Metal-Free Intermolecular Cyclopropanation Between Alkenes and Iodonium Ylides Mediated by $PhI(OAc)_2$•Bu_4NI

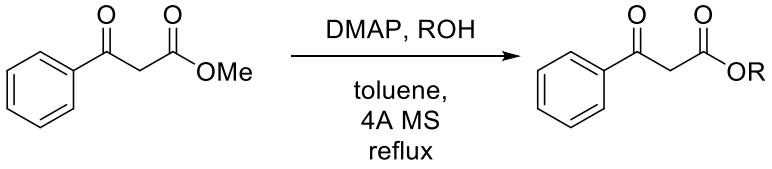
Jason Tao, Carl D. Estrada, Graham K. Murphy*

Department of Chemistry, University of Waterloo, 200 University Ave. W., Waterloo, ON, N2L3G1, Canada.

General Experimental Details. All reactions were performed using oven-dried or flame-dried glassware under a positive pressure of nitrogen unless otherwise stated. Reagents were obtained from commercial sources (e.g., Aldrich, Oakwood Chemicals) and were used without further purification. Anhydrous MeCN was obtained by allowing the solvent to sit over activated 3Å molecular sieves overnight and was used without further purification. Iodonium ylides **1e-k**[1] were synthesized through a method published by Schank and Lick[1] and their spectra matched those reported in the literature. Bu_4NI_3 was synthesized through the method published by Buckles and Yuk[2] and the melting point matched what had been reported. Thin layer chromatography was performed on glass plates pre-coated with 0.25 mm Kieselgel 60 F_{254} (Merck). Unless otherwise stated, flash chromatography columns were packed with 230-400 mesh silica gel (Silicycle). Proton nuclear magnetic resonance spectra (^1H NMR) were recorded at 300 MHz or 500 MHz and coupling constants (*J*) are reported in Hertz (Hz). Carbon nuclear magnetic resonance spectra (^{13}C NMR) were recorded at 125 MHz and are reported (ppm) relative to the center line of the triplet from chloroform-*d* (77.0 ppm). Positive ion electrospray ionization (ESI) was performed with a Thermo Scientific Q-Exactive hybrid mass spectrometer. Accurate mass determinations were performed at a mass resolution of 70,000. For ESI, samples were infused at 10 μL/min in either 1:1 CH_3OH/H_2O+0.1% formic acid or 1:1 CH_3OH/H_2O+0.2% NH_4OH.

Note: Ylides **1a-e** were prone to decomposition in solution. To minimize decomposition during NMR analysis, data was acquired as quickly as possible *immediately after* dissolving the ylides in $CDCl_3$.

General Synthesis of β-keto-esters (GP1)



Based on a modified transesterification procedure reported by Doyle:[3] Methyl benzoylacetate (5.45 g, 30 mmol, 1.0 equiv) was dissolved in toluene (15 mL). To this solution was added DMAP (183 mg, 1.5 mmol, 5 mol%) and alcohol (36 mmol, 1.2 equiv). The resulting mixture was heated to refluxed and the condensate was allowed to pass through a column of activated 4Å molecular sieves. After 16 h, the reaction mixture was concentrated via rotary evaporation and purified via flash chromatography (mobile phase: either varying concentrations of EtOAc in hexanes or 1% EtOAc in 1:1 CH_2Cl_2:hexanes) on silica gel to isolate the product away from the unreacted starting material.

General synthesis of phenyliodonium ylides of acyclic iodonium ylides (GP2-A)

Following the procedure reported by Lick:[1] 30% (w/v) KOH/MeOH (3.5 mL) solution was added slowly to a solution of acyclic 1,3-dicarbonyl (5 mmol) in MeOH (3.5 mL) cooled in an ice-brine bath. To this mixture, iodobenzene diacetate (5 mmol) in MeOH (8 mL) was added slowly to ensure reaction temperature remained < 0 °C. Stirring continued between 30 – 60 min and the resulting solution was poured onto ice (~100 mL) and diluted with water (75 mL) and transferred to a separatory funnel and extracted with CH_2Cl_2 (30 mL x 3). The combined organic extracts were dried over $MgSO_4$ and filtered through a sintered glass funnel and concentrated to ~20% of its original volume using a rotary evaporator. The resulting solution was precipitated by adding solvent (e.g., Et_2O and/or hexanes) followed by cooling to 0 °C. The solid is collected via filtration and dried in vacuo to yield the phenyliodonium ylides as typically white amorphous solids and were either used immediately or stored in a -20 °C freezer.

Note: Iodonium Ylides of acyclic 1,3-dicarbonyl compounds are typically thermally unstable. Especially in the case of ylides **1b** and **1c**, it is recommended that during work-up/isolation be performed as quickly as possible, while keeping the organic extracts cooled in an ice-water bath whenever possible.

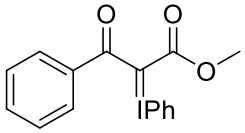
Iodonium ylides **1e-k**[1] were synthesized through a method published by Schank and Lick[1] and their spectra matched those reported in the literature.

General synthesis of phenyliodonium ylides of cyclic iodonium ylides (GP2-B)

Following the procedure reported by Lick:[1] Cyclic iodonium ylide (5 mmol) was dissolved in 10% aq. Na_2CO_3 (15 mL) at room temperature and was added to iodobenzene diacetate (5 mmol) in EtOH (15 mL). The resulting mixture was allowed to continue to stir for 30 min at room

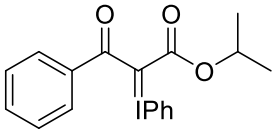
temperature and was then poured onto ice (~100 mL) and diluted with water (50 mL) and transferred to a seperatory funnel and extracted with CH_2Cl_2 (30 mL x 3). The combined organic extracts were dried over $MgSO_4$ and filtered through a sintered glass funnel and concentrated to ~20% of its original volume using a rotary evaporator. The resulting solution was precipitated by adding solvent (e.g., Et_2O and/or hexanes) followed by cooling to 0 °C. The solid is collected via filtration and dried in vacuo to yield the phenyliodonium ylides as typically white amorphous solids and were either used immediately or stored in a -20 °C freezer.

Phenyliodonium ylide of methyl benzoylacetate (1a)



The iodonium ylide was formed via **GP2-A** using methyl benzoylacetate[4] (1.78 g, 10 mmol). Following concentration of the organic extracts, the solution containing the crude iodonium ylide was diluted with CH_2Cl_2, Et_2O, then hexanes and concentrated in vacuo briefly to induce precipitation and the resulting suspension cooled to 0 °C. The solid was collected by vacuum filtration to yield the title compound as a white amorphous solid (2.07 g, 54% yield)
M.P. 80 – 82 °C.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.87 (d, J = 7.7 Hz, 2H), 7.55-7.54 (m, 3H), 7.42-7.36 (m, 5H), 3.50 (s, 3H).
^{13}C NMR (125, MHz, $CDCl_3$) δ 186.0, 165.0, 139.5, 133.1, 131.38, 131.21, 129.4, 128.1, 127.3, 112.9, 83.1, 51.6.
IR (ATR): 2953 (w), 1655 (s), 1429 (s), 1352 (s), 1126 (s) cm^{-1}.
HRMS calcd for $C_{16}H_{14}O_3I$ $(M+H)^+$ 380.9482, found 380.9481.

Phenyliodonium ylide of isopropyl benzoylacetate (1b)

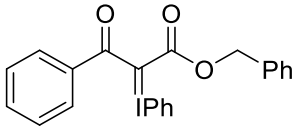


Isopropyl benzoylacetate was synthesized via **GP1** using 30 mmol methyl benzoylacetate and 36 mmol of *i*-PrOH. Purification of the crude material via gradient flash chromatography (silica gel, eluting with 5% then 10% EtOAc in hexanes) to give isopropyl benzoylacetate as an orange liquid (3.11 g, 50% yield).
R_f = 0.34 (10% EtOAc in hexanes)
^{1}H NMR (500 MHz, $CDCl_3$): δ 12.65 (s, 1H), 7.94 (d, J = 7.9 Hz, 7H), 7.77 (d, J = 7.4 Hz, 2H), 7.58 (s, 4H), 7.49-7.40 (m, 10H), 5.63 (s, 1H), 5.15 (s, 1H), 5.07 (dt, J = 12.5, 6.3 Hz, 3H), 3.95 (s, 7H), 1.31 (d, J = 6.3 Hz, 5H), 1.22 (d, J = 6.3 Hz, 21H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 192.8, 172.9, 171.4, 167.2, 136.2, 133.76, 133.66, 131.3, 128.9, 128.63, 128.58, 126.1, 88.0, 69.2, 67.9, 46.5, 22.1, 21.8
IR (ATR) 2981 (w), 1732 (s), 1686 (s), 1266 (s), 1200 (s), 1104 (s) cm^{-1}.
HRMS calcd for $C_{12}H_{15}O_3$ $(M+H)^+$ 207.1016, found 207.1016.

The iodonium ylide was formed via **GP2-A** using isopropyl benzoylacetate (2.06 g, 10 mmol). Following concentration of the organic extracts, the solution containing the crude iodonium ylide was diluted with CH_2Cl_2, Et_2O, then hexanes and concentrated in vacuo briefly to induce precipitation and the resulting suspension cooled to 0 °C. The solid was collected by vacuum filtration to yield the title compound as a white amorphous solid (802 mg, 20% yield)

M.P. 59 – 61 °C. ^{1}H-NMR (500 MHz, $CDCl_3$): δ 7.89 (dd, *J* = 8.3, 1.0 Hz, 2H), 7.55 (t, *J* = 7.4 Hz, 1H), 7.51-7.49 (m, 2H), 7.41 (t, *J* = 7.7 Hz, 2H), 7.35-7.30 (m, 3H), 4.81 (sept, *J* = 6.3 Hz, 1H), 0.93 (d, *J* = 6.2 Hz, 6H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 186.2, 164.3, 140.0, 133.5, 131.62, 131.48, 129.4, 128.3, 127.4, 112.9, 85.6, 68.1, 21.9
IR (ATR) 2977 (w), 1627 (m), 1469 (s), 1260 (s), 1105, (s), 1010 (s) cm^{-1}.
HRMS calcd $C_{18}H_{18}O_3I$ $(M+H)^+$ 409.0295, found 409.0295.

Phenyliodonium ylide of benzyl benzoylacetate (1c)

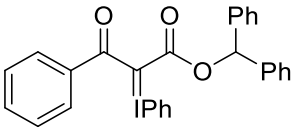


Benzyl benzoylacetate was synthesized following **GP1** using 30 mmol methyl benzoylacetate and 36 mmol of BnOH. Purification of the crude material via silica gel flash chromatography (1% EtOAc in 99% 1:1 CH_2Cl_2:hexanes solution) afforded title compound as an orange oil (4.66 g, 61% yield) in a 1:4 enol:keto ratio.

^{1}H NMR (500 MHz, $CDCl_3$): δ 12.54 (s, 1H), 7.94 (d, *J* = 7.9 Hz, 8H), 7.79 (d, *J* = 7.2 Hz, 2H), 7.59 (t, *J* = 7.4 Hz, 4H), 7.47-7.33 (m, 39H), 5.75 (s, 1H), 5.27 (s, 2H), 5.21 (s, 7H), 4.05 (s, 7H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 192.4, 173.0, 171.9, 167.4, 136.01, 135.88, 135.4, 133.4, 131.4, 129.8, 128.84, 128.69, 128.61, 128.55, 128.40, 128.30, 127.0, 126.2, 87.3, 77.36, 67.2, 66.1, 46.0
IR (ATR) 1738, 1684.9, 1264, 1209, 1183, 1141 cm^{-1}.
HRMS calcd for $C_{16}H_{15}O_3$ $(M+H)^+$ 255.1016, found 255.1015.

The iodonium ylide was formed via **GP2-A** using benzyl benzoylacetate (1.27 g, 5 mmol). Following concentration of the organic extracts, the solution containing the crude iodonium ylide was precipitated addition of Et_2O and hexanes. Vacuum filtration yielded the title compound as a white amorphous solid (724 mg, 32% yield).
M.P. 61 – 63 °C
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.83 (d, *J* = 7.5 Hz, 2H), 7.55-7.53 (m, 3H), 7.36 (t, *J* = 7.7 Hz, 3H), 7.33-7.29 (m, 2H), 7.24-7.23 (m, 3H), 7.00-6.99 (m, 2H), 4.98 (s, 2H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 186.4, 164.5, 139.7, 136.6, 133.6, 131.58, 131.49, 129.6, 128.3, 127.88, 127.76, 127.60, 113.0, 84.0, 66.6.
IR (ATR) 3057 (w), 1677 (m), 1646 (m), 1469 (s), 1262 (s), 1040 (s) cm^{-1}.
HRMS calcd for $C_{22}H_{18}IO_3$ $[M+H]^+$ 457.0295; 457.0294.

Phenyliodonium ylide of Benzhydrol benzoylacetate (1d)



Benzhydrol benzoylacetate was synthesized following **GP1** using 30 mmol methyl benzoylacetate and 36 mmol of benzhydrol. Purification via silica gel flash chromatography (1% EtOAc in 99% 1:1 CH_2Cl_2:hexanes solution) afforded title compound as an pink liquid which solidified upon standing to yield a pink solid (6.63 g, 20.1 mmol, 67% yield) in a 5:1 enol:keto ratio.
^{1}H NMR (500 MHz, $CDCl_3$) δ 12.45 (enol, s, 1H), 7.94 (keto, d, *J* = 8.0 Hz, 0.4H), 7.81 (enol, d, *J* = 7.2 Hz, 2H), 7.77 (keto, d, *J* = 7.2 Hz, 0.2H), 7.60 (keto, t, *J* = 7.5 Hz, 0.3H), 7.50-7.28 (m, 16H), 7.04 (s, 1H), 6.96 (keto, s, 0.1H), 5.87 (enol, s, 1H), 4.10 (keto, s, 0.3H).
^{13}C NMR (126 MHz, $CDCl_3$): δ 172.34, 172.23, 166.6, 140.2, 139.7, 136.1, 133.8, 133.4, 131.5, 128.9, 128.70, 128.68, 128.60, 128.13, 128.12, 128.05, 127.25, 127.23, 126.2, 87.5, 78.2, 77.0, 46.4
IR 3058 (w), 1747 (m), 1682 (m), 1636 (m), 1250 (s), 1194 (s) cm^{-1}.
HRMS calcd for $C_{22}H_{18}O_3Na$ $(M+Na)^+$ 353.1148, found 353.1129.

The iodonium ylide was formed via **GP2-A** using benhydrol benzoylacetate (1.27 g, 5 mmol). Following concentration of the organic extracts, the solution containing the crude iodonium ylide was precipitated addition of Et_2O and hexanes. Vacuum filtration yielded the title compound as a white amorphous solid (724 mg, 32% yield).
M.P. 120 – 122 °C.
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.80 (d, *J* = 7.8 Hz, 2H), 7.59 (d, *J* = 7.1 Hz, 2H), 7.52 (t, *J* = 7.5 Hz, 1H), 7.42 (t, *J* = 7.3 Hz, 1H), 7.37-7.32 (m, 4H), 7.24-7.21 (m, 6H), 7.07-7.03 (m, 4H), 6.80 (s, 1H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 186.4, 163.6, 140.8, 139.8, 133.2, 131.37, 131.20, 129.5, 128.30, 128.14, 127.6, 127.3, 126.9, 112.7, 77.6.
IR (ATR) 3053 (w), 1650 (s), 1529 (s), 1325 (m), 1252 (s), 1016 (s) cm^{-1}.
HRMS calcd for $C_{28}H_{22}O_3I$ $(M+H)^+$ 533.0608, found 533.0608.

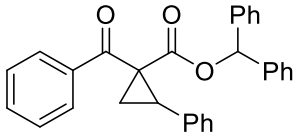
General Procedure for the Cyclopropanation of Iodonium Ylides Using $PhI(OAc)_2$ and Bu_4NI (GP3)

In a dry 10 mL round bottom flask, alkene (0.6 mmol, 2 equiv) was stirred in MeCN (3 mL) at room temperature. Bu_4NI (11 mg, 0.09 mmol, 30 mol%) was then added to the solution. In rapid succession, iodonium ylide (0.3 mmol, 1.0 equiv) and $PhI(OAc)_2$ (96 mg, 0.3 mmol, 1.0 equiv) were added, and stirred for 2 hours (1 hour for iodonium ylides of acyclic 1,3-dicarbonyls). The reaction mixture was then concentrated to dryness. If NMR yields were desired, HMDSO (1.5 μL/mmol of ylide) was added during ^{1}H NMR analysis. The crude reaction mixture was loaded onto a column of silica gel using a minimal amount of $CHCl_3$. Elution using mixtures of EtOAc/hexanes afforded the cyclopropanation products.

Note: Characterization, diastereoselectivities and NMR yields of cyclopropanes **2b-d** (where appropriate) were obtained in analogy to **2a** for which the *cis*-**2a** and *trans*-**2a** have been previously reported in the literature.[4-5]

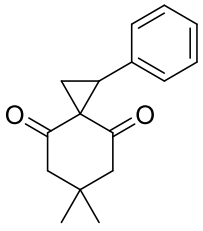
Cyclopropanes **2e**, **2f**, **2h** and **2k** are known in the literature.[6] NMR yields were determined by adding HMDSO (1.5 μL/mmol of ylide) during ^{1}H NMR analysis.

Benzhydryl 1-benzoyl-2-phenylcyclopropane-1-carboxylate (2d)



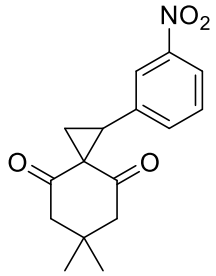
Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 3-nitrostyrene (89.5 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (eluting with, sequentially, 5% then 10% EtOAc in hexanes), led to the title compound to be isolated as a yellow liquid (55 mg, 42% yield) with a 2:1.2 ratio of diastereomers.
R_f = 0.3 (10% EtOAc in hexanes, UV active).
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.90 (d, *J* = 7.3 Hz, 1.8H), 7.70 (d, *J* = 7.3 Hz, 3.3H), 7.53-7.00 (m, 46H), 6.84 (d, *J* = 6.8 Hz, 3.3H), 6.77 (d, *J* = 7.6 Hz, 3.3H), 6.58 (d, *J* = 7.7 Hz, 1.8H), 6.51 (s, 0.6H), 3.69 (dd, *J* = 8.6 Hz, 1H), 3.58 (dd, *J* = 8.6 Hz, 1.9H), 2.55 – 2.51 (m, 2.6H), 1.84 (dd, *J* =9.2 Hz, 5.1 Hz, 1H), 1.74 (dd, *J* = 9.0, 4.7 Hz, 0.6H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 192.5, 170.2, 167.6, 139.7, 139.39, 139.32, 138.9, 137.44, 137.29, 134.5, 134.0, 133.0, 132.7, 129.2, 129.0, 128.79, 128.68, 128.60, 128.41, 128.35, 128.31, 128.28, 128.17, 128.03, 128.01, 127.80, 127.73, 127.52, 127.39, 127.33, 127.28, 127.18, 127.07, 126.97, 126.7, 78.5, 78.1, 42.7, 42.3, 34.3, 30.7, 20.3, 18.8
IR 3031 (w), 1725 (m), 1677 (m), 1258 (m), 1147 (m), 692 (s) cm^{-1}.
HRMS calcd for $C_{30}H_{24}O_3Li$ $(M+Li)^+$ 439.1880, found 439.1864.

6,6-Dimethyl-1-phenylspiro[2.5]octane-4,8-dione (2i)[7]



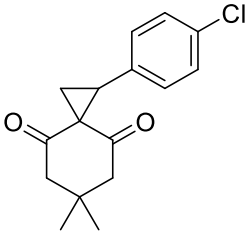
Synthesized according to **GP3** using 0.3 mmol of ylide and styrene (104.2 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (eluting with 5% EtOAc in hexanes, then 10% EtOAc in hexanes), led to the title compound to be isolated as a white solid (40 mg, 55% yield).
^{1}H NMR (300 MHz, $CDCl_3$): δ 7.49-7.23 (m, 5H), 3.30 (dd *J* = 10.2 Hz, 1H), 2.69-2.53 (m, 3H), 2.40-2.22 (m, 3H), 1.16 (s, 3H), 1.13 (s, 3H). This data matches what has been previously reported in the literature.

1-(3-nitrophenyl)-6,6-dimethylspiro[2.5]octane-4,8-dione (2m)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 3-nitrostyrene (89.5 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (eluting with, sequentially, 5% 10%, 15%, 30% EtOAc in hexanes), led to the title compound to be isolated as a white solid (51 mg, 60% yield).
R_f = 0.43 (20% EtOAc in hexanes, UV active).
M.P. 104 – 106 °C
^{1}H NMR (500 MHz, $CDCl_3$): δ 8.10-8.08 (m, 2H), 7.54 (d, *J* = 7.8 Hz, 1H), 7.46 (dd, *J* = 7.8 Hz, 1H), 3.33 (dd, *J* = 8.9 Hz, 1H), 2.68 - 2.63 (m, 1H), 2.62-2.58 (m, 1H), 2.49 (dd, *J* = 8.8, 3.8 Hz, 1H), 2.39 (d, *J* = 16.5 Hz, 1H), 2.34 (dd, *J* = 9.1, 3.8 Hz, 1H), 2.26 (d, *J* = 16.5 Hz, 1H), 1.12 (d, *J* = 0.2 Hz, 3H), 1.03 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 205.4, 202.2, 148.1, 135.76, 135.64, 129.0, 124.7, 123.0, 54.2, 53.3, 47.6, 45.7, 30.6, 29.3, 28.0, 23.7
IR (ATR) 2961 (w), 1699 (w), 1673 (s), 1527 (s), 1347 (s) 1334 (s), 1217 (m) cm^{-1}.
HRMS calcd for $C_{16}H_{18}O_4N$ $(M+H)^+$ 288.1230, found 288.1230.

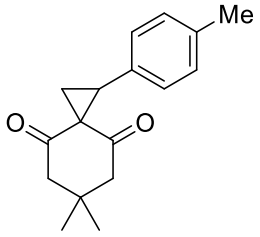
1-(4-chlorophenyl)-6,6-dimethylspiro[2.5]octane-4,8-dione (2n)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 4-chlorostyrene (2 equiv). Purification by gradient flash chromatography through a column of silica gel (eluting with 5% EtOAc in hexanes then 10% EtOAc in hexanes) led to the title compound to be isolated as a white solid (58 mg, 64% yield).
M.P. 106 – 108 °C.
R_f = 0.24 (10% EtOAc in hexanes, UV active)
^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.4 Hz, 2H), 7.18 (d, *J* = 8.3 Hz, 2H), 3.24 (dd, *J* = 9.0 Hz, 1H), 2.64 (d, *J* = 16.9 Hz, 1H), 2.60 (d, *J* = 16.9 Hz, 1H), 2.49 (dd, *J* = 8.9, 3.6 Hz, 1H), 2.39 (d, *J* = 16.6 Hz, 1H), 2.33 (dd, *J* = 9.1, 3.7 Hz, 1H), 2.25 (d, *J* = 16.7 Hz, 1H), 1.15 (s, 3H), 1.07 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 205.5, 201.7, 133.8, 131.7, 130.8, 128.2, 54.0, 53.2, 48.4, 47.3, 30.5, 29.2, 27.9, 22.5.
IR (ATR) 2958 (w), 1702 (w), 1675 (s), 1332 (m), 1015 (m) cm^{-1}.

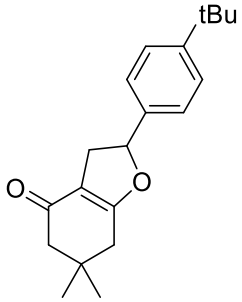
HRMS calcd for $C_{16}H_{18}O_2Cl$ $(M+H)^+$ 277.0990, found 277.0990.

1-(4-methylphenyl)-6,6-dimethylspiro[2.5]octane-4,8-dione (2o)



Synthesized following **GP3** using 0.3 mmol of ylide (1.0 equiv) and 4-methylstyrene (71 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (eluting with 5% EtOAc in hexanes then 10% EtOAc in hexanes) led to the title compound to be isolated as thick yellow oil (34 mg, 44% yield).
R_f = 0.17 (10% EtOAc in hexanes, UV active) ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.11 (d, *J* = 8.2 Hz, 2H), 7.08 (d, *J* = 8.2 Hz, 2H), 3.23 (t, *J* = 9.0 Hz, 1H), 2.62 (d, *J* = 16.8 Hz, 1H), 2.56 (d, *J* = 16.7 Hz, 1H), 2.51 (dd, *J* = 9.0, 3.7 Hz, 1H), 2.36-2.30 (m, 5H), 2.21 (d, *J* = 16.3 Hz, 1H), 1.12 (s, 3H), 1.04 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 205.7, 201.7, 137.7, 130.1, 129.4, 128.7, 54.0, 53.2, 48.93, 48.82, 30.5, 29.3, 27.9, 22.1, 21.2
IR 2954 (w), 1702 (m), 1674 (s), 1333 (m), 1273 (m) cm^{-1}.
HRMS calcd for $C_{17}H_{21}O_2$ $(M+H)^+$ 257.1542, found 257.1536.

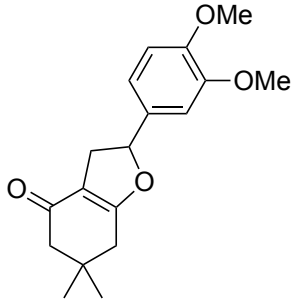
2-(4-(tert-butyl)phenyl)-6,6-dimethyl-3,5,6,7-tetrahydrobenzofuran-4(2H)-one (3p)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 4-*tert*-butylstyrene (96.3 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 5%, 10%, 20%, 40% EtOAc in hexanes) led to the title compound being isolated as a white solid (51 mg, 57% yield) which decomposed to a yellow liquid at room temperature. ^{1}H NMR analysis of this material showed a 2:1 mixture of the dihydrofuran and cyclopropane. Allowing this mixture to stand overnight at room temperature furnished quantitative conversion of cyclopropane to the title compound.
R_f = 0.23 (10% EtOAc in hexanes, UV active).
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.41 (d, *J* = 8.5 Hz, 2H), 7.26 (d, *J* = 8.2 Hz, 2H), 5.75 (dd, *J* = 10.5, 7.9 Hz, 1H), 3.26 (dddd, *J* = 14.5, 10.6, 1.8, 1.8 Hz, 1H), 2.91 (dddd, *J* = 14.6, 7.9, 1.9, 1.9 Hz, 1H), 2.36 (dd , *J* = 1.6, 1.6 Hz, 2H), 2.27 (d, *J* = 4.3 Hz, 2H), 1.32 (s, 9H), 1.14 (s, 3H), 1.13 (s, 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 194.7, 176.0, 151.7, 137.5, 125.7, 111.5, 100.0, 86.6, 51.0, 37.8, 34.6, 34.1, 33.5, 31.3, 28.9, 28.5.
IR (ATR) 2957 (m), 1739 (m), 1632 (s), 1399 (s), 1217 (s) cm^{-1}.
HRMS calcd for $C_{20}H_{27}O_2$ $(M+H)^+$ 299.2006, found 299.2006.

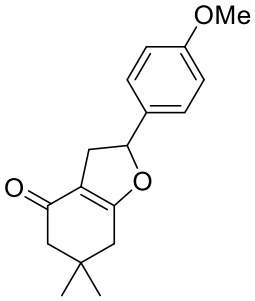
1-(3,4-dimethoxyphenyl)-6,6-dimethylspiro[2.5]octane-4,8-dione (3q)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 3,4-(dimethoxy)styrene (99.7 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 5%, 10%, 20%, 40% EtOAc in hexanes) led to the title compound to be isolated as a yellow liquid (74 mg, 82% yield).
R_f = 0.23 (10% EtOAc in hexanes, UV active).

^{1}H NMR (500 MHz, $CDCl_3$) δ 6.89-6.82 (m, 3H), 5.71 (dd, *J* = 10.4, 8.0 Hz, 1H), 3.88 (s, 3H), 3.87 (s, 3H), 3.25 (dd, *J* = 14.5, 10.5 Hz, 1H), 2.91 (dd, *J* = 14.6, 8.0 Hz, 1H), 2.36 (s, 2H), 2.29 (d, *J* = 16.2 Hz, 1H), 2.26 (d, *J* = 16.2 Hz, 1H), 1.14 (s, 3H), 1.13 (s, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 194.7, 175.9, 149.32, 149.27, 132.9, 118.7, 111.5, 111.1, 109.1, 86.8, 55.95, 55.89, 51.0, 37.9, 34.2, 33.4.
IR (ATR): 2955 (w), 1628 (s), 1516 (s), 1217 (s), 1137 (s) cm^{-1}.
HRMS calcd for $C_{18}H_{23}O_4$ $(M+H)^+$ 303.1591, found 303.1590.

2-(4-methoxyphenyl)-6,6-dimethyl-3,5,6,7-tetrahydrobenzofuran-4(2H)-one (3r)

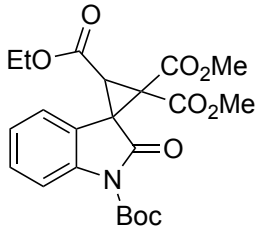


Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of 4-methoxystyrene (89.5 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 5%, 10%, 20%, 40% EtOAc in hexanes), led to the title compound to be isolated as a thick orange liquid (76 mg, 93% yield). An analytic sample was obtained by taking the above material and passing through another column of silica gel (5%, 10%, 20% EtOAc in benzene) to afford the title compound as a thick yellow liquid.
R_f = 0.13 (20% EtOAc in hexanes)

^{1}H NMR (500 MHz, $CDCl_3$): δ 7.27 (d, *J* = 8.6 Hz, 2H), 6.93 (d, *J* = 8.8 Hz, 2H), 5.74 (dd, *J* = 10.4, 7.9 Hz, 1H), 3.83 (s, 3H), 3.26 (dddd, *J* = 14.5, 10.6, 1.8, 1.8 Hz, 1H), 2.91 (dddd, *J* = 14.5, 7.9, 1.8, 1.8 Hz, 1H), 2.36 (dd, J = 1.8, 1.8 Hz, 2H), 2.29 (d, *J* = 3.5 Hz, 2H), 1.16 (s, 3H), 1.15 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 194.6, 175.9, 159.8, 132.6, 127.5, 114.1, 111.5, 86.6, 55.3, 50.9, 37.8, 34.1, 33.5, 28.8, 28.5
IR (ATR) 2957 (w), 1626 (s), 1514 (m), 1400 (m), 1217 (s), 1003 (m) cm^{-1}.
HRMS calcd for $C_{17}H_{21}O_3$ $(M+H)^+$ 273.1485, found 273.1485.

The substituted methylene compounds **4a-h**,**l**,**m** were prepared by Wittig olefinations of the isatins according to literature precedent.[8] Substrate **4j** was prepared via Peterson olefination of the *N*-Me isatin.[9] Substrate **4k** was prepared via malononitrile condensation on *N*-acetyl isatin.

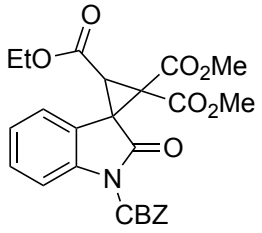
1'-(tert-butyl) 3-ethyl 2,2-dimethyl 2'-oxospiro[cyclopropane-1,3'-indoline]-1',2,2,3-tetracarboxylate (5a)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (95 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 10%, 20% EtOAc in hexanes) led to the title compound to be isolated as thick orange oil which slightly foamed when placed under high vacuum (96 mg, 71% yield).

^{1}H NMR (500 MHz; $CDCl_3$): δ 7.90 (d, *J* = 8.1 Hz, 1H), 7.41 (d, *J* = 7.9 Hz, 1H), 7.35 (ddd, *J* = 7.9, 7.9, 0.8 Hz, 1H), 7.12 (dd, *J* = 7.7 Hz, 1H), 4.25-4.13 (m, 2H), 3.80 (s, 6H), 3.42 (s, 1H), 1.62 (s, 9H), 1.23 (t, *J* = 7.1 Hz, 3H).
The data matches those previously reported in the literature.[10]

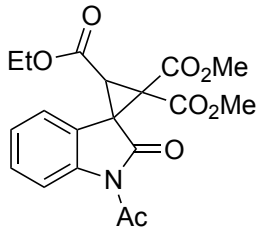
1'-benzyl 3-ethyl 2,2-dimethyl 2'-oxospiro[cyclopropane-1,3'-indoline]-1',2,2,3-tetracarboxylate (5b)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (105 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 10%, 20%, 30%, 40% EtOAc in hexanes) led to the title compound to be isolated as thick orange oil (117 mg, 81% yield as a 7.1:1 mixture of the diastereomers.

