Electronic supplementary materials *Mendeleev Commun.*, 2024, **34**, 496–498

A metal-templated synthesis of precursors for (2*S*)- and (2*R*)-2-(3-[^{18}F]fluoropropyl)tyrosines as potential radiotracers for positron emission tomography

Tat’yana F. Savel’yeva, Zalina T. Gugkaeva, Yulia V. Nelyubina, Alexander F. Smol’yakov, Margarita A. Moskalenko, Vladimir A. Larionov and Victor I. Maleev

Materials and Methods

General Information

All reactions were carried out using standard Schlenk techniques under argon atmosphere and anhydrous solvents, unless stated otherwise. Anhydrous solvents including EtOH and CH_2Cl_2 (99%+, extra dry AcroSeal®) were purchased from Acros Organics and used as supplied. Solvents were distilled under nitrogen atmosphere from calcium hydride (CH_3CN), sodium/benzophenone (THF) or magnesium turnings/iodine (MeOH). Reagents (including acrolein, MsCl, Et_3N, 1M Bu_4NF, KF) purchased from commercial suppliers (Across, TCI or Sigma-Aldrich (Merck)) were used without further purification. Unless otherwise stated, flash column chromatography was performed using silica gel 60 M from Macherey-Nagel. The chiral ligands (*S*)-**BBA** or (*S*)-**BPB** were synthesized according to a literature procedure.[S1-S3] Nickel(II) complexes **3** and **4** were prepared as described in the literature.[S4]

Instrumentation

^{1}H and ^{13}C NMR spectra were recorded on a Bruker Avance 600 and a Bruker Avance 400 spectrometers (CA, USA) operating at 600 (400) MHz (^{1}H) and (151) 101 MHz (^{13}C{^{1}H}). Chemical shifts are reported in ppm relative to the residual solvent peak ($CDCl_3$: δ = 7.26 ppm for ^{1}H NMR, δ = 77.1 for ^{13}C NMR). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, m = multiplet. High-resolution mass spectra were recorded on Bruker MicroTOF II instrument using ESI ionization method (BRUKER DALTONIK GmbH, Bremen, Germany). X-ray crystallography diffraction data were collected on a Bruker APEX-II CCD diffractometer (Bremen, Germany) [λ(MoKα) = 0.71073 Å, ω-scans, $2\theta<58°$] at 120 K. Elemental analyses were carried out in the Laboratory of Microanalysis of the A.N. Nesmeyanov Institute of Organoelement Compounds of the Russian Academy of Sciences (INEOS RAS). Reactions were monitored by thin-layer chromatography (TLC) carried out on 0.2±0.03 mm using UV light (254 nm) as a visualizing agent.

*Procedure for the synthesis of Ni^{II} complex **1***

A round-bottom flask equipped with a stirring bar was filled with a solution of (*S*)-**BBA**[S1,S2] (1.0 g, 3.24 mmol), racemic tyrosine (1.18 g, 6.48 mmol) and $Ni(NO_3)_2\times6H_2O$ (1.88 g, 6.48 mmol) in 40 mL of MeOH, heated to 45 °C with stirring, followed by the addition of a 2.4 N solution of MeONa in MeOH (5.4 mL, 12.96 mmol). The mixture was stirred for 1 h at 45 °C under argon, then cooled to room temperature and neutralized with 1 mL of acetic acid. The product was isolated by filtration after pouring the reaction mixture into 130 mL of water. The remaining amount of complex was isolated from aqueous solution by extraction with $CHCl_3$ (3×15 mL). The desired chiral Ni(II) complex **1** was isolated as a mixture of diastereomers (*dr* 3.5:1) as a red powder, combined yield 1.7 g (99%). The diastereomers were not separated and used in the next step without purification and full characterization.

HRMS calcd. for $C_{28}H_{28}N_3NiO_4$ $[M+H]^+$: 528.1428; found: 528.1429.

^{1}H NMR spectrum of the mixture of diastereomers (*the observed peaks for minor product are provided in the parentheses*) (400 MHz, $CDCl_3$): δ = 8.34 (*8.47*) (d, *J* = 8.7 Hz, 1H), 8.14 (s, 1H), 8.98 (*7.89*) (d, *J* = 7.2 Hz, 2H), 7.29 (*7.37*) (t, *J* = 7.6 Hz, 2H), 7.25–7.21 (m, 1H), 7.18 (*7.17*) (s, 1H), 7.15–7.09 (m, 1H), (*7.03, dd, J = 7.8, 1.4 Hz*), 6.97 (d, *J* = 8.4 Hz, 2H), 6.93–6.84 (m, 3H), (*6.79, d, J = 8.4 Hz*), 4.23 (d, *J* = 12.6 Hz, 1H), (*4.17–4.15, m*), 4.07 (t, *J* = 4.9 Hz, 1H), (*3.80–3.76, m*), 3.37 (d, *J* = 12.5 Hz, 1H), 3.32–3.26 (m, 2H), 3.22–3.15 (m, 1H), 3.06 (dd, *J* = 14.0, 4.5 Hz, 1H), (*2.94–2.87, m*), 2.74–2.65 (m, 1H), 2.36–2.30 (m, 2H), (*2.28–2.17, m*), 1.93–1.87 (m, 1H), 1.83–1.79 (m, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.7, 179.4, 162.3, 156.8, 142.3, 133.7, 133.4, 131.6, 131.5, 129.10, 128.9, 126.0, 123.9, 123.4, 121.7, 116.0, 73.6, 70.5, 63.2, 57.7, 41.3, 31.2, 23.2 ppm.

The ^{1}H and ^{13}C NMR spectra are provided in Figure S1 (*below*).

*Procedure for the synthesis of Ni^{II} complex **2***

A solution of the diastereomeric mixture of Ni^{II} complex **1** (0.5 g, 0.95 mmol) in 20 mL of dry CH_2Cl_2 was introduced into a round-bottomed flask equipped with a stirring bar, cooled to 0 ºC with stirring, followed by the addition of Et_3N (0.26 mL, 1.89 mmol) and methanesulfonyl chloride (0.15 mL, 1.89 mmol). The reaction mixture was stirred for 15 min at 0 ºC under argon and then for 8 h at room temperature. The solvent was then removed under reduced pressure and the residue was dissolved in 10 mL of dry acetone. The precipitated triethylamine hydrochloride was filtered and washed with dry acetone (3×5 mL). The organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure to afford the desired chiral Ni^{II} complex **2** as a mixture of diastereomers (*dr* 3.5:1) as a red powder, combined yield 0.57 g (98%). The diastereomers were not separated and used in the next step without purification and full characterization.

HRMS calcd. for $C_{29}H_{30}N_3NiO_6S$ $[M+H]^+$: 606.1203; found: 606.1204.

^{1}H NMR spectrum of the mixture of diastereomers (400 MHz, $CDCl_3$): δ = 8.39 (d, *J* = 8.7 Hz, 1H), 7.89 (d, *J* = 7.7 Hz, 2H), 7.24–7.06 (m, 8H), 7.04–6.96 (m, 2H), 6.82–6.76 (m, 1H), 4.17 (d, *J* = 12.6 Hz, 1H), 4.05–3.97 (m, 1H), 3.32 (d, *J* = 12.6 Hz, 1H), 3.26–3.10 (m, 3H), 3.05 (s, 3H, OMs), 2.73–2.59 (m, 1H), 2.34–2.12 (m, 3H), 1.91–1.76 (m, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.7, 162.6, 148.7, 142.7, 134.9, 134.1, 133.8, 133.2, 132.1, 131.9, 131.8, 131.6, 130.8, 129.1, 128.9, 123.7, 123.0, 122.7, 121.5, 70.2, 63.0, 57.5, 41.2, 37.7, 31.0, 23.4 ppm.

The ^{1}H and ^{13}C NMR spectra are provided in Figure S2 (*below*).

*Procedure for the synthesis of Ni^{II} complex **5***

A round-bottom flask equipped with a stirring bar was filled with a solution of the diastereomeric mixture of Ni^{II} complex **2** (0.57 g, 0.94 mmol) in 10 mL of dry MeOH, followed by the addition of Et_3N (0.2 mL, 1.4 mmol) and acrolein (0.13 mL, 1.88 mmol). The reaction mixture was stirred for 24 h at room temperature under argon. The solvent was then removed under reduced pressure and the residue was dissolved in 10 mL of $CHCl_3$. The mixture was washed with 10 mL of 0.5% aqueous acetic acid solution and water (2×7 mL). The organic layers were dried over Na_2SO_4 and the solvent was removed under reduced pressure, was additionally dried over P_2O_5 for 3 days to afford the desired chiral Ni(II) complex **5** as a mixture of diastereomers (*dr* 1.1:1) as a red powder, 0.6 g (96% yield). The diastereomers were not separated and used in the next step without purification and full characterization.

HRMS calcd. for $C_{32}H_{34}N_3NiO_7S$ $[M+H]^+$: 662.1465; found: 662.1469.

^{1}H NMR spectrum of the mixture of diastereomers (400 MHz, $CDCl_3$): δ = 9.85 (s, 1H, CHO), 9.82 (s, 1H, CHO), 8.47 (d, *J* = 8.6 Hz, 1H), 8.34 (d, *J* = 8.6 Hz, 1H), 7.96 (d, *J* = 7.4 Hz, 2H), 7.78–7.68 (m, 2H), 7.58

(s, 1H, -CH=N-), 7.46 (s, 1H, -CH=N-), 7.41–7.27 (m, 10H), 7.23–7.15 (m, 8H), 7.01–6.90 (m, 2H), 4.29 (d, *J* = 12.7 Hz, 1H, N-CH_2Ph), 4.10 (d, *J* = 12.7 Hz, 1H, N-CH_2Ph), 3.76–3.63 (m, 2H), 3.46–3.17 (m, 8H), 3.16 (s, 3H, OMs), 3.06 (s, 3H, OMs), 2.98–2.87 (m, 1H), 2.82 (d, *J* = 12.7 Hz, 1H, N-CH_2Ph), 2.71–2.61 (m, 1H), 2.56–2.44 (m, 1H), 2.38–2.24 (m, 6H), 2.20–2.11 (m, 2H), 1.95–1.86 (m, 2H), 1.80–1.71 (m, 2H), 1.66–1.56 (m, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.0, 182.2, 181.8, 180.3, 179.7, 162.4, 161.9, 148.8, 148.7, 143.2, 142.9, 134.5, 134.4, 134.3, 133.9, 133.8, 133.2, 132.4, 132.3, 131.7, 131.5, 129.3, 129.2, 129.0, 124.0, 123.0, 122.8, 122.5, 122.4, 121.7, 70.9, 69.6, 63.6, 63.2, 58.1, 57.9, 46.5, 44.7, 38.9, 38.7, 37.8, 37.6, 32.2, 31.1, 30.9, 30.7, 23.9, 23.1 ppm.

