Catalytic Anti-Markovnikov Transformations of Hindered Terminal Alkenes Enabled by Aldehyde-Selective Wacker-Type Oxidation

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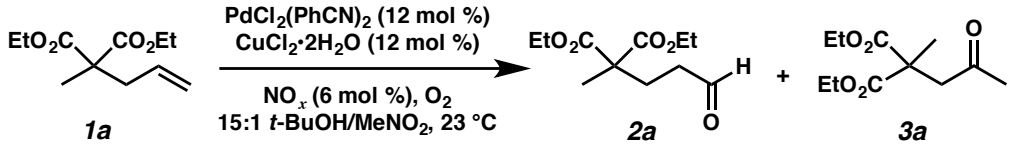
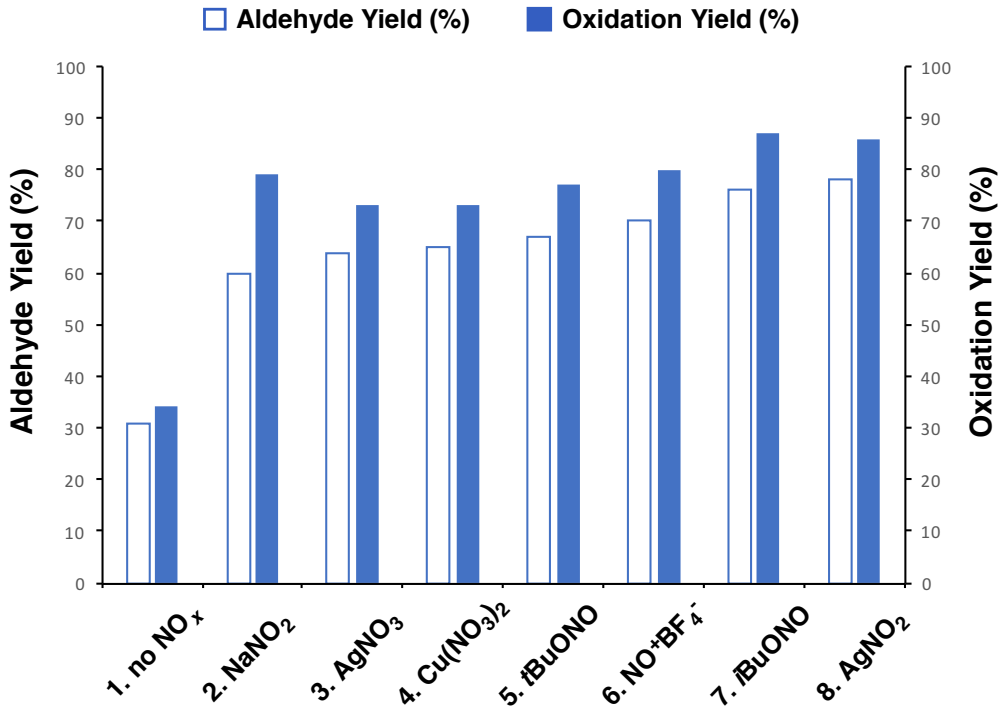
Materials and Methods

Unless noted in the specific procedure, reactions were performed in flame-dried glassware under argon atmosphere. Dried and deoxygenated solvents (Fisher Scientific) were prepared by passage through columns of activated aluminum before use.[1] Methanol (Fisher Scientific) was distilled from magnesium methoxide immediately prior to use. 1,2-dichloroethane (Fisher Scientific) was distilled from calcium hydride immediately prior to use. Anhydrous ethanol, *tert*-butanol, and *N,N*-dimethylformamide were purchased from Sigma Aldrich in sure-sealed bottles and used as received unless otherwise noted. Commercial reagents (Sigma Aldrich or Alfa Aesar) were used as received with the exception of palladium(II) acetate (Sigma Aldrich) and XPhos (Sigma Aldrich), which were stored in a nitrogen-filled govebox. The Ohira–Bestmann reagent[2] and carbomethoxy methylene triphenyl phosphorane ($Ph_3P{=}CHCO_2Me$)[3] were prepared according to known procedures. Triethylamine (Oakwood Chemical) and diisopropylethylamine (Oakwood Chemical) were distilled from calcium hydride immediately prior to use. Brine is defined as a saturated aqueous solution of sodium chloride. Reactions requiring external heat were modulated to the specified temperatures using an IKAmag temperature controller. Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-LCMS. TLC was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, potassium permanganate, or *p*-anisaldehyde staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040-0.063 mm) was used for flash chromatography. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 spectrometer (500 MHz and 126 MHz, respectively), a Bruker AV III HD spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe (400 MHz and 101 MHz, respectively), or a Varian Mercury 300 spectrometer (300 MHz and 75 MHz, respectively) and are reported in terms of chemical shift relative to residual $CHCl_3$ (δ 7.26 and δ 77.16 ppm, respectively). Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Abbreviations are used as follows: s = singlet, bs = broad singlet, d = doublet, t = triplet, q = quartet, m = complex multiplet. Infrared (IR) spectra were recorded on a Perkin Elmer Paragon 1000 spectrometer using thin film samples on KBr plates, and are reported in frequency of absorption (cm^{-1}). High-resolution mass spectra (HRMS) were obtained from the Caltech Mass Spectral Facility using a JEOL JMS-600H High Resolution Mass Spectrometer with fast atom bombardment (FAB+) ionization mode or were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+) mode.

Catalyst Optimization





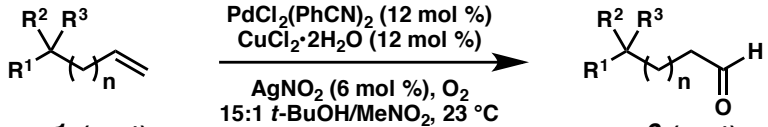
NO_x species	Aldehyde yield (%)[a]	Ketone yield (%)	Oxidation yield (%)[b]	Selectivity (aldehyde:ketone)
$AgNO_2$	78	8	86	10:1
$AgNO_3$	64	9	73	7:1
$NaNO_2$	60	19	79	3:1
$NO^+BF_4^-$	70	10	80	7:1
$Cu(NO_3)_2$	65	8	73	8:1
*t*BuONO	67	10	77	7:1
*i*BuONO	76	11	87	7:1
no NO_x	31	3	34	10:1

[a] Yields were calculated from the crude ^{1}H NMR spectrum.
[b] Oxidation yield is the sum of the yields of aldehyde **2a** and methyl ketone **3a**.

Procedure for Catalyst Optimization:
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012

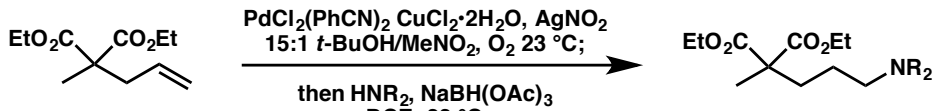
mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 14 hours, after which the reaction mixture was diluted with water (4 mL) and extracted with dichloromethane (3 x 5 mL). The organic extracts were dried over sodium sulfate, then filtered and concentrated in vacuo. Nitrobenzene (24.6 mg, 0.20 mmol, 1.00 equiv) was added as an internal standard immediately prior to NMR analysis, and the yield and selectivity of the formation of aldehyde **2a** was calculated from the ^{1}H NMR spectrum (d1 = 15s).[4,5]

General Experimental Procedures



1 **(n = 1)** ***2*** **(n = 1)**
4 **(n = 0)** ***5*** **(n = 0)**

General Procedure A. *Aldehyde-selective Wacker-type oxidation of alkenes.*
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1** or **4** (0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C until TLC analysis indicated consumption of starting material. The reaction mixture was diluted with water (4 mL) and extracted with dichloromethane (3 x 5 mL). The organic extracts were dried over sodium sulfate, then filtered and concentrated in vacuo. The crude residue was purified by silica gel column chromatography, using mixture of hexanes and ethyl acetate as eluent to afford aldehyde **2** or **5**.[6]



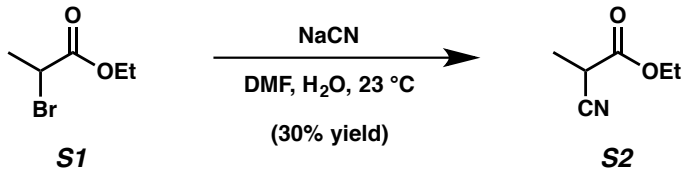
1a ***6a***

General Procedure B. *Hydroamination of diethyl 2-allyl-2-methylmalonate* ***(1a)****.*
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a**

(42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in 1,2-dichloroethane (4 mL) and treated with amine (0.22 mmol, 1.1 equiv) at 23 °C. After one hour, sodium triacetoxyborohydride (63.6 mg, 0.30 mmol, 1.50 equiv) was added in one portion. Stirring was continued at 23 °C for 5 hours, at which time the reaction was diluted with diethyl ether (3 mL), washed with saturated aqueous sodium bicarbonate (5 mL), and extracted with diethyl ether (3 x 5 mL). The organic extracts were dried over sodium sulfate, then filtered and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography, using mixture of hexanes and ethyl acetate with 0.5% triethylamine as eluent to afford amine **6a**.

Substrate Synthesis and Characterization Data

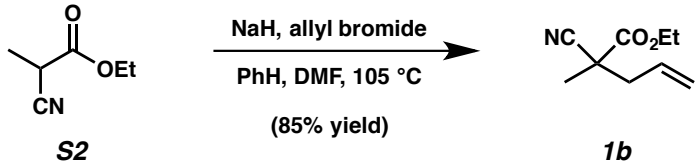
Compounds **1a** and **S5,**[7] **1e,**[8] **1g,**[9] **1h,**[10] **1i,**[6] **1f,**[9] and **4a–c,**[11] **S6**[9] may be prepared as previously reported by our research group.



S1 *S2*

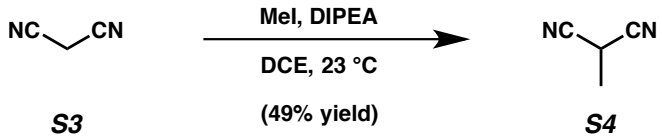
Ethyl-2-cyanopropanoate (S2):

A round-bottom flask equipped with a magnetic stir bar and thermometer was charged with sodium cyanide (2.44 g, 49.7 mmol, 1.50 equiv), *N,N*-dimethylformamide (22 mL), and water (2.2 mL). Alkyl bromide **S1** (4.30 mL, 33.1 mmol, 1.00 equiv) was added dropwise over 15 minutes, making sure the internal temperature did not exceed 35 °C throughout addition. After complete addition, the internal thermometer was removed, and the mixture was stirred at 23 °C for 12 hours, at which time the reaction mixture was diluted with diethyl ether and washed sequentially with cold 5% aqueous hydrochloric acid (15 mL) and saturated aqueous sodium bicarbonate (15 mL). The organic layer was dried over sodium sulfate, then filtered and concentrated under reduced pressure. The crude residue was purified by silica gel column chromatography (10% → 20% ethyl acetate in hexanes), furnishing cyanoester **S2** as a colorless oil (1.27 g, 30% yield). Characterization data match those reported in the literature.[12]



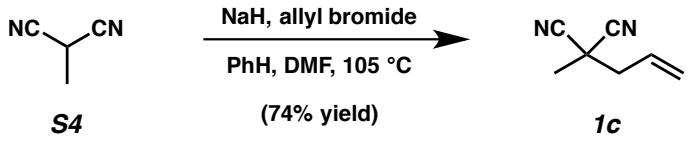
S2 *1b*

Ethyl 2-cyano-2-methylpent-4-enoate (1b):
To a suspension of sodium hydride (60% dispersion in mineral oil, 419 mg, 10.5 mmol, 1.05 equiv) in benzene (15 mL) was added a solution of cyanoester **S2** (1.27 g, 9.98 mmol, 1.00 equiv) in benzene (12 mL). *N*,*N*-dimethylformamide (8 mL) was added to stabilize the sodium enolate, and the mixture was stirred at 23 °C for 20 minutes before allyl bromide (910 μL mL, 10.5 mmol, 1.05 equiv) was added dropwise. Upon complete addition, the reaction mixture was heated to reflux (105 °C). After 12 hours, the reaction was allowed to cool to room temperature before quenching with water (15 mL) and extracting with diethyl ether (3 x 20 mL). The organic extracts were washed with brine (20 mL) and dried over magnesium sulfate before filtration and concentration under reduced pressure. The crude residue was purified by silica gel column chromatography (11% ethyl acetate in hexanes) to afford alkene **1b** as a colorless oil (1.43 g, 85% yield). R*f* = 0.68 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.81 (ddt, *J* = 16.1, 11.0, 7.3 Hz, 1H), 5.33–5.18 (m, 2H), 4.26 (qd, *J* = 7.1, 1.0 Hz, 2H), 2.67 (ddt, *J* = 13.8, 7.2, 1.2 Hz, 1H), 2.55–2.45 (m, 1H), 1.58 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 169.0, 130.7, 121.2, 119.8, 63.0, 43.8, 42.2, 22.8, 14.2; IR (Neat Film, KBr) 3083, 2985, 1744, 1455, 1233, 1174, 1017, 930; HRMS (FAB+) *m/z* calc'd for $C_9H_{14}NO_2$ $[M+H]^+$: 168.1024, found 168.1012.

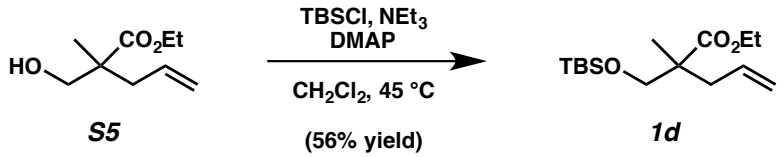


S3 *S4*

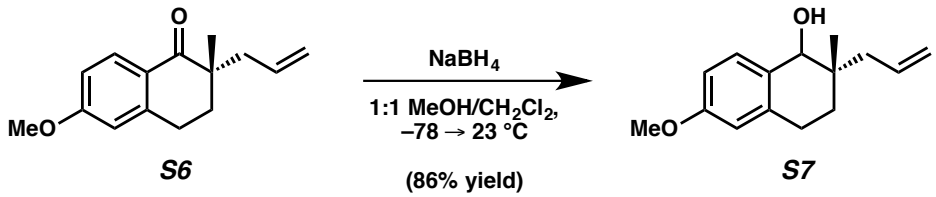
2-Methylmalononitrile (S4):
To a flame-dried round-bottom flask were added malononitrile **S3** (3.00 g, 45.4 mmol, 1.00 equiv) and 1,2-dichloroethane (90 mL). The suspension was cooled to 0 °C using an ice water bath, and diisopropylethylamine (7.91 mL, 45.4 mmol, 1.00 equiv) and methyl iodide (2.83 mL, 45.4 mmol, 1.00 equiv) were added dropwise sequentially. The resulting mixture was stirred at 23 °C for 24 hours, at which time the reaction was quenched with water and transferred to a separatory funnel. The aqueous layer was extracted with ethyl acetate (5 x 50 mL), and the combined organic extracts were washed with brine (50 mL) and dried over sodium sulfate. After filtration and concentration, the crude residue obtained was purified by silica gel column chromatography (5% → 10% → 15% ethyl acetate in hexanes) to furnish 2-methylmalononitrile (**S4**) as a white solid (1.77 g, 49% yield). Characterization data match those reported in the literature.[13]



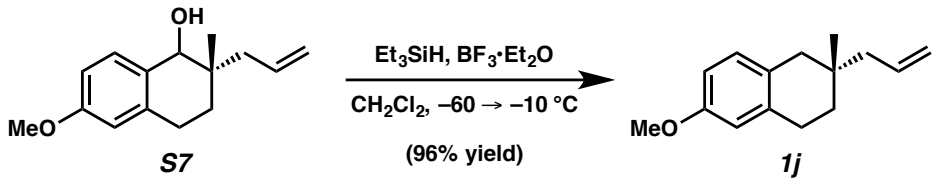
2-Allyl-2-methylmalononitrile (1c):
To a suspension of sodium hydride (60% dispersion in mineral oil, 309 mg, 7.72 mmol, 1.05 equiv) in benzene (7.1 mL) was added a solution of 2-methylmalononitrile **S4** (589 mg, 7.35 mmol, 1.00 equiv) in benzene (7.1 mL). *N*,*N*-dimethylformamide (3.5 mL) was added to stabilize the sodium enolate, and the mixture was stirred at 23 °C for 20 minutes before allyl bromide (670 μL mL, 7.72 mmol, 1.05 equiv) was added dropwise. Upon complete addition, the reaction mixture was heated to reflux (105 °C). After 12 hours, the reaction was allowed to cool to room temperature before quenching with water (8 mL) and extracting with diethyl ether (3 x 10 mL). The organic extracts were washed with brine (10 mL) and dried over magnesium sulfate before filtration and concentration under reduced pressure. The crude residue was purified by silica gel column chromatography (10% ethyl acetate in hexanes) to afford alkene **1c** as a colorless oil (653 mg, 74% yield). R*f* = 0.52 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 5.89 (ddt, *J* = 16.7, 10.1, 7.3 Hz, 1H), 5.55–5.31 (m, 2H), 2.68 (ddd, *J* = 7.3, 1.3, 0.8 Hz, 2H), 1.79 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 128.5, 123.6, 115.9, 43.0, 31.7, 24.2; IR (Neat Film, KBr) 3087, 2987, 2927, 1654, 1650, 1454, 1440, 1417, 1276, 1180, 994, 936, 729; HRMS (FAB+) *m/z* calc'd for $C_7H_9N_2$ $[M+H]^+$: 121.0760, found 121.0758.



Ethyl 2-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-methylpent-4-enoate (1d):[14]
To a flame-dried two-necked round-bottom flask equipped with a reflux condenser and magnetic stir bar were added alcohol **S5** (108.2 mg, 0.611 mmol, 1.00 equiv) and dichloromethane (12.2 mL). *tert*-Butyldimethylsilyl chloride (101.2 mg, 0.672 mmol, 1.10 equiv), triethylamine (0.17 mL, 1.22 mmol, 2.00 equiv), and 4-(dimethylamino)pyridine (7.5 mg, 0.0611 mmol, 0.10 equiv) were added at 23 °C, and the mixture was heated to reflux (45 °C). After 42 hours, the reaction was allowed to cool to 23 °C and washed with 2 M aqueous hydrochloric acid (2 x 10 mL) and brine (10 mL), then dried over sodium sulfate. After filtration and concentration under reduced pressure, the crude residue was purified by silica gel column chromatography (3% ethyl acetate in hexanes), delivering alkene **1d** as a colorless oil (98.1 mg, 56% yield). R*f* = 0.79 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 5.72 (ddt, *J* = 16.5, 10.6, 7.4 Hz, 1H), 5.14–4.96 (m, 2H), 4.12 (qd, *J* = 7.2, 0.9 Hz, 2H), 3.70–3.46 (m, 2H), 2.38 (ddt, *J* = 13.6, 7.2, 1.2 Hz, 1H), 2.22 (ddt, *J* = 13.6, 7.7, 1.1 Hz, 1H), 1.24 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H), 0.87 (s, 9H), 0.02 (s, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ175.8, 134.1, 118.1, 68.1, 60.4, 48.3, 39.5, 25.9, 19.3, 18.3, 14.4, -5.5; IR (Neat Film, KBr) 2956, 2929, 2857, 1732, 1472, 1386, 1251, 1227, 1101, 837, 776 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{31}O_3Si$ $[M+H]^+$: 287.2037, found 287.2040.



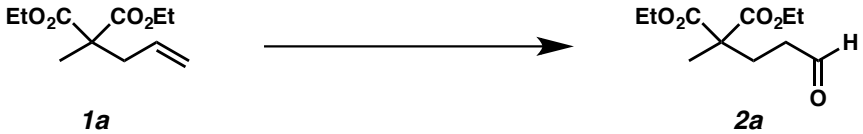
(2*S*)-2-Allyl-6-methoxy-2-methyl-1,2,3,4-tetrahydronaphthalen-1-ol (S7):
To a solution of ketone **S6** (64.9 mg, 0.282 mmol, 1.00 equiv) in dichloromethane (2.8 mL) and methanol (2.8 mL) was added a solution of sodium borohydride (21.3 mg, 0.564 mmol, 2.00 equiv) in dichloromethane (1.2 mL) and methanol (1.2 mL) at –78 °C. The reaction mixture was allowed to warm to 23 °C over the course of six hours. When TLC analysis indicated full consumption of starting material, the reaction was quenched with acetone (2.0 mL) and 2N NaOH (2.0 mL). The phases were separated, and the organic layer was immediately washed with brine (10 mL) and dried over sodium sulfate. After filtration and concentration under reduced pressure, the crude residue was purified by silica gel column chromatography (15% ethyl acetate in hexanes), furnishing alcohol **S7** as a 1:1 mixture of diastereomers (56.5 mg, 86% yield). R*f* = 0.26 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.35 (d, *J* = 8.5 Hz, 1H), 7.28 (d, *J* = 8.5 Hz, 1H), 6.79–6.73 (m, 2H), 6.64 (dt, *J* = 5.1, 1.8 Hz, 2H), 6.04–5.83 (m, 2H), 5.16–5.00 (m, 5H), 4.23 (s, 1H), 3.78 (s, 6H), 2.87–2.65 (m, 5H), 2.28 (ddt, *J* = 13.6, 7.3, 1.2 Hz, 1H), 2.13–2.01 (m, 3H), 1.87 (ddd, *J* = 13.5, 9.4, 6.7 Hz, 1H), 1.78 (ddd, *J* = 13.8, 7.5, 6.3 Hz, 1H), 1.55 (dt, *J* = 13.4, 6.6 Hz, 1H), 1.46 (dddd, *J* = 13.6, 5.9, 4.7, 1.0 Hz, 2H), 0.99 (s, 3H), 0.88 (s, 4H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 159.0, 158.9, 137.7, 137.4, 135.3, 135.0, 131.0, 130.9, 130.6, 130.2, 117.7, 117.6, 113.3, 113.2, 112.6, 75.1, 74.9, 55.3, 42.6, 41.6, 37.1, 36.9, 29.4, 29.1, 26.1, 26.0, 21.1, 19.9; IR (Neat Film, KBr) 3430 (br), 2928, 1610, 1501, 1456, 1263, 1159, 1104, 1038, 1015, 912, 802 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{20}O_2$ $[M\bullet]^+$: 232.1463, found 232.1439.



(*S*)-2-Allyl-6-methoxy-2-methyl-1,2,3,4-tetrahydronaphthalene (1j):
To a solution of alcohol **S7** (56.5 mg, 0.243 mmol, 1.00 equiv) in dichloromethane (5.0 mL) was added triethylsilane (0.12 mL, 0.730 mmol, 3.00 equiv) and boron trifluoride diethyl etherate (60 μL, 0.486 mmol, 2.00 equiv) at –60 °C. After 10 minutes, the reaction mixture was warmed to –10 °C and stirred at this temperature for 7 hours. A saturated aqueous solution of potassium carbonate was added, and the mixture was extracted with dichloromethane (2 x 20 mL). The combined organic extracts were dried over sodium sulfate before filtration and concentration under reduced pressure. The crude residue was purified by silica gel column chromatography (5% ethyl acetate in hexanes), affording tetralin **1j** as a colorless oil (50.3 mg, 96% yield). R*f* = 0.67 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 6.97 (d, *J* = 8.3 Hz, 1H), 6.73–6.63 (m, 2H), 5.91 (ddt, *J* = 16.9, 10.2, 7.5 Hz, 1H), 5.14–4.96 (m, 2H), 3.79 (s, 3H), 2.79 (t, *J* = 6.7 Hz, 2H), 2.60–2.39 (m, 2H), 2.06 (qdt, *J* = 13.7, 7.3, 1.2 Hz, 2H), 1.67–1.47

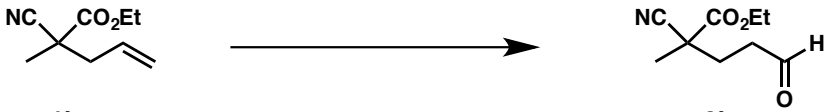
(m, 2H), 0.96 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 157.5, 137.0, 135.2, 130.5, 128.3, 117.3, 113.4, 112.0, 55.3, 45.4, 41.1, 33.8, 32.6, 26.5, 24.8; IR (Neat Film, KBr) 3073, 2951, 2914, 1611, 1503, 1464, 1267, 1254, 1236, 1153, 1042, 912, 808 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{21}O$ $[M+H]^+$: 217.1587, found 217.1584; $[\alpha]^{25}_D$ 6.47 (*c* 1.0, $CHCl_3$).

Aldehyde Characterization Data



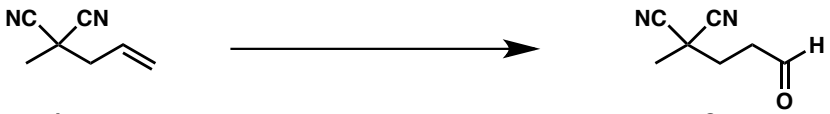
1a *2a*

Diethyl 2-methyl-2-(3-oxopropyl)malonate (2a):
Aldehyde **2a** was prepared from **1a** using General Procedure A, reaction time: 7 h, column eluent: 7% → 10% ethyl acetate in hexanes. 90% isolated yield. R*f* = 0.45 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.76 (t, *J* = 1.3 Hz, 1H), 4.18 (qd, *J* = 7.2, 0.6 Hz, 4H), 2.56–2.47 (m, 2H), 2.22–2.13 (m, 2H), 1.41 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 201.1, 171.9, 61.6, 52.9, 39.6, 27.9, 20.5, 14.2; IR (Neat Film, KBr) 2984, 1730, 1465, 1381, 1262, 1110, 1023, 861 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{11}H_{19}O_5$ $[M+H]^+$: 231.1227, found 231.1232.



1b *2b*

Ethyl 2-cyano-2-methyl-5-oxopentanoate (2b):
Aldehyde **2b** was prepared from **1b** using General Procedure A, reaction time: 7 h, column eluent: 20% ethyl acetate in hexanes. 81% isolated yield. R*f* = 0.39 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.77 (d, *J* = 0.9 Hz, 1H), 4.25 (qd, *J* = 7.1, 0.7 Hz, 2H), 2.83–2.53 (m, 2H), 2.27 (dddd, *J* = 14.4, 10.0, 5.6, 0.7 Hz, 1H), 2.15–2.02 (m, 1H), 1.61 (d, *J* = 0.7 Hz, 3H), 1.31 (td, *J* = 7.1, 0.7 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 199.2, 168.8, 119.5, 63.2, 43.1, 39.9, 30.1, 23.6, 14.1; IR (Neat Film, KBr) 2988, 2944, 1744, 1715, 1453, 1255, 1128, 1017, 857 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_9H_{14}NO_3$ $[M+H]^+$: 184.0974, found 184.0976.



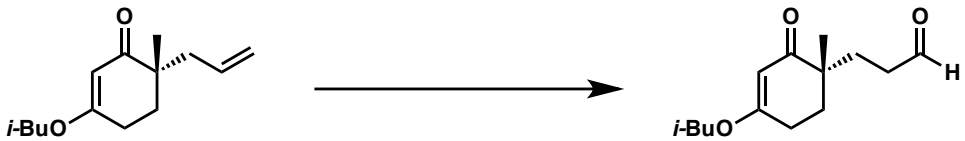
1c *2c*

2-Methyl-2-(3-oxopropyl)malononitrile (2c):
Aldehyde **2c** was prepared from **1c** using General Procedure A, reaction time: 17 h, column eluent: 20% ethyl acetate in hexanes. 89% isolated yield. R*f* = 0.25 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.85 (s, 1H), 3.00–2.84 (m, 2H),

2.38–2.21 (m, 2H), 1.84 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ197.7, 115.67, 39.9, 31.6, 31.2, 25.0; IR (Neat Film, KBr) 2848, 1724, 1454, 1389, 1150, 897, 629 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_7H_9N_2O$ $[M+H]^+$: 137.0715, found 137.0688.

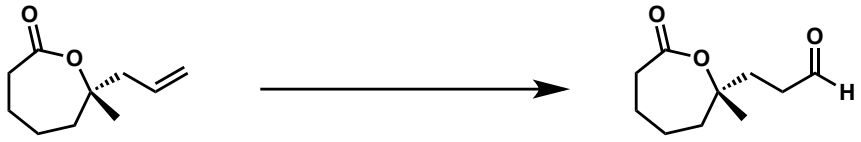
1d *2d*

Ethyl 2-(((*tert*-butyldimethylsilyl)oxy)methyl)-2-methyl-5-oxopentanoate (2d):
Aldehyde **2d** was prepared from **1d** using General Procedure A, reaction time: 15 h, column eluent: 7% ethyl acetate in hexanes. 87% isolated yield. R*f* = 0.70 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.74 (t, *J* = 1.6 Hz, 1H), 4.10 (q, *J* = 7.1 Hz, 2H), 3.64–3.57 (m, 2H), 2.46–2.40 (m, 2H), 1.97 (ddd, *J* = 14.0, 8.7, 7.1 Hz, 1H), 1.82–1.72 (m, 1H), 1.23 (t, *J* = 7.1 Hz, 3H), 1.13 (s, 3H), 0.85 (s, 9H), 0.01 s, 6 H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 202.1, 175.5, 68.4, 60.7, 47.6, 39.6, 27.2, 25.9, 19.7, 18.3, 14.3, -5.5; IR (Neat Film, KBr) 2955, 2930, 2857, 1728, 1472, 1252, 1184, 1100, 838, 777, 668 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{31}O_4Si$ $[M+H]^+$: 303.1986, found 303.1983.



1e *2e*

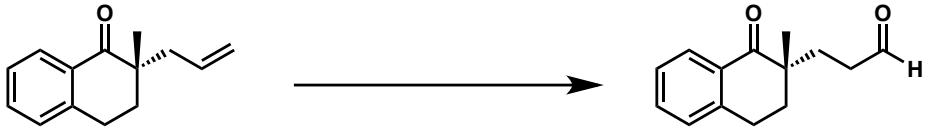
(*S*)-3-(4-Isobutoxy-1-methyl-2-oxocyclohex-3-en-1-yl)propanal (2e):
Aldehyde **2e** was prepared from **1e** using General Procedure A, reaction time: 14 h, column eluent: 15% ethyl acetate in hexanes. 60% isolated yield. R*f* = 0.34 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.76 (t, *J* = 1.5 Hz, 1H), 5.24 (s, 1H), 3.57 (d, *J* = 6.5 Hz, 2H), 2.53–2.36 (m, 4H), 2.02 (dq, *J* = 13.3, 6.7 Hz, 1H), 1.93–1.69 (m, 4H), 1.10 (s, 3H), 1.00–0.95 (m, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 203.2, 202.4, 176.3, 101.5, 75.0, 42.7, 39.4, 32.8, 29.1, 27.9, 26.0, 22.6, 19.2; IR (Neat Film, KBr) 2961, 2932, 1724, 1648, 1607, 1384, 1369, 1195, 993, 840 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{23}O_3$ $[M+H]^+$: 239.1642, found 239.1638; $[\alpha]^{25}_D$ –5.0 (*c* 0.94, $CHCl_3$).



1f *2f*

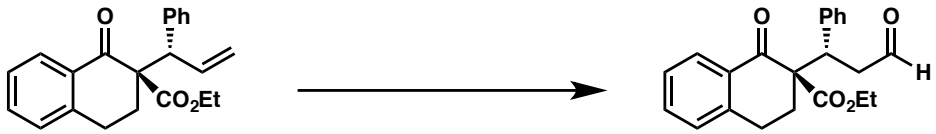
(*S*)-3-(2-Methyl-7-oxooxepan-2-yl)propanal (2f):
Aldehyde **2f** was prepared from **1f** using General Procedure A, reaction time: 15 h, column eluent: 20% → 40% ethyl acetate in hexanes. 67% isolated yield. R*f* = 0.30 (67% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.82 (d, *J* = 1.2 Hz, 1H), 2.80–2.57 (m, 4H), 2.11 (ddd, *J* = 14.9, 9.0, 6.3 Hz, 1H), 1.96–1.74 (m, 6H), 1.69–1.57

(m, 1H), 1.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 201.8, 174.9, 82.3, 39.4, 38.9, 37.6, 34.9, 24.7, 24.1, 23.7; IR (Neat Film, KBr) 2936, 1720, 1716, 1289, 1185, 1107, 1018, 858 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{10}H_{17}O_3$ $[M+H]^+$: 185.1178, found 185.1177; $[\alpha]^{25}_D$ 1.6 (*c* 2.46, $CHCl_3$).



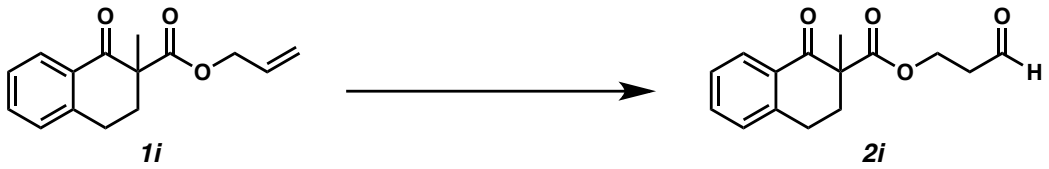
1g *2g*

(*S*)-3-(2-Methyl-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)propanal (2g):
Aldehyde **2g** was prepared from **1g** using General Procedure A, reaction time: 12 h, column eluent: 5% ethyl acetate in hexanes. 80% isolated yield. R*f* = 0.15 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.76 (t, *J* = 1.5 Hz, 1H), 8.01 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.49–7.42 (m, 1H), 7.33–7.26 (m, 1H), 7.22 (ddq, *J* = 7.6, 1.5, 0.8 Hz, 1H), 3.01 (t, *J* = 6.3 Hz, 2H), 2.61–2.30 (m, 2H), 2.13–1.82 (m, 4H), 1.21 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 202.2, 201.9, 143.1, 133.4, 131.5, 128.9, 128.1, 126.9, 44.1, 39.2, 34.2, 28.8, 25.3, 22.2; IR (Neat Film, KBr) 2929, 1722, 1682, 1600, 1454, 1224, 976, 798, 742 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{17}O_2$ $[M+H]^+$: 217.1229, found 217.1258; $[\alpha]^{25}_D$ –1.0 (*c* 1.65, $CHCl_3$).



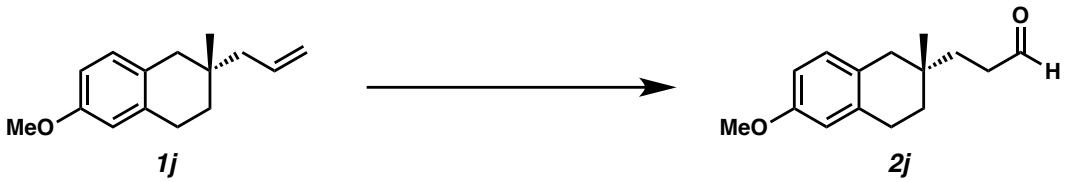
1h *2h*

Ethyl (*R*)-1-oxo-2-((*S*)-3-oxo-1-phenylpropyl)-1,2,3,4-tetrahydronaphthalene-2-carboxylate (2h):
Aldehyde **2h** was prepared from **1h** using General Procedure A, reaction time: 40 h, column eluent: 10% ethyl acetate in hexanes. 75% isolated yield. R*f* = 0.48 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.59 (t, *J* = 1.7 Hz, 1H), 8.00 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.44 (td, *J* = 7.5, 1.5 Hz, 1H), 7.40–7.34 (m, 2H), 7.31–7.24 (m, 2H), 7.24–7.12 (m, 3H), 4.19 (dd, *J* = 8.4, 6.2 Hz, 1H), 4.08 (q, *J* = 7.1 Hz, 2H), 3.13–3.07 (m, 2H), 3.07–2.97 (m, 1H), 2.88 (dt, *J* = 17.8, 4.5 Hz, 1H), 2.34 (ddd, *J* = 13.7, 4.8, 3.7 Hz, 1H), 1.98 (ddd, *J* = 13.8, 11.2, 5.1 Hz, 1H), 1.09 (t, *J* = 7.1 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 200.9, 194.7, 170.2, 142.7, 139.1, 133.6, 132.6, 130.5, 128.7, 128.4, 128.3, 127.5, 126.9, 61.8, 60.5, 46.3, 43.0, 30.5, 26.1, 14.0; IR (Neat Film, KBr) 2978, 2725, 1725, 1689, 1600, 1454, 1298, 1235, 1214, 1018, 909, 742, 703, 648 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{22}H_{23}O_5$ $[M+OH]^+$: 367.1540, found 367.1535; $[\alpha]^{25}_D$ 15.7 (*c* 1.52, $CHCl_3$).



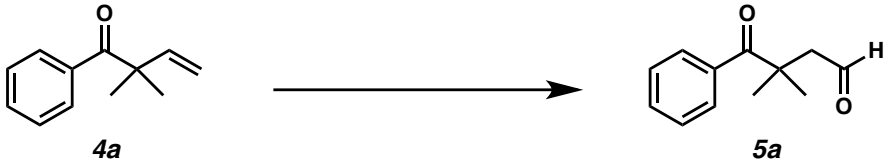
1i *2i*

3-Oxopropyl 2-methyl-1-oxo-1,2,3,4-tetrahydronaphthalene-2-carboxylate (2i):
Aldehyde **2i** was prepared from **1i** using General Procedure A, reaction time: 10 h, column eluent: 15% ethyl acetate in hexanes. 74% isolated yield. R*f* = 0.27 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.61 (t, *J* = 1.4 Hz, 1H), 8.02 (dd, *J* = 7.9, 1.4 Hz, 1H), 7.47 (td, *J* = 7.5, 1.5 Hz, 1H), 7.34 – 7.28 (m, 1H), 7.24 – 7.19 (m, 1H), 4.54 – 4.31 (m, 2H), 3.12 – 2.86 (m, 2H), 2.68 (ddt, *J* = 7.2, 6.0, 1.5 Hz, 2H), 2.58 (ddd, *J* = 13.7, 6.2, 4.9 Hz, 1H), 2.05 (ddt, *J* = 13.8, 9.0, 4.6 Hz, 1H), 1.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 199.0, 196.1, 172.9, 143.1, 133.7, 131.6, 128.9, 128.1, 127.0, 58.9, 54.0, 42.5, 33.7, 25.9, 20.4; IR (Neat Film, KBr) 2936, 1732, 1687, 1682, 1601, 1455, 1308, 1265, 1228, 1189, 1114, 743 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{17}O_4$ $[M+H]^+$: 261.1127, found 261.1155.



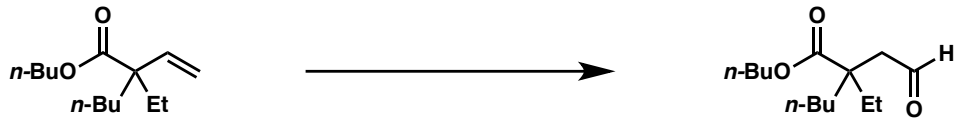
1j *2j*

(*S*)-3-(6-Methoxy-2-methyl-1,2,3,4-tetrahydronaphthalen-2-yl)propanal (2j):
Aldehyde **2j** was prepared from **1j** using General Procedure A, reaction time: 12 h, column eluent: 5% ethyl acetate in hexanes. 63% isolated yield. R*f* = 0.34 (20% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.79 (t, *J* = 1.9 Hz, 1H), 6.95 (d, *J* = 8.4 Hz, 1H), 6.71–6.66 (m, 1H), 6.64 (d, *J* = 2.7 Hz, 1H), 3.77 (s, 3H), 2.77 (td, *J* = 6.7, 4.2 Hz, 2H), 2.56–2.39 (m, 4H), 1.65–1.60 (m, 2H), 1.58 (t, *J* = 6.8 Hz, 2H), 0.93 (s, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 203.0, 157.7, 136.7, 130.5, 127.7, 113.4, 112.2, 55.4, 41.1, 39.1, 33.9, 32.6, 31.9, 26.4, 24.4; IR (Neat Film, KBr) 2916, 2834, 2719, 1724, 1610, 1503, 1267, 1242, 1040, 808 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{20}O_2$ $[M\bullet]^+$: 232.1463, found 232.1473; $[\alpha]^{25}_D$ 85.6 (*c* 1.00, $CHCl_3$).



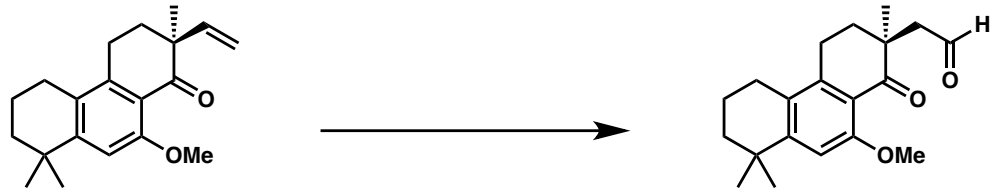
4a *5a*

3,3-Dimethyl-4-oxo-4-phenylbutanal (5a):
Aldehyde **5a** was prepared from **4a** using General Procedure A, reaction time: 20 h, column eluent: 10% ethyl acetate in hexanes. 85% isolated yield. R*f* = 0.30 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.74 (t, *J* = 1.4 Hz, 1H), 7.70–7.64 (m, 2H), 7.50–7.45 (m, 1H), 7.44–7.38 (m, 2H), 2.83 (d, *J* = 1.5 Hz, 2H), 1.46 (s, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 208.2, 200.6, 138.4, 131.2, 128.3, 127.8, 54.7, 46.1, 26.7; IR (Neat Film, KBr) 2974, 1784, 1712, 1450, 1291, 1114, 967, 714 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{12}H_{15}O_2$ $[M+H]^+$: 191.1067, found 191.1075.