R_f = 0.50 (40% EtOAc in hexanes, UV active)
^{1}H NMR (500 MHz; $CDCl_3$): δ 7.99 (d, *J* = 8.2 Hz, 1H), 7.48 (d, *J* = 7.0 Hz, 2H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.36 (dd, *J* = 12.8, 8.5 Hz, 4H), 7.15 (dd, *J* = 7.7 Hz, 1H), 5.44 (s, 2H), 4.29-4.13 (m, 2H), 3.80 (s, 3H), 3.78 (s, 3H), 3.44 (s, 1H), 1.23 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 170.1, 164.8, 164.4, 162.8, 150.2, 140.5, 134.8, 129.3, 128.69, 128.61, 128.2, 126.6, 124.2, 119.7, 114.9, 68.9, 62.1, 53.7, 53.4, 47.8, 40.5, 38.4, 14.1
IR (ATR) 2955 (w), 1796 (s), 1733 (s), 1251 (s), 1187 (s) cm^{-1}
HRMS calcd for $C_{25}H_{24}O_9N$ $[M+H]^+$ 482.1446; found 482.1445.

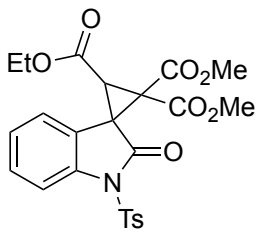
3-ethyl 2,2-dimethyl 1'-acetyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5c)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.6 mmol of alkene (155 mg, 0.6 mmol, 2 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 5%, 10%, 20%, 30% EtOAc in hexanes) led to the title compound to be isolated as an orange liquid containing a mixture of diastereomers (107 mg, 92% yield). An analytic sample of the major diastereomer was obtained by dissolving the above material in minimal $CHCl_3$ and passing through another column of silica gel (hexane followed by 10% EtOAc in hexanes 20% EtOAc in hexanes) to yield the major diastereomer as a yellow solid.

M.P. 84 – 86 °C.
R_f = 0.22 (20% EtOAc in hexanes, UV active)
^{1}H NMR (500 MHz; $CDCl_3$): δ 8.34 (d, *J* = 8.3 Hz, 1H), 7.46 (d, *J* = 7.4 Hz, 1H), 7.40 (ddd, *J* = 7.9, 7.9, 0.9 Hz, 1H), 7.21-7.18 (m, 1H), 4.28-4.18 (m, 2H), 2.66 (s, 3H), 1.27 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 172.8, 170.2, 164.62, 164.42, 162.6, 141.2, 129.3, 126.3, 124.5, 119.7, 116.1, 62.1, 53.6, 53.4, 47.8, 40.6, 38.2, 26.8, 14.0
IR (ATR) 2956 (w), 1751 (s), 1737 (s), 1721 (s), 1317 (m), 1188 (s), 1165 (s) cm^{-1}
HRMS calcd for $C_{19}H_{20}O_8N$ $[M+H]^+$ 390.1183; found 390.1182.

3-ethyl 2,2-dimethyl 2'-oxo-1'-tosylspiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5d)

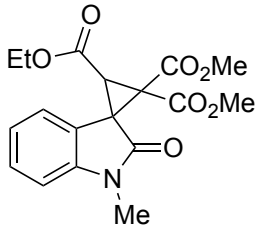


Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (111 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel

(sequentially eluting with pure hexanes followed by 10%, 20%, 30%, 40% EtOAc in hexanes) led to the major isomer of the title compound to be isolated as a yellow oil (102 mg, 68% yield) and the minor isomer of the title compound to be isolated as a yellow-brown solid (44 mg, 29% yield).

Major diastereomer
R_f = 0.39 (40% EtOAc in Hexanes)
^{1}H NMR (500 MHz; $CDCl_3$): δ 8.03 (d, *J* = 8.3 Hz, 1H), 8.00 (d, *J* = 8.4 Hz, 1H), 7.44 (dd, *J* = 7.9, 0.8 Hz, 1H), 7.41 (ddd, *J* = 8.0, 8.0, 1.3 Hz, 1H), 7.35 (d, *J* = 8.0 Hz, 2H), 7.16 (ddd, *J* = 7.8, 1.0 Hz, 1H), 4.25-4.16 (m, 2H), 3.78 (s, 3H), 3.67 (s, 3H), 3.38 (s, 1H), 2.45 (s, 3H), 1.26 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125MHz; $CDCl_3$): δ 170.1, 164.5, 163.9, 162.7, 145.9, 140.3, 134.8, 129.7, 129.4, 128.1, 127.1, 124.1, 119.6, 113.2, 62.1, 53.46, 53.35, 47.7, 40.1, 37.7, 21.7, 13.9
IR (ATR) 2956 (w), 1736 (s), 1235 (s), 1169 (s), 1088 (m) cm^{-1}.
HRMS calcd for $C_{24}H_{24}O_9SN$ $[M+H]^+$ 502.1166; found 502.1166.

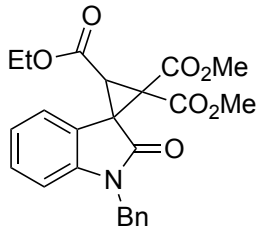
3-ethyl 2,2-dimethyl 1'-methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5e)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (69 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 10%, 20%, 30%, 40% EtOAc in hexanes) furnished a yellow oil (68 mg, 62% yield) containing an inseparable mixture of the title compound and tetramethyl ethene-1,1,2,2-tetracarboxylate in a 70:30 mol ratio (corrected yield of cyclopropane: 52 mg, 48% yield).

R_f = 0.32 (40% EtOAc in hexanes, UV active)
^{1}H NMR (500 MHz; $CDCl_3$): δ 7.41 (d, *J* = 7.8 Hz, 1H), 7.33 (dd, *J* = 7.8 Hz, 1H), 7.04 (dd, *J* = 7.6 Hz, 1H), 6.89 (d, *J* = 7.7 Hz, 1H), 4.19-4.13 (m, 2H), 3.85 (s, 2H), 3.80 (s, 6H), 3.39 (s, 1H), 3.24 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 171.3, 165.4, 164.8, 163.3, 144.7, 128.8, 126.9, 122.1, 120.6, 108.3, 61.8, 53.5, 53.2, 46.8, 40.1, 37.3, 26.8, 14.0
IR (ATR) 2982 (w), 1766 (m), 1746 (s), 1734 (s), 1712 (s), 1612 (m), 1328 (m), 1229 (s), 1028 (m) cm^{-1}.
HRMS calcd for $C_{18}H_{20}O_7N$ $[M+H]^+$ 362.1234; found 362.1233.

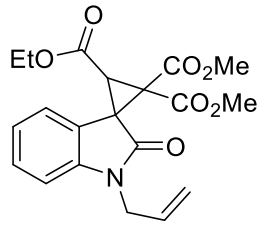
3-ethyl 2,2-dimethyl 1'-benzyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5f)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (92.2 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 5%, 10%, 15%, 20% EtOAc in hexanes) led to the title compound to be isolated as an orange foam (99 mg, 75% yield). An analytic sample was obtained by recrystallizing this material in using chloroform/hexanes, resulting in an off-white solid.

M.P. 164 – 166 °C
R_f = 0.50 (50% EtOAc in hexanes, UV hexanes)
^{1}H NMR (500 MHz; $CDCl_3$): δ 7.35 (d, *J* = 7.8 Hz, 1H), 7.24-7.17 (m, 5H), 7.14-7.10 (m, 1H), 6.91 (dd, *J* = 7.7 Hz, 1H), 6.71 (d, *J* = 7.8 Hz, 1H), 4.95 (d, *J* = 15.6 Hz, 1H), 4.72 (d, *J* = 15.9 Hz, 1H), 4.16-4.06 (m, 2H), 3.71 (s, 3H), 3.70 (s, 2H), 3.38 (s, 1H), 1.16 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 165.3, 164.8, 163.3, 143.9, 135.3, 128.75, 128.72, 127.7, 127.24, 127.08, 122.1, 120.6, 109.1, 61.8, 53.41, 53.23, 47.1, 44.3, 40.2, 37.3, 14.0
IR (ATR) 2994 (w), 1760 (m), 1744 (s), 1733 (s), 1714 (s), 1610 (m), 1356 (m), 1258 (s), 1157 (s).
HRMS calcd for $C_{24}H_{24}O_7N$ $(M+H)^+$ 438.1547; found 438.1548.

3-ethyl 2,2-dimethyl 1'-allyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5g)

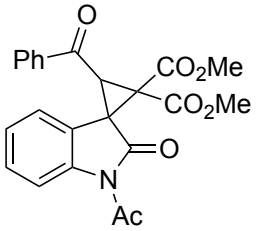


Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (77.8 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10%, 20%,40% EtOAc in hexanes) to recover the title compound as a thick orange oil (69 mg, 59% yield). An analytical sample was obtained by repeating chromatography stated above to yield an off-white solid.

R_f = 0.125 (20% EtOAc in hexanes, UV active)
M.P. = 103 – 105 °C
IR (ATR) 2950.0 (w), 1747.4 (s), 1737.3 (s), 1706.5 (s), 1613.2 (w), 1365.8 (m), 1192.3 (s)
^{1}H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, *J* = 7.9 Hz, 1H), 7.30 (ddd, *J* = 7.8, 7.8, 1.0 Hz, 1H), 7.03 (ddd, *J* = 7.7, 7.7, 0.8 Hz, 1H), 6.90 (d, *J* = 7.8 Hz, 1H), 5.84 (ddt, *J* = 16.8, 10.8, 5.6 Hz, 1H), 5.30 – 5.22 (m, 2H), 4.40 (ddt, 16.3, 5.0, 1.9, Hz, 1H), 4.32 (ddt, 16.3, 5.5, 1.3 Hz, 1H) 4.26-4.14 (m, 2H), 3.80 (s, 3H), 3.79 (s, 3H), 3.43-3.41 (m, 1H), 125 (t, *J* = 7.1 Hz, m 3H).

^{13}C NMR (125 MHz, $CDCl_3$): δ 171.2, 165.4, 164.8, 163.4, 144.0, 131.0, 128.8, 127.1, 122.1, 120.7, 117.9, 109.0, 61.9, 53.47, 53.28, 47.0, 43.0, 40.1, 37.4, 14.1
HRMS calcd for $C_{20}H_{22}O_7N$ $[M+H]^+$ 388.1391, found 388.1389.

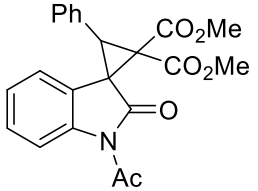
dimethyl 1'-acetyl-3-benzoyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2-dicarboxylate (5h)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (87 mg, 0.1 mmol, 1 equiv). Purification by flash chromatography through a column of silica gel (isocratic: 0.5% $MeOH/CH_2Cl_2$). Fractions containing the product were collected and concentrated by rotary evaporation and the resulting material dissolved in minimal $CHCl_3$ and passed through another column of silica (eluting sequentially with hexanes, followed by 10% EtOAc in hexanes, then 20% EtOAc in hexanes) led to the title compound to be isolated as a pale orange liquid which became of light yellow foam (106 mg, 83% yield) when placed under high vacuum. ^{1}H NMR analysis of this material showed 88:12 ratio between major and minor diastereomers.

R_f = 0.50 (40% EtOAc in hexanes, UV active)
IR (ATR) 2945, 1742 (s), 1720 (s), 1689 (m), 1252 (s), 1164 (s) cm^{-1}.
^{1}H NMR (500 MHz; $CDCl_3$): δ 8.33-8.31 (m, 1H), 8.15 (dd, *J* = 8.2, 1.1 Hz, 2H), 7.60 (dddd, *J* = 7.4, 1.2 Hz, 1H), 7.50 (dd, *J* = 7.8 Hz, 2H), 7.36 (ddd, *J* = 7.9, 1.3 Hz, 1H), 7.32 (d, *J* = 8.1 Hz, 1H), 7.15 (dd, *J* = 7.8 Hz, 1H), 4.08 (s, 1H), 3.87 (s, 3H), 3.68 (s, 3H), 2.68 (s, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 173.2, 170.2, 165.2, 163.2, 141.2, 136.4, 133.9, 129.2, 128.9, 128.4, 126.2, 124.6, 119.9, 116.1, 53.6, 53.4, 49.9, 41.6, 40.9, 26.8.
HRMS calcd for $C_{23}H_{20}O_7N$ $[M+H]^+$ 422.1234; found 422.1233.

Dimethyl 1'-acetyl-2'-oxo-3-phenylspiro[cyclopropane-1,3'-indoline]-2,2-dicarboxylate (5i)

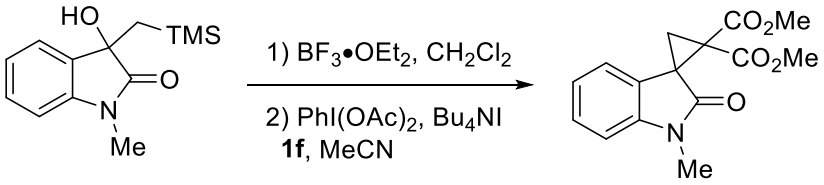


Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (79.0 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10% then 20% EtOAc in hexanes) to recover a thick yellow oil (34mg) which partially foamed when placed under hi-vacuum. This material was a 94:6 mol ratio between the title compound (corrected yield 28%, 2:1 ratio of diastereomers) and tetraethyl ethene-1,1,2,2-tetracarboxylate.

R_f = 0.13 (20% EtOAc in hexanes, UV active)
IR (ATR) 2954.2 (w), 1738.3 (s), 1715.6 (s), 1499.6 (w), 1463.2 (m), 1245.2 (s), 1523.0 (s), 1175.6 (s).

Major diastereomer: ^{1}H (500 Hz, $CDCl_3$) δ 8.36 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.25 (m, 6H), 7.21 (dd, *J* = 7.8, 7.8 Hz, 1H), 7.10 (d, J = 7.0 Hz, 1H), 4.28 (s, 1H), 3.79 (s, 3H), 3.71 (s, 3H), 2.57 (s, 3H).
Minor diastereomer: ^{1}H (500 Hz, $CDCl_3$) δ 8.36 (d, *J* = 8.0 Hz, 1H), 7.42 – 7.25 (m, 6H), 6.99 (dd, *J* = 7.7 Hz, 1H), 6.75 (d, J = 7.9 Hz, 1H), 4.08 (s, 1H), 3.85 (s, 3H), 3.70 (s, 3H), 2.69 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 174.1, 171.1, 170.67, 170.49, 166.3, 165.5, 164.1, 163.9, 141.2, 140.8, 130.2, 130.0, 129.7, 129.5, 129.0, 128.7, 128.3, 128.04, 127.93, 127.77, 127.72, 125.0, 124.1, 123.8, 122.0, 120.7, 116.5, 116.0, 54.6, 53.9, 53.00, 52.88, 51.9, 50.3, 42.2, 41.8, 40.6, 40.1, 26.87, 26.72
HRMS calcd for $C_{22}H_{20}O_6N$ $[M+H]^+$ 394.1285, found 394.1285.

dimethyl 1'-methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2-dicarboxylate (5j)



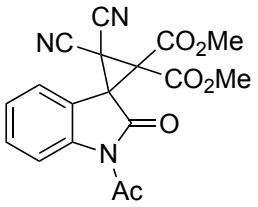
Step 1: In a flame-dried round bottom flask equipped with a magnetic stir bar, 3-hydroxy-1-methyl-3-((trimethylsilyl)methyl)indolin-2-one (235.4 mg, 1.0 mmol) was dissolved in CH_2Cl_2 (30 mL) and cooled to -78 °C, and BF_3•OEt_2 (1.5 mL, 1.725 g, 12.2 mmol) was added dropwise to the resulting solution. The reaction mixture was allowed to stir for 2 h at -78° C and then for 1 h at 0 °C and then quenched using a saturated solution of $NaHCO_3$ (20 mL) and diluted with dichloromethane (80 mL). The layers were separated and the aqueous layer was extracted with dichloromethane (40 mL x 2) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated to *near* dryness using a rotary evaporator.

Step 2: The resulting orange liquid was *immediately* transferred to a flame-dried 50 mL round bottom flask using anhydrous MeCN (10 mL) to assist in the transfer. To this flask, Bu_4NI (110 mg, 0.3 mmol, 30 mol%), ylide **1f** (334 mg, 10 mmol, 1.0 equiv), and $PhI(OAc)_2$ (322 mg, 10 mmol, 1.0 equiv) were sequentially added, and the resulting mixture was allowed to stir for 1 hour at ambient temperature. The reaction with quenched with a saturated solution of $Na_2S_2O_3$ (5 mL) and diluted with H_2O (10 mL). The organic layer was concentrated to approximately half its original volume and the biphasic mixture was extracted with CH_2Cl_2 (25 mL x 3). The combined organic layers were washed with brine, dried using $MgSO_4$, filtered and concentrated using rotary evaporation. The crude material was loaded onto a column of silica gel using a minimal amount of $CHCl_3$ and eluted by sequentially adding hexanes followed by 10%, 20%, 25% EtOAc in hexanes. Fractions containing the title compound were collected and concentrated to yield an orange solid (155 mg) containing a mixture of the title compound and tetramethyl ethene-1,1,2,2-tetracarboxylate in a 96:4 mol ratio. The corrected yield of the cyclopropane over the two steps is 145 mg (50% yield).

^{1}H NMR (500 MHz, $CDCl_3$) 7.36 – 7.30 (m, 2H), 7.02 (dd, *J* = 7.6 Hz, 1H), 6.89 (d, 7.8 Hz), 3.78 (s, 3H), 3.74 (s, 3H), 3.26 (s, 3H) 2.49 (d, *J* = 5.2 Hz), 2.45 (d, *J* = 5.2 Hz).

These data match those that have been reported previously in the literature.[9]

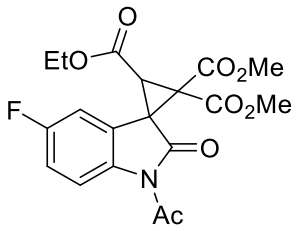
dimethyl 1'-acetyl-3,3-dicyano-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2-dicarboxylate (5k)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (71 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 10%, 20%, 30%, EtOAc in hexanes) led to the title compound to be isolated as slightly pink solid (56 mg, 51% yield)

M.P. 188 – 191 °C
R_f = 0.32 (20% EtOAc in hexanes, UV active)
^{1}H NMR (500 MHz; $CDCl_3$): δ 8.40 (d, *J* = 7.8 Hz, 1H), 7.56 (dd *J* = 7.6 Hz, 1H), 7.40 (d, *J* = 7.0 Hz, 1H), 7.32 (dd, *J* = 7.6 Hz, 1H), 3.95 (s, 3H), 3.91 (s, 3H), 2.69 (s, 3H).
^{13}C NMR (125MHz; $CDCl_3$): δ 169.7, 167.1, 159.4, 141.8, 132.0, 125.8, 124.3, 117.3, 116.2, 108.5, 108.0, 55.1, 54.8, 50.2, 44.3, 26.8, 22.9
IR (ATR) 2958 (w), 2259 (w), 1753 (s), 1739 (s), 1718 (s), 1465 (m), 1267 (s), 1174 (m) cm^{-1}.
HRMS calcd for $C_{18}H_{14}O_6N_3$ $[M+H]^+$ 368.0877; found 368.0879.

3-ethyl 2,2-dimethyl 1'-acetyl-5'-fluoro-2'-oxospiro[cyclopropane-1,3'-indoline]-2,2,3-tricarboxylate (5l)

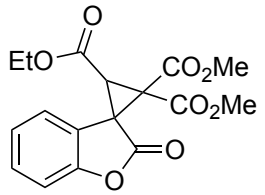


Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (83.2 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 5%, 10%, 15%, 20% EtOAc in hexanes) led to the title compound to be isolated as an orange liquid (117 mg, 96% yield) as a 3:1 mixture of diastereomers.

IR 2988 (w), 1733 (s), 1603 (w), 1476 (m), 1371 (m), 1254 (s), 1017 (m) cm^{-1}.
^{1}H NMR (500 MHz; $CDCl_3$): δ 8.31-8.28 (m, 1.4H), 7.21 (dd, *J* = 9.4, 2.6 Hz, 1H), 7.12 – 7.03 (m, 1.5H), 6.89 (dd, *J* = 8.4, 2.4 Hz, 0.4H), 4.25-4.19 (m, 3H), 3.83 (s, 1H), 3.81 (s, 6H), 3.73 (s, 1H), 3.64 (s, 0.3), 3.43 (s, 1H), 2.65 (s, 1H), 2.61 (s, 3H), 1.31-1.22 (m, 4H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5, 170.2, 169.97, 169.95, 164.4, 164.1, 164.0, 163.4, 162.50, 162.47, 159.8 (d, ^1J = 244.6 Hz), 159.4 (d, ^1J = 242.9), 137.3 (d, ^4J = 2.4 Hz), 137.0 (d, ^4J = 2.7 Hz), 124.3 (d, ^3J = 10.0 Hz), 121.8 (d, ^3J = 10.0 Hz), 117.9 (d, ^3J = 8.2 Hz), 117.2 (d, ^3J = 8.2 Hz), 116.0 (d, ^2J = 22.7 Hz), 115.8 (d, ^2J = 23.0 Hz), 114.2 (d, ^2J = 27.5 Hz), 109.3 (d, ^3J = 26.7 Hz), 62.3, 62.1, 54.1, 53.7, 53.6, 53.3, 49.9, 48.0, 40.4, 39.2, 38.4, 37.4, 26.7, 26.4, 14.0.

^{19}F (470 MHz, $CDCl_3$) -115.89 (minor), -116.45 (major).
HRMS calcd for $C_{19}H_{19}O_8NF$ $[M+H]^+$ 408.1089; found 408.1089.

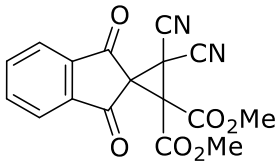
3'-ethyl 2',2'-dimethyl 2-oxo-2H-spiro[benzofuran-3,1'-cyclopropane]-2',2',3'-tricarboxylate (5m)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (65.5 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with pure hexanes followed by 10%, 20%, 30%, 40% EtOAc in hexanes) led to the major isomer of the title compound to be isolated as a yellow oil (65 mg, 62% yield) and the minor isomer of the title compound in 21% yield.

R_f = 0.25 (20% EtOAc in Hexanes, UV active)
IR (ATR) 2956 (w), 1802.9 (m), 1757 (s), 1728 (s), 1431 (m), 1256 (s), 159 (s), 1071 (s) cm^{-1}.
^{1}H NMR (500 MHz; $CDCl_3$): δ 7.43 (d, *J* = 7.8 Hz, 1H), 7.37 (dd, *J* = 7.8 Hz, 1H), 7.17-7.12 (m, 2H), 4.22-4.17 (m, 2H), 3.81 (d, *J* = 1.4 Hz, 6H), 3.45 (s, 1H), 1.24 (t, *J* = 7.1 Hz, 3H).
^{13}C NMR (125 MHz; $CDCl_3$): δ 171.9, 164.5, 163.7, 162.5, 154.5, 129.8, 127.3, 123.9, 119.5, 110.7, 62.2, 53.8, 53.4, 47.2, 38.18, 38.12, 14.0.
HRMS calcd for $C_{17}H_{17}O_8$ $[M+H]^+$ 349.0918; found 349.0918.

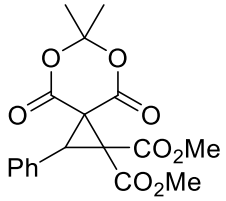
Dimethyl 3,3-dicyano-1',3'-dioxo-1',3'-dihydrospiro[cyclopropane-1,2'-indene]-2,2-dicarboxylate (5n)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (62.4 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10%, 20%, 40%, EtOAc in hexanes) led to the title compound to be isolated a thick orange liquid (36 mg, 35% yield)

R_f = 0.22 (40% EtOAc in heaxnes, UV active)
IR (ATR) 2195.2 (w), 2252.6 (w), 1741.4 (s), 1715.8 (s), 1591.6 (w), 1436.0 (m), 1239.7 (s).
^{1}H (500 MHz, $CDCl_3$) 8.13 – 8.00 (m, 4H), 3.93 (s, 6H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 185.9, 158.5, 141.6, 137.3, 124.5, 107.7, 55.0, 49.8, 444, 20.4
HRMS (ESI) calcd for $C_{17}H_{11}O_6N_2$ $[M+H]^+$ 339.06226, found 339.06119

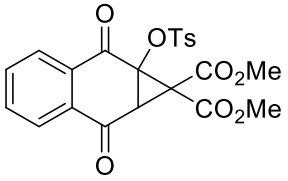
Dimethyl 6,6-dimethyl-4,8-dioxo-2-phenyl-5,7-dioxaspiro[2.5]octane-1,1-dicarboxylate (5o)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (70 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10%, 20%,40%, EtOAc in hexanes) led to the title compound to be isolated a white solid (80 mg, 74% yield).

M.P. = 135 – 137 °C
R_f = 0.48(40% EtOAc in hexanes, UV active)
IR (ATR) 2970.2 (w), 1735 (s), 1434 (w), 1332.9 (m) 1230.2 (m), 1081.2 (m) cm^{-1}.
^1H NMR (500 MHz, $CDCl_3$) δ 7.40 – 7.34 (m, 5H), 4.41 (s, 1H), 3.88 (s, 3H), 3.80 (s, 3), 2.07 (s, 3H), 1.86 (s, 3H).
^{13}C NMR (125 MHz, $CDCl_3$) δ 165.1, 164.1, 162.1, 161.4, 129.5, 129.3, 128.0 (2C), 105.9, 54.2, 53.7, 53.6, 43.9, 36.5 2, 27.63, 27.57.
HRMS calcd for $C_{18}H_{19}O_8$ $[M+H]^+$ 363.1074, found 363.1075.

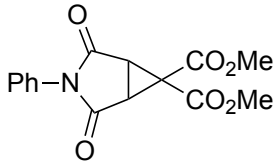
Dimethyl 2,7-dioxo-1a-(tosyloxy)-1a,2,7,7a-tetrahydro-1H-cyclopropa[b]naphthalene-1,1-dicarboxylate (5p)



Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (98.5 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10%, 20%,40%, EtOAc in hexanes) led to the title compound to be isolated a yellow-orange foam (109 mg, 79% yield).

R_f = 0.30 (40% EtOAc in Hexanes, UV active)
IR (ATR)2958.0 (w), 1753.5 (s), 1740.5 (m), 1693.0 (s), 1594.7 (m), 1246.0 (s), 1180.1 (s), 1077.3 (s)
^1H NMR (500 MHz, $CDCl_3$): δ 8.13 (d, J = 8.9 Hz, 1H), 8.03 (d, J = 6.6 Hz, 1H), 7.87 (d, J = 8.3 Hz, 2H), 7.78-7.76 (m, 2H), 7.38 (d, J = 8.1 Hz, 2H), 4.03 (s, 1H), 3.75 (s, 3H), 3.20 (s, 3H), 2.47 (s, 3H).
^{13}C (125 MHz, $CDCl_3$) δ 185.7, 183.9, 162.1, 161.5, 146.0, 134.83, 134.78, 133.0, 132.2, 131.5, 129.8, 128.5, 127.3, 126.9, 68.3, 54.2, 53.4, 47.9, 40.9, 21.8.
HRMS (ESI) calcd for $C_{22}H_{19}O_9S$ $[M+H]^+$ 459.0744, found 459.0743.

Dimethyl 2,4-dioxo-3-phenyl-3-azabicyclo[3.1.0]hexane-6,6-dicarboxylate (5q)

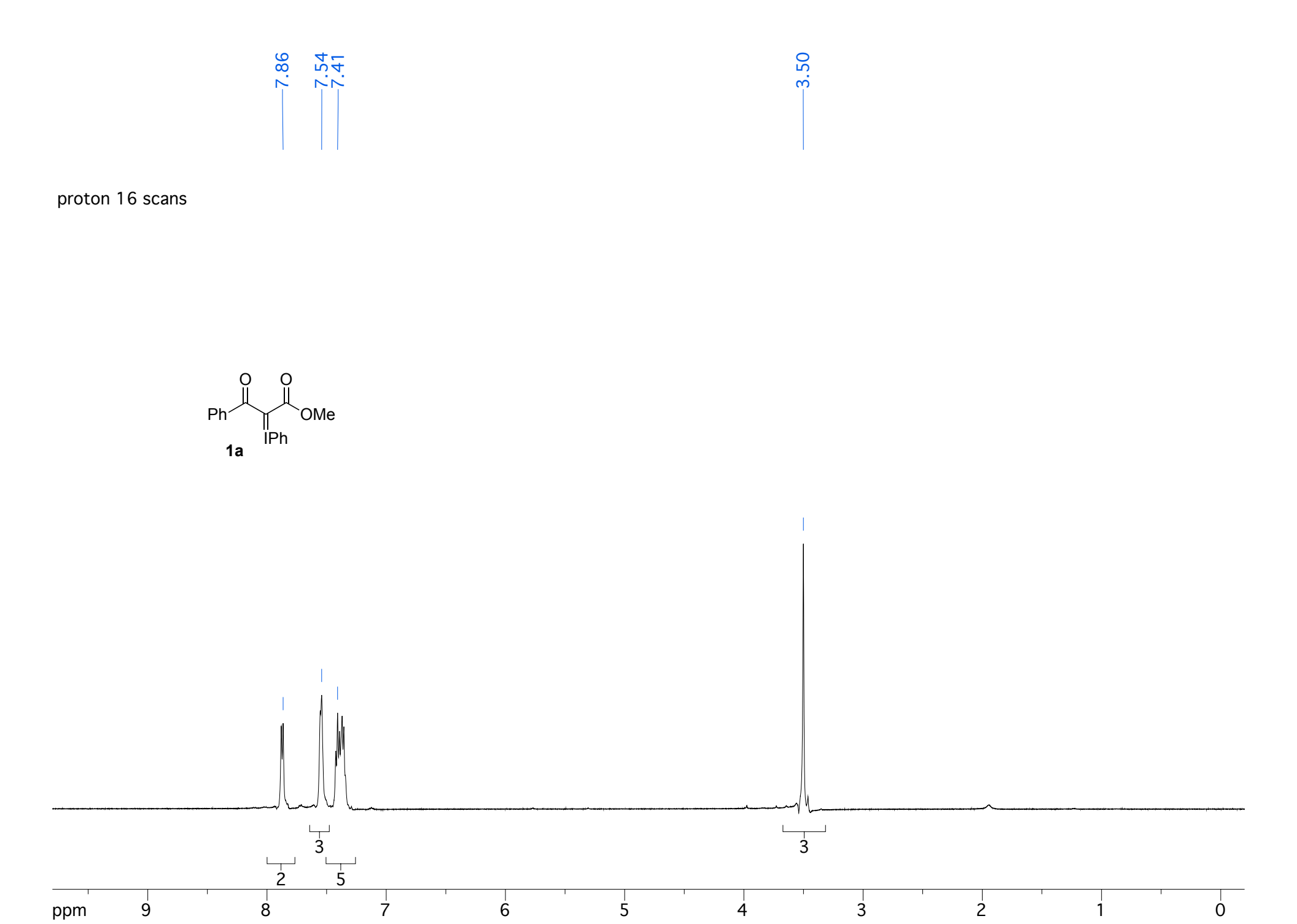


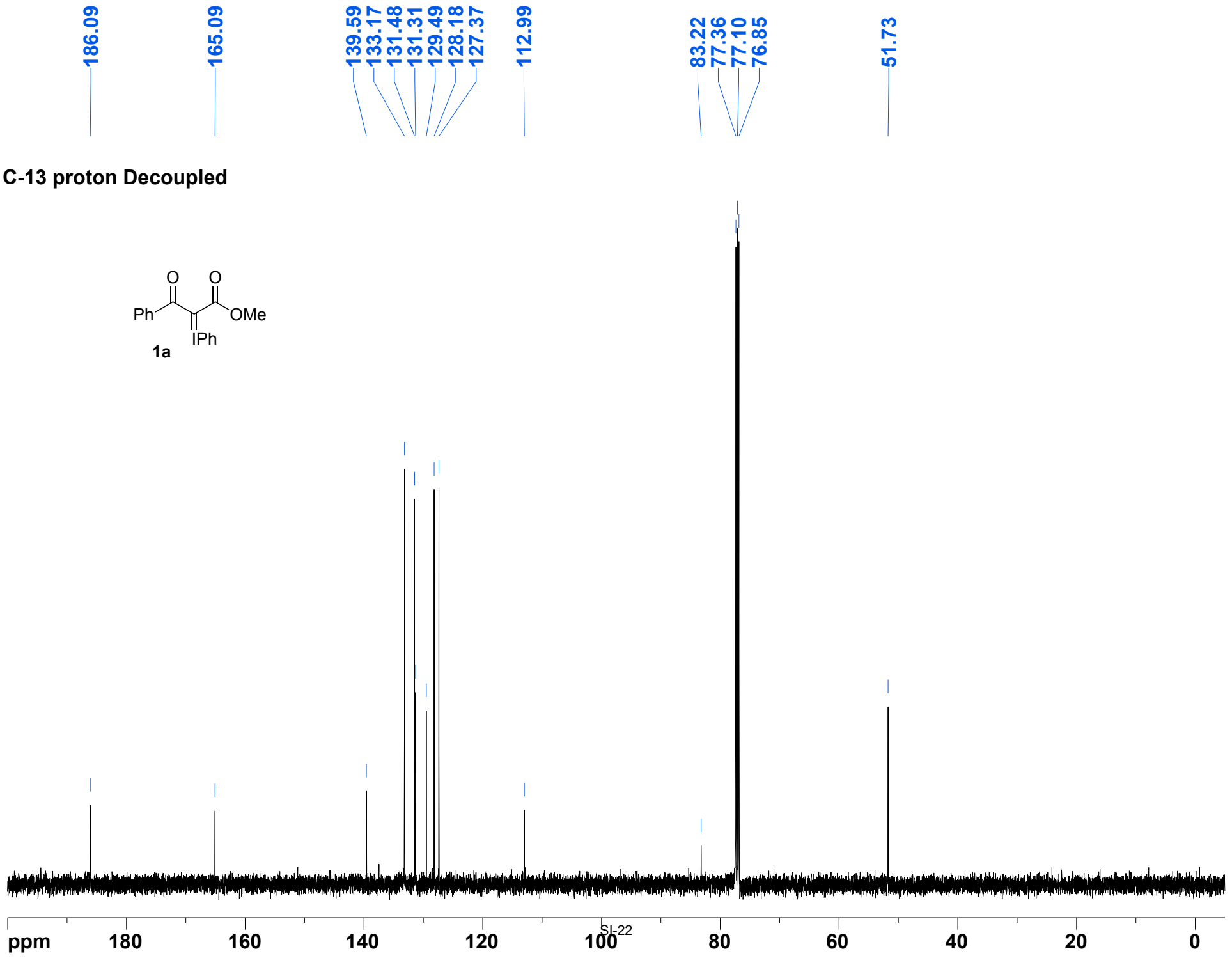
Synthesized according to **GP3** using 0.3 mmol of ylide and 0.3 mmol of alkene (52.0 mg, 0.3 mmol, 1 equiv). Purification by gradient flash chromatography through a column of silica gel (sequentially eluting with 10%, 20%,40%, EtOAc in hexanes) led to the title compound to be isolated a white solid (25 mg, 27% yield). An analytical sample of this material was obtained by triturating this material using Et_2O.

