

# SUPPORTING INFORMATION

## Rhodium (III)-catalyzed intramolecular annulations of acrylic and benzoic acids to alkynes

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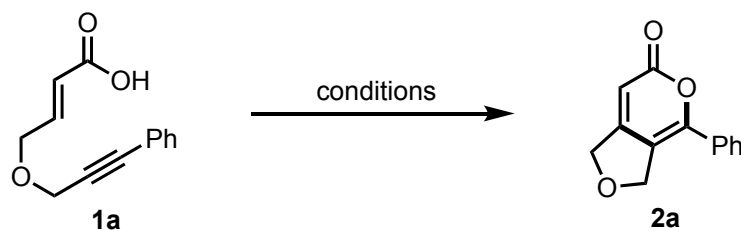
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## General Procedures

Dry solvents were freshly distilled under argon from an appropriate drying agent before use. Dried *N,N*-dimethylformamide were purchased from Aldrich and used without further purification.  $[\text{RhCp}^*\text{Cl}_2]_2$  (99%) [12354-85-7] and  $\text{Ag}_2\text{CO}_3$  (99%) [534-16-7] were purchased from Sigma-Aldrich. All other chemicals were purchased from Sigma-Aldrich, TCI, Alfa Aesar and Strem-Chemicals and used without further purification. All reactions dealing with air and moisture-sensitive compounds were carried out in oven-dried reaction flask under argon atmosphere with dry solvents. The abbreviation "rt" refers to reactions carried out approximately at 23 °C. Reaction mixtures were stirred using Teflon-coated magnetic stirring bars. Reaction temperatures were maintained using Thermowatch-controlled silicone oil baths. Thin-layer chromatography (TLC) was performed on silica gel plates and components were visualized by observation under UV light, and / or by treating the plates with *p*-anisaldehyde or phosphomolybdic acid solutions, followed by heating. Flash chromatography was carried out on silica gel unless otherwise stated. Drying was performed with anhydrous  $\text{Na}_2\text{SO}_4$  or  $\text{MgSO}_4$ . Concentration refers to the removal of volatile solvents via distillation using a Büchi rotary evaporator followed by residual solvent removal under high vacuum. Melting points (m.p.) were determined with an M-560 BÜCHI apparatus. NMR spectra were recorded in  $\text{CDCl}_3$ , at 300 MHz (Varian), 400 MHz (Varian) or 500 MHz (Varian), unless other solvent is specified. Carbon types and structure assignments were determined from DEPT-NMR. NMR spectra were analyzed using MestreNova© NMR data processing software ([www.mestrelab.com](http://www.mestrelab.com)). 1,3,5-Trimethoxybenzene was used as internal standard. The following abbreviations are used to indicate signal multiplicity: s, singlet; d, doublet; t, triplet; q, quartet; dd, double doublet; ddd, doublet of doublet of doublets; td, triple doublet; dt, doublet of triplets; dq, doublet of quartet; m, multiplet; brs, broad singlet. Mass spectra (ESI-MS) were acquired using IT-MS Bruker AmaZon SL at CIQUS and also using chemical ionization (CI) electron impact (EI), electrospray ionization (ESI) or (APCI) atmospheric-pressure chemical ionization at the CACTUS facility of the University of Santiago de Compostela. The reactions were monitored by TLC.

**Table S1. Optimization of the reaction conditions.<sup>a</sup>**

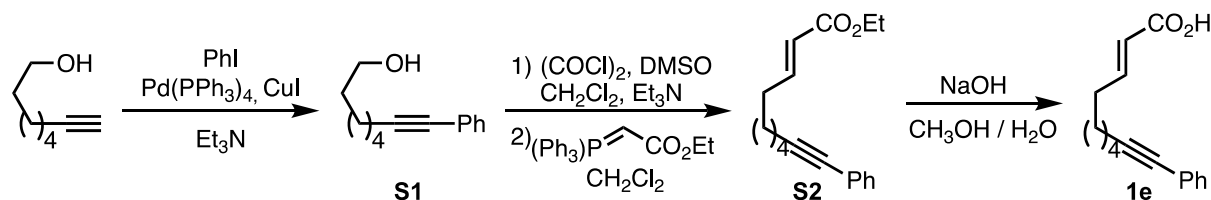


Entry	Catalyst	Oxidant	Solvent	T (°C)	Yield (%)
1	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Cu(OAc) <sub>2</sub> .H <sub>2</sub> O	<i>t</i> AmOH	100	50
2	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Cu(OAc) <sub>2</sub> .H <sub>2</sub> O	DMF	120	25
<b>3</b>	<b>[Cp*RhCl<sub>2</sub>]<sub>2</sub></b>	<b>Ag<sub>2</sub>CO<sub>3</sub></b>	<b>DMF</b>	<b>120</b>	<b>82<sup>b</sup></b>
4	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DCE	80	20
5	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	toluene	110	36
6	[( <i>p</i> -cymene) RuCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DMF	120	28
7	[Cp*IrCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DMF	120	-
8	[Cp*Rh(CH <sub>3</sub> CN) <sub>3</sub> ](SbF <sub>6</sub> ) <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DMF	120	21 <sup>b,c</sup>
9	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DMF	120	21 <sup>d</sup>
10	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	MeOH	80	71
11	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	HFIP	80	26 <sup>e</sup>
12	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	HFIP	80	48 <sup>b</sup>
13	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	1,3-DNB	DMF	120	28
14	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	BQ/AgOAc	DMF	120	<5 <sup>f</sup>
15	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Air	DMF	120	<5 <sup>g</sup>
16	[Cp*RhCl <sub>2</sub> ] <sub>2</sub>	Ag <sub>2</sub> CO <sub>3</sub>	DMF	120	31 <sup>h</sup>

<sup>a</sup> Reaction conditions: 0.20 mmol of **1a**, catalyst (2.5 mol%), 2 equiv. of oxidant, solvent (0.8 mL), 12 h. Yields determined by internal standard. <sup>b</sup> Isolated yield. <sup>c</sup> 5 mol% of catalyst. <sup>d</sup> AgSbF<sub>6</sub> (1 equiv.) was used as additive. <sup>e</sup> 1 mol% of catalyst, 0.5 equiv. oxidant. <sup>f</sup> 2 equiv. AgOAc, 1 equiv. 1,4-benzoquinone. <sup>g</sup> 1 equiv. NaOAc. <sup>h</sup> 1 equiv. Ag<sub>2</sub>CO<sub>3</sub>

## Synthesis of precursors

**General procedure (A) for preparation of acid precursors 1c, 1e, 1h, 1i, 1j, 1k and 1l** (exemplified for the synthesis of (*E*)-10-phenyldec-2-en-9-ynoic acid, **1e**).



**Scheme S1. General procedure A for preparation of acid precursors**

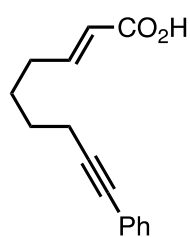
A flame-dried Schlenk flask under argon equipped with a Teflon septum and magnetic stir bar was charged with CuI (135.8 mg, 0.71 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (412.5 mg, 0.36 mmol). Et<sub>3</sub>N (47.5 mL), iodobenzene (4.0 mL, 35.66 mmol) and oct-7-yn-1-ol (3.0 g, 23.77 mmol) were sequentially added. The reaction mixture was stirred at rt. After 20 h, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (1:10 to 1:4 EtOAc: Hexane) afforded 8-phenyloct-7-yn-1-ol (**S1**) as a yellow oil (4.6 g, 96 % yield). <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.44 – 7.39 (m, 2H), 7.32 – 7.26 (m, 3H), 3.66 (td, *J* = 6.6, 2.4 Hz, 2H), 2.43 (t, *J* = 6.9 Hz, 2H), 2.08 – 1.93 (m, 1H), 1.69 – 1.55 (m, 4H), 1.54 – 1.37 (m, 4H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 131.60 (CH), 128.27 (CH), 127.58 (CH), 124.07 (C), 90.34 (C), 80.75 (C), 62.90 (CH<sub>2</sub>), 32.68 (CH<sub>2</sub>), 28.75 (CH<sub>2</sub>), 25.38 (CH<sub>2</sub>), 19.41 (CH<sub>2</sub>). HRMS (APCI-FIA-TOF): *m/z* calculated for C<sub>14</sub>H<sub>19</sub>O ([M+H]<sup>+</sup>) 203.1429, found 203.1430.

DMSO (1.3 mL, 17.79 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (1.9 mL) was added dropwise to a solution of oxalyl chloride (0.76 mL, 8.90 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (16.5 mL) at –78 °C. The reaction was stirred for 10 min and then a solution of 8-phenyloct-7-yn-1-ol (1.0 g, 4.94 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (3.5 mL) was added slowly. After 45 min Et<sub>3</sub>N (3.4 mL, 24.71 mmol) was added at –78 °C. After stirring at that temperature for 30 min, the mixture was warmed to rt and stirred for 45 min. H<sub>2</sub>O (30 mL) was then added, the organic phase was separated and washed with HCl (1.0 M solution), NaHCO<sub>3</sub> (sat) and brine. The organic phases were dried and carefully concentrated under vacuum at 0 °C. The crude 8-phenyloct-7-ynal was obtained in quantitative yield as yellow oil and submitted to the next step without purification. To a solution of ethyl 2-(triphenylphosphanyl)acetate (4.30 g, 12.35 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (10 mL) at 0 °C was added dropwise the crude 8-phenyloct-7-ynal (990 mg, 4.94 mmol). The reaction mixture was stirring at. After

18h, the solvent was evaporated *in vacuo* and the crude was purified by flash chromatography (pentane:diethylether 8:1) to obtain ethyl (*E*)-10-phenyldec-2-en-9-ynoate (**S2**) (940 mg, 70.5%). Colorless oil. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.56 – 7.49 (m, 2H), 7.43 – 7.36 (m, 3H), 7.10 (dt, *J* = 15.6, 6.9 Hz, 1H), 5.96 (dt, *J* = 15.6, 1.6 Hz, 1H), 4.31 (q, *J* = 7.1 Hz, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 2.42 – 2.29 (m, 2H), 1.79 – 1.69 (m, 2H), 1.69 – 1.56 (m, 4H), 1.40 (t, *J* = 7.1 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.7 (C), 149.1 (CH), 131.6 (CH), 128.2 (CH), 127.5 (CH), 124.0 (C), 121.5 (CH), 90.0 (C), 80.8 (C), 60.1 (CH<sub>2</sub>), 32.1 (CH<sub>2</sub>), 28.5 (CH<sub>2</sub>), 28.4 (CH<sub>2</sub>), 27.6 (CH<sub>2</sub>), 19.3 (CH<sub>2</sub>), 14.3 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>18</sub>H<sub>23</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) 271.1693, found 271.1693.

A NaOH aqueous solution (8.8 mL, 1M mmol) was added to solution that contains ethyl (*E*)-10-phenyldec-2-en-9-ynoate (**S2**, 600 mg, 2.21 mmol) in MeOH (4.1 mL). The reaction mixture was stirring at 45 °C. After 20 h, a solution of HCl (10 %) was added to adjust the pH to 1. The mixture was extracted with EtOAc (3 x 10 mL). The combined organic layers were dried, and the solvent removed *in vacuo*. Purification of the crude product by flash chromatography on silica gel (1:5 to 2:1 EtOAc: Hexane) afforded (*E*)-10-phenyldec-2-en-9-ynoic acid (**1e**) as a colorless oil. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.03 (s, 1H), 7.47 – 7.37 (m, 2H), 7.34 – 7.26 (m, 3H), 7.13 (dt, *J* = 15.6, 6.9 Hz, 1H), 5.87 (d, *J* = 15.6 Hz, 1H), 2.44 (t, *J* = 6.8 Hz, 2H), 2.35 – 2.25 (m, 2H), 1.71 – 1.47 (m, 6H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 172.3, 152.3, 131.7, 128.3, 127.7, 124.1, 120.9, 90.1, 80.9, 32.3, 28.6, 28.5, 27.5, 19.4. **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>16</sub>H<sub>19</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) 243.1373, found 243.1380.

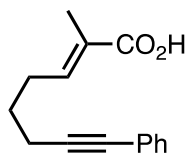
### (*E*)-9-Phenylnon-2-en-8-ynoic acid (**1c**)



This compound was prepared according to the previously described general procedure **A**, using 7-phenylhept-6-yn-1-ol instead of 8-phenyloct-7-yn-1-ol. White solid, **m.p.** 71 -72 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.45 – 7.35 (m, 2H), 7.33 – 7.23 (m, 3H), 7.10 (dt, *J* = 15.6, 6.9 Hz, 1H), 5.87 (dt, *J* = 15.6, 1.6 Hz, 1H), 2.47 – 2.39 (m, 2H), 2.36 – 2.25 (m, 2H), 1.74 – 1.59 (m, 4H).

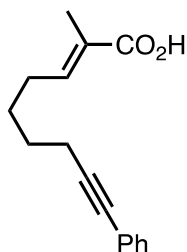
**<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.9 (C), 151.9 (CH), 131.7 (CH), 128.3 (CH), 127.7 (CH), 124.0 (C), 121.04 (CH), 89.7 (C), 81.2 (C), 32.0 (CH<sub>2</sub>), 28.3 (CH<sub>2</sub>), 27.2 (CH<sub>2</sub>), 19.3 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>15</sub>H<sub>17</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) 229.1221, found 229.1223.

**(E)-2-Methyl-8-phenyloct-2-en-7-ynoic acid (1h)**



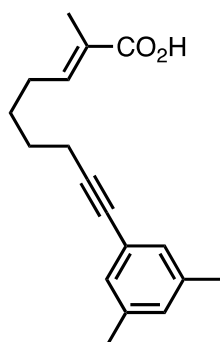
This compound was prepared according to the previously described general procedure **A**, using 6-phenylhex-5-yn-1-ol and ethyl ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)propanoate instead of 8-phenyloct-7-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)acetate. Light yellow solid, **m.p.** 77 -79 °C.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  11.94 (brs, 1H), 7.34 – 7.26 (m, 2H), 7.22 – 7.12 (m, 3H), 6.85 (t,  $J$  = 7.1 Hz, 1H), 2.38 – 2.24 (m, 4H), 1.79 (s, 3H), 1.66 (p,  $J$  = 7.1 Hz, 2H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  173.9 (C), 144.1 (CH), 131.6 (CH), 128.3 (CH), 128.1 (C), 127.7 (CH), 123.9 (C), 89.3 (C), 81.4 (C), 28.0 ( $\text{CH}_2$ ), 27.5 ( $\text{CH}_2$ ), 19.1 ( $\text{CH}_2$ ), 12.1 ( $\text{CH}_3$ ). **HRMS** (APCI-FIA-TOF):  $m/z$  calculated for  $\text{C}_{15}\text{H}_{16}\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ) 229.1225, found 229.1223.

**(E)-2-Methyl-9-phenylnon-2-en-8-ynoic acid (1i)**



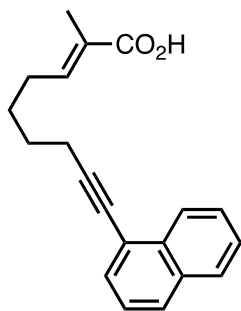
This compound was prepared according to the previously described general procedure **A**, using 7-phenylhept-6-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)propanoate instead of 8-phenyloct-7-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)acetate. Viscous oil.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  11.55 (brs, 1H), 7.45 – 7.40 (m, 2H), 7.33 – 7.27 (m, 3H), 7.01 – 6.94 (m, 1H), 2.49 – 2.42 (m, 2H), 2.31 – 2.23 (m, 2H), 1.88 (s, 3H), 1.70 – 1.61 (m, 4H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  174.0 (C), 144.9 (CH), 131.6 (CH), 128.2 (CH), 127.6 (CH), 127.4 (CH), 124.0 (C), 89.8 (C), 81.1 (C), 28.5 ( $\text{CH}_2$ ), 28.4 ( $\text{CH}_2$ ), 27.7 ( $\text{CH}_2$ ), 19.3 ( $\text{CH}_2$ ), 12.0 ( $\text{CH}_3$ ). **HRMS** (APCI-FIA-TOF):  $m/z$  calculated for  $\text{C}_{16}\text{H}_{19}\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ) 243.1378, found 243.1380.

**(E)-9-(3,5-Dimethylphenyl)-2-methylnon-2-en-8-ynoic acid (1j)**



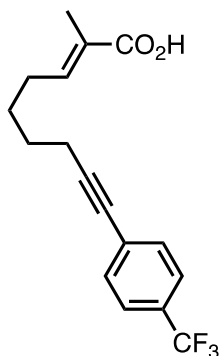
This compound was prepared according to the previously described general procedure **A**, using 7-phenylhept-6-yn-1-ol and ethyl ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)propanoate instead of 8-phenyloct-7-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)acetate. 1-bromo-3,5-dimethylbenzene was used for the Sonogashira coupling. Amorphous yellow solid.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ ):  $\delta$  11.54 (brs, 1H), 6.93 (s, 2H), 6.85 (t,  $J$  = 7.5 Hz, 1H), 6.79 (s, 1H), 2.37 – 2.26 (m, 2H), 2.17 (s, 6H), 1.79 – 1.72 (m, 3H), 1.59 – 1.49 (m, 4H).  $^{13}\text{C}$  NMR (75 MHz,  $\text{CDCl}_3$ ):  $\delta$  174.0 (C), 145.0 (CH), 137.8 (C), 129.6 (CH), 129.3 (CH), 127.4 (C), 123.6 (C), 89.0 (C), 81.3 (C), 28.5 ( $\text{CH}_2$ ), 28.5 ( $\text{CH}_2$ ), 27.7 ( $\text{CH}_2$ ), 21.2 ( $\text{CH}_3$ ), 19.3 ( $\text{CH}_2$ ), 12.1 ( $\text{CH}_3$ ). **HRMS** (APCI-FIA-TOF):  $m/z$  calculated for  $\text{C}_{15}\text{H}_{16}\text{O}_2$  ( $[\text{M}+\text{H}]^+$ ) 271.1695, found 271.1698.

**(E)-2-Methyl-9-(naphthalen-1-yl)non-2-en-8-ynoic acid (1k)**



This compound was prepared according to the previously described general procedure **A**, using 7-phenylhept-6-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene) propanoate instead of 8-phenyloct-7-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)acetate. 1-bromonaphthalene was used for the Sonogashira coupling. Light yellow solid, **m.p.** 72-74 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  12.10 (brs, 1H), 8.43 (d,  $J$  = 8.3 Hz, 1H), 7.92 – 7.79 (m, 2H), 7.71 (d,  $J$  = 7.1 Hz, 1H), 7.67 – 7.52 (m, 2H), 7.50 – 7.41 (m, 1H), 7.04 (t,  $J$  = 7.3 Hz, 1H), 2.63 (t,  $J$  = 6.4 Hz, 2H), 2.38 – 2.27 (m, 2H), 1.93 (s, 3H), 1.84 – 1.70 (m, 4H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  174.0 (C), 144.9 (CH), 133.5 (C), 133.3 (C), 130.1 (CH), 128.3 (CH), 128.1 (CH), 127.5 (C), 126.6 (CH), 126.3 (CH), 126.3 (CH), 125.3 (CH), 121.7 (C), 94.9 (C), 79.1 (C), 28.6 (CH<sub>2</sub>), 28.5 (CH<sub>2</sub>), 27.8 (CH<sub>2</sub>), 19.6 (CH<sub>2</sub>), 12.1 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF):  $m/z$  calculated for C<sub>20</sub>H<sub>21</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) 293.1537, found 293.1536.

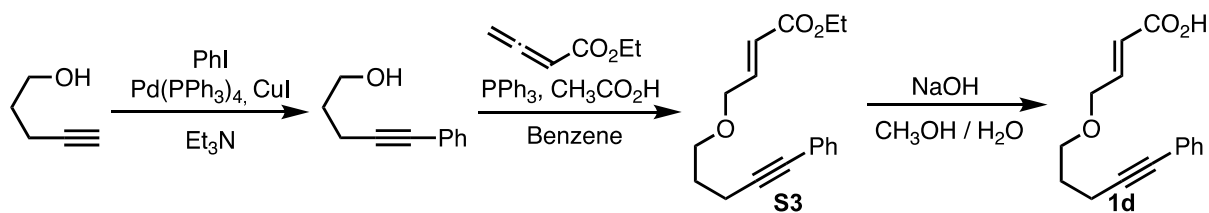
**(E)-2-Methyl-9-(4-(trifluoromethyl)phenyl)non-2-en-8-ynoic acid (1l)**



This compound was prepared according to the previously described general procedure **A**, using 7-phenylhept-6-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene) propanoate instead of 8-phenyloct-7-yn-1-ol and ethyl 2-(triphenyl- $\lambda^5$ -phosphaneylidene)acetate. 1-bromo-4-(trifluoromethyl) Benzene was used for the Sonogashira coupling. Amorphous yellowish solid. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>):  $\delta$  11.51 (brs, 1H), 7.46 – 7.35 (m, 4H), 6.88 – 6.81 (m, 1H), 2.39 – 2.29 (m, 2H), 2.21 – 2.10 (m, 2H), 1.75 (s, 3H), 1.58 – 1.50 (m, 4H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>):  $\delta$  174.0 (C), 144.8 (CH), 131.9 (CH), 129.4 (C, q,  $J$  = 32.8 Hz), 127.6 (C), 126.8 (C), 125.2 (CH, q,  $J$  = 4.0 Hz), 120.5 (CF<sub>3</sub>, q,  $J$  = 272.6 Hz), 92.7 (C), 80.0 (C), 28.5 (CH<sub>2</sub>), 28.2 (CH<sub>2</sub>), 27.7 (CH<sub>2</sub>), 19.3 (CH<sub>2</sub>), 12.0 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF):  $m/z$  calculated for C<sub>17</sub>H<sub>18</sub>F<sub>3</sub>O<sub>2</sub> ([M+H]<sup>+</sup>) 311.1257, found 311.1259.



**General procedure (B) for preparation of acid precursors 1a, 1b, 1d, 1f, 1g, 1m and 1n** (exemplified for the synthesis of (*E*)-4-((5-Phenylpent-4-yn-1-yl)oxy)but-2-enoic acid, **1d**).



**Scheme S2. General procedure B for preparation of acid precursors**

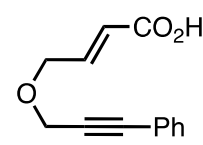
A flame-dried Schlenk flask under argon equipped with a Teflon septum and magnetic stir bar was charged with CuI (271.7 mg, 1.43 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (824.3 mg, 0.71 mmol). Et<sub>3</sub>N (95.0 mL), iodobenzene (8.0 mL, 71.33 mmol) and 4-pentyn-1-ol (4.0 g, 47.55 mmol) were sequentially added. The reaction mixture was stirred at rt, and after 20 h concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (1:10 to 1:2 EtOAc: Hexane) afforded 5-phenylpent-4-yn-1-ol as an orange oil (7.4 g, 97% yield). The NMR and MS data were consistent with those previously published.<sup>1</sup>

PPh<sub>3</sub> (163.7 mg, 0.62 mmol) was added to a solution of 5-phenylpent-4-yn-1-ol (2.0 g, 12.48 mmol) and ethyl buta-2,3-dienoate (2.9 mL, 24.97 mmol) in benzene (27.7 mL). To this orange solution, acetic acid (0.14 mL, 2.49 mmol) was added and the reaction was heated up to 60 °C. After 16 h, the solvent was removed in vacuo. Purification of the crude product by flash chromatography on silica gel (1:20 to 1:4 EtOAc: Hexane) afforded ethyl (*E*)-4-((5-Phenylpent-4-yn-1-yl)oxy)but-2-enoate as a pale yellow oil (1.9 g, 58 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.45 – 7.37 (m, 2H), 7.33 – 7.26 (m, 3H), 6.99 (dt, *J* = 15.7, 4.2 Hz, 1H), 6.11 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.26 – 4.16 (m, 4H), 3.65 (t, *J* = 6.0 Hz, 2H), 2.56 (t, *J* = 7.0 Hz, 2H), 1.91 (p, *J* = 6.9, 6.5 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.5 (C), 144.6 (CH), 131.7 (CH), 128.3 (CH), 127.7 (CH), 123.9 (C), 121.3 (CH), 89.4 (C), 81.1 (C), 69.6 (CH<sub>2</sub>), 60.5 (CH<sub>2</sub>), 29.0 (CH<sub>2</sub>), 16.3 (CH<sub>2</sub>), 14.4 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>17</sub>H<sub>21</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 273.1483, found 273.1485.

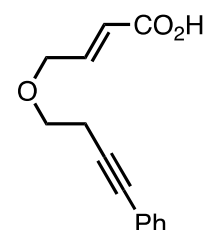
A NaOH aqueous solution (22.4 mL, 1M) was added to a solution that contains ethyl (*E*)-4-((5-Phenylpent-4-yn-1-yl)oxy)but-2-enoate (1500 mg, 5.51 mmol) in MeOH (10.2 mL). The reaction mixture was stirred at 45 °C. After 20 h, a solution of HCl (10 %) was added to adjust the pH to 1. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried and the solvent removed *in vacuo*. Purification of the crude product by flash chromatography on silica gel (1:5 to 2:1 EtOAc: Hexane) afforded (*E*)-4-((5-Phenylpent-4-yn-

1-yl)oxy)but-2-enoic acid (**1d**) as a white solid, **m.p.** 62-64 °C, (1.23 g, 92 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.64 (brs, 1H), 7.47 – 7.39 (m, 2H), 7.35 – 7.27 (m, 3H), 7.11 (dt, *J* = 15.7, 4.0 Hz, 1H), 6.15 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.24 – 4.18 (m, 2H), 3.66 (t, *J* = 6.1 Hz, 2H), 2.57 (t, *J* = 7.0 Hz, 2H), 1.93 (p, *J* = 6.5 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.9 (C), 147.5 (CH), 131.6 (CH), 128.3 (CH), 127.7 (CH), 123.9 (C), 120.4 (CH), 89.3 (C), 81.1 (C), 69.6 (CH<sub>2</sub>), 69.4 (CH<sub>2</sub>), 28.8 (CH<sub>2</sub>), 16.2 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>15</sub>H<sub>17</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 245.1172, found 245.1172.

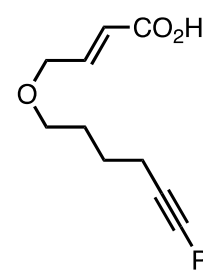
**(E)-4-((3-Phenylprop-2-yn-1-yl)oxy)but-2-enoic acid (1a)**

 This compound was prepared according to the previously described general procedure **B**, using prop-2-yn-1-ol instead of 4-pentyn-1-ol. White solid, **m.p.** 66 -67 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.51 – 7.39 (m, 2H), 7.36 – 7.28 (m, 3H), 7.19 – 7.04 (m, 1H), 6.22 – 6.08 (m, 1H), 4.45 (s, 2H), 4.34 (s, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.3 (C), 146.6 (CH), 131.9 (CH), 128.8 (CH), 128.5 (CH), 122.5 (C), 120.9 (CH), 87.1 (C), 84.4 (C), 68.2 (CH<sub>2</sub>), 59.0 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>13</sub>H<sub>13</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 217.0855, found 217.0859.

**(E)-4-((4-Phenylbut-3-yn-1-yl)oxy)but-2-enoic acid (1b)**

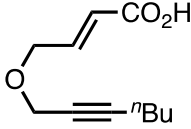
 This compound was prepared according to the previously described general procedure **B**, using but-3-yn-1-ol instead of 4-pentyn-1-ol. White solid, **m.p.** 80 -81 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.51 (brs, 1H), 7.48 – 7.40 (m, 2H), 7.35 – 7.27 (m, 3H), 7.11 (dt, *J* = 15.7, 4.0 Hz, 1H), 6.19 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.27 (dd, *J* = 4.1, 2.1 Hz, 2H), 3.72 (t, *J* = 6.9 Hz, 2H), 2.75 (t, *J* = 6.9 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.9 (C), 147.1 (CH), 131.7 (CH), 128.3 (CH), 127.9 (CH), 123.6 (C), 120.6 (CH), 86.5 (C), 81.8 (C), 69.5 (CH<sub>2</sub>), 69.4 (CH<sub>2</sub>), 20.9 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>14</sub>H<sub>15</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 231.1016, found 231.1016.

**(E)-4-((6-Phenylhex-5-yn-1-yl)oxy)but-2-enoic acid (1f)**

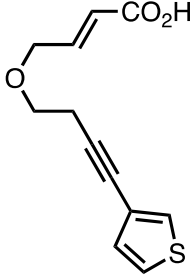
 This compound was prepared according to the previously described general procedure **B**, using hex-5-yn-1-ol instead of 4-pentyn-1-ol. White solid, **m.p.** 78 -79 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.31 (brs, 1H), 7.33 – 7.26 (m, 2H), 7.22 – 7.12 (m, 3H), 6.97 (dt, *J* = 15.7, 4.1 Hz, 1H), 6.00 (dt, *J* = 15.7, 2.0 Hz, 1H), 4.06 – 4.00 (m, 2H), 3.42 (t, *J* = 6.2 Hz, 2H), 2.35 (t, *J* = 6.7 Hz, 2H), 1.75 – 1.52 (m, 4H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.8 (C), 147.5 (CH), 131.6 (CH), 128.2 (CH), 127.6 (CH), 124.0 (C), 120.3 (CH), 89.9 (C), 81.0 (C), 70.7

(CH<sub>2</sub>), 69.2 (CH<sub>2</sub>), 28.8 (CH<sub>2</sub>), 25.4 (CH<sub>2</sub>), 19.2 (CH<sub>2</sub>). **HRMS** (IE-FIA-TOF): m/z calculated for C<sub>16</sub>H<sub>18</sub>O<sub>3</sub> ([M]<sup>+</sup>) 258.1256, found 258.1258.

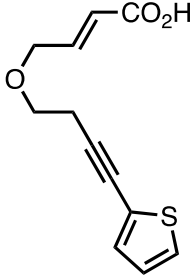
**(E)-4-(Hept-2-yn-1-yloxy)but-2-enoic acid (1g)**

 This compound was prepared according to the previously described general procedure **B**, using hept-2-yn-1-ol instead of 4-pentyn-1-ol. Viscous yellow oil. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 11.49 (brs, 1H), 7.11 – 6.99 (m, 1H), 6.12 – 6.02 (m, 1H), 4.24 – 4.19 (m, 2H), 4.16 (s, 2H), 2.25 – 2.14 (m, 2H), 1.56 – 1.28 (m, 4H), 0.88 (t, 3H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 173.8 (C), 148.7 (CH), 122.7 (CH), 89.9 (C), 77.2 (C), 69.8 (CH<sub>2</sub>), 60.7 (CH<sub>2</sub>), 32.6 (CH<sub>2</sub>), 24.0 (CH<sub>2</sub>), 20.4 (CH<sub>2</sub>), 15.6 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): m/z calculated for C<sub>11</sub>H<sub>17</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 197.1172, found 197.1172.

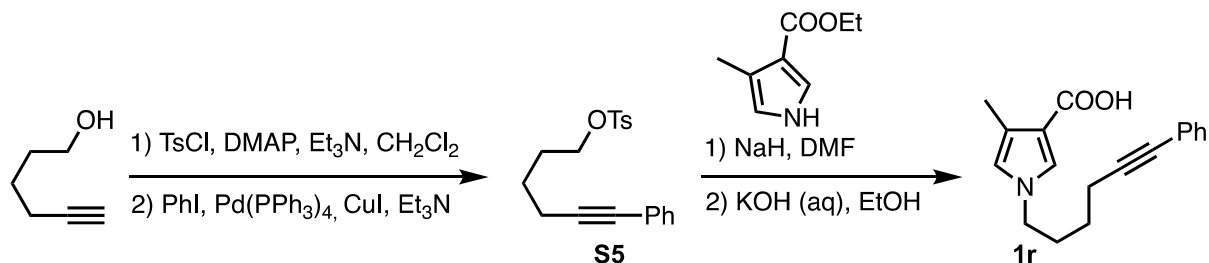
**(E)-4-((4-(Thiophen-3-yl)but-3-yn-1-yl)oxy)but-2-enoic acid (1m)**

 This compound was prepared according to the previously described general procedure **B**, using 3-bromothiophene (90%) instead of iodobenzene. Amorphous white solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 10.99 (brs, 1H), 7.41 (dd, *J* = 3.0, 1.2 Hz, 1H), 7.25 (dd, *J* = 5.0, 3.0 Hz, 1H), 7.17 – 7.03 (m, 2H), 6.18 (dt, *J* = 15.7, 2.1 Hz, 1H), 4.26 (dd, *J* = 4.1, 2.1 Hz, 2H), 3.70 (t, *J* = 6.9 Hz, 2H), 2.73 (t, *J* = 6.9 Hz, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 171.8 (C), 147.1 (CH), 130.1 (CH), 128.3 (CH), 125.2 (CH), 122.5 (C), 120.6 (CH), 86.0 (C), 76.9 (C), 69.5 (CH<sub>2</sub>), 69.3 (CH<sub>2</sub>), 20.9 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): m/z calculated for C<sub>12</sub>H<sub>13</sub>O<sub>3</sub>S ([M+H]<sup>+</sup>) 237.0577, found 237.0580.

