Supplementary Information

SmI_2-mediated reductive cyclisation reaction using trifluoroacetamide group as radical precursor

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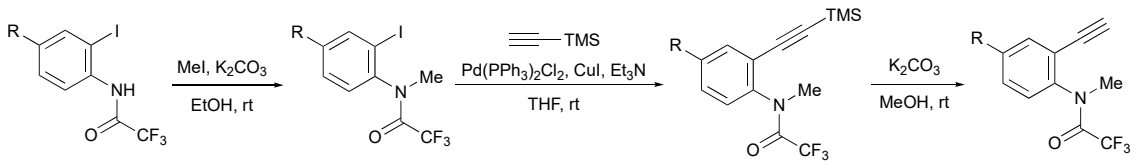
1. General Considerations

General Information: Melting points were measured using a Yanaco MP micro-melting point apparatus and were uncorrected. NMR spectra were recorded in the specified solvents using Bruker Ascend^{TM} 500 (^{1}H: 500 MHz; ^{13}C: 125 MHz), JEOL ECS-400 (^{1}H: 400 MHz; ^{13}C: 100 MHz) or Bruker UltrashieldTM 300 (^{1}H: 300 MHz; ^{13}C: 75 MHz, 19F: 283 MHz) spectrometers. Chemical shifts were recorded in ppm relative to that of the internal solvent signal [$CDCl_3$: 7.26 ppm (^{1}H NMR), 77.0 ppm (^{13}C NMR), methanol-d_4: 3.31ppm (^{1}H NMR), 49.0 ppm (^{13}C-NMR) or tetramethylsilane [0 ppm] and hexafluorobenzene [-164.9 ppm] used as the internal standard. The following abbreviations have been used: broad singlet = br s, singlet = s, doublet = d, triplet = t, quartet = q, quintet = quin, doublet of doublets = dd, doublet of triplets = dt and multiplets = m. IR absorption spectra (FT = diffuse reflectance spectroscopy) were recorded with single reflection ATR using a Jasco FTIR-4600, and only noteworthy absorptions (in cm^{-1}) were listed. Mass spectra were obtained using a JEOL JMS-600H, JEOL JMS-700, JEOL GC-mate II. Column chromatography was performed using a Kanto Chemical Silica Gel 60 N (spherical, neutral, 63–210 μm) column, and flash column chromatography was performed using a Merck Silica Gel 60 (40–63 μm) column. All air- and moisture-sensitive reactions were carried out in flame-dried glassware in an atmosphere consisting of Ar. Anhydrous THF was purchased from Kanto Chemicals Inc. and used without further purification. HMPA was distilled from CaH_2 under reduced pressure. All other chemicals were purchased at highest commercial grade and used without further purification. While organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated under reduced pressure using a rotary evaporator. The starting materials **1a**,[1] **1b**,[2] **1c**[1], **1i**[1], **7a**[3], **7b**[4] and by-product **3**[5] were known compound.

2. General Synthetic Procedure

A) General procedure for the synthesis of 1a

Trifluoroacetic anhydride (0.71 mL, 5.12 mmmol) was added to the solution of 2-ethynylaniline (500 mg, 4.27 mmol) in CH_2Cl_2 (13.0 mL), the reaction mixture then was stirred for 1.5 hours at rt. After completion of the reaction, saturated $NaHCO_3$ was added to the reaction mixture. The mixture was extracted with EtOAc, and the combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated in vacuo. Purification using column chromatography over silica gel with *n*-hexane/EtOAc (8:1) as eluent yielded **1a** (877 mg, 96%) as a colorless needle.



S1: R = H
S2: R = Me
S3: R = OMe
S4: R = Cl

S5: R = H
S6: R = Me
S7: R = OMe
S8: R = Cl

5a: R = H
5b: R = Me
5c: R = OMe
5e: R = Cl

B) General procedure for the synthesis of S1.

To a solution of 2,2,2-trifluoro-*N*-(2-iodophenyl)acetamide (2.23 g, 7.08 mmol) in EtOH (14.9 mL) was added K_2CO_3 (3.14 g, 22.7 mmol) and MeI (1.31 mL, 21.2 mmol), the reaction mixture was stirred for 46 hours at rt. After completion of the reaction, water was added to the mixture, and the whole was extracted with CH_2Cl_2. The organic layer was washed with brine prior to drying and solvent evaporation. Purification using column chromatography over silica gel with *n*-hexane/EtOAc (8:1) as eluent yielded **S1** (2.16 g, 93%) as a mixture of rotamers (9:1).

C) General procedure for the synthesis of S5.

To a solution of **S1** (2.30 g, 6.99 mmol) in THF (10.4 mL) was added $Pd(PPh_3)_2Cl_2$ (245 mg, 0.349 mmol), CuI (66.5 mg, 0.349 mmol), Et_3N (1.46 mL, 10.5 mmol) and trimethylsilylacetylene (1.48 mL, 10.5 mmol), the reaction mixture was stirred for 1 hour at rt. After completion of the reaction, water was added to the mixture, and the whole was extracted with Et_2O. The organic layer was washed with brine prior to drying and solvent evaporation. Purification using column chromatography over silica gel with *n*-hexane/EtOAc (10:1) as eluent yielded **S5** (1.79 g, 86%) as a mixture of rotamers (9:1).

D) General procedure for the synthesis of 5a.

To a solution of **S4** (1.79 g, 5.98 mmol) in MeOH (10.0 mL) was added K_2CO_3 (826 mg, 5.98 mmol), the reaction mixture was stirred for 1 hour at rt. After completion of the reaction, water was added to the mixture, and the whole was extracted with CH_2Cl_2. The organic layer was washed with brine prior to drying and solvent evaporation. Purification using column chromatography over silica gel with *n*-hexane/EtOAc (10:1) as eluent yielded **5a** (1.08 g, 79%) as a mixture of rotamers (9:1).

E) General procedure for samarium(II)-mediated reductive cyclisation reaction.

A mixture of samarium (186 mg, 1.24 mmol) and 1,2-diiodoethane (265 mg, 0.938 mmol) in THF (8.9 mL) was stirred for 2.0 hours at rt. HMPA (0.59 mL, 3.38 mmol) was added to the mixture at rt and stirring was continued for 40 min at same temperature. After cooling at 0 ºC, a solution of **1a** (80.0 mg, 0.375 mmol) and *i*-PrOH (57.5 μL, 0.750 mmil) in THF (9.4 mL) was added to the mixture, and the mixture was stirred for 1 hour at same temperature. After the reaction mixture was exposed to air, saturated $NaHCO_3$ was added to the mixture, and the whole was extracted with Et_2O. The organic layer was washed with saturated $NaHCO_3$ and brine prior to drying and solvent evaporation. Purification using column chromatography over silica gel with *n*-hexane/EtOAc (8:1) as eluent yielded **2a** (66.4 mg, 82%) as a colorless needle.

3. Characterization Data for the Products

***N*-(2-ethynylphenyl)-2,2,2-trifluoroacetamide (1a)**

Our data was in full agreement with previous reported in the literature.[1]

***N*-(2-ethynyl-3-methylphenyl)-2,2,2-trifluoroacetamide (1b)**

Following the general procedure A, the desired product **1b** (258 mg) was obtained in 66% yield as a orange solid. Our data was in full agreement with previous reported in the literature.[2]

***N*-(2-ethynyl-4-methylphenyl)-2,2,2-trifluoroacetamide (1c)**

Following the general procedure A, the desired product **1c** (172 mg) was obtained in 86% yield as a colorless prism. Our data was in full agreement with previous reported in the literature.[1]

***N*-(2-ethynyl-5-methylphenyl)-2,2,2-trifluoroacetamide (1d)**

Following the general procedure A, the desired product **1d** (125 mg) was obtained in 66% yield as a colorless needle. Colorless needle crystals: m.p. 89.2–90.2 ºC (*n*-hexane); IR (ATR) cm^{-1}: 3357 (N-H), 3260 (C≡C), 1714 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.71 (brs, 1H), 8.19 (s, 1H), 7.40 (d, J = 7.6 Hz, 1H), 6.99 (dd, J = 7.6, 0.4 Hz, 1H), 3.56 (s, 1H), 2.40 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.5 (q, J = 37.2 Hz), 141.2, 136.6, 132.0, 126.3, 120.2, 115.6 (q, J = 287.4 Hz), 109.1, 85.1, 78.0, 21.9; ^{19}F (283 MHz, $CDCl_3$) δ: -79.1, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{11}H_8F_3NO$ ($[M-H]^-$): 226.0485; found: 226.0487.

***N*-(2-ethynyl-6-methylphenyl)-2,2,2-trifluoroacetamide (1e)**

Following the general procedure A, the desired product **1e** (277 mg) was obtained in 87% yield as a white solid. Colorless crystals: m.p. 77.2–79.0 ºC (*n*-hexane); IR (ATR) cm^{-1}: 3362 (N-H), 3254 (C≡C), 1721 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.11 (brs, 1H), 7.34 (dd, J = 7.2, 1.6 Hz, 1H), 7.13-7.24 (m, 2H), 3.30 (s, 1H), 2.17 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 155.4 (q, J = 37.1 Hz), 135.7, 133.5, 131.7, 130.5, 128.0, 119.7, 115.8 (q, J = 286.8 Hz), 83.2, 79.0, 18.0; ^{19}F (283 MHz, $CDCl_3$) δ: -78.7, -164.9 (C_6F_6); HRMS (ESI) calcd. for $C_{11}H_8F_3NO$ ($[M+Na]^+$): 250.0450; found: 250.0445.

***N*-(2-ethynyl-4-methoxyphenyl)-2,2,2-trifluoroacetamide (1f)**

Following the general procedure A, the desired product **1f** (820 mg) was obtained in 93% yield as a pink solid. Pink solid: m.p. 90.8–91.2 °C (*n*-hexane/EtOAc); IR (ATR) cm^{-1}: 3275 (C≡C), 1701 (C=O); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.58 (brs, 1H), 8.24 (d, J = 9.2 Hz, 1H), 7.03 (s, 1H), 6.97 (dd, J = 9.2, 2.8 Hz, 1H), 3.81 (s, 3H), 3.58 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.3 (q, J = 37.1 Hz), 156.6, 130.2, 121.3, 116.9, 116.3, 115.7 (q, J = 287.0 Hz), 113.4, 85.4, 77.9, 55.6; ^{19}F (283 MHz,

$CDCl_3$) δ: -79.0, -164.9 (C_6F_6); MS (EI) *m/z* (%) 243 (M^+, 100.0), 228 (18), 200 (4), 146 (24), 119 (5); HRMS (EI) calcd for $C_{11}H_8F_3NO_2$ (M^+): 243.0507; found: 243.0504.

***N*-(4-bromo-2-ethynylphenyl)-2,2,2-trifluoroacetamide (1g)**

Following the general procedure A, the desired product **1g** (974 mg) was obtained in 95% yield as a colorless needle. Colorless needle crystals: m.p. 74.2–74.5 °C (*n*-hexane); IR (ATR) cm^{-1}:3385 (N-H), 3283 (C≡C), 1735 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 8.68 (s, 1H), 8.26 (d, J = 8.5 Hz, 1H), 7.65 (s, 1H), 7.55 (d, J = 8.5 Hz, 1H), 3.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 154.6 (q, J = 37.6 Hz), 136.0, 134.9, 133.5, 121.0, 118.1, 115.5 (q, J = 287.1 Hz), 113.9, 86.9, 76.5;; ^{19}F (283 MHz, $CDCl_3$) δ: -79.0, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{10}H_5BrF_3NO$ ($[M-H]^-$): 289.9434; found: 289.9435.

***N*-(4-chloro-2-ethynylphenyl)-2,2,2-trifluoroacetamide (1h)**

Following the general procedure A, the desired product **1h** (685 mg) was obtained in 89% yield as a colorless needle. Colorless needle crystals: m.p. 61.2–63.3 °C (*n*-hexane); IR (ATR) cm^{-1}:3350 (N-H), 3296 (C≡C), 1715 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 8.69 (s, 1H), 8.32 (d, J = 9.0 Hz, 1H), 7.49 (d, J = 2.5 Hz, 1H), 7.40 (dd, J = 9.0, 2.5 Hz, 1H), 3.66 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 154.6 (q, J = 37.6 Hz), 135.4, 132.0, 130.7, 130.6, 120.9, 115.5 (q, J = 287.3 Hz), 113.6, 86.8, 76.6; ^{19}F (283 MHz, $CDCl_3$) δ: -79.1, -164.9 (C_6F_6); HRMS (FAB^-) calcd for $C_{10}H_5F_3NOCl$ ($[M-H]^-$): 245.9939; found: 245.9941.

***N*-(4-cyano-2-ethynylphenyl)-2,2,2-trifluoroacetamide (1i)[1]**

Following the general procedure A, the desired product **1i** (1.07 g) was obtained in 94% yield as a colorless needle. Our data was in full agreement with previous reported in the literature.[1]

methyl 3-ethynyl-4-(2,2,2-trifluoroacetamido)benzoate (1j)

Following the general procedure A, the desired product **1j** (574 mg) was obtained in 93% yield as a colorless needle. Colorless needle crystals: m.p. 112.9–114.0 °C (*n*-hexane/EtOAc); IR (ATR) cm^{-1}:3375 (N-H), 3240 (C≡C), 1742 (C=O);^1H NMR (400 MHz, CD_3OD) δ: 8.89 (s, 1H), 8.48 (d, J = 8.8 Hz, 1H), 8.22 (d, J = 2.0 Hz, 1H), 8.11 (dd, J = 8.8, 2.0 Hz, 1H), 3.94 (s, 3H), 3.67 (s, 1H); ^{13}C NMR (100 MHz, CD_3OD) δ: 165.3, 154.7 (q, J = 37.8 Hz), 140.2, 133.7, 131.7, 127.1, 119.1, 115.4 (q, J = 287.3 Hz), 112.1, 86.6, 76.9, 52.4; ^{19}F (283 MHz, CD_3OD) δ: -79.0, -164.9 (C_6F_6); MS (EI) *m/z* (%) 272 ($M+H^+$, 12), 271 (M^+, 92), 241 (12), 240 (100); HRMS (EI) calcd for $C_{12}H_8BrF_3NO_3$ (M^+): 271.0456; found: 271.0451.

***N*-(2-ethynyl-4-nitrophenyl)-2,2,2-trifluoroacetamide (1k)**

Following the general procedure A, the desired product **1k** (697 mg) was obtained in 98% yield as a yellow needle. Yellow needle crystals: m.p. 126.9–127.9 °C (*n*-hexane); IR (ATR) cm^{-1}: 3260 (N-H), 1720 (C=O); 1510 (NO_2); ^1H NMR (400 MHz, $CDCl_3$) δ: 8.61 (d, J = 9.2 Hz, 1H), 8.96 (s, 1H), 8.41 (d, J = 2.6 Hz, 1H), 8.31 (dd, J = 9.2, 2.6 Hz, 1H), 3.81 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 154.9 (q, J = 38.2 Hz), 144.1, 141.6, 127.7, 125.8, 119.6, 115.2 (q, J = 287.1 Hz), 112.9, 88.2, 75.8; ^{19}F (283 MHz, $CDCl_3$) δ: -78.9, -164.9 (C_6F_6); HRMS (FAB^-) calcd for $C_{10}H_5F_3N_2O_3$ ($[M-H]^-$): 257.0179; found: 257.0179.

2,2,2-trifluoro-*N*-(2-iodophenyl)-*N*-methylacetamide (S1)

Yellow oil: IR (ATR) cm^{-1}:1701 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.94 (td, J = 8.0, 1.5 Hz, 1H), 7.43 (td, J = 7.5, 1.5 Hz, 1H), 7.31 (d, J = 7.5 Hz, 1H), 7.27 (dd, J = 7.5, 1.5 Hz, 1H), 3.43 (s, 0.4H), 3.31 (s, 2.6H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 156.7 (q, J = 36.2 Hz), 142.8, 140.1, 130.6, 129.4, 129.1, 115.9 (q, J = 288.3 Hz), 98.5, 38.2; ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.5, -164.9 (C_6F_6); HRMS (EI) calcd for $C_9H_7F_3INO$ (M^+): 328.9525; found: 328.9522.

2,2,2-trifluoro-*N*-(2-iodo-4-methylphenyl)-*N*-methylacetamide (S2)

Following the general procedure B, the desired product **S2** (716 mg) was obtained as a mixture of rotamers (9:1) in 98% yield as a yellow solid. Yellow solid: m.p. 42.7-44.6 °C; IR (ATR) cm^{-1}: 1698 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.75 (d, J = 2.0 Hz, 1H), 7.24 (d, J = 8.0 Hz, 0.1H), 7.21 (dd, J = 8.0, 2.0 Hz, 0.9H), 7.16 (d, J = 8.0 Hz, 0.9H), 7.12 (d, J = 8.0 Hz, 0.1H), 3.40 (s, 0.3H), 3.27 (s, 2.7H), 2.36 (s, 2.7H), 2.34 (s, 0.3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.9 (q, J = 36.0 Hz), 141.8, 141.2, 140.6, 140.5, 140.4, 140.3, 130.8, 130.1, 128.6, 127.2, 116.0 (q, J = 286.5 Hz), 98.3, 96.3, 38.3, 38.1, 20.6; ^{19}F (283 MHz, $CDCl_3$) δ:-73.43, -164.90 (C_6F_6); HRMS (FAB) calcd for $C_{10}H_{10}F_3INO$ ($[M+H]^+$): 343.9759; found: 343.9768.

2,2,2-trifluoro-*N*-(2-iodo-4-methoxyphenyl)-*N*-methylacetamide (S3)

Following the general procedure B, the desired product **S3** (530 mg) was obtained as a mixture of rotamers (9:1) in 86% yield as a light-yellow solid. Light-yellow solid: m.p. 81.6–83.0 °C; IR (ATR) cm^{-1}: 1697 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.42 (d, J = 2.5 Hz, 1H), 7.19 (d, J = 8.5 Hz, 1H), 7.13 (d, J = 8.5 Hz, 0.1H), 6.96 (dd, J = 8.5, 2.5 Hz, 0.1H), 6.91 (dd, J = 8.5, 2.5 Hz, 1H), 3.82 (s, 2.7H), 3.81 (s, 0.3H), 3.39 (s, 0.3H), 3.27 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.9, 159.6, 157.0 (q, J = 35.3 Hz), 137.2, 135.5, 129.3, 127.9, 125.0, 124.9, 116.0 (q, J = 286.5 Hz), 115.7, 114.7, 98.9, 96.8, 55.7, 38.5; ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.4, -164.9 (C_6F_6); HRMS (FAB) calcd for $C_{10}H_{10}F_3INO_2$ ($[M+H]^+$): 359.9708; found: 359.9701.

***N*-(4-chloro-2-iodophenyl)-2,2,2-trifluoro-*N*-methylacetamide (S4)**

Following the general procedure B, the desired product **S4** (1.07 g) was obtained as a mixture of rotamers (9:1) in 66% yield as a yellow oil. Yellow oil: IR (ATR) cm^{-1}: 1690 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.93 (d, J = 2.5 Hz, 1H), 7.42 (d, J = 2.0 Hz, 0.1H), 7.41 (dd, J = 8.5, 2.5 Hz, 0.9H), 7.24 (d, J = 8.5 Hz, 0.9H), 7.19 (d, J = 8.5 Hz, 0.1H), 3.40 (s, 0.4H), 3.28 (s, 2.6H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.6 (q, J = 36.1 Hz), 141.7, 139.7, 135.7, 135.1, 130.4, 129.8, 128.5, 116.0 (q, J = 286.5 Hz), 99.0, 97.0, 38.2, 38.1; ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.5, -164.9 (C_6F_6); MS (EI) *m/z* (%) 363 (4.1) [M^+], 110 (10), 138 (10), 139 (16), 236 (100), 237 (12), 238 (33); HRMS (EI) calcd for $C_9H_6ClF_3INO$ ([M]$^+$): 362.9135; found: 362.9124.

2,2,2-trifluoro-*N*-methyl-*N*-(2-((trimethylsilyl)ethynyl)phenyl)acetamide (S5)

Brown oil: IR (ATR) cm^{-1}: 2961 (C≡C), 1702 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.57 (d, J = 7.5 Hz, 0.1H), 7.53 (dd, J = 7.5, 2.5 Hz, 0.9H), 7.43-7.31 (m, 2H), 7.24 (d, J = 7.5 Hz, 0.9H), 7.21 (d, J = 7.5 Hz, 0.1H), 3.47 (s, 0.3H), 3.34 (s, 2.7H), 0.23 (s, 9H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 156.9 (q, J = 36.2 Hz), 142.4, 132.9, 129.4, 128.9, 128.1, 122.7, 116.2 (q, J = 288.3 Hz), 101.1, 99.6, 38.0, 0.5 (3C); ^{19}F (283 MHz, $CDCl_3$) δ: -71.6, -73.3, -164.9 (C_6F_6); HRMS (FAB) calcd. for $C_{14}H_{16}F_3NNaOSi$ ([M+Na]$^+$): 322.0851; found: 322.0841.

2,2,2-trifluoro-*N*-methyl-*N*-(4-methyl-2-((trimethylsilyl)ethynyl)phenyl)acetamide (S6)

Following the general procedure C, the desired product **S6** (189 mg) was obtained as a mixture of rotamers (9:1) in 99% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 2961 (C≡C), 1698 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.39 (s, 0.1H), 7.35 (s, 1H), 7.20 (d, J = 8.0 Hz, 0.1H), 7.17 (d, J = 8.0 Hz, 0.9H), 7.11 (d, J = 8.0 Hz, 1H), 3.44 (s, 0.3H), 3.31 (s, 2.7H), 2.36 (s, 2.7H), 2.34 (s, 0.3H), 0.22 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.2 (q, J = 35.3 Hz), 141.3, 139.9, 139.2, 138.4, 134.0, 133.4, 130.7, 130.1, 127.9, 126.7, 122.4, 120.9, 116.2 (q, J = 286.5 Hz), 100.6, 99.9, 38.1, 20.9, -0.4 (3C); ^{19}F NMR (282 MHz, $CDCl_3$) δ: -71.60, -73.22, -164.90 (C_6F_6); HRMS (FAB) calcd for $C_{15}H_{19}F_3NOSi$ ([M+H]$^+$): 314.1188; found: 314.1190.

2,2,2-trifluoro-*N*-methyl-*N*-(4-methoxy-2-((trimethylsilyl)ethynyl)phenyl)acetamide (S7)

Following the general procedure C, the desired product **S7** (275 mg) was obtained as a mixture of rotamers (9:1) in 82% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 2961 (C≡C), 1699 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.14 (d, J = 9.0 Hz, 0.9H), 7.11 (d, J = 9.0 Hz, 0.1H), 7.06 (d, J = 3.0 Hz, 0.1H), 7.01 (d, J = 3.0 Hz, 0.9H), 6.93 (dd, J = 9.0 Hz, 3.0 Hz, 0.1H), 6.88 (dd, J = 9.0, 3.0 Hz, 0.9H), 3.83 (s, 2.7H), 3.81 (s, 0.3H), 3.44 (s, 0.3H), 3.30 (s, 2.7H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.4, 158.9, 157.3 (q, J = 35.3 Hz), 135.2, 129.2, 128.0, 123.7, 122.1, 117.6, 117.1, 116.3 (q, J = 286.5 Hz), 116.3, 115.6, 100.9, 99.7, 55.6, 38.2, -0.4 (3C); ^{19}F (283 MHz, $CDCl_3$) δ: -71.6, -73.3, -164.9 (C_6F_6); HRMS (FAB) calcd for $C_{15}H_{18}F_3NNaO_2Si$ ([M+Na]$^+$): 352.0957; found: 352.0945.

***N*-(4-chloro-2-((trimethylsilyl)ethynyl)phenyl)-2,2,2-trifluoro-*N*-methylacetamide (S8)**

Following the general procedure C, the desired product **S8** (358 mg) was obtained as a mixture of rotamers (9:1) in 98% yield as a yellow oil. Yellow oil: IR (ATR) cm^{-1}: 1703 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.56 (d, J = 2.5 Hz, 0.1H), 7.52 (d, J = 2.5 Hz, 0.9H), 7.38 (d, J = 2.5 Hz, 0.1H), 7.35 (dd, J = 8.5, 2.5 Hz, 0.9H), 7.18 (d, J = 8.5 Hz, 0.9H), 7.15 (d, J = 8.5 Hz, 0.1H), 3.44 (s, 0.4H), 3.31 (s, 2.6H), 0.23 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.0 (q, J = 36.0 Hz), 142.3, 140.9, 134.9, 134.2, 133.3, 132.8, 130.0, 129.6, 129.4, 128.4, 124.4, 123.0, 116.1 (q, J = 286.5 Hz), 102.9, 102.0, 98.4, 98.2, 38.0, 37.7, -0.6 (3C); ^{19}F (283 MHz, $CDCl_3$) δ: -71.6, -73.4, -164.9 (C_6F_6); HRMS (EI) calcd. for $C_{14}H_{15}NOF_3SiCl$ (M^+) 333.0564; found: 333.0566.

***N*-(2-ethynylphenyl)-2,2,2-trifluoro-*N*-methylacetamide (5a)**

Yellow oil (1.08 g, 79%): IR (ATR) cm^{-1}: 3292 (C-H), 1693 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.60 (dd, J = 7.5, 1.5 Hz, 1H), 7.48-7.34 (m, 2H), 7.29-7.23 (m, 1H), 3.48 (s, 0.3H), 3.36 (s, 2.7H), 3.30 (s, 0.9H), 3.28 (s, 0.1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 38.2, 78.6, 83.0, 116.2 (q, J = 288.9 Hz), 121.8, 128.3, 129.1, 129.8, 133.7, 142.3, 157.0 (q, J = 36.2 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.4, -164.9 (C_6F_6); HRMS (FAB) calcd for $C_{33}H_{24}F_9NaO_3$ ([3M+Na]$^+$): 704.1572; found: 704.1574.

***N*-(2-ethynyl-4-methylphenyl)-2,2,2-trifluoro-*N*-methylacetamide (5b)**

Following the general procedure D, the desired product **5b** (115 mg) was obtained as a mixture of rotamers (9:1) in 75% yield as a yellow solid. Yellow solid; m.p. 72.5-74.1 °C; IR (ATR) cm^{-1}: 2930 (C≡C), 1696 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.42 (d, J = 1.5 Hz, 0.1H), 7.39 (d, J = 1.5 Hz, 0.9H), 7.26-7.23 (m, 0.1H), 7.21 (dd, J = 8.0, 1.5 Hz, 0.9H), 7.13 (d, J = 8.0 Hz, 1H), 3.45 (q, J = 1.5 Hz, 0.3H), 3.33 (s, 2.7H), 3.25 (s, 0.9H), 3.23 (0.1H), 2.37 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 157.1 (q, J = 36.0 Hz), 139.8, 139.3, 138.6, 134.4, 134.1, 131.1, 130.5, 128.1, 126.7, 121.4, 119.9, 116.2 (q, J = 286.5 Hz), 82.5, 81.9, 78.9, 78.8, 38.3, 20.9; ^{19}F NMR (282 MHz, $CDCl_3$) δ: -71.5, -73.3, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{12}H_{10}F_3NONa$ ([M+Na]$^+$): 264.0607; found: 264.0610.

***N*-(2-ethynyl-4-methoxyphenyl)-2,2,2-trifluoro-*N*-methylacetamide (5c)**

Following the general procedure D, the desired product **5c** (206 mg) was obtained as a mixture of rotamers (9:1) in 94% yield as an ocher oil. Ocher oil; IR (ATR) cm^{-1}: 2942 (C≡C), 1697 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.15 (d, J = 8.5 Hz, 1H), 7.07 (d, J = 2.5 Hz, 1H), 6.92 (dd, J = 8.5, 2.5 Hz, 1H), 3.84 (s, 2.7H), 3.82 (s, 0.3H), 3.44 (s, 0.3H), 3.33 (s, 2.7H), 3.26 (s, 0.9H), 3.25 (s, 0.1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 159.4, 159.0, 157.2 (q, J = 35.3 Hz), 136.9, 135.0, 129.4, 128.0, 122.7, 121.1, 118.3, 118.1, 116.5, 116.2 (q, J =285.0 Hz), 115.7, 82.6, 82.1, 78.7, 78.6, 55.6, 38.4; ^{19}F (283

MHz, $CDCl_3$) δ: -71.5, -73.4, -164.9 (C_6F_6); HRMS (FAB) calcd for $C_{12}H_{11}F_3NO_2$ ($[M+H]^+$): 258.0742; found: 258.0738.

***N*-(4-bromo-2-ethynylphenyl)-2,2,2-trifluoro-*N*-methylacetamide (5d)**

Following the general procedure for the synthesis of **S1**, the desired product **5d** (95.0 mg) was obtained as a mixture of rotamers (9:1) in 33% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 1698 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.73 (d, J = 2.5 Hz, 1H), 7.56 (dd, J = 8.5, 2.5 Hz, 1H), 7.14 (d, J = 8.5 Hz, 1H), 3.44 (s, 0.3H), 3.35 (s, 0.9H), 3.34 (s, 2.8H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.8 (q, J = 36.8 Hz), 143.0, 141.3, 136.6, 136.4, 133.5, 133.1, 129.8, 128.7, 123.7, 122.8, 122.3, 122.0, 116.0 (q, J = 275.0 Hz), 84.4, 83.8, 77.2, 38.1, 37.8; ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.5, -164.9 (C_6F_6); HRMS (FAB) calcd for $C_{11}H_8BrF_3NO$ ($[M+H]^+$): 305.9741; found: 305.9735.

***N*-(4-chloro-2-ethynylphenyl)-2,2,2-trifluoro-*N*-methylacetamide (5e)**

Following the general procedure D, the desired product **5e** (236 mg) was obtained as a mixture of rotamers (9:1) in 72% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 1690 (C=O); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.59 (d, J = 2.5 Hz, 0.1H), 7.57 (d, J = 2.5 Hz, 0.9H), 7.43 (d, J = 2.5 Hz, 0.1H), 7.40 (dd, J = 8.5, 2.5 Hz, 0.9H), 7.21-7.17 (m, 1H), 3.46 (s, 0.3H), 3.35 (s, 1H), 3.34 (s, 2.7H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 156.9 (J = 36.0 Hz), 140.8, 135.1, 134.3, 133.8, 133.5, 130.6, 130.1, 129.6, 128.5, 123.5, 116.1 (q, J = 214.8 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -71.5, -73.4, -164.9 (C_6F_6); MS (EI) *m/z* (%) 261 (85.8) [M^+], 57 (25), 69 (27), 110 (100), 129 (25), 149 (27), 263 (28); HRMS (EI) calcd for $C_{11}H_7ClF_3NO$ ($[M]^+$): 261.0168; found: 261.0174.

2,3-dihydroxy-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2a).

Colorless needle crystals: m.p. 87.1–88.0 ºC (*n*-hexane); IR (ATR) cm^{-1}: 3306 (N-H, O-H); ^1H NMR (400 MHz, $CDCl_3$) δ: 7.38 (d, J = 7.6 Hz, 1H), 7.19 (td, J = 7.6, 1.2 Hz, 1H), 6.85 (td, J = 7.6, 1.2 Hz, 1H), 6.71 (d, J = 7.6 Hz, 1H), 5.82 (s, 1H), 5.66 (s, 1H), 4.89 (brs, 1H), 2.86 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 147.9, 144.6, 130.8, 123.6, 123.1 (q, J = 240.0 Hz), 121.0, 120.1, 110.0, 109.0, 89.2 (q, J = 31.8 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -87.2, -164.9 (C_6F_6); MS (EI) *m/z* (%) 215 (68.4) $[M]^+$, 197 (37), 146 (100), 128 (54); HRMS (EI) Calcd for $C_{10}H_8F_3NO$: 215.0558; Found: 215.0551 $[M]^+$.

2,3-dihydroxy-4-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2b)

Following the general procedure E, the desired product **2b** (46.2 mg) was obtained in 57% yield as a colorless needle. Colorless needle crystals: m.p. 113.2-115.0 °C (*n*-hexane/EtOAc); IR (ATR) cm^{-1}: 3254 (N-H); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.07 (t, J = 7.5 Hz, 1H), 6.64 (d, J = 7.5 Hz, 1H), 6.56 (d, J = 7.5 Hz, 1H), 5.79 (s, 1H), 5.74 (s, 1H), 4.88 (s, 1H), 2.80 (s, 1H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 148.6, 145.7, 135.6, 130.3, 123.2 (q, J = 283.8 Hz), 122.7, 121.2, 112.4, 107.5, 89.3

(q, J = 32.1 Hz), 20.5; ^{19}F (283 MHz, $CDCl_3$) δ: -87.3, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{11}H_{10}F_3NO$ ([M-H]$^-$): 228.0642; found: 228.0640.

2,3-dihydroxy-5-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2c)

Following the general procedure E, the desired product **2c** (49.1 mg) was obtained in 70% yield as a pale-yellow needle. Pale-yellow needle crystals (49.1 mg, 70%): m.p. 107.0-119.7 °C (*n*-hexane); IR (ATR) cm^{-1}: 2922 (O-H), 3317 (N-H); ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.17 (d, J = 2.0 Hz, 1H), 6.99 (dd, J = 8.0, 2.0 Hz, 1H), 6.59 (d, J = 8.0 Hz, 1H), 5.75 (s, 1H), 5.59 (s, 1H), 4.74 (s, 1H), 2.99 (s, 1H), 2.28 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 145.9, 144.8, 131.6, 129.7, 123.8, 123.2 (q, J = 283.3 Hz), 121.5, 110.0, 108.7, 89.5 (q, J = 32.1 Hz), 20.7; ^{19}F (283 MHz, $CDCl_3$) δ: -87.2, -164.9 (C_6F_6); MS (EI) *m/z* (%) 229 (M^+, 48.2), 211 (44), 160 (100), 142 (31); HRMS (EI) calcd for $C_{11}H_{10}F_3NO$ (M^+): 229.0715; found: 229.0709.

2,3-dihydroxy-6-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2d)

Following the general procedure E, the desired product **2d** (79.3 mg) was obtained in 79% yield as a colorless needle. Colorless needle crystals: m.p. 100.6-101.7 °C (*n*-hexane/EtOAc); IR (ATR) cm^{-1}: 3283 (N-H); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, J = 7.6 Hz, 1H), 6.66 (d, J = 7.6 Hz, 1H), 6.50 (s, 1H), 5.71 (s, 1H), 5.55 (s, 1H), 4.79 (s, 1H) , 2.95 (s, 1H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 148.1, 144.4, 141.5, 123.1 (q, J = 283.1 Hz), 121.2, 121.0, 120.8, 110.6, 107.8, 89.4 (q, J = 32.1 Hz), 21.8; ^{19}F (283 MHz, $CDCl_3$) δ: -87.2, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{22}H_{20}F_6N_2O_2$ ([2M-H]$^-$): 457.1356; found: 457.1355.

2,3-dihydroxy-7-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2e)

Following the general procedure E, the desired product **2e** (55.5 mg) was obtained in 79% yield as a white solid. White solid: m.p. 82.3-84.1 ºC (*n*-hexane); IR (ATR) cm^{-1}: 3291 (N-H), 1602 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 (d, J = 7.6 Hz, 1H), 7.02 (d, J = 7.6 Hz, 1H), 6.79 (t, J = 7.6 Hz, 1H), 5.78 (s, 1H), 5.63 (s, 1H), 4.67 (brs, 1H), 2.88 (s, 1H), 2.17 (s, 3H);^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.7, 145.1, 131.7, 123.2 (q, J = 282.8 Hz), 123.0, 120.4, 119.5, 118.6, 108.9, 89.1 (q, J = 32.0 Hz), 16.3; ^{19}F (283 MHz, $CDCl_3$) δ: -87.1, -164.9 (C_6F_6); MS (EI) *m/z* (%) 229 (54.0) [M^+], 160 (100), 83 (36), 57 (67); HRMS (EI) calcd for $C_{11}H_{10}F_3NO$ ([M]$^+$): 229.0715; found: 229.0715.

5-methoxy-1-[(5-methoxy-2-(trifluoromethyl)-1*H*-indol-3-yl)methyl]-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (4)

Following the general procedure E, 5-methoxy-1-[(5-methoxy-2-(trifluoromethyl)-1*H*-indol-3-yl)methyl]-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol **4** (20.6 mg) instead of the desired product

2f was obtained in 30% yield as a yellow prism. Yellow prisms: m.p. 129.1-131.4 °C (*n*-hexane); IR (ATR) cm^{-1}: 3376 (N-H);^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.39 (brs, 1H), 7.28 (d, J = 9.0 Hz, 1H), 7.24 (d, J = 2.0 Hz, 1H), 6.95 (dd, J = 9.0, 2.0 Hz, 1H), 6.92 (d, J = 2.5 Hz, 1H), 6.61 (dd, J = 9.0, 2.5 Hz, 1H), 6.29 (d, J = 9.0 Hz, 1H), 5.81 (s, 1H), 5.71 (s, 1H), 4.98 (d, J = 16.5 Hz, 1H), 4.68 (d, J = 16.5 Hz, 1H), 3.72 (s, 3H), 3.63 (s, 3H), 3.07 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 154.7, 153.7, 145.7, 145.3, 130.3, 126.9, 124.2, 123.5 (q, J = 285.9 Hz), 121.9 (q, J = 37.3 Hz), 121.8 (q, J = 267.6 Hz), 117.2, 116.4, 114.7, 112.5, 110.2, 109.1, 106.1, 102.0, 91.4 (q, J = 31.4 Hz), 55.9, 55.3, 39.4; ^{19}F (283 MHz, $CDCl_3$) δ: -61.0, -83.8, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{22}H_{18}F_6N_2O_3$ ([M-H]$^-$): 471.1149; found: 471.1150.

2,3-dihydroxy-5-bromo-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2g)

Following the general procedure E, the desired product **2g** (43.4 mg) was obtained in 62% yield as a reddish-brown prism. Reddish-brown prisms: m.p. 63.7-64.2 °C (*n*-hexane/Et_2O); IR (ATR) cm^{-1}: 3407 (O-H), 1606 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.46 (d, J = 2.0 Hz, 1H), 7.28 (dd, J = 8.0, 2.0 Hz, 1H), 6.58 (d, J = 8.0 Hz, 1H), 5.81 (s, 1H), 5.68 (s, 1H), 4.90 (s, 1H), 3.03 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ:146.8, 143.4, 133.3, 125.6, 124.0, 122.9 (q, J = 283.7 Hz), 112.2, 111.3, 110.6, 89.4 (q, J = 32.3 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -85.4, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{10}H_7BrF_3NO$ ([M-H]$^-$): 291.9590; found: 291.9589.

2,3-dihydroxy-5-chloro-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (2h)

Following the general procedure E, the desired product **2h** (39.8 mg) was obtained in 56% yield as a yellow prism. Yellow prisms: m.p. 92.5-93.2 °C (*n*-hexane/Et_2O); IR (ATR) cm^{-1}: 3410 (O-H), 1649 (C=C); ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.32 (d, J = 2.0 Hz, 1H), 7.14 (dd, J = 8.4, 2.0 Hz, 1H), 6.63 (d, J = 8.4 Hz, 1H), 5.82 (s, 1H), 5.80 (s, 1H), 4.89 (s, 1H), 2.91 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 146.4, 143.6, 130.6, 125.3, 125.1, 122.9 (q, J = 283.4 Hz), 121.2, 110.9, 110.6, 89.6 (q, J = 32.4 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -87.3, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{10}H_7ClF_3NO$ ([M-H]$^-$): 248.0095; found: 248.0094.