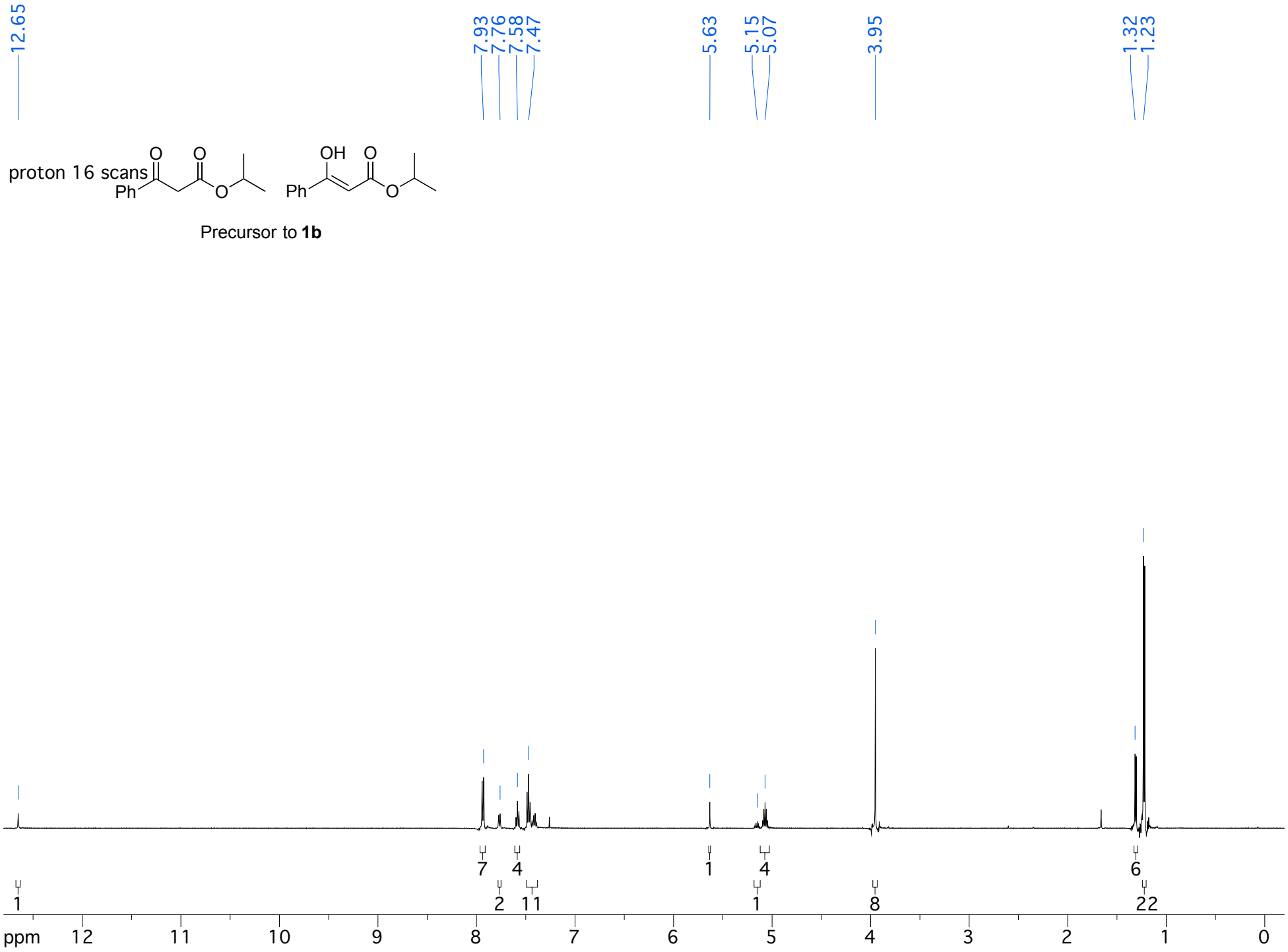
R_f = 0.49 (40% EtOAc in hexanes, UV active)
M.P. = 176 – 178 °C
IR (ATR) 3078.5 (w), 1724.2 (s), 1256.1 (s), 1160.5 (m).
^{1}H NMR (500 MHz; $CDCl_3$) δ 7.44 (t, *J* = 7.5 Hz, 2H), 7.42 (s, 2H), 7.39-7.36 (m, 1H), 7.39-7.36 (m, 1H), 7.17 (d, *J* = 7.2 Hz, 2H), 7.17 (d, *J* = 7.2 Hz, 2H), 3.85 (s, 3H), 3.85 (s, 3H), 3.78 (s, 3H), 3.78 (s, 3H), 3.26 (s, 2H), 3.26 (s, 2H).
^{13}C NMR (125 MHz, $CDCl_3$): δ 168.7, 165.5, 164.0, 130.9, 129.2, 128.8, 126.0, 54.09, 53.99, 44.3, 31.2.
HRMS (ESI) calcd for $C_{15}H_{14}NO_6$ $[M+H]^+$ 304.08156, found 304.08151.

1. Schank, K.; Lick, C. *Synthesis* **1983**, *1983*, 392-395.
2. Buckles, R. E.; Yuk, J. P. *J. Am. Chem. Soc.* **1953**, *75*, 5048-5052.
3. Xu, X.; Wang, X.; Zavalij, P. Y.; Doyle, M. P. *Org. Lett.* **2015**, *17*, 790-793.
4. Tao, J.; Tuck, T. N.; Murphy, G. K. *Synthesis* **2016**, *48*, 772-782.
5. Marcoux, D.; Charette, A. B. *Angew. Chem. Int. Ed. Engl.* **2008**, *47*, 10155-10158.
6. For **2e** see Müller, P.; Bernardinelli, G.; Allenbach, Y. F.; Ferri, M.; Flack, H. D. *Org. Lett.* **2004**, *6*, 1725–1728. For **2f** see Nishimura, T.; Maeda, Y.; Hayashi, T. *Angew. Chem. Int. Ed.* **2010**, *49*, 7324. For **2h** see Bosnidou, A.-E.; Kalpogiannaki, D.; Karanestora, S.; Nixas, J. A.; Hadjiarapoglou, L. P. *J. Org. Chem.* **2015**, *80*, 1279. For **2k** see Qian, P.; Du, B.; Song, R.; Wu, X.; Mei, H.; Han, J.; Pan, Y. *J. Org. Chem.* **2016**, *81*, 6546.
7. Xia, L.; Lee, Y. R. *Adv. Synth. Catal.* **2013**, *355*, 2361-2374.
8. Liu, Y.-Y.; Duan, S.-W.; Zhang, R.; Liu, Y.-H.; Chen, J.-R.; Xiao, W.-J. *Org. Biomol. Chem.* **2016**, *14*, 5224-5228.
9. Wilson, E. E.; Rodriguez, K. X.; Ashfeld, B. L. *Tetrahedron* **2015**, *71*, 5765-5775.
10. Guo, J.; Liu, Y.; Li, X.; Liu, X.; Lin, L.; Feng, X., *Chem. Sci.* **2016**, *7*, 2717.

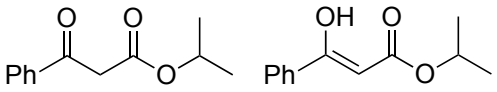
^{1}H and ^{13}C NMR Spectra


7.86
7.54
7.41
3.50
proton 16 scans
O
O
Ph
OMe
IPh
1a
3
3
2
5
ppm
9
8
7
6
5
4
3
2
1
0

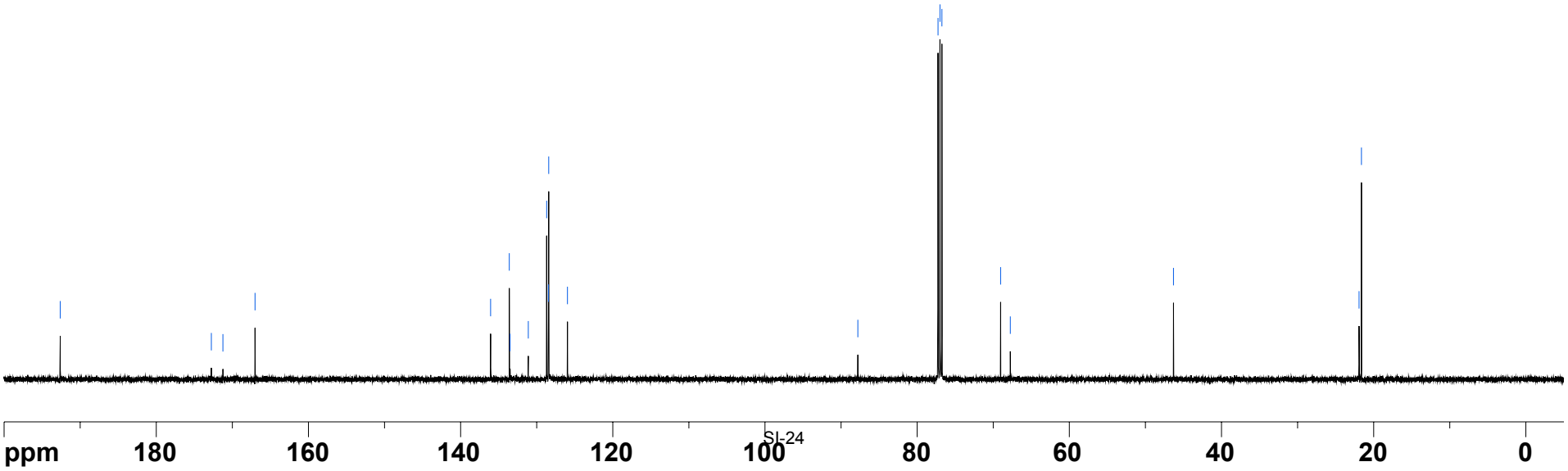

186.09
165.09
139.59
133.17
131.48
131.31
129.49
128.18
127.37
112.99
83.22
77.36
77.10
76.85
51.73
C-13 proton Decoupled
O
O
Ph
OMe
IPh
1a
ppm
180
160
140
120
100
80
60
40
20
0

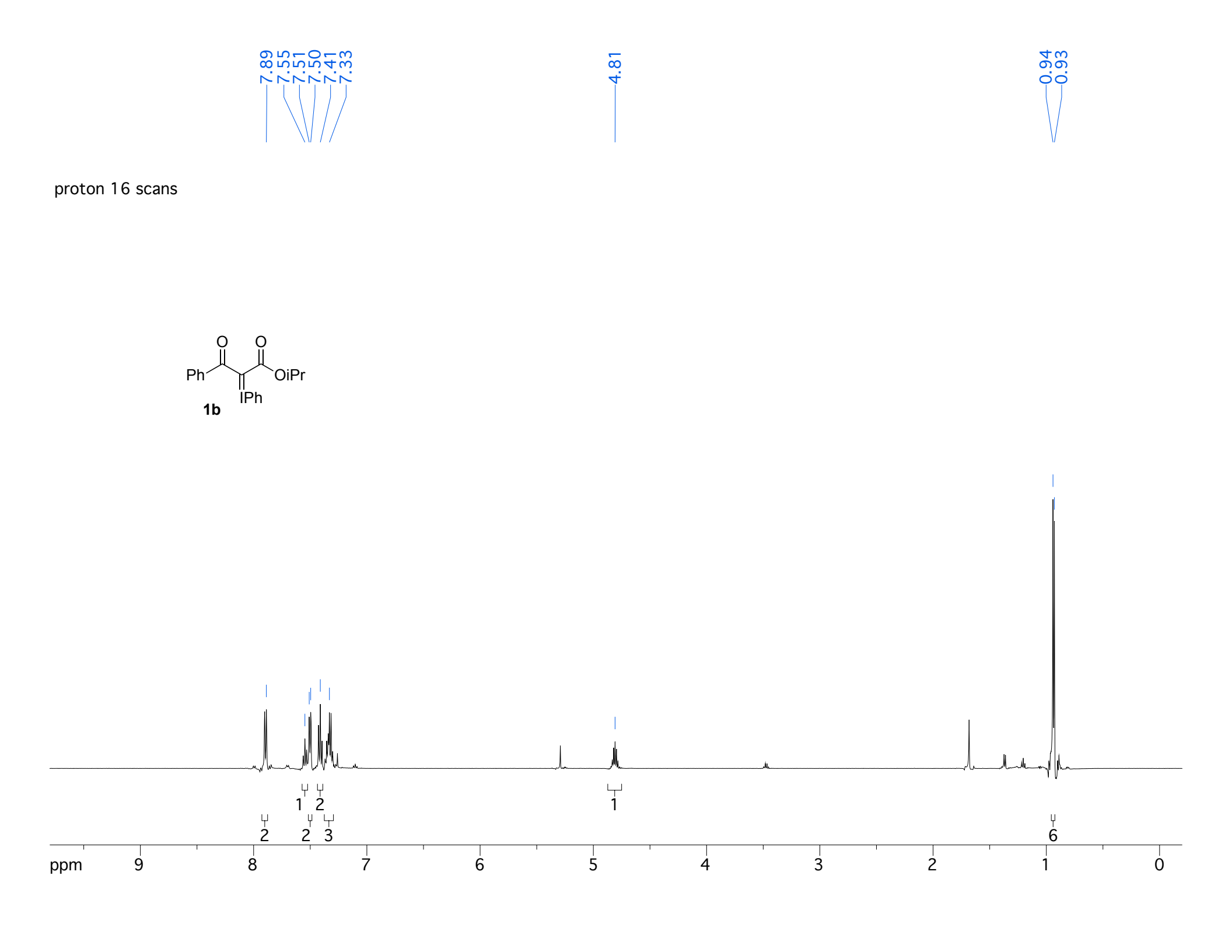

12.65
7.93
7.76
7.58
7.47
5.63
5.15
5.07
3.95
1.32
1.23
proton 16 scans
Ph
O
O
O
OH
O
Ph
O
Precursor to **1b**
7
4
1
4
6
1
2
11
1
8
22
ppm
12
11
10
9
8
7
6
5
4
3
2
1
0

C-13 proton Decoupled



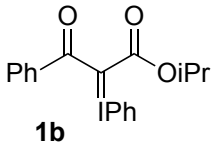
Precursor to **1b**



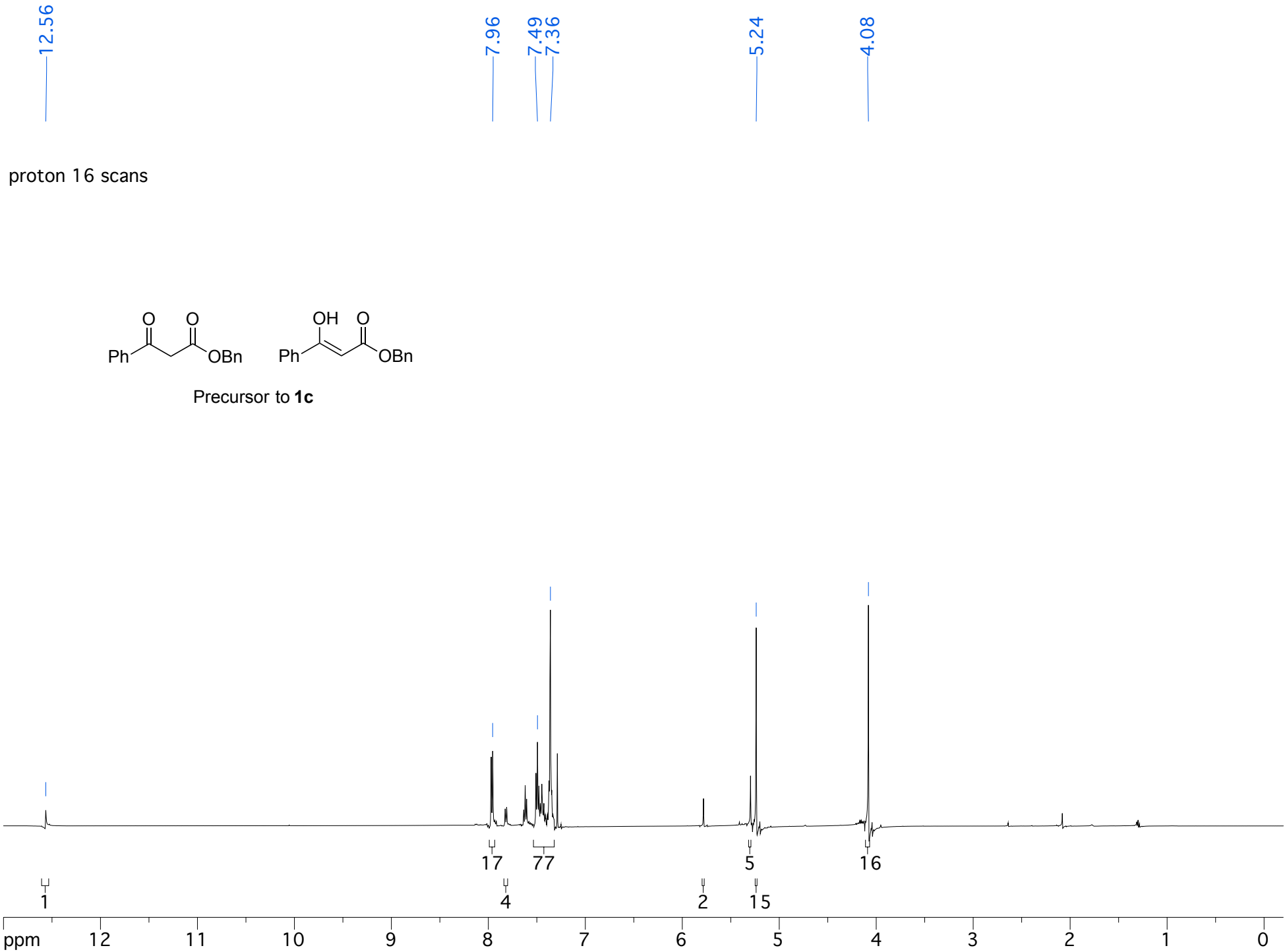

7.89
7.55
7.51
7.50
7.41
7.33
4.81
0.94
0.93
proton 16 scans
O
O
Ph
OiPr
IPh
1b
1
2
1
2
2
3
6
ppm
9
8
7
6
5
4
3
2
1
0

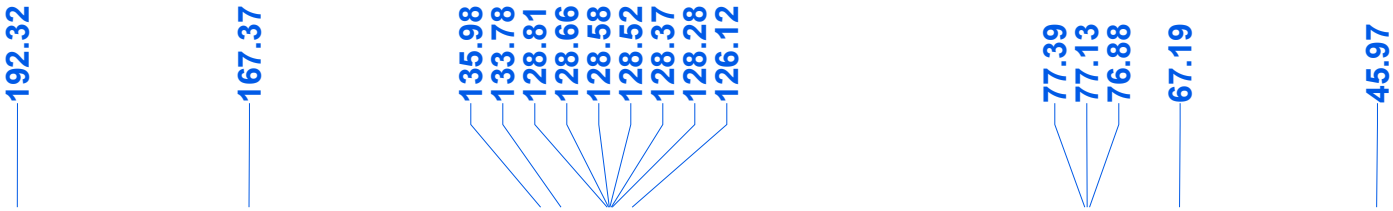
186.08
164.15
139.89
133.38
131.46
131.32
129.19
128.10
127.29
112.79
85.42
77.00
67.91
21.79

C-13 proton Decoupled

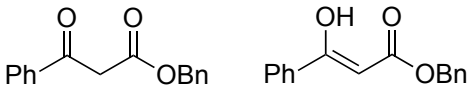


1b

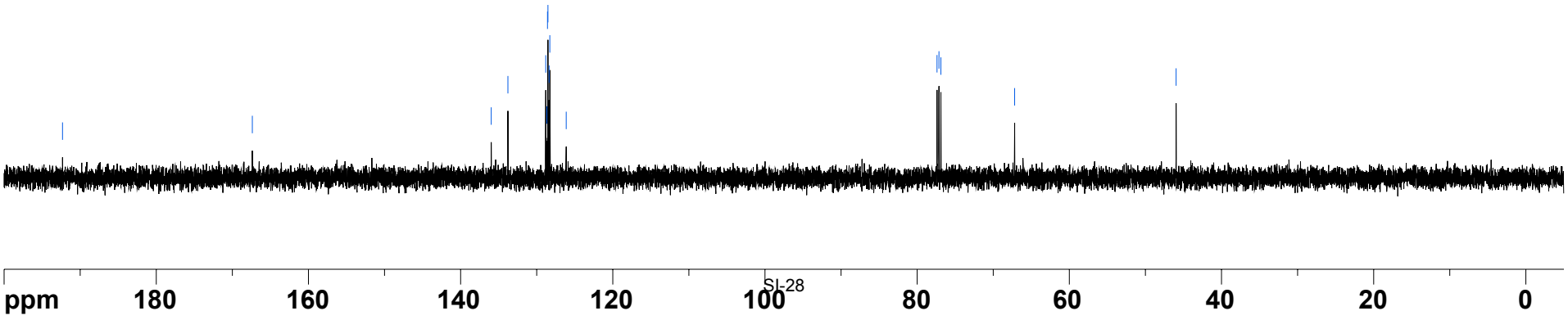

12.56
7.96
7.49
7.36
5.24
4.08
proton 16 scans
O
O
Ph
OBn
OH
O
Ph
OBn
Precursor to 1c
17
77
5
16
1
4
2
15
ppm
12
11
10
9
8
7
6
5
4
3
2
1
0

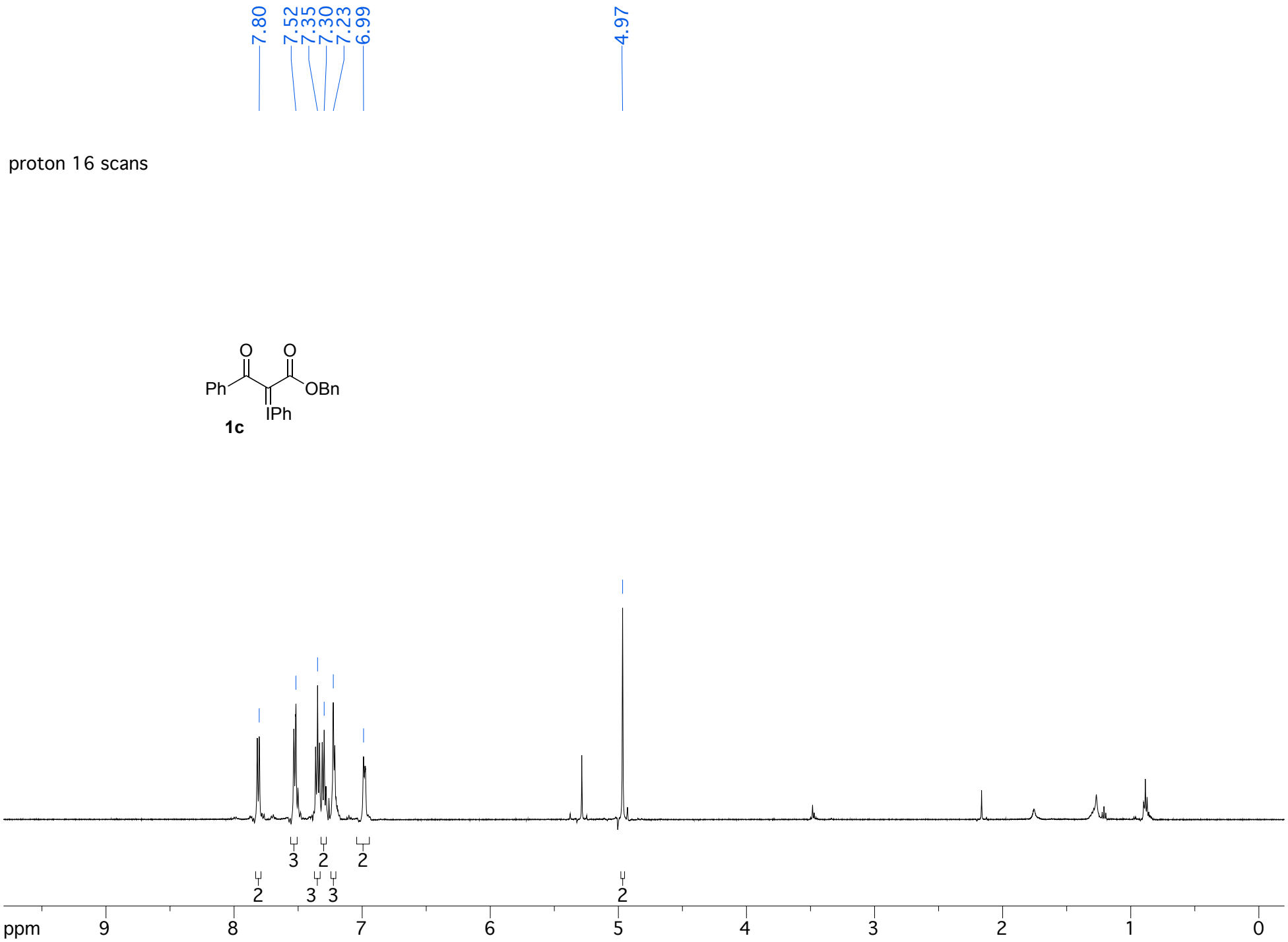


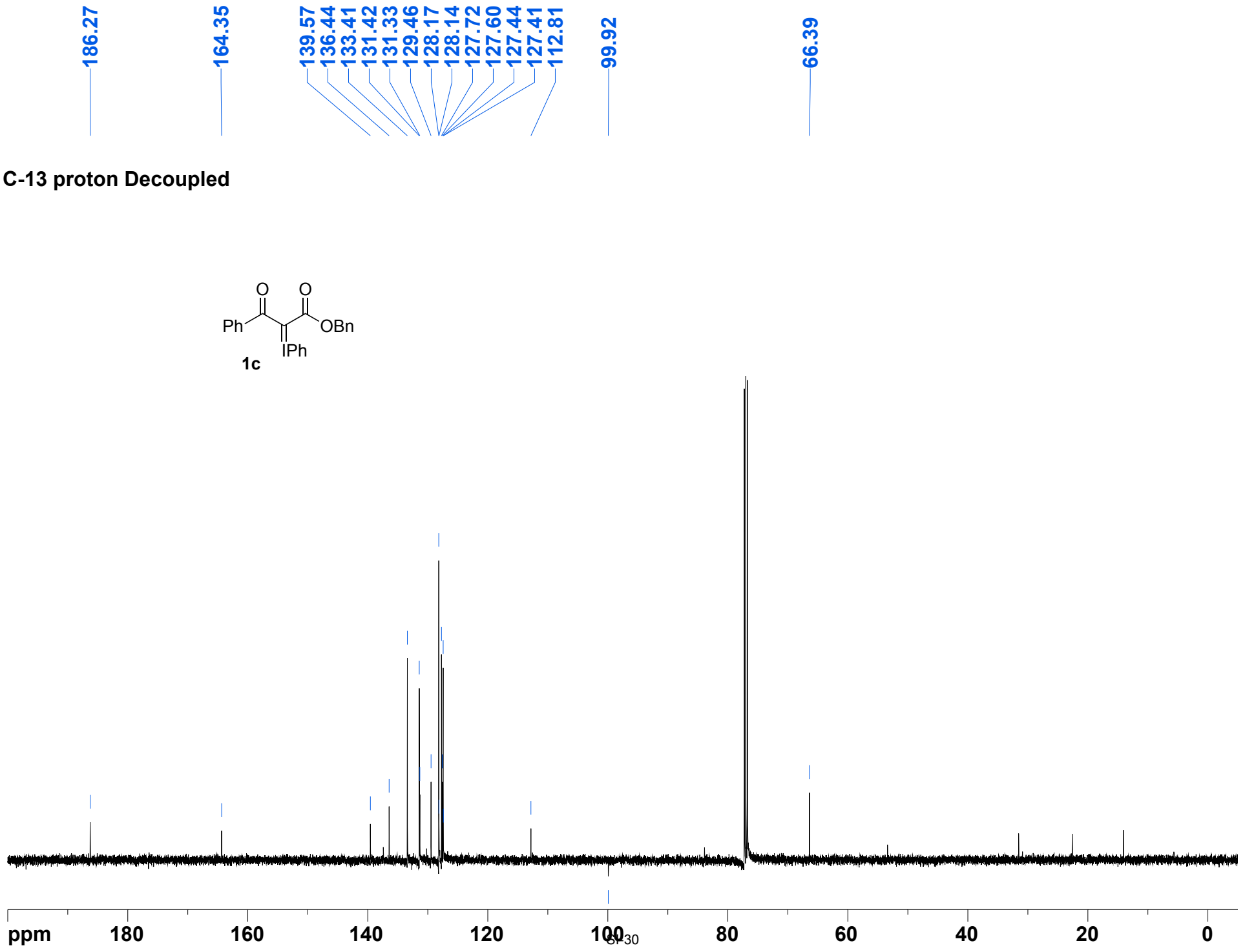
C-13 proton Decoupled

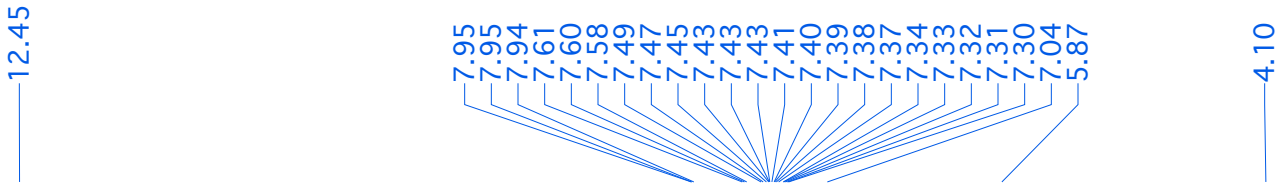


Precursor to **1c**

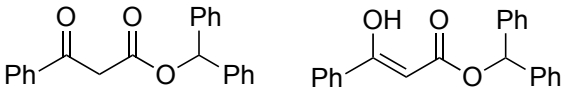



7.80
7.52
7.35
7.30
7.23
6.99
4.97
proton 16 scans
O
O
Ph
OBn
IPh
1c
3
2
2
2
3
3
2
ppm
9
8
7
6
5
4
3
2
1
0

