Supplementary Information (SI) for Organic & Biomolecular Chemistry.

Supporting Information

Design, Synthesis, and Structural Analysis of an Inhibitor of the Gastric Proton Pump with a Diaza-tricyclic Skeleton

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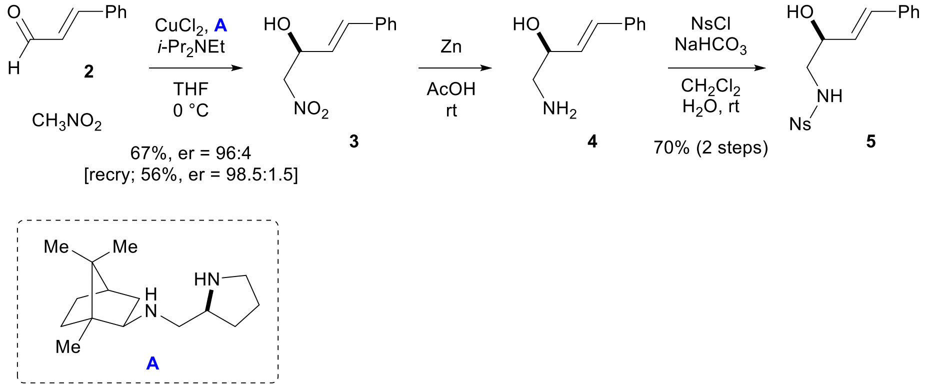
General Remarks: Nuclear magnetic resonance (NMR) spectra were determined on a JEOL-ECS400 or JEOL-ECZ400 instrument unless otherwise noted. Chemical shifts for ^{1}H NMR are reported in parts per million (ppm) using residual chloroform (7.26 ppm for $CDCl_3$). Coupling constants were reported as *J* values in hertz (Hz). The following abbreviations are used for spin multiplicity: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, m = multiplet, brs = broad singlet. Chemical shifts for ^{13}C NMR were reported in ppm using residual solvent as the internal standard (77.16 ppm for $CDCl_3$). High resolution mass spectra (HRMS) were obtained on a Bruker Daltonics compact in electrospray ionization (ESI) method, using ESI-L Low Concentration Tuning Mix (Agilent Technologies) as the internal standard. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 Fourier Transform Infrared Spectrophotometer and were reported in wavenumbers (cm^{-1}). Melting points (mp) were determined on a Yanaco Micro Melting Point Apparatus. Analytical thin layer chromatography (TLC) was performed on Merck precoated analytical plates, 0.25 mm thick, silica gel 60 F254. Preparative TLC separations were performed on Merck analytical plates (0.25 or 0.50 mm thick) precoated with silica gel 60 F254 unless otherwise noted. Flash chromatography separations were performed on KANTO CHEMICAL Silica Gel 60 (spherical, 40-100 mesh) unless otherwise noted. Reagents were commercial grades and were used without any purification. Dehydrated tetrahydrofuran and dichloromethane were purchased from FUJIFILM Wako Pure Chemical Co. *N*,*N*-dimethylformamide and toluene was purchased from FUJIFILM Wako Pure Chemical Co. and stored over activated MS4A. Dehydrated methanol and ethanol were also purchased from FUJIFILM Wako Pure Chemical Co. and stored over activated MS3A. All reactions sensitive to oxygen or moisture were conducted under an argon atmosphere. Reactions that require heating were conducted in an oil bath unless otherwise noted. Optical rotations were measured on a JASCO P-2200 Polarimeter at room temperature using the sodium D line. High pressure liquid chromatography (HPLC) was performed on a JASCO instrument using a DAICEL-CHIRALCEL-IG (4.6 x 250 mm) and DAICEL-CHIRALCEL-IC(4.6 x 250 mm). Racemic **3** was prepared according to the literature.[2] *N*-Methyl-2-nitrobenzanesulfonamide (**S1**) was prepared according to the literature.[3]

Experimental Procedure for Compounds

Compound 5



Ligand **A** (456 mg, 1.93 mmol), copper(II) chloride dihydrate (329 mg, 1.93 mmol), cinnamaldehyde (9.70 ml, 77.1 mmol), nitro methane (41.3 ml, 77.1 mmol), *N*,*N*-diisopropylethylamine (13.1 ml, 77.1 mmol), THF (385 ml), was transformed into compound **3** (10.0 g, 52.0 mmol, 67% yield, er =95.7 :4.3, yellow solid) according to the literature,[1] witch was recrystallized from *m*-xylene to give **3** (8.27g, 42.8 mmol, 56% yield, er =98.5 :1.5, yellow solid). The enantiomeric excess was determined by HPLC analysis with a DAICEL CHRALPAK IG (*n*-hexane:2-propanol = 7.0:3.0, 1.0ml/min at 40 °C, UV 235 nm). The retention times corresponding to **3** and its enantiomer were 6.9 and 7.6 min, respectively. The melting point was 81.4-83.2 °C.

To a stirred solution of **3** (193 mg, 1.00 mmol) in acetic acid (10.0 mL) was added zinc powder (654 mg, 10.0 mmol) portionwise at room temperature. After stirring for 16 h, the reaction mixture was filtered through a glass filter and washed with DCM. The filtrate was concentrated *in vacuo* until the volume was reduced to one-tenth. The resulting mixture was neutralized by 30% NaOH aqueous solution until the pH reached 10 and subsequently extracted with DCM. The combined organic phase was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo* to afford **4** (165 mg, white solid), which was directly used for the next steps without further purification. To a stirred solution of the solid and NsCl (244 mg, 1.10 mmol) in DCM (1.50 mL) was added saturated $NaHCO_3$ aqueous solution (1.50 mL) at 0 °C. After stirring at the same temperature for 30 min, the reaction mixture was partitioned between DCM and water and the organic phase was dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 4:1 to 1:1) to afford **5** (244 mg, 0.700 mmol, 70% yield, yellow oil).

$[\alpha]_D^{23} = -18°$ (*c* 1.8, $CHCl_3$)

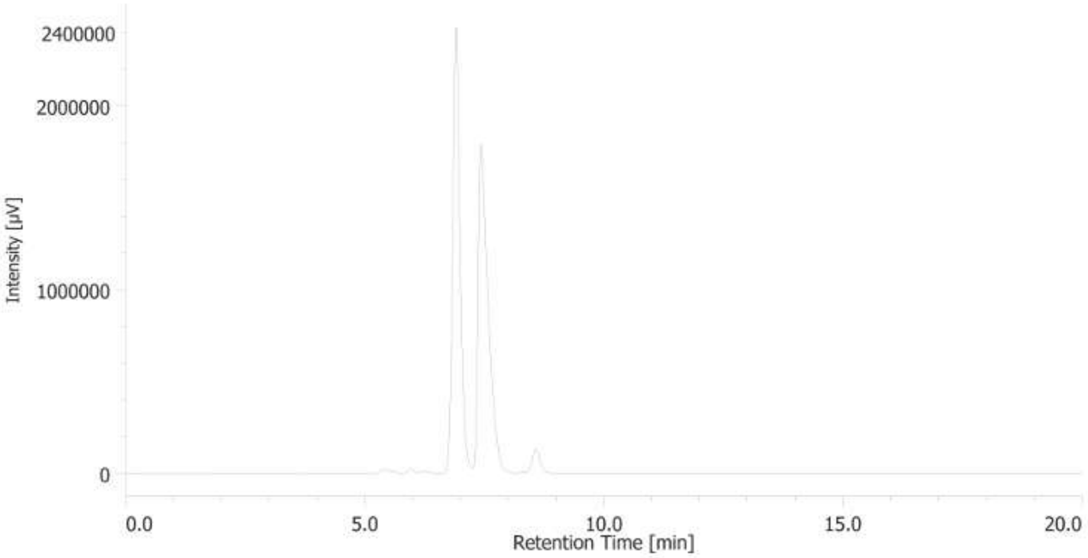
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.09 (m, 1H), 7.77 (m, 1H), 7.69-7.61 (m, 2H), 7.32-7.19 (m, 5H), 6.57 (d, *J* = 16.0 Hz, 1H), 6.06 (dd, *J* = 15.8, 6.2 Hz, 1H), 5.89 (m, 1H), 4.42 (dd, *J* = 9.2, 5.2 Hz, 1H), 3.36 (m, 1H), 3.13 (ddd, *J* = 12.9, 7.4, 5.5 Hz, 1H), 2.46 (brs, 1H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.0 (C), 136.0 (C), 133.7 (CH), 133.6 (C), 132.9 (CH), 132.6 (CH), 131.0 (CH), 128.7 (CH), 128.2 (CH), 127.8 (CH), 126.7 (CH), 125.5 (CH), 71.2 (CH), 49.1 (CH_2)

IR (film, cm^{-1}) 3525, 3345, 3026, 1539, 1361, 1166, 970, 751, 742, 587

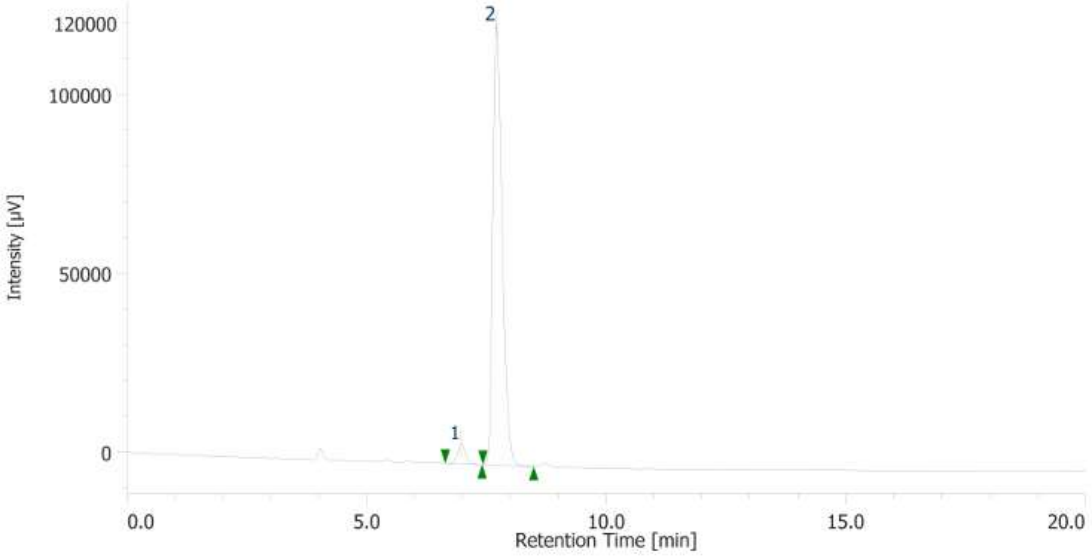
HRMS (ESI-QTOF) m/z: [M + Na]$^+$ Calcd for $C_{16}H_{16}N_2NaO_5S^+$ 371.0672; Found 371.0679

HPLC chart of 3 (racemic)



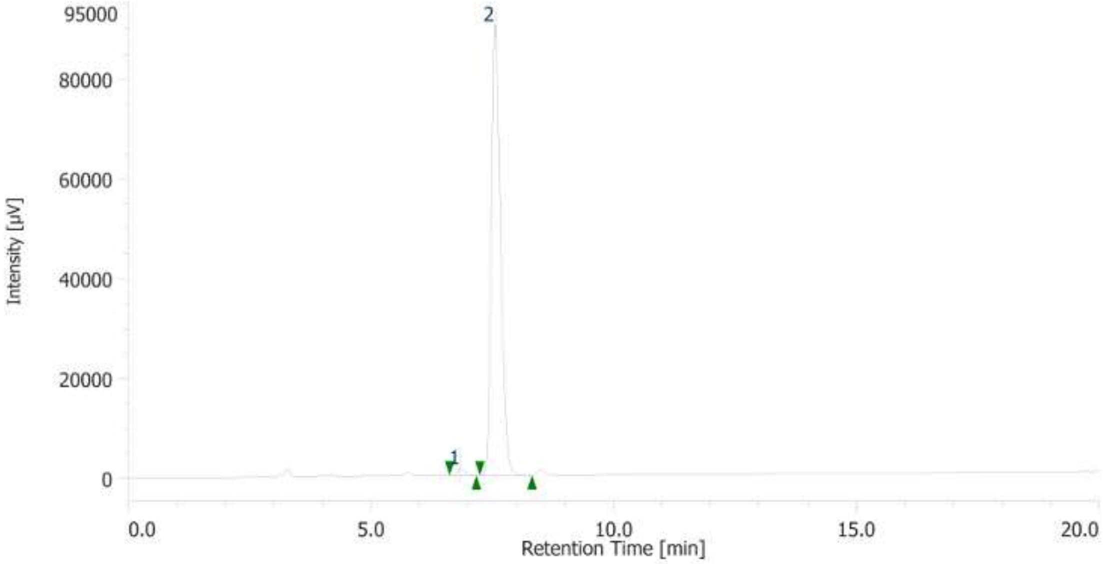
No.	tR (min)	Area (μV･sec)	Height (μV)	Area (%)
1	6.903	25095202	2410062	49.639
2	7.427	25459823	1764966	50.361

HPLC chart of 3 (before recrystallization)



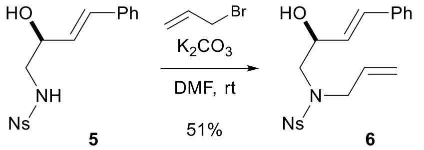
No.	tR (min)	Area (μV·sec)	Height (μV)	Area (%)
1	6.97	64164	5534	4.295
2	7.707	1674881	123323	95.705

HPLC chart of 3 (after recrystallization)



No.	tR (min)	Area (μV·sec)	Height (μV)	Area (%)
1	6.847	15944	1360	1.316
2	7.557	1195529	90292	98.684

Compound 6



To a stirred solution of **5** (205 mg, 0.588 mmol) and K_2CO_3 (122 mg , 0.882 mmol) in DMF (1.50 mL) was added allyl bromide (0.124 mL, 1.47 mmol) at room temperature. After stirring for 3 h, the reaction mixture was quenched with water and extracted with DCM. The organic phase was washed with brine and dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 3:2) to afford **6** (117 mg, 0.300 mmol, 51%, yellow oil).

$[\alpha]_D^{23}$ = +6.3° (*c* 1.8, $CHCl_3$)

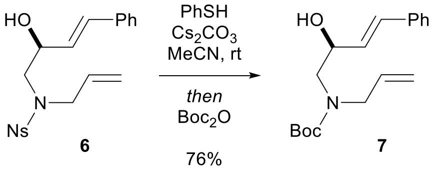
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.11-8.06 (m, 1H), 7.70-7.64 (m, 2H), 7.63-7.58 (m, 1H), 7.36-7.29 (m, 4H), 7.27-7.23 (m, 1H), 6.64 (d, *J* =16.0 Hz, 1H), 6.11 (dd, *J* = 15.8, 6.18 Hz, 1H), 5.75 (dddd, *J* = 17.0, 10.4, 6.4, 6.4 Hz, 1H), 5.25 (ddd, *J* = 18.3, 13.3, 0.91 Hz, 2H), 4.54 (quin, *J* = 5.49 Hz, 1H), 4.15 (dd, *J* = 16.0, 6.4 Hz, 1H), 4.07 (dd, *J* = 16.0, 6.4 Hz, 1H), 3.48 (d, *J* = 6.4 Hz, 2H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 148.0 (C), 136.3 (C), 133.8 (CH), 133.4 (C), 132.5 (CH), 132.0 (CH), 131.9 (CH), 131.1 (CH), 128.7 (CH), 128.5 (CH), 128.0 (CH), 126.7 (CH), 124.3 (CH), 119.8 (CH_2), 70.8 (CH), 52.5 (CH_2), 51.4 (CH_2)

IR (film, cm^{-1}) 3544, 2036, 1541, 1348, 1160, 970, 933, 778, 750, 580

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{20}N_2NaO_5S^+$ 411.0985; Found 411.0987

Compound 7



To a stirred solution of **6** (1.36 g, 3.52 mmol) in MeCN (49.0 mL) were added Cs_2CO_3 (1.72g, 5.28 mmol) and PhSH (0.565 mL, 5.28 mmol) at room temperature. After stirring for 3 h, Boc_2O (1.53 g, 7.00 mmol) was added at the same temperature. After stirring for 30 min, the reaction was quenched with water at the same temperature. Then, the mixture was extracted twice with EtOAc and the combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc =

10:1 to 1:1) to afford **7** (808 mg, 2.66 mmol, 76% yield, yellow oil).

$[\alpha]_D^{24}$ = +4.3° (*c* 0.32, $CHCl_3$)

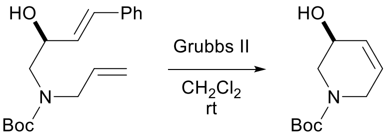
^{1}H NMR ($CDCl_3$, 400 MHz, mixture of rotamers) δ 7.37 (d, *J* = 7.8 Hz, 2H), 7.31 (t, *J* = 7.8 Hz, 2H), 7.26-7.20 (m, 1H), 6.67 (d, *J* = 15.1 Hz, 1H), 6.18 (dd, *J* = 16.0, 6.0 Hz, 1H), 5.79 (m, 1H), 5.16 (s, 1H), 5.12 (d, *J* = 8.2 Hz, 1H), 4.51 (brs, 1H), 3.86 (m, 2H), 3.37 (m, 2H), 1.46 (s, 9H)

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of rotamers) δ 157.7 (C), 155.5 (C), 136.8 (C), 136.7(C), 133.9 (CH), 131.4 (CH), 130.9 (CH), 129.8 (CH), 128.6 (CH), 128.5 (CH), 127.8 (CH), 127.7 (CH), 126.6 (CH), 116.6 (CH_2), 80.6 (C), 72.6 (CH), 72.1 (CH), 53.8 (CH_2), 53.0 (CH_2), 51.9 (CH_2), 50.9 (CH_2), 28.4 (CH_3)

IR (film, cm^{-1}) 3424, 2981, 2928, 1670, 1462, 1413, 1256, 1161, 967, 744

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{18}H_{25}NNaO_3^+$ 326.1727; Found 326.1742

Compound 8a



7 84% **8a**

A solution of **7** (808 mg, 2.66 mmol) in DCM (270 mL) was carefully degassed by Ar bubbling. To the degassed solution was added Grubbs second generation catalyst (137 mg, 0.160 mmol) at room temperature. After stirring for 15 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 1:1) to afford **8a** (453 mg, 2.30 mmol, 84% yield, brown oil).

$[\alpha]_D^{23}$ = +40° (*c* 1.8, $CHCl_3$)

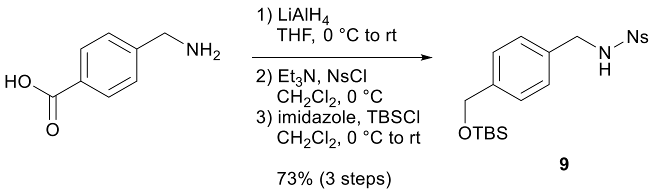
^{1}H NMR ($CDCl_3$, 400 MHz, mixture of rotamers) δ 5.89-5.76 (dd, *J* = 10.1, 2.3 Hz, 1H), 5.79 (brs, 1H), 4.18 (brs, 1H), 3.90 (d, *J* = 18.3 Hz, 1H), 3.80 (dd, *J* = 17.8, 1.8 Hz, 1H), 3.63 (brs, 1H), 3.39 (brs, 1H), [2.72 (brs), 2.35 (brs), *all sum to* 1H], 1.44 (s, 9H)

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of rotamers) δ 157.2 (C), 128.6 (CH), 128.5 (CH), 127.5(CH), 126.7 (CH), 80.2 (C), 63.7 (CH), 48.2 (CH_2), 47.0 (CH_2), 43.6 (CH_2), 43.0 (CH_2), 28.5 (CH_3)

IR (film, cm^{-1}) 3420, 2978, 2925, 1702, 1646, 1417, 1361, 1234, 1164, 1063

HRMS (ESI-QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{18}NO_3^+$ 220.1281; Found 220.1291

Compound 9



9

To a solution of *p*-(aminomethyl)benzoic acid (5.00 g, 33.0 mmol) in THF (50.0 mL) was added lithium aluminum hydride (5.01 g, 0.132 mol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. To the resulting mixture were successively added water (5.00 mL), 15% aqueous NaOH (7.50 mL), and water (15.0 mL) at 0 °C. The solution was filtered through a glass filter with EtOAc. The filtrate was concentrated *in vacuo.* To the residue in DCM (30.0 mL) were added triethylamine (3.65 mL, 26.2 mmol) and NsCl (4.88 g, 22.0 mmol) at 0 °C. After stirring for 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$. Then, the mixture was extracted teice with EtOAc and the combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*. The residue was dissolved in DCM (30.0 ml) and to this residue were added imidazole (1.78 g, 26.2 mmol) and TBSCl (3.32 g, 22.0 mmol) at 0 °C. After stirring for 5 h, the reaction was quenched with saturated aqueous $NaHCO_3$. Then, the mixture was extracted twice with EtOAc and the combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 6:1) to afford **9** (10.5 g, 24.0 mmol, 73% yield, white solid).