4b *5b*

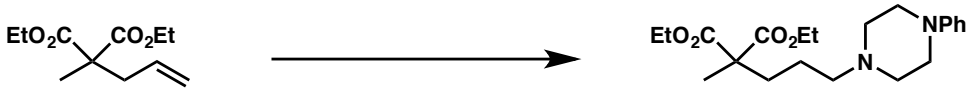
Butyl 2-ethyl-2-(2-oxoethyl)hexanoate (5b):
Aldehyde **5b** was prepared from **4b** using General Procedure A, reaction time: 45 h, column eluent: 10% ethyl acetate in hexanes. 69% isolated yield. R*f* = 0.36 (10% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.76 (t, *J* = 2.3 Hz, 1H), 4.10 (t, *J* = 6.6 Hz, 2H), 2.62 (d, *J* = 2.3 Hz, 2H), 1.79–1.56 (m, 6H), 1.42–1.32 (m, 2H), 1.31–1.24 (m, 2H), 1.23–1.08 (m, 2H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.2 Hz, 3H), 0.83 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 201.7, 176.0, 64.8, 48.1, 47.3, 35.7, 30.7, 29.0, 26.5, 23.2, 19.3, 14.1, 13.8, 8.7; IR (Neat Film, KBr) 2961, 2936, 2874, 1724, 1459, 1383, 1203, 1139, 1022, 737 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{26}O_3$ $[M+H]^+$: 243.1955, found 243.1961.



4c *5c*

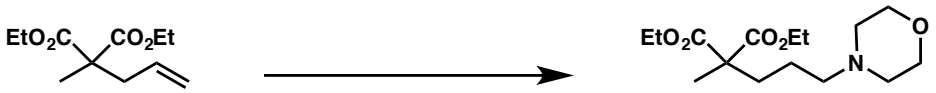
(*S*)-2-(10-methoxy-2,8,8-trimethyl-1-oxo-1,2,3,4,5,6,7,8-octahydrophenanthren-2-yl)acetaldehyde (5c):
Aldehyde **5c** was prepared from **4c** using General Procedure A, reaction time: 48 h, column eluent: 5% ethyl acetate in hexanes. 64% isolated yield. R*f* = 0.40 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 9.89 (t, *J* = 2.5 Hz, 1H), 6.85 (s, 1H), 3.88 (s, 3H), 2.80 (dd, *J* = 8.0, 4.9 Hz, 2H), 2.67 (dd, *J* = 15.5, 2.3 Hz, 1H), 2.60–2.45 (m, 3H), 2.22–2.11 (m, 1H), 1.96 (dt, *J* = 13.6, 4.9 Hz, 1H), 1.89–1.78 (m, 2H), 1.68–1.61 (m, 2H), 1.30 (s, 9H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 202.3, 200.6, 158.9, 153.1, 143.4, 126.3, 118.9, 108.6, 56.0, 51.3, 45.4, 38.4, 35.0, 33.8, 31.8, 31.7, 27.0, 23.7, 22.0, 19.4; IR (Neat Film, KBr) 2959, 2930, 2866, 1717, 1676, 1591, 1558, 1459, 1401, 1318, 1246, 1227, 1104, 1042, 1013, 972, 850, 734 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{20}H_{26}O_3$ $[M+H]^+$: 315.1955, found 315.1947; $[\alpha]^{25}_D$ 4.03 (*c* 1.00, $CHCl_3$).

Amine Characterization Data



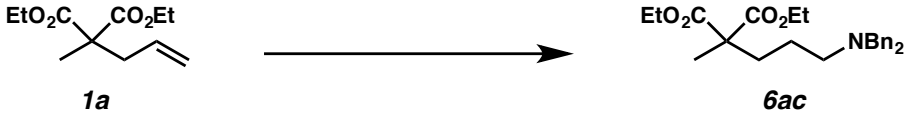
1a *6aa*

Diethyl 2-methyl-2-(3-(4-phenylpiperazin-1-yl)propyl)malonate (6aa):
Amine **6aa** was prepared from **1a** using General Procedure B, column eluent: 25% ethyl acetate in hexanes with 0.5% triethylamine. 98% isolated yield. R*f* = 0.16 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.29–7.18 (m, 2H), 6.92 (dt, *J* = 7.9, 1.0 Hz, 2H), 6.88–6.79 (m, 1H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.26–3.12 (m, 4H), 2.66–2.53 (m, 4H), 2.45–2.33 (m, 2H), 1.94–1.82 (m, 2H), 1.55–1.44 (m, 2H), 1.41 (d, *J* = 4.4 Hz, 3H), 1.25 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 172.4, 151.4, 129.2, 119.8, 116.1, 61.3, 58.7, 53.6, 53.3, 49.2, 33.5, 21.9, 20.1, 14.2; IR (Neat Film, KBr) 2816, 1731, 1600, 1502, 1257, 1235, 1110, 759, 692 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{21}H_{33}N_2O_5$ $[M+OH]^+$: 393.2384, found 393.2386.



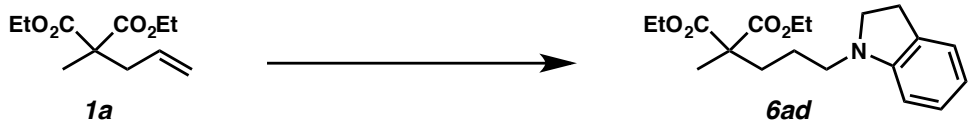
1a *6ab*

Diethyl 2-methyl-2-(3-morpholinopropyl)malonate (6ab):
Amine **6ab** was prepared from **1a** using General Procedure B, column eluent: 8% → 25% ethyl acetate in hexanes with 0.5% triethylamine. 91% isolated yield. ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.17 (q, *J* = 7.1 Hz, 4H), 3.76 – 3.65 (m, 4H), 2.41 (dd, *J* = 5.8, 3.6 Hz, 4H), 2.37 – 2.29 (m, 2H), 1.89 – 1.81 (m, 2H), 1.52 – 1.36 (m, 5H), 1.23 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 172.4, 66.8, 61.4, 58.9, 53.6, 53.5, 33.4, 21.4, 20.1, 14.2; IR (Neat Film, KBr) 2958, 1730, 1457, 1256, 1232, 1118, 1023, 862 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{28}NO_5$ $[M+H]^+$: 302.1962, found 302.1961.

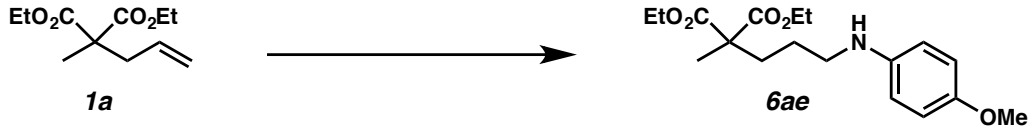


1a *6ac*

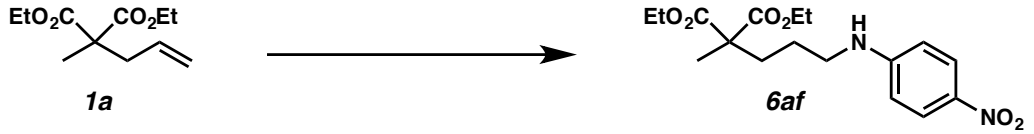
Diethyl 2-(3-(dibenzylamino)propyl)-2-methylmalonate (6ac):
Amine **6ac** was prepared from **1a** using General Procedure B, column eluent: 8% ethyl acetate in hexanes with 0.5% triethylamine. 76% isolated yield. R*f* = 0.72 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.38–7.27 (m, 8H), 7.25–7.20 (m, 2H), 4.22–4.10 (m, 4H), 3.54 (s, 4H), 2.43 (t, *J* = 7.0 Hz, 2H), 1.88–1.80 (m, 2H), 1.50–1.41 (m, 2H), 1.38 (d, *J* = 0.8 Hz, 3H), 1.22 (td, *J* = 7.1, 0.6 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 172.5, 139.8, 128.9, 128.3, 126.9, 61.2, 58.3, 53.6, 53.5, 33.3, 21.9, 20.1, 14.2; IR (Neat Film, KBr) 2981, 2796, 1731, 1453, 1245, 1111, 1028, 746, 699 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{25}H_{34}NO_4$ $[M+H]^+$: 412.2482, found 412.2494.



Diethyl 2-(3-(indolin-1-yl)propyl)-2-methylmalonate (6ad):
Amine **6ad** was prepared from **1a** using General Procedure B, column eluent: 6% ethyl acetate in hexanes with 0.5% triethylamine. 96% isolated yield. R*f* = 0.66 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.12–7.00 (m, 2H), 6.64 (t, *J* = 7.5 Hz, 1H), 6.45 (d, *J* = 7.8 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.32 (t, *J* = 8.3 Hz, 2H), 3.06 (t, *J* = 7.2 Hz, 2H), 2.95 (t, *J* = 8.2 Hz, 2H), 2.01–1.89 (m, 2H), 1.61–1.54 (m, 2H), 1.43 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 7H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 172.5, 152.7, 130.2, 127.4, 124.5, 117.5, 107.0, 61.4, 53.6, 53.1, 49.6, 33.3, 28.7, 22.5, 20.2, 14.2; IR (Neat Film, KBr) 2980, 1730, 1607, 1490, 1254, 1232, 1113, 1022, 746 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{19}H_{28}NO_4$ $[M+H]^+$: 334.2013, found 334.2019.

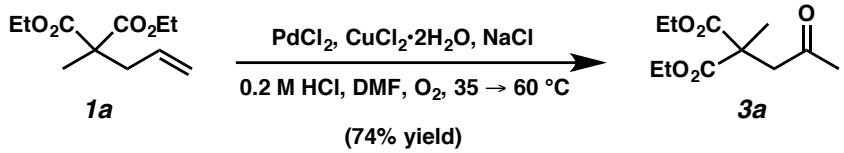


Diethyl 2-(3-((4-methoxyphenyl)amino)propyl)-2-methylmalonate (6ae):
Amine **6ae** was prepared from **1a** using General Procedure B, column eluent: 10% ethyl acetate in hexanes with 0.5% triethylamine. 86% isolated yield. R*f* = 0.45 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 400 MHz) δ 6.81–6.71 (m, 2H), 6.60–6.51 (m, 2H), 4.17 (q, *J* = 7.1 Hz, 4H), 3.74 (s, 3H), 3.08 (t, *J* = 6.9 Hz, 2H), 2.00–1.89 (m, 2H), 1.62–1.48 (m, 2H), 1.41 (s, 3H), 1.23 (t, *J* = 7.1 Hz, 7H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 172.4, 152.2, 142.6, 115.1, 114.2, 61.4, 56.0, 53.6, 45.1, 33.3, 24.7, 20.1, 14.2; IR (Neat Film, KBr) 2982, 1730, 1514, 1235, 1187, 1110, 1037, 820 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{18}H_{28}NO_5$ $[M+H]^+$: 338.1962, found 338.1953.

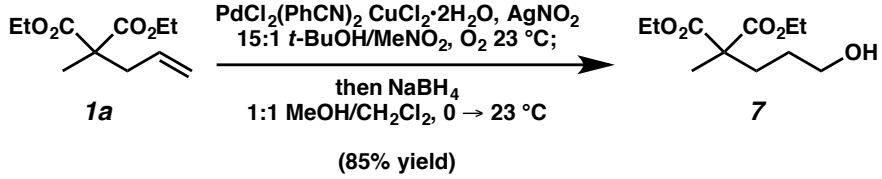


Diethyl 2-methyl-2-(3-((4-nitrophenyl)amino)propyl)malonate (6af):
Amine **6af** was prepared from **1a** using General Procedure B, column eluent: 10% → 20% ethyl acetate in hexanes with 0.5% triethylamine. 95% isolated yield. R*f* = 0.31 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.12–8.04 (m, 2H), 6.54–6.48 (m, 2H), 4.18 (q, *J* = 7.1 Hz, 4H), 3.22 (t, *J* = 6.8 Hz, 2H), 1.98–1.92 (m, 2H), 1.69–1.61 (m, 2H), 1.43 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 172.3, 153.3, 138.1, 126.6, 111.1, 61.6, 53.5, 43.5, 33.1, 24.2, 20.2, 14.2; IR (Neat Film, KBr) 3383, 2836, 1748, 1721, 1610, 1475, 1314, 1328, 1190, 1114, 829 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{17}H_{25}N_2O_6$ $[M+H]^+$: 353.1707, found 353.1707.

Alkene Transformation Procedures and Characterization Data

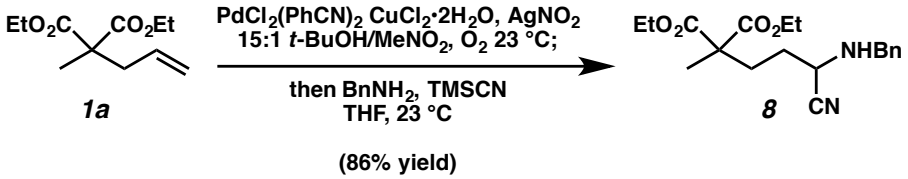


Diethyl 2-methyl-2-(2-oxopropyl)malonate (3a):
To a two-necked round-bottom flask were added palladium(II) chloride (10.6 mg, 0.06 mmol, 0.30 equiv), copper(II) chloride dihydrate (20.5 mg, 0.12 mmol, 0.60 equiv), and sodium chloride (15.0 mg, 0.26 mmol, 1.30 equiv). The mixture was diluted with 0.2 M aqueous hydrochloric acid (3.1 mL) and stirred vigorously at 35 °C under oxygen atmosphere (balloon) for 30 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added as a solution in *N,N*-dimethylformamide (1.0 mL), and the resulting solution was heated stirred vigorously under oxygen atmosphere at 60 °C for 6 hours. The reaction mixture was allowed to cool to 23 °C and extracted with chloroform (2 x 5 mL). The organic extracts were dried over magnesium sulfate, filtered, and concentrated. The crude residue was purified by silica gel column chromatography (8% ethyl acetate in hexanes) to afford ketone **3a** as a colorless oil (34.3 mg, 74% yield). R*f* = 0.24 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.18 (q, *J* = 7.1 Hz, 4H), 3.08 (s, 2H), 2.15 (s, 3H), 1.51 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 205.1, 171.6, 61.7, 51.6, 48.8, 30.5, 20.6, 14.1; IR (Neat Film, KBr) 2984, 1732, 1463, 1376, 1242, 1109, 1024, 863, 798 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{11}H_{19}O_5$ $[M+H]^+$: 231.1227, found 231.1226.

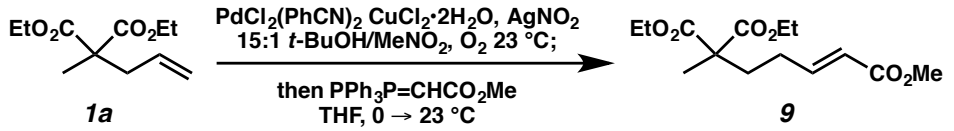


Diethyl 2-(3-hydroxypropyl)-2-methylmalonate (7):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in 1:1 MeOH/CH_2Cl_2 (4 mL total volume) and cooled to 0 °C using an ice water bath. Sodium borohydride (11.3 mg, 0.30 mmol, 1.50 equiv) was added in one portion, and the resulting mixture was

stirred at 23 °C for 2 hours, at which time the reaction was quenched with acetone and 2 N aqueous sodium hydroxide (2 mL). The phases were separated, and the organic layer was immediately washed with brine (5 mL) and dried over sodium sulfate. Filtration and concentration delivered the crude product, which was purified by silica gel column chromatography (35% ethyl acetate in hexanes) to afford alcohol **7** as a colorless oil (39.7 mg, 85% yield). R*f* = 0.18 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.18 (q, *J* = 7.1 Hz, 4H), 3.64 (t, *J* = 6.4 Hz, 2H), 1.98–1.88 (m, 2H), 1.59–1.49 (m, 2H), 1.42 (d, *J* = 2.4 Hz, 3H), 1.24 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 172.5, 62.9, 61.4, 53.5, 32.0, 27.8, 20.1, 14.2; IR (Neat Film, KBr) 3469 (br), 2982, 2939, 1730, 1460, 1270, 1119, 1020, 859 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{11}H_{21}O_5$ $[M+H]^+$: 233.1389, found 233.1382.

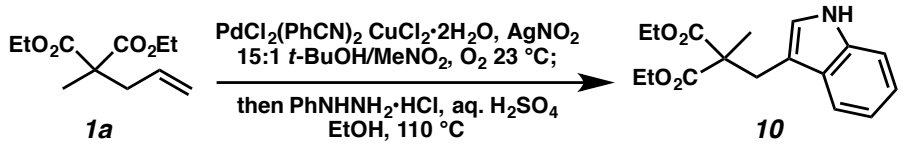


Diethyl 2-(3-(benzylamino)-3-cyanopropyl)-2-methylmalonate (8):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in THF (4 mL total volume) and treated with benzylamine (23 μL, 0.21 mmol, 1.05 equiv) at 23 °C. After one hour, trimethylsilyl cyanide (26 μL, 0.21 mmol, 1.05 equiv) was added, and the resulting mixture was stirred at 23 °C for 7 hours, at which time the volatiles were removed under reduced pressure. The crude residue obtained was purified by silica gel column chromatography (20% ethyl acetate in hexanes) to furnish α-aminonitrile **8** as a colorless oil (59.6 mg, 86% yield). R*f* = 0.42 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 7.37–7.31 (m, 4H), 7.31–7.26 (m, 1H), 4.18 (qd, *J* = 7.1, 2.2 Hz, 4H), 4.06 (d, *J* = 12.9 Hz, 1H), 3.82 (d, *J* = 12.9 Hz, 1H), 3.49 (t, *J* = 7.0 Hz, 1H), 2.17–2.05 (m, 1H), 2.00 (ddd, *J* = 13.7, 9.5, 7.4 Hz, 1H), 1.81–1.73 (m, 2H), 1.41 (s, 3H), 1.24 (td, *J* = 7.1, 2.3 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 171.9, 138.2, 128.7, 128.5, 127.7, 119.8, 61.6, 53.2, 51.7, 49.8, 31.8, 28.9, 20.2, 14.2; IR (Neat Film, KBr) 3325, 2983, 1728, 1454, 1261, 1189, 1112, 1027, 738, 700 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{19}H_{27}N_2O_4$ $[M+H]^+$: 347.1965, found 347.1970.



(86% yield)

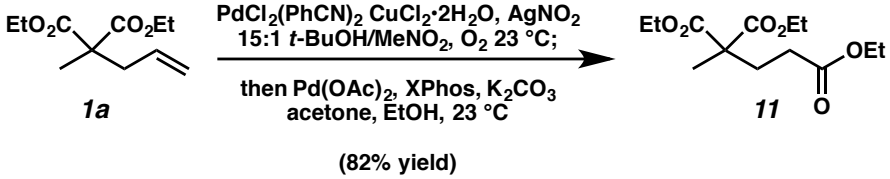
5,5-Diethyl 1-methyl (*E*)-hex-1-ene-1,5,5-tricarboxylate (9):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in THF (4 mL total volume) and cooled to 0 °C using an ice water bath. Carbomethoxy methylene triphenyl phosphorane (100.3 mg, 0.30 mmol, 1.50 equiv) was added in one portion, and the resulting mixture was stirred at 23 °C for 20 hours, at which time the reaction was transferred to a separatory funnel with diethyl ether and washed sequentially with water (5 mL) and brine (5 mL). The organic layer was dried over sodium sulfate, filtered, and concentrated to a crude yellow oil. Purification by silica gel column chromatography (10% ethyl acetate in hexanes) afforded α,β-unsaturated methyl ester **9** as a colorless oil (49.3 mg, 86% yield). R*f* = 0.56 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 6.93 (dtd, *J* = 15.3, 6.7, 1.8 Hz, 1H), 5.83 (dt, *J* = 15.7, 1.7 Hz, 1H), 4.17 (qd, *J* = 7.2, 1.7 Hz, 4H), 3.71 (d, *J* = 1.9 Hz, 3H), 2.26–2.10 (m, 2H), 2.04–1.92 (m, 2H), 1.41 (d, *J* = 1.7 Hz, 3H), 1.24 (td, *J* = 7.1, 1.7 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 172.0, 167.0, 148.1, 121.5, 61.5, 53.4, 51.6, 33.9, 27.3, 20.1, 14.2; IR (Neat Film, KBr) 2984, 2951, 1734, 1730, 1659, 1437, 1268, 1234, 1110, 1024, 858 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{14}H_{23}O_6$ $[M+H]^+$: 287.1489, found 287.1485.



(57% yield)

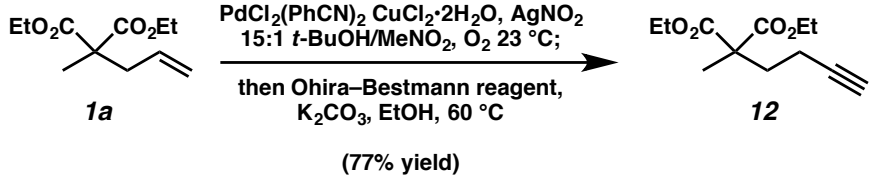
Diethyl 2-((1*H*-indol-3-yl)methyl)-2-methylmalonate (10):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (23.0 mg, 0.060 mmol, 0.12 equiv), copper(II) chloride dihydrate (10.2 mg, 0.060 mmol, 0.12 equiv), and silver nitrite (4.6 mg, 0.030 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (9.4 mL) and nitromethane (0.60 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a**

(107 mg, 0.50 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then diluted with a pre-heated solution (50 °C) of 4% aqueous sulfuric acid (4.7 mL) and phenyl hydrazine hydrochloride (79.5 mg, 0.550 mmol, 1.10 equiv). After addition of ethanol (3.5 mL), the mixture was heated to reflux at 110 °C for 7 hours. The reaction mixture was cooled to 23 °C and treated with saturated aqueous sodium bicarbonate and ethyl acetate. The phases were separated, and the aqueous layer was extracted with ethyl acetate (2 x 20 mL). The combined organic extracts were dried over sodium sulfate before filtration and concentration under reduced pressure. The crude residue was purified by silica gel column chromatography (20% ethyl acetate in hexanes) to afford indole **10** as yellow oil (86.1 mg, 57% yield). R*f* = 0.44 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 8.17 (s, 1H), 7.59 (d, *J* = 7.9 Hz, 1H), 7.32 (dt, *J* = 8.1, 1.0 Hz, 1H), 7.11 (ddd, *J* = 8.0, 7.0, 1.1 Hz, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 6.98 (d, *J* = 2.4 Hz, 1H), 4.27–4.10 (m, 4H), 3.41 (d, *J* = 0.9 Hz, 2H), 1.44 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 6H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 172.6, 135.9, 128.5, 123.5, 121.9, 119.5, 111.2, 110.5, 61.4, 55.4, 30.7, 20.4, 14.1; IR (Neat Film, KBr) 3403, 2983, 1728, 1458, 1293, 1254, 1106, 1021, 861, 743 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{17}H_{22}NO_4$ $[M+H]^+$: 304.1543, found 304.1548.



Triethyl butane-1,3,3-tricarboxylate (11):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in degassed ethanol (2 mL), and oven-dried potassium carbonate (10.0 mg, 0.072 mmol, 0.36 equiv) was added. After stirring for 20 minutes, a solution of palladium(II) acetate (2.2 mg, 0.01 mmol, 0.05 equiv) and XPhos (9.5 mg, 0.02 mmol, 0.10 equiv) in acetone (2 mL) that had been stirring at 23 °C for 20 minutes was added via syringe under argon atmosphere. The resulting dark green solution was stirred at 23 °C for 6 hours, at which time the volatiles

were removed under reduced pressure. The crude residue obtained was purified by silica gel column chromatography (8% ethyl acetate in hexanes) to furnish tri-ester **11** as a colorless oil (45.0 mg, 82% yield). R*f* = 0.53 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 500 MHz) δ 4.16 (q, *J* = 7.1, 0.8 Hz, 4H), 4.11 (q, *J* = 7.2, 0.9 Hz, 2H), 2.38–2.27 (m, 2H), 2.23–2.13 (m, 2H), 1.39 (s, 3H), 1.23 (td, *J* = 7.1, 0.8 Hz, 9H); ^{13}C NMR ($CDCl_3$, 126 MHz) δ 173.0, 171.9, 61.5, 60.6, 53.0, 30.7, 29.9, 20.2, 14.3; IR (Neat Film, KBr) 2982, 2941, 1738, 1732, 1466, 1380, 1243, 1185, 1109, 1025, 860 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{13}H_{23}O_6$ $[M+H]^+$: 275.1489, found 275.1483.



Diethyl 2-(but-3-yn-1-yl)-2-methylmalonate (12):
To a flame-dried 25-mL round-bottom flask with a magnetic stir bar were added bis(benzonitrile)palladium(II) chloride (9.2 mg, 0.024 mmol, 0.12 equiv), copper(II) chloride dihydrate (4.1 mg, 0.024 mmol, 0.12 equiv), and silver nitrite (1.8 mg, 0.012 mmol, 0.06 equiv). The flask was capped with a rubber septum, and *tert*-butyl alcohol (3.75 mL) and nitromethane (0.25 mL) were added sequentially by syringe. The mixture was stirred at 23 °C and sparged with oxygen gas (balloon) for 3 minutes. Alkene **1a** (42.9 mg, 0.20 mmol, 1.00 equiv) was added dropwise by syringe, and the reaction mixture was sparged with oxygen for another minute. The reaction was stirred under oxygen atmosphere at 23 °C for 12 hours, when TLC analysis indicated consumption of starting material. The solvent was removed under reduced pressure, and the residue was loaded onto a short plug of silica gel, eluting with 30% ethyl acetate in hexanes (100 mL). The oil obtained upon concentration was then redissolved in ethanol (4 mL), and potassium carbonate (33.2 mg, 0.24 mmol, 1.20 equiv) and Ohira–Bestmann reagent (46.1 mg, 0.24 mmol, 1.20 equiv) were added. The resulting mixture was stirred at 60 °C for 24 hours, at which time the reaction was quenched with water (4 mL), diluted with diethyl ether (2 mL), and washed with 5% aqueous sodium bicarbonate. The organic layer was dried over magnesium sulfate, filtered, and concentrated. The crude residue obtained was purified by silica gel column chromatography (8% ethyl acetate in hexanes) to furnish alkyne **12** as a colorless oil (35.0 mg, 77% yield). R*f* = 0.72 (33% ethyl acetate in hexanes); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 4.18 (q, *J* = 7.1 Hz, 4H), 2.28–2.06 (m, 4H), 1.95 (t, *J* = 2.5 Hz, 1H), 1.42 (s, 3H), 1.25 (t, *J* = 7.1 Hz, 7H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 171.9, 83.5, 68.8, 61.5, 53.2, 34.6, 20.0, 14.3, 14.2; IR (Neat Film, KBr) 3291, 2983, 1731, 1465, 1381, 1265, 1189, 1109, 1025, 861, 659 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{20}O_4$ $[M+H]^+$: 227.1283, found 227.1287.

Notes and References

1. Pangborn, A. B.; Giardello, M. A.; Grubbs, R. H.; Rosen, R. K.; Timmers, F. J. *Organometallics* **1996**, *15*, 1518–1520.
2. Pietruszka, J.; Witt, A. *Synthesis* **2006**, *24*, 4266–4268.
3. Boers, R. B.; Randulfe, Y. P.; van der Haas, H. N. S.; van Rossum-Baan, M.; Lugtenburg, J. *Eur. J. Org. Chem.* **2002**, 2094–2108.
4. Anhydrous CuCl and $CuCl_2$ were also examined as copper sources, but use of $CuCl_2$•$2H_2O$ resulted in the highest yields.
5. While investigations into the complex mechanism of this transformation are still ongoing, evidence suggests that a *t*-BuOH-ligated nitrite Pd–Cu species promotes selective formation of the aldehyde. For more mechanistic analysis, see: a) Jiang, Y.-Y.; Zhang, Q.; Yu, H.-Z.; Fu, Y. *ACS Catal.* **2015**, *5*, 1414–1423; b) Anderson, B. J.; Keith, J. A.; Sigman, M. S. *J. Am. Chem. Soc.* **2010**, *132*, 11872–11874; c) Keith, J. A.; Nielsen, R. J.; Oxgaard, J.; Goddard, W. A., III *J. Am. Chem. Soc.* **2007**, *129*, 12342–12343.
6. Lactam substrates bearing quaternary carbons at the homoallylic position were also investigated, but these substrates reacted sluggishly, and only low yields (32–37%) of the aldehyde product were obtained, often contaminated by enal side product.
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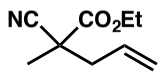
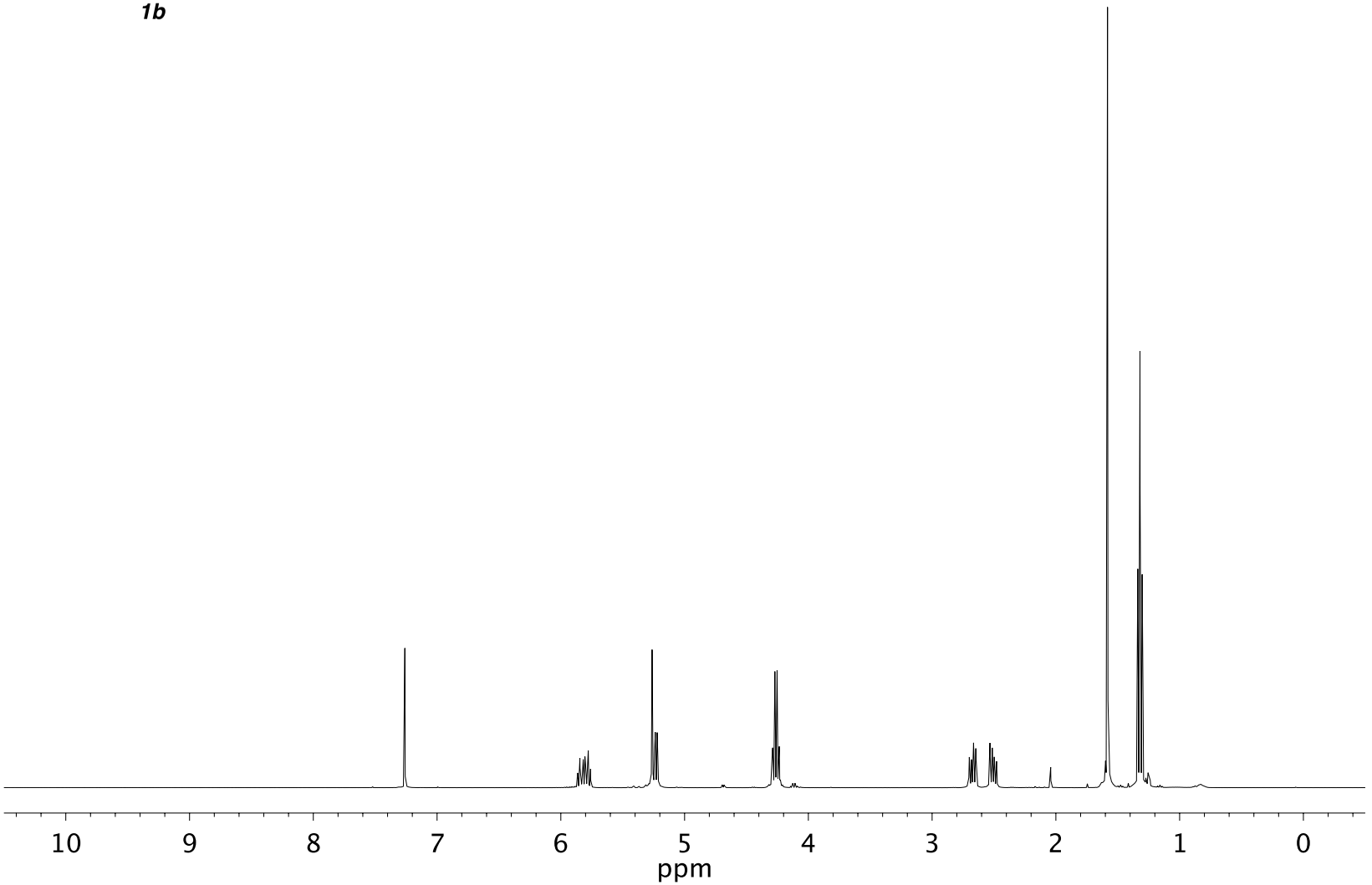
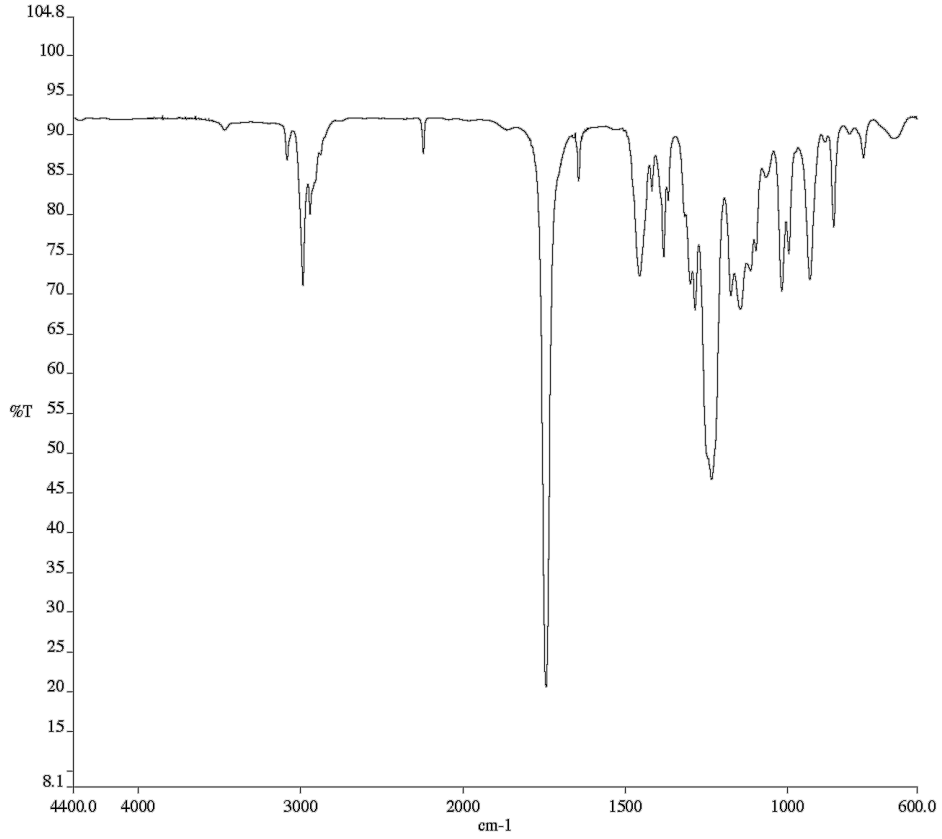
14. When unprotected **1d** was subjected to the aldehyde-selective Wacker conditions, mixtures containing several inseparable compounds were obtained after purification.



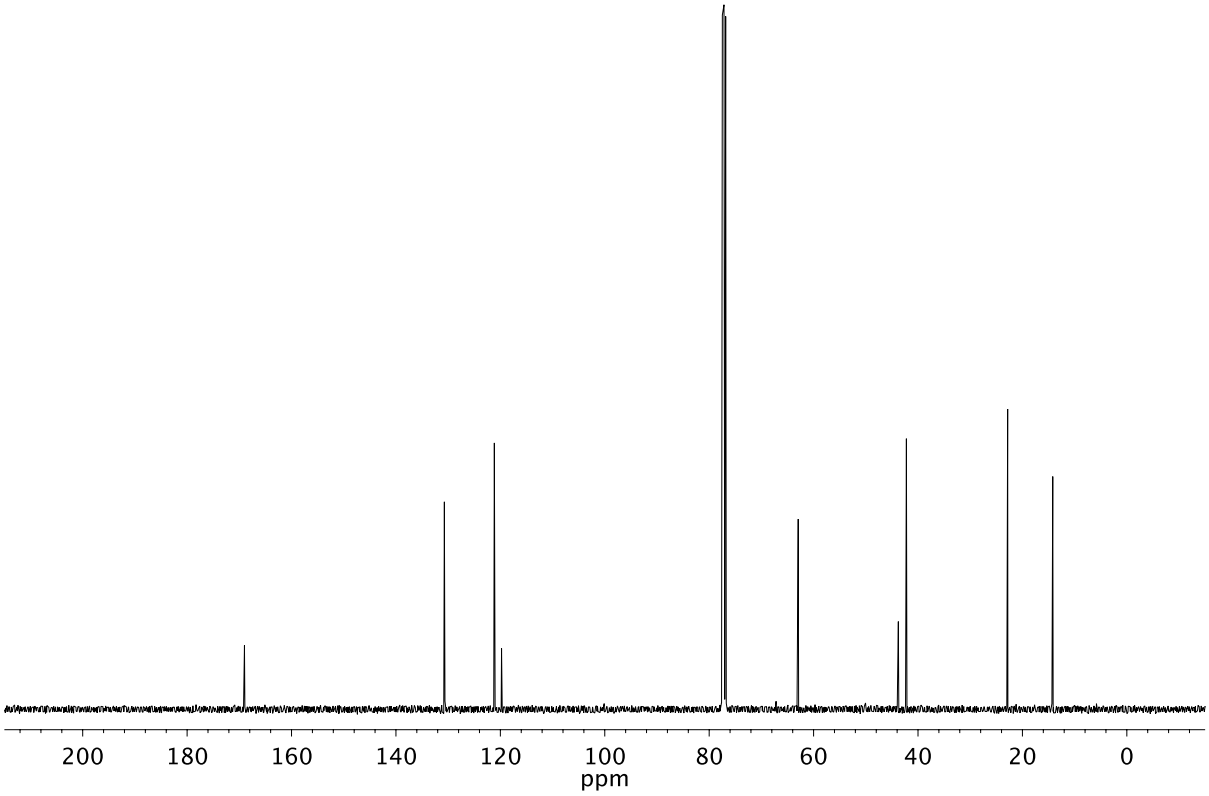
1b



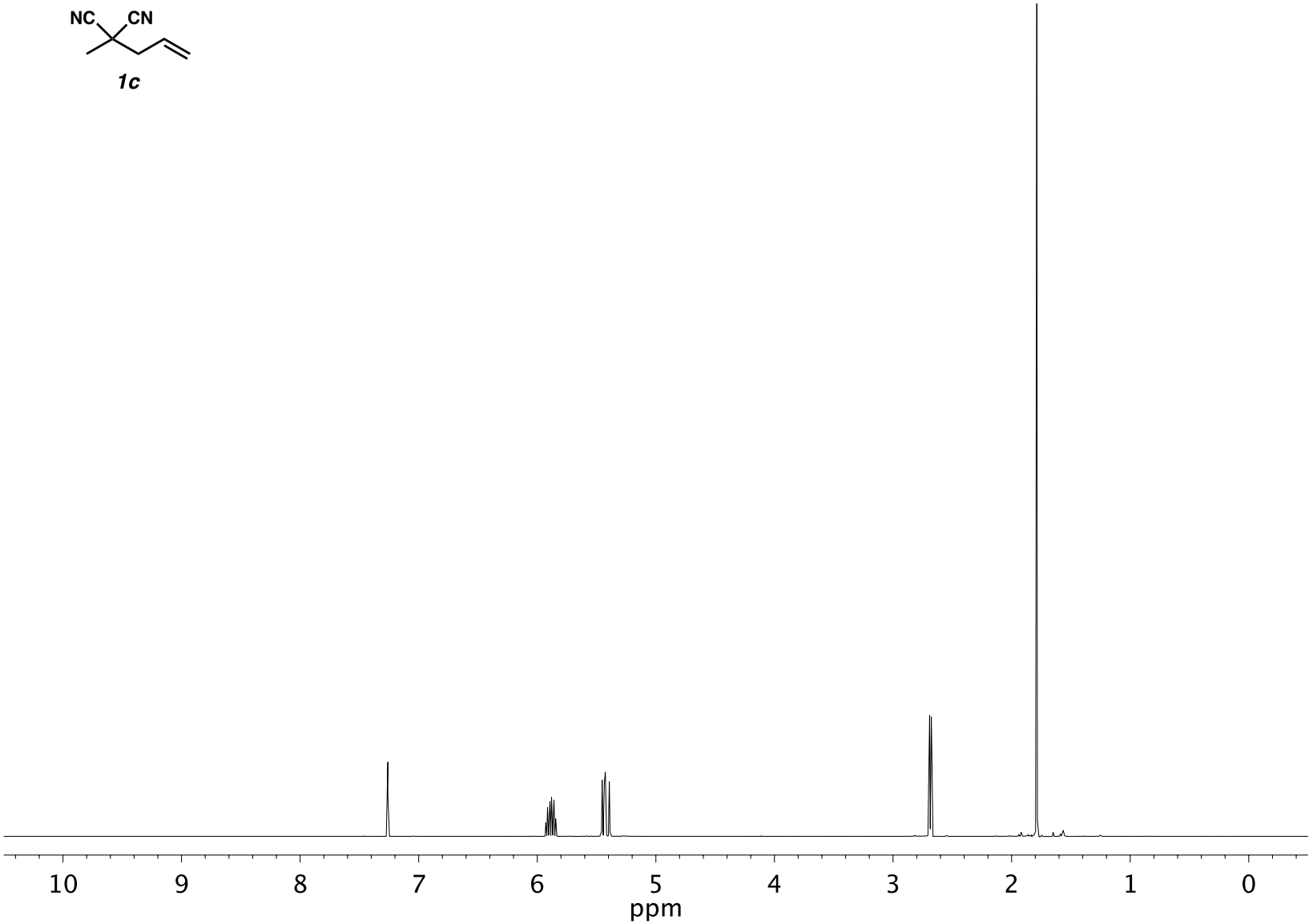
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1b**.