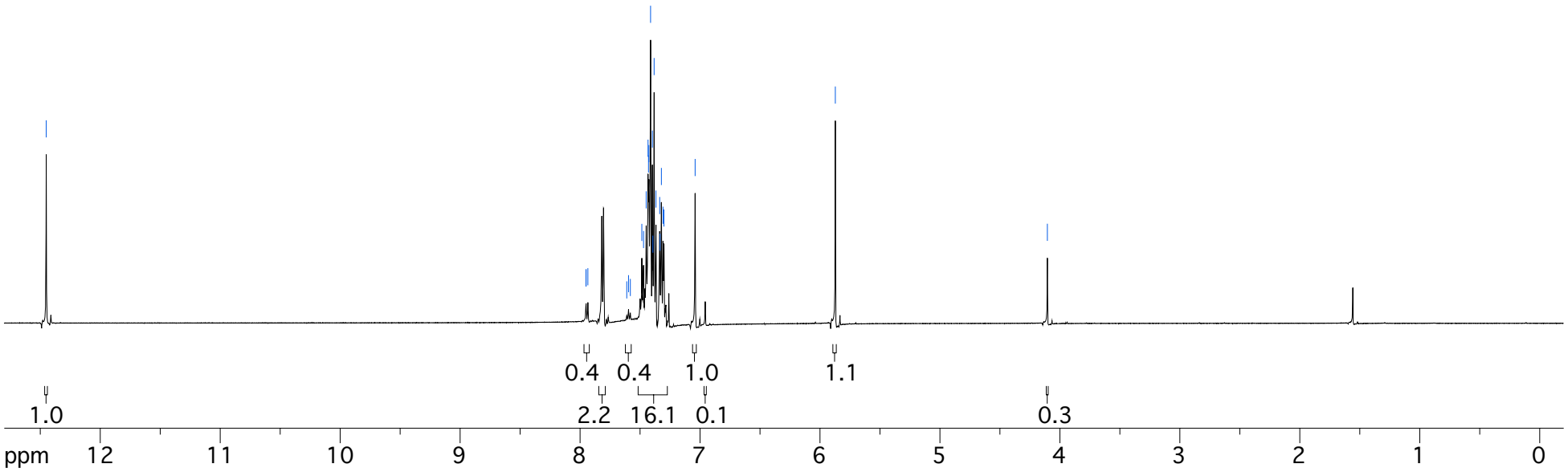

186.27
164.35
139.57
136.44
133.41
131.42
131.33
129.46
128.17
128.14
127.72
127.60
127.44
127.41
112.81
99.92
66.39
C-13 proton Decoupled
O
O
Ph
OBn
IPh
1c
ppm
180
160
140
120
100
80
60
40
20
0
CF-30

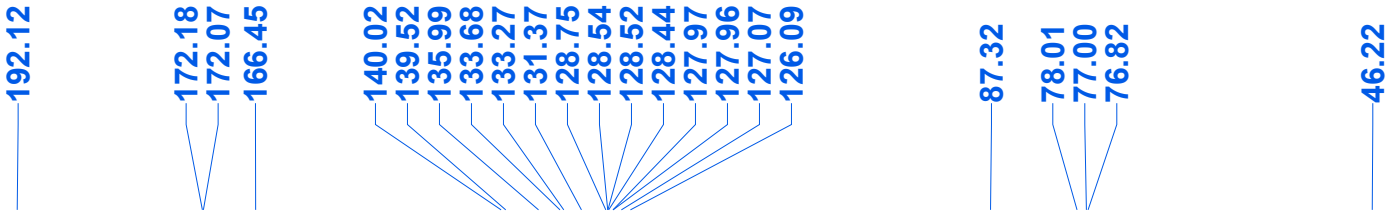


proton 16 scans

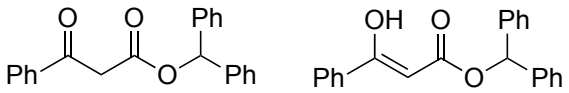


Precursor to **1d**

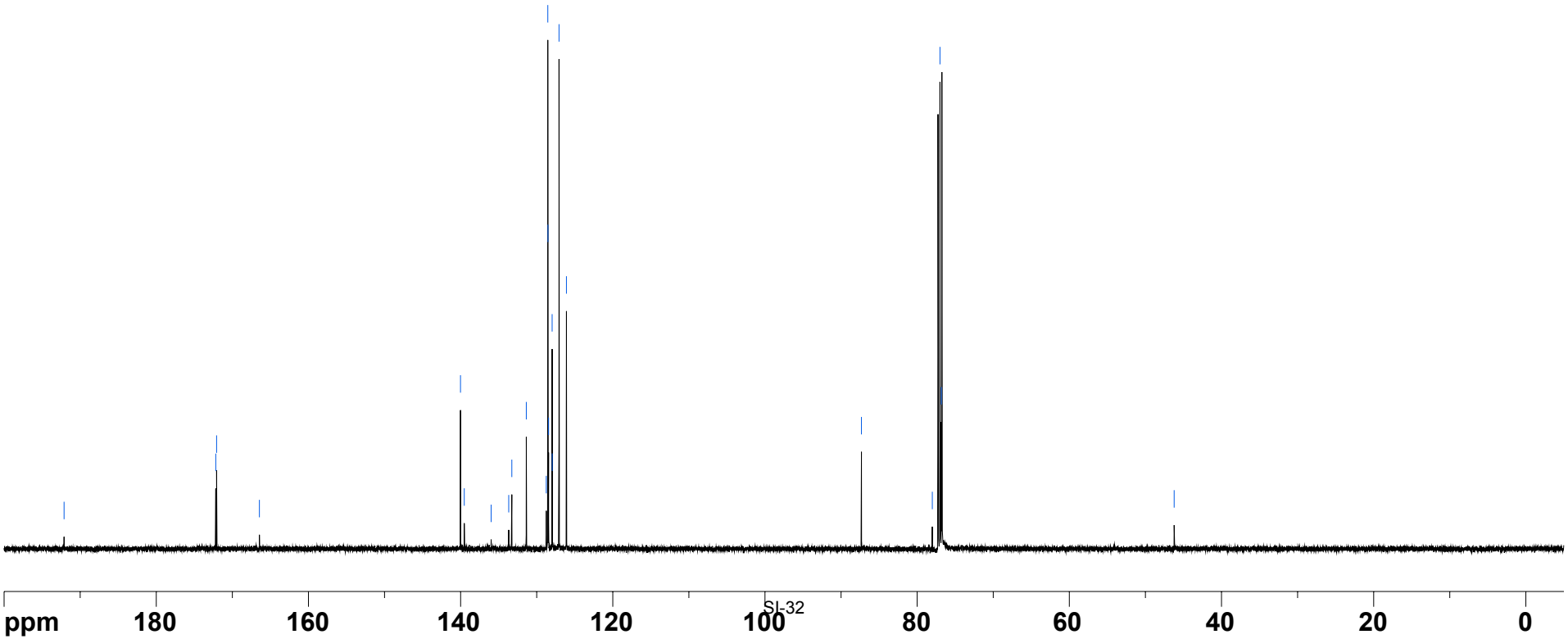


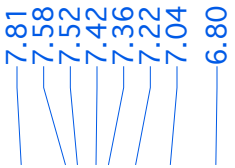


C-13 proton Decoupled

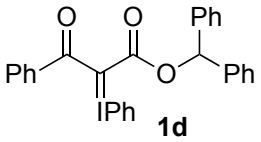


Precursor to **1d**

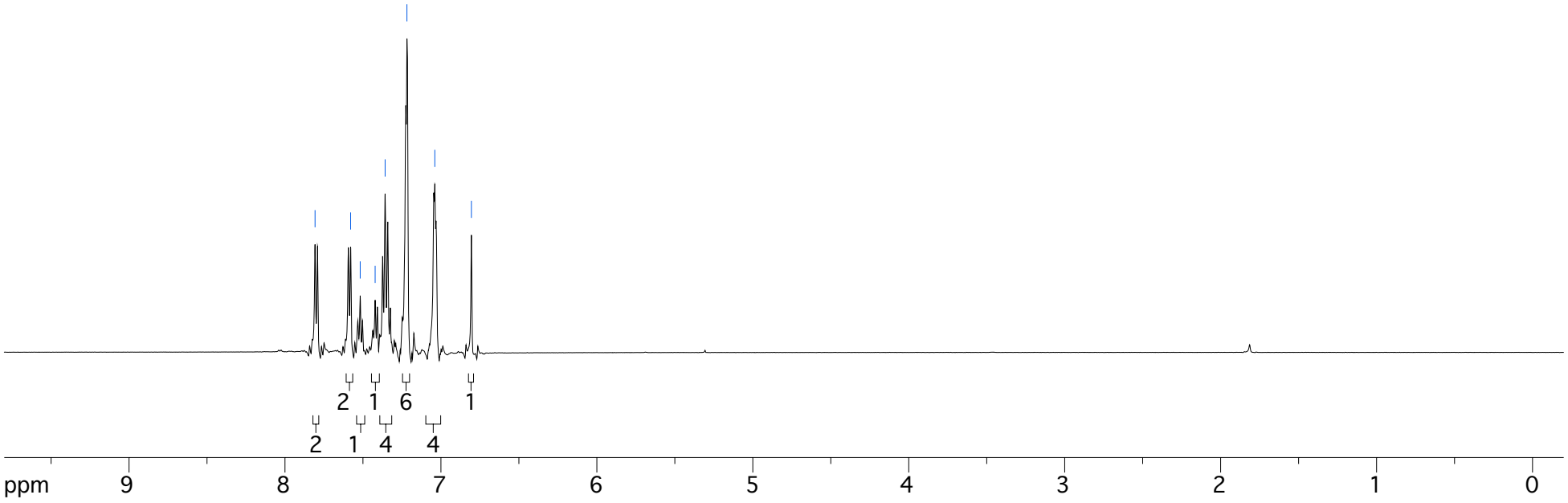


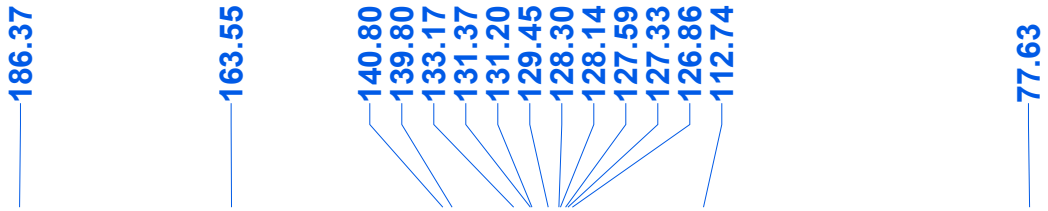


proton 16 scans

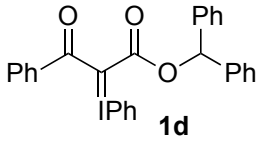


1d

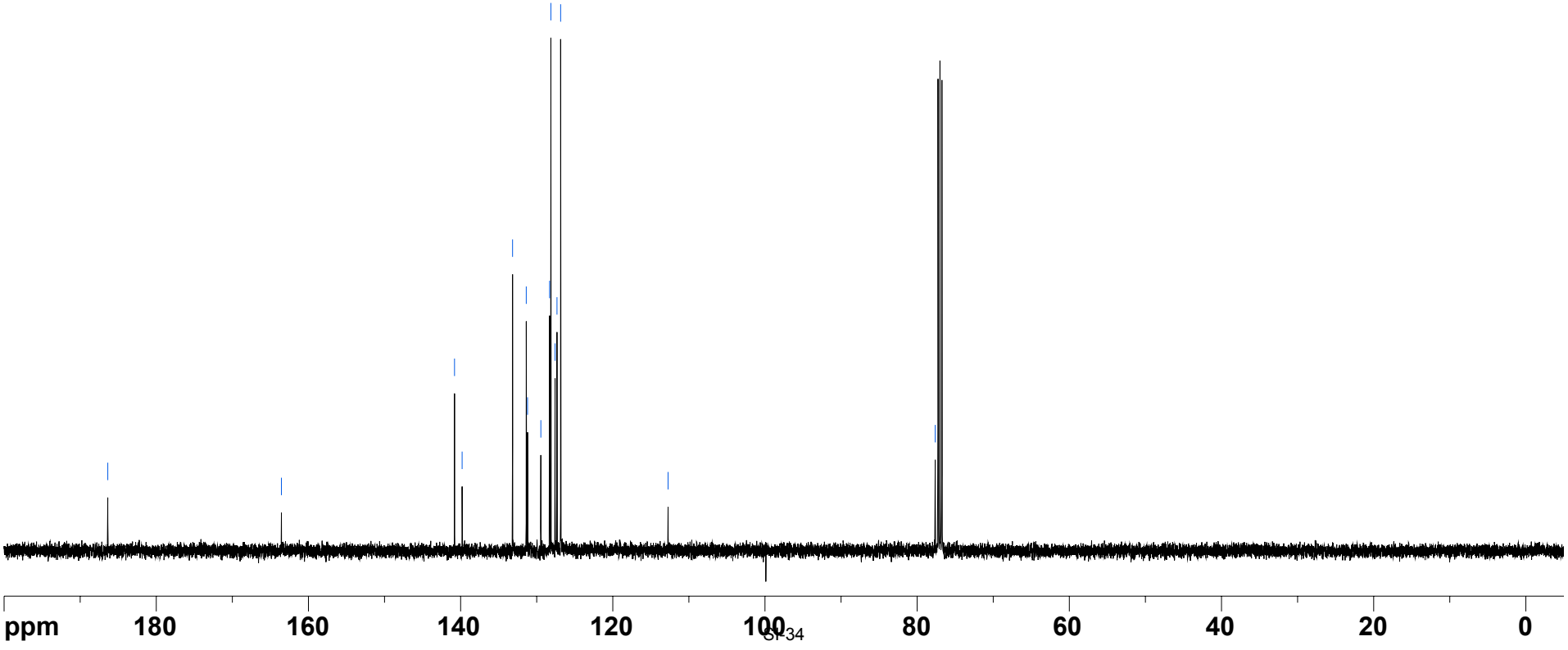


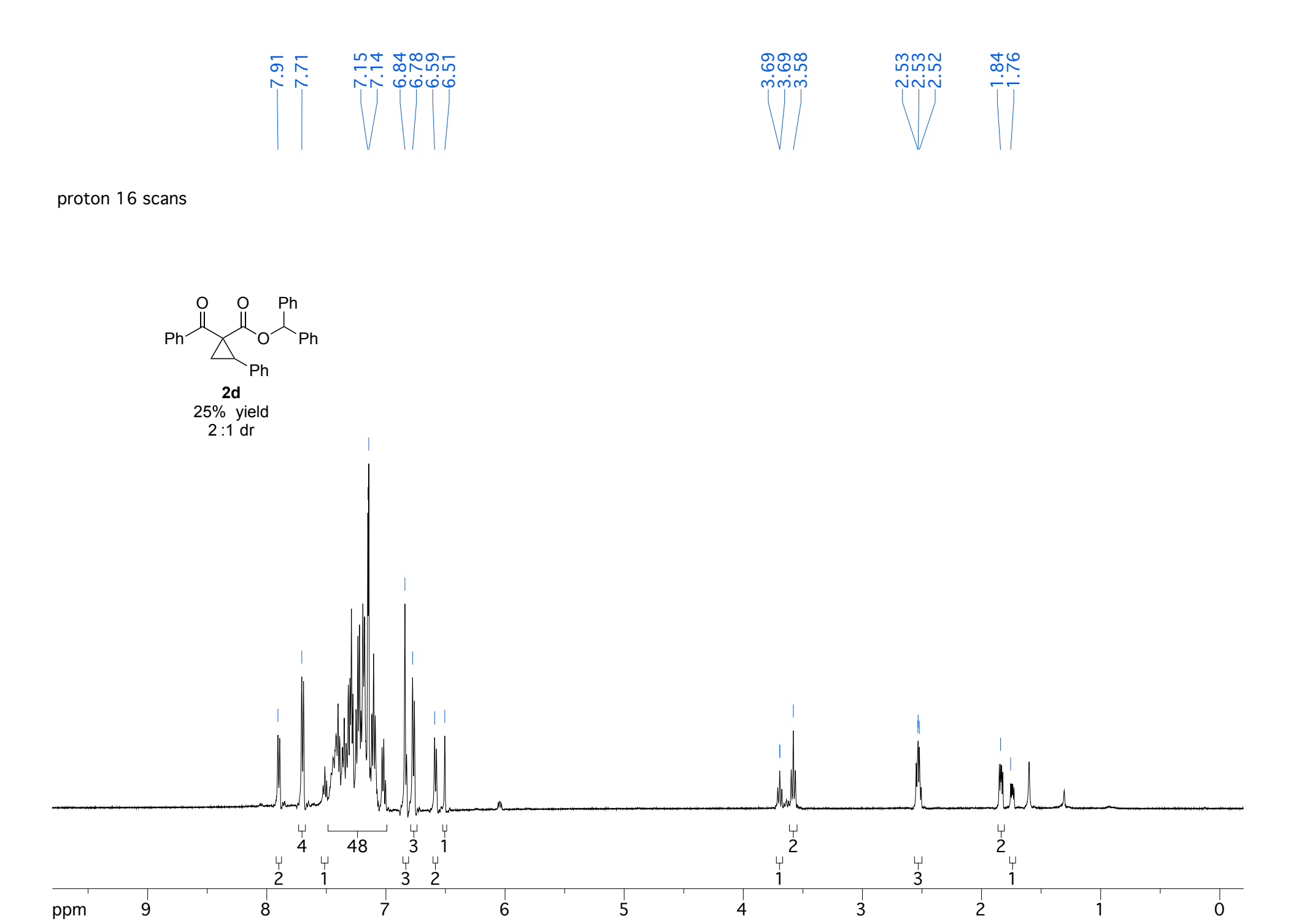


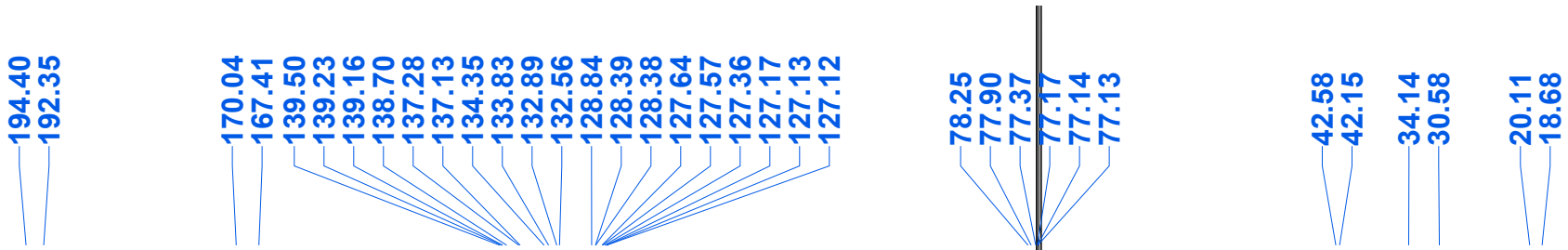
C-13 proton Decoupled



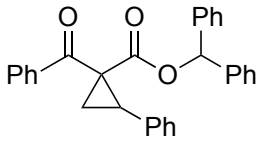
1d



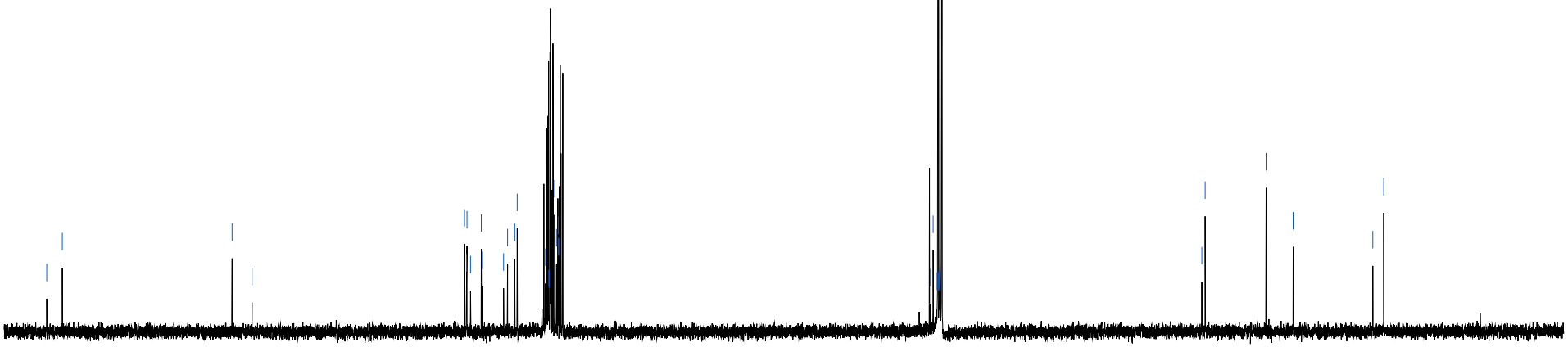

7.91
7.71
7.15
7.14
6.84
6.78
6.59
6.51
3.69
3.69
3.58
2.53
2.53
2.52
1.84
1.76
proton 16 scans
O
O
Ph
Ph
O
Ph
Ph
2d
25% yield
2 :1 dr
4
48
3
1
2
2
2
1
3
2
1
3
2
1
ppm
9
8
7
6
5
4
3
2
1
0

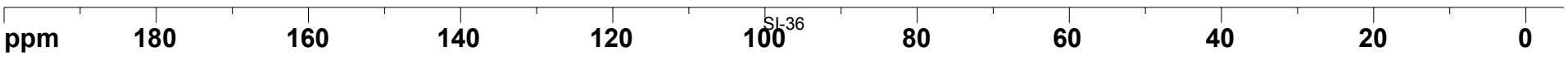


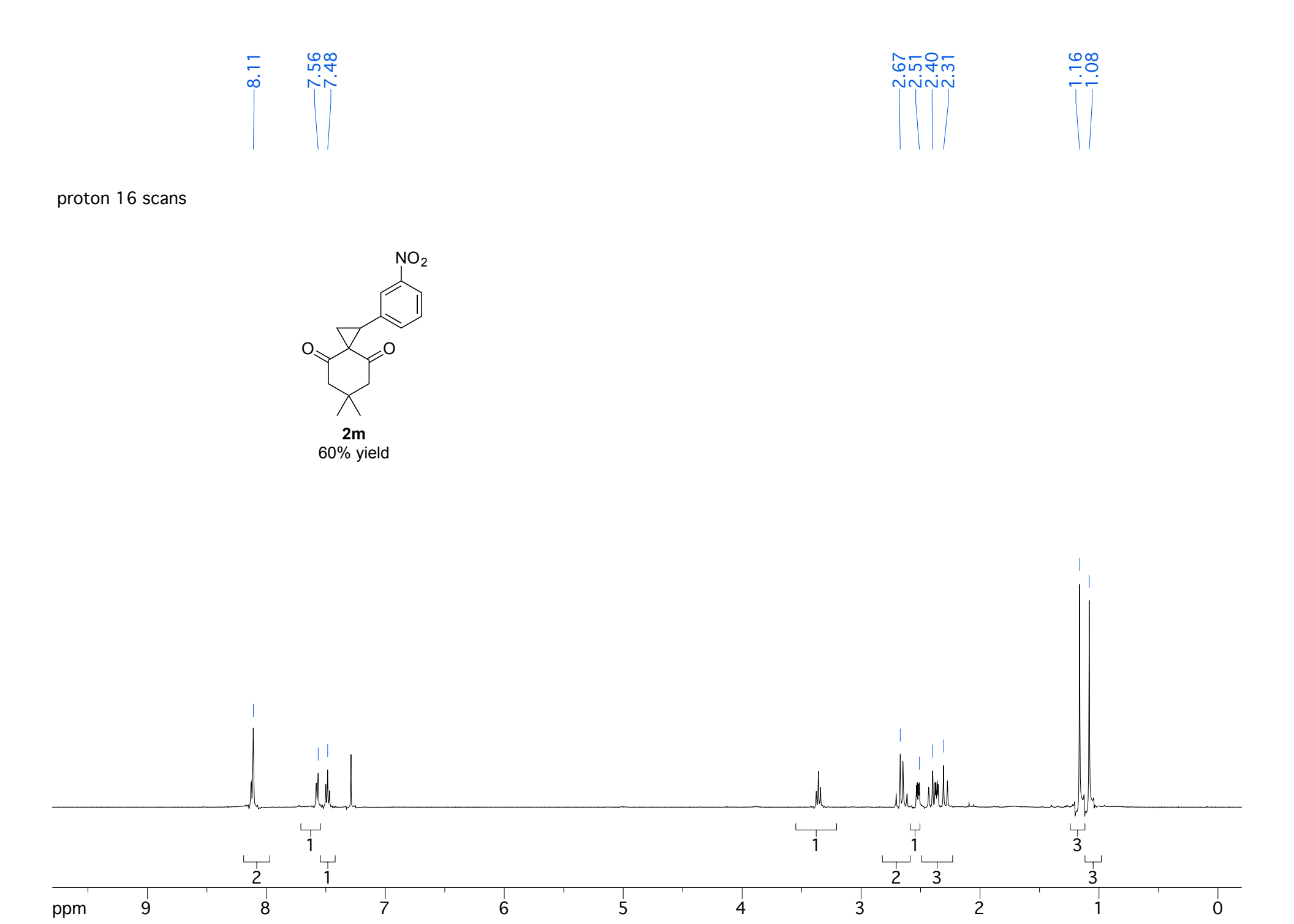
C-13 proton Decoupled



2d
25% yield
2 :1 dr

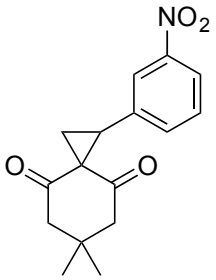




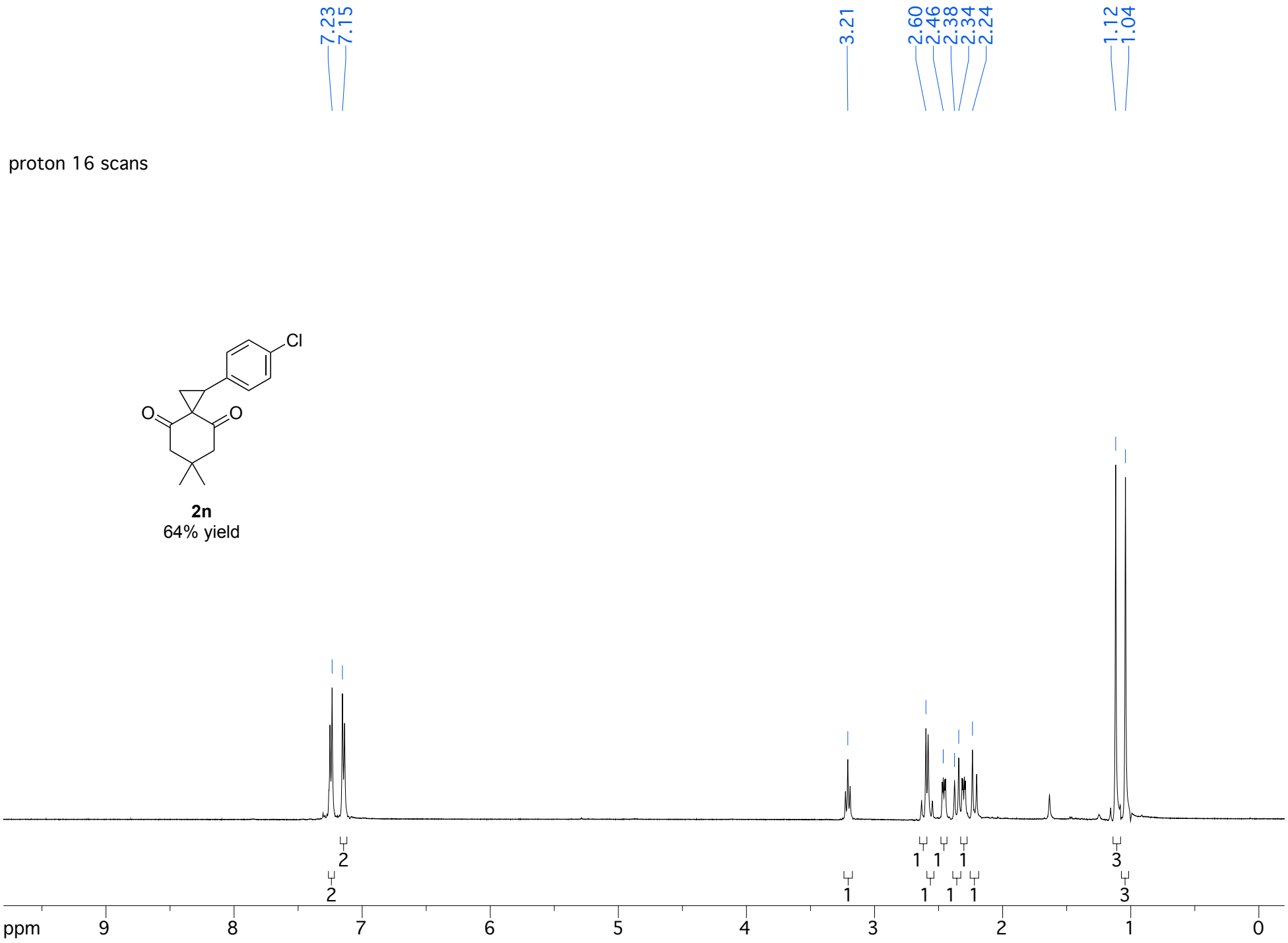

8.11
7.56
7.48
2.67
2.51
2.40
2.31
1.16
1.08
proton 16 scans
NO2
O
O
2m
60% yield
1
1
1
1
3
2
1
2
3
3
ppm
9
8
7
6
5
4
3
2
1
0

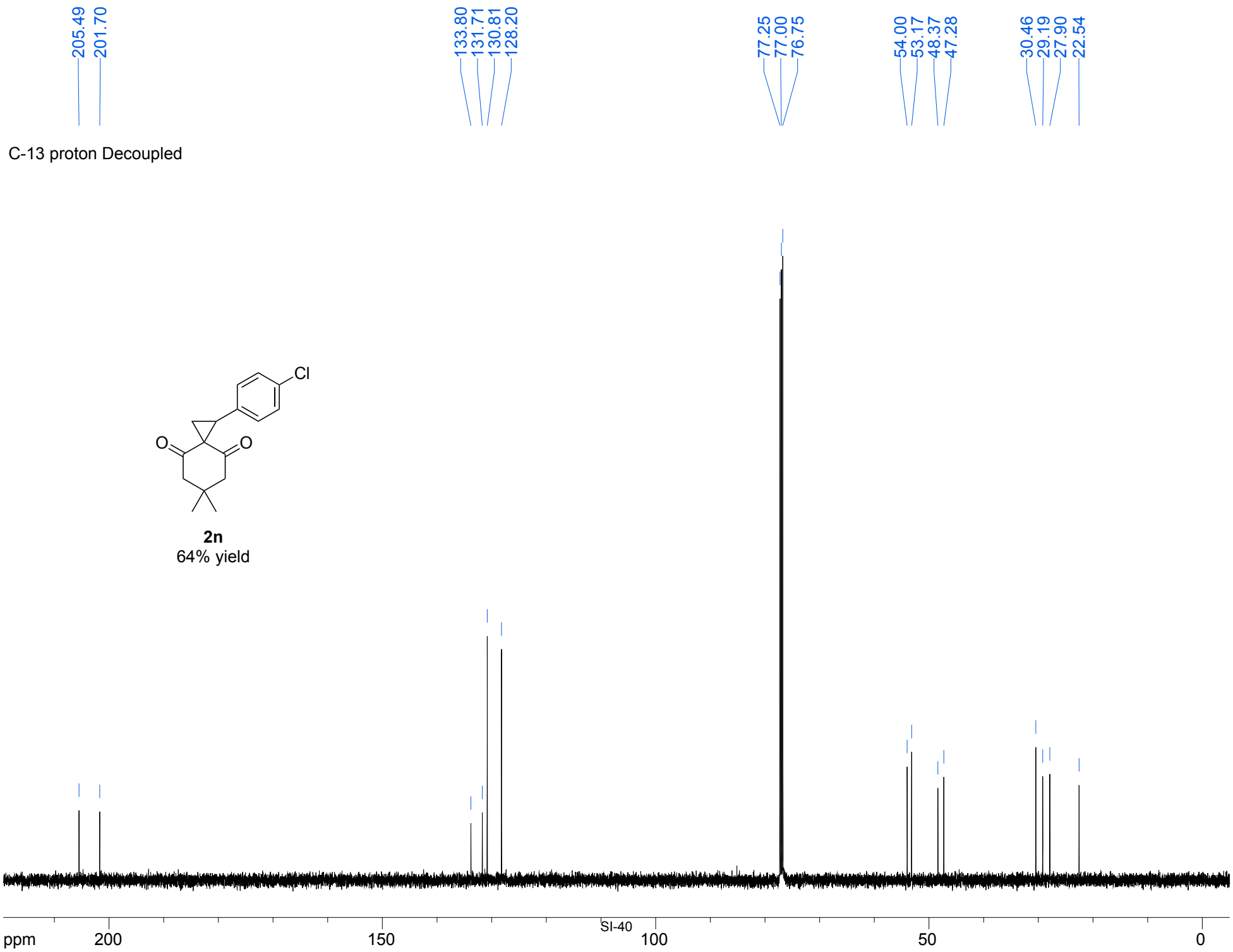
205.30
202.10
147.98
135.54
128.95
124.63
122.85
77.31
77.06
76.80
54.12
53.16
47.51
45.62
30.50
29.20
27.91
23.59

