Allylic Alkylation and Ring-Closing Metathesis in Sequence: a Successful Cohabitation of Pd and Ru

Claire Kammerer, Guillaume Prestat*, Thomas Gaillard, David Madec and Giovanni Poli*

Laboratoire de Chimie Organique UMR CNRS 7611
Institut de Chimie Moléculaire FR2769
Université Pierre et Marie Curie-Paris 6, Case 183
4, Place Jussieu, F-75252 Paris, France

guillaume.prestat@upmc.fr, giovanni.poli@upmc.fr

Supporting Information

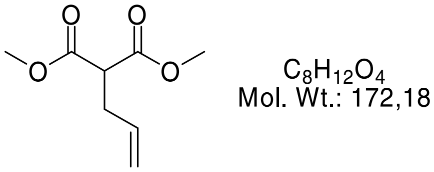
Table of contents

I. General remarks

Dichloromethane was distilled on CaH_2. THF and toluene were distilled on sodium/benzophenone. Tetrakis(triphenylphosphine)palladium was synthesized according to a published procedure.[1] All other reagents and solvents were used without further purification. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) were recorded on a Brüker ARX-400 spectrometer using the residual peak of chloroform-*d* as internal standard (7.27 ppm for ^{1}H NMR and 77.2 ppm for ^{13}C NMR). Chemical shifts are reported in ppm and coupling constants *J* in Hertz. IR spectra were recorded on a Brüker Tensor 27 (pike) instrument and only the strongest or structurally most important peaks were listed. Flash chromatography was conducted using 40-63 µm silica. Analytical TLC were performed on Merck precoated silica 60-F_{254} plates.

II. Preparation of starting materials

Dimethyl 2-allylmalonate 1a



Dimethyl malonate (1 mL, 8.8 mmol, 1.5 equiv.) and 3-bromoprop-1-ene (0.5 mL, 5.8 mmol, 1 equiv.) were added to a solution of potassium carbonate (2.4 g, 17.4 mmol, 3 equiv.) in acetone (30 mL). The reaction mixture was allowed to stir for 24 h at room temperature and was then quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with methylene chloride. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with cyclohexane / AcOEt 80 : 20 to afford 917 mg (91%) of the expected product **1a** as a yellow oil.

Data in agreement with: Curran, D. P.; Fairweather, N. *J. Org. Chem.* **2003**, *68*, 2972-2974. Commercially available.

^{1}H NMR ($CDCl_3$, 400 MHz) : δ = 2.55 (tt, *J* = 1.5, 7.5 Hz, 2H), 3.38 (t, *J* = 7.5 Hz, 1H), 3.64 (s, 6H), 4.96 (dd, *J* = 1.0, 10.5 Hz, 1H), 5.02 (ddt, *J* = 1.5, 2.0, 17.0 Hz, 1H), 5.68 (ddt, *J* = 7.0, 10.0, 17.0 Hz, 1H).

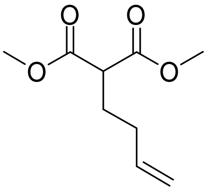
^{13}C NMR ($CDCl_3$, 100 MHz) : δ = 32.8, 51.2, 52.3, 117.5, 133.9, 169.1.

IR (ATR) : 2955, 1732, 1644, 1435 cm^{-1}

---

[1] Coulson, D. R. *Inorg. Synth.* **1972**, *13*, 121-124.

Dimethyl 2-(but-3'-enyl)malonate 1b

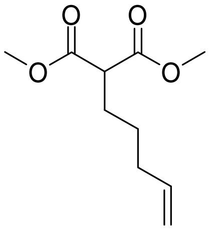


$C_9H_{14}O_4$
Mol. Wt.: 186,21

At 0 °C, dimethyl malonate (1 mL, 8.8 mmol, 1 equiv.) was added dropwise to a suspension of sodium hydride (390 mg, 9.7 mmol, 1.1 equiv., 60% in mineral oil) in DMF (20 mL). The mixture was allowed to warm up to room temperature and 4-bromobut-1-ene (1.05 mL, 8.8 mmol, 1 equiv.) was introduced. The reaction mixture was allowed to stir for 24 h at room temperature and was then quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with pentane / Et_2O 95 : 5 to afford 1.14 g (70%) of the expected product **1b** as a yellow oil.

Data in agreement with: Laidig, G. J.; Hegedus, L. S. *Synthesis* **1995**, 527-532.
^{1}H NMR ($CDCl_3$, 400 MHz) : δ = 1.99 - 2.13 (m, 4H), 3.41 (t, *J* = 7.5 Hz, 1H), 3.75 (s, 6H), 5.00 – 5.07 (m, 2H), 5.77 (ddt, *J* = 6.5, 10.5, 16.5 Hz, 1H).
^{13}C NMR ($CDCl_3$, 100 MHz) : δ = 28.0, 31.4, 51.0, 52.6, 116.2, 136.9, 170.0.
IR (ATR) : 2955, 1732, 1642, 1435 cm^{-1}

Dimethyl 2-(pent-4'-enyl)malonate 1c



$C_{10}H_{16}O_4$
Mol. Wt.: 200,23

At 0 °C, dimethyl malonate (0.5 mL, 4.4 mmol, 1 equiv.) was added dropwise to a suspension of sodium hydride (196 mg, 4.9 mmol, 1.1 equiv., 60% in mineral oil) in DMF (10 mL). The mixture was allowed to warm up to room temperature and 5-bromopent-1-ene (0.4 mL, 3.4 mmol, 0.8 equiv.) was introduced. The reaction mixture was allowed to stir for 24 h at room temperature and was then quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with pentane / Et_2O 95 : 5 to afford 292 mg (43%) of the expected product **1c** as a yellow oil.

Data in agreement with: Fournet, G.; Balme, G.; Gore, J. *Tetrahedron* **1990**, *46*, 7763-7774.

^{1}H NMR ($CDCl_3$, 400 MHz) : δ = 1.25 – 1.33 (m, 2H), 1.74 – 1.80 (m, 2H), 1.95 (q, *J* = 7.5 Hz, 2H), 3.24 (t, *J* = 7.5 Hz, 1H), 3.59 (s, 6H), 4.82 (br d, *J* = 10.0 Hz, 1H), 4.88 (dd, *J* = 1.5, 17.0 Hz, 1H), 5.64 (ddt, *J* = 6.5, 10.0, 17.0 Hz, 1H).

^{13}C NMR ($CDCl_3$, 100 MHz) : δ = 26.3, 28.1, 33.0, 51.3, 52.1, 114.8, 137.6, 169.5.

IR (ATR) : 2954, 1734, 1641, 1435 cm^{-1}

III. Typical procedures

III.1. Typical procedures for the *pseudo* domino reactions

"Allylic alkylation – ring-closing metathesis" PDOM sequence

The palladium catalyst was dissolved in 0.5 mL of methylene chloride, and the appropriate ligand was added if required. The resulting source of palladium(0) was diluted with 10 mL of methylene chloride and the ruthenium catalyst was introduced, followed by allyl acetate (113 µL, 1.05 mmol, 1.05 equiv.). In another flask, the appropriate monosubstituted malonate (1 mmol, 1 equiv.) dissolved in 6 mL of methylene chloride was deprotonated with sodium hydride (44 mg, 1.1 mmol, 1.1 equiv., 60% in mineral oil) before being added *via* cannula to the solution containing the catalytic systems. The resulting mixture was refluxed for 1 h, and then allowed to cool down to room temperature. The reaction was quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with methylene chloride. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with pentane / Et_2O 90 : 10, to afford the expected pure product.

"Allylic alkylation – allylic alkylation – ring-closing metathesis" PDOM sequence

Sequential addition of the catalytic systems :

Precursor (**4**, **7-12**) (1 mmol, 1 equiv.), allyl acetate (226 µl, 2.1 mmol, 2.1 equiv.) and sodium hydride (88 mg, 2.2 mmol, 2.2 equiv., 60% in mineral oil) were successively added to a solution of tetrakis(triphenylphosphine)palladium (29 mg, 25 µmol, 2.5 mol %) in 17 mL of methylene chloride. The reaction mixture was stirred at room temperature until disappearance of the starting material (TLC monitoring). Grubbs' catalyst 2nd generation (64 mg, 75 µmol, 7.5 mol %) was then introduced and the resulting mixture was refluxed for 4 h. After cooling to room temperature, the reaction was quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer was extracted with methylene chloride. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure.

The crude product was purified by flash chromatography on silica gel eluting with cyclohexane / AcOEt to afford the expected product (**2a**, **13**-**18**).

Real *pseudo*-domino reaction :

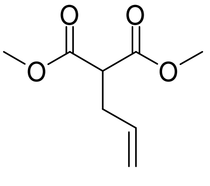
Allyl acetate (226 µl, 2.1 mmol, 2.1 equiv.), dimethyl malonate (114 µL, 1 mmol, 1 equiv.), sodium hydride (88 mg, 2.2 mmol, 2.2 equiv., 60% in mineral oil) and Grubbs' catalyst 2nd generation (64 mg, 75 µmol, 7.5 mol %) were successively added to a solution of tetrakis(triphenylphosphine)palladium (29 mg, 25 µmol, 2.5 mol %) in 17 mL of methylene chloride. The resulting mixture was refluxed for 12 h. After cooling down to room temperature, the reaction was quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with methylene chloride. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with pentane / AcOEt 95 : 5 to afford 83 mg (45%) of the expected product **2a** as a bright yellow oil.

III.2. Typical procedure for the allylic alkylation with ruthenium

Sodium hydride (42 mg, 1.05 mmol, 1.05 equiv., 60% in mineral oil), Grubbs'catalyst (62 mg, 75 µmol, 7.5 mol %) and allyl acetate (108 µL, 1 mmol, 1 equiv.) were successively added to a solution of the appropriate malonate **1a** or **4** (1 mmol, 1 equiv.) in freshly distilled THF (5 mL). The resulting mixture was stirred at room temperature during 30 min and then refluxed during 12 h. After cooling down to room temperature, the reaction was quenched with a saturated solution of NH_4Cl. The organic layer was separated and the aqueous layer extracted with diethyl ether. The combined organic layers were washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography on silica gel eluting with cyclohexane / AcOEt 95 : 5 to afford the expected products **1a** and/or **3**.

IV. Characterization data for the reaction products

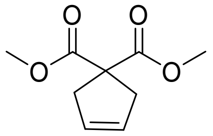
Dimethyl 2-allylmalonate 1a



$C_8H_{12}O_4$
Mol. Wt.: 172,18

See: II. Preparation of starting materials

Dimethyl cyclopent-3-ene-1,1-dicarboxylate 2a



$C_9H_{12}O_4$
Mol. Wt.: 184,19

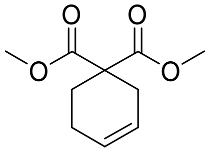
Data in agreement with: Quinkert, G.; Schwartz, U.; Stark, H.; Weber, W.-D.; Adam, F.; Baier, H.; Frank, G.; Dürner, G. *Liebigs Ann. Chem.* **1982**, *11*, 1999-2040. Commercially available.

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 3.03 (s, 4H), 3.75 (s, 6H), 5.62 (s, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 41.1, 53.0, 58.9, 128.0, 172.8.

IR (ATR) : 2954, 1731, 1624, 1434 cm^{-1}

Dimethyl cyclohex-3-ene-1,1-dicarboxylate 2b



$C_{10}H_{14}O_4$
Mol. Wt.: 198,22

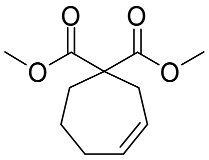
Data in agreement with: Snider, B. B.; Merritt, J. E.; Dombroski, M. A.; Buckman, B. O. *J. Org. Chem.* **1991**, *56*, 5544-5553.

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 2.07 – 2.16 (m, 4H), 2.55 (m, 2H), 3.72 (s, 6H), 5.66 (m, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 22.4, 27.6, 30.6, 52.7, 53.0, 124.0, 126.2, 172.2.

IR (ATR) : 2954, 1731, 1434 cm^{-1}

Dimethyl cyclohept-3-ene-1,1-dicarboxylate 2c



$C_{11}H_{16}O_4$
Mol. Wt.: 212,24

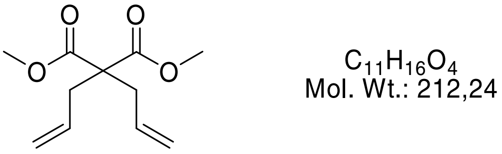
^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 1.61 – 1.67 (m, 2H), 2.16 (q, J = 5.5 Hz, 2H), 2.23 – 2.26 (m, 2H), 2.68 (d, J = 6.5 Hz, 2H), 3.71 (s, 6H), 5.65 – 5.71 (m, 1H), 5.83 – 5.89 (m, 1H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 22.9, 28.4, 32.5, 36.9, 52.6, 56.3, 127.2, 134.4, 172.4.

IR (ATR) : 2952, 1730, 1434 cm^{-1}

HRMS *m/z* calculated for $C_{11}H_{16}O_4Na$ (M^+): 235.0941. Found: 235.0942.

Dimethyl 2,2-diallylmalonate 3

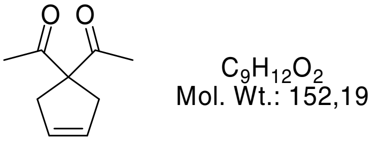


Data in agreement with: Hayashi, Y.; Gotoh, H.; Tamura, T.; Yamaguchi, H.; Masui, R.; Shoji, M. *J. Am. Chem. Soc.* **2005**, *127*, 16028 – 16029. Commercially available.

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 2.64 (dd, *J* = 1.0, 6.5 Hz, 4H), 3.72 (s, 6H), 5.09 – 5.13 (m, 4H), 5.59 – 5.70 (m, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 37.0, 52.5, 57.8, 119.4, 132.3, 171.3.

1,1-diacetylcyclopent-3-ene 13



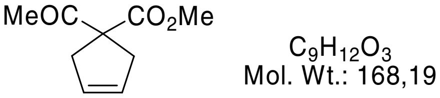
Data in agreement with: Bose, G.; Ullah, E.; Langer, P. *Chem. Eur. J.* **2004**, *10*, 6015-6028.

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 2.13 (s, 6H), 2.89 (s, 4H), 5.57 (s, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ =. 26.5, 37.8, 73.3, 128.0, 205.1.