**(E)-4-((4-(Thiophen-2-yl)but-3-yn-1-yl)oxy)but-2-enoic acid (1n)**

 This compound was prepared according to the previously described general procedure **B**, using 2-bromothiophene instead of iodobenzene. Amorphous yellow solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 11.64 (brs, 1H), 7.22 – 7.12 (m, 2H), 7.07 (dt, *J* = 15.7, 4.1 Hz, 1H), 6.93 (dd, *J* = 5.2, 3.6 Hz, 1H), 6.14 (dd, *J* = 15.7, 2.2 Hz, 1H), 4.23 (dd, *J* = 4.2, 2.1 Hz, 2H), 3.68 (t, *J* = 6.9 Hz, 2H), 2.74 (t, *J* = 6.9 Hz, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 171.8 (C), 147.0 (CH), 131.6 (CH), 126.9 (CH), 126.4 (CH), 123.6 (C), 120.6 (CH), 90.5 (C), 75.0 (C), 69.5 (CH<sub>2</sub>), 69.1 (CH<sub>2</sub>), 21.1 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): m/z calculated for C<sub>12</sub>H<sub>13</sub>O<sub>3</sub>S ([M+H]<sup>+</sup>) 237.0577, found 237.0580.

**General procedure (C) for preparation of acid precursors 1p, 1q, 1r, 1s, 1t and 1u** (exemplified for the synthesis of 4-Methyl-1-(6-phenylhex-5-yn-1-yl)-1*H*-pyrrole-3-carboxylic acid, **1r**).



**Scheme S3. General procedure C for preparation of acid precursors**

5-Hexyn-1-ol (4.0 g, 40.8 mmol) was added to a solution of Et<sub>3</sub>N (11.3 mL, 81.5 mmol), Tosyl chloride (8.2 g, 42.8 mmol) and 4-Dimethylaminopyridine (747 mg, 6.1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (60.8 mL) at 0°C. The mixture was warmed to rt and stirred for 3 h. NH<sub>4</sub>Cl (sat) (80 mL) was then added, the organic phase separated, and the aqueous phase extracted twice with CH<sub>2</sub>Cl<sub>2</sub> (30 mL). The organic phases were dried and concentrated under vacuum. Purification of the crude residue by flash chromatography on silica gel (1:20 to 1:3 EtOAc: Hexanes) afforded hex-5-yn-1-yl 4-methylbenzenesulfonate (**S4**) as colorless oil (10.1 g, 98 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.74 (d, *J* = 8.4 Hz, 2H), 7.31 (d, *J* = 8.0 Hz, 2H), 4.01 (t, *J* = 6.3 Hz, 2H), 2.41 (s, 3H), 2.12 (td, *J* = 6.9, 2.7 Hz, 2H), 1.90 (t, *J* = 2.7 Hz, 1H), 1.80 – 1.67 (m, 2H), 1.51 (p, *J* = 6.9 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 144.8 (C), 133.0 (C), 129.9 (CH), 127.8 (CH), 83.4 (C), 70.0 (CH<sub>2</sub>), 69.0 (CH), 27.7 (CH<sub>2</sub>), 24.2 (CH<sub>2</sub>), 21.6 (CH<sub>3</sub>), 17.7 (CH<sub>2</sub>). **HRMS** (ESI-TOF): *m/z* calculated for C<sub>13</sub>H<sub>17</sub>O<sub>3</sub>S ([M+H]<sup>+</sup>) 253.0893, found 253.0893.

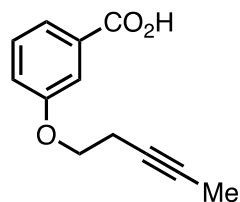
A Schlenk tube under argon equipped with a Teflon septum and magnetic stir bar was charged with CuI (22.6 mg, 0.12 mmol) and Pd(PPh<sub>3</sub>)<sub>4</sub> (68.7 mg, 0.06 mmol). Et<sub>3</sub>N (7.9 mL), iodobenzene (0.53 mL, 4.7 mmol) and hex-5-yn-1-yl 4-methylbenzenesulfonate (**S4**, 600 mg, 2.38 mmol) were sequentially added. The reaction mixture was stirred at rt. After 20 h, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (1:20 to 1:4 EtOAc: Hexane) afforded 6-phenylhex-5-yn-1-yl-4-methylbenzenesulfonate (**S5**) as a colorless oil (723 mg, 93% yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.79 – 7.74 (m, 2H), 7.37 – 7.33 (m, 2H), 7.30 – 7.28 (m, 1H), 7.28 – 7.22 (m, 4H), 4.06 (t, *J* = 6.3 Hz, 2H), 2.38 – 2.30 (m, 5H), 1.85 – 1.73 (m, 2H), 1.65 – 1.53 (m, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 144.7 (C), 132.9 (C), 131.3 (CH), 129.8 (CH), 128.1 (CH), 127.6 (CH), 127.5 (CH), 123.6 (C), 89.0 (C), 81.2 (C), 70.0 (CH<sub>2</sub>), 27.8 (CH<sub>2</sub>), 24.4 (CH<sub>2</sub>), 21.4 (CH<sub>3</sub>),

18.6 (CH<sub>2</sub>). **HRMS** (ESI-TOF): *m/z* calculated for C<sub>19</sub>H<sub>21</sub>O<sub>3</sub>S ([M+H]<sup>+</sup>) 329.1208, found 329.1206.

Following a modified procedure described by Schreiber and co-workers<sup>2</sup>, to a solution of ethyl 4-methyl-1*H*-pyrrole-3-carboxylate (250 mg, 1.63 mmol) in anhydrous DMF (4 mL) at 0 °C was added sodium hydride (60 % mineral oil) (97.9 mg, 2.45 mmol). After 20 minutes, 6-phenylhex-5-yn-1-yl-4-methylbenzenesulfonate (540 mg, 1.64 mmol) was added. The reaction mixture was stirred at 85 °C for 16 hours. The reaction mixture was allowed to cool to room temperature, water (30 mL) and Et<sub>2</sub>O (10 mL) were successively added, and the layers were separated. The aqueous phase was extracted with Et<sub>2</sub>O (4 x 10 mL) and the combined organic phases were dried and concentrated. Purification of the crude residue by flash chromatography on silica gel (1:10 to 1:2 EtOAc: Hexanes) afforded ethyl 4-methyl-1-(6-phenylhex-5-yn-1-yl)-1*H*-pyrrole-3-carboxylate (**S6**) as yellow pale oil (396 mg, 78 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.45 – 7.39 (m, 2H), 7.33 – 7.25 (m, 4H), 6.42 – 6.38 (m, 1H), 4.28 (q, *J* = 7.1 Hz, 2H), 3.82 (t, *J* = 7.0 Hz, 2H), 2.43 (t, *J* = 6.9 Hz, 2H), 2.31 (s, 3H), 1.97 – 1.84 (m, 2H), 1.63 – 1.50 (m, 2H), 1.35 (t, *J* = 7.1 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 165.3 (C), 131.4 (CH), 128.2 (CH), 127.6 (CH), 126.4 (CH), 123.7 (C), 121.4 (C), 120.2 (C), 120.1 (CH), 114.0 (C), 89.2 (C), 81.2 (C), 59.1 (CH<sub>2</sub>), 49.3 (CH<sub>2</sub>), 30.2 (CH<sub>2</sub>), 25.5 (CH<sub>2</sub>), 18.9 (CH<sub>2</sub>), 14.5 (CH<sub>3</sub>), 11.7 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>20</sub>H<sub>24</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) 310.1798, found 310.1802.

Following a modified procedure described by Sieber and co-workers<sup>3</sup>, to a solution of ethyl 4-methyl-1-(6-phenylhex-5-yn-1-yl)-1*H*-pyrrole-3-carboxylate (**S6**, 390 mg, 1.26 mmol) in EtOH (6.3 mL) was added an aqueous solution of KOH (0.5 mL, 10 M) and the reaction mixture was stirred for 24 h at room temperature. The solution was acidified by adding aqueous 1 M HCl, the reaction mixture extracted with EtOAc (4 x 10 mL), and the combined organic extracts were washed with brine (40 mL), dried and concentrated under reduced. Purification of the crude residue by flash chromatography on silica gel (1:5 to 2:1 EtOAc: Hexanes) afforded 4-methyl-1-(6-phenylhex-5-yn-1-yl)-1*H*-pyrrole-3-carboxylic acid (**1r**) as a light-yellow solid, **m.p.** 77 -88 °C, (323 mg, 91 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.45 – 7.40 (m, 2H), 7.38 – 7.35 (m, 1H), 7.35 – 7.27 (m, 3H), 6.46 – 6.42 (m, 1H), 3.89 (t, *J* = 6.9 Hz, 2H), 2.47 (t, *J* = 6.9 Hz, 2H), 2.31 (s, 3H), 1.97 (p, *J* = 7.1 Hz, 2H), 1.61 (p, *J* = 7.1 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.2 (C), 131.7 (CH), 128.4 (CH), 128.0 (CH), 127.8 (CH), 123.8 (C), 122.4 (C), 120.6 (CH), 113.4 (C), 89.2 (C), 81.5 (C), 49.6 (CH<sub>2</sub>), 30.3 (CH<sub>2</sub>), 25.7 (CH<sub>2</sub>), 19.1 (CH<sub>2</sub>), 11.8 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>18</sub>H<sub>20</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) 282.1491, found 282.1489.

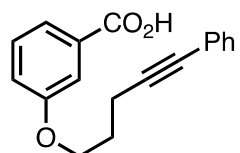
### 3-(Pent-3-yn-1-yloxy)benzoic acid (1p)



This compound was prepared according to the previously described general procedure **C**, using pent-3-yn-1-ol and methyl 3-hydroxybenzoate instead of 5-Hexyn-1-ol and ethyl 4-methyl-1H-pyrrole-3-carboxylate.

White solid, **m.p.** 146 -147 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 10.37 (brs, 1H), 7.73 (d, *J* = 7.7 Hz, 1H), 7.64 (s, 1H), 7.38 (t, *J* = 8.0 Hz, 1H), 7.17 (dd, *J* = 8.3, 2.7 Hz, 1H), 4.11 (t, *J* = 7.1 Hz, 2H), 2.72 – 2.60 (m, 2H), 1.81 (t, *J* = 2.5 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 172.2 (C), 158.8 (C), 130.7 (C), 129.7 (CH), 123.1 (CH), 121.2 (CH), 115.4 (CH), 77.7 (C), 75.0 (C), 67.0 (CH<sub>2</sub>), 19.9 (CH<sub>2</sub>), 3.7 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>12</sub>H<sub>12</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 205.0859, found 205.0859.

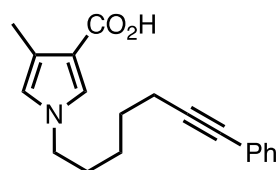
### 3-((5-Phenylpent-4-yn-1-yl)oxy)benzoic acid (1q)



This compound was prepared according to the previously described general procedure **C**, using pent-4-yn-1-ol and methyl 3-hydroxybenzoate instead of 5-Hexyn-1-ol and ethyl 4-methyl-1H-pyrrole-3-carboxylate.

White solid, **m.p.** 116 -117 °C. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.44 (brs, 1H), 7.75 (d, *J* = 7.7 Hz, 1H), 7.68 (s, 1H), 7.47 – 7.38 (m, 3H), 7.33 – 7.26 (m, 3H), 7.20 (dd, *J* = 8.3, 2.6 Hz, 1H), 4.20 (t, *J* = 6.1 Hz, 2H), 2.67 (t, *J* = 6.9 Hz, 2H), 2.13 (p, *J* = 6.5 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 172.4 (C), 159.1 (C), 131.7 (CH), 130.7 (C), 129.7 (CH), 128.3 (CH), 127.8 (CH), 123.8 (C), 122.8 (CH), 121.1 (CH), 115.3 (CH), 89.0 (C), 81.4 (C), 66.8 (CH<sub>2</sub>), 28.5 (CH<sub>2</sub>), 16.3 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>18</sub>H<sub>17</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 281.1171, found 281.1172.

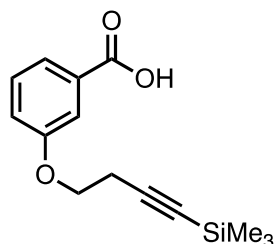
### 4-Methyl-1-(7-phenylhept-6-yn-1-yl)-1H-pyrrole-3-carboxylic acid (1s)



This compound was prepared according to the previously described general procedure **C**, using hept-6-yn-1-ol instead of 5-Hexyn-1-ol.

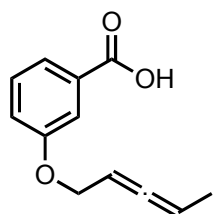
Viscous orange oil. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 12.00 (brs, 1H), 7.45 – 7.39 (m, 2H), 7.38 – 7.34 (m, 1H), 7.34 – 7.27 (m, 3H), 6.43 (s, 1H), 3.84 (t, *J* = 6.9 Hz, 2H), 2.44 (t, *J* = 6.9 Hz, 2H), 2.31 (s, 3H), 1.83 (p, *J* = 7.1 Hz, 2H), 1.65 (p, *J* = 7.0 Hz, 2H), 1.55 – 1.43 (m, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.3 (C), 131.6 (CH), 128.3 (CH), 128.0 (CH), 127.7 (CH), 123.9 (C), 122.3 (C), 120.6 (CH), 113.3 (C), 89.7 (C), 81.1 (C), 49.9 (CH<sub>2</sub>), 30.7 (CH<sub>2</sub>), 28.2 (CH<sub>2</sub>), 25.9 (CH<sub>2</sub>), 19.3 (CH<sub>2</sub>), 11.8 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>19</sub>H<sub>22</sub>NO<sub>2</sub> F<sub>3</sub> ([M+H]<sup>+</sup>) 296.1650, found 296.1645.

### 3-((4-(Trimethylsilyl)but-3-yn-1-yl)oxy)benzoic acid (1t)



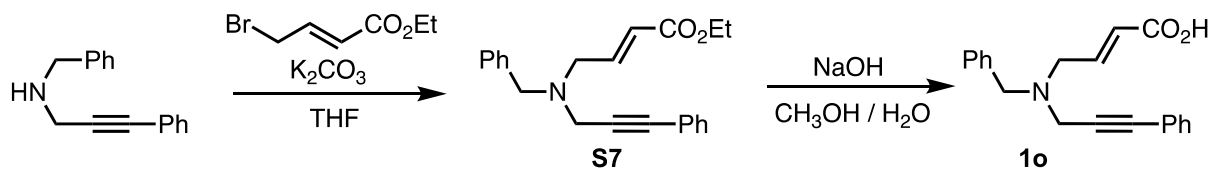
This compound was prepared according to the previously described general procedure **C**, using but-3-yn-1-ol and methyl 3-hydroxybenzoate instead of 5-Hexyn-1-ol and ethyl 4-methyl-1H-pyrrole-3-carboxylate<sup>4</sup>. White solid (5:1, SiMe<sub>3</sub> : H). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.74 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.64 (dd, *J* = 2.7, 1.5 Hz, 1H), 7.39 (t, *J* = 7.9 Hz, 1H), 7.22 – 7.12 (m, 1H), 4.14 (t, *J* = 7.2 Hz, 2H), 2.75 (t, *J* = 7.3 Hz, 2H), 0.17 (s, 9H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 172.3 (C), 151.8 (C), 130.7 (C), 129.7 (CH), 123.1 (CH), 121.2 (CH), 115.3 (CH), 102.4 (C), 86.8 (C), 66.5 (CH<sub>2</sub>), 21.0 (CH<sub>2</sub>), 0.2 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>14</sub>H<sub>19</sub>O<sub>3</sub>Si ([M+H]<sup>+</sup>) 263.1097, found 263.1098.

### 3-(Penta-2,3-dien-1-yloxy)benzoic acid (1u)



This compound was prepared according to the previously described general procedure **C**, using penta-2,3-dien-1-ol and methyl 3-hydroxybenzoate instead of 5-Hexyn-1-ol and ethyl 4-methyl-1H-pyrrole-3-carboxylate. White solid. **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 9.20 (s, 1H), 7.71 (dt, *J* = 7.7, 1.3 Hz, 1H), 7.65 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.36 (t, *J* = 7.9 Hz, 1H), 7.16 (ddd, *J* = 8.3, 2.6, 1.0 Hz, 1H), 5.37 – 5.20 (m, 2H), 4.60 (dd, *J* = 6.4, 2.6 Hz, 2H), 1.68 (dd, *J* = 6.8, 3.4 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 206.3 (C), 172.2 (C), 158.5 (C), 130.9 (C), 129.6 (CH), 122.9 (CH), 121.40 (CH), 115.7 (CH), 87.9 (CH), 86.8 (CH), 66.7 (CH<sub>2</sub>), 14.0 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>12</sub>H<sub>13</sub>O<sub>3</sub> ([M+H]<sup>+</sup>) 205.0858, found 205.0859.

### Procedure for preparation of (E)-4-(Benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoic acid 1o.



### Scheme S4. Synthesis of (E)-4-(Benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoic acid 1o.

Following a modified procedure described by ourselves<sup>5</sup>, N-Benzyl-3-phenylprop-2-yn-1-amine (2.5 g, 11.3 mmol) was added to a suspension of K<sub>2</sub>CO<sub>3</sub> (2.6 g, 19.2 mmol) in THF (39 mL) at -10 °C. After stirring for 15 min, ethyl (E)-4-bromobut-2-enoate (2.7 mL, 14.7 mmol) was added dropwise and the mixture was stirred overnight at rt. Then, the mixture was poured into

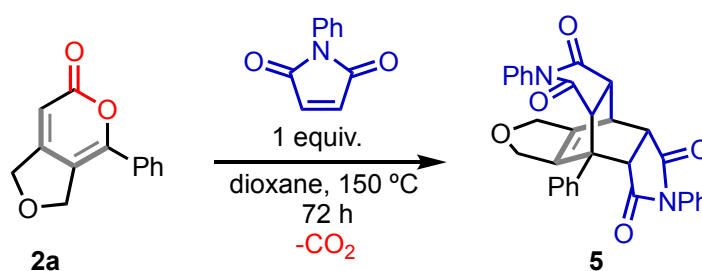
water and extracted with Et<sub>2</sub>O (3x40 mL). The organic phases were dried, filtered and concentrated. Purification of the crude residue by flash chromatography on silica gel gave (1:20 to 1:1 EtOAc: Hexanes) ethyl (E)-4-(benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoate (**S7**) as a light-yellow oil, (3.1 g, 84 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 7.54 – 7.48 (m, 2H), 7.46 – 7.39 (m, 2H), 7.39 – 7.30 (m, 6H), 7.05 (dtd, *J* = 15.7, 6.0, 1.1 Hz, 1H), 6.15 (dt, *J* = 15.7, 1.3 Hz, 1H), 4.24 (q, *J* = 7.2 Hz, 2H), 3.78 (s, 2H), 3.58 (s, 2H), 3.43 (dd, *J* = 6.0, 1.7 Hz, 2H), 1.33 (t, *J* = 7.1 Hz, 3H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 166.4 (C), 145.8 (CH), 138.4 (C), 131.9 (CH), 129.1 (CH), 128.5 (CH), 128.4 (CH), 128.3 (CH), 127.4 (CH), 123.4 (CH), 123.2 (C), 86.1 (C), 84.0 (C), 60.5 (CH<sub>2</sub>), 58.0 (CH<sub>2</sub>), 54.4 (CH<sub>2</sub>), 42.8 (CH<sub>2</sub>), 14.4 (CH<sub>3</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>22</sub>H<sub>23</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) 333.1729, found 333.1727.

A NaOH aqueous solution (3 mL, 1M) was added to a solution that contains ethyl (E)-4-(benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoate (1.0 g, 3.0 mmol) in MeOH (4.5 mL). The reaction mixture was stirred at rt. After 8 h, a solution of HCl (5 %) was added to adjust the pH to 2. The mixture was extracted with EtOAc (3 x 20 mL). The combined organic layers were dried and the solvent removed *in vacuo*. Purification of the crude product by flash chromatography on silica gel (1:5 to 2:1 EtOAc: Hexane) afforded (E)-4-(benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoic acid (**1o**) as a colorless oil, (450 mg, 49 % yield). **<sup>1</sup>H NMR** (300 MHz, CDCl<sub>3</sub>): δ 11.05 (s, 1H), 7.51 – 7.46 (m, 1H), 7.40 (ddd, *J* = 8.3, 6.8, 1.7 Hz, 2H), 7.36 – 7.27 (m, 4H), 7.14 (dt, *J* = 15.7, 6.0 Hz, 1H), 6.14 (dd, *J* = 15.7, 1.6 Hz, 1H), 3.78 (s, 2H), 3.58 (s, 2H), 3.46 (dd, *J* = 6.1, 1.7 Hz, 2H). **<sup>13</sup>C NMR** (75 MHz, CDCl<sub>3</sub>): δ 171.4 (C), 148.0 (CH), 137.9 (C), 131.9 (CH), 129.3 (CH), 128.6 (CH), 128.47 (CH), 128.46 (C), 128.4 (CH), 127.6 (CH), 123.1 (CH), 86.4 (C), 83.6 (C), 58.0 (CH<sub>2</sub>), 54.4 (CH<sub>2</sub>), 42.7 (CH<sub>2</sub>). **HRMS** (APCI-FIA-TOF): *m/z* calculated for C<sub>20</sub>H<sub>20</sub>NO<sub>2</sub> ([M+H]<sup>+</sup>) 306.1489, found 306.1489.



## Further insights into the cascade DA transformation

Preliminary tests on the amount of dienophile used were performed with **2a**, as in this way we would also confirm the viability of the tandem process on other substrates than **2d**. Heating **2a** in presence of 1 equiv of the maleimide led exclusively to the cascade DA adduct **5** (47 %), and recovery of the remaining starting material **2a** (52 %). This result suggests that the intermediate resulting from the initial cycloadditions reacts faster than the initial pyrone.



**Scheme S5. Cascade Diels-Alder reaction**

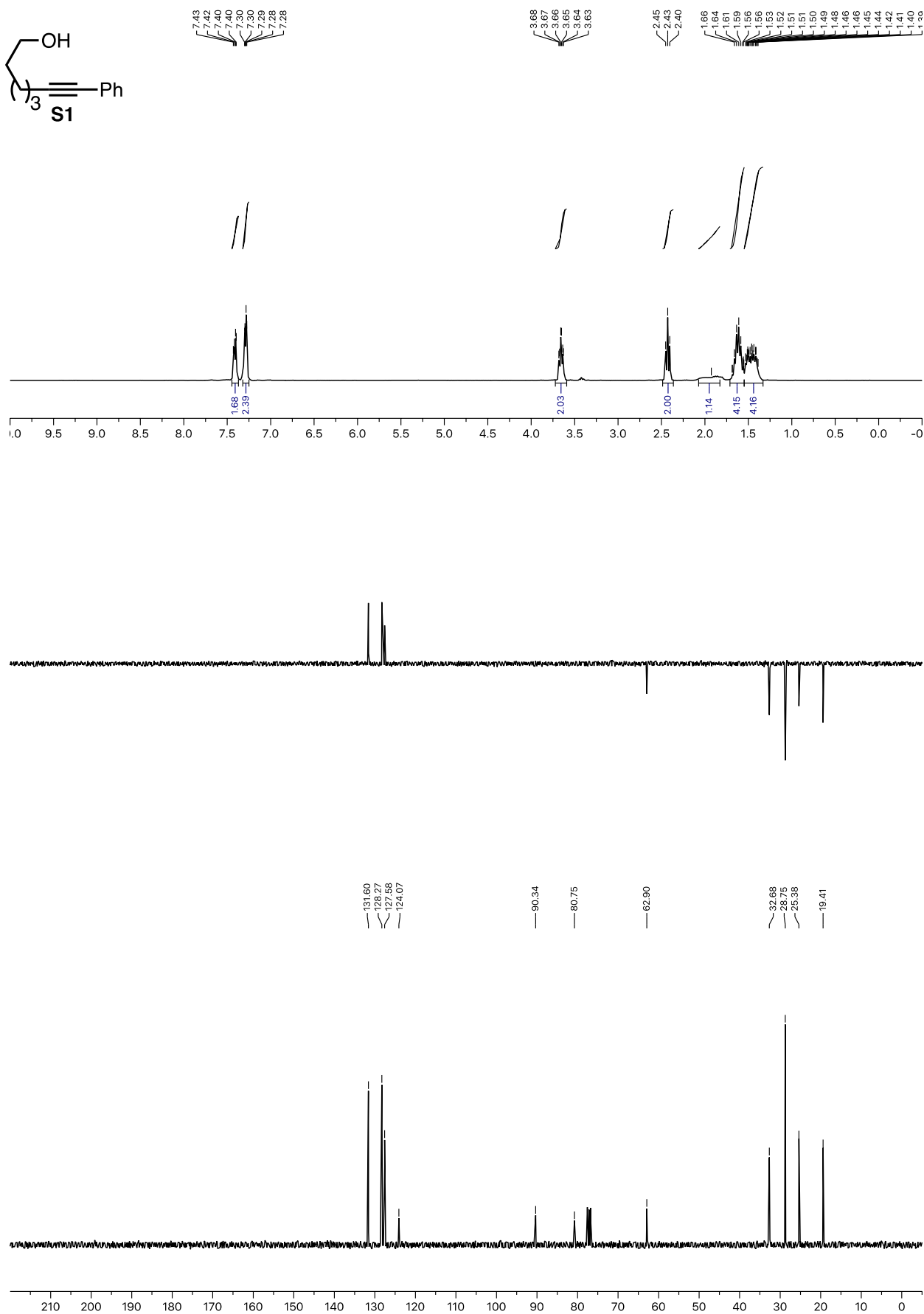
An oven dried sealed tube equipped with a magnetic stir bar was charged with *N*-phenylmaleimide (28.3 mg, 0.16 mmol), 4-phenyl-3*H*-furo[3,4-*c*]pyran-6(1*H*)-one (**2a**) (35 mg, 0.16 mmol) and dioxane (1.3 mL). The reaction mixture was then stirred at 150 °C. After 72 h, the reaction mixture was concentrated in vacuo. Purification of the crude product by flash chromatography on silica gel (1:10 to 2:1 EtOH: Hexane) afforded the cascade product **5** as a white solid (39.6 mg, 47 % yield). Light yellow solid. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>): δ 7.49 – 7.31 (m, 10H), 7.11 – 7.04 (m, 5H), 5.08 (t, *J* = 5.2 Hz, 2H), 4.72 (t, *J* = 5.2 Hz, 2H), 4.18 (t, *J* = 3.0 Hz, 1H), 3.62 (d, *J* = 8.0 Hz, 2H), 3.34 (dd, *J* = 8.0, 3.0 Hz, 2H). <sup>13</sup>C NMR (75 MHz, CDCl<sub>3</sub>): δ 175.0 (C), 173.5 (C), 138.9 (C), 137.5 (C), 137.1 (C), 131.3 (C), 129.5 (CH), 129.2 (CH), 128.0 (CH), 126.5 (CH), 76.4 (CH<sub>2</sub>), 75.2 (CH<sub>2</sub>), 51.2 (C), 49.8 (CH), 44.4 (CH), 34.2 (CH).

## X-Ray Crystallographic Details

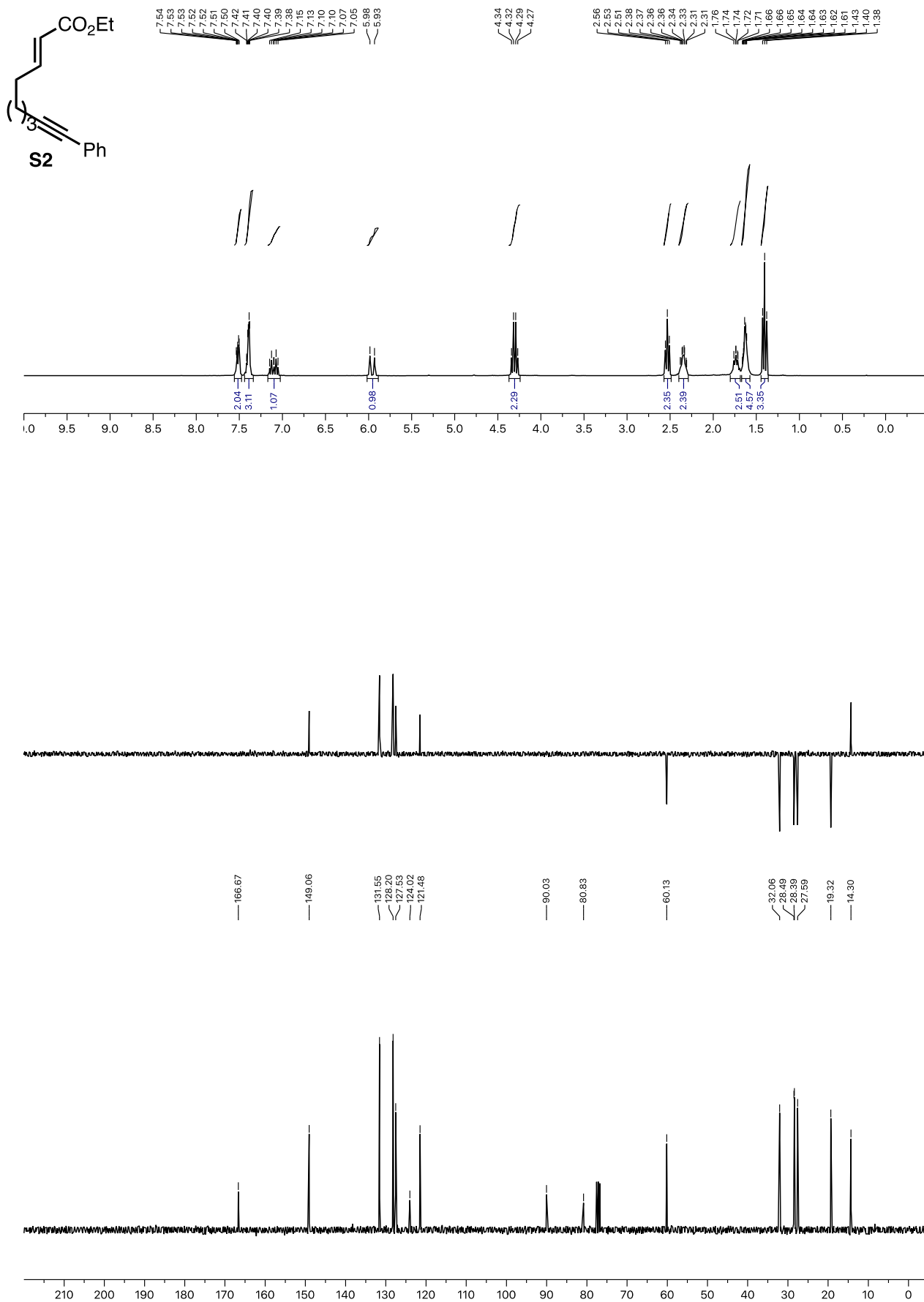
CCDC 1885153 (**2c**) and CCDC 1885154 (**4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via [www.ccdc.cam.ac.uk/data\\_request/cif](http://www.ccdc.cam.ac.uk/data_request/cif).

## References

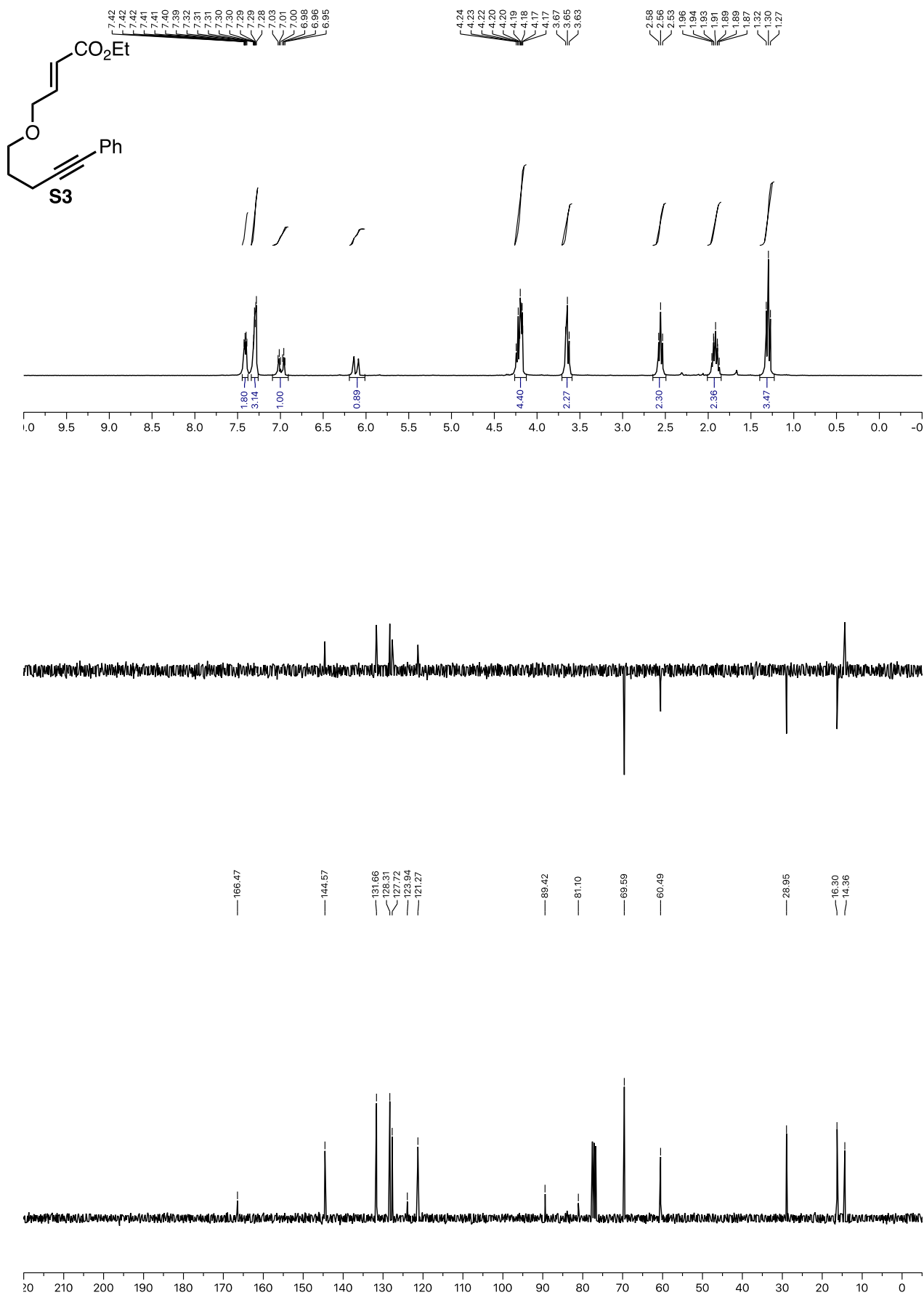
- (1) Ferrand, L.; Tang, Y.; Aubert, C.; Fensterbank, L.; Mouriès-Mansuy, V.; Petit, M.; Amatore, M. Niobium-Catalyzed Intramolecular Addition of O–H and N–H Bonds to Alkenes: A Tool for Hydrofunctionalization. *Org. Lett.* **2017**, *19*, 2062 – 2065.
- (2) Schreiber, S. L. et al; Real-Time Biological Annotation of Synthetic Compounds. *J. Am. Chem. Soc.*, **2016**, *138*, 8920 – 8927.
- (3) Sieber, S. A. et al; Natural-Product-Inspired Aminoepoxybenzoquinones Kill Members of the Gram-Negative Pathogen Salmonella by Attenuating Cellular Stress Response. *Angew. Chem. Int. Ed.*, **2016**, *55*, 14852 – 14857.
- (4) Srihari, P.; Sridhar, Y. Total Synthesis of Both Enantiomers of Macrocyclic Lactone Aspergillide C. *Eur. J. Org. Chem.* **2011**, *33*, 6690 – 6697.
- (5) Verdugo, F.; Villarino, L.; Durán, J.; Gullías, M.; Mascareñas, J. L.; López, F. Enantioselective Palladium-Catalyzed [3C + 2C] and [4C + 3C] Intramolecular Cycloadditions of Alkylidenecyclopropanes. *ACS Catal.* **2018**, *8*, 6100 – 6105.



