Supporting Information for

Palladium-Catalyzed Decarboxylative Asymmetric Allylic Alkylation of 1,4-diazepan-5-ones

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Materials and Methods

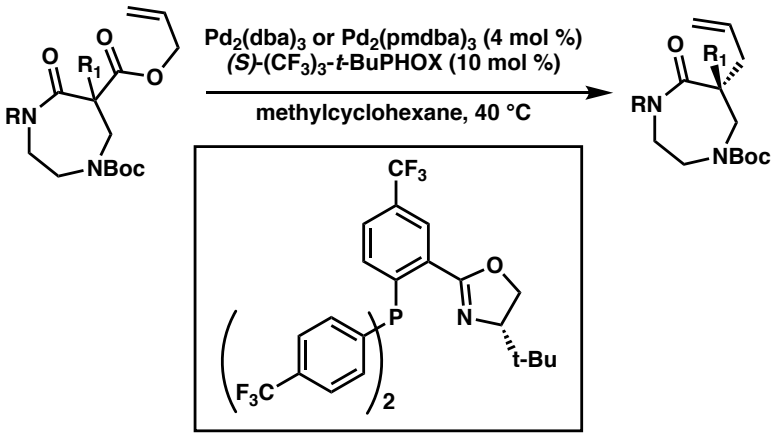
Unless otherwise stated, reactions were performed in flame-dried glassware under an argon or nitrogen atmosphere using dry, deoxygenated solvents. Solvents were dried by passage through an activated alumina column under argon.[1] Reaction progress was monitored by thin-layer chromatography (TLC) or Agilent 1290 UHPLC-MS. TLC was performed using E. Merck silica gel 60 F254 precoated glass plates (0.25 mm) and visualized by UV fluorescence quenching or $KMnO_4$ staining. Silicycle Silia*Flash*® P60 Academic Silica gel (particle size 40–63 nm) was used for flash chromatography. ^{1}H NMR spectra were recorded on Varian Inova 500 MHz, Varian 400 MHz, and Bruker 400 MHz spectrometers and are reported relative to residual $CHCl_3$ (δ 7.26 ppm). ^{13}C NMR spectra were recorded on a Varian Inova 500 MHz spectrometer (125 MHz), a Varian 400 MHz spectrometer (100 MHz), and Bruker 400 MHz spectrometers (100 MHz) and are reported relative to $CHCl_3$ (δ 77.16 ppm). Data for ^{1}H NMR are reported as follows: chemical shift (δ ppm) (multiplicity, coupling constant (Hz), integration). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, sept = septuplet, m = multiplet, br s = broad singlet, br d = broad doublet. Data for ^{13}C NMR are reported in terms of chemical shifts (δ ppm) Some reported spectra include minor solvent impurities of water (δ 1.56ppm), 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. Most NMR spectra are complicated by rotational isomerism about amide bonds. This behavior is illustrated by variable-temperature NMR spectra of compound **4e** in DMSO (p. S102). IR spectra were obtained by use of a Perkin Elmer Spectrum BXII spectrometer or Nicolet 6700 FTIR spectrometer using thin films deposited on NaCl plates and reported in frequency of absorption (cm^{-1}). Optical rotations were measured with a Jasco P-2000 polarimeter operating on the sodium D-line (589 nm), using a 100 mm path-length cell. Analytical SFC was performed with a Mettler SFC supercritical CO_2 analytical chromatography system utilizing Chiralpak (AD-H, AS-H or IC) or Chiralcel (OD-H, OJ-H, or OB-H) columns (4.6 mm x 25 cm) obtained from Daicel Chemical Industries, Ltd. High resolution mass spectra (HRMS) were obtained from 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+). Absolute stereochemistry is assigned by analogy to previous results by our group.[2]

Reagents were purchased from commercial sources and used as received unless otherwise stated. Ligands (*S*)-$(CF_3)_3$-*t*-BuPHOX and (*S*)-Ty-PHOX were prepared according to literature procedures.[3,4]

List of Abbreviations:

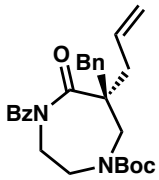
ee – enantiomeric excess, SFC – supercritical fluid chromatography, TLC – thin-layer chromatography, IPA – isopropanol, An = 4-anisoyl, MeCy = methylcyclohexane

General Procedure for Pd-Catalyzed Allylic Alkylation Reactions



(S)-$(CF_3)_3$-*t*-BuPHOX

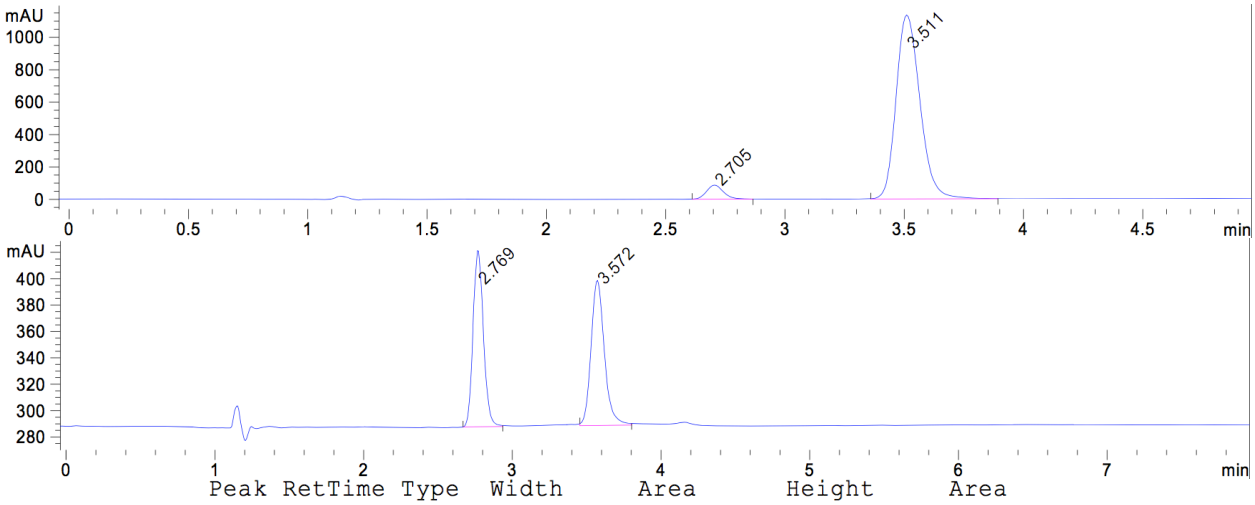
In a N_2 filled glovebox, $Pd_2(dba)_3$ (4 mol %) or $Pd_2(pmdba)_3$ (4 mol %) and (*S*)-$(CF_3)_3$-*t*-BuPHOX (10 mol %) were suspended in methylcyclohexane (2 mL) in a 20 mL glass vial. After stirring for 20 minutes at 25 °C, the appropriate diazepanone (1.0 equiv) and methylcyclohexane (5.2 mL, total substrate concentration 0.014 M) were added to the pre-stirred catalyst solution. The vial was then sealed and heated to 40 °C. After full consumption of starting material, as monitored by TLC, the reaction mixture was exposed to air. The crude reaction mixture was loaded directly onto a flash column and the product was isolated by silica gel flash chromatography.



***tert*-butyl (*S*)-6-allyl-4-benzoyl-6-benzyl-5-oxo-1,4-diazepane-1-carboxylate (4a)**

Prepared according to the general procedure with allyl ester **3a** (51.2 mg, 0.104 mmol, 1.0

equiv), $Pd_2(pmdba)_3$ (4.4 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (15% EtOAc/hexanes) to provide benzyl diazepanone **4a** as a colorless oil (43.4 mg, 0.0967 mmol, 93% yield, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 – 7.40 (m, 3H), 7.40 – 7.32 (m, 2H), 7.32 – 7.19 (m, 3H), 7.19 – 7.00 (m, 2H), 5.88 (br s, 1H), 5.26 – 5.07 (m, 2H), 4.26 – 4.03 (m, 1H), 3.94 (d, *J* = 15.4 Hz, 1H), 3.73 (d, *J* = 42.2 Hz, 1H), 3.54 (d, *J* = 15.3 Hz, 1H), 3.40 (s, 2H), 3.09 (dd, *J* = 61.0, 13.7 Hz, 1H), 2.94 – 2.34 (m, 3H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 174.8, 156.0, 155.4, 136.6, 136.4, 133.0, 131.5, 130.8, 128.6, 128.4, 127.8, 127.1, 120.0, 119.7, 80.8, 54.3, 53.9, 49.1, 47.4, 46.9, 42.5, 42.0, 41.5, 40.3, 28.5; IR (Neat Film, NaCl) 3062, 2975, 2928, 1693, 1682, 1601, 1452, 1415, 1392, 1365, 1322, 1283, 1246, 1156, 1044, 978, 917, 865, 728, 697 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{27}H_{33}N_2O_4$ $[M+H]^+$: 449.2435, found 449.2429; $[\alpha]_D^{22.4}$ +14.19 (*c* 0.66, $CHCl_3$); SFC conditions: 20% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 3.51, minor = 2.71.



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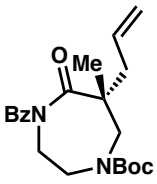
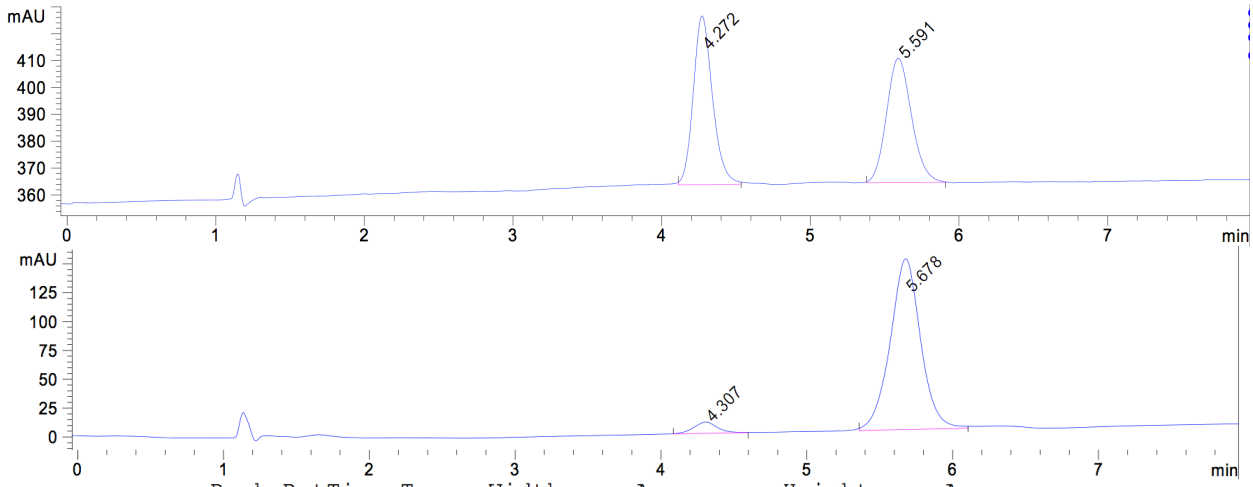


tert-butyl (*R*)-6-allyl-4-benzoyl-6-methyl-5-oxo-1,4-diazepane-1-carboxylate (4b)

Prepared according to the general procedure with allyl ester **3b** (39.0 mg, 0.0937 mmol, 1.0 equiv), $Pd_2(pmdba)_3$ (4.4 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide methyl diazepanone **4b** as a colorless, waxy solid (32.3 mg, 0.868 mmol, 93% yield, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.43 (m, 3H), 7.43 – 7.32 (m, 2H), 5.74 (ddt, *J* = 17.1, 9.9, 7.4 Hz, 1H), 5.19 – 5.06 (m, 2H), 4.30 – 3.89 (m, 3H), 3.85 – 3.69 (m, 1H), 3.66 – 3.34 (m, 2H), 2.63 – 2.20 (m, 2H), 1.50 (s, 9H), 1.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.8, 174.5, 155.4, 155.0, 136.3, 132.9, 131.4, 128.3, 127.5, 119.5, 80.7, 50.9, 49.9, 47.2, 46.5, 42.5, 42.1, 41.8, 28.4, 23.5, 23.1; IR (Neat Film, NaCl) 2976, 2933, 1694, 1450, 1418, 1392, 1366, 1323, 1284, 1246, 1146, 1057, 983, 917, 868, 768, 729, 696 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{21}H_{29}N_2O_4$ $[M+H]^+$: 373.2122, found 373.2117; $[\alpha]_D^{22.31}$ –12.69 (*c* 1.0, $CHCl_3$); SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): minor = 4.31, major = 5.68.



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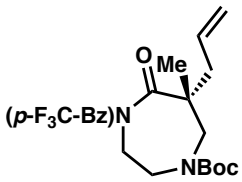
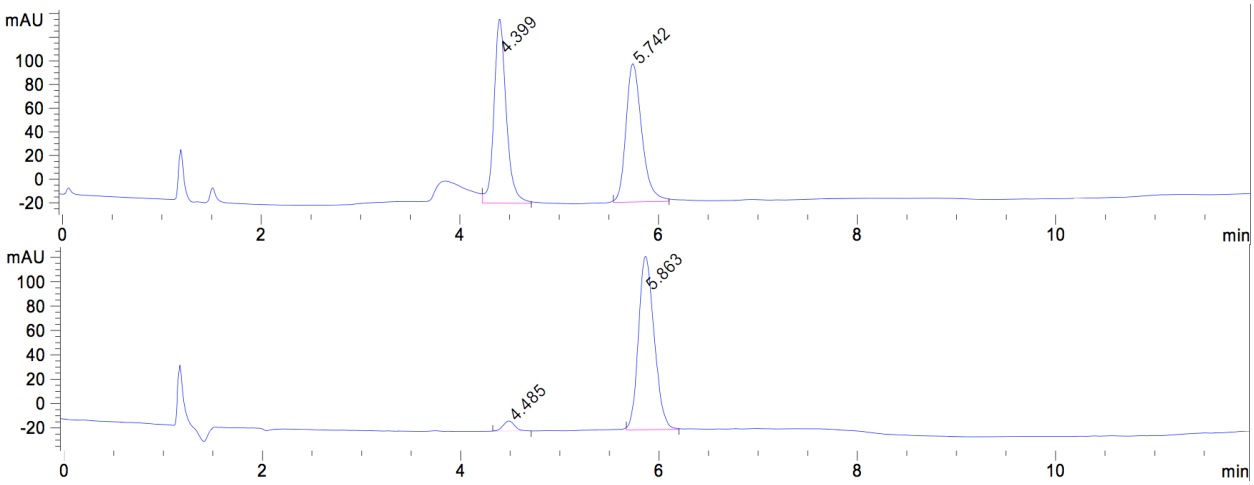
2	5.678	BB	0.2215	2149.23340	147.92346	95.0636
Totals :				2260.83681	157.80833	



tert-butyl (_R_)-6-allyl-6-methyl-5-oxo-4-(4-(trifluoromethyl)benzoyl)-1,4-diazepane-1-carboxylate (4c)

Prepared according to the general procedure with allyl ester **3c** (55.3 mg, 0.114 mmol, 1.0 equiv), $Pd_2(dba)_3$ (4.2 mg, 4.57 μmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (6.7 mg, 0.011 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide methyl diazepanone **4c** as a colorless oil (45.1 mg, 0.102 mmol, 90% yield, 92% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (d, J = 8.2 Hz, 2H), 7.55 (d, J = 8.2 Hz, 2H), 5.71 (ddt, J = 17.2, 10.1, 7.4 Hz, 1H), 5.23 – 5.07 (m, 2H), 4.21 – 4.03 (m, 2H), 4.02 – 3.64 (m, 2H), 3.58 – 3.38 (m, 2H), 2.59 – 2.21 (m, 2H), 1.49 (s, 9H), 1.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.0, 180.8, 173.1, 155.4, 155.1 140.0, 132.8 (q, $J_{C\text{-}F}$ = 32.9 Hz), 132.7, 127.6, 125.5 (q, $J_{C\text{-}F}$ = 3.7 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 119.9, 81.0, 50.9, 50.0, 47.2, 46.4, 42.4, 42.0, 41.8, 28.5, 23.6, 23.3; IR (Neat Film, NaCl) 3366, 3077, 2978, 2934, 1694, 1452, 1410, 1394, 1367, 1326, 1248, 1167, 1147, 1066, 1014, 984, 925, 852, 764 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{31}F_3N_3O_4$ $[M+NH_4]^+$: 458.2261, found 458.2250; $[\alpha]_D^{22.6}$ –12.32 (*c* 1.0, $CHCl_3$); SFC Conditions: 5% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 4.49, major = 5.86.



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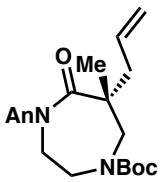
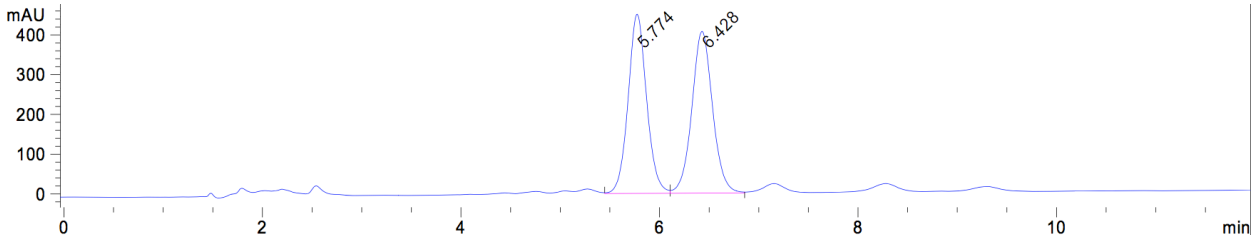
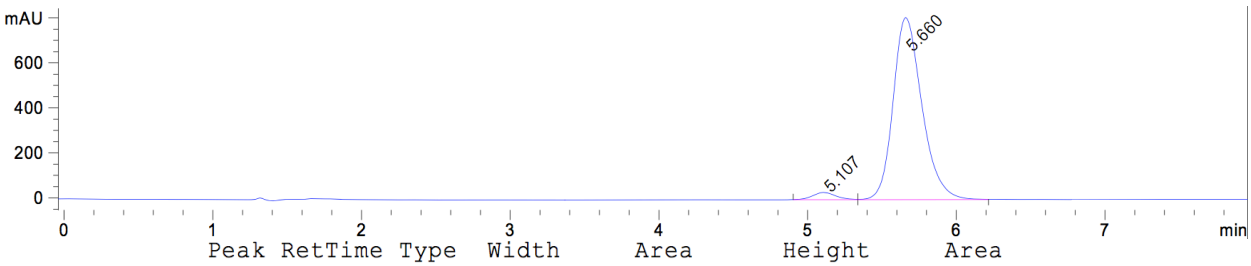
1	4.485	BB	0.1259	66.46159	8.25322	4.0582
2	5.863	BB	0.1731	1571.26794	142.02565	95.9418
Totals :				1637.72953	150.27887	



tert-butyl (_R_)-6-allyl-4-(4-methoxybenzoyl)-6-methyl-5-oxo-1,4-diazepane-1-carboxylate (4d)

Prepared according to the general procedure with allyl ester **3d** (45.8 mg, 0.103 mmol, 1.0 equiv), $Pd_2(dba)_3$ (3.7 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide methyl diazepanone **4d** as a colorless oil (38.9 mg, 0.0966 mmol, 94% yield, 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.44 (m, 2H), 6.95 – 6.75 (m, 2H), 5.76 (m, 1H), 5.26 – 4.99 (m, 2H), 4.24 – 3.87 (m, 3H), 3.83 (s, 3H), 3.75 (m, 1H), 3.59 – 3.37 (m, 2H), 2.60 – 2.25 (m, 2H), 1.49 (s, 9H), 1.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.7, 180.6, 174.3, 162.5, 155.4, 155.0, 133.0, 130.1, 128.1, 119.4, 113.6, 80.7, 55.4, 50.8, 49.8, 47.4, 46.6, 42.7, 42.4, 28.4, 23.5, 23.1; IR (Neat Film, NaCl) 3352, 3076, 2975, 2932, 2841, 2568, 1690, 1605, 1579, 1542, 1511, 1458, 1420, 1392, 1366, 1322, 1284, 1256, 1214, 1168, 1146, 1056, 1032, 984, 924, 868, 842, 807, 762, 743, 736, 650, 633, 621, 608 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{31}N_2O_5$ $[M+H]^+$: 403.2227, found 403.2225; $[\alpha]_D^{22.45}$ –40.51 (*c* 1.0, $CHCl_3$); SFC Conditions: 20% MeOH, 2.5 mL/min, Chiralpak IC column, λ = 210 nm, t_R (min): minor = 5.11, major = 5.66.





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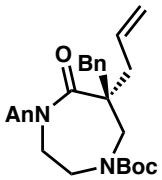
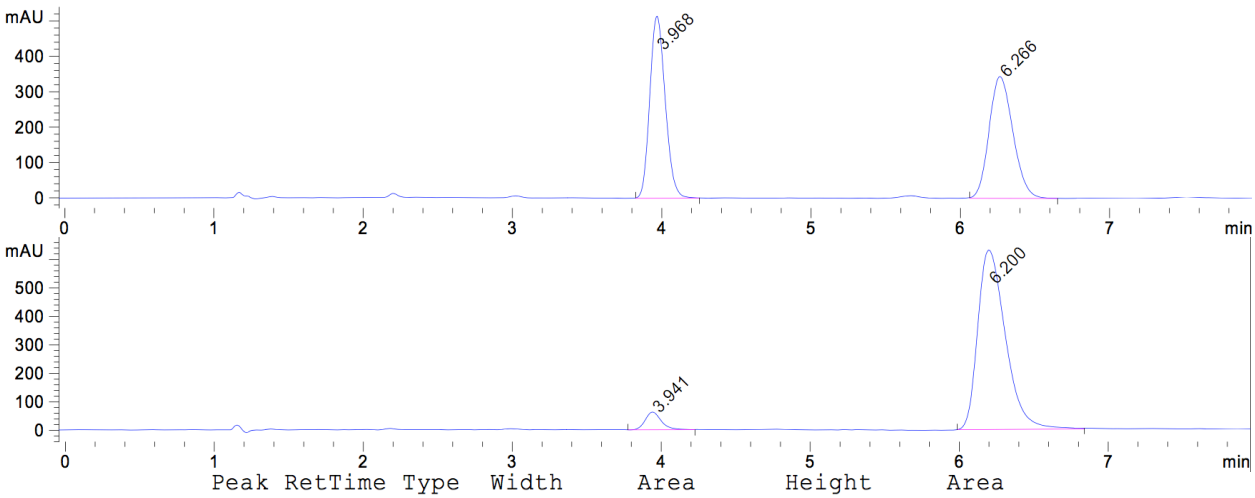
Totals :				1.12435e4	841.02899	



***tert*-butyl (*S*)-6-allyl-6-benzyl-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (4e)**

Prepared according to the general procedure with allyl ester **3e** (52.3 mg, 0.100 mmol, 1.0 equiv), $Pd_2(dba)_3$ (3.7 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide benzyl diazepanone **4e** as a colorless oil (48.1 mg, 0.100 mmol, >99% yield, 89% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 – 7.44 (m, 2H), 7.32 – 7.20 (m, 3H), 7.18 – 7.09 (m, 2H), 6.87 – 6.81 (m, 2H), 5.93 (br s, 1H), 5.26 – 5.12 (m, 2H), 4.09 – 3.88 (m, 2H), 3.84 (s, 3H), 3.78 – 2.41 (m, 8H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.0, 174.6, 162.6, 156.0, 155.4, 136.7, 133.1, 130.8, 130.5, 128.5, 128.2, 127.0, 119.9, 119.6, 113.7, 80.9, 80.7, 55.5, 54.2, 53.8, 49.1, 47.5, 47.3, 42.4, 42.0, 41.2, 40.9, 40.0, 28.5; IR (Neat Film, NaCl) 3374, 2974, 2927, 1694, 1604, 1581, 1510, 1454, 1416, 1392, 1365, 1320, 1282, 1256, 1211, 1166, 1028, 979, 925, 838, 762, 742, 705, 678, 636, 610 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{28}H_{35}N_2O_5$ $[M+H]^+$: 479.2540, found 479.2533; $[\alpha]_D^{22.81}$ +19.02 (*c* 1.0, $CHCl_3$); SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 3.94, major = 6.20.



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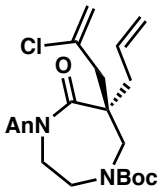
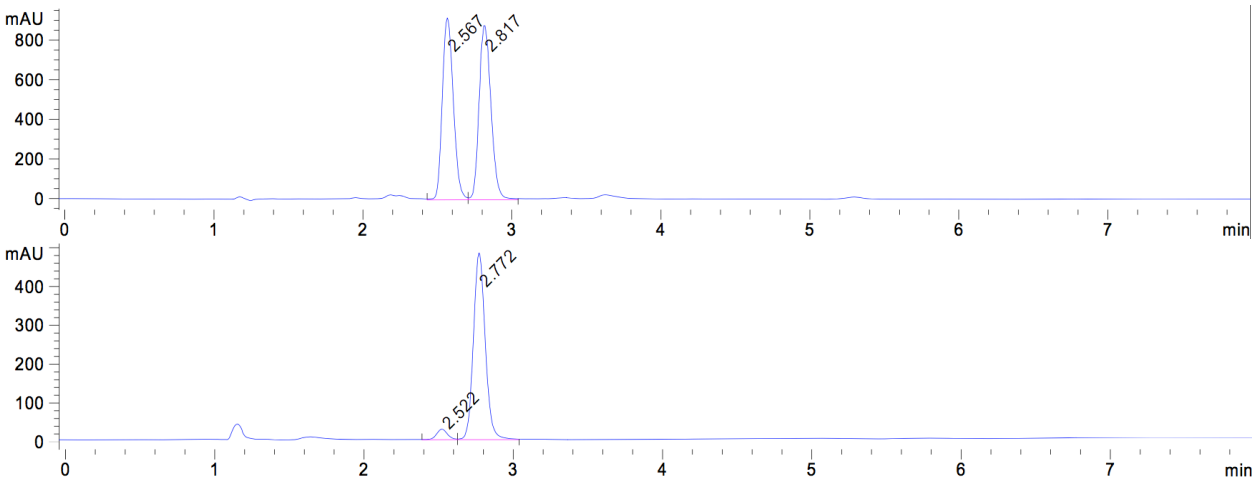
Totals :				8634.09113	692.14267	



tert-butyl (*S*)-6-allyl-6-(2-chloroallyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (4f)

Prepared according to the general procedure with allyl ester **3f** (48.1 mg, 0.0949 mmol, 1.0 equiv), $Pd_2(dba)_3$ (3.7 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide alkenyl chloride **4f** as a colorless oil (36.7 mg, 0.0793 mmol, 84% yield, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.8 Hz, 2H), 6.87 (d, *J* = 8.8 Hz, 2H), 5.93 – 5.71 (m, 1H), 5.36 – 5.07 (m, 4H), 4.36 – 3.84 (m, 4H), 3.83 (s, 3H), 3.82 – 3.51 (m, 2H), 3.00 – 2.33 (m, 4H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.2, 174.6, 162.7, 155.8, 155.2, 137.5, 132.9, 130.5, 128.3, 120.1, 118.2, 113.7, 81.1, 80.9, 55.5, 52.6, 49.2, 47.7, 47.4, 47.0, 44.5, 43.8, 42.8, 42.0, 41.8, 40.3, 28.5; IR (Neat Film, NaCl) 2976, 2930, 1694, 1631, 1604, 1580, 1510, 1456, 1421, 1393, 1366, 1320, 1282, 1256, 1212, 1167, 1150, 1030, 980, 928, 840, 765, 682, 636, 610 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{24}H_{32}ClN_2O_5$ $[M+H]^+$: 463.1994, found 463.2005;

$[\alpha]_D^{22.68}$ –24.10 (*c* 0.5, $CHCl_3$); SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 2.52, major = 2.77.



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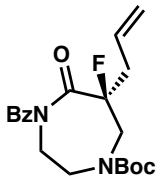
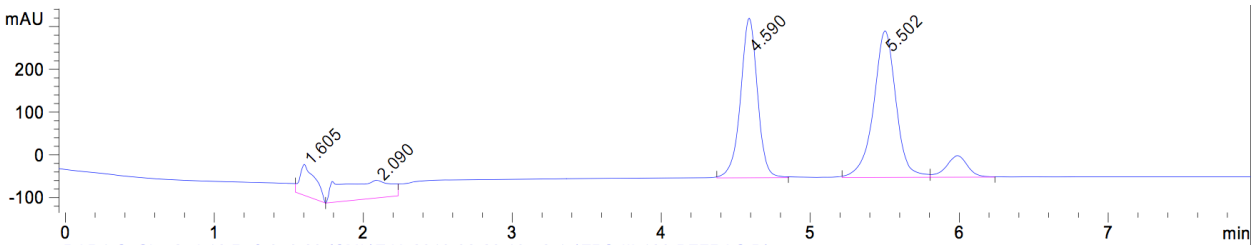
2	2.772	VB	0.0848	2661.86450	478.89621	94.9984
Totals :				2802.00838	506.17488	

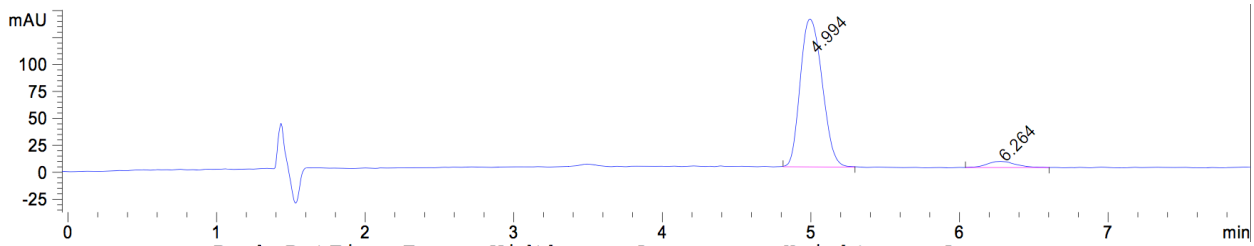


tert-butyl (*S*)-6-allyl-4-benzoyl-6-fluoro-5-oxo-1,4-diazepane-1-carboxylate (4g)

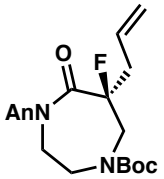
Prepared according to the general procedure with allyl ester **3g** (43.2 mg, 0.103 mmol, 1.0 equiv), $Pd_2(pmdba)_3$ (4.4 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide alkyl fluoride **4g** as a white, amorphous solid (32.6 mg, 0.0866 mmol, 84% yield, 90% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 2H), 7.53 – 7.45 (m, 1H), 7.45 – 7.34 (m, 2H), 5.94 – 5.72 (m, 1H), 5.34 – 5.17 (m, 2H), 4.58 – 4.38 (m, 1H), 4.26 – 4.02 (m, 2H), 3.99 – 3.74 (m, 1H), 3.39 – 3.10 (m, 2H), 2.96 – 2.74 (m, 1H), 2.73 – 2.43 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 173.9 (d, $J_{C\text{-}F}$ = 26.3 Hz), 155.1, 135.2, 132.1, 130.3, 128.4, 128.2, 121.0, 97.7 (dd, $J_{C\text{-}F}$ = 193.9, 47.2 Hz), 81.1, 49.8 (dd, $J_{C\text{-}F}$ = 35.3, 23.1 Hz), 47.2, 46.6, 42.6, 39.7 (dd, $J_{C\text{-}F}$ = 27.6, 21.9 Hz), 28.3; IR (Neat Film, NaCl) 2978, 2926, 1694, 1450, 1414, 1393, 1367,

1329, 1246, 1152, 1042, 999, 979, 926, 857, 766, 724, 694, 672, 648 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{20}H_{29}FN_3O_4$ $[M+NH_4]^+$: 438.2035, found 438.2040; $[\alpha]_D^{22.85}$ +28.89 (*c* 1.0, $CHCl_3$); SFC Conditions: 10% IPA, 2.5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): minor = 6.26, major = 4.99.





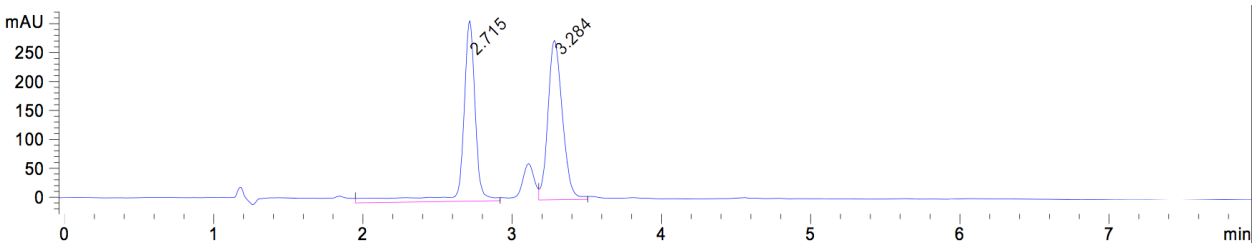
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.994	BB	0.1643	1412.55457	137.04532	94.8798
2	6.264	BB	0.1858	76.22813	5.63548	5.1202
Totals :				1488.78269	142.68080	

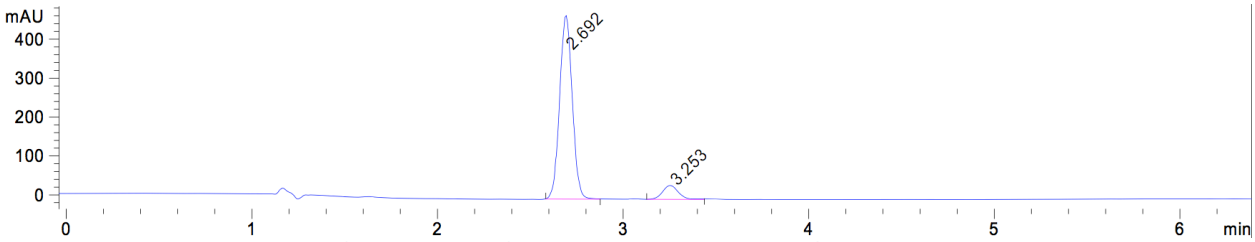


***tert*-butyl (*S*)-6-allyl-6-fluoro-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (4h)**

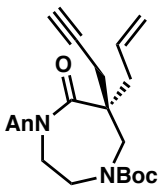
Prepared according to the general procedure with allyl ester **3h** (60 mg, 0.133 mmol, 1.0 equiv), $Pd_2(dba)_3$ (4.9 mg, 0.0053 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (7.9 mg, 0.013 mmol, 10 mol %). Purified by automated silica gel flash chromatography (0→50% acetone/hexanes) to provide alkyl fluoride **4h** as a colorless oil (45 mg, 0.111 mmol, 84% yield, 83% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.53 (m, 2H), 6.92 – 6.84 (m, 2H), 5.93 – 5.78 (m, 1H), 5.30 – 5.21 (m, 2H), 4.35 (t, *J* = 16.0 Hz, 1H), 4.22 – 4.02 (m, 2H), 3.96 – 3.85 (m, 1H), 3.84 (s, 3H), 3.40 – 3.19 (m, 2H), 2.94 – 2.78 (m, 1H), 2.71 – 2.48 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 173.7, 163.1, 155.3, 131.0, 130.6, 127.1, 121.0, 113.8, 97.8 (dd, J_{C-F} = 193.7,

52.5 Hz), 81.2, 55.5, 49.8 (dd, $J_{C\text{-}F}$ = 33.5, 23.3 Hz), 47.5, 46.9, 43.2, 39.8 (dd, $J_{C\text{-}F}$ = 32.1, 21.8 Hz), 28.3; IR (Neat Film, NaCl) 2977, 2932, 1696, 1603, 1578, 1511, 1448, 1413, 1366, 1327, 1256, 1169, 1152, 1029, 1000, 977, 923, 835, 766 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{21}H_{28}FN_2O_5$ $[M+H]^+$: 407.1977, found 407.1973; $[\alpha]_D^{22.5}$ +46.99 (*c* 1.7, $CHCl_3$); SFC conditions: 20% IPA, 2.5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 2.69, minor = 3.25.





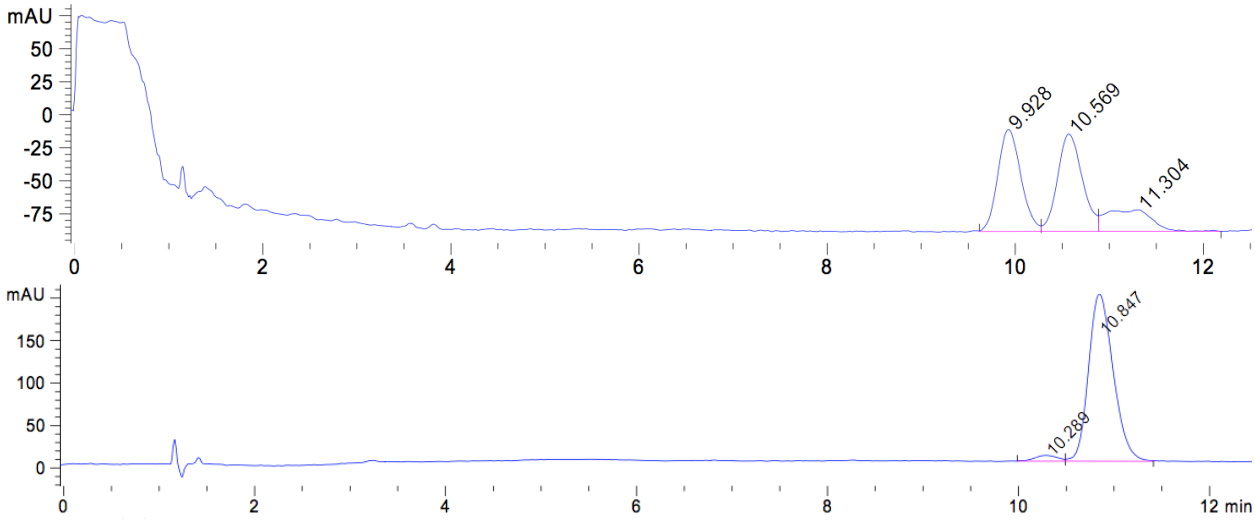
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	2.692	BB	0.0755	2233.58398	469.76068	91.4020
2	3.253	BB	0.0929	210.10995	35.55383	8.5980
Totals :				2443.69394	505.31451	



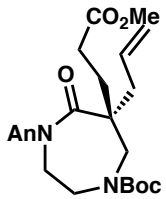
tert-butyl (*S*)-6-allyl-4-(4-methoxybenzoyl)-5-oxo-6-(prop-2-yn-1-yl)-1,4-diazepane-1-carboxylate (4i)

Prepared according to the general procedure with allyl ester **3i** (70.0 mg, 0.149 mmol, 1.0 equiv), $Pd_2(pmdba)_3$ (5.4 mg, 4.9 μmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (8.8 mg, 0.015 mmol, 10 mol %) at 50 °C. Purification by automated silica gel flash chromatography (Teledyne ISCO, 0→40% acetone/hexanes) provided alkyne **4i** as a colorless oil (28.0 mg, 0.0656 mmol, 44%

yield, 94% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 8.2 Hz, 2H), 6.89 – 6.82 (m, 2H), 5.93 – 5.63 (m, 1H), 5.30 – 5.10 (m, 2H), 4.36 – 4.15 (m, 1H), 4.09 – 3.68 (m, 4H), 3.83 (s, 3H), 3.62 – 3.37 (m, 1H), 2.83 – 2.43 (m, 4H), 2.20 – 1.99 (m, 1H), 1.51 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.5, 174.6, 162.9, 155.6, 155.2, 132.1, 130.7, 127.9, 120.0, 113.7, 81.1, 80.9, 80.5, 72.1, 55.6, 52.7, 49.1, 46.9, 47.7, 43.0, 42.3, 39.1, 37.5, 28.5, 26.5, 25.9; IR (Neat Film, NaCl) 3283, 2972, 2922, 1692, 1603, 1511, 1454, 1418, 1365, 1322, 1255, 1169, 1031, 980, 926, 839, 766, 670 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{24}H_{31}N_2O_5$ $[M+H]^+$: 427.2227, found 427.2238; $[\alpha]_D^{22.1}$ –7.69 (*c* 1.0, $CHCl_3$); SFC conditions: 10% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): major = 10.85, minor = 10.29.

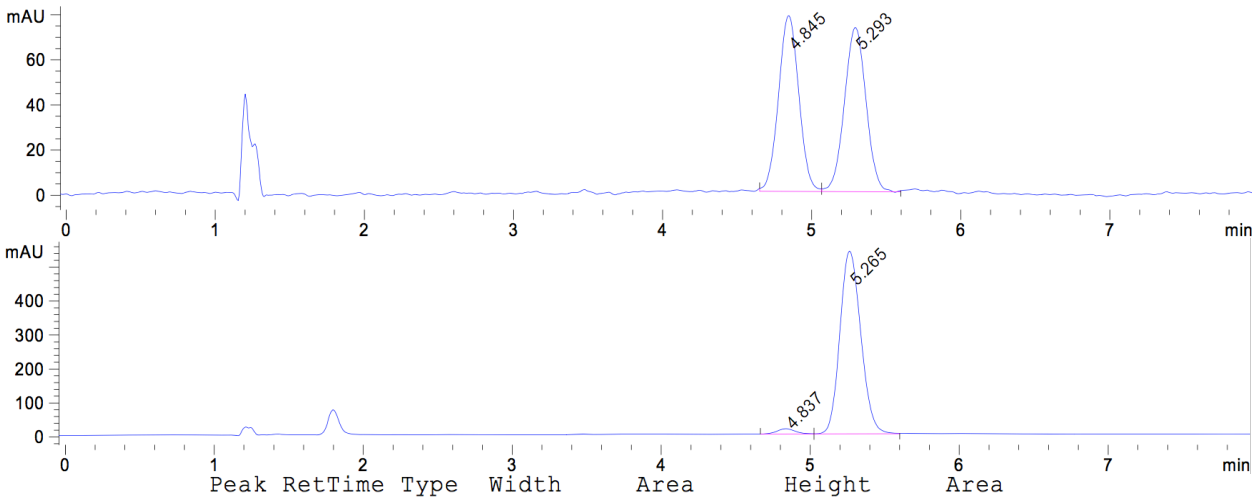


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.289	BV	0.2467	110.53387	6.90531	3.0290
2	10.847	VB	0.2737	3538.59668	196.86908	96.9710
Totals :				3649.13055	203.77439	

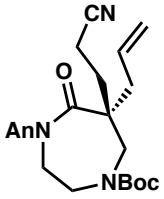


tert-butyl (*R*)-6-allyl-6-(3-methoxy-3-oxopropyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (4j)

Prepared according to the general procedure with allyl ester **3j** (51.9 mg, 0.100 mmol, 1.0 equiv), $Pd_2(dba)_3$ (3.7 mg, 0.004 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (5.9 mg, 0.01 mmol, 10 mol %). Purified by silica gel flash chromatography (33% EtOAc/hexanes) to provide methyl ester **4j** as a white, amorphous solid (45.8 mg, 0.0965 mmol, 96% yield, 95% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.48 (m, 2H), 6.92 – 6.83 (m, 2H), 5.80 – 5.64 (m, 1H), 5.22 – 5.09 (m, 2H), 4.21 (ddd, *J* = 15.7, 6.6, 2.1 Hz, 1H), 4.13 – 3.85 (m, 3H), 3.83 (s, 3H), 3.62 (s, 3H), 3.51 (d, *J* = 15.2 Hz, 1H), 3.42 – 3.29 (m, 1H), 2.64 – 2.20 (m, 4H), 2.20 – 1.86 (m, 2H), 1.49 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.2, 174.7, 173.6, 173.4, 162.7, 155.4, 155.0, 132.7, 132.5, 130.3, 128.3, 120.0, 113.8, 81.1, 80.9, 55.5, 51.8, 50.1, 48.9, 47.6, 46.8, 43.2, 42.9, 40.3, 39.7, 29.3, 28.8, 28.5; IR (Neat Film, NaCl) 2975, 2360, 1736, 1694, 1605, 1580, 1510, 1426, 1393, 1366, 1321, 1283, 1254, 1167, 1031, 980, 927, 842, 811, 762, 647, 610 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{25}H_{35}N_2O_7$ $[M+H]^+$: 475.2439, found 475.2438; $[\alpha]_D^{22.52}$ +7.73 (*c* 1.0, $CHCl_3$); SFC conditions: 15% IPA, 2.5 mL/min, Chiralcel OD-H column, λ = 210 nm, t_R (min): major = 5.27, minor = 4.84.

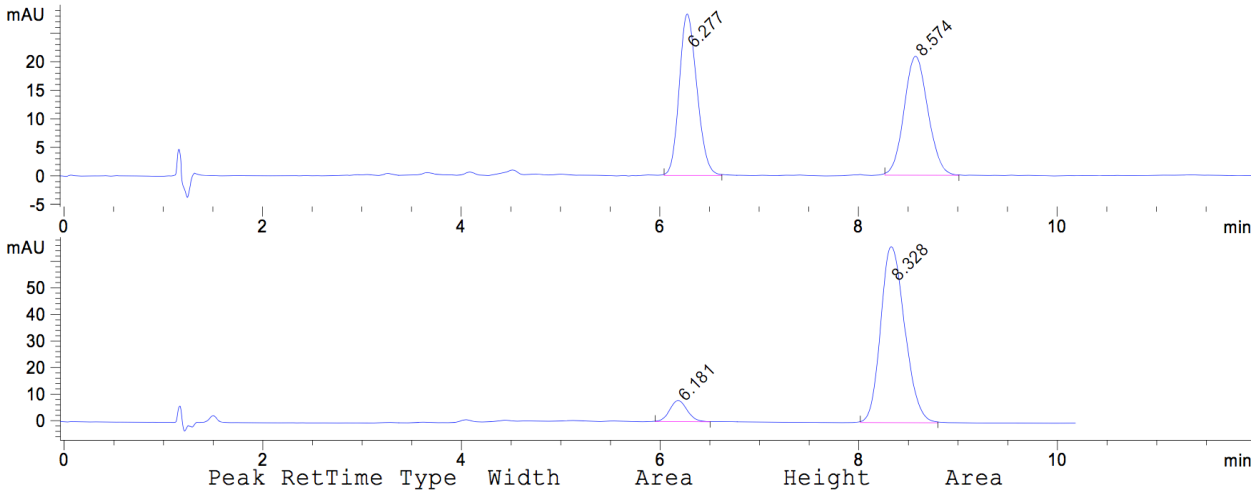


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.837	BV	0.1353	131.40652	15.43421	2.4390
2	5.265	VB	0.1501	5256.27393	537.28778	97.5610
Totals :				5387.68045	552.72199	

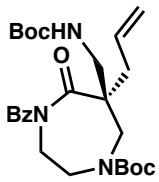


tert-butyl (_R_)-6-allyl-6-(2-cyanoethyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (4k)

Prepared according to the general procedure with allyl ester **3k** (62.2 mg, 0.128 mmol, 1.0 equiv), $Pd_2(dba)_3$ (4.7 mg, 0.00512 mmol, 4 mol %), and (*S*)-$(CF_3)_3$-*t*-BuPHOX (7.6 mg, 0.0128 mmol, 10 mol %), using 9:1 methylcyclohexane-toluene as the reaction solvent. Purified by silica gel flash chromatography (33% EtOAc/hexanes) to provide nitrile **4k** as a white, amorphous solid (48.6 mg, 0.110 mmol, 86% yield, 84% ee); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.47 (m, 2H), 6.96 – 6.85 (m, 2H), 5.82 – 5.64 (m, 1H), 5.30 – 5.11 (m, 2H), 4.09 – 3.93 (m, 2H), 3.93 – 3.72 (m, 2H), 3.85 (s, 3H), 3.70 – 3.38 (m, 2H), 2.60 – 2.25 (m, 4H), 2.22 – 1.93 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.0, 174.5, 163.0, 155.6, 154.9, 131.7, 130.3, 127.9, 120.7, 119.7, 113.9, 81.4, 55.6, 52.2, 49.6, 48.0, 47.4, 46.8, 43.0, 42.6, 39.9, 39.0, 32.1, 31.5, 28.4, 12.4; IR (Neat Film, NaCl) 2975, 2931, 2361, 2246, 1690, 1604, 1579, 1510, 1456, 1419, 1366, 1321, 1256, 1168, 1148, 1031, 980, 926, 840, 811, 766, 607 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{24}H_{35}N_4O_5$ $[M+NH_4]^+$: 459.2602, found 459.2602; $[\alpha]_D^{22.4}$ +9.31 (*c* 0.5, $CHCl_3$); SFC conditions: 20% IPA, 2.5 mL/min, Chiralcel OD-H column, λ = 310 nm, t_R (min): major = 8.33, minor = 6.18.

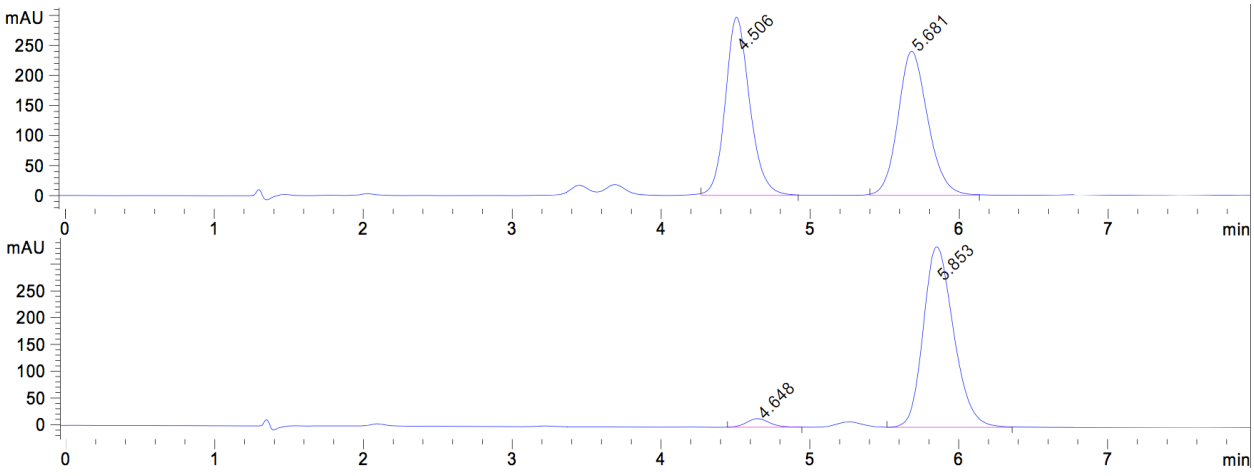


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.181	BB	0.1914	97.48795	7.93404	8.0193
2	8.328	BB	0.2649	1118.18079	66.25080	91.9807
Totals :				1215.66874	74.18484	

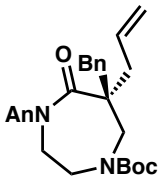


tert-butyl (*S*)-6-allyl-4-benzoyl-6-(((tert-butoxycarbonyl)amino)methyl)-5-oxo-1,4-diazepane-1-carboxylate (4l)

Prepared according to the general procedure with allyl ester **3l** (53 mg, 0.0997 mmol, 1.0 equiv) and $Pd_2(dba)_3$. Purification by automated silica gel flash chromatography (0→50% EtOAc/hexanes) provided carbamate **4l** as a white foam (37 mg, 0.0759 mmol, 76% yield, 93% ee). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.44 (m, 3H), 7.44 – 7.35 (m, 2H), 5.74 (ddt, *J* = 15.7, 10.5, 7.4 Hz, 1H), 5.35 (br s, 0.5H), 5.21 – 5.06 (m, 2H), 4.79 (br s, 0.5H), 4.48 – 4.28 (m, 1H), 4.14 – 3.09 (m, 7H), 2.69 – 2.18 (m, 2H), 1.50 (s, 9H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.3, 178.8, 174.5, 156.3, 155.9, 155.1, 136.3, 132.5, 132.1, 131.7, 128.5, 127.7, 120.1, 81.3, 81.1, 79.5, 54.8, 48.9, 47.3, 46.8, 46.3, 42.6, 41.1, 38.7, 37.1, 28.5, 28.5; IR (Neat Film, NaCl) 2977, 1687, 1502, 1422, 1391, 1365, 1322, 1282, 1245, 1168, 978, 916, 753 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{26}H_{37}N_3O_6$ $[M+H]^+$: 488.2755, found 488.2747; $[\alpha]_D^{23.2}$ –3.70 (*c* 1.85, $CHCl_3$); SFC conditions: 20% IPA, 2.5 mL/min, Chiralpak IC column, λ = 254 nm, t_R (min): major = 5.85, minor = 4.65.