2-hydroxy-3-methylene-2-(trifluoromethyl)indoline-5-carbonitrile (2i)

Following the general procedure E, the desired product **2i** (20.6 mg) was obtained in 29% yield as a colorless prism. Colorless prisms: m.p. 121.8-123.7 °C ($CHCl_3$); IR (ATR) cm^{-1}:3347 (N-H), 2224 (C≡N), 1616 (C=C), ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.57 (s, 1H), 7.45 (d, J = 8.0 Hz, 1H), 6.73 (d, J = 8.0 Hz, 1H), 5.94 (s, 1H), 5.82 (s, 1H), 5.36 (s, 1H), 3.22 (s, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ: 151.0, 142.3, 135.3, 125.0, 124.1, 122.7 (q, J = 283.3 Hz), 119.4, 112.2, 109.6, 102.6, 89.3 (q, J = 32.6 Hz); ^{19}F (283 MHz, $CDCl_3$) δ: -87.4, -164.9 (C_6F_6); HRMS (FAB$^-$) calcd for $C_{11}H_7F_3N_2O$ ([M-H]$^-$): 239.0438; found: 239.0439.

methyl 2-hydroxy-3-methylene-2-(trifluoromethyl)indoline-5-carboxlate (2j)

Following the general procedure E, the desired product **2j** (14.3 mg) was obtained in 18% yield as a colorless prism. Colorless prisms: m.p. 139.0-140.3 °C ($CHCl_3$); IR (ATR) cm^{-1}: 3358 (O-H), 3291 (N-H), 1665 (C=O), 1616 (C=C), ^1H NMR (400 MHz, methanol-d_4) δ: 8.00 (d, J = 1.6 Hz, 1H), 7.82 (dd, J = 8.4, 1.6 Hz, 1H), 6.65 (d, J = 8.4 Hz, 1H), 5.92 (s, 1H), 5.60 (s, 1H), 3.84 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 168.8, 155.1, 145.8, 134.1, 124.9 (q, J = 283.9 Hz), 124.8, 123.4, 120.8, 109.9, 108.9, 90.6 (q, J = 32.9 Hz), 52.2; ^{19}F (283 MHz, $CDCl_3$) δ: -85.5, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{12}H_{10}F_3NO_3$ ($[M-H]^-$): 272.0540; found: 272.0536.

2,3-dihydroxy-1-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (6a)

Following the general procedure E, the desired product **6a** (55.5 mg) was obtained in 69% yield as a yellow oil. Yellow oil: IR (ATR) cm^{-1}: 3394 (O-H), 1608 (C=C); ^1H NMR (300 MHz, $CDCl_3$) δ: 7.33 (dd, J = 7.5, 0.9 Hz, 1H), 7.22 (td, J = 7.5, 0.9 Hz, 1H), 6.75 (td, J = 7.5, 0.9 Hz, 1H), 6.53 (d, J = 8.1 Hz, 1H), 5.80 (s, 1H), 5.66 (s, 1H), 2.98 (q, J = 1.4 Hz, 3H), 2.61 (s, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ: 150.7, 145.0, 131.1, 123.1 (q, J = 287.6 Hz), 122.5, 120.3, 118.4, 109.1, 106.5, 90.4 (q, J = 31.9 Hz), 27.9; ^{19}F (283 MHz, $CDCl_3$) δ: -84.4, -164.9 (C_6F_6); MS (EI) *m/z* (%) 229 (M^+,45), 71 (21), 158 (10), 200 (13), 202 (10), 212 (100), 226 (11), 228 (14), 230 (23) HRMS (EI) calcd. for $C_{11}H_{10}NOF_3$ (M^+) 229.0715; found: 229.0714.

2,3-dihydroxy-5-methyl-1-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (6b)

Following the general procedure E, the desired product **6b** (43.4 mg) was obtained in 69% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 3371 (O-H); ^1H NMR (500 MHz, $CDCl_3$) δ: 7.16 (bs, 1H), 7.04 (d, J = 8.0 Hz, 1H), 6.45 (d, J = 8.0 Hz, 1H), 5.7 (s, 1H), 5.64 (s, 1H), 2.67 (d, J = 1.5 Hz, 3H), 2.51 (bs, 1H), 2.28 (s, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 148.8, 145.3, 131.6, 127.9, 123.2 (q, J = 286.0 Hz), 122.7, 121.0, 108.7 (q, J = 2.3 Hz), 106.6, 90.7 (q, J = 31.3 Hz), 28.1, 20.7; ^{19}F (283 MHz, $CDCl_3$) δ: -84.3, -164.9 (C_6F_6); MS (EI) *m/z* (%) 243 (M^+, 54.5), 226 (35), 174 (100); HRMS (EI) calcd for $C_{12}H_{12}F_3NO$ (M^+): 243.0871; found: 243.0879.

2,3-dihydroxy-5-methoxy-1-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (6c)

Following the general procedure E, the desired product **6c** (59.8 mg) was obtained in 75% yield as a red oil. Red oil; IR (ATR) cm^{-1}: 3371 (O-H); ^1H NMR (500 MHz, $CDCl_3$) δ: 6.93 (d, J = 2.5 Hz, 1H), 6.83 (dd, J = 8.5, 2.5 Hz, 1H), 6.47 (d, J = 8.5 Hz, 1H), 5.78 (s, 1H), 5.68 (s, 1H), 3.78 (s, 3H), 2.95 (s, 3H), 2.48 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 153.0, 145.5, 145.2, 123.4, 123.2 (q, J = 285.8 Hz), 117.1, 109.3 (q, J = 2.3 Hz), 107.3, 106.5, 90.9 (q, J = 30.8 Hz), 56.2, 28.3; ^{19}F (283 MHz, $CDCl_3$) δ: -85.5, -164.9 (C_6F_6); HRMS (ESI) calcd for $C_{24}H_{25}N_2O_4F_6$ ($[2M+H]^+$): 519.1713; found: 519.1710.

2,3-dihydroxy-5-bromo-1-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (6d)

Following the general procedure E, the desired product **6d** (33.4 mg) was obtained in 47% yield as a yellow oil. Yellow oil; IR (ATR) cm^{-1}: 3419 (O-H); ^1H NMR (300 MHz, $CDCl_3$) δ: 7.40 (d, J = 1.5 Hz, 1H), 7.28 (d, J = 8.4 Hz, 1H), 6.38 (dd, J = 8.4, 1.5 Hz, 1H), 5.78 (s, 1H), 5.69 (s, 1H), 2.95 (s, 3H), 1.26 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.5, 143.7, 133.4, 124.6, 123.3, 122.9 (q, J = 286.5 Hz), 110.7, 110.3, 108.0, 90.7 (q, J = 31.5 Hz), 27.9; ^{19}F (283 MHz, $CDCl_3$) δ: -87.1, -164.9 (C_6F_6); MS (EI) *m/z* (%) 307 (M^+, 38.7), 309 ($M+2^+$, 37.1), 240 (100), 238 (99), 159 (34); HRMS (EI) calcd. for $C_{11}H_9BrF_3NO$ (M^+): 306.9820; found: 306.9821.

2,3-dihydroxy-5-chloro-1-methyl-3-methylene-2-trifluoromethyl-1*H*-indole-2-ol (6e)

Following the general procedure E, the desired product **6e** (46.8 mg) was obtained in 58% yield as a yellow oil. IR (ATR) cm^{-1}: 3420 (O-H); ^1H NMR (300 MHz, $CDCl_3$) δ: 7.28 (d, J = 2.1 Hz, 1H), 7.16 (dd, J = 8.4, 2.1 Hz, 1H), 6.44 (d, J = 8.4 Hz, 1H), 5.81 (s, 1H), 5.71 (s, 1H), 2.97 (q, J = 1.5 Hz, 3H), 2.59 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 149.1, 144.0, 130.7, 124.1, 123.5, 123.0 (q, J = 286.1 Hz), 120.6, 110.7 (q, J = 2.2 Hz), 107.5, 90.8 (q, J = 31.7 Hz), 28.0; ^{19}F (283 MHz, $CDCl_3$) δ: -84.6, -164.9 (C_6F_6); MS (EI) *m/z* (%) 263 (M^+, 71.3), 265 ($M+2^+$, 31.6), 246 (100), 236 (32), 194 (68), 83 (40); HRMS (EI) calcd. for $C_{11}H_9ClF_3NO$ (M^+): 263.0325; found: 263.0331.

(*E*,*Z*)-3-benzylidene-2-(trifluoromethyl)indolin-2-ol (8a)

Following the general procedure E, the desired product **8a** (70.5 mg) was obtained as a mixture of isomers in 87% yield. Yellow oil; IR (ATR) cm^{-1}: 3313 (O-H); ^1H NMR (300 MHz, $CDCl_3$) δ: 8.44 (brs, 1H), 7.73 (d, J = 7.8 Hz, 1H), 7.64 (d, J = 7.8 Hz, 1H), 7.55-7.22 (m, 12H), 7.21-7.02 (m, 3H), 6.85 (t, J = 7.5 Hz, 0.4 H), 6.66 (d, J = 7.8 Hz, 1H), 6.59 (t, J = 7.8 Hz, 0.6H), 6.39 (s, 1H), 4.96 (s, 0.4H), 4.93 (s, 0.6H), 3.24 (s, 0.4H), 2.99 (s, 0.6H), 2.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 170.0, 153.4, 148.8, 147.0, 145.7, 142.65, 142.62, 142.4, 139.2, 137.1, 135.8, 135.4, 135.2, 134.8, 134.3, 134.0, 133.1, 130.9, 130.6, 130.37, 129.98, 129.94, 128.9, 128.6, 128.43,128.37, 128.32, 128.2, 128.13, 128.09, 128.06, 127.9, 127.81, 127.78, 127.74, 127.4, 127.3, 126.6, 126.0, 125.3, 125.0, 123.8, 123.5, 123.0, 122.8, 122.5, 122.3, 122.1, 121.8, 121.3, 121.1, 120.2, 120.0, 119.84, 119.80, 119.6, 111.9, 111.7, 109.7, 109.4, 90.6 (q, J = 32.9 Hz), 90.4 (q, J = 31.6 Hz), 70.0, 68.4;^{19}F (283 MHz, $CDCl_3$) δ: -60.3, -64.7, -84.4, -87.3 -164.9 (C_6F_6); MS (EI) *m/z* (%) 291 (M^+, 62.9), 273 (100), 252 (29), 204 (93), 186 (32); HRMS (EI) calcd. for $C_{16}H_{12}F_3NO$ (M^+): 291.0871; found: 291.0861.

(*E*,*Z*)-2-(trifluoromethyl)-3-((trimethylsilyl)methylene)indolin-2-ol (8b)

Following the general procedure E, the desired product **8b** (117.9 mg) was obtained as a mixture of isomers in 58% yield. White powder; IR (ATR) cm^{-1}: 3502 (O-H); ^1H NMR (300 MHz, $CDCl_3$) δ:

8.25 (brs, 1H), 7.97 (d, J = 8.1 Hz, 1H), 7.46-7.27 (m, 3H), 7.22-7.10 (m, 2H), 6.86-6.78 (m, 1H), 6.70 (d, J = 8.1 Hz, 0.5H), 6.66 (d, J = 8.1 Hz, 0.5H), 6.39 (s, 0.5H), 6.25 (s, 0.5H), 5.07 (s, 1H), 4.94 (s, 0.5H), 4.91 (s, 0.5H), 2.73 (s, 0.5H), 2.70 (s, 0.5H), 1.82 (s, 1H), 0.30 (s, 4H), 0.24 (s, 5H), 0.08 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 151.2, 147.7, 135.6, 128.9 (q, J = 274 Hz), 127.1, 126.3, 124.9 (2C), 123.8 (2C), 122.4 (q, J = 279 Hz), 120.3 (2C), 120.1, 119.8, 111.5 (2C), 109.9, 109.7, 63.2, 0.52, -0.59 (2C), -2.99 (3C); ^{19}F (283 MHz, $CDCl_3$) δ: -60.1, -86.3, -87.3 -164.9 (C_6F_6); MS (EI) *m/z* (%) 287 (M^+, 84.0), 254 (53), 215 (100), 174 (57), 79 (81); HRMS (EI) calcd. for $C_{13}H_{16}F_3NOSi$ (M^+): 287.0953; found: 287.0959.

3-(piperidine-1-yl)methyl)-2-(trifluoromethyl)-1*H*-indole (9)

To a solution of **2a** (50.0 mg, 0.232 mmol) in THF (0.83 mL) was added TMSCl (29.3 μL, 0.232 mmol) and piperidine (0.275 mL, 0.278 mmol), the reaction mixture was stirred for 22 hours at rt. After completion of the reaction, the reaction mixture was evaporated. Purification using column chromatography over silica gel with $CHCl_3$/MeOH (100:1) as eluent yielded **7a** (45 mg, 69%) as a pale-yellow solid. IR (ATR) cm^{-1}: 3069; ^{1}H NMR (500 MHz, $CDCl_3$) δ: 8.31 (brs, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.32 (t, J = 8.0 Hz, 1H), 7.18 (t, J = 8.0 Hz, 1H), 3.77 (s, 2H), 2.42 (brs, 4H), 1.55 (quin, J = 5.5 Hz, 4H), 1.41-1.35 (m, 2H); ^{13}C NMR (75 MHz, $CDCl_3$) δ: 135.2, 128.0, 124.7, 122.9 (q, J = 36.9 Hz), 122.1, 121.9 (q, J = 267.5 Hz), 120.5, 115.4, 111.4, 54.4 (2C), 52.4, 26.0 (2C), 24.3; ^{19}F (283 MHz, $CDCl_3$) δ: -60.8, -164.9 (C_6F_6); MS (EI) *m/z* (%) 282 (M^+, 90.0), 198 (97), 178 (40), 84 (100); HRMS (EI) calcd. for $C_{15}H_{17}F_3N$ (M^+): 282.1344; found: 282.1350.

4. References

1. J. Wang, G. Wang, X. Cheng, Y. Liu and J. Zhang, *Org. Biomol. Chem*., 2021, **19**, 1329–1333.
2. U. F. Röhrig, S. R. Majjigapu, A. Grosdidier, A. Bron, V. Stroobant, L. Pilotte, D. Colau, P. Vogel, B. J. Van den Eynde, V. Zoete and O. Michielin, *J. Med. Chem*., 2012, **55**, 5270–5290.
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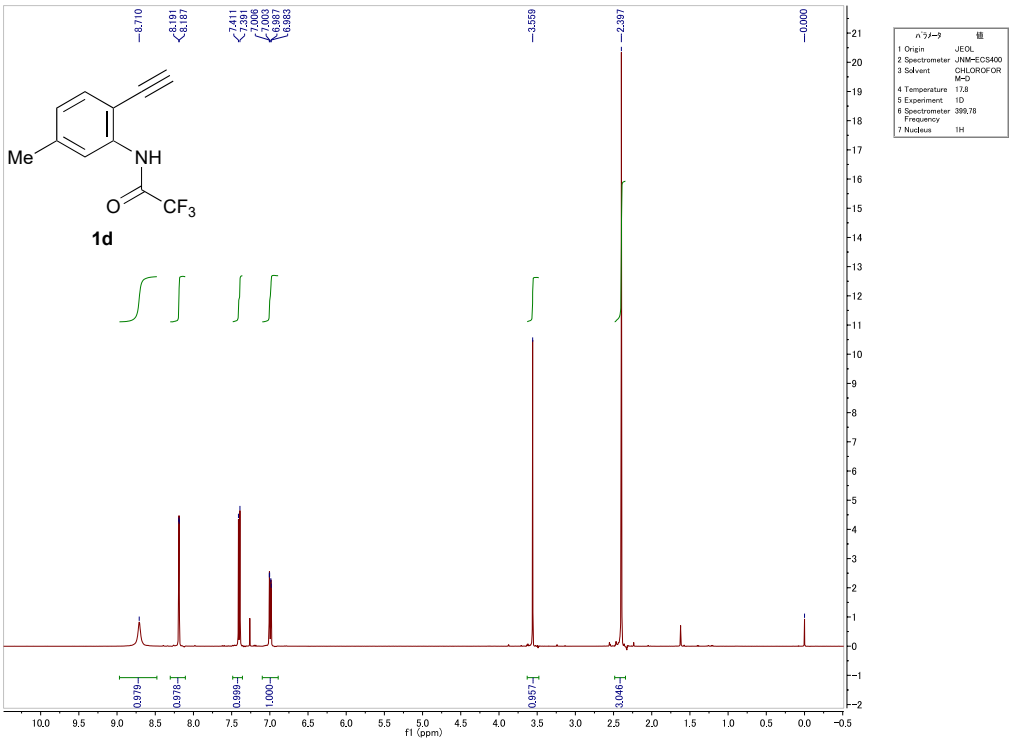
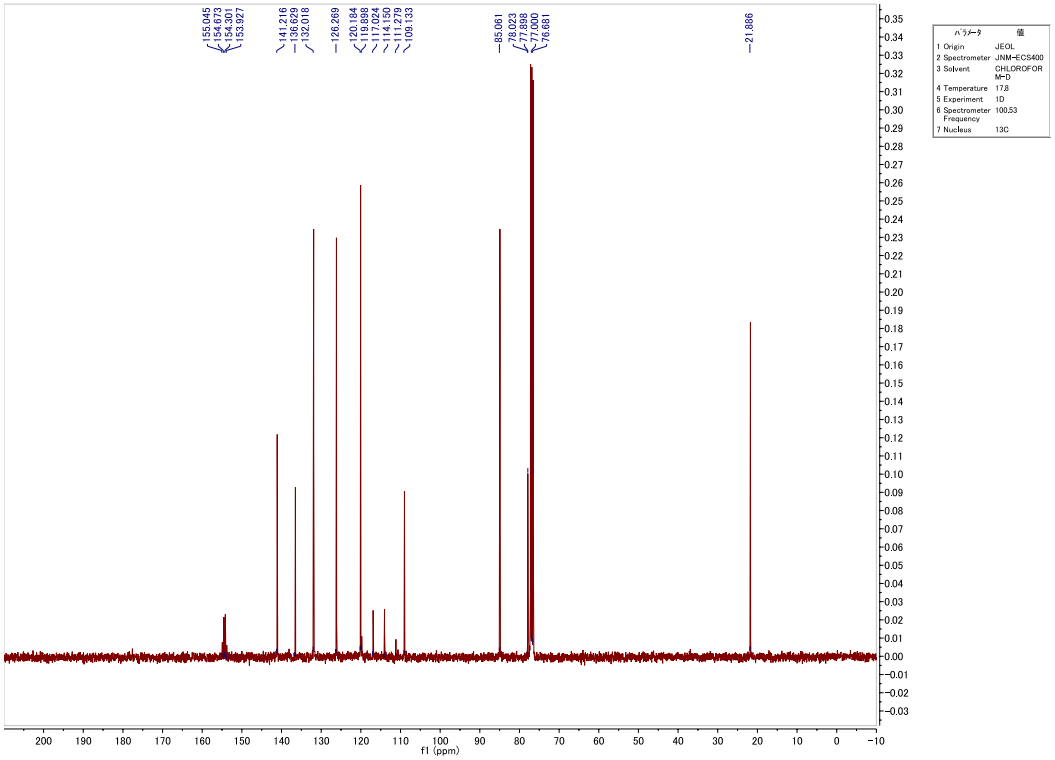
4. P. Cironi, J. T. Puche, G. Barany, F. Albericio and M. Álvarez, *Org. Lett.* 2004, **6**, 1405-1408.
5. J. R. Box, M. E. Avanthay, D. L. Poole and A. J. J. Lennox, *Angew. Chem. Int. Ed.,* 2023, **62**, e202218195.

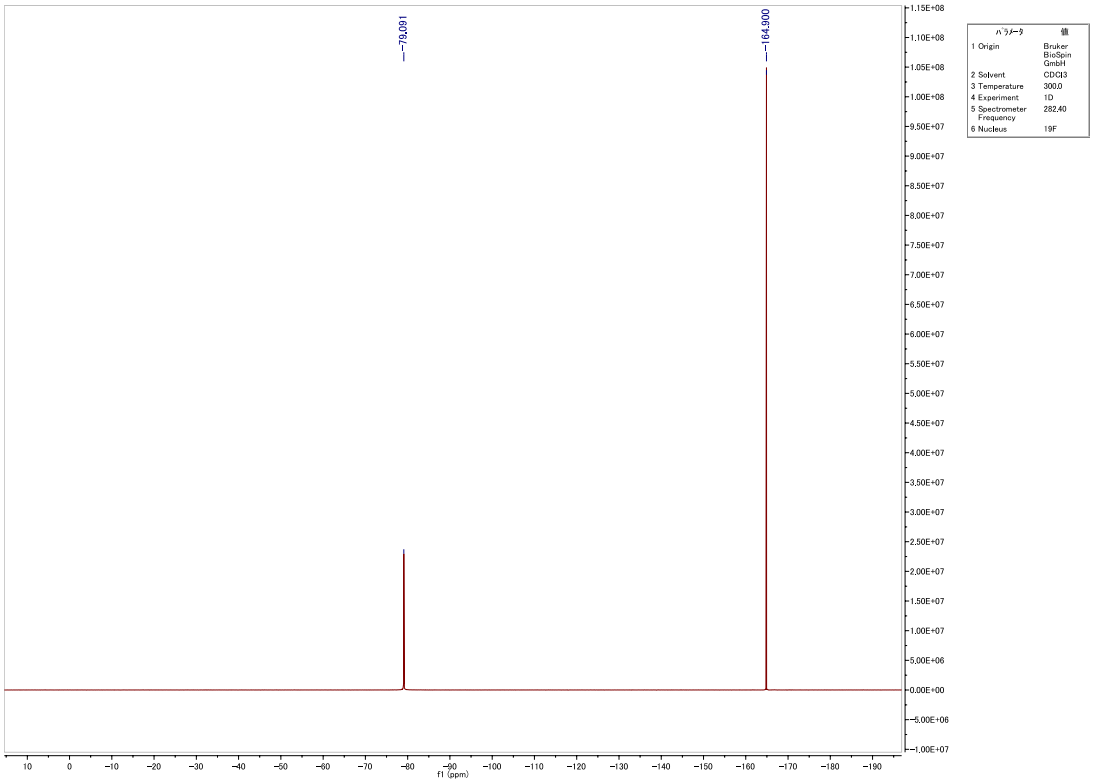
5. Copies of the ^{1}H NMR, ^{13}C NMR and ^{19}F NMR Spectra



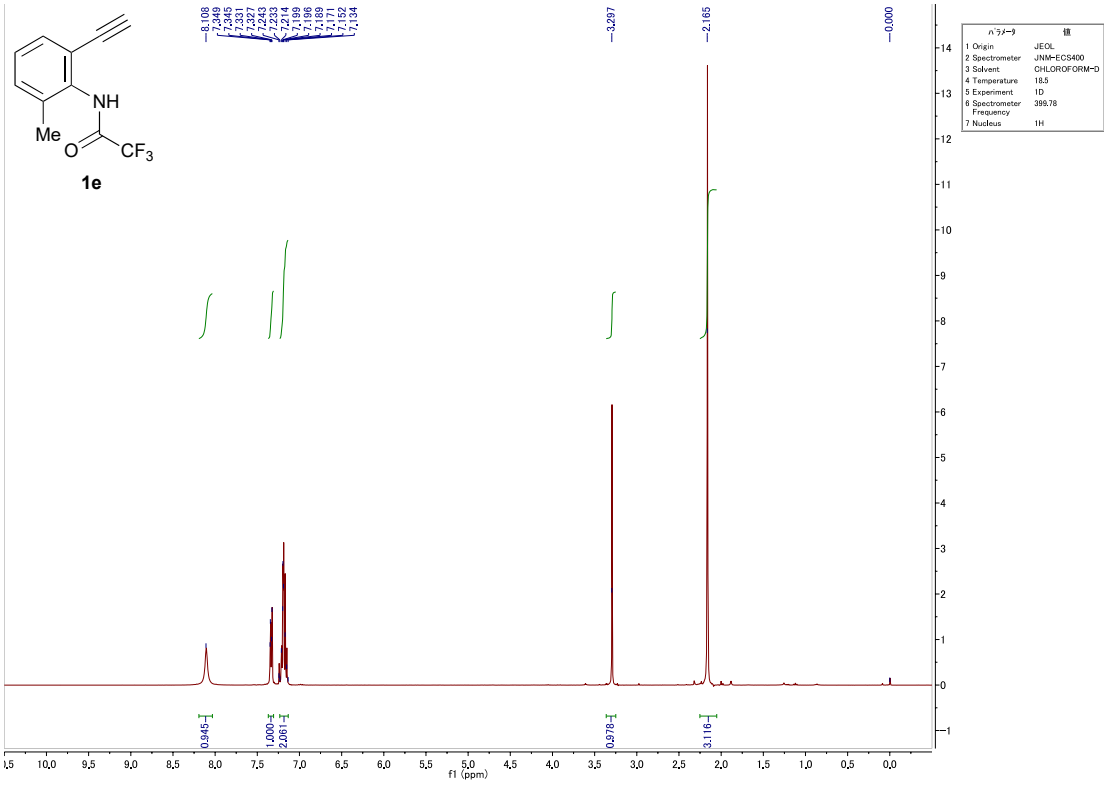
^{1}H NMR (400 MHz, $CDCl_3$) of **1d**



^{13}C NMR (100 MHz, $CDCl_3$) of **1d**



^{19}F NMR (283 MHz, $CDCl_3$) of **1d**



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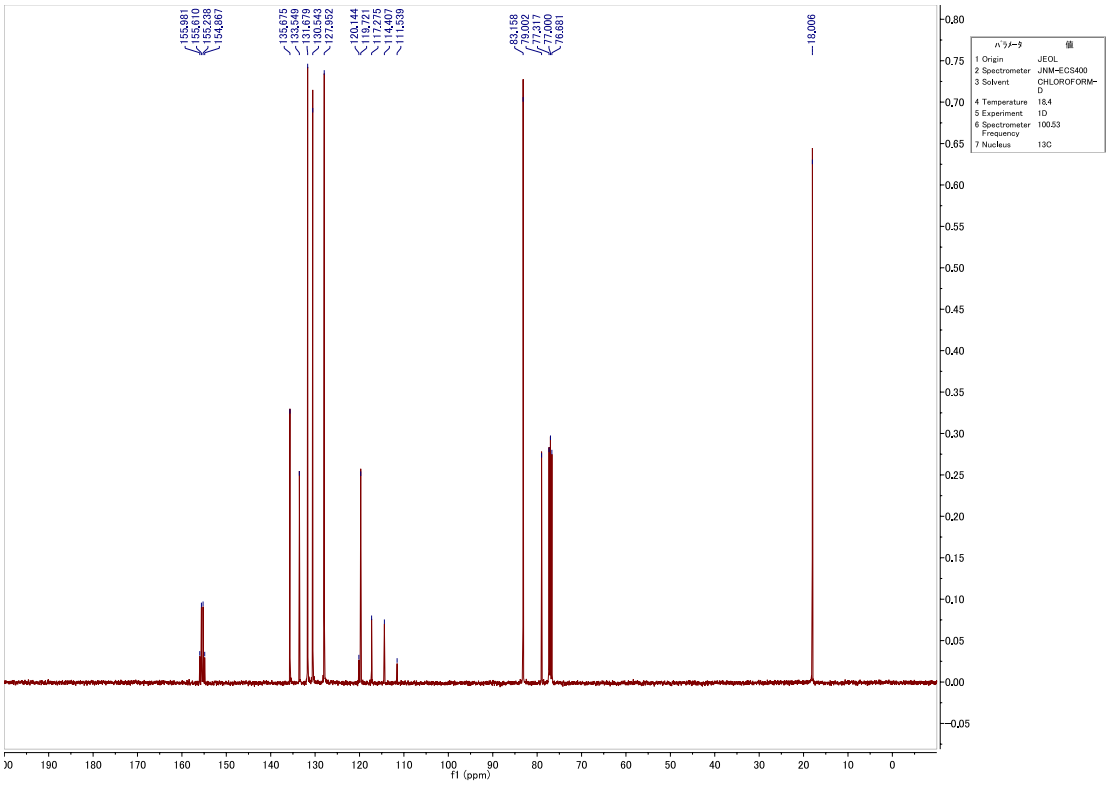
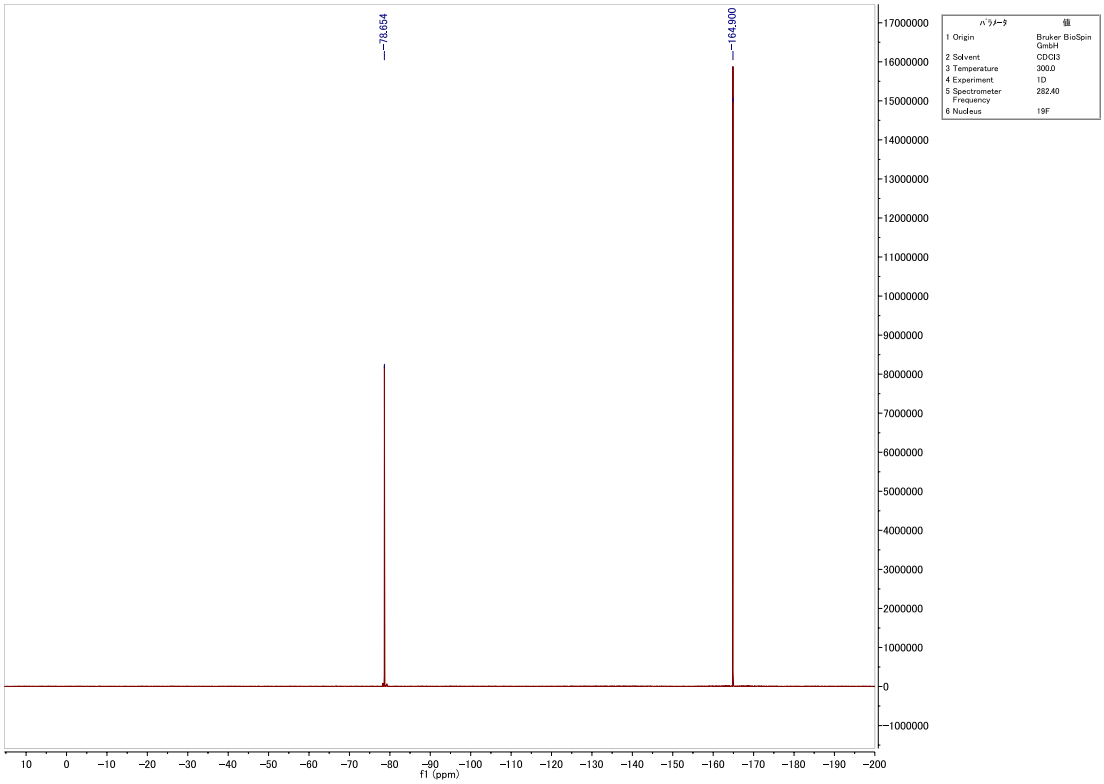
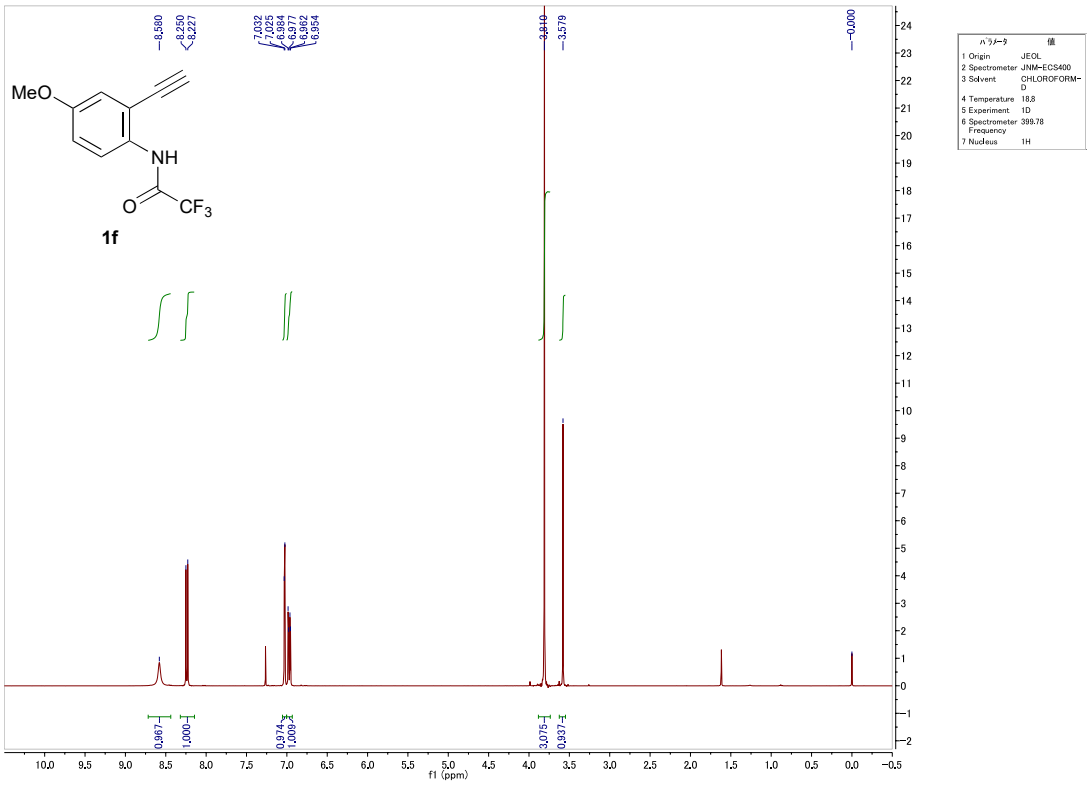


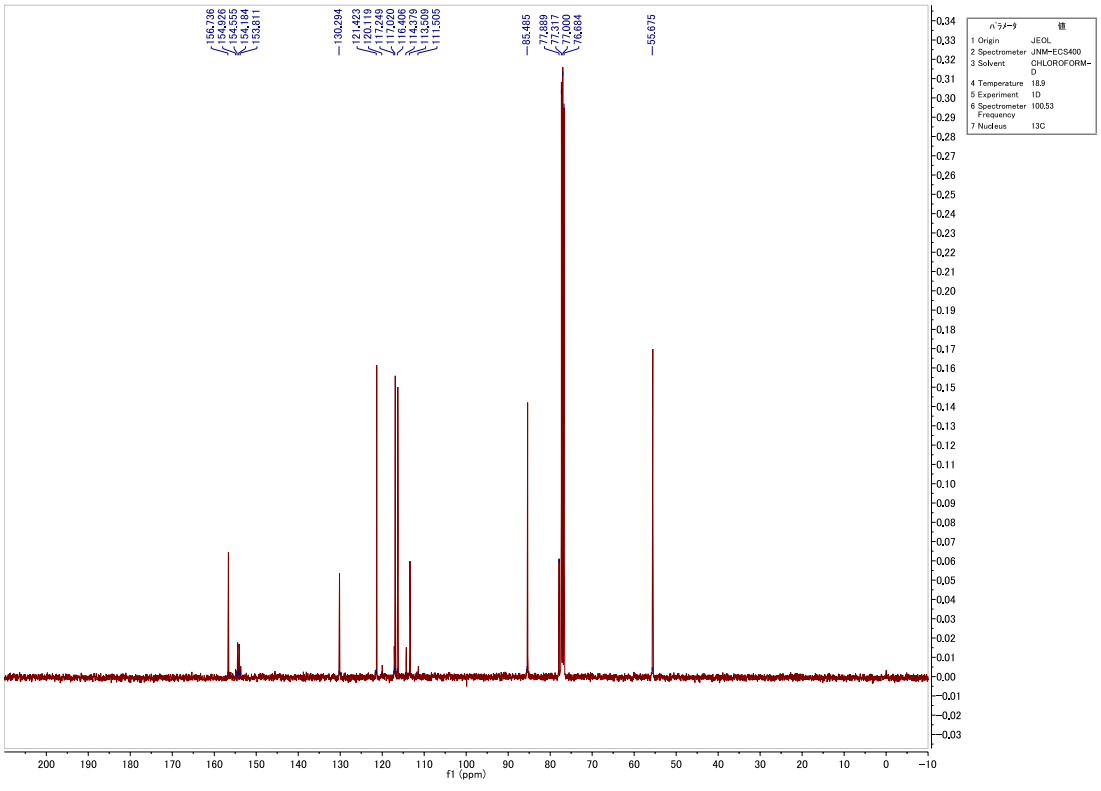
^{13}C NMR (100 MHz, $CDCl_3$) of **1e**



