Electronic Supplementary Material (ESI) for Chemical Communications.

Supplementary Information

$Cu(OTf)_2$ Catalyzed Ugi-type Reaction of *N,O*-Acetals with Isocyanides for Synthesis of Pyrrolidinyl and Piperidinyl 2-Carboxamides

Zhuo-Ya Mao,[a] Xiao-Di Nie,[a] Yi-Man Feng,[a] Chang-Mei Si,[a] Bang-Guo Wei*[a] and Guo-Qiang Lin [b]

[a]*School of Pharmacy and Institutes of Biomedical Sciences, Fudan University, 826 Zhangheng Road, Shanghai, 201203, China.*

[b]*Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Lingling Road, Shanghai 200032, China.*

Table of Contents

Mechanism Study:

The “inside attack” model and electronic effects have been proposed to explain the stereoselective reactions of nucleophiles with five-membered-ring oxocarbenium ions (Figure S1a). The “inside attack” model was used to explain the direction of the nuclear attack. The preferred conformation of a five-membered-ring oxocarbenium ion is an envelope conformation where the $C{=}O^{+}$ unit resides in the flattened portion of the envelope. Approach of the nucleophile onto the cation can occur from either side. Attack from “inside” the cation forms the all-staggered conformer. Attack from “outside” results in a conformer that suffers from eclipsed interactions. Because the staggered product is lower in energy than the eclipsed product, attack from “inside” the envelope should be favored. The electronic effect was used to explain the stability of the two conformations. When the C-4 alkoxy group in a pseudoaxial orientation, the electrostatic effect can be maximized to stabilize the conformation, placing the partially negatively charged substituent in closest proximity to the cationic carbon of the oxocarbenium ion. On the contrary, due to the lack of electrostatic effect, the conformation with C-4 aryl group in the equatorial orientation is more stable.

In order to verify the applicability of these model in five-membered-ring iminium ion, 4-Ar-*N,O*-acetal was carry out under standard conditions and 2,4-*trans* product was obtained in 84% yield with 92:8 diastereoselectivity as expected. This result in good agreement with the theoretical model. Therefore, the theoretical model for oxocarbenium ions is also applicable to iminium ion (Figure S1b).

Stereoselective for $Cu(OTf)_2$ catalyzed Ugi-type reaction of *N,O*-acetals with isocyanides can be explained by the “inside attack” model and electronic effect (Figure S1c). When the C-4 alkoxy group in a pseudoaxial orientation, the electrostatic effect can be maximized to stabilize the conformation. Although there is an syn-butanol interaction when attacking from the “inside”, but this interaction is considerably smaller than a syn-pentane interaction, so it is not destabilizing enough to hinder attack from this trajectory to generated the 2,4-*cis* product. When the C-4 alkoxy group is replaced by C-4 aryl group, the electrostatic effect disappears, so the C-4 aryl group will be more

stable in the equatorial orientation. Meanwhile, a C-4 aryl group would experience a syn-pentane interaction upon attack of the C-4 axial conformer, so attack occurs on the analogous equatorial cation, leading to the 2,4-*trans* product.

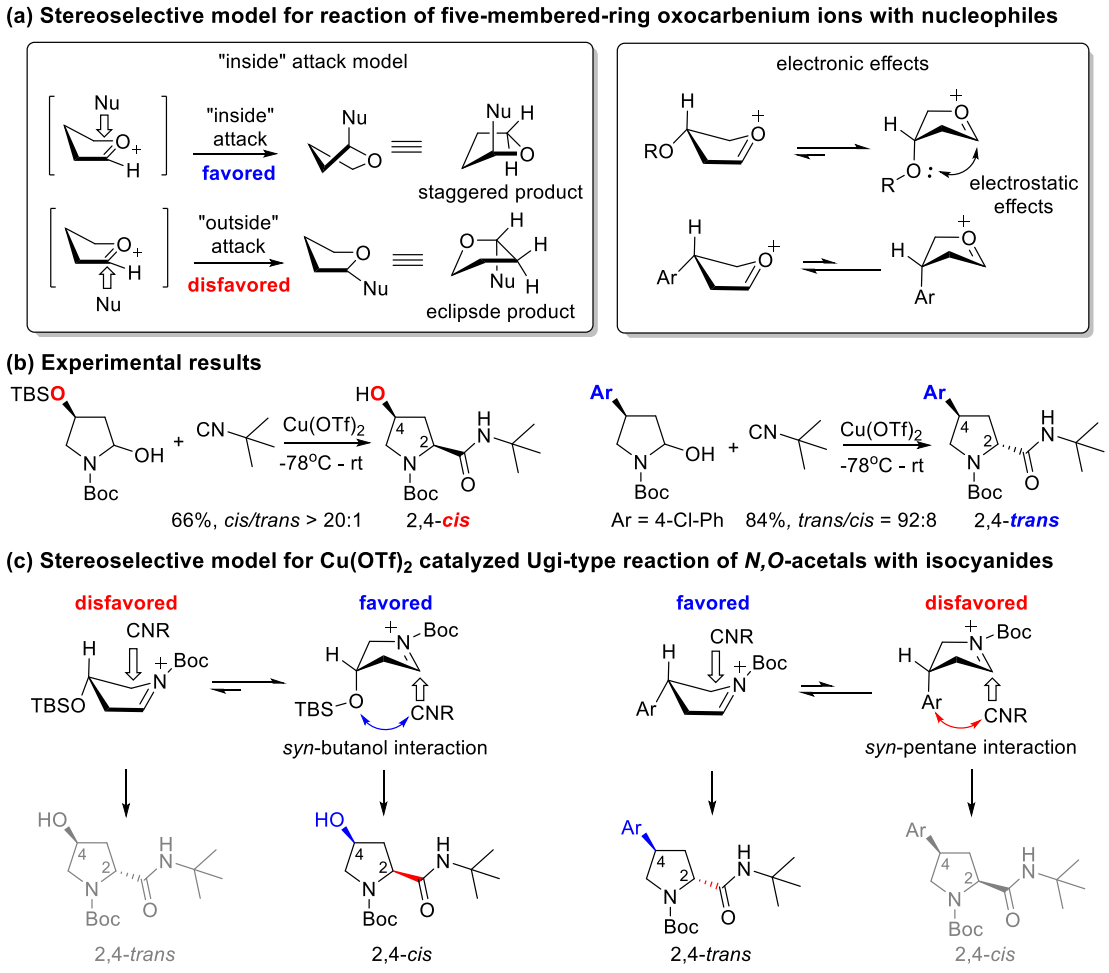


Figure S1. (a) Stereoselective model for reaction of five-membered-ring oxocarbenium ions with nucleophiles; (b) Experimental results; (c) Stereoselective model for $Cu(OTf)_2$ catalyzed Ugi-type reaction of *N,O*-acetals with isocyanides

General: Reactions were monitored by thin layer chromatography (TLC) on glass plates coated with silica gel with fluorescent indicator. Flash chromatography was performed on silica gel (300–400) with petroleum/EtOAc as eluent. Optical rotations were measured on a polarimeter with a sodium lamp. HRMS were measured on a LTQ-Orbitrap-XL apparatus. IR spectra were recorded using film on a Fourier Transform Infrared Spectrometer. NMR spectra were recorded at 400 MHz, and chemical shifts are reported in δ (ppm) referenced to an internal CD_3OD (3.31) standard for ^1H NMR and CD_3OD (49.00) for ^{13}C NMR.

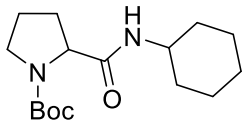
General Procedure A: Synthesis of 4

To a solution of imide (2 mmol) in MeOH (5 mL) was added $NaBH_4$ (3.0 equiv, 227 mg) at 0 °C in one portion. The reaction mixture was stirred for 1 h at the same temperature, and the reaction was quenched with saturated aqueous $NaHCO_3$ (5 mL) and warmed to room temperature. The mixture was extracted with DCM (20 mL × 3), and the combined organic layers were washed with brine. Dried, fifiltered , and concentrated to give the *N,O*-acetal **4** without further purifications.

General Procedure B: Synthesis of 6

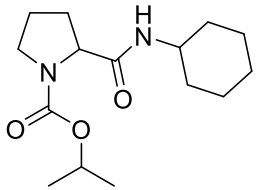
N,O-acetal **4** (1.0 mmol), isocyanides **3** (1.0 mmol) were dissolved in THF (5 mL) at room temperature, then $Cu(OTf)_2$ (0.2 mmol) was added. The reaction was stirred at room temperature overnight then quenched with a saturated $NaHCO_3$ aqueous solution and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine, dried, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA = 2:1 - 1:1) to give the desired product **6**.

***tert*-Butyl 2-(cyclohexylcarbamoyl)pyrrolidine-1-carboxylate (6a)**



Eluent: PE/EA = 2:1, White Solid (247 mg, 84%); mp 149-150 °C; IR (film): ν_{max} 2934, 2419, 1699, 1640, 1451, 1401, 1363, 1161, 1116. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.17-4.06 (m, 1H), 3.68-3.59 (m, 1H), 3.54-3.47 (m, 1H), 3.44-3.36 (m, 1H), 2.26-2.10 (m, 1H), 1.95-1.73 (m, 7H), 1.67-1.60 (m, 1H), 1.46 (s, 2.5H), 1.42 (s, 6.5H), 1.38-1.17 (m, 5H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.7, 174.3, 156.4, 156.1, 81.3, 81.2, 61.7, 61.5, 49.8, 48.0, 33.9, 33.8, 32.8, 31.6, 28.7, 26.6, 26.2, 25.4, 24.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{28}N_2O_3Na^+$: 319.1992, found: 319.1993.

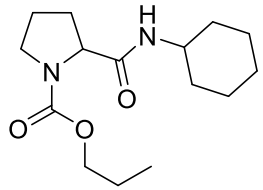
Isopropyl 2-(cyclohexylcarbamoyl)pyrrolidine-1-carboxylate (6b)



Eluent: PE/EA = 2:1, White Solid (260 mg, 92%); mp 120-121 °C; IR (film): ν_{max} 2932, 2480, 2426, 1705, 1650, 1449, 1411, 1385, 1115,^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.87-4.83 (m, 1H), 4.20-4.14 (m, 1H), 3.68-3.59 (m, 1H), 3.57-3.50 (m, 1H), 3.48-3.41 (m, 1H), 2.28-2.13 (m, 1H), 1.96-1.73 (m, 7H), 1.67-1.60 (m, 1H), 1.41-1.31 (m, 2H), 1.29-1.17 (m, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.5, 174.1, 156.8, 156.4, 70.2, 61.8, 61.5, 49.8, 48.3, 48.0, 33.9, 33.7, 32.7, 31.7, 26.7, 26.2, 25.4, 24.7, 22.6, 22.5 ppm;

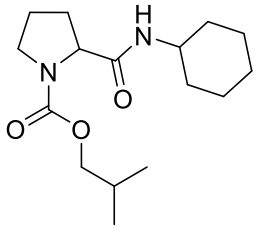
HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{26}N_2O_3Na^+$: 305.1836, found: 305.1834.

Propyl 2-(cyclohexylcarbamoyl)pyrrolidine-1-carboxylate (6c)



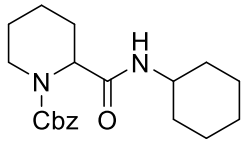
Eluent: PE/EA = 2:1, White Solid (246 mg, 87%); mp 110-111 ºC; IR (film): ν_{max} 2933, 2421, 1703, 1645, 1446, 1425, 1365, 1120. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.21-4.16 (m, 1H), 4.06-3.92 (m, 2H), 3.67-3.59 (m, 1H), 3.58-3.51 (m, 1H), 3.50-3.43 (m, 1H), 2.27-2.13 (m, 1H), 2.00-1.73 (m, 7H), 1.69-1.56 (m, 3H), 1.37-1.16 (m, 5H), 0.99-0.90 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.4, 174.1, 157.2, 156.9, 68.2, 61.8, 61.5, 49.7, 48.1, 33.8, 33.7, 32.8, 31.7, 26.7, 26.2, 25.4, 24.6, 23.5, 10.9, 10.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{26}N_2O_3Na^+$: 305.1836, found: 305.1835.

Isobutyl 2-(cyclohexylcarbamoyl)pyrrolidine-1-carboxylate (6d)



Eluent: PE/EA = 2:1, White Solid (255 mg, 86%); mp 123-125 ºC; IR (film): ν_{max} 2932, 2855, 1708, 1646, 1449, 1420, 1385, 1359, 1121. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.22-4.16 (m, 1H), 3.89-3.75 (m, 2H), 3.66-3.58 (m, 1H), 3.57-3.51 (m, 1H), 3.50-3.44 (m, 1H), 2.29-2.14 (m, 1H), 1.97-1.72 (m, 8H), 1.68-1.60 (m, 1H), 1.38-1.14 (m, 5H), 0.98-0.89 (m, 6H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.3, 174.0, 157.1, 156.8, 72.7, 61.8, 61.4, 49.8, 48.4, 33.7, 32.9, 31.6, 29.3, 26.6, 26.1, 25.3, 24.6, 19.4 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{28}N_2O_3Na^+$: 319.1992, found: 319.1998.

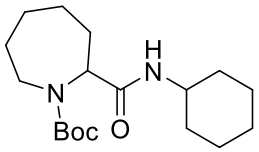
Benzyl 2-(cyclohexylcarbamoyl)piperidine-1-carboxylate (6e)



Eluent: PE/EA = 2:1, White Solid (214 mg, 62%); mp 76-77 ºC; IR (film): ν_{max} 2930, 2854, 2360, 1699, 1645, 1416, 1254, 1169. ^{1}H NMR (400 MHz, CD_3OD) δ 7.40-7.25 (m, 5H), 5.19-5.14 (m, 1H), 5.13-5.02 (m, 1H), 4.71-4.65 (m, 1H), 4.05-3.98 (m, 1H), 3.70-3.57 (m, 1H), 3.25-3.15 (m, 1H), 2.19-2.01 (m, 1H), 1.83-1.58 (m, 8H), 1.45-1.28 (m, 4H), 1.26-1.10 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 172.8, 158.2, 138.0,

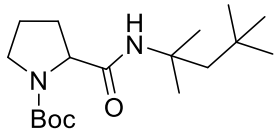
129.5, 129.1, 128.8, 68.4, 56.2, 49.9, 43.3, 33.7, 33.7, 28.5, 26.6, 25.7, 21.0 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{28}N_2O_3Na^+$: 367.1992, found: 367.1992.

***tert*-Butyl 2-(cyclohexylcarbamoyl)azepane-1-carboxylate (6f)**



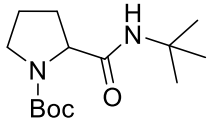
Eluent: PE/EA = 2:1, White Solid (123 mg, 38%); mp 118-120 °C; IR (film): ν_{max} 2928, 2854, 1695, 1647, 1448, 1407, 1365, 1163. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.36 (dd, *J* = 12.4, 6.0 Hz, 0.42H), 4.22 (dd, *J* = 12.4, 5.2 Hz, 0.58H), 3.96 (dd, *J* = 14.8, 4.8 Hz, 0.58H), 3.87-3.80 (m, 0.42H), 3.66-3.57 (m, 1H), 3.14-3.02 (m, 1H), 2.23-2.10 (m, 1H), 2.00-1.90 (m, 1H), 1.86-1.60 (m, 8H), 1.47 (s, 3.78H), 1.44 (s, 5.22H), 1.40-1.15 (m, 8H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.8, 174.3, 157.8, 157.4, 81.5, 81.2, 62.4, 60.5, 49.6, 49.6, 45.2, 44.8, 34.0, 33.8, 33.7, 33.5, 32.8, 32.2, 31.3, 30.9, 30.4, 30.3, 28.7, 27.8, 26.9, 26.6, 26.2, 26.0 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{32}N_2O_3Na^+$: 347.2305, found: 347.2305.

***tert*-Butyl 2-((2,4,4-trimethylpentan-2-yl)carbamoyl)pyrrolidine-1-carboxylate (6g)**



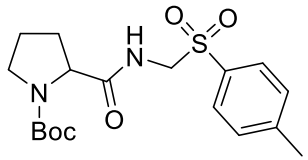
Eluent: PE/EA = 2:1, White Solid (239 mg, 73%); mp 67-68 °C; IR (film): ν_{max} 2955, 1702, 1679, 1396, 1366, 1165, 1120. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.15-4.09 (m, 1H), 3.50-3.36 (m, 2H), 2.25-2.07 (m, 1H), 1.97-1.76 (m, 4H), 1.70-1.55 (m, 1H), 1.46 (s, 9H), 1.42 (s, 3H), 1.38 (s, 3H), 1.01 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.1, 173.6, 156.5, 156.1, 81.3, 62.0, 56.2, 56.1, 52.3, 48.0, 32.4, 32.0, 30.6, 29.9, 29.6, 29.4, 28.8, 25.4, 24.5 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{34}N_2O_3Na^+$: 349.2462, found: 349.2458.

***tert*-Butyl 2-(tert-butylcarbamoyl)pyrrolidine-1-carboxylate (6h)**



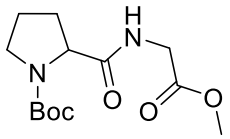
Eluent: PE/EA = 2:1, White Solid (216 mg, 80%); mp 125-126 °C; IR (film): ν_{max} 2972, 2876, 1670, 1678, 1396, 1364, 1250, 1165, 1121.^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.13-4.05 (m, 1H), 3.53-3.45 (m, 1H), 3.44-3.36 (m, 1H), 2.25-2.10 (m, 1H), 1.97-1.78 (m, 3H), 1.44 (s, 9H), 1.35 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.8, 174.4, 156.4, 156.1, 81.2, 61.8, 51.9, 48.0, 32.7, 31.4, 29.0, 28.8, 25.3, 24.6 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{26}N_2O_3Na^+$: 293.1836, found: 293.1834.

***tert*-Butyl 2-((tosylmethyl)carbamoyl)pyrrolidine-1-carboxylate (6i)**



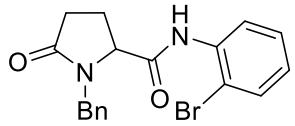
Eluent: PE/EA = 2:1, White Solid (256 mg, 67%); mp 69-71 ºC; IR (film): ν_{max} 2927, 2883, 2853, 1683, 1521, 1253, 1049, 834.^{1}H NMR (400 MHz, $CDCl_3$, mixture of rotamers) δ 7.83-7.79 (m, 2H), 7.47-7.41 (m, 2H), 4.96-4.80 (m, 3H), 4.59-4.51 (m, 1H), 4.17-4.10 (m, 1H), 3.47-3.40 (m, 1H), 2.46 (s, 3H), 2.19-2.03 (m, 1H), 1.85-1.63 (m, 3H), 1.47 (s, 3.7H), 1.40 (s, 5.3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$, mixture of rotamers) δ 175.5, 175.0, 156.4, 155.8, 146.8, 146.7, 136.1, 136.0, 131.0, 130.2, 130.1, 81.6, 81.4, 61.6, 61.4, 61.2, 48.2, 47.8, 32.4, 31.2, 28.8, 28.7, 28.6, 25.2, 24.5, 21.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{26}N_2O_5SNa^+$: 405.1455, found: 405.1455.

***tert*-Butyl 2-((2-methoxy-2-oxoethyl)carbamoyl)pyrrolidine-1-carboxylate (6j)**



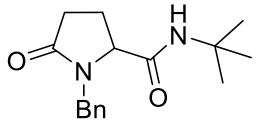
Eluent: PE/EA = 2:1, White Solid (203 mg, 71%); mp 138-139 ºC; IR (film): ν_{max} 2975, 1755, 1698, 1670, 1453, 1396, 1367, 1207, 1166, 1123. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.29-4.20 (m, 1H), 4.04-3.89 (m, 2H), 3.74 (s, 3H), 3.58-3.51 (m, 1H), 3.47-3.40 (m, 1H), 2.34-2.16 (m, 1H), 2.08-1.85 (m, 3H), 1.49 (s, 2.7H), 1.45 (s, 6.3H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 176.4, 176.0, 171.6, 171.4, 156.5, 156.1, 81.6, 81.4, 61.9, 61.5, 52.6, 47.9, 41.8, 32.4, 31.4, 28.7, 28.6, 25.3, 24.6 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{13}H_{22}N_2O_5Na^+$: 309.1421, found: 309.1416.

1-Benzyl-*N*-(2-bromophenyl)-5-oxopyrrolidine-2-carboxamide (6k)



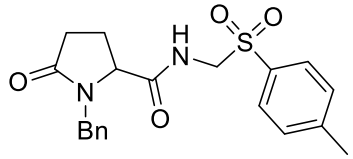
Eluent: PE/EA = 1:1, White Solid (298 mg, 80%); mp 159-160 ºC; IR (film): ν_{max} 3030, 1670, 1584, 1527, 1437, 1285, 1177, 752. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28-8.24 (m, 1H), 7.57-7.53 (m, 1H), 7.35-7.23 (m, 6H), 7.06-7.01 (m, 1H), 5.19 (d, *J* = 14.8 Hz, 1H), 4.03-4.01 (m, 1H), 4.00-3.96 (m, 1H), 2.73-2.64 (m, 1H), 2.53-2.44 (m, 1H), 2.42-2.33 (m, 1H), 2.23-2.14 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.7, 169.6, 169.5, 135.6, 134.8, 134.7, 132.4, 129.1, 128.8, 128.6, 128.2, 126.2, 122.2, 114.1, 114.0, 61.5, 46.1, 29.7, 23.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{17}BrN_2O_2Na^+$: 395.0366, 397.0345, 398.0379, found: 395.0367, 397.0345, 398.0375.

1-Benzyl-*N*-(*tert*-butyl)-5-oxopyrrolidine-2-carboxamide (6l)



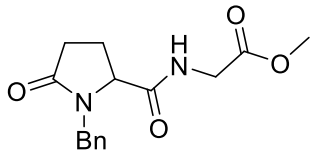
Eluent: PE/EA = 1:1, White Solid (192 mg, 70%); mp 116-118 ºC; IR (film): ν_{max} 2968, 2422, 1670, 1431, 1361, 1227, 701. ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.26 (m, 3H), 7.23-7.19 (m, 2H), 4.96 (d, *J* = 14.8 Hz, 1H), 3.93 (dd, *J* = 8.8, 4.4 Hz, 1H), 3.84 (d, *J* = 14.8 Hz, 1H), 2.61-2.51 (m, 1H), 2.43-2.34 (m, 1H), 2.26-2.16 (m, 1H), 1.95-1.86 (m, 1H), 1.31 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 178.3, 172.6, 137.2, 129.8, 129.4, 128.8, 61.8, 52.2, 46.5, 30.9, 28.7, 24.1 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{22}N_2O_2Na^+$: 297.1574, found: 297.1579.

1-Benzyl-5-*oxo*-*N*-(tosylmethyl)pyrrolidine-2-carboxamide (6m)



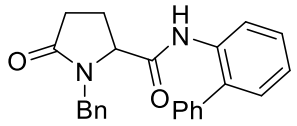
Eluent: PE/EA = 1:1, White Solid (340 mg, 88%); mp 152-153 ºC; IR (film): ν_{max} 3284, 2919, 2850, 1672, 1596, 1265, 1142, 746. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82-7.77 (m, 2H), 7.38-7.35 (m, 2H), 7.34-7.27 (m, 3H), 7.17-7.14 (m, 2H), 5.02 (d, *J* = 14.8 Hz, 1H), 4.67-4.64 (m, 2H), 3.83 (dd, *J* = 9.2, 3.2 Hz, 1H), 3.76 (d, *J* = 14.8 Hz, 1H), 2.54-2.46 (m, 1H), 2.45 (s, 3H), 2.43-2.35 (m, 1H), 2.25-2.13 (m, 1H), 1.82-1.73 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 175.8, 171.3, 145.9, 135.6, 134.3, 130.2, 129.1, 128.9, 128.6, 128.2, 60.3, 60.2, 45.8, 29.6, 23.5, 21.9 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{22}N_2O_4SNa^+$: 409.1193, 410.1223, 411.1151, found: 409.1194, 410.1220, 411.1151.

Methyl (1-benzyl-5-oxopyrrolidine-2-carbonyl)glycinate (6n)



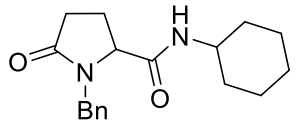
Eluent: PE/EA = 1:1, White Solid (197 mg, 68%); mp 61-63 ºC; IR (film): ν_{max} 2952, 1751, 1668, 1452, 1414, 1210, 704. ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.25 (m, 5H), 5.03 (d, *J* = 6.8 Hz, 1H), 4.03 (dd, *J* = 8.8, 4.0 Hz, 1H), 3.96-3.91 (m, 2H), 3.89-3.84 (m, 1H), 3.74 (s, 3H), 2.61-2.51 (m, 1H), 2.46-2.36 (m, 1H), 2.32-2.22 (m, 1H), 2.07-1.98 (m, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 178.2, 174.3, 171.4, 137.1, 129.8, 129.5, 128.8, 61.3, 52.7, 46.3, 41.8, 30.7, 23.9 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{15}H_{18}N_2O_4Na^+$: 313.1159, found: 313.1157.

***N*-([1,1'-biphenyl]-2-yl)-1-benzyl-5-oxopyrrolidine-2-carboxamide (6o)**



Eluent: PE/EA = 1:1, White Solid (248 mg, 67%); mp 117-119 °C; IR (film): ν_{max} 3028, 1667,1482, 1438, 1417, 1356, 752, 701. ^{1}H NMR (400 MHz, CD_3OD) δ 7.43-7.23 (m, 12H), 7.19-7.13 (m, 2H), 4.91 (d, *J* = 14.8 Hz, 1H), 3.99 (dd, *J* = 8.8, 3.2 Hz, 1H), 3.69 (d, *J* = 14.8 Hz, 1H), 2.48-2.38 (m, 1H), 2.37-2.28 (m, 1H), 2.20-2.09 (m, 1H), 1.84-1.75 (m, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 178.2, 172.5, 140.6, 140.0, 137.0, 134.8, 131.6, 130.1, 129.8, 129.5, 129.1, 128.9, 128.6, 128.2, 61.4, 46.4, 30.6, 24.1 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{22}N_2O_4Na^+$: 393.1574, found: 393.1574.

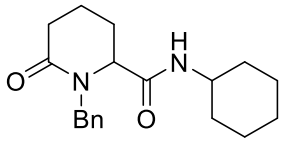
1-Benzyl-*N*-cyclohexyl-5-oxopyrrolidine-2-carboxamide (6p)



Eluent: PE/EA = 1:1, White Solid (228 mg, 76%); mp 140-141 °C; IR (film): ν_{max} 2931, 2854, 2422, 1671, 1450, 1416, 1249, 702. ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.26 (m, 3H), 7.23-7.19 (m, 2H), 4.96 (d, *J* = 14.8 Hz, 1H), 3.94 (dd, *J* = 8.8, 4.0 Hz, 1H), 3.83 (d, *J* = 14.8 Hz, 1H), 3.65-3.56 (m, 1H), 2.61-2.52 (m, 1H), 2.44-2.35 (m, 1H), 2.27-2.17 (m, 1H), 1.97-1.88 (m, 1H), 1.85-1.70 (m, 4H), 1.66-1.60 (m, 1H), 1.39-1.28 (m, 2H), 1.23-1.13 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 176.9, 171.0, 135.7, 128.5, 128.1, 127.5, 60.2, 48.5, 45.1, 32.4, 32.1, 29.5,

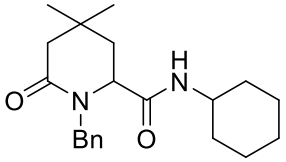
25.2, 24.7, 22.9 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{18}H_{24}N_2O_2Na^+$: 323.1730, found: 323.1728.

1-Benzyl-*N*-cyclohexyl-6-oxopiperidine-2-carboxamide (6q)



Eluent: PE/EA = 1:1, White Solid (257 mg, 82%); mp 113-115 ºC; IR (film): ν_{max} 2931, 2854, 1626, 1450, 1330, 1249, 701. ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.27 (m, 3H), 7.26-7.21 (m, 2H), 5.44 (d, *J* = 15.2 Hz, 1H), 3.96 (dd, *J* = 4.8, 4.0 Hz, 1H), 3.70-3.62 (m, 2H), 2.56-2.41 (m, 2H), 1.97-1.94 (m, 2H), 1.93-1.70 (m, 6H), 1.70-1.63 (m, 1H), 1.42-1.31 (m, 2H), 1.28-1.14 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 173.5, 172.2, 137.9, 129.7, 129.2, 128.6, 60.6, 50.0, 49.9, 33.7, 33.5, 32.7, 28.4, 26.6, 26.1, 19.1 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{26}N_2O_2Na^+$: 337.1887, found: 337.1887.

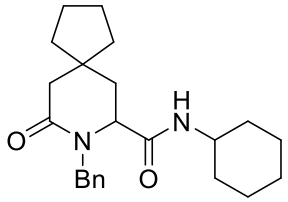
1-Benzyl-*N*-cyclohexyl-4,4-dimethyl-6-oxopiperidine-2-carboxamide (6r)



Eluent: PE/EA = 1:1, White Solid (246 mg, 72%); mp 126-128 ºC; IR (film): ν_{max} 2931, 2855, 2412, 1625, 1449, 1345, 1306, 1249. ^{1}H NMR (400 MHz, CD_3OD) δ 7.38-7.30 (m, 3H), 7.28-7.24 (m, 2H), 5.62 (d, *J* = 14.8 Hz, 1H), 3.85 (dd, *J* = 10.8, 6.4 Hz, 1H), 3.75-3.67 (m, 1H), 3.62 (d, *J* = 14.8 Hz, 1H), 2.37 (d, *J* = 16.8 Hz, 1H), 2.24 (dd, *J* = 16.8, 2.8 Hz, 1H), 2.00-1.93 (m, 1H), 1.85-1.73 (m, 5H), 1.70-1.65 (m, 1H), 1.45-1.33 (m, 2H), 1.30-1.15 (m, 3H), 1.03 (s, 3H), 0.87 (s, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 173.0, 172.9, 137.8, 129.8, 129.7, 128.9,

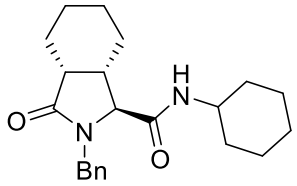
59.3, 50.0, 48.3, 46.4, 40.8, 33.8, 33.5, 30.9, 30.5, 26.6, 26.1, 26.0, 24.7 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{30}N_2O_2Na^+$: 365.2200, found: 365.2199.

8-Benzyl-*N*-cyclohexyl-9-oxo-8-azaspiro[4.5]decane-7-carboxamide (6s)



Eluent: PE/EA = 1:1, White Solid (269 mg, 73%); mp 111-112 °C; IR (film): ν_{max} 2930, 2854, 2413, 1623, 1448, 1344, 709. ^{1}H NMR (400 MHz, CD_3OD) δ 7.35-7.25 (m, 3H), 7.24-7.19 (m, 2H), 5.59 (d, *J* = 14.8 Hz, 1H), 3.85 (dd, *J* = 10.4, 6.4 Hz, 1H), 3.72-3.63 (m, 1H), 3.59 (d, *J* = 14.8 Hz, 1H), 2.45 (d, *J* = 16.8 Hz, 1H), 2.34 (dd, *J* = 16.8, 2.4 Hz, 1H), 1.96-1.89 (m, 1H), 1.87-1.72 (m, 5H), 1.70-1.61 (m, 5H), 1.50-1.44 (m, 2H), 1.40-1.28 (m, 4H), 1.26-1.12 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 173.3, 172.5, 137.8, 129.7, 129.6, 128.8, 59.8, 50.0, 45.2, 42.0, 40.8, 39.2, 35.8, 33.8, 33.5, 26.6, 26.1, 26.1, 25.5, 24.8 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{32}N_2O_2Na^+$: 391.2356, found: 391.2358.

(1*S*,3a*R*,7a*S*)-2-Benzyl-*N*-cyclohexyl-3-oxooctahydro-1H-isoindole-1-carboxamide (6t)



Eluent: PE/EA = 1:1, White Solid (322 mg, 91%); mp 131-133 °C; IR (film): ν_{max} 2929, 2853, 1669, 1446, 1349, 1302, 1248. ^{1}H NMR (400

MHz, CD_3OD) δ 7.39-7.30 (m, 3H), 7.26-7.22 (m, 2H), 5.02 (d, *J* = 14.8 Hz, 1H), 3.81 (d, *J* = 14.4 Hz, 1H), 3.68-3.59 (m, 1H), 3.45 (d, *J* = 2.8 Hz, 1H), 2.80 (dd, *J* = 10.8, 6.4 Hz, 1H), 3.34-3.27 (m, 1H), 1.98-1.90 (m, 1H), 1.87-1.72 (m, 5H), 1.68-1.60 (m, 2H), 1.55-1.48 (m, 2H), 1.40-1.31 (m, 2H), 1.27-1.14 (m, 5H), 1.13-1.02 (m, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 179.0, 171.4, 137.3, 129.9, 129.7, 129.0, 65.6, 50.0, 46.8, 41.7, 39.5, 33.8, 33.6, 29.1, 26.6, 26.1, 24.5, 24.4, 24.0 ppm; HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{30}N_2O_2Na^+$: 377.2200, found: 377.2198.

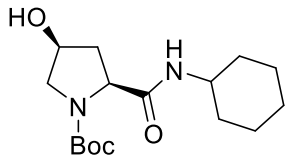
General Procedure C: Synthesis of 7

To a solution of *trans*- 4-hydroxy-5-substituted 2-pyrrolidinones[1] (2 mmol) in dry THF (8 mL) was added a solution of $LiHBEt_3$ in THF (1 M, 1.1 equiv, 2.2 mL) at −78 °C. The reaction mixture was stirred for 1 h at the same temperature, and the reaction was quenched with water (5 mL) and warmed to room temperature. To the mixture were added saturated aqueous $NaHCO_3$ (20 mL) and 30% H_2O_2 solution (5 mL). After stirring for 1 h, the mixture was extracted with ethyl acetate (20 mL × 3), and the combined organic layers were washed with brine. Dried, fifiltered , and concentrated to give the *N,O*-acetal **7** without further purifications[2].

General Procedure D: Synthesis of 8

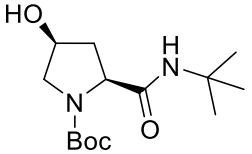
N,O-acetal **7** (1.0 mmol), isocyanides **3** (1.0 mmol) were dissolved in THF (5 mL) at -78ºC, then $Cu(OTf)_2$ (0.2 mmol) was added. The reaction was stirred at -78 ºC to room temperature overnight then quenched with a saturated $NaHCO_3$ aqueous solution and extracted with EtOAc (30 mL × 3). The combined organic layers were washed with brine, dried, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA =2:1 - 1:1) to give the desired product **8**.

***tert*-butyl (2*S*,4*S*)-2-(cyclohexylcarbamoyl)-4-hydroxypyrrolidine-1-carboxylate (8a)**



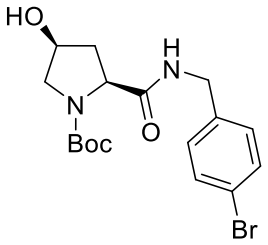
Eluent: PE/EA = 1:1, White Solid (237 mg, 76%); mp 129-131 °C; $[\alpha]_D^{22}$ = -49.2 (*c* 2.00, $CHCl_3$), IR (film): ν_{max} 2933, 1701, 1677, 1646, 1452, 1396, 1367, 1163, 1125, 1085. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.33-4.25 (m, 1H), 4.20-4.10 (m, 1H), 3.58-3.51 (m, 1H), 3.50-3.43 (m, 1H), 2.47-2.30 (m, 1H), 2.00-1.86 (m, 1H), 1.48 (s, 9H), 1.37 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 175.2, 174.9, 156.3, 156.1, 81.8, 81.5, 71.3, 70.5, 61.4, 56.8, 56.3, 52.1, 39.7, 38.7, 30.3, 28.8, 28.7. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{16}H_{28}N_2O_4Na^+$: 335.1941, found: 335.1938.

***tert*-butyl (2*S*,4*S*)-2-(*tert*-butylcarbamoyl)-4-hydroxypyrrolidine-1-carboxylate (8b)**



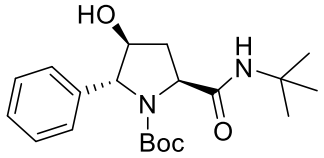
Eluent: PE/EA = 1:1, White Solid (188 mg, 66%); mp 139-142 °C; $[\alpha]_D^{22}$ = -68.1 (*c* 1.00, CD_3OD, mixture of rotamers), IR (film): ν_{max} 2972, 1701, 1651, 1394, 1365, 1162, 1123. ^{1}H NMR (400 MHz, CD_3OD) δ 4.37-4.27 (m, 1H), 4.23-4.15 (m, 1H), 3.72-3.63 (m, 1H), 3.60-3.53 (m, 1H), 3.50-3.43 (m, 1H), 2.50-2.35 (m, 1H), 1.95-1.63 (m, 6H), 1.46 (s, 9H), 1.43-1.34 (m, 2H), 1.32-1.21 (m, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 175.0, 174.7, 156.4, 156.1, 81.8, 81.5, 71.3, 70.5, 61.5, 56.8, 56.2, 39.9, 38.9, 33.7, 28.7, 26.6, 26.0 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{14}H_{26}N_2O_4Na^+$: 309.1785, found: 309.1784.

***tert*-butyl (2*S*,4*S*)-2-((4-bromobenzyl)carbamoyl)-4-hydroxypyrrolidine-1-carboxylate (8c)**



Eluent: PE/EA = 1:1, White Solid (259 mg, 65%); mp 109-111 °C; $[\alpha]_D^{23}$ = -12.6 (*c* 0.50, CD_3OD, mixture of rotamers), IR (film): ν_{max} 2977, 1653, 1488, 1403, 1162, 1125. ^1H NMR (400 MHz, CD_3OD) δ 6.73-6.59 (m, 2H), 6.53-6.39 (m, 2H), 3.65-3.40 (m, 4H), 2.82-2.75 (m, 1H), 2.67-2.60 (m, 1H), 1.69-1.56 (m, 1H), 1.25-1.17 (m, 1H), 0.68 (s, 3.5H), 0.55 (s, 5.5H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.1, 151.3, 136.5, 129.8, 128.2, 127.6, 79.1, 78.9, 68.5, 67.7, 58.5, 58.4, 53.9, 53.4, 40.8, 40.7, 37.2, 36.2, 25.8 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{27}BrN_2O_4Na^+$: 421.0733, 427.0717, found: 421.0735, 423.0714.

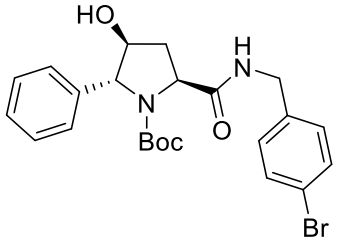
***tert*-butyl (2*R*,3*S*,5*S*)-5-(*tert*-butylcarbamoyl)-3-hydroxy-2-phenylpyrrolidine-1-carboxylate (8d)**



Eluent: PE/EA = 2:1, White Solid (235 mg, 65%); mp 138-140 °C; $[\alpha]_D^{21}$ = +78.7 (*c* 2.00, $CHCl_3$), IR (film): ν_{max} 2793, 1701, 1681, 1651, 1450, 1390, 1366, 1163, 1126. ^1H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.40-7.34 (m, 2H), 7.30-7.23 (m, 1H), 7.20-7.15 (m, 2H), 5.10-5.03 (m, 0.59H), 4.94-4.92 (m, 0.41H), 4.54-4.49 (m, 0.41H), 4.49-4.44 (m, 0.59H), 4.06-4.00 (m, 1H), 2.47-2.37 (m, 1H), 1.90-1.79 (m, 1H), 1.49 (s, 5.31H), 1.42 (s, 5.31H), 1.39 (s, 3.69H), 1.21 (s, 3.69H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 175.6, 175.1,

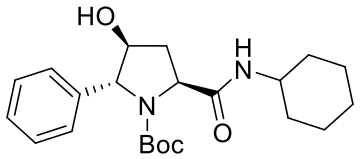
156.0, 155.7, 142.5, 141.4, 129.8, 129.7, 128.39, 128.36, 126.3, 82.2, 81.5, 79.4, 78.8, 73.7, 73.1, 62.8, 62.7, 52.30, 52.26, 36.3, 35.6, 28.9, 28.8, 28.7, 28.4 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{30}N_2O_4Na^+$: 385.2098, found: 385.2095.

***tert*-butyl (2*R*,3*S*,5*S*)-5-((4-bromobenzyl)carbamoyl)-3-hydroxy-2-phenylpyrrolidine-1-carboxylate (8e)**



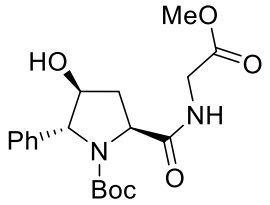
Eluent: PE/EA = 2:1, White Solid (314 mg, 66%); mp 111-113 °C; $[\alpha]_D^{24}$ = -28.9 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2977, 1650, 1488, 1390, 1162, 1129, 1067, 750, 700. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.61-7.41 (m, 2H), 7.40-7.23 (m, 5H), 7.22-7.10 (m, 2H), 5.12-4.88 (m, 1H), 4.68-4.54 (m, 1H), 4.52-4.33 (m, 2H), 4.12-4.02 (m, 1H), 2.57-2.39 (m, 1H), 1.98-1.87 (m, 1H), 1.36 (s, 4H), 1.20 (s, 5H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 174.7, 174.5, 154.8, 154.1, 141.2, 140.0, 137.7, 131.3, 131.1, 129.7, 129.0, 128.3, 128.2, 127.0, 125.1, 124.9, 120.8, 120.4, 80.8, 80.2, 78.0, 77.4, 72.2, 71.6, 61.0, 60.8, 42.5, 42.2, 35.0, 34.4, 27.1, 26.9 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{27}BrN_2O_4Na^+$: 497.1046, 499.1026 found: 497.1045, 499.1024.

***tert*-butyl (2*R*,3*S*,5*S*)-5-(cyclohexylcarbamoyl)-3-hydroxy-2-phenylpyrrolidine-1-carboxylate (8f)**



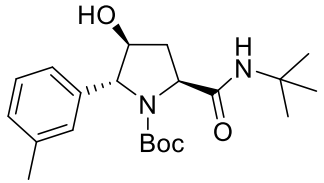
Eluent: PE/EA = 2:1, White Solid (217 mg, 56%); mp 127-129 °C; $[\alpha]_D^{23}$ = -41.2 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2931, 2855, 2435, 1700, 1645, 1452, 1386, 1162, 1127. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.41-7.34 (m, 2H), 7.31-7.24 (m, 1H), 7.20-7.15 (m, 2H), 5.10-5.04 (m, 0.54H), 4.96-4.90 (m, 0.46H), 4.60-4.54 (m, 0.46H), 4.54-4.49 (m, 0.54H), 4.07-4.02 (m, 1H), 3.76-3.67 (m, 1H), 2.52-2.37 (m, 1H), 2.00-1.75 (m, 5H), 1.72-1.63 (m, 1H), 1.46 (s, 4.86H), 1.43-1.24 (m, 5H), 1.21 (s, 4.14H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 175.4, 174.8, 156.0, 155.6, 142.5, 141.4, 129.8, 129.7, 128.39, 128.36, 126.5, 126.3, 82.3, 81.5, 79.4, 78.8, 73.6, 73.1, 62.3, 62.1, 50.2, 50.0, 36.5, 35.7, 33.72, 33.69, 33.5, 33.3, 28.7, 28.3, 26.7, 26.6, 26.0, 25.9 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{22}H_{32}N_2O_4Na^+$: 411.2254, found: 411.2253.

***tert*-Butyl (2*R*,3*S*,5*S*)-3-hydroxy-5-((2-methoxy-2-oxoethyl)carbamoyl)-2-phenylpyrrolidine-1-carboxylate (8g)**



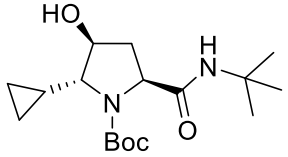
Eluent: PE/EA = 2:1, White Solid (197 mg, 52%); mp 107-109 °C; $[\alpha]_D^{23}$ = -22.2 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2976, 1650, 1488, 1390, 1162, 1129, 1067, 750, 700. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.46-7.42 (m, 2H), 7.38-7.33 (m, 1H), 7.29-7.24 (m, 2H), 5.15-5.00 (m, 1H), 4.75-4.65 (m, 1H), 4.15-4.00 (m, 4H), 3.84 (s, 1.47H), 3.83 (s, 1.53H), 2.65-2.47 (m, 1H), 2.12-1.98 (m, 1H), 1.52 (s, 4.6H), 1.27 (s, 4.4H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 176.9, 176.3, 156.2, 155.6, 142.6, 142.4, 129.8, 129.7, 128.4, 128.0, 126.5, 126.4, 82.4, 81.6, 79.4, 78.8, 62.2, 61.9, 52.6, 42.2, 42.1, 36.3, 36.7, 28.6, 28.3 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{19}H_{26}N_2O_6Na^+$: 401.1683 found: 401.1685.

***tert*-butyl (2*R*,3*S*,5*S*)-5-(*tert*-butylcarbamoyl)-3-hydroxy-2-(m-tolyl)pyrrolidine-1-carboxylate (8h)**



Eluent: PE/EA = 2:1, White Solid (229 mg, 61%); mp 153-155 °C; $[\alpha]_D^{22}$ = +54.0 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2972, 2436, 1652, 1607, 1390, 1366, 1165, 1124. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.27-7.21 (m, 1H), 7.13-7.06 (m, 1H), 7.01-6.92 (m, 2H), 5.04-5.00 (m, 1H), 4.52-4.43 (m, 1H), 4.05-3.98 (m, 1H), 2.47-2.38 (m, 1H), 2.36-2.34 (m, 3H), 1.89-1.78 (m, 1H), 1.49 (s, 5.13H), 1.41 (s, 5.13H), 1.39 (s, 3.87H), 1.22 (s, 3.87H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 178.1, 177.6, 158.6, 158.2, 145.0, 143.9, 142.1, 142.0, 132.2, 132.1, 131.6, 131.5, 129.6, 129.5, 126.0, 125.8, 84.7, 84.0, 81.9, 81.3, 76.2, 75.6, 65.4, 65.2, 54.81, 54.77, 38.9, 38.1, 31.7, 31.4, 31.3, 31.2, 30.9, 24.1, 24.0 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{21}H_{32}N_2O_4Na^+$: 399.2254, found: 399.2255.

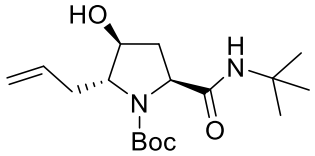
***tert*-butyl (2*R*,3*S*,5*S*)-5-(*tert*-butylcarbamoyl)-2-cyclopropyl-3-hydroxypyrrolidine-1-carboxylate (8i)**



Eluent: PE/EA = 2:1, White Solid (235 mg, 72%); mp 135-136 °C; $[\alpha]_D^{21}$ = -41.5 (*c* 0.20, $CHCl_3$), IR (film): ν_{max} 2972, 1698, 1650, 1388, 1366, 1171, 1121. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 4.20-4.15 (m, 1H), 4.14-4.08 (m, 1H), 3.53-3.47 (m, 0.63H), 3.33-3.28 (m, 0.41H), 2.65-2.52 (m, 1H), 1.90-1.80 (m, 1H), 1.49 (s, 3.33H), 1.47 (s, 5.67H), 1.37 (s, 5.67H), 1.34 (s, 3.33H), 0.75-0.66 (m, 1H), 0.64-0.42 (m,

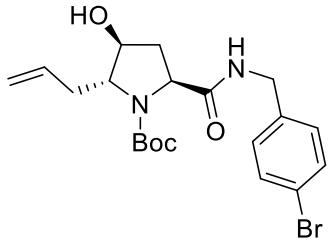
3H), 0.30-0.22 (m, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.9, 173.3, 154.2, 154.0, 79.5, 79.3, 74.8, 73.9, 71.1, 70.6, 59.9, 50.0, 35.5, 34.3, 26.7, 26.6, 26.5, 13.0, 12.8, 3.5, 2.6 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{30}N_2O_4Na^+$: 349.2098, found: 349.2098.

***tert*-butyl (2*R*,3*S*,5*S*)-2-allyl-5-(*tert*-butylcarbamoyl)-3-hydroxypyrrolidine-1-carboxylate (8j)**



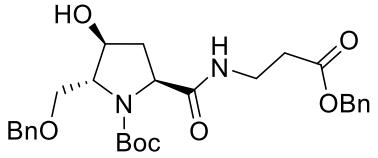
Eluent: PE/EA = 2:1, White Solid (238 mg, 73%); mp 131-133 °C; $[\alpha]_D^{23}$ = -29.2 (*c* 0.50, $CHCl_3$), IR (film): ν_{max} 2974, 2430, 1698, 1679, 1650, 1440, 1392, 1366, 1171, 1127. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 5.09-4.96 (m, 1H), 4.35-4.26 (m, 2H), 3.36-3.28 (m, 1H), 3.27-3.20 (m, 1H), 3.16-3.04 (m, 1H), 1.75-1.57 (m, 2H), 1.33-1.21 (m, 1H), 1.06-0.98 (m, 1H), 0.69 (s, 2.8H), 0.67 (s, 6.2H), 0.56 (s, 6.2H), 0.54 (s, 2.8H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.1, 172.7, 153.0, 152.9, 133.0, 132.9, 115.44, 115.38, 79.1, 78.8, 72.4, 71.5, 66.3, 66.1, 59.43, 59.38, 49.44, 49.40, 35.5, 34.7, 34.4, 33.6, 26.1, 26.0 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{30}N_2O_4Na^+$: 349.2098, found: 349.2098.

***tert*-butyl (2*R*,3*S*,5*S*)-2-allyl-5-((4-bromobenzyl)carbamoyl)-3-hydroxypyrrolidine-1-carboxylate (8k)**



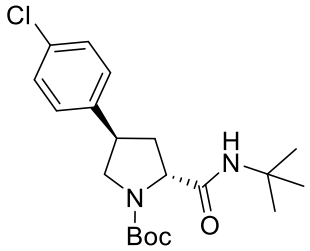
Eluent: PE/EA = 2:1, White Solid (285 mg, 65%); mp 121-123 °C; $[\alpha]_D^{24}$ = +13.0 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2977, 1651, 1391, 1254, 1168, 1130, 772, 631. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 6.73-6.60 (m, 2H), 6.51-6.41 (m, 2H), 5.10-4.95 (m, 1H), 4.38-4.26 (m, 2H), 3.63-3.40 (m, 3H), 3.31-3.24 (m, 1H), 3.19-3.04 (m, 1H), 1.80-1.60 (m, 2H), 1.37-1.25 (m, 1H), 1.15-1.05 (m, 1H), 0.70 (s, 3.7H), 0.54 (s, 5.3H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.7, 173.5, 153.2, 152.8, 136.31, 136.29, 132.92, 132.86, 130.0, 129.8, 128.4, 127.7, 119.4, 119.1, 115.5, 79.2, 79.0, 72.5, 71.5, 66.2, 66.0, 59.0, 58.8, 41.1, 40.8, 35.4, 34.8, 34.3, 33.8, 26.0, 25.8 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{27}BrN_2O_4Na^+$: 461.1046, 463.1026, found: 461.1049, 463.1028.

***tert*-butyl (2*R*,3*S*,5*S*)-5-((3-(benzyloxy)-3-oxopropyl)carbamoyl)-2-((benzyloxy)methyl)-3-hydroxypyrrolidine-1-carboxylate (8l)**



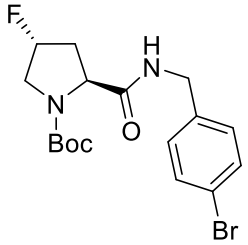
Eluent: PE/EA = 2:1, White Solid (246 mg, 48%), $[\alpha]_D^{22}$ = -16.7 (*c* 1.00, $CHCl_3$), IR (film): ν_{max} 2975, 1734, 1658, 1454, 1389, 1255, 1171, 1127, 1085, 739, 698. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.40-7.29 (m, 10H), 5.17-5.12 (m, 2H), 4.56-4.46 (m, 2H), 4.27-4.17 (m, 2H), 4.07-3.92 (m, 1H), 3.61-3.56 (m, 2H), 3.52-3.40 (m, 2H), 2.65-2.53 (m, 3H), 1.85-1.77 (m, 1H), 1.42 (s, 5.3H), 1.40 (s, 3.7H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 176.8, 176.3, 173.2, 173.0, 155.8, 155.5, 139.7, 139.6, 137.6, 137.5, 129.6, 129.5, 129.4, 129.33, 129.28, 129.25, 129.2, 128.8, 128.71, 128.68, 82.0, 81.8, 75.3, 74.4, 74.35, 74.27, 70.1, 69.5, 68.9, 68.8, 67.5, 67.4, 62.1, 62.0, 38.4, 37.3, 36.44, 36.38, 34.8, 34.7, 28.7 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{28}H_{36}N_2O_7Na^+$: 535.2415, found: 535.2418.

(±) *tert*-Butyl (2*R*,4*R*)-2-(*tert*-butylcarbamoyl)-4-(4-chlorophenyl)pyrrolidine-1-carboxylate (14)



(±) *tert*-butyl (4R)-4-(4-chlorophenyl)-2-hydroxypyrrolidine-1-carboxylate (**13**) was synthesized according to the General Procedure C from (±) *tert*-butyl (R)-4-(4-chlorophenyl)-2-oxopyrrolidine-1-carboxylate[3]. **14** was synthesized from *N,O*-acetal **13** according to the General Procedure D. Eluent: PE/EA = 4:1, White Solid (320 mg, 84%), mp 121-123 °C; IR (film): ν_{max} 2813, 2071, 1906, 1762, 1594, 1423. ^{1}H NMR (400 MHz, CD_3OD) δ 7.36-7.30 (m, 2H), 7.29-7.24 (m, 2H), 4.36-4.25 (m, 1H), 3.98-3.88 (m, 1H), 3.63-3.53 (m, 1H), 3.40-3.33 (m, 1H), 2.41-2.18 (m, 2H), 1.48 (s, 9H), 1.38 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ 174.4, 155.9, 141.2, 133.7, 129.8, 81.6, 61.8, 54.1, 52.0, 42.3, 39.7, 29.0, 28.7 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + H]^+$ Calcd for $C_{20}H_{30}ClN_2O_3^+$: 381.1940, found: 381.1940.

***tert*-Butyl (2*S*,4*R*)-2-((4-bromobenzyl)carbamoyl)-4-fluoropyrrolidine-1-carboxylate (9)**

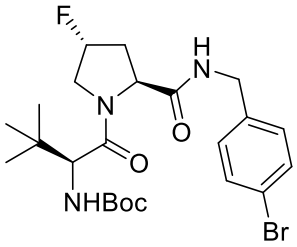


A solution of **8c** (400 mg, 1.0 mmol) in DCM (3 mL) was added DAST (0.67 mL, 5 mmol) at 0°C. After been stirred at 0°C to room temperature for 4 h, saturated $NaHCO_3$ aqueous solution was added and extracted with DCM (10 mL × 3). The combined organic layers were washed with

brine, dried, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA = 1:1) to give the desired product **9**.

White Solid (188 mg, 47%); mp 130-131 °C; $[\alpha]_D^{22}$ = -36.8 (*c* 0.50, $CHCl_3$), IR (film): ν_{max} 2978, 1663, 1554, 1488, 1406, 1367, 1162, 1128, 773. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.51-7.44 (m, 2H), 7.30-7.21 (m, 2H), 5.35-5.15 (m, 1H), 4.45-4.27 (m, 3H), 3.90-3.78 (m, 1H), 3.72-3.53 (m, 1H), 2.64-2.48 (m, 1H), 2.24-2.01 (m, 1H), 1.50 (s, 3.5H), 1.36 (s, 5.5H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.5, 173.3, 154.8, 154.5, 137.7, 131.2, 131.1, 130.9, 129.6, 128.9, 128.6, 120.7, 120.3, 91.0 (d, $^1J_{C\text{-}F}$ = 174.8 MHz), 91.2 (d, $^1J_{C\text{-}F}$ = 175.5 MHz), 80.6, 80.4, 58.9, 58.7, 53.6 (d, $^2J_{C\text{-}F}$ = 22.4 MHz), 53.1 (d, $^2J_{C\text{-}F}$ = 22.5 MHz), 43.1, 42.2, 41.9, 40.8, 37.7 (d, $^2J_{C\text{-}F}$ = 22.0 MHz), 36.7 (d, $^2J_{C\text{-}F}$ = 22.3 MHz), 27.2, 27.0 ppm; ^{19}F NMR (376 MHz, CD_3OD, mixture of rotamers) δ -180.4, -180.9 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{17}H_{22}BrFN_2O_3Na^+$: 423.0690, 425.0670, found: 423.0690, 425.0668.

***tert*-butyl ((*S*)-1-((2*S*,4*R*)-2-((4-bromobenzyl)carbamoyl)-4-fluoropyrrolidin-1-yl)-3,3-dimethyl-1-oxobutan-2-yl)carbamate (10)**

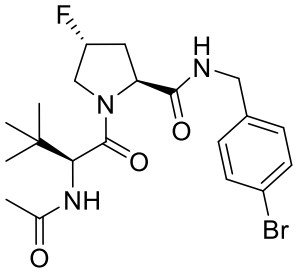


A solution of **9** (150 mg, 0.37 mmol) in TFA/DCM (1/1 mL) was stirred at room temperature for 1 h. The mixture was evaporated under reduced pressure to give the corresponding intermediate further purification. The corresponding intermediate was dissolved in DMF (1 mL), Boc-*L*-*te*rt-Leu (86 mg, 0.37 mmol), HATU (156 mg, 0.41 mmol) and DIPEA (0.26 mL, 1.48 mmol) were added. After been stirred at room

temperature for 3 h, water was added and extracted with EtOAc (10 mL × 3). The combined organic layers were washed with brine, dried, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (PE/EA = 1:1) to give the desired product **10**.

White Foam (158 mg, 83%) $[\alpha]_D^{22}$ = -23.0 (*c* 0.50, $CHCl_3$), IR (film): ν_{max} 2972, 1674, 1641, 1492, 1402, 1362, 1166. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.49-7.43 (m, 2H), 7.33-7.24 (m, 2H), 5.46-5.26 (m, 1H), 4.61-4.53 (m, 1H), 4.51-4.43 (m, 1H), 4.35-4.20 (m, 3H), 3.95-3.78 (m, 1H), 2.63-2.48 (m, 1H), 2.28-2.08 (m, 1H), 1.46 (s, 9H), 1.03 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.8, 173.0, 157.9, 139.1, 132.5, 130.4, 121.8, 93.5 (d, $^1J_{C\text{-}F}$ = 178.4 MHz), 80.8, 60.5, 56.2 (d, $^2J_{C\text{-}F}$ = 22.3 MHz), 43.5, 38.9, 37.2 (d, $^2J_{C\text{-}F}$ = 21.8 MHz), 36.6, 28.8, 28.7, 26.9, 26.7 ppm; ^{19}F NMR (376 MHz, CD_3OD, mixture of rotamers) δ -178.8, -179.0 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{23}H_{33}BrFN_3O_4Na^+$: 536.1531, 538.1510, found: 536.1536, 538.1513.

(2*S*,4*R*)-1-((*S*)-2-acetamido-3,3-dimethylbutanoyl)-*N*-(4-bromobenzyl)-4-fluoropyrrolidine-2-carboxamide (11)

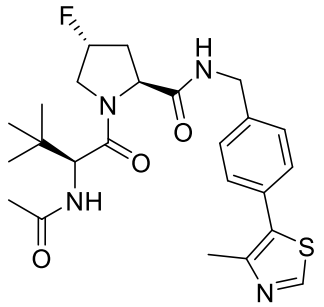


A solution of **10** (150 mg, 0.29 mmol) in TFA/DCM (1/1 mL) was stirred at room temperature for 1 h. The mixture was evaporated under reduced pressure to give the corresponding intermediate further purification. The corresponding intermediate was dissolved in DCM (2 mL), and triethylamine (120 μL, 0.88 mmol) was added to the solution. After stirring the mixture for 10 min at room temperature, acetic anhydride (41 μL, 0.44 mmol) was added and the reaction was stirred 3 h at room temperature then the solvents were evaporated. The residue was purified by flash

chromatography on silica gel (PE/EA = 1:1) to give the desired product **11**.

White Foam (112 mg, 85%) $[\alpha]_D^{22}$ = -22.0 (*c* 0.25, $CHCl_3$), IR (film): ν_{max} 1633, 1582, 1535, 1425, 1280, 1120. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 7.52-7.43 (m, 2H), 7.32-7.27 (m, 2H), 5.43-5.25 (m, 1H), 4.60-4.45 (m, 3H), 4.38-4.24 (m, 2H), 3.95-3.78 (m, 1H), 2.59-2.46 (m, 1H), 2.27-2.09 (m, 1H), 2.02 (s, 3H), 1.06 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 175.2, 173.8, 173.3, 173.1, 172.5, 172.3, 139.2, 138.9, 132.7, 132.5, 131.0, 130.5, 122.1, 121.8, 93.5 (d, $^1J_{C\text{-}F}$ = 176.7 MHz), 91.9 (d, $^1J_{C\text{-}F}$ = 175.1 MHz), 60.5, 60.4, 59.5, 58.5, 56.3 (d, $^2J_{C\text{-}F}$ = 22.5 MHz), 54.7 (d, $^2J_{C\text{-}F}$ = 23.6 MHz), 44.1, 43.5, 39.7 (d, $^2J_{C\text{-}F}$ = 22.3 MHz), 38.9, 37.5, 37.3 (d, $^2J_{C\text{-}F}$ = 21.8 MHz), 36.2, 27.0, 26.9, 22.6, 22.2 ppm; ^{19}F NMR (376 MHz, CD_3OD, mixture of rotamers) δ -178.7, -178.8 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{20}H_{27}BrFN_3O_3Na^+$: 478.1112, 480.1092, found: 478.1112, 480.1091.