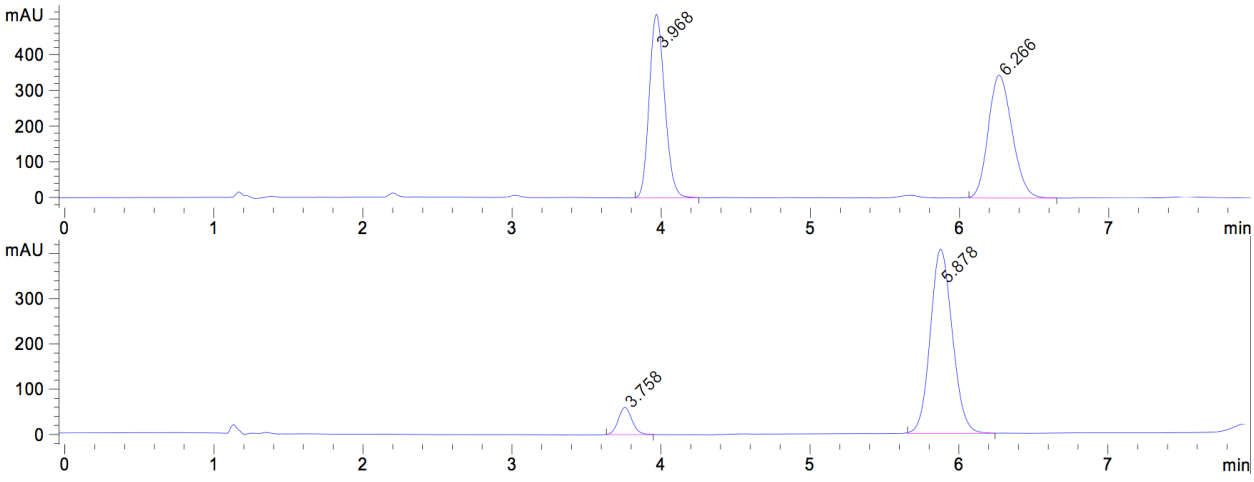


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.648	BB	0.1676	175.76628	16.06920	3.5426
2	5.853	VB	0.2176	4785.68066	337.25015	96.4574
Totals :				4961.44695	353.31935	



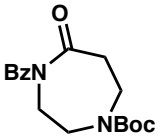
Procedure for the large scale preparation of diazepanone 4e

To a 500 mL Schlenk flask was added $Pd_2(dba)_3$ (37 mg, 0.04 mmol, 4 mol %), (*S*)-$(CF_3)_3$-*t*-BuPHOX (59 mg, 0.1 mmol, 10 mol %), and MeCy (20 mL). After stirring for 20 minutes at 25 °C, allyl ester **3e** (523 mg, 1.0 mmol, 1.0 equiv) and methylcyclohexane (52 mL, total substrate concentration 0.014 M) were added to the pre-stirred catalyst solution. After stirring for 23 h at 40 °C, the reaction mixture was directly loaded onto a flash column and purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide benzyl diazepanone **4e** as a colorless oil (393 mg, 0.82 mmol, 82% yield, 83% ee); All characterization data matched those reported above for compound **4e**; $[\alpha]_D^{21.96}$ +14.757 (*c* 1.0, $CHCl_3$); SFC Conditions: 20% IPA, 2.5 mL/min, Chiralpak AD-H column, λ = 210 nm, t_R (min): minor = 3.76, major = 5.90.



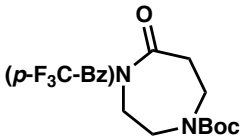
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	3.758	BB	0.0989	386.25449	60.12492	8.4266
2	5.878	BB	0.1604	4197.52441	406.90225	91.5734
Totals :				4583.77890	467.02718	

Synthesis of Allylic Alkylation Substrates



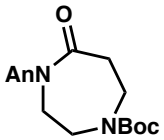
***tert*-butyl 4-benzoyl-5-oxo-1,4-diazepane-1-carboxylate (SI1)**

To a solution of *tert*-butyl 5-oxo-1,4-diazepane-1-carboxylate (5.00 g, 23.3 mmol, 1.0 equiv) in THF (230 mL, 0.1 M) at –78 °C was slowly added *n*-BuLi (2.18 M in hexanes, 12.8 mL, 27.9 mmol, 1.2 equiv). The opaque mixture was allowed to warm to ambient temperature until the solution became homogeneous, at which point it was again cooled to –78 °C. Then, benzoyl chloride (3.52 mL, 30.3 mmol, 1.3 equiv) was added dropwise and the reaction turned light orange over several minutes. The reaction was stirred for 1 h at –78 °C, then poured into saturated aqueous NH_4Cl (200 mL) and extracted with EtOAc (3 x 100 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated. The crude product was purified by silica gel flash chromatography (20% acetone/hexanes) to afford benzoyl-protected lactam **SI1** as a white solid (7.43 g, 23.3 mmol, >99% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 – 7.49 (m, 2H), 7.49 – 7.41 (m, 1H), 7.41 – 7.32 (m, 2H), 4.03 – 3.96 (m, 2H), 3.71 (m, 4H), 2.82 – 2.75 (m, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.6, 173.7, 154.5, 135.9, 131.7, 128.2, 127.9, 80.7, 47.8, 47.10, 45.4, 41.6, 41.0, 40.6, 28.3; IR (Neat Film, NaCl) 2976, 2932, 2251, 1682, 1599, 1582, 1450, 1422, 1392, 1366,1327, 1285, 1247, 1229, 1157, 1115, 1032, 1018, 976, 954, 915,862, 793,769, 729, 696, 647 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{17}H_{26}N_3O_4$ $[M+NH_4]^+$: 336.1918, found 336.1912.



***tert*-butyl 5-oxo-4-(4-(trifluoromethyl)benzoyl)-1,4-diazepane-1-carboxylate (SI2)**

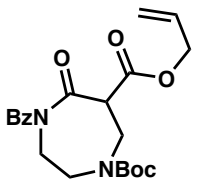
To a solution of *tert*-butyl 5-oxo-1,4-diazepane-1-carboxylate (500 mg, 2.33 mmol, 1 equiv) in THF (25 mL, 0.1 M) at –78 °C was slowly added *n*-BuLi (2.5 M in hexanes, 1.02 mL, 2.56 mmol, 1.1 equiv), and the reaction mixture was stirred at –78 °C for 15 min. Then, 4-trifluoromethylbenzoyl chloride (450 µL, 3.03 mmol, 1.3 equiv) was added dropwise, and the reaction was stirred for 30 min at –78 °C. The reaction mixture was then poured into saturated aqueous NH_4Cl (20 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (25% EtOAc/hexanes) to afford the title compound as a white solid (698 mg, 1.81 mmol, 77% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (d, J = 8.2 Hz, 2H), 7.60 (d, J = 8.1 Hz, 2H), 4.14 – 4.02 (m, 2H), 3.84 – 3.66 (m, 4H), 2.91 – 2.77 (m, 2H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 172.5, 154.6, 139.6, 133.0 (q, $J_{C\text{-}F}$ = 32.8 Hz), 130.6, 128.0, 125.5 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.6 Hz), 81.2, 47.7 (br), 45.3, 41.4 (br), 40.8, 28.5; IR (Neat Film, NaCl) 2981, 1689, 1455, 1422, 1367, 1326, 1301, 1249, 1230, 1159, 1127, 1066, 1028, 1015, 977, 955, 852, 832, 769 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{18}H_{25}F_3N_3O_4$ $[M+NH_4]^+$: 404.1742, found 404.1797.



***tert*-butyl 4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1-carboxylate (SI3)**

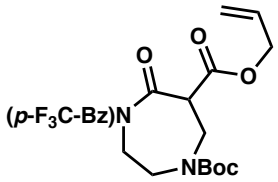
To a solution of *tert*-butyl 5-oxo-1,4-diazepane-1-carboxylate (800 mg, 3.73 mmol, 1 equiv) in THF (37 mL, 0.1 M) at –78 °C was slowly added *n*-BuLi (2.5 M in hexanes, 1.64 mL, 4.1 mmol, 1.1 equiv). The opaque mixture was allowed to warm to ambient temperature until the solution became homogeneous, at which point it was again cooled to –78 °C. Then, 4-methoxybenzoyl chloride (657 µL, 4.85 mmol, 1.3 equiv) was added dropwise and the reaction was stirred for 30 min at –78 °C. The reaction mixture was then poured into saturated aqueous NH_4Cl (30 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (3 x 10 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated under reduced pressure. The crude product was purified by automated silica gel flash chromatography (Teledyne ISCO, 0→100% EtOAc/hexanes) to afford the title compound as a white solid (1.2 g, 3.44 mmol, 92%

yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 2H), 6.93 – 6.84 (m, 2H), 4.00 – 3.93 (m, 2H), 3.83 (s, 3H), 3.78 – 3.69 (m, 4H), 2.85 – 2.78 (m, 2H), 1.48 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 173.4, 162.9, 154.6, 130.9, 130.6, 127.7, 113.7, 80.8, 55.5, 48.0, 47.4, 46.1, 41.9, 41.3, 40.8, 28.5; IR (Neat Film, NaCl) 2974, 2936, 1774, 1687, 1604, 1578, 1510, 1458, 1420, 1391, 1366, 1327, 1284, 1249, 1166, 1114, 1023, 977, 956, 916, 860, 842, 809, 767, 632 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{18}H_{25}N_2O_5$ $[M+H]^+$: 349.1758, found 349.1760.



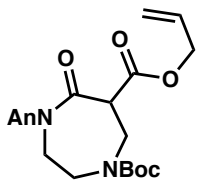
6-allyl 1-(*tert*-butyl) 4-benzoyl-5-oxo-1,4-diazepane-1,6-dicarboxylate (2a)

To a solution of diisopropylamine (266 μL, 1.88 mmol, 1.2 equiv) in THF (10 mL) at –78 °C in a flame-dried round-bottom flask was added *n*-BuLi (2.5 M in hexanes, 792 μL, 1.73 mmol, 1.1 equiv), the resulting solution was stirred at –78 °C for 45 min. To this solution was then added lactam **SI1** (500 mg, 1.57 mmol, 1.0 equiv) in THF (6 mL, 0.1 M total concentration) dropwise while stirring at −78 °C. The reaction mixture was stirred for 75 min at −78 °C. Allyl cyanoformate (201 μL, 1.88 mmol, 1.2 equiv) was then added dropwise at −78 °C. After stirring for 3 h at −78 °C, the reaction mixture was poured into saturated aqueous NH_4Cl (10 mL) and extracted with ethyl acetate (3 x 20 mL). The combined organic extracts were concentrated under reduced pressure onto silica (4 g). The silica-adsorbed crude mixture was purified by silica gel flash chromatography (20→30% EtOAc/hexanes) to provide allyl ester **2a** as an off-white solid (550 mg, 1.37 mmol, 87% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.65 – 7.57 (m, 2H), 7.53 – 7.45 (m, 1H), 7.42 – 7.34 (m, 2H), 5.92 (ddt, *J* = 17.2, 10.4, 5.9 Hz, 1H), 5.40 – 5.22 (m, 2H), 4.79 – 4.59 (m, 2H), 4.33 – 4.03 (m, 2H), 4.02 – 3.88 (m, 3H), 3.87 – 3.66 (m, 1H), 3.55 – 3.40 (m, 1H), 1.48 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 171.4, 167.5, 154.7, 135.3, 132.2, 131.4, 128.4, 128.4, 119.5, 81.3, 66.6, 56.0, 46.7 (br), 44.5, 43.3 (br), 28.4; IR (Neat Film, NaCl) 3374, 3062, 2977, 2934, 1746, 1694, 1600, 1582, 1450, 1419, 1393, 1367, 1327, 1246, 1156, 1037, 1020, 995, 968, 939, 857, 792, 769, 727, 695, 616 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{21}H_{30}N_3O_6$ $[M+NH_4]^+$: 420.2129, found 420.2109.



6-allyl 1-(*tert*-butyl) 5-oxo-4-(4-(trifluoromethyl)benzoyl)-1,4-diazepane-1,6-dicarboxylate (2b)

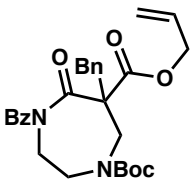
To a solution of lactam **SI2** (500 mg, 1.29 mmol, 1.0 equiv) in THF (8 mL, 0.1 M total concentration) at −78 °C was added LiHMDS (303 mg, 1.81 mmol, 1.4 equiv) in THF (5 mL) dropwise. The resulting yellow reaction mixture was stirred for 15 min at −78 °C. Then, allyl cyanoformate (166 μL, 1.55 mmol, 1.2 equiv) was added dropwise at −78 °C, after which the solution slowly became colorless. After stirring for 1 h at −78 °C, the reaction was poured into 2 M HCl (20 mL) and extracted with ethyl acetate (4 x 20 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and $NaHCO_3$, passed through filter paper, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20→33% EtOAc/hexanes) to provide allyl ester **2b** as a white solid (266 mg, 0.565 mmol, 44% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (d, J = 8.3 Hz, 2H), 7.64 (d, J = 8.4 Hz, 2H), 5.92 (ddt, J = 17.2, 10.4, 5.9 Hz, 1H), 5.42 – 5.23 (m, 2H), 4.79 – 4.59 (m, 2H), 4.46 – 3.63 (m, 6H), 3.52 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.4, 171.4, 167.4, 154.6, 138.9, 133.3 (q, $J_{C\text{-}F}$ = 32.6 Hz), 131.2, 128.3, 125.4 (q, $J_{C\text{-}F}$ = 3.8 Hz), 123.7 (q, $J_{C\text{-}F}$ = 272.5 Hz), 119.8, 81.5, 66.8, 56.0, 47.4, 46.3, 44.2, 43.0, 28.4; IR (Neat Film, NaCl) 3377, 3083, 2980, 2935, 2463, 2358, 1928, 1798, 1747, 1694, 1652, 1619, 1584, 1513, 1455, 1414, 1394, 1368, 1327, 1246, 1156, 1131, 1067, 1034, 1016, 994, 970, 940, 879, 853, 824, 770, 723, 679, 639, 630, 612 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{29}F_3N_3O_6$ $[M+NH_4]^+$: 488.2003, found 488.2022.



6-allyl 1-(*tert*-butyl) 4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (2c)

To a solution of lactam **SI3** (1.00 g, 2.87 mmol, 1.0 equiv) in THF (20 mL, 0.1 M total concentration) at −78 °C was added LiHMDS (528 mg, 3.16 mmol, 1.1 equiv) in THF (9 mL)

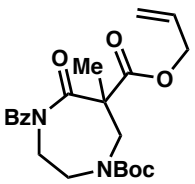
dropwise. The resulting pale yellow reaction mixture was stirred for 15 min at −78 °C. Allyl cyanoformate (368 μL, 3.44 mmol, 1.2 equiv) was then added dropwise at −78 °C, resulting in a clear solution. After stirring for 1.5 h at −78 °C, the reaction was poured into 1 M HCl (10 mL) and diluted with ethyl acetate (20 mL). The layers were separated and the aqueous phase was extracted with ethyl acetate (3 x 30 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and $NaHCO_3$, filtered, and concentrated under reduced pressure onto silica. The silica-adsorbed crude mixture was purified by silica gel flash chromatography (10→20% EtOAc/hexanes) to provide allyl ester **2c** as a colorless oil (600 mg, 1.39 mmol, 48% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 – 7.60 (m, 2H), 6.91 – 6.79 (m, 2H), 5.92 (ddt, *J* = 17.3, 10.4, 5.9 Hz, 1H), 5.42 – 5.20 (m, 2H), 4.77 – 4.56 (m, 2H), 4.40 – 3.92 (m, 4H), 3.92 – 3.62 (m, 2H), 3.82 (s, 3H), 3.58 – 3.24 (m, 1H), 1.46 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 171.3, 167.6, 163.2, 154.6, 131.4, 131.2, 127.0, 119.4, 113.7, 81.1, 66.5, 55.9, 55.4, 47.7 and 46.7, 45.1, 43.3, 42.8, 28.3; IR (Neat Film, NaCl) 2977, 1746, 1693, 1603, 1578, 1511, 1454, 1419, 1392, 1366, 1324, 1255, 1168, 1025, 995, 965, 842, 766 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{28}N_2O_7$ $[M+H]^+$: 433.1969, found 433.1966.



6-allyl 1-(*tert*-butyl) 4-benzoyl-6-benzyl-5-oxo-1,4-diazepane-1,6-dicarboxylate (3a)

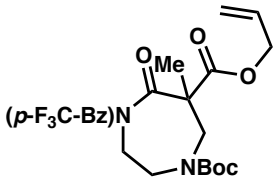
To a flame-dried round bottom flask containing a solution of allyl ester **2a** (1.00 g, 2.49 mmol, 1.0 equiv) in THF (25 mL, 0.1 M) at 0 °C was added NaH (60% dispersion in mineral oil, 107 mg, 2.74 mmol, 1.1 equiv) and the mixture was stirred at 0 °C for 30 min. BnBr (1.50 mL, 12.45 mmol, 5.0 equiv) was then added dropwise and the reaction mixture was warmed to 45 °C. After 16 h, the temperature was further increased to 53 °C due to sluggish reactivity. After another 45 min of stirring at 53 °C, the reaction mixture was cooled to 23 °C and poured into saturated aqueous NH_4Cl (25 mL), the layers were separated, and the aqueous layer was extracted with ethyl acetate (3 x 10 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide the title compound as a colorless foam (922 mg, 1.87 mmol, 75% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, *J* = 7.6 Hz, 2H), 7.55 –

7.46 (m, 1H), 7.37 (t, J = 7.7 Hz, 2H), 7.31 – 7.25 (m, 3H), 7.24 – 7.12 (m, 2H), 5.86 (tq, *J* = 22.8, 6.5 Hz, 1H), 5.42 – 5.26 (m, 2H), 4.71 – 4.55 (m, 2H), 4.22 (dd, *J* = 75.3, 15.5 Hz, 1H), 4.05 – 3.57 (m, 4H), 3.57 – 3.36 (m, 2H), 3.22 (dd, *J* = 68.5, 13.7 Hz, 1H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (174.4, 174.0, 172.2, 172.0, 170.8, 170.2, 155.5, 155.0, 135.7, 135.6, 135.5, 132.0, 131.1, 130.9, 130.8, 130.6, 128.5, 128.5, 128.3, 127.5, 127.4, 120.6, 120.2, 81.2, 81.0, 67.0, 66.9, 62.6, 62.2, 47.3, 46.7, 46.2, 45.8, 42.4, 42.1, 42.0, 28.5; IR (Neat Film, NaCl) 3063, 3030, 2977, 2933, 1694, 1601, 1583, 1495, 1450, 1416, 1393, 1366, 1325, 1280, 1247, 1154, 1132, 1092, 1041, 1023, 980, 939, 868, 796, 768, 728, 703, 662 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{24}H_{25}N_2O_6$ [M–^{t}Bu+2H]$^+$: 437.1707, found 437.1697.



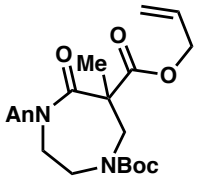
6-allyl 1-(*tert*-butyl) 4-benzoyl-6-methyl-5-oxo-1,4-diazepane-1,6-dicarboxylate (3b)

To a solution of allyl ester **2a** (240 mg, 0.596 mmol, 1.0 equiv) in THF (6 mL, 0.1 M) at 0 °C was added 60 % NaH (26 mg, 0.657 mmol, 1.1 equiv). The solution was stirred at 0 °C for 40 min, after which MeI (186 µL, 2.98 mmol, 5.0 equiv) was added rapidly. The reaction was heated to 45 °C and stirred for 16 h, cooled to 23 °C, poured into saturated aqueous NH_4Cl (5 mL), and extracted with EtOAc (3 x 3 mL). The combined organic extracts were dried over Na_2SO_4 and concentrated onto silica gel. The silica-adsorbed crude product was purified by silica gel flash chromatography (20% EtOAc/hexanes) to afford the title compound as a light yellow oil (200 mg, 0.480 mmol, 81% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 – 7.63 (m, 2H), 7.58 – 7.43 (m, 1H), 7.38 (t, *J* = 7.6 Hz, 2H), 5.96 (ddt, *J* = 16.6, 10.4, 6.0 Hz, 1H), 5.49 – 5.26 (m, 2H), 4.85 – 4.64 (m, 2H), 4.46 – 4.22 (m, 1H), 4.10 (br d, *J* = 14.8 Hz, 1H), 3.86 – 3.42 (m, 4H), 1.57 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.5 174.1, 173.0, 171.7, 155.1, 154.9, 135.7, 132.0, 131.2, 128.3, 128.2, 120.2, 81.1, 66.9, 57.7, 49.8, 49.0, 47.1, 46.0, 43.2, 28.4, 23.6; IR (Neat Film, NaCl) 2977, 1693, 1449, 1416, 1366, 1325, 1281, 1249, 1139, 1104, 1047, 983, 938, 768, 727, 694 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{29}N_2O_6$ [M+H]$^+$: 417.2020, found 417.2010.



6-allyl 1-(*tert*-butyl) 6-methyl-5-oxo-4-(4-(trifluoromethyl)benzoyl)-1,4-diazepane-1,6-dicarboxylate (3c)

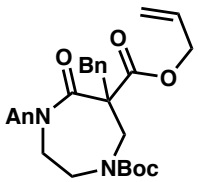
To a suspension of allyl ester **2b** (150 mg, 0.319 mmol, 1.0 equiv) and Cs_2CO_3 (208 mg, 0.638 mmol, 2.0 equiv) in acetonitrile (3.2 mL, 0.1 M) was added MeI (99 µL, 1.59 mmol, 5.0 equiv) at 23 °C. The reaction was heated to 45 °C and stirred for 5 h, then cooled to 23 °C, poured into saturated aqueous NH_4Cl (6 mL), and extracted with EtOAc (3 x 3 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (15% EtOAc/petroleum ether) to provide the title compound as a colorless oil (146 mg, 0.301 mmol, 95% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 5.97 (ddt, J = 17.3, 10.3, 6.1 Hz, 1H), 5.48 – 5.29 (m, 2H), 4.84 – 4.68 (m, 2H), 4.49 – 4.30 (m, 1H), 4.18 – 3.98 (m, 1H), 3.90 – 3.39 (m, 4H), 1.57 (s, 3H), 1.45 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.2, 172.7, 171.7, 154.9, 139.2, 133.1 (q, $J_{C\text{-}F}$ = 32.5 Hz), 131.1, 128.2, 125.4, 123.8 (q, $J_{C\text{-}F}$ = 272.7 Hz), 120.5, 81.3, 67.0, 57.7, 49.7, 49.0, 46.9, 45.8, 43.1, 42.9, 28.4, 23.7; IR (Neat Film, NaCl) 3384, 3083, 2979, 2937, 1698, 1619, 1584, 1514, 1478, 1453, 1416, 1394, 1367, 1326, 1285, 1250, 1207, 1166, 1136, 1110, 1066, 1022, 1012, 985, 938, 855, 832, 817, 790, 769, 740, 722, 680 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{23}H_{28}F_3N_2O_6$ $[M+H]^+$: 485.1894, found 485.1907.



6-allyl 1-(tert-butyl) 4-(4-methoxybenzoyl)-6-methyl-5-oxo-1,4-diazepane-1,6-dicarboxylate (3d)

To a suspension of allyl ester **2c** (200 mg, 0.462 mmol, 1.0 equiv), Cs_2CO_3 (301 mg, 0.925 mmol, 2.0 equiv) in acetonitrile (4.6 mL, 0.1 M) was added MeI (143 µL, 2.31 mmol, 5.0 equiv) at 23 °C. The reaction was heated to 45 °C and stirred for 40 min, then cooled to 23 °C, poured

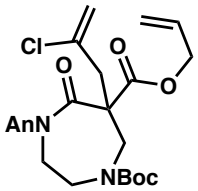
into saturated aqueous NH_4Cl (10 mL), and extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by automated silica gel flash chromatography (Teledyne ISCO, 0→90% EtOAc/hexanes) to provide the title compound as a colorless oil (70 mg, 0.157 mmol, 34% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.75 – 7.65 (m, 2H), 6.90 – 6.82 (m, 2H), 5.96 (ddt, *J* = 17.3, 10.4, 6.0 Hz, 1H), 5.44 – 5.29 (m, 2H), 4.77 – 4.66 (m, 2H), 4.27 – 4.15 (m, 1H), 4.14 – 4.04 (m, 1H), 3.83 (s, 3H), 3.80 – 3.70 (m, 1H), 3.67 – 3.58 (m, 2H), 3.56 – 3.46 (m, 1H), 1.57 (s, 3H), 1.44 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.0, 173.6, 172.9, 172.0, 171.8, 162.9, 155.2, 154.9, 131.2, 131.2, 131.0, 127.6, 120.1, 120.0, 113.6, 81.0, 66.8, 57.5, 55.5, 49.6, 48.9, 47.2, 46.1, 43.7, 28.4, 23.7; IR (Neat Film, NaCl) 2974, 2937, 1698, 1604, 1578, 1511, 1453, 1416, 1392, 1366, 1324, 1280, 1256, 1169, 1139, 1103, 1031, 1001, 983, 929, 840, 768, 733 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{23}H_{31}N_2O_7$ $[M+H]^+$: 447.2126, found 447.2128.



6-allyl 1-(*tert*-butyl) 6-benzyl-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3e)

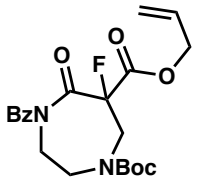
To a flame-dried round bottom flask containing a solution of allyl ester **2c** (300 mg, 0.694 mmol, 1.0 equiv) in THF (7 mL, 0.1 M) at 0 °C was added NaH (60% dispersion in mineral oil, 38 mg, 0.972 mmol, 1.4 equiv) and the mixture was stirred at 0 °C for 15 min and then allowed to warm to 23 °C over 15 min. BnBr (412 μL, 3.47 mmol, 5.0 equiv) was then added dropwise and the reaction mixture was heated to 50 °C. After stirring for 8 h, the reaction mixture was allowed to cool to 23 °C and poured into saturated aqueous NH_4Cl (5 mL), the layers were separated, and the aqueous phase was extracted with ethyl acetate (3 x 2 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% EtOAc/hexanes) to provide the title compound as a colorless foam (303 mg, 0.580 mmol, 84% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.72 (d, J = 8.5 Hz, 2H), 7.31 – 7.12 (m, 5H), 6.90 – 6.80 (m, 2H), 5.95 – 5.75 (m, 1H), 5.41 – 5.26 (m, 2H), 4.69 – 4.54 (m, 2H), 4.21 – 4.05 (m, 1H), 4.02 – 3.86 (m, 2H), 3.83 (s, 3H),

3.78 – 3.62 (m, 2H), 3.56 – 3.49 (m, 1H), 3.43 – 3.10 (m, 2H), 1.45 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 173.4, 172.0, 171.7, 170.8, 170.2, 162.9, 155.4, 154.8, 135.7, 135.6, 131.1, 130.9, 130.7, 130.5, 128.5, 128.3, 128.2, 127.5, 127.3, 127.0, 120.2, 119.9, 113.5, 80.9, 80.7, 66.6, 62.4, 62.0, 55.3, 47.1, 46.8, 46.0, 45.8, 42.8, 42.5, 41.9, 28.3; IR (Neat Film, NaCl) 2976, 2359, 1698, 1604, 1512, 1455, 1416, 1366, 1324, 1258, 1155, 1028, 979, 840, 741, 703, 671, 634 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{29}H_{35}N_2O_7$ $[M+H]^+$: 523.2439, found 523.2446.



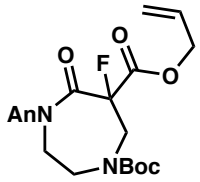
6-allyl 1-(*tert*-butyl) 6-(2-chloroallyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3f)

To a suspension of allyl ester **2c** (300 mg, 0.694 mmol, 1.0 equiv) and Cs_2CO_3 (453 mg, 1.39 mmol, 2.0 equiv) in acetonitrile (7 mL, 0.1 M) was added 2,3-dichloropropene (320 μL, 3.47 mmol, 5.0 equiv) at 23 °C. The reaction mixture was heated to 50 °C and stirred for 19 h, after which starting material remained as judged by TLC. Tetrabutylammonium iodide (25.6 mg, 0.0694 mmol, 0.1 equiv) was added and the reaction mixture was stirred at 50 °C for an additional 9 h, then allowed to cool to 23 °C. The mixture was filtered through a cotton plug and concentrated under reduced pressure. The crude product was purified by silica gel flash chromatography (20% EtOAc/petroleum ether) to provide the title compound as a colorless oil (196 mg, 0.387 mmol, 56% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, *J* = 8.8 Hz, 2H), 6.85 (d, *J* = 8.9 Hz, 2H), 6.12 – 5.94 (m, 1H), 5.60 – 5.25 (m, 4H), 4.78 (qdt, *J* = 12.8, 6.0, 1.2 Hz, 2H), 4.25 (br t, *J* = 13.9 Hz, 1H), 4.17 – 3.87 (m, 3H), 3.84 (s, 3H), 3.76 – 3.51 (m, 1H), 3.48 – 3.30 (m, 1H), 3.29 – 2.99 (m, 2H), 1.43 (d, *J* = 16.9 Hz, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.9, 173.3, 170.3, 163.1, 155.9, 155.1, 137.0, 136.7, 131.1, 127.2, 120.6, 120.3, 119.4, 118.4, 113.6, 81.4, 81.0, 67.5, 60.0, 55.5, 47.1, 45.9, 46.0, 45.2, 45.6, 44.7, 43.1, 42.8, 28.4; IR (Neat Film, NaCl) 3356, 3080, 2977, 2933, 2841, 2568, 2254, 1700, 1629, 1605, 1579, 1512, 1456, 1417, 1393, 1367, 1326, 1281, 1257, 1217, 1196, 1153, 1029, 988, 910, 842, 811, 780, 757, 732, 668, 634, 621 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{25}H_{32}ClN_2O_7$ $[M+H]^+$: 507.1893, found 507.1902.



6-allyl 1-(*tert*-butyl) 4-benzoyl-6-fluoro-5-oxo-1,4-diazepane-1,6-dicarboxylate (3g)

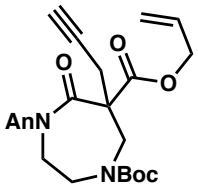
To a 20 mL vial containing allyl ester **2a** (250 mg, 0.621 mmol, 1.0 equiv) in THF (7.4 mL, 0.1 M) at 23 °C was added NaH (60% dispersion in mineral oil, 27.3 mg, 0.683 mmol, 1.1 equiv). After stirring for 12 min, Selectfluor™ (264 mg, 0.745 mmol, 1.2 equiv) was added in a single portion, and the reaction mixture was warmed to 50 °C and stirred for 24 h, after which starting material remained as judged by TLC. Additional Selectfluor™ (264 mg, 0.745 mmol, 1.2 equiv) was then added, and the reaction mixture was stirred for an additional 8 h at 50 °C. The reaction mixture was allowed to cool to 23 °C and water (5 mL) was added. The layers were separated and the aqueous layer was extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by silica gel flash chromatography (25% EtOAc/hexanes) to provide the title compound (167 mg, 0.397 mmol, 64% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.64 – 7.56 (m, 2H), 7.52 – 7.43 (m, 1H), 7.36 (t, J = 7.7 Hz, 2H), 5.99 – 5.80 (m, 1H), 5.43 – 5.19 (m, 2H), 4.83 – 4.56 (m, 2H), 4.52 – 4.17 (m, 3H), 4.03 – 3.56 (m, 2H), 3.27 – 3.08 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.1, 169.6, 169.4, 164.8, 164.6, 154.9, 134.3, 132.5, 130.7, 128.5, 128.4, 119.7, 95.7 (d, J = 204.8 Hz), 81.5, 67.2, 47.6 (dd, $J_{C\text{-}F}$ = 137.5, 24.1 Hz), 47.3, 46.4, 42.8, 28.3; IR (Neat Film, NaCl) 2978, 2926, 1694, 1450, 1414, 1393, 1367, 1329, 1246, 1152, 1042, 999, 979, 926, 857, 766, 724, 694, 672, 648 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{21}H_{29}FN_3O_6$ $[M+NH_4]^+$: 438.2035, found 438.2040.



6-allyl 1-(tert-butyl) 6-fluoro-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3h)

To a 20 mL vial containing allyl ester **2c** (320 mg, 0.740 mmol, 1.0 equiv) and NaH (60% dispersion in mineral oil, 32.5 mg, 0.814 mmol, 1.1 equiv) was added THF (7.4 mL, 0.1 M) at 23 °C. After stirring for 30 min, Selectfluor™ (315 mg, 0.889 mmol, 1.2 equiv) was added in a

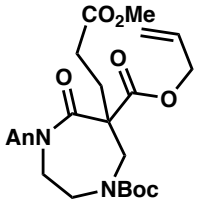
single portion, and the reaction mixture was warmed to 50 °C and stirred for 5 h. The crude reaction mixture was then concentrated under reduced pressure and purified by silica gel flash chromatography (30% acetone/hexanes) to provide the title compound (290 mg, 0.644 mmol, 87% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.58 (m, 2H), 6.90 – 6.82 (m, 2H), 5.91 (ddt, *J* = 16.3, 10.9, 5.7 Hz, 1H), 5.43 – 5.21 (m, 2H), 4.84 – 4.40 (m, 3H), 4.40 – 4.16 (m, 2H), 4.00 – 3.86 (m, 1H), 3.82 (s, 3H), 3.77 – 3.56 (m, 1H), 3.22 – 3.09 (m, 1H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.6, 169.6 (dd, $J_{C\text{-}F}$ = 48.2, 25.4 Hz), 164.9 (d, $J_{C\text{-}F}$ = 25.8 Hz), 163.4, 155.0, 131.3, 130.8, 126.1, 119.8, 113.9, 95.7 (dd, $J_{C\text{-}F}$ = 205.6, 14.6 Hz), 81.5, 67.3, 55.5, 47.5 (dd, $J_{C\text{-}F}$ = 109.0, 23.7 Hz), 47.2 (d, $J_{C\text{-}F}$ = 92.2 Hz), 43.4, 28.3; IR (Neat Film, NaCl) 2976, 2936, 2844, 1759, 1698, 1603, 1578, 1512, 1449, 1414, 1367, 1327, 1258, 1168, 1151, 1076, 1030, 997, 977, 942, 929, 841, 817, 770, 760, 730, 698 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{28}FN_2O_7$ $[M+H]^+$: 451.1875, found 451.1877.



6-allyl 1-(tert-butyl) 4-(4-methoxybenzoyl)-5-oxo-6-(prop-2-yn-1-yl)-1,4-diazepane-1,6-dicarboxylate (3i)

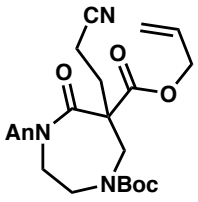
To a solution of allyl ester **2c** (250 mg, 0.578 mmol, 1.0 equiv) in THF (5.8 mL, 0.1 M) was added NaH (60% dispersion in mineral oil, 25 mg, 0.636 mmol, 1.1 equiv) at 0 °C. After stirring for 30 min at 0 °C, propargyl bromide (80% wt/wt in toluene, 125 µL, 1.16 mmol, 2.0 equiv) was added at 0 °C. The reaction mixture was heated to 50 °C and stirred for 16 h. The mixture was allowed to cool to 23 °C, quenched with aqueous $NaHCO_3$ (10 mL) and extracted with EtOAc (3 x 5 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by automated silica gel flash chromatography (Teledyne ISCO, 0→50% acetone/hexanes) to provide propargyl allyl ester **3i** as a colorless oil (220 mg, 0.468 mmol, 81% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.73 – 7.59 (m, 2H), 6.84 (d, *J* = 8.6 Hz, 2H), 5.99 (ddt, *J* = 17.3, 10.4, 6.0 Hz, 1H), 5.54 – 5.27 (m, 2H), 4.85 – 4.69 (m, 2H), 4.33 – 3.85 (m, 4H), 3.82 (s, 3H), 3.76 – 3.56 (m, 1H), 3.56 – 3.39 (m, 1H), 3.14 – 2.90 (m, 2H), 2.08 (s, 1H), 1.42 (d, *J* = 14.3 Hz, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7, 173.2, 170.5, 170.3, 169.7, 169.3, 163.0, 155.6, 154.9, 131.2, 131.0, 127.1, 120.3, 120.0,

113.6, 81.1, 81.0, 78.9, 78.6, 72.3, 67.3, 60.7, 60.4, 55.5, 47.1, 46.5, 46.2, 46.0, 43.0, 28.3, 27.0, 26.9; IR (Neat Film, NaCl) 3280, 2975, 2936, 1737, 1694, 1604, 1579, 1547, 1512, 1454, 1416, 1393, 1366, 1326, 1280, 1258, 1156, 1134, 1030, 994, 980, 841, 778, 770, 737, 706, 677, 634, 622 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{25}H_{31}N_2O_7$ $[M+H]^+$: 471. 2126, found 471.2130.



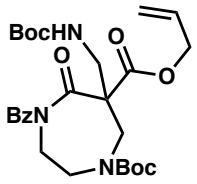
6-allyl 1-(*tert*-butyl) 6-(3-methoxy-3-oxopropyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3j)

To a 20 mL vial containing allyl ester **2c** (300 mg, 0.694 mmol, 1.0 equiv) and K_2CO_3 (480 mg, 3.47 mmol, 5.0 equiv) was added acetone (2.8 mL, 0.25 M) and methyl acrylate (126 μL, 1.39 mmol, 2.0 equiv) at 23 °C. The vessel was sealed and heated to 50 °C. After stirring for 5 h, additional methyl acrylate (126 μL, 1.39 mmol, 2.0 equiv) was added and the reaction was stirred for an additional 14 h. The reaction mixture was then filtered through a plug of cotton, concentrated under reduced pressure, and purified by silica gel flash chromatography (33% EtOAc/petroleum ether) to provide diester **3j** as a colorless, waxy solid (185 mg, 0.357 mmol, 51% yield); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.77 – 7.65 (m, 2H), 6.92 – 6.79 (m, 2H), 5.96 (ddt, *J* = 17.2, 10.3, 6.1 Hz, 1H), 5.48 – 5.27 (m, 2H), 4.82 – 4.63 (m, 2H), 4.32 – 3.84 (m, 3H), 3.83 (s, 3H), 3.81 – 3.66 (m, 1H), 3.62 (s, 3H), 3.58 – 3.40 (m, 2H), 2.56 – 2.13 (m, 4H), 1.44 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.8, 173.5, 173.0, 171.9, 170.9, 170.6, 163.0, 155.1, 154.8, 131.1, 131.0, 127.5, 120.6, 113.6, 81.2, 67.0, 60.4, 55.5, 51.7, 48.7, 47.8, 47.0, 46.0, 43.4, 31.4, 29.8, 28.3; IR (Neat Film, NaCl) 3354, 2976, 2843, 2568, 2255, 2044, 1694, 1605, 1579, 1556, 1513, 1416, 1393, 1367, 1260, 1168, 1030, 982, 916, 843, 811, 782, 766, 732, 648, 634 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{26}H_{38}N_3O_9$ $[M+NH_4]^+$: 536.2603, found 536.2603.



6-allyl 1-(tert-butyl) 6-(2-cyanoethyl)-4-(4-methoxybenzoyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3k)

To a 20 mL vial containing allyl ester **2c** (300 mg, 0.694 mmol, 1.0 equiv) and K_2CO_3 (480 mg, 3.47 mmol, 5.0 equiv) was added acetone (2.8 mL, 0.25 M) and acrylonitrile (182 µL, 2.78 mmol, 4.0 equiv) at 23 °C. The vessel was sealed and heated to 50 °C. After 17 h of stirring, the reaction mixture was filtered through a plug of cotton, concentrated under reduced pressure, and purified by silica gel flash chromatography (33% EtOAc/petroleum ether) to provide **3k** as a colorless foam (176 mg, 0.362 mmol, 52% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, *J* = 8.8 Hz, 2H), 6.89 (d, *J* = 8.9 Hz, 2H), 6.01 (ddt, *J* = 16.7, 10.3, 6.3 Hz, 1H), 5.51 – 5.36 (m, 2H), 4.89 – 4.75 (m, 2H), 4.32 – 3.88 (m, 3H), 3.86 (s, 3H), 3.84 – 3.34 (m, 3H), 2.71 – 2.09 (m, 4H), 1.53 – 1.34 (m, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.8, 170.3, 163.2, 155.3, 131.0, 130.6, 127.1, 121.4, 121.1, 119.1, 113.7, 81.4, 67.5, 60.2, 55.5, 47.5, 46.8, 43.6, 32.9, 28.3, 13.6; IR (Neat Film, NaCl) 2975, 2934, 2250, 1694, 1605, 1579, 1512, 1455, 1419, 1393, 1367, 1326, 1255, 1164, 1031, 1000, 979, 941, 916, 842, 813, 781, 762, 733, 648, 634 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{25}H_{35}N_4O_7$ $[M+NH_4]^+$: 503.2500, found 503.2505.

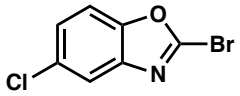


6-allyl 1-(*tert*-butyl) 4-benzoyl-6-(((tert-butoxycarbonyl)amino)methyl)-5-oxo-1,4-diazepane-1,6-dicarboxylate (3l)

A solution of allyl ester **2a** (200 mg, 0.497 mmol, 1.0 equiv) and *tert*-butyl ((phenylsulfonyl)methyl)carbamate[5,6] (162 mg, 0.597 mmol, 1.2 equiv) in CH_2Cl_2 (2.5 mL, 0.2 M) at 23 °C was stirred for 5 min, after which time Cs_2CO_3 (405 mg, 1.24 mmol, 2.5 equiv) was added at the same temperature. After an additional 30 min of stirring, saturated aqueous NH_4Cl (1 mL) was added and the biphasic mixture was vigorously stirred for 20 min. The layers were separated and the aqueous phase was extracted with CH_2Cl_2 (3 x 3 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure onto silica gel (2 g). The silica-adsorbed crude reaction mixture was purified by automated silica gel flash chromatography (Teledyne ISCO, 10→40% acetone/hexanes) to provide carbamate **3l**

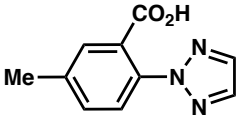
as a white foam (200 mg, 0.376 mmol, 76% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 – 7.71 (m, 2H), 7.59 – 7.46 (m, 1H), 7.46 – 7.36 (m, 2H), 6.00 (ddt, *J* = 16.6, 10.3, 6.1 Hz, 1H), 5.51 – 5.25 (m, 2H), 5.17 (br s, 1H), 4.79 – 4.64 (m, 2H), 4.48 – 4.23 (m, 1H), 4.14 – 3.20 (m, 7H), 1.44 (s, 9H), 1.42 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 174.1, 173.8, 172.7, 170.1, 169.6, 156.0, 155.2, 154.7, 135.5, 132.2, 131.4, 128.5, 128.4, 120.2, 81.4, 79.6, 67.4, 62.7, 47.1, 46.8, 45.9, 43.2, 28.5, 28.4; IR (Neat Film, NaCl) 3457, 2977, 2934, 2253, 1704, 1600, 1503, 1450, 1417, 1392, 1367, 1325, 1283, 1248, 1158, 1042, 980, 913,77 860, 767, 729, 693, 663 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{27}H_{38}N_3O_8$ $[M+H]^+$: 532.2653, found 532.2664.

Derivatization of Allylic Alkylation Products



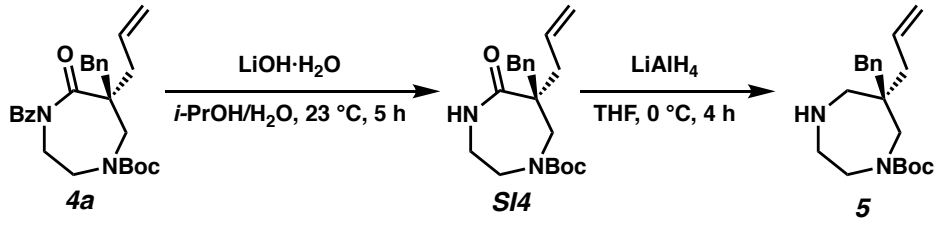
2-bromo-5-chlorobenzo[*d*]oxazole (6)

Prepared according to the literature procedure by Mangion and coworkers[7] and used directly in the synthesis of **7**.



5-methyl-2-(2*H*-1,2,3-triazol-2-yl)benzoic acid (8)

Prepared according to the literature procedure by Mangion and coworkers.[7] All characterization data matched those reported in the literature.



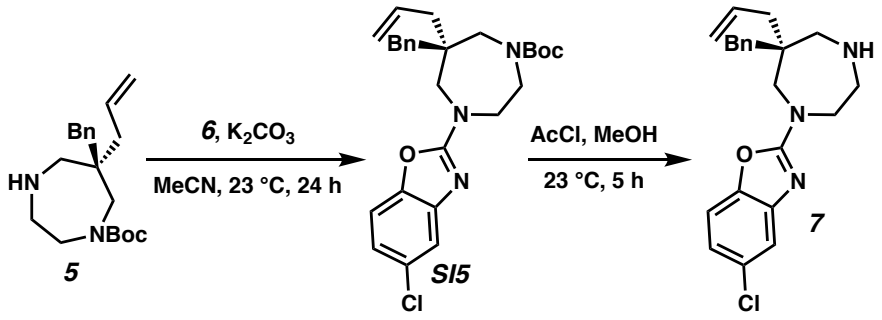
***tert*-butyl (*S*)-6-allyl-6-benzyl-5-oxo-1,4-diazepane-1-carboxylate (SI4)**

To a flask containing benzoyl-protected diazepanone **4a** (460 mg, 1.03 mmol, 1.0 equiv) was added isopropyl alcohol (100 mL, 0.01 M) and water (10 mL), followed by LiOH·H_2O (61 mg, 1.45 mmol, 1.5 equiv) at 23 °C. After stirring for 4 h at 23 °C, the isopropyl alcohol was removed under reduced pressure and the resulting aqueous mixture extracted with EtOAc (4 x 50

mL). The combined organic extracts were dried with sodium sulfate, filtered, and concentrated under reduced pressure to yield a crude oil (400 mg) that was used without further purification.

***tert*-butyl (*R*)-6-allyl-6-benzyl-1,4-diazepane-1-carboxylate (5)**

Crude lactam **SI4** (350 mg [theoretical maximum 310 mg lactam], 0.903 mmol, 1 equiv) was dissolved in THF (10.2 mL, 0.1 M) and cooled to 0 °C. $LiAlH_4$ (77 mg, 2.03 mmol, 2.25 equiv) was then added, and the reaction mixture was stirred at 0 °C for 4 h, over the course of which an additional 3.37 equiv (116 mg, 3.05 mmol) of $LiAlH_4$ were added in total (77 mg, followed by 39 mg, at equal intervals). The reaction mixture was then diluted with diethyl ether (10 mL) and water (300 μL) was added. After gas generation subsided, 15% aqueous NaOH (300 μL) was added, followed by additional water (900 μL). After stirring at 0 °C for 15 min, anhydrous $MgSO_4$ was added, and the mixture was stirred for an additional 10 min, whereafter it was filtered through celite and concentrated under reduced pressure. Purification by automated silica gel flash chromatography (Teledyne ISCO, 0→20% MeOH/CH_2Cl_2) provided the product as a light yellow oil (130 mg, 0.393 mmol, 44% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 – 7.14 (m, 5H), 6.01 (dq, *J* = 17.1, 7.8 Hz, 1H), 5.18 (d, *J* = 15.9 Hz, 2H), 3.67 – 3.30 (m, 4H), 2.97 (m, 2H), 2.88 – 2.48 (m, 4H), 2.30 – 2.06 (m, 3H), 1.50 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.8, 138.1, 134.6, 130.7, 128.0, 126.2, 118.2, 79.8, 79.5, 57.9, 57.2, 55.3, 54.2, 50.9, 49.8, 49.3, 43.5, 41.3, 39.8, 39.4, 28.5; IR (Neat Film, NaCl) 3357, 3066, 3028, 2976, 2928, 1694, 1602, 1464, 1455, 1416, 1391, 1365, 1334, 1302, 1248, 1166, 1031, 996, 952, 912, 866, 771, 733, 703, 685, 672, 659, 644, 612 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{20}H_{31}N_2O_2$ $[M+H]^+$: 331.2380, found 331.2399; $[\alpha]_D^{22.24}$ –6.496 (c 2.0, $CHCl_3$).



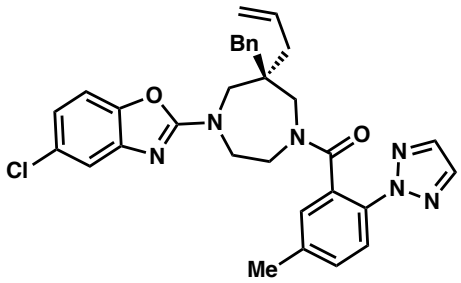
***tert*-butyl (*R*)-6-allyl-6-benzyl-4-(5-chlorobenzo[*d*]oxazol-2-yl)-1,4-diazepane-1-carboxylate (SI5)**

To a 1 dram vial containing diazepane **5** (9.5 mg, 0.0287 mmol, 1.0 equiv), aryl bromide **6** (10.0 mg, 0.0431 mmol, 1.5 equiv), and K_2CO_3 (7.9 mg, 0.0574 mmol, 2 equiv) was added

MeCN (0.3 mL, 0.1 M) at 23 °C. After stirring for 24 h at 23 °C, saturated aqueous NH_4Cl (1 mL) was added, and the mixture was extracted with EtOAc (3 x 1 mL). The combined organic extracts were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The crude material (15.4 mg) thus obtained was carried forward without further purification.

(*S*)-2-(6-allyl-6-benzyl-1,4-diazepan-1-yl)-5-chlorobenzo[*d*]oxazole (7)

Crude carbamate **SI5** was dissolved in MeOH (0.3 mL, 0.1 M) and AcCl (20.5 µL, 0.288 mmol, 10 equiv) was added at 23 °C. After stirring for 5 h at 23 °C, the reaction mixture was concentrated under reduced pressure and purified by silica gel flash chromatography (66% EtOAc/benzene + 1% Et_3N) to provide **7** as a beige, amorphous solid (4.3 mg, 0.0113 mmol, 39% yield from **5**) of sufficient purity for use in the next reaction, however, further purification was possible by silica gel flash chromatography with 2% Et_3N in Et_2O; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 – 7.27 (m, 3H), 7.25 – 7.17 (m, 3H), 7.12 (d, *J* = 8.4 Hz, 1H), 6.94 (dd, *J* = 8.4, 2.3 Hz, 1H), 5.99 (ddt, *J* = 14.5, 10.4, 7.2 Hz, 1H), 5.30 (d, *J* = 3.1 Hz, 1H), 5.20 – 5.10 (m, 1H), 3.87 – 3.61 (m, 3H), 3.15 – 3.00 (m, 2H), 2.90 – 2.66 (m, 3H), 2.57 (d, *J* = 13.9 Hz, 1H), 2.22 – 2.10 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.5, 137.8, 134.1, 130.8, 129.4, 128.2, 126.4, 120.1, 118.8, 116.2, 109.2, 57.8, 56.5, 53.3, 49.2, 43.8, 41.3, 39.8; IR (Neat Film, NaCl) 2922, 1638, 1570, 1458, 1249, 1167, 921, 792, 710 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{22}H_{25}ClN_3O$ $[M+H]^+$: 382.1681, found 382.1695; $[\alpha]_D^{21.89}$ +7.524 (c 0.07, $CHCl_3$).