^{1}H and ^{13}C NMR spectra of the mixture of diastereomers are provided in Figure S3 (*below*).

*Procedure for the synthesis of Ni^{II} complex **6***

A round-bottom flask equipped with a stirring bar was filled with a solution of the diastereomeric mixture of Ni^{II} complex **5** (0.6 g, 0.91 mmol) in 25 mL of dry EtOH, followed by the addition of $NaBH_4$ (34 mg, 0.91 mmol). The reaction mixture was stirred for 30 min at room temperature under argon. Then 25 mL of H_2O, 15 mL of $CHCl_3$ and 0.2 mL of acetic acid were added to the mixture. The organic layer was separated, washed with water (3×10 mL) and dried over Na_2SO_4. The solvent was removed under reduced pressure and the resulting residue was purified by preparative TLC on silica gel (eluent: $CHCl_3$/acetone 1:1) to isolate the diastereomers of the Ni(II) complex **6**. The first eluted diastereomer was identified as (*S,S*)-**6** (R_f = 0.55) and the second eluted diastereomer was assigned as (*S,R*)-**6** (R_f = 0.35). Each fraction was further purified using Sephadex LH-20 resin (eluent: benzene/EtOH 3:1).

Nickel(II) complex (*S,S*)-6

The desired Ni^{II} complex (*S,S*)-**6** was isolated as a red powder (0.17 g, 27% yield).

^{1}H NMR (400 MHz, $CDCl_3$+CD_3OD): δ = 8.13 (d, *J* = 8.7 Hz, 1H), 7.90 (d, *J* = 7.4 Hz, 2H), 7.63 (s, 1H, -CH=N-), 7.30–7.26 (m, 1H), 7.19–7.12 (m, 5H), 7.05–6.99 (m, 3H), 6.82 (t, *J* = 7.4 Hz, 1H), 3.82 (d, *J* = 12.4 Hz, 1H, N-CH_2Ph), 3.51–3.39 (m, 2H), 3.24 (d, *J* = 12.4 Hz, 1H, N-CH_2Ph), 3.13–3.03 (m, 2H), 3.02 (s, 3H, OMs), 2.95–2.91 (m, 1H), 2.70 (d, *J* = 13.6 Hz, 1H), 2.17–2.10 (m, 1H), 2.06–2.00 (m, 1H), 1.96–1.84 (m, 3H), 1.77–1.71 (m, 1H), 1.66–1.58 (m, 1H), 1.45–1.33 (m, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$+CD_3OD): δ = 181.9, 181.2, 162.4, 148.5, 141.9, 134.7, 134.2, 134.0, 133.8, 132.0, 131.1, 128.8, 128.7, 123.4, 123.4, 122.1, 121.7, 78.4, 70.9, 63.7, 61.1, 57.7, 46.3, 37.2, 35.3, 30.7, 26.7, 22.7 ppm. ^{1}H and ^{13}C NMR spectra of the diastereomer are provided in Figure S4 (*below*).

Elemental analysis calcd. for $C_{32}H_{35}N_3NiO_7S\times1.2H_2O$ (%): C, 56.03; H, 5.50; N, 6.13. Found: C, 56.05; H, 5.45; N, 5.91.

The structure of (*S,S*)-**6** was unambiguously established by single crystal X-ray diffraction analysis (see Figure 1 in the main text and X-Ray part *below*).

Nickel(II) complex (*S,R*)-6

The desired Ni^{II} complex (*S,R*)-**6** was isolated as a red powder (0.12 g, 19% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (d, *J* = 8.7 Hz, 1H), 7.78–7.75 (m, *2*H), 7.46 (s, 1H, -CH=N-), 7.29–7.26 (m, 3H), 7.25–7.18 (m, 6H), 6.93 (t, *J* = 7.4 Hz, 1H), 4.29 (d, *J* = 12.6 Hz, 1H, N-CH_2Ph), 3.83–3.64 (m, 3H), 3.36 (d, *J* = 14.3 Hz, 1H), 3.31 (d, *J* = 7.8 Hz, 1H), 3.27 (d, *J* = 12.6 Hz, 1H, N-CH_2Ph), 3.21–3.14 (m, 1H), 3.06 (s, 3H, OMs), 3.02 (d, *J* = 14.3 Hz, 1H), 2.36–2.30 (m, 2H), 2.24–2.17 (m, 1H), 2.16–1.88 (m, 5H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.1, 181.0, 161.9, 148.6, 142.8, 134.8, 134.0, 133.7, 133.4, 132.3, 131.6, 129.1, 128.9, 124.0, 123.9, 122.3, 121.5, 78.0, 69.7, 63.2, 62.0, 58.1, 45.0, 37.6, 36.8, 30.9, 27.5, 23.7 ppm. ^{1}H and ^{13}C NMR spectra of the diastereomer are provided in Figure S5 (*below*).

Elemental analysis calcd. for $C_{32}H_{35}N_3NiO_7S$ (%): C, 57.85; H, 5.31; N, 6.32. Found: C, 58.22; H, 5.62; N, 6.07.

Procedure for the synthesis of Ni^{II} complex 7

A round-bottom flask equipped with a stirring bar was filled with a solution of the Ni^{II} complex (*S*,*S*)-**6** (0.2 g, 0.3 mmol) in 10 mL of dry CH_2Cl_2, cooled to 0 °C with stirring, followed by the addition of Et_3N (0.084 mL, 0.6 mmol) and methanesulfonyl chloride (0.069 mL, 0.6 mmol). The reaction mixture was stirred for 15 min at 0 °C under argon and then for 8 h at room temperature. The solvent was then removed under reduced pressure and the residue was dissolved in 5 mL of dry acetone. The precipitated triethylamine hydrochloride was filtered and washed with dry acetone (3×5 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed under reduced pressure and the resulting residue was purified by preparative TLC on silica gel (eluent: $CHCl_3$/acetone 1:1, $R_f = 0.62$) to afford the desired chiral Ni(II) complex (*S*,*S*)-**7** as a red powder (0.14 g, 64% yield). In addition, the complex was purified using Sephadex LH-20 resin (eluent: benzene/EtOH 3:1).

Nickel(II) complex (*S*,*S*)-7

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 8.7 Hz, 1H), 7.96 (d, *J* = 7.3 Hz, 2H), 7.60 (s, 1H, -CH=N-), 7.37–7.23 (m, 7H), 7.23–7.14 (m, 2H), 6.97 (t, *J* = 7.4 Hz, 1H), 4.39–4.34 (m, 1H), 4.26–4.20 (m, 1H), 4.08 (d, *J* = 12.6 Hz, 1H, N-CH_2Ph), 3.45(d, *J* = 12.6 Hz, 1H, N-CH_2Ph), 3.28–3.21 (m, 3H), 3.15 (s, 3H, OMs), 3.02 (s, 3H, OMs), 2.79 (d, *J* = 13.5 Hz, 1H), 2.31–2.09 (m, 5H), 1.89–1.77 (m, 4H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.6, 179.6, 161.7, 148.9, 143.3, 134.6, 134.4, 133.9, 132.4, 131.5, 129.2, 129.0, 128.4, 123.9, 123.1, 122.4, 121.6, 77.8, 70.9, 69.6, 63.6, 57.8, 46.9, 37.8 (2C, OMs), 34.9, 31.0, 24.2, 23.1 ppm. ^{1}H and ^{13}C NMR spectra of the diastereomer are provided in Figure S6 (*below*).

Elemental analysis calcd. for $C_{33}H_{37}N_3NiO_9S_2 \times 0{,}4C_6H_6$ (%): C, 54.95; H, 5.13; N, 5.43. Found: C, 54.99; H, 5.20; N, 5.45.

Nickel(II) complex (*S*,*R*)-7

The desired chiral Ni^{II} complex (*S,R*)-**7** was obtained as a red powder by the *above* Procedure (65% yield).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.33 (d, *J* = 8.5 Hz, 1H), 7.77–7.68 (m, 2H), 7.48 (s, 1H, -CH=N-), 7.30–7.23 (m, 4H), 7.21–7.15 (m, 5H), 6.94 (t, *J* = 7.1 Hz, 1H), 4.35–4.27 (m, 3H), 3.70–3.65 (m, 1H), 3.37–3.27 (m, 3H), 3.17–3.02 (m, 2H), 3.05 (s, 3H, OMs), 2.99 (s, 3H, OMs), 2.35–2.31 (m, 3H), 2.23–2.11 (m, 3H), 2.02–1.90 (m, 2H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.2, 180.4, 162.2, 148.7, 142.9, 134.5, 134.2, 133.9, 133.2, 132.3, 131.7, 129.2, 128.9, 124.0, 122.9, 122.4, 121.6, 69.5, 69.3, 63.1, 58.0, 44.5, 37.7, 37.6, 36.4, 30.9, 24.3, 23.8 ppm. ^{1}H and ^{13}C NMR spectra of the diastereomer are provided in Figure S7 (*below*).

Elemental analysis calcd. for $C_{33}H_{37}N_3NiO_9S_2 \times 0.4H_2O$ (%): C, 52.87; H, 5.08; N, 5.61. Found: C, 52.90; H, 5.34; N, 5.84.