Melting point 71.5-72.5 °C

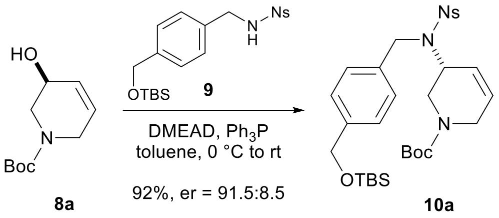
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.00 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.81 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.67 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 7.63 (ddd, *J* = 7.6, 7.6, 1.8 Hz, 1H), 7.27-7.12 (m, 4H), 5.70 (brs, 1H), 4.66 (s, 2H), 4.30 (d, *J* = 6.4 Hz, 2H), 0.93 (s, 9H), 0.08 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 147.9 (C), 141.6 (C), 134.3 (C), 134.1 (C), 133.5 (CH), 132.8 (CH), 131.2 (CH), 127.9 (CH), 126.4 (CH), 125.3 (CH), 64.6 (CH_2), 47.8 (CH_2), 26.0 (CH_3), 18.5 (C), −5.2 (CH_3)

IR (film, cm^{-1}) 3360, 2957, 2858, 1540, 1360, 1256, 1161, 843, 673, 585

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{28}N_2NaO_5SSi^+$ 459.1380; Found 459.1397

Compound 10a



To a stirred solution of **8a** (1.26 g, 6.35 mmol) in toluene (64.0 mL) were added **9** (3.05 g, 6.98 mmol) and triphenylphosphine (2.00 g, 7.62 mmol) at 0 °C, then bis(2-methoxyethyl) azodicarboxylate (1.78 g, 7.62 mmol) was added portionwise to the reaction mixture at same temperature over 30 min. The resulting mixture was allowed to warm up to room temperature. After stirring for 5 h, the resulting mixture was diluted with EtOAc and water. The aqueous phase was extracted twice with EtOAc. The combined organic phases were washed with brine, and dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 6:1) to afford **10a** (3.61 g, 5.84 mmol, 92% yield, brown oil). The enantiomeric excess was determined by HPLC analysis with a DAICEL CHRALPAK IC (*n*-hexane:2-propanol = 8.0:3.0, 1.0ml/min at 40 °C, UV 235 nm). The retention times corresponding to **10a** and its enantiomer were 12.9 and 14.9 min, respectively.

$[\alpha]_D^{22}$ = −27° (*c* 0.6, $CHCl_3$)

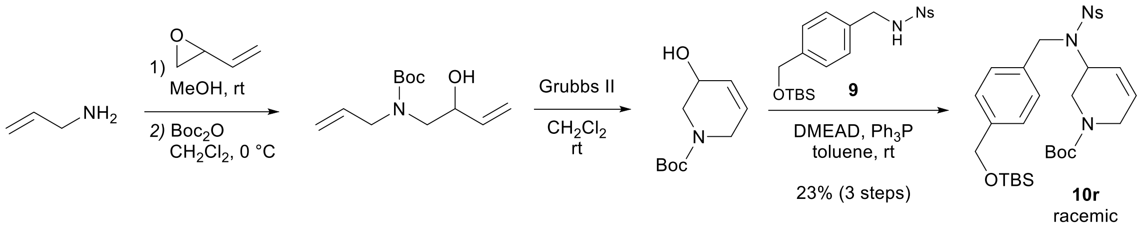
^{1}H NMR ($CDCl_3$, 400 MHz, mixture of rotamers) δ [8.00 (d, *J* = 7.3 Hz), 7.81 (d, *J* = 7.3 Hz), *all sum to* 1H], 7.70-7.50 (m, 3H), 7.43-7.00 (m, 4H), [5.94 (brs), 5.78 (brs), 5.70 (m), *all sum to* 2H], 4.65 (brs, 1H), [4.65 (s), 4.61 (s), *all sum to* 2H], 4.54 (d, *J* = 15.6 Hz, 1H), 4.44 (d, *J* = 15.6 Hz, 1H), [4.29 (d, *J* = 6.4 Hz), 3.90-3.64 (m), 3.61-3.48 (m), *all sum to* 4H], 1.46 (s, 9H), 0.92 (s, 9H), 0.07 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of rotamers) δ 154.5 (C), 147.9 (C), 147.5 (C), 141.6 (C), 141.0 (C), 135.4 (C), 134.6 (C), 134.4 (C), 134.1 (C), 133.5 (CH), 133.1 (CH), 132.9 (CH), 131.6 (CH), 131.4 (CH), 131.2 (CH), 125.0 (CH), 124.1 (CH), 130.5 (CH), 128.4 (CH), 127.9 (CH), 126.4 (CH), 126.0 (CH), 125.0 (CH), 80.5 (C), 64.7 (CH_2), 64.6 (CH_2), 52.9 (CH), 48.5 (CH_2), 42.6 (CH_2), 47.8 (CH_2), 46.7 (CH_2), 28.5 (CH_3), 26.1 (CH_3), 18.5 (C), −5.1 (CH_3)

IR (film, cm^{-1}) 2932, 2854, 1695, 1543, 1362, 1245, 1165, 836, 776, 588

HRMS (ESI-QTOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{44}N_3O_7SSi^+$ 618.2664; Found 618.2693

Compound 10r

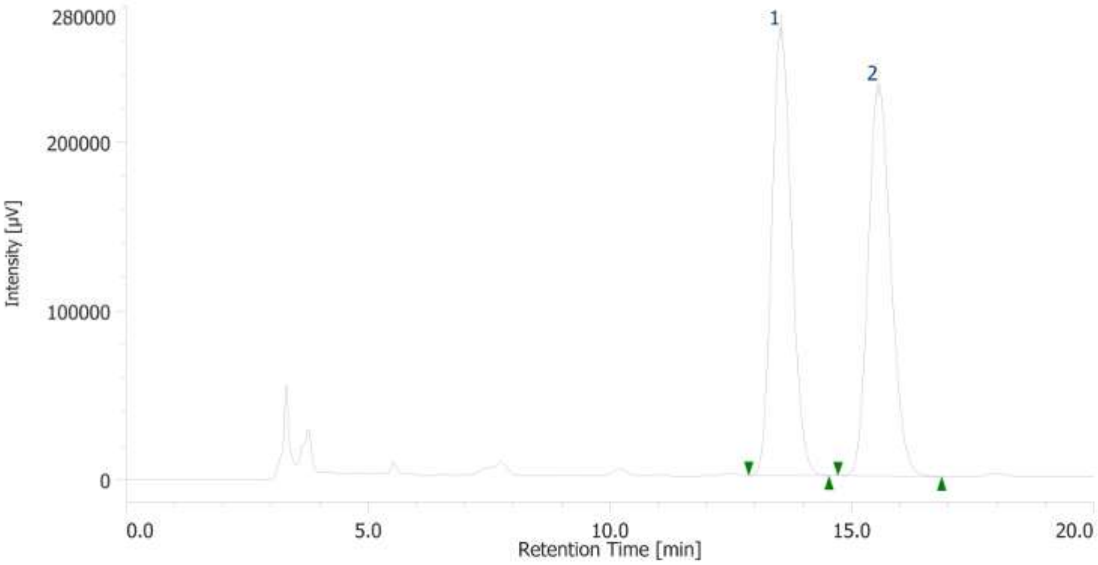


To a stirred solution of allylamine (0.750 mL, 10.0 mmol) in MeOH (1.00 mL) was added 1,3-butadiene monoepoxide (0.805 mL, 10.0 mmol) at room temperature. After stirring for 16 h, the reaction mixture was concentrated *in vacuo.* The residue was dissolved in DCM (2.00 mL), and to this solution was added Boc$_2$O (2.18 g, 10.0 mmol) at 0 °C. After stirring for 1 h, the reaction was quenched with saturated aqueous NaHCO$_3$ at same temperature. Then, the mixture was extracted twice with DCM and the combined organic phases were dried over Na$_2$SO$_4$. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 3:1) to give crude mixture as a brown oil.

The brown oil was dissolved in DCM (240 mL) and the resulting solution was carefully degassed by Ar bubbling. To the degassed solution was added Grubbs second generation catalyst (101 mg, 0.110 mmol) at room temperature. After stirring for 15 h, the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 2:1 to 1:1) to give crude mixture as a brown oil.

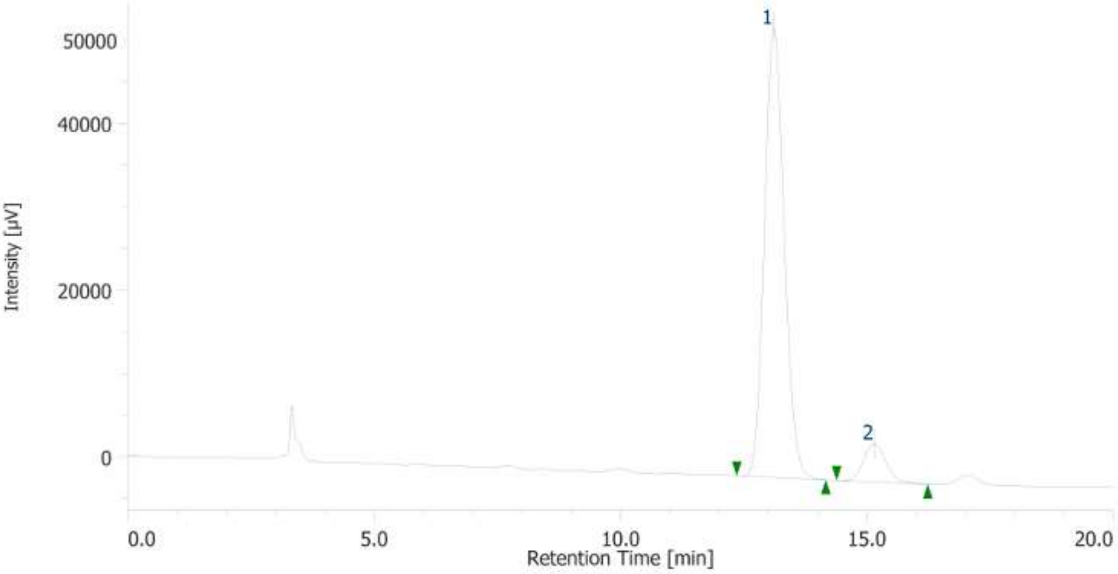
The brown oil was dissolved in toluene (21.0 mL) and to this solution were added **9** (1.00 g, 2.30 mmol) and triphenylphosphine (656 mg, 2.51 mmol) at 0 °C. Bis(2-methoxyethyl) azodicarboxylate (586 mg, 2.52 mmol) was then added portionwise to the reaction mixture at the same temperature over 30 min. The resulting mixture was allowed to warm up to room temperature. After stirring for 5 h, the resulting mixture was diluted with EtOAc and water. The aqueous phase was extracted twice with EtOAc. The combined organic phases were washed with brine, and dried over Na$_2$SO$_4$. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 6:1) to afford **10r** (1.45 g, 2.35 mmol, 23% yield, brown oil). The enantiomeric excess was determined by HPLC analysis with a DAICEL CHRALPAK IC (*n*-hexane:2-propanol = 8.0:3.0, 1.0ml/min at 40 °C, UV 235 nm). The retention times corresponding to each enantiomer were 13.5 and 15.6 min, respectively.

HPLC chart of 10r (racemic)



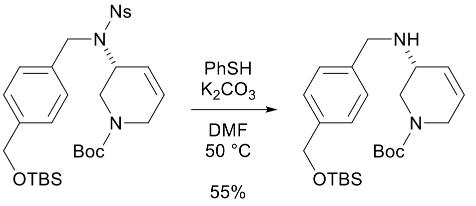
No.	tR (min)	Area (μV·sec)	Height (μV)	Area (%)
1	13.533	7558848	265219	49.958
2	15.553	7571662	231997	50.042

HPLC chart of (–)-10a



No.	tR (min)	Area (μV·sec)	Height (μV)	Area (%)
1	13.11	1502875	53984	91.147
2	15.15	145980	4574	8.853

Compound 11a



10a **11a**

To a stirred solution of **10a** (2.50 g, 3.69 mmol) in DMF (8.00 mL) were added K_2CO_3 (765 mg, 5.54 mmol) and PhSH (0.414 mL, 4.06 mmol) at room temperature. The reaction mixture was stirred at 50 °C for 2.5 h. The reaction was quenched with water. After the mixture was extracted twice with EtOAc, the combined organic phases were washed with brine and dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 6:1) to afford **11a** (873 mg, 2.02 mmol, 55% yield, yellow oil).

$[\alpha]_D^{23} = -40°$ (*c* 2.4, $CHCl_3$)

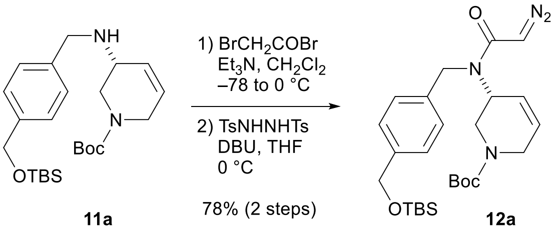
^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.33-7.26 (m, 4H), 5.88-5.84 (m, 1H), 5.74 (brs, 1H), 4.72 (s, 2H), 4.02-3.77 (m, 4H), 3.68-3.39 (m, 2H), 3.25 (brs, 1H), 1.48 (s, 9H), 0.93 (s, 9H), 0.09 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 155.2 (C), 140.3 (C), 138.9 (C), 128.8 (CH), 128.2 (CH), 128.1 (CH), 126.3 (CH), 125.7 (CH), 79.9 (C), 64.9 (CH_2), 51.2 (CH), 50.8 (CH_2), 43.9 (CH_2), 43.3 (CH_2), 28.6 (CH_3), 26.1 (CH_3), 18.5 (C), −5.1 (CH_3)

IR (film, cm^{-1}) 2931, 2854, 1698, 1420, 1364, 1245, 1172, 1091, 837, 770

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{40}N_2NaO_3Si^+$ 455.2700; Found 455.2703

Compound 12a



11a **12a**

To a stirred solution of **11a** (349 mg, 0.807 mmol) in DCM (8.00 mL) were added triethylamine (0.123 mL, 0.887 mmol) and bromoacetyl bromide (77.2 µL, 0.887 mmol) at –78 °C. After stirring for 30 min, the reaction mixture was warmed to 0 °C. After stirring for 1 h at 0 °C, the reaction was quenched with water and the resulting mixture was extracted twice with EtOAc. The combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*. To the residue in THF (8.00 mL) were added 1,8-diazabicyclo[5.4.0]-7-undecene (0.601 mL, 4.04 mmol) and TsNHNHTs (274 mg, 0.807 mmol) at 0 °C. After stirring for 1 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted twice with Et_2O. The combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to 6:1) to afford **12a** (313 mg, 0.628 mmol, 78% yield, yellow oil).

$[\alpha]_D^{23} = -61°$ (*c* 1.8, $CHCl_3$)

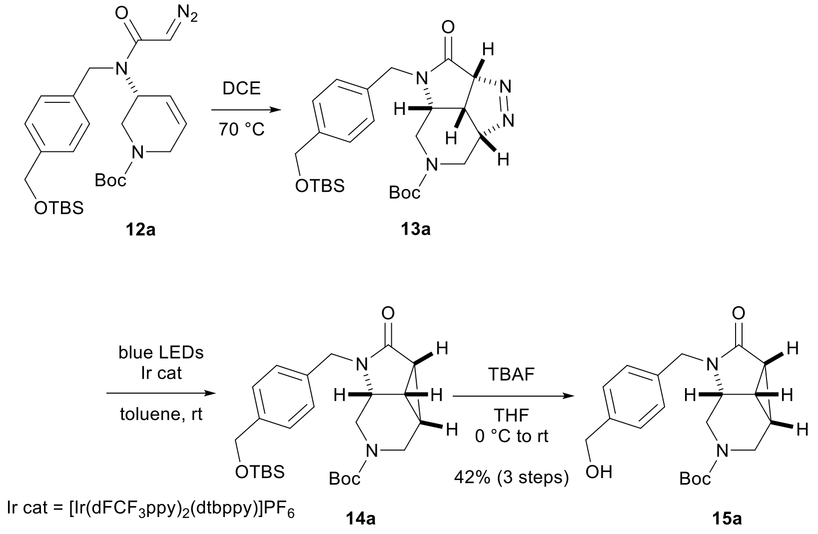
^{1}H NMR ($CDCl_3$, 400 MHz, mixture of rotamers) δ 7.35-7.05 (m, 4H), [5.69 (d, *J* = 10.0 Hz), 5.63 (d, *J* = 9.2 Hz), *all sum to* 1H], [5.18 (d, *J* = 15.2 Hz), 5.08 (d, *J* = 14.4 Hz), *all sum to* 1H], 4.72 (s, 2H), 4.68 (m, 1H), [4.06-3.74 (m), 3.44 (d, *J* = 14.8 Hz), 3.42 (d, *J* = 14.8 Hz), *all sum to* 1H], 3.40 (m, 1H), 6.00-2.64 (multiplets and broadening peaks, all sum to 5H), [1.45 (s), 1.42 (s), *all sum to* 9H], 0.94 (s, 9H), 0.10 (s, 6H)

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of rotamers) δ 167.1 (C), 154.8 (C), 154.6 (C), 141.3 (C), 140.7 (C), 136.8 (C), 133.9 (C), 128.6 (CH), 126.7 (CH), 126.6 (CH), 126.0 (CH), 98.2 (CH), 87.5 (CH), 81.1 (C), 80.2 (C), 64.7 (CH_2), 51.2 (CH), 47.9 (CH_2), 47.5 (CH_2), 43.9 (CH_2), 42.7 (CH_2), 41.6 (CH_2), 28.5 (CH_3), 28.3 (CH_3), 26.6 (CH), 26.1 (CH_3), 18.5 (CH_3), –5.2 (CH_3)

IR (film, cm^{-1}) 2930, 2856, 2107, 1695, 1417, 1246, 1166, 1119, 1092, 839, 777

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{26}H_{40}N_4NaO_4Si^+$ 523.2711; Found 523.2705

Compound 15a



Compound **12a** (0.11 g, 0.22 mmol) was dissolved in 1,2-dichloroethane (11 mL) at room temperature. After heating at 70 °C for 2 h, the resulting mixture was concentrated *in vacuo*.

The residue was dissolved in toluene (11 mL), and the residue was carefully degassed by successive freeze-thaw cycles. After the addition of [Ir(dFCF$_3$ppy)$_2$(dtbppy)]PF$_6$ (7.4 mg, 6.6 μmol), the resulting solution was irradiated with LED (365 nm) at room temperature for 4 h. The resulting mixture was concentrated under reduced pressure, and the residue was used for the next step without further purification.

The residue was dissolved in THF (1.1 mL), and to this solution were added TBAF (1.0 M solution in THF, 0.44 mL, 0.44 mmol) at 0 °C. After stirring for 1 h at the same temperature, the reaction was quenched with aqueous NH$_4$Cl and the resulting mixture was extracted twice with EtOAc. The combined organic phases were dried over Na$_2$SO$_4$. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 1:1 to EtOAc:MeOH=9:1) to afford **15a** (32 mg, 0.092 mmol, 42% yield, yellow oil).

$[\alpha]_D^{22}$ = −18° (*c* 0.26, CHCl$_3$)

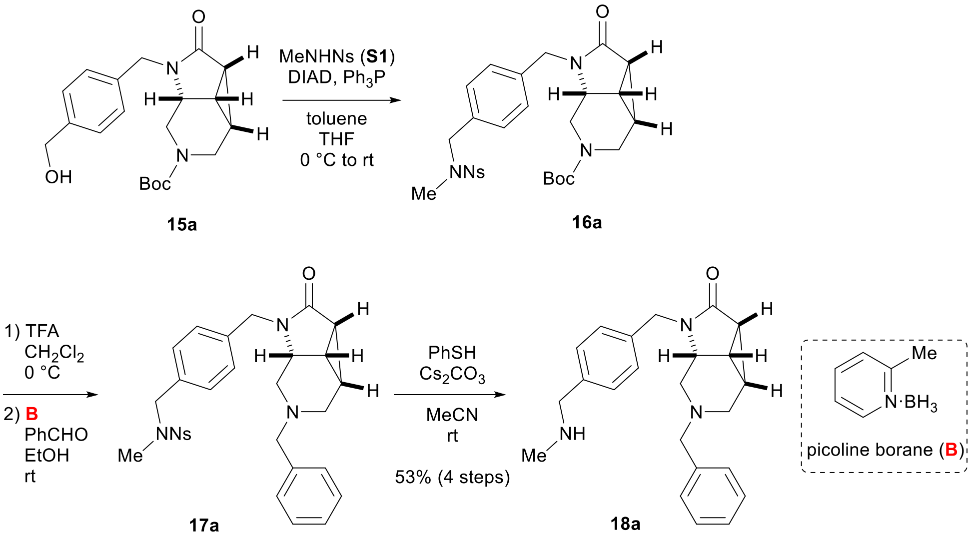
^{1}H NMR (CDCl$_3$, 400 MHz, mixture of rotamers) δ 7.39-7.32 (m, 2H), 7.27-7.18 (m, 2H), [4.94 (d, *J* = 15.1 Hz), 4.92 (d, *J* = 15.6 Hz), 3.59 (d, *J* = 15.6 Hz), *all sum to* 2H], 4.68 (s, 2H), [4.00 (dd, *J* = 13.7, 2.3 Hz), 3.74-3.69 (m), 2.96 (d, *J* = 12.8 Hz), 2.82 (d, *J* = 13.7 Hz), *all sum to* 2H], [3.87 (dd, *J* = 14.6 Hz), 3.70-3.66 (m), 3.32 (dd, *J* = 14.4, 2.1 Hz), *all sum to* 2H], 2.30 (brs, 1H), 2.22-2.04 (m, 2H), [1.66 (m) , 1.52 (m), *all sum to* 1H], 1.47 (s, 9H)

^{13}C NMR (CDCl$_3$, 100 MHz, mixture of rotamers) δ 172.4 & 172.3 (C), 155.4 & 155.0 (C), 140.8 & 140.6 (C), 135.3 (C), 128.7 & 128.5 (CH), 127.5 (CH), 80.5 & 80.3 (C), 65.0 (CH$_2$), 50.4 (CH), 43.2 (CH), 40.1 & 39.4 (CH$_2$), 38.1 & 36.6 (CH$_2$), 28.6 & 28.5 (CH$_3$), 25.4 (CH), 19.0 & 18.1 (CH), 16.7 & 16.6 (CH)

IR (film, cm^{-1}) 3410, 2929, 1685, 1415, 1362, 1249, 1168, 1122, 1017, 752

HRMS (ESI-QTOF) m/z: [M + Na]$^+$ Calcd for $C_{20}H_{26}N_2NaO_4^+$ 381.1785; Found 381.1783

Compound 18a



To a solution of **15a** (30 mg, 0.084 mmol) and triphenylphosphine (33 mg, 0.13 mmol) and NsNHMe (27 mg, 0.13 mmol) in toluene (3.5 mL) and tetrahydrofuran (0.50 mL) was added a solution of DIAD (25 µL, 0.13 mmol) in toluene (2.0 mL) at 0 °C. After stirring for 16 h at room temperature, the reaction mixture was concentrated *in vacuo*, and the residue was purified by preparative TLC (EtOAc only) to give containing **16a** and impurities as a yellow oil.