(*R*)-(6-allyl-6-benzyl-4-(5-chlorobenzo[*d*]oxazol-2-yl)-1,4-diazepan-1-yl)(5-methyl-2-(2*H*-1,2,3-triazol-2-yl)phenyl)methanone (9)

To a vial containing carboxylic acid **8** (35 mg, 0.172 mmol, 1.0 equiv) in CH_2Cl_2 (1.8 mL) at 23 °C was added DMF (4 µL, 0.0517 mmol, 0.3 equiv) and oxalyl chloride (18 µL, 0.207 mmol, 1.2 equiv). After stirring for 1 h, Et_3N (48 µL, 0.344 mmol, 2.0 equiv) was added, followed by amine **7** (60 mg, 0.155 mmol, 0.9 equiv) in CH_2Cl_2 (1.8 mL, 0.05 M total concentration). After stirring for an additional 1 h at 23 °C, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ (3 mL), the layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3

x 2 mL). The combined organic extracts were dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by automated silica gel flash chromatography (Teledyne ISCO, 0→40% Et_2O/hexanes) to provide amide **9** as a beige oil (29.6 mg, 0.0522 mmol, 34% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73 (s, 1H), 7.55 (s, 1H), 7.34 – 7.27 (m, 6H), 7.20 – 7.09 (m, 3H), 7.04 – 6.92 (m, 2H), 6.11 (ddt, *J* = 17.6, 10.4, 7.3 Hz, 1H), 5.26 – 5.12 (m, 2H), 4.24 – 4.07 (m, 1H), 3.96 (dd, *J* = 17.1, 14.4 Hz, 1H), 3.90 – 3.75 (m, 1H), 3.70 – 3.40 (m, 4H), 3.38 – 3.12 (m, 2H), 2.99 – 2.80 (m, 2H), 2.43 – 2.38 (m, 2H), 2.38 – 2.33 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 170.7, 170.5, 170.0, 163.0, 147.2, 144.4, 138.7, 138.6, 138.5, 136.9, 135.9, 135.8, 135.8, 135.7, 135.7, 135.6, 135.6, 134.2, 133.9, 133.8, 133.6, 133.5, 133.2, 132.9, 130.9, 130.8, 130.6, 130.6, 130.4, 130.4, 129.9, 129.5, 129.5, 129.0, 129.0, 128.3, 128.3, 128.2, 128.2, 128.2, 128.1, 128.1, 126.6, 126.6, 122.2, 122.0, 121.9, 120.5, 120.5, 119.2, 119.1, 119.0, 116.3, 116.3, 109.3, 109.2, 56.2, 56.1, 55.5, 54.3, 52.9, 52.2, 49.5, 49.3, 49.2, 48.9, 47.6, 45.0, 43.5, 43.1, 42.4, 42.2, 42.0, 41.8, 39.5, 39.5, 37.6, 21.0, 21.0, 20.9; IR (Neat Film, NaCl) 3431, 2923, 2854, 2356, 1644, 1634, 1574, 1568, 1538, 1505, 1462, 1454, 1428, 1372, 1308, 1251, 1216, 1172, 1054, 952, 921, 852, 822, 794, 737, 704 cm^{-1}; HRMS (MM: ESI-APCI): *m/z* calc'd for $C_{32}H_{32}ClN_6O_2$ $[M+H]^+$: 567.2270, found 567.2294; $[\alpha]_D^{22.24}$ +41.90 (c 1.0, $CHCl_3$).

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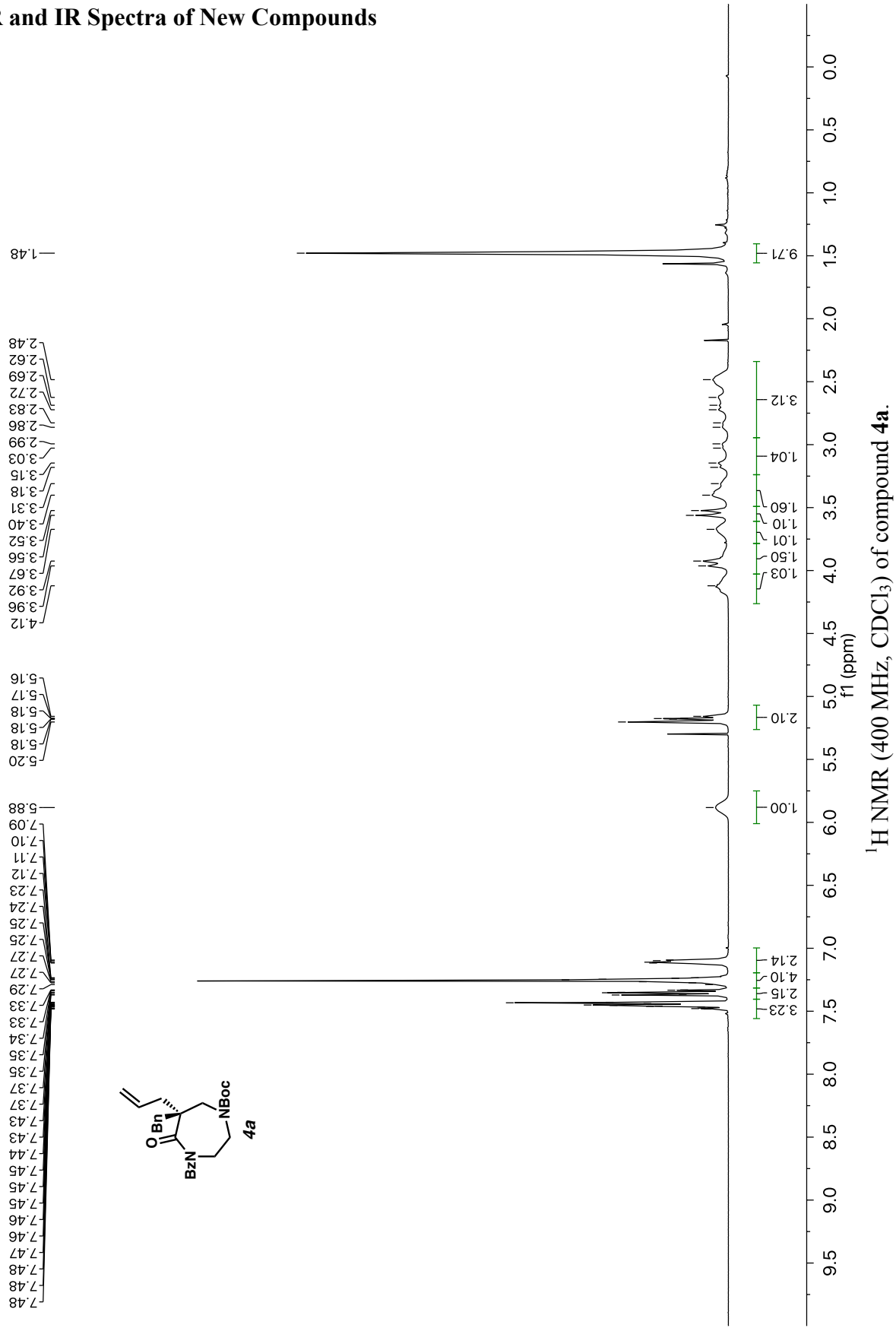
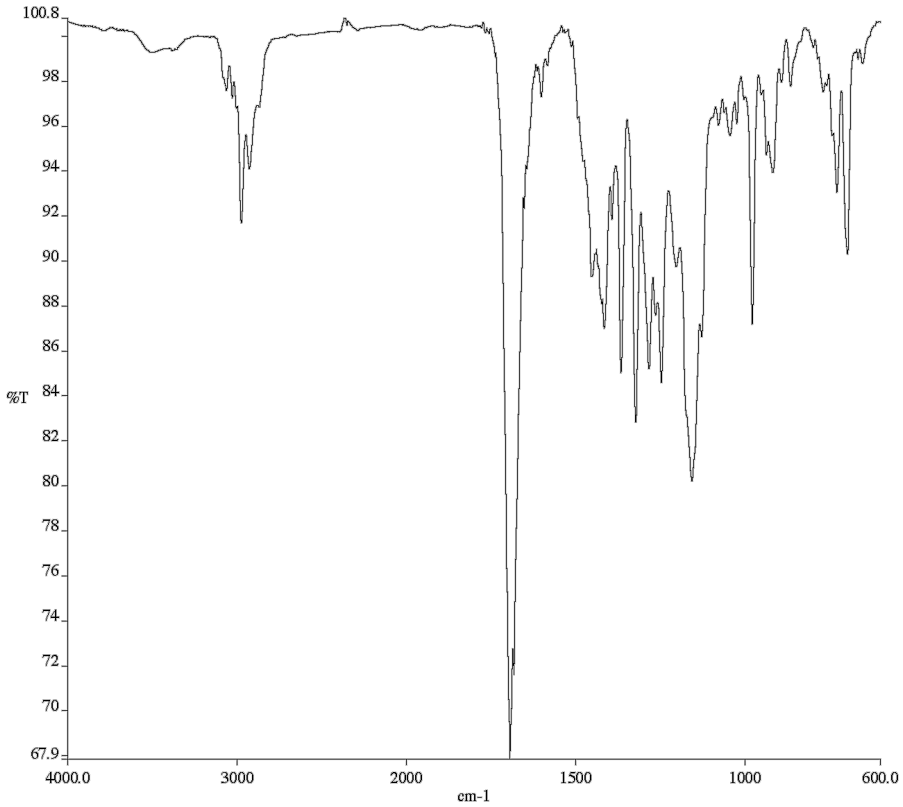
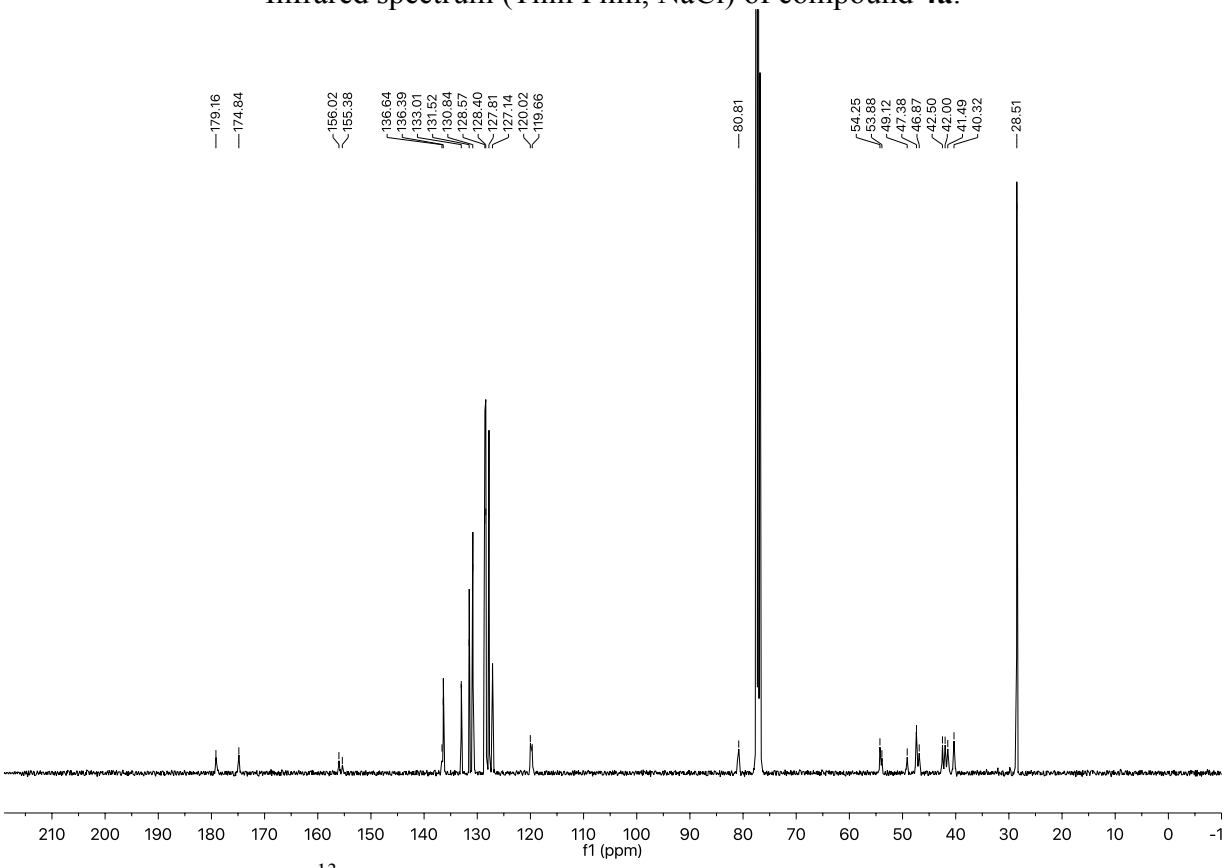
NMR and IR Spectra of New Compounds



^{1}H NMR (400 MHz, $CDCl_3$) of compound **4a**.



Infrared spectrum (Thin Film, NaCl) of compound **4a**.



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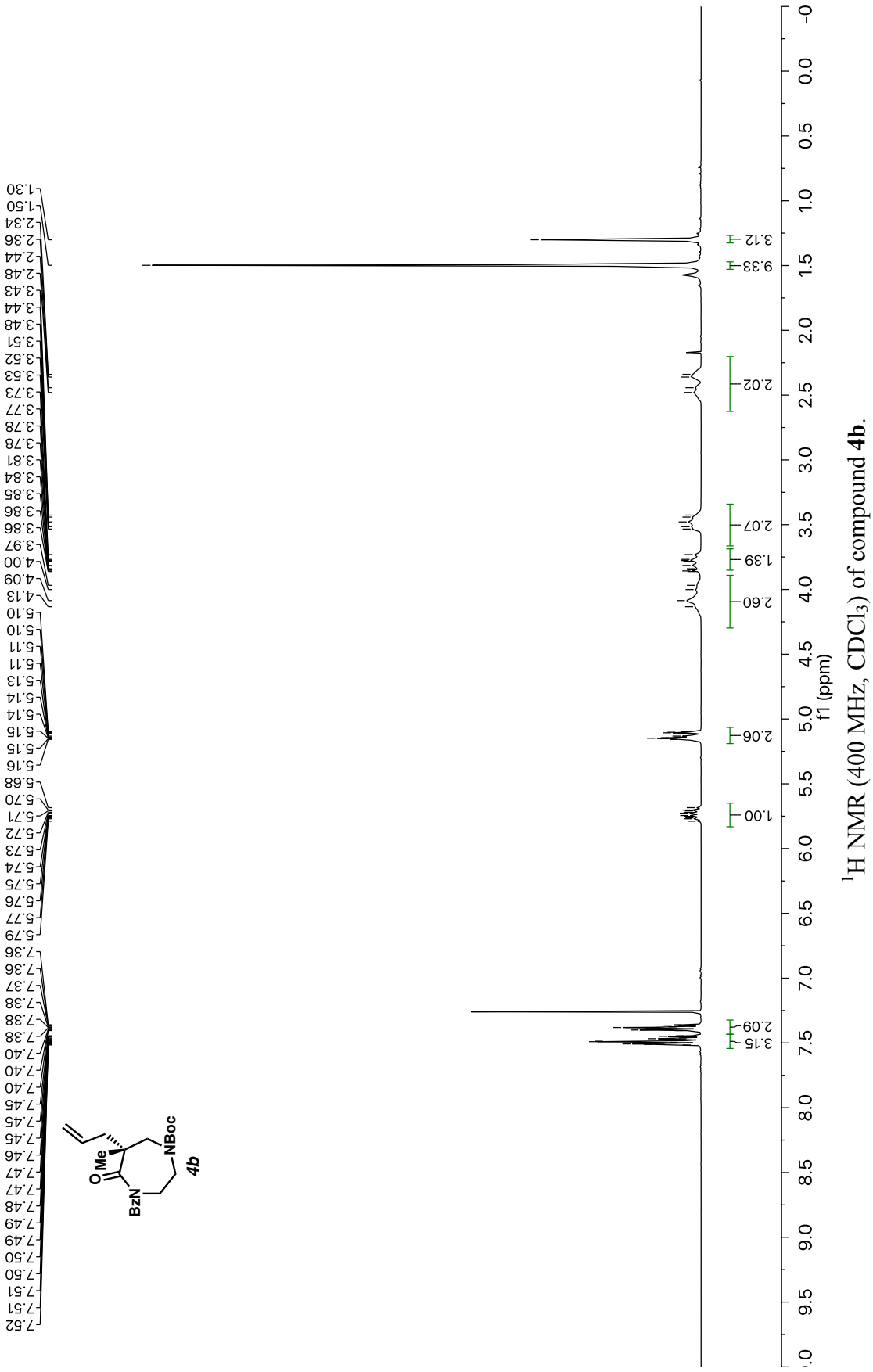
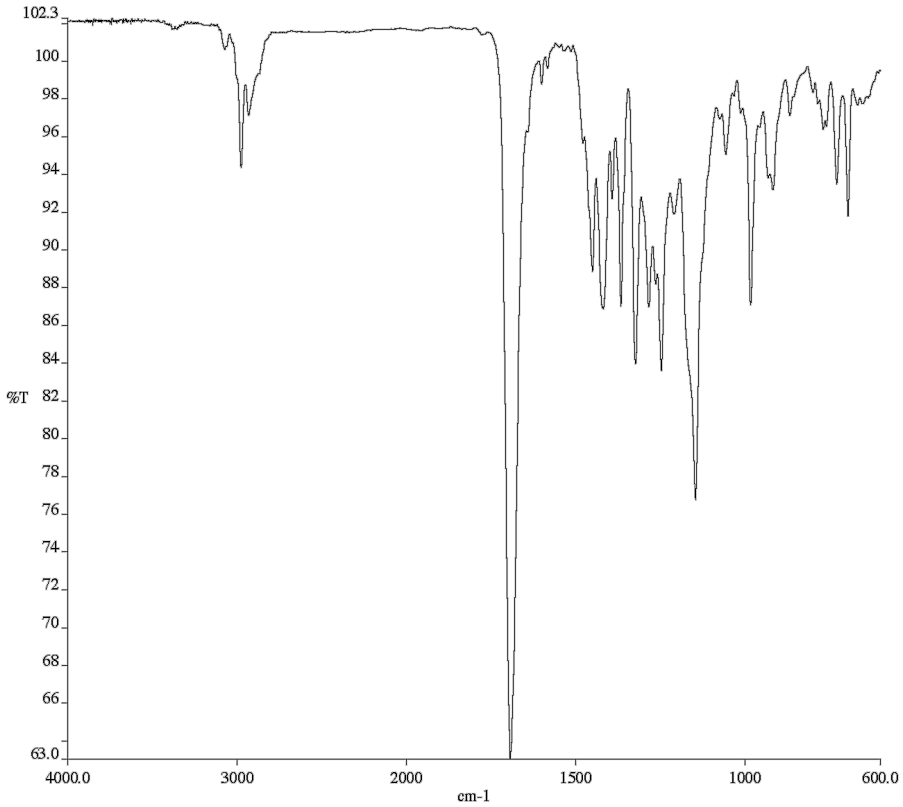
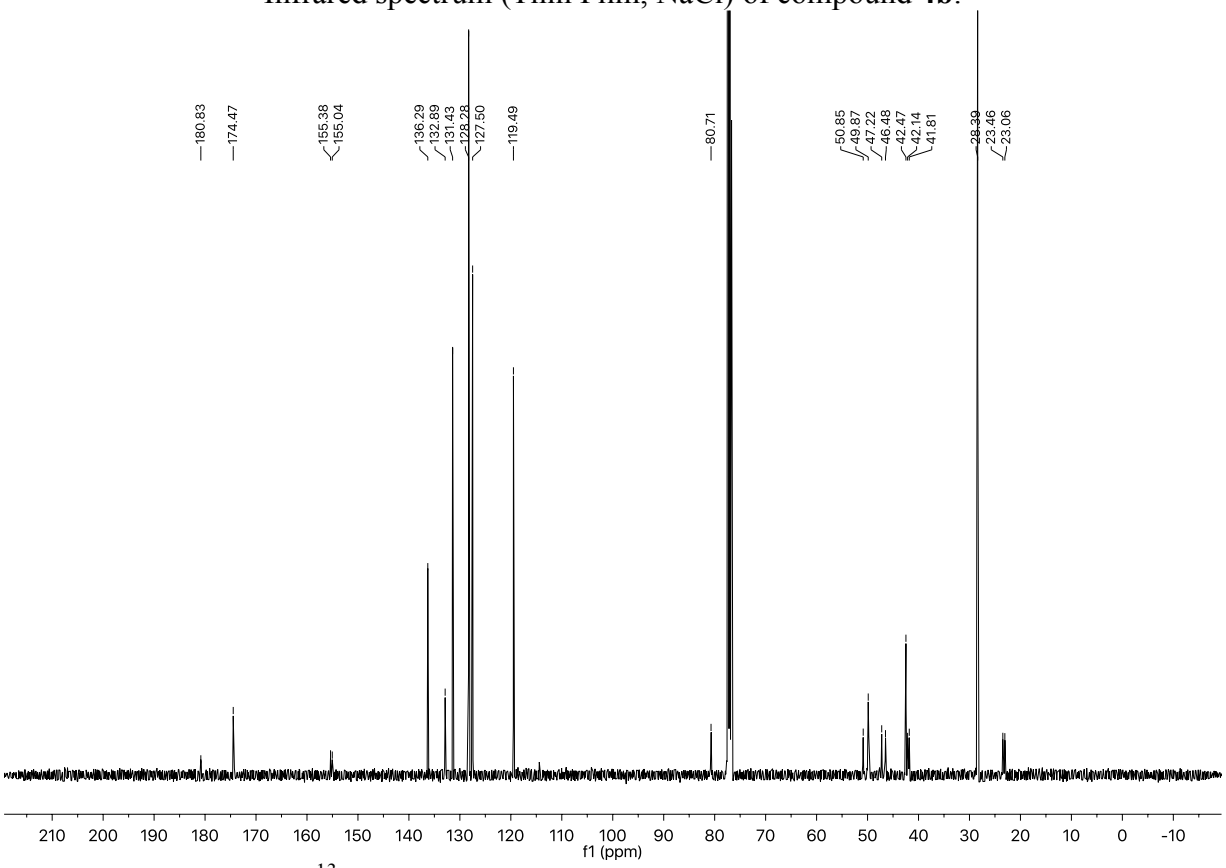


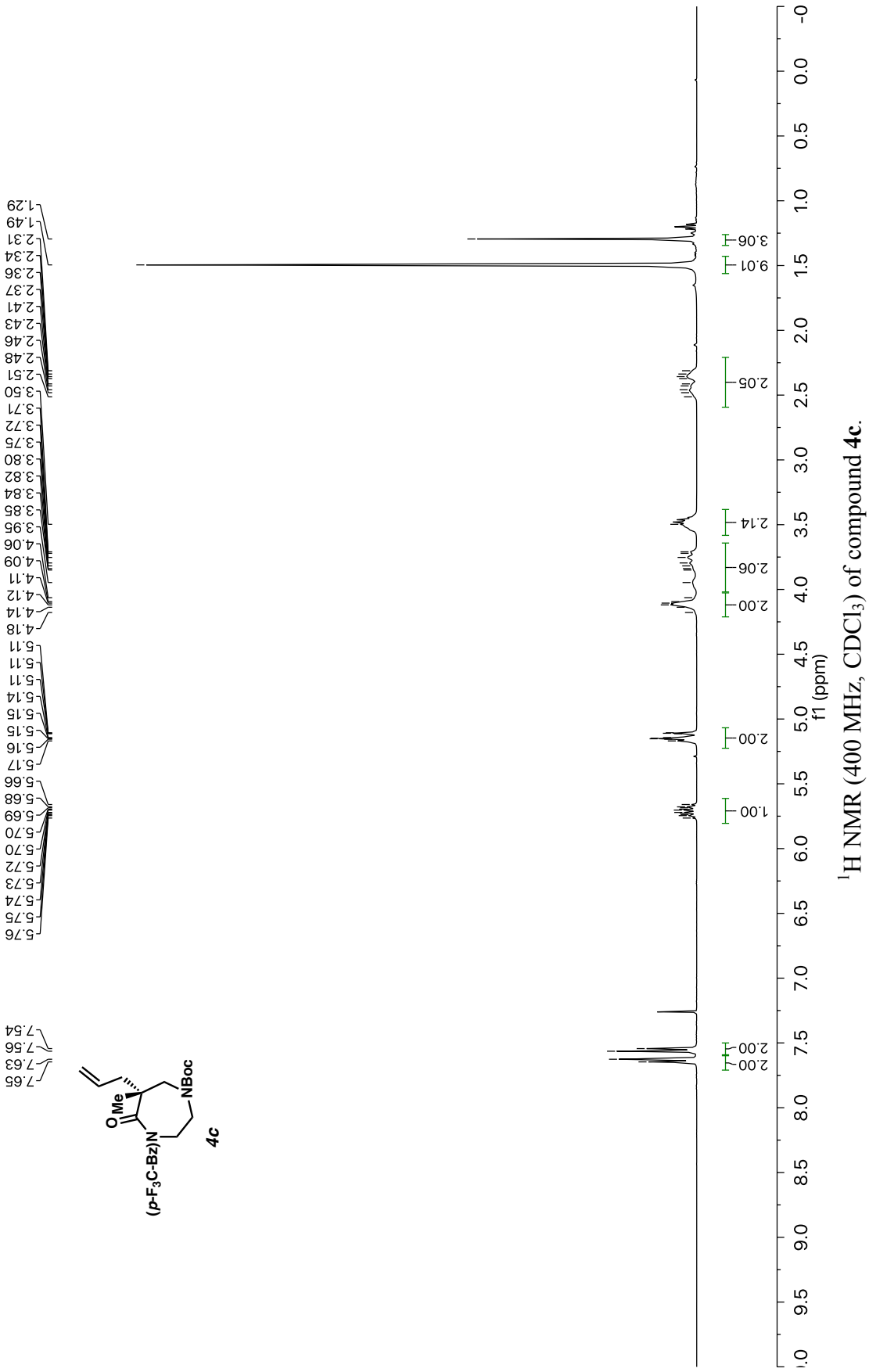
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4b**.



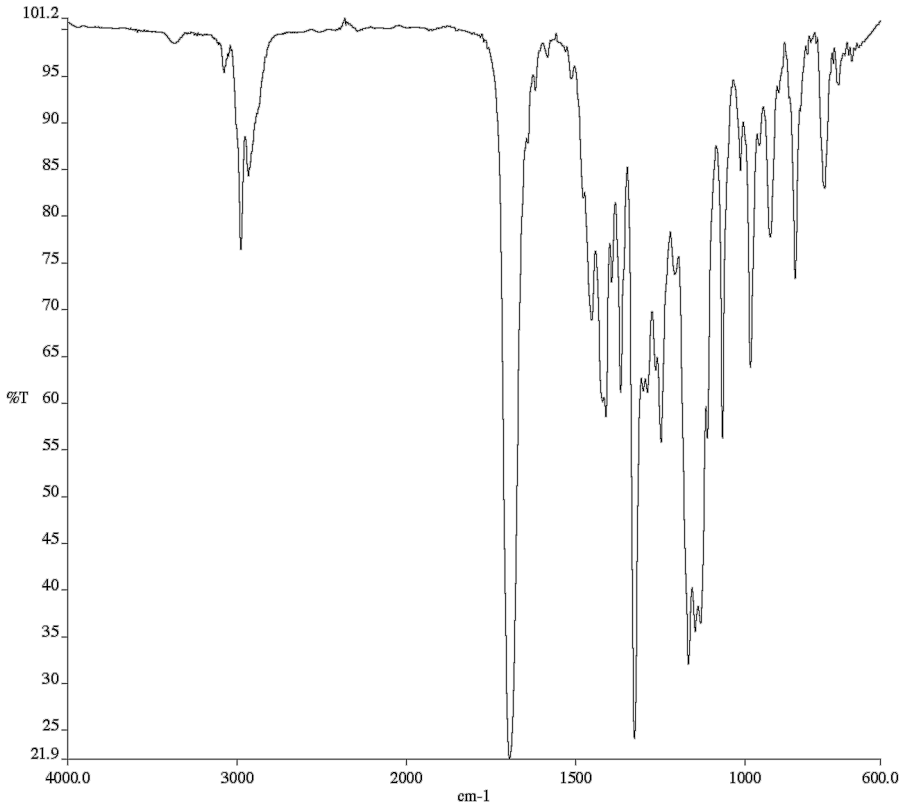
Infrared spectrum (Thin Film, NaCl) of compound **4b**.



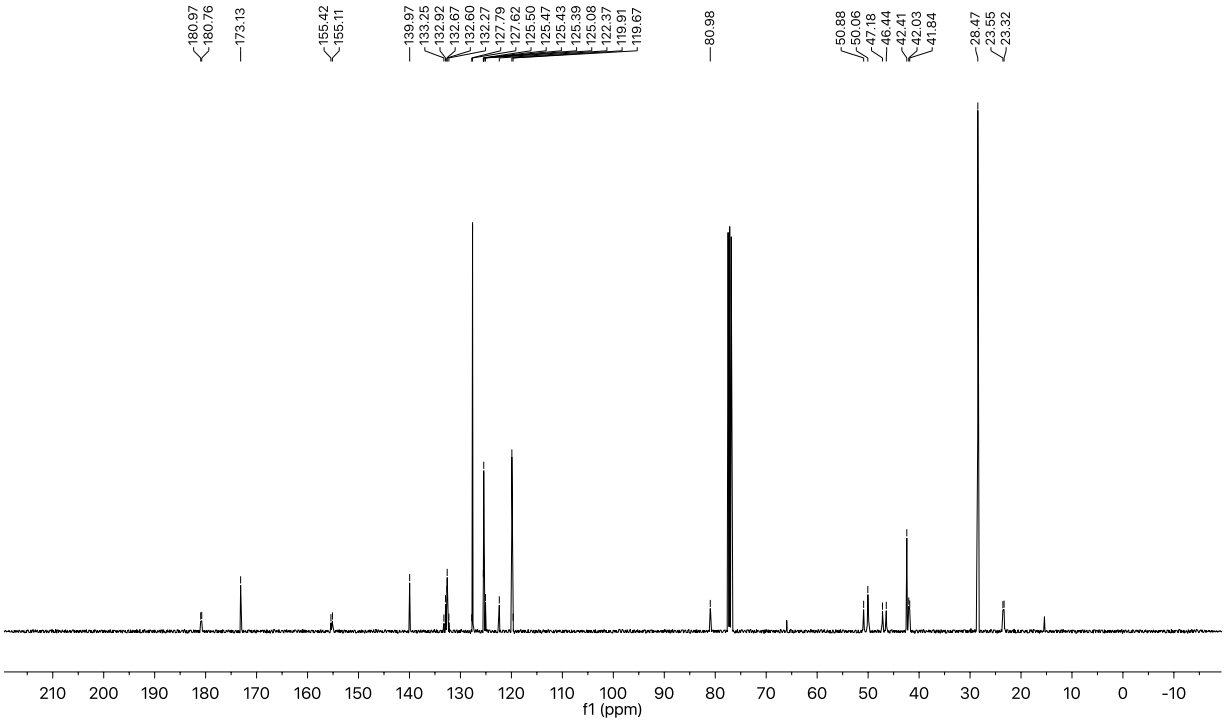
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4b**.



^{1}H NMR (400 MHz, $CDCl_3$) of compound **4c**.



Infrared spectrum (Thin Film, NaCl) of compound **4c**.



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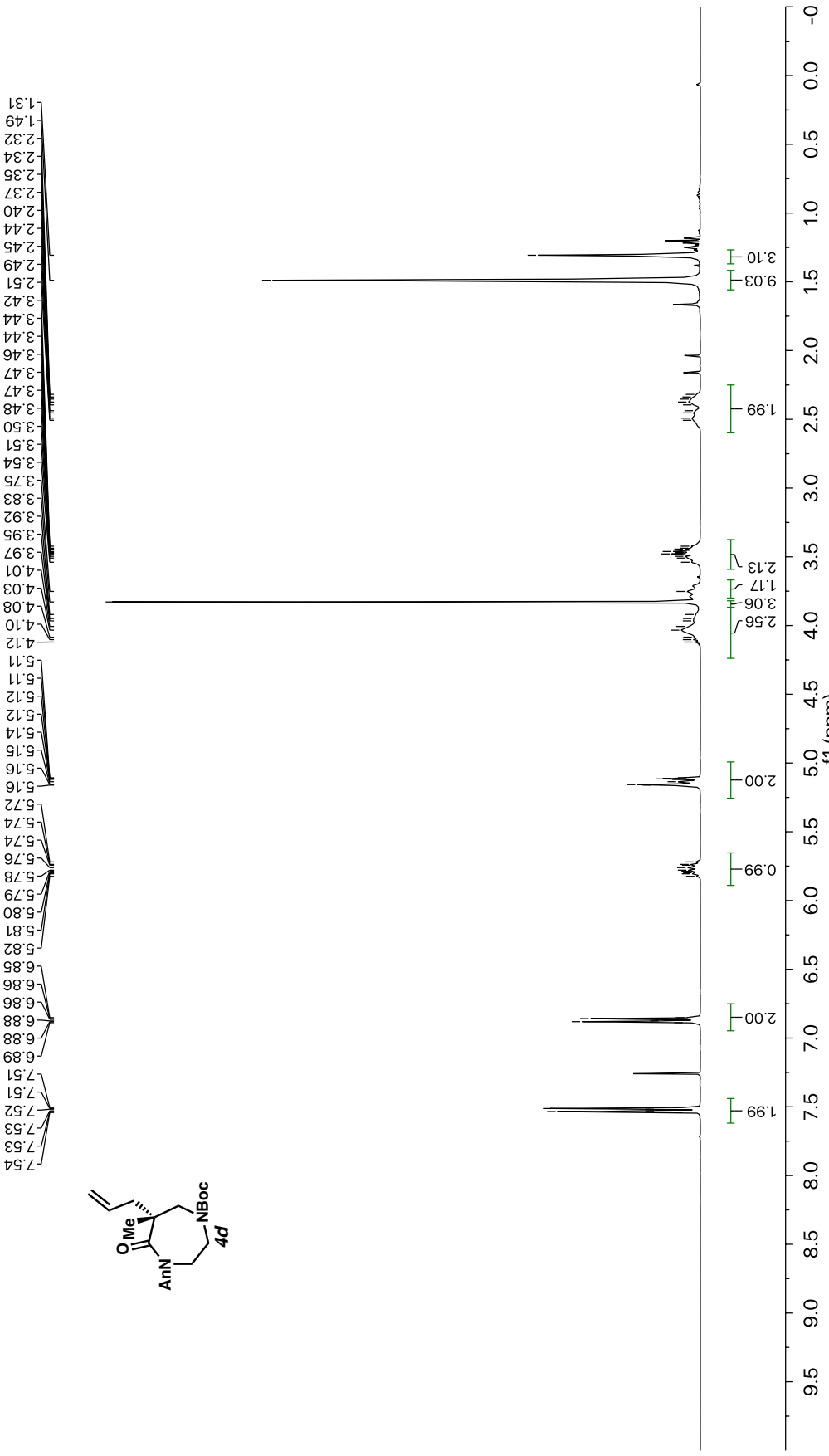
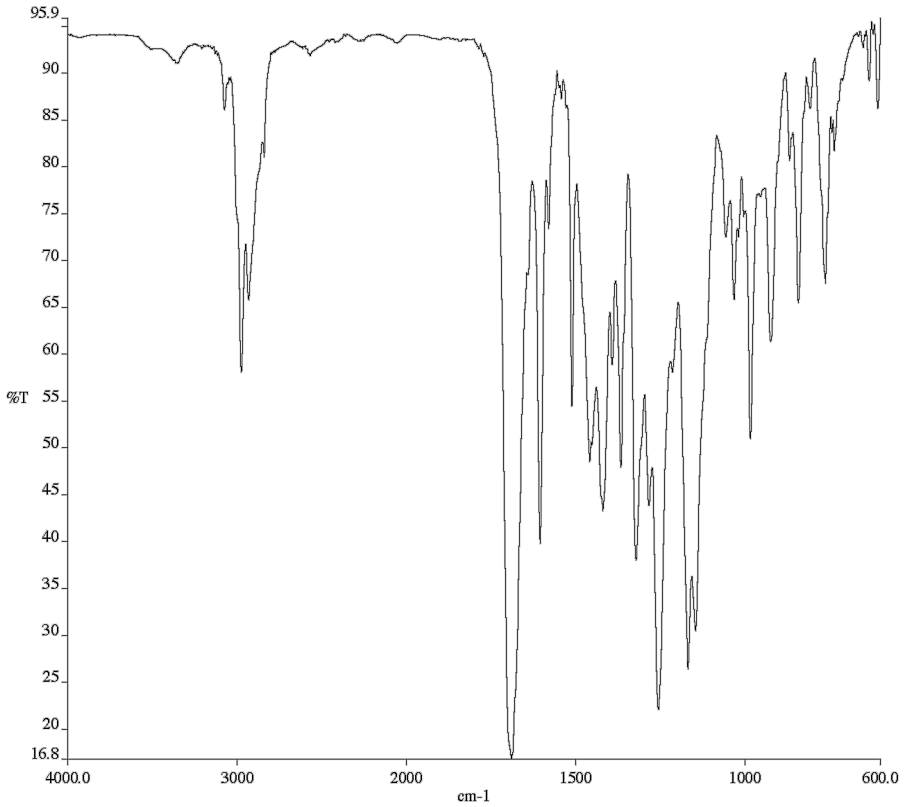


^{1}H NMR (400 MHz, $CDCl_3$) of compound **4d**.



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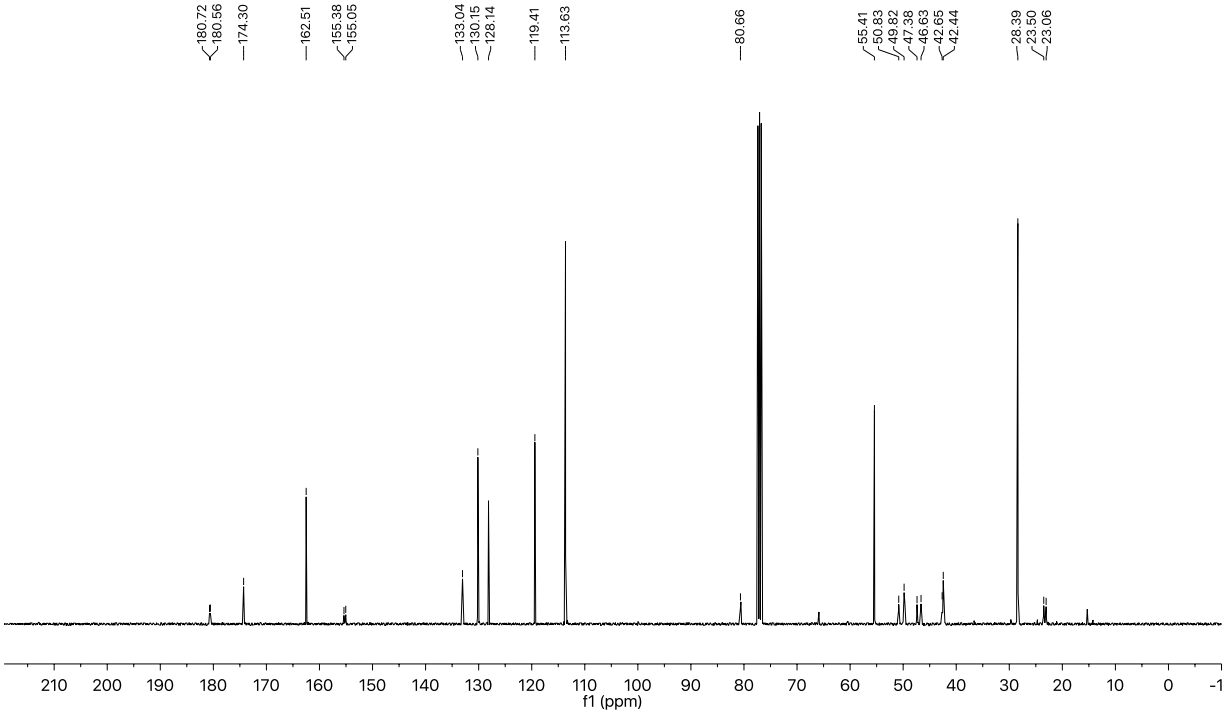

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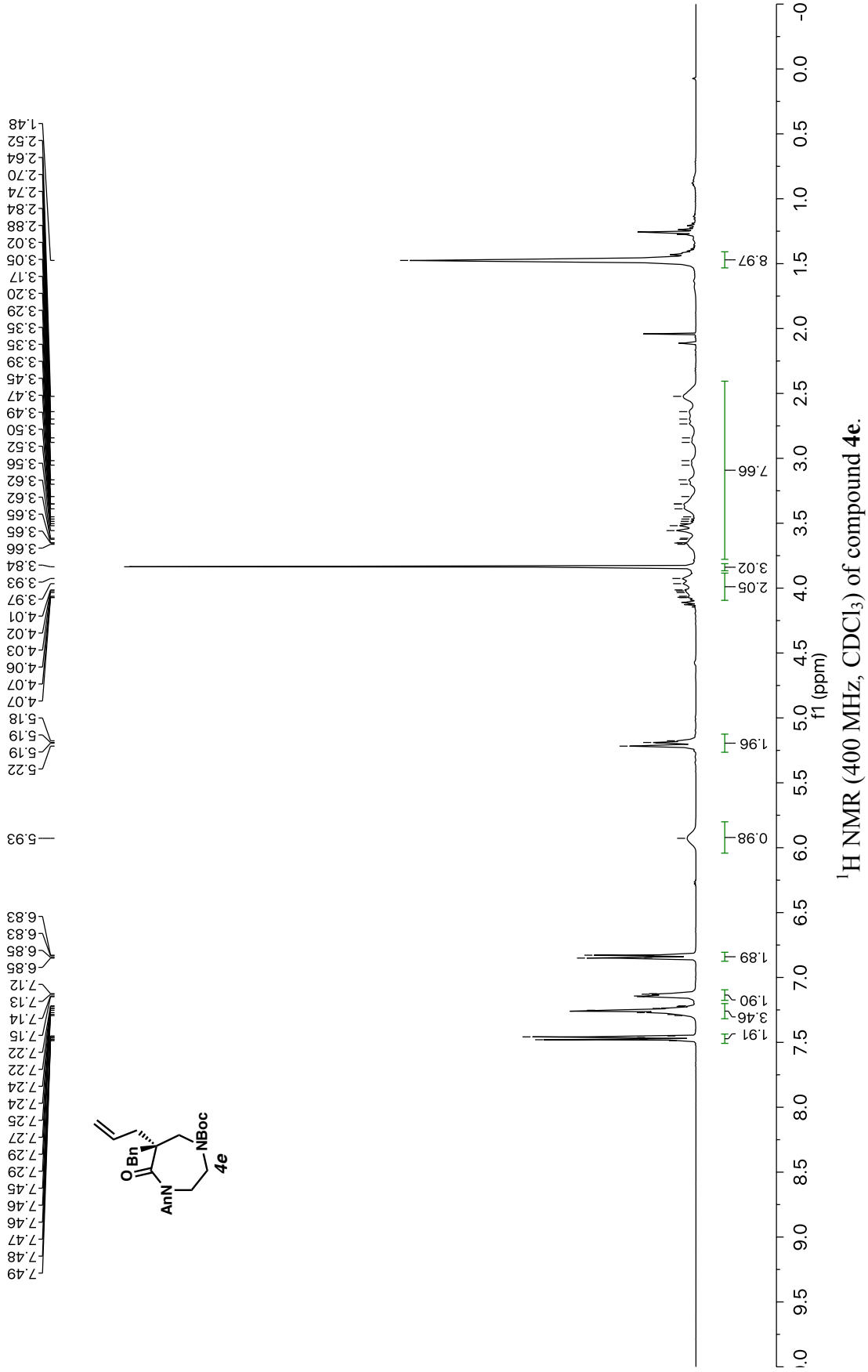

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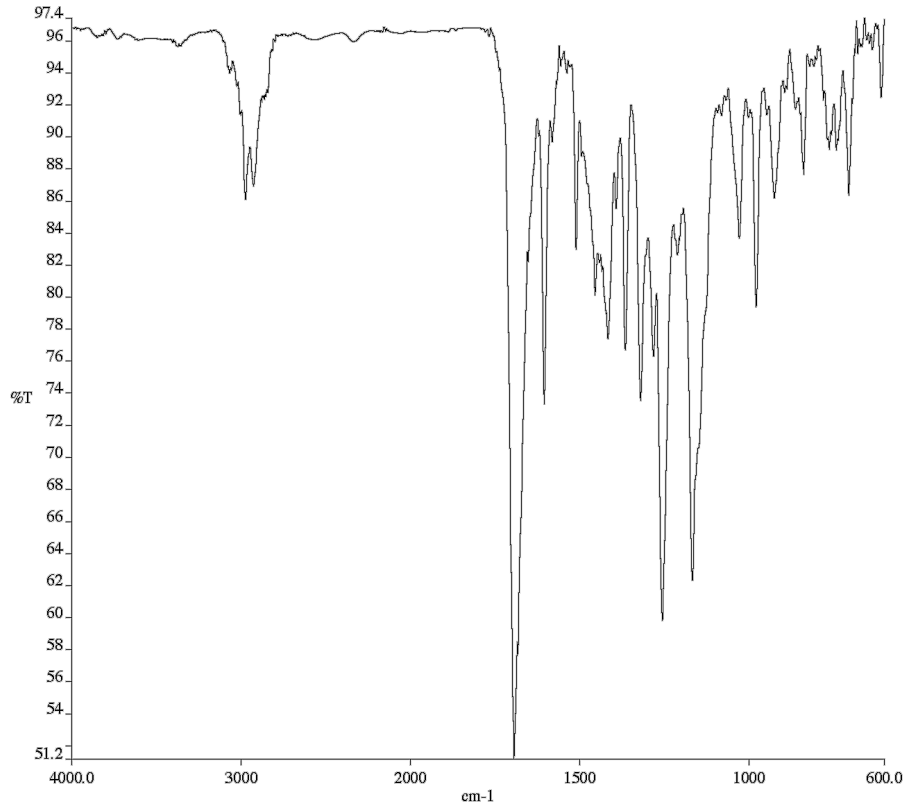
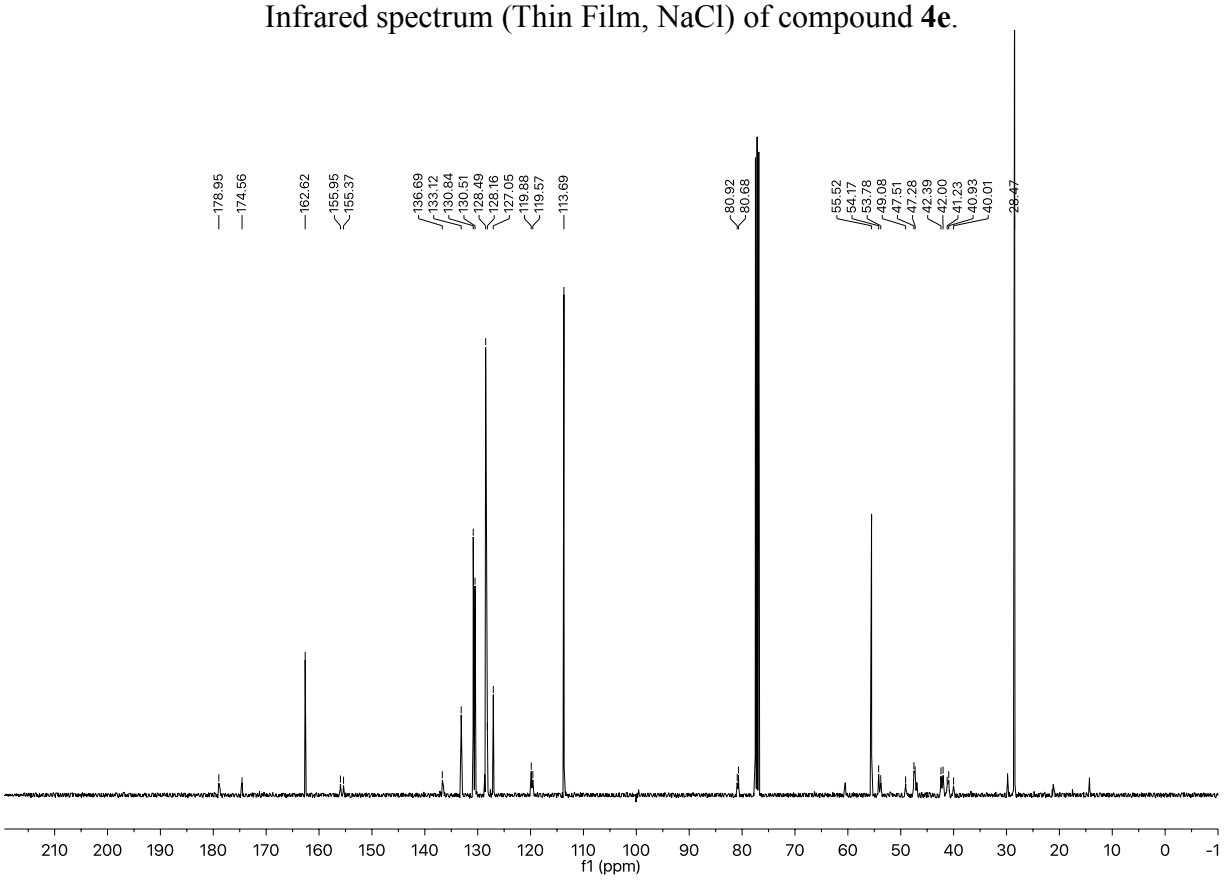


Infrared spectrum (Thin Film, NaCl) of compound **4e**.



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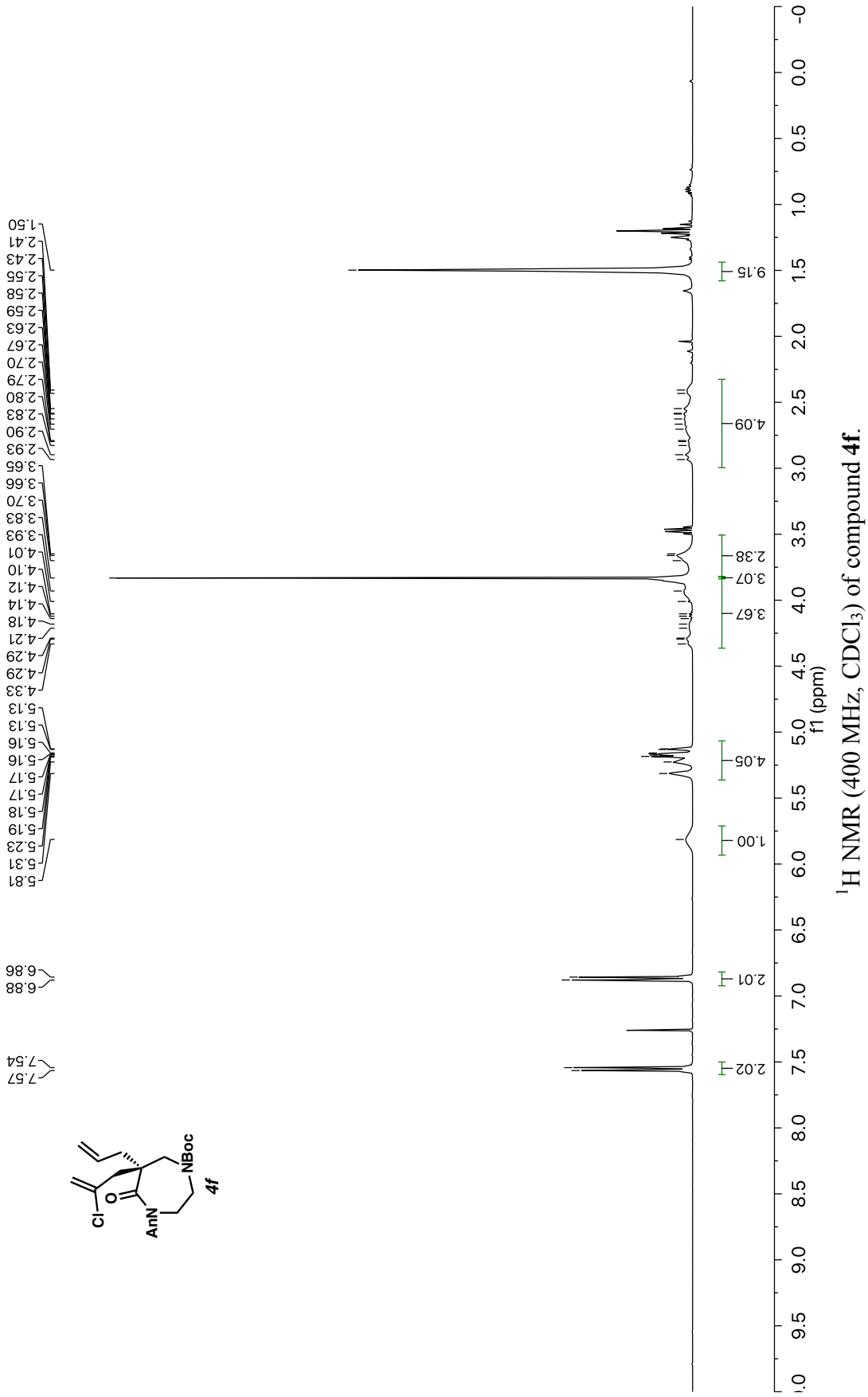

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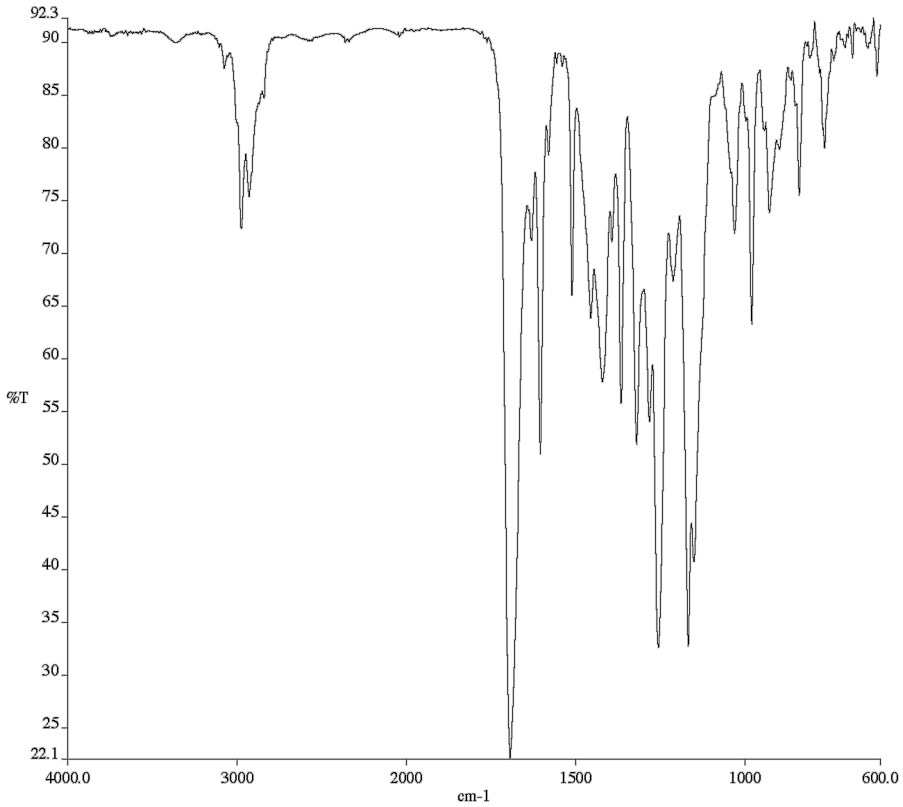
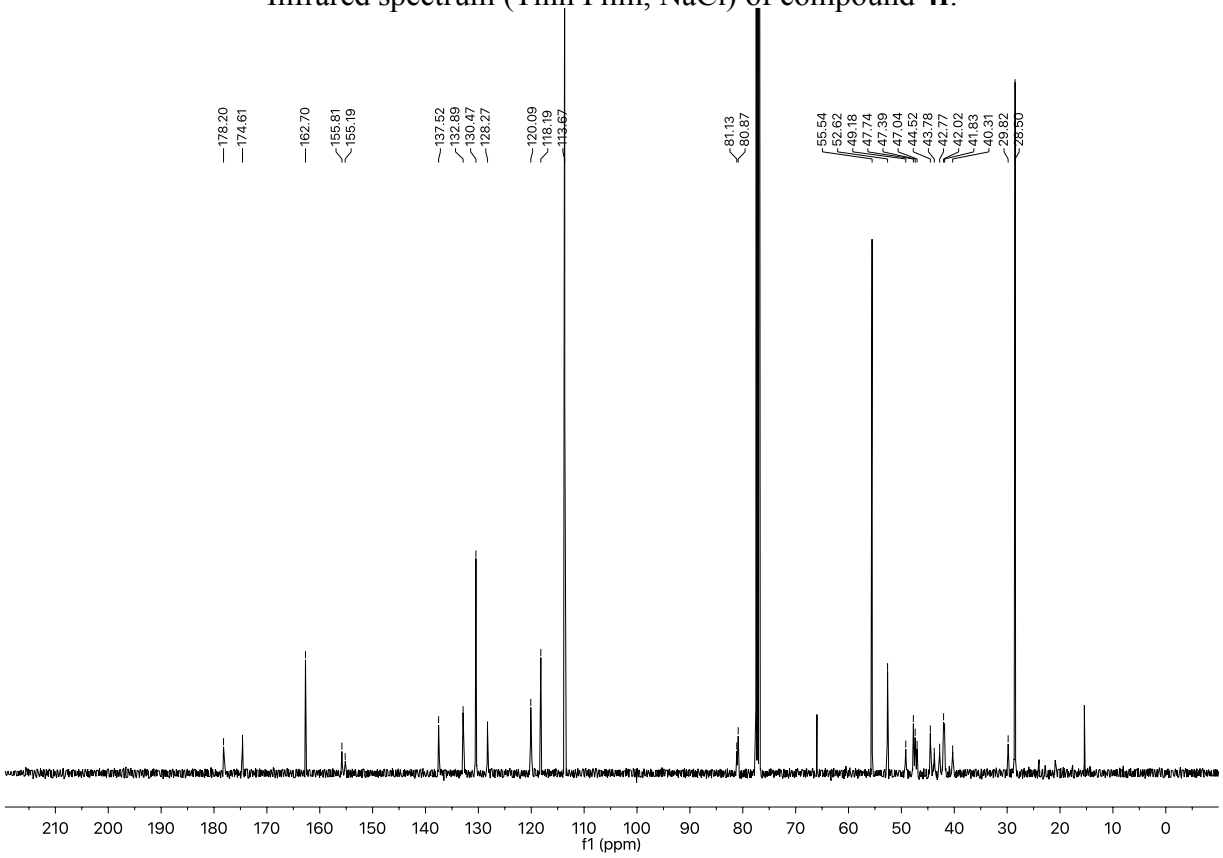


Infrared spectrum (Thin Film, NaCl) of compound **4f**.



