Asymmetric Synthesis of Sterically and Electronically Demanding Linear ω-Trifluoromethyl Containing Amino Acids via Alkylation of Chiral Equivalents of Nucleophilic Glycine and Alanine

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(A) General Methods

The reagents (chemicals) were purchased from commercial sources, and used without further purification. Analytical thin layer chromatography (TLC) was HSGF 254 (0.15-0.2 mm thickness). All products were characterized by their NMR and MS spectra. ^{1}H and ^{13}C NMR spectra were recorded in deuterochloroform ($CDCl_3$) on a 300MHz instrument. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Low- and high-resolution mass spectra (LRMS and HRMS) were measured on spectrometer. Optical rotations were reported as follows: $[\alpha]_D^{22}$ (c: g/100 mL, in solvent).

(B) General Procedure for the Asymmetric Alkylation Reactions

General Procedure for the Synthesis of (*S*,2*S*)-3a:

The Ni(II) complex of glycine (*S*)-**1a** (200 mg, 0.40 mmol) was dissolved in DMF (2 mL). The sodium hydroxide (19.2 mg, 0.48 mmol) was added at ambient conditions. Then the 1,1,1-trifluoro-4-iodobutane **2a** (104 mg, 0.44 mmol) was added and the reaction mixture was stirred for 0.5 h. The reaction was quenched by pouring the crude reaction mixture over 30 mL aq. sat. NH_4Cl. The suspension was extracted with ethyl acetate (3 times). The combined organic layers were dried with $MgSO_4$, concentrated, and purified by column chromatography on silica gel (petroleum ether/ ethyl acetate = 1/1) to give (*S*,2*S*)-**3a** as a red solid.

Procedure for the Synthesis of (*S*,2*S*)-3d: The Ni(II) complex of alanine (*S*)-**1b** (200 mg, 0.39 mmol) was dissolved in DMF (2 mL). The sodium hydroxide (131 mg, 1.17 mmol) was added at ambient conditions. Then the 1,1,1-trifluoro-4-iodobutane **2a** (232 mg, 0.98 mmol) was added and the reaction mixture was stirred for 1h. The reaction was quenched by pouring the crude reaction mixture over 30 mL aq. sat. NH_4Cl. The suspension was extracted with ethyl acetate (3 times). The combined organic layers were dried with $MgSO_4$, concentrated, and purified by column chromatography on silica gel (petroleum ether/ ethyl acetate = 1/1) to give (*S*,2*S*)-**3d** as a red solid. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 6.0 min, t_{major} = 9.2 min, de = 99%.

Procedure for the Synthesis of (*S*)-4a: The crystallized complex (*S*,2*S*)-**3a** (1 g, 1.65 mmol) was decomposed by refluxing a suspension in a mixture of aqueous 6 N HCl (1 mL) and MeOH (15 mL) for 30 min, until the red color of the solution disappeared, as described previously. The reaction was cooled to room temperature and then evaporated to dryness. Water (20 mL) was added to the residue to form a clear solution, and this solution was then separated by column chromatography on C_{18}-reversed phase (230-400 mesh) silica gel. Pure water as an eluent was employed to remove the green $NiCl_2$ and excess HCl; water was then used to obtain optically pure product (*S*)-**4a** (293 mg, 96%): $[\alpha]_D^{24}$ = +7.9 (*c* = 0.38 g/100 mL, 6 N HCl). The ligand BPB that decomposed from (*S*,2*S*)-**3a** was recovered by MeOH eluent (608 mg, 96%), and the column chromatography was washed with 100 mL of MeOH for further use.

Procedure for the synthesis of (*S*)-1[1].

(*S*)-BPB (1 g, 2.60 mmol), Gly (976 mg, 13.0 mmol), $Ni(NO_3)_2 \cdot 6H_2O$ (1.52 g, 5.21 mmol), MeOH (50 mL) was added as solvent. And NaH (55-65% in oil, 1.04 g, 26 mmol), KOH (437 mg, 7.81 mmol) were added successively. The resulting mixture was refluxed for 2 h and then the reaction was terminated and cooled. The solution was neutralized with acetic acid. After 12 h the separated crystalline solid was filtered and washed with 100 mL of ethanol, followed by stirring in methane/water (v/v) 1:2, 200 mL), then filtered to form a red crystal (1.27 g, yield 98%). The complex was sufficiently pure for further use without additional purification.

(C) Analytical Characterization Data of Asymmetric Alkylation Products

Ni(II)-(*S*)-BPB/(*S*)-2-Amino-6,6,6-Trifluorohexanoic Acid Schiff Base Complex 3a. Mp 183-185 ºC; $[\alpha]_D^{24}$ = +1667 (*c* = 0.3 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.13 (d, *J* = 8.4 Hz, 1H), 8.07 (d, *J* = 7.5 Hz, 2H), 7.55-7.43 (m, 3H), 7.35 (t, *J* = 7.5 Hz, 2H), 7.29-7.26 (m, 1H), 7.22-7.11 (m, 2H), 6.92 (d, *J* = 6.6 Hz, 1H), 6.70-6.62 (m, 2H), 4.42 (d, *J* = 12.6 Hz, 1H), 3.90 (dd, J_1 = 8.4 Hz, J_2 = 3.6 Hz, 1H). 3.60-3.44 (m, 4H), 2.78-2.70 (m, 1H), 2.58-2.49 (m, 1H), 2.37-2.31 (m, 1H), 2.22-1.94 (m, 6H), 1.90-1.79 (m, 2H), 1.73-1.62 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.0, 23.5, 30.6, 33.0 (q, *J* = 28.7 Hz), 34.0, 57.0, 63.1, 69.4, 70.2, 120.7, 123.6, 125.3, 126.2, 126.7 (q, *J* = 274.9 Hz), 127.0, 127.2, 128.8, 128.9, 129.8, 131.4, 132.2, 133.1, 133.5, 142.2, 170.8, 178.8, 180.3 ppm. LRMS (EI) $[M]^+$ found *m/z* 607. HRMS (EI) $[M]^+$ found *m/z* 607.1593, calcd. for $C_{31}H_{30}F_3N_3NiO_3$ 607.1598. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 6.0 min, t_{major} = 12.3 min, de = 97%.

Ni(II)-(*R*)-BPB/(*R*)-2-Amino-6,6,6-Trifluorohexanoic Acid Schiff Base Complex 3a. Mp 182-184 ºC; $[\alpha]_D^{24}$ = -2248 (*c* = 0.3 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.11 (d, *J* = 8.7 Hz, 1H), 8.04 (d, *J* = 7.8 Hz, 2H), 7.52-7.45 (m, 3H), 7.36-7.31 (m, 2H), 7.26-7.20 (m, 3H), 6.90 (d, *J* = 7.2 Hz, 1H), 6.65-6.61 (m, 2H), 4.40 (d, *J* = 12.6 Hz, 1H), 3.89 (dd, J_1 = 8.1 Hz, J_2 = 3.3 Hz, 1H). 3.58-3.43 (m, 4H), 2.77-2.71 (m, 1H), 2.55-2.49 (m, 1H), 2.40-2.33 (m, 1H), 2.18-1.88 (m, 6H), 1.81-1.79 (m, 2H), 1.70-1.62 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.0, 23.5, 30.6, 33.0 (q, *J* = 28.7 Hz), 34.0, 57.0, 63.0, 69.6, 70.1, 120.7, 123.6, 125.3, 126.2, 127.0, 127.2, 128.8, 128.9, 129.8, 131.4, 132.2, 133.1, 133.5, 142.2, 170.8, 178.8, 180.3 ppm. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{major} = 6.0 min, de > 99%.

Ni(II)-(*S*)-BPB/(*S*)-2-Amino-5,5,5-Trifluoropentanoic Acid Schiff Base Complex 3b. Mp 201-203 ºC; $[\alpha]_D^{23}$ = +1774 (*c* = 0.1 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.13 (d, *J* = 8.7 Hz, 1H), 8.06 (d, *J* = 7.5 Hz, 2H), 7.56-7.45 (m, 3H), 7.36 (t, *J* = 7.5 Hz, 2H), 7.28-7.24 (m, 1H), 7.23-7.12 (m, 2H), 6.95 (d, *J* = 6.6 Hz, 1H), 6.71-6.63 (m, 2H), 4.42 (d, *J* = 13.6 Hz, 1H), 3.84 (dd, J_1 = 9.6 Hz, J_2 = 3.3 Hz, 1H). 3.59-3.46 (m, 4H), 2.77-2.68 (m, 2H), 2.59-2.54 (m, 1H), 2.42-2.38 (m, 1H), 2.24-2.20 (m, 1H), 2.14-2.04(m, 2H), 1.89-1.84 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 23.8, 28.0, 30.1 (q, *J* = 29.4 Hz), 30.7, 57.2, 63.2, 68.5, 70.2, 120.8, 123.8, 124.9, 126.1, 126.3 (q, *J* = 274.7 Hz), 126.9, 127.2, 128.9, 129.0, 129.1, 129.9, 131.5, 132.5, 133.2, 133.3, 142.4, 171.4, 178.3, 180.4 ppm. LRMS (EI) $[M]^+$ found *m/z* 593. HRMS (EI) $[M]^+$ found *m/z* 593.1436, calcd. for $C_{30}H_{28}F_3N_3NiO_3$ 593.1442. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 6.0 min, t_{major} = 12.2 min, de > 99%.

Ni(II)-(*R*)-BPB/(*R*)-2-Amino-5,5,5-Trifluoropentanoic Acid Schiff Base Complex 3b. Mp 200-202 ºC; $[\alpha]_D^{23}$ = -1868 (*c* = 0.31 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.12 (d, *J* = 8.7 Hz, 1H), 8.05 (d, *J* = 7.5 Hz, 2H), 7.54-7.51 (m, 3H), 7.36 (t, J = 7.8 Hz, 3H), 7.20-7.13 (m, 2H), 6.95 (d, J = 7.2 Hz, 1H), 6.68-6.63 (m, 2H), 4.42 (d, J = 12.6 Hz, 1H), 3.84 (dd, J_1 = 10.2 Hz, J_2 = 3.9 Hz, 1H). 3.59-3.46 (m, 4H), 2.75-2.70 (m, 2H), 2.58-2.53 (m, 1H), 2.43-2.39 (m, 1H), 2.25-2.21 (m, 1H), 2.11-2.05 (m, 2H), 1.90-1.85 (m, 1H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 19.2, 23.9, 28.1, 29.7, 30.7, 57.1, 63.1, 68.5, 70.21, 120.9, 123.8, 124.9, 126.1, 126.9, 127.2, 127.7, 128.8, 128.9, 129.0, 129.1, 130.0, 131.5, 131.8, 132.5, 133.1, 133.3, 133.4, 142.3, 171.4, 178.3, 180.6 ppm. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 6.0 min, t_{major} = 12.3 min, de = 96%.