The yellow oil was dissolved in DCM (0.80 mL) and to the resulting solution was added TFA (0.20 mL) at 0 °C. After stirring for 1.5 h, the reaction was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted twice with DCM. The combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was used for the next step without further purification.

To a stirred solution of the residue in EtOH (1.0 mL) were added benzaldehyde (43 µL, 0.42 mmol) and 2-picoline borane (**B**, 11 mg, 0.10 mmol) at room temperature. After stirring for 16 h at the same temperature, the reaction was quenched with saturated aqueous $NaHCO_3$ and the resulting mixture was extracted twice with DCM. The combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by preparative TLC (EtOAc:MeOH = 30:1) to give crude mixture as a yellow oil.

The resulting crude mixture was dissolved in MeCN (2.0 mL) and to the resulting solution were added Cs_5CO_3 (41 mg, 0.13 mmol) and PhSH (13 µL, 0.13 mmol) at room temperature. After stirring for 5 h, the reaction was quenched with water and the resulting mixture was extracted twice with EtOAc. The mixture was washed with saturated aqueous K_2CO_3 and the combined organic phases were dried over Na_2SO_4. After filtration, the filtrate was concentrated *in vacuo*, and the residue was purified by preparative TLC (NH_2 SiO_2, EtOAc:MeOH = 9:1) to afford **18a** (16 mg, 44 µmol, 53% yield, yellow oil).

$[\alpha]_D^{22}$ = +36° (*c* 0.28, CHCl$_3$)

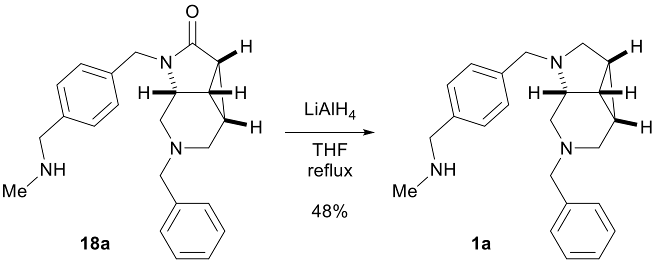
^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.51-7.49 (m, 2H), 7.37-7.21 (m, 3H), 7.19 (d, *J* = 7.8 Hz, 2H), 6.88 (d, *J* = 7.8 Hz, 2H), 4.82 (d, *J* = 13.7 Hz, 2H), 3.70 (dd, *J* = 18.5, 18.5 Hz, 2H), 3.62 (d, *J* = 12.8 Hz, 1H), 3.51 (dd, *J* = 7.3, 2.7 Hz, 1H), 3.38 (d, *J* = 8.7 Hz, 1H), 3.35 (d, *J* = 9.6 Hz, 1H), 2.95 (d, *J* = 15.6 Hz, 1H), 2.67 (dd, *J* = 11.9, 4.1 Hz, 1H), 2.57 (dd, *J* = 11.9, 3.2 Hz, 1H), 2.44 (s, 3H), 2.14 (dd, *J* = 14.6, 7.3 Hz, 1H), 2.00 (dd, *J* = 7.6, 7.6 Hz 1H), 1.91 (d, *J* = 12.4 Hz,1H), 1.45 (ddd, *J* = 7.8, 7.8, 4.6 Hz, 1H)

^{13}C NMR (CDCl$_3$, 100 MHz) δ 174.3 (C), 138.7 (C), 138.0 (C), 135.2 (C), 129.8 (CH), 129.2 (CH), 128.5 (CH), 128.4 (CH), 127.6 (CH), 62.4 (CH$_2$), 55.6 (CH$_2$), 51.3 (CH), 49.8 (CH), 48.3 (CH), 44.3 (CH$_2$), 35.9 (CH$_3$), 26.0 (CH), 20.8 (CH), 19.4 (CH)

IR (film, cm^{-1}) 3732, 3052, 2925, 2799, 1681, 1509, 1436, 1241, 740, 691

HRMS (ESI-QTOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{28}N_3O^+$ 362.2227; Found 362.2235

Compound 1a



To a solution of **18a** (19 mg, 51 µmol) in THF (1.0 mL) was added lithium aluminum hydride (5.8 mg, 0.15 mmol) at 0 °C. The reaction mixture was warmed to room temperature and then heated at reflux for 16 h. After the reaction mixture was cooled at 0 °C, water (10 µl), 15% aqueous NaOH (10 µl), and water (10 µl) were successively added. The resulting suspension was filtered through a glass filter with EtOAc. The filtrate was concentrated *in vacuo*, and the residue was purified by preparative TLC (NH$_2$ SiO$_2$, EtOAc:MeOH = 9:1) to afford **1a** (8.5 mg, 24 µmol, 48% yield, yellow oil).

$[\alpha]_D^{24}$ = +30° (*c* 0.28, CHCl$_3$)

^{1}H NMR (CDCl$_3$, 400 MHz) δ 7.38-7.26 (m, 5H), 7.19 (d, *J* = 7.8 Hz, 2H), 7.08 (d, *J* = 7.8 Hz, 2H), 3.70 (s, 2H), 3.61 (d, *J* = 12.8 Hz, 1H), 3.53 (d, *J* = 13.2 Hz, 1H), 3.36 (ddd, *J* = 11.1, 11.1, 11.1 Hz, 2H), 3.29-3.11 (m, 4H), 2.78 (dd, *J* = 11.9, 2.8 Hz, 2H), 2.50 (dd, *J* = 11.5, 4.1 Hz, 1H), 2.45 (s, 3H), 1.97 (ddd, *J* = 7.6, 7.6, 7.6 Hz, 1H), 1.82 (d, *J* =11.9 Hz, 1H), 1.63 (dddd, *J* = 7.6, 7.6, 7.6, 2.3 Hz, 1H), 1.83-1.59 (m, 1H), 1.05 (ddd, *J* =7.8, 7.8, 3.7 Hz, 1H)

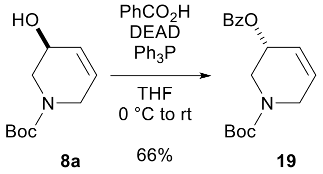
^{13}C NMR (CDCl$_3$, 100 MHz) δ 138.9 (C), 138.6 (C), 138.5 (C), 129.8 (CH), 128.8 (CH), 128.3 (CH), 128.1 (CH), 127.3 (CH), 64.0 (CH$_2$), 56.1 (CH$_2$), 55.7 (CH), 53.7 (CH$_2$), 53.5 (CH$_2$), 52.4 (CH$_2$), 50.4 (CH$_2$), 36.3

(CH_3), 22.3 (CH), 21.3 (CH), 19.2 (CH)

IR (film, cm^{-1}) 3729, 3027, 2881, 2794, 1510, 1455, 1374, 1154, 698, 670

HRMS (ESI-QTOF) m/z: [M + H]$^+$ Calcd for $C_{23}H_{30}N_3^+$ 348.2434; Found 348.2430

Compound 19



To a stirred solution of **8a** (19.9 mg, 0.100 mmol) in THF (0.700 mL) were added benzoic acid (14.2 mg, 0.150 mmol) and triphenylphosphine (39.3 mg, 0.150 mmol) at 0 °C. Diethyl azodicarboxylate 40 % in toluene (68.0 µL, 0.150 mmol) was then added dropwise to the reaction mixture at the same temperature over 30 min. The resulting mixture was allowed to warm up to room temperature. After stirring for 16 h, the reaction was quenched with MeOH. The resulting mixture was concentrated *in vacuo*, and the residue was purified by preparative TLC (*n*-hexane:EtOAc = 1:1) to afford **19** (20.0 mg, 66.0 µmol, 66% yield, brown oil).

$[\alpha]_D^{23} = -121°$ (*c* 1.1, $CHCl_3$)

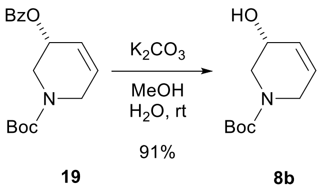
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.04 (d, *J* = 7.8 Hz, 2H), 7.59-7.51 (m, 1H), 7.46-7.40 (m, 2H), 6.12-5.83 (m, 2H), 5.39 (brs, 1H), 4.54-3.38 (m, 4H) 1.54-1.45 (m, 9H)

^{13}C NMR ($CDCl_3$, 100 MHz, mixture of rotamers) δ 166.2 (C), 154.9 (C), 133.2 (CH), 131.3 (CH), 130.2 (C), 129.9 (CH), 128.4 (CH), 123.7 (CH), 80.2 (C), 66.4 (CH), 45.2 (CH_2), 42.9 (CH_2), 28.4 (C)

IR (film, cm^{-1}) 2981, 2928, 1706, 1451, 1423, 1267, 1164, 1108, 1026, 713

HRMS (ESI-QTOF) m/z: [M + Na]$^+$ Calcd for $C_{17}H_{21}NNaO_4^+$ 326.1363; Found 326.1369

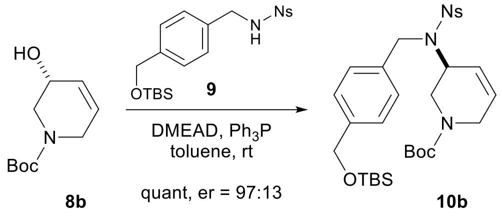
Compound 8b



To a stirred solution of **19** (558 mg, 1.84 mmol) in MeOH (5.40 mL) was added a solution of K_2CO_3 (298 mg, 1.20 mmol) in water (0.900 mL) at room temperature. After stirring for 3 h, the reaction was quenched with saturated aqueous NH_4Cl and extracted with DCM. The resulting mixture was washed with brine and concentrated *in vacuo*, and the residue was purified by flash silica gel column chromatography (*n*-hexane:EtOAc = 10:1 to EtOAc:MeOH=1:1) to afford **8a** (327 mg, 1.64 mmol, 91% yield, colorless oil).

[α]$_D$^{23} = −53° (*c* 1.8, CHCl$_3$)
Spectral data were consistent with **8a**.

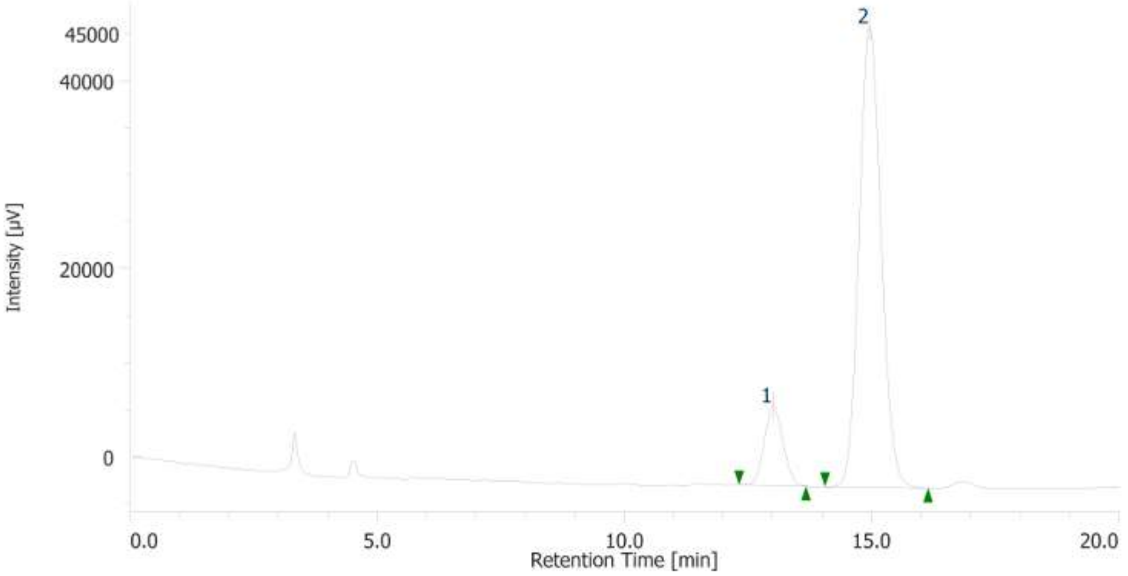
Compound 10b



Compound **10b** was prepared following the procedure for the transformation of **8a** into **10b**.
The enantiomeric excess was determined by HPLC analysis with a DAICEL CHRALPAK IC (*n*-hexane:2-propanol = 8.0:3.0, 1.0ml/min at 40 °C, UV 235 nm). The retention times corresponding to **10b** and its enantiomer were 13.0 and 15.0 min, respectively.

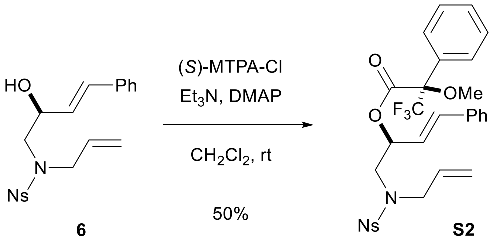
[α]$_D$^{23} = (+)23° (*c* 1.8, CHCl$_3$)
Spectral data were consistent with **10a**.

HPLC chart of (+)-10b



No.	tR (min)	Area (μV･sec)	Height (μV)	Area (%)
1	13.007	223066	8382	12.789
2	14.963	1508903	48489	87.121

Compound S2



To a stirred solution of **6** (26.1 mg, 0.0750 mmol), 4-dimethylaminopyridine (32.5 mg, 0.305 mmol) and triethylamine (45.2 µL, 0.325 mmol) in DCM (2.50 mL) was added (*S*)-MTPA-Cl (28.0 µL, 0.150 mmol) at room temperature. After stirring for 2 h, 3-dimethylaminopropylamine (18.5 µL, 0.145 mmol) was added at the same temperature. After stirring for 10 min at the same temperature, the reaction mixture was concentrated *in vacuo*, and the residue was purified by preparative TLC (*n*-hexane:EtOAc = 1:1) to afford **20** (22.8 mg, 50% yield, yellow oil).

$[\alpha]_D^{23}$ = +40° (*c* 1.1, $CHCl_3$)

^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.99 (m, 1H),7.62-7.58 (m, 2H), 7.55-7.48 (m, 3H), 7.42-7.36 (m, 3H), 7.33-7.27 (m, 5H), 6.74 (d, *J* = 16.0 Hz, 1H), 6.05 (dd, *J* = 15.8, 8.0 Hz, 1H), 5.81 (dd, *J* = 12.8, 7.8 Hz, 1H), 5.47 (dddd, *J* = 16.8, 10.4, 6.4, 6.4 Hz, 1H), 5.10 (dd, *J* = 14.2, 14.2 Hz, 2H), 3.93 (dd, *J* = 16.3, 5.7 Hz, 1H), 3.66 (m, 2H), 3.59-3.51 (m, 4H)

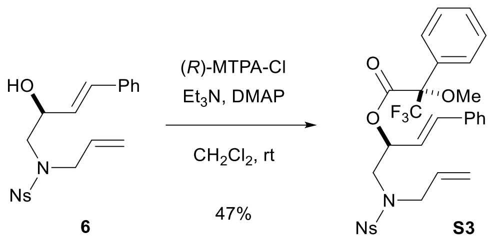
^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9 (C), 148.0 (C), 136.8 (CH), 135.5 (C), 133.8 (CH), 133.5 (C), 132.3 (C), 131.8 (CH), 131.3 (CH), 129.8 (CH), 128.8 (CH), 128.7 (CH), 127.4 (CH), 126.1 (q, $J_{C\text{-}F}$ = 257.8 Hz, C), 127.0 (CH), 124.4 (CH), 122.7 (CH), 120.2 (CH_2), 84.6 (q, $J_{C\text{-}F}$ = 25.9 Hz, C), 76.1 (C), 55.8 (CH_3), 51.1 (CH_2), 49.1 (CH_2) Two tertiary carbons of the benzene ring were not observed perhaps due to overlapping.

^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.2

IR (film, cm^{-1}) 2947, 1755, 1547, 1360, 1243, 1161, 1126, 970, 715, 575

HRMS (ESI-QTOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{28}F_3N_2O_7S^+$ 605.1564; Found 605.1579

Compound S3



To a stirred solution of **6** (26.1 mg, 0.0750 mmol), 4-dimethylaminopylidine (32.5 mg, 0.305 mmol) and triethylamine (45.2 μL, 0.325 mmol) in DCM (2.50 mL) was added (*R*)-MTPA-Cl (28.0 μL, 0.150 mmol) at room temperature. After stirring for 2 h, dimethylaminopropylamine (18.5 μL, 0.145 mmol) was added at the same temperature. After stirring for 10 min at the same temperature, the reaction mixture was concentrated *in vacuo*, and the residue was purified by preparative TLC (*n*-hexane:EtOAc = 1:1) to afford **21** (21.0 mg, 47% yield, yellow oil).

$[\alpha]_D^{23}$ = −6.0° (*c* 1.1, $CHCl_3$)

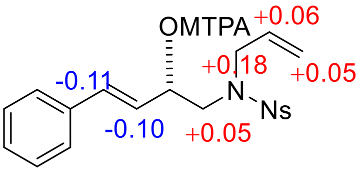
^{1}H NMR ($CDCl_3$, 400 MHz) δ 8.02 (m, 1H),7.65-7.53 (m, 3H), 7.52-7.47 (m, 2H), 7.43-7.24 (m, 8H), 6.63 (d, *J* = 16.0 Hz, 1H), 5.94 (dd, *J* = 15.8, 7.6 Hz, 1H), 5.79 (dd, *J* = 12.8, 7.3 Hz, 1H), 5.53 (dddd, *J* = 17.3, 10.2, 6.4, 6.4 Hz, 1H), 5.17 (s, 1H), 5.13 (d, *J* = 5.0 Hz, 1H), 4.05 (dd, *J* = 16.0, 6.0 Hz, 1H), 3.90 (dd, *J* = 16.2, 6.6 Hz, 1H), 3.65 (m, 2H), 3.55 (s, 3H)

^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.9 (C), 148.0 (C), 136.2 (CH), 135.5 (C), 133.9 (CH), 133.5 (C), 132.0 (C), 131.9 (CH), 131.7 (CH), 131.3 (CH), 129.9 (CH), 128.7 (CH), 127.6 (CH), 127.0 (CH), 124.4 (CH), 123.4 (q, $J_{C\text{-}F}$ = 288.5 Hz, C), 122.6 (CH), 120.4 (CH_2), 84.9 (q, $J_{C\text{-}F}$ = 27.8 Hz, C), 75.8 (C), 55.8 (CH_3), 51.3 (CH_2), 49.3 (CH_2)

^{19}F NMR ($CDCl_3$, 376 MHz) δ −71.1

IR (film, cm^{-1}) 2947, 1744, 1540, 1362, 1246, 1165, 1116, 970, 715, 581

HRMS (ESI-QTOF) m/z: $[M + Na]^+$ Calcd for $C_{29}H_{27}F_3N_2NaO_7S^+$ 627.1383; Found 627.1403



$\Delta\delta_H$ values [δ_H of (*S*)-MTPA ester **S3** – δ_H of (*R*)-MTPA ester **S2**]

Pharmacophore fitting and binding affinity score calculation

Pharmacophore fitting was conducted using LigandScout 4.5[4] to identify the binding modes of **10a** and **10b**. The pharmacophore was constructed based on the binding interactions between DQ-18 and the gastric proton pump (PDB: 8IJX) using the Structure-Based mode in LigandScout 4.5. The pharmacophore consisted of three hydrophobic features, one positive ionization feature, and one hydrogen bond donor feature. Three-dimensional conformations of **10a** and **10b** were generated using the icon-best mode of the 'idbgen' module in LigandScout 4.5. Pharmacophore fitting was then performed with the ‘iscreen’ module, applying the Relative Pharmacophore-Fit score, with the conformation match mode set to BEST and exclusion volume clashes disabled. Binding affinity scores between each compound and the gastric proton pump were calculated ‘iaffinity’ module with default parameters in LigandScout 4.5.

Cryo-EM analysis of gastric H^+,K^+-ATPase bound to compound 1b

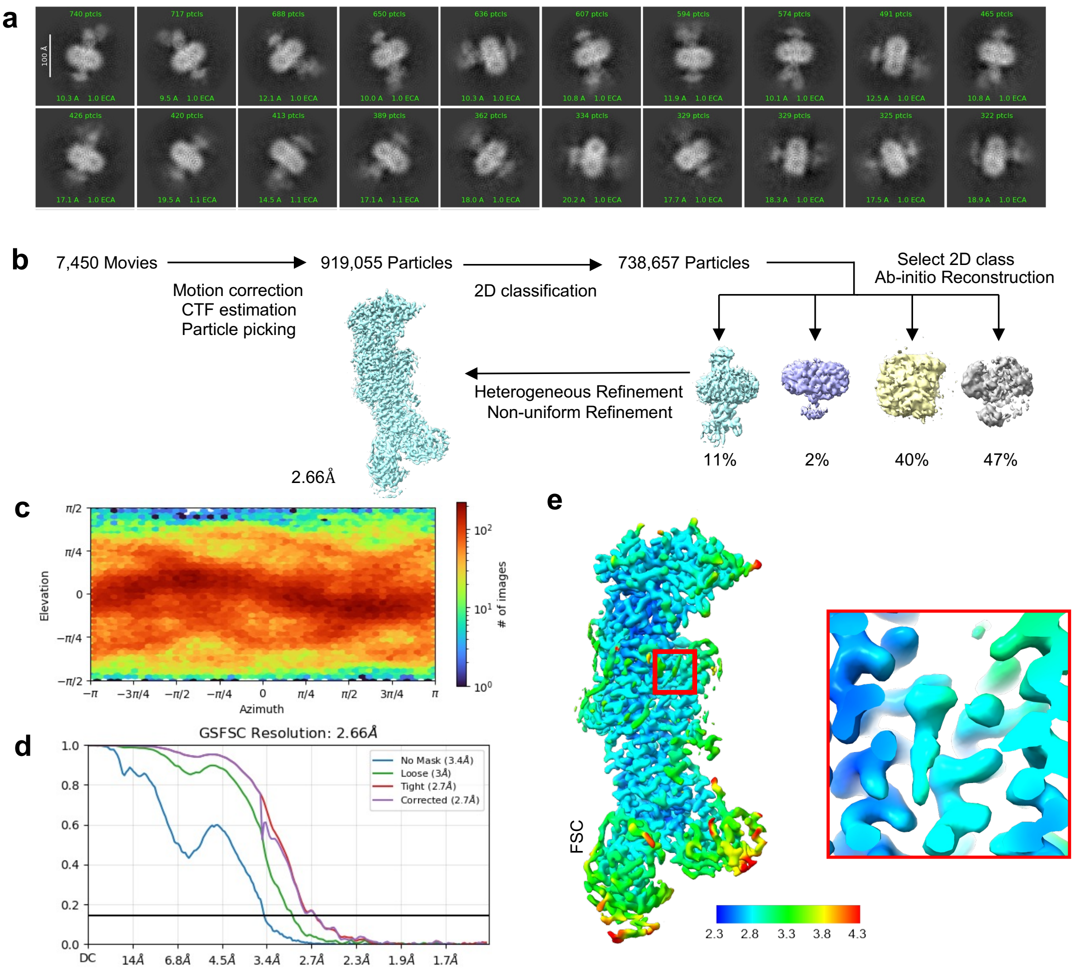
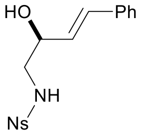


Figure S1. **a** Representative 2D class averages. **b** Cryo-EM workflow. **c** Angular distribution plot of particles included in the final 3D reconstruction. The number of views at each angular orientation is represented by the color (blue to red). **d** FSC plot used for resolution estimation (blue: no mask, green: loose, red: tight, purple: corrected). Black straight line indicate FSC value of 0.143. **e** Unsharpened maps colored by local resolution as calculated by cryoSPARC (scale is indicated in the figure). Inset images correspond to the close-up view of the compound binding site.

