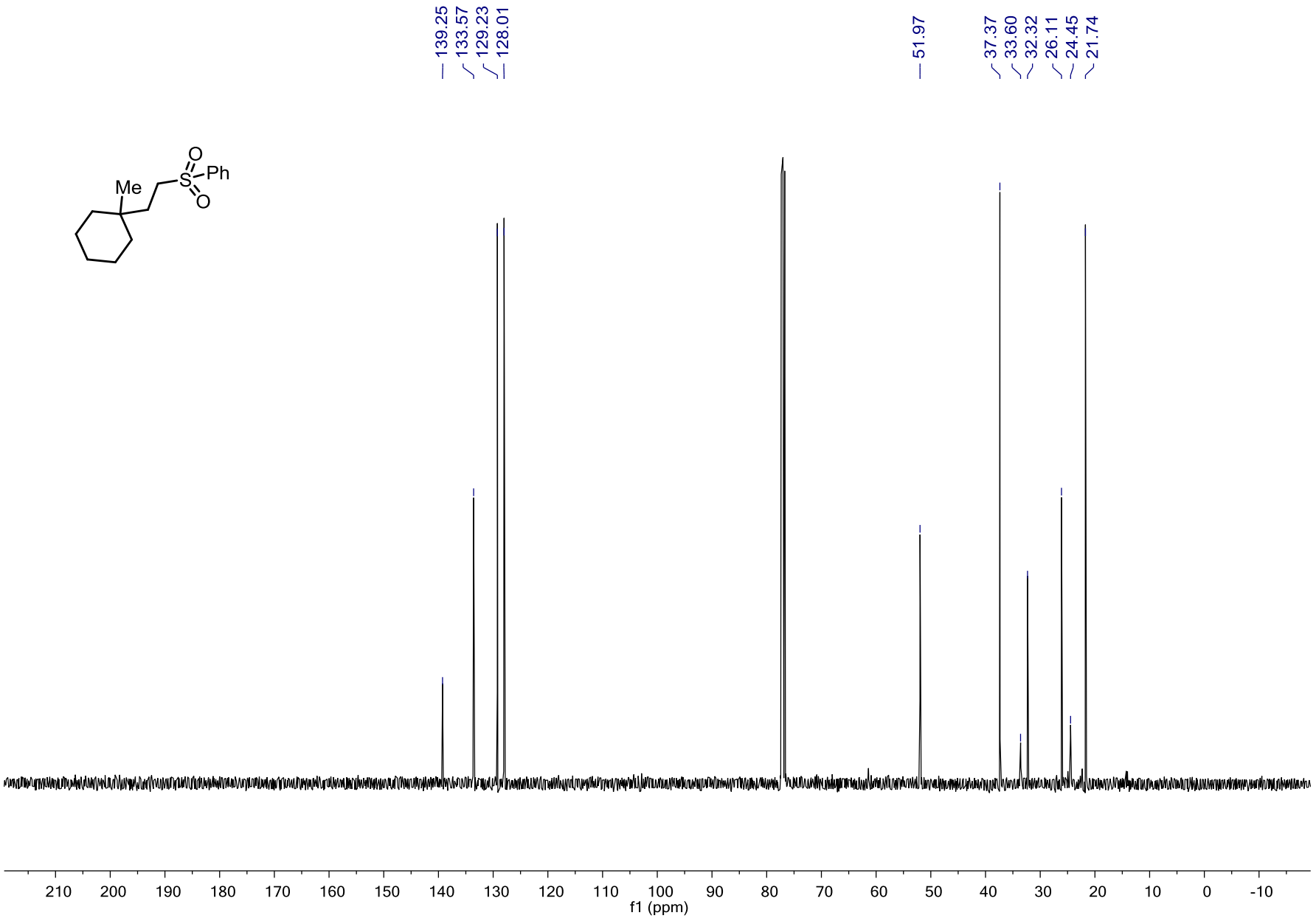
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4f***



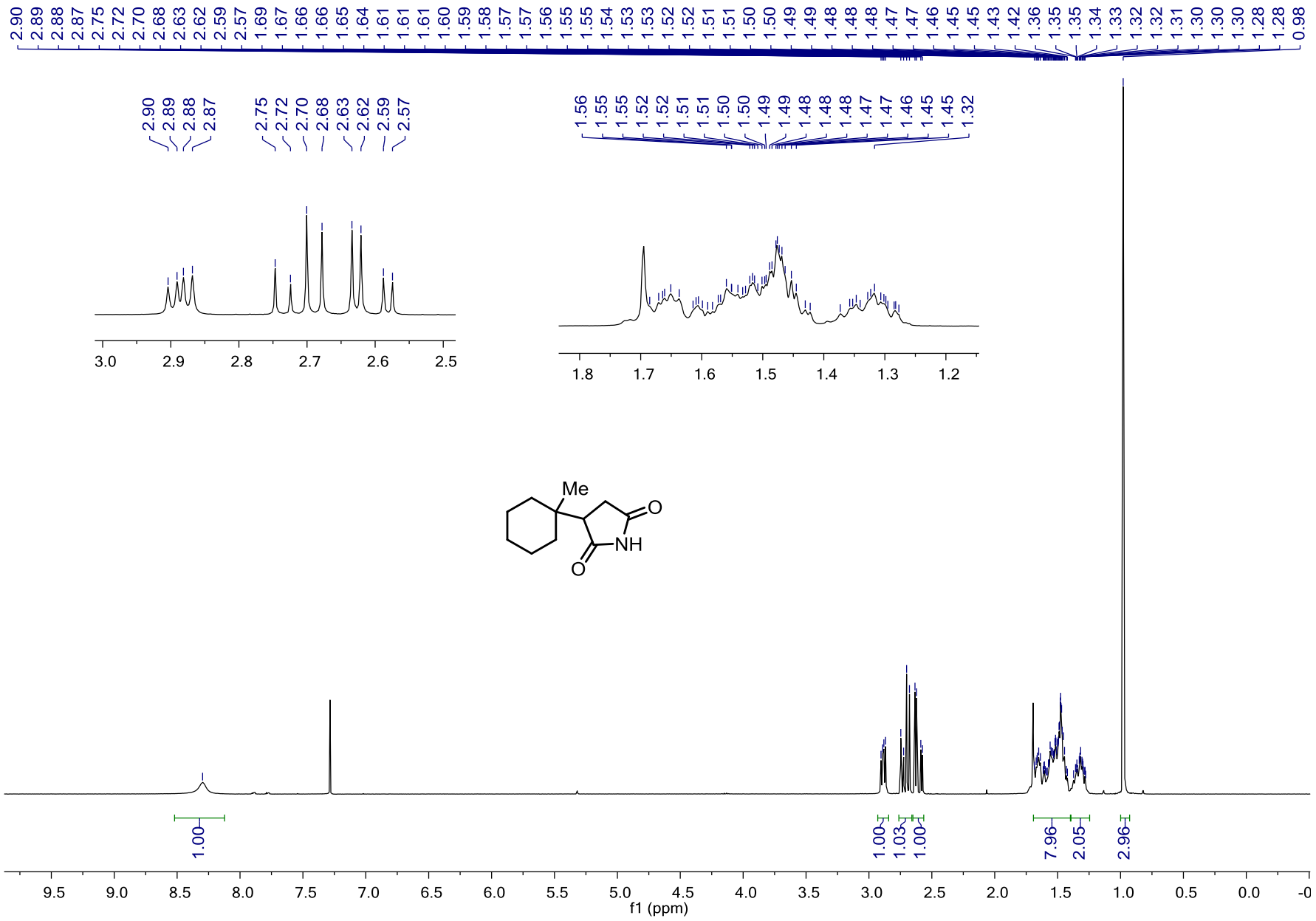
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4g***



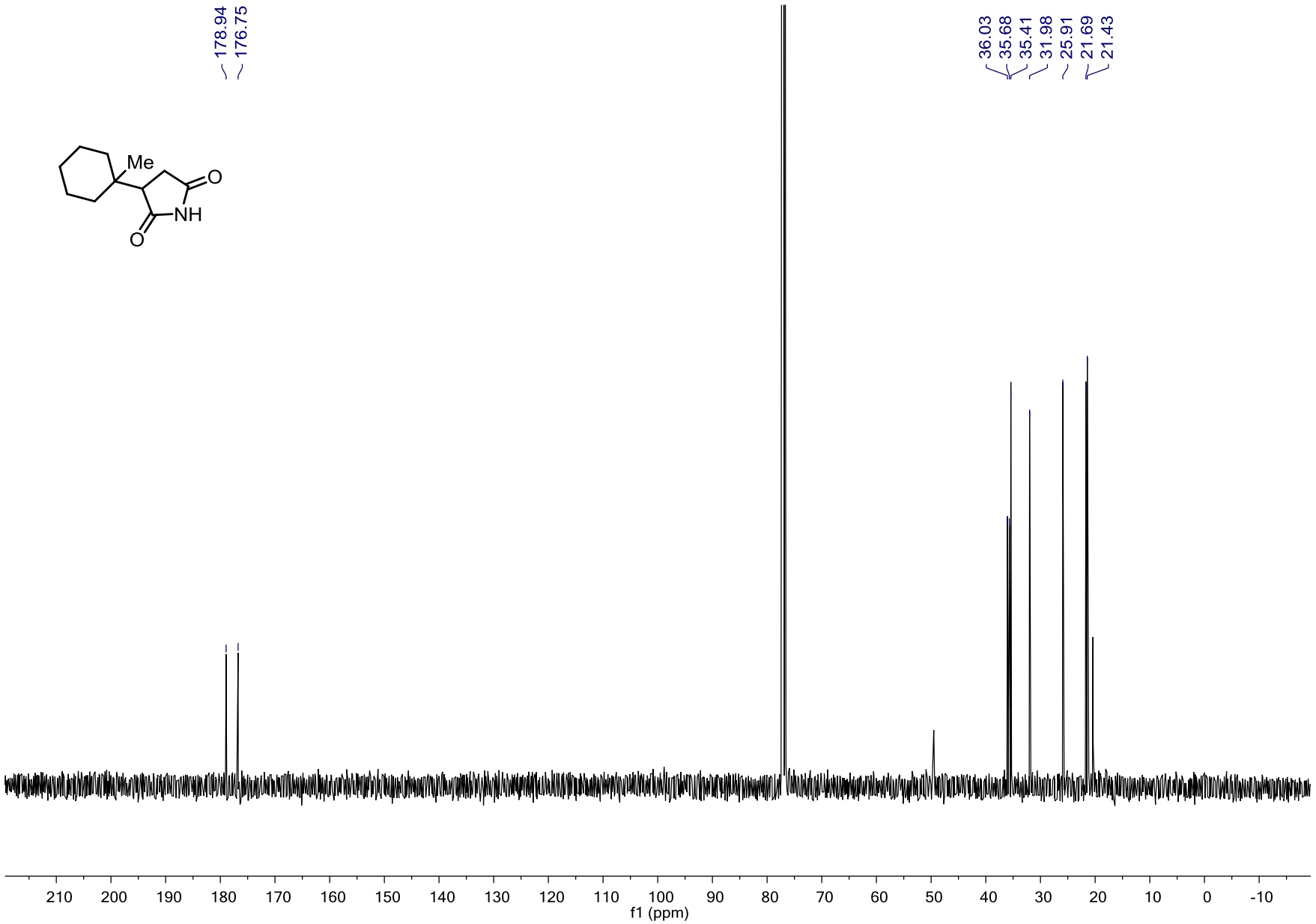
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4g***



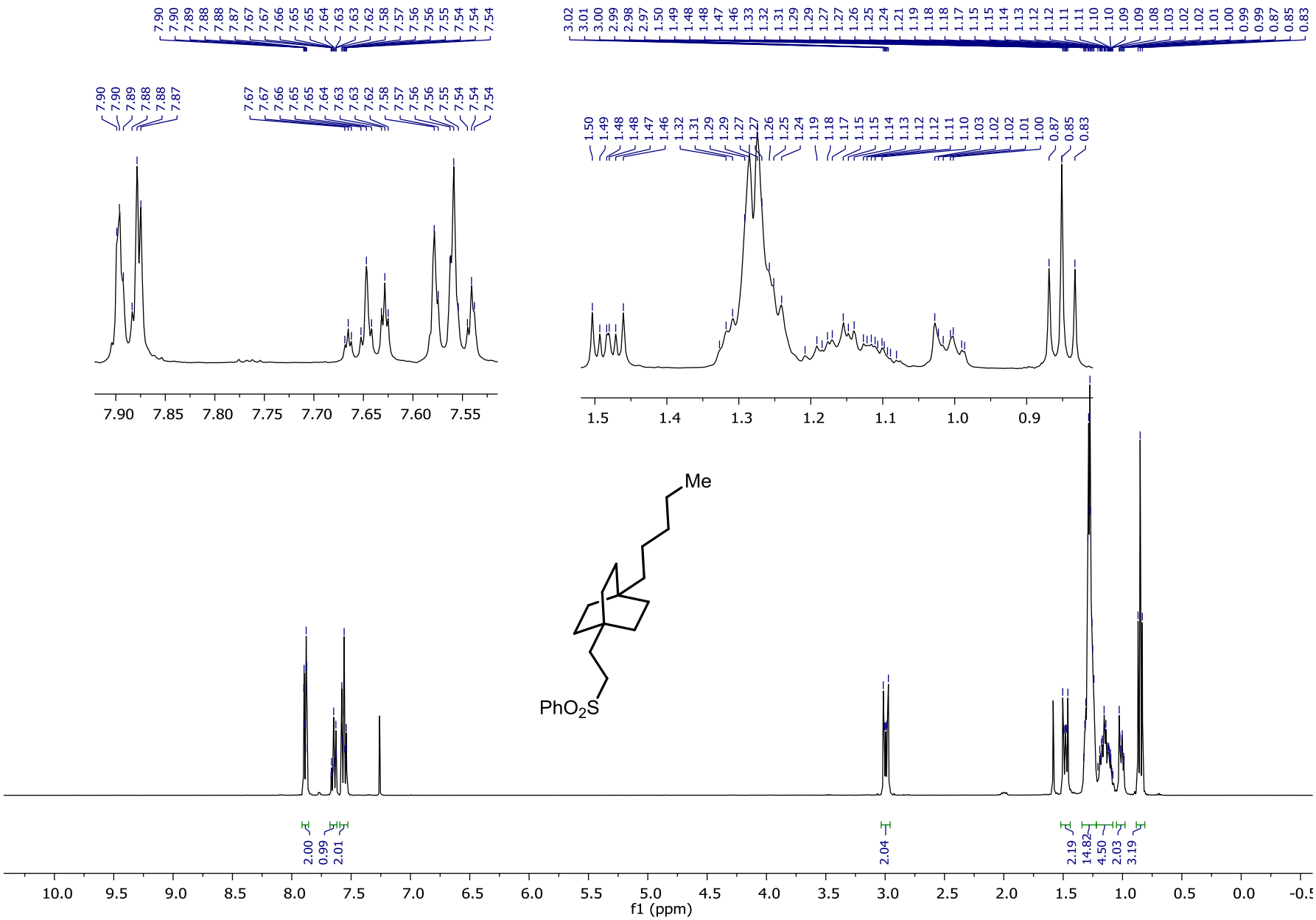
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4h***



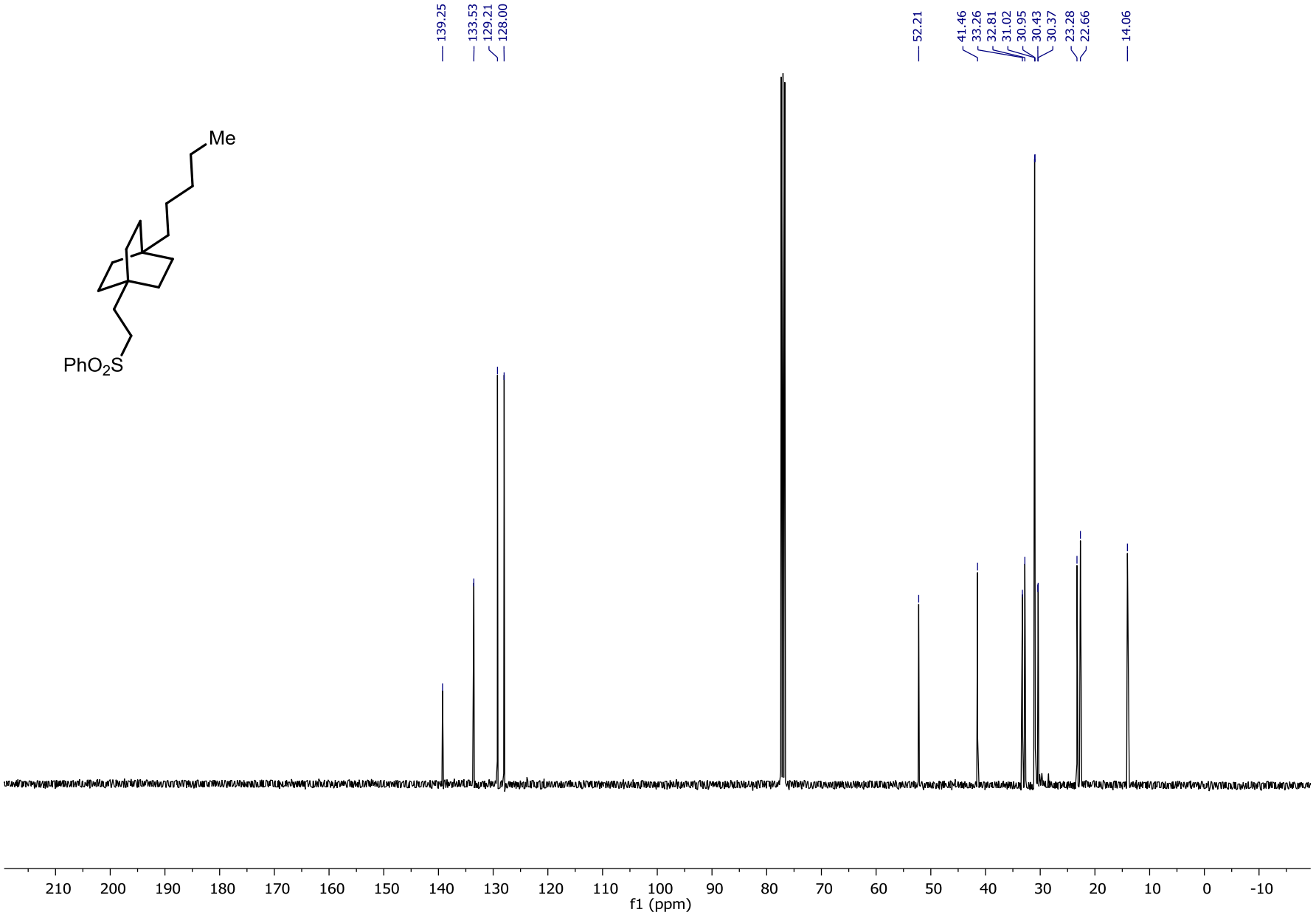
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4h***



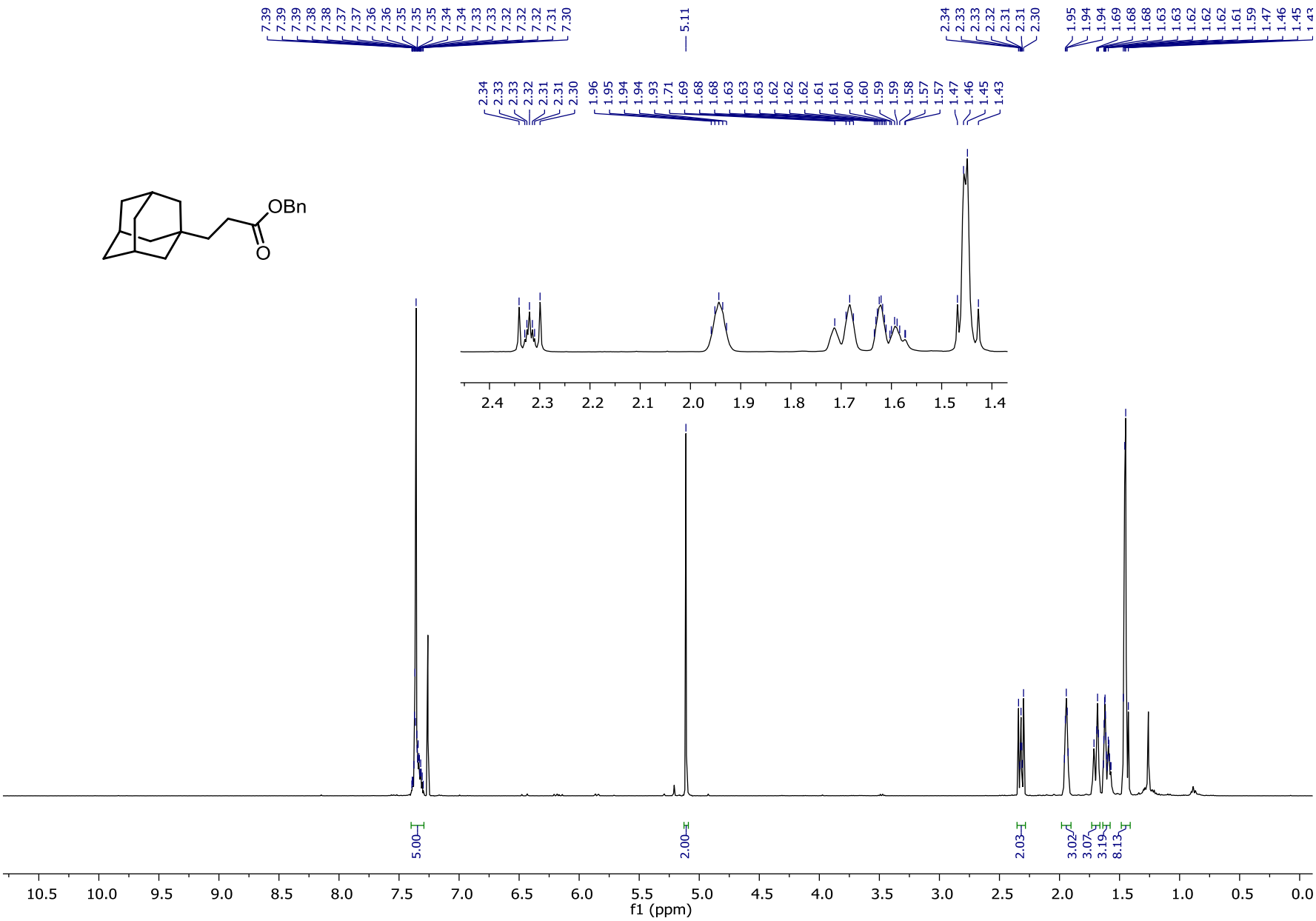
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4i***