^{19}F NMR (283 MHz, $CDCl_3$) of **1e**



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



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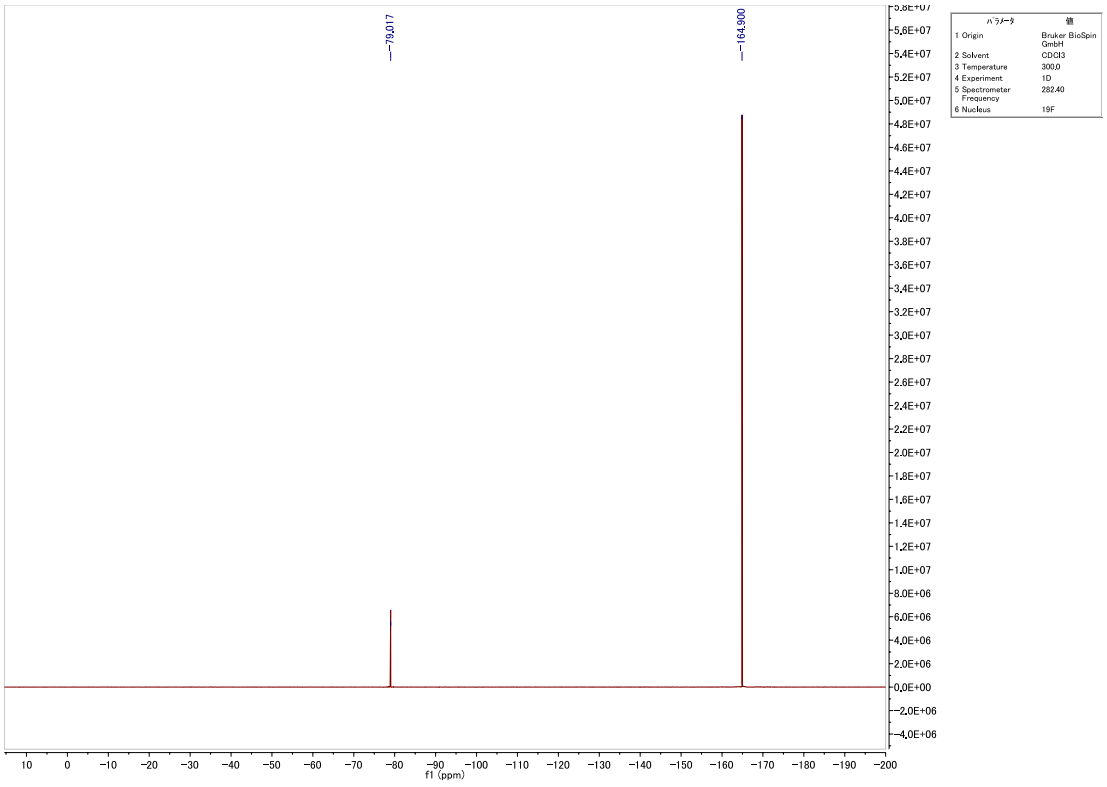
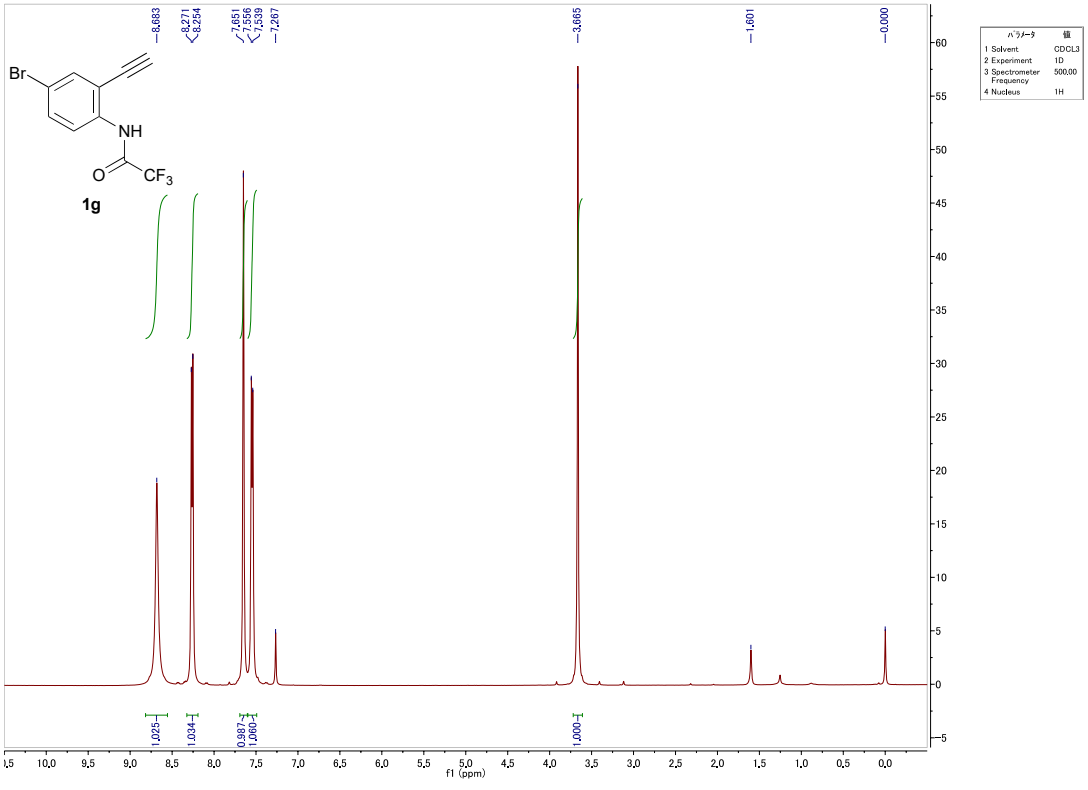
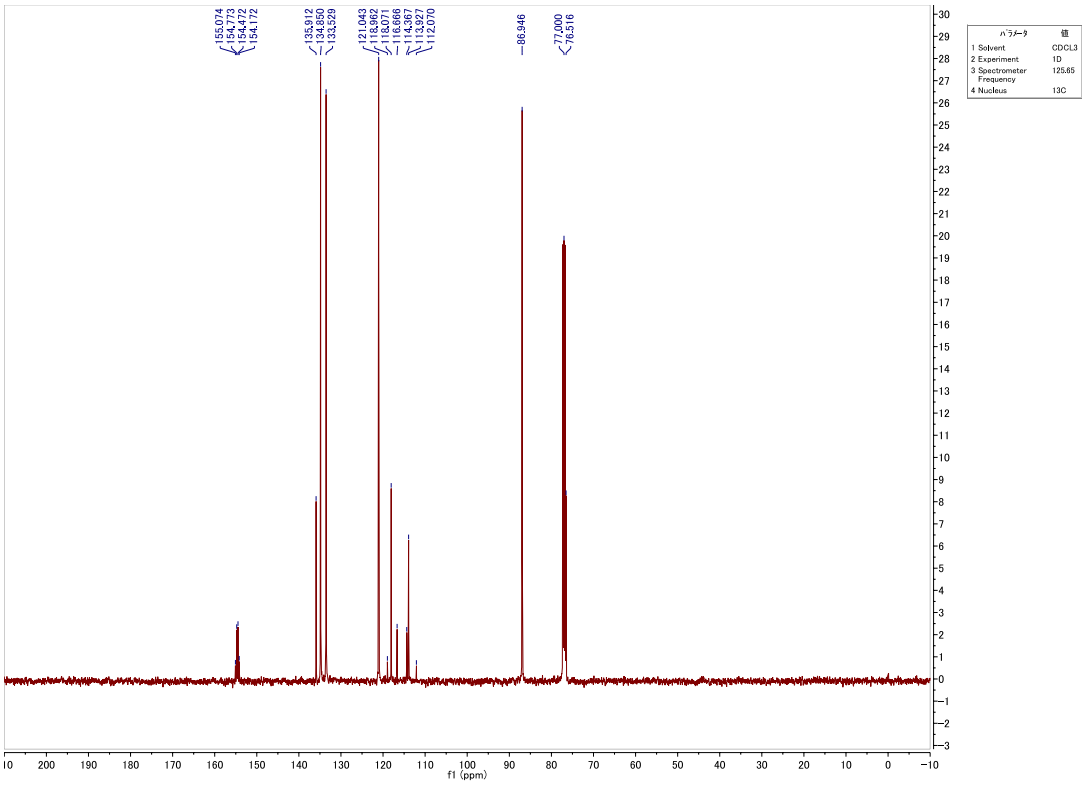


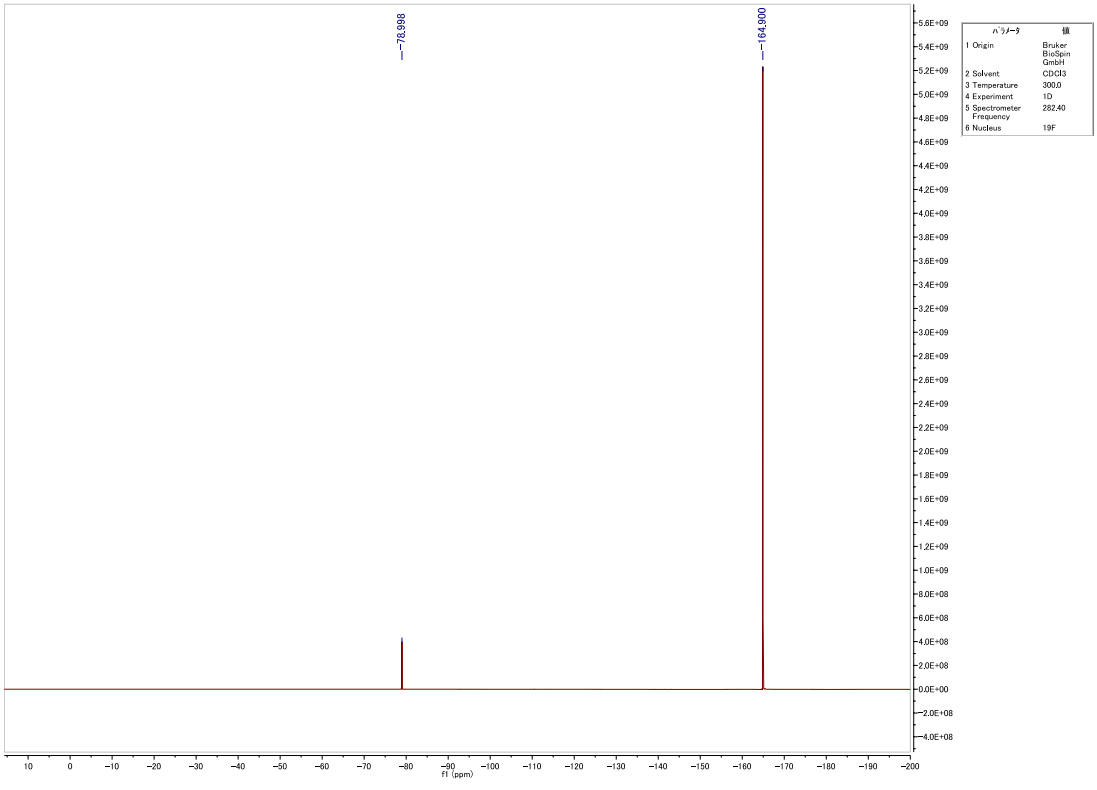
^{19}F NMR (283 MHz, $CDCl_3$) of **1f**



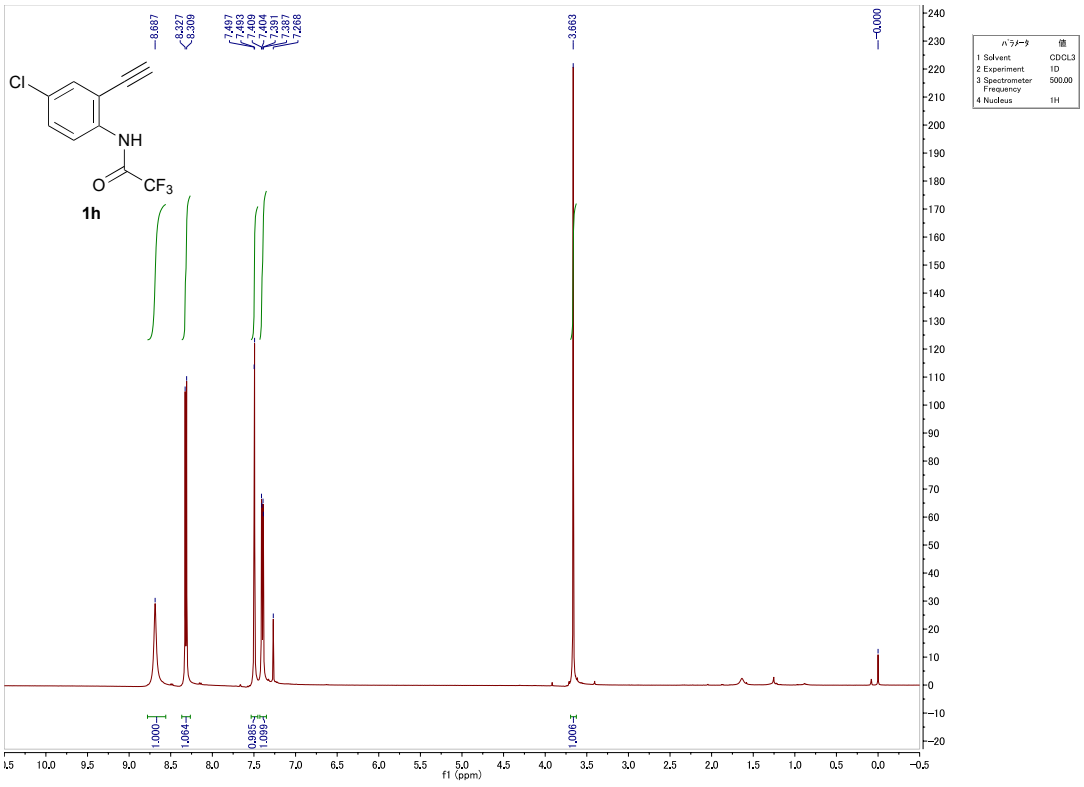
^{1}H NMR (500 MHz, $CDCl_3$) of **1g**



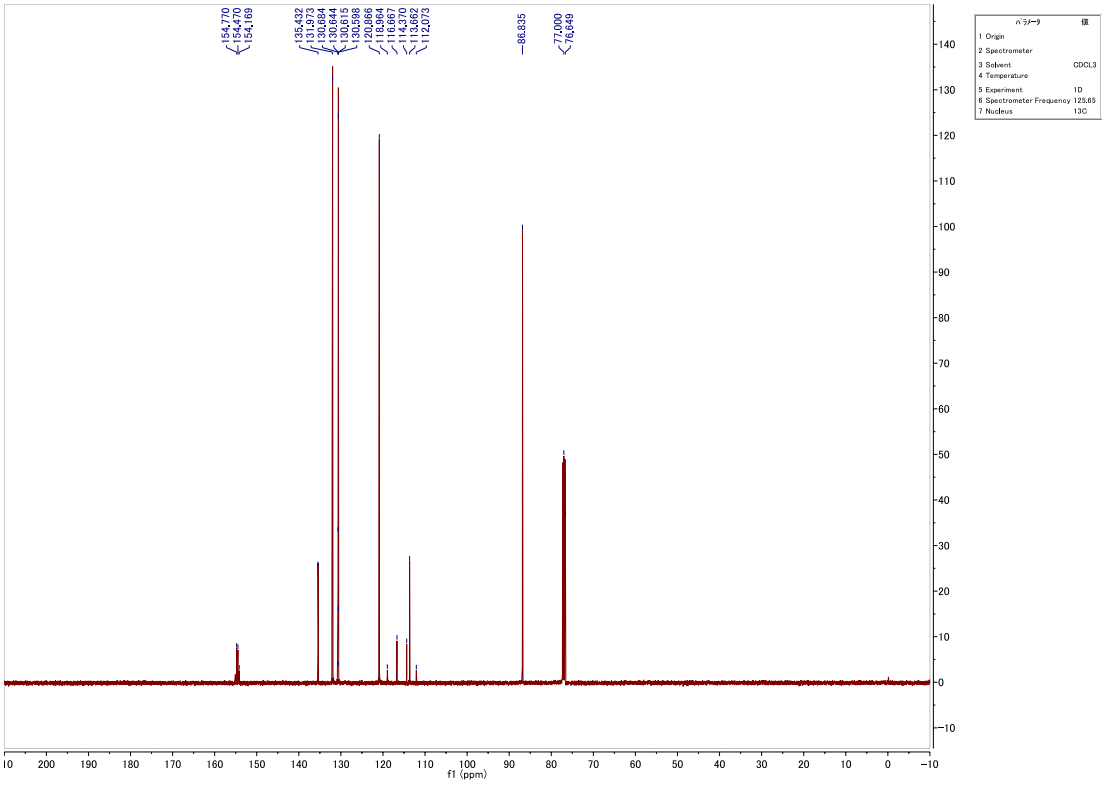
^{13}C NMR (125 MHz, $CDCl_3$) of **1g**



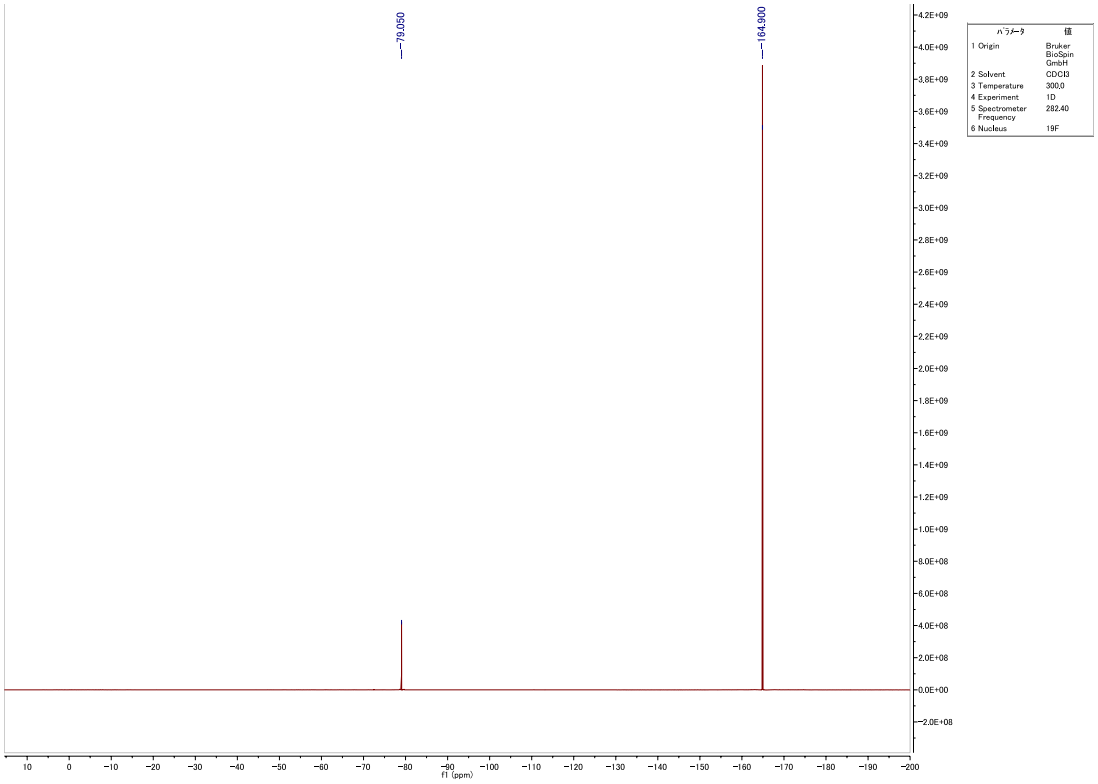
^{19}F NMR (283 MHz, $CDCl_3$) of **1g**



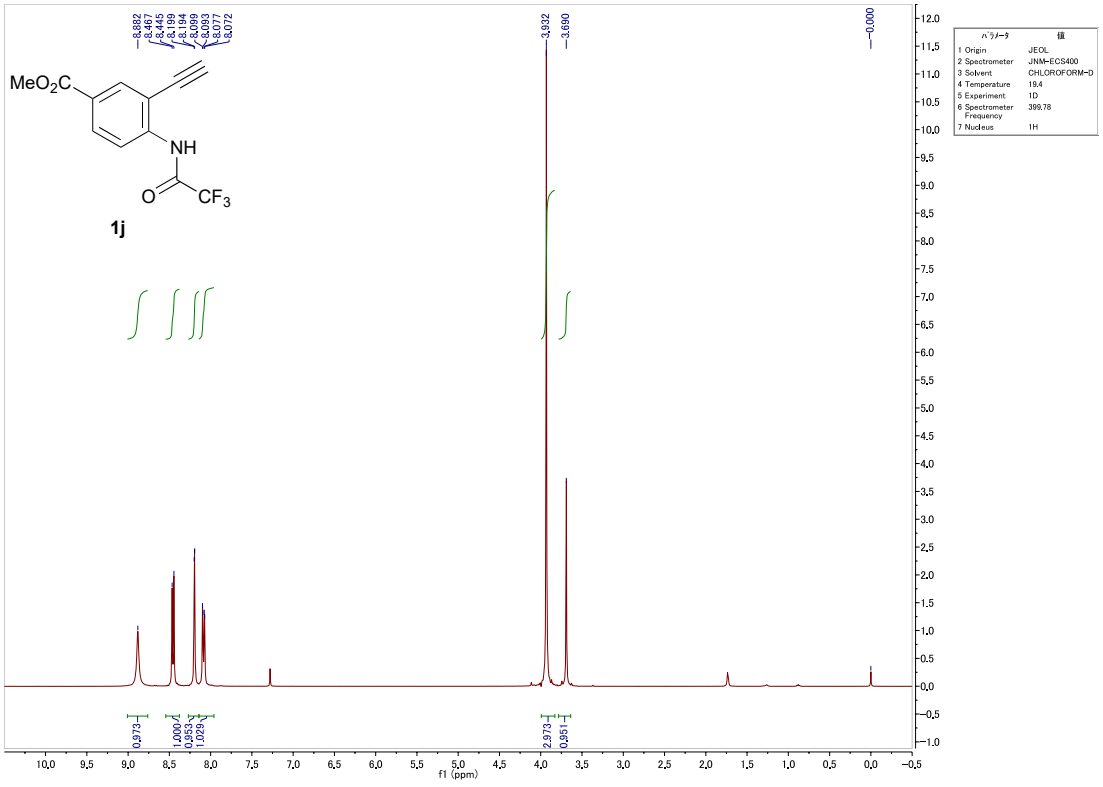
^{1}H NMR (500 MHz, $CDCl_3$) of **1h**



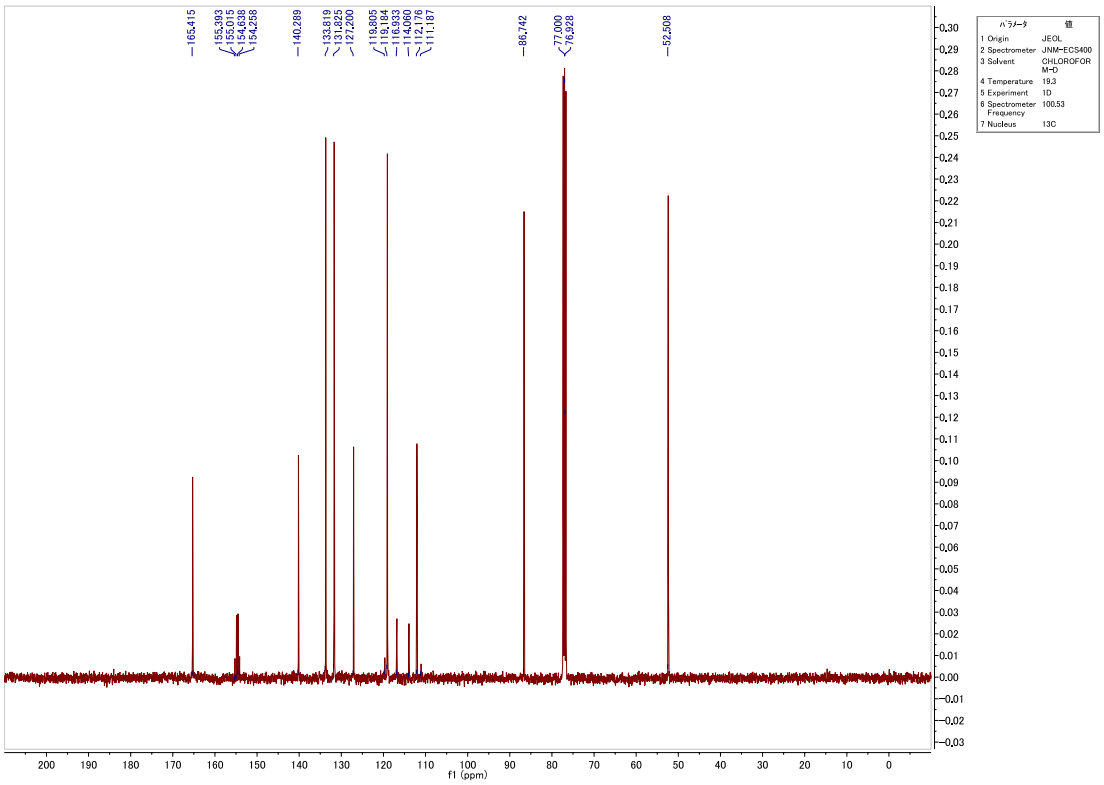
^{13}C NMR (125 MHz, $CDCl_3$) of **1h**



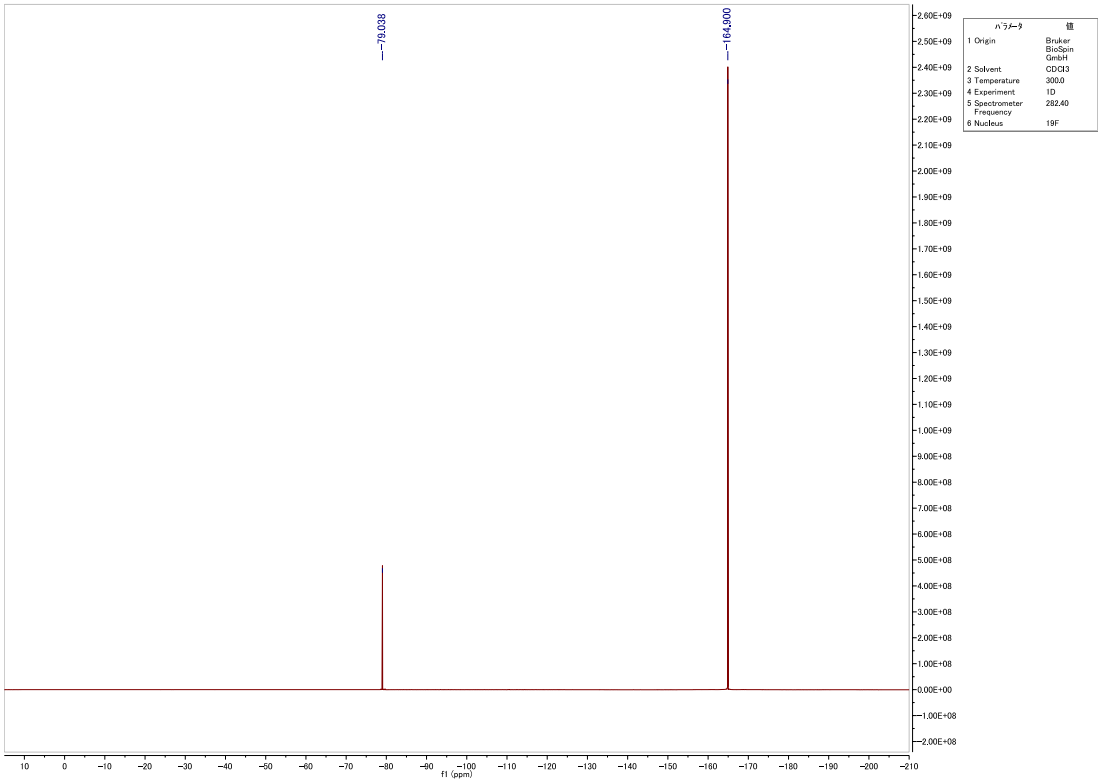
^{19}F NMR (283 MHz, $CDCl_3$) of **1h**



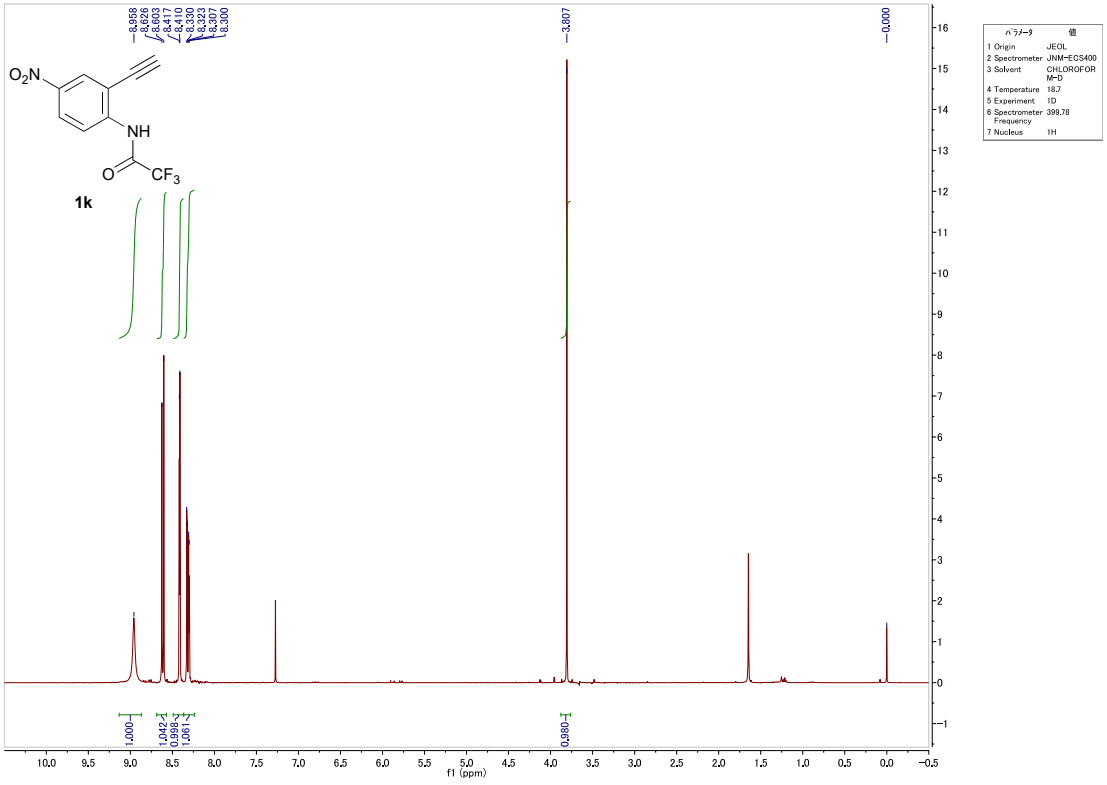
^{1}H NMR (400 MHz, $CDCl_3$) of **1j**



^{13}C NMR (100 MHz, $CDCl_3$) of **1j**



^{19}F NMR (283 MHz, $CDCl_3$) of **1j**



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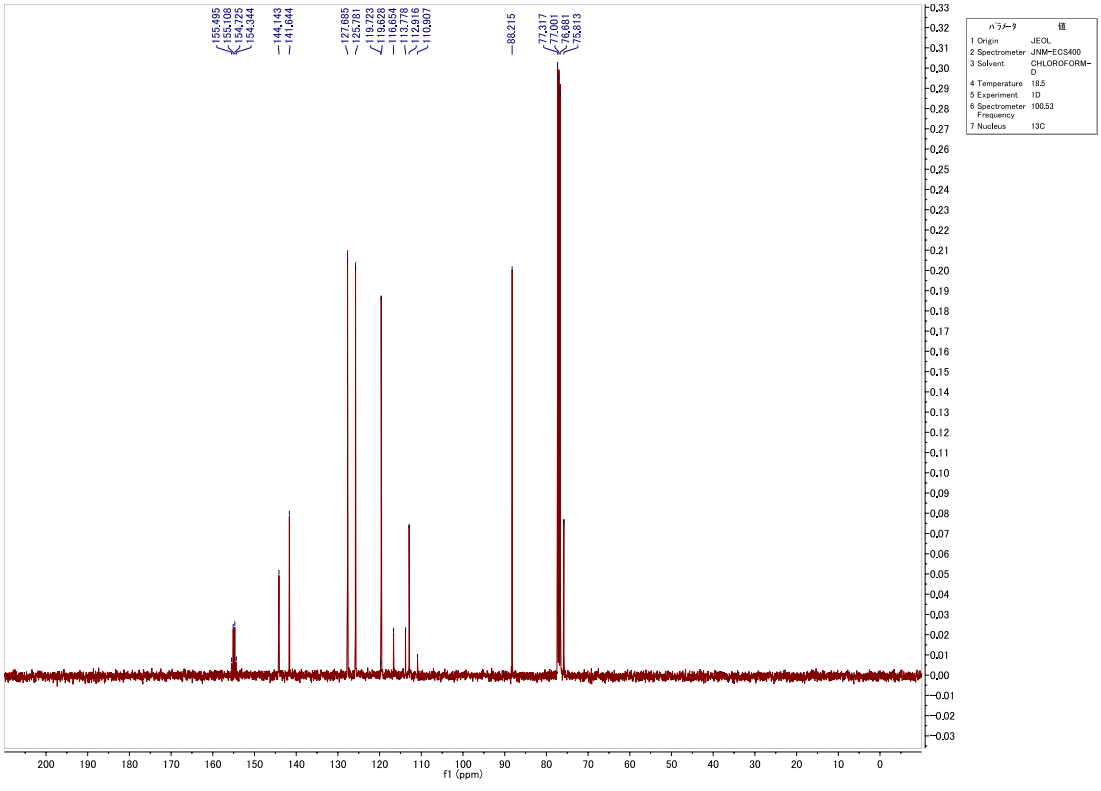

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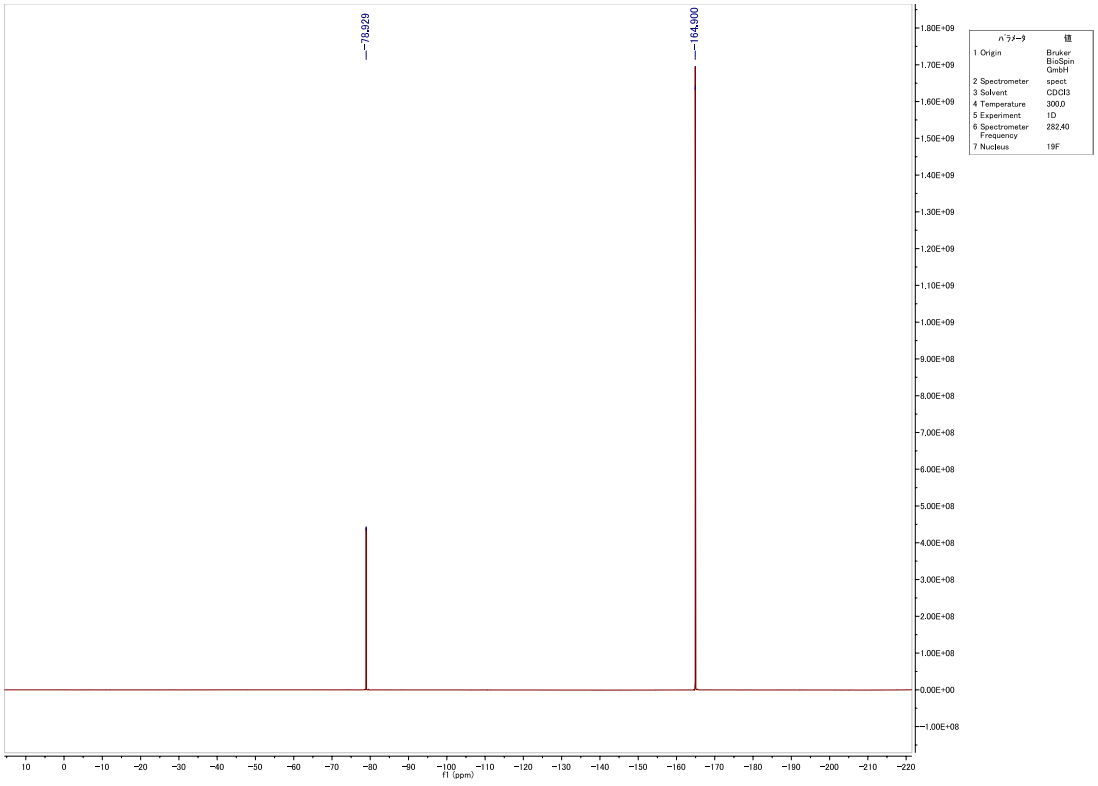

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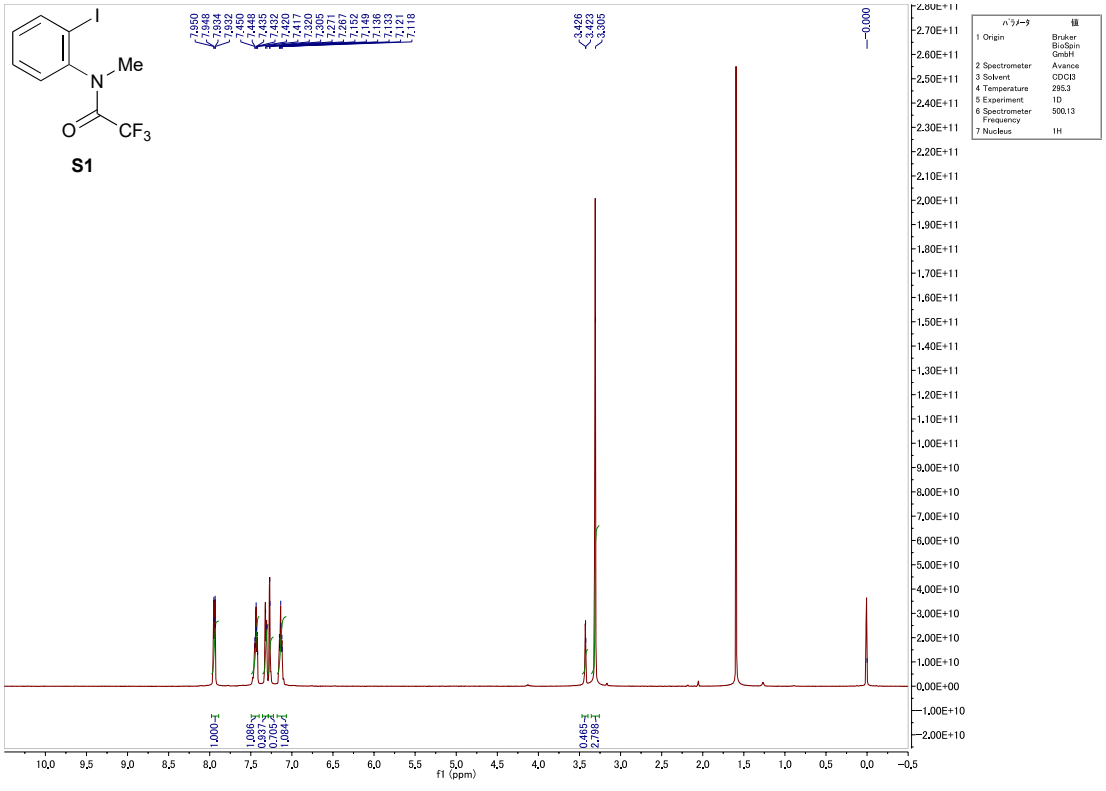
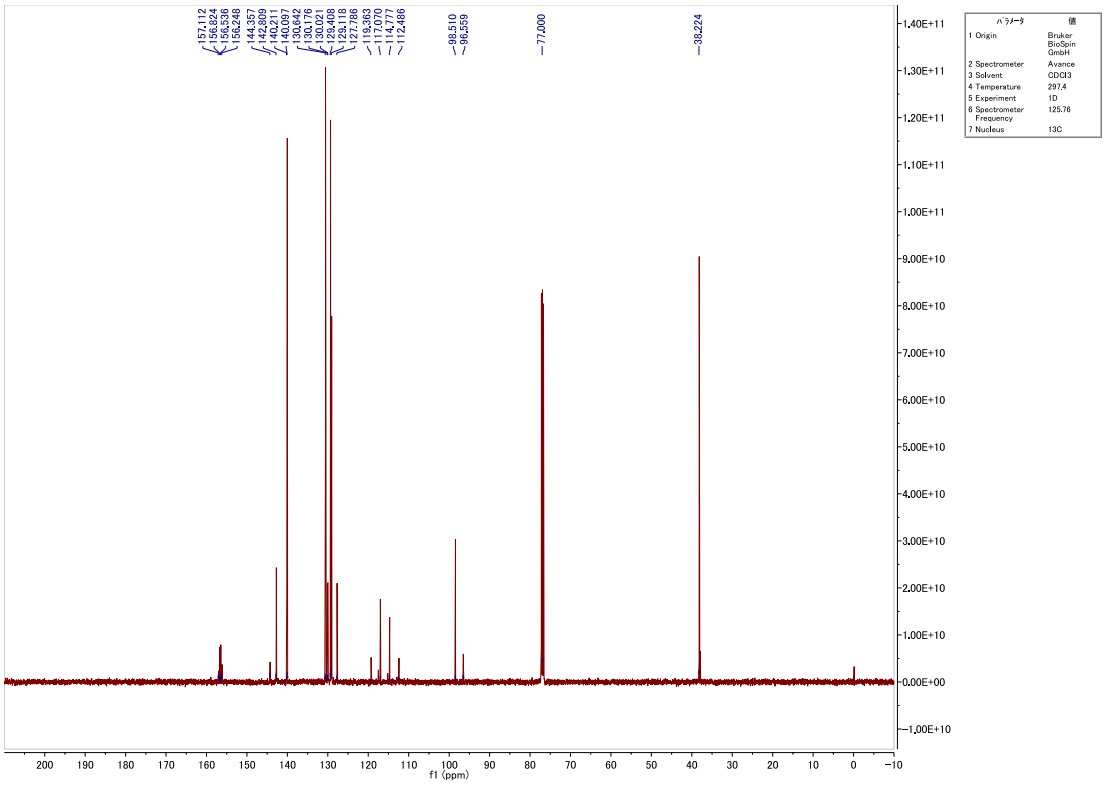
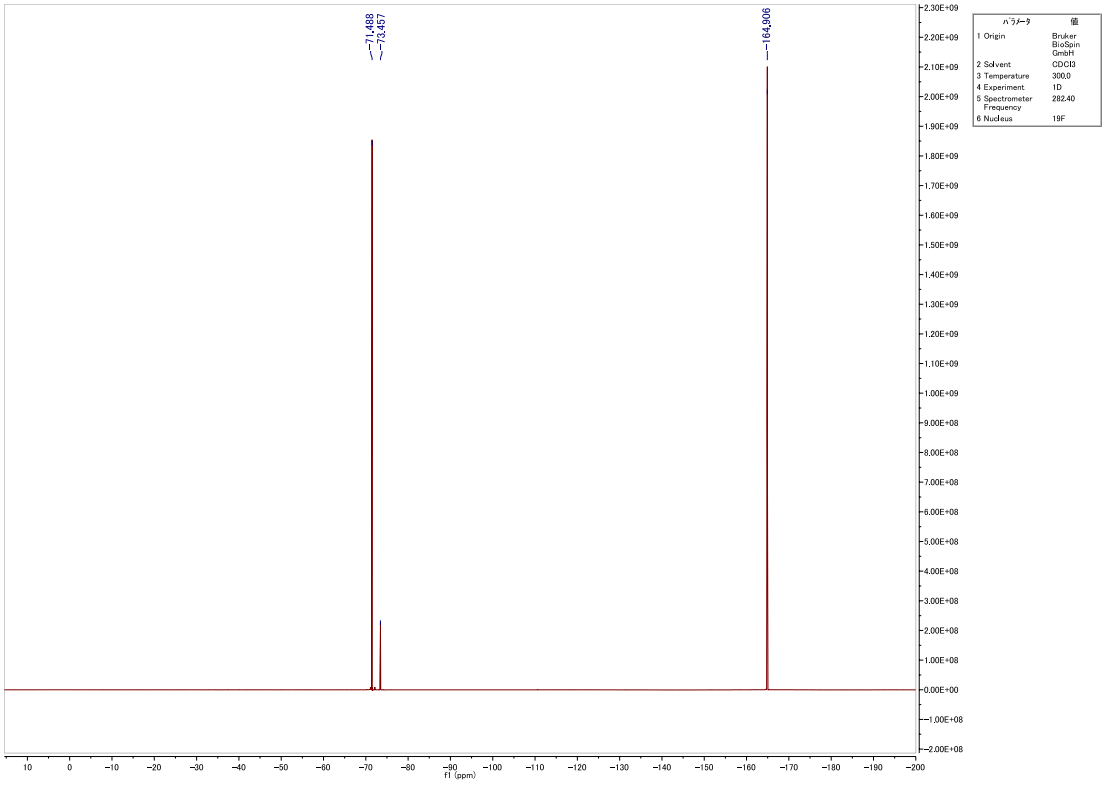