Procedure for the synthesis of Ni^{II} complex ***8***

A round-bottom flask equipped with a stirring bar was filled with a solution of the Ni^{II} complex (*S*,*S*)-**7** (0.14 g, 0.19 mmol) in 6 mL of dry CH_3CN, followed by the addition of anhydrous KF (0.44 g, 7.55 mmol) and 1 M solution of Bu_4NF in THF (0.38 mL). Then, the reaction mixture was stirred for 5 h at 80 °C under argon. The solvent was then removed under reduced pressure and the residue was dissolved in 5 mL of dry acetone. The precipitated KF was filtered and washed with dry acetone (2×5 mL). The combined organic layers were dried over Na_2SO_4, the solvent was removed under reduced pressure and the resulting residue was purified by preparative TLC on silica gel (eluent: $CHCl_3$/acetone 1:1) to afford the desired chiral Ni^{II} complex (*S*,*S*)-**8** as a red powder (0.06 g, 46% yield).

Nickel(II) complex (*S*,*S*)-8

^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.48 (d, *J* = 8.6 Hz, 1H), 8.00 (d, *J* = 7.6 Hz, 2H), 7.60 (s, 1H, -CH=N), 7.39–7.32 (m, 4H), 7.31–7.16 (m, 5H), 6.97 (t, *J* = 7.4 Hz, 1H), 4.69–4.34 (m, 2H, CH_2F), 4.10 (d, *J* = 12.5, 1H, N-CH_2Ph), 3.43 (d, *J* = 12.5 Hz, 1H, N-CH_2Ph), 3.32–3.20 (m, 3H), 3.16 (s, 3H, OMs), 2.81 (d, *J* = 13.5 Hz, 1H), 2.36–2.02 (m, 5H), 1.98–1.87 (m, 1H), 1.86–1.72 (m, 3H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 181.7, 179.8, 161.5, 148.7, 143.1, 134.7, 134.2, 134.1, 133.9, 132.3, 131.4, 129.1, 128.9, 123.9, 123.1, 122.3, 121.5, 83.3 (d, J = 166.0 Hz), 77.8, 70.8, 63.6, 57.9, 46.8, 37.7, 34.8, 30.9, 25.1 (d, J = 20.3 Hz), 23.0 ppm.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –218.72 ppm. ^1H, ^{13}C and ^{19}F NMR spectra of the diastereomer are provided in Figure S8 (*below*).

Elemental analysis calcd. for $C_{32}H_{34}FN_3NiO_6S \times 0{,}15CHCl_3$ (%): C, 56.43; H, 5.03; N, 6.14; F, 2.78. Found: C, 56.78; H, 4.87; N, 5.92; F, 2.62.

The structure of (*S,S*)-**8** was unambiguously established by single crystal X-ray diffraction analysis (see Figure 1 in the main text and X-Ray part *below*).

Nickel(II) complex (*S*,*R*)-8

The desired chiral Ni^{II} complex (*S,R*)-**8** was obtained as a red powder by the *above* Procedure (45% yield).

^1H NMR (400 MHz, $CDCl_3$): δ = 8.32 (d, J = 8.7 Hz, 1H), 7.78–7.74 (m, 2H), 7.47 (s, 1H, -CH=N-), 7.30–7.24 (m, 4H), 7.21–7.14 (m, 5H), 6.93 (t, J = 7.4 Hz, 1H), 4.68–4.40 (m, 2H, CH_2F), 4.29 (d, J = 12.6 Hz, 1H, N-CH_2Ph), 3.70–3.64 (m, 1H), 3.38 (d, J = 14.0 Hz, 1H), 3.33–3.26 (m, 2H), 3.19–3.12 (m, 1H), 3.06 (s, 3H, OMs), 3.03 (d, J = 14.0 Hz, 1H), 2.36–2.28 (m, 3H), 2.24–2.15 (m, 2H), 2.13–2.01 (m, 2H), 1.95–1.89 (m, 1H) ppm.

^{13}C NMR (101 MHz, $CDCl_3$): δ = 182.1, 180.3, 162.0, 148.7, 142.9, 134.7, 134.2, 133.8, 133.3, 132.3, 131.7, 129.2, 129.0, 124.0, 123.0, 122.4, 121.6, 83.4 (d, J = 166.0 Hz), 77.7, 69.6, 63.2, 58.1, 44.9, 37.6, 36.4, 31.0, 25.5 (d, J = 20.3 Hz), 23.8 ppm.

^{19}F NMR (376 MHz, $CDCl_3$): δ = –219.08 ppm. ^1H, ^{13}C and ^{19}F NMR spectra of the diastereomer are provided in Figure S9 (*below*).

HRMS calcd. for $C_{32}H_{35}FN_3NiO_6S$ $[M+H]^+$: 666.1579; found: 666.1583.

References

S1. Y. N. Belokon, V. I. Maleyev, S. V. Vitt, M. G. Ryzhov, Y. D. Kondrashov, S. N. Golubev, Y. P. Vauchskii, A. I. Kazika, M. I. Novikova, P. A. Krasutskii, A. G. Yurchenko, I. L. Dubchak, V. E. Shklover, Y. T. Struchkov, V. I. Bakhmutov and V. M. Belikov, *J. Chem. Soc., Dalton Trans.*, 1985, 17.

S2. Y. N. Belokon', S. M. Motsishkite, V. I. Tararov and V. I. Maleev, *Bull. Acad. Sci. USSR, Div. Chem. Sci*, 1991, **40**, 1355 (*Izv. Akad. Nauk SSSR, Ser. Khim.*, 1991, 1536).

S3. Y. N. Belokon', V. I. Tararov, V. I. Maleev, T. F. Savel'yeva and M. G. Ryzhov, *Tetrahedron: Asymmetry*, 1998, **9**, 4249.

S4. R. N. Krasikova, O. F. Kuznetsova, O. S. Fedorova, V. I. Maleev, T. F. Savel'eva and Yu. N. Belokon, *Bioorg. Med. Chem.*, 2008, **16**, 4994.

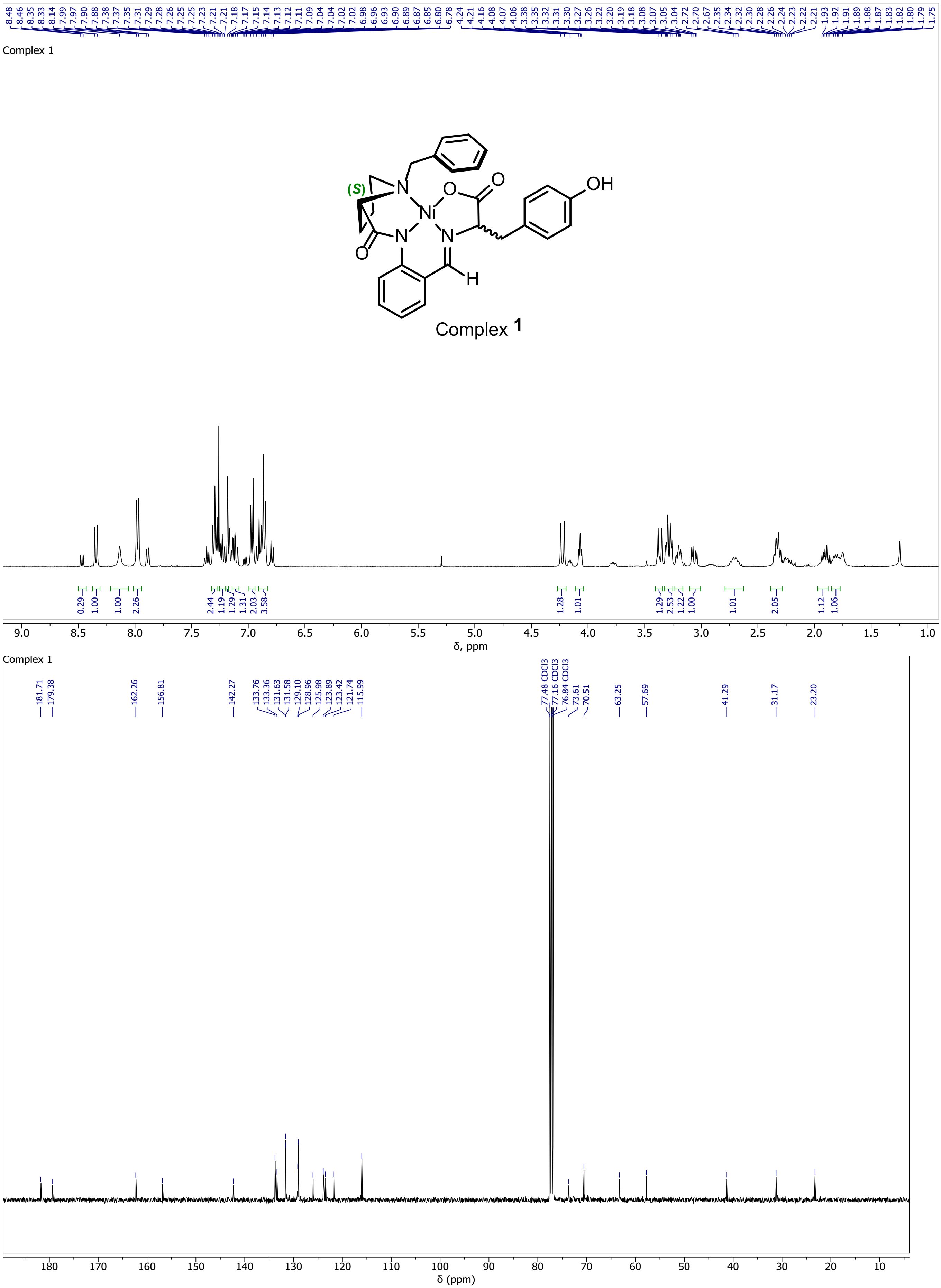


Figure S1. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex **1** in $CDCl_3$ (a mixture of diastereomers *dr* 3.5:1).

