Supplementary Material (ESI) for Chemical Communications

SUPPLEMENTARY INFORMATION

The First Example of Enamine-Lewis Acid Cooperative Bifunctional Catalysis: Application to the Asymmetric Aldol Reaction.

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General Experimental

All ^{1}H NMR were recorded with either of Varian Mercury-400, Bruker Avance-400 or Varian Inova-500 spectrometers. ^{13}C NMR were recorded on Varian Mercury-400, Bruker Avance-400 or Varian Inova-500 spectrometers at frequencies of 100 or 126 MHz. ^{11}B NMR were recorded with the Bruker Avance-400 at a frequency of 128 MHz. ^{19}F NMR were recorded with the Varian inova-500 at a frequency of 500 MHz. Chemical shifts are expressed as parts per million (ppm) downfield from the internal standard TMS for ^{1}H and ^{13}C, to external $BF_3.Et_2O$ for ^{11}B and to $CFCl_3$ for ^{19}F. EI mass spectrometry was performed on a Micromass Autospec, Finnigan MAT 900XLT or Finnigan MAT 95XP with electrospray methods, both +ve and –ve, conducted on a VG platform. IR spectra were recorded on a Perkin-Elmer 298 spectrometer employing NaCl plates or KBr discs. Elemental analysis was performed using an Exeter Analytical E-440 Elemental Analyser. Melting points were determined using an Electrothermal melting point apparatus. TLC was performed on Polygram SIL G/UV_{254} plastic backed silica gel plates with visualization achieved using a UV lamp, or by staining with $KMnO_4$ or vanillin. $[\alpha]_D$ values are given in deg cm^2 g^{-1} and were recorded at the Δ-line of sodium (589 nm) in a 0.05 dm cell. All evaporations were carried out on a Büchi rotary evaporator, followed by drying *in vacuo*. HPLC analyses were performed on a Gilson HPLC system equipped with a Gilson 321 Pump, a Gilson 234 Autoinjector, two Gilson Valvemate, a MetaChem Technologies Degassit degasser, a Gilson UV/Vis Detector 118 using a Chiralcel OJ-H (Daicel) column.

(*S*)-*N*-(1,1-Dimethylethoxycarbonyl)-pinacol-(pyrrolidin-2-yl)methylboronate (*S*)-4

To a stirred solution of (-)-sparteine (1.79 mL, 7.8 mmol) in dry Et_2O (30 mL) under argon at -78 °C, was added *s*-BuLi (5.6 mL, 1.4 M in cyclohexane, 7.8 mmol) dropwise and the solution stirred for 10 min. To this was added N-Boc-pyrrolidine **5** (1.05 mL, 6 mmol) in Et_2O (5 mL) dropwise and the reaction mixture stirred at -78 °C for 4.5 h. Pinacol chloromethylboronate (1.27 g, 7.2 mmol) was added dropwise followed by $ZnCl_2$ (11.4 mL, 1.0 M in Et_2O, 11.4 mmol), the mixture warmed to room temperature and stirred overnight (16 h). The reaction was quenched with 5 % (w/v) HCl (20 mL) and filtered through Celite©. Phases were separated and the aqueous layer extracted into Et_2O (2 × 10 mL). Combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (petroleum ether:EtOAc, 9:1) afforded boronate (*S*)-**4** (1.28 g, 69%) as a colourless oil. $[\alpha]_D^{22}$ +20.0 (*c* 1.00 in CH_2Cl_2); ν_{max} (film) 2976, 1694s, 1397, 1144 cm^{-1}; ^1H NMR (400 MHz; $CDCl_3$) δ 0.80-1.00 (m, 2H), 1.20 (s, 6H), 1.21 (s, 6H), 1.43 (s, 9H), 1.50-1.60 (br m, 1H), 1.65-1.75 (m, 1H), 1.77-1.88 (m, 1H), 1.96-2.04 (m, 1H), 3.20-3.40 (br m, 2H), 3.92 (br s, 1H); ^{13}C NMR (125.7 MHz; $CDCl_3$) δ 18.2, 23.6, 24.6, 28.5, 33.1, 46.1, 54.0, 78.8, 82.8, 154.4; ^{11}B NMR (128.4 MHz; $CDCl_3$) δ 33.0; *m/z* (ES+) 334.2 (100%); HRMS (ES+) $[M+Na]^+$ calcd for $C_{16}H_{30}BNO_4Na^+$ 334.2166; found 334.2160.

(*S*)-*N*-(1,1-Dimethylethoxycarbonyl)-pinacol-(pyrrolidin-2-yl)methylboronate (*S*)-4 **(by homologation)**

To a stirred solution of bromochloromethane (0.12 mL, 1.90 mmol) and (*S*)-**3** (0.47 g, 1.58 mmol) in dry THF (20 mL) under argon at -78 °C was added *n*-BuLi (0.88 mL, 2.5 M, 2.21 mmol) dropwise. The mixture was stirred for 1 h at -78 °C. $ZnCl_2$ (0.95 mL, 1.0 M in Et_2O, 0.95 mmol) was then added, the mixture warmed to room temperature and stirred overnight (16 h). The reaction was quenched with 5 % (w/v) HCl (10 mL) and extracted into Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (15 mL), dried over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (petroleum ether:EtOAc, 9:1) afforded boronate (*S*)-**4** (0.13 g, 26%) as a colourless oil. Analytical and spectroscopic properties were identical to those reported above.

***N*-(1,1-Dimethylethoxycarbonyl)-pinacol-(pyrrolidin-2-yl)methylboronate racemic** 4

To a stirred solution of *N*-Boc-pyrrolidine **5** (0.35 mL, 2 mmol) and TMEDA in dry Et_2O (15 mL) under argon at -78 °C, *s*-BuLi (1.9 mL, 1.4 M, 2.6 mmol) was added dropwise and the reaction mixture stirred at -78 °C for 4 h. Pinacol chloromethylboronate (0.42 g, 2.4 mmol) was added dropwise followed by $ZnCl_2$ (3.8 mL, 1.0 M in Et_2O, 3.8 mmol), the mixture warmed to room temperature and stirred overnight (18 h). The reaction was quenched with 5% (w/v) HCl (10 mL) and filtered through Celite©. Phases were separated and the aqueous layer extracted into Et_2O (2 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried

over $MgSO_4$ and concentrated *in vacuo*. Silica gel chromatography (petroleum ether:EtOAc, 9:1) afforded racemic boronate **4** (0.44 g, 71%) as a colourless oil. Analytical and spectroscopic properties were identical to those reported above.

(*S*)-*N*-(1,1-Dimethylethoxycarbonyl)-(pyrrolidin-2-yl)methylboronic acid (*S*)-6

To a stirred solution of (*S*)-**4** (1.16 g, 3.73 mmol) in Et_2O (10 mL) was added diethanolamine (4.1 mL, 1.0 M in isopropanol, 4.1 mmol). The solvent was removed *in vacuo* and pinacol removed by distillation at reduced pressure (4 mbar). After cooling, the resulting glassy solid was stirred in THF (7 mL) and 5% (w/v) HCl (7 mL) for 50 min. Another portion of 5% (w/v) HCl (3 mL) was added and the mixture extracted into Et_2O (3 × 10 mL). The combined organic extracts were washed with brine (10 mL), dried over $MgSO_4$ and concentrated *in vacuo* to afford boronic acid (*S*)-**6** (0.48 g, 56%) as a white solid. Slow re-crystallisation from THF afforded crystals suitable for X-ray analysis. Mp 99-100 °C; $[\alpha]_D^{22}$ -60.0 (*c* 1.00 in CH_2Cl_2); IR (film) 3386, 2974, 1691, 1400, 1167cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.22 (m, 2H), 1.45 (s, 9H), 1.55-1.65 (br m, 1H), 1.68-2.08 (br m, 3H), 3.31 (m, 2H), 4.11 (br m, 1H), 6.81 (br s, 2H); ^{13}C NMR (125.7 MHz; $CDCl_3$) δ 23.1, 28.4, 34.4, 46.2, 54.0, 80.5, 156.9; ^{11}B (128.4 MHz; $CDCl_3$) δ 32.1; *m/z* (ES+) 656.4 (100%, [boroxine+Na]$^+$); Elemental anal. calc. for $C_{10}H_{20}BNO_4$: C, 52.43; H, 8.80; N, 6.11. Found: C, 53.02; H, 8.76; N, 5.67.

(*S*)-(Pyrrolidinium-2-yl)-methylboronic acid trifluoroacetate (*S*)-2.TFA

(*S*)-**6** (141 mg, 0.62 mmol) was stirred at reflux in TFA:DCM (1:1, 5 mL) for 2 h. The mixture was cooled to room temperature and concentrated *in vacuo*. The residue was redissolved in DCM (5 mL) and concentrated *in vacuo*. Azeotroping of TFA with DCM was repeated a further three times to afford (*S*)-(pyrrolidinium-2-yl)-methylboronic acid trifluoroacetate (*S*)-**2**.TFA (140.3 mg, 93%) as a brown oil. $[\alpha]_D^{22}$ –53.7 (*c* 0.44 in H_2O); IR (film)/ 2982, 1671, 1392, 1182, 1135; ^{1}H NMR (500 MHz; D_2O) δ 1.15 (unsymmetrical dd, *J* = 15.7, 8.9 Hz, 1H), 1.28 (unsymmetrical dd, *J* = 15.7, 6.5 Hz, 1H), 1.49-1.58 (m, 1H), 1.85-2.04 (m, 2H), 2.12-2.20 (m, 1H), 3.15-3.27 (m, 2H), 3.59-3.67 (m, 1H); ^{13}C NMR (125.7 MHz; D_2O) δ 18.2, 23.2, 31.6, 44.8, 58.3, 116.4 (q, J = 291.5 Hz), 163.1 (q, J = 35.6); ^{11}B NMR (128.4 MHz; $CDCl_3$) δ 30.6; ^{19}F (470.3 MHz; D_2O) δ –76; *m/z* (ES+ in CH_3CN/MeOH) 129.1 [30%, M^+ (^{10}B)], 130.1 [100%, M^+(^{10}B)]; HRMS (ES+) [M^+ (^{10}B)] calcd for $C_5H_{13}BNO_2^+$ 129.1070; found 129.1071.

(*S*)-(Pyrrolidinium-2-yl)-methylboronic acid chloride (*S*)-2.HCl

(*S*)-**4** (0.63 g, 2.02 mmol) was stirred at reflux with 20% (w/v) HCl (7 mL) for 2 h. The mixture was cooled to room temperature, washed with Et_2O (2 × 10 mL) and concentrated *in vacuo*. The residue was redissolved in water (1 mL), toluene (5 mL) was added and the mixture concentrated *in vacuo*. Azeotroping with toluene was

repeated a further three times to afford (*S*)-(pyrrolidinium-2-yl)-methylboronic acid chloride (*S*)-**2**.HCl (0.32 g, 96%) as a pale brown oil. $[\alpha]_D^{22}$ +20.0 (*c* 1.00 in H_2O); IR (film)/ 3299, 2975, 1597, 1385, 1215, 1021; ^{1}H NMR (400 MHz; D_2O) δ 1.21 (unsymmetrical dd, *J* = 15.6, 8.8 Hz, 1H), 1.34 (unsymmetrical dd, *J* = 15.6, 6.4 Hz, 1H), 1.54-1.64 (m, 1H), 1.90-2.10 (m, 2H), 2.17-2.25 (m, 1H), 3.21-3.33 (m, 2H), 3.65-3.73 (m, 1H); ^{13}C NMR (125.7 MHz; D_2O) δ 18.4, 23.1, 31.5, 44.8, 58.3; ^{11}B NMR (128.4 MHz; D_2O) δ 30.7; *m/z* (ES+) 130.1 (80%); HRMS (ES+) [M^+ (^{11}B)] calcd for $C_5H_{13}BNO_2^+$ 130.1034; found 130.1033.

(*S*)-Pinacol-(pyrrolidinium-2-yl)-methylboronic acid chloride (*S*)-7.HCl

A mixture of (*S*)-**2**.HCl (0.13 g, 0.79 mmol) and pinacol (92.9 mg, 0.79 mmol) in $CHCl_3$ (30 mL), was stirred vigorously at room temperature for 3 h and then concentrated *in vacuo*. Recrystallisation from acetone afforded (*S*)-pinacol-(pyrrolidinium-2-yl)-methylboronic acid chloride, (*S*)-**7**.HCl (0.09 g, 46%) as a white crystalline solid, with crystals suitable for X-ray analysis. Mp 202-203 °C; $[\alpha]_D^{22}$ +20.0 (*c* 1.00 in CH_2Cl_2); IR (film) 3392, 2979, 1636, 1380, 1145 cm^{-1}; ^{1}H NMR (400 MHz; $CDCl_3$) δ 1.21 (s, 12H), 1.35-1.43 (m, 1H), 1.56-1.64 (m, 2H), 1.89-2.12 (m, 2H), 2.20-2.30 (m, 1H), 3.22-3.44 (m, 2H), 3.65-3.77 (m, 1H), 9.03 (bs, 1H), 9.82 (bs, 1H); ^{13}C (100.6 MHz; $CDCl_3$) δ 23.4, 24.7, 24.9, 31.9, 44.1, 57.7, 83.8; ^{11}B (128.4 MHz; $CDCl_3$) δ 32.1; *m/z* (ES+) 212.2 (100%, $[M+H]^+$); Elemental anal. calc. for $C_{11}H_{22}BNO_2$: C, 53.37; H, 9.36; N, 5.66. Found: C, 53.24; H, 9.28; N, 5.43.