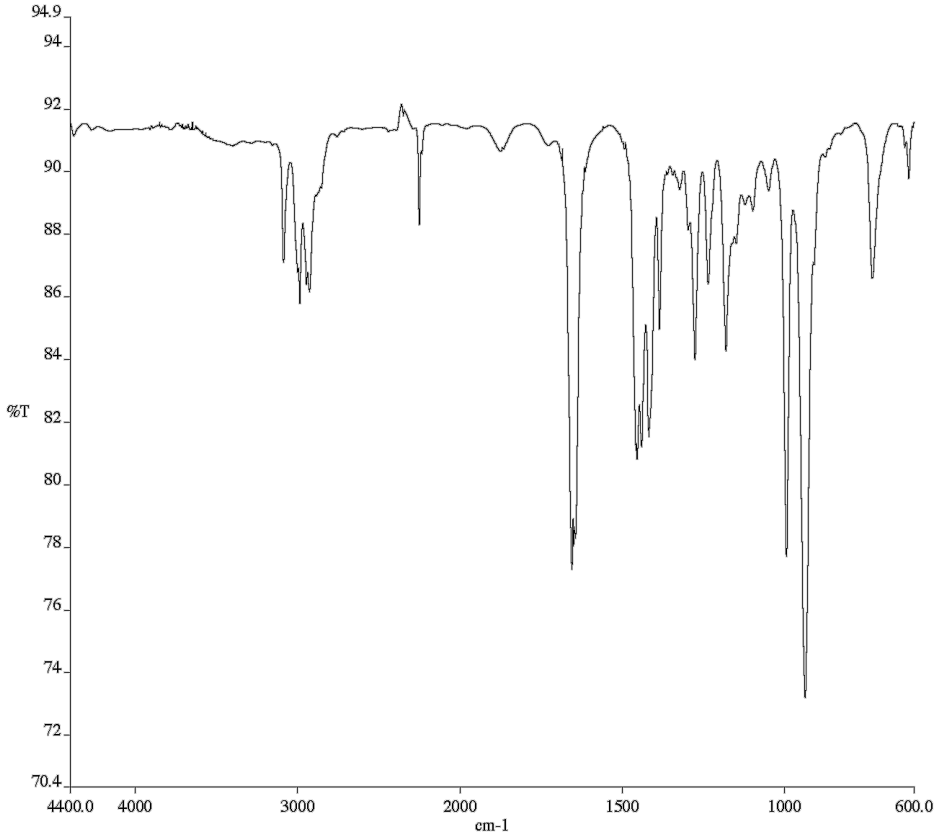
Infrared spectrum (Thin Film, KBr) of compound **1b**.



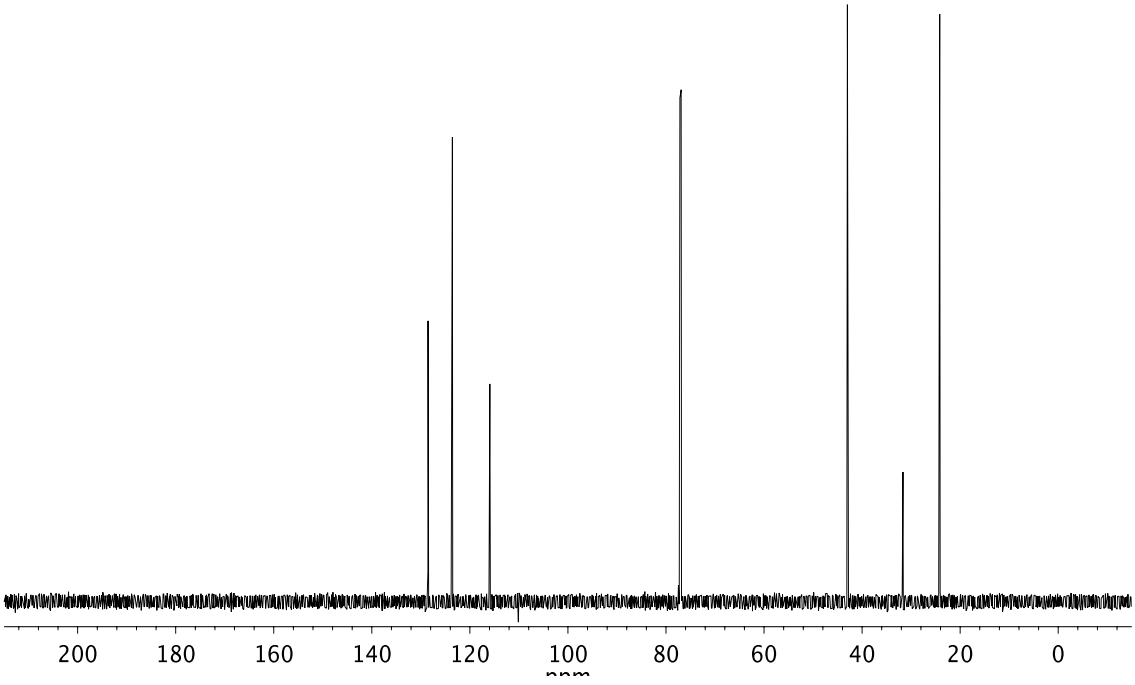
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1b**.



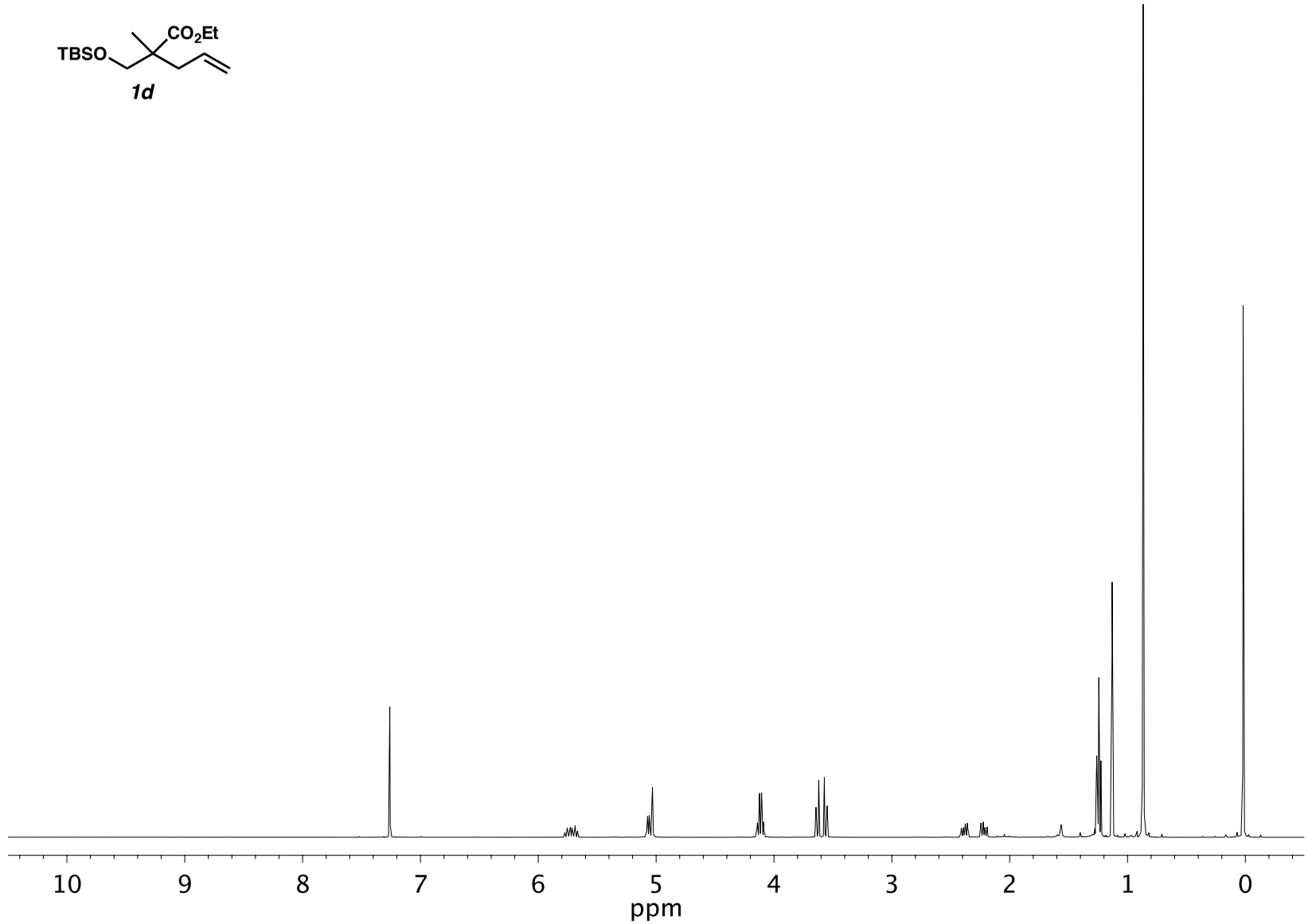
^{1}H NMR (500 MHz, $CDCl_3$) of compound **1c**.



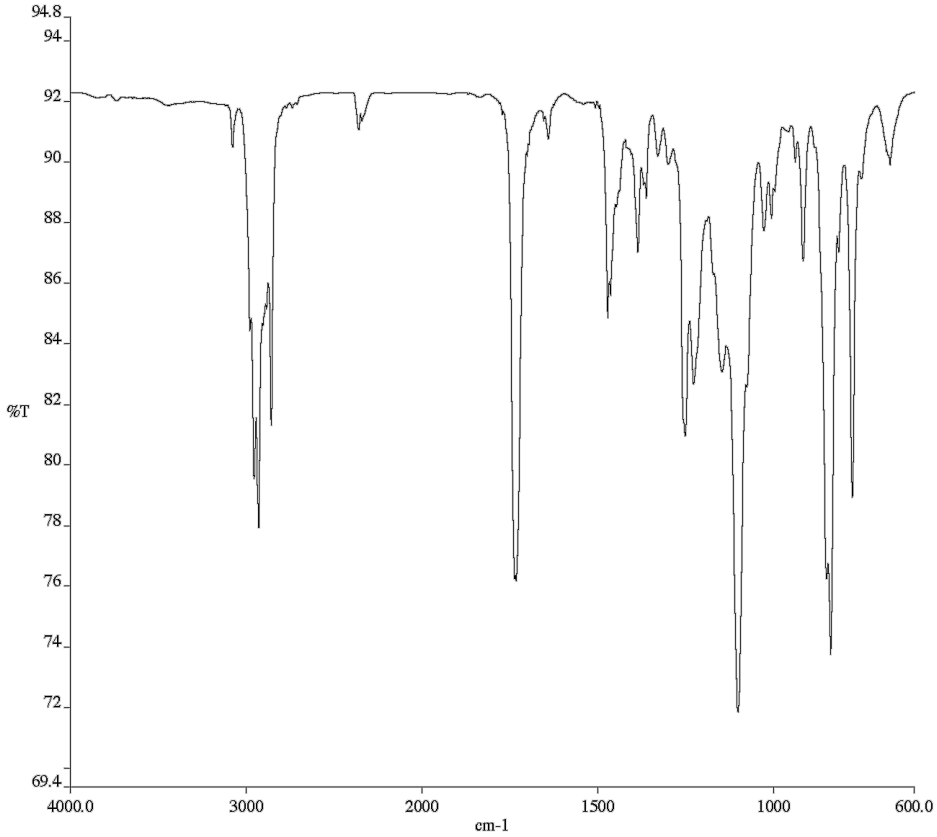
Infrared spectrum (Thin Film, KBr) of compound **1c**.



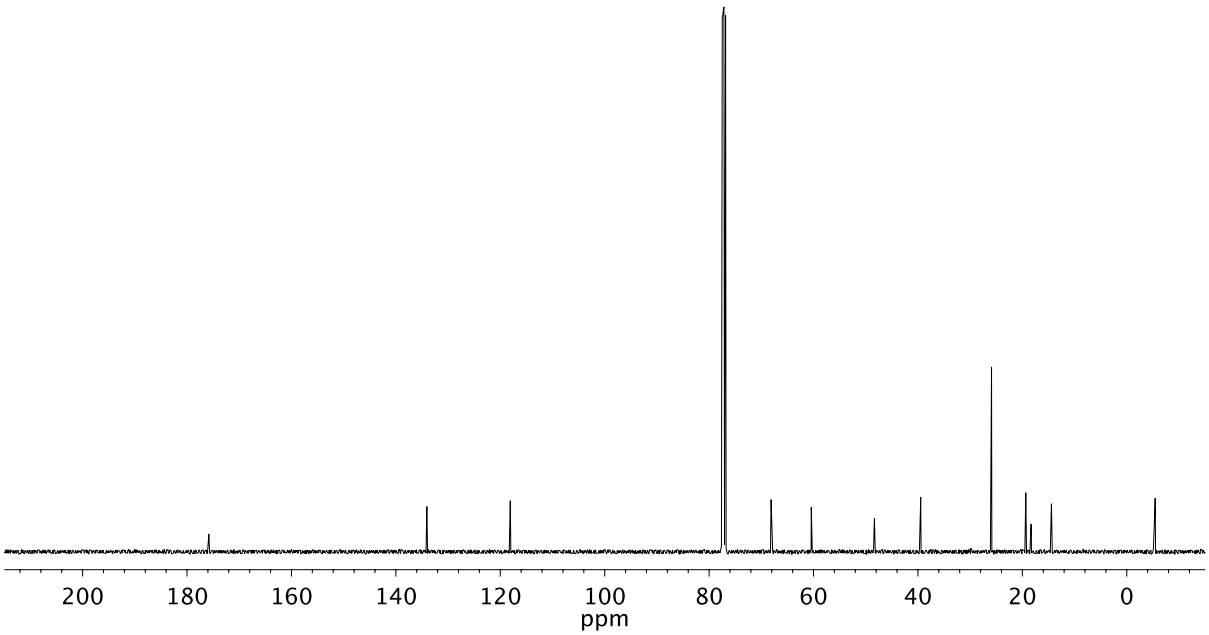
^{13}C NMR (126 MHz, $CDCl_3$) of compound **1c**.



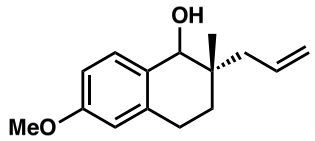
^{1}H NMR (400 MHz, $CDCl_3$) of compound **1d**.



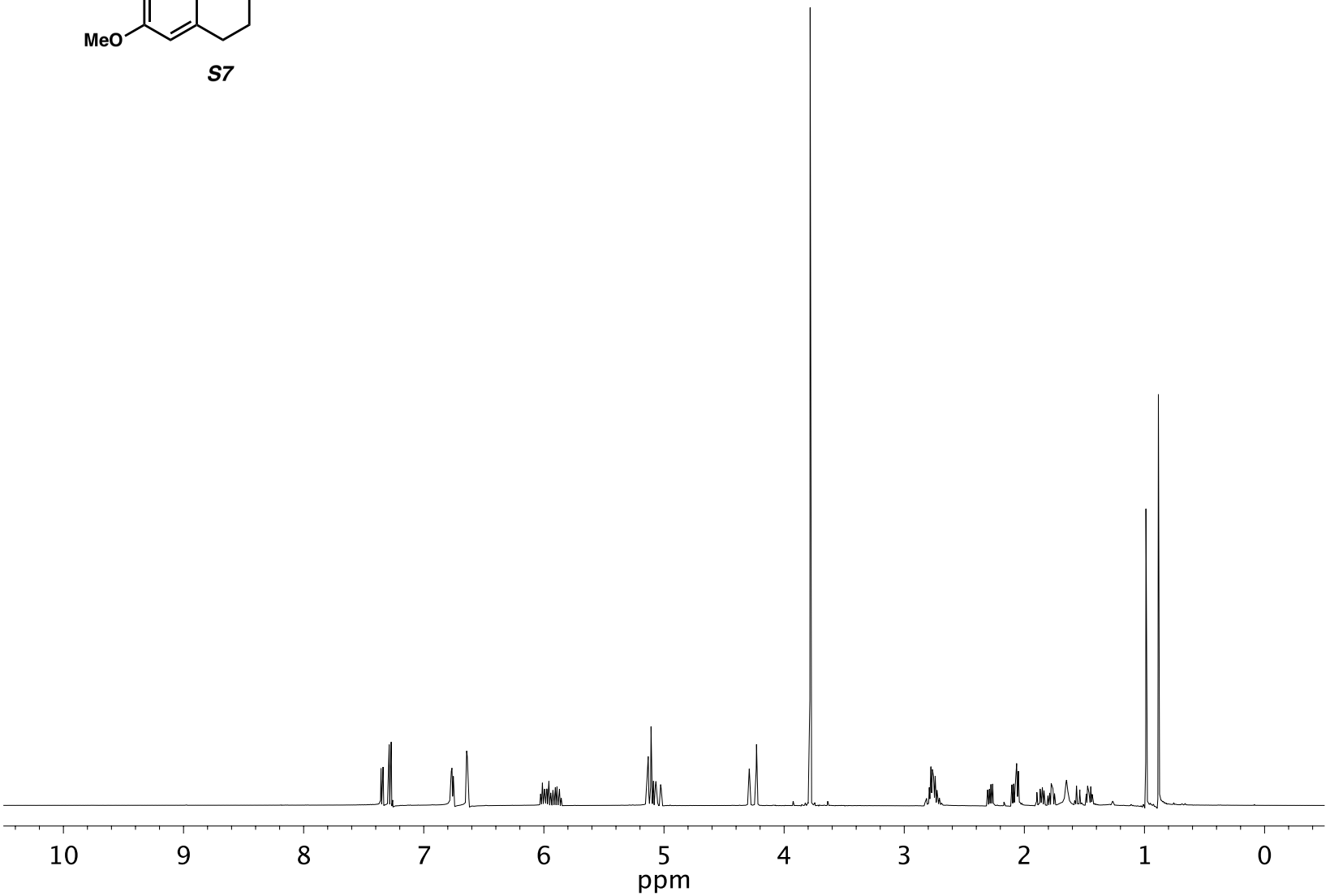
Infrared spectrum (Thin Film, KBr) of compound **1d**.



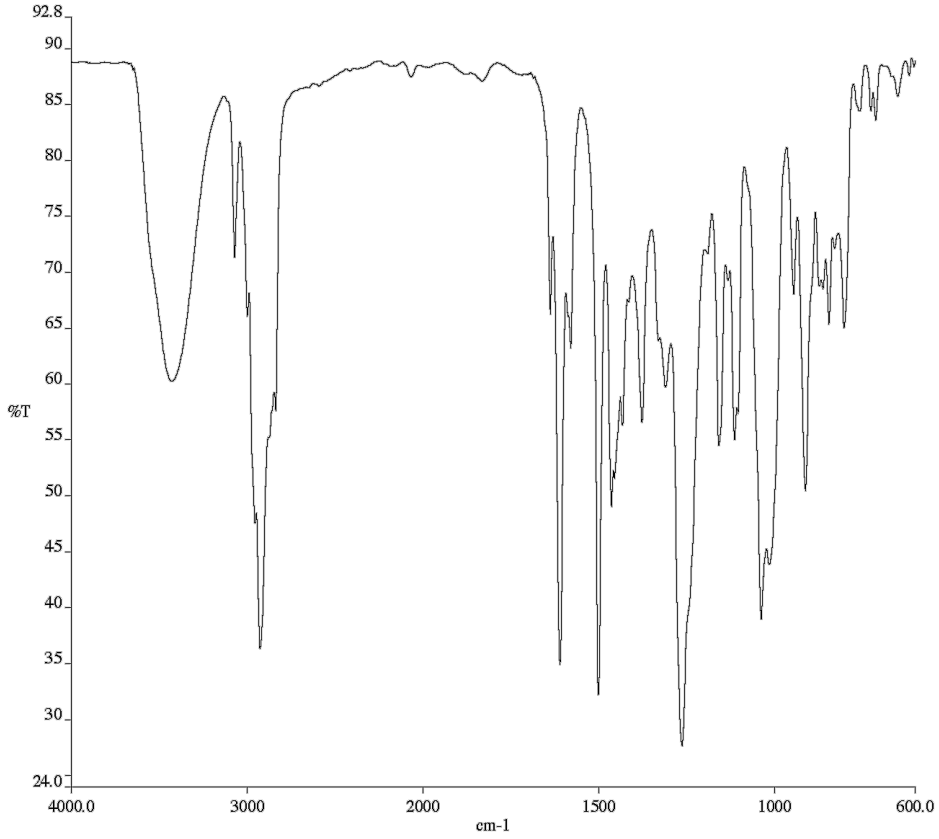
^{13}C NMR (101 MHz, $CDCl_3$) of compound **1d**.



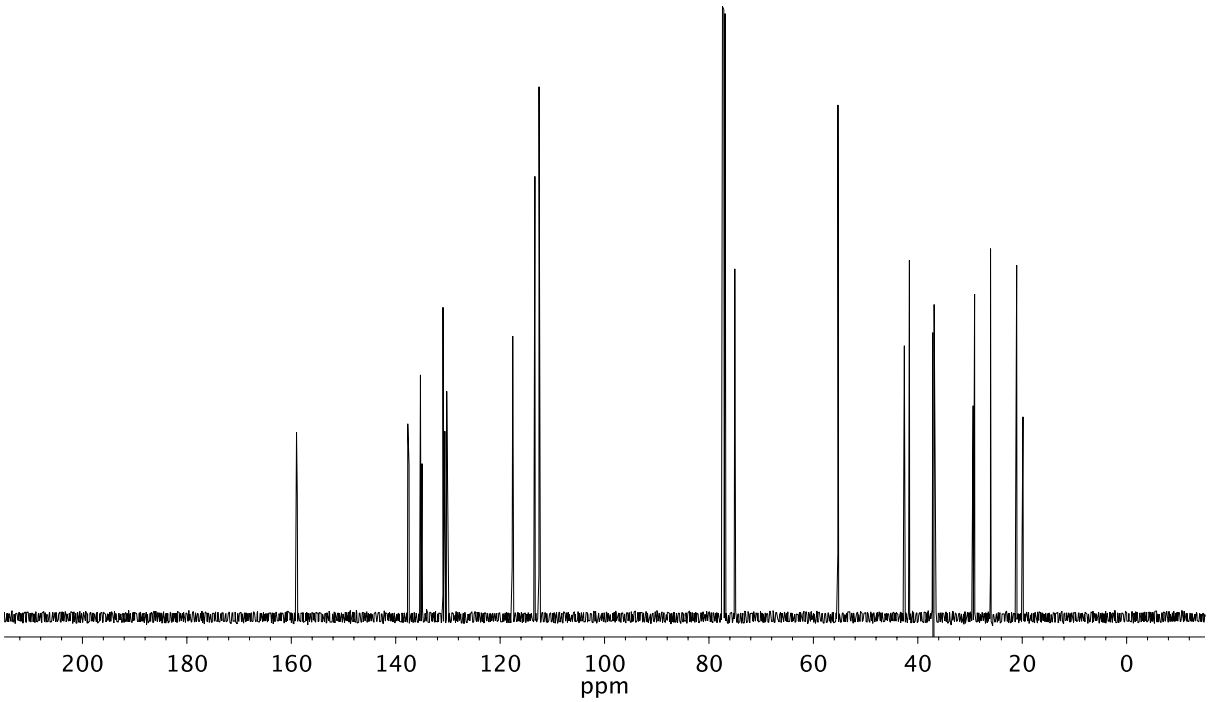
S7



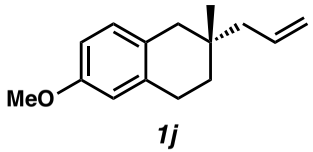
^{1}H NMR (500 MHz, $CDCl_3$) of compound **S7**.



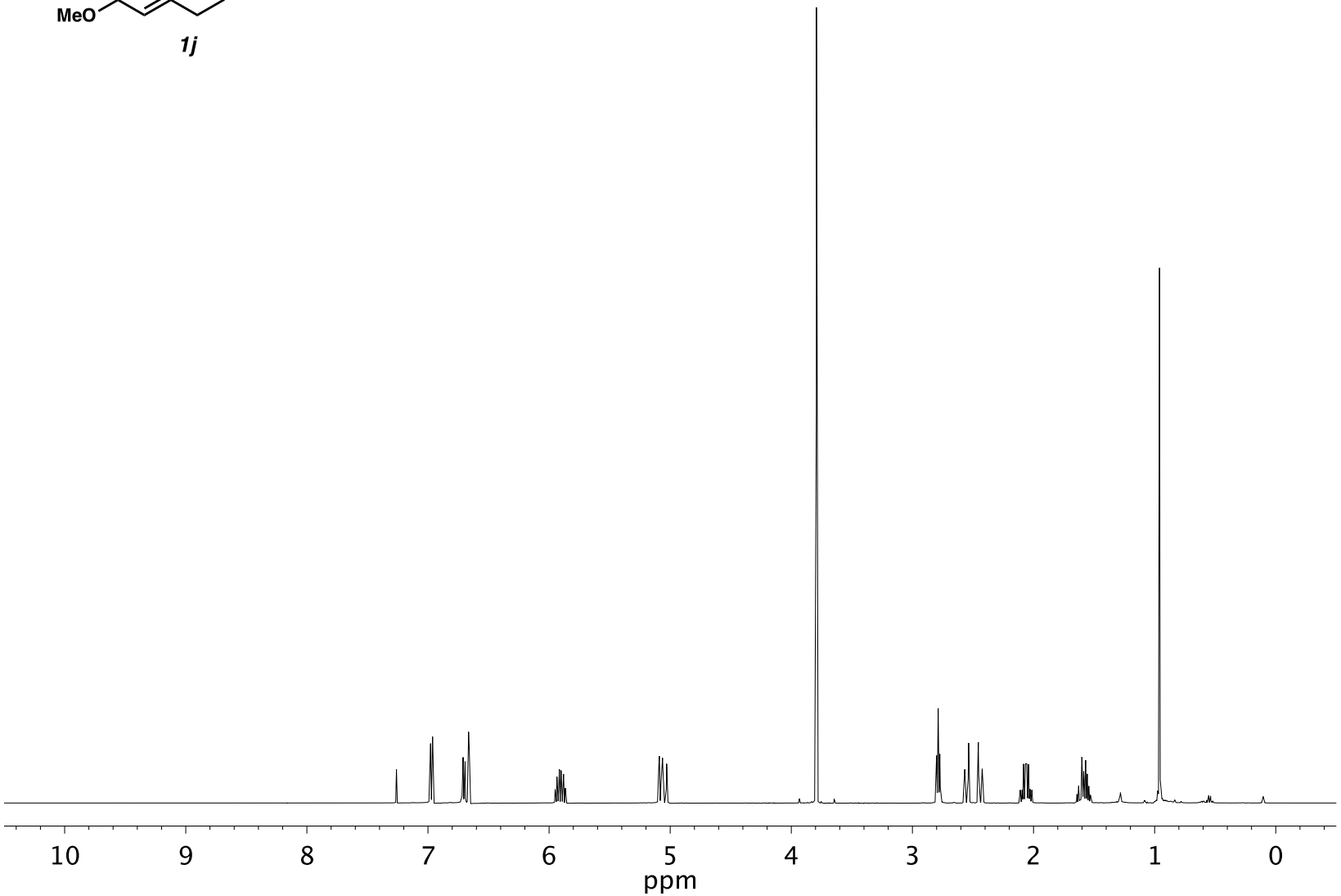
Infrared spectrum (Thin Film, KBr) of compound **S7**.



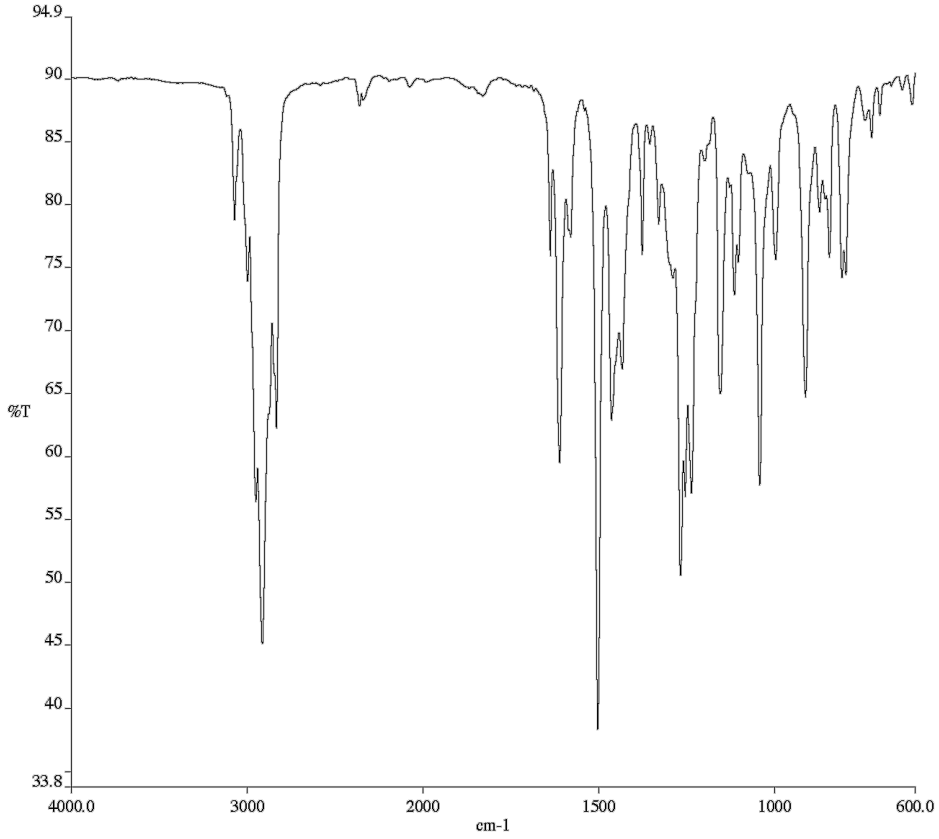
^{13}C NMR (126 MHz, $CDCl_3$) of compound **S7**.



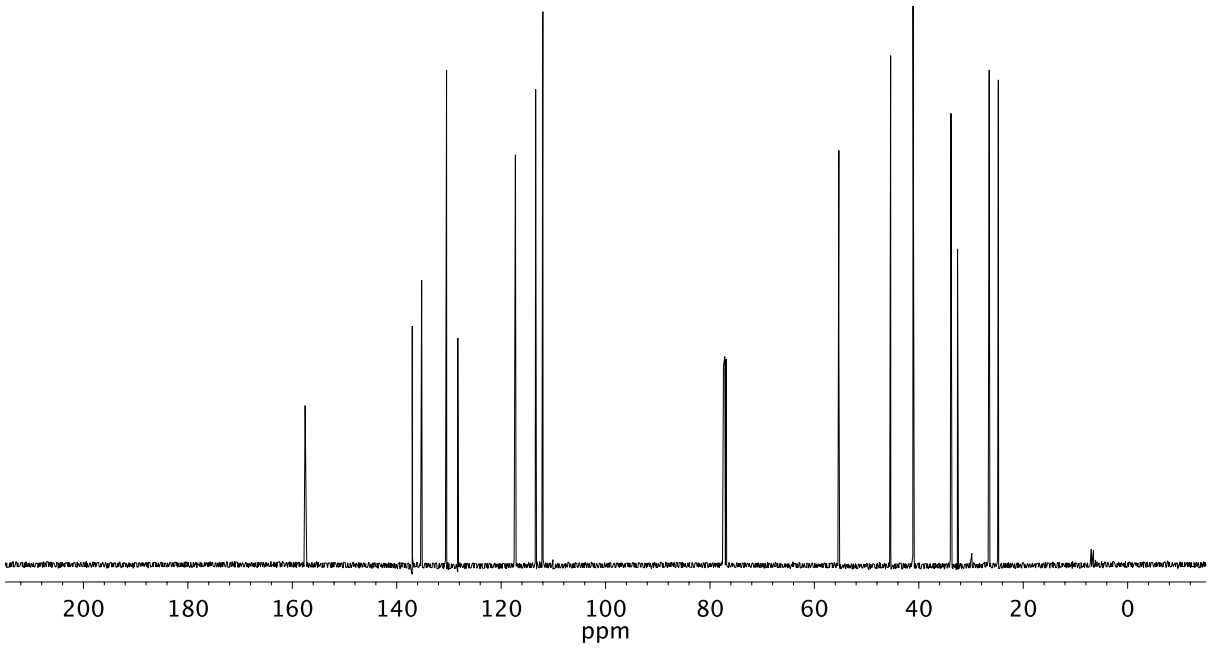
1j



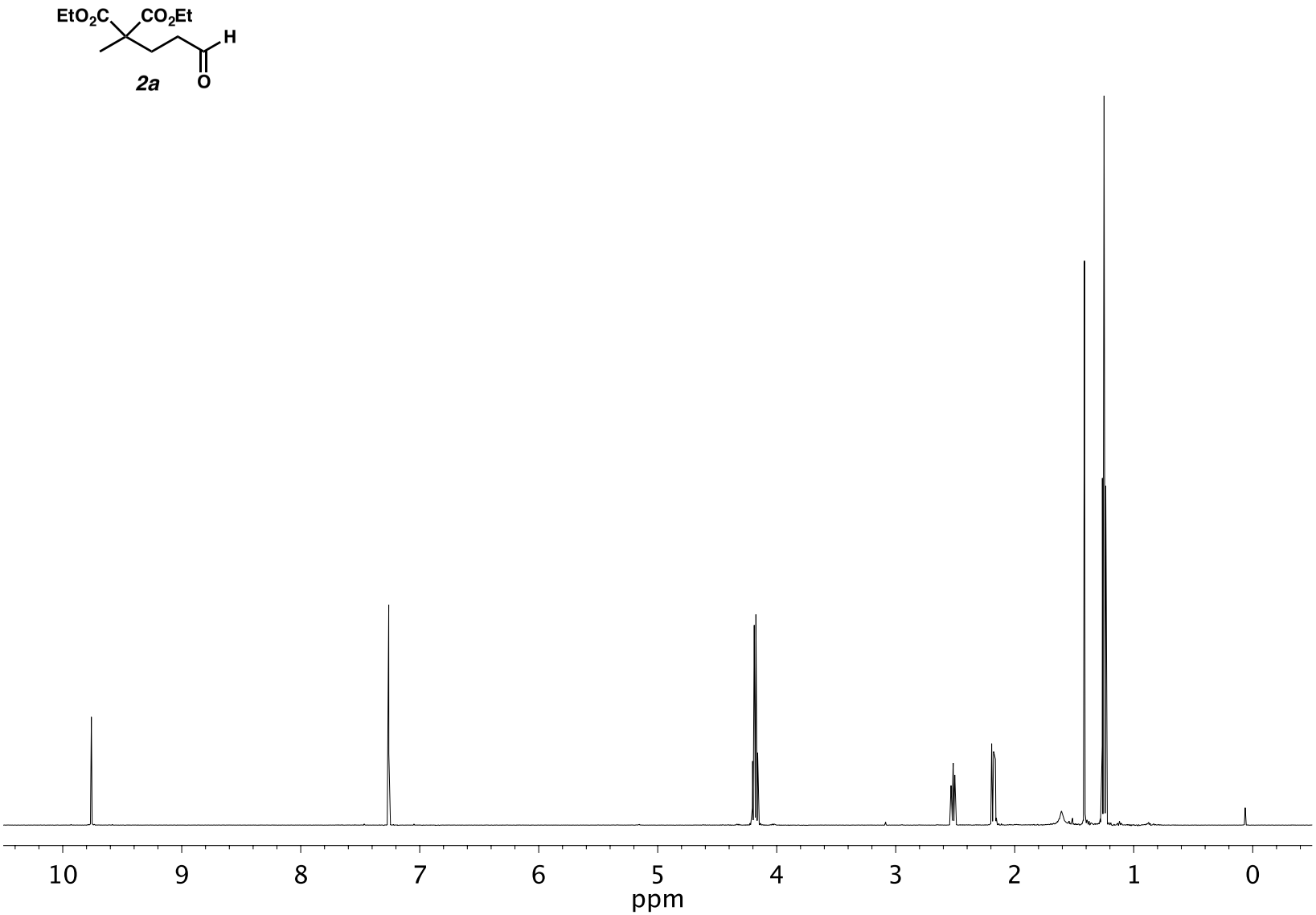
^{1}H NMR (500 MHz, $CDCl_3$) of compound **1j**.



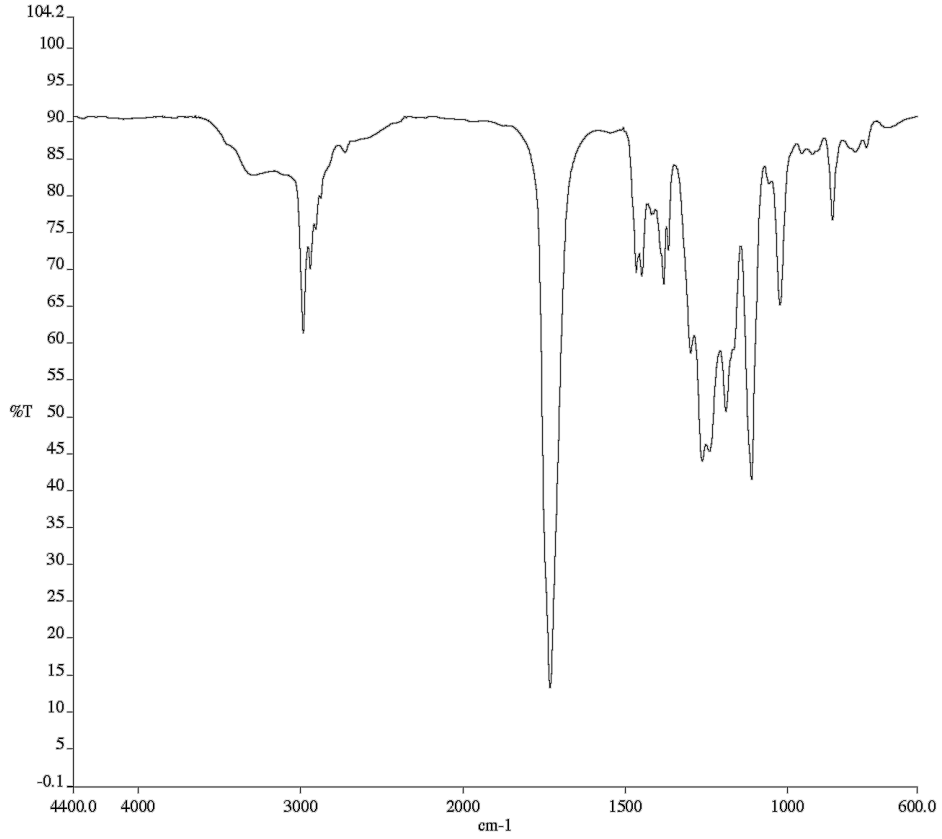
Infrared spectrum (Thin Film, KBr) of compound **1j**.