(2*S*,4*R*)-1-((*S*)-2-acetamido-3,3-dimethylbutanoyl)-4-fluoro-*N*-(4-(4-methylthiazol-5-yl)benzyl)pyrrolidine-2-carboxamide (12)



To a solution of **11** (100 mg, 0.22 mmol) and $Pd(OAc)_2$ (1 mg, 2 mol %) in DMAc (2 mL) were added KOAc (43 mg, 0.44 mmol) and 4-methylthiazole (44 mg, 0.44 mmol). The resulting mixture was heated to 150 °C and stirred for 12 h. The mixture was diluted with water and extracted with DCM (3×10 mL). The combined organic phases were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was

purified by flash chromatography on silica gel (PE/EA = 1:1) to give the desired product **12**.

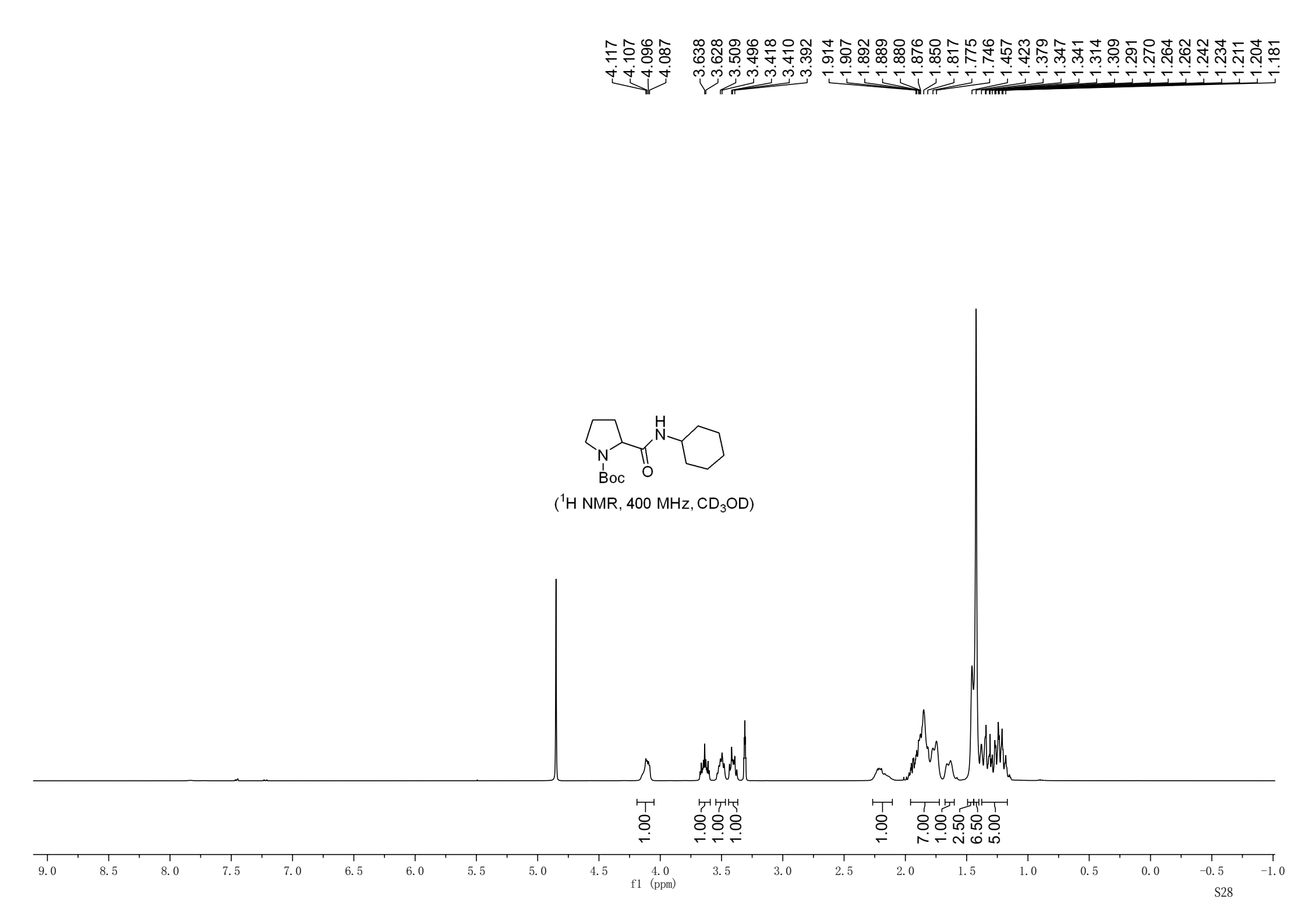
White Foam (70 mg, 67%) $[\alpha]_D^{22}$ = -8.4 (*c* 0.25, $CHCl_3$), IR (film): ν_{max} 1635, 1544, 1425, 1370, 1283, 1118, 769. ^{1}H NMR (400 MHz, CD_3OD, mixture of rotamers) δ 8.89 (s, 1H), 7.54-7.40 (m, 4H), 5.45-5.28 (m, 1H), 4.62-4.55 (m, 3H), 4.40-4.28 (m, 2H), 3.96-3.81 (m, 1H), 2.65-2.52 (m, 1H), 2.49 (s, 3H), 2.29-2.12 (m, 1H), 2.02 (s, 3H), 1.07 (s, 9H) ppm; ^{13}C NMR (100 MHz, CD_3OD, mixture of rotamers) δ 173.9, 173.4, 172.5, 152.8, 149.1, 140.2, 131.6, 130.4, 129.0, 93.5 (d, $^1J_{C\text{-}F}$ = 176.7 MHz), 60.5, 59.6, 56.3 (d, $^2J_{C\text{-}F}$ = 22.4 MHz), 43.8, 37.3 (d, $^2J_{C\text{-}F}$ = 20.0 MHz), 36.2, 27.0, 22.2, 15.8 ppm; ^{19}F NMR (376 MHz, CD_3OD) δ -178.8 ppm. HRMS (ESI-Orbitrap) *m/z*: $[M + Na]^+$ Calcd for $C_{24}H_{31}FN_4O_3SNa^+$: 497.1993, found: 497.1995.

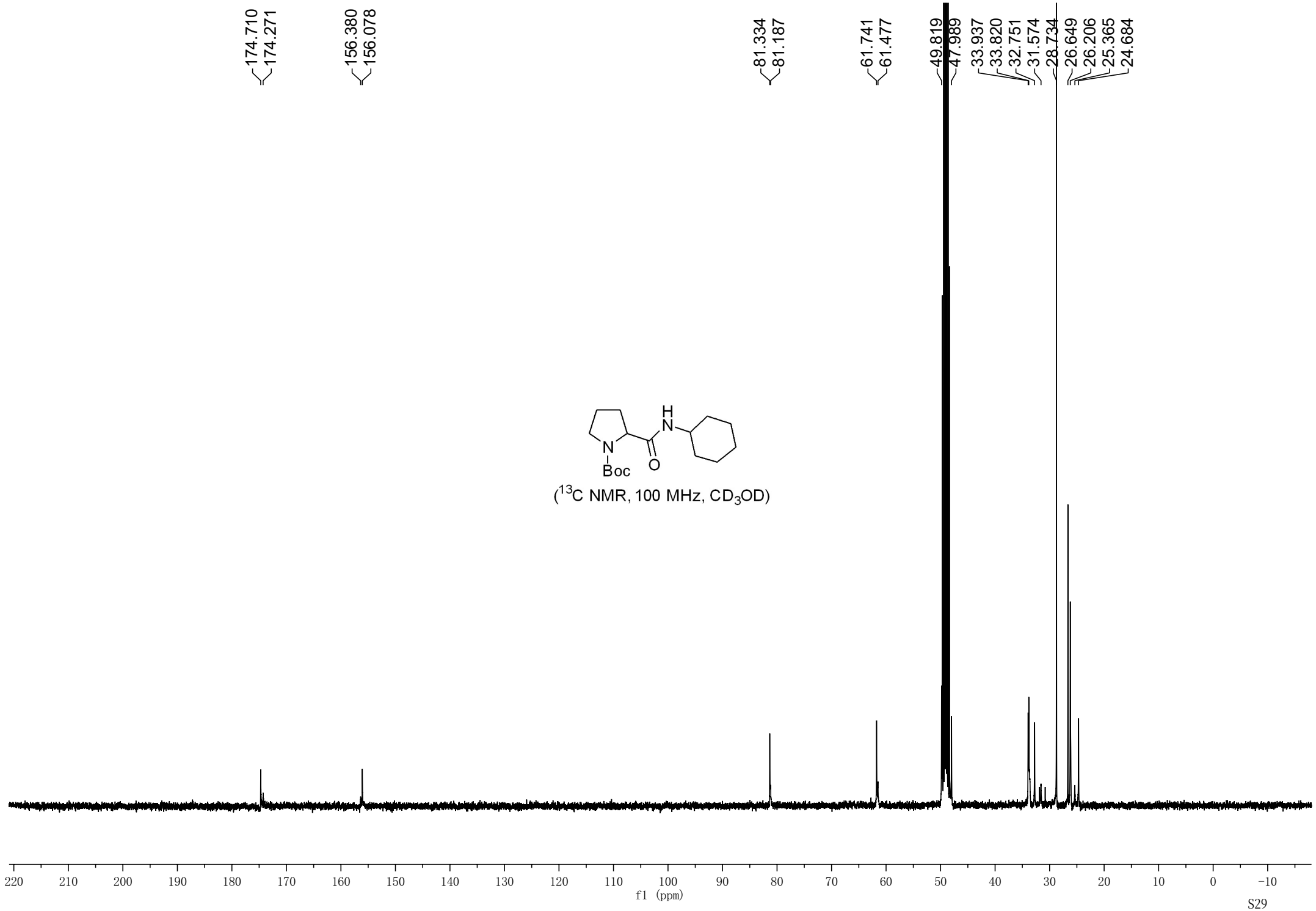
References:

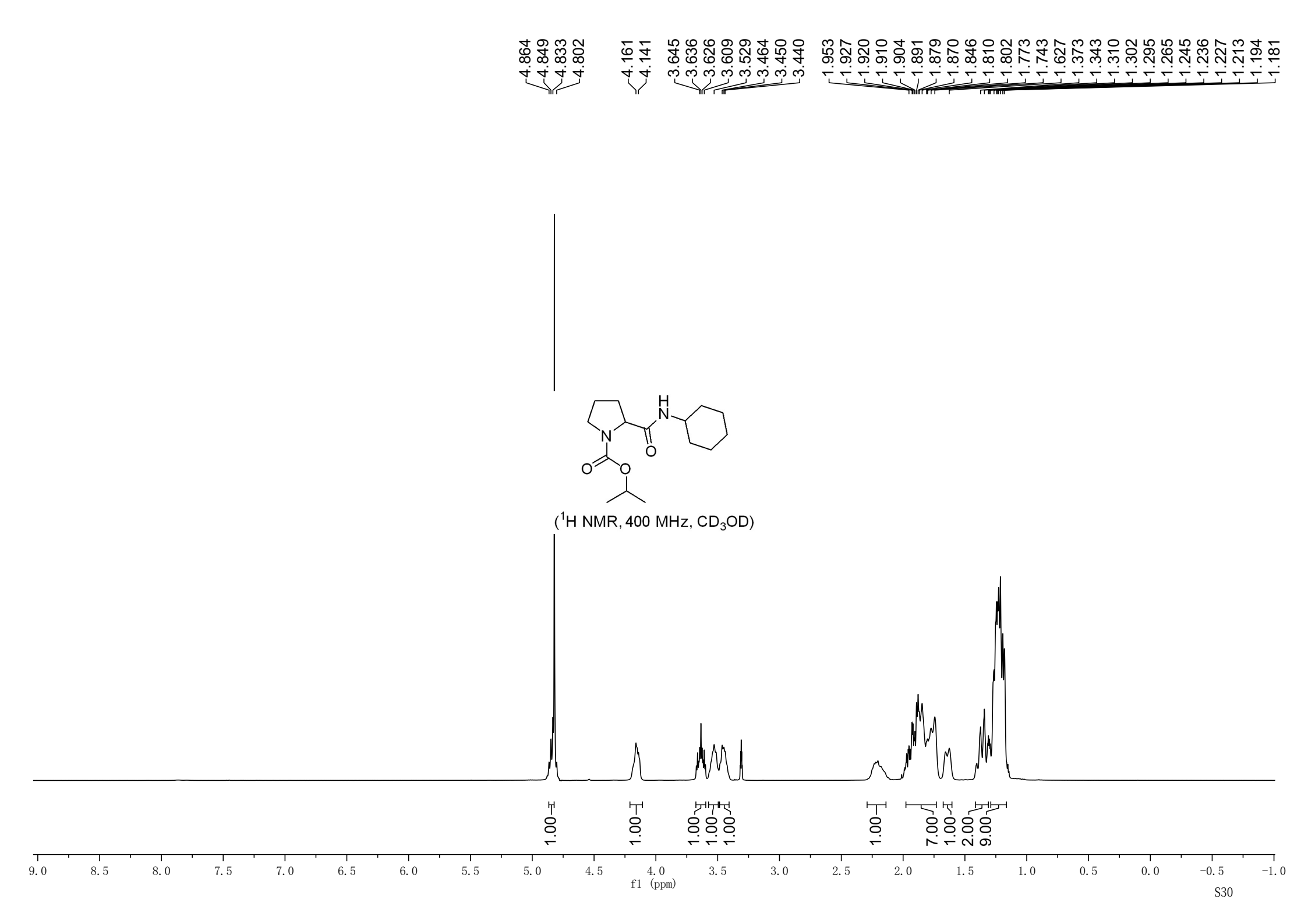
1 C.-M. Si, Z.-Y. Mao, Y.-W. Liu, Z.-T. Du, B.-G. Wei and G.-Q. Lin, *Org. Chem. Front.*, 2015, **2**, 1485-1499.

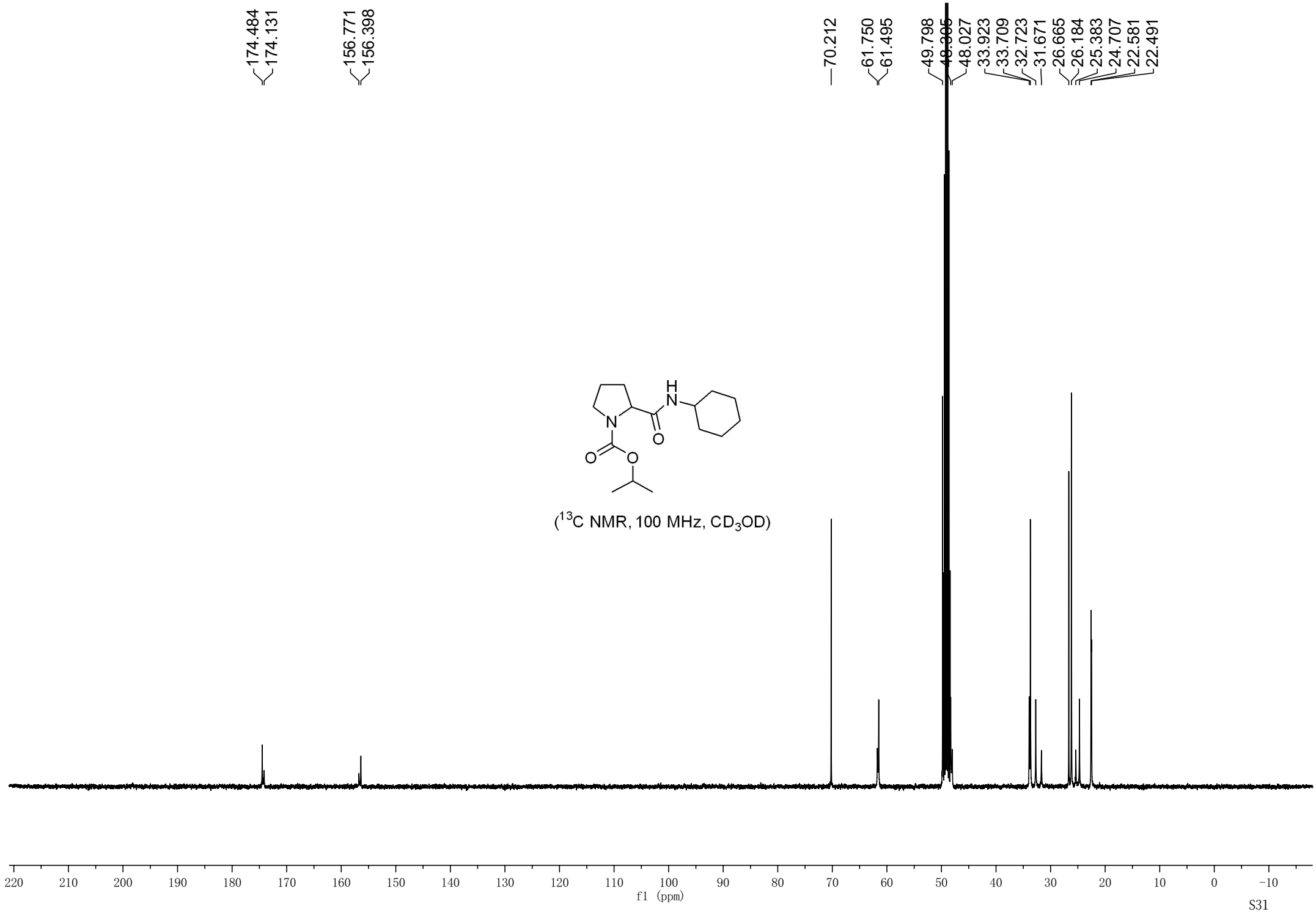
2 (a) Y. X. Zhang, L. Y. Chen, J. T. Sun, C. M. Si and B. G. Wei, *J. Org. Chem.*, 2020, **85**, 12603-12613; (b) X.-M. Wang, Y.-W. Liu, Q.-E. Wang, Z. Zhou, C.-M. Si and B.-G. Wei, *Tetrahedron*, 2019, **75**, 260-268; (c) W. Huang, J.-Y. Ma, M. Yuan, L.-F. Xu and B.-G. Wei, *Tetrahedron*, 2011, **67**, 7829-7837.

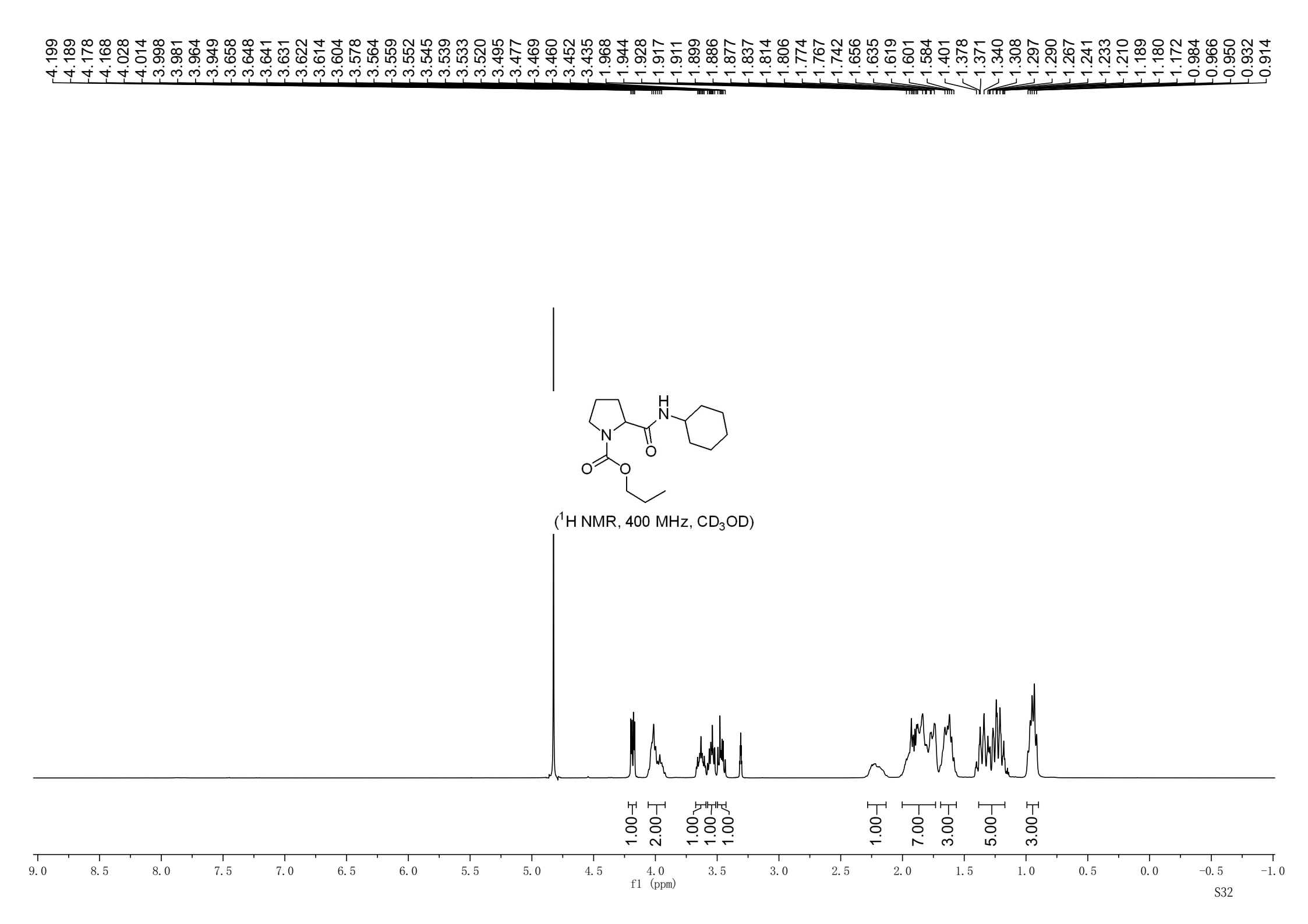
3 A. Greb, J.-S. Poh, S. Greed, C. Battilocchio, P. Pasau, D. C. Blakemore and S. V. Ley, *Angew. Chem. Int. Ed.*, 2017, **56**, 16602-16605.

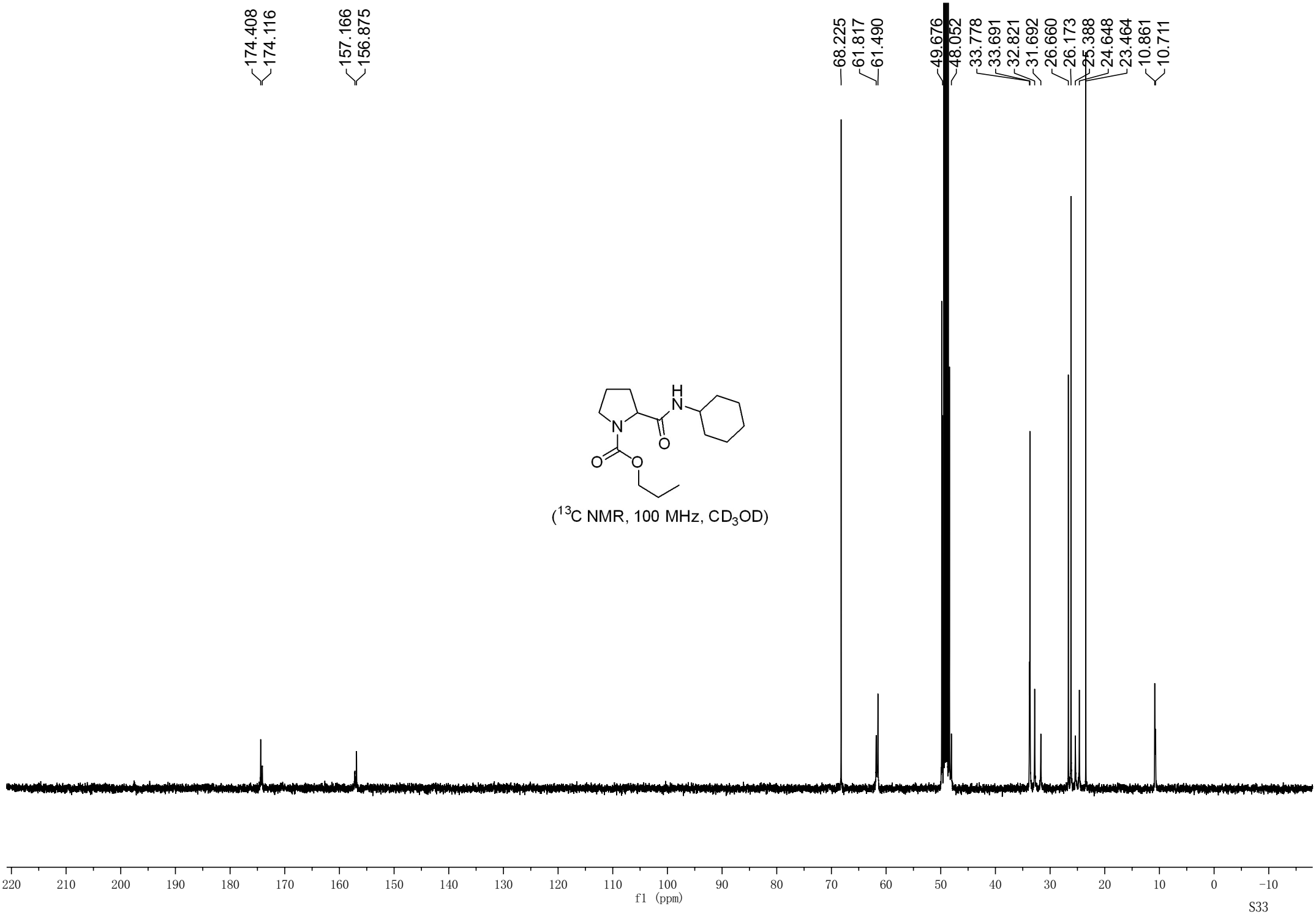

4.117
4.107
4.096
4.087
3.638
3.628
3.509
3.496
3.418
3.410
3.392
1.914
1.907
1.892
1.889
1.880
1.876
1.850
1.817
1.775
1.746
1.457
1.423
1.379
1.347
1.341
1.314
1.309
1.291
1.270
1.264
1.262
1.242
1.234
1.211
1.204
1.181
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.00
1.00
1.00
1.00
1.00
7.00
1.00
2.50
6.50
5.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

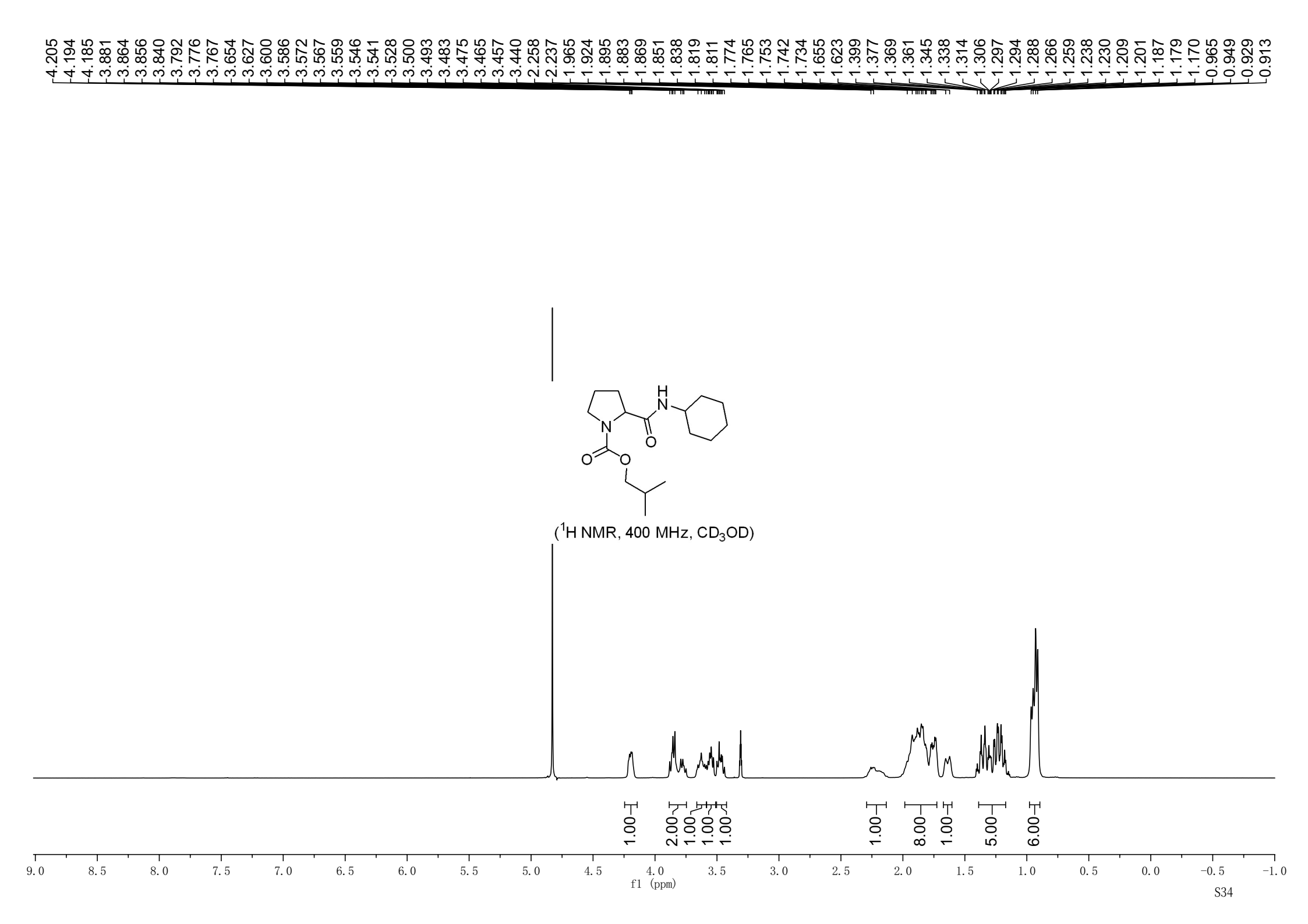

174.710
174.271
156.380
156.078
81.334
81.187
61.741
61.477
49.819
47.989
33.937
33.820
32.751
31.574
28.734
26.649
26.206
25.365
24.684
H
N
N
Boc
O
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

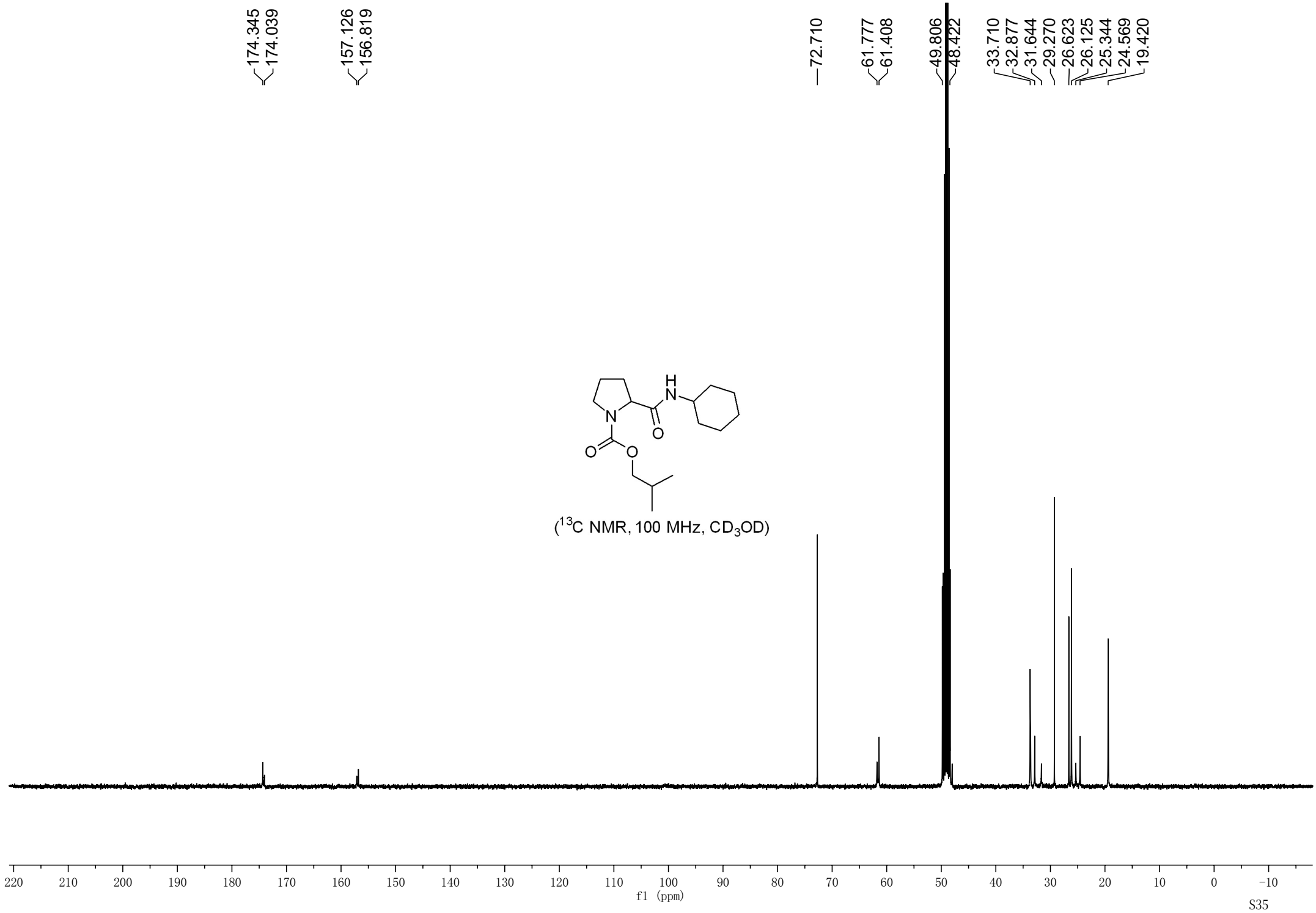

4.864
4.849
4.833
4.802
4.161
4.141
3.645
3.636
3.626
3.609
3.529
3.464
3.450
3.440
1.953
1.927
1.920
1.910
1.904
1.891
1.879
1.870
1.846
1.810
1.802
1.773
1.743
1.627
1.373
1.343
1.310
1.302
1.295
1.265
1.245
1.236
1.227
1.213
1.194
1.181
H
N
N
O
O
O
(^{1}H NMR, 400 MHz, CD$_3$OD)
1.00
1.00
1.00
1.00
1.00
1.00
7.00
1.00
2.00
9.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

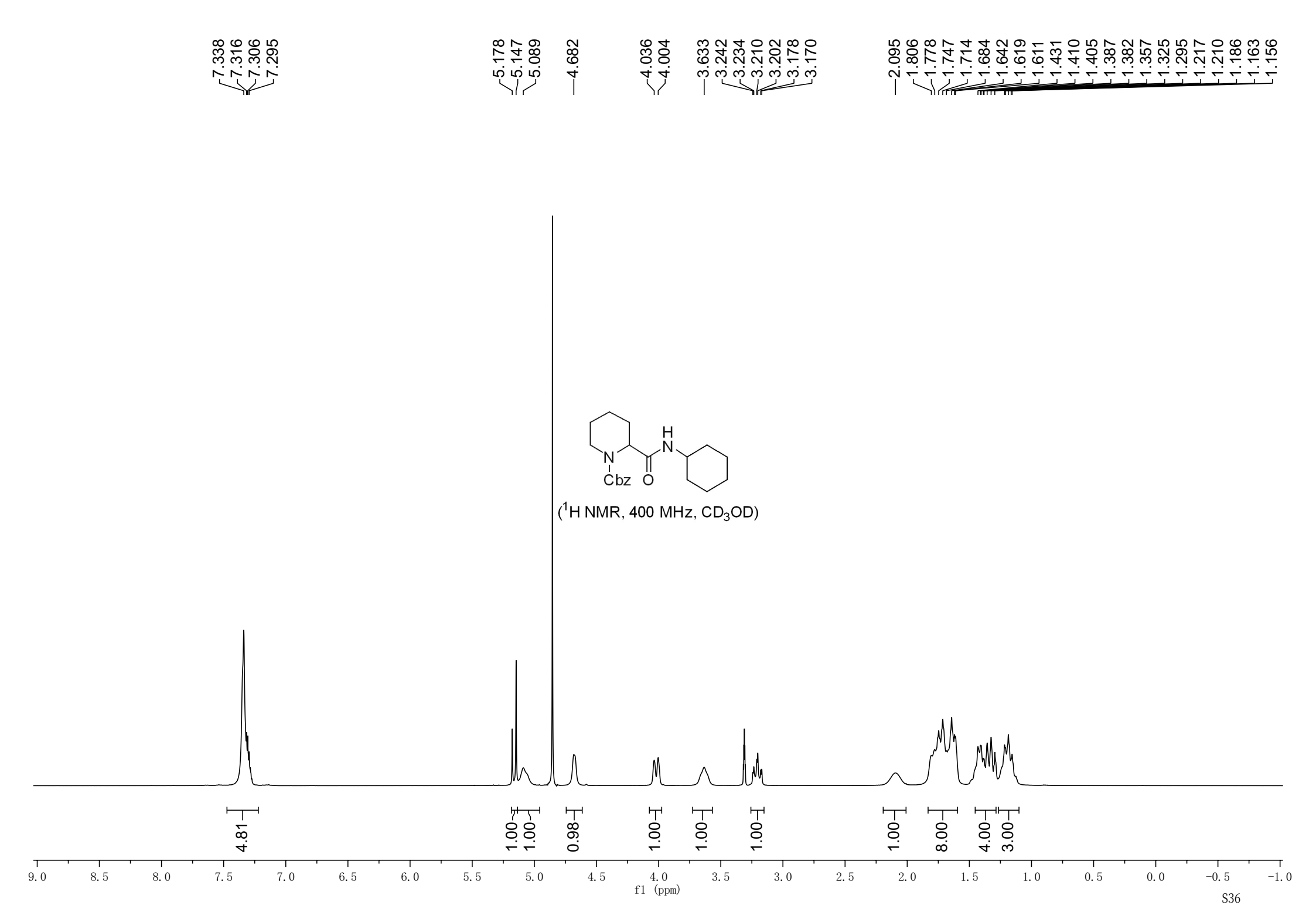

174.484
174.131
156.771
156.398
70.212
61.750
61.495
49.798
48.305
48.027
33.923
33.709
32.723
31.671
26.665
26.184
25.383
24.707
22.581
22.491
H
N
N
O
O
O
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

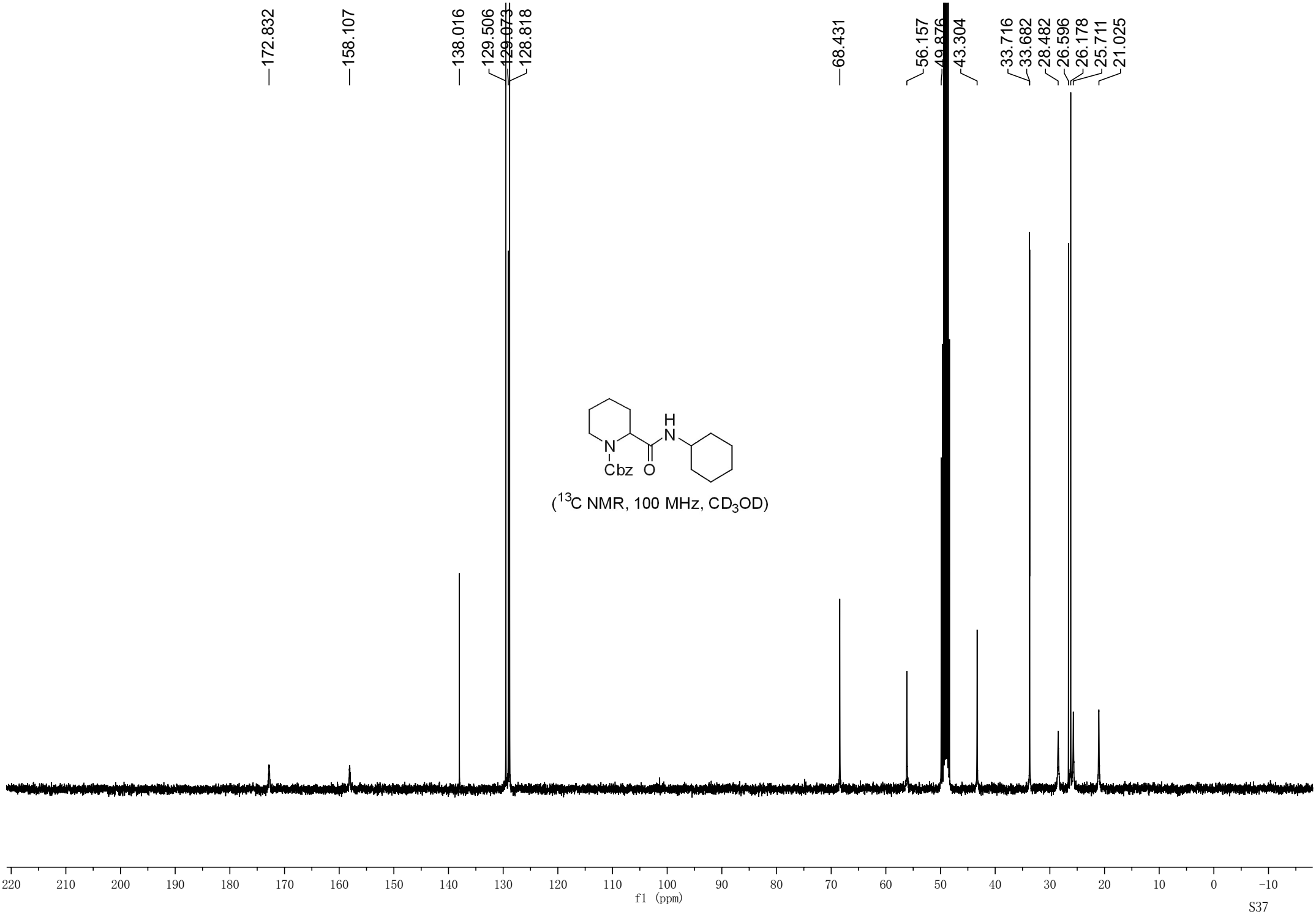

4.199
4.189
4.178
4.168
4.028
4.014
3.998
3.981
3.964
3.949
3.658
3.648
3.641
3.631
3.622
3.614
3.604
3.578
3.564
3.559
3.552
3.545
3.539
3.533
3.520
3.495
3.477
3.469
3.460
3.452
3.435
1.968
1.944
1.928
1.917
1.911
1.899
1.886
1.877
1.837
1.814
1.806
1.774
1.767
1.742
1.656
1.635
1.619
1.601
1.584
1.401
1.378
1.371
1.340
1.308
1.297
1.290
1.267
1.241
1.233
1.210
1.189
1.180
1.172
0.984
0.966
0.950
0.932
0.914
H
N
N
O
O
O
(^{1}H NMR, 400 MHz, CD_3OD)
1.00
2.00
1.00
1.00
1.00
1.00
7.00
3.00
5.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

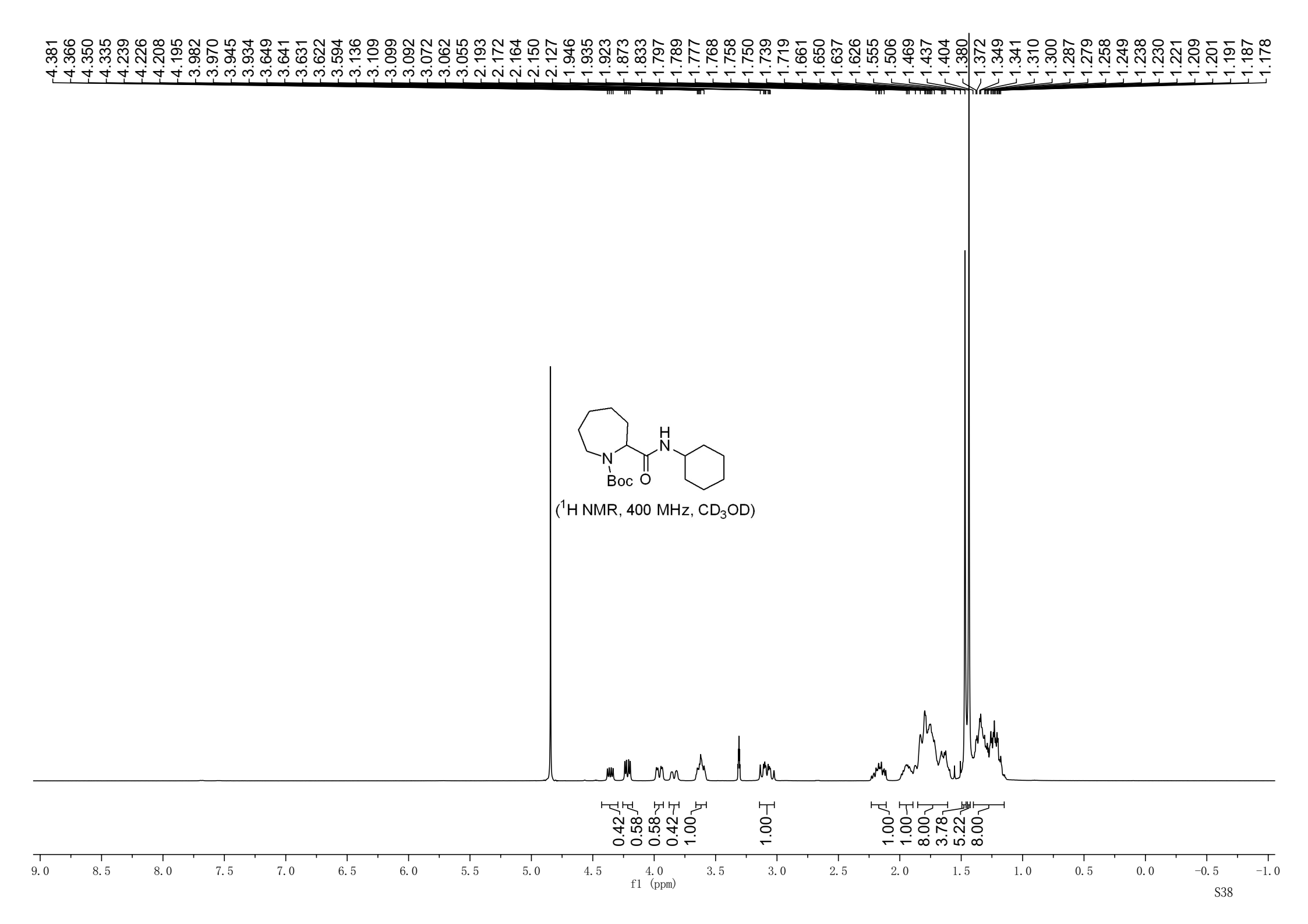

174.408
174.116
157.166
156.875
68.225
61.817
61.490
49.676
48.052
33.778
33.691
32.821
31.692
26.660
26.173
25.388
24.648
23.464
10.861
10.711
H
N
N
O
O
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

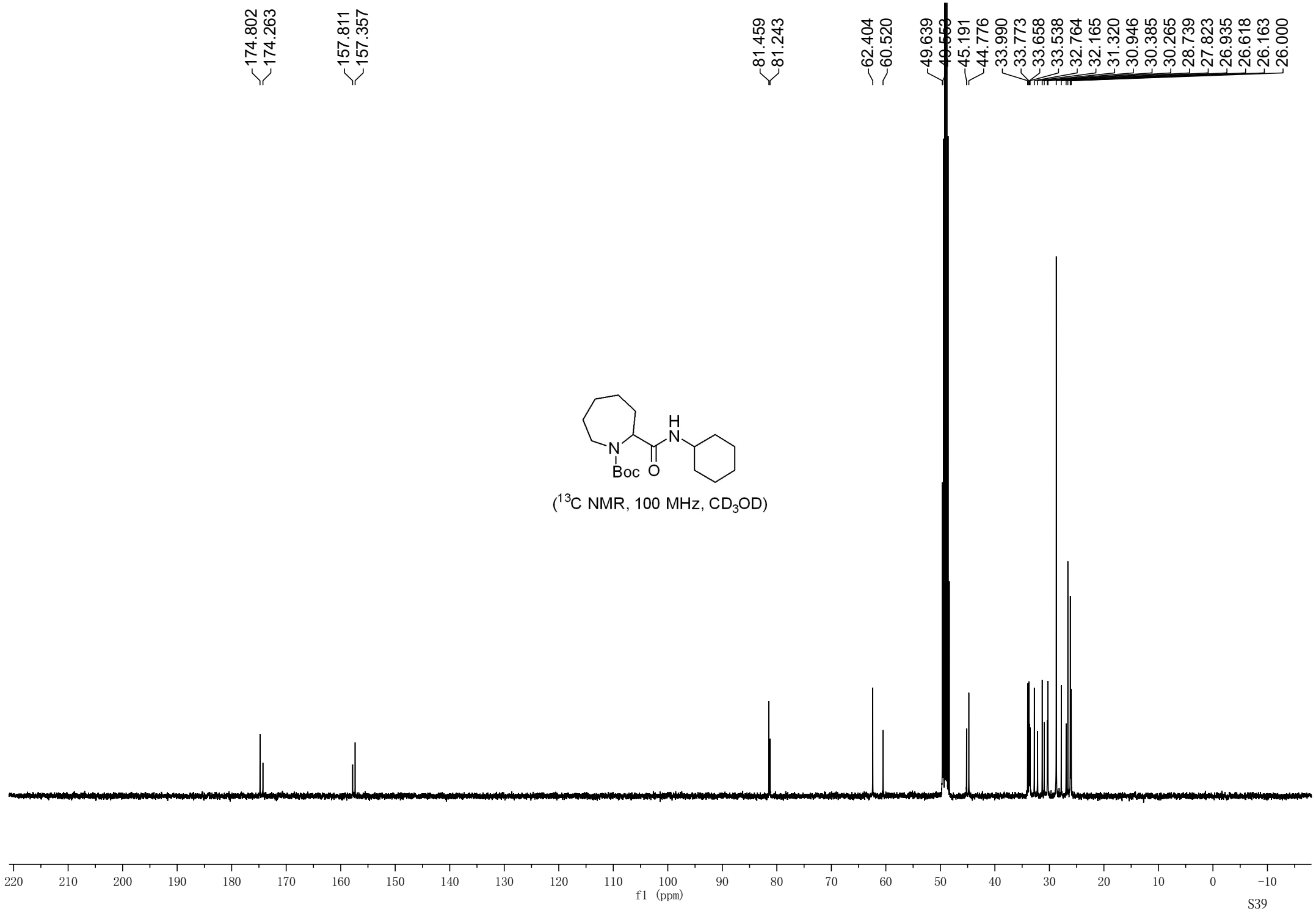

4.205
4.194
4.185
3.881
3.864
3.856
3.840
3.792
3.776
3.767
3.654
3.627
3.600
3.586
3.572
3.567
3.559
3.546
3.541
3.528
3.500
3.493
3.483
3.475
3.465
3.457
3.440
2.258
2.237
1.965
1.924
1.895
1.883
1.869
1.851
1.838
1.819
1.811
1.774
1.765
1.753
1.742
1.734
1.655
1.623
1.399
1.377
1.369
1.361
1.345
1.338
1.314
1.306
1.297
1.294
1.288
1.266
1.259
1.238
1.230
1.209
1.201
1.187
1.179
1.170
0.965
0.949
0.929
0.913
H
N
N
O
O
O
(^{1}H NMR, 400 MHz, CD_3OD)
1.00
2.00
1.00
1.00
1.00
1.00
8.00
1.00
5.00
6.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

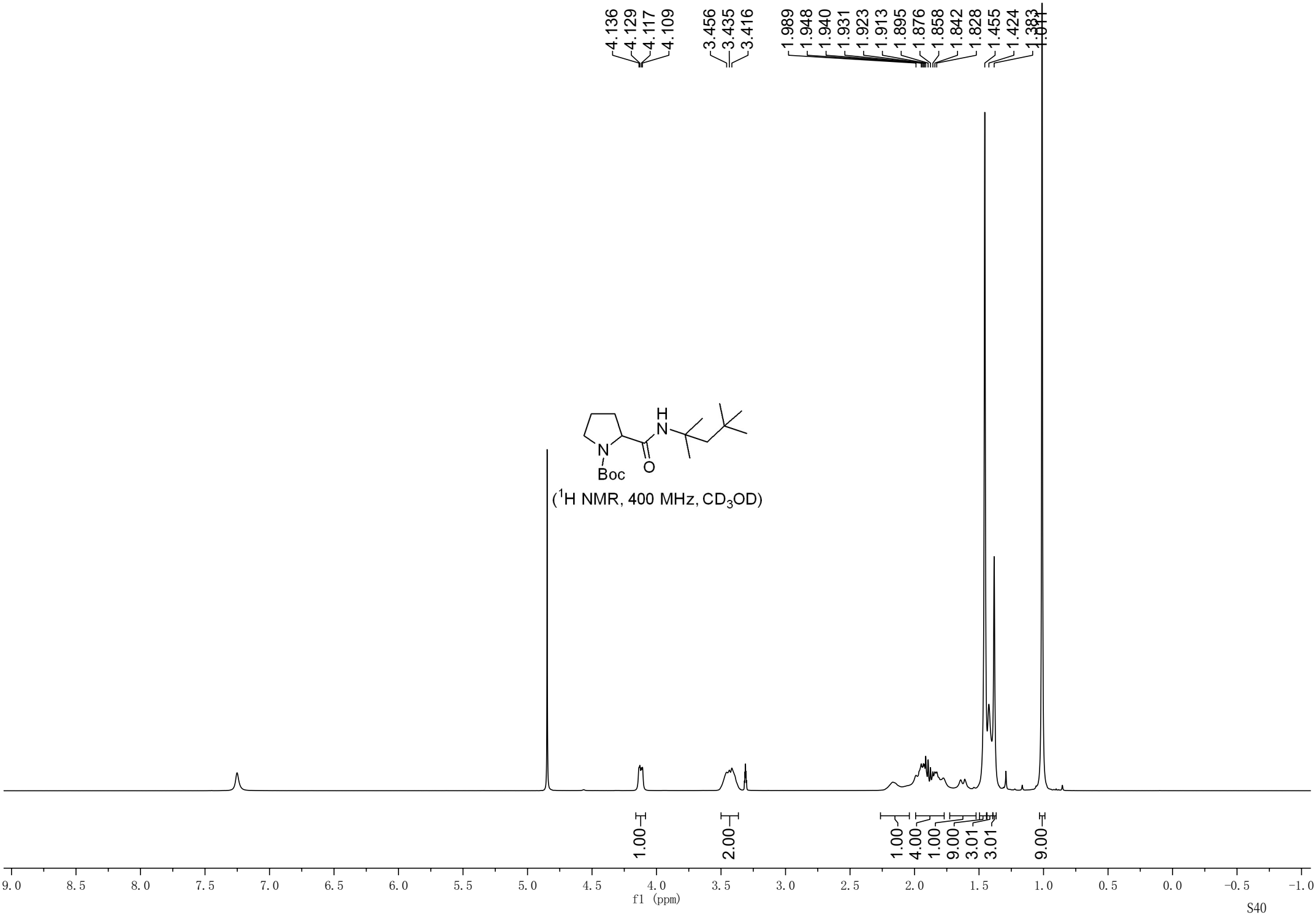

174.345
174.039
157.126
156.819
72.710
61.777
61.408
49.806
48.422
33.710
32.877
31.644
29.270
26.623
26.125
25.344
24.569
19.420
H
N
N
O
O
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

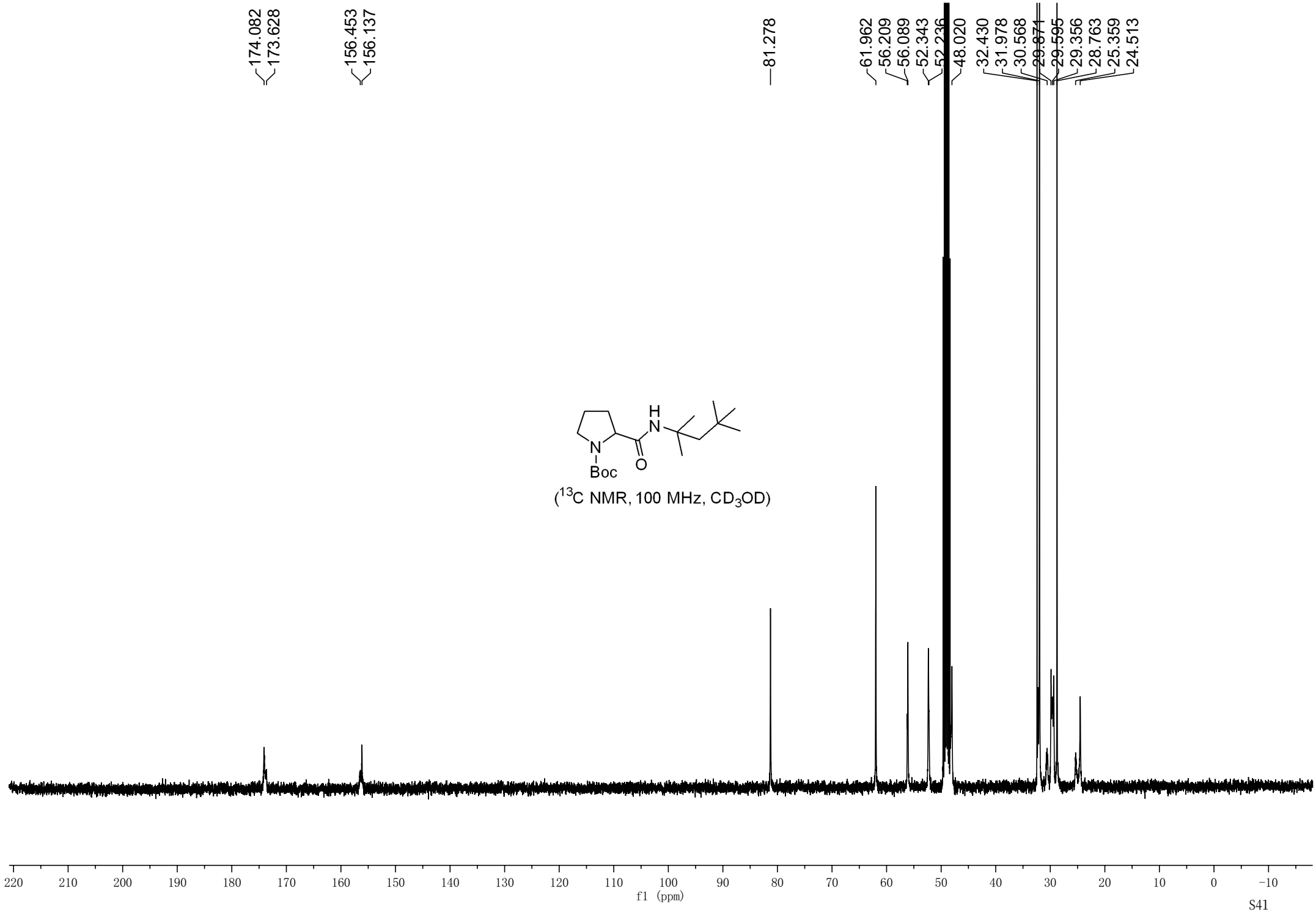

7.338
7.316
7.306
7.295
5.178
5.147
5.089
4.682
4.036
4.004
3.633
3.242
3.234
3.210
3.202
3.178
3.170
2.095
1.806
1.778
1.747
1.714
1.684
1.642
1.619
1.611
1.431
1.410
1.405
1.387
1.382
1.357
1.325
1.295
1.217
1.210
1.186
1.163
1.156
Cbz
O
N
H
N
(1H NMR, 400 MHz, CD3OD)
4.81
1.00
1.00
0.98
1.00
1.00
1.00
1.00
8.00
4.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

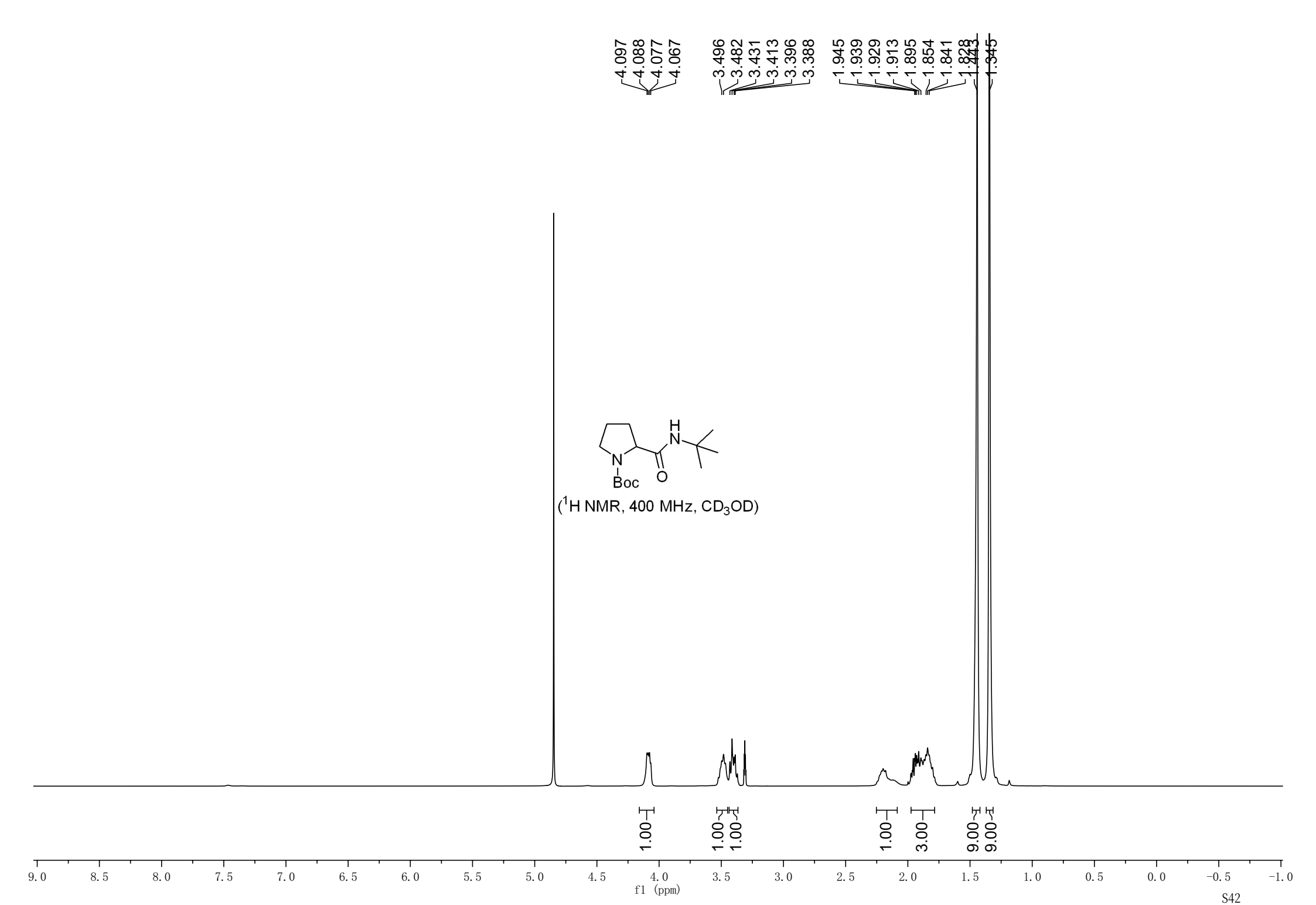

172.832
158.107
138.016
129.506
129.073
128.818
68.431
56.157
49.876
43.304
33.716
33.682
28.482
26.596
26.178
25.711
21.025
H
N
N
Cbz
O
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