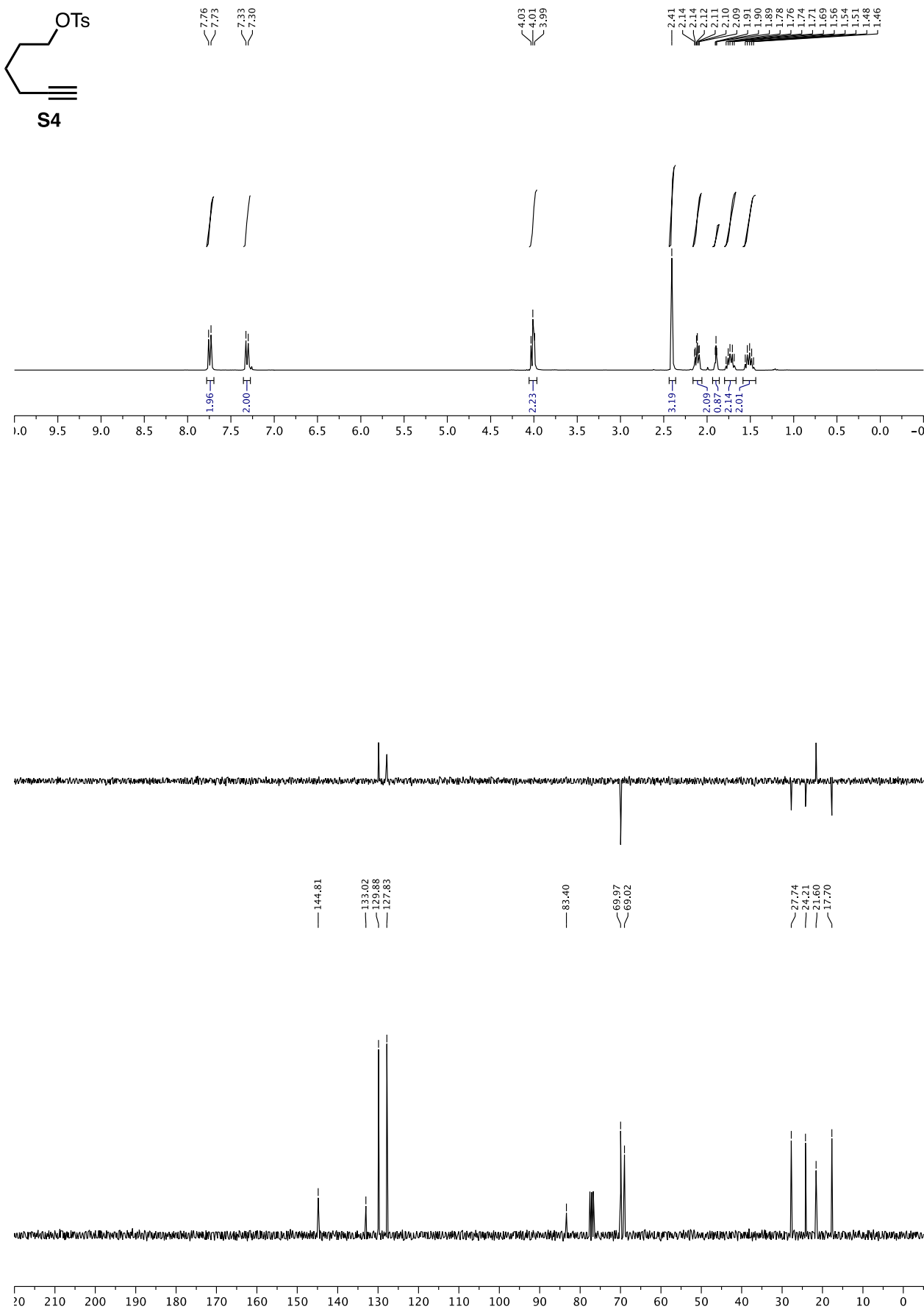
**Figure S1.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 8-phenyloct-7-yn-1-ol (**S1**)



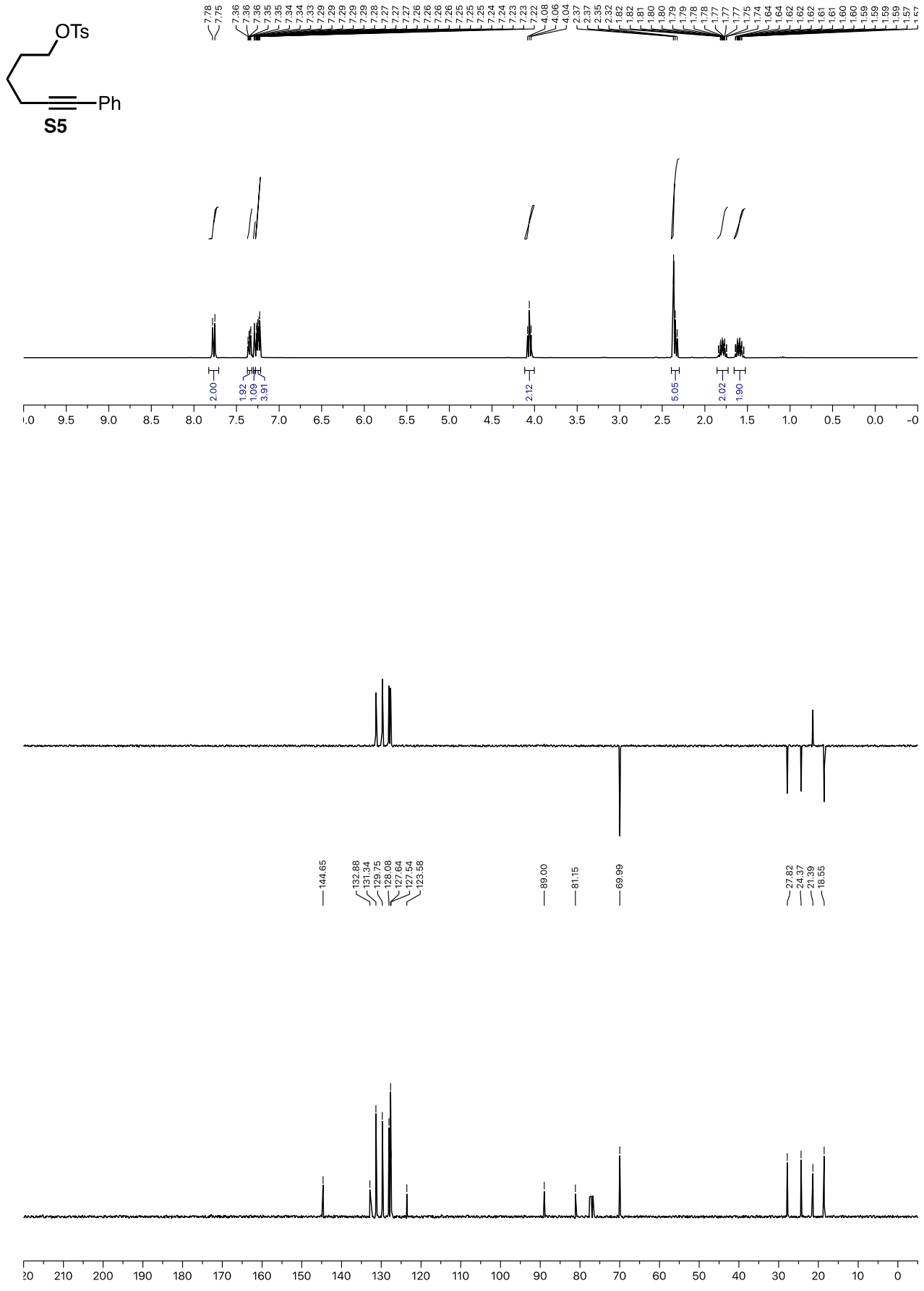
**Figure S2.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of ethyl (E)-10-phenyldec-2-en-9-ynoate (S2)



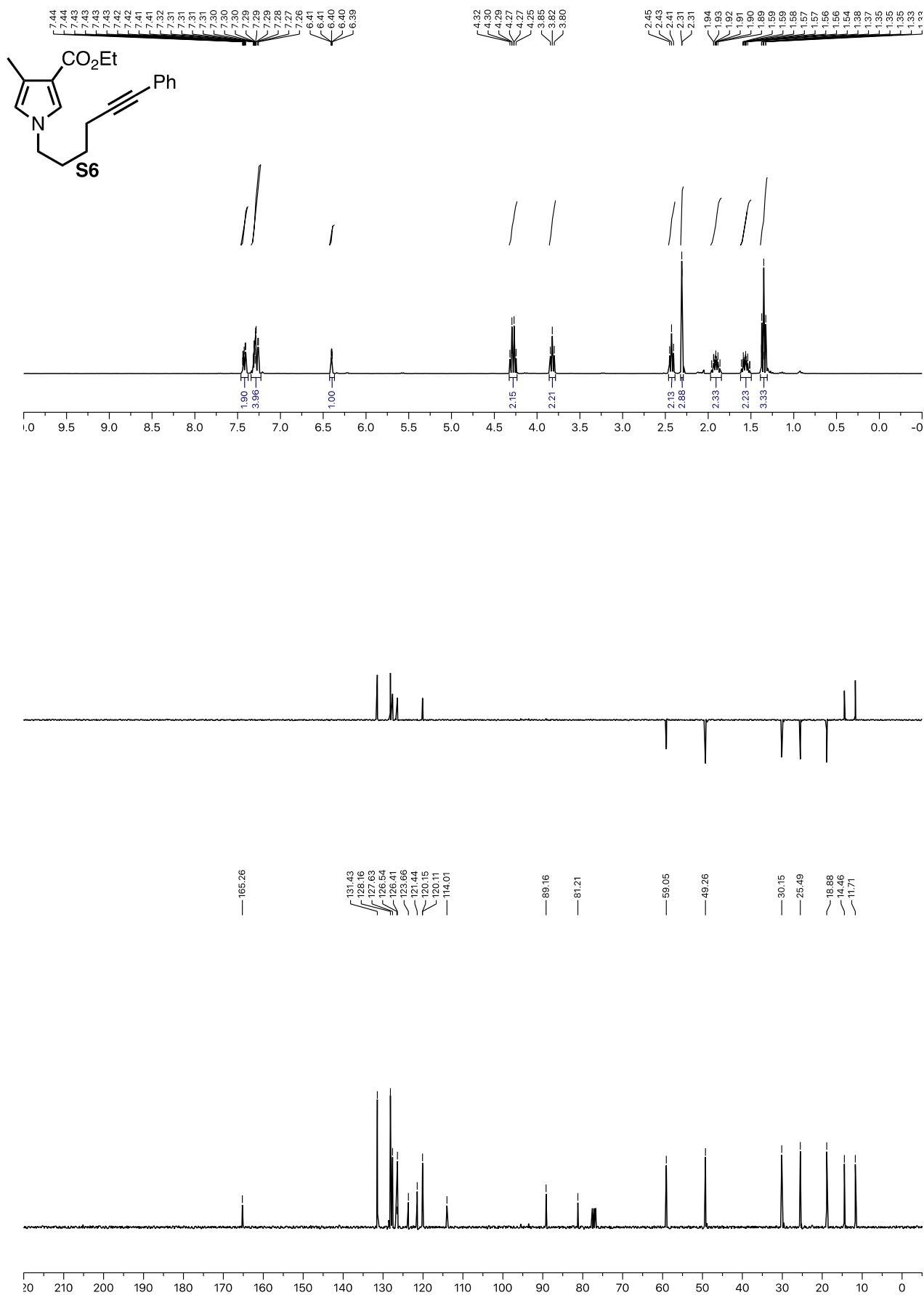
**Figure S3.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of ethyl (*E*)-4-((5-Phenylpent-4-yn-1-yl)oxy)but-2-enoate (**S3**)



**Figure S4.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of hex-5-yn-1-yl 4-methylbenzenesulfonate (**S4**)

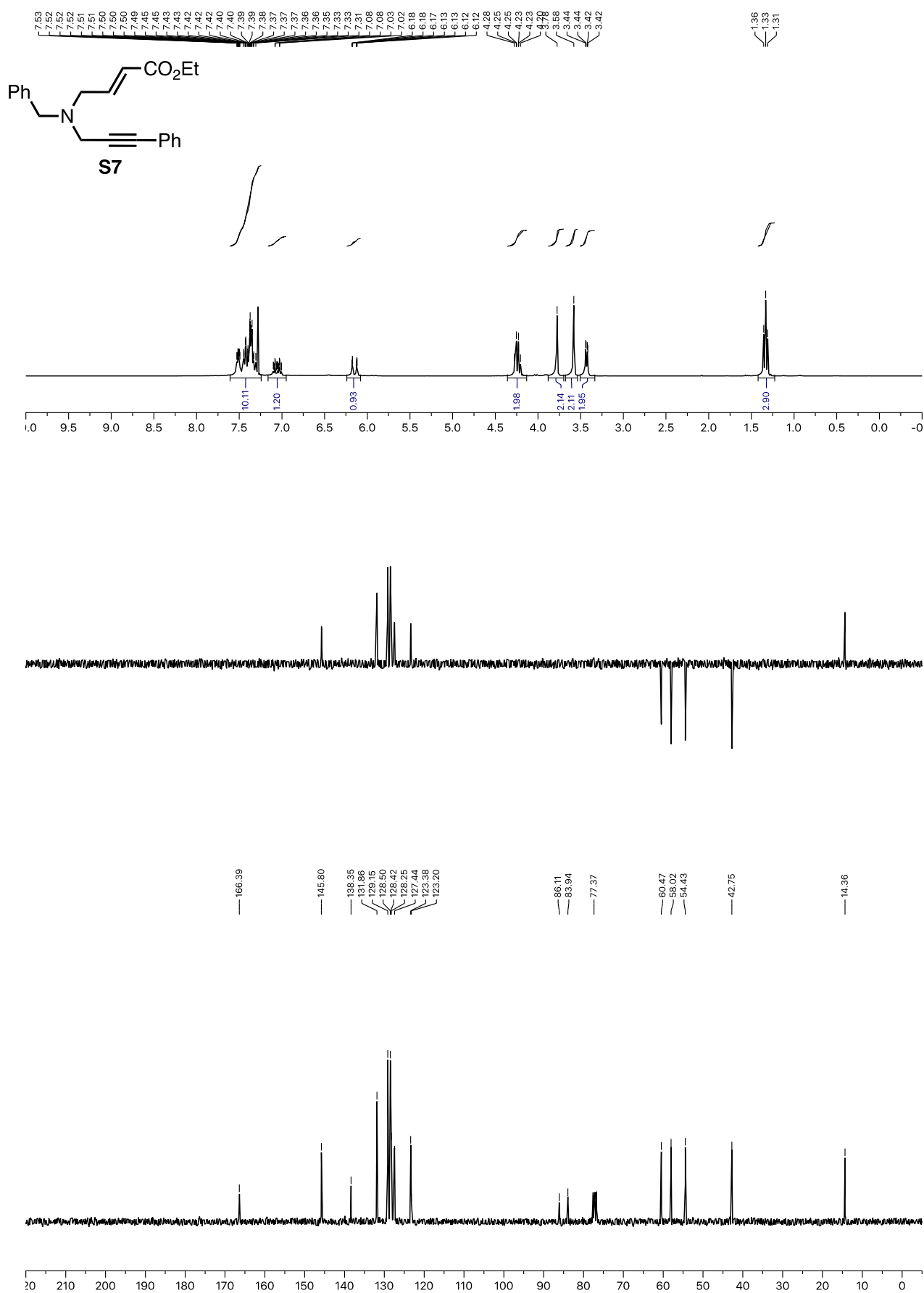


**Figure S5.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 6-phenylhex-5-yn-1-yl-4-methylbenzenesulfonate (**S5**)

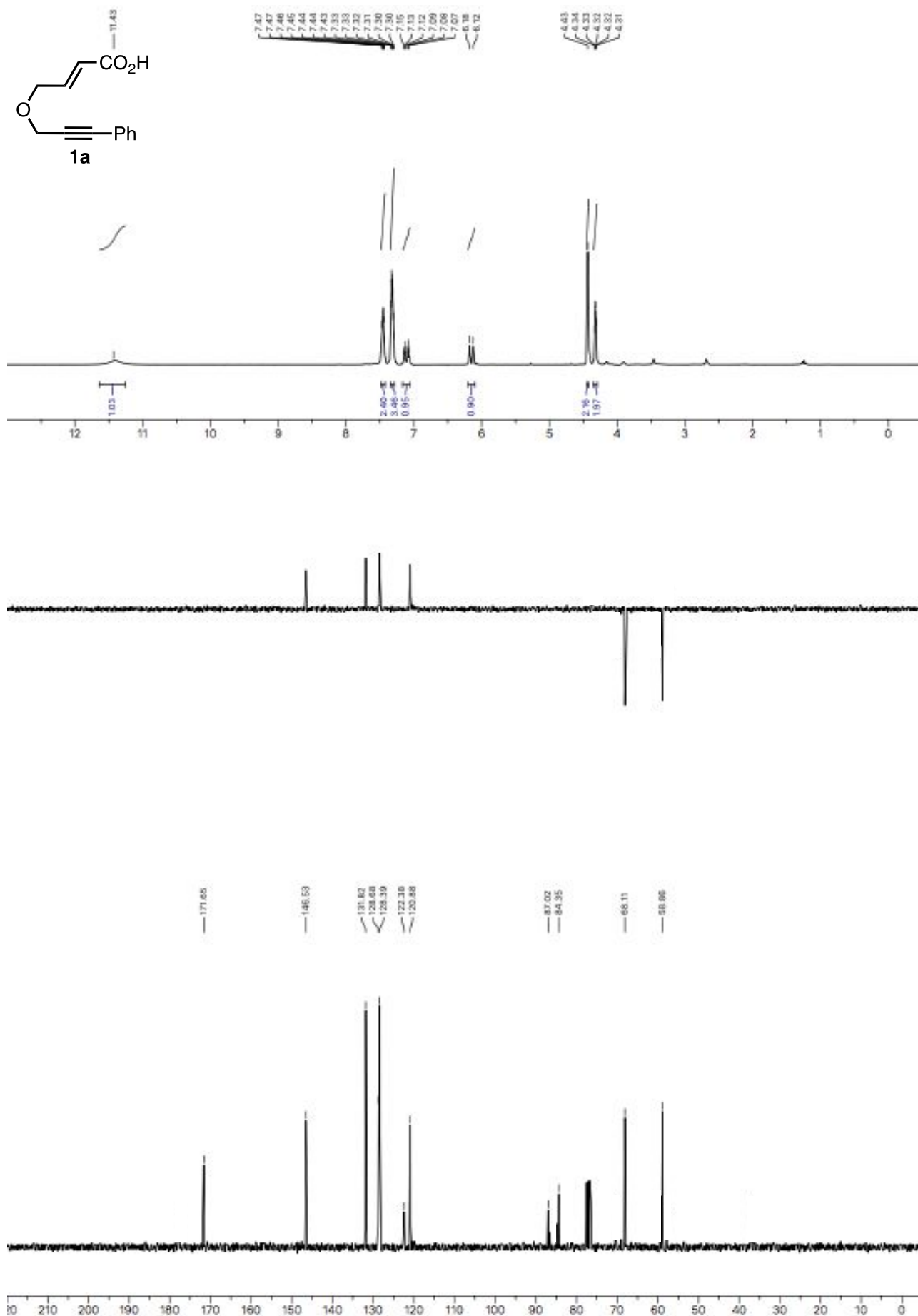


**Figure S6.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of ethyl 4-methyl-1-(6-phenylhex-5-yn-1-yl)-1H-pyrrole-3-carboxylate (**S6**)

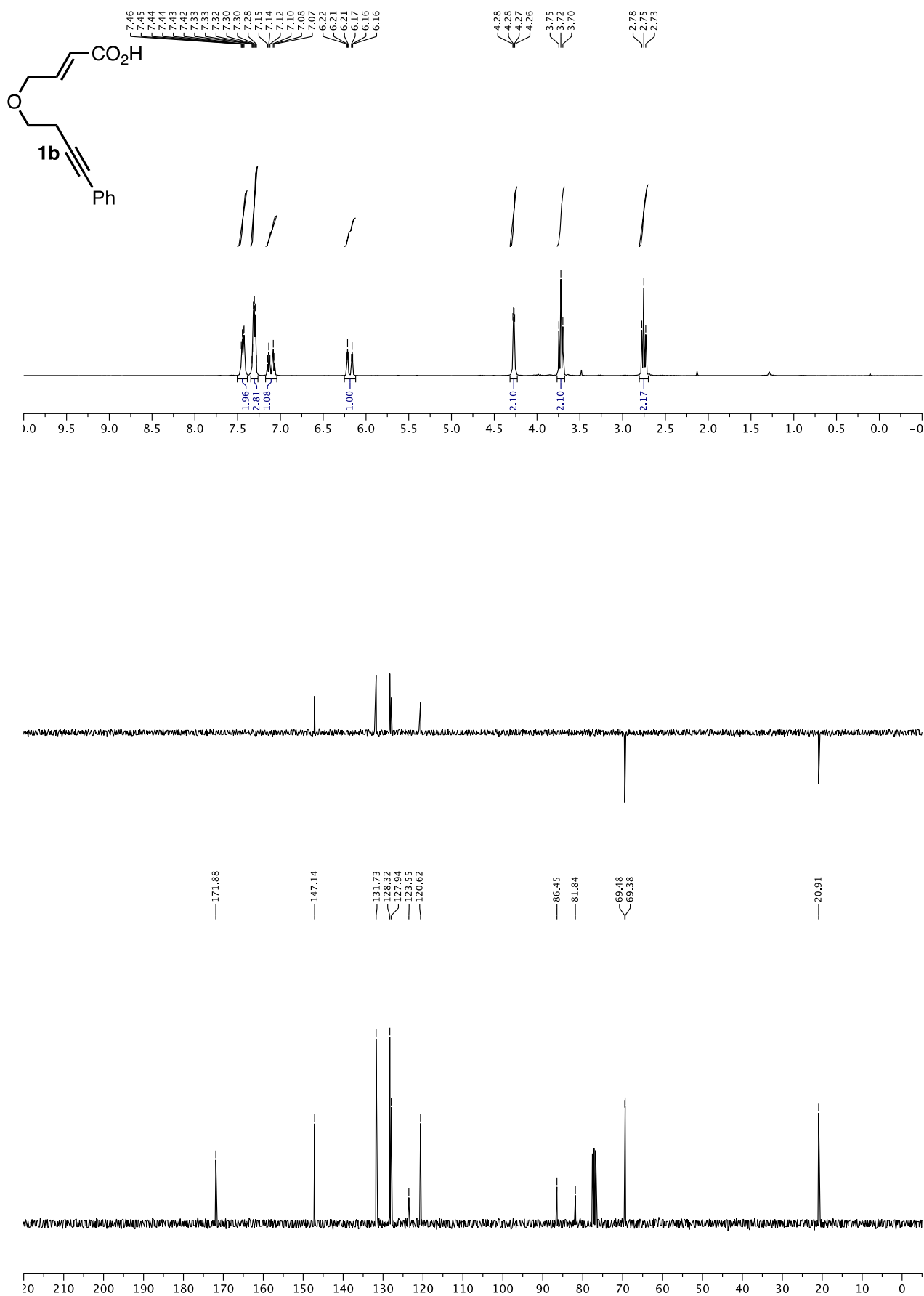




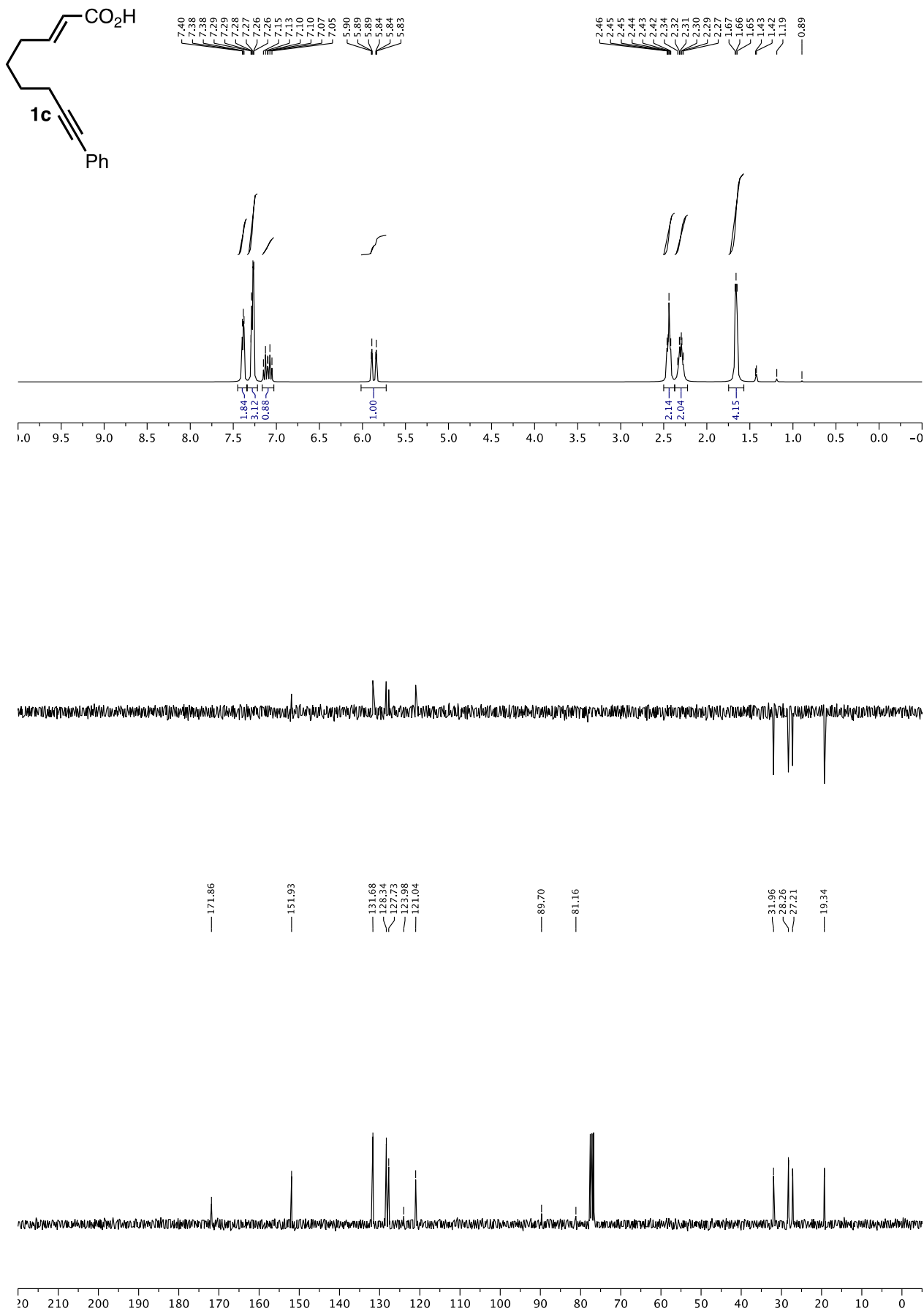
**Figure S7.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of ethyl (*E*)-4-(benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoate (**S7**)



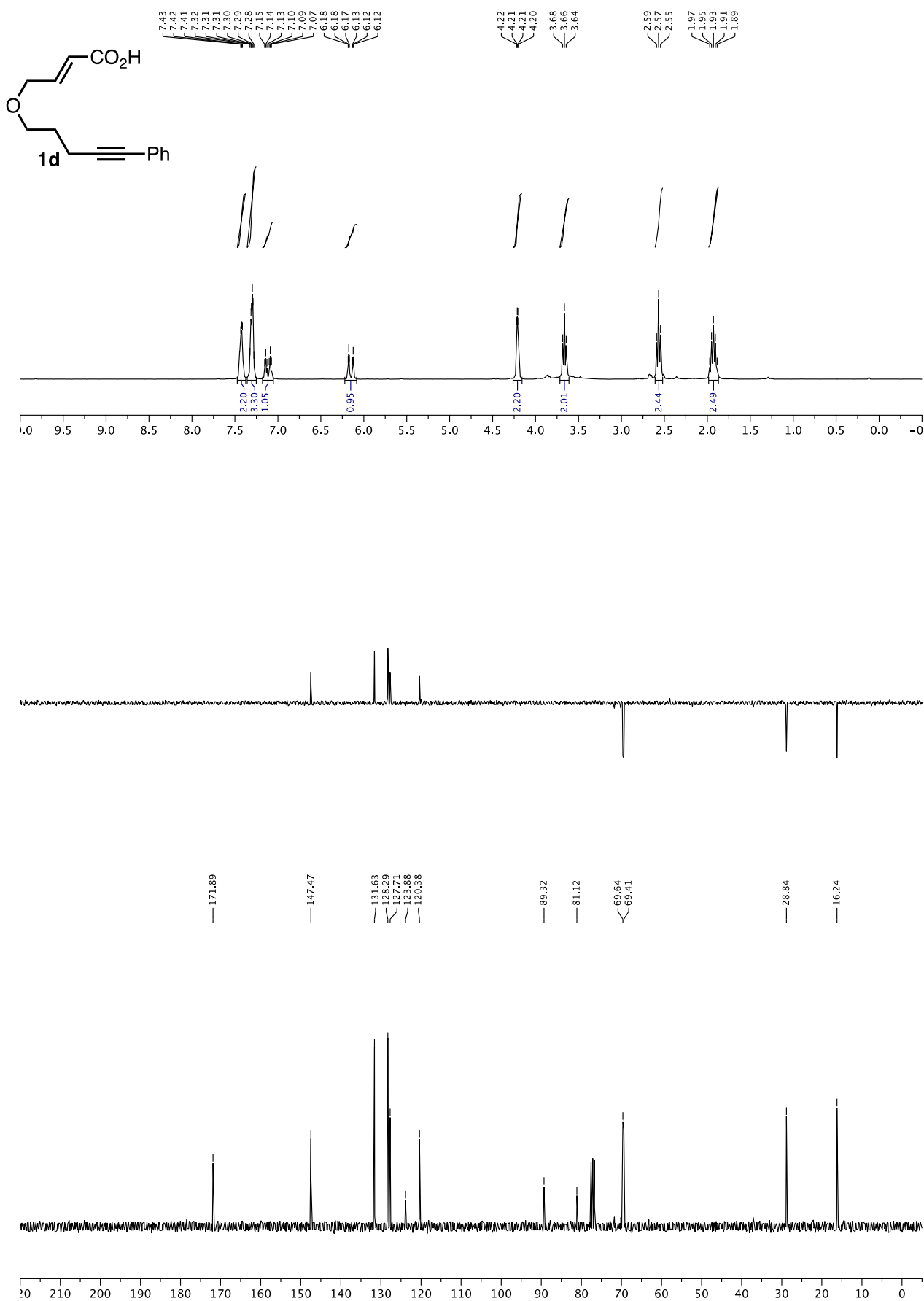
**Figure S8.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of *(E)*-4-((3-Phenylprop-2-yn-1-yl)oxy)but-2-enoic acid (**1a**)