***N*-(1,1-Dimethylethoxycarbonyl)-(2-hydroxymethyl)-pyrrolidine (*R*)-8**

(*S*)-**4** (0.52 g, 1.67 mmol) was dissolved in THF (5 mL), cooled to 0 °C with an ice bath and treated with NaOH (1.8 mL, 3 N solution). Hydrogen peroxide (500 μL, 30% w/v solution) was then added and the mixture heated at reflux for 6.5 h. The solution was then cooled, diluted with brine and extracted with Et_2O (6 × 10 mL). The combined organic phase was then dried over $MgSO_4$ and concentrated *in vacuo*. Successive silica gel chromatography purifications (DCM:MeOH, 10:1, followed by PetEther:Ethyl Acetate 1:1) afforded (*R*)-**8** (0.22 g, 66%) as a white solid. $[\alpha]_D^{22}$ +50.8 (*c* 1.17 in $CHCl_3$). The other analytical and spectroscopic properties were identical to those reported in the literature.[1]

(*S*)-(Pyrrolidinium-2-yl)-methylboronic acid bromide (*S*)-2.HBr

(*S*)-**4** (48 mg, 0.2 mmol) was stirred at reflux with 20% (w/v) HBr (5 mL) for 2 h. The mixture was cooled to room temperature, washed with Et_2O (2 × 10 mL) and concentrated *in vacuo*. The residue was redissolved in water (1 mL), toluene (5 mL) was added and the mixture concentrated *in vacuo*. Azeotroping with toluene was repeated a further three times to afford (*S*)-(pyrrolidinium-2-yl)-methylboronic acid bromide (*S*)-**2**.HBr (44 mg, 100%) as a dark brown oil. $[\alpha]_D^{22}$ +166 (*c* 0.44 in H_2O); IR (film)/ 3299, 2984, 1620, 1367, 1218, 1013; ^{1}H

NMR (400 MHz; D_2O) δ 1.21 (unsymmetrical dd, *J* = 15.8, 9 Hz, 1H), 1.34 (unsymmetrical dd, *J* = 15.8, 6.8 Hz, 1H), 1.54-1.64 (m, 1H), 1.9-2.1 (m, 2H), 2.18-2.25 (m, 1H), 3.21-3.33 (m, 2H), 3.65-3.73 (m, 1H); ^{13}C NMR (125.7 MHz; D_2O) δ 18.7, 23.2, 31.6, 44.9, 58.3; ^{11}B NMR (128.4 MHz; $CDCl_3$) δ 30.2; *m/z* (ES+ in CH_3CN/MeOH) 158.1 (93%, [M+2×MeOH]), 144.1 (100%, [M+MeOH]), 130.1 (30%); HRMS (ES+) [M^+] calcd for $C_5H_{13}BNO_2^+$ 130.1034; found 130.1035.

(*S*)-(Pyrrolidinium-2-yl)-methylboronic acid iodide (*S*)-2.HI

(*S*)-**4** (83 mg, 0.2 mmol) was stirred at reflux with 28% (w/v) HI (5 mL) for 2 h. The mixture was cooled to room temperature, washed with Et_2O (2 × 10 mL) and concentrated *in vacuo*. The residue was redissolved in water (1 mL), toluene (5 mL) was added and the mixture concentrated *in vacuo*. Azeotroping with toluene was repeated a further three times to afford (*S*)-(pyrrolidinium-2-yl)-methylboronic acid iodide (*S*)-**2**.HI (150 mg, *ca*. 100%) as a crude yellow oil. $[\alpha]_D^{22}$ – 92.3 (*c* 52.0 in H_2O); IR (film)/ 2984, 1623, 1389, 993; ^1H NMR (400 MHz; D_2O) δ 1.04 (unsymmetrical dd, *J* = 15.7, 8.9 Hz, 1H), 1.13 (unsymmetrical dd, *J* = 15.7, 6.5 Hz, 1H), 1.33-1.45 (m, 1H), 1.69-1.89 (m, 2H), 1.96-2.05 (m, 1H), 3.00-3.14 (m, 2H), 3.44-3.54 (m, 1H); ^{13}C NMR (125.7 MHz; D_2O) δ 18.1, 23.1, 31.5, 44.8, 58.2; ^{11}B NMR (128.4 MHz; $CDCl_3$) δ 30.2; *m/z* (ES+ in CH_3CN/MeOH) 158.2 (7%, [M+2×MeOH]), 144.1 (28%, [M+MeOH]), 130.1 (100%); HRMS (ES+) [M^+] calcd for $C_5H_{13}{}^{10}BNO_2^+$ 129.1070; found 129.1070.

General Procedures for the Aldol Reactions

4-Hydroxy-4-(p-nitrophenyl)-butan-2-one **9**. (*S*)-**2**.HCl (0.2 mmol, 20 mol%), *p*-nitrobenzaldehyde (151 mg, 1 mmol), triethylamine (28 μL, 0.2 mmol) and acetone (10 mL) were stirred at room temperature for the appropriate time. The reaction was quenched with sat. aq. NH_4Cl (10 mL) and extracted into EtOAc (2 × 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated in vacuo. Silica gel chromatography (petroleum ether:EtOAc, 7:3) afforded **9** as a yellow oil and **10** as a yellow solid. Analytical and spectroscopic properties were identical to those reported in the literature.[2]

General Procedures for the Aldol Reactions using boronate esters

4-Hydroxy-4-(p-nitrophenyl)-butan-2-one **9**. (*S*)-**2**.HCl (0.05 mmol, 20 mol%) and diol (0.05 mmol) were stirred in acetone (2.5 ml) for 1 h before triethylamine (7 μl, 0.05 mmol) and *p*-nitrobenzaldehyde (38 mg, 0.25 mmol)l) were added. After stirring at room temperature for the appropriate time the reaction was quenched with sat. aq. NH_4Cl (5 mL) and extracted into EtOAc (2 × 10 mL). Combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo*. Analytical and spectroscopic properties were identical to those reported in the literature.[2]

X-Ray Crystallography.

Single-crystal diffraction experiments (Table 1) were carried out on a Siemens 3-circle diffractometer with a SMART 1K CCD area detector, using graphite-monochromated Mo-K_α radiation (λ=0.71073 Å) and an Oxford Cryosystems open-flow N_2 cryostat. The structures were solved by direct methods and refined by full-matrix least squares against F^2 of all data, using SHELXTL software.[3] In (*S*)-**6** all non-hydrogen atoms were refined in anisotropic, all H atoms in isotropic approximation, the absolute configuration was assigned by inference. Crystals of (*S*)-**6** undergo a phase transition between 160 and 175 K, whereupon they turn polycrystalline. At 200 K, the pinacol moiety is disordered between two conformations with estimated occupancies of 85% and 15% (Fig. S1). Non-hydrogen atoms were refined in anisotropic (major component) and isotropic (minor component), with 'riding' H atoms. The asymmetric unit comprises one cation and two halves of Cl^- anions (both of which lie on a crystallographic twofold axis); two anions and two cations are hydrogen-bonded into a closed unit. The absolute configuration of **7** was determined from anomalous scattering of Cl, by refining the Flack parameter[4] which converged at 0.09(8). Given the relatively low inversion-distinguishing power,[5] we repeated the experiment on another crystal, which gave the same absolute structure with the Flack parameter of 0.12(12). Full crystallographic data, excluding structure factors, have been deposited at the Cambridge Crystallographic Data Centre.

X-ray diffraction experiment: SMART 1K CCD area detector diffractometer, graphite-monochromated Mo-K_α radiation ($\bar{\lambda}$=0.71073 Å), computations: SHELXTL 6.14 software, Bruker AXS, Madison WI, USA, 2003. *Crystal data*: (*S*)-**6**, $C_{10}H_{20}BNO_4$, *M*=229.08, *T*=120 K, orthorhombic, space group $P2_12_12_1$ (no 19), *a*=9.3385(9), *b*=11.500(1), *c*=12.064(1) Å, *U*=1295.6(2) Å^3, *Z*=4, D_c=1.174 g cm^{-3}, μ=0.09 mm^{-1}, 13209 reflections (1968 unique+1466 Friedels), R_{int}=0.037, *R(F)*=0.031 [$I \geq 2\sigma(I)$], w$R(F^2)$=0.077, CCDC-666984; (*S*)-**7**, $C_{11}H_{23}BNO_2^+Cl^-$, *M*=229.08, *T*=200 K (phase transition between 160 and 175 K), monoclinic, space group *C*2 (no 5), *a*=22.004(4), *b*=6.598(1), *c*=10.039(2) Å, β=93.68(1)°, *U*=1454.5(5) Å^3, *Z*=4, D_c=1.131 g cm^{-3}, μ=0.25 mm^{-1}, 8899 reflections (1821 unique+1527 Friedels), R_{int}=0.022, *R(F)*=0.051 [$I \geq 2\sigma(I)$], w$R(F^2)$=0.132, Flack parameter 0.09(8) [0.12(12) from second sample], CCDC-666985.

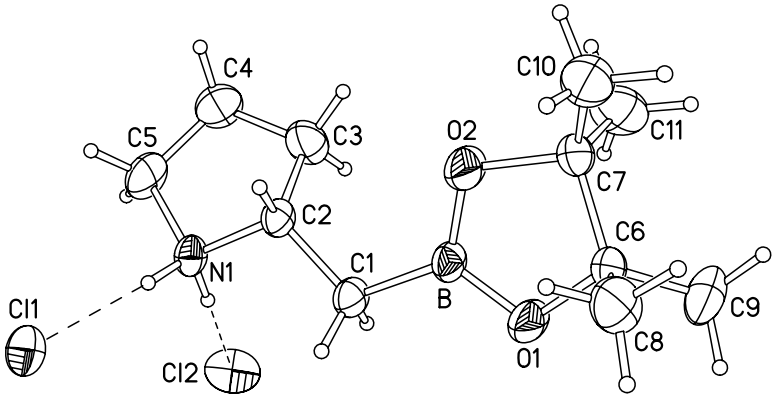

Fig. 2 Principal conformation of (*S*)-**7**.HCl (50% probability thermal ellipsoids). $Cl(1)^-$ and $Cl(2)^-$ anions lie on crystallographic twofold axes [½ *y* 0] and [½ *y* ½] and link cations into a zig-zag chain parallel to the *z* axis.

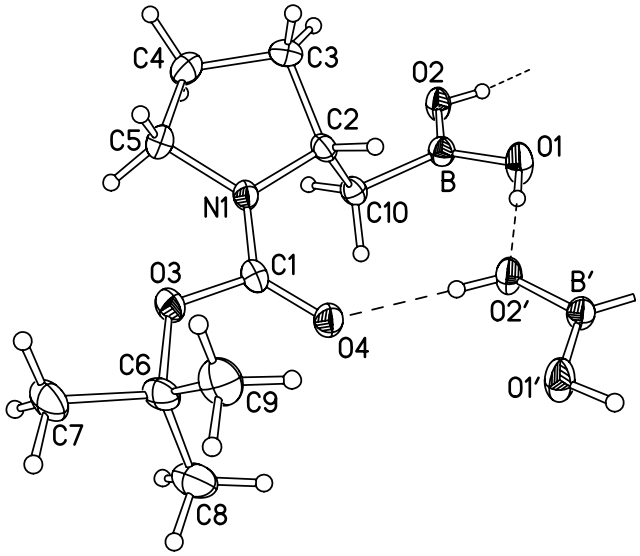

Fig. 1 X-ray molecular structure (*S*)-**6** showing 50% probability thermal ellipsoids (symmetry transformation for primed atoms: *x*+½, ½−*y*, 1−*z*. Molecules are hydrogen-bonded into a chain parallel to the *x* axis.

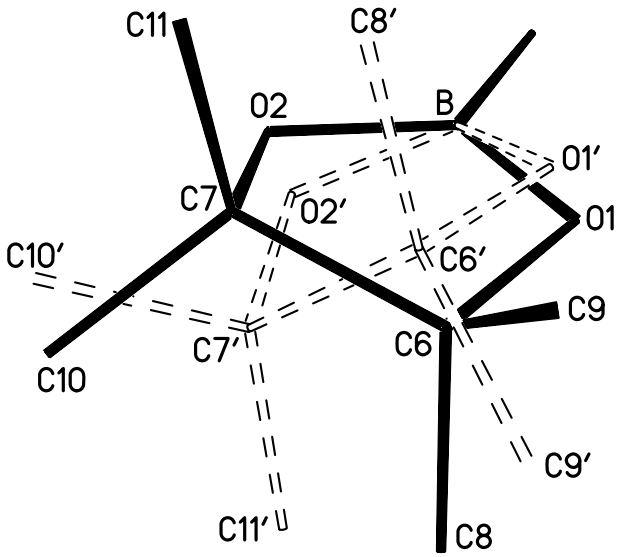

Fig. 3 Disorder of the moiety in (*S*)-**7**

Table 1. Crystal data

Compound	(*S*)-**6**	(*S*)-**7**
CCDC dep. no.	666984	666985
Formula	$C_{10}H_{20}BNO_4$	$C_{11}H_{23}BNO_2^+Cl^-$
Formula weight	229.08	247.56
T, K	120	200
Symmetry	orthorhombic	monoclinic
Space group	$P2_12_12_1$ (# 19)	$C2$ (# 5)
a, Å	9.3385(9)	22.004(4)
b, Å	11.500(1)	6.598(1)
c, Å	12.064(1)	10.039(2)
β, °	90	93.68(1)
V, Å^3	1295.6(2)	1454.5(5)
Z,	4	4
D_x, g/cm^3	1.174	1.131
Refls collected	13209	8899
Unique refls	3434, 1968[a]	3349, 1821[a]
R_{int}[a], %	3.7	2.2
R_1, wR_2, %[b]	3.1, 7.7	5.1, 13.2

[a] With Friedel equivalents merged.