References for Supporting Information

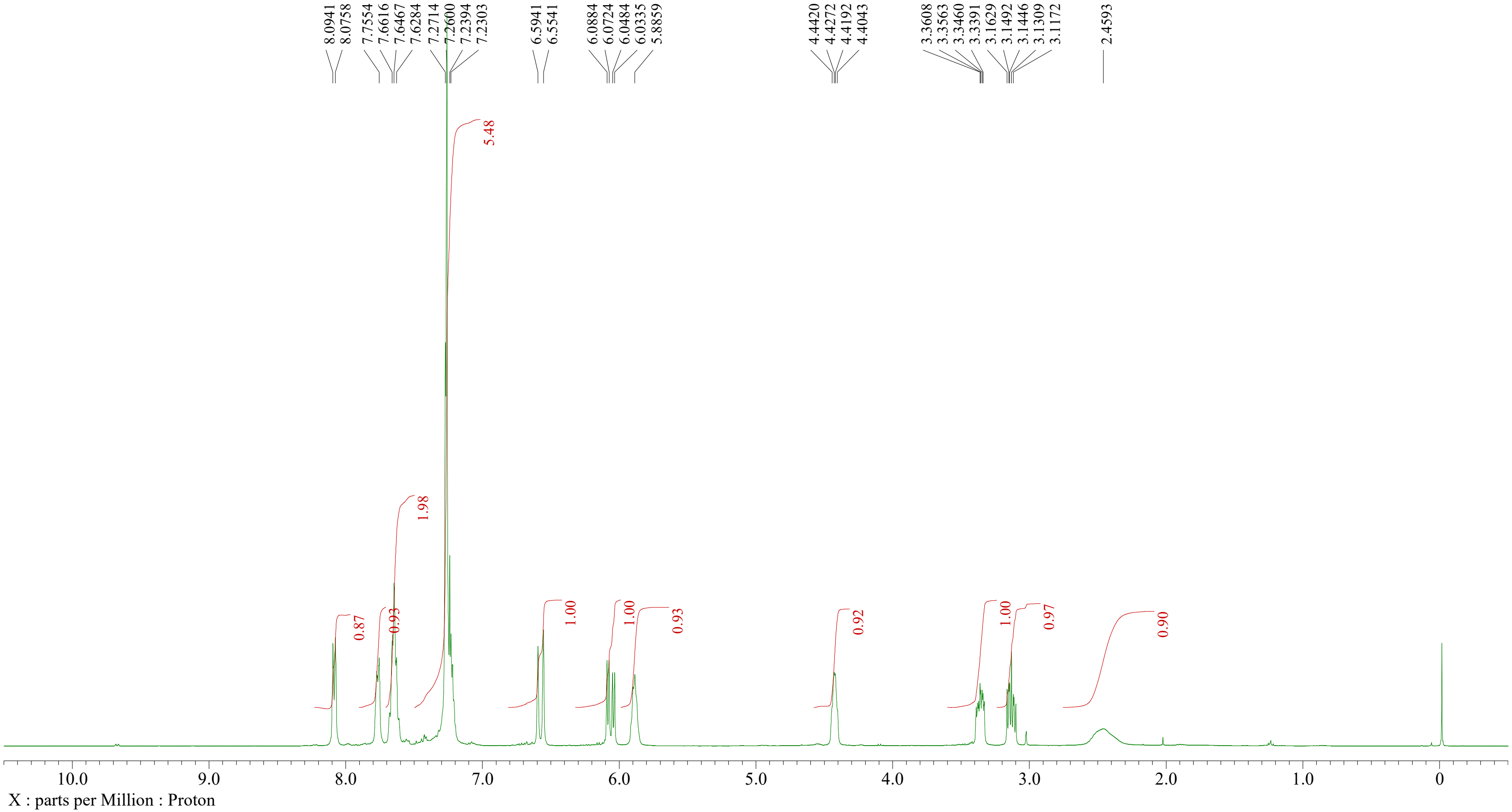
1. Zhou, Y.; Dong, J.; Zhang, F. Gong, Y. *J. Org. Chem.* 2011, **76**, 588.
2. Youn, S.; Kim, Y. *Synlett* 2000, **6**, 880.
3. Gonçalves, C. R.; Lemmerer, M.; Teskey, C. J.; Adler, P.; Kaiser, D.; Maryasin, B.; Gonzáles, L.; Maulide, N. *J. Am. Chem. Soc.* 2019, **141**, 18437.
4. Wolber, G; Langer, T. *J. Chem. Inf. Model.* 2005, **45**, 160.

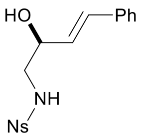


5

^{1}H-NMR

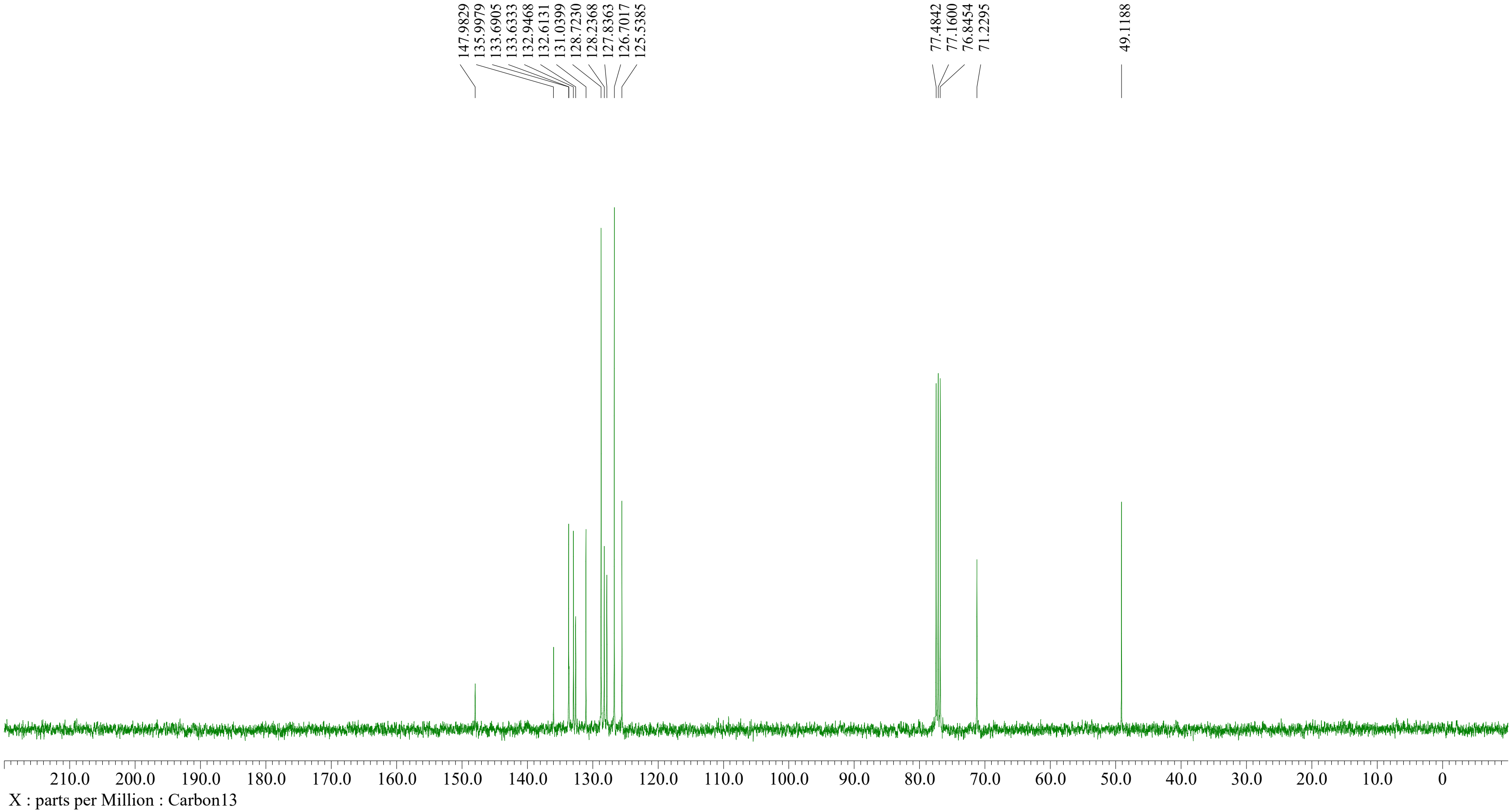
(400 MHz, $CDCl_3$)

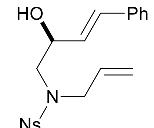




5

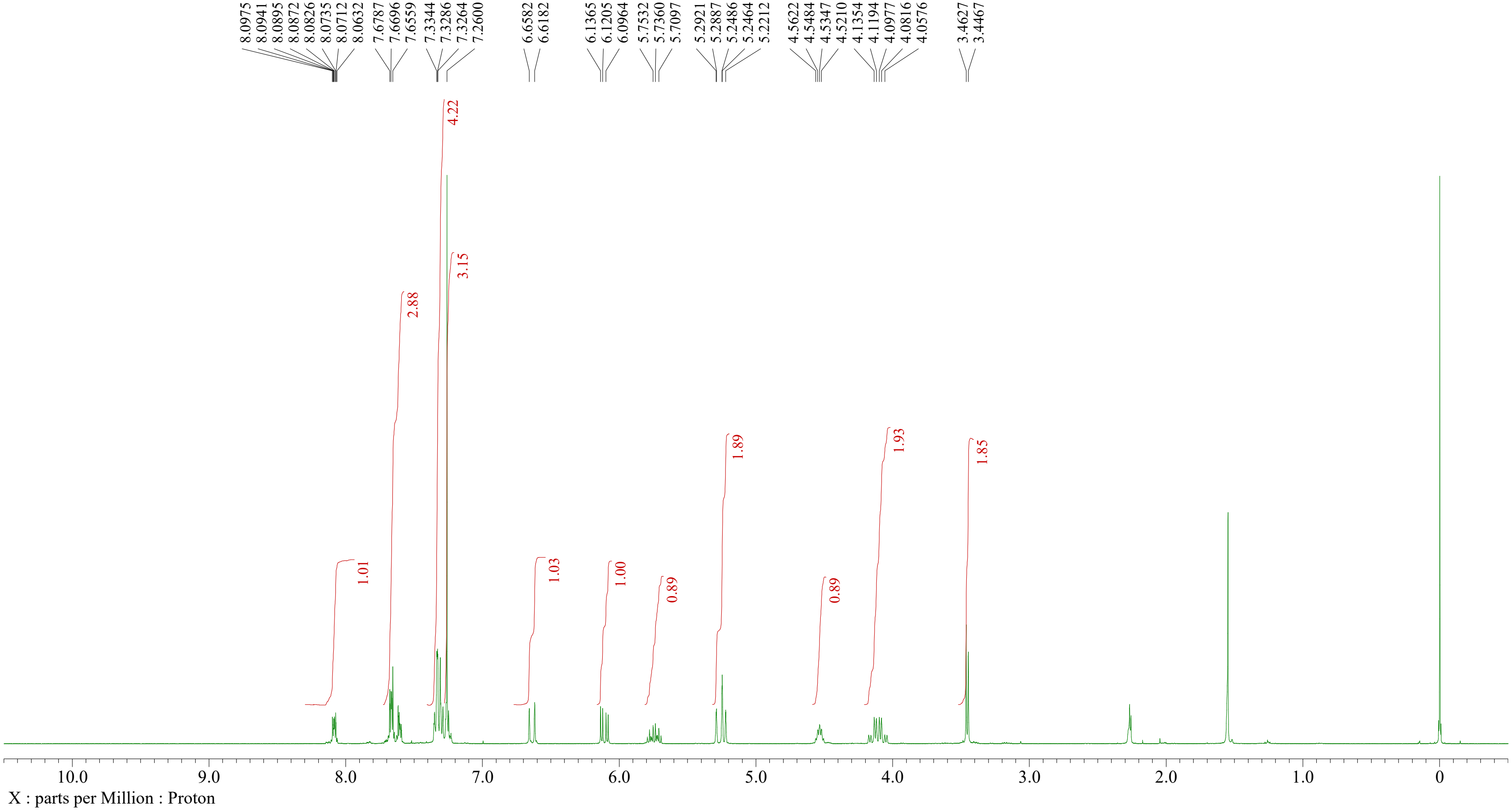
^{13}C-NMR
(100 MHz, $CDCl_3$)

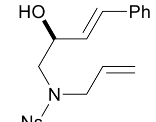




6

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





6

^{13}C-NMR
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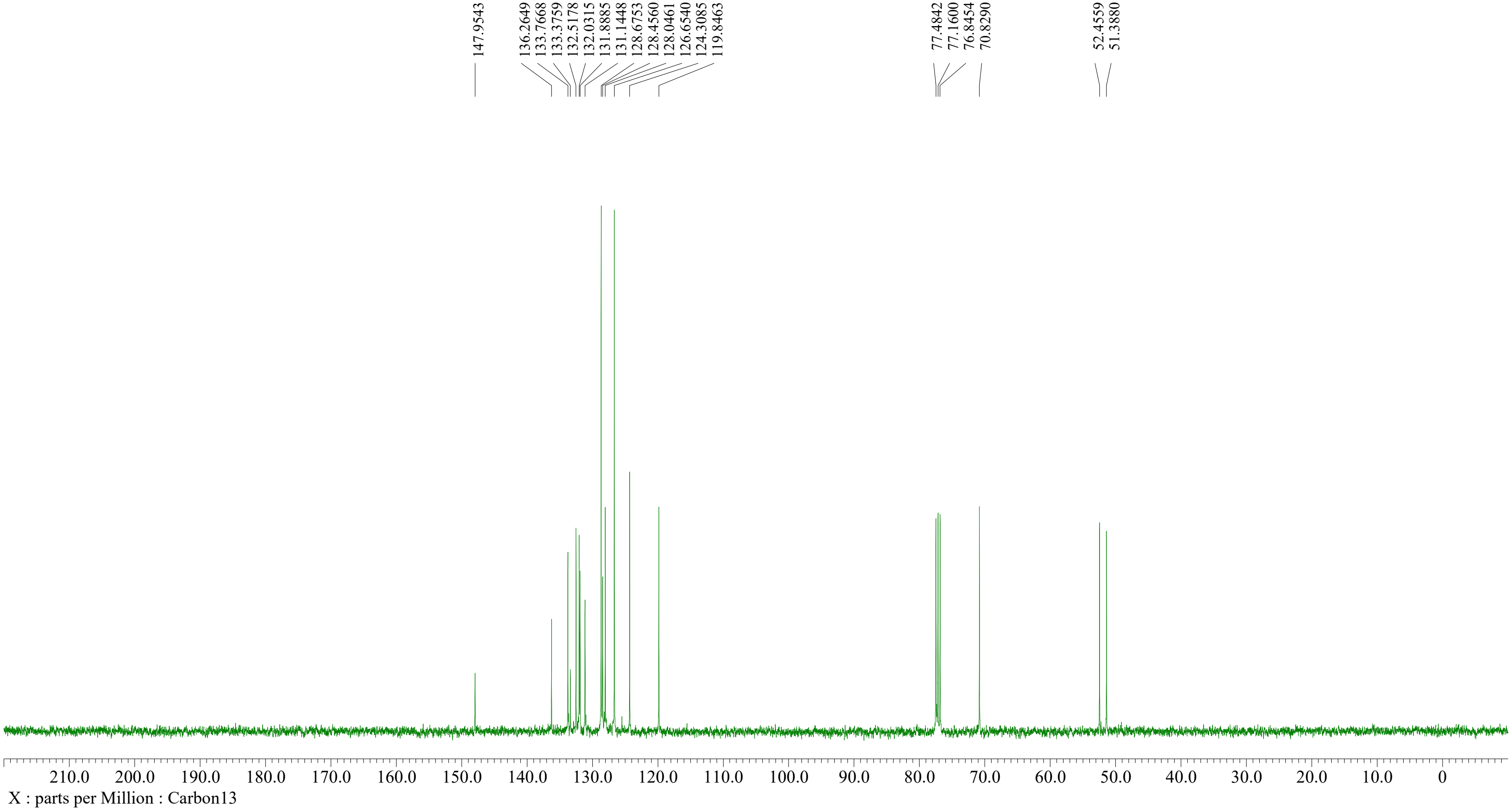
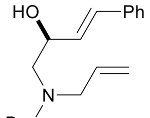
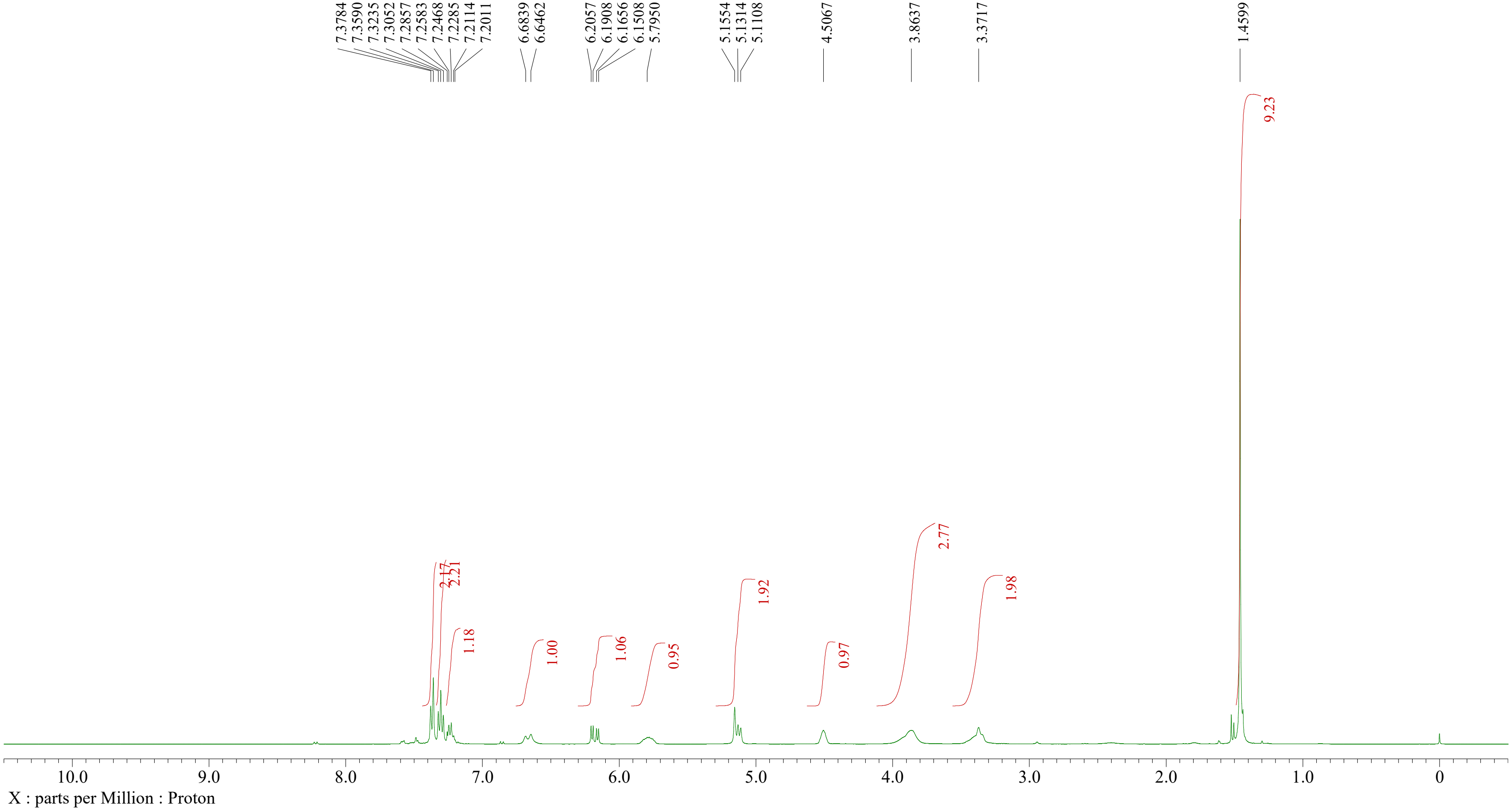
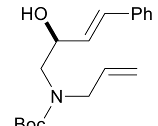