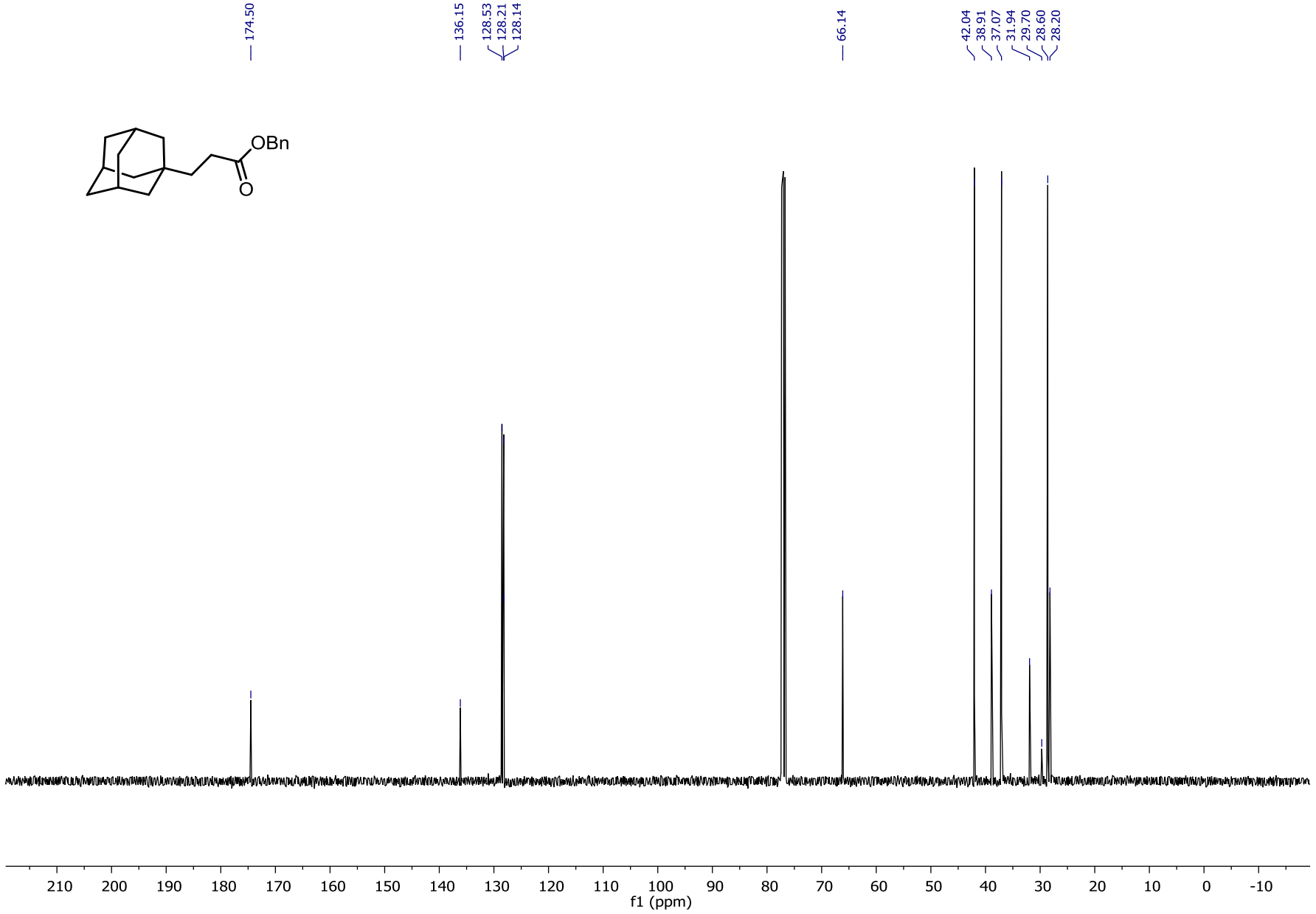
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4i***



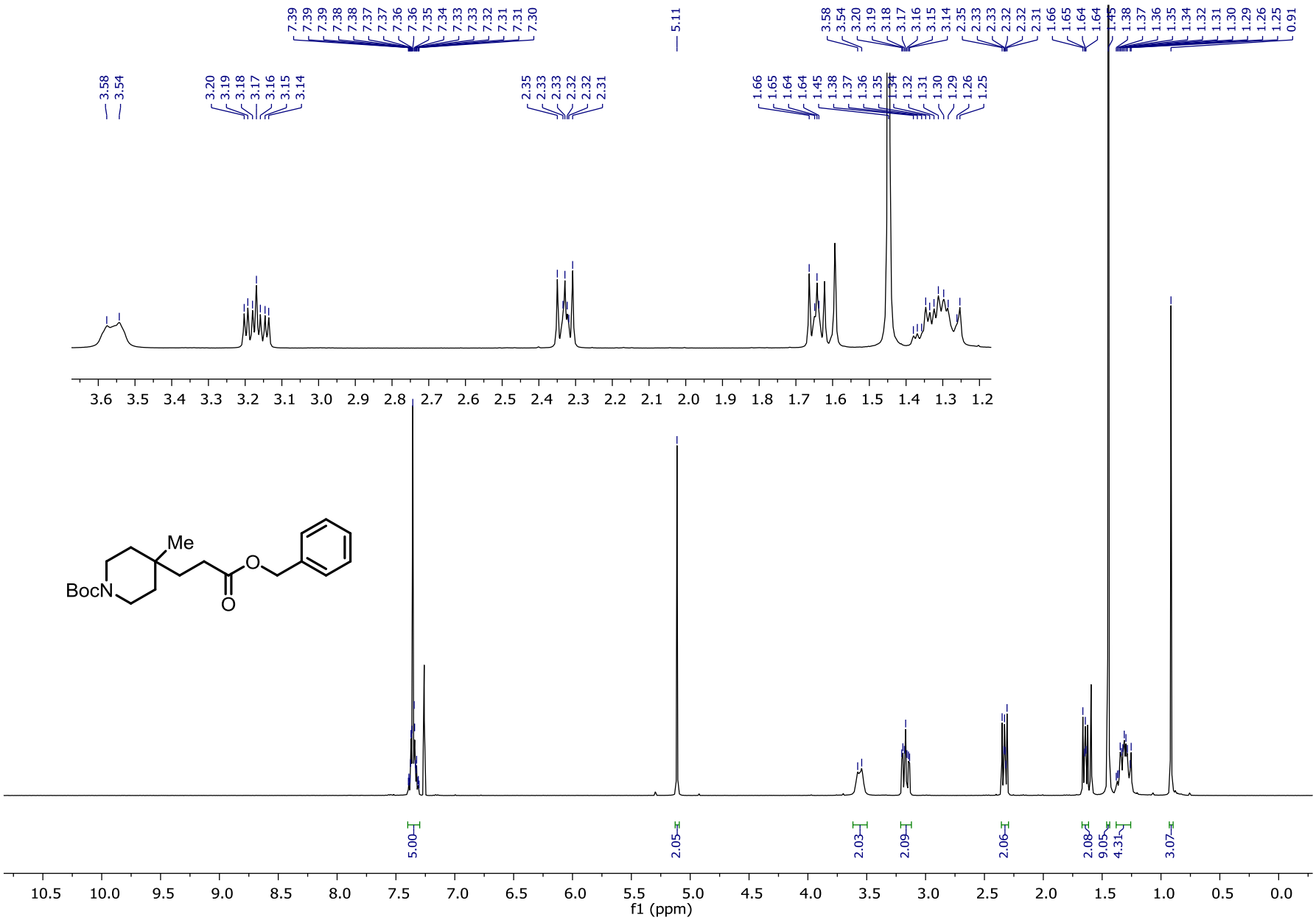
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4j***



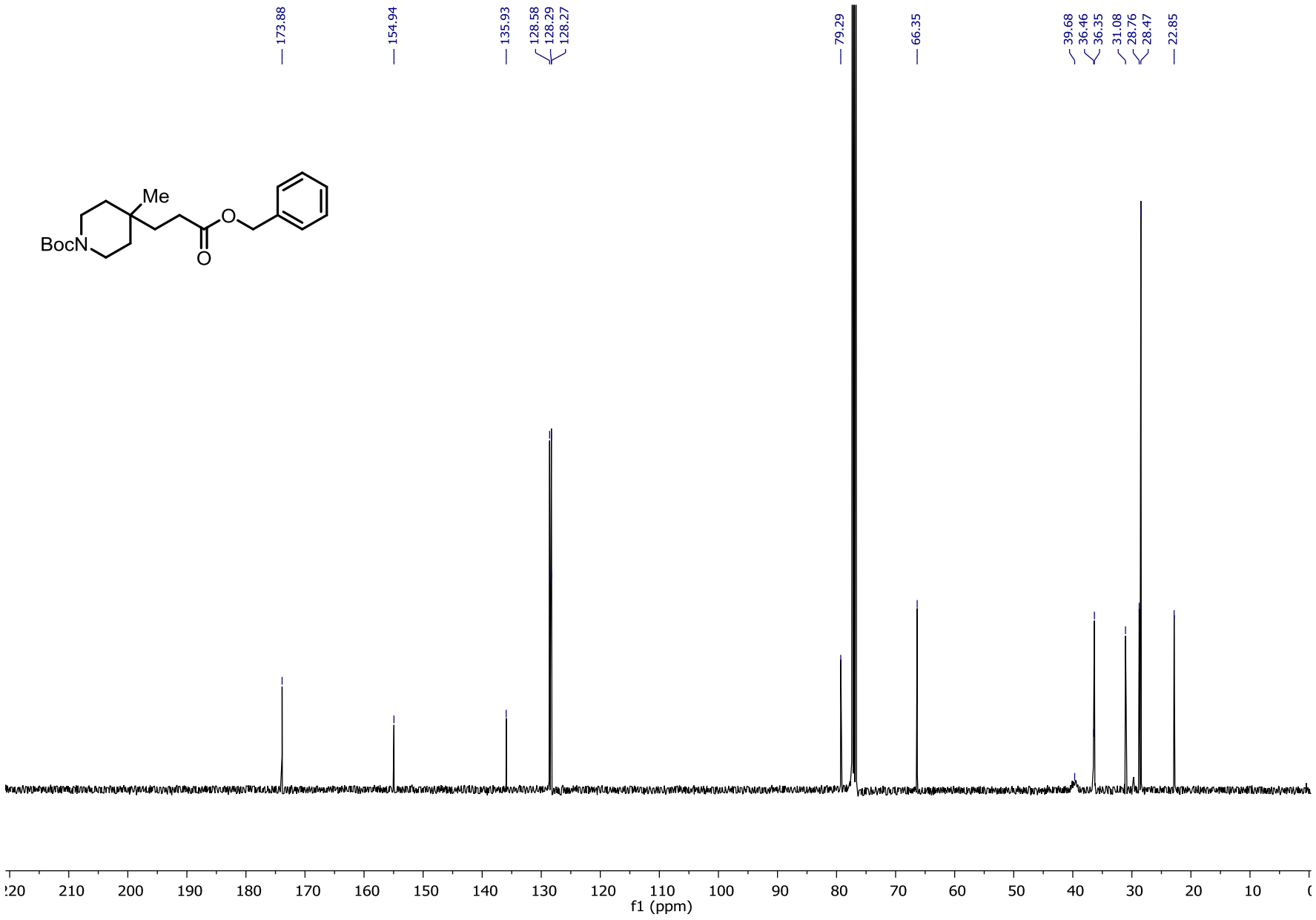
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4j***



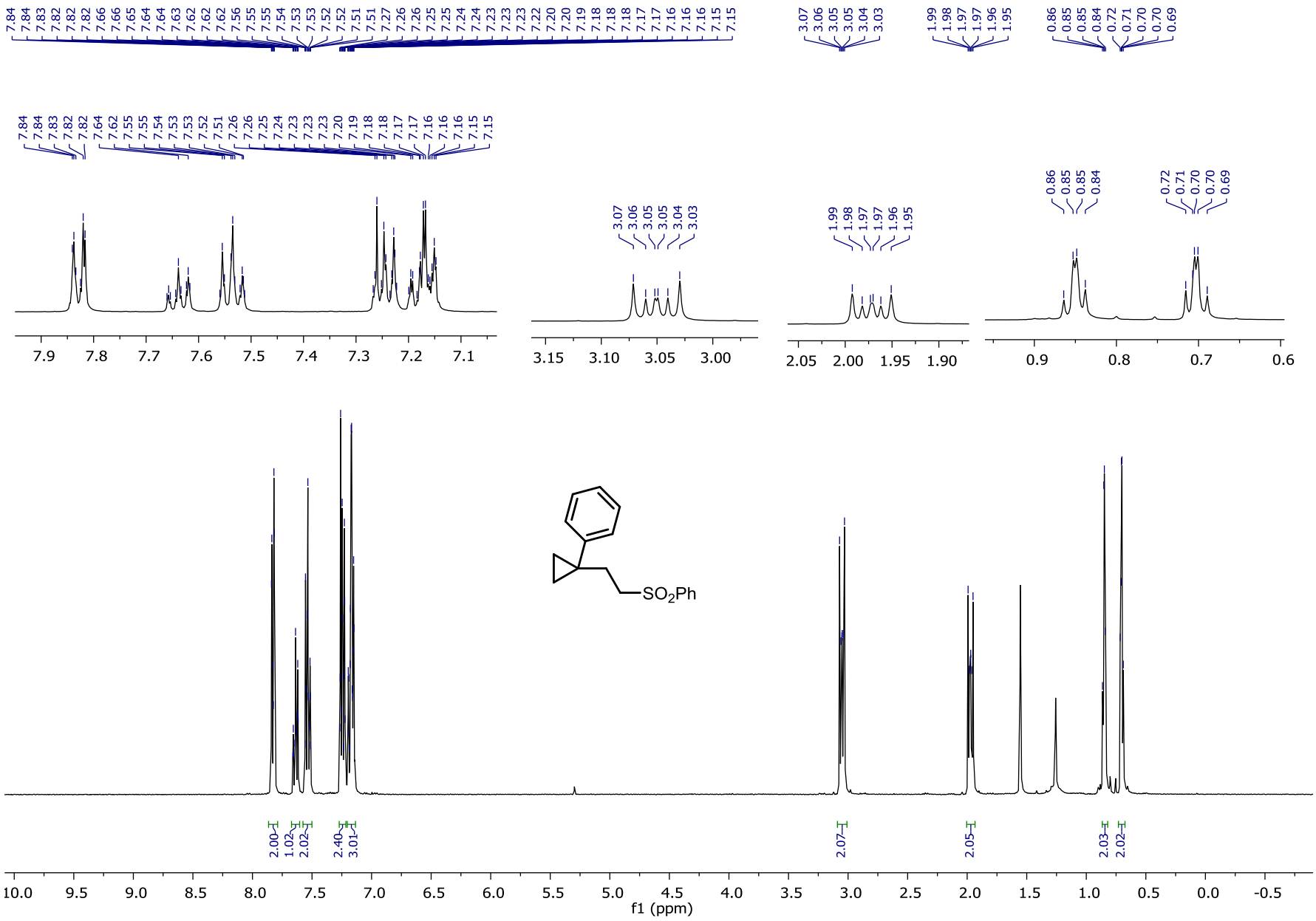
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4k***



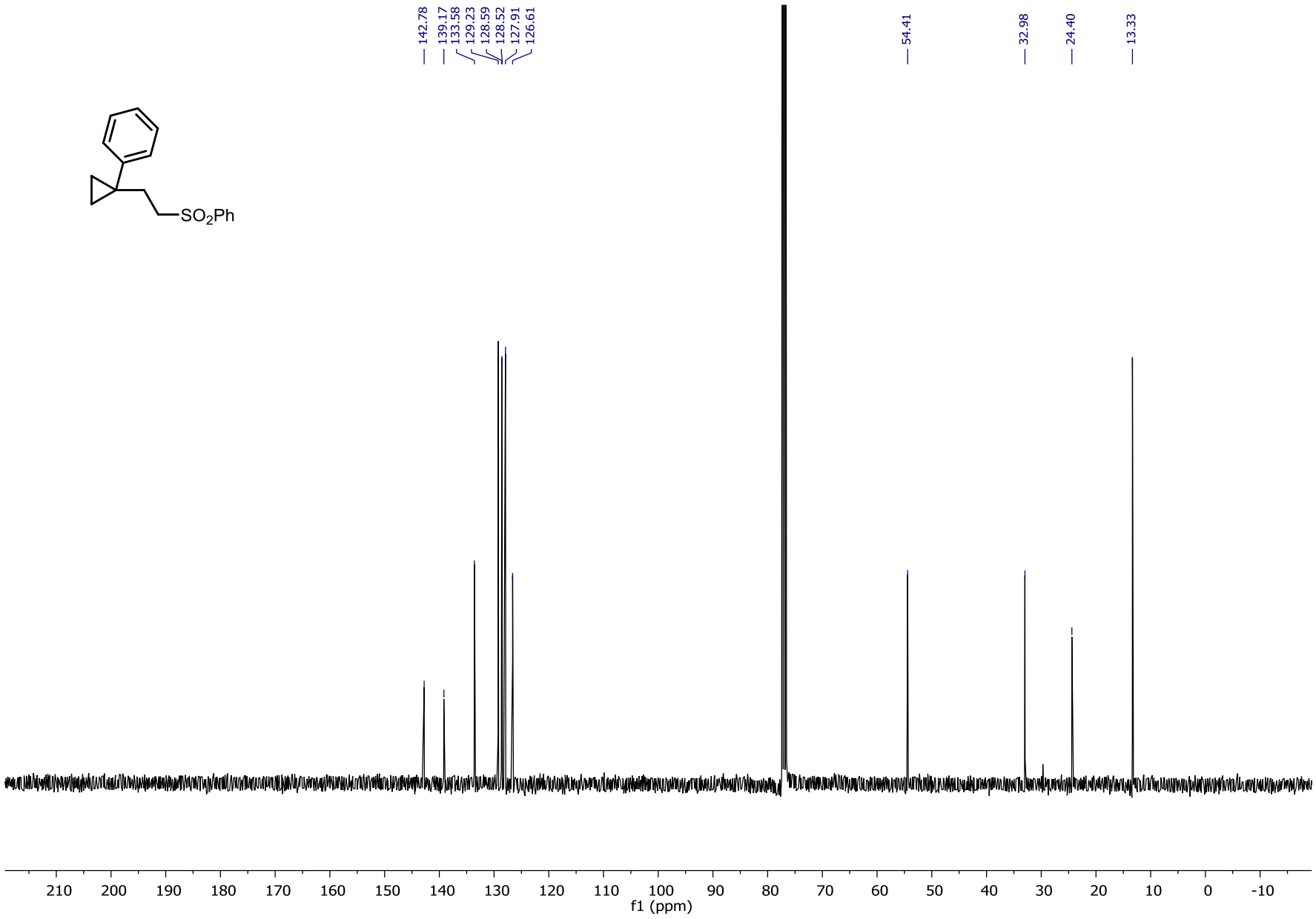
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4k***



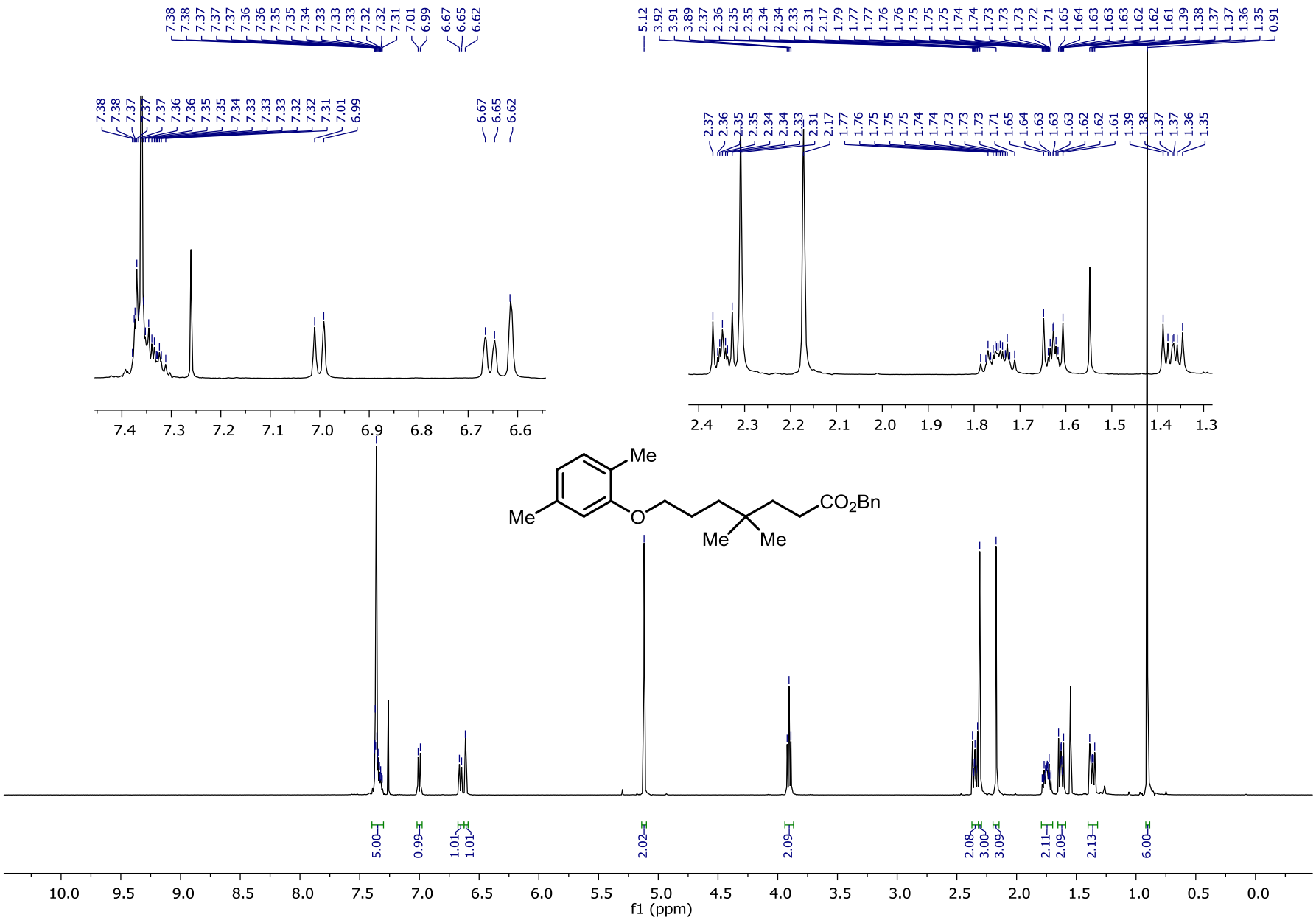
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4l***



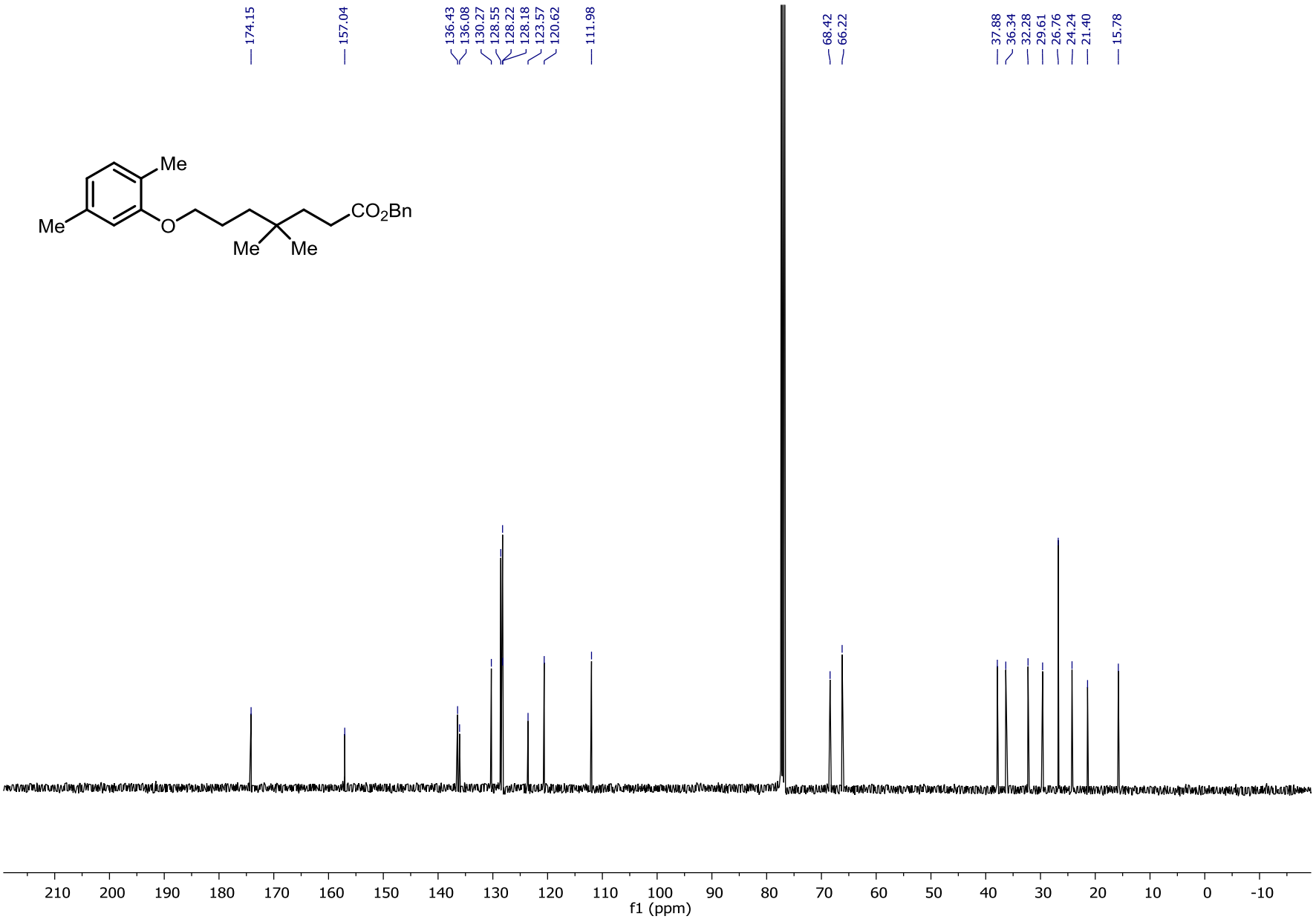
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4l***