IR (ATR) : 2923, 1696, 1626, 1431, 1356 cm^{-1}

Methyl 1-acetyl-cyclopent-3-enecarboxylate 14



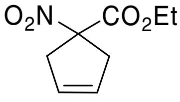
Data in agreement with:. Deprès, J.-P.; Greene, A. P. *J. Org. Chem.* **1984**, *49*, 928-931.

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 2.19 (s, 3H), 2.95 (s, 4H), 3.76 (s, 3H), 5.60 (s, 2H).

^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 26.1, 39.5, 52.9, 65.5, 127.9, 173.6, 202.9.

IR (ATR) : 3063, 2928, 2854, 1744, 1714, 1435, 1358 cm^{-1}

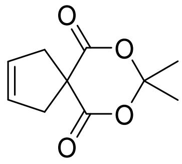
Ethyl-1-nitro-cyclopent-3-enecarboxylate 15



$C_8H_{11}NO_4$
Mol. Wt.: 185,18

^{1}H NMR (CDCl$_3$, 400 MHz) : δ = 1.30 (t, 3H, ^3J= 7.0 Hz), 3.24 (d, 2H, ^2J= 17 Hz, part of AB system), 3.48 (d, 2H, ^2J= 17 Hz, part of AB system), 4.29 (q, 2H, ^3J= 7.0 Hz), 5.69 (s, 2H).
^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 13.9, 42.8, 63.2, 98.0, 127.1, 167.4;
IR (ATR) : 2984, 1746, 1550, 1428, 1353, 1270, 1208 cm^{-1}

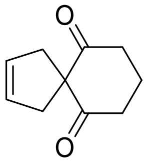
8,8-dimethyl-7,9-dioxaspiro[4.5]dec-2-ene-6,10-dione 16



$C_{10}H_{12}O_4$
Mol. Wt.: 196,2

Data in agreement with: Kotha, S.; Manivannan, E.; Ganesh, T.; Sreenivasachary, N.; Deb, A. *Synlett* **1999**, 1618-1620.
^{1}H NMR (CDCl$_3$, 400 MHz) : δ =. 1.74 (s, 6H), 3.12 (s, 4H), 5.69 (s, 2H).
^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 29.0, 46.7, 50.7, 104.8, 127.2, 170.8.
IR (ATR) : 3062, 2928, 1743, 1666 cm^{-1}

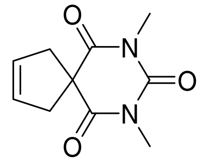
Spiro[4.5]dec-2-ene-6,10-dione 17



$C_{10}H_{12}O_2$
Mol. Wt.: 164,2

Data in agreement with: Kotha, S.; Manivannan, E. *Arkivoc* **2003**, 67-76.
^{1}H NMR (CDCl$_3$, 400 MHz) : δ =. 1.97 (quint., 2H, ^3J= 6.5 Hz), 2.69 (t, 4H, ^3J= 6.5 Hz), 2.85 (s, 4H), 5.52 (s, 2H).
^{13}C NMR (CDCl$_3$, 100 MHz) : δ = 17.6, 37.7, 39.2, 70.9, 127.1, 207.1.
IR (ATR) : 2926, 2852, 1723, 1688, 1629 cm^{-1}

7,9-dimethyl-9-diazaspiro[4.5]dec-2-ene-6,8,10-trione 18



$C_{10}H_{12}N_2O_3$
Mol. Wt.: 208,21

Data in agreement with: Kotha, S.; Deb, A. C.; Kumar, R. V. *Bioorg. Med. Chem.* **2005**, *16*, 1039-1043.

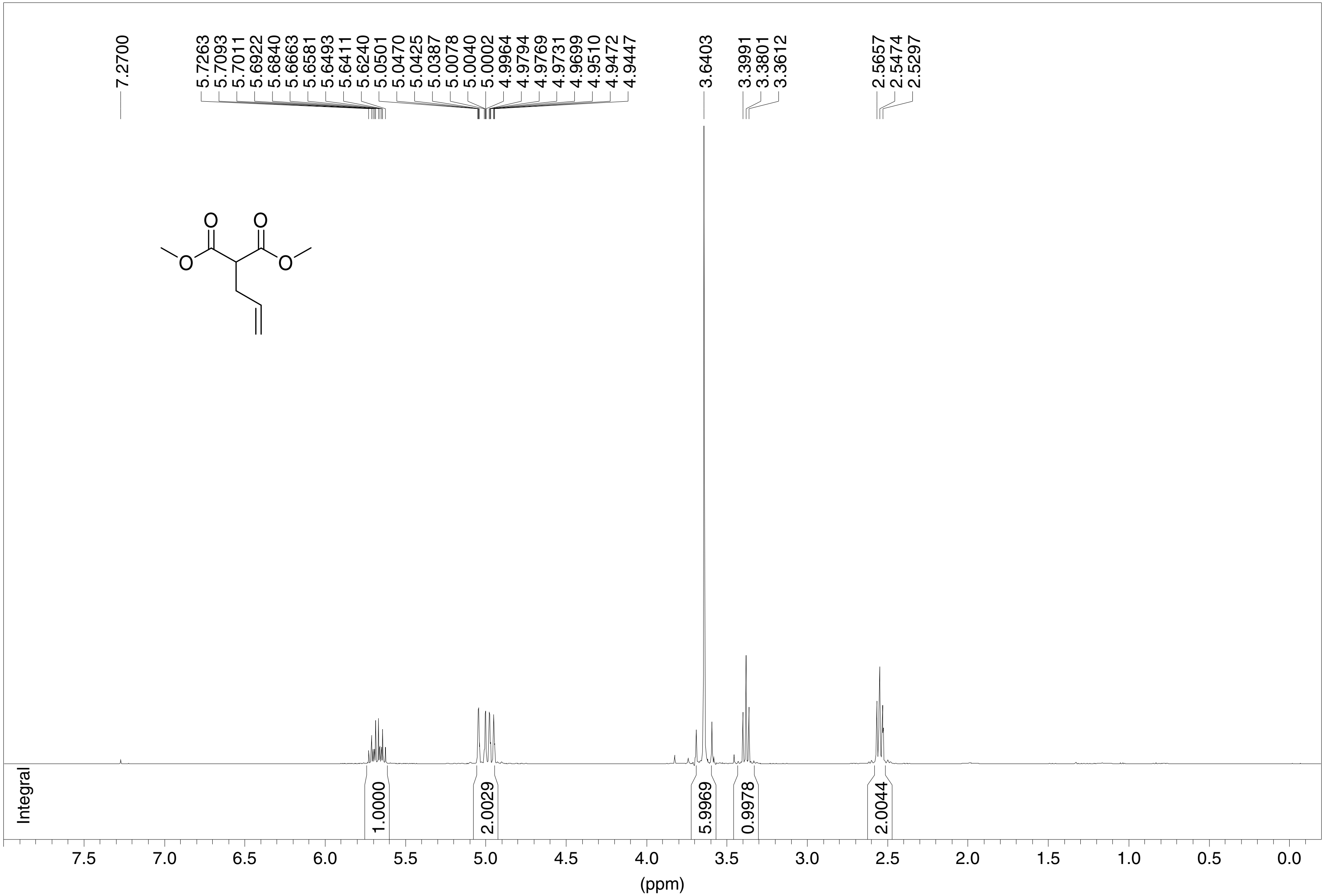
^{1}H NMR ($CDCl_3$, 400 MHz) : δ =. 2.97 (s, 4H), 3.27 (s, 6H), 5.63 (s, 2H).

^{13}C NMR ($CDCl_3$, 100 MHz) : δ =. 29.0, 45.5, 54.6, 127.4, 151.4, 172.5.

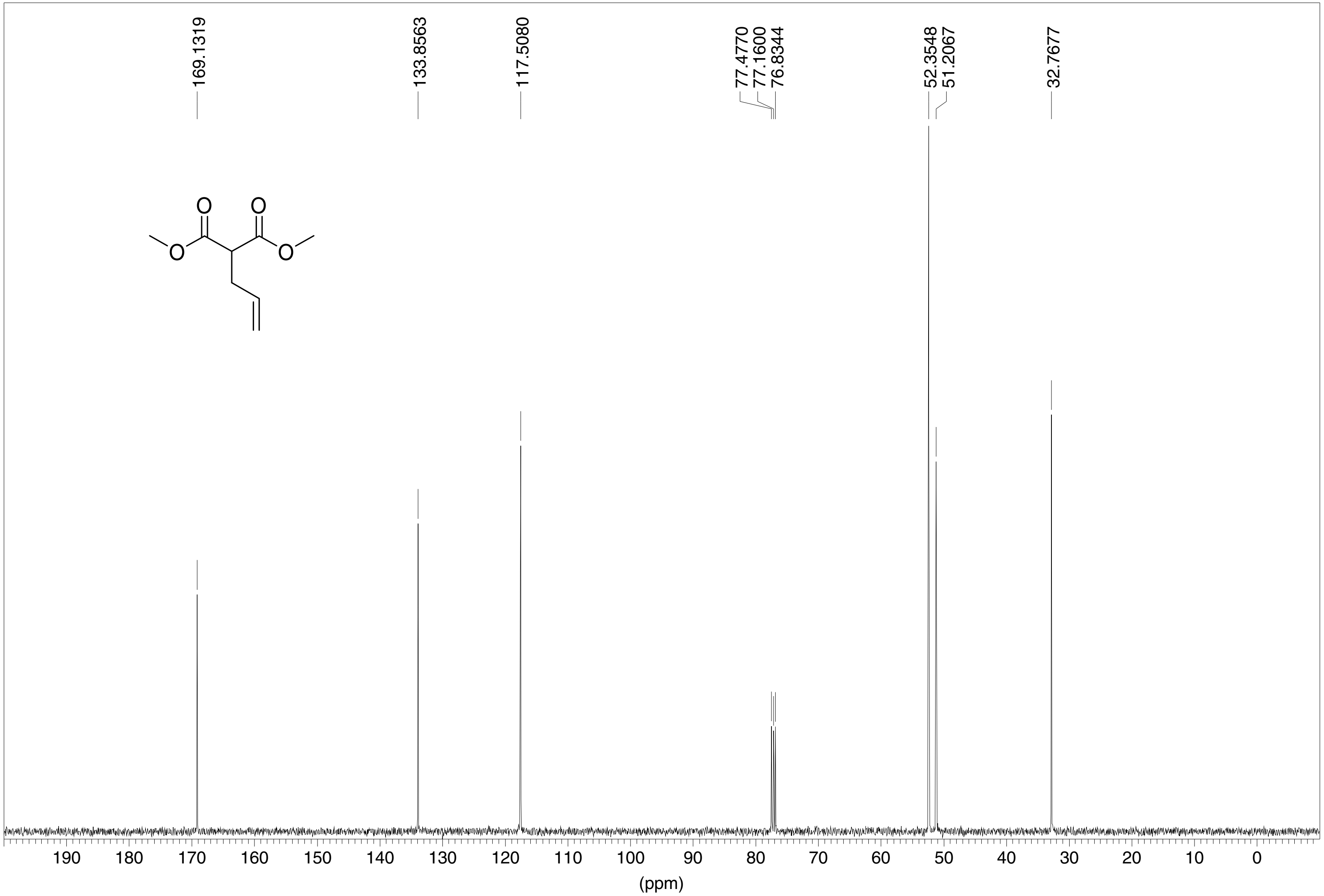
IR (ATR) : 3059, 3003, 2933, 2852, 1763, 1733 cm^{-1}