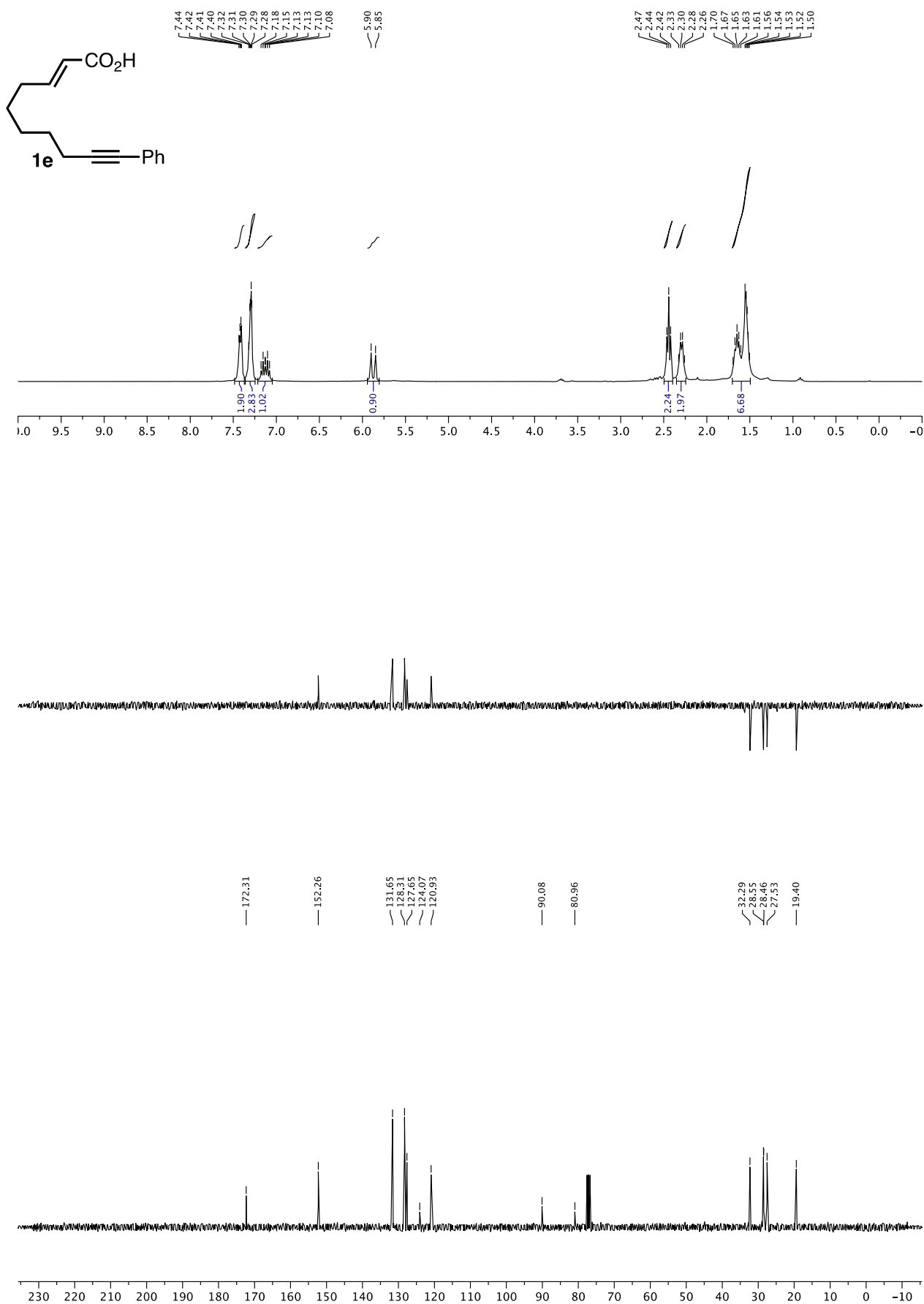
**Figure S9.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-4-((4-Phenylbut-3-yn-1-yl)oxy)but-2-enoic acid (**1b**)



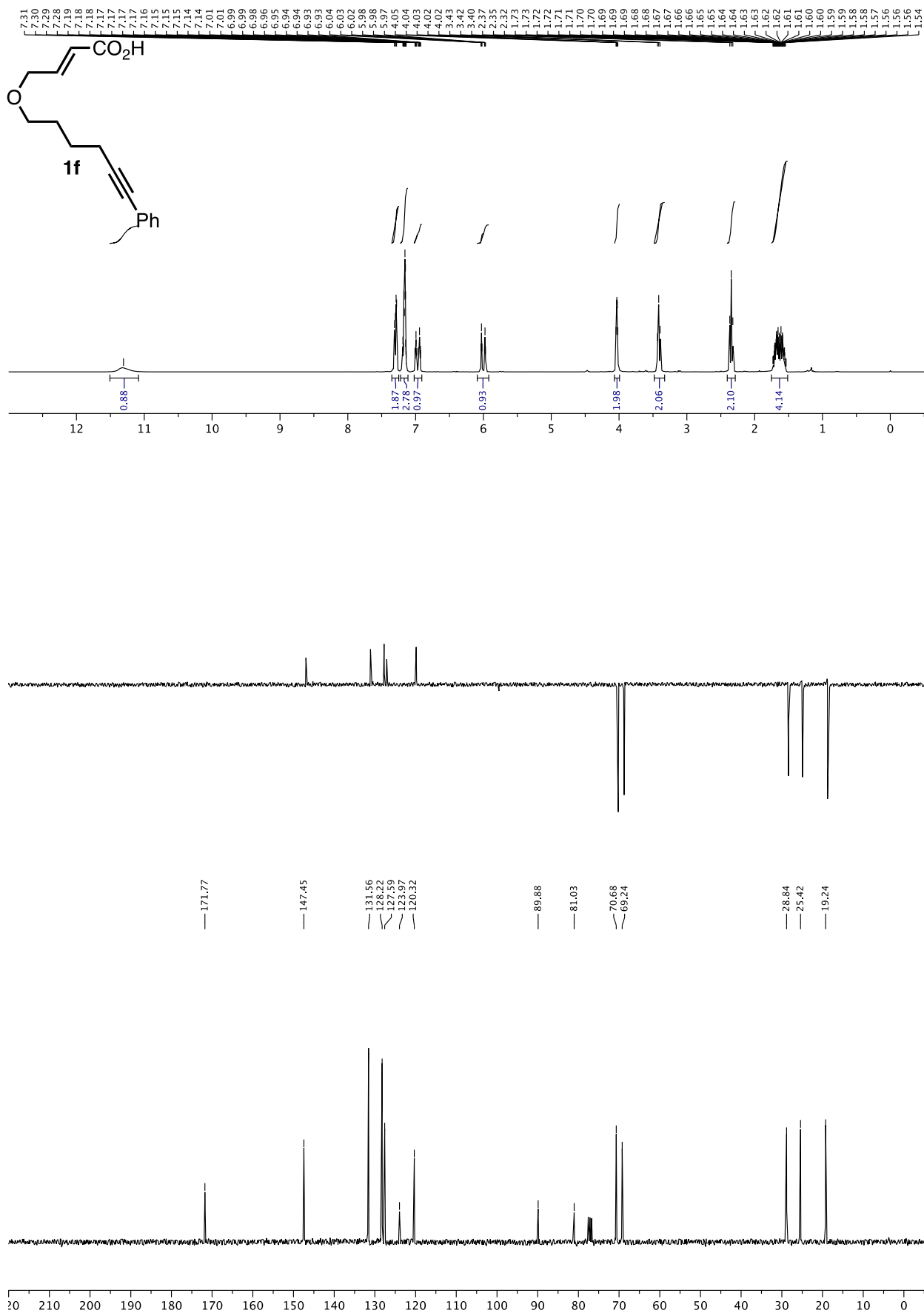
**Figure S10.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-9-Phenylnon-2-en-8-ynoic acid (**1c**)



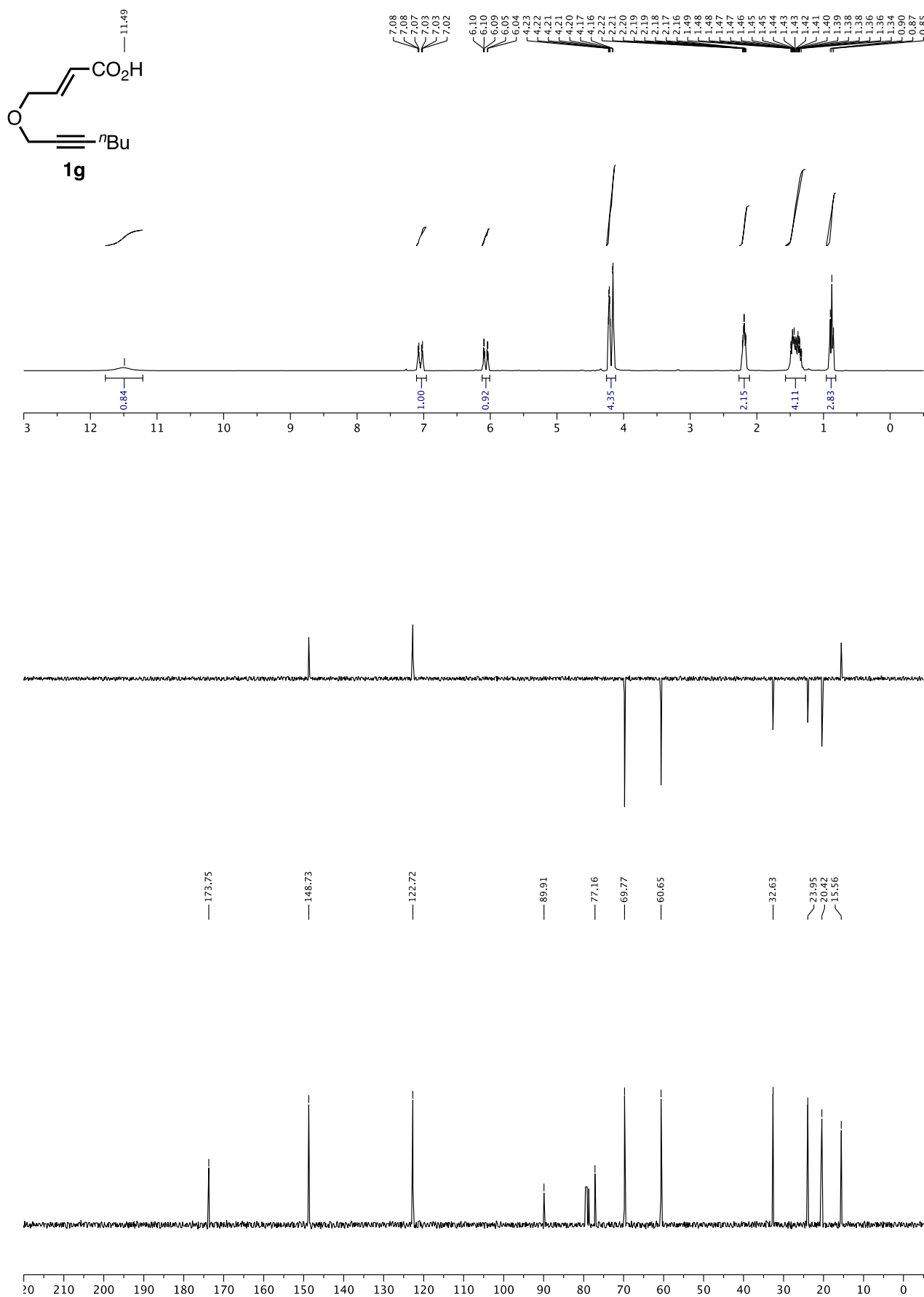
**Figure S11.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of *(E)*-4-((5-Phenylpent-4-yn-1-yl)oxy)but-2-enoic acid (**1d**)



**Figure S12.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-10-Phenyldec-2-en-9-ynoic acid (**1e**)

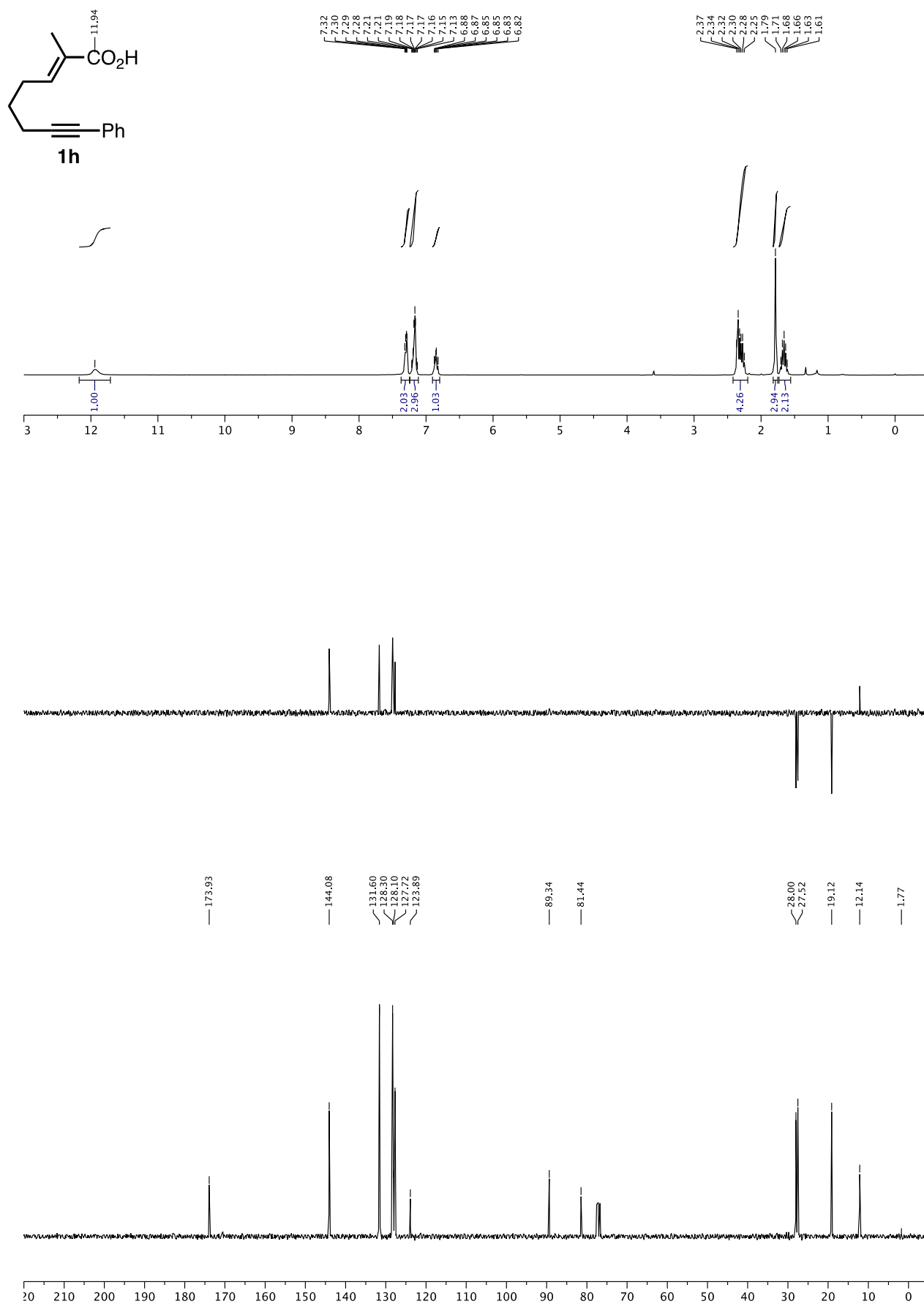


**Figure S13.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-4-((6-Phenylhex-5-yn-1-yl)oxy)but-2-enoic acid (**1f**)

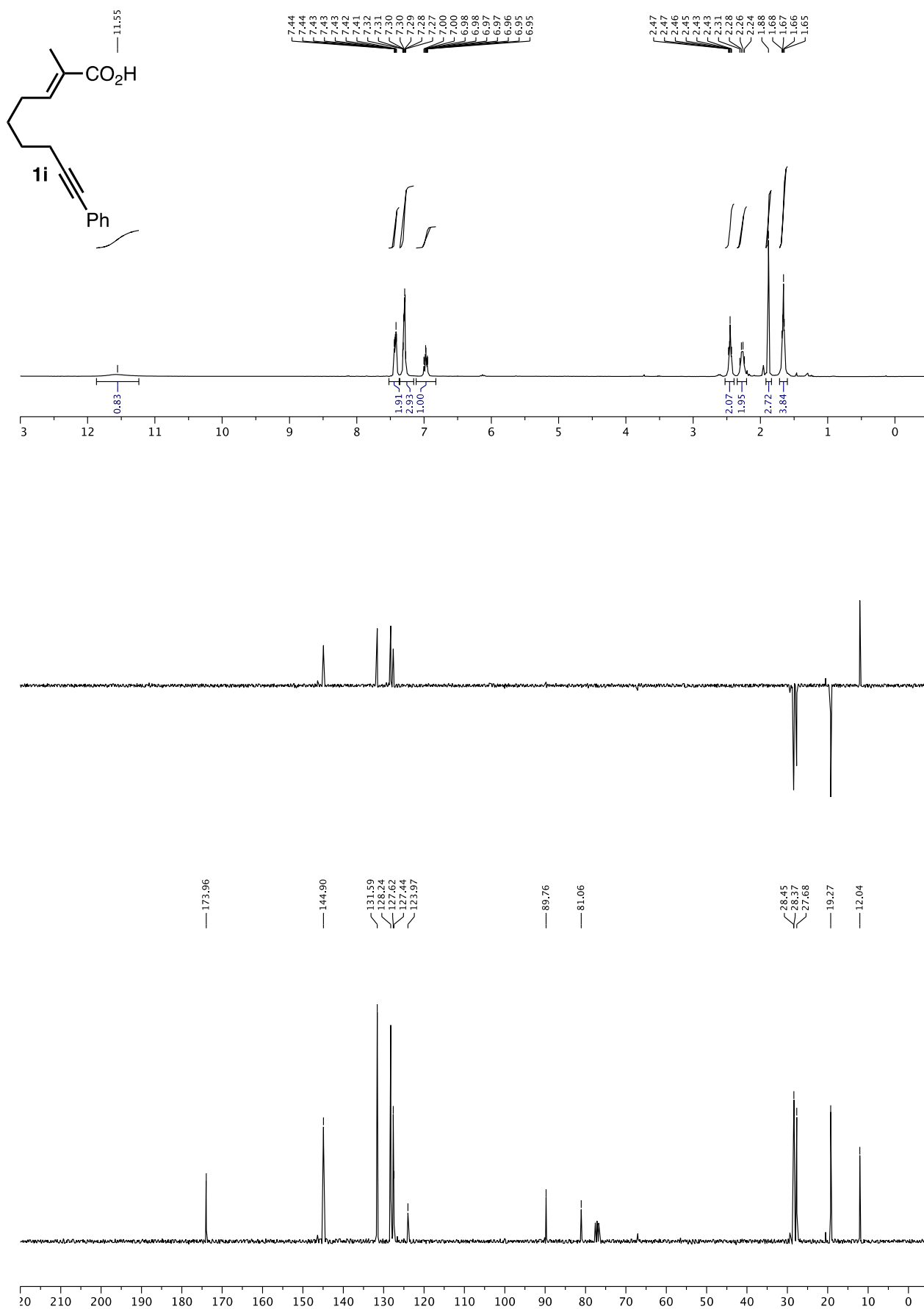


**Figure S14.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-4-(Hept-2-yn-1-yloxy)but-2-enoic acid (**1g**)

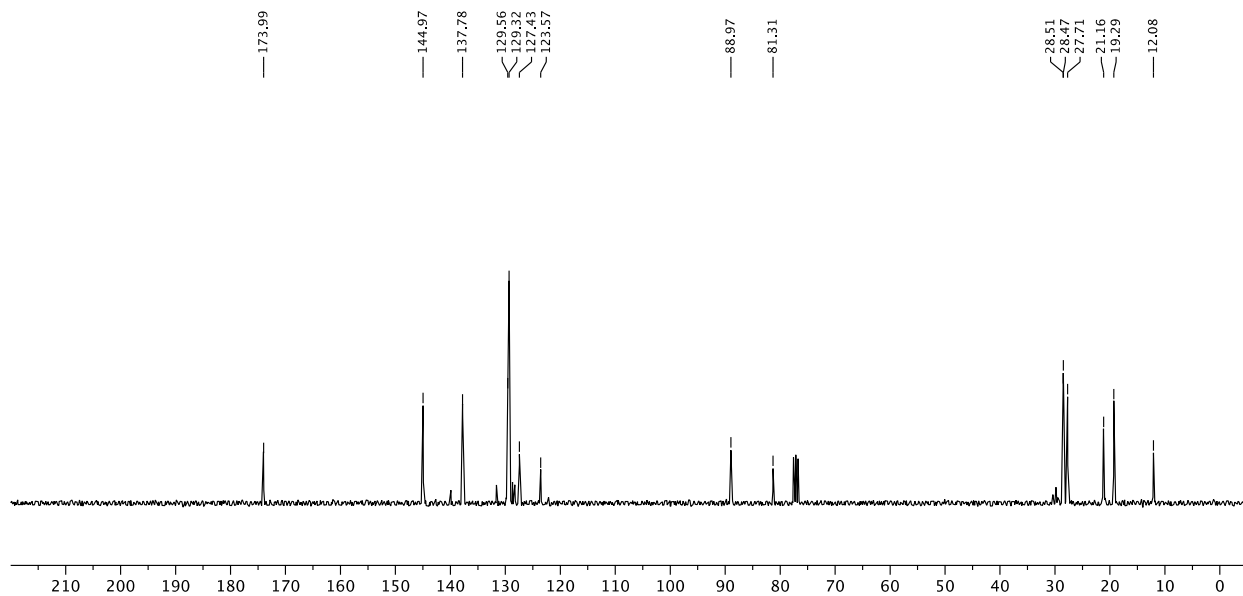
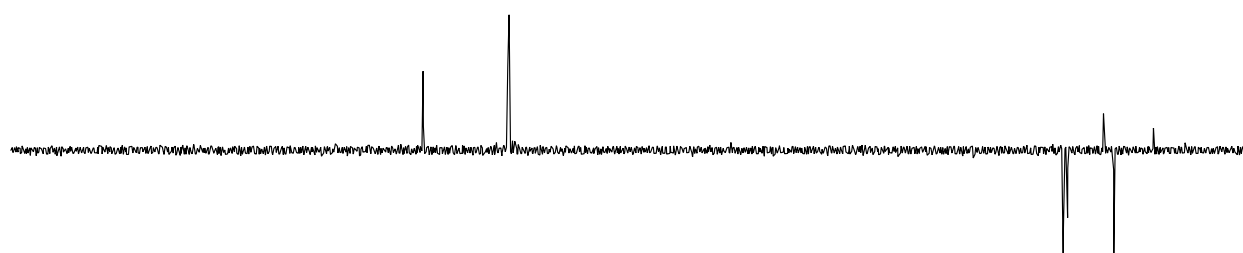
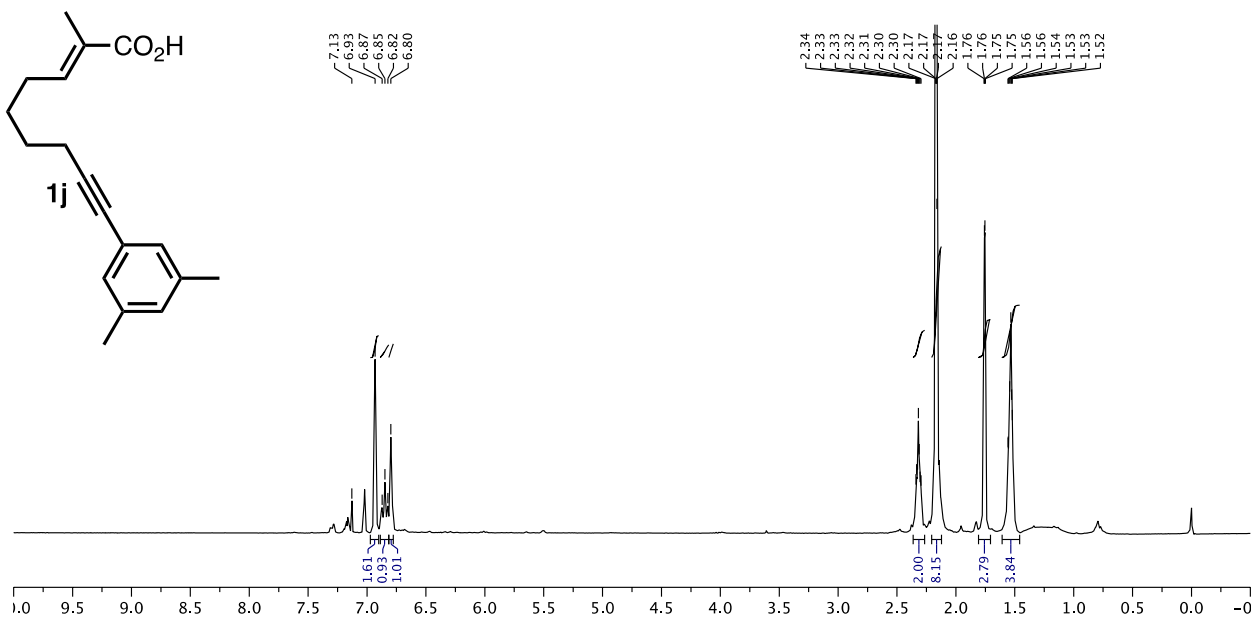




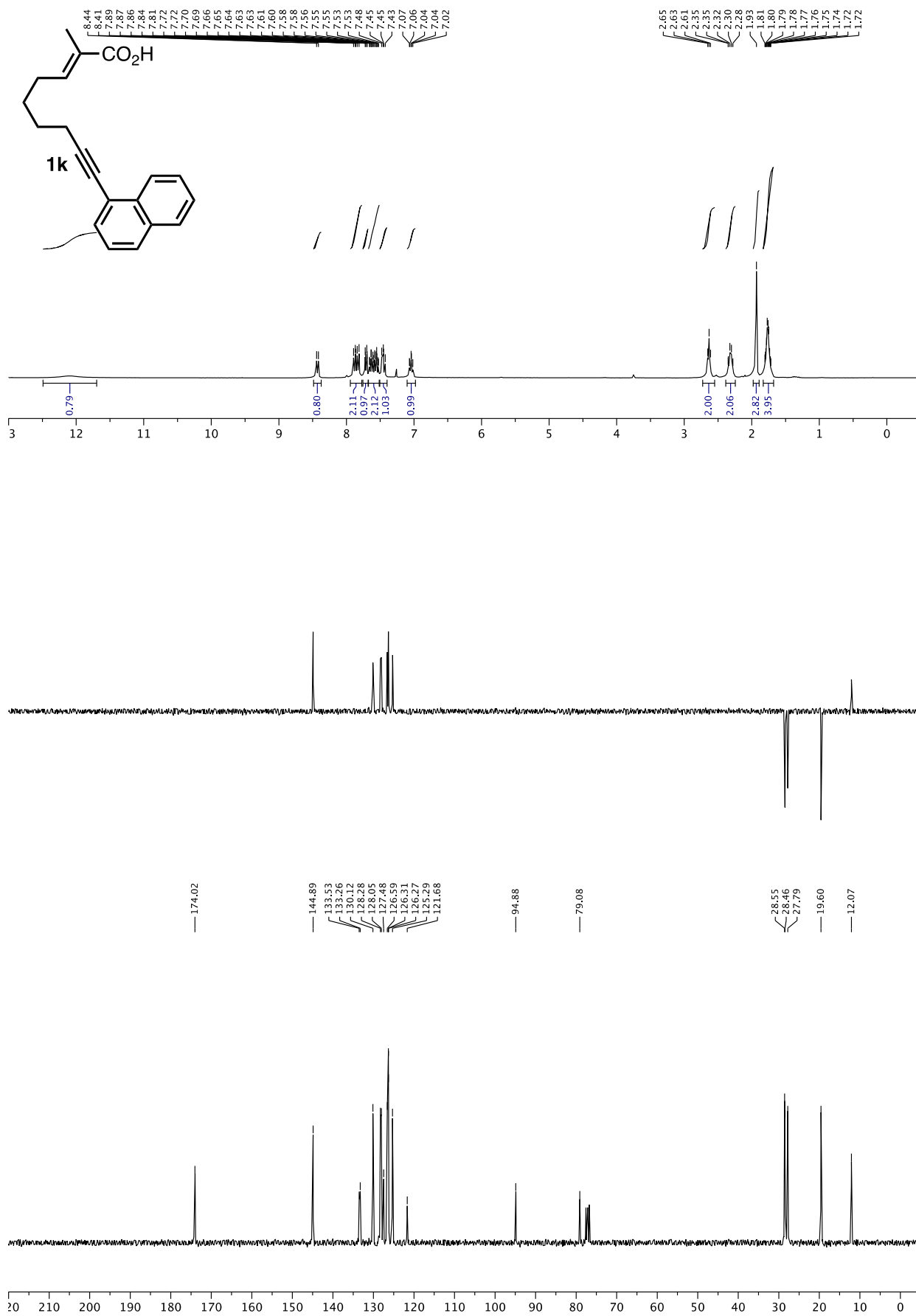
**Figure S15.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-2-Methyl-8-phenyloct-2-en-7-ynoic acid (**1h**)



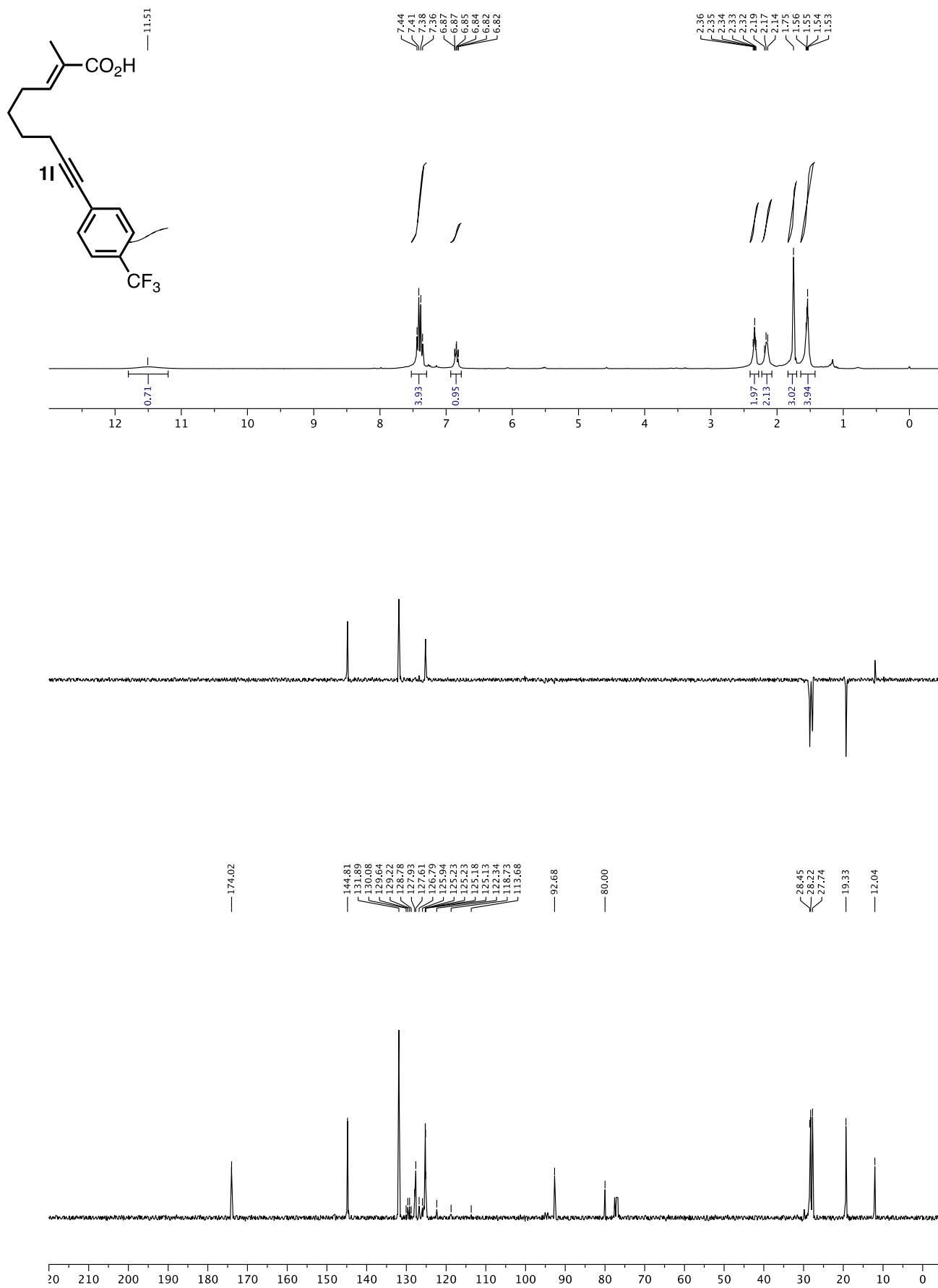
**Figure S16.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-2-Methyl-9-phenylnon-2-en-8-ynoic acid (**1i**)