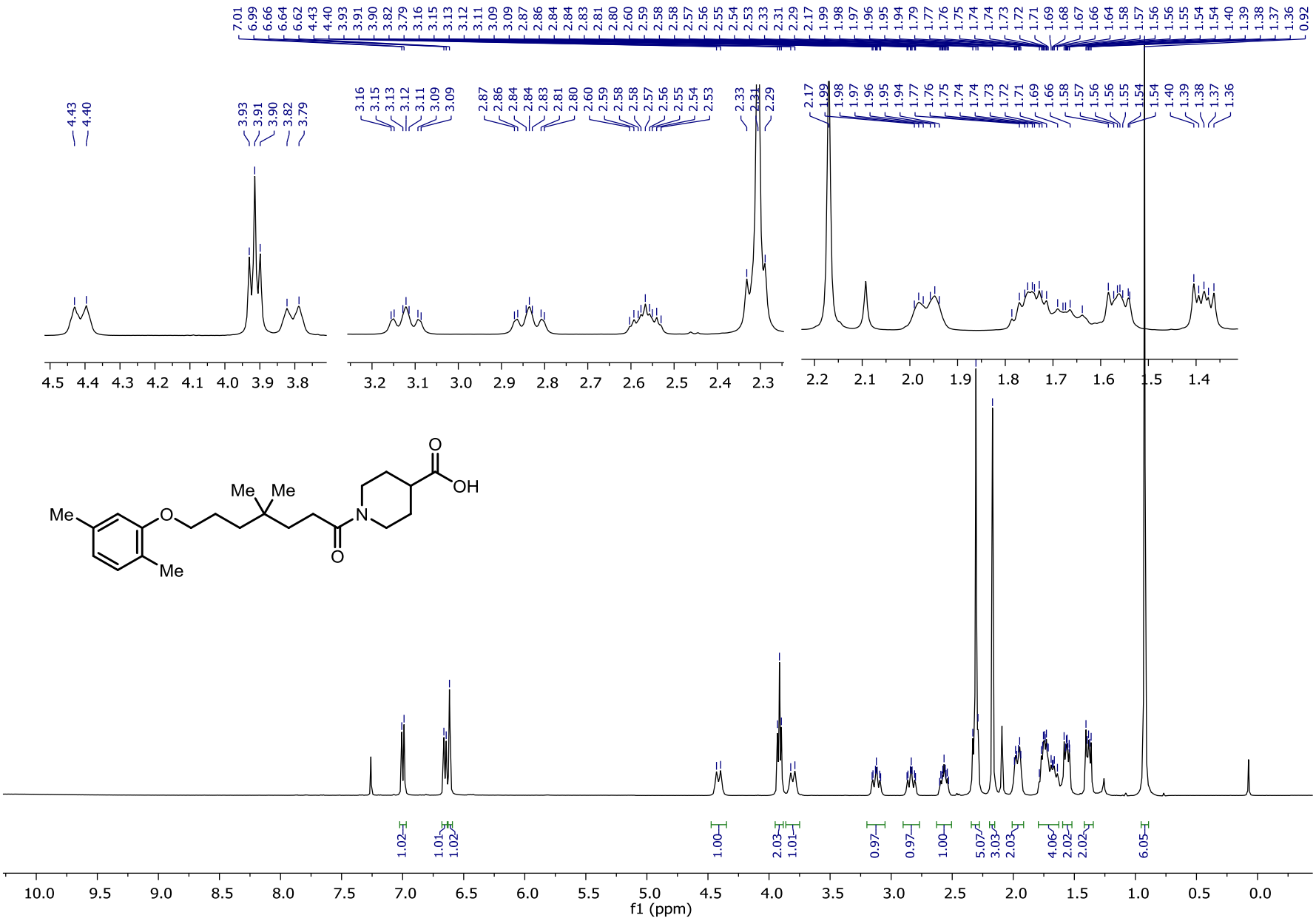
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4m***



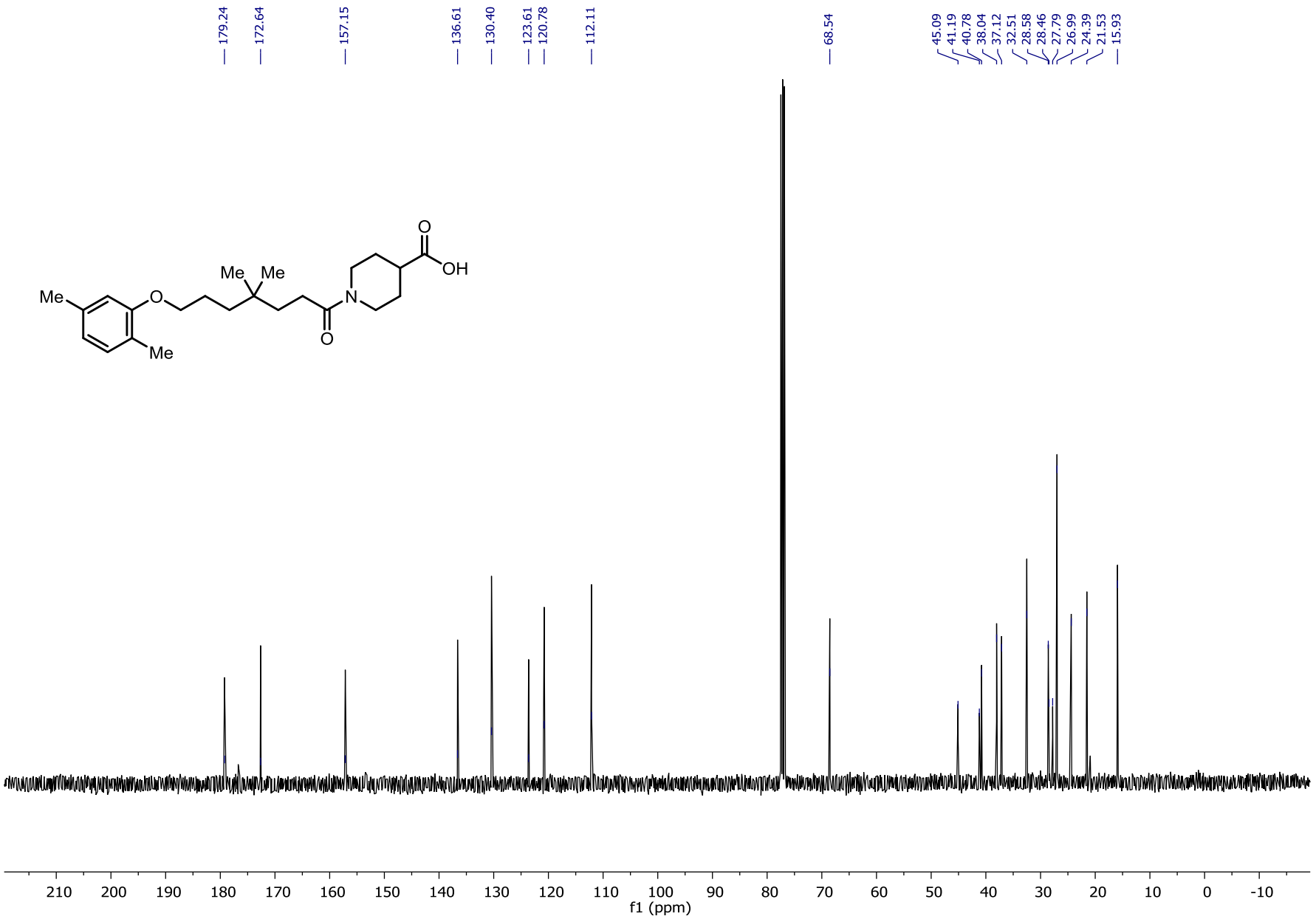
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4m***



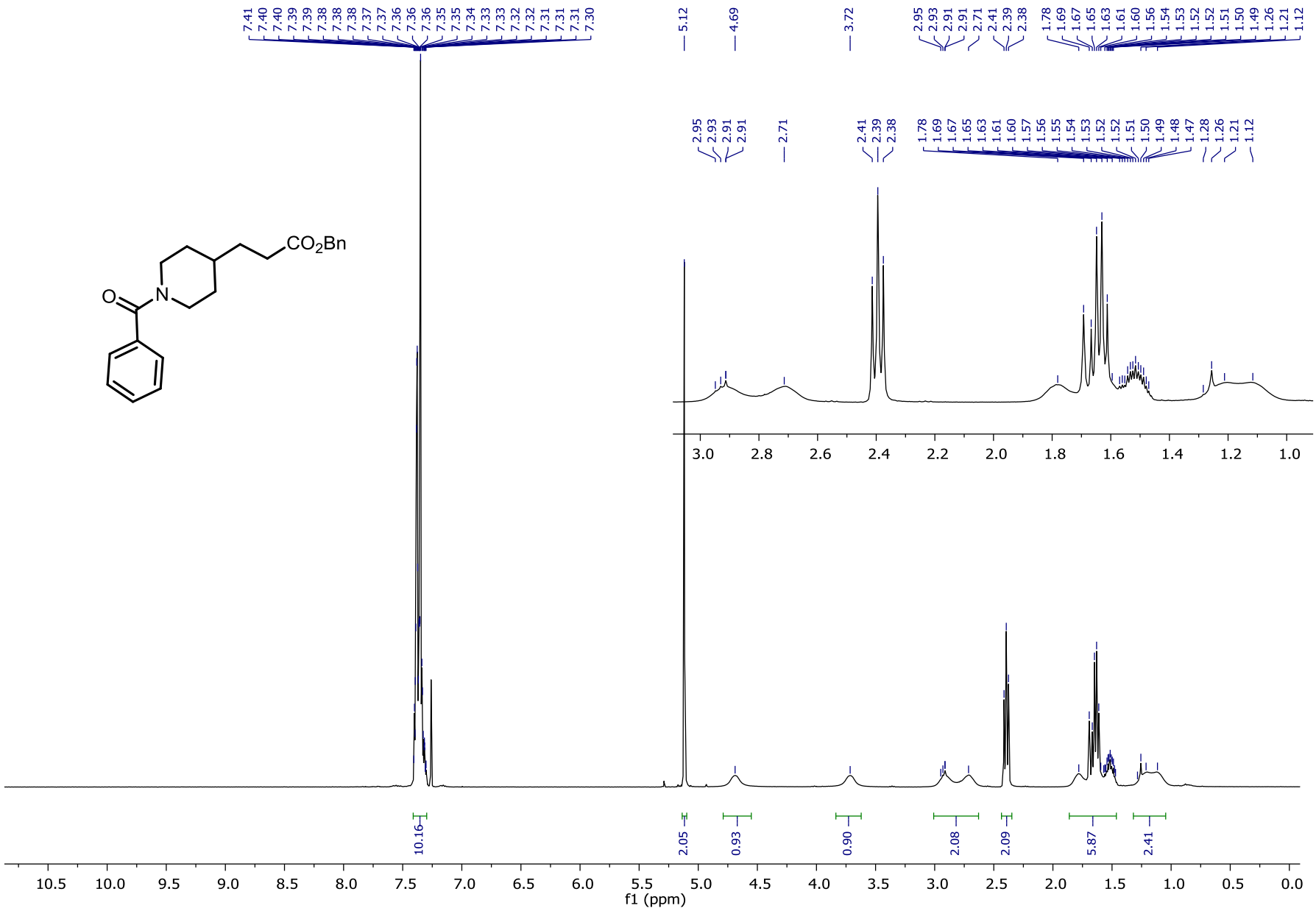
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4n***



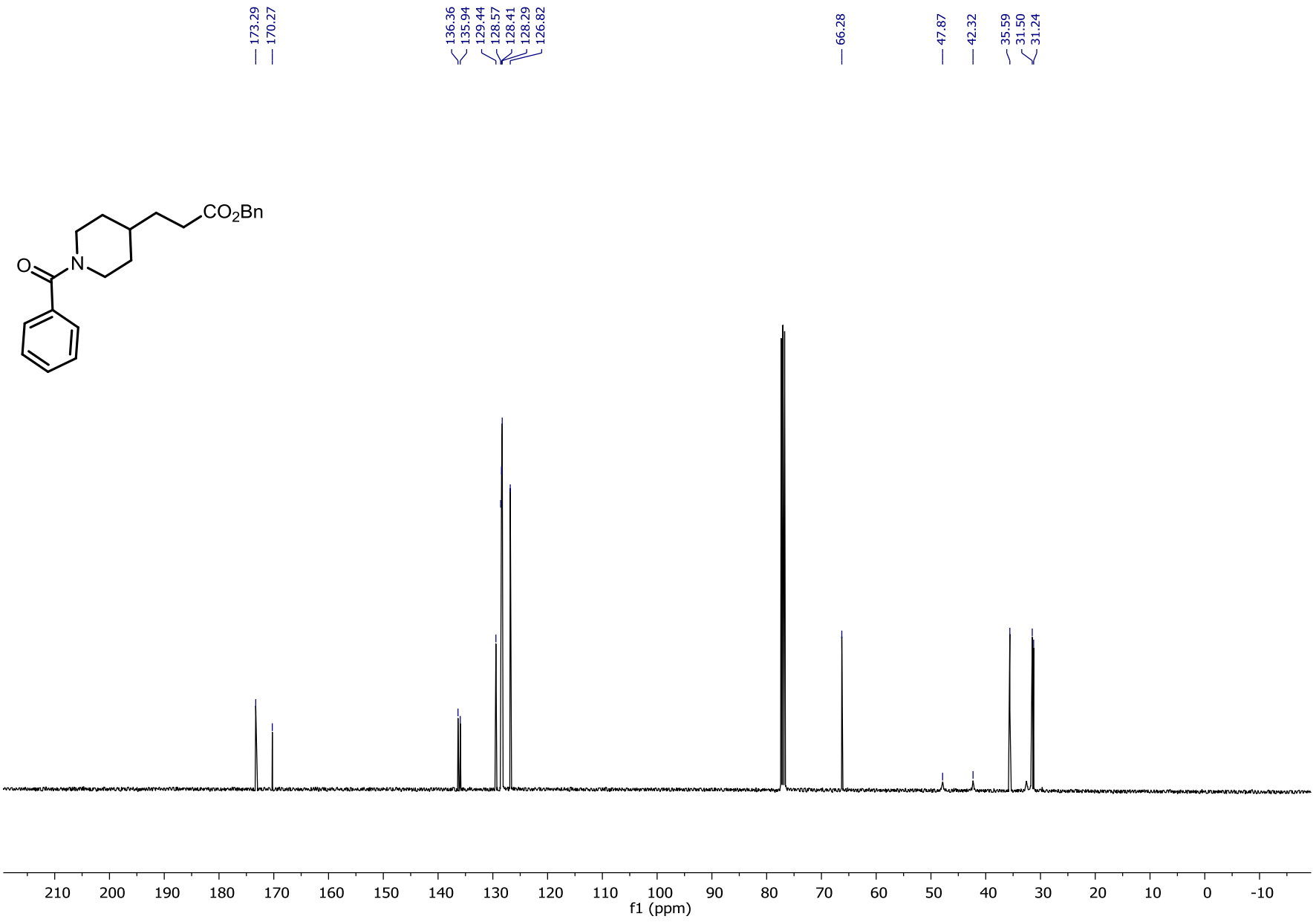
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4n***



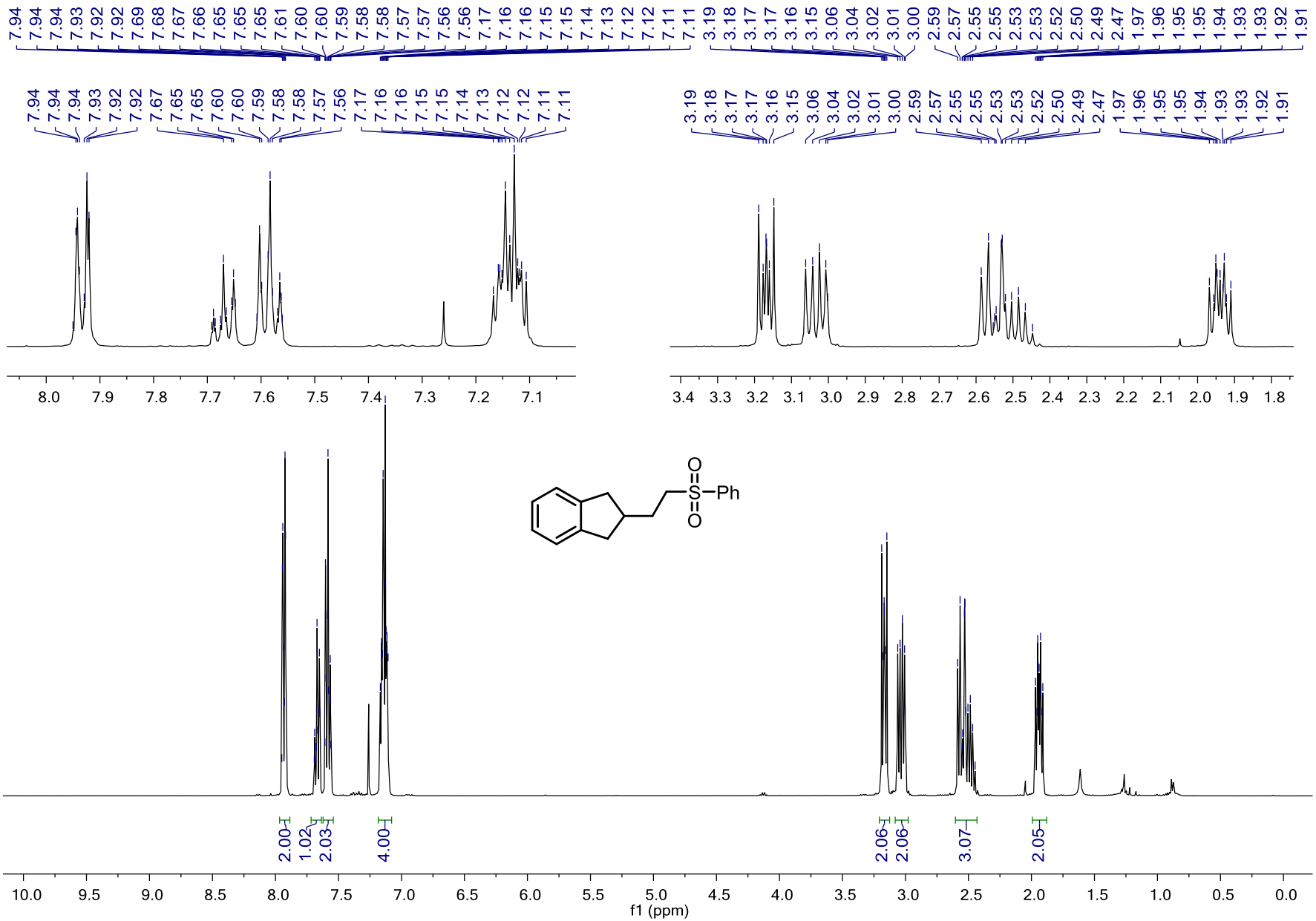
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4o***



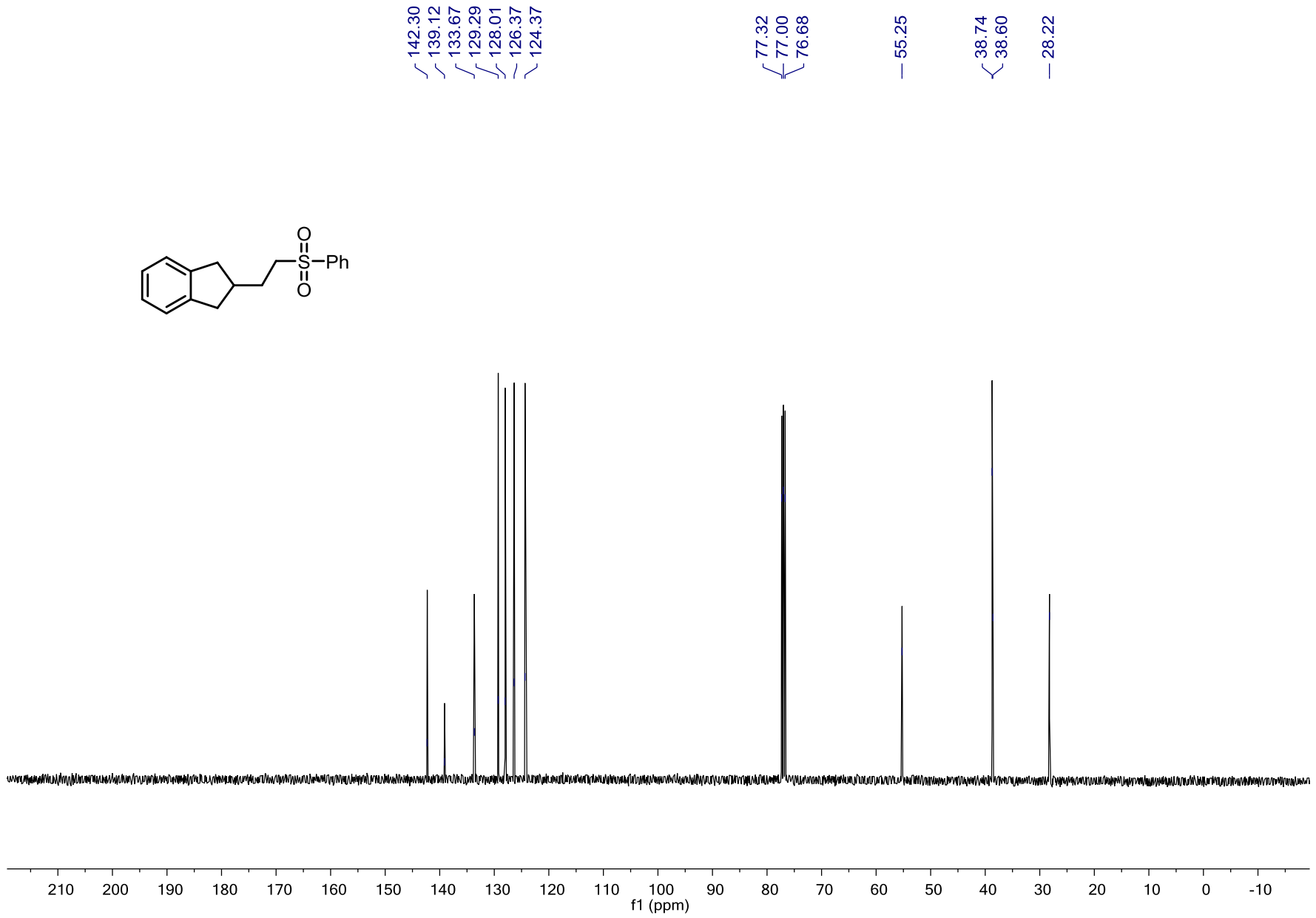
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4o***