V. ^{1}H and ^{13}C NMR spectra

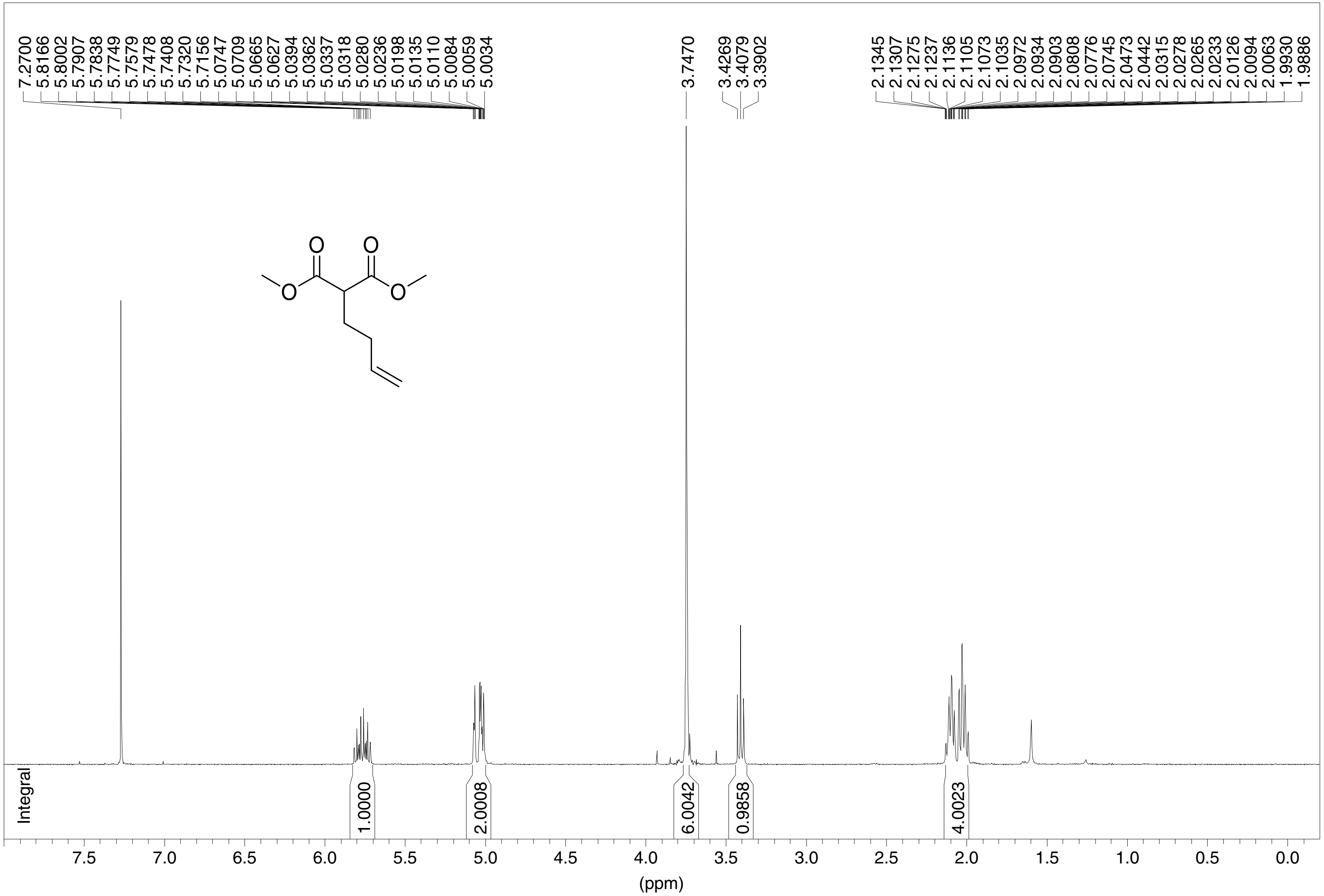
Dimethyl 2-allylmalonate 1a



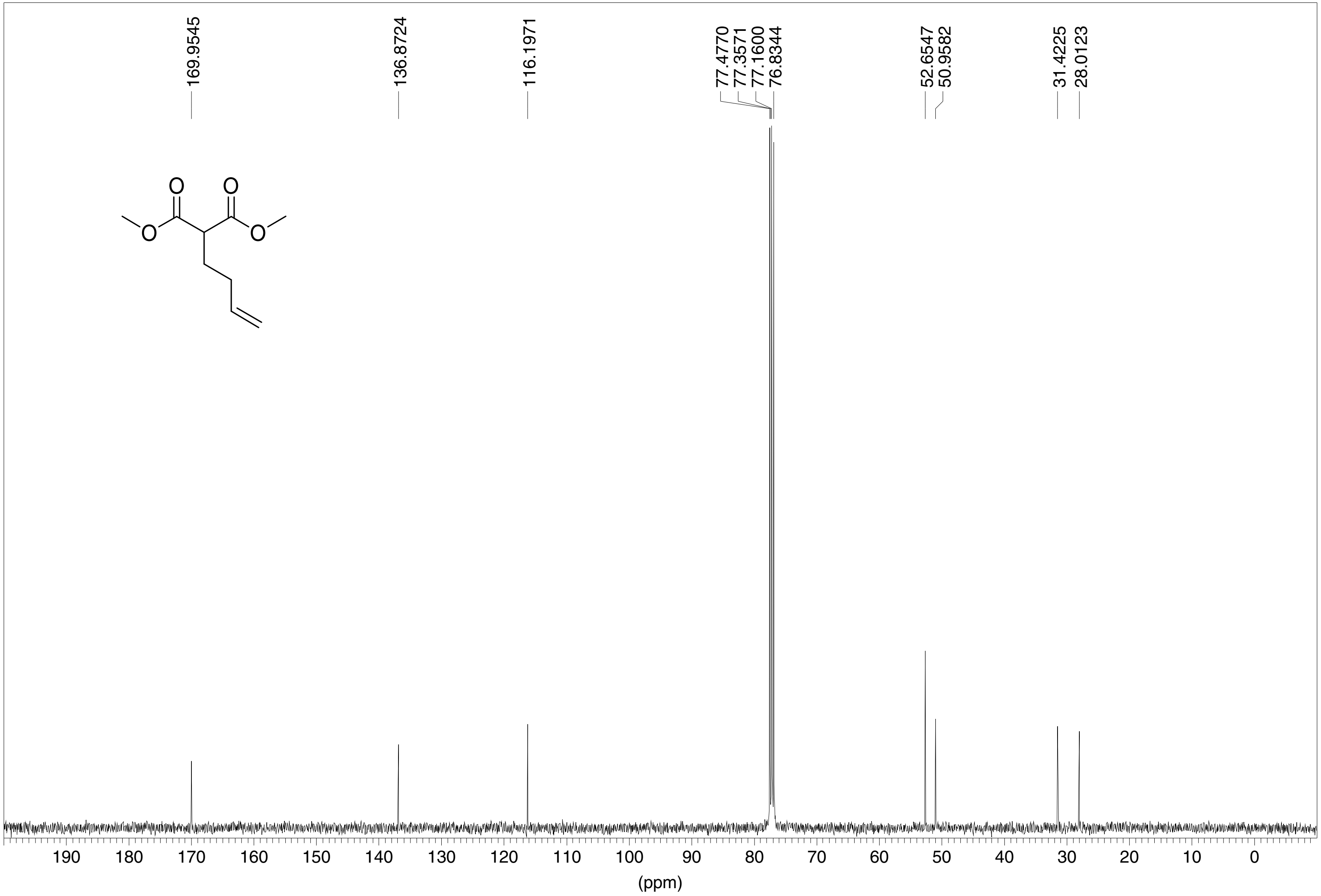
Dimethyl 2-allylmalonate 1a



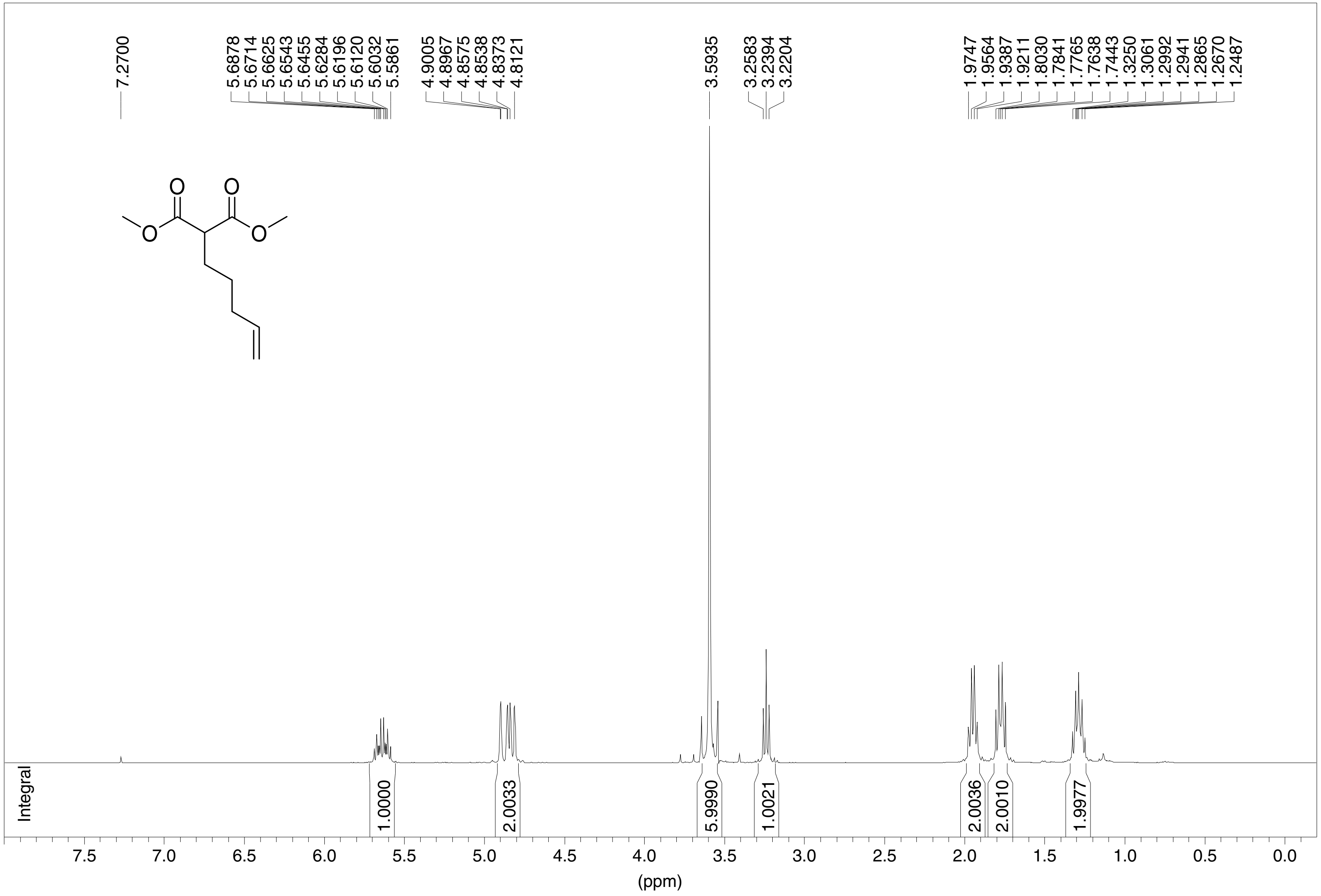
Dimethyl 2-(but-3’-enyl)malonate 1b



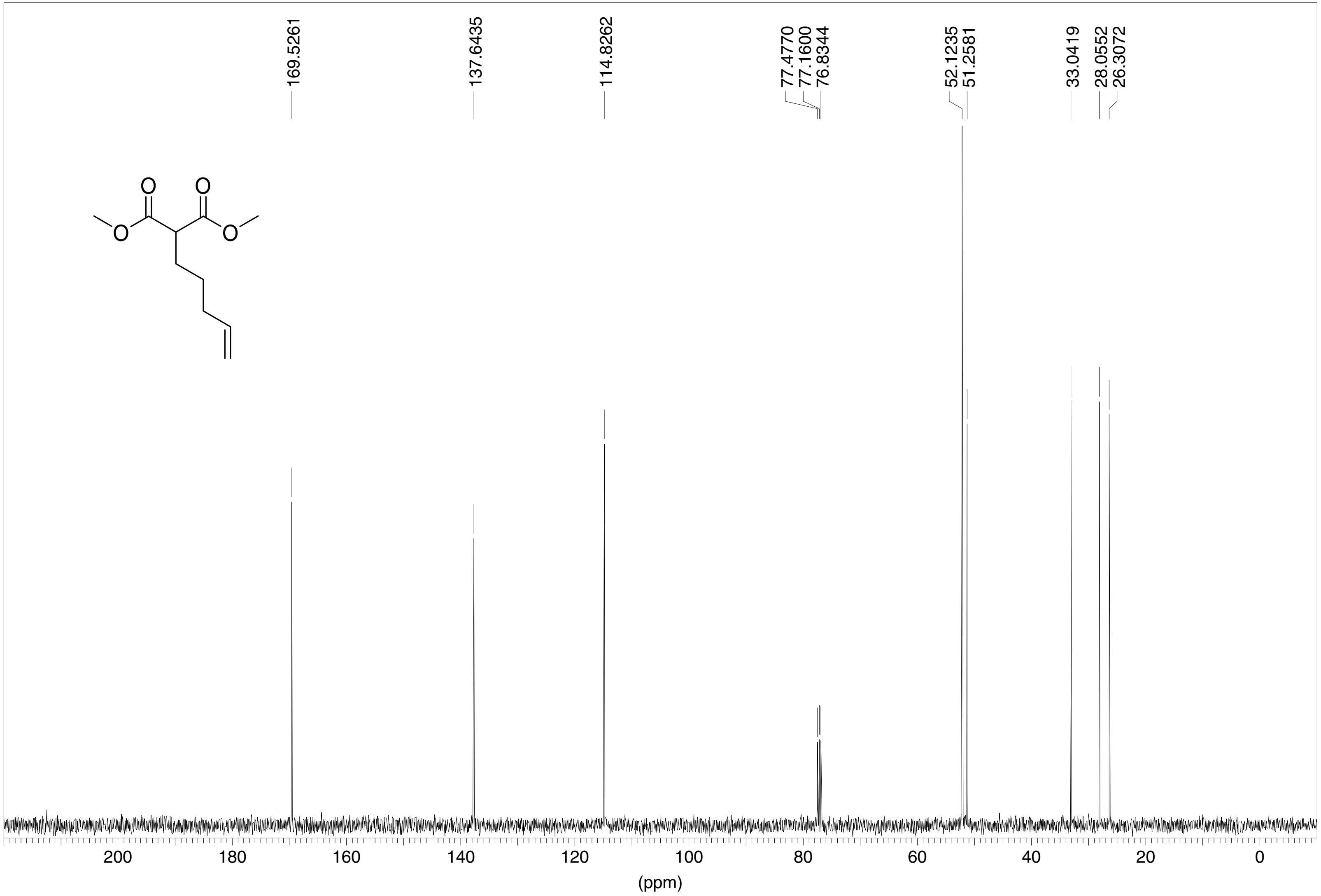
Dimethyl 2-(but-3'-enyl)malonate 1b