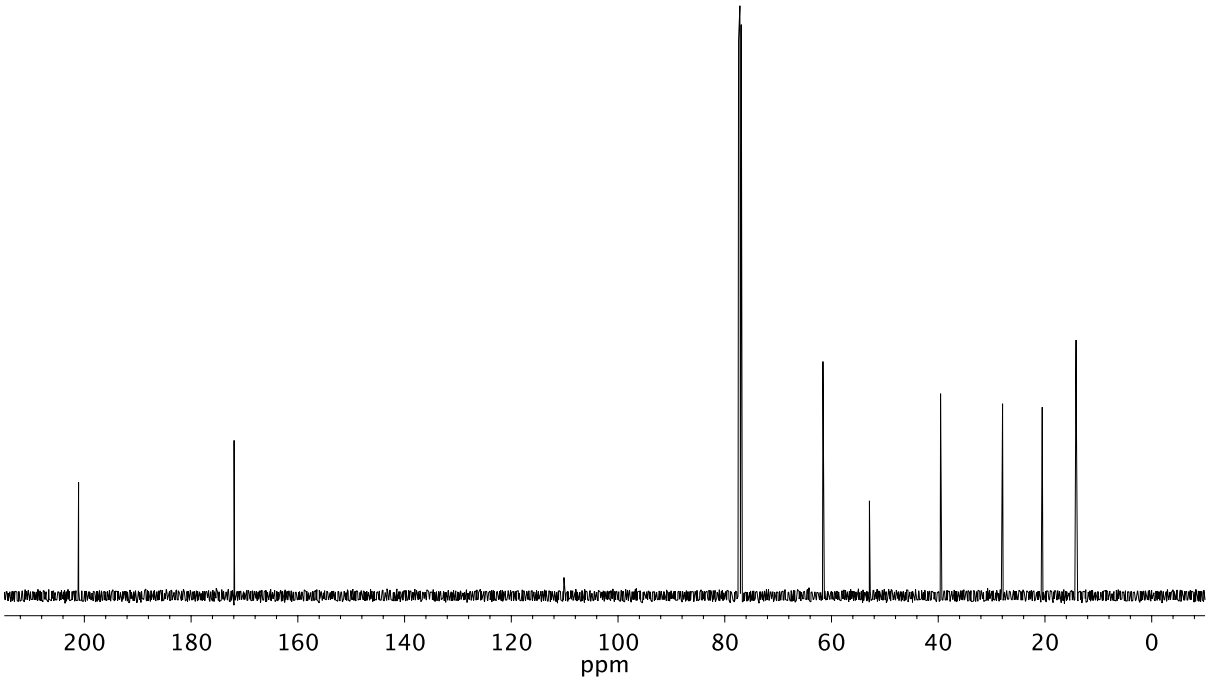
^{13}C NMR (126 MHz, $CDCl_3$) of compound **1j**.



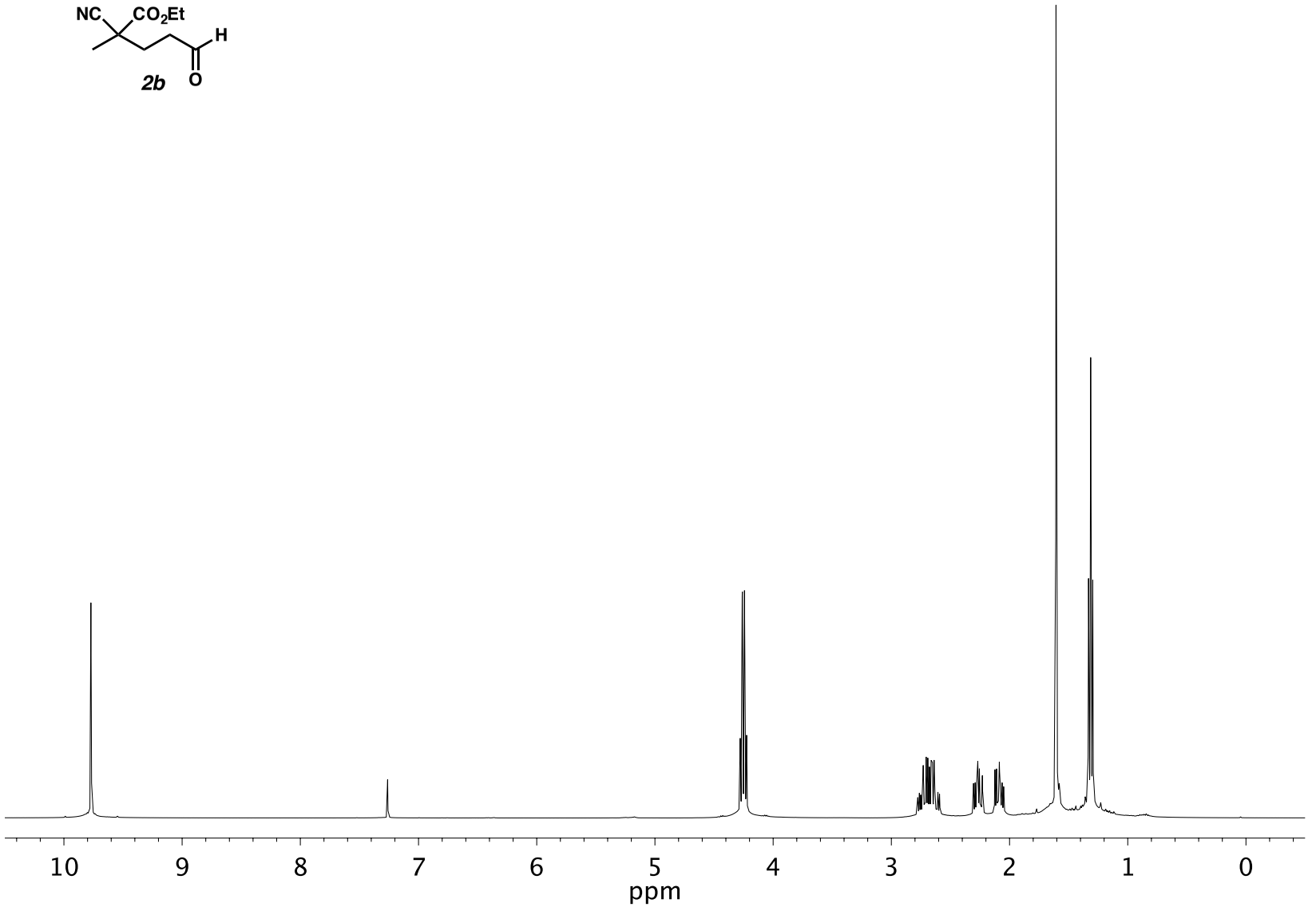
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**.



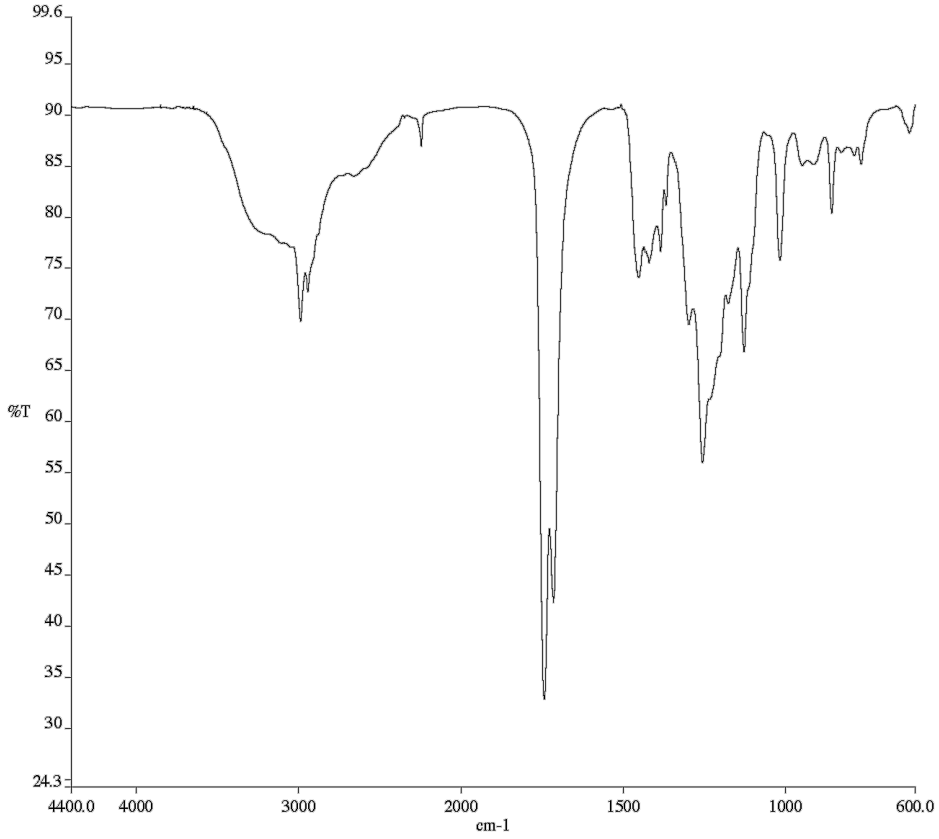
Infrared spectrum (Thin Film, KBr) of compound **2a**.



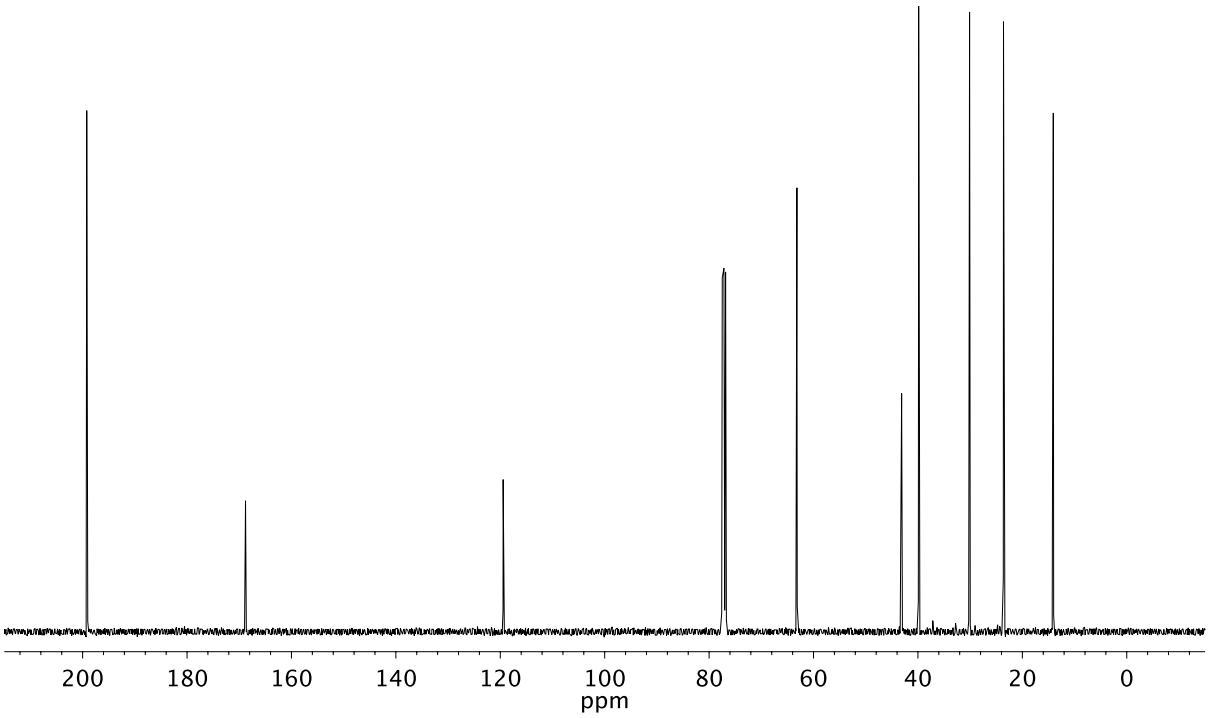
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2a**.



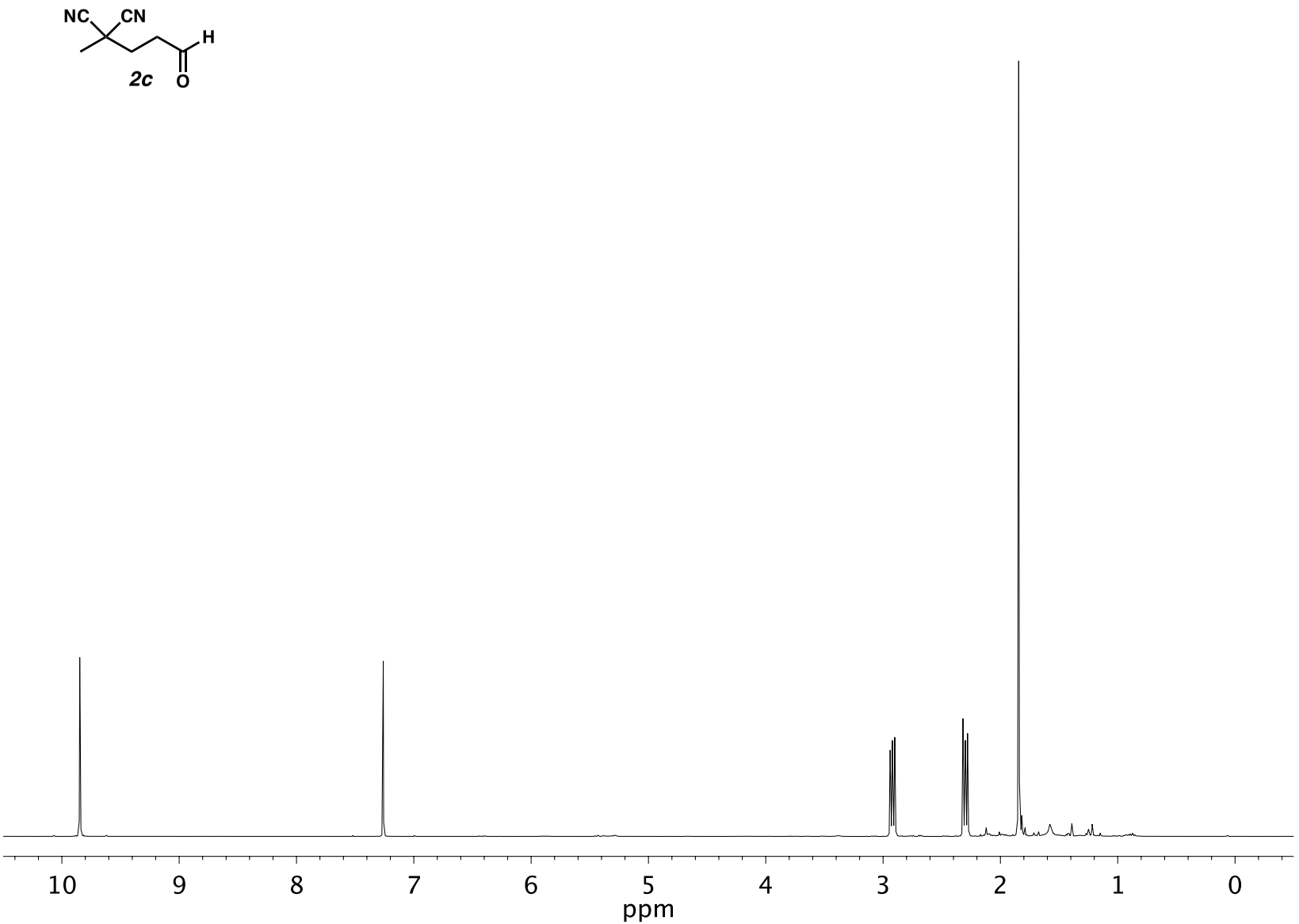
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2b**.



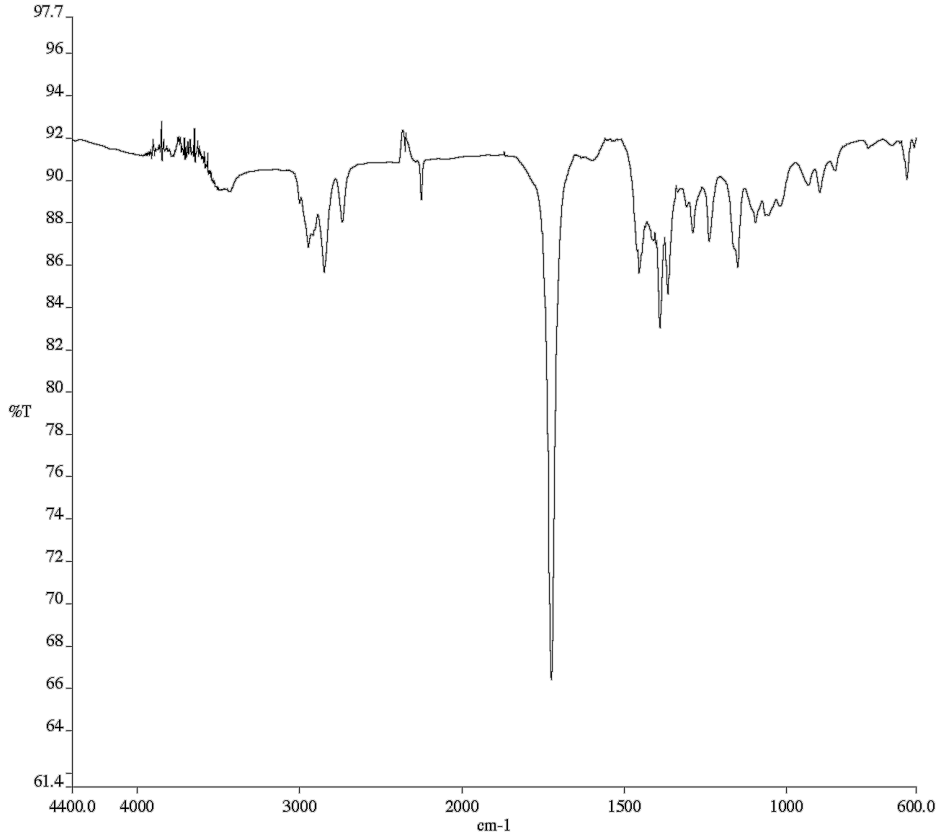
Infrared spectrum (Thin Film, KBr) of compound **2b**.



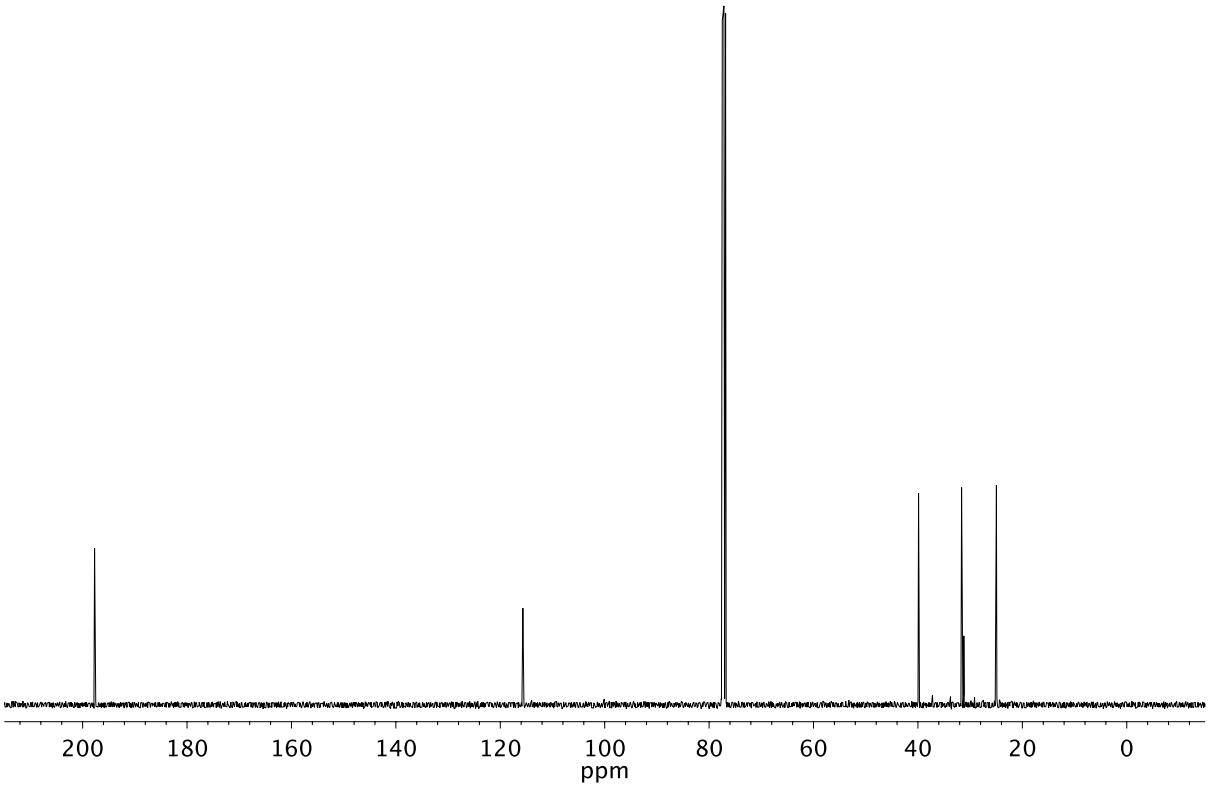
^{13}C NMR (101 MHz, $CDCl_3$) of compound **2b**.



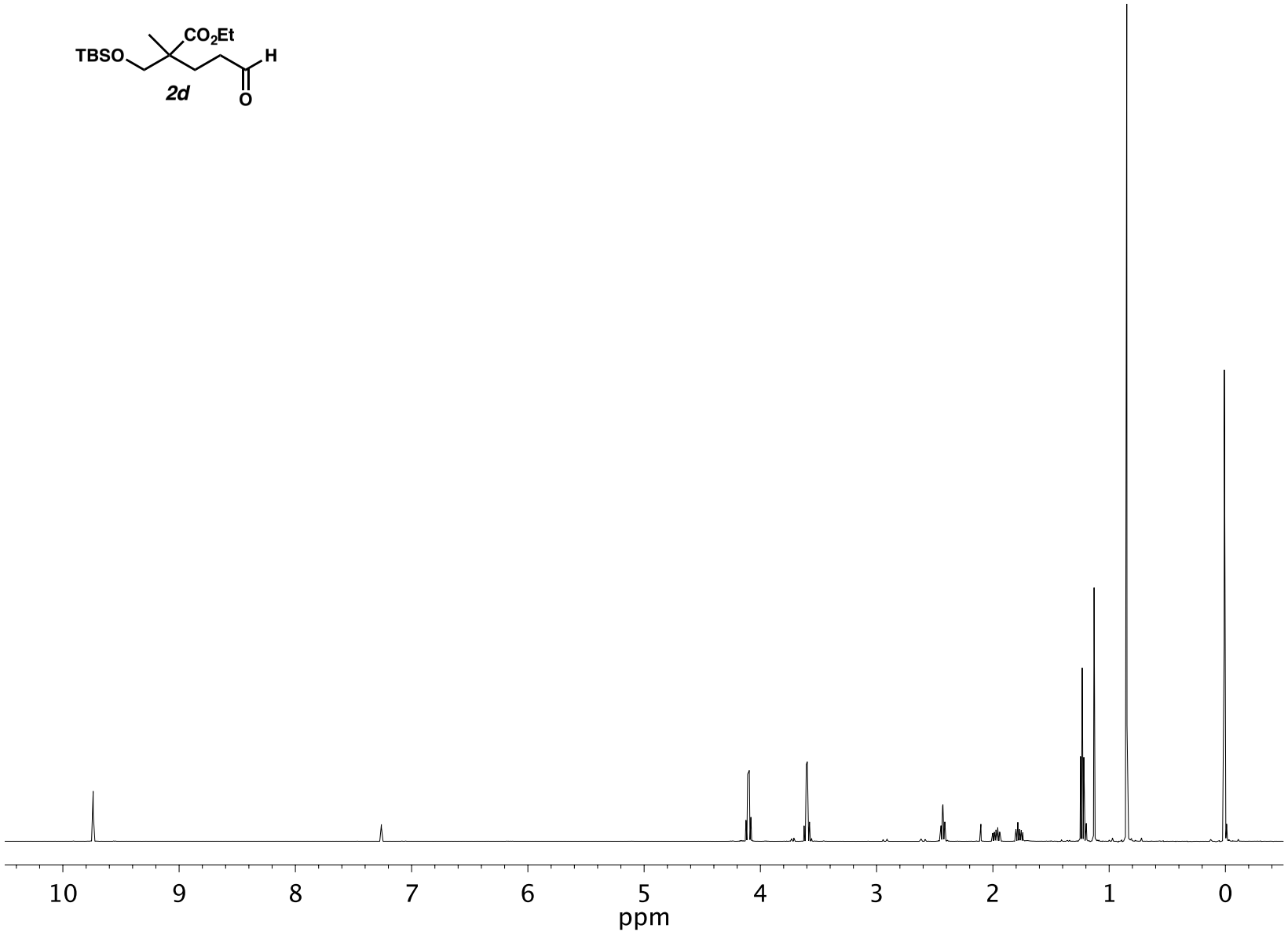
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2c**.



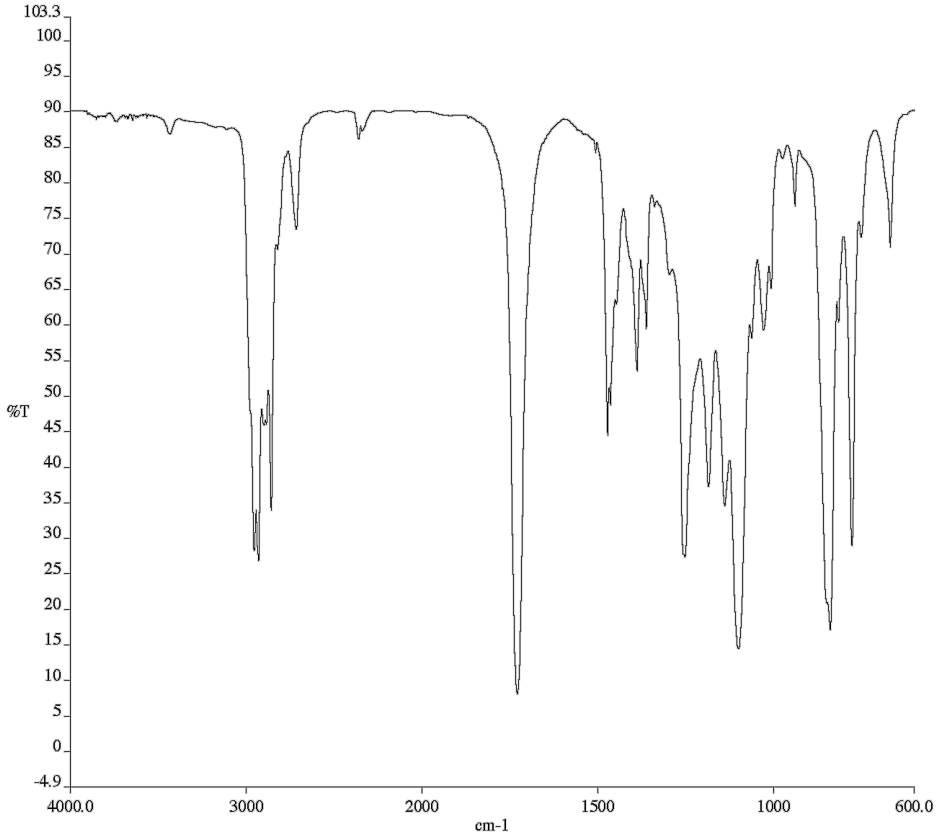
Infrared spectrum (Thin Film, KBr) of compound **2c**.



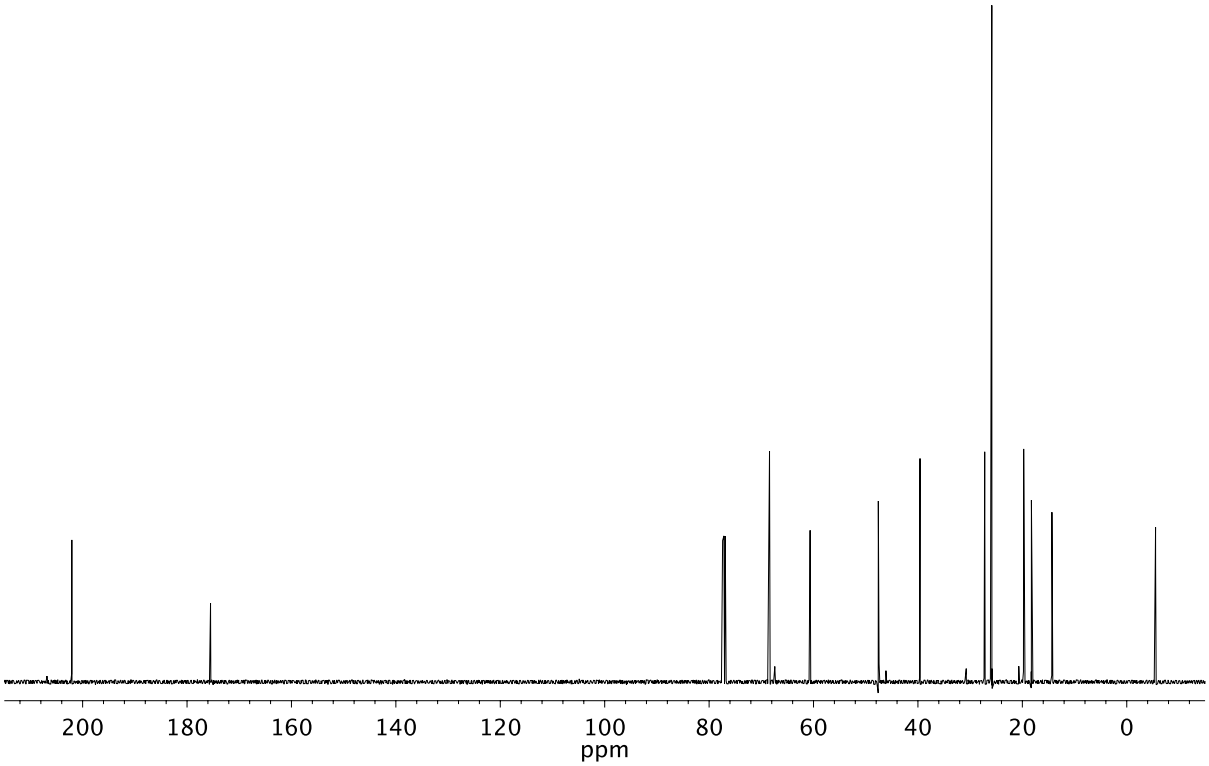
^{13}C NMR (101 MHz, $CDCl_3$) of compound **2c**.



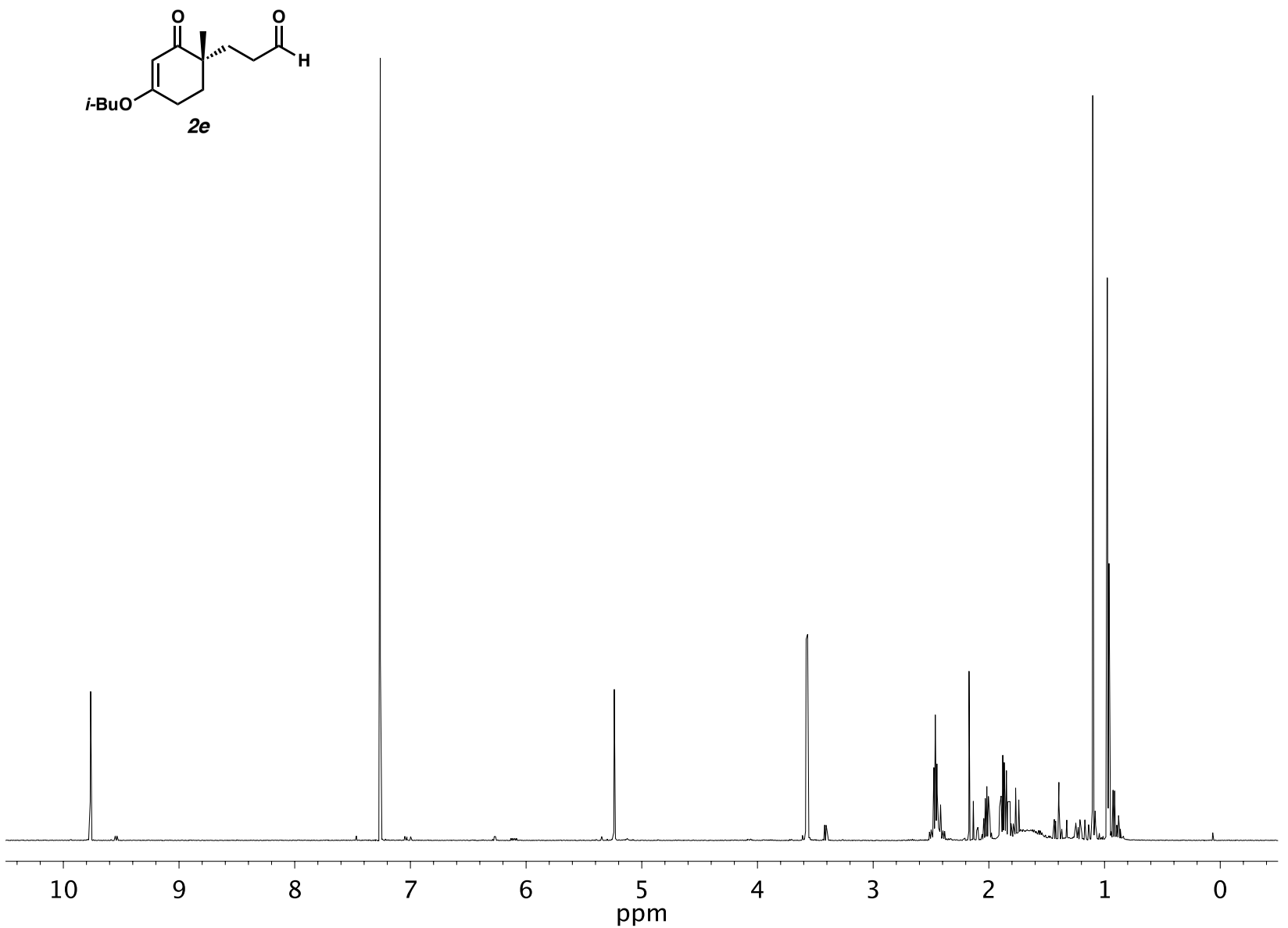
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2d**.



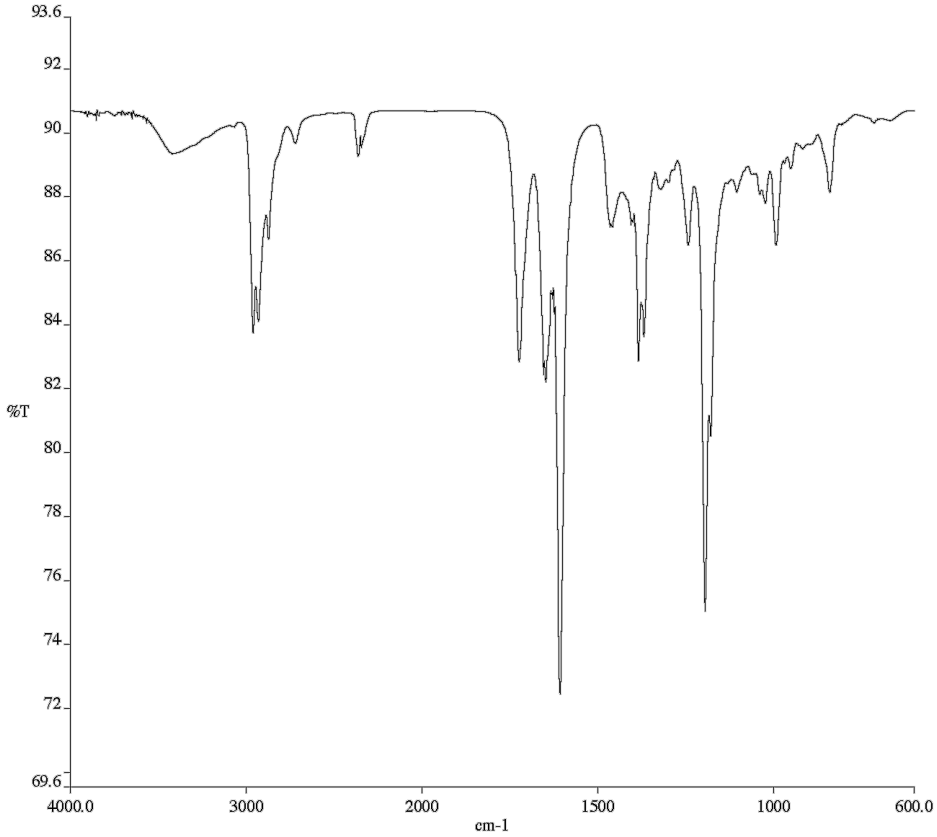
Infrared spectrum (Thin Film, KBr) of compound **2d**.



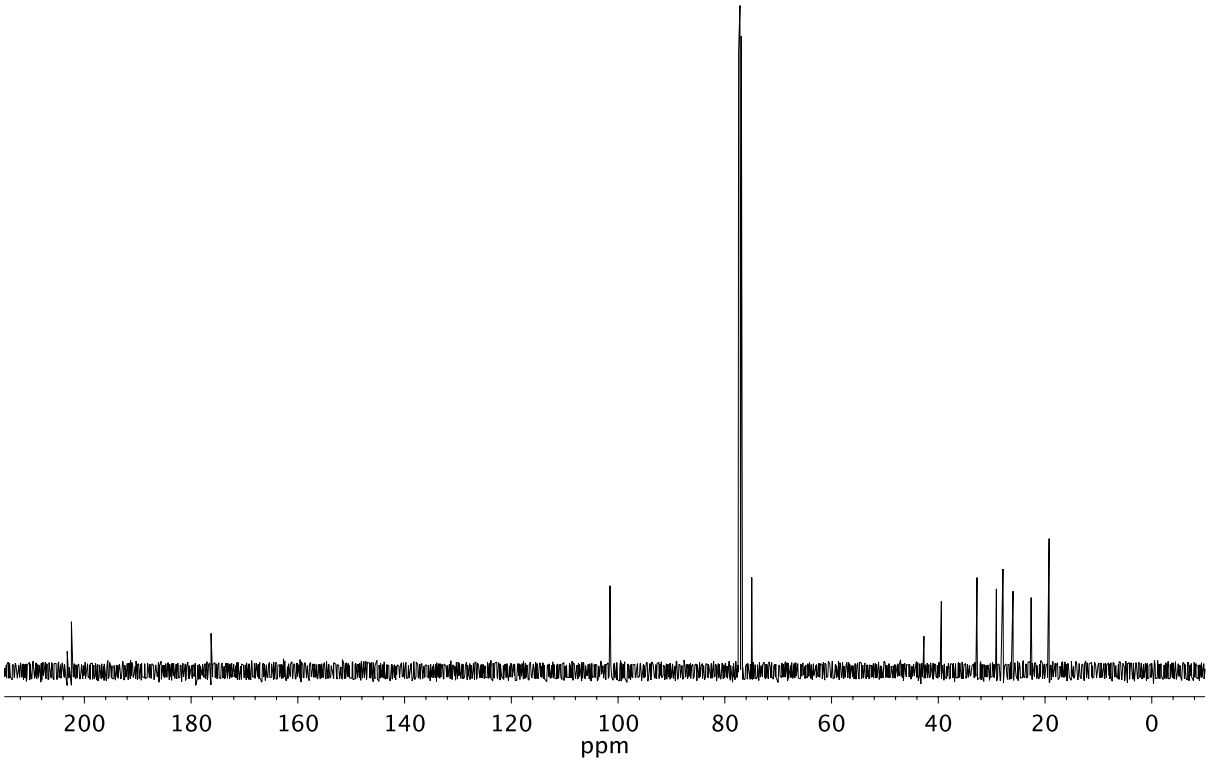
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2d**.



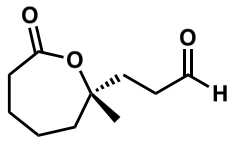
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2e**.