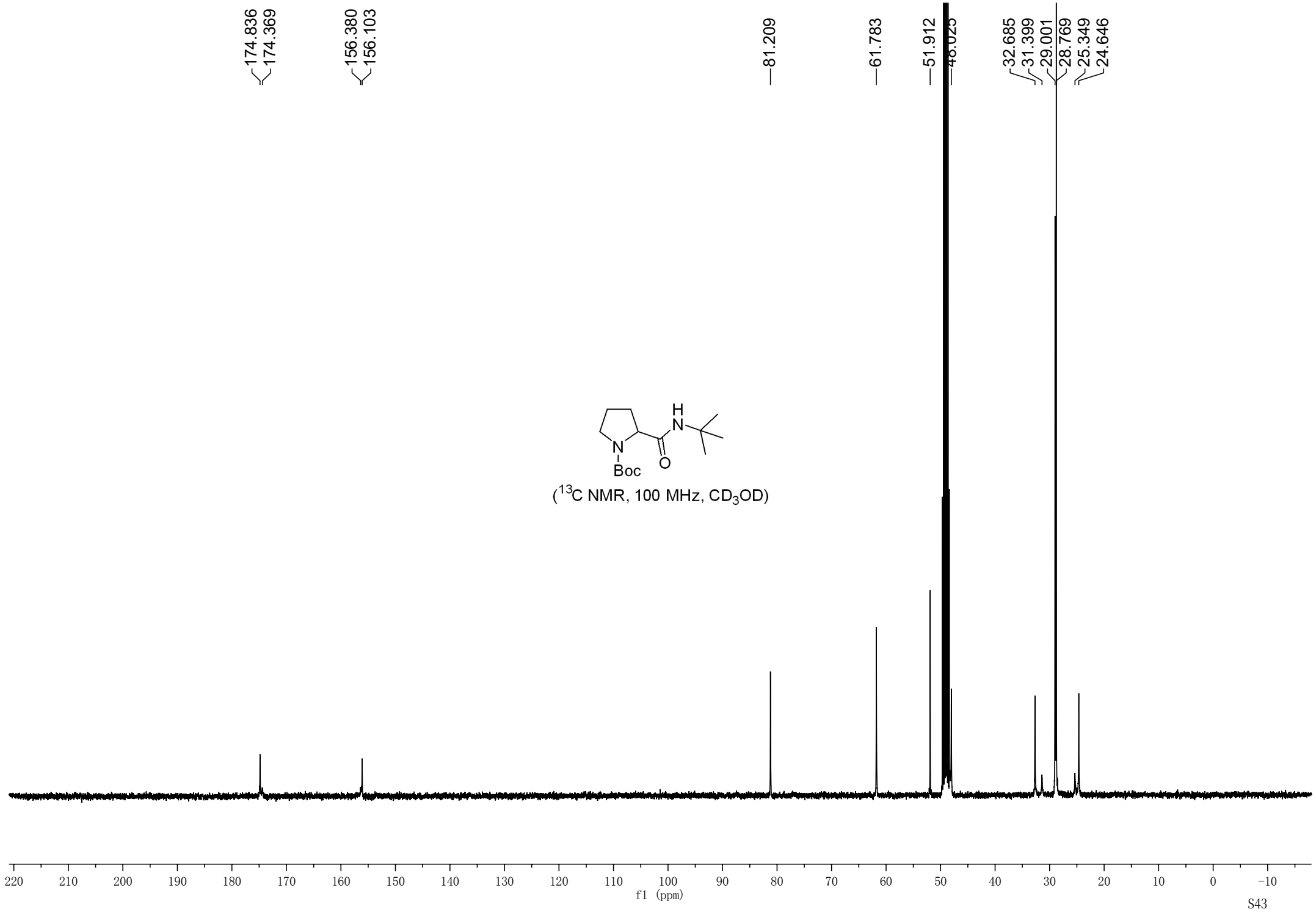

4.381
4.366
4.350
4.335
4.239
4.226
4.208
4.195
3.982
3.970
3.945
3.934
3.649
3.641
3.631
3.622
3.594
3.136
3.109
3.099
3.092
3.072
3.062
3.055
2.193
2.172
2.164
2.150
2.127
1.946
1.935
1.923
1.873
1.833
1.797
1.789
1.777
1.768
1.758
1.750
1.739
1.719
1.661
1.650
1.637
1.626
1.555
1.506
1.469
1.437
1.404
1.380
1.372
1.349
1.341
1.310
1.300
1.287
1.279
1.258
1.249
1.238
1.230
1.221
1.209
1.201
1.191
1.187
1.178
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
0.42
0.58
0.58
0.42
1.00
1.00
1.00
1.00
8.00
3.78
5.22
8.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

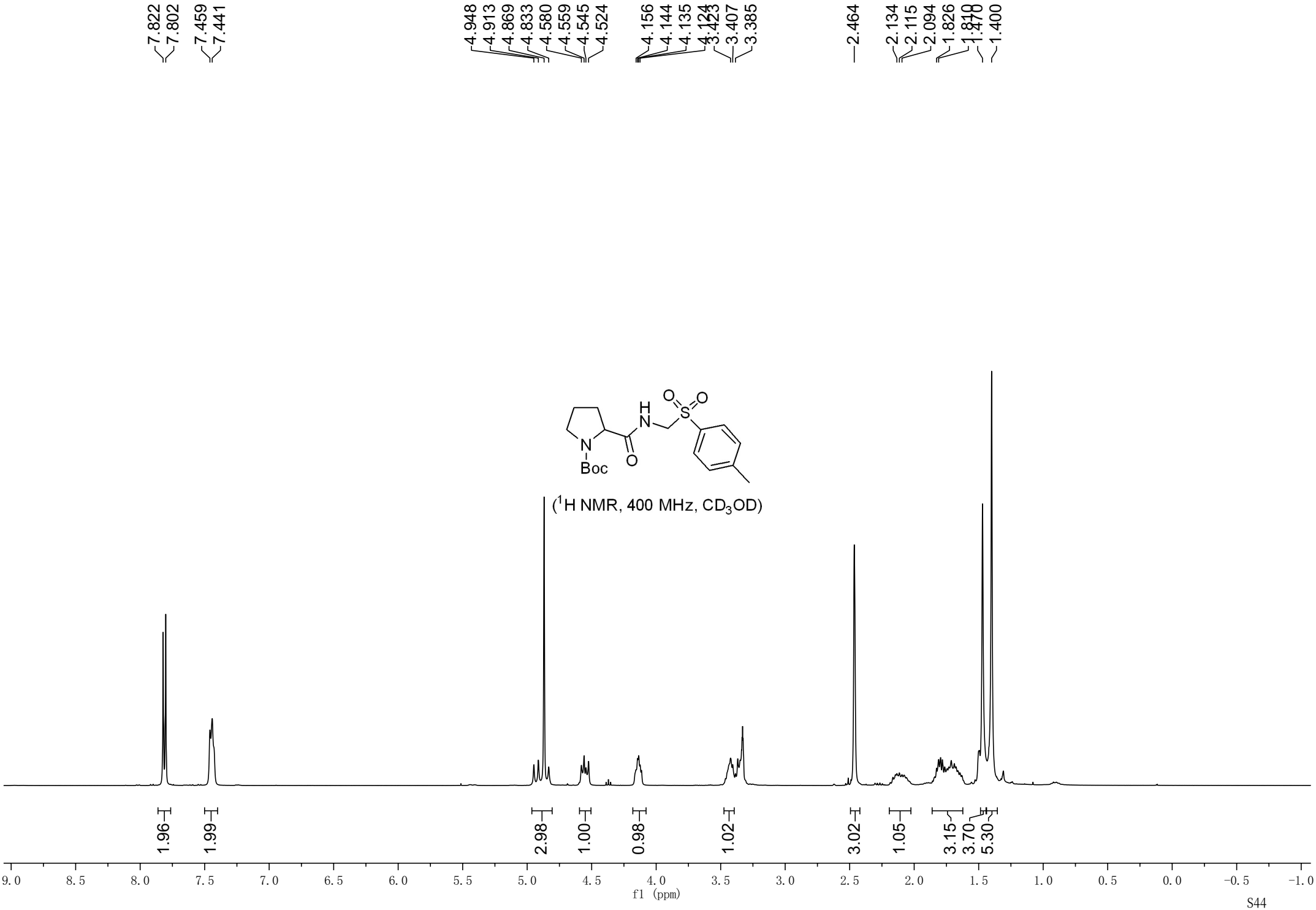

174.802
174.263
157.811
157.357
81.459
81.243
62.404
60.520
49.639
49.553
45.191
44.776
33.990
33.773
33.658
33.538
32.764
32.165
31.320
30.946
30.385
30.265
28.739
27.823
26.935
26.618
26.163
26.000
H
N
N
Boc
O
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

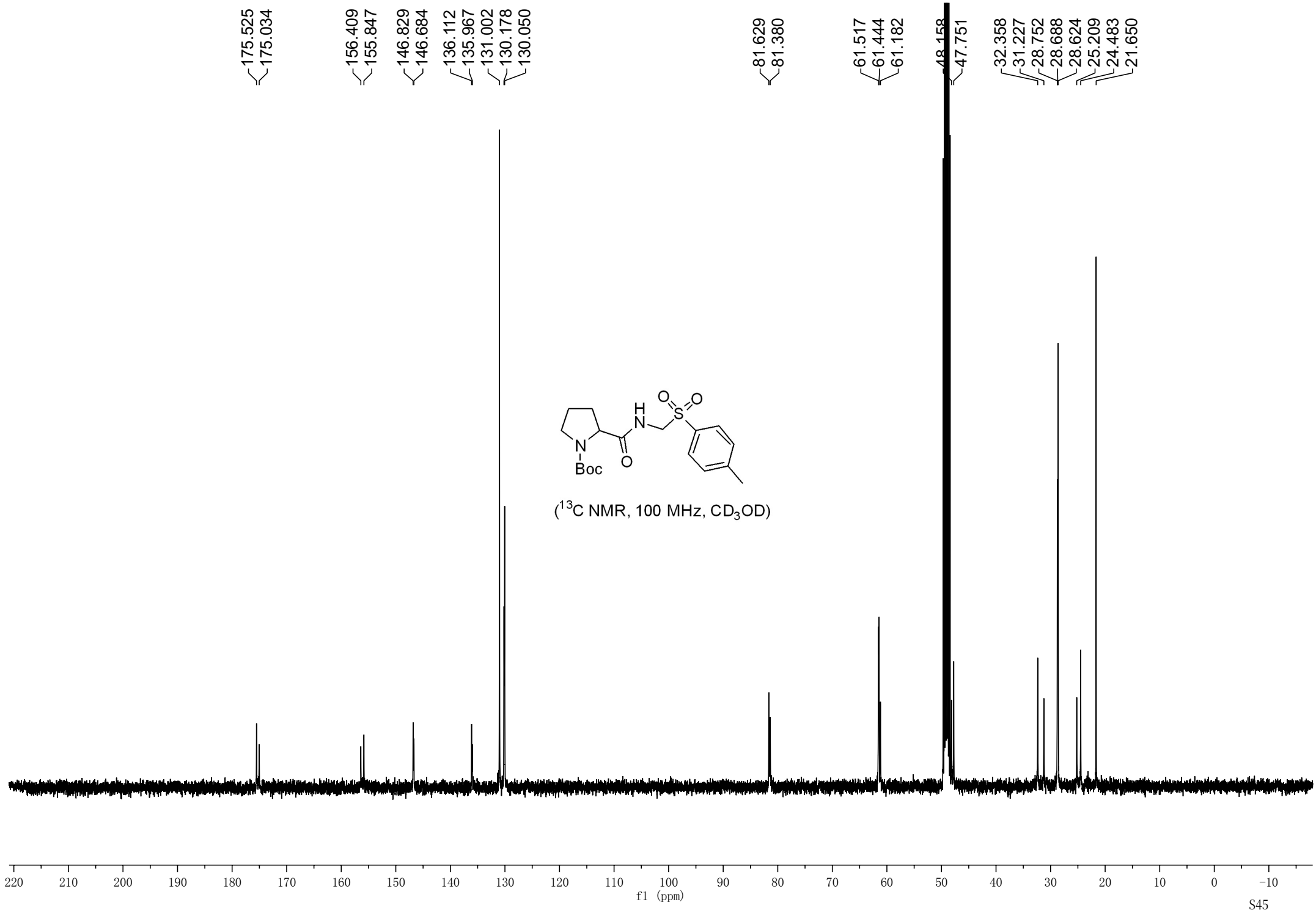

4.136
4.129
4.117
4.109
3.456
3.435
3.416
1.989
1.948
1.940
1.931
1.923
1.913
1.895
1.876
1.858
1.842
1.828
1.455
1.424
1.383
1.341
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.00
2.00
1.00
4.00
1.00
9.00
3.01
3.01
9.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

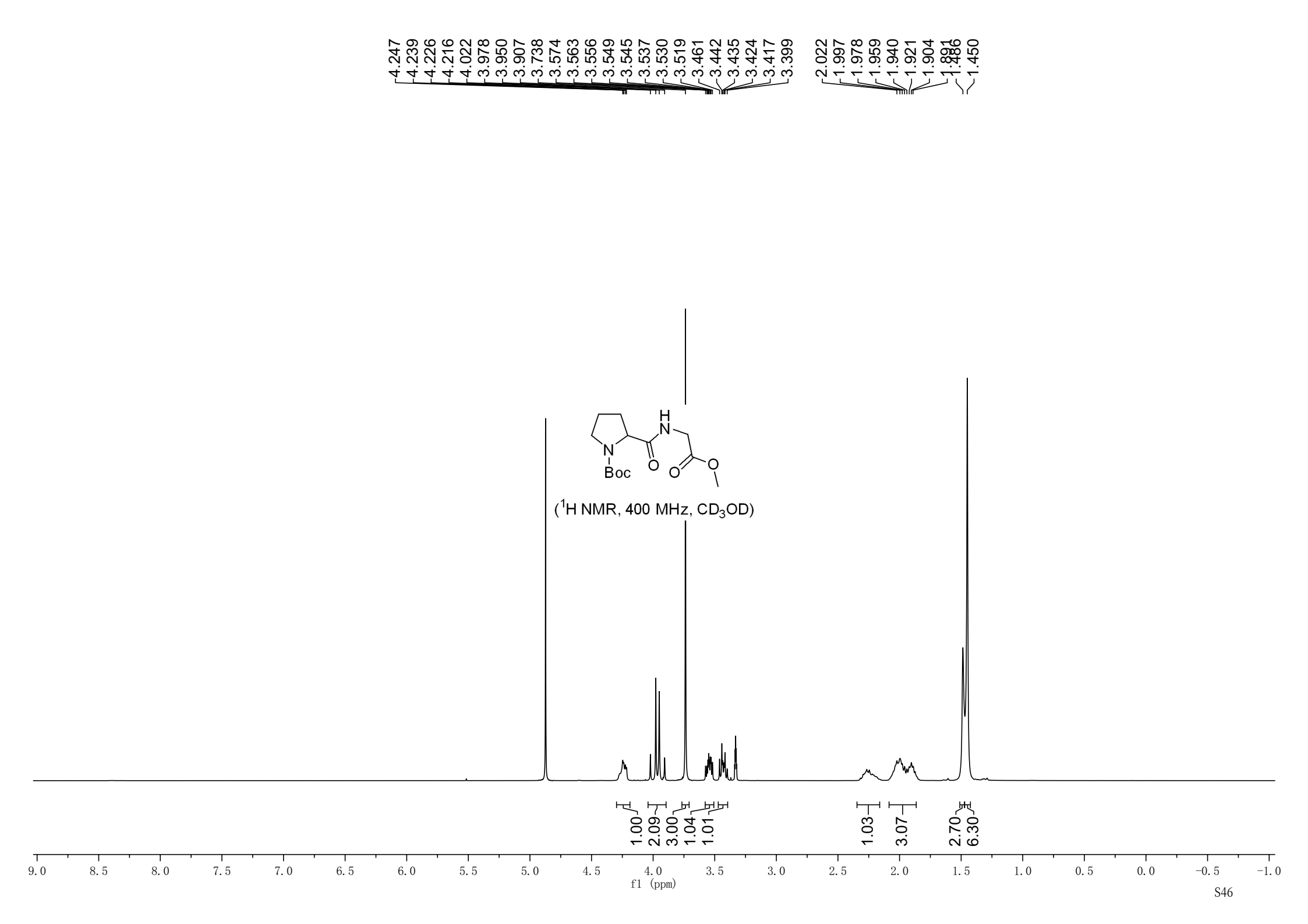

174.082
173.628
156.453
156.137
81.278
61.962
56.209
56.089
52.343
52.236
48.020
32.430
31.978
30.568
29.871
29.595
29.356
28.763
25.359
24.513
N
H
N
O
Boc
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

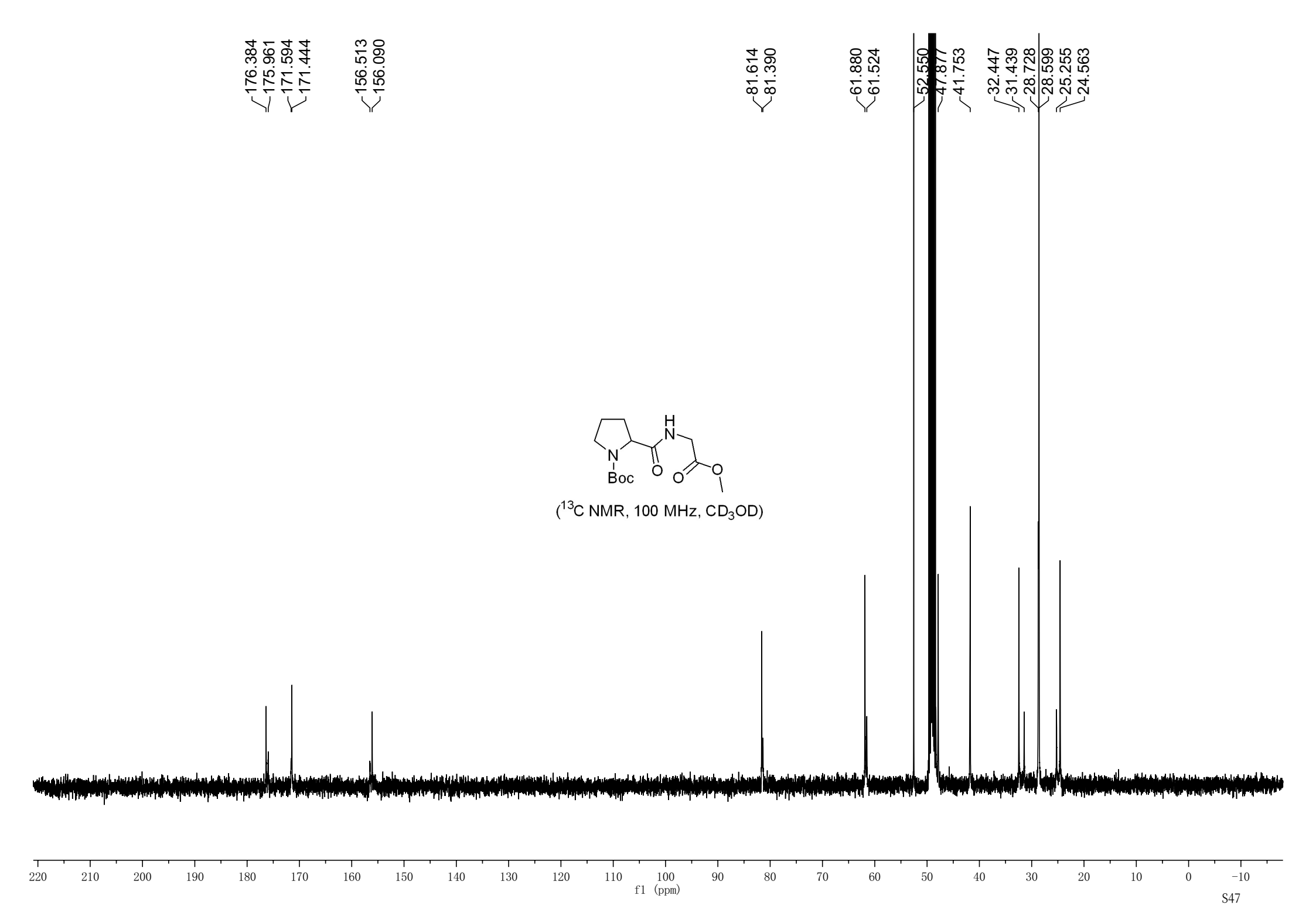

4.097
4.088
4.077
4.067
3.496
3.482
3.431
3.413
3.396
3.388
1.945
1.939
1.929
1.913
1.895
1.854
1.841
1.828
1.443
1.345
Boc
(1H NMR, 400 MHz, CD3OD)
1.00
1.00
1.00
1.00
3.00
9.00
9.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

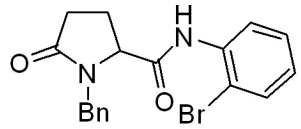

174.836
174.369
156.380
156.103
81.209
61.783
51.912
48.025
32.685
31.399
29.001
28.769
25.349
24.646
H
N
N
O
Boc
(^{13}C NMR, 100 MHz, CD_3OD)
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10
f1 (ppm)


7.822
7.802
7.459
7.441
4.948
4.913
4.869
4.833
4.580
4.559
4.545
4.524
4.156
4.144
4.135
4.124
4.123
3.407
3.385
2.464
2.134
2.115
2.094
1.826
1.810
1.470
1.400
Boc
(1H NMR, 400 MHz, CD3OD)
1.96
1.99
2.98
1.00
0.98
1.02
3.02
1.05
3.15
3.70
5.30
f1 (ppm)

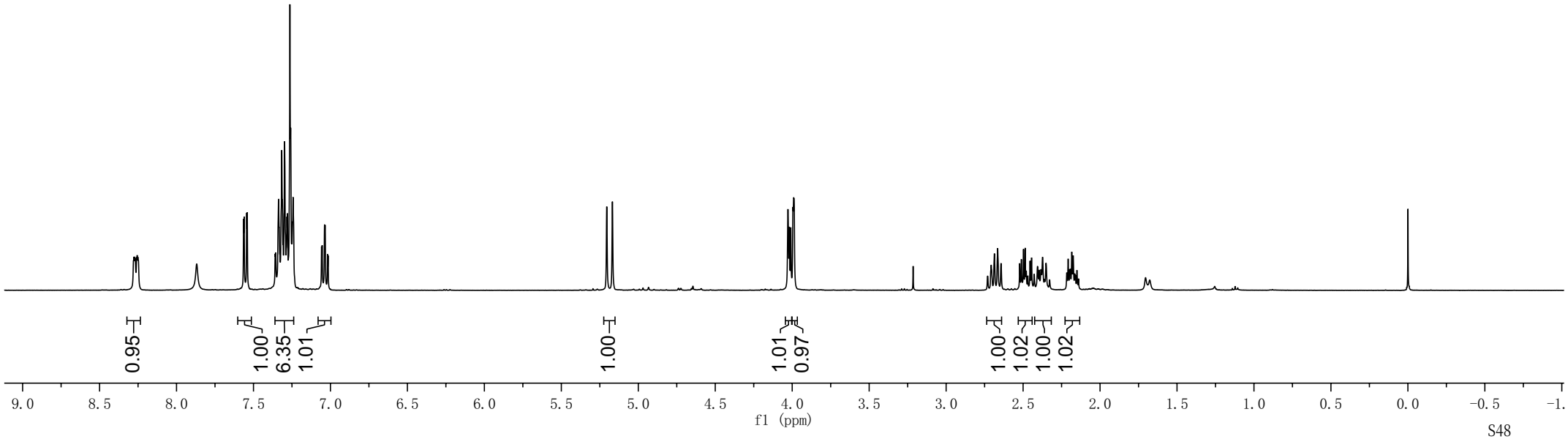

175.525
175.034
156.409
155.847
146.829
146.684
136.112
135.967
131.002
130.178
130.050
81.629
81.380
61.517
61.444
61.182
48.158
47.751
32.358
31.227
28.752
28.688
28.624
25.209
24.483
21.650
Boc
(^{13}C NMR, 100 MHz, CD_3OD)
f1 (ppm)

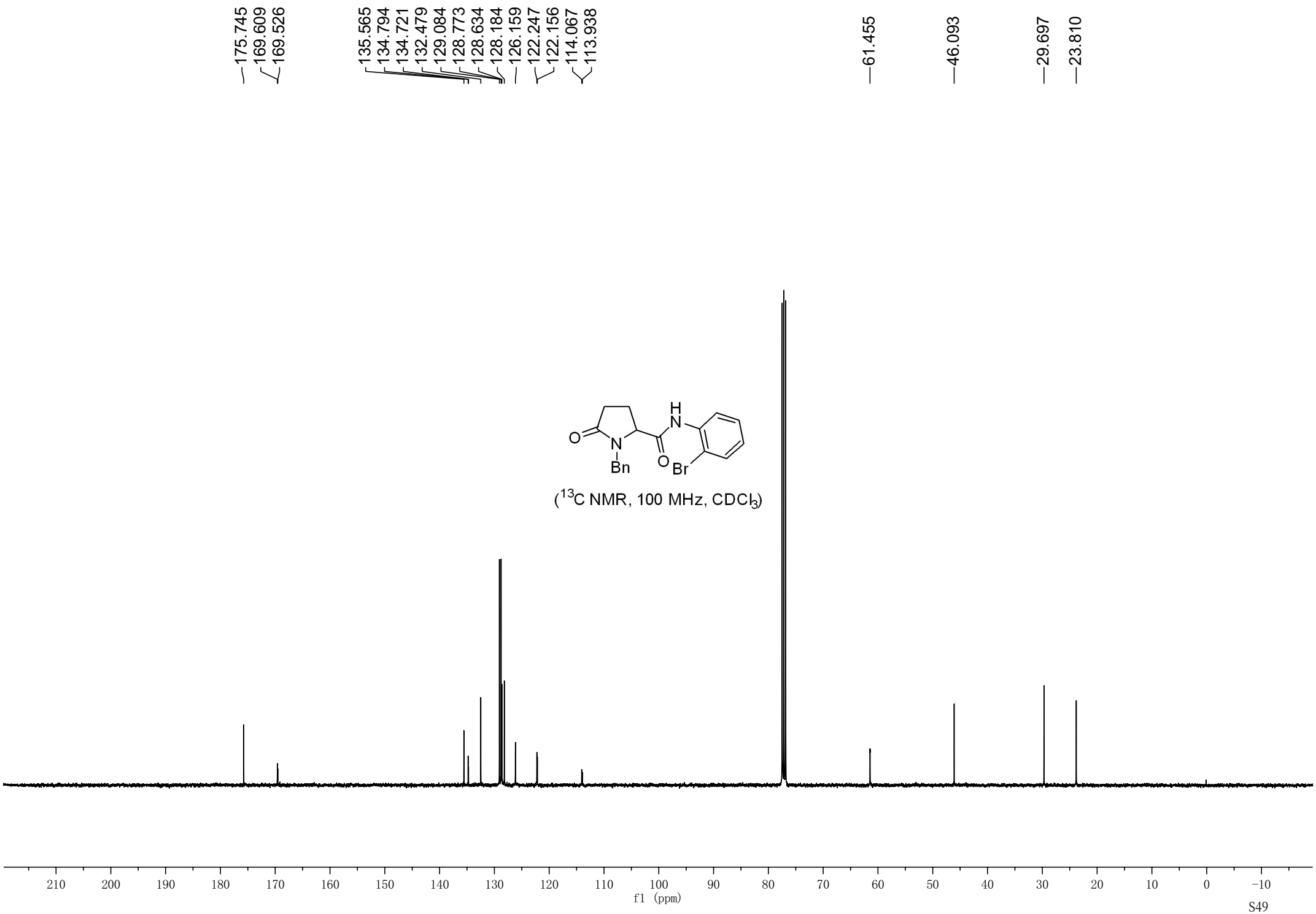

4.247
4.239
4.226
4.216
4.022
3.978
3.950
3.907
3.738
3.574
3.563
3.556
3.549
3.545
3.537
3.530
3.519
3.461
3.442
3.435
3.424
3.417
3.399
2.022
1.997
1.978
1.959
1.940
1.921
1.904
1.891
1.886
1.450
N
H
N
Boc
O
O
O
(^{1}H NMR, 400 MHz, CD$_3$OD)
1.00
2.09
3.00
1.04
1.01
1.03
3.07
2.70
6.30
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

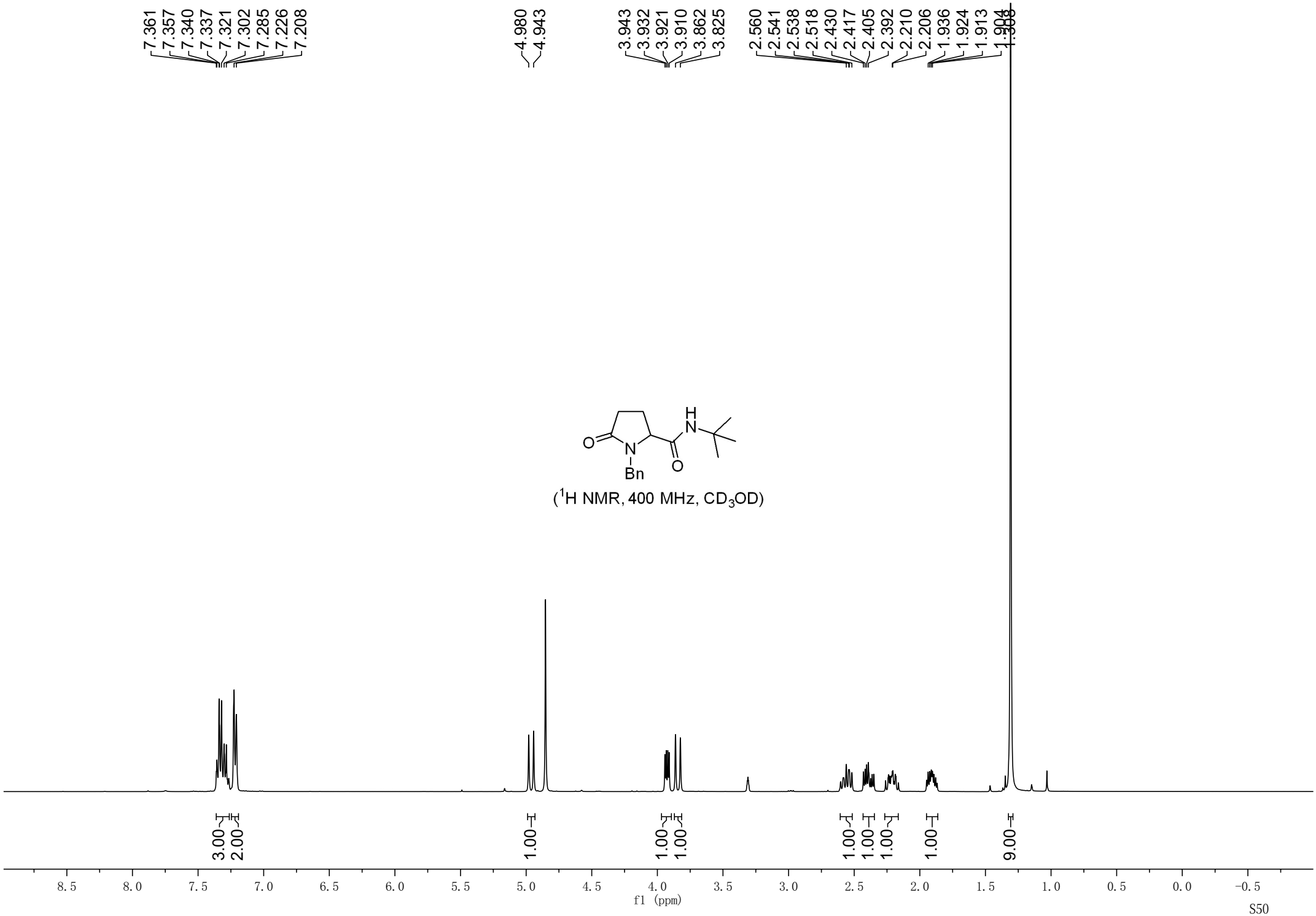

176.384
175.961
171.594
171.444
156.513
156.090
81.614
81.390
61.880
61.524
52.550
47.877
41.753
32.447
31.439
28.728
28.599
25.255
24.563
H
N
N
Boc
O
O
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

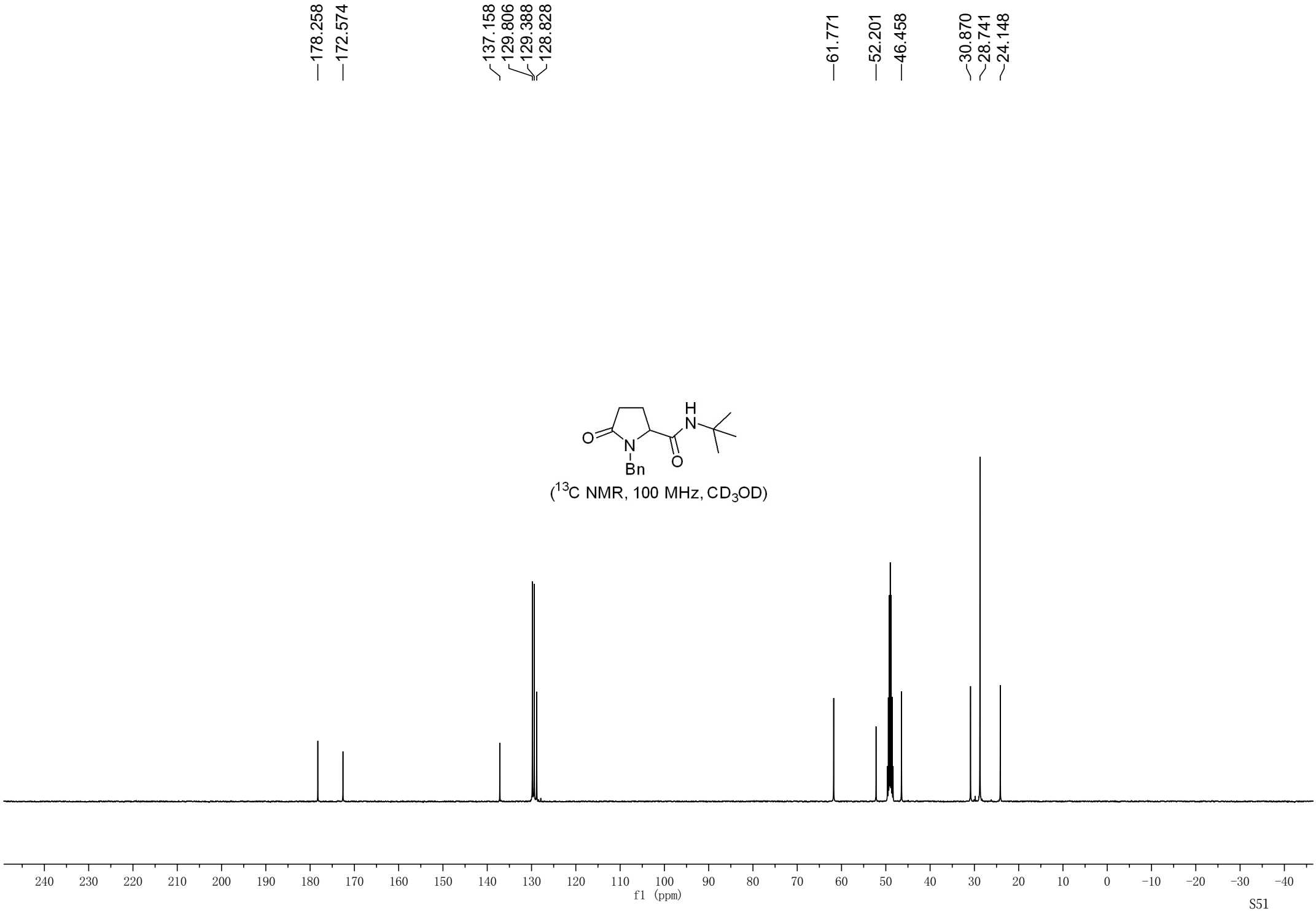


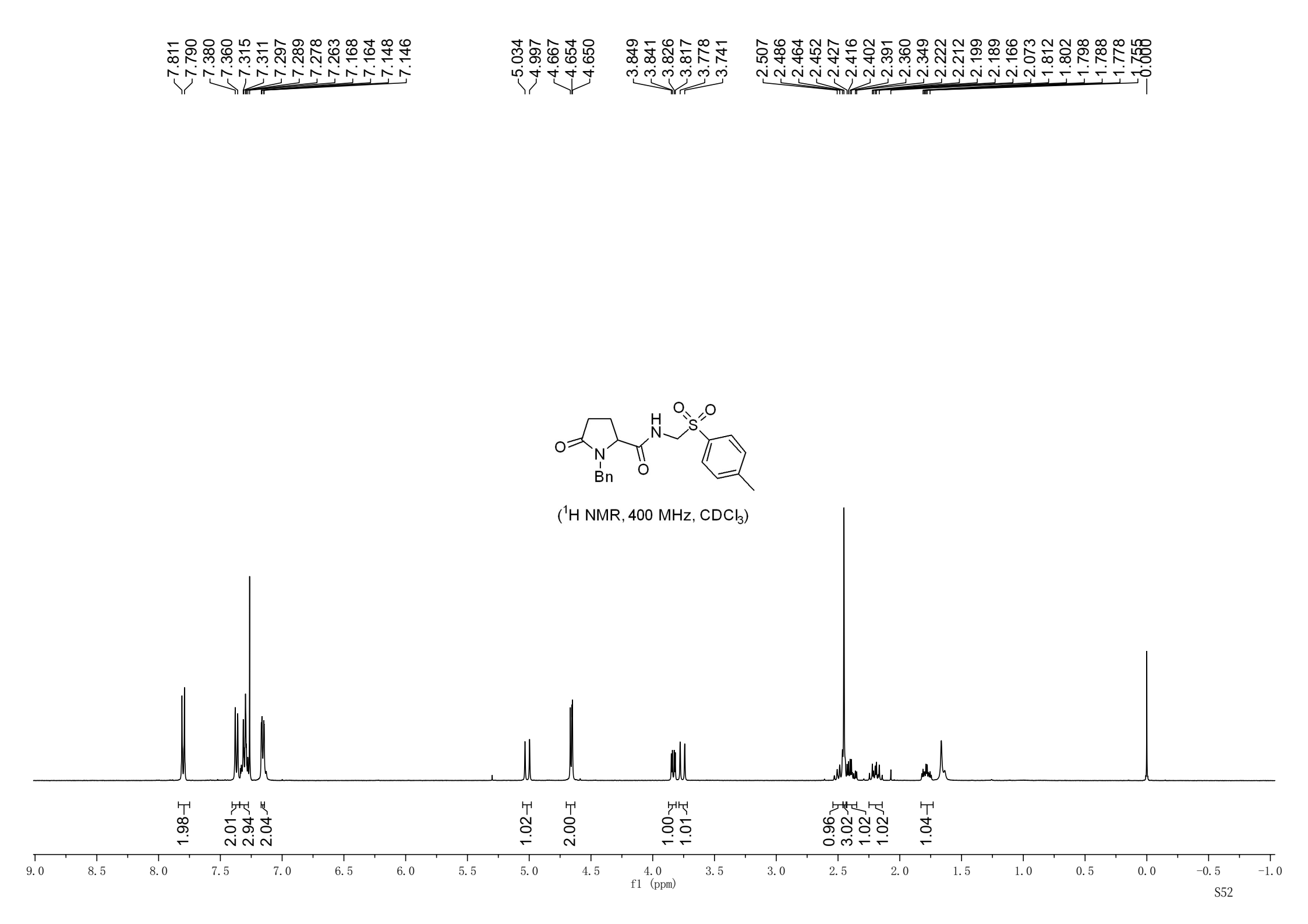
(^{1}H NMR, 400 MHz, $CDCl_3$)

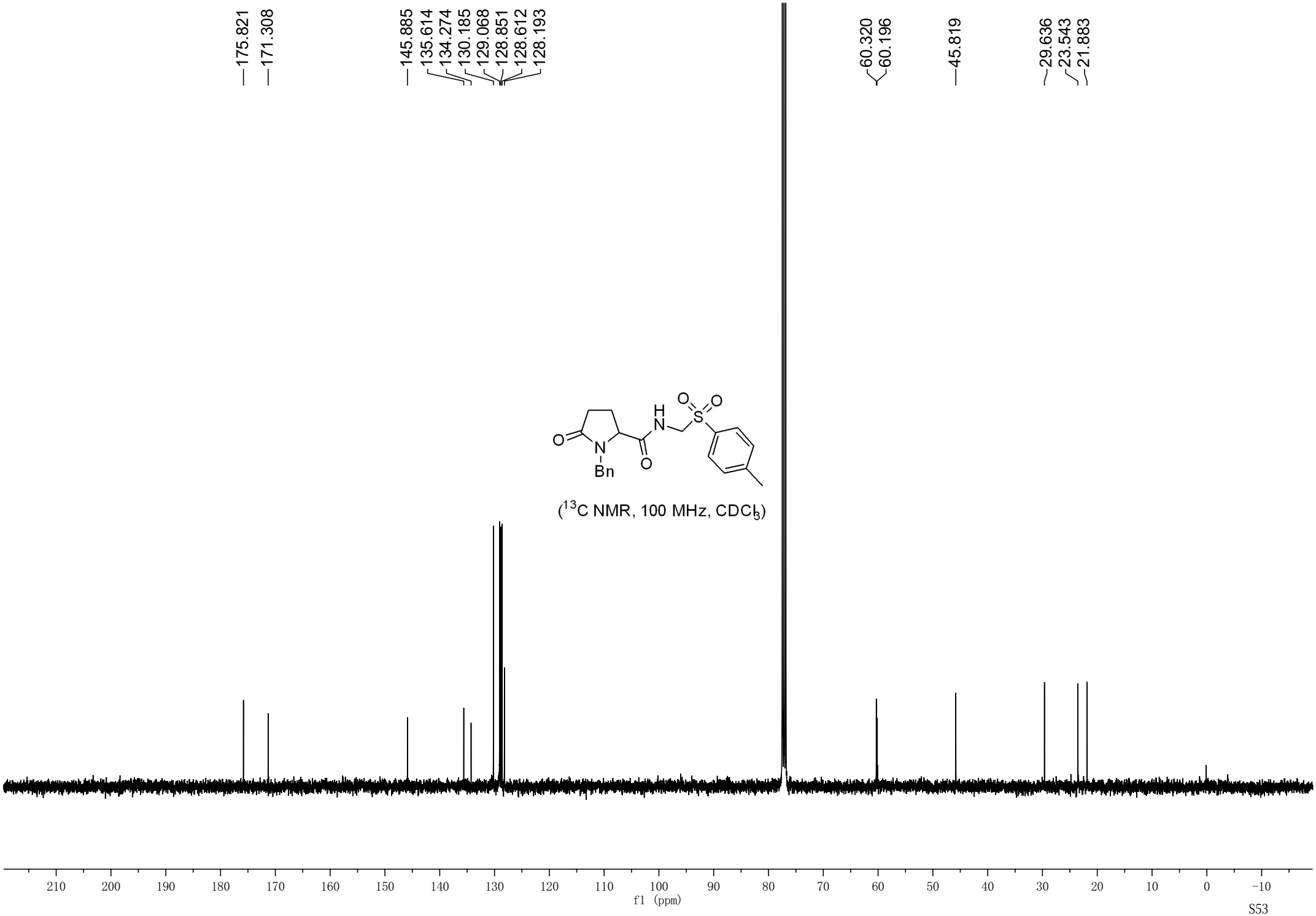


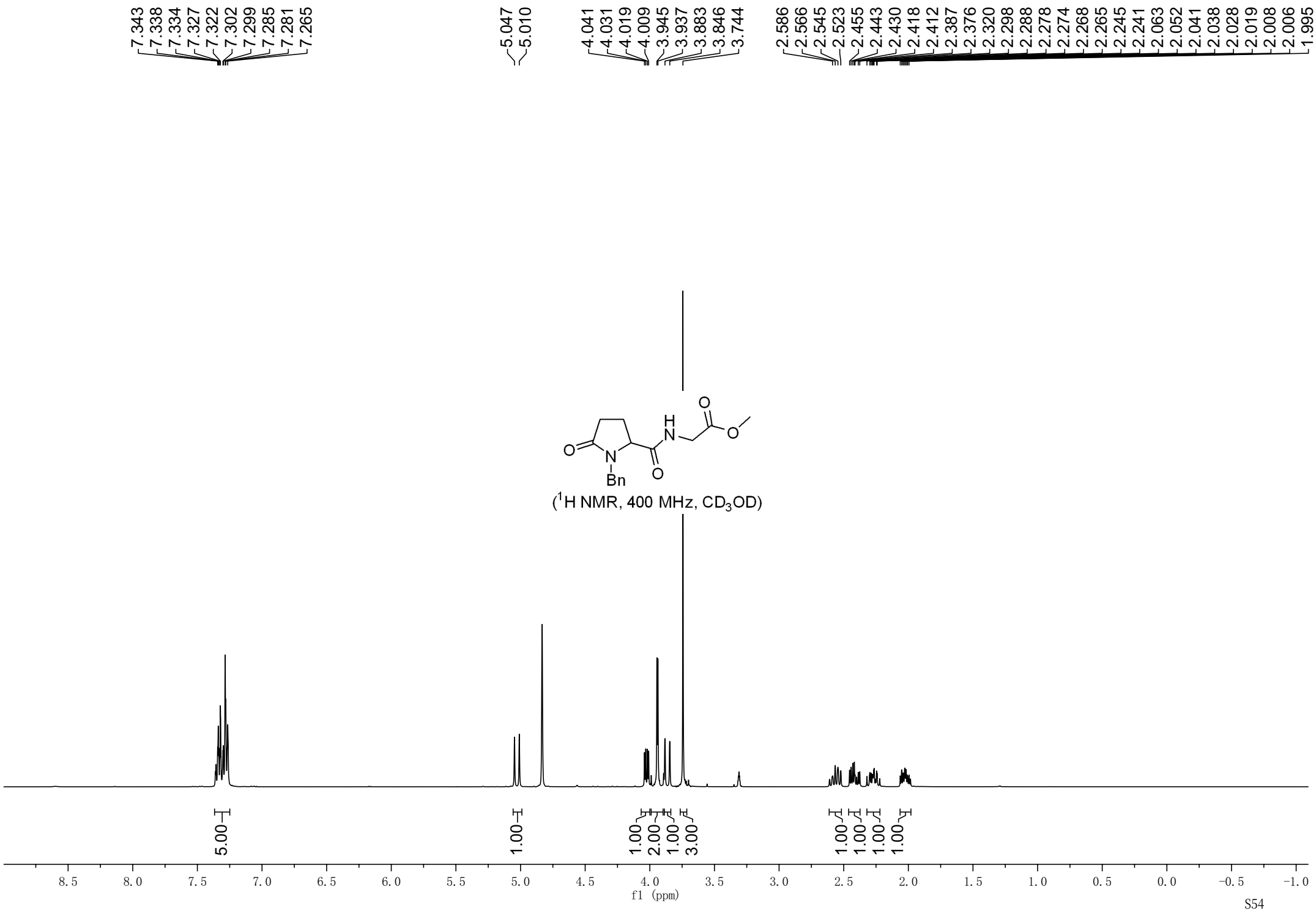

175.745
169.609
169.526
135.565
134.794
134.721
132.479
129.084
128.773
128.634
128.184
126.159
122.247
122.156
114.067
113.938
61.455
46.093
29.697
23.810
O
N
Bn
O
H
N
Br
(13C NMR, 100 MHz, CDCl3)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

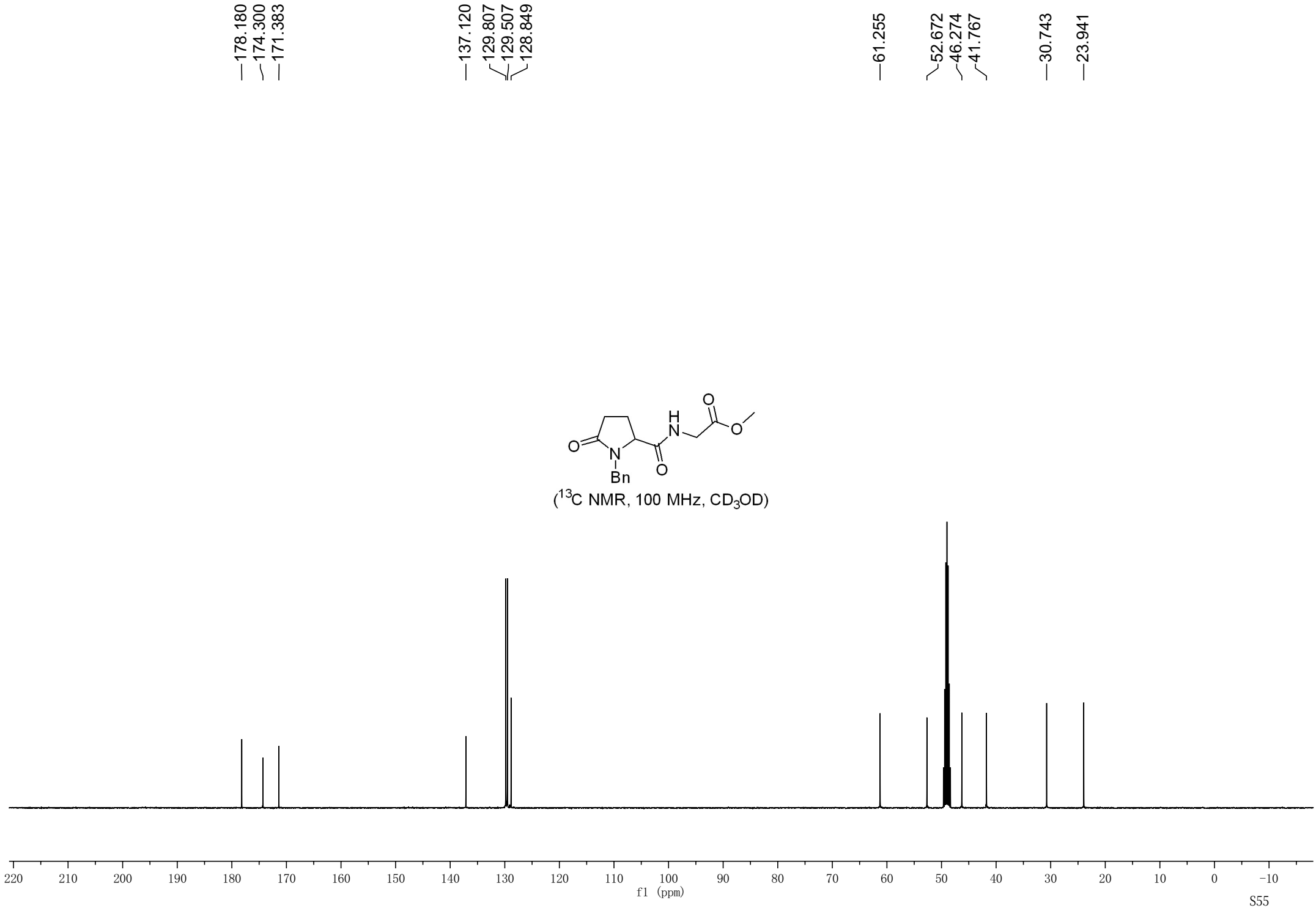

7.361
7.357
7.340
7.337
7.321
7.302
7.285
7.226
7.208
4.980
4.943
3.943
3.932
3.921
3.910
3.862
3.825
2.560
2.541
2.538
2.518
2.430
2.417
2.405
2.392
2.210
2.206
1.936
1.924
1.913
1.904
1.308
O
N
Bn
O
H
N
(1H NMR, 400 MHz, CD3OD)
3.00
2.00
1.00
1.00
1.00
1.00
1.00
1.00
9.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
f1 (ppm)

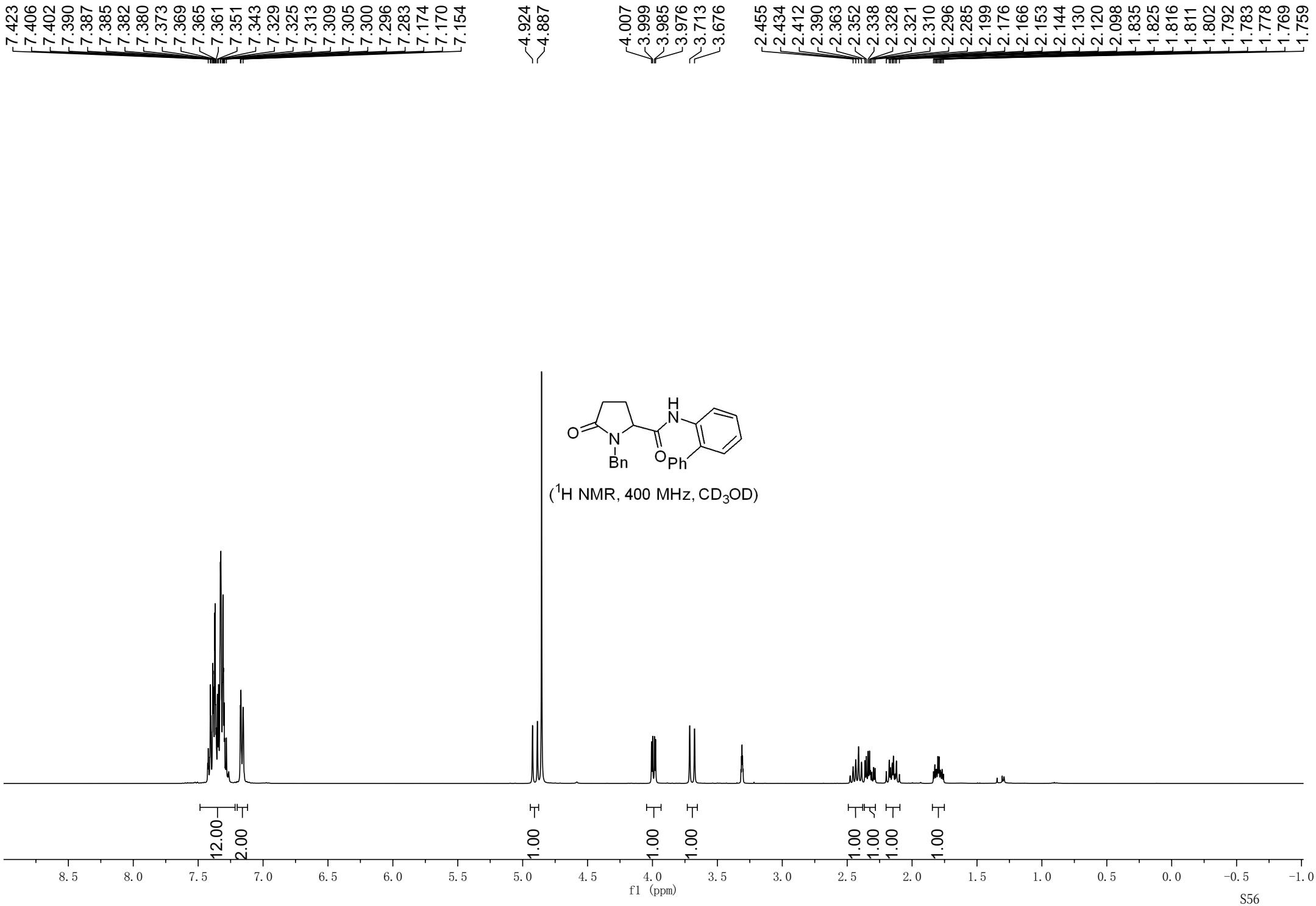

178.258
172.574
137.158
129.806
129.388
128.828
61.771
52.201
46.458
30.870
28.741
24.148
O
N
Bn
H
N
O
(13C NMR, 100 MHz, CD3OD)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40
f1 (ppm)

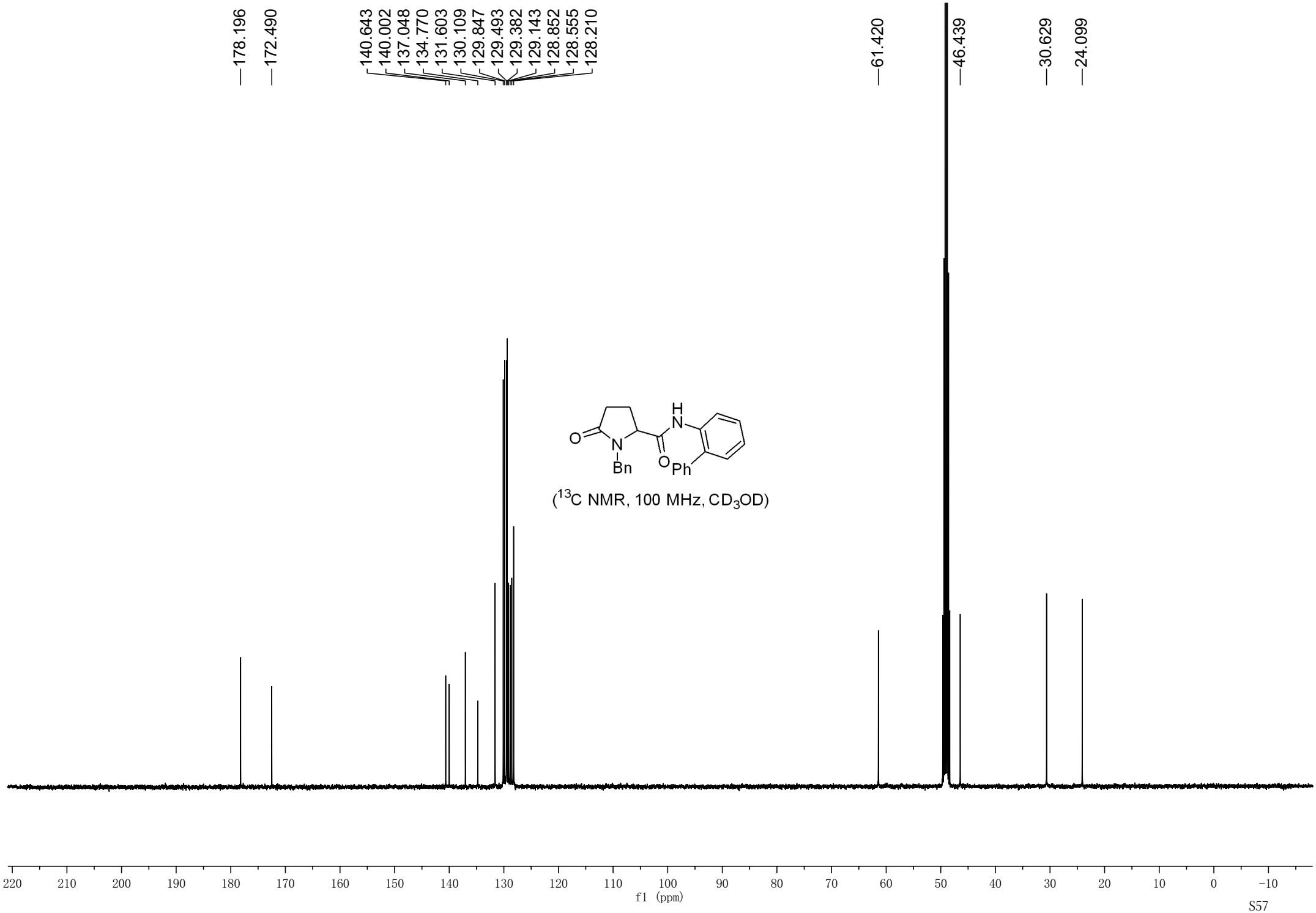

7.811
7.790
7.380
7.360
7.315
7.311
7.297
7.289
7.278
7.263
7.168
7.164
7.148
7.146
5.034
4.997
4.667
4.654
4.650
3.849
3.841
3.826
3.817
3.778
3.741
2.507
2.486
2.464
2.452
2.427
2.416
2.402
2.391
2.360
2.349
2.222
2.212
2.199
2.189
2.166
2.073
1.812
1.802
1.798
1.788
1.778
1.755
0.000
O
N
Bn
O
H
N
O
S
O
(^{1}H NMR, 400 MHz, $CDCl_3$)
1.98
2.01
2.94
2.04
1.02
2.00
1.00
1.01
0.96
3.02
1.02
1.02
1.04
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