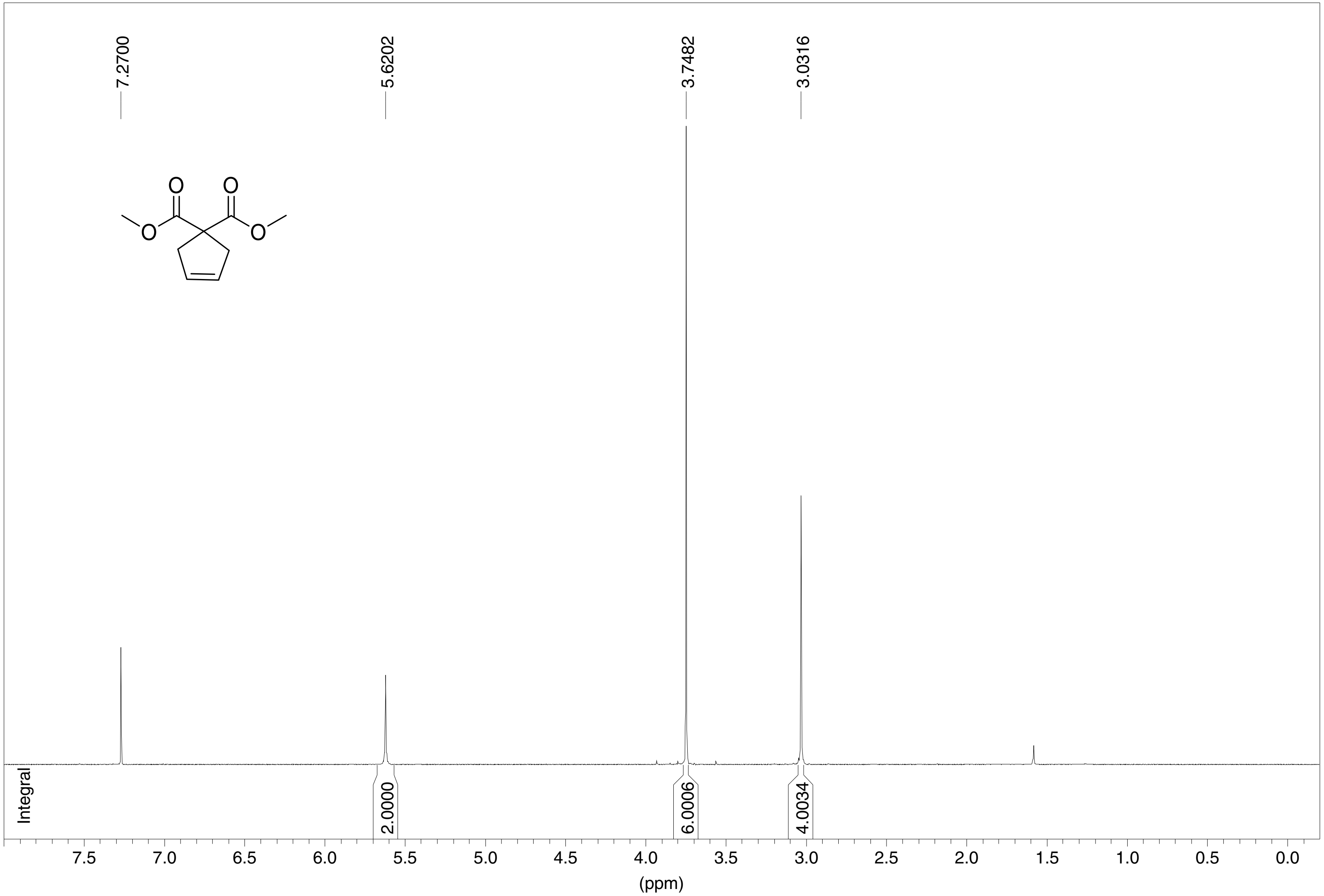
Dimethyl 2-(pent-4’-enyl)malonate 1c



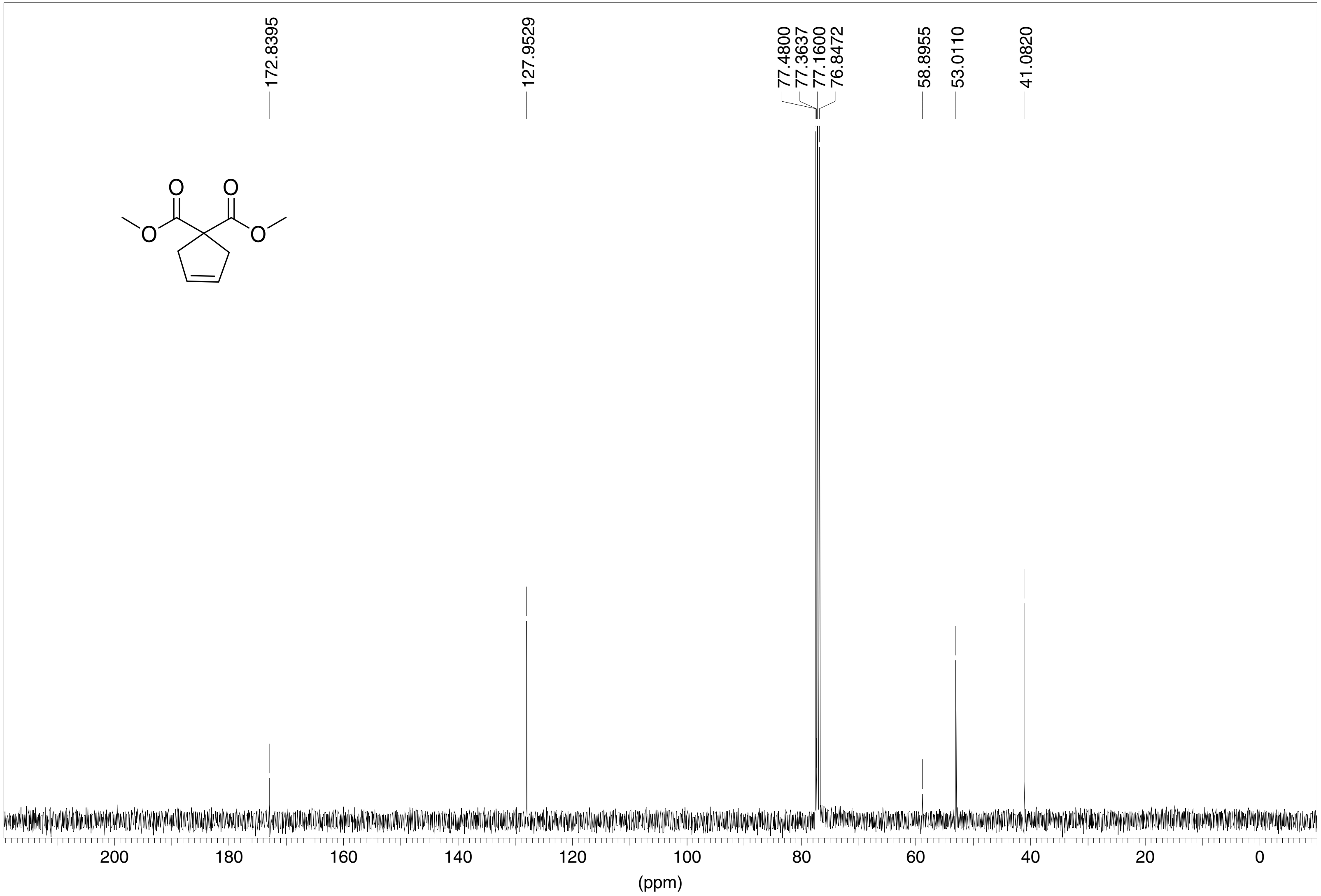
Dimethyl 2-(pent-4’-enyl)malonate 1c



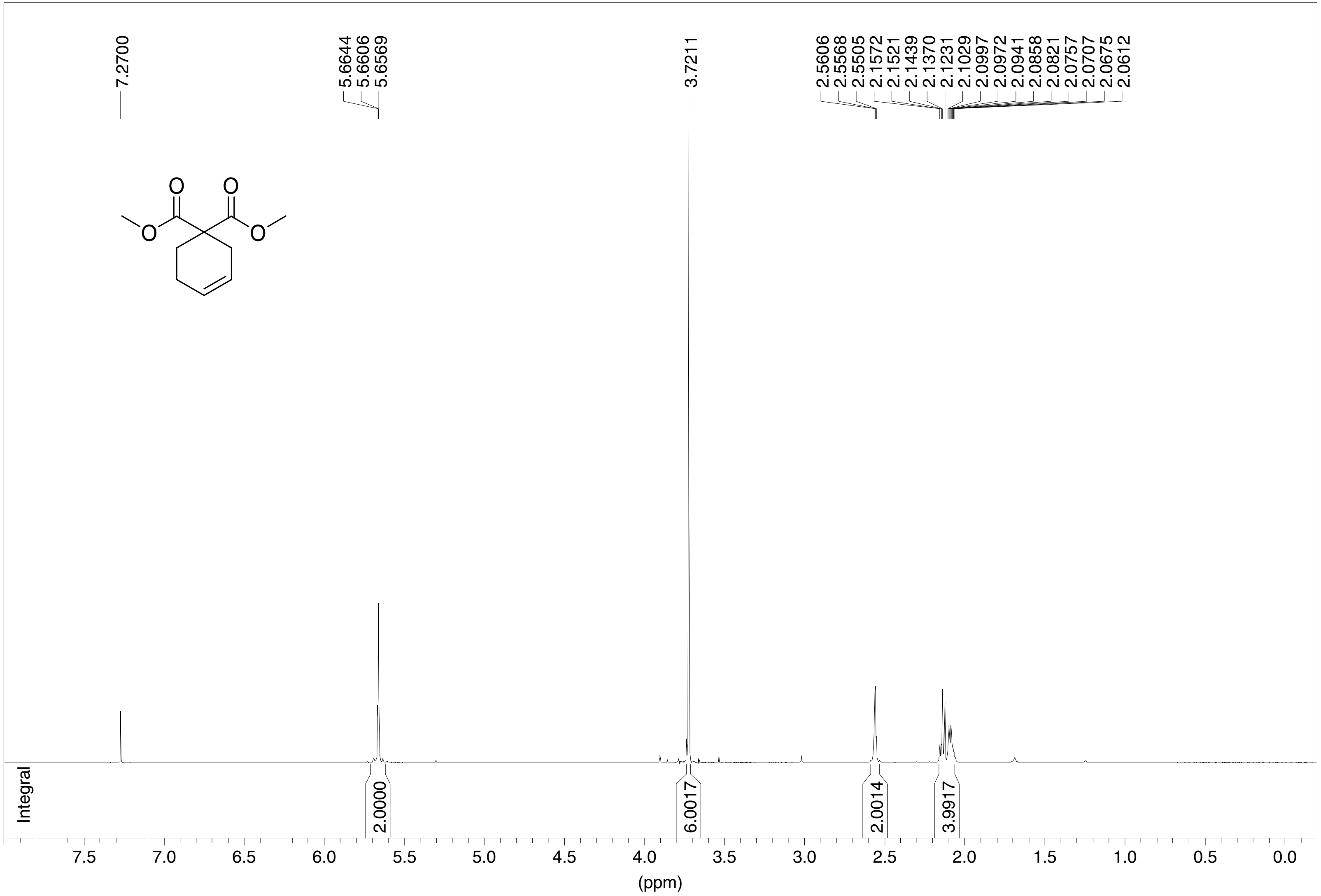
Dimethyl cyclopent-3-ene-1,1-dicarboxylate 2a



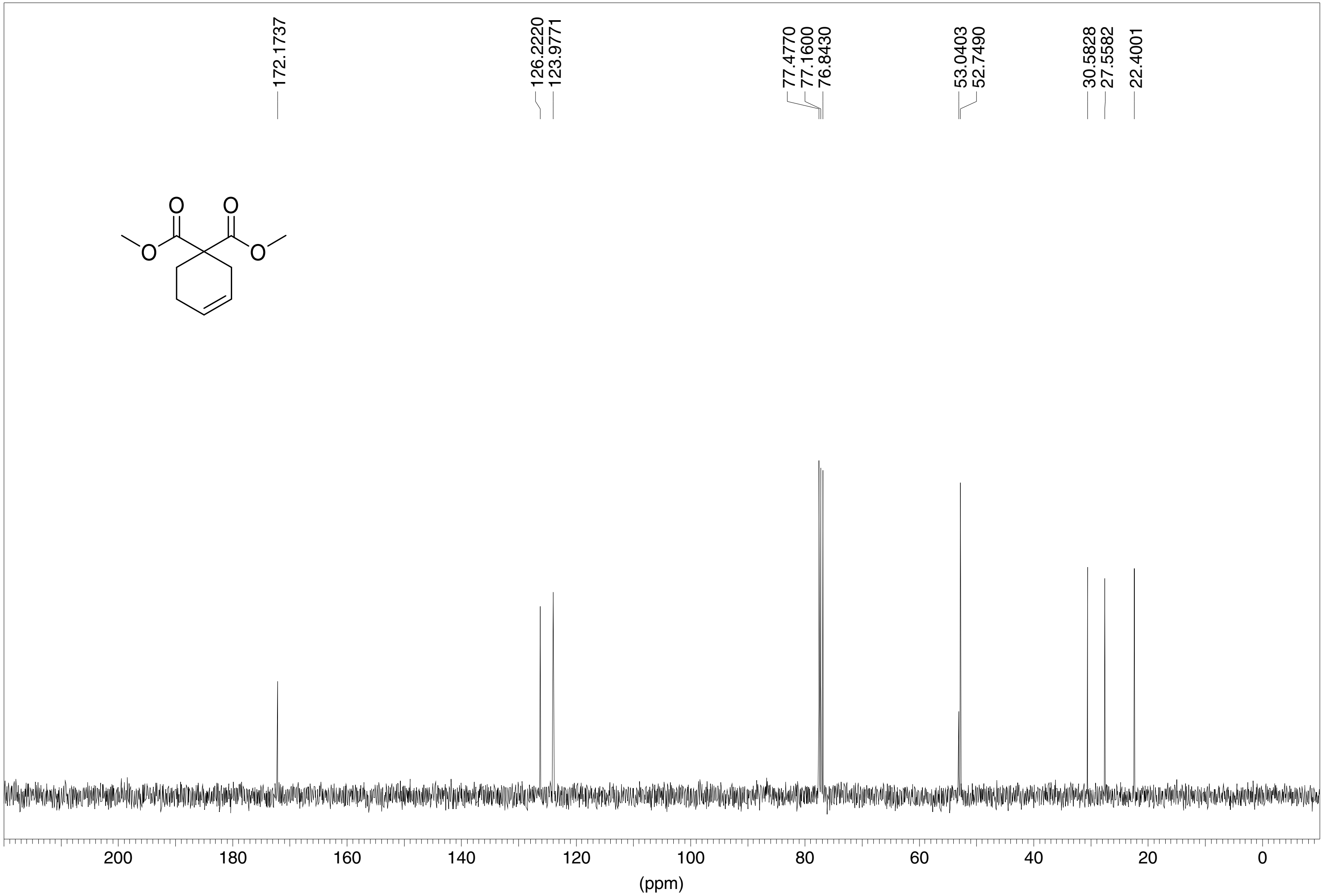
Dimethyl cyclopent-3-ene-1,1-dicarboxylate 2a