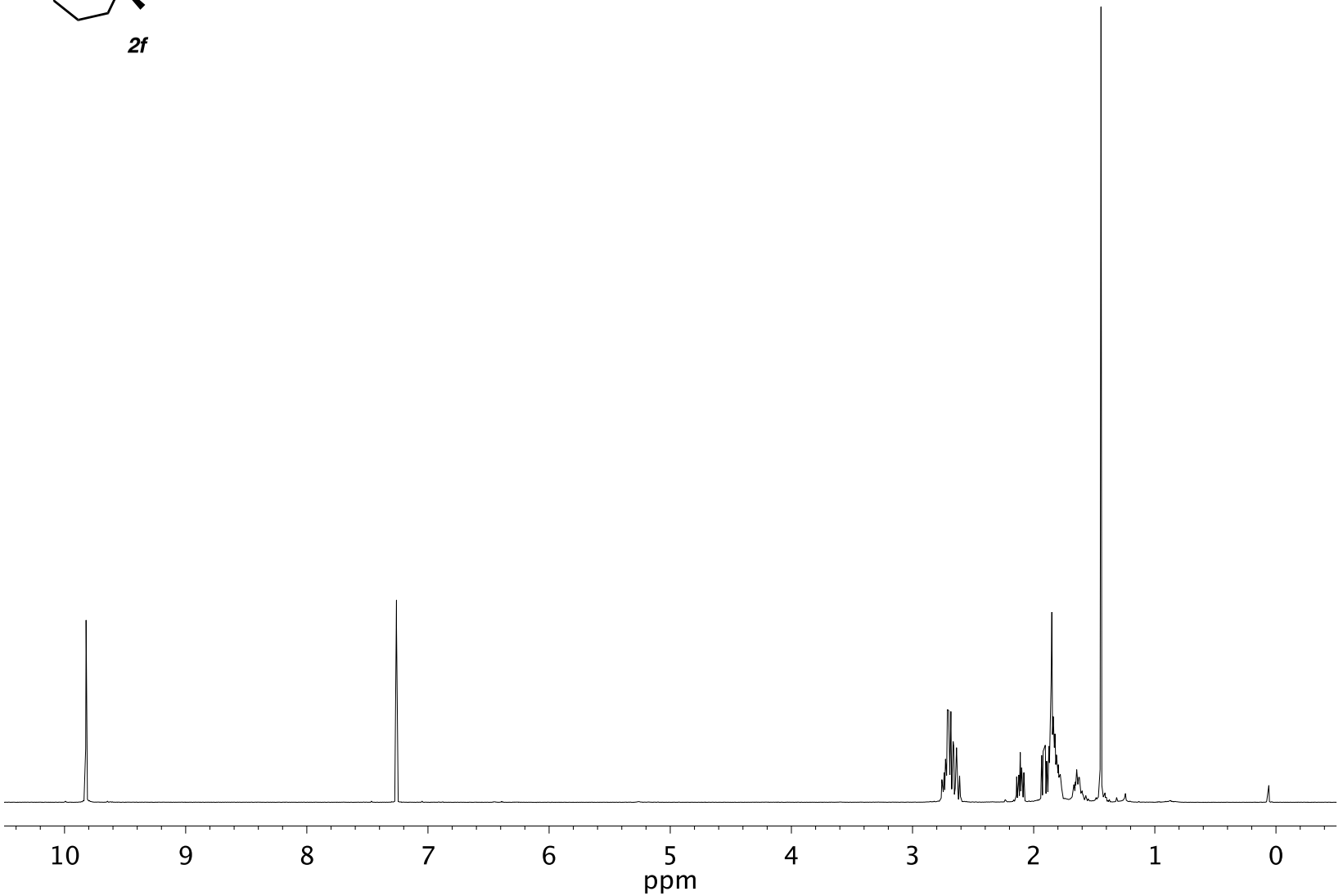
Infrared spectrum (Thin Film, KBr) of compound **2e**.



^{13}C NMR (126 MHz, $CDCl_3$) of compound **2e**.



2f



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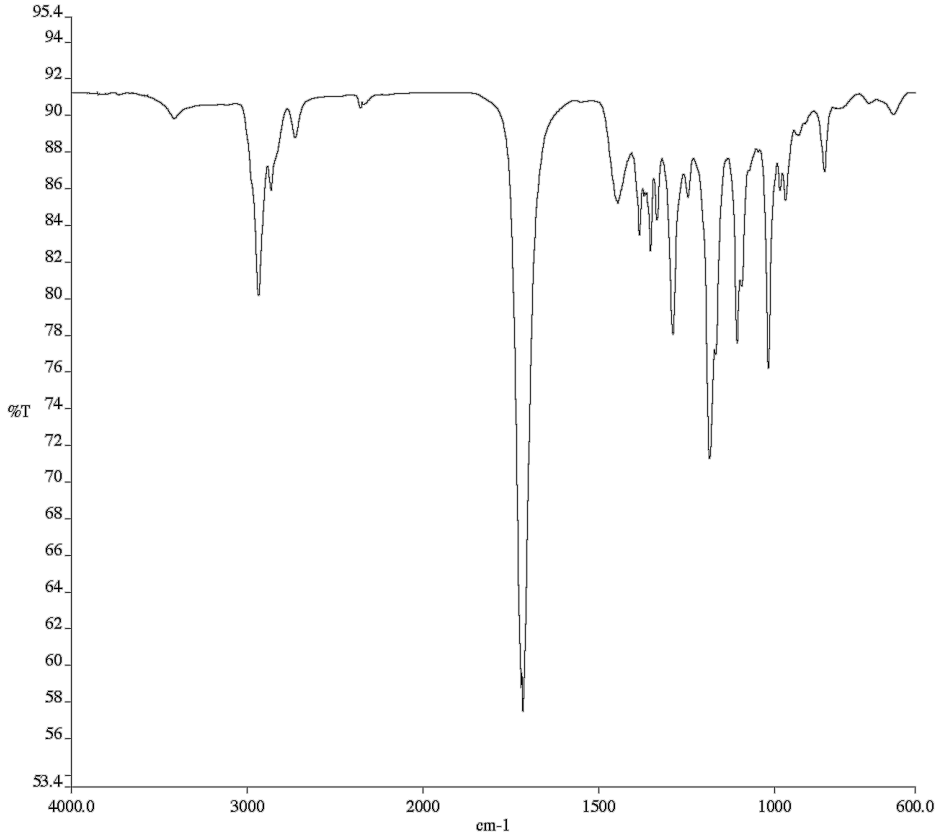
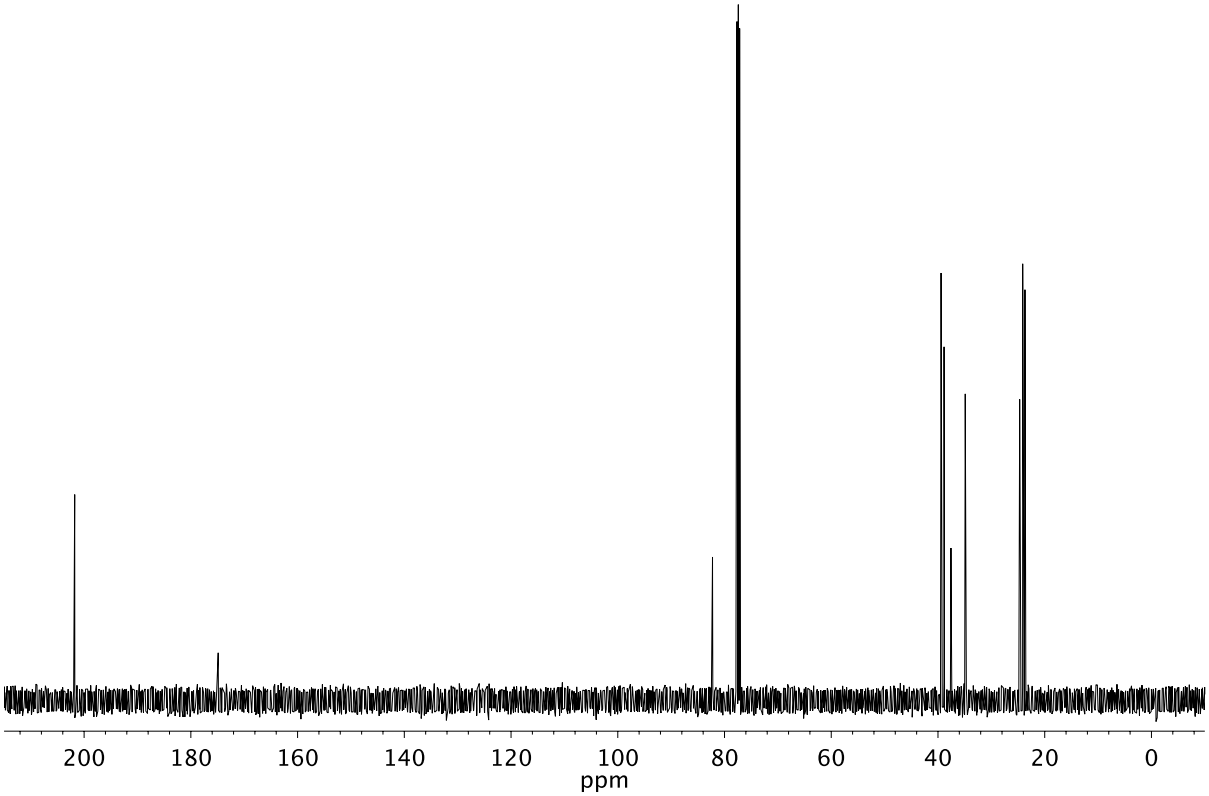
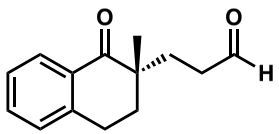


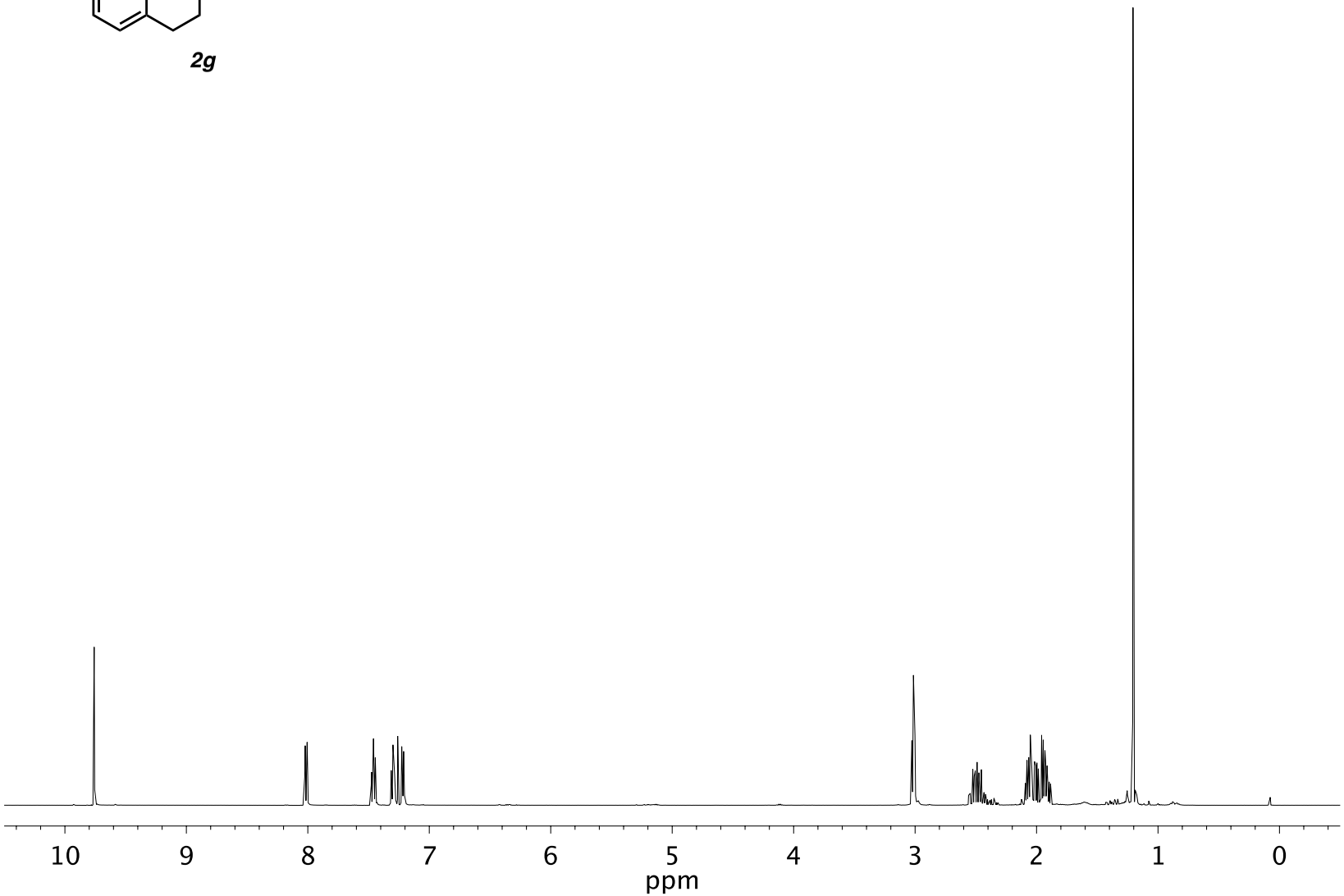
Infrared spectrum (Thin Film, KBr) of compound **2f**.



^{13}C NMR (126 MHz, $CDCl_3$) of compound **2f**.



2g



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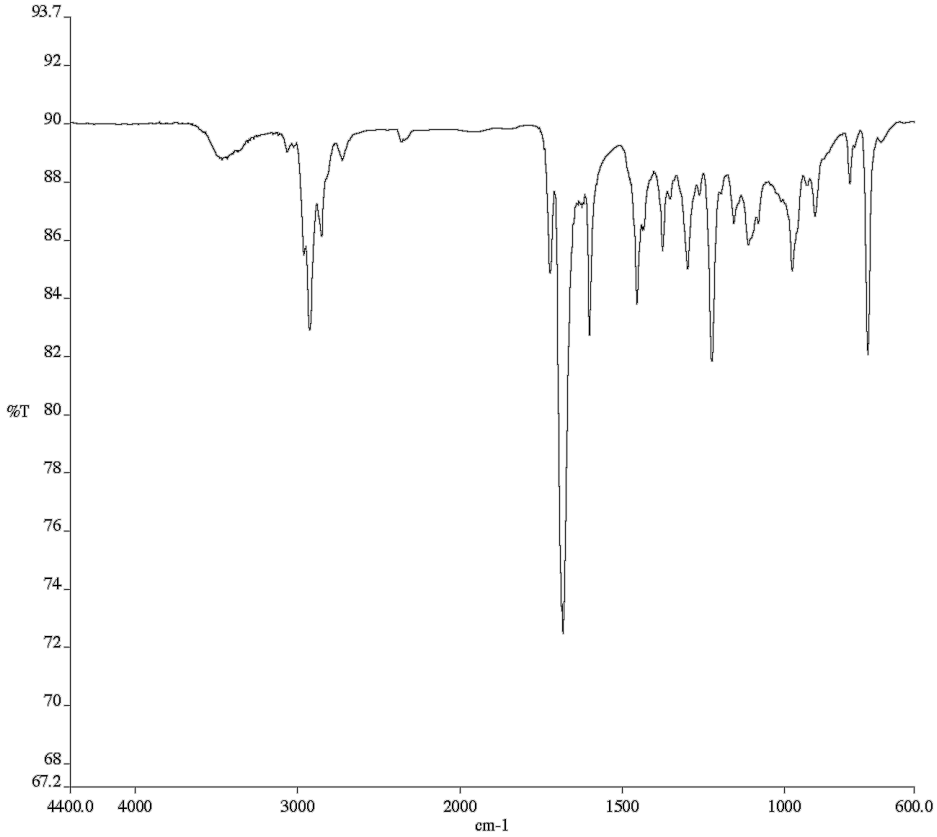
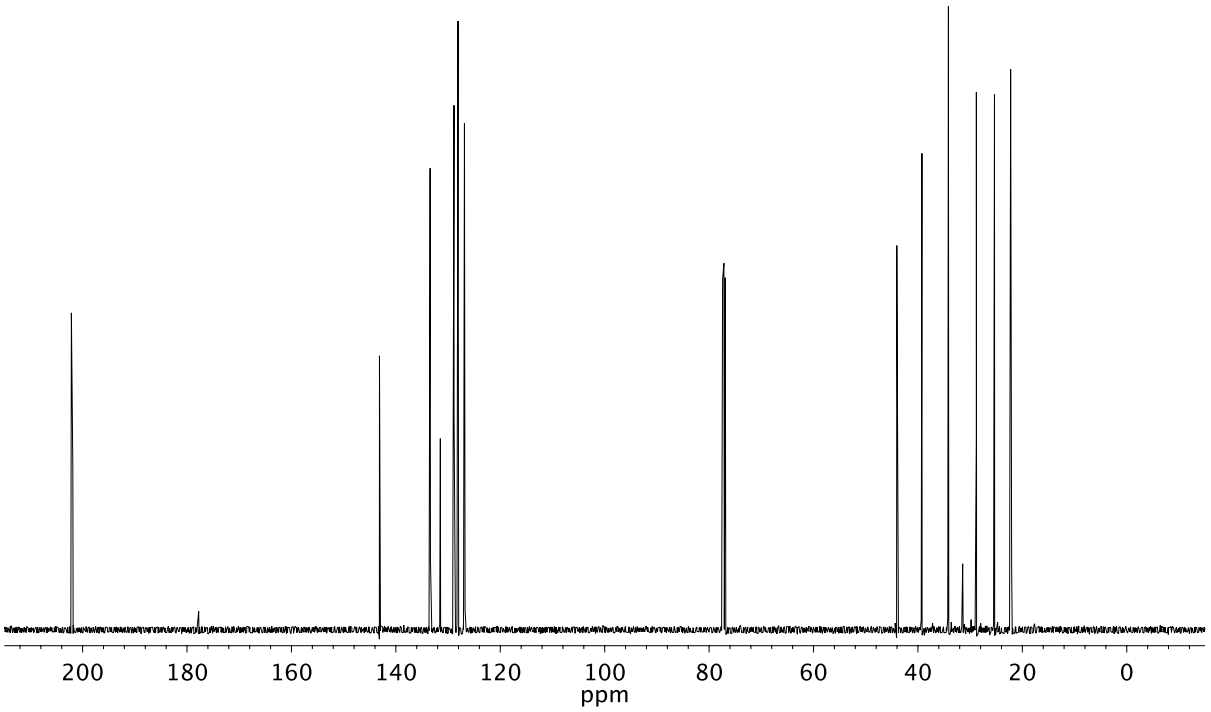
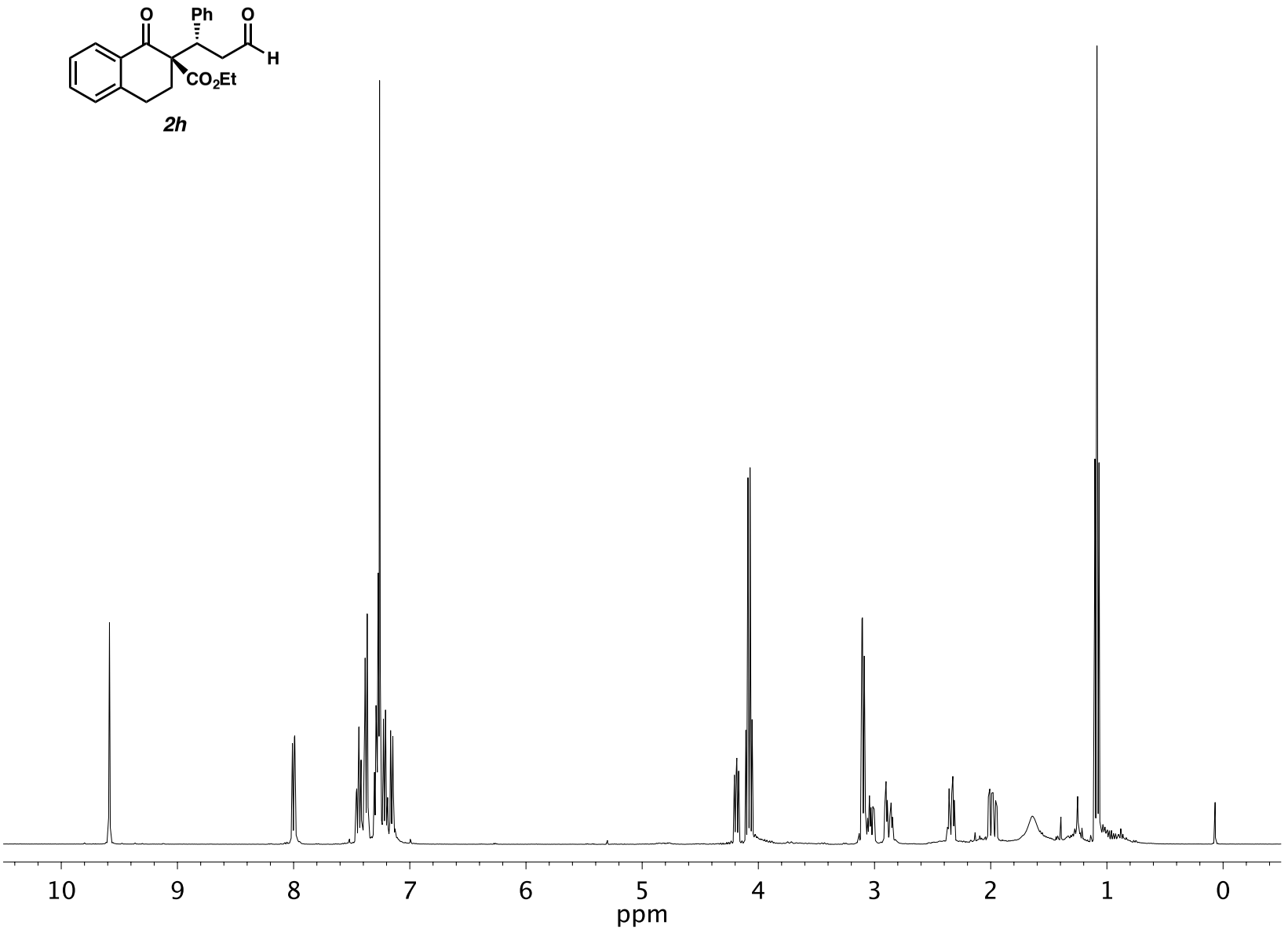


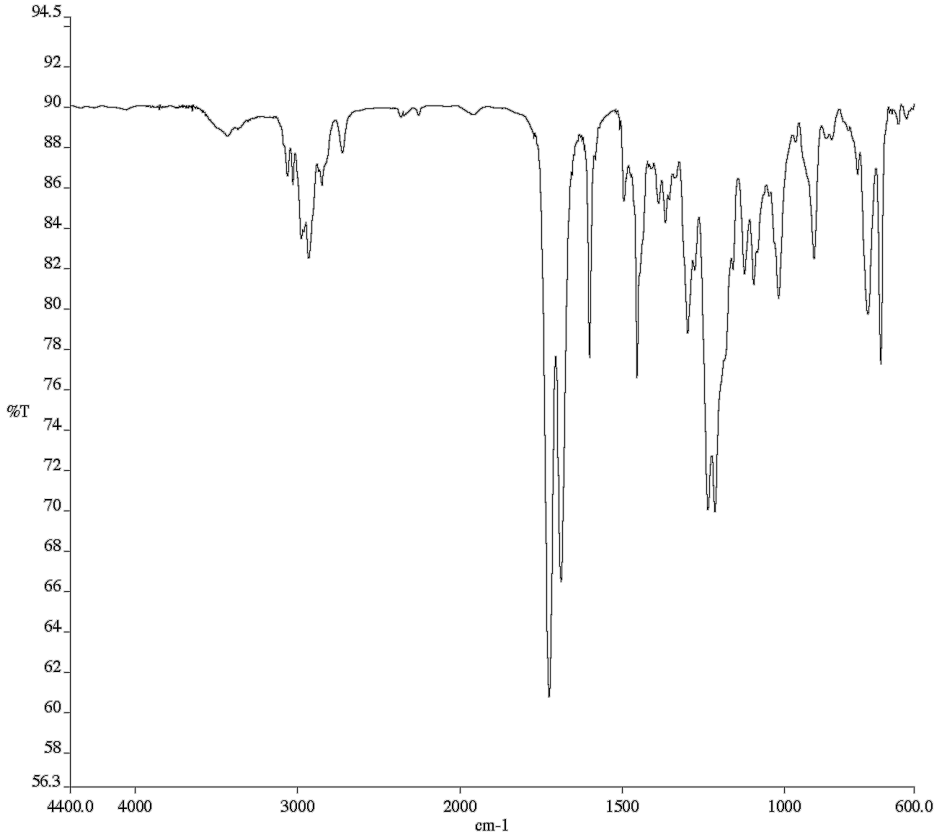
Infrared spectrum (Thin Film, KBr) of compound **2g**.



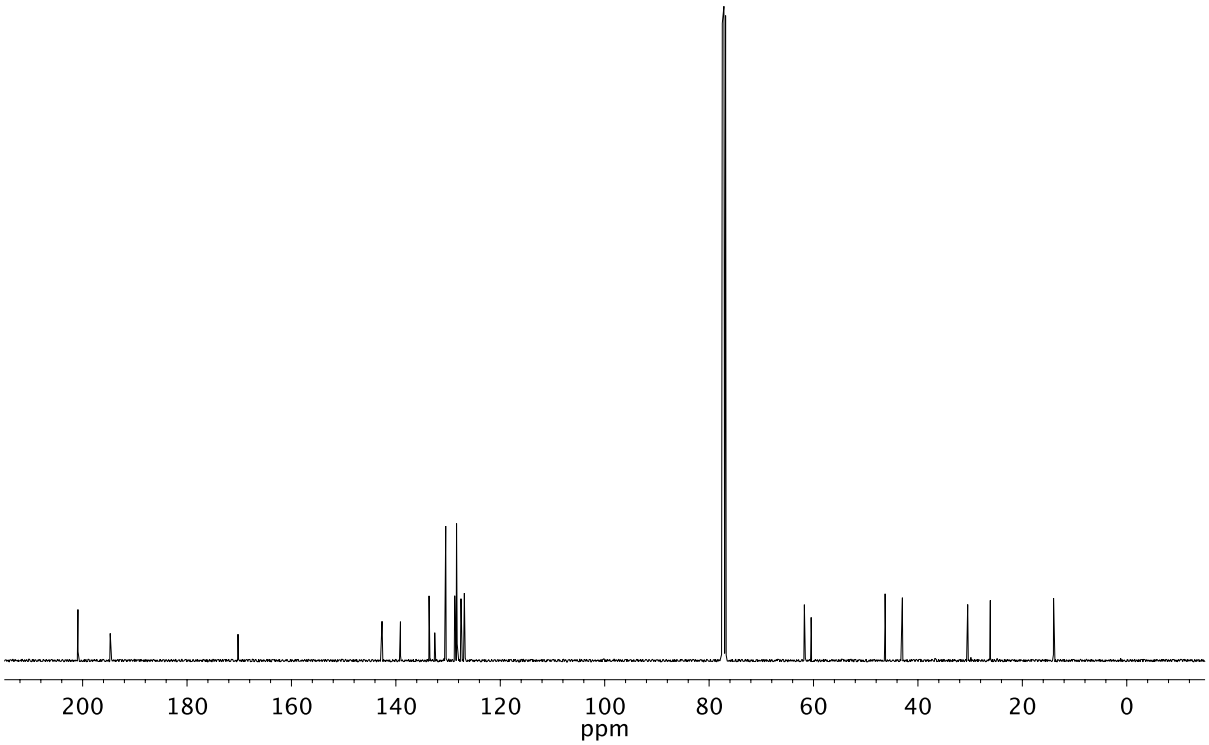
^{13}C NMR (126 MHz, $CDCl_3$) of compound **2g**.



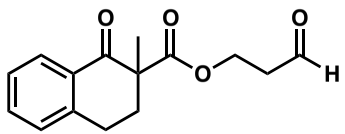
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2h**.



Infrared spectrum (Thin Film, KBr) of compound **2h**.

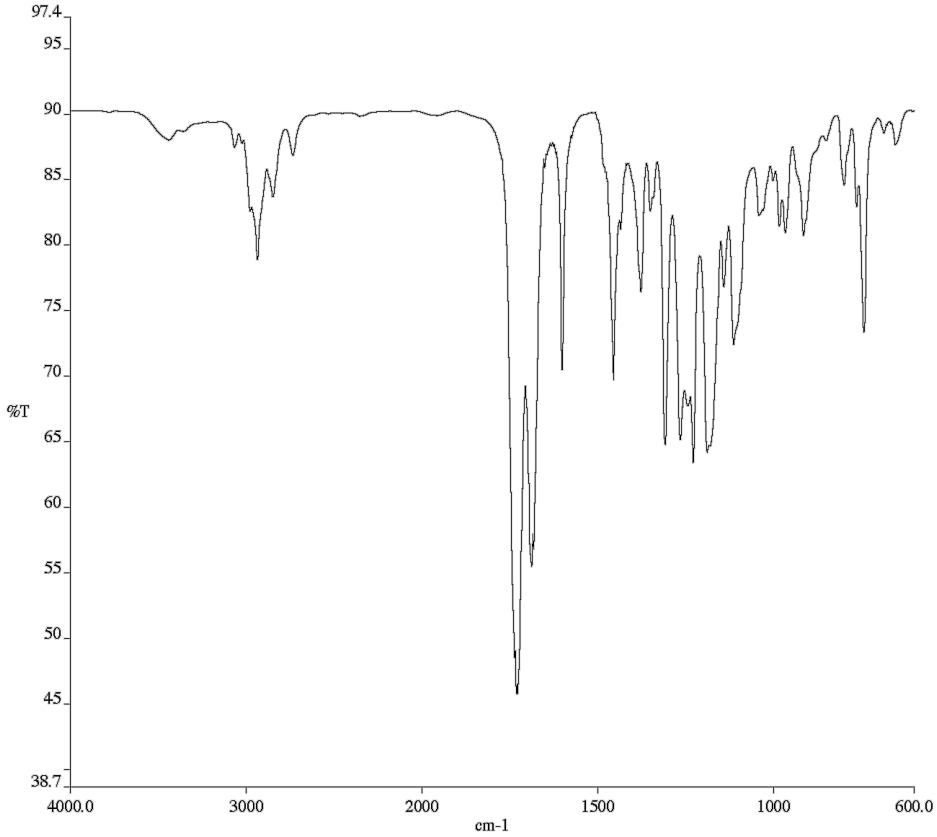


^{13}C NMR (101 MHz, $CDCl_3$) of compound **2h**.

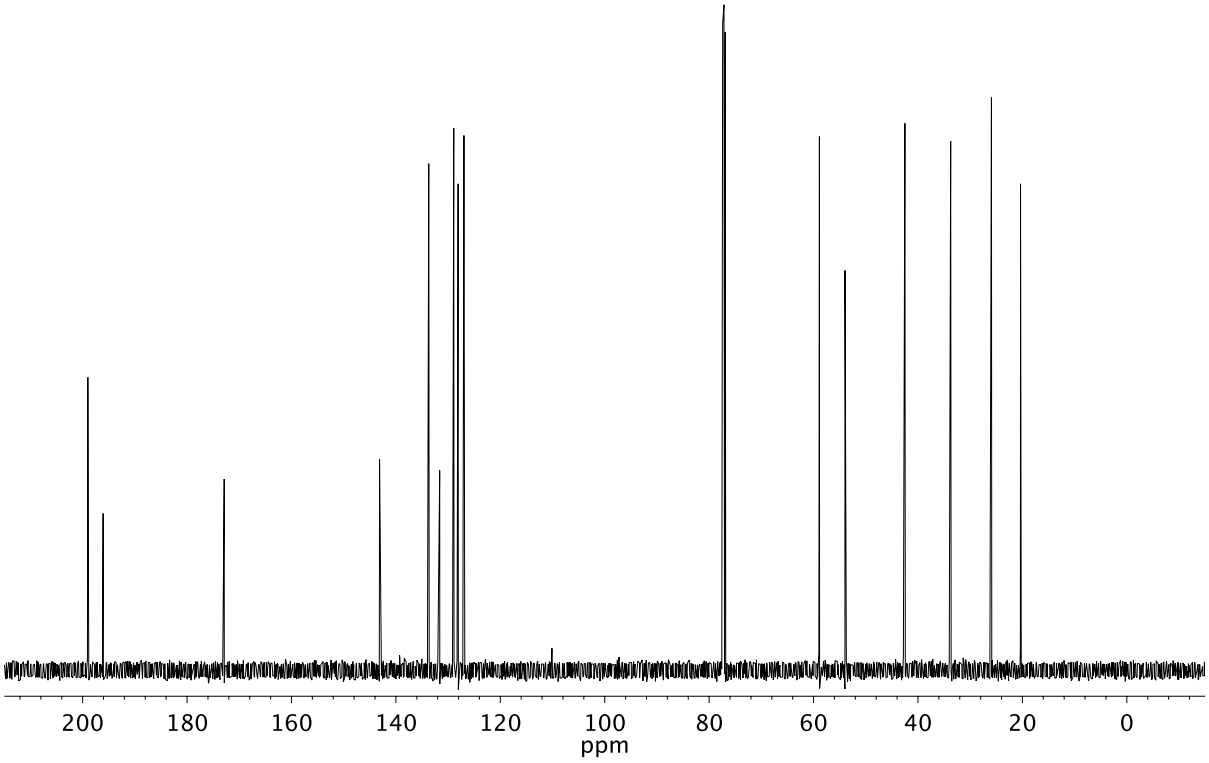


2i

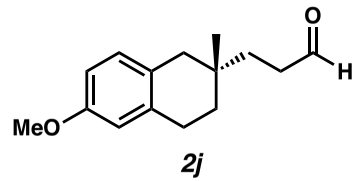
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2i**.



Infrared spectrum (Thin Film, KBr) of compound **2i**.

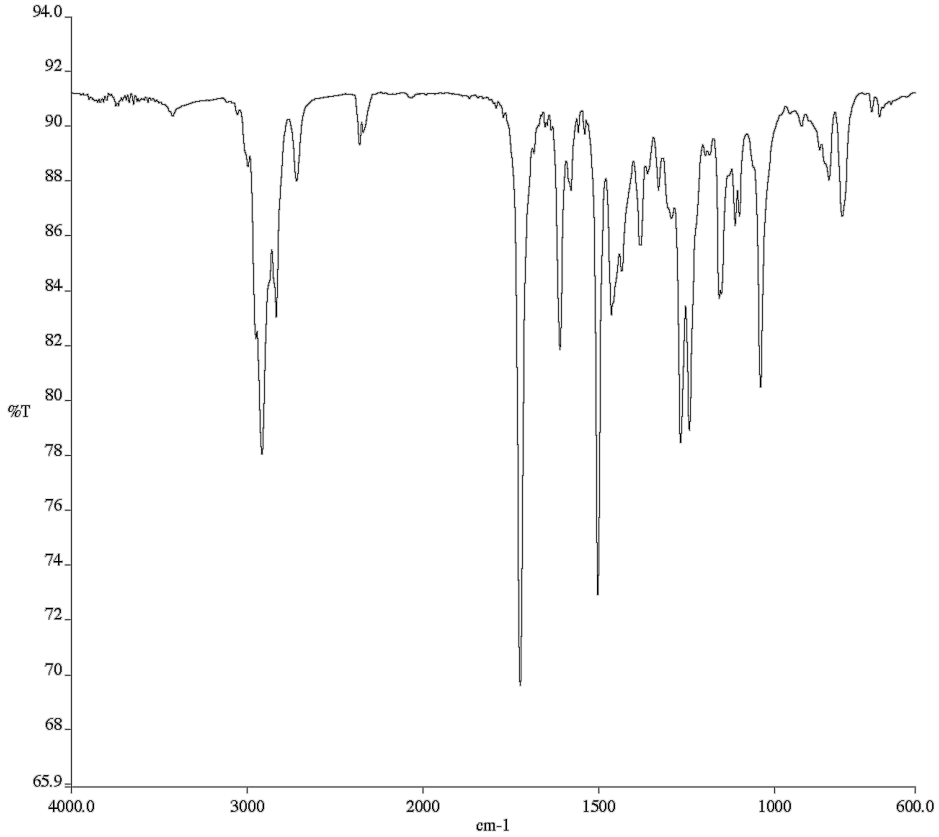


^{13}C NMR (126 MHz, $CDCl_3$) of compound **2i**.

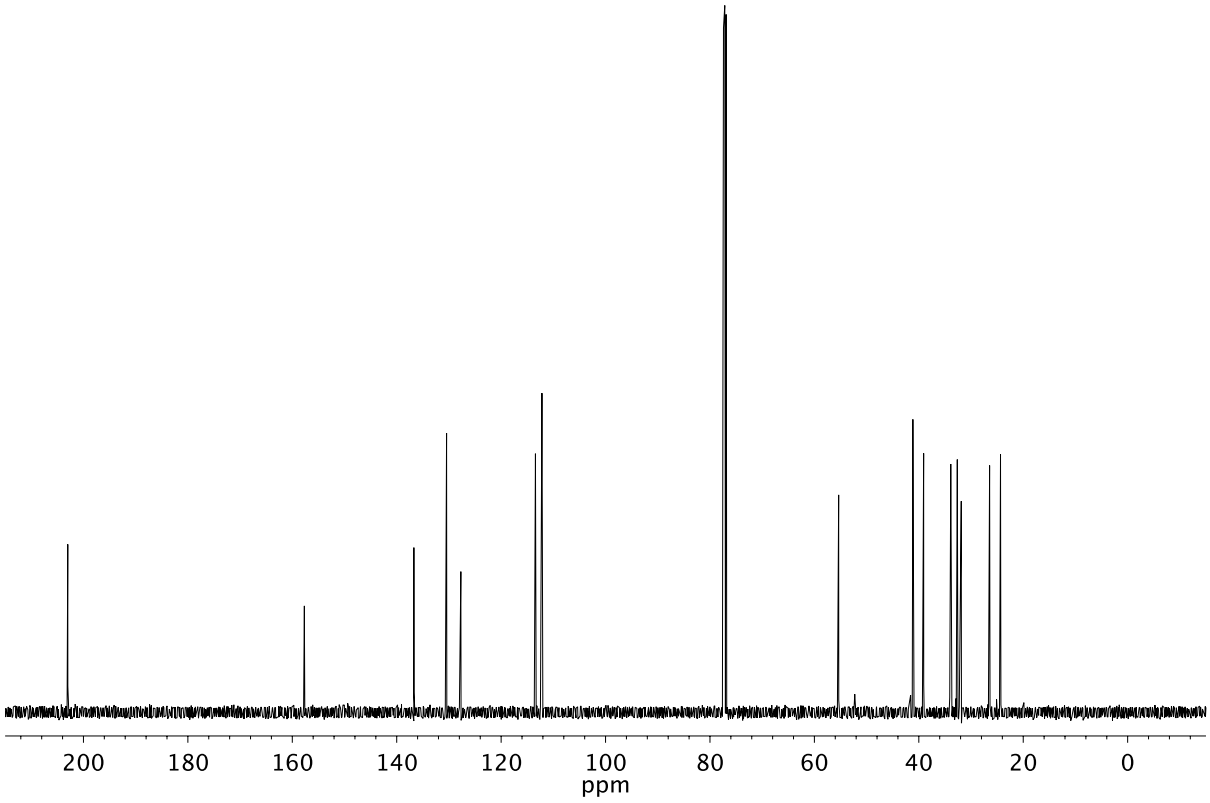


2j

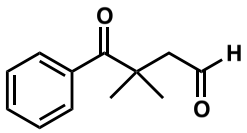
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2j**.



Infrared spectrum (Thin Film, KBr) of compound **2j**.

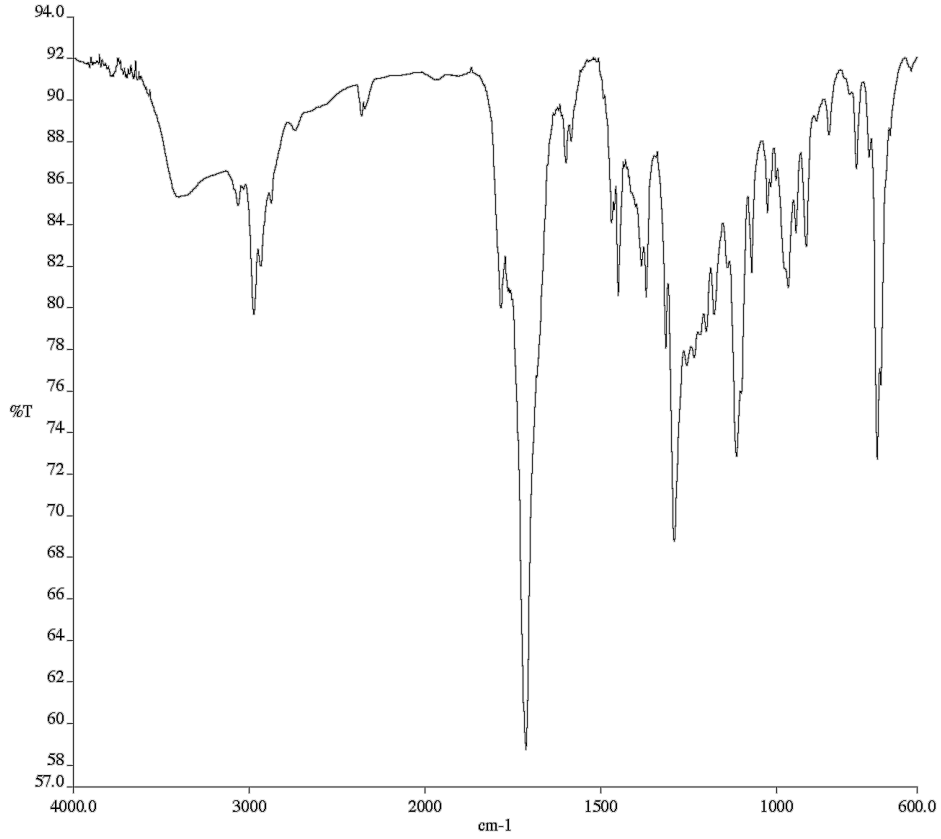


^{13}C NMR (126 MHz, $CDCl_3$) of compound **2j**.