7

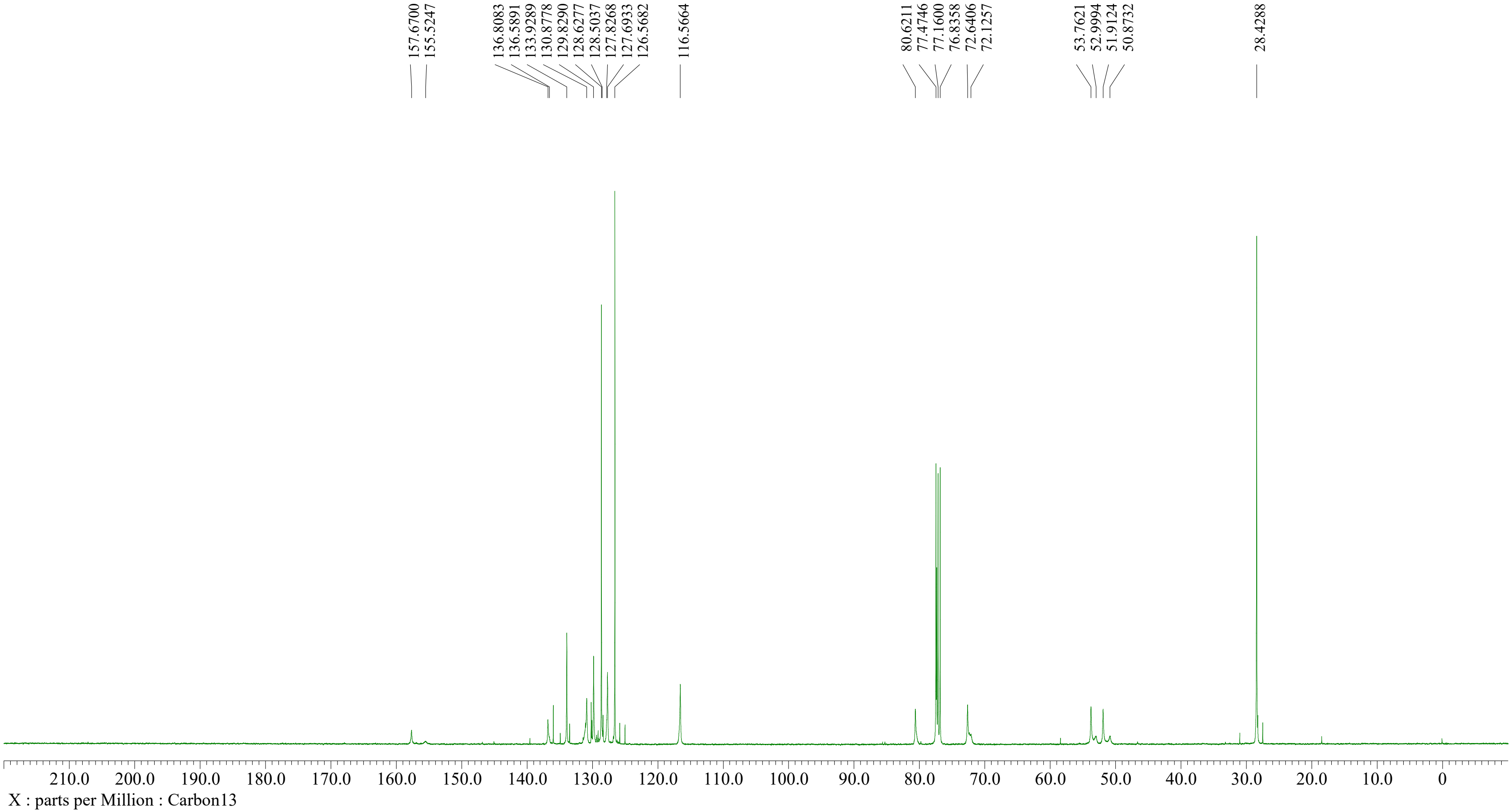
^{1}H-NMR
(400 MHz, $CDCl_3$)

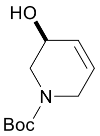




7

^{13}C-NMR
(100 MHz, CDCl$_3$)

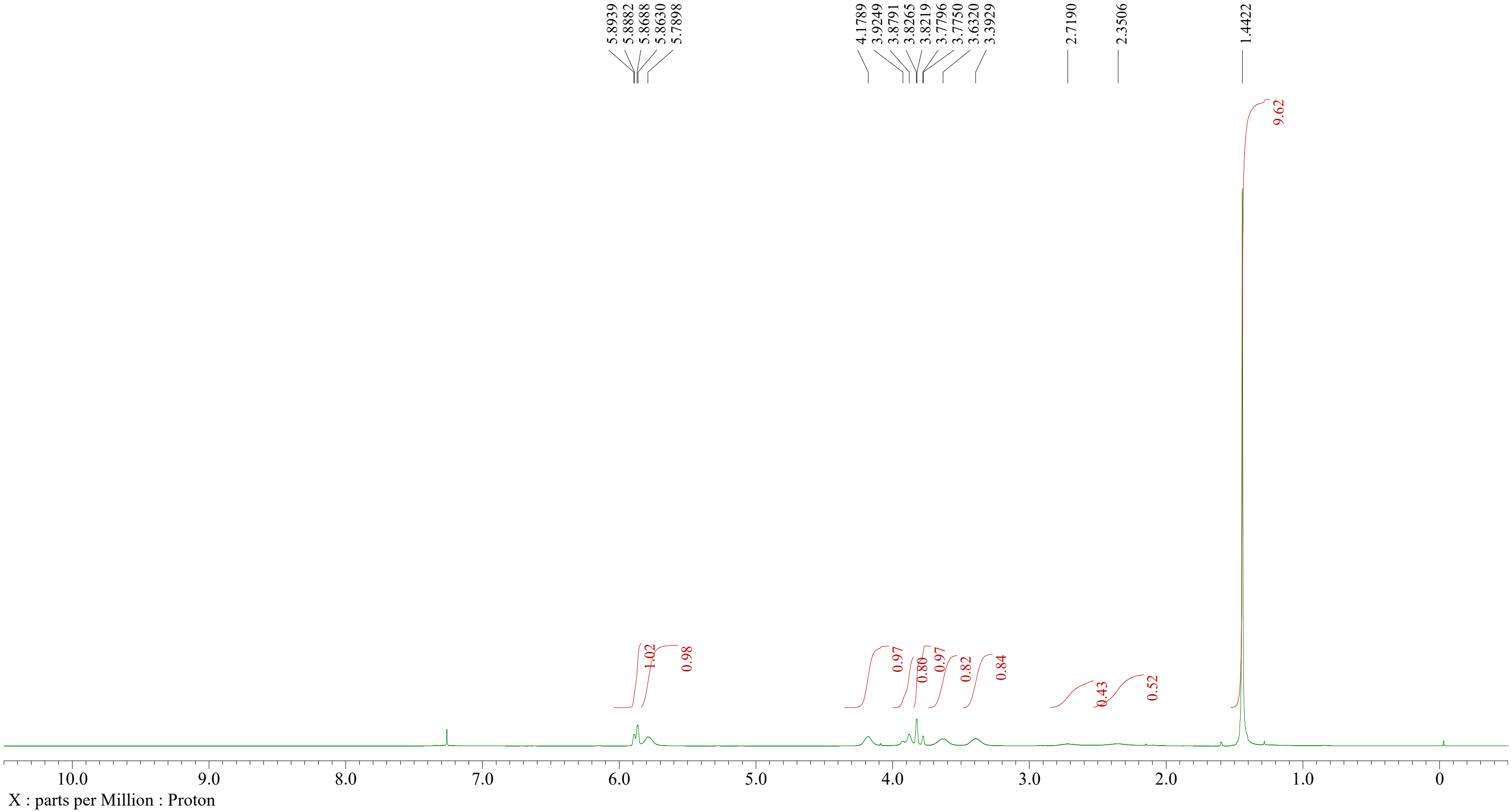


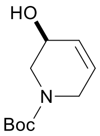


8a

^{1}H-NMR

(400 MHz, $CDCl_3$)

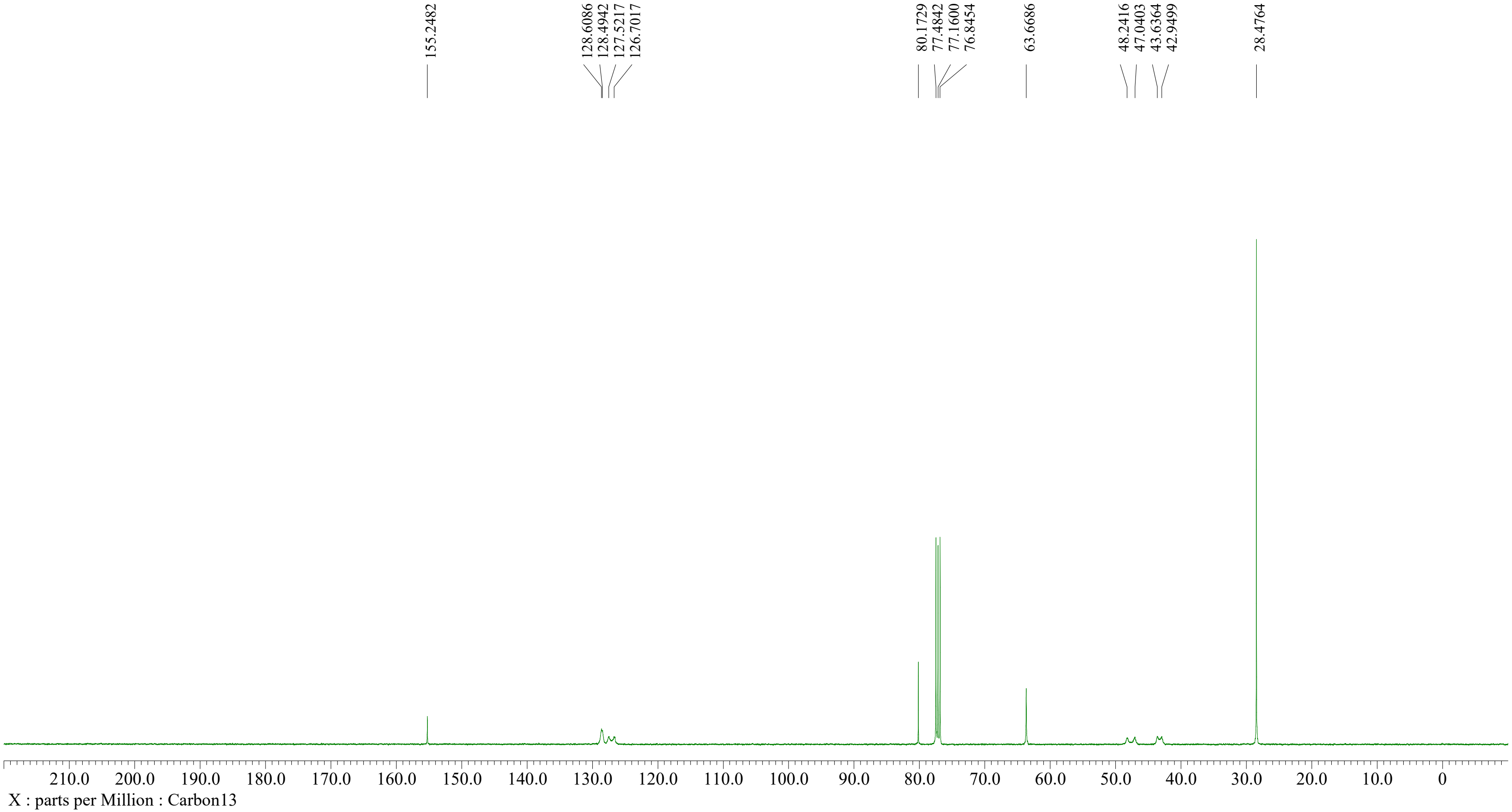


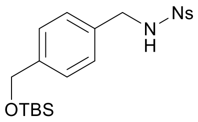


8a

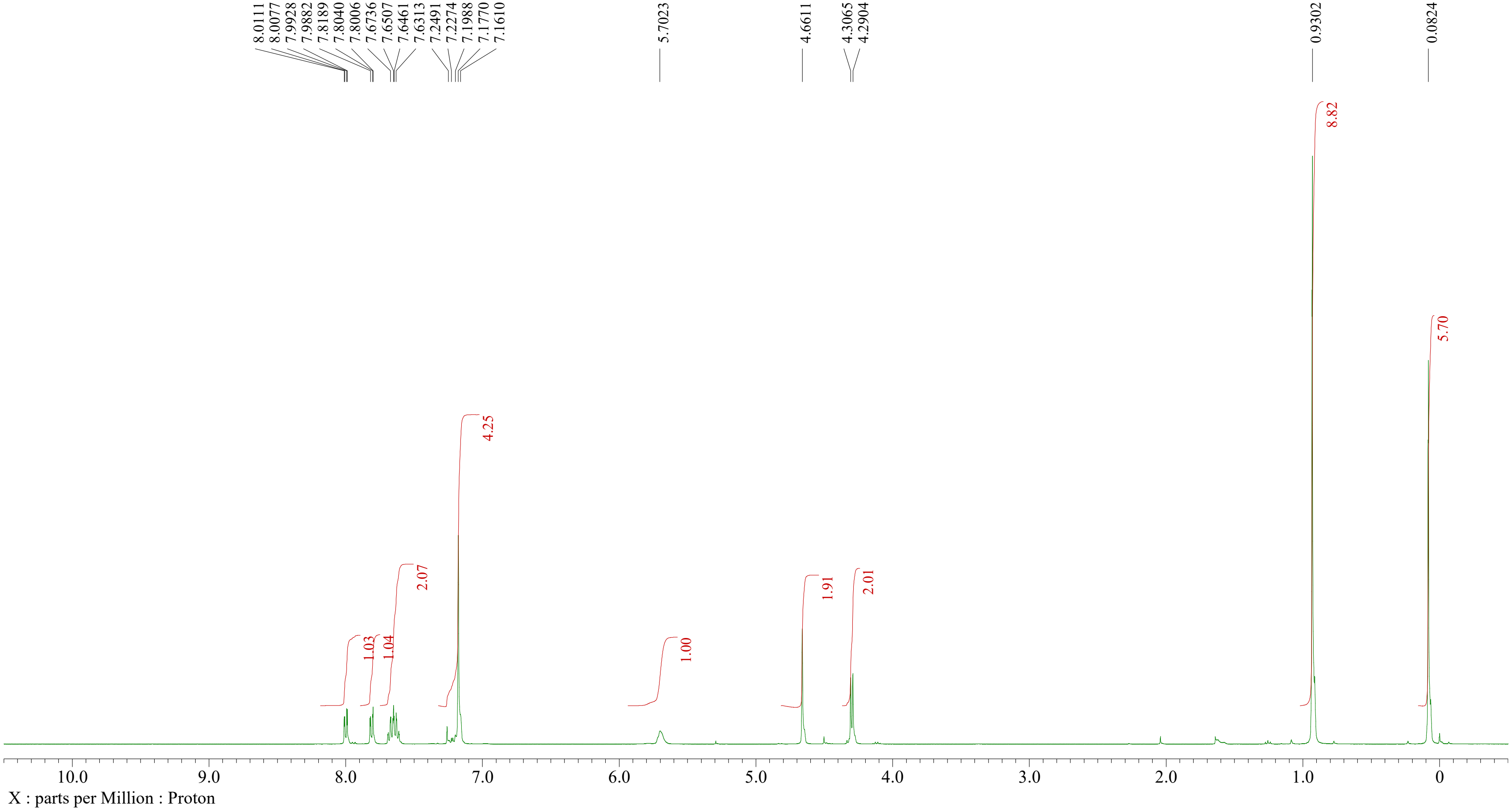
^{13}C-NMR

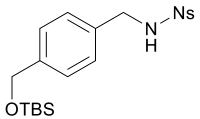
(100 MHz, $CDCl_3$)





9
^{1}H-NMR
(400 MHz, $CDCl_3$)





9
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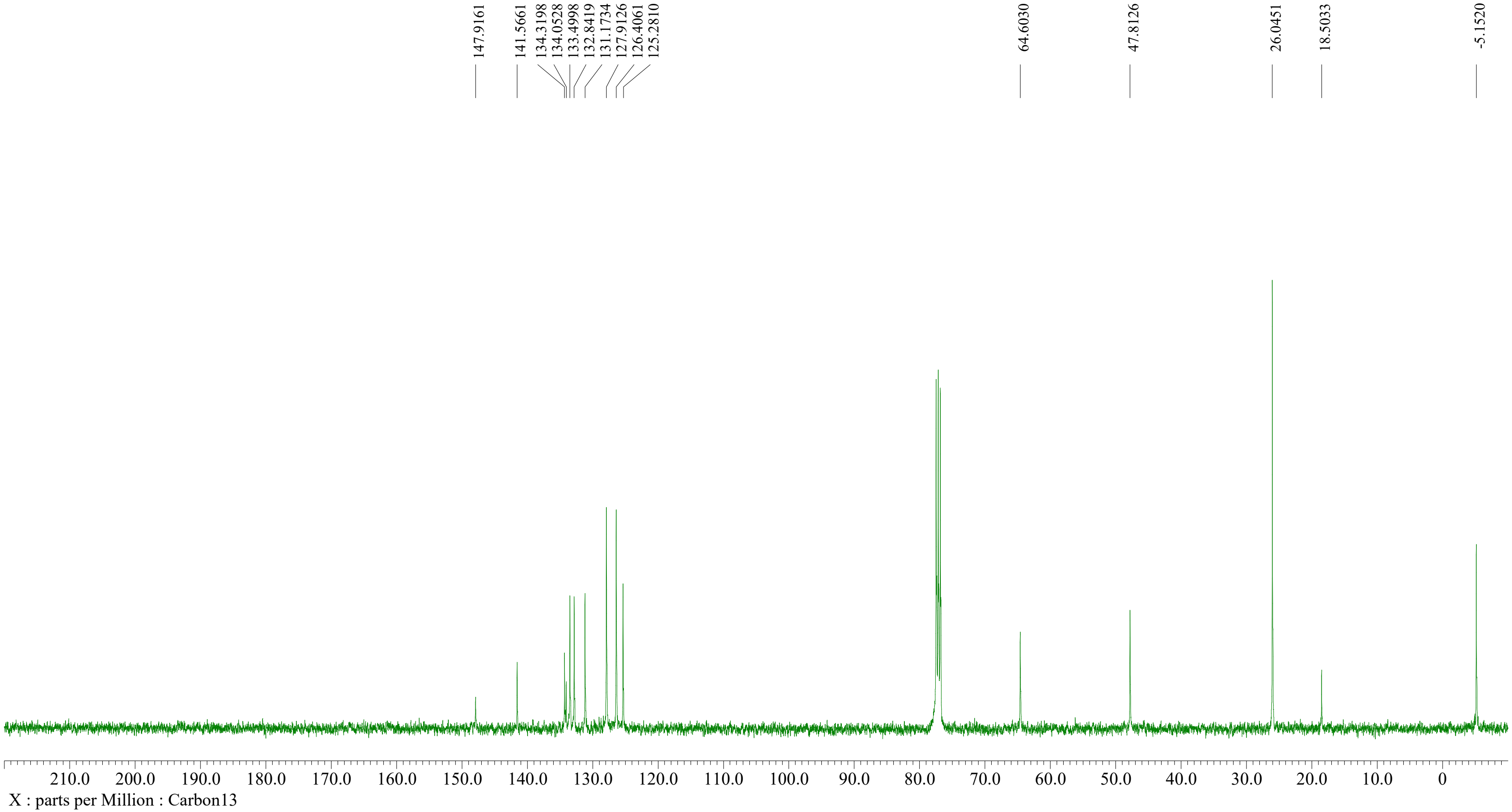
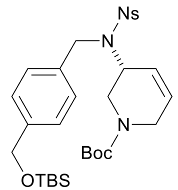
(100 MHz, $CDCl_3$)

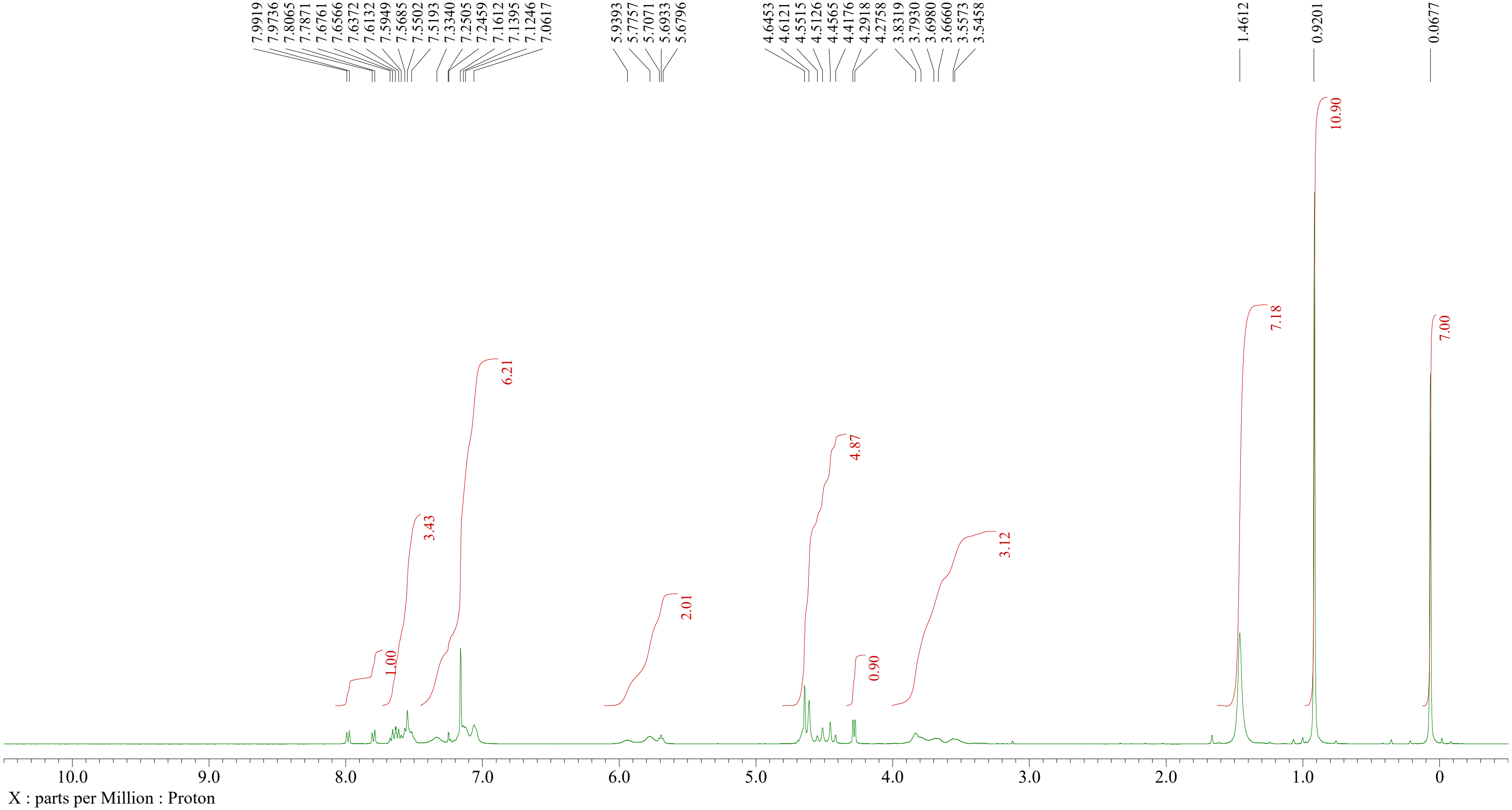


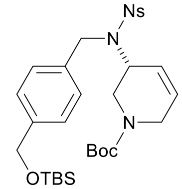


10a

^{1}H-NMR

(400 MHz, $CDCl_3$)