^{1}H NMR (500 MHz, $CDCl_3$) of **S1**



^{13}C NMR (125 MHz, $CDCl_3$) of **S1**



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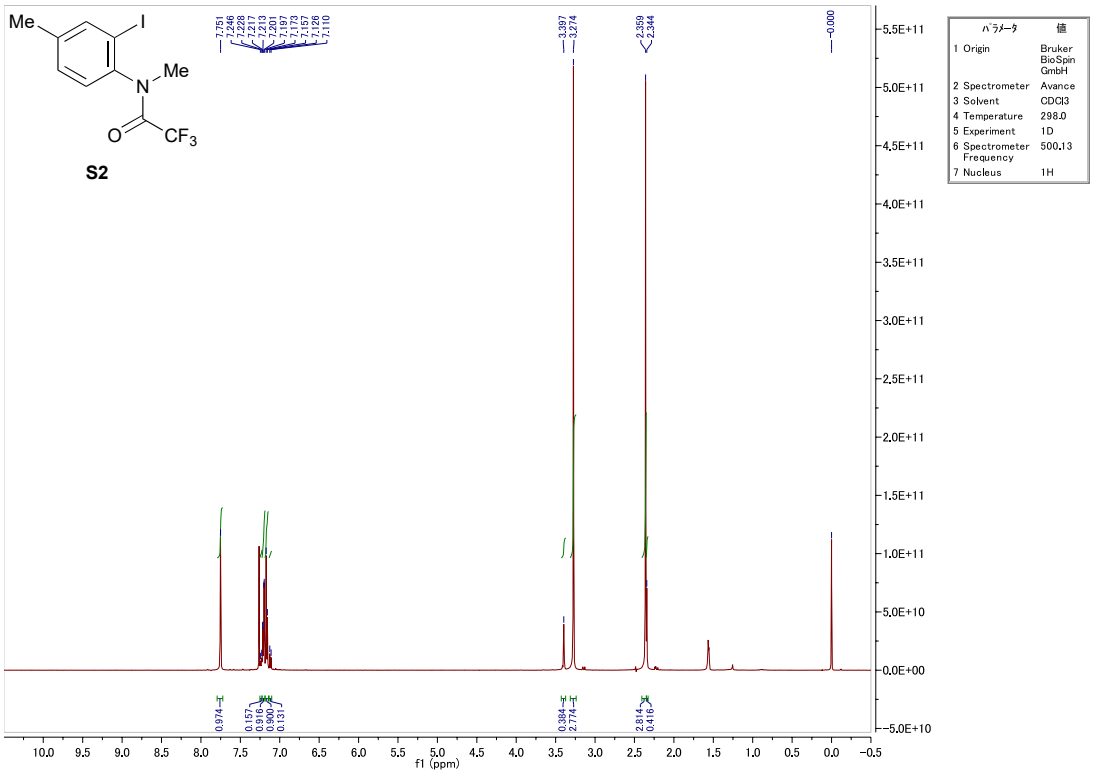
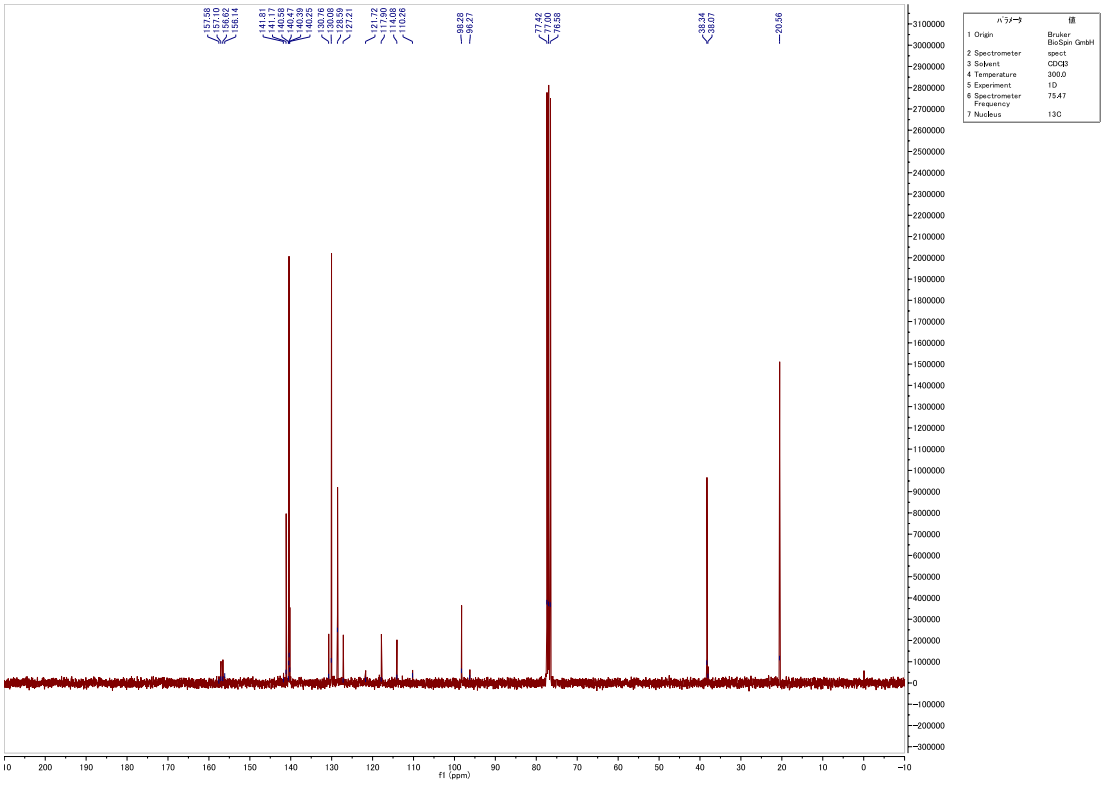
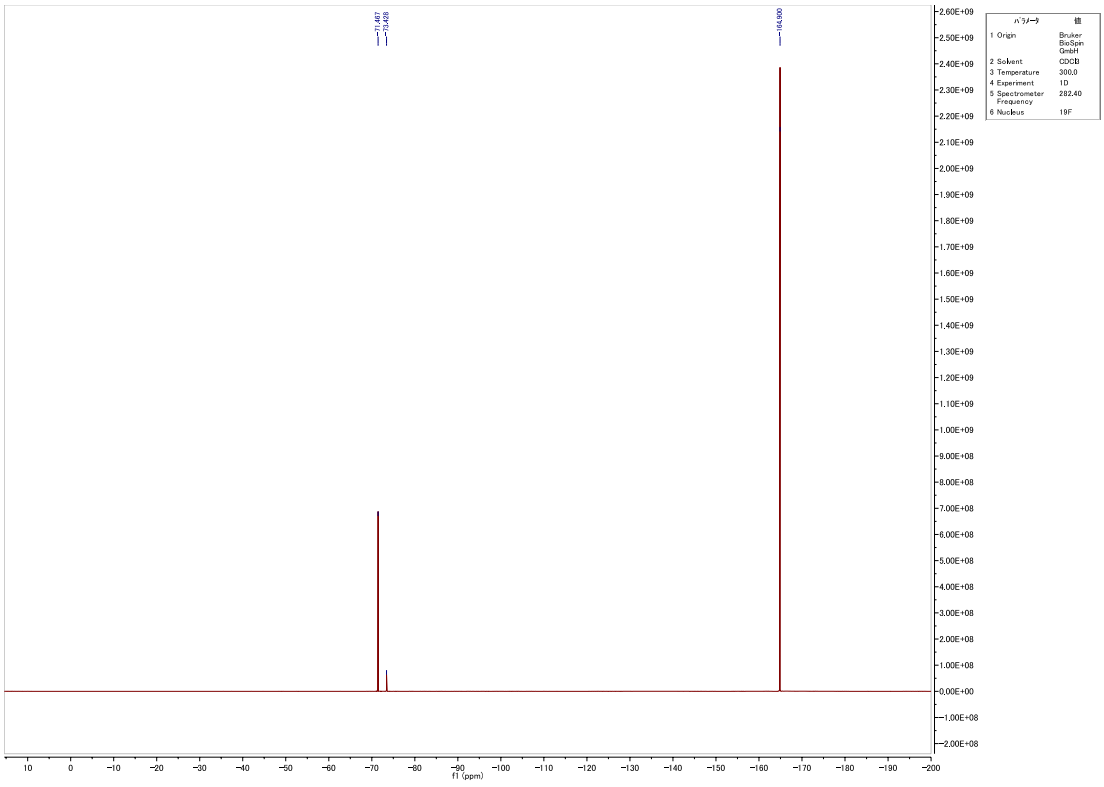


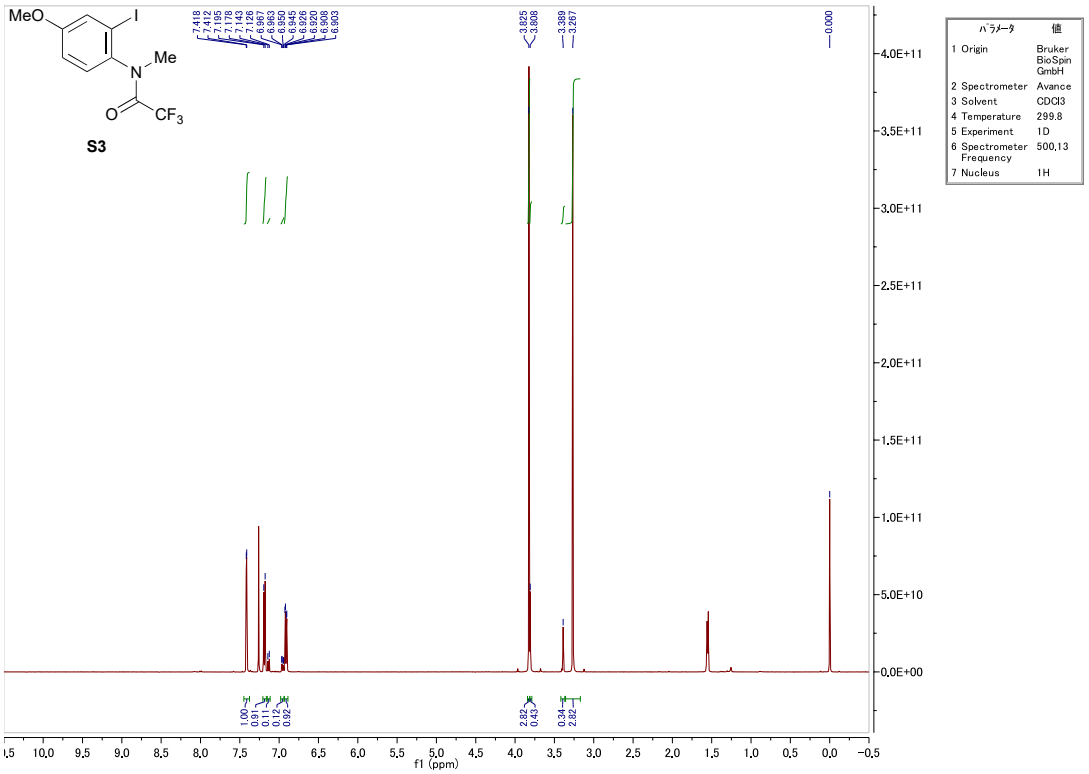
^{1}H NMR (500 MHz, $CDCl_3$) of **S2**



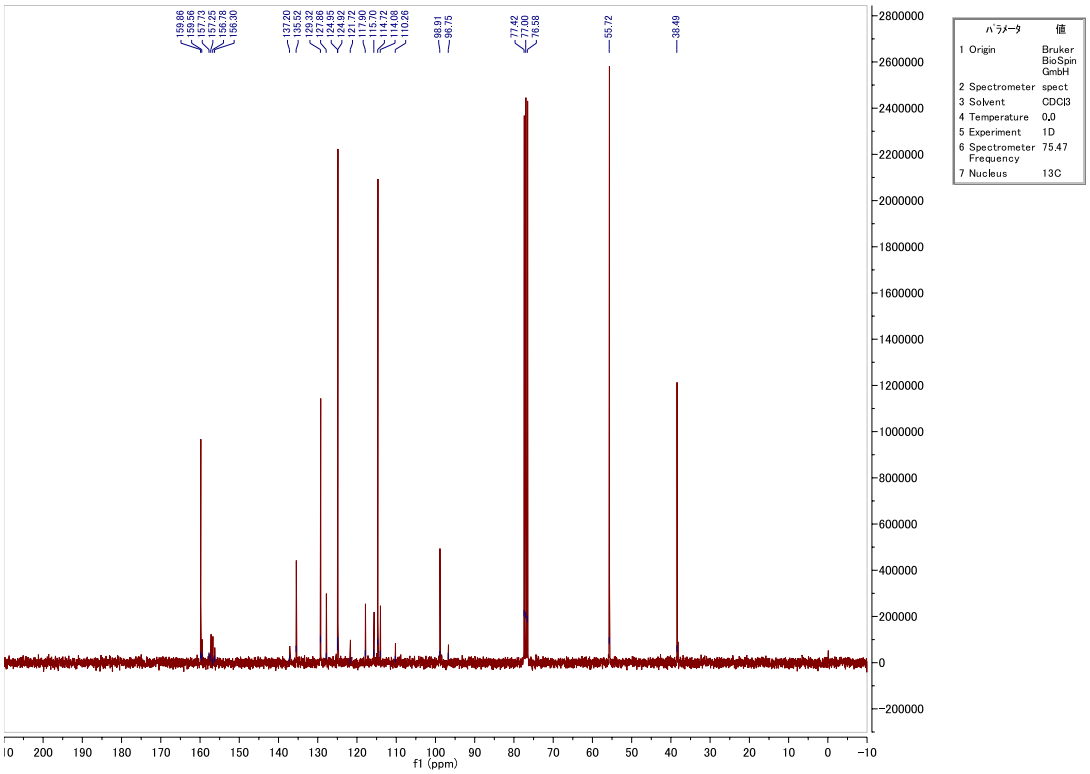
^{13}C NMR (75 MHz, $CDCl_3$) of **S2**



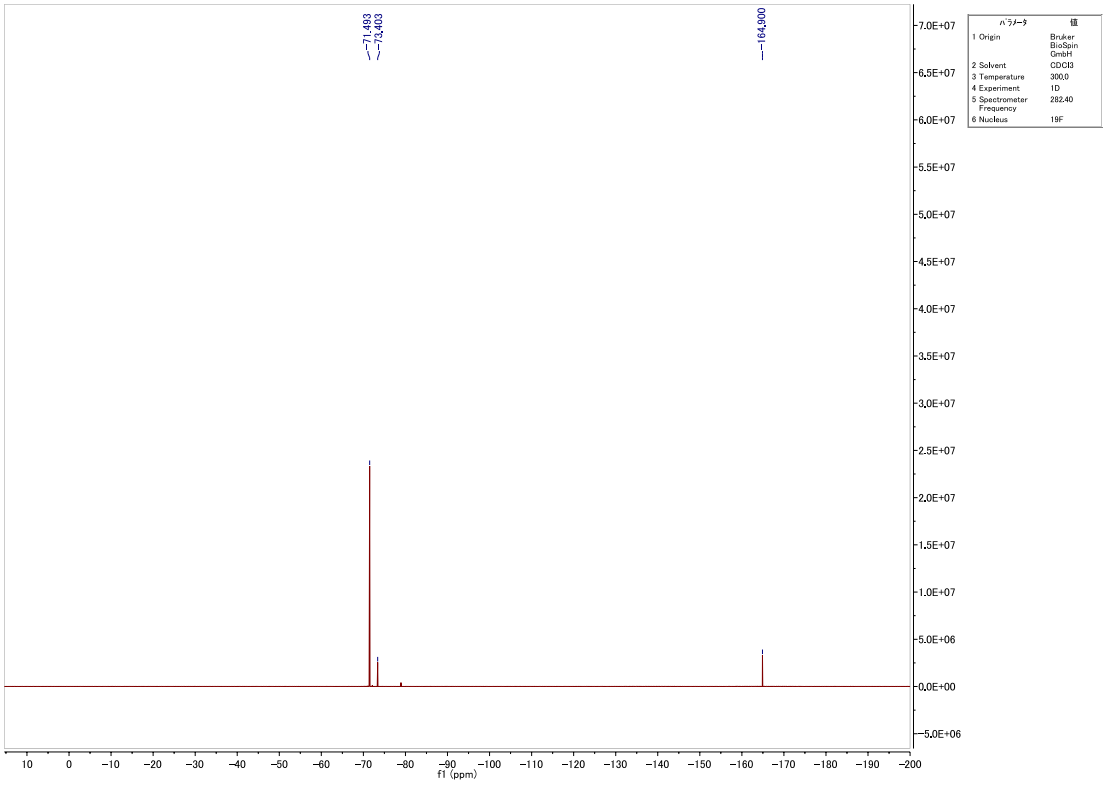
^{19}F NMR (283 MHz, $CDCl_3$) of **S2**



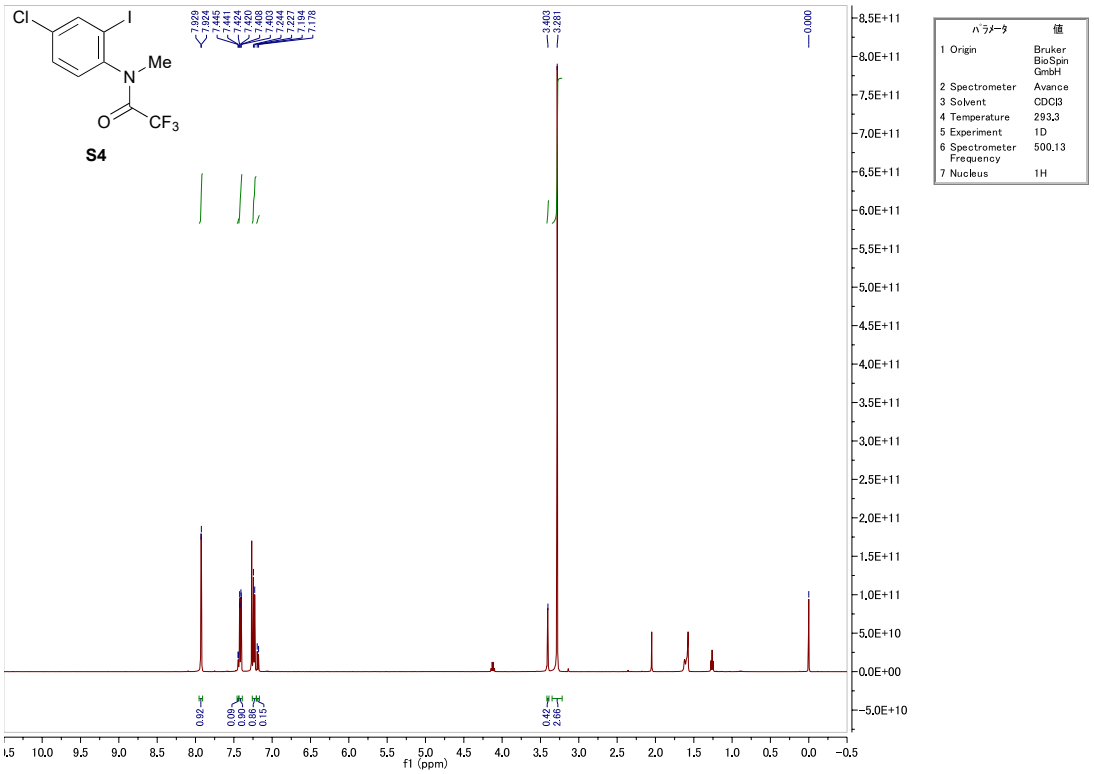
^{1}H NMR (500 MHz, $CDCl_3$) of **S3**



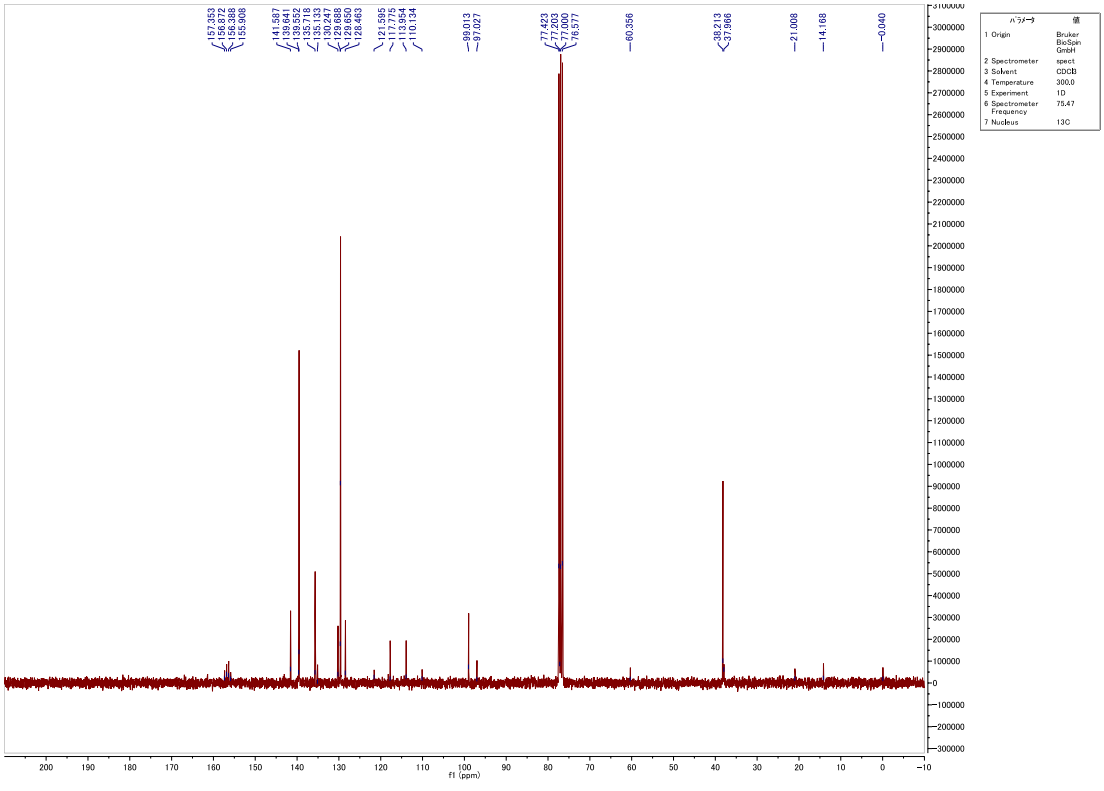
^{13}C NMR (75 MHz, $CDCl_3$) of **S3**



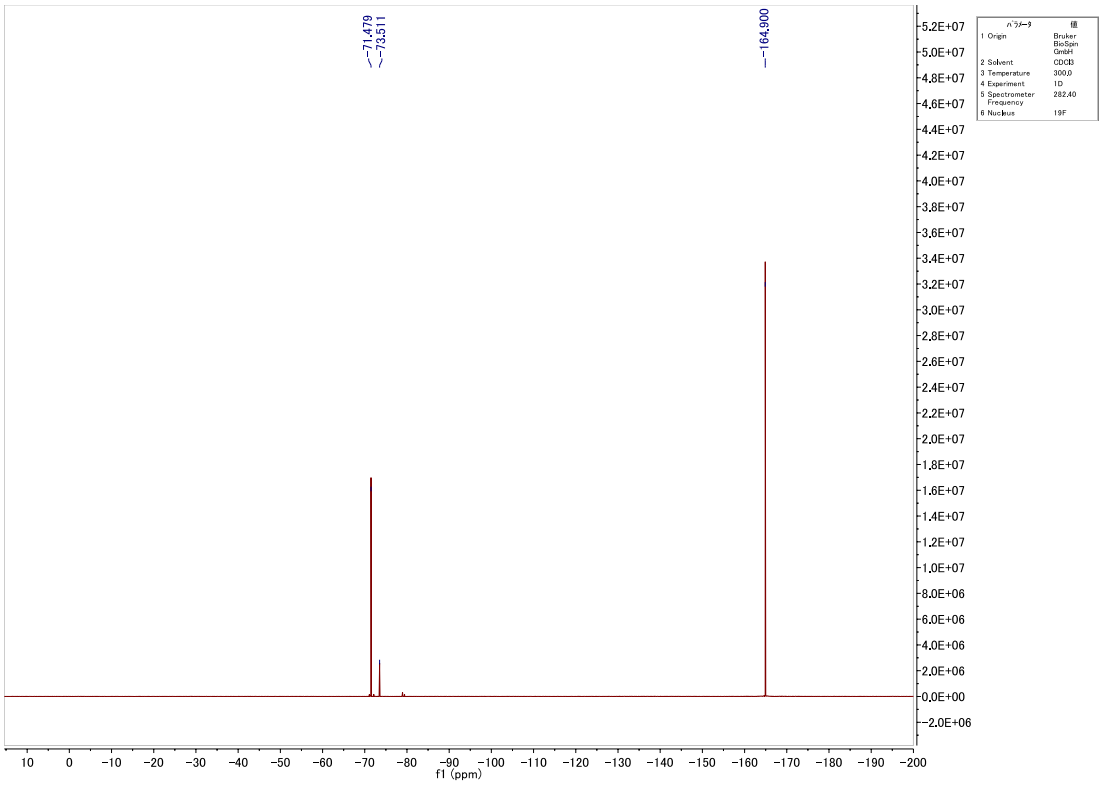
^{19}F NMR (283 MHz, $CDCl_3$) of **S3**



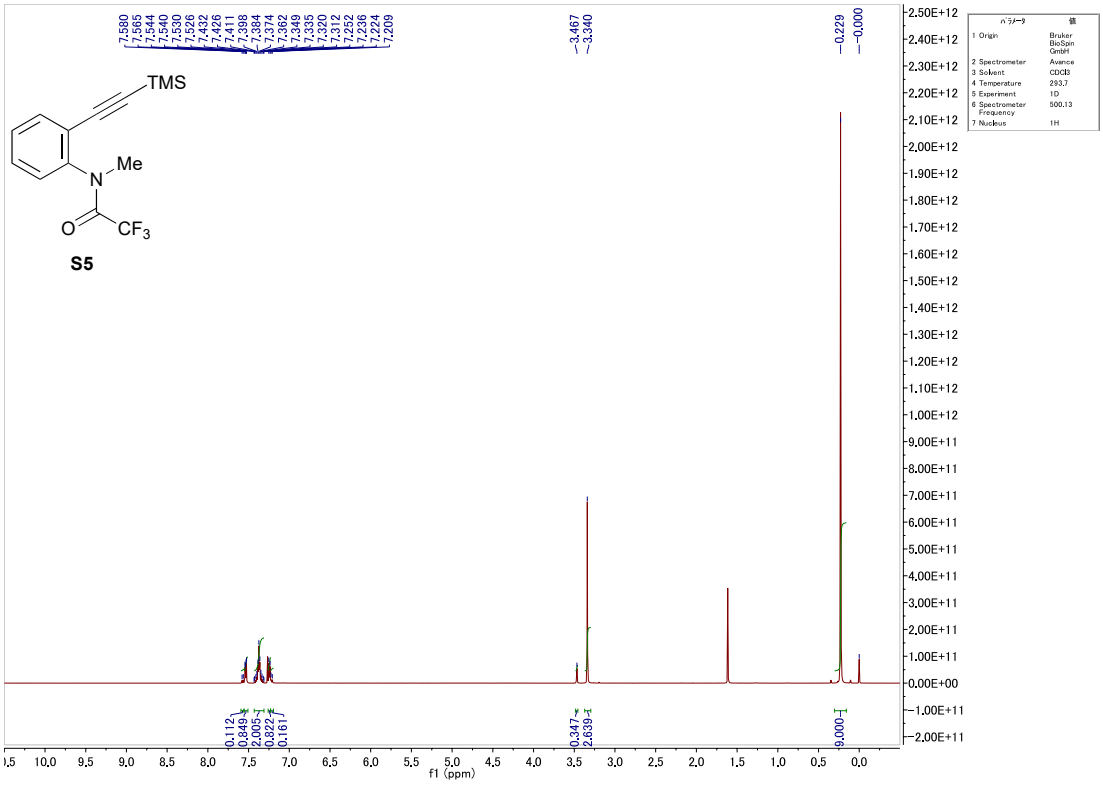
^{1}H NMR (500 MHz, $CDCl_3$) of **S4**



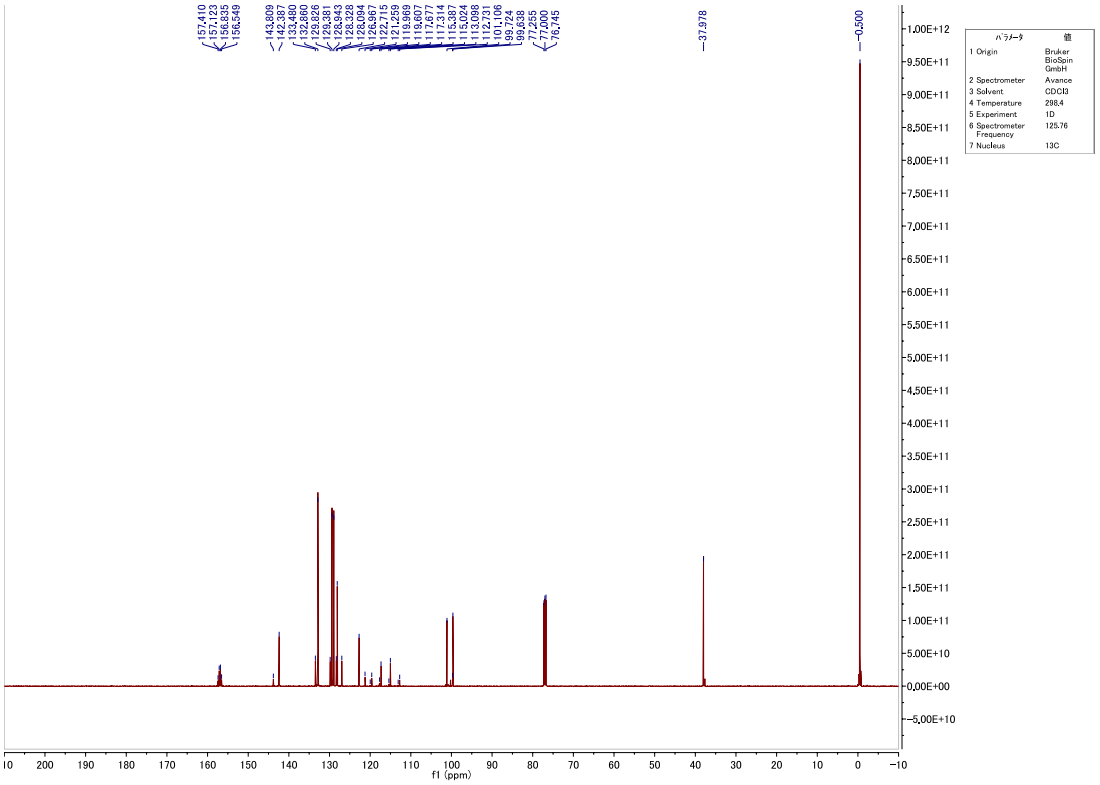
^{13}C NMR (75 MHz, $CDCl_3$) of **S4**



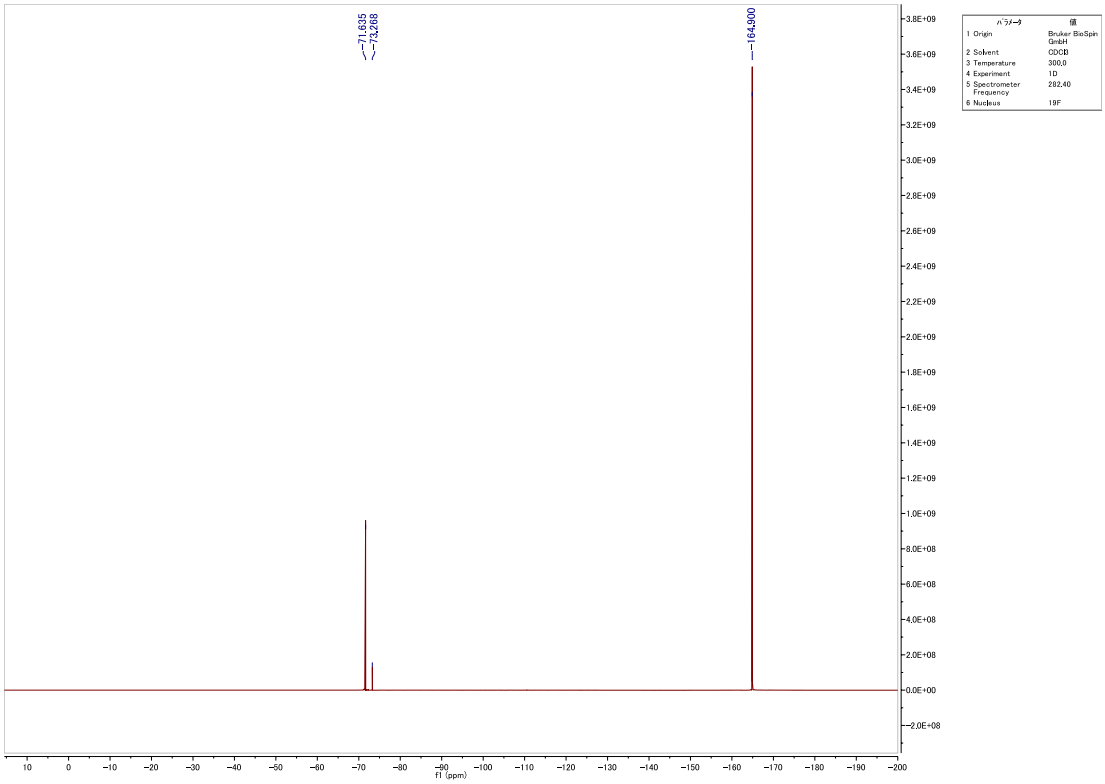
^{19}F NMR (283 MHz, $CDCl_3$) of **S4**