Ni(II)-(*S*)-BPB/(*S*)-2-Amino-4,4,4-Trifluorobutanoic Acid Schiff Base Complex 3c. Mp 173-175 ºC; $[\alpha]_D^{24}$ = +2821 (c = 0.19 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.24 (d, J = 8.4 Hz, 1H), 8.06 (d, J = 7.6 Hz, 2H), 7.57-7.48 (m, 3H), 7.36 (t, J = 7.6 Hz, 2H), 7.28-7.25 (m, 1H), 7.23-7.15 (m, 2H), 6.96 (d, J = 7.6 Hz, 1H), 6.69-6.61 (m, 2H), 4.41 (d, J = 12.8 Hz, 1H), 4.20 (dd, J_1 = 6.8 Hz, J_2 = 2.8 Hz, 1H). 3.62-3.52(m, 2H), 3.46-3.40 (m, 2H), 2.85-2.81 (m, 1H), 2.59-2.49 (m, 2H), 2.16-2.03 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.8, 30.8, 35.8 (q, J = 28.7 Hz), 57.1, 63.3, 64.3, 70.5, 120.6, 123.7, 126.0, 126.5, 127.7, 128.8, 128.9, 129.2, 130.2, 131.5, 132.8, 133.2, 133.4, 133.9, 143.1, 172.7, 177.5, 180.5 ppm. LRMS (EI) $[M]^+$ found m/z 579. HRMS (EI) $[M]^+$ found m/z 579.1280, calcd. for $C_{29}H_{26}F_3N_3NiO_3$ 579.1283. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 7.1 min, t_{major} = 14.0 min, de > 96%.

Ni(II)-(*R*)-BPB/(*R*)-2-Amino-4,4,4-Trifluorobutanoic Acid Schiff Base Complex 3c. Mp 174-176 ºC; $[\alpha]_D^{24}$ = -2634 (c = 0.29 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 8.22 (d, *J* = 8.4 Hz, 1H), 8.05 (d, *J* = 7.8 Hz, 2H), 7.56-7.50 (m, 3H), 7.36 (t, *J* = 7.8 Hz, 2H), 7.26-7.15 (m, 3H), 6.95 (d, *J* = 7.2 Hz, 1H), 6.65-6.60 (m, 2H), 4.39 (d, *J* = 12.9 Hz, 1H), 4.19 (d, *J* = 4.2 Hz, 1H). 3.61-3.41 (m, 4H), 2.87-2.77 (m, 1H), 2.54-2.51 (m, 2H), 2.09-2.03 (m, 3H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 22.8, 30.7, 57.1, 63.3, 64.4, 70.5, 120.6, 123.6, 126.0, 126.5, 127.0, 127.7, 128.8, 128.9, 129.2, 130.2, 131.5, 132.7, 133.2, 133.4, 133.9, 143.0, 172.7, 177.8, 180.6 ppm. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 7.1 min, t_{major} = 14.1 min, de = 94%.

Ni(II)-(*S*)-BPB/(*S*)-2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid Schiff Base Complex 3d. Mp 203-205 ºC; $[\alpha]_D^{24}$ = +1932 (*c* = 0.23 g/100 mL, $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 8.08 (d, *J* = 7.5 Hz, 2H), 8.00 (d, *J* = 8.7 Hz, 1H), 7.51-7.27 (m, 7H), 7.18-7.12 (m, 1H), 6.98 (d, *J* = 7.5 Hz, 1H), 6.64 (d, *J* = 3.6 Hz, 2H), 4.49 (d, *J* = 13.6 Hz, 1H), 4.12 (q, *J* = 7.2 Hz, 1H), 3.72-3.62 (m, 2H), 3.49-3.41 (m, 1H), 3.27-3.19 (m, 1H), 2.66-2.63 (m, 1H), 2.52-2.44 (m, 2H), 2.05 (s, 3H), 1.31-1.23 (m, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.5, 23.1, 29.7, 30.6, 33.6 (q, *J* = 29.1 Hz), 38.4, 57.2, 63.4, 70.0, 120.8, 124.1, 126.9, 127.1, 128.0, 128.6, 128.9, 129.0, 129.6, 130.1, 131.6, 131.7, 133.3, 136.4, 141.5, 173.0, 180.6, 182.0 ppm. LRMS (EI) $[M]^+$ found *m/z* 621. HRMS (EI) $[M]^+$ found *m/z* 621.1749, calcd. for $C_{32}H_{32}F_3N_3NiO_3$ 621.1759. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 6.0 min, t_{major} = 9.2 min, de = 99%.

Ni(II)-(*R*)-BPB/(*R*)-2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid Schiff Base Complex 3d. Mp 201-203 ºC; $[\alpha]_D^{20}$ = -1336 (*c* = 0.36 g/100 mL, $CHCl_3$). ^{1}H NMR

($CDCl_3$, 300 MHz): δ = 8.07 (d, *J* = 7.2 Hz, 2H), 7.98 (d, *J* = 8.7 Hz, 1H), 7.50-7.34 (m, 7H), 7.15-7.13 (m, 1H), 6.96 (d, *J* = 7.5 Hz, 1H), 6.64-6.63 (m, 2H), 4.48 (d, *J* = 12.6 Hz, 1H), 4.32-4.10 (m, 1H), 3.70-3.64 (m, 2H), 3.45-3.40 (m, 1H), 3.28-3.18 (m, 1H), 2.69-2.63 (m, 1H), 2.51-2.45 (m, 2H), 2.20-2.00 (s, 6H), 1.30 (s, 6H) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 18.5, 23.1, 29.7, 30.6, 33.6 (q, *J* = 29.2 Hz), 38.4, 57.1, 63.4, 70.0, 120.8, 124.1, 126.8, 127.1, 128.0, 128.6, 128.8, 128.9, 129.0, 129.5, 130.1, 131.6, 131.7, 133.3, 136.4, 141.5, 173.0, 180.6, 182.0 ppm. HPLC (Chiralpak IA, *i*-propanol/*n*-hexane = 40/60, flow rate 1.0 mL/min, λ = 254 nm), t_{minor} = 5.8 min, t_{major} = 9.0 min, de > 97%.

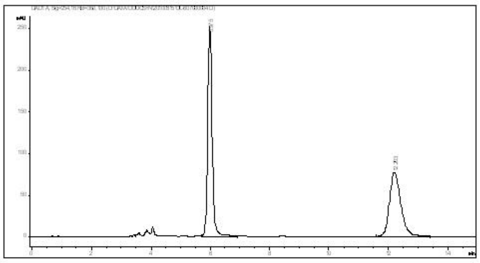
2-Amino-6,6,6-Trifluorohexanoic Acid 4a: Mp 193-195 ºC;; $[\alpha]_D^{24}$ = +7.9 (*c*= 0.38 g/100 mL, 6 *N* HCl).^1H NMR (D_2O, 300 MHz): δ = 3.78-3.73 (m, 1H), 2.21-2.06 (m, 2H), 1.87-1.81 (m, 2H), 1.62-1.52 (m, 2H) ppm. ^{13}C NMR (D_2O, 100 MHz): δ = 19.8, 31.2, 34.6 (q, *J* = 28.2 Hz), 55.1, 129.6 (q, *J* = 274.4 Hz), 174.3 ppm. LRMS (ESI) $[M+H]^+$ found *m/z* 186. HRMS (ESI) $[M+Na]^+$ found *m/z* 208.0561, calcd. for $C_6H_{10}F_3NO_2Na$ 208.0557.

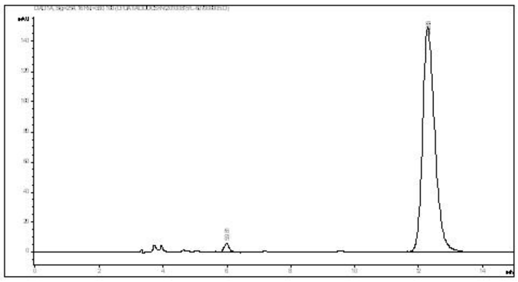
2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid 4d: Mp 193-195 ºC; $[\alpha]_D^{27}$ = +8.3 (*c*= 0.4 g/100 mL, 6 *N* HCl).^1H NMR (D_2O, 300 MHz): δ = 2.31-2.20 (m, 2H), 2.04-1.85 (m, 2H) 1.75-1.67 (m, 1H), 1.55 (s, 3H), 1.53-1.49 (m, 1H) ppm. ^{13}C NMR (D_2O, 100 MHz): δ = 18.6, 24.4, 34.7 (q, *J* = 28.3 Hz), 38.2, 63.2, 129.5 (q, *J* = 274.5 Hz), 178.0 ppm. LRMS (ESI) $[M+H]^+$ found *m/z* 200. HRMS (ESI) $[M+Na]^+$ found *m/z* 222.0718, calcd. for $C_7H_{12}F_3NO_2Na$ 222.0718.

Analytical high performance liquid chromatography was carried out using the Dionex

ASI-100 automated sampler, using the Chiralpak IA column. The loading loop was 5 μL. The eluting employed was an isocratic mixture of *n*-hexane and *i*-propanol (60:40 respectively) at a flow of 1 mL/min unless stated. Retention times are reported in minutes. The enantiomeric excess was calculated from the integration of the absorption peaks at 254 nm.

(*S*,2*S*)-**3a**: R_t(minor) = 6.0 min, R_t(major) = 12.3 min, de = 97%;

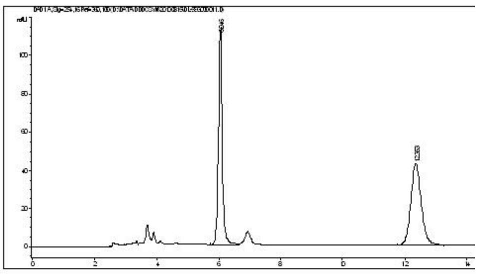


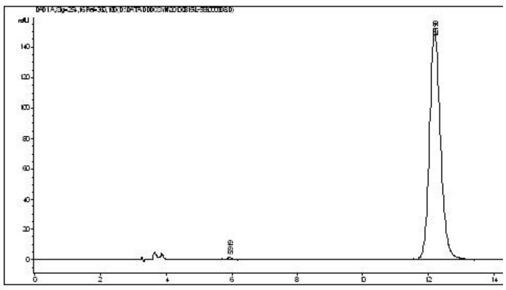


Peak #	Time [Min]	Area	Height [μV]	Width [min]	Area [%]
1	5.975	2532.8	252.7	0.151	55.656
2	12.203	2018	77.5	0.3956	44.344

Peak #	Time [Min]	Area	Height [μV]	Width [min]	Area [%]
1	5.981	60	5.6	0.1636	1.497
2	12.283	3945.3	149	0.4068	98.503

(*S*,2*S*)-**3b**: R_t(minor) = 6.0 min, R_t(major) = 12.2 min, de > 99%.