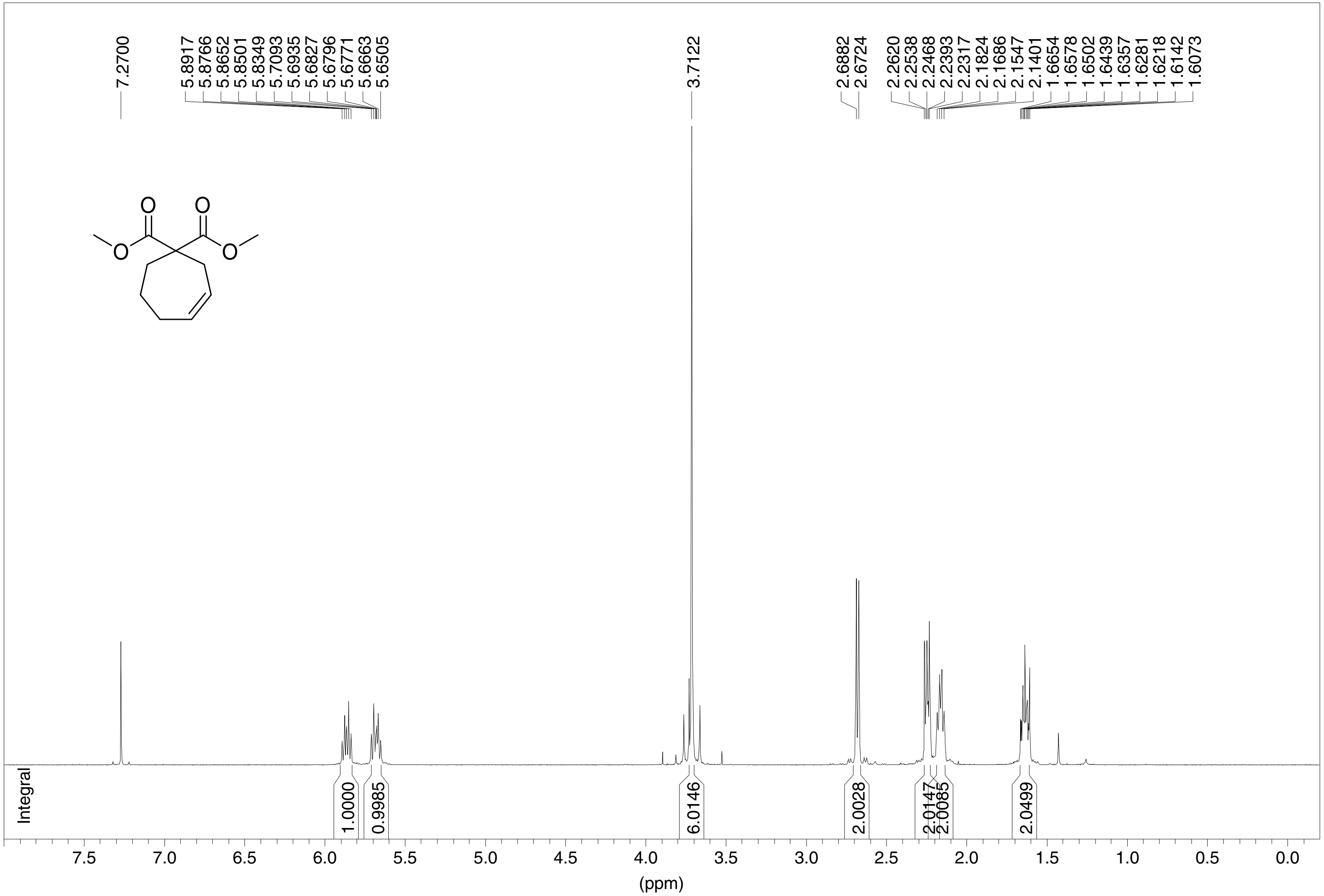
Dimethyl cyclohex-3-ene-1,1-dicarboxylate 2b



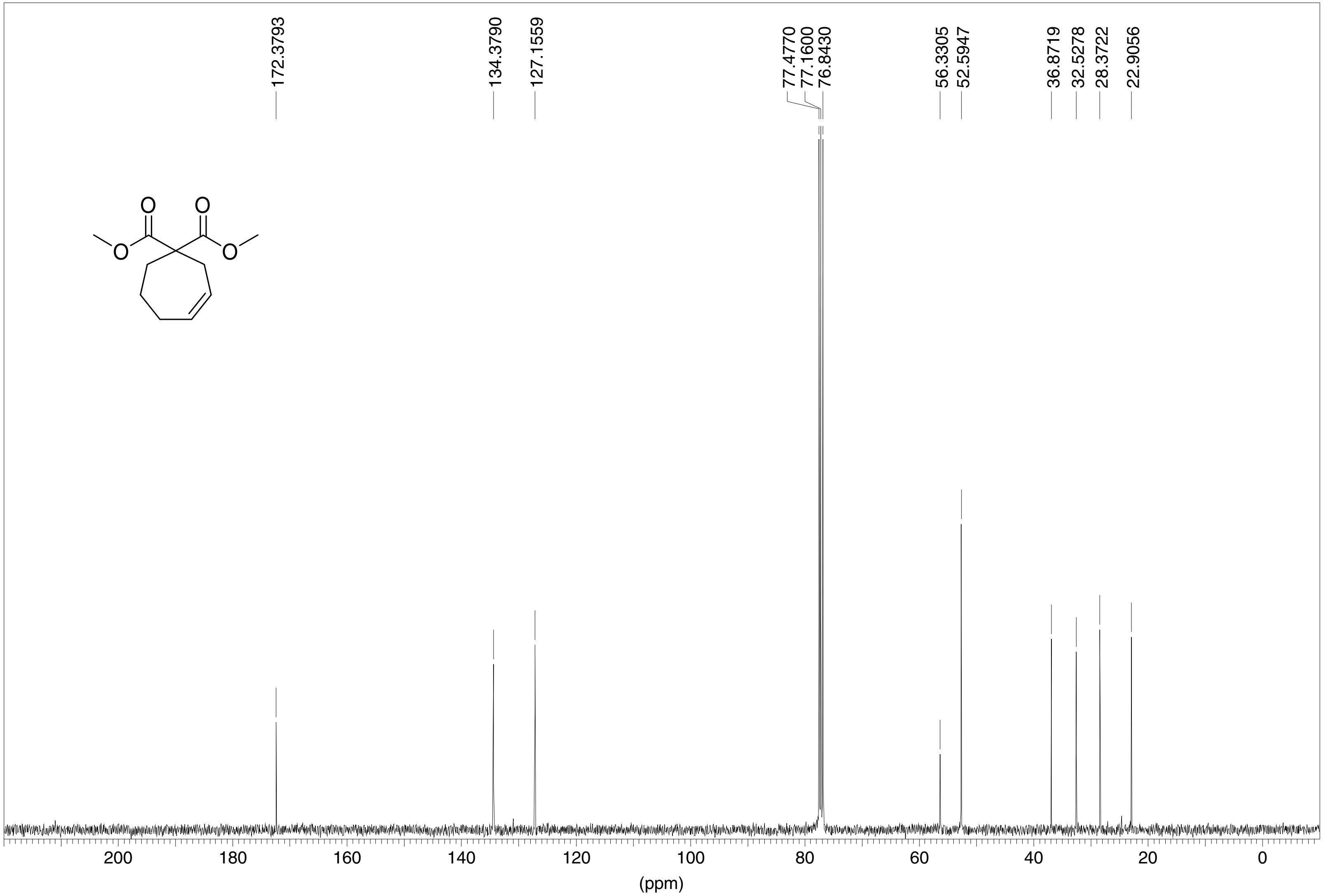
Dimethyl cyclohex-3-ene-1,1-dicarboxylate 2b



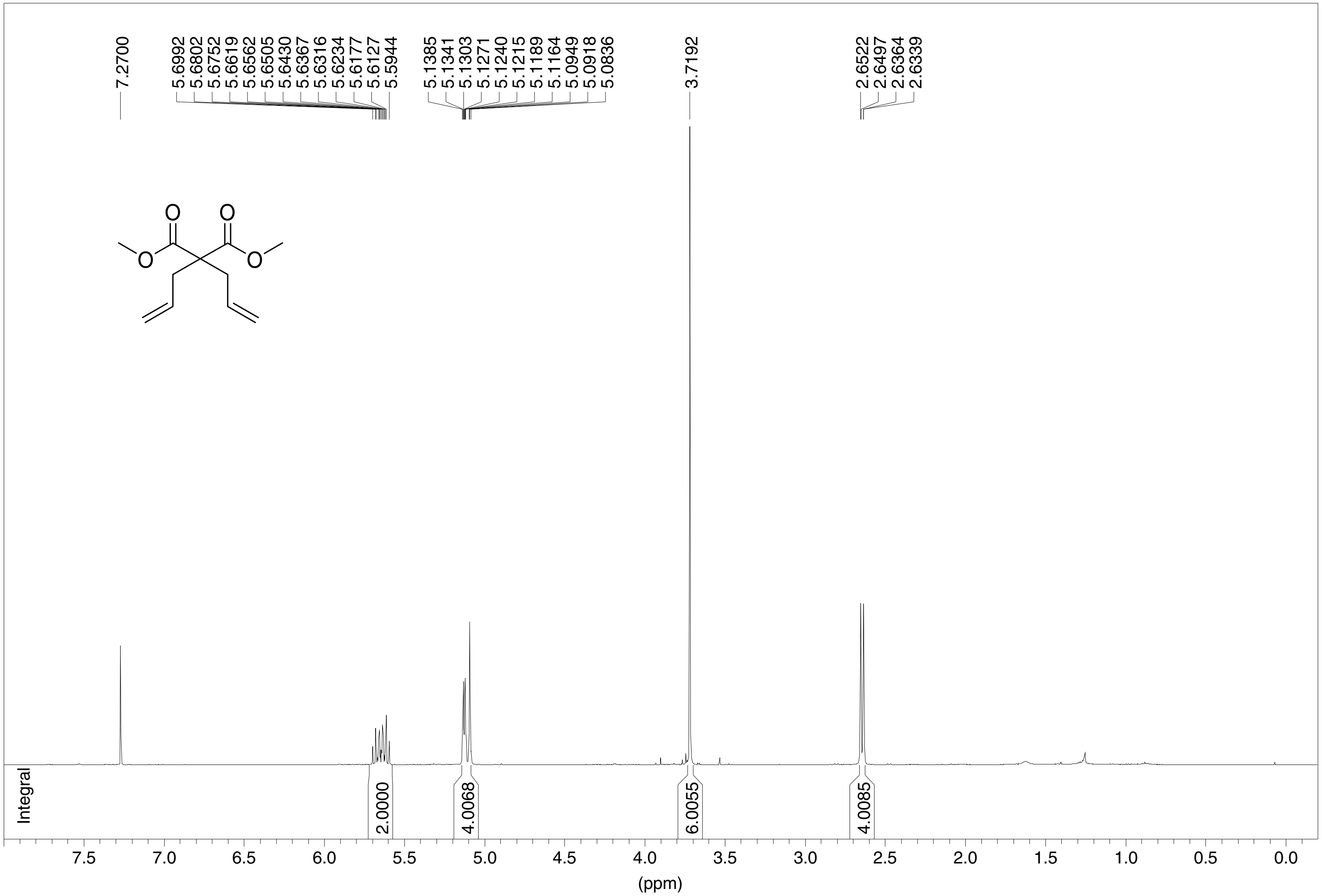
Dimethyl cyclohept-3-ene-1,1-dicarboxylate 2c



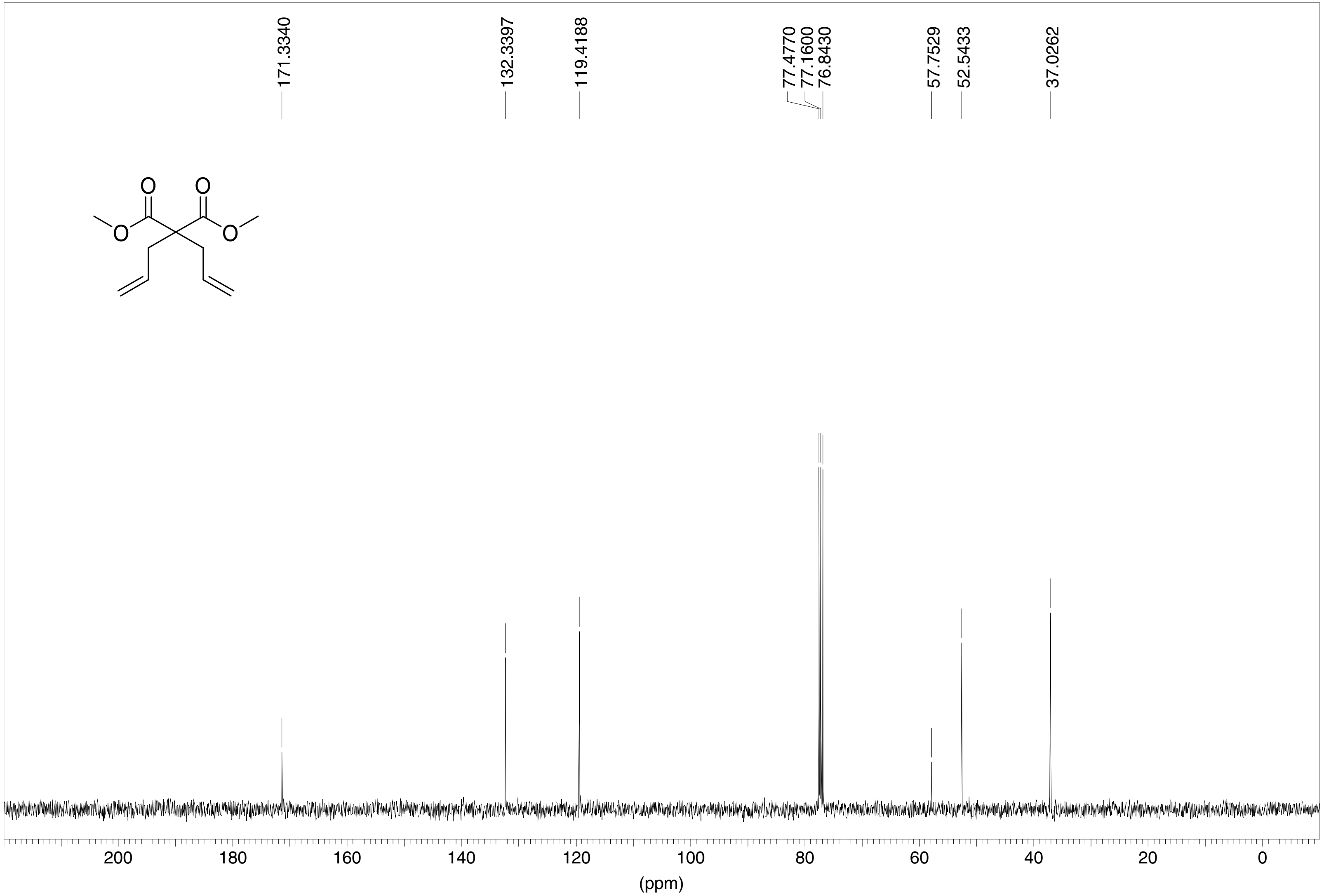
Dimethyl cyclohept-3-ene-1,1-dicarboxylate 2c