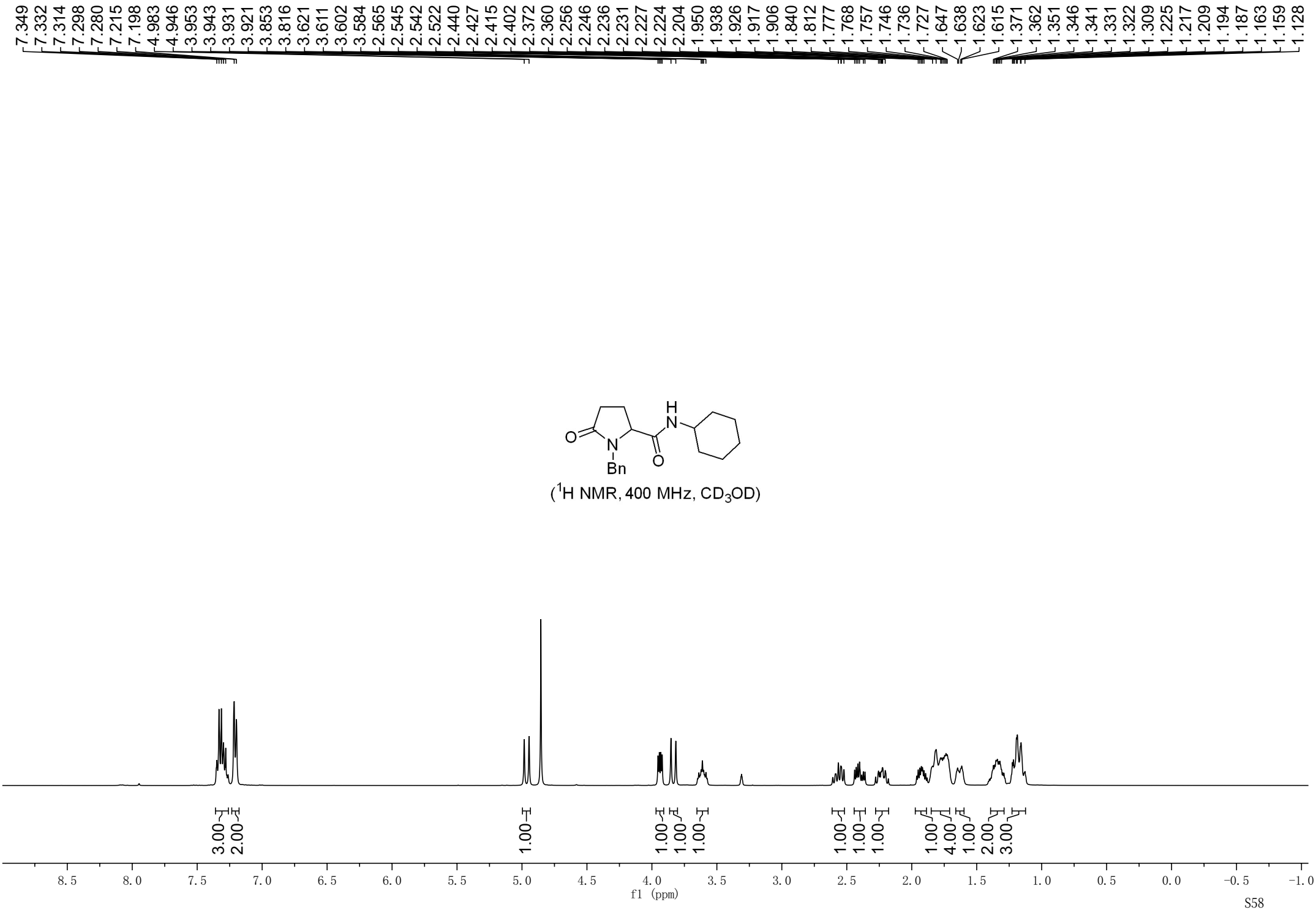

175.821
171.308
145.885
135.614
134.274
130.185
129.068
128.851
128.612
128.193
60.320
60.196
45.819
29.636
23.543
21.883
O
N
Bn
O
H
N
O
S
O
(^{13}C NMR, 100 MHz, $CDCl_3$)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

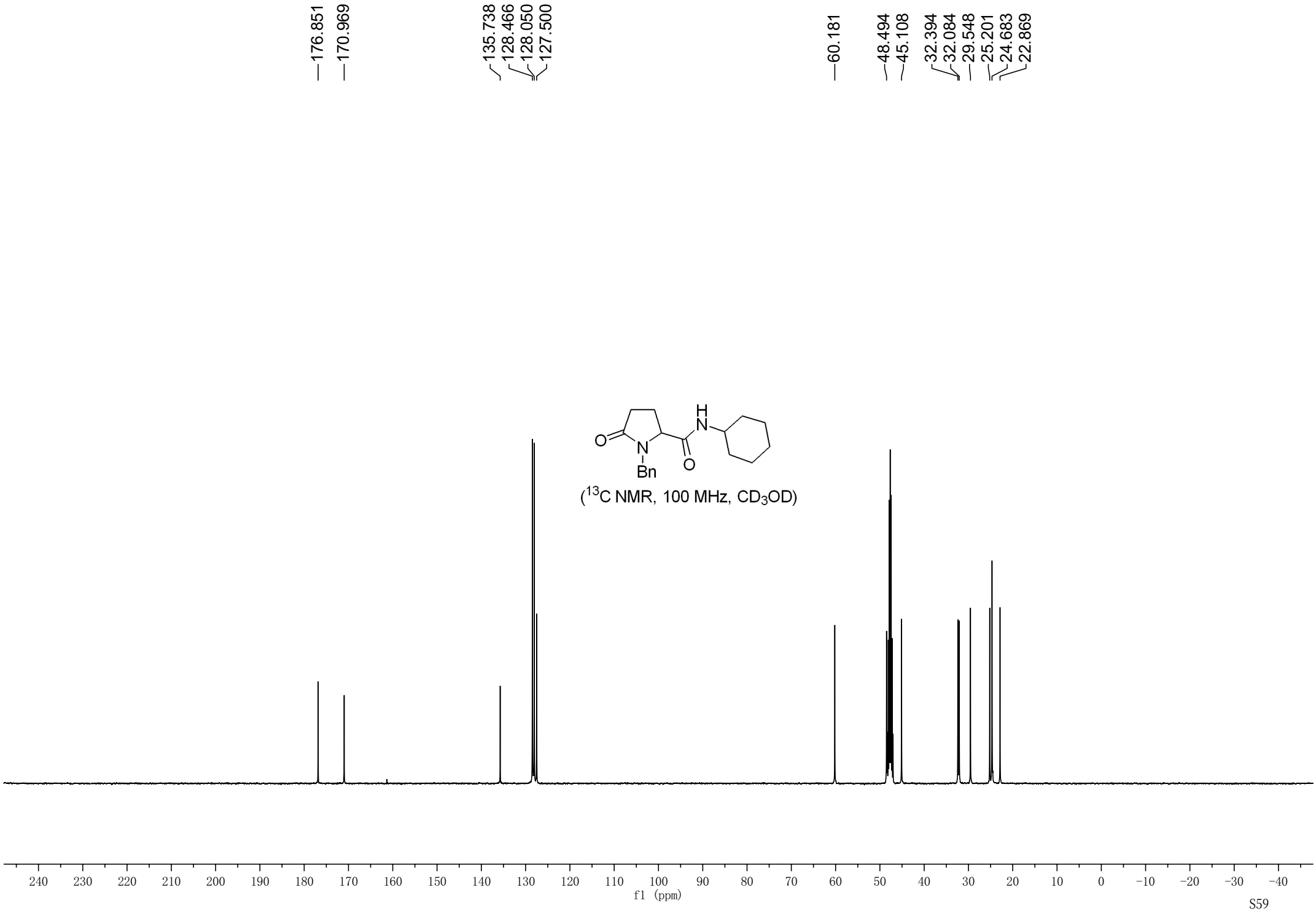

7.343
7.338
7.334
7.327
7.322
7.302
7.299
7.285
7.281
7.265
5.047
5.010
4.041
4.031
4.019
4.009
3.945
3.937
3.883
3.846
3.744
2.586
2.566
2.545
2.523
2.455
2.443
2.430
2.418
2.412
2.387
2.376
2.320
2.298
2.288
2.278
2.274
2.268
2.265
2.245
2.241
2.063
2.052
2.041
2.038
2.028
2.019
2.008
2.006
1.995
O
H
N
O
O
N
O
Bn
(1H NMR, 400 MHz, CD3OD)
5.00
1.00
1.00
2.00
1.00
3.00
1.00
1.00
1.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

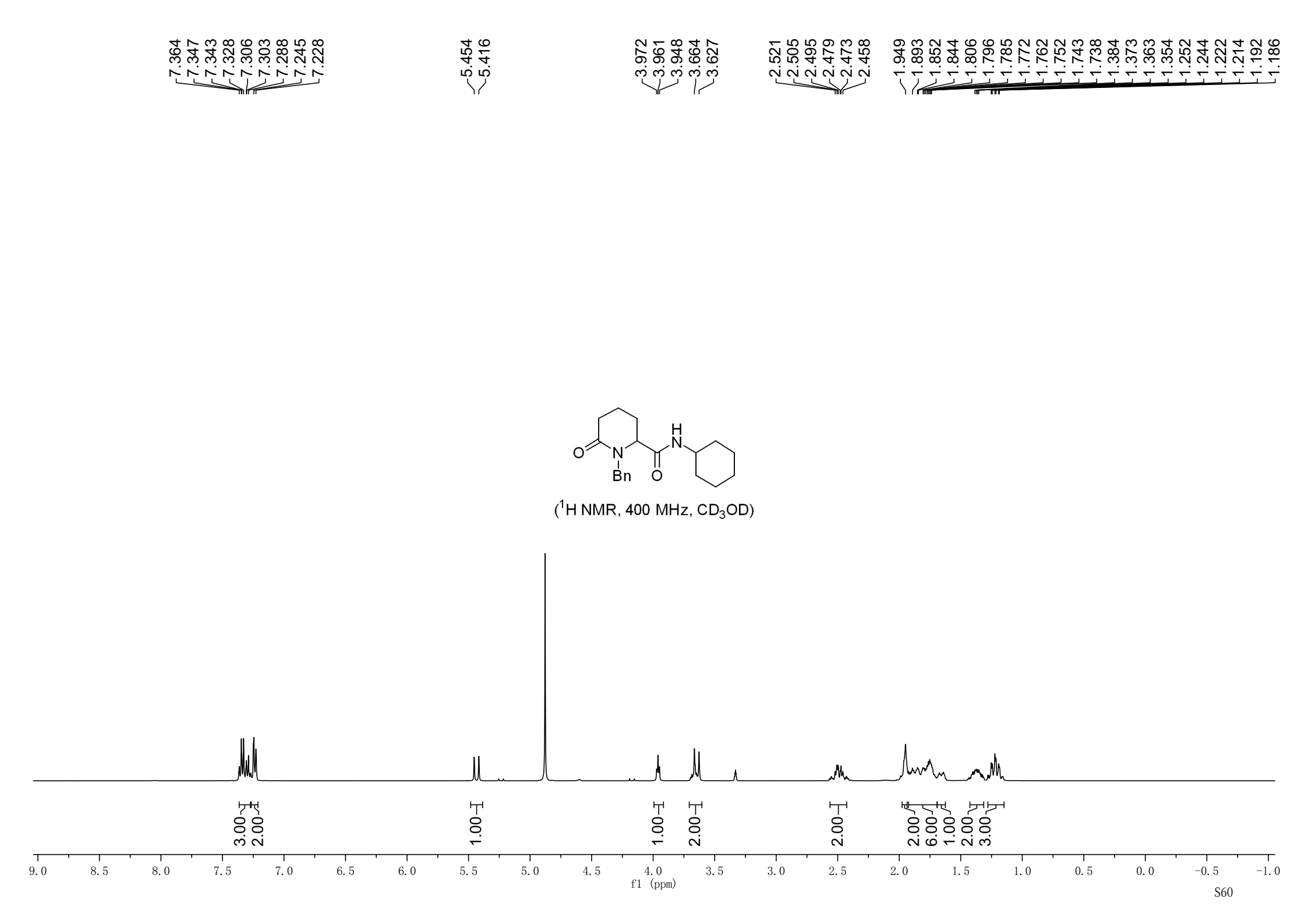

178.180
174.300
171.383
137.120
129.807
129.507
128.849
61.255
52.672
46.274
41.767
30.743
23.941
O
H
N
O
O
N
O
Bn
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

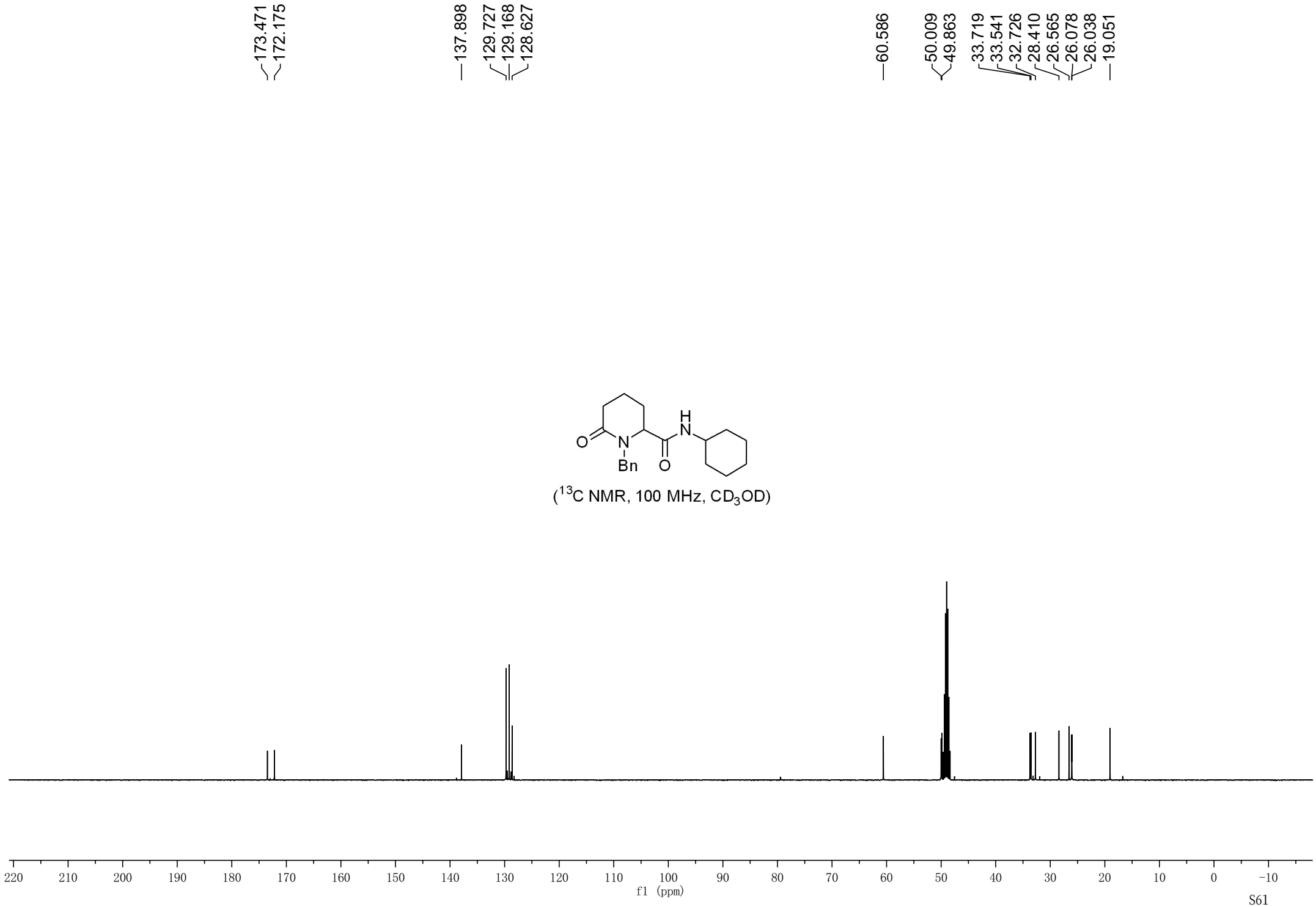

7.423
7.406
7.402
7.390
7.387
7.385
7.382
7.380
7.373
7.369
7.365
7.361
7.351
7.343
7.329
7.325
7.313
7.309
7.305
7.300
7.296
7.283
7.174
7.170
7.154
4.924
4.887
4.007
3.999
3.985
3.976
3.713
3.676
2.455
2.434
2.412
2.390
2.363
2.352
2.338
2.328
2.321
2.310
2.296
2.285
2.199
2.176
2.166
2.153
2.144
2.130
2.120
2.098
1.835
1.825
1.816
1.811
1.802
1.792
1.783
1.778
1.769
1.759
H
N
O
N
Bn
O
Ph
(^{1}H NMR, 400 MHz, CD_3OD)
12.00
2.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)


178.196
172.490
140.643
140.002
137.048
134.770
131.603
130.109
129.847
129.493
129.382
129.143
128.852
128.555
128.210
61.420
46.439
30.629
24.099
O
N
Bn
H
N
O
Ph
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

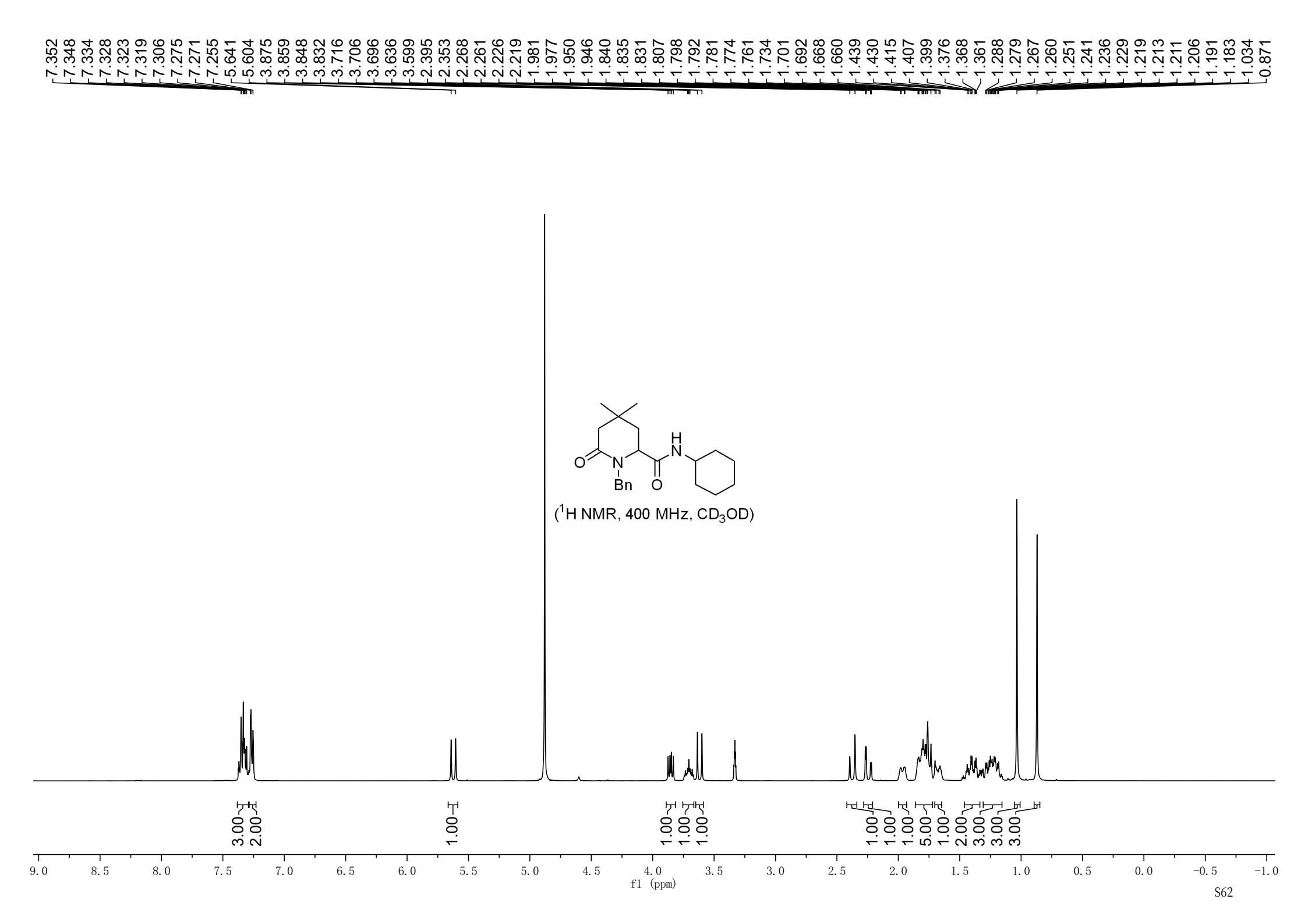

7.349
7.332
7.314
7.298
7.280
7.215
7.198
4.983
4.946
3.953
3.943
3.931
3.921
3.853
3.816
3.621
3.611
3.602
3.584
2.565
2.545
2.542
2.522
2.440
2.427
2.415
2.402
2.372
2.360
2.256
2.246
2.236
2.231
2.227
2.224
2.204
1.950
1.938
1.926
1.917
1.906
1.840
1.812
1.777
1.768
1.757
1.746
1.736
1.727
1.647
1.638
1.623
1.615
1.371
1.362
1.351
1.346
1.341
1.331
1.322
1.309
1.225
1.217
1.209
1.194
1.187
1.163
1.159
1.128
O
N
Bn
O
H
N
O
(1H NMR, 400 MHz, CD3OD)
3.00
2.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
4.00
1.00
2.00
3.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

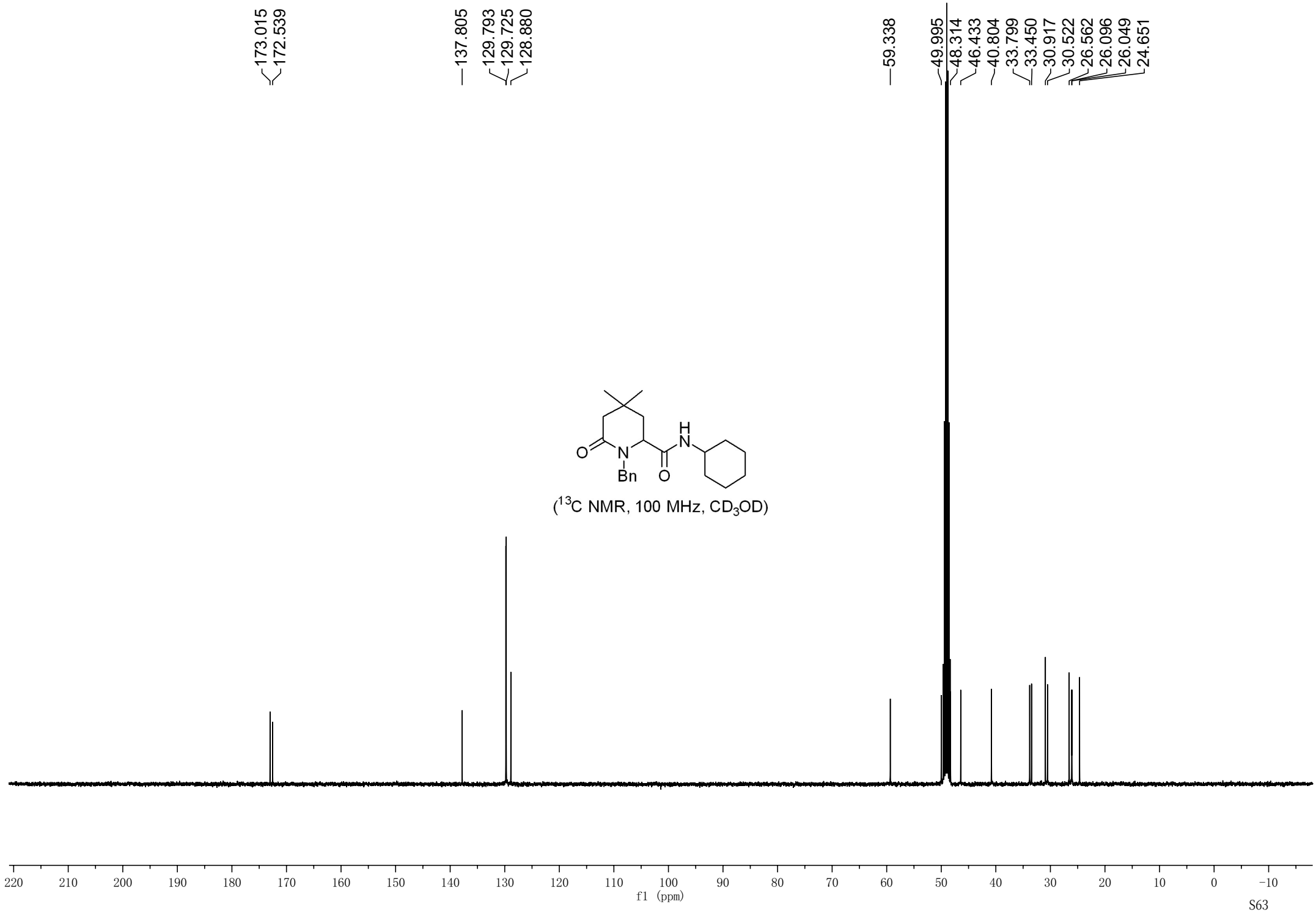

176.851
170.969
135.738
128.466
128.050
127.500
60.181
48.494
45.108
32.394
32.084
29.548
25.201
24.683
22.869
O
N
Bn
O
H
N
(^{13}C NMR, 100 MHz, CD_3OD)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20 −30 −40
f1 (ppm)


7.364
7.347
7.343
7.328
7.306
7.303
7.288
7.245
7.228
5.454
5.416
3.972
3.961
3.948
3.664
3.627
2.521
2.505
2.495
2.479
2.473
2.458
1.949
1.893
1.852
1.844
1.806
1.796
1.785
1.772
1.762
1.752
1.743
1.738
1.384
1.373
1.363
1.354
1.252
1.244
1.222
1.214
1.192
1.186
O
N
H
N
Bn
O
(1H NMR, 400 MHz, CD3OD)
3.00
2.00
1.00
1.00
2.00
2.00
2.00
6.00
1.00
2.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

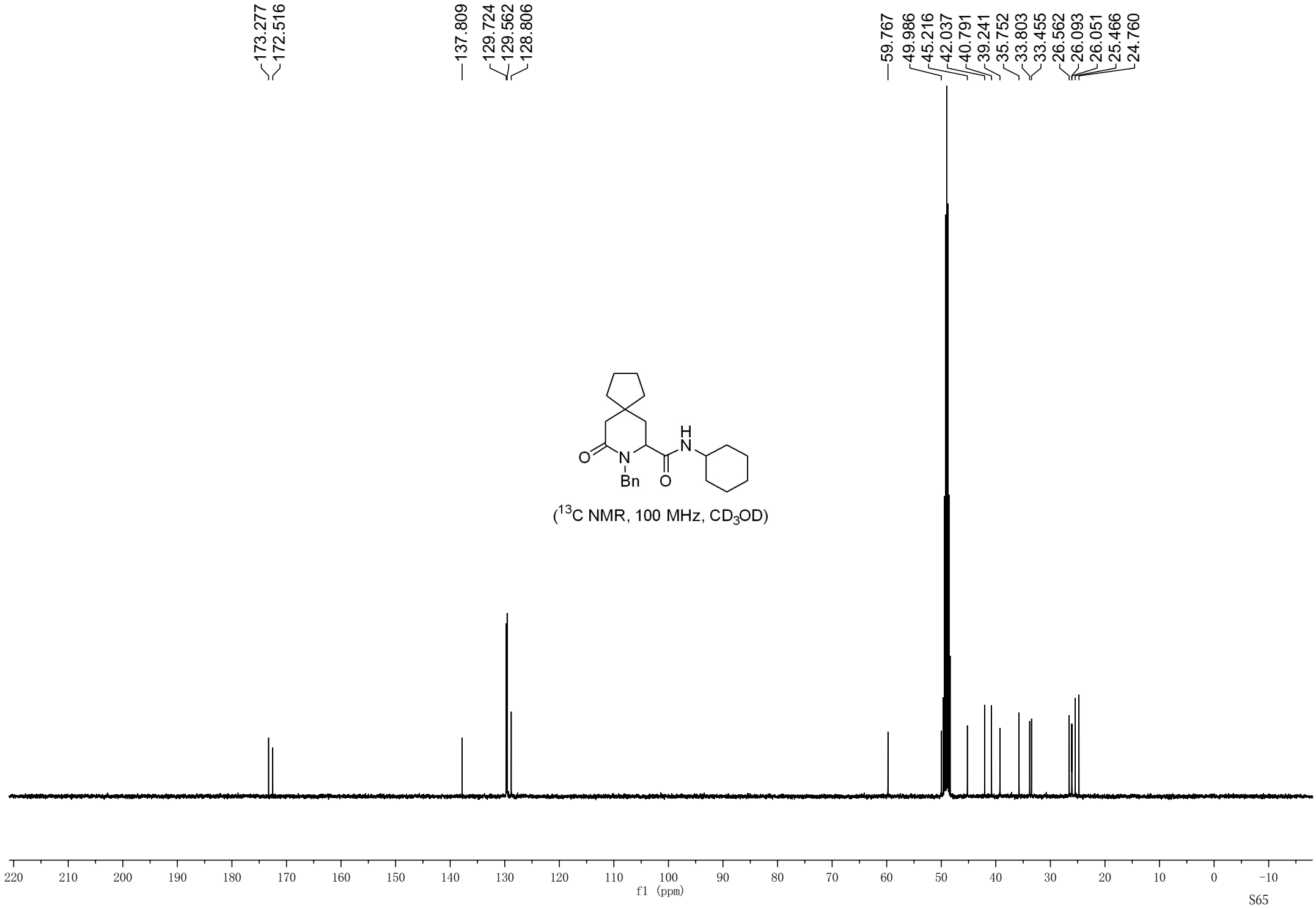


(^{13}C NMR, 100 MHz, CD_3OD)

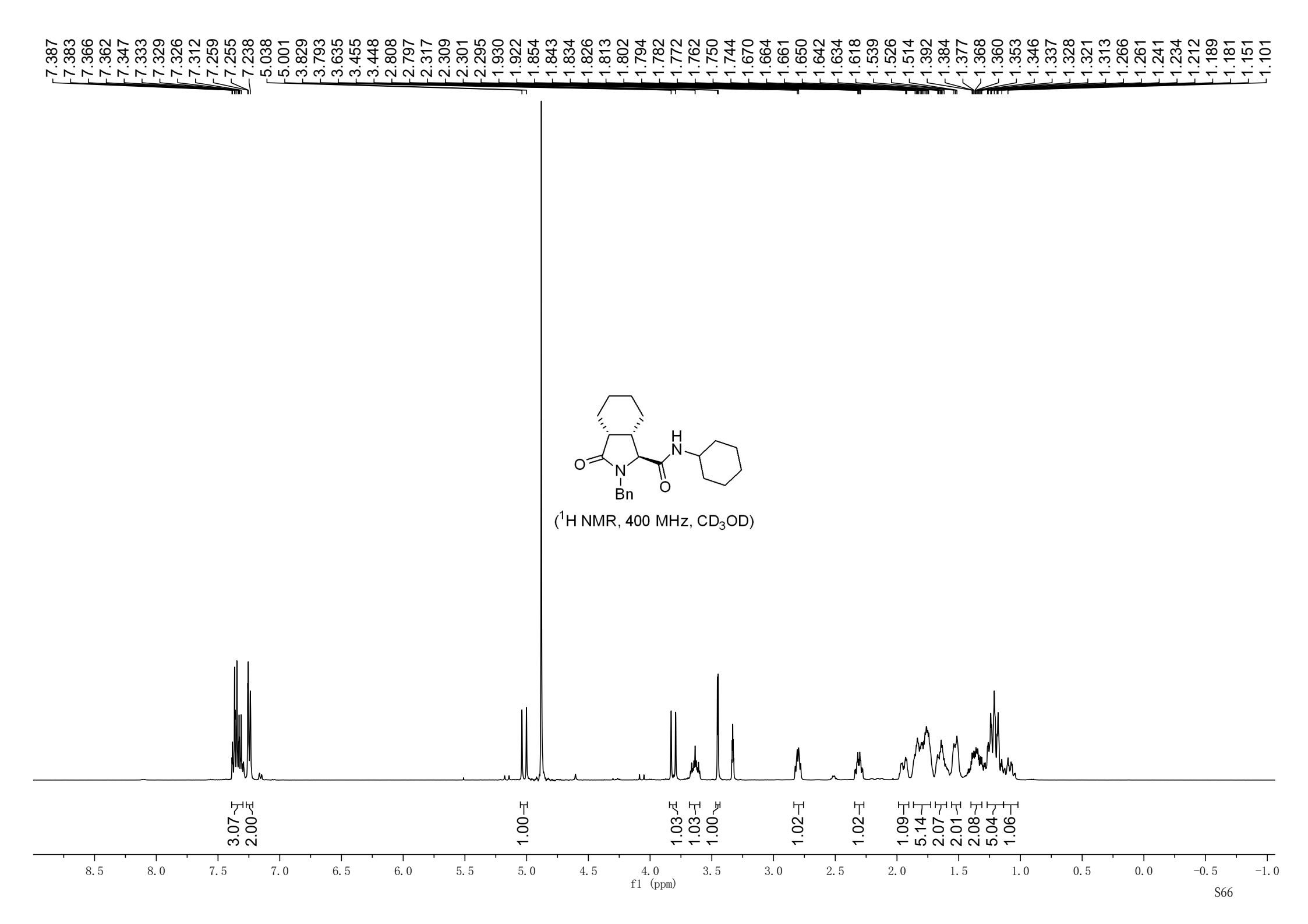

7.352
7.348
7.334
7.328
7.323
7.319
7.306
7.275
7.271
7.255
5.641
5.604
3.875
3.859
3.848
3.832
3.716
3.706
3.696
3.636
3.599
2.395
2.353
2.268
2.261
2.226
2.219
1.981
1.977
1.950
1.946
1.840
1.835
1.831
1.807
1.798
1.792
1.781
1.774
1.761
1.734
1.701
1.692
1.668
1.660
1.439
1.430
1.415
1.407
1.399
1.376
1.368
1.361
1.288
1.279
1.267
1.260
1.251
1.241
1.236
1.229
1.219
1.213
1.211
1.206
1.191
1.183
1.034
0.871
O
N
Bn
O
H
N
(^{1}H NMR, 400 MHz, CD_3OD)
3.00
2.00
1.00
1.00
1.00
1.00
1.00
1.00
5.00
1.00
2.00
3.00
3.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

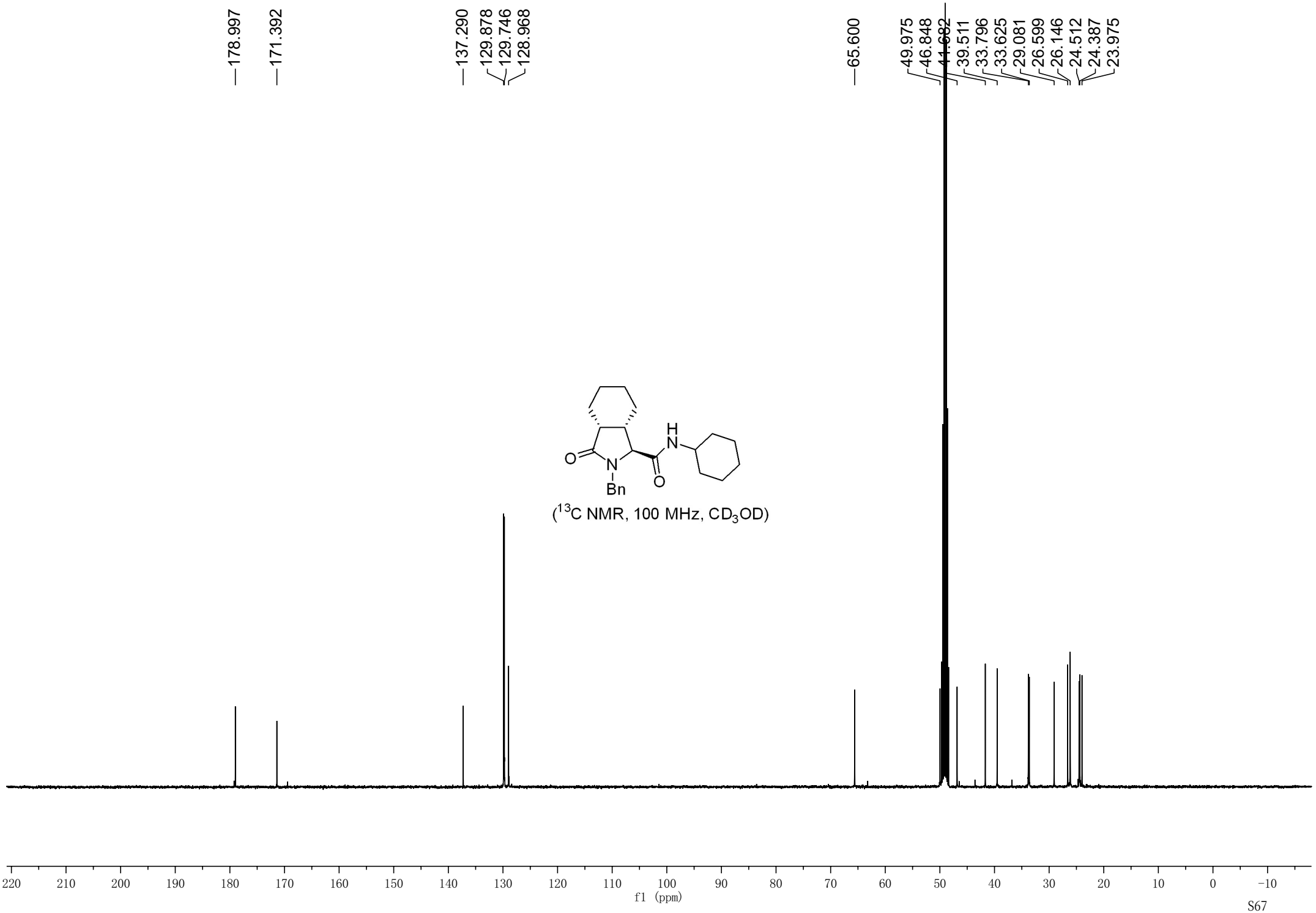

173.015
172.539
137.805
129.793
129.725
128.880
59.338
49.995
48.314
46.433
40.804
33.799
33.450
30.917
30.522
26.562
26.096
26.049
24.651
O
N
Bn
O
H
N
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

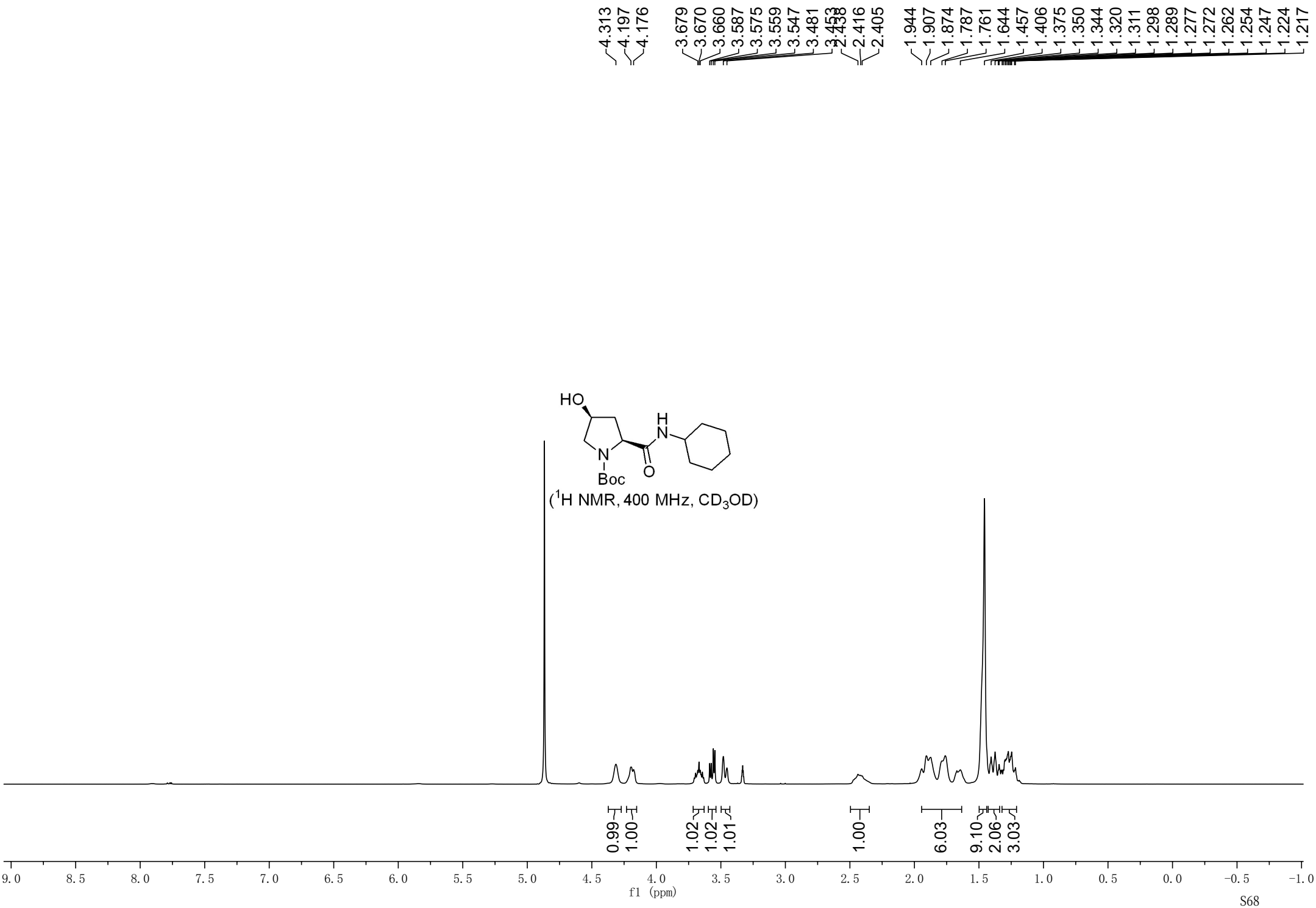

7.349
7.332
7.328
7.314
7.303
7.299
7.295
7.282
7.227
7.224
7.207
5.605
5.568
3.866
3.850
3.840
3.824
3.677
3.610
3.573
2.467
2.425
2.367
2.361
2.325
2.319
1.864
1.857
1.844
1.818
1.812
1.793
1.784
1.772
1.763
1.730
1.727
1.695
1.688
1.682
1.670
1.664
1.655
1.644
1.636
1.619
1.615
1.491
1.480
1.471
1.454
1.413
1.382
1.374
1.366
1.350
1.342
1.333
1.320
1.303
1.253
1.248
1.244
1.223
1.217
1.192
1.186
1.164
1.156
O
N
Bn
O
H
N
(^{1}H NMR, 400 MHz, CD_3OD)
3.00
2.00
1.00
1.00
1.00
1.00
1.00
1.00
5.00
2.00
4.00
3.00
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

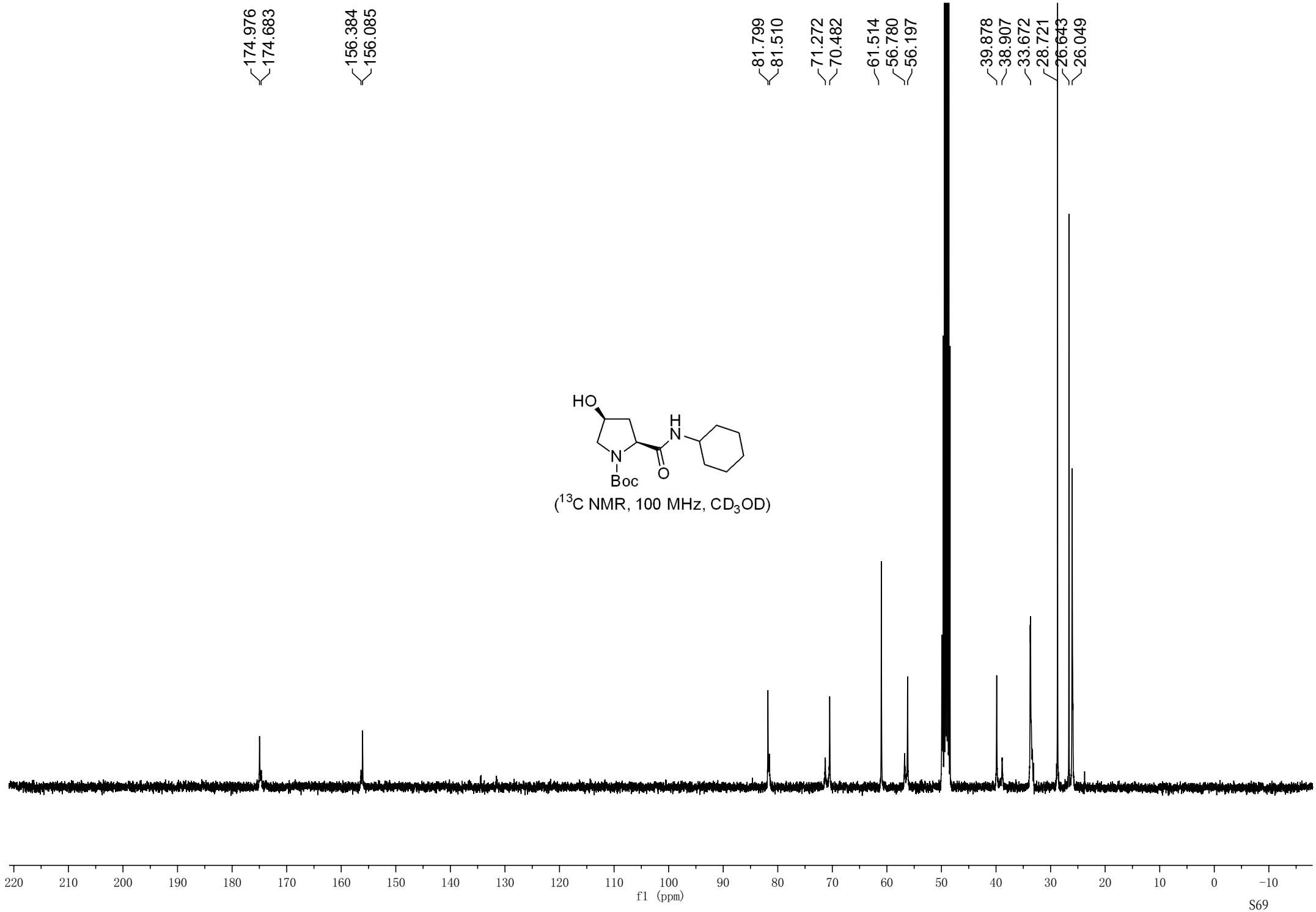


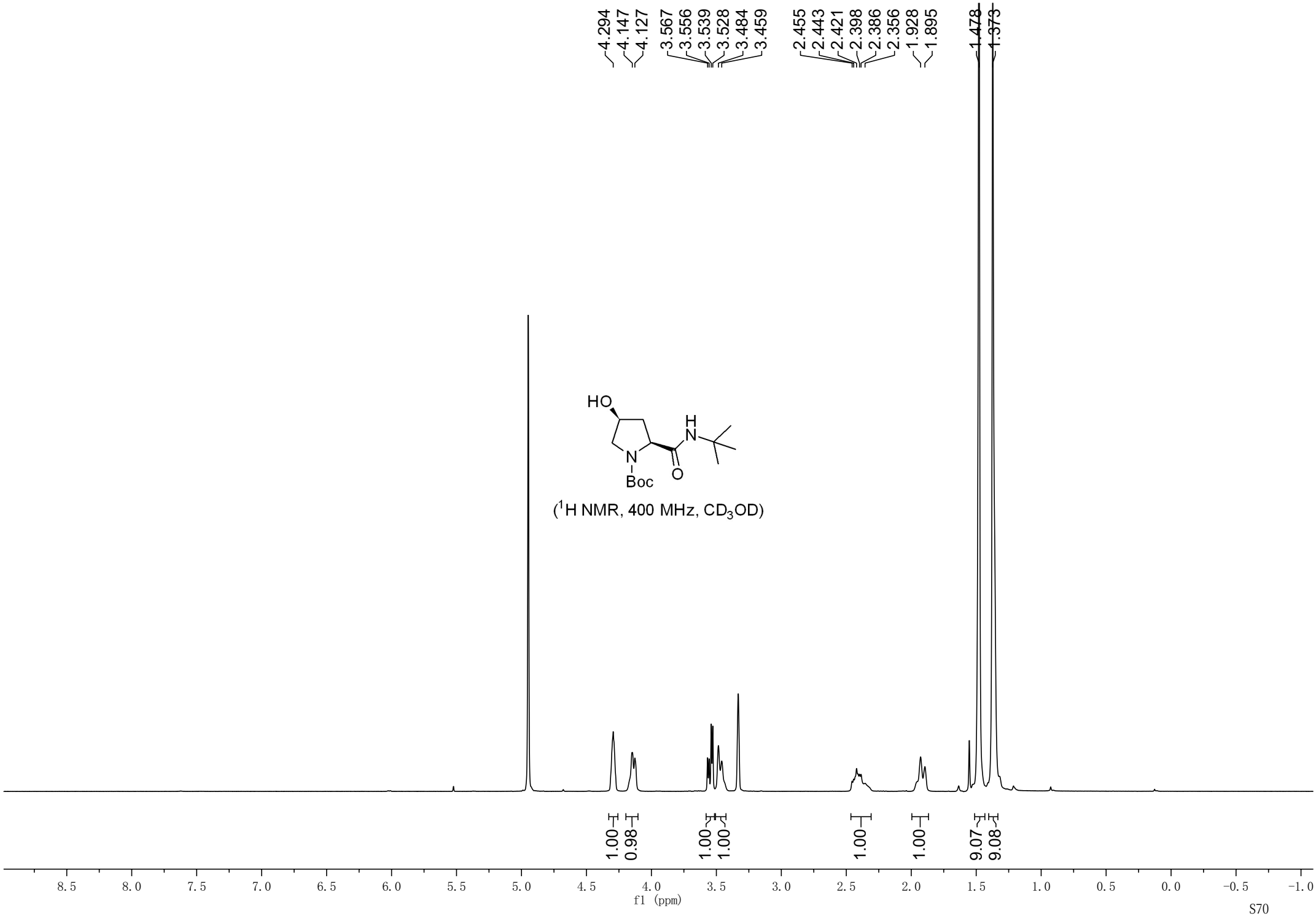
(^{13}C NMR, 100 MHz, CD_3OD)

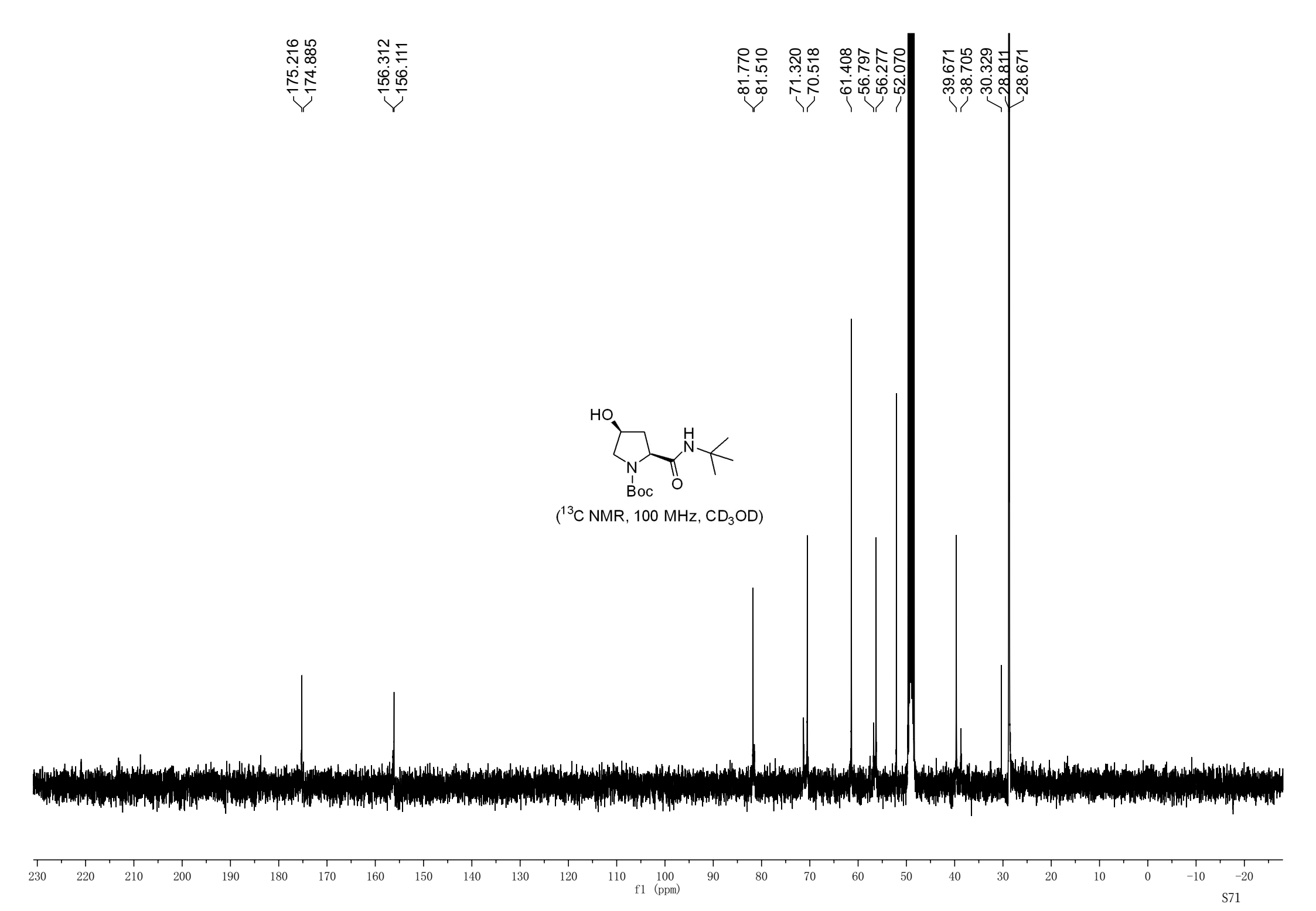

7.387
7.383
7.366
7.362
7.347
7.333
7.329
7.326
7.312
7.259
7.255
7.238
5.038
5.001
3.829
3.793
3.635
3.455
3.448
2.808
2.797
2.317
2.309
2.301
2.295
1.930
1.922
1.854
1.843
1.834
1.826
1.813
1.802
1.794
1.782
1.772
1.762
1.750
1.744
1.670
1.664
1.661
1.650
1.642
1.634
1.618
1.539
1.526
1.514
1.392
1.384
1.377
1.368
1.360
1.353
1.346
1.337
1.328
1.321
1.313
1.266
1.261
1.241
1.234
1.212
1.189
1.181
1.151
1.101
O
N
Bn
O
H
N
(^{1}H NMR, 400 MHz, CD_3OD)
3.07
2.00
1.00
1.03
1.03
1.00
1.02
1.02
1.09
5.14
2.07
2.01
2.08
5.04
1.06
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

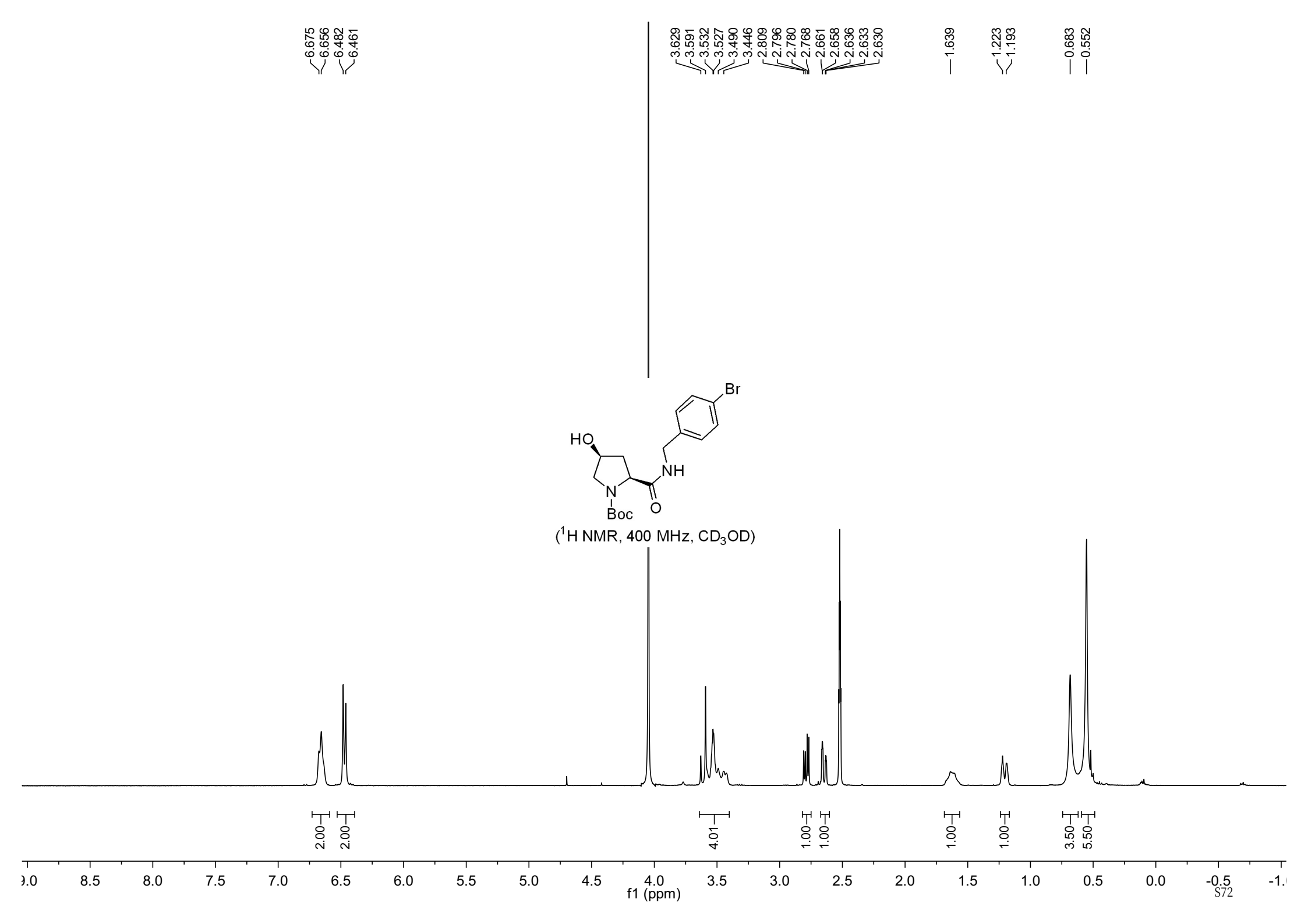

178.997
171.392
137.290
129.878
129.746
128.968
65.600
49.975
46.848
41.682
39.511
33.796
33.625
29.081
26.599
26.146
24.512
24.387
23.975
O
N
Bn
H
N
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

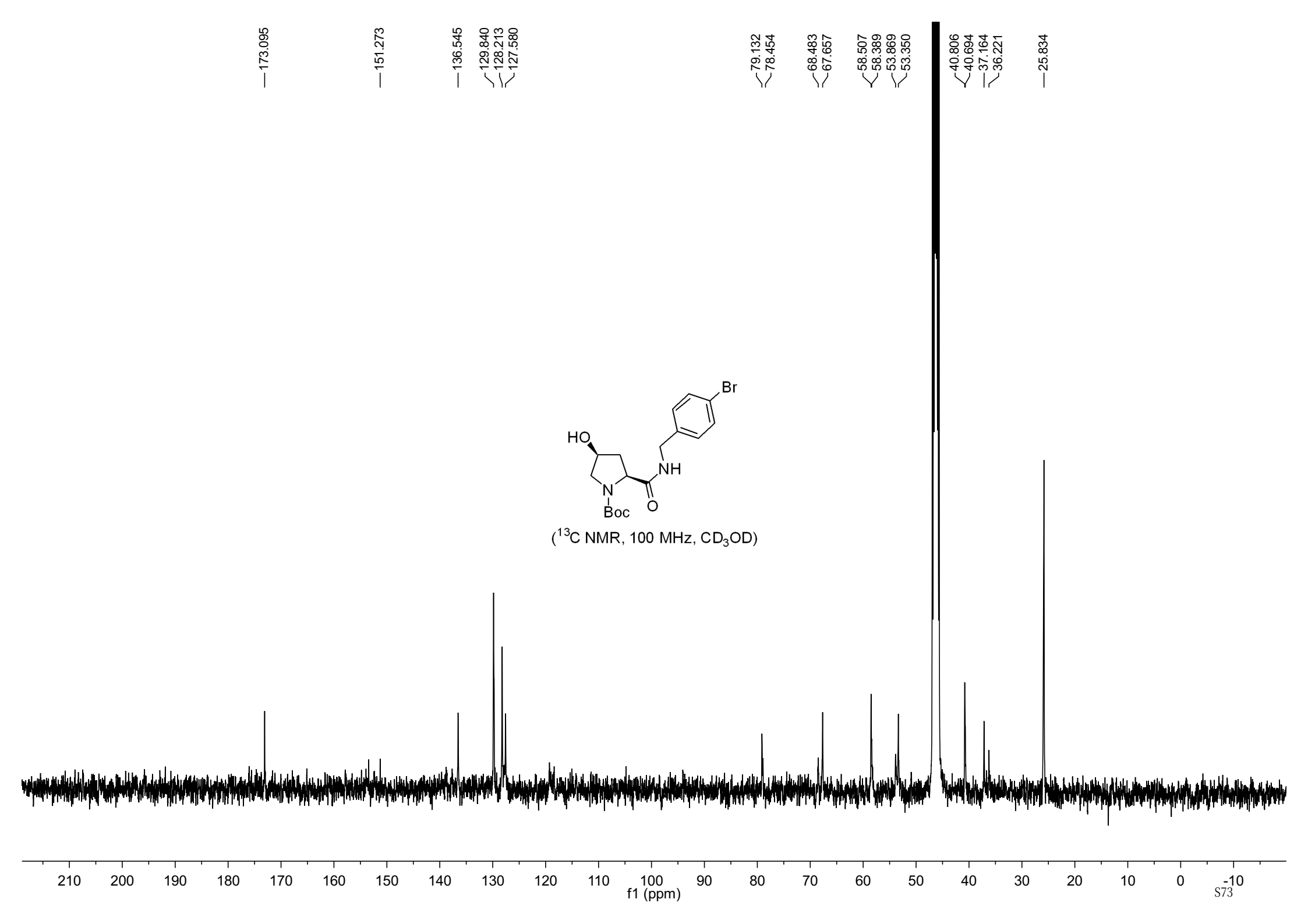

4.313
4.197
4.176
3.679
3.670
3.660
3.587
3.575
3.559
3.547
3.481
3.453
3.438
2.416
2.405
1.944
1.907
1.874
1.787
1.761
1.644
1.457
1.406
1.375
1.350
1.344
1.320
1.311
1.298
1.289
1.277
1.272
1.262
1.254
1.247
1.224
1.217
HO
H
N
N
O
Boc
(1H NMR, 400 MHz, CD3OD)
0.99
1.00
1.02
1.02
1.01
1.00
6.03
9.10
2.06
3.03
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
−0.5
−1.0
f1 (ppm)

