Synthesis of Aryl Ketoamides via Aryne Insertion Into Imides

Austin C. Wright, Christopher K. Haley, Guillaume LaPointe, and Brian M. Stoltz

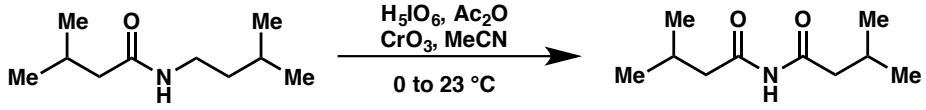
The Warren and Katharine Schlinger Laboratory for Chemistry and Chemical Engineering, Division of Chemistry and Chemical Engineering, California Institute of Technology, Pasadena, California, 91125, United States

Table of Contents

Materials and Methods

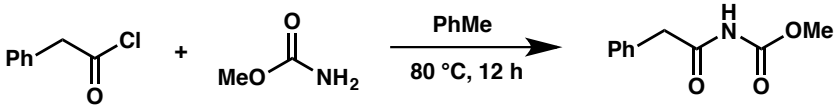
Unless otherwise stated, reactions were performed in flame-dried glassware under nitrogen atmosphere using dry, deoxygenated solvents (distilled or passed over a column of activated alumina). Reaction temperatures were controlled by an IKAmag temperature modulator. Thin layer chromatography (TLC) was performed using E. Merck silica gel 60 F254 precoated plates (0.25 mm) and visualized by UV fluorescence quenching. 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 either on a Bruker AV III HD spectrometer equipped with a Prodigy liquid nitrogen temperature cryoprobe (400 MHz and 101 MHz, respectively) or on a Varian Inova 500 (500 MHz and 125 MHz, respectively) and are reported relative to Me_4Si (δ 0.0). IR spectra were recorded on a Perkin Elmer Paragon 1000 Spectrometer and are reported in frequency of absorption (cm^{-1}). Preparatory HPLC was performed using an Agilent 1100 Series HPLC utilizing a Zorbax XDB-C18 column purchased from Agilent Technologies. HRMS were acquired using an Agilent 6200 Series TOF with an Agilent G1978A Multimode source in electrospray ionization (ESI), atmospheric pressure chemical ionization (APCI) or mixed (MM) ionization mode or with a JEOL JMS-600H in fast atom bombardment (FAB+).

Imide Synthesis and Characterization Data



S1 ***S2***

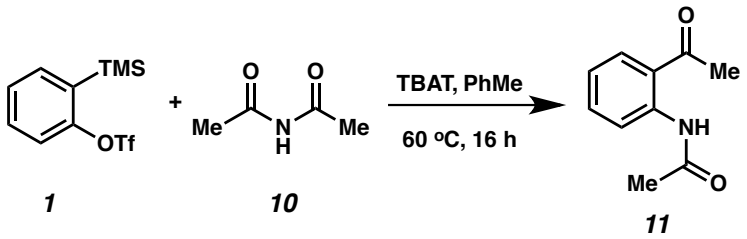
3-methyl-*N*-(3-methylbutanoyl)butanamide (**S1**): In air, H_5IO_6 (4.42 g, 19.4 mmol, 6.0 equiv), CrO_3 (16.2 mg, 0.16 mmol, 5.0 mol %), and MeCN (46 mL) were sequentially added to a round bottom flask equipped with a magnetic stir bar. The reaction mixture was stirred for 30 minutes at ambient temperature, at which point acetic anhydride (1.8 mL, 19.4 mmol, 6.0 equiv) was added. The mixture was cooled to 0 °C, and **S1** (553 mg, 3.23 mmol, 1.0 equiv) was added slowly. The resulting mixture was allowed to warm to ambient temperature over 12 h. The reaction was quenched with ice water and extracted with EtOAc (4 x 40 mL). The resulting organic layers were concentrated in vacuo and purified by column chromatography (20% EtOAc in hexanes) to afford **S2** (89 mg, 15% yield) as a white solid; R_f = 0.15 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.72 (br s, 1H), 2.47 (d, *J* = 9.4, 4H), 2.14 (heptet, *J* = 9.0 Hz, 2H), 0.98 (s, 12 H); ^{13}C (101 MHz, $CDCl_3$) δ 173.9, 46.3, 25.2, 22.4. IR (Neat Film, NaCl) 3272.4, 3170.7, 2957.7, 2871.5, 1728.6, 1505.7, 1466.8, 1386.4, 1367.0, 1294.4, 1246.8, 1181.5, 1160.6, 1120.1, 1090.0 cm^{-1}; HRMS (FAB+) *m/z* calc'd for $C_{10}H_{20}NO_2$ $[M+H]^+$: 186.1494, found 186.1500.



S3 ***S4*** ***S5***

Methyl (2-phenylacetyl)carbamate (S5): In air, 2-phenylacetyl chloride (**S3**, 309.2 mg, 0.26 mL, 2.00 mmol, 1.0 equiv), methyl carbamate (**S4**, 450.4 mg, 6.00 mmol, 3.0 equiv), and PhMe (10 mL) were added. The reaction vessel was heated to 80 °C for 12 h. The reaction was cooled to 23 °C, concentrated, and purified by column chromatography (10% EtOAc in hexanes) to afford **S5** (34.1 mg, 9% yield) as white solid; R_f = 0.40 (50% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.48 (br s, 1H), 7.36–7.33 (m, 2H), 7.31–7.27 (m, 3H), 4.07 (s, 2H), 3.78 (s, 3H); ^{13}C (126 MHz, $CDCl_3$) δ 152.0, 138.5, 133.3, 129.6, 128.6, 127.4, 110.0, 53.1. IR (Neat Film, NaCl) 3246.1, 3172.3, 3014.0, 2259.7, 1788.1, 1757.5, 1686.2, 1520.2, 1455.7, 1257.2, 1216.1, 1192.1, 1144.1, 1049.9, 781.9, 705.3 cm^{-1}; HRMS (ESI-APCI) *m/z* calc'd for $C_{10}H_{12}NO_3$ $[M+H]^+$: 194.0817, found 194.0817.

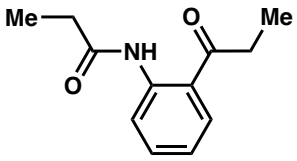
Aryl Ketoamide Synthesis and Characterization Data



1 ***10*** ***11***

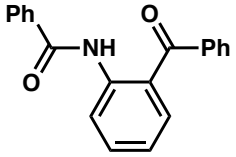
Representative Procedure for Acylamination

A 2-dram vial equipped with a magnetic stir bar was charged with TBAT (144.7 mg, 0.268 mmol, 2.0 equiv) and imide **10** (13.6 mg, 0.134 mmol, 1.0 equiv). The vial was purged with nitrogen, and PhMe (1.6 mL) was added via syringe followed by silyl triflate **1** (60.0 mg, 0.201 mmol, 1.5 equiv). The vial was sealed and placed in an aluminum block preheated to 60 °C. The reaction mixture was stirred at this temperature for 16 h, then it was allowed to cool to 23 °C. The mixture was concentrated in vacuo and purified by column chromatography (10% EtOAc in hexanes) to afford **11** (23.6 mg, 89% yield) as a white solid. Characterization data match those previously reported;[1] ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.70 (s, 1H), 8.74 (d, *J* = 8.6 Hz, 1H), 7.90 (d, *J* = 8.2 Hz, 1H), 7.56 (dd, *J* = 7.3, 8.6 Hz, 1H), 7.12 (dd, *J* = 8.2, 7.3 Hz, 1H), 2.67 (s, 3H), 2.23 (s, 3H).



13a

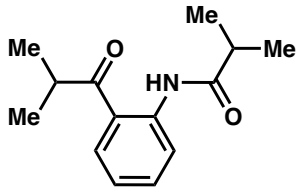
***N*-(2-propionylphenyl)propionamide (13a)**: Prepared according to the representative procedure using *N*-propionylpropionamide (17.3 mg, 0.134 mmol) and silyl triflate **1** (60.0 mg, 0.201 mmol). The reaction was purified by column chromatography (10% EtOAc in hexanes) to afford **13a** (24.0 mg, 88% yield) as a white solid. Characterization data match those previously reported.[2] ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.78 (s, 1H), 8.78 (d, *J* = 9.0 Hz, 1H), 7.93 (d, *J* = 9.0 Hz, 1H), 7.57–7.51 (m, 1H), 7.13–7.07 (m, 1H), 3.06 (q, *J* = 7.2 Hz, 2H), 2.50 (q, *J* = 7.6, 2H), 1.31–1.20 (m, 6H).



13b

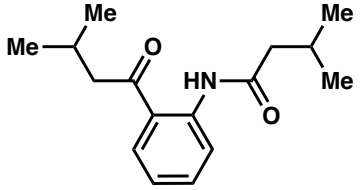
N-(2-benzoylphenyl)benzamide (13b): Prepared according to the representative procedure using *N*-benzoylbenzamide (30.2 mg, 0.134 mmol) and silyl triflate **1** (60.0 mg, 0.201 mmol). The reaction was purified by column chromatography (10% EtOAc in hexanes) to afford **13b** (27.4 mg, 68% yield) as a white solid. Characterization data match those previously reported.[3]

^{1}H NMR (400 MHz, $CDCl_3$) δ 12.00 (s, 1H), 8.92 (d, *J* = 8.2 Hz, 1H), 8.11–8.08 (m, 2H), 7.74 (t, *J* = 4.3 Hz, 2H), 7.66–7.59 (m, 3H), 7.56–7.49 (m, 5H), 7.14 (s, 1H).



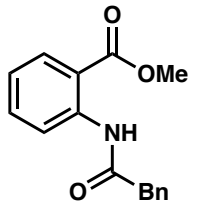
13c

***N*-(2-isobutyrylphenyl)isobutyramide** (**13c**): Prepared according to the representative procedure using *N*-isobutyrylisobutyramide (23.6 mg, 0.150 mmol) and silyl triflate **1** (67.1 mg, 0.225 mmol). Purification was achieved by prep HPLC to afford **13c** (27.3 mg, 78% yield) as a white solid; R_f = 0.4 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.80 (br s, 1H), 8.79 (d, *J* = 6 Hz, 1H), 7.93 (d, *J* = 6 Hz, 1H), 7.53 (t, *J* = 4.5 Hz, 1H), 7.10 (t, *J* = 6 Hz, 1H), 3.65 (sept, *J* = 6 Hz, 1H), 2.62 (sept, *J* = 6 Hz, 1H), 1.28 (d, *J* = 6 Hz, 6H), 1.23 (d, *J* = 6.0 Hz, 6H); ^{13}C (101 MHz, $CDCl_3$) δ 209.2, 176.6, 141.7, 134.8, 130.6, 122.2, 121.1, 120.7, 37.6, 36.3, 19.6 (2 unresolved signals); IR (Neat Film, NaCl) 3251.4, 2970.8, 2903.3, 2872.9, 1700.1, 1653.0, 1604.8, 1583.4, 1521.7, 1517.1, 1467.7, 1450.3, 1383.3, 1356.5, 1350.9, 1301.9, 1239.0, 1211.6, 1157.4, 1099.6, 1083.7, 976.8, 755.1 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1489, found: 234.1490.



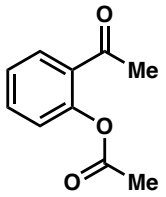
13d

3-methyl-*N*-(2-(3-methylbutanoyl)phenyl)butanamide (**13d**): Prepared according to the representative procedure using imide **S2** (37.1 mg, 0.200 mmol) and silyl triflate **1** (89.5 mg, 0.300 mmol). Purification was achieved by prep HPLC to afford **13d** (41.3 mg, 79% yield) as a white solid. R_f = 0.30 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.73 (br s, 1H), 8.77 (d, *J* = 1.6 Hz, 1H), 7.90 (d, *J* = 10.8 Hz, 1H), 7.53 (t, *J* = 9.8 Hz, 1H), 7.10 (t, *J* = 9.8 Hz, 1H), 2.88 (d, *J* = 9.2 Hz, 2H), 2.33–2.19 (m, 4H), 1.03–0.99 (m, 12H); ^{13}C (126 MHz, $CDCl_3$) 205.0, 172.1, 141.0, 134.9, 130.4, 122.2, 121.92, 120.9, 49.0, 48.1, 26.3, 25.6, 22.7, 22.5. IR (Neat Film, NaCl) 3255.4, 2957.6, 2929.9, 2870.7, 1698.8, 1651.9, 1583.5, 1520.0, 1450.7, 1386.2, 1366.0, 1298.9, 1281.3, 1258.1, 1201.8, 1163.5, 1114.3, 1003.9, 947.5, 754.1 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{16}H_{24}NO_2$ $[M+H]^+$: 262.1802, found: 262.1804.



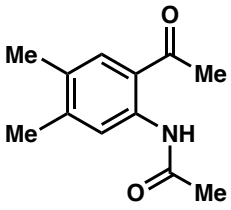
13e

Methyl 2-(2-phenylacetamido)benzoate (13e): Prepared according to the representative procedure using imide **S5** (25.9 mg, 0.134 mmol) and silyl triflate **1** (60.0 mg, 0.201 mmol). The reaction was purified by column chromatography (10% EtOAc in hexanes) to afford **13e** (8.7 mg, 24% yield) as a white solid. R_f = 0.30 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.04 (br s, 1H), 8.70 (dd, *J* = 8.0 Hz, 1.2 Hz, 1H), 7.99 (dd, *J* = 8.0, 1.2 Hz, 1H), 7.54–7.49 (m, 1H), 7.41–7.28 (m, 5H), 7.08–7.01 (m, 1H), 3.86 (s, 3H), 3.76 (s, 2H); ^{13}C (101 MHz, $CDCl_3$) 170.0, 168.5, 141.4, 134.6, 134.4, 130.8, 129.5, 129.3, 128.9, 127.3, 122.6, 120.4, 52.3, 45.9. IR (Neat Film, NaCl) 2917.9, 1687.6, 1588.4, 1523.0, 1448.6, 1309.3, 1263.3, 1193.6, 1088.9, 756.5 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{16}H_{15}NO_3$ $[M+H]^+$: 270.1125, found: 270.1129.



13g

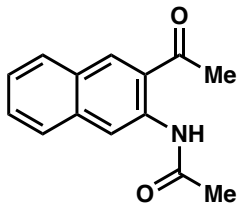
2-Acetylphenyl acetate (13g): Prepared according to the representative procedure using acetic anhydride (13.7 mg, 0.134 mmol) and silyl triflate **1** (60.0 mg, 0.201 mmol). The reaction was purified by column chromatography (10% EtOAc in hexanes) to afford **13g** (12.8 mg, 54% yield) as a white solid. Characterization data match those previously reported.[4] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.78 (d, *J* = 7.8 Hz, 1H), 7.50 (t, *J* = 7.7 Hz, 1H), 7.28 (t, *J* = 7.6 Hz, 1H), 7.10 (d, *J* = 8.0 Hz, 1H), 2.52 (s, 3H), 2.32 (s, 3H).



15a

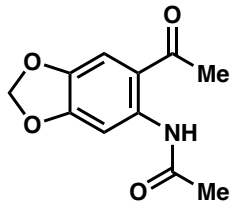
N*-(2-acetyl-4,5-dimethylphenyl)acetamide** (**15a**): Prepared according to the representative procedure using imide ***10 (8.4 mg, 0.083 mmol) and silyl triflate **14a** (40.5 mg, 0.124 mmol). Purified by column chromatography (10% EtOAc in hexanes) to afford **15a** (6.5 mg, 31% yield) as a white solid. R_f = 0.15 (10% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.63 (br s, 1H), 8.53 (s, 1H), 7.61 (s, 1H), 2.63 (s, 3H), 2.31 (s, 3H), 2.26 (s, 3H), 2.21 (s, 3H); ^{13}C (101 MHz, $CDCl_3$) δ 202.4, 169.4, 145.3, 139.1, 132.4, 130.6, 121.5, 119.8, 28.6, 25.6, 20.6, 19.4. IR (Neat Film, NaCl) 3238.4, 2917.3, 1692.5, 1643.4, 1579.0, 1514.1, 1450.2, 1397.3, 1353.6,

1286.8, 1270.0, 1235.1, 1018.7, 876.4, 758.9, 659.3 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{12}H_{16}NO_2$ $[M+H]^+$: 206.1176, found: 206.1171.