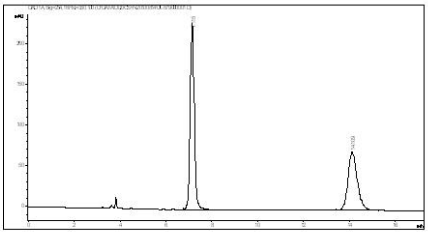


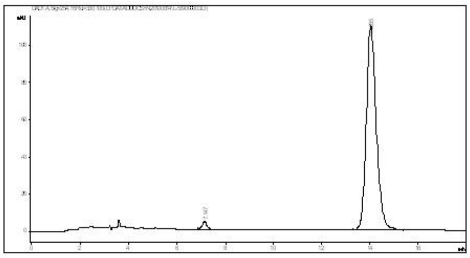


Peak #	Time [Min]	Area	Height [μV]	Width [min]	Area [%]
1	6.046	1163.6	113.8	0.1552	53.864
2	12.353	996.6	43.2	0.3533	46.136

Peak #	Time [Min]	Area	Height [μV]	Width [min]	Area [%]
1	5.919	13.9	1.4	0.1526	0.395
2	12.19	3508	151.7	0.3538	99.605

(*S*,2*S*)-**3c**: R_t(minor) = 7.147 min, R_t(major) = 14.035 min, de > 96%.

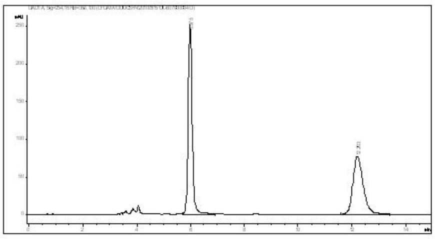


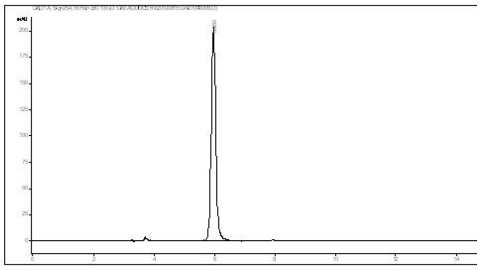


Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	7.115	2863.8	228.7	0.1901	58.766
2	14.109	2009.4	71.2	0.4293	41.234

Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	7.147	54.7	4.3	0.1956	1.733
2	14.035	3099.4	109.4	0.4324	98.267

(*R*,2*R*)-**3a**: R_t(major) = 6.0 min, de > 99%.

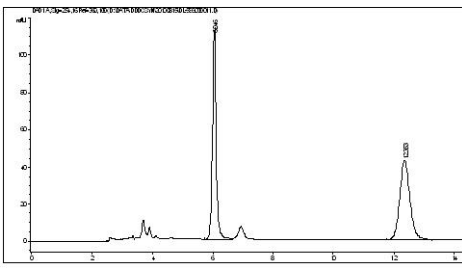


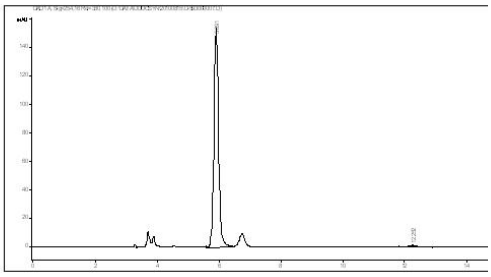


Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	5.975	2532.8	252.7	0.151	55.656
2	12.203	2018	77.5	0.3956	44.344

Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	5.950	2147	203.8	0.1589	100.000

(*R*,2*R*)-**3b**: R_t(major) = 6.0 min, R_t(minor) = 12.3 min, de = 96%.

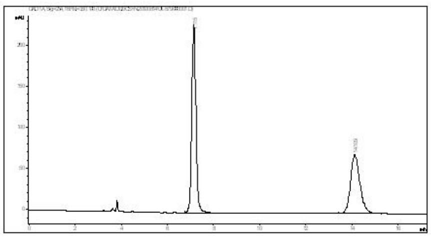


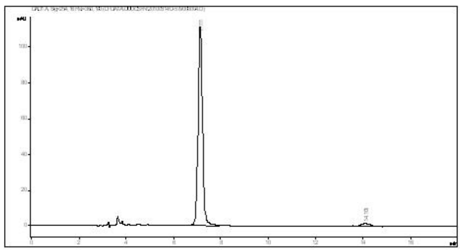


Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	6.046	1163.6	113.8	0.1552	53.864
2	12.353	996.6	43.2	0.3533	46.136

Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	5.891	1557.6	154	0.152	98.145
2	12.252	29.4	1.2	0.3415	1.855

(*R*,2*R*)-**3c**: R_t(minor) = 7.1 min, R_t(major) = 14.1 min, de = 94%.

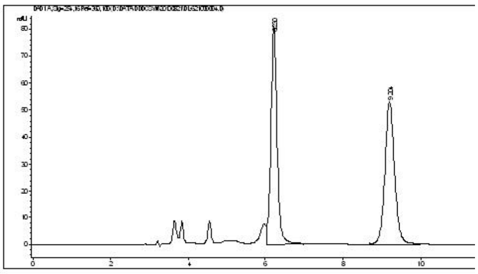




Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	7.115	2863.8	228.7	0.1901	58.766
2	14.109	2009.4	71.2	0.4293	41.234

Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	7.111	1419.5	111.6	0.1924	97.189
2	14.103	41.1	1.5	0.3741	2.811

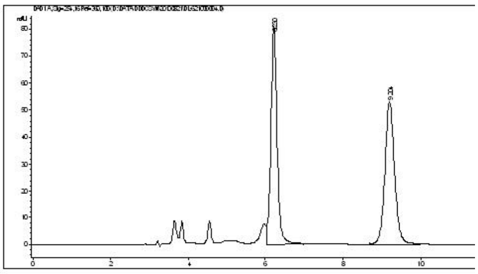
(*S*,2*S*)-**3d**: R_t(minor) = 6.0 min, R_t(major) = 9.2 min, de = 99%.

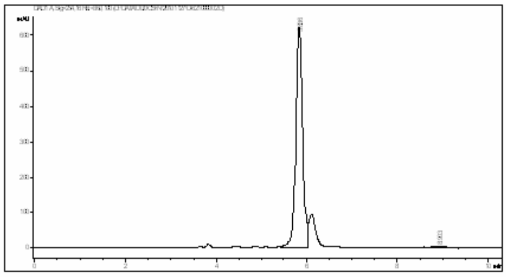


Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	6.23	902.5	81	0.1681	49.767
2	9.204	910.9	53.1	0.262	50.233

Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	5.962	6	0.6	0.1512	0.569
2	9.184	1049.5	61.6	0.2588	99.431

(*S*,2*S*)-**3d**: R_t(minor) = 5.8 min, R_t(major) = 9.0 min, de > 97%.





Peak #	Time [Min]	Area	Height [µV]	Width [min]	Area [%]
1	6.23	902.5	81	0.1681	49.767
2	9.204	910.9	53.1	0.262	50.233

Peak #	Time [min]	Area	Height [µV]	Width[min]	Area%
1	5.836	6394.4	620.8	0.1562	98.808
2	8.903	77.1	4.6	0.2599	1.192

(D) The Absolute Configuration of 3a and Quantum Chemical Calculation

X-ray Single Crystal Stucture Analysis of (*S*,2*S*)-**3a** :

X-ray crystallographic data of (*S*,2*S*)-**3a** were solutions at T = 293(2) K: $C_{39}H_{40}N_4NiO_5$, M_r = 647.36, monoclinic. Space group *P2* (1), a = 11.393 (2) Å, b = 22.375 (4) Å, c = 11.623 (2) Å, α = 90°, β = 103.254 (3)°, γ = 90°, *V* = 2883.9 (10) Å^3, *Z* = 2.

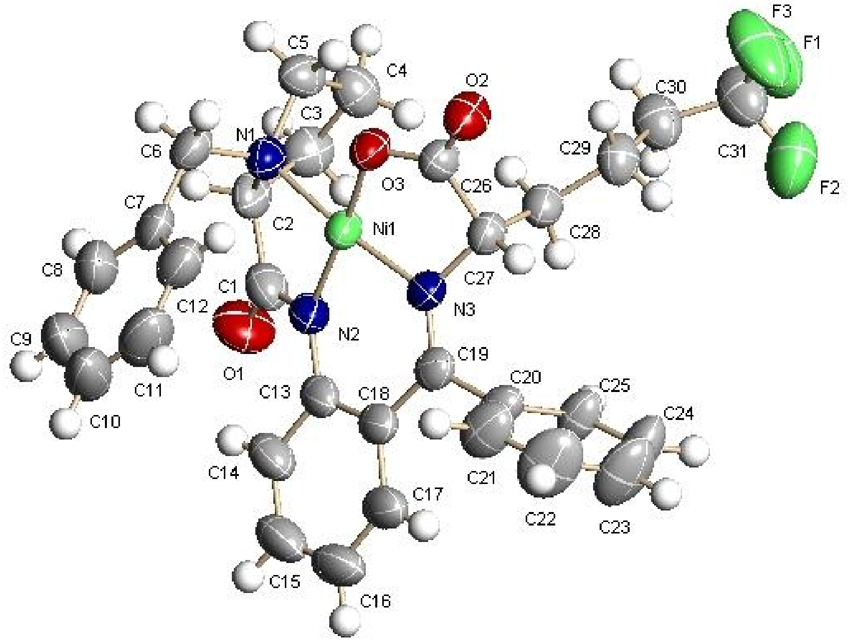
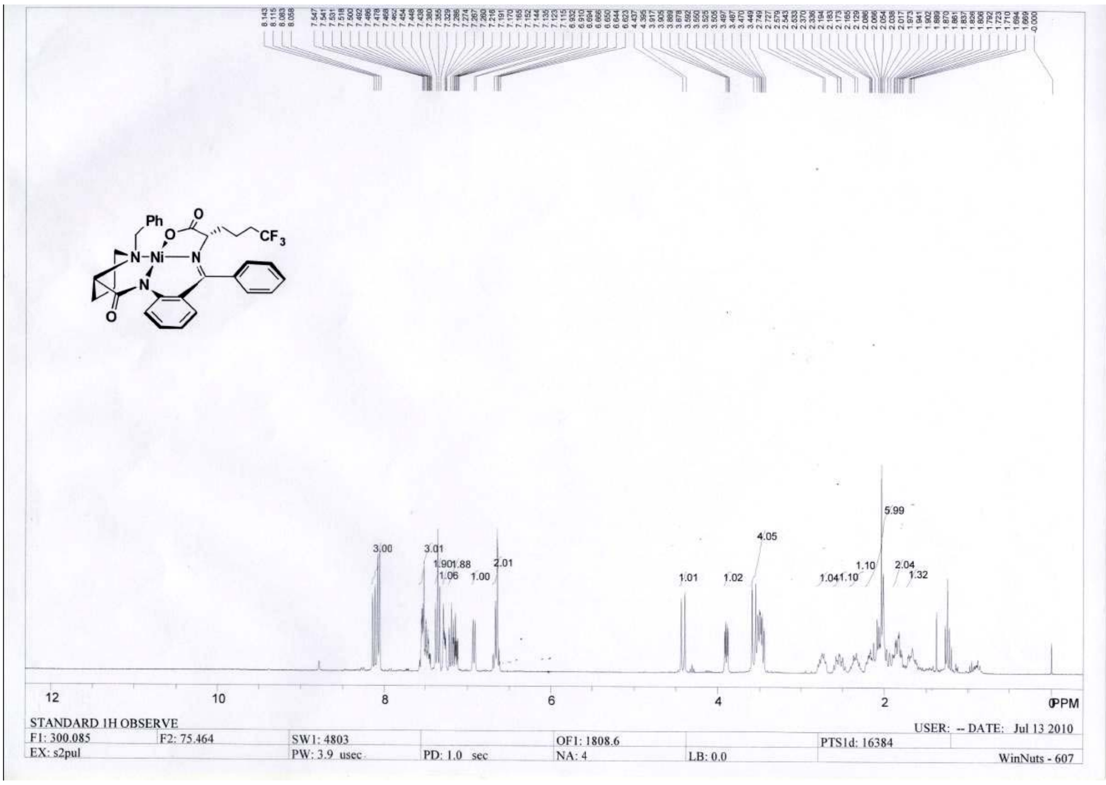