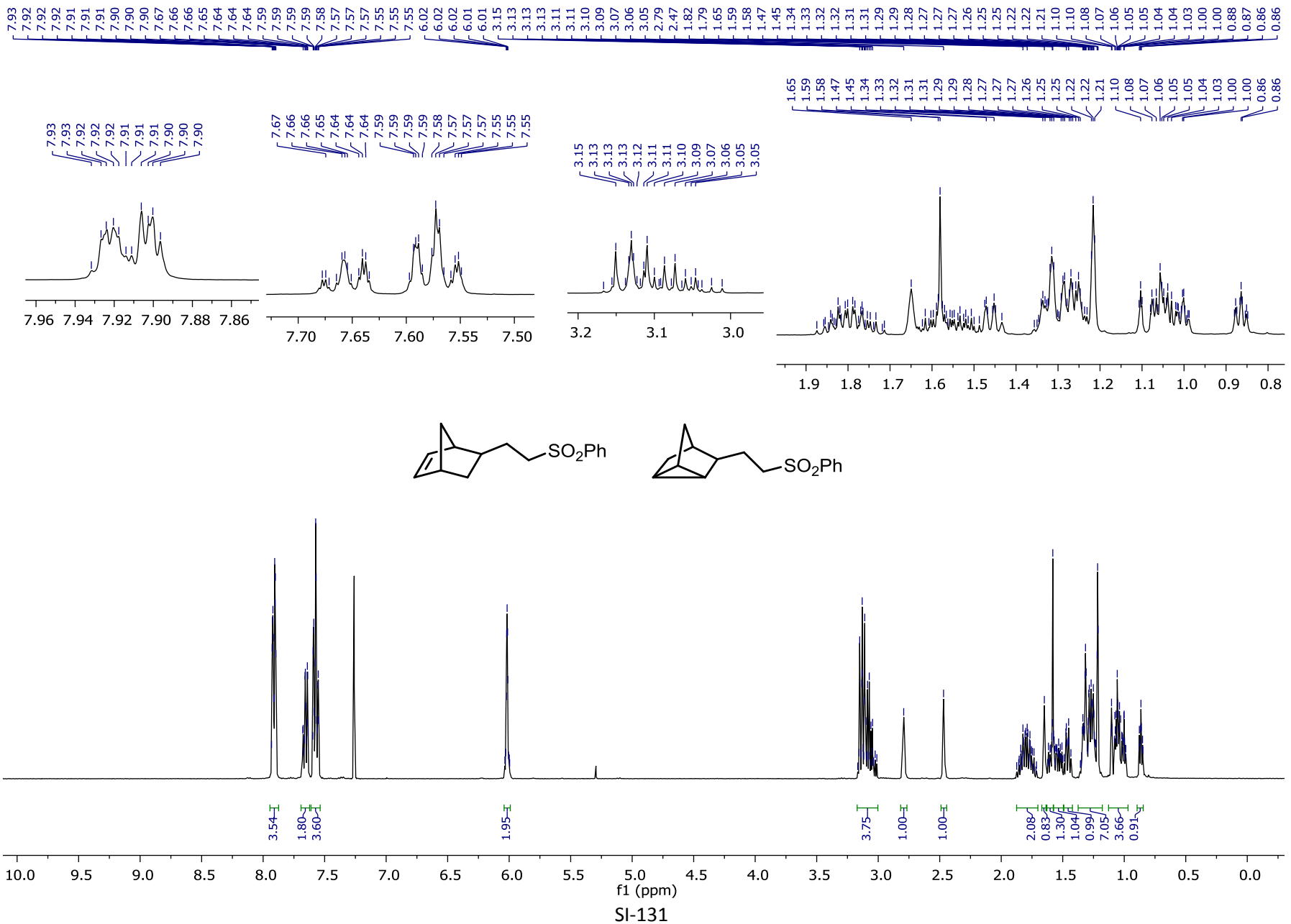
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4p***



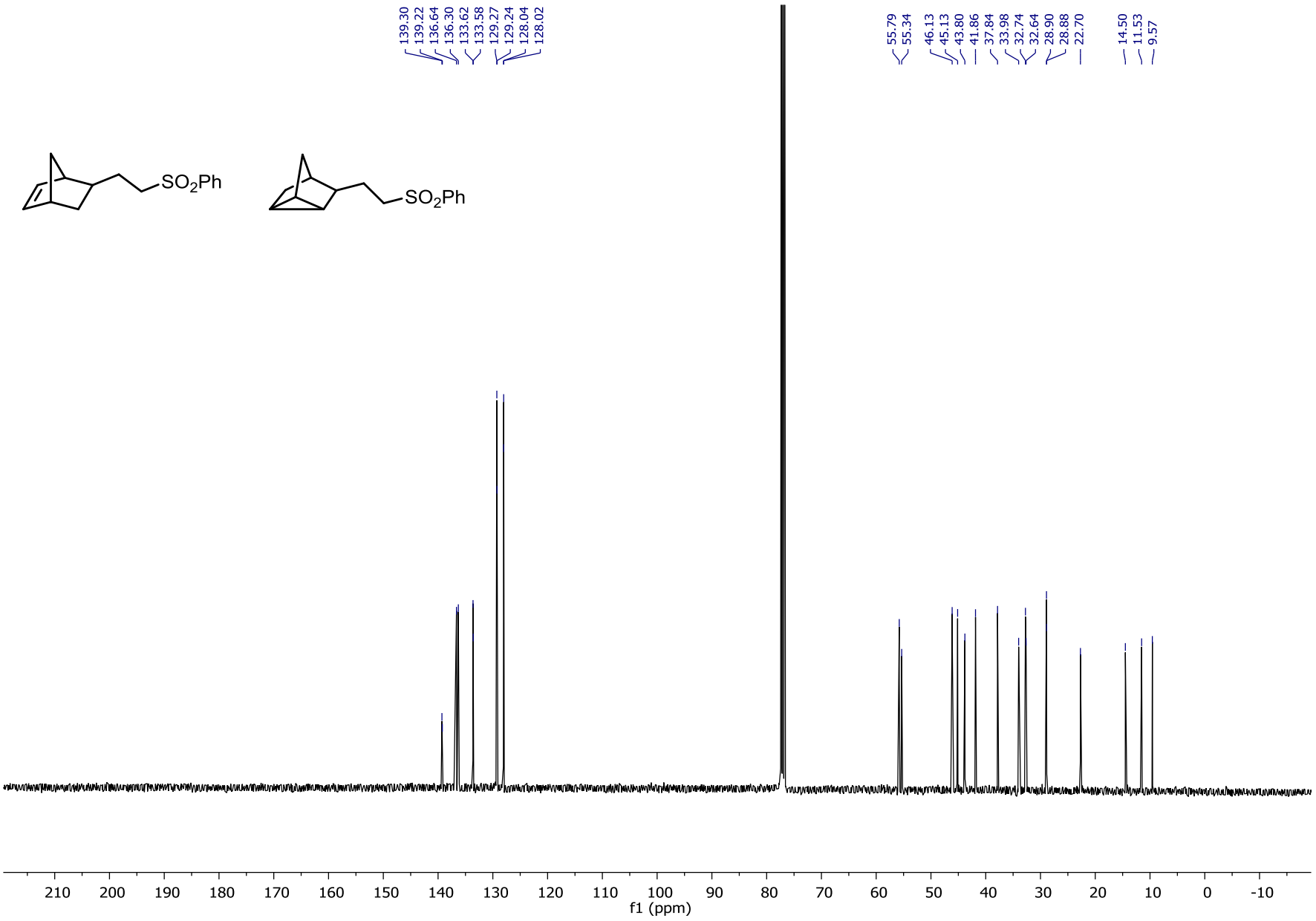
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4p***



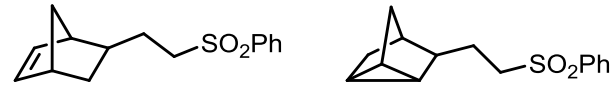
*^{1}H-NMR (400 MHz, CDCl3) for compound **4q** and **4q'***

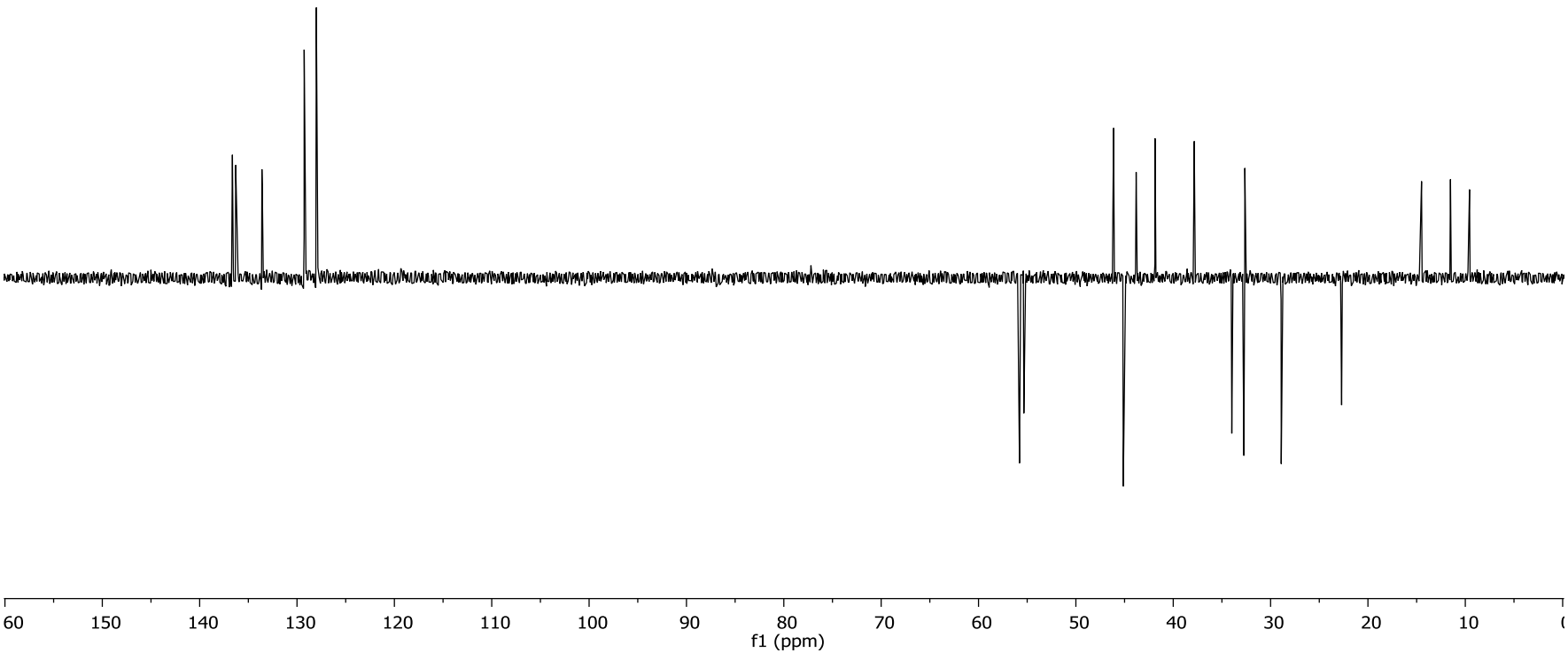


*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4q** and **4q'***

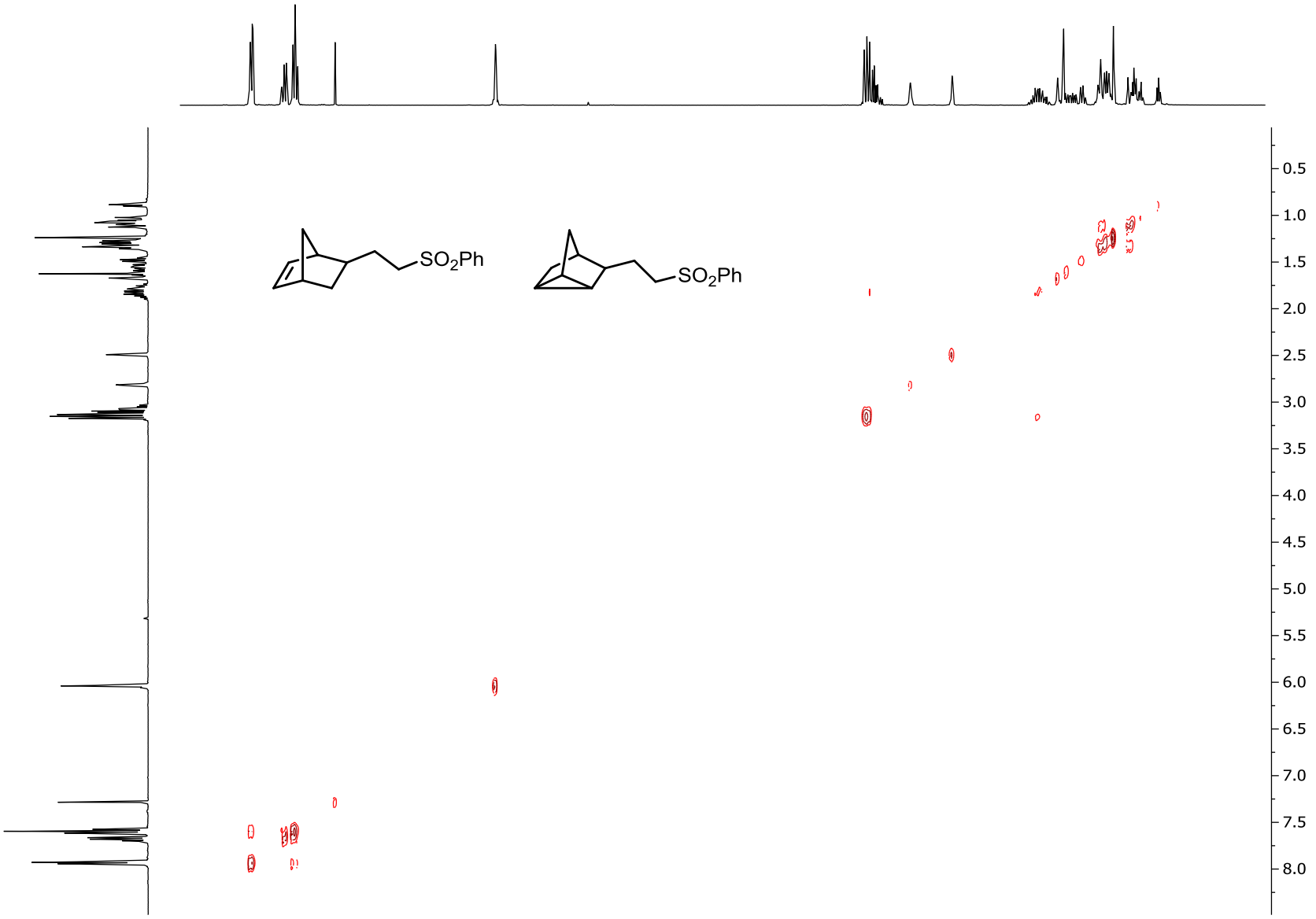


*DEPT 135 NMR (101 MHz, $CDCl_3$) for compound **4q** and **4q'***

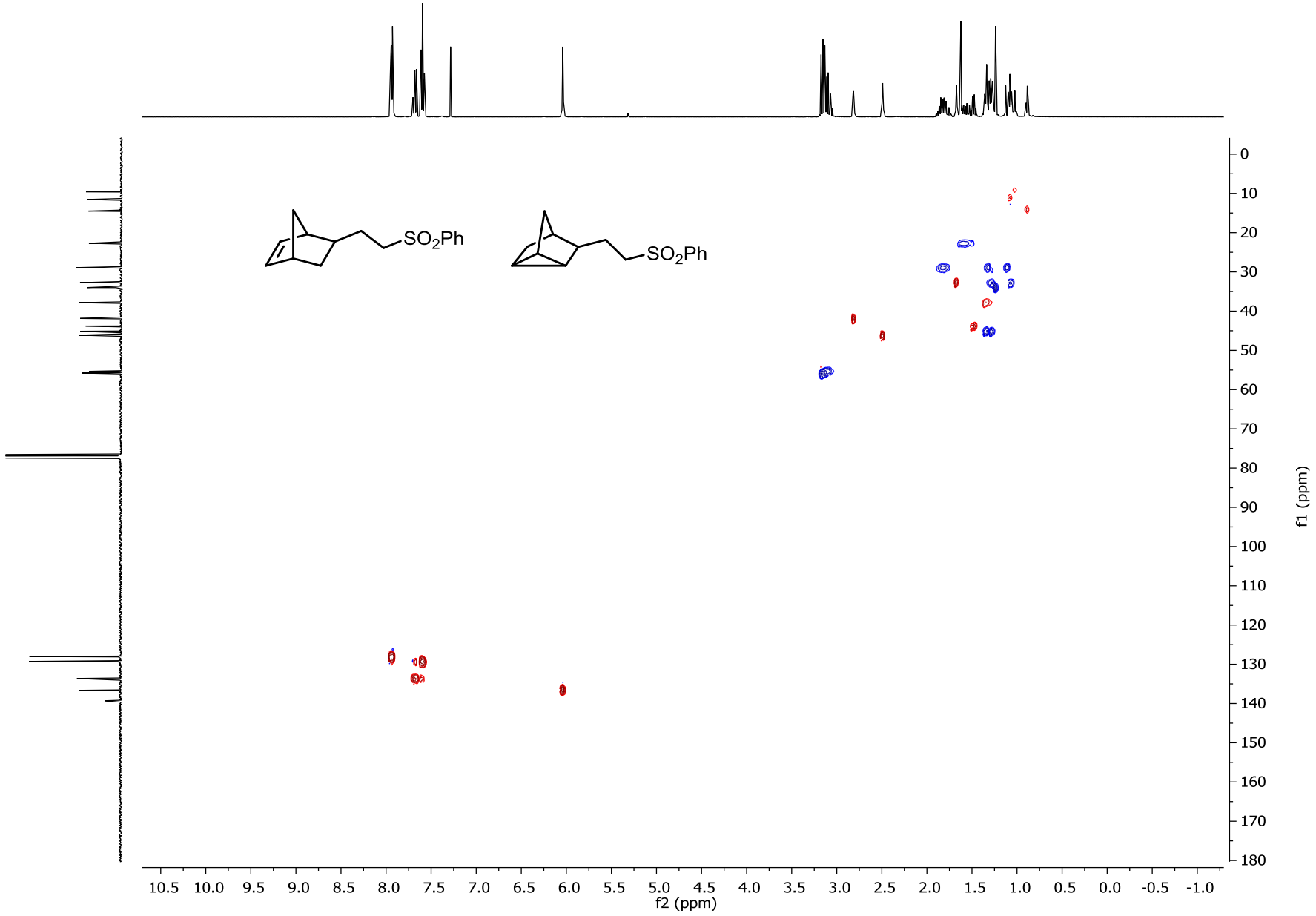




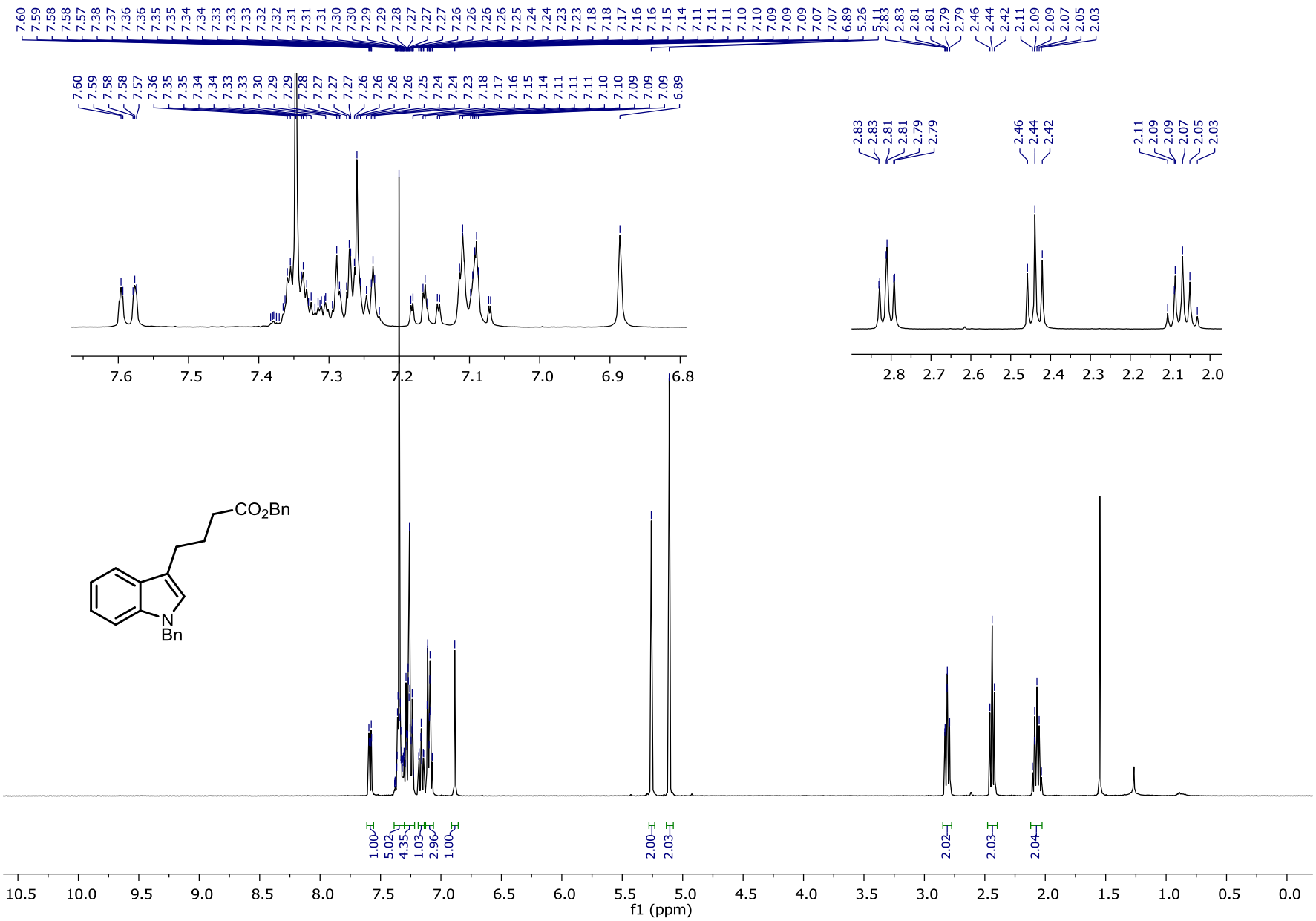
*COSY NMR (400 MHz, $CDCl_3$) for compound **4q** and **4q'***



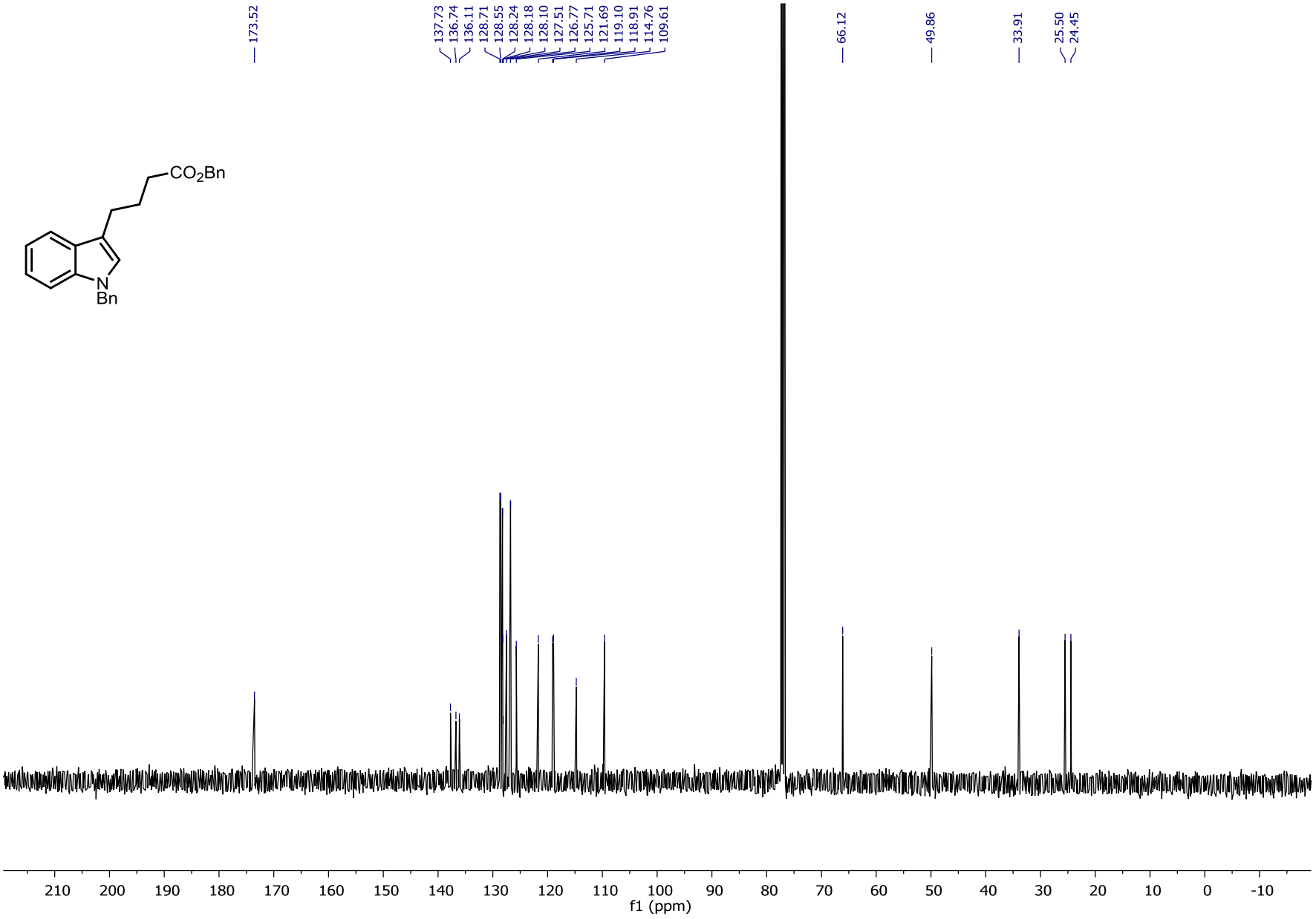
*HSQC-NMR (400 MHz, $CDCl_3$) for compound **4q** and **4q'***