[b] $R_1=\Sigma||F_o| - |F_c||/\Sigma|F_o|$ for reflections with $I>2\sigma(I)$; $wR_2=\{\Sigma[w(F_o^2 - F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$

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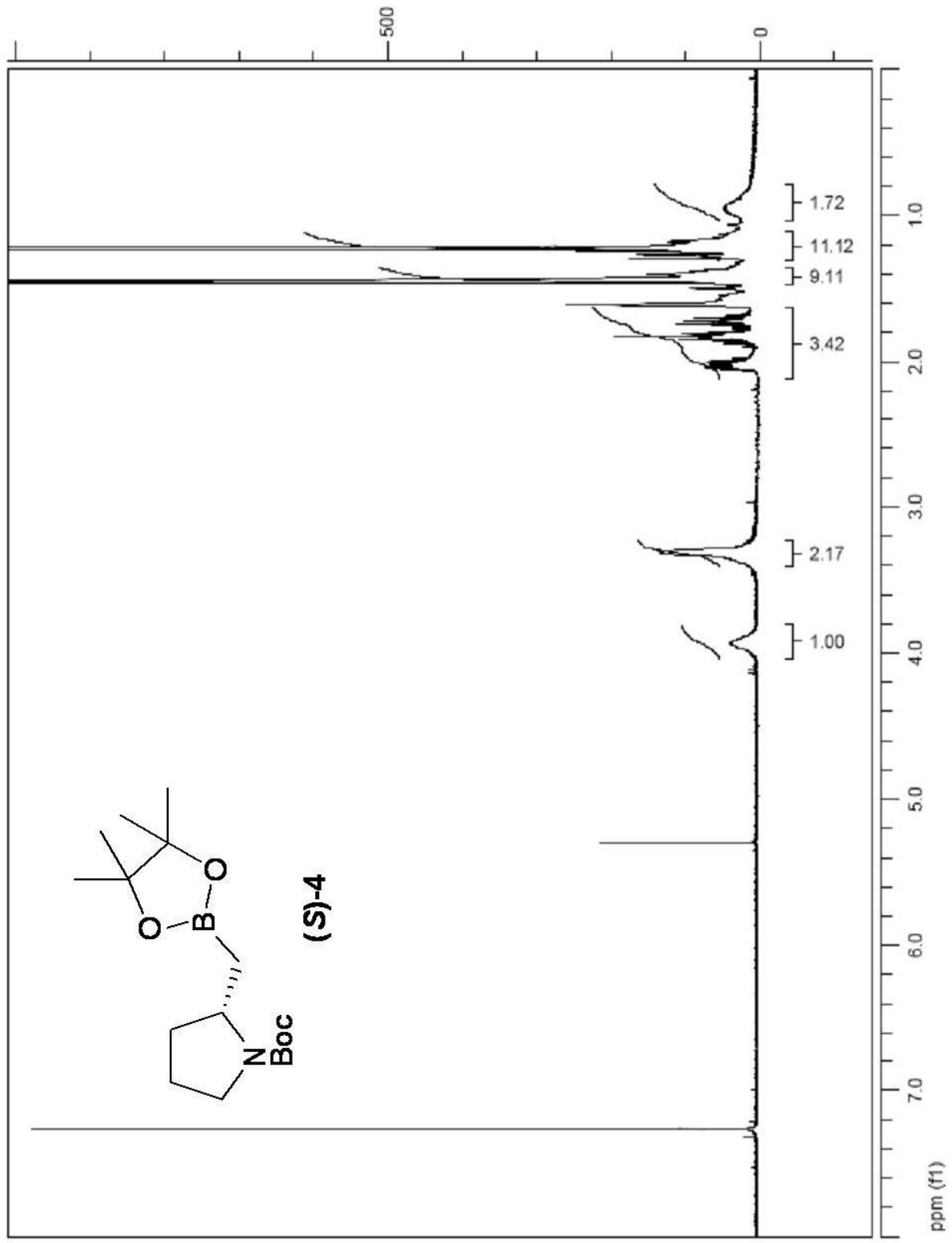
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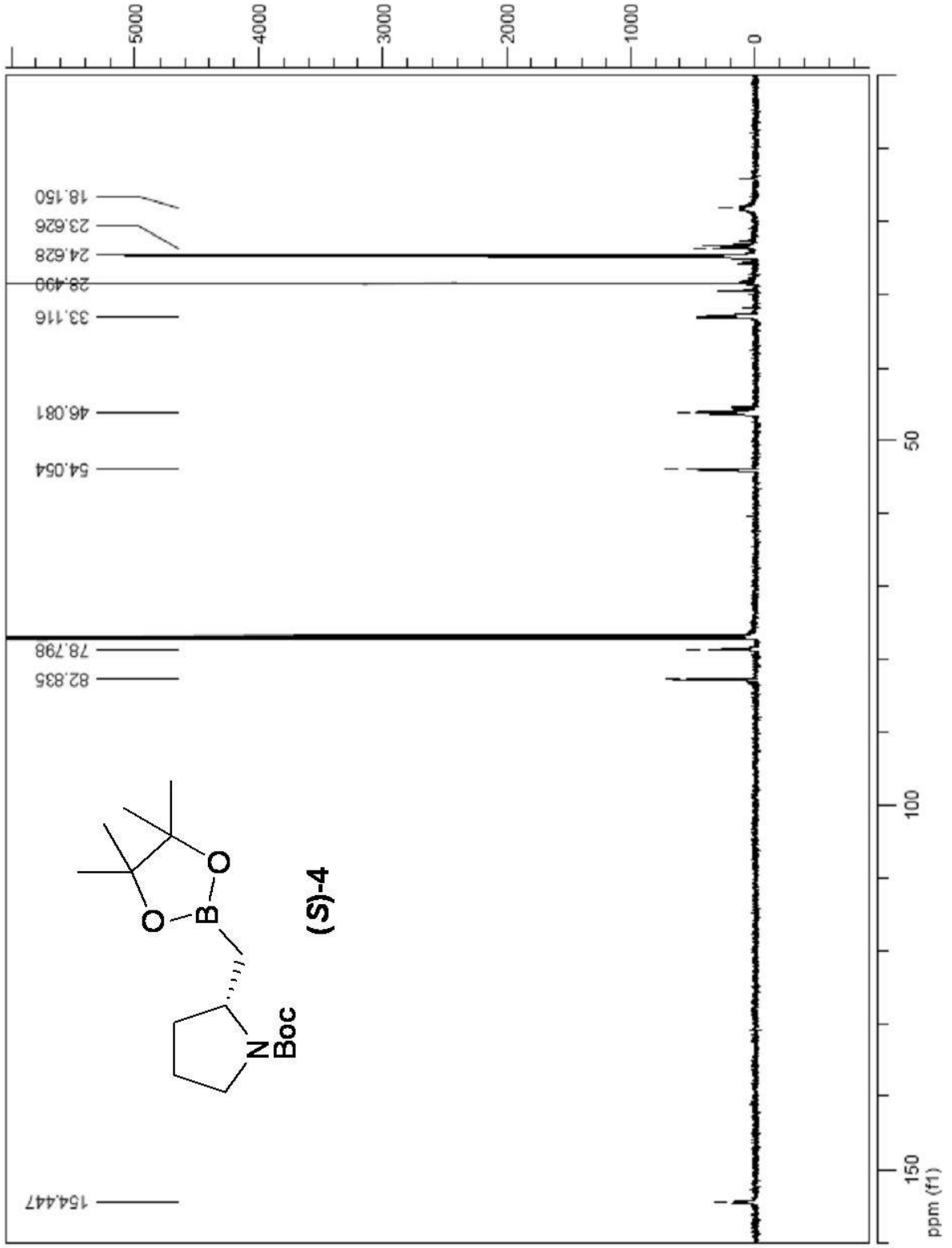