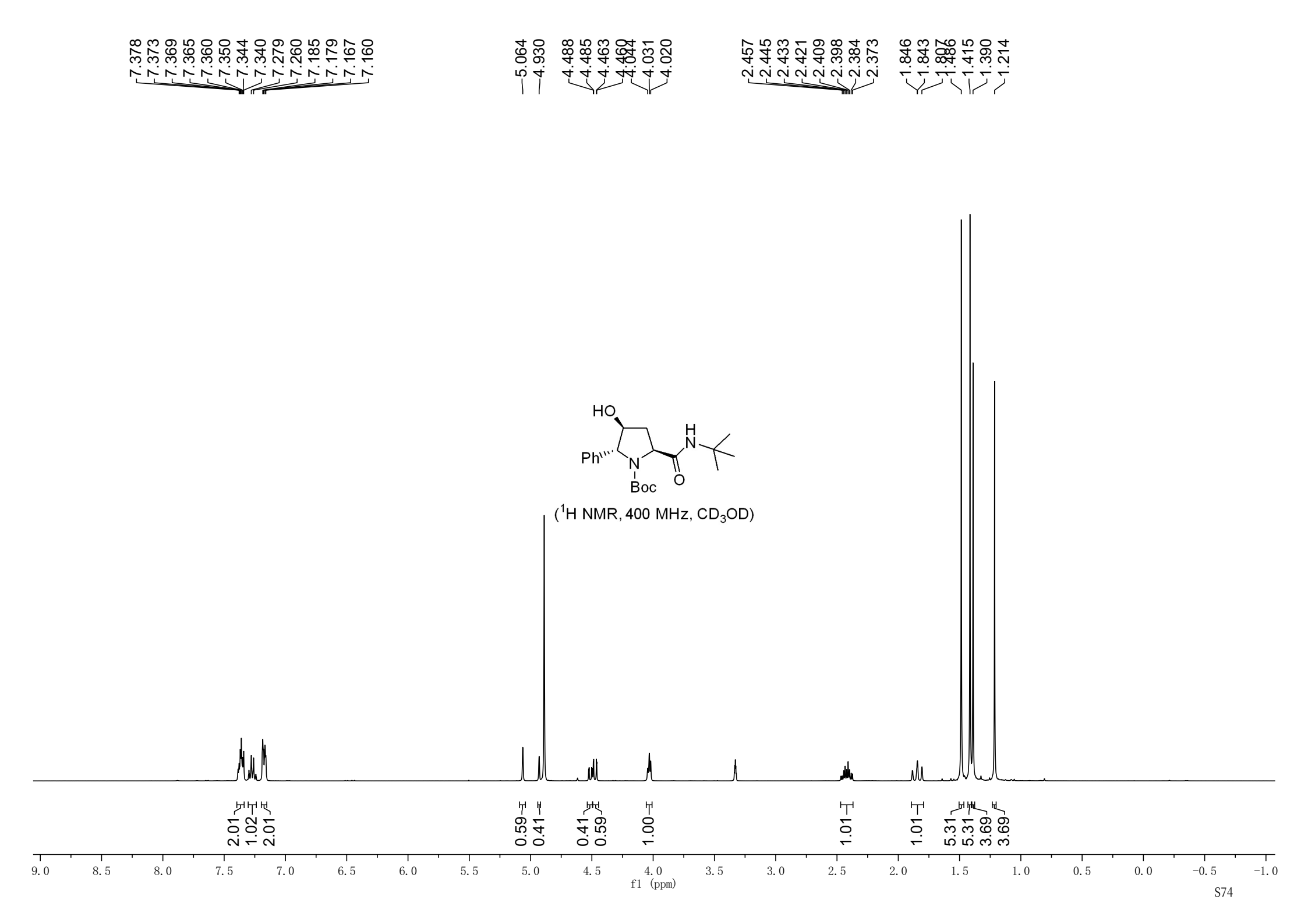

174.976
174.683
156.384
156.085
81.799
81.510
71.272
70.482
61.514
56.780
56.197
39.878
38.907
33.672
28.721
26.643
26.049
HO
H
N
N
Boc
O
(^{13}C NMR, 100 MHz, CD_3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

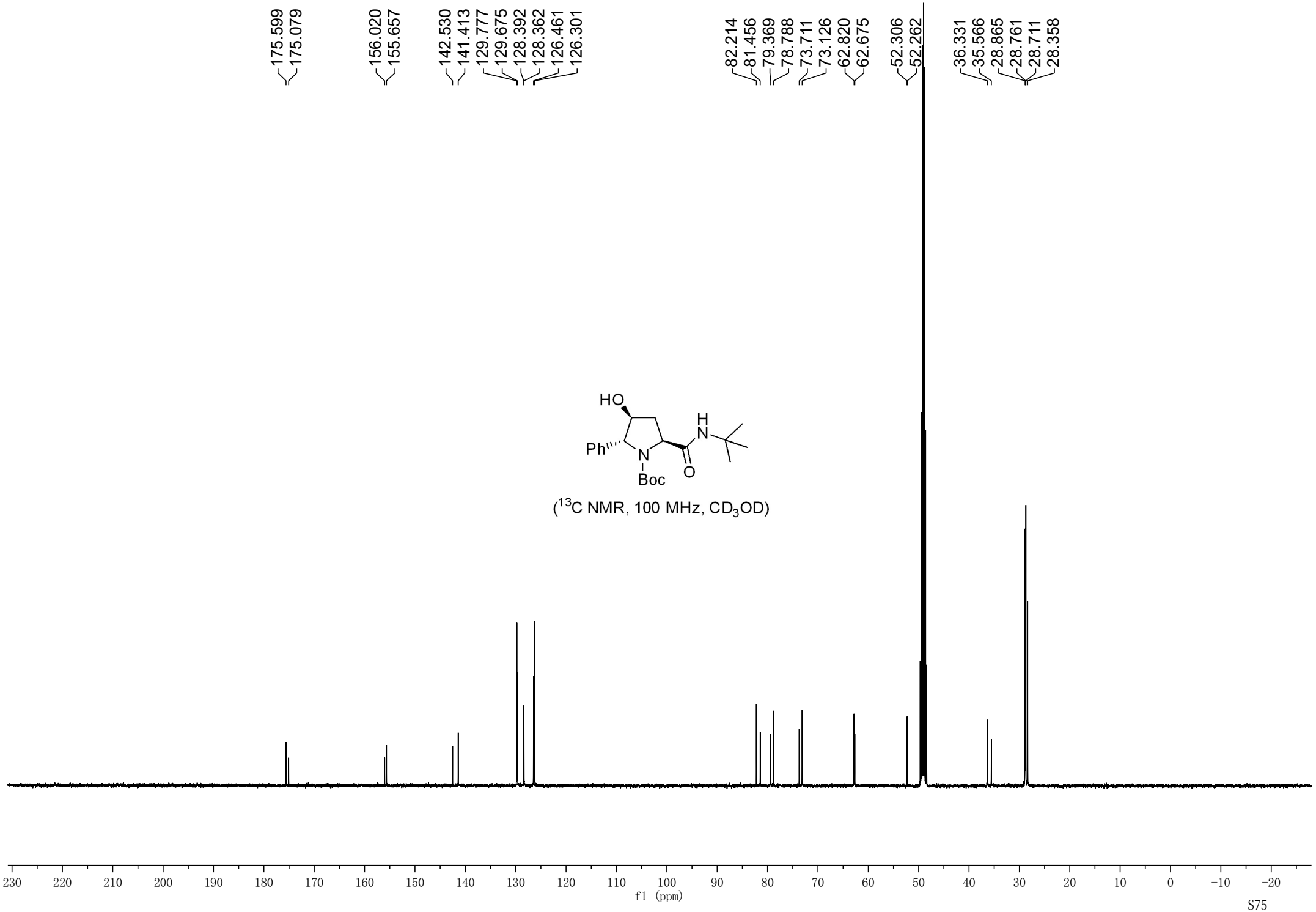

4.294
4.147
4.127
3.567
3.556
3.539
3.528
3.484
3.459
2.455
2.443
2.421
2.398
2.386
2.356
1.928
1.895
1.478
1.373
HO
N
H
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.00
0.98
1.00
1.00
1.00
1.00
9.07
9.08
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

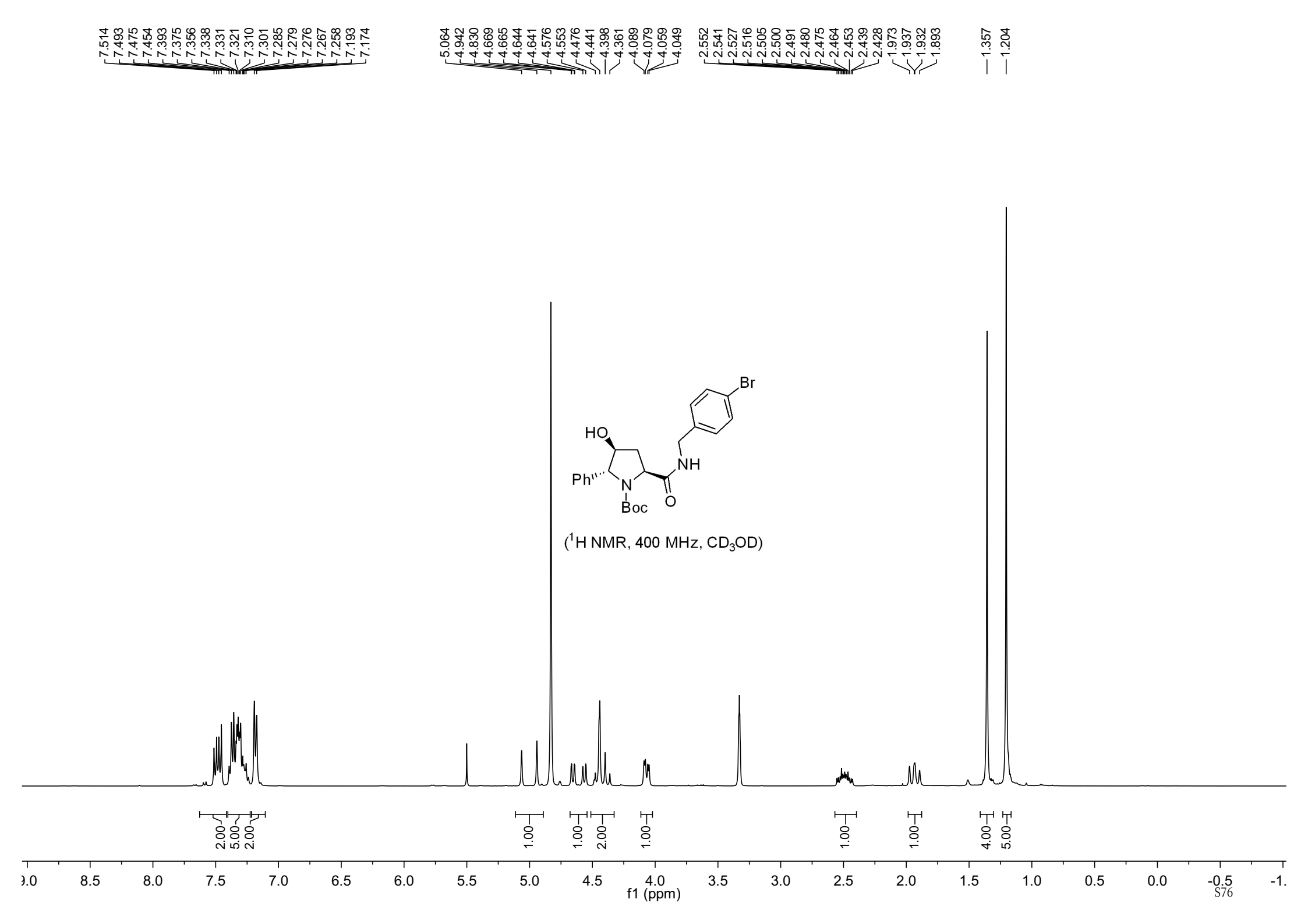

175.216
174.885
156.312
156.111
81.770
81.510
71.320
70.518
61.408
56.797
56.277
52.070
39.671
38.705
30.329
28.811
28.671
HO
H
N
N
Boc
O
(^{13}C NMR, 100 MHz, CD_3OD)
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 −10 −20
f1 (ppm)

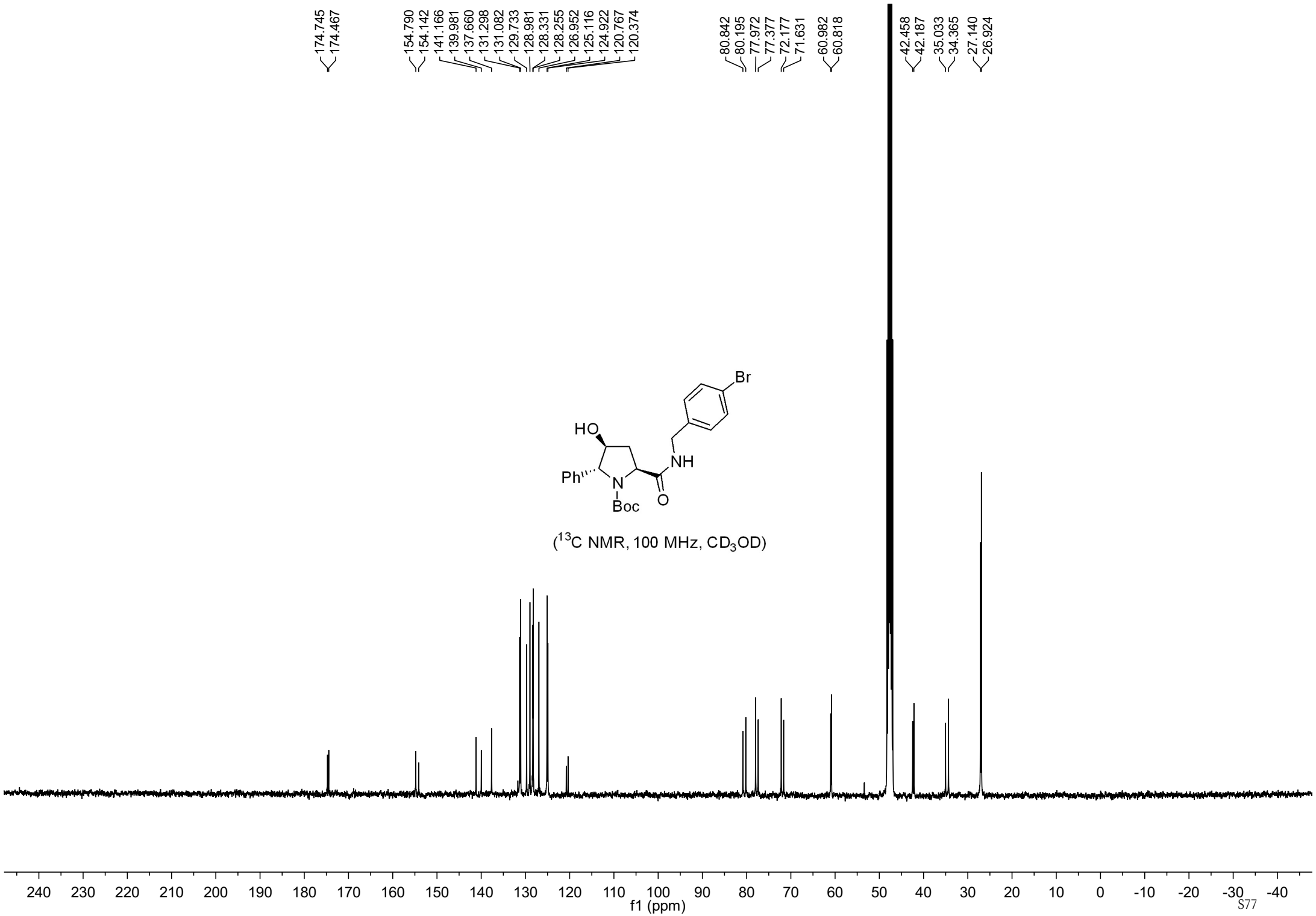

6.675
6.656
6.482
6.461
3.629
3.591
3.532
3.527
3.490
3.446
2.809
2.796
2.780
2.768
2.661
2.658
2.636
2.633
2.630
1.639
1.223
1.193
0.683
0.552
Br
HO
NH
N
O
Boc
(1H NMR, 400 MHz, CD3OD)
2.00
2.00
4.01
1.00
1.00
1.00
1.00
3.50
5.50
f1 (ppm)

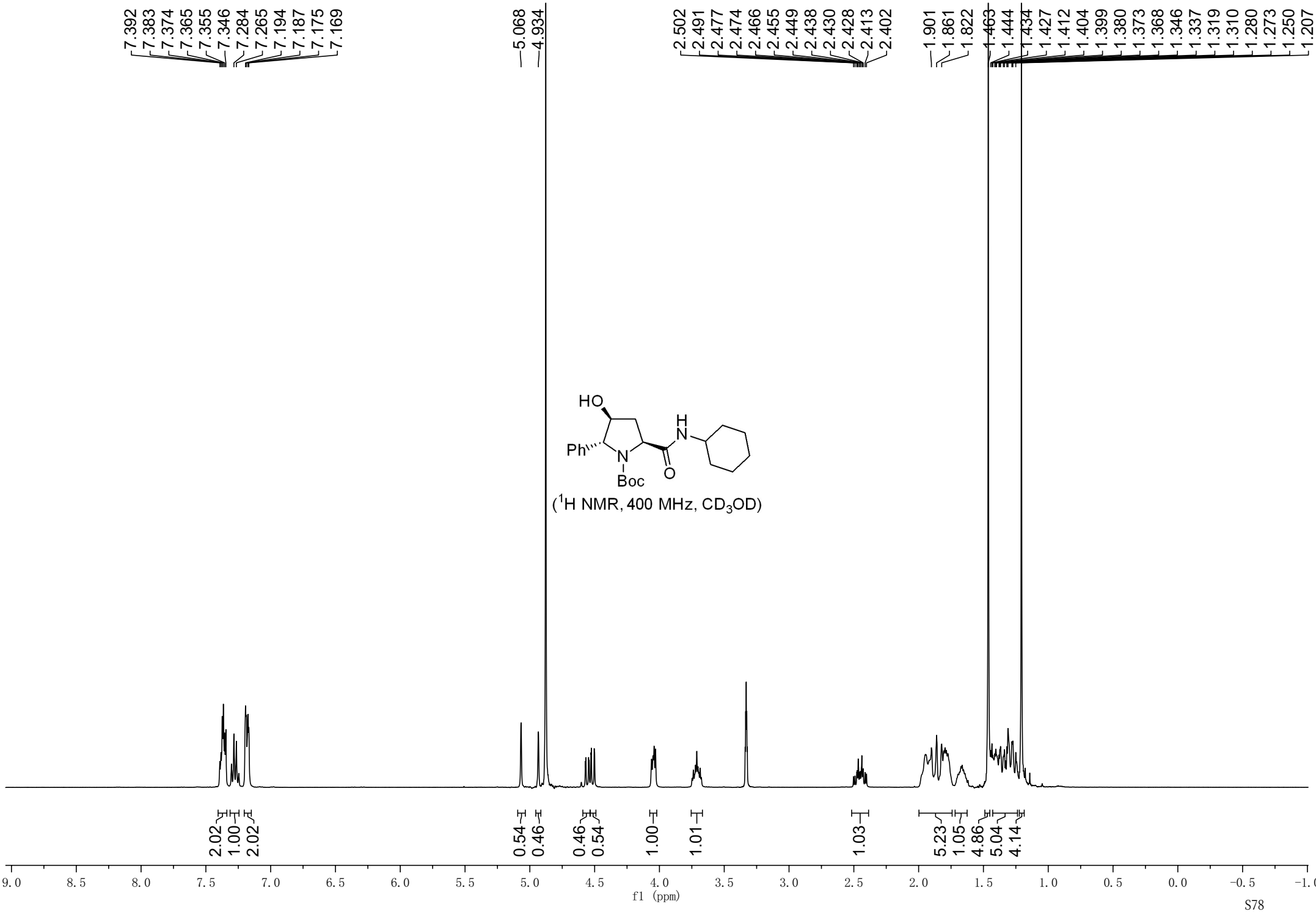

173.095
151.273
136.545
129.840
128.213
127.580
79.132
78.454
68.483
67.657
58.507
58.389
53.869
53.350
40.806
40.694
37.164
36.221
25.834
Br
HO
NH
N
O
Boc
(^{13}C NMR, 100 MHz, CD_3OD)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

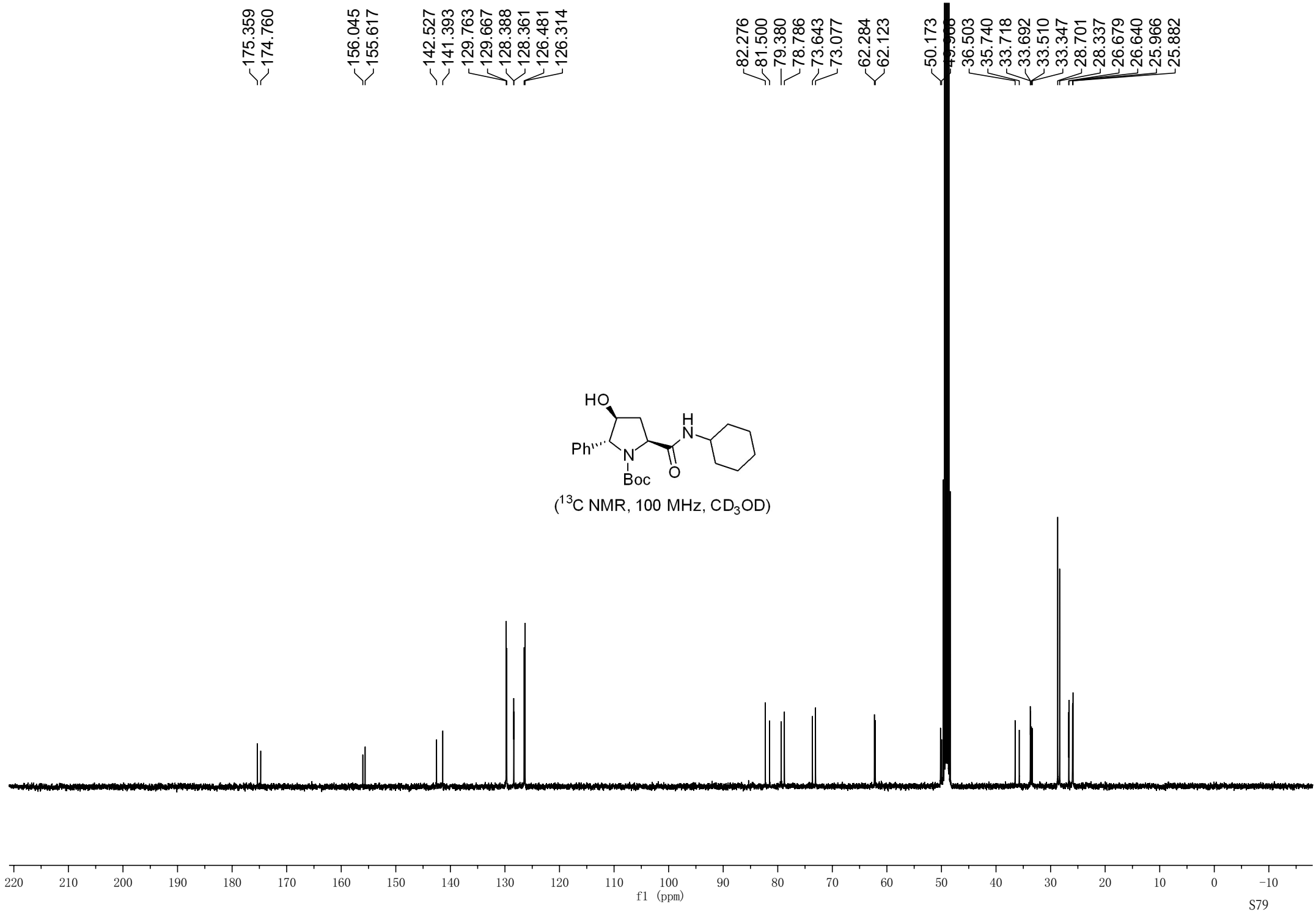

7.378
7.373
7.369
7.365
7.360
7.350
7.344
7.340
7.279
7.260
7.185
7.179
7.167
7.160
5.064
4.930
4.488
4.485
4.463
4.460
4.044
4.031
4.020
2.457
2.445
2.433
2.421
2.409
2.398
2.384
2.373
1.846
1.843
1.807
1.486
1.415
1.390
1.214
HO
Ph
N
Boc
H
N
O
(1H NMR, 400 MHz, CD3OD)
2.01
1.02
2.01
0.59
0.41
0.41
0.59
1.00
1.01
1.01
5.31
5.31
3.69
3.69
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

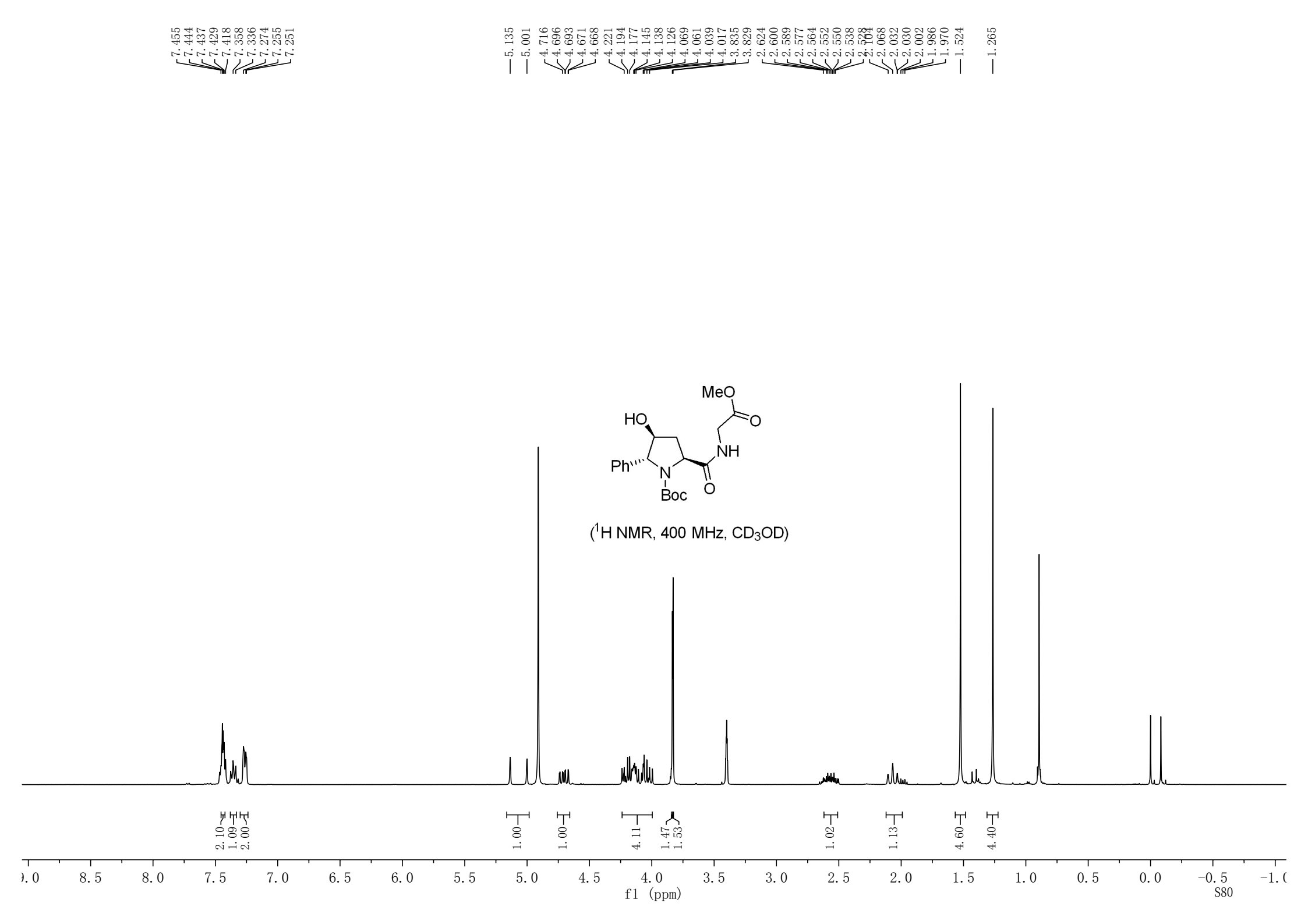

175.599
175.079
156.020
155.657
142.530
141.413
129.777
129.675
128.392
128.362
126.461
126.301
82.214
81.456
79.369
78.788
73.711
73.126
62.820
62.675
52.306
52.262
36.331
35.566
28.865
28.761
28.711
28.358
HO
Ph
N
Boc
H
N
O
(13C NMR, 100 MHz, CD3OD)
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
f1 (ppm)

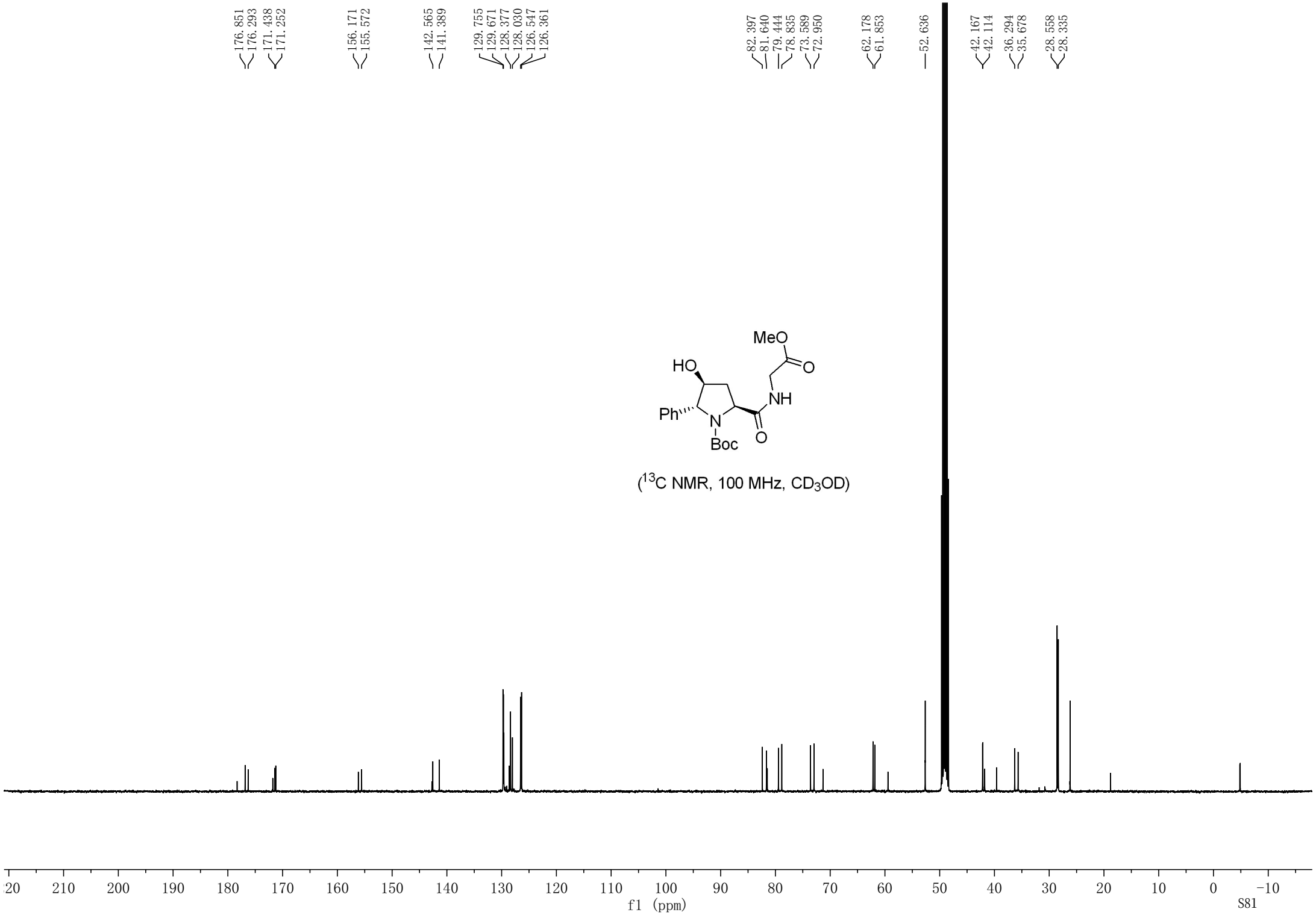

7.514
7.493
7.475
7.454
7.393
7.375
7.356
7.338
7.331
7.321
7.310
7.301
7.285
7.279
7.276
7.267
7.258
7.193
7.174
5.064
4.942
4.830
4.669
4.665
4.644
4.641
4.576
4.553
4.476
4.441
4.398
4.361
4.089
4.079
4.059
4.049
2.552
2.541
2.527
2.516
2.505
2.500
2.491
2.480
2.475
2.464
2.453
2.439
2.428
1.973
1.937
1.932
1.893
1.357
1.204
Br
HO
NH
Ph
N
Boc
O
(^{1}H NMR, 400 MHz, CD_3OD)
2.00
5.00
2.00
1.00
1.00
2.00
1.00
1.00
1.00
4.00
5.00
f1 (ppm)

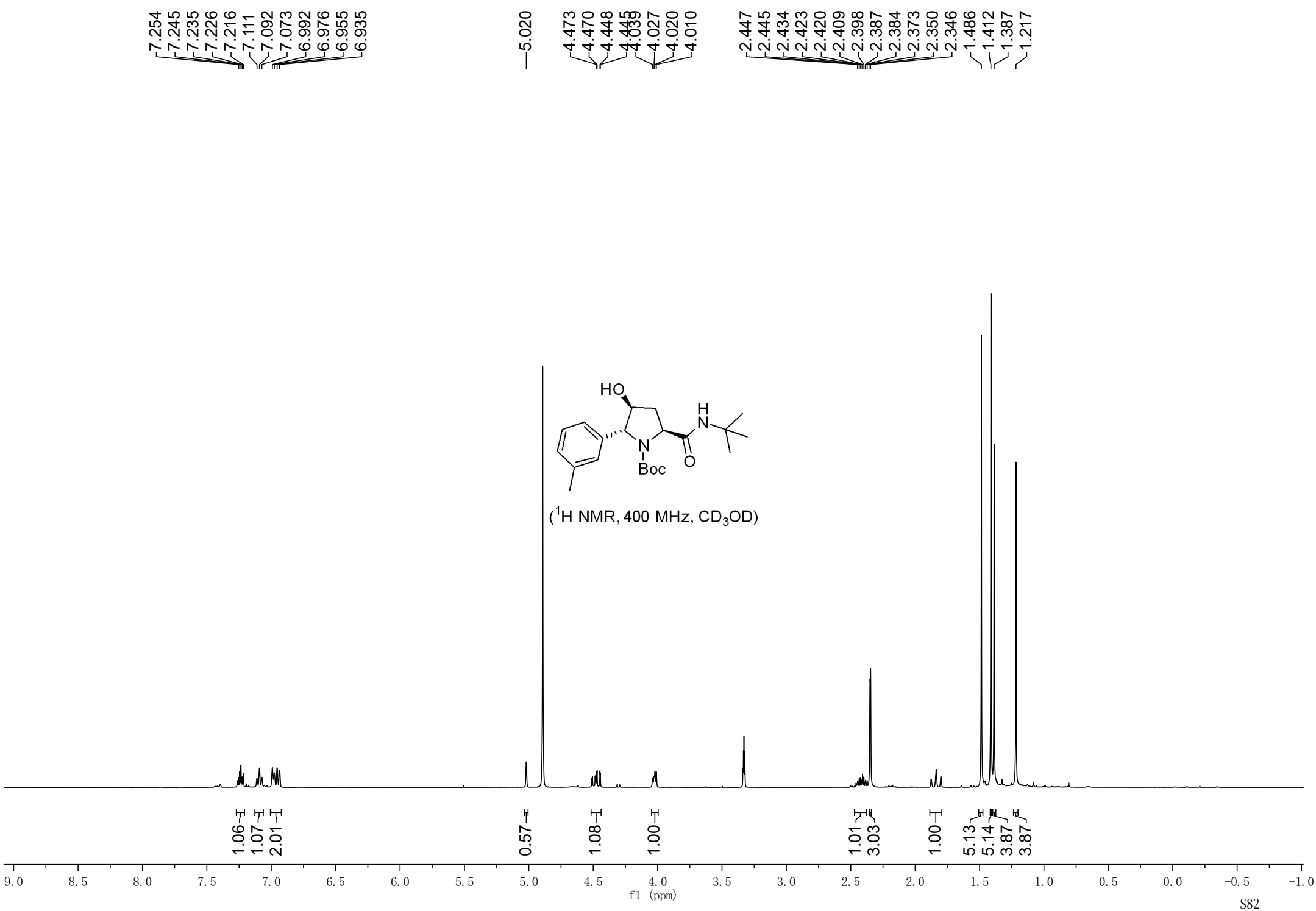

174.745
174.467
154.790
154.142
141.166
139.981
137.660
131.298
131.082
129.733
128.981
128.331
128.255
126.952
125.116
124.922
120.767
120.374
80.842
80.195
77.972
77.377
72.177
71.631
60.982
60.818
42.458
42.187
35.033
34.365
27.140
26.924
Br
HO
NH
Ph
N
O
Boc
(^{13}C NMR, 100 MHz, CD_3OD)
240 230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40
f1 (ppm)

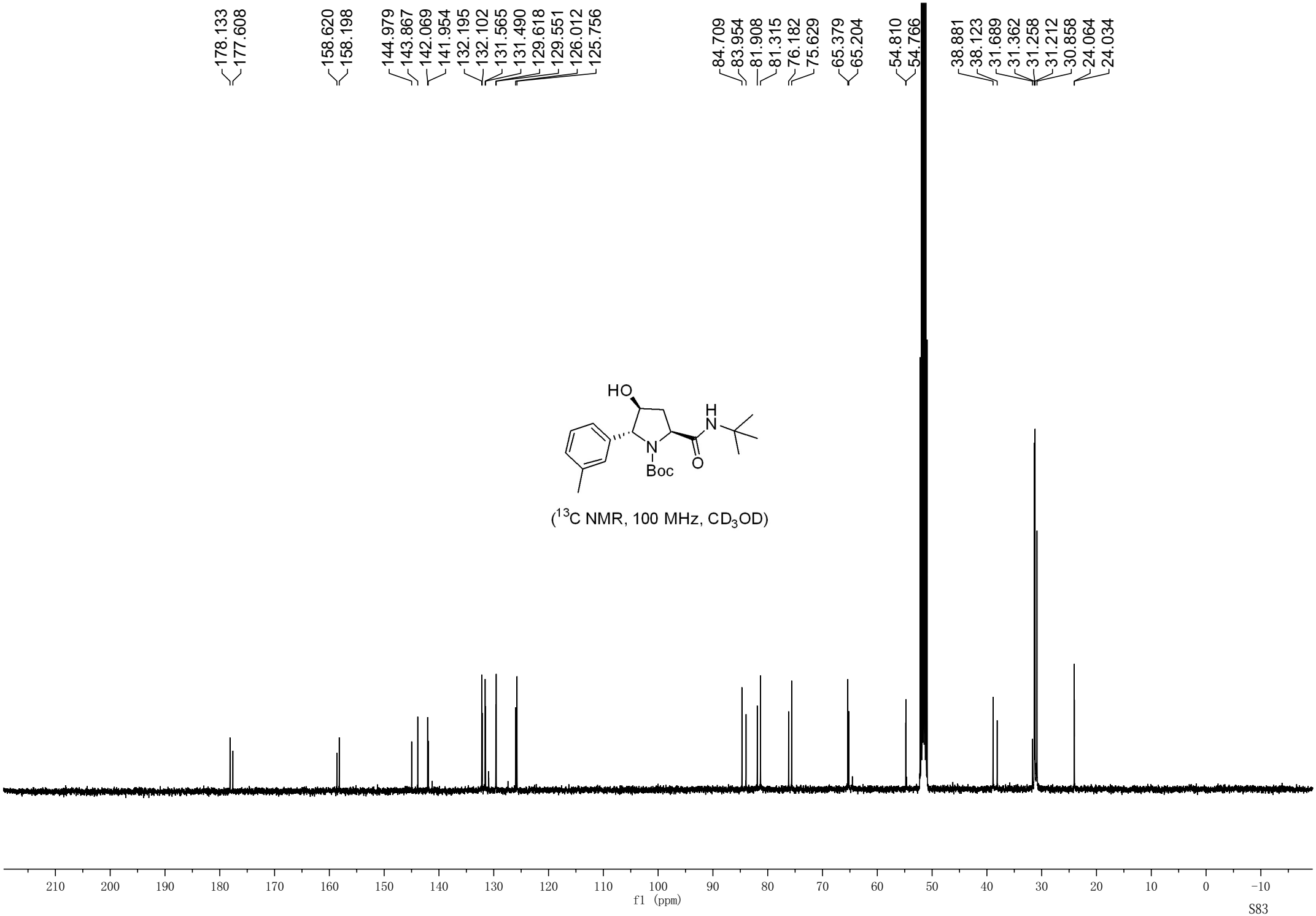

7.392
7.383
7.374
7.365
7.355
7.346
7.284
7.265
7.194
7.187
7.175
7.169
5.068
4.934
2.502
2.491
2.477
2.474
2.466
2.455
2.449
2.438
2.430
2.428
2.413
2.402
1.901
1.861
1.822
1.463
1.444
1.434
1.427
1.412
1.404
1.399
1.380
1.373
1.368
1.346
1.337
1.319
1.310
1.280
1.273
1.250
1.207
HO
Ph
N
Boc
H
N
O
(1H NMR, 400 MHz, CD3OD)
2.02
1.00
2.02
0.54
0.46
0.46
0.54
1.00
1.01
1.03
5.23
1.05
4.86
5.04
4.14
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


175.359
174.760
156.045
155.617
142.527
141.393
129.763
129.667
128.388
128.361
126.481
126.314
82.276
81.500
79.380
78.786
73.643
73.077
62.284
62.123
50.173
36.503
35.740
33.718
33.692
33.510
33.347
28.701
28.337
26.679
26.640
25.966
25.882
HO
H
N
Ph
N
O
Boc
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
f1 (ppm)

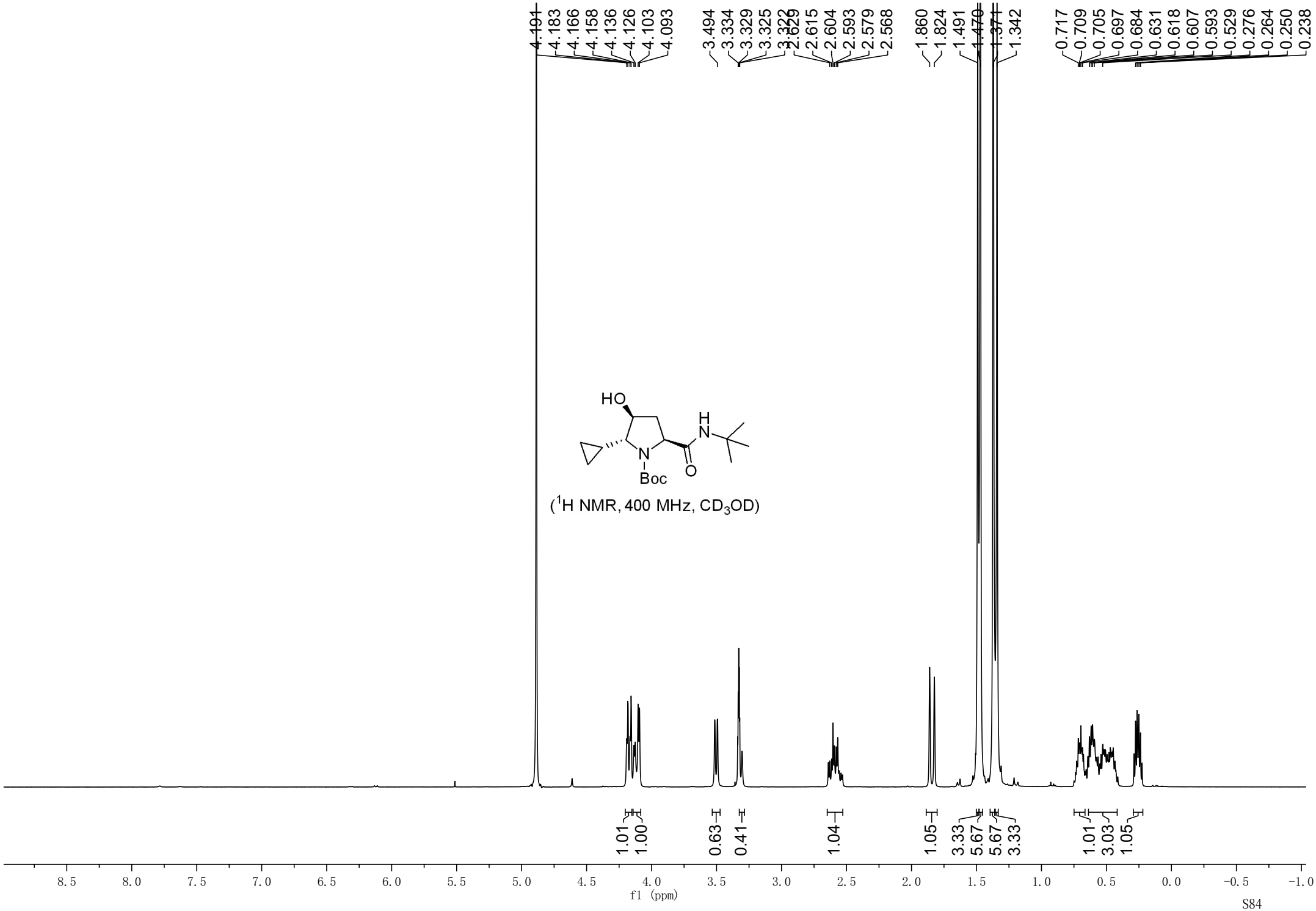

7.455
7.444
7.437
7.429
7.418
7.358
7.336
7.274
7.255
7.251
5.135
5.001
4.716
4.696
4.693
4.671
4.668
4.221
4.194
4.177
4.145
4.138
4.126
4.069
4.061
4.039
4.017
3.835
3.829
2.624
2.600
2.589
2.577
2.564
2.552
2.550
2.538
2.068
2.032
2.030
2.002
1.986
1.970
1.524
1.265
MeO
HO
NH
Ph
N
Boc
O
O
(^{1}H NMR, 400 MHz, CD_3OD)
2.10
1.09
2.00
1.00
1.00
4.11
1.47
1.53
1.02
1.13
4.60
4.40
f1 (ppm)

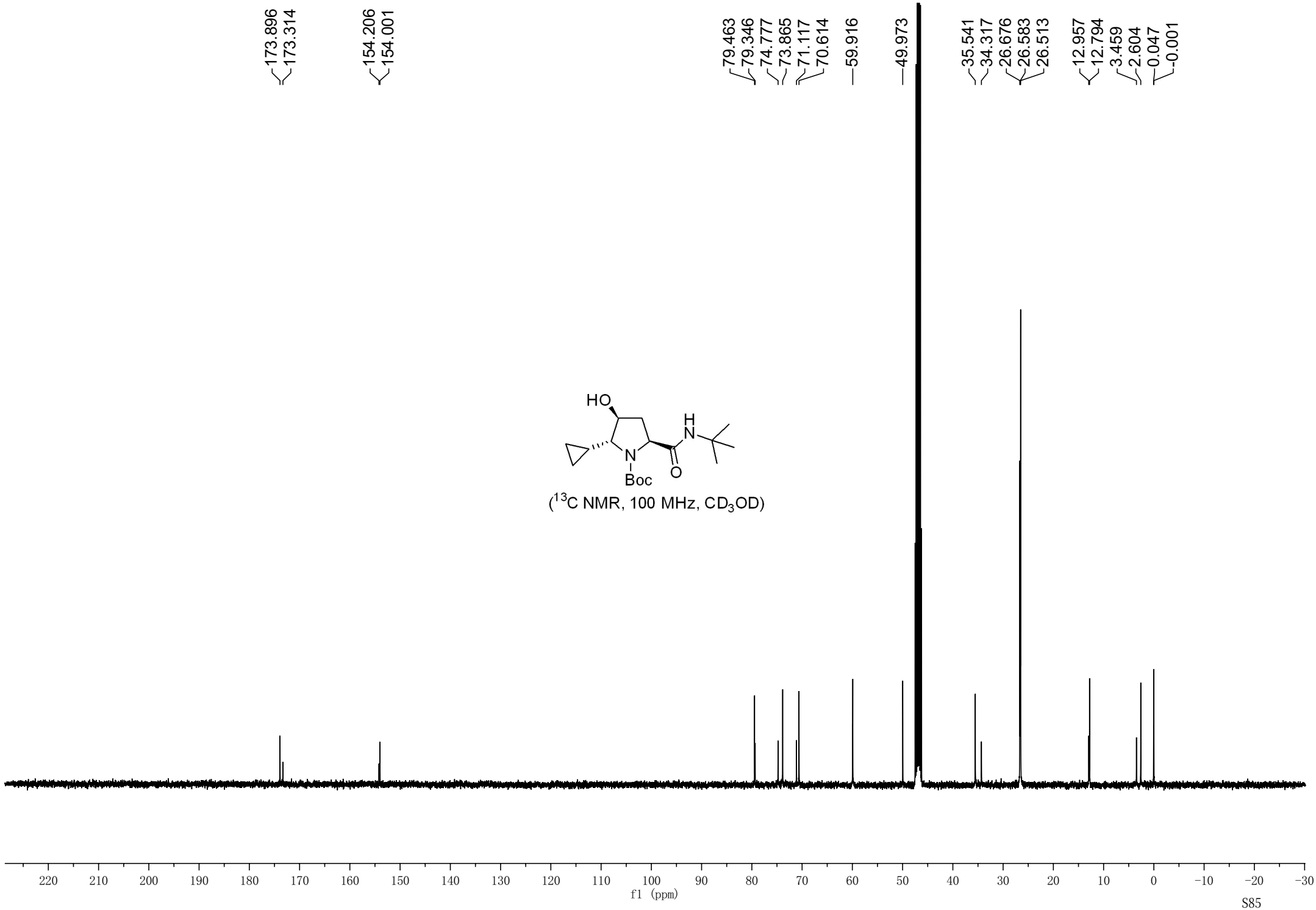

176.851
176.293
171.438
171.252
156.171
155.572
142.565
141.389
129.755
129.671
128.377
128.030
126.547
126.361
82.397
81.640
79.444
78.835
73.589
72.950
62.178
61.853
52.636
42.167
42.114
36.294
35.678
28.558
28.335
MeO
O
HO
NH
Ph
N
O
Boc
(^{13}C NMR, 100 MHz, CD_3OD)
f1 (ppm)

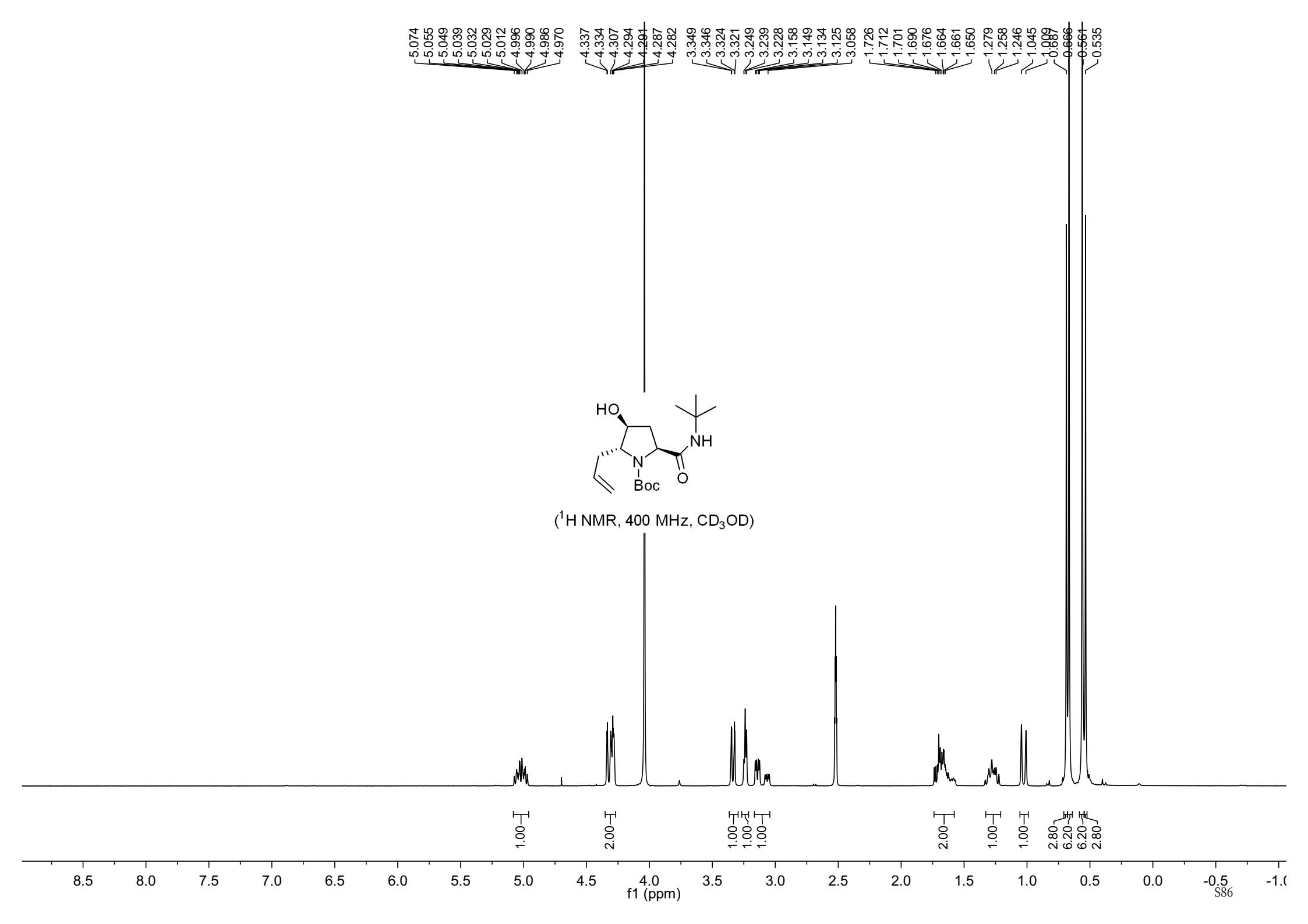

7.254
7.245
7.235
7.226
7.216
7.111
7.092
7.073
6.992
6.976
6.955
6.935
5.020
4.473
4.470
4.448
4.445
4.039
4.027
4.020
4.010
2.447
2.445
2.434
2.423
2.420
2.409
2.398
2.387
2.384
2.373
2.350
2.346
1.486
1.412
1.387
1.217
HO
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.06
1.07
2.01
0.57
1.08
1.00
1.01
3.03
1.00
5.13
5.14
3.87
3.87
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

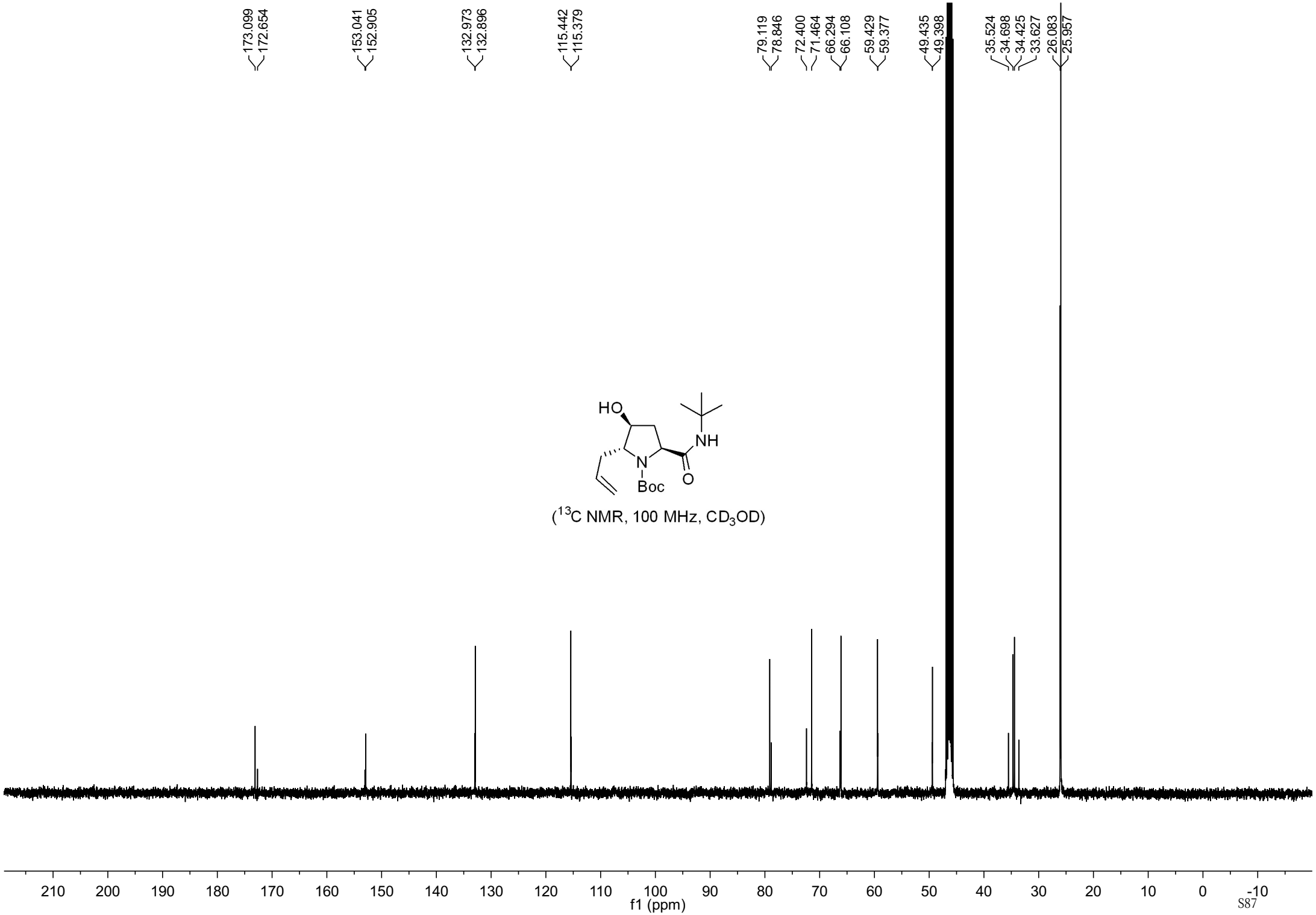


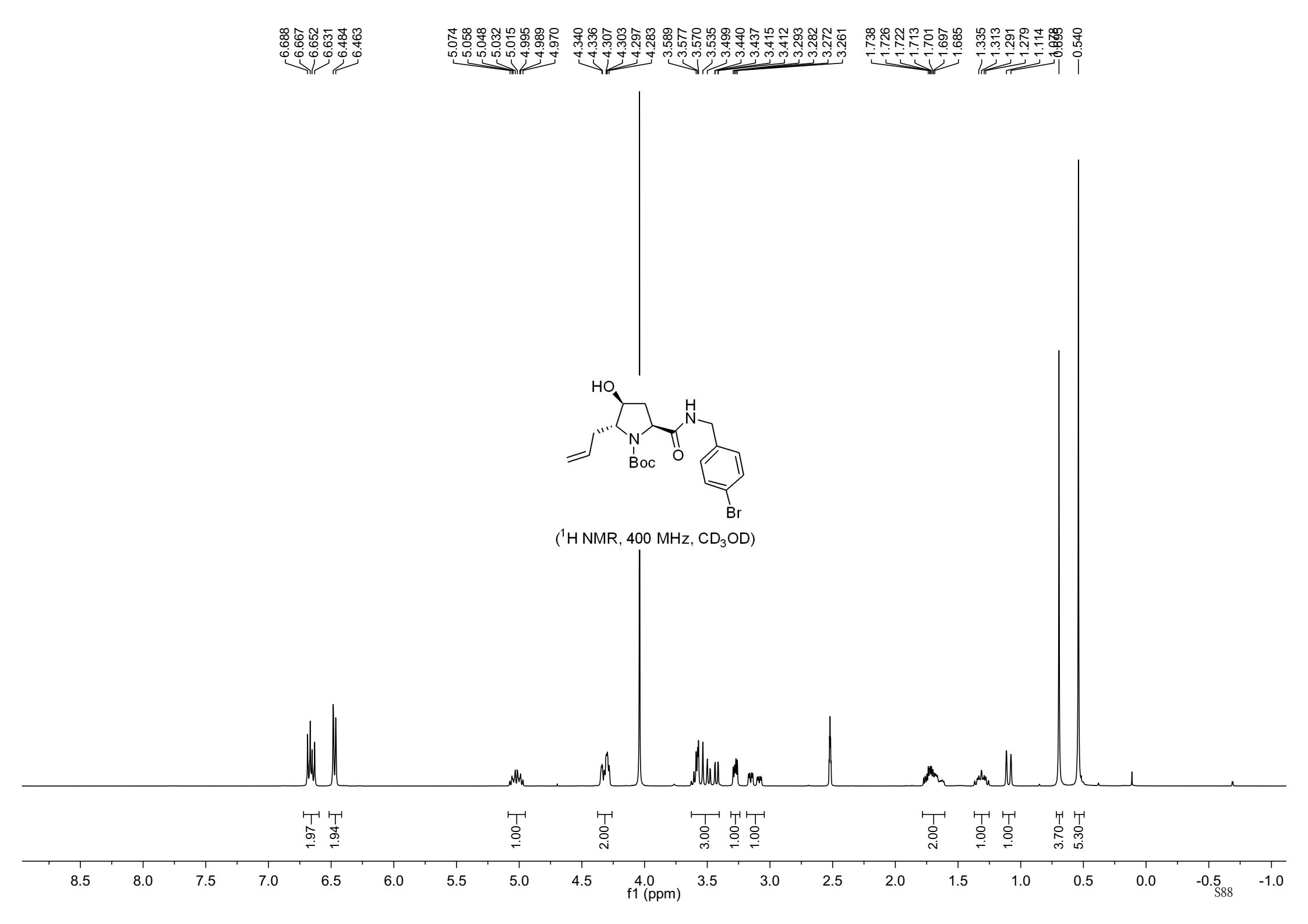
(^{13}C NMR, 100 MHz, CD_3OD)