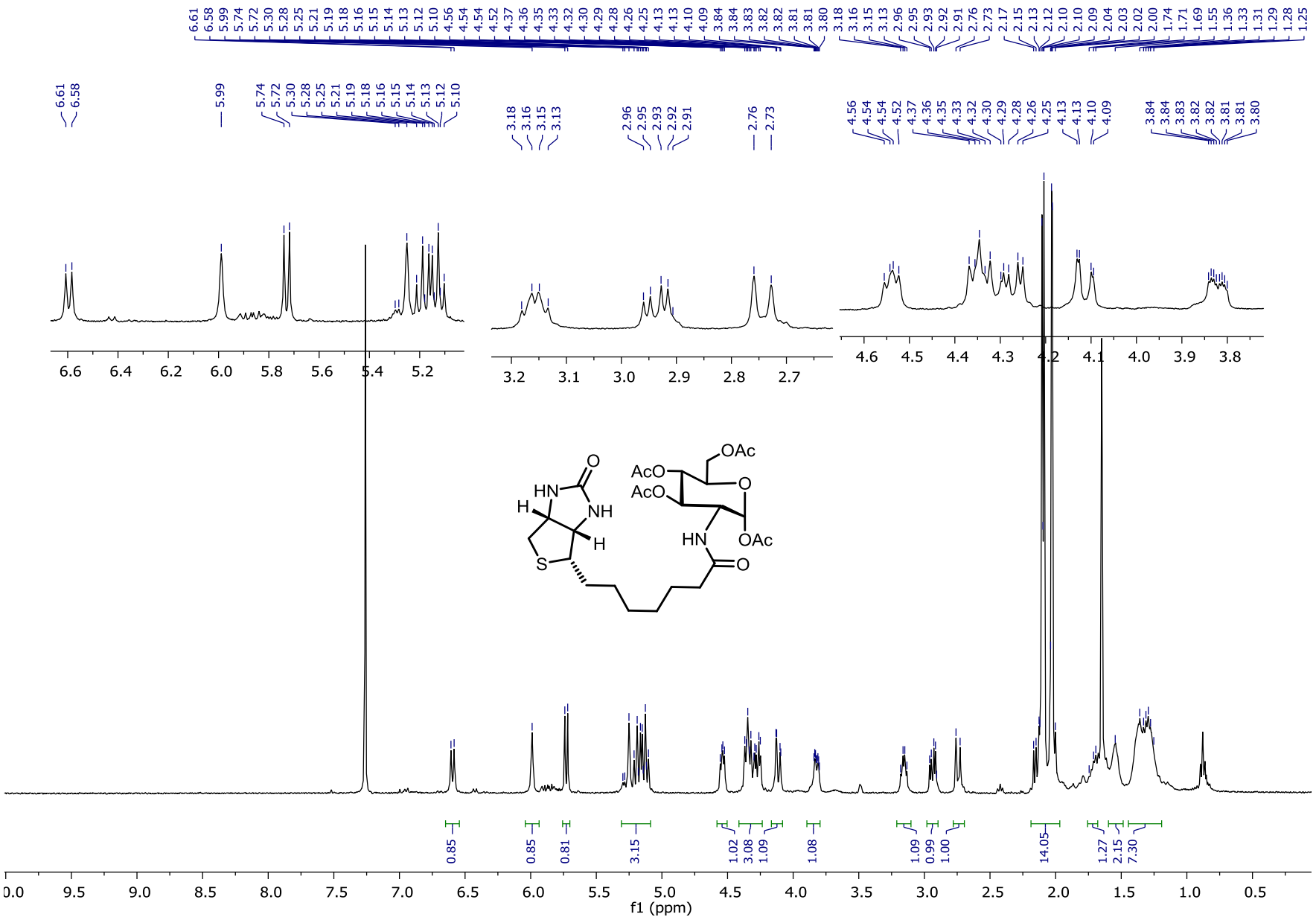
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4r***



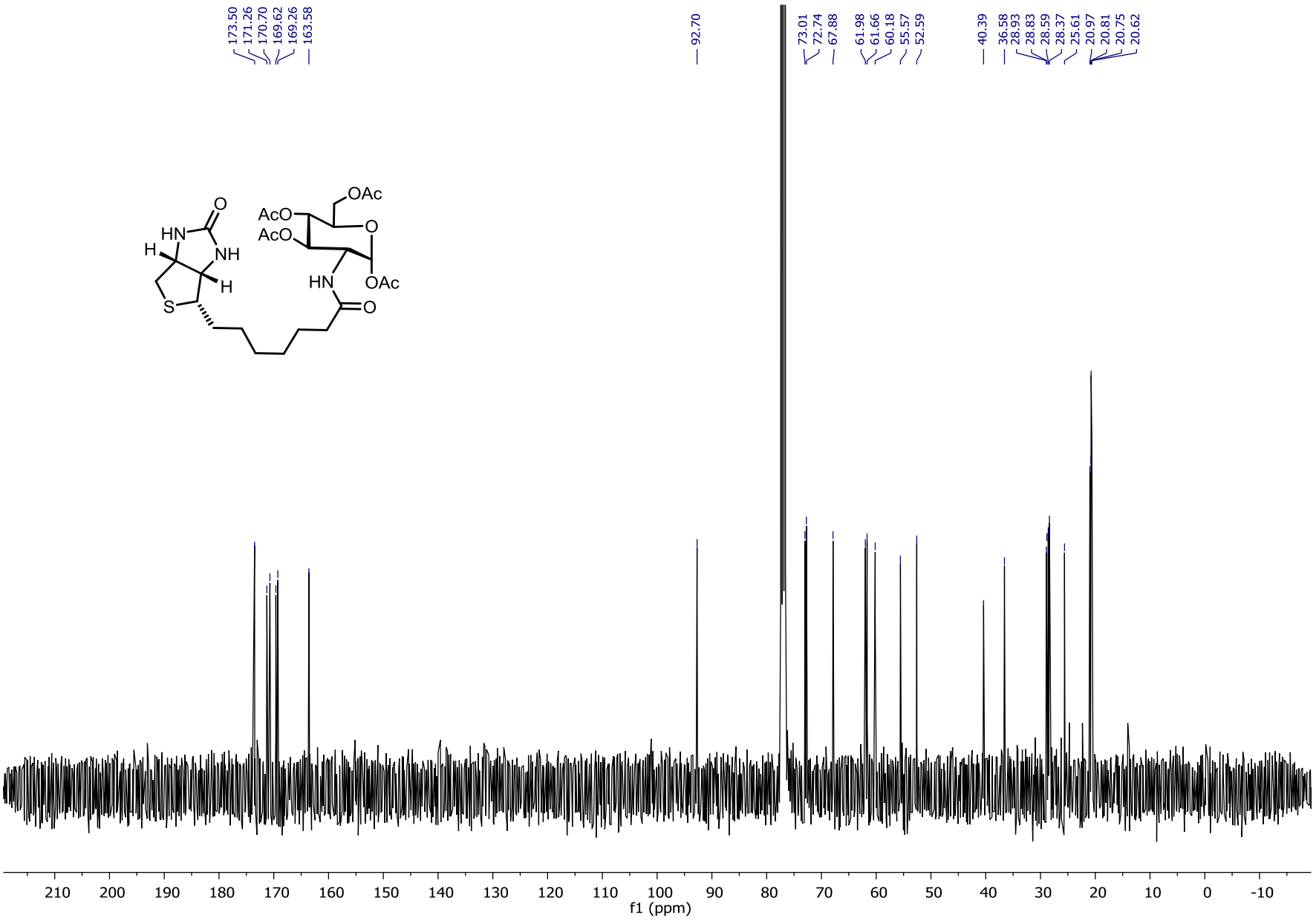
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4r***



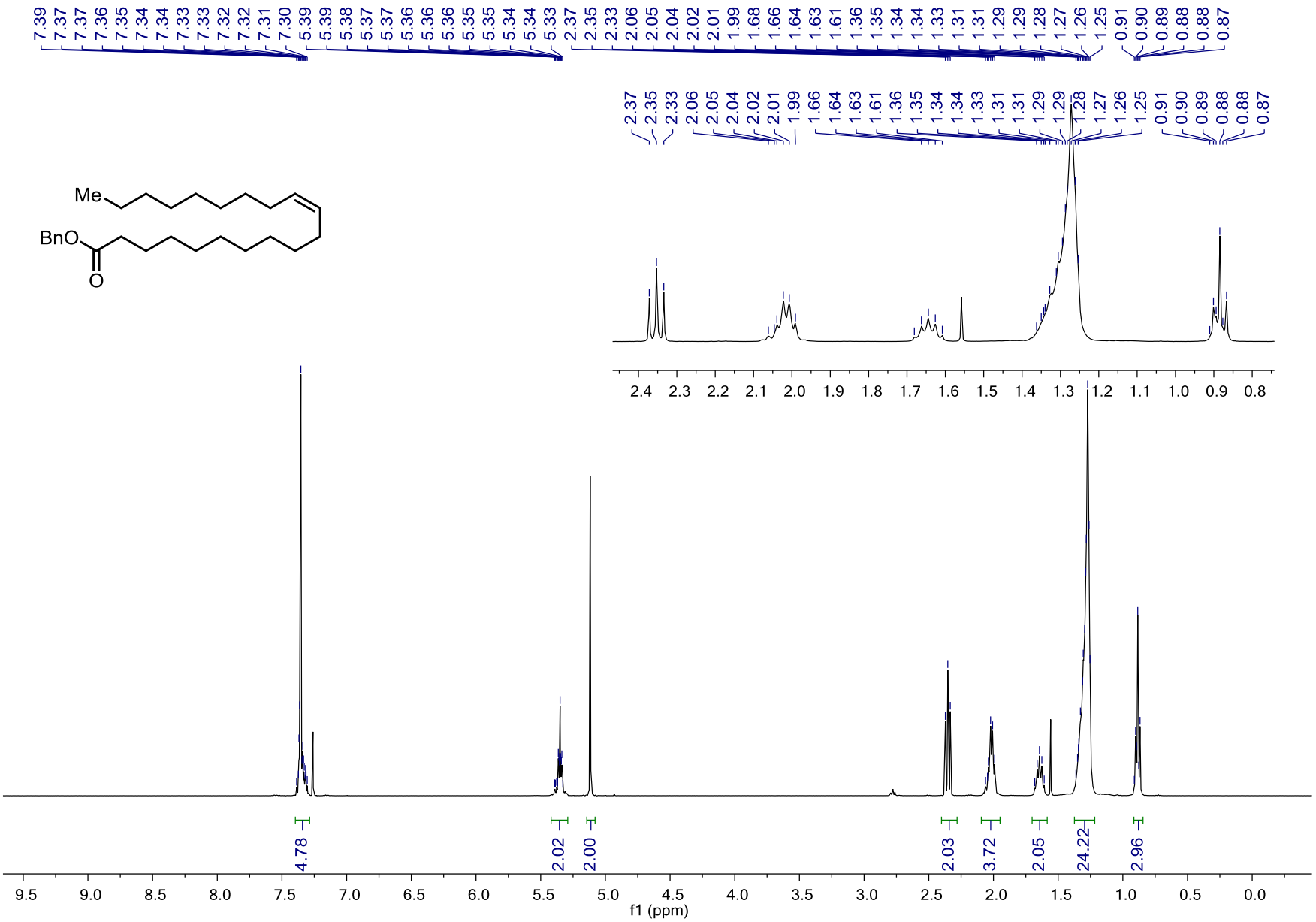
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4s***



*^{13}C-NMR (101MHz, $CDCl_3$) for compound **4s***



*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4t***



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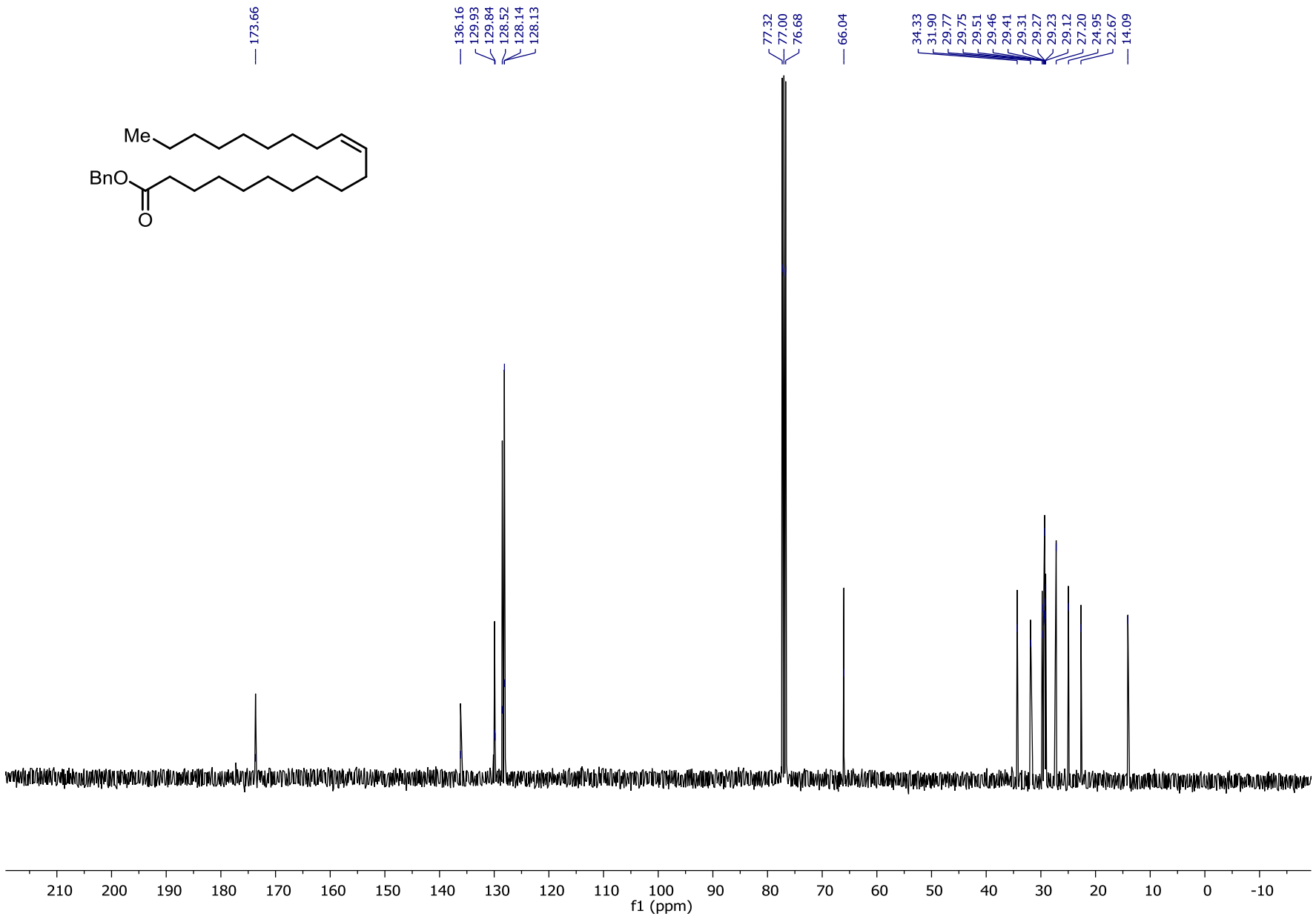
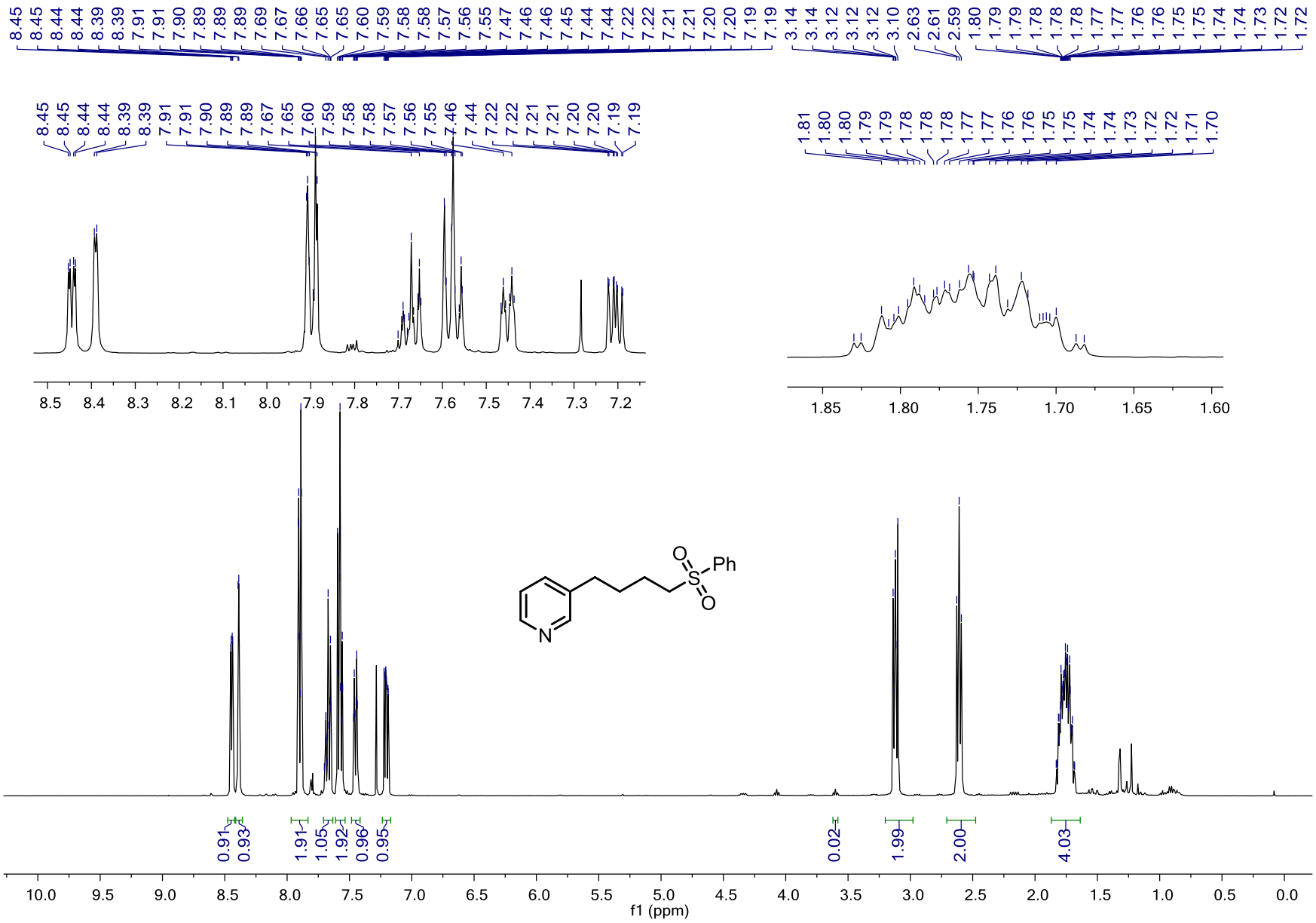
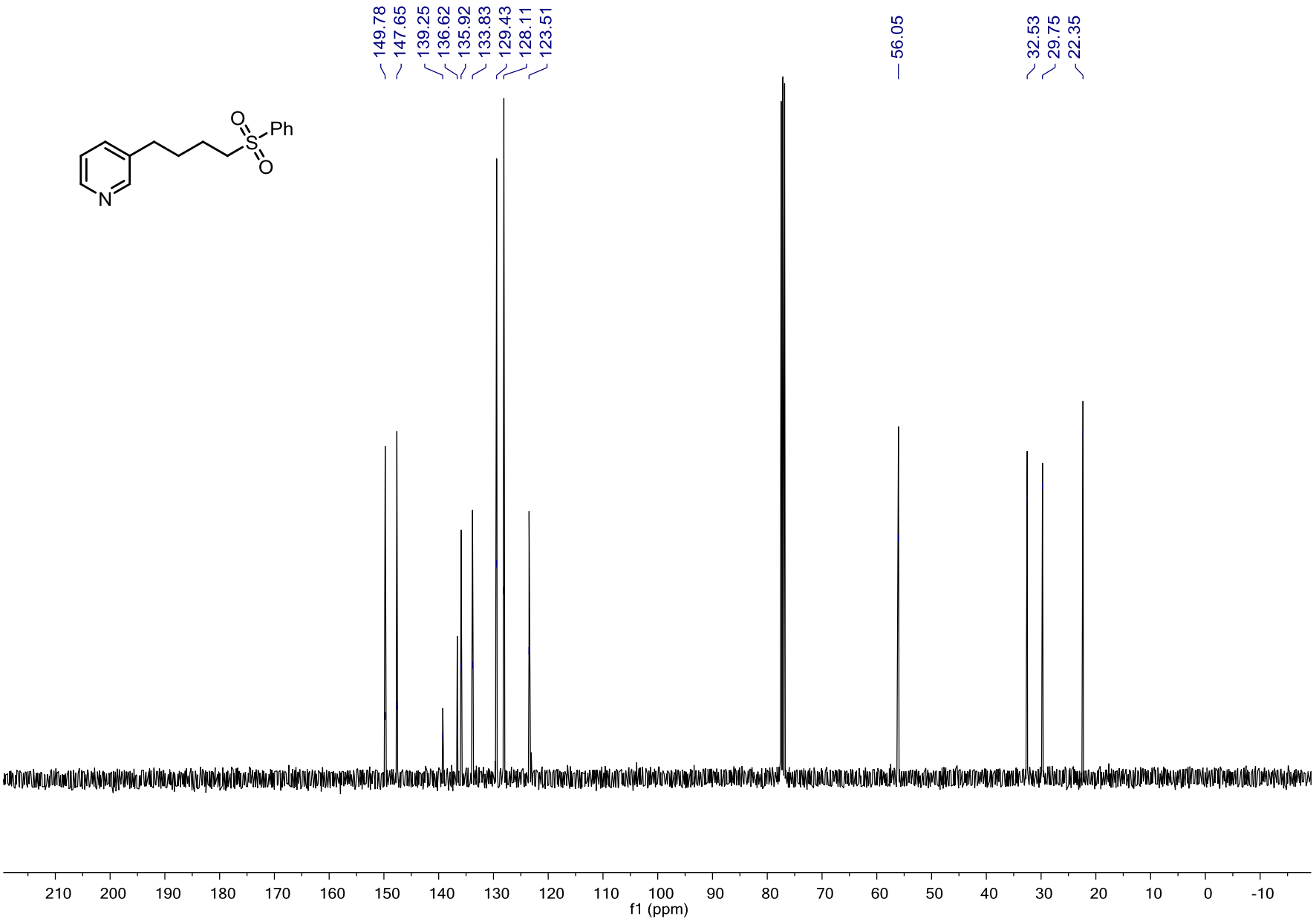