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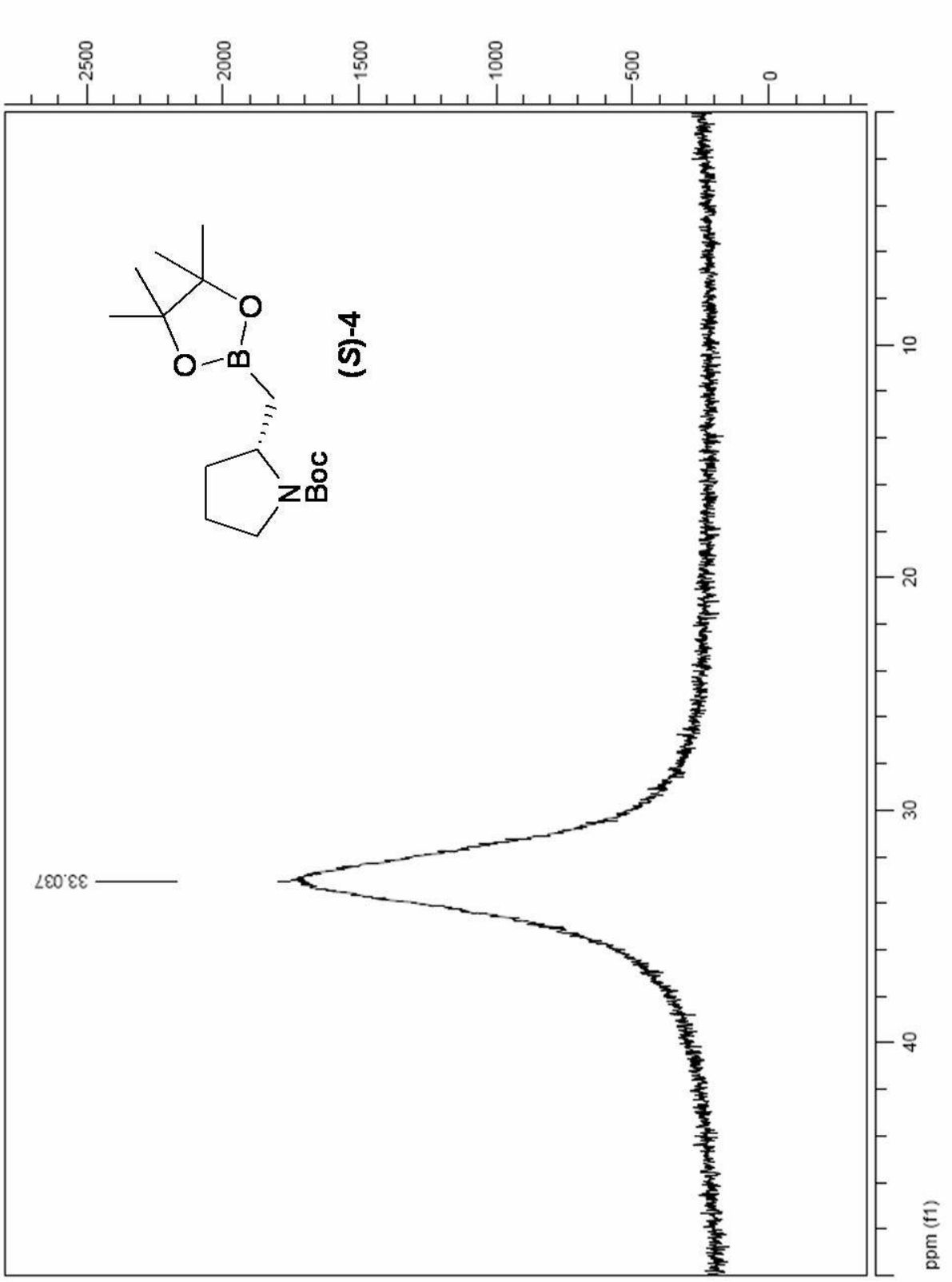
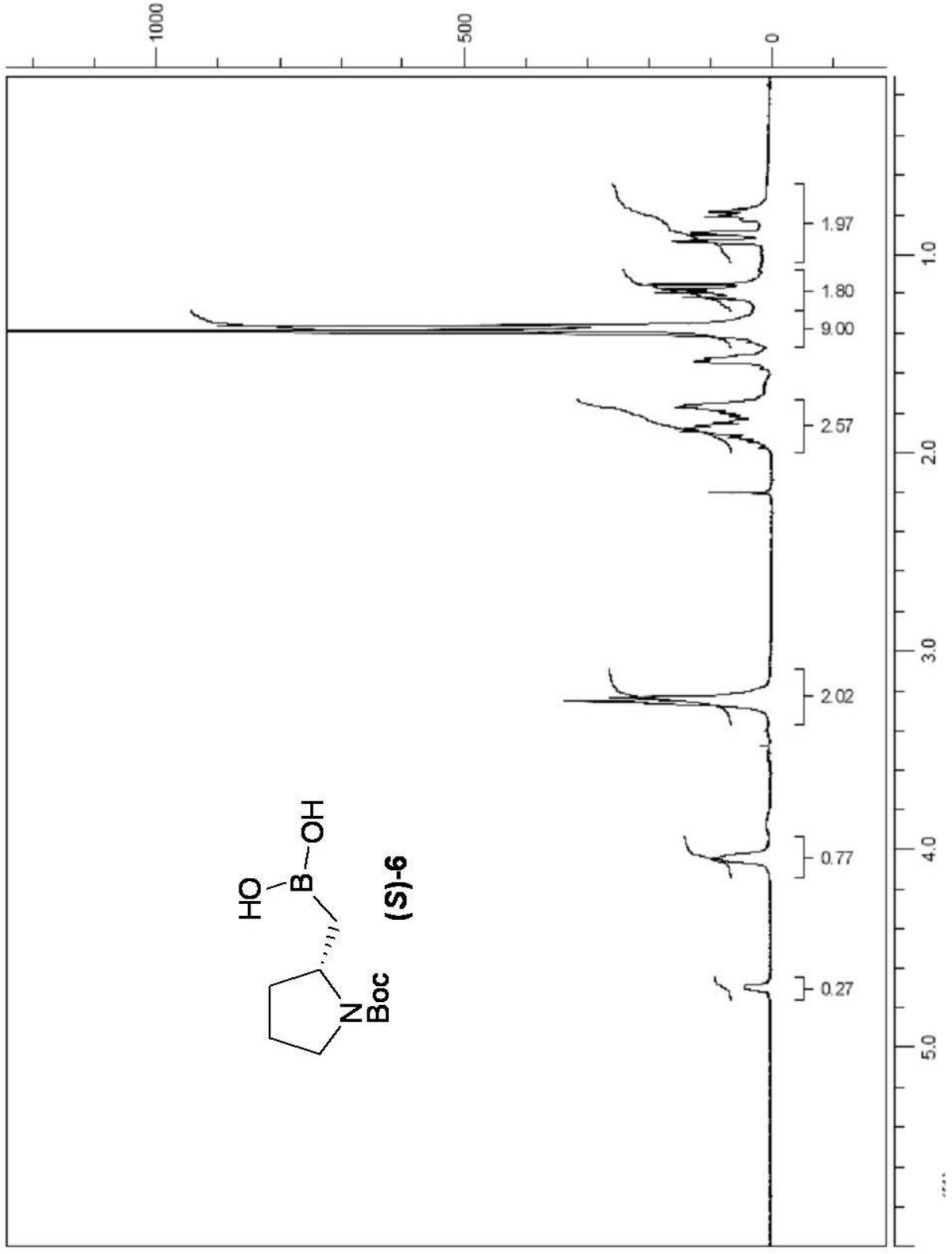
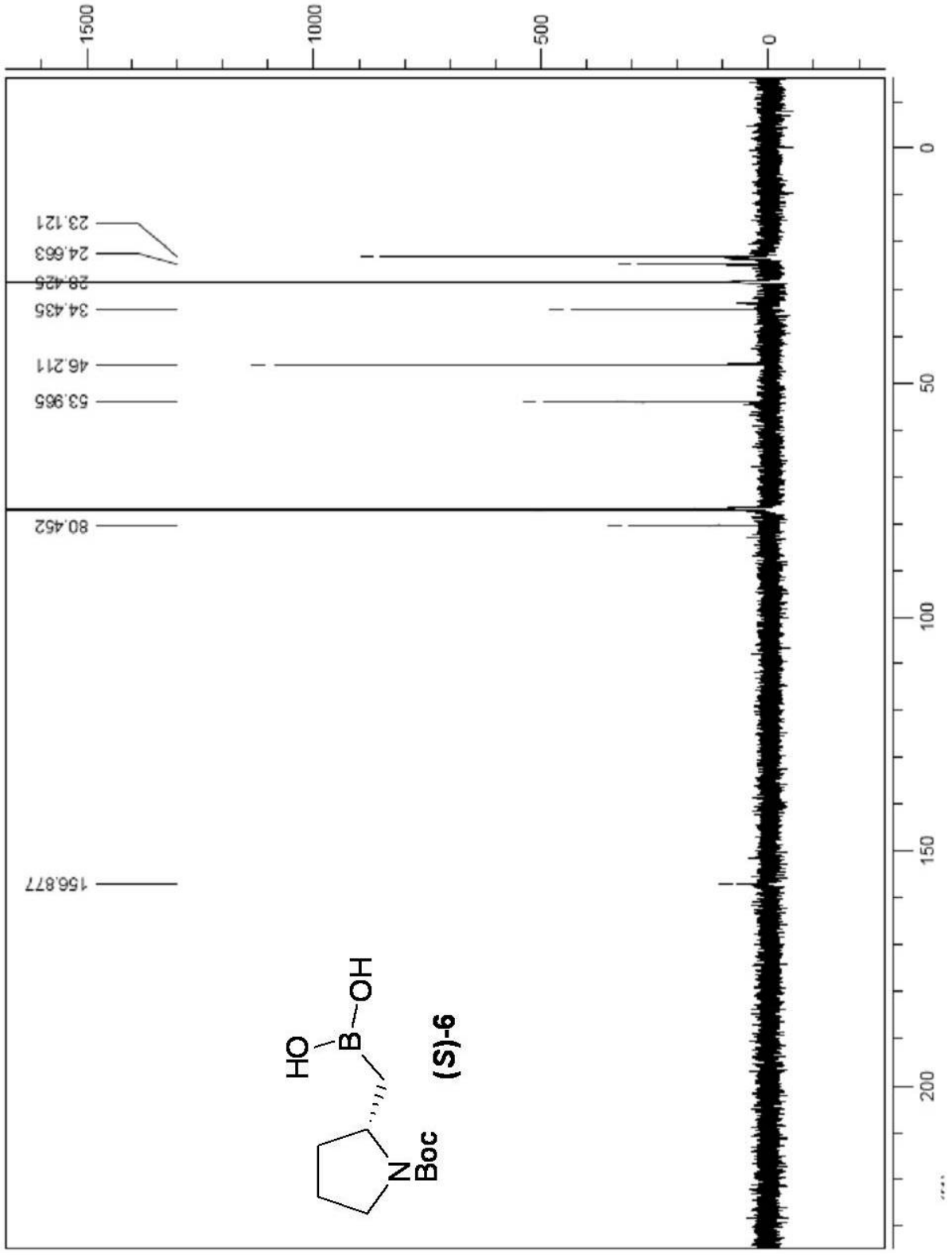
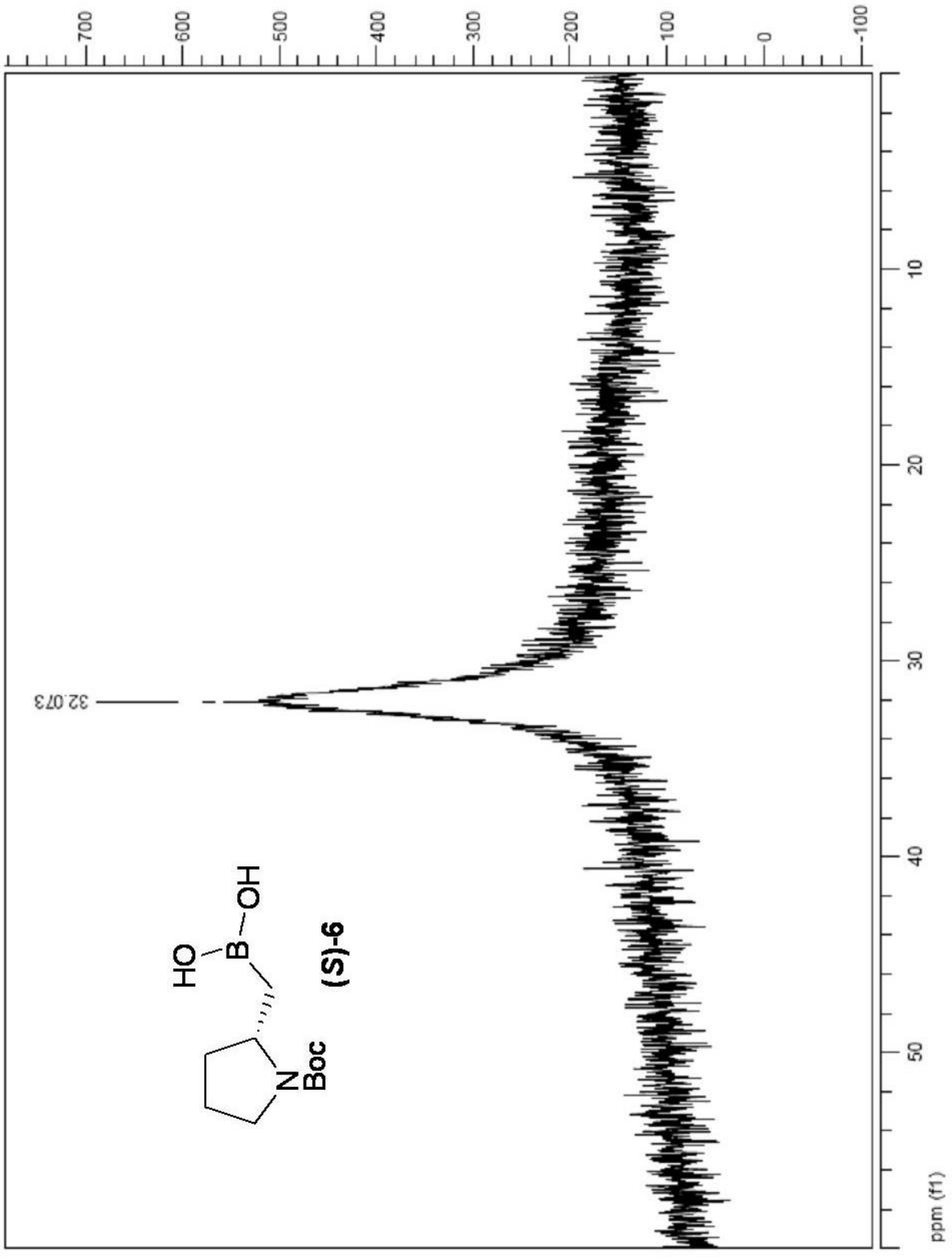
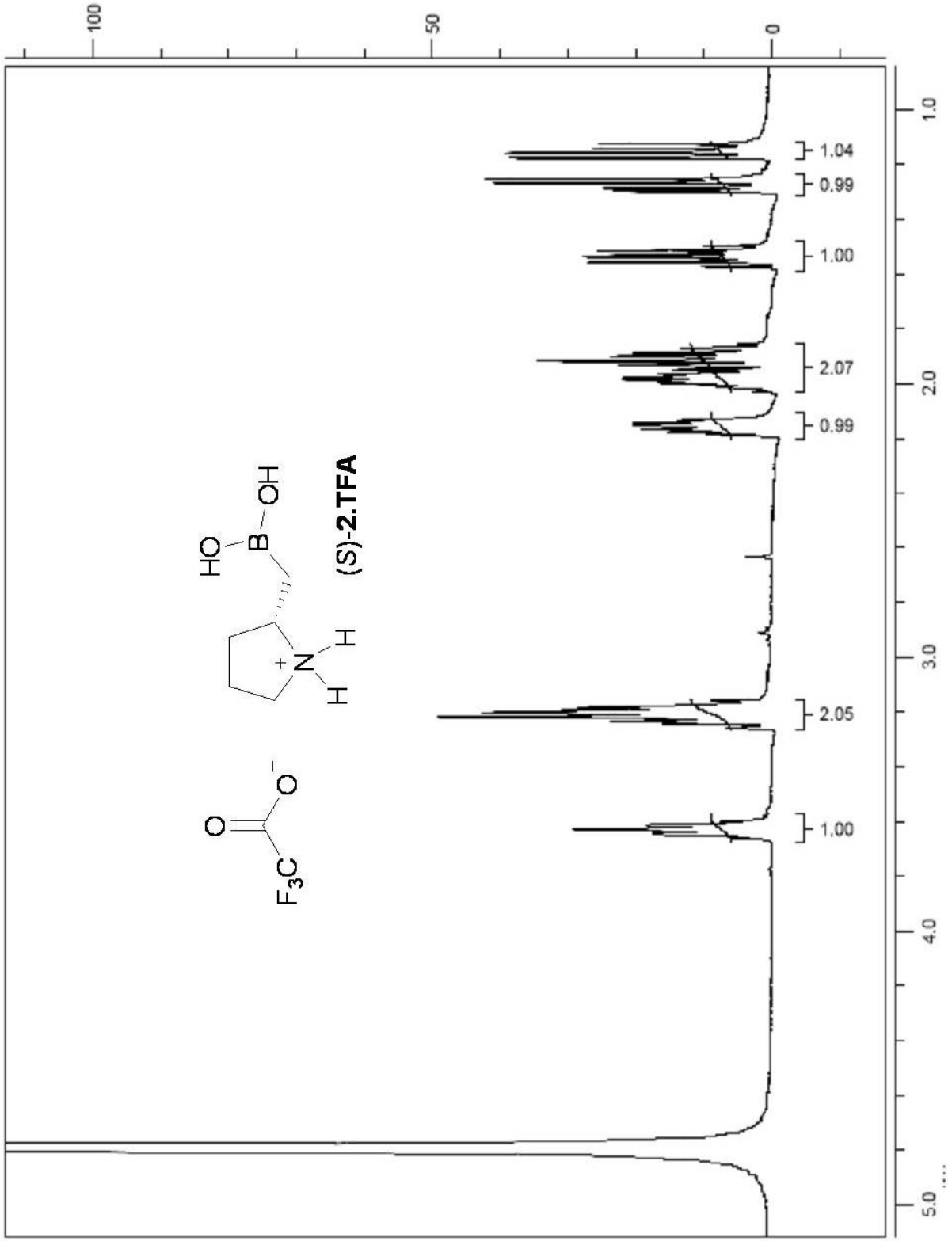
Boc
(S)-4