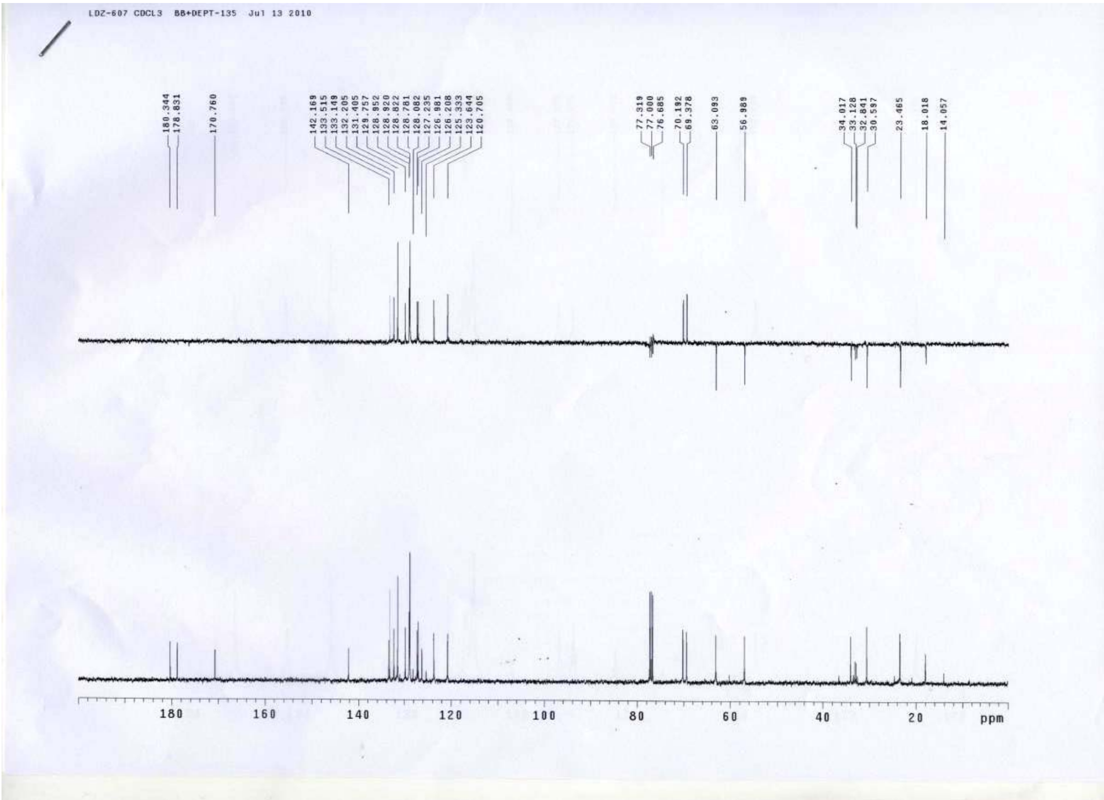
FIGURE S1. The crystal structure of (*S*,2*S*)-**3a** by X-ray analysis.

These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

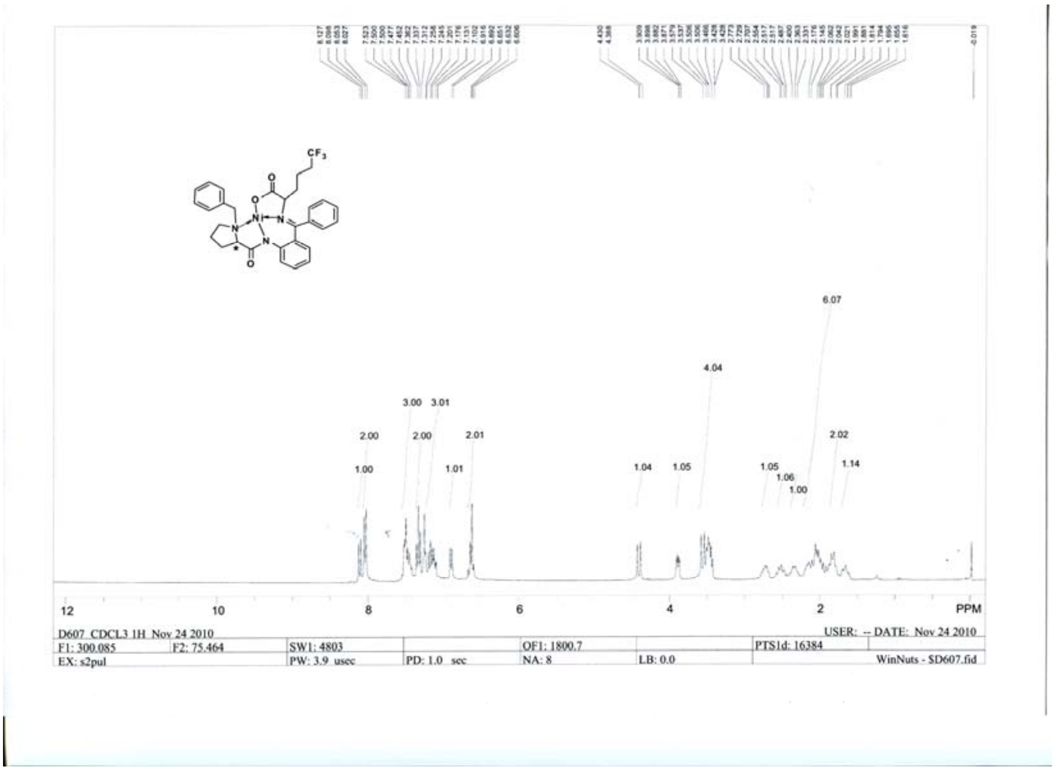
(E) Copies of ^{1}H NMR and ^{13}C NMR Spectra for the Products

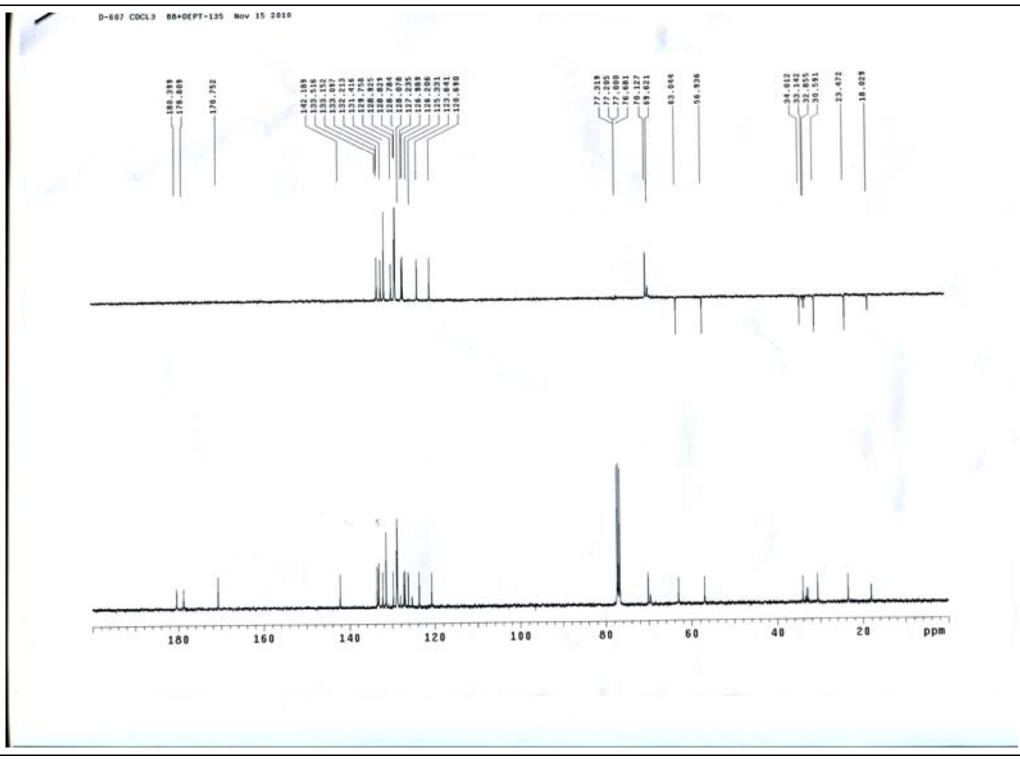
Ni(II)-(*S*)-BPB/(*S*)-2-Amino-6,6,6-Trifluorohexanoic Acid Schiff Base Complex 3a.