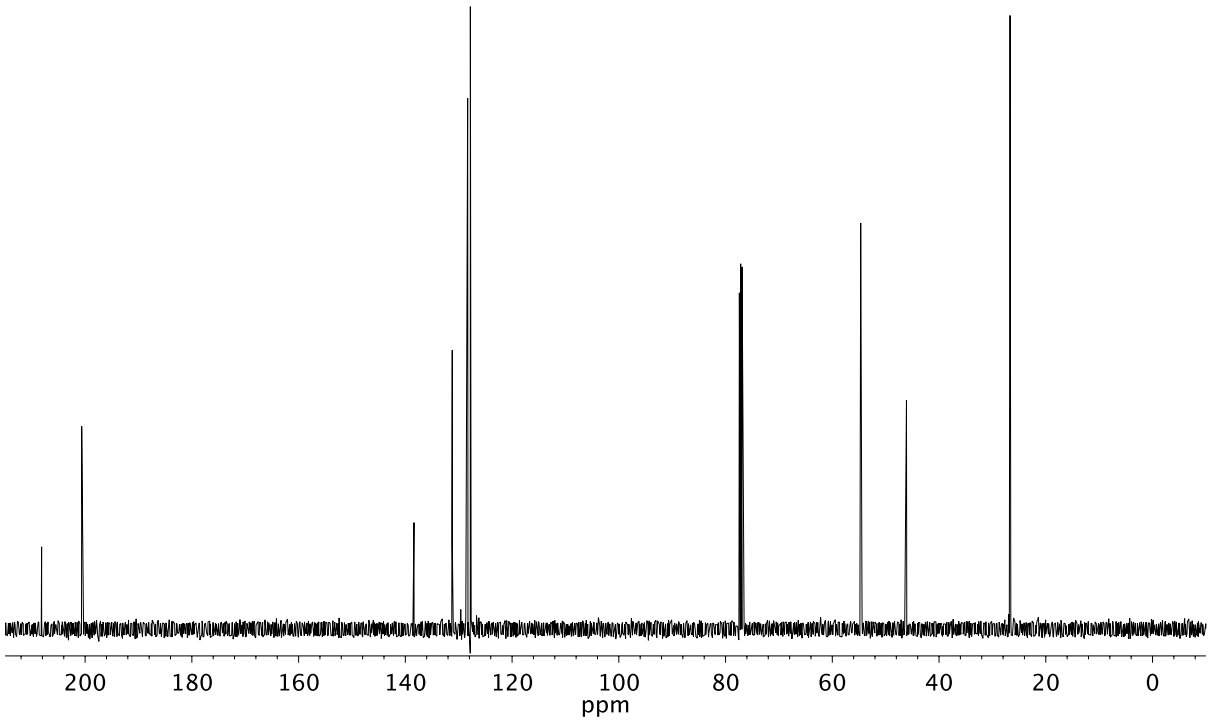


5a

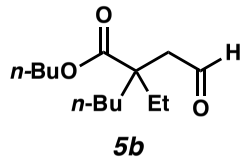
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5a**.



Infrared spectrum (Thin Film, KBr) of compound **5a**.

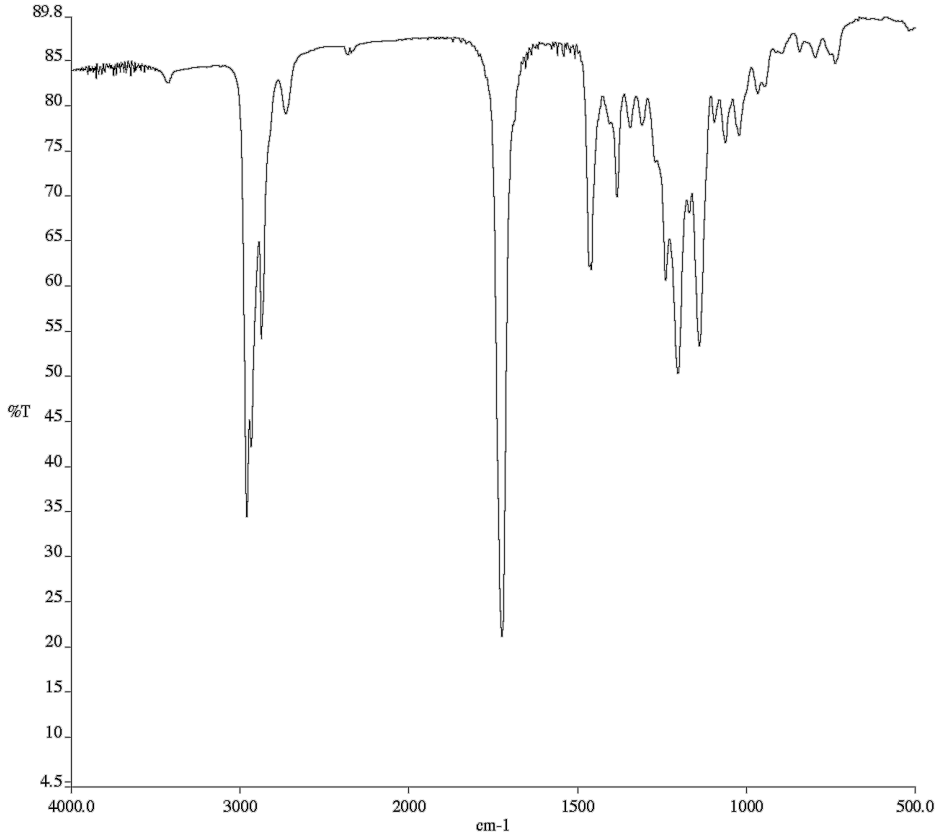


^{13}C NMR (126 MHz, $CDCl_3$) of compound **5a**.

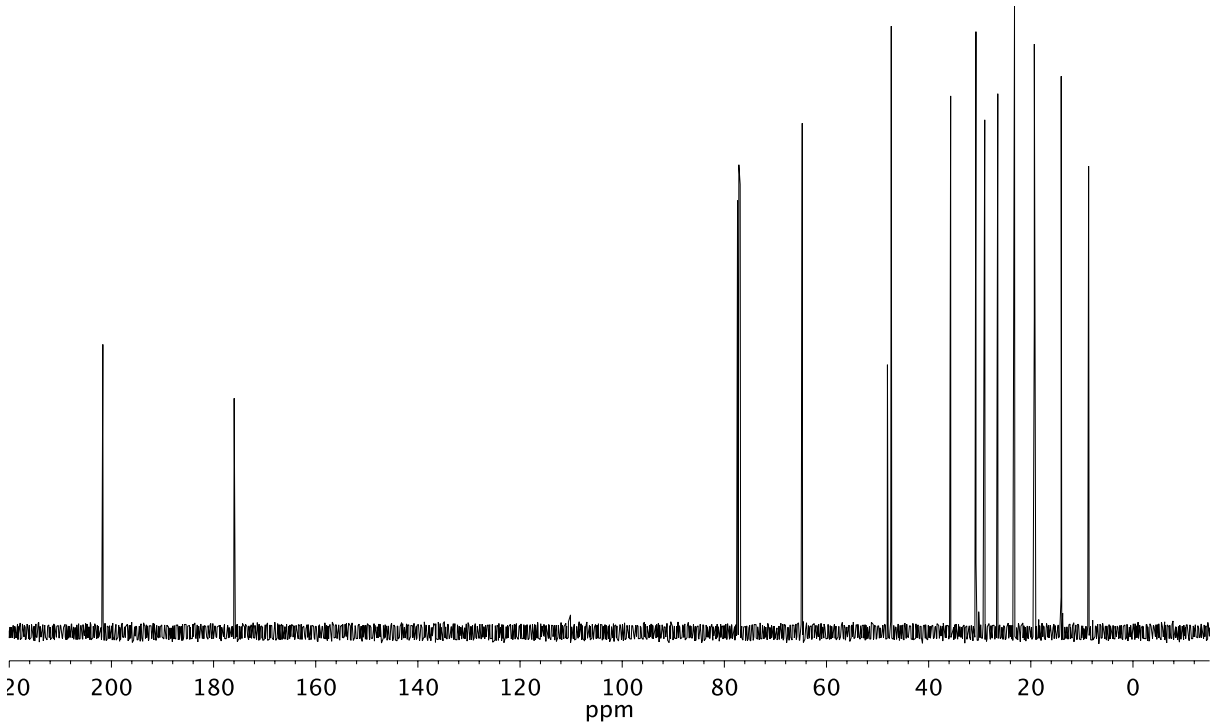


5b

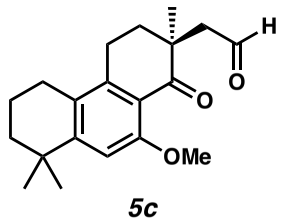
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5b**.



Infrared spectrum (Thin Film, KBr) of compound **5b**.

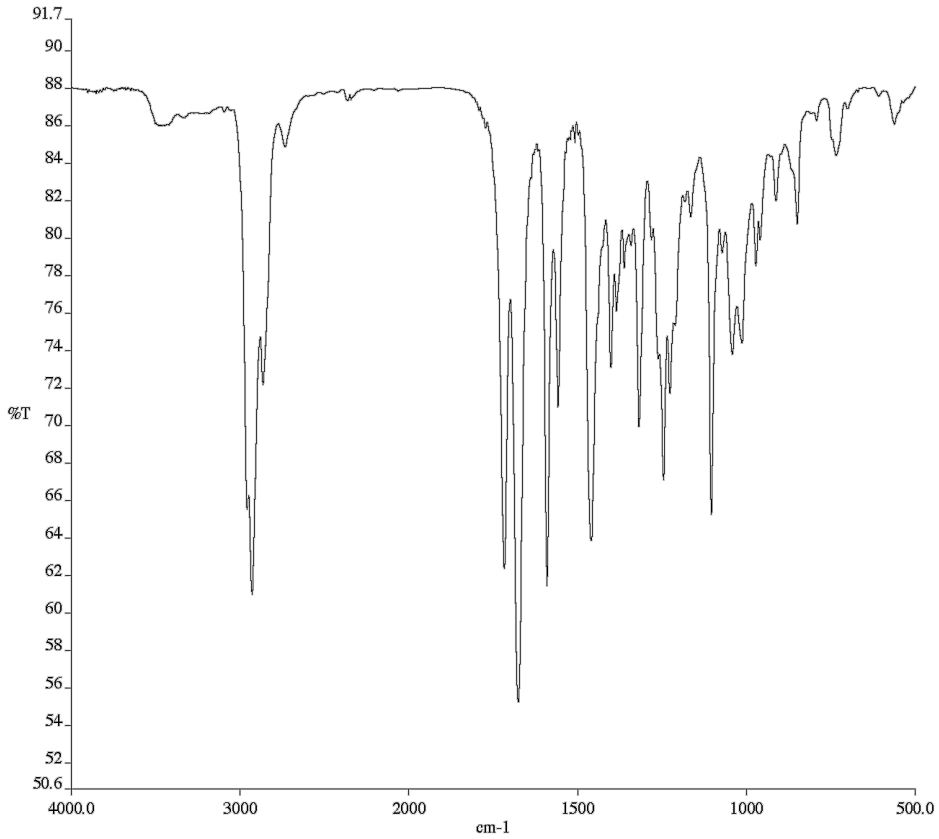


^{13}C NMR (126 MHz, $CDCl_3$) of compound **5b**.

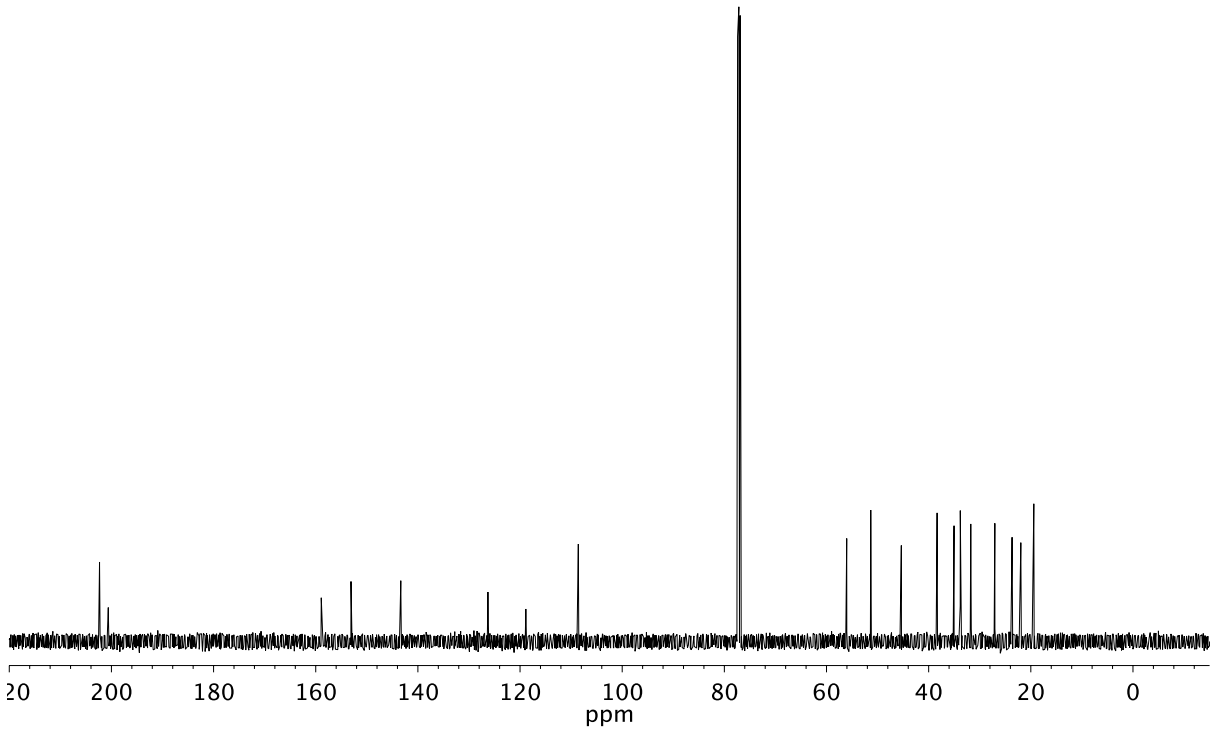


5c

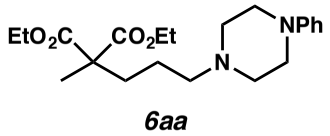
^{1}H NMR (500 MHz, $CDCl_3$) of compound **5c**.



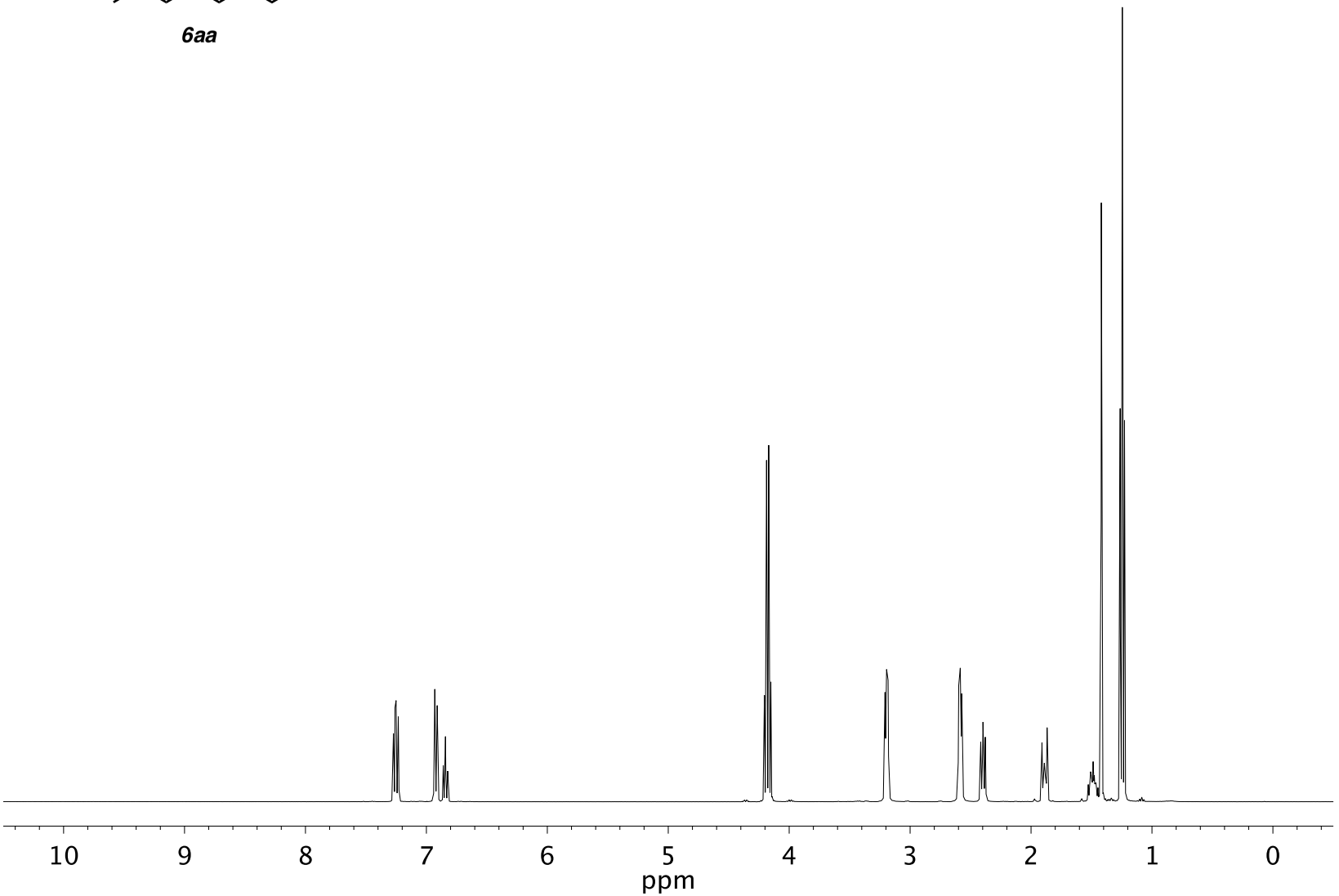
Infrared spectrum (Thin Film, KBr) of compound **5c**.



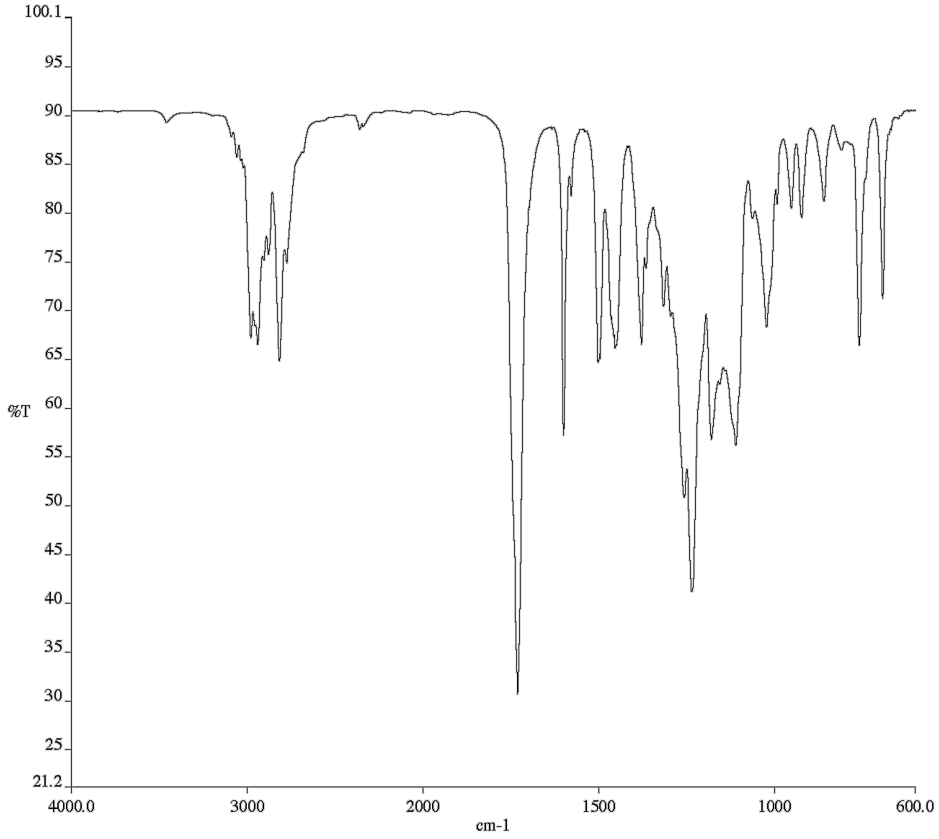
^{13}C NMR (126 MHz, $CDCl_3$) of compound **5c**.



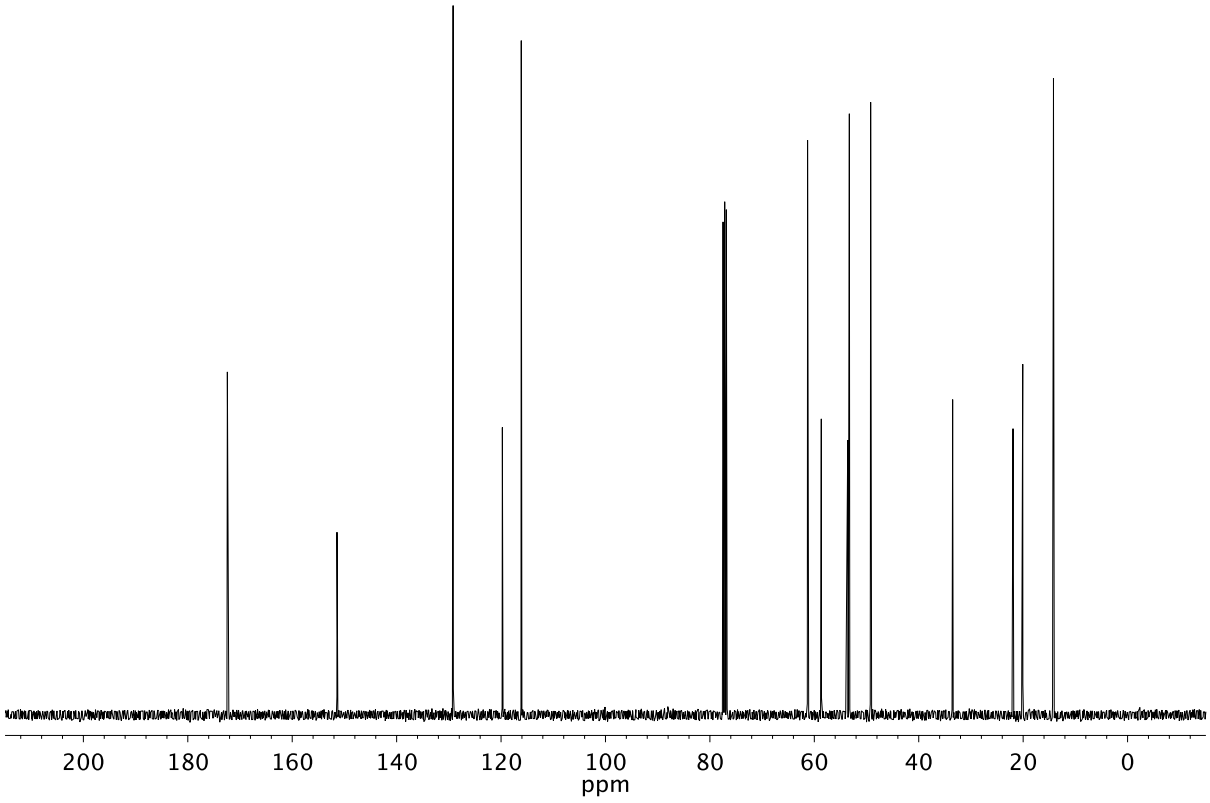
6aa



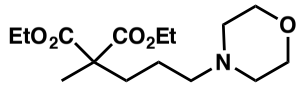
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6aa**.



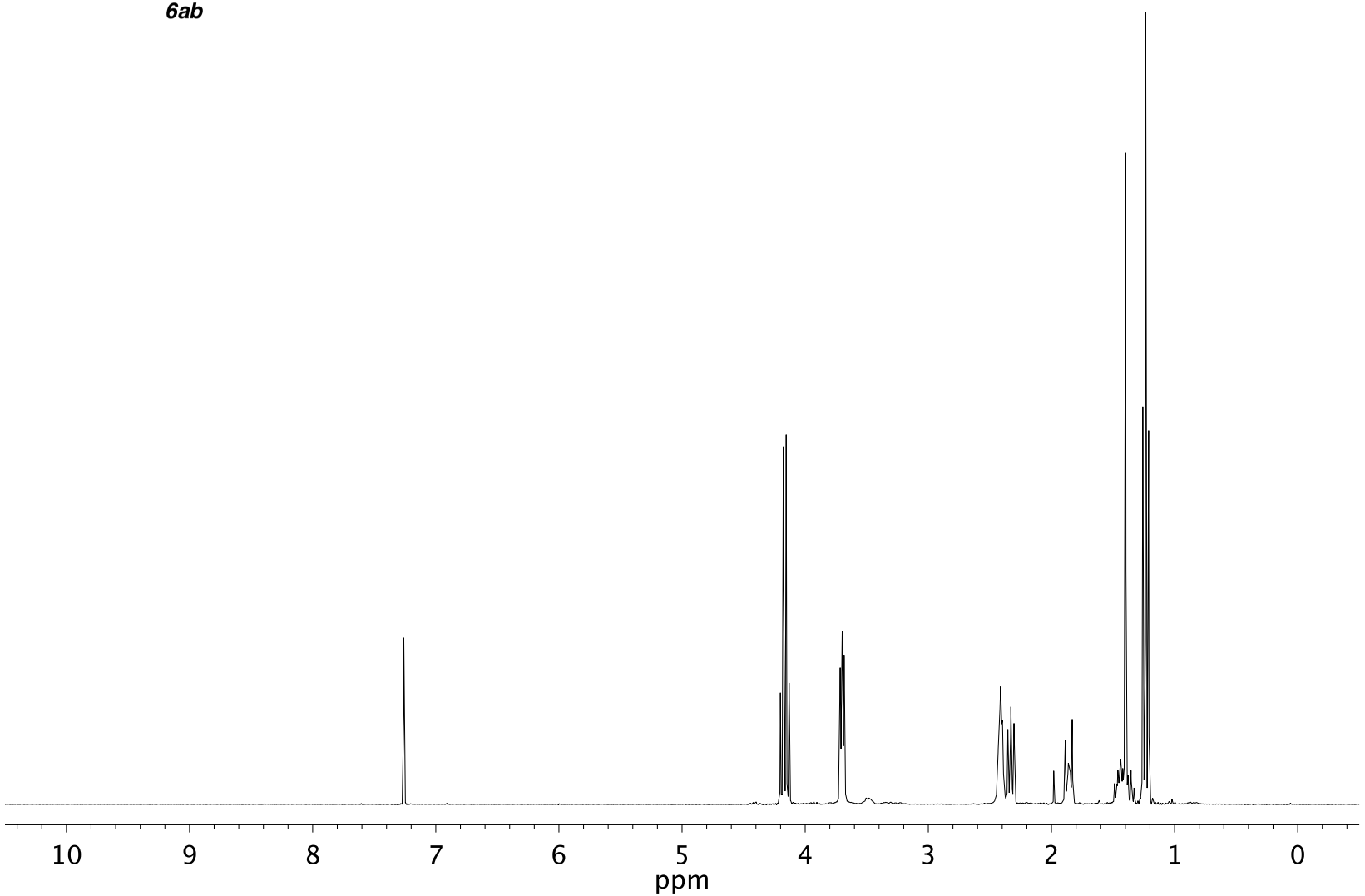
Infrared spectrum (Thin Film, KBr) of compound **6aa**.



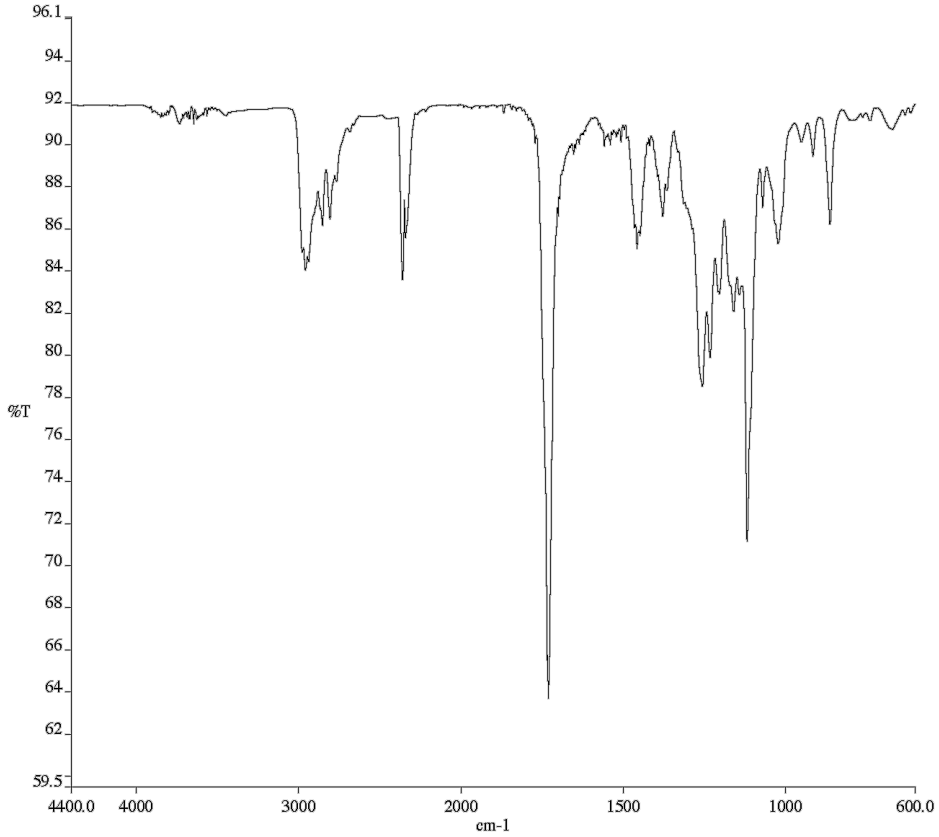
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6aa**.



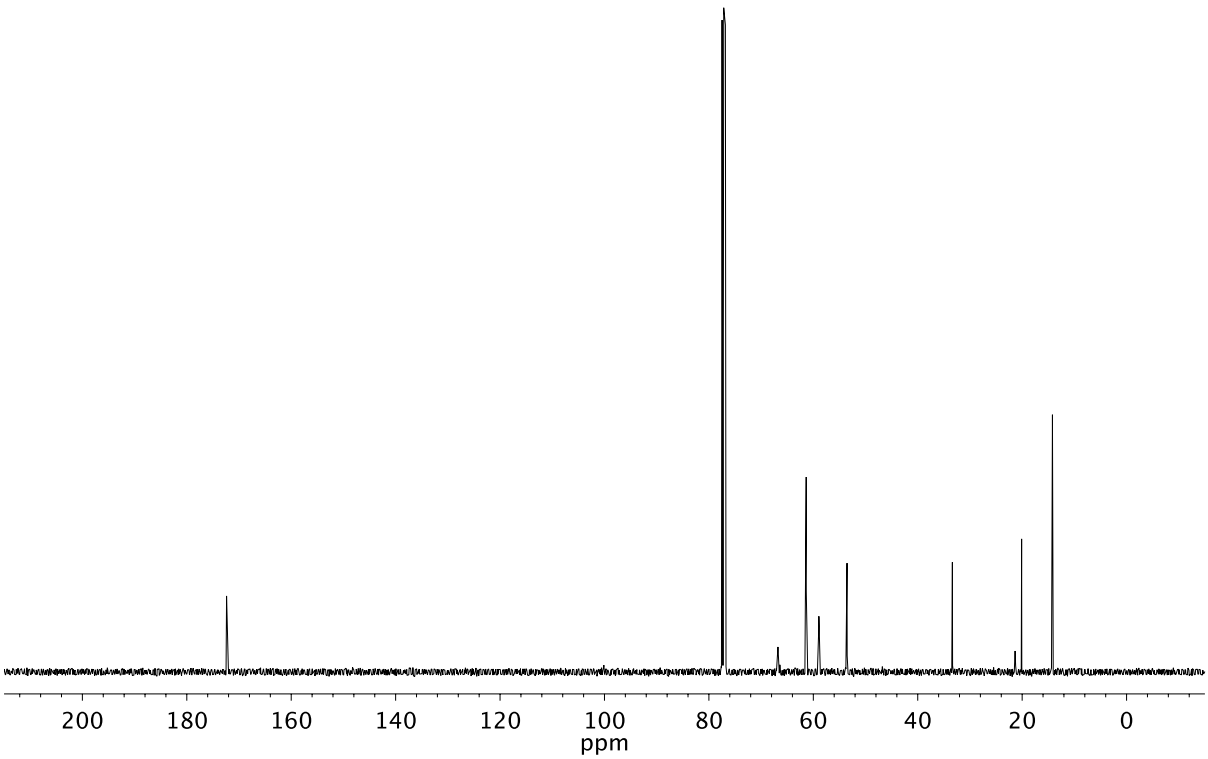
6ab



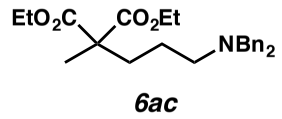
^{1}H NMR (300 MHz, $CDCl_3$) of compound **6ab**.



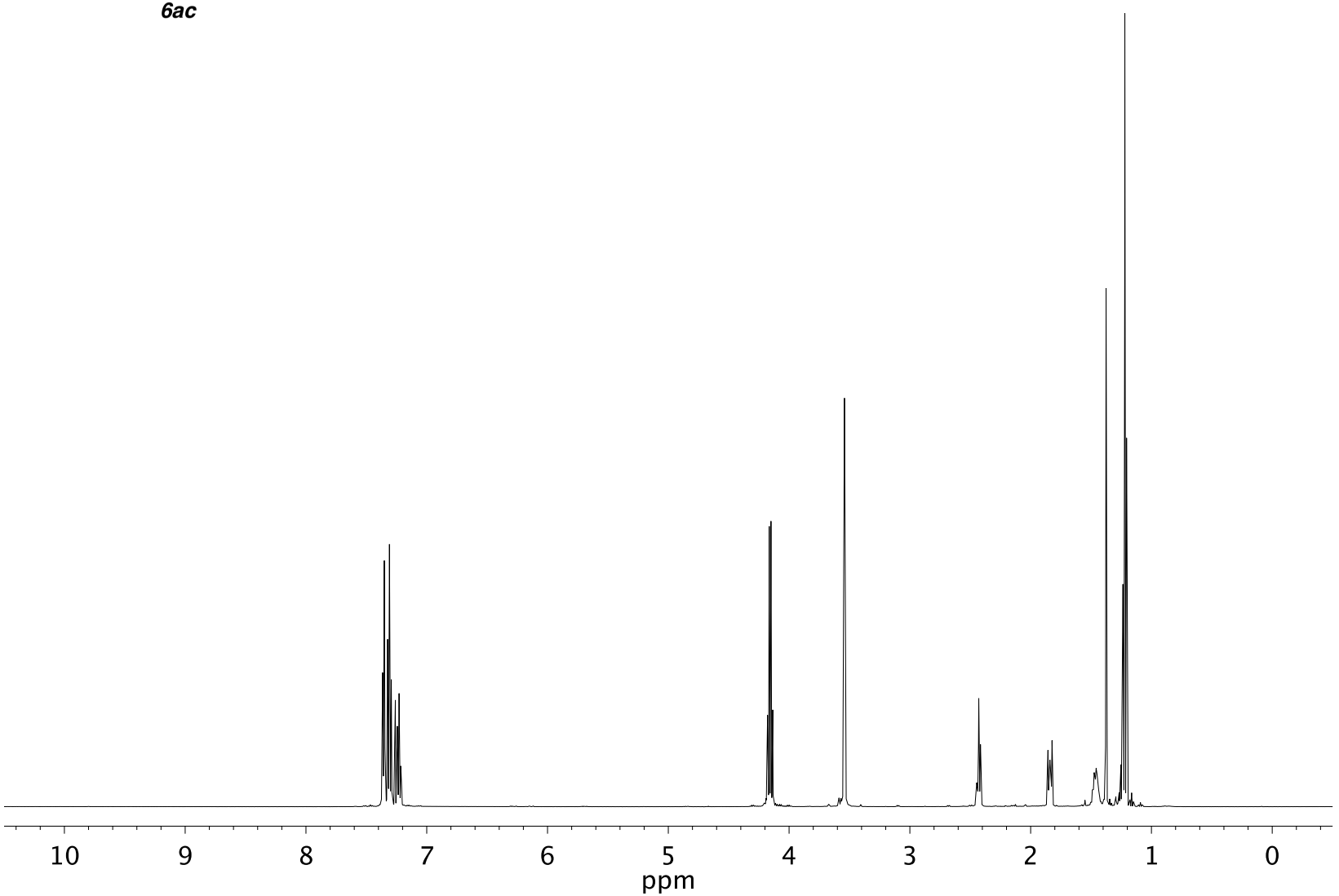
Infrared spectrum (Thin Film, KBr) of compound **6ab**.



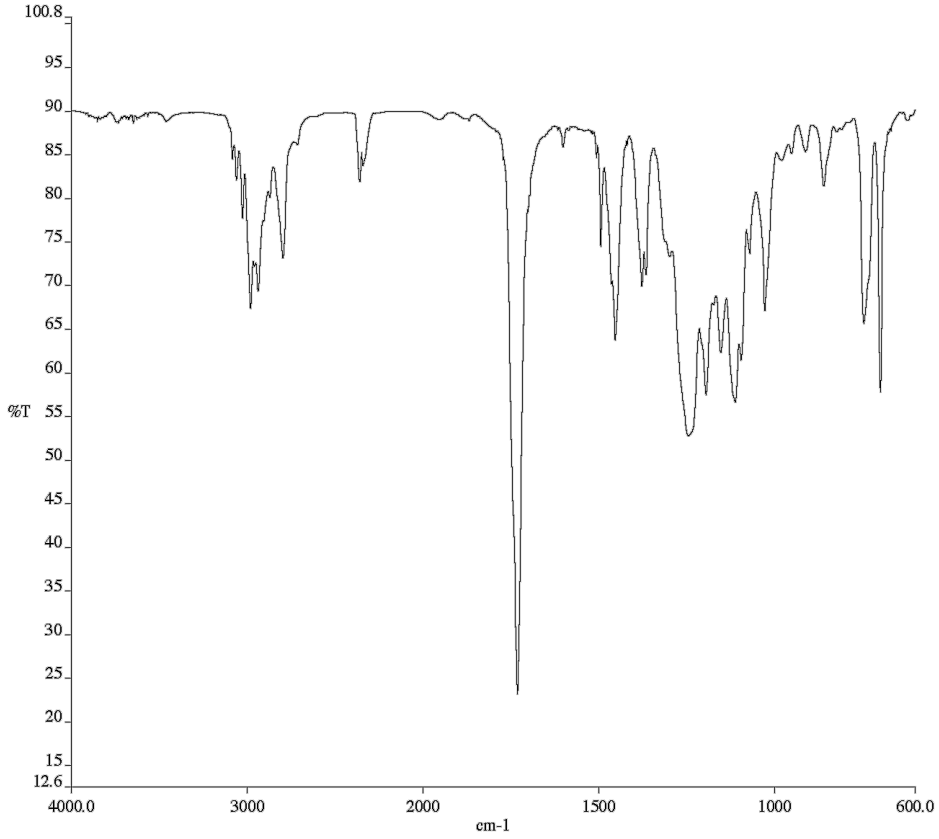
^{13}C NMR (101 MHz, $CDCl_3$) of compound **6ab**.



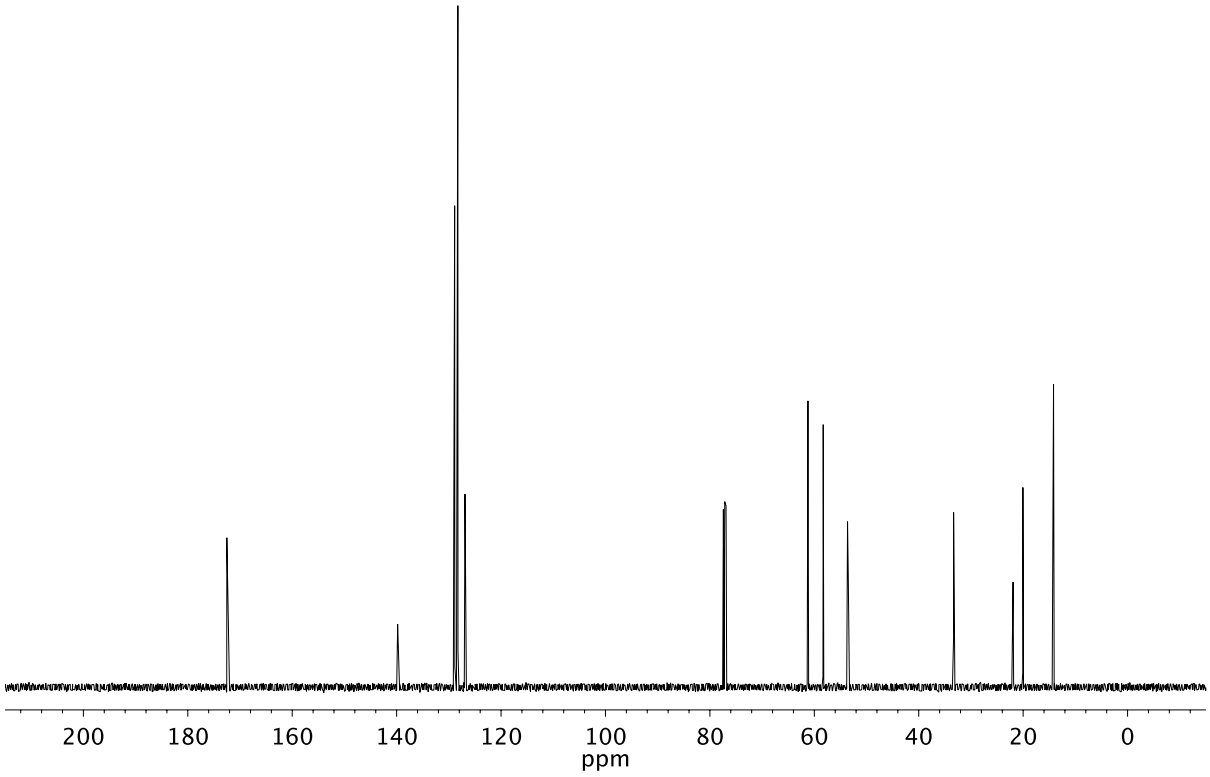
6ac



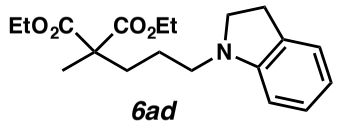
^{1}H NMR (500 MHz, $CDCl_3$) of compound **6ac**.