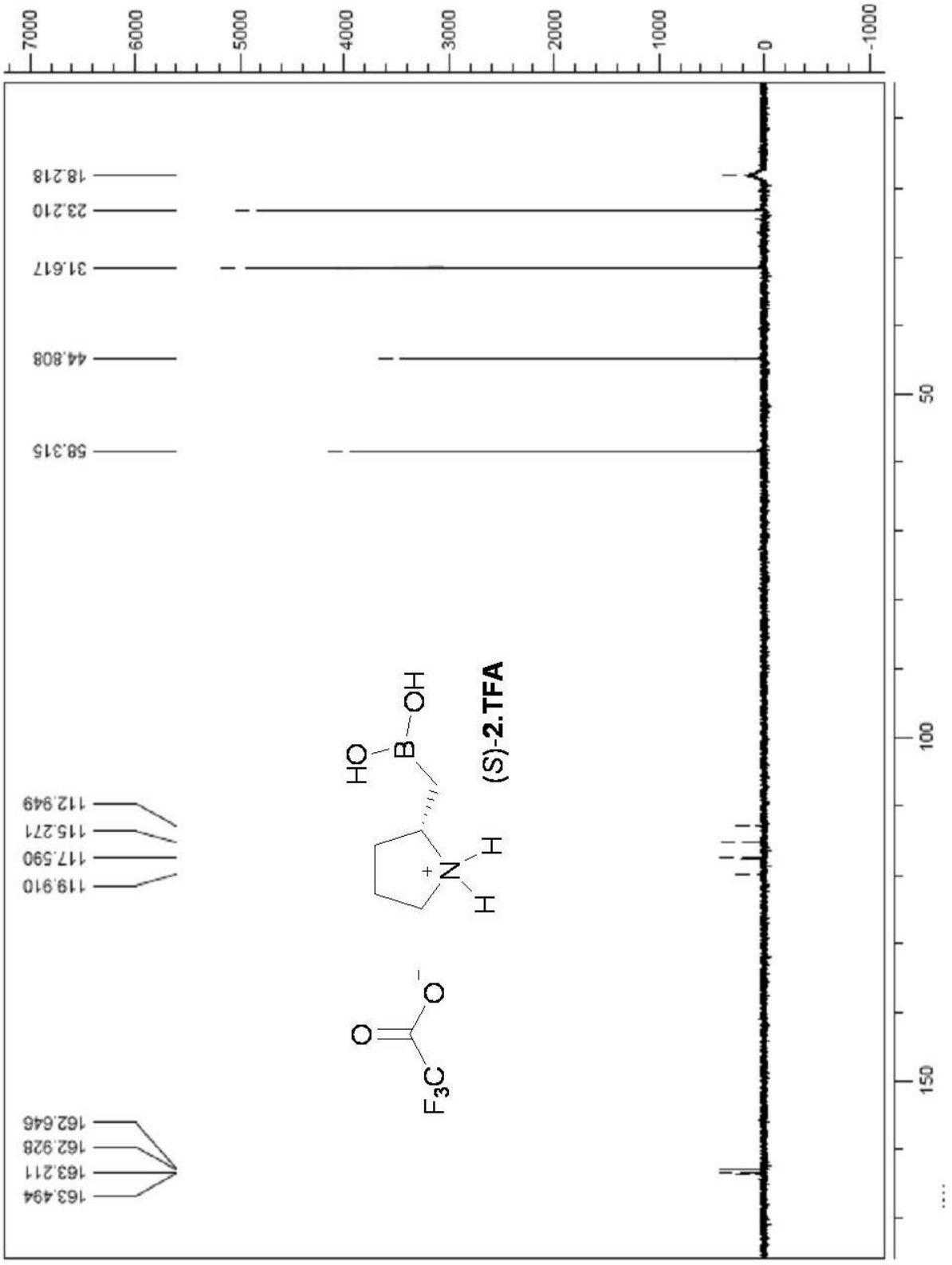

2500
2000
1500
1000
500
0
33.037
10
20
30
40
ppm (f1)
O
B
O
N
Boc
(S)-4

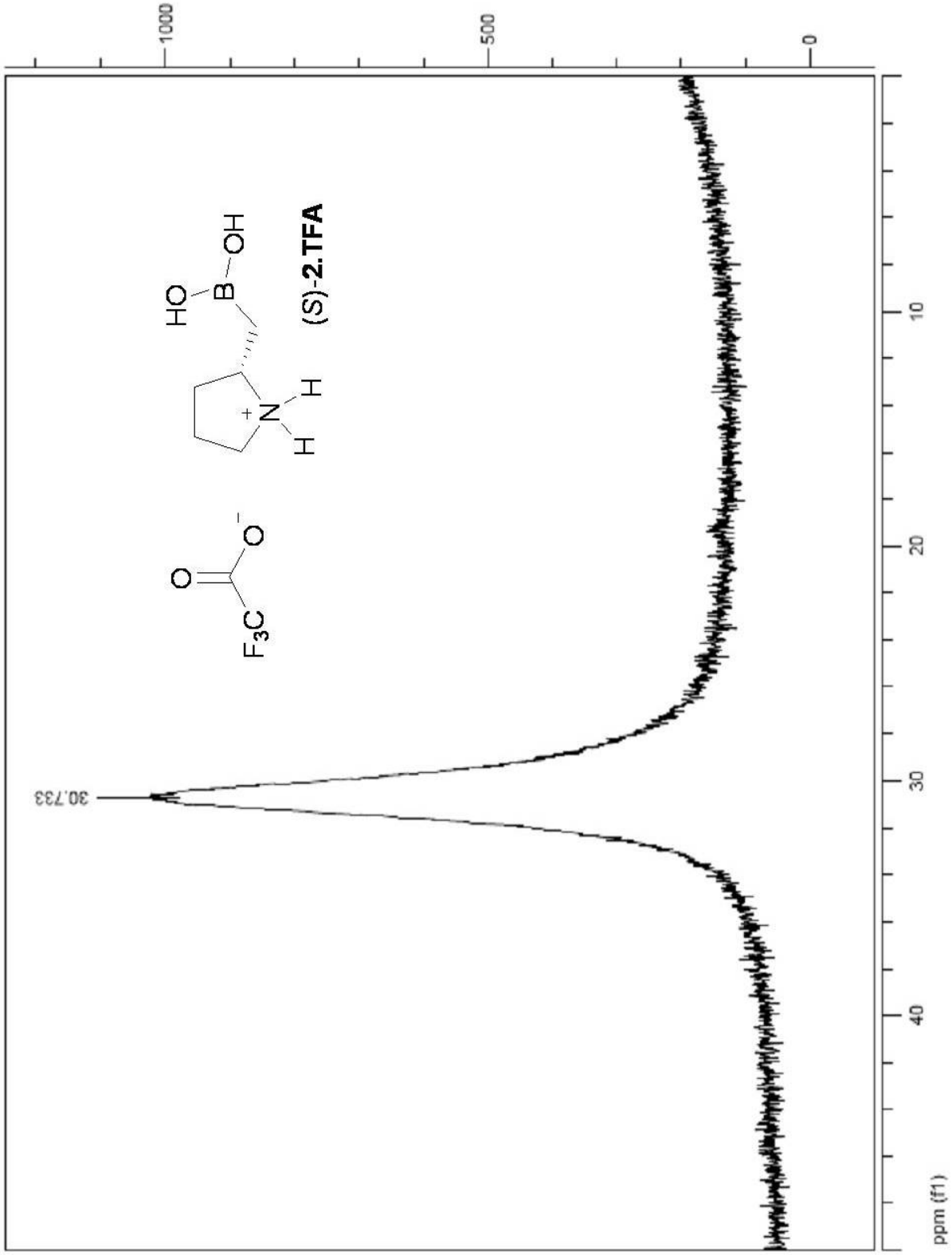

1000
500
0
1.97
1.80
9.00
2.57
2.02
0.77
0.27
1.0
2.0
3.0
4.0
5.0
HO
B
OH
N
Boc
(S)-6

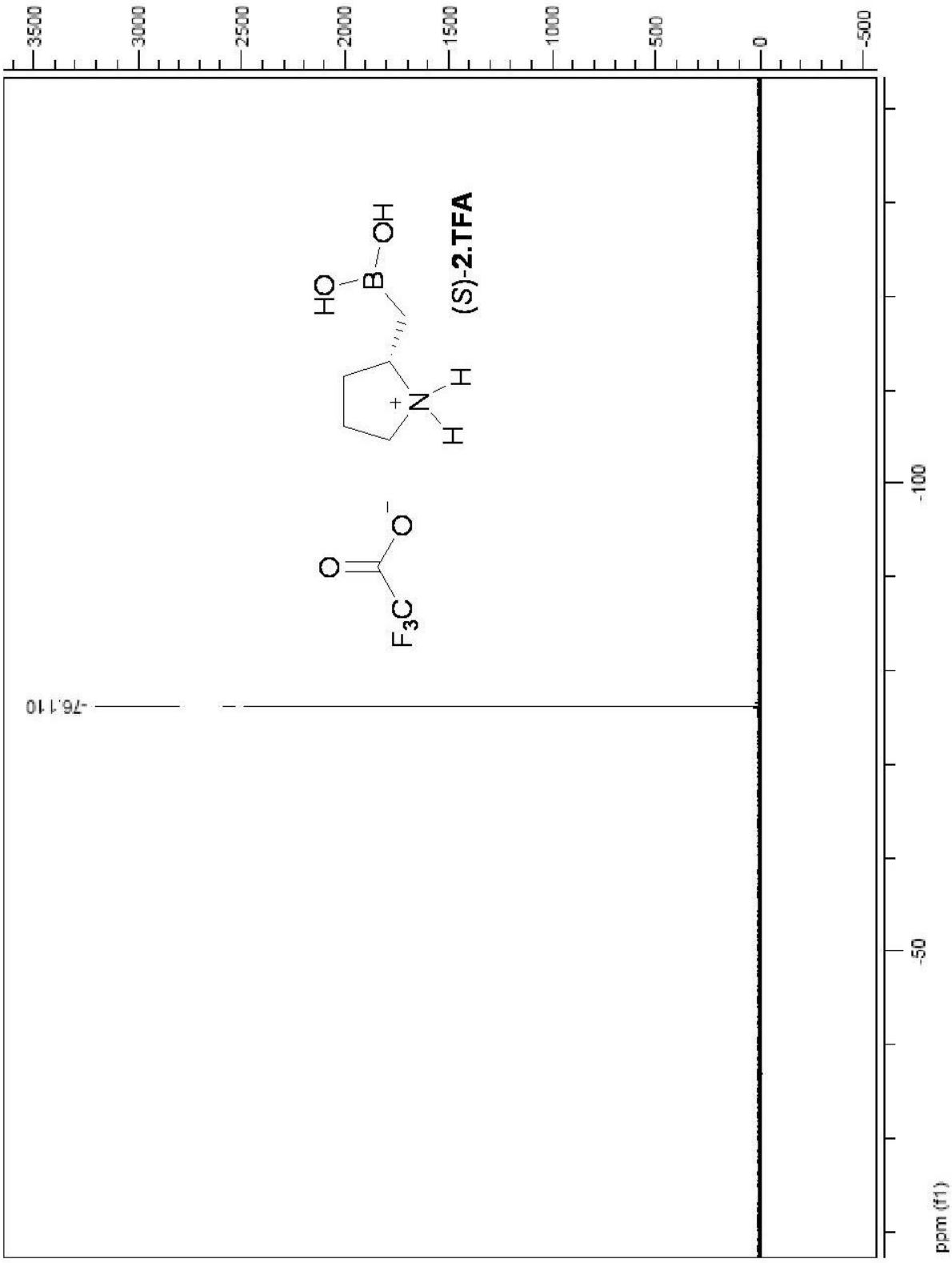

1500
1000
500
0
23.121
24.663
28.425
34.435
46.211
53.965
80.452
156.877
0
50
100
150
200
HO
B
OH
N
Boc
(S)-6

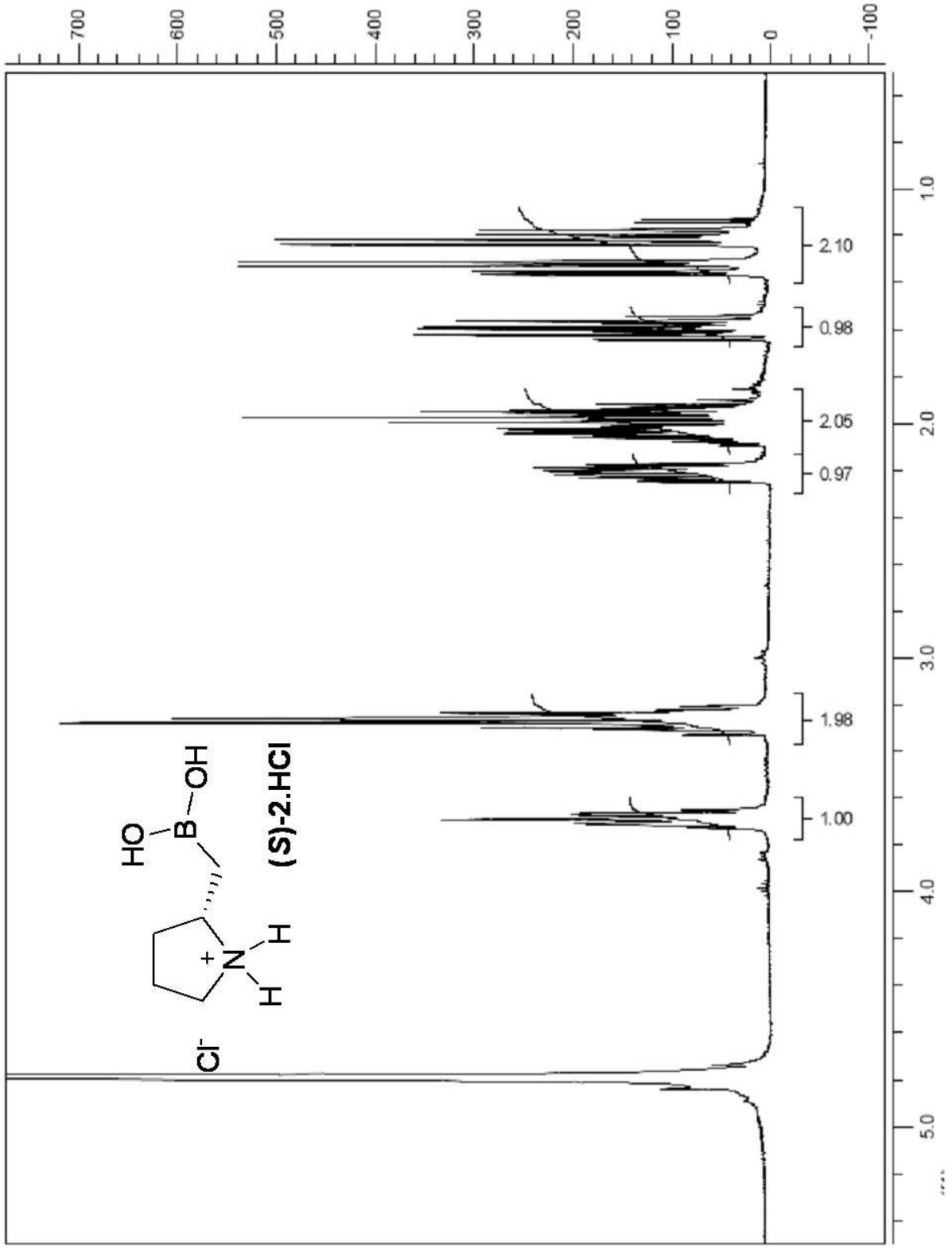

700
600
500
400
300
200
100
0
-100
32.073
10
20
30
40
50
ppm (f1)
HO
B
OH
N
Boc
(S)-6