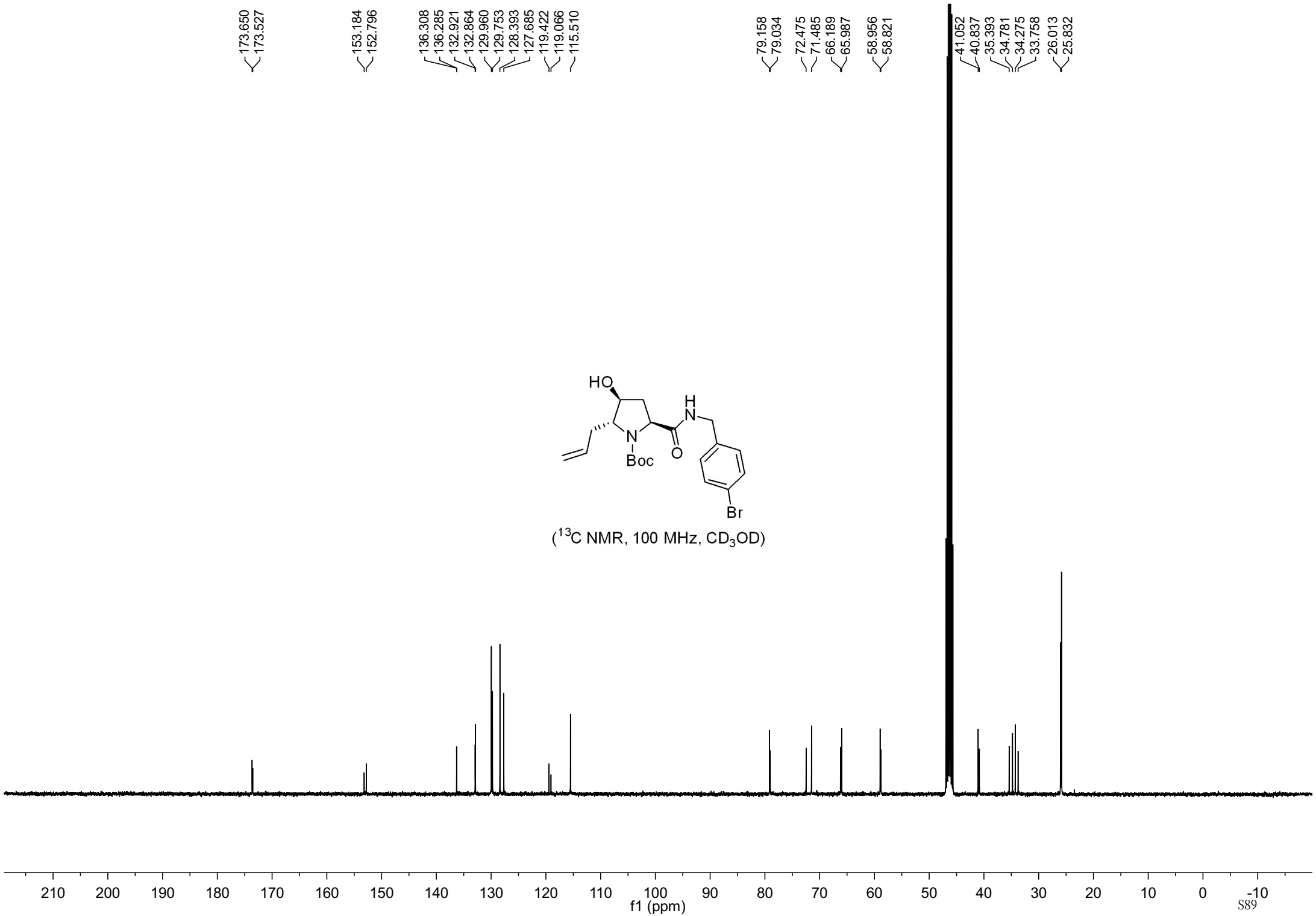

4.191
4.183
4.166
4.158
4.136
4.126
4.103
4.093
3.494
3.334
3.329
3.325
2.615
2.604
2.593
2.579
2.568
1.860
1.824
1.491
1.470
1.371
1.342
0.717
0.709
0.705
0.697
0.684
0.631
0.618
0.607
0.593
0.529
0.276
0.264
0.250
0.238
HO
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.01
1.00
0.63
0.41
1.04
1.05
3.33
5.67
5.67
3.33
1.01
3.03
1.05
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)

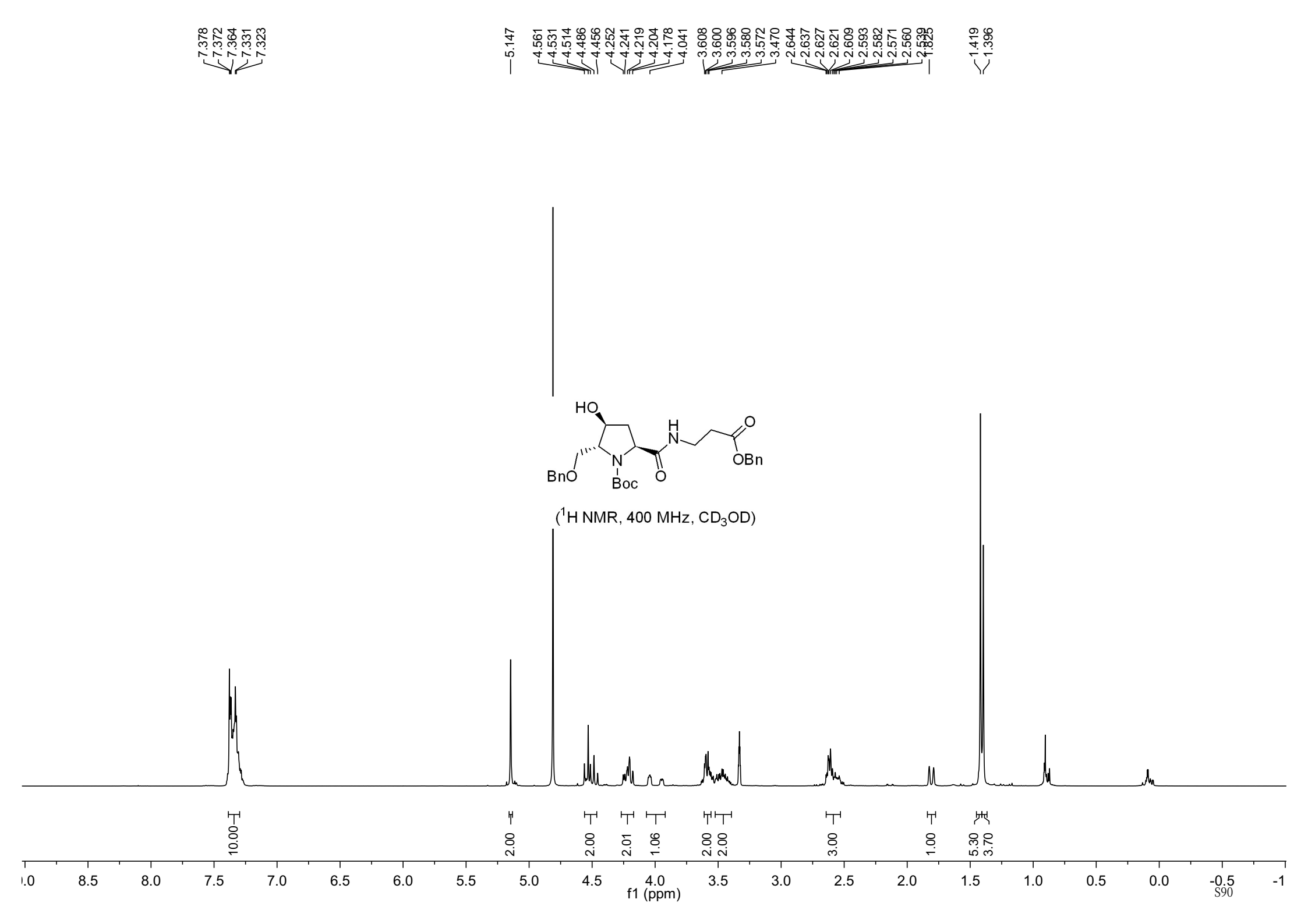

173.896
173.314
154.206
154.001
79.463
79.346
74.777
73.865
71.117
70.614
59.916
49.973
35.541
34.317
26.676
26.583
26.513
12.957
12.794
3.459
2.604
0.047
-0.001
HO
H
N
N
Boc
O
(13C NMR, 100 MHz, CD3OD)
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
−10
−20
−30
f1 (ppm)

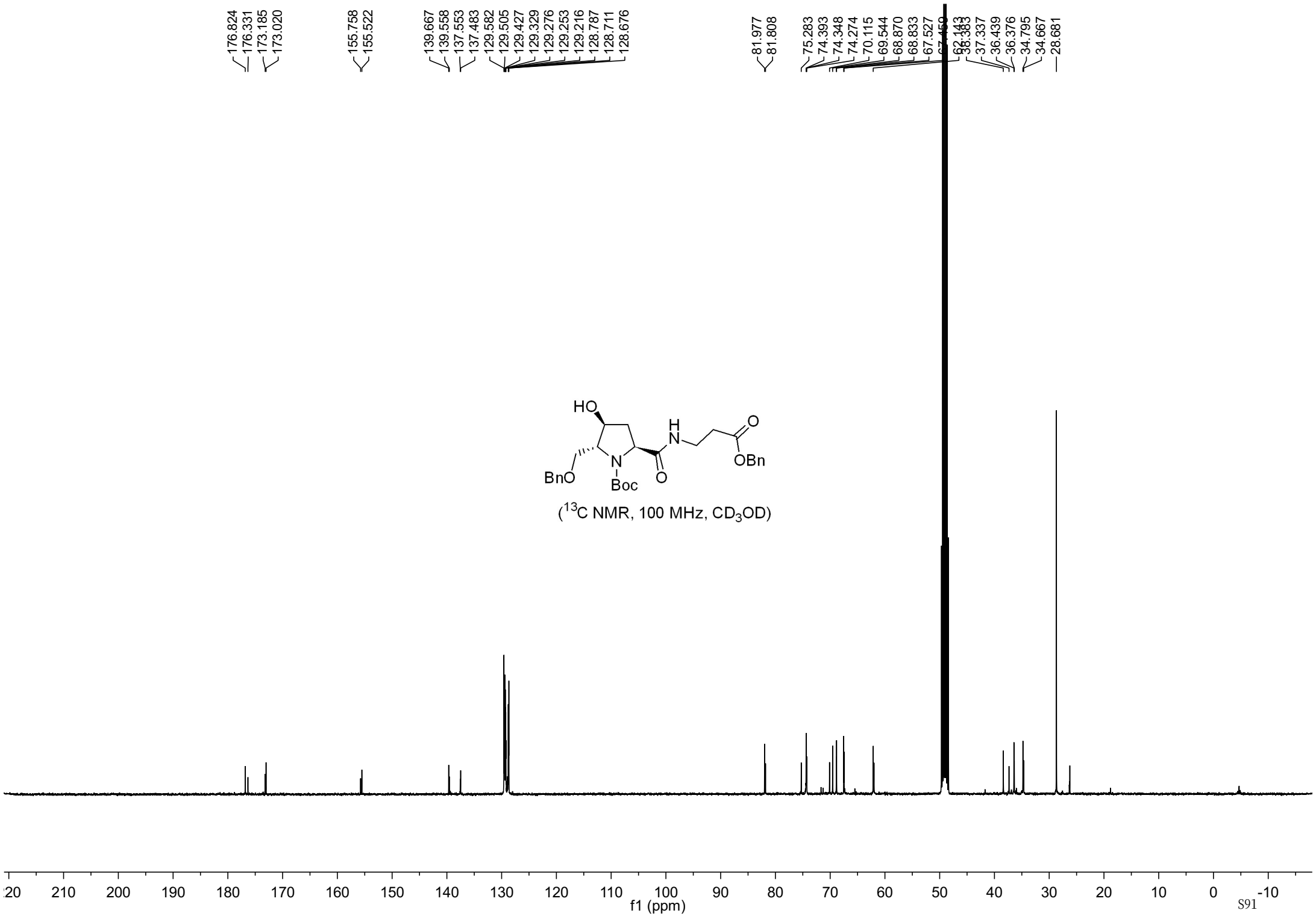

5.074
5.055
5.049
5.039
5.032
5.029
5.012
4.996
4.990
4.986
4.970
4.337
4.334
4.307
4.294
4.291
4.287
4.282
3.349
3.346
3.324
3.321
3.249
3.239
3.228
3.158
3.149
3.134
3.125
3.058
1.726
1.712
1.701
1.690
1.676
1.664
1.661
1.650
1.279
1.258
1.246
1.045
1.009
0.887
0.666
0.561
0.535
HO
NH
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
1.00
2.00
1.00
1.00
1.00
2.00
1.00
1.00
2.80
6.20
6.20
2.80
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)

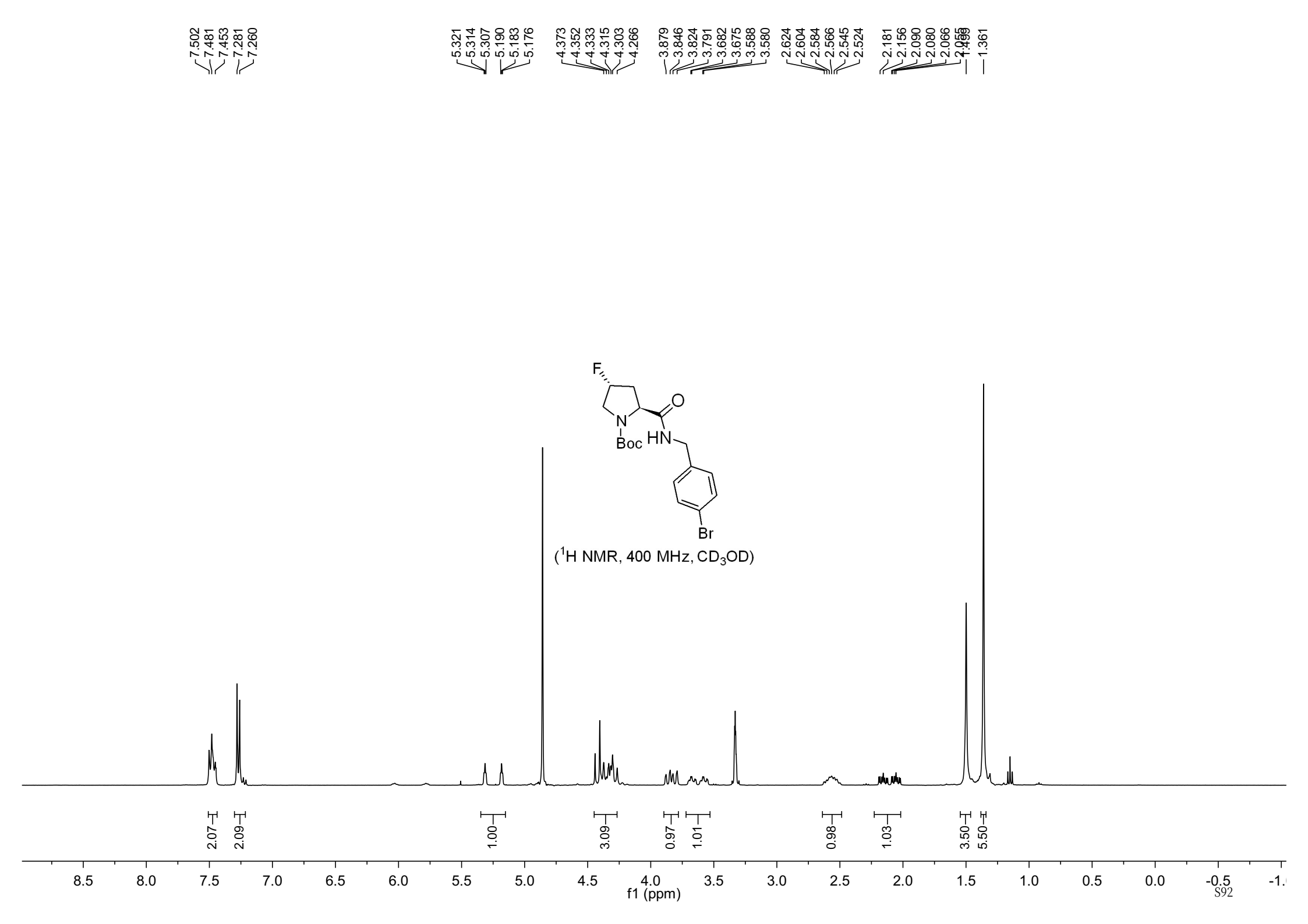

173.099
172.654
153.041
152.905
132.973
132.896
115.442
115.379
79.119
78.846
72.400
71.464
66.294
66.108
59.429
59.377
49.435
49.398
35.524
34.698
34.425
33.627
26.083
25.957
HO
NH
N
O
Boc
(13C NMR, 100 MHz, CD3OD)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

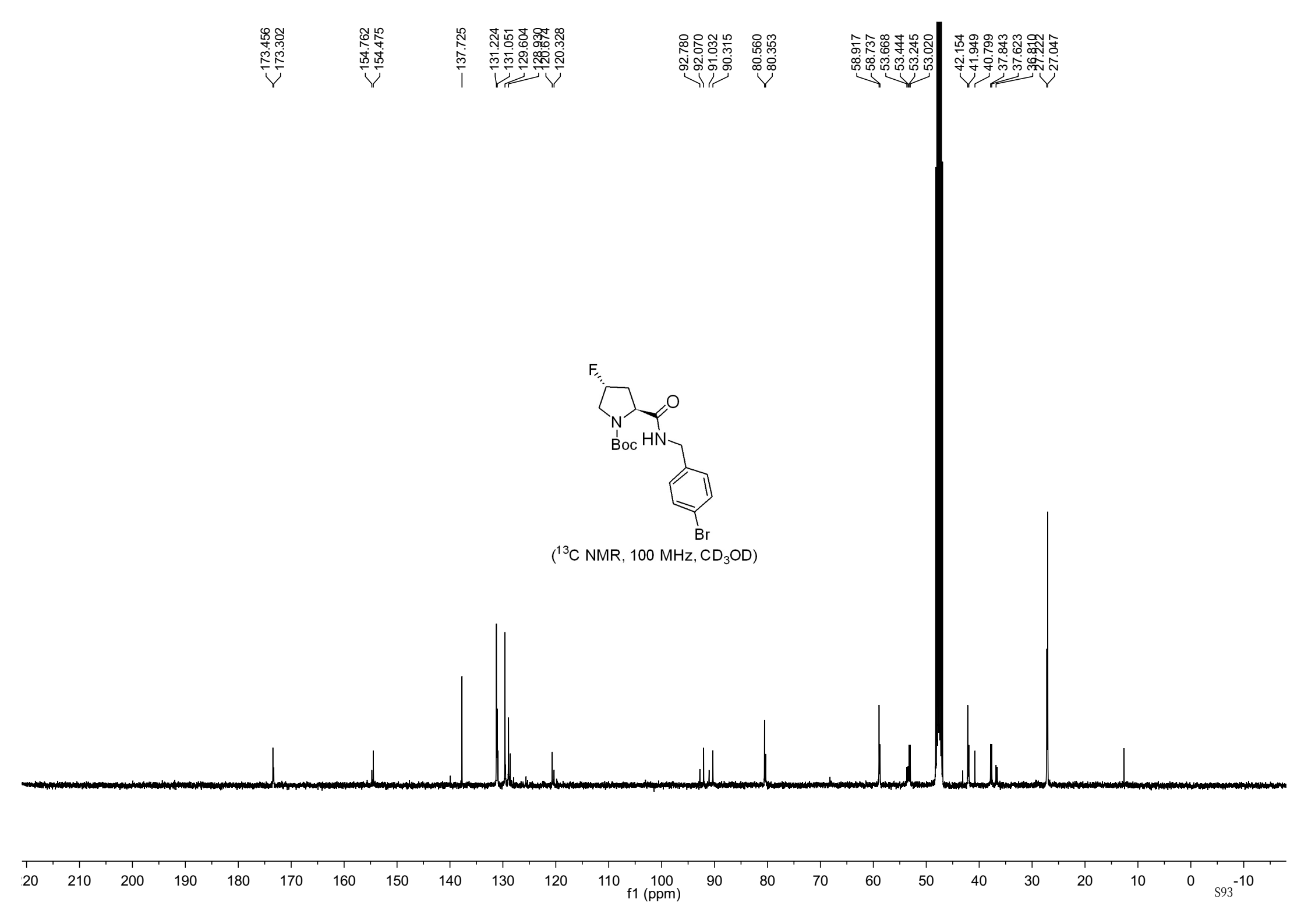

6.688
6.667
6.652
6.631
6.484
6.463
5.074
5.058
5.048
5.032
5.015
4.995
4.989
4.970
4.340
4.336
4.307
4.303
4.297
4.283
3.589
3.577
3.570
3.535
3.499
3.440
3.437
3.415
3.412
3.293
3.282
3.272
3.261
1.738
1.726
1.722
1.713
1.701
1.697
1.685
1.335
1.313
1.291
1.279
1.114
0.540
HO
H
N
N
Boc
O
Br
(1H NMR, 400 MHz, CD3OD)
1.97
1.94
1.00
2.00
3.00
1.00
1.00
2.00
1.00
1.00
3.70
5.30
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


173.650
173.527
153.184
152.796
136.308
136.285
132.921
132.864
129.960
129.753
128.393
127.685
119.422
119.066
115.510
79.158
79.034
72.475
71.485
66.189
65.987
58.956
58.821
41.052
40.837
35.393
34.781
34.275
33.758
26.013
25.832
HO
H
N
N
Boc
O
Br
(^{13}C NMR, 100 MHz, CD_3OD)
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)

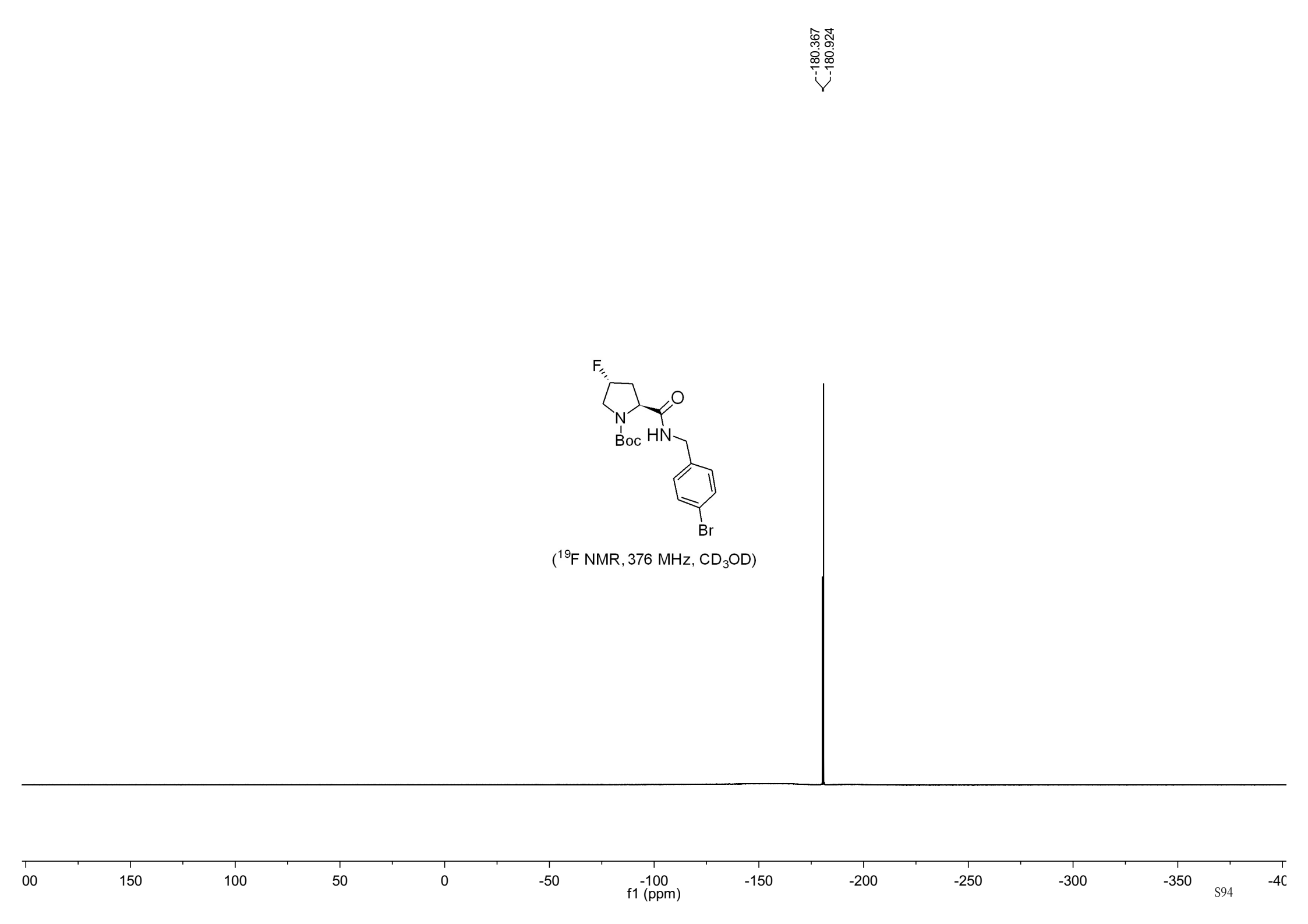

7.378
7.372
7.364
7.331
7.323
5.147
4.561
4.531
4.514
4.486
4.456
4.252
4.241
4.219
4.204
4.178
4.041
3.608
3.600
3.596
3.580
3.572
3.470
2.644
2.637
2.627
2.621
2.609
2.593
2.582
2.571
2.560
1.825
1.419
1.396
HO
H
N
O
OBn
BnO
N
Boc
O
(^{1}H NMR, 400 MHz, CD_3OD)
10.00
2.00
2.00
2.01
1.06
2.00
2.00
3.00
1.00
5.30
3.70
f1 (ppm)

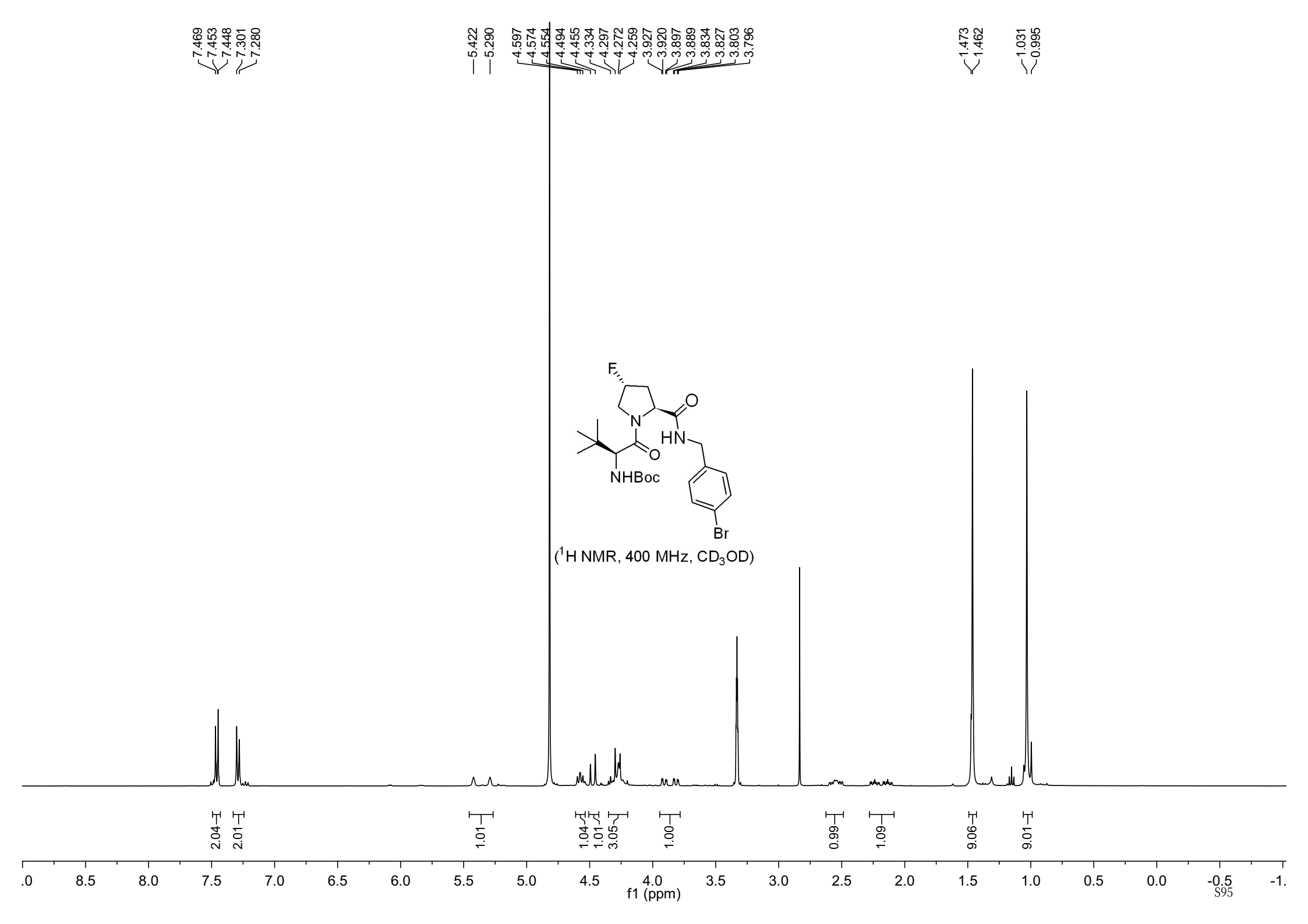

176.824
176.331
173.185
173.020
155.758
155.522
139.667
139.558
137.553
137.483
129.582
129.505
129.427
129.329
129.276
129.253
129.216
128.787
128.711
128.676
81.977
81.808
75.283
74.393
74.348
74.274
70.115
69.544
68.870
68.833
67.527
62.143
38.383
37.337
36.439
36.376
34.795
34.667
28.681
HO
H
N
O
OBn
BnO
N
Boc
O
(^{13}C NMR, 100 MHz, CD_3OD)
f1 (ppm)

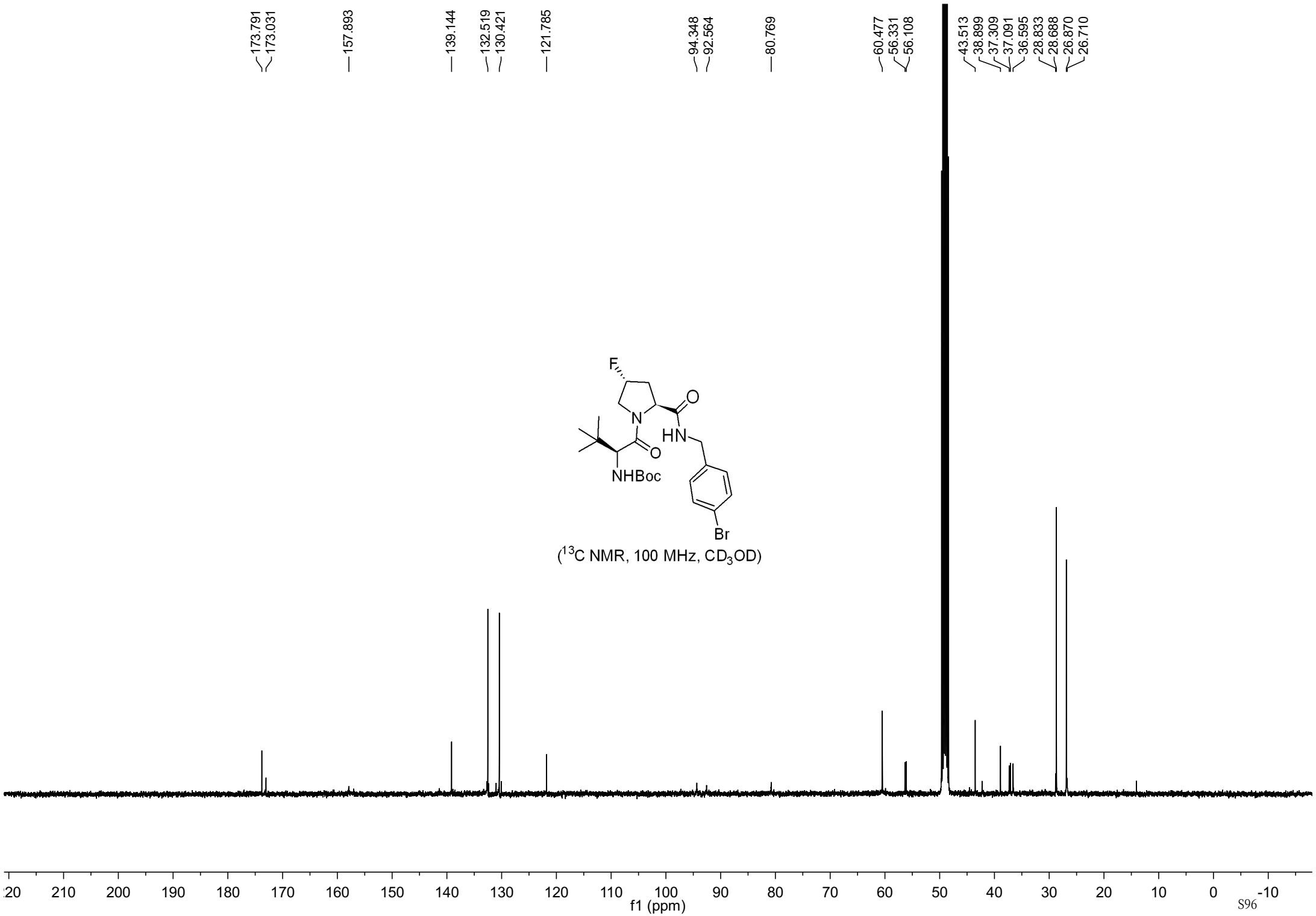

7.502
7.481
7.453
7.281
7.260
5.321
5.314
5.307
5.190
5.183
5.176
4.373
4.352
4.333
4.315
4.303
4.266
3.879
3.846
3.824
3.791
3.682
3.675
3.588
3.580
2.624
2.604
2.584
2.566
2.545
2.524
2.181
2.156
2.090
2.080
2.066
1.361
F
O
N
Boc
HN
Br
(^{1}H NMR, 400 MHz, CD_3OD)
2.07
2.09
1.00
3.09
0.97
1.01
0.98
1.03
3.50
5.50
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)



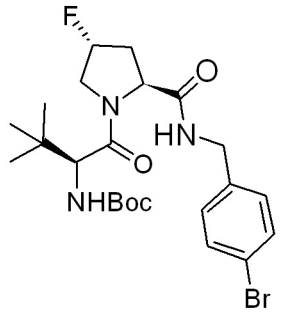
(^{13}C NMR, 100 MHz, CD_3OD)


-180.367
-180.924
F
O
N
Boc
HN
Br
(19F NMR, 376 MHz, CD3OD)
00
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
-40
f1 (ppm)

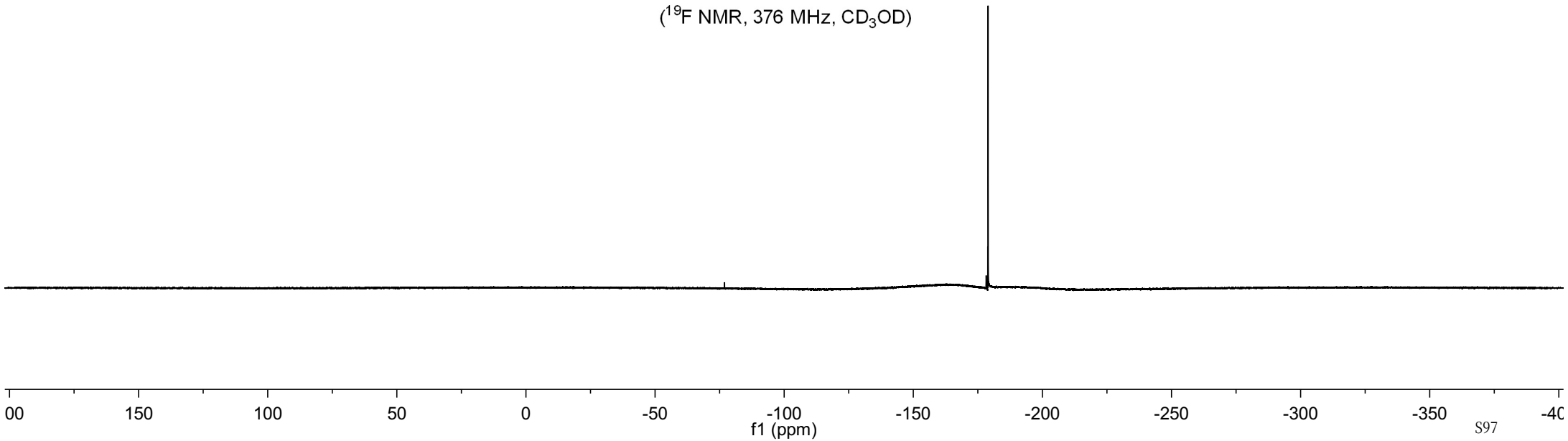

7.469
7.453
7.448
7.301
7.280
5.422
5.290
4.597
4.574
4.554
4.494
4.455
4.334
4.297
4.272
4.259
3.927
3.920
3.897
3.889
3.834
3.827
3.803
3.796
1.473
1.462
1.031
0.995
F
O
N
HN
O
NHBoc
Br
(1H NMR, 400 MHz, CD3OD)
2.04
2.01
1.01
1.04
1.01
3.05
1.00
0.99
1.09
9.06
9.01
f1 (ppm)

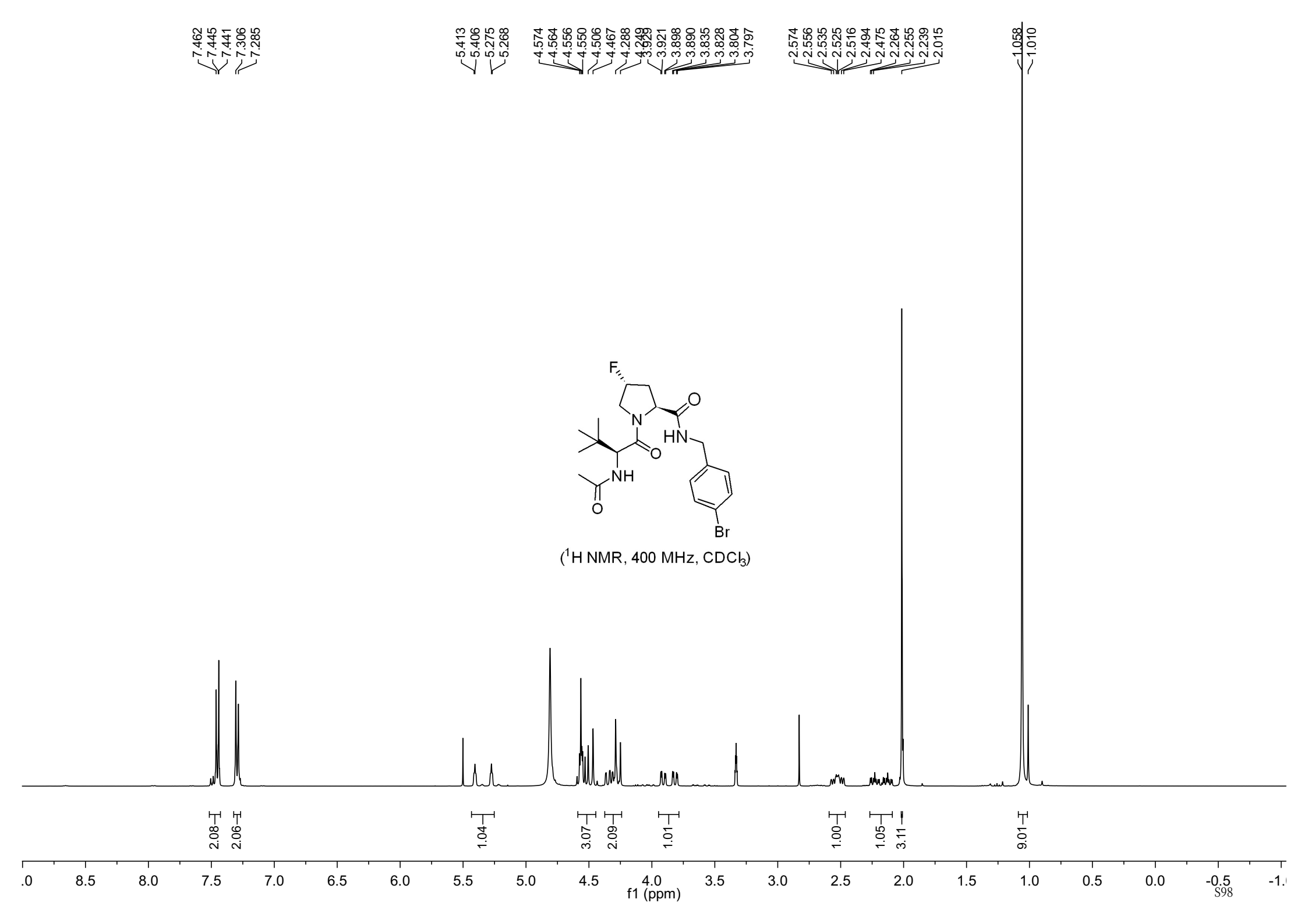

173.791
173.031
157.893
139.144
132.519
130.421
121.785
94.348
92.564
80.769
60.477
56.331
56.108
43.513
38.899
37.309
37.091
36.595
28.833
28.688
26.870
26.710
F
O
N
HN
O
NHBoc
Br
(13C NMR, 100 MHz, CD3OD)
f1 (ppm)

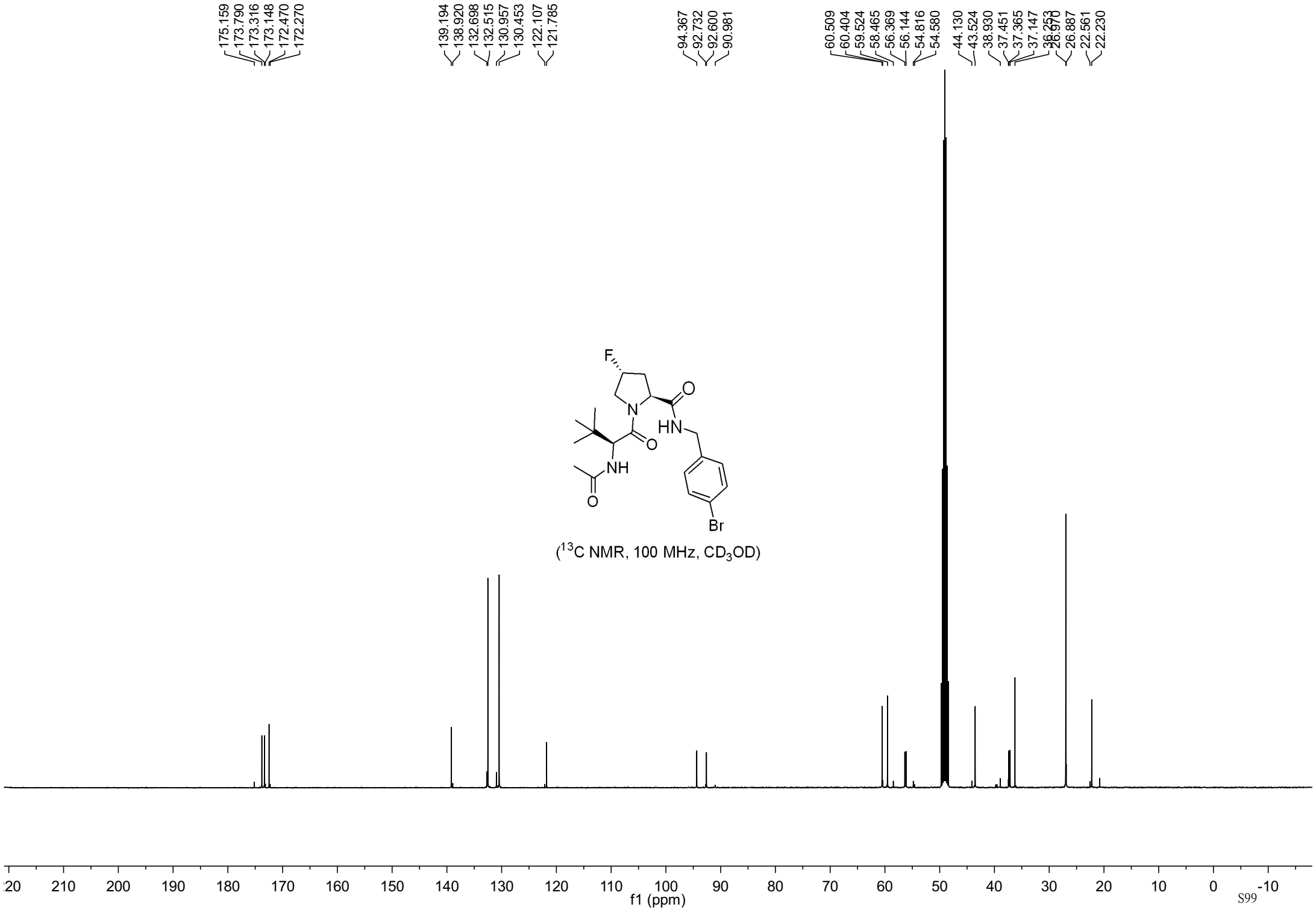
-178.832
-178.981

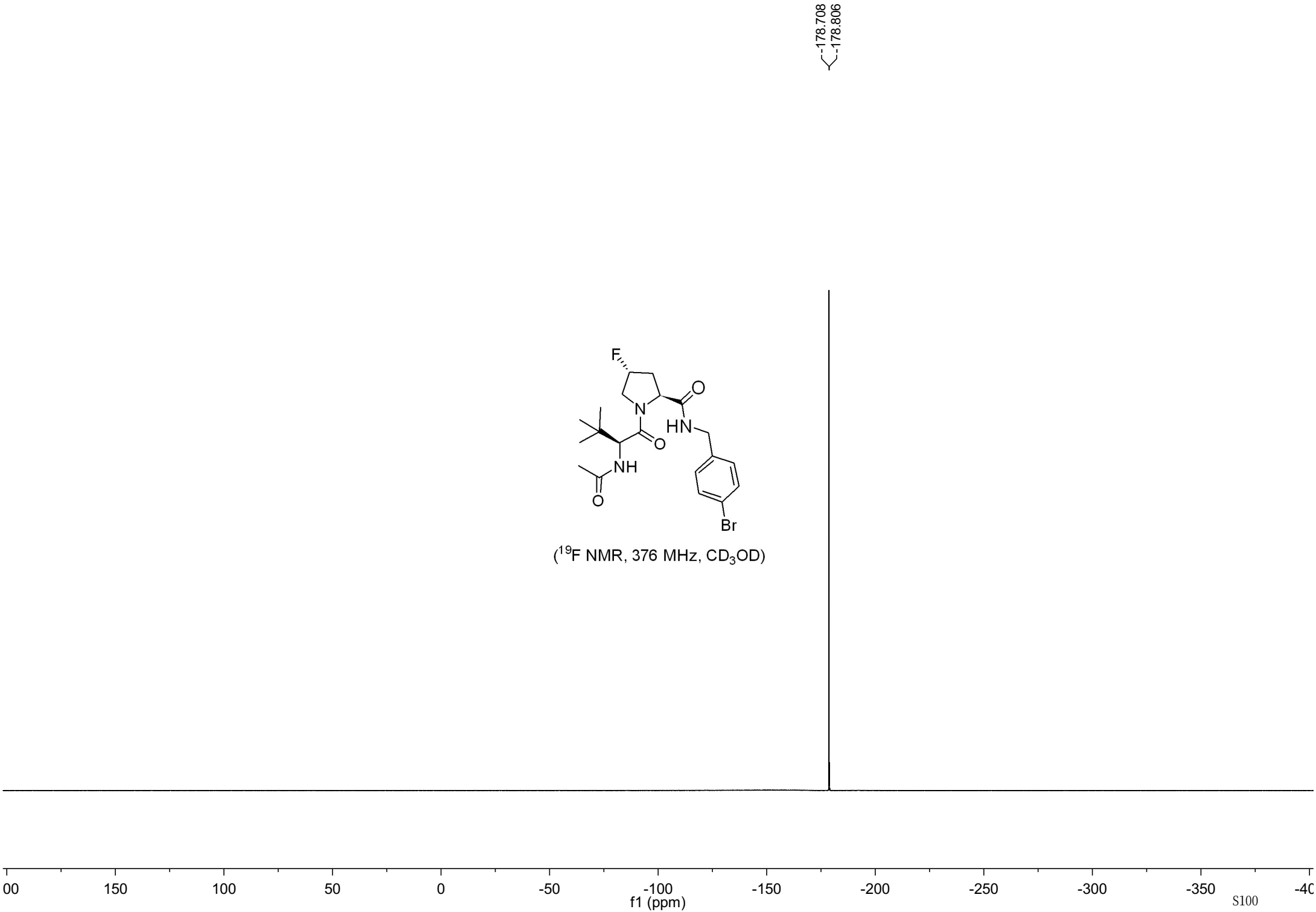


(^{19}F NMR, 376 MHz, CD_3OD)

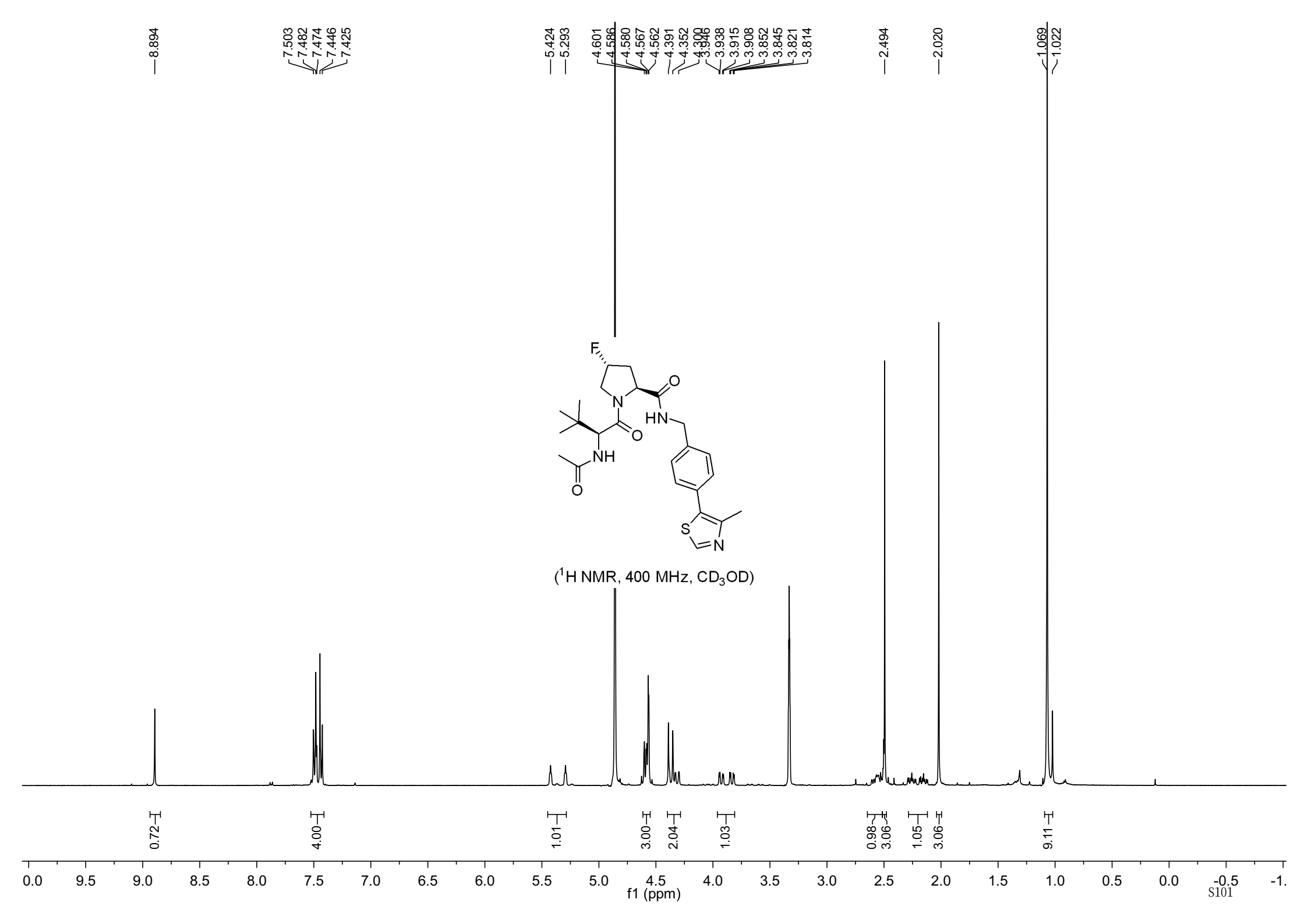


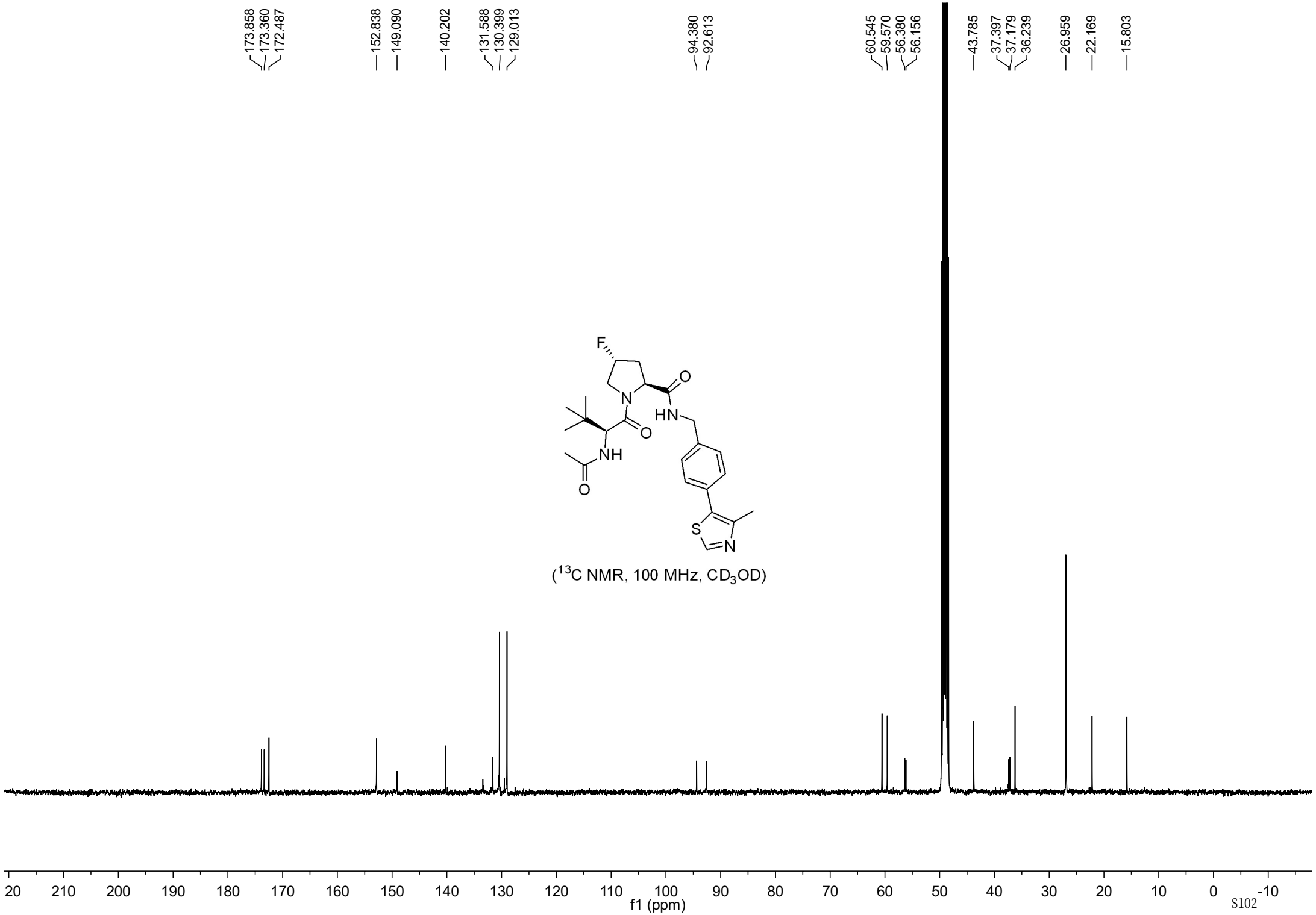

7.462
7.445
7.441
7.306
7.285
5.413
5.406
5.275
5.268
4.574
4.564
4.556
4.550
4.506
4.467
4.288
4.249
3.929
3.921
3.898
3.890
3.835
3.828
3.804
3.797
2.574
2.556
2.535
2.525
2.516
2.494
2.475
2.264
2.255
2.239
2.015
1.058
1.010
F
O
N
HN
O
NH
O
Br
(1H NMR, 400 MHz, CDCl3)
2.08
2.06
1.04
3.07
2.09
1.01
1.00
1.05
3.11
9.01
f1 (ppm)

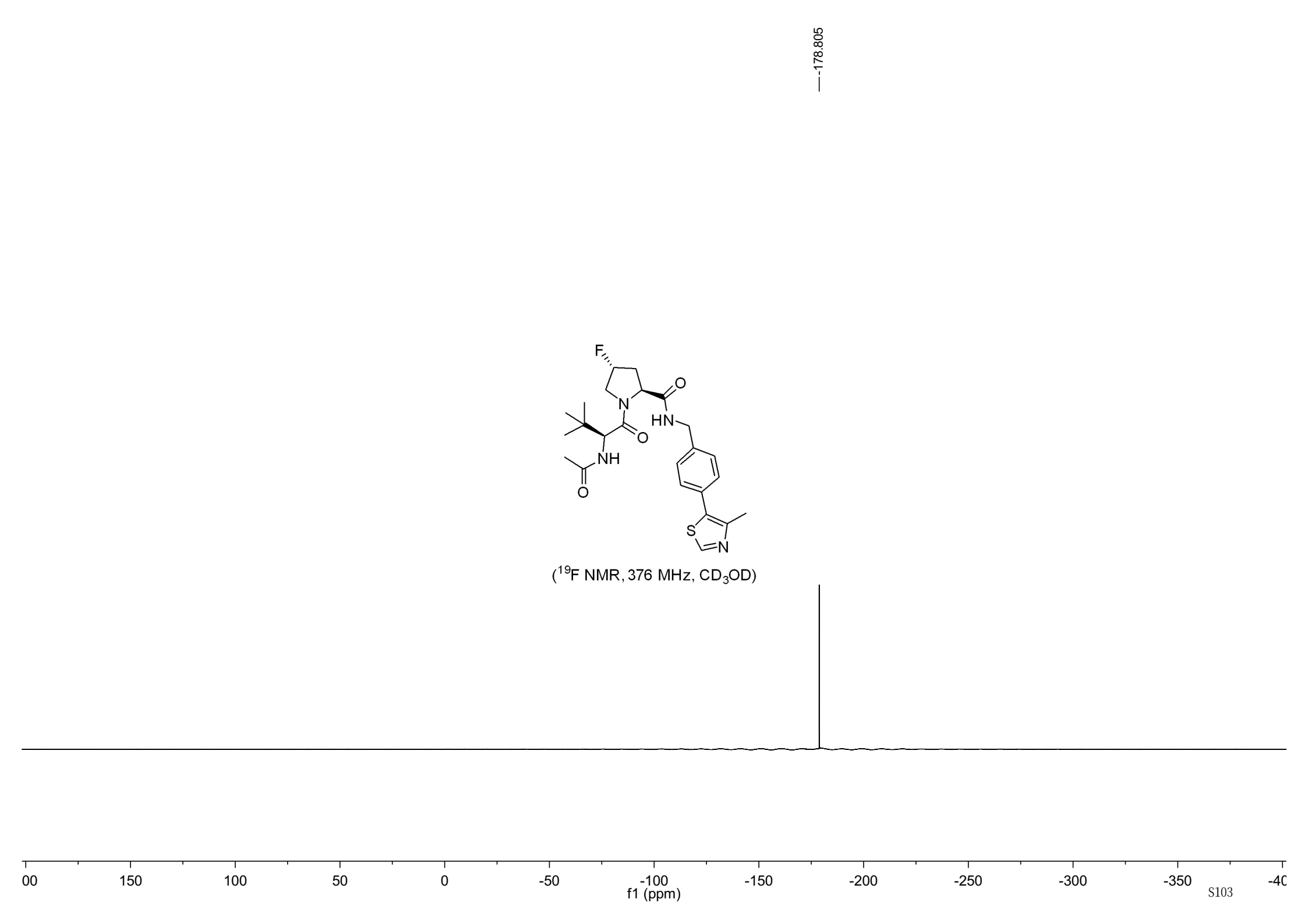

175.159
173.790
173.316
173.148
172.470
172.270
139.194
138.920
132.698
132.515
130.957
130.453
122.107
121.785
94.367
92.732
92.600
90.981
60.509
60.404
59.524
58.465
56.369
56.144
54.816
54.580
44.130
43.524
38.930
37.451
37.365
37.147
26.970
26.887
22.561
22.230
F
O
N
HN
O
NH
O
Br
(^{13}C NMR, 100 MHz, CD_3OD)
f1 (ppm)