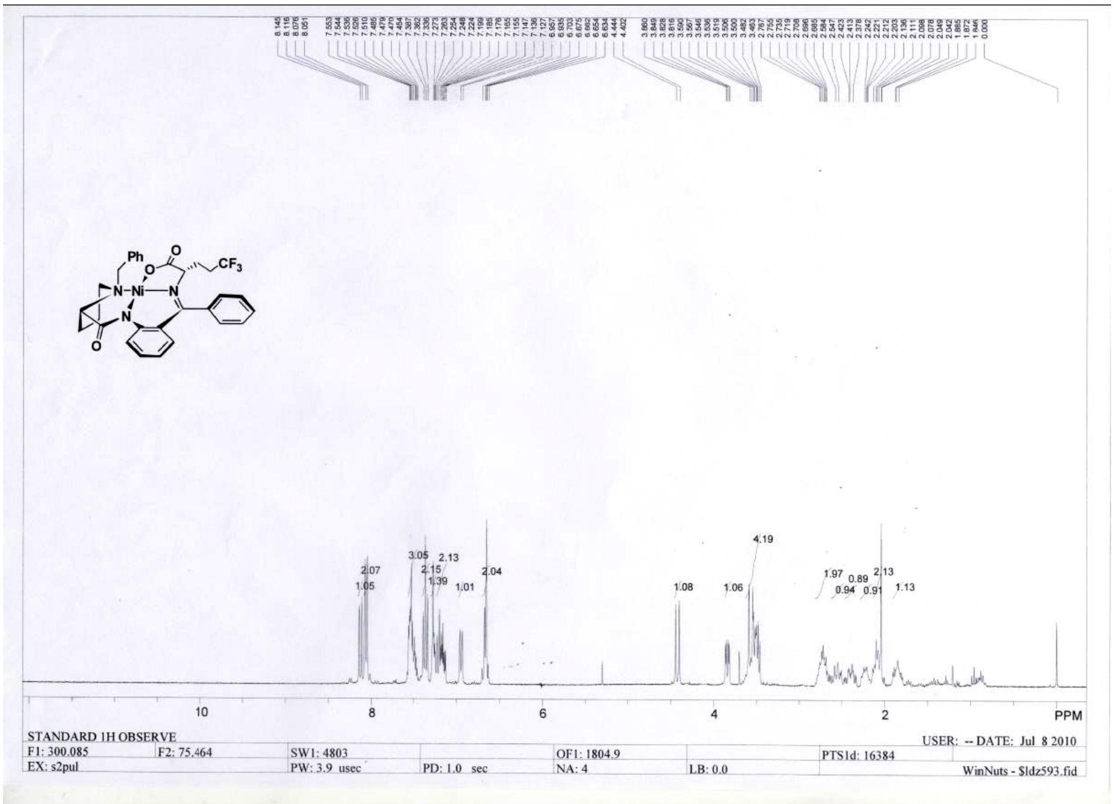


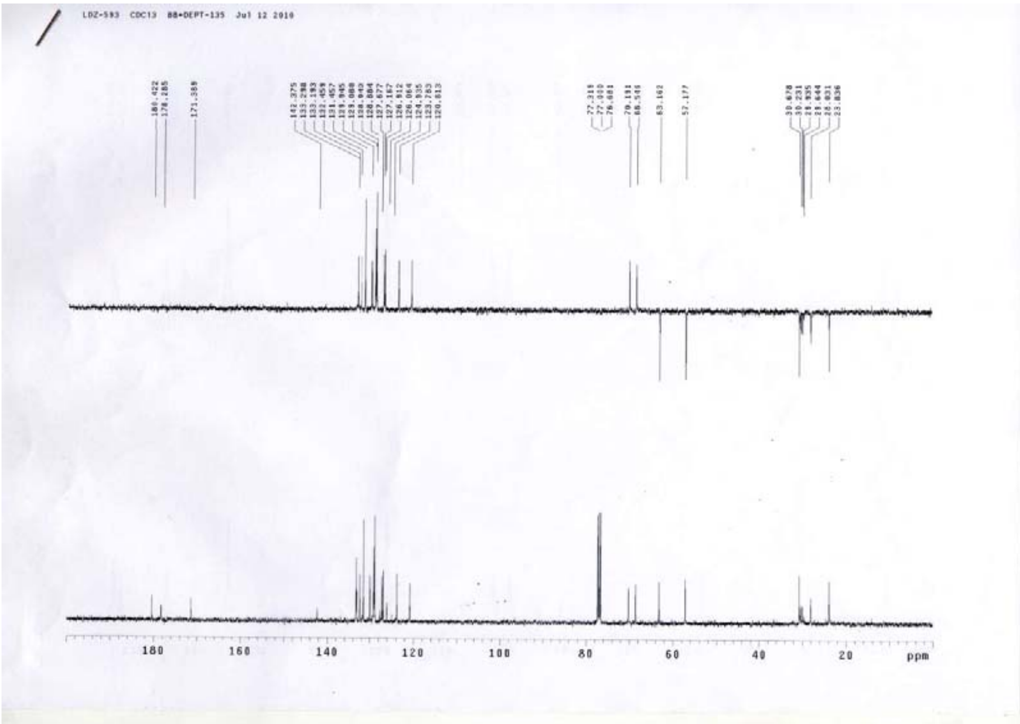
Ni(II)-(*R*)-BPB/(*R*)-2-Amino-6,6,6-Trifluorohexanoic Acid Schiff Base Complex 3a.



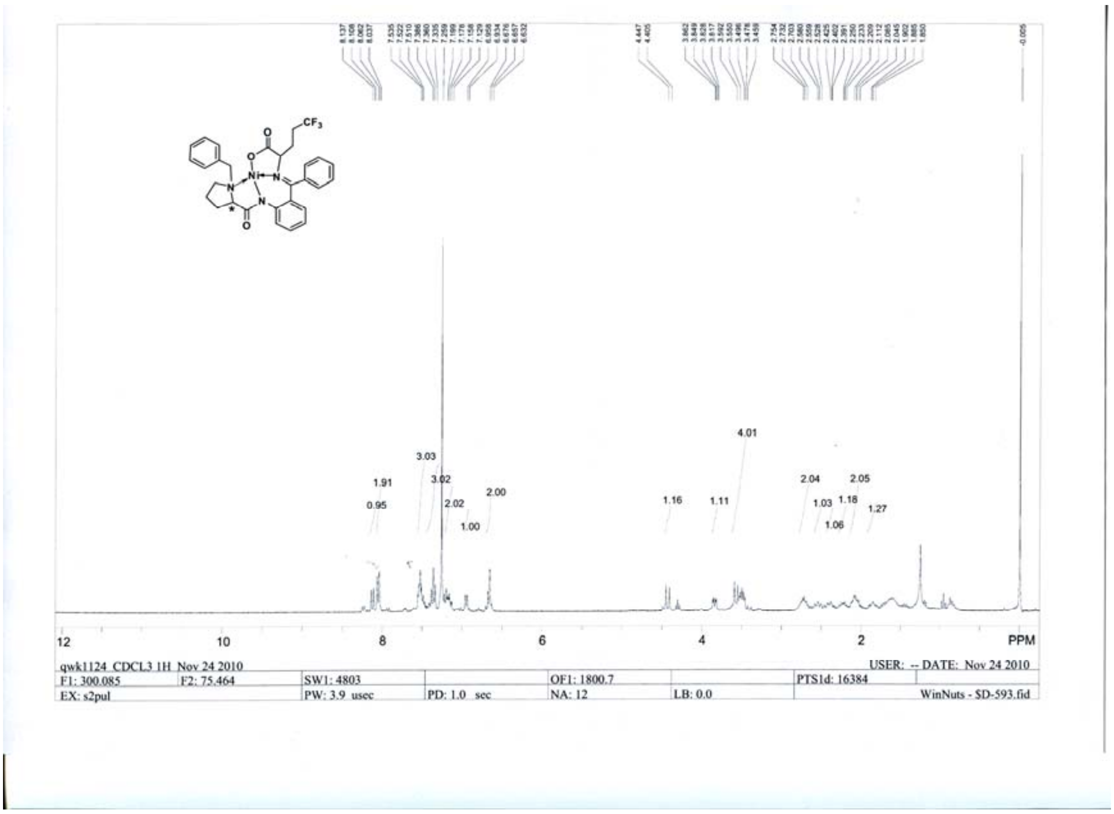


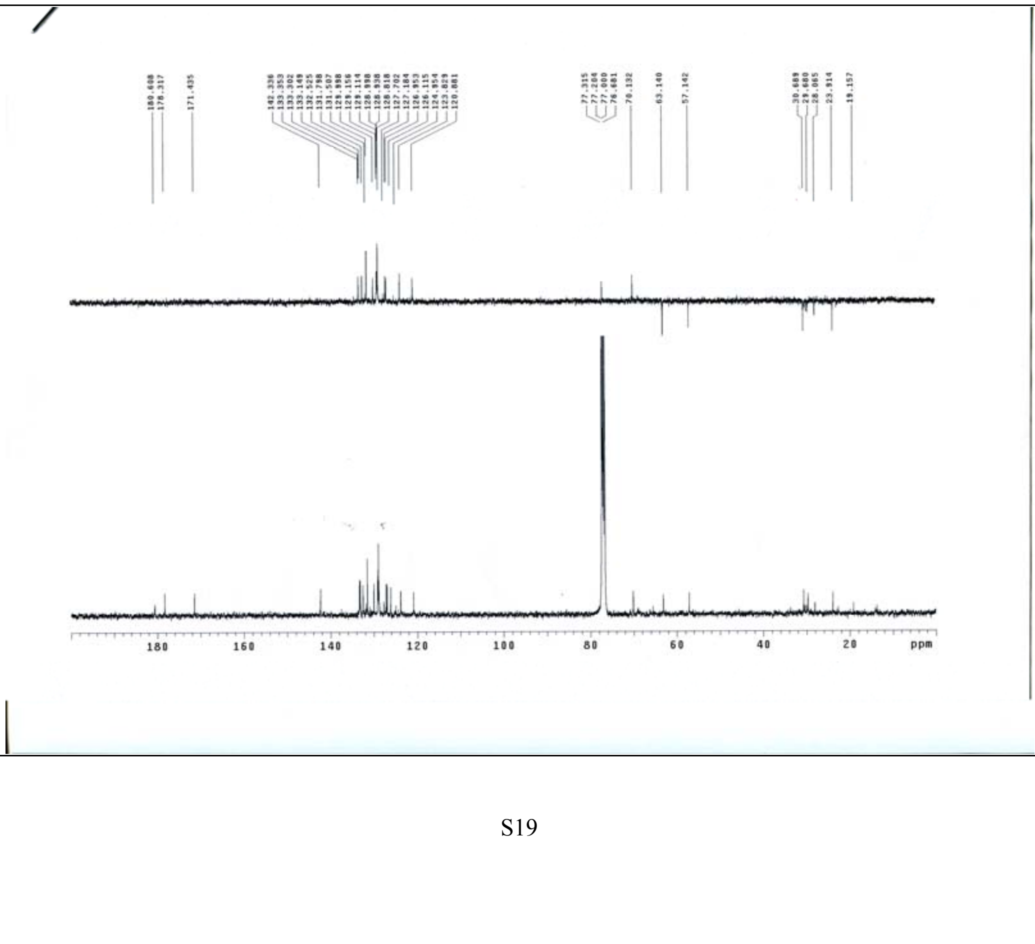
Ni(II)-(*S*)-BPB/(*S*)-2-Amino-5,5,5-Trifluoropentanoic Acid Schiff Base Complex 3b.