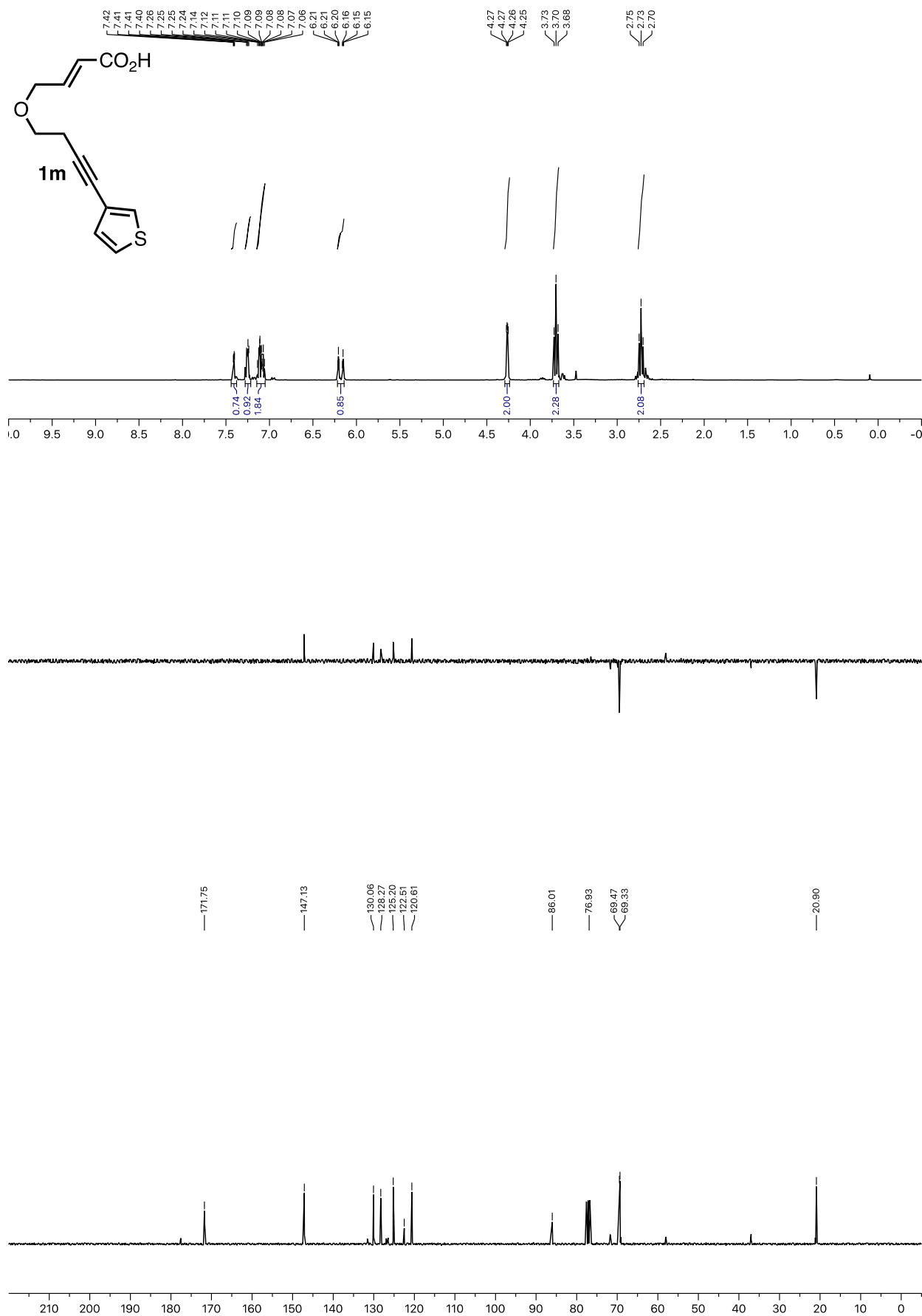
**Figure S17.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-9-(3,5-Dimethylphenyl)-2-methylnon-2-en-8-ynoic acid (**1j**)



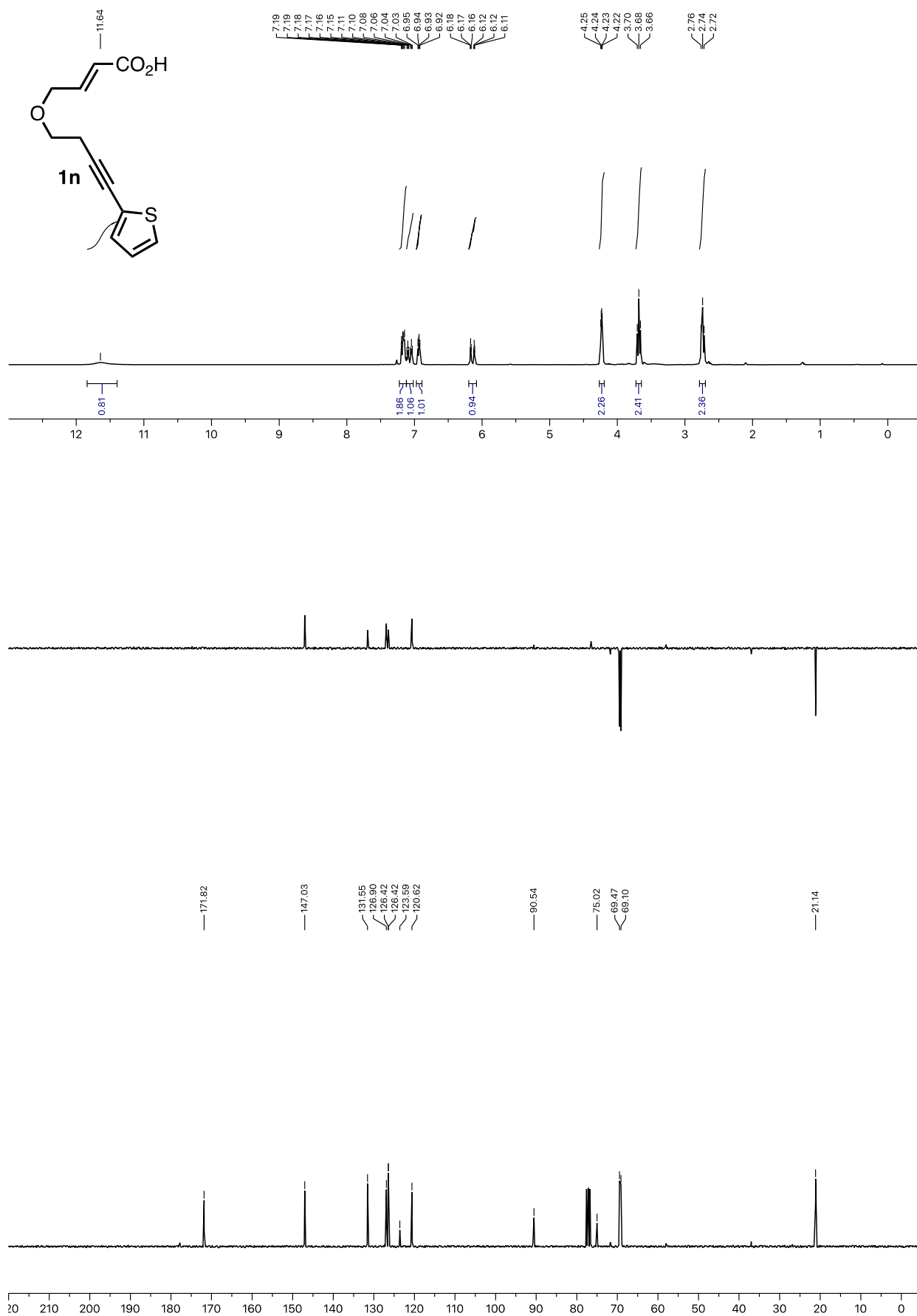
**Figure S18.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-2-Methyl-9-(naphthalen-1-yl)non-2-en-8-ynoic acid (**1k**)

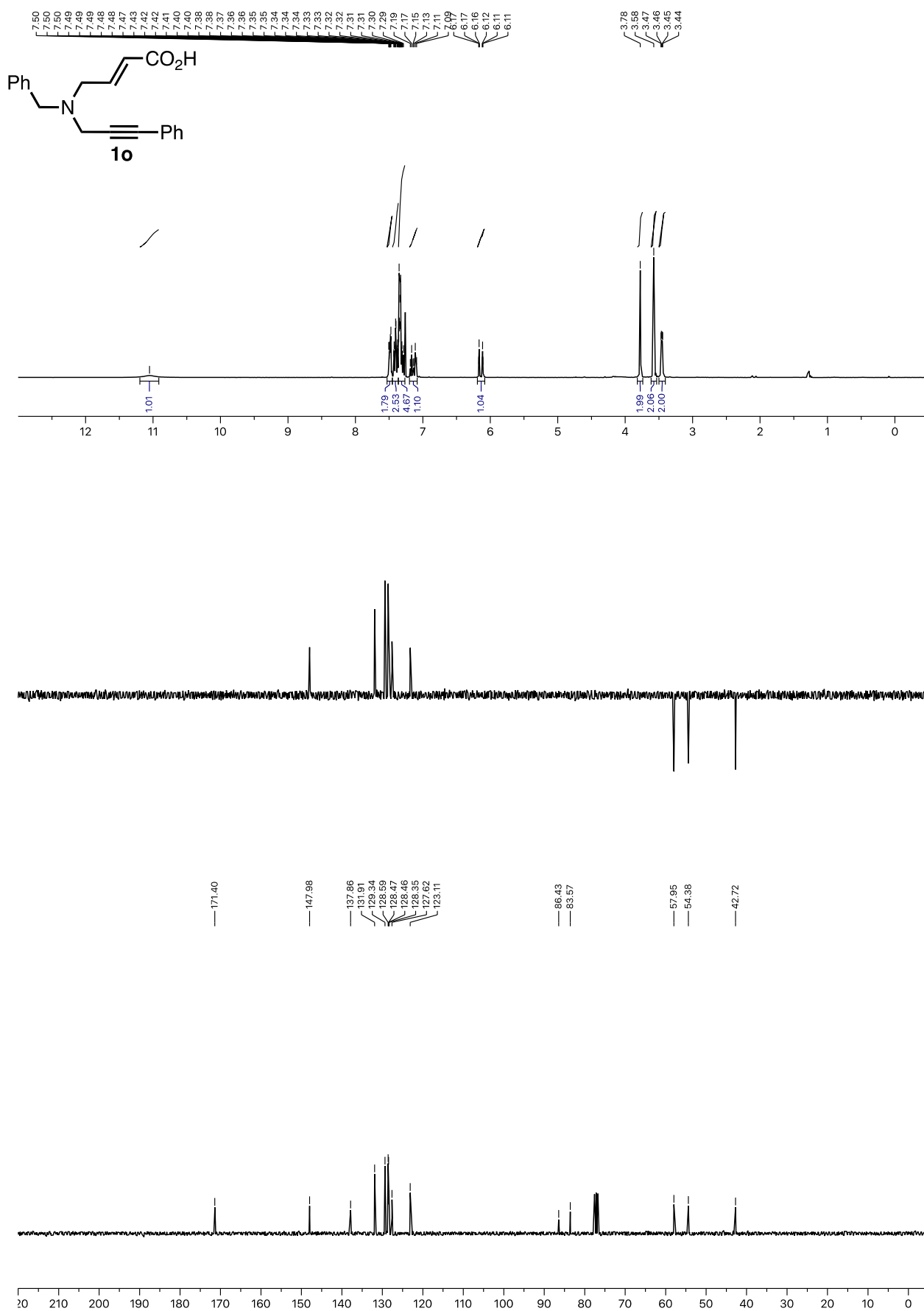


**Figure S19.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-2-Methyl-9-(4-(trifluoromethyl)phenyl)non-2-en-8-ynoic acid (**11**)



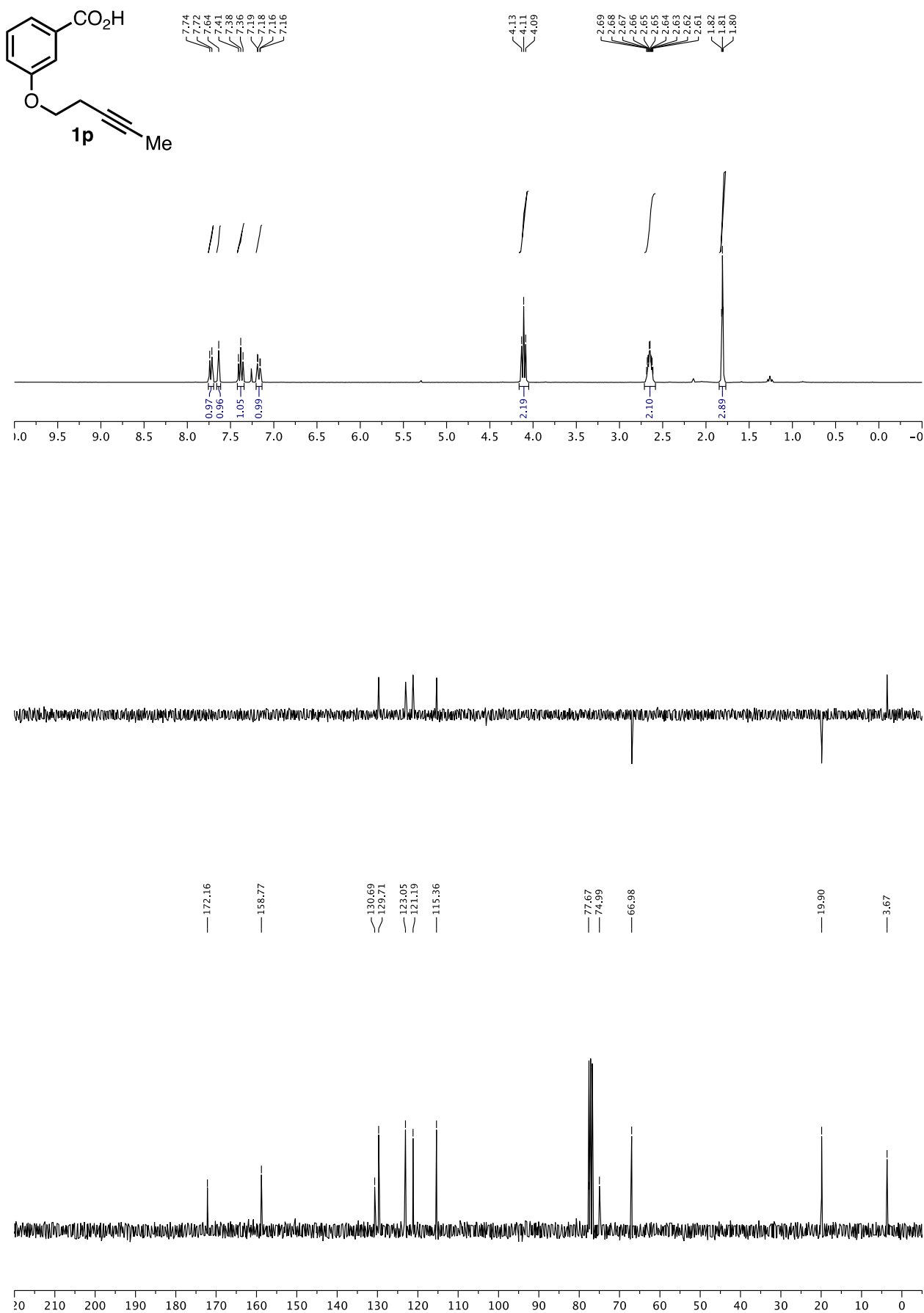
**Figure S20.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of *(E)*-4-((4-(Thiophen-3-yl)but-3-yn-1-yl)oxy)but-2-enoic acid (**1m**)



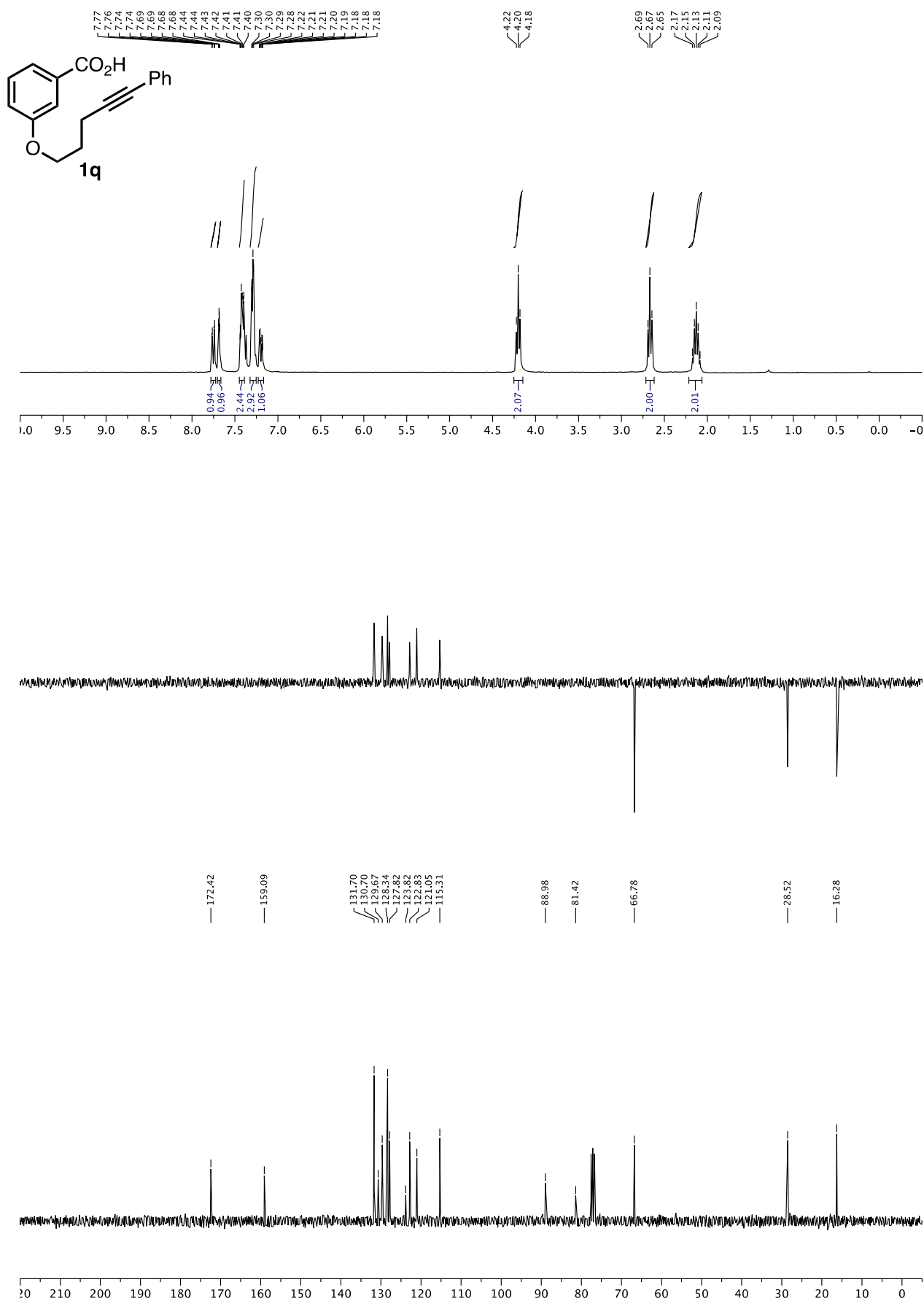


**Figure S22.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of (*E*)-4-(Benzyl(3-phenylprop-2-yn-1-yl)amino)but-2-enoic acid (**1o**)

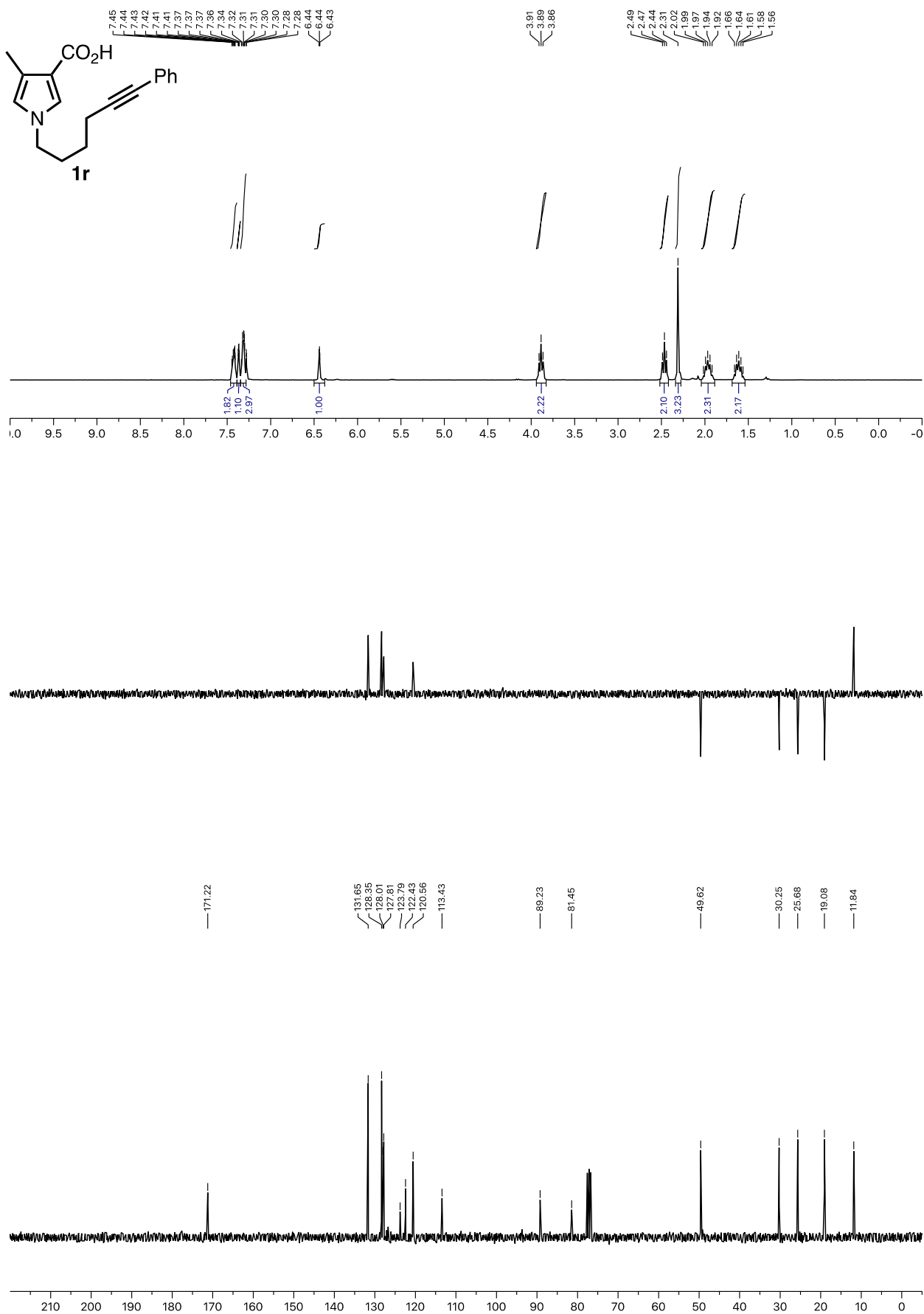




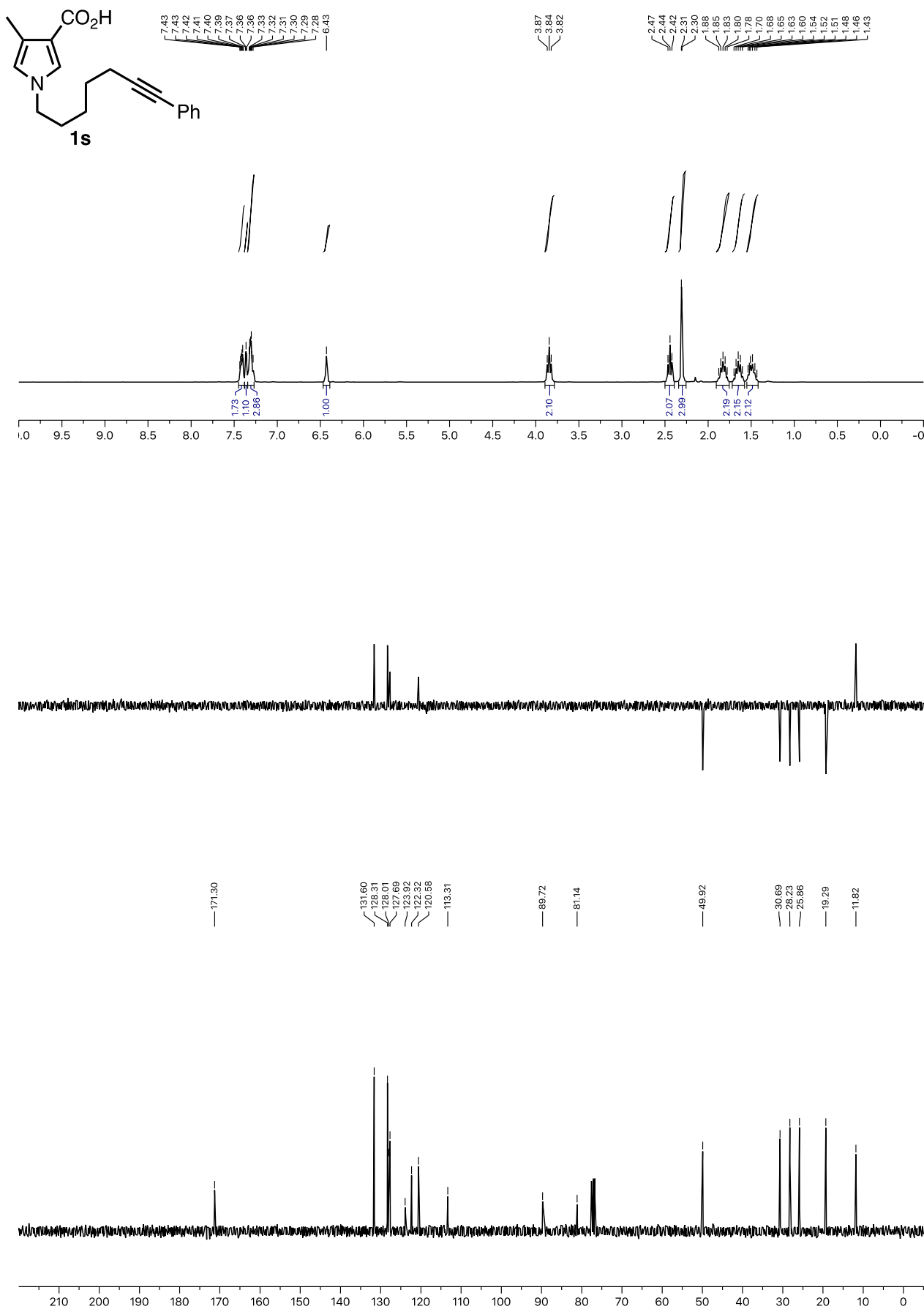
**Figure S23.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 3-(Pent-3-yn-1-yloxy)benzoic acid (**1p**)



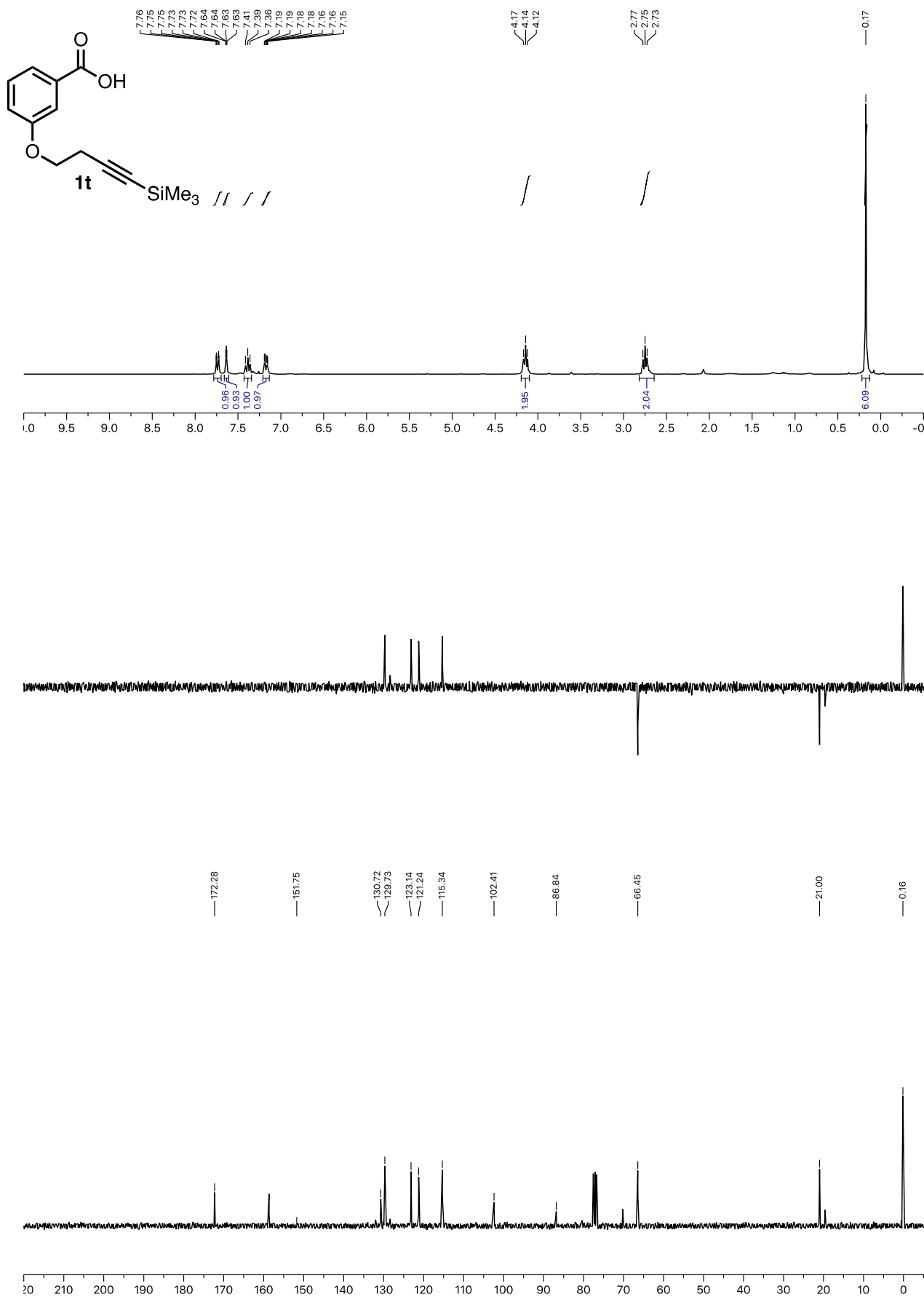
**Figure S24.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 3-((5-Phenylpent-4-yn-1-yl)oxy)benzoic acid (**1q**)



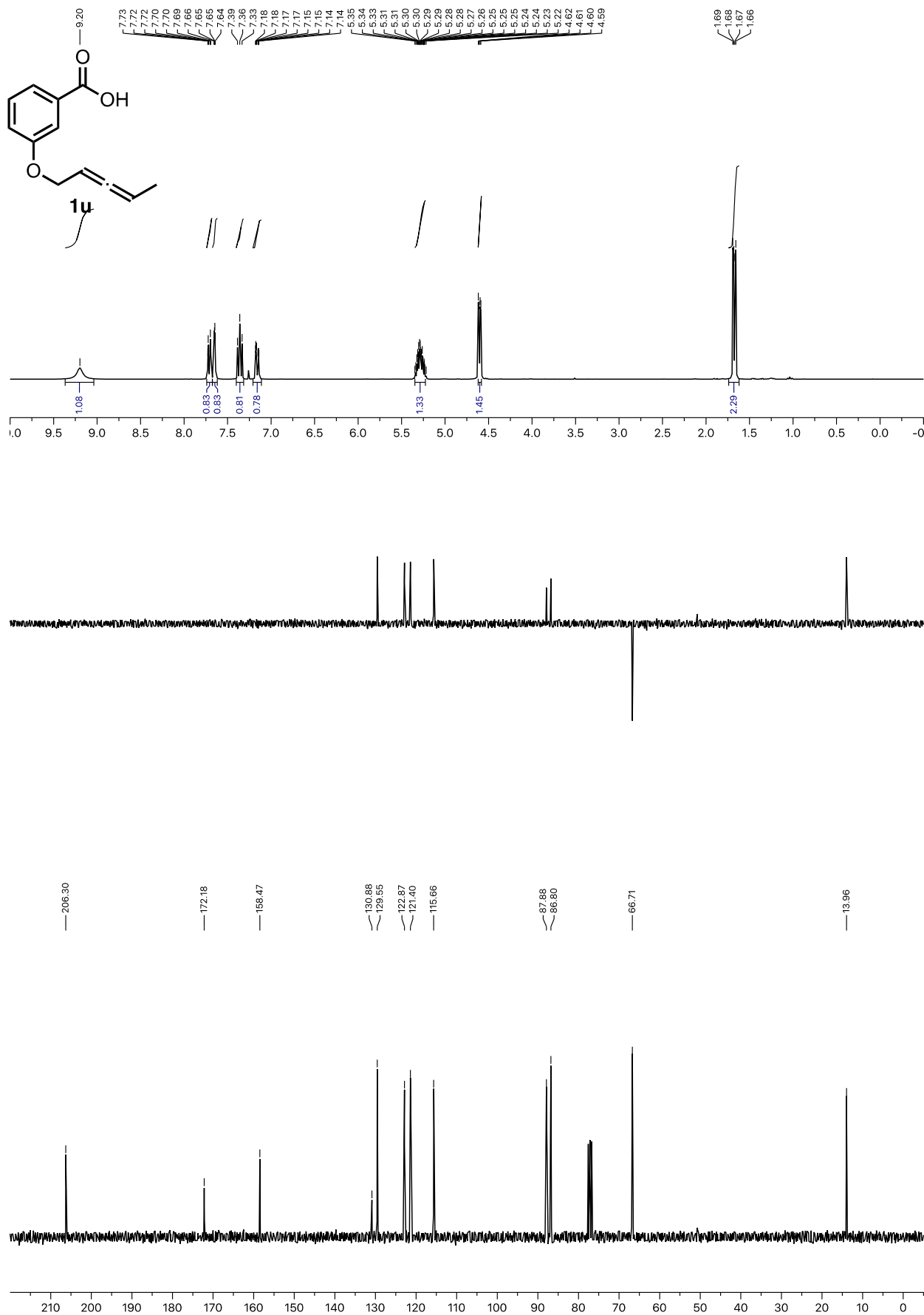
**Figure S25.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-(6-phenylhex-5-yn-1-yl)-1H-pyrrole-3-carboxylic acid (**1r**)