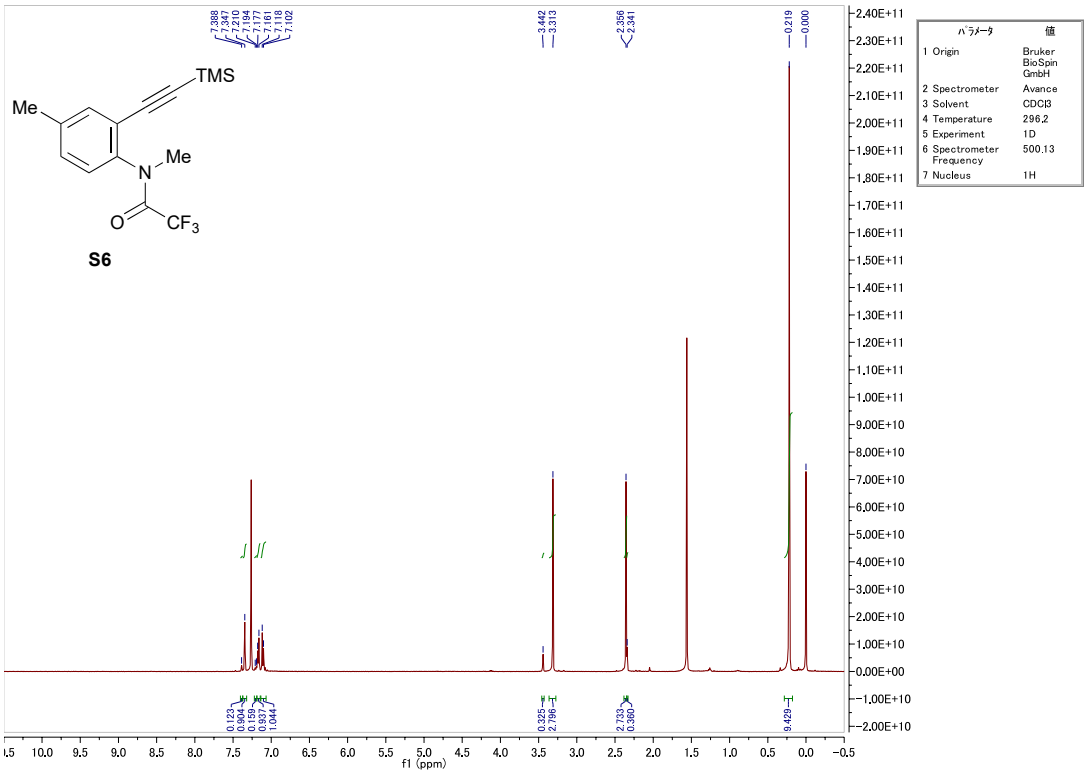
^{1}H NMR (500 MHz, $CDCl_3$) of **S5**



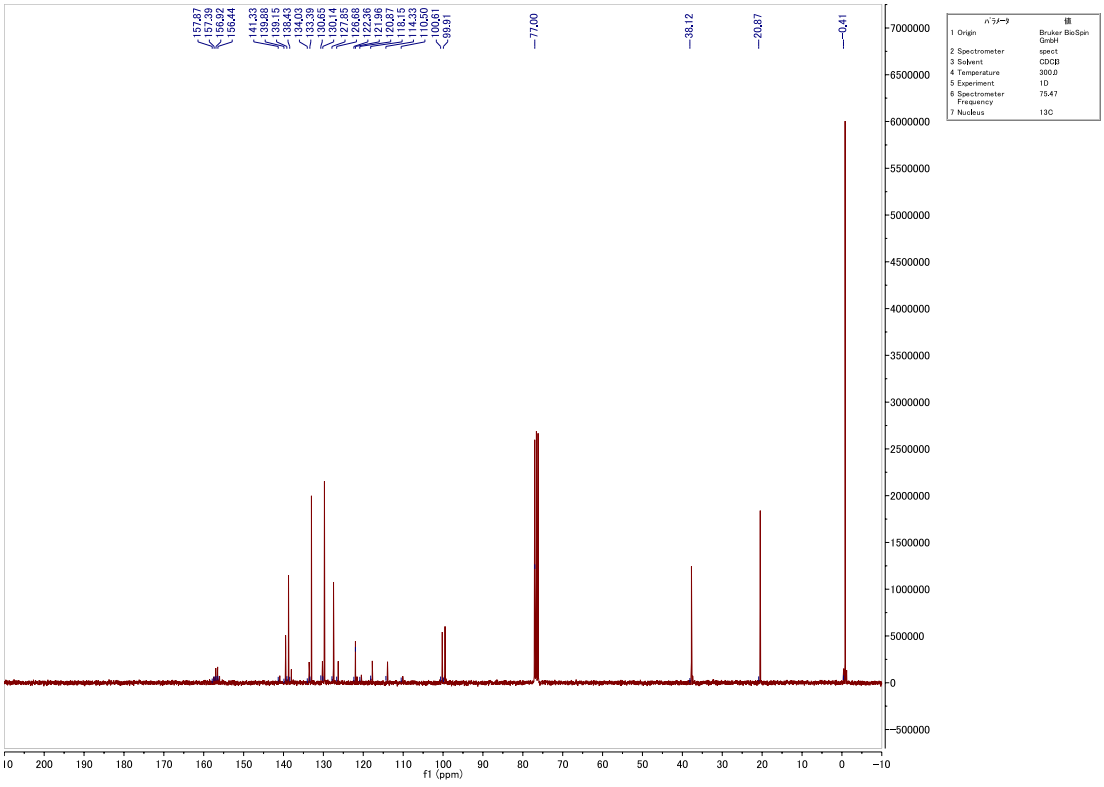
^{13}C NMR (125 MHz, $CDCl_3$) of **S5**



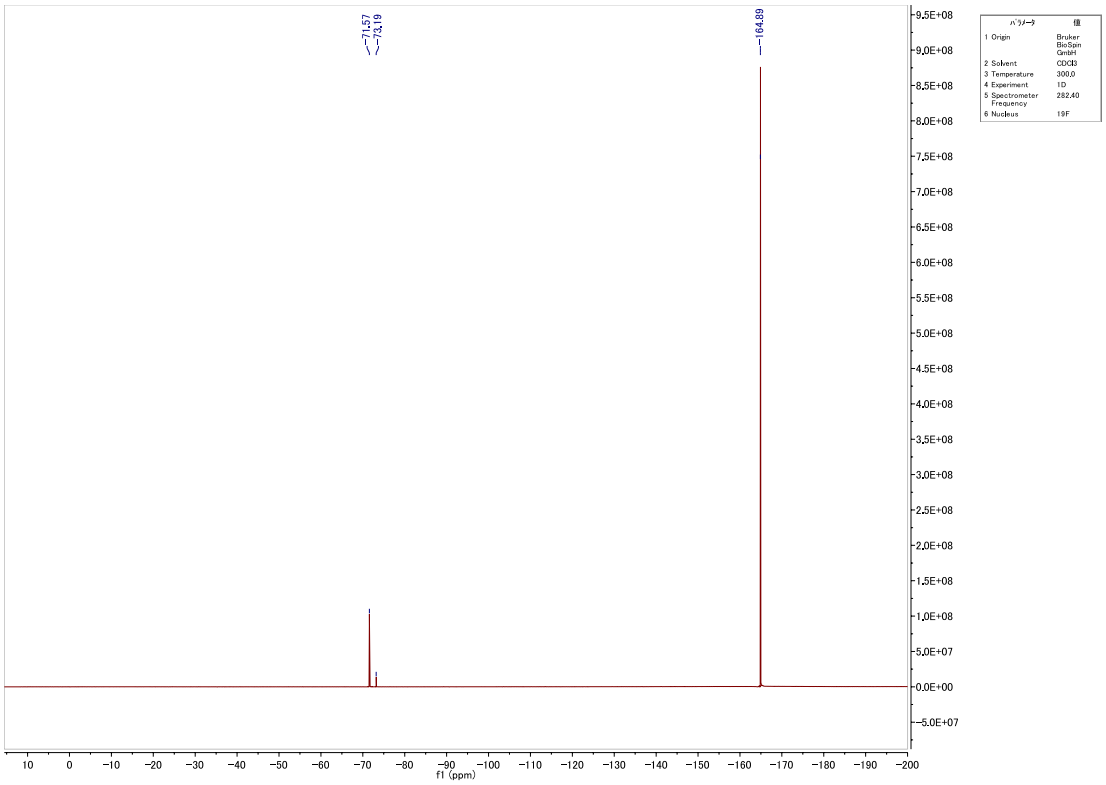
^{19}F NMR (283 MHz, $CDCl_3$) of **S5**



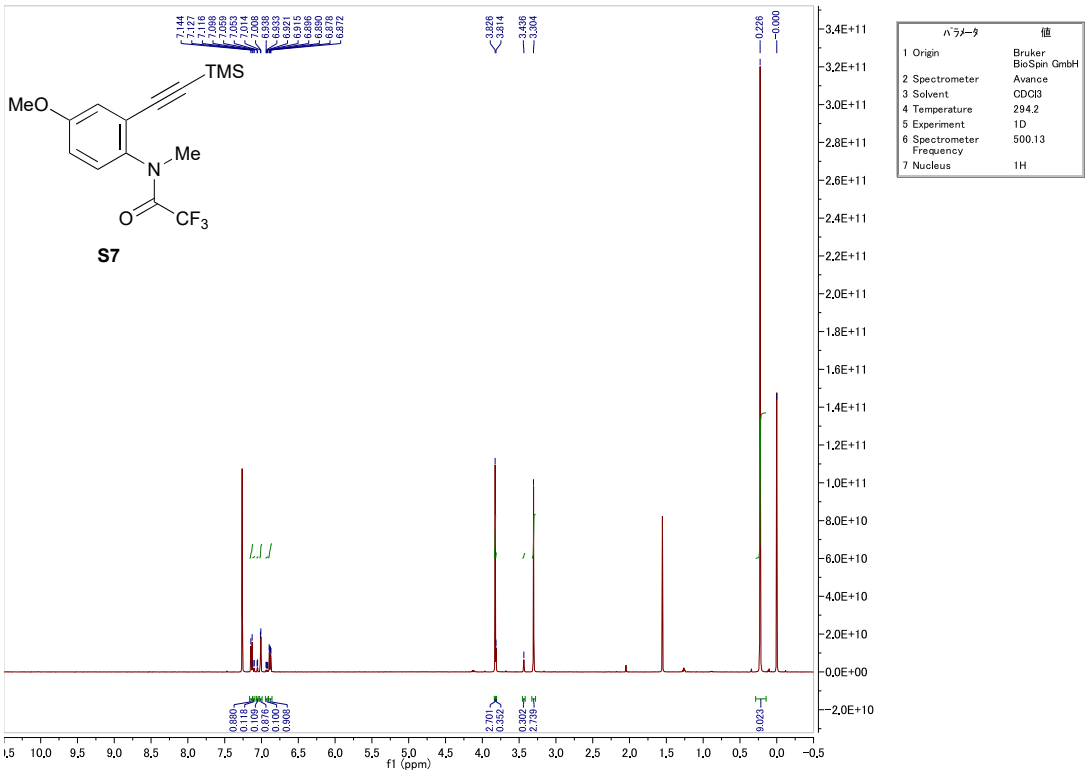
^{1}H NMR (500 MHz, $CDCl_3$) of **S6**



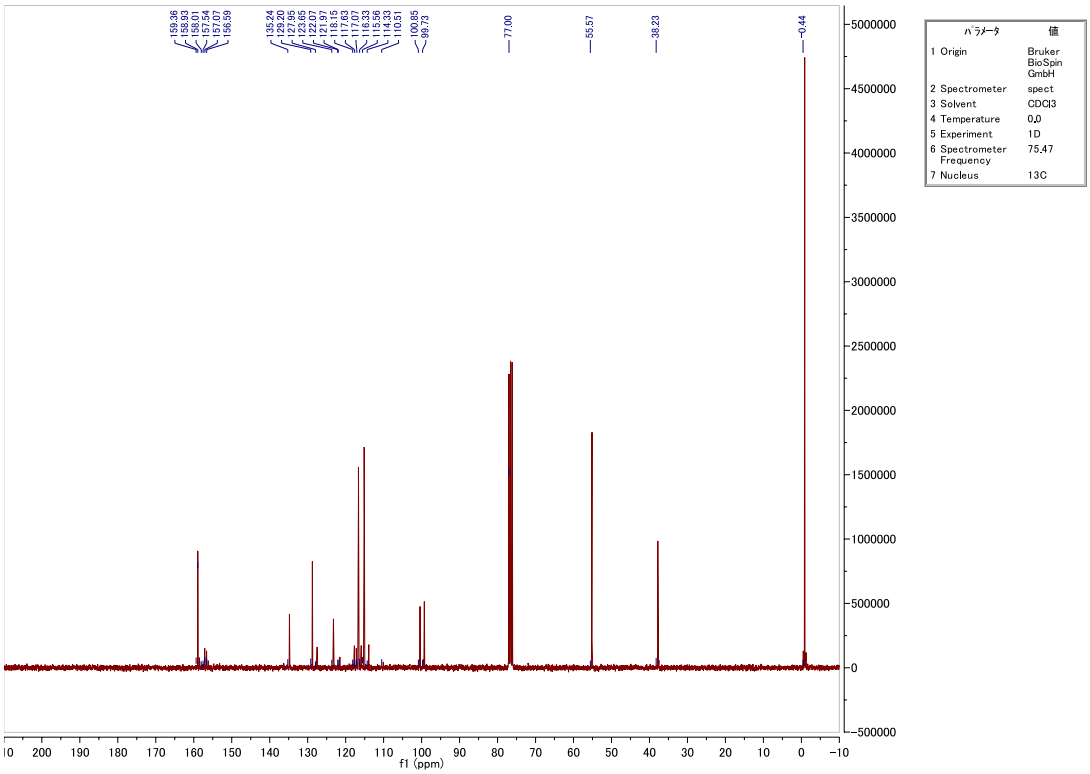
^{13}C NMR (75 MHz, $CDCl_3$) of **S6**



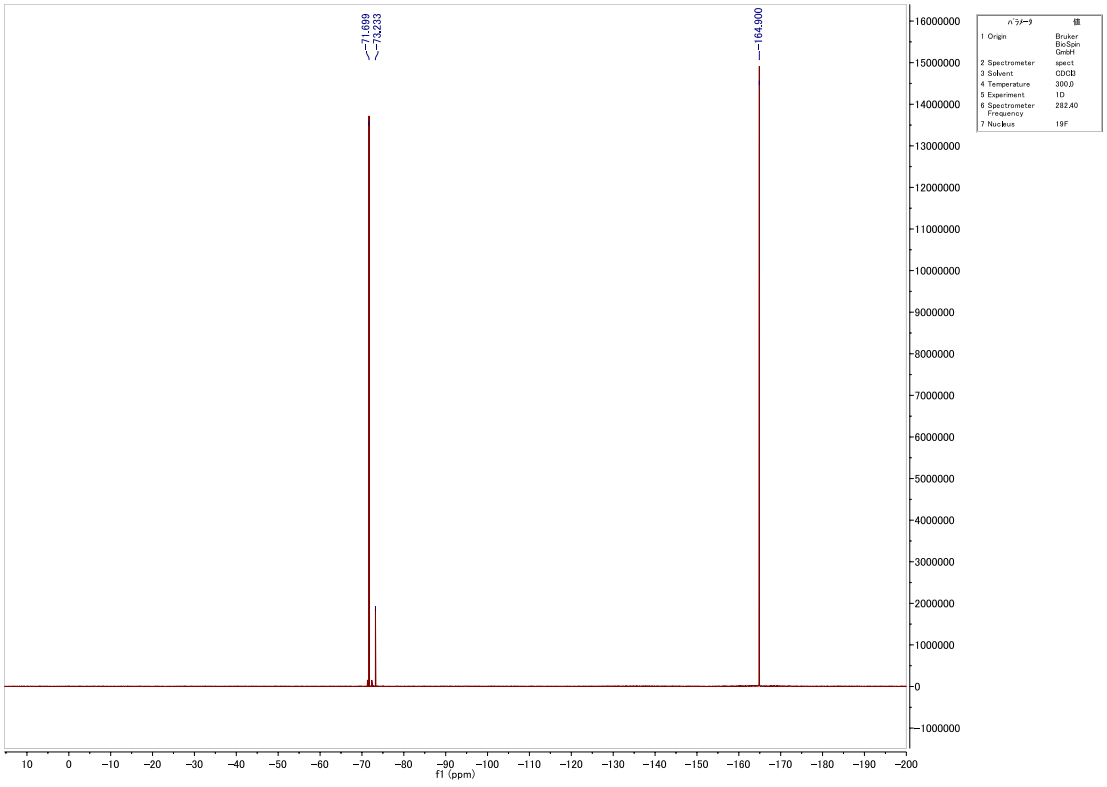
^{19}F NMR (283 MHz, $CDCl_3$) of **S6**



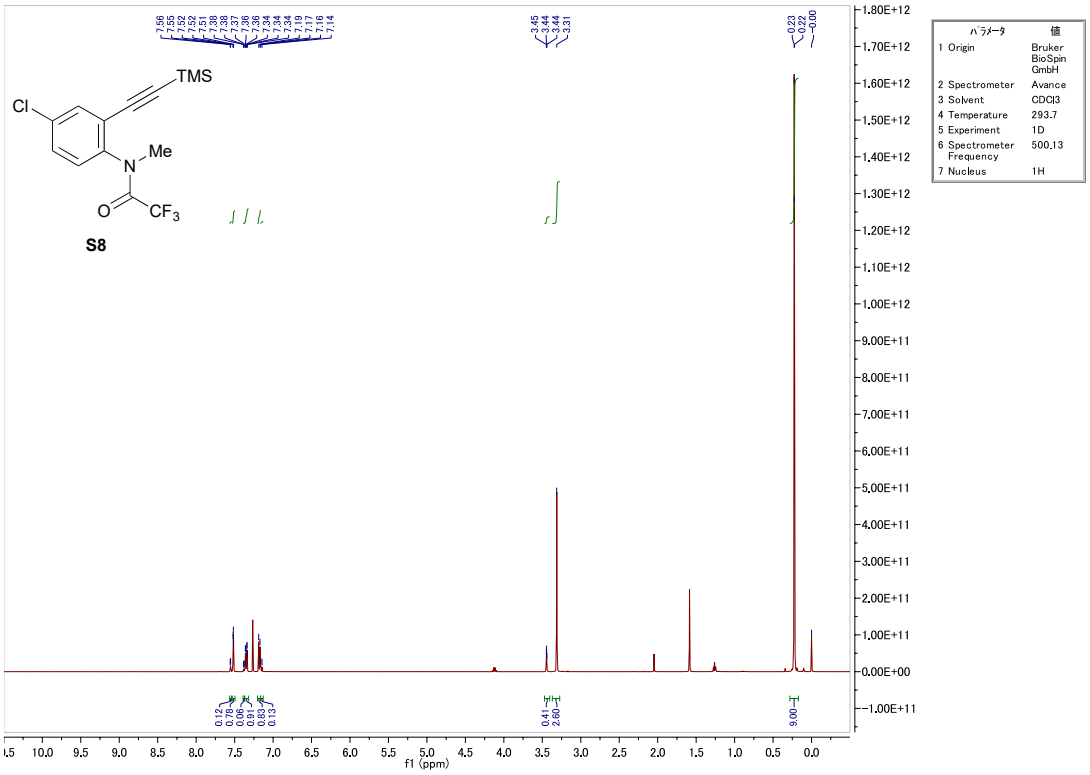
^{1}H NMR (500 MHz, $CDCl_3$) of **S7**



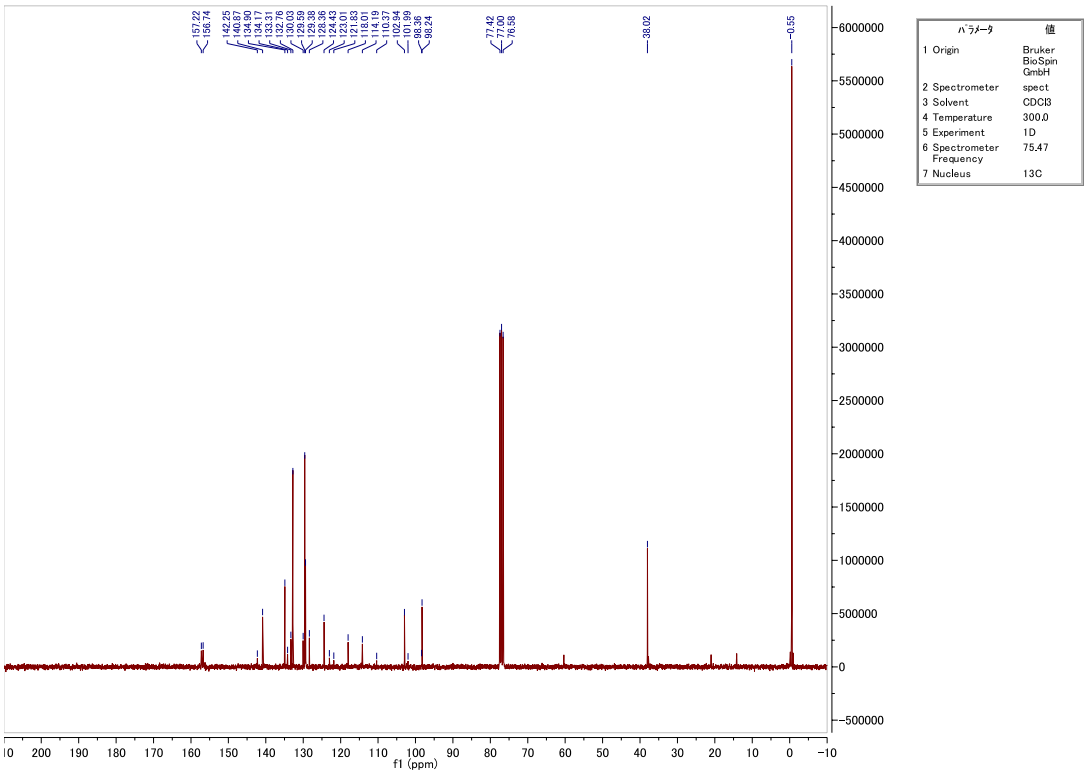
^{13}C NMR (75 MHz, $CDCl_3$) of **S7**



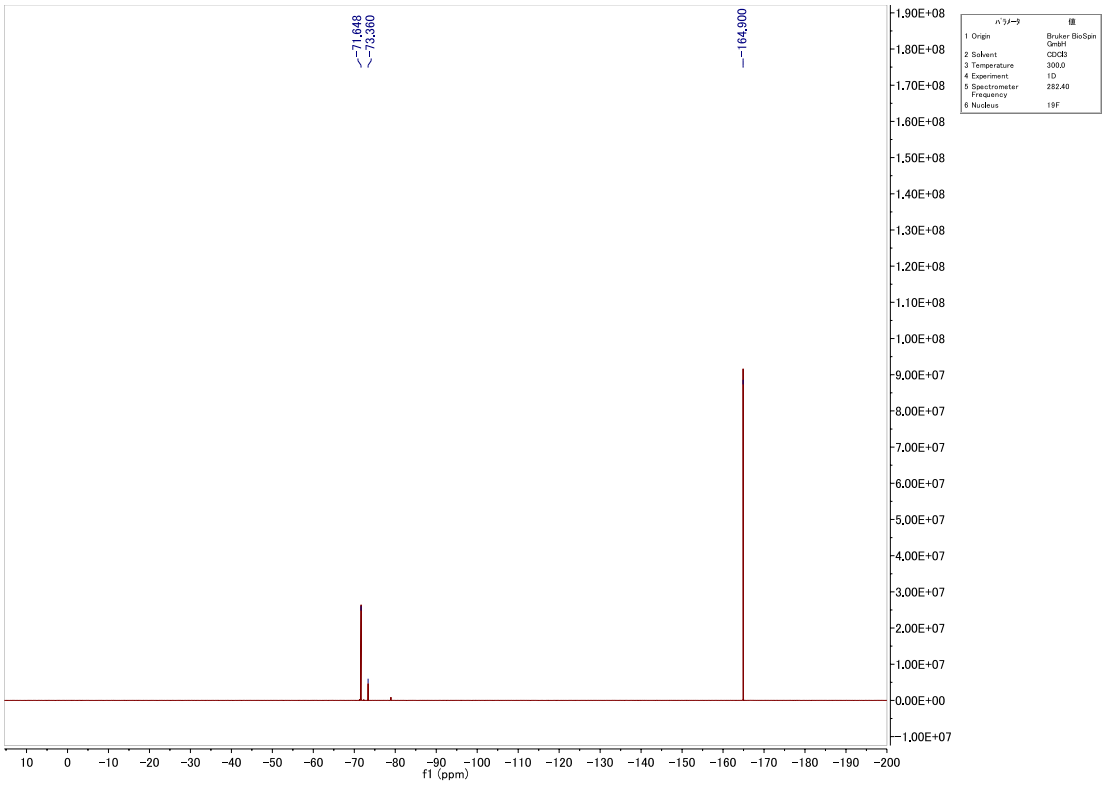
^{19}F NMR (283 MHz, $CDCl_3$) of **S7**



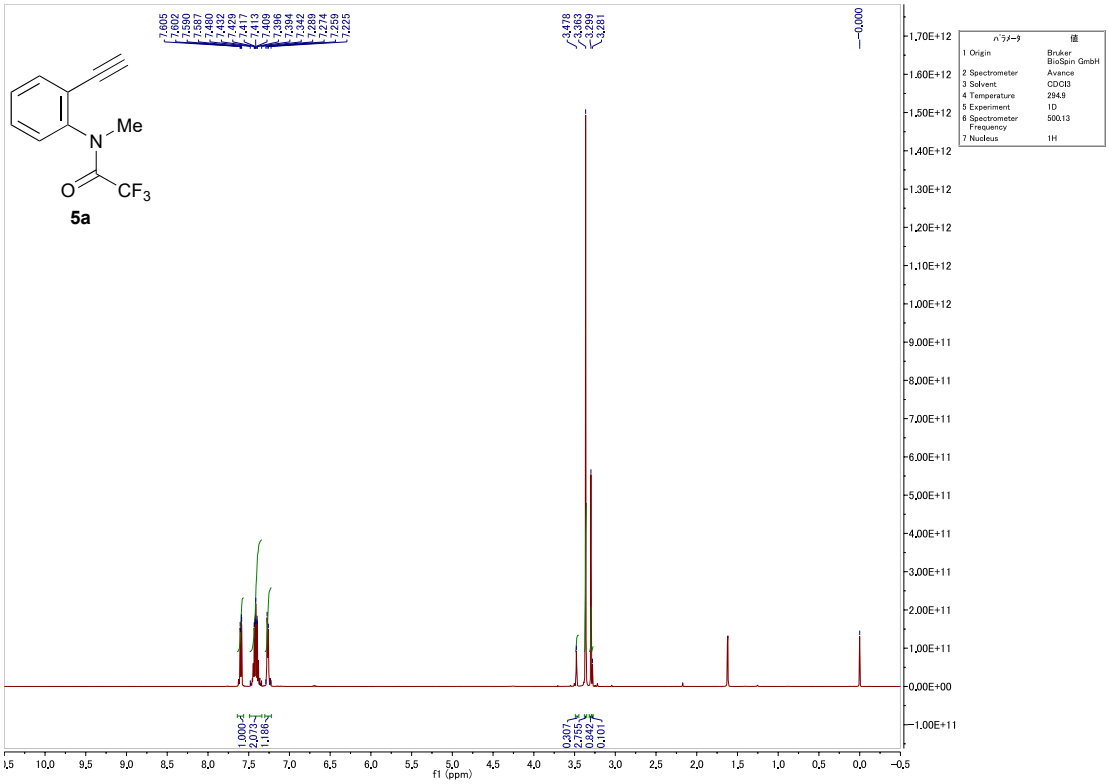
^{1}H NMR (500 MHz, $CDCl_3$) of **S8**



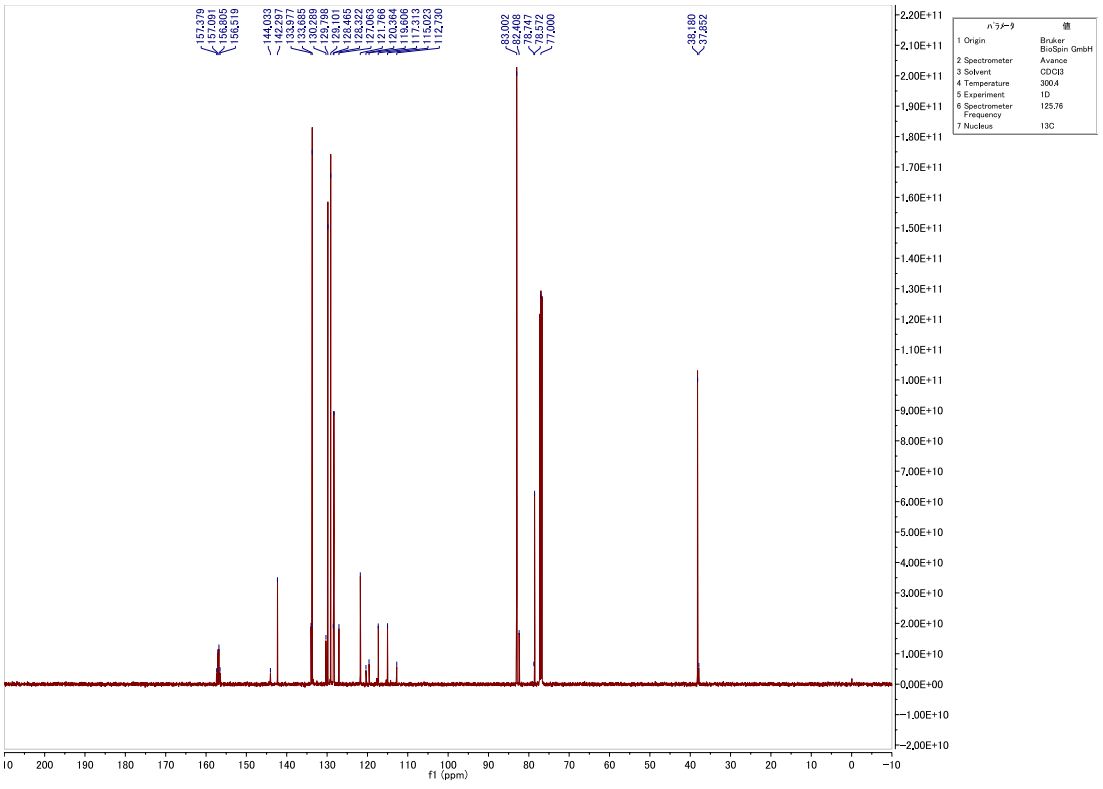
^{13}C NMR (75 MHz, $CDCl_3$) of **S8**



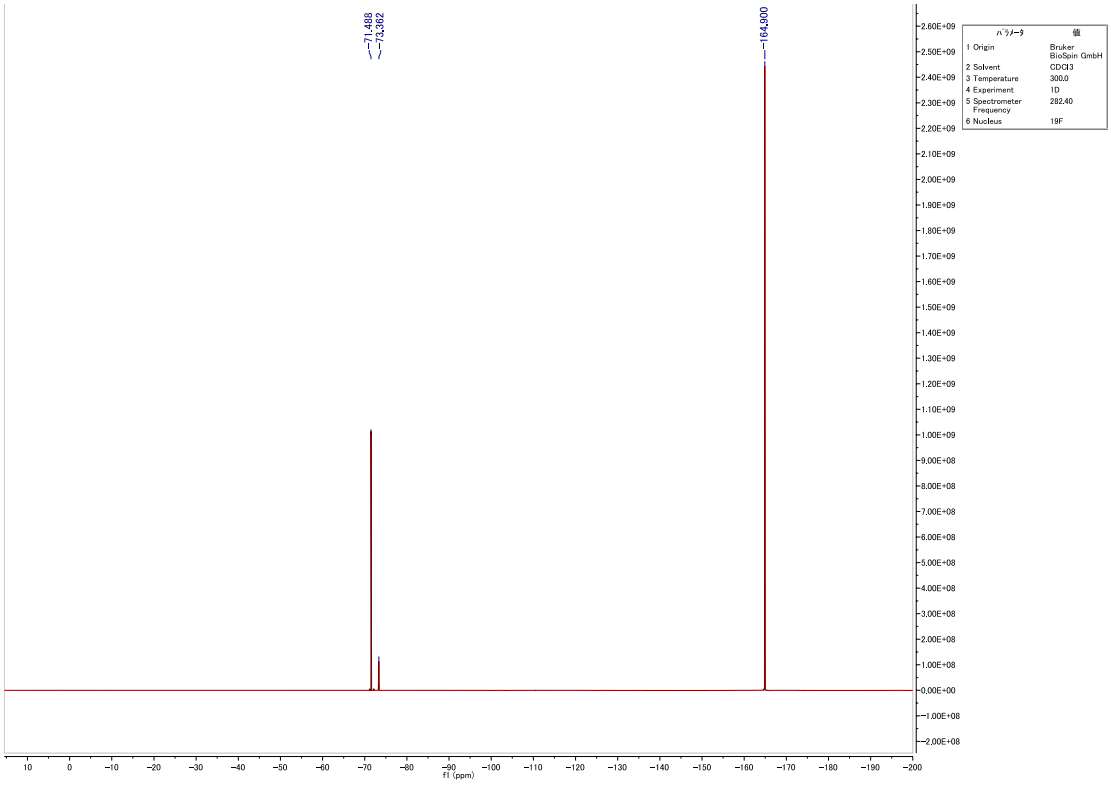
^{19}F NMR (283 MHz, $CDCl_3$) of **S8**



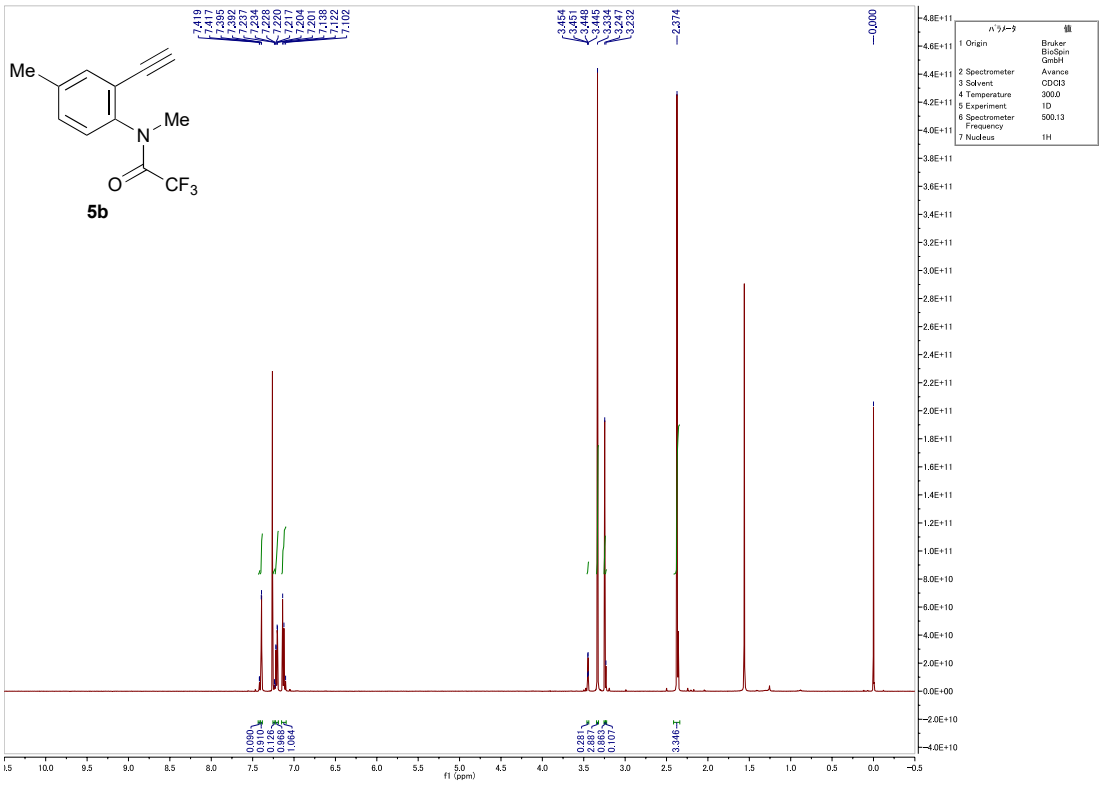
^{1}H NMR (500 MHz, $CDCl_3$) of **5a**



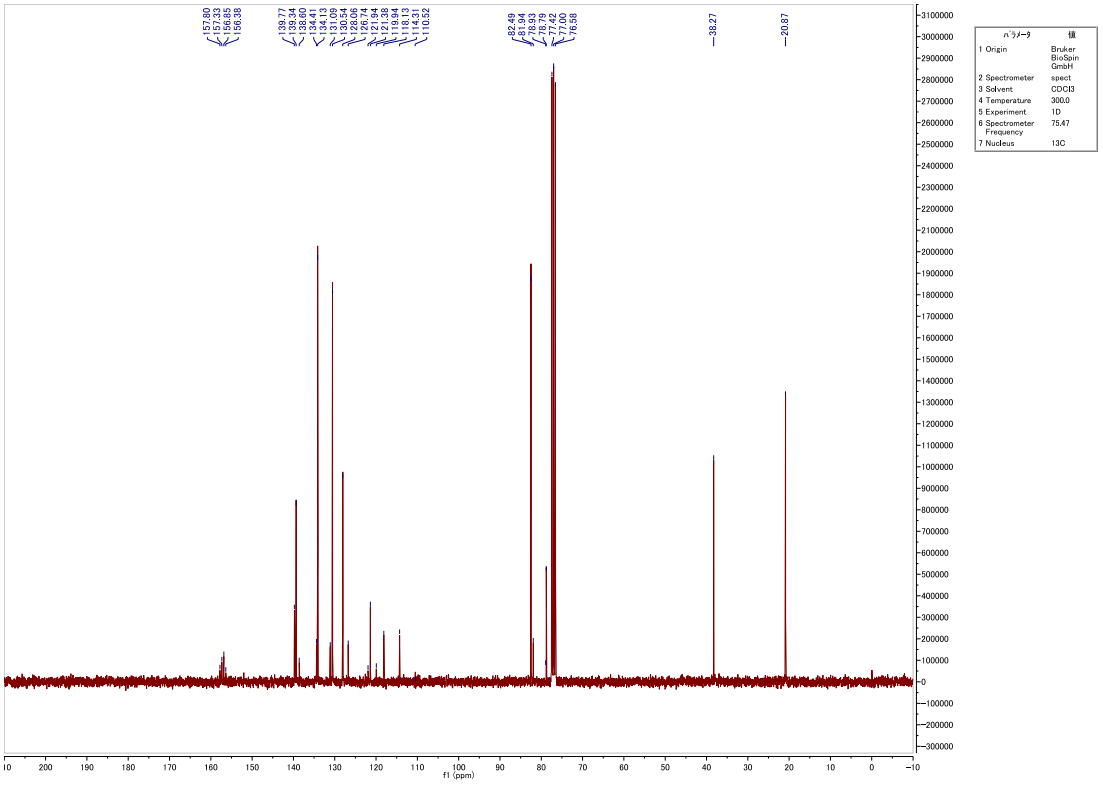
^{13}C NMR (125 MHz, $CDCl_3$) of **5a**



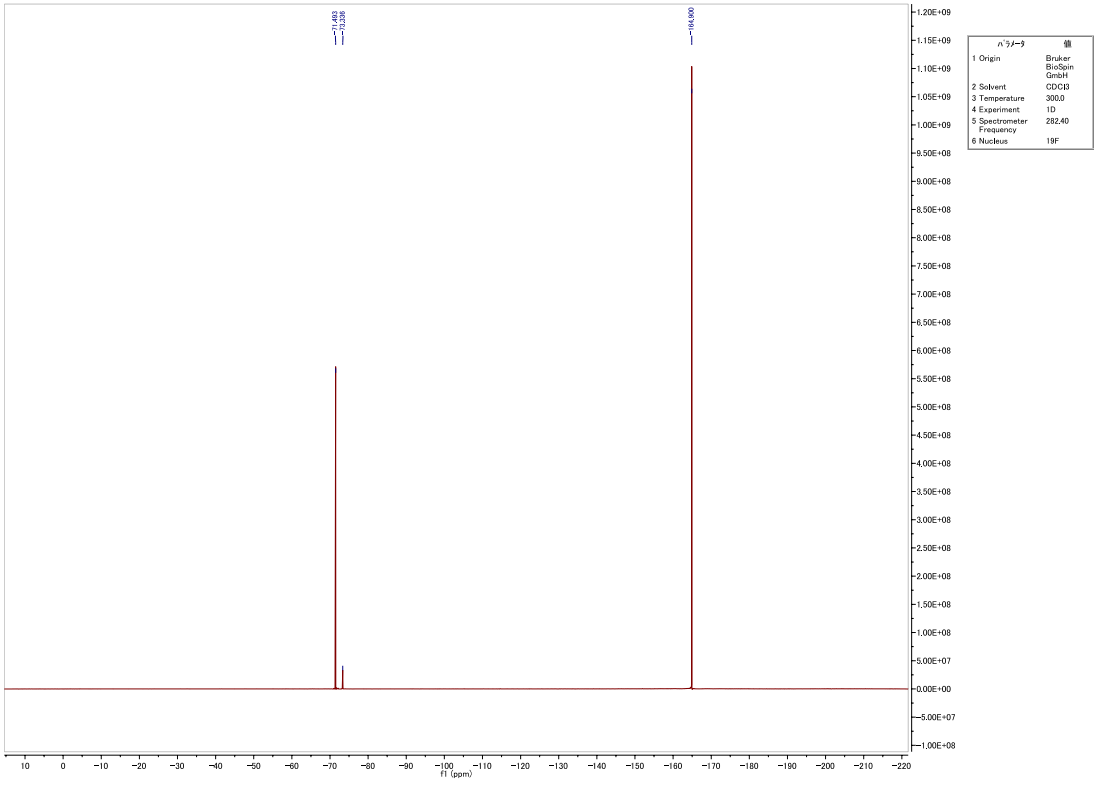
^{19}F NMR (283 MHz, $CDCl_3$) of **5a**