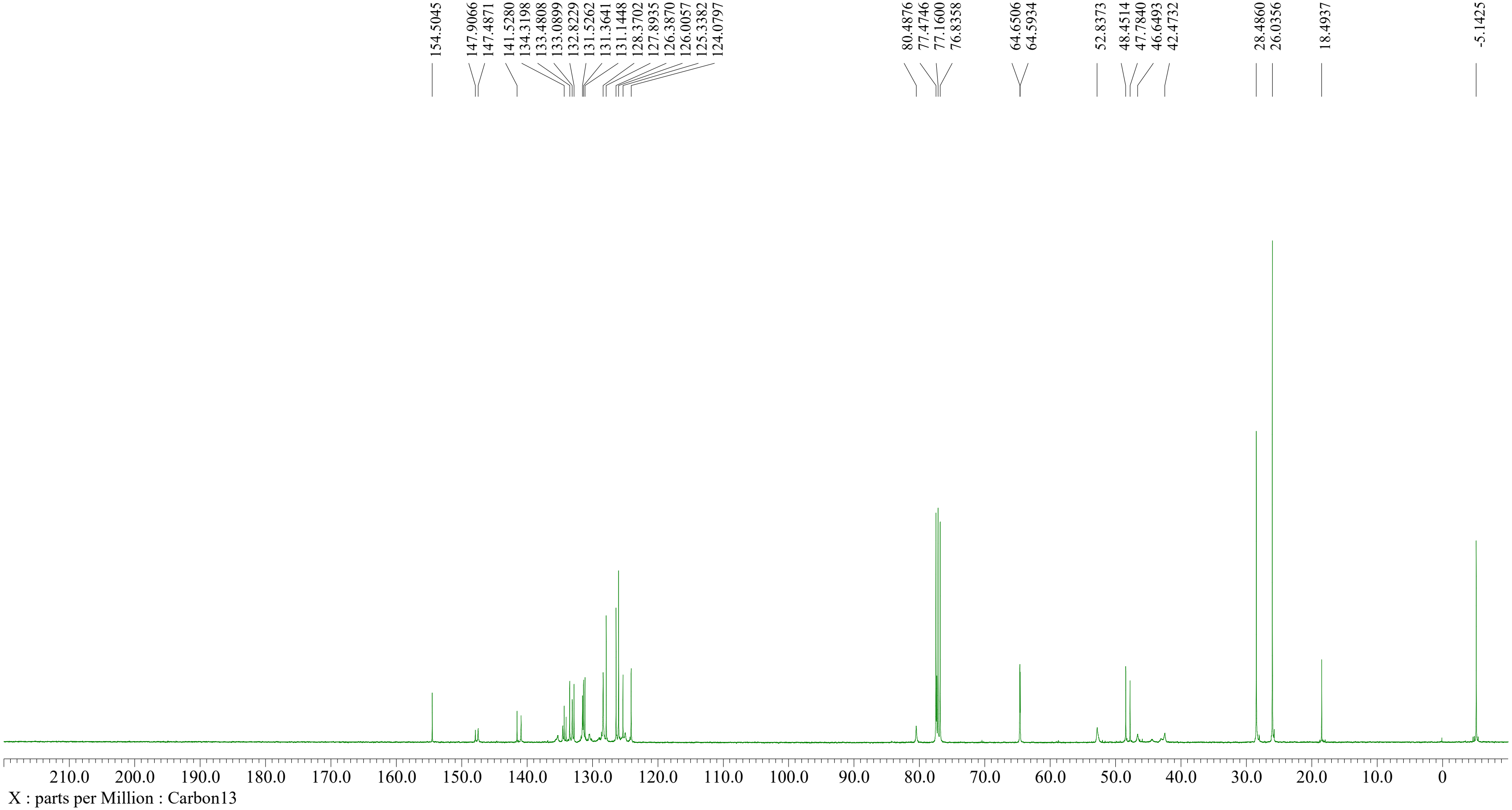


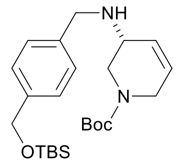


10a

^{13}C-NMR

(100 MHz, CDCl$_3$)

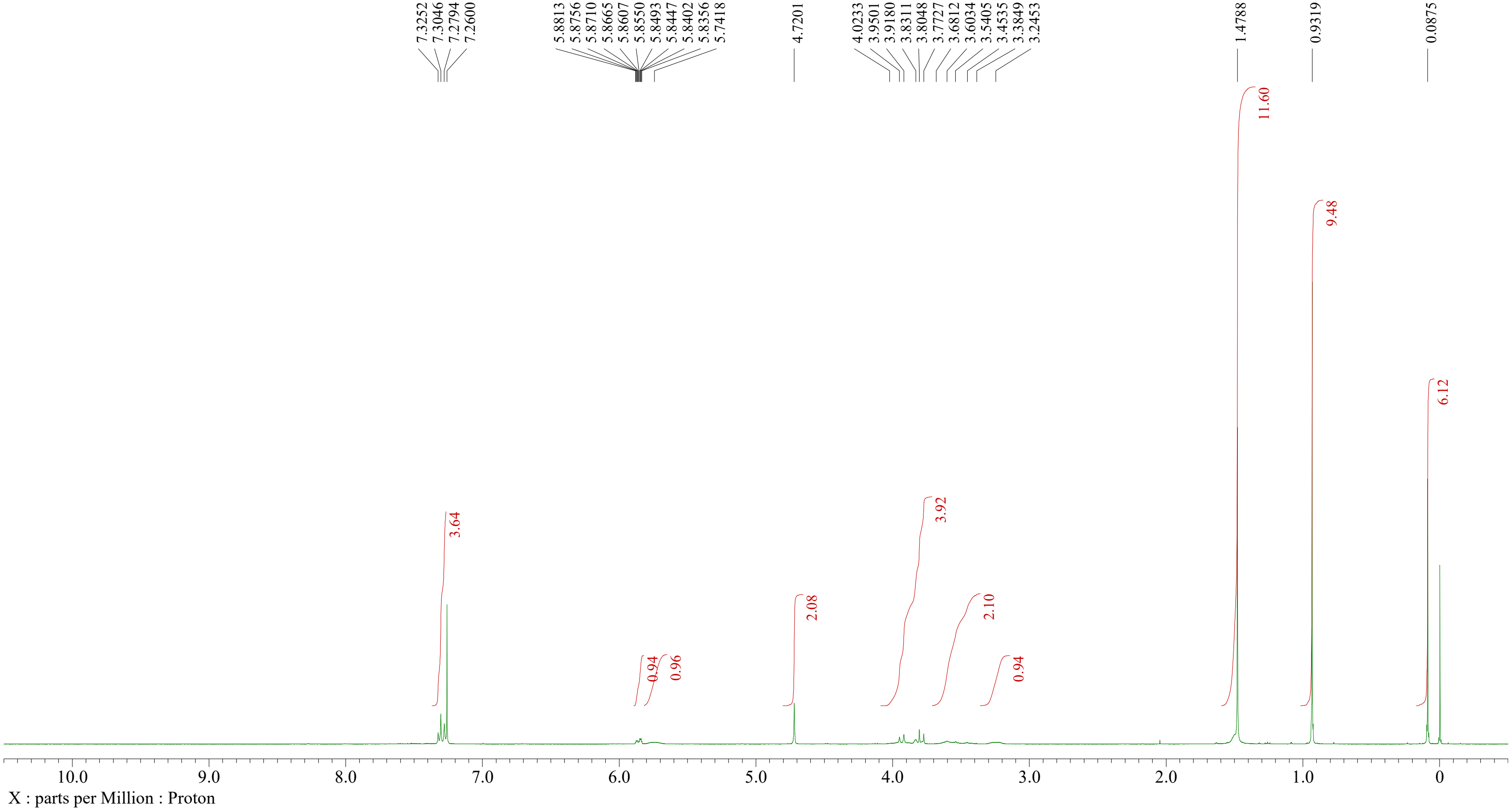


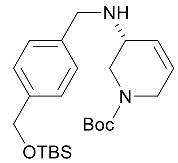


11a

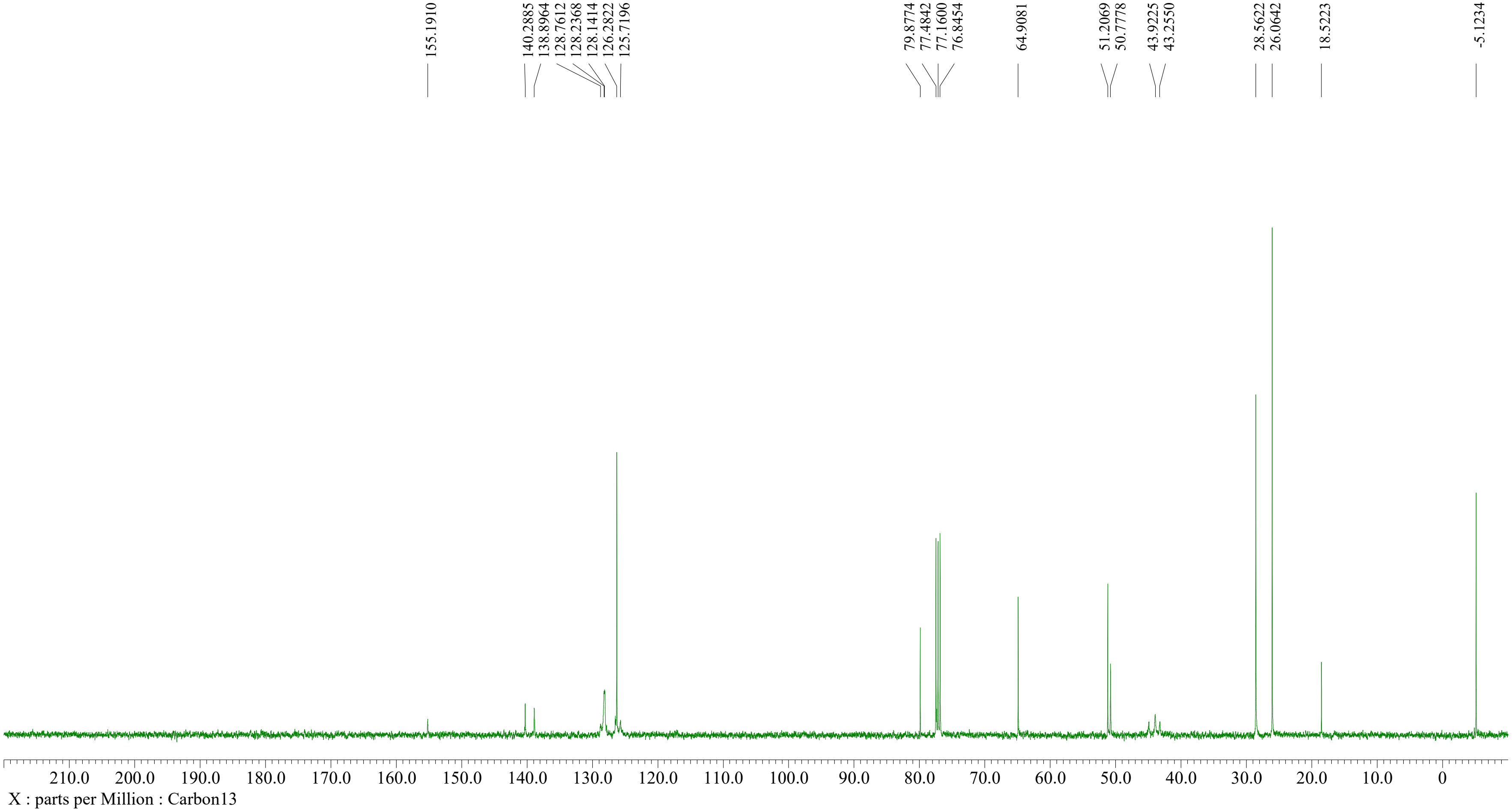
^{1}H-NMR

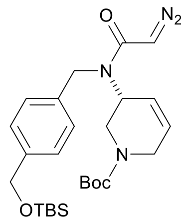
(400 MHz, $CDCl_3$)





11a
^{13}C-NMR
(100 MHz, $CDCl_3$)





12a
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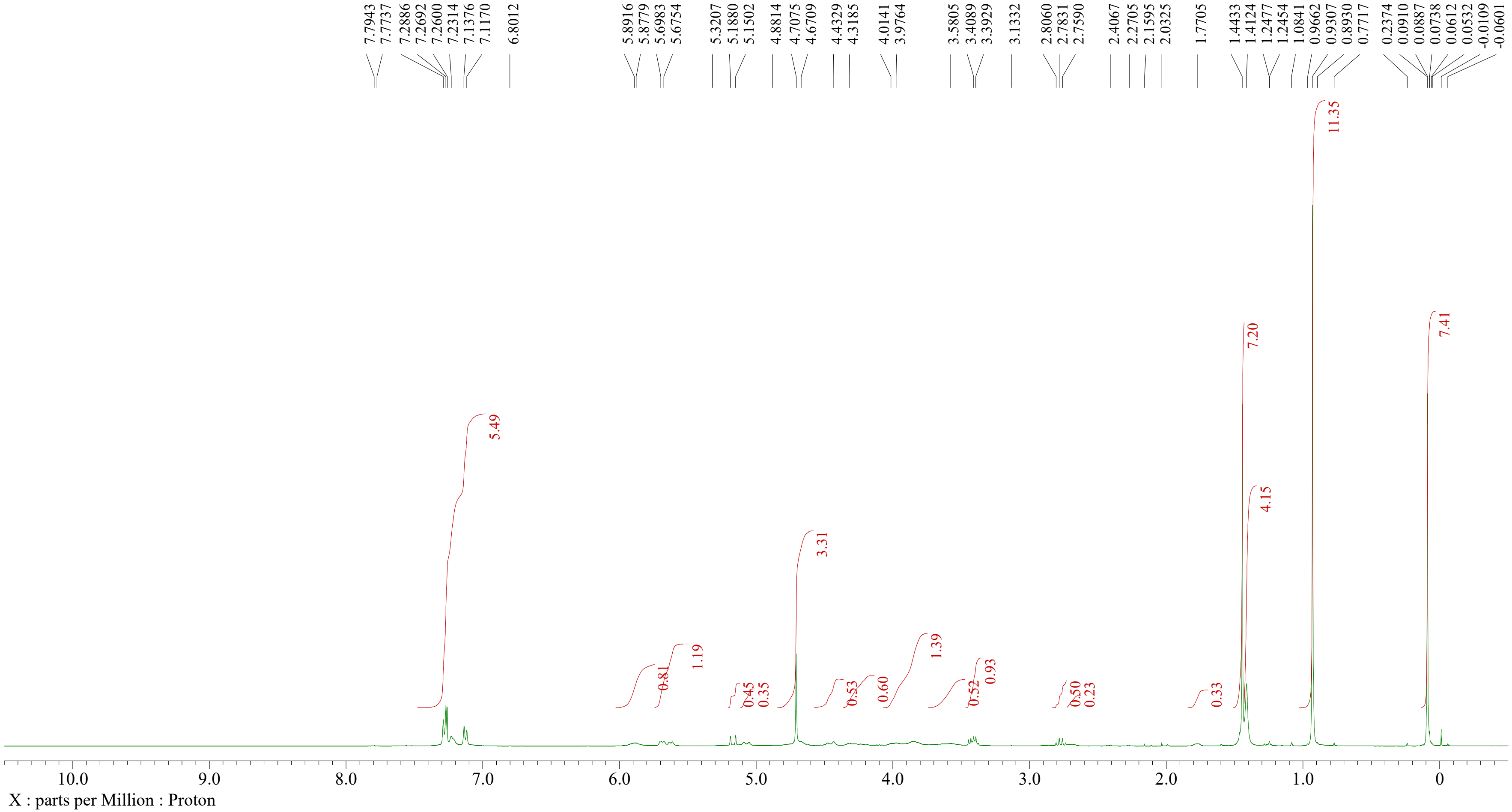
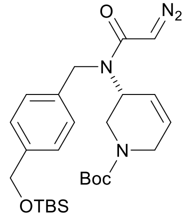
(400 MHz, $CDCl_3$)