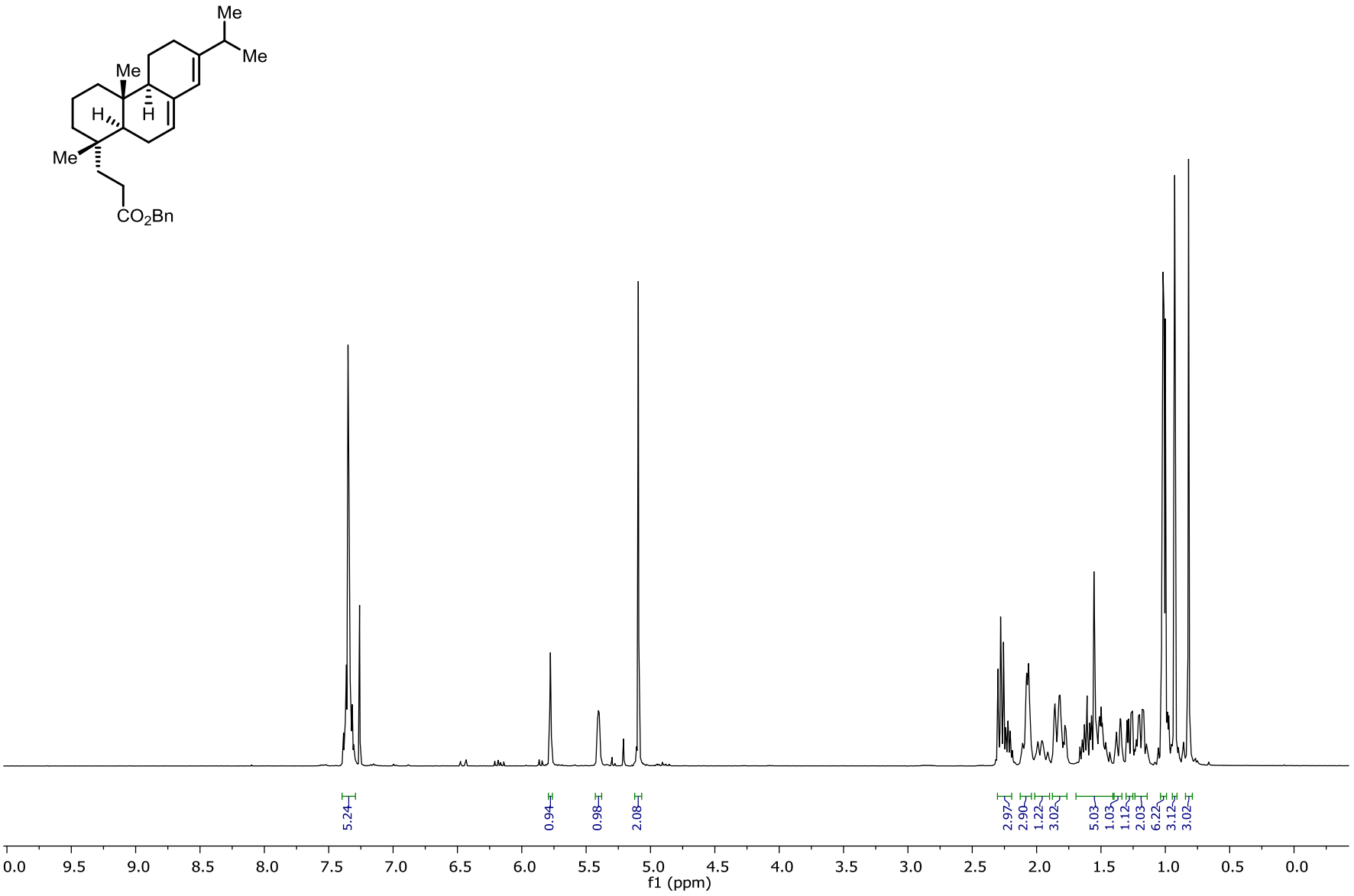
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4u***



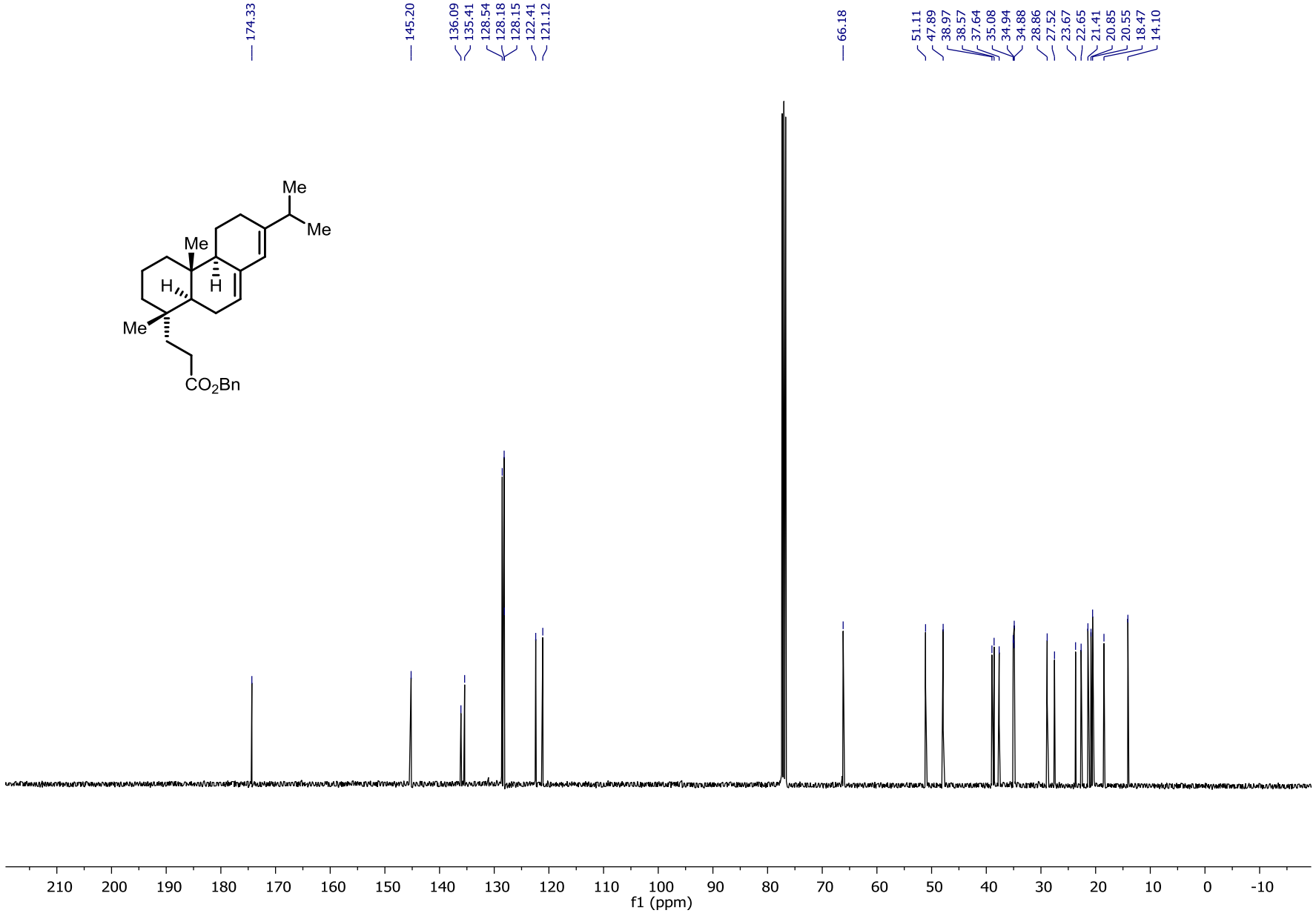
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4u***



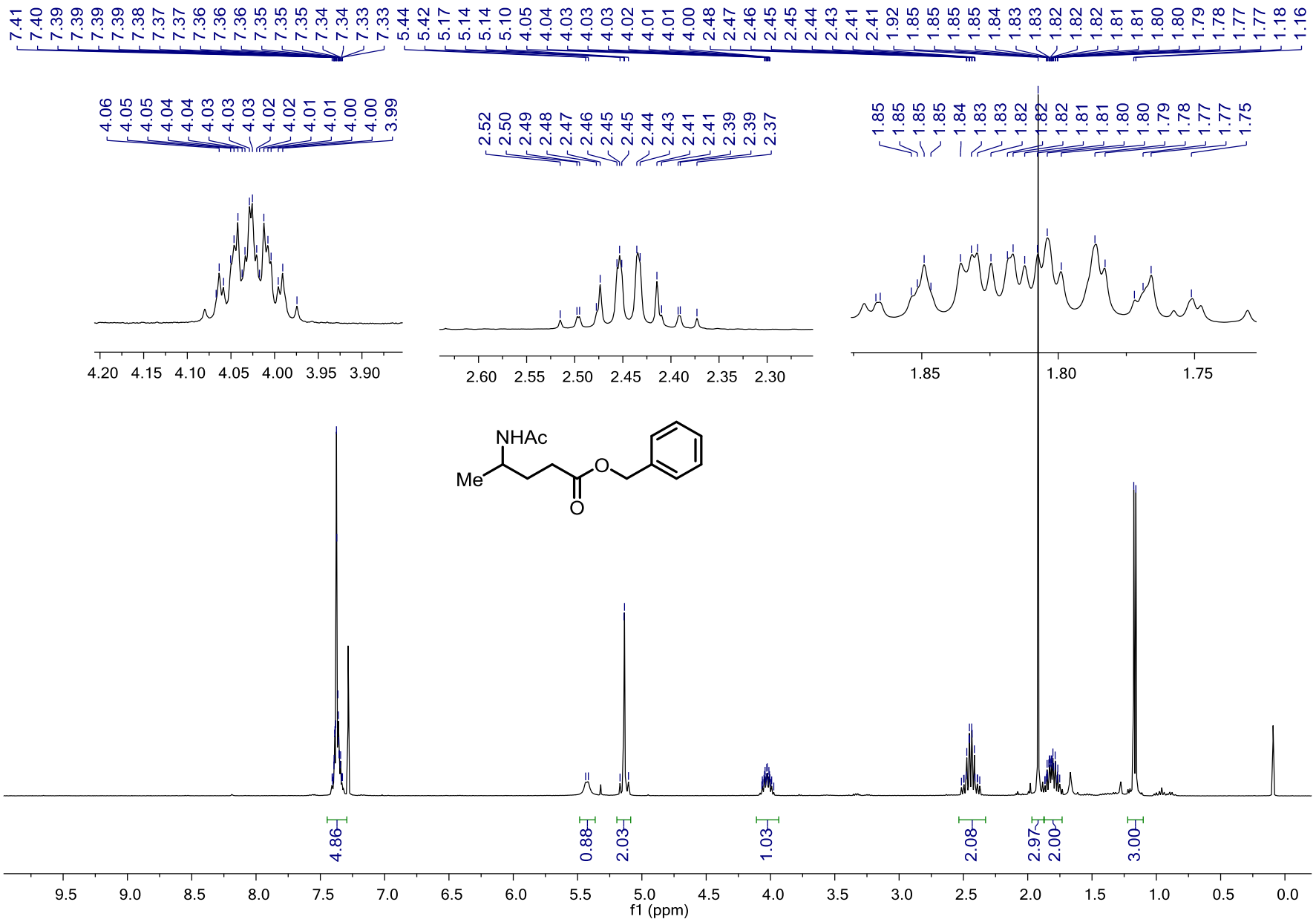
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4v***



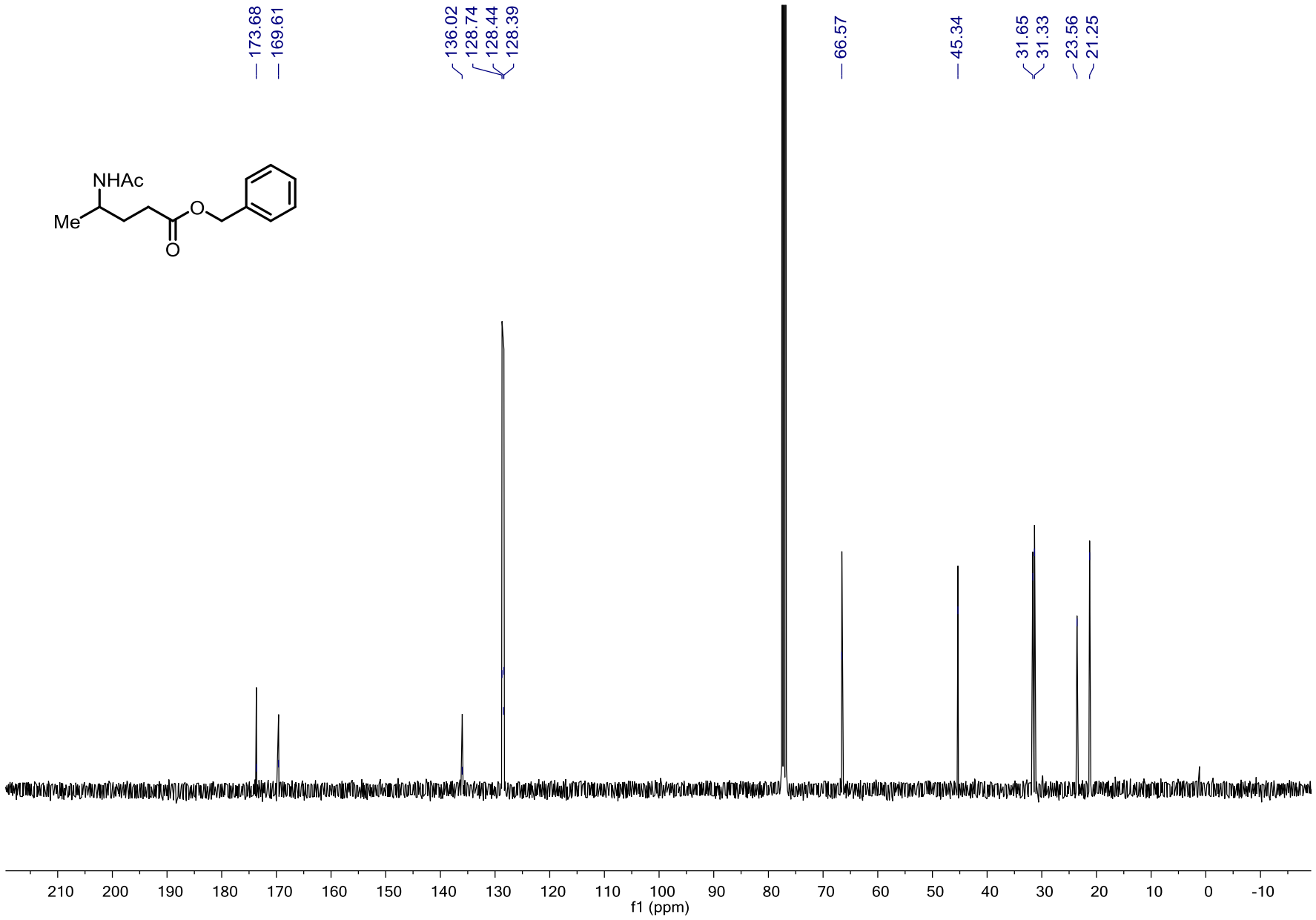
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4v***



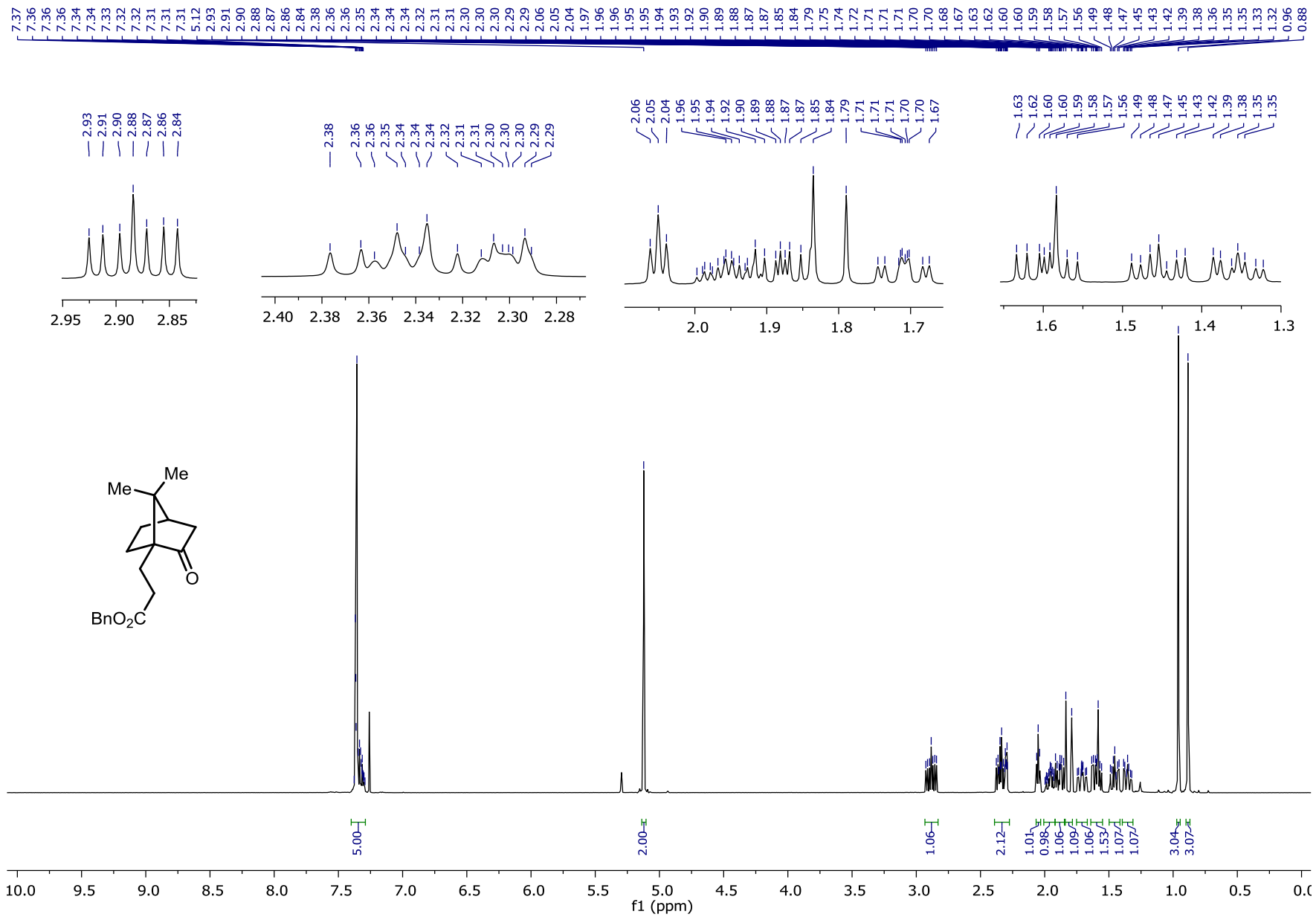
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4w***



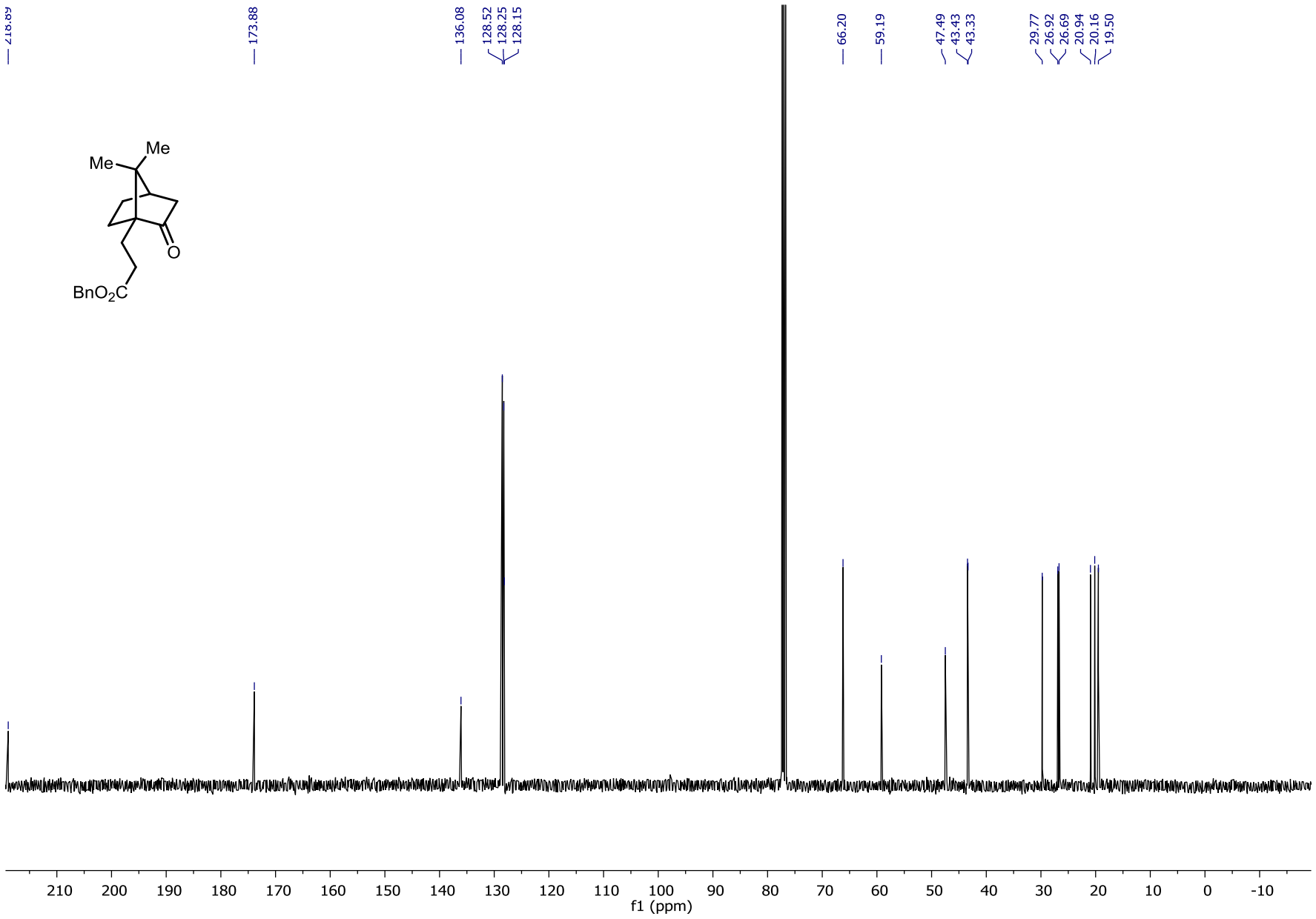
*^{13}C-NMR (101 MHz, CDCl3) for compound **4w***



