Enantioselective Synthesis of Vicinal All-Carbon Quaternary Centers via Iridium-Catalyzed Allylic Alkylation

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Materials and Methods

Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon. Chemicals were purchased from Sigma Aldrich/Strem/Alfa Aesar/Oakwood Chemicals and used as received. Reaction temperatures were controlled by an IKAmag temperature modulator. Glove box manipulations were performed under a nitrogen atmosphere. Thin-layer chromatography (TLC) and preparatory TLC was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching, $KMnO_4$, or *p*-anisaldehyde staining. Silia*Flash* P60 Academic Silica gel (particle size 0.040–0.063 mm) was used for flash chromatography. Analytical chiral HPLC was performed with an Agilent

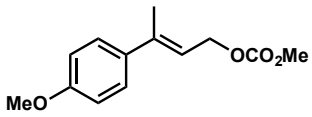
1100 Series HPLC utilizing a Chiralpak OJ column (4.6 mm x 25 cm) or a Chiralpak AD-H column (4.6 mm x 25 cm), both obtained from Daicel Chemical Industries, Ltd. with visualization at 210 nm. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing a Chiralpak OJ–H column (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. with visualization at 210 nm. ^{1}H NMR spectra were recorded on a Bruker Avance HD 400 MHz spectrometer and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Bruker Avance HD 400 MHz spectrometer and are reported relative to residual $CDCl_3$ (δ 77.16 ppm). Data for ^{1}H NMR are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm). Some reported spectra include minor solvent impurities of water (δ 1.56 ppm), ethyl acetate (δ 4.12, 2.05, 1.26 ppm), methylene chloride (δ 5.30 ppm), acetone (δ 2.17 ppm), grease (δ 1.26, 0.86 ppm), and/or silicon grease (δ 0.07 ppm), which do not impact product assignments. IR spectra were obtained using a Perkin Elmer Paragon 1000 spectrometer using thin films deposited on NaCl plates and 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 in fast atom bombardment (FAB+) or electron ionization (EI+) mode, or an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI+), atmospheric pressure chemical ionization (APCI+), or mixed ionization mode (MM: ESI-APCI+). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm pathlength cell and are reported as: $[\alpha]_D^T$ (concentration in g/100 mL, solvent).

Key Considerations: All synthesized reagents (i.e., (S_a)-**L**, **1**, **2**, **4**, and **6**) were dried over P_2O_5 and drierite in a vacuum desiccator under vacuum overnight before use in the iridium-catalyzed allylic alkylation reaction. THF was taken directly from an activated alumina column under argon and used immediately to eliminate the possibility of peroxides. Mesitylene or 1,2,4,5-tetrachloro-3-nitrobenzene were used as the internal standard for determining ^{1}H NMR yields. Prolonged storage of electrophiles **2** and **6** at room temperature under an air atmosphere results in the formation of an unidentified impurity; storage in a –30 °C freezer allows for prolonged storage.

List of Abbreviations: ee – enantiomeric excess, HPLC – high-performance liquid chromatography, SFC – super critical fluid chromatography, TLC – thin-layer chromatography, EtOAc – ethyl acetate, Et_2O – diethyl ether, THF – tetrahydrofuran, MeOH – methanol, TBD – 1,5,7-triazabicyclo[4.4.0]dec-5-ene, cod – *cis,cis*-1,5-cyclooctadiene, DIBAL – diisobutylaluminium hydride, dppp – 1,3-bis(diphenylphosphino)propane, DABCO – 1,4-diazabicyclo[2.2.2]octane

Preparation of Known Compounds: Previously reported methods were used to prepare ligand (S_a)-**L**[1] as well as starting materials **1**[2], **2**[3], **4a**[4], **4b**[2], **4c**[5], **4d**[6], **4e**[7], **4f**[7], **4g**[8], **4h**[9], **6a**[10], **6d**[11], **6e**[10], **6g**[11], **6h**[11], **6i**[10], **6j**[10], **6k**[12], and **6l**[10].

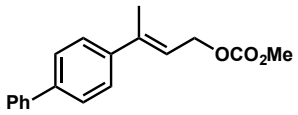
Representative Procedure for the Synthesis of Electrophiles:



(*E*)-3-(4-Methoxyphenyl)but-2-en-1-yl methyl carbonate (6b). To a solution of methyl (*E*)-3-(4-methoxyphenyl)but-2-enoate[13] (0.21 g, 1.0 mmol, 1 equiv) in THF (6.0 mL) at –78 °C was added DIBAL (0.62 mL, 3.0 mmol, 3.5 equiv) dropwise. The resulting reaction mixture was stirred at –78 °C for 2.5 h, whereupon the reaction was quenched with a saturated aqueous Rochelle's salt solution (10 mL). The cooling bath was then removed and the reaction was stirred for 18 h at ambient temperature. The aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL) and the combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure.

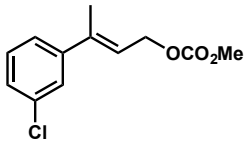
The crude material was dissolved in CH_2Cl_2 (4.0 mL) and cooled to 0 °C. Pyridine (0.64 mL, 8.3 mmol, 8.3 equiv) was added followed by methyl chloroformate (0.20 mL, 2.3 mmol, 2.3 equiv) dropwise. The resulting solution was allowed to warm to ambient temperature and was stirred for 18 h. The reaction was quenched with the addition of 1 M HCl (5 mL) and the aqueous layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (5% EtOAc/hexanes) to give carbonate **6b** as a colorless solid (0.13 g, 53% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 8.8 Hz, 2H), 6.86 (d, *J* = 8.8 Hz, 2H), 5.92 – 5.82 (m, 1H), 4.84 (dd, *J* = 7.2, 0.8 Hz, 2H), 3.81 (s, 3H), 3.80 (s, 3H), 2.16 – 2.05 (m, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.4, 156.0, 140.7, 134.9, 127.1, 119.1, 113.8, 65.2, 55.4, 54.9, 16.4; IR (Neat Film, NaCl) 2958, 2832, 1753, 1740, 1440, 1381, 1336, 1249, 1028, 942, 819, 798 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{13}H_{16}O_3$ $[M]^{+\bullet}$: 236.1049, found 236.1053.

Spectroscopic Data for the Synthesis of Electrophiles



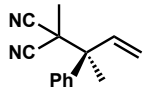
(*E*)-3-([1,1'-Biphenyl]-4-yl)but-2-en-1-yl methyl carbonate (6c). Carbonate **6c** was prepared from methyl (*E*)-3-([1,1'-biphenyl]-4-yl)but-2-enoate[14] according to the representative procedure and isolated by silica gel flash column chromatography (5% EtOAc/hexanes) as a colorless oil (0.17 g, 52% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, *J* = 19.6 Hz, 4H), 7.51 – 7.41 (m, 4H), 7.35 (t, *J* = 7.3 Hz, 1H), 6.00 (td, *J* = 7.0, 1.4 Hz, 1H), 4.88 (dq, *J* = 7.0, 0.8 Hz, 2H), 3.81 (s, 3H), 2.17 (dt, *J* = 1.3, 0.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 156.0, 141.4, 140.7, 140.7, 140.6, 128.9, 127.5, 127.1, 126.4, 120.8, 65.1, 55.0, 16.4; IR (Neat Film, NaCl) 3032, 2968, 1750, 1740, 1441, 1408, 1340,

1245, 992, 943, 827, 794, 759, 689 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{18}H_{18}O_3$ $[M]^{+\bullet}$: 282.1256, found 282.1253.



(*E*)-3-(3-Chlorophenyl)but-2-en-1-yl methyl carbonate (6f). Carbonate **6f** was prepared from methyl (*E*)-3-(3-chlorophenyl)but-2-enoate[15] according to the representative procedure and isolated by silica gel flash column chromatography (10% EtOAc/hexanes) as a colorless oil (0.43 g, 88% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (q, *J* = 1.5 Hz, 1H), 7.30 – 7.22 (m, 3H), 5.92 (ddt, *J* = 6.9, 5.6, 1.4 Hz, 1H), 4.84 (dq, *J* = 7.0, 0.8 Hz, 2H), 3.81 (s, 3H), 2.10 (dt, *J* = 1.4, 0.7 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 144.4, 139.8, 134.4, 129.7, 127.8, 126.3, 124.2, 122.0, 64.9, 55.0, 16.4; IR (Neat Film, NaCl) 2957, 1748, 1594, 1564, 1443, 1377, 1333, 1268, 1172, 1102, 997, 948, 906, 884, 782, 691 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{12}H_{13}ClO_3$ $[M]^{+\bullet}$: 240.0553, found 240.0564.

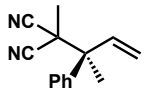
General Procedure for Optimization of the Ir-Catalyzed Allylic Alkylation (Table 1)



(*S*)-2-Methyl-2-(2-phenylbut-3-en-2-yl)malononitrile (3). In a nitrogen-filled glove box, to a 1 dram vial (vial A) equipped with a stir bar was added $[Ir(cod)Cl]_2$ (1.3 mg, 0.0020 mmol, 2 mol %), ligand (S_a)-**L** (2.0 mg, 0.004 mmol, 4 mol %), TBD (1.4 mg, 0.010 mmol, 10 mol %), and THF (0.5 mL). Vial A was stirred at 25 °C (ca. 10 min) while another 1 dram vial (vial B) was charged with nucleophile **1** (0.10 mmol or 0.20 mmol, as specified), THF (0.5 mL), and the base additive (0 or 200 mol %). The pre-formed catalyst solution (vial A) was then transferred to vial B followed immediately by carbonate **2** (0.20 mmol, 0.10 mmol, or 0.20 mmol, as specified). The vial was sealed and stirred at 60 °C. After 18 h, the vial was removed from the glove box concentrated under reduced pressure. To the crude reaction mixture was added 1,2,4,5-tetrachloro-3-nitrobenzene (0.10 mmol in 0.5 mL $CDCl_3$). The NMR yield (measured in reference to 1,2,4,5-tetrachloro-3-nitrobenzene δ 7.74 ppm (s, 1H)) was determined by ^{1}H NMR analysis of the crude mixture. The residue was purified by preparatory TLC (15% Et_2O/hexanes, eluted twice) to afford allylic alkylation product **3** as a pale yellow oil.

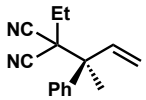
General Procedure for the Ir-Catalyzed Allylic Alkylation

Please note that the absolute configuration was determined only for compound **7c** via X-ray crystallographic analysis. The absolute configuration for all other products has been inferred by analogy. For respective HPLC and SFC conditions, please refer to Table S1.

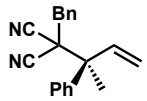


(*S*)-2-Methyl-2-(2-phenylbut-3-en-2-yl)malononitrile (3). In a nitrogen-filled glove box, to a 1 dram vial (vial A) equipped with a stir bar was added $[Ir(cod)Cl]_2$ (2.7 mg, 0.0040 mmol, 2 mol %), ligand (S_a)-**L** (4.0 mg, 0.008 mmol, 4 mol %), TBD (2.8 mg, 0.020 mmol, 10 mol %), and THF (1 mL). Vial A was stirred at 25 °C (ca. 10 min) while another 1 dram vial (vial B) was charged with nucleophile **1** (18 mg, 0.20 mmol, 100 mol %), THF (1 mL), DABCO (45 mg, 0.40 mmol, 200 mol %), and BEt_3 (400 μL, 1M in hexanes). The pre-formed catalyst solution (vial A) was then transferred to vial B followed immediately by carbonate **2** (83 mg, 0.40 mmol, 200 mol %). The vial was sealed and stirred at 60 °C. After 18 h, the vial was removed from the glove box, transferred to a 20 mL vial with CH_2Cl_2, and concentrated under reduced pressure. The crude residue was purified by preparatory TLC (15% Et_2O/hexanes, eluted twice) to afford allylic alkylation product **3** as a pale yellow oil (37 mg, 89% yield): 95% ee; $[\alpha]_D^{25}$ +32.9 (*c* 1.9, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.52 (m, 2H), 7.44 – 7.33 (m, 3H), 6.49 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.63 – 5.31 (m, 2H), 1.80 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.2, 138.3, 128.7, 128.6, 128.1, 119.0, 116.1, 116.0, 49.4, 41.9, 21.8, 21.5; IR (Neat Film, NaCl) 3095, 3062, 2992, 2951, 2247, 1749, 1639, 1600, 1496, 1447, 1417, 1386, 1270, 1217, 1165, 1102, 1074, 1031, 1003, 937, 802, 751, cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{14}N_2$ $[M]^{+\bullet}$: 210.1157, found 210.1156; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.832, minor = 4.594.

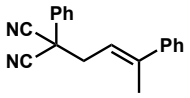
Spectroscopic Data for the Ir-Catalyzed Allylic Alkylation Products



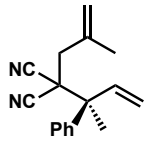
(*S*)-2-Ethyl-2-(2-phenylbut-3-en-2-yl)malononitrile (5a). Allylic alkylation product **5a** was prepared according to the general procedure and isolated by preparatory TLC (100% toluene, eluted twice) to give a pale yellow oil (34 mg, 76% yield): 95% ee; $[\alpha]_D^{25}$ +19.0 (*c* 0.87, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.51 (m, 2H), 7.45 – 7.31 (m, 3H), 6.51 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.52 (d, *J* = 11.0 Hz, 1H), 5.40 (d, *J* = 17.3 Hz, 1H), 1.90 – 1.72 (m, 5H), 1.27 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.6, 138.7, 128.6, 128.5, 128.2, 118.7, 115.2, 115.1, 49.9, 49.7, 27.7, 22.0, 10.7; IR (Neat Film, NaCl) 3094, 3061, 2959, 2931, 2874, 2244, 1730, 1640, 1600, 1496, 1461, 1446, 1416, 1382, 1271, 1175, 1074, 1031, 1002, 937, 793, 750, 701 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1395; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.378, minor = 4.088.



(*S*)-2-Benzyl-2-(2-phenylbut-3-en-2-yl)malononitrile (5b). Allylic alkylation product **5b** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a pale yellow oil (39 mg, 69% yield): 93% ee; $[\alpha]_D^{25}$ +11.0 (*c* 1.0, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.62 (m, 2H), 7.51 – 7.29 (m, 8H), 6.64 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.60 (d, *J* = 11.0 Hz, 1H), 5.47 (d, *J* = 17.2 Hz, 1H), 3.07 – 2.90 (m, 2H), 1.93 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 138.5, 132.6, 130.5, 128.9, 128.7, 128.7, 128.6, 128.3, 119.1, 114.9, 114.7, 50.6, 50.3, 39.6, 22.1; IR (Neat Film, NaCl) 3092, 3063, 3034, 2990, 2927, 2245, 1957, 1884, 1810, 1748, 1602, 1498, 1456, 1446, 1416, 1383, 1270, 1212, 1159, 1110, 1080, 1032, 1004, 938, 766, 749 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{20}H_{19}N_2$ $[M+H]^+$: 287.1548, found 287.1553; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 10.960, minor = 11.727.

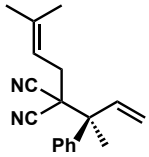


(*E*)-2-Phenyl-2-(3-phenylbut-2-en-1-yl)malononitrile (SI-1). Linear allylic alkylation product **SI-1** was prepared according to the general procedure in 99% conversion by ^1H NMR yield but was inseparable from unreacted electrophile **2**. **SI-1** was prepared via an alternate route for verification and characterization. In a nitrogen-filled glove box, to a 1 dram vial equipped with a stir bar was added $Pd(PPh_3)_4$ (11 mg, 0.01 mmol, 0.1 mol %), nucleophile **4c** (21 mg, 0.15 mmol, 1.5 equiv), electrophile **2** (21 mg, 0.10 mmol, 1.0 equiv), and THF (1 mL). The reaction was stirred for 18 h whereupon the vial was removed from the glove box, transferred to a 20 mL vial with CH_2Cl_2, and concentrated under reduced pressure. The crude residue was purified by preparatory TLC (20% Et_2O/hexanes, eluted twice) to afford **SI-1** as a colorless crystalline solid (23 mg, 43% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.28 (m, 10H), 5.75 (td, *J* = 7.8, 1.5 Hz, 1H), 3.23 – 3.01 (m, 2H), 1.95 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.8, 142.6, 131.7, 130.1, 129.8, 128.5, 128.0, 126.1, 126.1, 117.2, 115.0, 42.5, 42.0, 16.6; IR (Neat Film, NaCl) 3062, 3032, 2983, 2930, 2246, 1599, 1494, 1451, 1383, 1277, 1027, 861, 756, 692 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{19}H_{17}N_2$ $[M+H]^+$: 273.1292, found 273.1387.

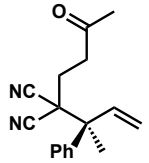


(*S*)-2-(2-methylallyl)-2-(2-phenylbut-3-en-2-yl)malononitrile (5d). Allylic alkylation product **5d** was prepared according to the general procedure and isolated by preparatory TLC (100% toluene, eluted twice) to give a pale yellow oil (17 mg, 33% yield): 92% ee;

$[\alpha]_D^{25}$ +26.0 (*c* 0.94, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.45 – 7.32 (m, 3H), 6.54 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.55 (d, *J* = 11.0 Hz, 1H), 5.41 (d, *J* = 17.3 Hz, 1H), 5.11 (t, *J* = 1.4 Hz, 1H), 5.01 (p, *J* = 1.0 Hz, 1H), 2.50 – 2.35 (m, 2H), 1.91 (dd, *J* = 1.6, 0.8 Hz, 3H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 138.5, 137.9, 128.7, 128.6, 128.3, 119.1, 118.7, 115.4, 115.2, 50.4, 47.6, 41.5, 23.2, 22.0; IR (Neat Film, NaCl) 3085, 2988, 2242, 1747, 1650, 1496, 1445, 1416, 1381, 1264, 1072, 1004, 910, 792, 750, 698 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{19}N_2$ $[M+H]^+$: 251.1548, found 251.1539; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.138, minor = 3.923.

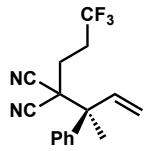


(*S*)-2-(3-Methylbut-2-en-1-yl)-2-(2-phenylbut-3-en-2-yl)malononitrile (5e). Allylic alkylation product **5e** was prepared according to the general procedure and isolated by preparatory TLC (5% Et_2O/hexanes, eluted twice) to give a colorless oil (49 mg, 92% yield): 96% ee; $[\alpha]_D^{25}$ +7.87 (*c* 6.3, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.47 – 7.31 (m, 3H), 6.54 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.54 (d, *J* = 11.0 Hz, 1H), 5.41 (d, *J* = 17.3 Hz, 1H), 5.34 – 5.24 (m, 1H), 2.46 (qd, *J* = 14.1, 7.6 Hz, 2H), 1.84 (s, 3H), 1.78 (d, *J* = 1.4 Hz, 3H), 1.60 (d, *J* = 1.4 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.4, 139.6, 138.7, 128.6, 128.5, 128.1, 118.7, 115.3, 115.3, 115.2, 49.6, 48.9, 32.7, 26.1, 21.9, 18.4; IR (Neat Film, NaCl) 3089, 2987, 2926, 2242, 1497, 1446, 1416, 1383, 1004, 935, 838, 750, 700 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{18}H_{21}N_2$ $[M+H]^+$: 265.1705, found 265.1709; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.095, minor = 4.061.

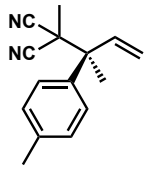


(*S*)-2-(3-oxobutyl)-2-(2-phenylbut-3-en-2-yl)malononitrile (5f). Allylic alkylation product **5f** was prepared according to the general procedure and isolated by preparatory TLC (20% Et_2O/hexanes, eluted twice) to give a colorless oil (28 mg, 52% yield): 96% ee; $[\alpha]_D^{25}$ +16.8 (*c* 1.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.53 (m, 2H), 7.46 – 7.30 (m, 3H), 6.50 (dd, *J* = 17.2, 10.9 Hz, 1H), 5.54 (d, *J* = 11.0 Hz, 1H), 5.41 (d, *J* = 17.2 Hz, 1H), 2.86 – 2.75 (m, 2H), 2.19 (s, 3H), 2.17 – 1.97 (m, 2H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 205.1, 139.2, 138.2, 128.7, 128.6, 128.1, 119.1, 115.0, 114.9, 49.8, 47.7, 40.0, 30.2, 27.8, 21.8; IR (Neat Film, NaCl) 3094, 3061, 2991, 2957, 2246, 1721, 1640, 1601, 1582, 1496, 1446, 1418, 1370, 1288, 1215, 1170, 1118, 1080, 1032, 1002, 938, 754, 702 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{17}H_{19}N_2O$ $[M+H]^+$: 267.1497, found

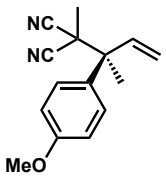
267.1499; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 5.022, minor = 7.267.



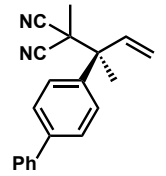
(*S*)-2-(2-Phenylbut-3-en-2-yl)-2-(3,3,3-trifluoropropyl)malononitrile (5g). Allylic alkylation product **5g** was prepared according to the general procedure and isolated by preparatory TLC (100% toluene, eluted twice) to give a colorless oil (29 mg, 50% yield): 91% ee; $[\alpha]_D^{25}$ +16.6 (*c* 1.8, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.32 (m, 5H), 6.50 (dd, *J* = 17.2, 10.9 Hz, 1H), 5.59 (d, *J* = 11.0 Hz, 1H), 5.44 (d, *J* = 17.2 Hz, 1H), 2.57 – 2.39 (m, 2H), 2.12 – 1.93 (m, 2H), 1.84 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 137.7, 128.87, 128.86, 127.9, 125.7 (q, *J* = 276.4 Hz), 119.5, 114.3, 114.1, 49.9, 47.5, 31.7, 31.3 (q, *J* = 30.3 Hz), 27.1 (q, *J* = 3.4 Hz); IR (Neat Film, NaCl) 3096, 3063, 2992, 2928, 2242, 1496, 1447, 1400, 1318, 1257, 1157, 1089, 1046, 940, 845, 752, 701, 624 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{16}H_{15}F_2N_2$ $[M]^{+\bullet}$: 292.1187, found 292.1173; SFC conditions: 1% IPA, 3.0 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 1.651, minor = 1.868.



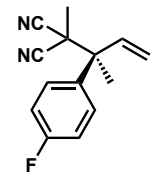
(*S*)-2-Methyl-2-(2-(*p*-tolyl)but-3-en-2-yl)malononitrile (7a). Allylic alkylation product **7a** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a pale yellow oil (36 mg, 80% yield): 96% ee; $[\alpha]_D^{25}$ +48.7 (*c* 1.1, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.39 (m, 2H), 7.23 – 7.16 (m, 2H), 6.48 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.52 (d, *J* = 11.0 Hz, 1H), 5.40 (d, *J* = 17.3 Hz, 1H), 2.35 (s, 3H), 1.77 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.44, 138.42, 136.2, 129.3, 128.0, 118.8, 116.2, 116.1, 49.2, 42.0, 21.8, 21.5, 21.1; IR (Neat Film, NaCl) 3094, 2992, 2953, 2925, 2247, 1748, 1682, 1639, 1614, 1515, 1454, 1416, 1383, 1268, 1198, 1102, 1074, 1019, 937, 825, 804, 774 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{16}N_2$ $[M]^{+\bullet}$: 224.1314, found 224.1306; SFC conditions: 1% IPA, 3.0 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.658, minor = 4.375.



(*S*)-2-(2-(4-Methoxyphenyl)but-3-en-2-yl)-2-methylmalononitrile (7b). Allylic alkylation product **7b** was prepared according to the general procedure and isolated by preparatory TLC (20% Et_2O/hexanes, eluted twice) to give a pale yellow oil (34 mg, 70% yield): 96% ee; $[\alpha]_D^{25}$ +25.4 (*c* 2.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.42 (m, 2H), 6.95 – 6.88 (m, 2H), 6.47 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.52 (d, *J* = 11.0 Hz, 1H), 5.39 (d, *J* = 17.3 Hz, 1H), 3.82 (s, 3H), 1.77 (s, 3H), 1.65 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.5, 138.5, 131.0, 129.4, 118.7, 116.2, 116.1, 113.9, 55.4, 49.0, 42.1, 21.7, 21.6; IR (Neat Film, NaCl) 2998, 2934, 2832, 2242, 1609, 1514, 1458, 1298, 1257, 1188, 1029, 932, 832, 808, 774 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{15}ON_2$ $[(M+H)–H_2]^+$: 239.1184, found 239.1198; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 5.019, minor = 5.890.

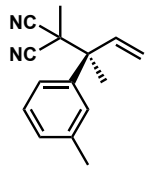


(*S*)-2-(2-([1,1'-Biphenyl]-4-yl)but-3-en-2-yl)-2-methylmalononitrile (7c). Allylic alkylation product **7c** was prepared according to the general procedure and isolated by preparatory TLC (20% Et_2O/hexanes, eluted twice) to give a colorless crystalline solid (58 mg, 99% yield): 95% ee; $[\alpha]_D^{25}$ +42.3 (*c* 1.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.67 – 7.32 (m, 9H), 6.53 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.58 (d, *J* = 10.9 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 1.84 (s, 3H), 1.71 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.3, 140.1, 138.2, 138.1, 129.0, 128.5, 127.8, 127.24, 127.21, 119.1, 116.1, 116.0, 49.3, 41.9, 21.8, 21.5; IR (Neat Film, NaCl) 3059, 3032, 2992, 2952, 2247, 1749, 1488, 1450, 1416, 1386, 1267, 1214, 1168, 1102, 1076, 1007, 937, 842, 766, 749, 698 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{20}H_{18}N_2$ $[M]^{+\bullet}$: 286.1470, found 286,1466; SFC conditions: 1% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 43.531, minor = 40.798.

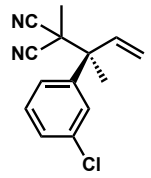


(*S*)-2-(2-(4-fluorophenyl)but-3-en-2-yl)-2-methylmalononitrile (7d). Allylic alkylation product **7d** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a colorless oil (45 mg, 99% yield): 94% ee;

$[\alpha]_D^{25}$ +23.5 (*c* 3.4, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.54 (dd, *J* = 9.0, 5.1 Hz, 2H), 7.09 (dd, *J* = 9.1, 8.3 Hz, 2H), 6.46 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.55 (d, *J* = 11.0 Hz, 1H), 5.41 (d, *J* = 17.3 Hz, 1H), 1.78 (s, 3H), 1.67 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.6 (d, *J* = 249.0 Hz), 138.1, 135.1 (d, *J* = 3.3 Hz), 130.1, 130.0, 119.3, 115.9 (d, *J* = 10.2 Hz), 115.6 (d, *J* = 21.4 Hz), 49.1, 42.0, 21.7, 21.7; IR (Neat Film, NaCl) 3074, 2993, 2247, 1752, 16001, 1509, 1453, 1416, 1386, 1239, 1170, 1097, 1014, 936, 838, 820, 782, 643 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{13}FN_2$ $[M]^{+\bullet}$: 228.1063, found 228.1036; HPLC conditions: 3% IPA, 1 mL/min, Chiralpak OJ column, λ = 210 nm, t_R (min): major = 22.493, minor = 29.003.

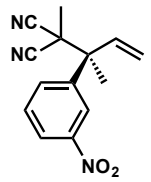


(*S*)-2-Methyl-2-(2-(*m*-tolyl)but-3-en-2-yl)malononitrile (7e). Allylic alkylation product **7e** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a colorless oil (30 mg, 67% yield): 95% ee; $[\alpha]_D^{25}$ +29.8 (*c* 1.8, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.32 – 7.22 (m, 1H), 7.17 (ddt, *J* = 7.4, 1.4, 0.7 Hz, 1H), 6.48 (dd, *J* = 17.3, 11.0 Hz, 1H), 5.53 (d, *J* = 11.0 Hz, 1H), 5.42 (d, *J* = 17.3 Hz, 1H), 2.38 (d, *J* = 0.8 Hz, 3H), 1.78 (s, 3H), 1.66 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.1, 138.4, 138.3, 129.2, 128.7, 128.5, 125.1, 118.8, 116.1, 116.0, 49.2, 41.8, 21.8, 21.8, 21.4; IR (Neat Film, NaCl) 3092, 2992, 2951, 2924, 2246, 1638, 1606, 1588, 1492, 1454, 1417, 1384, 1250, 1162, 1106, 1042, 1002, 937, 794, 766, 705 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1387; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 2.897, minor = 3.290.

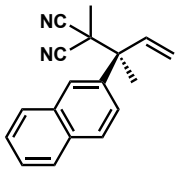


(*S*)-2-(2-(3-Chlorophenyl)but-3-en-2-yl)-2-methylmalononitrile (7f). Allylic alkylation product **7f** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a pale yellow oil (48 mg, 99% yield): 99% ee; $[\alpha]_D^{25}$ +3.2 (*c* 3.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.43 (m, 2H), 7.40 – 7.30 (m, 2H), 6.43 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.58 (d, *J* = 11.0 Hz, 1H), 5.43 (d, *J* = 17.3 Hz, 1H), 1.78 (s, 3H), 1.68 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.4, 137.6, 134.7, 129.9, 128.8, 128.5, 126.2, 119.6, 115.8, 115.7, 49.3, 41.7, 21.7, 21.4; IR (Neat Film, NaCl) 3071, 2992, 2957, 2247, 1880, 1752, 1637, 1594, 1571, 1478, 1458, 1414, 1261, 1217, 1168, 1094, 999, 938, 885, 811, 739, 695 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{13}ClN_2$

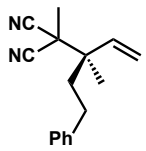
$[M]^{+\bullet}$: 244.0767, found 244.0773; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.255, minor = 4.955.



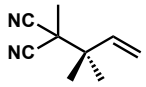
(*S*)-2-Methyl-2-(2-(3-nitrophenyl)but-3-en-2-yl)malononitrile (7g). Allylic alkylation product **7g** was prepared according to the general procedure and isolated by preparatory TLC (25% Et_2O/hexanes) to give a pale yellow solid (43 mg, 84% yield): 93% ee; $[\alpha]_D^{25}$ +38.6 (*c* 2.2, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.41 (t, *J* = 2.1 Hz, 1H), 8.25 (ddd, *J* = 8.3, 2.2, 1.0 Hz, 1H), 7.98 (ddd, *J* = 8.0, 2.1, 1.0 Hz, 1H), 7.63 (t, *J* = 8.1 Hz, 1H), 6.50 (dd, *J* = 17.2, 10.9 Hz, 1H), 5.66 (d, *J* = 11.0 Hz, 1H), 5.46 (d, *J* = 17.2 Hz, 1H), 1.85 (s, 3H), 1.73 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 141.8, 136.9, 134.1, 129.8, 123.7, 123.3, 120.5, 115.4, 115.3, 49.4, 41.7, 21.7, 21.3; IR (Neat Film, NaCl) 3093, 2994, 2957, 2927, 2248, 1749, 1534, 1455, 1418, 1379, 1351, 1266, 1218, 1107, 1002, 942, 906, 854, 812, 795, 739, 721, 688 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{13}N_2O_2$ $[M]^{+\bullet}$: 255.1008, found 255.0983; HPLC conditions: 6% IPA, 1 mL/min, Chiralpak AD–H column, λ = 210 nm, t_R (min): major = 12.542, minor = 11.851.



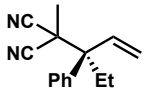
(*S*)-2-Methyl-2-(2-(naphthalen-2-yl)but-3-en-2-yl)malononitrile (7h). Allylic alkylation product **7h** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a colorless oil (48 mg, 93% yield): 95% ee; $[\alpha]_D^{25}$ +57.9 (*c* 3.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 8.01 (d, *J* = 2.2 Hz, 1H), 7.93 – 7.80 (m, 3H), 7.70 (dd, *J* = 8.8, 2.1 Hz, 1H), 7.57 – 7.49 (m, 2H), 6.60 (dd, *J* = 17.3, 10.9 Hz, 1H), 5.60 (d, *J* = 11.0 Hz, 1H), 5.46 (d, *J* = 17.3 Hz, 1H), 1.91 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.4, 136.5, 132.9, 132.8, 128.6, 128.3, 127.8, 127.5, 127.0, 126.7, 125.4, 119.2, 116.1, 116.0, 49.6, 41.8, 21.8 (2C); IR (Neat Film, NaCl) 3060, 2992, 2950, 2246, 1748, 1637, 1598, 1507, 1453, 1416, 1386, 1277, 1194, 1164, 1130, 1103, 999, 937, 902, 859, 819, 779, 747, 666 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{18}H_{17}N_2$ $[M+H]^+$: 261.1392, found 261.1378; SFC conditions: 4% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 11.637, minor = 13.691.



(*R*)-2-Methyl-2-(3-methyl-5-phenylpent-1-en-3-yl)malononitrile (7j). Allylic alkylation product **7j** was prepared according to the general procedure and isolated by preparatory TLC (20% Et_2O/hexanes, eluted twice) to give a pale yellow oil (31 mg, 65% yield as a 1:1.5 mixture of linear to branched products): 84% ee; $[\alpha]_D^{25}$ +17.0 (*c* 1.9, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.28 – 7.06 (m, 13.5H), 5.80 (dd, *J* = 17.3, 10.8 Hz, 1.5H), 5.48 (dd, *J* = 10.8, 0.5 Hz, 1.5H), 5.30 (dd, *J* = 17.4, 0.6 Hz, 1.5H), 5.19 – 5.11 (m, 1H), 2.70 (dd, *J* = 8.9, 6.7 Hz, 2.5H), 2.57 (dq, *J* = 7.7, 0.7 Hz, 2H), 2.54 – 2.40 (m, 3H), 2.34 (ddd, *J* = 8.6, 6.4, 1.1 Hz, 2H), 1.94 (ddd, *J* = 10.3, 6.8, 5.6 Hz, 3H), 1.71 – 1.67 (m, 3H), 1.64 (s, 4.5H), 1.55 (s, 3H), 1.30 (s, 4.5H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.7, 141.4, 141.1, 137.0, 128.7, 128.5, 128.4, 126.4, 126.1, 120.5, 116.3, 115.8, 115.7, 115.3, 46.2, 41.8, 41.5, 38.7, 37.4, 34.2, 31.8, 30.9, 23.8, 20.5, 17.1, 16.9; IR (Neat Film, NaCl) 3087, 3064, 3028, 2989, 2930, 2864, 2247, 1949, 1871, 1812, 1638, 1604, 1497, 1453, 1418, 1385, 1277, 1179, 1104, 1074, 1030, 1002, 936, 751, 714, 699, 624 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{16}H_{19}N_2$ $[M+H]^+$: 239.1548, found 239.1530; SFC conditions: 0.1% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 7.621, minor = 7.163.



2-Methyl-2-(2-methylbut-3-en-2-yl)malononitrile (7k). Allylic alkylation product **7k** was prepared according to the general procedure and isolated by preparatory TLC (20% Et_2O/hexanes, eluted twice) to give a colorless oil (18 mg, 61% yield): ^1H NMR (400 MHz, $CDCl_3$) δ 5.92 (dd, *J* = 17.2, 10.8 Hz, 1H), 5.45 – 5.04 (m, 2H), 1.68 (s, 3H), 1.35 (s, 6H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.8, 118.2, 115.8, 42.9, 41.2, 22.9, 20.6; IR (Neat Film, NaCl) 3095, 2981, 2941, 2885, 2248, 1643, 1459, 1419, 1383, 1176, 1155, 1112, 998, 934, 735, 688 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_9H_{11}N_2$ $[(M+H)–H_2]^+$: 147.0922, found 147.0945.



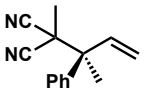
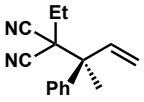
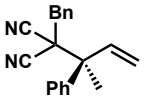
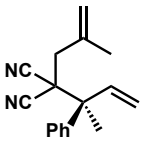
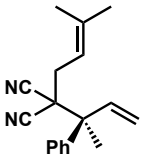
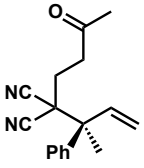
(*S*)-2-Methyl-2-(3-phenylpent-1-en-3-yl)malononitrile (7l). Allylic alkylation product **7l** was prepared according to the general procedure and isolated by preparatory TLC (15% Et_2O/hexanes, eluted twice) to give a colorless oil (23 mg, 50% yield): 96% ee; $[\alpha]_D^{25}$ +30.4 (*c* 1.6, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.46 (m, 2H), 7.46 – 7.29 (m, 3H), 6.19 (ddd, *J* = 17.6, 11.3, 0.7 Hz, 1H), 5.69 (d, *J* = 11.3 Hz, 1H), 5.42 (d, *J* = 17.6 Hz, 1H), 2.50 (dqd, *J* = 14.3, 7.2, 0.7 Hz, 1H), 2.15 (dq, *J* = 14.4, 7.2 Hz, 1H), 1.60 (s, 3H), 0.87 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.8, 134.7, 129.8, 128.58, 128.57, 121.2,

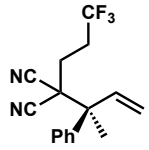
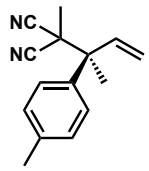
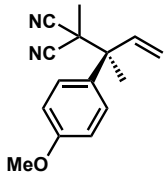
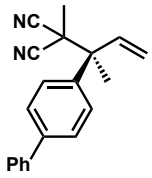
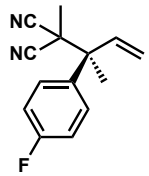
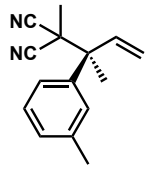
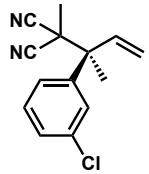
116.3, 116.1, 54.4, 42.6, 26.4, 21.9, 9.1; IR (Neat Film, NaCl) 3094, 3061, 2981, 2944, 2884, 2246, 1638, 1601, 1496, 1448, 1414, 1382, 1180, 1161, 1083, 1002, 940, 751, 704 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{15}H_{17}N_2$ $[M+H]^+$: 225.1392, found 225.1377; SFC conditions: 3% IPA, 2.5 mL/min, Chiralpak OJ–H column, λ = 210 nm, t_R (min): major = 3.270, minor = 4.727.

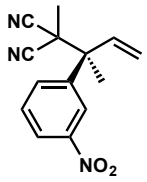
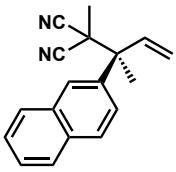
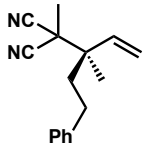
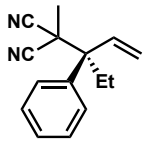
Determination of Enantiomeric Excess

Please note racemic products were synthesized using racemic **L**.