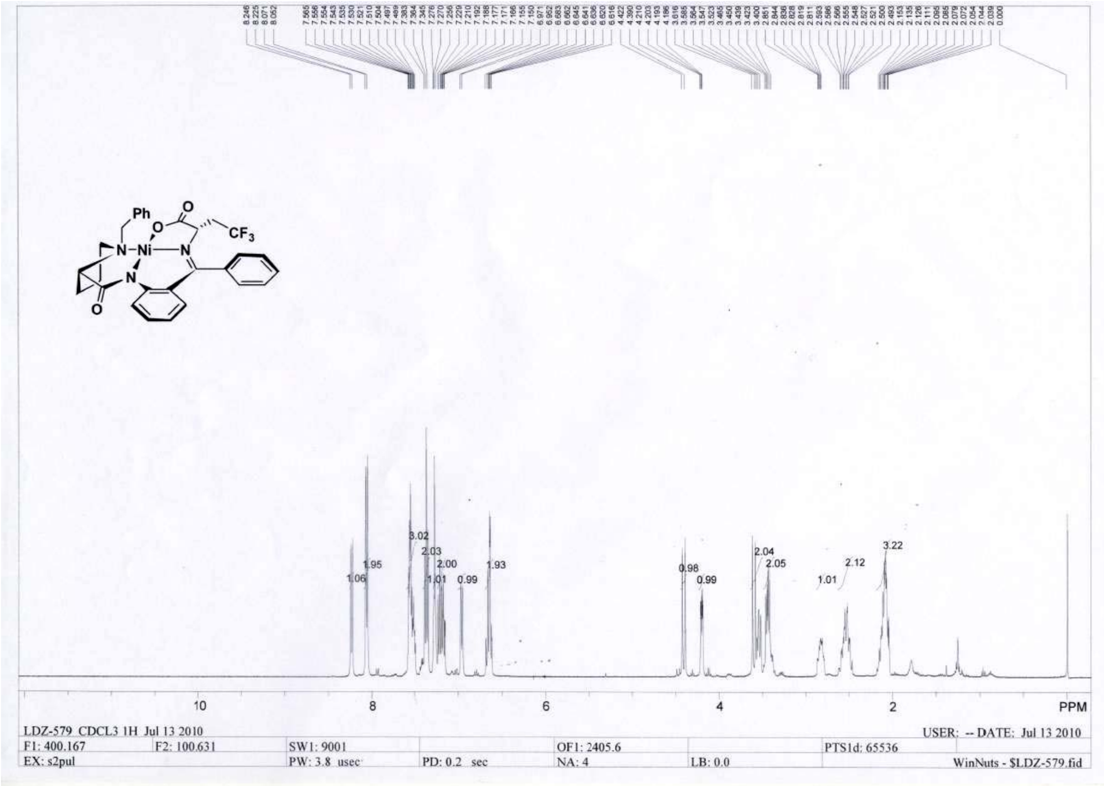


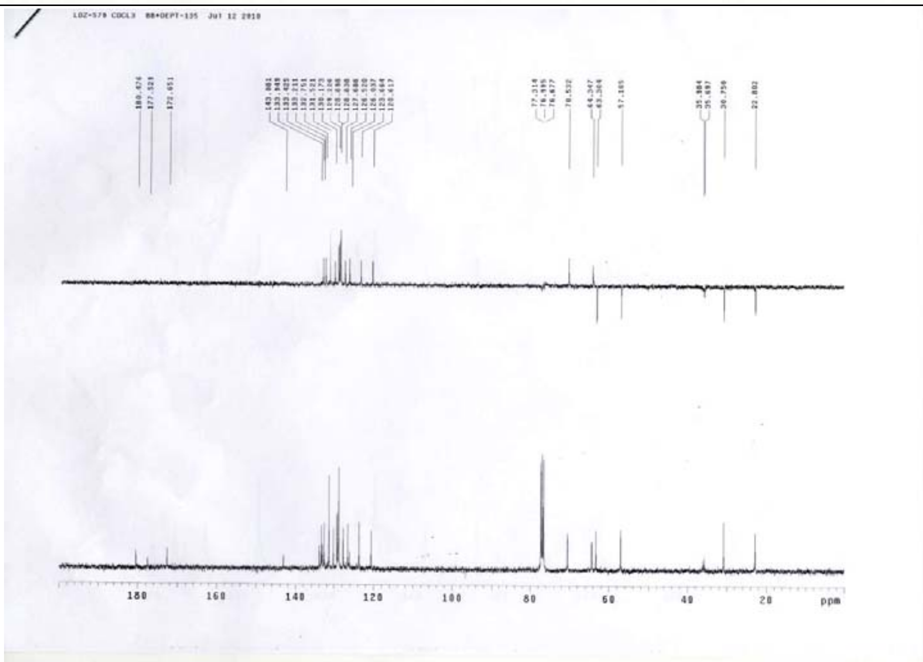
Ni(II)-(*R*)-BPB/(*R*)-2-Amino-5,5,5-Trifluoropentanoic Acid Schiff Base Complex 3b.



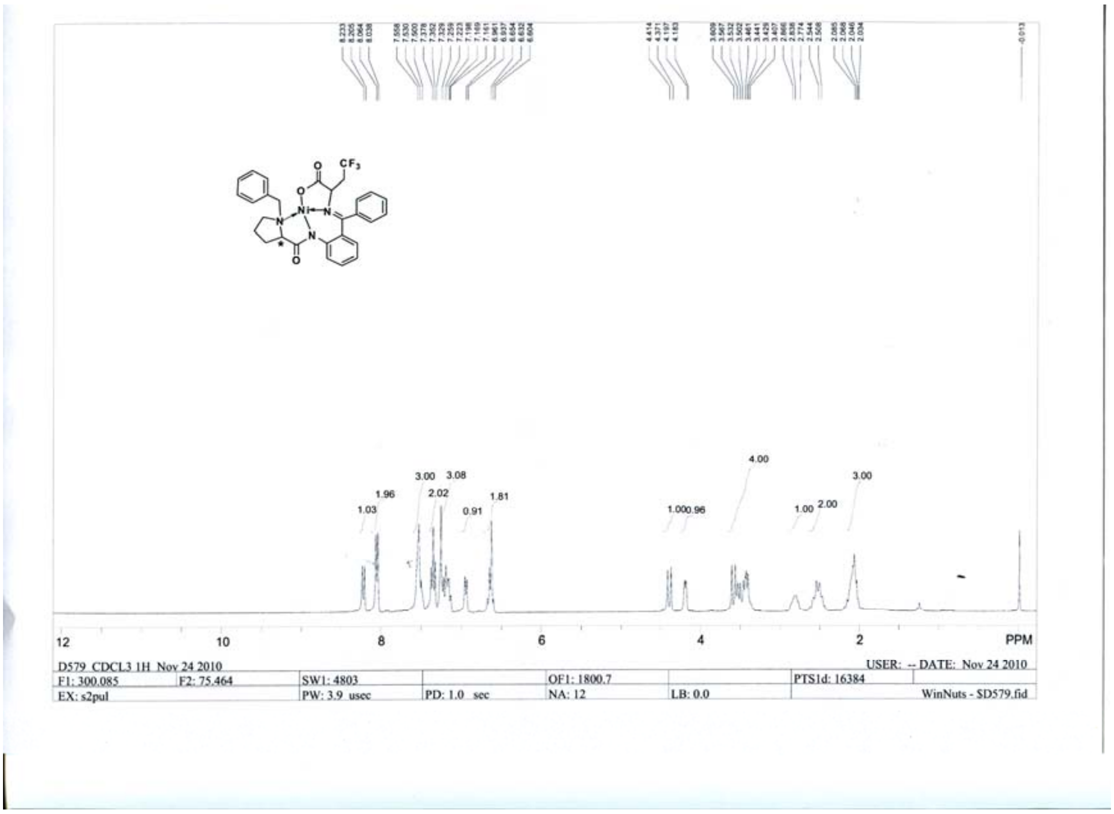


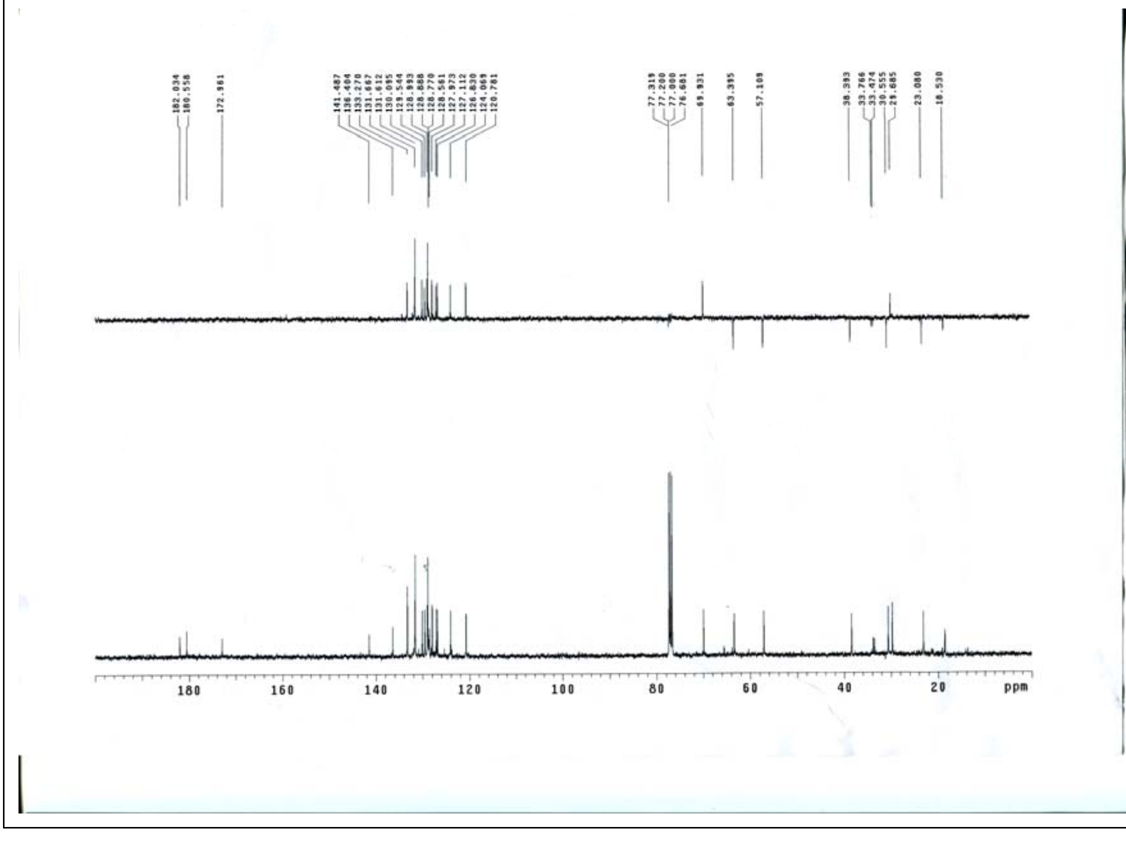
Ni(II)-(*S*)-BPB/(*S*)-2-Amino-4,4,4-Trifluorobutanoic Acid Schiff Base Complex 3c.