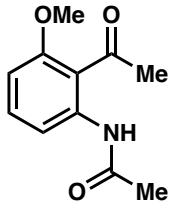
15b

***N*-(3-acetylnaphthalen-2-yl)acetamide** (**15b**): Prepared according to the representative procedure using imide **10** (29.0 mg, 0.287 mmol) and silyl triflate **14b** (150.0 mg, 0.431 mmol). Purification was achieved by prep HPLC to afford **15b** (28.7 mg, 44% yield) as a white solid; R_f = 0.35 (30% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.50 (br s, 1H), 9.12, (s, 1H), 8.44 (s, 1H), 7.83 (d, *J* = 9.0 Hz, 2H), 7.57 (t, *J* = 7.5 Hz, 1H), 7.43 (t, *J* = 7.5 Hz, 1H), 2.80 (s, 3H), 2.27 (s, 3H); ^{13}C (101 MHz, $CDCl_3$) 203.0, 169.3, 136.7, 136.1, 134.3, 129.7, 128.9, 128.2, 127.7, 125.6, 122.7, 117.7, 28.7, 25.6; IR (Neat Film, NaCl) 3217.8, 1682.2, 1654.4, 1577.0, 1546.1, 1480.7, 1437.2, 1352.5, 1386.4, 1286.3, 1277.9, 1203.7, 1148.0, 1020.5, 953.6, 885.1, 742.1, 656.2 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{14}H_{14}NO_2$ $[M+H]^+$: 228.1019, found: 228.1022.



15c

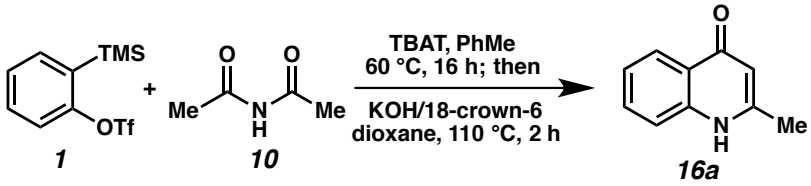
***N*-(6-acetylbenzo[*d*][1,3]dioxol-5-yl)acetamide** (**15c**): Prepared according to the the representative procedure using imide **10** (20.4 mg, 0.201 mmol) and silyl triflate **14c** (103.4 mg, 0.302 mmol). Purification was achieved by prep HPLC to afford **15c** (28.9 mg, 65% yield) as a white solid; R_f = 0.55 (50% EtOAc in hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.08 (br s, 1H), 8.37 (s, 1H), 7.25 (s, 1H), 6.02 (s, 2H), 2.57 (s, 3H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, CDCl3) δ 200.6, 169.5, 152.9, 142.4, 139.3, 115.1, 109.6, 102.1, 101.5, 28.8, 25.6. IR (Neat Film, NaCl) 2916.7, 1692.6, 1611.8, 1502.7, 1483.5, 1433.8, 1370.2, 1342.5, 1243.2, 1178.9, 1118.8, 1044.8, 927.0 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{11}H_{12}NO_4$ $[M+H]^+$: 222.0761, found: 222.0766.



15d

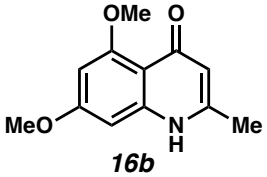
***N*-(2-acetyl-3-methoxyphenol)acetamide (15d)**: Prepared according to the representative procedure using imide **10** (13.6 mg, 0.134 mmol) and silyl triflate **14d** (66.0 mg, 0.201 mmol). The reaction was purified by column chromatography (10% EtOAc in hexanes) to afford **15d** (13.0 mg, 47% yield) as a white solid; R_f = 0.20 (20% EtOAc in hexanes); ^{1}H NMR (500 MHz, $CDCl_3$) δ 10.49 (s, 1H), 8.07 (d, *J* = 8.3 Hz, 1H), 7.40 (td, *J* = 8.4, 0.5 Hz, 1H), 6.69 (dd, *J* = 8.4, 0.9 Hz, 1H), 2.57 (s, 3H), 3.90 (s, 3H), 2.61 (s, 3H); ^{13}C NMR (126 MHz, $CDCl_3$) δ 204.6, 169.2, 160.0, 139.2, 133.7, 116.5, 114.0, 106.2, 55.8, 33.7, 25.5; IR (Neat Film, NaCl) 3086.8, 2947.7, 1698.6, 1639.6, 1634.0, 1528.8, 1470.6, 1403.5, 1273.1, 1243.4, 1195.9, 1093.2, 1017.3, 967.4, 802.3, 735.2, 610.8 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{11}H_{14}NO_3$ $[M+H]^+$: 262.1802, found: 262.1804.

Quinolone Synthesis and Characterization Data



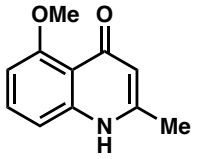
<u>*Representative Procedure for Quinolone Synthesis*</u>

A 2-dram vial equipped with a magnetic stir bar was charged with TBAT (144.7 mg, 0.268 mmol, 2.0 equiv) and imide **10** (13.6 mg, 0.134 mmol, 1.0 equiv). The vial was purged with nitrogen, and PhMe (1.6 mL) was added via syringe followed by silyl triflate **1** (60.0 mg, 0.201 mmol, 1.5 equiv). The vial was sealed and placed in an aluminum block preheated to 60 °C. The reaction mixture was stirred at this temperature for 16 h, then it was allowed to cool to 23 °C. The mixture was concentrated in vacuo and then charged with dioxane (1.6 mL), KOH (22.6 mg, 0.402 mmol, 3.0 equiv), and 18-crown-6 (106.3 mg, 0.402 mmol, 3.0 equiv). The reaction vial was sealed and heated to 110 °C and stirred for 2 h. The reaction was allowed to cool, diluted with CH_2Cl_2 (10 mL), neutralized to pH ~7, and washed with brine (10 mL). The layers were separated, and the aqueous layer was back extracted with CH_2Cl_2 (2 x 10 mL). The combined organic layers were dried (Na_2SO_4), concentrated, and purified by column chromatography (CH_2Cl_2 to 5% MeOH in CH_2Cl_2) to provide **16a** (15.1 mg, 71% yield) as a yellow solid. Characterization data match those previously reported.[5] ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.04 (s, 1H), 7.79 (d, *J* = 10.8 Hz, 1H), 7.65–7.62 (m, 2H), 7.40–7.36 (m, 1H), 6.74 (s, 1H), 2.61 (d, *J* = 1.4 Hz, 3H).



16b

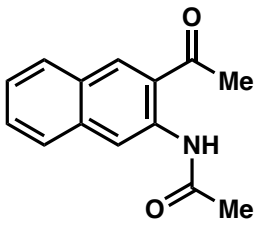
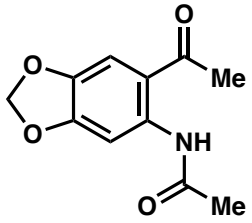
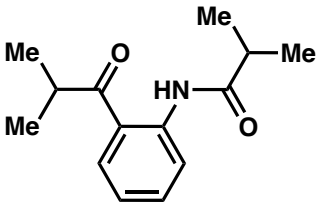
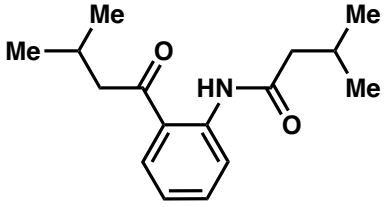
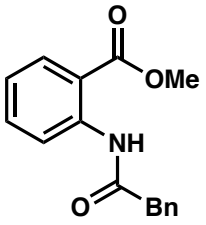
6,8-Dimethoxy-3-methylnaphthalen-1–(4*H*)-one (16b): Prepared according to the representative procedure using imide **10** (13.6 mg, 0.134 mmol) and 3,5-dimethoxy-2-(trimethylsilyl)phenyl trifluoromethanesulfonate (**S2**, 66.0 mg, 0.201 mmol) to provide quinolone **16b** (11.8 mg, 40% yield) as a brown solid. Characterization data match those previously reported.[6] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.08 (s, 1H), 6.75 (s, 1H), 6.74 (s, 1H), 6.24–6.23 (m, 1H), 3.78 (s, 6H), 2.17 (s, 3H).



16c

8-Methoxy-3-methylnaphthalen-1–(4*H*)-one (16c): Prepared according to the representative procedure using imide **10** (13.6 mg, 0.134 mmol) and silyl triflate **13d** (66.0 mg, 0.201 mmol) to provide quinolone **16c** (10.6 mg, 42% yield) as a beige solid. R_f = 0.35 (10% MeOH in CH_2Cl_2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29–7.27 (m, 1H), 7.21 (t, *J* = 8.2, 1H), 7.11 (br s, 1H), 6.95 (d, *J* = 8.0 Hz, 1H), 6.67 (dd, *J* = 12.0, 11.2 Hz, 1H), 3.81 (s, 3H), 2.18 (s, 3H); ^{13}C (126 MHz, $CDCl_3$) 168.2, 160.2, 139.1, 134.8, 129.7, 111.8, 110.1, 105.6, 100.0 55.3, 24.8. IR (Neat Film, NaCl) 2920.7, 1664.8, 1598.3, 1548.7, 1492.8, 1425.9, 1369.9, 1252.6, 1156.1, 1044.1, 775.1 cm^{-1}; HRMS (MM: ESI-APCI) *m/z* calc'd for $C_{11}H_{12}NO_2$ $[M+H]^+$: 190.0863, found: 190.0866.

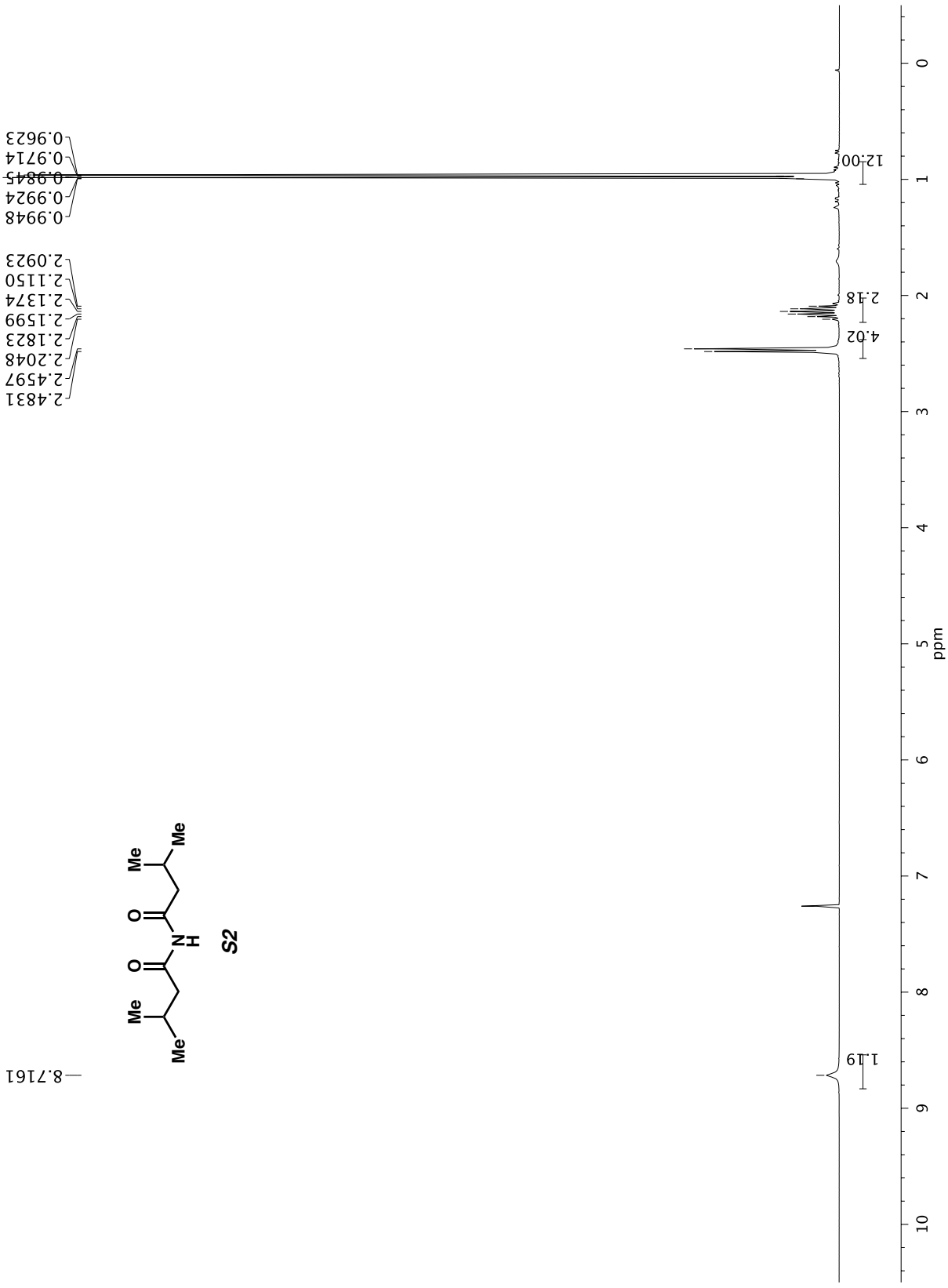
Preparatory HPLC Conditions

Entry	Product	Conditions	Retention Time (min)
1	 ***15b***	**HPLC Zorbax XDB-C18 column 20% to 60% MeCN in H_2O 15 min, 30.0 mL/min**	**13.90**
2	 ***15c***	**HPLC Zorbax XDB-C18 column 20% to 60% MeCN in H_2O 15 min, 30.0 mL/min**	**12.75**
3	 ***13c***	**HPLC Zorbax XDB-C18 column 40% to 80% MeCN in H_2O 15 min, 30.0 mL/min**	**14.36**
4	 ***13d***	**HPLC Zorbax XDB-C18 column 40% to 80% MeCN in H_2O 20 min, 30.0 mL/min**	**17.35**
5	 ***13e***	**HPLC Zorbax XDB-C18 column 0% to 80% MeCN in H_2O 10 min, 15 mL/min**	**9.79**

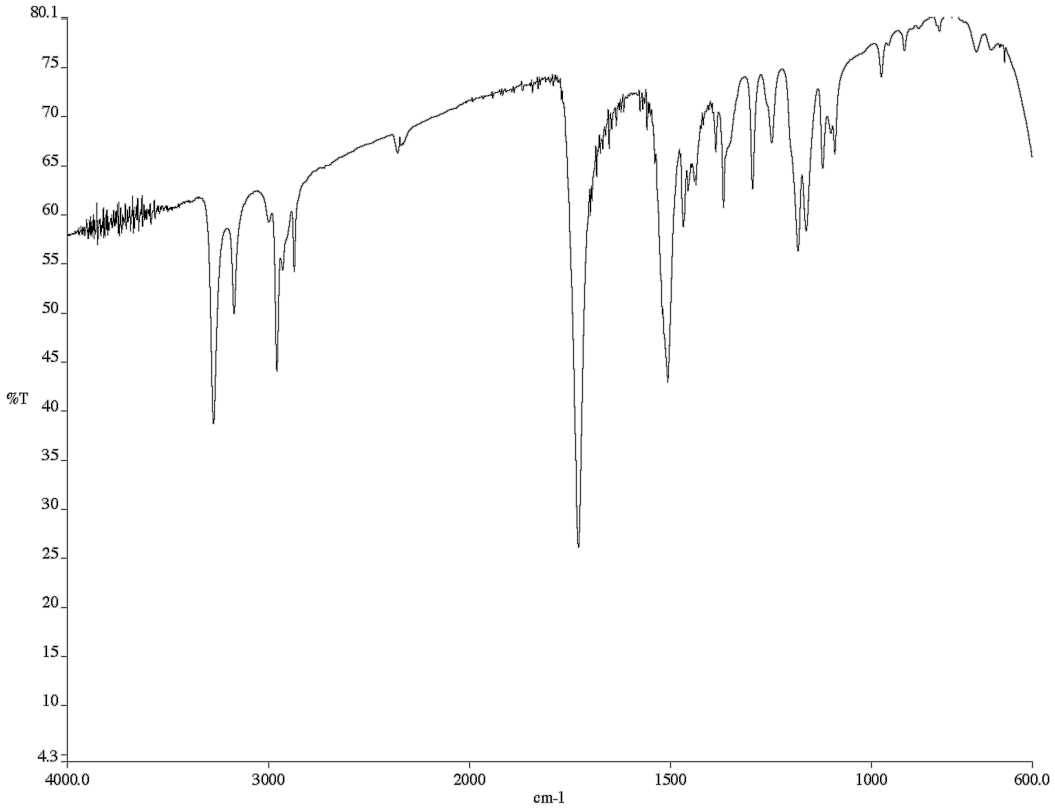
Notes & References

(1) Tobisu, M.; Ano, Y.; Chatani, N. *Org. Lett*. **2009**, *11*, 3250-3252.
(2) Canonne, P.; Boulanger, R.; Chantegrel, B. *Tetrahedron* **1987**, *43*, 663–668.
(3) Yin, Z.; Sun, P. *Org. Lett.* **2012**, *77*, 11339–11344.
(4) Rodriguez–Ramos, F.; Navarette, A.; Gonzalez–Andrade, M.; Alarcon, C.; Aguilera–Cruz, A.; Reyes–Ramirez, Adelfo. *Bioorg. Chem.* **2013**, *50*, 17–25.
(5) Cross, R. M.; Manetsch, R. *J. Org. Chem.* **2010**, *75*, 8654–8657.
(6) Liu, G.-B.; Xu, J.-L.; He, C.-C.; Chen, G.; Xu, Q.; Xu, H.-X.; Li, J.-X. *Bioorg. Med. Chem.* **2009**, *17*, 5433–5441.