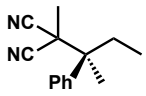
Table S1: Determination of Enantiomeric Excess

Entry	Product	Assay Conditions	Retention time of major isomer (min)	Retention time of minor isomer (min)	%ee
1		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.832	4.594	95%
2		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.378	4.088	95%
3		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	10.960	11.727	93%
4		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.138	3.923	92%
5		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.095	4.061	96%
6		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	5.022	7.267	96%

Entry	Product	Assay Conditions	Retention time of major isomer (min)	Retention time of minor isomer (min)	%ee
7		SFC Chiralpak OJ–H 1% IPA isocratic, 3.0 mL/min	1.651	1.868	91%
8		SFC Chiralpak OJ–H 1% IPA isocratic, 3.0 mL/min	3.658	4.375	96%
9		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	5.019	5.890	96%
10		SFC Chiralpak OJ–H 1% IPA isocratic, 2.5 mL/min	43.531	40.798	95%
11		HPLC Chiralpak OJ 3% IPA isocratic, 1 mL/min	22.493	29.003	94%
12		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	2.897	3.290	95%
13		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.255	4.955	99%

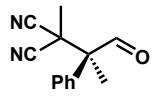
Entry	Product	Assay Conditions	Retention time of major isomer (min)	Retention time of minor isomer (min)	%ee
14		HPLC Chiralpak AD–H 6% IPA isocratic, 1 mL/min	12.542	11.851	93%
15		SFC Chiralpak OJ–H 4% IPA isocratic, 2.5 mL/min	11.637	13.691	95%
16		SFC Chiralpak OJ–H 0.1% IPA isocratic, 2.5 mL/min	7.621	7.163	84%
17		SFC Chiralpak OJ–H 3% IPA isocratic, 2.5 mL/min	3.270	4.727	96%

Experimental Procedures and Spectroscopic Data for the Product Transformations

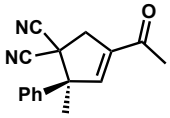


(*S*)-2-Methyl-2-(2-phenylbutan-2-yl)malononitrile (8). In a nitrogen-filled glove box, to a 1 dram vial equipped with a stir bar was added olefin **3** (25 mg, 0.12 mmol, 1 equiv), $RhCl(PPh_3)_3$ (11 mg, 0.012 mmol, 10 mol %) and benzene (1.2 mL). The reaction mixture was removed from the glove box, sparged with hydrogen (balloon) for 5 minutes, and stirred under a hydrogen atmosphere for 18 h, whereupon the reaction was concentrated under reduced pressure. The crude residue was purified by preparatory TLC (20% EtOAc/hexanes) to give alkyl **8** as a colorless oil (23 mg, 92% yield): $[\alpha]_D^{25}$ +16.6 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 – 7.31 (m, 5H), 2.58 – 2.46 (m, 1H), 1.94 (dq, *J* = 13.6, 7.2 Hz, 1H), 1.65 (d, *J* = 0.9 Hz, 3H), 1.56 (s, 3H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.9, 128.7, 128.3 (2C), 116.3, 116.3, 47.3, 43.3, 29.5, 21.2,

20.5, 8.8; IR (Neat Film, NaCl) 3059, 2979, 2943, 2885, 2245, 1602, 15001, 1451, 1391, 1192, 1164, 1098, 1030, 806, 774, 741, 702, 662 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{14}H_{16}N_2$ $[M]^{+\bullet}$: 212.1314, found 212.1291.



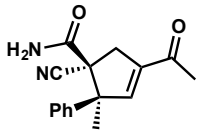
(*S*)-2-Methyl-2-(1-oxo-2-phenylpropan-2-yl)malononitrile (9). A solution of olefin **3** (40.0 mg, 0.19 mmol, 1 equiv) and pyridine (0.038 mL, 0.48 mmol, 2.5 equiv) in CH_2Cl_2 (2.0 mL) was cooled to –78 °C. Ozone was bubbled through the resulting solution for 4 min, whereupon the reaction mixture was sparged with O_2, warmed to ambient temperature, and diluted with CH_2Cl_2 (5.0 mL). The reaction mixture was washed with saturated aqueous $NaHCO_3$ (5 mL) and the aqueous layer was further extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with 1 M HCl (5 mL), brine (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure to give aldehyde **9** as a colorless solid (37 mg, 93% yield): $[\alpha]_D^{25}$ –46.9 (*c* 2.1, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ 9.45 (s, 1H), 7.55 – 7.45 (m, 3H), 7.41 – 7.30 (m, 2H), 1.88 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.9, 131.1, 130.2, 129.6, 128.9, 115.3, 115.2, 58.3, 37.4, 21.4, 16.3; IR (Neat Film, NaCl) 3033, 3063, 2985, 2954, 2832, 2720, 2249, 1726, 1498, 1448, 1395, 1376, 1262, 1190, 1172, 1080, 923, 869, 764, 703 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{13}H_{12}N_2O$ $[M]^{+\bullet}$: 212.0950, found 212.0948.



(*S*)-4-Acetyl-2-methyl-2-phenylcyclopent-3-ene-1,1-dicarbonitrile (SI-2). A solution of olefin **5f** (42 mg, 0.16 mmol, 1 equiv) and pyridine (0.031 mL, 0.39 mmol, 2.5 equiv) in CH_2Cl_2 (2.0 mL) was cooled to –78 °C. Ozone was bubbled through the resulting solution for 4 min, whereupon the reaction mixture was sparged with O_2, warmed to ambient temperature, and diluted with CH_2Cl_2 (5.0 mL). The reaction mixture was washed with saturated aqueous $NaHCO_3$ (5 mL) and the aqueous layer was further extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were washed with 1 M HCl (5 mL), brine (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure.

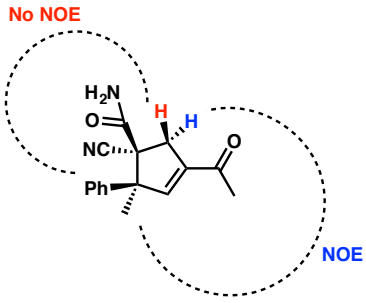
The crude material was dissolved in benzene (10 mL) and *p*-toluenesulfonic acid (30.0 mg, 0.16 mmol, 1 equiv) was added. The resulting solution was stirred at ambient temperature for 0.5 h and then heated under reflux for 18 h, whereupon the reaction mixture was cooled to ambient temperature and diluted with Et_2O (10 mL). Saturated aqueous $NaHCO_3$ (10 mL) was added to the resulting solution and allowed to stir for 5 min. The organic layer was then separated and washed further with saturated aqueous $NaHCO_3$ (10 mL), brine (10 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude residue was purified by preparatory TLC (33% acetone/hexanes) to give enone **SI-2** as a colorless oil (19 mg, 47% yield over two steps): $[\alpha]_D^{25}$ –27.3 (*c* 1.2, $CHCl_3$); ^1H NMR (400 MHz,

$CDCl_3$) δ 7.52 – 7.36 (m, 5H), 6.91 (dd, *J* = 2.2, 1.2 Hz, 1H), 3.56 (dd, *J* = 16.7, 1.2 Hz, 1H), 3.39 (dd, *J* = 16.7, 2.1 Hz, 1H), 2.48 (s, 3H), 1.82 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.6, 145.4, 140.5, 138.8, 129.5 (d, *J* = 2.6 Hz), 126.3, 114.7, 114.4, 61.4, 45.7, 42.2, 26.8, 23.6; IR (Neat Film, NaCl) 3063, 2978, 2934, 2249, 1676, 1629, 1499, 1446, 1371, 1335, 1267, 1098, 1026, 953, 896, 764, 699 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{15}ON_2$ $[M+H]^+$: 251.1184, found 251.1197.

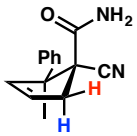


(1*S*,2*S*)-4-acetyl-1-cyano-2-methyl-2-phenylcyclopent-3-ene-1-carboxamide (10). A solution of bis-nitrile **SI-2** (19 mg, 0.074 mmol, 1 equiv), NaOH (10 mg, 0.25 mmol, 3.4 equiv) in EtOH/H_2O (1:1, 1.0 mL) was heated to 60 °C for 18 h, whereupon the resulting mixture was cooled to ambient temperature and diluted with EtOAc (5 mL). The solution was washed with brine (5 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by preparatory TLC (50% acetone/hexanes) to give amide **10** as a colorless oil (7.5 mg, 38% yield, 1:11 dr): $[\alpha]_D^{25}$ +4.4 (*c* 1.2, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.38 (m, 5H), 6.65 (dd, *J* = 2.3, 1.1 Hz, 1H), 5.76 (s, 2H), 3.71 (dd, *J* = 17.0, 2.3 Hz, 1H), 3.22 (dd, *J* = 17.0, 1.1 Hz, 1H), 2.44 (s, 3H), 1.58 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 195.4, 165.9, 146.5, 141.9, 129.8, 129.0, 127.4, 124.9, 120.6, 60.5, 59.0, 39.2, 26.9, 21.4; IR (Neat Film, NaCl) 3338, 3201, 3062, 2980, 2929, 2854, 2242, 1732, 1694, 1673, 1604, 1498, 1446, 1371, 1338, 1259, 1102, 1046, 913, 767. 734, 702 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{16}H_{17}O_2N_2$ $[M+H]^+$: 269.1290, found 269.1282. *Please note* that the NMR data listed is for the major diastereomer, though both diastereomers can be seen in the NMR spectra in a 1:11 ratio.

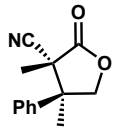
Stereochemical Assignment:



There is an NOE between the bottom allylic proton (blue) and the methyl group, but not the phenyl group and the top allylic proton (red) leading us to believe that it exists in the conformer below

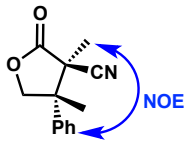


There is a HMBC between the bottom proton (blue) and the amide, thus we believe that the amide is on the top face which provides a great angle for coupling as opposed to if the amide were in the equatorial position which would be approaching 90 °



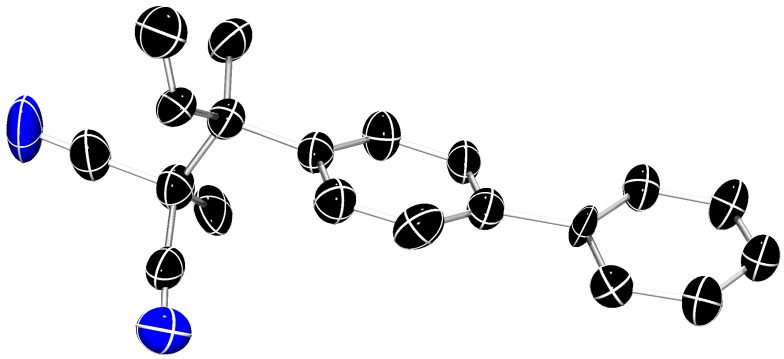
(3*R*,4*S*)-3,4-dimethyl-2-oxo-4-phenyltetrahydrofuran-3-carbonitrile (11). A solution of olefin **3** (100.0 mg, 0.48 mmol, 1 equiv) in MeOH (5.0 mL) was cooled to –78 °C. Ozone was bubbled through the reaction mixture for 0.5 h, whereupon the resulting solution was sparged with O_2 and $NaBH_4$ (0.80 mg, 2.1 mmol, 4.4 equiv) was added. The reaction was then warmed to 0 °C and stirred for 3 h. The reaction mixture was quenched with the addition of 1 M HCl (5 mL) and the aqueous layer was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine (20 mL), dried over Na_2SO_4, and concentrated under reduced pressure. The crude product was purified by silica gel flash column chromatography (20% acetone/hexanes) to give lactone **11** as a colorless solid (66 mg, 65% yield, 1:2.5 dr): $[\alpha]_D^{25}$ +21.3 (*c* 3.0, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 – 7.33 (m, 3H), 7.26 – 7.23 (m, 2H), 4.78 (dt, *J* = 9.1, 0.8 Hz, 1H), 4.50 (d, *J* = 9.1 Hz, 1H), 1.74 (d, *J* = 0.8 Hz, 3H), 1.33 (s, 3H); ^{13}C NMR (101 MHz, $CDCl_3$) δ 171.7, 138.7, 129.6, 128.5, 125.6, 117.7, 74.6, 49.6, 49.0, 27.1, 18.9; IR (Neat Film, NaCl) 2979, 2930, 2355, 2242, 1783, 1498, 1445, 1381, 1279, 1172, 1092, 1012, 764, 699 cm^{-1}; HRMS (ESI+) *m/z* calc'd for $C_{13}H_{13}NO_2$ $[M]^{+\bullet}$: 215.0946, found 215.0966. *Please note* that the NMR data listed is for the major diastereomer.

Stereochemical Assignment:



Crystal Structure Data for Allylic Alkylation Product 7c

Allylic alkylation product **7c** was recrystallized from boiling hexanes to provide crystals suitable for X-ray analysis.



Low-temperature diffraction data (ϕ-and ω-scans) were collected on a Bruker AXS D8 VENTURE KAPPA diffractometer coupled to a PHOTON II CPAD detector with Cu K_α radiation (λ = 1.54178 Å) from an IμS micro-source for the structure of compound **7c**. The structure was solved by direct methods using SHELXS[16] and refined against F^2 on all data by full-matrix least squares with SHELXL-2016[17] using established refinement techniques.[18] All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were included into the model at geometrically calculated positions and refined using a riding model. The isotropic displacement parameters of all hydrogen atoms were fixed to 1.2 times the U value of the atoms they are linked to (1.5 times for methyl groups). All disordered atoms were refined with the help of similarity restraints on the 1,2- and 1,3-distances and displacement parameters as well as enhanced rigid bond restraints for anisotropic displacement parameters.

Compound **7c** crystallizes in the tetragonal space group $I4_1$ with half a molecule in the asymmetric unit. The molecule is located near a crystallographic 2-fold rotation axis and is disordered by the rotation. The phenyl moiety was disordered over four positions, two of which are pairwise related to the other two by the 2-fold rotation. This requires a number of SADI restraints during refinement. We note that a Bayesian analysis of the Friedel pairs (performed using the "Bijvoet-Pair Analysis" routine of PLATON) confirms the absolute stereochemical assignment based on the Flack x. The output of this analysis gives:

Bayesian Statistics
Student_T Nu 99
Select Pairs 752
Theta_Min .. 5.23
Theta_Max ..74.45
P2(true).... 1.000
P3(true).... 0.999
P3(rac-twin) 0.8E-03
P3(false) ..0.8E-08

G 2.0938
G (su) 0.4726
Hooft y .... -0.5(2)

*Table S2. Crystal data and structure refinement for **7c**.*

Empirical formula	C20 H18 N2	
Formula weight	286.36	
Temperature	100(2) K	
Wavelength	1.54178 Å	
Crystal system	Tetragonal	
Space group	$I4_1$	
Unit cell dimensions	a = 10.0971(4) Å	a= 90°.
	b = 10.0971(4) Å	b= 90°.
	c = 15.5215(7) Å	g = 90°.
Volume	1582.44(14) $Å^3$	
Z	4	
Density (calculated)	1.202 Mg/m^3	
Absorption coefficient	0.545 mm^{-1}	
F(000)	608	
Crystal size	0.600 x 0.150 x 0.150 mm^3	
Theta range for data collection	5.226 to 74.482°.	
Index ranges	-12<=h<=12, -12<=k<=12, -17<=l<=19	
Reflections collected	10160	
Independent reflections	1590 [R(int) = 0.0381]	

Completeness to theta = 67.679°	99.6 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7538 and 0.5549
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	1590 / 823 / 256
Goodness-of-fit on F^2	1.044
Final R indices [I>2sigma(I)]	R1 = 0.0422, wR2 = 0.1227
R indices (all data)	R1 = 0.0433, wR2 = 0.1248
Absolute structure parameter	-0.6(3)
Extinction coefficient	n/a
Largest diff. peak and hole	0.211 and -0.114 e.$Å^{-3}$

Table S3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **7c**. *U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.*

	x	y	z	U(eq)
C(11)	4978(4)	4611(3)	4288(2)	41(1)
C(12)	3831(6)	4487(6)	4770(4)	50(1)
C(13)	3815(16)	4637(13)	5665(6)	44(2)
C(14)	4960(20)	4930(50)	6109(3)	47(3)
C(15)	6113(19)	5045(15)	5612(9)	58(3)
C(16)	6135(6)	4925(6)	4736(4)	50(1)
C(21)	5150(20)	4990(50)	7046(10)	44(3)
C(22)	4028(19)	5180(30)	7561(12)	58(4)
C(23)	4064(18)	5150(30)	8460(12)	68(4)
C(24)	5262(18)	4980(40)	8853(12)	63(5)
C(25)	6388(16)	4750(30)	8376(10)	69(4)
C(26)	6337(17)	4800(30)	7479(10)	54(3)
C(21A)	4840(30)	4910(40)	7104(13)	43(5)
C(22A)	3718(19)	4470(30)	7512(12)	47(4)
C(23A)	3681(18)	4450(20)	8410(11)	57(4)
C(24A)	4750(30)	4830(40)	8896(17)	56(6)
C(25A)	5830(20)	5330(30)	8484(15)	57(4)
C(26A)	5890(20)	5390(30)	7587(15)	52(4)
C(1)	5012(4)	4373(4)	3312(3)	45(1)
C(2)	6410(11)	3889(10)	3042(7)	52(2)
C(3)	6731(6)	2674(6)	2858(5)	78(2)
C(4)	3908(17)	3438(17)	3046(13)	70(5)
C(5)	4782(5)	5744(4)	2825(3)	51(1)
C(6)	3509(14)	6450(11)	3020(8)	65(3)
C(7)	5866(16)	6713(17)	3030(10)	50(2)
N(1)	6596(5)	7446(5)	3232(4)	78(1)
C(8)	4876(5)	5491(6)	1886(3)	64(1)
N(2)	5010(30)	5250(20)	1173(3)	100(6)

Table S4. Bond lengths [Å] and angles [°] for ***7c****.*

C(11)-C(12)	1.385(7)
C(11)-C(16)	1.396(7)
C(11)-C(1)	1.534(6)
C(12)-C(13)	1.398(11)
C(12)-H(12)	0.9500
C(13)-C(14)	1.380(16)
C(13)-H(13)	0.9500
C(14)-C(15)	1.400(16)
C(14)-C(21)	1.467(18)
C(15)-C(16)	1.366(14)
C(15)-H(15)	0.9500
C(16)-H(16)	0.9500
C(21)-C(26)	1.390(17)
C(21)-C(22)	1.397(17)
C(22)-C(23)	1.396(17)
C(22)-H(22)	0.9500
C(23)-C(24)	1.366(18)
C(23)-H(23)	0.9500
C(24)-C(25)	1.376(16)
C(24)-H(24)	0.9500
C(25)-C(26)	1.394(15)
C(25)-H(25)	0.9500
C(26)-H(26)	0.9500
C(21A)-C(22A)	1.374(19)
C(21A)-C(26A)	1.384(19)
C(22A)-C(23A)	1.395(17)
C(22A)-H(22A)	0.9500
C(23A)-C(24A)	1.37(2)
C(23A)-H(23A)	0.9500
C(24A)-C(25A)	1.36(2)
C(24A)-H(24A)	0.9500
C(25A)-C(26A)	1.395(18)
C(25A)-H(25A)	0.9500
C(26A)-H(26A)	0.9500

C(1)-C(4)	1.518(16)
C(1)-C(2)	1.551(11)
C(1)-C(5)	1.594(6)
C(2)-C(3)	1.301(10)
C(2)-H(2)	0.9500
C(3)-H(3A)	0.9500
C(3)-H(3B)	0.9500
C(4)-H(4A)	0.9800
C(4)-H(4B)	0.9800
C(4)-H(4C)	0.9800
C(5)-C(8)	1.482(7)
C(5)-C(6)	1.501(13)
C(5)-C(7)	1.503(15)
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(6)-H(6C)	0.9800
C(7)-N(1)	1.091(15)
C(8)-N(2)	1.141(9)

C(12)-C(11)-C(16)	116.9(3)
C(12)-C(11)-C(1)	122.6(4)
C(16)-C(11)-C(1)	120.5(4)
C(11)-C(12)-C(13)	122.5(8)
C(11)-C(12)-H(12)	118.8
C(13)-C(12)-H(12)	118.8
C(14)-C(13)-C(12)	120.7(9)
C(14)-C(13)-H(13)	119.7
C(12)-C(13)-H(13)	119.7
C(13)-C(14)-C(15)	116.0(5)
C(13)-C(14)-C(21)	127.6(17)
C(15)-C(14)-C(21)	115.9(18)
C(16)-C(15)-C(14)	123.8(11)
C(16)-C(15)-H(15)	118.1
C(14)-C(15)-H(15)	118.1
C(15)-C(16)-C(11)	120.1(9)
C(15)-C(16)-H(16)	119.9

C(11)-C(16)-H(16)	119.9
C(26)-C(21)-C(22)	116.1(14)
C(26)-C(21)-C(14)	126(2)
C(22)-C(21)-C(14)	118(2)
C(23)-C(22)-C(21)	123.3(16)
C(23)-C(22)-H(22)	118.3
C(21)-C(22)-H(22)	118.3
C(24)-C(23)-C(22)	118.1(16)
C(24)-C(23)-H(23)	121.0
C(22)-C(23)-H(23)	121.0
C(23)-C(24)-C(25)	120.9(15)
C(23)-C(24)-H(24)	119.5
C(25)-C(24)-H(24)	119.5
C(24)-C(25)-C(26)	120.0(15)
C(24)-C(25)-H(25)	120.0
C(26)-C(25)-H(25)	120.0
C(21)-C(26)-C(25)	121.3(13)
C(21)-C(26)-H(26)	119.3
C(25)-C(26)-H(26)	119.3
C(22A)-C(21A)-C(26A)	119.6(19)
C(21A)-C(22A)-C(23A)	119.1(16)
C(21A)-C(22A)-H(22A)	120.5
C(23A)-C(22A)-H(22A)	120.5
C(24A)-C(23A)-C(22A)	121.7(17)
C(24A)-C(23A)-H(23A)	119.1
C(22A)-C(23A)-H(23A)	119.1
C(25A)-C(24A)-C(23A)	118(2)
C(25A)-C(24A)-H(24A)	120.8
C(23A)-C(24A)-H(24A)	120.8
C(24A)-C(25A)-C(26A)	121(2)
C(24A)-C(25A)-H(25A)	119.5
C(26A)-C(25A)-H(25A)	119.5
C(21A)-C(26A)-C(25A)	119.8(18)
C(21A)-C(26A)-H(26A)	120.1
C(25A)-C(26A)-H(26A)	120.1
C(4)-C(1)-C(11)	110.4(8)

C(4)-C(1)-C(2)	113.5(9)
C(11)-C(1)-C(2)	109.7(6)
C(4)-C(1)-C(5)	107.7(7)
C(11)-C(1)-C(5)	109.2(3)
C(2)-C(1)-C(5)	106.2(5)
C(3)-C(2)-C(1)	125.7(8)
C(3)-C(2)-H(2)	117.1
C(1)-C(2)-H(2)	117.1
C(2)-C(3)-H(3A)	120.0
C(2)-C(3)-H(3B)	120.0
H(3A)-C(3)-H(3B)	120.0
C(1)-C(4)-H(4A)	109.5
C(1)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	109.5
C(1)-C(4)-H(4C)	109.5
H(4A)-C(4)-H(4C)	109.5
H(4B)-C(4)-H(4C)	109.5
C(8)-C(5)-C(6)	109.6(7)
C(8)-C(5)-C(7)	105.9(7)
C(6)-C(5)-C(7)	105.8(8)
C(8)-C(5)-C(1)	107.9(4)
C(6)-C(5)-C(1)	116.2(5)
C(7)-C(5)-C(1)	111.0(8)
C(5)-C(6)-H(6A)	109.5
C(5)-C(6)-H(6B)	109.5
H(6A)-C(6)-H(6B)	109.5
C(5)-C(6)-H(6C)	109.5
H(6A)-C(6)-H(6C)	109.5
H(6B)-C(6)-H(6C)	109.5
N(1)-C(7)-C(5)	174.5(14)
N(2)-C(8)-C(5)	176(2)

*Table S5. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **7c**. The anisotropic displacement factor exponent takes the form: $-2p^2[\ h^2\ a^{*2}U^{11} + \ldots + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$*

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
C(11)	47(2)	43(2)	34(2)	1(1)	1(1)	4(2)
C(12)	42(2)	67(3)	43(2)	2(3)	5(2)	2(3)
C(13)	53(3)	48(5)	32(3)	2(3)	8(2)	3(3)
C(14)	65(3)	39(7)	37(2)	1(4)	6(5)	7(3)
C(15)	55(3)	62(8)	58(4)	-15(4)	-8(3)	-3(4)
C(16)	49(2)	56(3)	46(3)	-3(3)	4(2)	-5(3)
C(21)	56(8)	31(5)	44(5)	-5(6)	10(5)	1(8)
C(22)	63(9)	67(8)	45(6)	1(6)	4(5)	-1(8)
C(23)	80(9)	83(9)	40(6)	-1(6)	9(6)	-2(10)
C(24)	85(10)	69(10)	36(6)	-5(6)	11(6)	-3(10)
C(25)	82(9)	89(9)	36(5)	-11(4)	5(5)	-14(8)
C(26)	64(8)	72(8)	26(4)	-3(4)	3(4)	-7(7)
C(21A)	64(10)	47(10)	18(6)	-10(7)	4(7)	2(9)
C(22A)	51(8)	55(9)	36(6)	0(5)	5(5)	7(7)
C(23A)	64(9)	69(10)	37(6)	-11(6)	5(6)	5(7)
C(24A)	75(11)	58(11)	35(8)	-3(6)	2(7)	-2(8)
C(25A)	71(10)	63(10)	38(7)	1(7)	-4(7)	-4(9)
C(26A)	64(10)	46(8)	46(7)	1(7)	4(6)	-3(9)
C(1)	48(2)	47(2)	39(2)	-5(2)	4(2)	-2(1)
C(2)	66(3)	41(4)	49(3)	-11(3)	19(2)	-3(3)
C(3)	82(3)	66(3)	86(4)	-8(3)	32(3)	0(3)
C(4)	79(7)	73(8)	57(6)	-24(5)	15(5)	-25(6)
C(5)	57(2)	59(2)	37(3)	2(2)	-3(2)	-2(2)
C(6)	91(5)	51(6)	53(3)	21(3)	18(3)	17(3)
C(7)	67(4)	48(3)	36(4)	-1(3)	-2(3)	2(3)
N(1)	86(3)	62(2)	84(3)	-4(2)	7(2)	-12(2)
C(8)	64(3)	84(3)	45(3)	4(2)	0(2)	-21(3)
N(2)	100(3)	164(18)	35(2)	-7(4)	8(4)	-60(11)

Table S6. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for ***7c****.*

	x	y	z	U(eq)
H(12)	3024	4292	4482	61
H(13)	3007	4534	5971	53
H(15)	6925	5212	5901	70
H(16)	6940	5055	4430	60
H(22)	3202	5331	7286	70
H(23)	3277	5256	8789	81
H(24)	5318	5012	9463	76
H(25)	7201	4562	8658	83
H(26)	7131	4701	7157	65
H(22A)	2977	4171	7187	57
H(23A)	2893	4179	8693	68
H(24A)	4744	4738	9506	67
H(25A)	6561	5645	8813	69
H(26A)	6643	5751	7309	62
H(2)	7091	4536	3009	62
H(3A)	6082	1995	2883	93
H(3B)	7615	2467	2698	93
H(4A)	3973	3256	2428	104
H(4B)	3049	3848	3172	104
H(4C)	3988	2607	3368	104
H(6A)	3559	7361	2805	98
H(6B)	3364	6462	3644	98
H(6C)	2773	5988	2738	98

Table S7. Torsion angles [°] for ***7c****.*

C(16)-C(11)-C(12)-C(13)	-1.3(8)
C(1)-C(11)-C(12)-C(13)	176.6(7)
C(11)-C(12)-C(13)-C(14)	1(3)
C(12)-C(13)-C(14)-C(15)	-1(5)
C(12)-C(13)-C(14)-C(21)	-173(4)
C(13)-C(14)-C(15)-C(16)	3(5)
C(21)-C(14)-C(15)-C(16)	175(3)
C(14)-C(15)-C(16)-C(11)	-3(3)
C(12)-C(11)-C(16)-C(15)	2.5(9)
C(1)-C(11)-C(16)-C(15)	-175.4(8)
C(13)-C(14)-C(21)-C(26)	154(3)
C(15)-C(14)-C(21)-C(26)	-18(6)
C(13)-C(14)-C(21)-C(22)	-22(6)
C(15)-C(14)-C(21)-C(22)	166(3)
C(26)-C(21)-C(22)-C(23)	-1(3)
C(14)-C(21)-C(22)-C(23)	175(4)
C(21)-C(22)-C(23)-C(24)	2(3)
C(22)-C(23)-C(24)-C(25)	-4(4)
C(23)-C(24)-C(25)-C(26)	5(4)
C(22)-C(21)-C(26)-C(25)	2(3)
C(14)-C(21)-C(26)-C(25)	-174(4)
C(24)-C(25)-C(26)-C(21)	-4(3)
C(26A)-C(21A)-C(22A)-C(23A)	-3(3)
C(21A)-C(22A)-C(23A)-C(24A)	-2(3)
C(22A)-C(23A)-C(24A)-C(25A)	6(5)
C(23A)-C(24A)-C(25A)-C(26A)	-4(5)
C(22A)-C(21A)-C(26A)-C(25A)	4(3)
C(24A)-C(25A)-C(26A)-C(21A)	-1(4)
C(12)-C(11)-C(1)-C(4)	-25.7(9)
C(16)-C(11)-C(1)-C(4)	152.2(8)
C(12)-C(11)-C(1)-C(2)	-151.5(6)
C(16)-C(11)-C(1)-C(2)	26.4(6)
C(12)-C(11)-C(1)-C(5)	92.6(5)
C(16)-C(11)-C(1)-C(5)	-89.6(5)

C(4)-C(1)-C(2)-C(3)	-20.9(15)
C(11)-C(1)-C(2)-C(3)	103.2(11)
C(5)-C(1)-C(2)-C(3)	-138.9(9)
C(4)-C(1)-C(5)-C(8)	-62.4(9)
C(11)-C(1)-C(5)-C(8)	177.7(4)
C(2)-C(1)-C(5)-C(8)	59.5(6)
C(4)-C(1)-C(5)-C(6)	61.1(11)
C(11)-C(1)-C(5)-C(6)	-58.8(8)
C(2)-C(1)-C(5)-C(6)	-177.0(8)
C(4)-C(1)-C(5)-C(7)	-178.0(10)
C(11)-C(1)-C(5)-C(7)	62.1(7)
C(2)-C(1)-C(5)-C(7)	-56.1(8)

References

(1) Hamilton, J. Y.; Sarlah, D.; Carreira, E. M. *Org. Synth.* **2015**, *92*, 1–12.

(2) Ghorai, M. K.; Talukdar, R.; Tiwari, D. P. *Org. Lett.* **2014**, *16*, 2204–2207.

(3) Matsubara, R.; Jamison, T. F. *J. Am. Chem. Soc.* **2010**, *132*, 6880–6881.

(4) Díez-Barra, E.; de la Hoz, A.; Moreno, A.; Sánchez-Verdú, P. *J. Chem. Soc., Perkin Trans. 1* **1991**, *0*, 2589–2592.

(5) Gao, C.; Tao, X.; Qian, Y.; Huang, J. *Synlett* **2003**, *11*, 1716–1718.

(6) Fernández-Mateos, A.; Teijón, P. H.; Burón, L. M.; Clemente, R. R.; González, R. R. *J. Org. Chem.* **2007**, *72*, 9973–9982.

(7) Benati, L.; Bencivenni, G.; Leardini, R.; Minozzi, M.; Nanni, D.; Scialpi, R.; Spagnolo, P.; Zanardi, G.; Rizzoli, C. *Org. Lett.* **2004**, *6*, 417–420.

(8) Paganelli, S.; Sehionato, A.; Botteghi, C. *Tetrahedron Lett.* **1991**, *32*, 2807–2810.

(9) Okada, S.; Oohira, D.; Otaka, K. Patent WO2004020399 (A1), March 11, 2004.

(10) Guzman-Martinez, A.; Hoveyda, A. H. *J. Am. Chem. Soc.* **2010**, *132*, 10634–10637.

(11) Shockley, S. E.; Hethcox, J. C.; Stoltz, B. M. *Angew. Chem. Int. Ed.* **2017**, *56*, 11545–11548.

(12) Ghosh, S.; Chaudhuri, S.; Bisai, A. *Org. Lett.* **2015**, *17*, 1373–1376.

(13) Sharma, S.; Kumar, S.; Shil, A. K.; Guha, N. R.; Bandna; Das, P. *Tetrahedron Lett.* **2012**, *53*, 7044–7051.

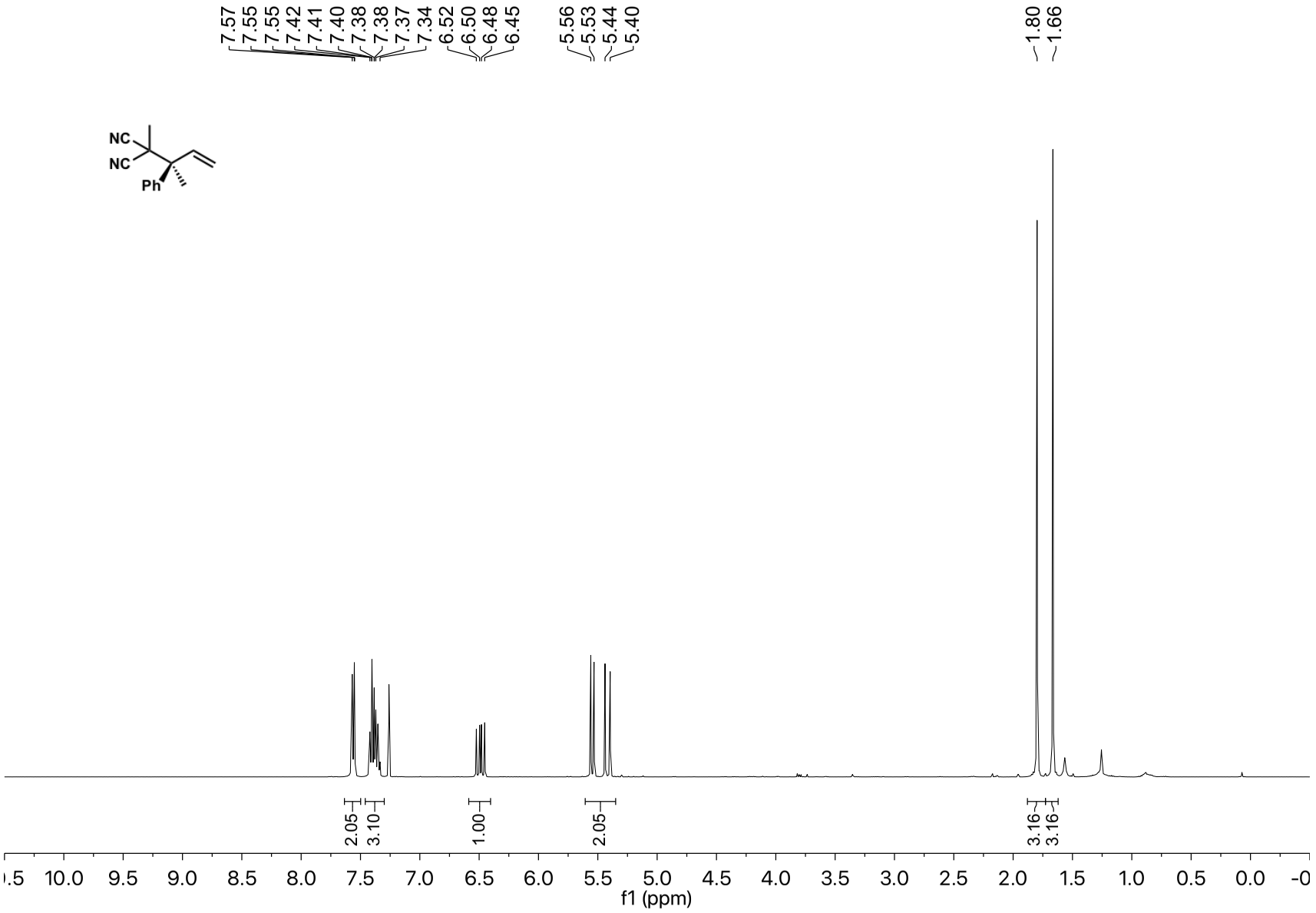
(14) (a) Franke, A.; Mattern, G.; Traber, W. *Helv. Chim. Acta* **1975**, *58*, 268–278; (b) Rossi, D.; Baraglia, A. C.; Serra, M.; Azzolina, O.; Collina, S. *Molecules* **2010**, *15*, 5928–5942.

(15) Zhang, T.; Jiang, J.; Yao, L.; Geng, H.; Zhang, X. *Chem. Commun.* **2017**, *53*, 9258–9261.

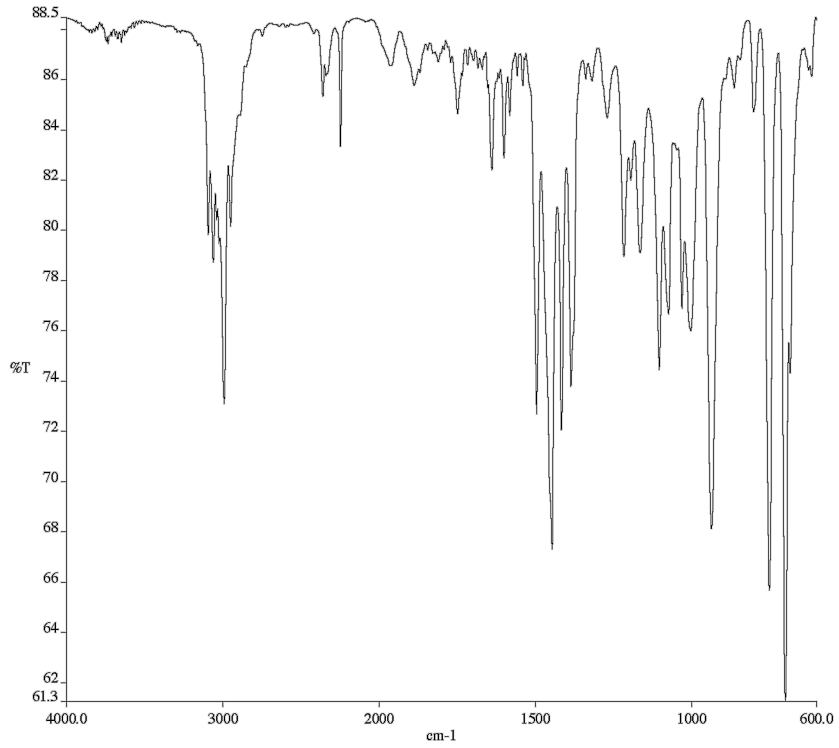
(16) Sheldrick, G. M. *Acta Cryst.* **1990**, A46, 467–473.

(17) Sheldrick, G. M. *Acta Cryst.* **2015**, C71, 3–8.

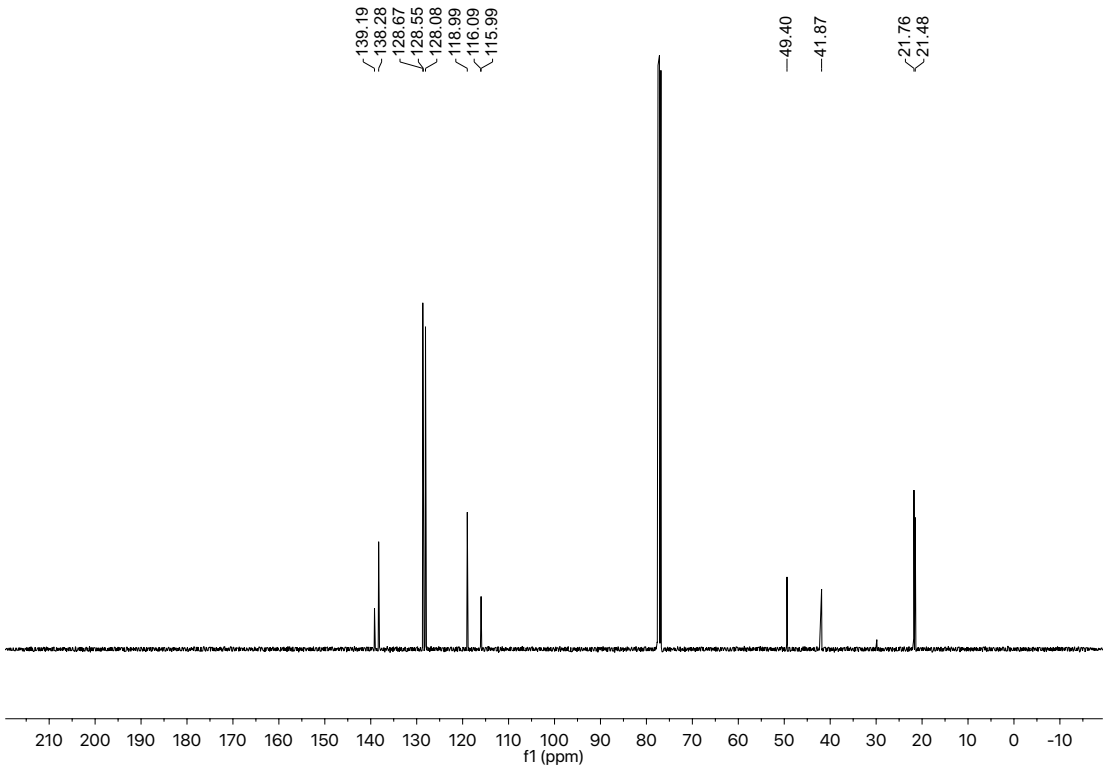
(18) Müller, P. *Crystallography Reviews* **2009**, *15*, 57–83.