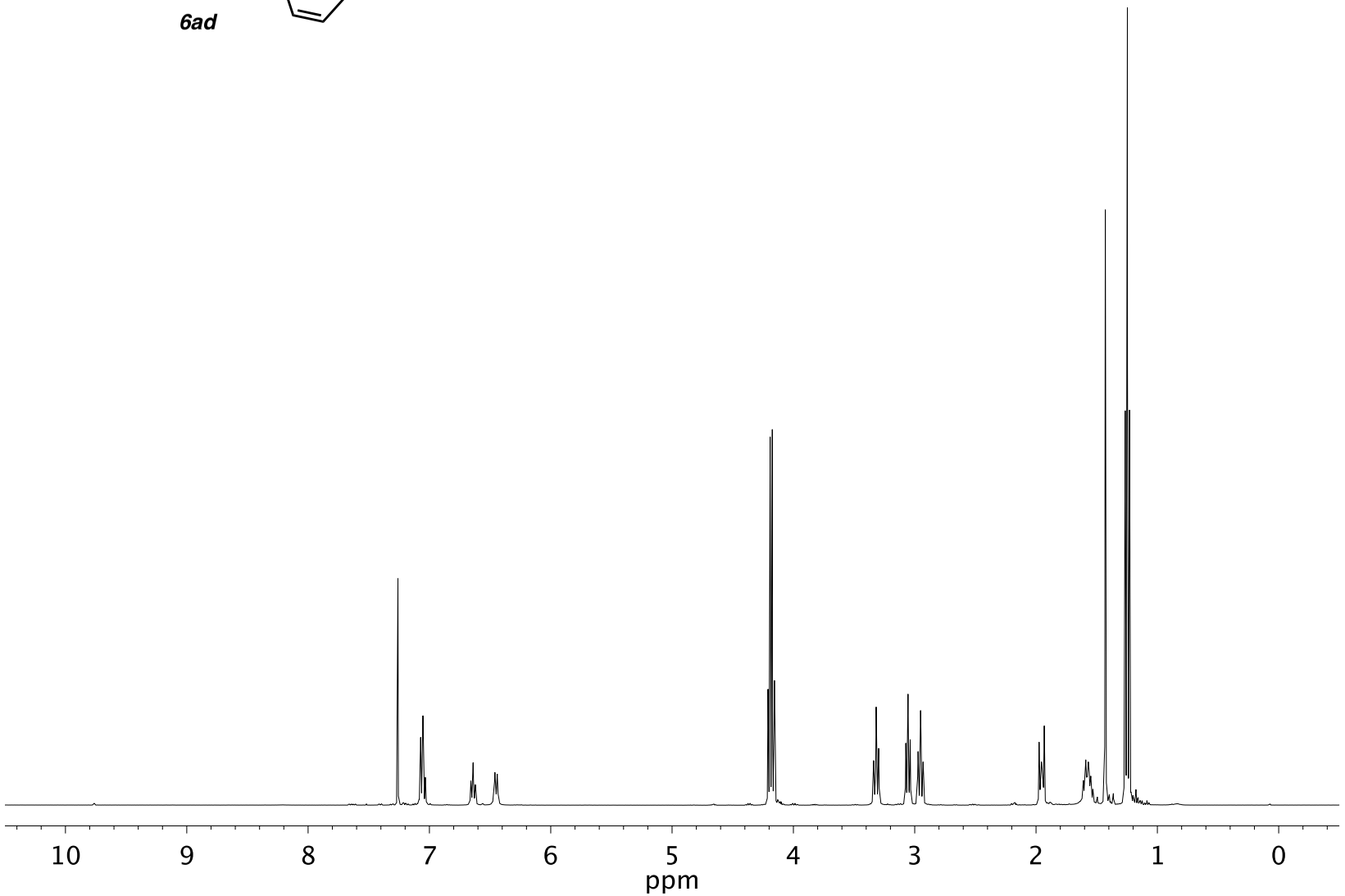
Infrared spectrum (Thin Film, KBr) of compound **6ac**.



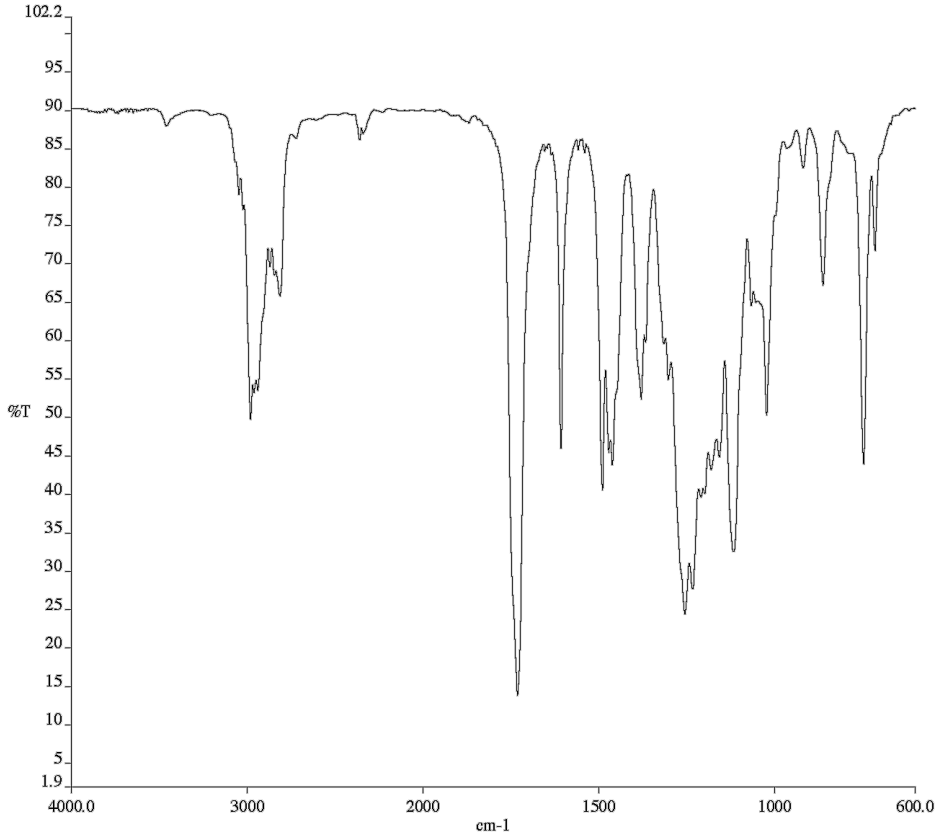
^{13}C NMR (126 MHz, $CDCl_3$) of compound **6ac**.



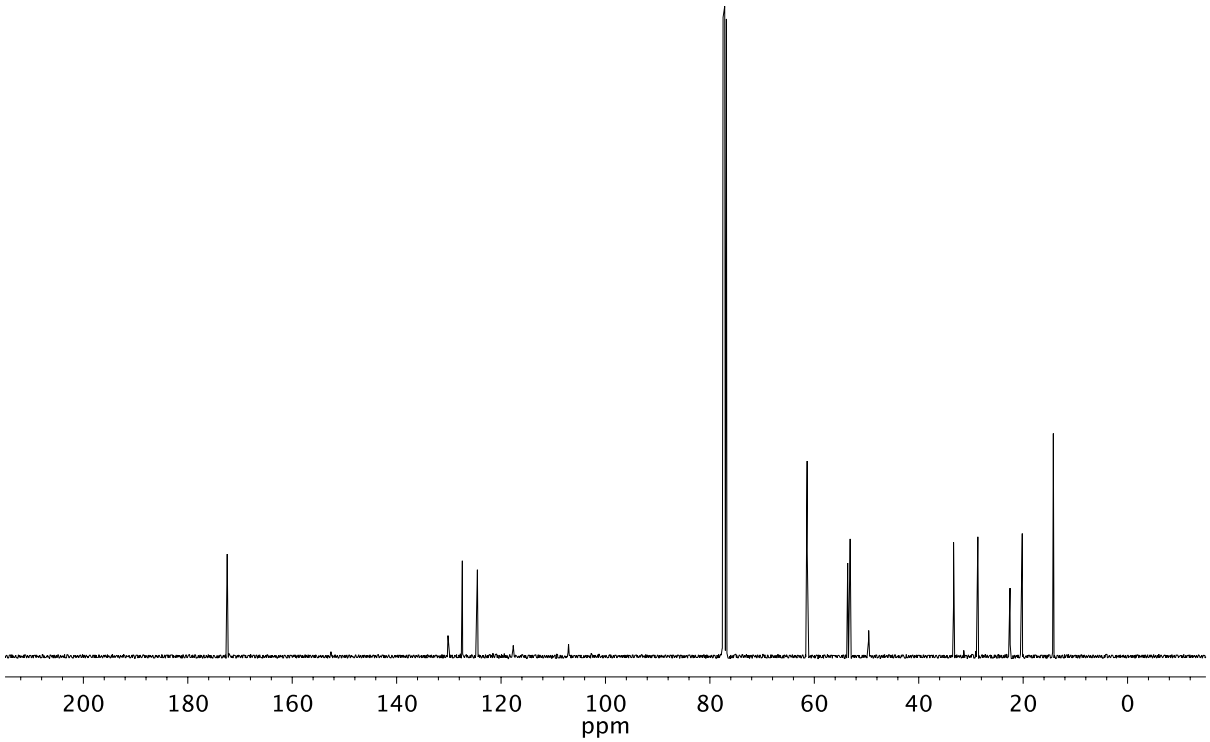
6ad



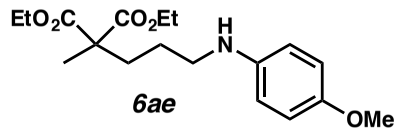
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6ad**.



Infrared spectrum (Thin Film, KBr) of compound **6ad**.

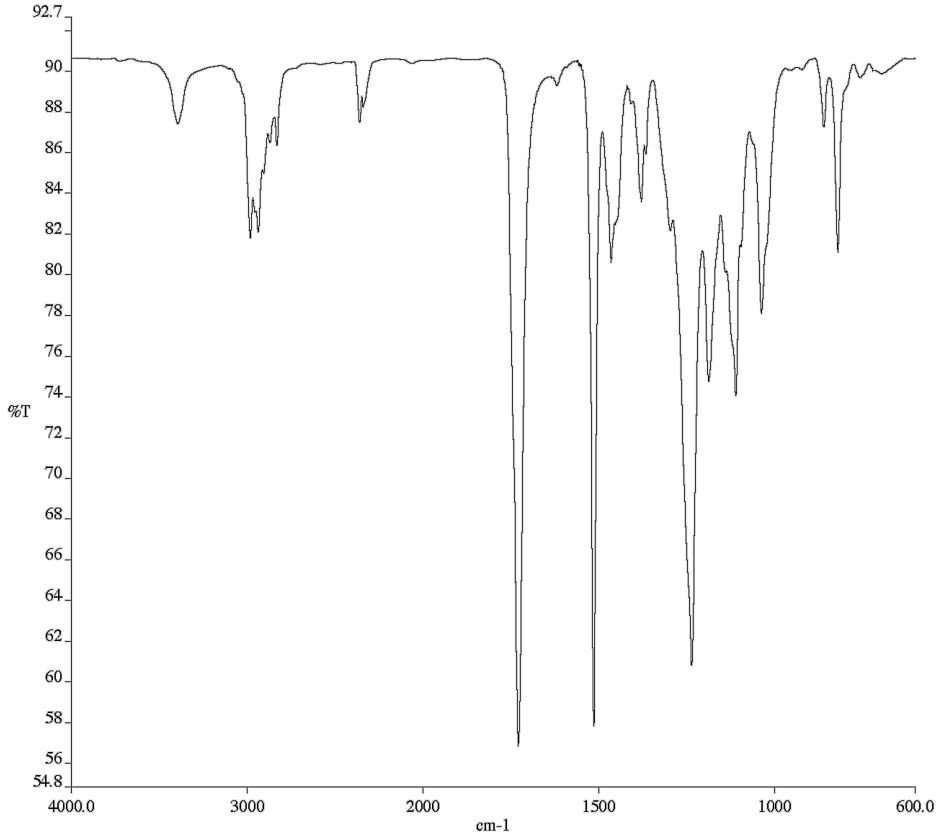


^{13}C NMR (101 MHz, $CDCl_3$) of compound **6ad**.

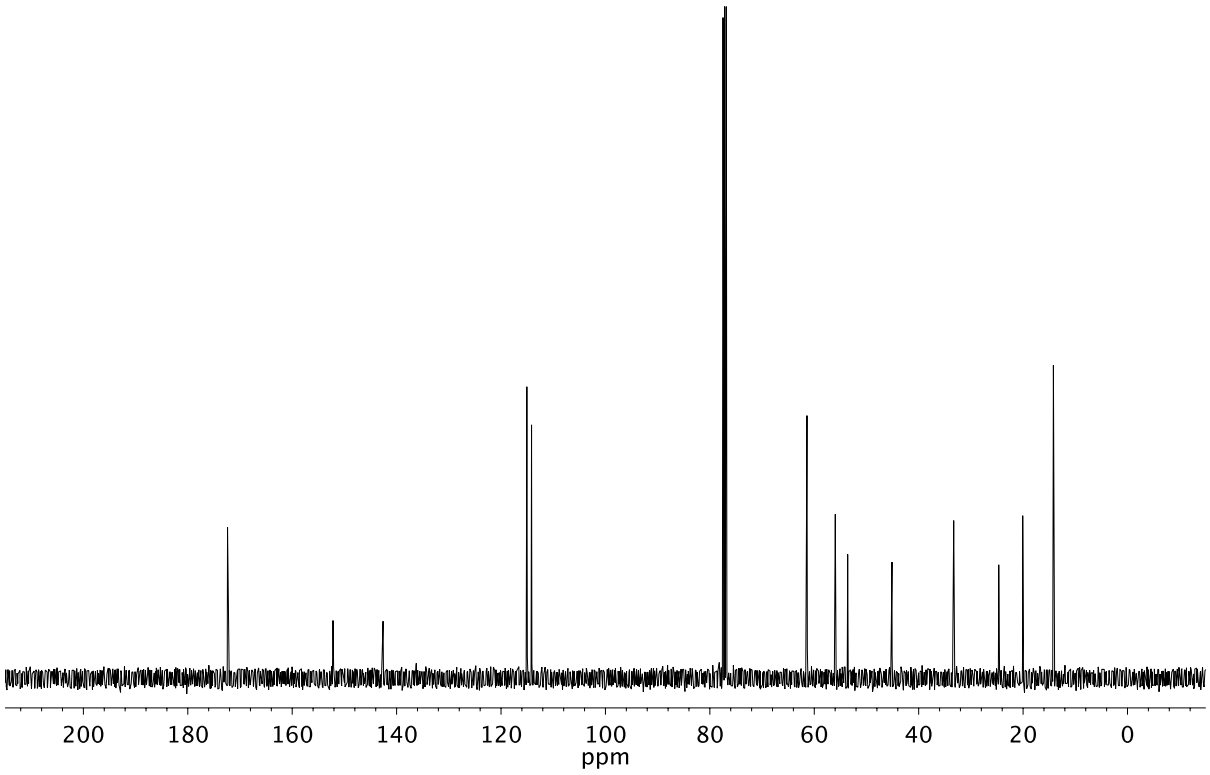


6ae

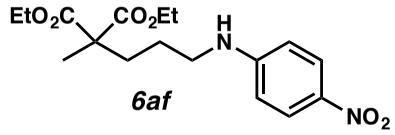
^{1}H NMR (400 MHz, $CDCl_3$) of compound **6ae**.



Infrared spectrum (Thin Film, KBr) of compound **6ae**.

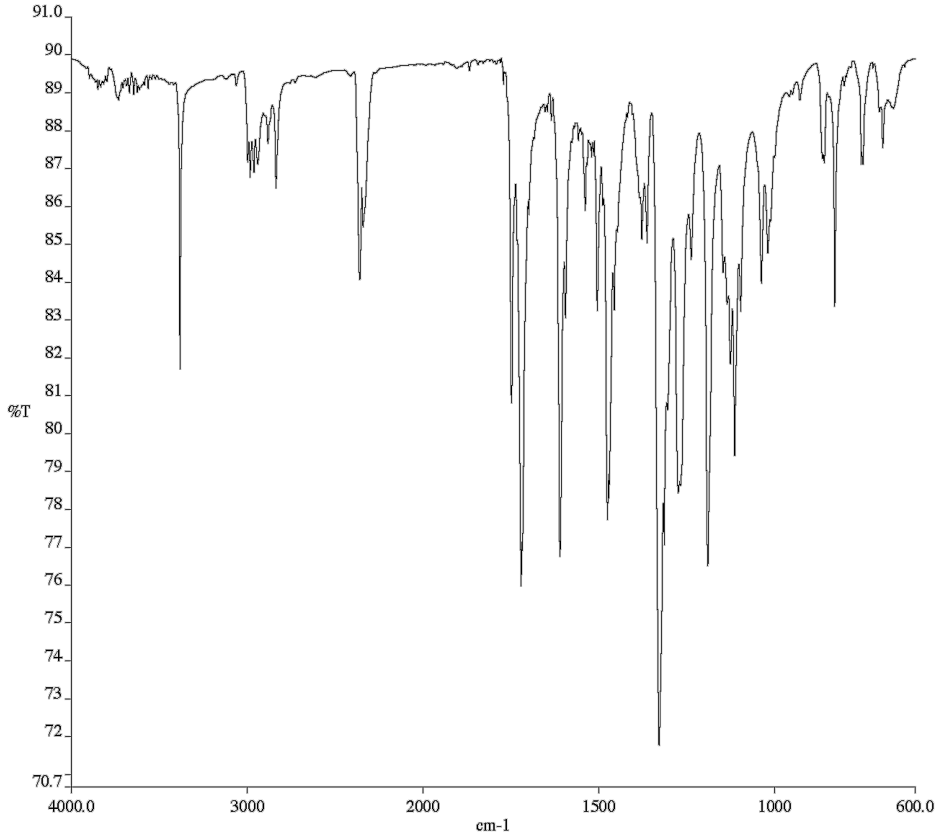


^{13}C NMR (101 MHz, $CDCl_3$) of compound **6ae**.

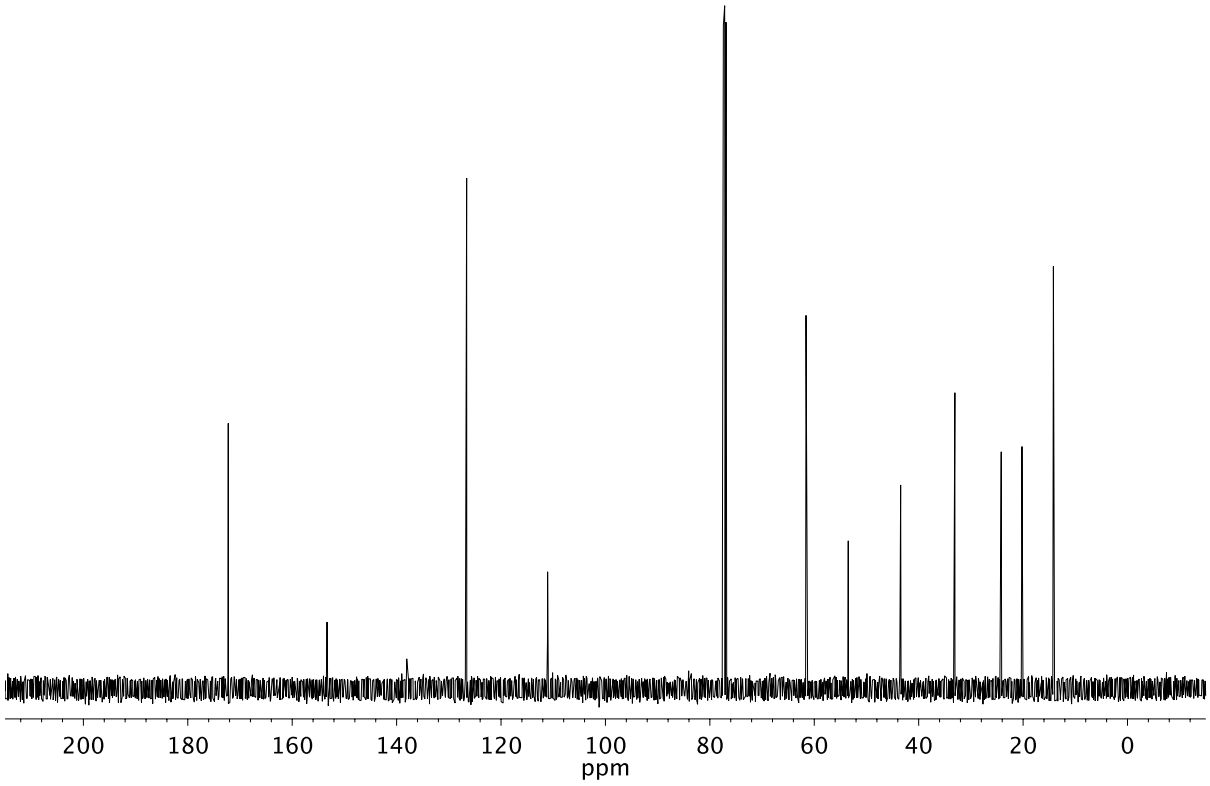


6af

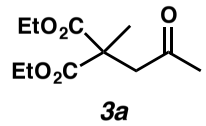
^{1}H NMR (500 MHz, $CDCl_3$) of compound **6af**.



Infrared spectrum (Thin Film, KBr) of compound **6af**.

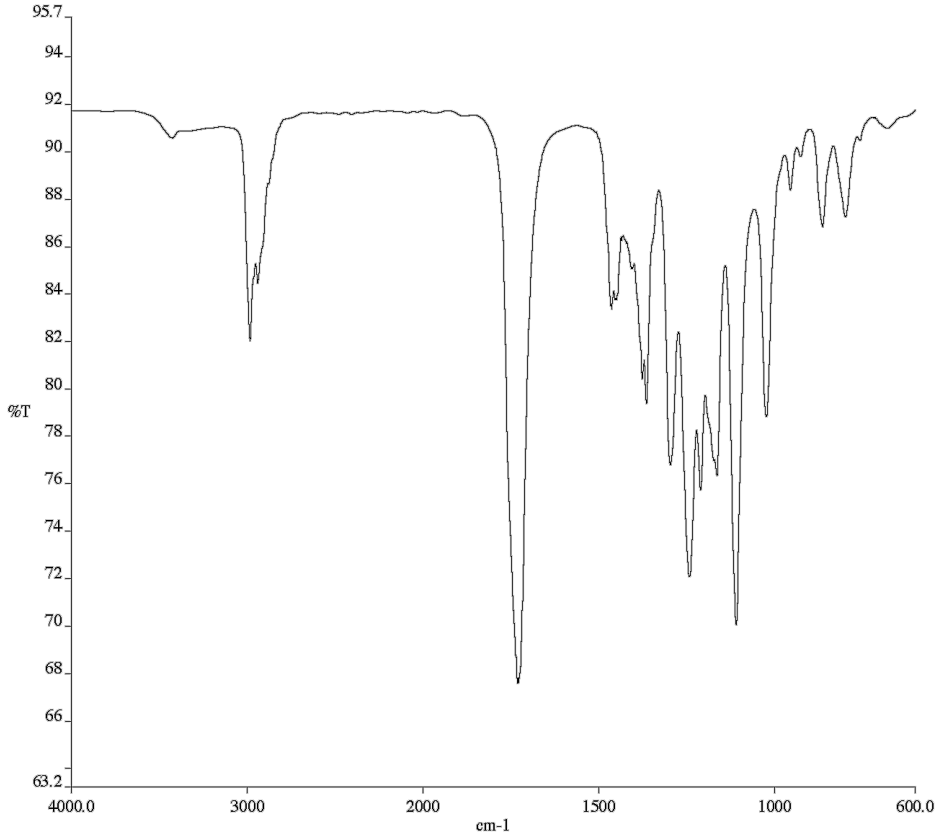


^{13}C NMR (126 MHz, $CDCl_3$) of compound **6af**.

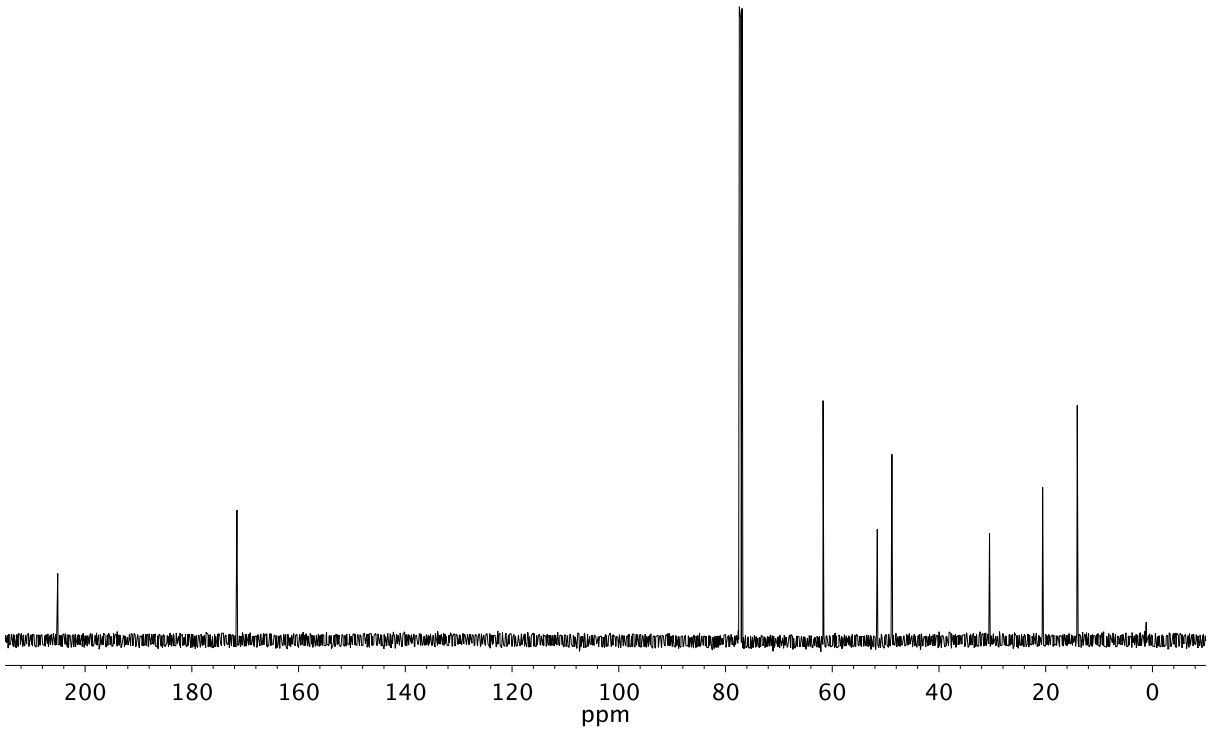


3a

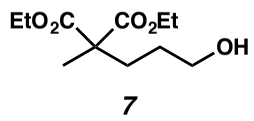
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3a**.



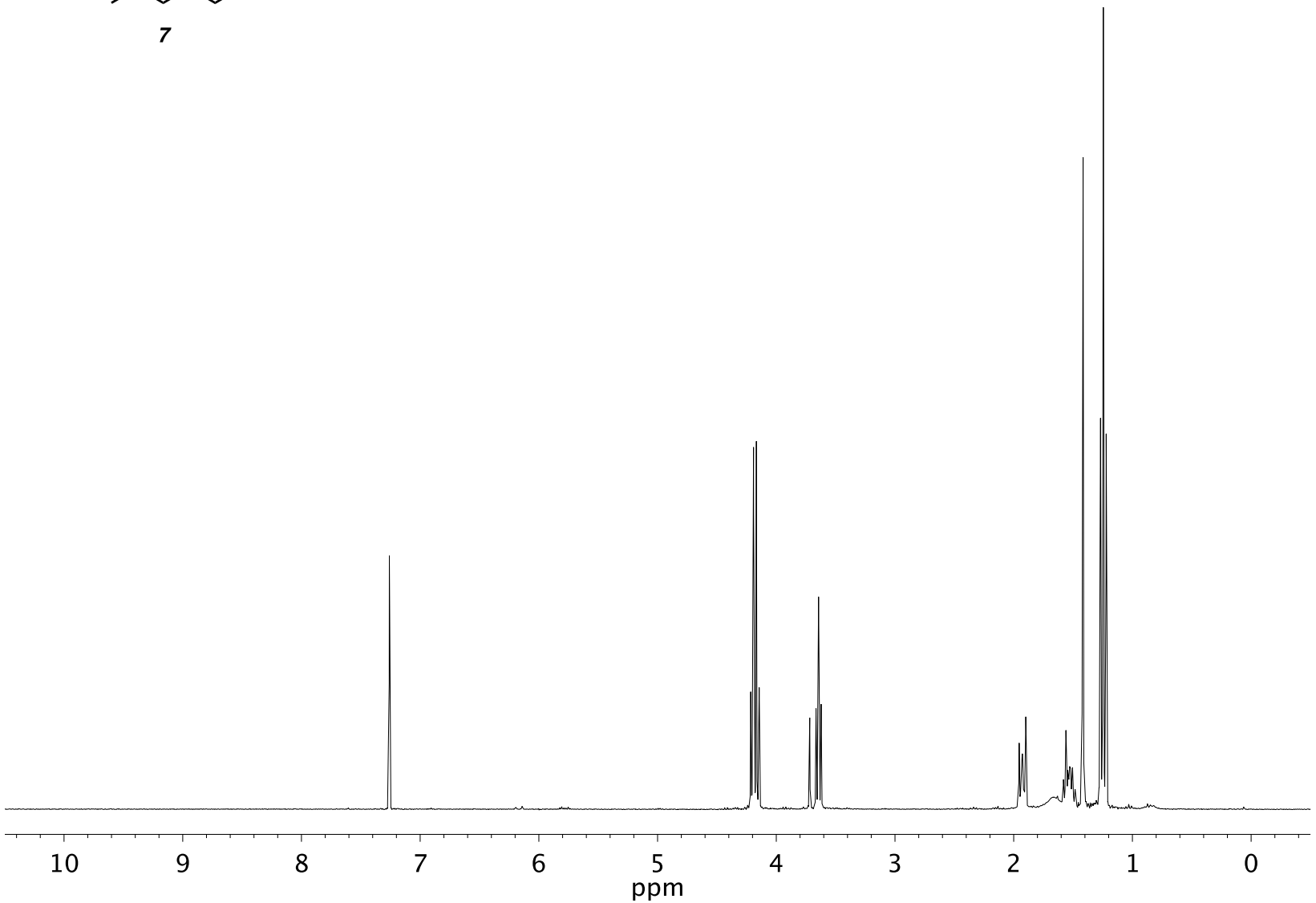
Infrared spectrum (Thin Film, KBr) of compound **3a**.



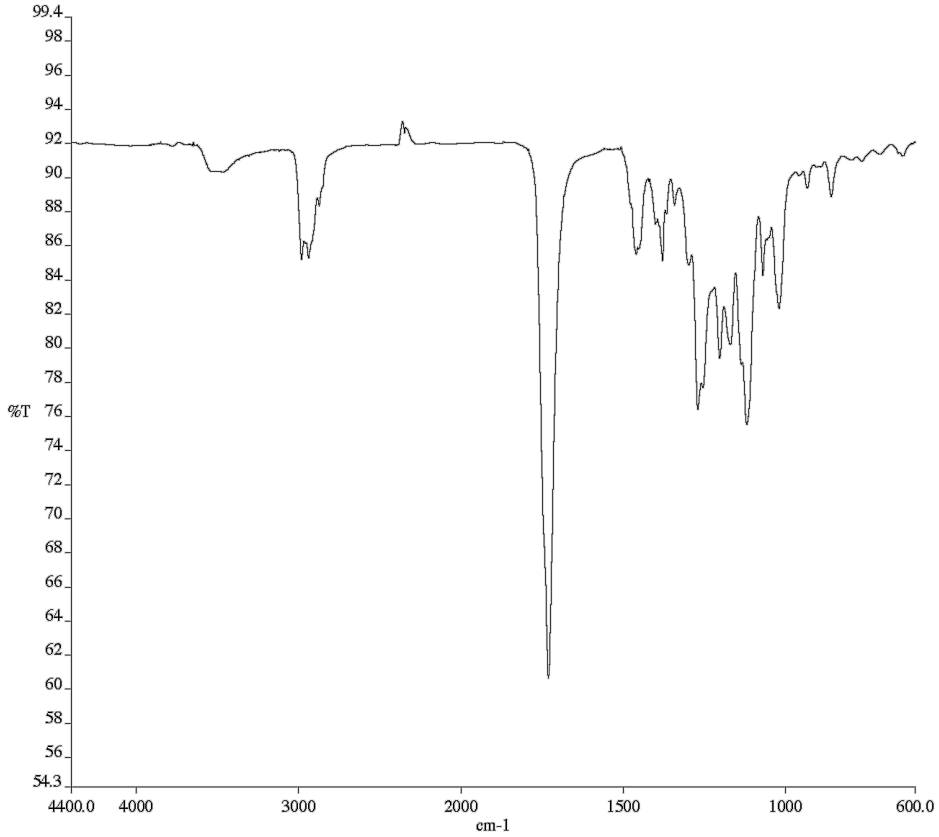
^{13}C NMR (126 MHz, $CDCl_3$) of compound **3a**.



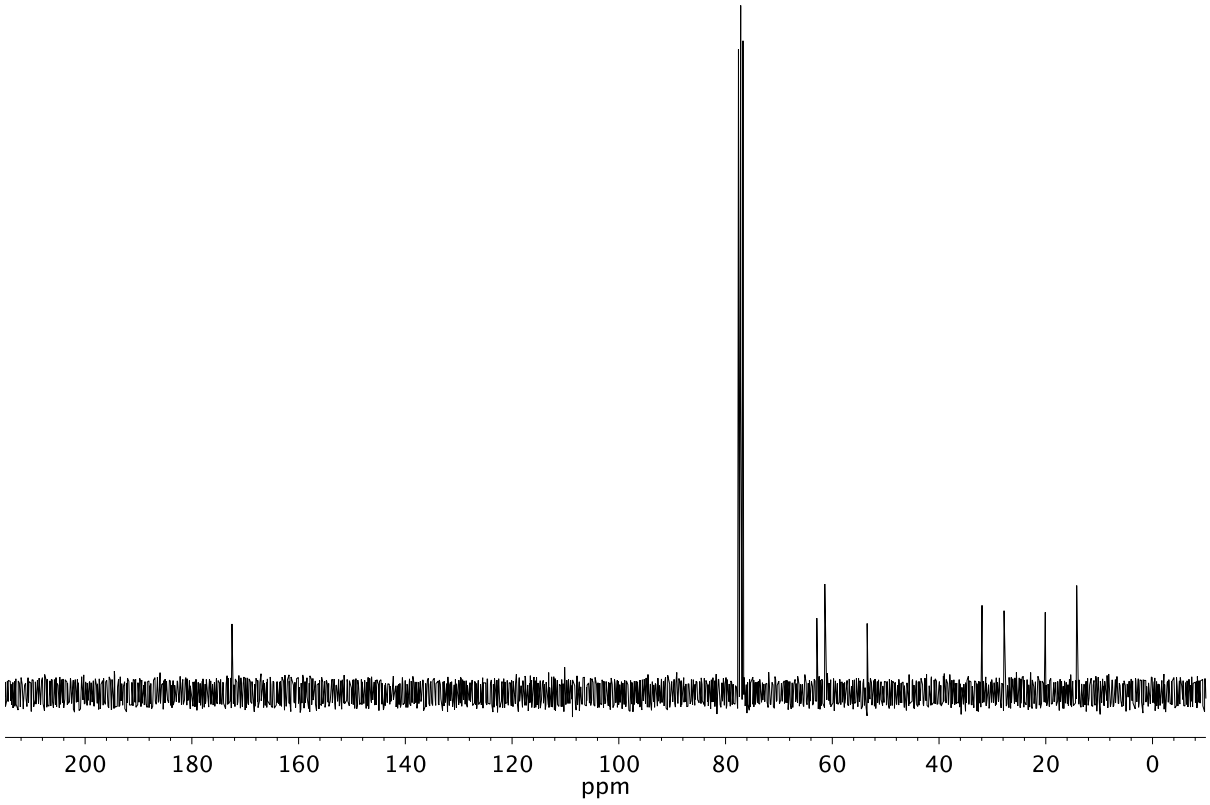
7



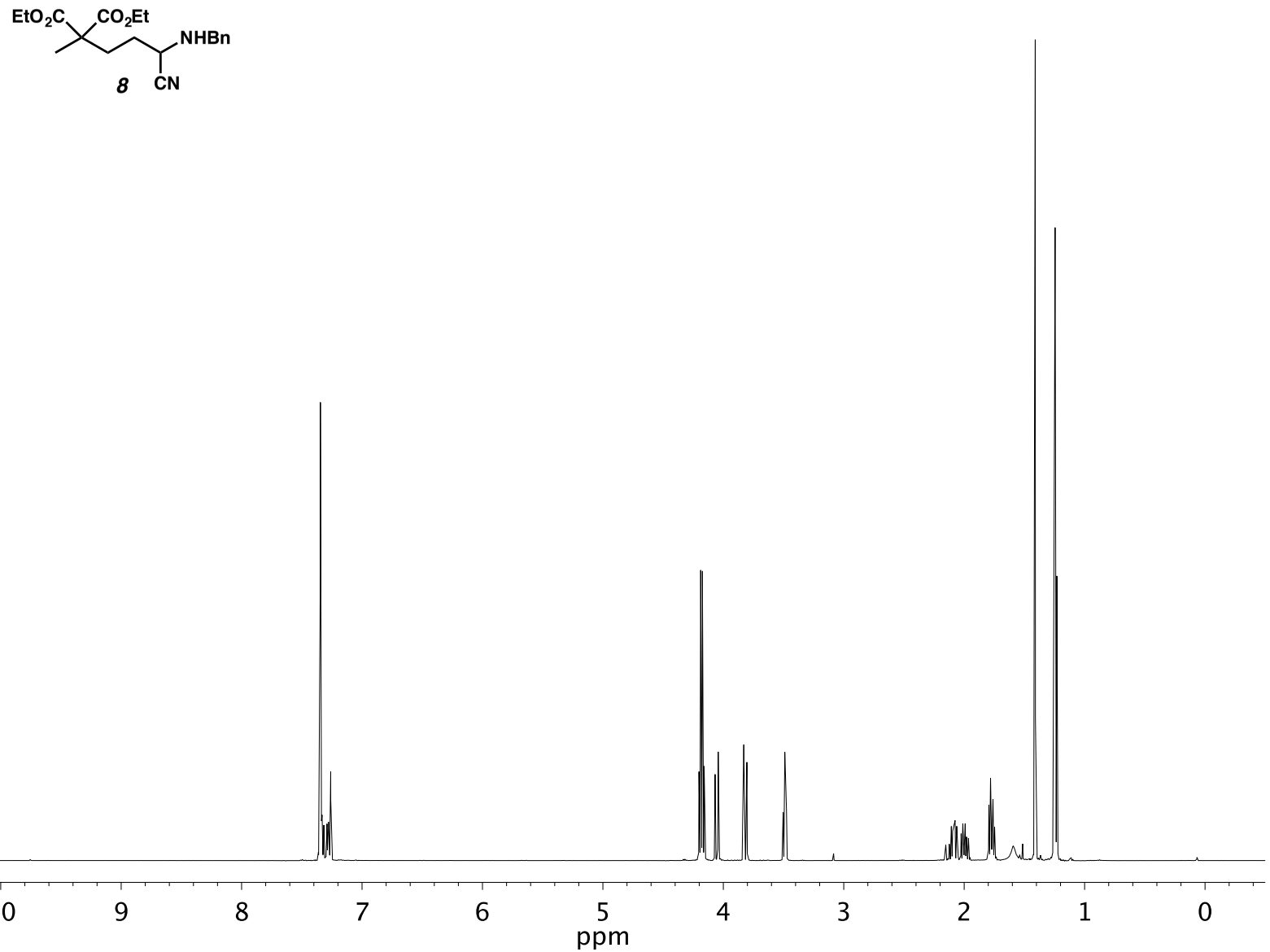
^{1}H NMR (300 MHz, $CDCl_3$) of compound **7**.