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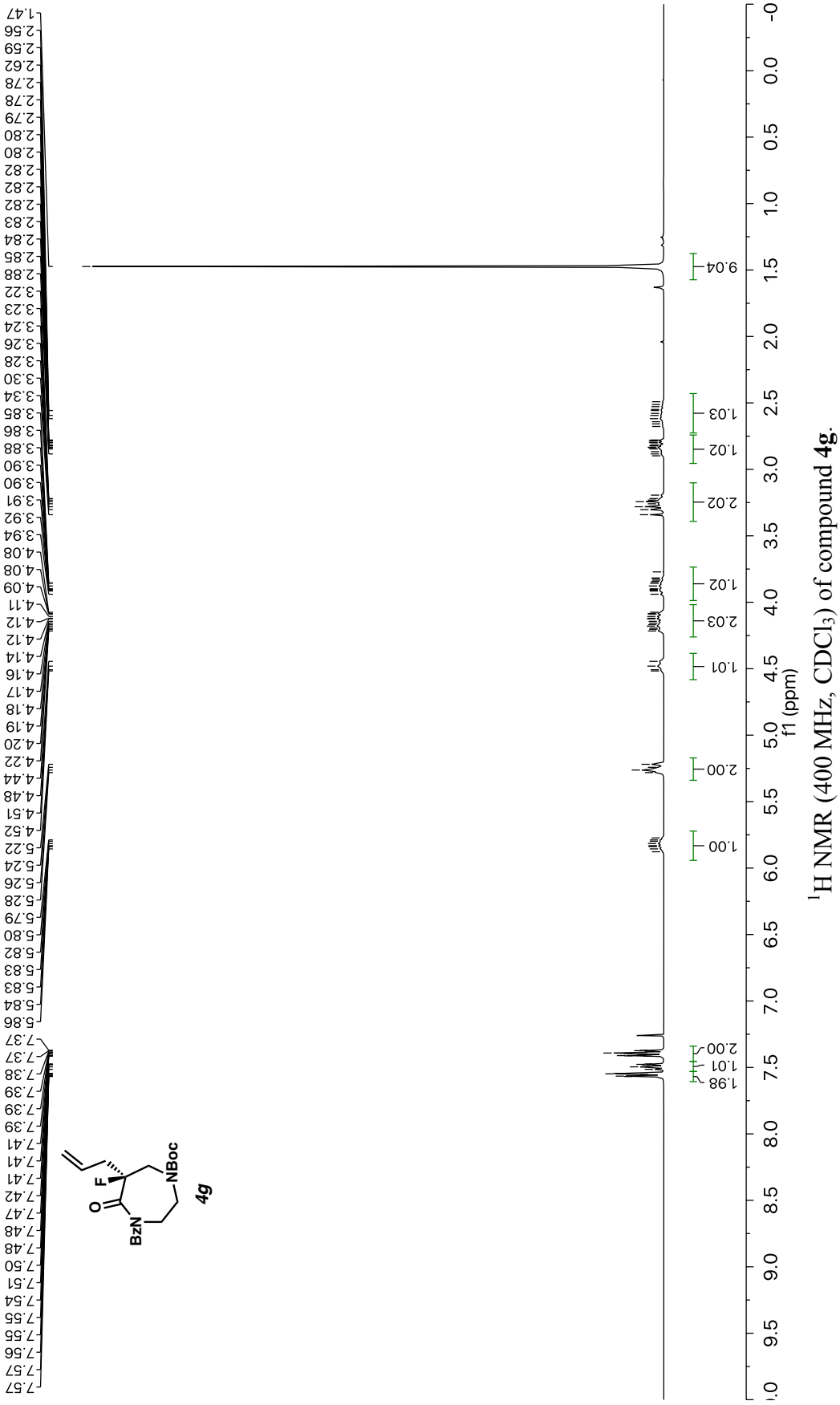
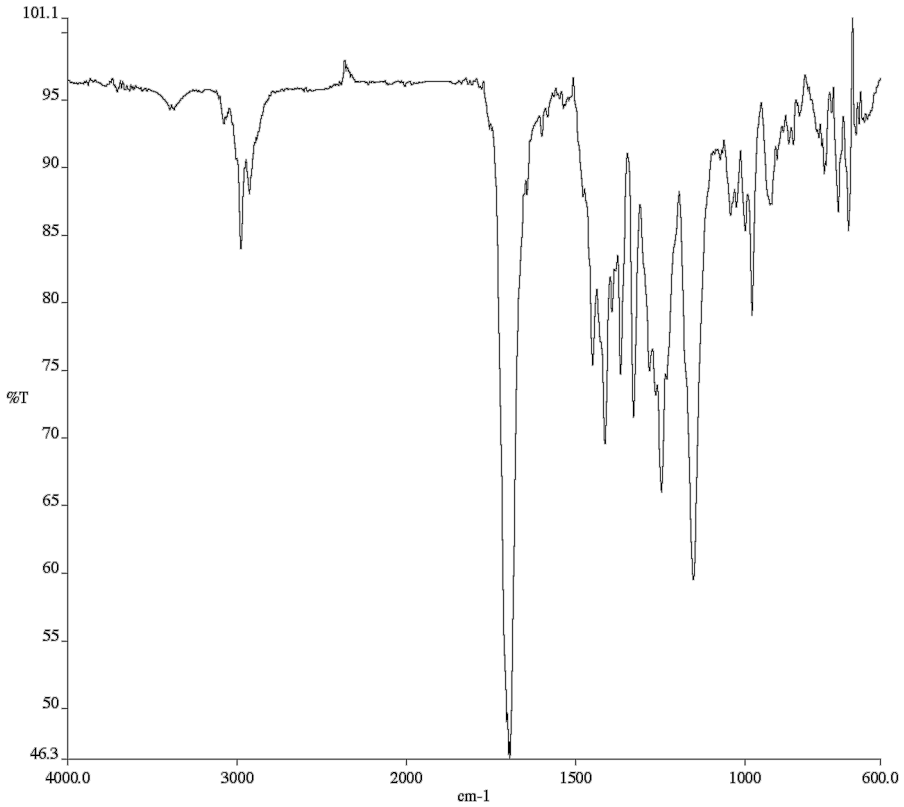
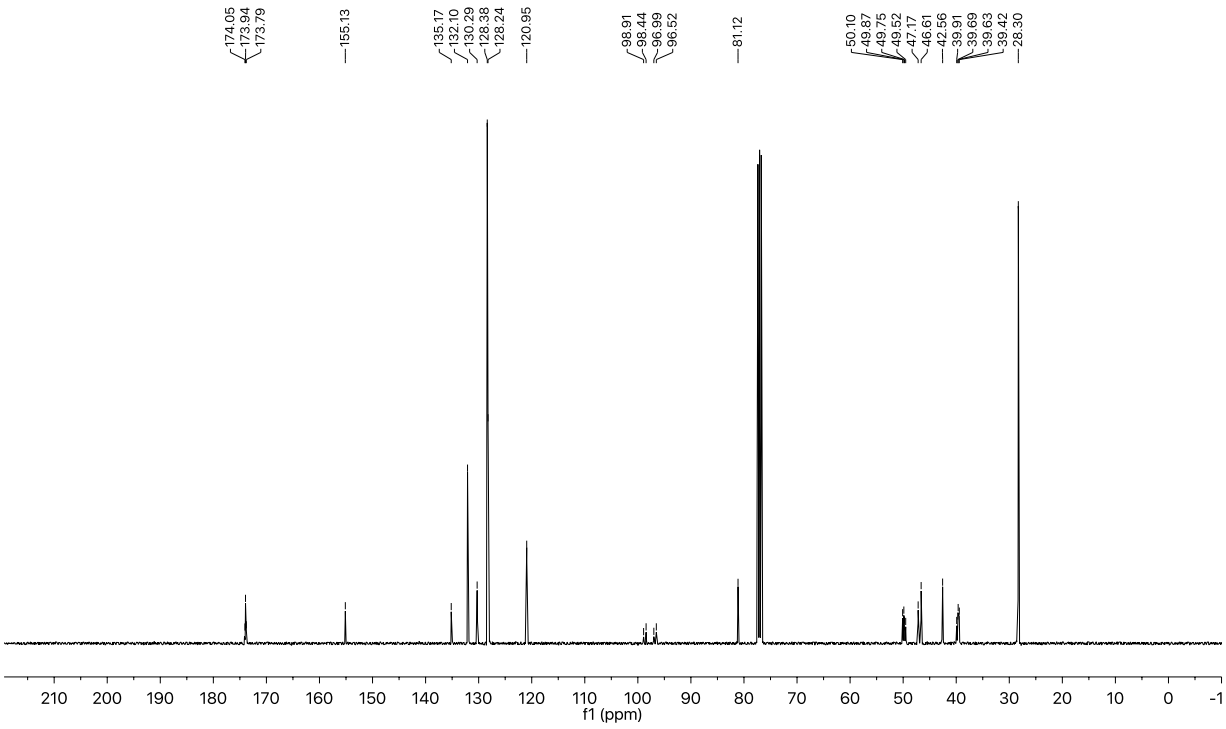


^{1}H NMR (400 MHz, $CDCl_3$) of compound **4g**.



Infrared spectrum (Thin Film, NaCl) of compound **4g**.



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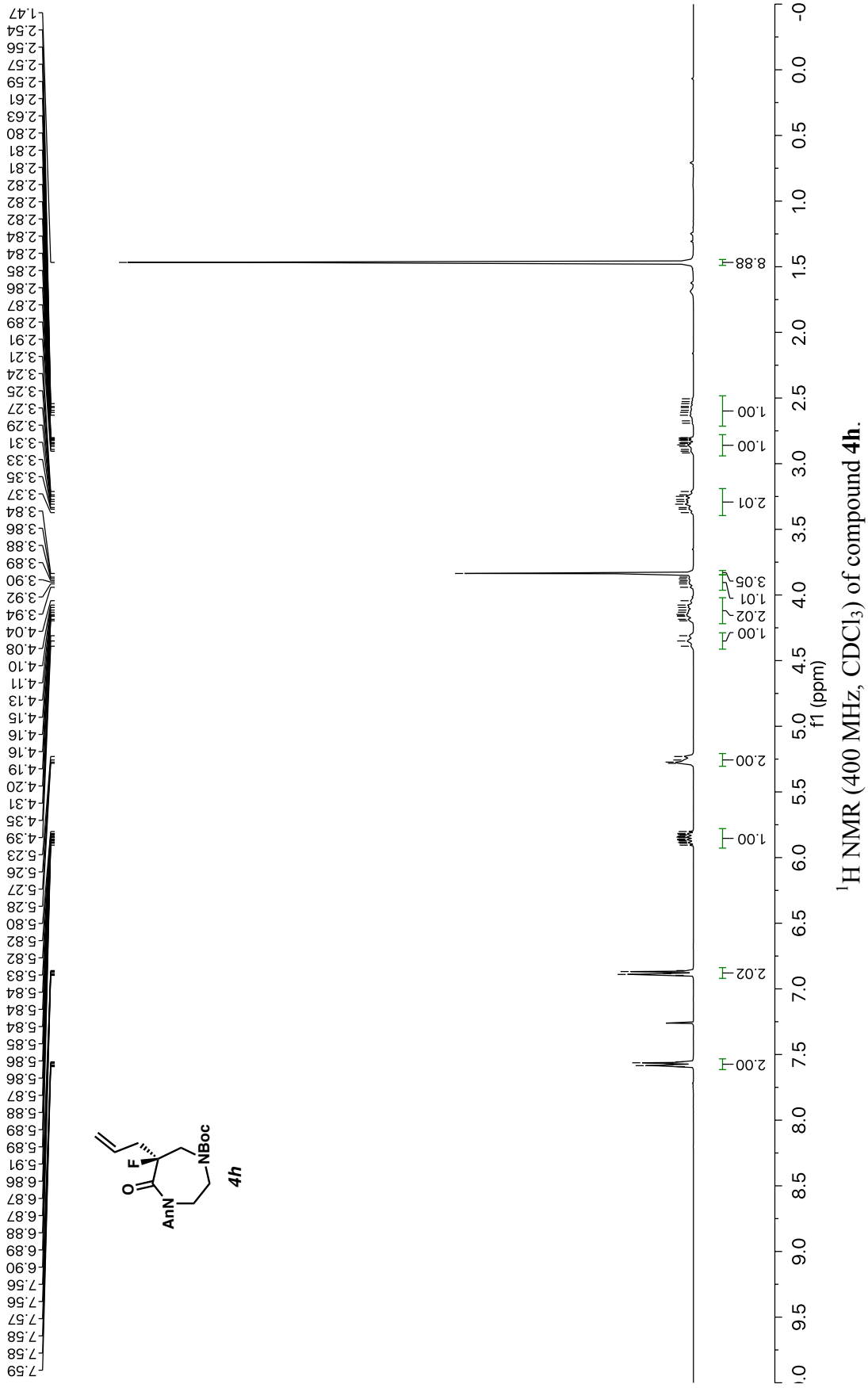
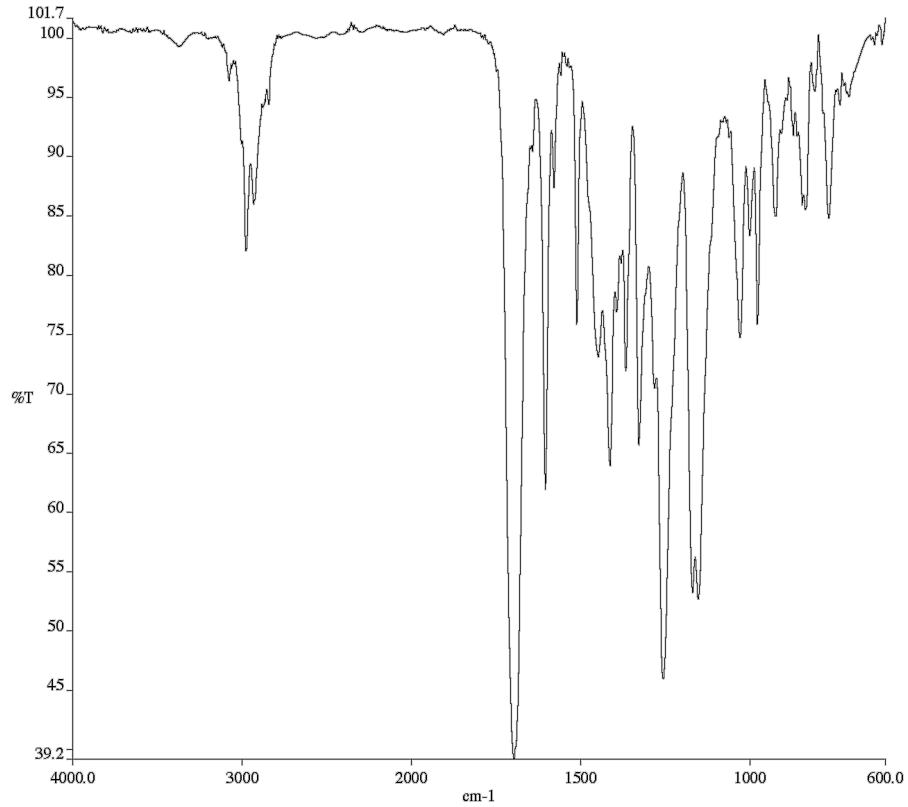
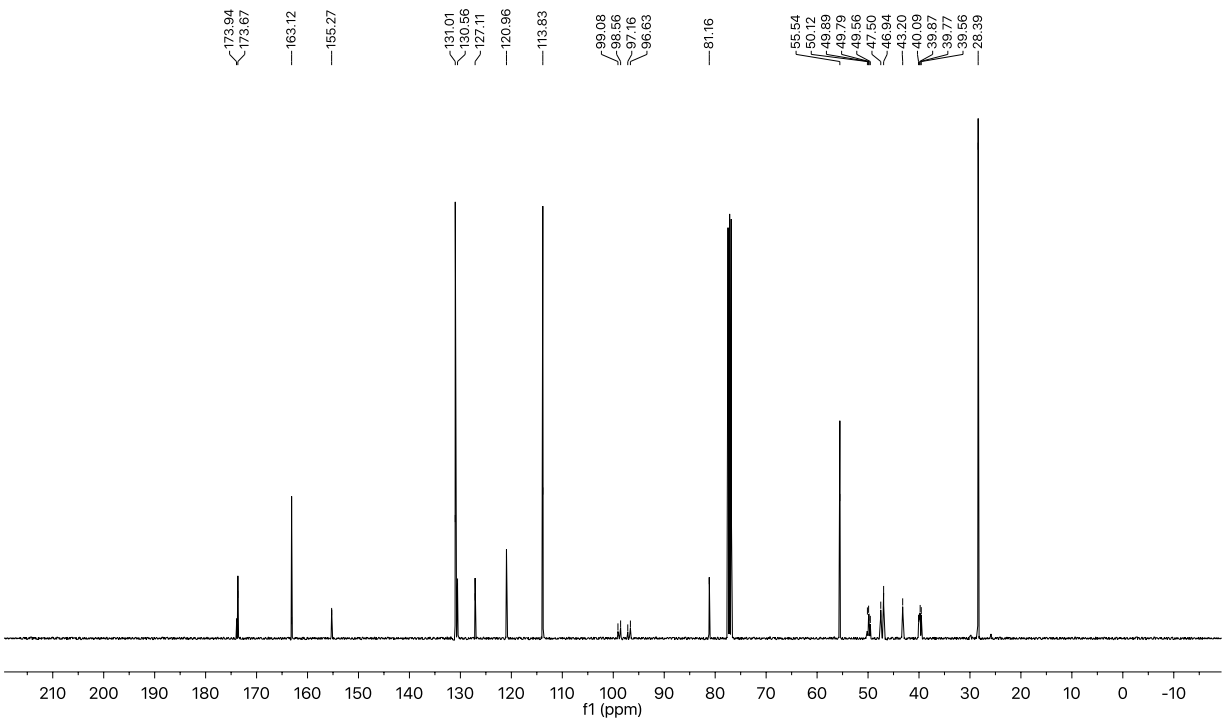


^{1}H NMR (400 MHz, $CDCl_3$) of compound **4h**.



Infrared spectrum (Thin Film, NaCl) of compound **4h**.



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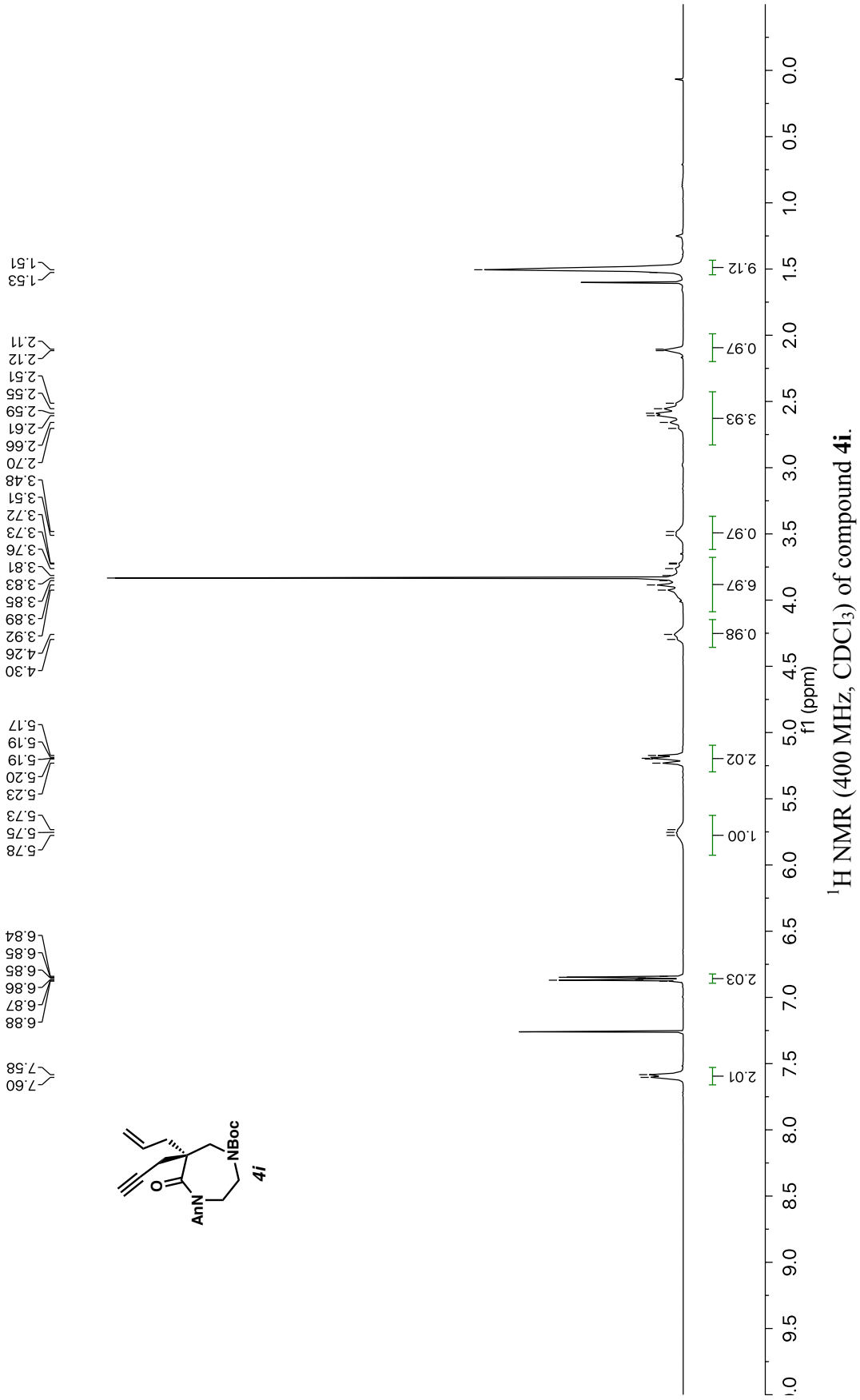

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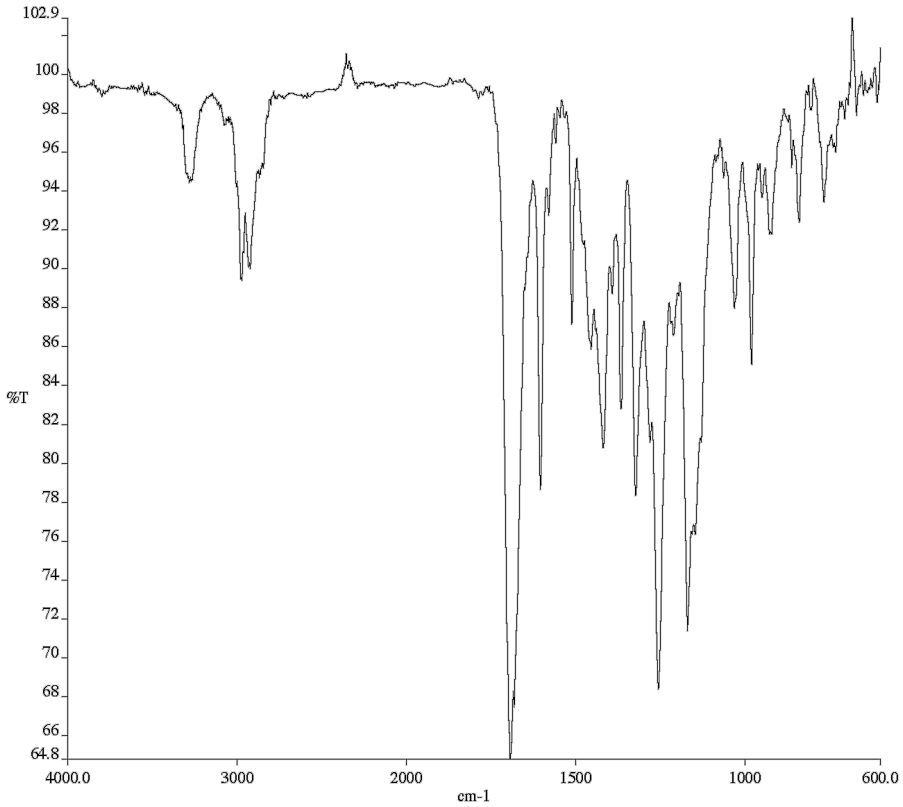
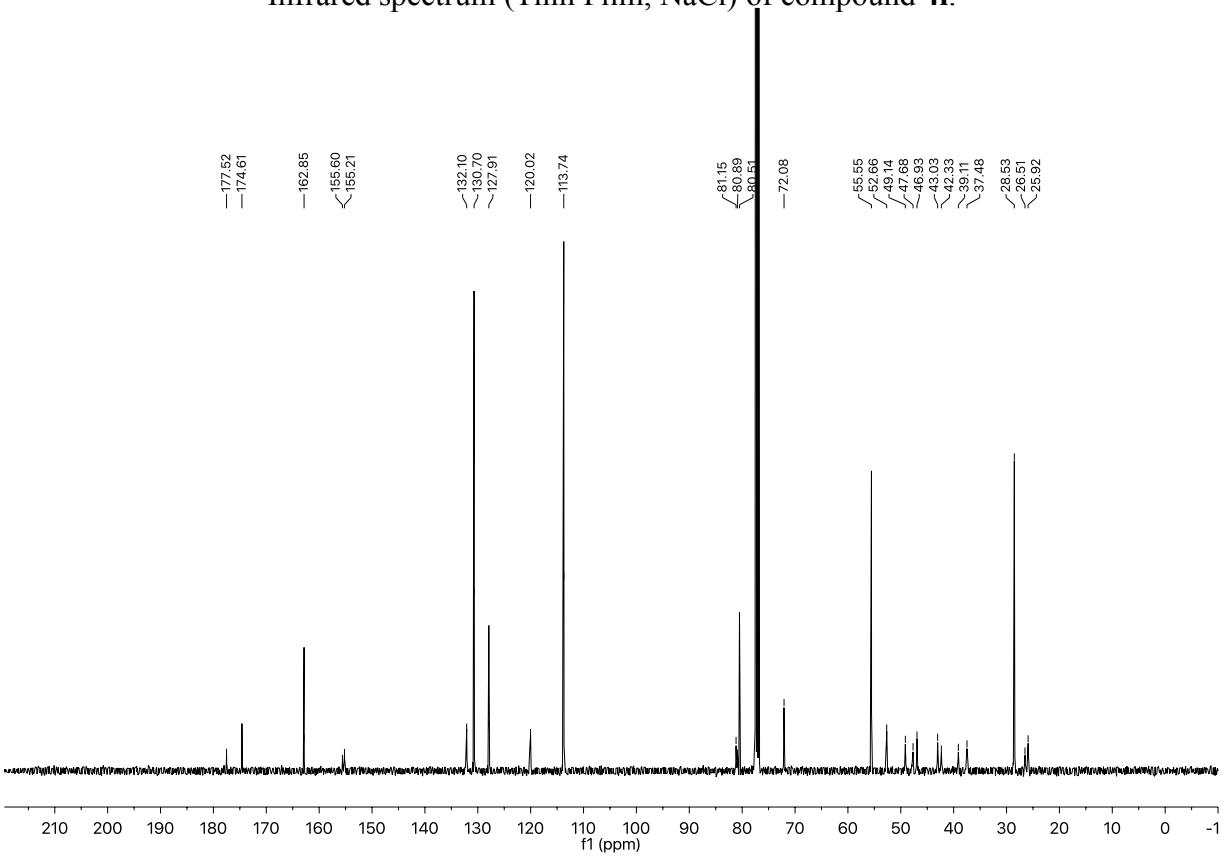
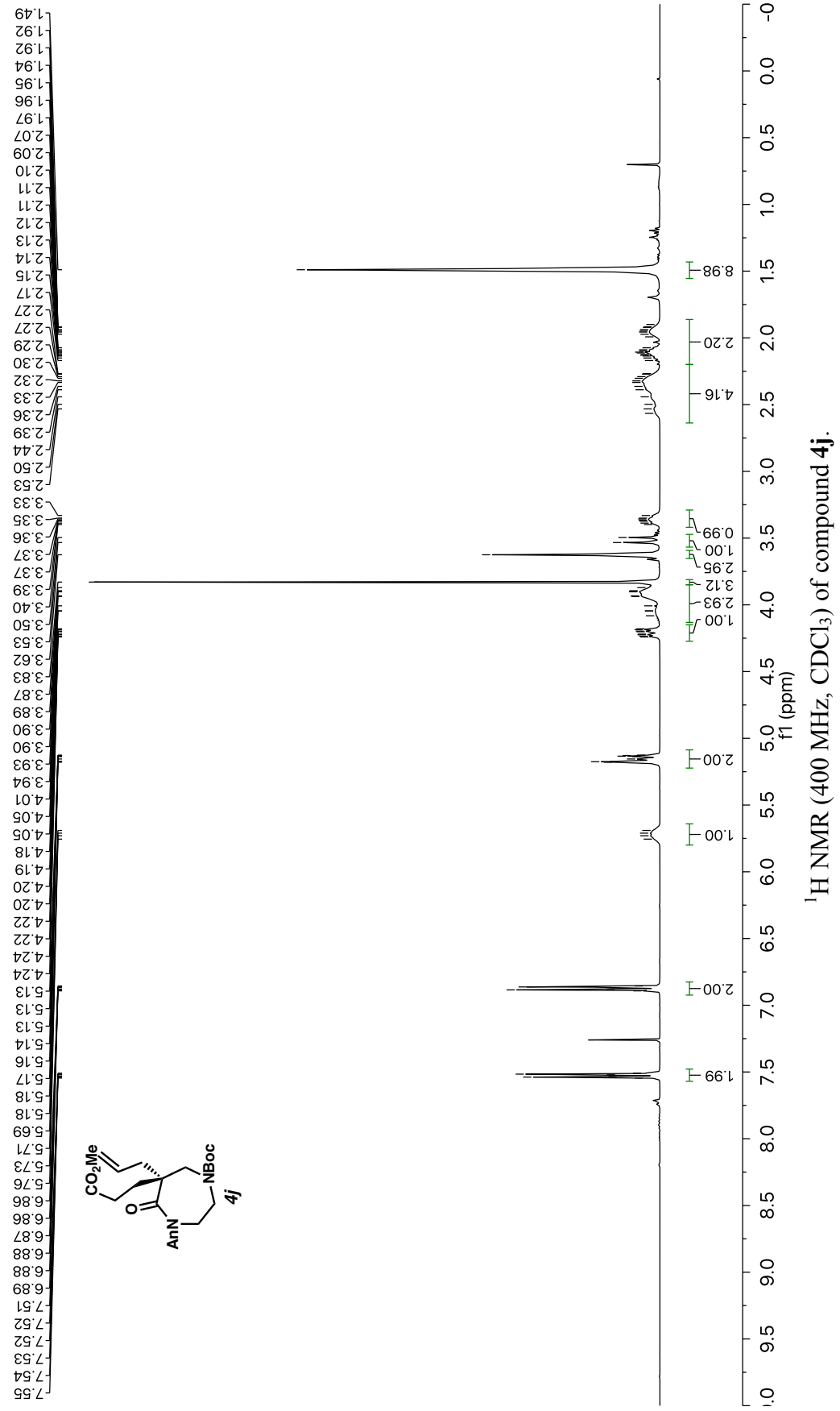


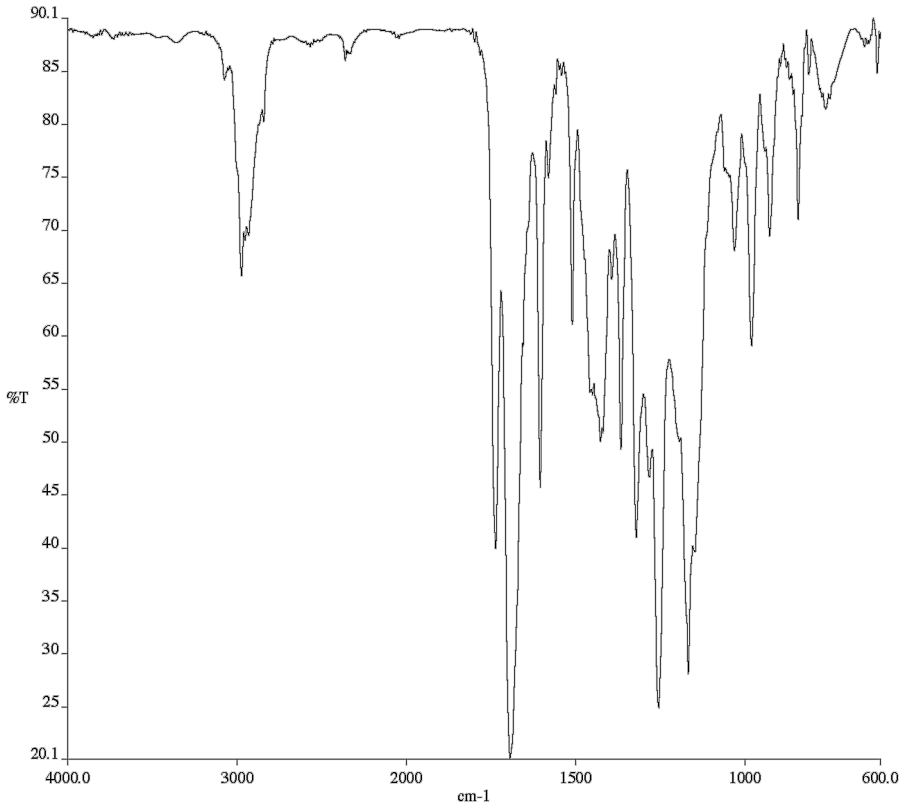
Infrared spectrum (Thin Film, NaCl) of compound **4i**.



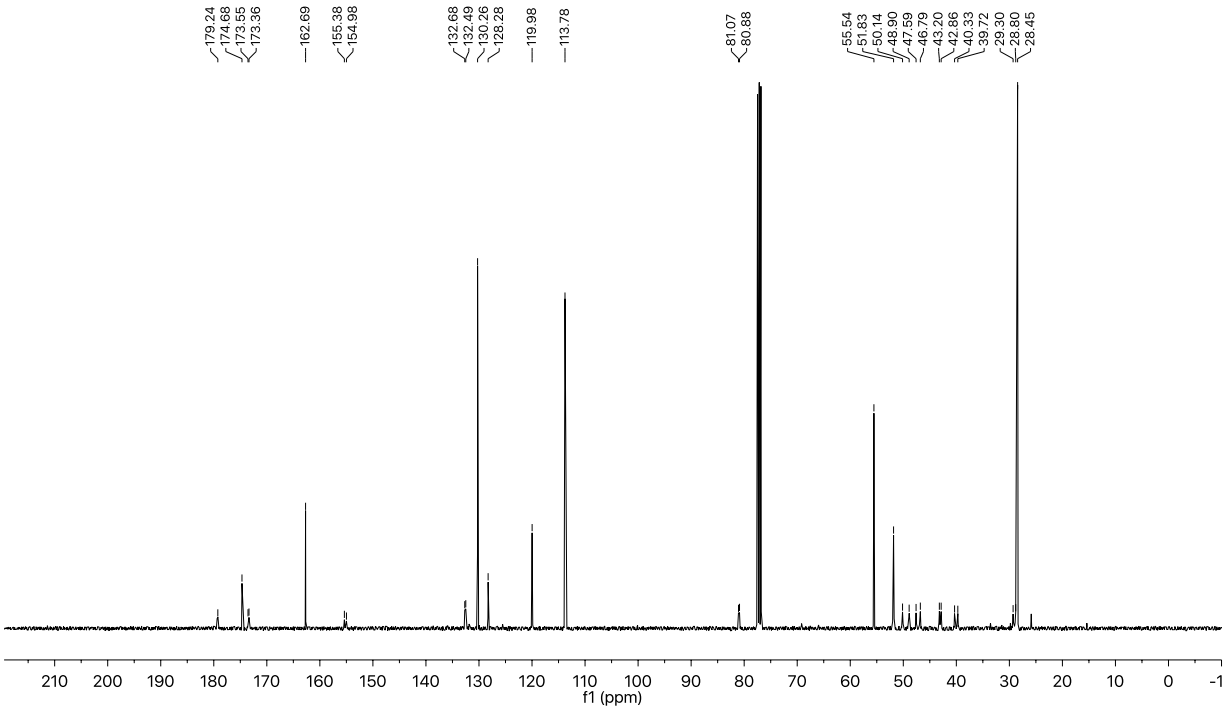
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4i**.



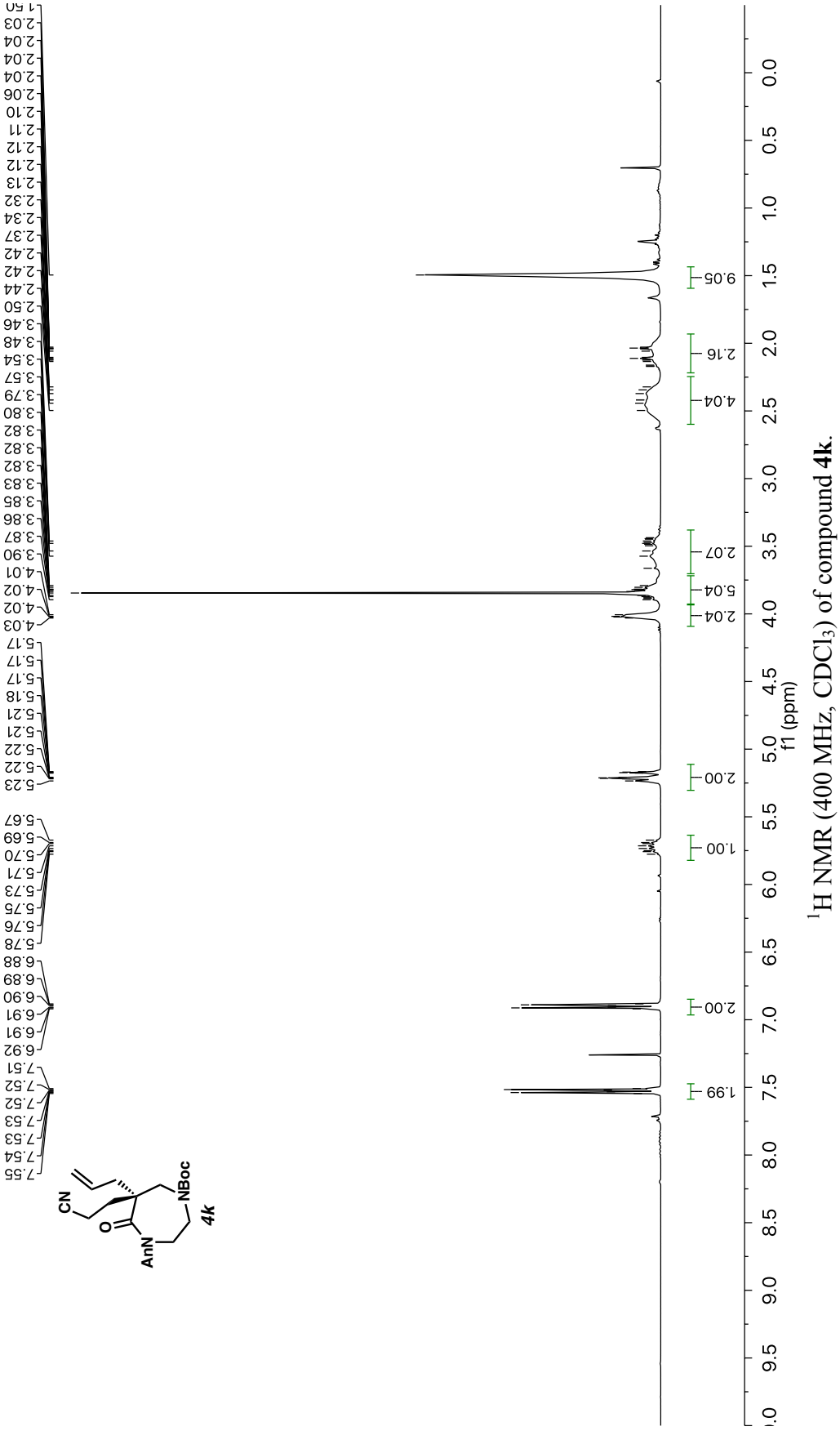
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4j**.



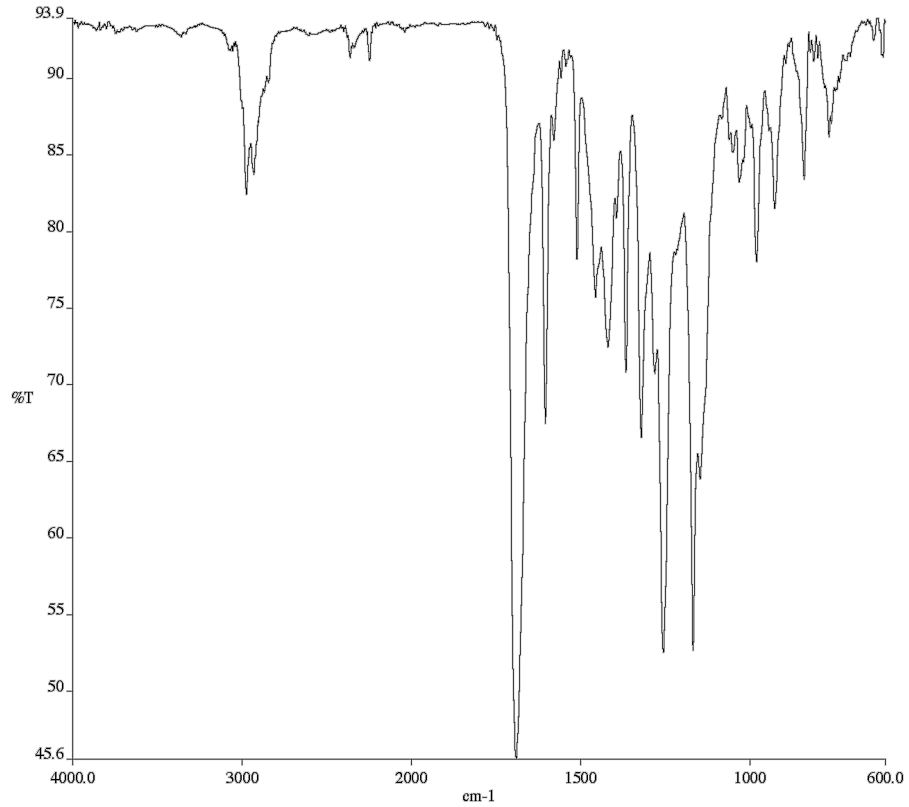
Infrared spectrum (Thin Film, NaCl) of compound **4j**.



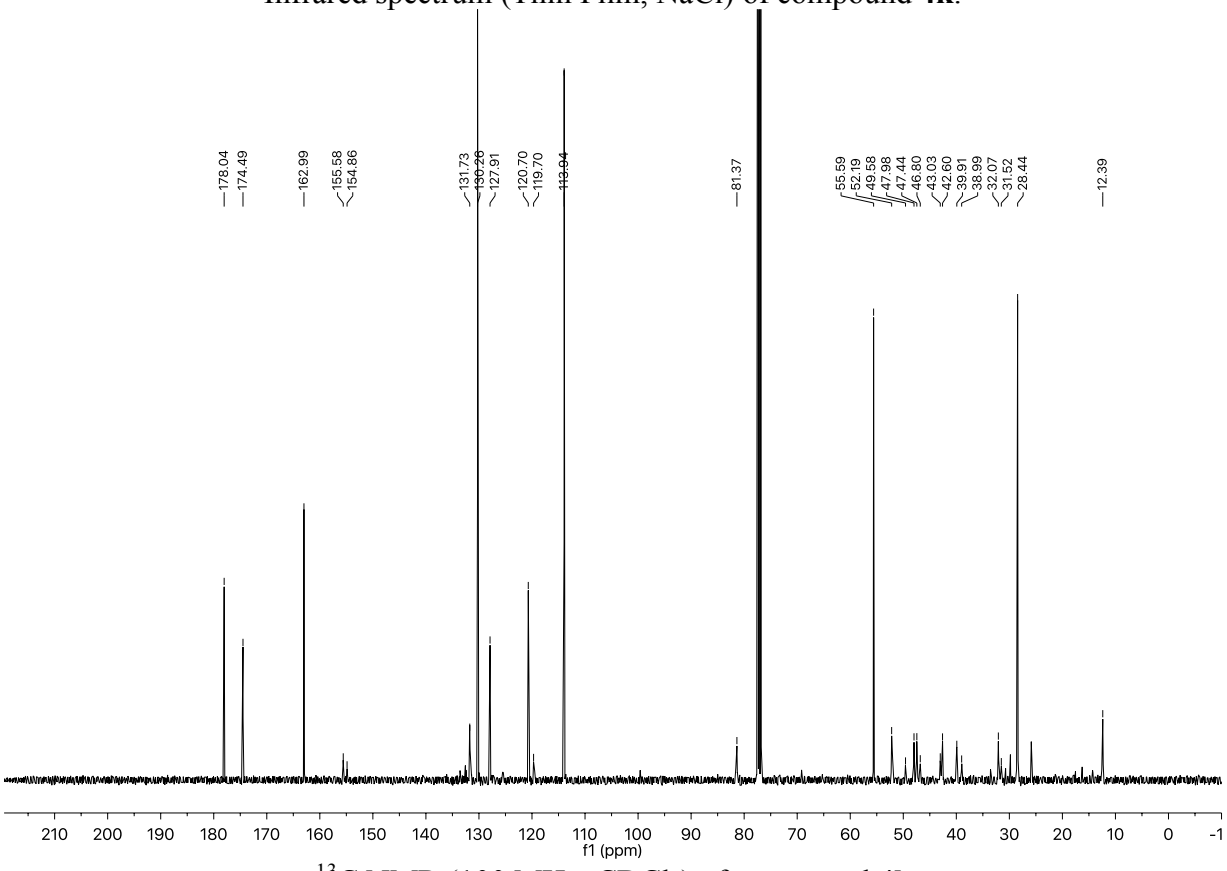
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4j**.



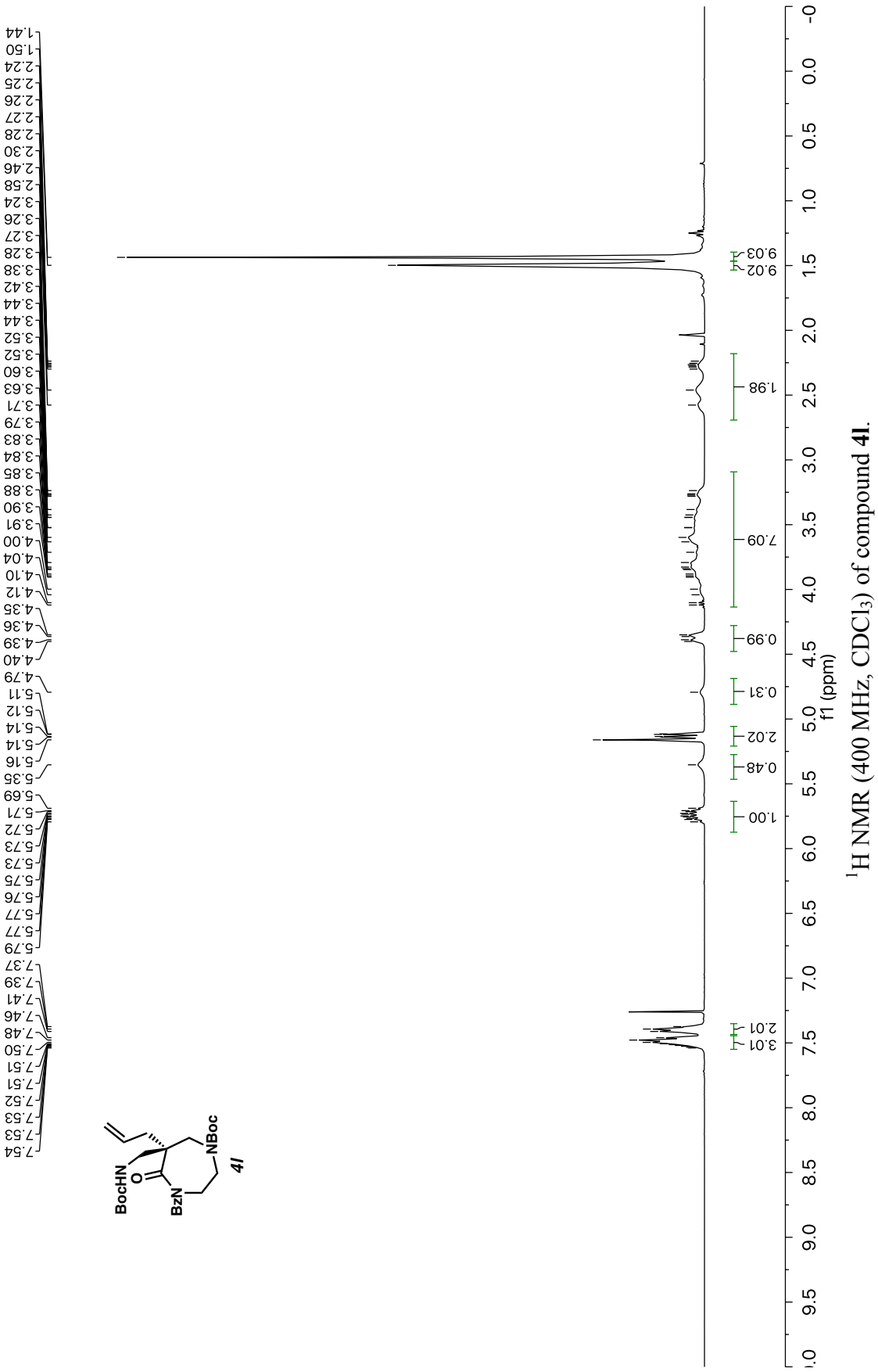
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4k**.