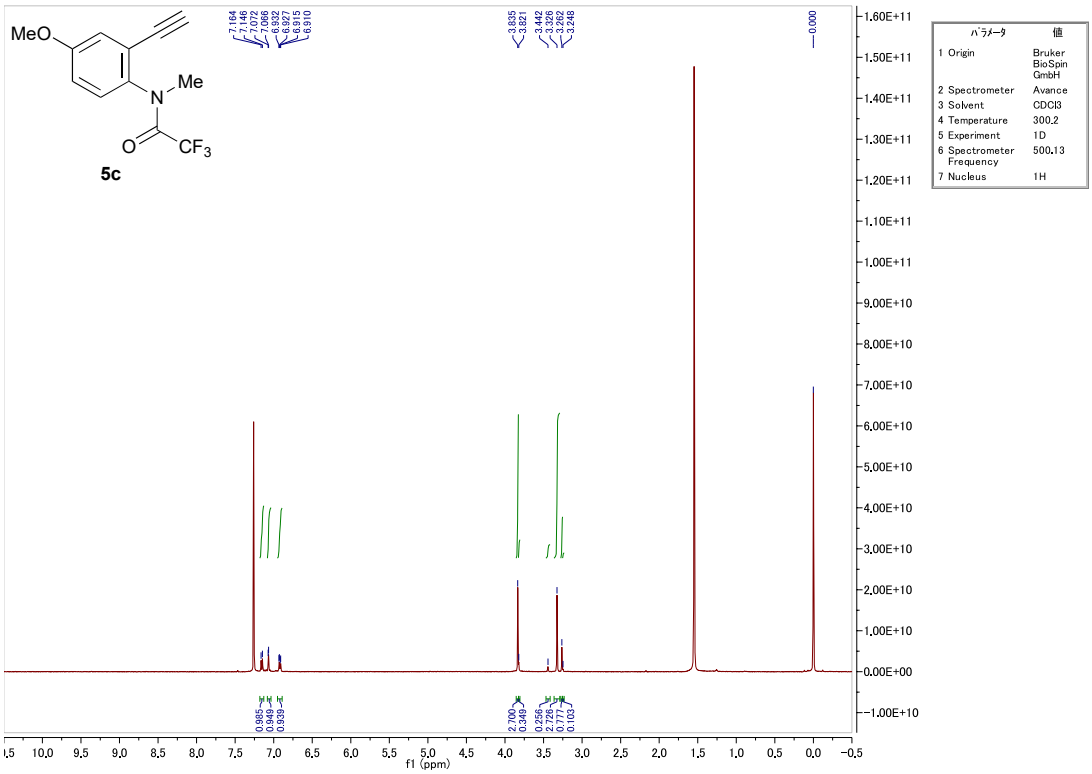
^{1}H NMR (500 MHz, $CDCl_3$) of **5b**



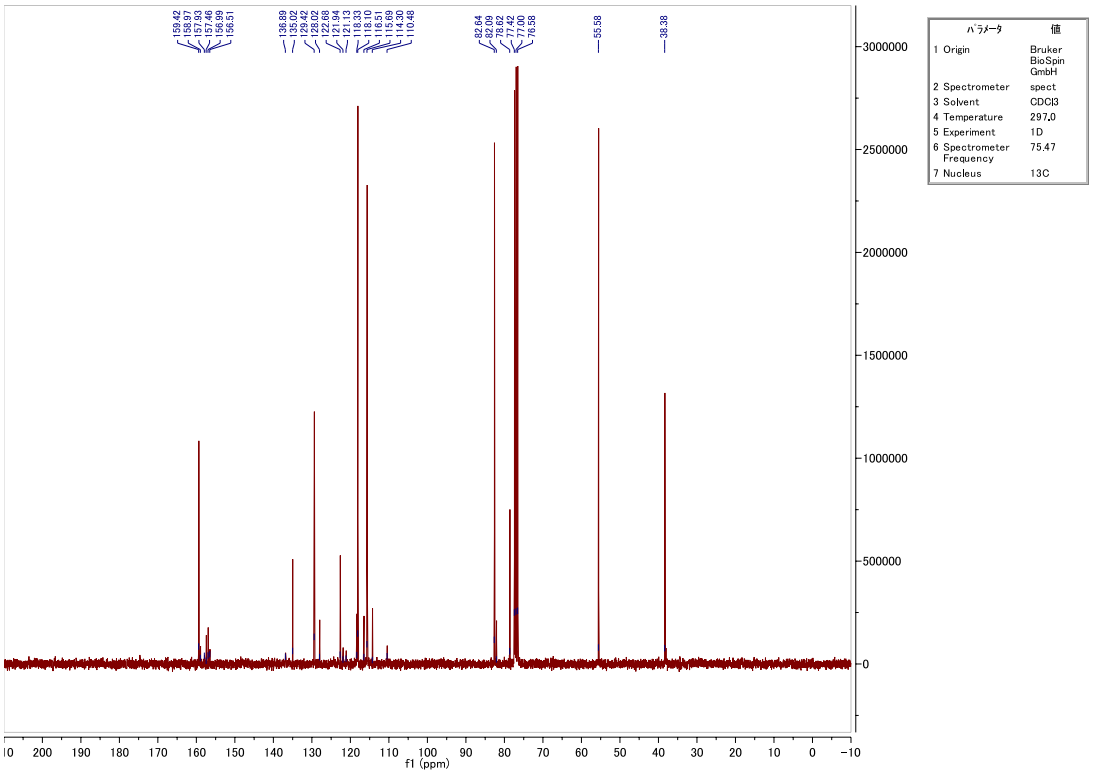
^{13}C NMR (75 MHz, $CDCl_3$) of **5b**



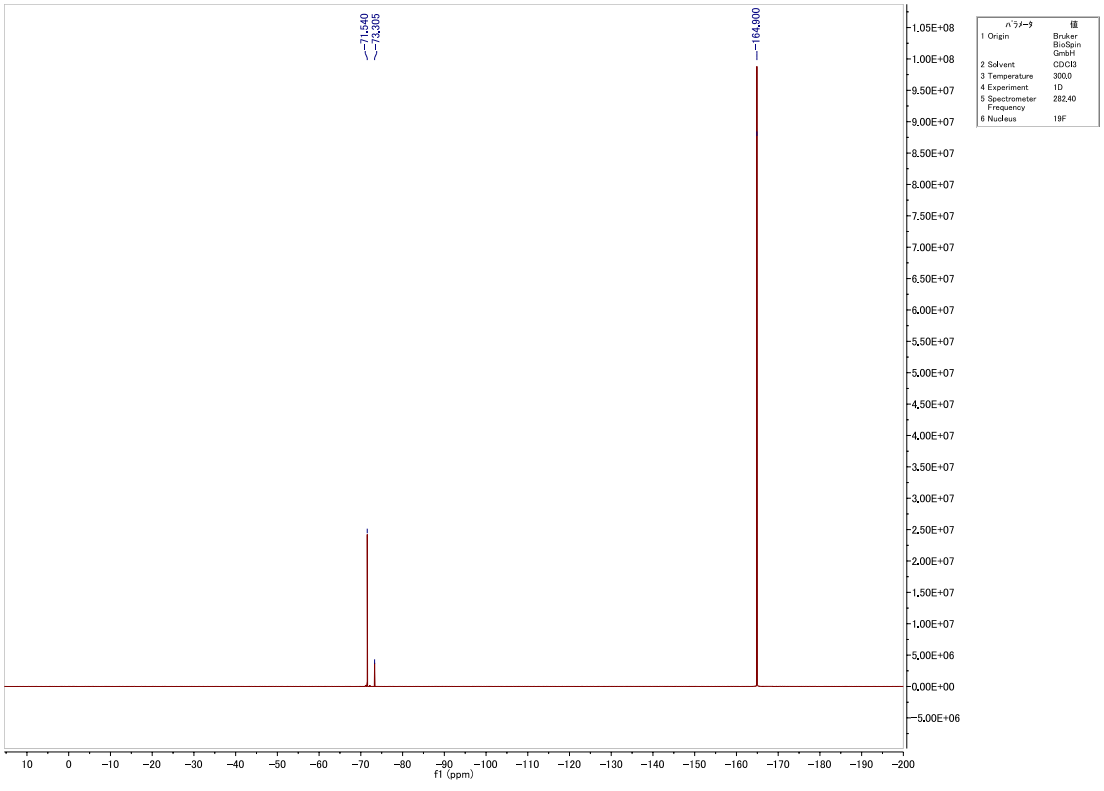
^{19}F NMR (283 MHz, $CDCl_3$) of **5b**



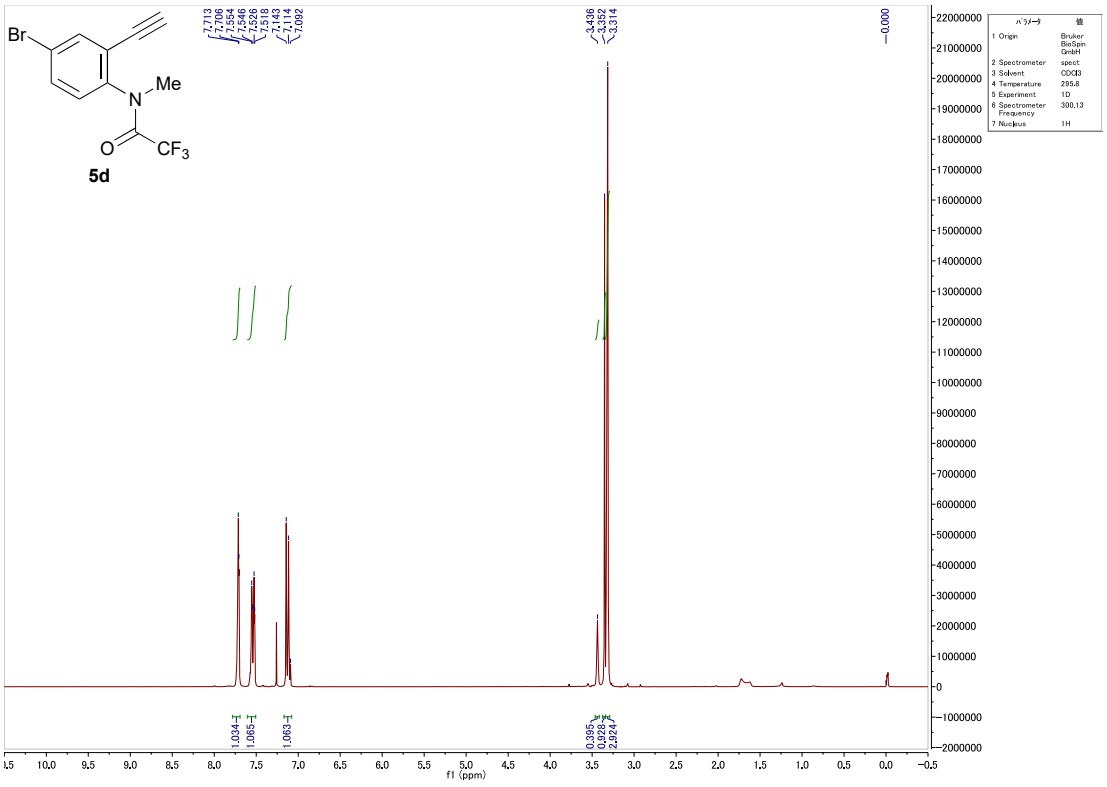
^{1}H NMR (500 MHz, $CDCl_3$) of **5c**



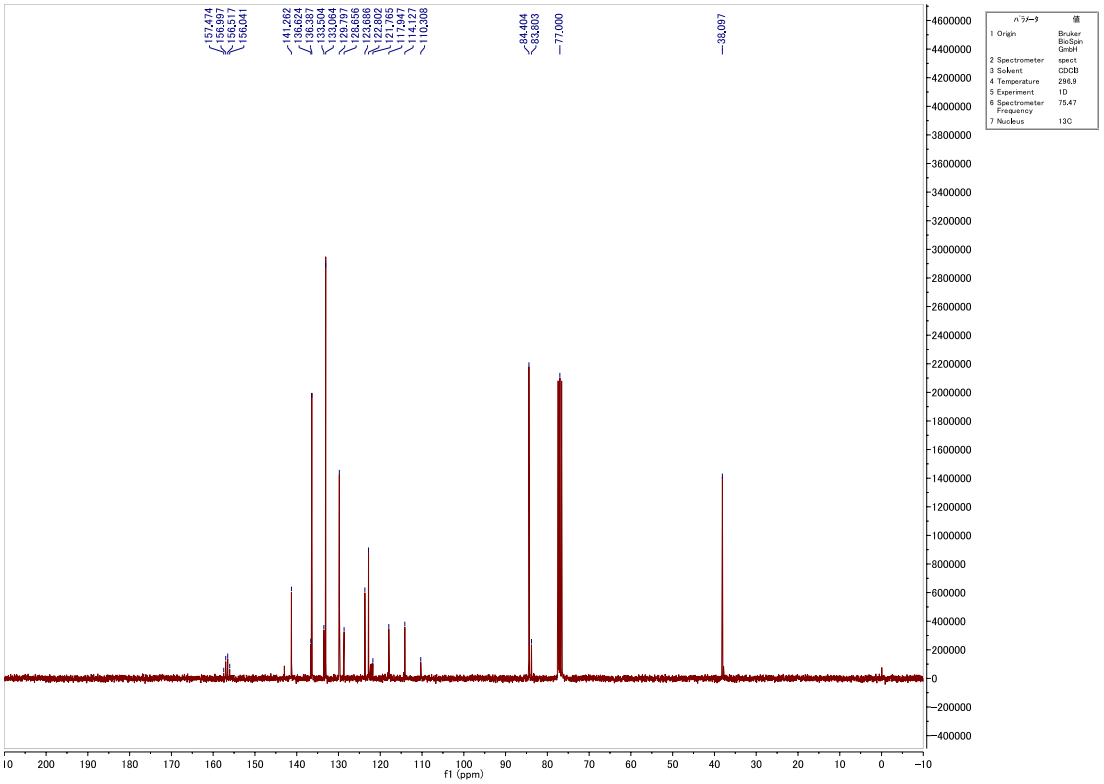
^{13}C NMR (75 MHz, $CDCl_3$) of **5c**



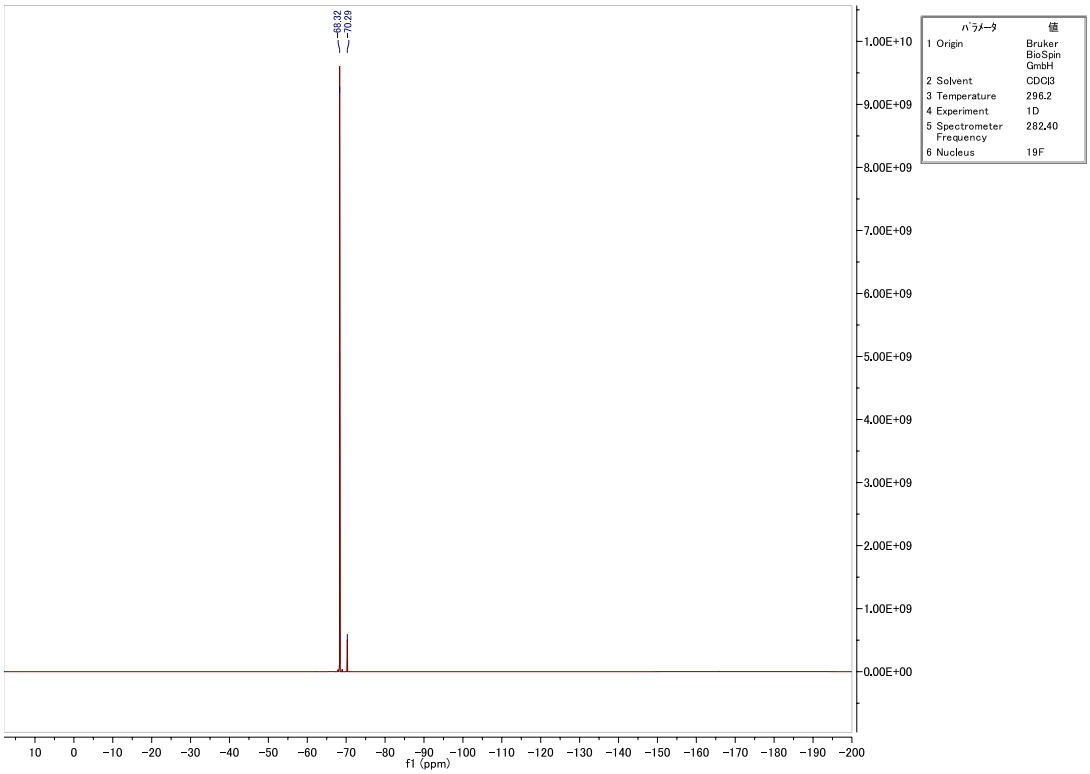
^{19}F NMR (283 MHz, $CDCl_3$) of **5c**



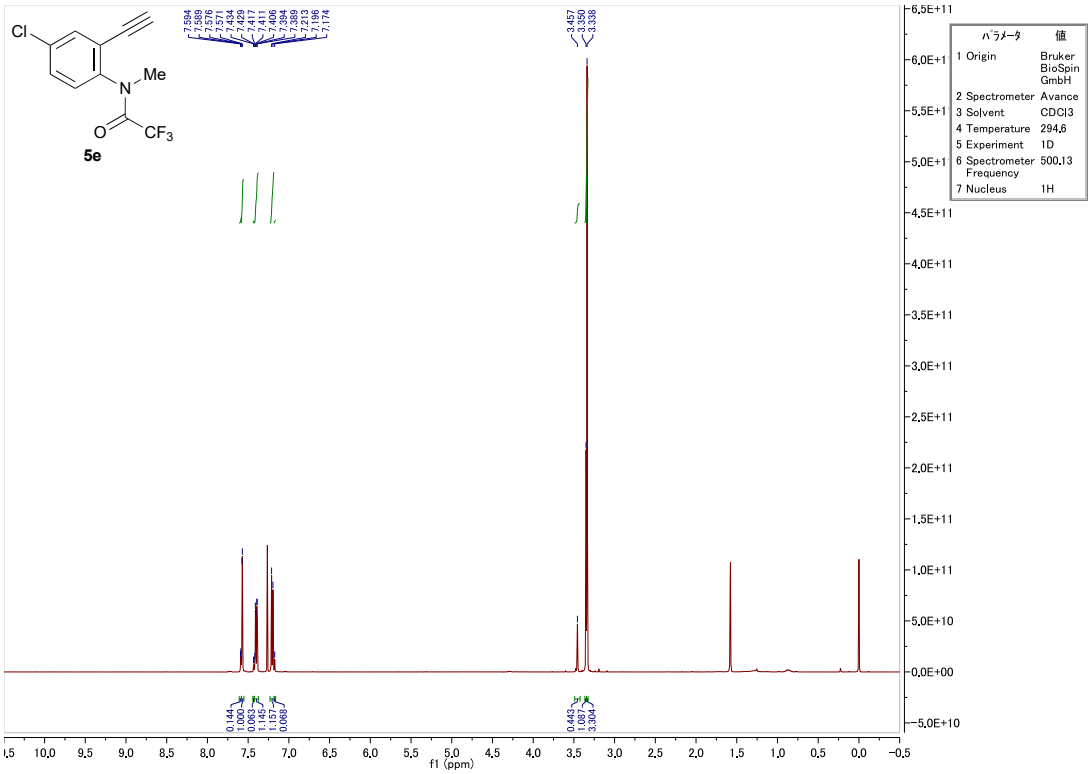
^{1}H NMR (300 MHz, $CDCl_3$) of **5d**



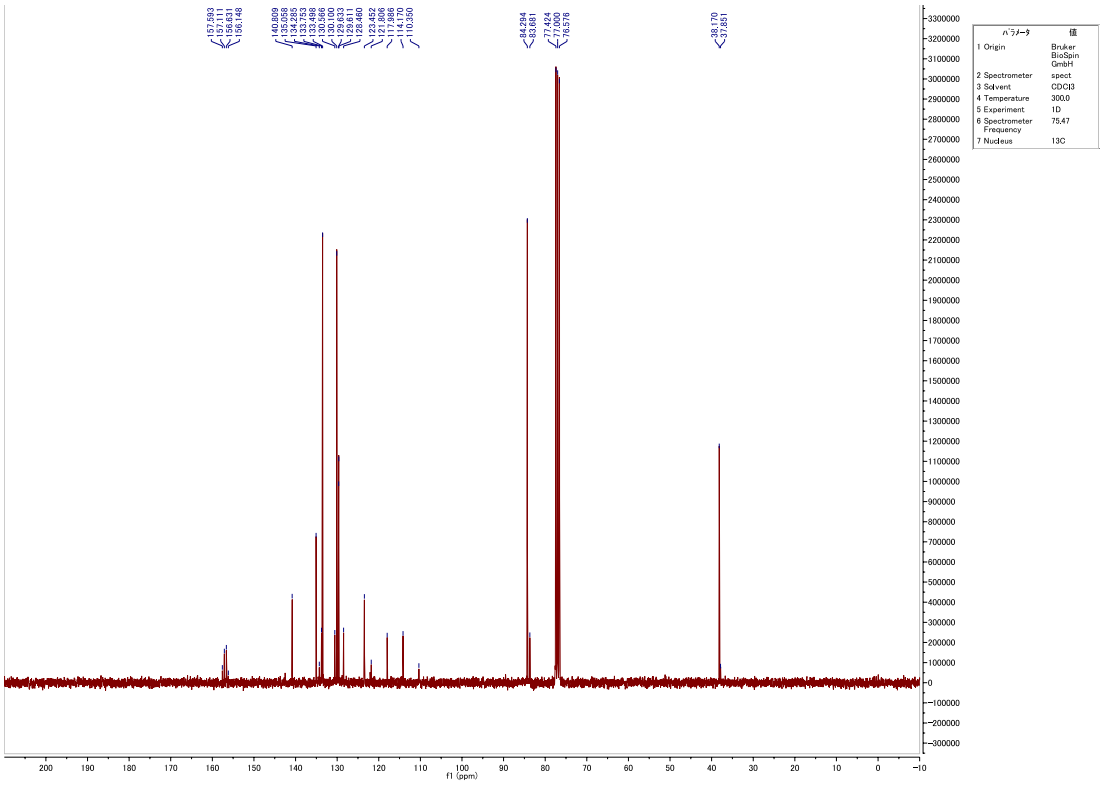
^{13}C NMR (75 MHz, $CDCl_3$) of **5d**



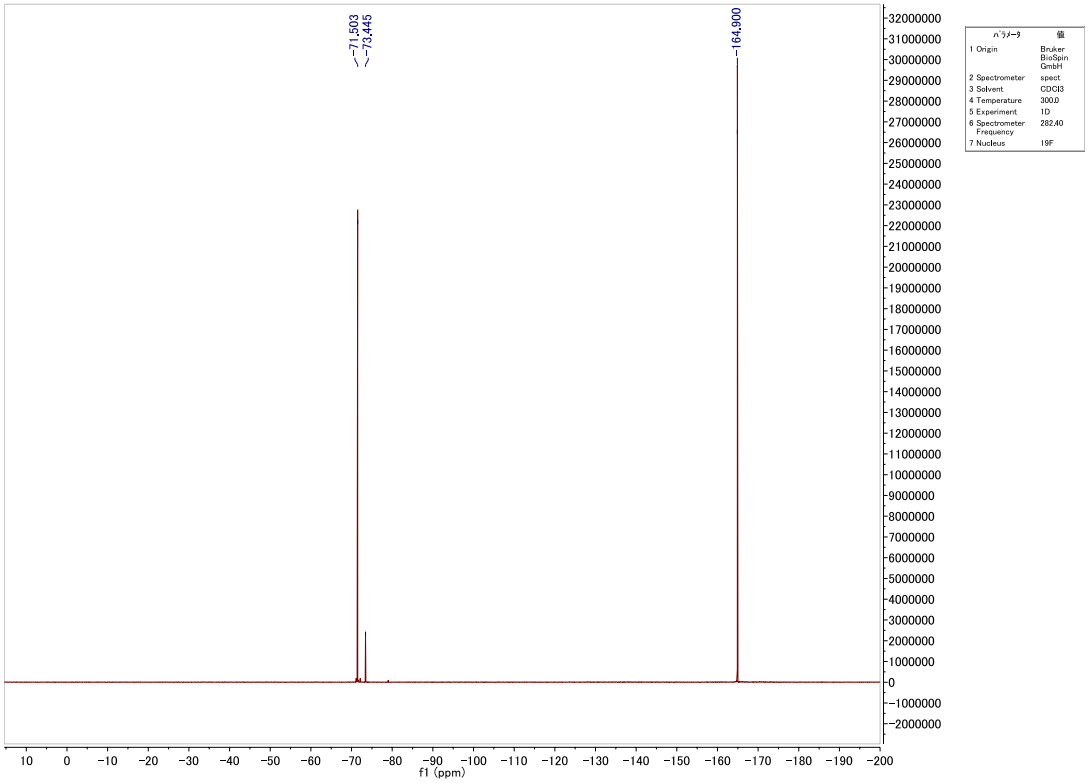
^{19}F NMR (283 MHz, $CDCl_3$) of **5d**



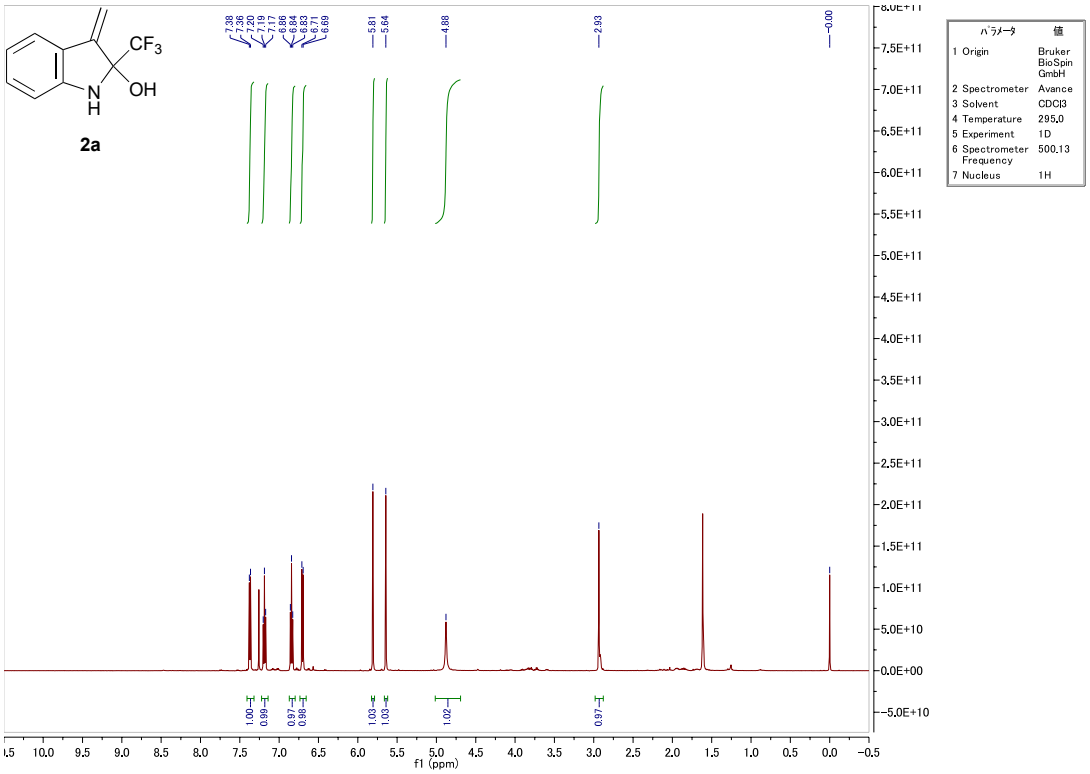
^{1}H NMR (500 MHz, $CDCl_3$) of **5e**



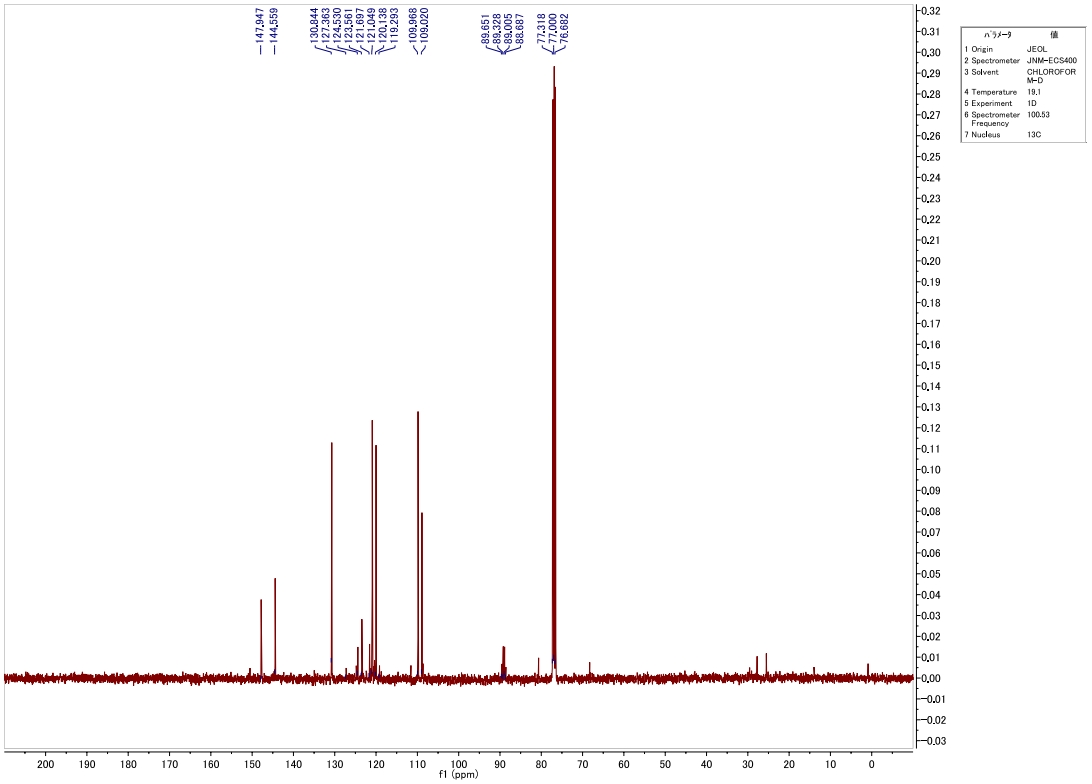
^{13}C NMR (75 MHz, $CDCl_3$) of **5e**



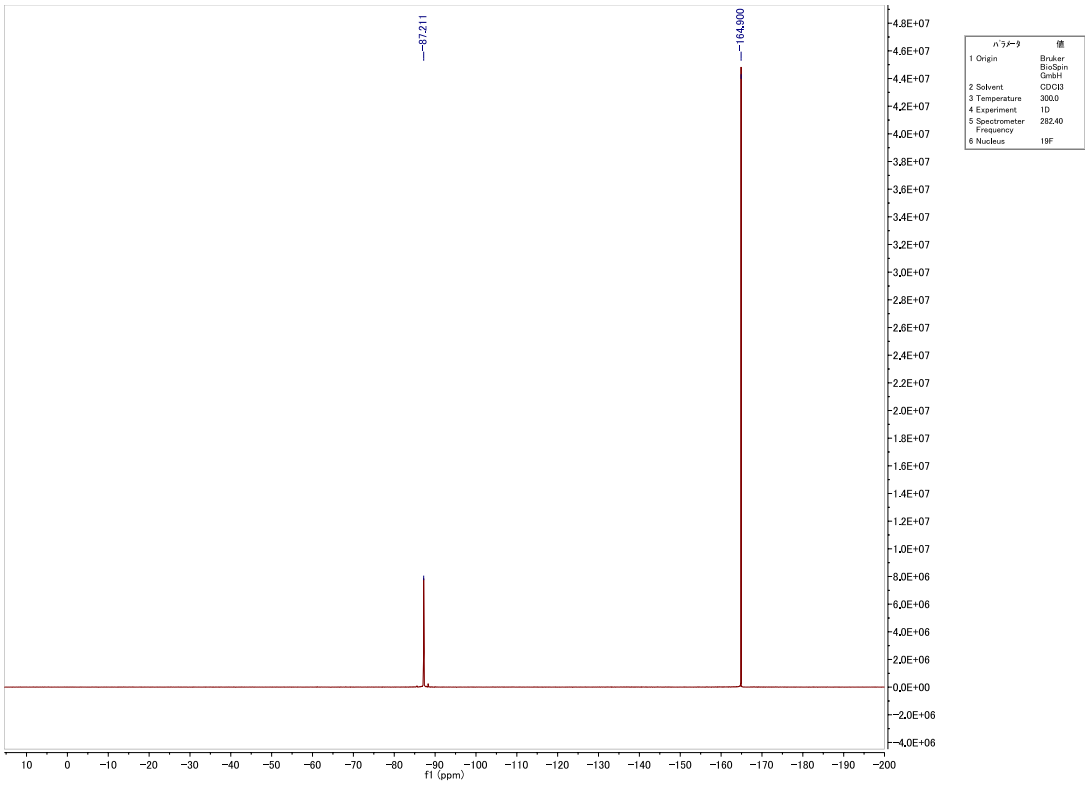
^{19}F NMR (283 MHz, $CDCl_3$) of **5e**



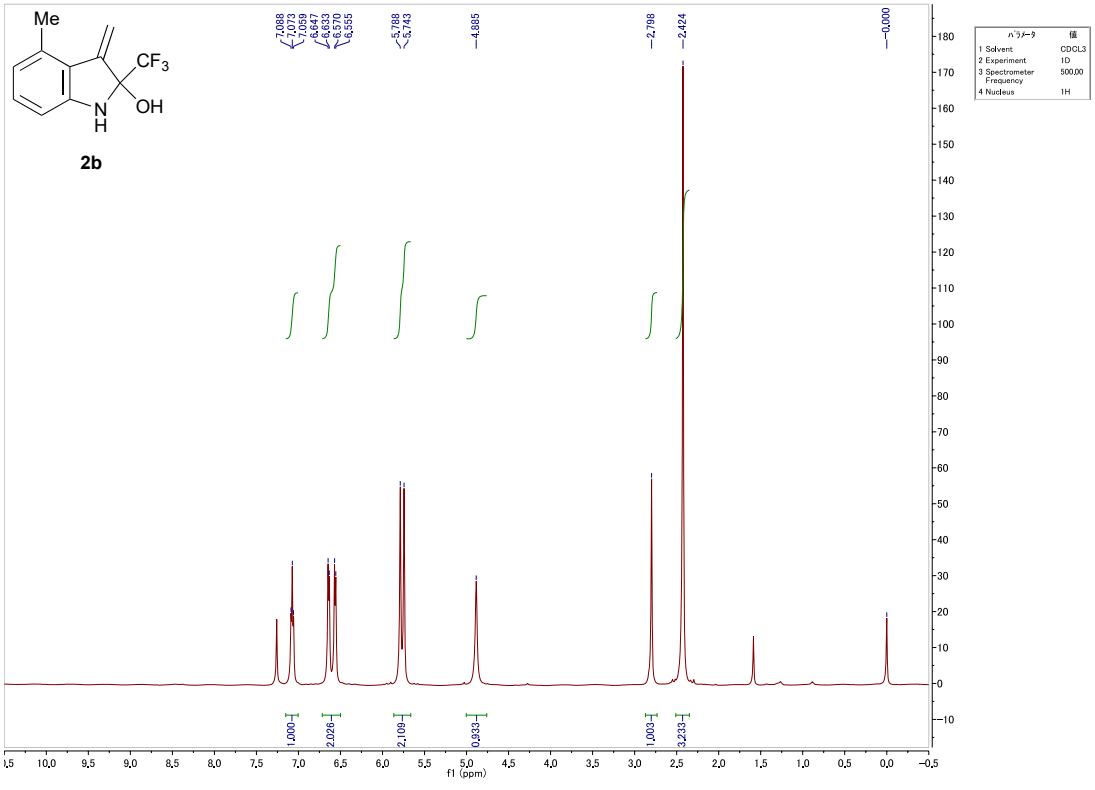
^{1}H NMR (400 MHz, $CDCl_3$) of **2a**



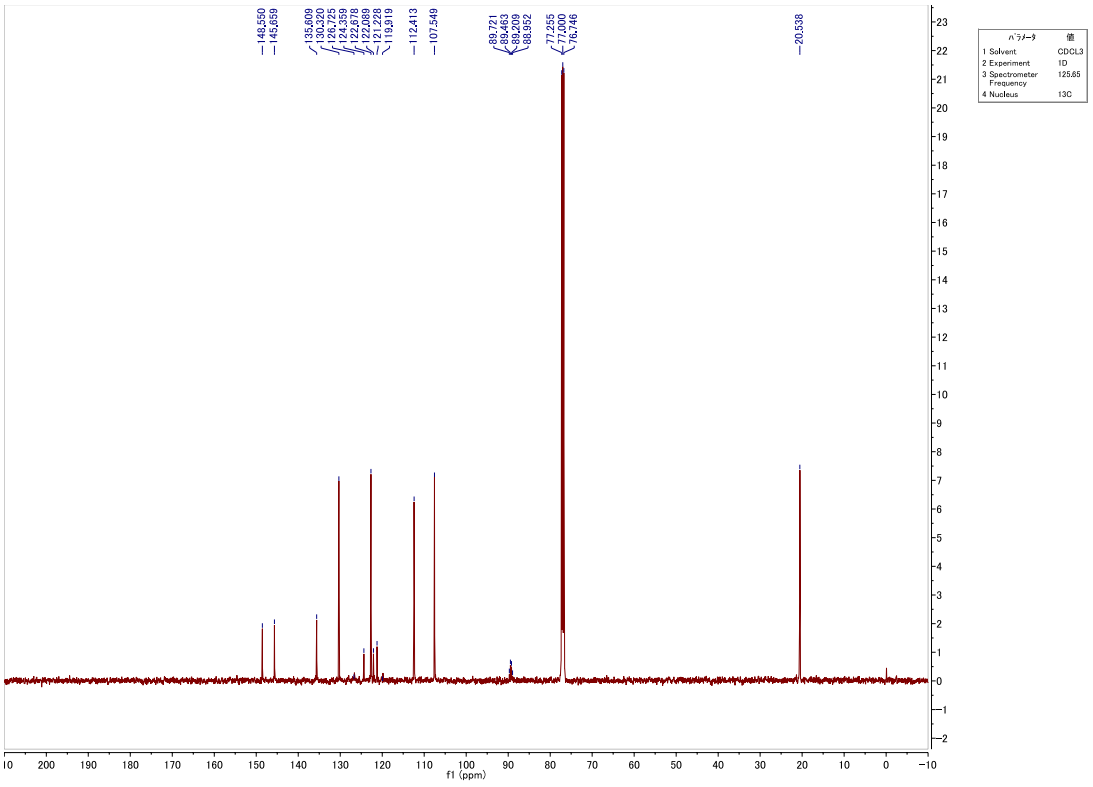
^{13}C NMR (100 MHz, $CDCl_3$) of **2a**