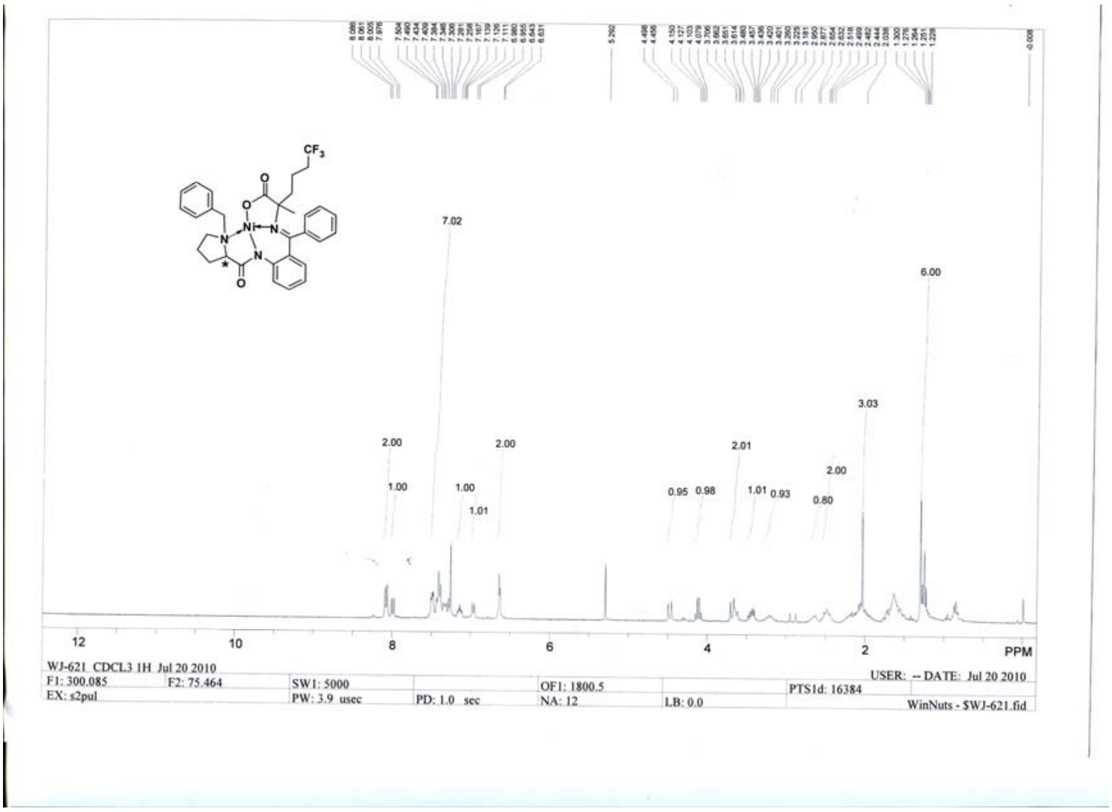


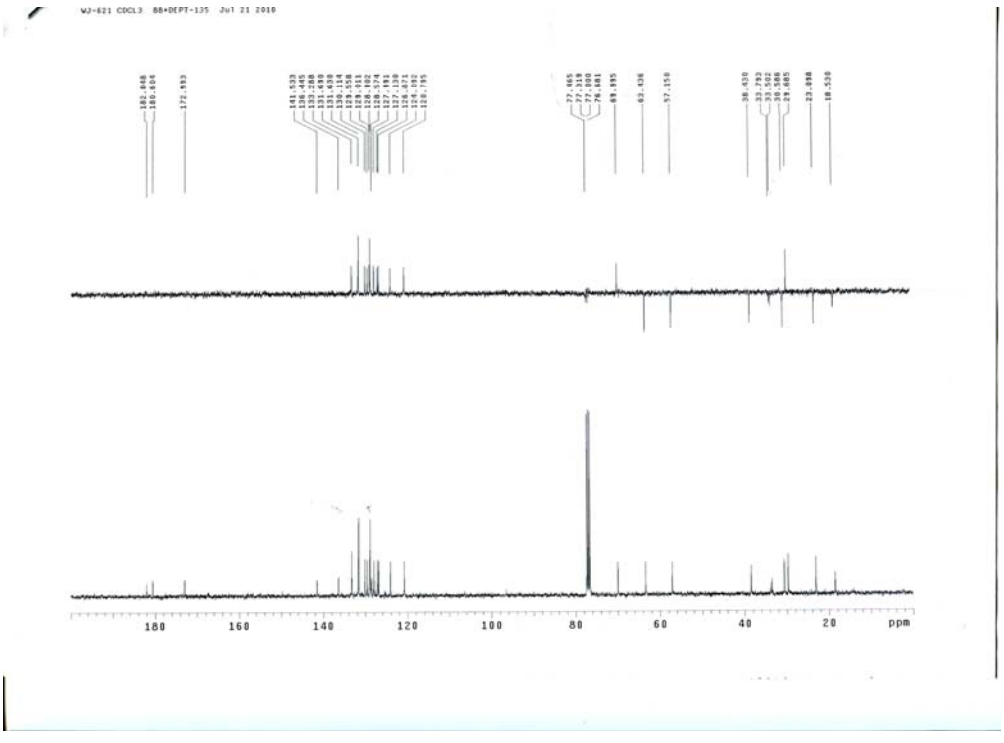
Ni(II)-(*R*)-BPB/(*R*)-2-Amino-4,4,4-Trifluorobutanoic Acid Schiff Base Complex 3c.



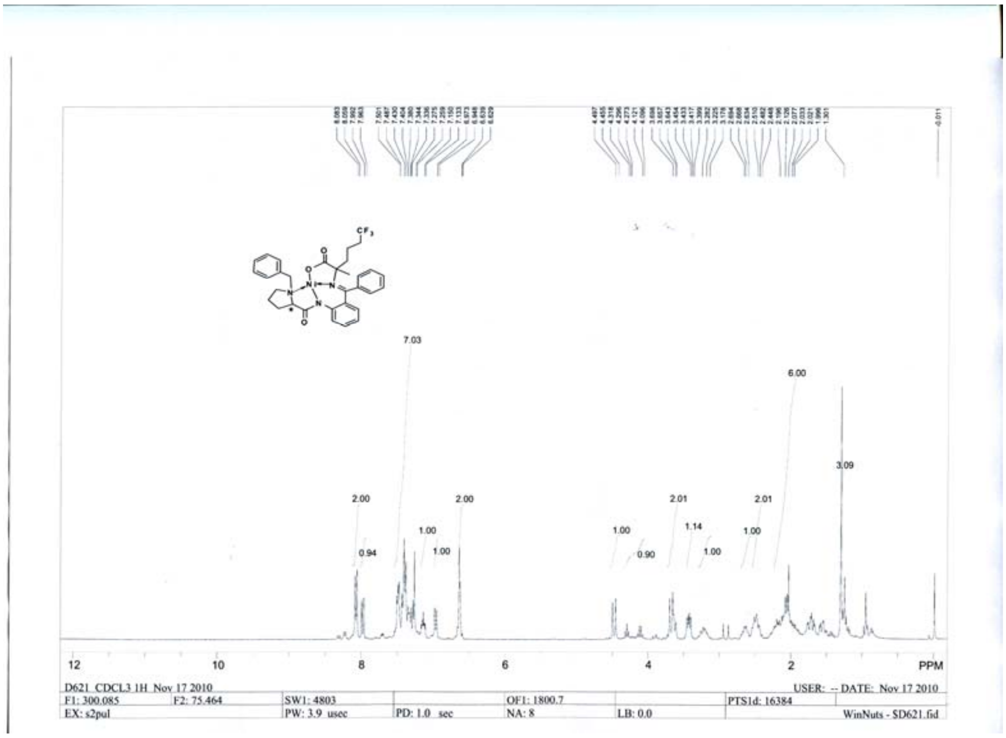


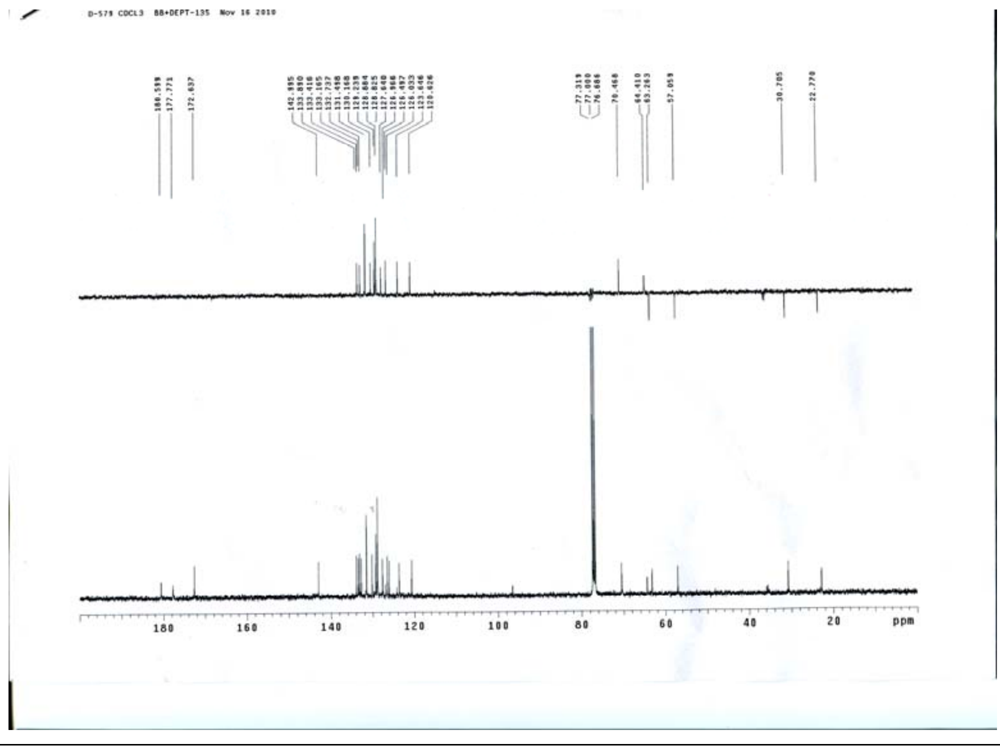
Ni(II)-(*S*)-BPB/(*S*)-2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid Schiff Base Complex 3d.