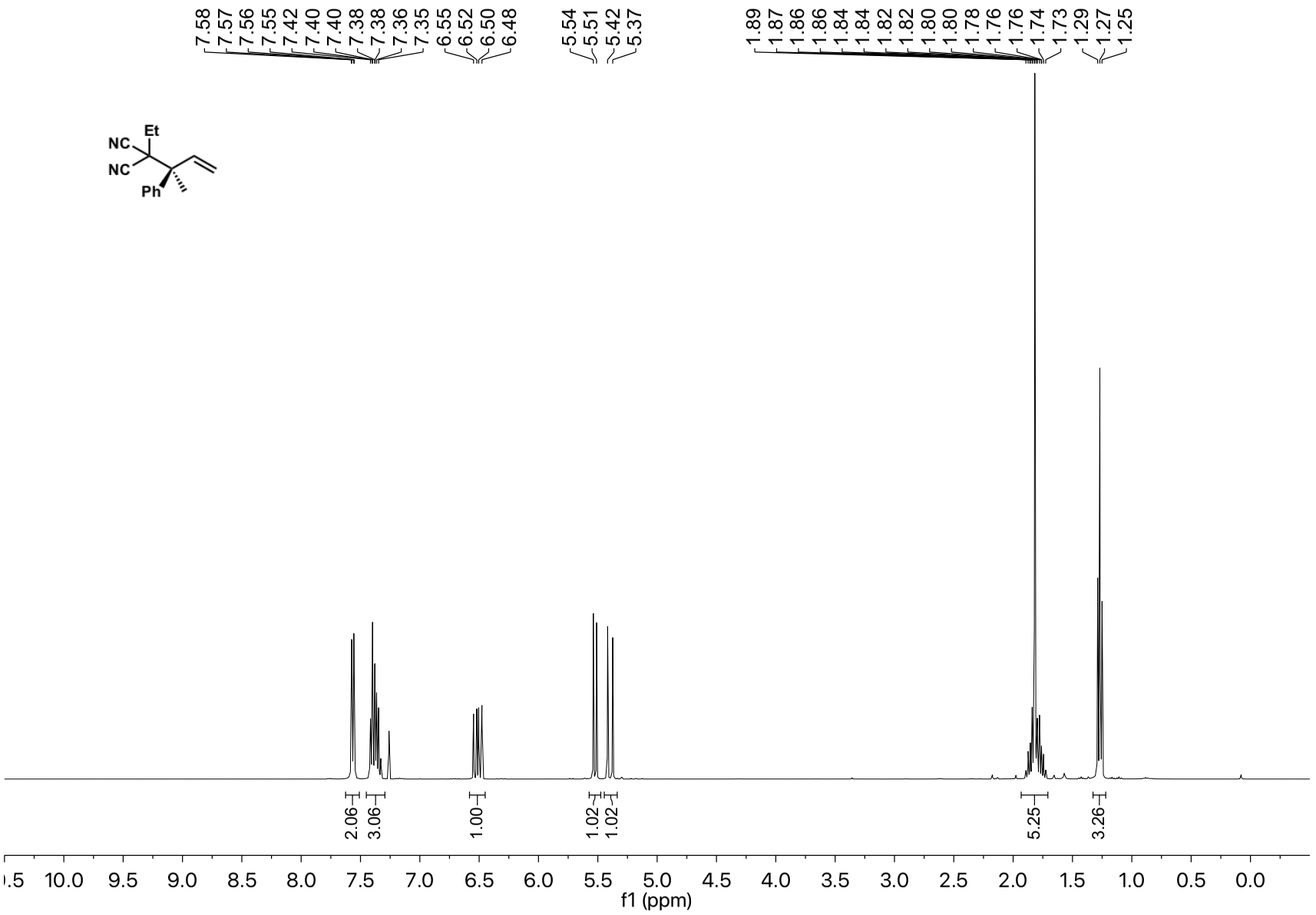
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3**.



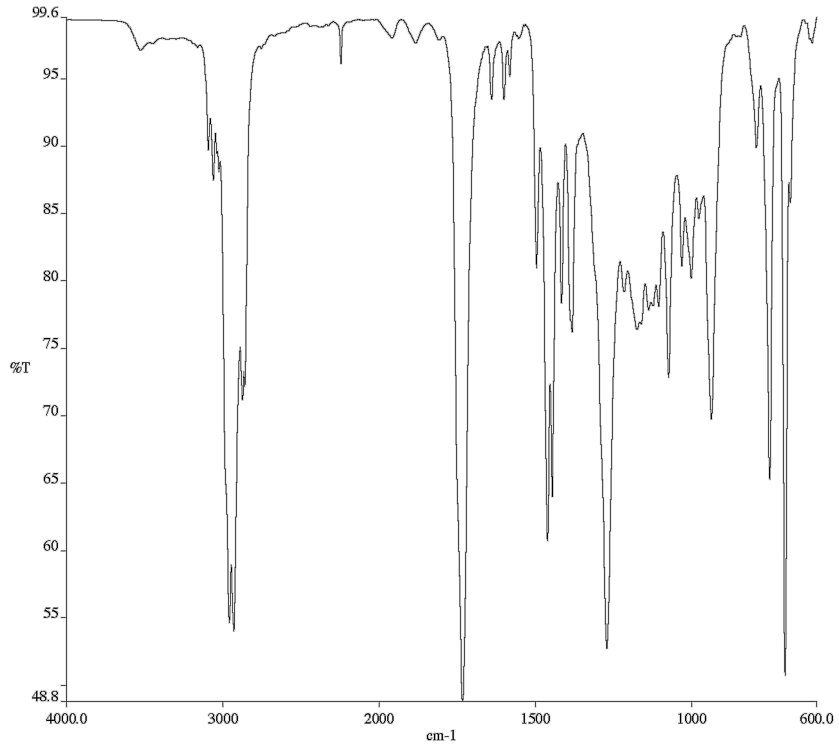
Infrared spectrum (Thin Film, NaCl) of compound **3**.



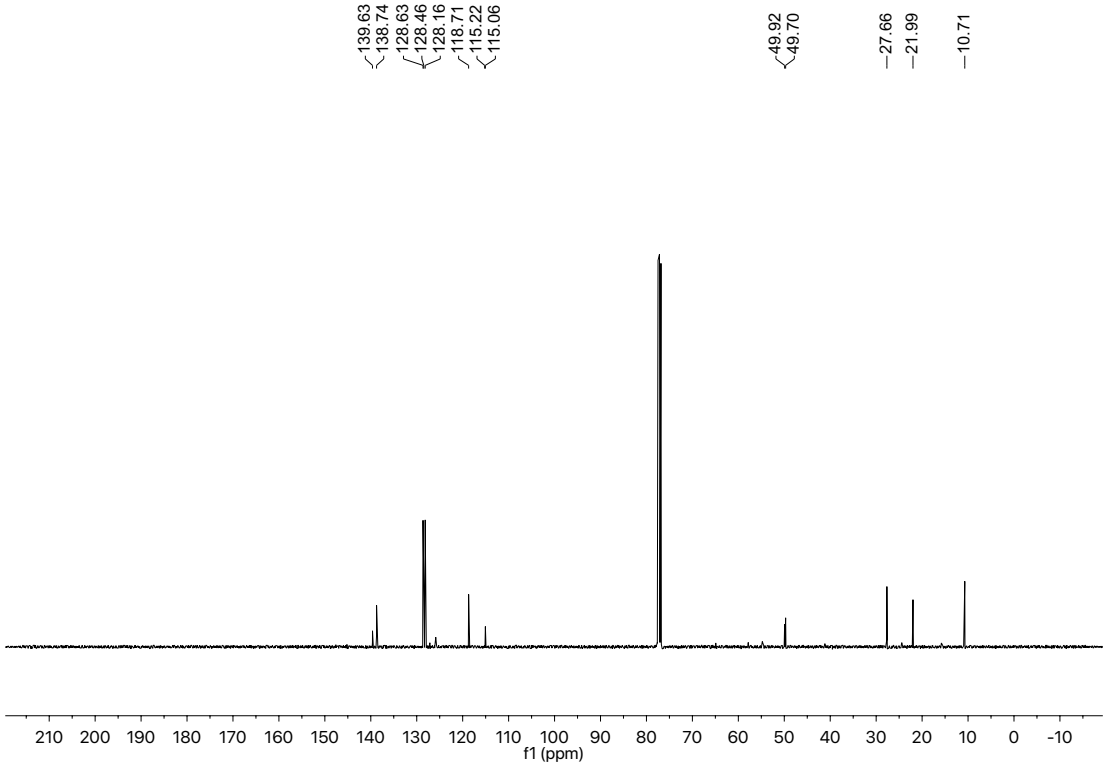
^{13}C NMR (101 MHz, $CDCl_3$) of compound **3**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **5a**.



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



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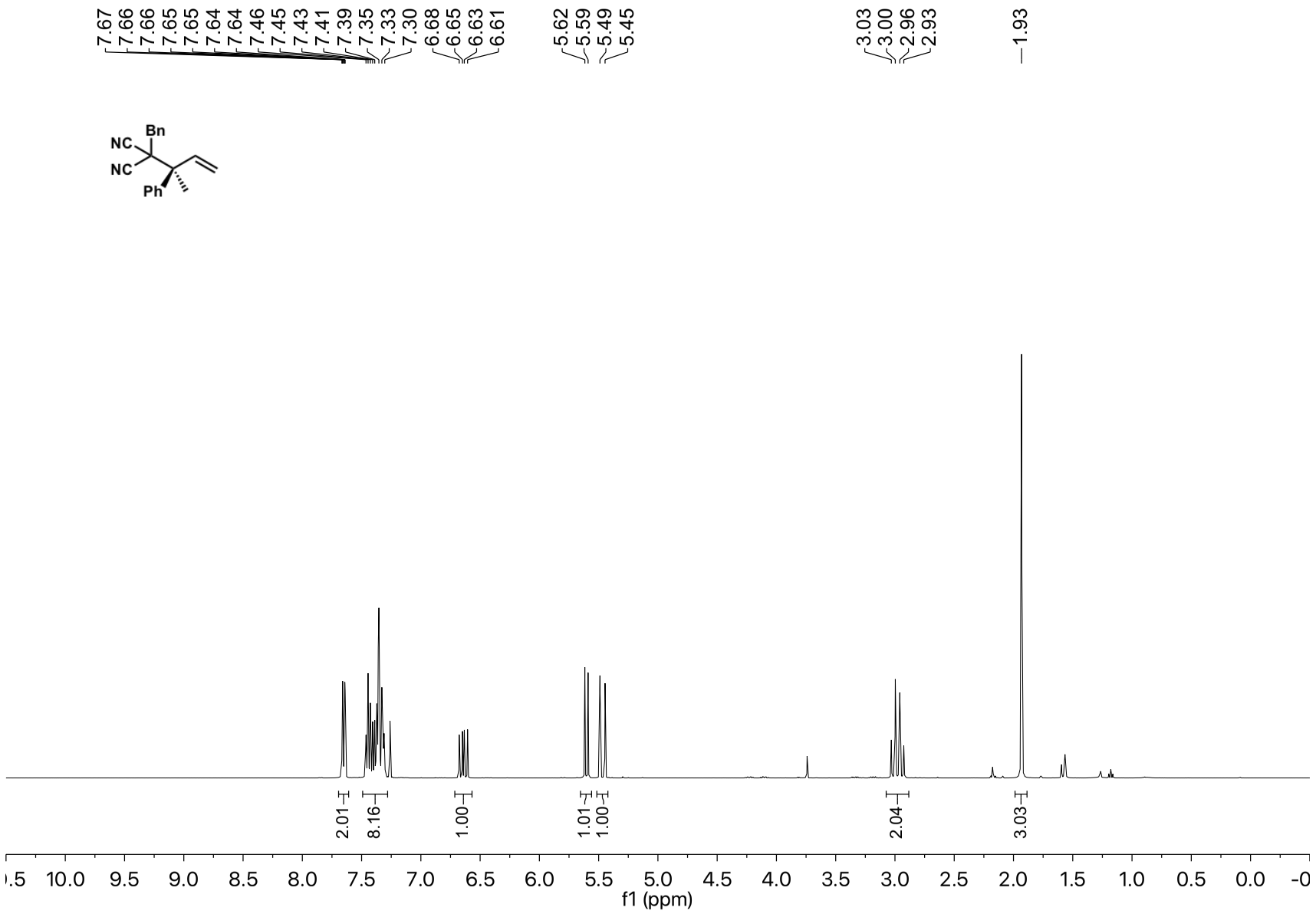

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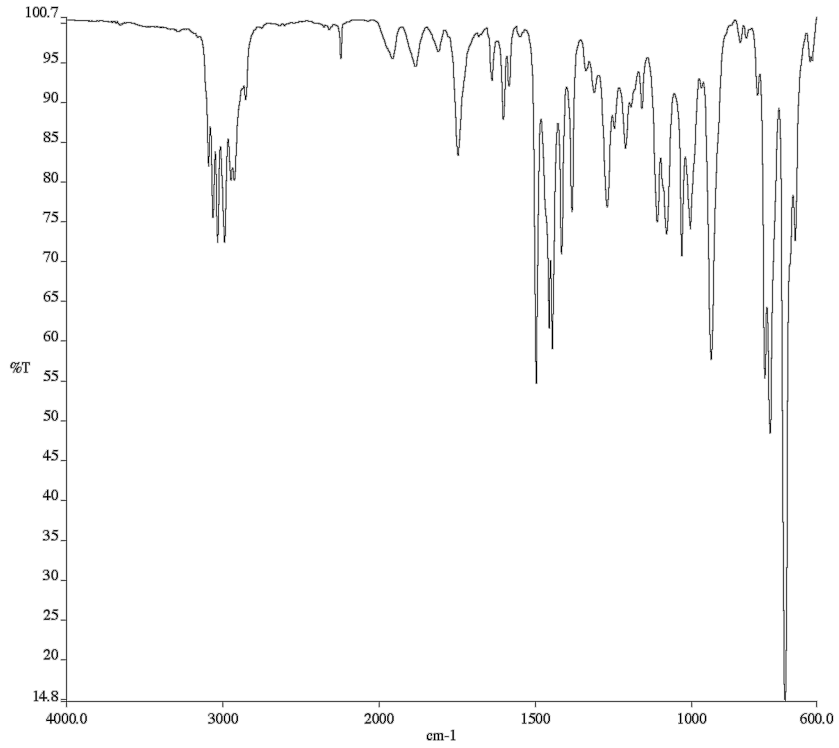
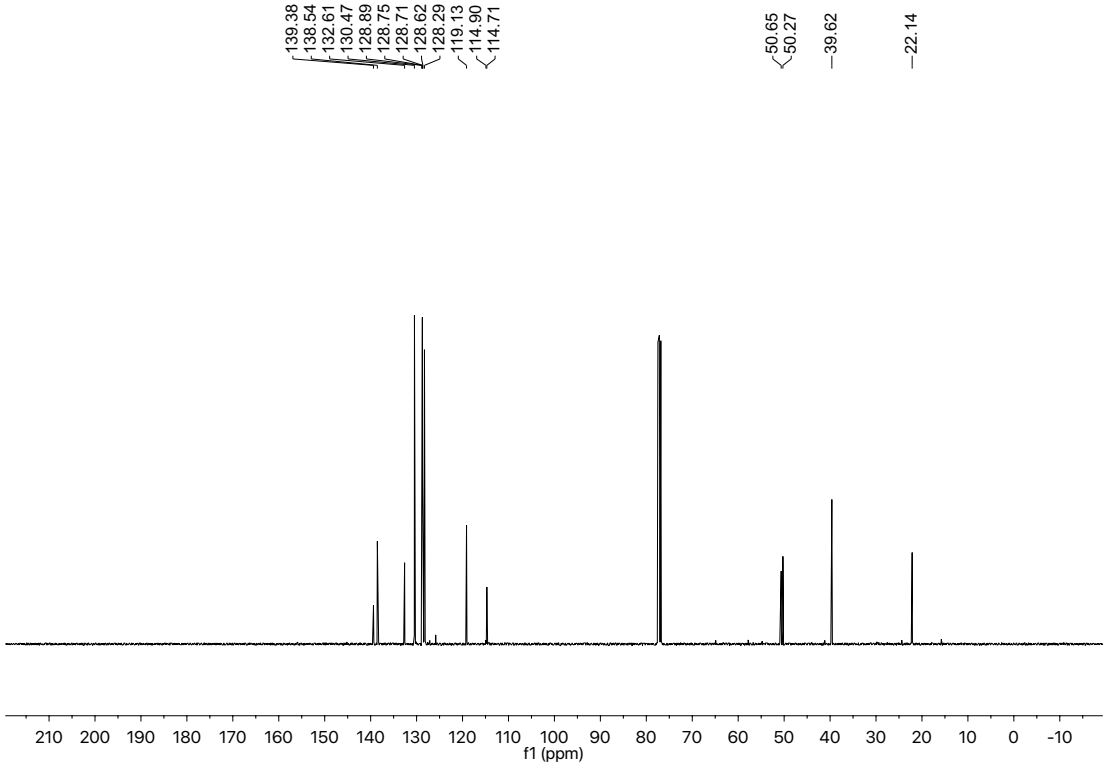


Infrared spectrum (Thin Film, NaCl) of compound **5b**.



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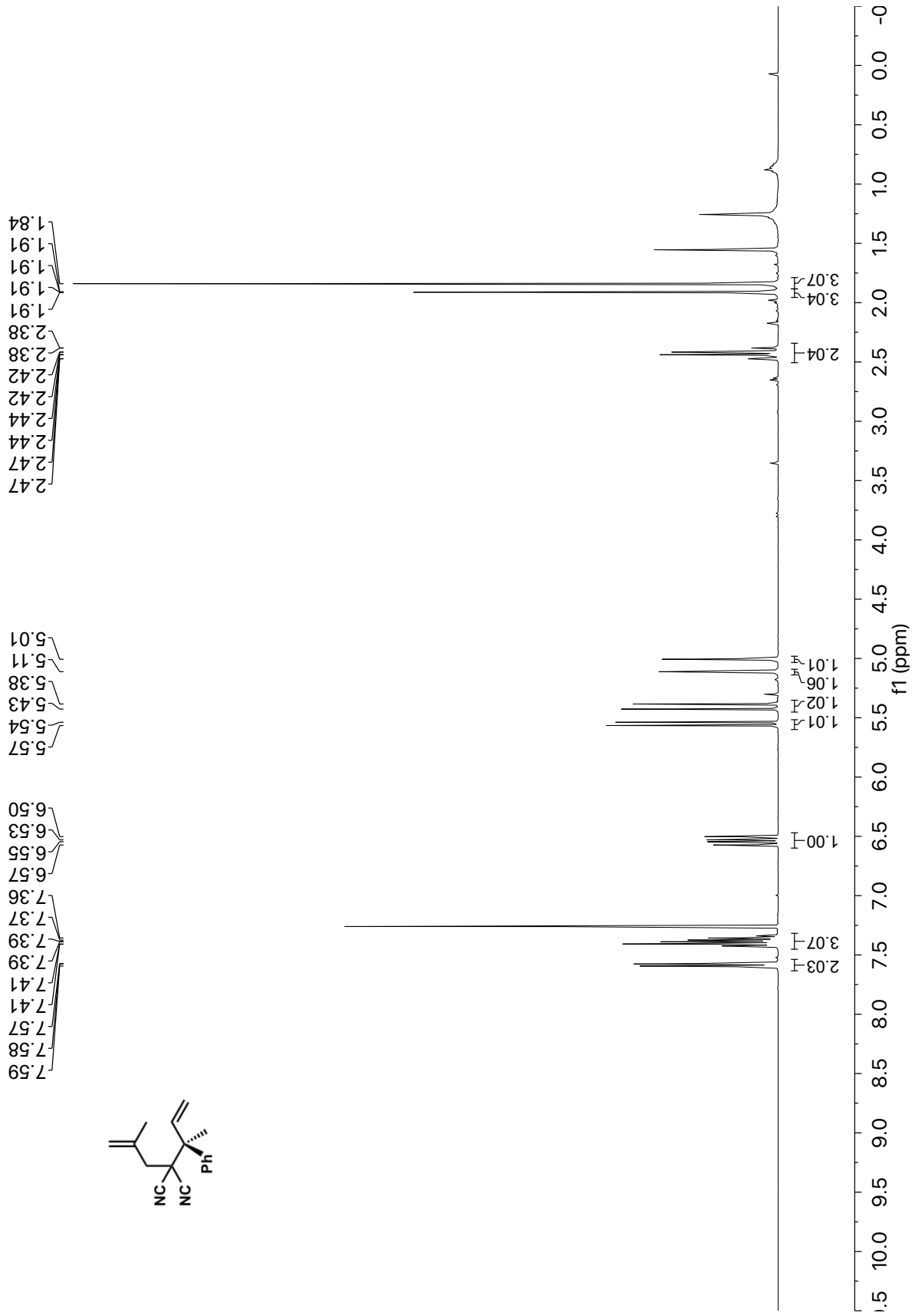

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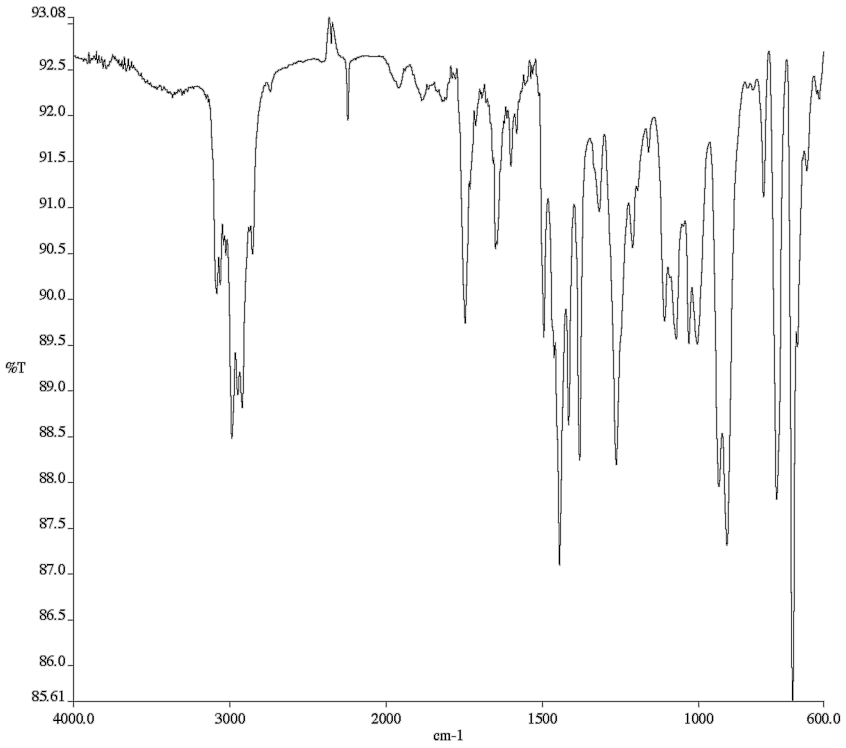

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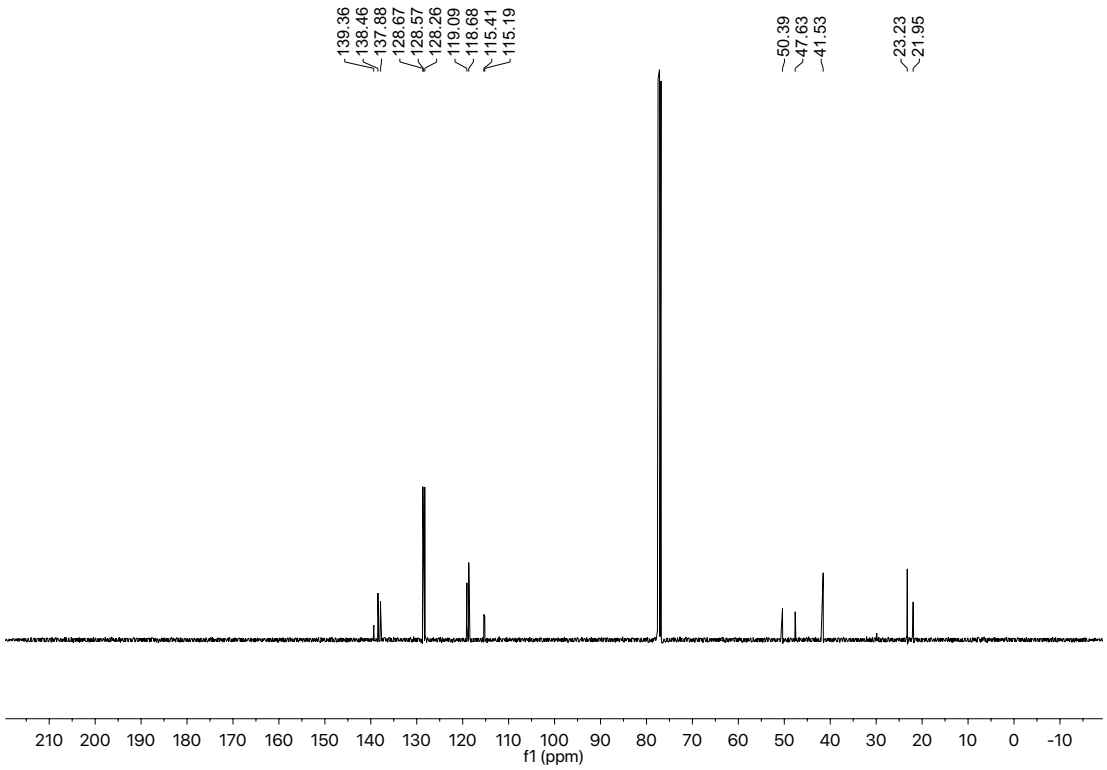

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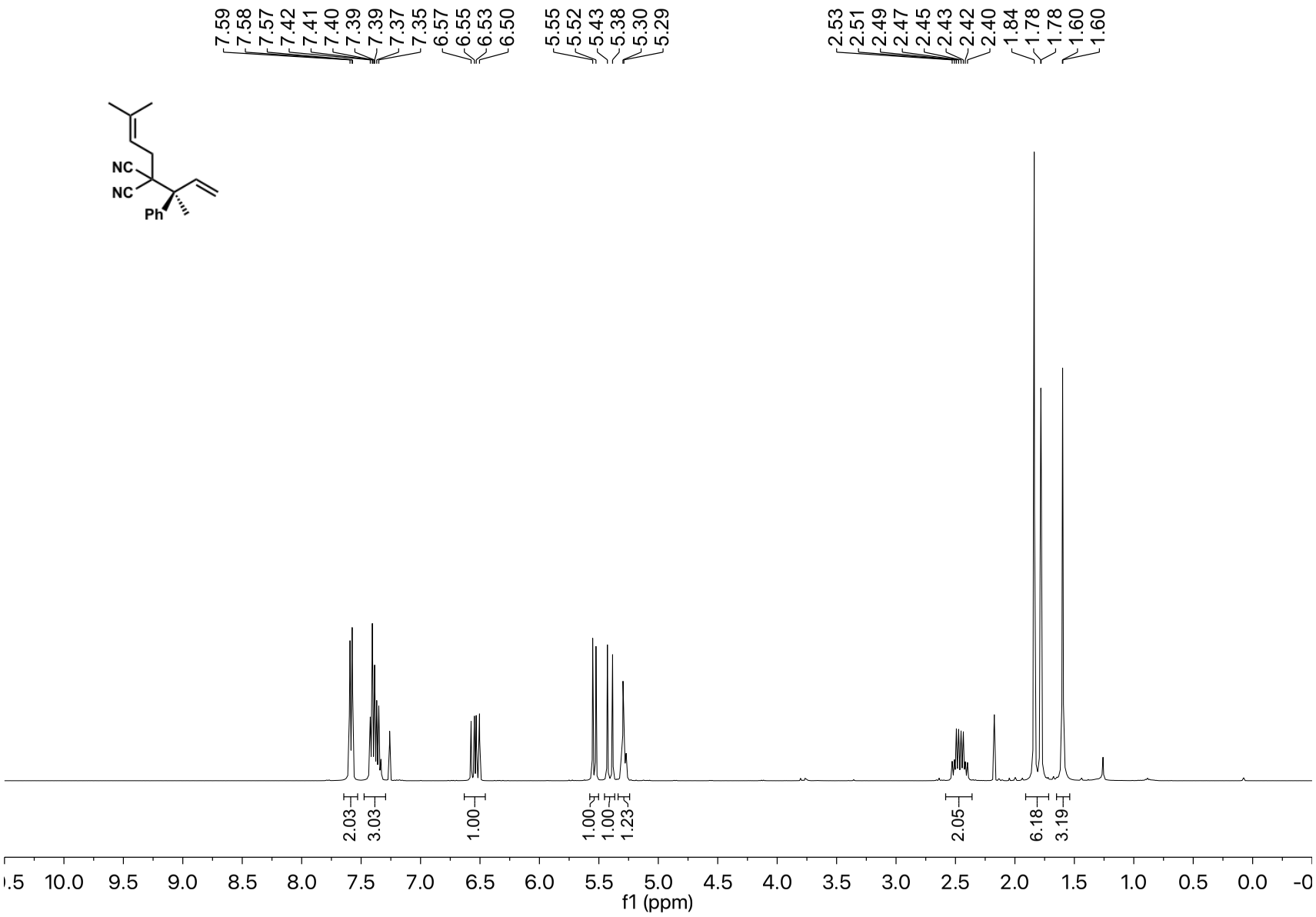

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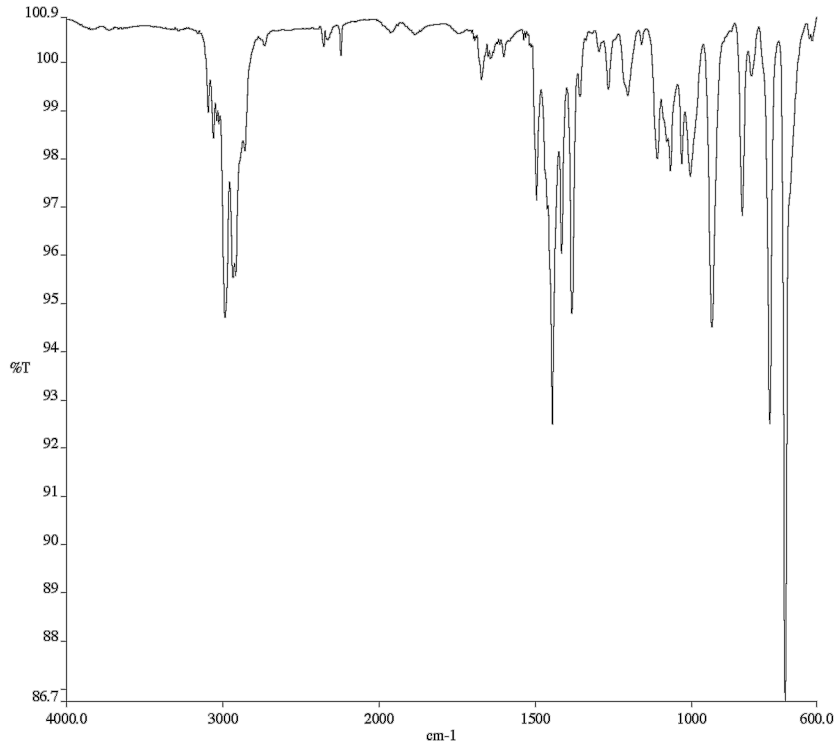
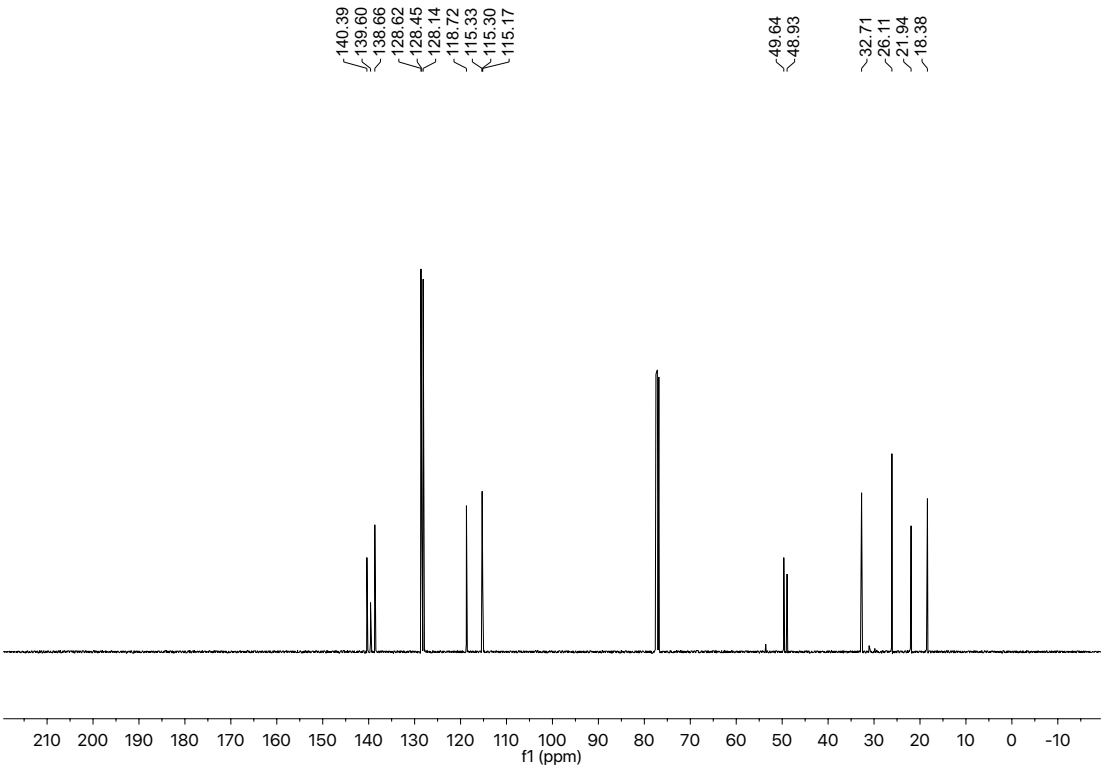
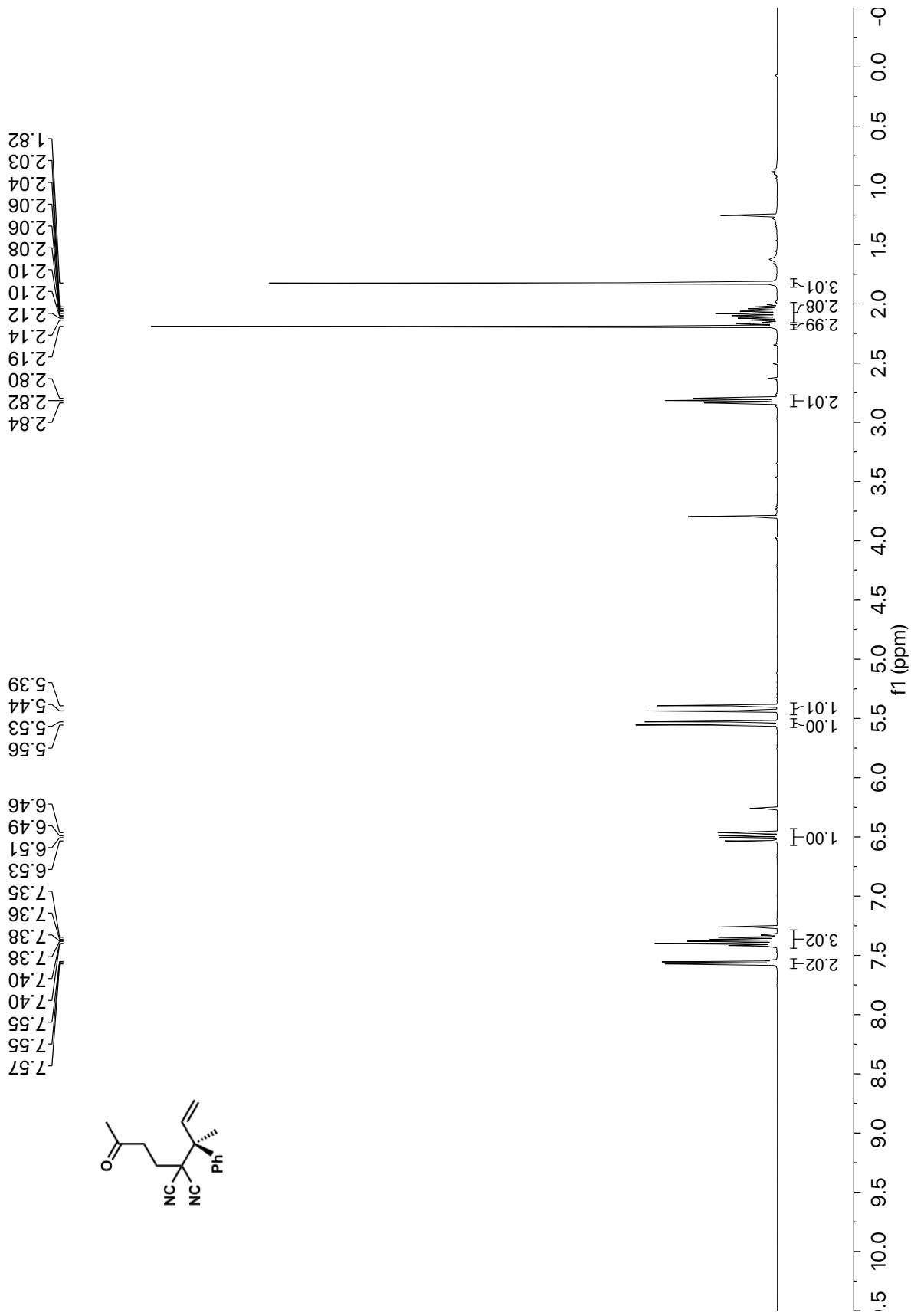


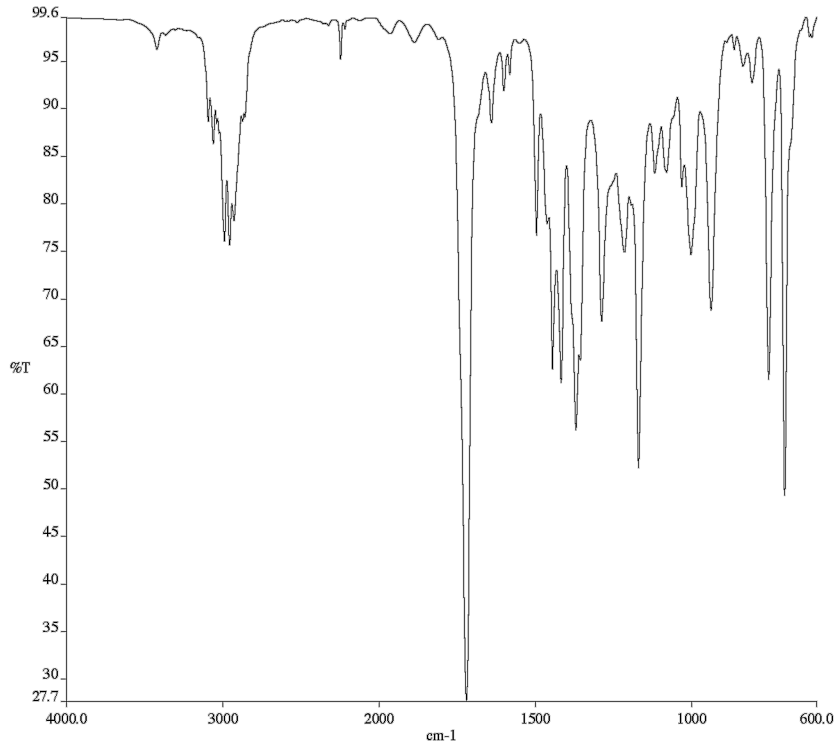
Infrared spectrum (Thin Film, NaCl) of compound **5e**.