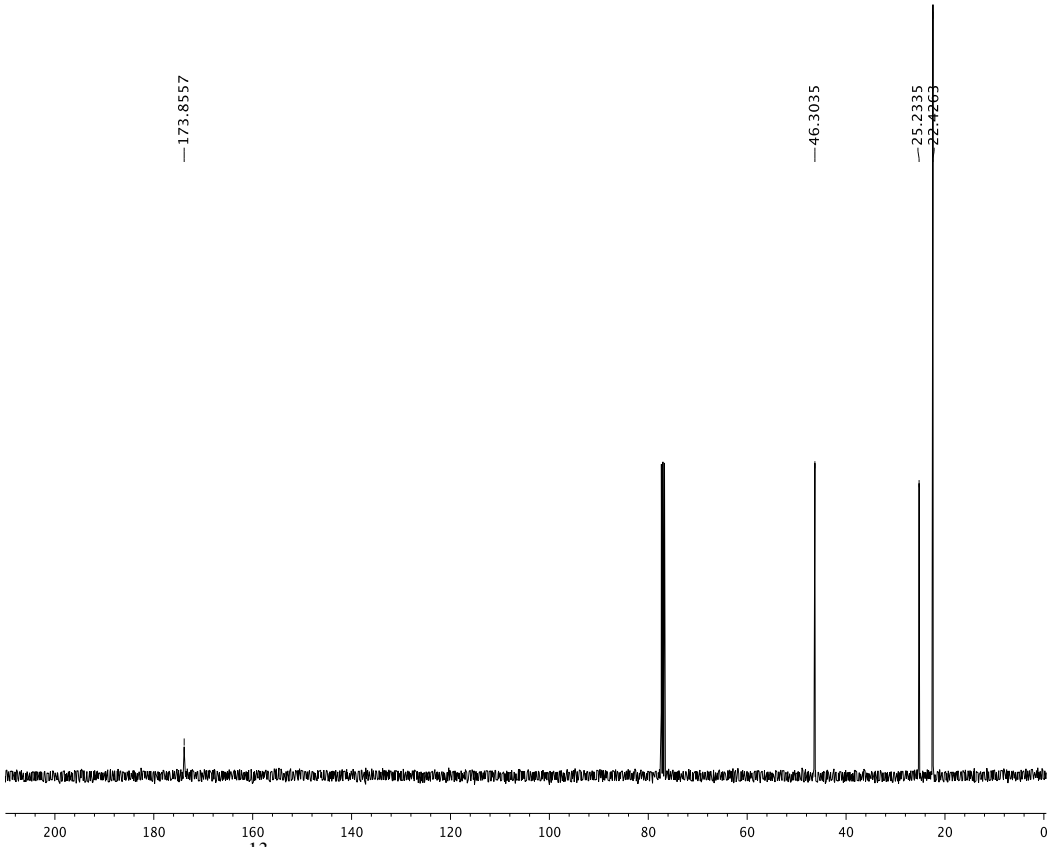
NMR and IR Spectra



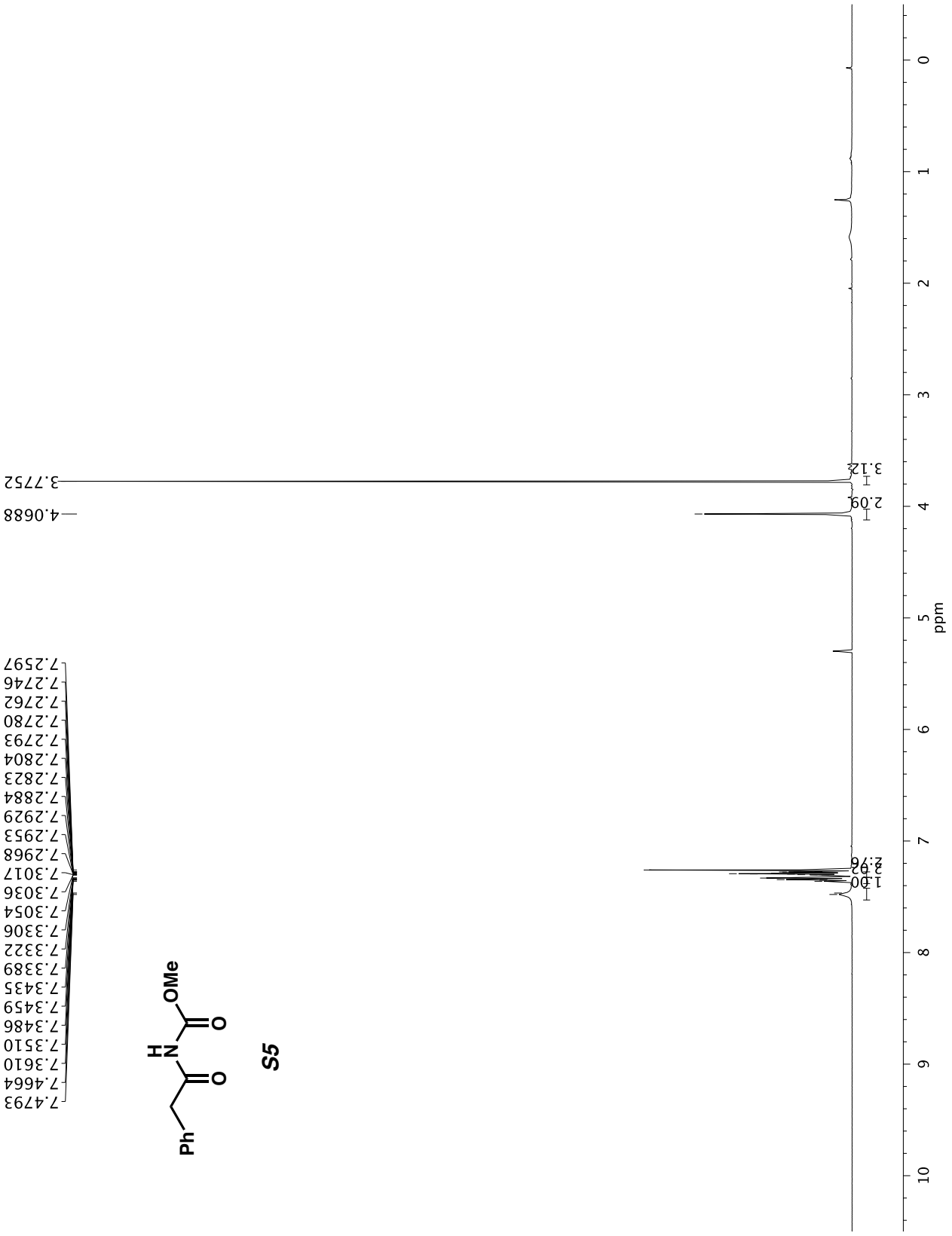
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S2.**



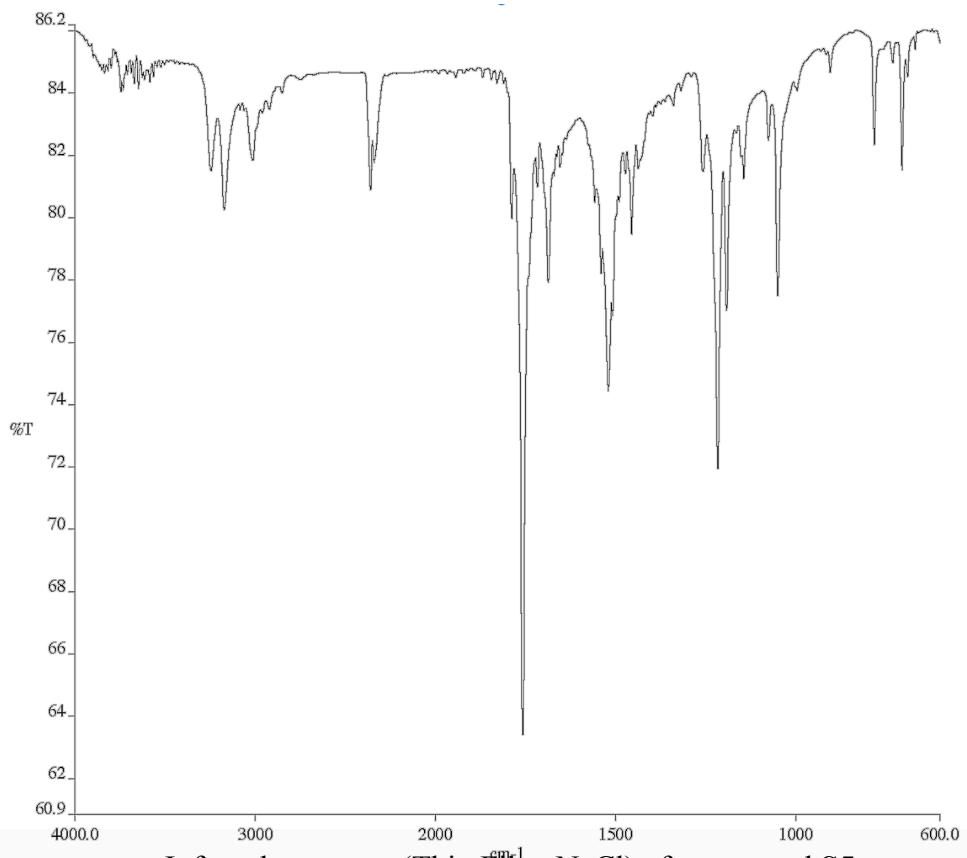
Infrared spectrum (Thin Film, NaCl) of compound **S2**.



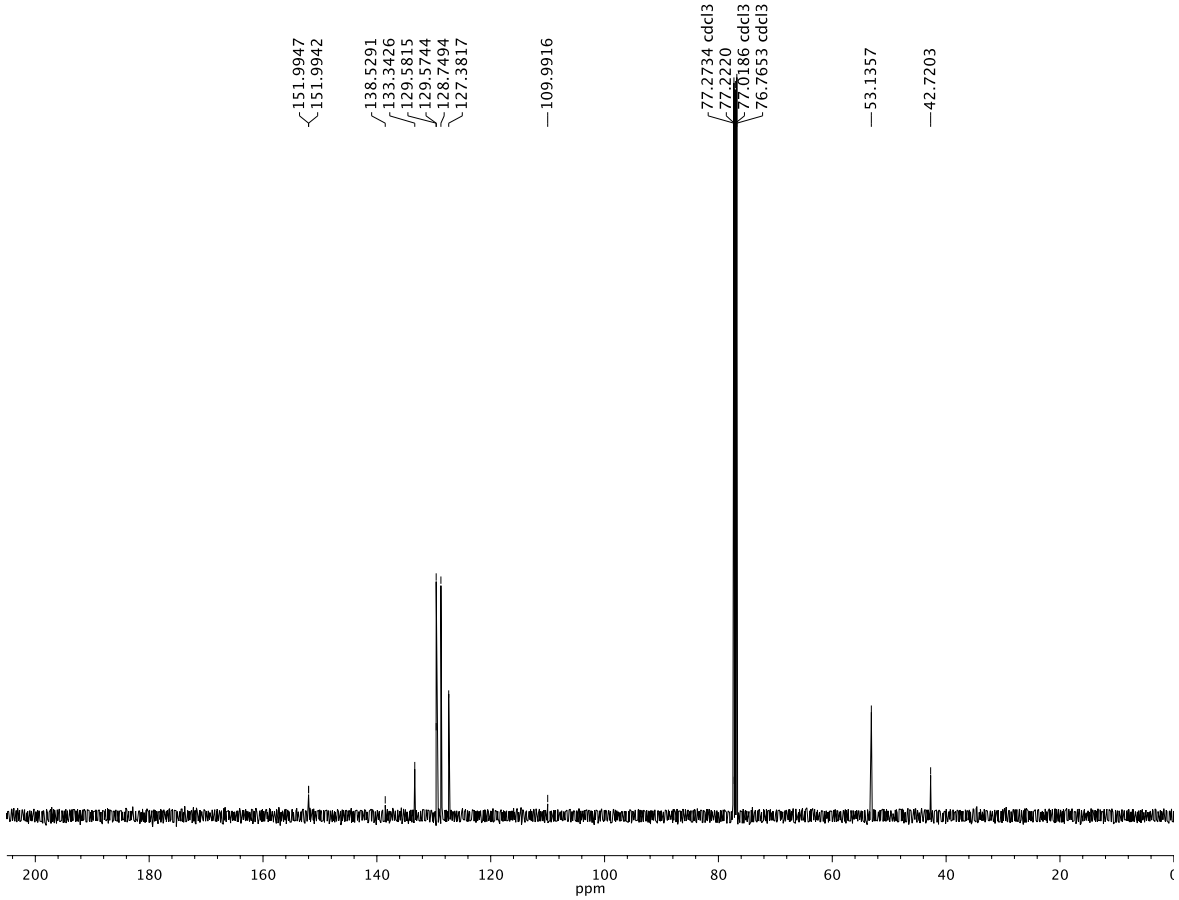
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S2**.



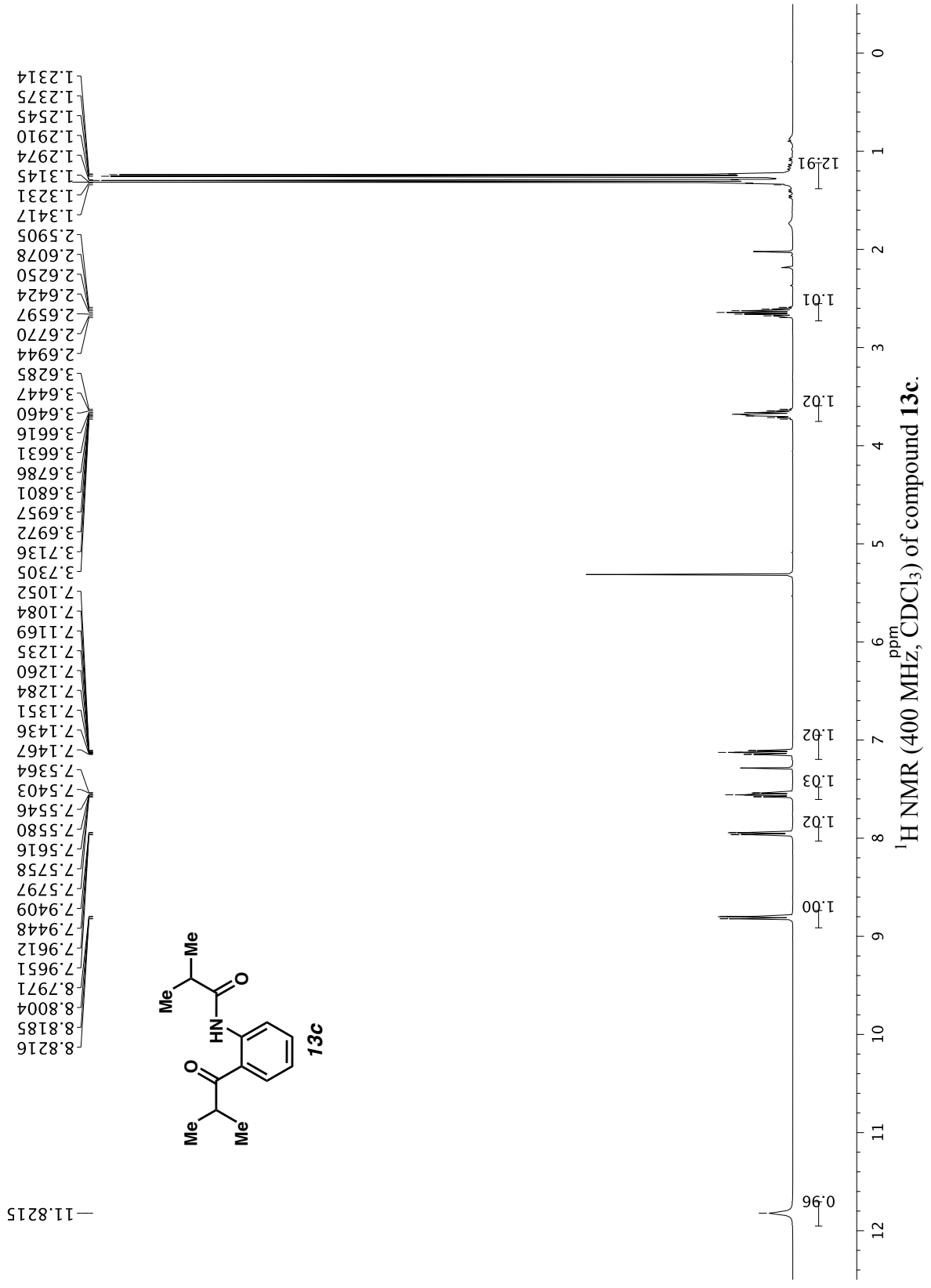
^{1}H NMR (400 MHz, $CDCl_3$) of compound **S5.**