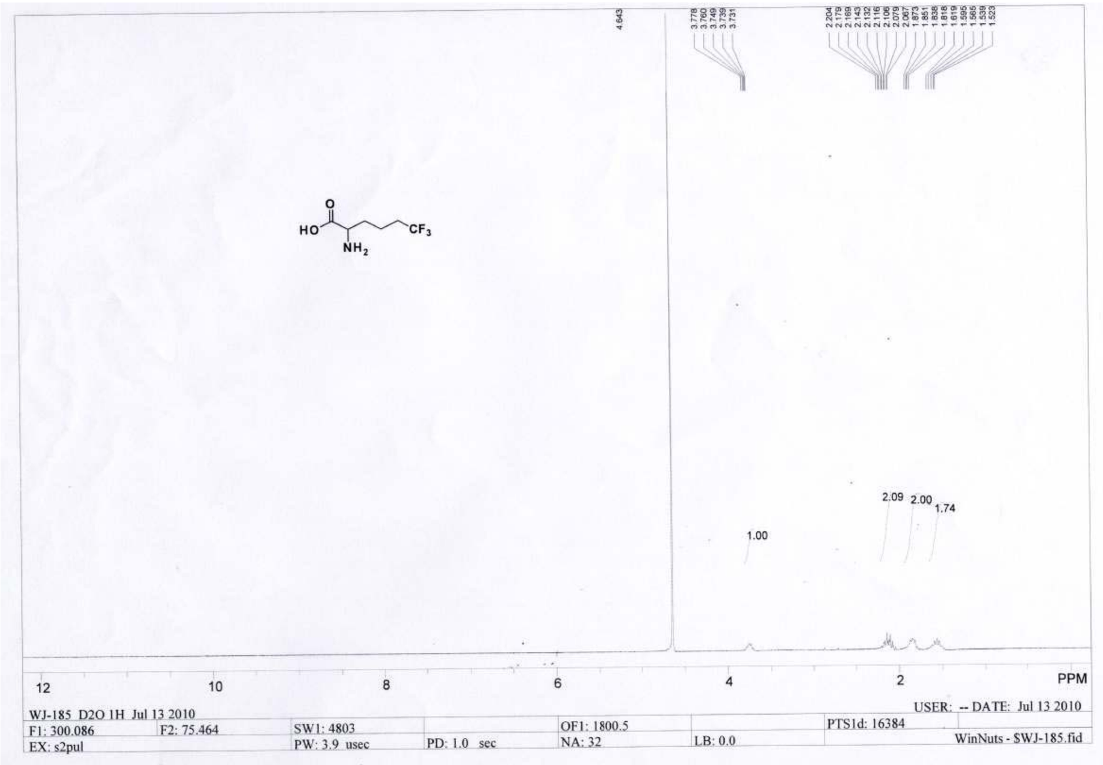


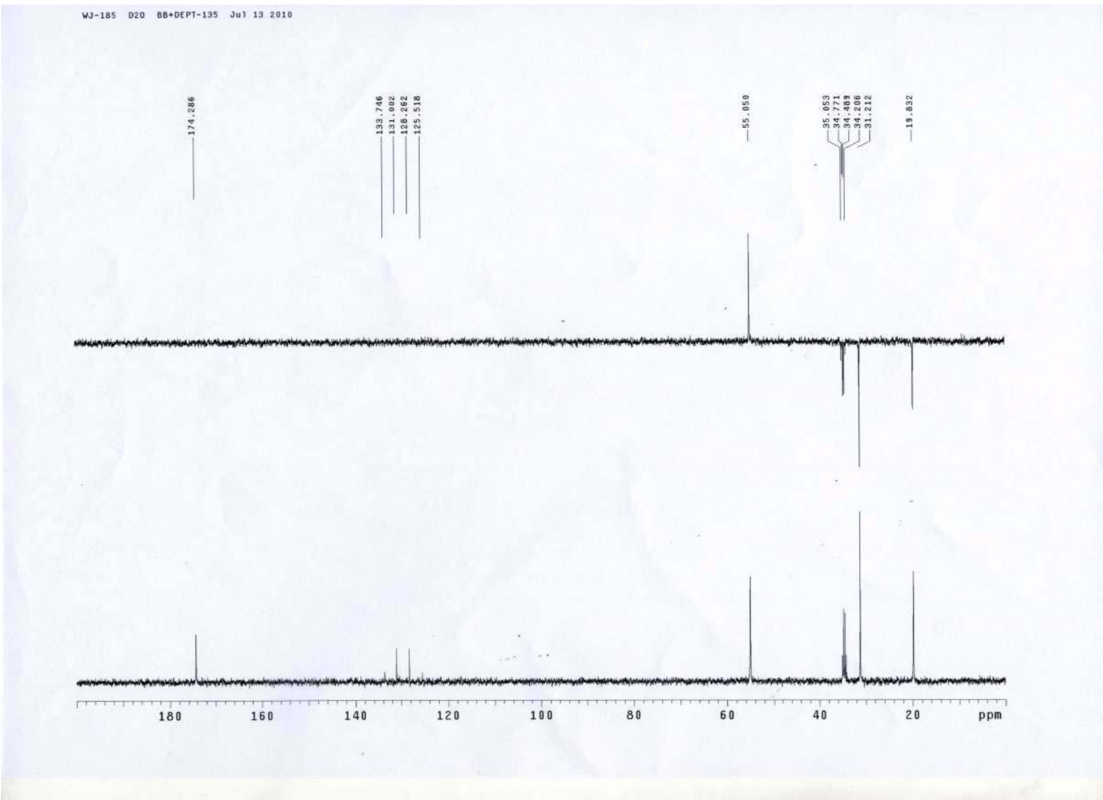
Ni(II)-(*R*)-BPB/(*R*)-2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid Schiff Base Complex 3d.



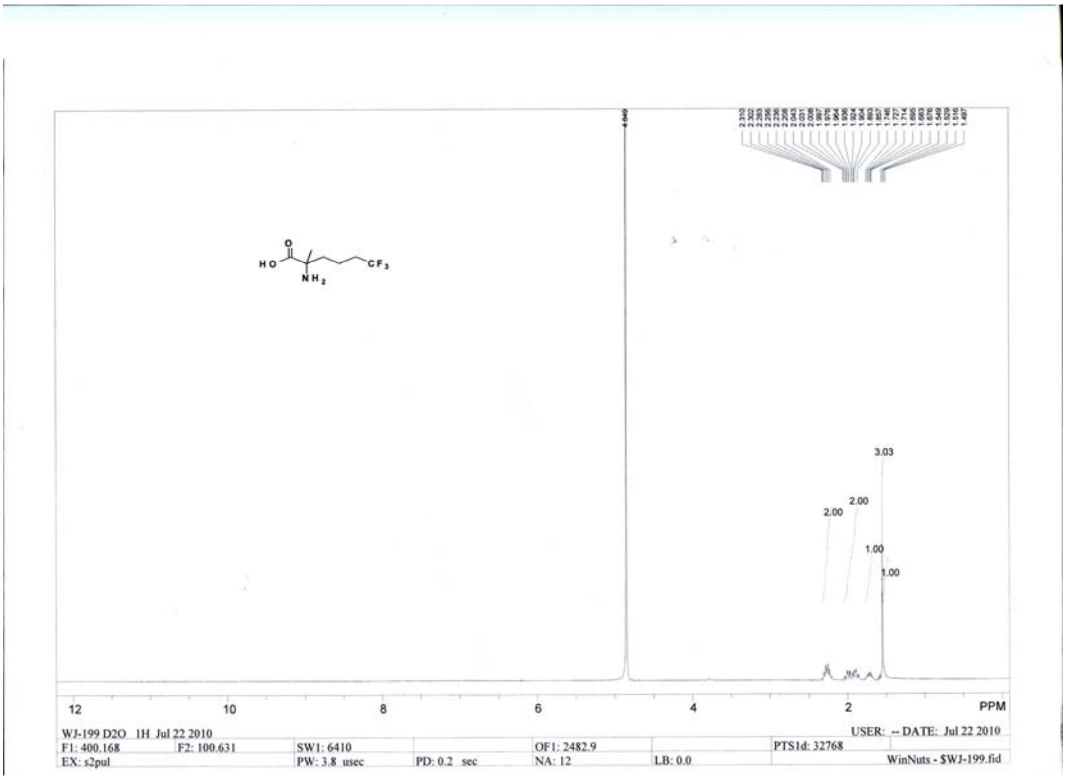


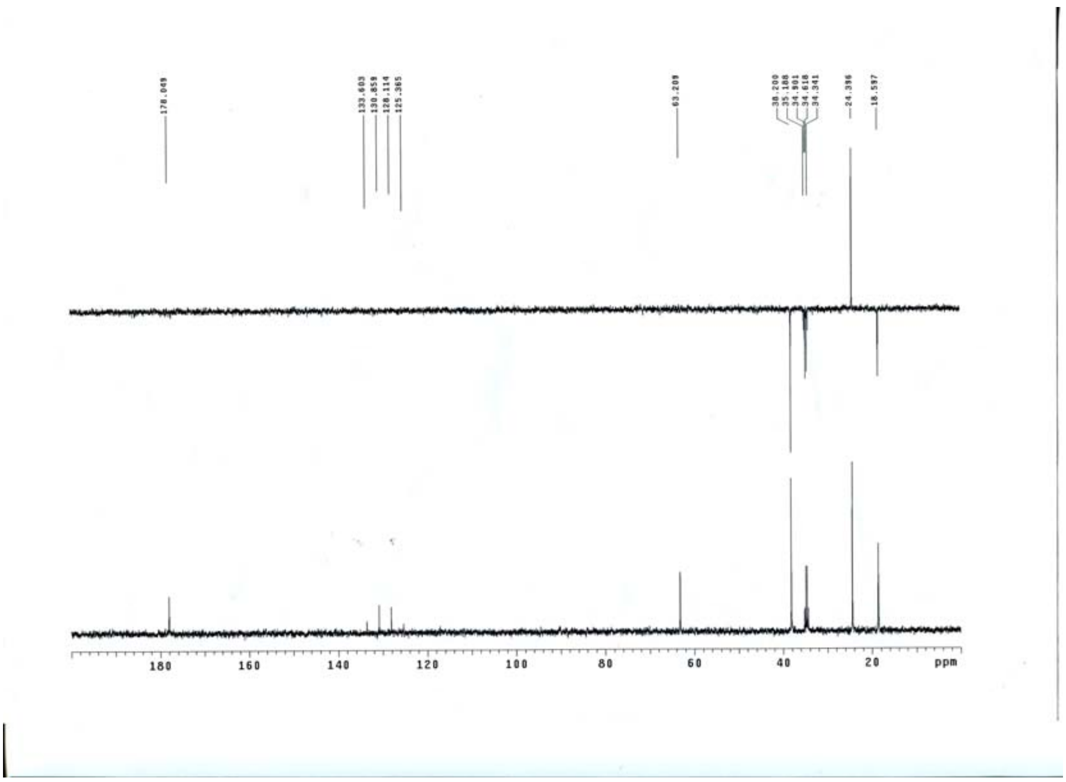
2-Amino-6,6,6-Trifluorohexanoic Acid 4a





2-Amino-6,6,6-Trifluoro-2-Methylhexanoic Acid 4d.





(F) Reference

[1] Deng, G. H.; Wang, J.; Zhou, Y.; Jiang, H. L.; Liu, H. *J. Org. Chem.* **2007**, *72*, 8932.