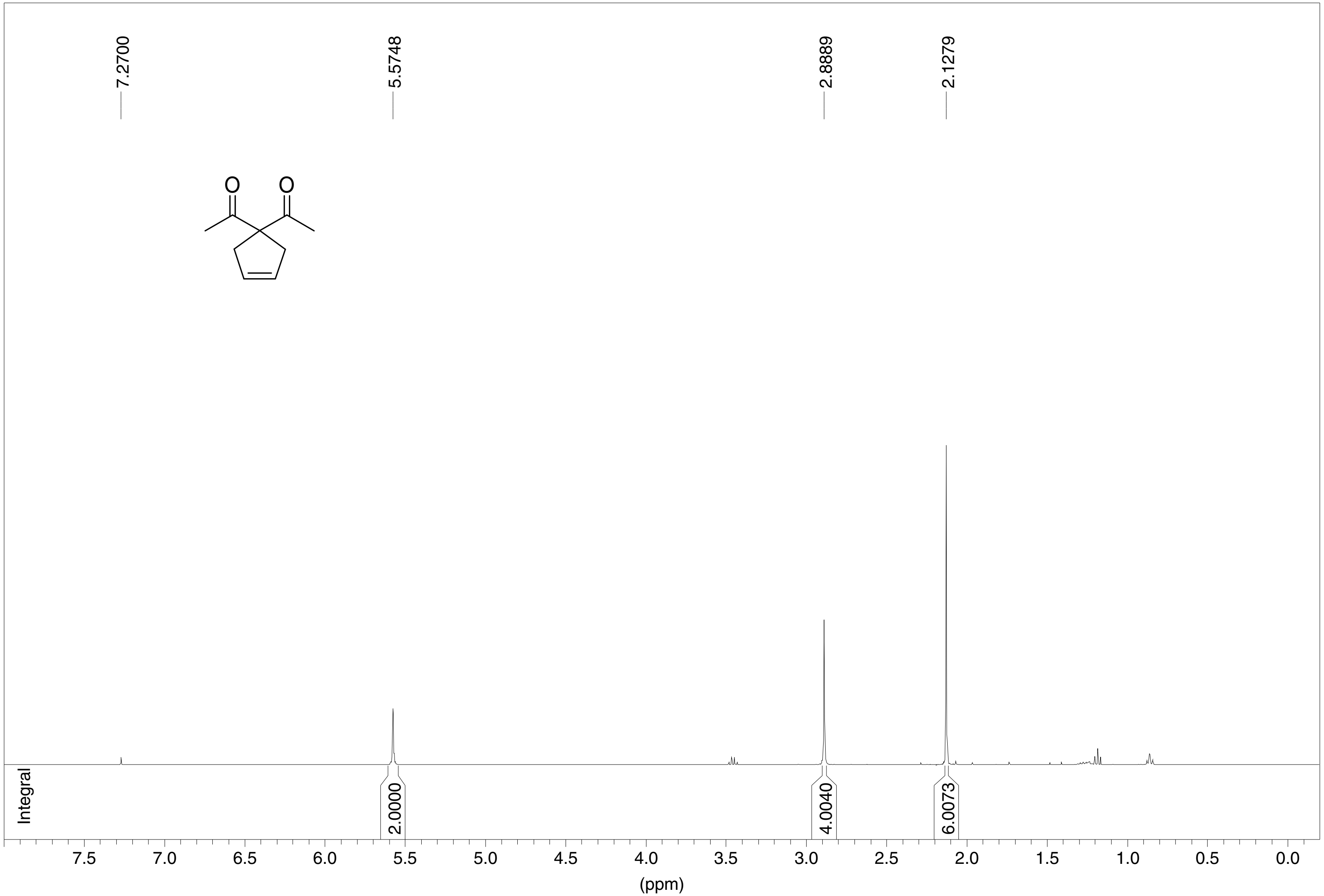
Dimethyl 2,2-diallylmalonate 3



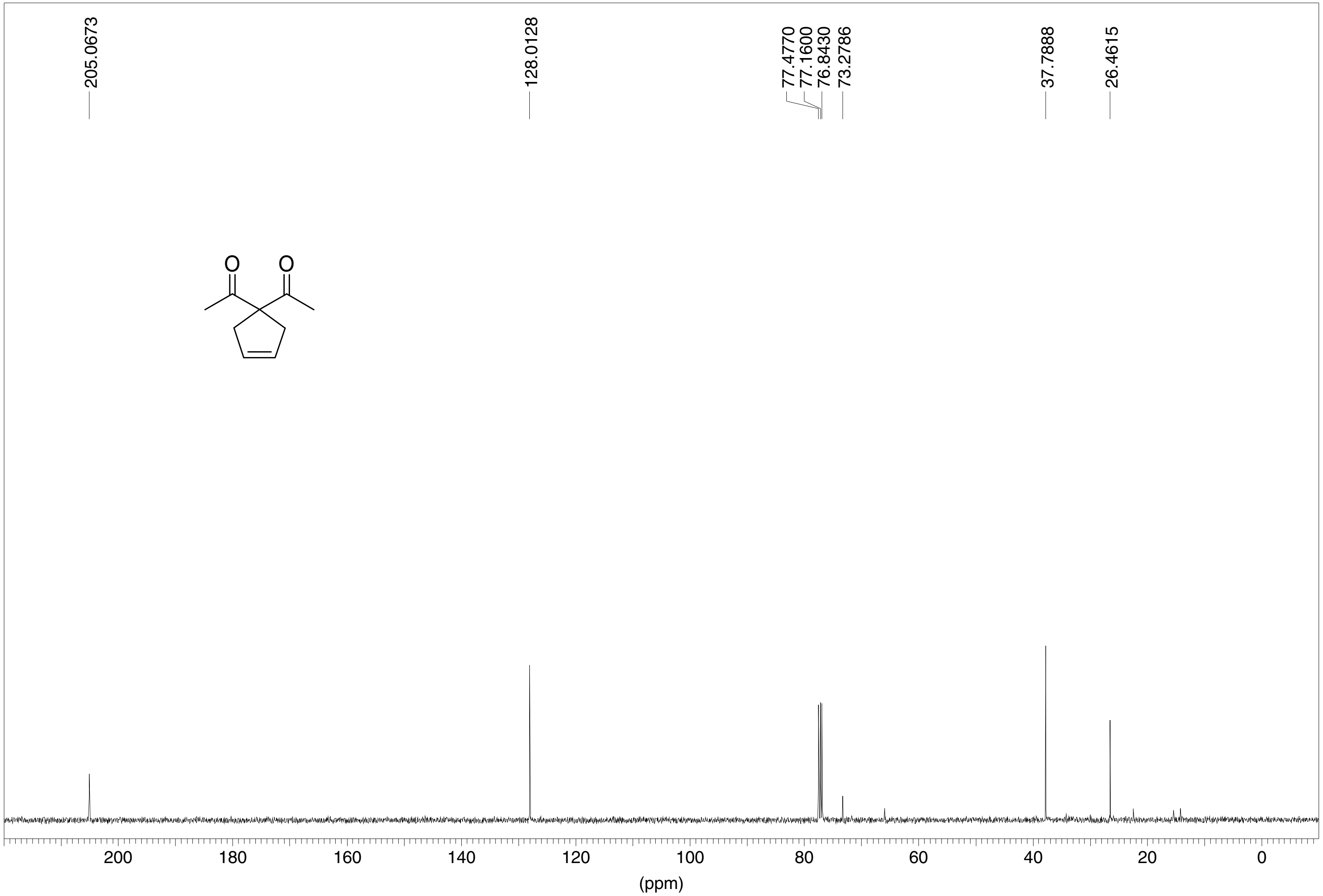
Dimethyl 2,2-diallylmalonate 3



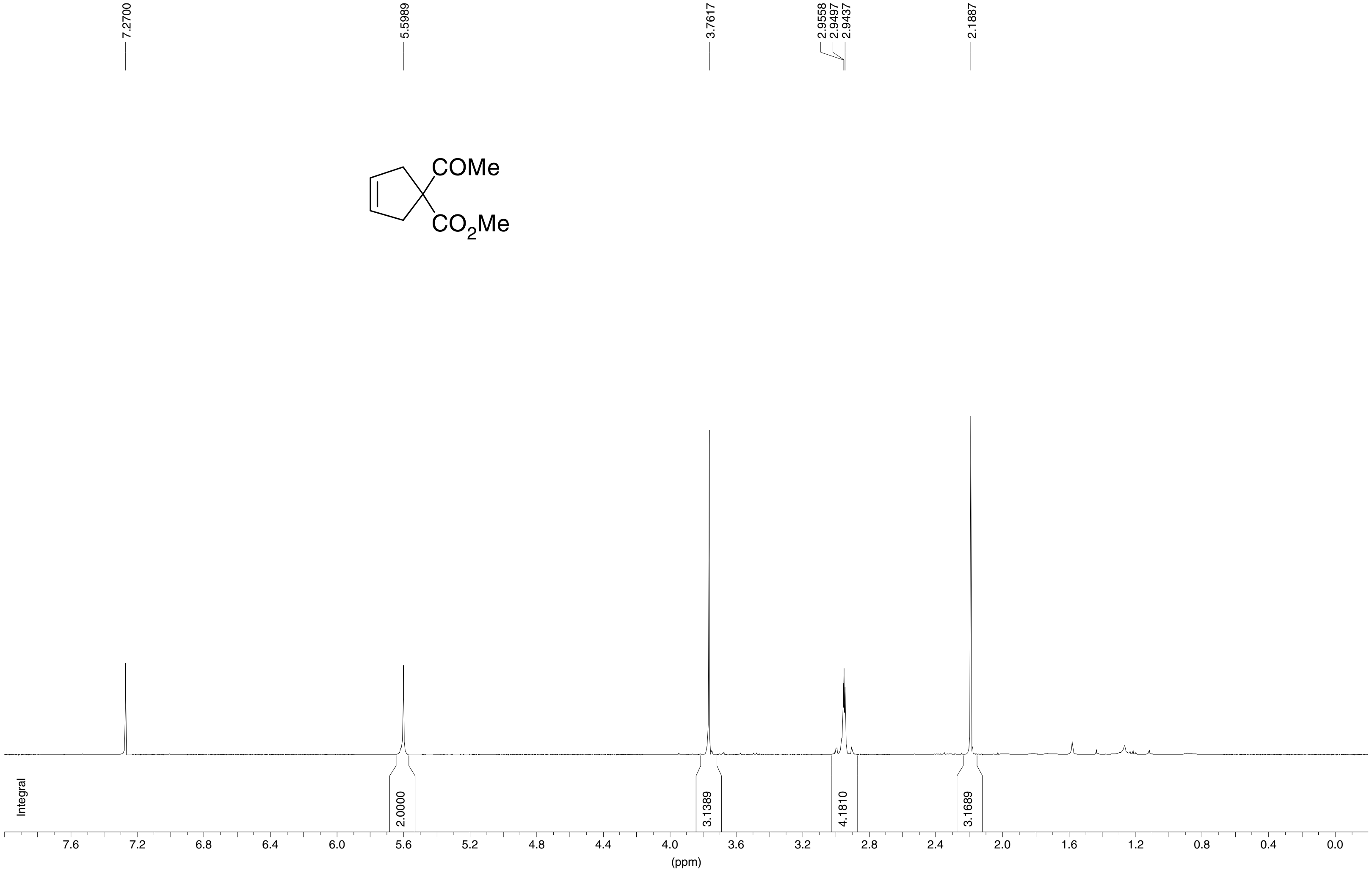
1,1-diacetylcyclopent-3-ene 13



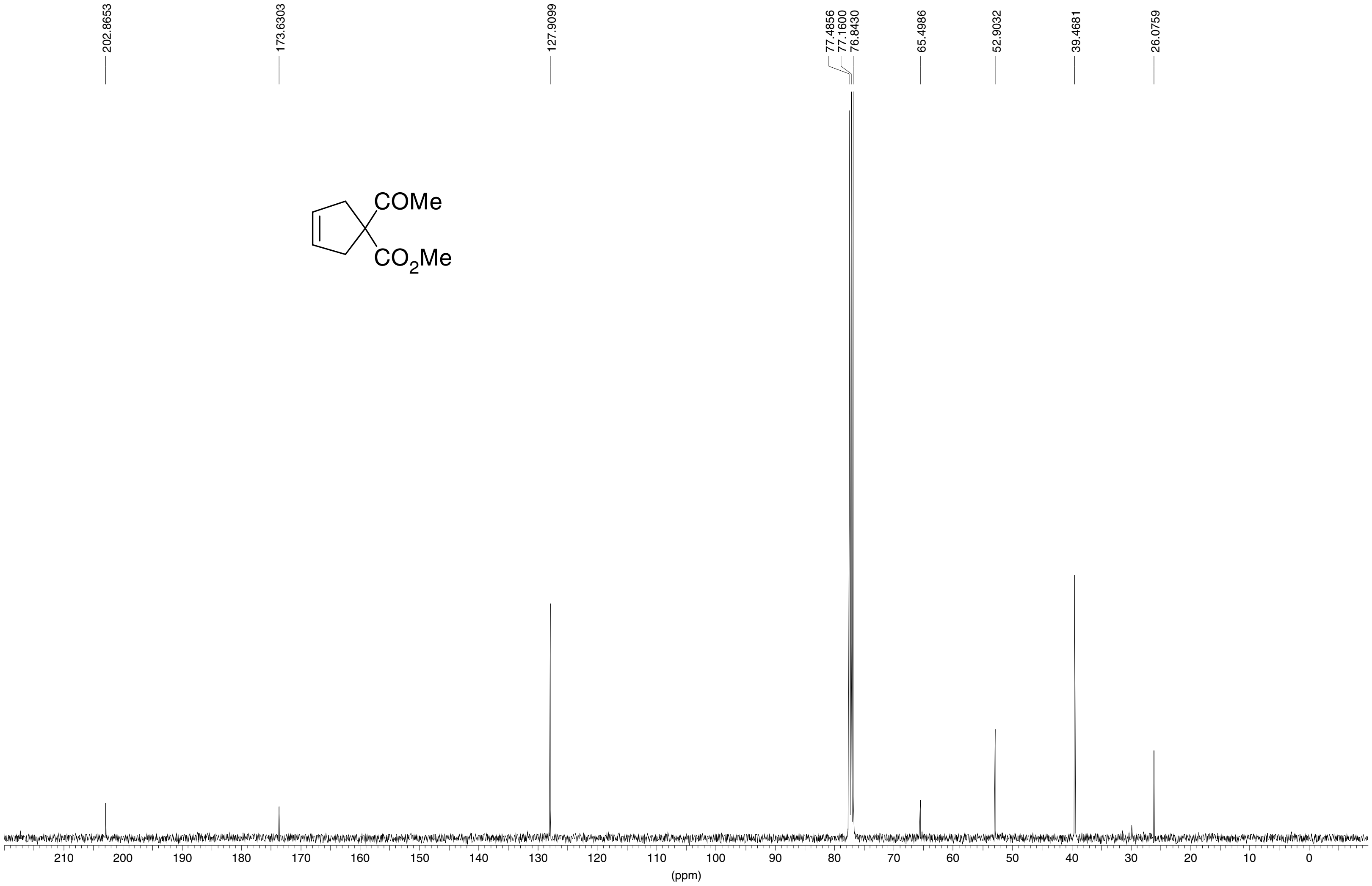
1,1-diacetylcyclopent-3-ene 13