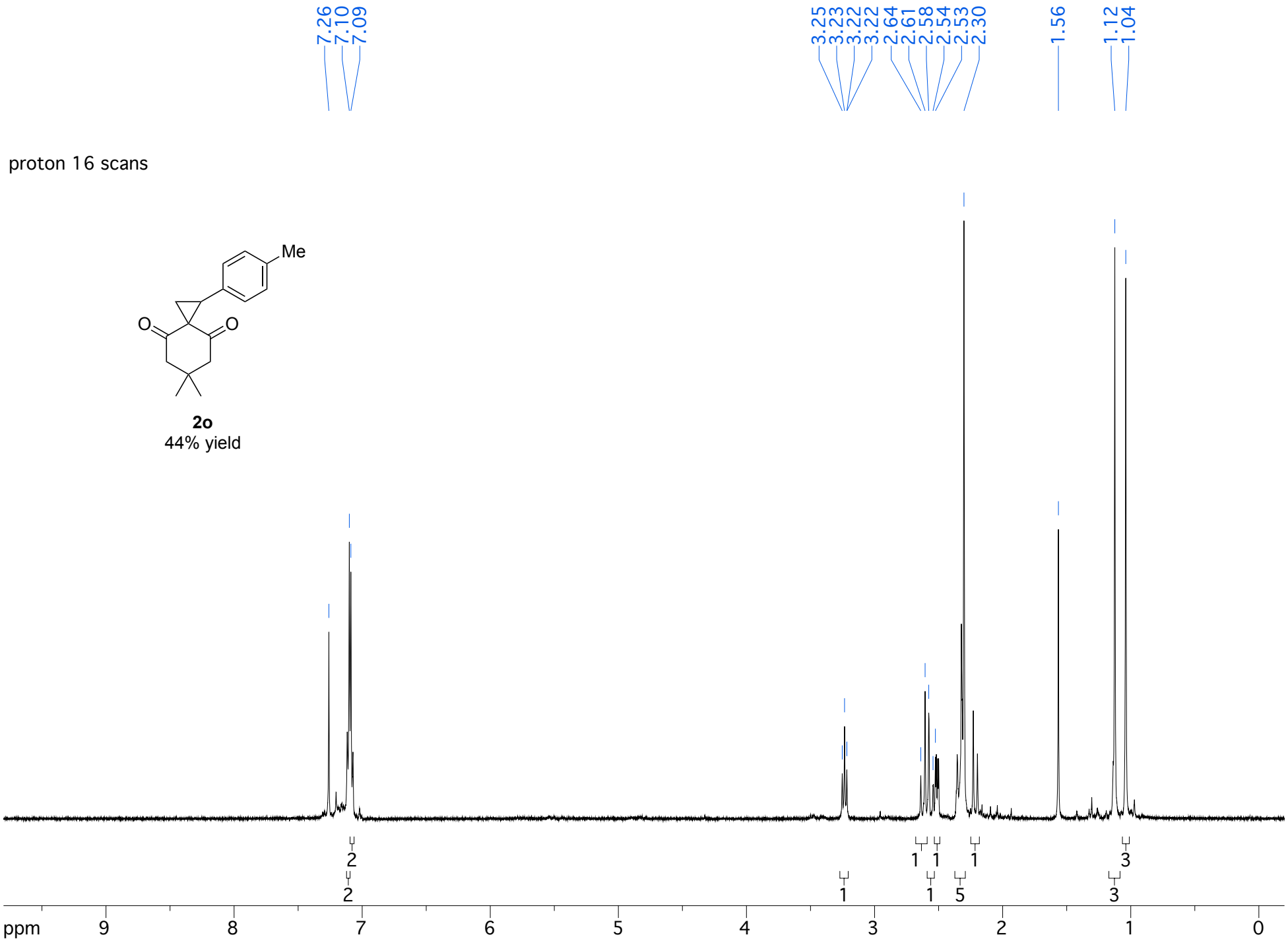
C-13 proton Decoupled



2m
60% yield

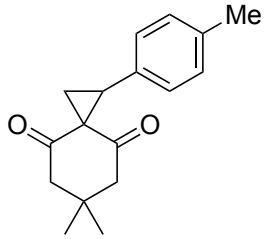

7.23
7.15
3.21
2.60
2.46
2.38
2.34
2.24
1.12
1.04
proton 16 scans
Cl
O
O
2n
64% yield
2
2
1
1
1
1
1
1
3
3
ppm
9
8
7
6
5
4
3
2
1
0


205.49
201.70
133.80
131.71
130.81
128.20
77.25
77.00
76.75
54.00
53.17
48.37
47.28
30.46
29.19
27.90
22.54
C-13 proton Decoupled
Cl
O
O
2n
64% yield
ppm
200
150
100
50
0

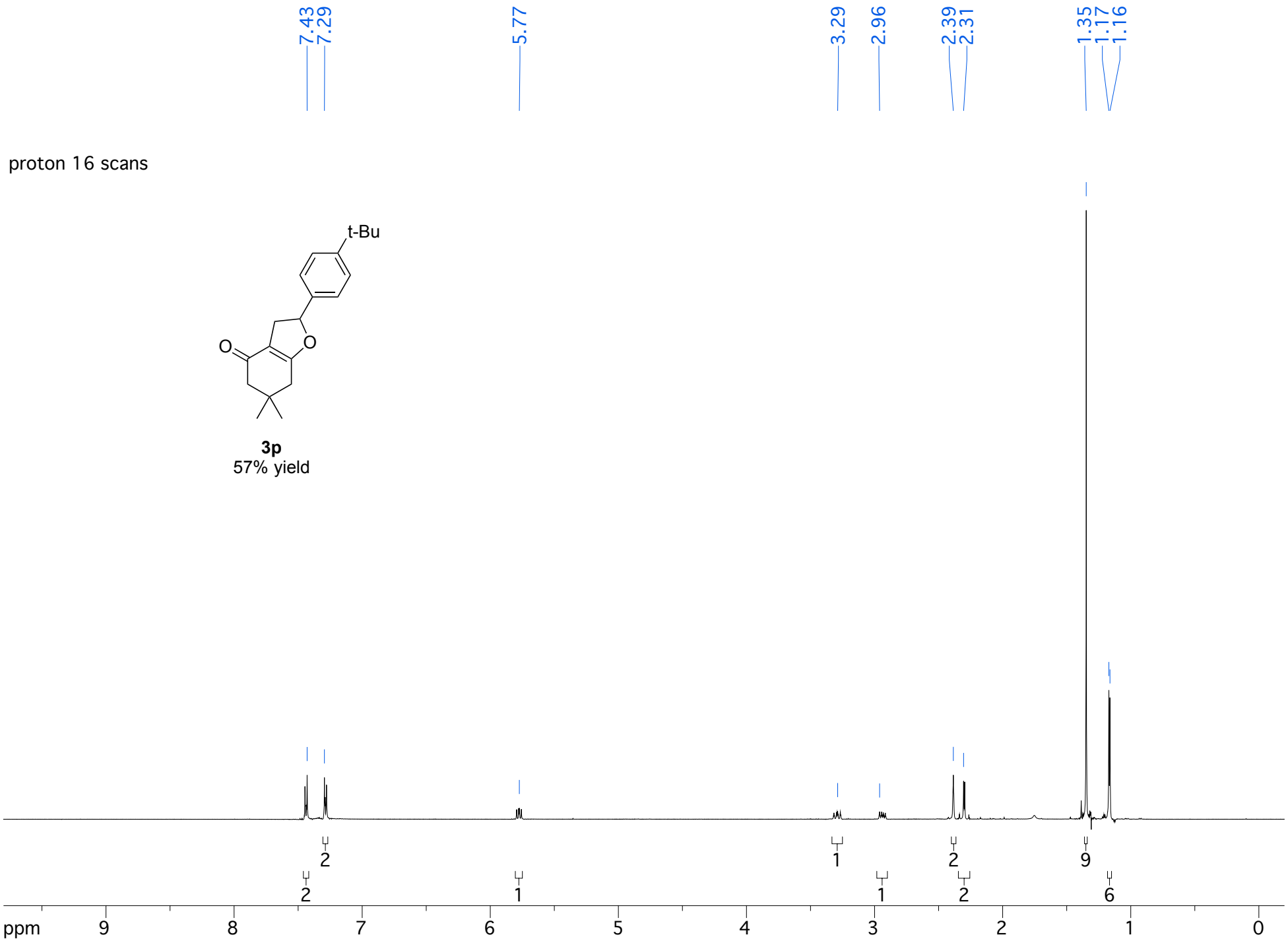

7.26
7.10
7.09
3.25
3.23
3.22
3.22
2.64
2.61
2.58
2.54
2.53
2.30
1.56
1.12
1.04
proton 16 scans
Me
O
O
2o
44% yield
2
2
1
1
1
1
5
1
3
3
ppm
9
8
7
6
5
4
3
2
1
0

205.75
201.68
137.74
130.07
129.40
128.74
77.25
77.00
76.75
53.99
53.21
48.93
48.82
30.49
29.30
27.87
22.11
21.17

C-13 proton Decoupled

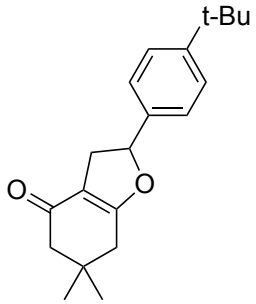


2o
44% yield

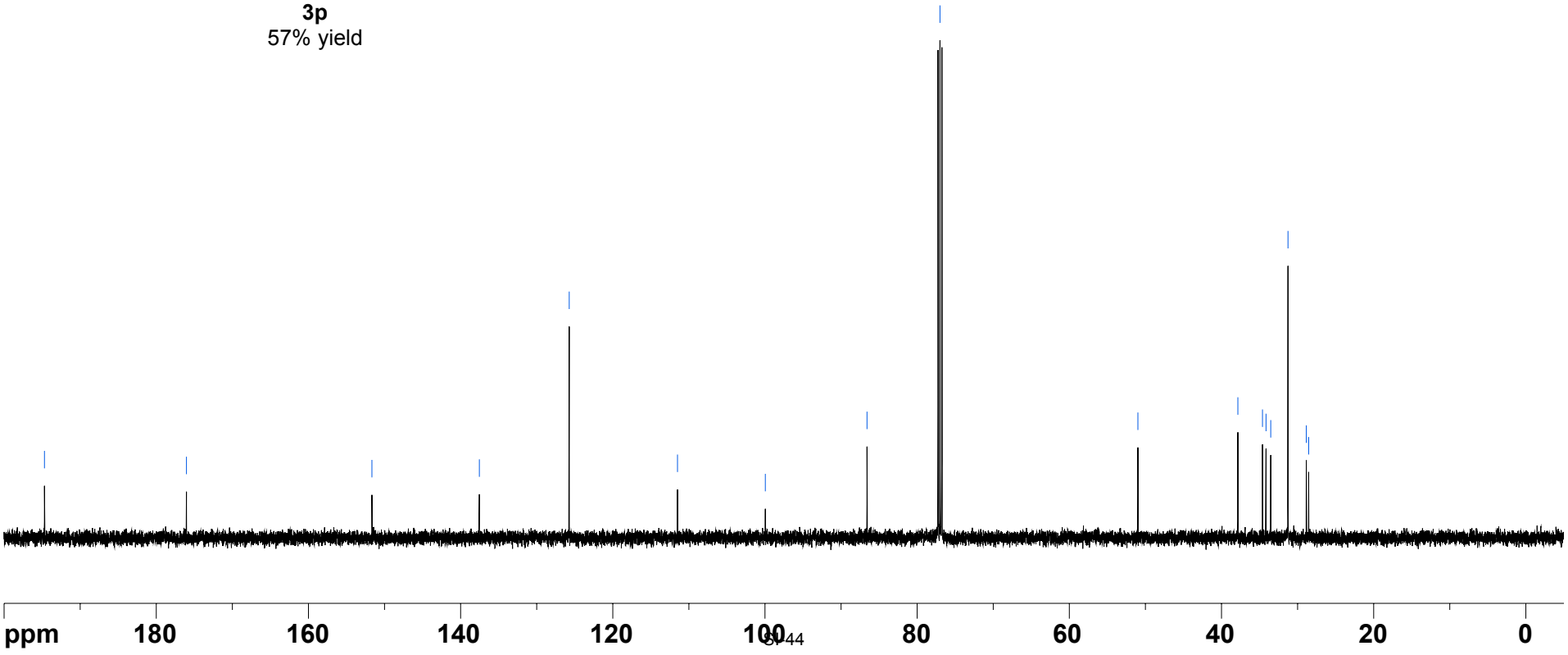

7.43
7.29
5.77
3.29
2.96
2.39
2.31
1.35
1.17
1.16
proton 16 scans
t-Bu
O
O
3p
57% yield
2
1
2
9
2
1
1
2
6
ppm
9
8
7
6
5
4
3
2
1
0

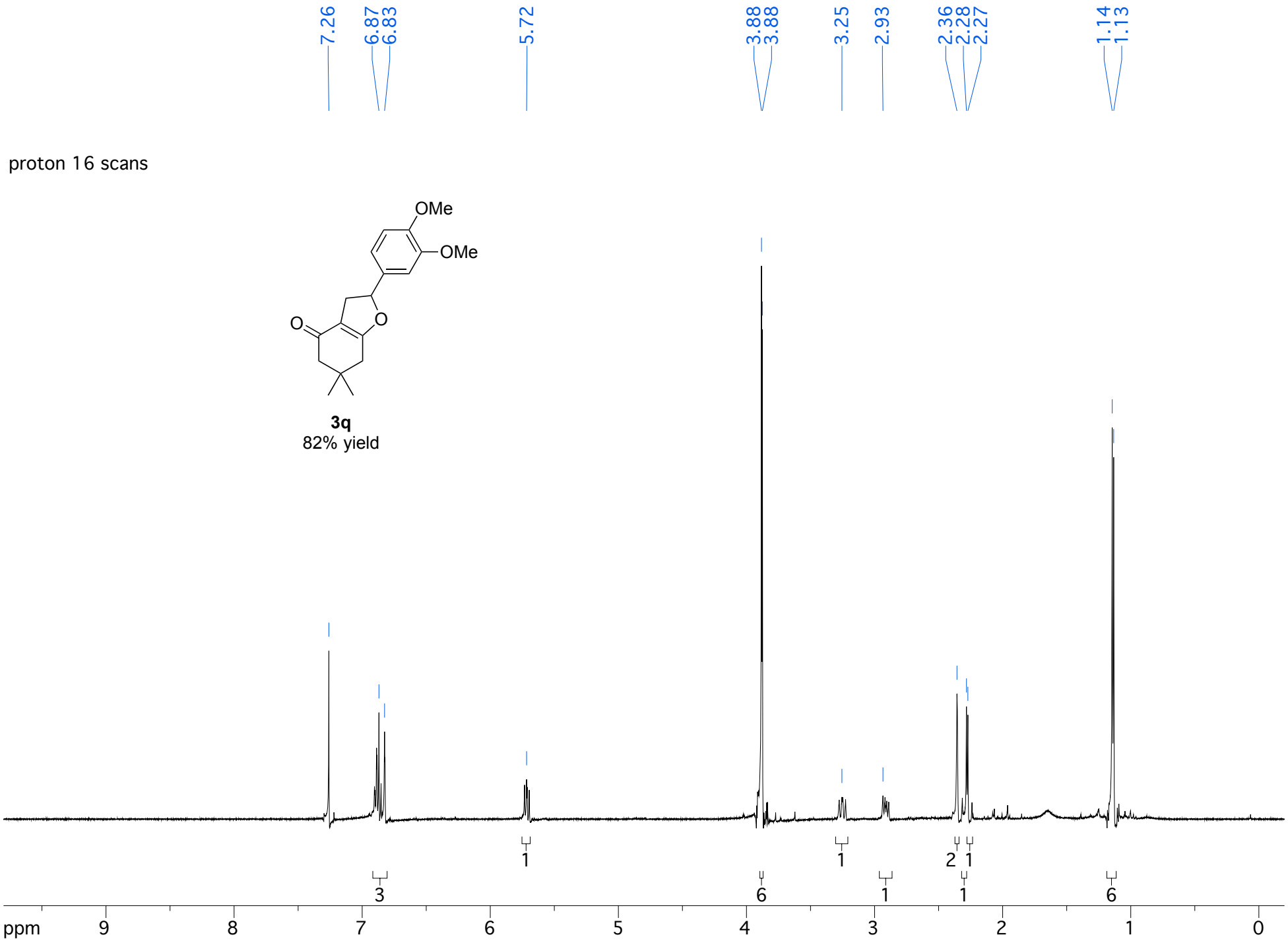
194.69 176.03 151.66 137.54 125.73 111.50 99.95 86.59 77.00 50.99 37.85 34.61 34.15 33.53 31.26 28.86 28.54

C-13 proton Decoupled



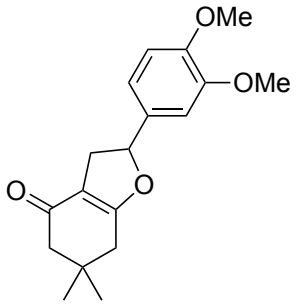
3p
57% yield



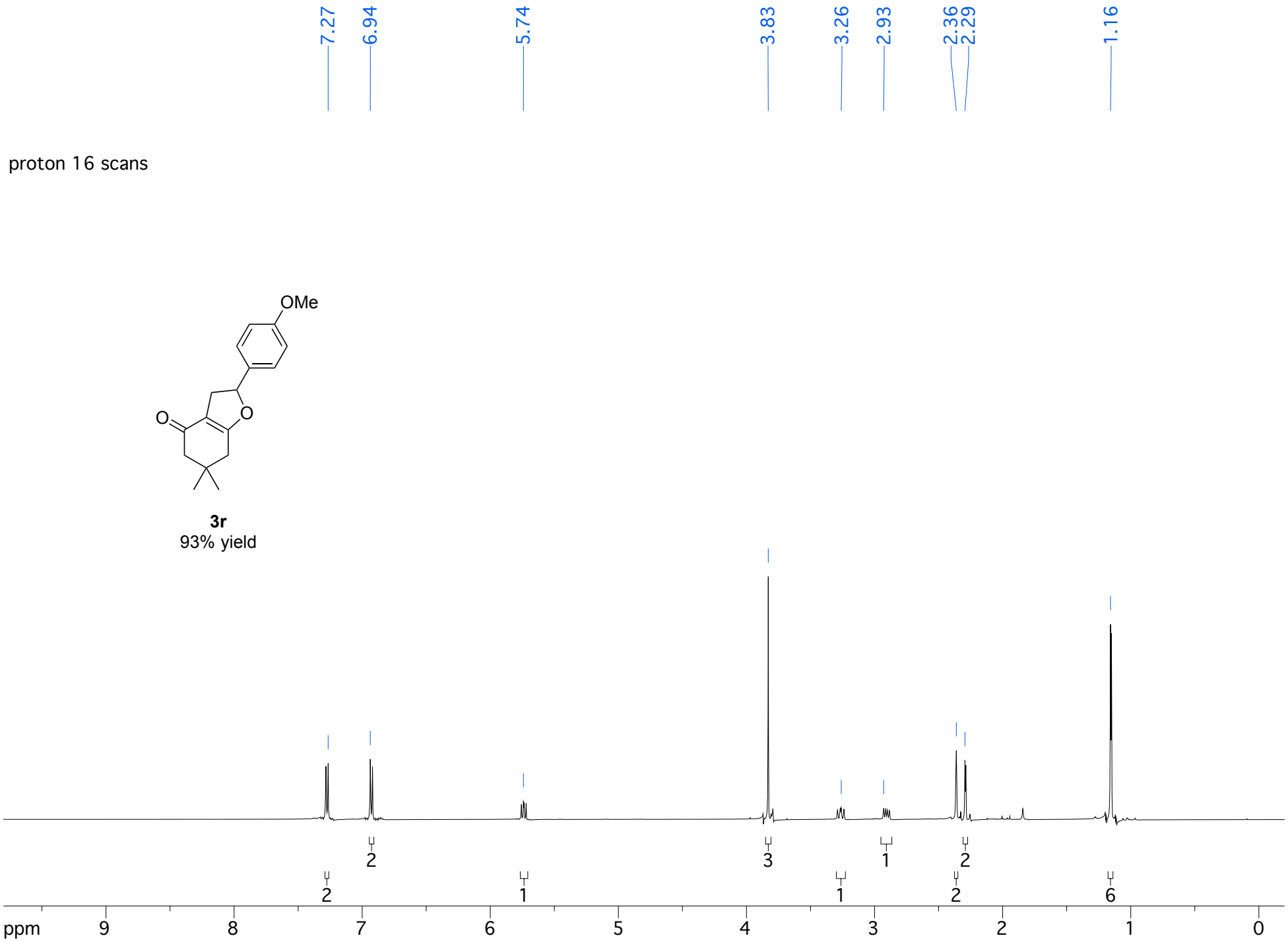

7.26
6.87
6.83
5.72
3.88
3.88
3.25
2.93
2.36
2.28
2.27
1.14
1.13
proton 16 scans
OMe
OMe
O
O
3q
82% yield
1
1
2
1
3
6
1
1
6
ppm
9
8
7
6
5
4
3
2
1
0

194.71
175.94
149.32
149.27
132.92
111.54
111.13
109.13
86.82
55.95
55.89
50.96
37.87
34.17
33.43

C-13 proton Decoupled

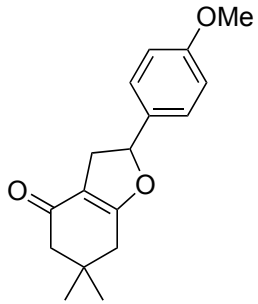


3q
82% yield

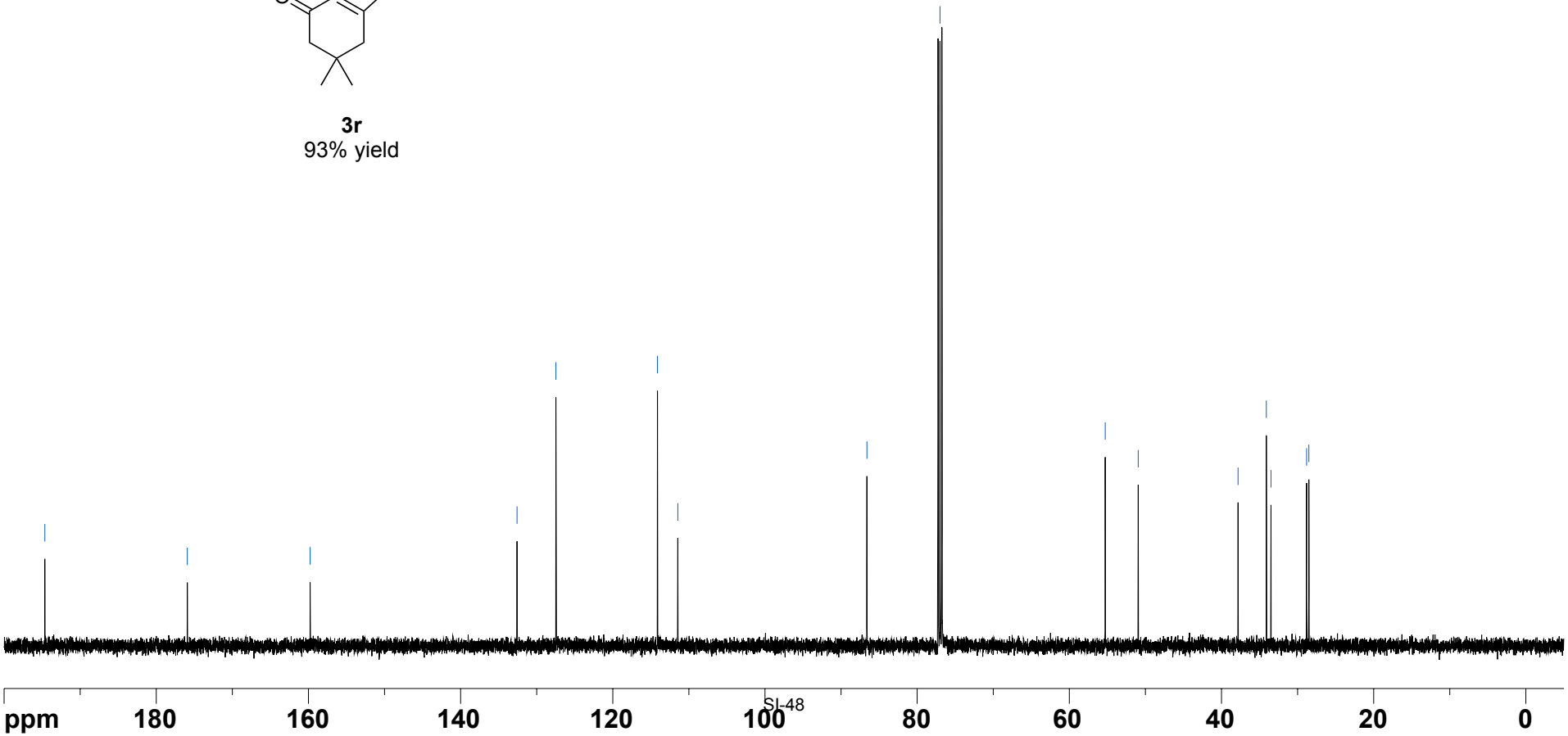

7.27
6.94
5.74
3.83
3.26
2.93
2.36
2.29
1.16
proton 16 scans
OMe
O
O
3r
93% yield
2
3
1
2
2
1
1
2
6
ppm
9
8
7
6
5
4
3
2
1
0

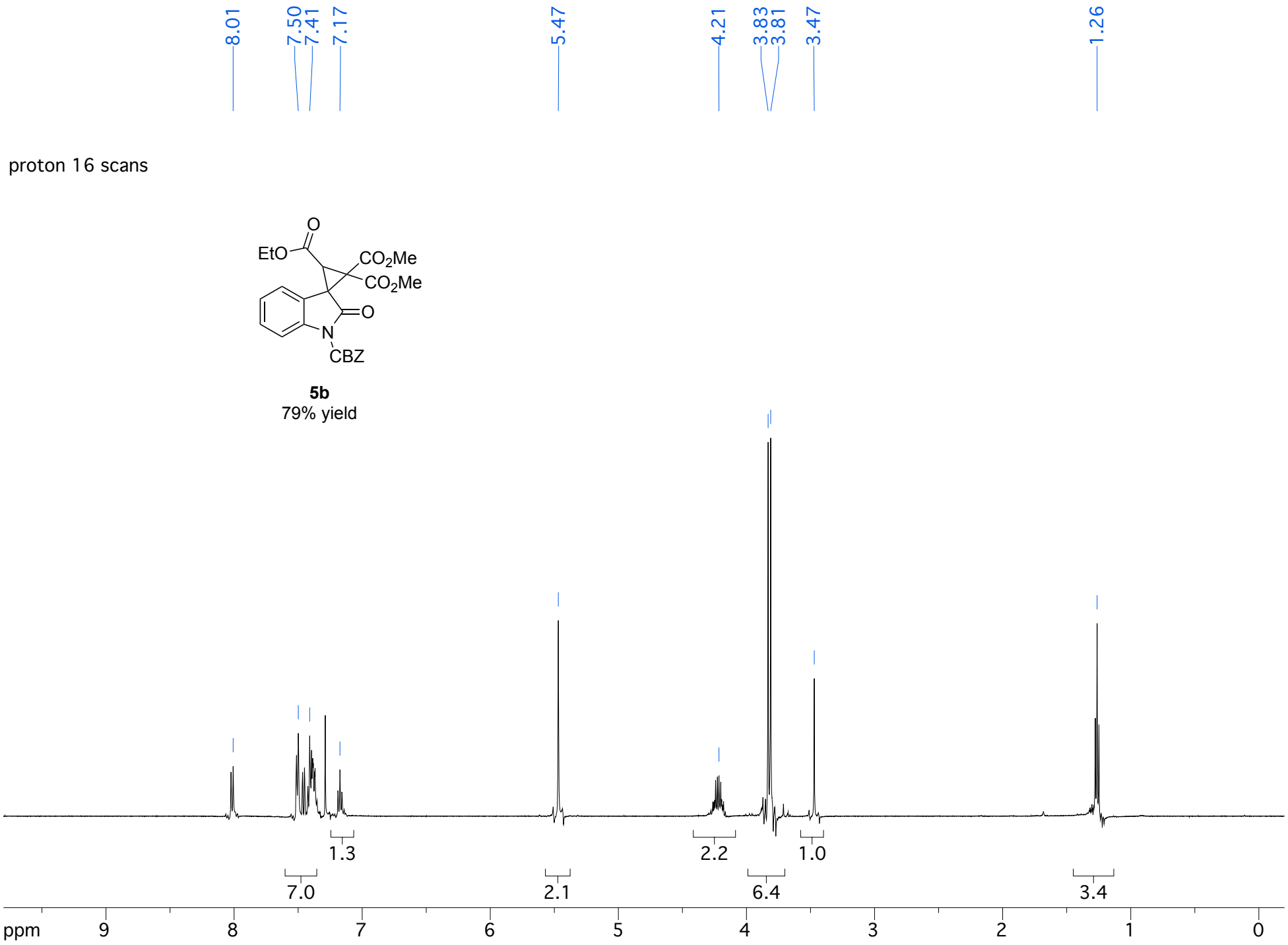
194.65
175.92
159.78
132.59
127.48
114.13
111.45
86.60
77.00
55.28
50.95
37.82
34.11
33.50
28.82
28.52