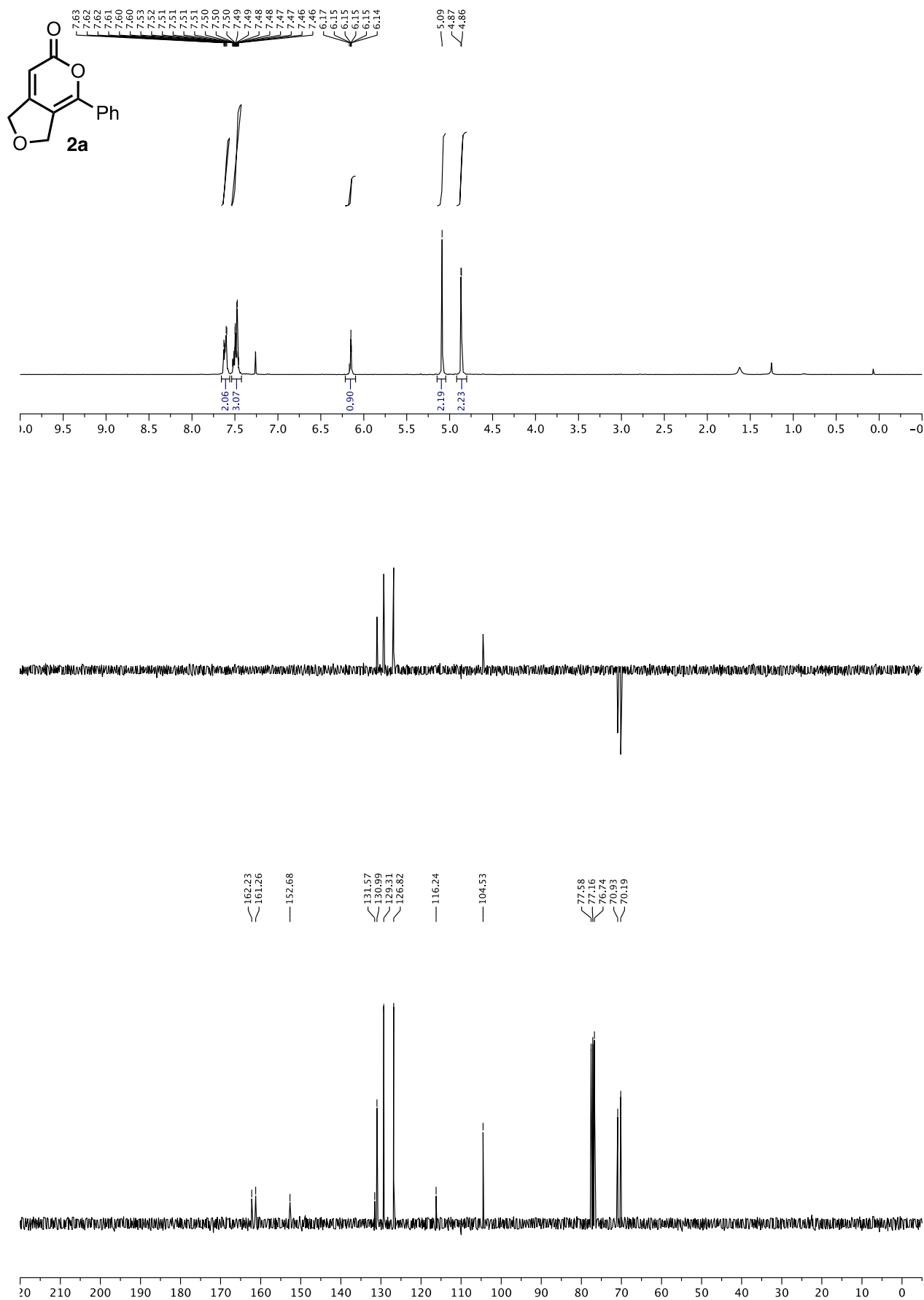
**Figure S26.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-(7-phenylhept-6-yn-1-yl)-1H-pyrrole-3-carboxylic acid (**1s**)



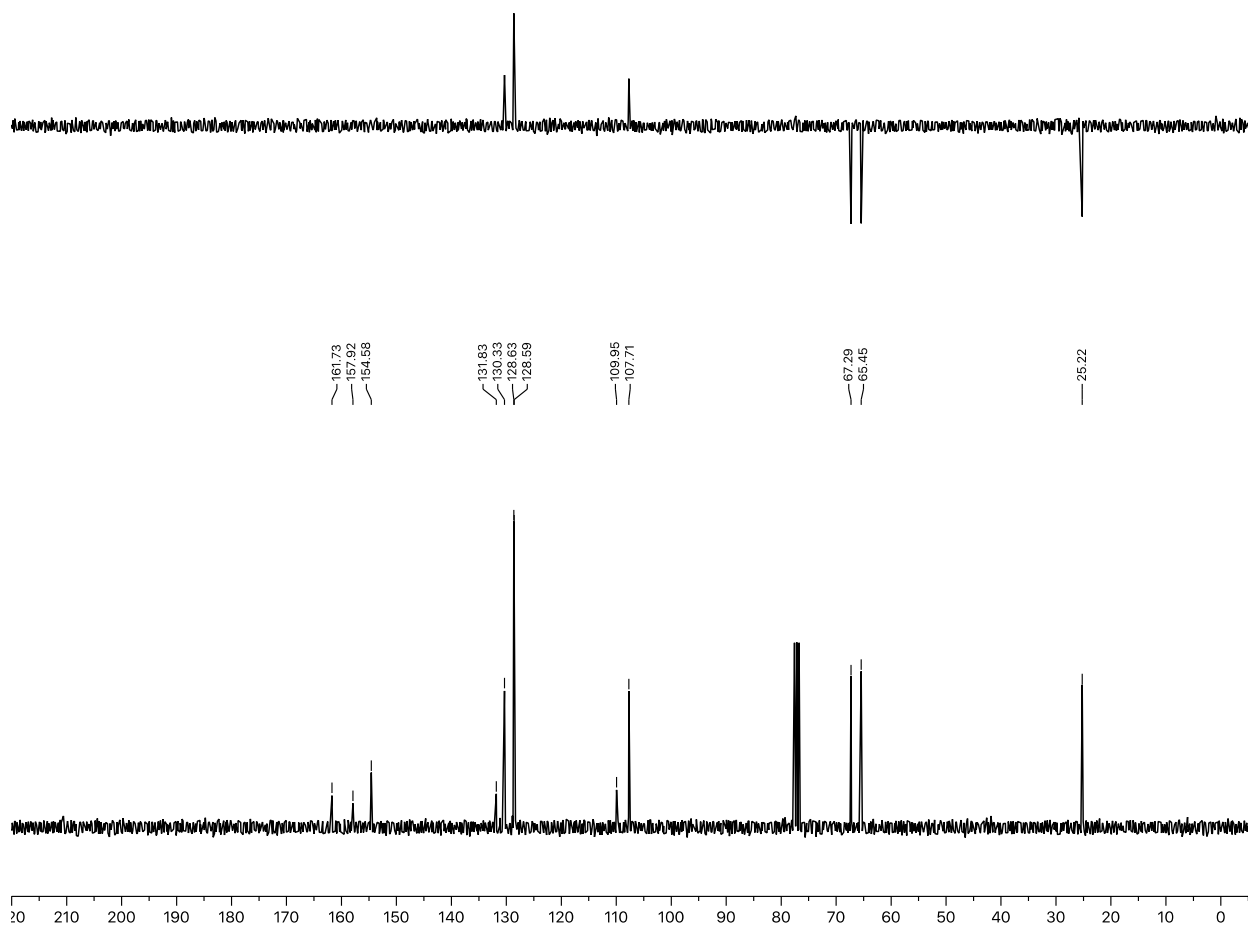
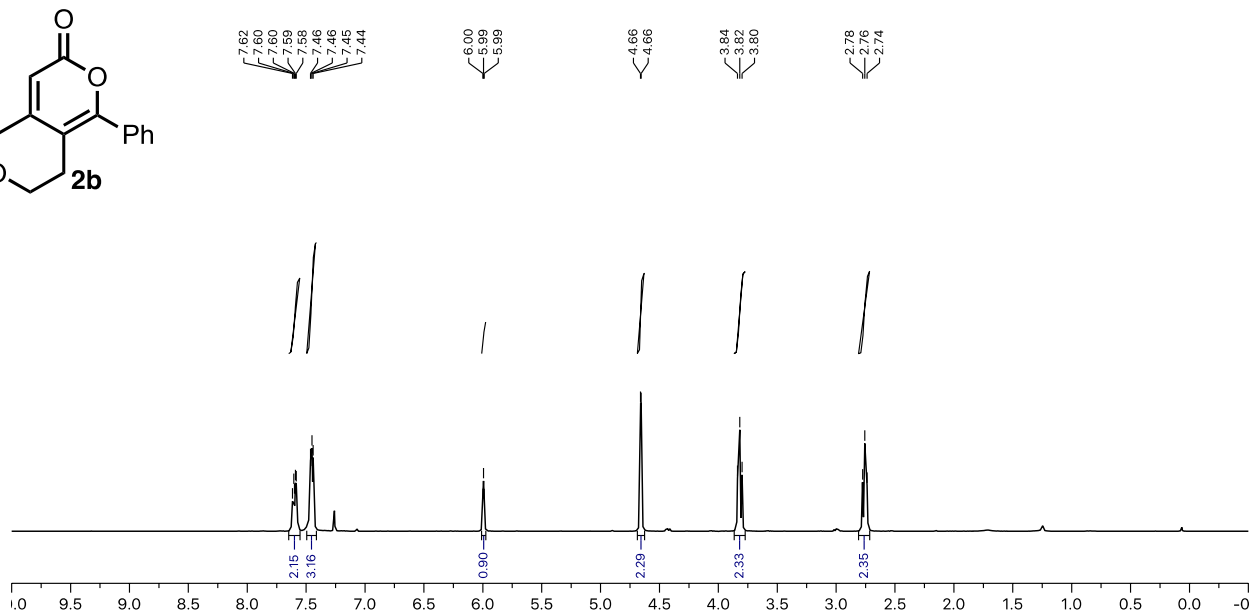
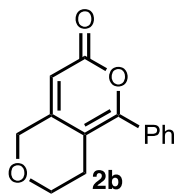
**Figure S27.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 3-((4-(Trimethylsilyl)but-3-yn-1-yl)oxy)benzoic acid (**1t**)



**Figure S28.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 3-(Penta-2,3-dien-1-yloxy)benzoic acid (**1u**)

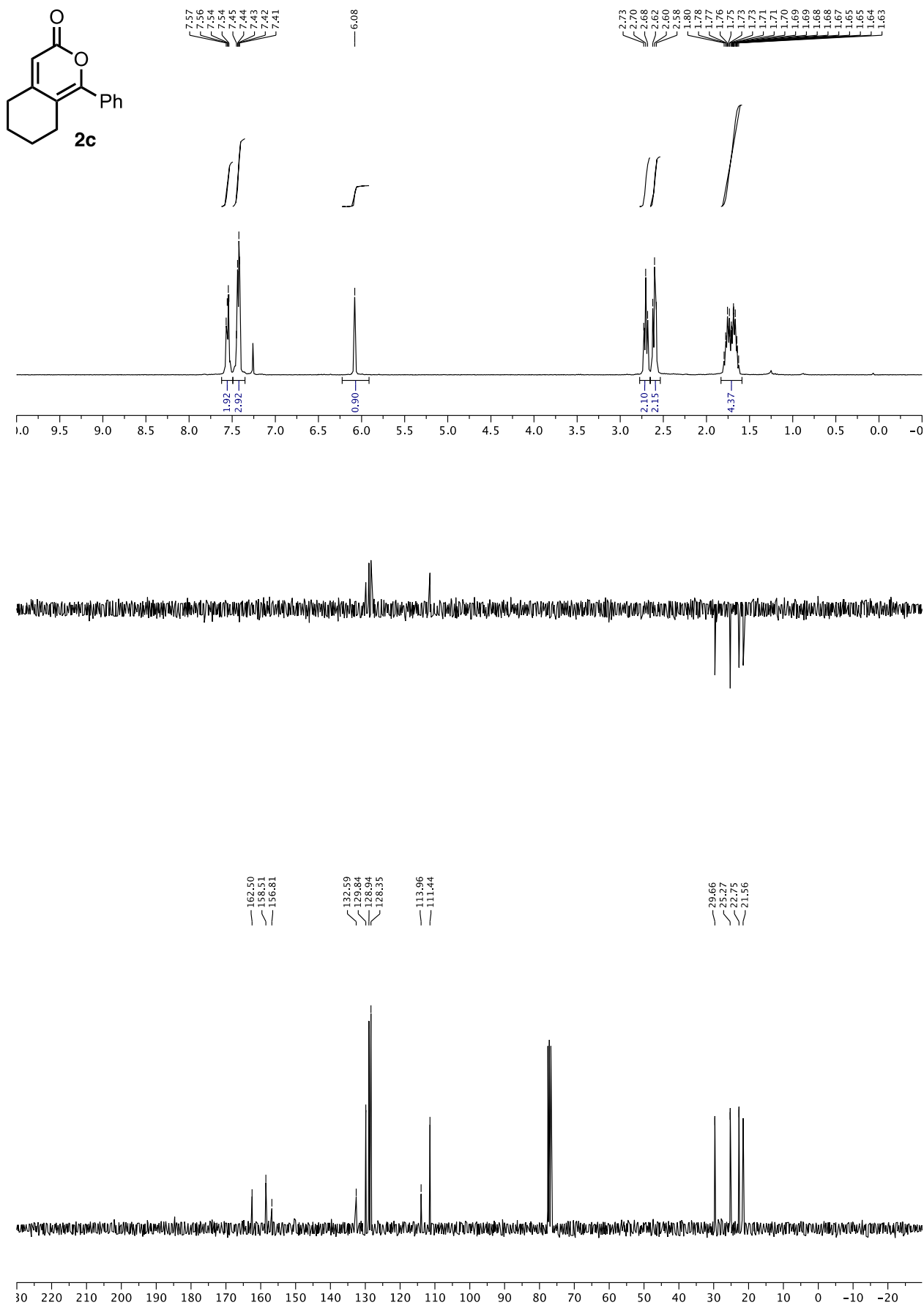


**Figure S29.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Phenyl-3H-furo[3,4-c]pyran-6(1H)-one (**2a**)

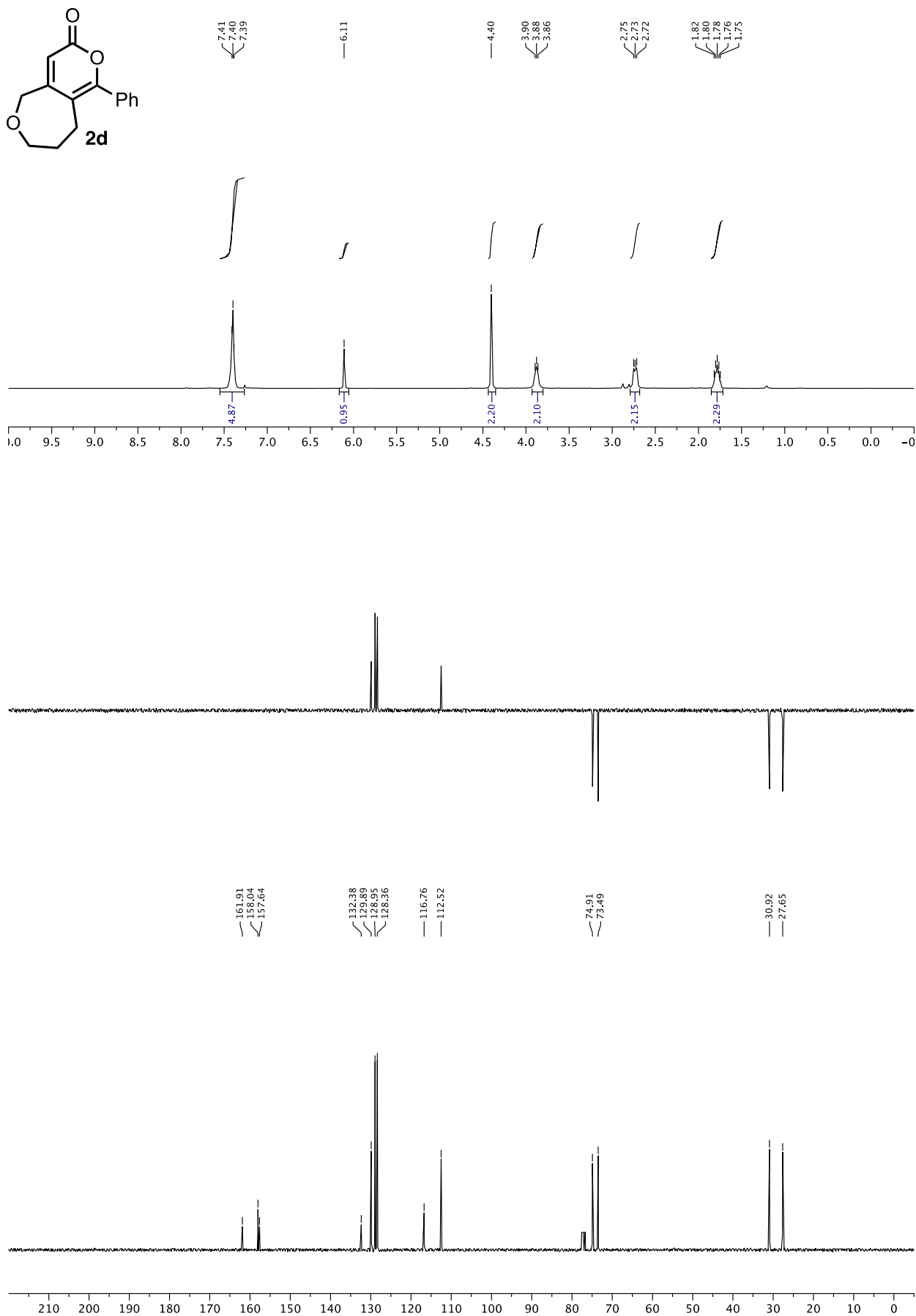


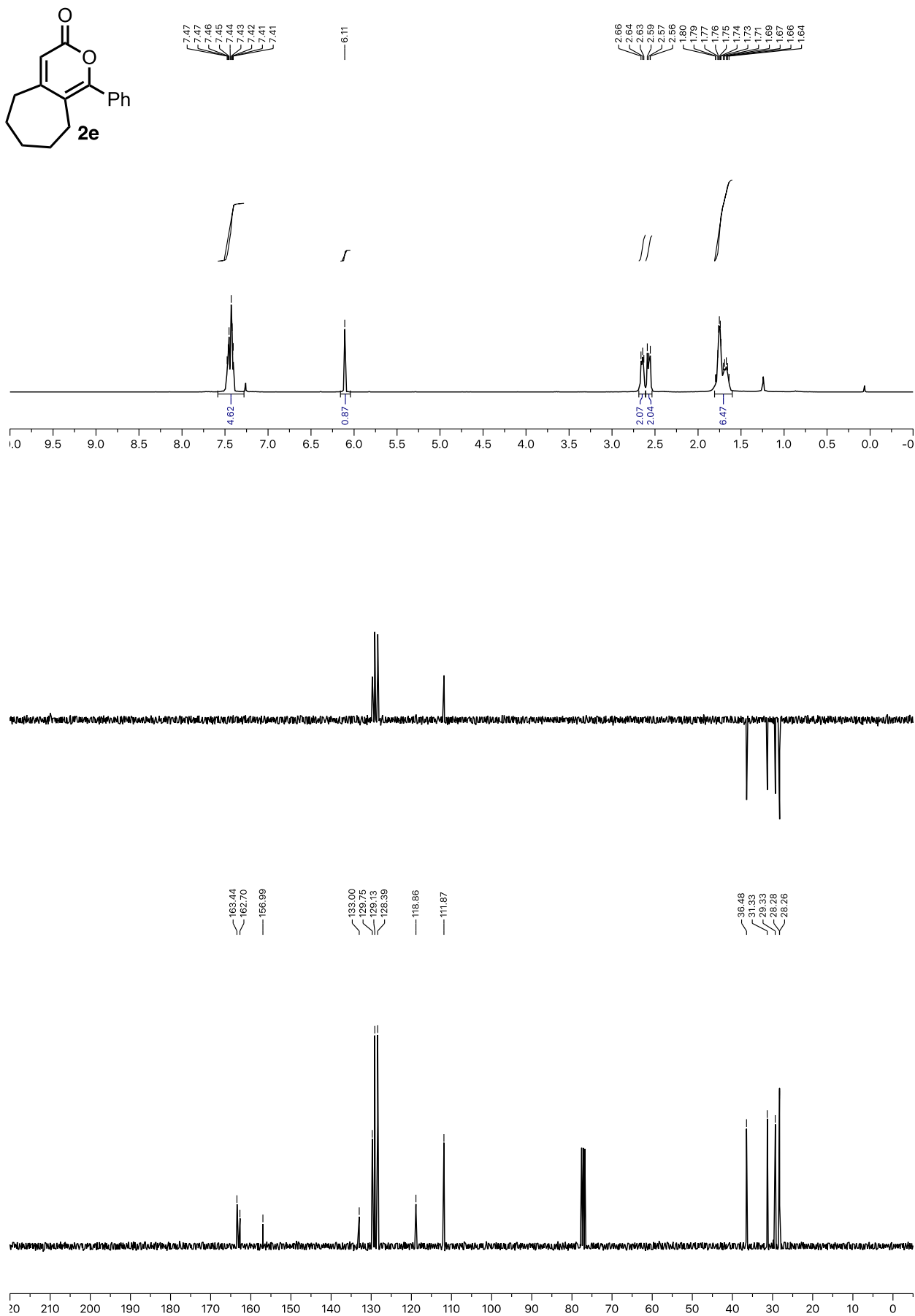
**Figure S30.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-Phenyl-7,8-dihydropyrano[4,3-c]pyran-3(5H)-one (**2b**)



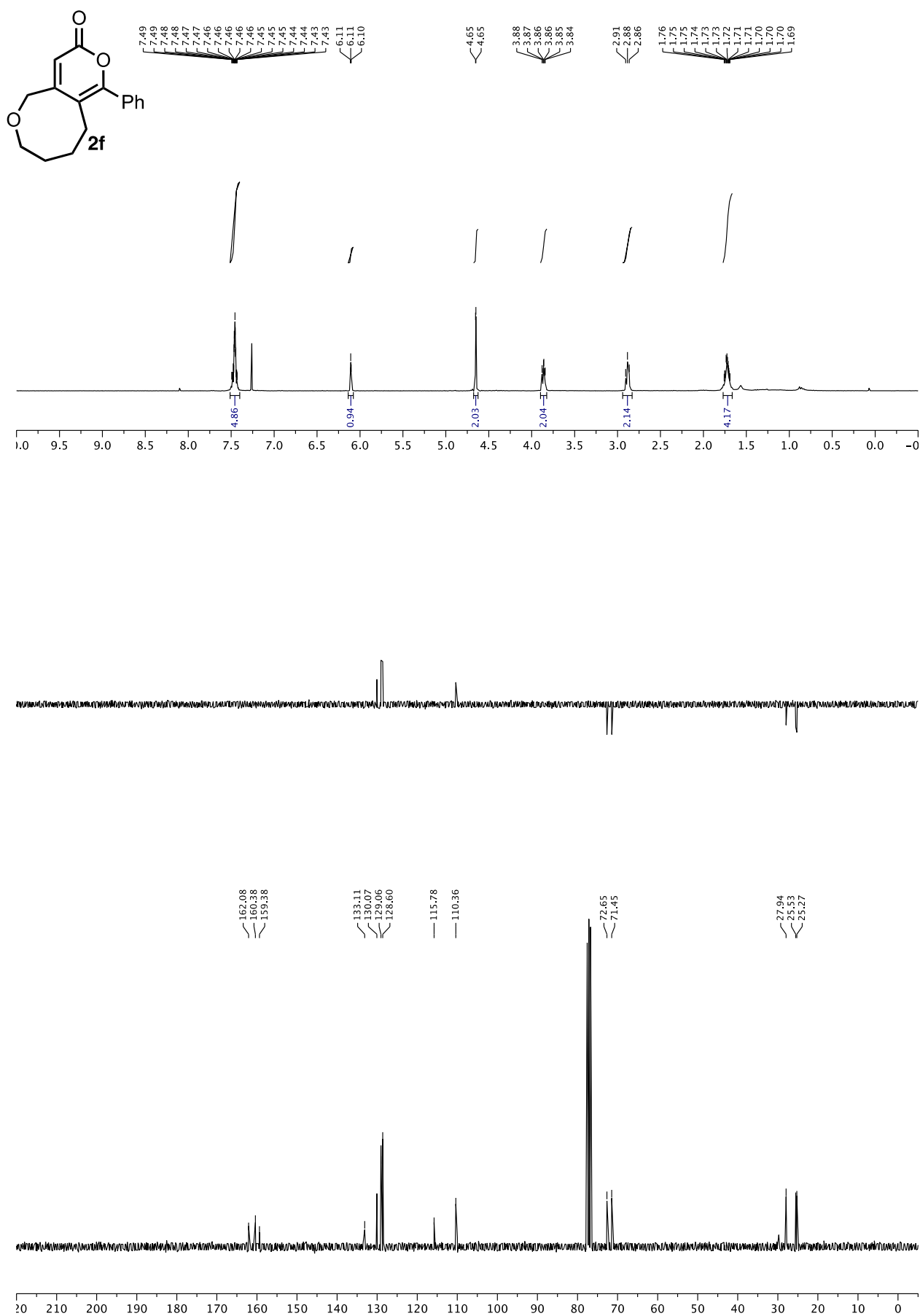


**Figure S31.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-Phenyl-5,6,7,8-tetrahydro-3H-isochromen-3-one (**2c**)

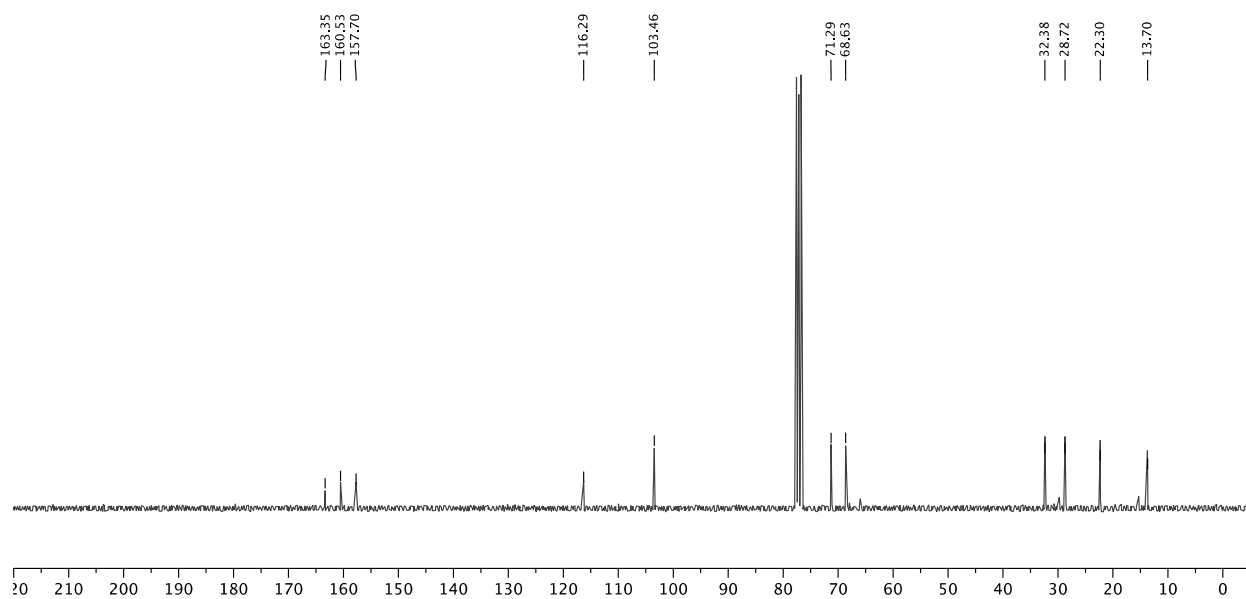
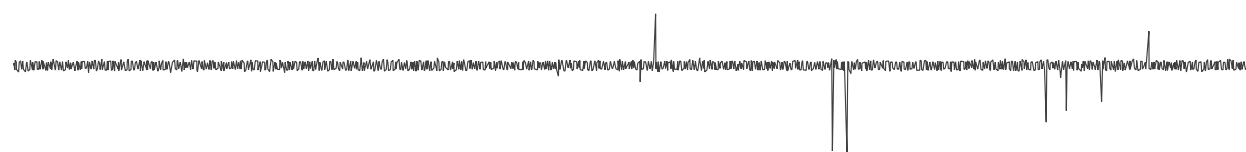
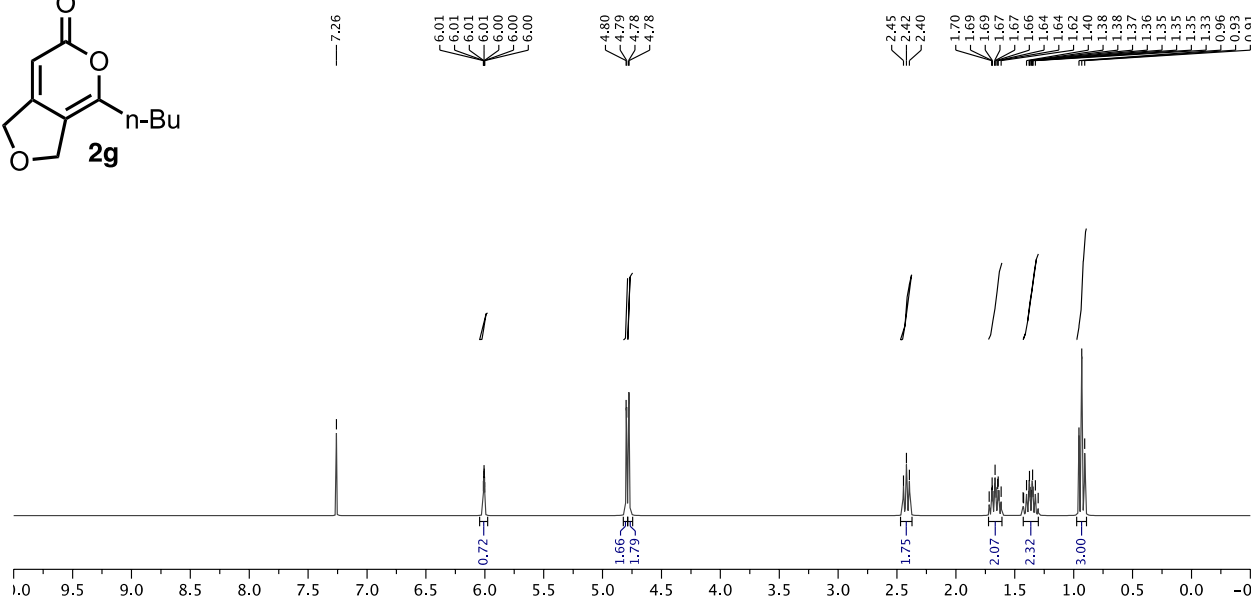
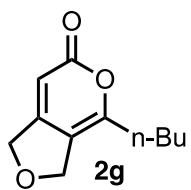