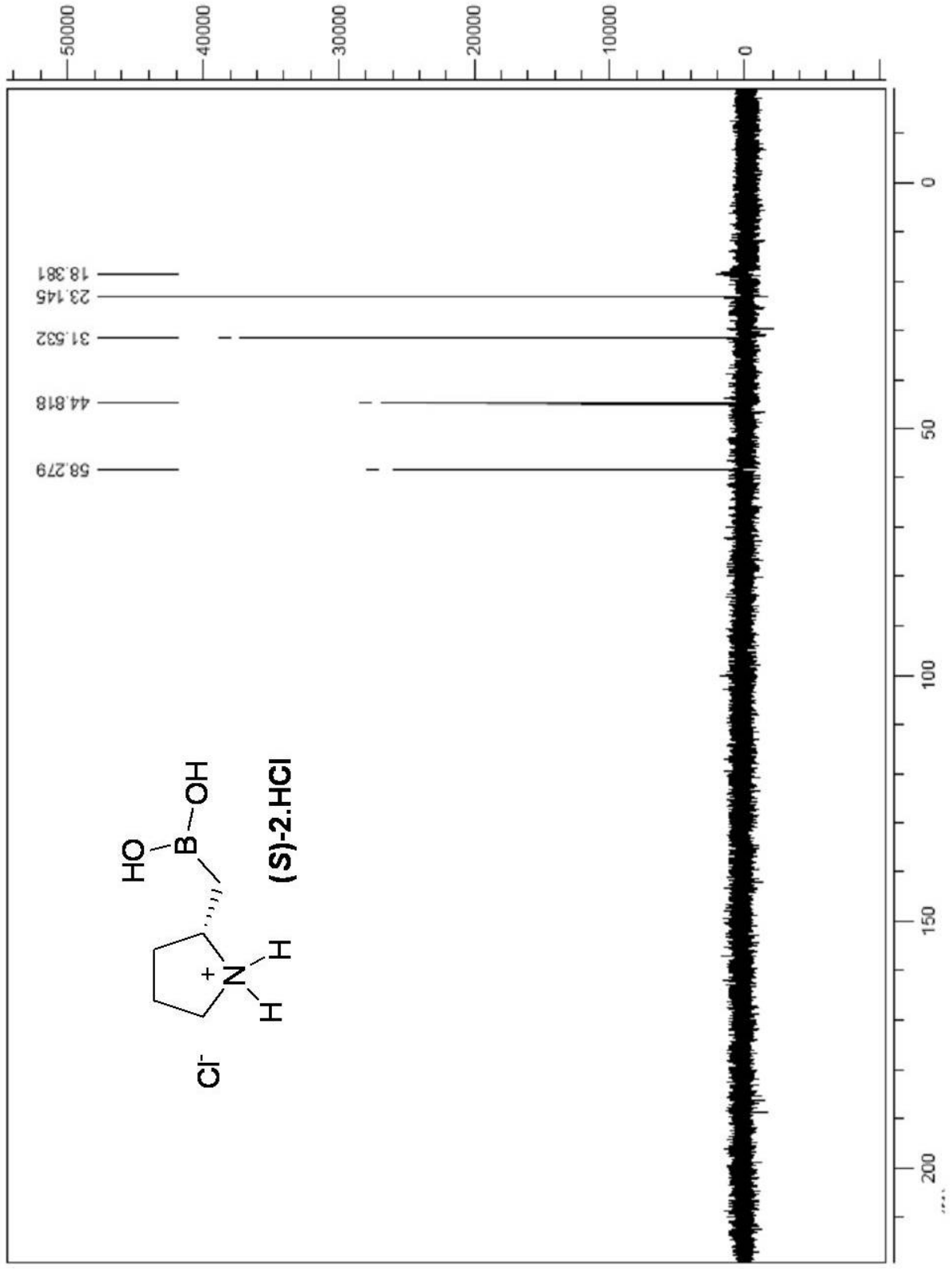

100
50
0
1.0
2.0
3.0
4.0
5.0
1.04
0.99
1.00
2.07
0.99
2.05
1.00
HO
B
OH
H
N
+
H
O
O
F3C
(S)-2.TFA

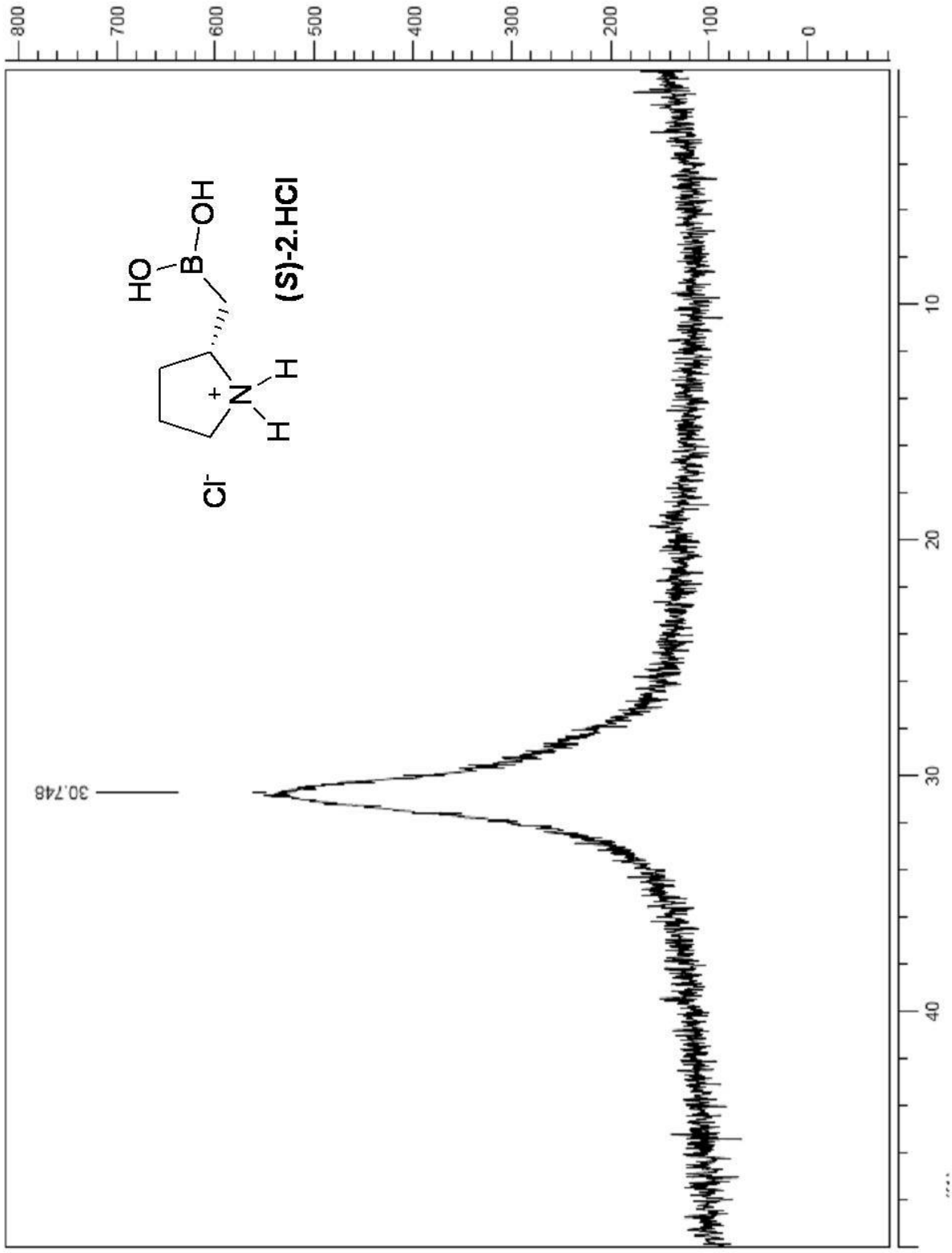

7000
6000
5000
4000
3000
2000
1000
0
-1000
18.218
23.210
31.617
44.808
58.315
112.949
115.271
117.590
119.910
162.646
162.928
163.211
163.494
50
100
150
HO
B
OH
(S)-2.TFA
H
H
N
+
O
O
F3C

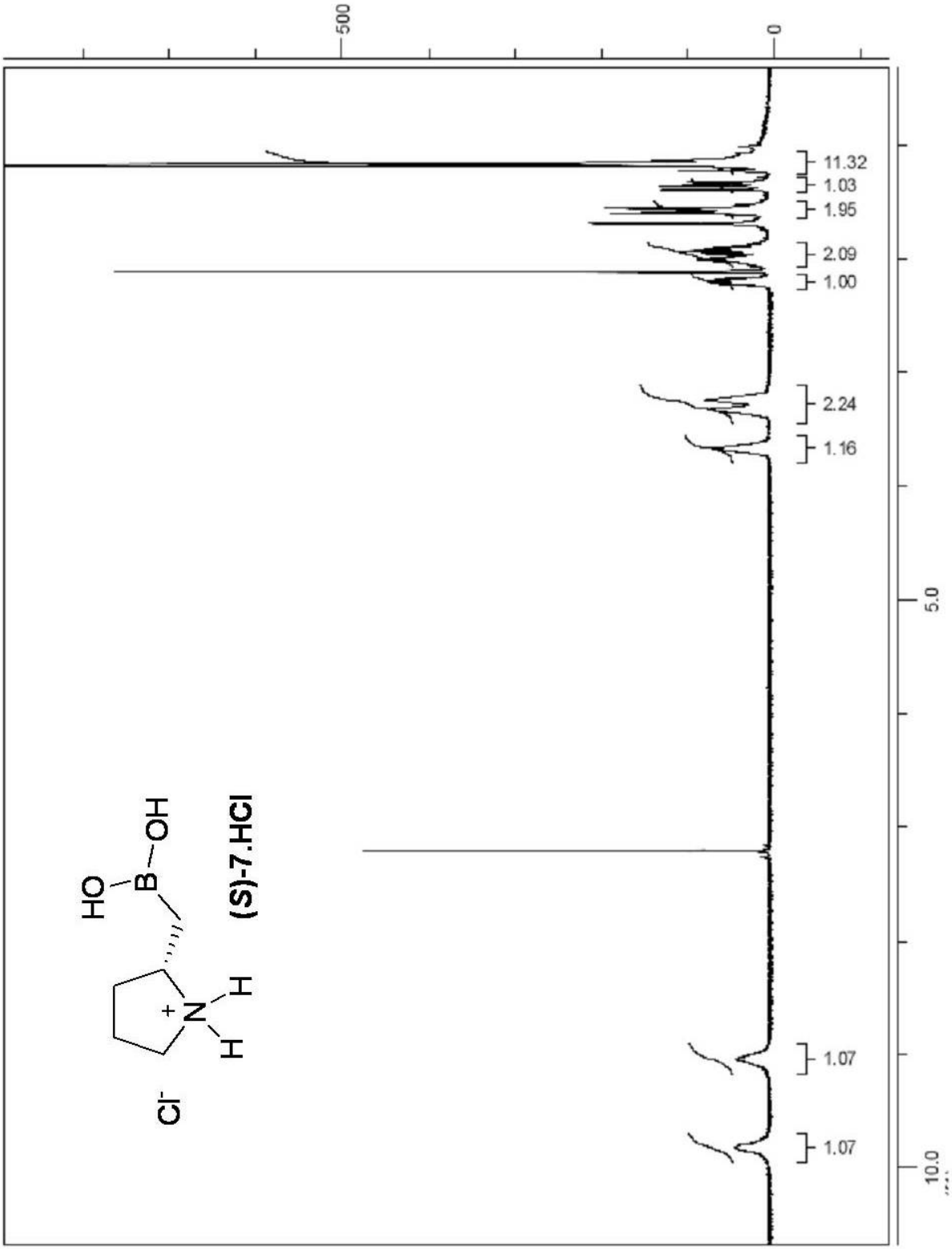

1000
500
0
30.733
10
20
30
40
ppm (f1)
HO
B
OH
(S)-2.TFA
H
N
H
+
O
O
F3C

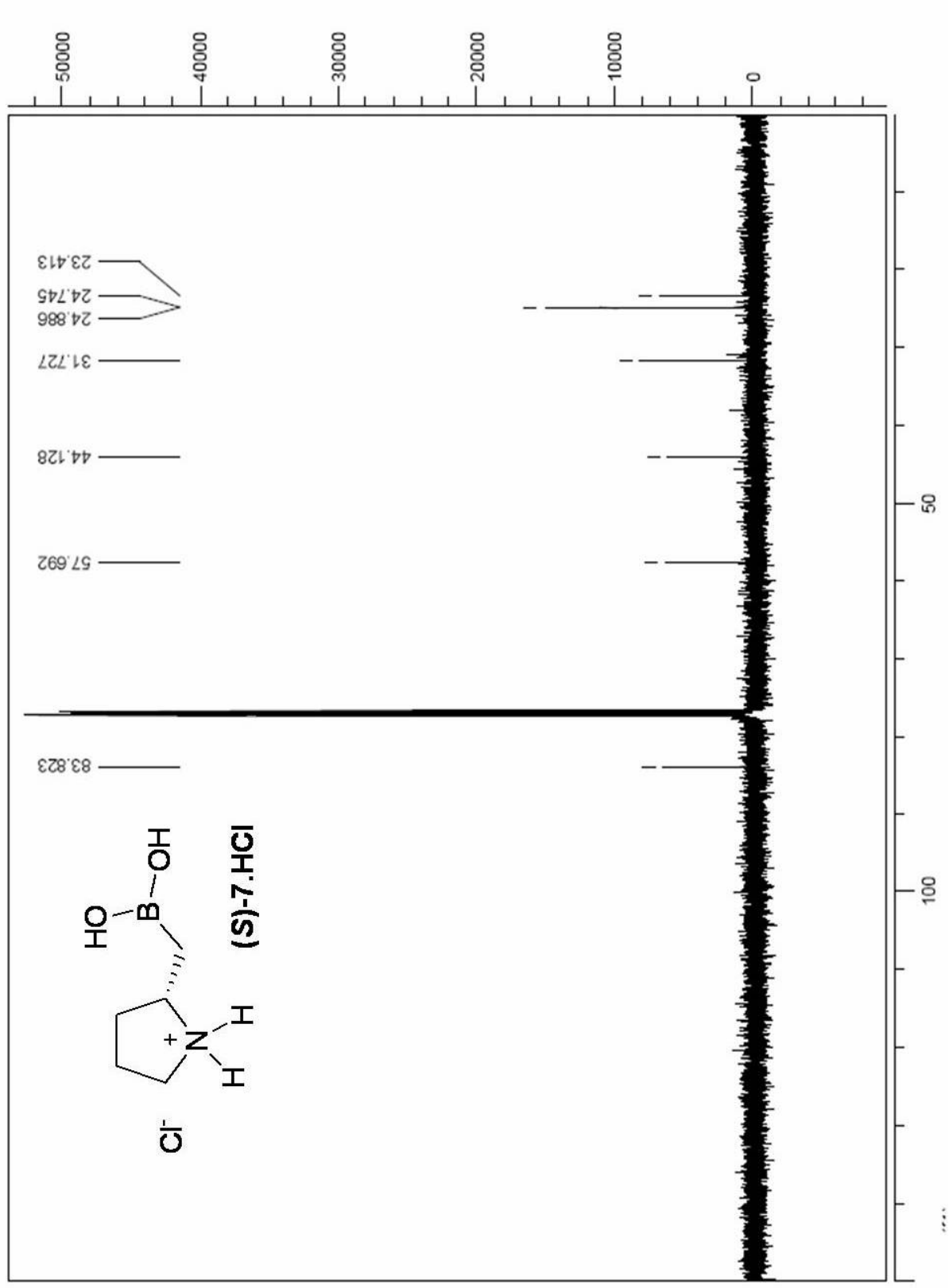

3500
3000
2500
2000
1500
1000
500
0
-500
-100
-50
ppm (f1)
-76.110
HO
B
OH
(S)-2.TFA
H
N
H
O
O
F3C