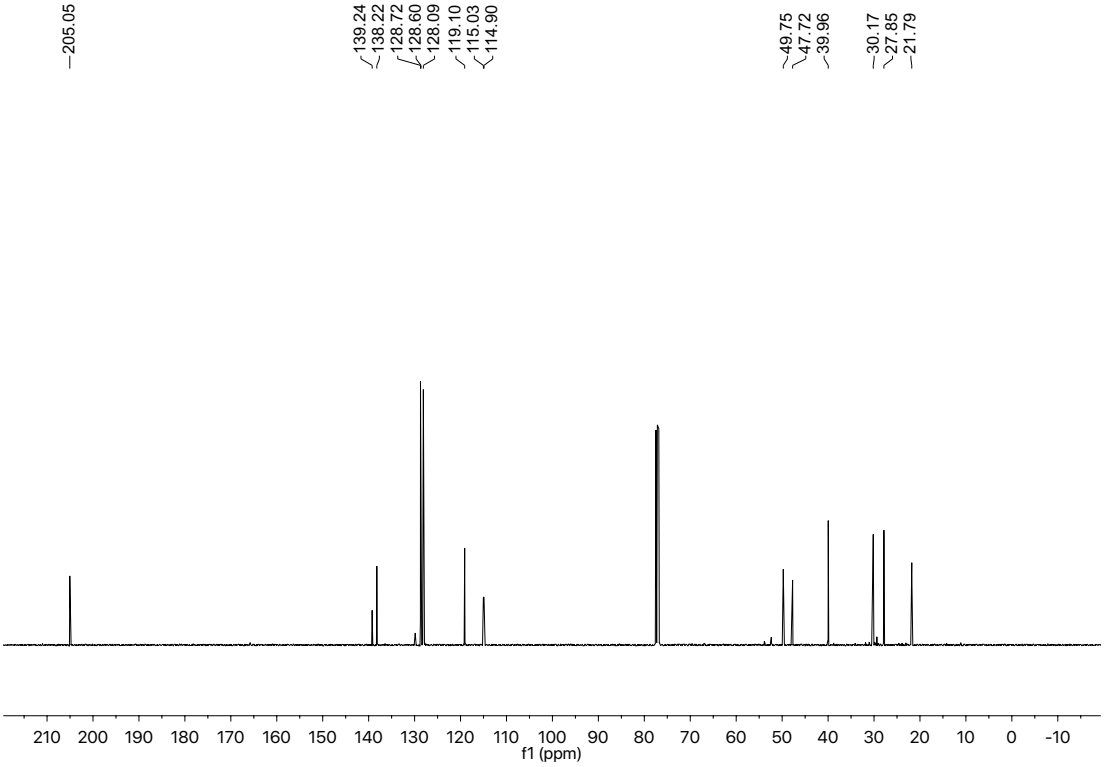
^{13}C NMR (101 MHz, $CDCl_3$) of compound **5e**.



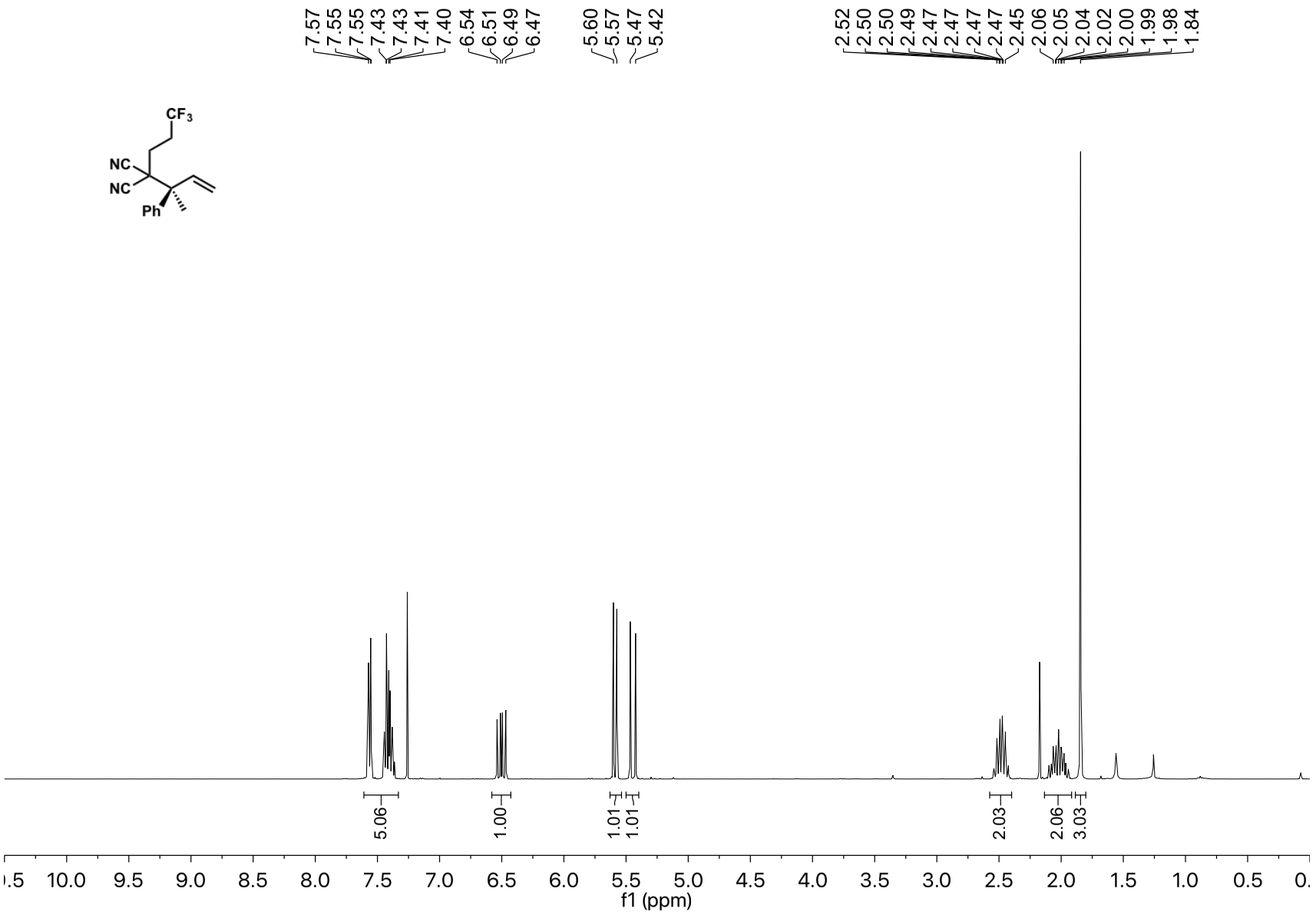
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5f.**



Infrared spectrum (Thin Film, NaCl) of compound **5f**.



^{13}C NMR (101 MHz, $CDCl_3$) of compound **5f**.



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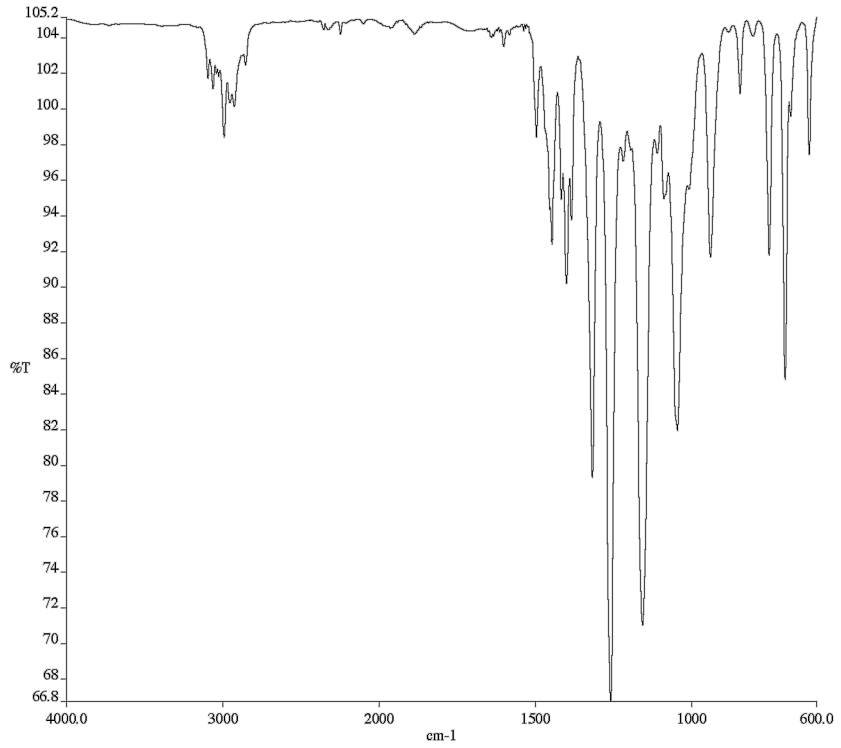
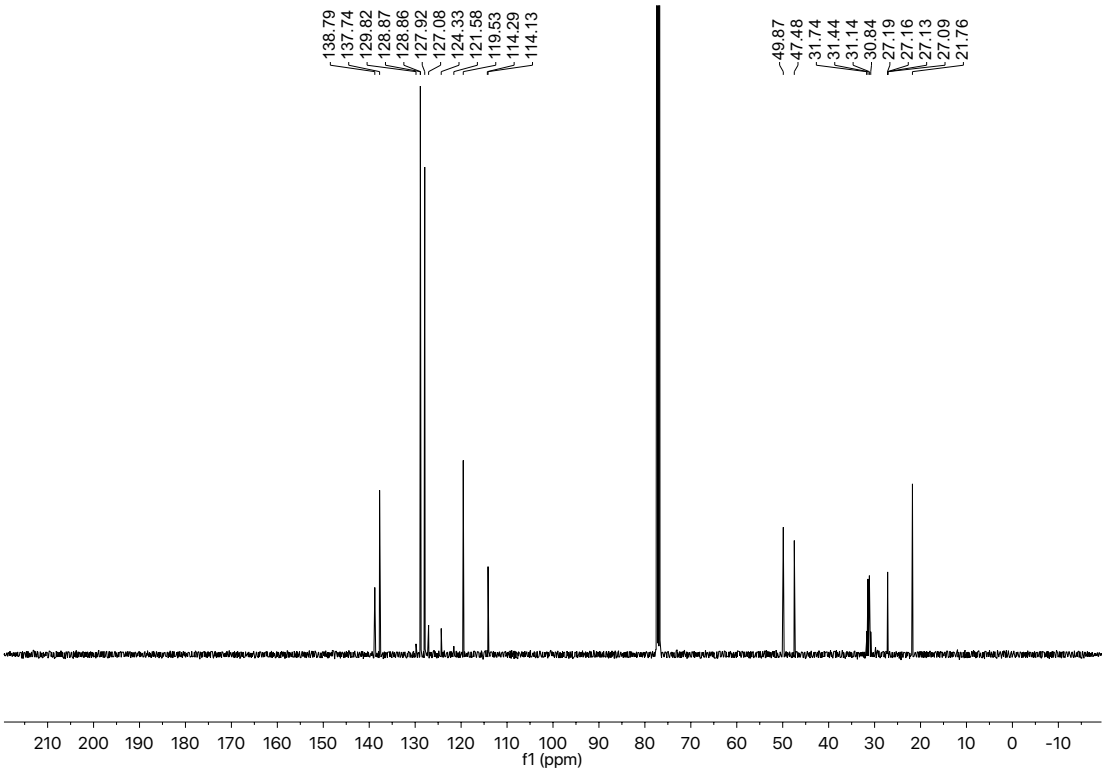


Infrared spectrum (Thin Film, NaCl) of compound **5g**.



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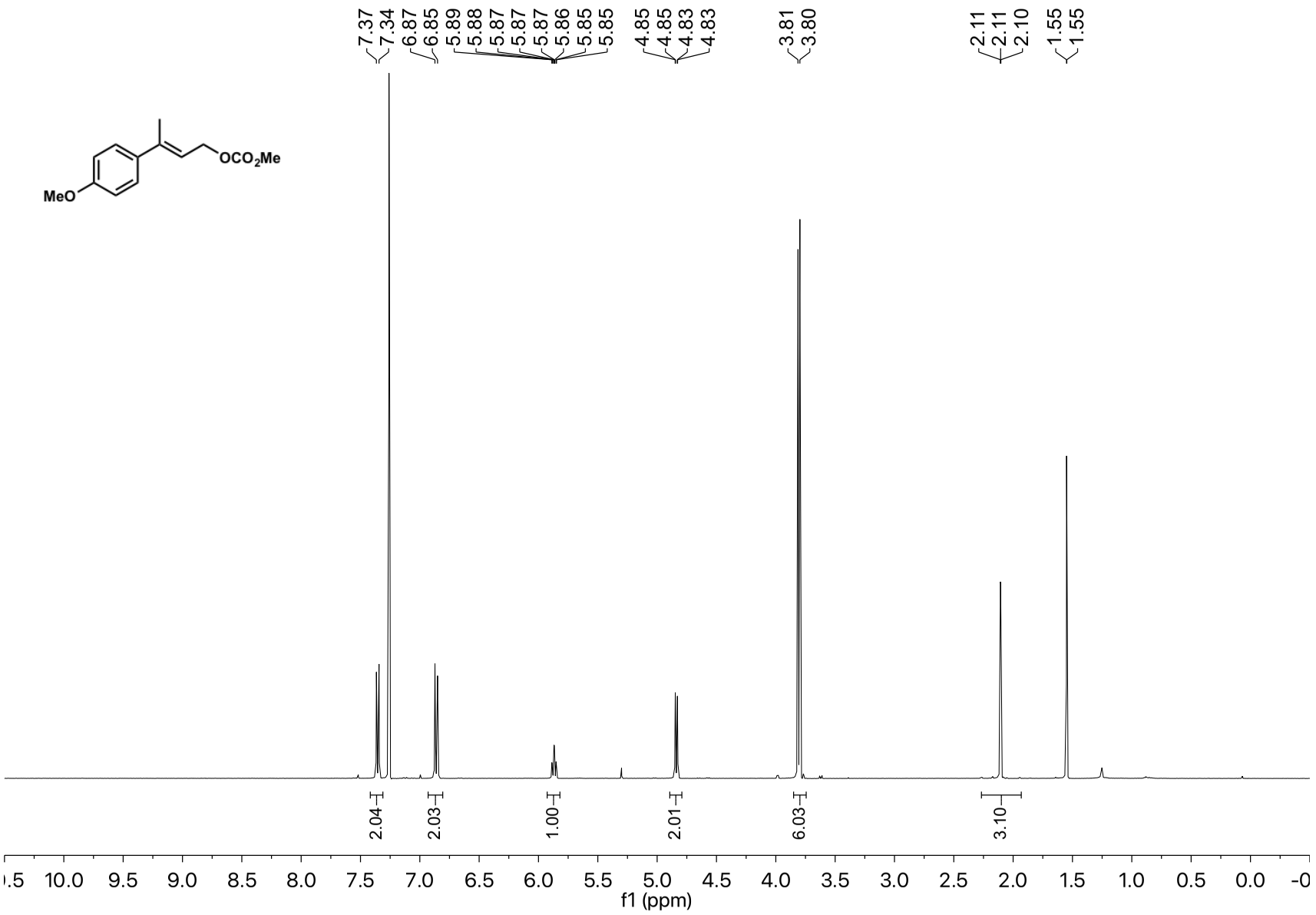

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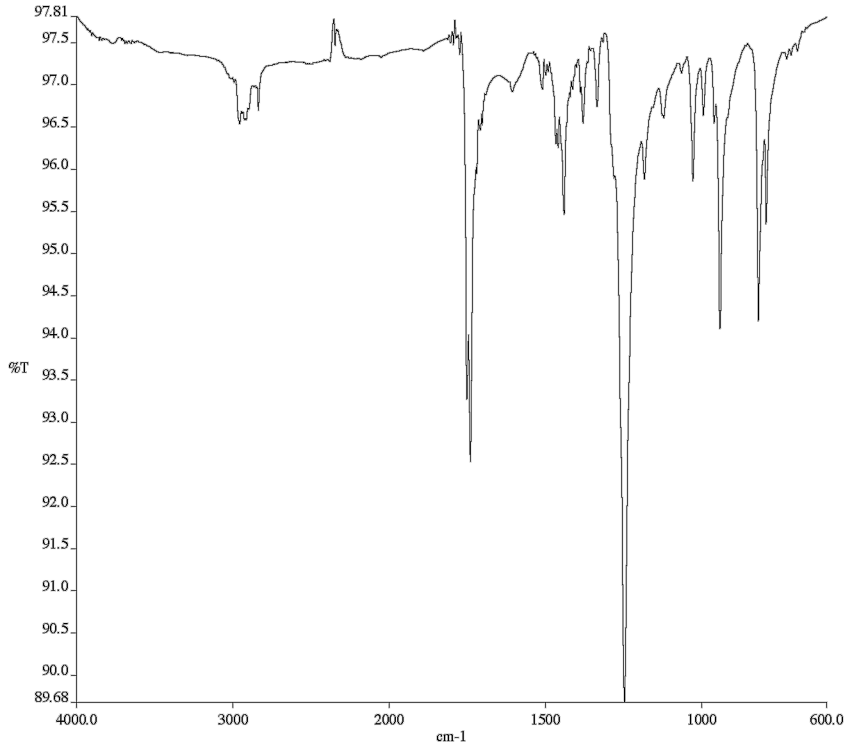
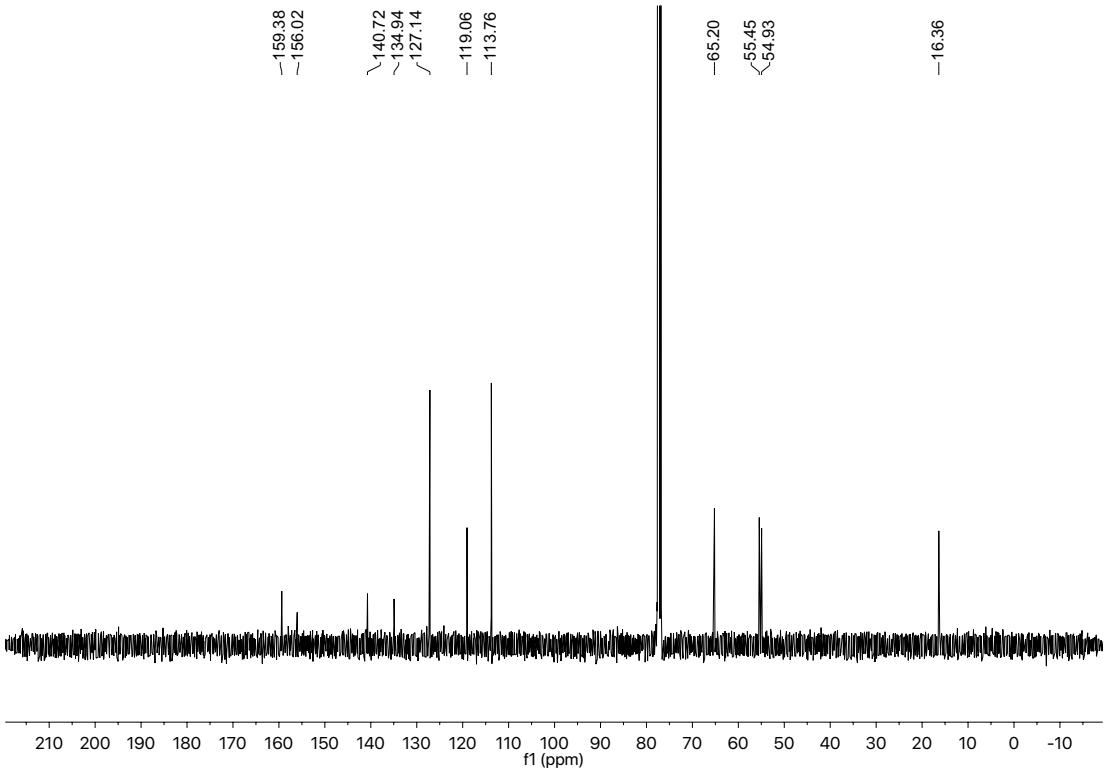


Infrared spectrum (Thin Film, NaCl) of compound **6b**.



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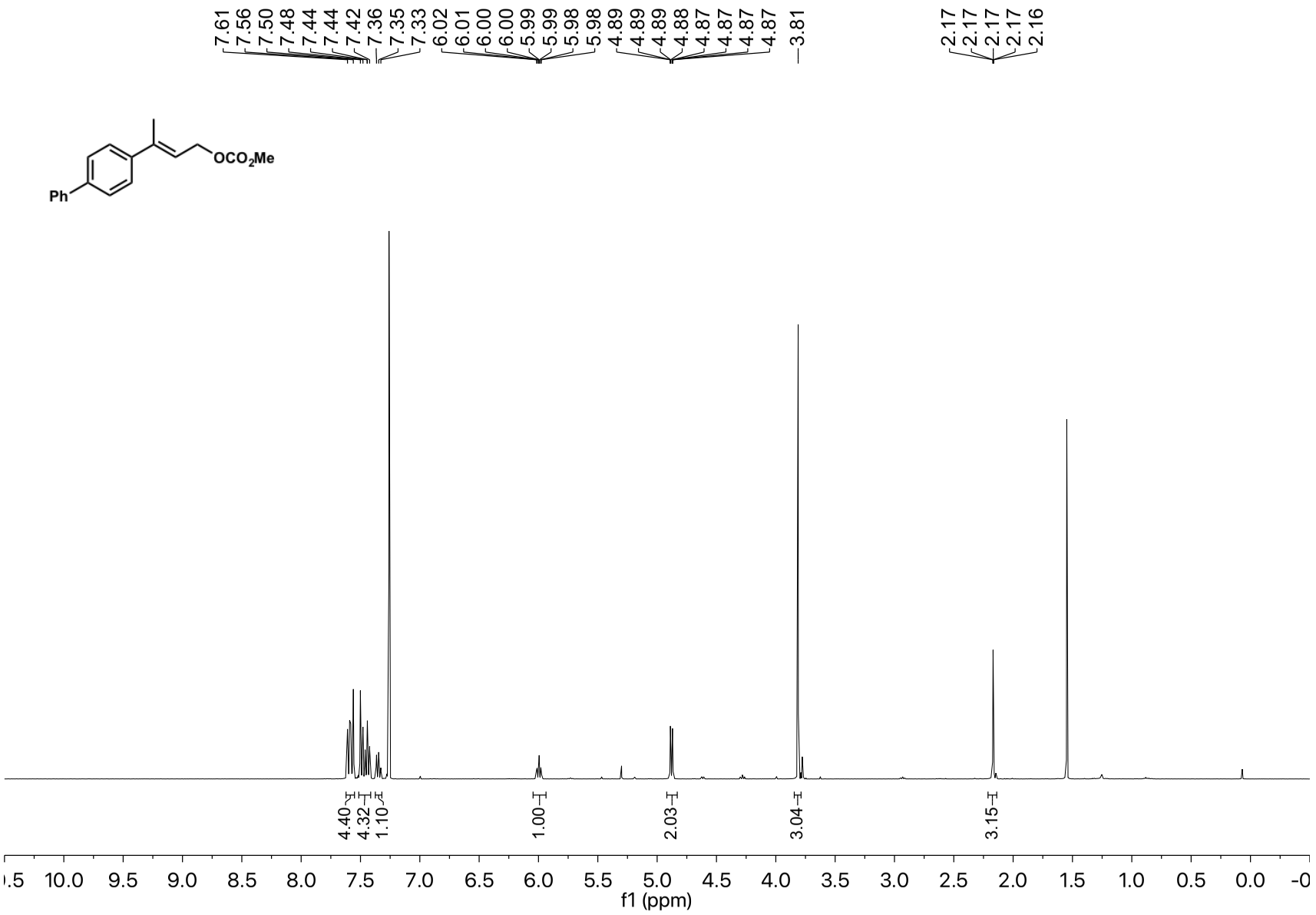

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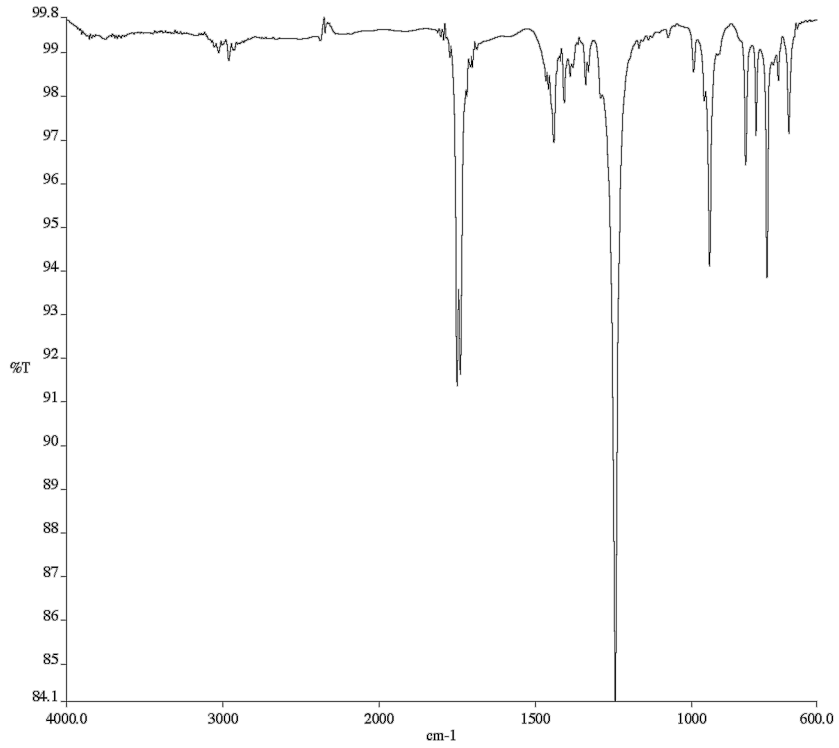
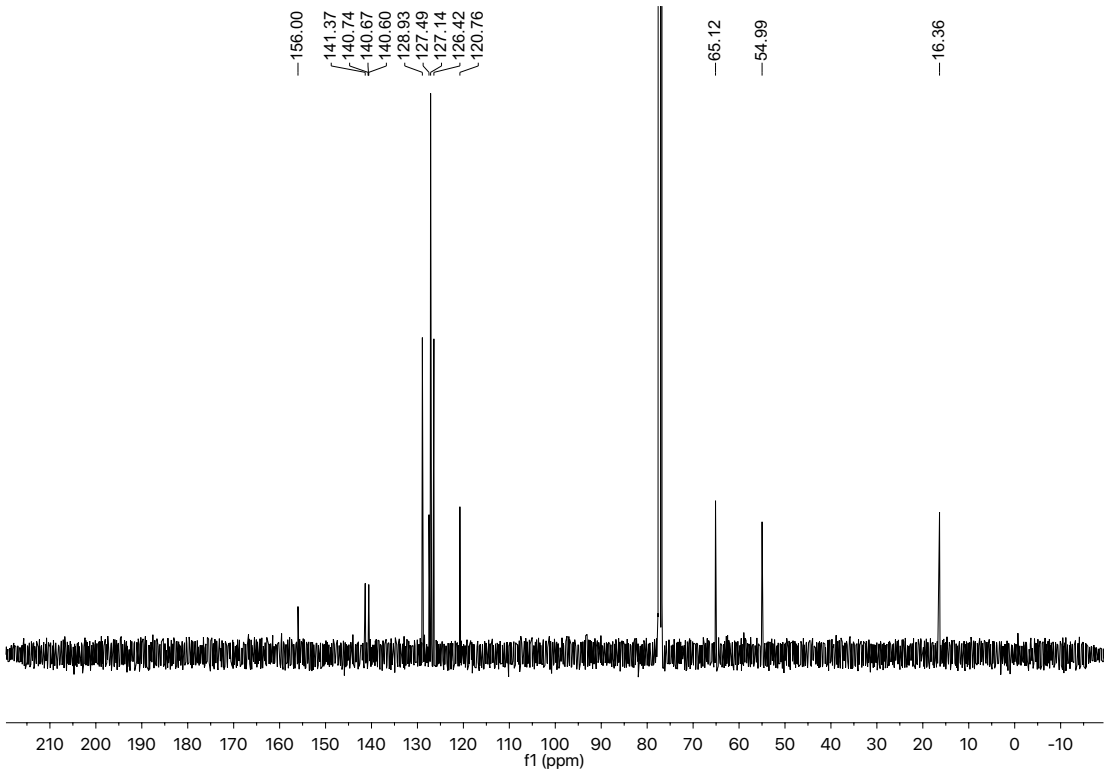


Infrared spectrum (Thin Film, NaCl) of compound **6c**.



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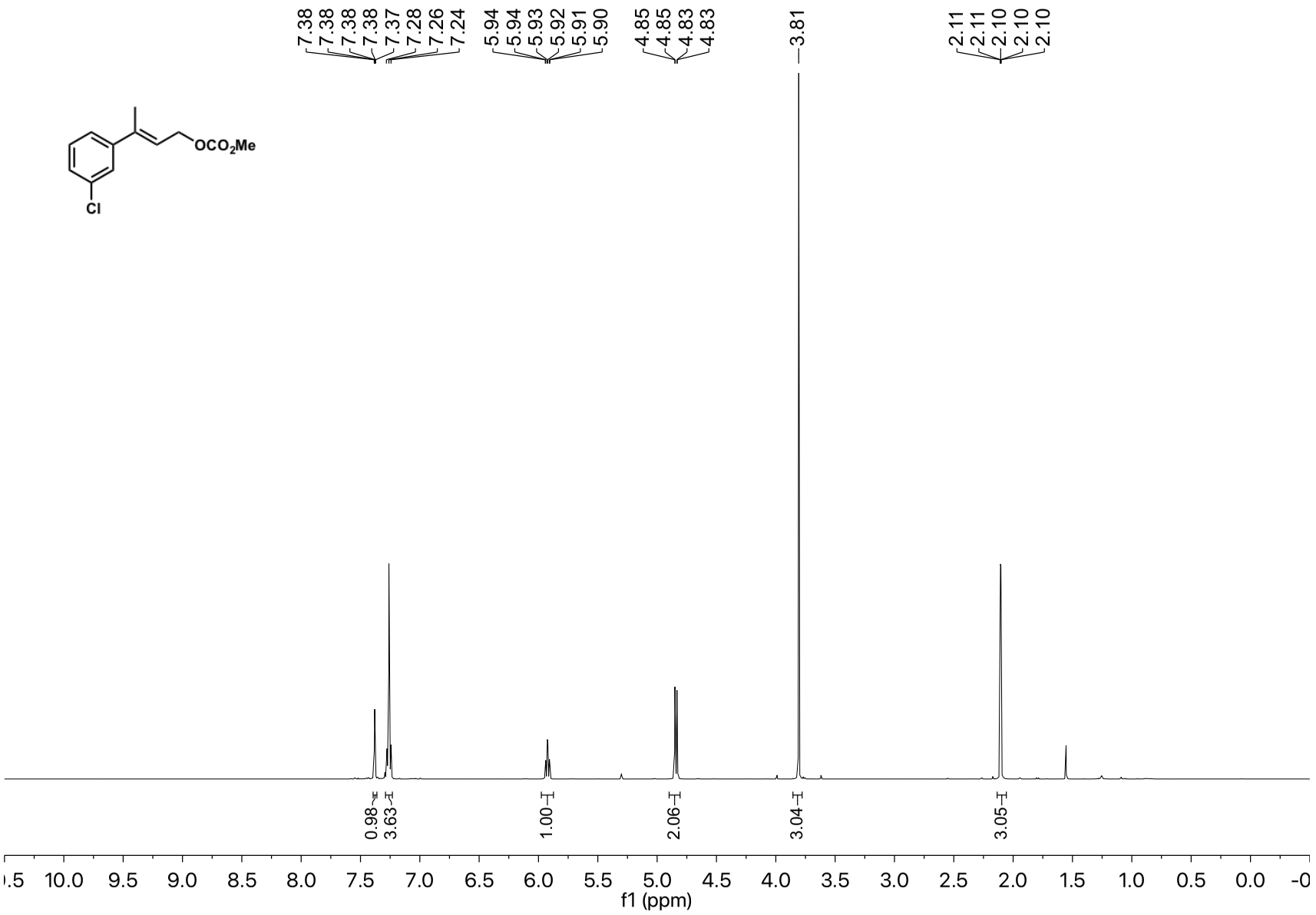

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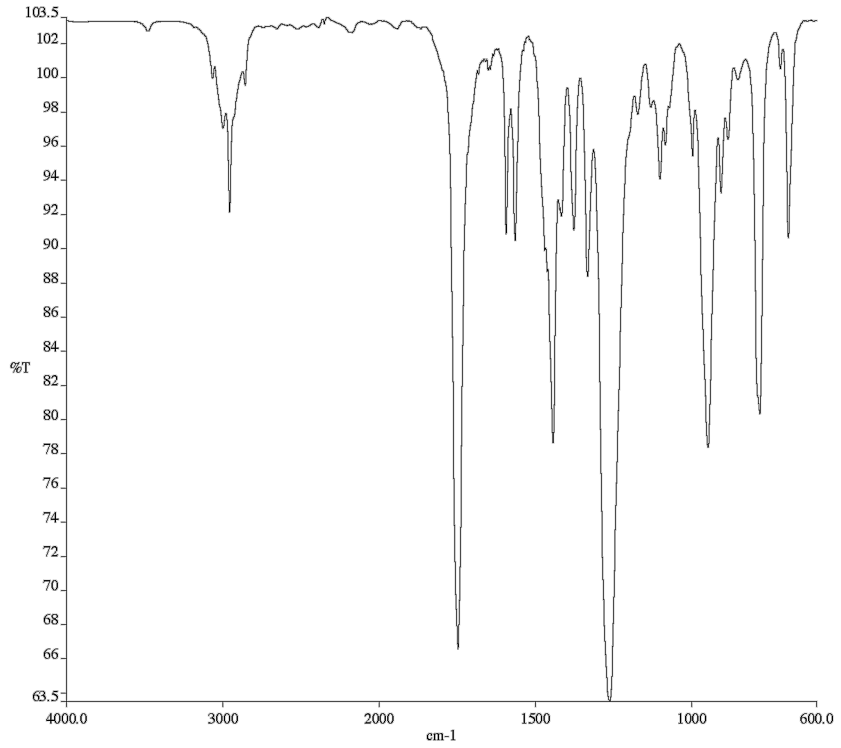
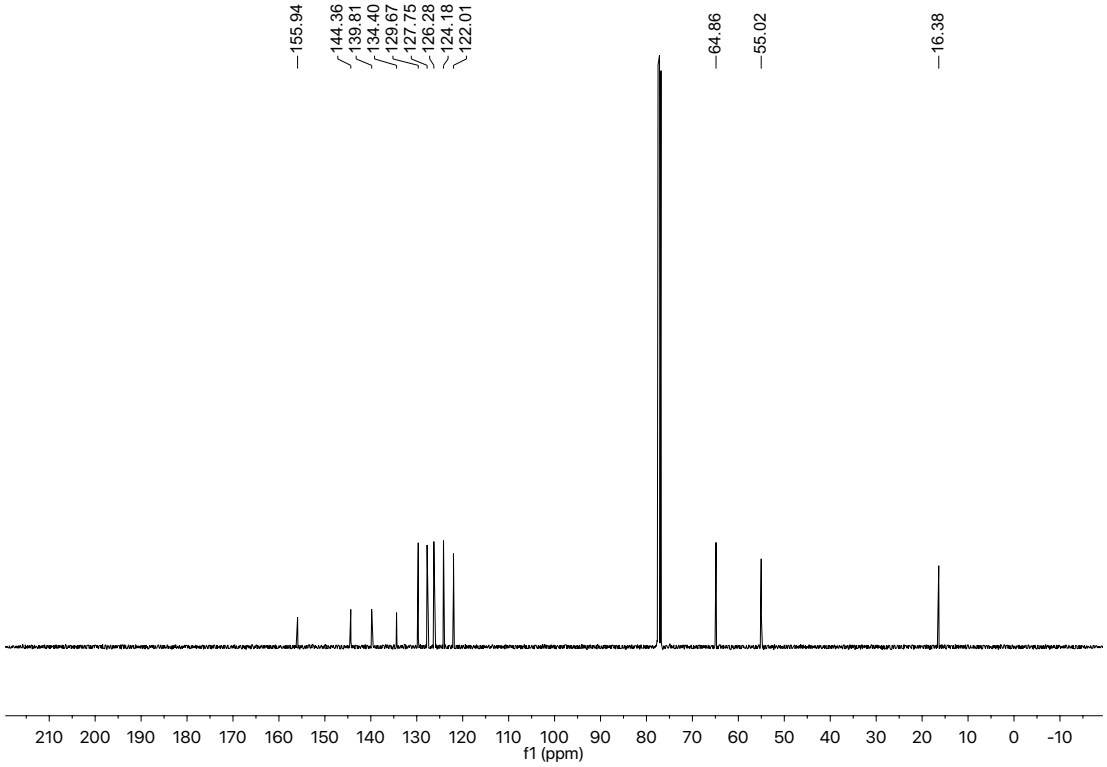


Infrared spectrum (Thin Film, NaCl) of compound **6f**.