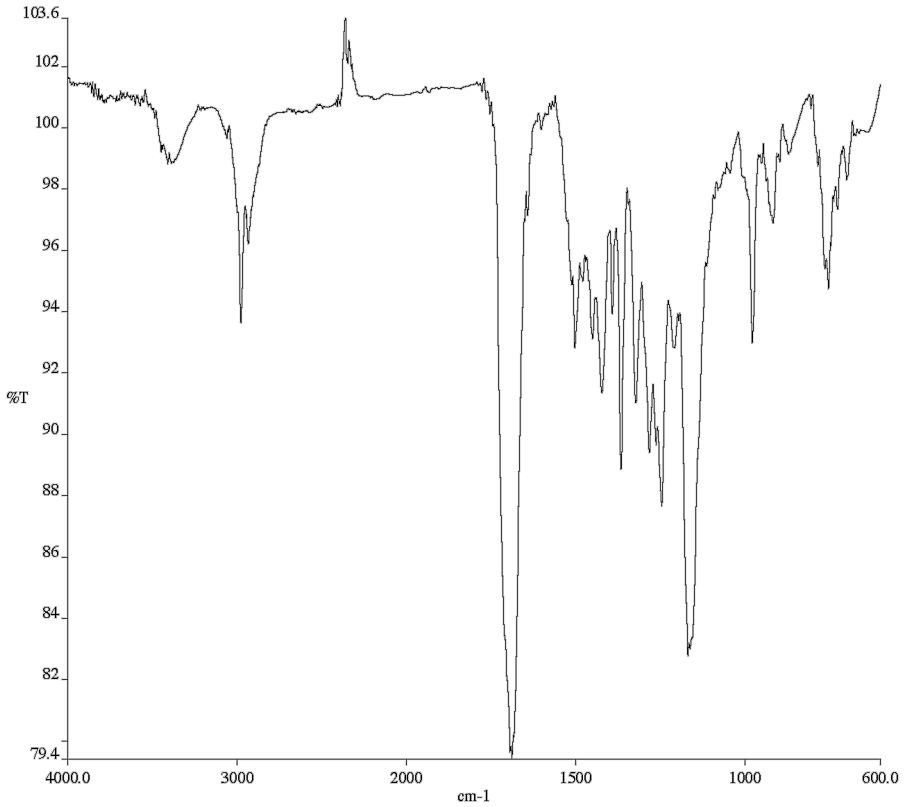
Infrared spectrum (Thin Film, NaCl) of compound **4k**.



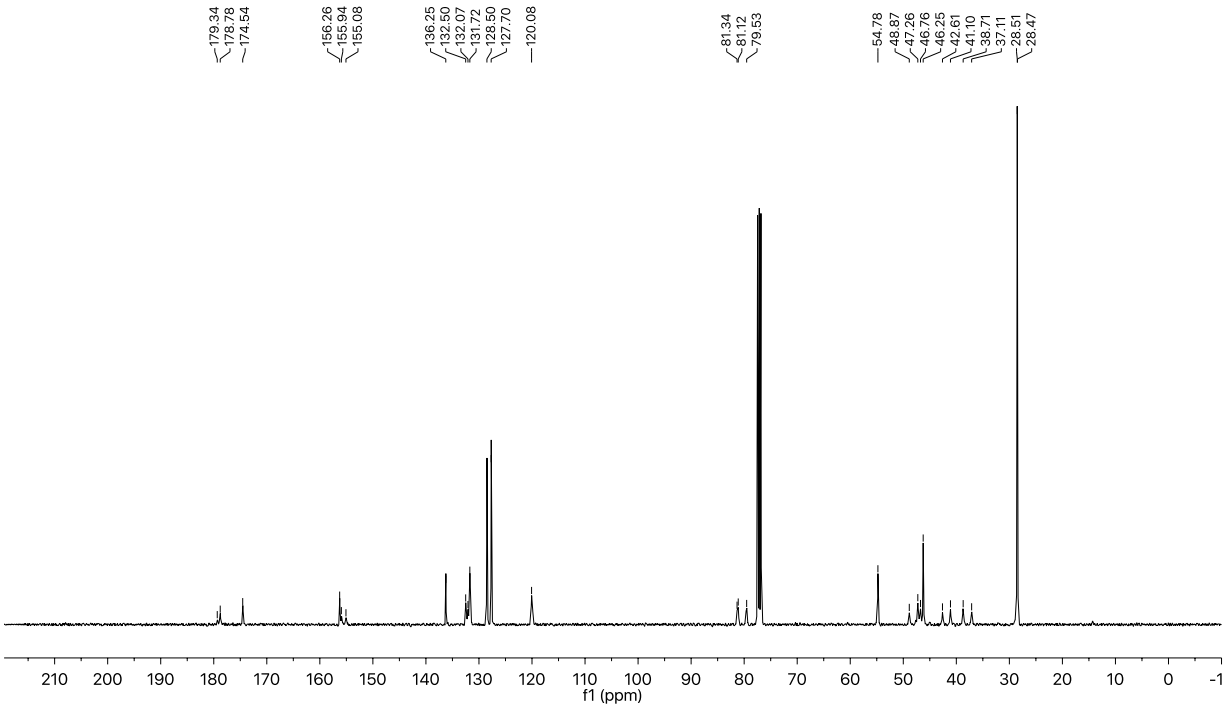
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4k**.



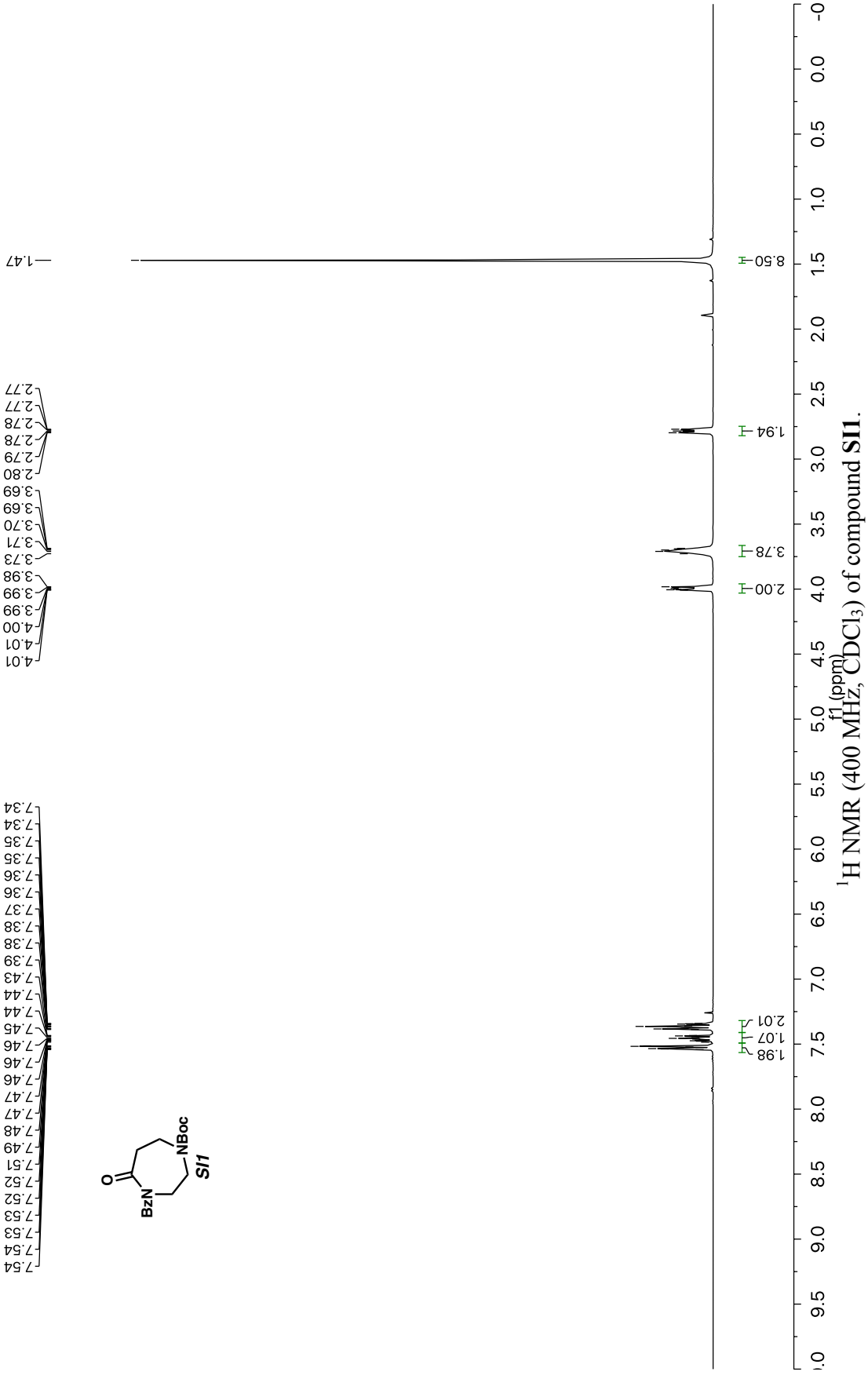
^{1}H NMR (400 MHz, $CDCl_3$) of compound **4l**.



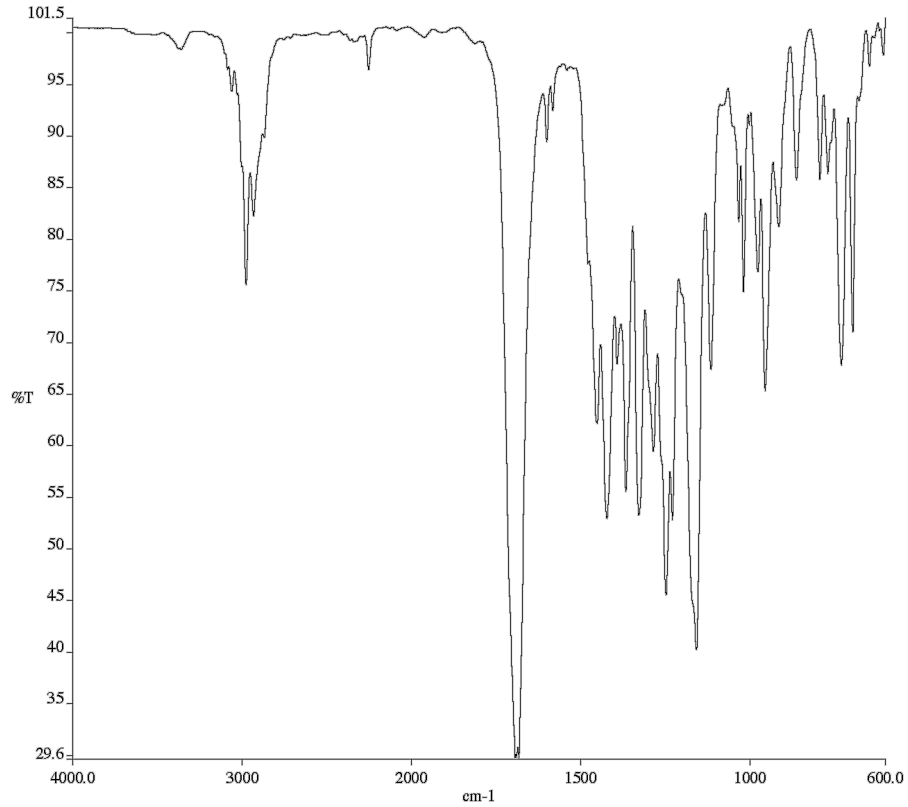
Infrared spectrum (Thin Film, NaCl) of compound **4l**.



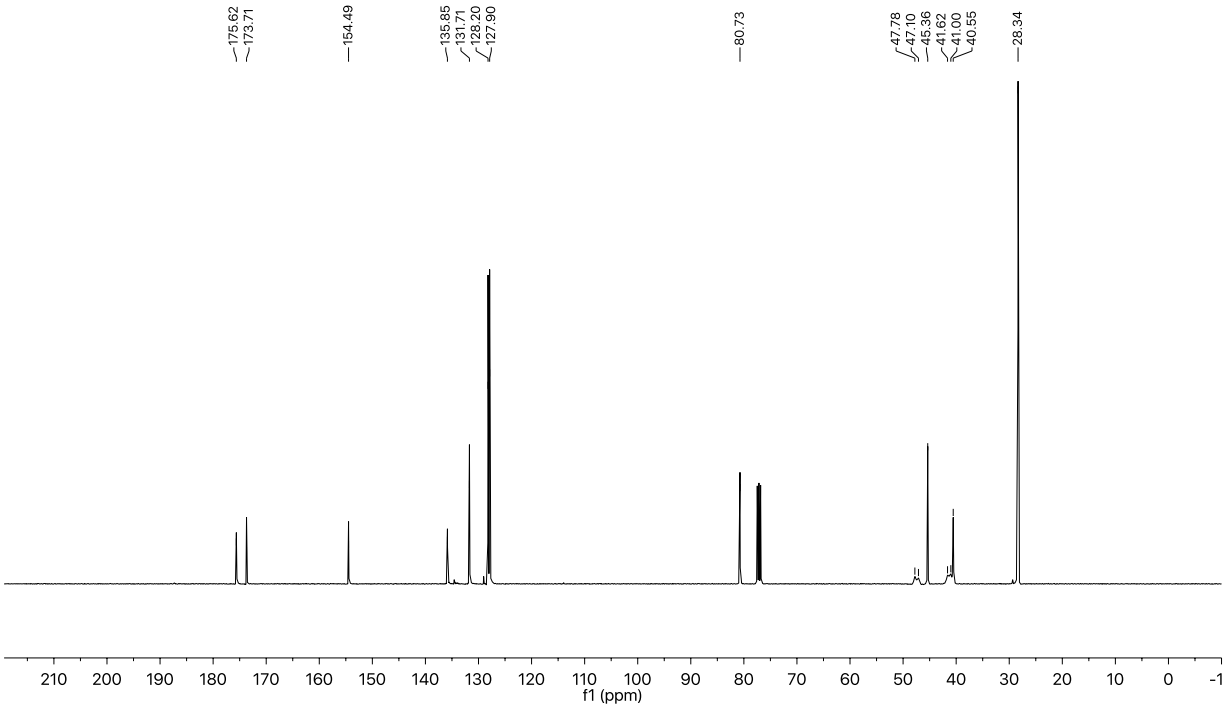
^{13}C NMR (100 MHz, $CDCl_3$) of compound **4l**.



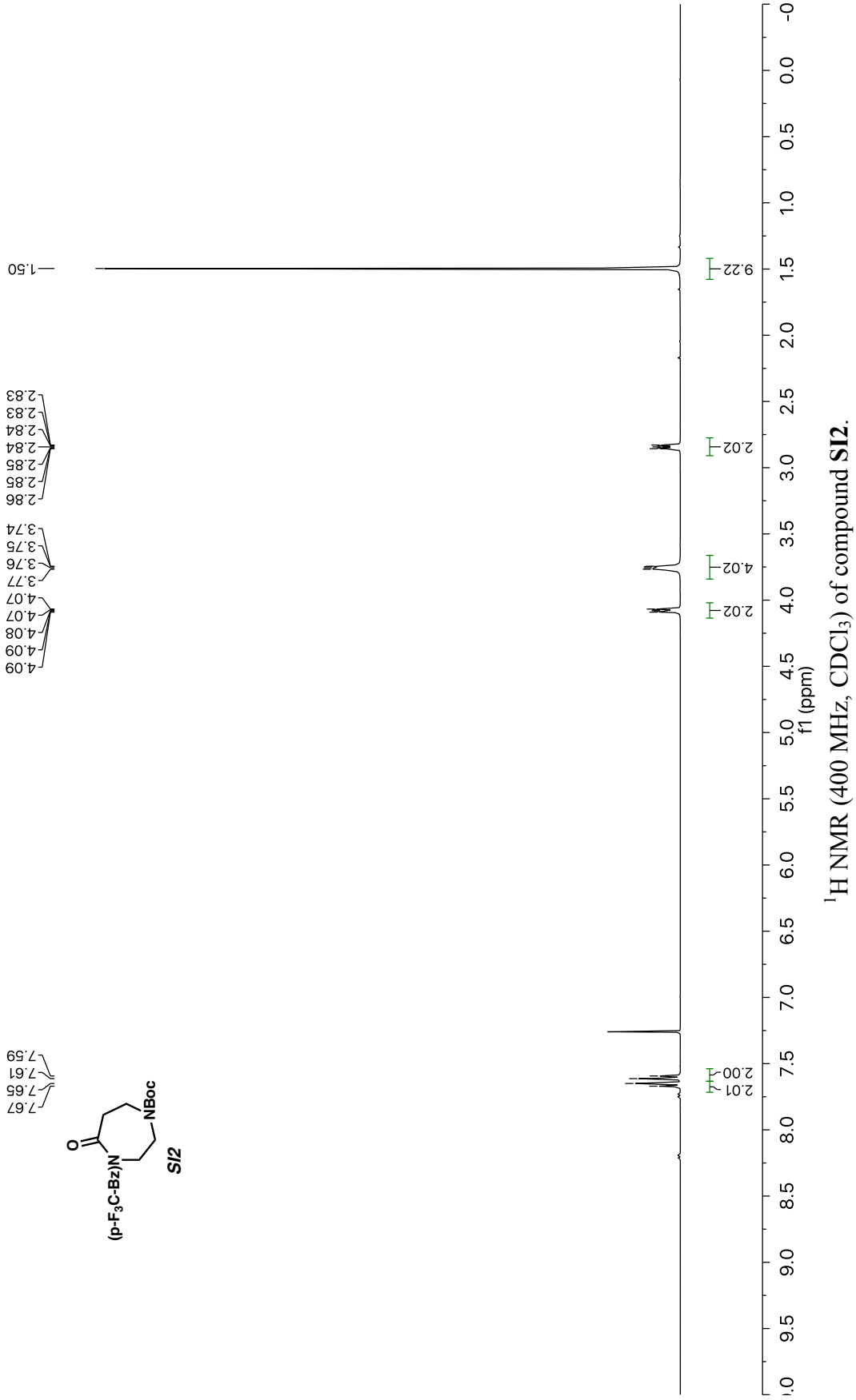
^{1}H NMR (400 MHz, $CDCl_3$) of compound **SI1**.



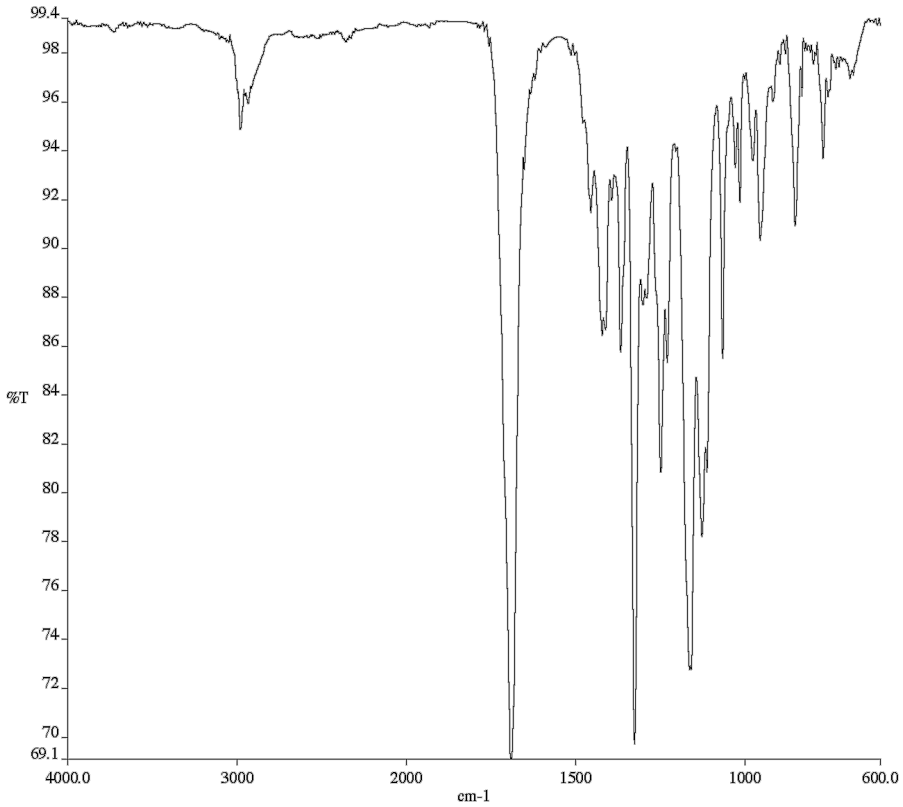
Infrared spectrum (Thin Film, NaCl) of compound **SI1**.



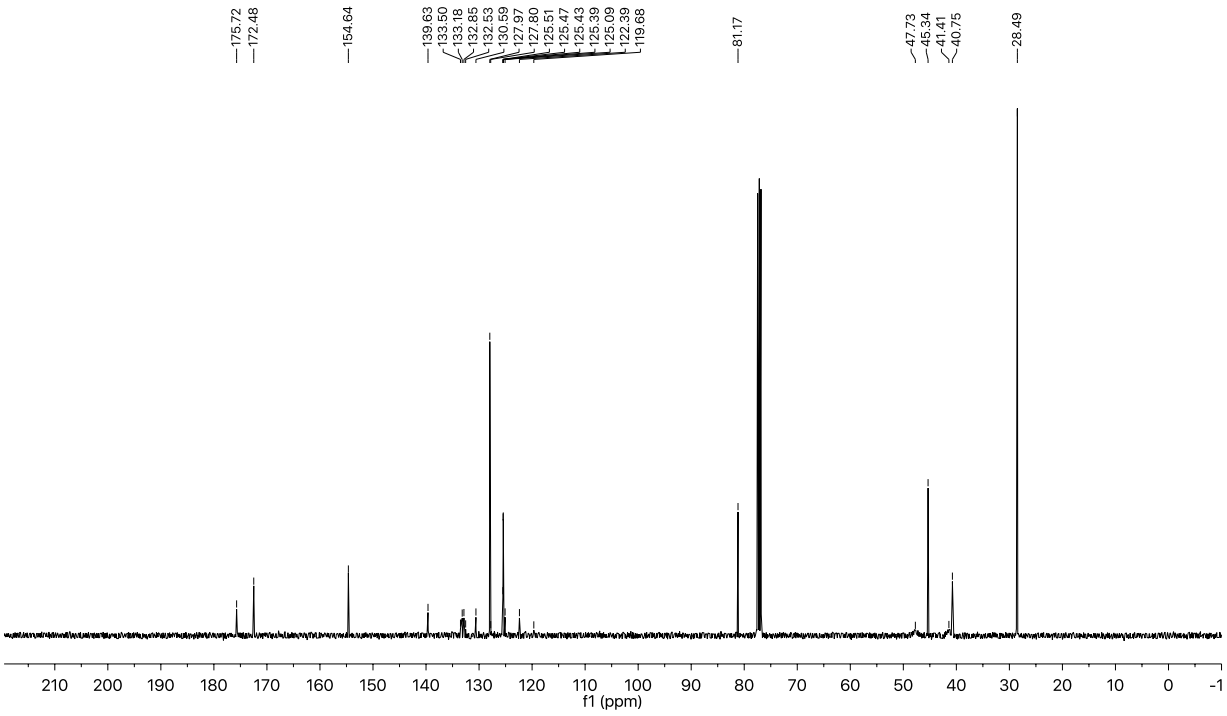
^{13}C NMR (100 MHz, $CDCl_3$) of compound **SI1**.



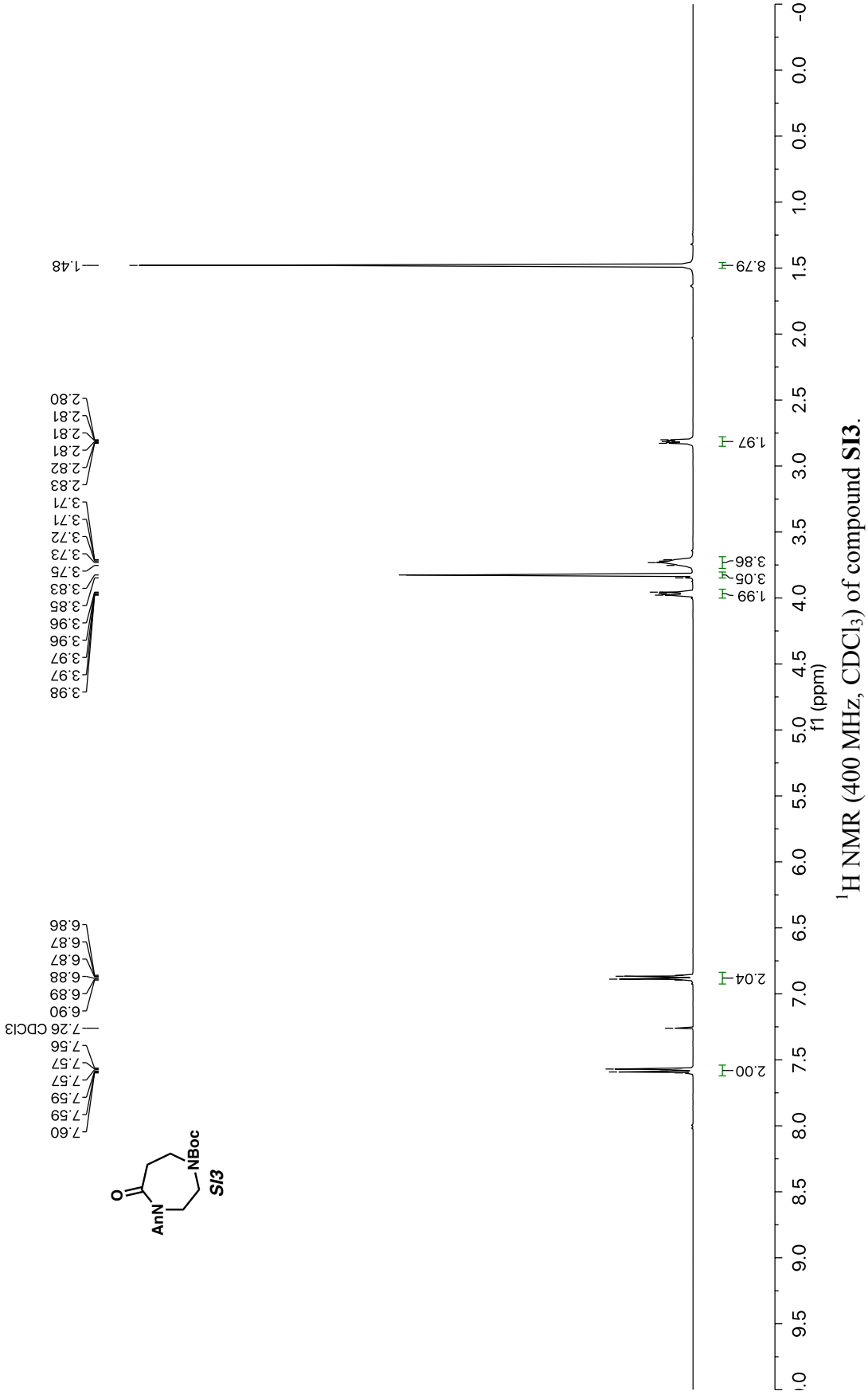
^{1}H NMR (400 MHz, $CDCl_3$) of compound **SI2**.



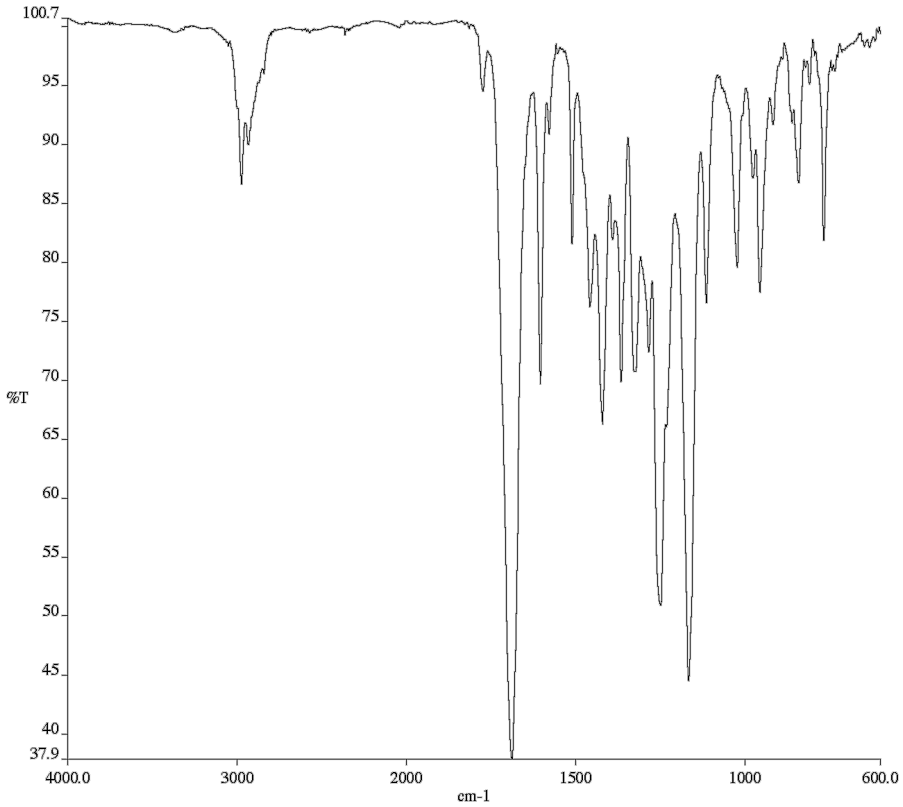
Infrared spectrum (Thin Film, NaCl) of compound **SI2**.



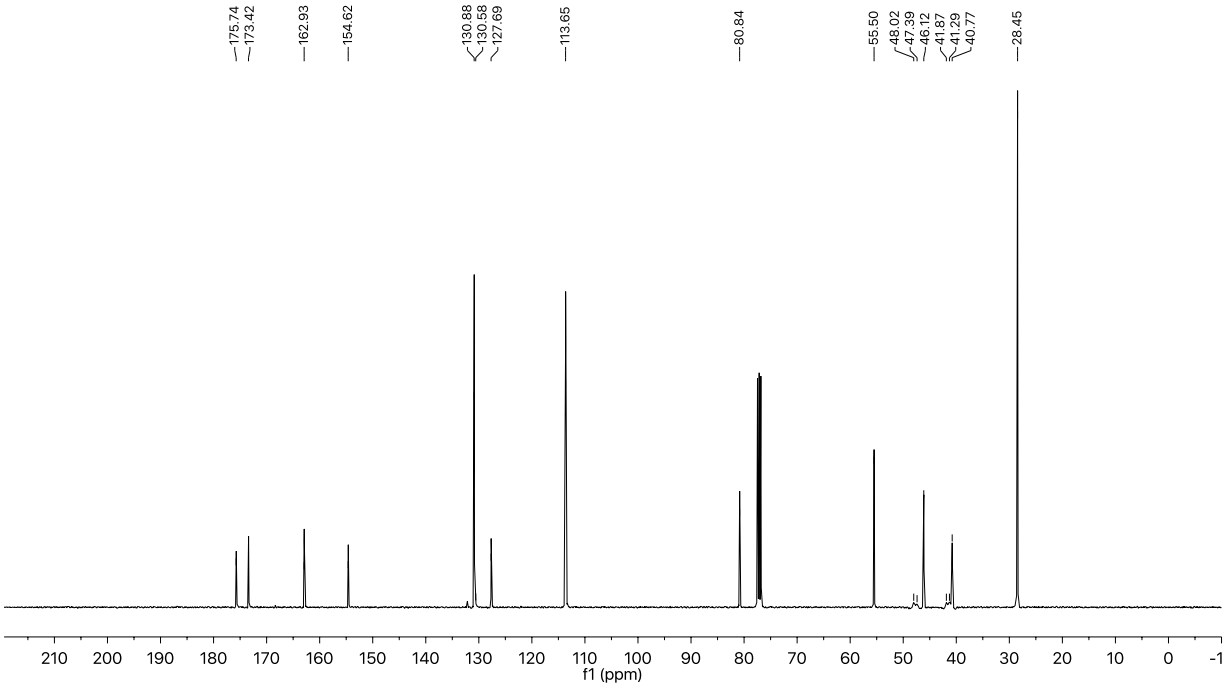
^{13}C NMR (100 MHz, $CDCl_3$) of compound **SI2**.



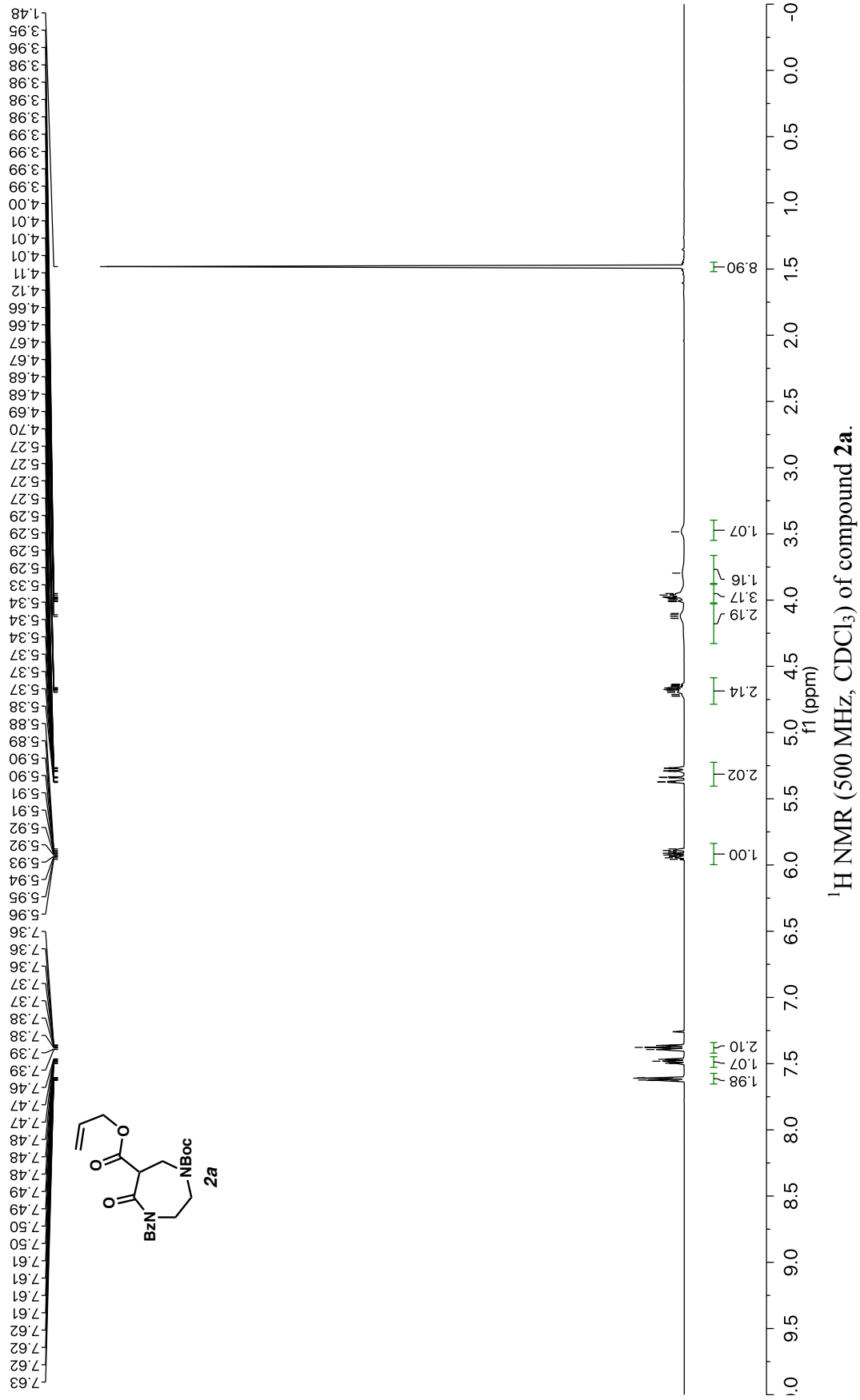
^{1}H NMR (400 MHz, $CDCl_3$) of compound **SI3**.



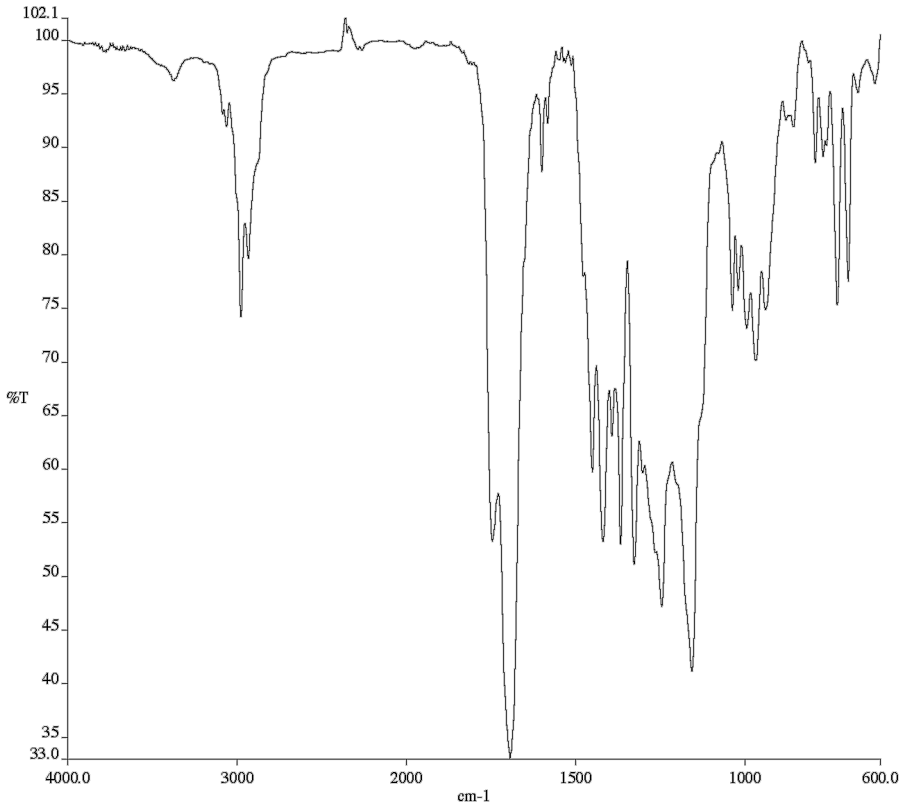
Infrared spectrum (Thin Film, NaCl) of compound **SI3**.



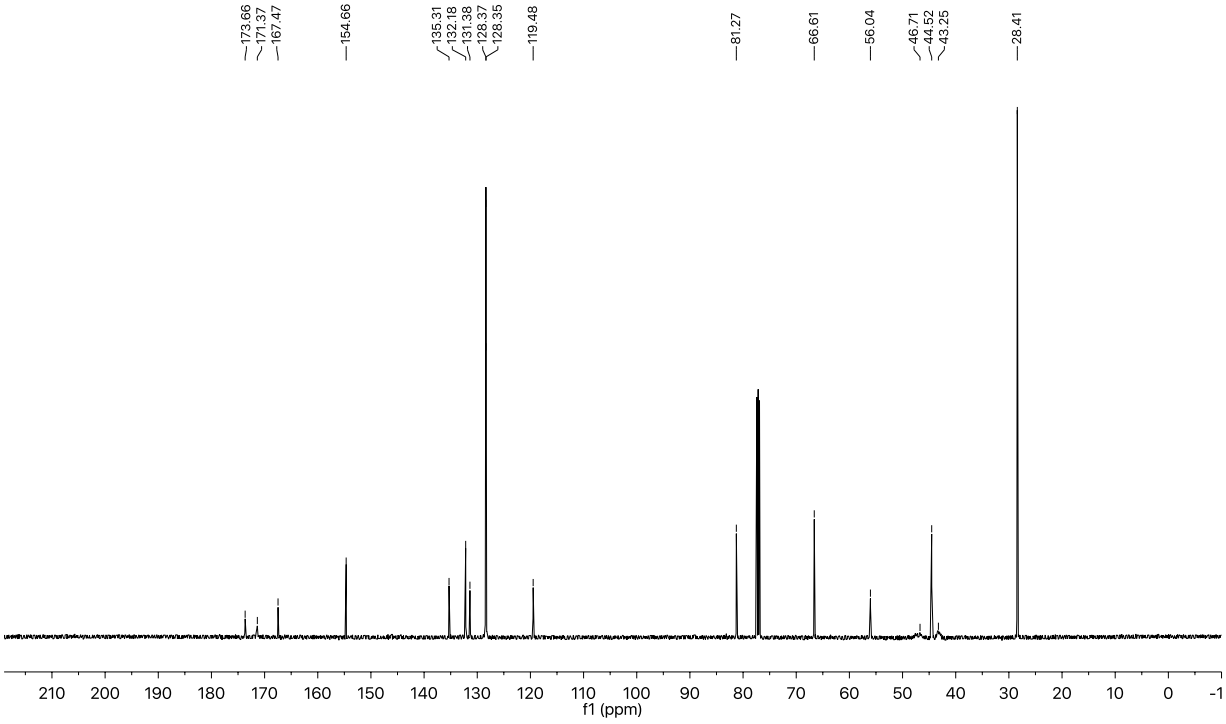
^{13}C NMR (100 MHz, $CDCl_3$) of compound **SI3**.



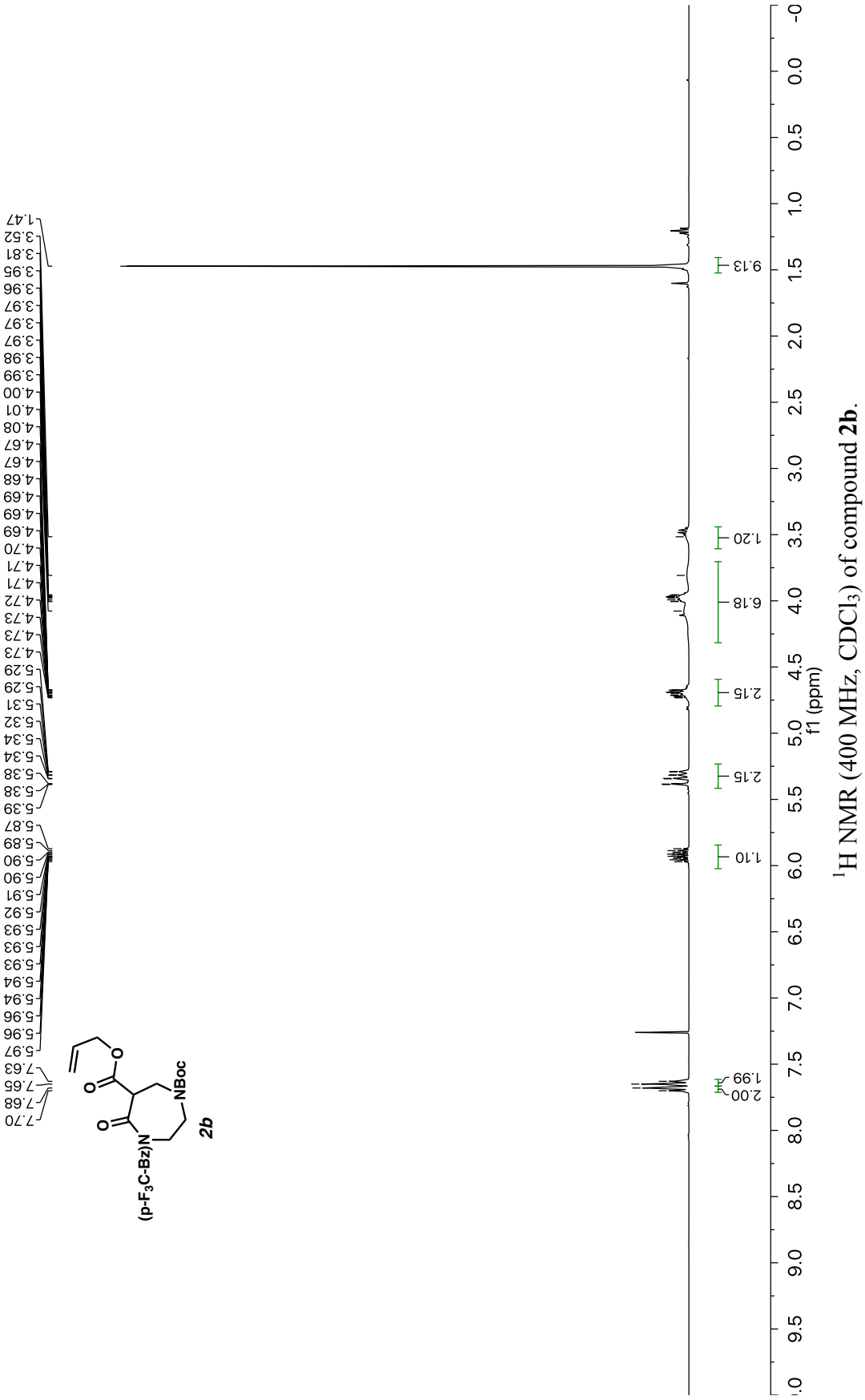
^{1}H NMR (500 MHz, $CDCl_3$) of compound **2a**.



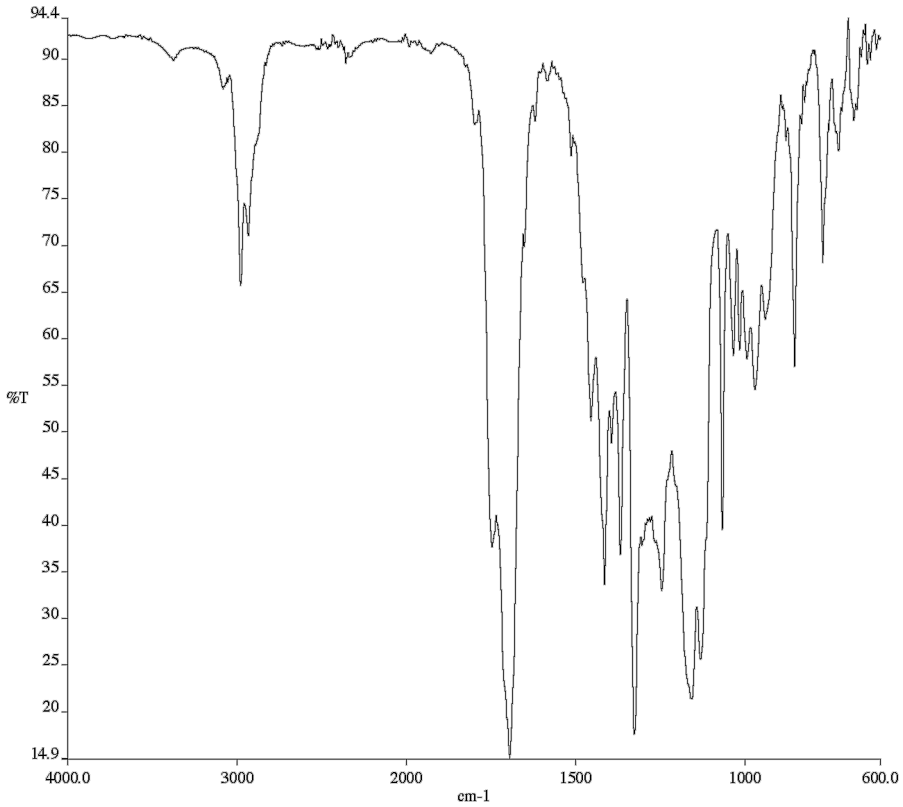
Infrared spectrum (Thin Film, NaCl) of compound **2a**.



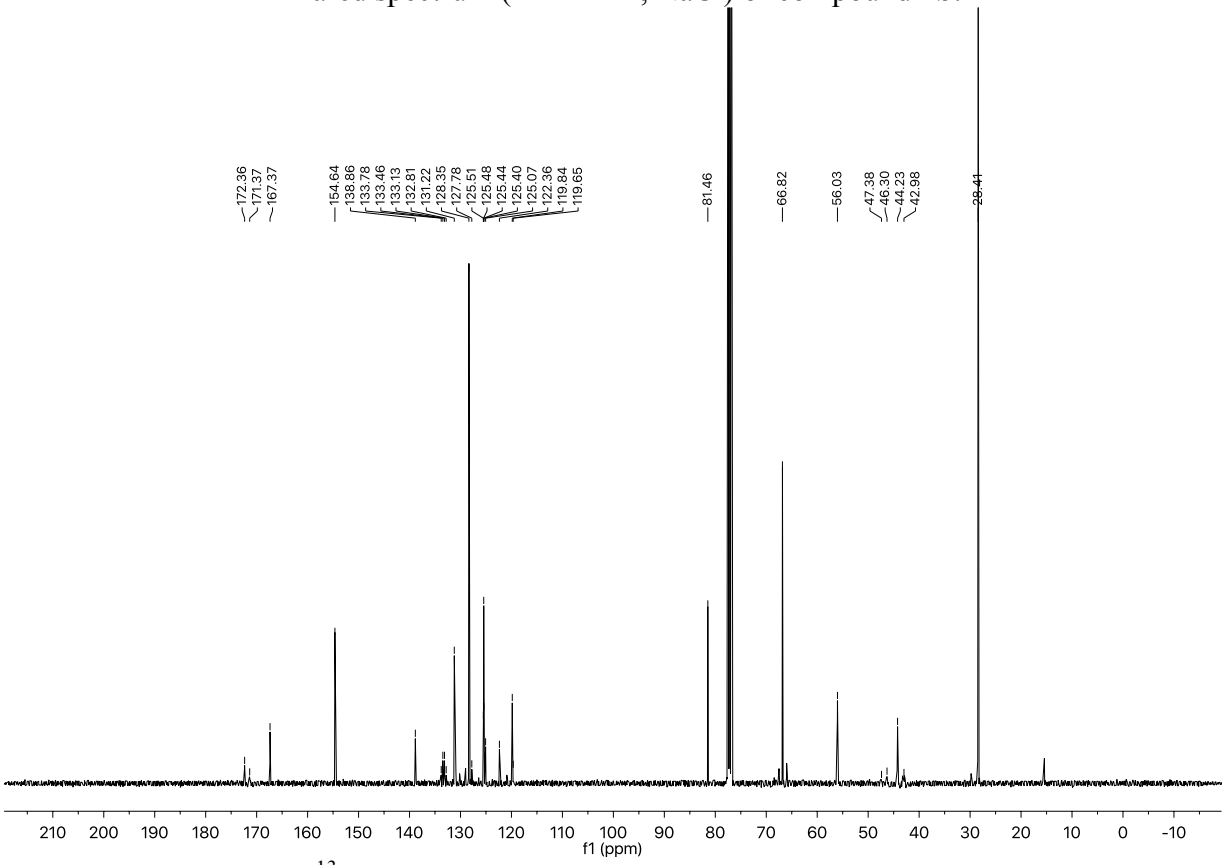
^{13}C NMR (125 MHz, $CDCl_3$) of compound **2a**.