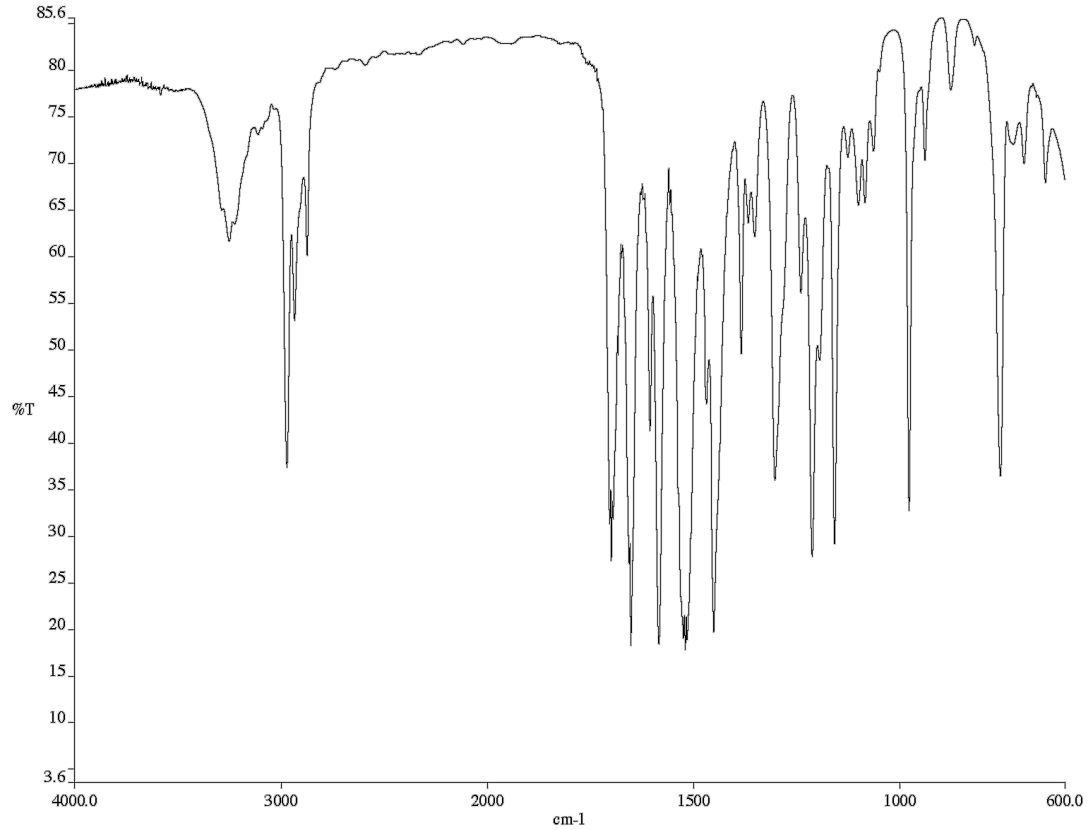
Infrared spectrum (Thin Film, NaCl) of compound **S5**.



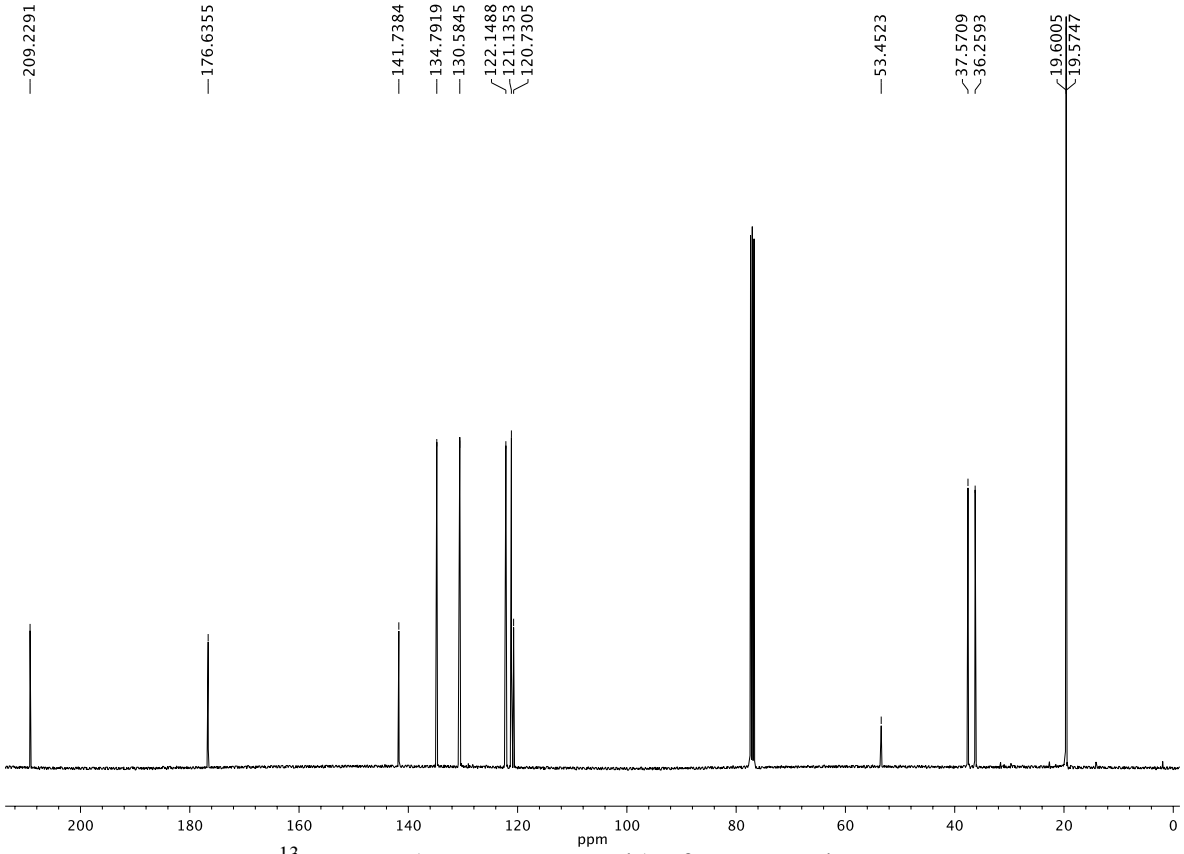
^{13}C NMR (101 MHz, $CDCl_3$) of compound **S5**.



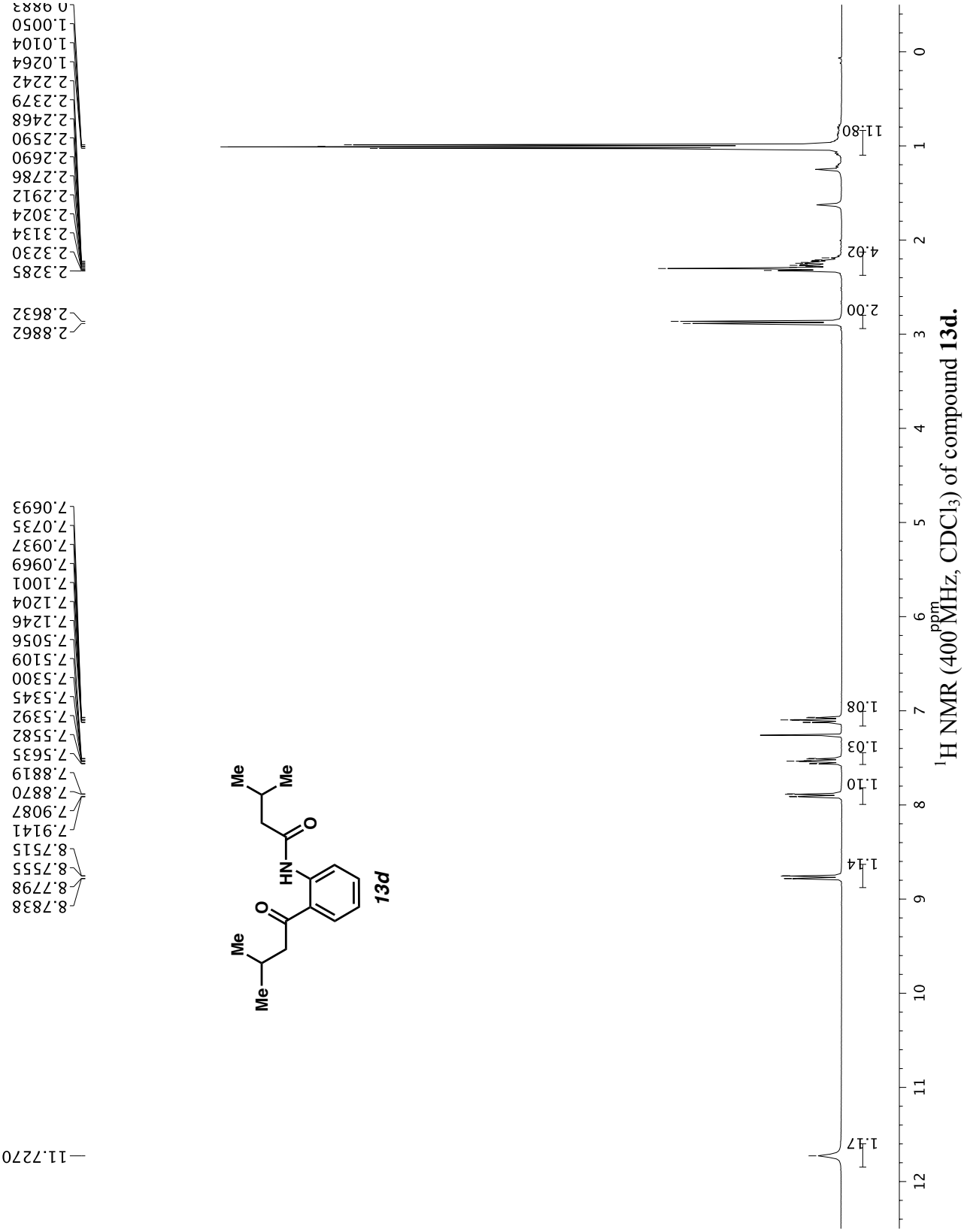
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13c**.



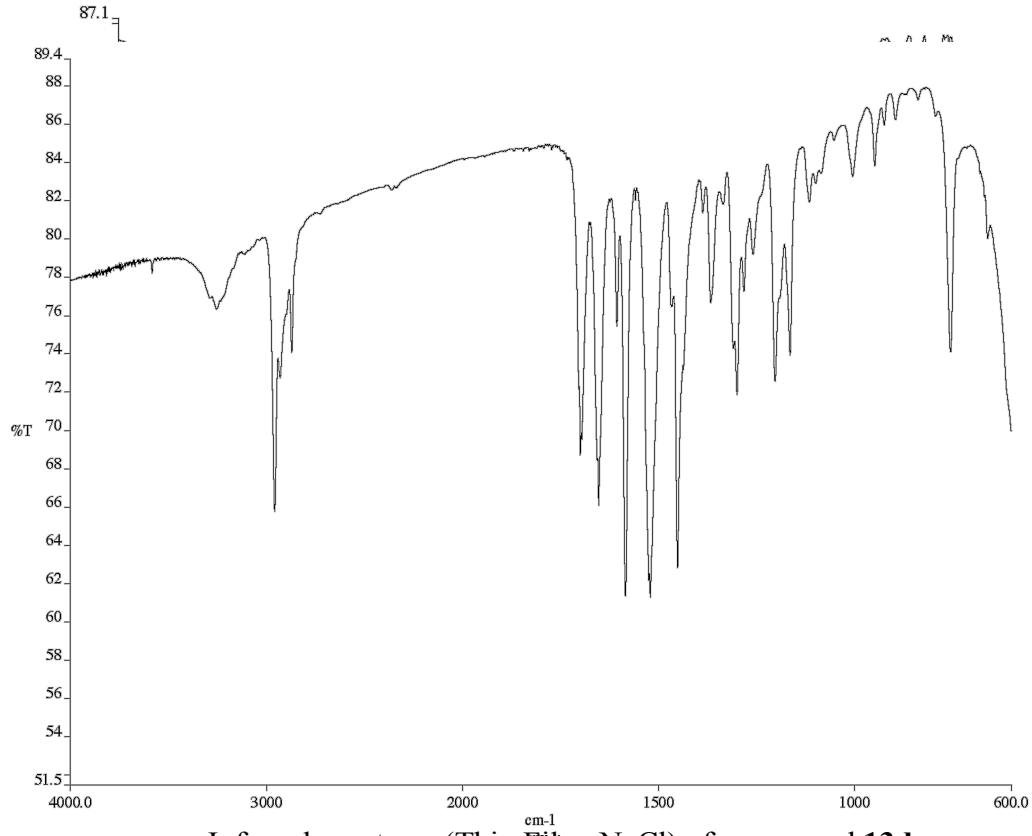
Infrared spectrum (Thin Film, NaCl) of compound **13c**.



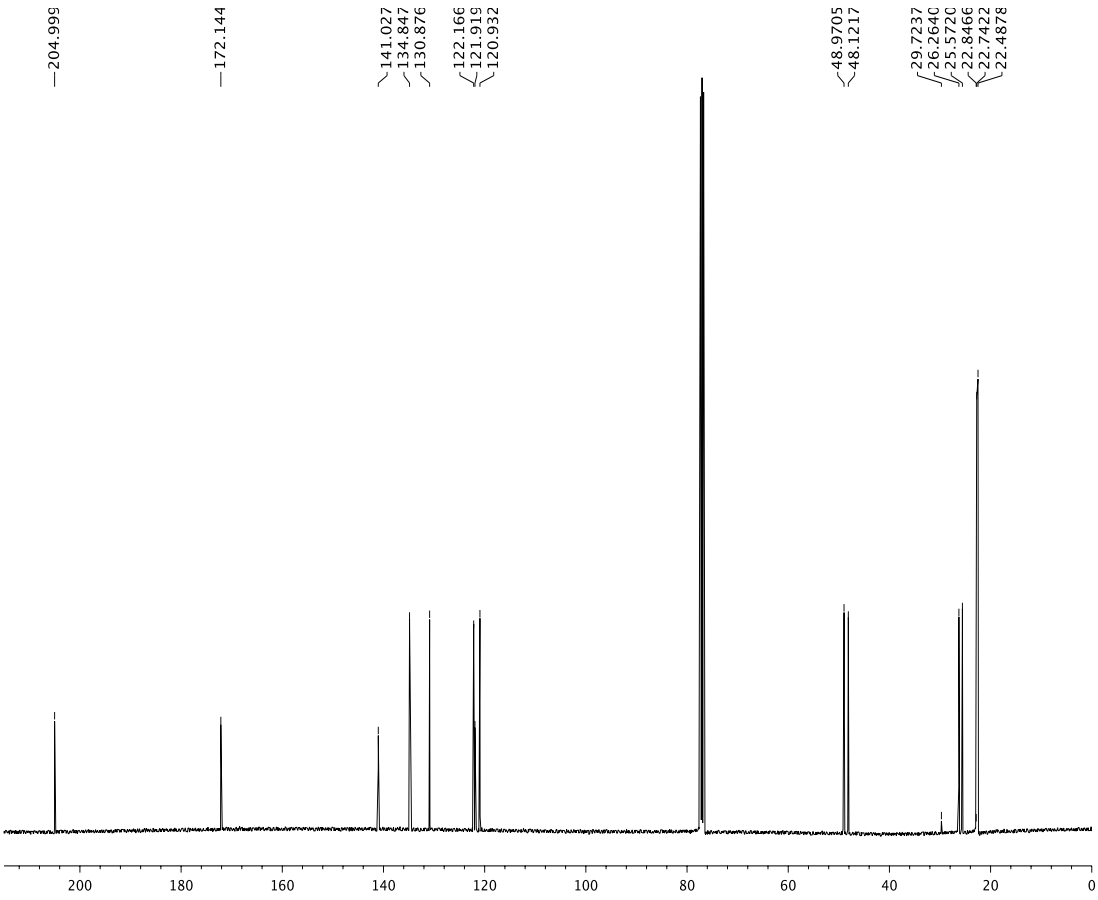
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13c**.