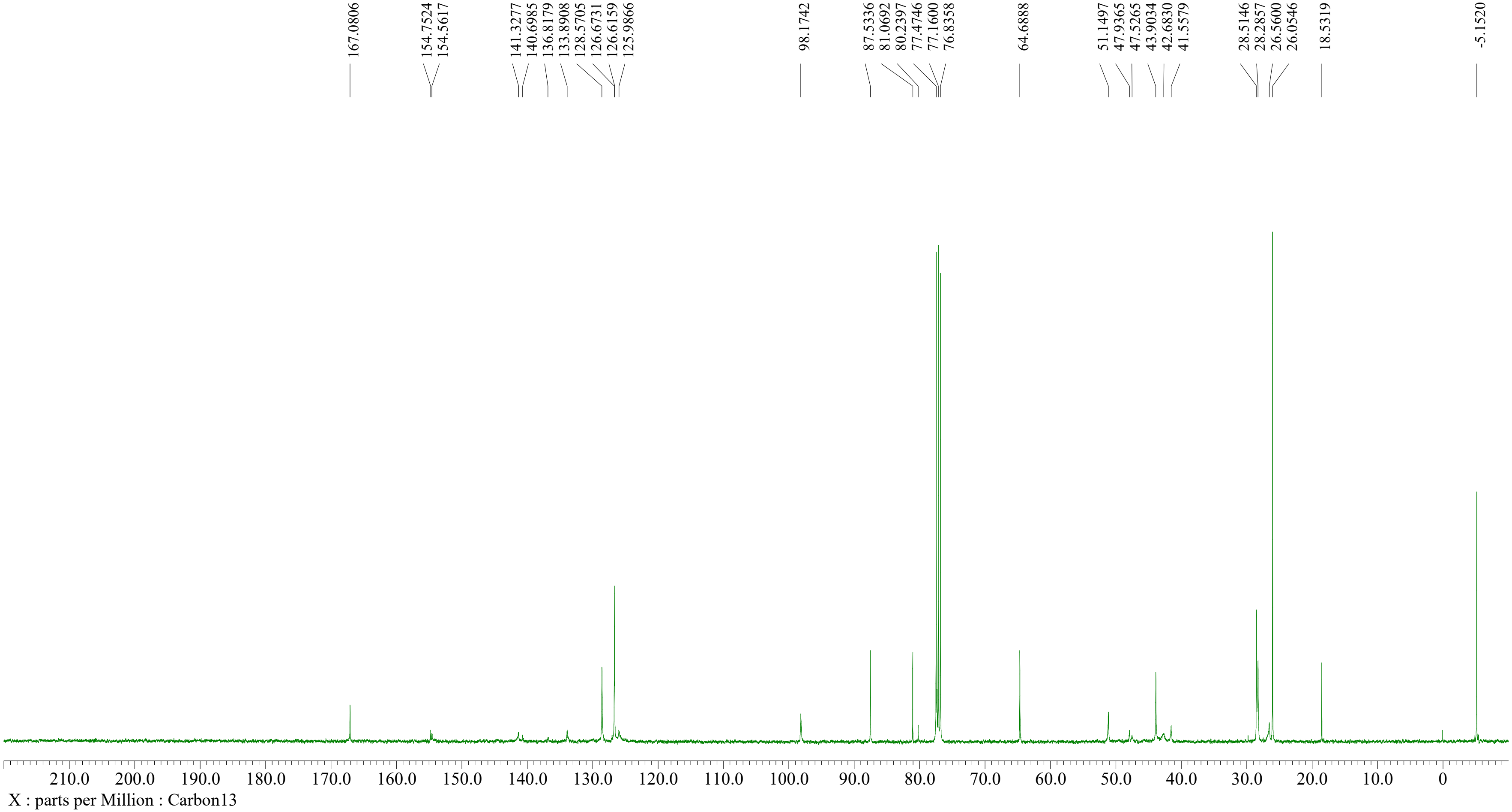


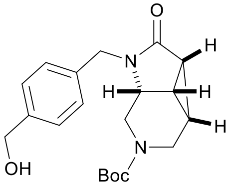


12a

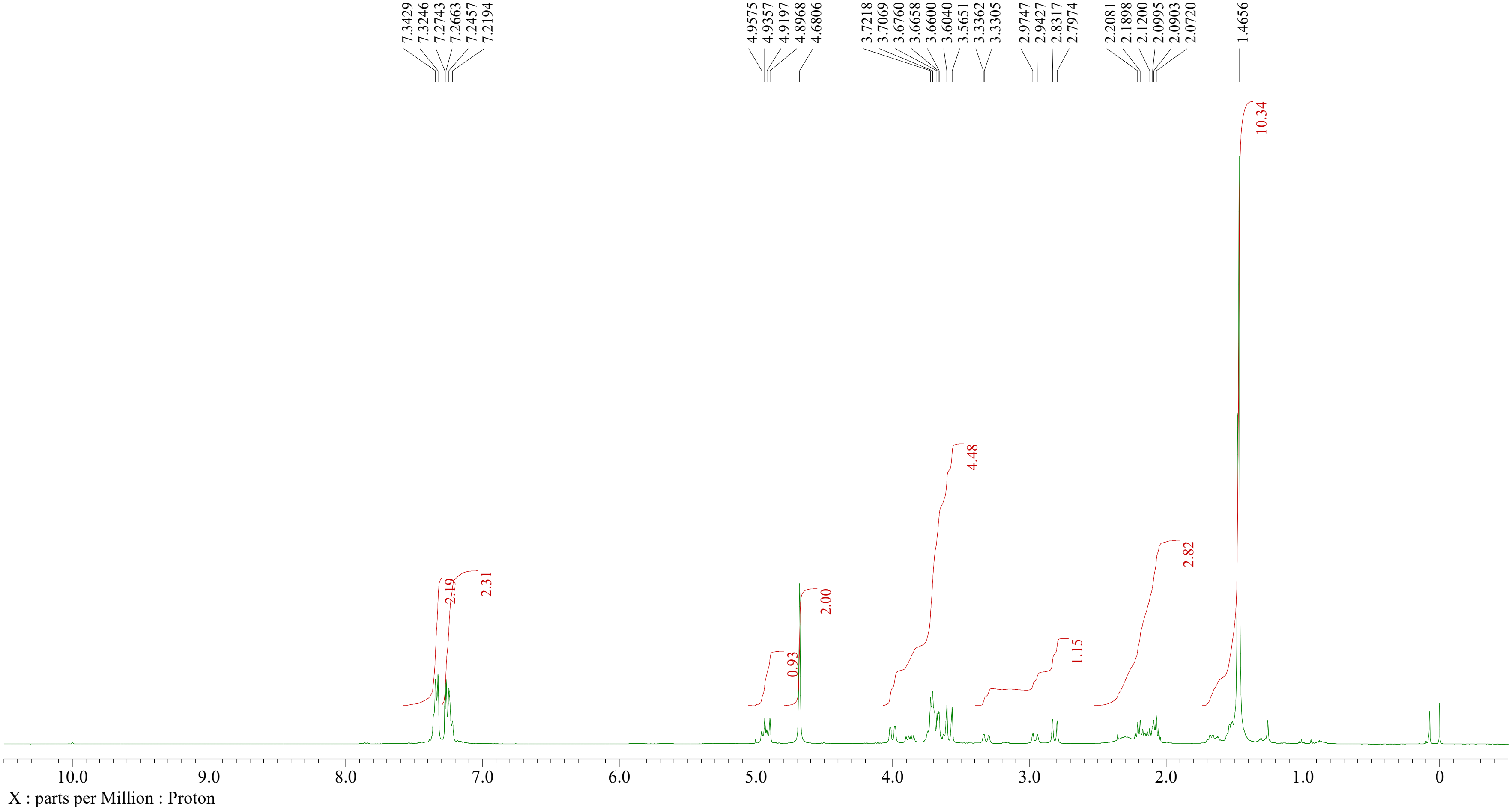
^{13}C-NMR

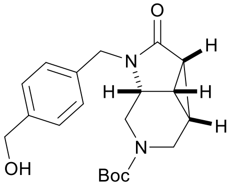
(100 MHz, $CDCl_3$)



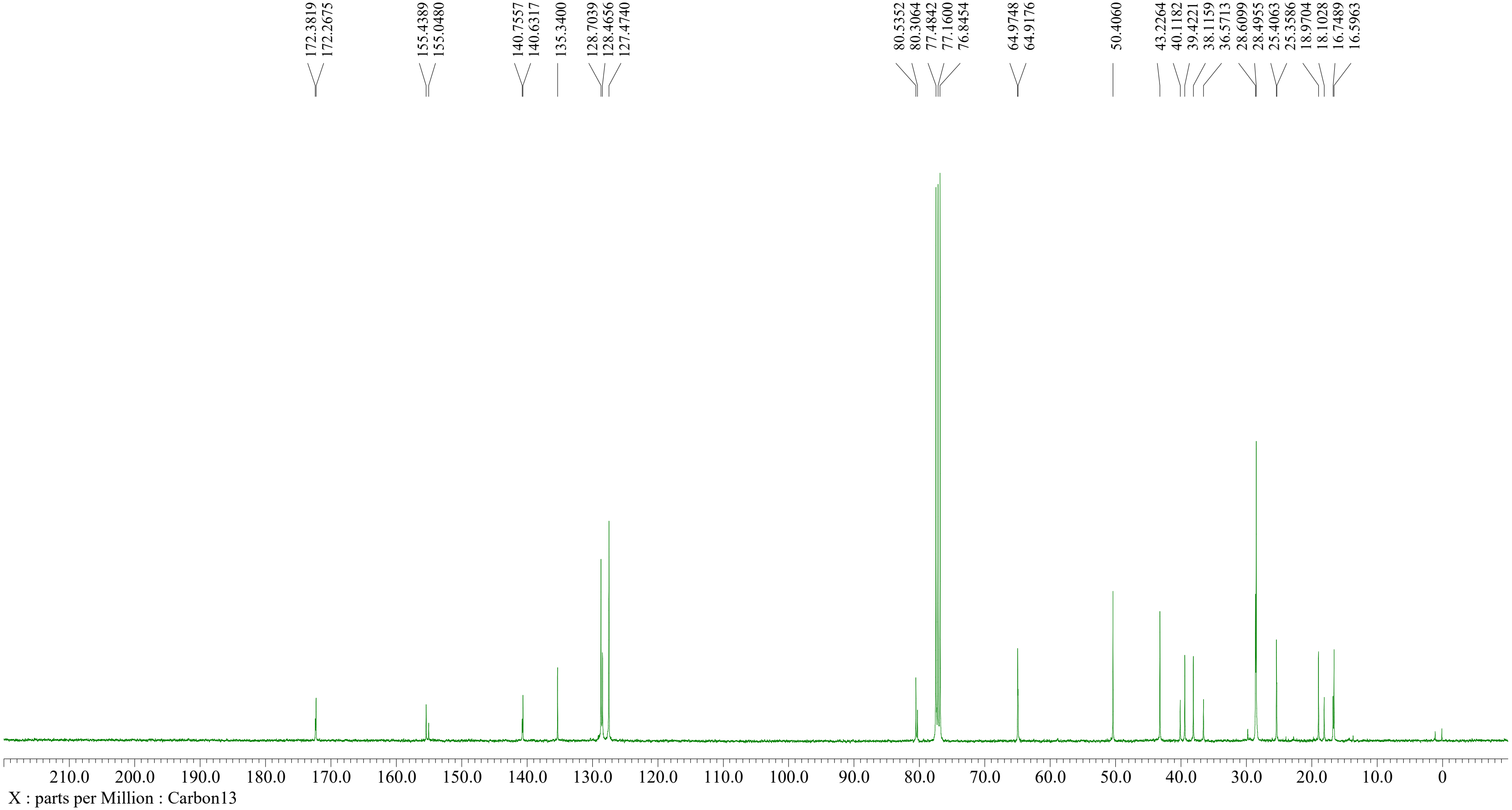


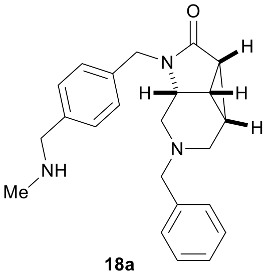
15a
^{1}H-NMR
(400 MHz, $CDCl_3$)





15a
^{13}C-NMR
(100 MHz, $CDCl_3$)

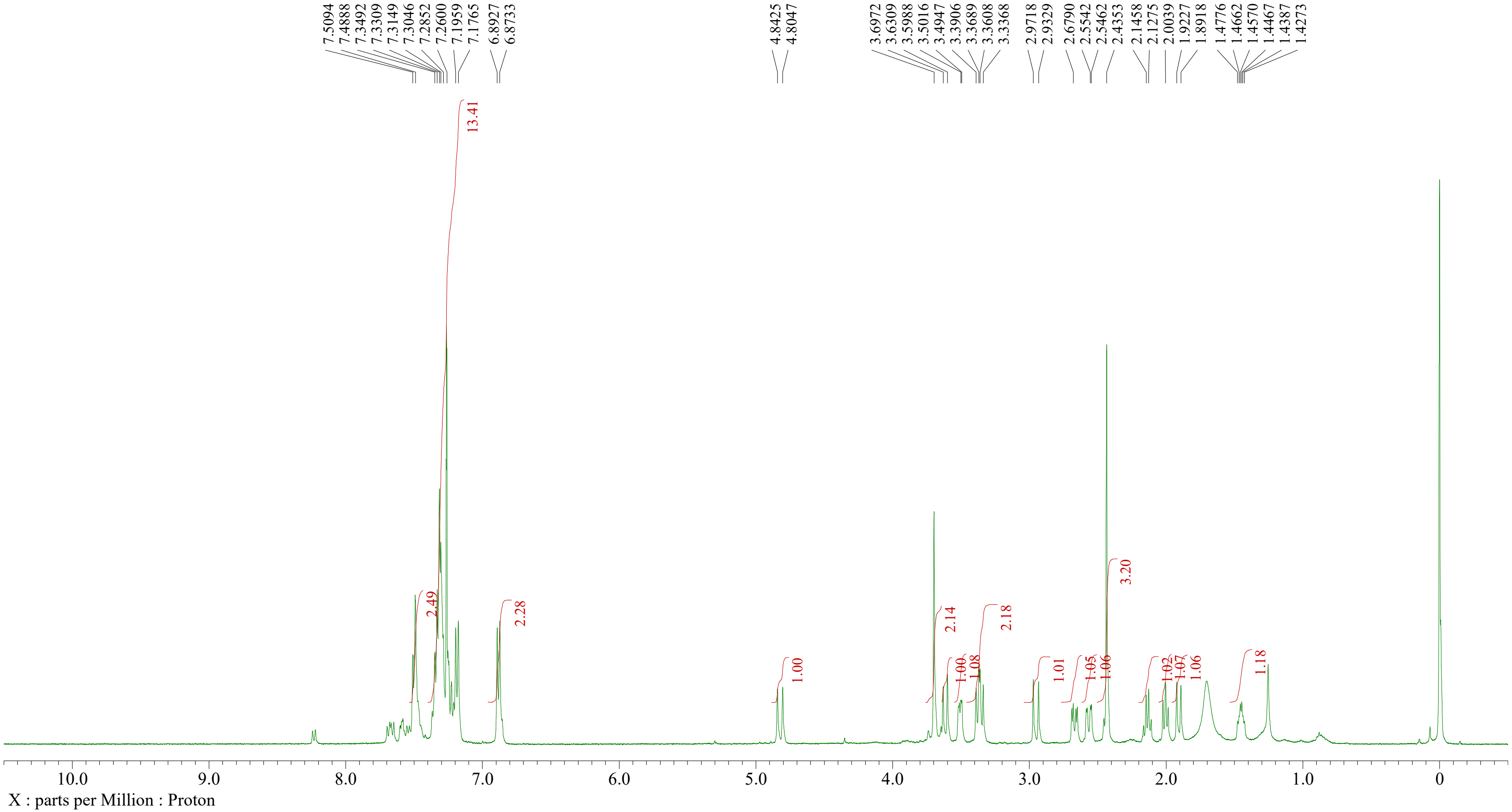


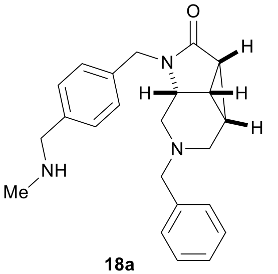


18a

^{1}H-NMR

(400 MHz, $CDCl_3$)

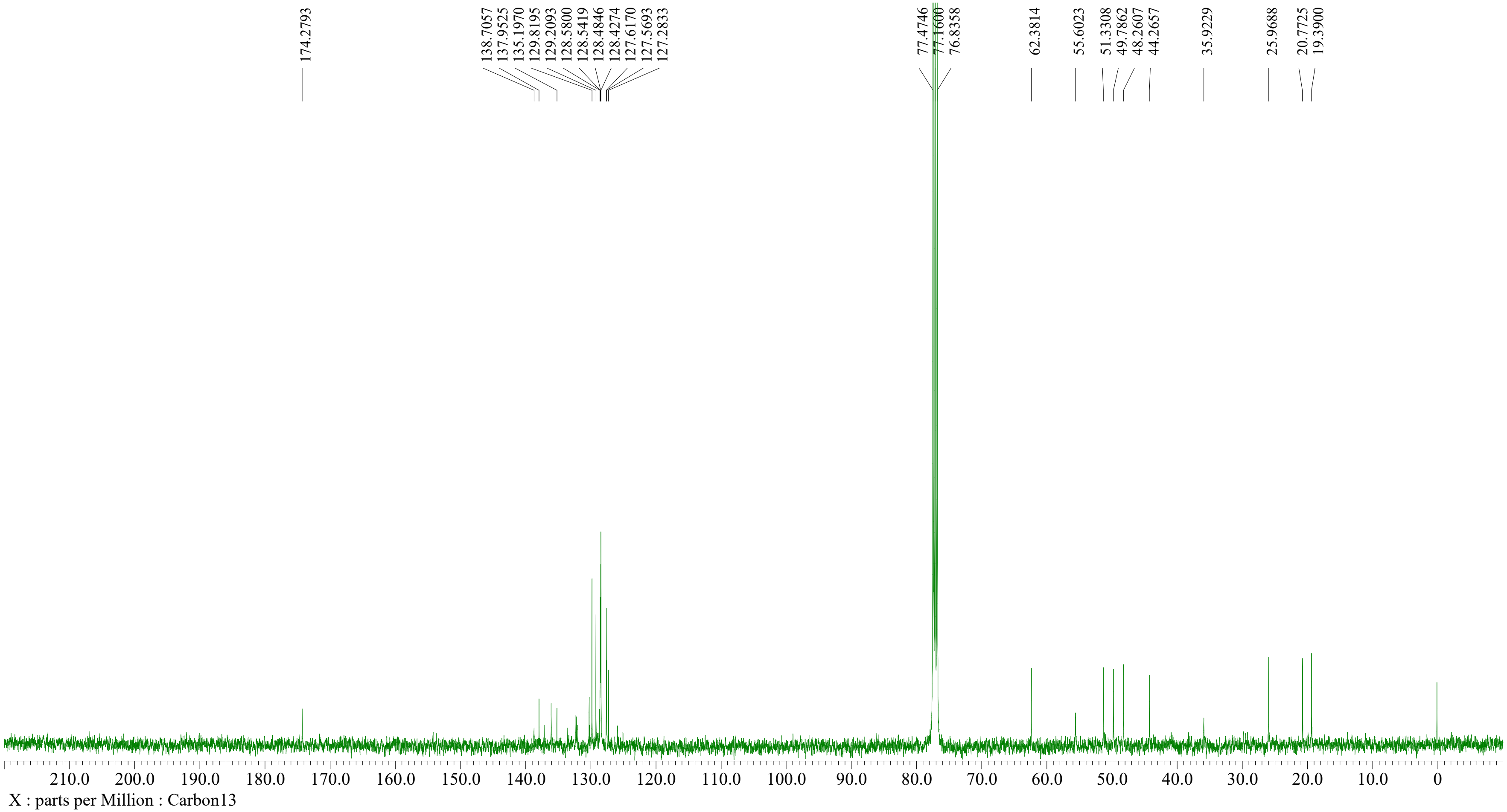


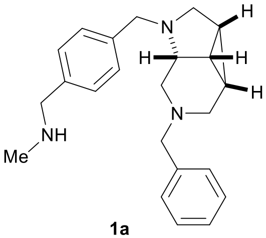


18a

^{13}C-NMR

(100 MHz, $CDCl_3$)

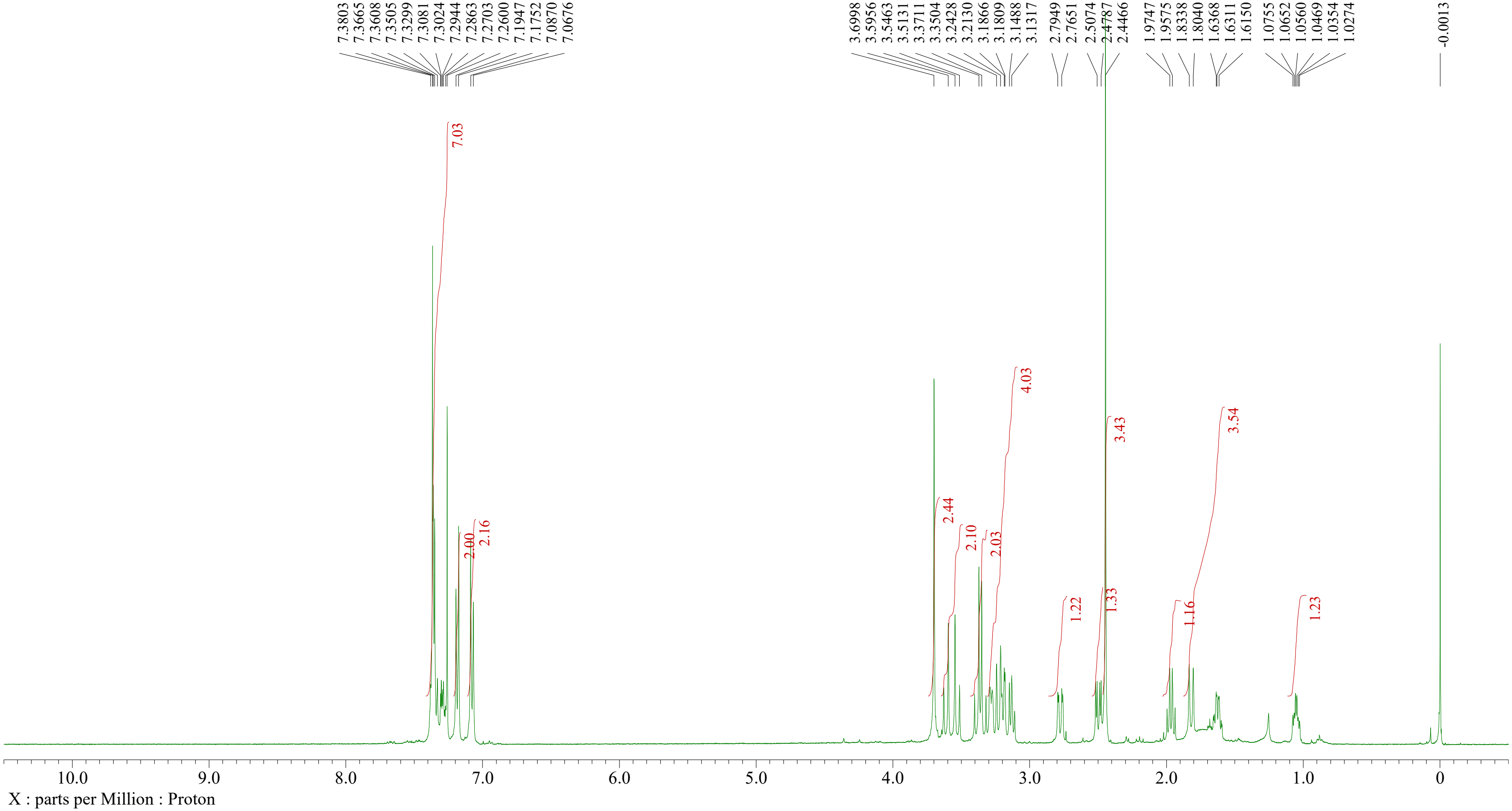


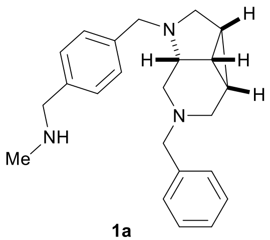


1a

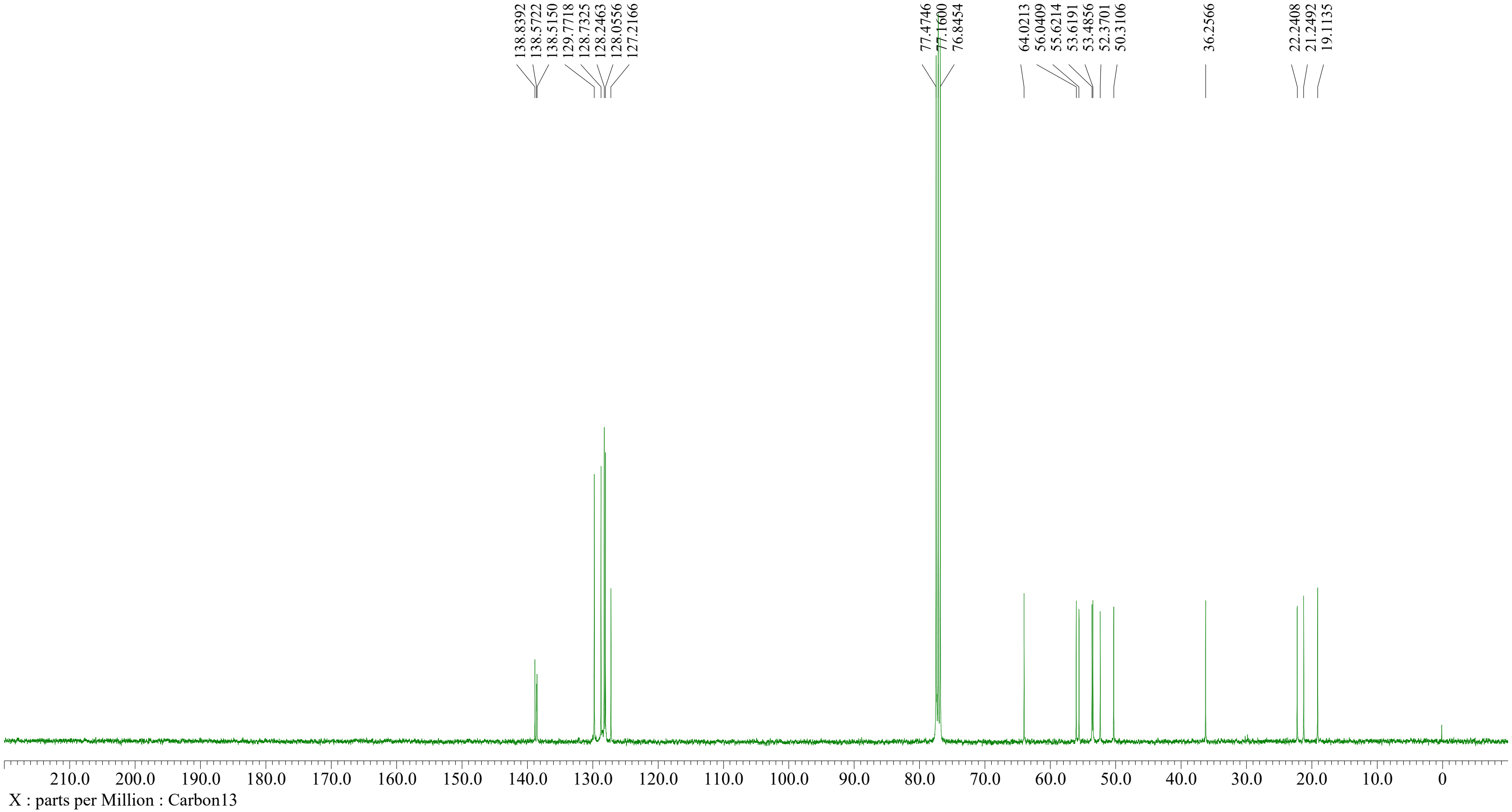
^{1}H-NMR

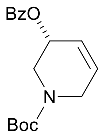
(400 MHz, $CDCl_3$)