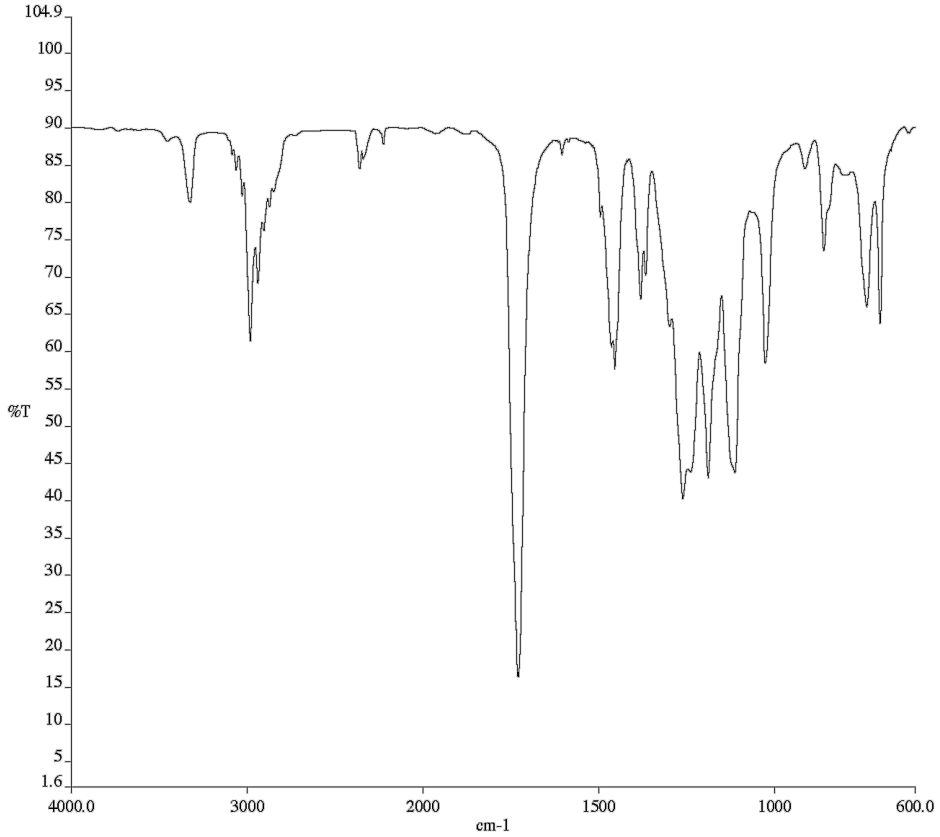
Infrared spectrum (Thin Film, KBr) of compound **7**.



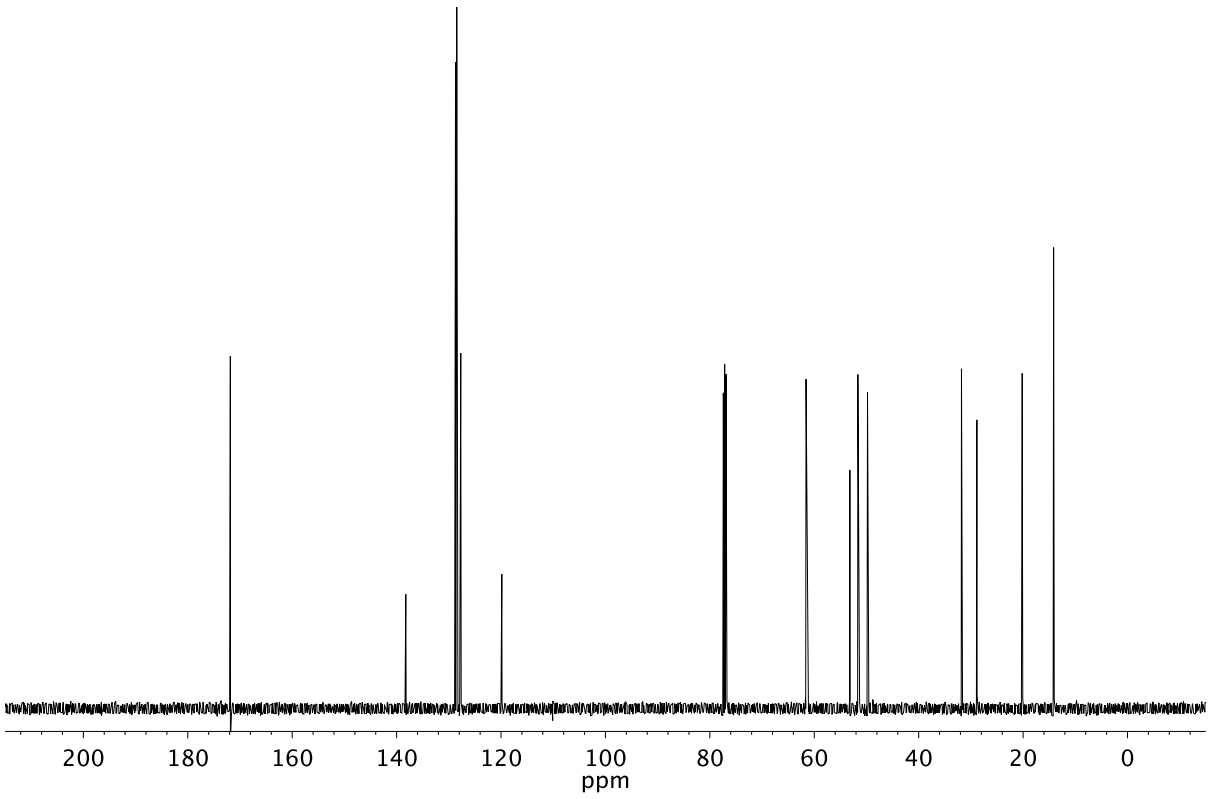
^{13}C NMR (75 MHz, $CDCl_3$) of compound **7**.



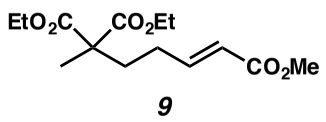
^{1}H NMR (500 MHz, $CDCl_3$) of compound **8**.



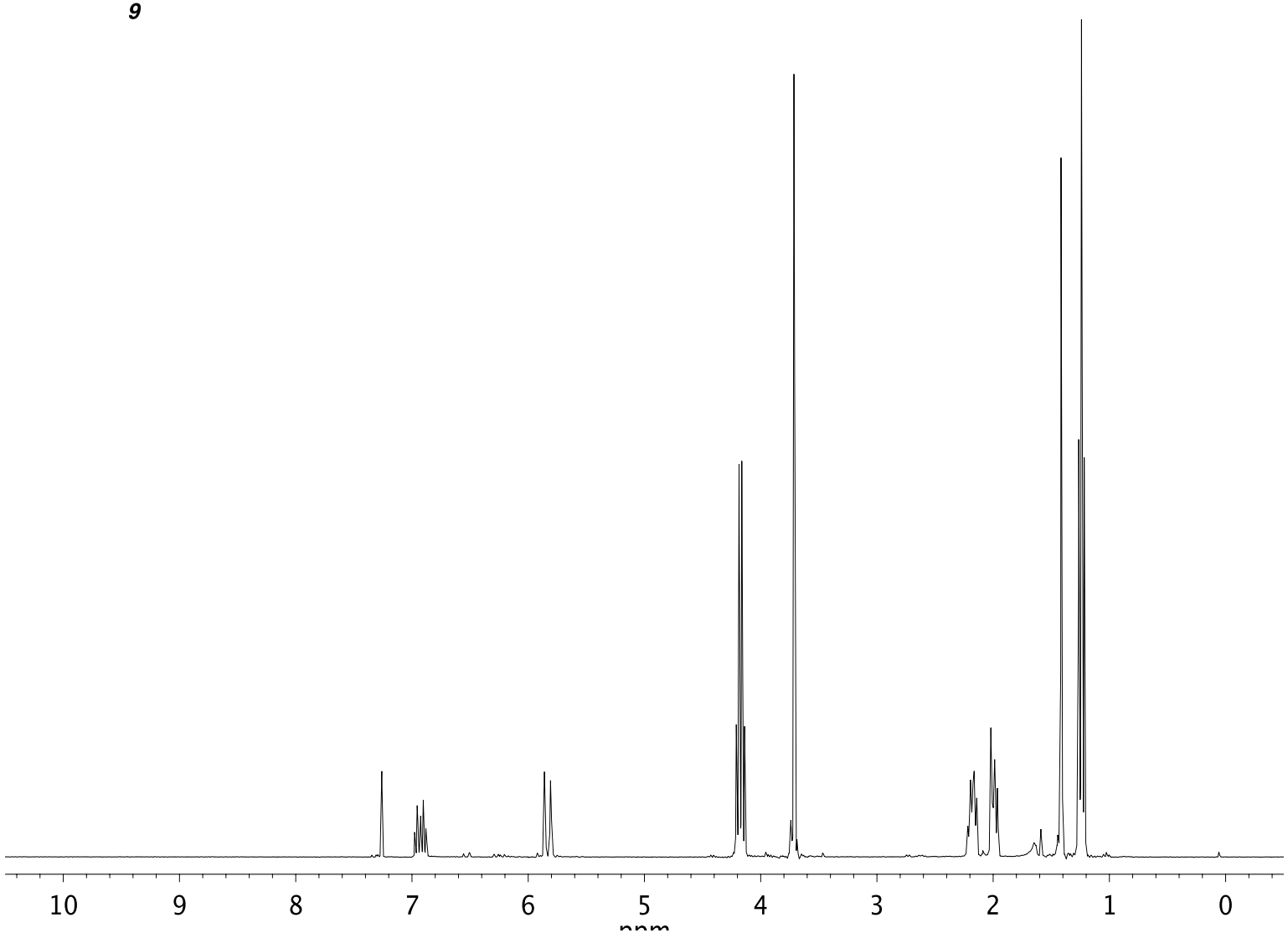
Infrared spectrum (Thin Film, KBr) of compound **8**.



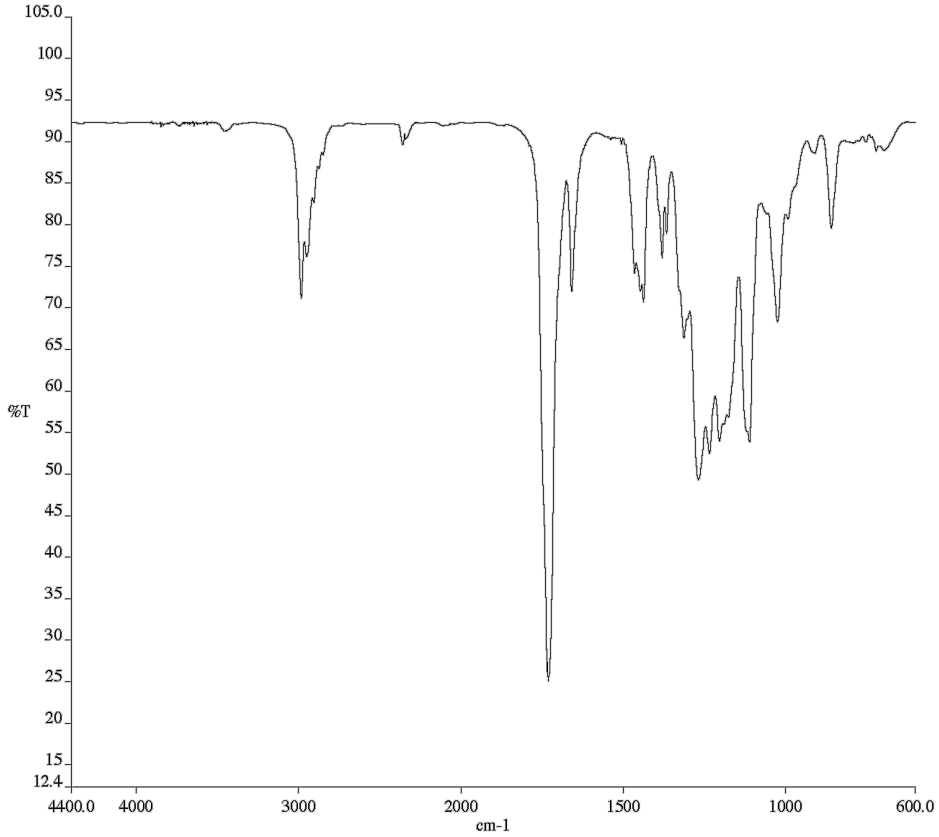
^{13}C NMR (126 MHz, $CDCl_3$) of compound **8**.



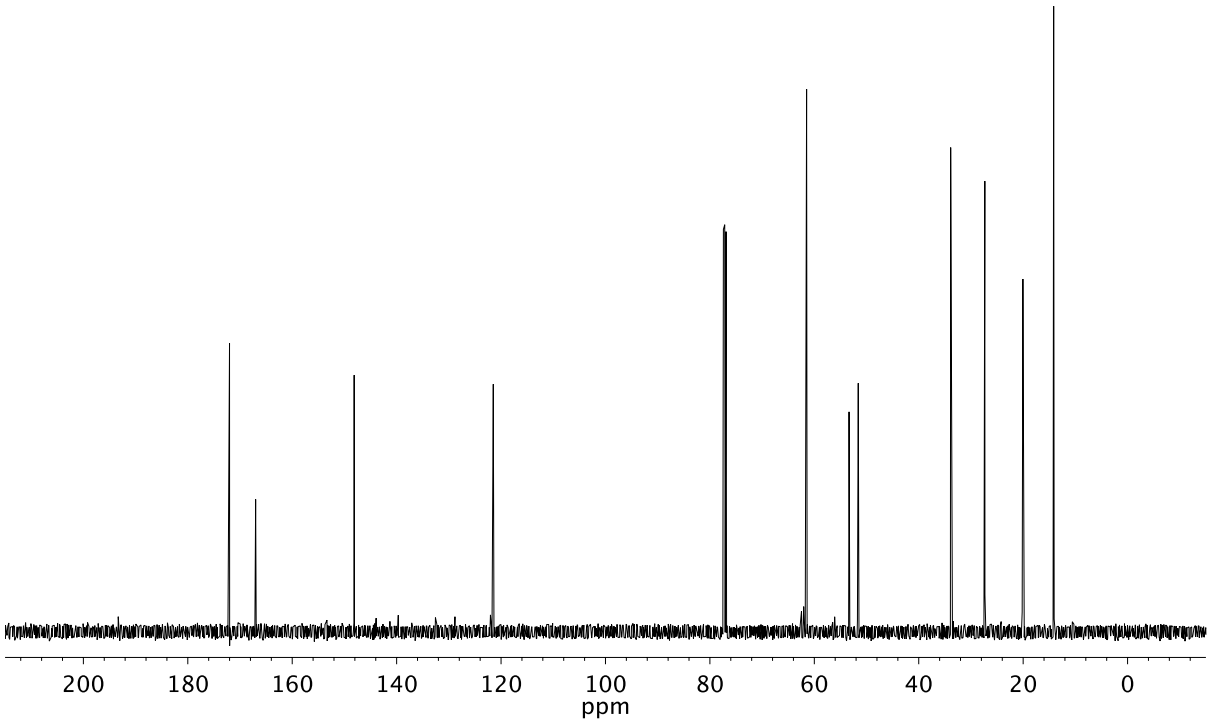
9



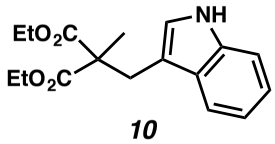
^{1}H NMR (300 MHz, $CDCl_3$) of compound **9**.



Infrared spectrum (Thin Film, KBr) of compound **9**.

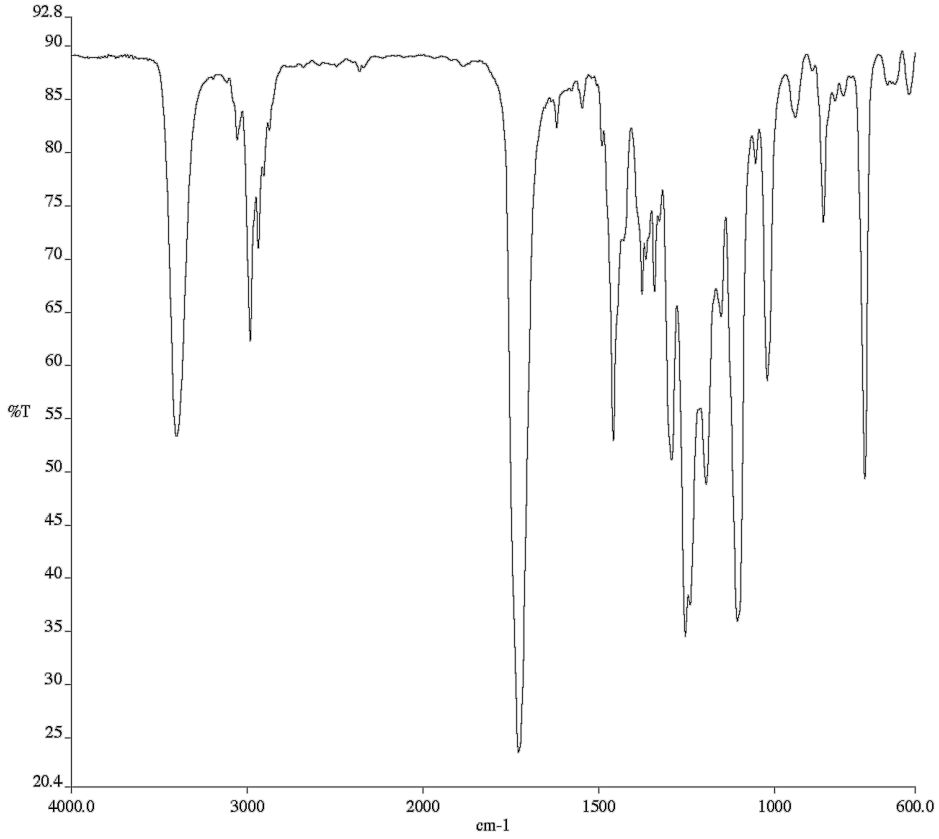


^{13}C NMR (126 MHz, $CDCl_3$) of compound **9**.

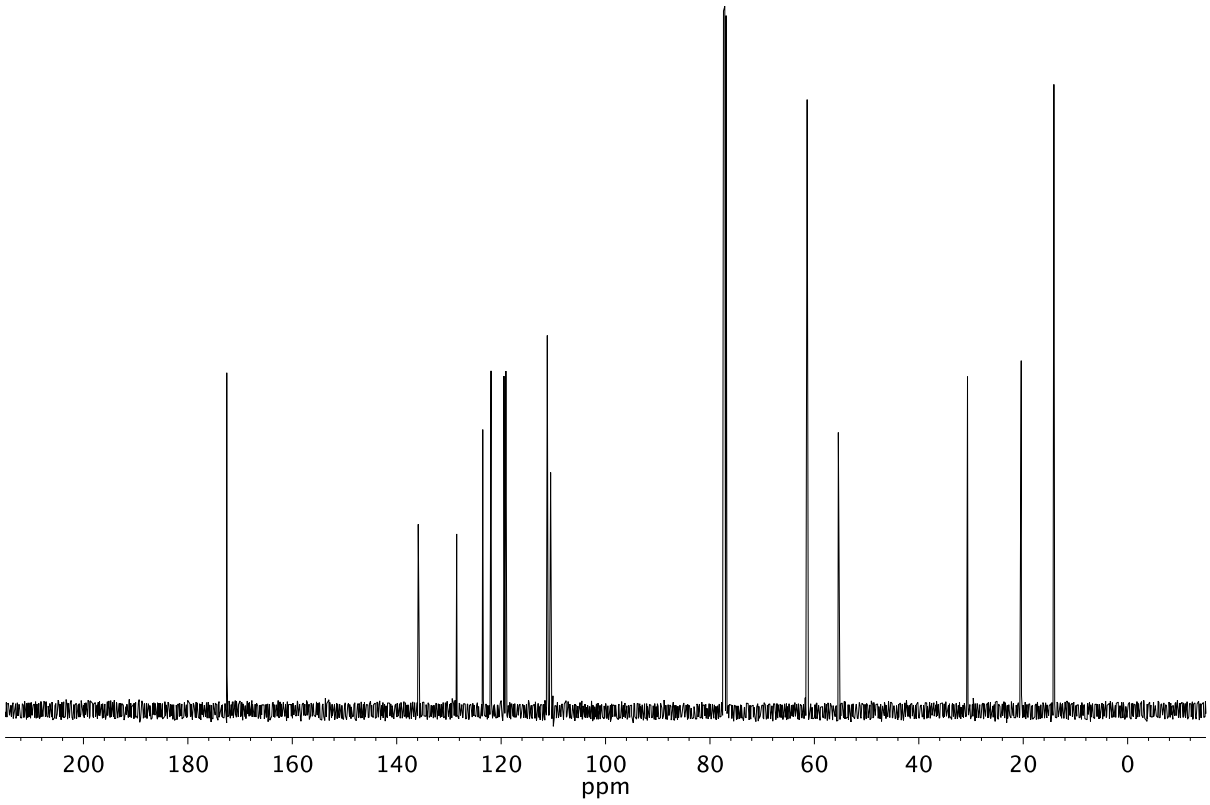


10

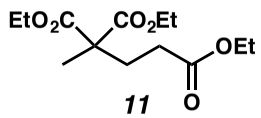
^{1}H NMR (500 MHz, $CDCl_3$) of compound **10**.

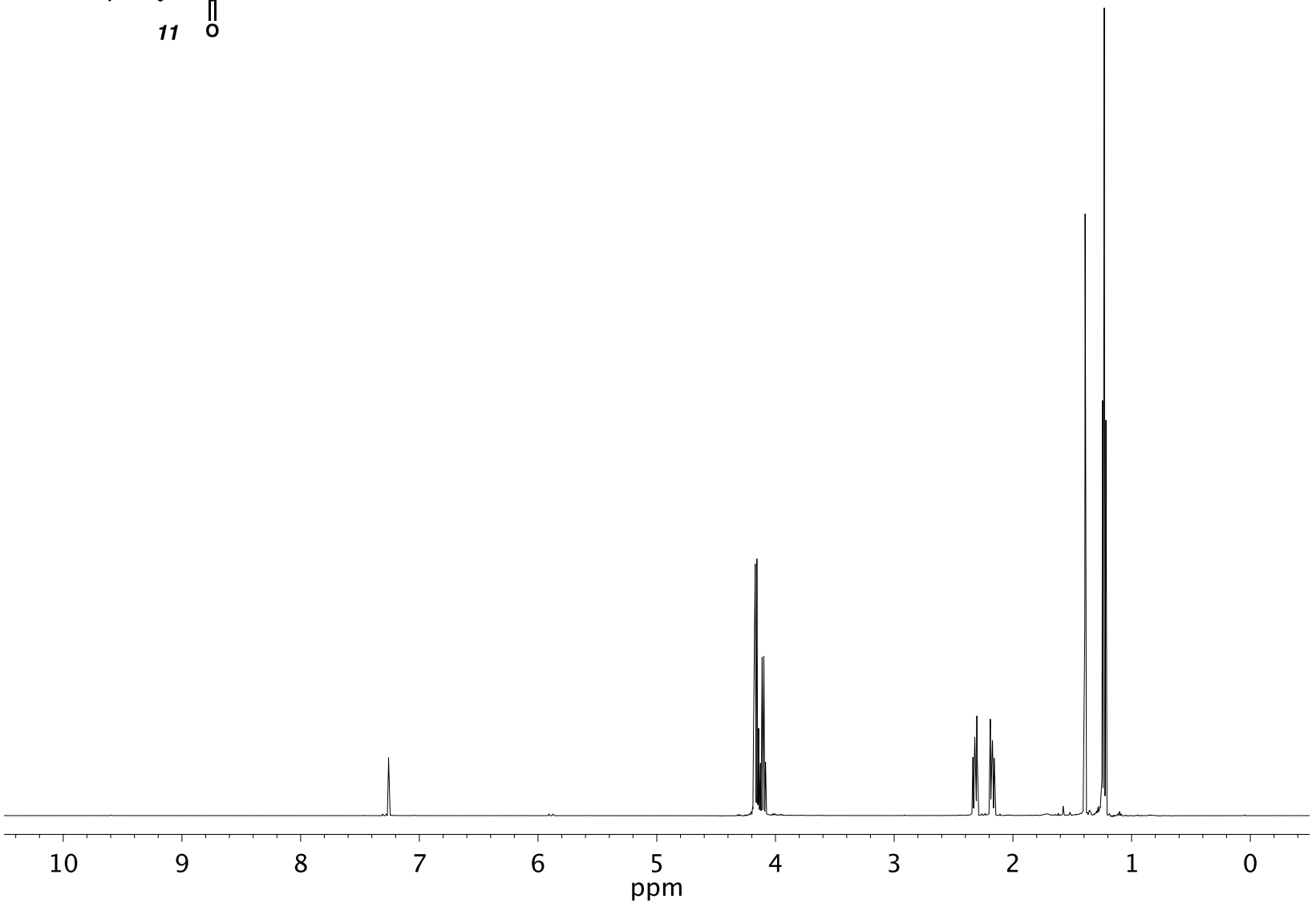


Infrared spectrum (Thin Film, KBr) of compound **10**.

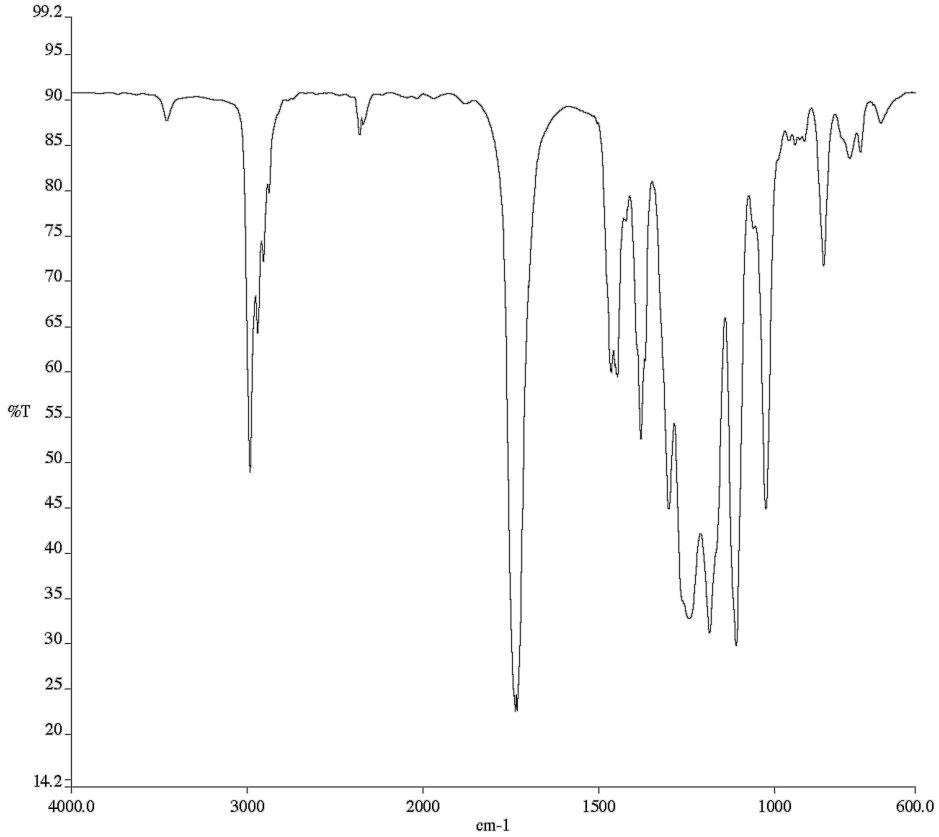


^{13}C NMR (126 MHz, $CDCl_3$) of compound **10**.

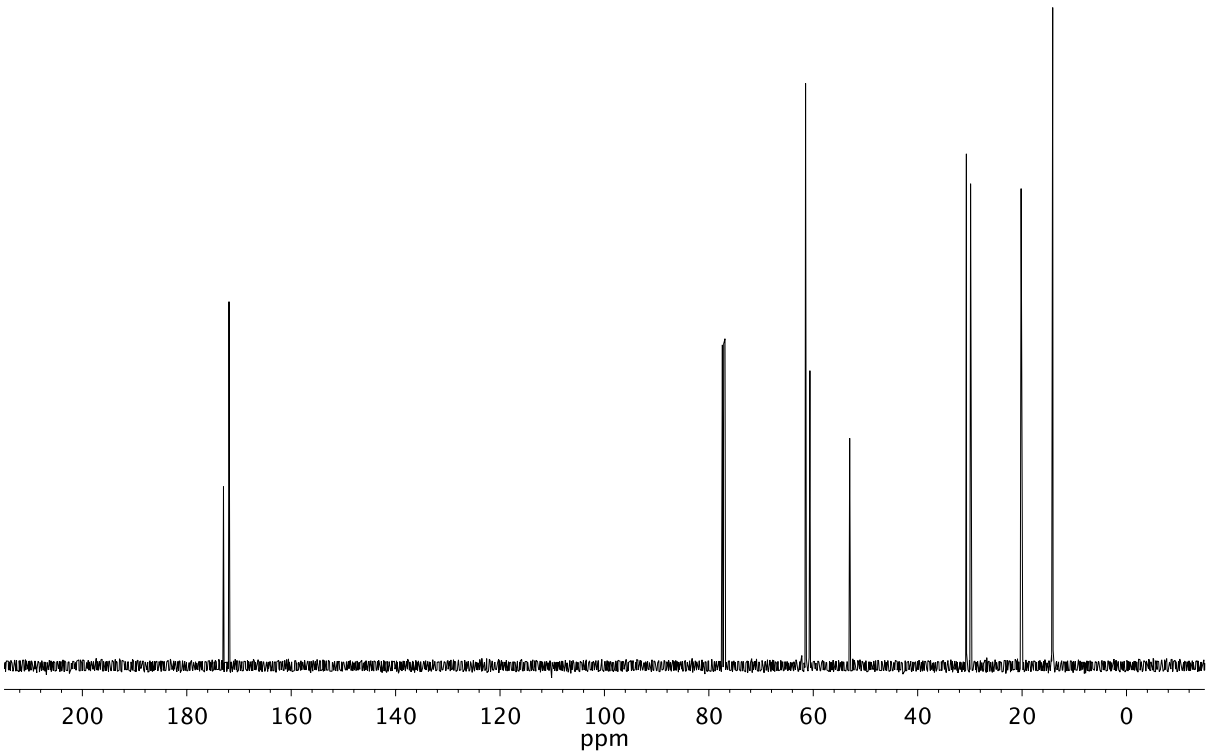




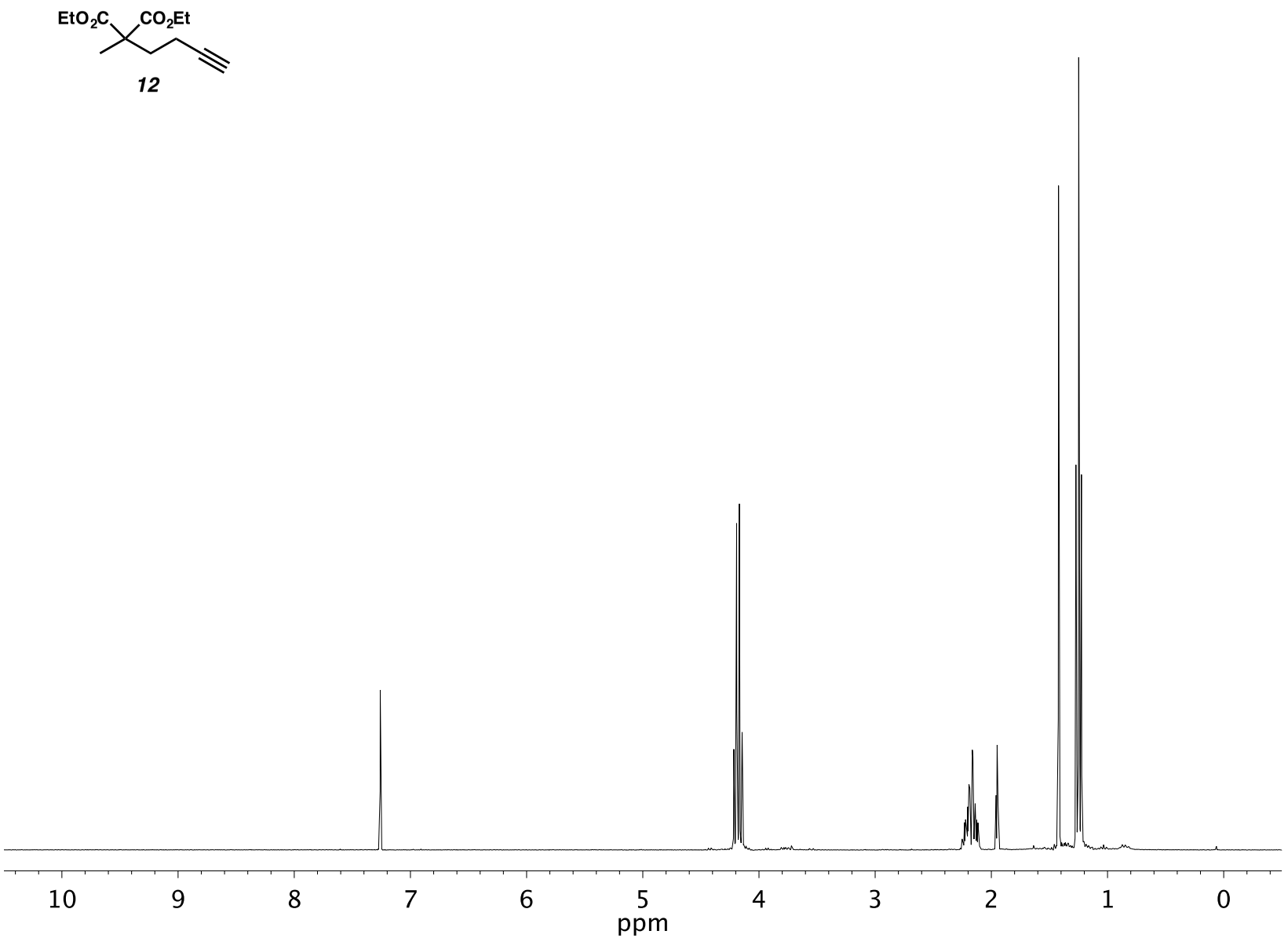
^{1}H NMR (500 MHz, $CDCl_3$) of compound **11**.



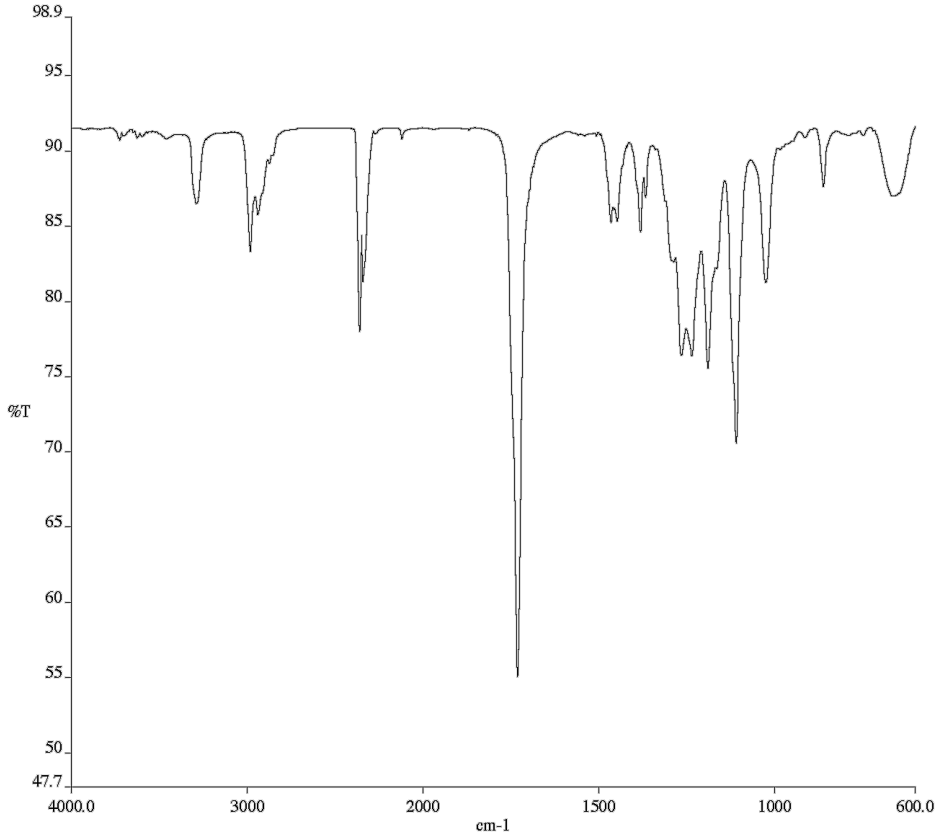
Infrared spectrum (Thin Film, KBr) of compound **11**.



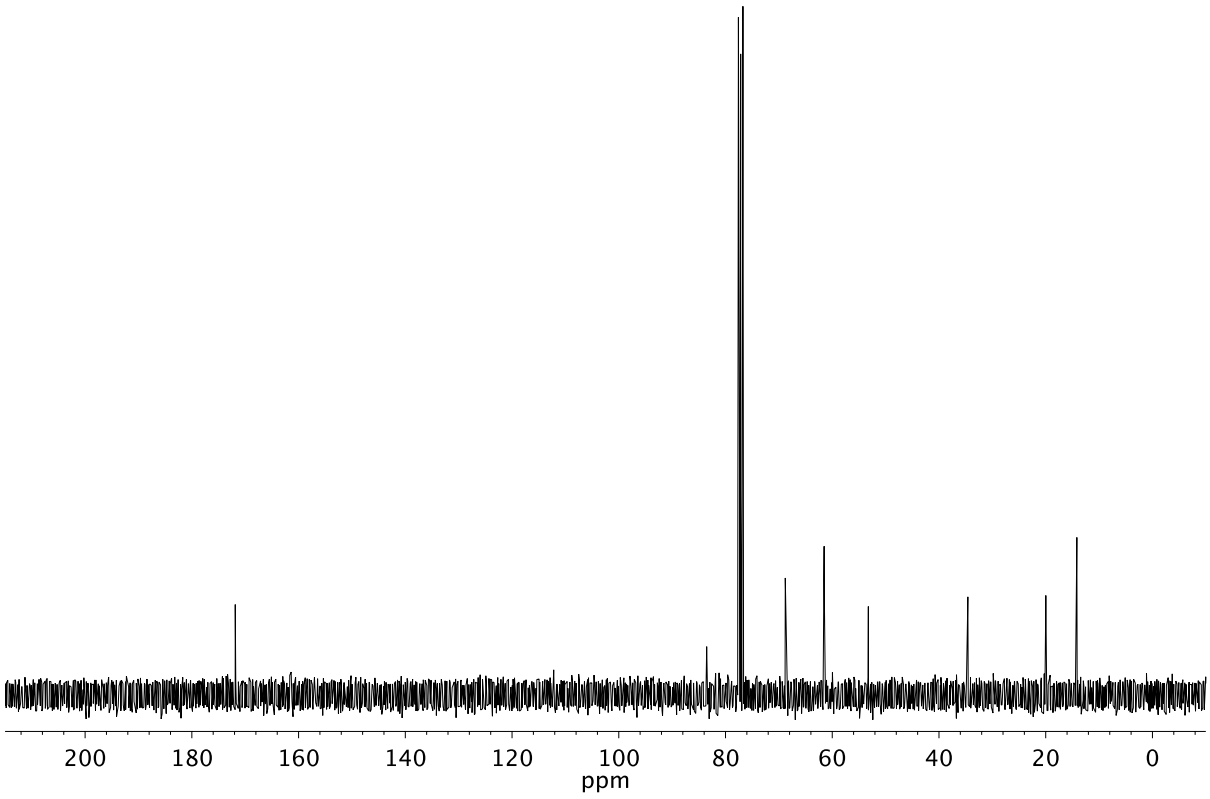
^{13}C NMR (126 MHz, $CDCl_3$) of compound **11**.



^{1}H NMR (300 MHz, $CDCl_3$) of compound **12**.



Infrared spectrum (Thin Film, KBr) of compound **12**.



^{13}C NMR (75 MHz, $CDCl_3$) of compound **12**.