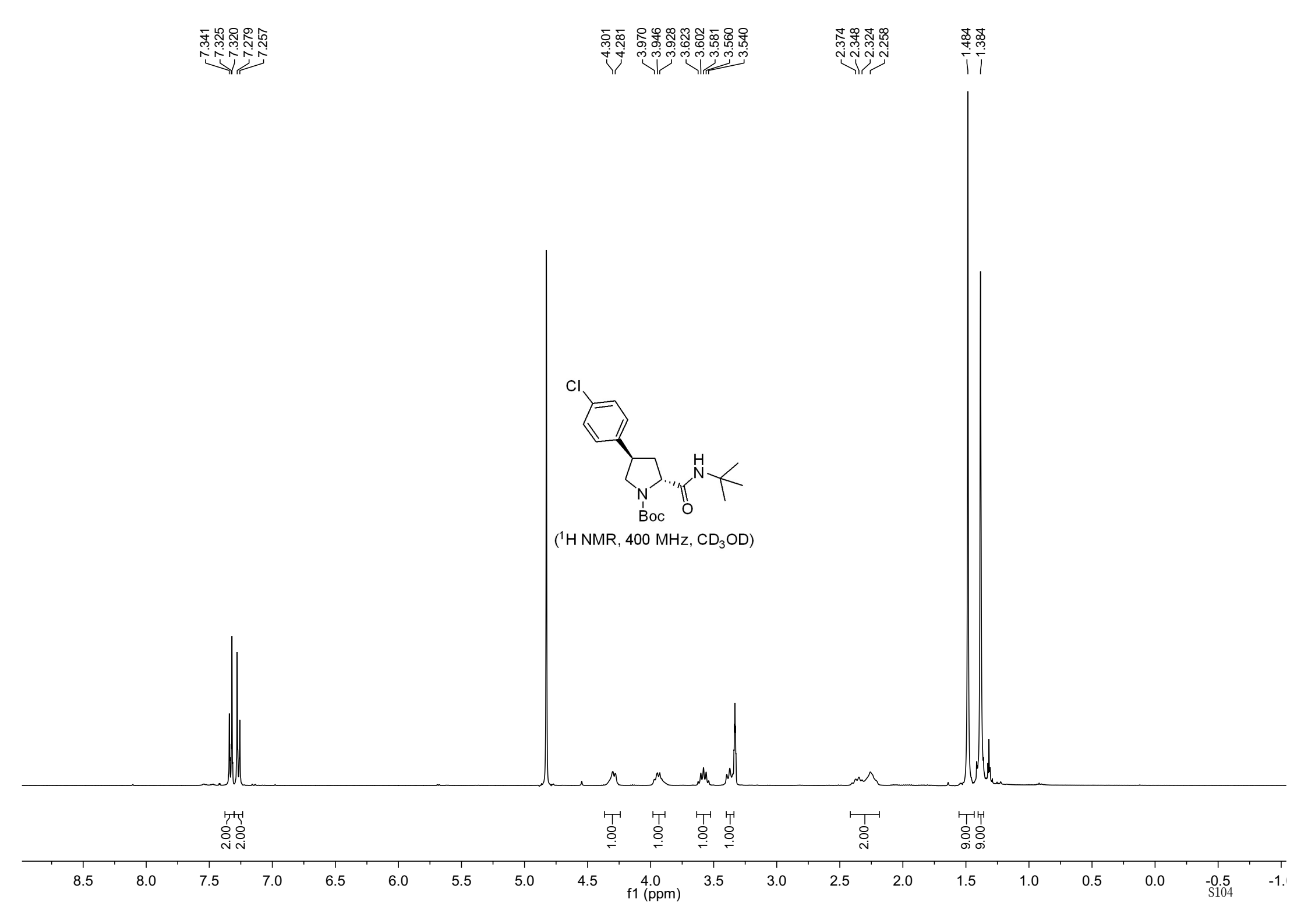


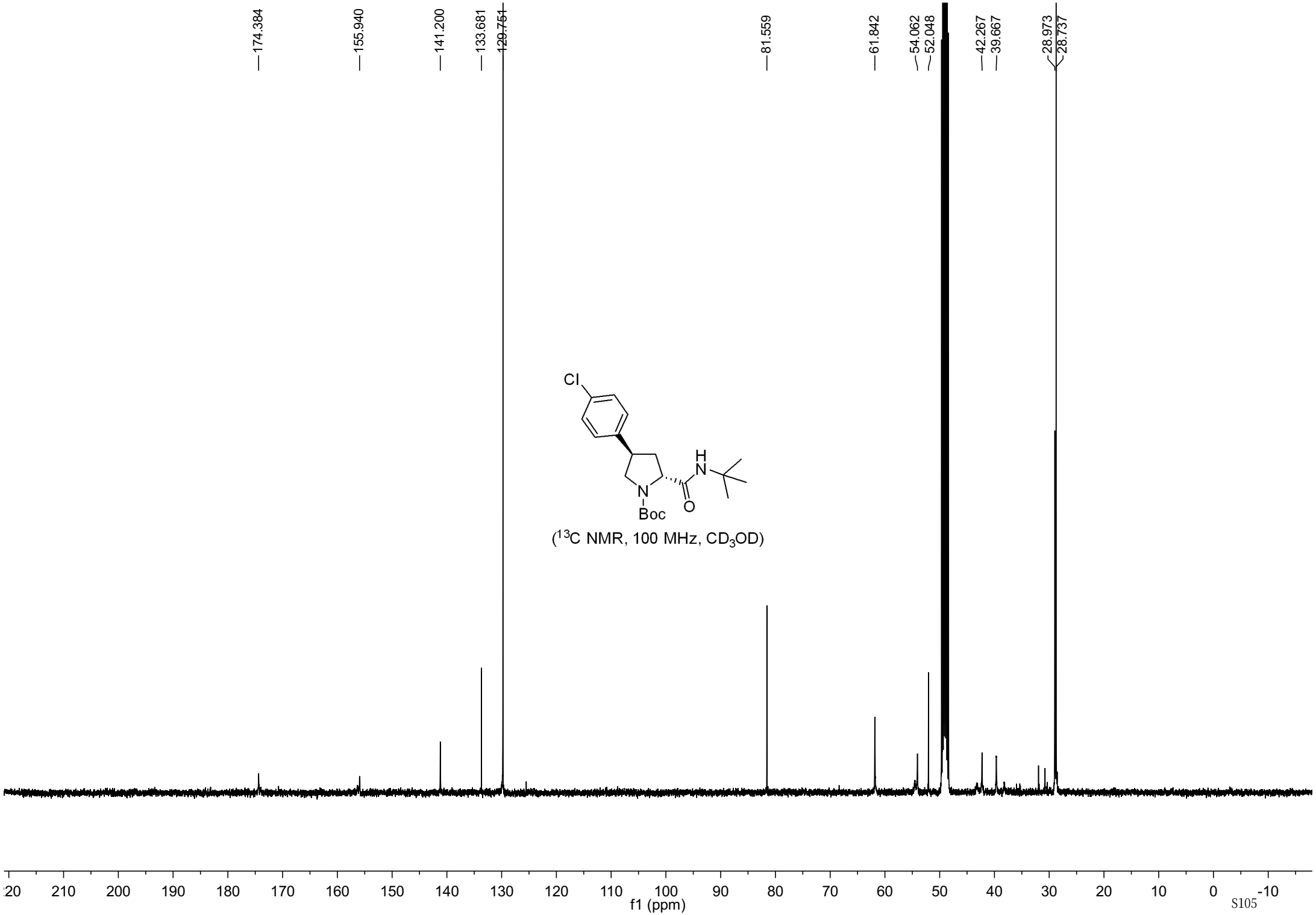
(^{19}F NMR, 376 MHz, CD_3OD)

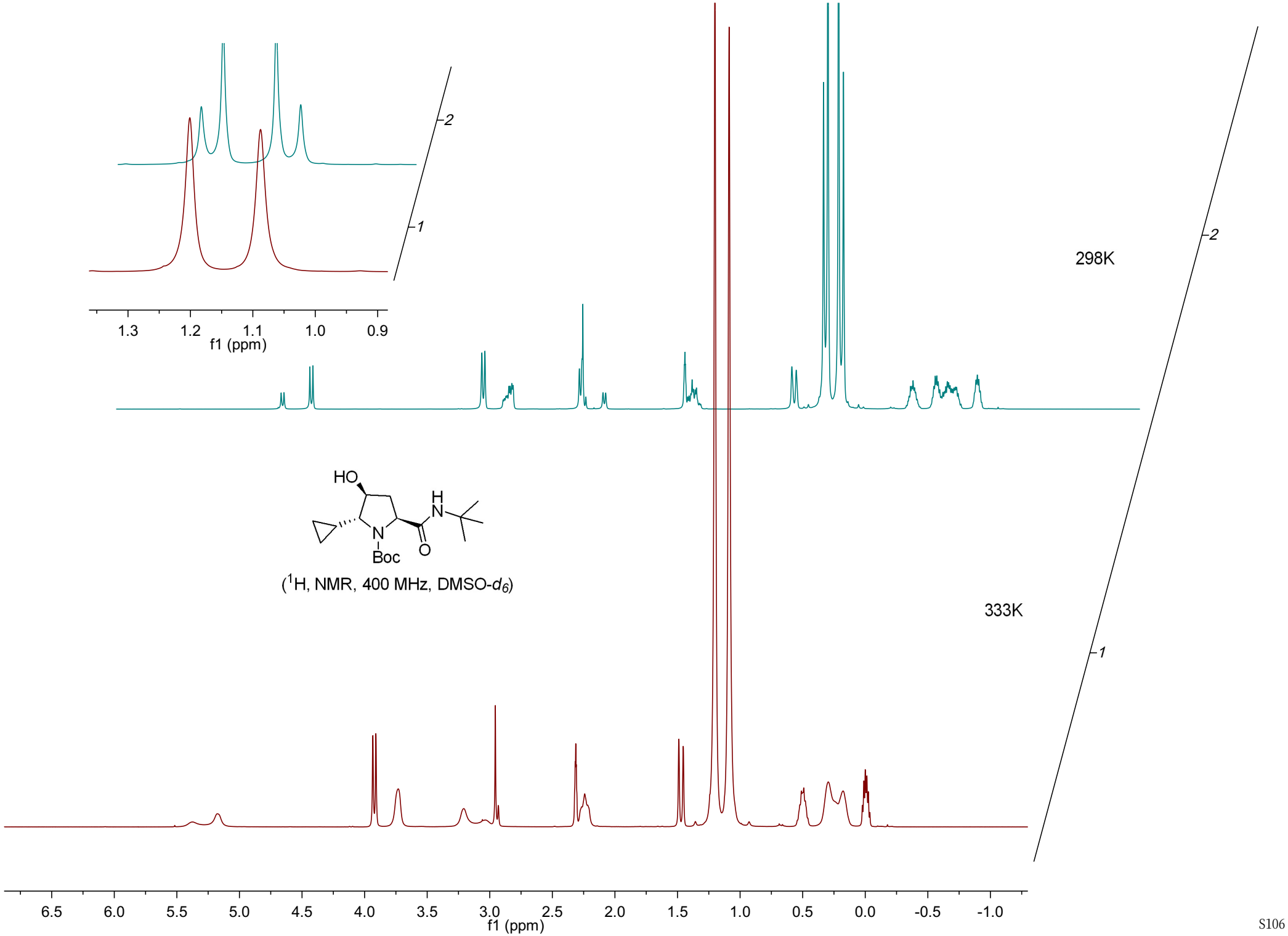

8.894
7.503
7.482
7.474
7.446
7.425
5.424
5.293
4.601
4.586
4.580
4.567
4.562
4.391
4.352
4.300
3.946
3.938
3.915
3.908
3.852
3.845
3.821
3.814
2.494
2.020
1.069
1.022
F
O
N
HN
O
NH
O
S
N
(1H NMR, 400 MHz, CD3OD)
0.72
4.00
1.01
3.00
2.04
1.03
0.98
3.06
1.05
3.06
9.11
0.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.
f1 (ppm)

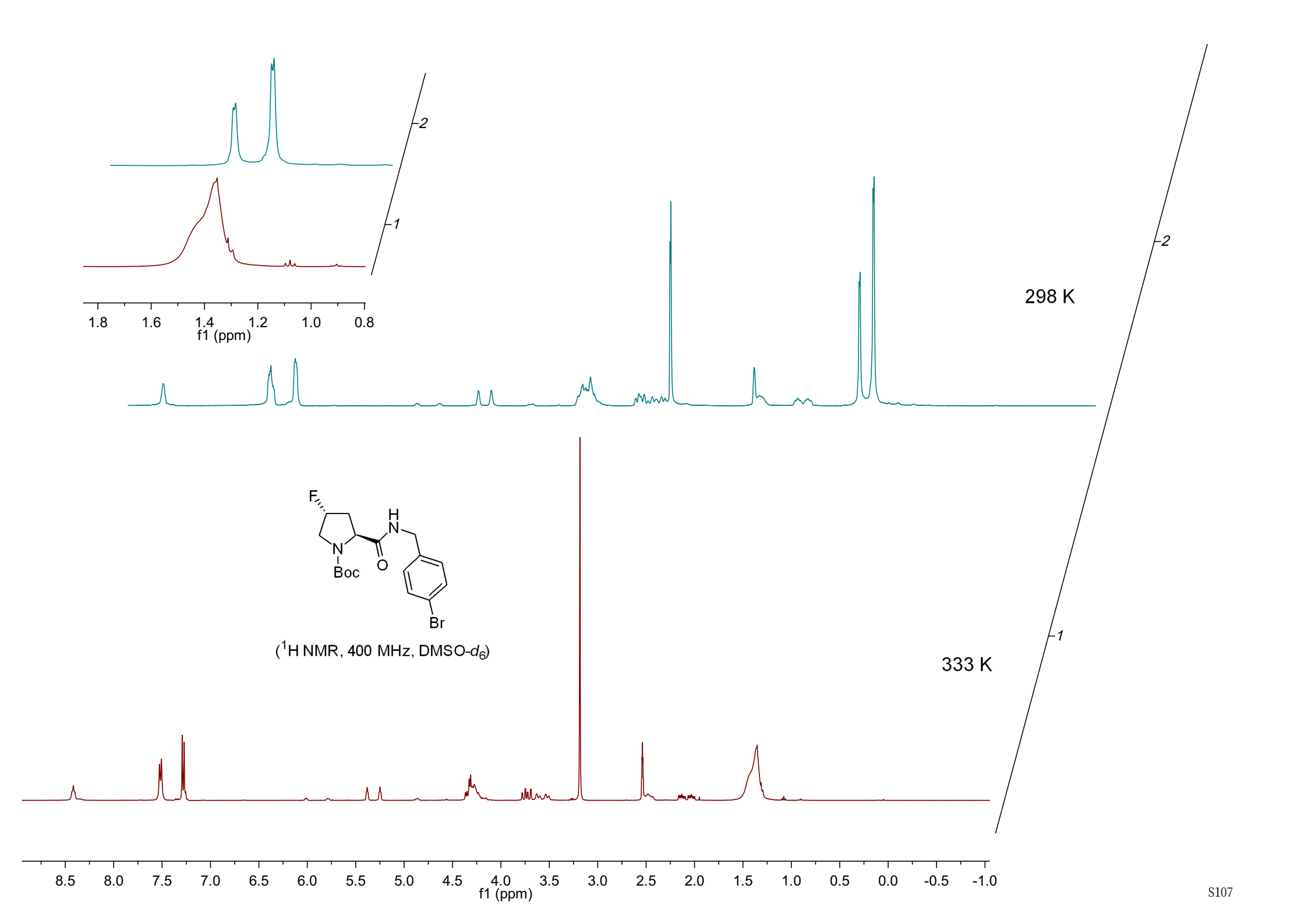

173.858
173.360
172.487
152.838
149.090
140.202
131.588
130.399
129.013
94.380
92.613
60.545
59.570
56.380
56.156
43.785
37.397
37.179
36.239
26.959
22.169
15.803
F
O
N
HN
O
NH
O
S
N
(13C NMR, 100 MHz, CD3OD)
f1 (ppm)


-178.805
F
O
N
HN
O
NH
O
S
N
(19F NMR, 376 MHz, CD3OD)
00
150
100
50
0
-50
-100
-150
-200
-250
-300
-350
-40
f1 (ppm)

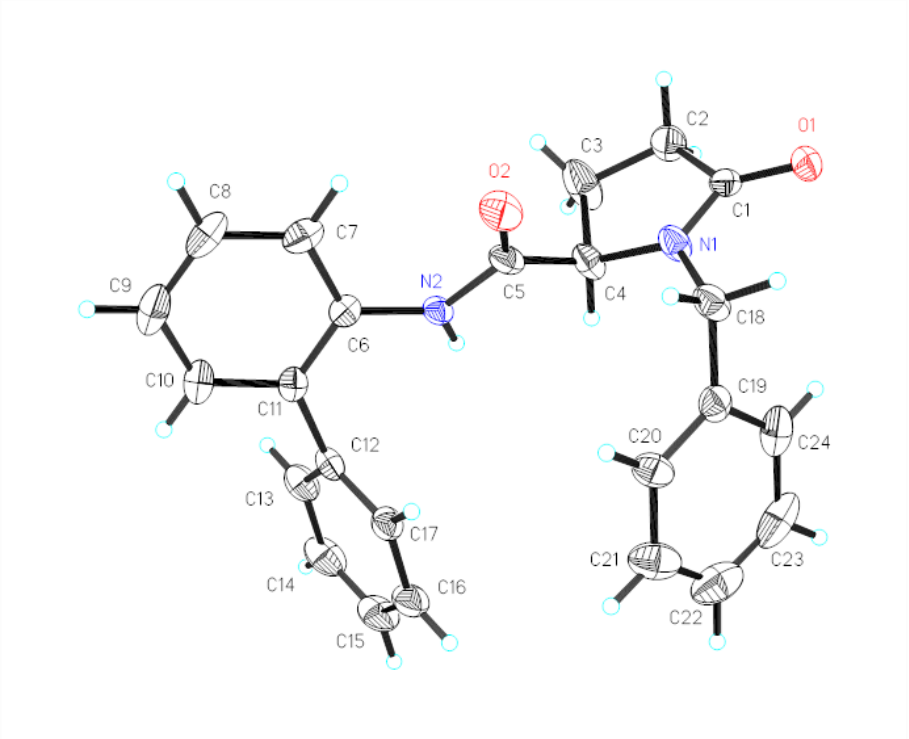

7.341
7.325
7.320
7.279
7.257
4.301
4.281
3.970
3.946
3.928
3.623
3.602
3.581
3.560
3.540
2.374
2.348
2.324
2.258
1.484
1.384
Cl
H
N
N
Boc
O
(1H NMR, 400 MHz, CD3OD)
2.00
2.00
1.00
1.00
1.00
1.00
2.00
9.00
9.00
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
f1 (ppm)


174.384
155.940
141.200
133.681
129.751
81.559
61.842
54.062
52.048
42.267
39.667
28.973
28.737
Cl
H
N
N
Boc
O
(^{13}C NMR, 100 MHz, CD_3OD)
f1 (ppm)


2
1
1.3
1.2
1.1
1.0
0.9
f1 (ppm)
298K
2
HO
H
N
N
Boc
O
(1H, NMR, 400 MHz, DMSO-d6)
333K
1
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
-0.5
-1.0
f1 (ppm)


298 K
333 K
F
H
N
N
Boc
O
Br
(1H NMR, 400 MHz, DMSO-d6)
f1 (ppm)
f1 (ppm)

ORTEP drawing of the X-ray crystallographic structure of **6o**



The single crystal of compound **6o** was prepared from its solution in petroleum ether/ethylacetate (1:1) by slow evaporation of the solvent.

CCDC 2089259. For detailed crystallographic data, please refer to the Cambridge Crystallographic Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for dd20119.

Identification code	dd20119	
Empirical formula	C24 H22 N2 O2	
Formula weight	370.43	
Temperature	192(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P n a 21	
Unit cell dimensions	a = 9.8421(19) Å	α= 90°.
	b = 19.150(4) Å	β= 90°.
	c = 10.450(2) Å	γ = 90°.
Volume	1969.5(7) $Å^3$	
Z	4	
Density (calculated)	1.249 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	784	
Crystal size	0.200 x 0.100 x 0.060 mm^3	
Theta range for data collection	2.220 to 25.495°.	

Index ranges	-11<=h<=9, -23<=k<=22, -12<=l<=12
Reflections collected	8842
Independent reflections	3627 [R(int) = 0.0496]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6421
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3627 / 1 / 258
Goodness-of-fit on F^2	1.094
Final R indices [I>2sigma(I)]	R1 = 0.0544, wR2 = 0.0999
R indices (all data)	R1 = 0.0915, wR2 = 0.1203
Absolute structure parameter	-0.4(10)
Extinction coefficient	0.018(2)
Largest diff. peak and hole	0.186 and -0.170 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for dd20119. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	-253(3)	4177(2)	802(3)	51(1)
O(2)	3280(4)	5659(2)	2262(3)	62(1)
N(1)	1185(4)	4652(2)	2267(4)	46(1)
N(2)	2810(4)	5923(2)	4349(3)	34(1)
C(1)	70(5)	4649(2)	1536(4)	39(1)
C(2)	-670(5)	5317(2)	1740(5)	53(1)
C(3)	96(7)	5715(3)	2694(6)	83(2)
C(4)	1219(5)	5221(2)	3193(5)	46(1)
C(5)	2553(5)	5610(2)	3201(4)	42(1)
C(6)	3833(4)	6424(2)	4603(4)	36(1)
C(7)	4380(5)	6836(2)	3639(5)	50(1)
C(8)	5319(6)	7344(2)	3921(6)	64(2)
C(9)	5717(6)	7463(3)	5170(7)	70(2)
C(10)	5167(5)	7058(2)	6128(5)	52(1)
C(11)	4239(4)	6527(2)	5867(4)	38(1)
C(12)	3763(4)	6098(2)	6974(4)	39(1)
C(13)	3107(5)	6414(3)	8003(4)	52(1)
C(14)	2829(6)	6037(4)	9097(5)	66(2)
C(15)	3163(6)	5344(3)	9171(5)	65(2)

C(16)	3800(5)	5022(3)	8163(5)	56(1)
C(17)	4094(5)	5395(2)	7058(4)	44(1)
C(18)	2152(5)	4072(2)	2316(4)	50(1)
C(19)	2165(5)	3712(2)	3592(5)	45(1)
C(20)	3263(5)	3784(3)	4409(5)	49(1)
C(21)	3295(7)	3465(3)	5591(5)	68(2)
C(22)	2237(9)	3067(3)	5975(7)	82(2)
C(23)	1134(8)	2973(3)	5180(8)	85(2)
C(24)	1075(6)	3309(3)	4000(6)	67(2)

Table 3. Bond lengths [Å] and angles [°] for dd20119.

O(1)-C(1)	1.227(5)
O(2)-C(5)	1.218(5)
N(1)-C(1)	1.337(5)
N(1)-C(4)	1.457(5)
N(1)-C(18)	1.464(5)
N(2)-C(5)	1.366(5)
N(2)-C(6)	1.415(5)
N(2)-H(2)	0.92(5)
C(1)-C(2)	1.487(6)
C(2)-C(3)	1.464(7)
C(2)-H(2A)	0.9900
C(2)-H(2B)	0.9900
C(3)-C(4)	1.546(7)
C(3)-H(3A)	0.9900
C(3)-H(3B)	0.9900
C(4)-C(5)	1.509(7)
C(4)-H(4)	1.0000
C(6)-C(7)	1.389(6)
C(6)-C(11)	1.394(6)
C(7)-C(8)	1.374(7)
C(7)-H(7)	0.9500
C(8)-C(9)	1.382(8)
C(8)-H(8)	0.9500
C(9)-C(10)	1.377(7)
C(9)-H(9)	0.9500
C(10)-C(11)	1.394(6)

C(10)-H(10)	0.9500
C(11)-C(12)	1.494(6)
C(12)-C(17)	1.388(6)
C(12)-C(13)	1.393(6)
C(13)-C(14)	1.379(7)
C(13)-H(13)	0.9500
C(14)-C(15)	1.370(7)
C(14)-H(14)	0.9500
C(15)-C(16)	1.373(8)
C(15)-H(15)	0.9500
C(16)-C(17)	1.388(6)
C(16)-H(16)	0.9500
C(17)-H(17)	0.9500
C(18)-C(19)	1.501(6)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-C(20)	1.384(6)
C(19)-C(24)	1.388(7)
C(20)-C(21)	1.378(7)
C(20)-H(20)	0.9500
C(21)-C(22)	1.350(8)
C(21)-H(21)	0.9500
C(22)-C(23)	1.379(9)
C(22)-H(22)	0.9500
C(23)-C(24)	1.393(8)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500

C(1)-N(1)-C(4)	113.7(4)
C(1)-N(1)-C(18)	123.4(4)
C(4)-N(1)-C(18)	121.9(3)
C(5)-N(2)-C(6)	126.5(4)
C(5)-N(2)-H(2)	113(3)
C(6)-N(2)-H(2)	121(3)
O(1)-C(1)-N(1)	124.9(4)
O(1)-C(1)-C(2)	126.6(4)
N(1)-C(1)-C(2)	108.4(4)
C(3)-C(2)-C(1)	107.0(4)

C(3)-C(2)-H(2A)	110.3
C(1)-C(2)-H(2A)	110.3
C(3)-C(2)-H(2B)	110.3
C(1)-C(2)-H(2B)	110.3
H(2A)-C(2)-H(2B)	108.6
C(2)-C(3)-C(4)	106.2(4)
C(2)-C(3)-H(3A)	110.5
C(4)-C(3)-H(3A)	110.5
C(2)-C(3)-H(3B)	110.5
C(4)-C(3)-H(3B)	110.5
H(3A)-C(3)-H(3B)	108.7
N(1)-C(4)-C(5)	113.1(4)
N(1)-C(4)-C(3)	102.5(4)
C(5)-C(4)-C(3)	108.7(4)
N(1)-C(4)-H(4)	110.7
C(5)-C(4)-H(4)	110.7
C(3)-C(4)-H(4)	110.7
O(2)-C(5)-N(2)	124.4(5)
O(2)-C(5)-C(4)	123.0(4)
N(2)-C(5)-C(4)	112.5(4)
C(7)-C(6)-C(11)	119.7(4)
C(7)-C(6)-N(2)	121.7(4)
C(11)-C(6)-N(2)	118.6(4)
C(8)-C(7)-C(6)	120.5(5)
C(8)-C(7)-H(7)	119.7
C(6)-C(7)-H(7)	119.7
C(7)-C(8)-C(9)	120.6(5)
C(7)-C(8)-H(8)	119.7
C(9)-C(8)-H(8)	119.7
C(10)-C(9)-C(8)	118.8(5)
C(10)-C(9)-H(9)	120.6
C(8)-C(9)-H(9)	120.6
C(9)-C(10)-C(11)	121.8(5)
C(9)-C(10)-H(10)	119.1
C(11)-C(10)-H(10)	119.1
C(10)-C(11)-C(6)	118.5(4)
C(10)-C(11)-C(12)	117.1(4)
C(6)-C(11)-C(12)	124.4(4)

C(17)-C(12)-C(13)	118.8(4)
C(17)-C(12)-C(11)	120.6(4)
C(13)-C(12)-C(11)	120.3(4)
C(14)-C(13)-C(12)	120.3(5)
C(14)-C(13)-H(13)	119.8
C(12)-C(13)-H(13)	119.8
C(15)-C(14)-C(13)	120.4(5)
C(15)-C(14)-H(14)	119.8
C(13)-C(14)-H(14)	119.8
C(14)-C(15)-C(16)	120.1(5)
C(14)-C(15)-H(15)	119.9
C(16)-C(15)-H(15)	119.9
C(15)-C(16)-C(17)	120.1(5)
C(15)-C(16)-H(16)	119.9
C(17)-C(16)-H(16)	119.9
C(16)-C(17)-C(12)	120.2(5)
C(16)-C(17)-H(17)	119.9
C(12)-C(17)-H(17)	119.9
N(1)-C(18)-C(19)	112.7(4)
N(1)-C(18)-H(18A)	109.1
C(19)-C(18)-H(18A)	109.1
N(1)-C(18)-H(18B)	109.1
C(19)-C(18)-H(18B)	109.1
H(18A)-C(18)-H(18B)	107.8
C(20)-C(19)-C(24)	118.0(5)
C(20)-C(19)-C(18)	120.6(4)
C(24)-C(19)-C(18)	121.4(5)
C(21)-C(20)-C(19)	121.7(5)
C(21)-C(20)-H(20)	119.1
C(19)-C(20)-H(20)	119.1
C(22)-C(21)-C(20)	119.9(6)
C(22)-C(21)-H(21)	120.0
C(20)-C(21)-H(21)	120.0
C(21)-C(22)-C(23)	120.1(7)
C(21)-C(22)-H(22)	119.9
C(23)-C(22)-H(22)	119.9
C(22)-C(23)-C(24)	120.4(6)
C(22)-C(23)-H(23)	119.8

C(24)-C(23)-H(23)	119.8
C(19)-C(24)-C(23)	119.8(6)
C(19)-C(24)-H(24)	120.1
C(23)-C(24)-H(24)	120.1

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for dd20119. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	57(2)	43(2)	52(2)	-3(2)	-20(2)	-5(2)
O(2)	84(3)	73(2)	30(2)	-9(2)	14(2)	-8(2)
N(1)	44(3)	46(2)	49(2)	-14(2)	-17(2)	14(2)
N(2)	38(2)	41(2)	23(2)	-1(2)	2(2)	-3(2)
C(1)	42(3)	40(3)	36(2)	8(2)	-6(2)	-1(2)
C(2)	44(3)	52(3)	62(3)	0(3)	-11(3)	6(3)
C(3)	65(4)	79(4)	106(5)	-41(4)	-47(4)	35(3)
C(4)	43(3)	52(3)	44(3)	-17(2)	-11(2)	9(2)
C(5)	51(3)	47(3)	28(2)	-3(2)	-5(2)	7(2)
C(6)	38(3)	34(2)	35(2)	-1(2)	7(2)	3(2)
C(7)	61(4)	42(3)	48(3)	9(2)	13(3)	5(3)
C(8)	69(4)	40(3)	83(4)	14(3)	25(3)	-8(3)
C(9)	64(4)	42(3)	103(5)	-3(3)	6(4)	-15(3)
C(10)	48(3)	42(3)	67(3)	-11(3)	6(3)	-11(3)
C(11)	32(3)	34(2)	46(3)	-5(2)	2(2)	1(2)
C(12)	32(2)	51(3)	32(2)	-7(2)	-3(2)	-7(2)
C(13)	48(3)	68(3)	39(3)	-14(3)	0(2)	1(3)
C(14)	61(4)	105(5)	32(3)	-11(3)	5(3)	-3(3)
C(15)	63(4)	100(5)	32(3)	12(3)	3(3)	-18(3)
C(16)	58(4)	69(3)	40(3)	10(3)	-7(3)	-13(3)
C(17)	47(3)	49(3)	35(2)	-1(2)	0(2)	-8(2)
C(18)	50(3)	53(3)	46(3)	-12(2)	-14(3)	15(2)
C(19)	46(3)	36(2)	53(3)	-9(2)	-4(2)	8(2)
C(20)	40(3)	61(3)	47(3)	2(3)	-4(2)	11(2)
C(21)	66(4)	86(4)	52(4)	5(3)	4(3)	30(4)
C(22)	106(6)	60(4)	79(5)	14(4)	25(5)	26(4)

C(23)	98(6)	40(3)	118(6)	2(4)	46(5)	-8(4)
C(24)	58(4)	48(3)	96(5)	-19(3)	2(3)	-8(3)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for dd20119.

	x	y	z	U(eq)
H(2A)	-730	5582	929	63
H(2B)	-1603	5225	2052	63
H(3A)	-505	5863	3403	100
H(3B)	503	6136	2300	100
H(4)	992	5046	4069	56
H(7)	4103	6766	2778	60
H(8)	5699	7616	3250	77
H(9)	6359	7818	5365	83
H(10)	5426	7143	6989	63
H(13)	2851	6891	7952	62
H(14)	2402	6260	9803	79
H(15)	2954	5086	9922	78
H(16)	4041	4543	8221	67
H(17)	4523	5169	6357	52
H(18A)	3075	4251	2130	59
H(18B)	1916	3728	1644	59
H(20)	4015	4060	4148	59
H(21)	4059	3525	6135	82
H(22)	2254	2852	6793	98
H(23)	411	2676	5439	102
H(24)	290	3264	3477	81
H(2)	2200(50)	5800(20)	4980(40)	49(14)

Table 6. Torsion angles [°] for dd20119.

C(4)-N(1)-C(1)-O(1)	-170.9(4)
C(18)-N(1)-C(1)-O(1)	-2.3(7)
C(4)-N(1)-C(1)-C(2)	10.8(5)
C(18)-N(1)-C(1)-C(2)	179.4(4)

O(1)-C(1)-C(2)-C(3)	-179.7(5)
N(1)-C(1)-C(2)-C(3)	-1.4(6)
C(1)-C(2)-C(3)-C(4)	-7.5(6)
C(1)-N(1)-C(4)-C(5)	-131.9(4)
C(18)-N(1)-C(4)-C(5)	59.3(6)
C(1)-N(1)-C(4)-C(3)	-14.9(5)
C(18)-N(1)-C(4)-C(3)	176.3(5)
C(2)-C(3)-C(4)-N(1)	12.9(6)
C(2)-C(3)-C(4)-C(5)	132.9(5)
C(6)-N(2)-C(5)-O(2)	9.1(7)
C(6)-N(2)-C(5)-C(4)	-167.9(4)
N(1)-C(4)-C(5)-O(2)	28.5(6)
C(3)-C(4)-C(5)-O(2)	-84.7(6)
N(1)-C(4)-C(5)-N(2)	-154.4(4)
C(3)-C(4)-C(5)-N(2)	92.4(5)
C(5)-N(2)-C(6)-C(7)	23.5(6)
C(5)-N(2)-C(6)-C(11)	-160.0(4)
C(11)-C(6)-C(7)-C(8)	0.0(7)
N(2)-C(6)-C(7)-C(8)	176.5(4)
C(6)-C(7)-C(8)-C(9)	-1.2(8)
C(7)-C(8)-C(9)-C(10)	0.7(9)
C(8)-C(9)-C(10)-C(11)	1.0(8)
C(9)-C(10)-C(11)-C(6)	-2.2(7)
C(9)-C(10)-C(11)-C(12)	177.0(4)
C(7)-C(6)-C(11)-C(10)	1.6(6)
N(2)-C(6)-C(11)-C(10)	-174.9(4)
C(7)-C(6)-C(11)-C(12)	-177.5(4)
N(2)-C(6)-C(11)-C(12)	5.9(6)
C(10)-C(11)-C(12)-C(17)	-113.9(5)
C(6)-C(11)-C(12)-C(17)	65.3(6)
C(10)-C(11)-C(12)-C(13)	59.1(6)
C(6)-C(11)-C(12)-C(13)	-121.8(5)
C(17)-C(12)-C(13)-C(14)	1.7(7)
C(11)-C(12)-C(13)-C(14)	-171.3(5)
C(12)-C(13)-C(14)-C(15)	-1.6(8)
C(13)-C(14)-C(15)-C(16)	1.1(8)
C(14)-C(15)-C(16)-C(17)	-0.7(8)
C(15)-C(16)-C(17)-C(12)	0.9(7)

C(13)-C(12)-C(17)-C(16)	-1.4(6)
C(11)-C(12)-C(17)-C(16)	171.7(4)
C(1)-N(1)-C(18)-C(19)	-112.9(5)
C(4)-N(1)-C(18)-C(19)	54.8(6)
N(1)-C(18)-C(19)-C(20)	-108.9(5)
N(1)-C(18)-C(19)-C(24)	69.8(5)
C(24)-C(19)-C(20)-C(21)	0.5(7)
C(18)-C(19)-C(20)-C(21)	179.3(4)
C(19)-C(20)-C(21)-C(22)	0.3(8)
C(20)-C(21)-C(22)-C(23)	0.8(9)
C(21)-C(22)-C(23)-C(24)	-2.7(9)
C(20)-C(19)-C(24)-C(23)	-2.4(7)
C(18)-C(19)-C(24)-C(23)	178.8(4)
C(22)-C(23)-C(24)-C(19)	3.5(8)

Symmetry transformations used to generate equivalent atoms:

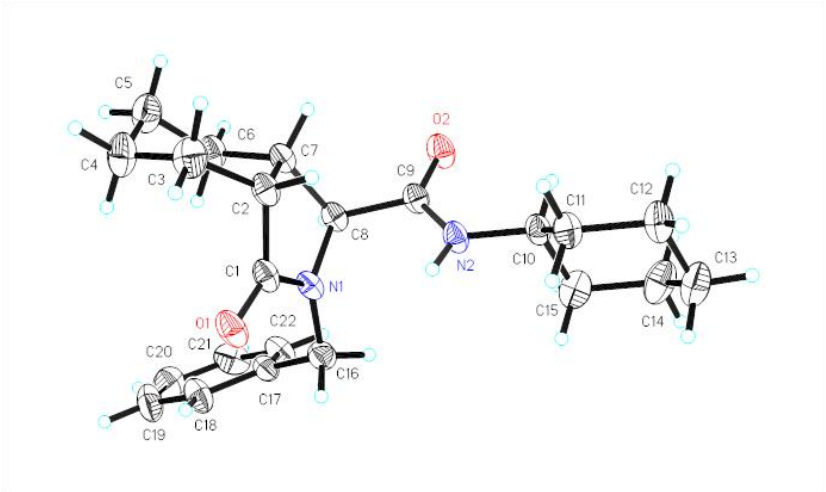
Table 7. Hydrogen bonds for dd20119 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2)...O(1)#1	0.92(5)	2.11(5)	2.945(5)	151(4)
C(7)-H(7)...O(2)	0.95	2.33	2.885(6)	116.5
C(4)-H(4)...O(1)#1	1.00	2.45	3.110(6)	122.7
C(3)-H(3A)...O(1)#1	0.99	2.62	3.259(7)	122.6
C(3)-H(3A)...O(1)#1	0.99	2.62	3.259(7)	122.6
C(4)-H(4)...O(1)#1	1.00	2.45	3.110(6)	122.7
C(7)-H(7)...O(2)	0.95	2.33	2.885(6)	116.5
N(2)-H(2)...O(1)#1	0.92(5)	2.11(5)	2.945(5)	151(4)

Symmetry transformations used to generate equivalent atoms:

#1 -x,-y+1,z+1/2

ORTEP drawing of the X-ray crystallographic structure of **6t**



The single crystal of compound **6t** was prepared from its solution in petroleum ether/ethylacetate (1:1) by slow evaporation of the solvent.

CCDC 2089257. For detailed crystallographic data, please refer to the Cambridge Crystallographic Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for mo_ddz20072_0m.

Identification code	mo_ddz20072_0m	
Empirical formula	C22 H30 N2 O2	
Formula weight	354.48	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 9.9031(14) Å	α= 72.827(4)°.
	b = 9.9209(15) Å	β= 89.188(4)°.
	c = 10.8025(14) Å	γ = 78.782(5)°.
Volume	993.6(2) $Å^3$	
Z	2	
Density (calculated)	1.185 Mg/m^3	
Absorption coefficient	0.076 mm^{-1}	
F(000)	384	
Crystal size	0.180 x 0.150 x 0.110 mm^3	
Theta range for data collection	2.717 to 25.500°.	
Index ranges	-11<=h<=11, -12<=k<=12, -13<=l<=13	
Reflections collected	22231	
Independent reflections	3683 [R(int) = 0.0909]	
Completeness to theta = 25.242°	99.8 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.2216	

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3683 / 0 / 236
Goodness-of-fit on F^2	1.029
Final R indices [I>2sigma(I)]	R1 = 0.0574, wR2 = 0.1469
R indices (all data)	R1 = 0.0787, wR2 = 0.1651
Extinction coefficient	0.075(10)
Largest diff. peak and hole	0.257 and -0.212 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mo_ddz20072_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	3819(1)	6280(2)	4881(1)	57(1)
O(2)	6267(1)	5810(2)	232(1)	58(1)
N(1)	4018(1)	5866(2)	2904(1)	41(1)
N(2)	6509(2)	4408(2)	2325(1)	46(1)
C(1)	4266(2)	6526(2)	3786(2)	43(1)
C(2)	5189(2)	7571(2)	3192(2)	45(1)
C(3)	5052(2)	8852(3)	3719(2)	64(1)
C(4)	3736(3)	9965(3)	3214(2)	73(1)
C(5)	3600(3)	10402(2)	1745(2)	70(1)
C(6)	3555(2)	9099(2)	1295(2)	54(1)
C(7)	4842(2)	7908(2)	1738(2)	43(1)
C(8)	4577(2)	6458(2)	1648(2)	41(1)
C(9)	5870(2)	5508(2)	1342(2)	42(1)
C(10)	7694(2)	3347(2)	2169(2)	45(1)
C(11)	8774(2)	2968(2)	3265(2)	51(1)
C(12)	10000(2)	1861(2)	3080(2)	65(1)
C(13)	9560(3)	530(3)	2961(3)	77(1)
C(14)	8464(3)	906(3)	1882(3)	79(1)
C(15)	7243(2)	2011(2)	2072(2)	64(1)
C(16)	3146(2)	4805(2)	3117(2)	50(1)
C(17)	1665(2)	5498(2)	2691(2)	42(1)
C(18)	806(2)	6110(2)	3484(2)	59(1)
C(19)	-530(2)	6805(3)	3070(3)	72(1)
C(20)	-1010(2)	6899(3)	1864(3)	73(1)
C(21)	-179(2)	6284(3)	1070(2)	70(1)
C(22)	1155(2)	5584(2)	1486(2)	56(1)

Table 3. Bond lengths [Å] and angles [°] for mo_ddz20072_0m.

O(1)-C(1)	1.229(2)
O(2)-C(9)	1.226(2)
N(1)-C(1)	1.354(2)
N(1)-C(16)	1.454(2)
N(1)-C(8)	1.458(2)
N(2)-C(9)	1.336(2)
N(2)-C(10)	1.460(2)
N(2)-H(2)	0.8600
C(1)-C(2)	1.511(3)
C(2)-C(3)	1.522(3)
C(2)-C(7)	1.535(2)
C(2)-H(2A)	0.9800
C(3)-C(4)	1.523(3)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.517(3)
C(4)-H(4A)	0.9700
C(4)-H(4B)	0.9700
C(5)-C(6)	1.517(3)
C(5)-H(5A)	0.9700
C(5)-H(5B)	0.9700
C(6)-C(7)	1.532(2)
C(6)-H(6A)	0.9700
C(6)-H(6B)	0.9700
C(7)-C(8)	1.542(3)
C(7)-H(7)	0.9800
C(8)-C(9)	1.530(2)
C(8)-H(8)	0.9800
C(10)-C(15)	1.511(3)
C(10)-C(11)	1.517(3)
C(10)-H(10)	0.9800
C(11)-C(12)	1.525(3)
C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700
C(12)-C(13)	1.509(3)

C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-C(14)	1.516(3)
C(13)-H(13A)	0.9700
C(13)-H(13B)	0.9700
C(14)-C(15)	1.522(3)
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(16)-C(17)	1.509(2)
C(16)-H(16A)	0.9700
C(16)-H(16B)	0.9700
C(17)-C(22)	1.376(3)
C(17)-C(18)	1.383(3)
C(18)-C(19)	1.380(3)
C(18)-H(18)	0.9300
C(19)-C(20)	1.364(3)
C(19)-H(19)	0.9300
C(20)-C(21)	1.371(3)
C(20)-H(20)	0.9300
C(21)-C(22)	1.380(3)
C(21)-H(21)	0.9300
C(22)-H(22)	0.9300

C(1)-N(1)-C(16)	124.11(15)
C(1)-N(1)-C(8)	112.92(16)
C(16)-N(1)-C(8)	122.57(15)
C(9)-N(2)-C(10)	123.41(14)
C(9)-N(2)-H(2)	118.3
C(10)-N(2)-H(2)	118.3
O(1)-C(1)-N(1)	124.76(19)
O(1)-C(1)-C(2)	127.14(17)
N(1)-C(1)-C(2)	108.09(15)
C(1)-C(2)-C(3)	114.98(16)
C(1)-C(2)-C(7)	101.67(14)
C(3)-C(2)-C(7)	116.71(17)
C(1)-C(2)-H(2A)	107.7

C(3)-C(2)-H(2A)	107.7
C(7)-C(2)-H(2A)	107.7
C(2)-C(3)-C(4)	112.51(17)
C(2)-C(3)-H(3A)	109.1
C(4)-C(3)-H(3A)	109.1
C(2)-C(3)-H(3B)	109.1
C(4)-C(3)-H(3B)	109.1
H(3A)-C(3)-H(3B)	107.8
C(5)-C(4)-C(3)	110.92(18)
C(5)-C(4)-H(4A)	109.5
C(3)-C(4)-H(4A)	109.5
C(5)-C(4)-H(4B)	109.5
C(3)-C(4)-H(4B)	109.5
H(4A)-C(4)-H(4B)	108.0
C(4)-C(5)-C(6)	110.09(19)
C(4)-C(5)-H(5A)	109.6
C(6)-C(5)-H(5A)	109.6
C(4)-C(5)-H(5B)	109.6
C(6)-C(5)-H(5B)	109.6
H(5A)-C(5)-H(5B)	108.2
C(5)-C(6)-C(7)	112.95(17)
C(5)-C(6)-H(6A)	109.0
C(7)-C(6)-H(6A)	109.0
C(5)-C(6)-H(6B)	109.0
C(7)-C(6)-H(6B)	109.0
H(6A)-C(6)-H(6B)	107.8
C(6)-C(7)-C(2)	111.36(14)
C(6)-C(7)-C(8)	111.09(15)
C(2)-C(7)-C(8)	102.29(14)
C(6)-C(7)-H(7)	110.6
C(2)-C(7)-H(7)	110.6
C(8)-C(7)-H(7)	110.6
N(1)-C(8)-C(9)	114.99(14)
N(1)-C(8)-C(7)	102.32(13)
C(9)-C(8)-C(7)	112.66(15)
N(1)-C(8)-H(8)	108.9
C(9)-C(8)-H(8)	108.9
C(7)-C(8)-H(8)	108.9

O(2)-C(9)-N(2)	124.26(16)
O(2)-C(9)-C(8)	118.76(15)
N(2)-C(9)-C(8)	116.97(15)
N(2)-C(10)-C(15)	110.58(16)
N(2)-C(10)-C(11)	111.56(14)
C(15)-C(10)-C(11)	110.63(16)
N(2)-C(10)-H(10)	108.0
C(15)-C(10)-H(10)	108.0
C(11)-C(10)-H(10)	108.0
C(10)-C(11)-C(12)	110.58(16)
C(10)-C(11)-H(11A)	109.5
C(12)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
C(12)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	108.1
C(13)-C(12)-C(11)	111.63(19)
C(13)-C(12)-H(12A)	109.3
C(11)-C(12)-H(12A)	109.3
C(13)-C(12)-H(12B)	109.3
C(11)-C(12)-H(12B)	109.3
H(12A)-C(12)-H(12B)	108.0
C(12)-C(13)-C(14)	111.17(19)
C(12)-C(13)-H(13A)	109.4
C(14)-C(13)-H(13A)	109.4
C(12)-C(13)-H(13B)	109.4
C(14)-C(13)-H(13B)	109.4
H(13A)-C(13)-H(13B)	108.0
C(13)-C(14)-C(15)	110.97(18)
C(13)-C(14)-H(14A)	109.4
C(15)-C(14)-H(14A)	109.4
C(13)-C(14)-H(14B)	109.4
C(15)-C(14)-H(14B)	109.4
H(14A)-C(14)-H(14B)	108.0
C(10)-C(15)-C(14)	111.19(19)
C(10)-C(15)-H(15A)	109.4
C(14)-C(15)-H(15A)	109.4
C(10)-C(15)-H(15B)	109.4
C(14)-C(15)-H(15B)	109.4

H(15A)-C(15)-H(15B)	108.0
N(1)-C(16)-C(17)	111.75(15)
N(1)-C(16)-H(16A)	109.3
C(17)-C(16)-H(16A)	109.3
N(1)-C(16)-H(16B)	109.3
C(17)-C(16)-H(16B)	109.3
H(16A)-C(16)-H(16B)	107.9
C(22)-C(17)-C(18)	118.59(18)
C(22)-C(17)-C(16)	120.75(16)
C(18)-C(17)-C(16)	120.61(17)
C(19)-C(18)-C(17)	120.6(2)
C(19)-C(18)-H(18)	119.7
C(17)-C(18)-H(18)	119.7
C(20)-C(19)-C(18)	119.9(2)
C(20)-C(19)-H(19)	120.1
C(18)-C(19)-H(19)	120.1
C(19)-C(20)-C(21)	120.3(2)
C(19)-C(20)-H(20)	119.9
C(21)-C(20)-H(20)	119.9
C(20)-C(21)-C(22)	119.8(2)
C(20)-C(21)-H(21)	120.1
C(22)-C(21)-H(21)	120.1
C(17)-C(22)-C(21)	120.8(2)
C(17)-C(22)-H(22)	119.6
C(21)-C(22)-H(22)	119.6

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for mo_ddz20072_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	52(1)	79(1)	32(1)	-14(1)	6(1)	4(1)
O(2)	60(1)	71(1)	32(1)	-13(1)	9(1)	5(1)
N(1)	34(1)	56(1)	33(1)	-13(1)	4(1)	-5(1)
N(2)	44(1)	55(1)	32(1)	-12(1)	6(1)	4(1)
C(1)	33(1)	58(1)	31(1)	-12(1)	-2(1)	6(1)
C(2)	34(1)	60(1)	41(1)	-19(1)	-2(1)	-2(1)

C(3)	68(1)	74(2)	60(1)	-33(1)	-3(1)	-12(1)
C(4)	84(2)	71(2)	69(2)	-40(1)	2(1)	4(1)
C(5)	77(2)	58(1)	68(2)	-20(1)	1(1)	7(1)
C(6)	51(1)	59(1)	44(1)	-13(1)	-2(1)	7(1)
C(7)	36(1)	53(1)	38(1)	-13(1)	5(1)	-3(1)
C(8)	35(1)	55(1)	29(1)	-12(1)	-1(1)	-2(1)
C(9)	42(1)	53(1)	32(1)	-18(1)	2(1)	-4(1)
C(10)	46(1)	49(1)	35(1)	-14(1)	7(1)	1(1)
C(11)	47(1)	58(1)	51(1)	-24(1)	0(1)	-2(1)
C(12)	51(1)	67(1)	71(2)	-24(1)	-4(1)	9(1)
C(13)	80(2)	58(1)	81(2)	-21(1)	-11(1)	16(1)
C(14)	100(2)	57(1)	82(2)	-35(1)	-14(2)	5(1)
C(15)	70(1)	59(1)	63(1)	-24(1)	-14(1)	-4(1)
C(16)	42(1)	54(1)	51(1)	-13(1)	5(1)	-7(1)
C(17)	38(1)	48(1)	44(1)	-16(1)	8(1)	-11(1)
C(18)	47(1)	82(2)	62(1)	-42(1)	10(1)	-16(1)
C(19)	47(1)	81(2)	106(2)	-57(2)	18(1)	-10(1)
C(20)	42(1)	68(2)	104(2)	-20(1)	-6(1)	-4(1)
C(21)	56(1)	94(2)	58(1)	-13(1)	-8(1)	-21(1)
C(22)	48(1)	79(2)	47(1)	-24(1)	10(1)	-16(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for mo_ddz20072_0m.

	x	y	z	U(eq)
H(2)	6206	4320	3089	55
H(2A)	6144	7042	3364	54
H(3A)	5840	9306	3477	77
H(3B)	5061	8513	4659	77
H(4A)	2946	9567	3576	88
H(4B)	3747	10808	3492	88
H(5A)	4376	10824	1380	84
H(5B)	2763	11121	1442	84
H(6A)	3460	9399	356	65
H(6B)	2749	8715	1630	65
H(7)	5627	8173	1227	52

H(8)	3863	6646	966	49
H(10)	8114	3770	1355	54
H(11A)	8371	2583	4086	61
H(11B)	9084	3831	3286	61
H(12A)	10458	2285	2305	78
H(12B)	10654	1594	3814	78
H(13A)	9201	40	3775	92
H(13B)	10353	-121	2786	92
H(14A)	8153	42	1867	95
H(14B)	8856	1291	1054	95
H(15A)	6579	2270	1347	76
H(15B)	6797	1591	2857	76
H(16A)	3197	4271	4032	60
H(16B)	3484	4128	2639	60
H(18)	1132	6053	4305	70
H(19)	-1102	7208	3613	87
H(20)	-1904	7382	1579	88
H(21)	-513	6338	252	85
H(22)	1715	5167	945	67

Table 6. Torsion angles [°] for mo_ddz20072_0m.

C(16)-N(1)-C(1)-O(1)	2.2(3)
C(8)-N(1)-C(1)-O(1)	174.95(15)
C(16)-N(1)-C(1)-C(2)	-178.76(14)
C(8)-N(1)-C(1)-C(2)	-5.96(18)
O(1)-C(1)-C(2)-C(3)	-27.9(2)
N(1)-C(1)-C(2)-C(3)	152.99(16)
O(1)-C(1)-C(2)-C(7)	-155.00(16)
N(1)-C(1)-C(2)-C(7)	25.94(17)
C(1)-C(2)-C(3)-C(4)	-74.8(2)
C(7)-C(2)-C(3)-C(4)	44.2(3)
C(2)-C(3)-C(4)-C(5)	-52.4(3)
C(3)-C(4)-C(5)-C(6)	60.1(3)
C(4)-C(5)-C(6)-C(7)	-59.2(3)
C(5)-C(6)-C(7)-C(2)	48.9(2)
C(5)-C(6)-C(7)-C(8)	162.16(17)
C(1)-C(2)-C(7)-C(6)	84.15(18)

C(3)-C(2)-C(7)-C(6)	-41.8(2)
C(1)-C(2)-C(7)-C(8)	-34.57(15)
C(3)-C(2)-C(7)-C(8)	-160.49(16)
C(1)-N(1)-C(8)-C(9)	105.85(17)
C(16)-N(1)-C(8)-C(9)	-81.22(19)
C(1)-N(1)-C(8)-C(7)	-16.62(17)
C(16)-N(1)-C(8)-C(7)	156.31(14)
C(6)-C(7)-C(8)-N(1)	-87.49(16)
C(2)-C(7)-C(8)-N(1)	31.42(15)
C(6)-C(7)-C(8)-C(9)	148.47(15)
C(2)-C(7)-C(8)-C(9)	-92.62(16)
C(10)-N(2)-C(9)-O(2)	-5.8(3)
C(10)-N(2)-C(9)-C(8)	175.47(16)
N(1)-C(8)-C(9)-O(2)	168.02(17)
C(7)-C(8)-C(9)-O(2)	-75.3(2)
N(1)-C(8)-C(9)-N(2)	-13.2(2)
C(7)-C(8)-C(9)-N(2)	103.51(19)
C(9)-N(2)-C(10)-C(15)	-97.5(2)
C(9)-N(2)-C(10)-C(11)	138.97(19)
N(2)-C(10)-C(11)-C(12)	180.00(17)
C(15)-C(10)-C(11)-C(12)	56.5(2)
C(10)-C(11)-C(12)-C(13)	-55.9(3)
C(11)-C(12)-C(13)-C(14)	55.2(3)
C(12)-C(13)-C(14)-C(15)	-55.0(3)
N(2)-C(10)-C(15)-C(14)	178.87(17)
C(11)-C(10)-C(15)-C(14)	-57.0(2)
C(13)-C(14)-C(15)-C(10)	56.2(3)
C(1)-N(1)-C(16)-C(17)	89.8(2)
C(8)-N(1)-C(16)-C(17)	-82.31(19)
N(1)-C(16)-C(17)-C(22)	96.5(2)
N(1)-C(16)-C(17)-C(18)	-80.9(2)
C(22)-C(17)-C(18)-C(19)	-0.6(3)
C(16)-C(17)-C(18)-C(19)	176.9(2)
C(17)-C(18)-C(19)-C(20)	-0.4(4)
C(18)-C(19)-C(20)-C(21)	1.2(4)
C(19)-C(20)-C(21)-C(22)	-0.9(4)
C(18)-C(17)-C(22)-C(21)	0.8(3)
C(16)-C(17)-C(22)-C(21)	-176.6(2)

C(20)-C(21)-C(22)-C(17)	-0.1(4)

Symmetry transformations used to generate equivalent atoms:

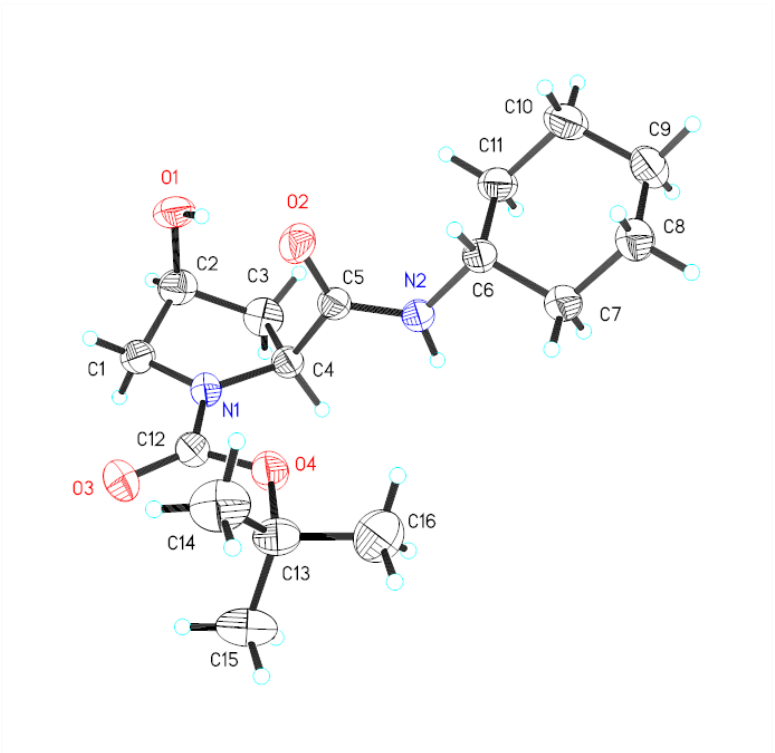
Table 7. Hydrogen bonds for mo_ddz20072_0m [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(11)-H(11A)...O(1)#1	0.97	2.64	3.340(2)	129.7
N(2)-H(2)...O(1)#1	0.86	2.10	2.9202(19)	159.9

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,-y+1,-z+1

ORTEP drawing of the X-ray crystallographic structure of **8a**



The single crystal of compound **8a** was prepared from its solution in petroleum ether/ethylacetate (1:1) by slow evaporation of the solvent.

CCDC 2089256. For detailed crystallographic data, please refer to the Cambridge Crystallographic Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for mo_ddz20132_0m.

Identification code	mo_ddz20132_0m	
Empirical formula	C16 H28 N2 O4	
Formula weight	312.40	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Orthorhombic	
Space group	P 21 21 21	
Unit cell dimensions	a = 9.6865(7) Å	α= 90°.
	b = 10.3400(8) Å	β= 90°.
	c = 17.7546(11) Å	γ = 90°.
Volume	1778.3(2) $Å^3$	
Z	4	
Density (calculated)	1.167 Mg/m^3	
Absorption coefficient	0.083 mm^{-1}	
F(000)	680	
Crystal size	0.190 x 0.150 x 0.130 mm^3	

Theta range for data collection	2.294 to 25.989°.
Index ranges	-11<=h<=10, -12<=k<=12, -21<=l<=19
Reflections collected	8722
Independent reflections	3456 [R(int) = 0.0266]
Completeness to theta = 25.242°	99.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6306
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3456 / 0 / 204
Goodness-of-fit on F^2	1.039
Final R indices [I>2sigma(I)]	R1 = 0.0389, wR2 = 0.0833
R indices (all data)	R1 = 0.0546, wR2 = 0.0935
Absolute structure parameter	0.0(6)
Extinction coefficient	0.043(7)
Largest diff. peak and hole	0.087 and -0.097 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mo_ddz20132_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	4807(2)	-212(2)	1447(1)	74(1)
O(2)	6627(2)	558(2)	2526(1)	67(1)
O(3)	7742(2)	3127(2)	552(1)	73(1)
O(4)	7830(2)	3553(2)	1811(1)	63(1)
N(1)	6094(2)	2430(2)	1354(1)	52(1)
N(2)	6243(2)	2157(2)	3363(1)	52(1)
C(1)	5266(3)	1781(3)	780(1)	61(1)
C(2)	4253(3)	1010(3)	1239(2)	66(1)
C(3)	4014(3)	1882(3)	1917(2)	66(1)
C(4)	5436(2)	2460(2)	2093(1)	48(1)
C(5)	6184(2)	1648(2)	2677(1)	49(1)
C(6)	6706(3)	1450(2)	4026(1)	51(1)
C(7)	7255(3)	2383(3)	4606(1)	66(1)
C(8)	7705(3)	1678(3)	5314(2)	75(1)
C(9)	6569(4)	858(3)	5636(2)	77(1)
C(10)	6003(3)	-65(3)	5060(2)	76(1)
C(11)	5559(3)	632(3)	4348(2)	64(1)
C(12)	7275(3)	3048(2)	1181(1)	55(1)

C(13)	9173(3)	4211(3)	1797(2)	65(1)
C(14)	10284(3)	3309(3)	1510(2)	98(1)
C(15)	9076(4)	5417(3)	1330(2)	98(1)
C(16)	9387(4)	4531(4)	2617(2)	98(1)

Table 3. Bond lengths [Å] and angles [°] for mo_ddz20132_0m.