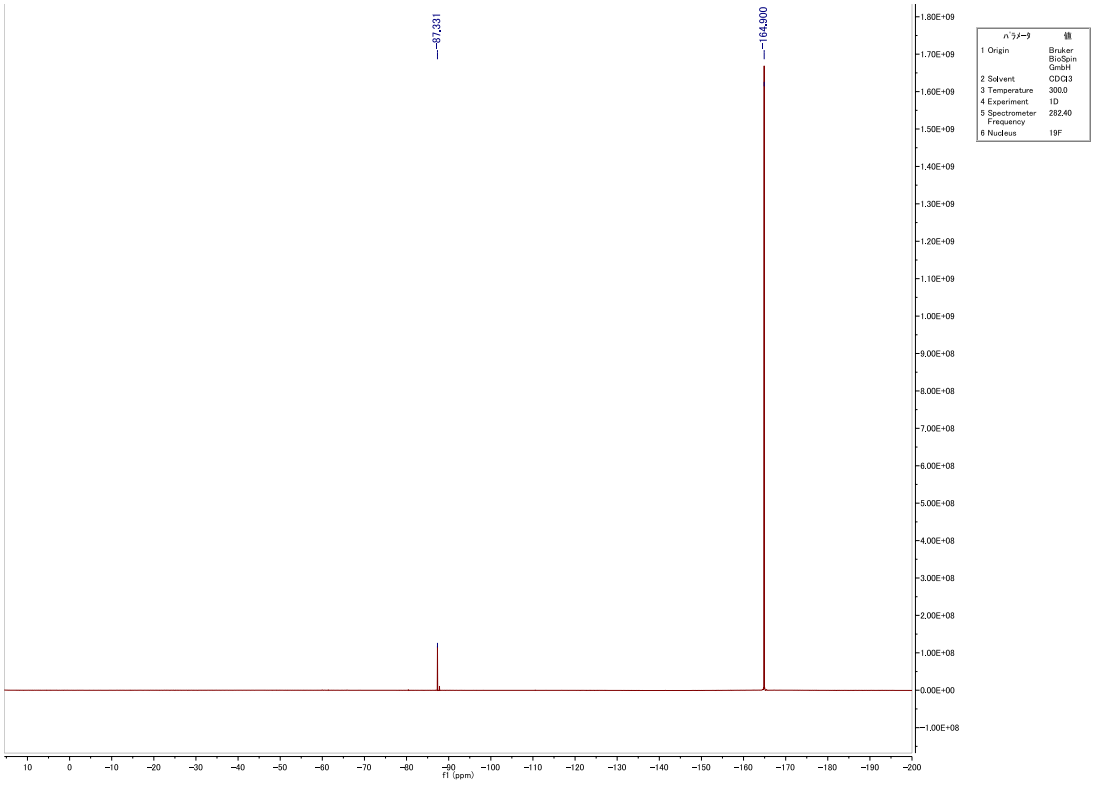
^{19}F NMR (283 MHz, $CDCl_3$) of **2a**



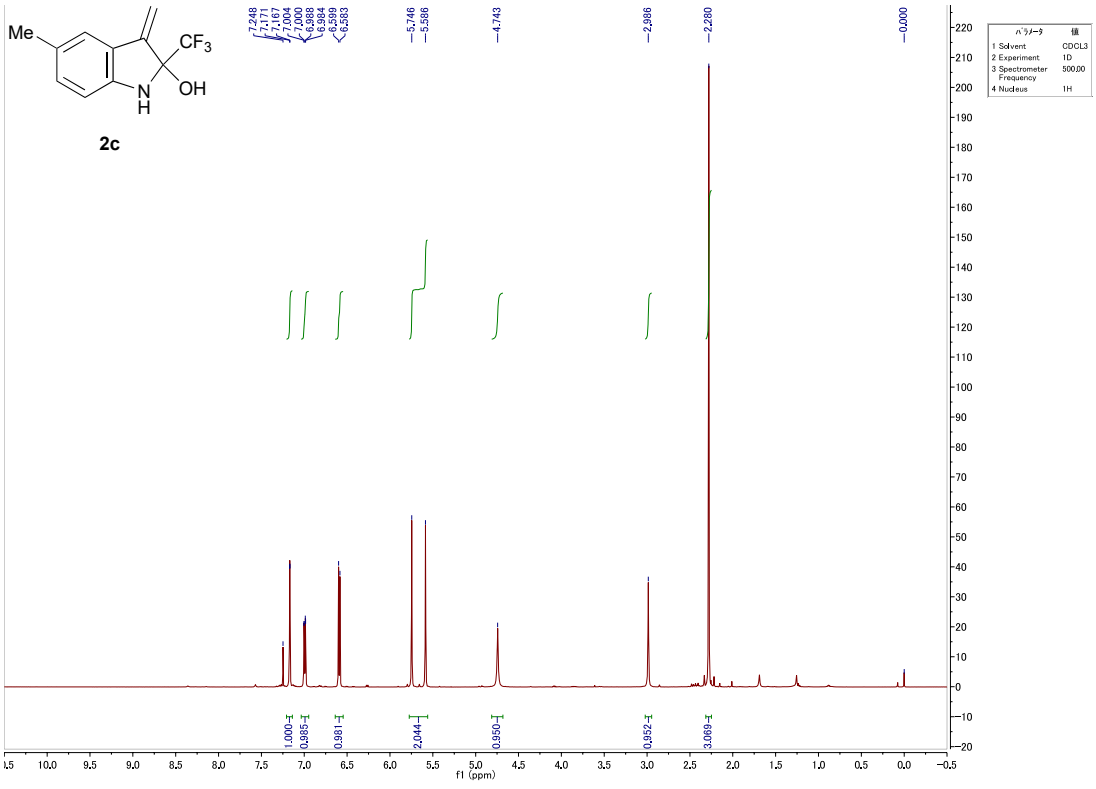
^{1}H NMR (500 MHz, $CDCl_3$) of **2b**



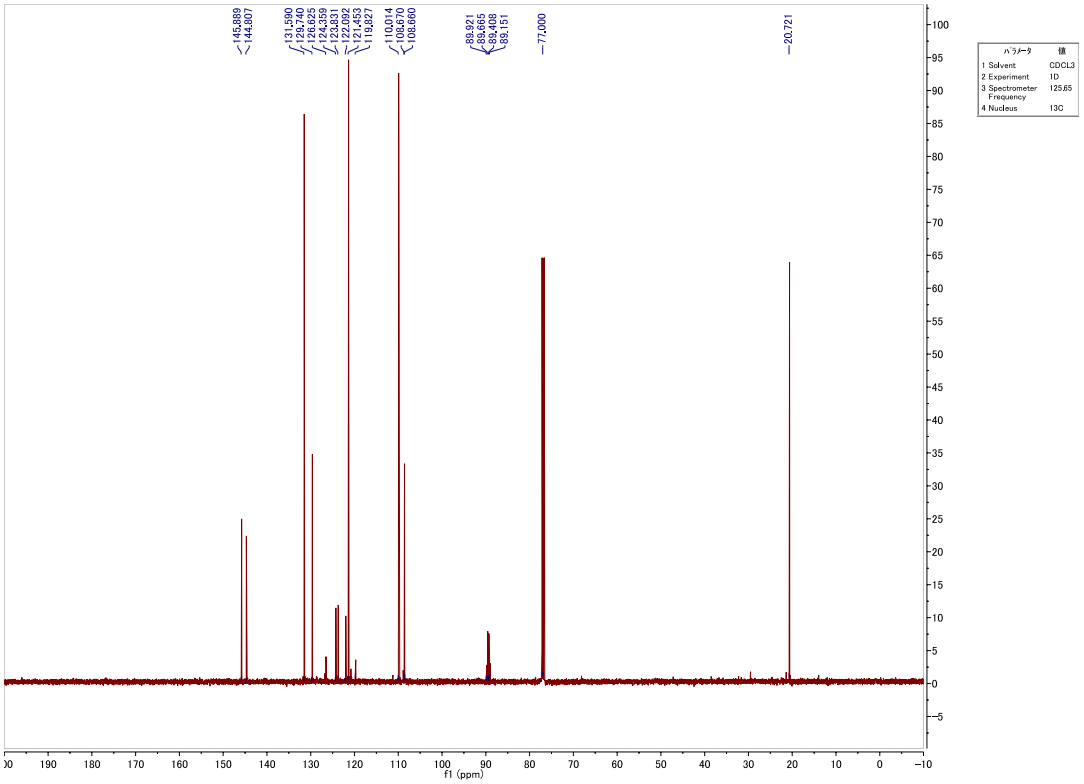
^{13}C NMR (125 MHz, $CDCl_3$) of **2b**



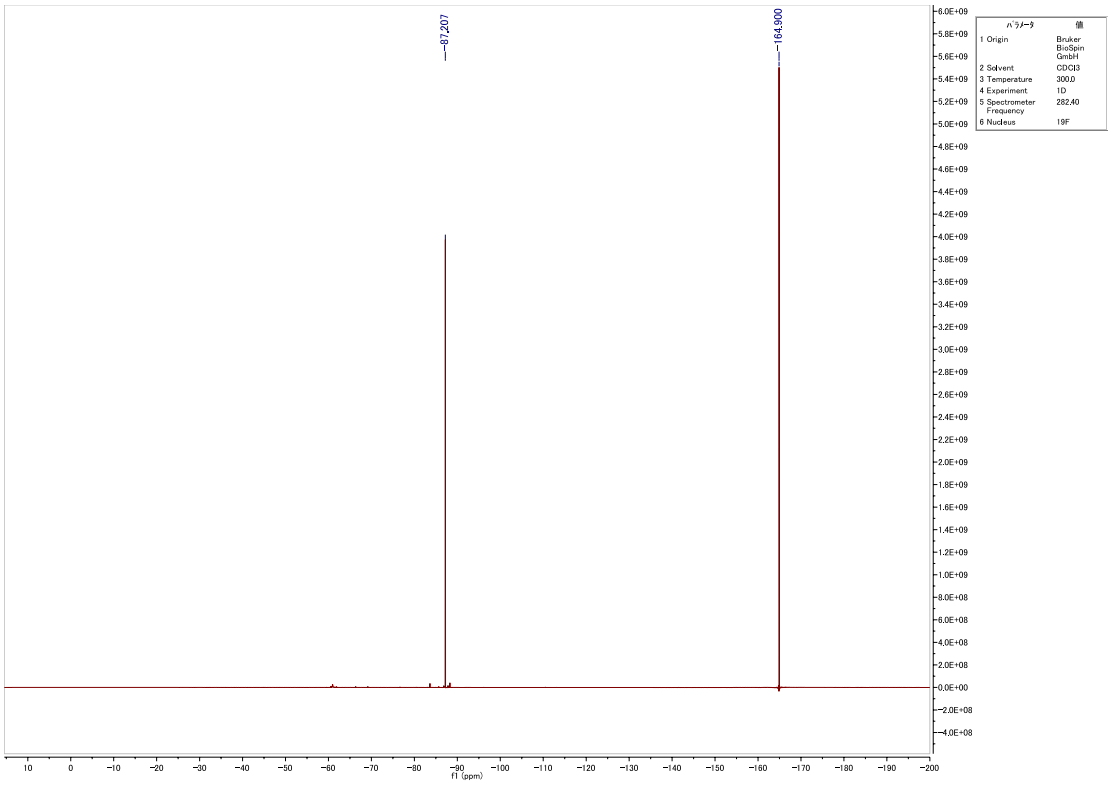
^{19}F NMR (283 MHz, $CDCl_3$) of **2b**



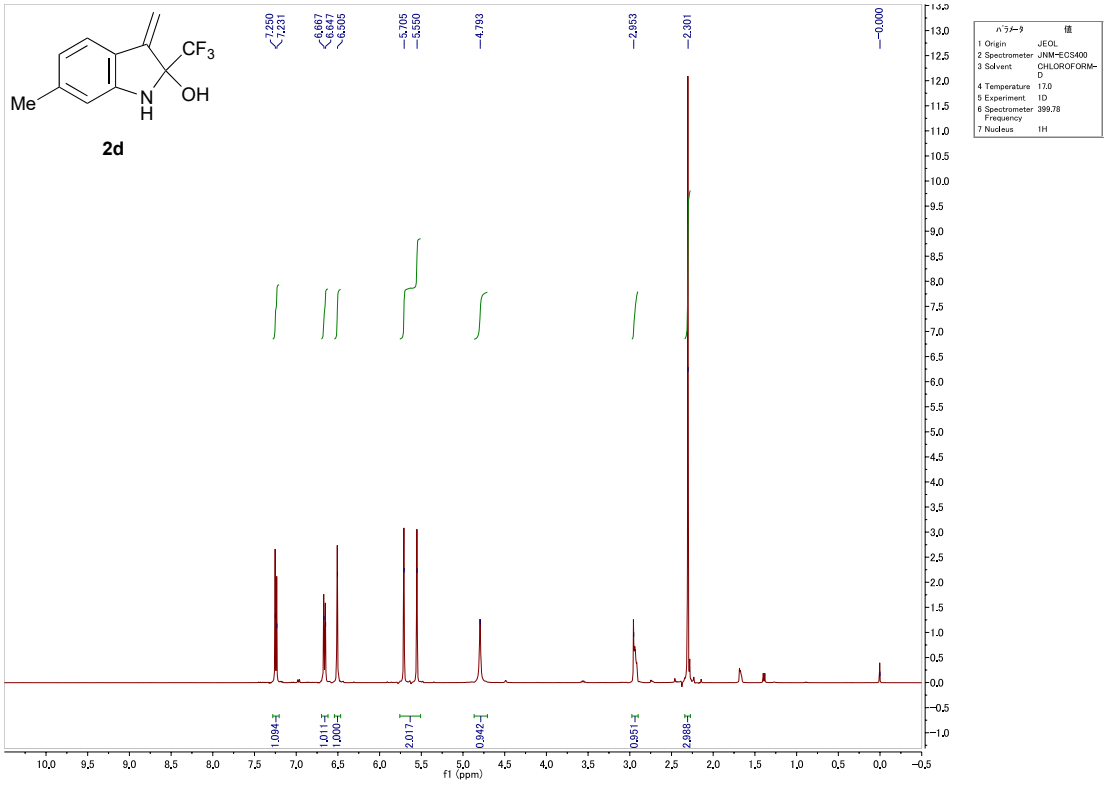
^{1}H NMR (500 MHz, $CDCl_3$) of **2c**



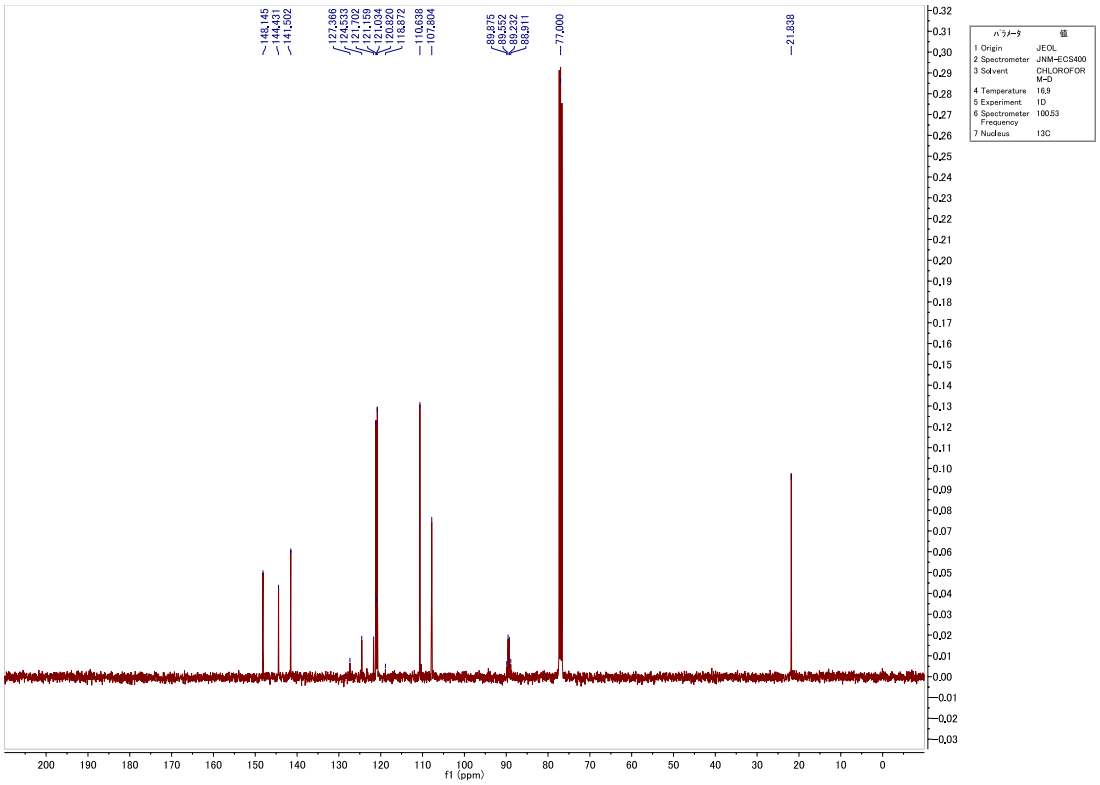
^{13}C NMR (125 MHz, $CDCl_3$) of **2c**



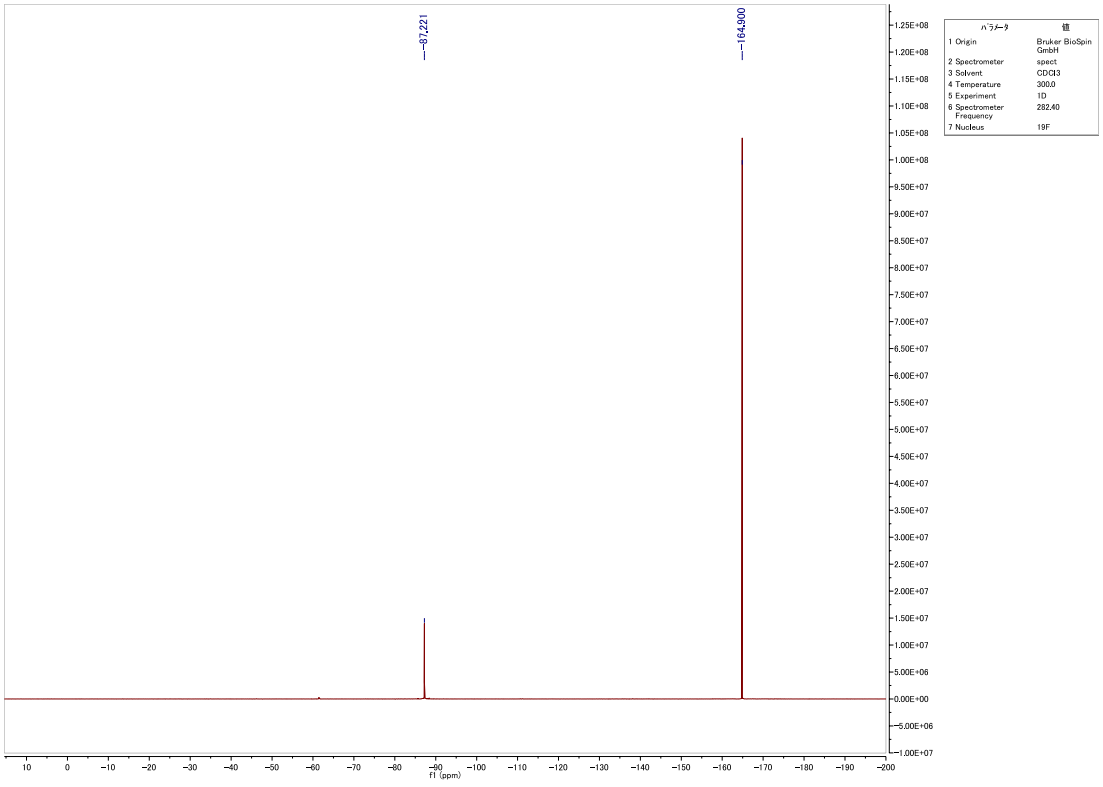
^{19}F NMR (283 MHz, $CDCl_3$) of **2c**



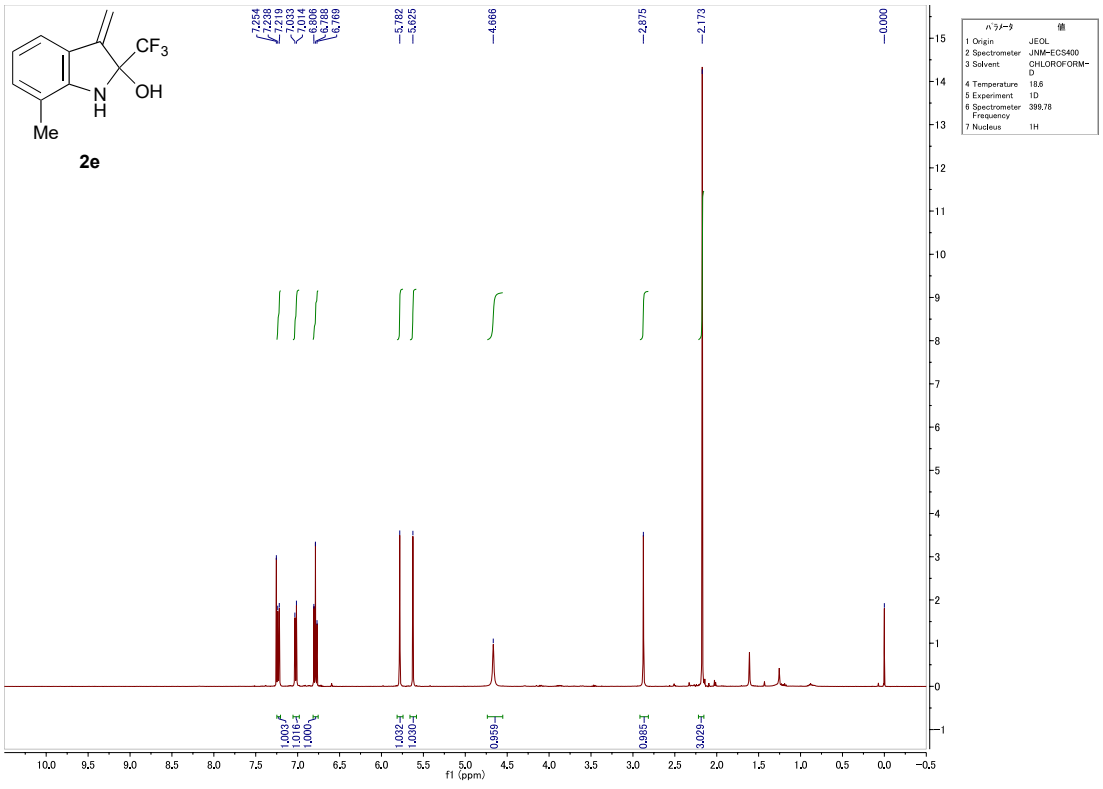
^{1}H NMR (400 MHz, $CDCl_3$) of **2d**



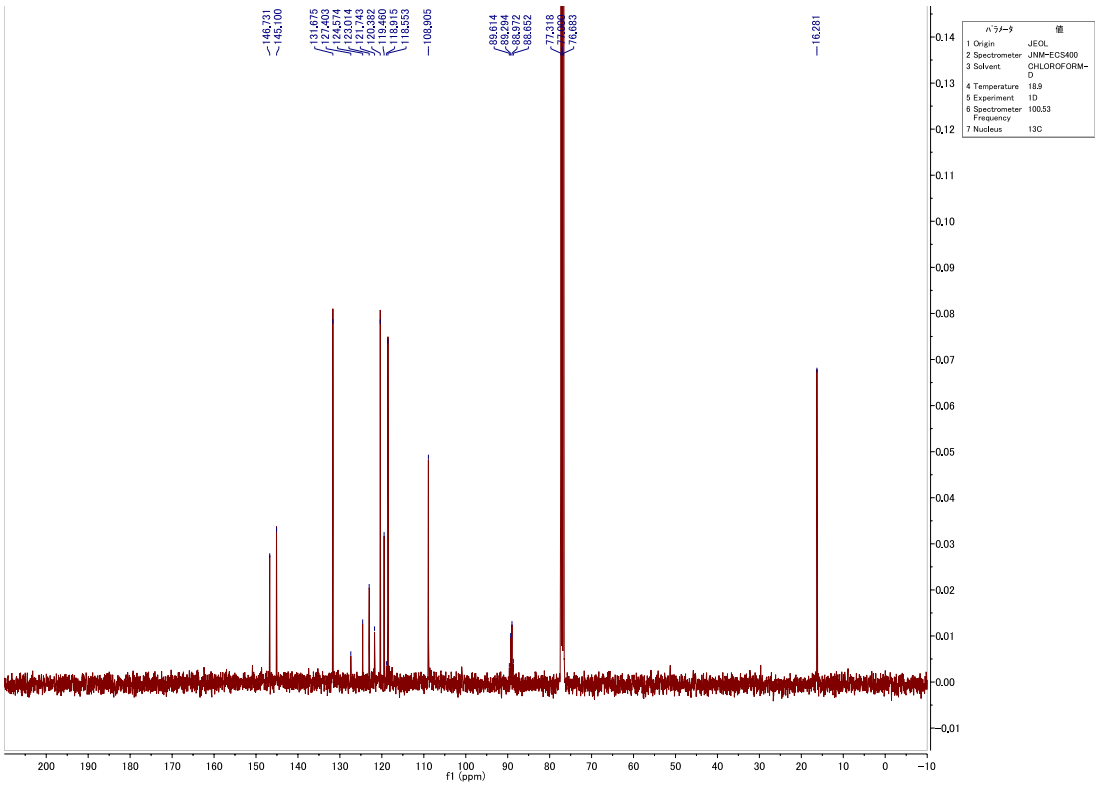
^{13}C NMR (100 MHz, $CDCl_3$) of **2d**



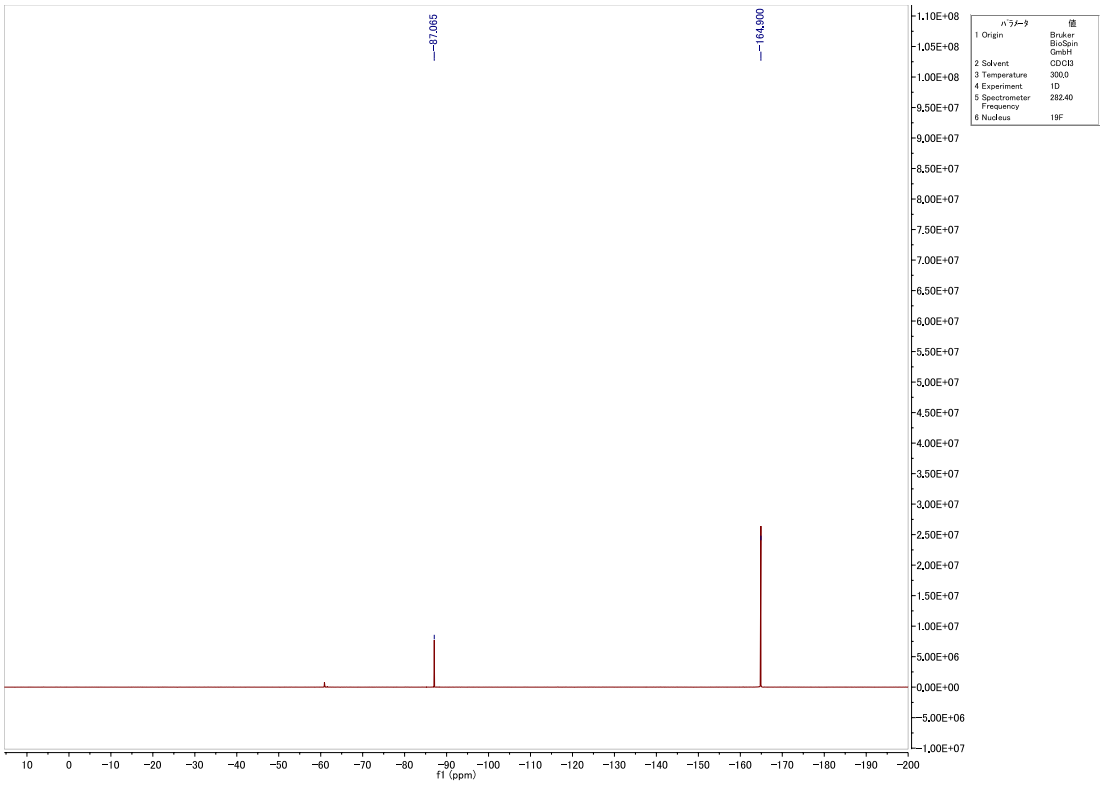
^{19}F NMR (283 MHz, $CDCl_3$) of **2d**



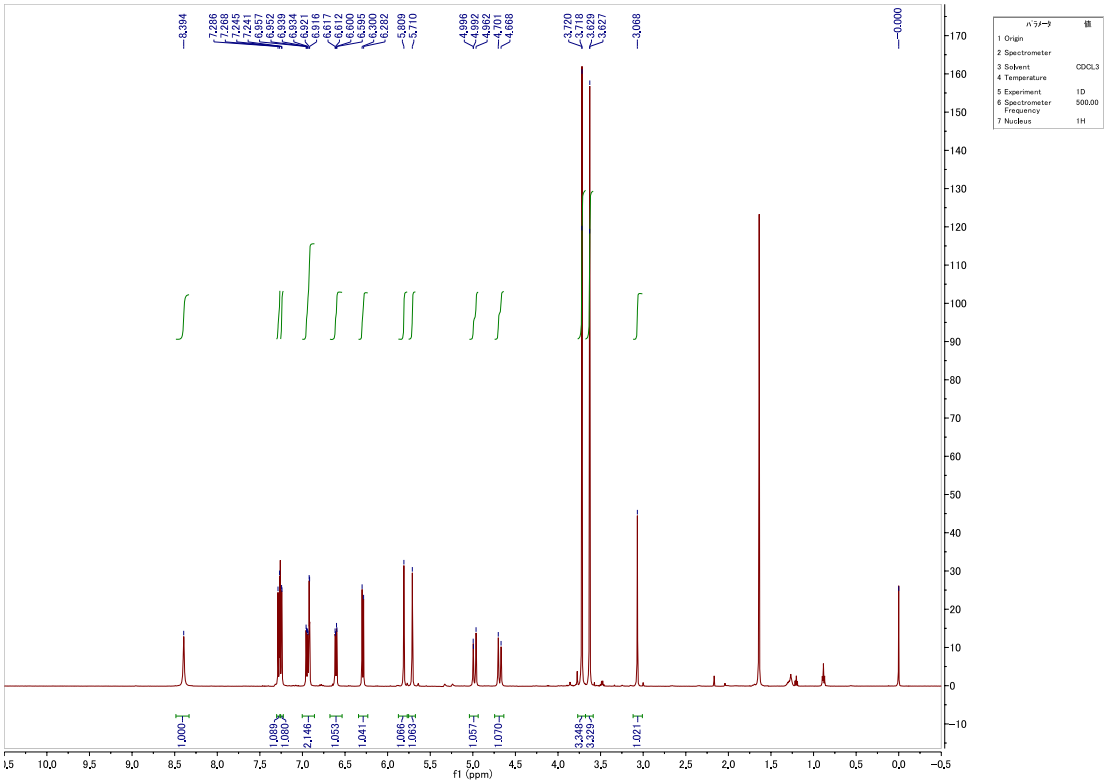
^{1}H NMR (400 MHz, $CDCl_3$) of **2e**



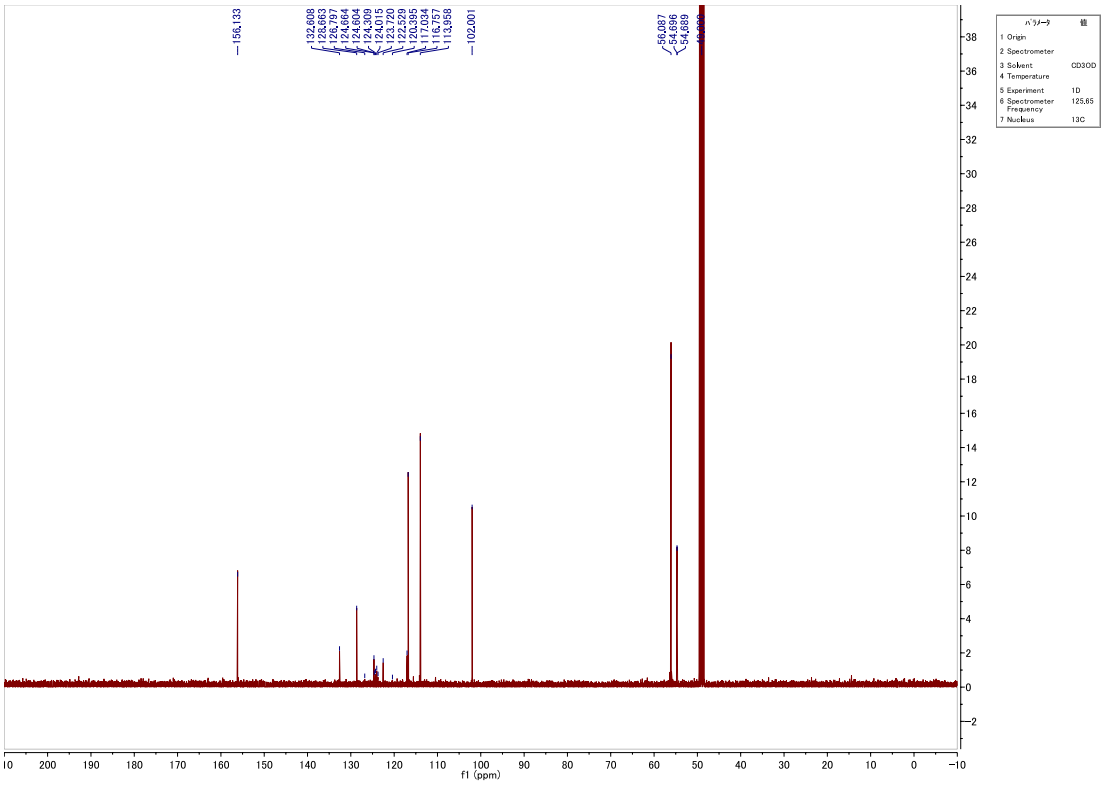
^{13}C NMR (100 MHz, $CDCl_3$) of **2e**



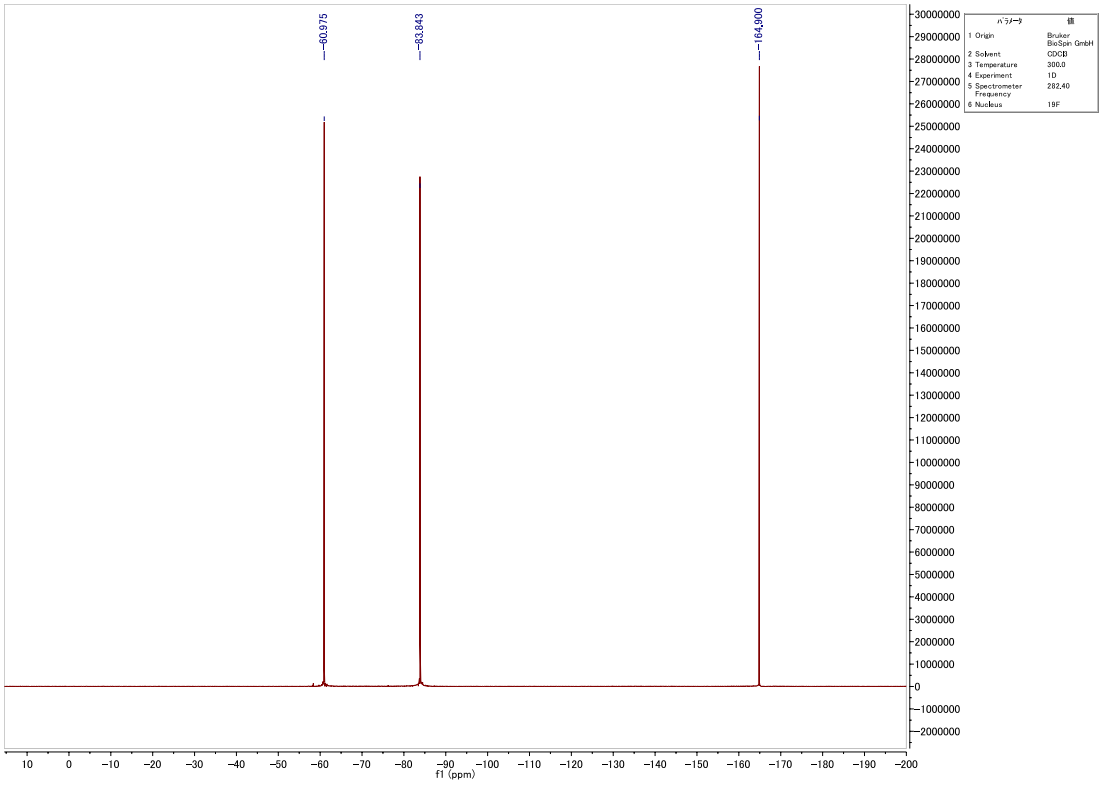
^{19}F NMR (283 MHz, $CDCl_3$) of **2e**