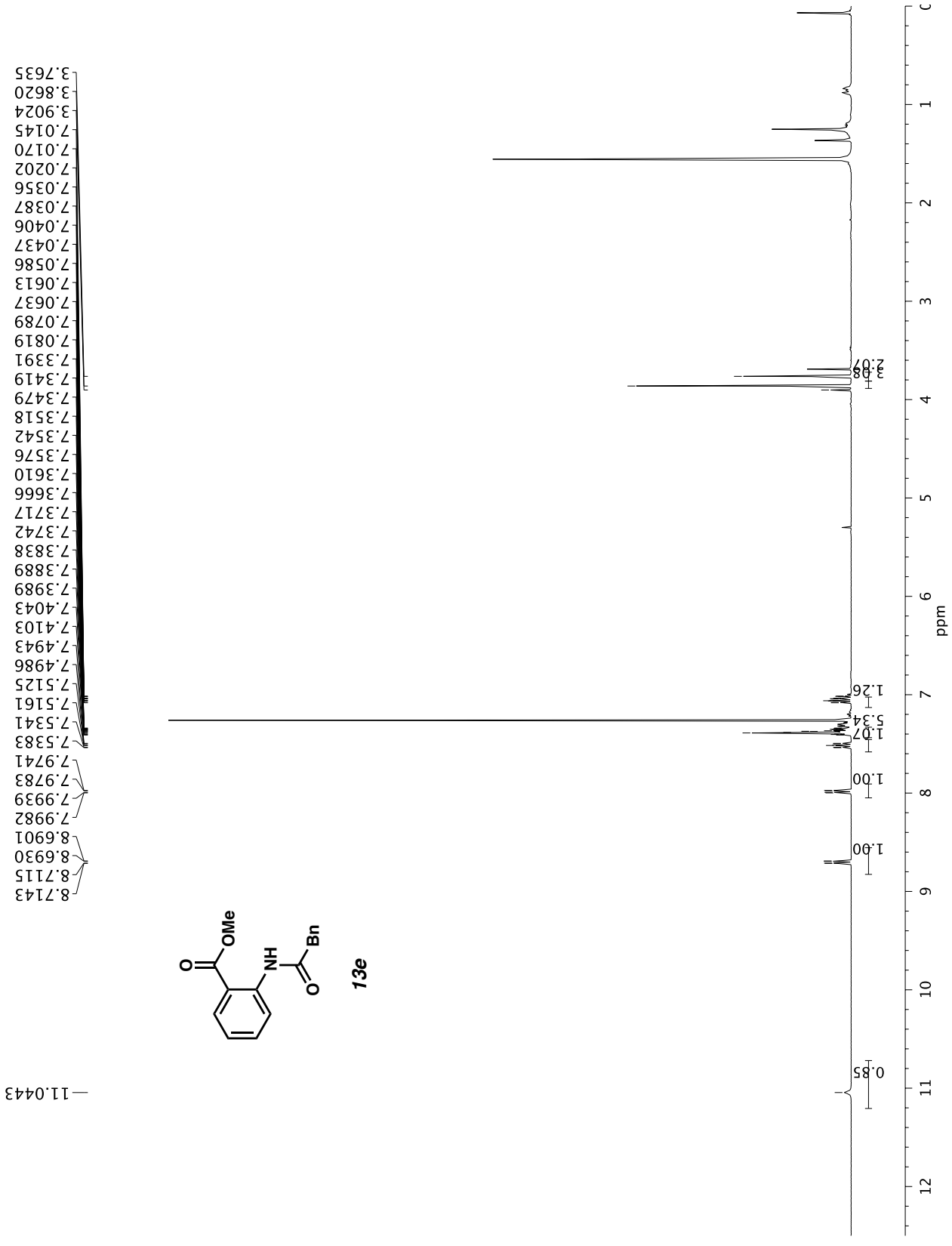
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13d.**



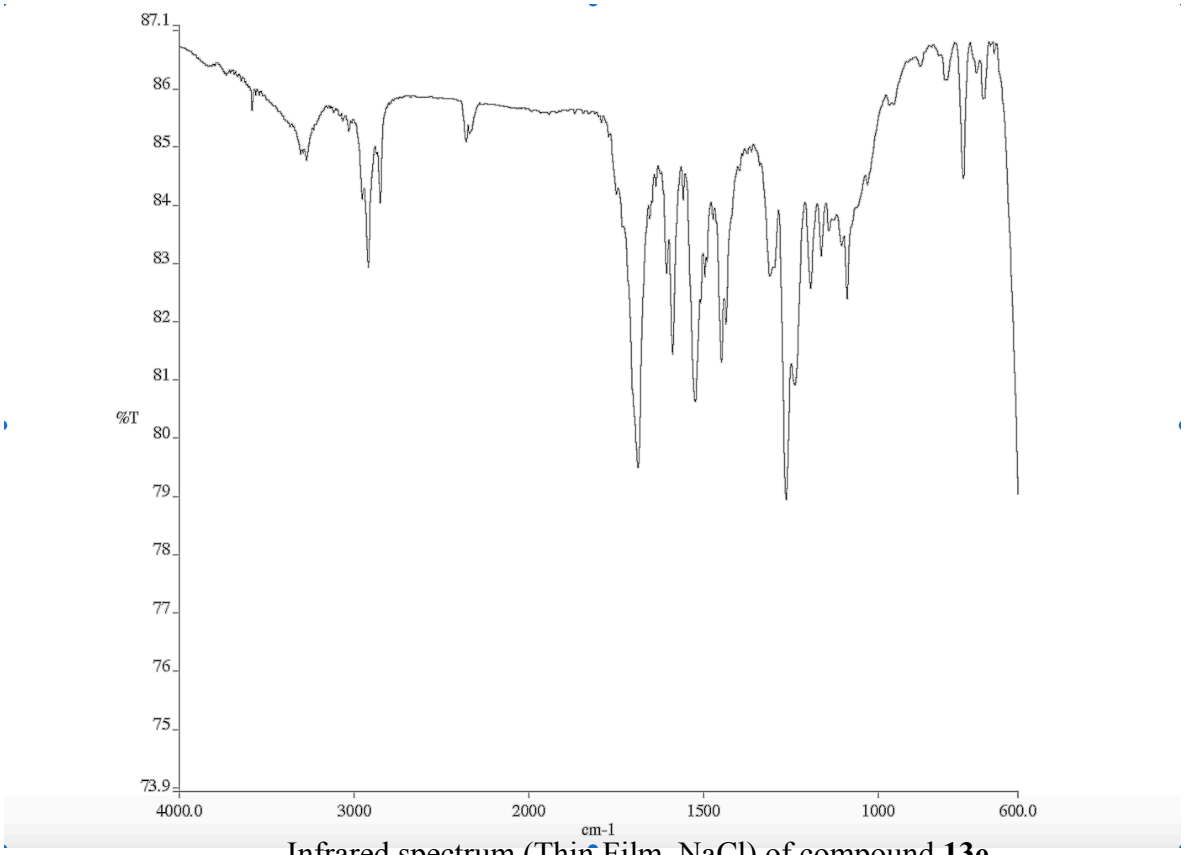
Infrared spectrum (Thin Film, NaCl) of compound **13d**.



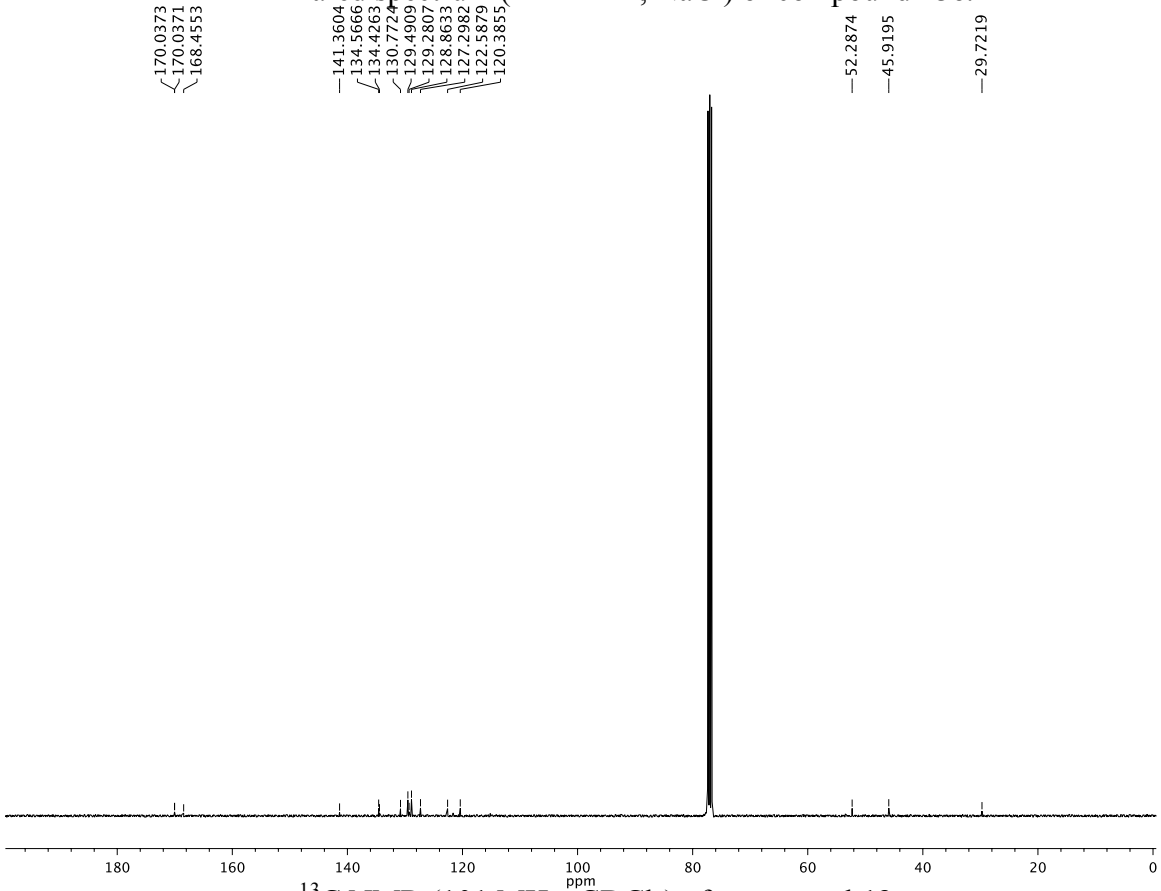
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13d**.



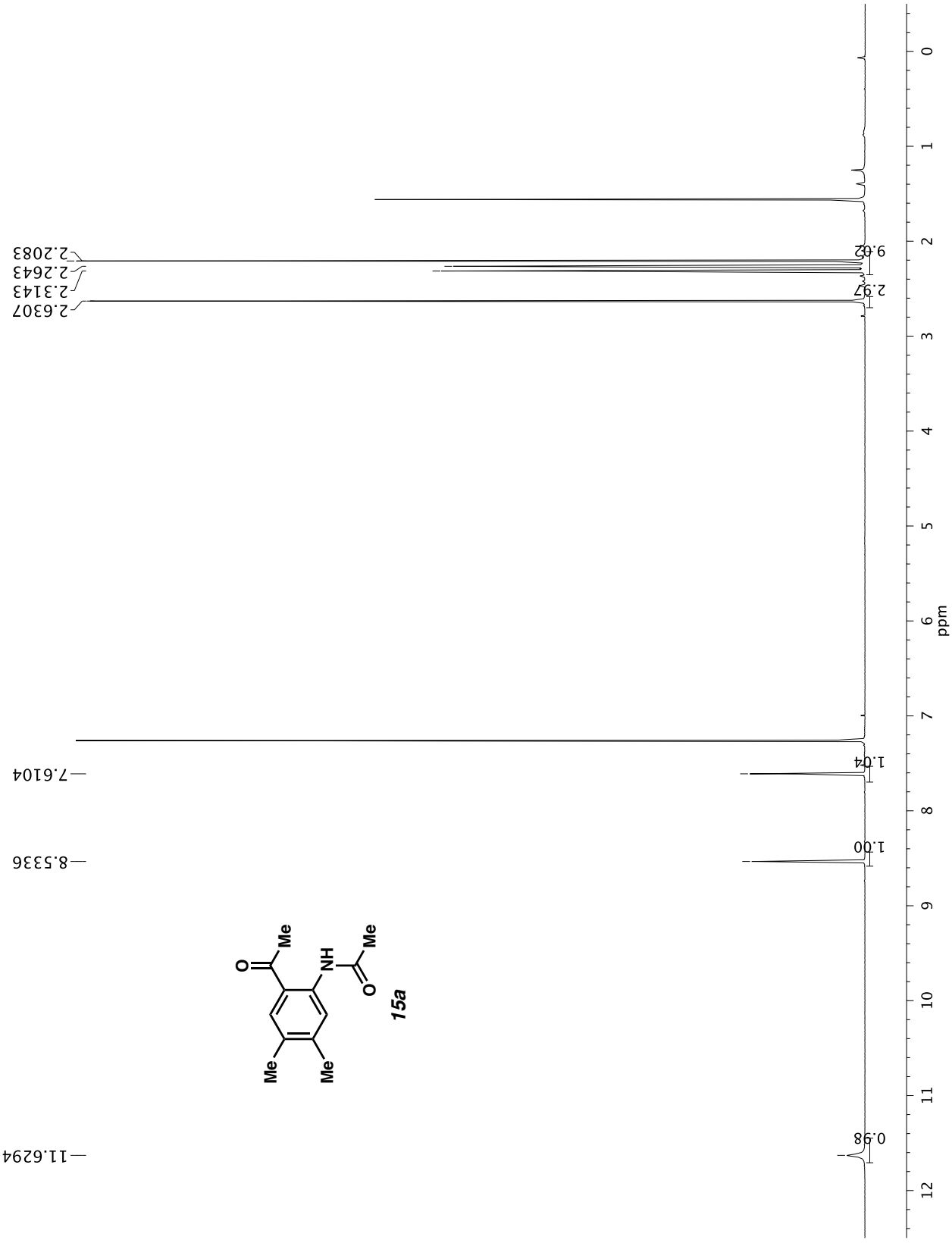
^{1}H NMR (400 MHz, $CDCl_3$) of compound **13e.**



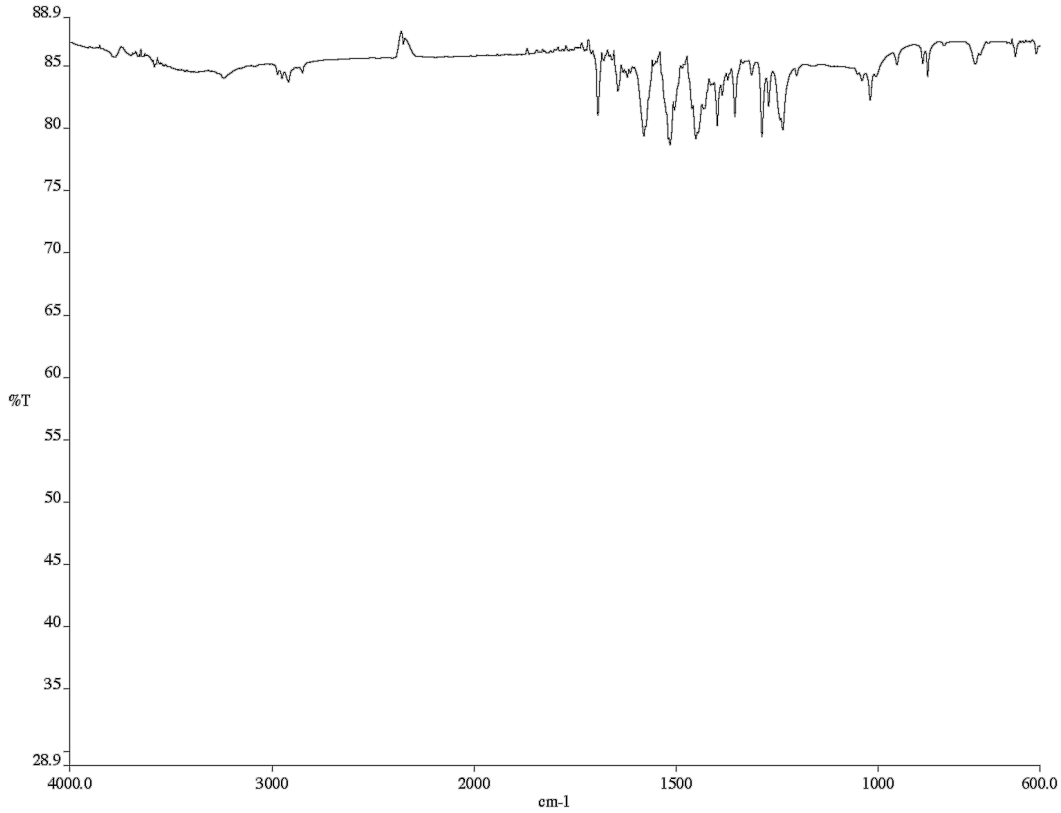
Infrared spectrum (Thin Film, NaCl) of compound **13e**.