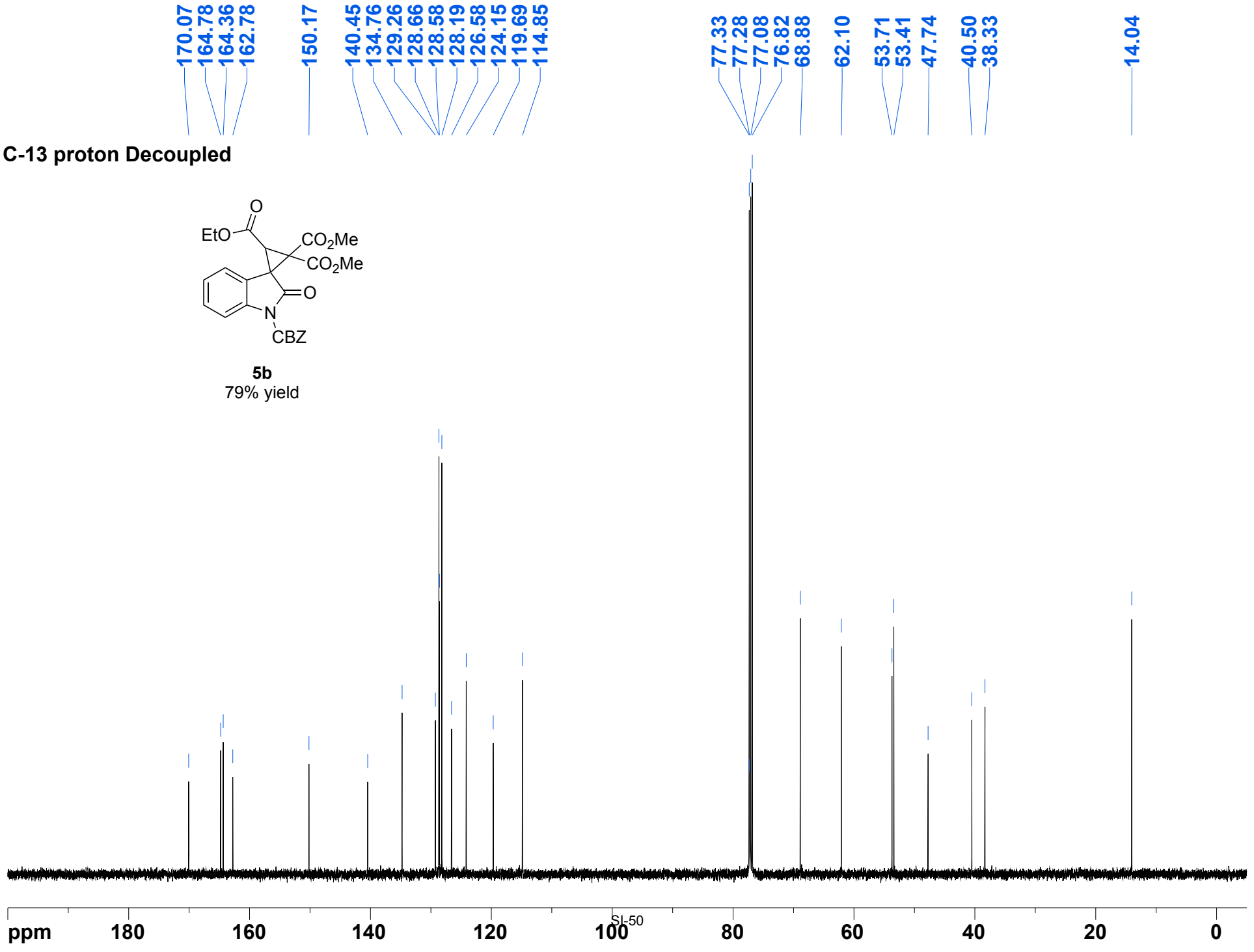
C-13 proton Decoupled

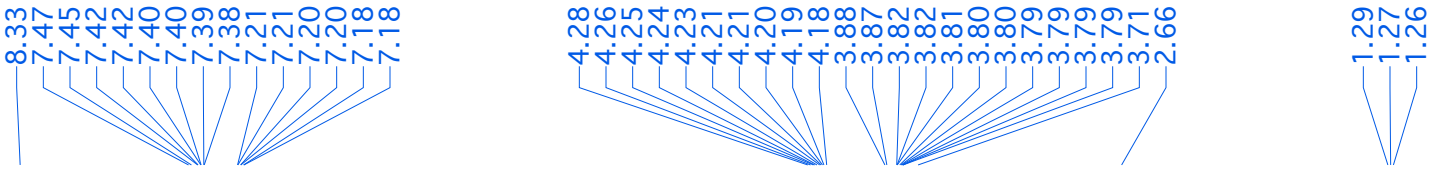


3r
93% yield

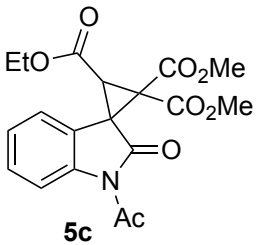



8.01
7.50
7.41
7.17
5.47
4.21
3.83
3.81
3.47
1.26
proton 16 scans
O
EtO
CO2Me
CO2Me
O
N
CBZ
5b
79% yield
1.3
2.2
1.0
7.0
2.1
6.4
3.4
ppm
9
8
7
6
5
4
3
2
1
0

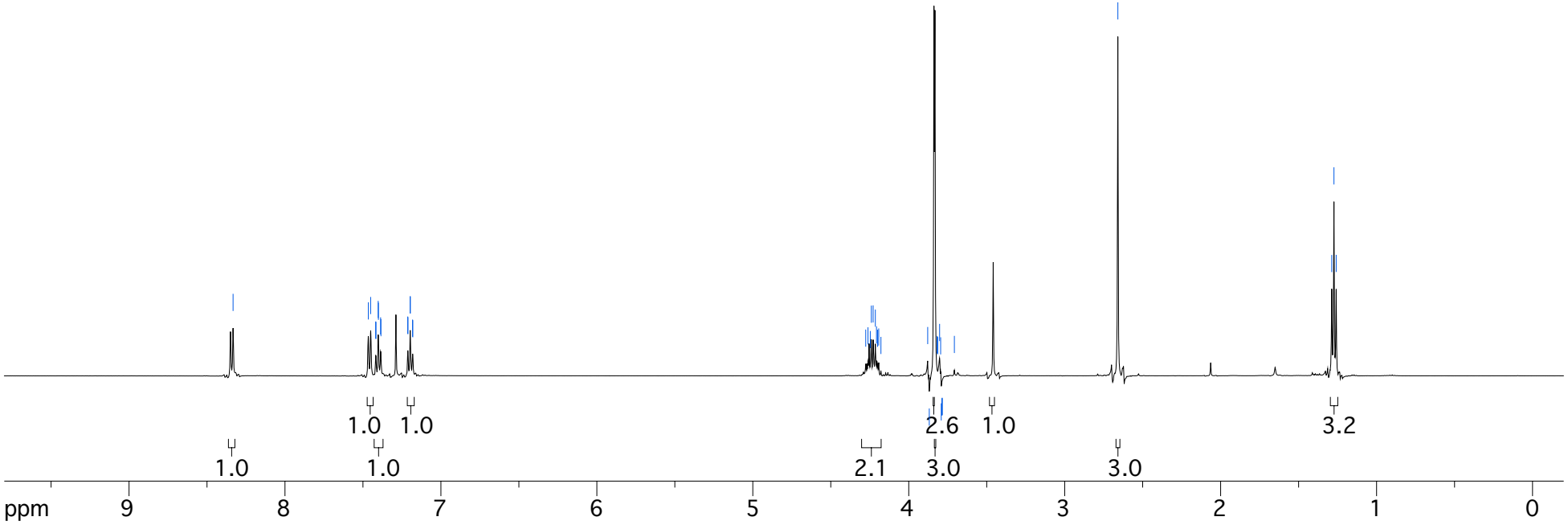

170.07
164.78
164.36
162.78
150.17
140.45
134.76
129.26
128.66
128.58
128.19
126.58
124.15
119.69
114.85
77.33
77.28
77.08
76.82
68.88
62.10
53.71
53.41
47.74
40.50
38.33
14.04
C-13 proton Decoupled
EtO
O
CO2Me
CO2Me
O
N
CBZ
5b
79% yield
ppm
180
160
140
120
100
80
60
40
20
0

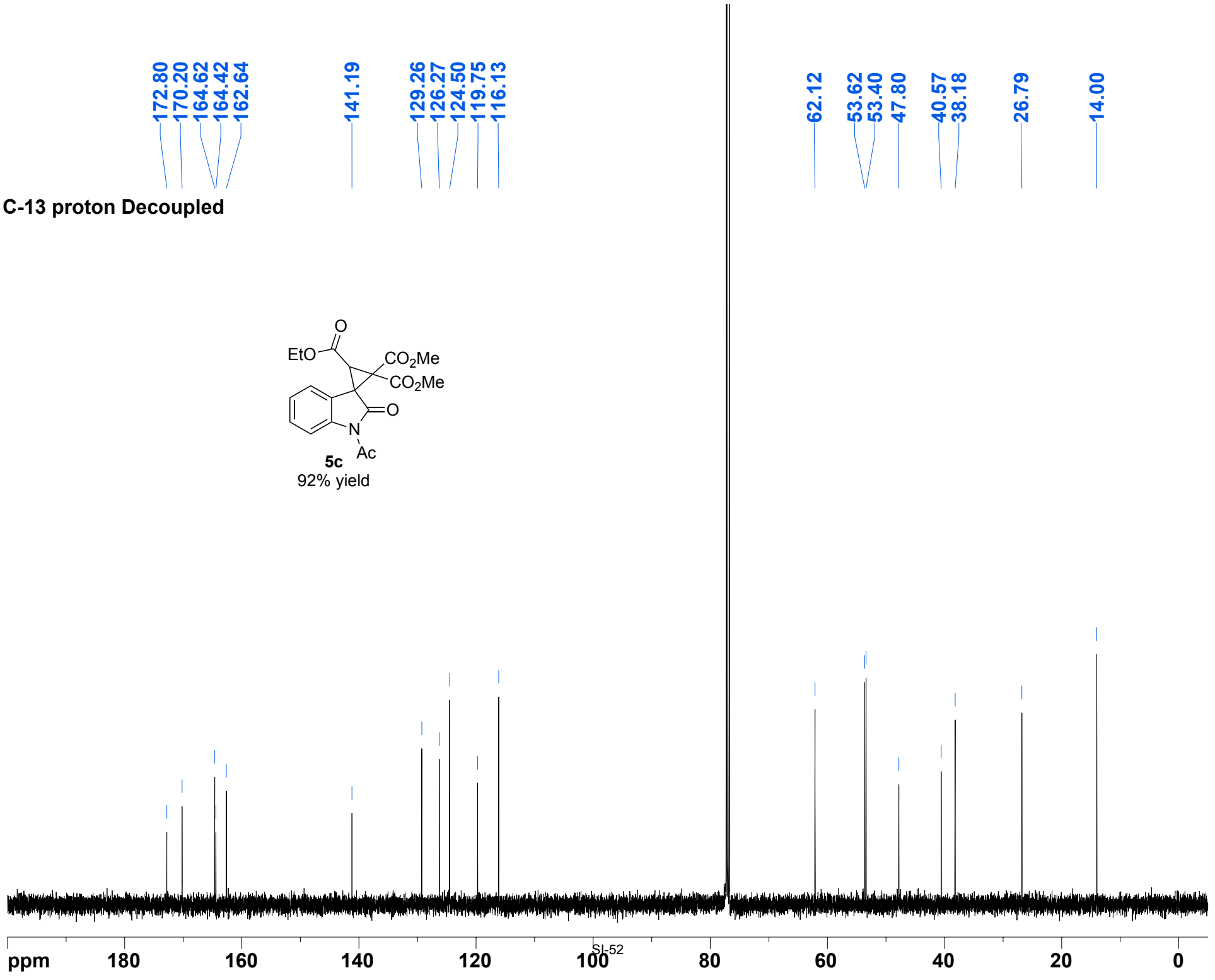


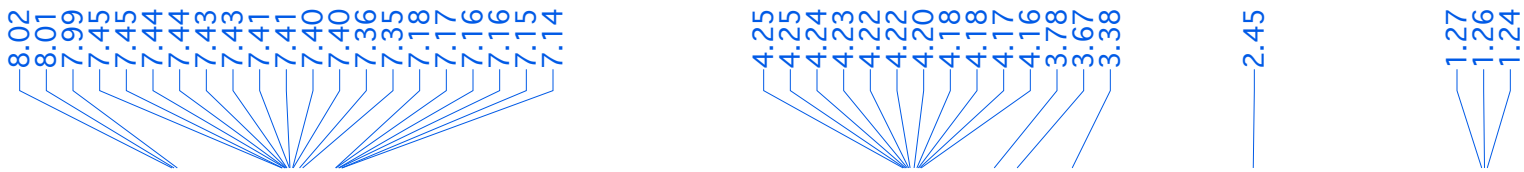
proton 16 scans



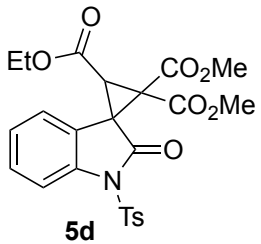
5c
92% yield



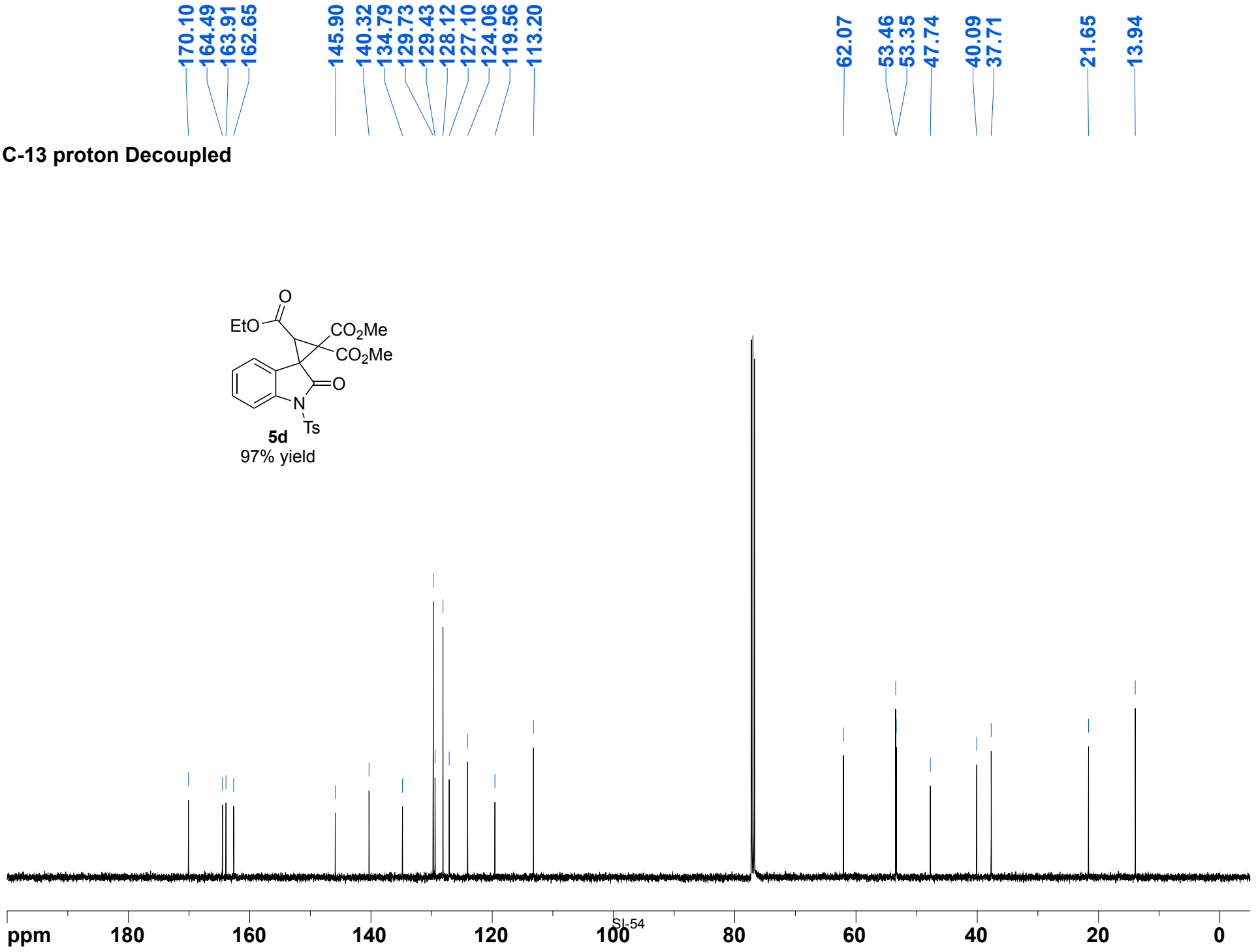

172.80
170.20
164.62
164.42
162.64
141.19
129.26
126.27
124.50
119.75
116.13
62.12
53.62
53.40
47.80
40.57
38.18
26.79
14.00
C-13 proton Decoupled
EtO
O
CO2Me
CO2Me
O
N
Ac
5c
92% yield
ppm
180
160
140
120
100
80
60
40
20
0

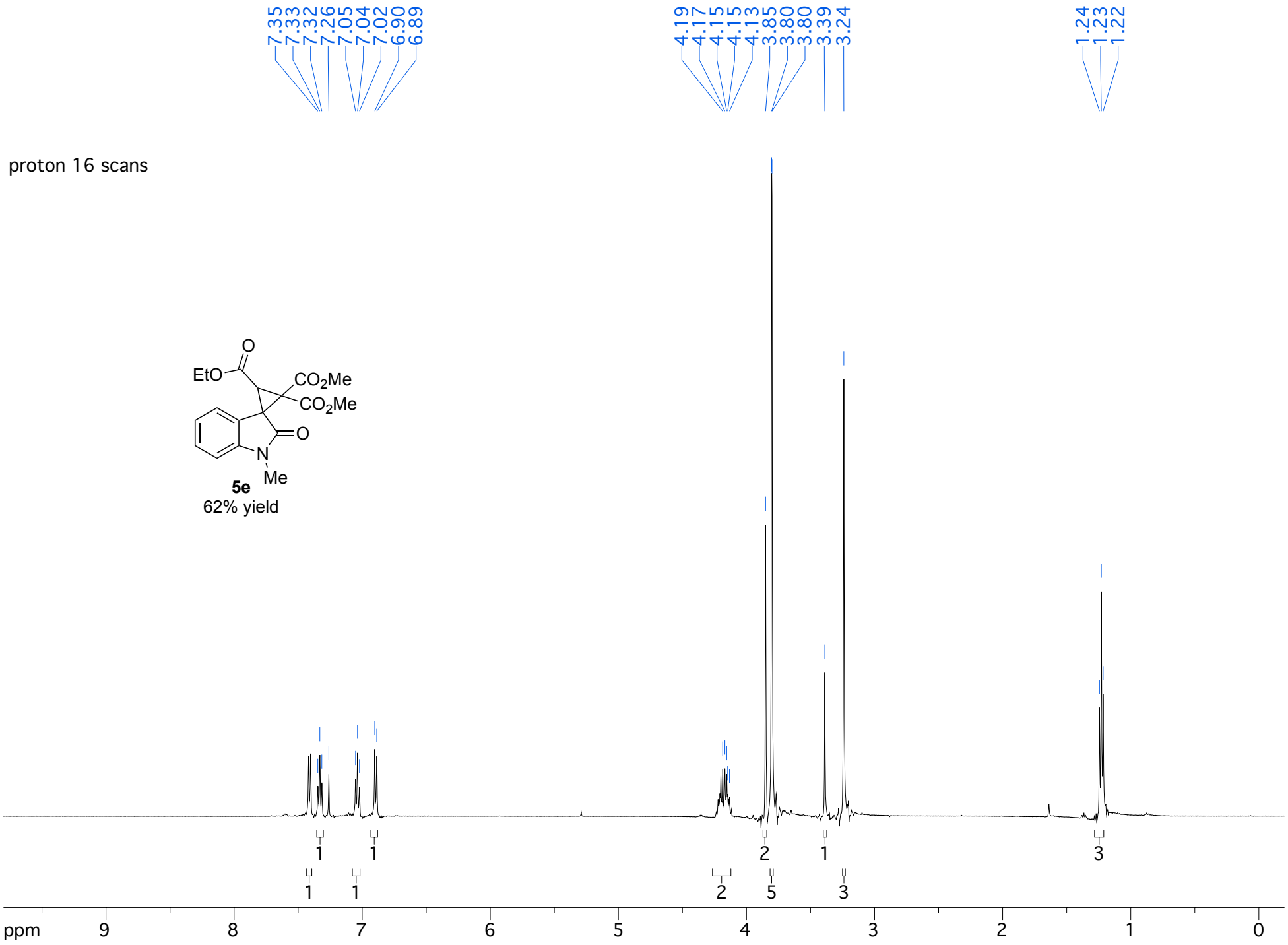


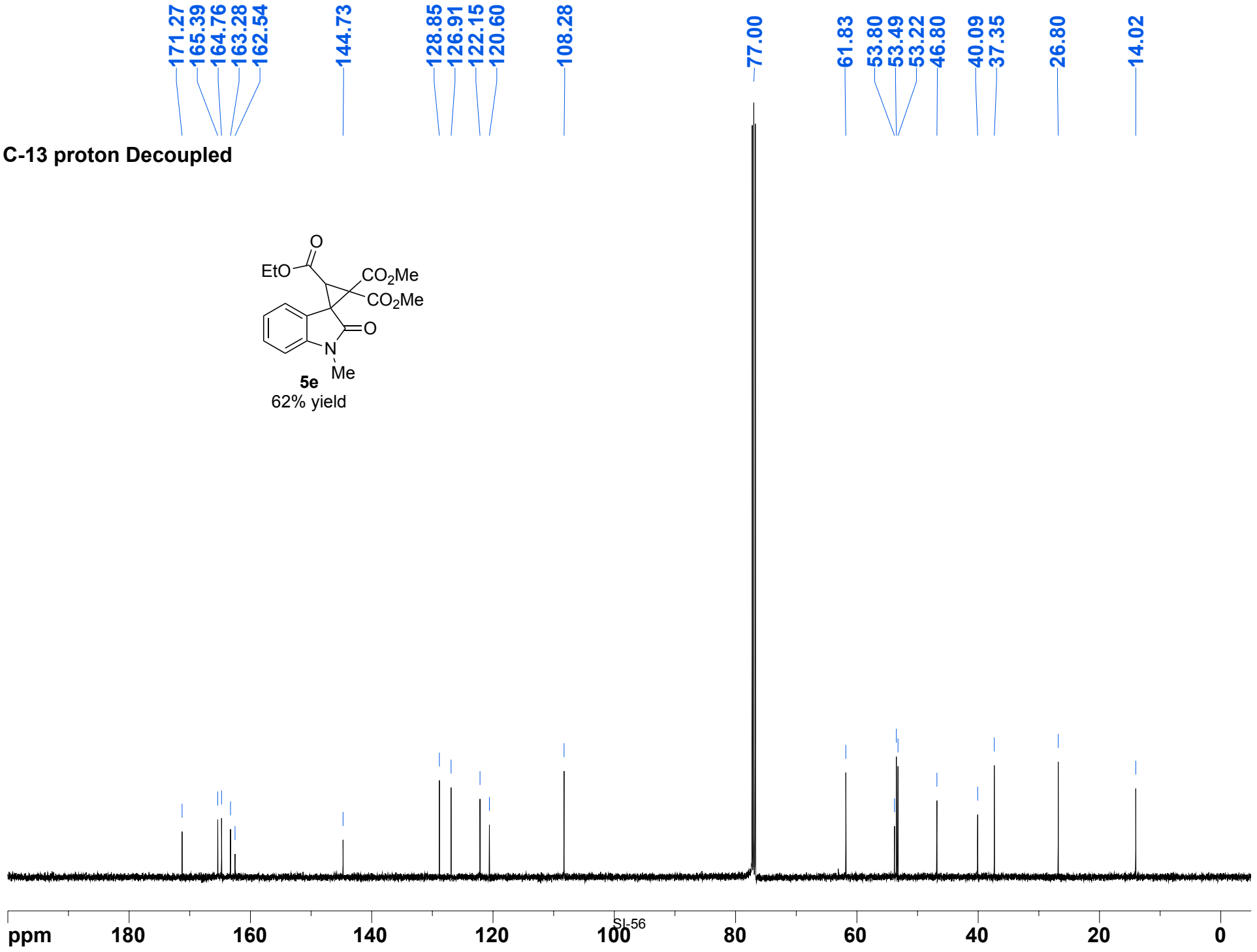
proton 16 scans

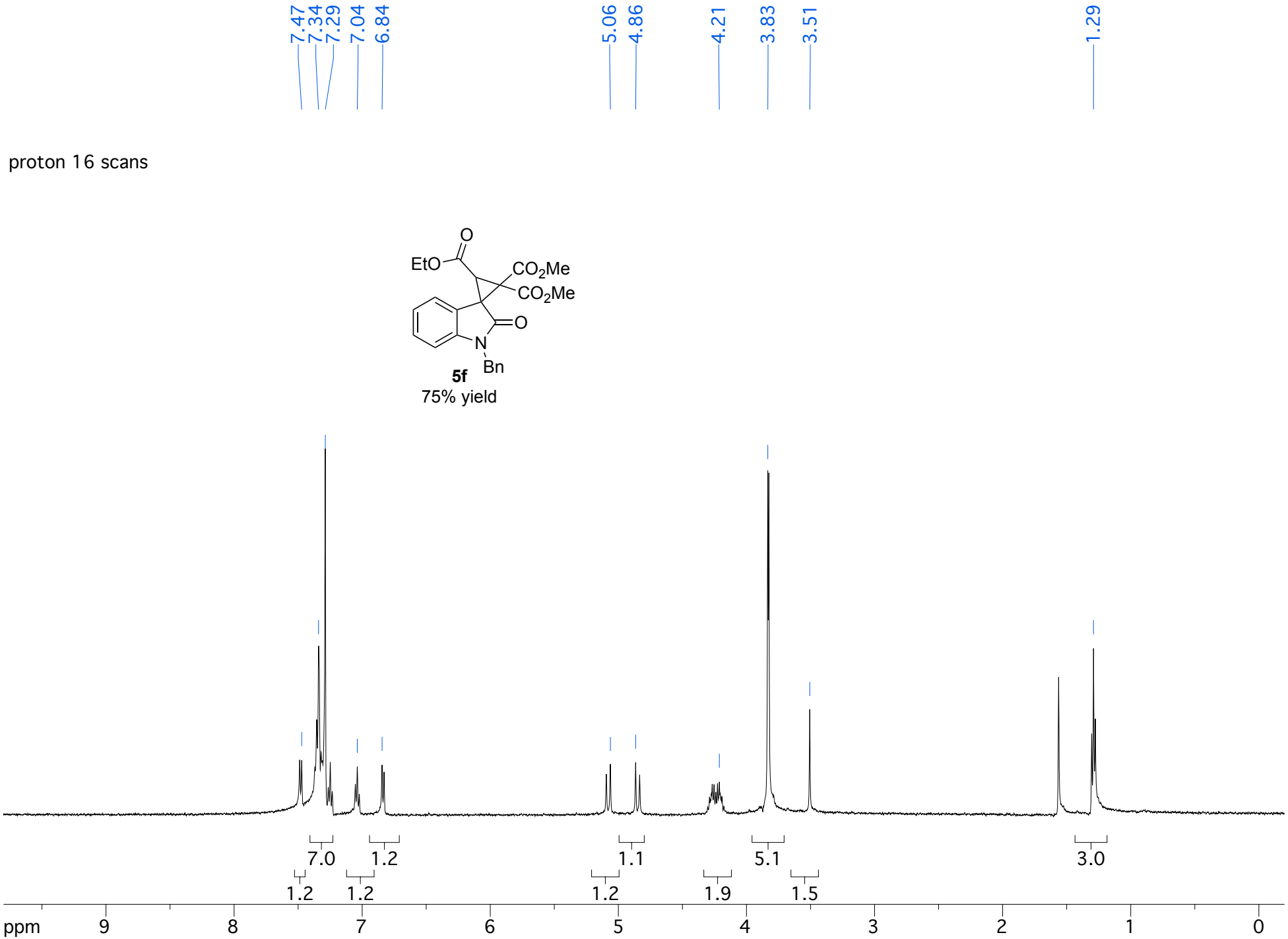


5d
97% yield


170.10
164.49
163.91
162.65
145.90
140.32
134.79
129.73
129.43
128.12
127.10
124.06
119.56
113.20
62.07
53.46
53.35
47.74
40.09
37.71
21.65
13.94
C-13 proton Decoupled
EtO
O
CO2Me
CO2Me
O
N
Ts
5d
97% yield
ppm
180
160
140
120
100
80
60
40
20
0

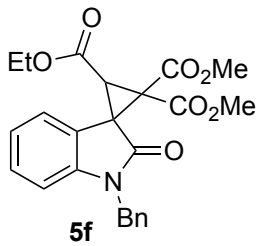

7.35
7.33
7.32
7.26
7.05
7.04
7.02
6.90
6.89
4.19
4.17
4.15
4.15
4.13
3.85
3.80
3.80
3.39
3.24
1.24
1.23
1.22
proton 16 scans
O
EtO
CO2Me
CO2Me
O
N
Me
5e
62% yield
1
1
1
1
2
5
1
3
ppm
9
8
7
6
5
4
3
2
1
0


171.27
165.39
164.76
163.28
162.54
144.73
128.85
126.91
122.15
120.60
108.28
77.00
61.83
53.80
53.49
53.22
46.80
40.09
37.35
26.80
14.02
C-13 proton Decoupled
EtO
O
CO2Me
CO2Me
O
N
Me
5e
62% yield
ppm
180
160
140
120
100
80
60
40
20
0

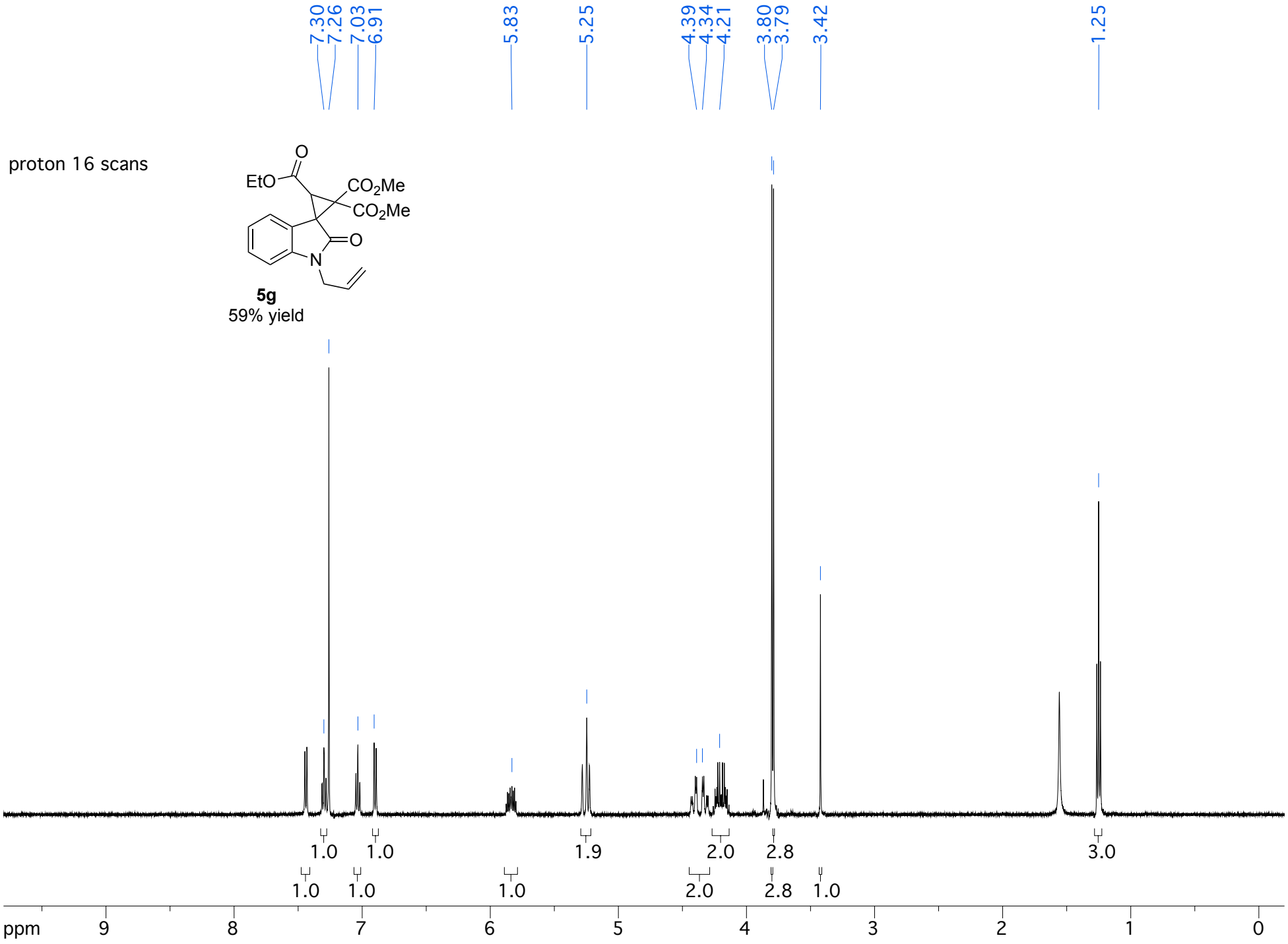

7.47
7.34
7.29
7.04
6.84
5.06
4.86
4.21
3.83
3.51
1.29
proton 16 scans
O
EtO
CO2Me
CO2Me
O
N
Bn
5f
75% yield
7.0
1.2
1.1
5.1
3.0
1.2
1.2
1.2
1.9
1.5
ppm
9
8
7
6
5
4
3
2
1
0