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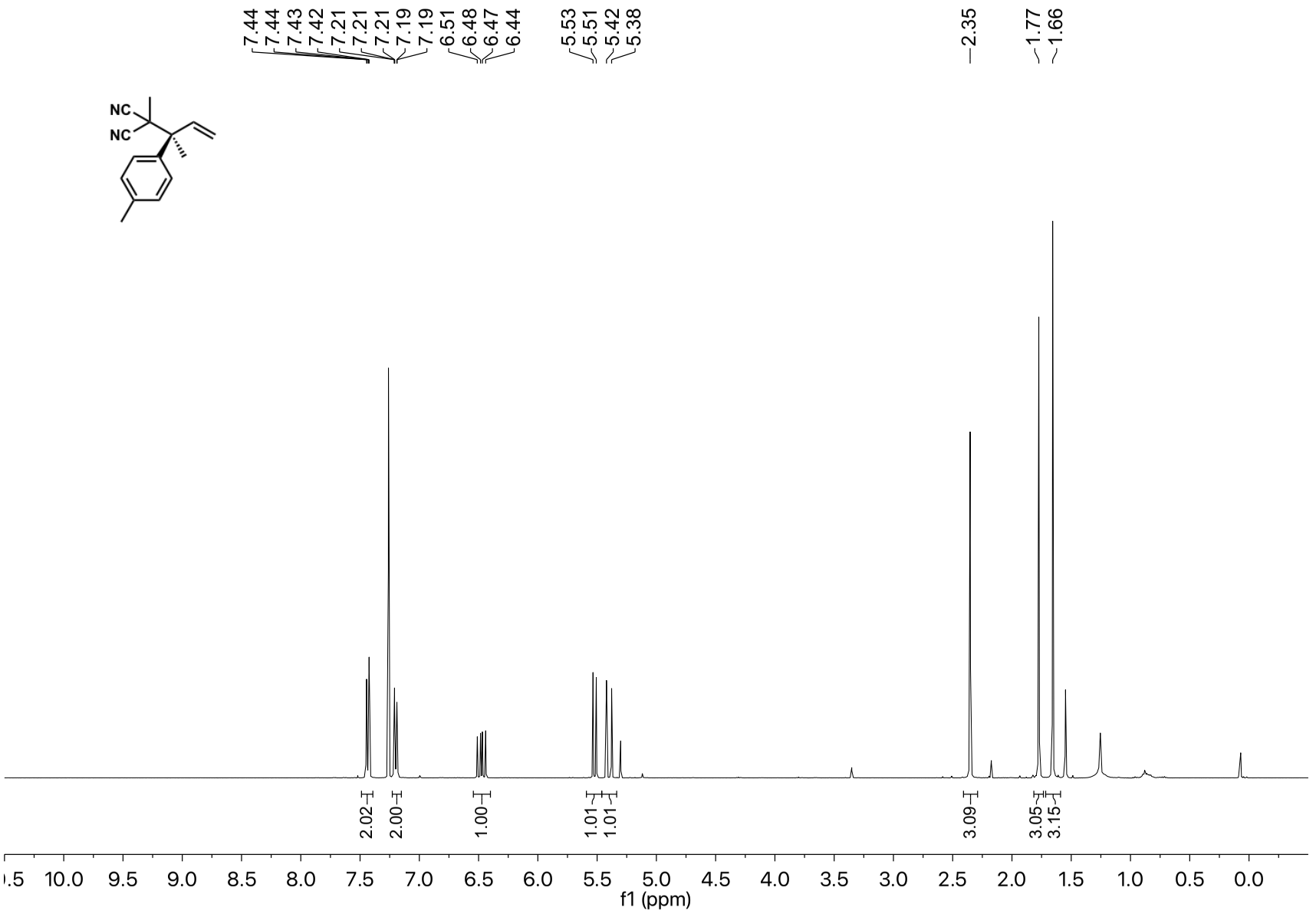

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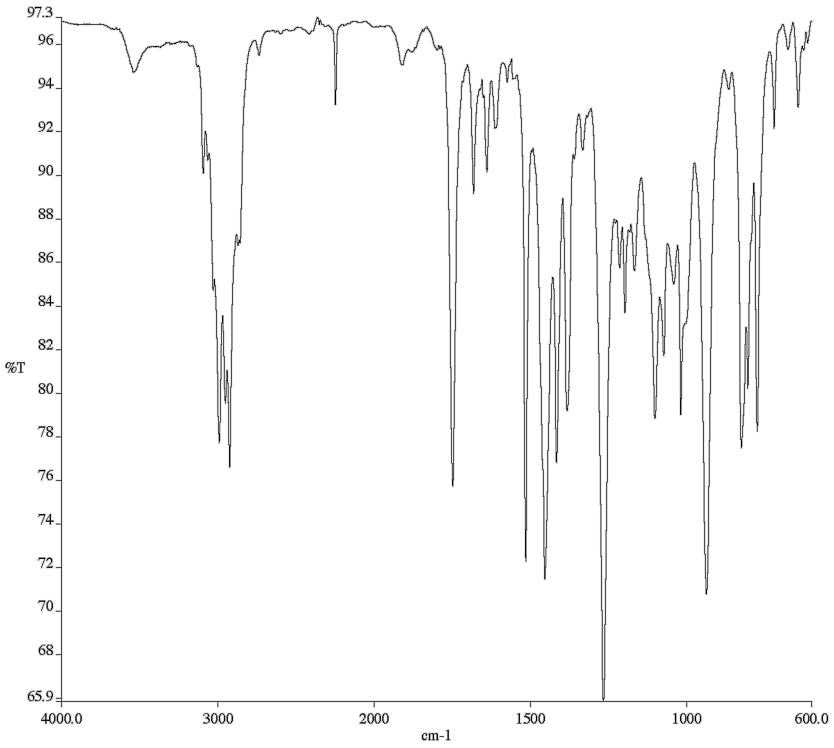
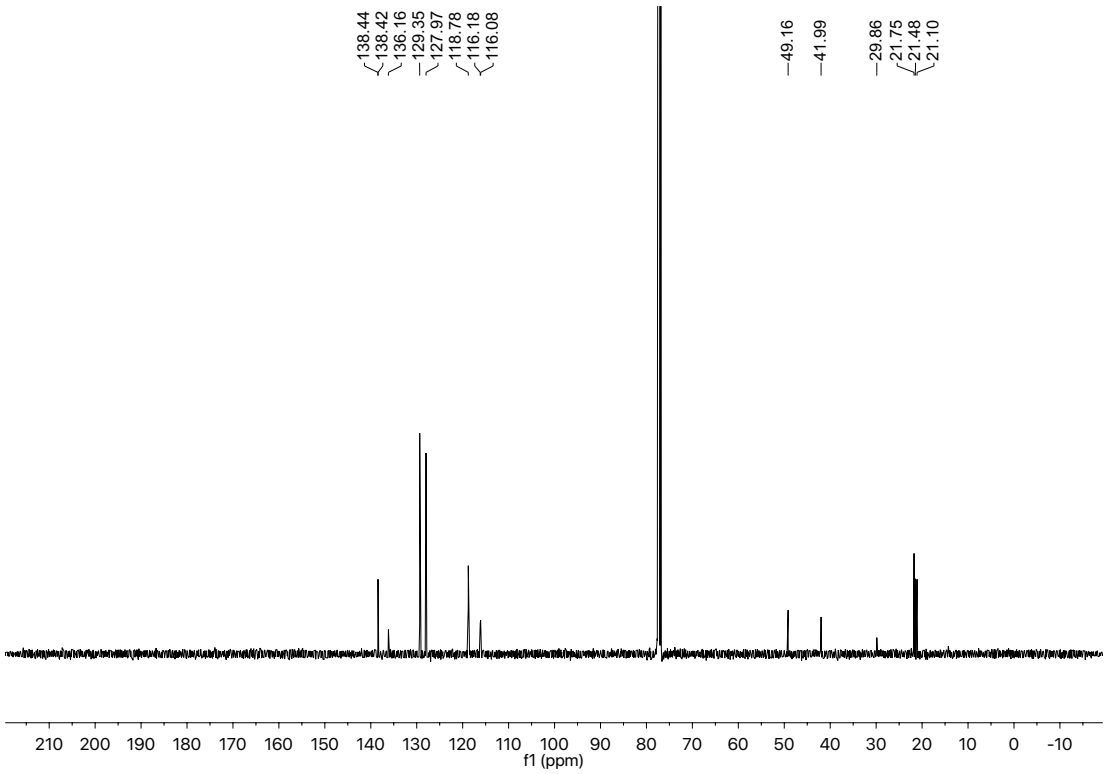


Infrared spectrum (Thin Film, NaCl) of compound **7a**.



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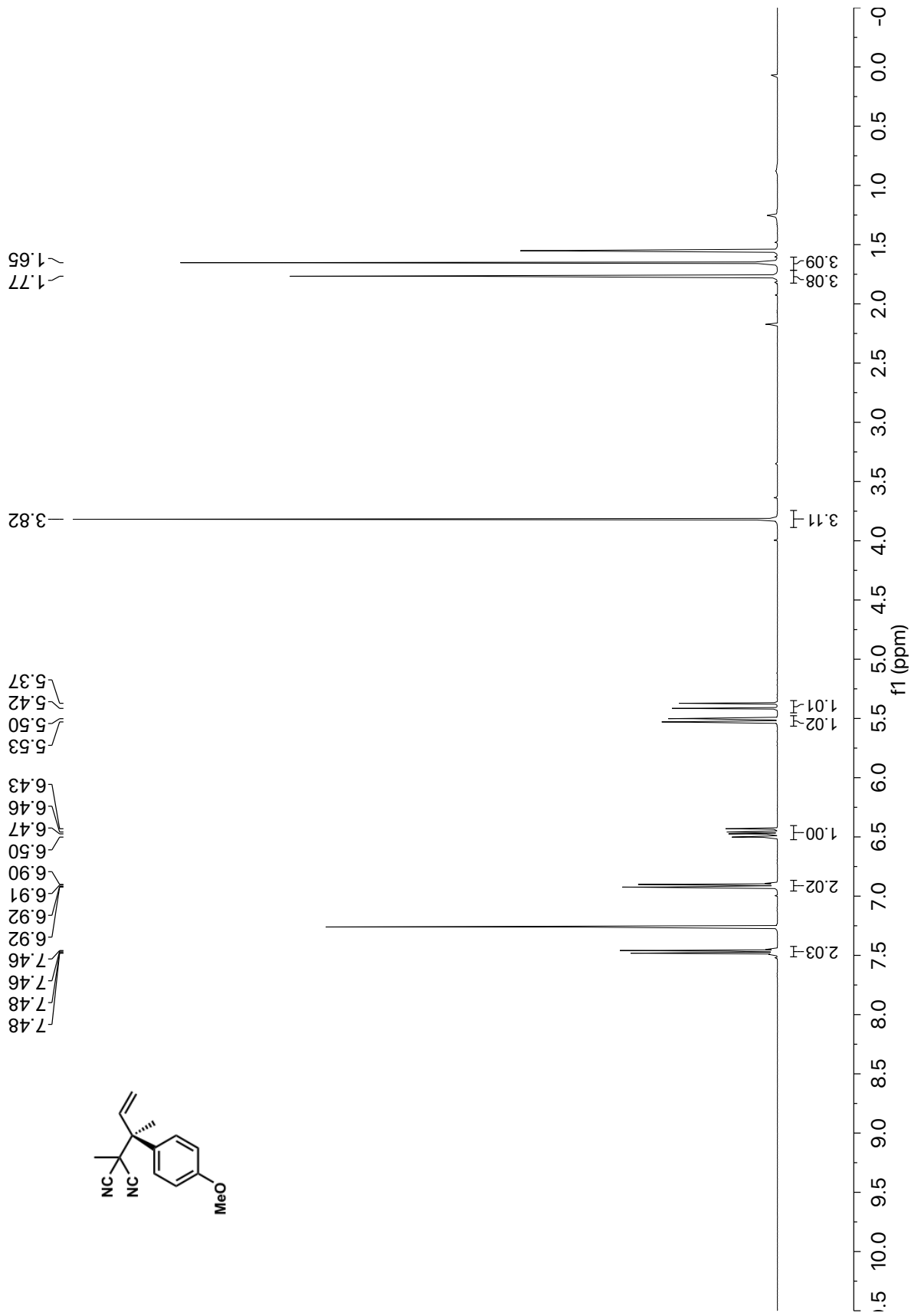

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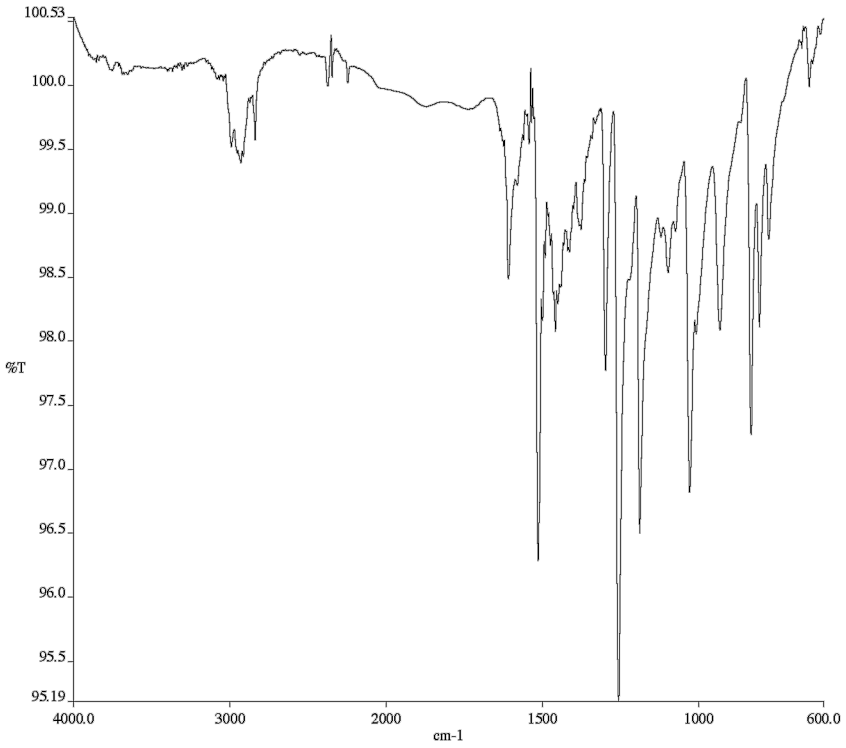
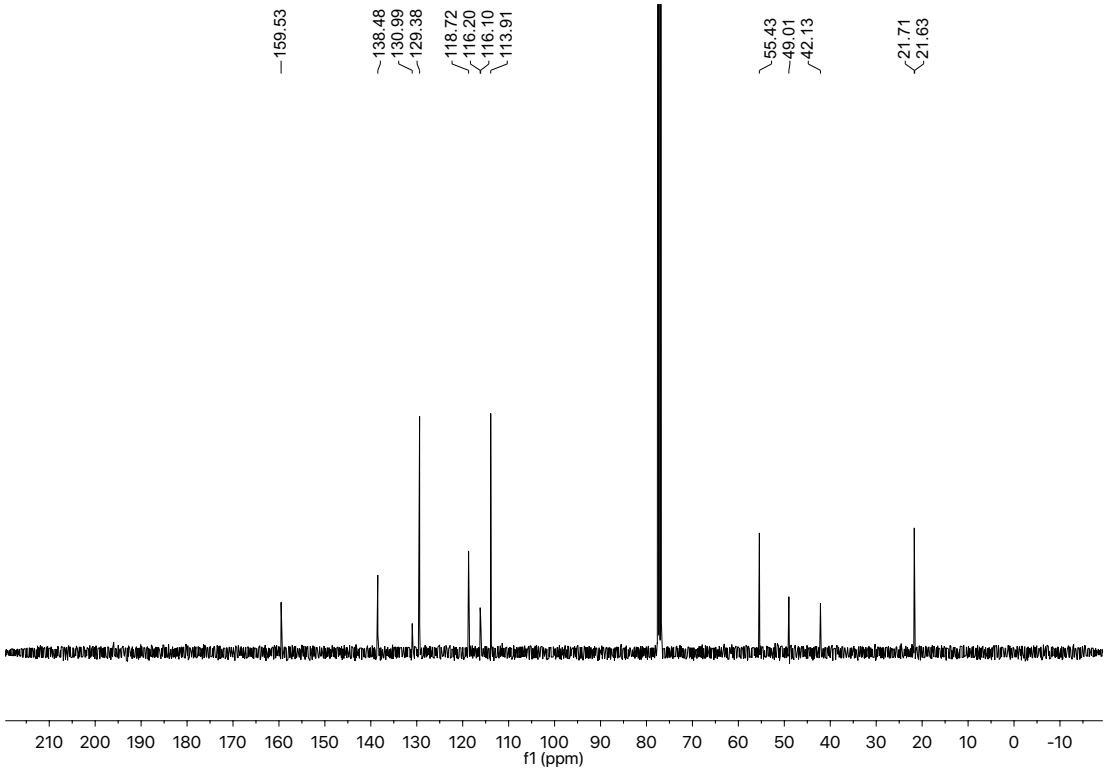


Infrared spectrum (Thin Film, NaCl) of compound **7b**.



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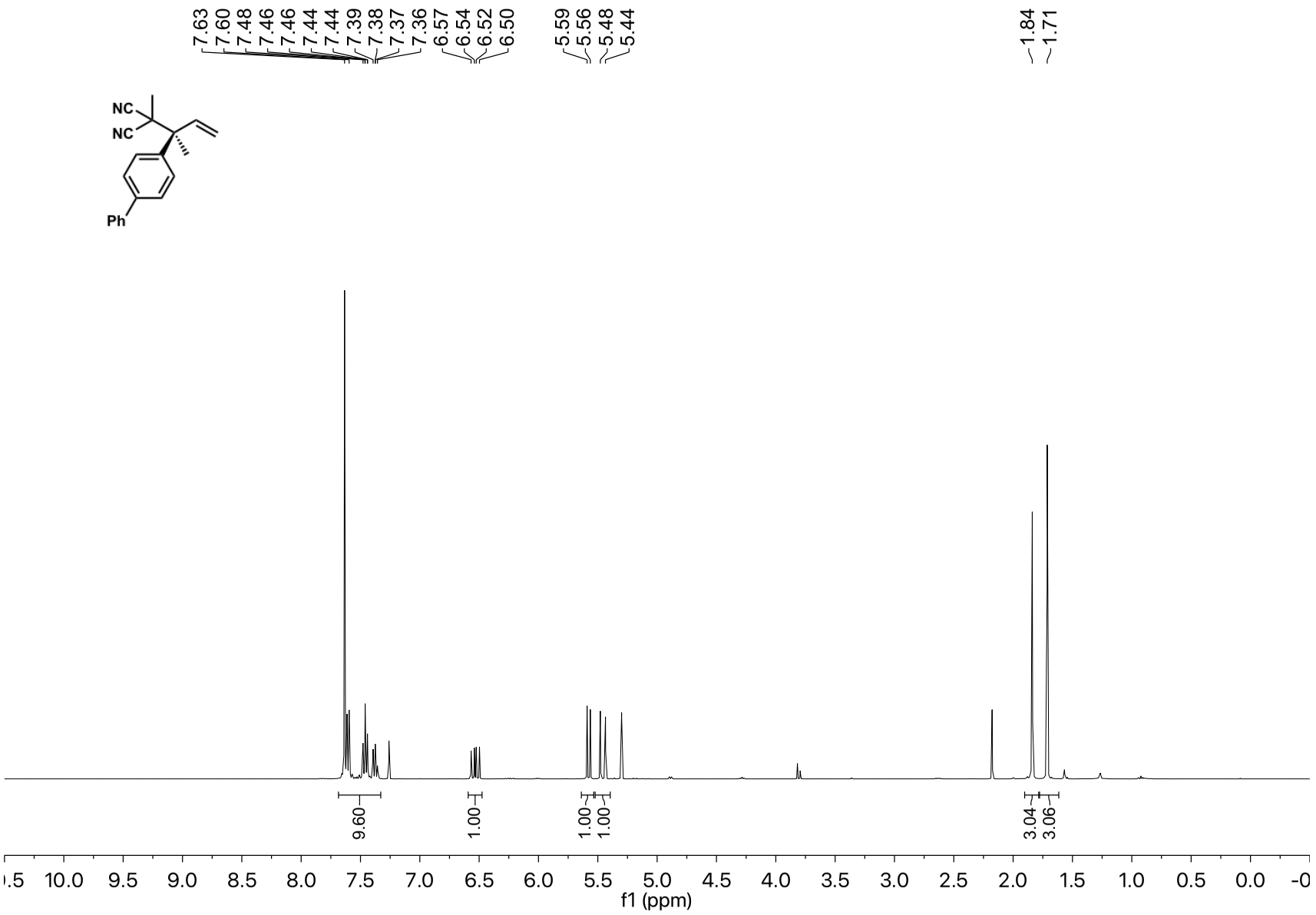

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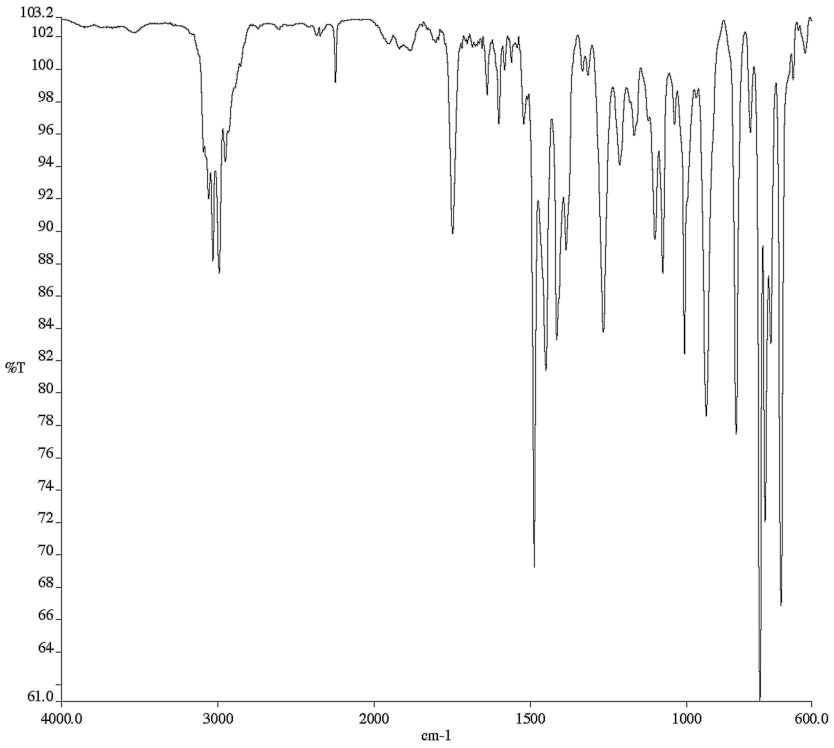
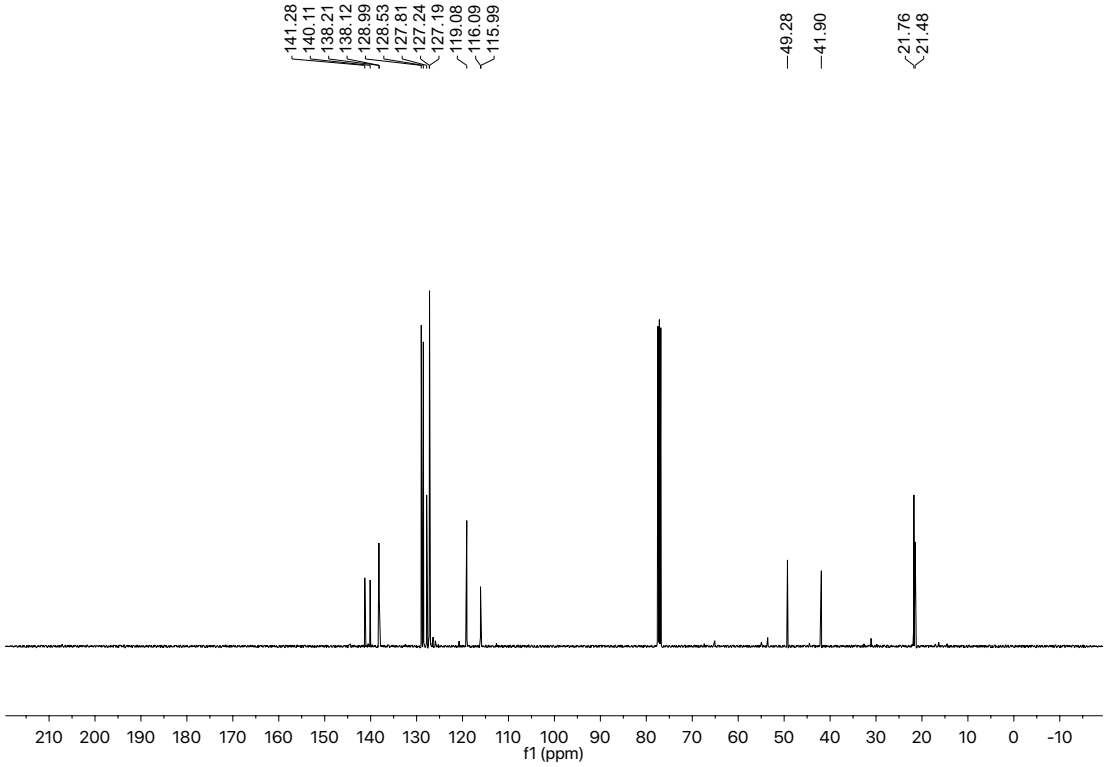


Infrared spectrum (Thin Film, NaCl) of compound **7c**.



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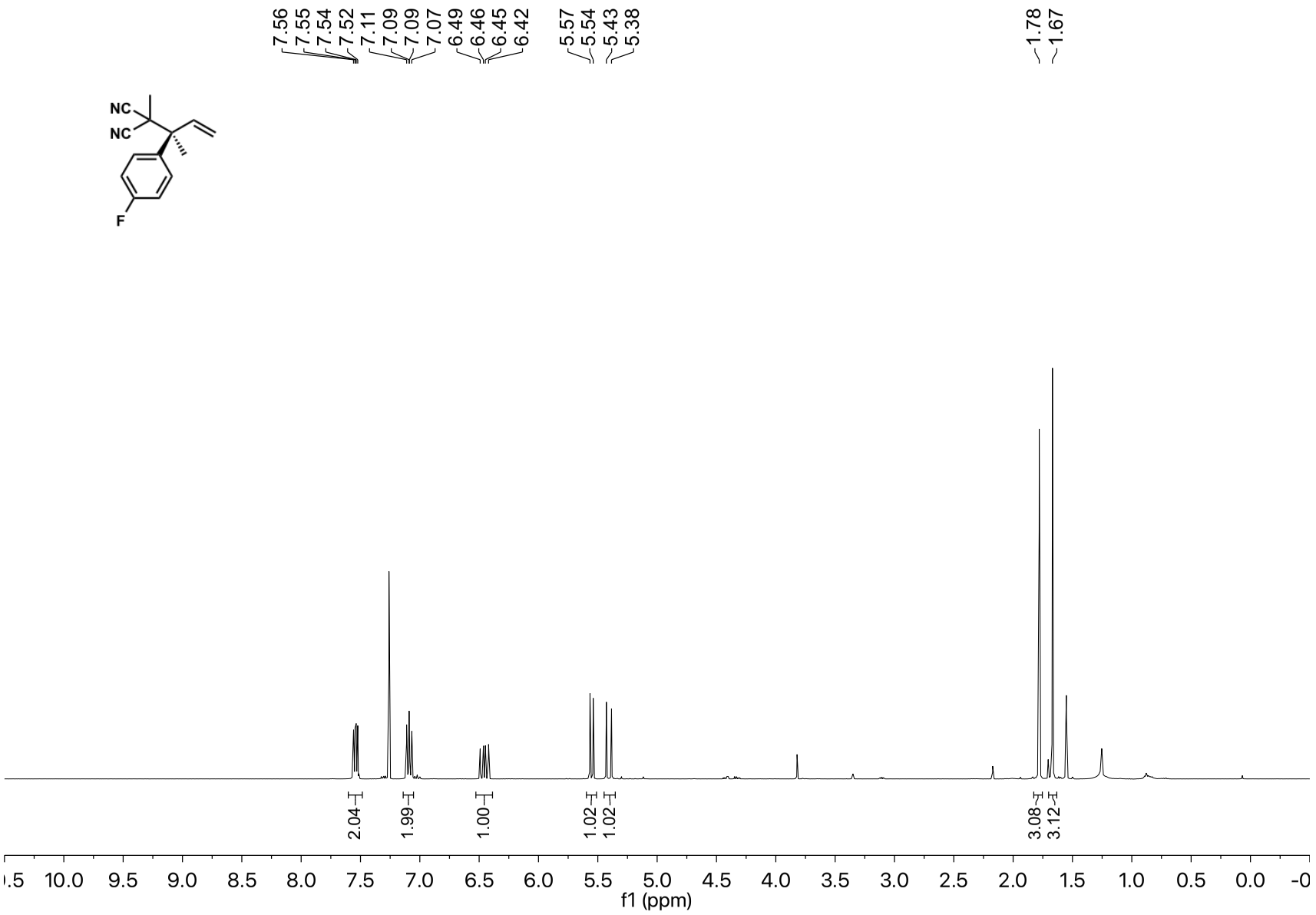

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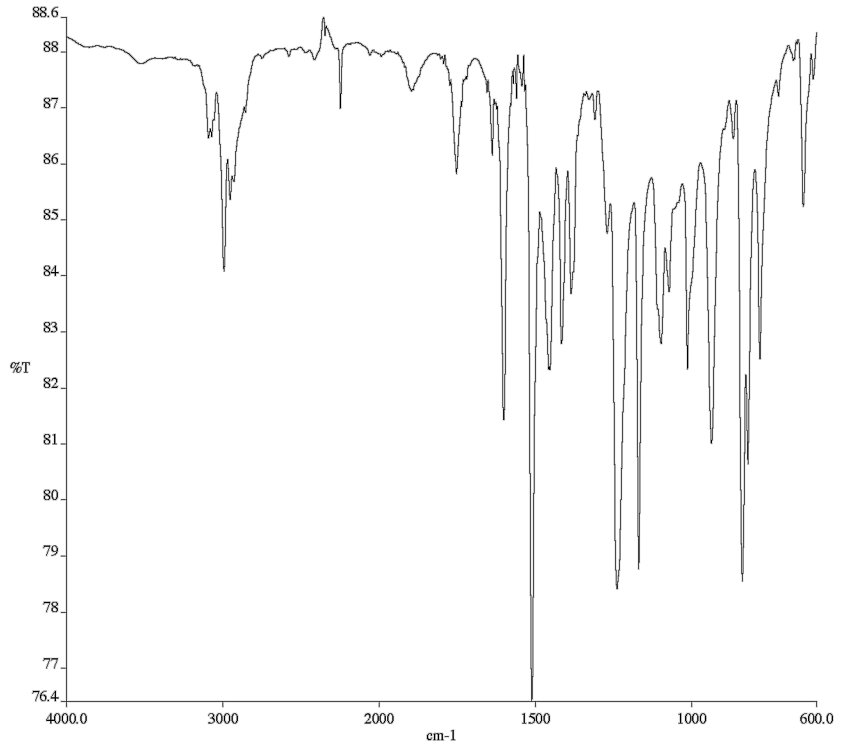
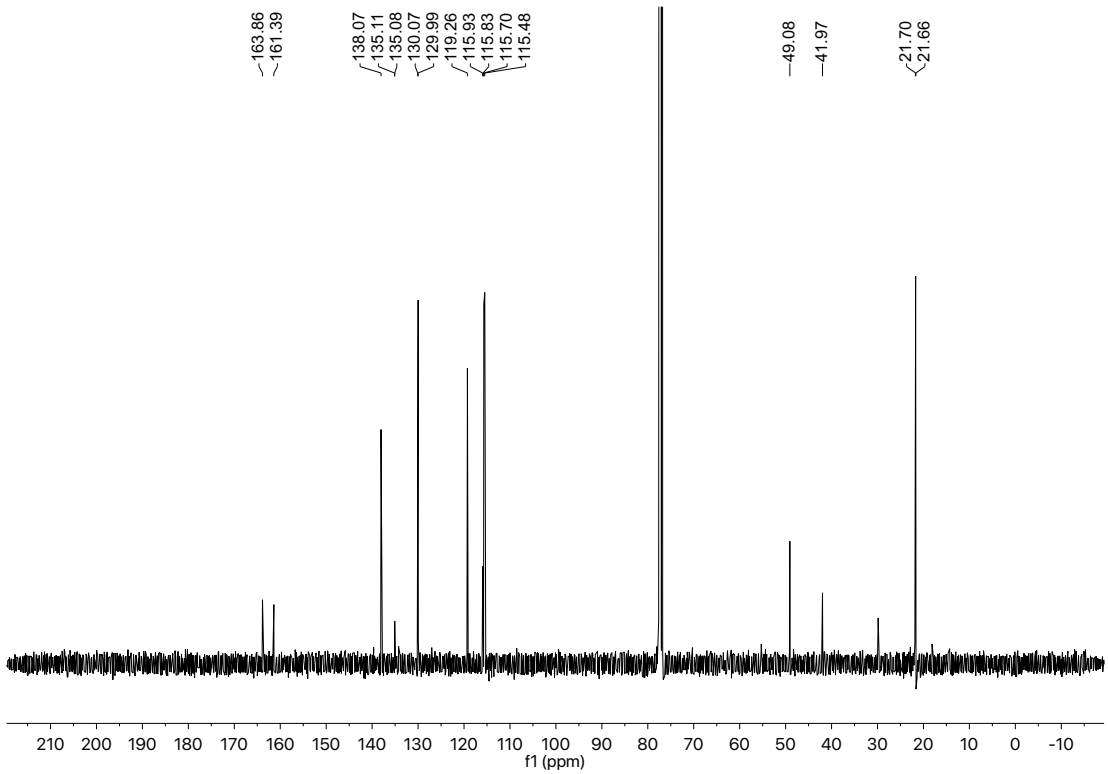


Infrared spectrum (Thin Film, NaCl) of compound **7d**.



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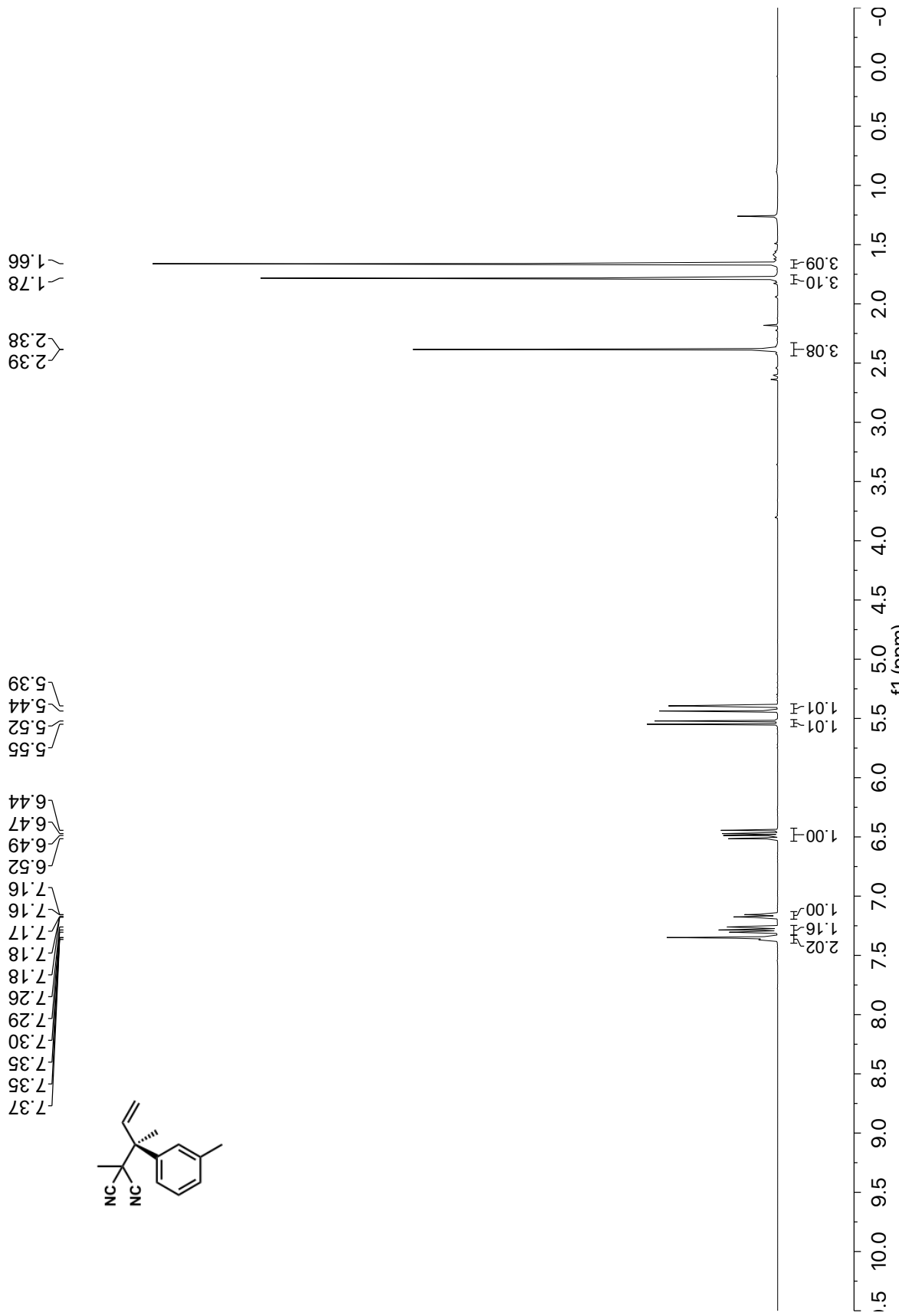

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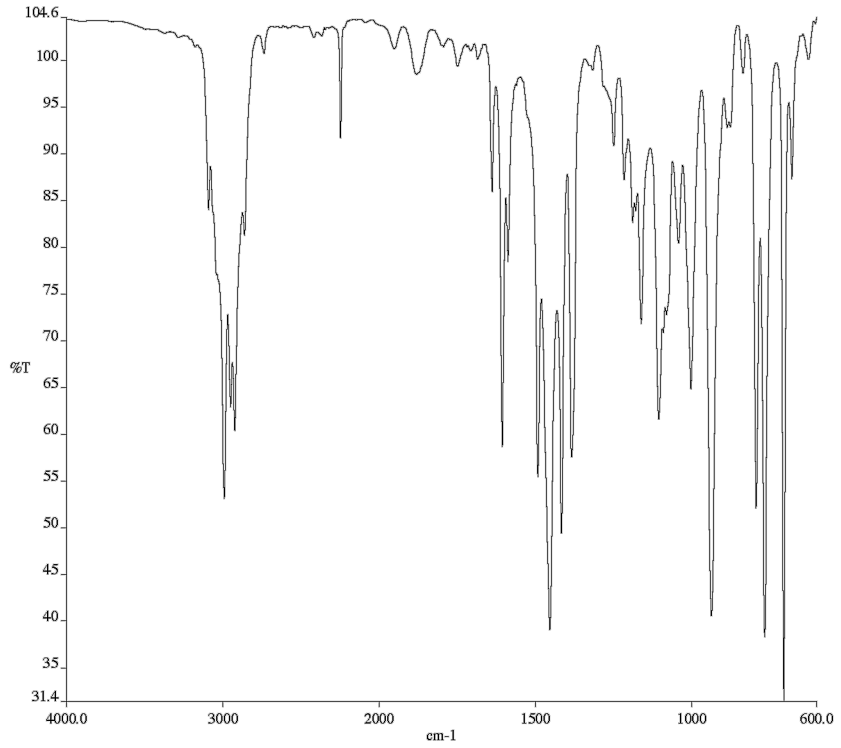

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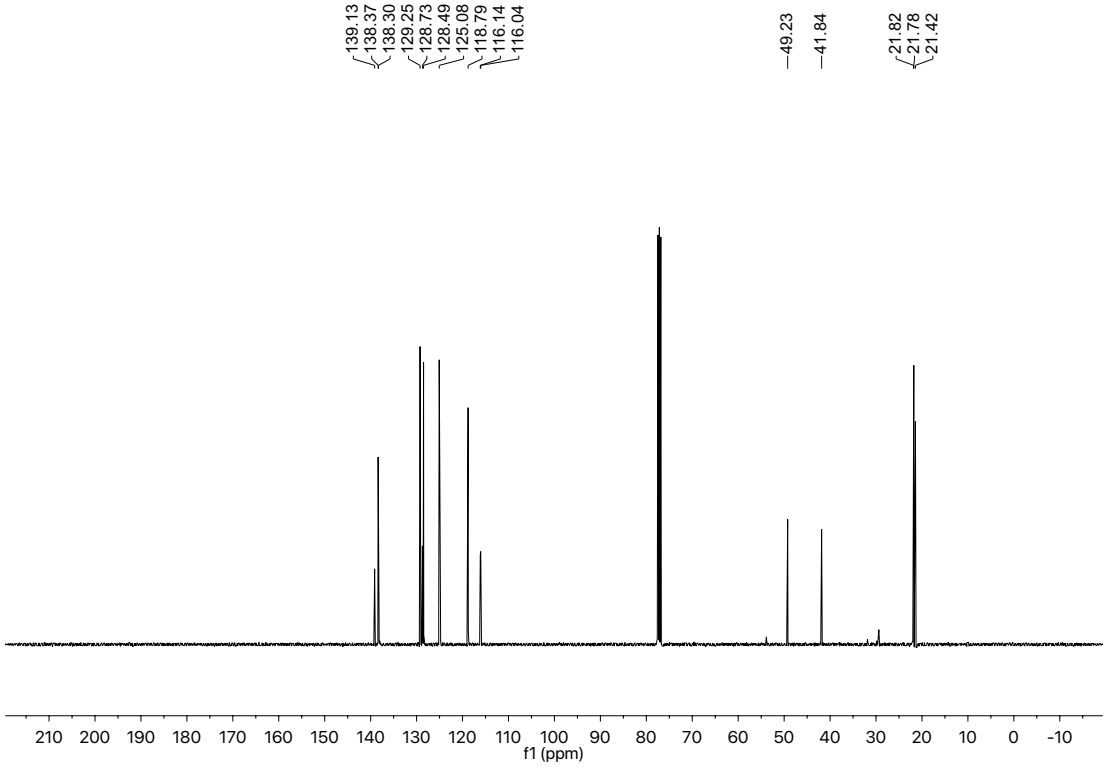