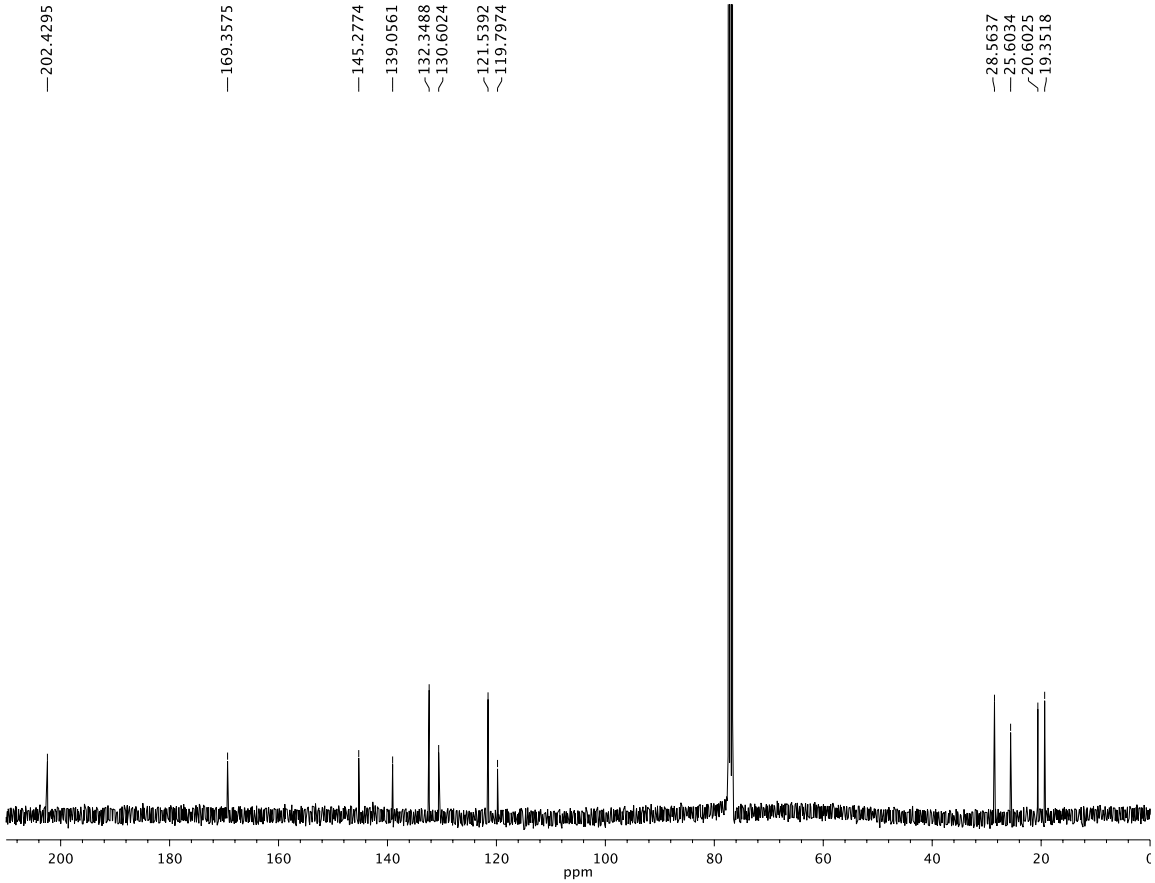
^{13}C NMR (101 MHz, $CDCl_3$) of compound **13e**.



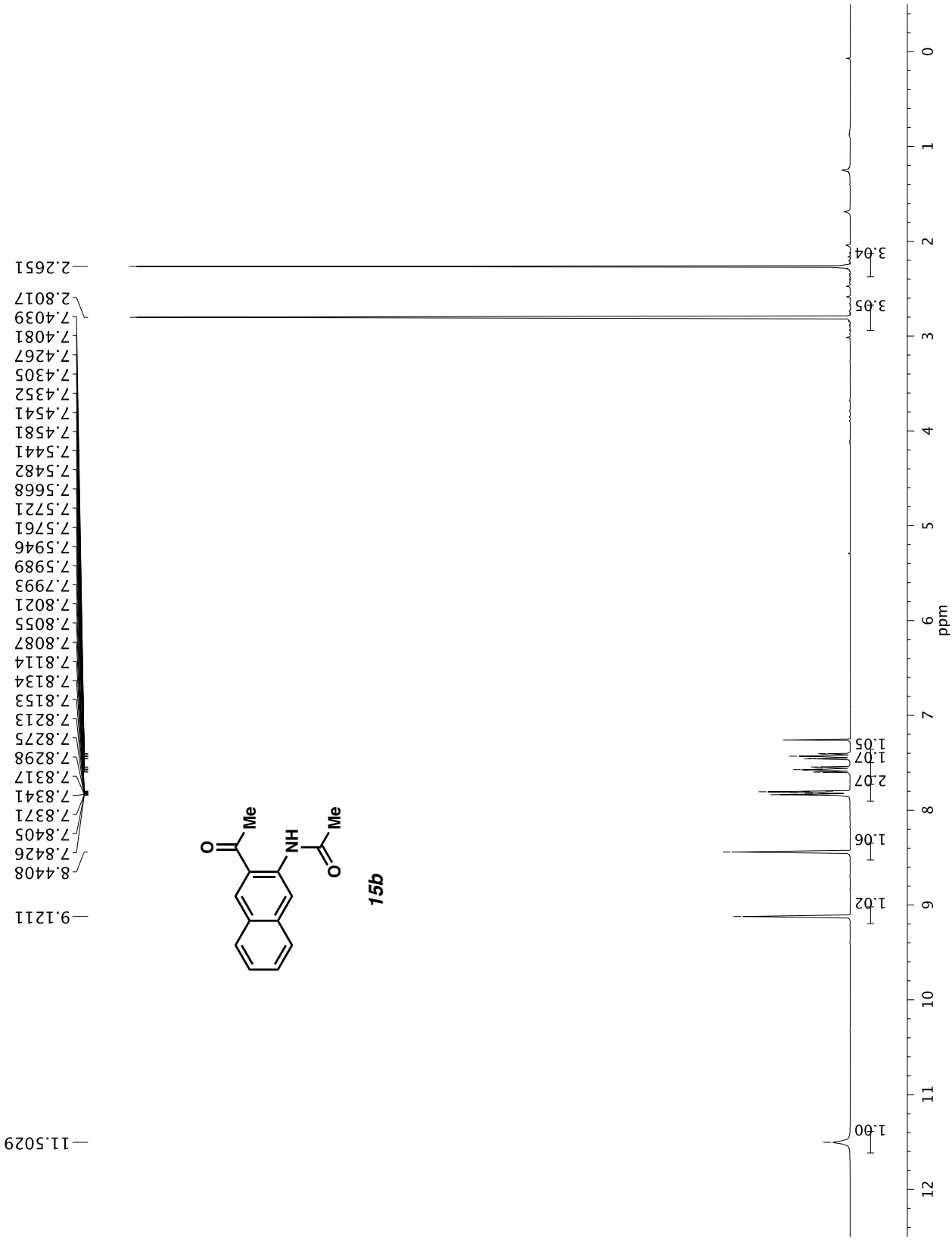
^{1}H NMR (400 MHz, $CDCl_3$) of compound **15a.**



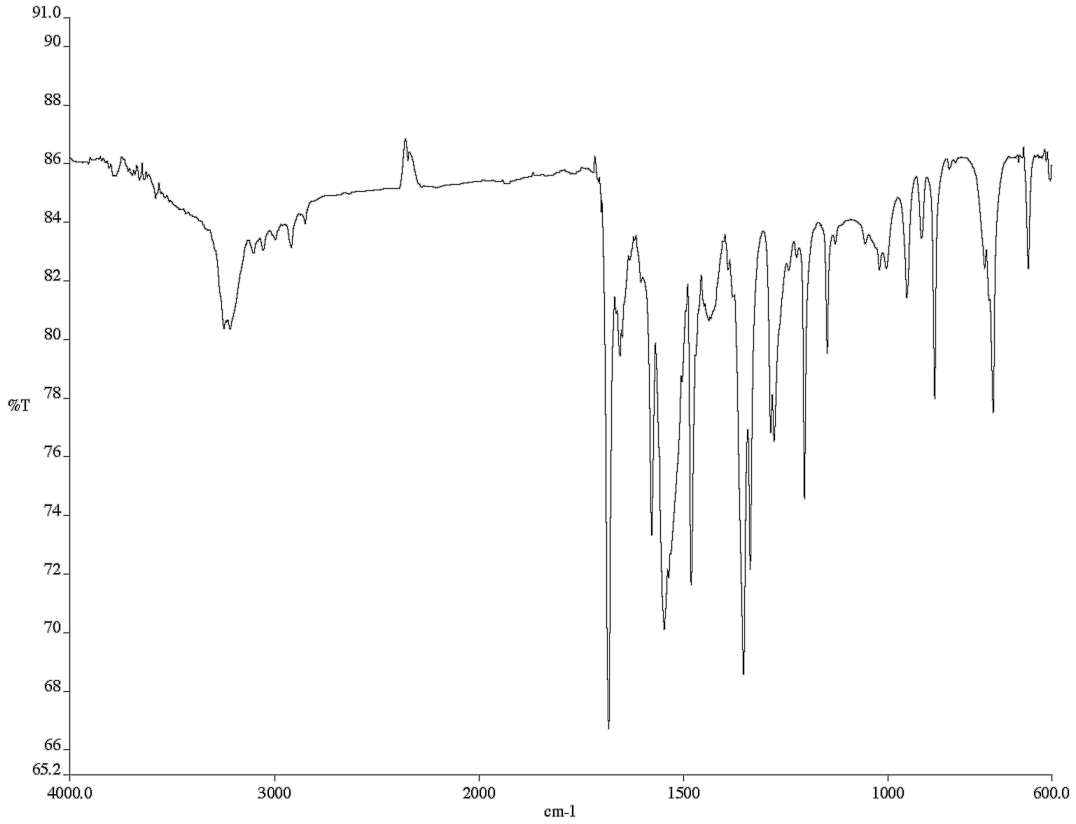
Infrared spectrum (Thin Film, NaCl) of compound **15a**.



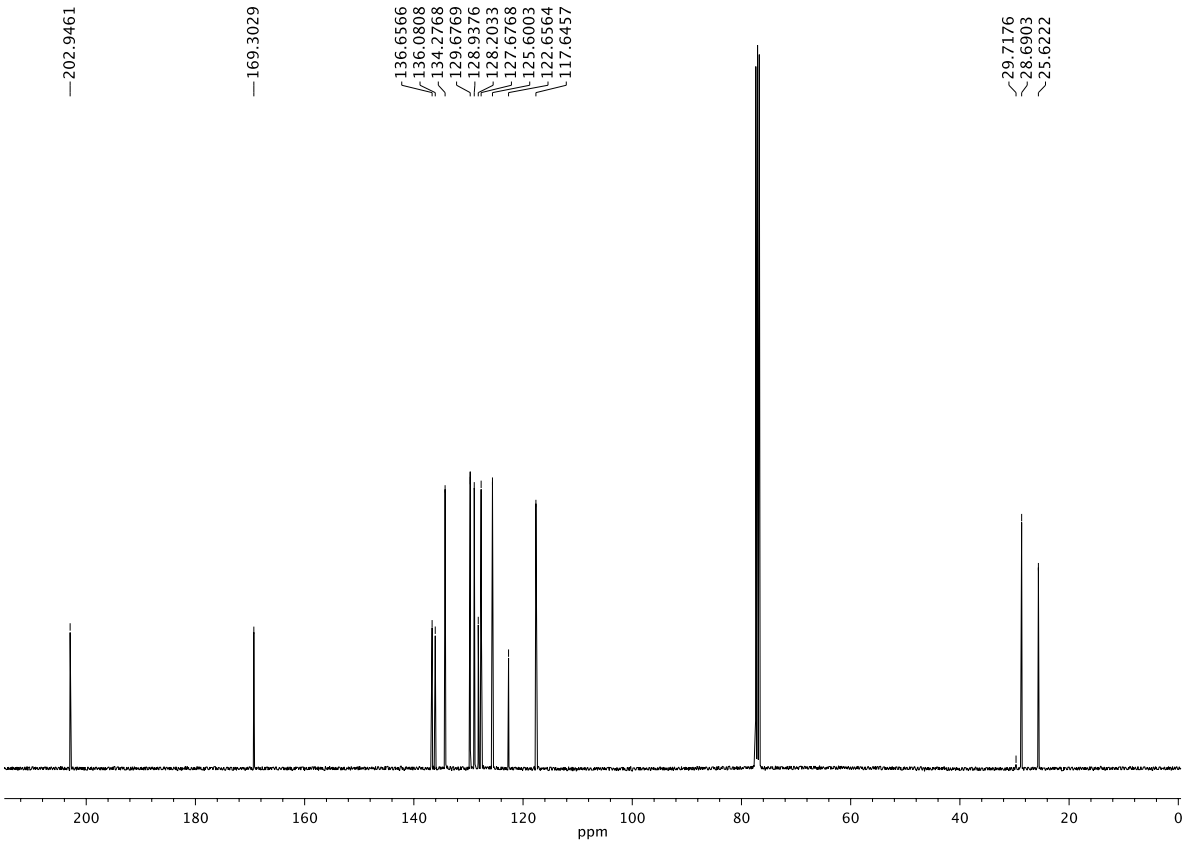
^{13}C NMR (101 MHz, $CDCl_3$) of compound **15a**.



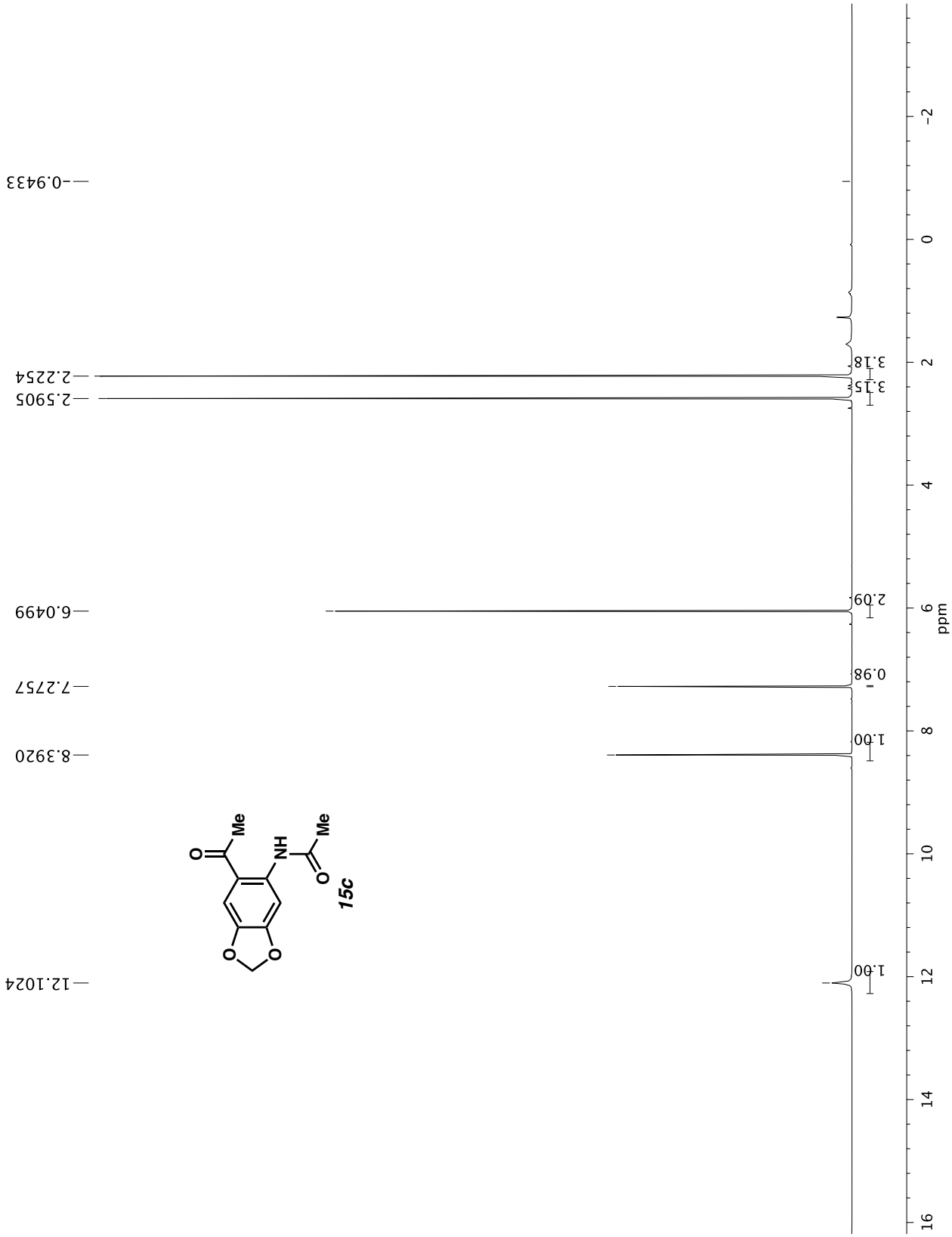
^{1}H NMR (400 MHz, $CDCl_3$) of compound **15b.**