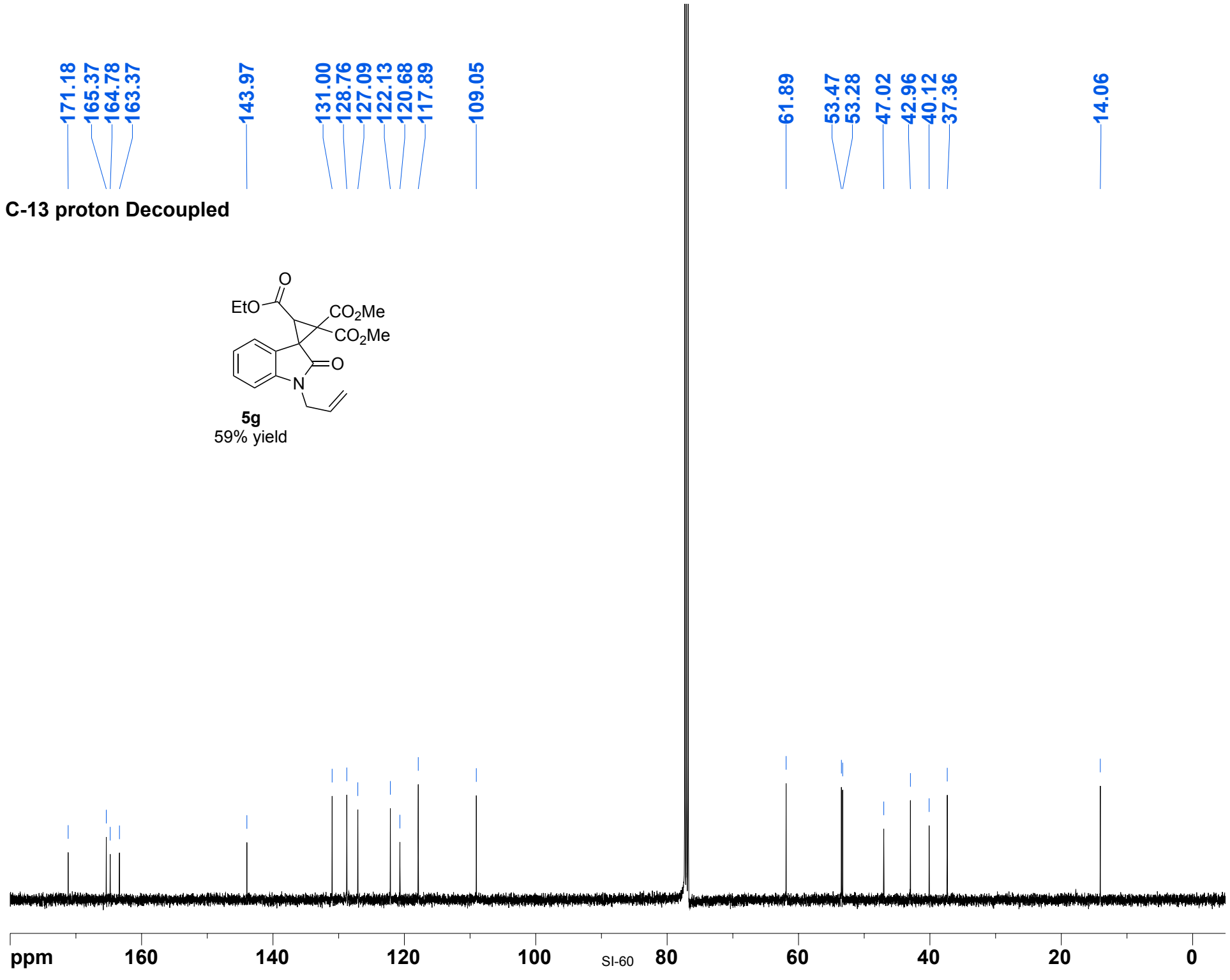
171.60
165.28
164.76
163.34
143.86
135.29
128.75
128.72
127.69
127.24
127.08
122.14
120.65
109.11
61.85
53.41
53.23
47.08
44.30
40.15
37.30
14.00

C-13 proton Decoupled

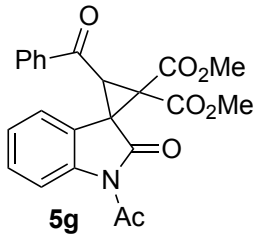


5f
75% yield

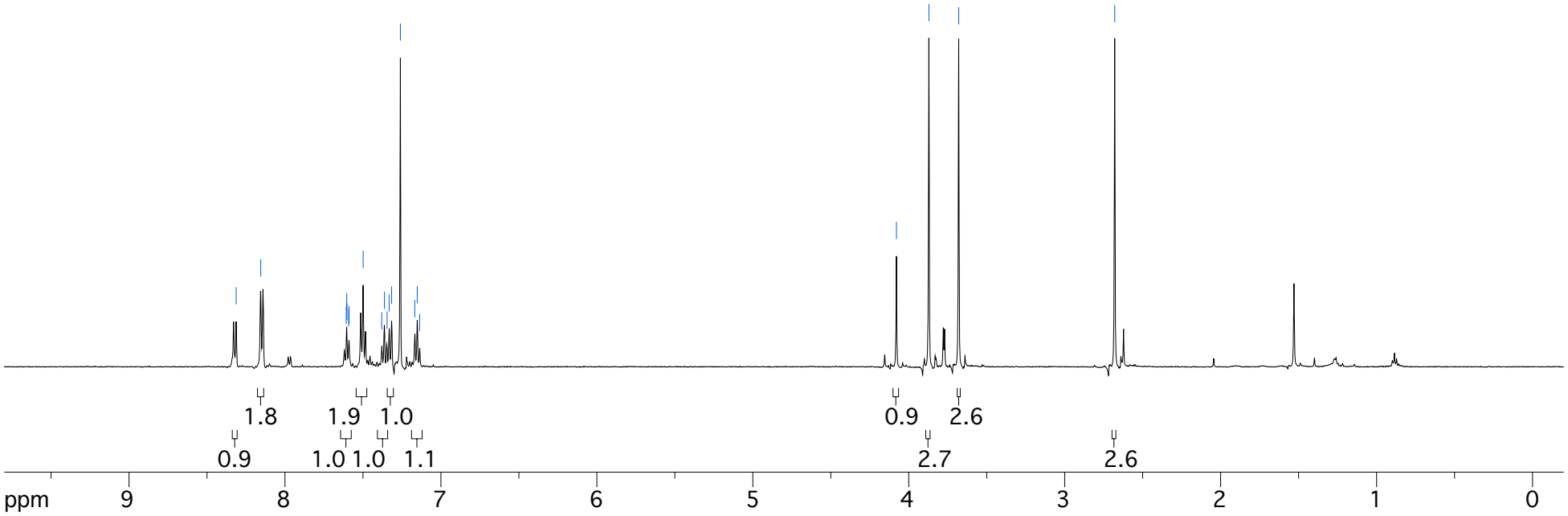

7.30
7.26
7.03
6.91
5.83
5.25
4.39
4.34
4.21
3.80
3.79
3.42
1.25
proton 16 scans
EtO
O
CO2Me
CO2Me
O
N
5g
59% yield
1.0
1.0
1.9
2.0
2.8
3.0
1.0
1.0
1.0
2.0
2.8
1.0
ppm
9
8
7
6
5
4
3
2
1
0

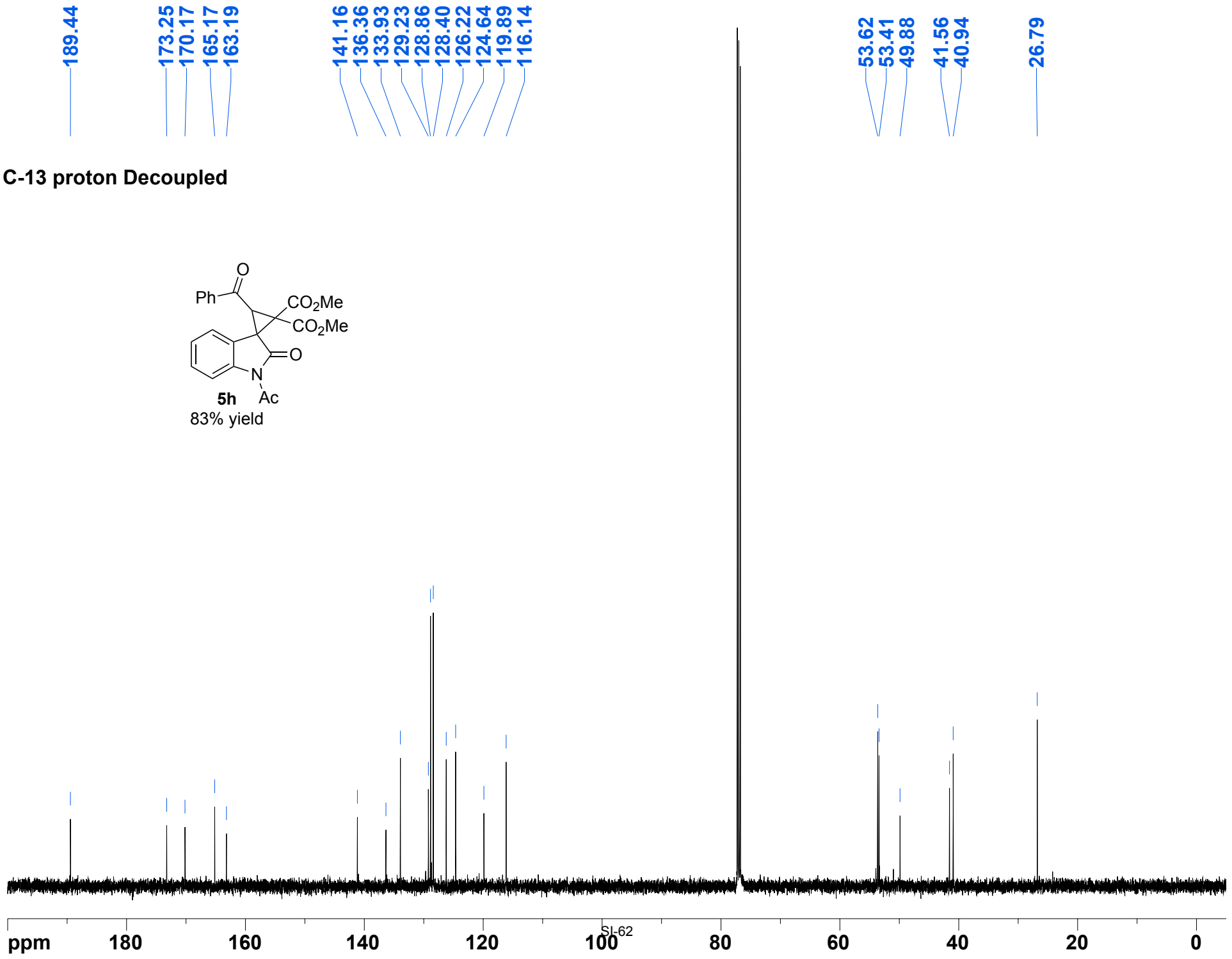

171.18
165.37
164.78
163.37
143.97
131.00
128.76
127.09
122.13
120.68
117.89
109.05
61.89
53.47
53.28
47.02
42.96
40.12
37.36
14.06
C-13 proton Decoupled
O
EtO
CO2Me
CO2Me
O
N
5g
59% yield
ppm
160
140
120
100
80
60
40
20
0

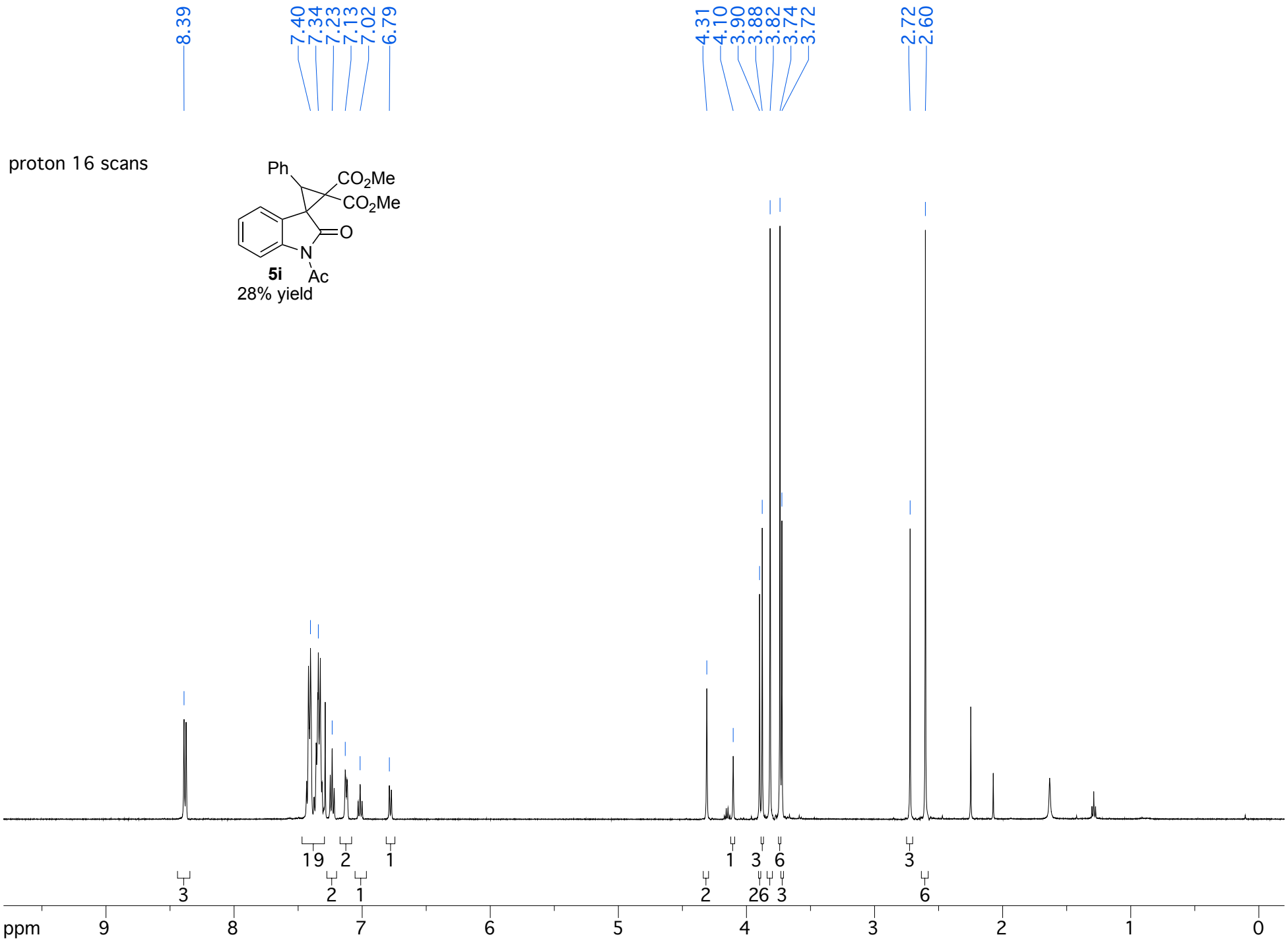
proton 16 scans

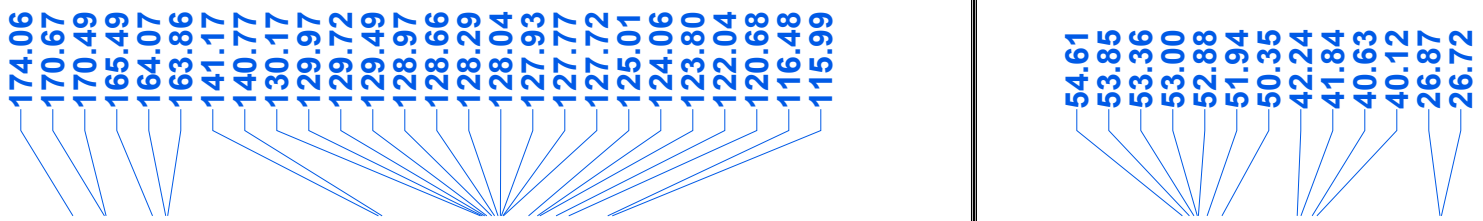


5g
83% yield

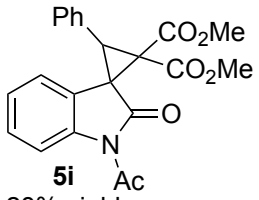



189.44
173.25
170.17
165.17
163.19
141.16
136.36
133.93
129.23
128.86
128.40
126.22
124.64
119.89
116.14
53.62
53.41
49.88
41.56
40.94
26.79
C-13 proton Decoupled
O
Ph
CO2Me
CO2Me
O
N
Ac
5h
83% yield
ppm
180
160
140
120
100
80
60
40
20
0

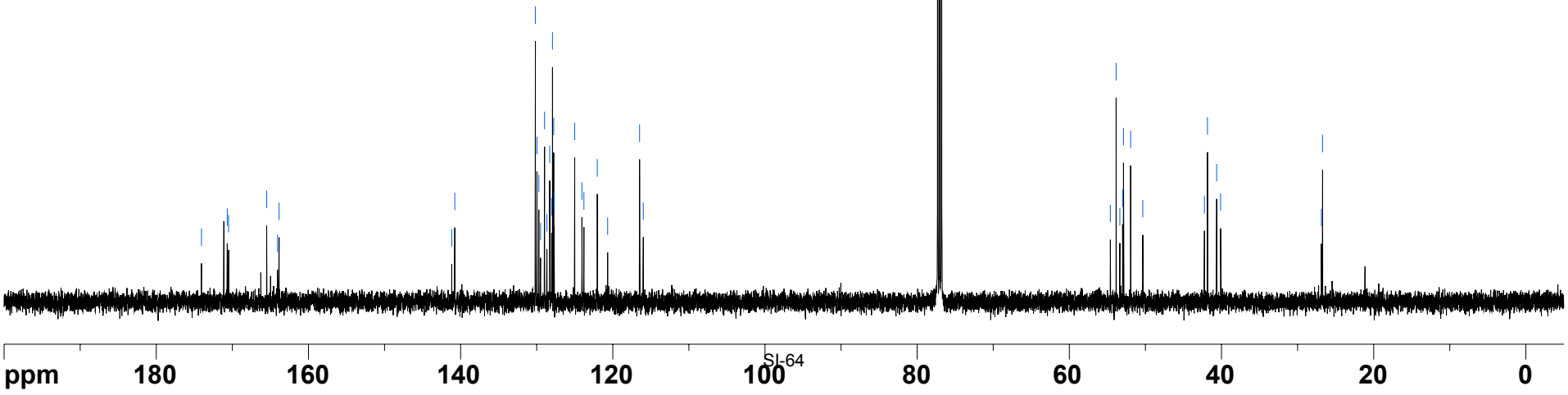

8.39
7.40
7.34
7.23
7.13
7.02
6.79
4.31
4.10
3.90
3.88
3.82
3.74
3.72
2.72
2.60
proton 16 scans
Ph
CO2Me
CO2Me
O
N
Ac
5i
28% yield
19
2
1
1
3
6
3
3
2
1
2
26
3
6
ppm
9
8
7
6
5
4
3
2
1
0

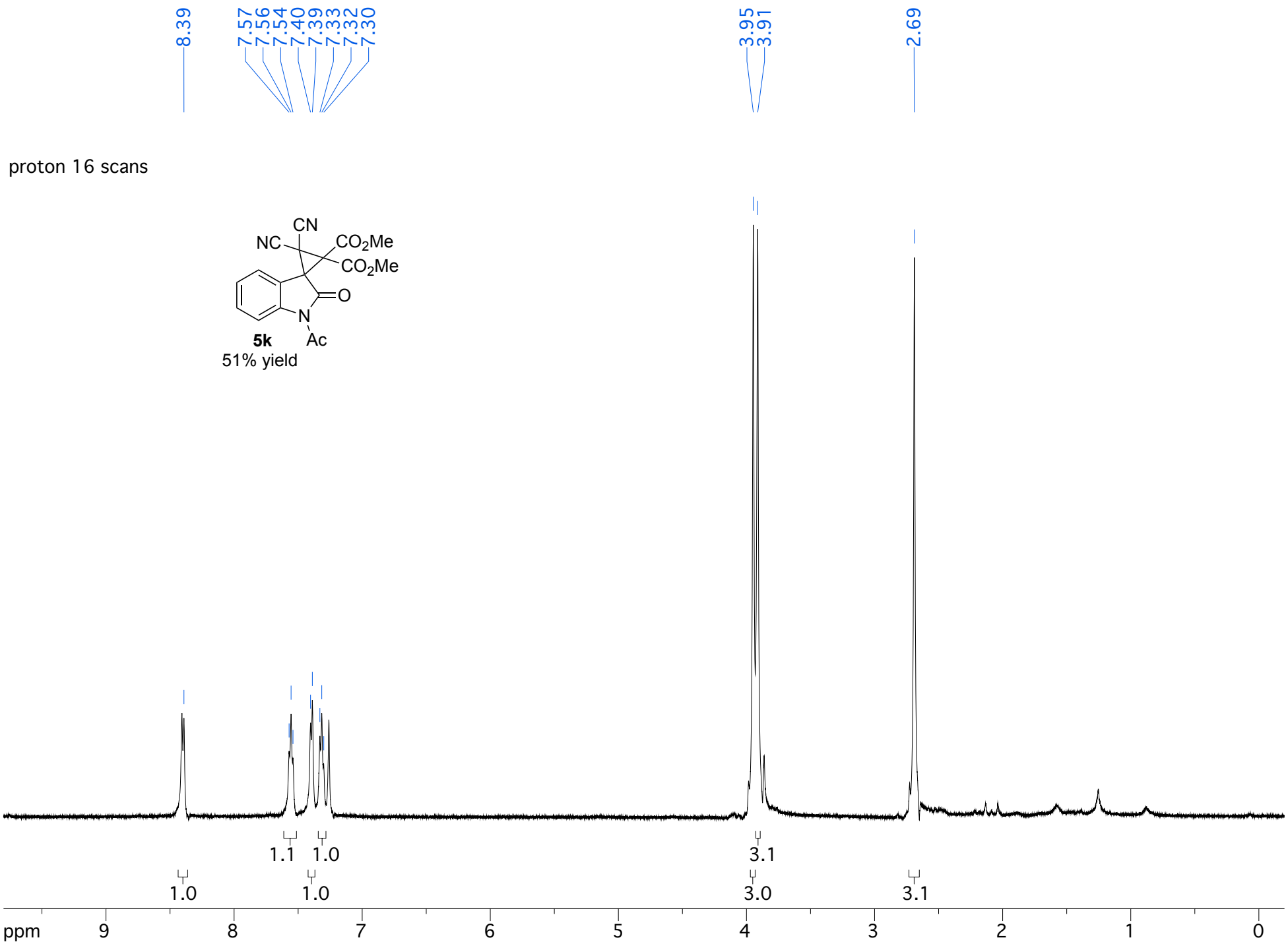


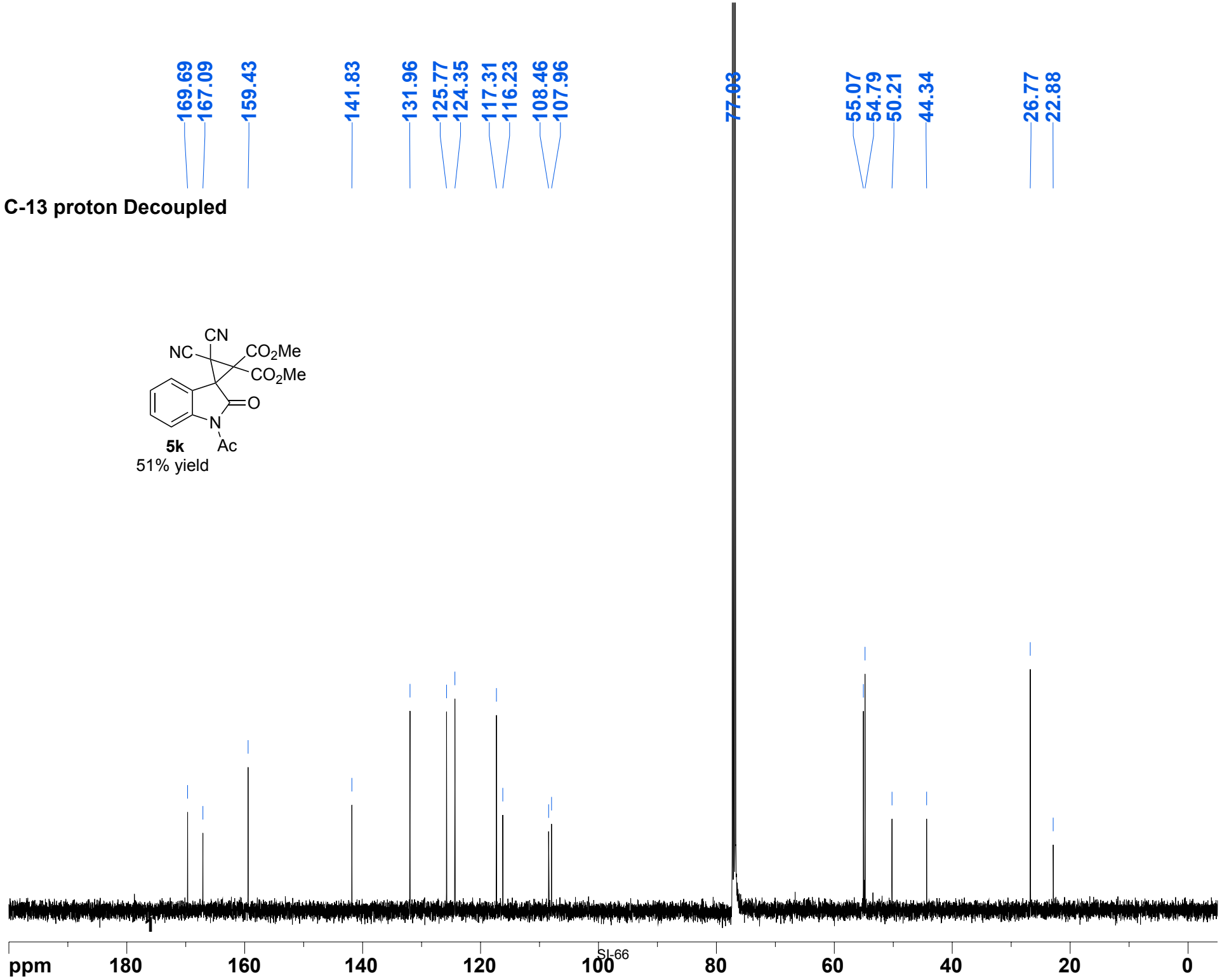
C-13 proton Decoupled

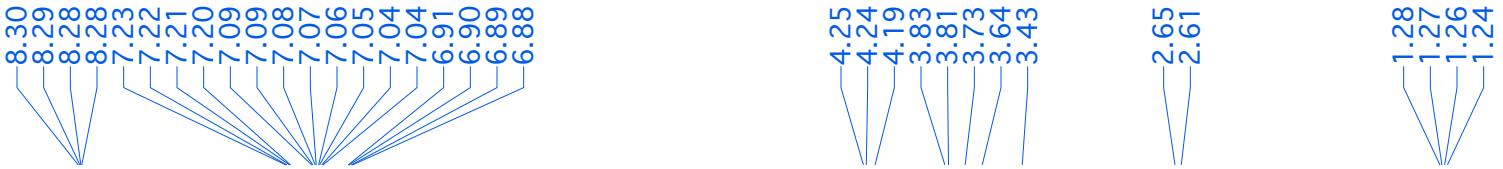


5i
28% yield

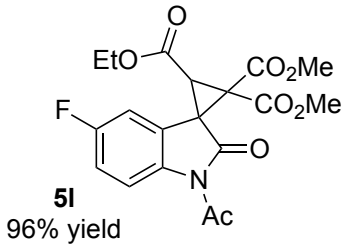



8.39
7.57
7.56
7.54
7.40
7.39
7.33
7.32
7.30
3.95
3.91
2.69
proton 16 scans
CN
NC
CO2Me
CO2Me
O
N
Ac
5k
51% yield
1.1
1.0
3.1
1.0
1.0
3.0
3.1
ppm
9
8
7
6
5
4
3
2
1
0

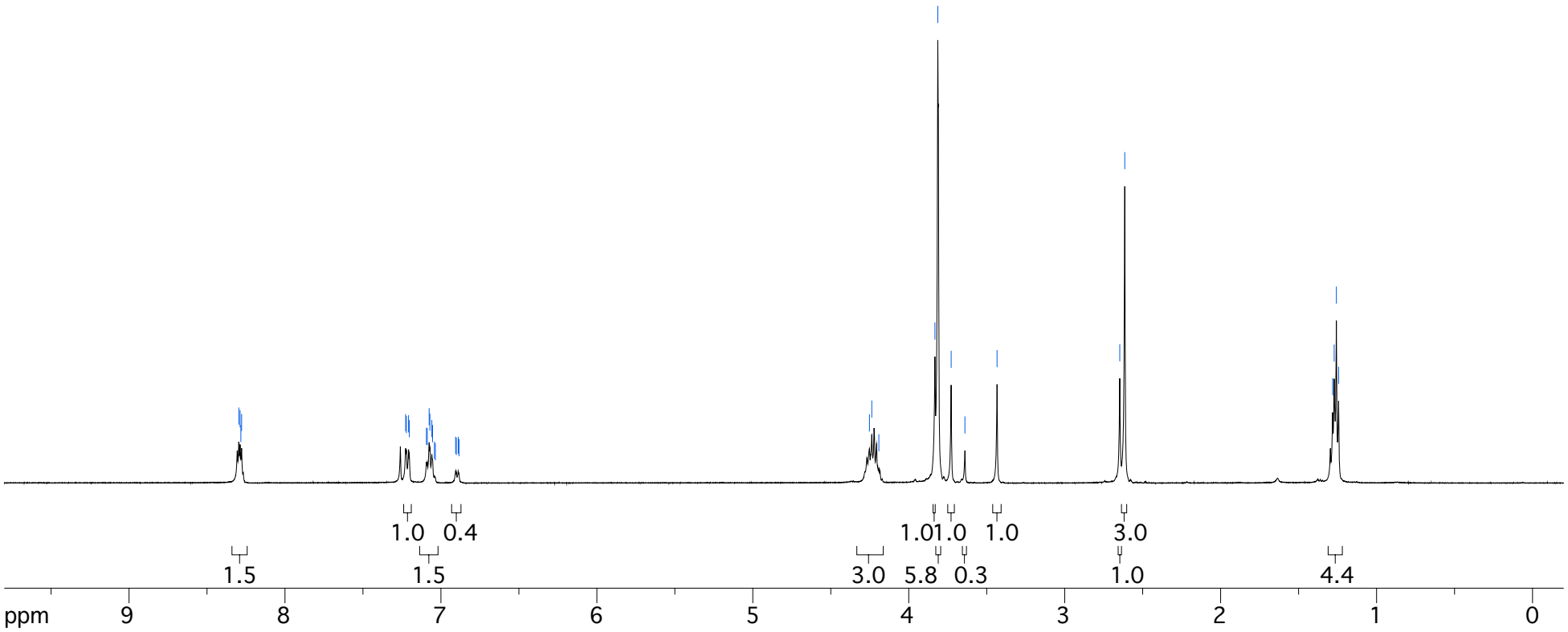

169.69
167.09
159.43
141.83
131.96
125.77
124.35
117.31
116.23
108.46
107.96
77.03
55.07
54.79
50.21
44.34
26.77
22.88
C-13 proton Decoupled
CN
NC
CO2Me
CO2Me
O
N
Ac
5k
51% yield
ppm
180
160
140
120
100
80
60
40
20
0
SL-66



proton 16 scans



5l
96% yield

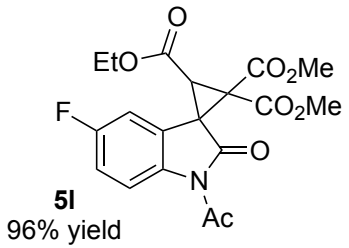


172.47
170.22
169.97
169.95
164.40
164.13
164.02
163.41
162.50
162.47
160.75
160.38
158.80
158.45
137.26
137.24
136.97
136.95
124.35
124.27
121.80
121.72
117.98
117.91
117.25
117.18
116.08
115.94
115.89
115.75
114.31
114.09
109.45
109.24

62.30
62.10
54.05
53.69
53.55
53.33
49.93
48.03
40.37
39.16
38.39
37.39
26.67
26.35