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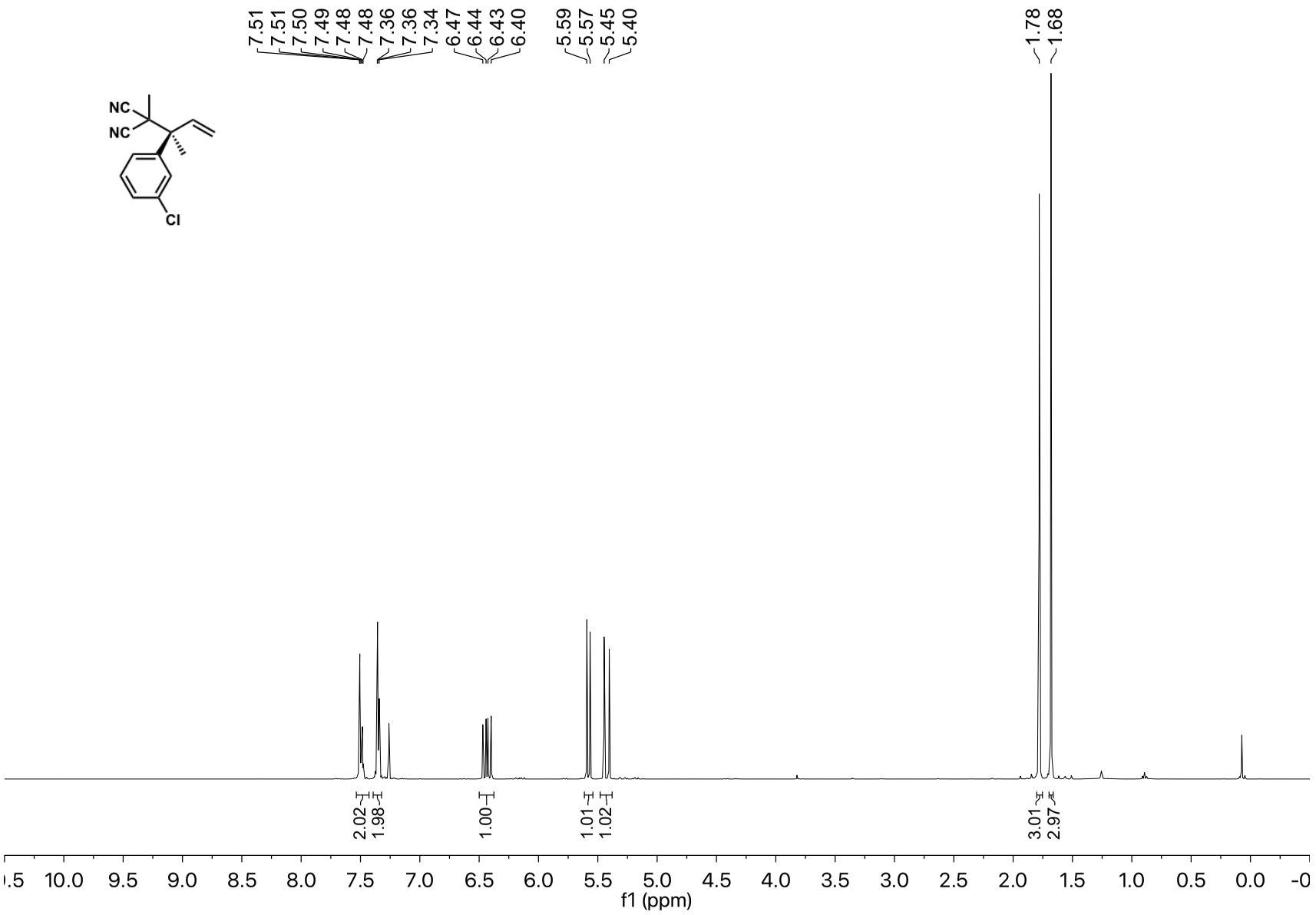
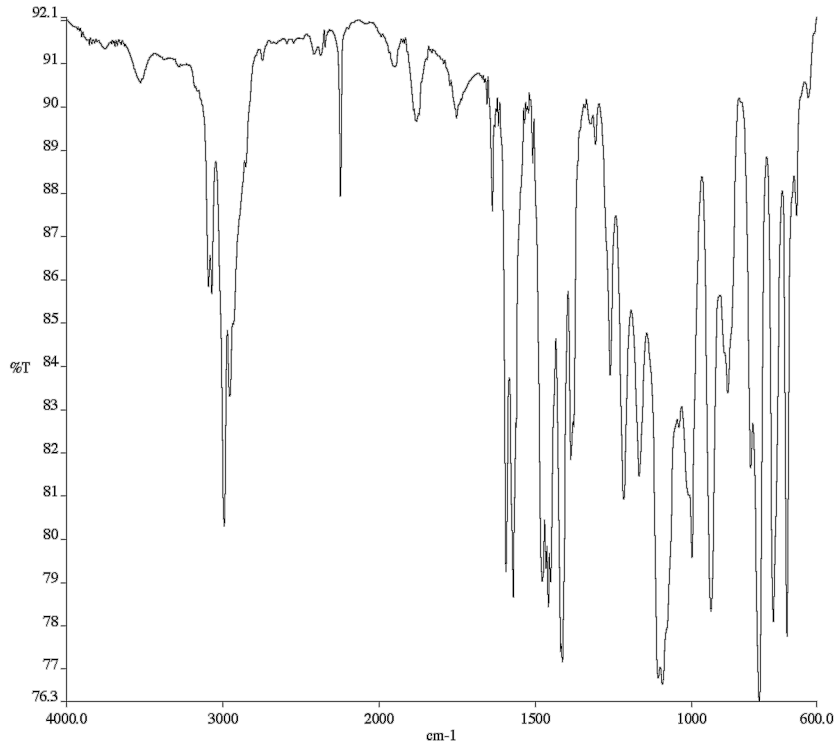
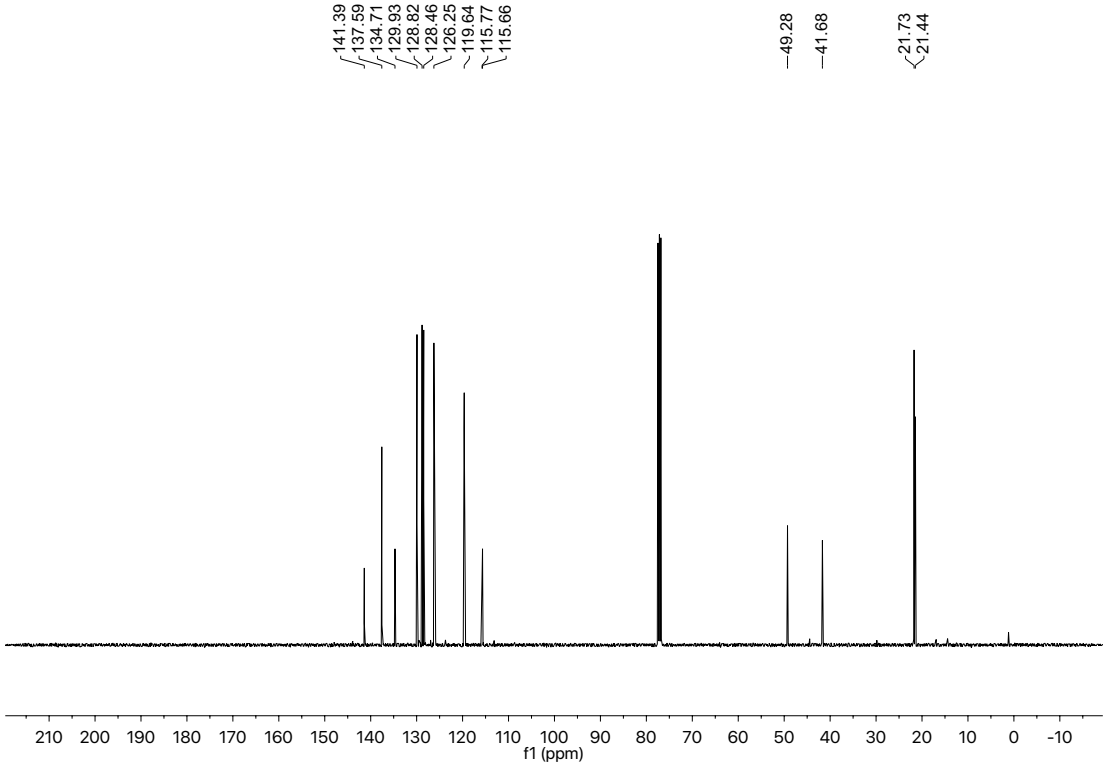


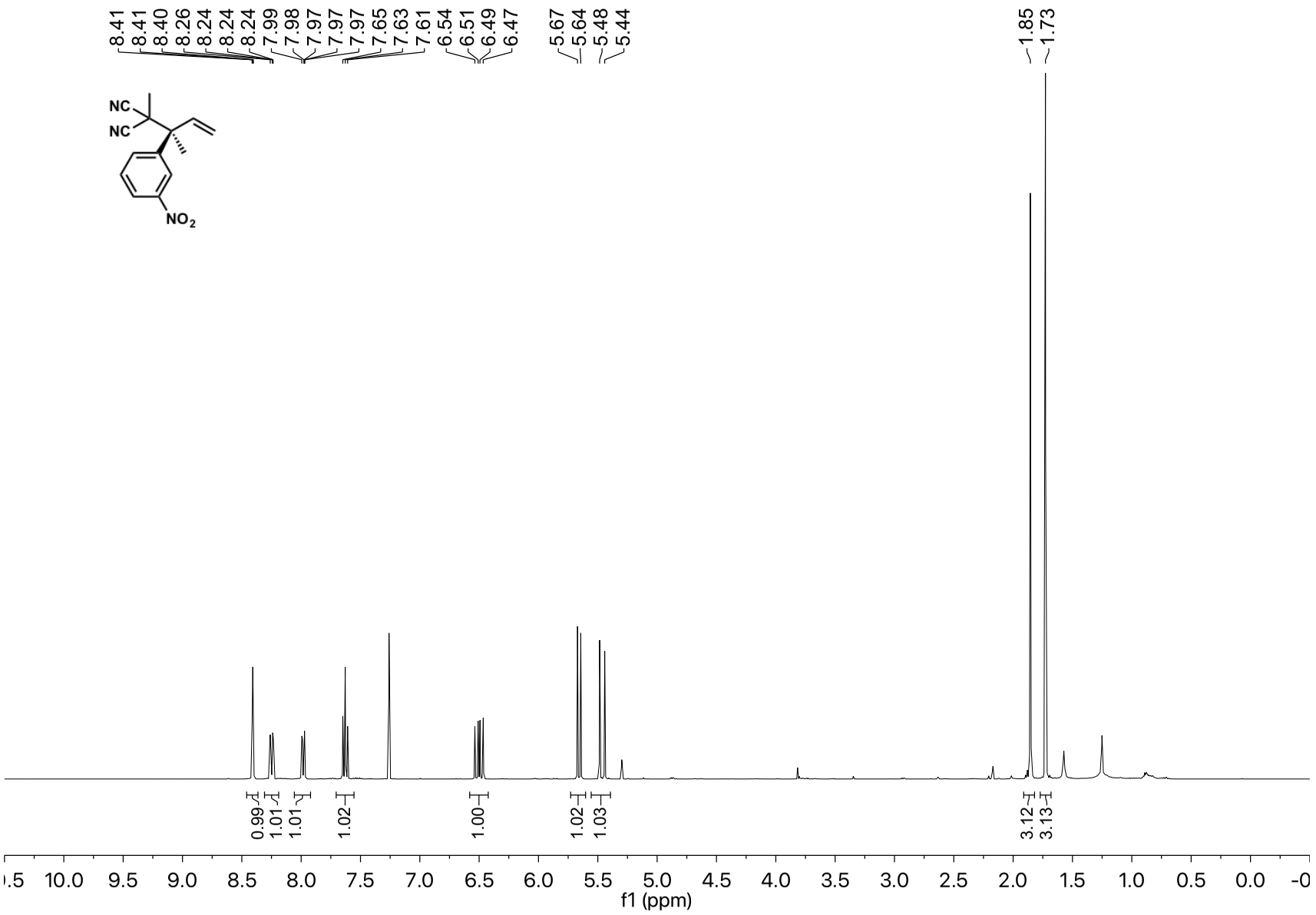
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7f.**



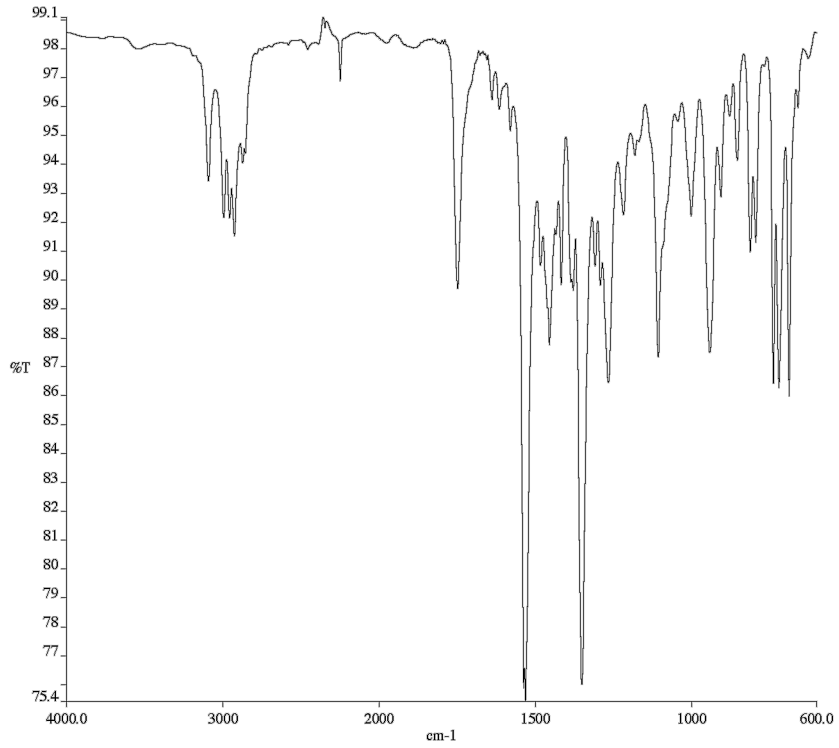
Infrared spectrum (Thin Film, NaCl) of compound **7f**.



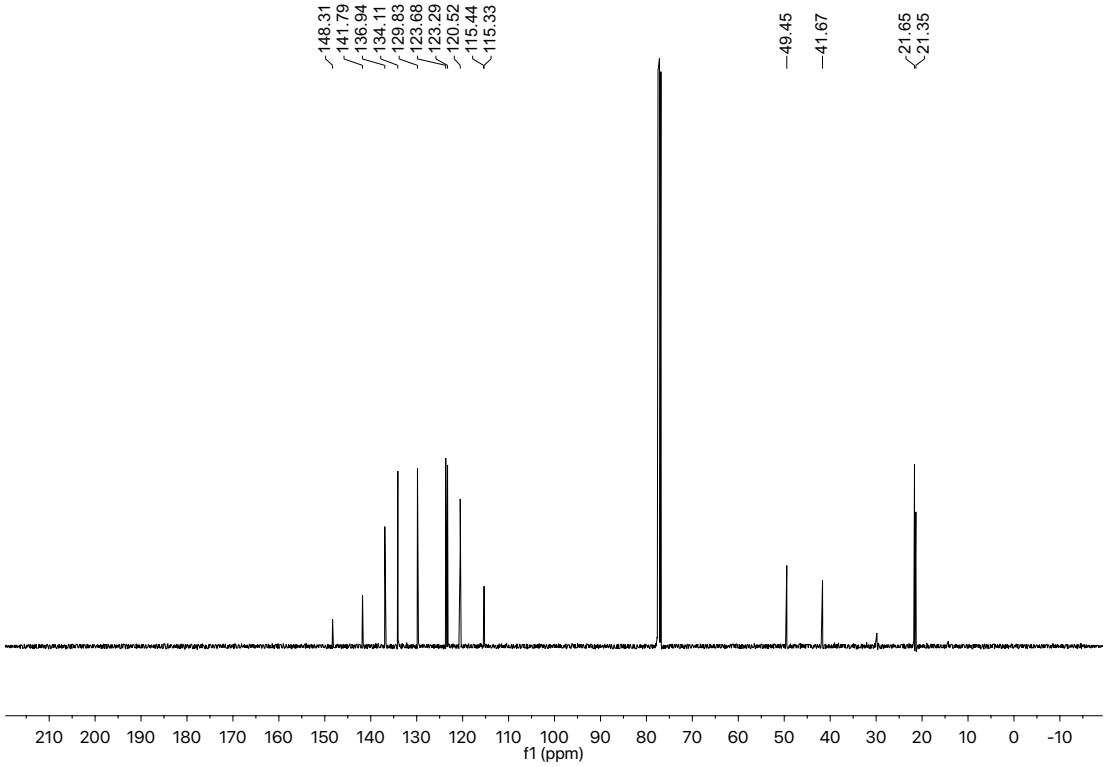
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7f**.



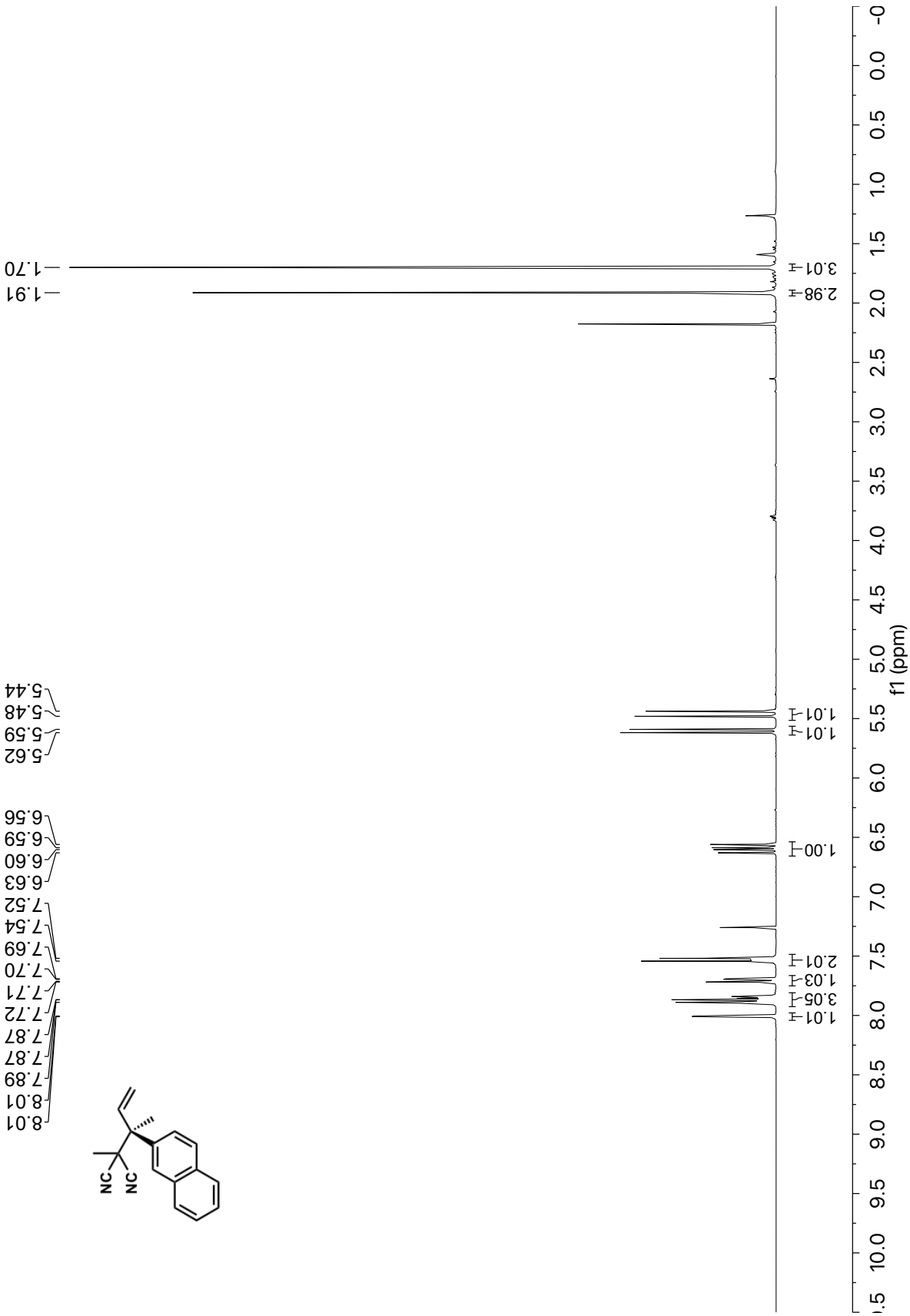
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7g.**



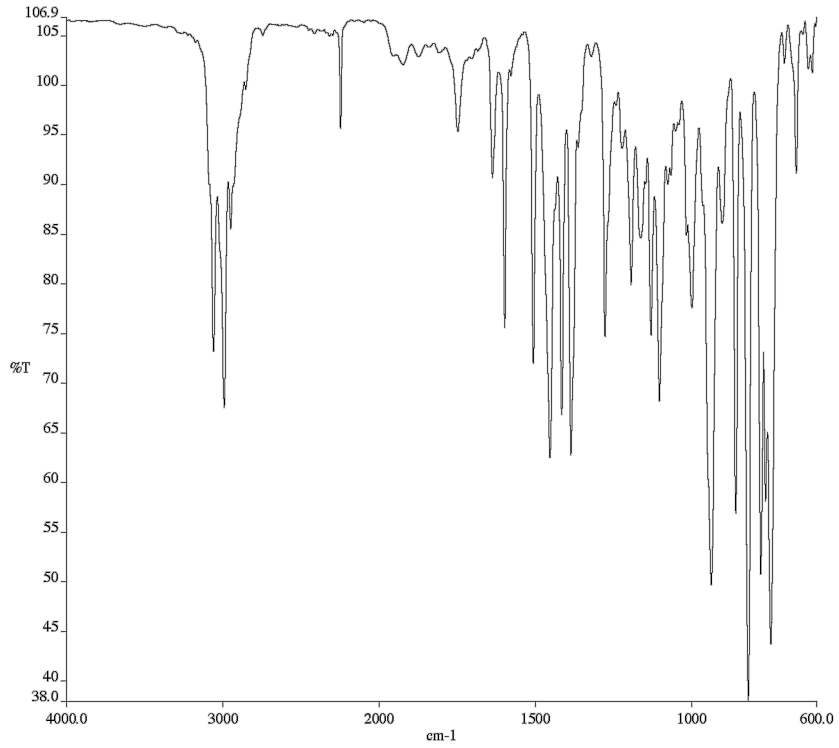
Infrared spectrum (Thin Film, NaCl) of compound **7g**.



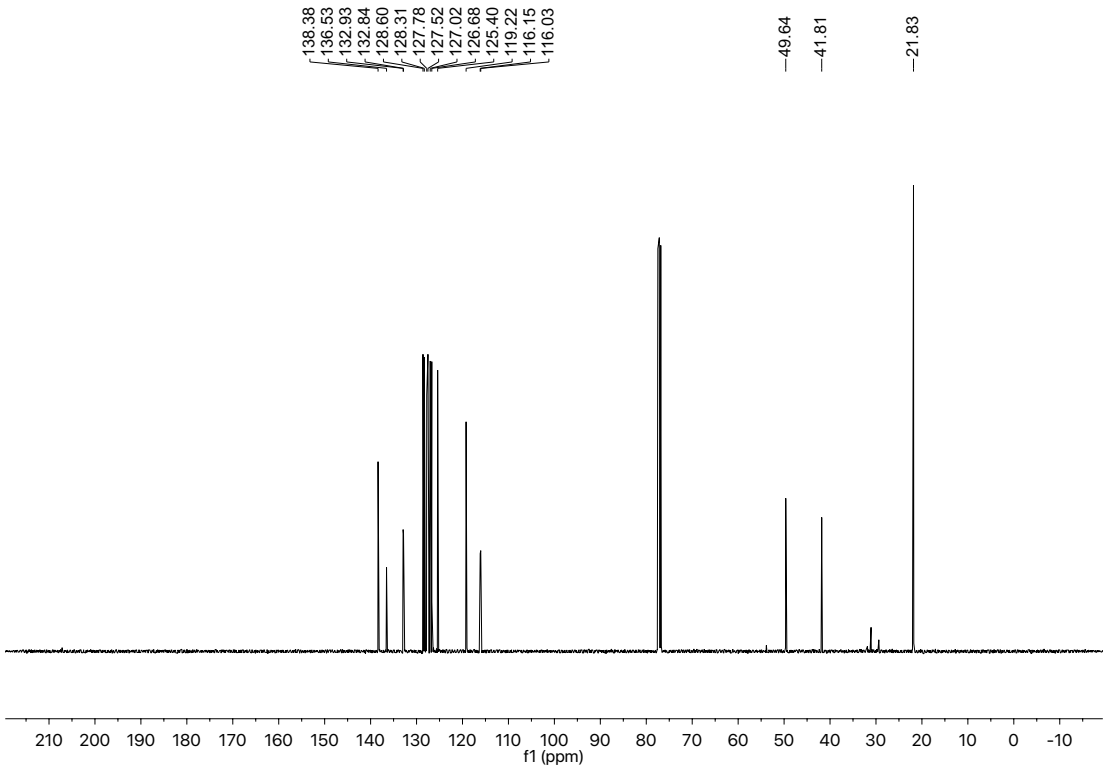
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7g**.



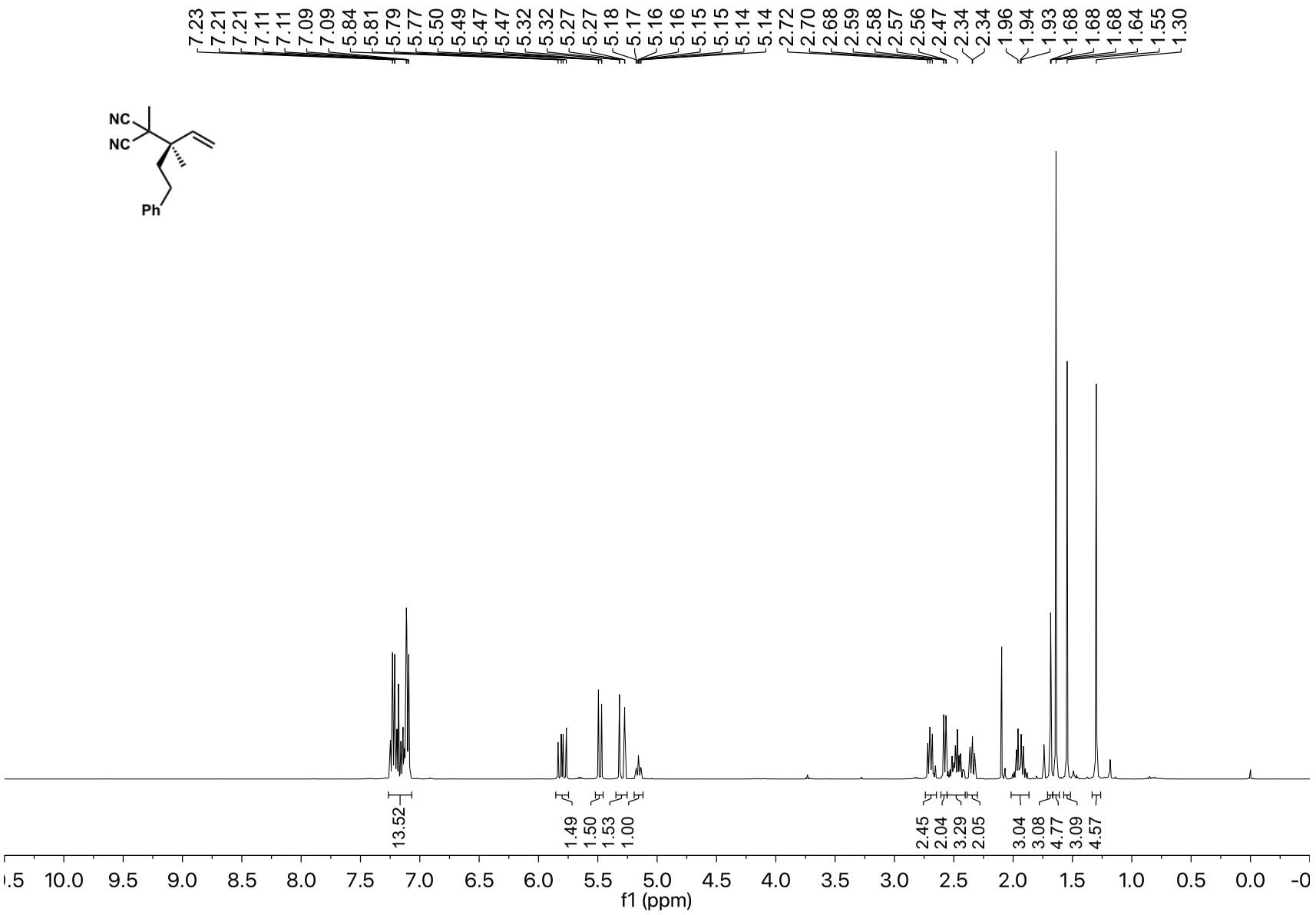
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7h.**



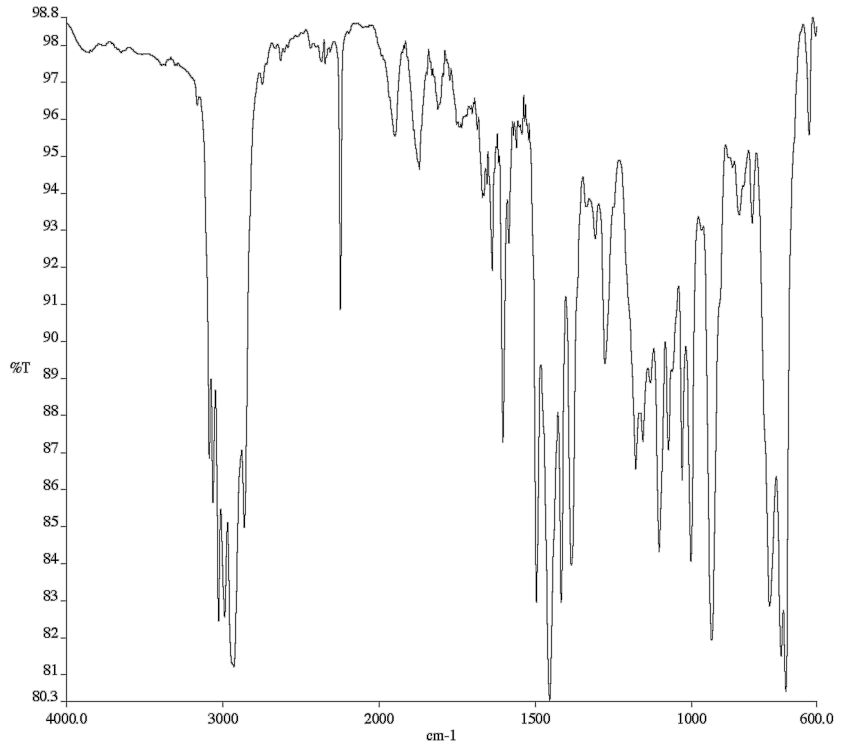
Infrared spectrum (Thin Film, NaCl) of compound **7h**.



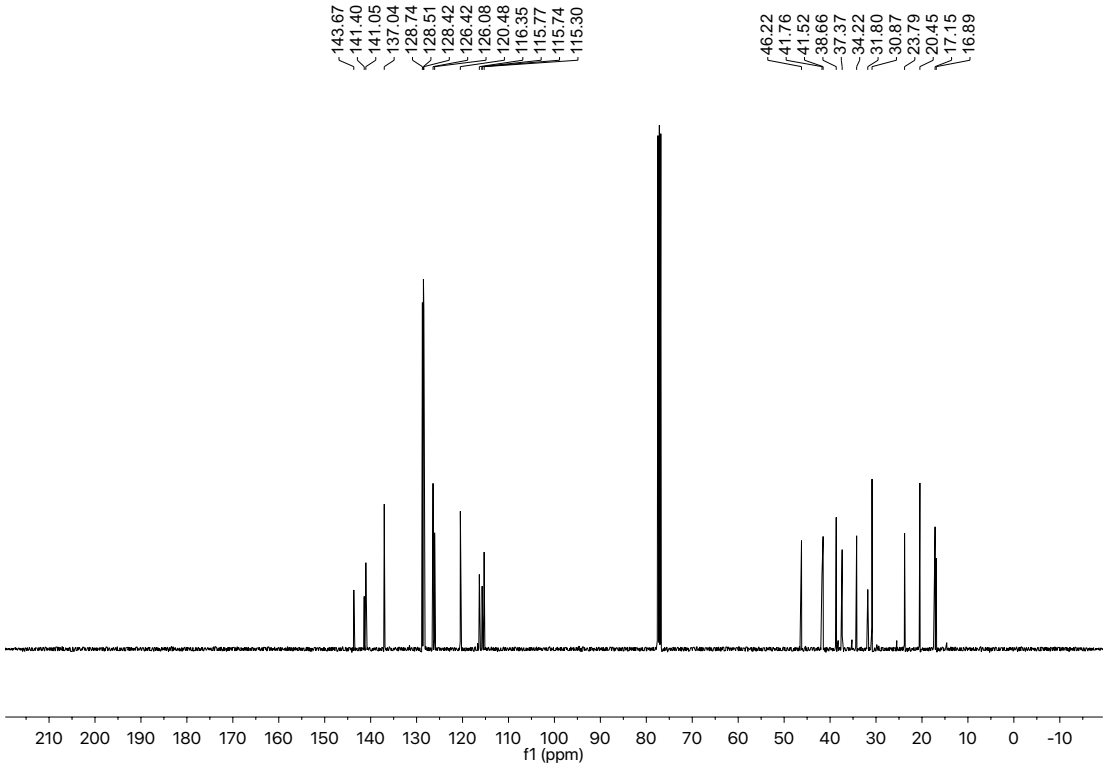
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7h**.



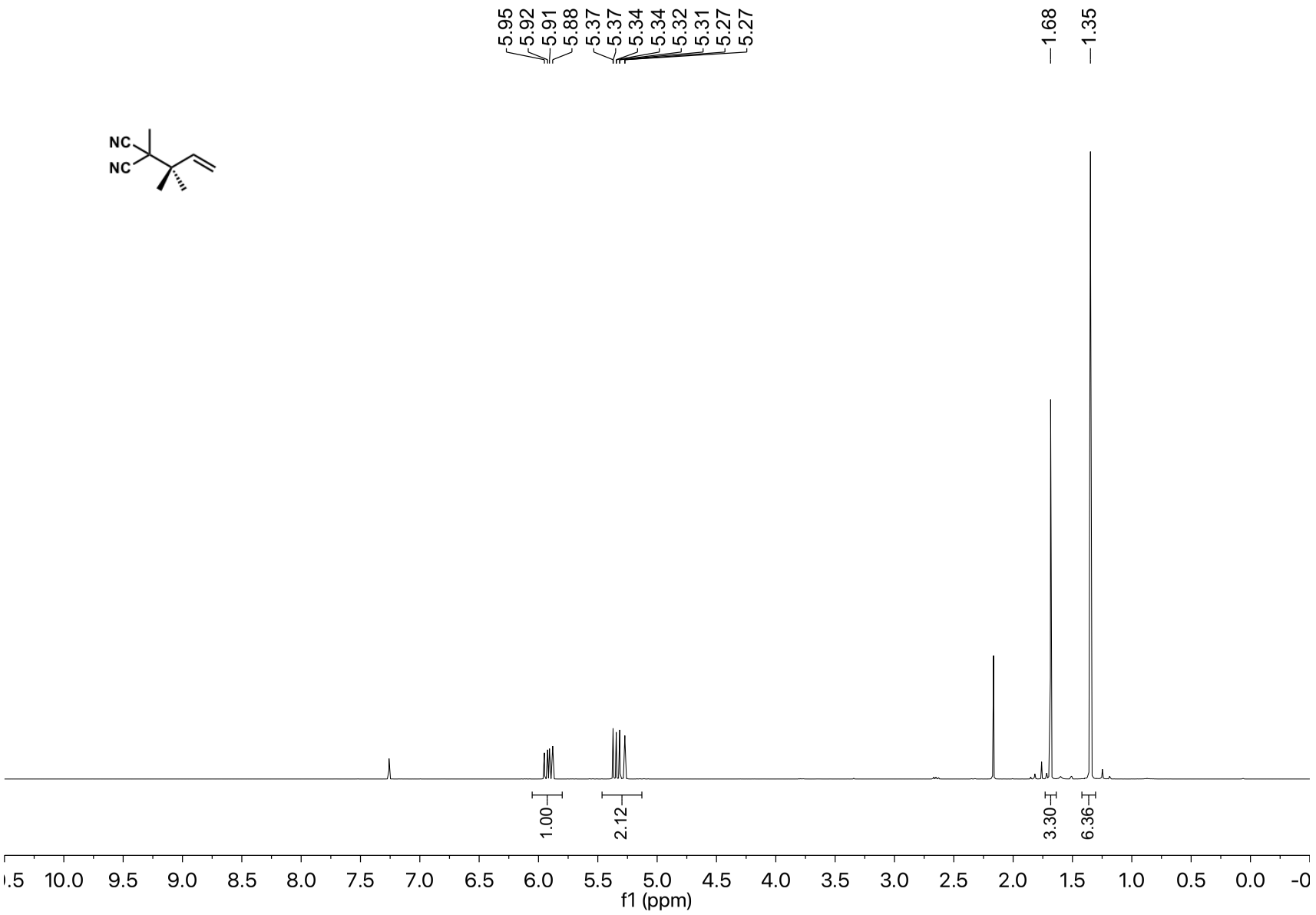
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7j.**



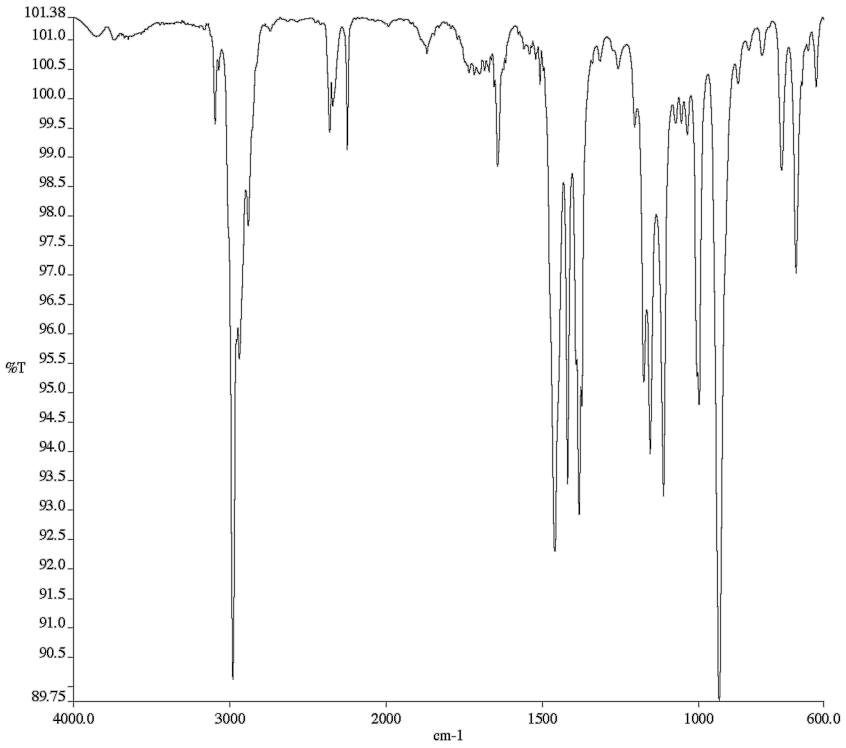
Infrared spectrum (Thin Film, NaCl) of compound **7j**.



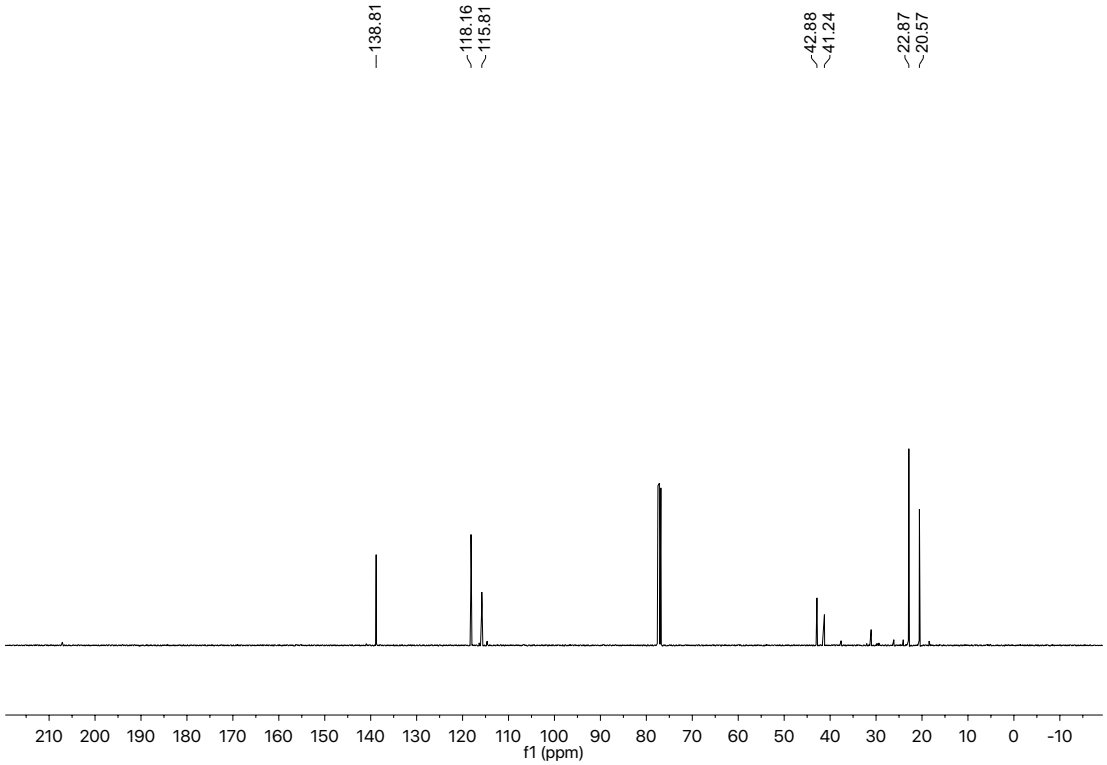
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7j**.