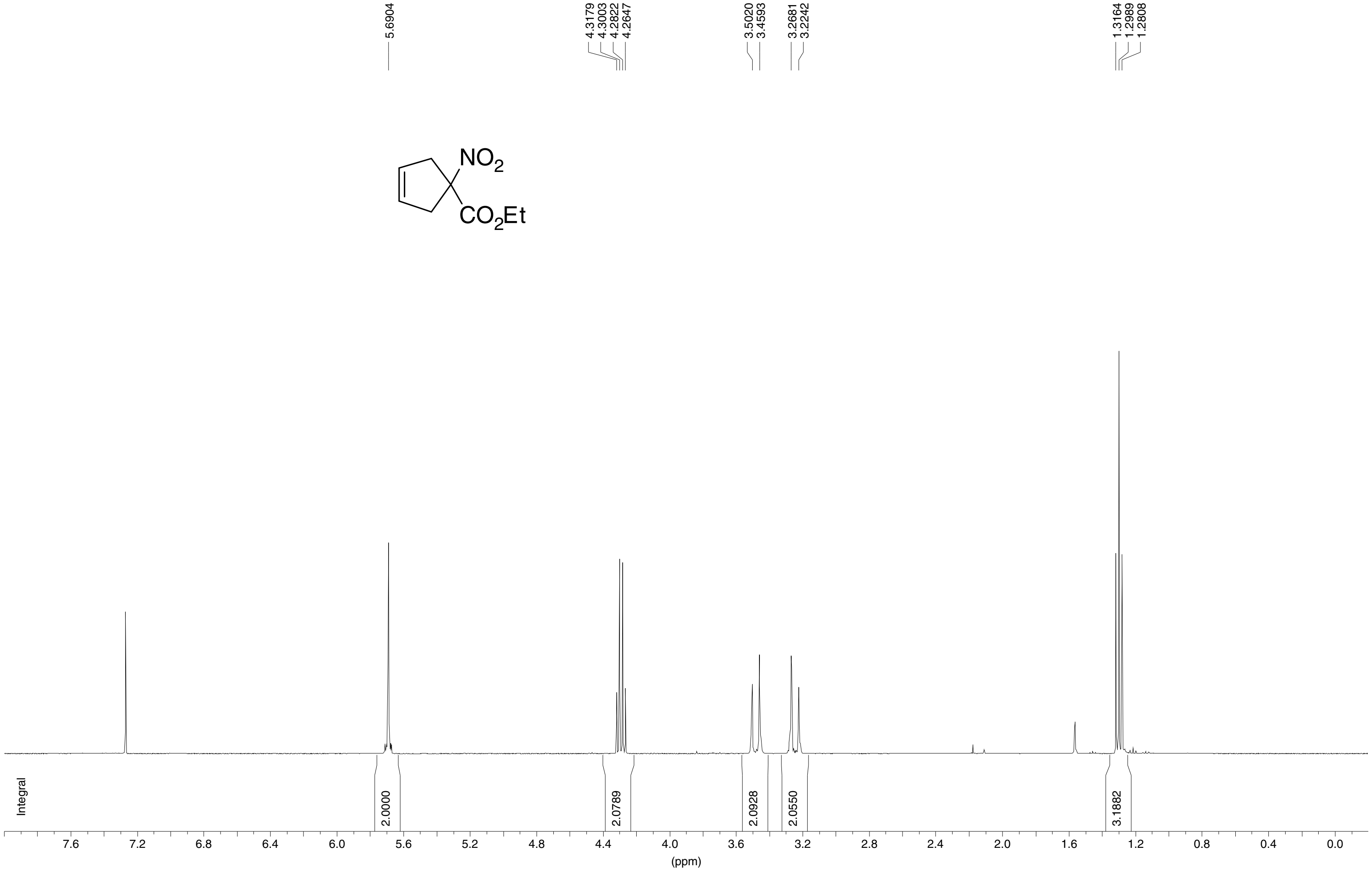
Methyl 1-acetyl-cyclopent-3-enecarboxylate 14



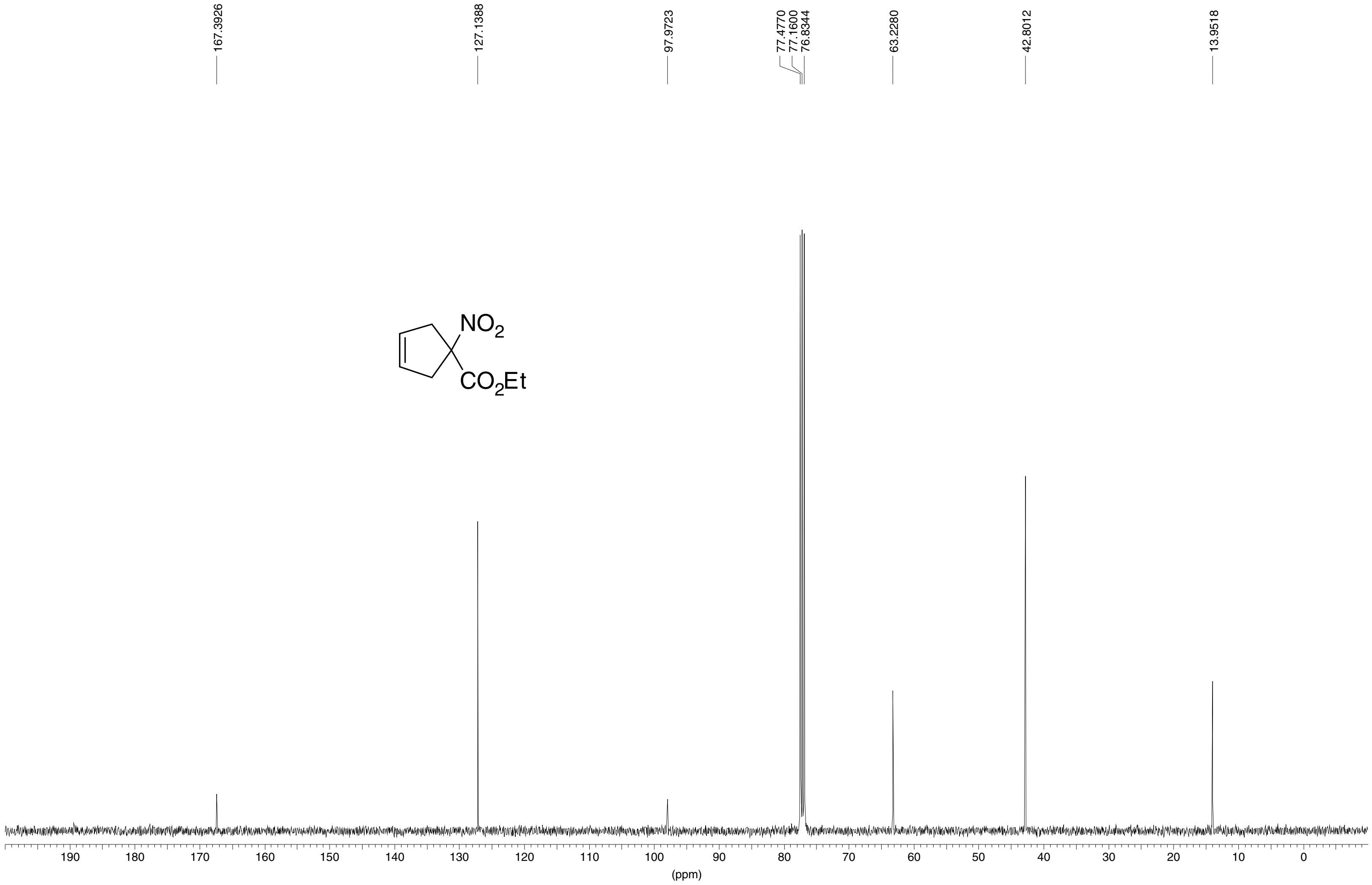
Methyl 1-acetyl-cyclopent-3-enecarboxylate 14



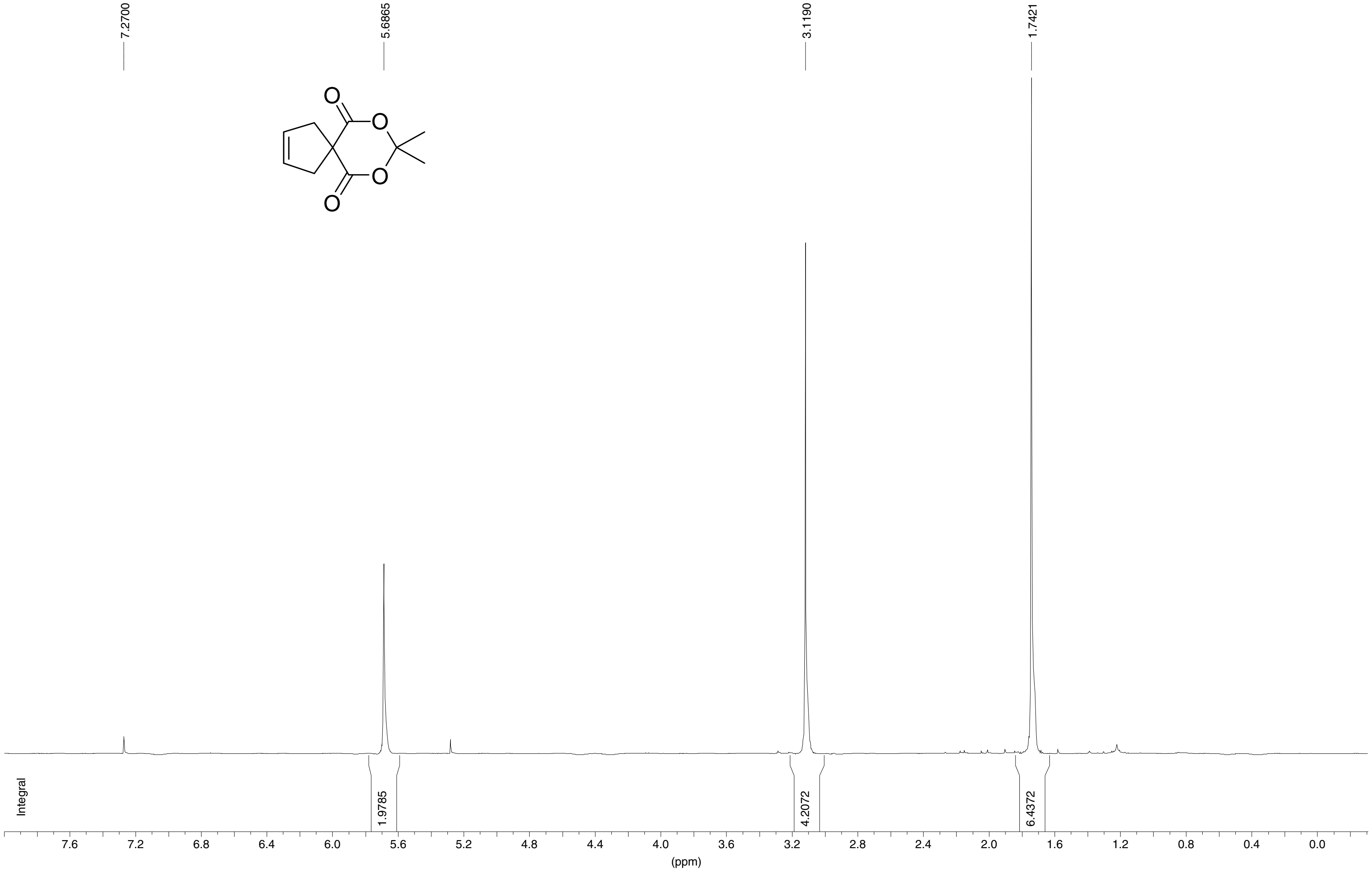
Ethyl-1-nitro-cyclopent-3-enecarboxylate 15