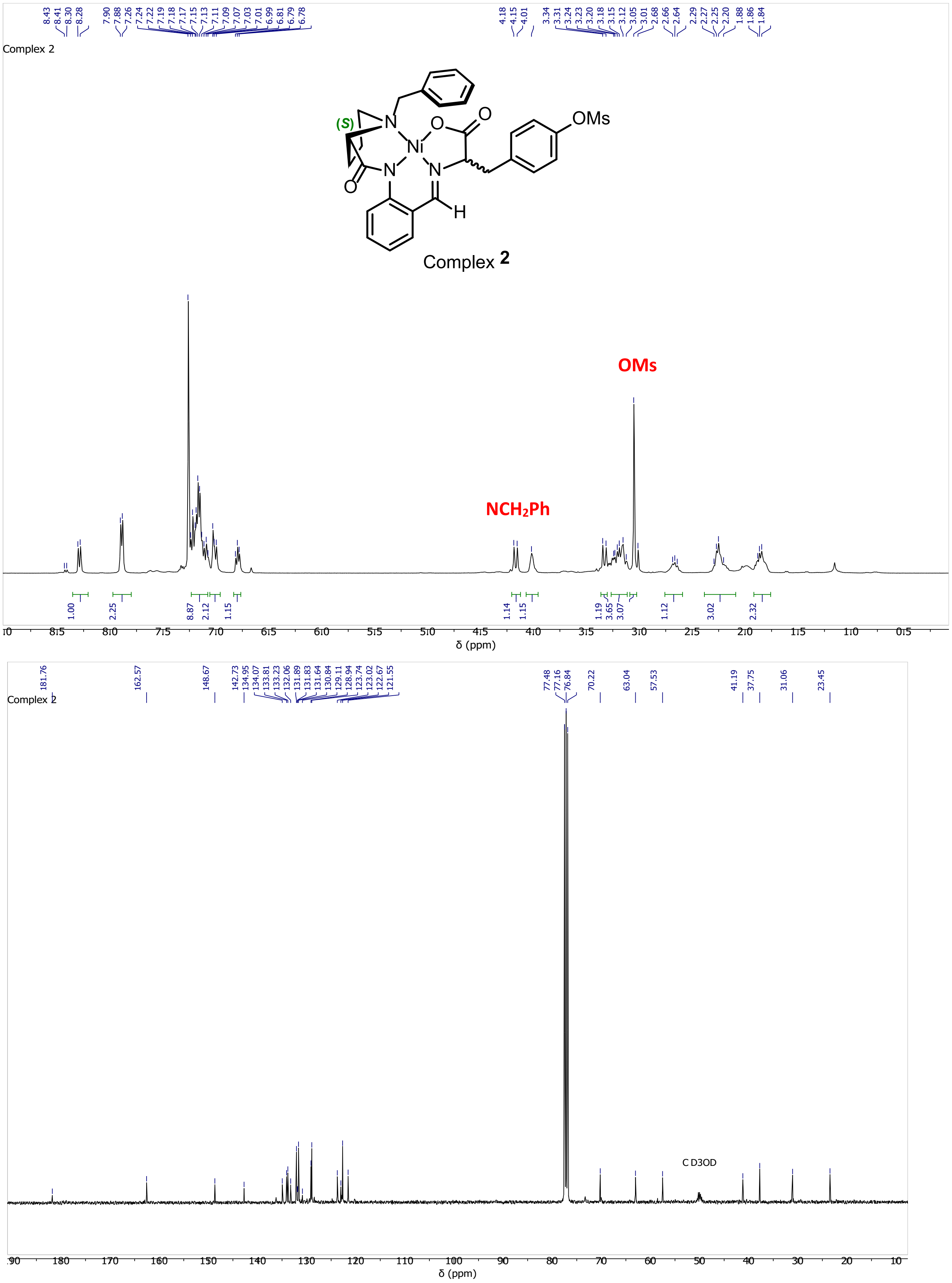


Figure S2. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex **2** in $CDCl_3$.

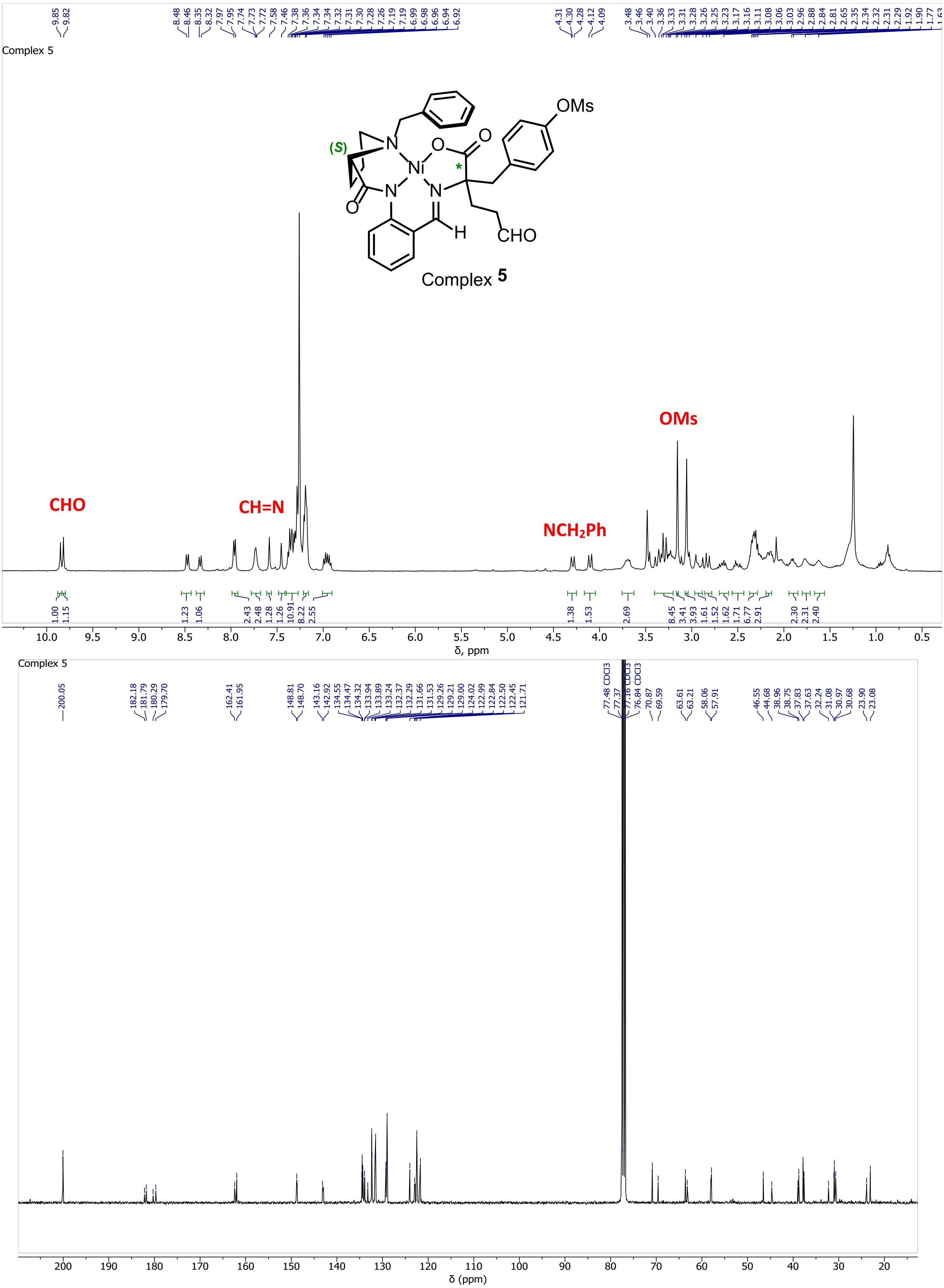


Figure S3. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex **5** in CDCl$_3$ (a mixture of diastereomers *dr* 1.1:1).