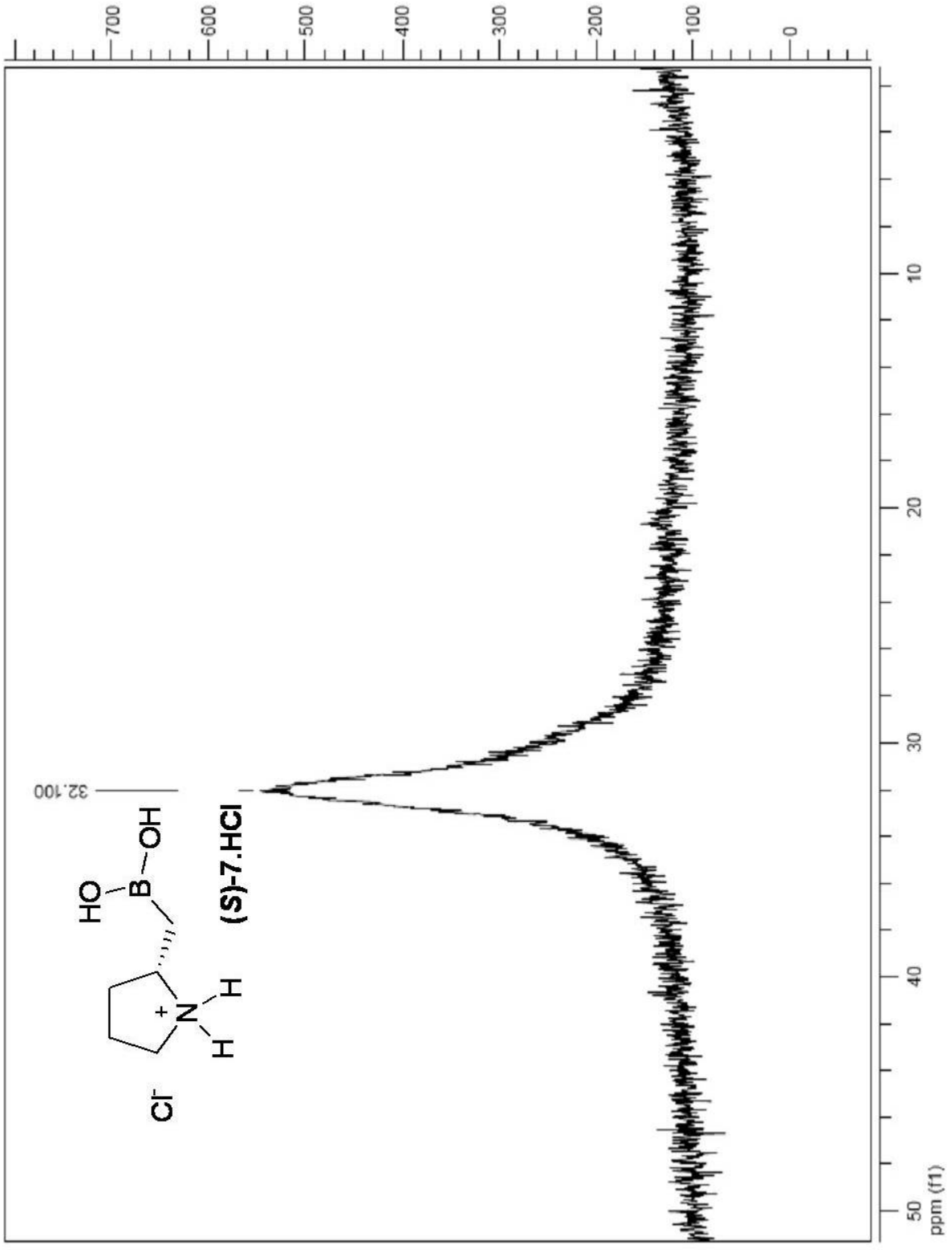

700
600
500
400
300
200
100
0
-100
1.0
2.0
3.0
4.0
5.0
2.10
0.98
2.05
0.97
1.98
1.00
HO
B
OH
H
N
H
+
Cl-
(S)-2.HCl

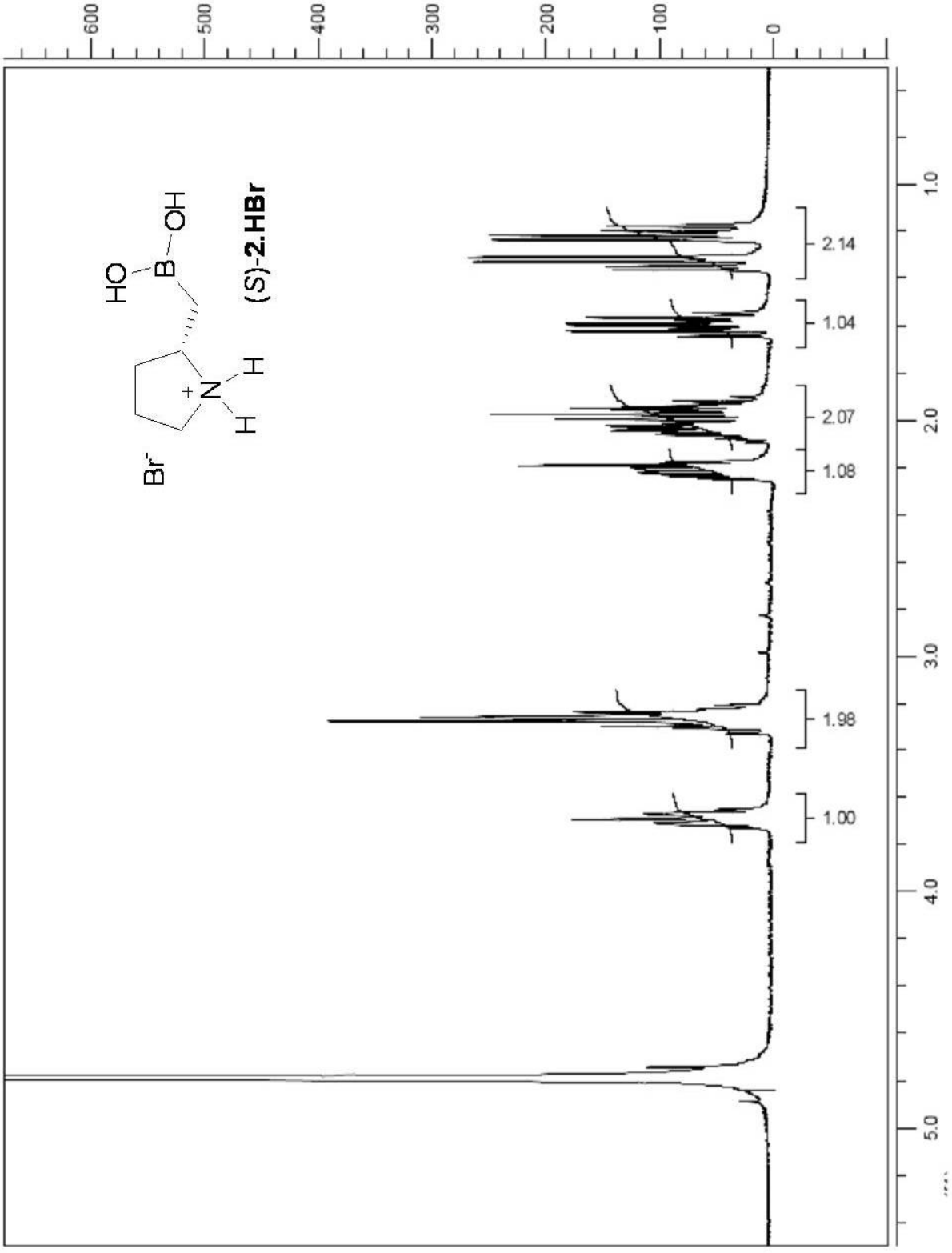

50000
40000
30000
20000
10000
0
18.381
23.145
31.532
44.818
58.279
0
50
100
150
200
HO
B
OH
H
N
H
Cl-
(S)-2.HCl

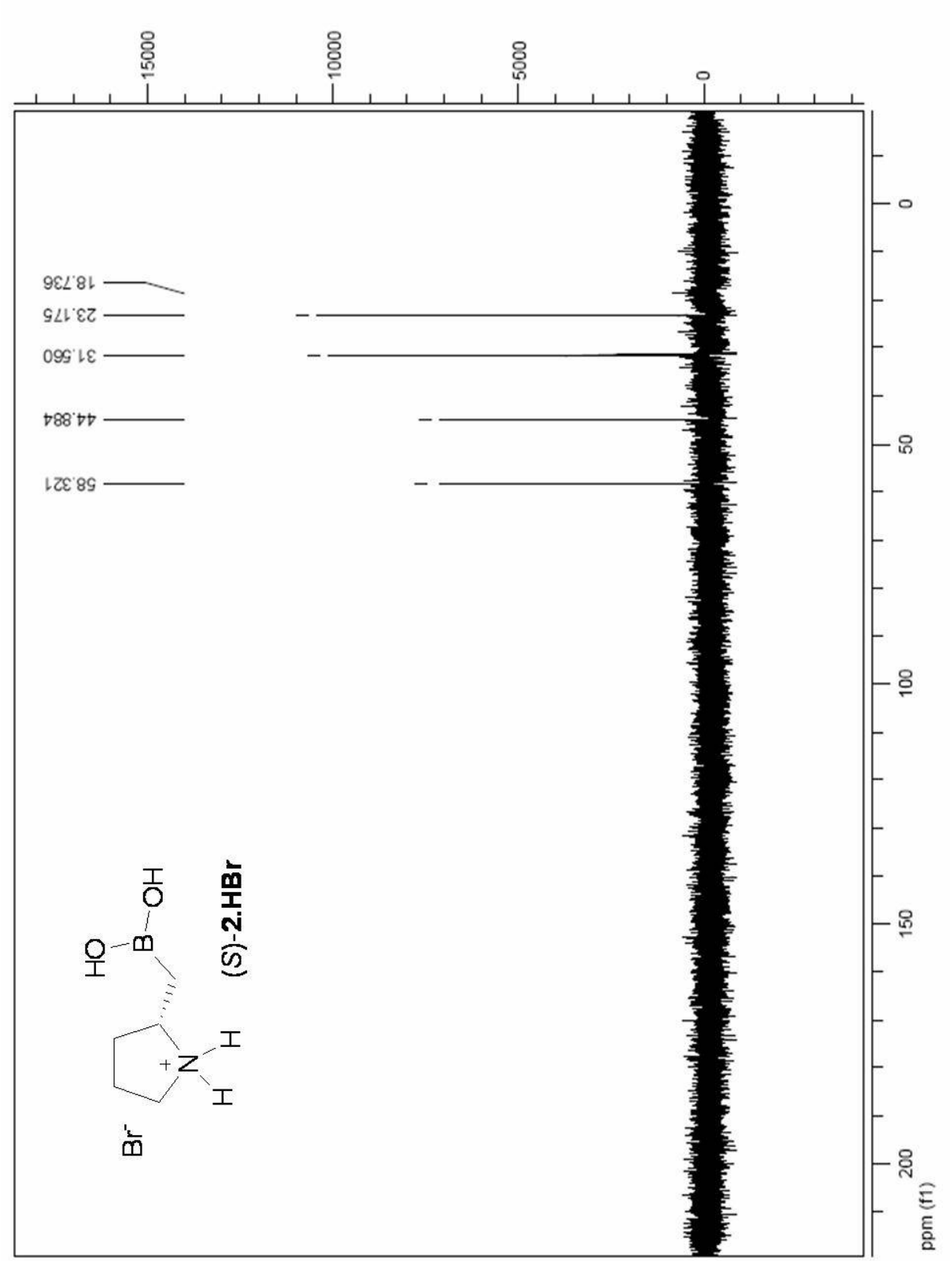

800
700
600
500
400
300
200
100
0
10
20
30
40
30.748
HO
B
OH
H
N
H
Cl-
(S)-2.HCl

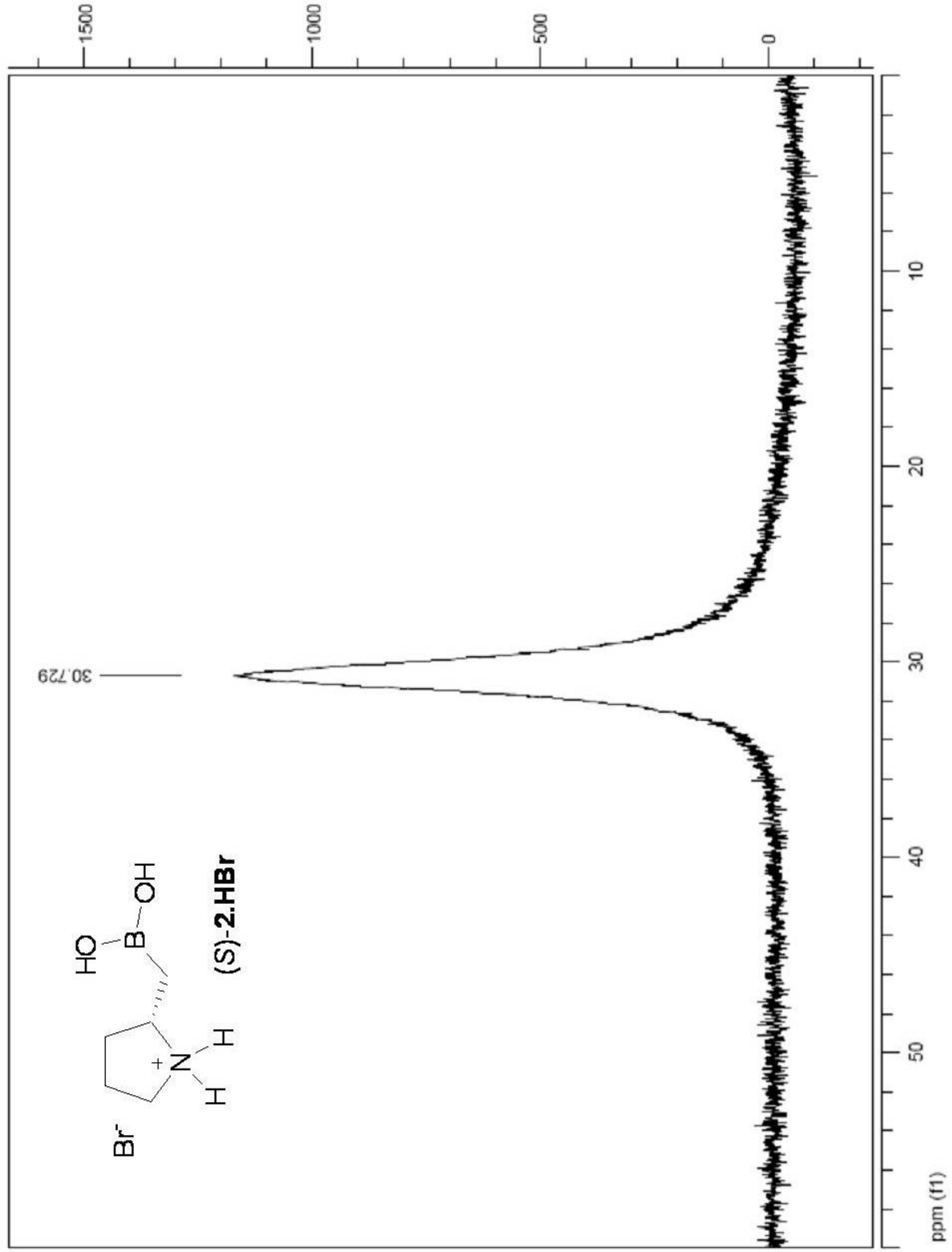

500
0
11.32
1.03
1.95
2.09
1.00
2.24
1.16
1.07
1.07
5.0
10.0
HO
B
OH
H
N
H
Cl-
(S)-7.HCl

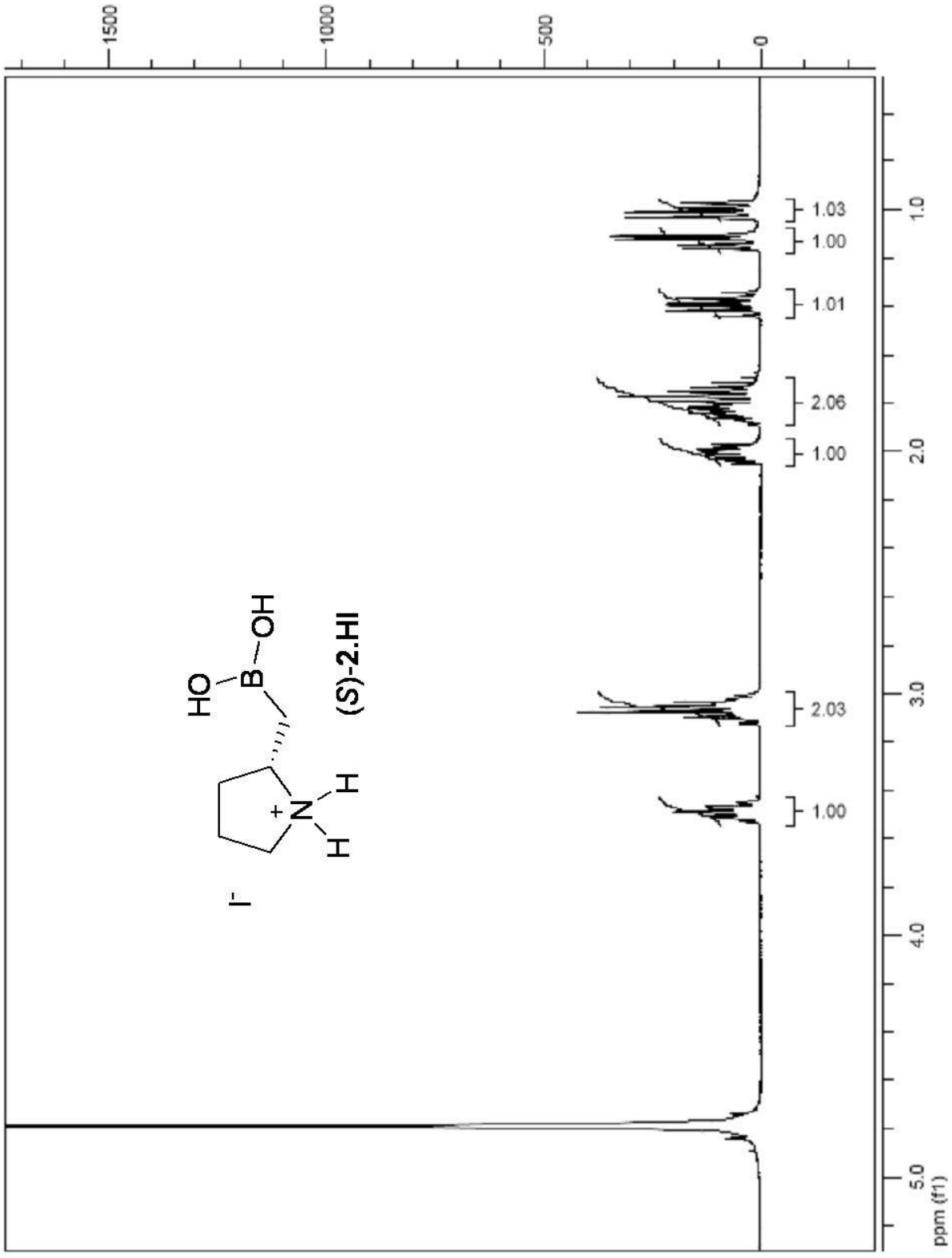

50000
40000
30000
20000
10000
0
23.413
24.745
24.886
31.727
44.128
57.692
83.823
50
100
(S)-7.HCl
HO
B
OH
H
N
H
Cl-