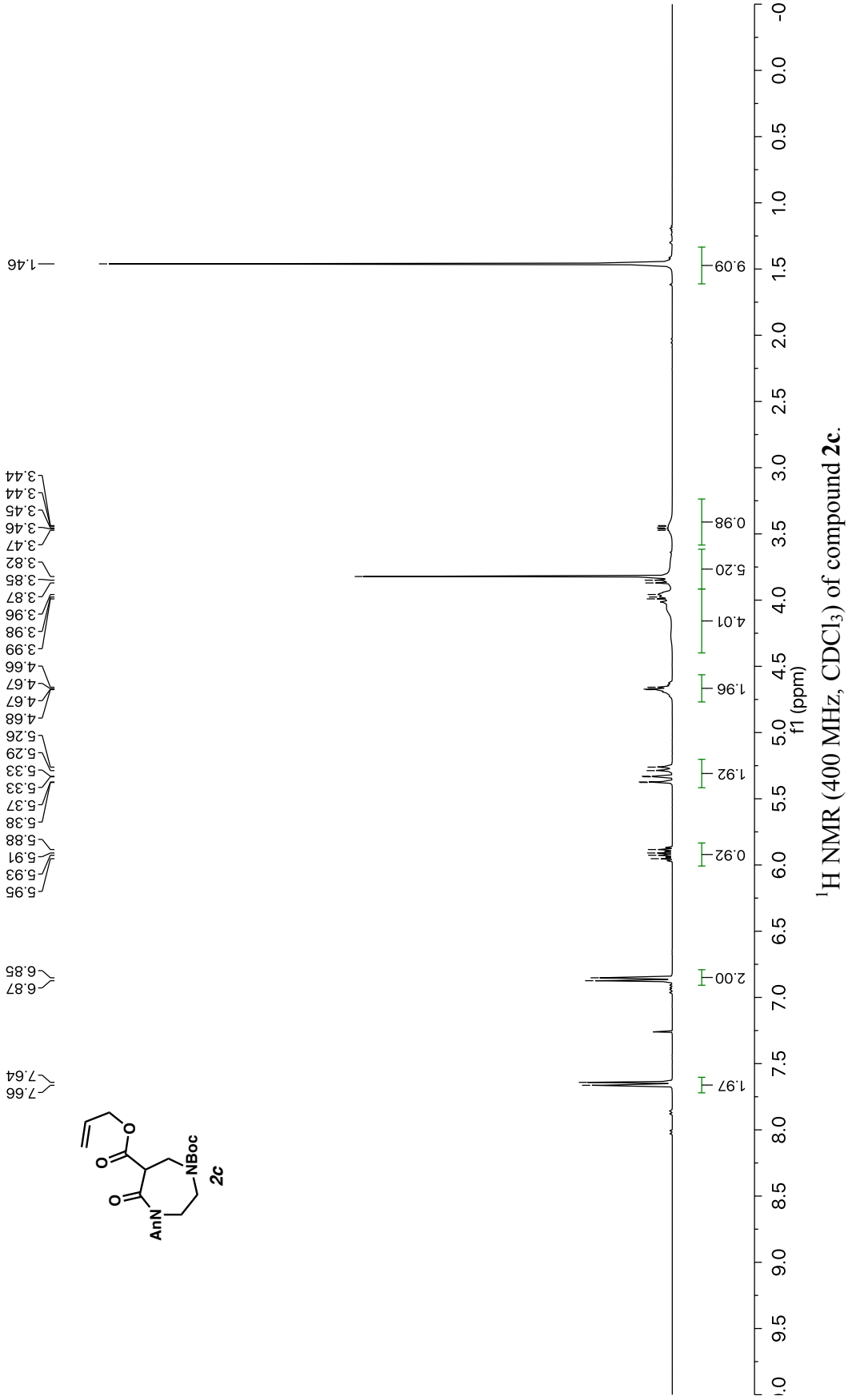
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2b**.



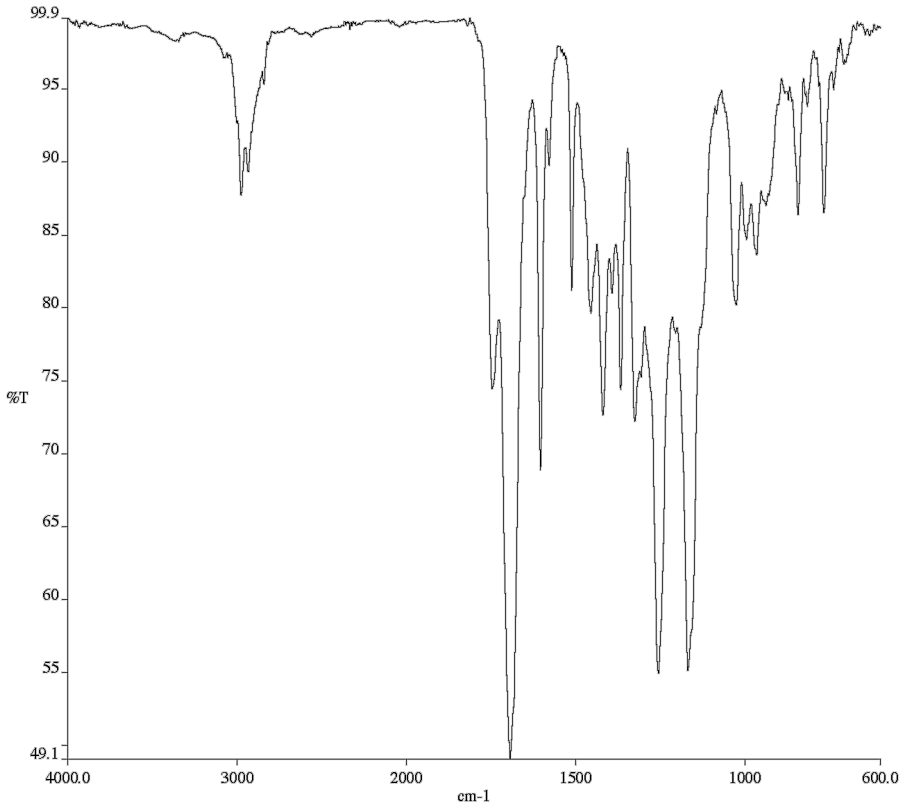
Infrared spectrum (Thin Film, NaCl) of compound **2b**.



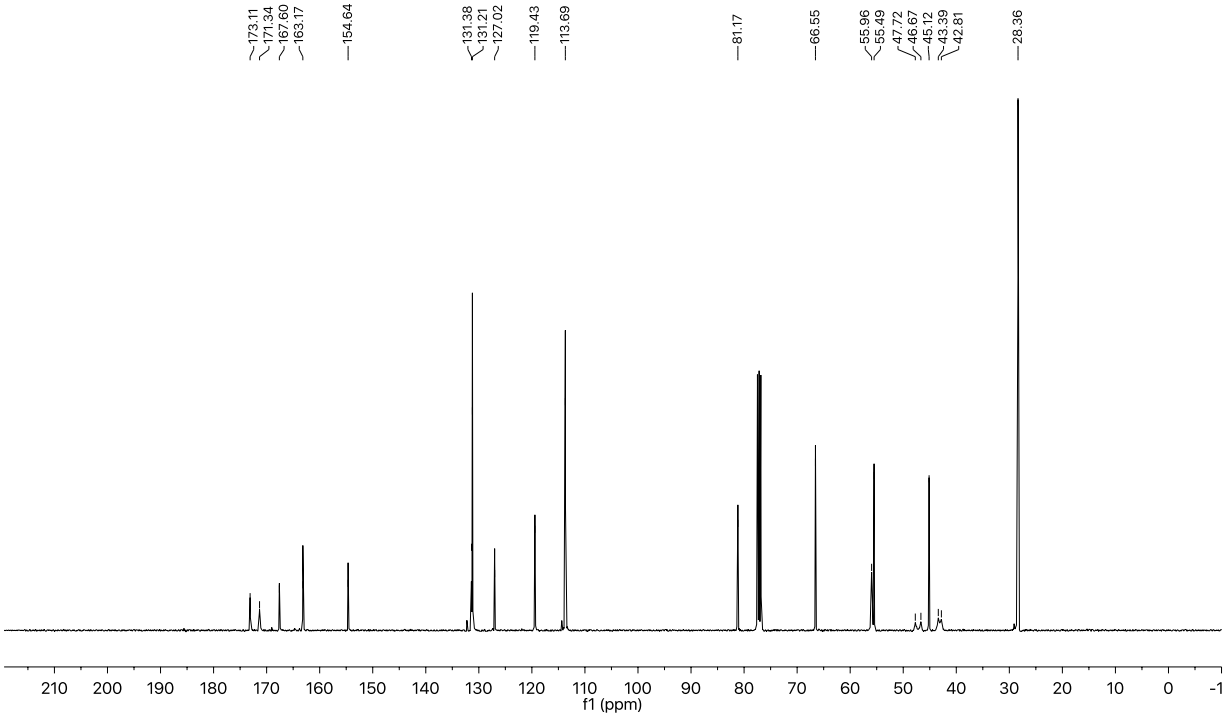
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2b**.



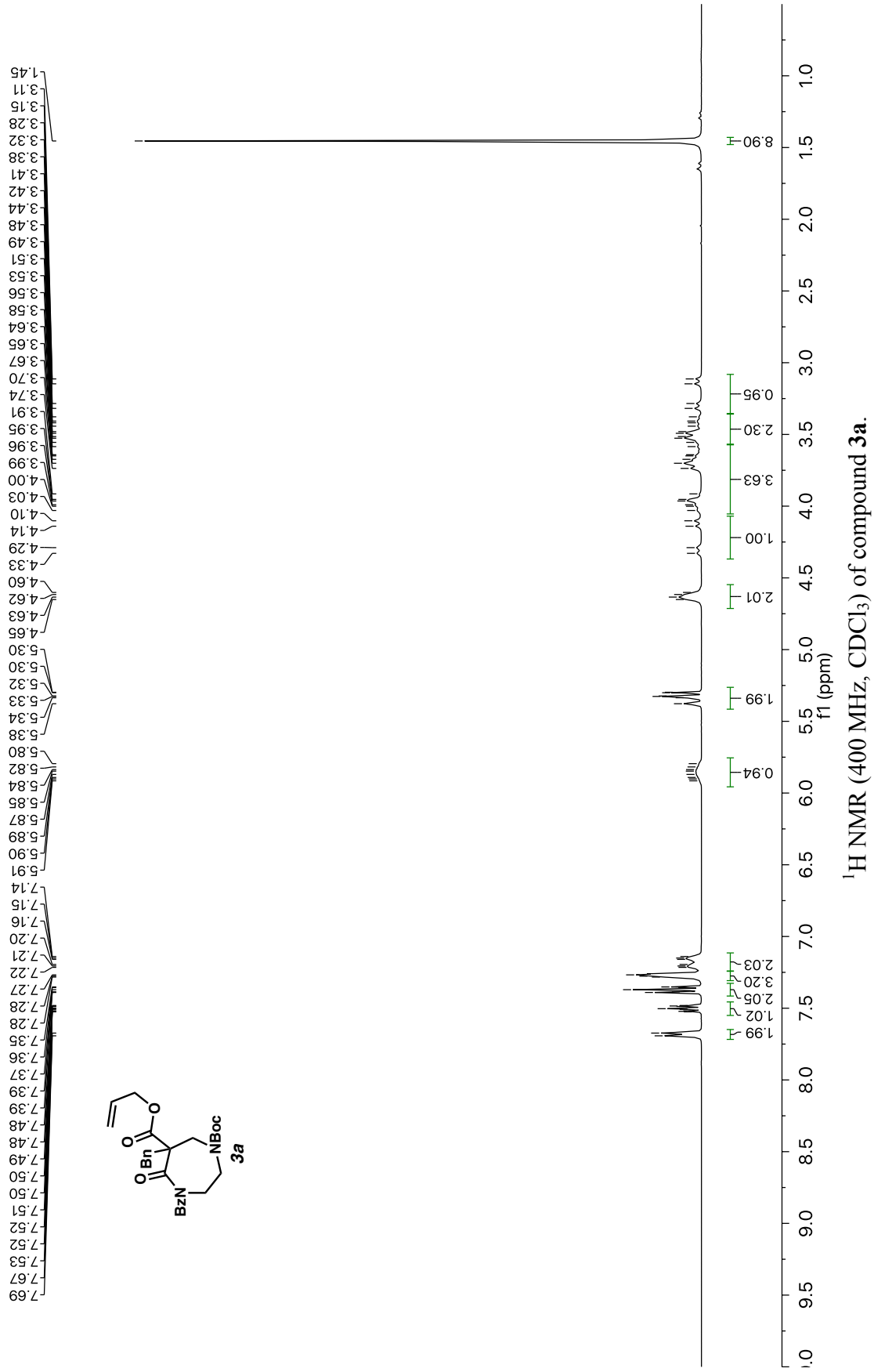
^{1}H NMR (400 MHz, $CDCl_3$) of compound **2c**.



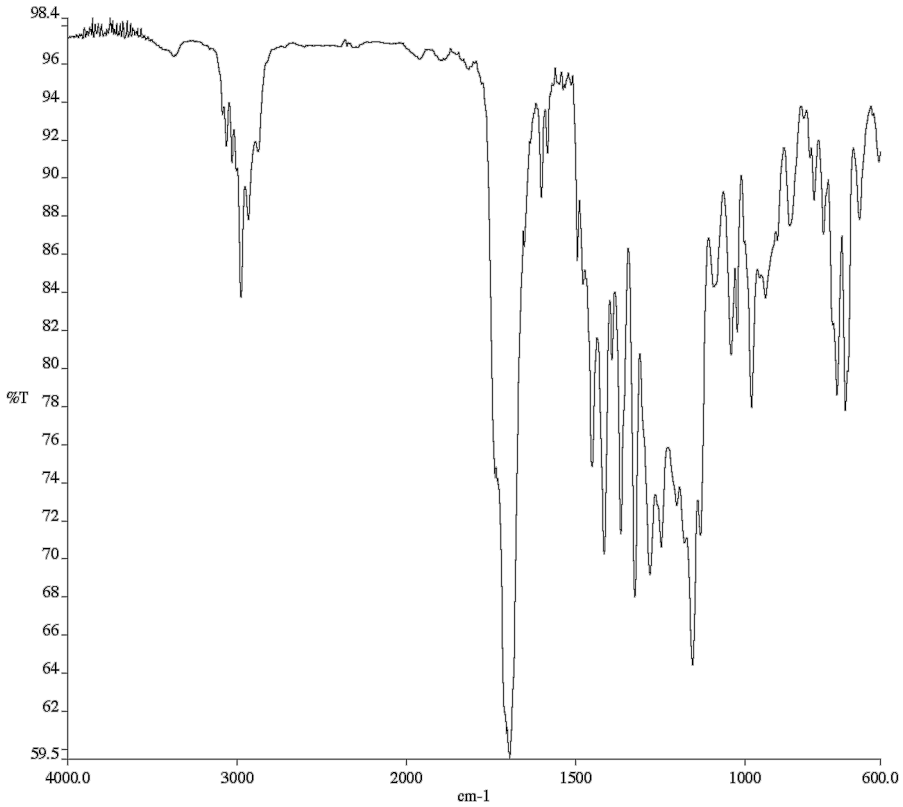
Infrared spectrum (Thin Film, NaCl) of compound **2c**.



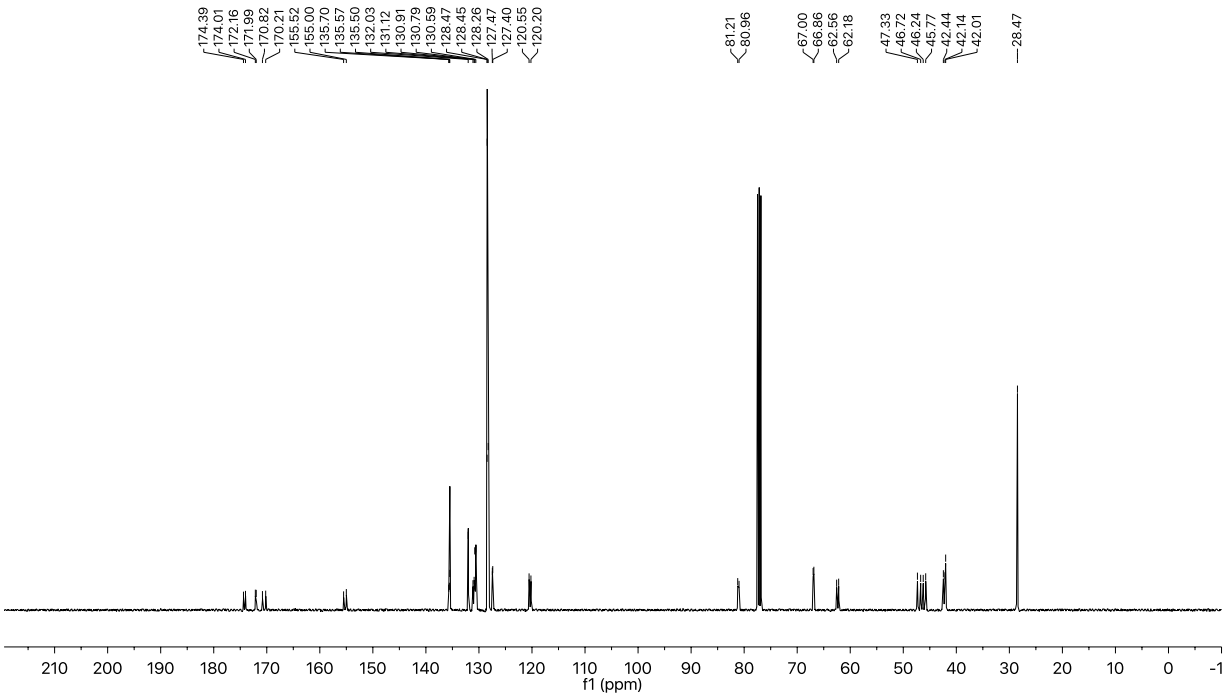
^{13}C NMR (100 MHz, $CDCl_3$) of compound **2c**.



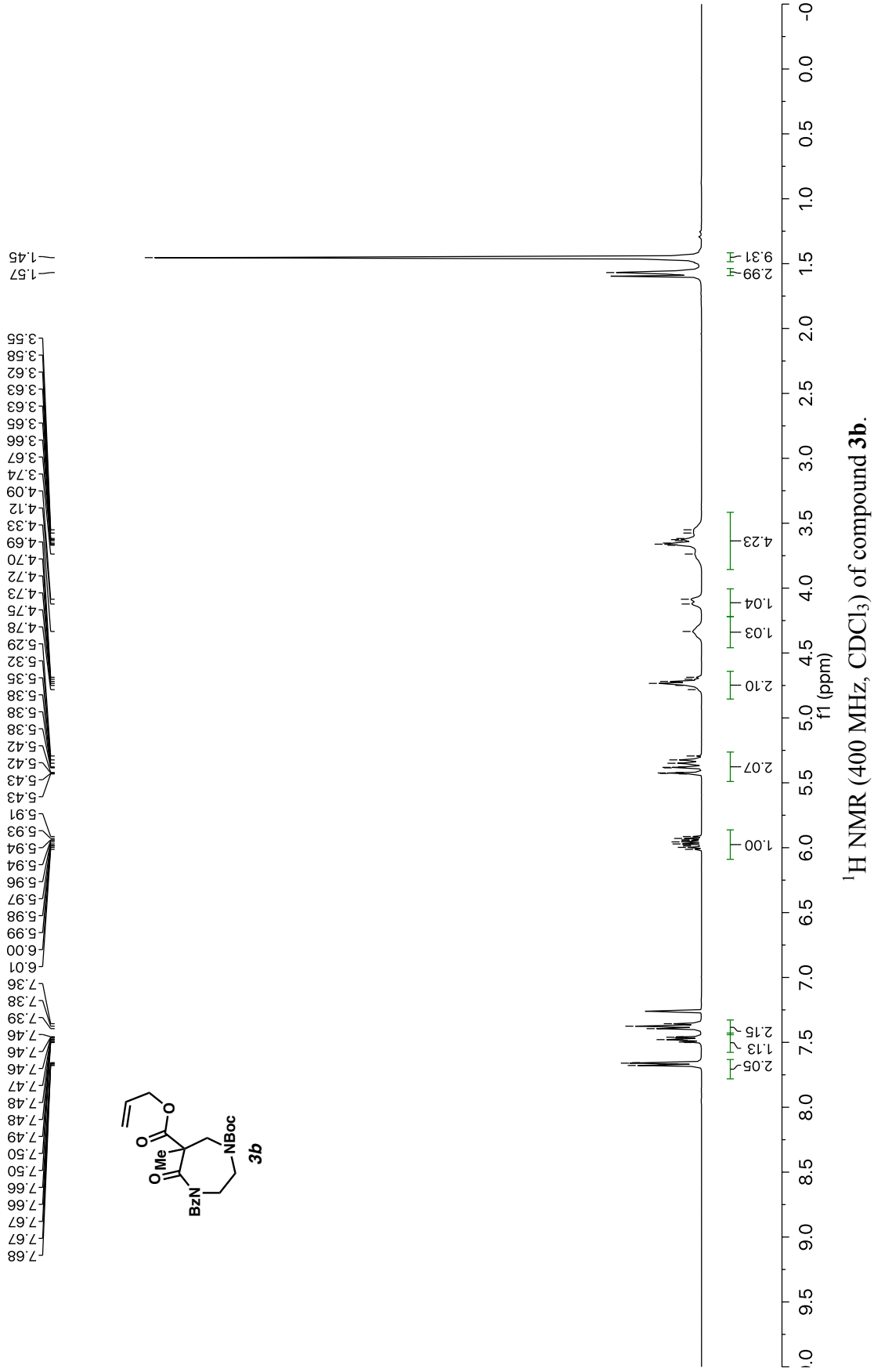
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3a**.



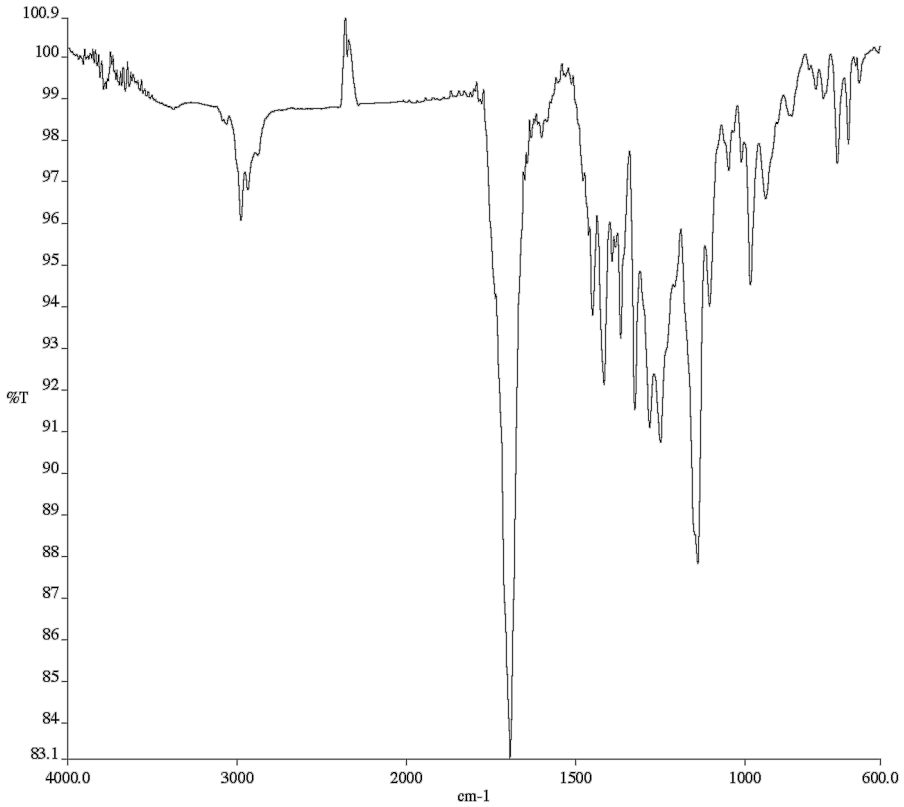
Infrared spectrum (Thin Film, NaCl) of compound **3a**.



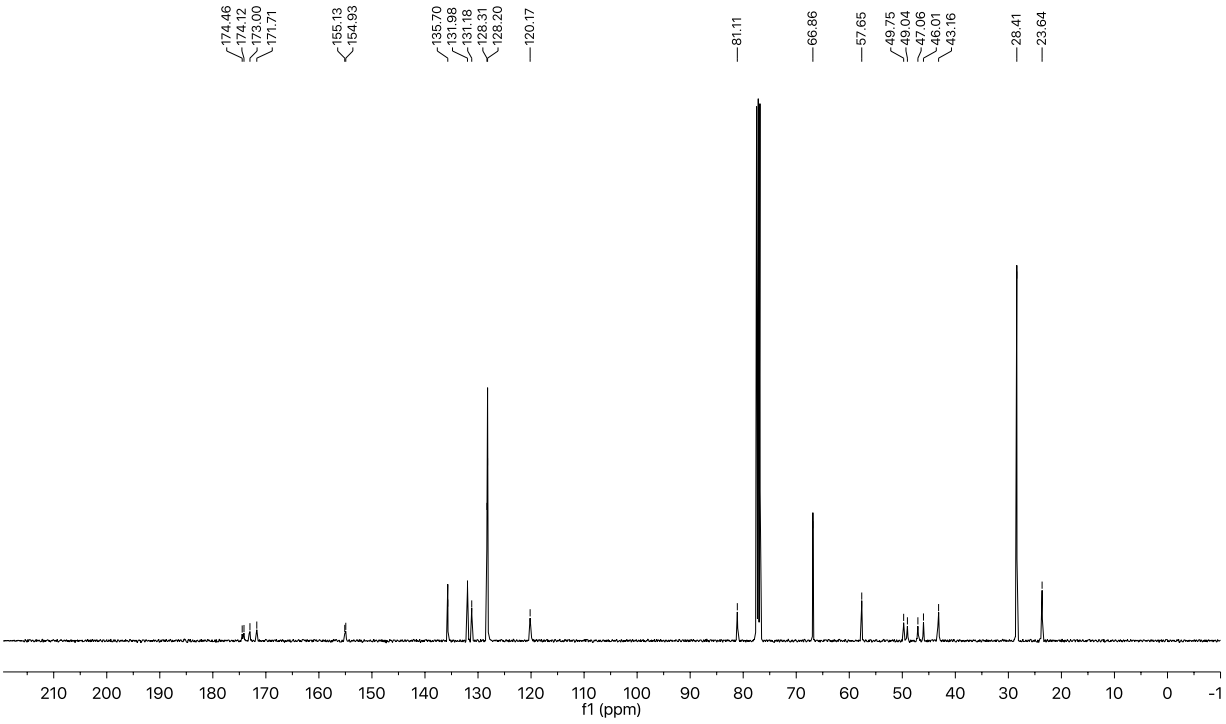
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3a**.



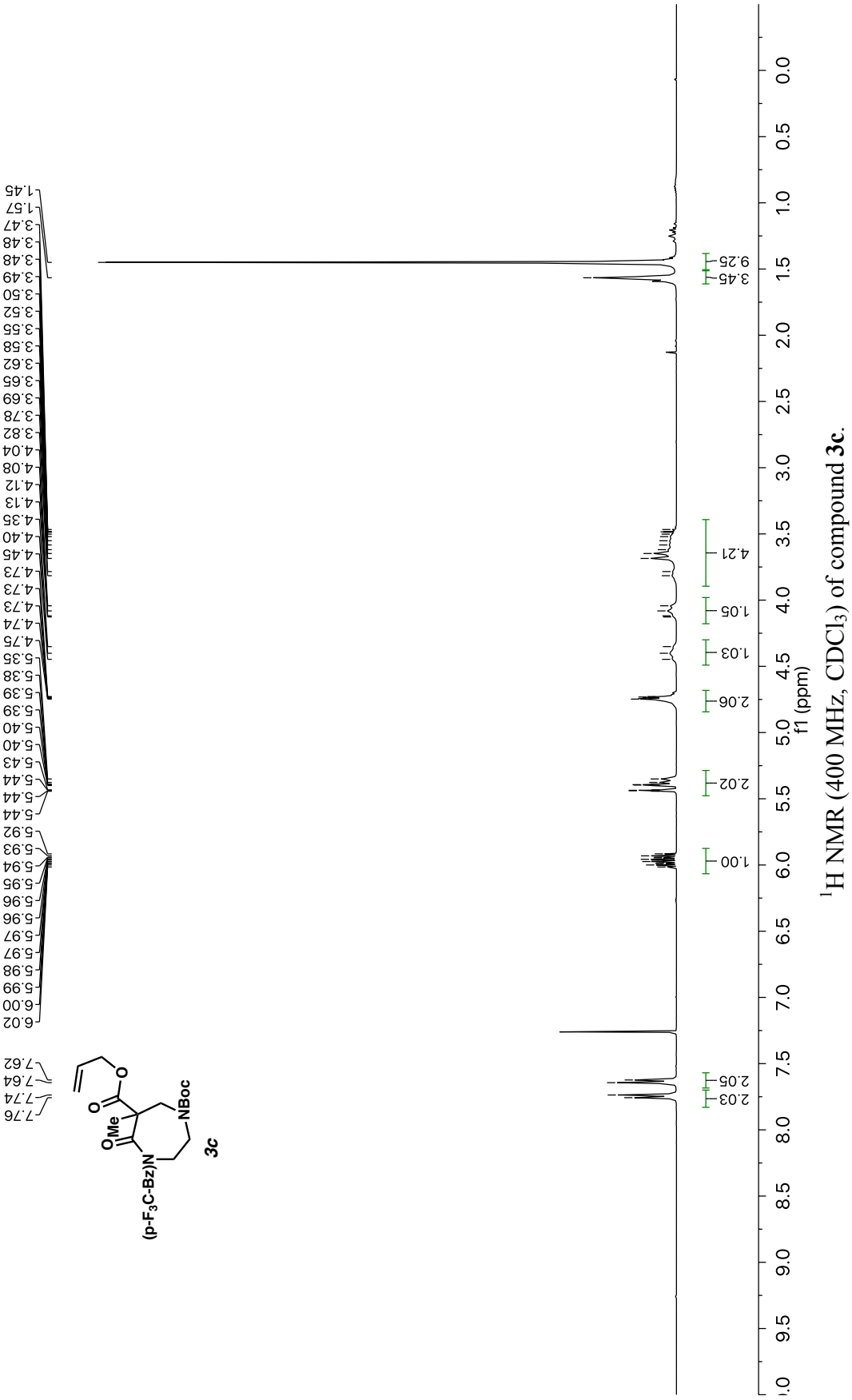
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3b**.



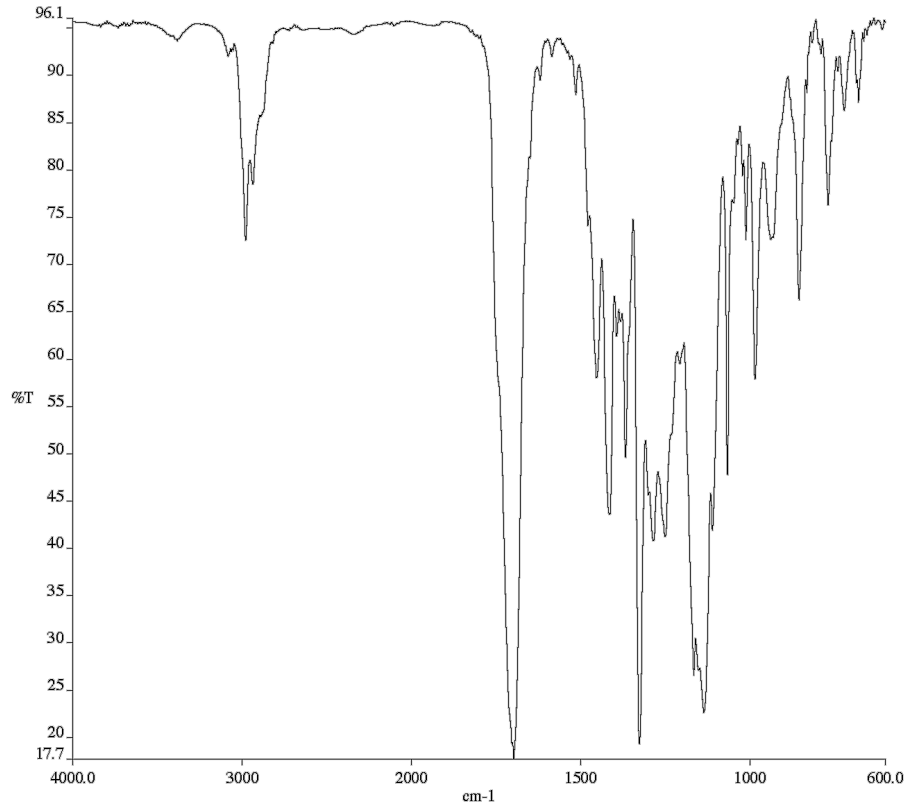
Infrared spectrum (Thin Film, NaCl) of compound **3b**.



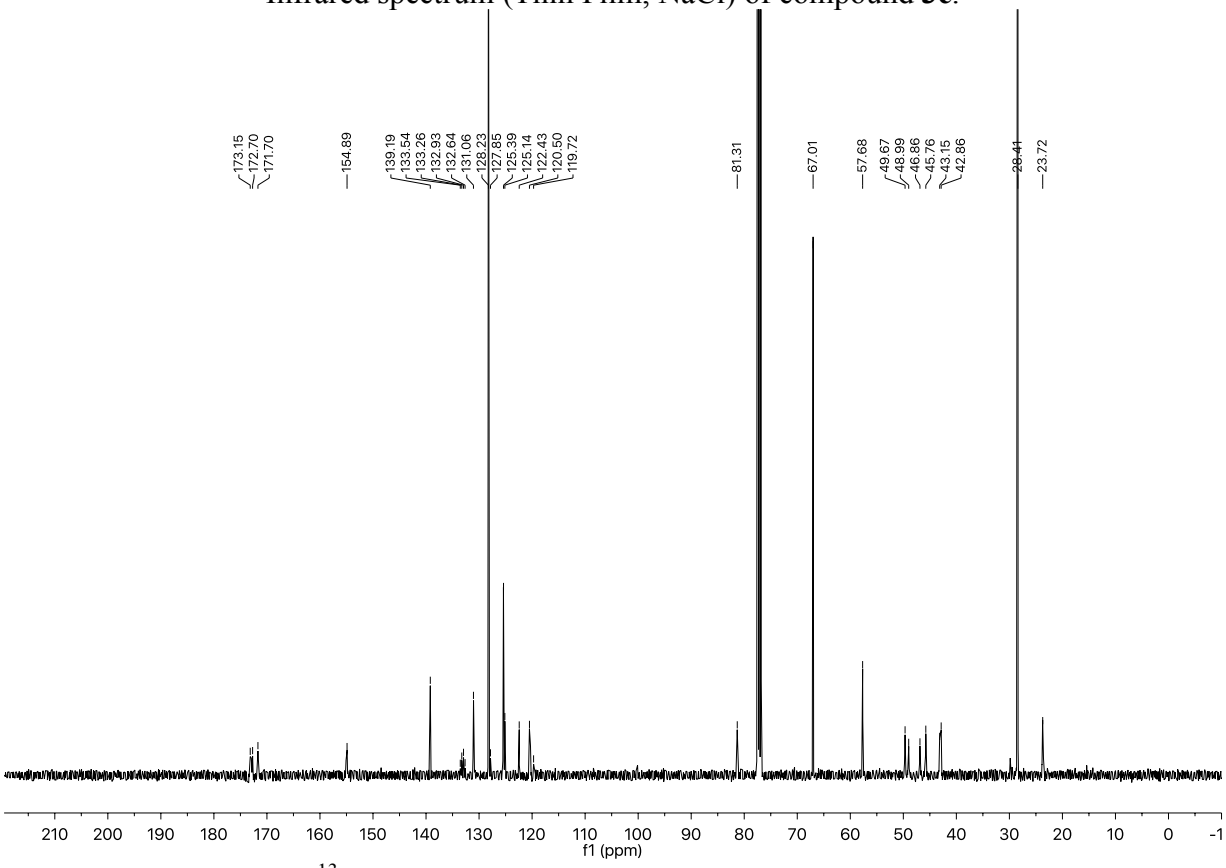
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3b**.



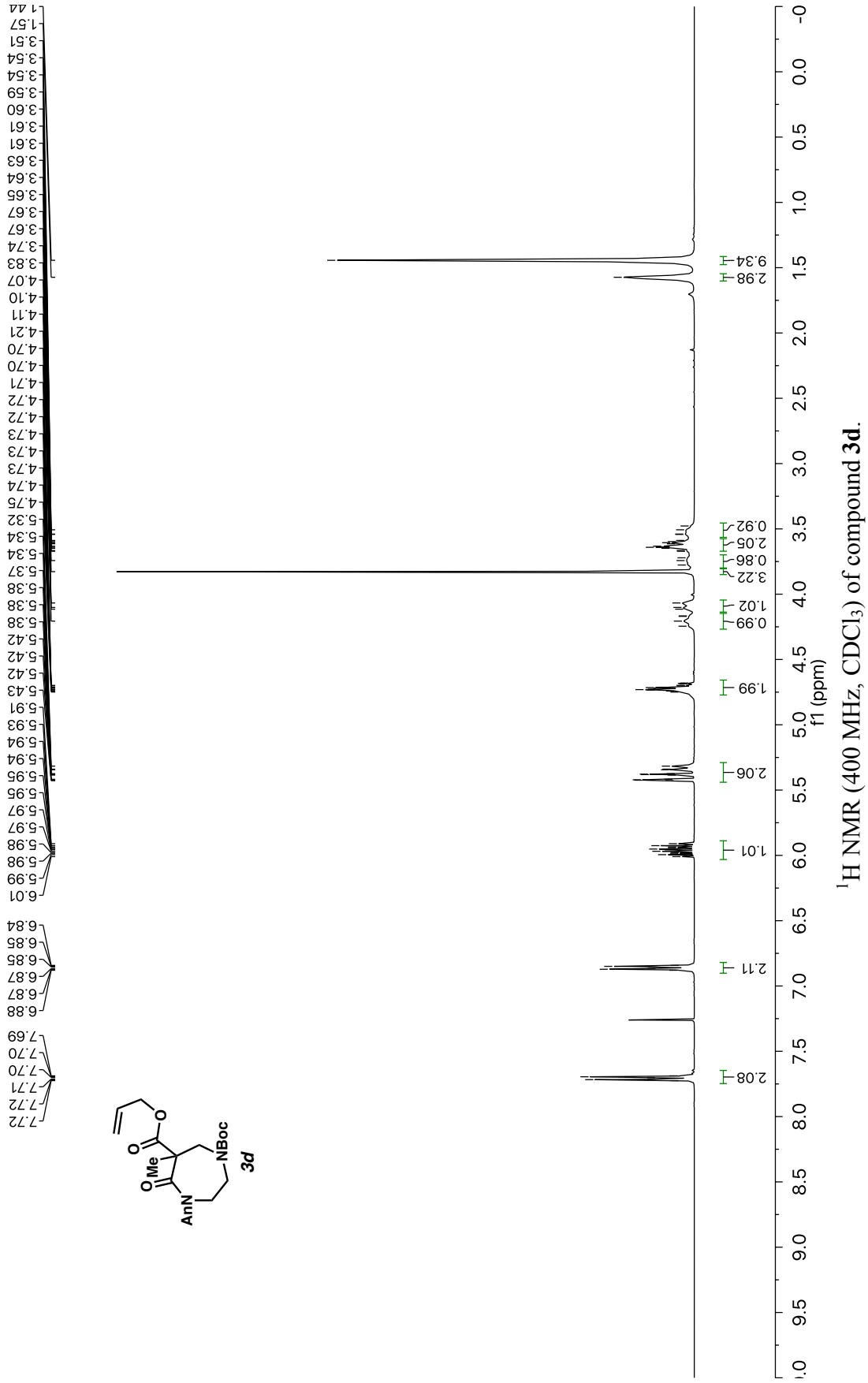
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3c**.



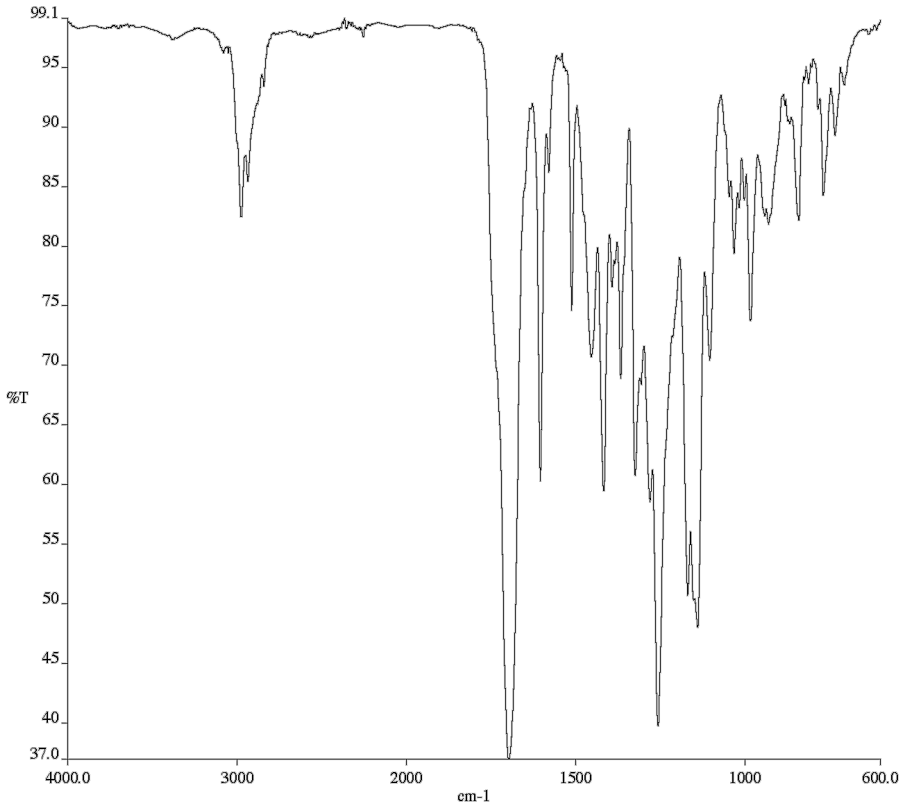
Infrared spectrum (Thin Film, NaCl) of compound **3c**.



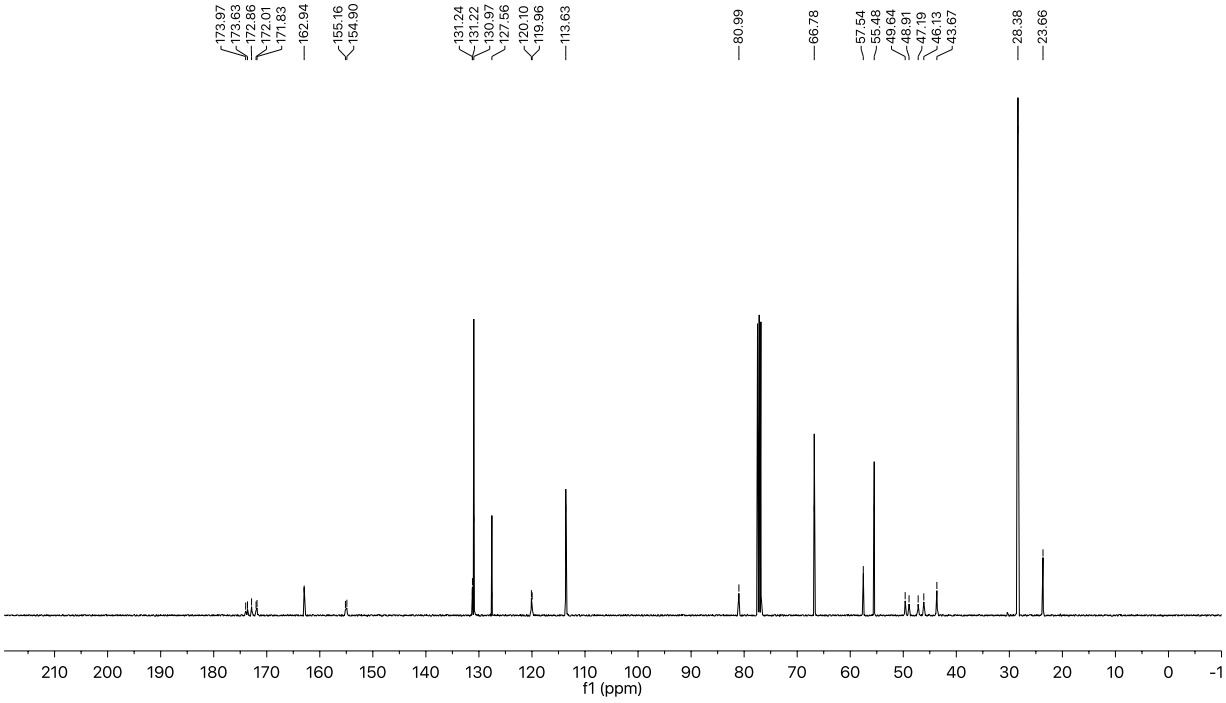
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3c**.



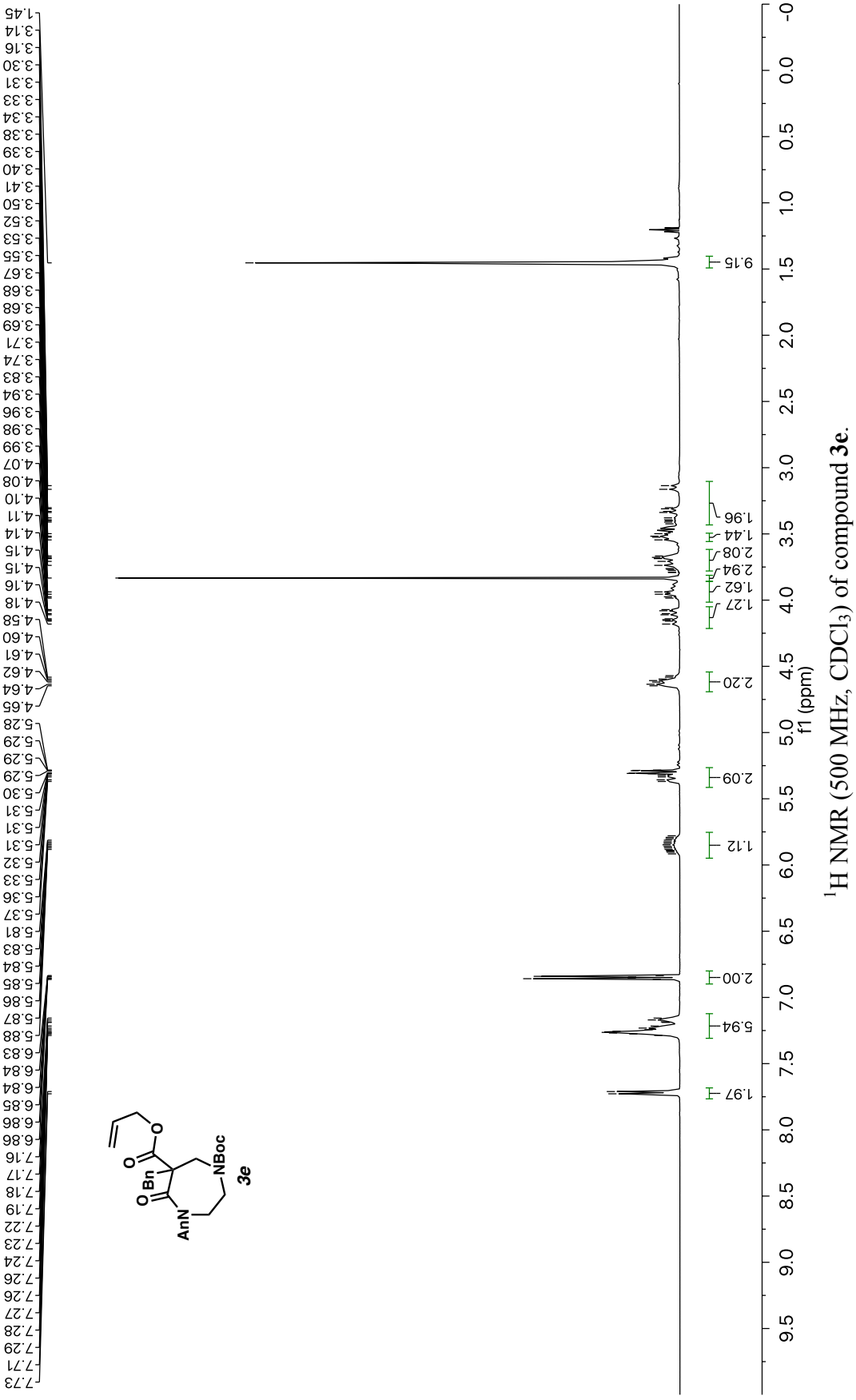
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3d**.



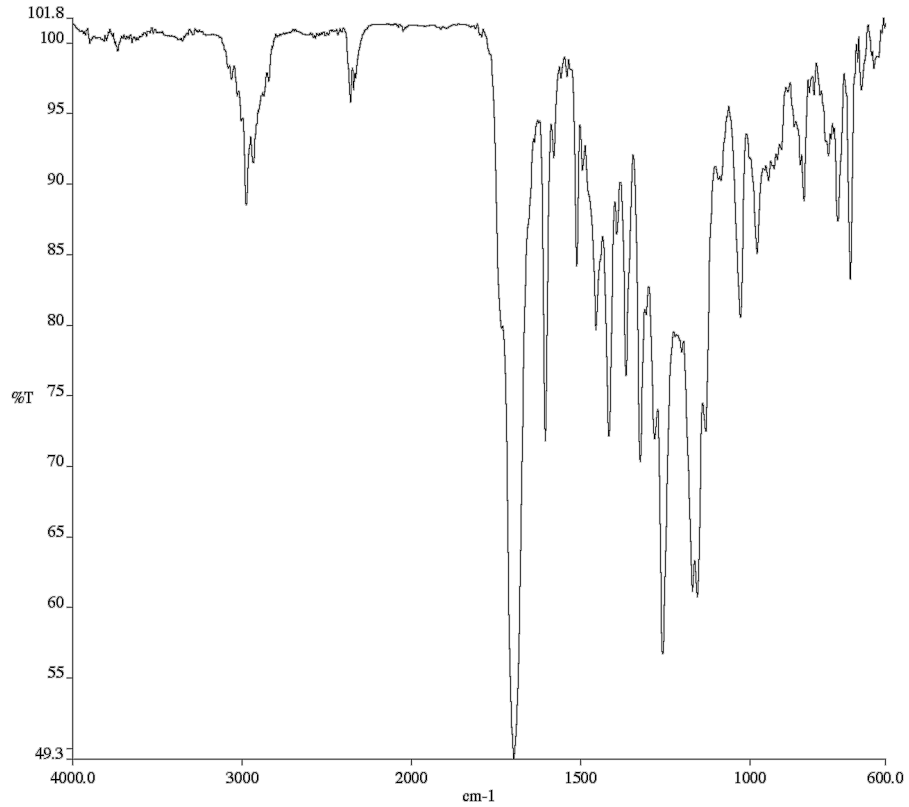
Infrared spectrum (Thin Film, NaCl) of compound **3d**.



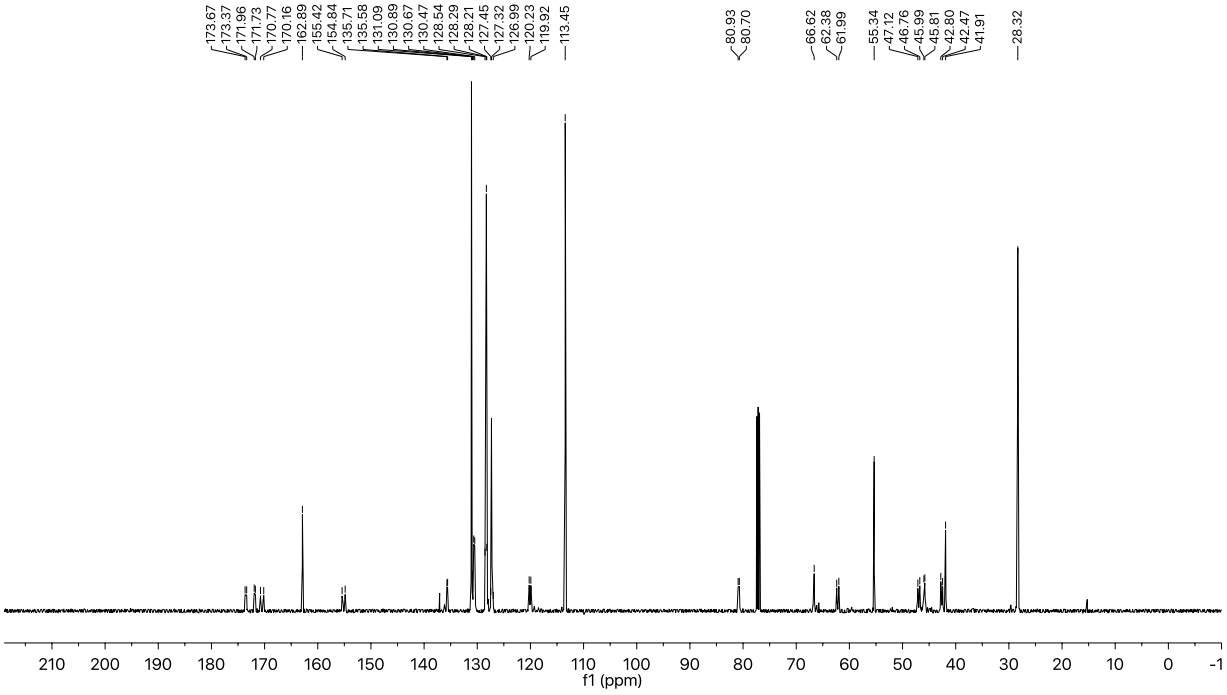
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3d**.