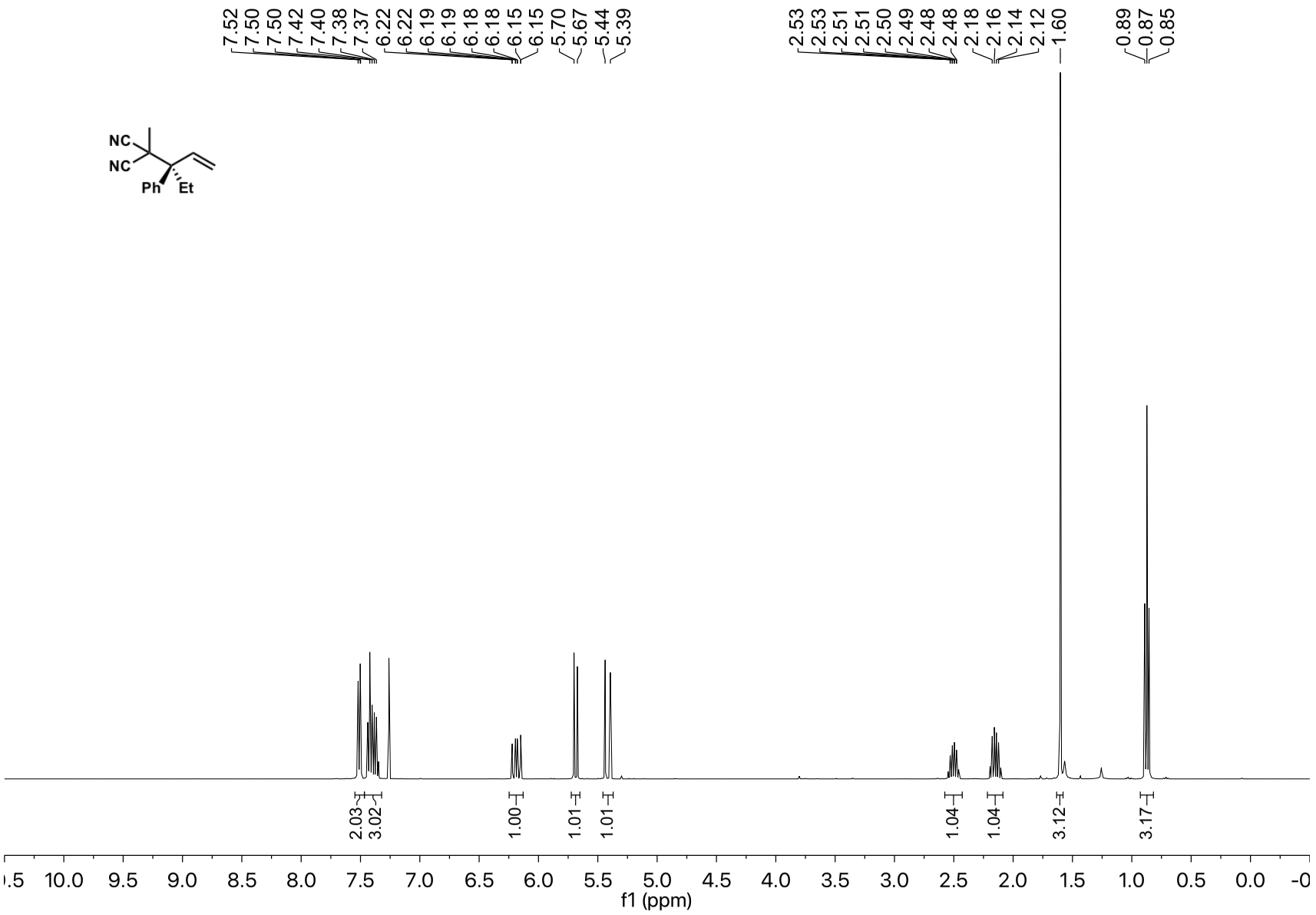
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7k.**



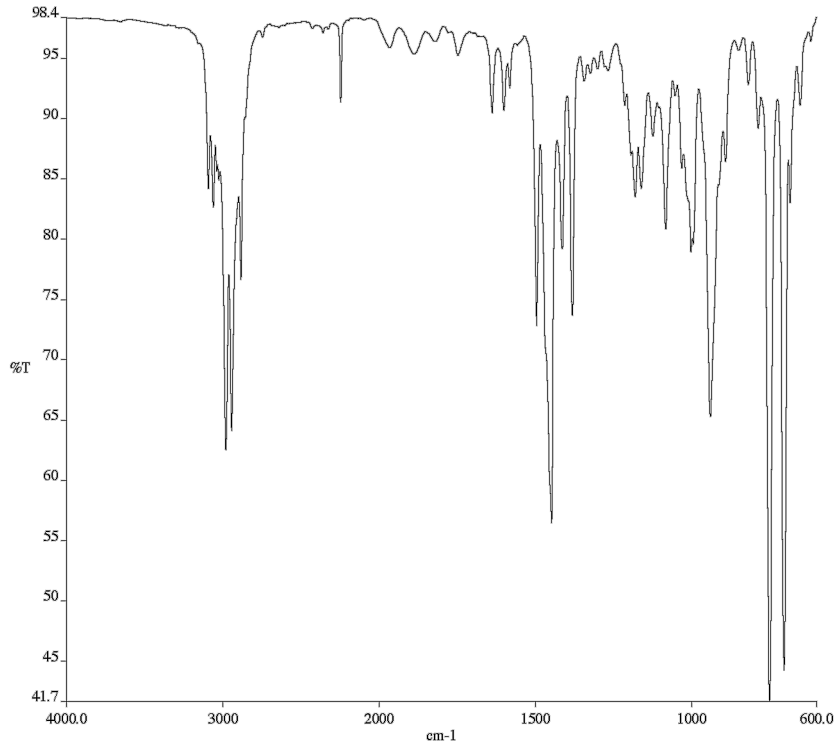
Infrared spectrum (Thin Film, NaCl) of compound **7k**.



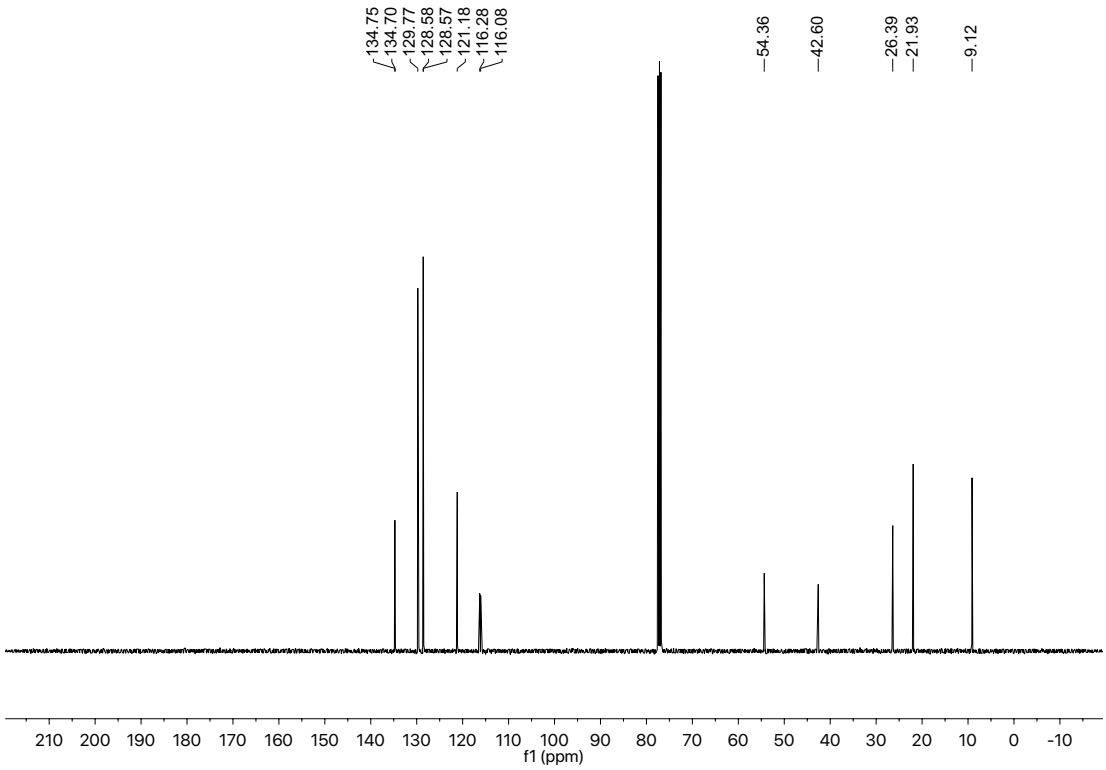
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7k**.



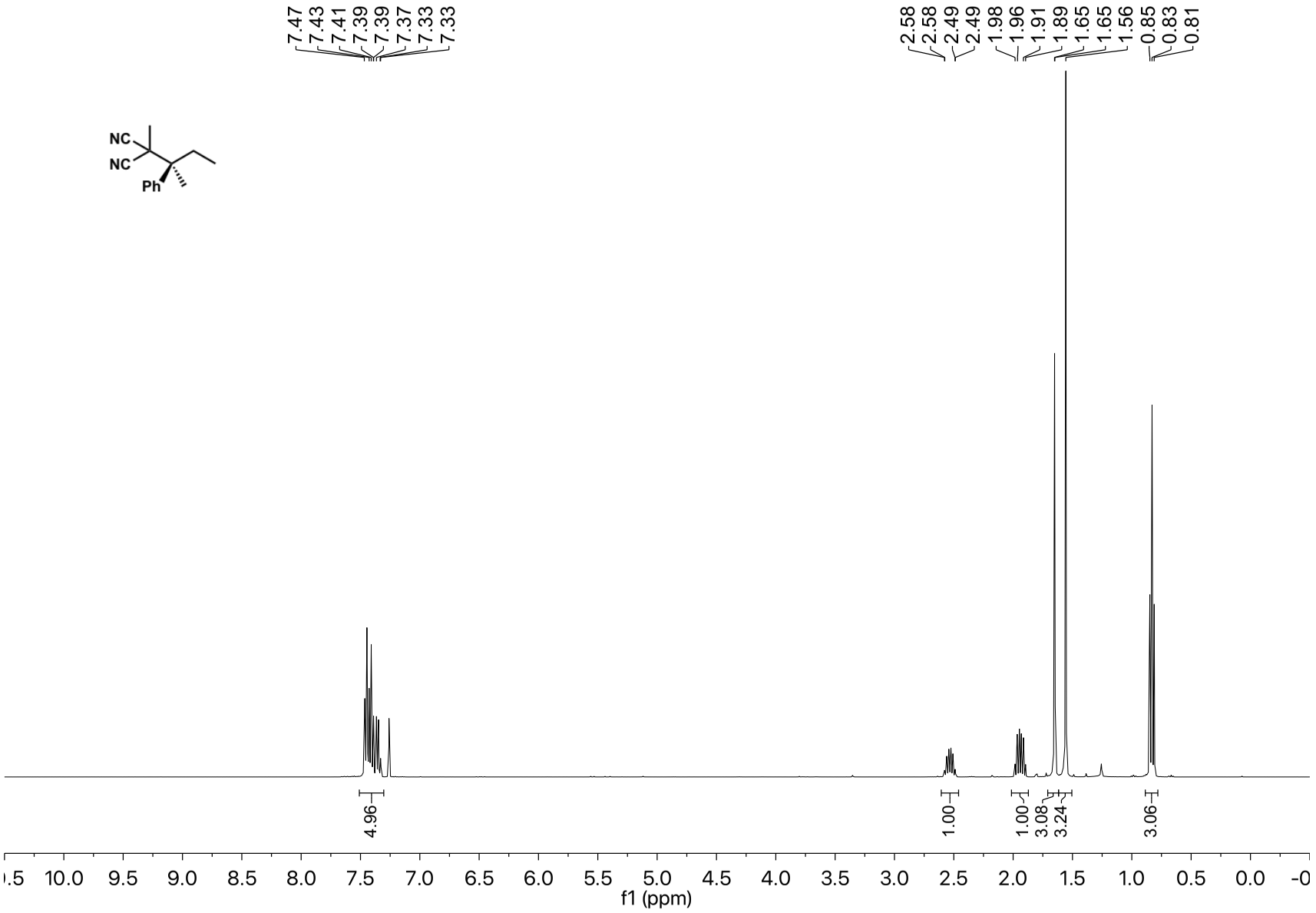
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7l.**



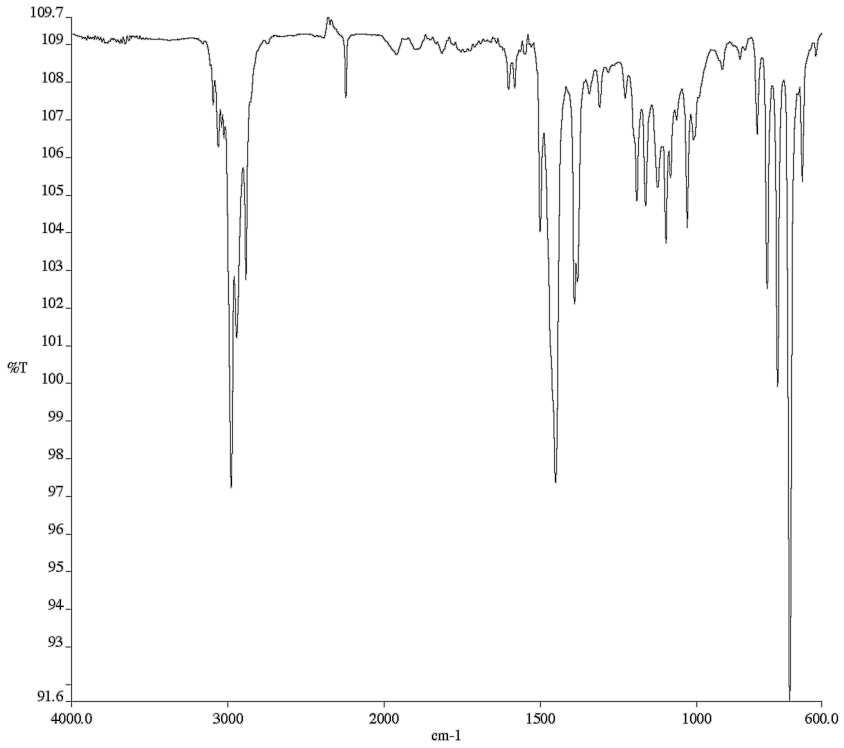
Infrared spectrum (Thin Film, NaCl) of compound **7l**.



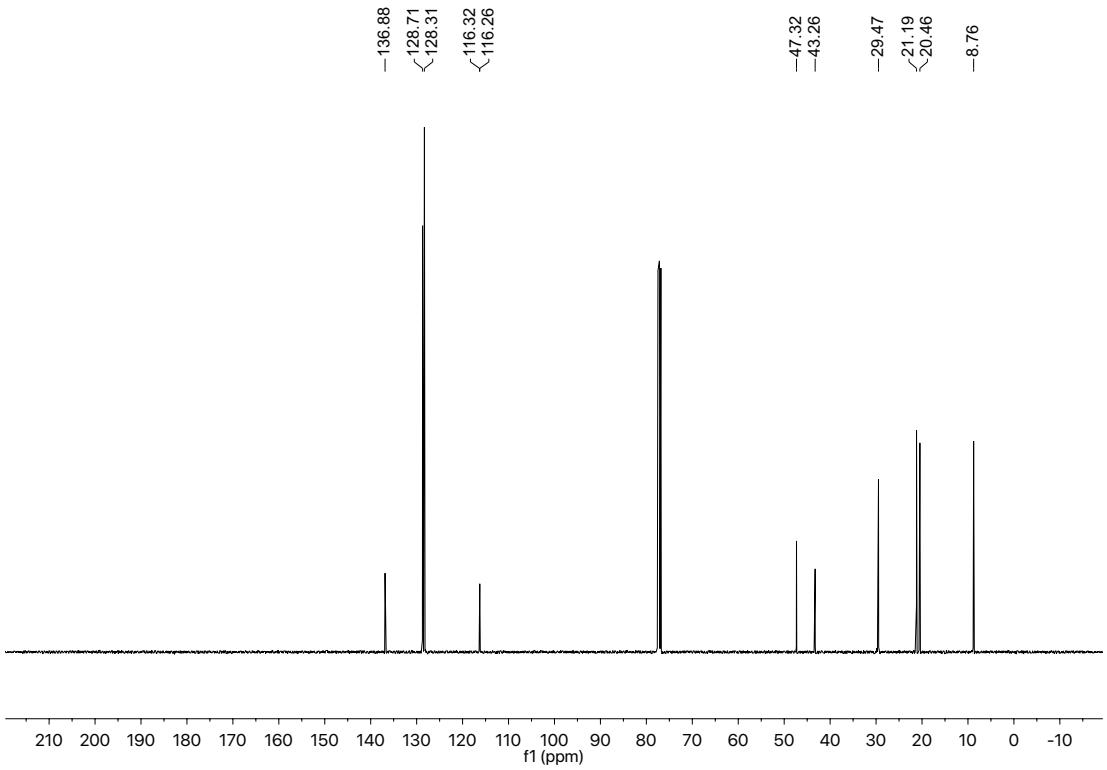
^{13}C NMR (101 MHz, $CDCl_3$) of compound **7l**.



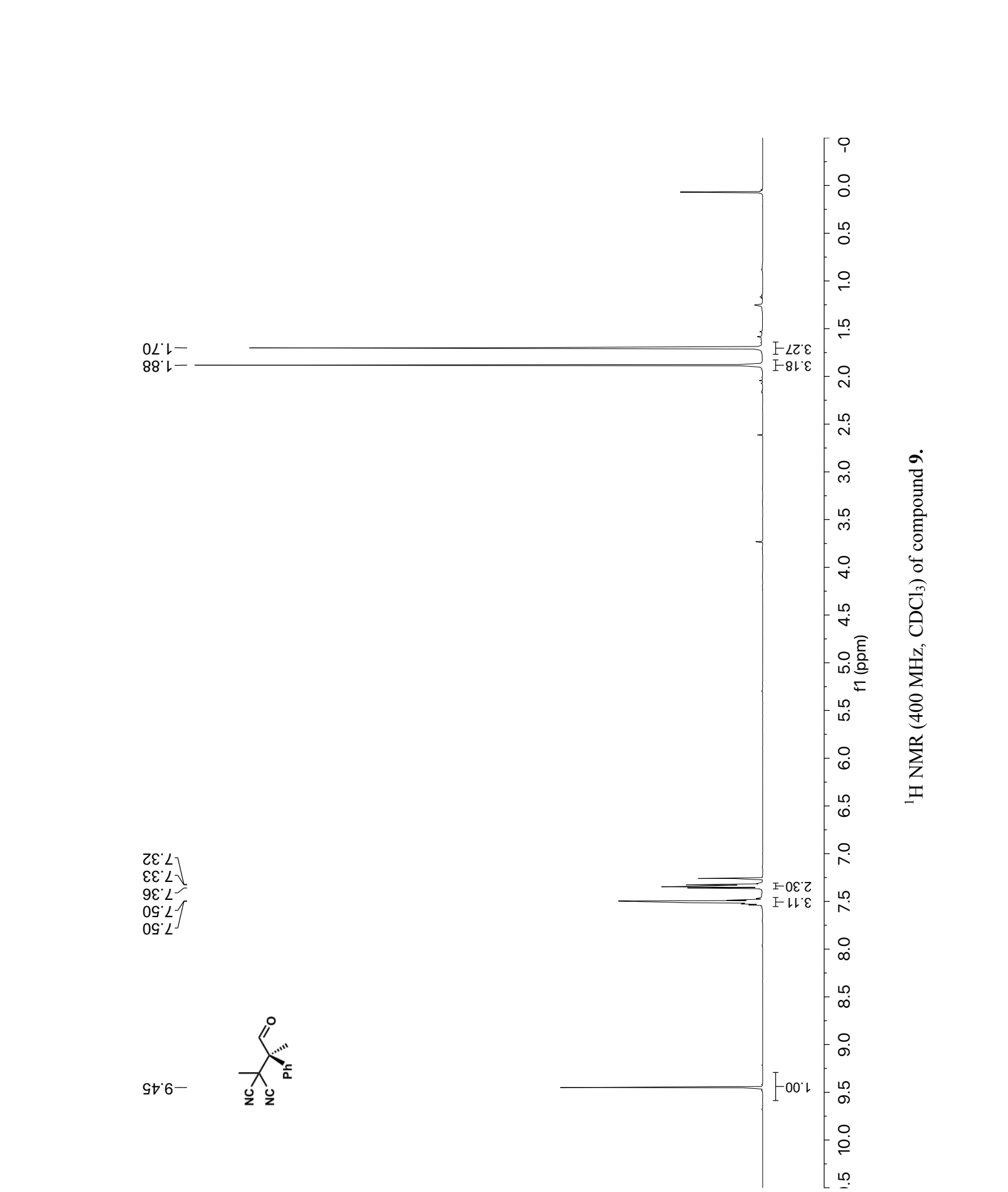
^{1}H NMR (400 MHz, $CDCl_3$) of compound **8.**



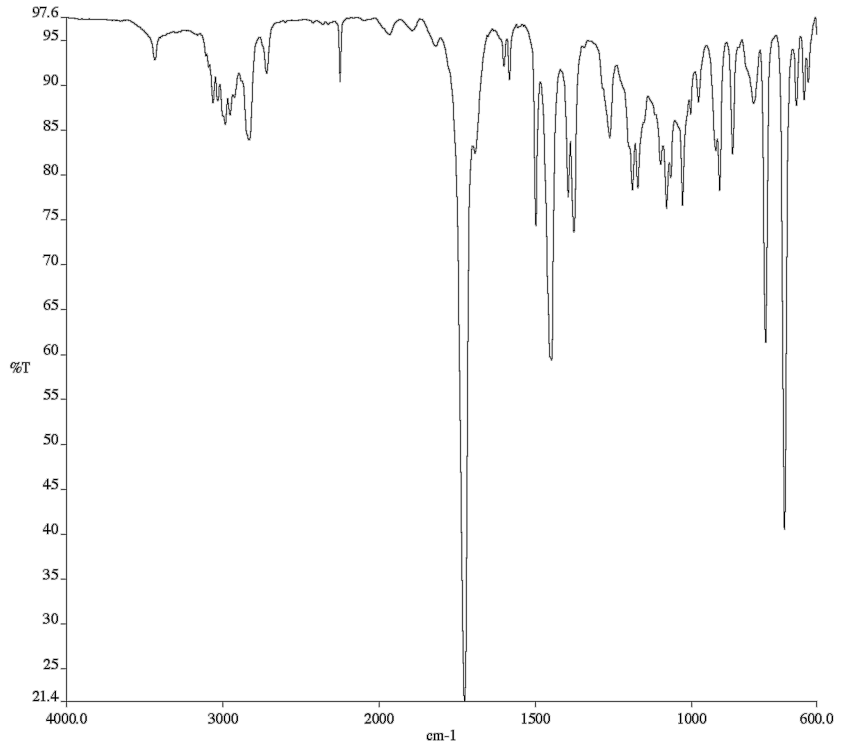
Infrared spectrum (Thin Film, NaCl) of compound **8**.



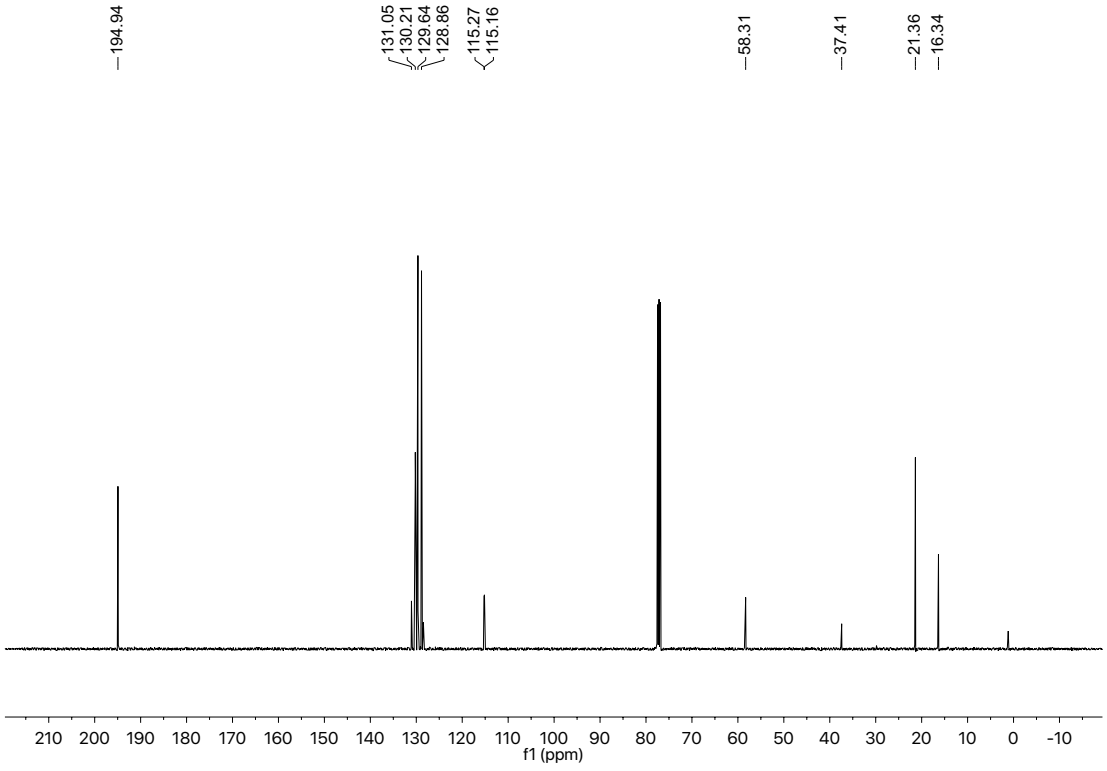
^{13}C NMR (101 MHz, $CDCl_3$) of compound **8**.



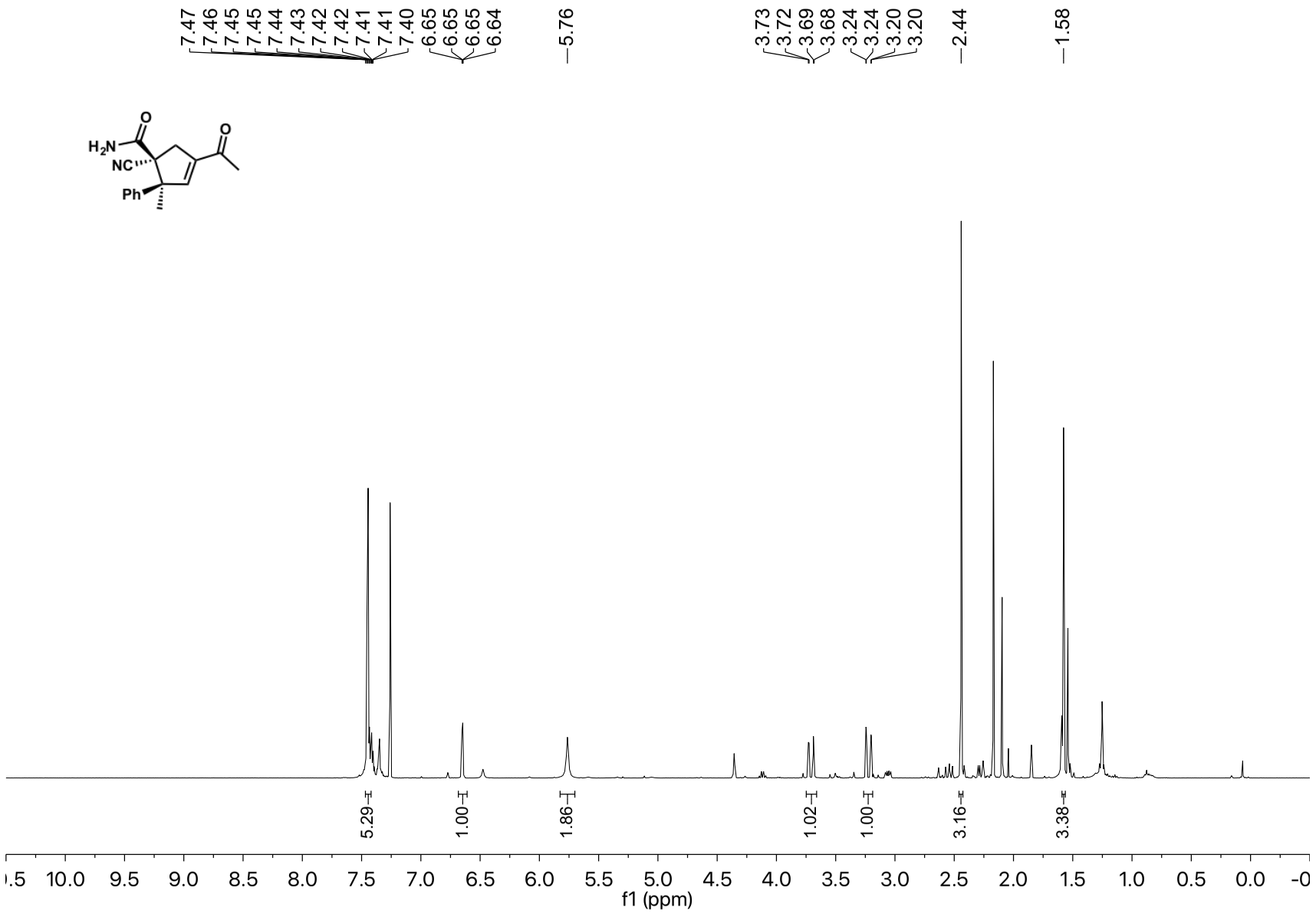
^{1}H NMR (400 MHz, $CDCl_3$) of compound **9.**



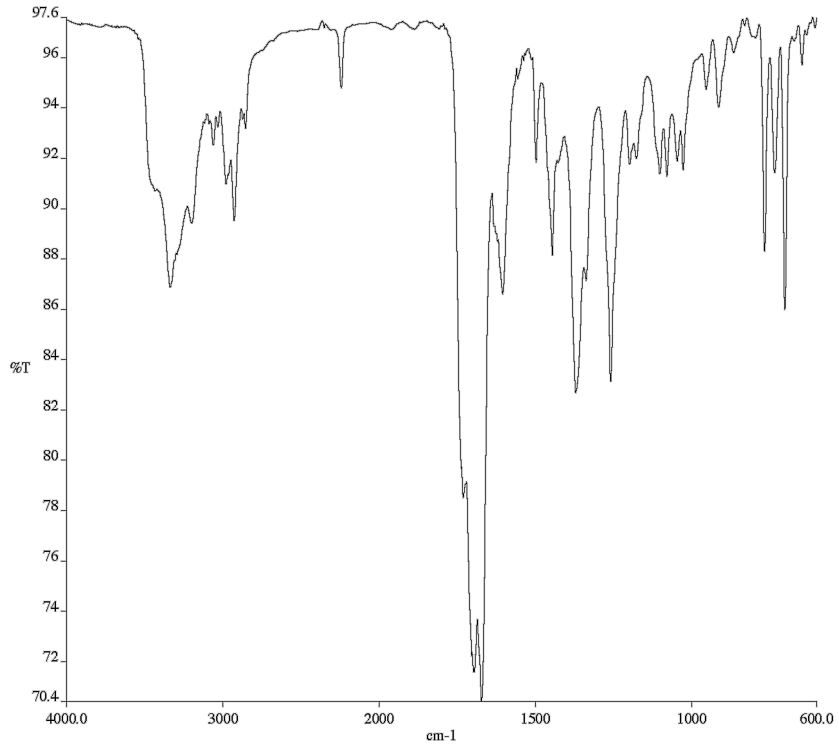
Infrared spectrum (Thin Film, NaCl) of compound **9**.



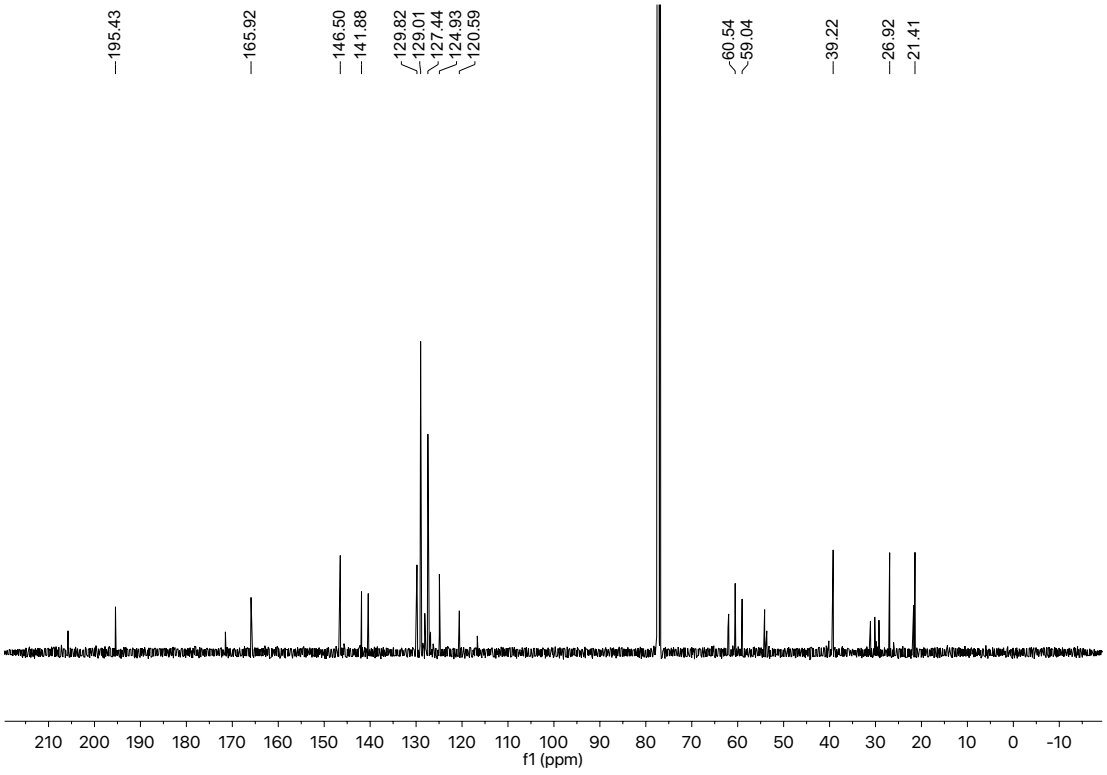
^{13}C NMR (101 MHz, $CDCl_3$) of compound **9**.



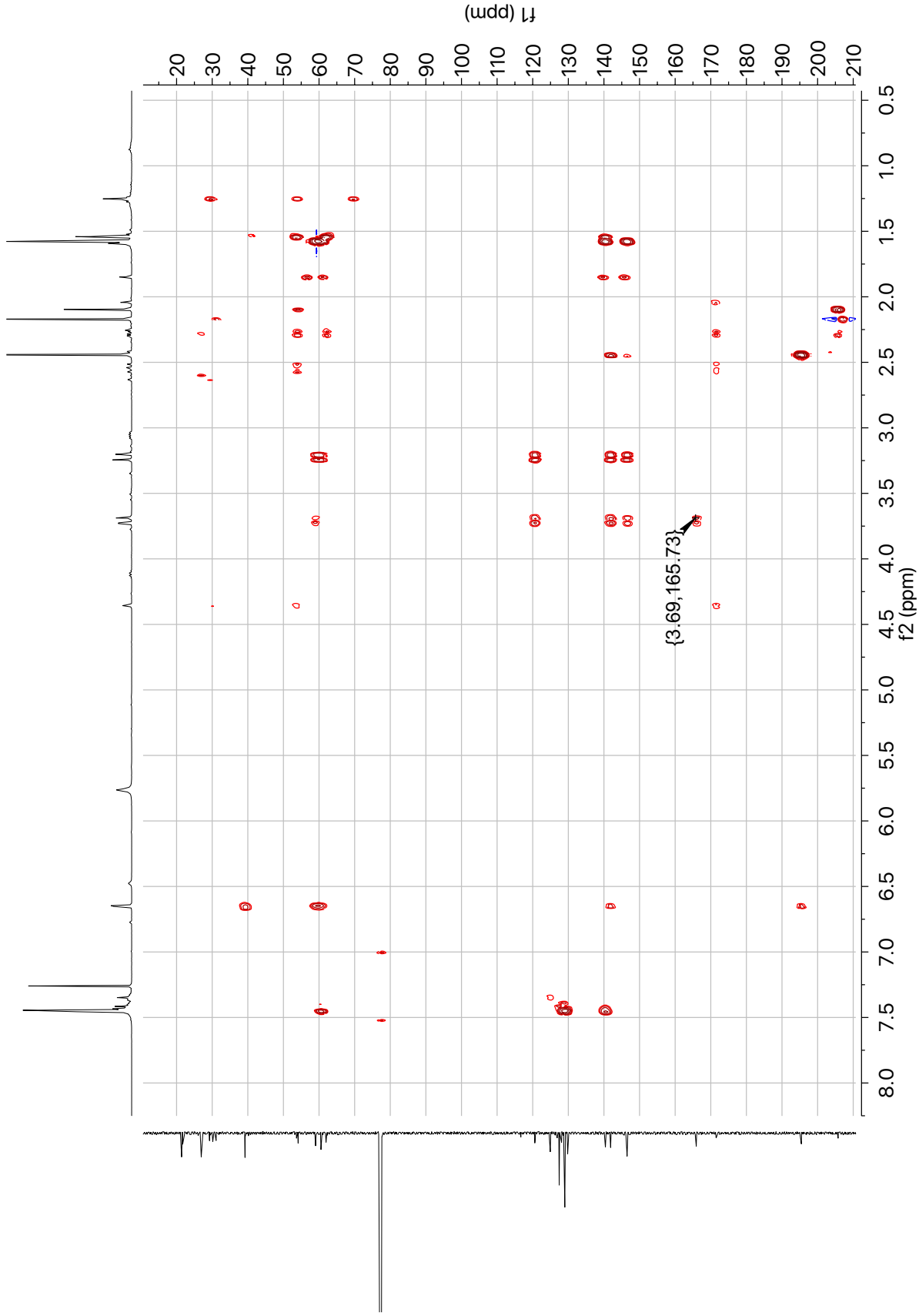
^{1}H NMR (400 MHz, $CDCl_3$) of compound **10.**



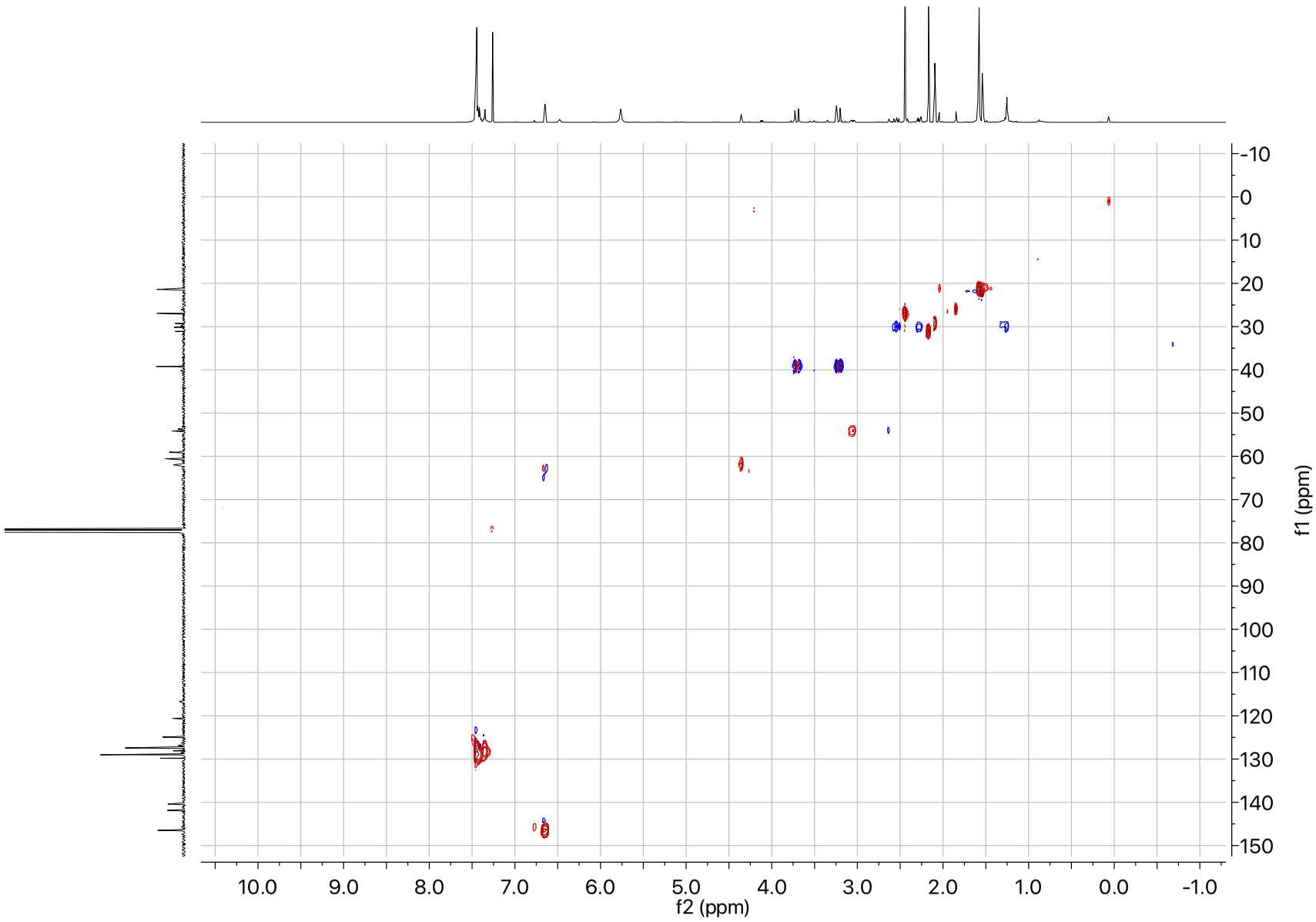
Infrared spectrum (Thin Film, NaCl) of compound **10**.