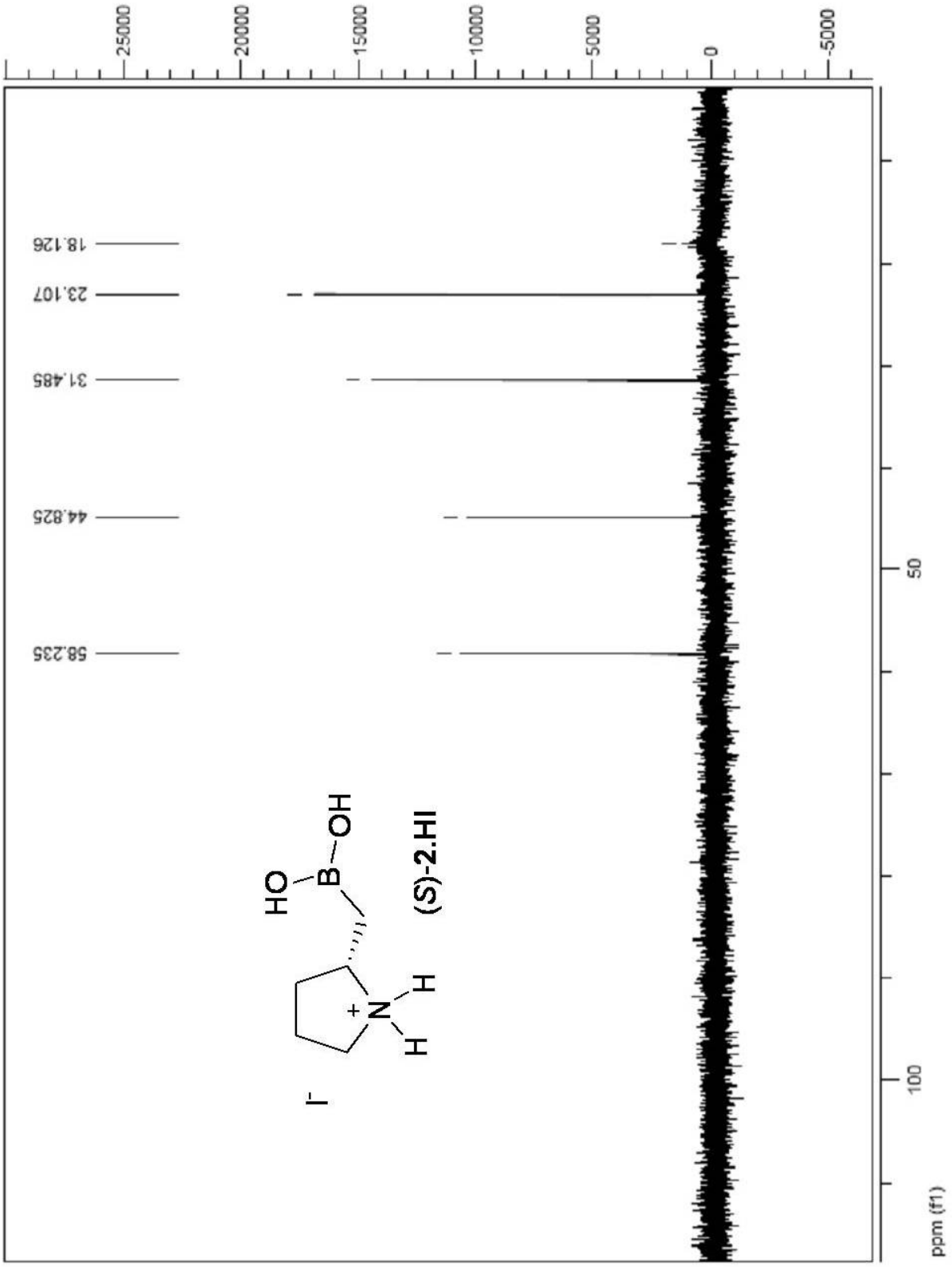

700
600
500
400
300
200
100
0
10
20
30
40
50
ppm (f1)
32.100
HO
B
OH
N
H
H
Cl⁻
(S)-7.HCl

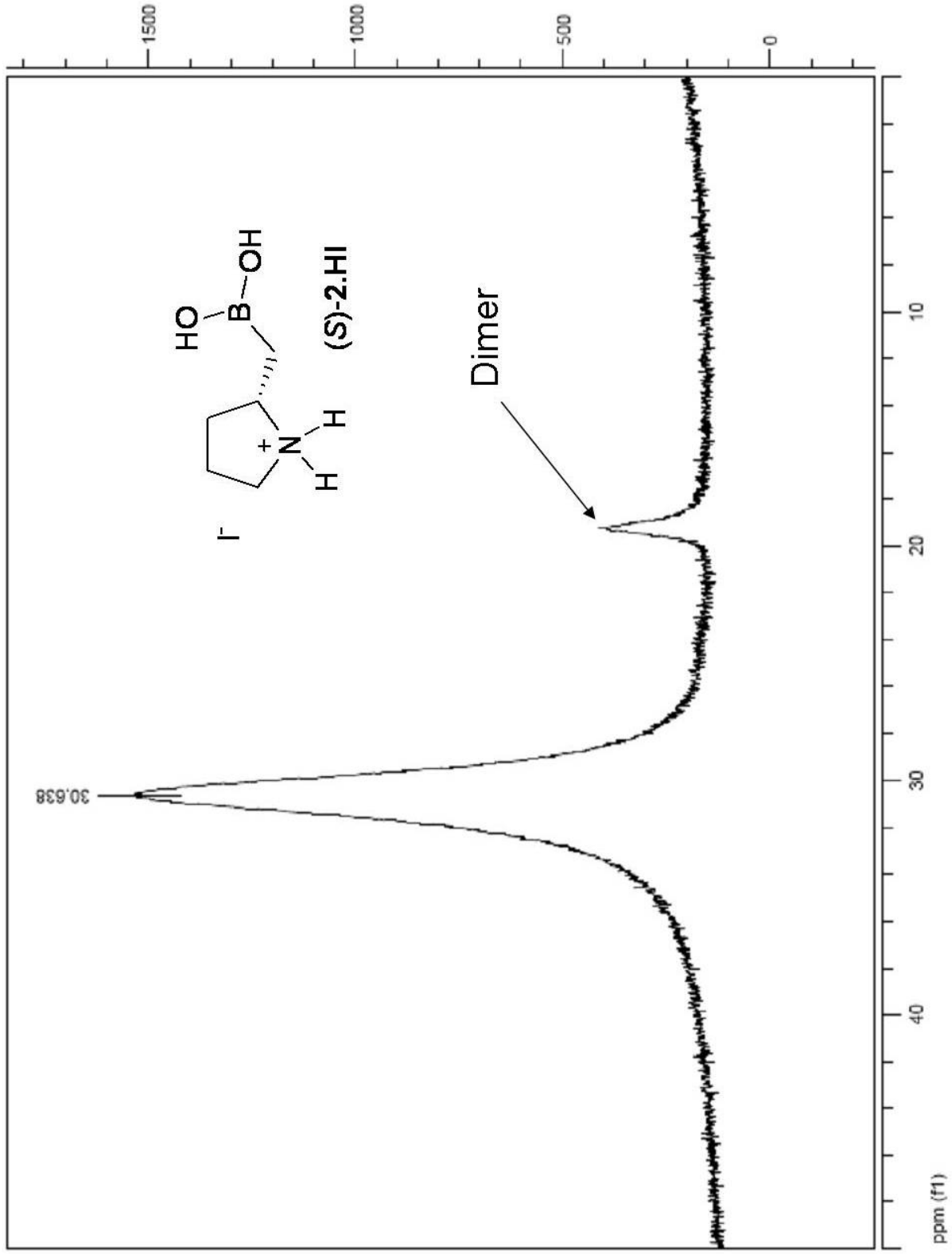

600
500
400
300
200
100
0
HO
B
OH
H
N
H
Br-
(S)-2.HBr
2.14
1.04
2.07
1.08
1.98
1.00
1.0
2.0
3.0
4.0
5.0


15000
10000
5000
0
18.736
23.175
31.560
44.884
58.321
0
50
100
150
200
ppm (f1)
HO
B
OH
H
N
H
Br⁻
(S)-2.HBr


1500
1000
500
0
30.729
10
20
30
40
50
ppm (f1)
HO
B
OH
H
N
H
Br
(S)-2.HBr


1500
1000
500
0
1.03
1.00
1.01
2.06
1.00
2.03
1.00
1.0
2.0
3.0
4.0
5.0
ppm (f1)
HO
B
OH
H
N
H
I⁻
(S)-2.HI


25000
20000
15000
10000
5000
0
-5000
18.126
23.107
31.485
44.825
58.235
50
100
ppm (f1)
HO
B
OH
H
N
H
+
I-
(S)-2.HI


1500
1000
500
0
HO
B
OH
(S)-2.HI
Dimer
30.638
10
20
30
40
ppm (f1)