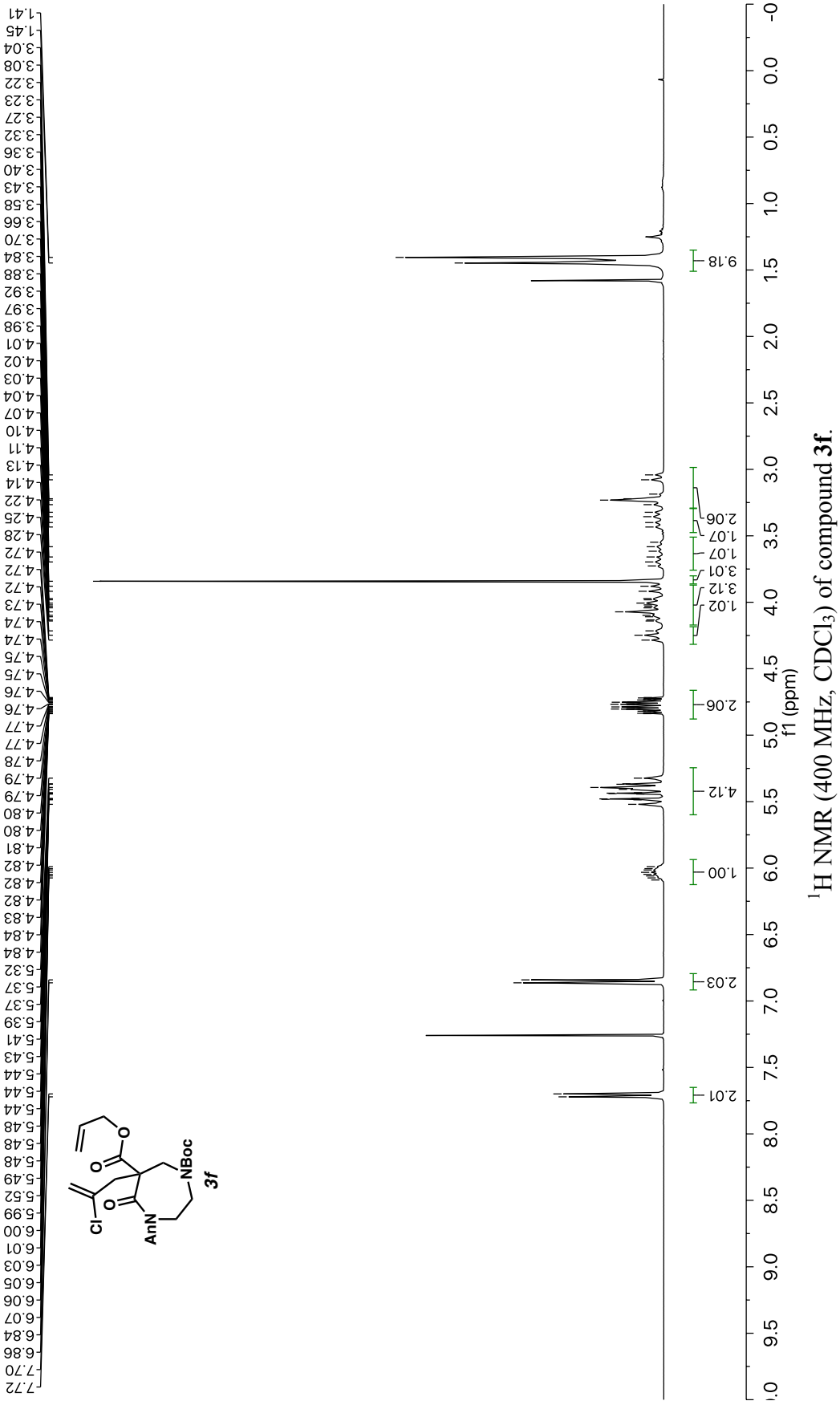
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3e**.



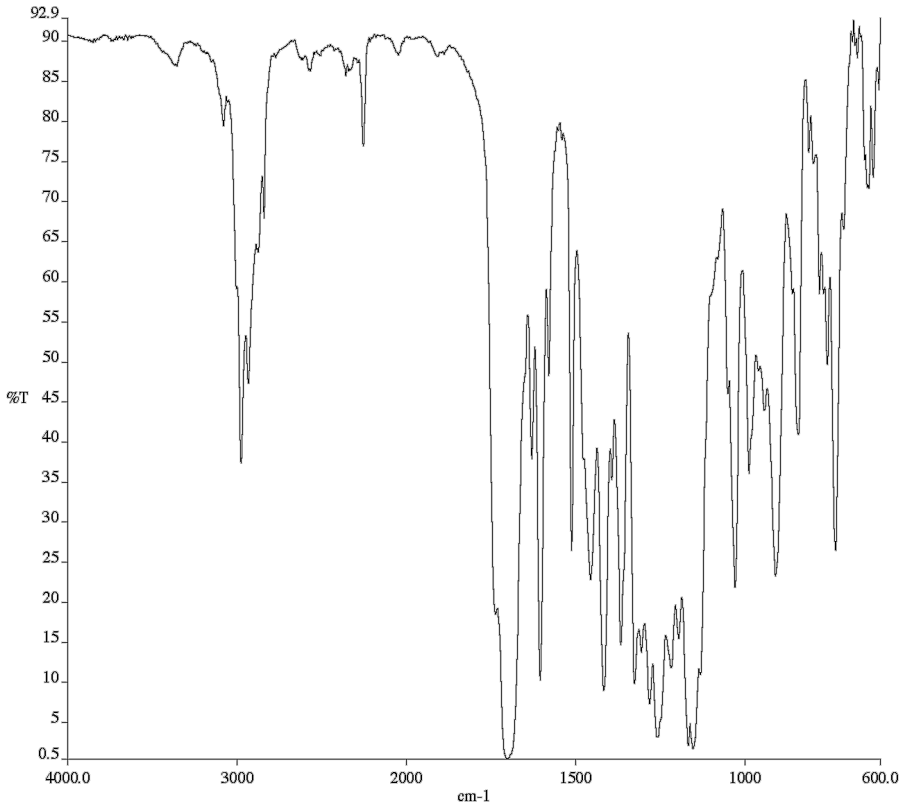
Infrared spectrum (Thin Film, NaCl) of compound **3e**.



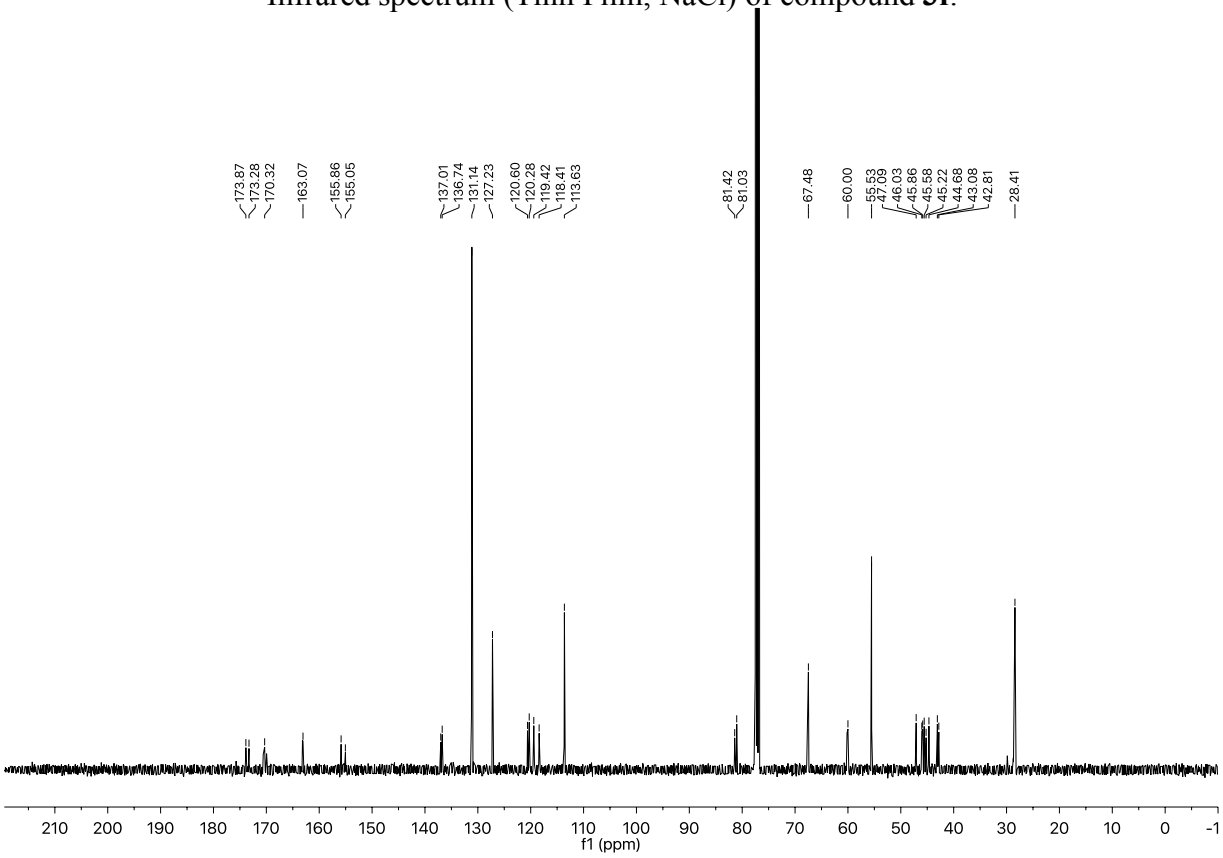
^{13}C NMR (125 MHz, $CDCl_3$) of compound **3e**.



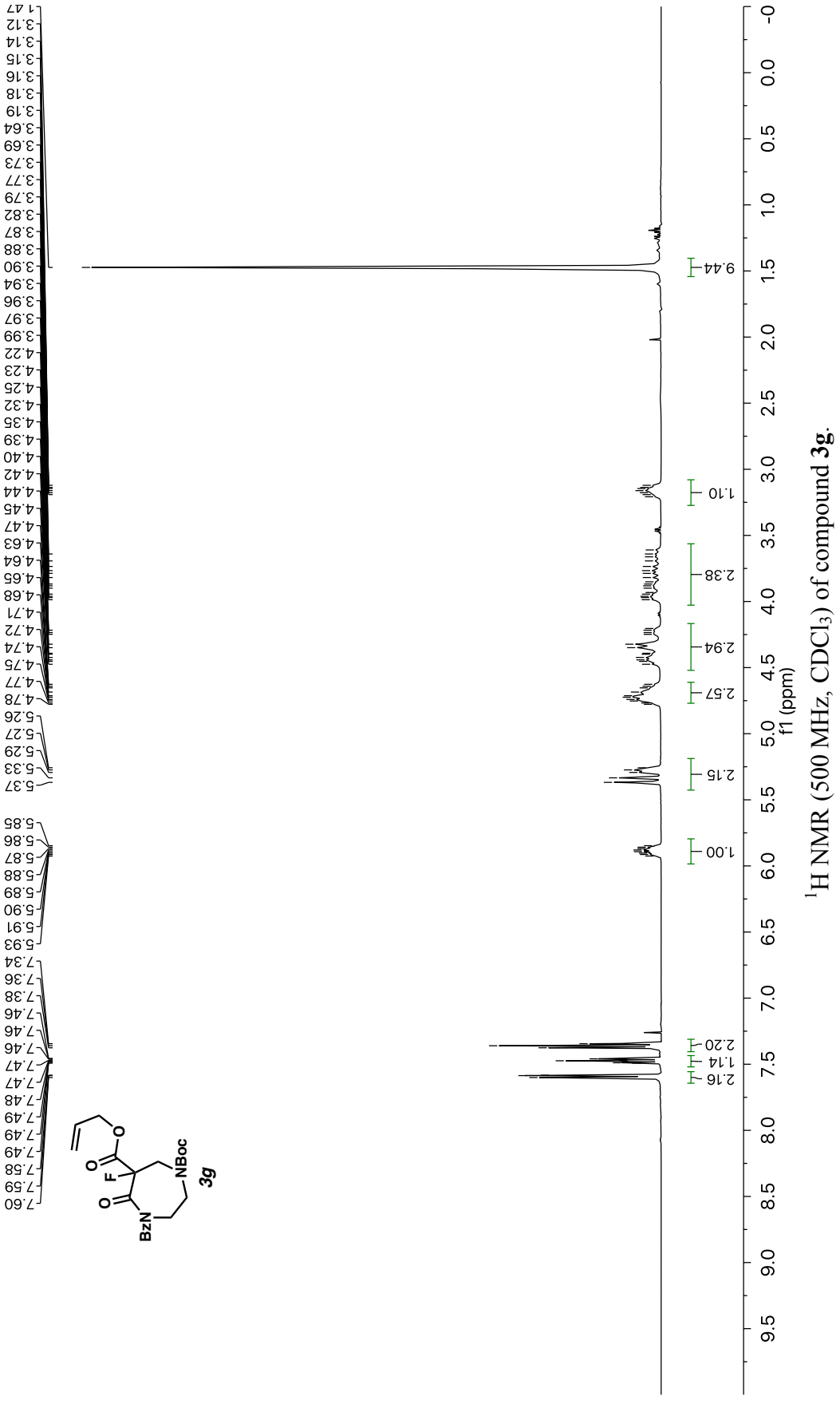
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3f**.



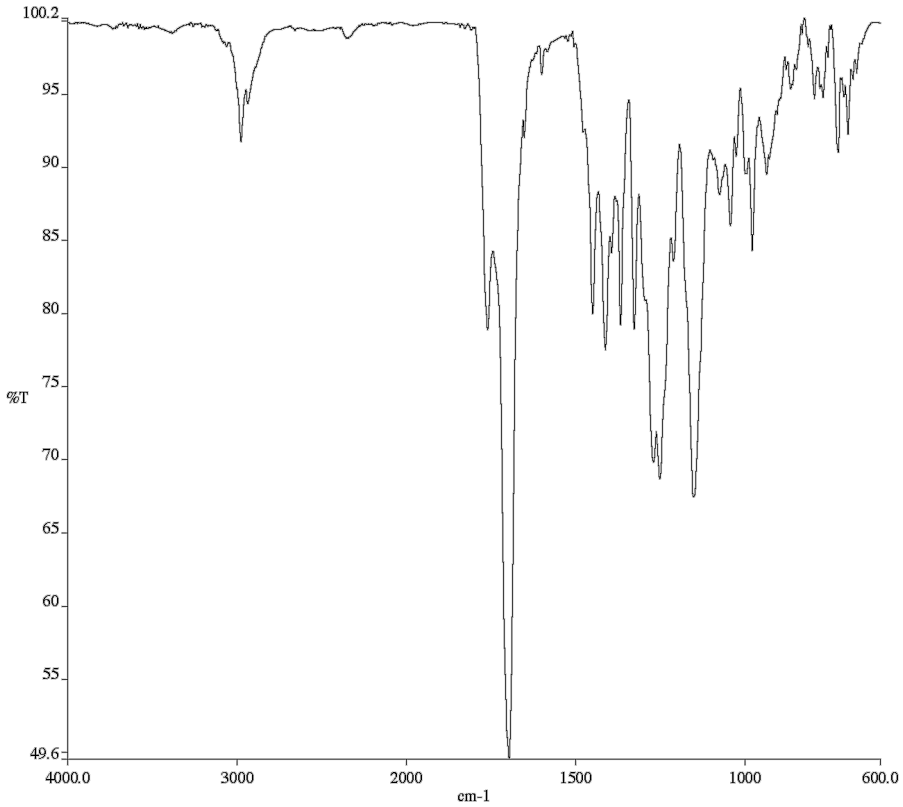
Infrared spectrum (Thin Film, NaCl) of compound **3f**.



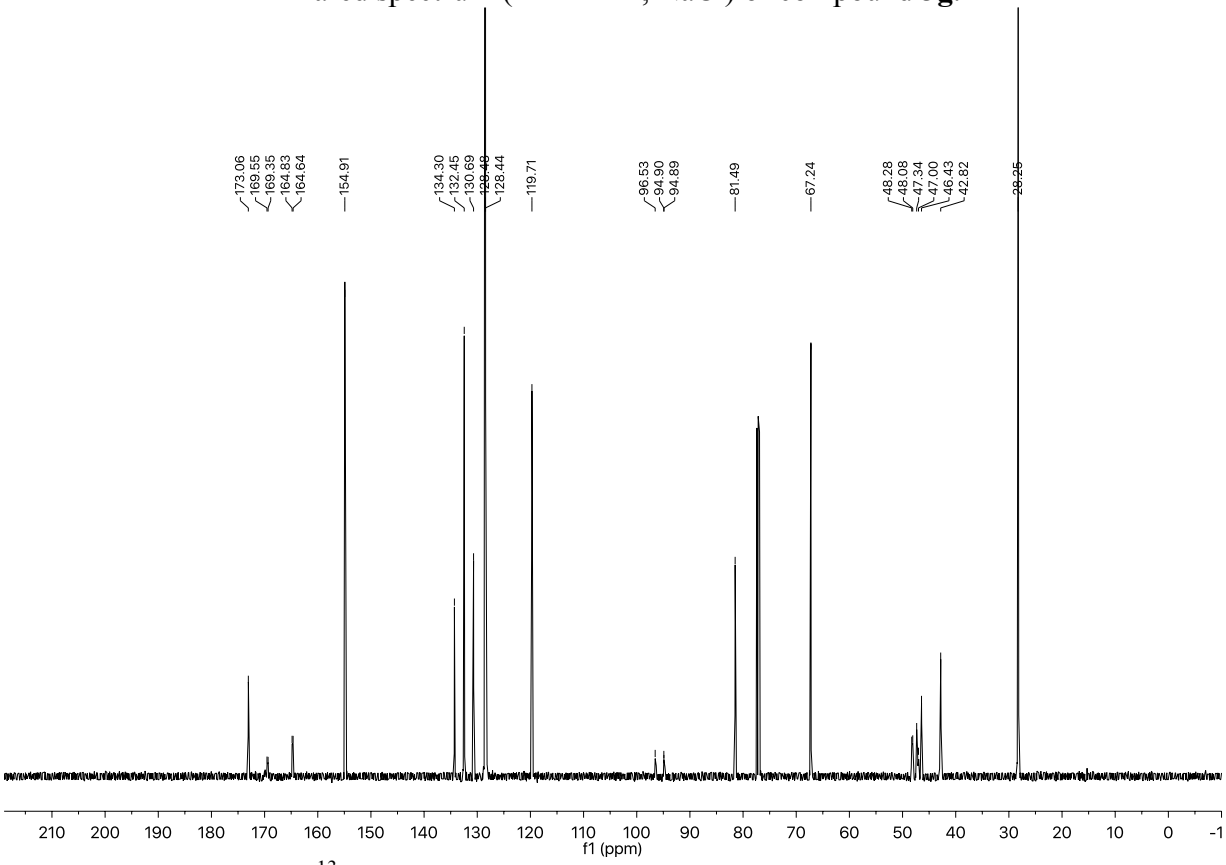
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3f**.



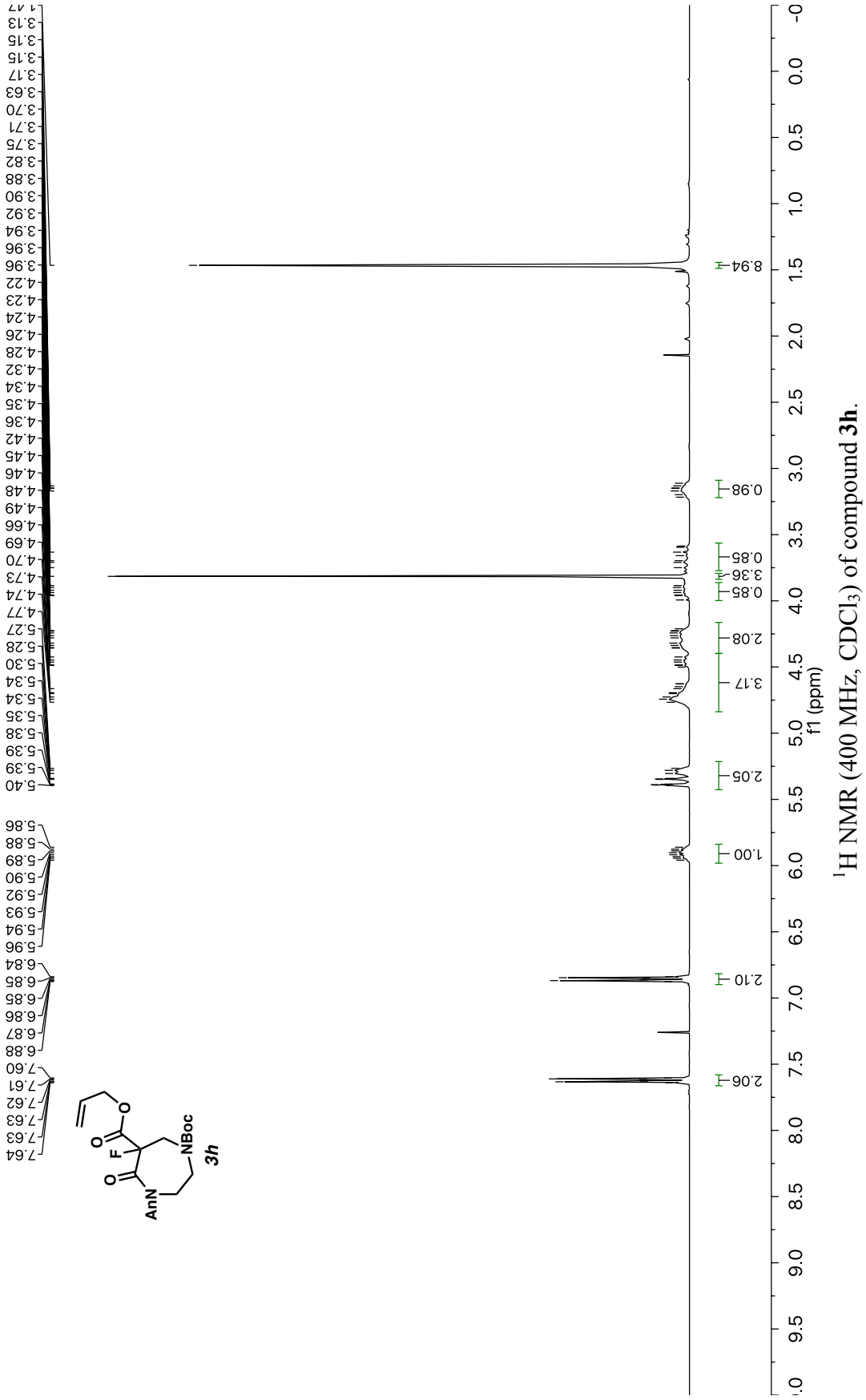
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3g**.



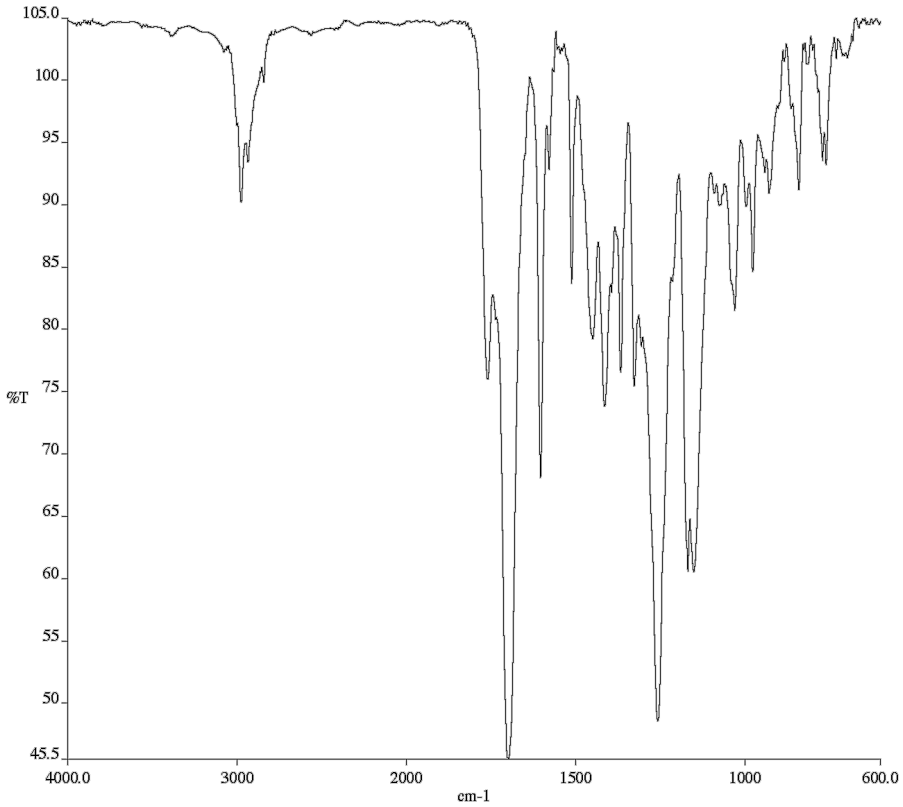
Infrared spectrum (Thin Film, NaCl) of compound **3g**.



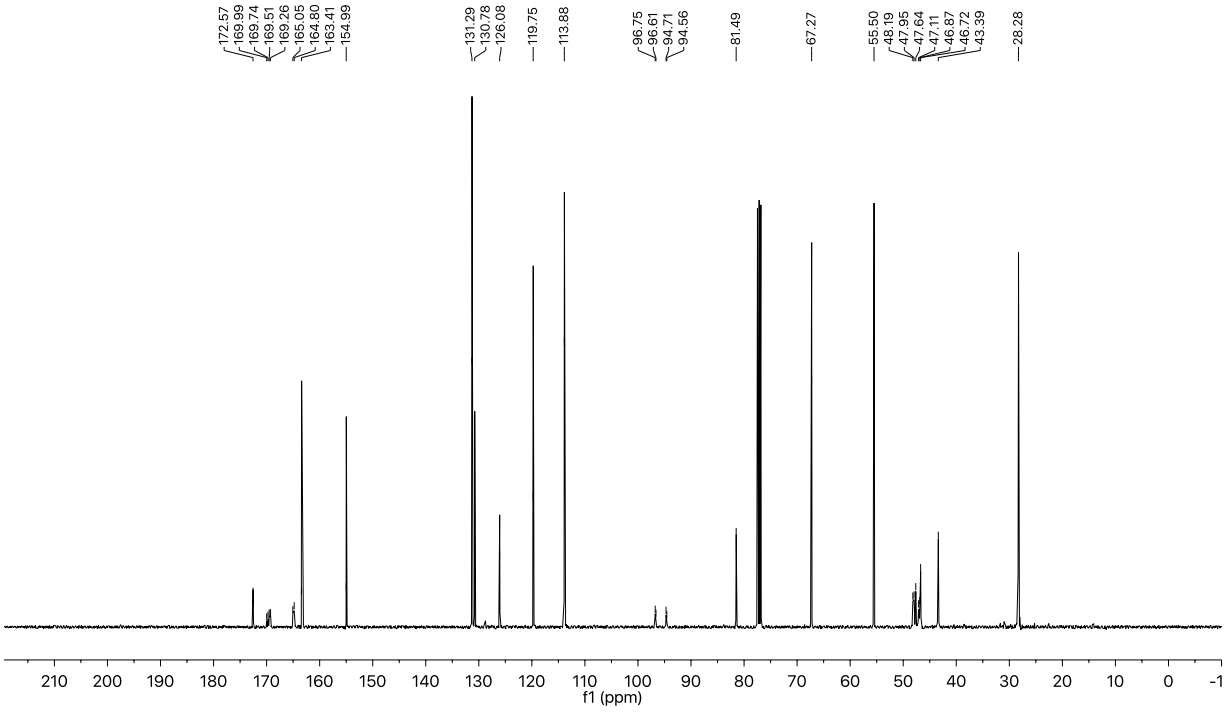
^{13}C NMR (125 MHz, $CDCl_3$) of compound **3g**.



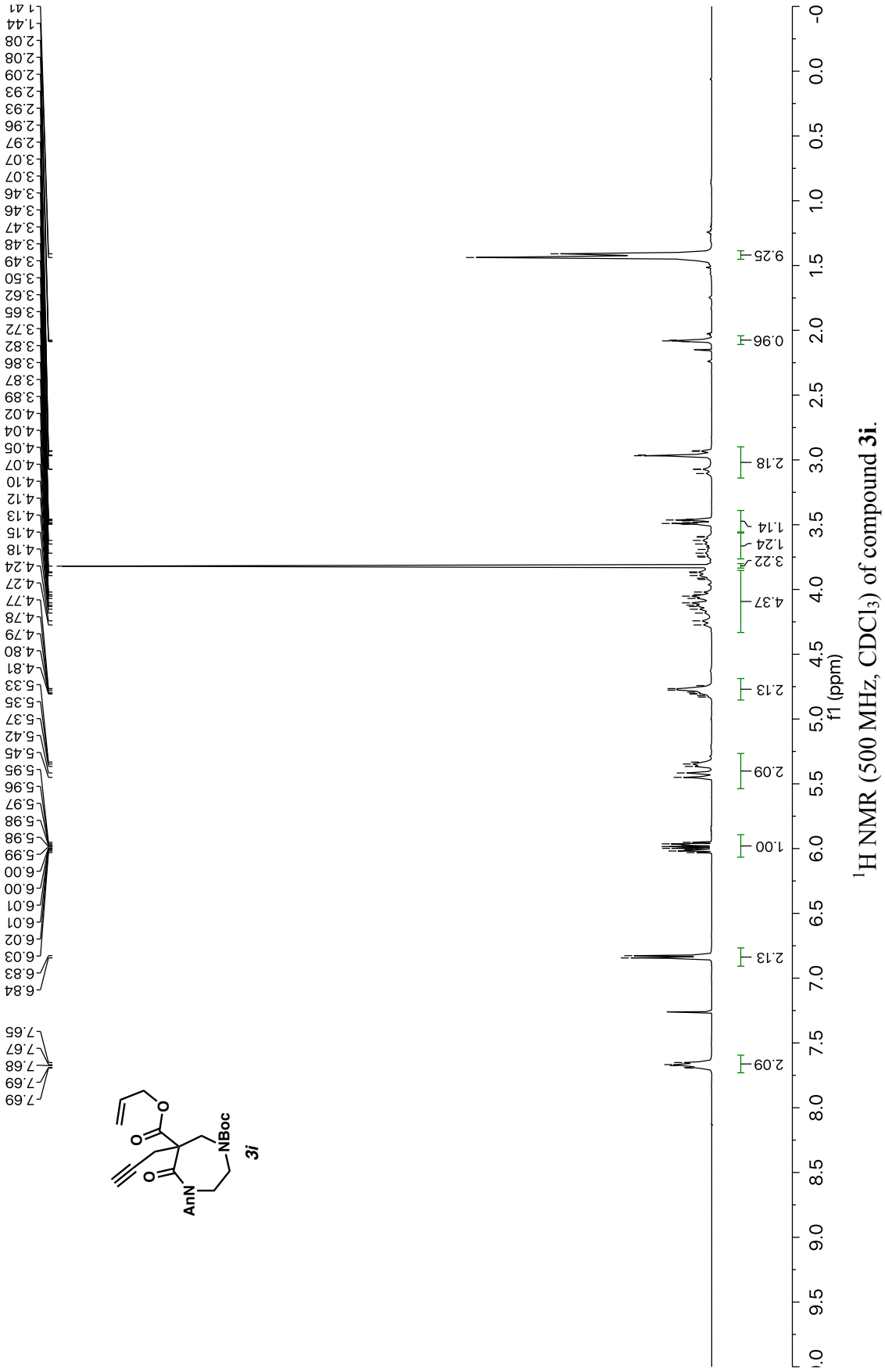
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3h**.



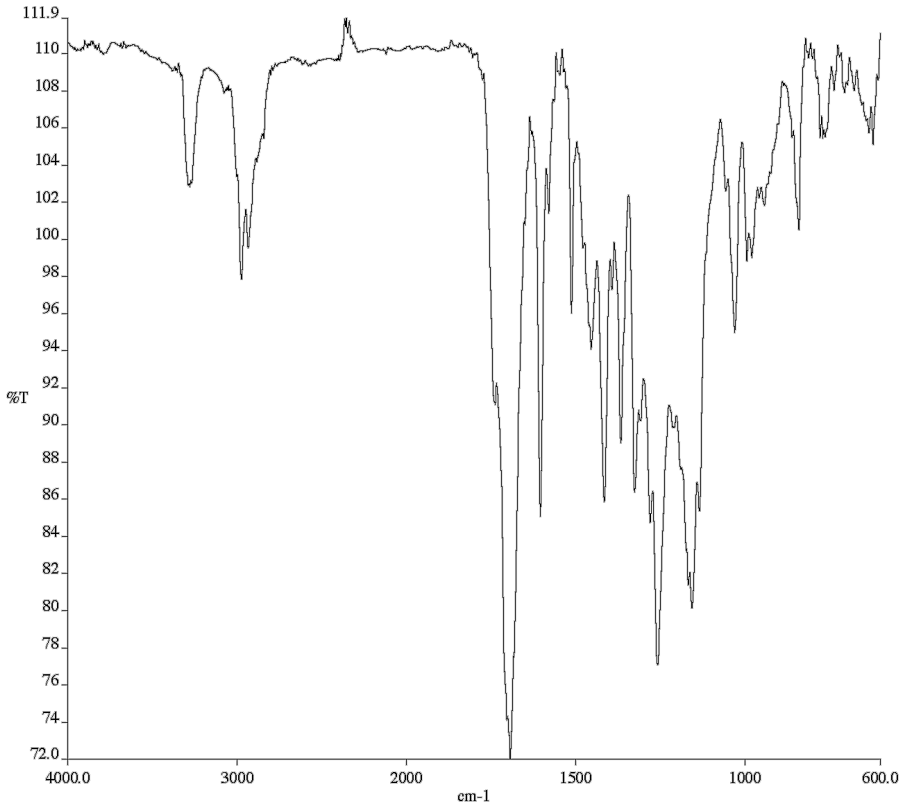
Infrared spectrum (Thin Film, NaCl) of compound **3h**.



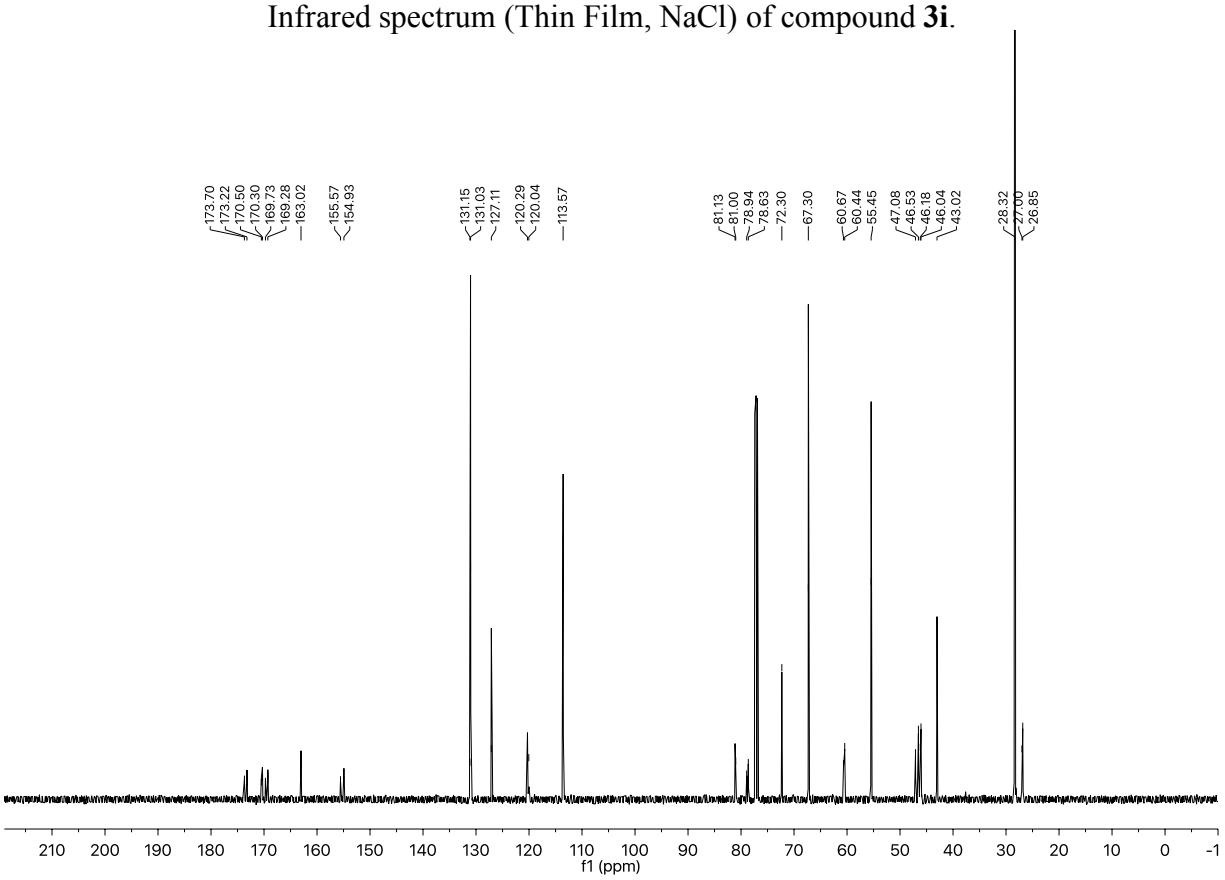
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3h**.



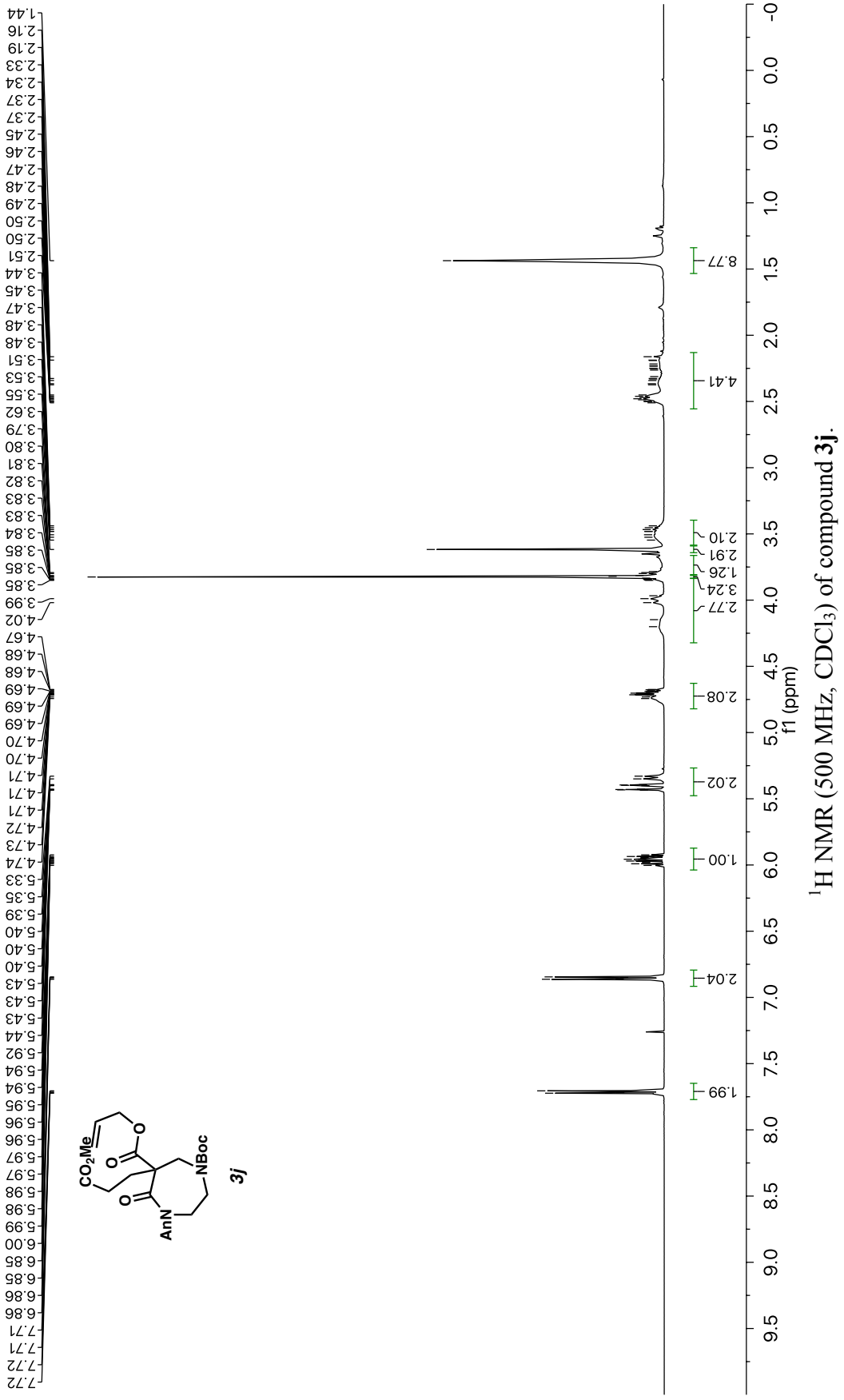
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3i**.



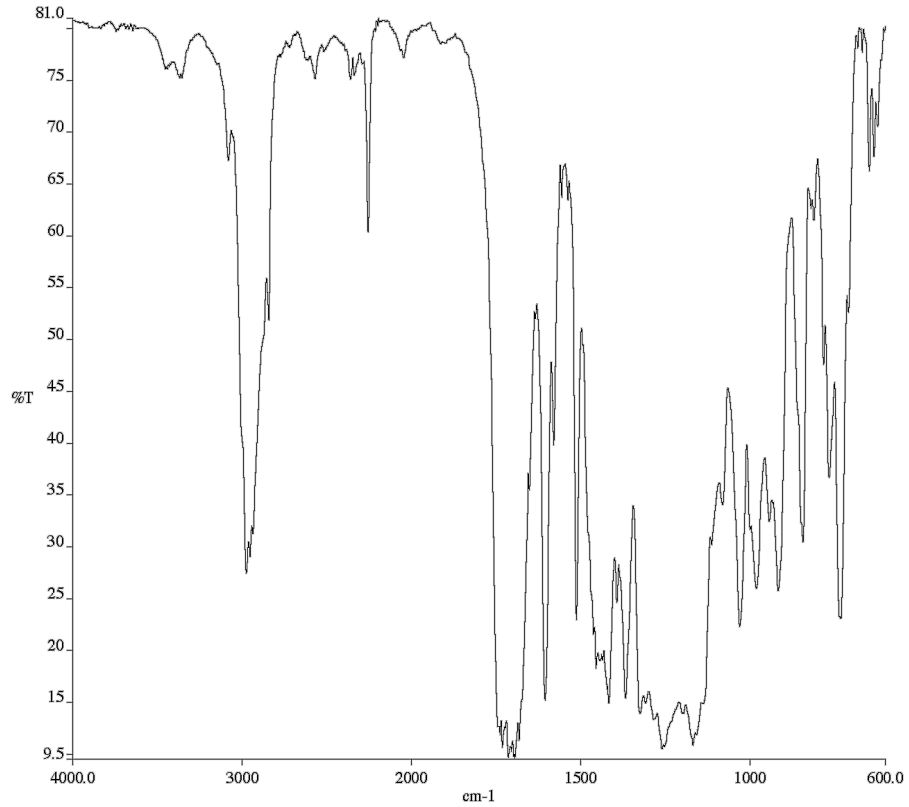
Infrared spectrum (Thin Film, NaCl) of compound **3i**.



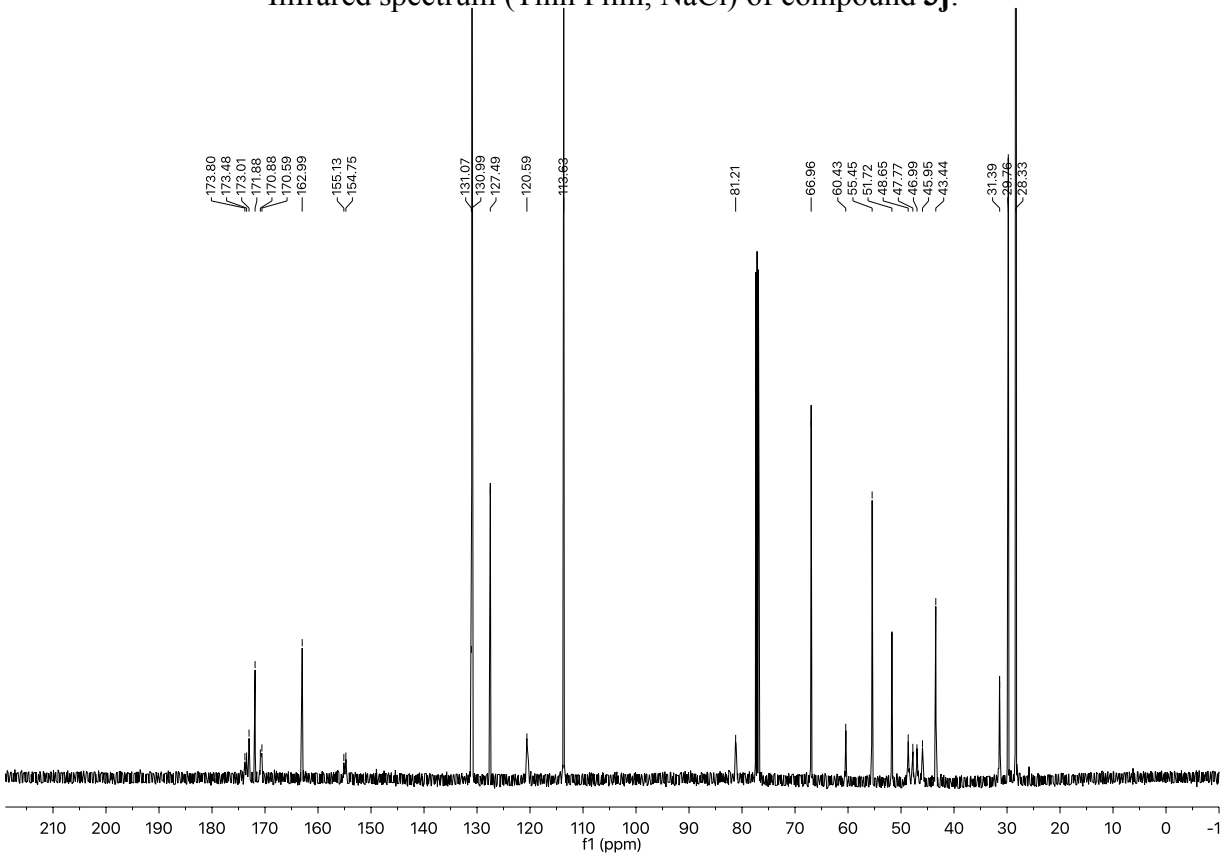
^{13}C NMR (125 MHz, $CDCl_3$) of compound **3i**.



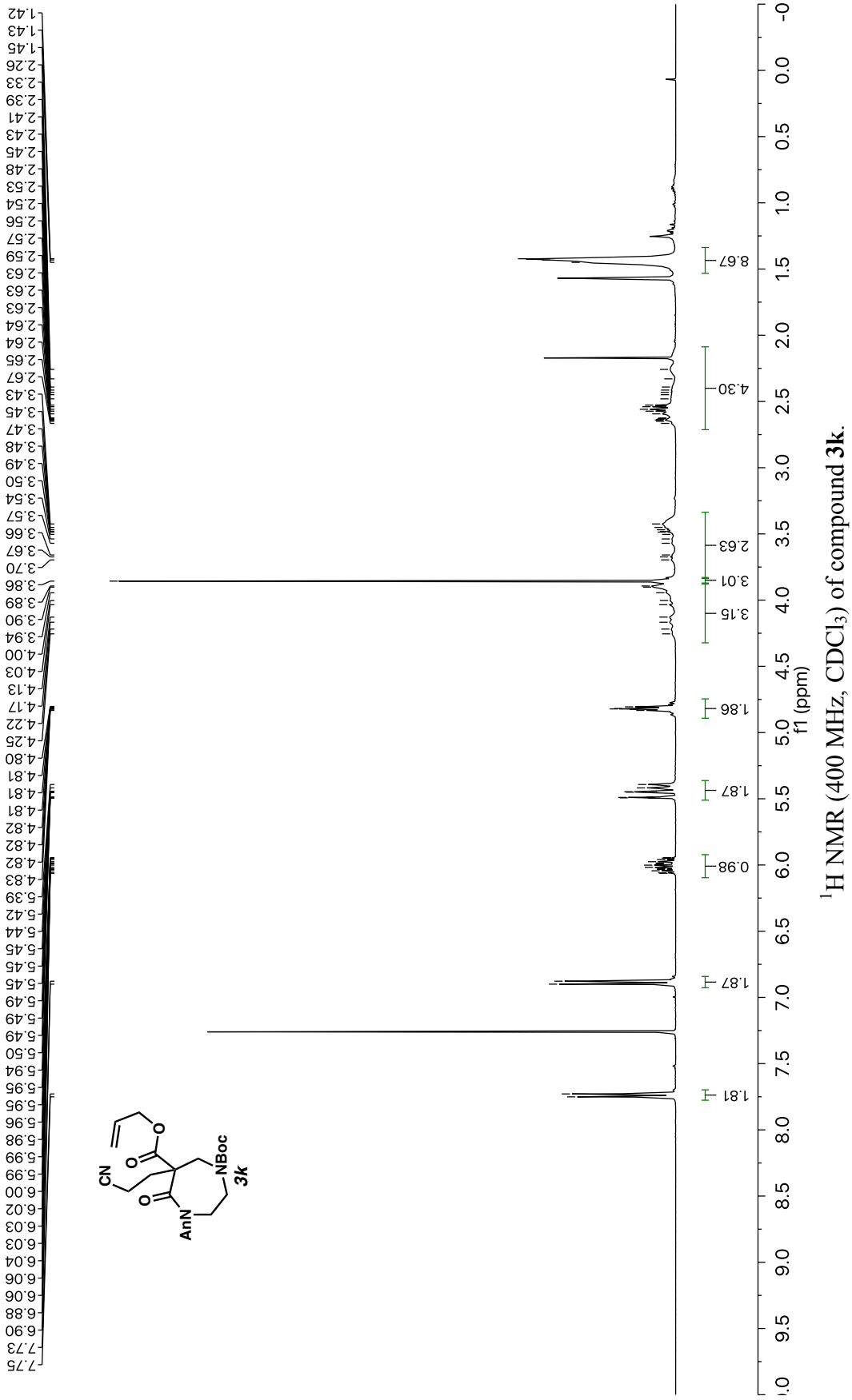
^{1}H NMR (500 MHz, $CDCl_3$) of compound **3j**.



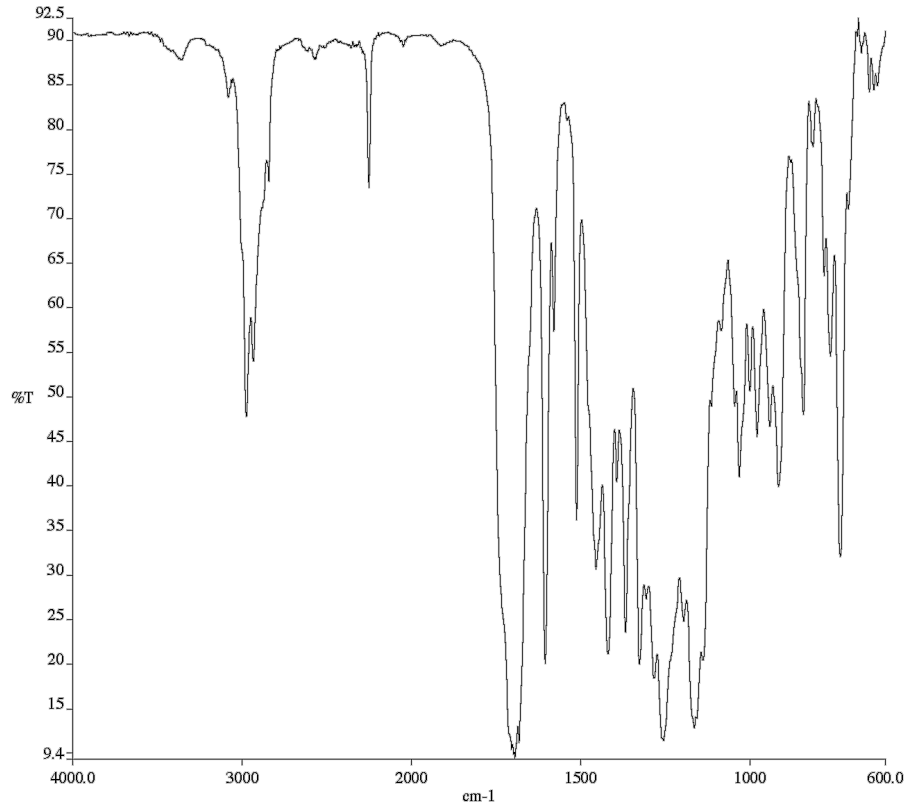
Infrared spectrum (Thin Film, NaCl) of compound **3j**.