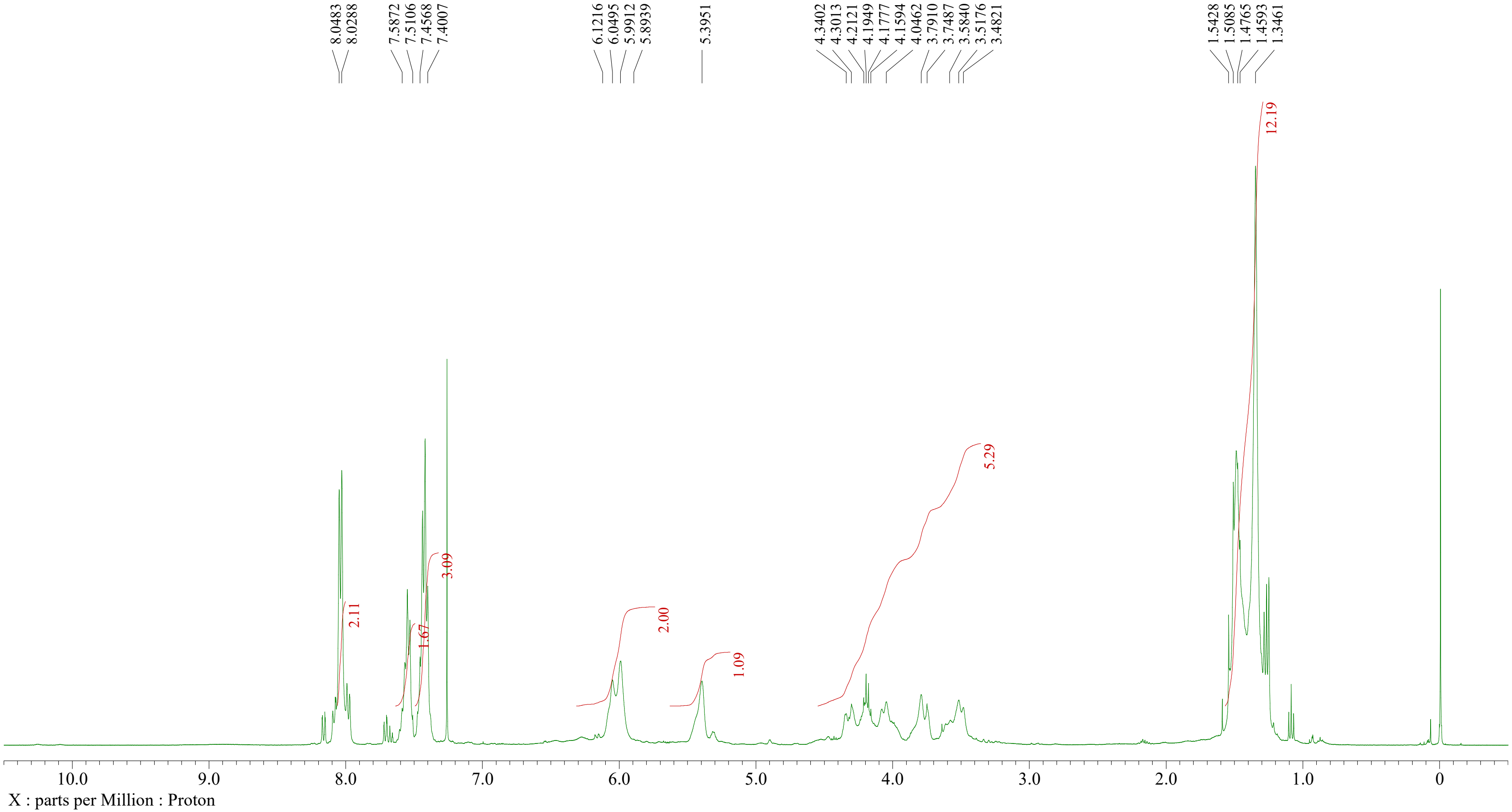


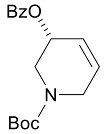
1a
^{13}C-NMR
(100 MHz, $CDCl_3$)





19
^{1}H-NMR
(400 MHz, $CDCl_3$)

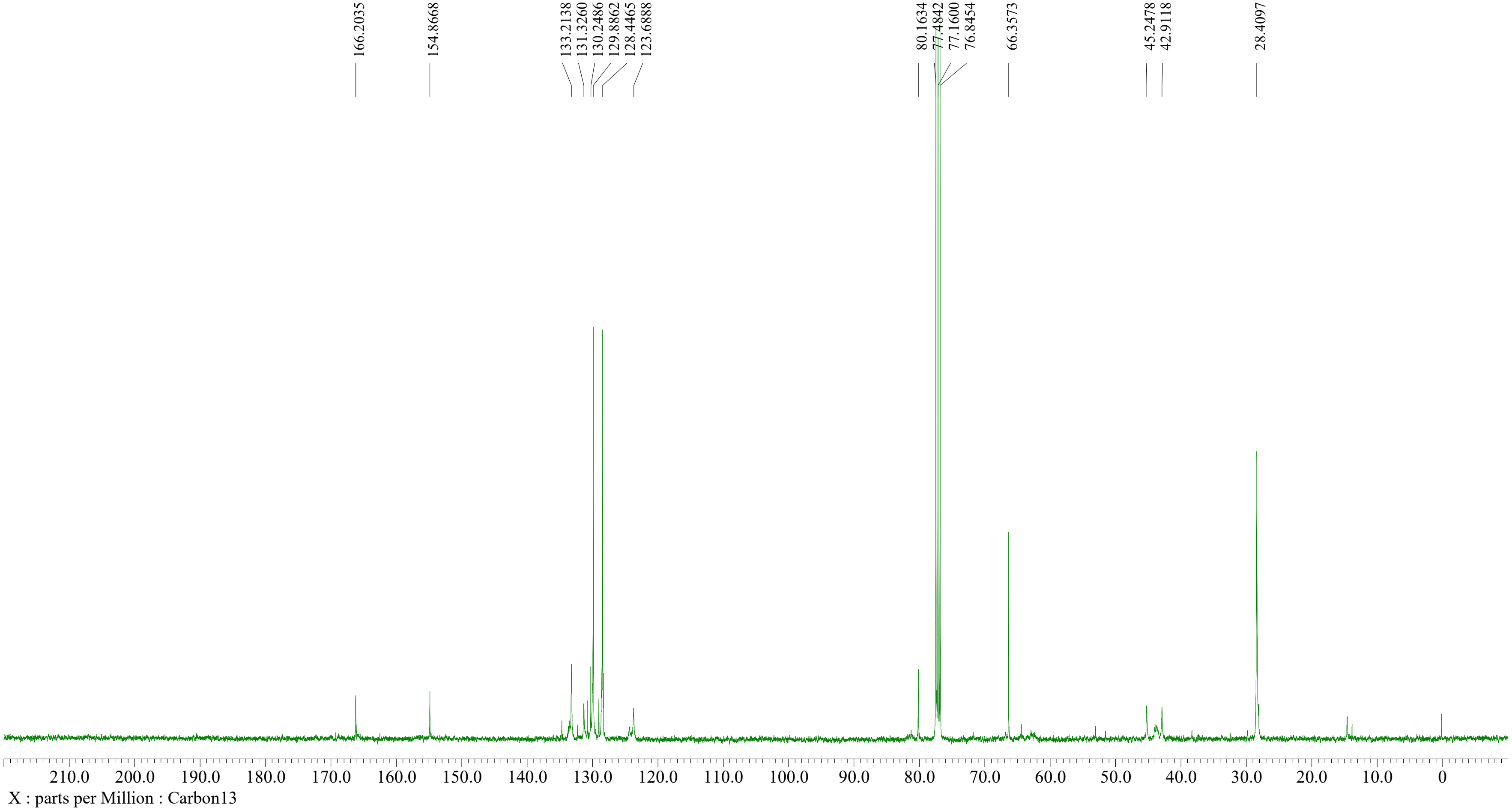


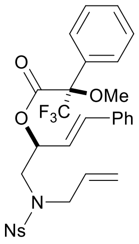


19

^{13}C-NMR

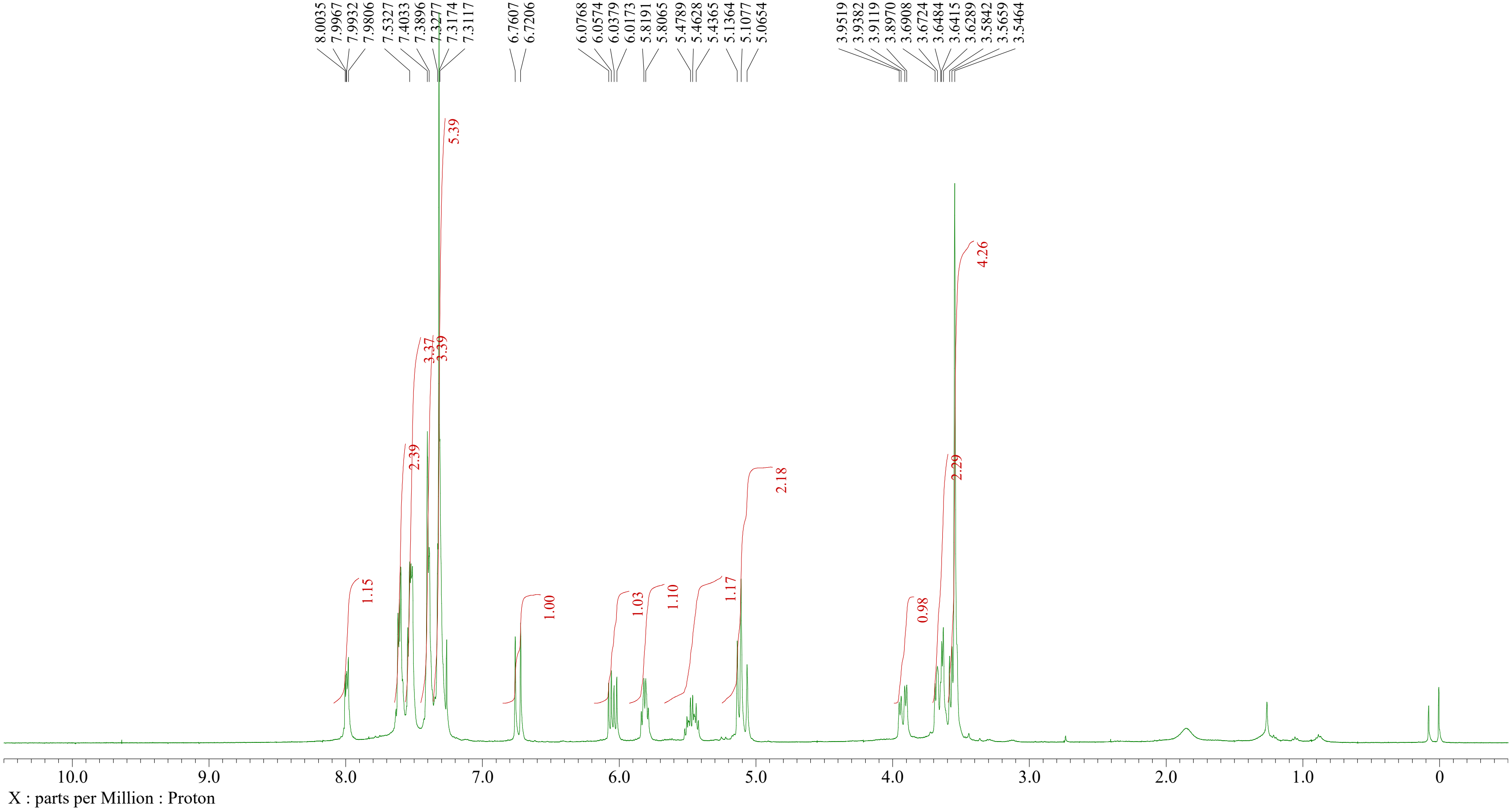
(100 MHz, $CDCl_3$)

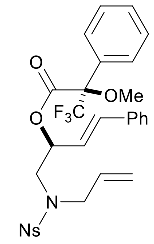




S2

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

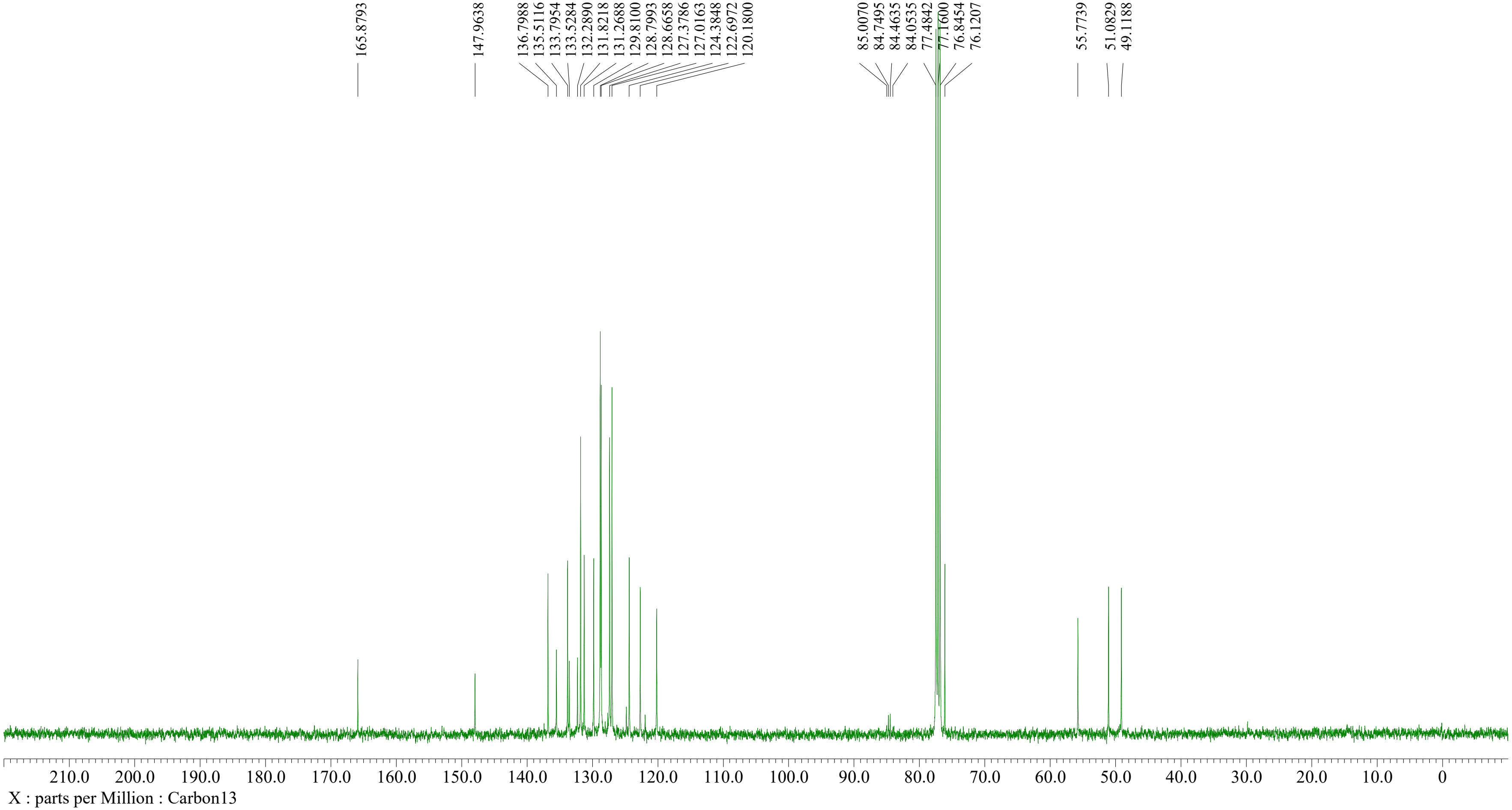


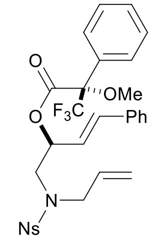


S2

^{13}C-NMR

(100 MHz, $CDCl_3$)

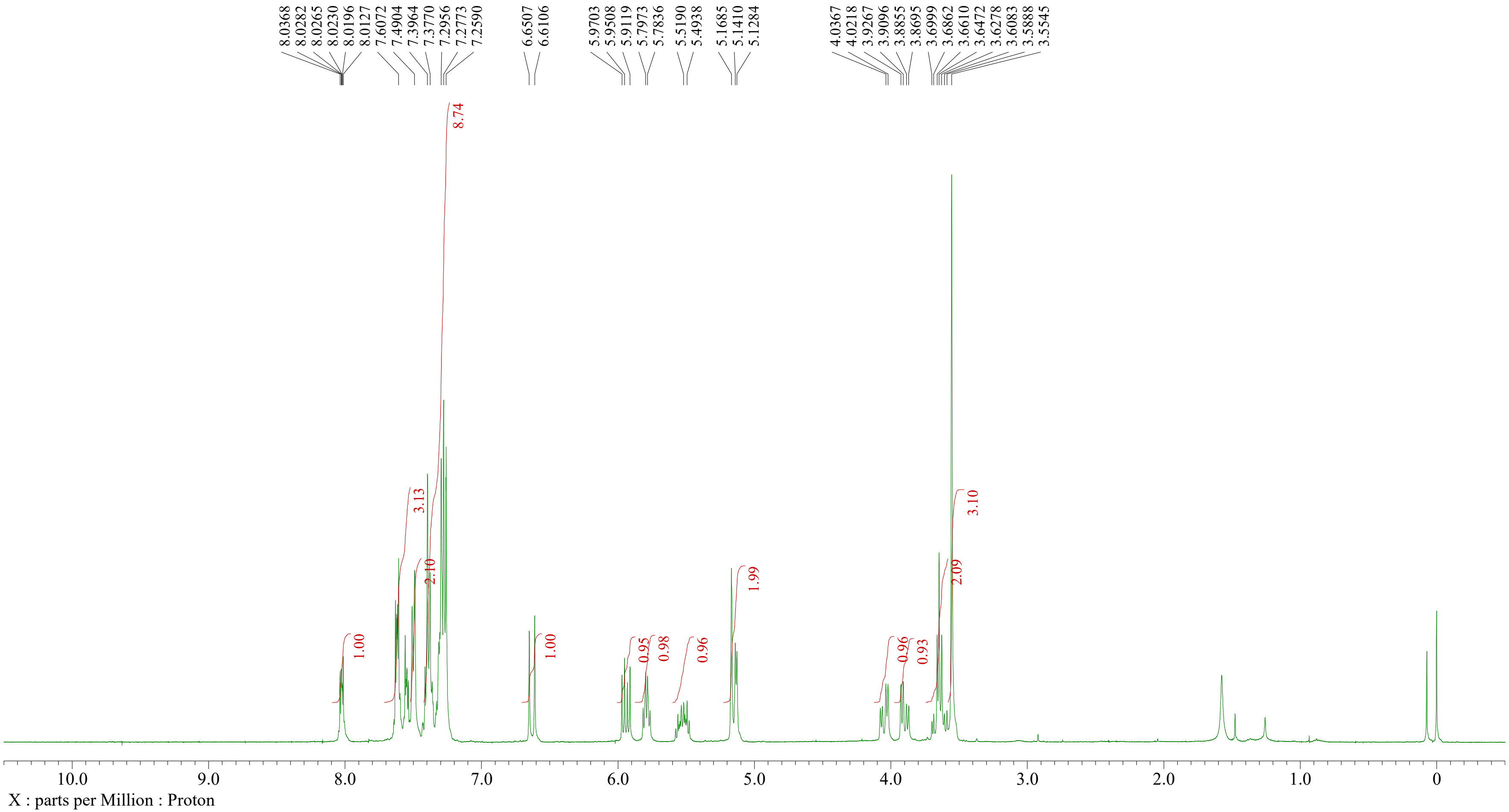


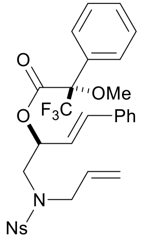


S3

^{1}H-NMR

(400 MHz, CDCl$_3$)





S3

^{13}C-NMR

(100 MHz, $CDCl_3$)