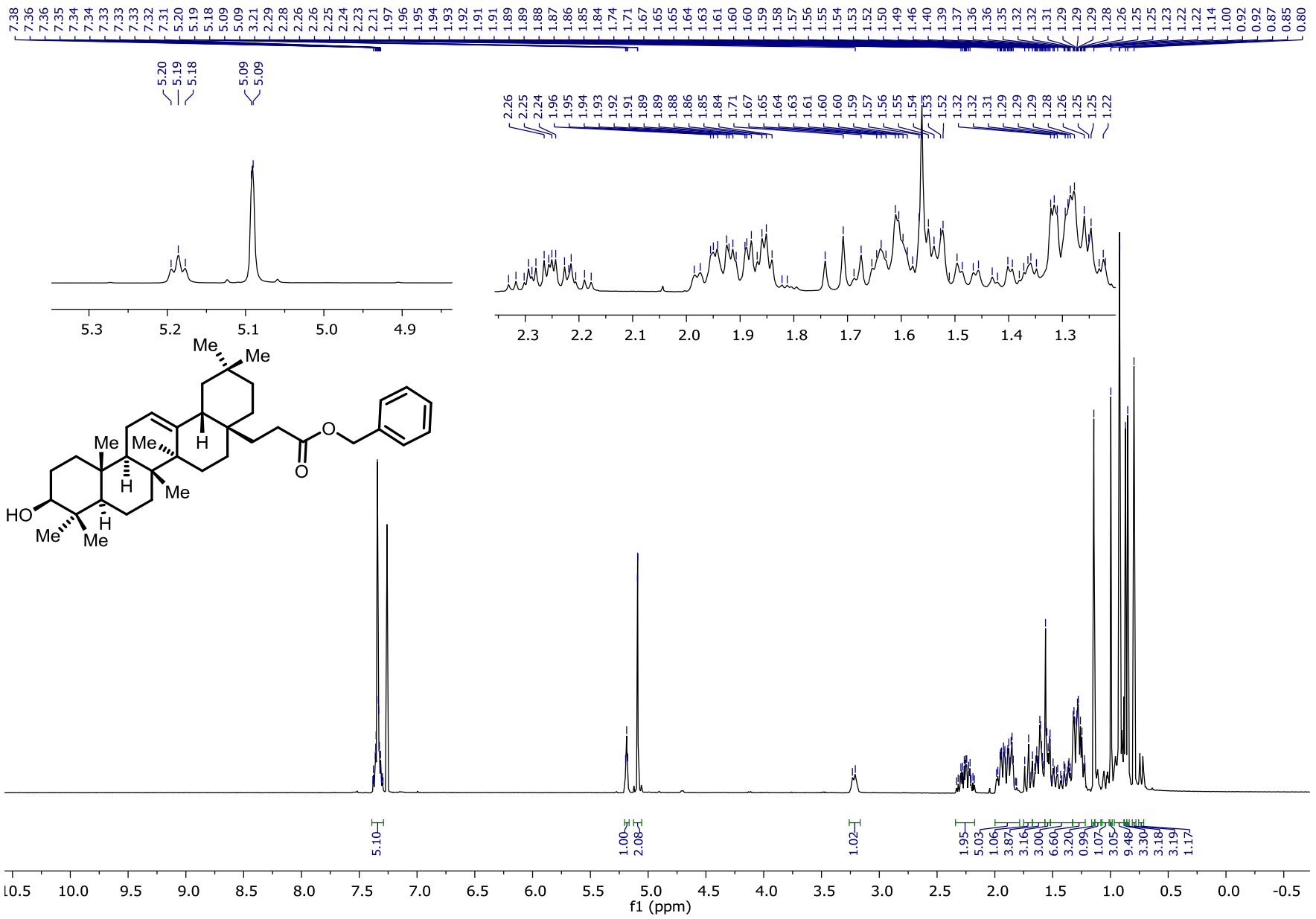
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4x***



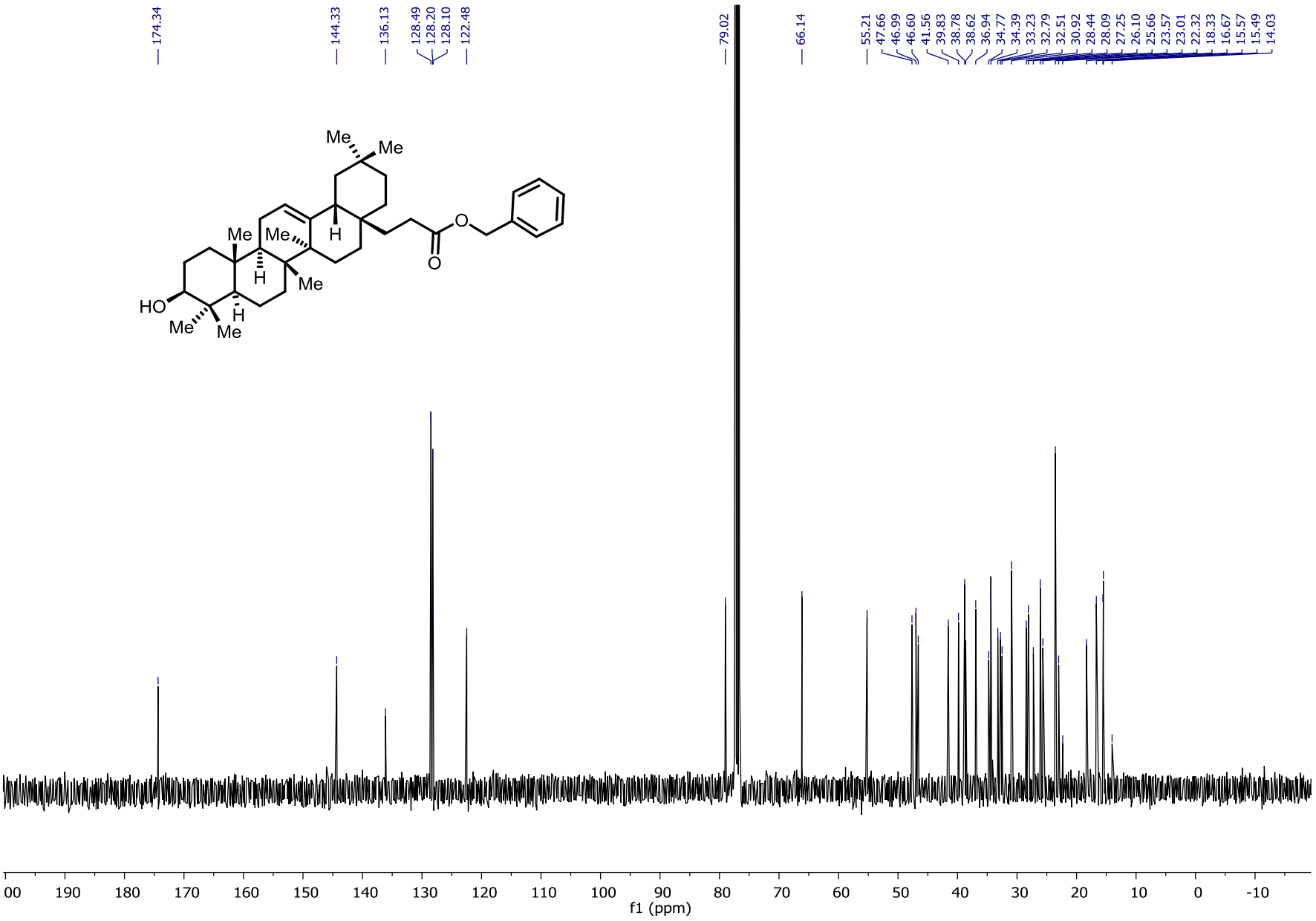
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4x***



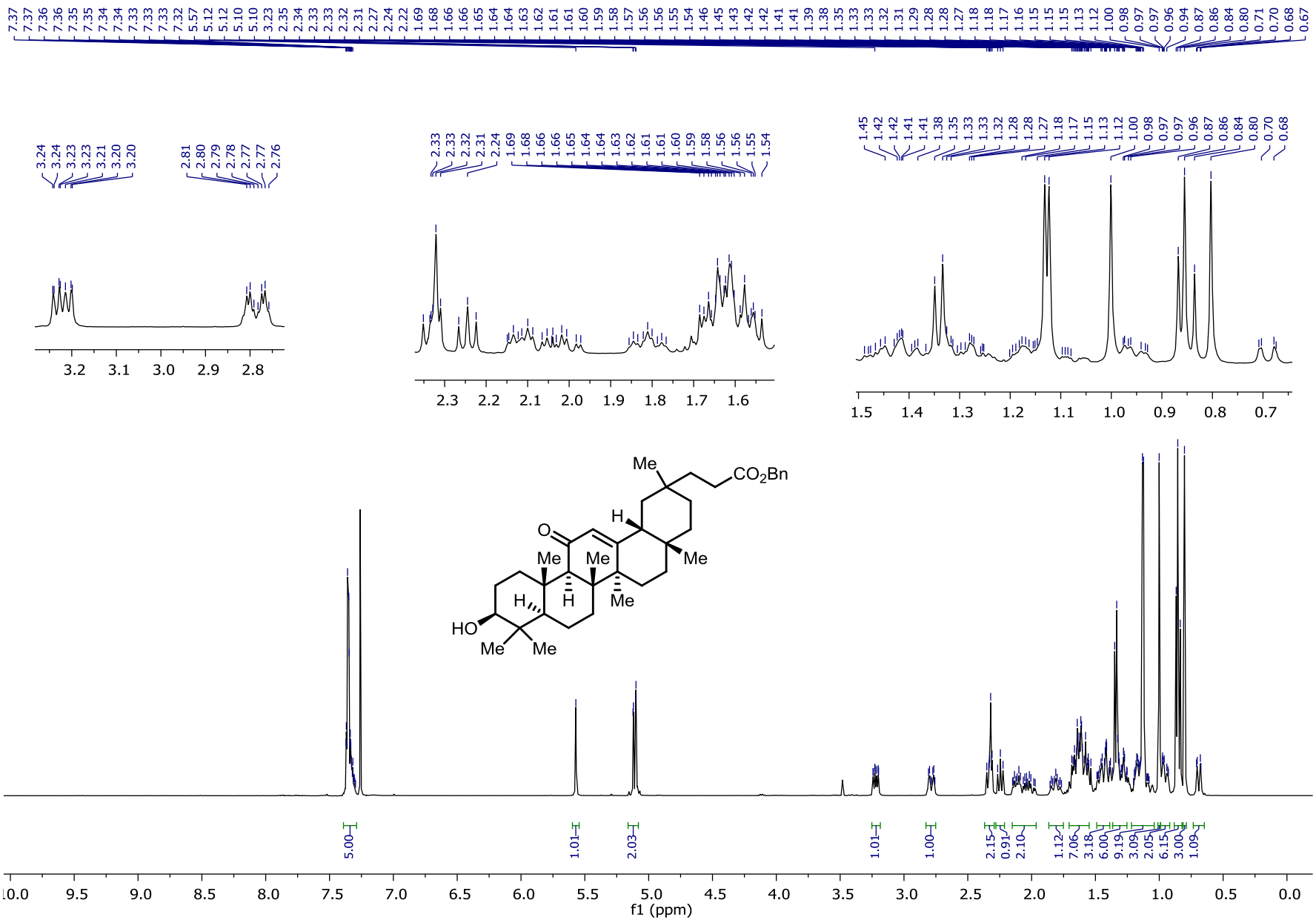
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4y***



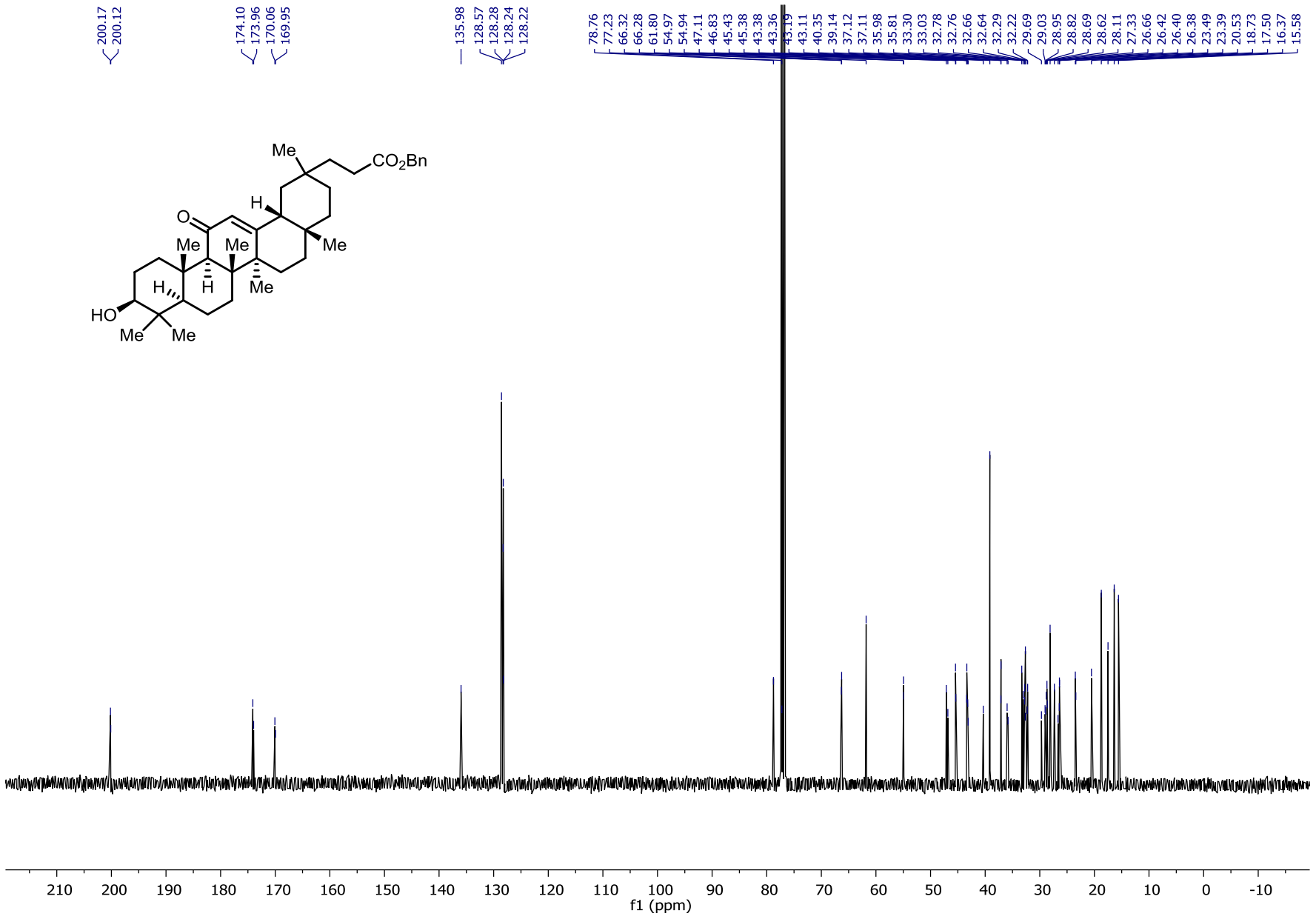
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4y***



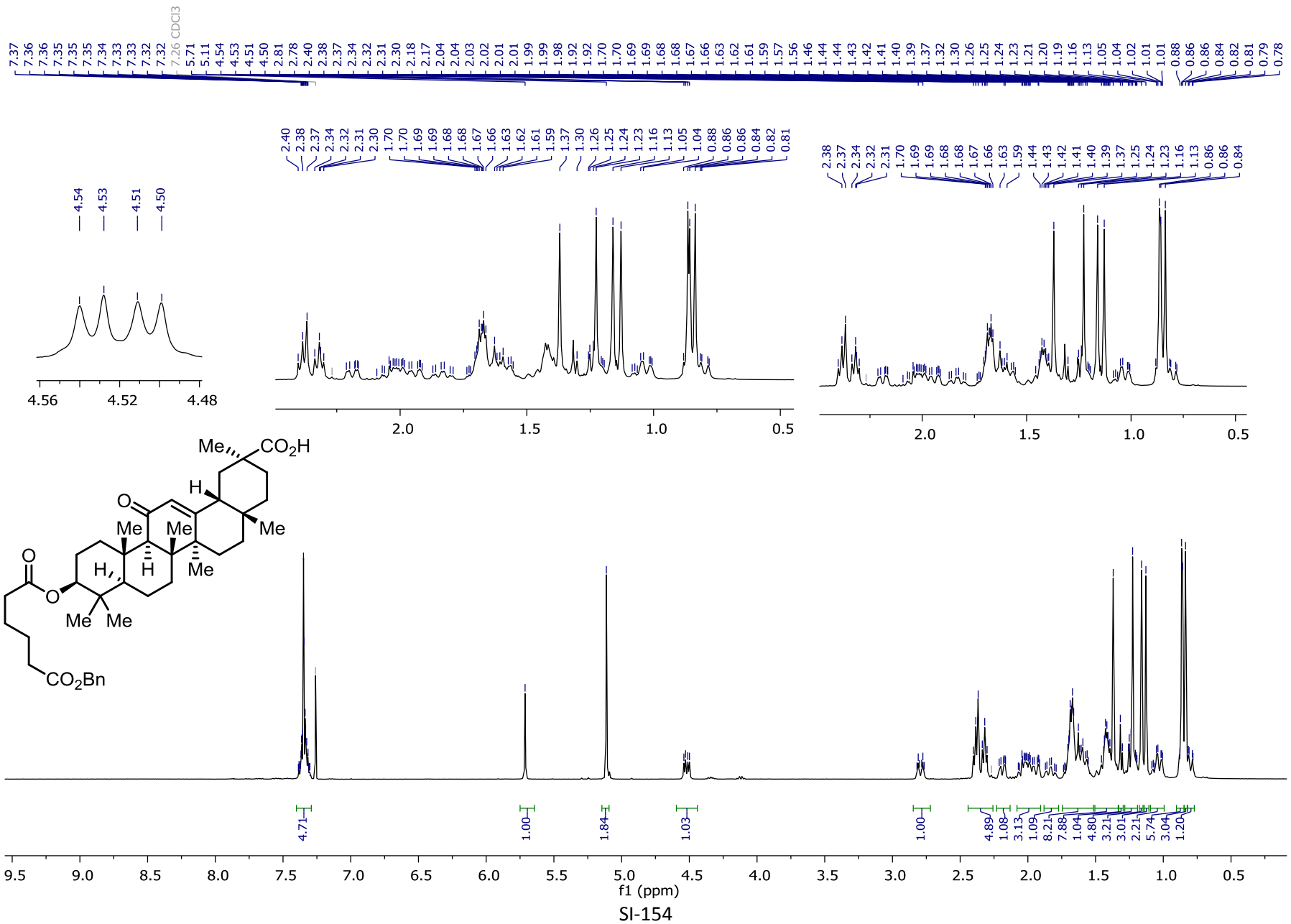
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4z***



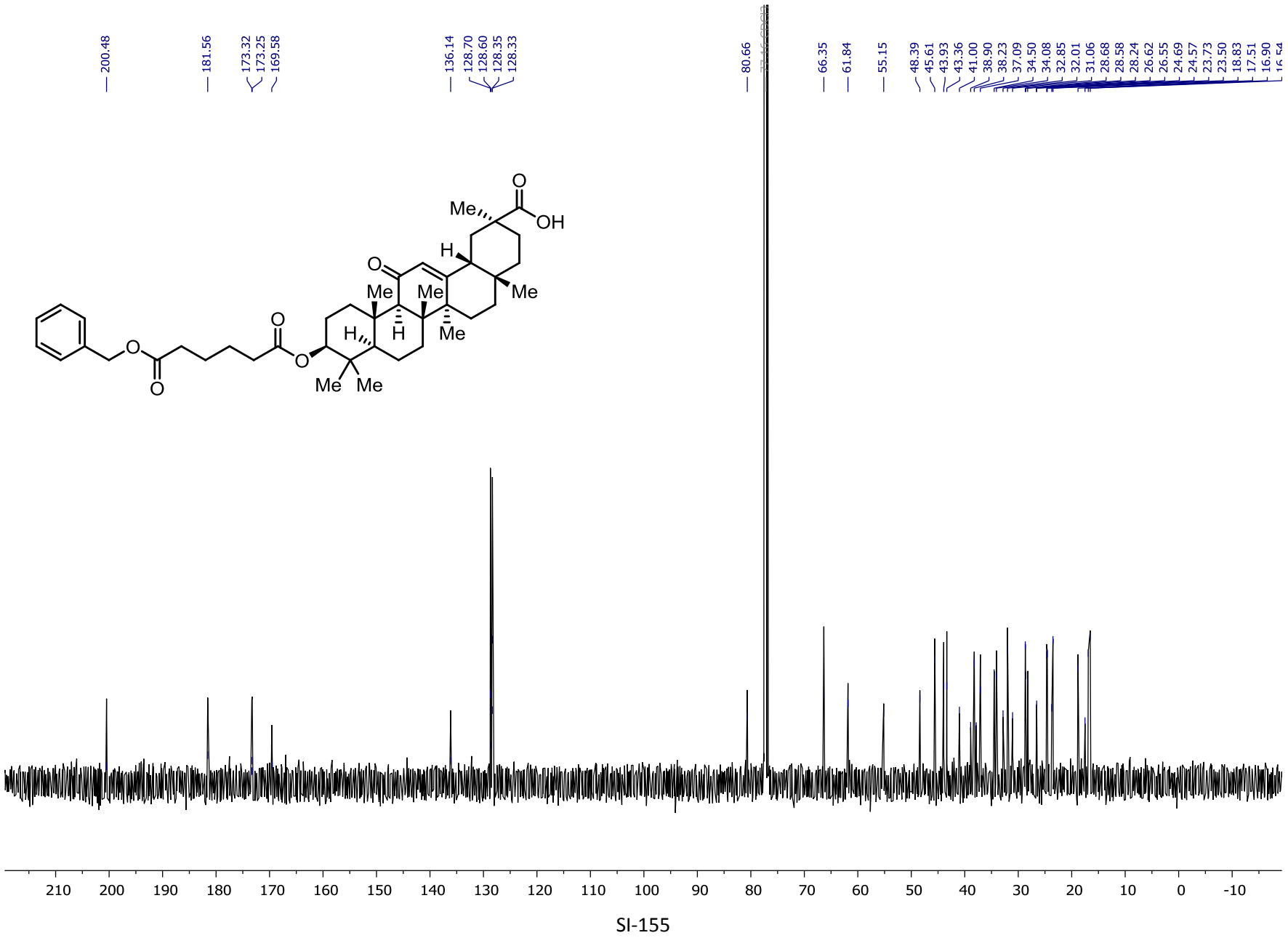
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4z***



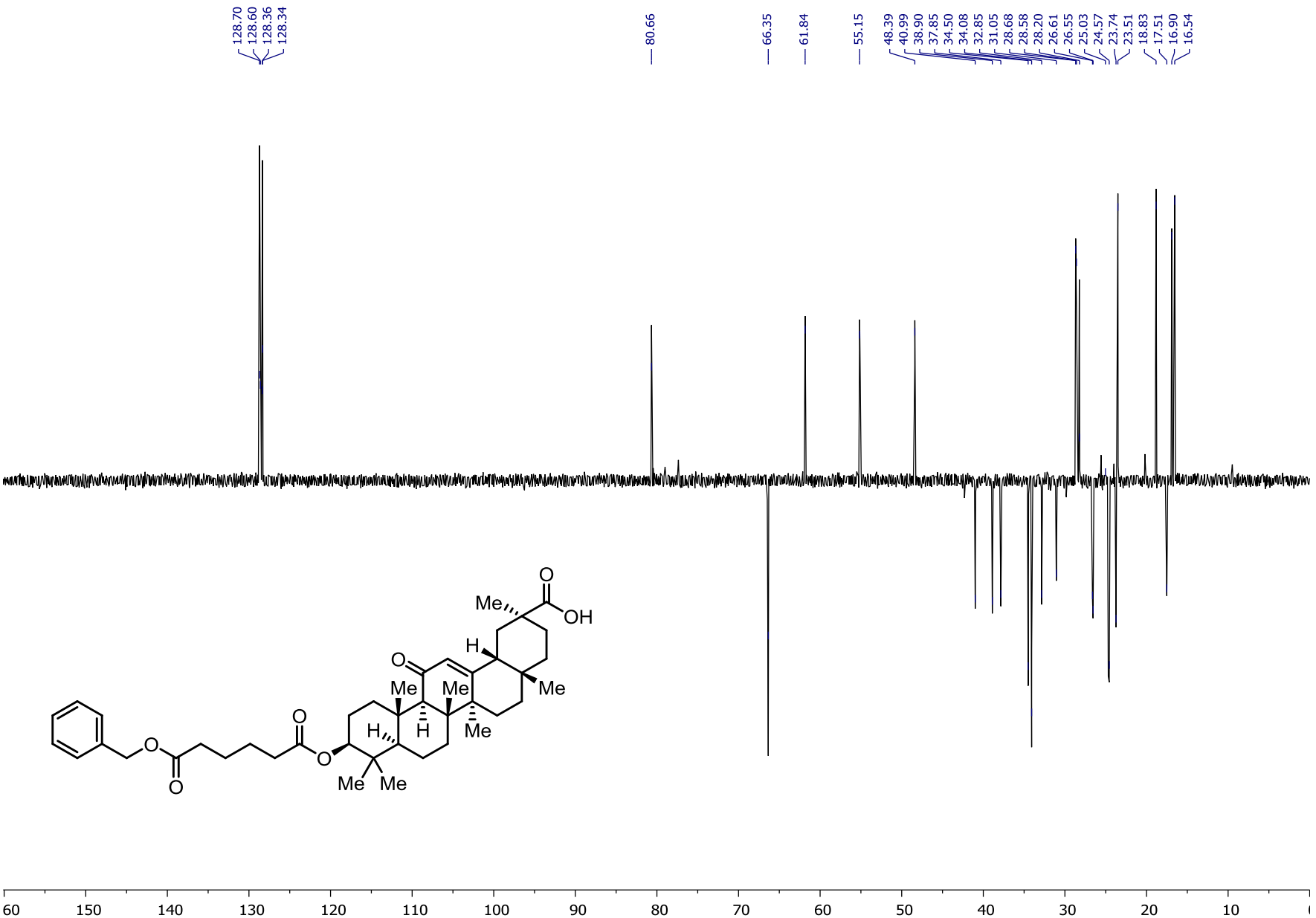
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4aa***