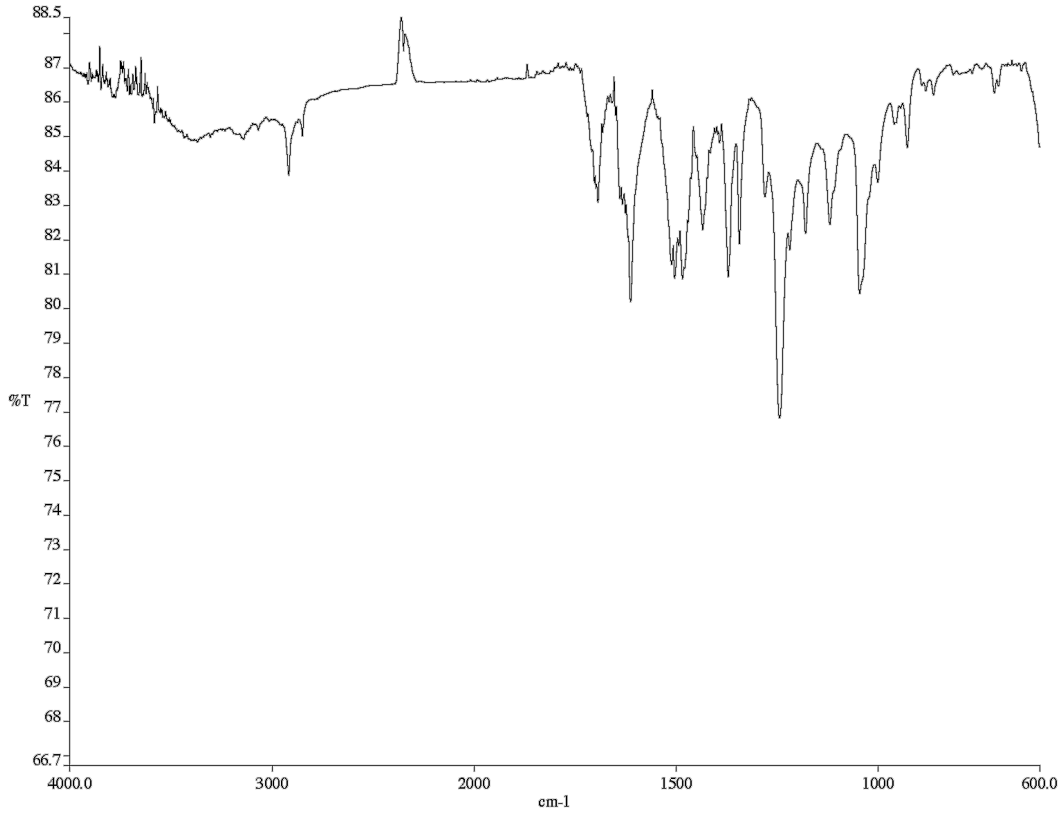
Infrared spectrum (Thin Film, NaCl) of compound **15b**.



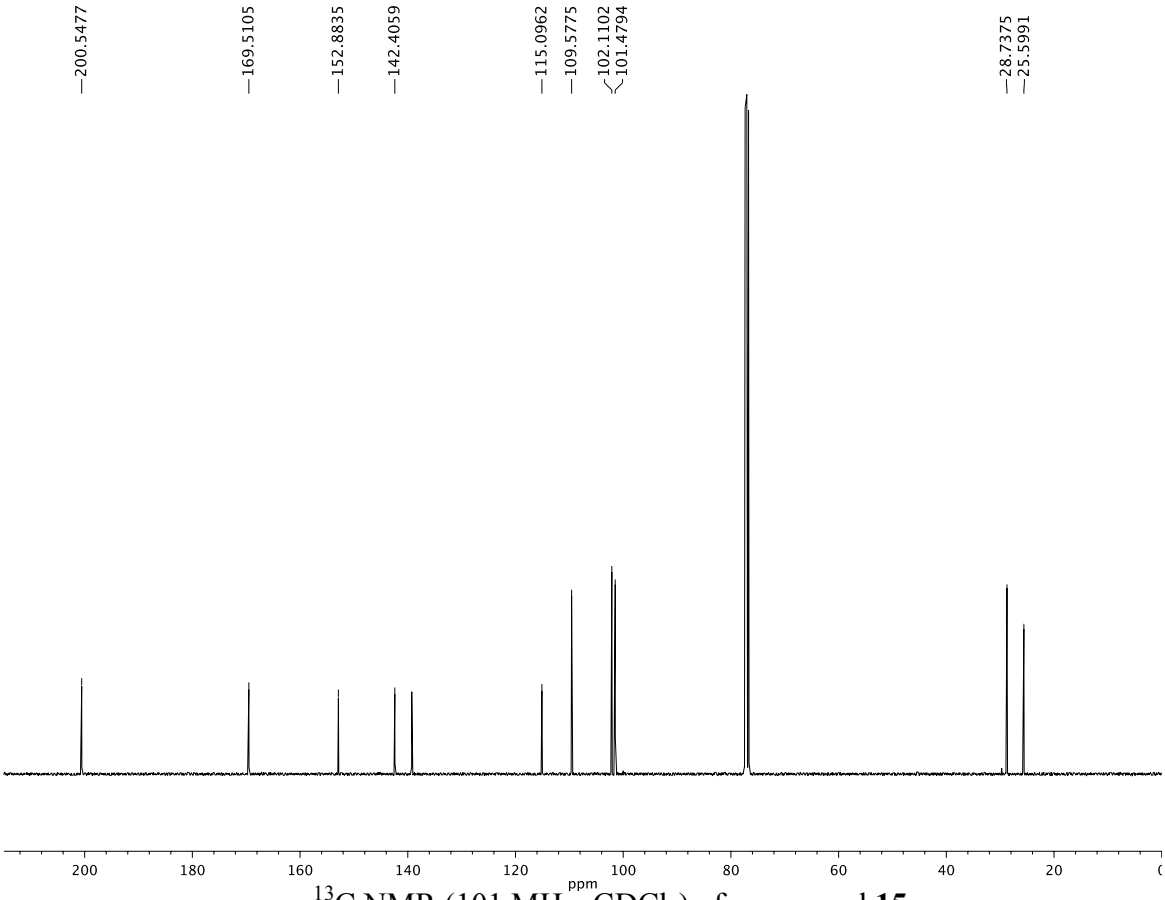
^{13}C NMR (101 MHz, $CDCl_3$) of compound **15b**.



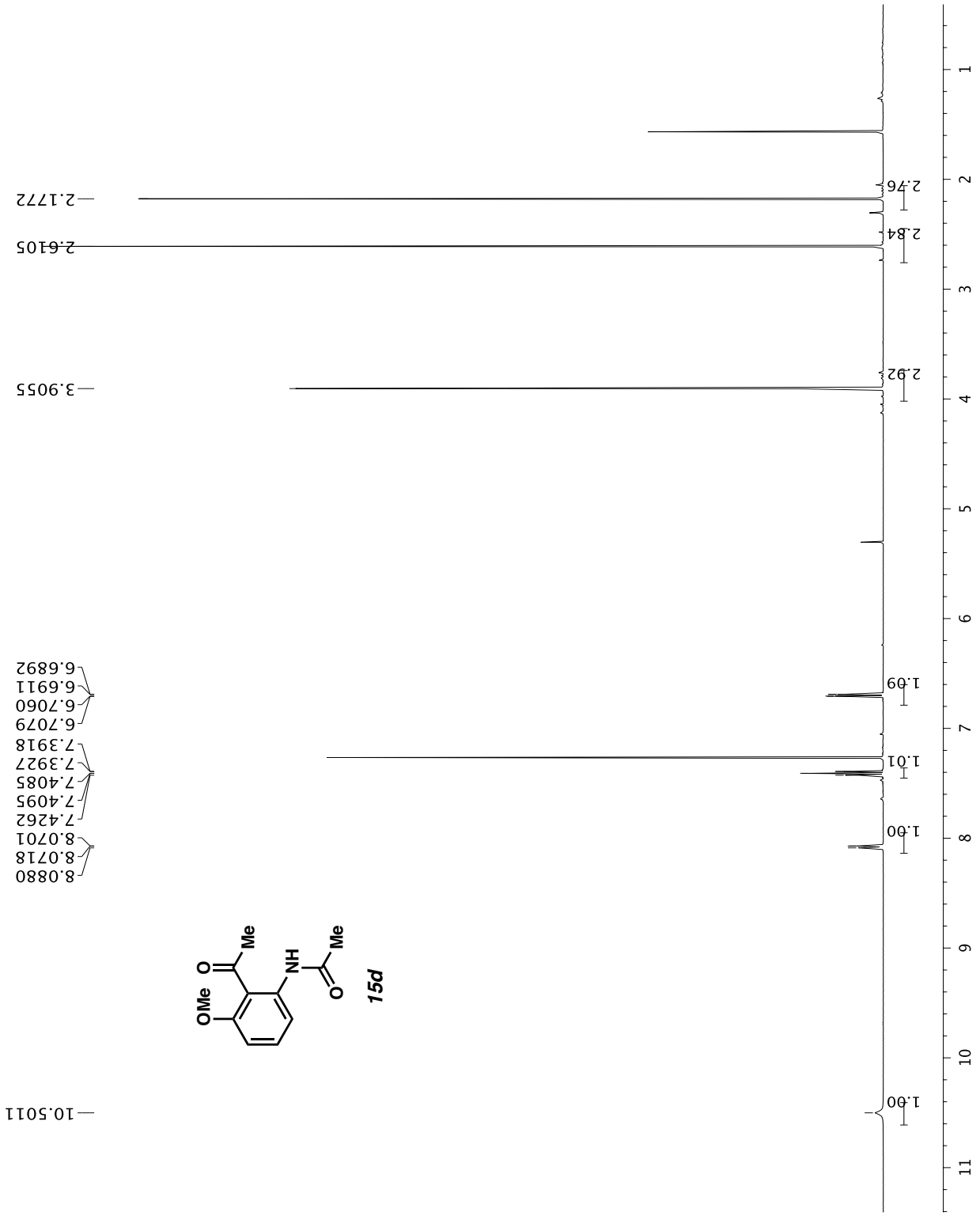
^{1}H NMR (400 MHz, $CDCl_3$) of compound **15c.**



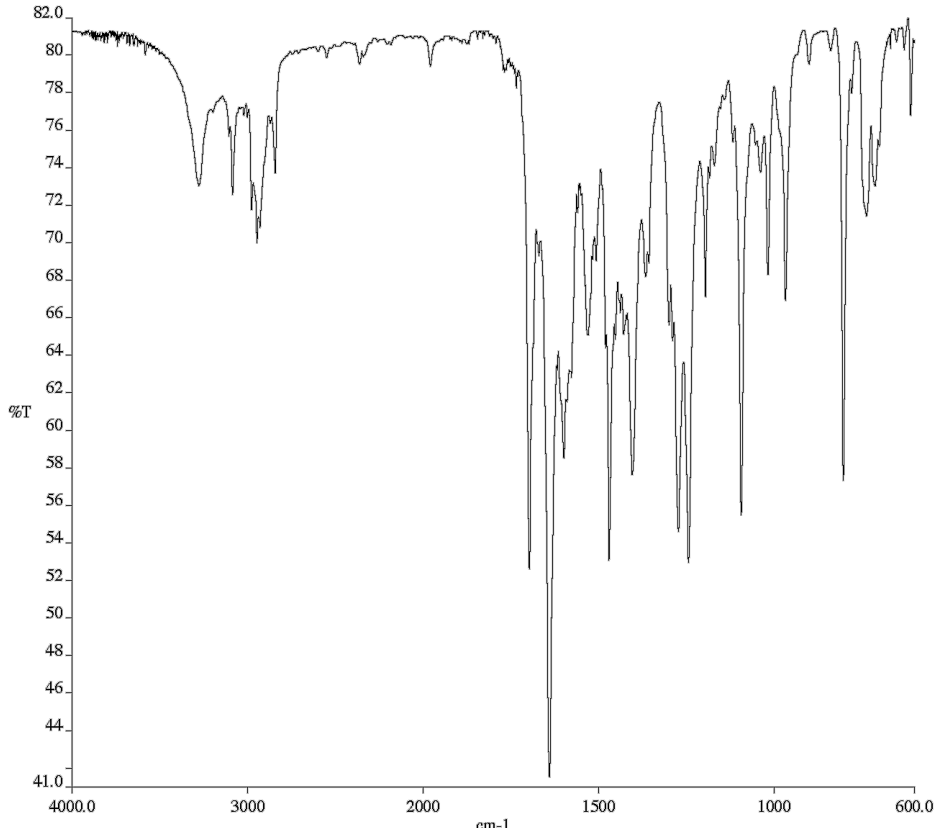
Infrared spectrum (Thin Film, NaCl) of compound **15c**.



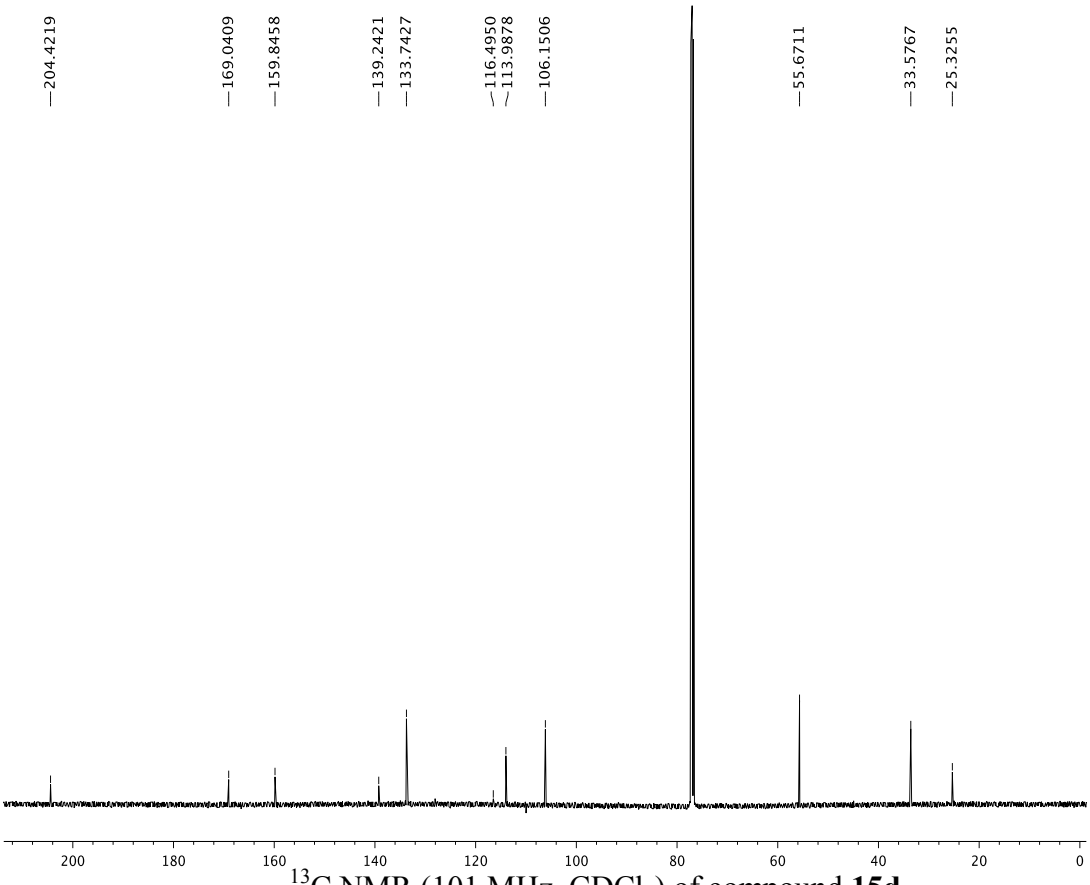
^{13}C NMR (101 MHz, $CDCl_3$) of compound **15c**.