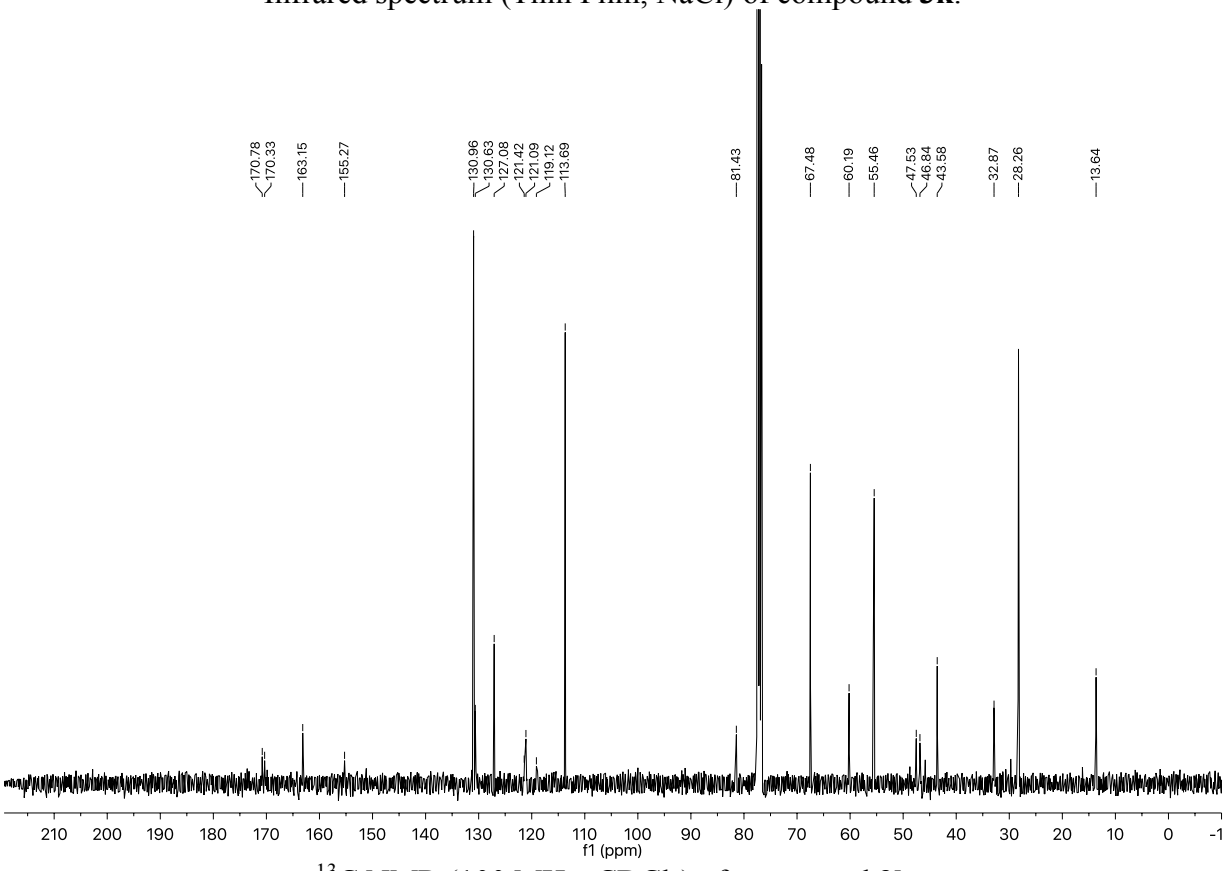
^{13}C NMR (125 MHz, $CDCl_3$) of compound **3j**.



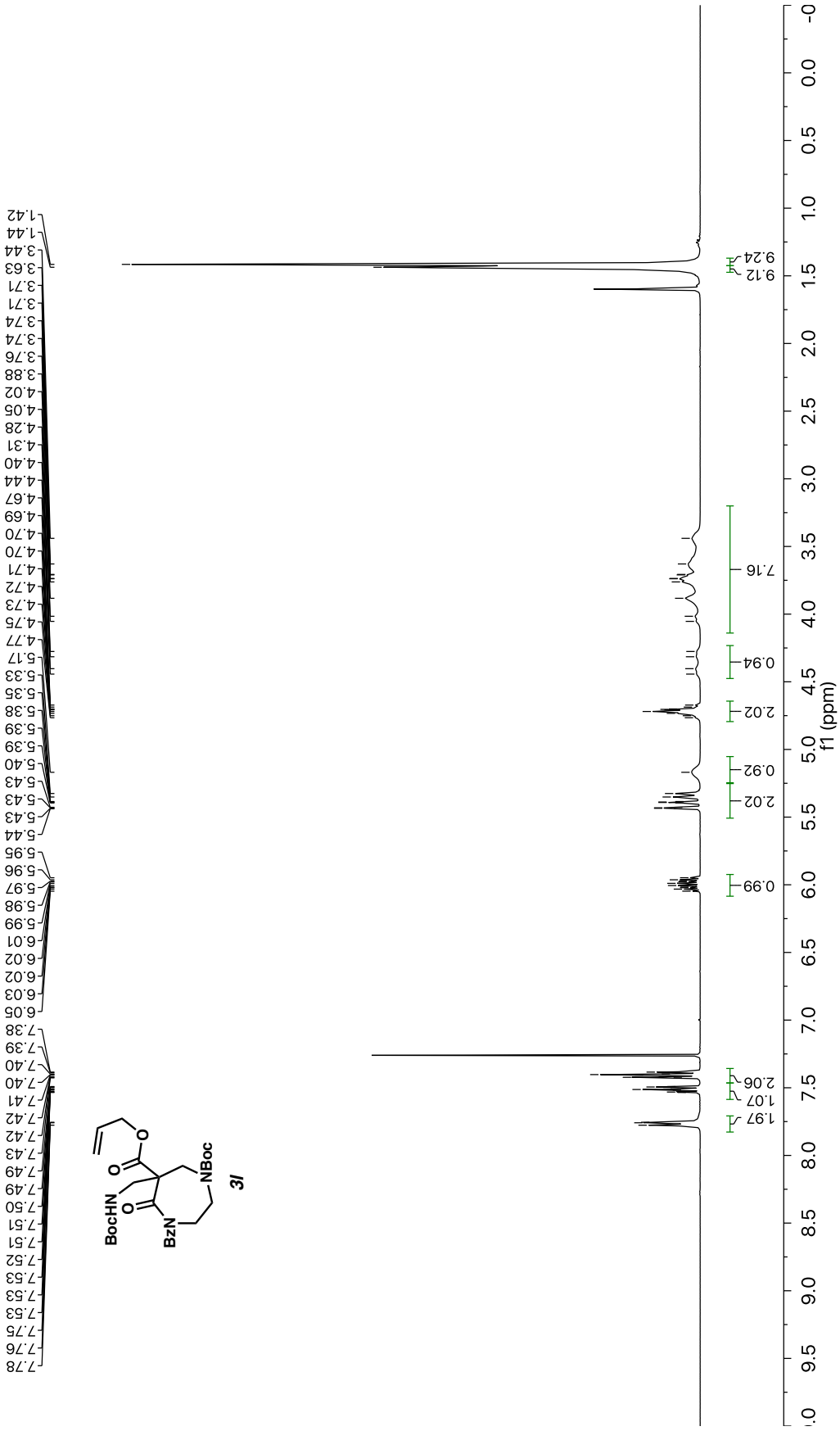
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3k**.



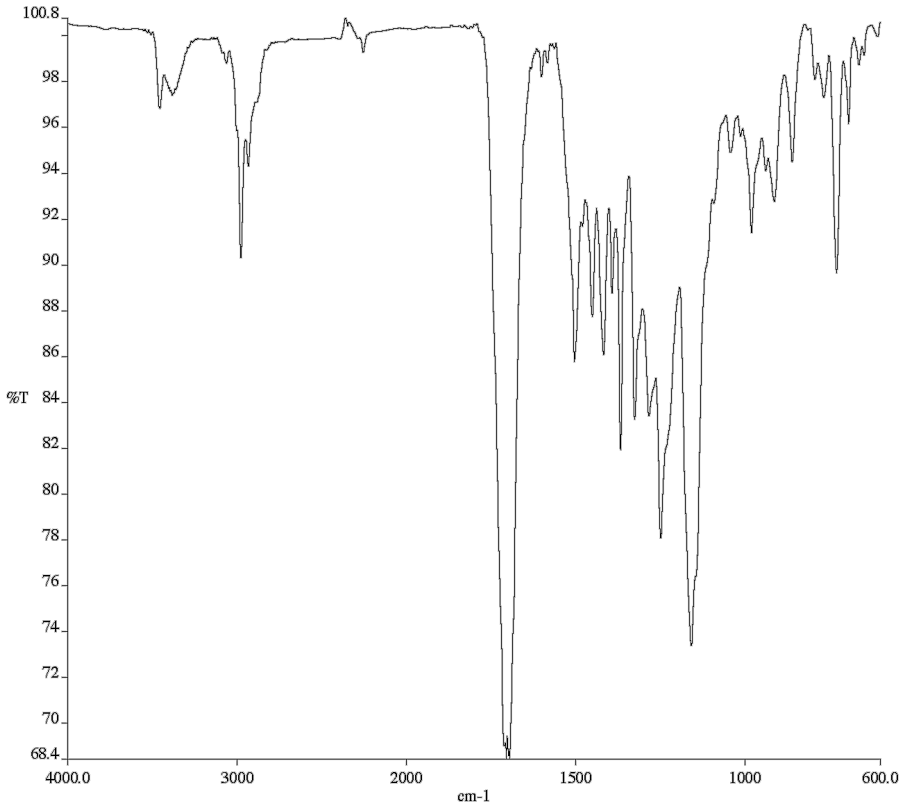
Infrared spectrum (Thin Film, NaCl) of compound **3k**.



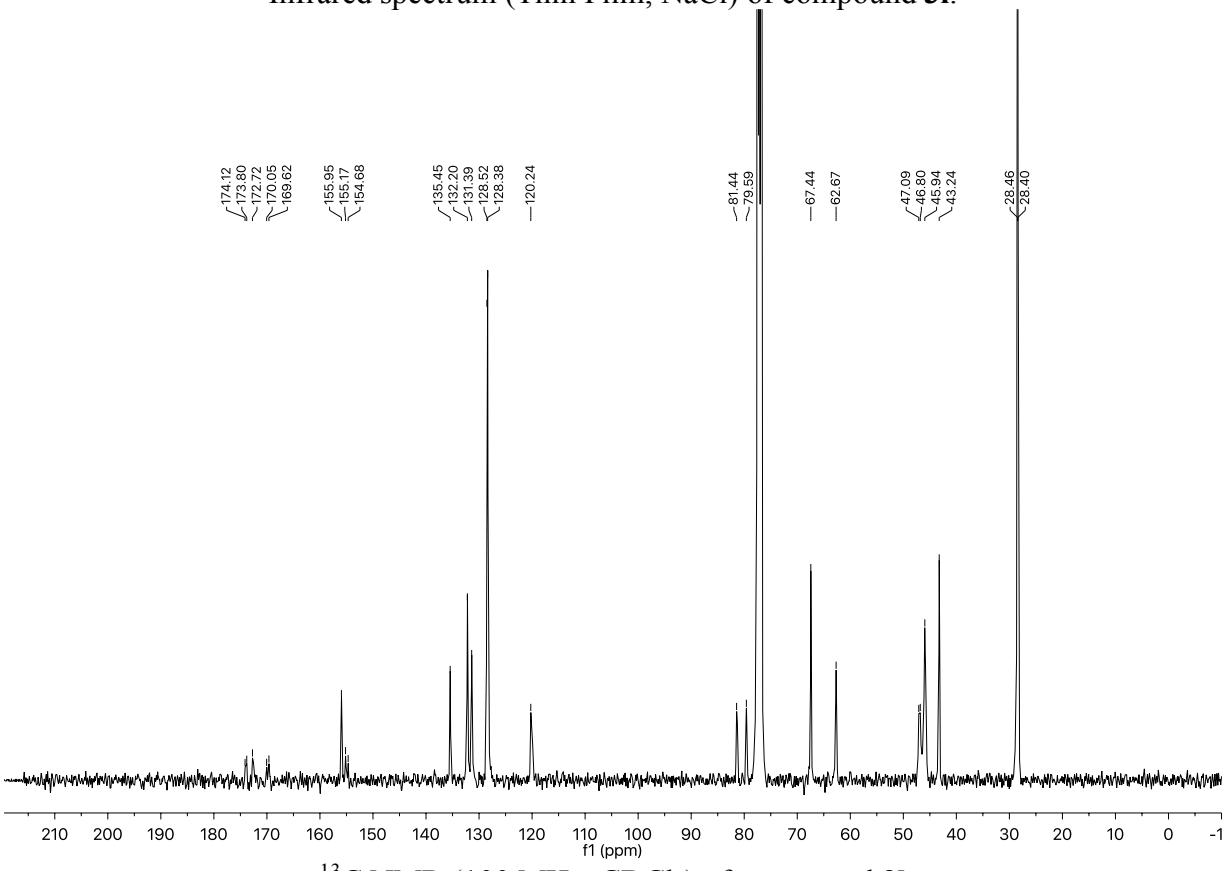
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3k**.



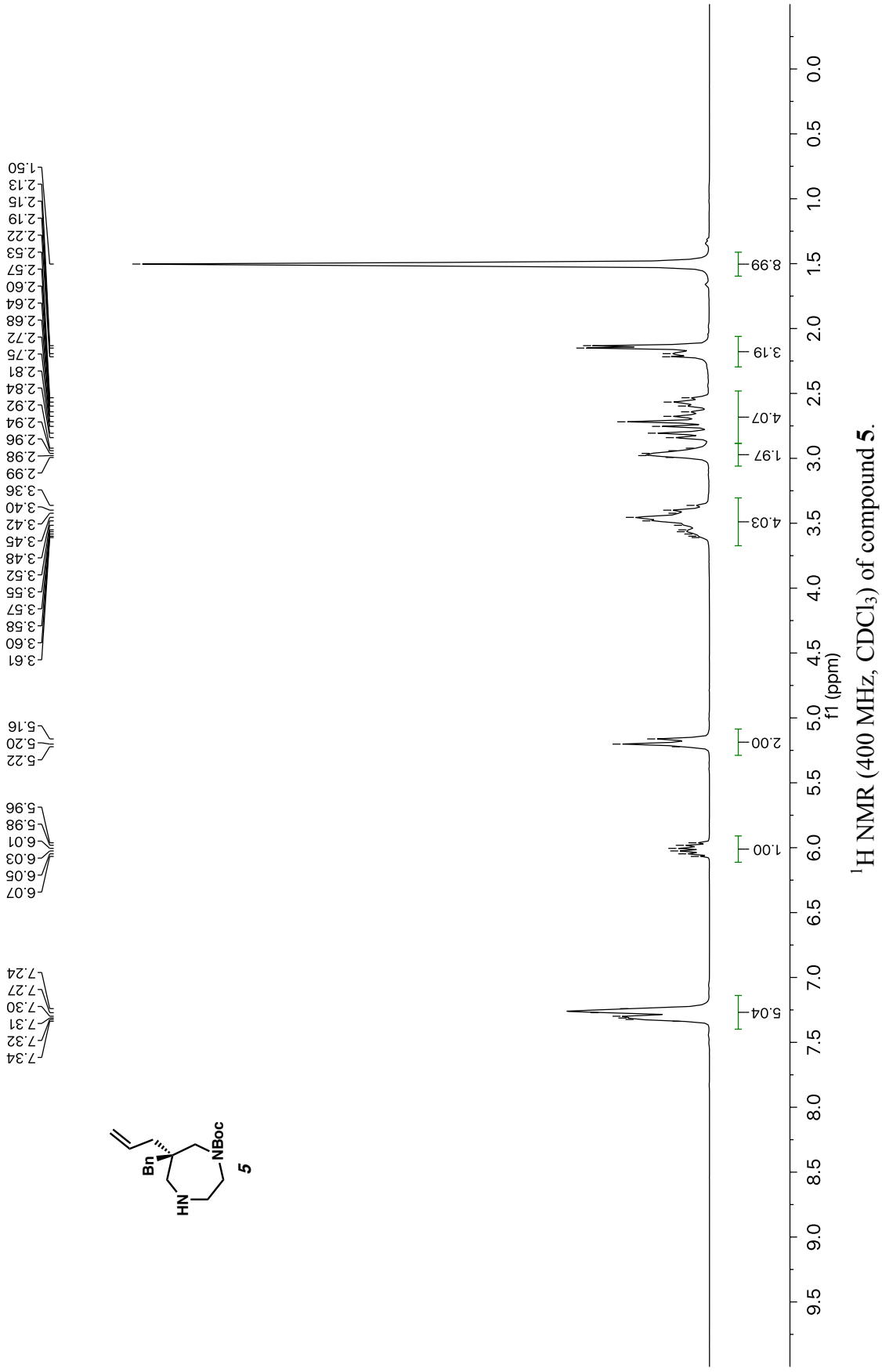
^{1}H NMR (400 MHz, $CDCl_3$) of compound **3l**.



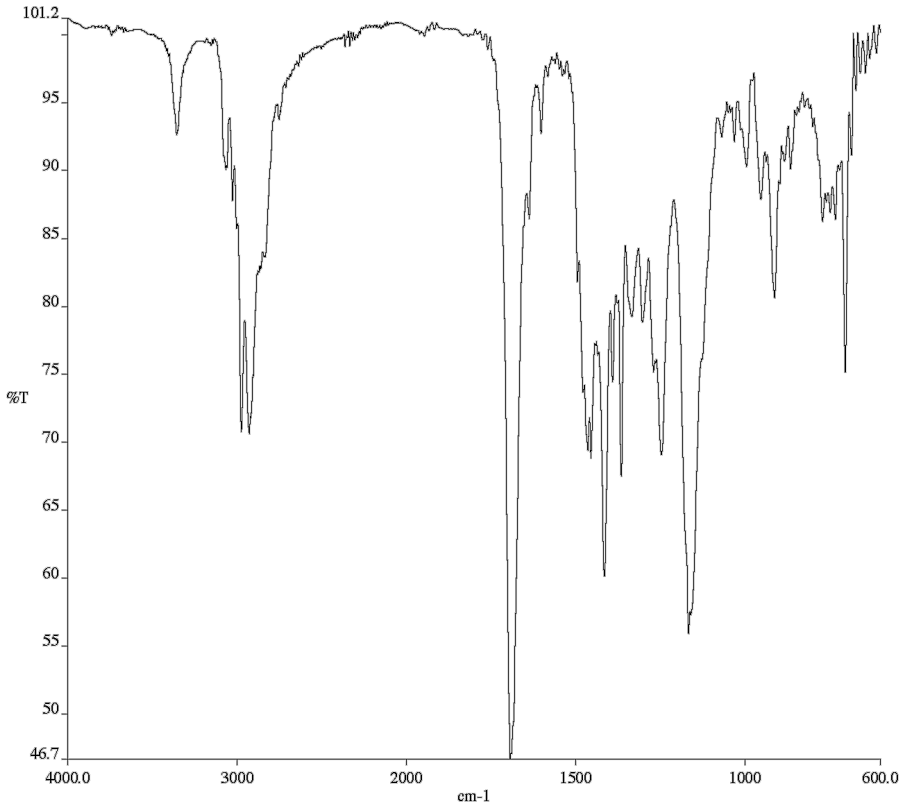
Infrared spectrum (Thin Film, NaCl) of compound **3l**.



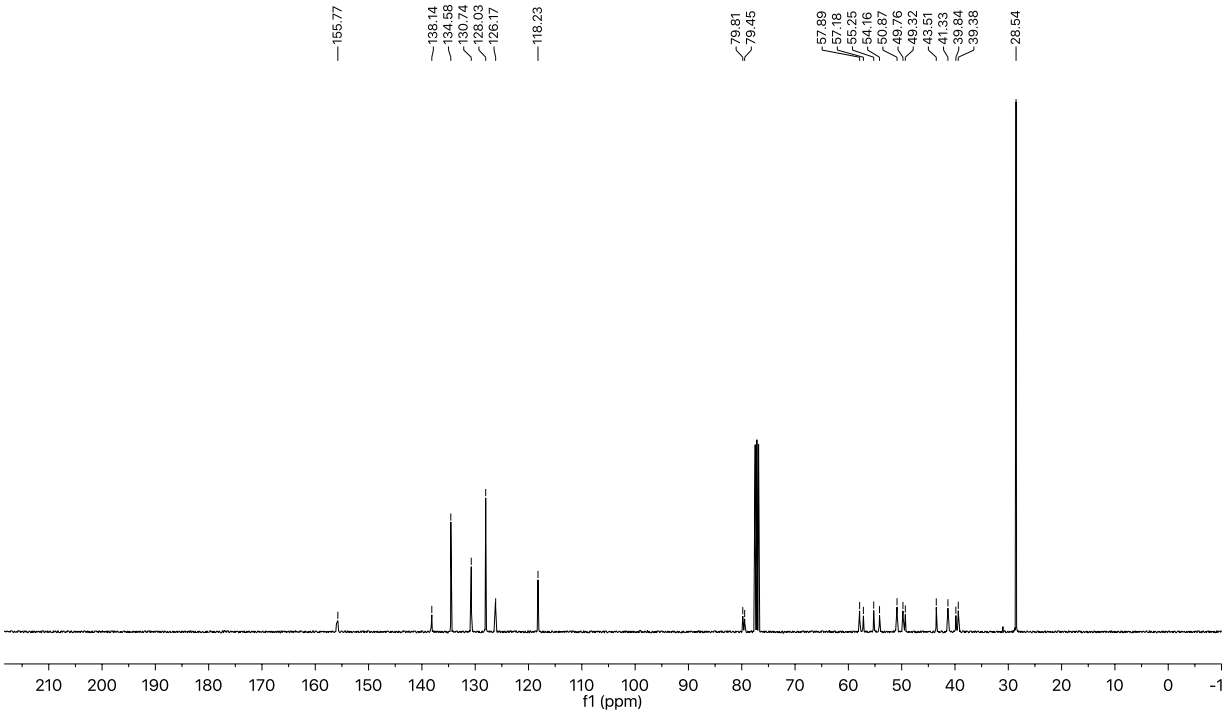
^{13}C NMR (100 MHz, $CDCl_3$) of compound **3l**.



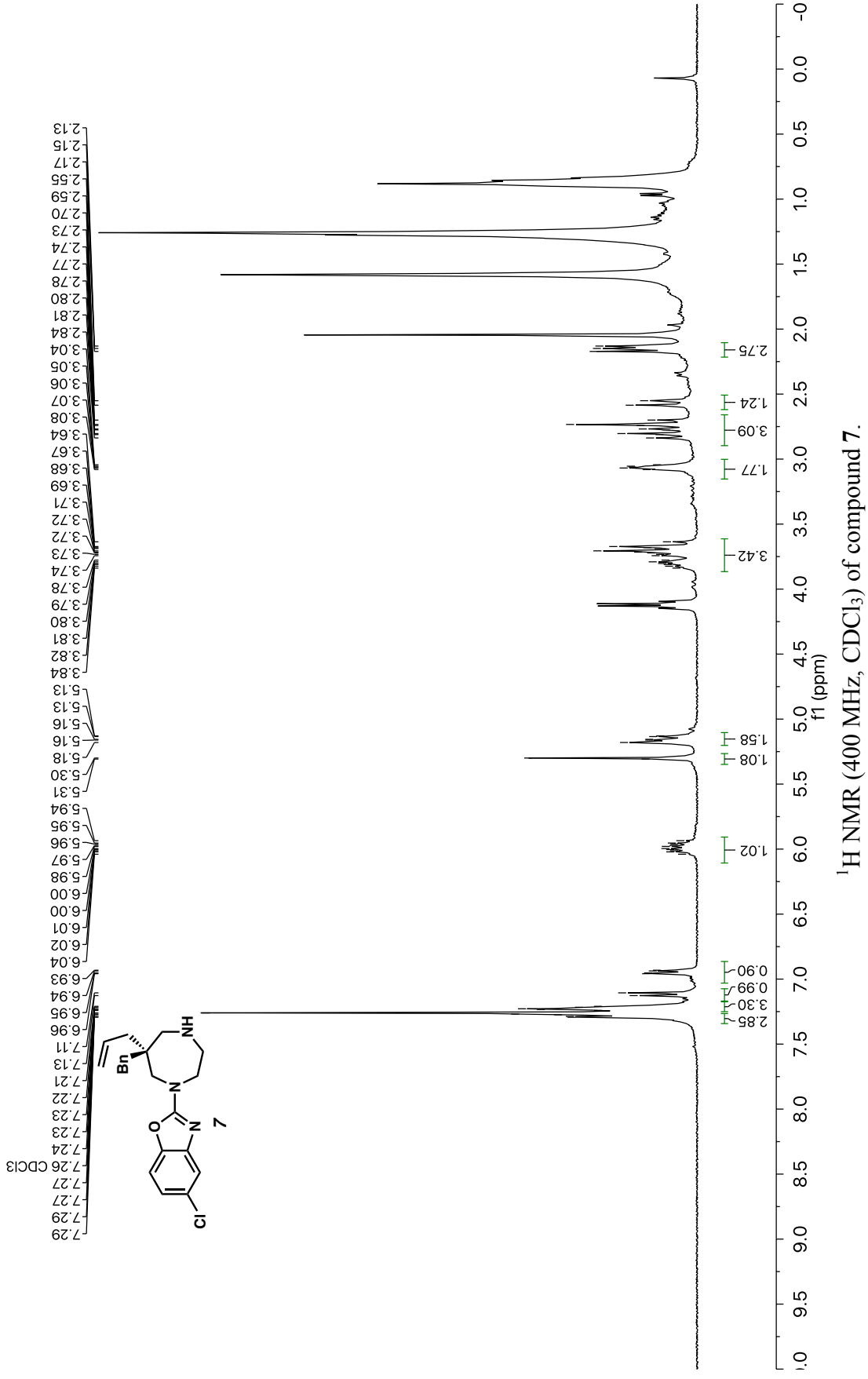
^{1}H NMR (400 MHz, $CDCl_3$) of compound **5**.



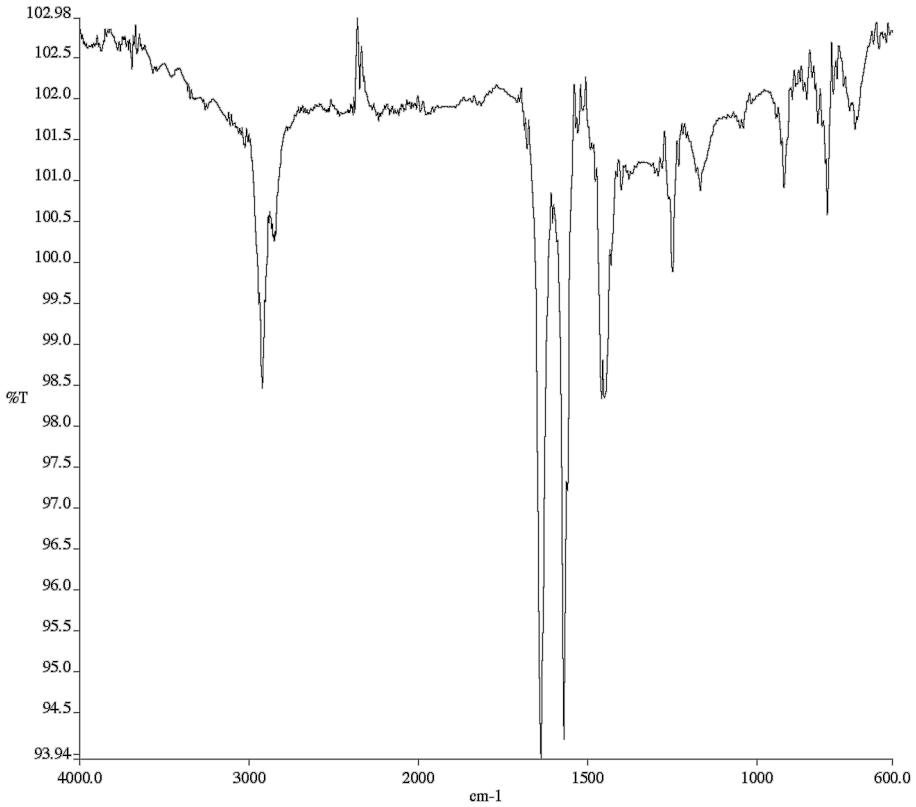
Infrared spectrum (Thin Film, NaCl) of compound **5**.



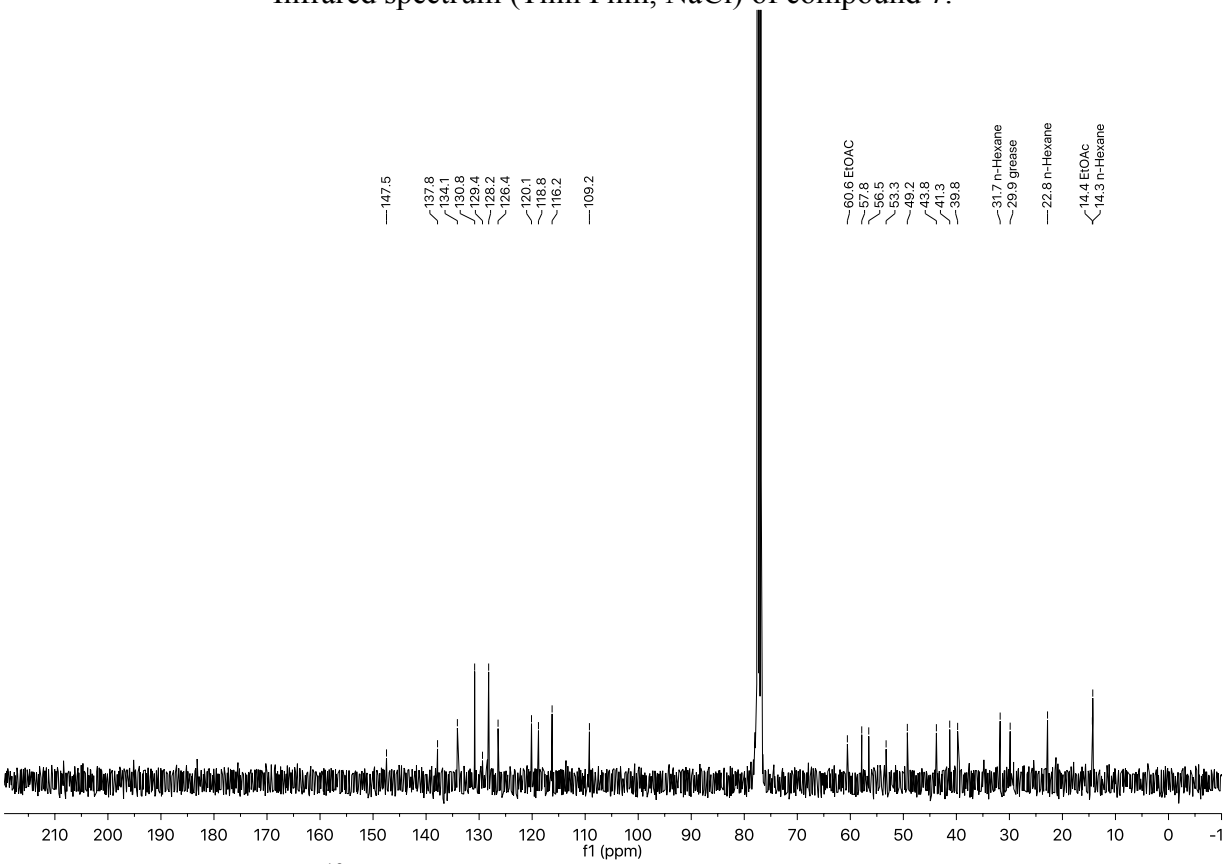
^{13}C NMR (100 MHz, $CDCl_3$) of compound **5**.



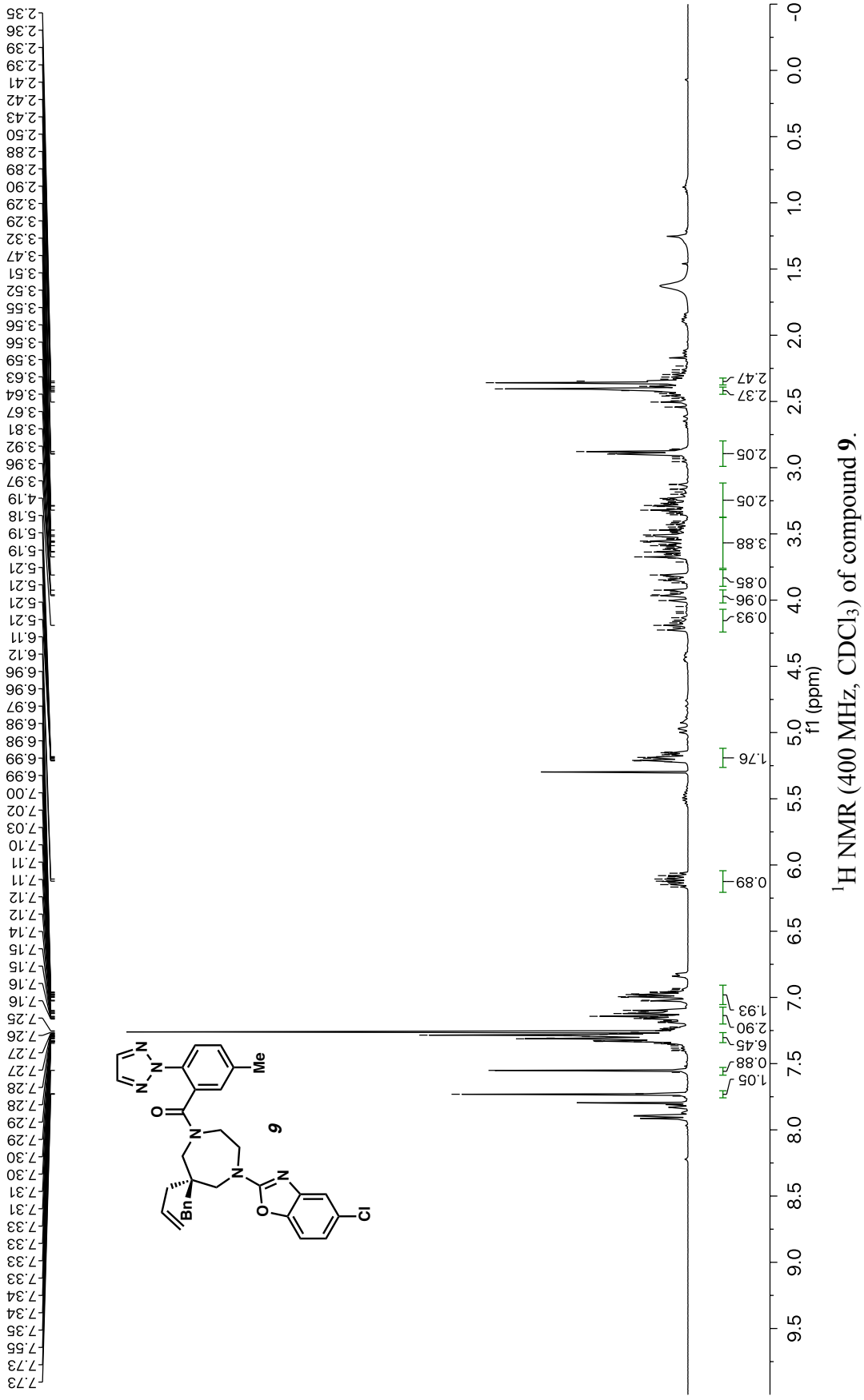
^{1}H NMR (400 MHz, $CDCl_3$) of compound **7**.



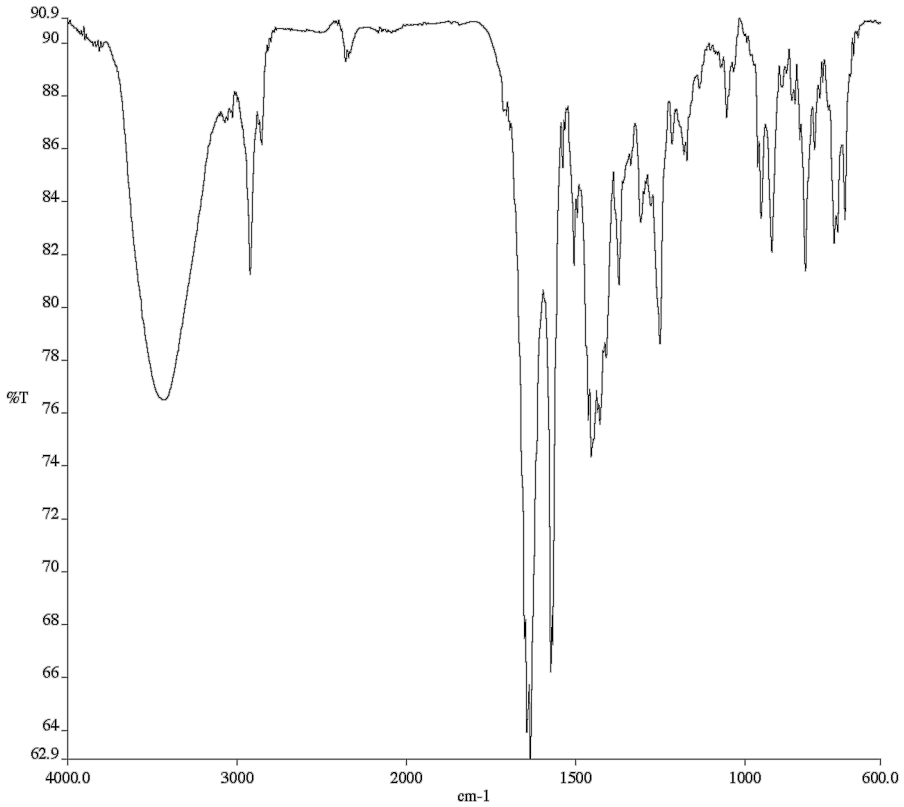
Infrared spectrum (Thin Film, NaCl) of compound **7**.



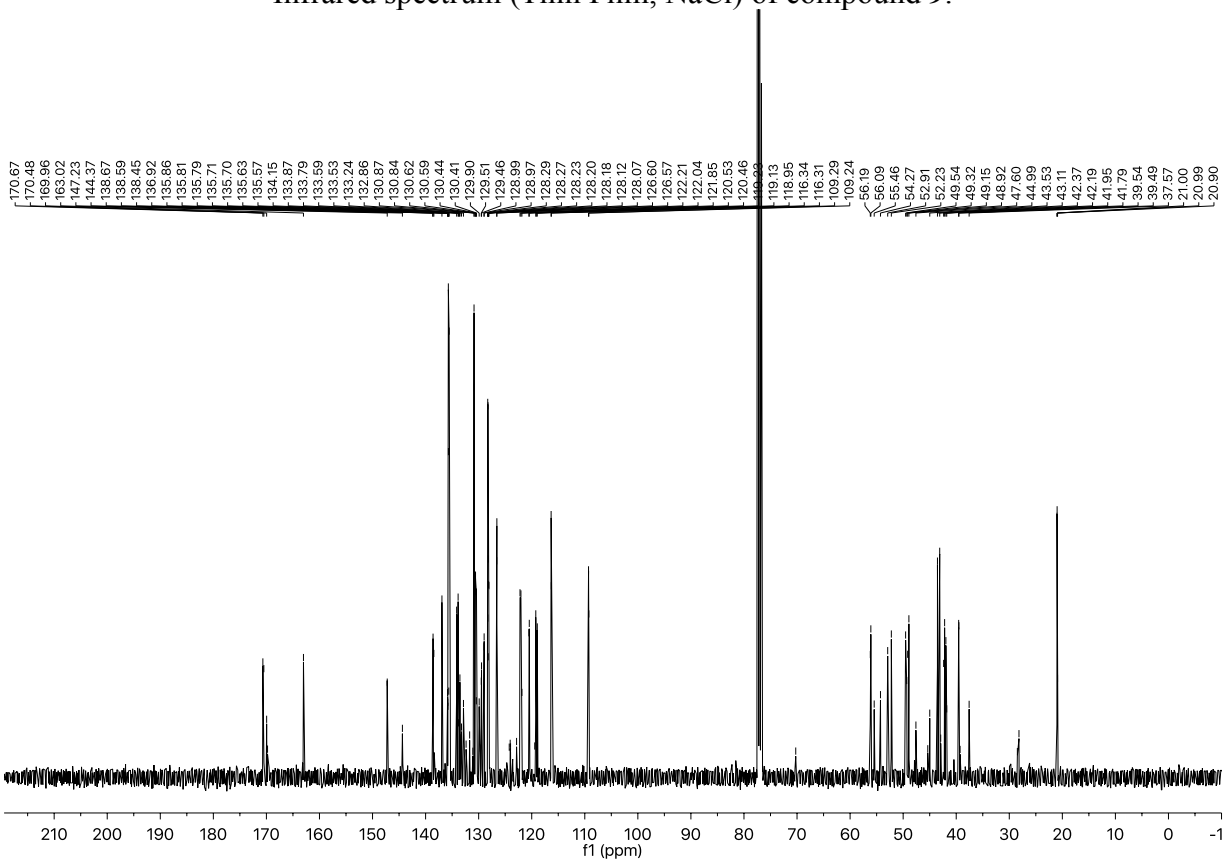
^{13}C NMR (100 MHz, $CDCl_3$) of compound **7**.



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

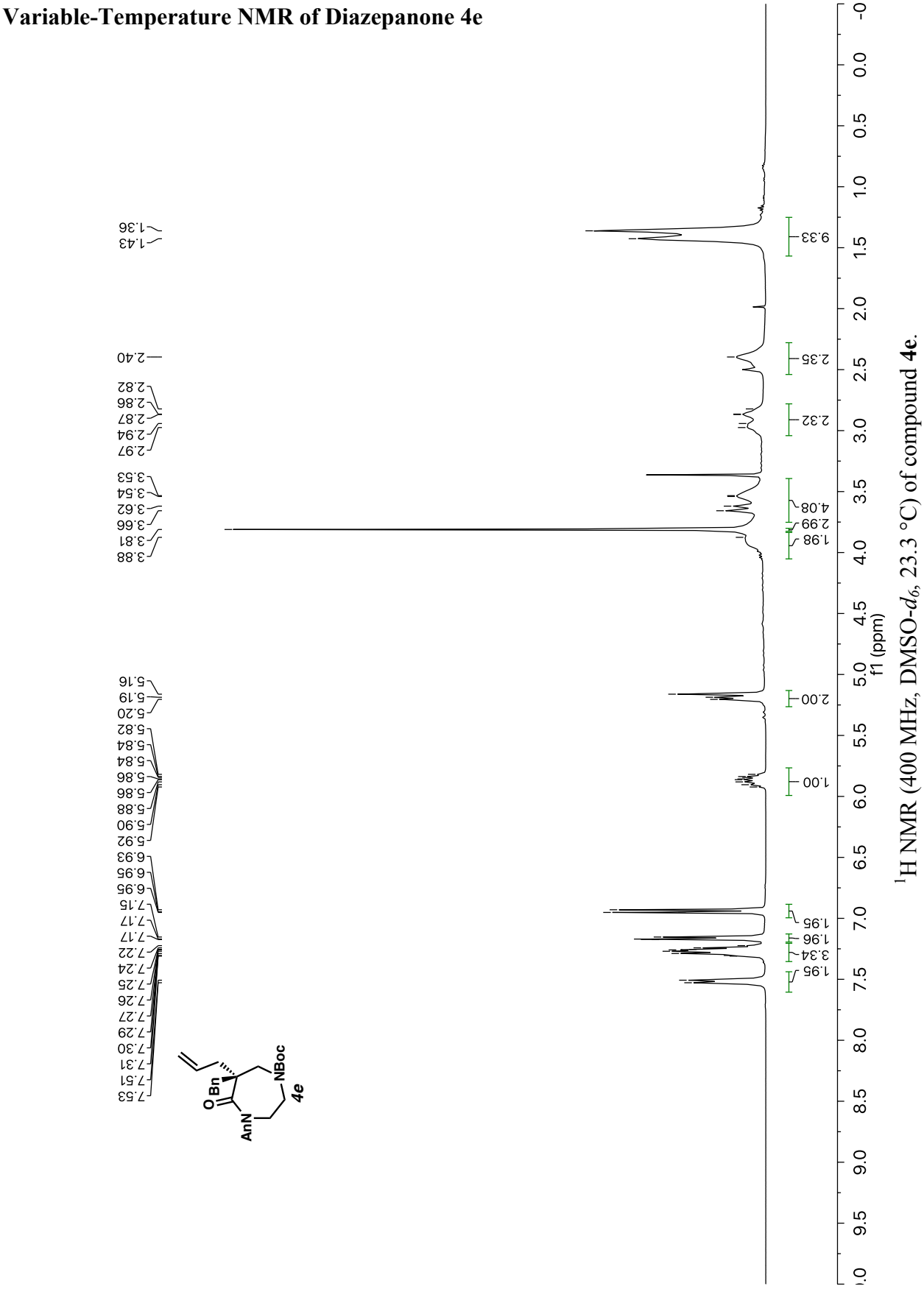


Infrared spectrum (Thin Film, NaCl) of compound **9**.

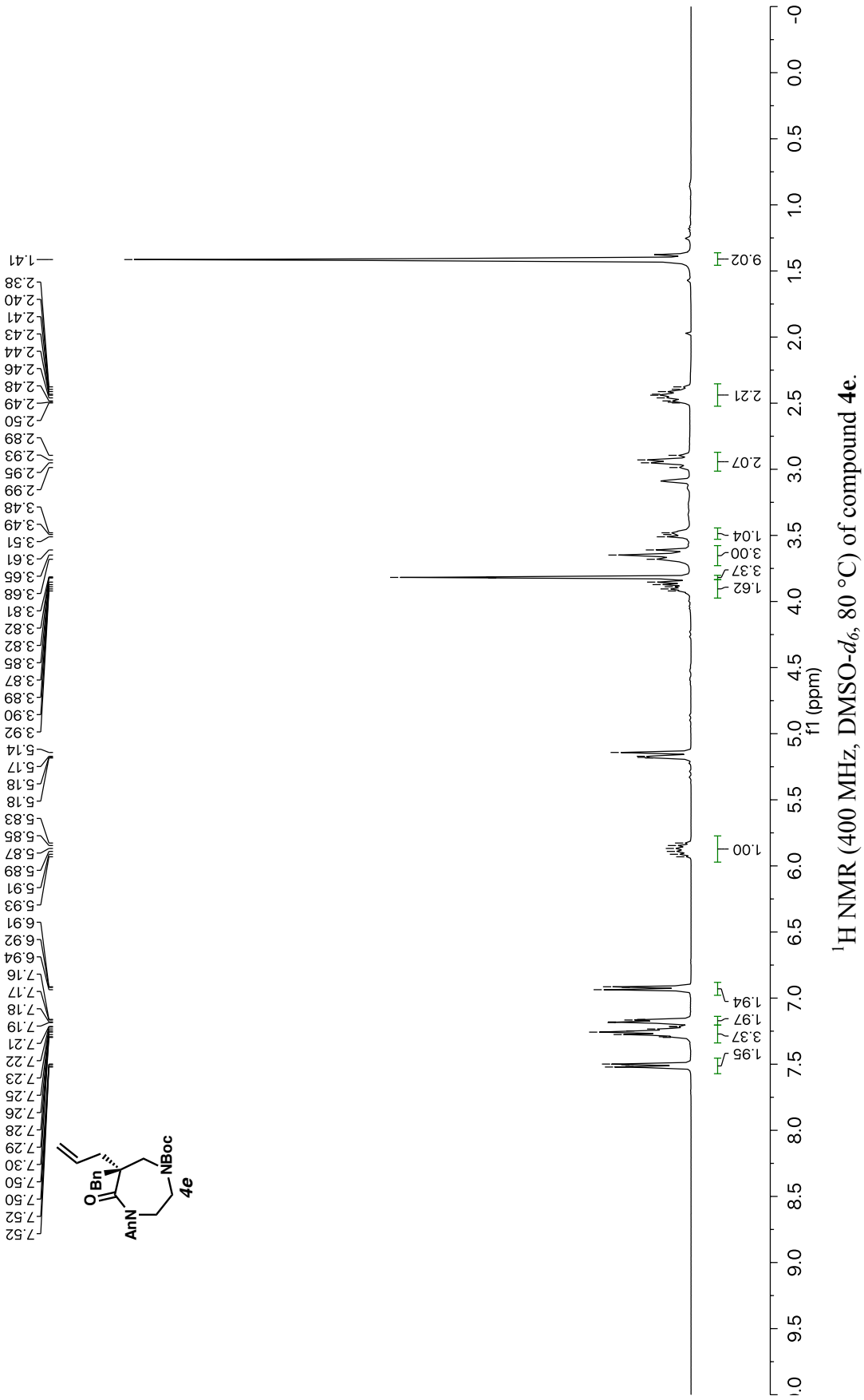


^{13}C NMR (100 MHz, $CDCl_3$) of compound **9**.

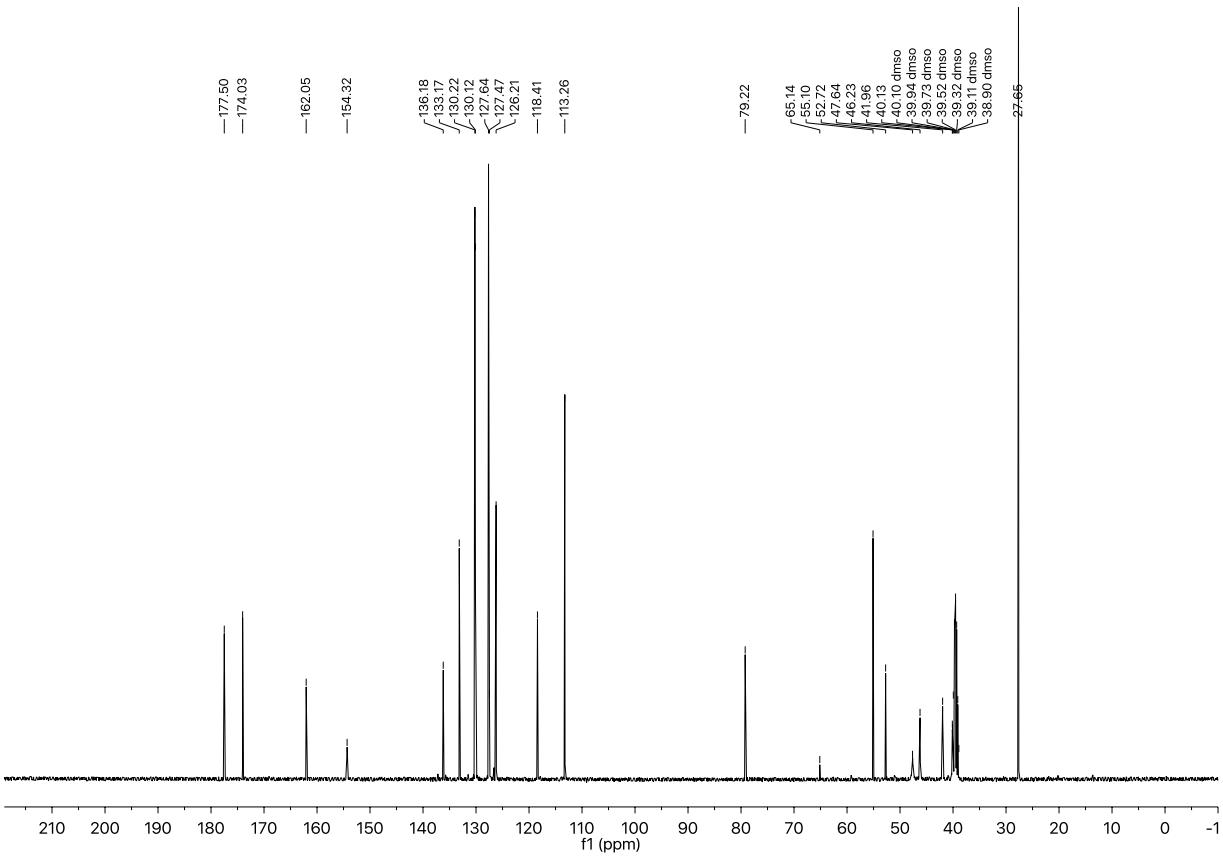
Variable-Temperature NMR of Diazepanone 4e



^{1}H NMR (400 MHz, DMSO-d_6, 23.3 °C) of compound **4e**.



^{1}H NMR (400 MHz, DMSO-d_6, 80 °C) of compound **4e**.



^{13}C NMR (100 MHz, DMSO-d_6, 80 °C) of compound **4e**.