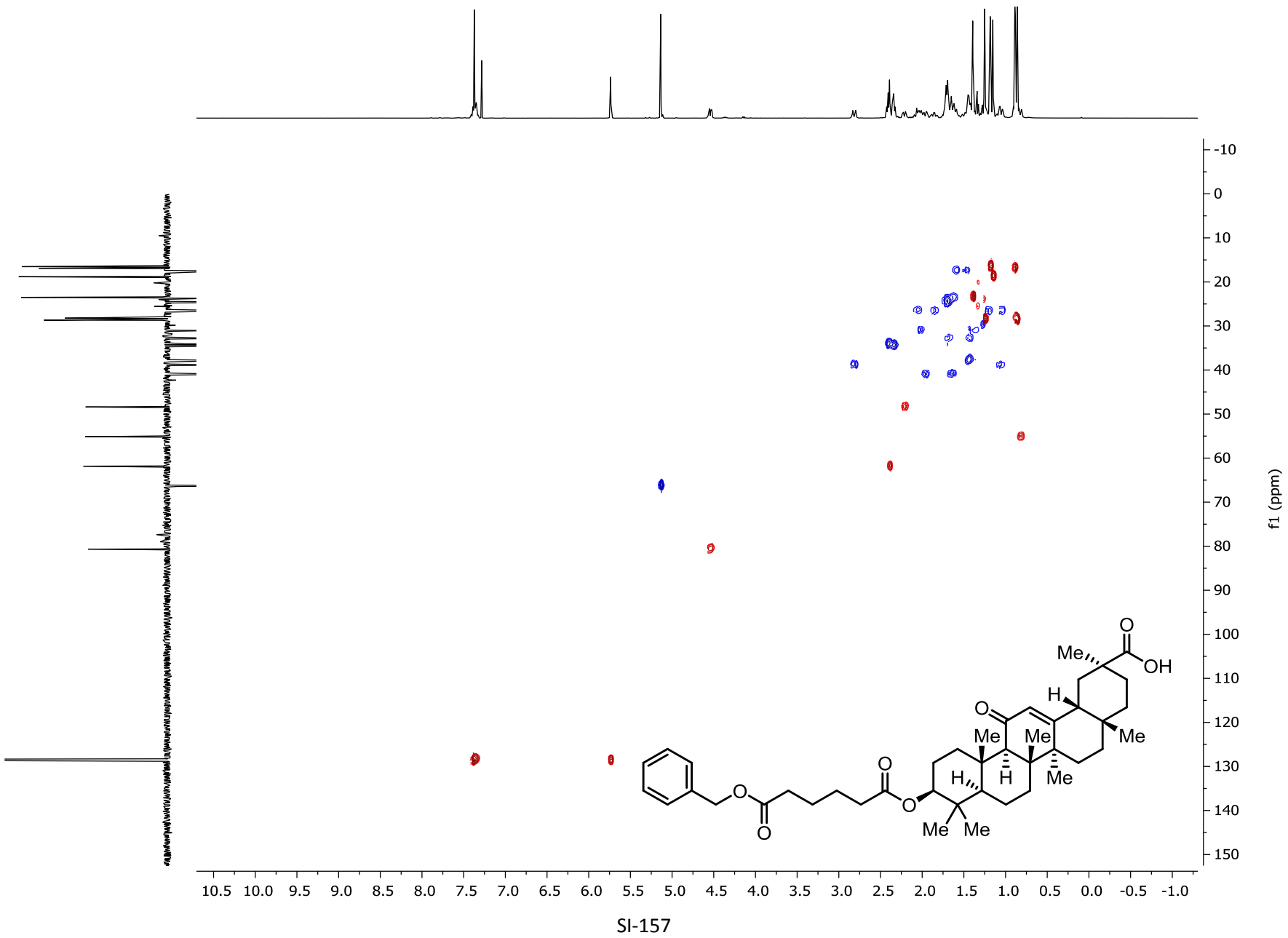
*^{13}C-NMR (400 MHz, $CDCl_3$) for compound **4aa***



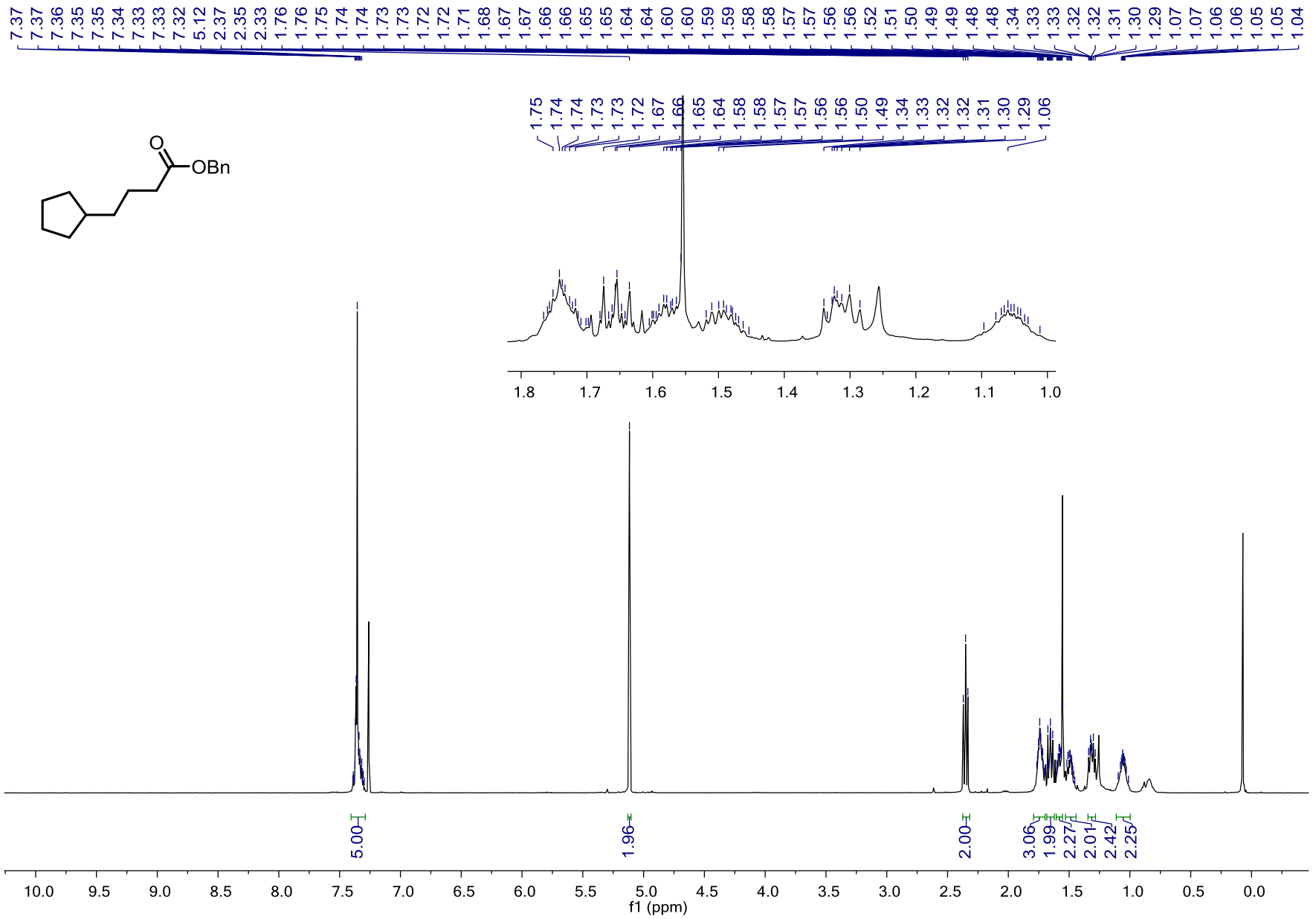
*DEPT 135 NMR (101 MHz, $CDCl_3$) for compound **4aa***



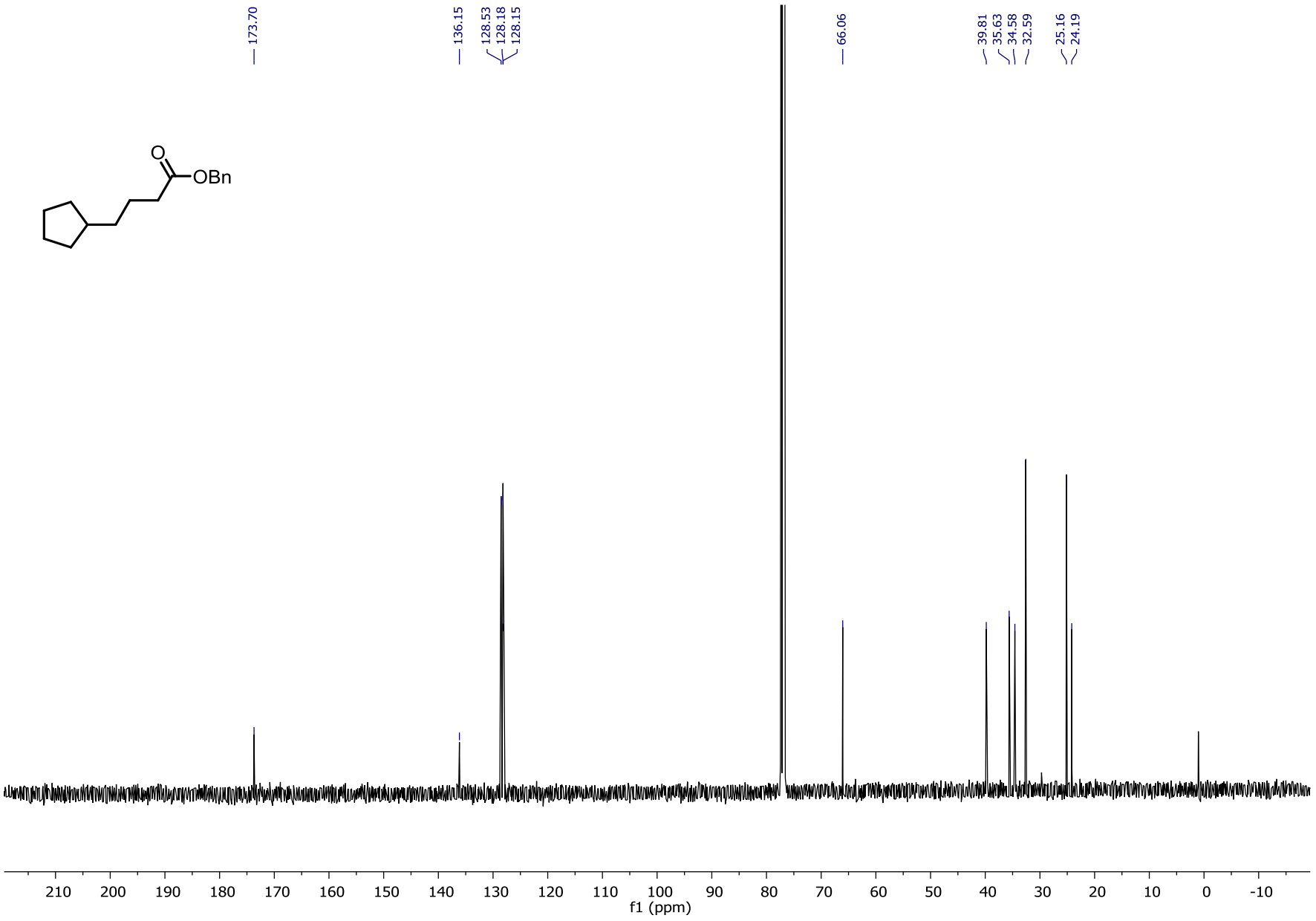
*HSQC NMR ($CDCl_3$) for compound **4aa***



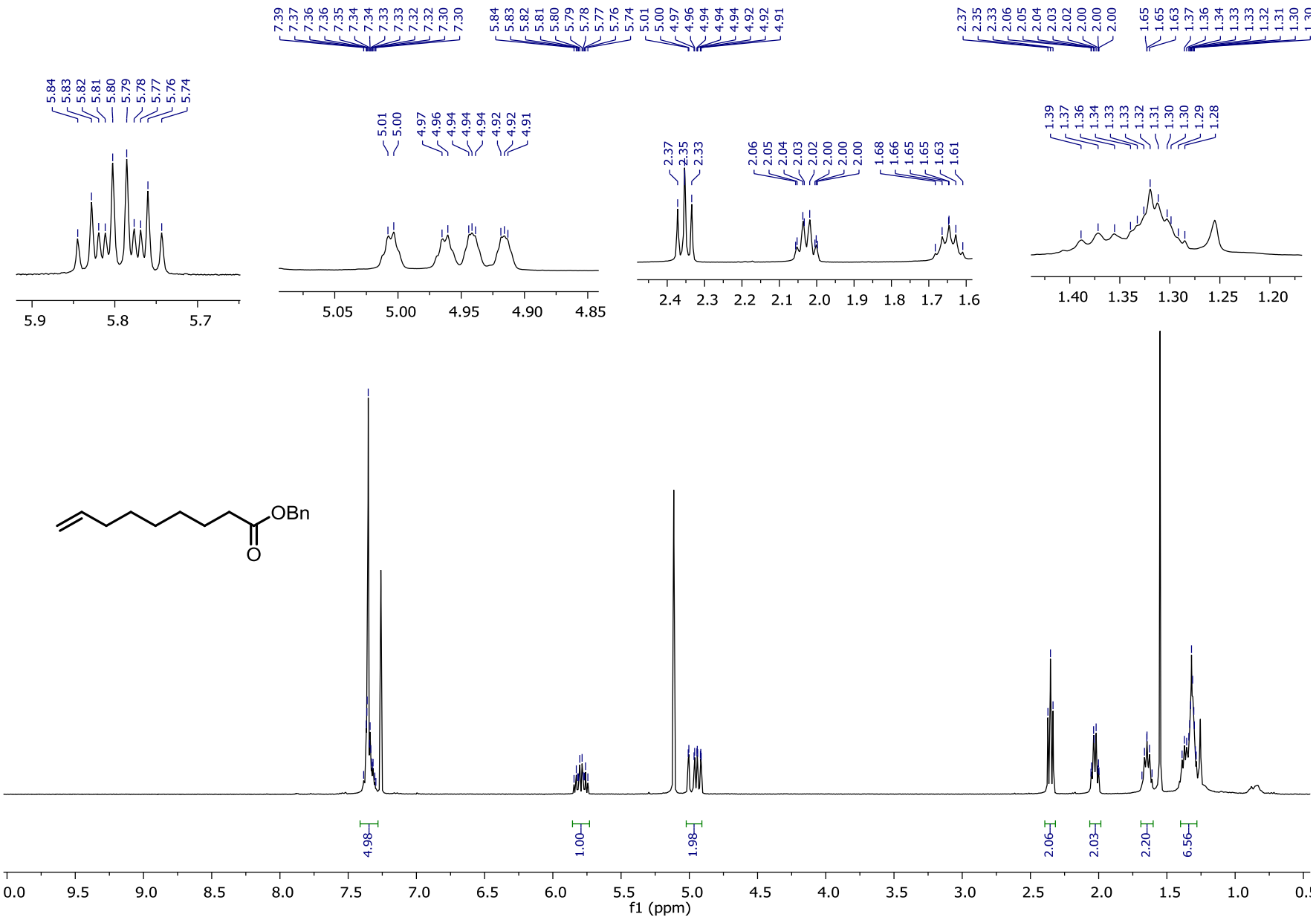
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4ab***



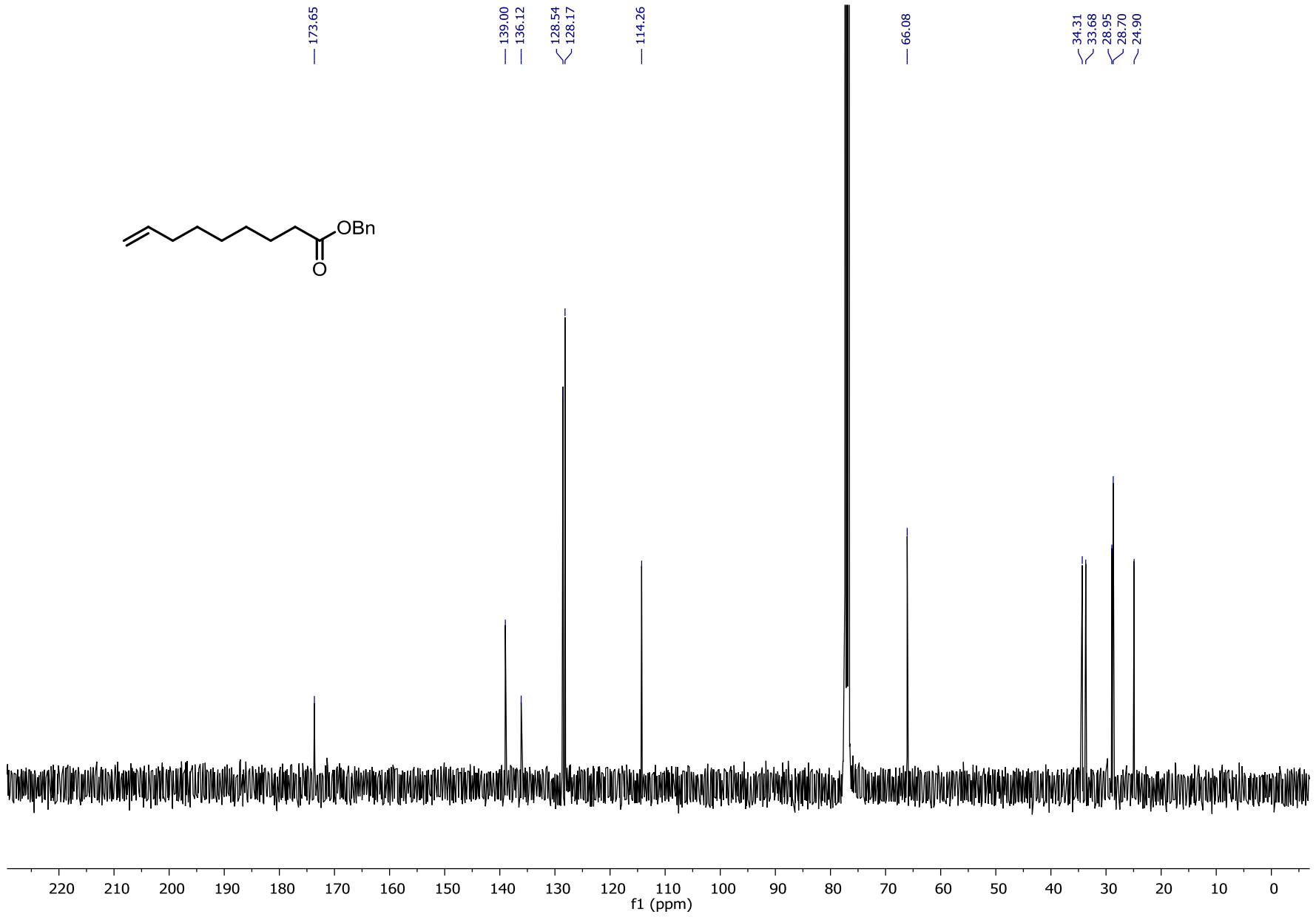
*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4ab***



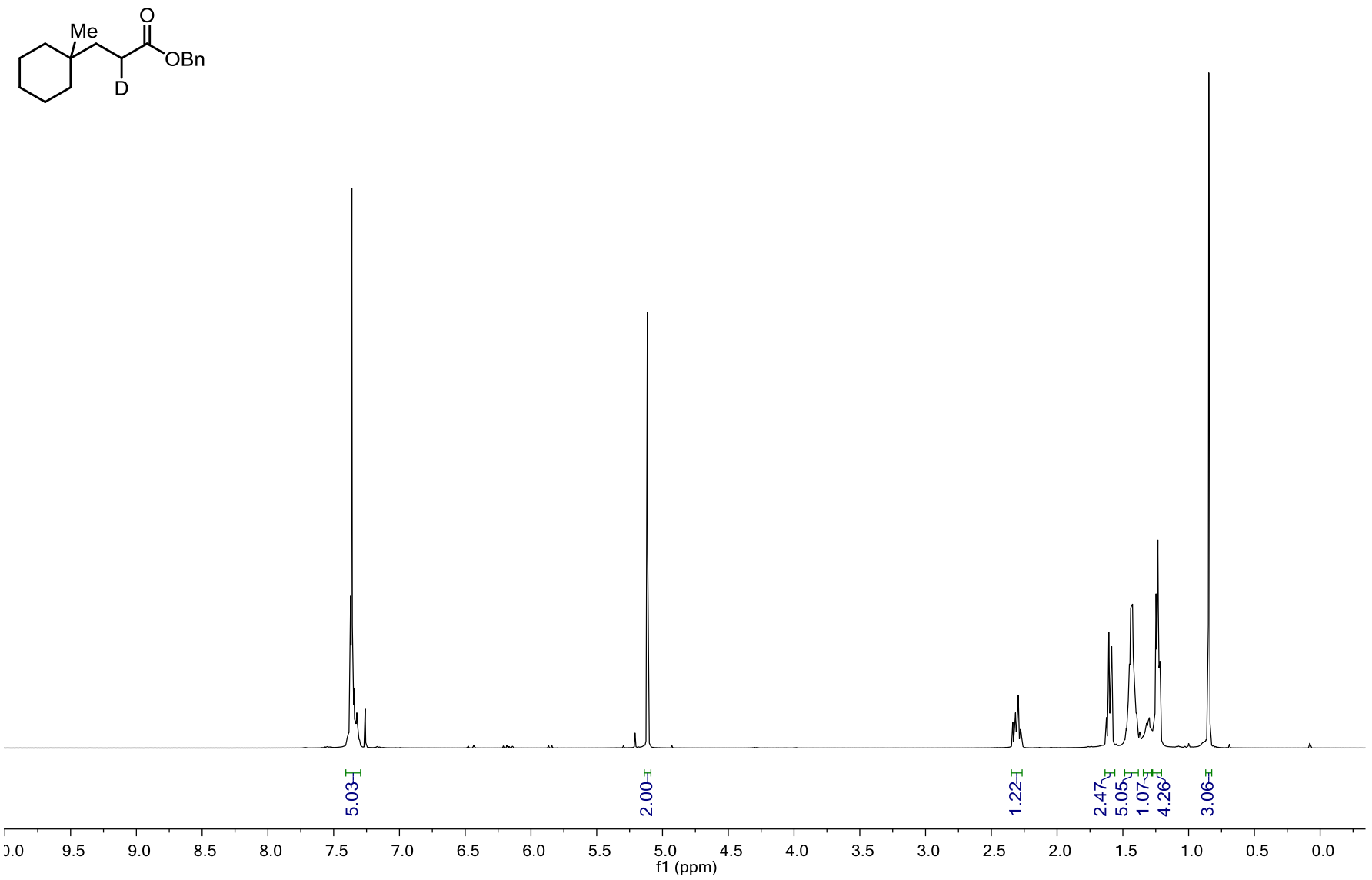
*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4ab'***



*^{13}C-NMR (101 MHz, $CDCl_3$) for compound **4ab'***



*^{1}H-NMR (400 MHz, $CDCl_3$) for compound **4a-d_1***



^{13}C-NMR (101 MHz, $CDCl_3$) for compound ***4a-d$_1$***