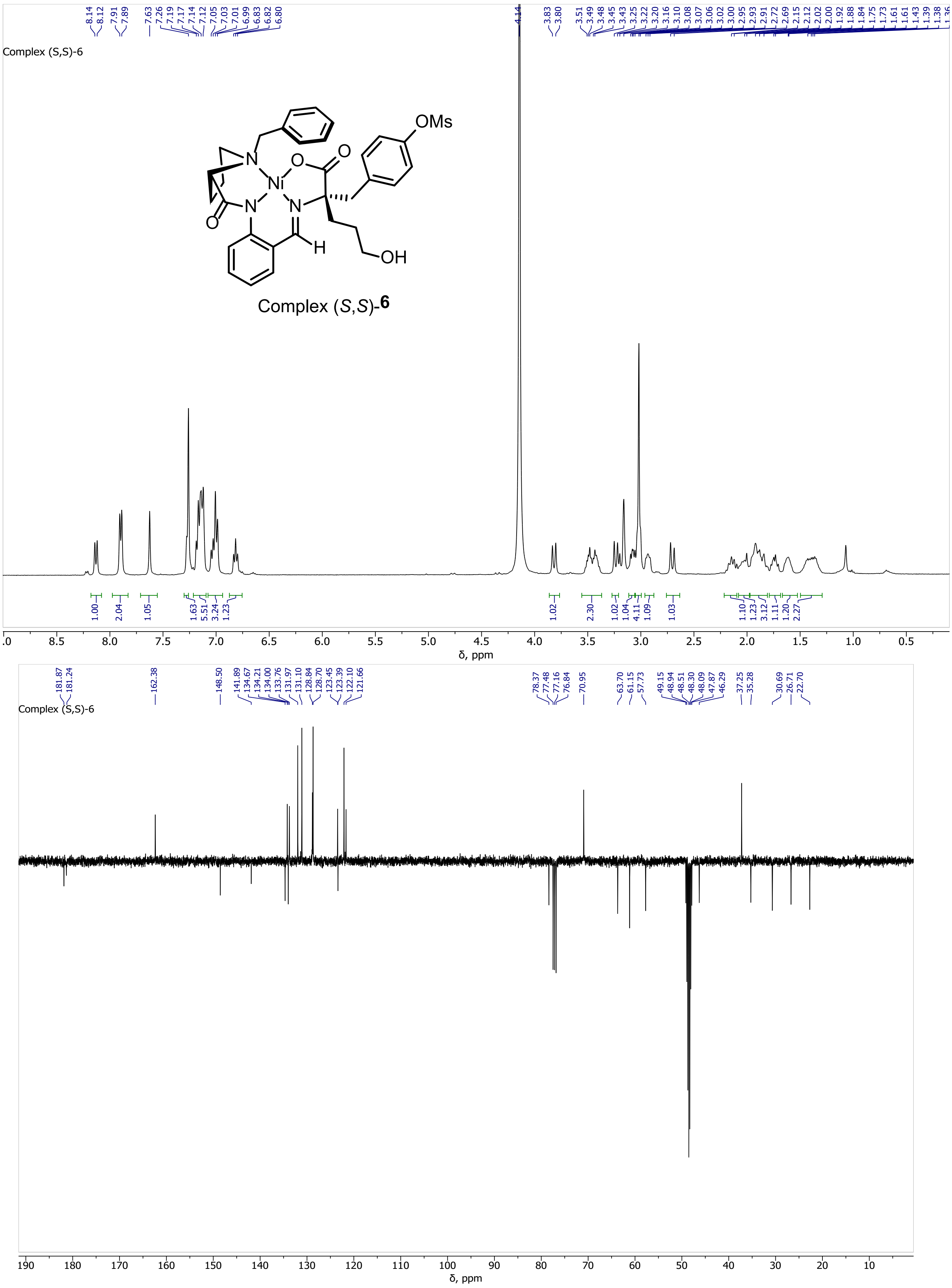


Figure S4. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex (*S*,*S*)-**6** in CDCl$_3$+CD$_3$OD.

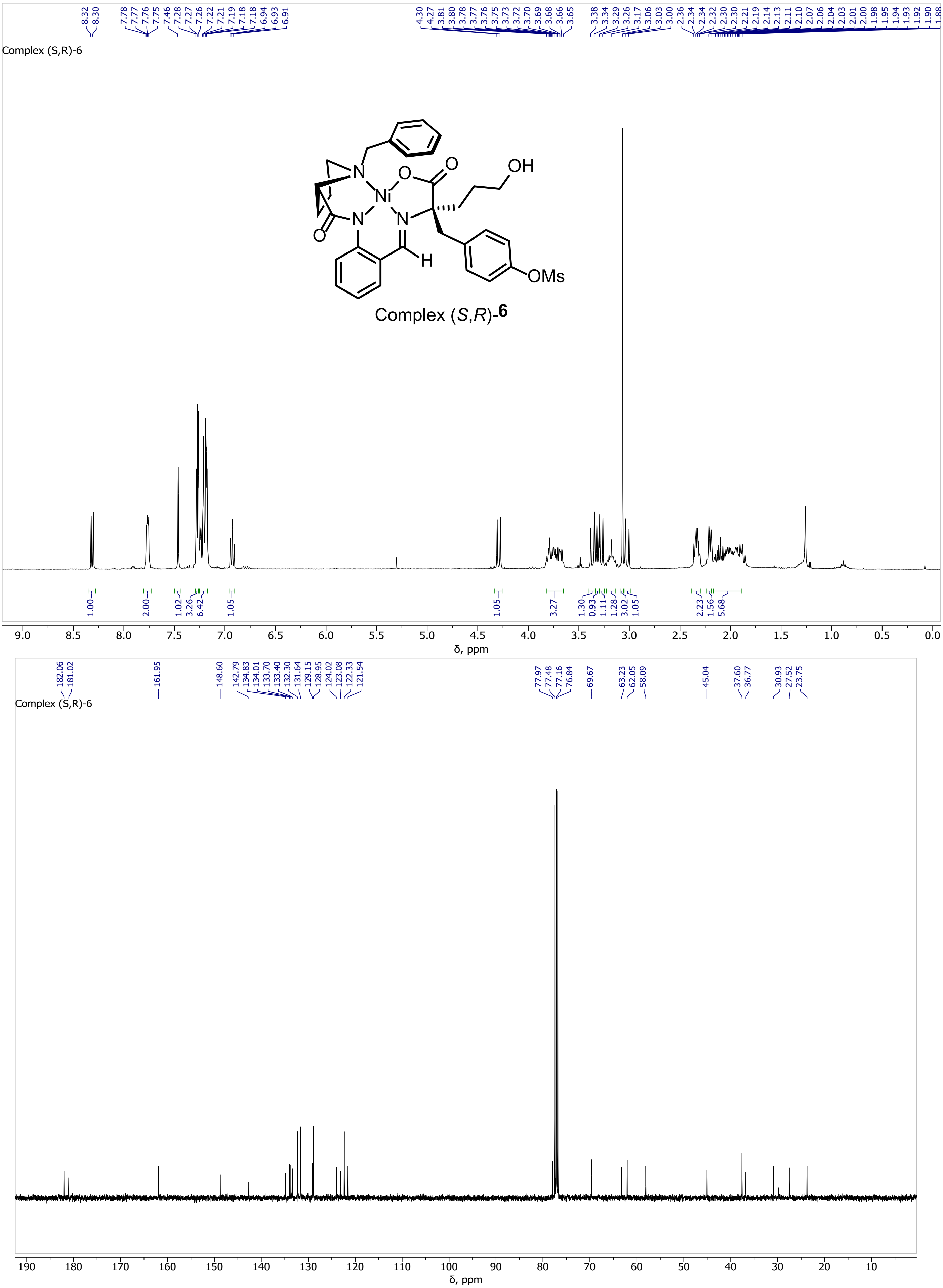


Figure S5. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex (*S*,*R*)-**6** in $CDCl_3$.

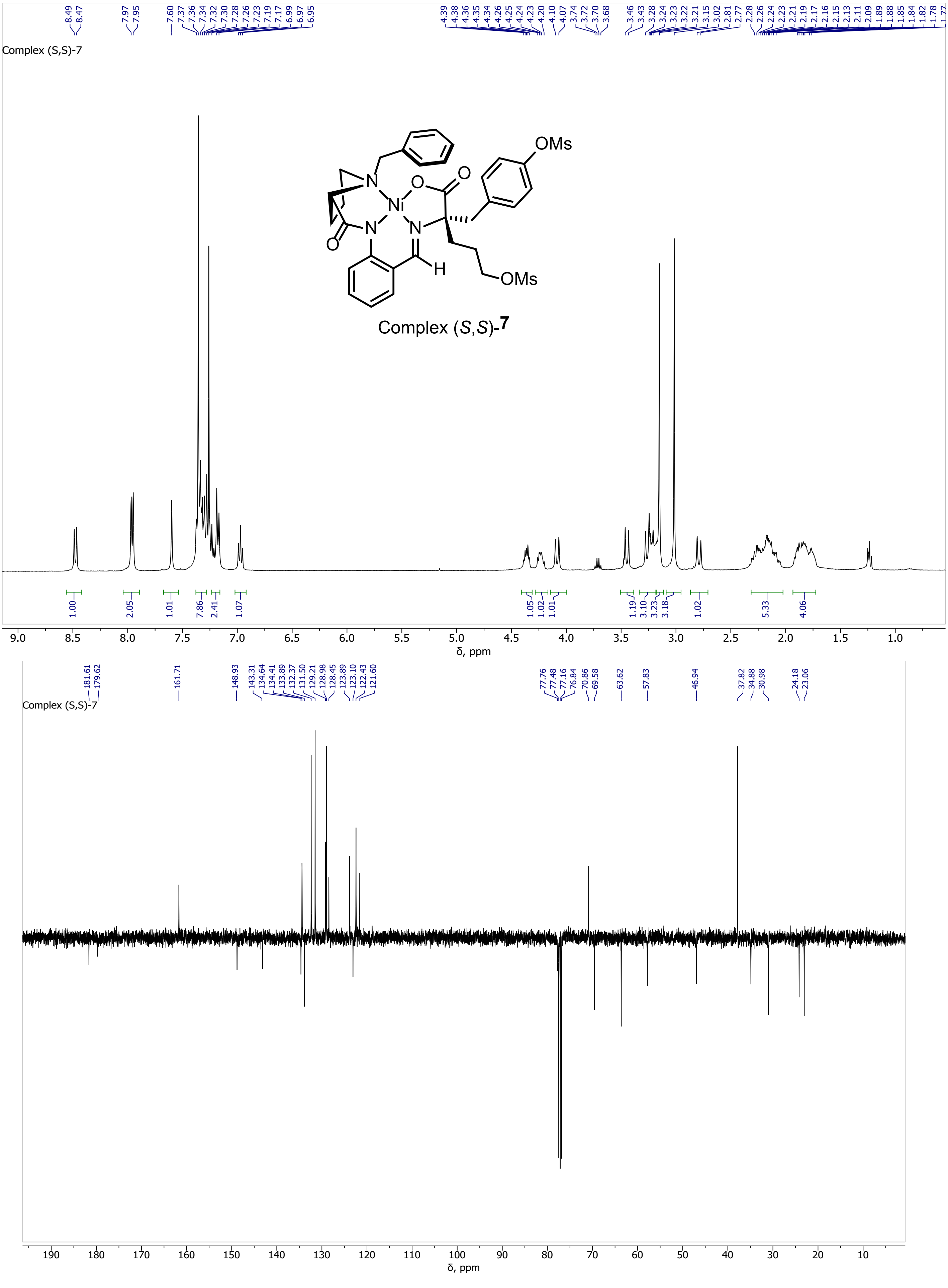


Figure S6. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex (*S*,*S*)-**7** in CDCl$_3$.