O(1)-C(2)	1.421(3)
O(1)-H(1)	0.8200
O(2)-C(5)	1.235(3)
O(3)-C(12)	1.208(3)
O(4)-C(12)	1.347(3)
O(4)-C(13)	1.468(3)
N(1)-C(12)	1.346(3)
N(1)-C(4)	1.459(3)
N(1)-C(1)	1.461(3)
N(2)-C(5)	1.328(3)
N(2)-C(6)	1.456(3)
N(2)-H(2)	0.8600
C(1)-C(2)	1.505(4)
C(1)-H(1A)	0.9700
C(1)-H(1B)	0.9700
C(2)-C(3)	1.522(4)
C(2)-H(2A)	0.9800
C(3)-C(4)	1.534(4)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.518(3)
C(4)-H(4)	0.9800
C(6)-C(7)	1.508(3)
C(6)-C(11)	1.509(3)
C(6)-H(6)	0.9800
C(7)-C(8)	1.517(3)
C(7)-H(7A)	0.9700
C(7)-H(7B)	0.9700
C(8)-C(9)	1.502(4)
C(8)-H(8A)	0.9700
C(8)-H(8B)	0.9700

C(9)-C(10)	1.502(4)
C(9)-H(9A)	0.9700
C(9)-H(9B)	0.9700
C(10)-C(11)	1.517(3)
C(10)-H(10A)	0.9700
C(10)-H(10B)	0.9700
C(11)-H(11A)	0.9700
C(11)-H(11B)	0.9700
C(13)-C(15)	1.502(4)
C(13)-C(16)	1.508(4)
C(13)-C(14)	1.513(4)
C(14)-H(14A)	0.9600
C(14)-H(14B)	0.9600
C(14)-H(14C)	0.9600
C(15)-H(15A)	0.9600
C(15)-H(15B)	0.9600
C(15)-H(15C)	0.9600
C(16)-H(16A)	0.9600
C(16)-H(16B)	0.9600
C(16)-H(16C)	0.9600

C(2)-O(1)-H(1)	109.5
C(12)-O(4)-C(13)	121.3(2)
C(12)-N(1)-C(4)	124.5(2)
C(12)-N(1)-C(1)	121.7(2)
C(4)-N(1)-C(1)	113.5(2)
C(5)-N(2)-C(6)	123.75(19)
C(5)-N(2)-H(2)	118.1
C(6)-N(2)-H(2)	118.1
N(1)-C(1)-C(2)	102.88(19)
N(1)-C(1)-H(1A)	111.2
C(2)-C(1)-H(1A)	111.2
N(1)-C(1)-H(1B)	111.2
C(2)-C(1)-H(1B)	111.2
H(1A)-C(1)-H(1B)	109.1
O(1)-C(2)-C(1)	111.4(2)
O(1)-C(2)-C(3)	112.3(2)
C(1)-C(2)-C(3)	102.3(2)

O(1)-C(2)-H(2A)	110.2
C(1)-C(2)-H(2A)	110.2
C(3)-C(2)-H(2A)	110.2
C(2)-C(3)-C(4)	104.8(2)
C(2)-C(3)-H(3A)	110.8
C(4)-C(3)-H(3A)	110.8
C(2)-C(3)-H(3B)	110.8
C(4)-C(3)-H(3B)	110.8
H(3A)-C(3)-H(3B)	108.9
N(1)-C(4)-C(5)	113.19(19)
N(1)-C(4)-C(3)	101.58(19)
C(5)-C(4)-C(3)	110.6(2)
N(1)-C(4)-H(4)	110.4
C(5)-C(4)-H(4)	110.4
C(3)-C(4)-H(4)	110.4
O(2)-C(5)-N(2)	123.0(2)
O(2)-C(5)-C(4)	121.5(2)
N(2)-C(5)-C(4)	115.3(2)
N(2)-C(6)-C(7)	109.90(19)
N(2)-C(6)-C(11)	111.16(19)
C(7)-C(6)-C(11)	111.1(2)
N(2)-C(6)-H(6)	108.2
C(7)-C(6)-H(6)	108.2
C(11)-C(6)-H(6)	108.2
C(6)-C(7)-C(8)	111.1(2)
C(6)-C(7)-H(7A)	109.4
C(8)-C(7)-H(7A)	109.4
C(6)-C(7)-H(7B)	109.4
C(8)-C(7)-H(7B)	109.4
H(7A)-C(7)-H(7B)	108.0
C(9)-C(8)-C(7)	112.1(3)
C(9)-C(8)-H(8A)	109.2
C(7)-C(8)-H(8A)	109.2
C(9)-C(8)-H(8B)	109.2
C(7)-C(8)-H(8B)	109.2
H(8A)-C(8)-H(8B)	107.9
C(8)-C(9)-C(10)	111.5(2)
C(8)-C(9)-H(9A)	109.3

C(10)-C(9)-H(9A)	109.3
C(8)-C(9)-H(9B)	109.3
C(10)-C(9)-H(9B)	109.3
H(9A)-C(9)-H(9B)	108.0
C(9)-C(10)-C(11)	111.7(2)
C(9)-C(10)-H(10A)	109.3
C(11)-C(10)-H(10A)	109.3
C(9)-C(10)-H(10B)	109.3
C(11)-C(10)-H(10B)	109.3
H(10A)-C(10)-H(10B)	107.9
C(6)-C(11)-C(10)	111.9(2)
C(6)-C(11)-H(11A)	109.2
C(10)-C(11)-H(11A)	109.2
C(6)-C(11)-H(11B)	109.2
C(10)-C(11)-H(11B)	109.2
H(11A)-C(11)-H(11B)	107.9
O(3)-C(12)-N(1)	124.2(2)
O(3)-C(12)-O(4)	126.3(2)
N(1)-C(12)-O(4)	109.5(2)
O(4)-C(13)-C(15)	109.8(2)
O(4)-C(13)-C(16)	102.0(2)
C(15)-C(13)-C(16)	111.1(3)
O(4)-C(13)-C(14)	110.5(2)
C(15)-C(13)-C(14)	111.7(3)
C(16)-C(13)-C(14)	111.3(3)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(13)-C(15)-H(15A)	109.5
C(13)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(13)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(13)-C(16)-H(16A)	109.5

C(13)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(13)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for mo_ddz20132_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	95(2)	48(1)	78(1)	4(1)	-10(1)	-16(1)
O(2)	87(1)	55(1)	58(1)	-7(1)	-7(1)	23(1)
O(3)	87(1)	79(1)	53(1)	2(1)	18(1)	-9(1)
O(4)	62(1)	74(1)	54(1)	-1(1)	2(1)	-18(1)
N(1)	61(1)	53(1)	41(1)	-2(1)	2(1)	-6(1)
N(2)	68(1)	41(1)	46(1)	0(1)	1(1)	8(1)
C(1)	78(2)	52(2)	52(1)	2(1)	-11(1)	-3(1)
C(2)	63(2)	63(2)	71(2)	3(1)	-15(1)	-8(1)
C(3)	50(1)	73(2)	76(2)	2(2)	0(1)	3(1)
C(4)	53(1)	45(1)	47(1)	2(1)	3(1)	5(1)
C(5)	52(1)	44(1)	49(1)	1(1)	6(1)	3(1)
C(6)	57(1)	46(1)	50(1)	0(1)	0(1)	7(1)
C(7)	82(2)	58(2)	58(1)	4(1)	-9(1)	-14(2)
C(8)	89(2)	74(2)	61(2)	4(1)	-15(2)	-9(2)
C(9)	97(2)	80(2)	54(2)	12(1)	2(2)	4(2)
C(10)	87(2)	66(2)	76(2)	21(2)	-3(2)	-10(2)
C(11)	70(2)	54(2)	67(2)	7(1)	-7(1)	-7(1)
C(12)	64(2)	51(1)	49(1)	2(1)	4(1)	1(1)
C(13)	51(2)	59(2)	85(2)	6(1)	-1(1)	-8(1)
C(14)	71(2)	89(3)	133(3)	6(2)	2(2)	16(2)
C(15)	88(2)	67(2)	137(3)	28(2)	0(2)	-10(2)
C(16)	86(2)	109(3)	99(2)	-8(2)	-22(2)	-20(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for mo_ddz20132_0m.

	x	y	z	U(eq)
H(1)	5481	-104	1720	111
H(2)	5992	2949	3419	62
H(1A)	5832	1222	468	73
H(1B)	4795	2403	461	73
H(2A)	3390	893	959	79
H(3A)	3671	1387	2342	80
H(3B)	3354	2557	1798	80
H(4)	5341	3354	2269	58
H(6)	7460	875	3874	61
H(7A)	6544	3007	4732	79
H(7B)	8035	2850	4398	79
H(8A)	8492	1133	5198	89
H(8B)	7994	2305	5688	89
H(9A)	5831	1413	5815	92
H(9B)	6921	372	6062	92
H(10A)	5217	-519	5271	91
H(10B)	6703	-701	4936	91
H(11A)	5274	0	3975	76
H(11B)	4772	1179	4459	76
H(14A)	10244	2508	1783	147
H(14B)	11173	3700	1581	147
H(14C)	10140	3145	983	147
H(15A)	8988	5187	808	146
H(15B)	9895	5927	1399	146
H(15C)	8284	5909	1483	146
H(16A)	8633	5053	2793	147
H(16B)	10236	4999	2676	147
H(16C)	9427	3746	2905	147

Table 6. Torsion angles [°] for mo_ddz20132_0m.

C(12)-N(1)-C(1)-C(2)	168.4(2)
C(4)-N(1)-C(1)-C(2)	-18.2(3)
N(1)-C(1)-C(2)-O(1)	-86.1(3)
N(1)-C(1)-C(2)-C(3)	34.1(3)
O(1)-C(2)-C(3)-C(4)	80.8(3)
C(1)-C(2)-C(3)-C(4)	-38.8(3)
C(12)-N(1)-C(4)-C(5)	-73.9(3)
C(1)-N(1)-C(4)-C(5)	112.9(2)
C(12)-N(1)-C(4)-C(3)	167.5(2)
C(1)-N(1)-C(4)-C(3)	-5.7(3)
C(2)-C(3)-C(4)-N(1)	27.3(2)
C(2)-C(3)-C(4)-C(5)	-93.2(2)
C(6)-N(2)-C(5)-O(2)	-6.2(4)
C(6)-N(2)-C(5)-C(4)	169.5(2)
N(1)-C(4)-C(5)-O(2)	-43.2(3)
C(3)-C(4)-C(5)-O(2)	70.1(3)
N(1)-C(4)-C(5)-N(2)	141.1(2)
C(3)-C(4)-C(5)-N(2)	-105.7(2)
C(5)-N(2)-C(6)-C(7)	154.5(2)
C(5)-N(2)-C(6)-C(11)	-82.1(3)
N(2)-C(6)-C(7)-C(8)	178.2(2)
C(11)-C(6)-C(7)-C(8)	54.8(3)
C(6)-C(7)-C(8)-C(9)	-55.1(3)
C(7)-C(8)-C(9)-C(10)	54.4(3)
C(8)-C(9)-C(10)-C(11)	-53.6(3)
N(2)-C(6)-C(11)-C(10)	-177.4(2)
C(7)-C(6)-C(11)-C(10)	-54.7(3)
C(9)-C(10)-C(11)-C(6)	54.1(3)
C(4)-N(1)-C(12)-O(3)	-172.3(3)
C(1)-N(1)-C(12)-O(3)	0.4(4)
C(4)-N(1)-C(12)-O(4)	7.5(3)
C(1)-N(1)-C(12)-O(4)	-179.8(2)
C(13)-O(4)-C(12)-O(3)	-4.2(4)
C(13)-O(4)-C(12)-N(1)	176.0(2)
C(12)-O(4)-C(13)-C(15)	65.1(3)
C(12)-O(4)-C(13)-C(16)	-177.0(2)

C(12)-O(4)-C(13)-C(14)	-58.6(3)

Symmetry transformations used to generate equivalent atoms:

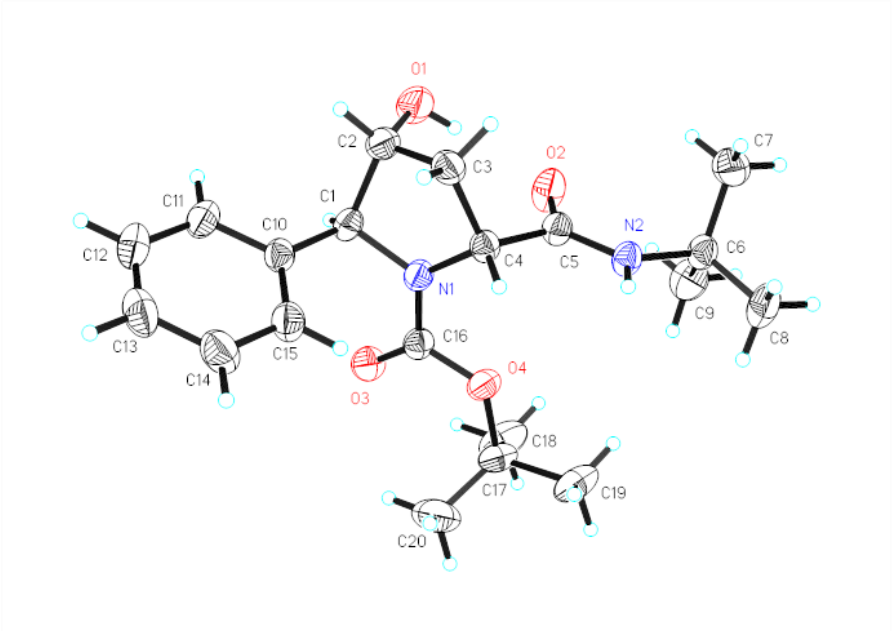
Table 7. Hydrogen bonds for mo_ddz20132_0m [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(15)-H(15A)...O(3)	0.96	2.49	3.031(4)	115.5
C(14)-H(14C)...O(3)	0.96	2.45	2.999(4)	116.4
N(2)-H(2)...O(1)#1	0.86	2.07	2.924(3)	174.4
O(1)-H(1)...O(2)	0.82	1.94	2.723(3)	160.1
O(1)-H(1)...O(2)	0.82	1.94	2.723(3)	160.1
N(2)-H(2)...O(1)#1	0.86	2.07	2.924(3)	174.4
C(14)-H(14C)...O(3)	0.96	2.45	2.999(4)	116.4
C(15)-H(15A)...O(3)	0.96	2.49	3.031(4)	115.5

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y+1/2,-z+1/2

ORTEP drawing of the X-ray crystallographic structure of **8d**



The single crystal of compound **8d** was prepared from its solution in petroleum ether/ethylacetate (1:1) by slow evaporation of the solvent.

CCDC 2089258. For detailed crystallographic data, please refer to the Cambridge Crystallographic Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for ddz20133.

Identification code	ddz20133	
Empirical formula	C20 H30 N2 O4	
Formula weight	362.46	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 13.4680(13) Å	α= 90°.
	b = 14.2172(13) Å	β= 92.363(3)°.
	c = 10.9007(10) Å	γ = 90°.
Volume	2085.5(3) $Å^3$	
Z	4	
Density (calculated)	1.154 Mg/m^3	
Absorption coefficient	0.080 mm^{-1}	
F(000)	784	
Crystal size	0.160 x 0.130 x 0.090 mm^3	
Theta range for data collection	2.758 to 25.499°.	
Index ranges	-16<=h<=16, -17<=k<=17, -13<=l<=13	
Reflections collected	29338	

Independent reflections	3881 [R(int) = 0.0666]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6955
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3881 / 0 / 243
Goodness-of-fit on F^2	1.085
Final R indices [I>2sigma(I)]	R1 = 0.0521, wR2 = 0.1082
R indices (all data)	R1 = 0.0908, wR2 = 0.1293
Extinction coefficient	0.0173(19)
Largest diff. peak and hole	0.154 and -0.143 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for ddz20133. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	10076(1)	2794(1)	2912(2)	78(1)
O(2)	8868(1)	1225(1)	2967(1)	73(1)
O(3)	6831(1)	3456(1)	1607(1)	62(1)
O(4)	6439(1)	2301(1)	2951(1)	57(1)
N(1)	7891(1)	3019(1)	3177(1)	49(1)
N(2)	7849(1)	745(1)	4446(2)	51(1)
C(1)	8606(2)	3782(1)	3007(2)	50(1)
C(2)	9536(2)	3390(2)	3679(2)	59(1)
C(3)	9105(2)	2870(2)	4756(2)	56(1)
C(4)	8150(2)	2412(1)	4231(2)	46(1)
C(5)	8317(2)	1398(1)	3817(2)	50(1)
C(6)	7864(2)	-284(1)	4248(2)	55(1)
C(7)	8896(2)	-670(2)	4546(3)	82(1)
C(8)	7120(2)	-684(2)	5117(3)	81(1)
C(9)	7555(2)	-512(2)	2931(2)	82(1)
C(10)	8262(2)	4713(1)	3511(2)	49(1)
C(11)	8784(2)	5524(2)	3270(2)	65(1)
C(12)	8494(2)	6380(2)	3718(3)	82(1)
C(13)	7686(2)	6436(2)	4425(3)	84(1)
C(14)	7152(2)	5644(2)	4682(2)	77(1)
C(15)	7438(2)	4791(2)	4216(2)	64(1)
C(16)	7035(2)	2966(2)	2499(2)	50(1)

C(17)	5463(2)	2084(2)	2358(2)	64(1)
C(18)	5614(2)	1694(2)	1091(2)	96(1)
C(19)	5073(2)	1328(2)	3186(3)	90(1)
C(20)	4806(2)	2939(2)	2356(3)	105(1)

Table 3. Bond lengths [Å] and angles [°] for ddz20133.

O(1)-C(2)	1.413(2)
O(1)-H(1)	0.8200
O(2)-C(5)	1.235(2)
O(3)-C(16)	1.218(2)
O(4)-C(16)	1.347(2)
O(4)-C(17)	1.473(3)
N(1)-C(16)	1.346(3)
N(1)-C(1)	1.467(2)
N(1)-C(4)	1.468(2)
N(2)-C(5)	1.328(2)
N(2)-C(6)	1.479(3)
N(2)-H(2)	0.8600
C(1)-C(10)	1.512(3)
C(1)-C(2)	1.530(3)
C(1)-H(1A)	0.9800
C(2)-C(3)	1.523(3)
C(2)-H(2A)	0.9800
C(3)-C(4)	1.532(3)
C(3)-H(3A)	0.9700
C(3)-H(3B)	0.9700
C(4)-C(5)	1.529(3)
C(4)-H(4)	0.9800
C(6)-C(9)	1.514(3)
C(6)-C(8)	1.518(3)
C(6)-C(7)	1.517(3)
C(7)-H(7A)	0.9600
C(7)-H(7B)	0.9600
C(7)-H(7C)	0.9600
C(8)-H(8A)	0.9600
C(8)-H(8B)	0.9600
C(8)-H(8C)	0.9600

C(9)-H(9A)	0.9600
C(9)-H(9B)	0.9600
C(9)-H(9C)	0.9600
C(10)-C(11)	1.381(3)
C(10)-C(15)	1.381(3)
C(11)-C(12)	1.375(3)
C(11)-H(11)	0.9300
C(12)-C(13)	1.361(4)
C(12)-H(12)	0.9300
C(13)-C(14)	1.371(4)
C(13)-H(13)	0.9300
C(14)-C(15)	1.376(3)
C(14)-H(14)	0.9300
C(15)-H(15)	0.9300
C(17)-C(20)	1.504(4)
C(17)-C(18)	1.509(3)
C(17)-C(19)	1.511(3)
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-H(19A)	0.9600
C(19)-H(19B)	0.9600
C(19)-H(19C)	0.9600
C(20)-H(20A)	0.9600
C(20)-H(20B)	0.9600
C(20)-H(20C)	0.9600

C(2)-O(1)-H(1)	109.5
C(16)-O(4)-C(17)	121.43(16)
C(16)-N(1)-C(1)	121.57(17)
C(16)-N(1)-C(4)	124.59(17)
C(1)-N(1)-C(4)	113.46(16)
C(5)-N(2)-C(6)	127.36(17)
C(5)-N(2)-H(2)	116.3
C(6)-N(2)-H(2)	116.3
N(1)-C(1)-C(10)	112.92(16)
N(1)-C(1)-C(2)	101.51(16)
C(10)-C(1)-C(2)	113.65(17)

N(1)-C(1)-H(1A)	109.5
C(10)-C(1)-H(1A)	109.5
C(2)-C(1)-H(1A)	109.5
O(1)-C(2)-C(3)	112.76(18)
O(1)-C(2)-C(1)	111.49(19)
C(3)-C(2)-C(1)	102.38(17)
O(1)-C(2)-H(2A)	110.0
C(3)-C(2)-H(2A)	110.0
C(1)-C(2)-H(2A)	110.0
C(2)-C(3)-C(4)	105.04(17)
C(2)-C(3)-H(3A)	110.7
C(4)-C(3)-H(3A)	110.7
C(2)-C(3)-H(3B)	110.7
C(4)-C(3)-H(3B)	110.7
H(3A)-C(3)-H(3B)	108.8
N(1)-C(4)-C(5)	110.90(15)
N(1)-C(4)-C(3)	102.16(15)
C(5)-C(4)-C(3)	112.34(17)
N(1)-C(4)-H(4)	110.4
C(5)-C(4)-H(4)	110.4
C(3)-C(4)-H(4)	110.4
O(2)-C(5)-N(2)	124.06(19)
O(2)-C(5)-C(4)	120.63(18)
N(2)-C(5)-C(4)	115.30(17)
N(2)-C(6)-C(9)	110.16(18)
N(2)-C(6)-C(8)	105.48(17)
C(9)-C(6)-C(8)	110.4(2)
N(2)-C(6)-C(7)	110.19(18)
C(9)-C(6)-C(7)	109.8(2)
C(8)-C(6)-C(7)	110.7(2)
C(6)-C(7)-H(7A)	109.5
C(6)-C(7)-H(7B)	109.5
H(7A)-C(7)-H(7B)	109.5
C(6)-C(7)-H(7C)	109.5
H(7A)-C(7)-H(7C)	109.5
H(7B)-C(7)-H(7C)	109.5
C(6)-C(8)-H(8A)	109.5
C(6)-C(8)-H(8B)	109.5

H(8A)-C(8)-H(8B)	109.5
C(6)-C(8)-H(8C)	109.5
H(8A)-C(8)-H(8C)	109.5
H(8B)-C(8)-H(8C)	109.5
C(6)-C(9)-H(9A)	109.5
C(6)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(6)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
C(11)-C(10)-C(15)	117.7(2)
C(11)-C(10)-C(1)	119.76(19)
C(15)-C(10)-C(1)	122.51(18)
C(12)-C(11)-C(10)	121.2(2)
C(12)-C(11)-H(11)	119.4
C(10)-C(11)-H(11)	119.4
C(13)-C(12)-C(11)	119.9(2)
C(13)-C(12)-H(12)	120.1
C(11)-C(12)-H(12)	120.1
C(12)-C(13)-C(14)	120.5(2)
C(12)-C(13)-H(13)	119.8
C(14)-C(13)-H(13)	119.8
C(13)-C(14)-C(15)	119.3(3)
C(13)-C(14)-H(14)	120.3
C(15)-C(14)-H(14)	120.3
C(14)-C(15)-C(10)	121.4(2)
C(14)-C(15)-H(15)	119.3
C(10)-C(15)-H(15)	119.3
O(3)-C(16)-N(1)	124.5(2)
O(3)-C(16)-O(4)	125.1(2)
N(1)-C(16)-O(4)	110.38(17)
O(4)-C(17)-C(20)	110.2(2)
O(4)-C(17)-C(18)	109.05(18)
C(20)-C(17)-C(18)	113.4(2)
O(4)-C(17)-C(19)	102.31(18)
C(20)-C(17)-C(19)	110.9(2)
C(18)-C(17)-C(19)	110.4(2)
C(17)-C(18)-H(18A)	109.5

C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(17)-C(19)-H(19A)	109.5
C(17)-C(19)-H(19B)	109.5
H(19A)-C(19)-H(19B)	109.5
C(17)-C(19)-H(19C)	109.5
H(19A)-C(19)-H(19C)	109.5
H(19B)-C(19)-H(19C)	109.5
C(17)-C(20)-H(20A)	109.5
C(17)-C(20)-H(20B)	109.5
H(20A)-C(20)-H(20B)	109.5
C(17)-C(20)-H(20C)	109.5
H(20A)-C(20)-H(20C)	109.5
H(20B)-C(20)-H(20C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for ddz20133. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	62(1)	66(1)	109(1)	-7(1)	31(1)	1(1)
O(2)	93(1)	54(1)	75(1)	-9(1)	42(1)	-6(1)
O(3)	64(1)	72(1)	49(1)	14(1)	3(1)	-1(1)
O(4)	47(1)	67(1)	56(1)	10(1)	0(1)	-10(1)
N(1)	49(1)	47(1)	50(1)	5(1)	1(1)	-6(1)
N(2)	58(1)	41(1)	54(1)	-3(1)	14(1)	-3(1)
C(1)	51(1)	48(1)	51(1)	3(1)	10(1)	-9(1)
C(2)	49(1)	53(1)	75(2)	-7(1)	7(1)	-2(1)
C(3)	56(1)	50(1)	63(1)	-3(1)	-4(1)	4(1)
C(4)	51(1)	45(1)	44(1)	2(1)	7(1)	2(1)
C(5)	56(1)	46(1)	50(1)	-2(1)	8(1)	-1(1)
C(6)	62(2)	39(1)	65(1)	-6(1)	6(1)	-6(1)
C(7)	74(2)	55(2)	116(2)	-8(1)	-2(2)	7(1)

C(8)	94(2)	53(1)	98(2)	2(1)	25(2)	-19(1)
C(9)	96(2)	70(2)	80(2)	-21(1)	-2(2)	-15(2)
C(10)	54(1)	45(1)	48(1)	7(1)	1(1)	-2(1)
C(11)	64(2)	55(2)	77(2)	1(1)	6(1)	-14(1)
C(12)	91(2)	49(2)	107(2)	0(1)	5(2)	-14(1)
C(13)	106(2)	49(2)	97(2)	-7(1)	-2(2)	11(2)
C(14)	84(2)	64(2)	84(2)	4(1)	19(2)	19(2)
C(15)	72(2)	51(1)	69(2)	6(1)	16(1)	2(1)
C(16)	52(1)	51(1)	46(1)	1(1)	12(1)	-1(1)
C(17)	42(1)	88(2)	61(1)	2(1)	4(1)	-8(1)
C(18)	84(2)	139(3)	65(2)	-20(2)	7(2)	-39(2)
C(19)	63(2)	119(2)	90(2)	9(2)	10(2)	-33(2)
C(20)	63(2)	129(3)	125(3)	13(2)	9(2)	25(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^{3}) for ddz20133.

	x	y	z	U(eq)
H(1)	9768	2303	2795	118
H(2)	7498	943	5034	61
H(1A)	8729	3849	2132	60
H(2A)	9961	3908	3981	71
H(3A)	8959	3304	5412	68
H(3B)	9566	2398	5076	68
H(4)	7629	2436	4832	56
H(7A)	9359	-396	4002	123
H(7B)	8891	-1341	4443	123
H(7C)	9091	-519	5379	123
H(8A)	7328	-539	5948	122
H(8B)	7082	-1354	5016	122
H(8C)	6478	-412	4936	122
H(9A)	6898	-275	2752	123
H(9B)	7560	-1181	2816	123
H(9C)	8011	-224	2390	123
H(11)	9342	5490	2796	78
H(12)	8849	6921	3539	99

H(13)	7495	7015	4735	101
H(14)	6601	5683	5167	92
H(15)	7069	4256	4380	76
H(18A)	5877	2178	582	144
H(18B)	4990	1480	739	144
H(18C)	6073	1178	1147	144
H(19A)	5530	809	3224	136
H(19B)	4438	1114	2864	136
H(19C)	5003	1579	3995	136
H(20A)	4788	3188	3174	158
H(20B)	4146	2769	2072	158
H(20C)	5065	3407	1821	158

Table 6. Torsion angles [°] for ddz20133.

C(16)-N(1)-C(1)-C(10)	73.5(2)
C(4)-N(1)-C(1)-C(10)	-99.72(19)
C(16)-N(1)-C(1)-C(2)	-164.46(18)
C(4)-N(1)-C(1)-C(2)	22.3(2)
N(1)-C(1)-C(2)-O(1)	84.60(19)
C(10)-C(1)-C(2)-O(1)	-153.86(17)
N(1)-C(1)-C(2)-C(3)	-36.20(19)
C(10)-C(1)-C(2)-C(3)	85.3(2)
O(1)-C(2)-C(3)-C(4)	-81.4(2)
C(1)-C(2)-C(3)-C(4)	38.5(2)
C(16)-N(1)-C(4)-C(5)	68.3(2)
C(1)-N(1)-C(4)-C(5)	-118.73(18)
C(16)-N(1)-C(4)-C(3)	-171.81(18)
C(1)-N(1)-C(4)-C(3)	1.2(2)
C(2)-C(3)-C(4)-N(1)	-24.7(2)
C(2)-C(3)-C(4)-C(5)	94.21(19)
C(6)-N(2)-C(5)-O(2)	-1.8(3)
C(6)-N(2)-C(5)-C(4)	179.44(18)
N(1)-C(4)-C(5)-O(2)	49.6(3)
C(3)-C(4)-C(5)-O(2)	-64.0(3)
N(1)-C(4)-C(5)-N(2)	-131.55(19)
C(3)-C(4)-C(5)-N(2)	114.8(2)
C(5)-N(2)-C(6)-C(9)	-54.7(3)

C(5)-N(2)-C(6)-C(8)	-173.8(2)
C(5)-N(2)-C(6)-C(7)	66.6(3)
N(1)-C(1)-C(10)-C(11)	-170.94(19)
C(2)-C(1)-C(10)-C(11)	74.1(2)
N(1)-C(1)-C(10)-C(15)	9.3(3)
C(2)-C(1)-C(10)-C(15)	-105.7(2)
C(15)-C(10)-C(11)-C(12)	0.1(3)
C(1)-C(10)-C(11)-C(12)	-179.7(2)
C(10)-C(11)-C(12)-C(13)	0.8(4)
C(11)-C(12)-C(13)-C(14)	-0.7(4)
C(12)-C(13)-C(14)-C(15)	-0.2(4)
C(13)-C(14)-C(15)-C(10)	1.1(4)
C(11)-C(10)-C(15)-C(14)	-1.0(3)
C(1)-C(10)-C(15)-C(14)	178.8(2)
C(1)-N(1)-C(16)-O(3)	9.3(3)
C(4)-N(1)-C(16)-O(3)	-178.22(18)
C(1)-N(1)-C(16)-O(4)	-170.23(16)
C(4)-N(1)-C(16)-O(4)	2.2(3)
C(17)-O(4)-C(16)-O(3)	1.9(3)
C(17)-O(4)-C(16)-N(1)	-178.51(17)
C(16)-O(4)-C(17)-C(20)	-61.0(3)
C(16)-O(4)-C(17)-C(18)	64.1(3)
C(16)-O(4)-C(17)-C(19)	-178.99(19)

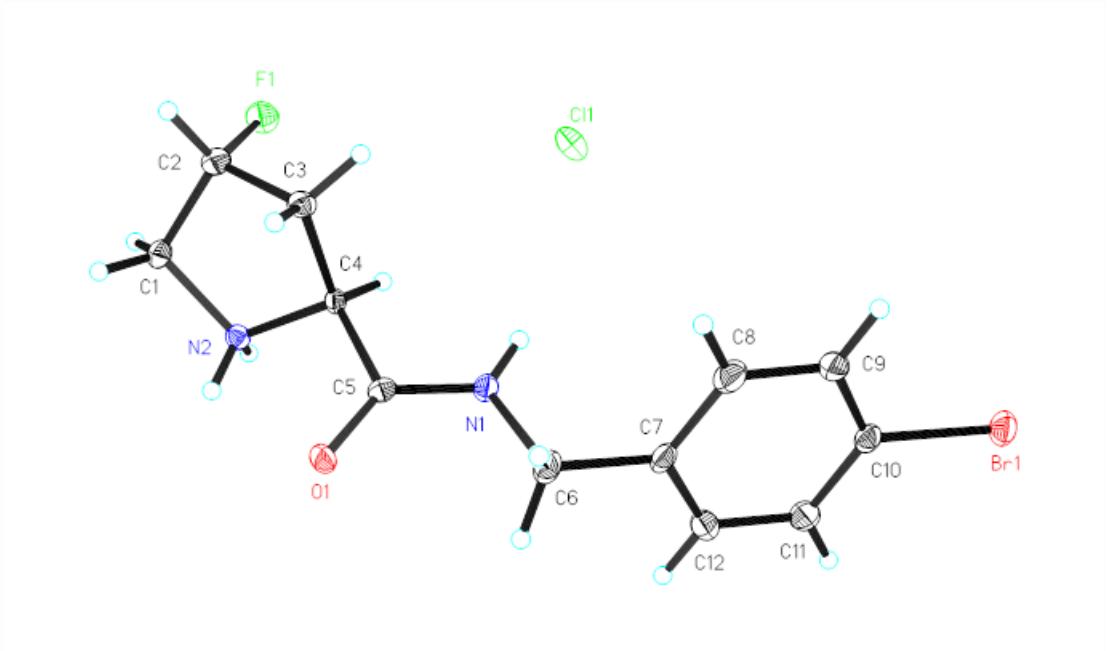
Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for ddz20133 [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(20)-H(20C)...O(3)	0.96	2.40	2.970(3)	117.7
C(18)-H(18A)...O(3)	0.96	2.47	3.033(3)	117.6
C(9)-H(9C)...O(2)	0.96	2.43	3.036(3)	120.7
C(7)-H(7A)...O(2)	0.96	2.64	3.197(3)	117.5
C(4)-H(4)...O(3)#1	0.98	2.58	3.431(2)	144.5
N(2)-H(2)...O(3)#1	0.86	2.15	2.998(2)	171.0
O(1)-H(1)...O(2)	0.82	1.97	2.763(2)	163.5

Symmetry transformations used to generate equivalent atoms: #1 x,-y+1/2,z+1/2

ORTEP drawing of the X-ray crystallographic structure of deprotected **9**



The compound **9** (20 mg) was dissolved in HCl/MeOH (6 M, 5 mL) and stirred at rt for 2h, than concentrated to give the deprotected **9** as its hydrochloride. The single crystal was prepared from its solution in methanol/acetonitrile (1:10) by slow evaporation of the solvent.

CCDC 2094462. For detailed crystallographic data, please refer to the Cambridge Crystallographic Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for mo_d8v21545_0m.

Identification code	mo_d8v21545_0m	
Empirical formula	C15 H22 Cl2 N2 O	
Formula weight	317.24	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21/c	
Unit cell dimensions	a = 6.0632(3) Å	α= 90°.
	b = 26.8654(12) Å	β= 92.299(2)°.
	c = 10.3001(5) Å	γ = 90°.
Volume	1676.44(14) $Å^3$	
Z	4	
Density (calculated)	1.257 Mg/m^3	
Absorption coefficient	0.385 mm^{-1}	
F(000)	672	
Crystal size	0.140 x 0.100 x 0.060 mm^3	
Theta range for data collection	3.015 to 25.998°.	
Index ranges	-6<=h<=7, -33<=k<=31, -12<=l<=12	

Reflections collected	12631
Independent reflections	3288 [R(int) = 0.0461]
Completeness to theta = 25.242°	99.8 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6686
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3288 / 0 / 184
Goodness-of-fit on F^2	1.075
Final R indices [I>2sigma(I)]	R1 = 0.0458, wR2 = 0.0894
R indices (all data)	R1 = 0.0703, wR2 = 0.1028
Extinction coefficient	n/a
Largest diff. peak and hole	0.208 and -0.270 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mo_d8v21545_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	2384(1)	5292(1)	3349(1)	56(1)
O(1)	6731(3)	1880(1)	5455(2)	41(1)
N(1)	4033(3)	1646(1)	3969(2)	34(1)
N(2)	8377(3)	2570(1)	3858(2)	29(1)
C(1)	5636(4)	1943(1)	4432(2)	31(1)
C(2)	6056(4)	2396(1)	3597(2)	28(1)
C(3)	4625(4)	2849(1)	3929(2)	32(1)
C(4)	6251(4)	3260(1)	4390(2)	29(1)
C(5)	8337(4)	3120(1)	3705(2)	30(1)
C(6)	5391(4)	3780(1)	4162(2)	29(1)
C(7)	3429(4)	3923(1)	4708(2)	34(1)
C(8)	2513(4)	4385(1)	4479(2)	40(1)
C(9)	3580(4)	4714(1)	3691(2)	37(1)
C(10)	5561(5)	4593(1)	3170(2)	40(1)
C(11)	6452(4)	4126(1)	3402(2)	36(1)
C(12)	3207(4)	1189(1)	4596(2)	38(1)
C(13)	2192(5)	1319(1)	5877(3)	49(1)
C(14)	1452(6)	973(1)	3653(3)	66(1)
C(15)	5099(5)	819(1)	4798(3)	50(1)
Cl(2)	957(1)	2160(1)	1625(1)	38(1)

Table 3. Bond lengths [Å] and angles [°] for mo_d8v21545_0m.

Cl(1)-C(9)	1.745(3)
O(1)-C(1)	1.234(3)
N(1)-C(1)	1.332(3)
N(1)-C(12)	1.485(3)
N(1)-H(1)	0.8700
N(2)-C(5)	1.484(3)
N(2)-C(2)	1.497(3)
N(2)-H(2A)	0.9800
N(2)-H(2B)	0.9800
C(1)-C(2)	1.518(3)
C(2)-C(3)	1.541(3)
C(2)-H(2)	0.9900
C(3)-C(4)	1.541(3)
C(3)-H(3A)	0.9800
C(3)-H(3B)	0.9800
C(4)-C(6)	1.508(3)
C(4)-C(5)	1.520(3)
C(4)-H(4)	0.9900
C(5)-H(5A)	0.9800
C(5)-H(5B)	0.9800
C(6)-C(7)	1.390(3)
C(6)-C(11)	1.389(3)
C(7)-C(8)	1.377(3)
C(7)-H(7)	0.9400
C(8)-C(9)	1.378(4)
C(8)-H(8)	0.9400
C(9)-C(10)	1.374(4)
C(10)-C(11)	1.382(4)
C(10)-H(10)	0.9400
C(11)-H(11)	0.9400
C(12)-C(13)	1.518(4)
C(12)-C(15)	1.525(4)
C(12)-C(14)	1.527(4)
C(13)-H(13A)	0.9700
C(13)-H(13B)	0.9700

C(13)-H(13C)	0.9700
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(14)-H(14C)	0.9700
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(15)-H(15C)	0.9700

C(1)-N(1)-C(12)	126.4(2)
C(1)-N(1)-H(1)	116.8
C(12)-N(1)-H(1)	116.8
C(5)-N(2)-C(2)	106.23(17)
C(5)-N(2)-H(2A)	110.5
C(2)-N(2)-H(2A)	110.5
C(5)-N(2)-H(2B)	110.5
C(2)-N(2)-H(2B)	110.5
H(2A)-N(2)-H(2B)	108.7
O(1)-C(1)-N(1)	125.7(2)
O(1)-C(1)-C(2)	119.8(2)
N(1)-C(1)-C(2)	114.5(2)
N(2)-C(2)-C(1)	109.03(18)
N(2)-C(2)-C(3)	104.33(18)
C(1)-C(2)-C(3)	113.52(19)
N(2)-C(2)-H(2)	109.9
C(1)-C(2)-H(2)	109.9
C(3)-C(2)-H(2)	109.9
C(2)-C(3)-C(4)	105.93(18)
C(2)-C(3)-H(3A)	110.6
C(4)-C(3)-H(3A)	110.6
C(2)-C(3)-H(3B)	110.6
C(4)-C(3)-H(3B)	110.6
H(3A)-C(3)-H(3B)	108.7
C(6)-C(4)-C(5)	116.5(2)
C(6)-C(4)-C(3)	113.73(19)
C(5)-C(4)-C(3)	102.33(18)
C(6)-C(4)-H(4)	107.9
C(5)-C(4)-H(4)	107.9
C(3)-C(4)-H(4)	107.9

N(2)-C(5)-C(4)	101.97(18)
N(2)-C(5)-H(5A)	111.4
C(4)-C(5)-H(5A)	111.4
N(2)-C(5)-H(5B)	111.4
C(4)-C(5)-H(5B)	111.4
H(5A)-C(5)-H(5B)	109.2
C(7)-C(6)-C(11)	117.9(2)
C(7)-C(6)-C(4)	119.2(2)
C(11)-C(6)-C(4)	122.9(2)
C(8)-C(7)-C(6)	121.6(2)
C(8)-C(7)-H(7)	119.2
C(6)-C(7)-H(7)	119.2
C(7)-C(8)-C(9)	118.9(2)
C(7)-C(8)-H(8)	120.6
C(9)-C(8)-H(8)	120.6
C(10)-C(9)-C(8)	121.1(2)
C(10)-C(9)-Cl(1)	119.6(2)
C(8)-C(9)-Cl(1)	119.2(2)
C(9)-C(10)-C(11)	119.2(2)
C(9)-C(10)-H(10)	120.4
C(11)-C(10)-H(10)	120.4
C(10)-C(11)-C(6)	121.2(2)
C(10)-C(11)-H(11)	119.4
C(6)-C(11)-H(11)	119.4
N(1)-C(12)-C(13)	110.1(2)
N(1)-C(12)-C(15)	109.5(2)
C(13)-C(12)-C(15)	111.1(2)
N(1)-C(12)-C(14)	106.0(2)
C(13)-C(12)-C(14)	110.1(2)
C(15)-C(12)-C(14)	109.9(2)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
C(12)-C(14)-H(14A)	109.5
C(12)-C(14)-H(14B)	109.5

H(14A)-C(14)-H(14B)	109.5
C(12)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
C(12)-C(15)-H(15A)	109.5
C(12)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(12)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for mo_d8v21545_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Cl(1)	69(1)	44(1)	53(1)	8(1)	5(1)	19(1)
O(1)	43(1)	46(1)	34(1)	6(1)	-14(1)	-7(1)
N(1)	38(1)	34(1)	28(1)	3(1)	-9(1)	-5(1)
N(2)	26(1)	36(1)	24(1)	-2(1)	1(1)	3(1)
C(1)	29(1)	34(1)	28(1)	-2(1)	-2(1)	2(1)
C(2)	25(1)	34(1)	24(1)	-1(1)	-1(1)	-1(1)
C(3)	26(1)	31(1)	40(1)	6(1)	3(1)	0(1)
C(4)	30(1)	34(1)	22(1)	-1(1)	1(1)	1(1)
C(5)	26(1)	34(1)	30(1)	-1(1)	0(1)	-2(1)
C(6)	30(1)	32(1)	24(1)	-2(1)	0(1)	-3(1)
C(7)	32(1)	34(1)	35(1)	-2(1)	4(1)	-2(1)
C(8)	39(2)	41(2)	39(2)	-7(1)	6(1)	2(1)
C(9)	45(2)	32(1)	34(1)	-2(1)	-4(1)	7(1)
C(10)	50(2)	36(2)	34(1)	3(1)	6(1)	-5(1)
C(11)	34(2)	38(2)	36(1)	-1(1)	6(1)	-2(1)
C(12)	44(2)	34(2)	34(1)	1(1)	-3(1)	-7(1)
C(13)	46(2)	53(2)	49(2)	3(1)	8(1)	4(1)
C(14)	80(2)	57(2)	58(2)	6(2)	-20(2)	-35(2)
C(15)	66(2)	37(2)	49(2)	3(1)	11(2)	9(1)
Cl(2)	36(1)	54(1)	24(1)	-3(1)	-1(1)	11(1)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for mo_d8v21545_0m.

	x	y	z	U(eq)
H(1)	3407	1728	3224	40
H(2A)	8890	2479	4741	35
H(2B)	9366	2419	3240	35
H(2)	5827	2310	2667	34
H(3A)	3619	2765	4617	39
H(3B)	3751	2960	3162	39
H(4)	6545	3217	5336	34
H(5A)	8240	3216	2787	36
H(5B)	9645	3274	4124	36
H(7)	2710	3698	5248	40
H(8)	1182	4475	4853	47
H(10)	6301	4825	2660	48
H(11)	7800	4041	3040	43
H(13A)	3318	1457	6467	73
H(13B)	1586	1021	6256	73
H(13C)	1025	1561	5725	73
H(14A)	288	1216	3496	99
H(14B)	836	674	4023	99
H(14C)	2116	891	2838	99
H(15A)	5713	741	3967	76
H(15B)	4550	517	5186	76
H(15C)	6236	964	5370	76

Table 6. Torsion angles [°] for mo_d8v21545_0m.

C(12)-N(1)-C(1)-O(1)	1.5(4)
C(12)-N(1)-C(1)-C(2)	-177.6(2)
C(5)-N(2)-C(2)-C(1)	-147.34(18)
C(5)-N(2)-C(2)-C(3)	-25.8(2)
O(1)-C(1)-C(2)-N(2)	25.2(3)
N(1)-C(1)-C(2)-N(2)	-155.7(2)

O(1)-C(1)-C(2)-C(3)	-90.7(3)
N(1)-C(1)-C(2)-C(3)	88.5(3)
N(2)-C(2)-C(3)-C(4)	-0.9(2)
C(1)-C(2)-C(3)-C(4)	117.7(2)
C(2)-C(3)-C(4)-C(6)	152.64(19)
C(2)-C(3)-C(4)-C(5)	26.1(2)
C(2)-N(2)-C(5)-C(4)	42.6(2)
C(6)-C(4)-C(5)-N(2)	-166.27(18)
C(3)-C(4)-C(5)-N(2)	-41.6(2)
C(5)-C(4)-C(6)-C(7)	176.8(2)
C(3)-C(4)-C(6)-C(7)	58.1(3)
C(5)-C(4)-C(6)-C(11)	-1.9(3)
C(3)-C(4)-C(6)-C(11)	-120.6(2)
C(11)-C(6)-C(7)-C(8)	2.0(4)
C(4)-C(6)-C(7)-C(8)	-176.7(2)
C(6)-C(7)-C(8)-C(9)	-0.2(4)
C(7)-C(8)-C(9)-C(10)	-2.0(4)
C(7)-C(8)-C(9)-Cl(1)	177.81(19)
C(8)-C(9)-C(10)-C(11)	2.4(4)
Cl(1)-C(9)-C(10)-C(11)	-177.40(19)
C(9)-C(10)-C(11)-C(6)	-0.6(4)
C(7)-C(6)-C(11)-C(10)	-1.6(4)
C(4)-C(6)-C(11)-C(10)	177.1(2)
C(1)-N(1)-C(12)-C(13)	63.4(3)
C(1)-N(1)-C(12)-C(15)	-59.0(3)
C(1)-N(1)-C(12)-C(14)	-177.5(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for mo_d8v21545_0m [Å and °].

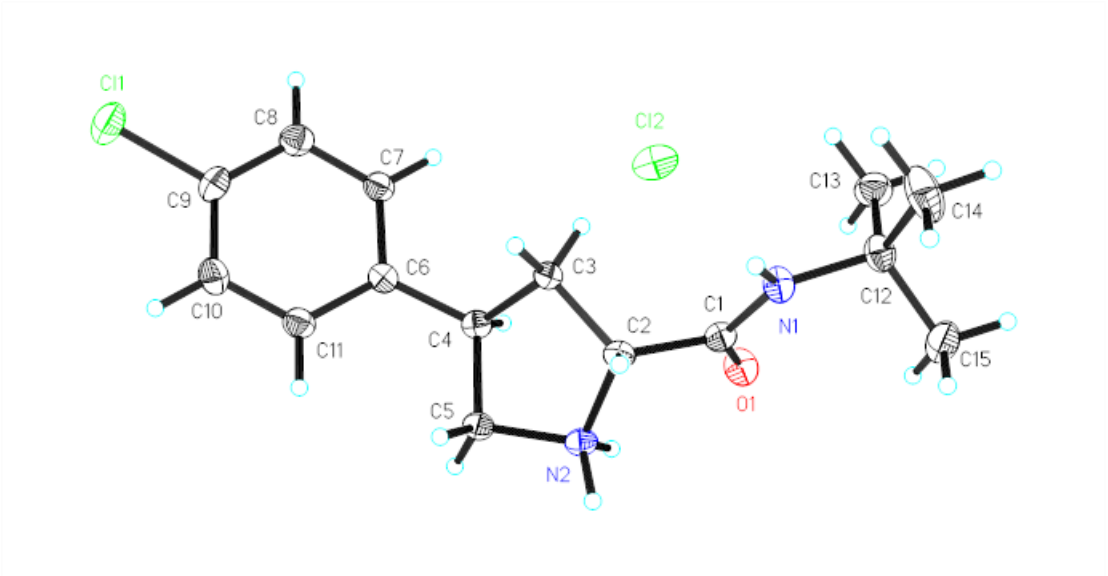
D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(15)-H(15C)...O(1)	0.97	2.48	3.084(3)	120.1
C(15)-H(15A)...Cl(1)#1	0.97	2.95	3.904(3)	168.1
C(13)-H(13A)...O(1)	0.97	2.61	3.183(3)	117.7
C(8)-H(8)...Cl(1)#2	0.94	2.97	3.886(3)	165.6
C(5)-H(5B)...Cl(2)#3	0.98	2.91	3.428(2)	114.1
C(5)-H(5A)...O(1)#4	0.98	2.55	3.449(3)	152.7
C(3)-H(3A)...Cl(2)#5	0.98	2.68	3.627(2)	162.2
N(2)-H(2B)...Cl(2)#6	0.98	2.08	3.040(2)	167.3
N(2)-H(2A)...Cl(2)#3	0.98	2.47	3.2768(19)	139.8
N(1)-H(1)...Cl(2)	0.87	2.46	3.294(2)	159.8

Symmetry transformations used to generate equivalent atoms:

#1 -x+1,y-1/2,-z+1/2 #2 -x,-y+1,-z+1 #3 x+1,-y+1/2,z+1/2

#4 x,-y+1/2,z-1/2 #5 x,-y+1/2,z+1/2 #6 x+1,y,z

ORTEP drawing of the X-ray crystallographic structure of **15**



The compound **14** (20 mg) was dissolved in HCl/MeOH (6 M, 5 mL) and stirred at rt for 2h then concentrated to give the deprotected **15** as its hydrochloride. The single crystal was prepared from its solution in methanol/acetonitrile (1:10) by slow evaporation of the solvent.

CCDC 2094460. For detailed crystallographic data, please refer to the Cambridge Crystallographic
Data Centre at http://ccdc.cam.ac.uk.

Table 1. Crystal data and structure refinement for mo_d8v21544_0m.

Identification code	mo_d8v21544_0m	
Empirical formula	C12 H15 Br Cl F N2 O	
Formula weight	337.62	
Temperature	213(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P 21	
Unit cell dimensions	a = 6.5060(4) Å	α= 90°.
	b = 4.7861(3) Å	β= 96.991(2)°.
	c = 21.3358(10) Å	γ = 90°.
Volume	659.42(7) $Å^3$	
Z	2	
Density (calculated)	1.700 Mg/m^3	
Absorption coefficient	3.321 mm^{-1}	
F(000)	340	
Crystal size	0.170 x 0.140 x 0.100 mm^3	
Theta range for data collection	2.886 to 25.995°.	
Index ranges	-8<=h<=8, -5<=k<=5, -26<=l<=25	
Reflections collected	6384	

Independent reflections	2446 [R(int) = 0.0301]
Completeness to theta = 25.242°	98.4 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.4967
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2446 / 1 / 172
Goodness-of-fit on F^2	0.998
Final R indices [I>2sigma(I)]	R1 = 0.0195, wR2 = 0.0487
R indices (all data)	R1 = 0.0205, wR2 = 0.0490
Absolute structure parameter	0.030(6)
Extinction coefficient	0.014(4)
Largest diff. peak and hole	0.244 and -0.219 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mo_d8v21544_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Br(1)	13631(1)	-147(1)	9460(1)	34(1)
Cl(1)	8696(1)	2172(1)	6530(1)	27(1)
F(1)	2956(3)	3616(4)	5316(1)	33(1)
O(1)	4009(3)	10159(5)	7246(1)	25(1)
N(1)	6396(4)	6742(5)	7454(1)	22(1)
N(2)	1618(4)	7010(5)	6391(1)	19(1)
C(1)	1112(4)	7408(8)	5690(1)	25(1)
C(2)	3046(5)	6529(7)	5420(2)	23(1)
C(3)	4783(4)	7151(7)	5933(1)	22(1)
C(4)	3871(4)	6284(6)	6534(1)	17(1)
C(5)	4772(4)	7902(6)	7122(1)	18(1)
C(6)	7527(5)	8136(7)	8000(1)	30(1)
C(7)	9008(5)	6118(6)	8360(1)	24(1)
C(8)	10869(5)	5439(7)	8141(1)	34(1)
C(9)	12226(5)	3552(7)	8456(1)	29(1)
C(10)	11738(5)	2359(7)	9004(1)	24(1)
C(11)	9905(5)	2972(7)	9237(1)	28(1)
C(12)	8537(4)	4812(9)	8910(1)	29(1)

Table 3. Bond lengths [Å] and angles [°] for mo_d8v21544_0m.

Br(1)-C(10)	1.900(3)
F(1)-C(2)	1.412(3)
O(1)-C(5)	1.231(4)
N(1)-C(5)	1.320(4)
N(1)-C(6)	1.461(4)
N(1)-H(1)	0.8700
N(2)-C(4)	1.501(3)
N(2)-C(1)	1.503(3)
N(2)-H(2B)	0.86(3)
N(2)-H(2A)	1.02(5)
C(1)-C(2)	1.507(4)
C(1)-H(1A)	0.9800
C(1)-H(1B)	0.9800
C(2)-C(3)	1.505(4)
C(2)-H(2)	0.9900
C(3)-C(4)	1.534(3)
C(3)-H(3A)	0.9800
C(3)-H(3B)	0.9800
C(4)-C(5)	1.529(4)
C(4)-H(4)	0.9900
C(6)-C(7)	1.507(4)
C(6)-H(6A)	0.9800
C(6)-H(6B)	0.9800
C(7)-C(8)	1.388(4)
C(7)-C(12)	1.396(4)
C(8)-C(9)	1.379(4)
C(8)-H(8)	0.9400
C(9)-C(10)	1.373(4)
C(9)-H(9)	0.9400
C(10)-C(11)	1.378(4)
C(11)-C(12)	1.379(5)
C(11)-H(11)	0.9400
C(12)-H(12)	0.9400
C(5)-N(1)-C(6)	121.9(2)
C(5)-N(1)-H(1)	119.1
C(6)-N(1)-H(1)	119.1
C(4)-N(2)-C(1)	108.8(2)
C(4)-N(2)-H(2B)	113(2)

C(1)-N(2)-H(2B)	108(2)
C(4)-N(2)-H(2A)	112(3)
C(1)-N(2)-H(2A)	108(2)
H(2B)-N(2)-H(2A)	108(3)
N(2)-C(1)-C(2)	104.7(2)
N(2)-C(1)-H(1A)	110.8
C(2)-C(1)-H(1A)	110.8
N(2)-C(1)-H(1B)	110.8
C(2)-C(1)-H(1B)	110.8
H(1A)-C(1)-H(1B)	108.9
F(1)-C(2)-C(3)	108.8(3)
F(1)-C(2)-C(1)	108.4(3)
C(3)-C(2)-C(1)	104.7(2)
F(1)-C(2)-H(2)	111.5
C(3)-C(2)-H(2)	111.5
C(1)-C(2)-H(2)	111.5
C(2)-C(3)-C(4)	102.9(2)
C(2)-C(3)-H(3A)	111.2
C(4)-C(3)-H(3A)	111.2
C(2)-C(3)-H(3B)	111.2
C(4)-C(3)-H(3B)	111.2
H(3A)-C(3)-H(3B)	109.1
N(2)-C(4)-C(5)	108.5(2)
N(2)-C(4)-C(3)	103.5(2)
C(5)-C(4)-C(3)	113.6(2)
N(2)-C(4)-H(4)	110.3
C(5)-C(4)-H(4)	110.3
C(3)-C(4)-H(4)	110.3
O(1)-C(5)-N(1)	124.8(3)
O(1)-C(5)-C(4)	119.8(3)
N(1)-C(5)-C(4)	115.4(2)
N(1)-C(6)-C(7)	110.0(2)
N(1)-C(6)-H(6A)	109.7
C(7)-C(6)-H(6A)	109.7
N(1)-C(6)-H(6B)	109.7
C(7)-C(6)-H(6B)	109.7
H(6A)-C(6)-H(6B)	108.2
C(8)-C(7)-C(12)	117.9(3)

C(8)-C(7)-C(6)	120.5(3)
C(12)-C(7)-C(6)	121.6(3)
C(9)-C(8)-C(7)	121.5(3)
C(9)-C(8)-H(8)	119.2
C(7)-C(8)-H(8)	119.2
C(10)-C(9)-C(8)	119.1(3)
C(10)-C(9)-H(9)	120.5
C(8)-C(9)-H(9)	120.5
C(9)-C(10)-C(11)	121.2(3)
C(9)-C(10)-Br(1)	119.7(2)
C(11)-C(10)-Br(1)	119.1(2)
C(10)-C(11)-C(12)	119.2(3)
C(10)-C(11)-H(11)	120.4
C(12)-C(11)-H(11)	120.4
C(11)-C(12)-C(7)	121.1(3)
C(11)-C(12)-H(12)	119.4
C(7)-C(12)-H(12)	119.4

Symmetry transformations used to generate equivalent atoms:

Table 4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for mo_d8v21544_0m. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ... + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
Br(1)	34(1)	32(1)	32(1)	-1(1)	-8(1)	9(1)
Cl(1)	20(1)	20(1)	42(1)	-3(1)	7(1)	0(1)
F(1)	37(1)	28(1)	32(1)	-12(1)	-2(1)	2(1)
O(1)	27(1)	19(1)	26(1)	-4(1)	-2(1)	7(1)
N(1)	28(1)	18(1)	20(1)	-4(1)	-5(1)	5(1)
N(2)	17(1)	19(1)	20(1)	-1(1)	2(1)	0(1)
C(1)	22(2)	32(2)	19(1)	-1(1)	-3(1)	3(2)
C(2)	26(2)	23(2)	21(1)	-1(1)	3(1)	-2(1)
C(3)	17(1)	28(2)	22(1)	-2(1)	4(1)	-1(1)
C(4)	15(2)	17(1)	18(1)	1(1)	-1(1)	2(1)
C(5)	21(2)	18(1)	16(1)	1(1)	5(1)	-4(1)
C(6)	35(2)	27(2)	25(2)	-4(1)	-9(1)	4(1)
C(7)	29(2)	22(1)	18(1)	-3(1)	-6(1)	1(1)

C(8)	33(2)	47(3)	21(1)	4(1)	3(1)	0(2)
C(9)	23(2)	41(2)	24(1)	-3(1)	4(1)	2(1)
C(10)	27(2)	22(2)	22(1)	-5(1)	-4(1)	2(1)
C(11)	32(2)	32(2)	22(1)	5(1)	6(1)	3(1)
C(12)	26(2)	34(1)	28(1)	3(2)	5(1)	7(2)

Table 5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for mo_d8v21544_0m.

	x	y	z	U(eq)
H(1)	6803	5101	7344	27
H(1A)	779	9366	5589	30
H(1B)	-68	6241	5524	30
H(2)	3212	7562	5027	28
H(3A)	5140	9141	5942	27
H(3B)	6019	6053	5878	27
H(4)	4041	4249	6606	20
H(6A)	6548	8844	8276	36
H(6B)	8298	9728	7858	36
H(8)	11211	6285	7770	40
H(9)	13469	3089	8297	35
H(11)	9590	2146	9613	34
H(12)	7266	5193	9060	35
H(2B)	1290(50)	8530(70)	6572(14)	19(8)
H(2A)	680(60)	5450(110)	6523(18)	73(14)

Table 6. Torsion angles [°] for mo_d8v21544_0m.

C(4)-N(2)-C(1)-C(2)	7.2(3)
N(2)-C(1)-C(2)-F(1)	86.9(3)
N(2)-C(1)-C(2)-C(3)	-29.1(3)
F(1)-C(2)-C(3)-C(4)	-76.2(3)
C(1)-C(2)-C(3)-C(4)	39.6(3)
C(1)-N(2)-C(4)-C(5)	137.8(3)
C(1)-N(2)-C(4)-C(3)	16.8(3)
C(2)-C(3)-C(4)-N(2)	-34.3(3)

C(2)-C(3)-C(4)-C(5)	-151.8(3)
C(6)-N(1)-C(5)-O(1)	-2.9(4)
C(6)-N(1)-C(5)-C(4)	175.2(3)
N(2)-C(4)-C(5)-O(1)	-28.1(3)
C(3)-C(4)-C(5)-O(1)	86.5(3)
N(2)-C(4)-C(5)-N(1)	153.7(2)
C(3)-C(4)-C(5)-N(1)	-91.7(3)
C(5)-N(1)-C(6)-C(7)	168.6(2)
N(1)-C(6)-C(7)-C(8)	77.6(4)
N(1)-C(6)-C(7)-C(12)	-100.4(3)
C(12)-C(7)-C(8)-C(9)	-0.4(5)
C(6)-C(7)-C(8)-C(9)	-178.6(3)
C(7)-C(8)-C(9)-C(10)	-1.2(5)
C(8)-C(9)-C(10)-C(11)	1.3(5)
C(8)-C(9)-C(10)-Br(1)	-177.9(2)
C(9)-C(10)-C(11)-C(12)	0.2(5)
Br(1)-C(10)-C(11)-C(12)	179.4(3)
C(10)-C(11)-C(12)-C(7)	-1.9(5)
C(8)-C(7)-C(12)-C(11)	2.0(5)
C(6)-C(7)-C(12)-C(11)	-179.9(3)

Symmetry transformations used to generate equivalent atoms:

Table 7. Hydrogen bonds for mo_d8v21544_0m [Å and °].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
N(2)-H(2A)...Cl(1)#1	1.02(5)	2.03(5)	3.034(3)	164(3)
N(2)-H(2B)...O(1)	0.86(3)	2.28(3)	2.708(3)	111(2)
N(2)-H(2B)...Cl(1)#2	0.86(3)	2.42(3)	3.153(3)	143(3)
C(4)-H(4)...O(1)#3	0.99	2.39	3.298(4)	152.3
C(3)-H(3B)...Cl(1)	0.98	2.80	3.605(3)	140.1
C(3)-H(3A)...Cl(1)#4	0.98	2.89	3.618(3)	132.3
C(1)-H(1A)...F(1)#4	0.98	2.59	3.338(4)	133.6
C(1)-H(1A)...Cl(1)#2	0.98	2.89	3.401(3)	113.7
N(1)-H(1)...Cl(1)	0.87	2.65	3.410(2)	146.6

Symmetry transformations used to generate equivalent atoms:

#1 x-1,y,z #2 x-1,y+1,z #3 x,y-1,z #4 x,y+1,z