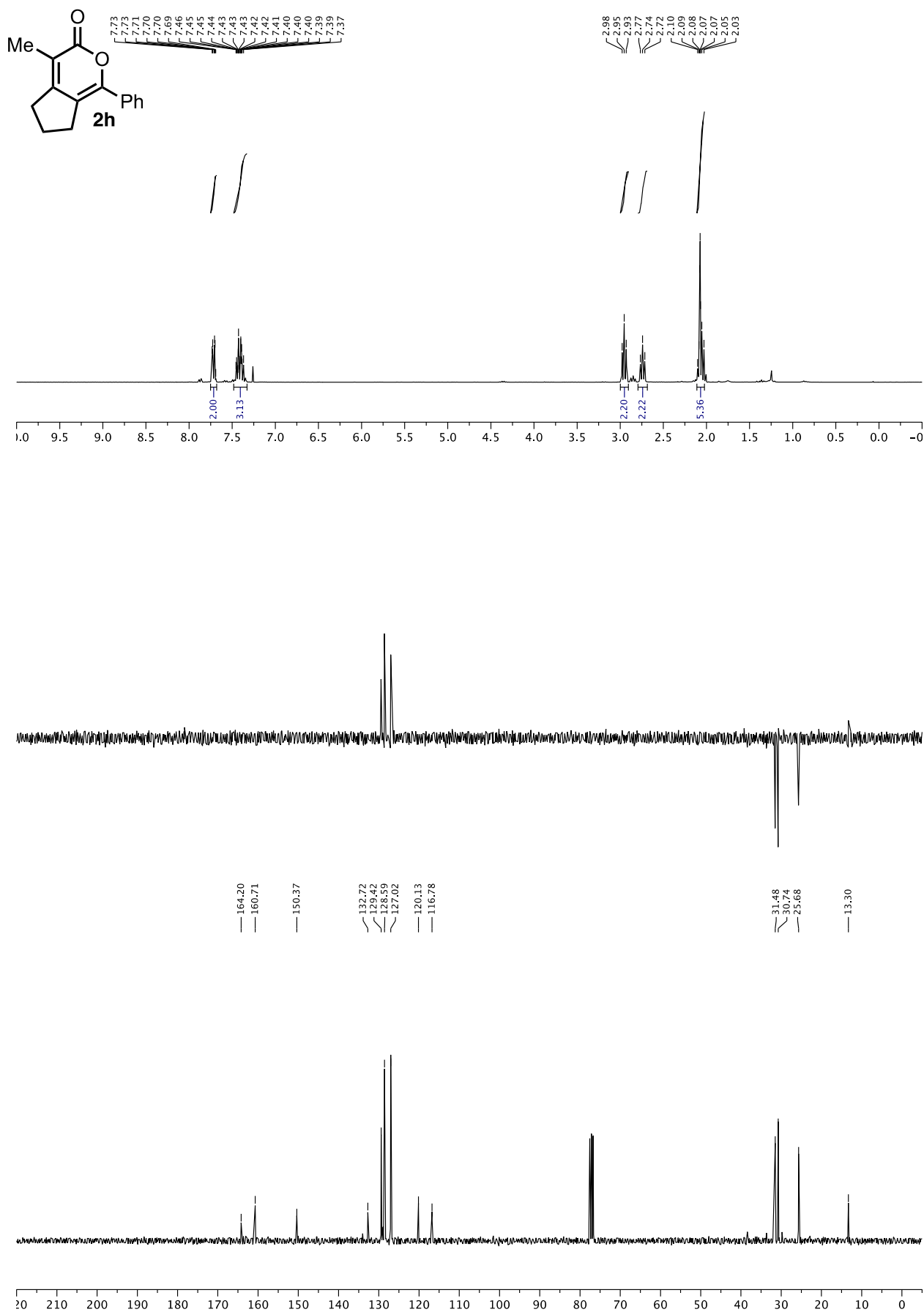
**Figure S33.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-Phenyl-6,7,8,9-tetrahydrocyclohepta[*c*]pyran-3(5*H*)-one (**2e**)



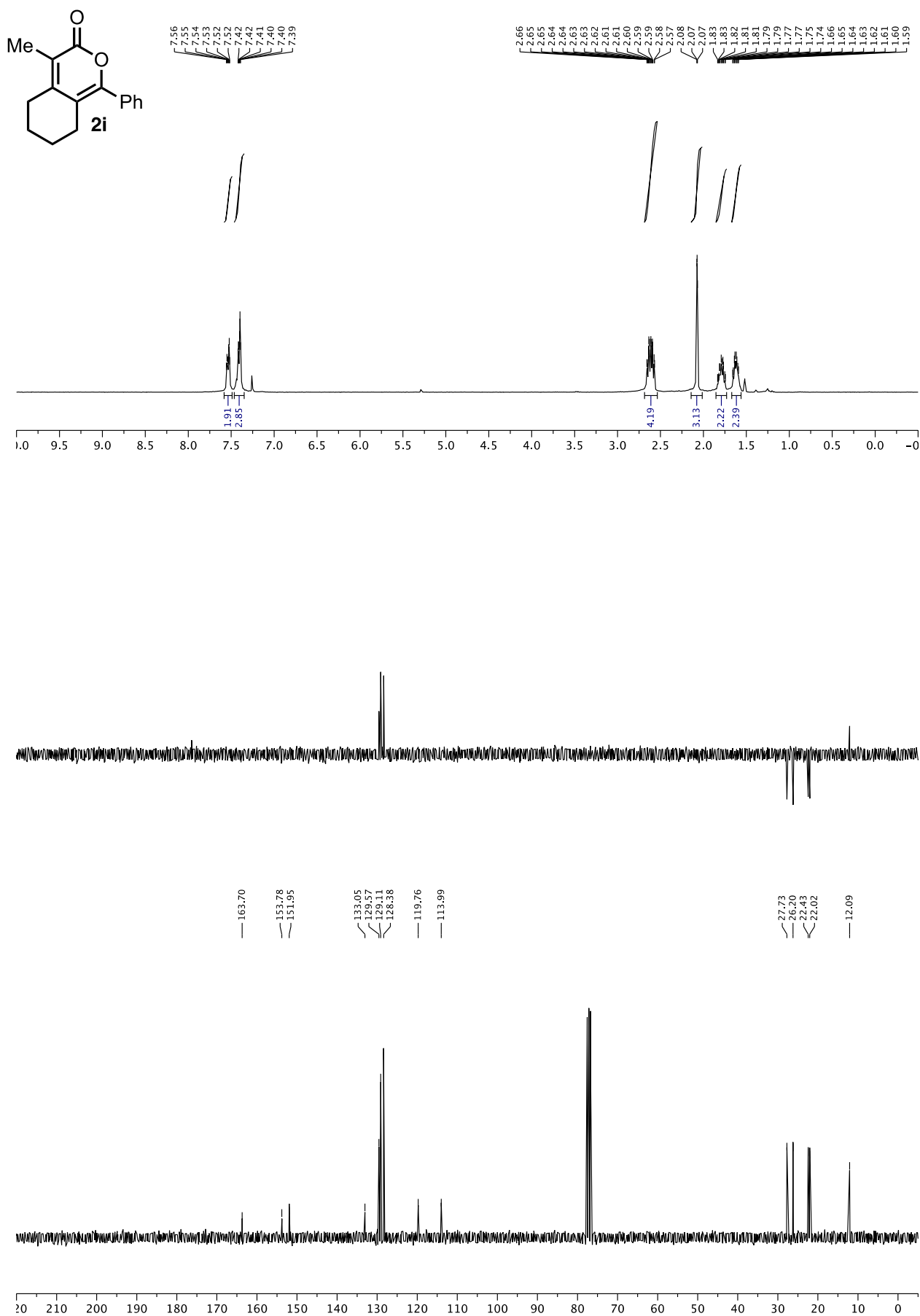
**Figure S34.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-Phenyl-7,8,9,10-tetrahydropyrano[4,3-c]oxocin-3(5H)-one (**2f**)



**Figure S35.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Butyl-3H-furo[3,4-c]pyran-6(1H)-one (**2g**)



**Figure S36.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-phenyl-6,7-dihydrocyclopenta [c]pyran-3(5H)-one (**2h**)



**Figure S37.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-phenyl-5,6,7,8-tetrahydro-3H-isochromen-3-one (**2i**)

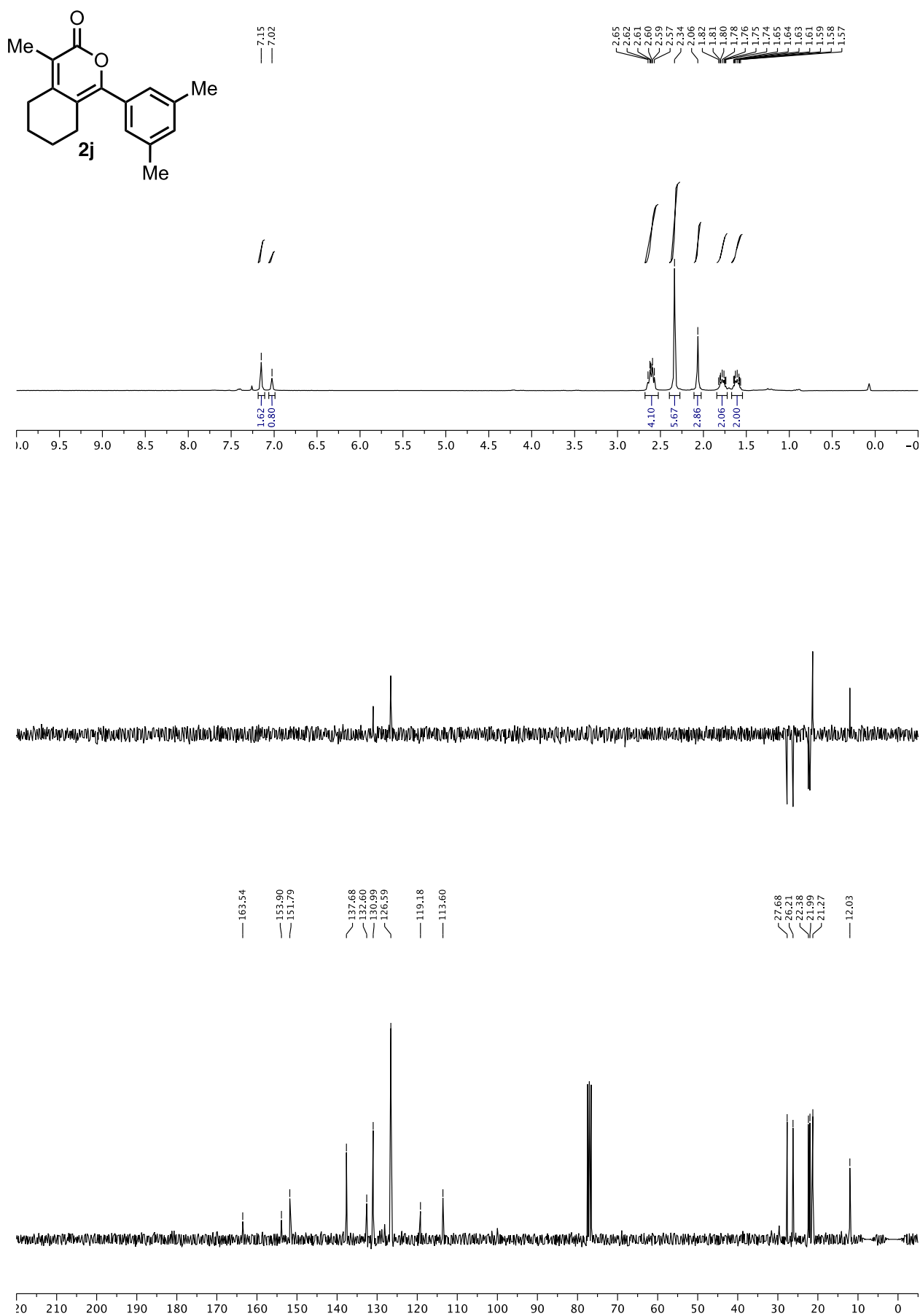
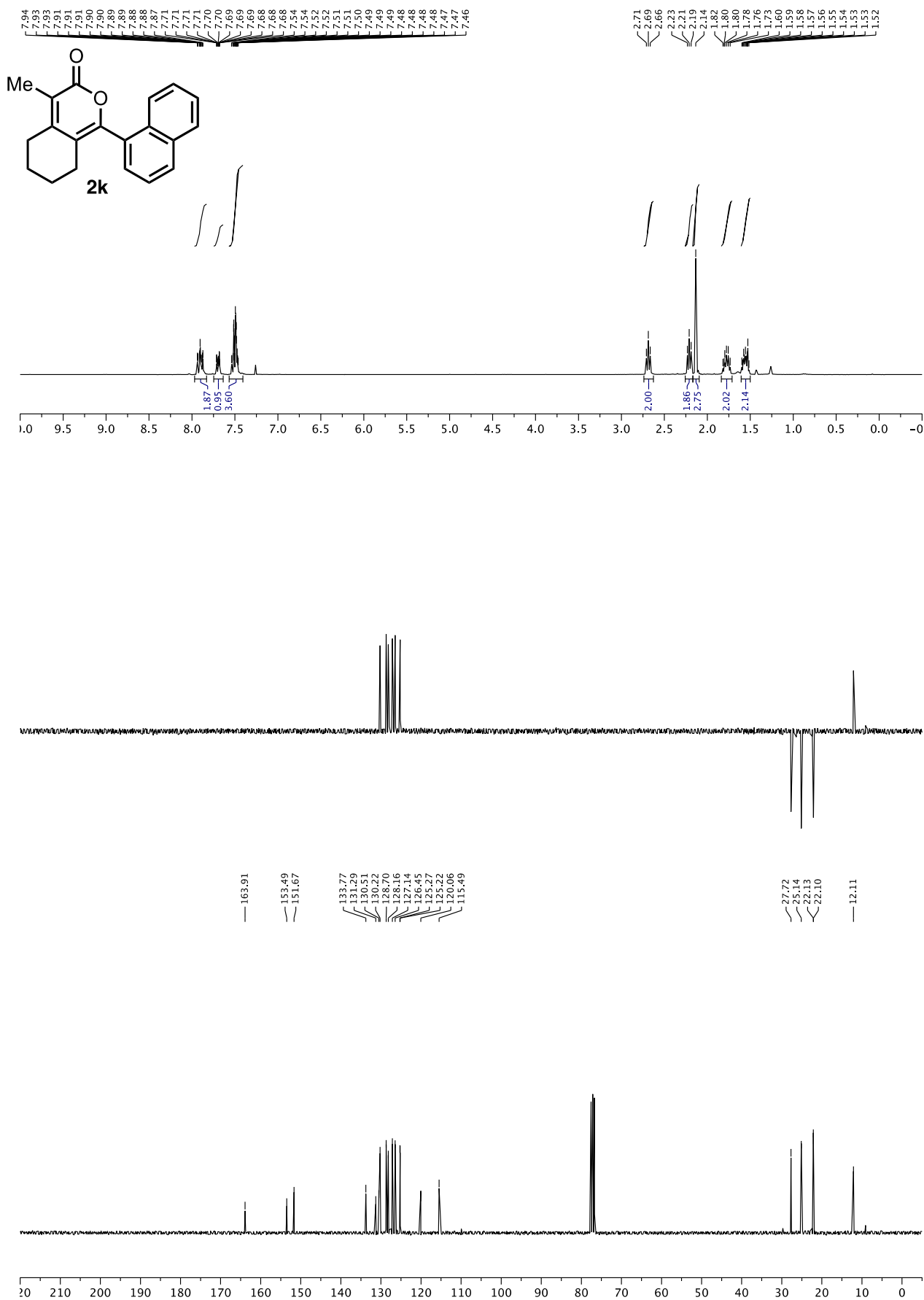
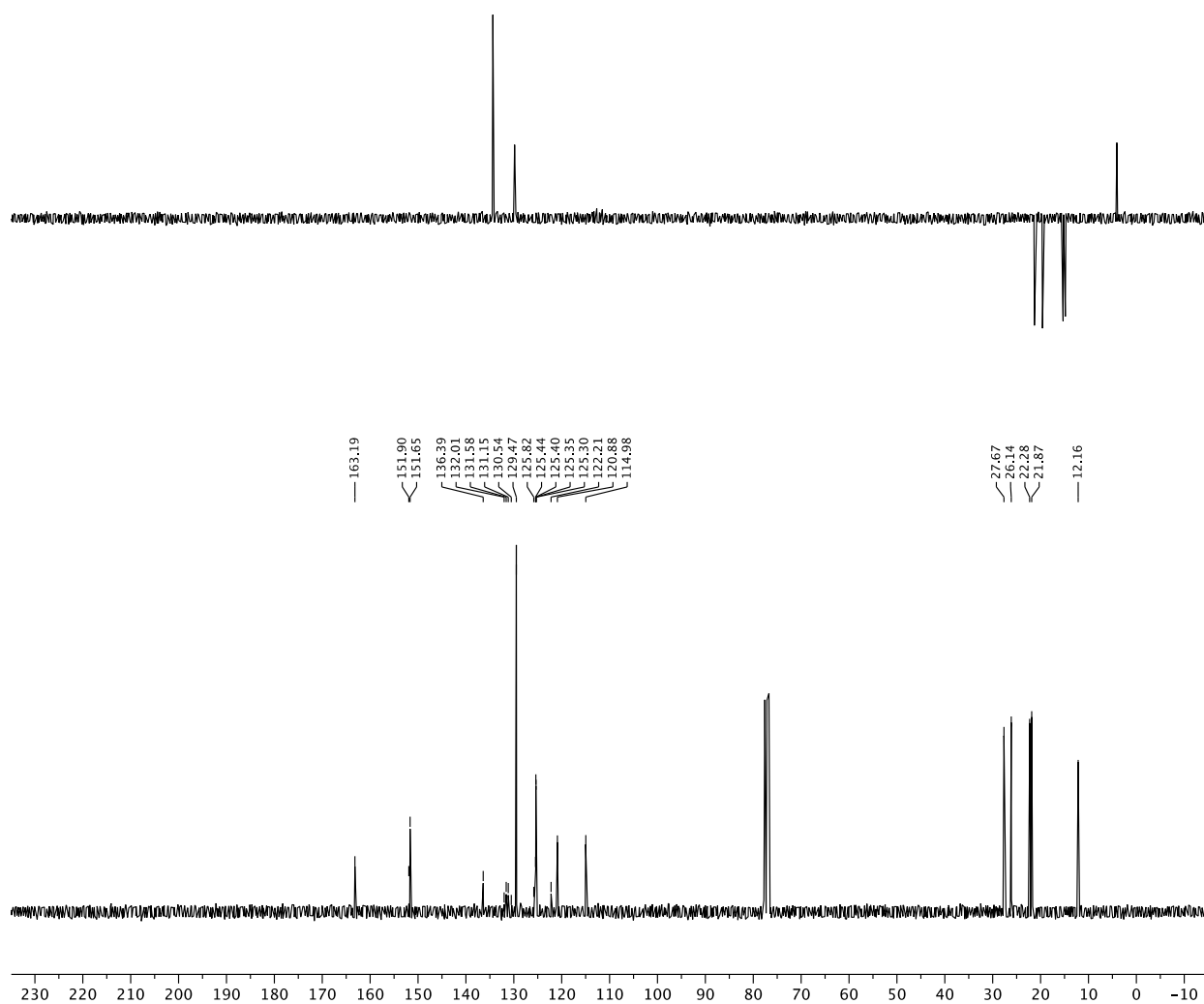
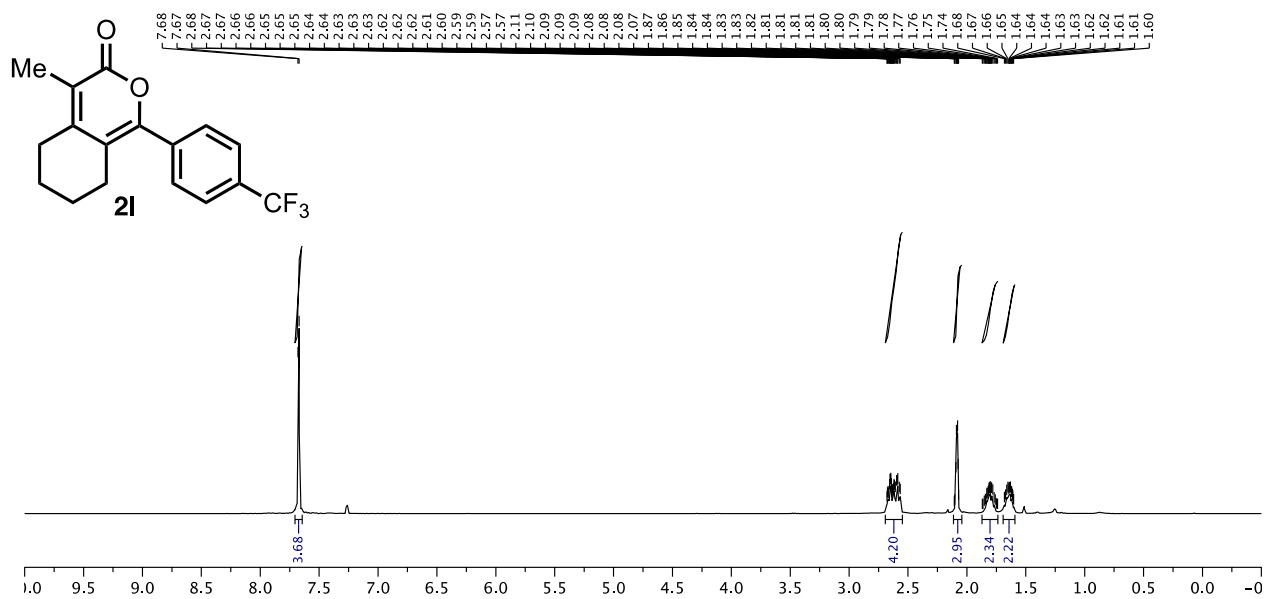


Figure S38.  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 300 MHz), DEPT  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 75 MHz) and  $^{13}\text{C}$  NMR Spectra ( $\text{CDCl}_3$ , 75 MHz) of 1-(3,5-Dimethylphenyl)-4-methyl-5,6,7,8-tetrahydro-3*H*-isochromen-3-one (**2j**)

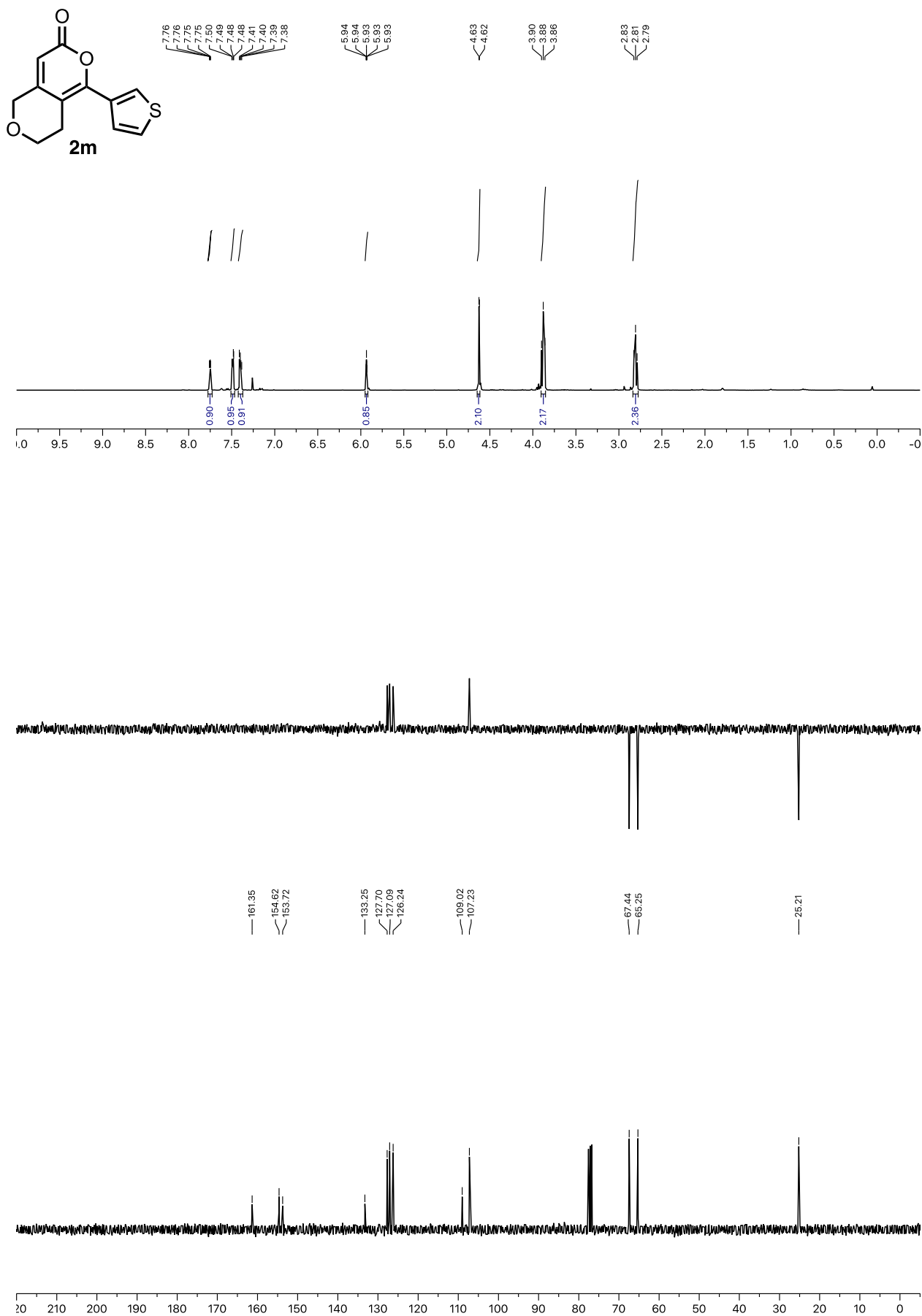




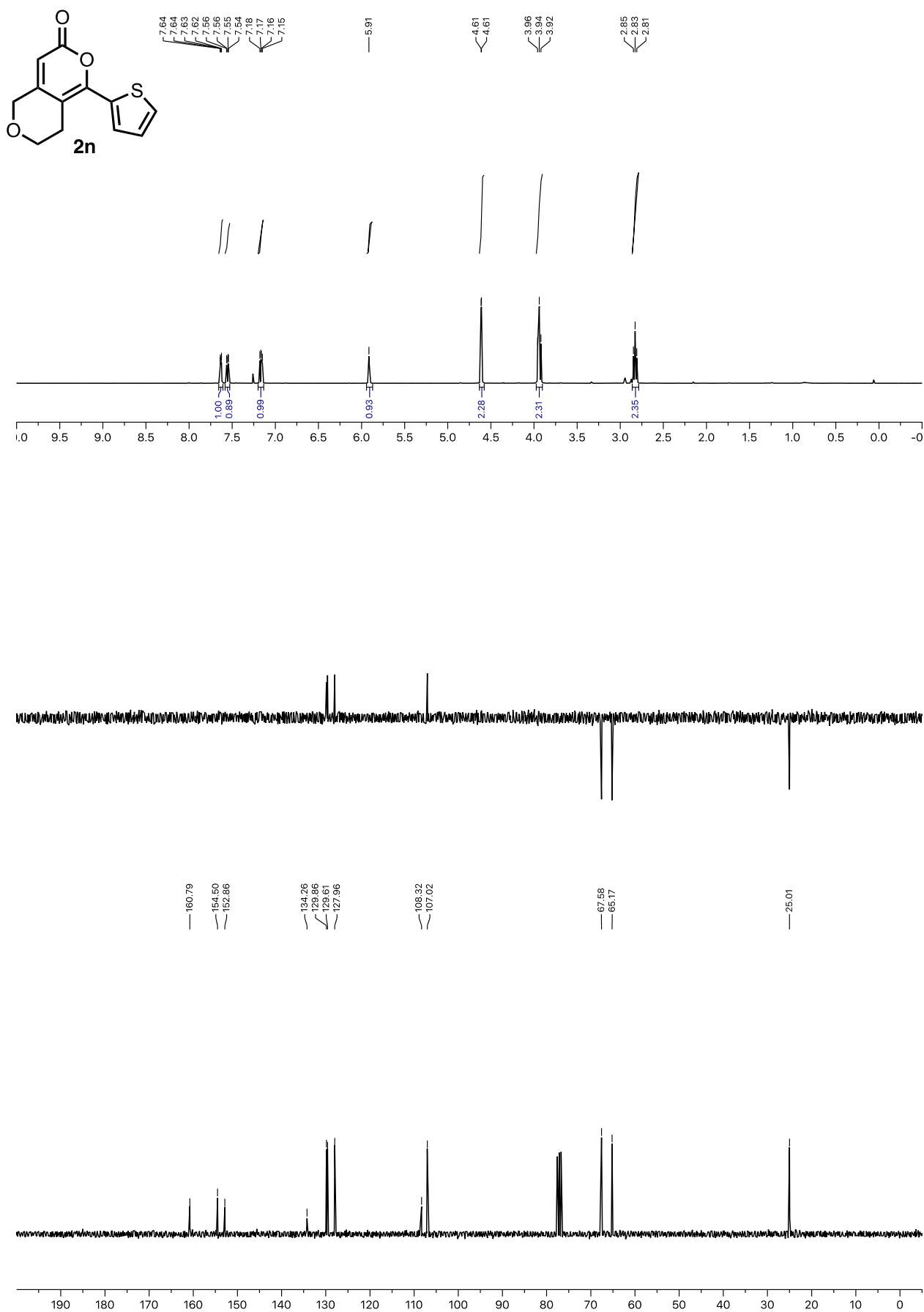
**Figure S39.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-(naphthalen-1-yl)-5,6,7,8-tetrahydro-3H-isochromen-3-one (**2k**)



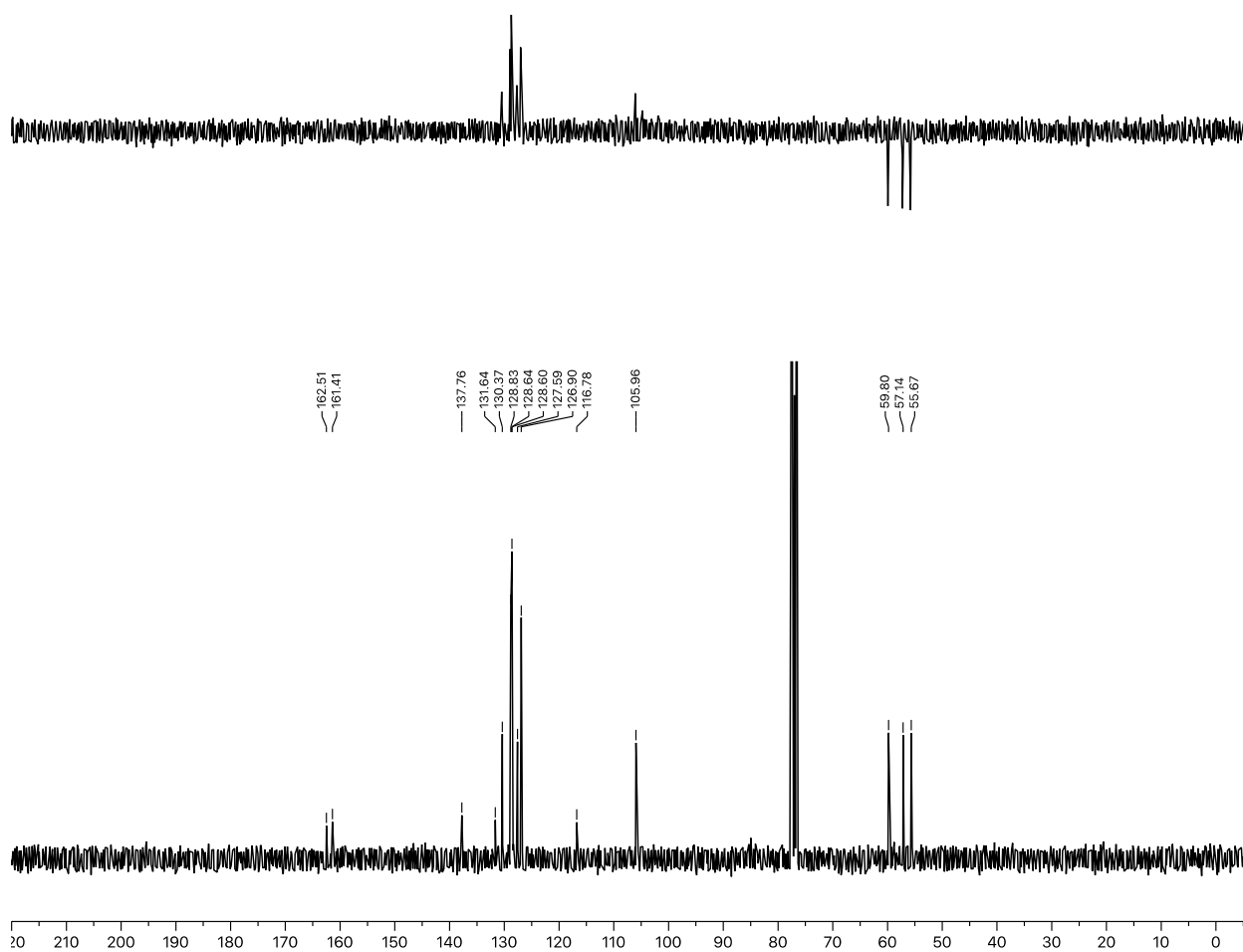
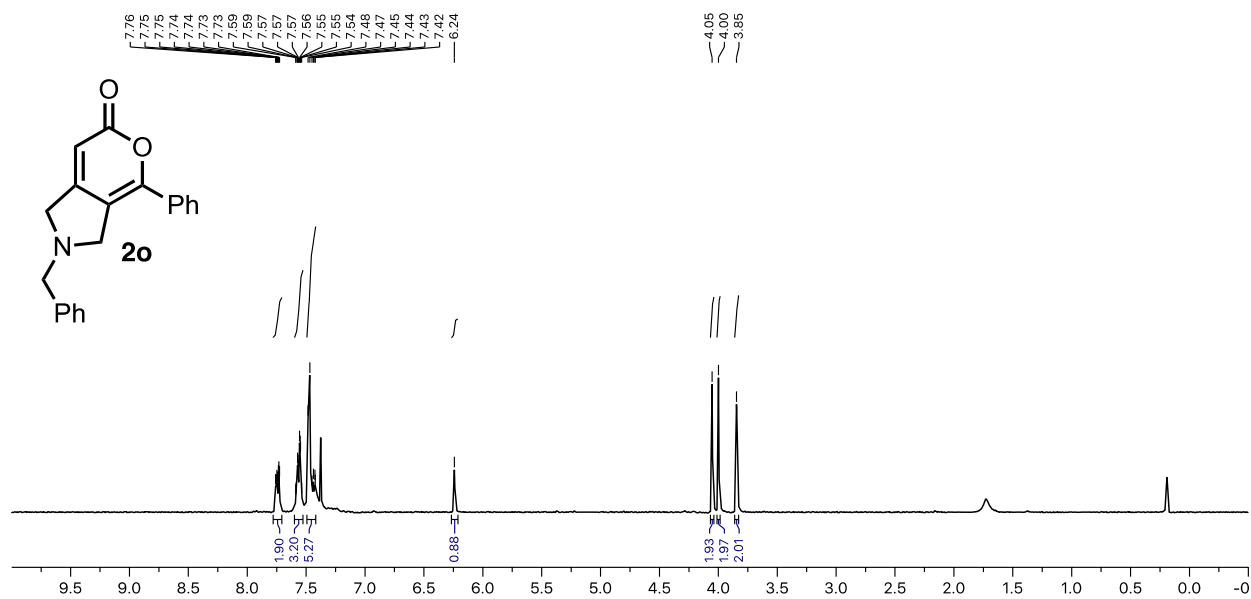
**Figure S40.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-1-(4-(trifluoromethyl)phenyl)-5,6,7,8-tetrahydro-3H-isochromen-3-one (**21**)