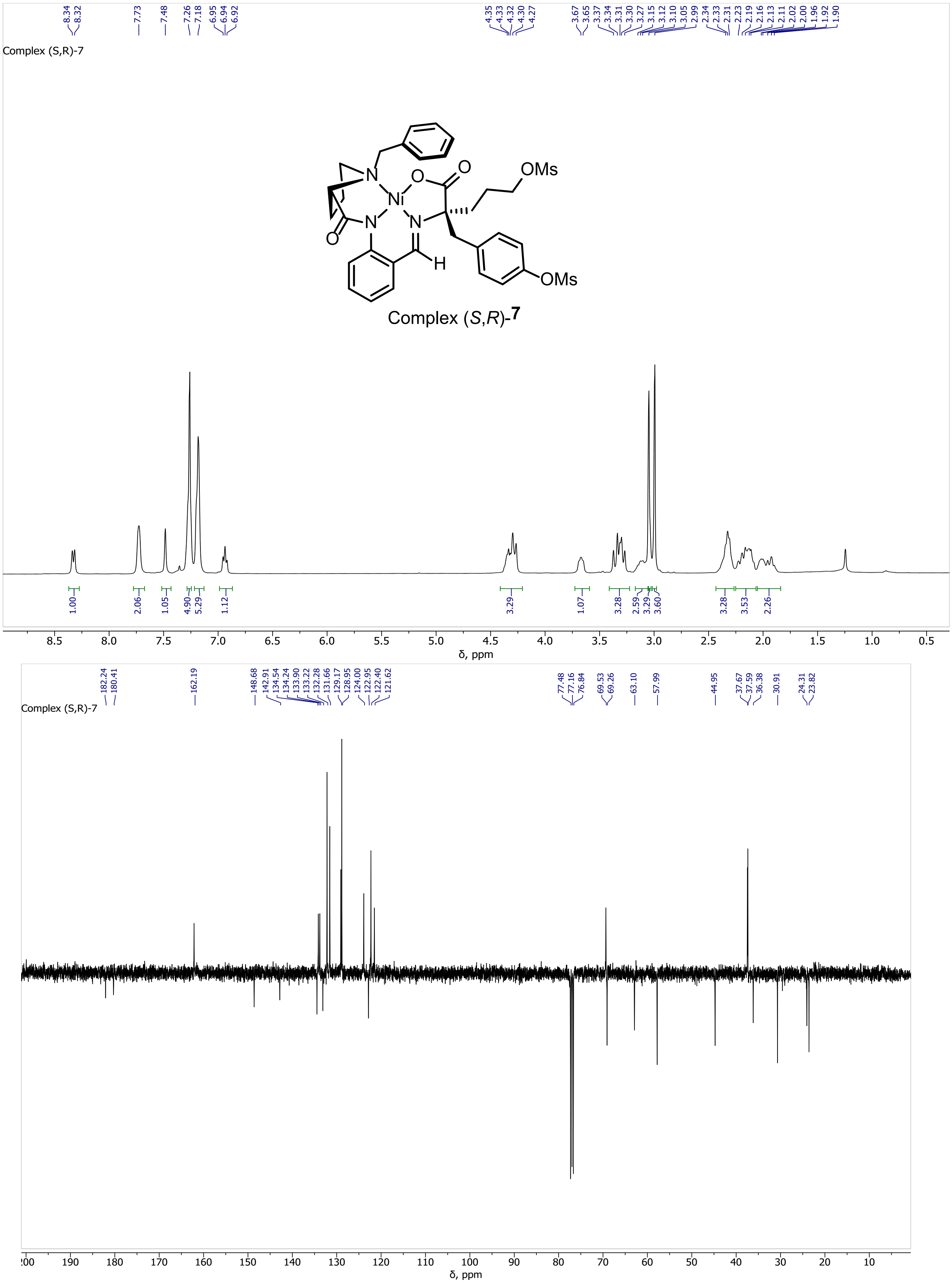
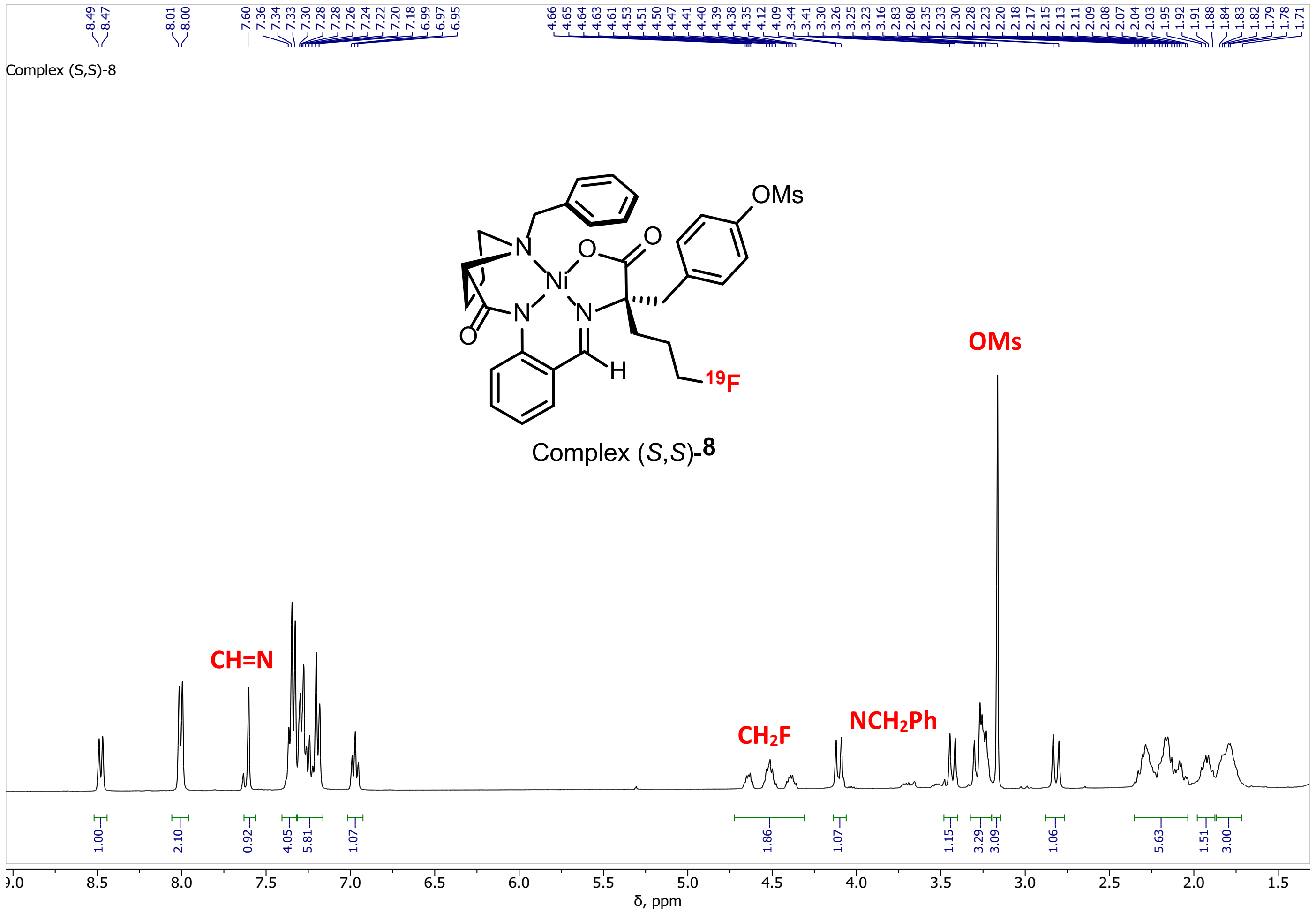
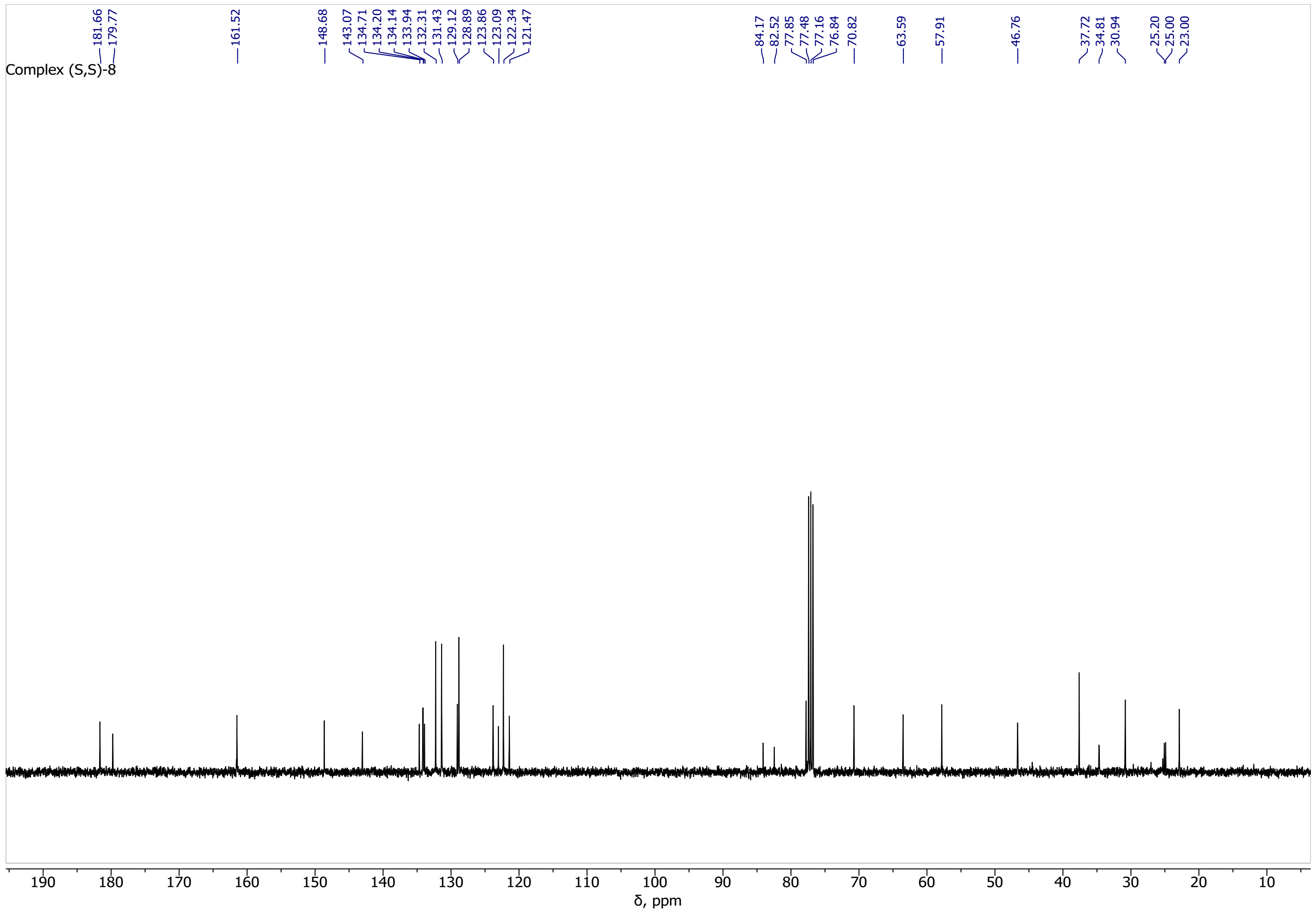


Figure S7. ^{1}H and ^{13}C NMR spectra of the Ni^{II} complex (*S*,*R*)-**7** in CDCl$_3$.