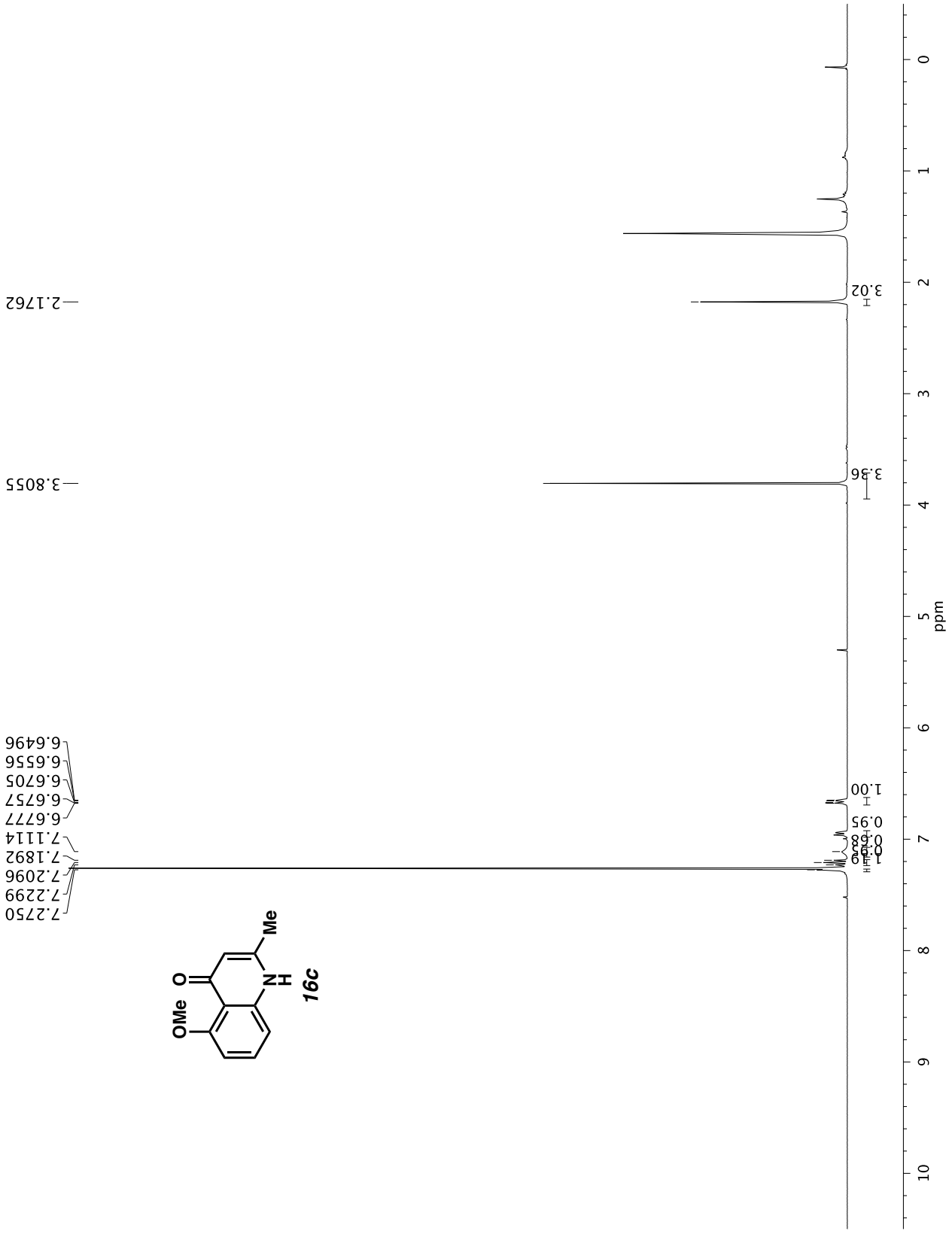
^{1}H NMR (500 MHz, $CDCl_3$) of compound **15d.**



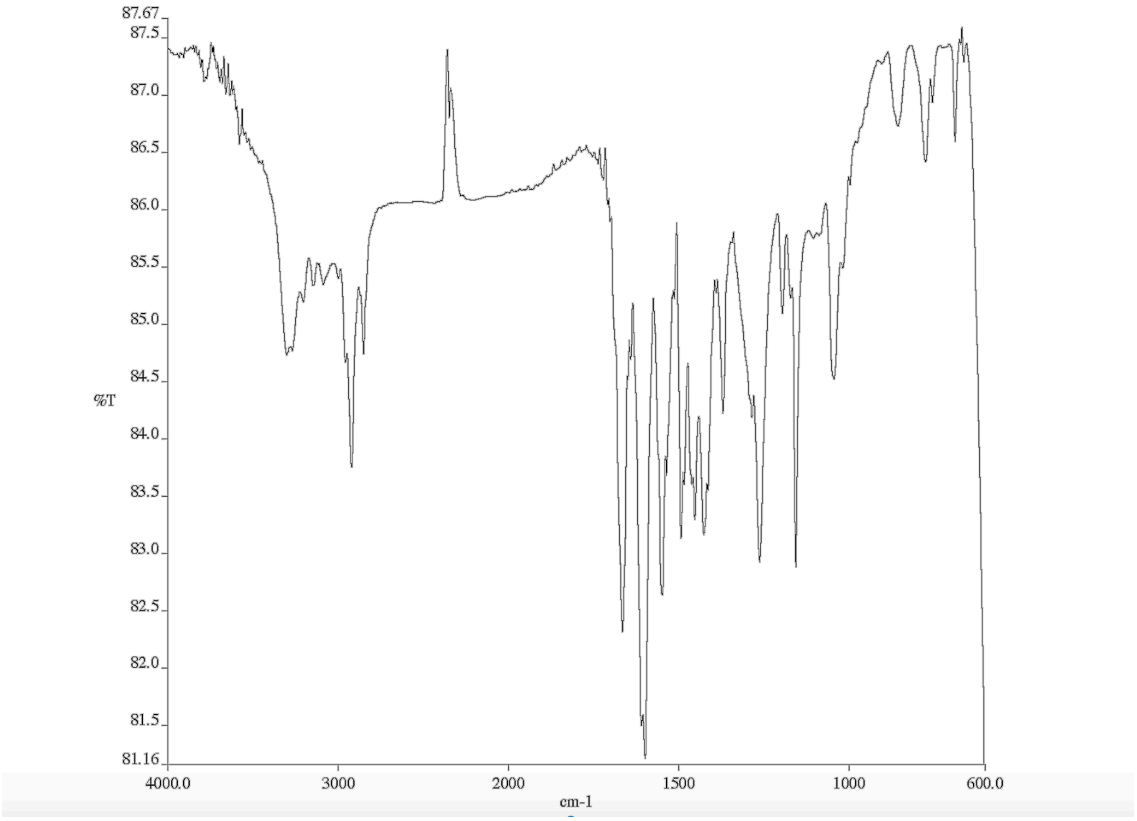
Infrared spectrum (Thin Film, NaCl) of compound **15d**.



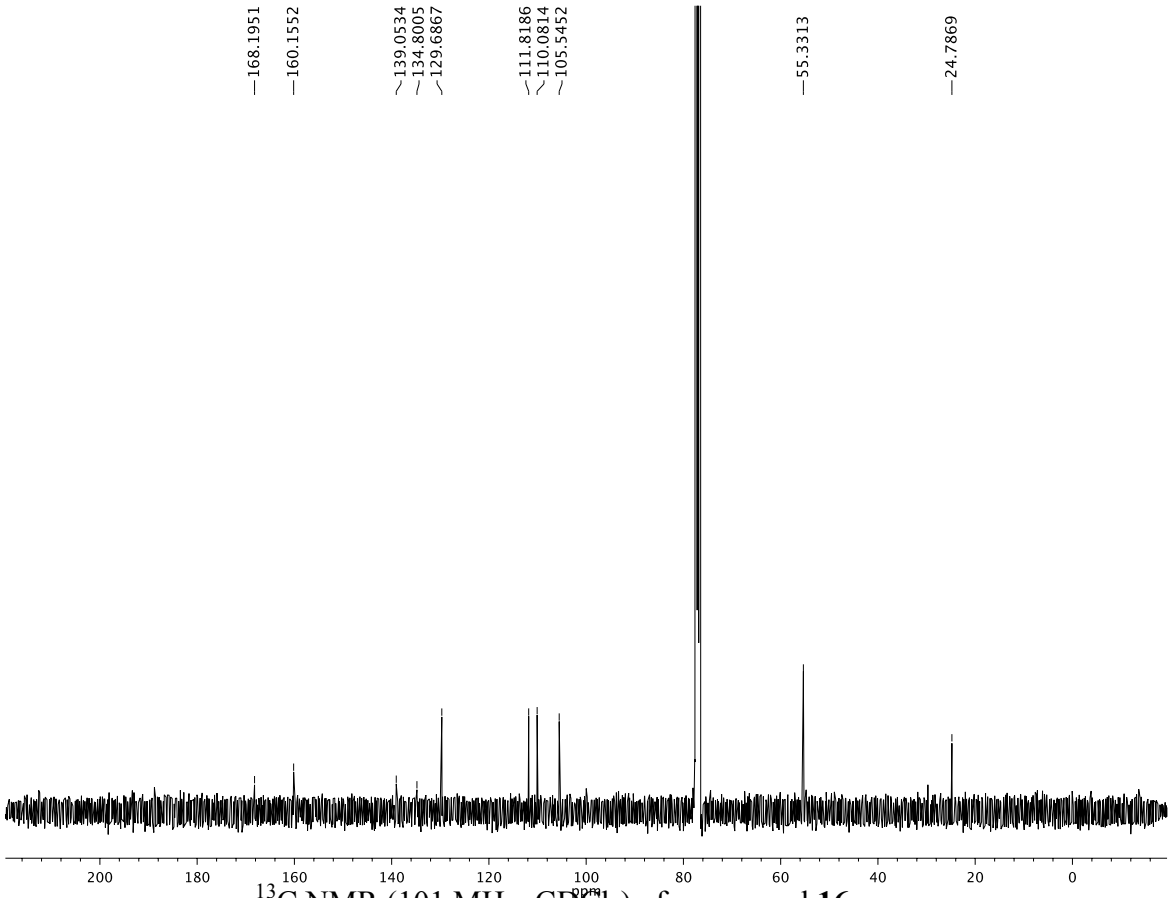
^{13}C NMR (101 MHz, $CDCl_3$) of compound **15d**.



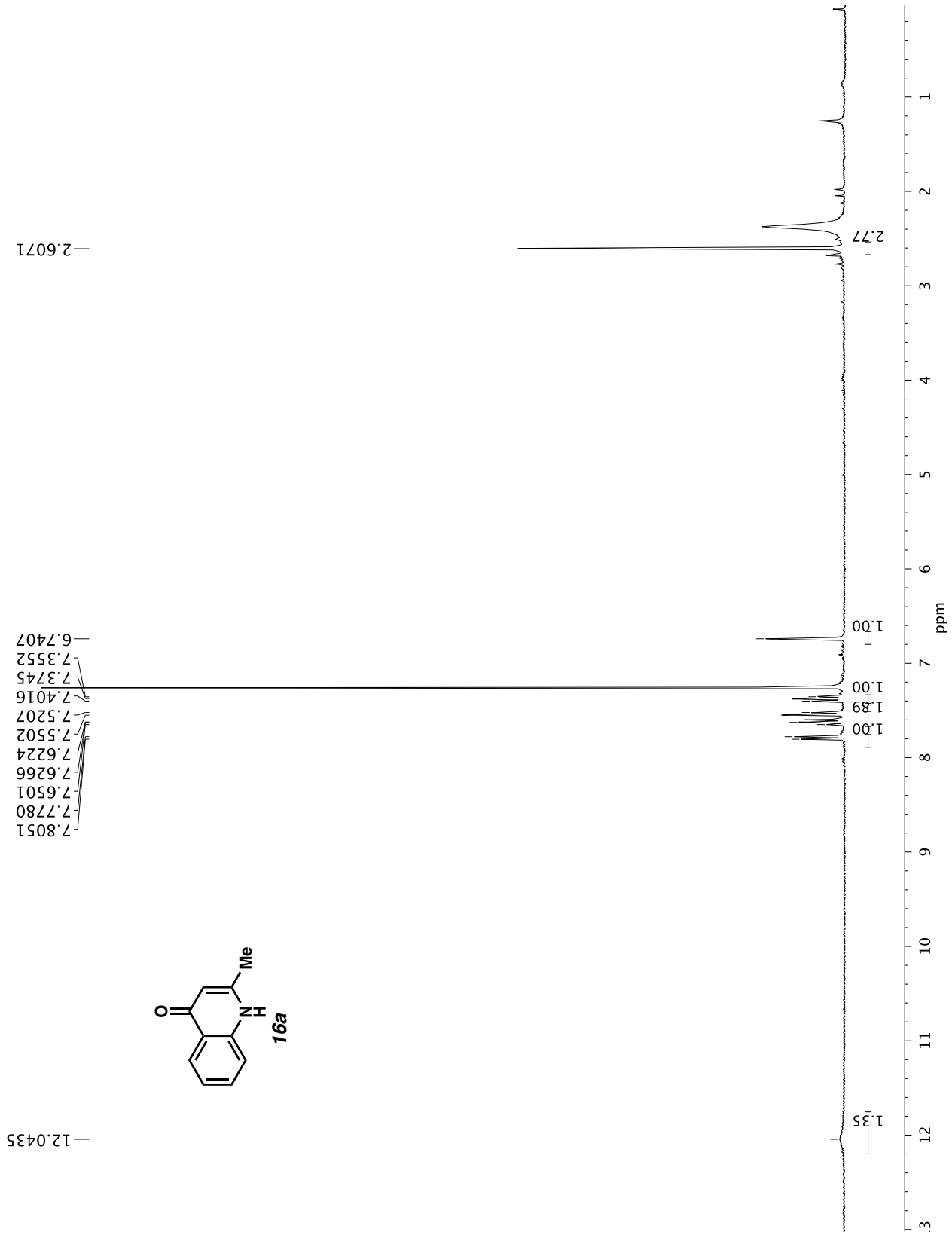
^{1}H NMR (400 MHz, $CDCl_3$) of compound **16c.**



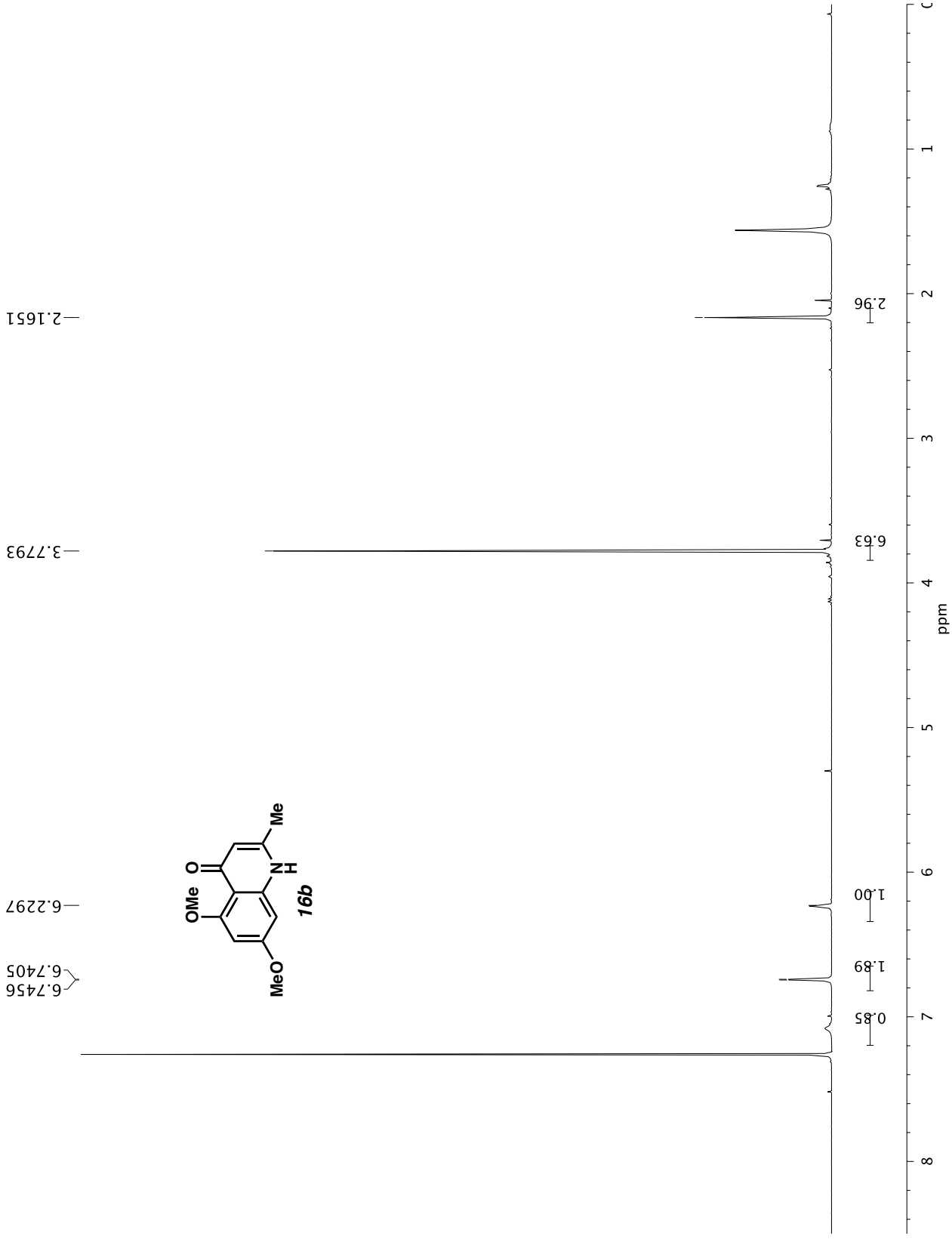
Infrared spectrum (Thin Film, NaCl) of compound **16c**.



^{13}C NMR (101 MHz, $CDCl_3$) of compound **16c**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **16a.**



^{1}H NMR (400 MHz, $CDCl_3$) of compound **16b.**