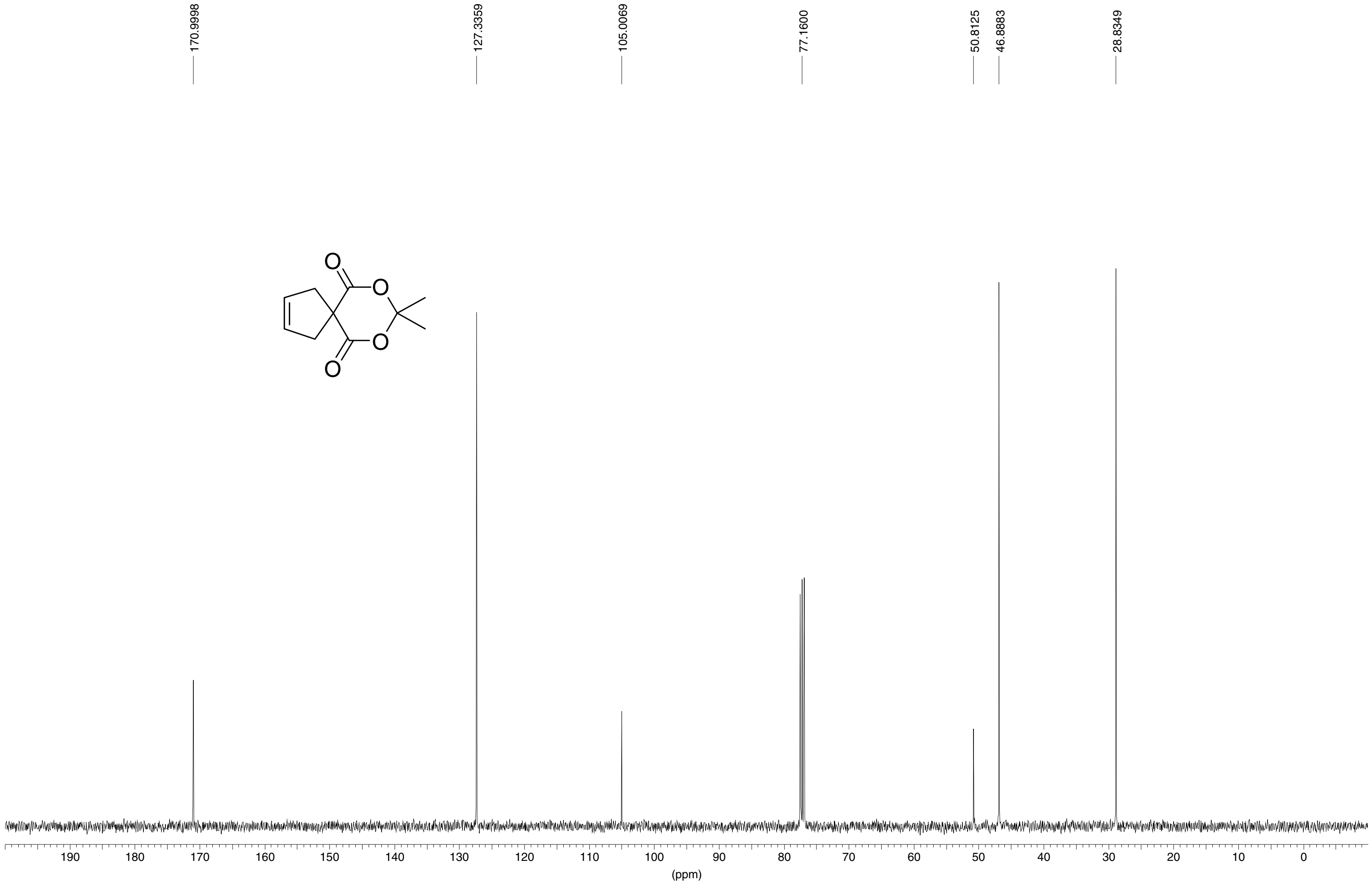
Ethyl-1-nitro-cyclopent-3-enecarboxylate 15



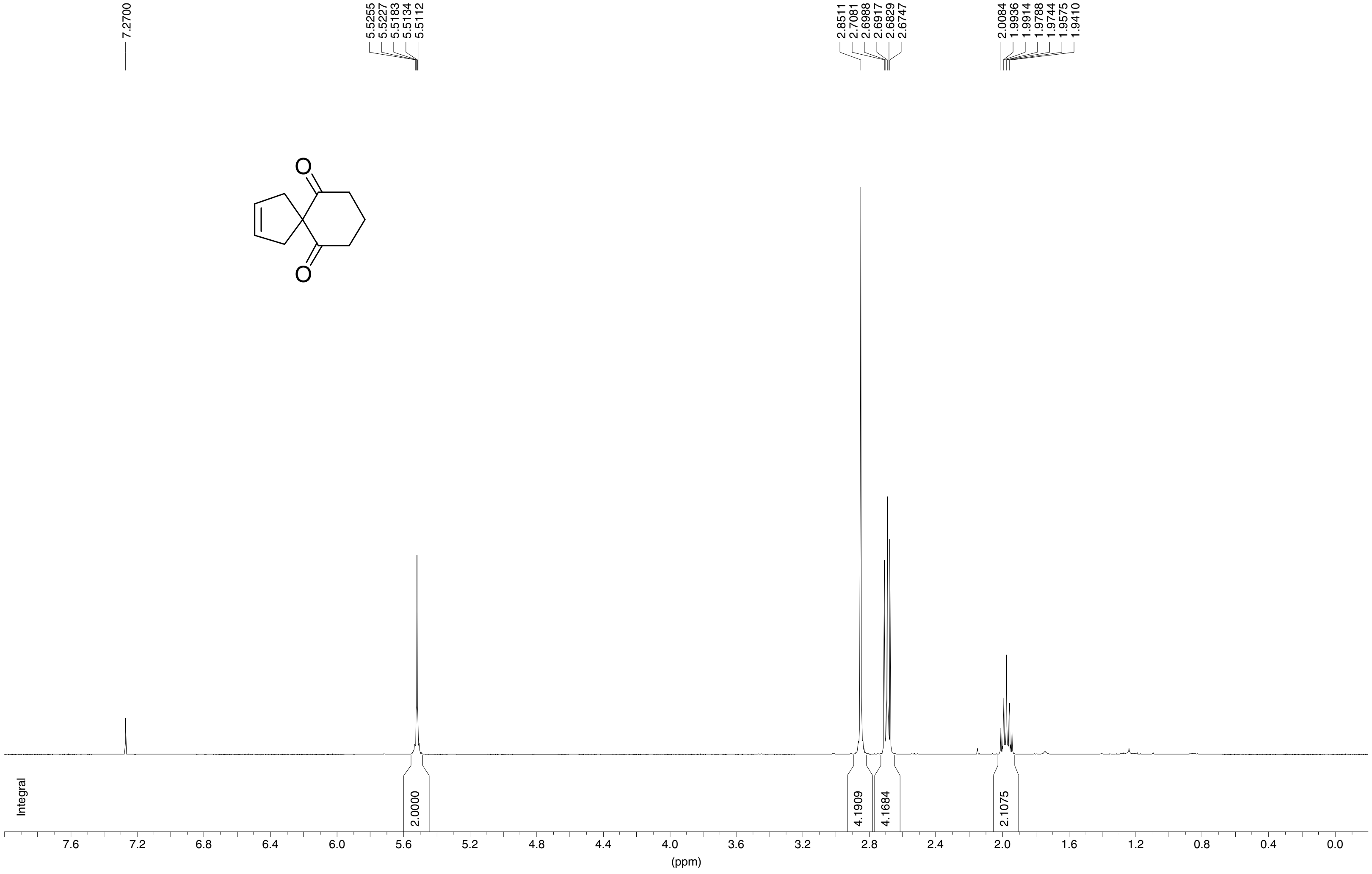
8,8-dimethyl-7,9-dioxaspiro[4.5]dec-2-ene-6,10-dione 16



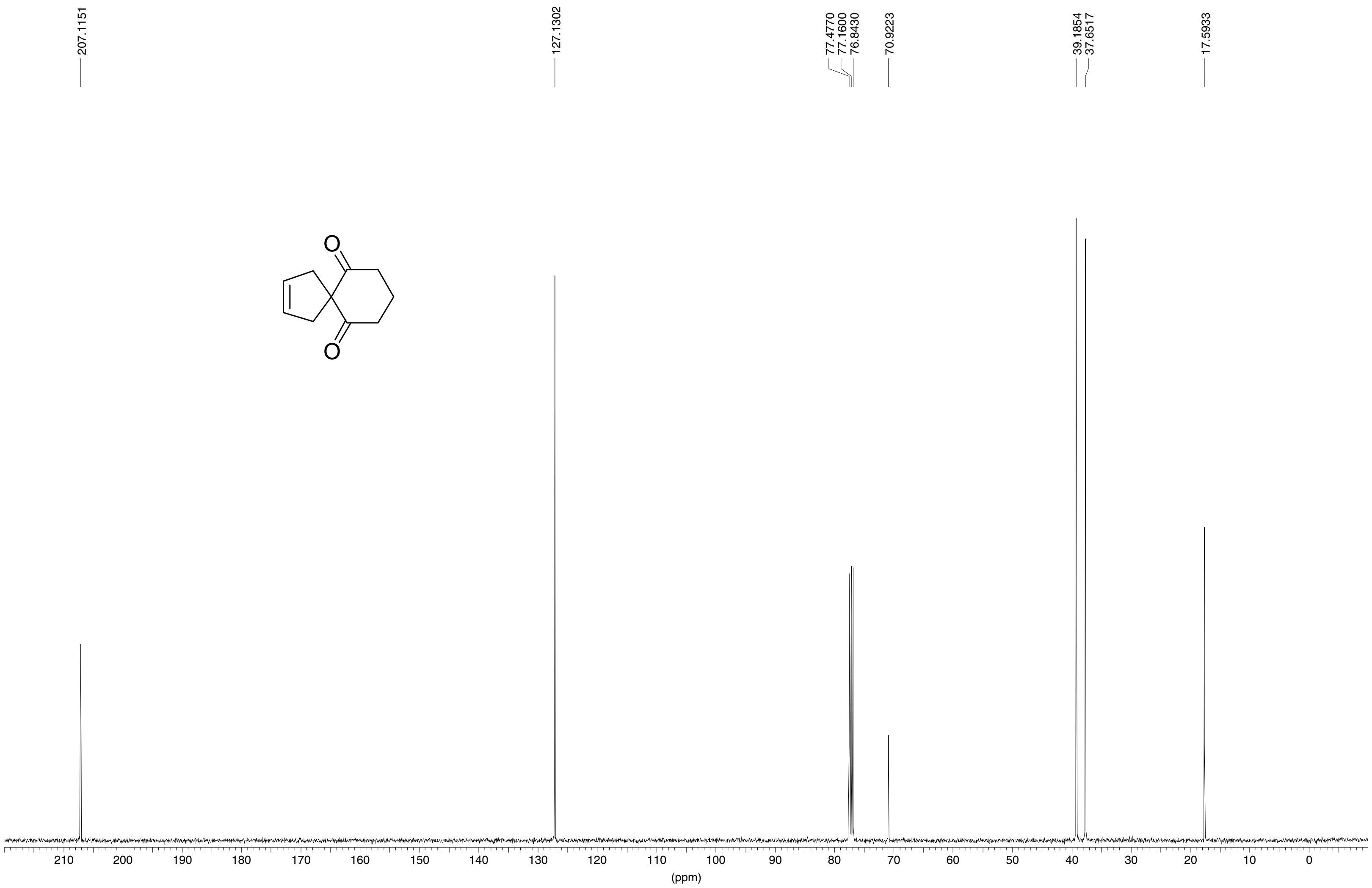
8,8-dimethyl-7,9-dioxaspiro[4.5]dec-2-ene-6,10-dione 16



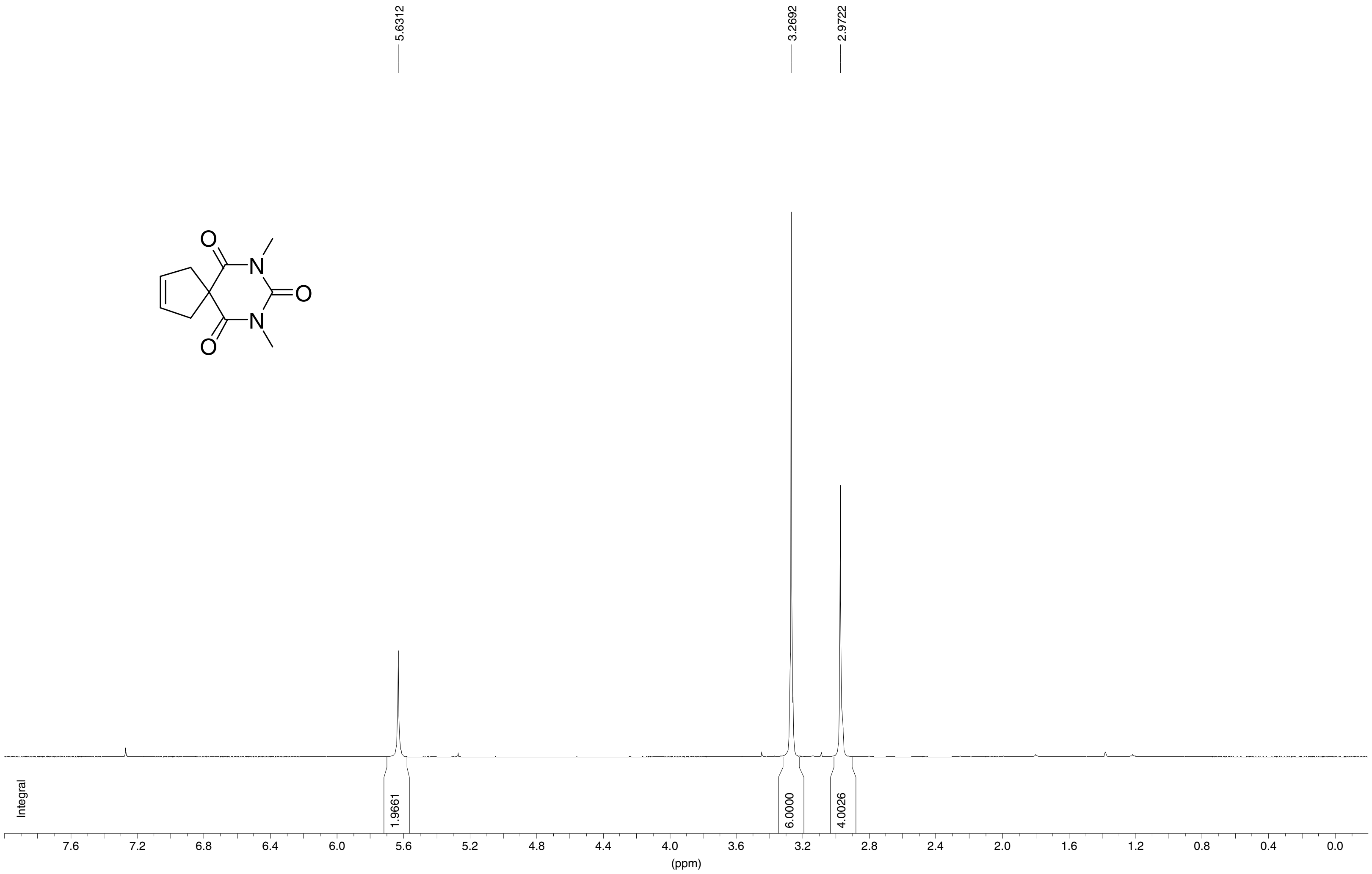
Spiro[4.5]dec-2-ene-6,10-dione 17



Spiro[4.5]dec-2-ene-6,10-dione 17



7,9-dimethyl-9-diazaspiro[4.5]dec-2-ene-6,8,10-trione 18



7,9-dimethyl-9-diazaspiro[4.5]dec-2-ene-6,8,10-trione 18