8.49
8.47
8.01
8.00
7.60
7.36
7.34
7.33
7.30
7.28
7.28
7.26
7.24
7.22
7.20
7.18
6.99
6.97
6.95
4.66
4.65
4.64
4.63
4.61
4.53
4.51
4.50
4.47
4.41
4.40
4.39
4.38
4.35
4.12
4.09
3.44
3.41
3.30
3.26
3.25
3.23
3.16
2.83
2.80
2.35
2.33
2.30
2.28
2.23
2.20
2.18
2.17
2.15
2.13
2.11
2.09
2.08
2.07
2.04
2.03
1.95
1.92
1.91
1.88
1.84
1.83
1.82
1.79
1.78
1.71
Complex (S,S)-8
OMs
O
O
N
Ni
O
N
N
H
19F
Complex (S,S)-8
OMs
CH=N
CH2F
NCH2Ph
1.00
2.10
0.92
4.05
5.81
1.07
1.86
1.07
1.15
3.29
3.09
1.06
5.63
1.51
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
δ, ppm


181.66
179.77
161.52
148.68
143.07
134.71
134.20
134.14
133.94
132.31
131.43
129.12
128.89
123.86
123.09
122.34
121.47
84.17
82.52
77.85
77.48
77.16
76.84
70.82
63.59
57.91
46.76
37.72
34.81
30.94
25.20
25.00
23.00
Complex (S,S)-8
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
δ, ppm

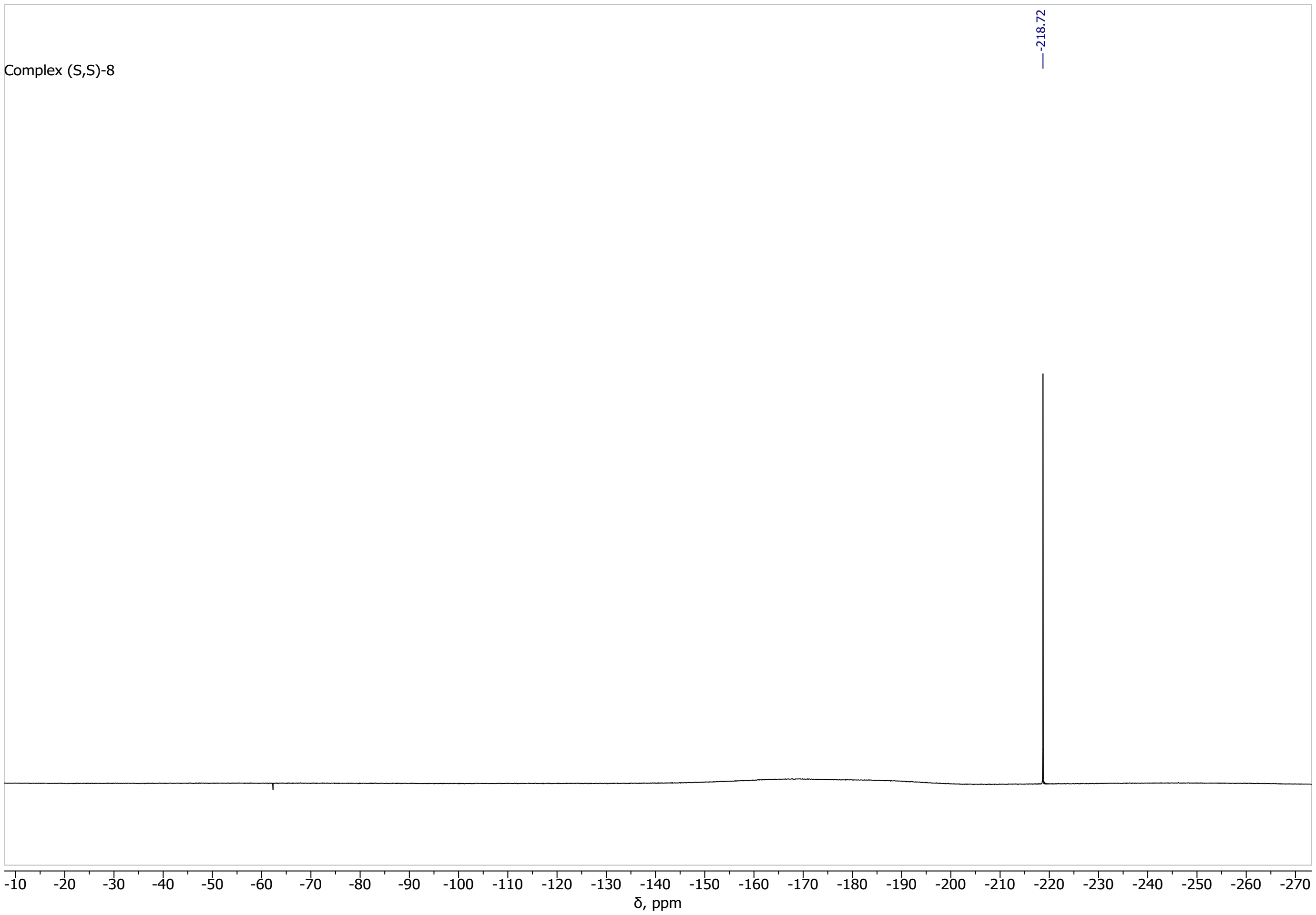
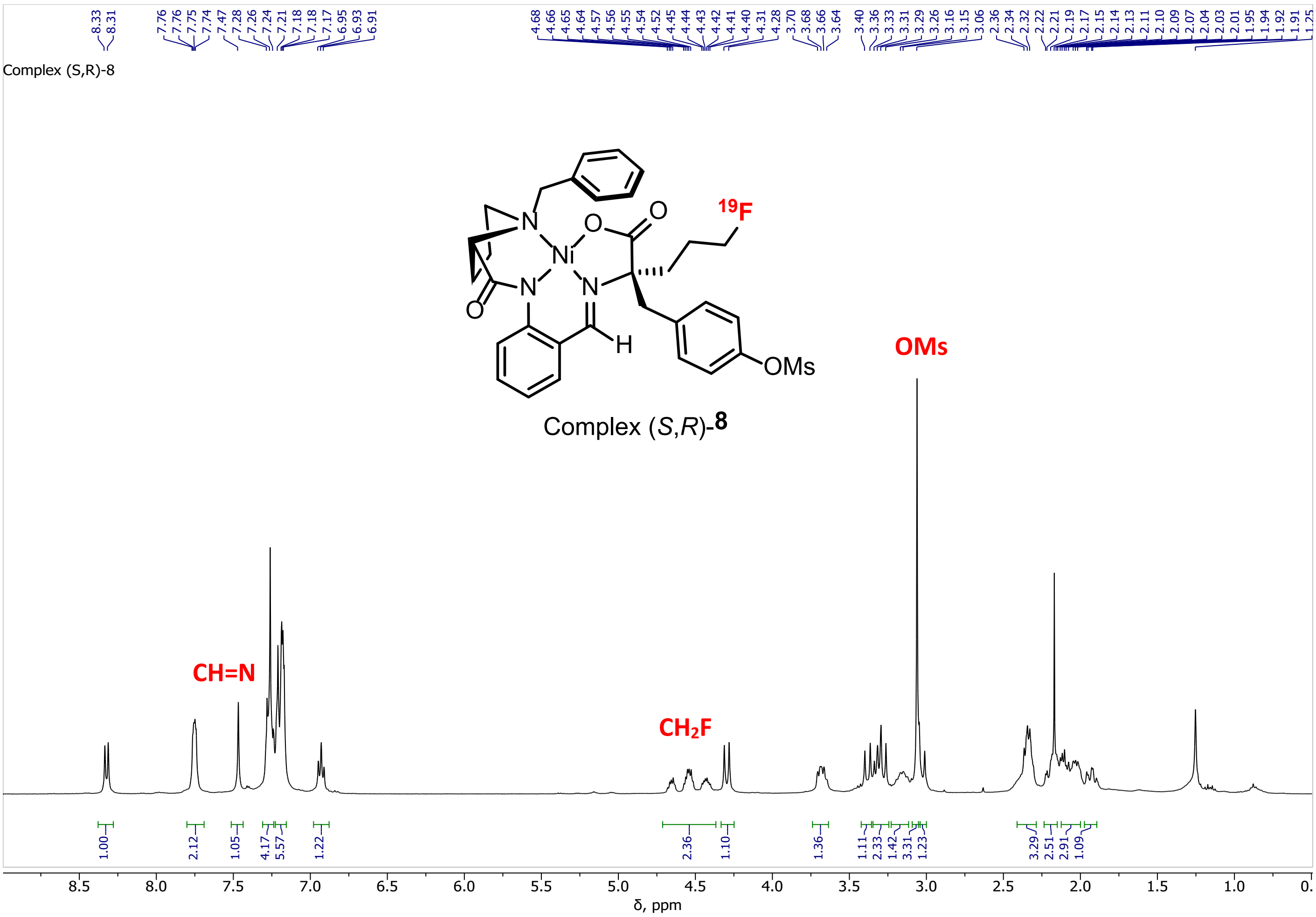
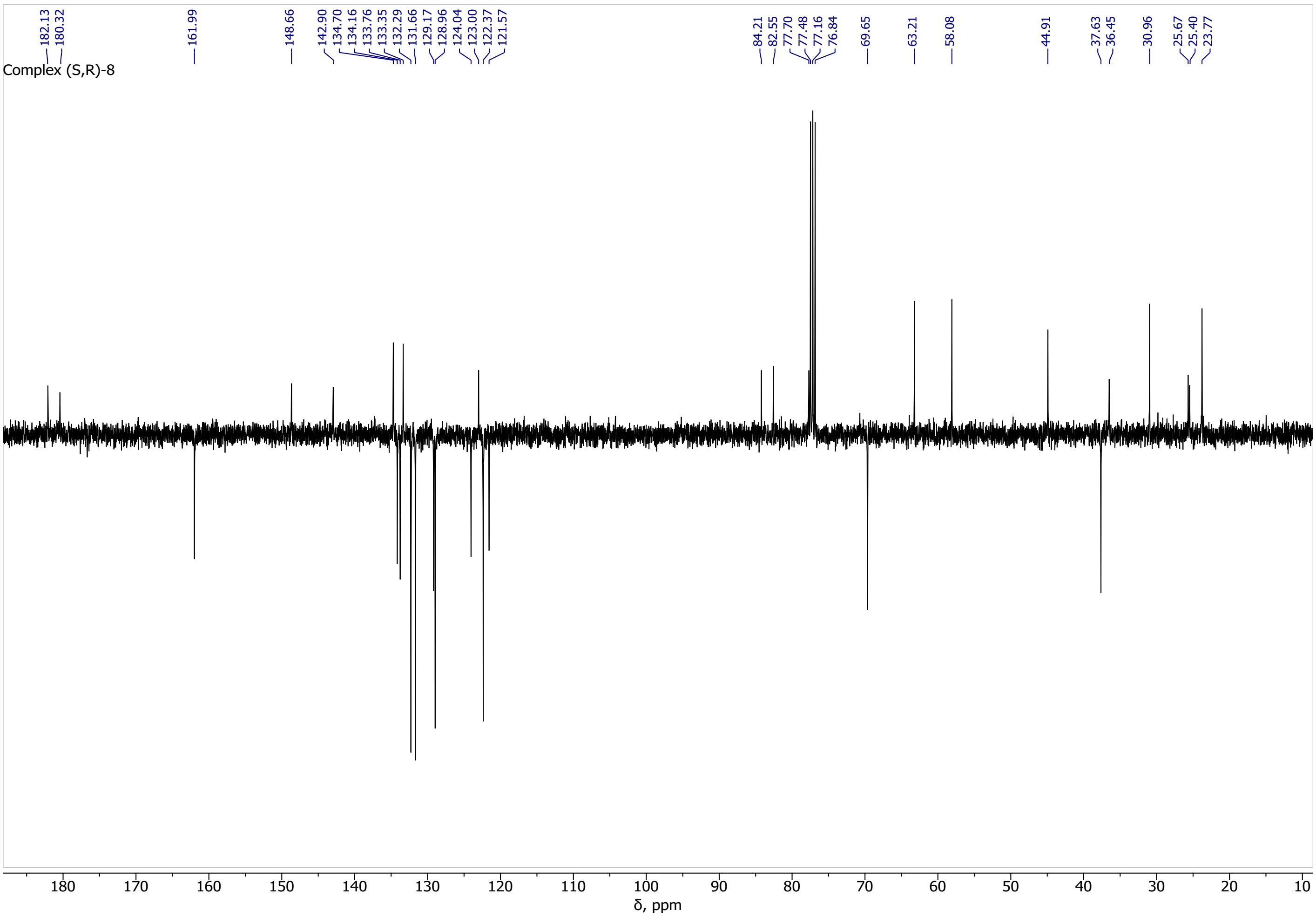