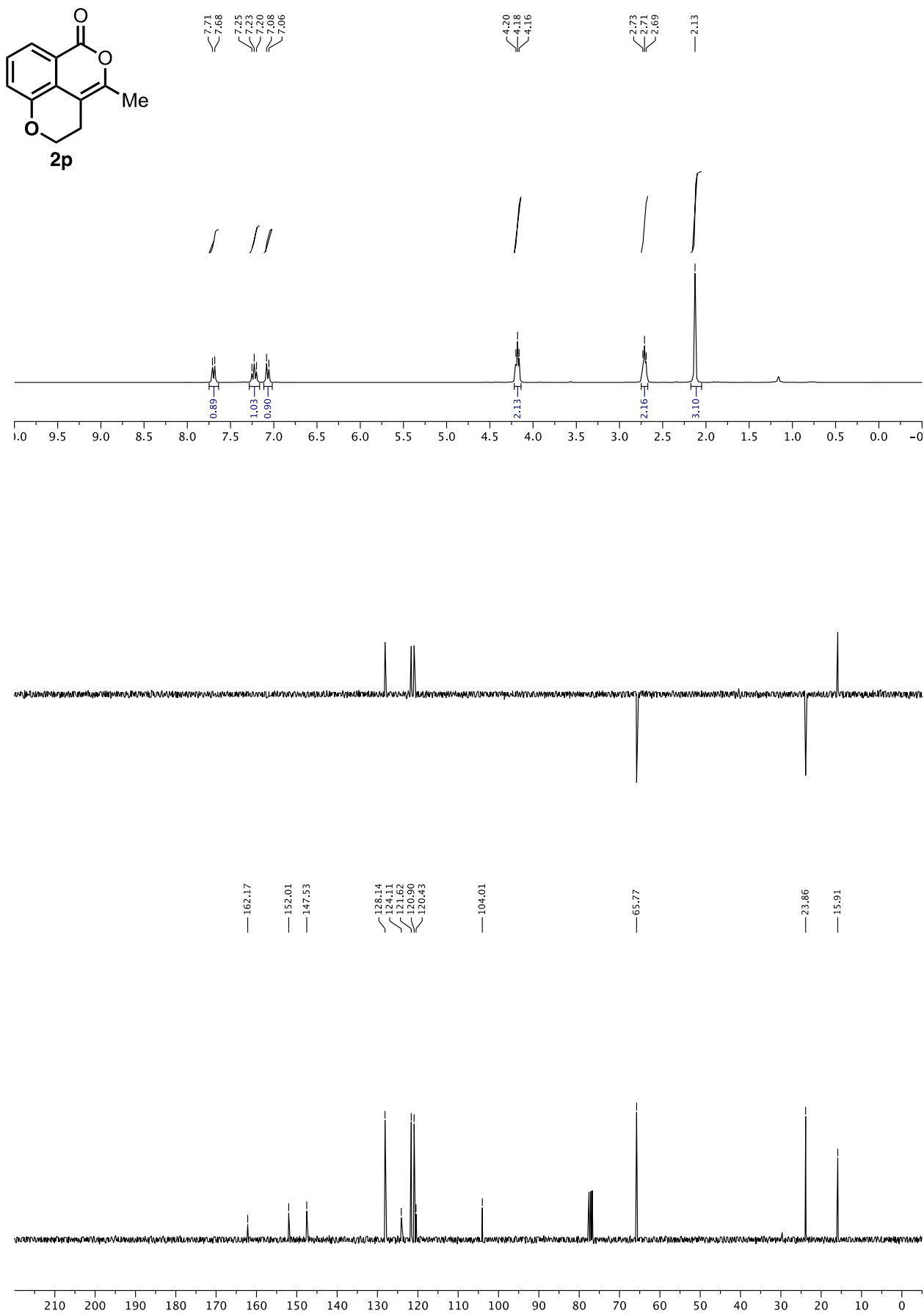
**Figure S41.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-(Thiophen-3-yl)-7,8-dihydropyrano[4,3-c]pyran-3(5H)-one (**2m**)



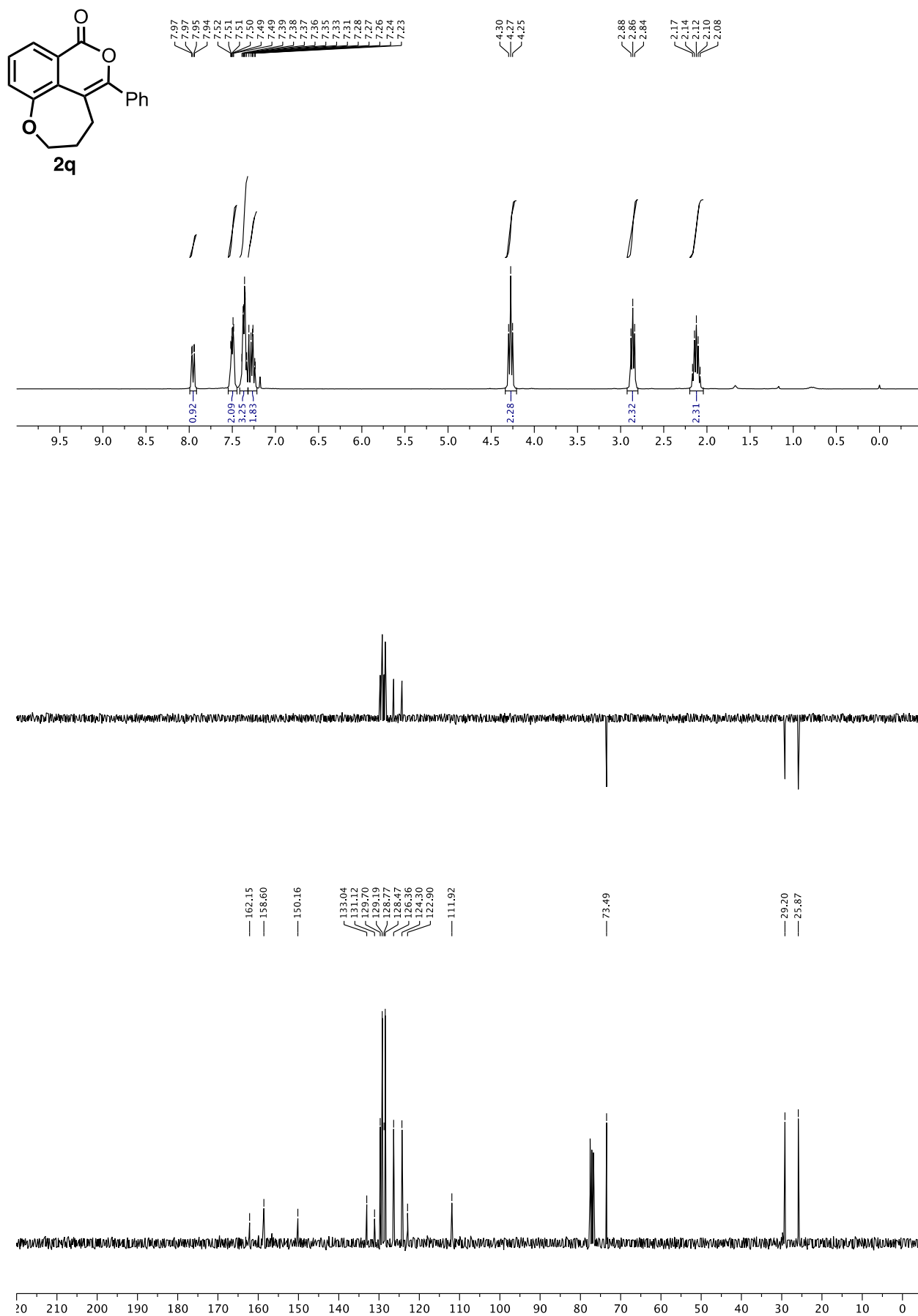
**Figure S42.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 1-(Thiophen-2-yl)-7,8-dihydropyrano[4,3-c]pyran-3(5H)-one (**2n**)



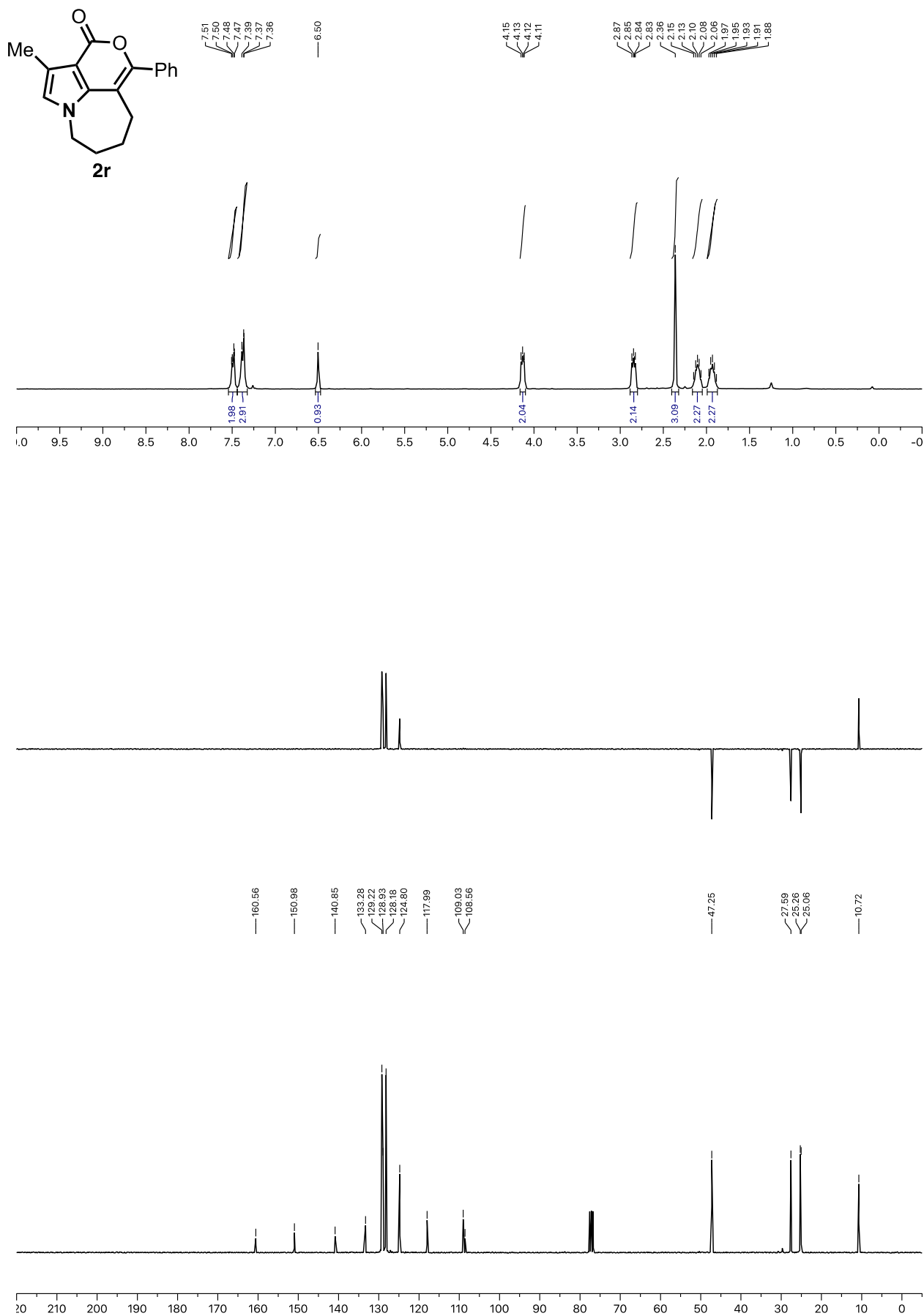
**Figure S43.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 2-Benzyl-4-phenyl-2,3-dihydropyrano[3,4-c]pyrrol-6(1*H*)-one (**2o**)



**Figure S44.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 4-Methyl-2,3-dihydro-6H-pyrano[3,4,5-de]chromen-6-one (**2p**)

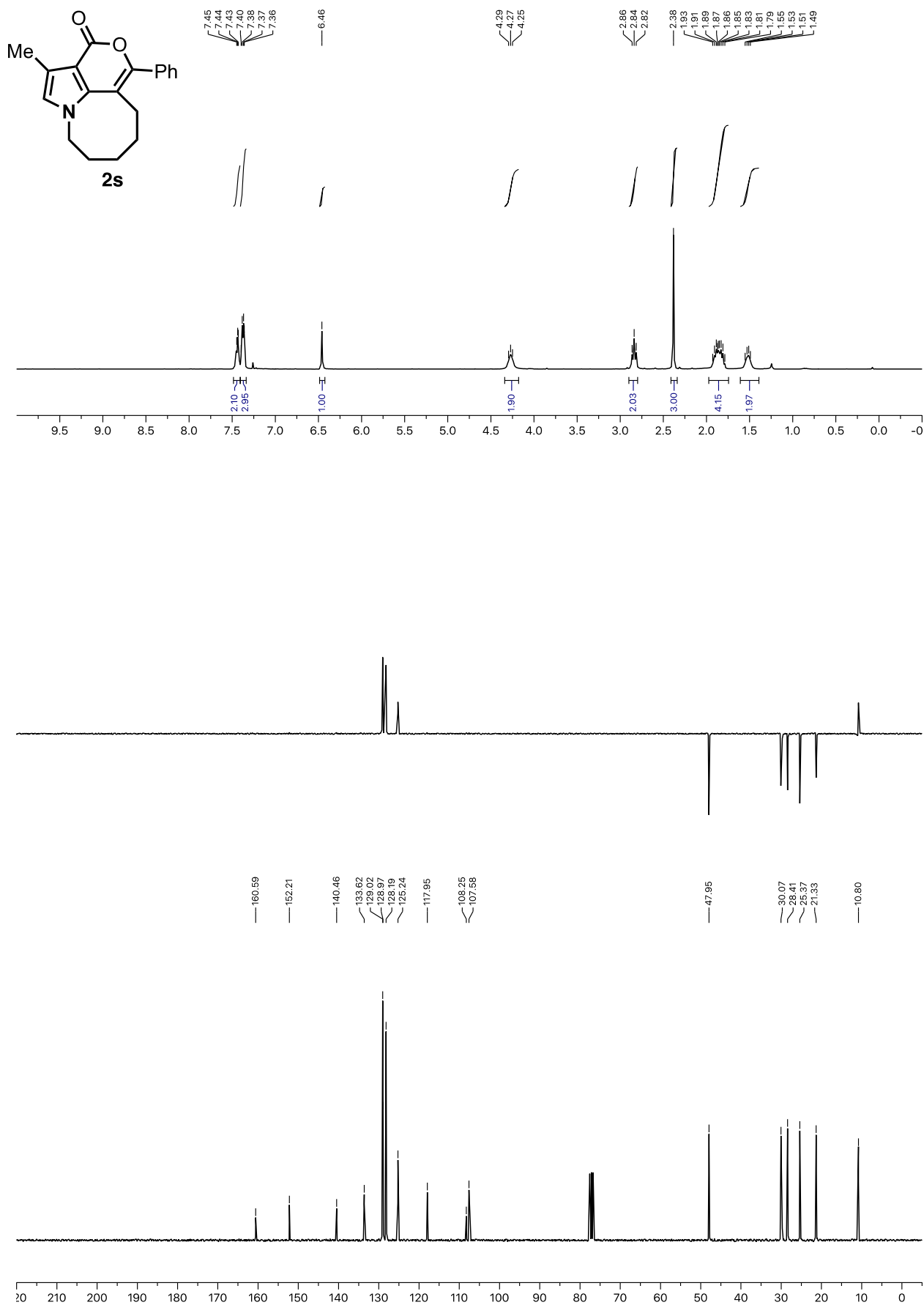


**Figure S45.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 5-Phenyl-3,4-dihydro-2*H*,7*H*-oxepino[4,3,2-*d*]isochromen-7-one (**2q**)

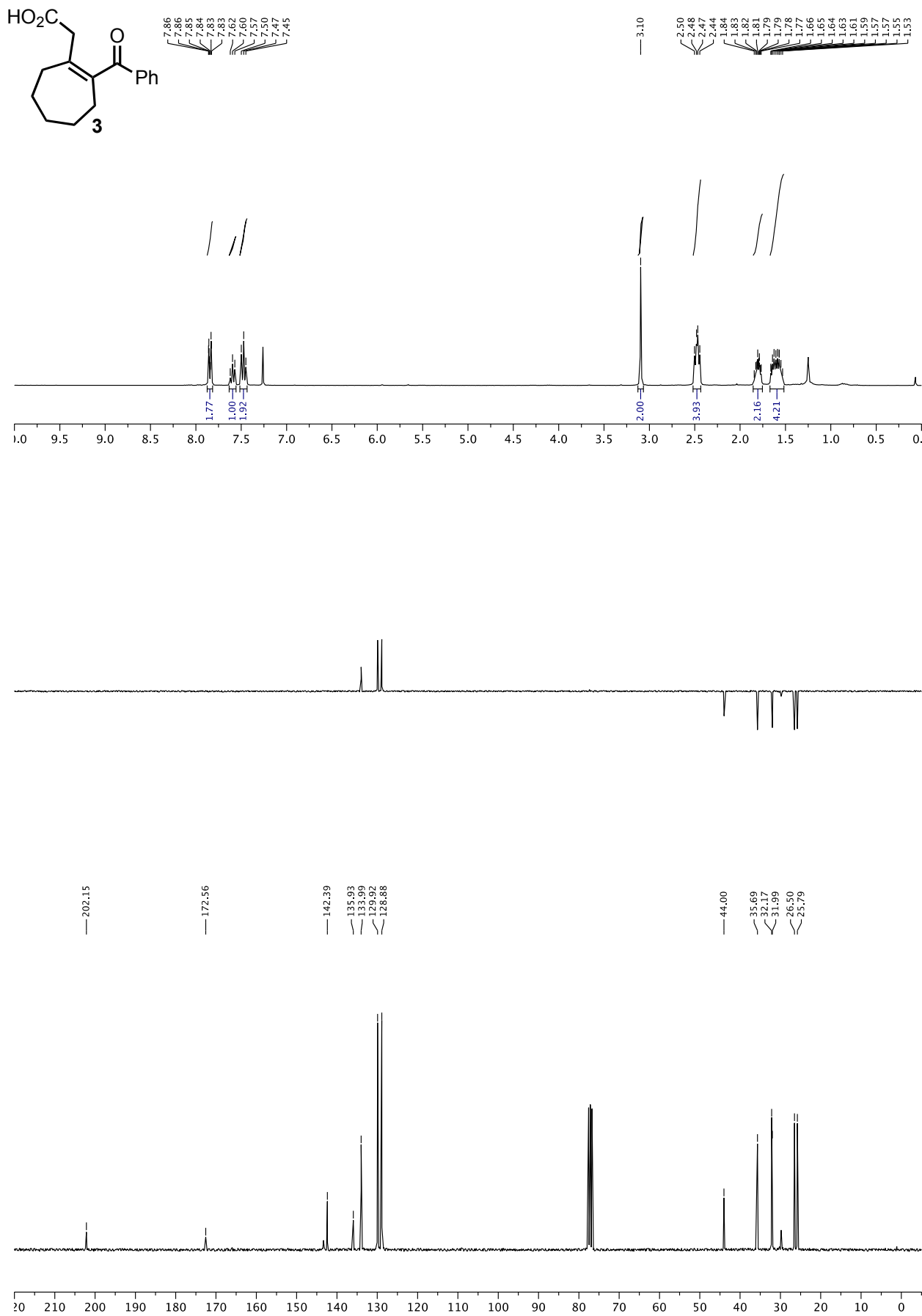


**Figure S46.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 2-Methyl-5-phenyl-6,7,8,9-tetrahydro-3H-4-oxa-9a-azabenzoc[cd]azulen-3-one (**2r**)

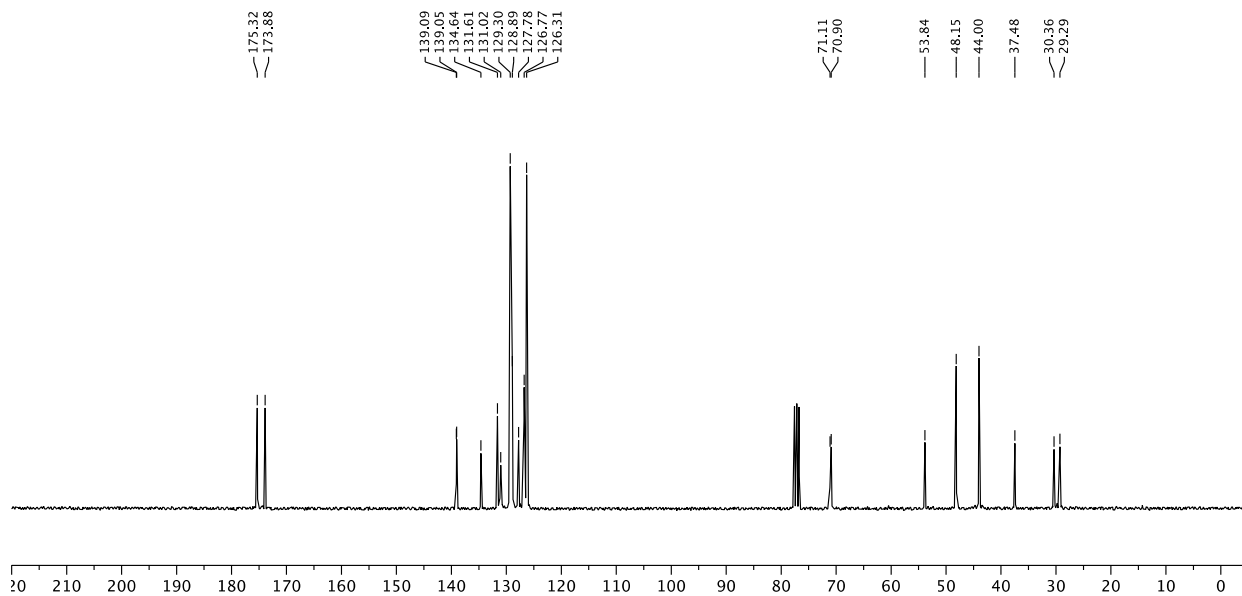
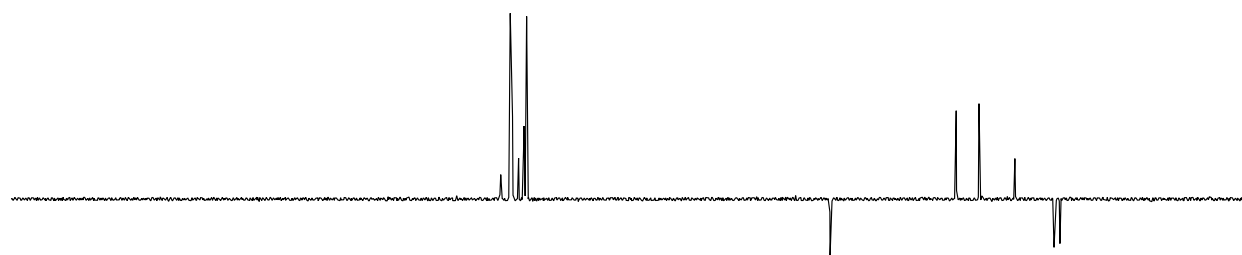
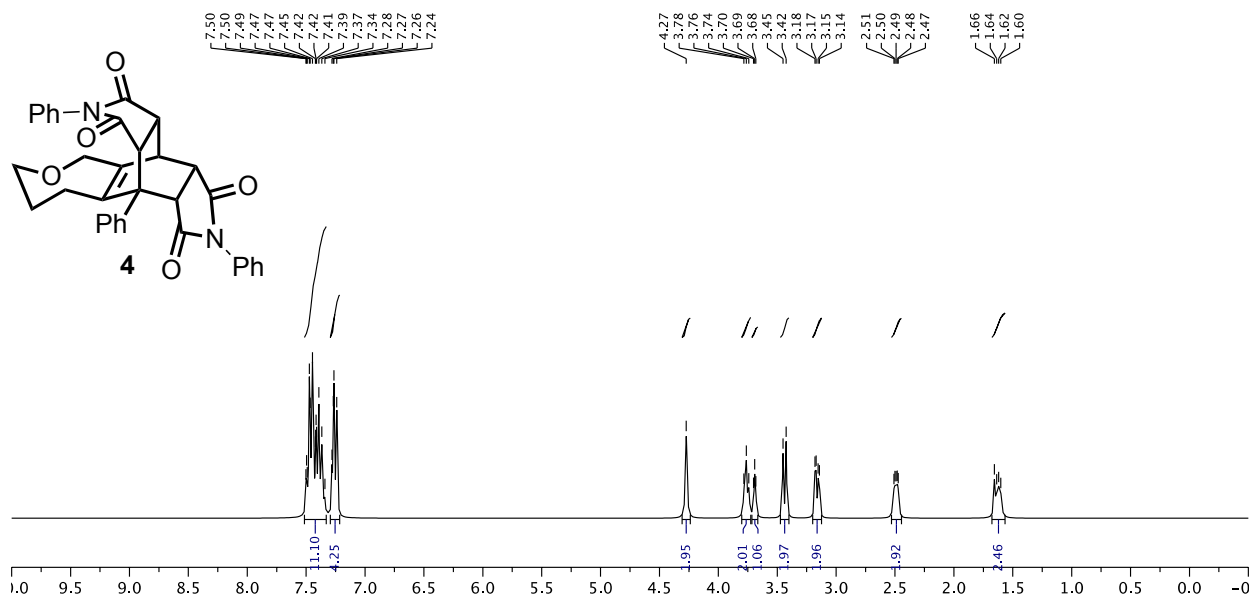




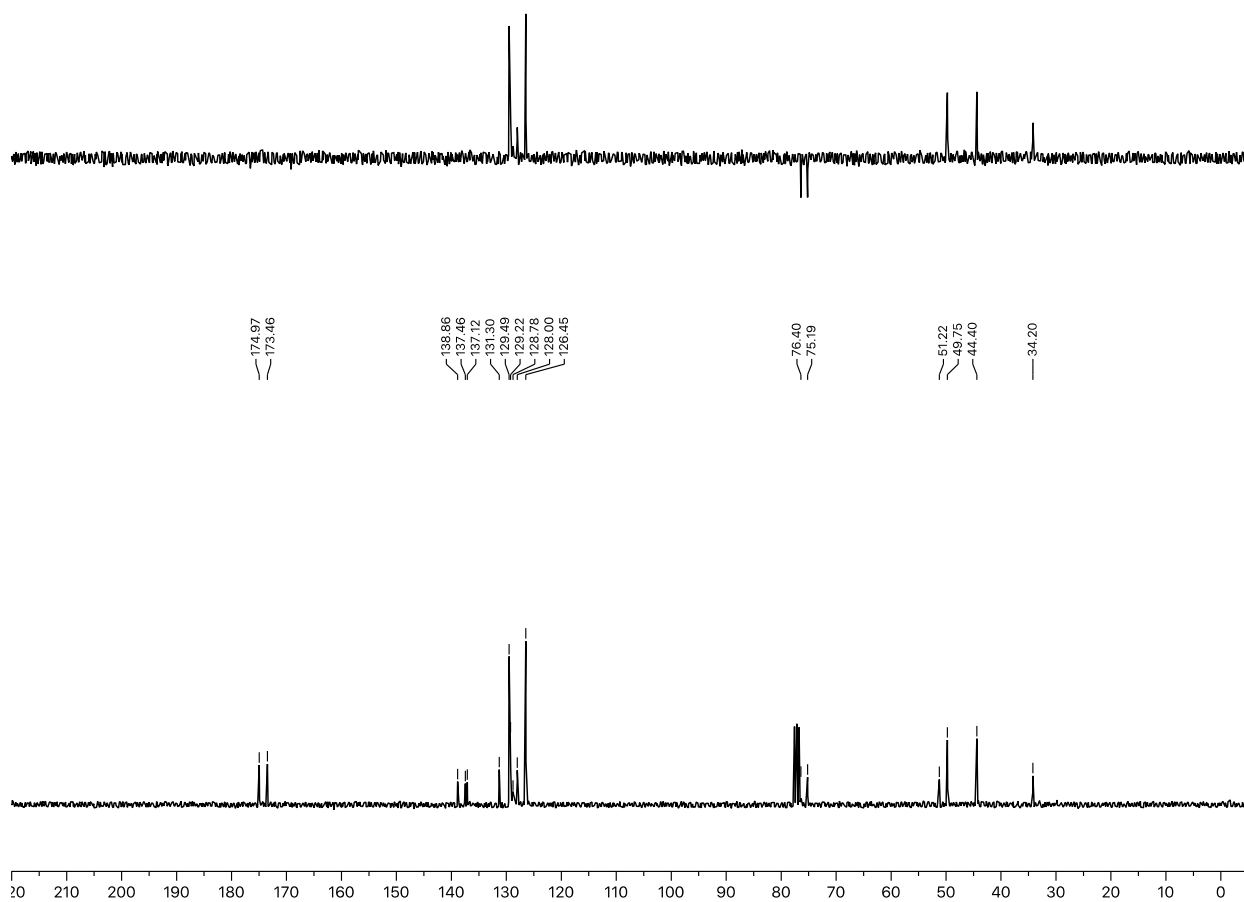
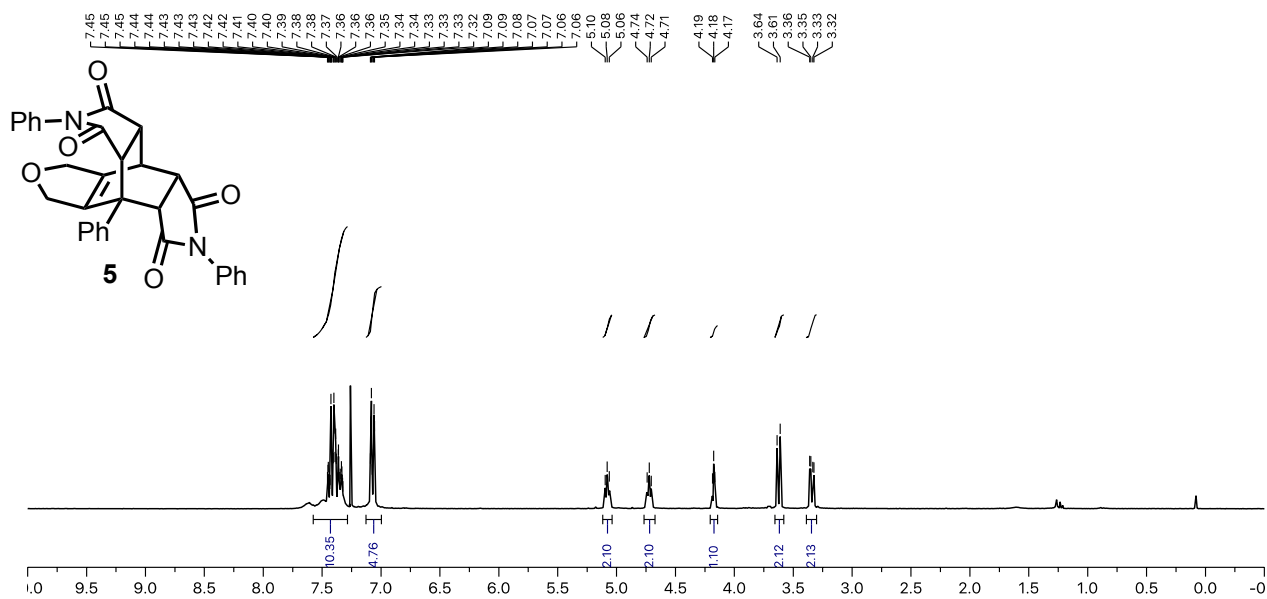
**Figure S47.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 2-Methyl-5-phenyl-7,8,9,10-tetrahydro-3H,6H-4-oxa-10a-azacycloocta[cd]inden-3-one (**2s**)



**Figure S48.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of 2-(2-benzoylcyclohept-1-en-1-yl)acetic acid (**3**)



**Figure S49.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of compound **4**



**Figure S50.** <sup>1</sup>H NMR (CDCl<sub>3</sub>, 300 MHz), DEPT <sup>13</sup>C NMR (CDCl<sub>3</sub>, 75 MHz) and <sup>13</sup>C NMR Spectra (CDCl<sub>3</sub>, 75 MHz) of compound **5**