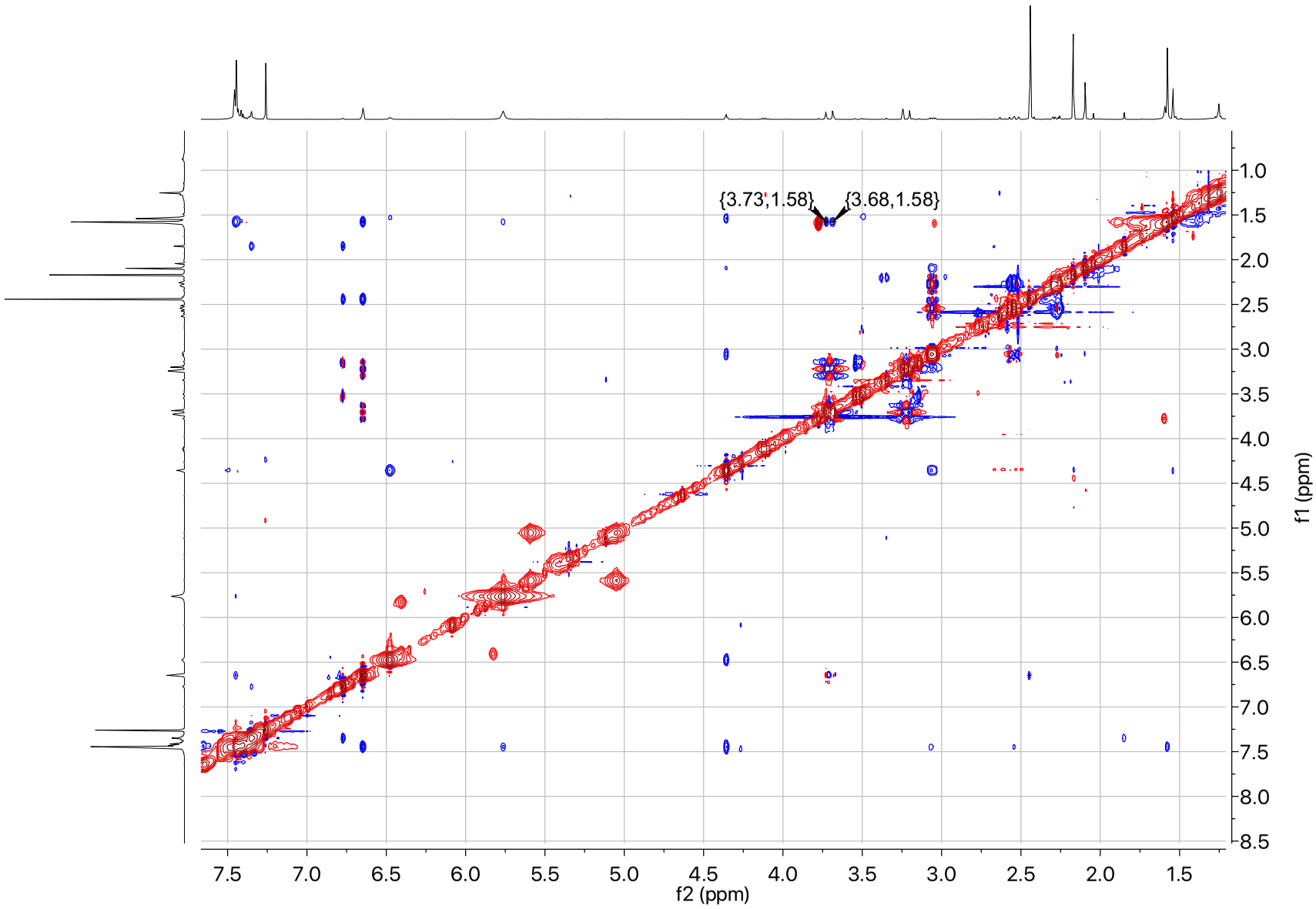
^{13}C NMR (101 MHz, $CDCl_3$) of compound **10**.



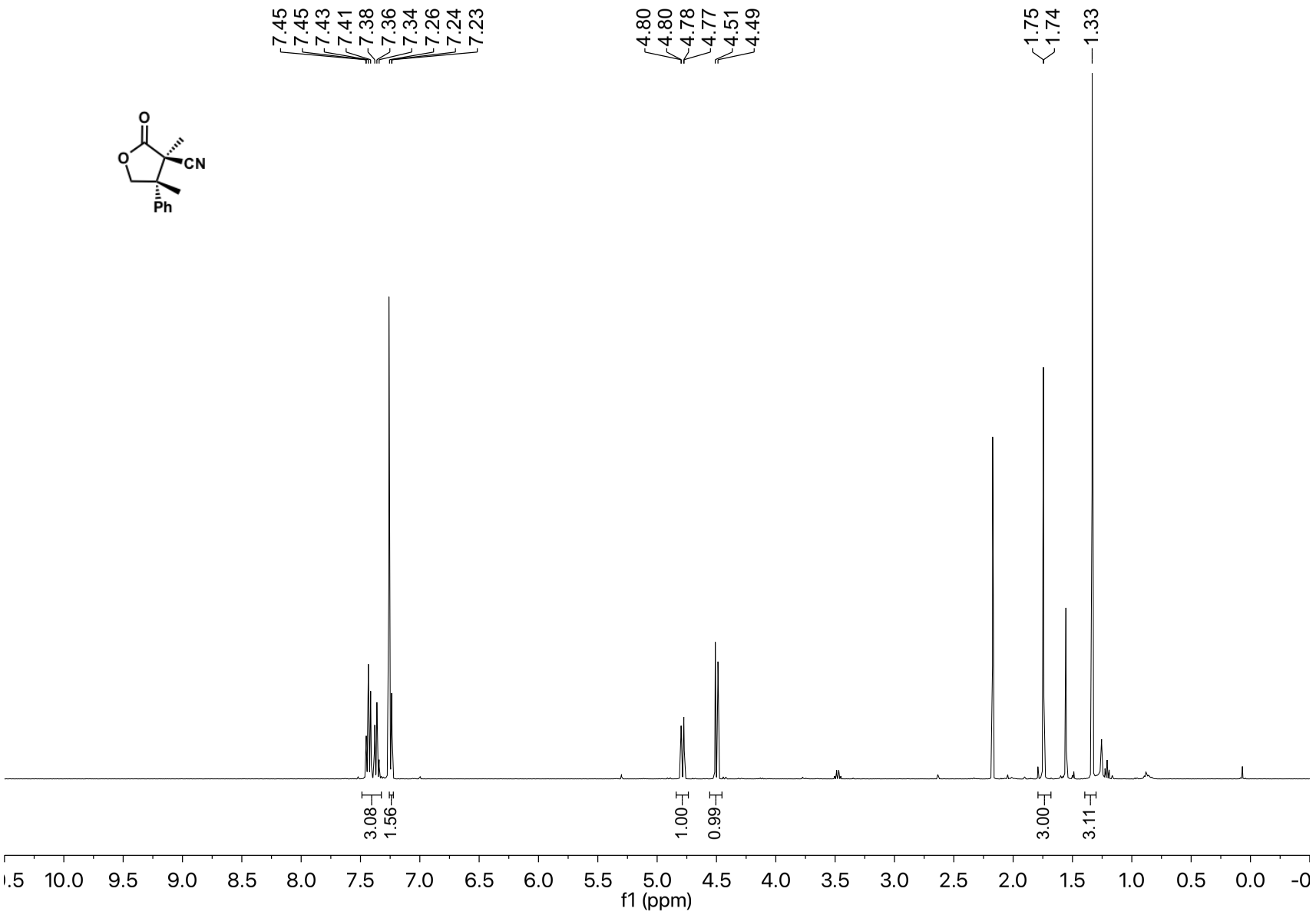
HMBC (400 MHz, $CDCl_3$) of compound **10**.



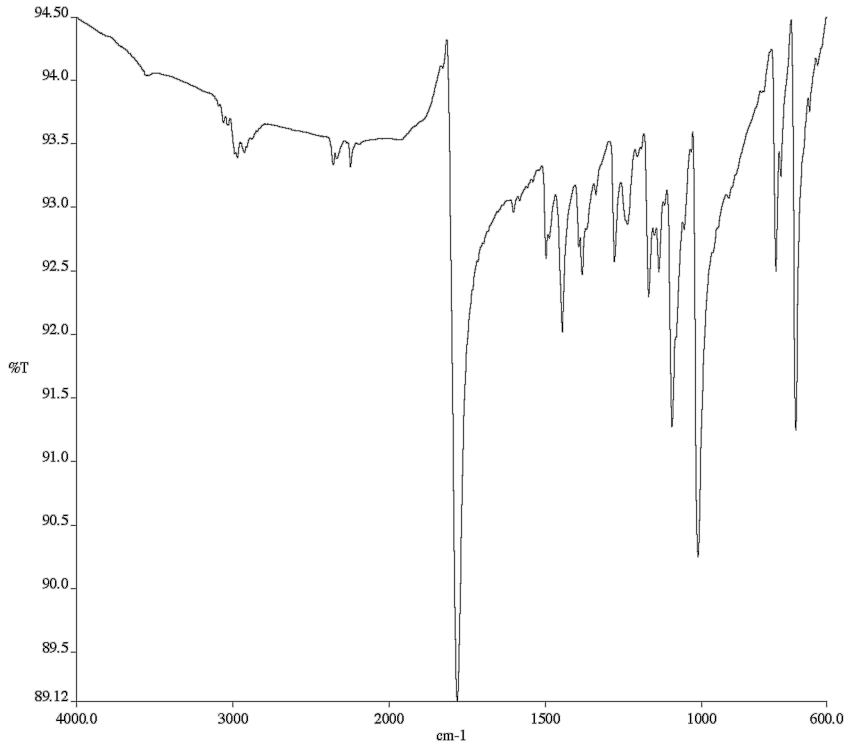
HSQC (400 MHz, $CDCl_3$) of compound **10**.



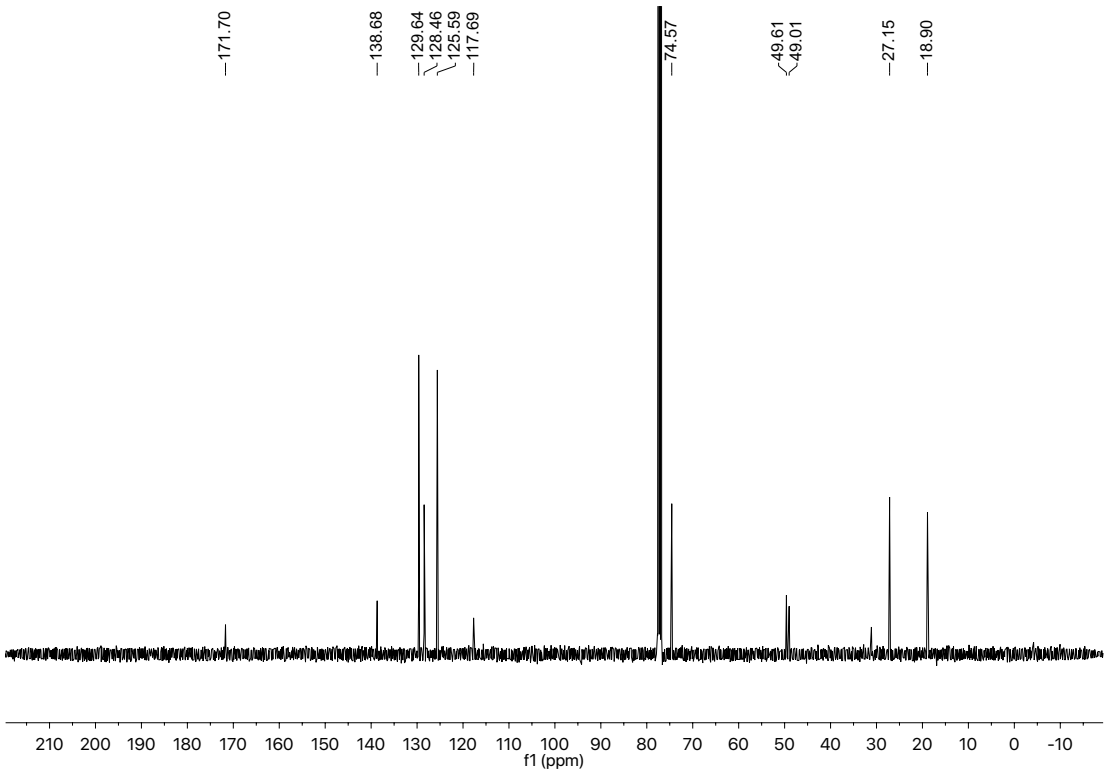
NOESY (400 MHz, $CDCl_3$) of compound **10**.



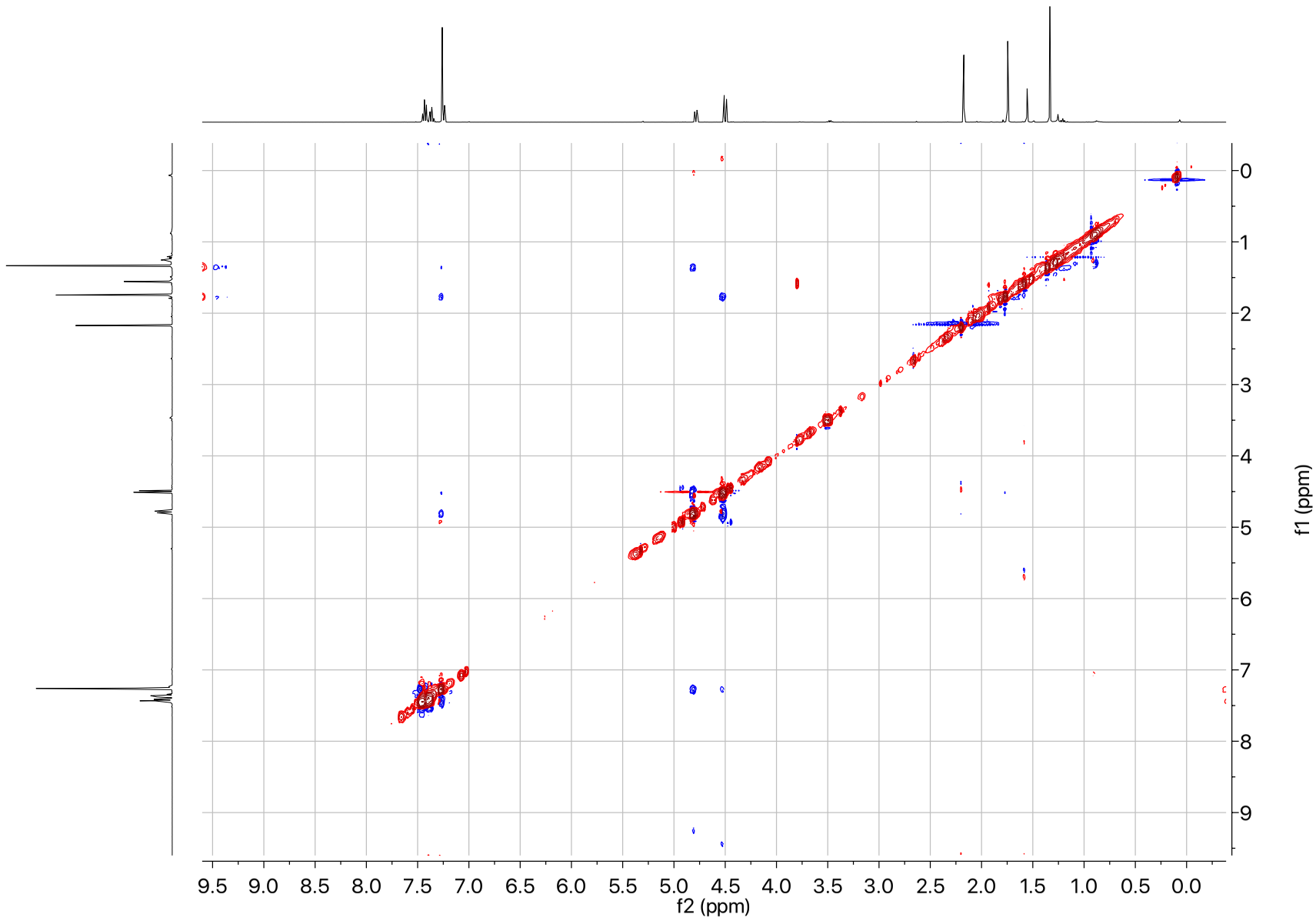
^{1}H NMR (400 MHz, $CDCl_3$) of compound **11.**



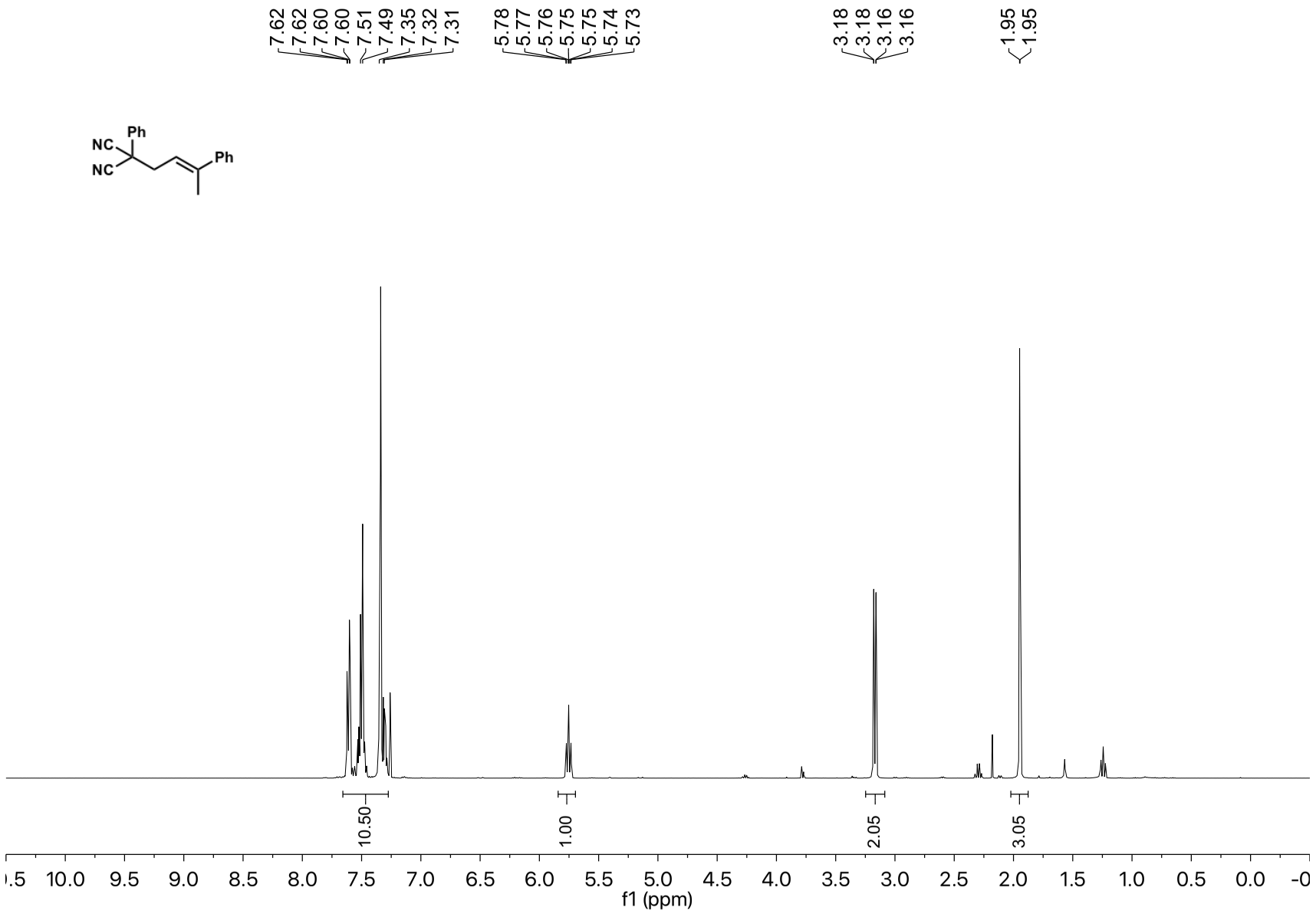
Infrared spectrum (Thin Film, NaCl) of compound **11**.



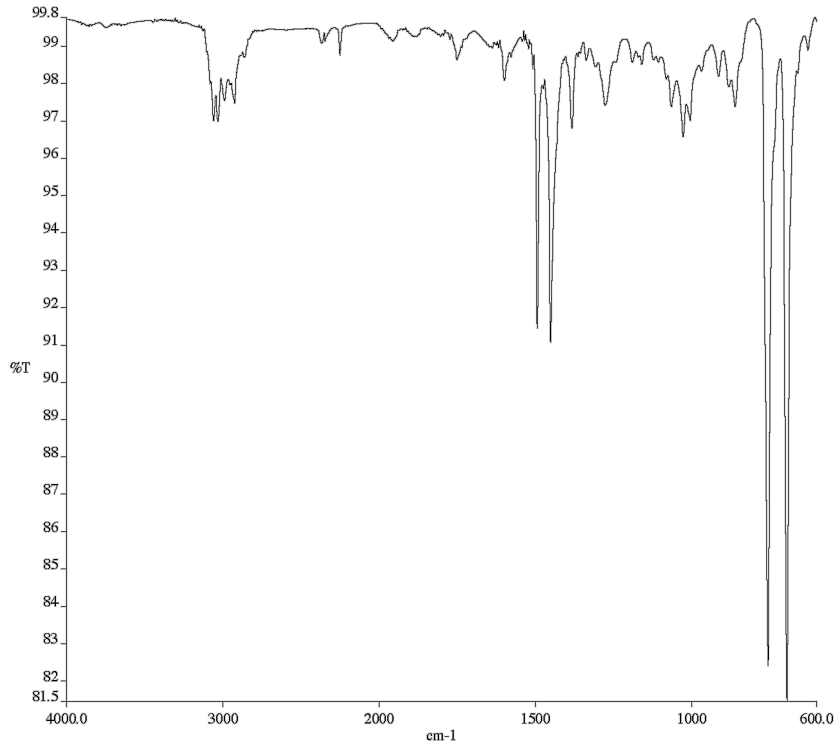
^{13}C NMR (101 MHz, $CDCl_3$) of compound **11**.



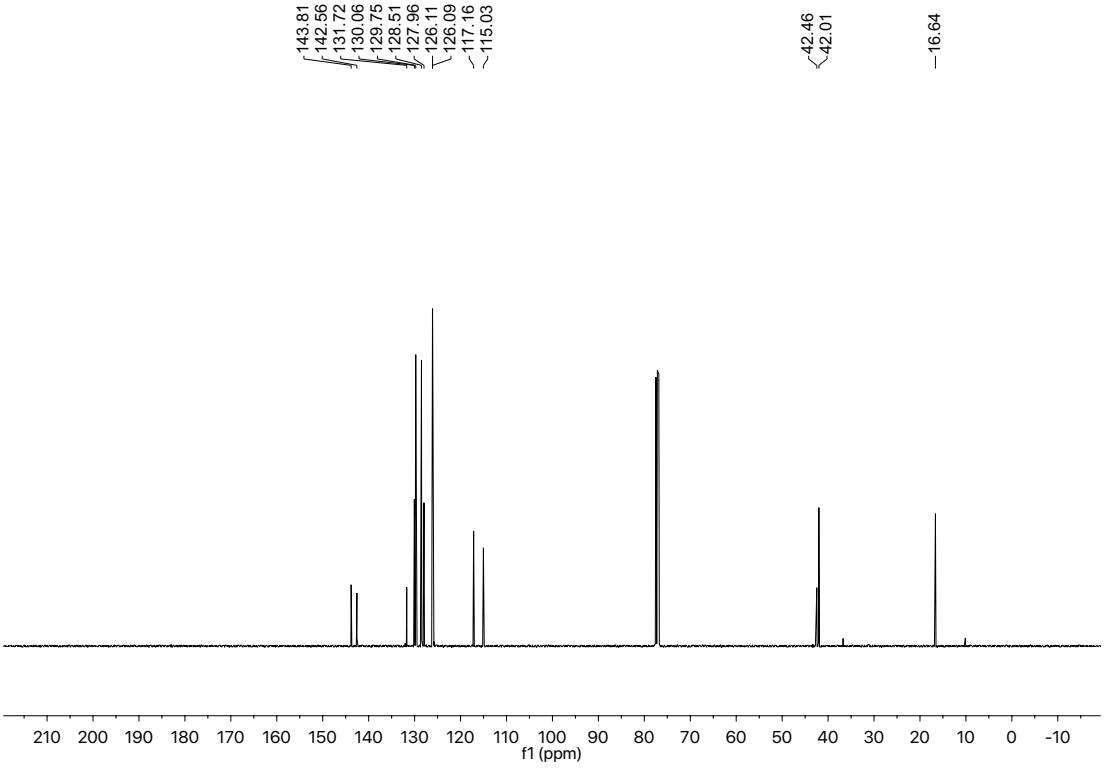
NOESY (400 MHz, $CDCl_3$) of compound **11**.



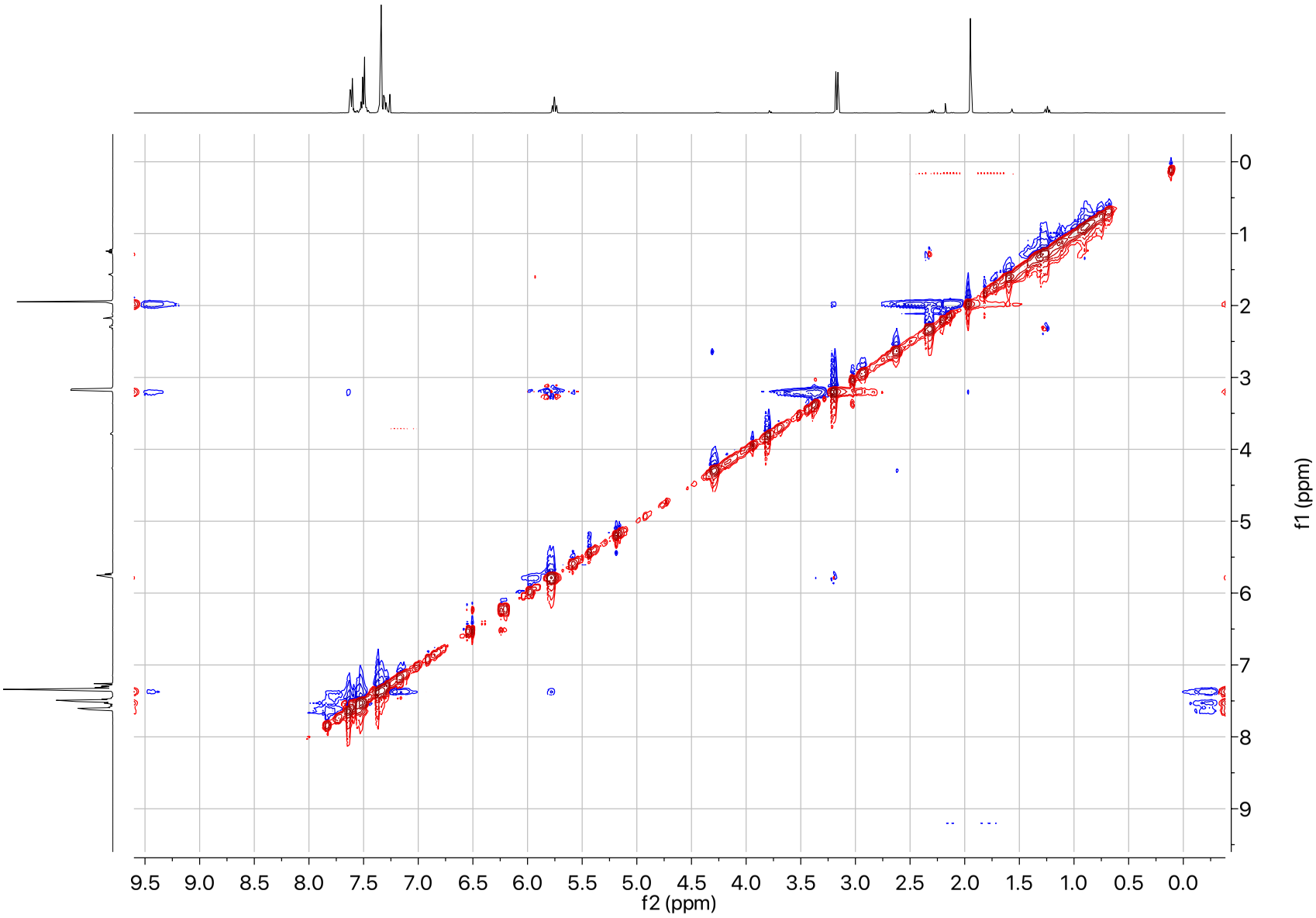
^{1}H NMR (400 MHz, $CDCl_3$) of compound **SI-1**.



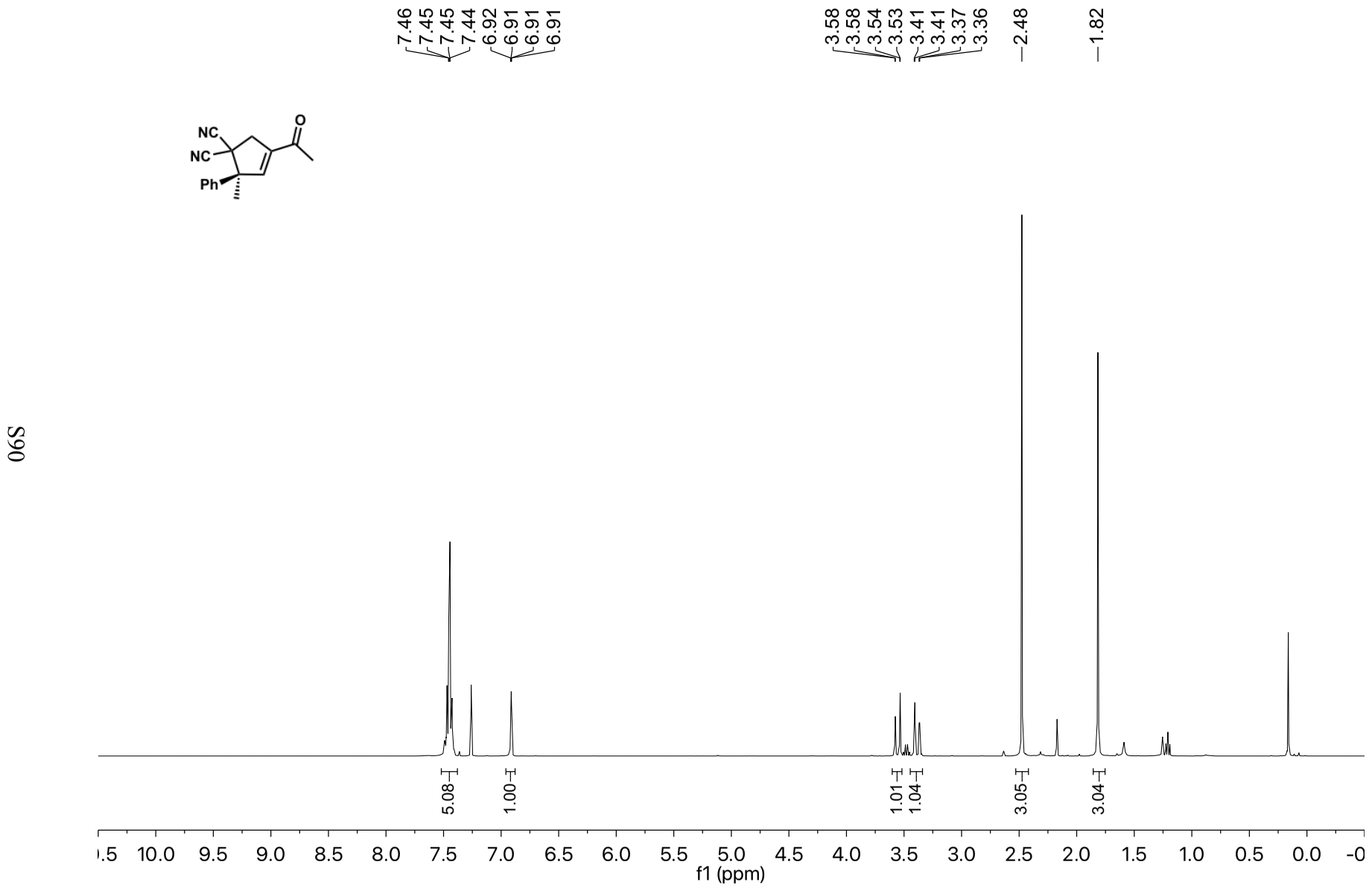
Infrared spectrum (Thin Film, NaCl) of compound **SI-1**.



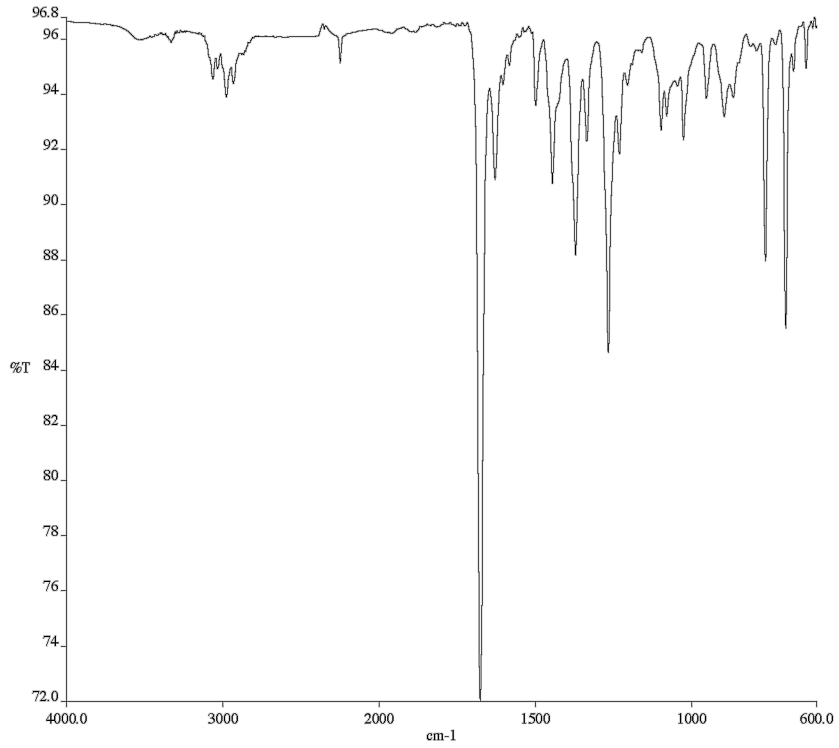
^{13}C NMR (101 MHz, $CDCl_3$) of compound **SI-1**.



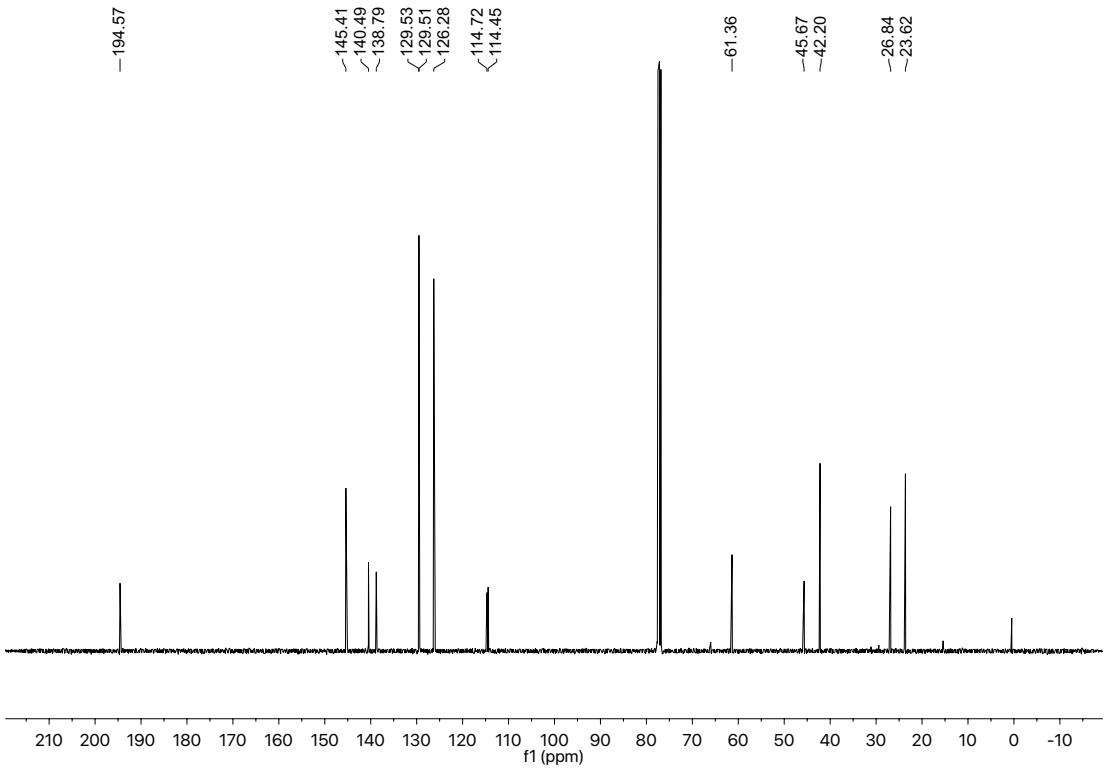
NOESY (400 MHz, $CDCl_3$) of compound **SI-1**.



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



Infrared spectrum (Thin Film, NaCl) of compound **SI-2**.



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