Figure S8. ^{1}H, ^{13}C and ^{19}F NMR spectra of the Ni^{II} complex (*S*,*S*)-**8** in $CDCl_3$.


Complex (S,R)-8
8.33 8.31
7.76 7.76 7.75 7.74 7.47 7.28 7.26 7.24 7.21 7.18 7.17 6.95 6.93 6.91
4.68 4.66 4.65 4.64 4.57 4.56 4.55 4.54 4.52 4.45 4.44 4.43 4.42 4.41 4.40 4.31 4.28 3.70 3.68 3.66 3.64
3.40 3.36 3.33 3.31 3.29 3.26 3.16 3.15 3.06 2.36 2.34 2.32 2.22 2.21 2.19 2.17 2.15 2.14 2.13 2.11 2.10 2.09 2.07 2.04 2.03 2.01 1.95 1.94 1.92 1.91 1.25
19F
O
O
N
Ni
N
N
O
H
OMs
Complex (S,R)-8
OMs
CH=N
CH2F
1.00
2.12
1.05
4.17
5.57
1.22
2.36
1.10
1.36
1.11
2.33
1.42
3.31
1.23
3.29
2.51
2.91
1.09
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.
δ, ppm


182.13
180.32
161.99
148.66
142.90 134.70 134.16 133.76 133.35 132.29 131.66 129.17 128.96 124.04 123.00 122.37 121.57
84.21 82.55 77.70 77.48 77.16 76.84
69.65
63.21
58.08
44.91
37.63 36.45
30.96
25.67 25.40 23.77
Complex (S,R)-8
180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
δ, ppm

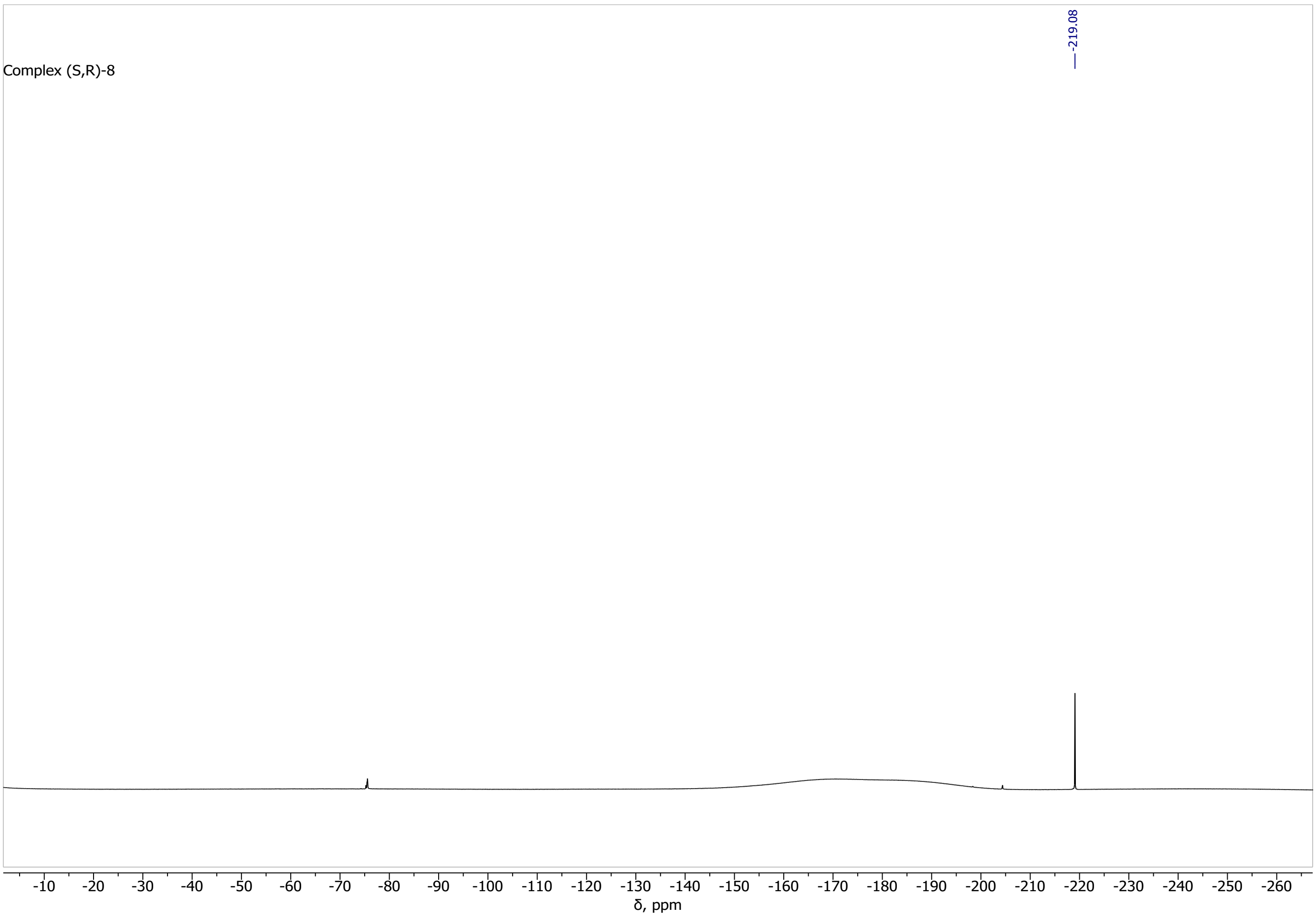


Figure S9. ^{1}H, ^{13}C and ^{19}F NMR spectra of the Ni^{II} complex (*S*,*R*)-**8** in CDCl$_3$.