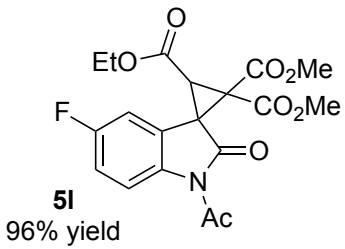
13.98

C-13 proton Decoupled



5l
96% yield

F19 Decoupled



5l
96% yield

-115.61
-116.17

-0

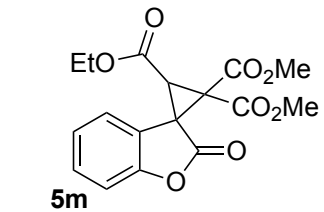
ppm -0 -50 -100 -150

7.43 7.38 7.36 7.35 7.17 7.15 7.14 7.12 7.12

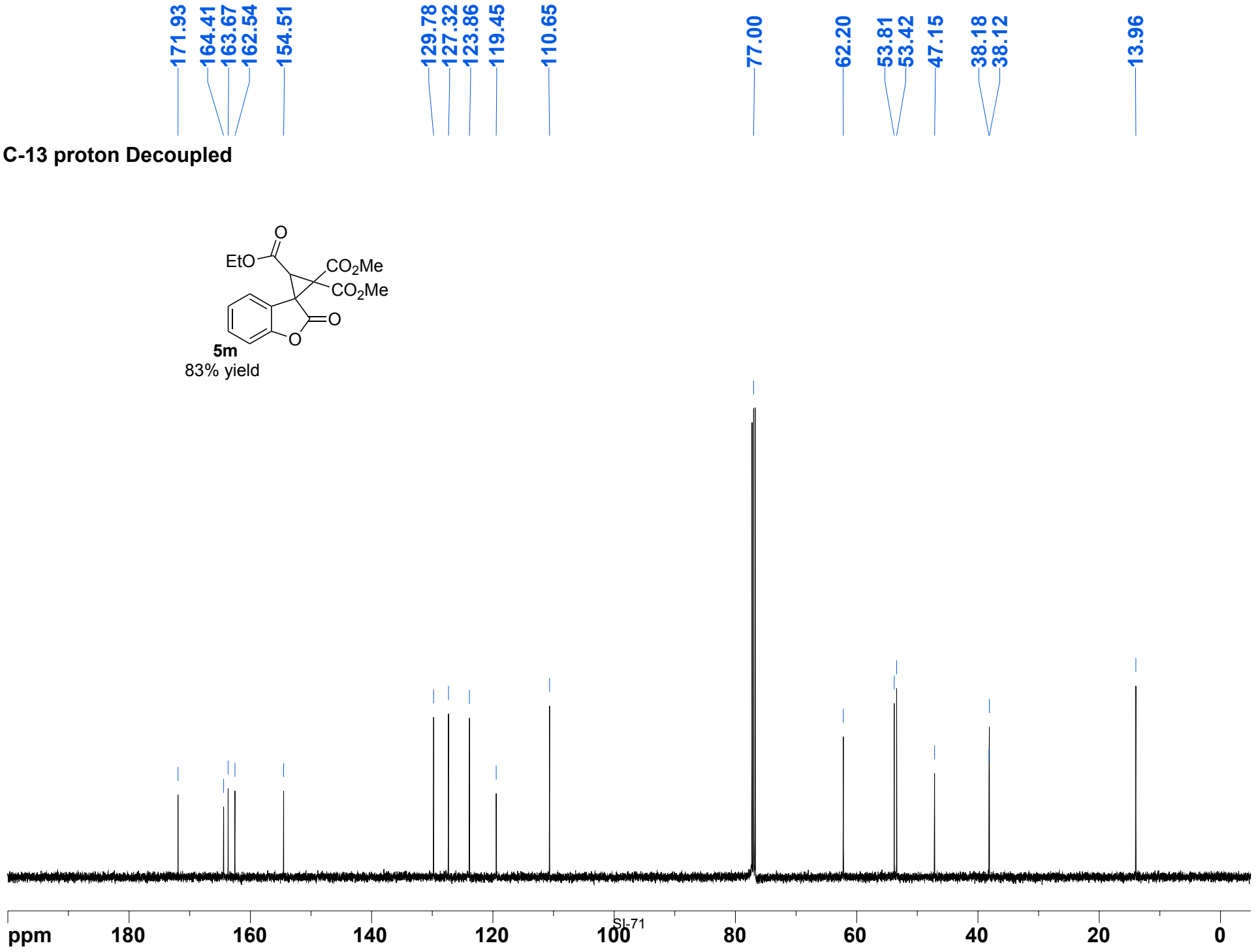
4.22 4.20 4.19 4.19 4.17 4.17 3.81 3.81 3.45

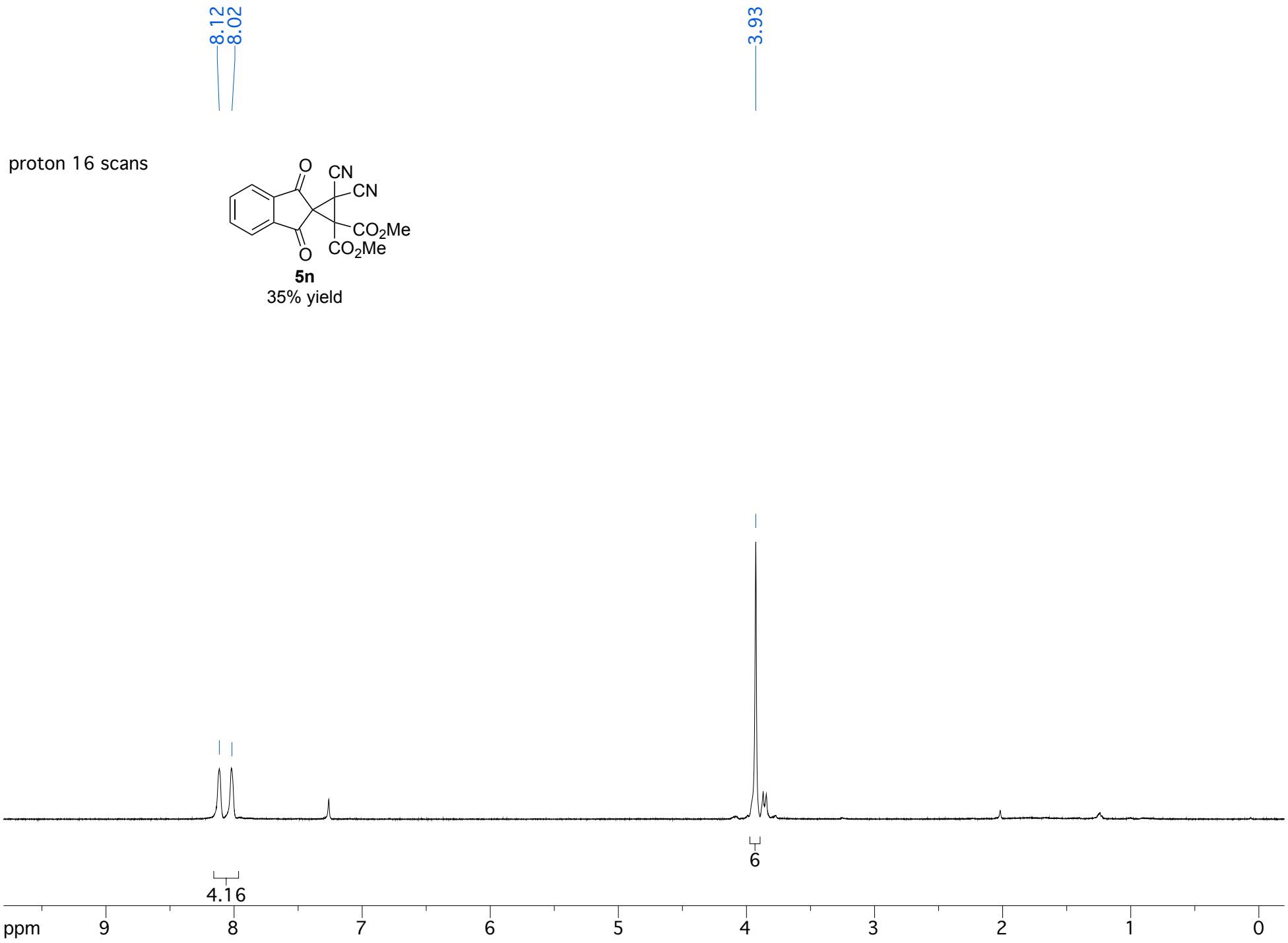
1.25 1.24 1.23

proton 16 scans



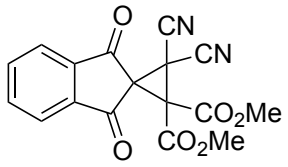
5m
83% yield


171.93
164.41
163.67
162.54
154.51
129.78
127.32
123.86
119.45
110.65
77.00
62.20
53.81
53.42
47.15
38.18
38.12
13.96
C-13 proton Decoupled
EtO
O
CO2Me
CO2Me
O
O
5m
83% yield
ppm
180
160
140
120
100
80
60
40
20
0

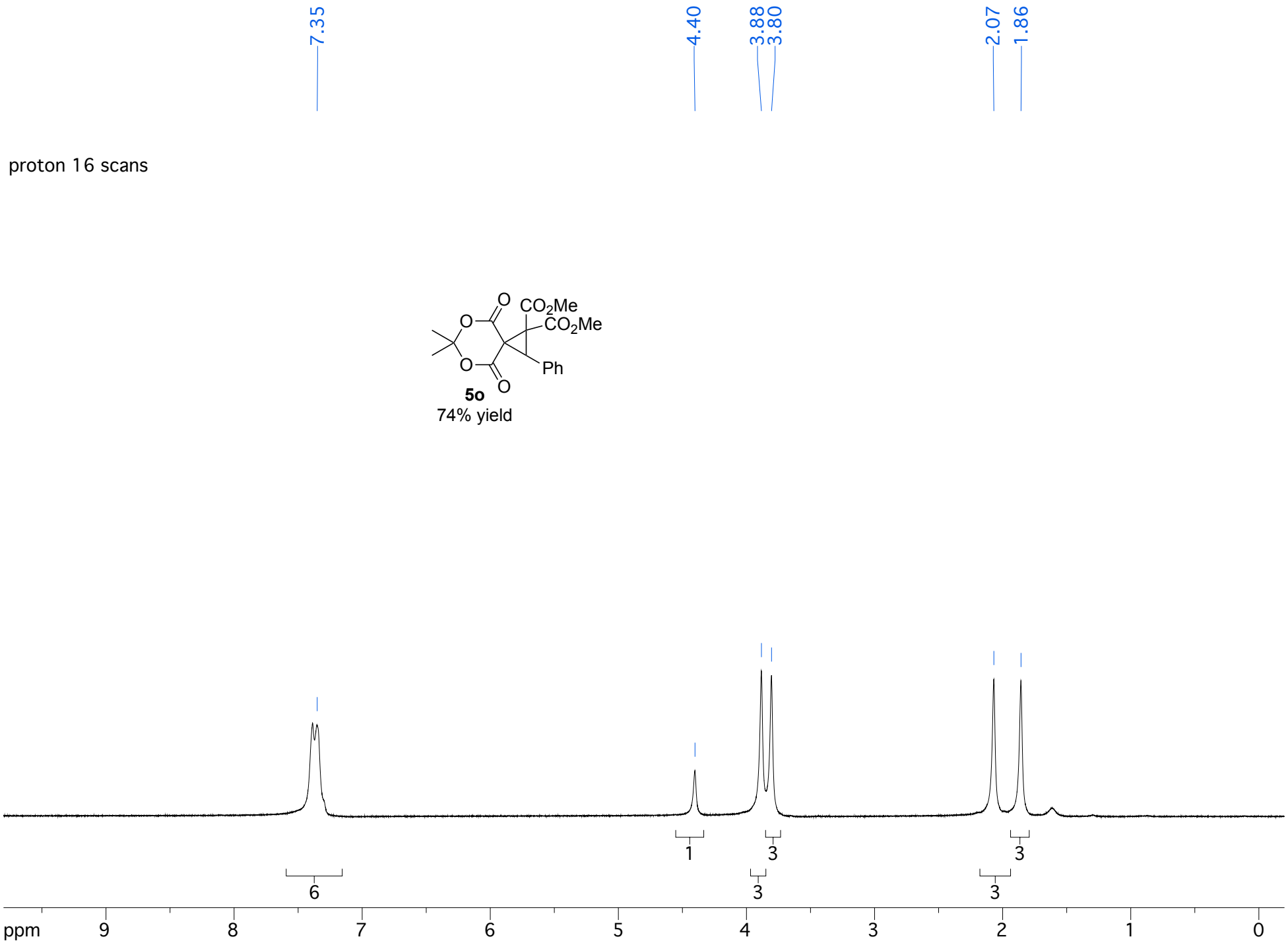

8.12
8.02
3.93
proton 16 scans
O
CN
CN
CO2Me
CO2Me
O
5n
35% yield
4.16
6
ppm
9
8
7
6
5
4
3
2
1
0

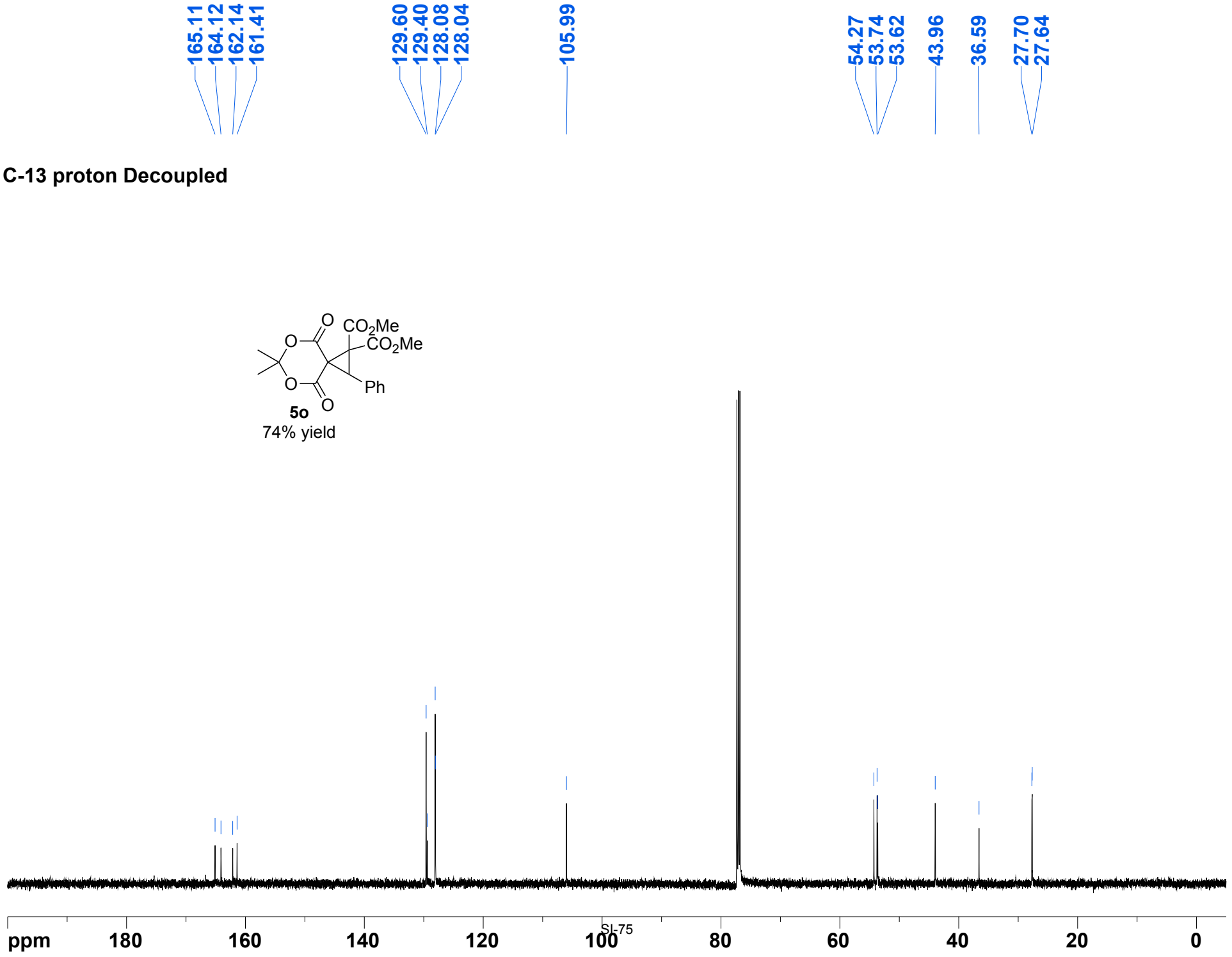
185.97
158.59
141.67
137.35
124.60
107.76
55.04
49.86
44.47
20.50

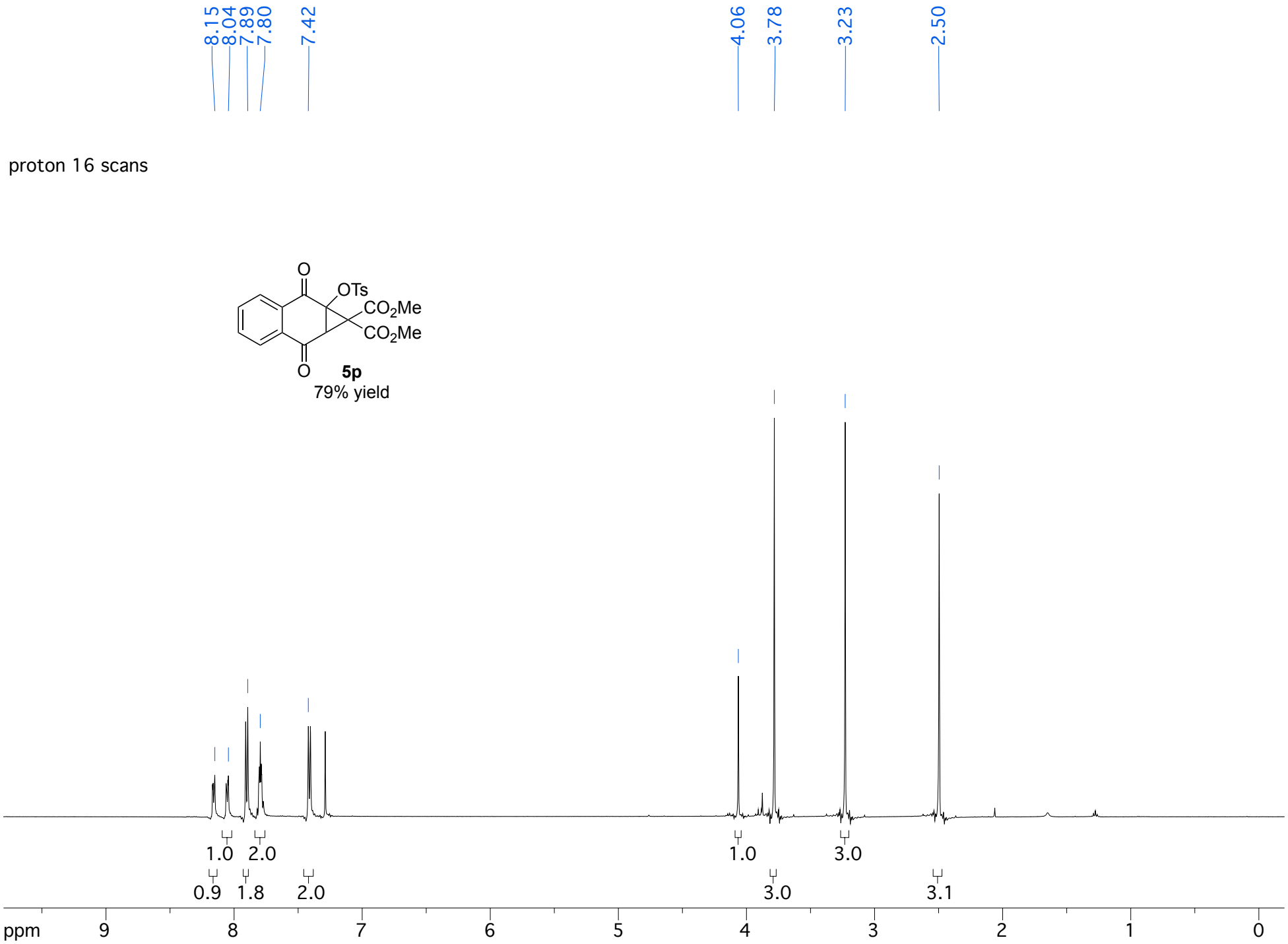
C-13 proton Decoupled

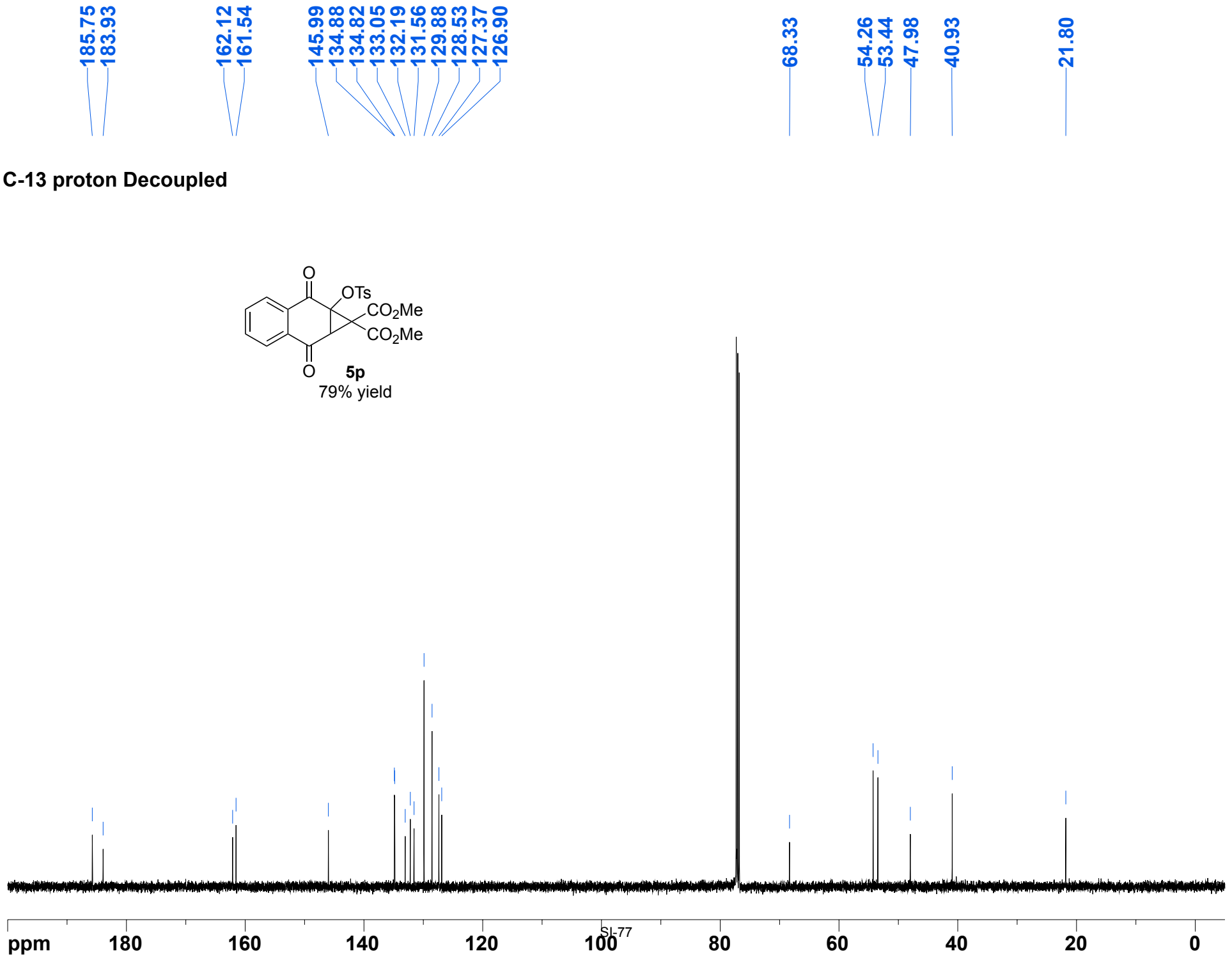


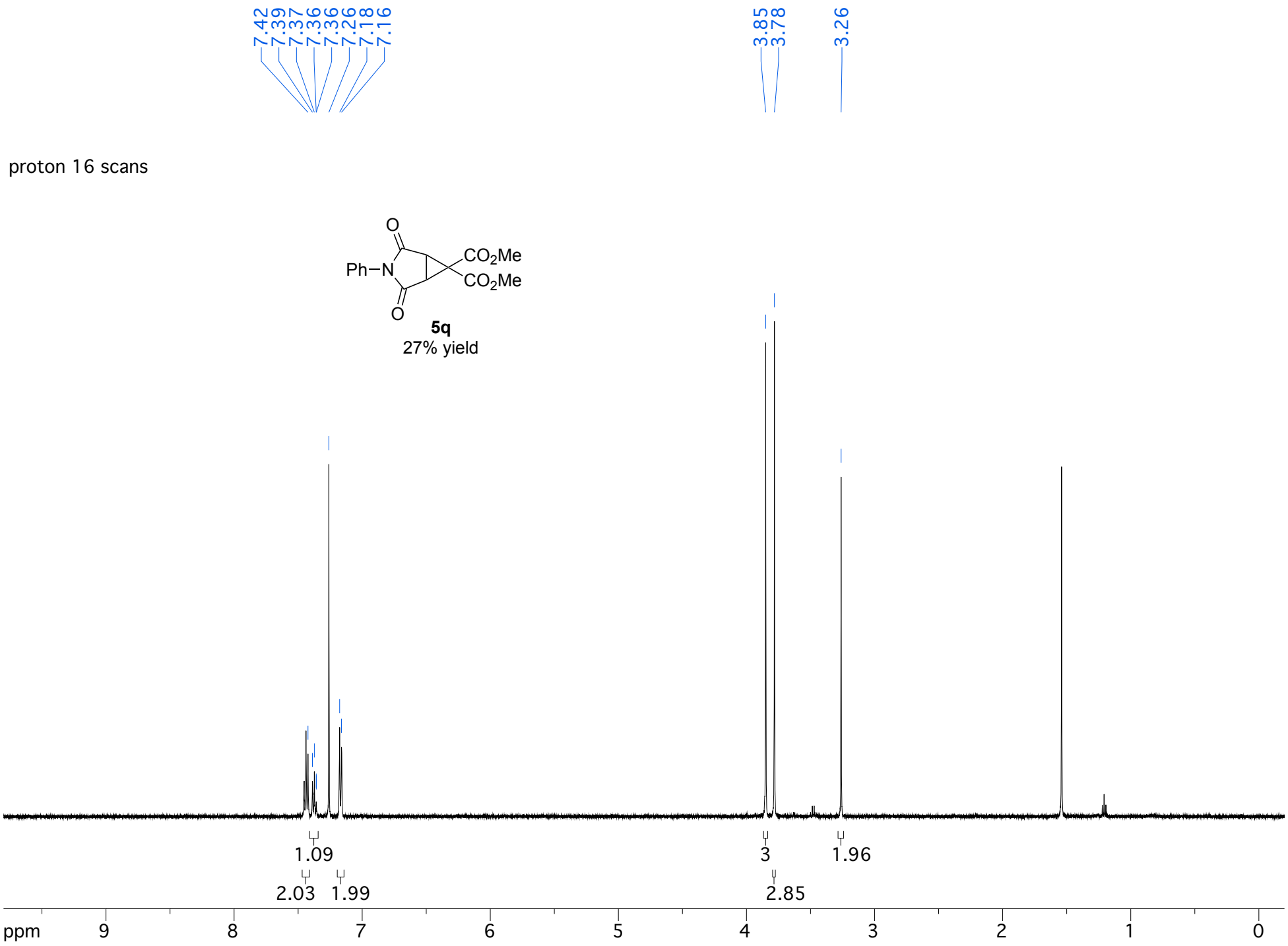
5n
35% yield

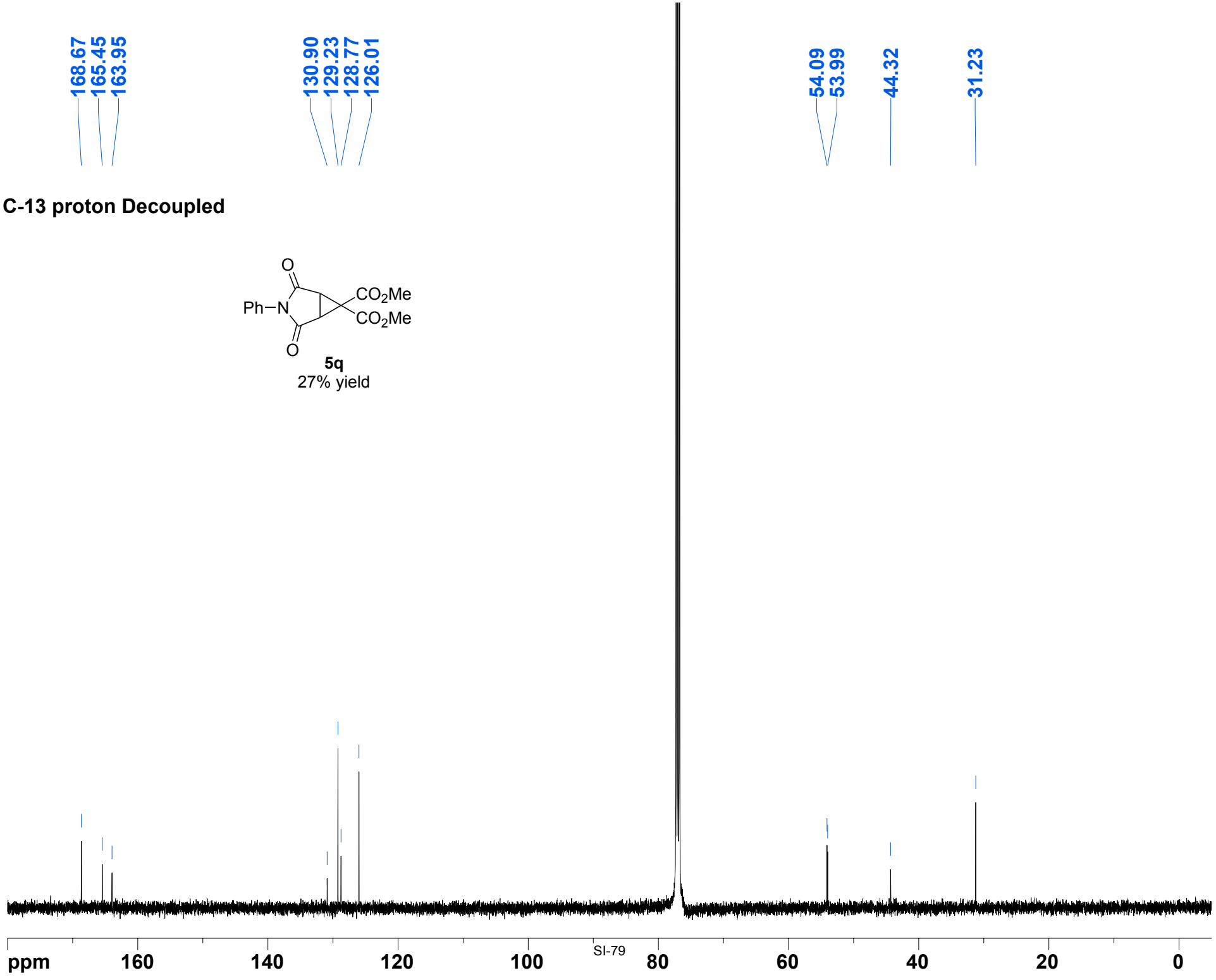

7.35
4.40
3.88
3.80
2.07
1.86
proton 16 scans
O
CO2Me
O
CO2Me
O
Ph
O
5o
74% yield
1
3
3
6
3
3
ppm
9
8
7
6
5
4
3
2
1
0


165.11
164.12
162.14
161.41
129.60
129.40
128.08
128.04
105.99
54.27
53.74
53.62
43.96
36.59
27.70
27.64
C-13 proton Decoupled
O
CO2Me
O
CO2Me
O
Ph
O
5o
74% yield
ppm
180
160
140
120
100
80
60
40
20
0


8.15
8.04
7.89
7.80
7.42
4.06
3.78
3.23
2.50
proton 16 scans
O
OTs
CO2Me
CO2Me
O
5p
79% yield
1.0
2.0
1.0
3.0
0.9
1.8
2.0
3.0
3.1
ppm
9
8
7
6
5
4
3
2
1
0


185.75
183.93
162.12
161.54
145.99
134.88
134.82
133.05
132.19
131.56
129.88
128.53
127.37
126.90
68.33
54.26
53.44
47.98
40.93
21.80
C-13 proton Decoupled
O
OTs
CO2Me
CO2Me
O
5p
79% yield
ppm
180
160
140
120
100
80
60
40
20
0
SL-77


7.42
7.39
7.37
7.36
7.36
7.26
7.18
7.16
3.85
3.78
3.26
proton 16 scans
O
Ph–N
O
CO2Me
CO2Me
5q
27% yield
1.09
2.03
1.99
3
2.85
1.96
ppm
9
8
7
6
5
4
3
2
1
0


168.67
165.45
163.95
130.90
129.23
128.77
126.01
54.09
53.99
44.32
31.23
C-13 proton Decoupled
O
Ph–N
O
CO2Me
CO2Me
5q
27% yield
ppm
160
140
120
100
80
60
40
20
0