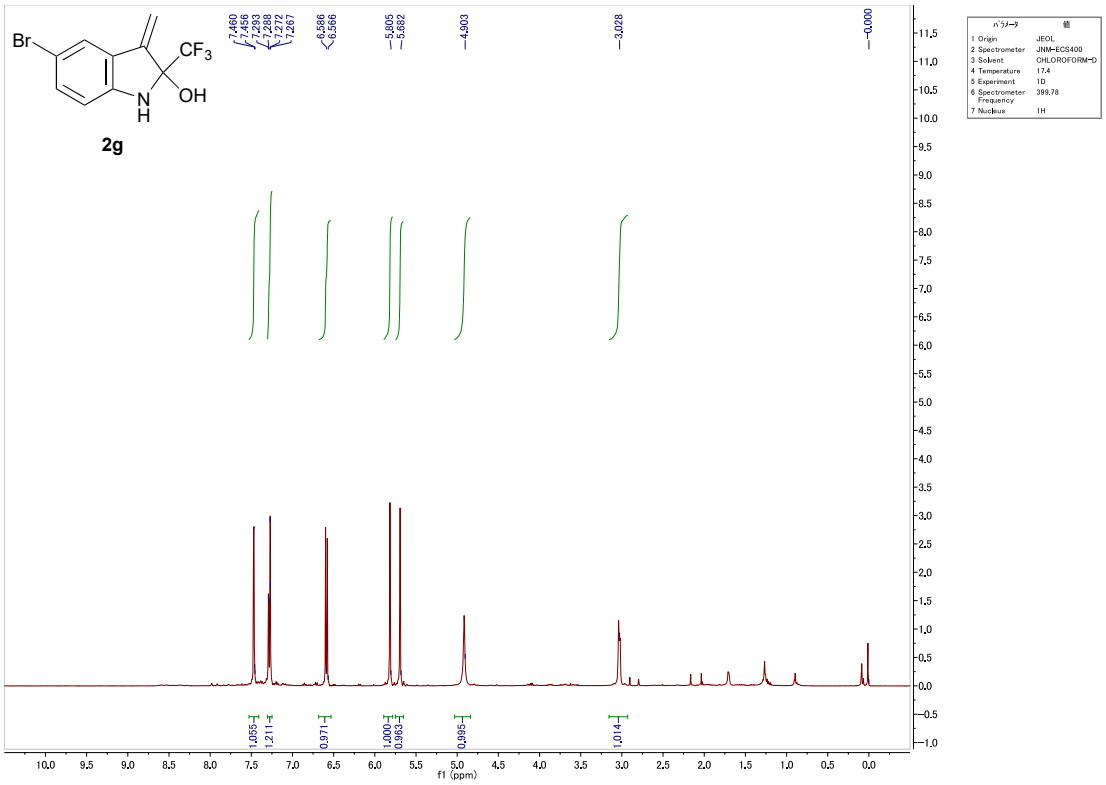
^{1}H NMR (500 MHz, $CDCl_3$) of **4**



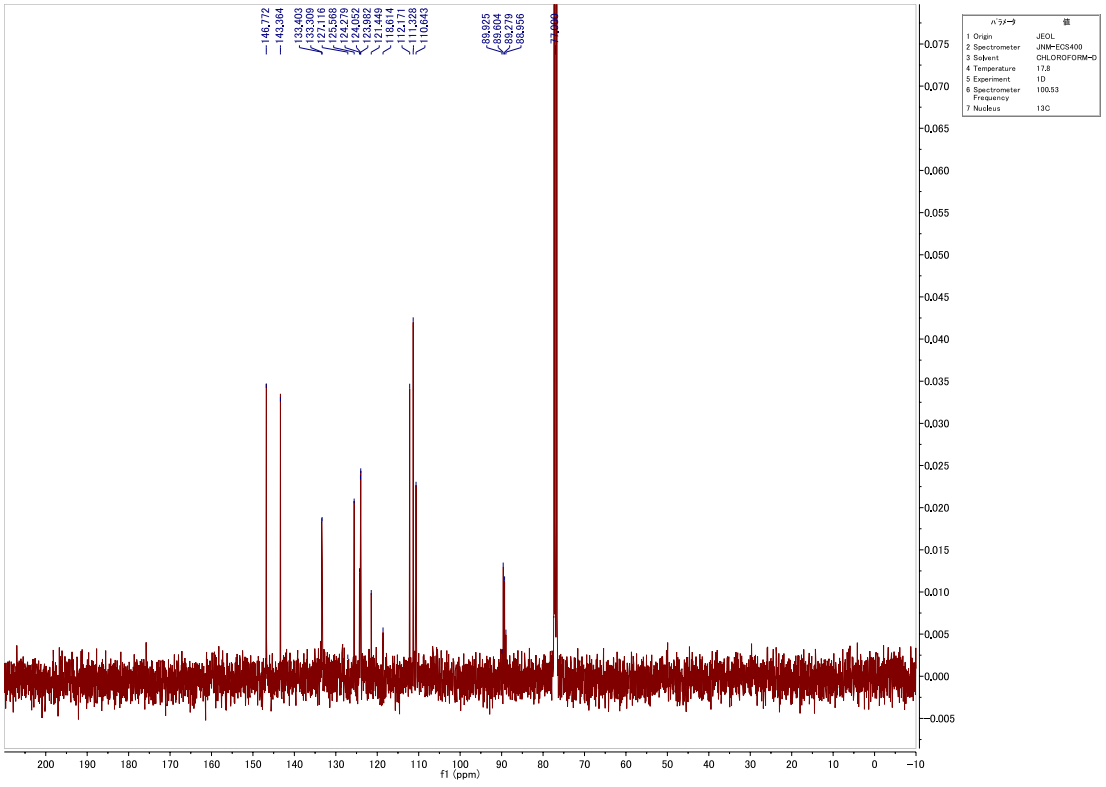
^{13}C NMR (125 MHz, CD_3OD) of **4**



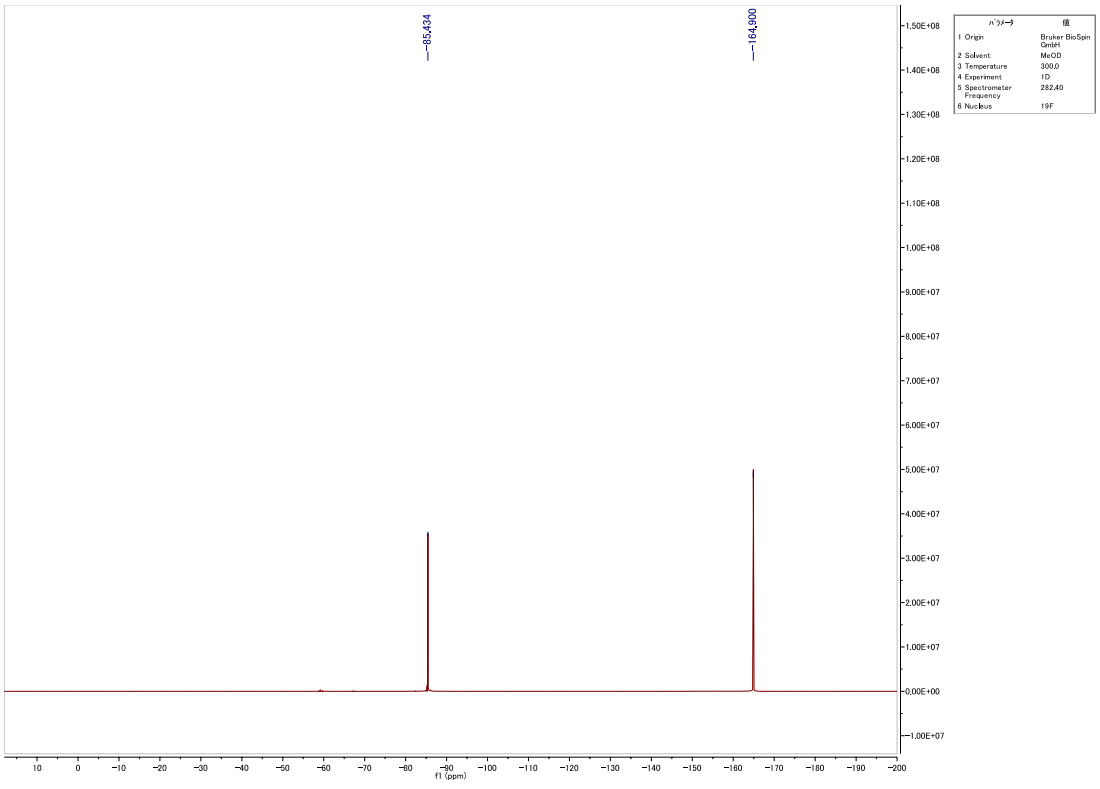
^{19}F NMR (283 MHz, $CDCl_3$) of **4**



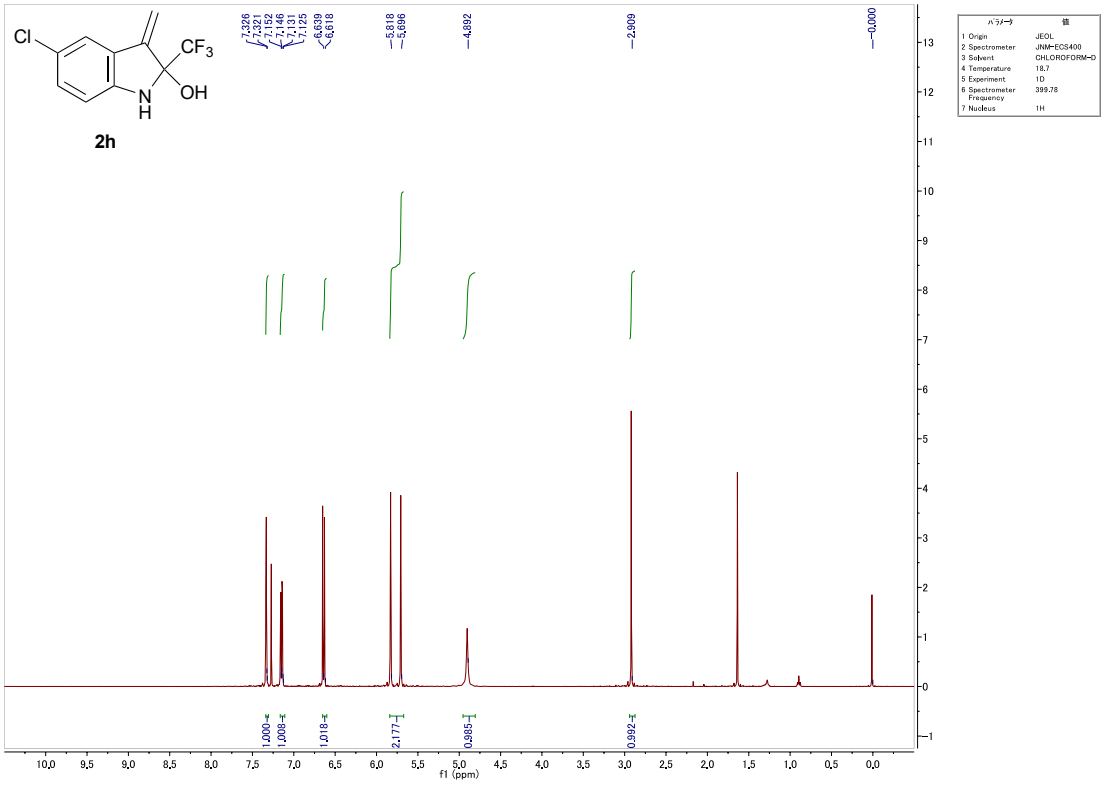
^{1}H NMR (400 MHz, $CDCl_3$) of **2g**



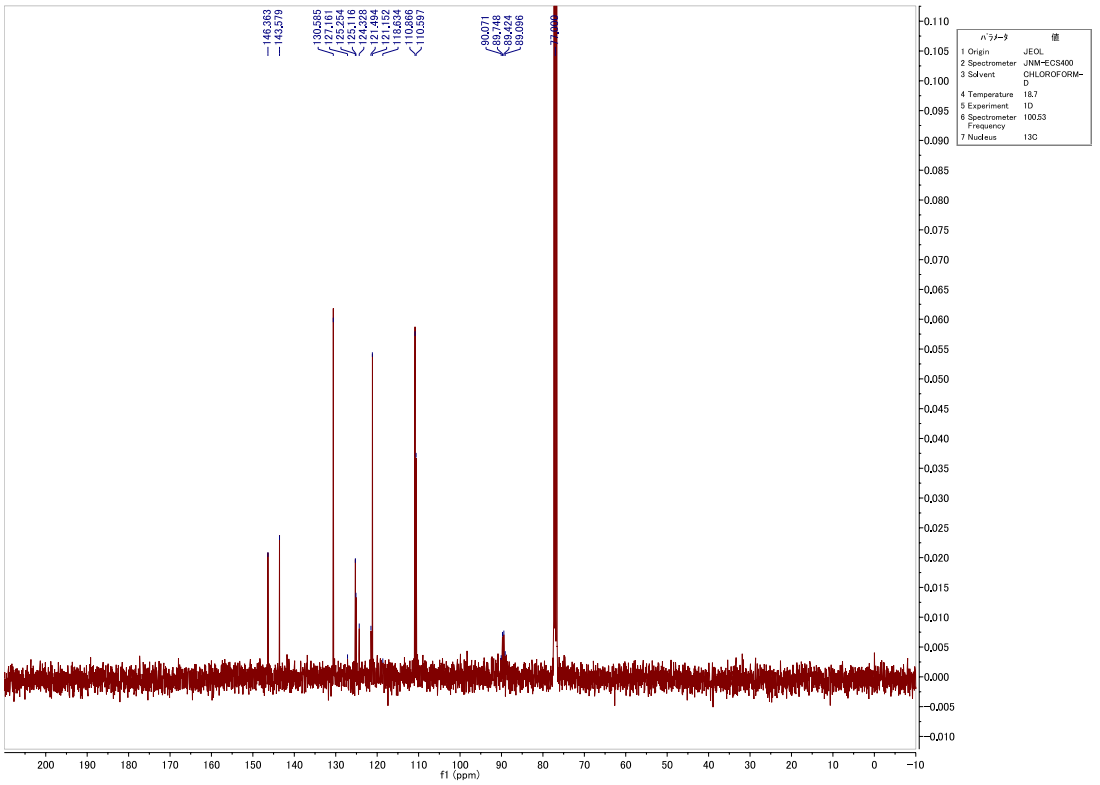
^{13}C NMR (100 MHz, $CDCl_3$) of **2g**



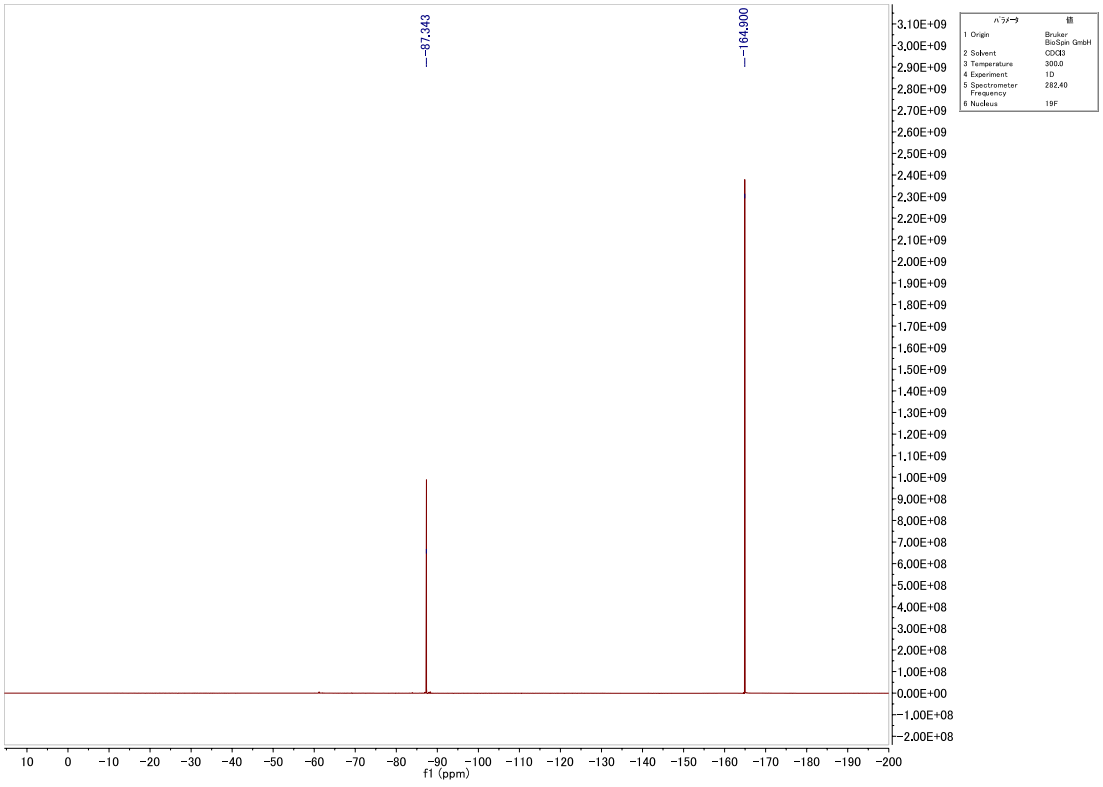
^{19}F NMR (283 MHz, $CDCl_3$) of **2g**



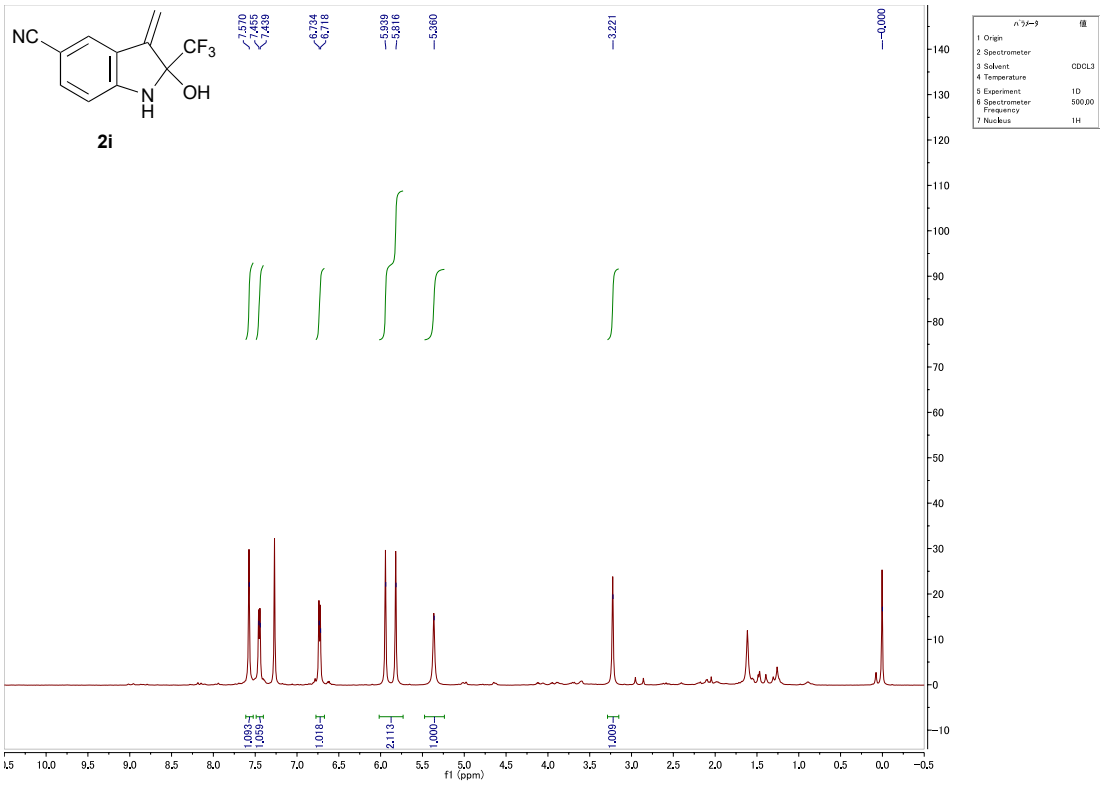
^{1}H NMR (400 MHz, $CDCl_3$) of **2h**



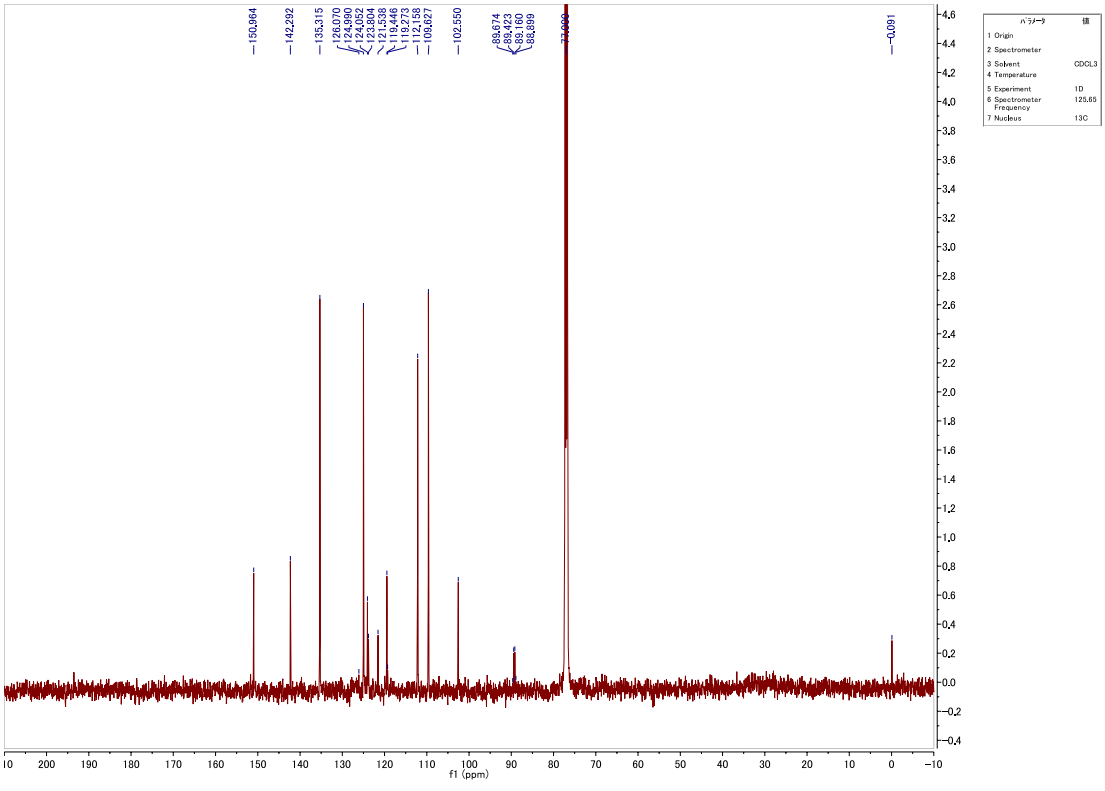
^{13}C NMR (100 MHz, $CDCl_3$) of **2h**



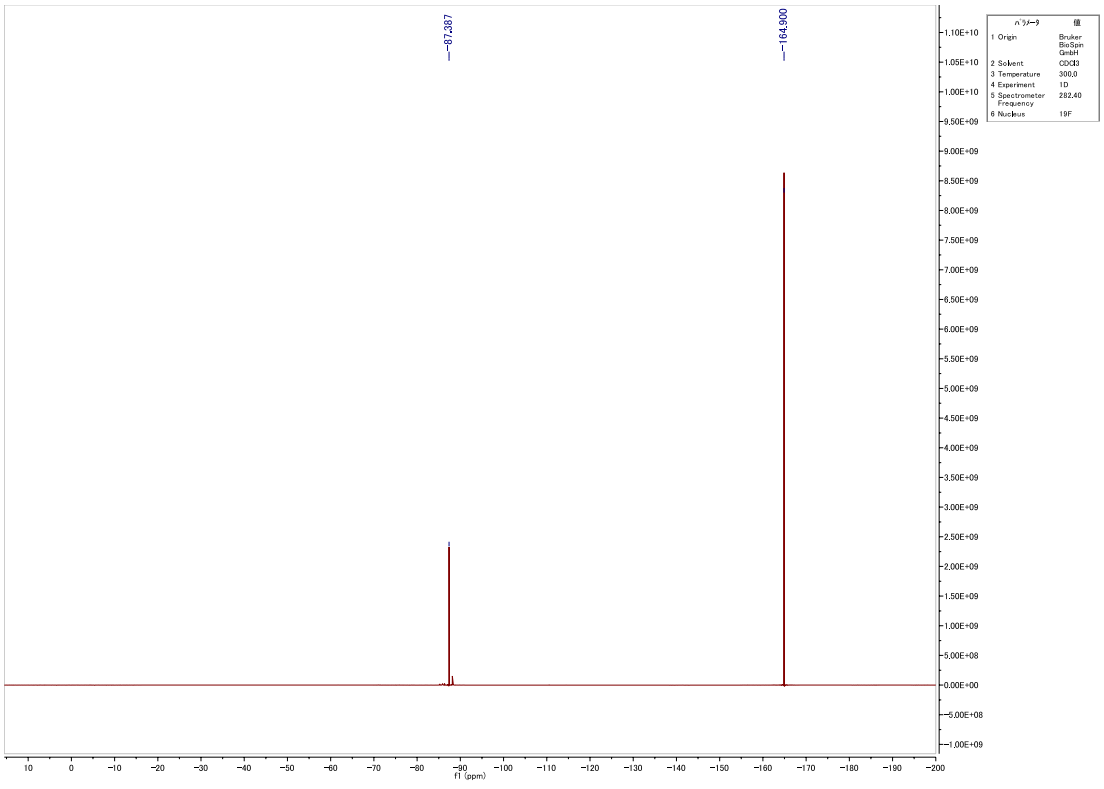
^{19}F NMR (283 MHz, $CDCl_3$) of **2h**



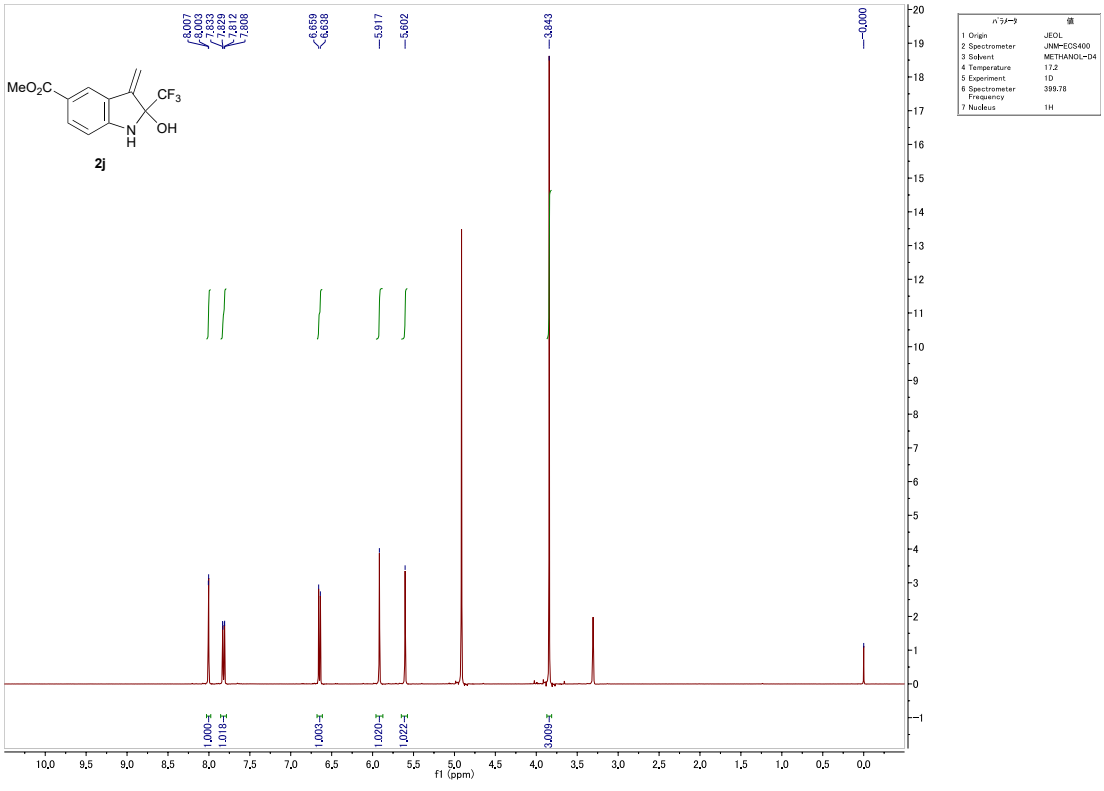
^{1}H NMR (500 MHz, $CDCl_3$) of **2i**



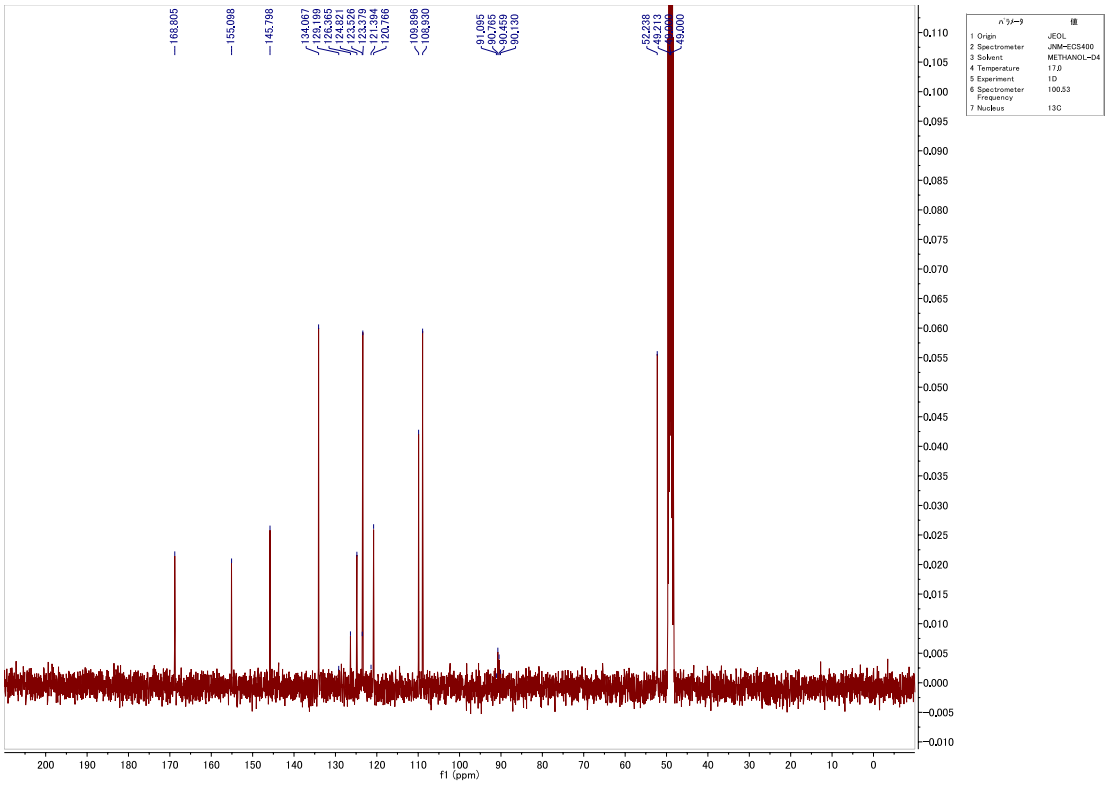
^{13}C NMR (125 MHz, $CDCl_3$) of **2i**



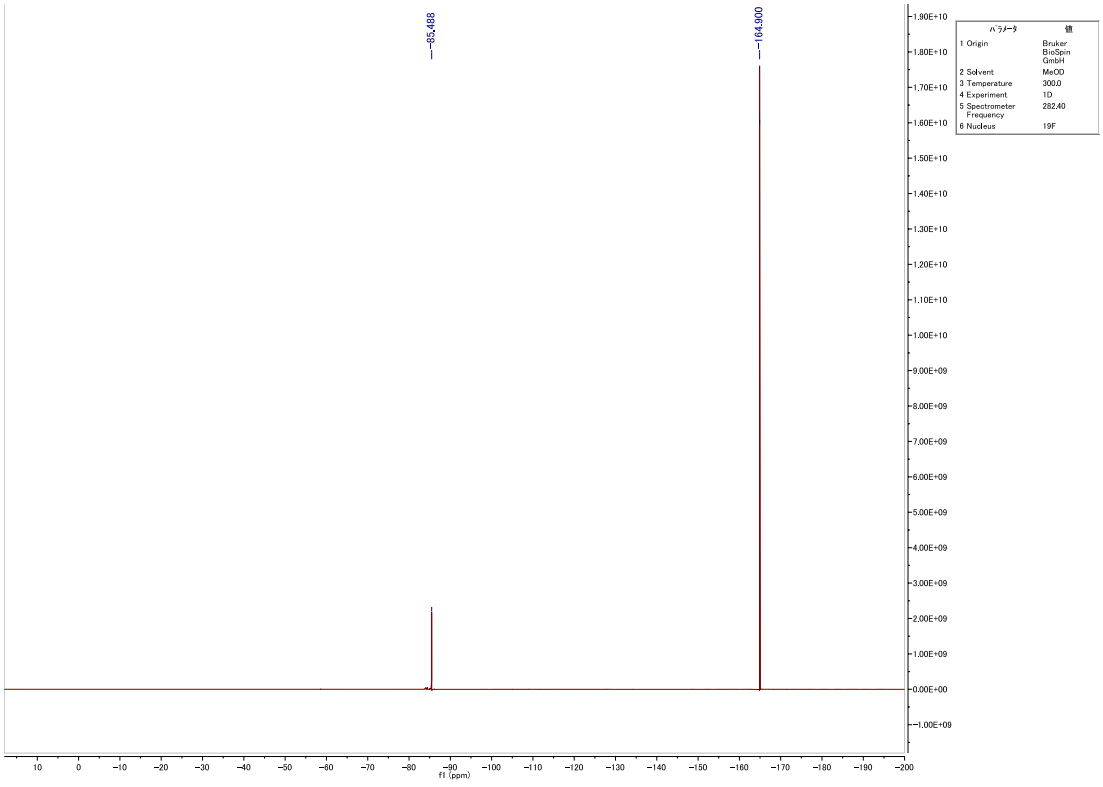
^{19}F NMR (283 MHz, $CDCl_3$) of **2i**



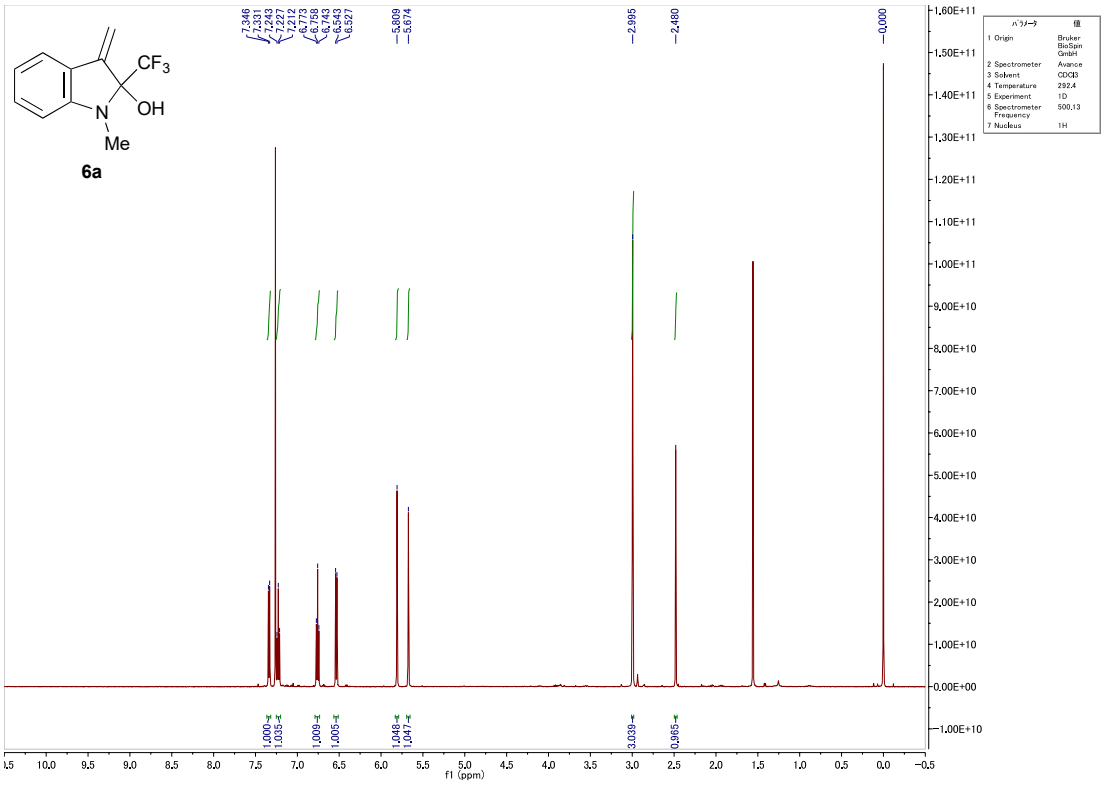
^{1}H NMR (400 MHz, CD_3OD) of **2j**



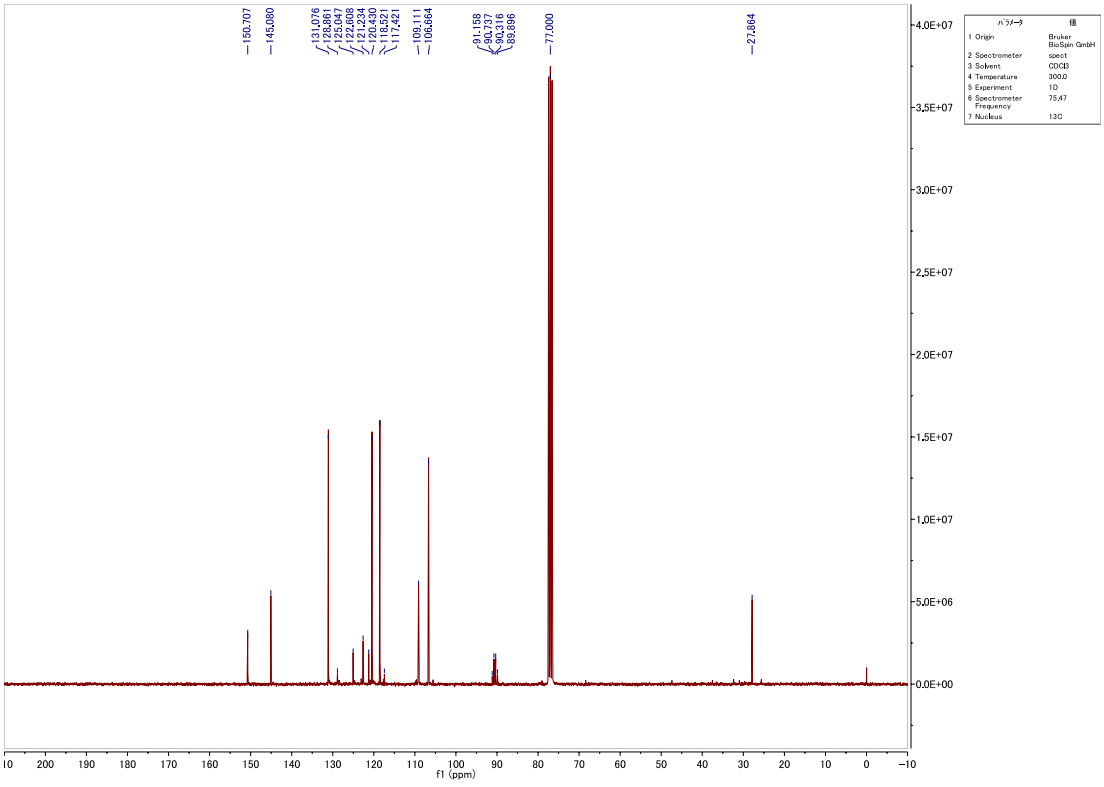
^{13}C NMR (100 MHz, CD_3OD) of **2j**



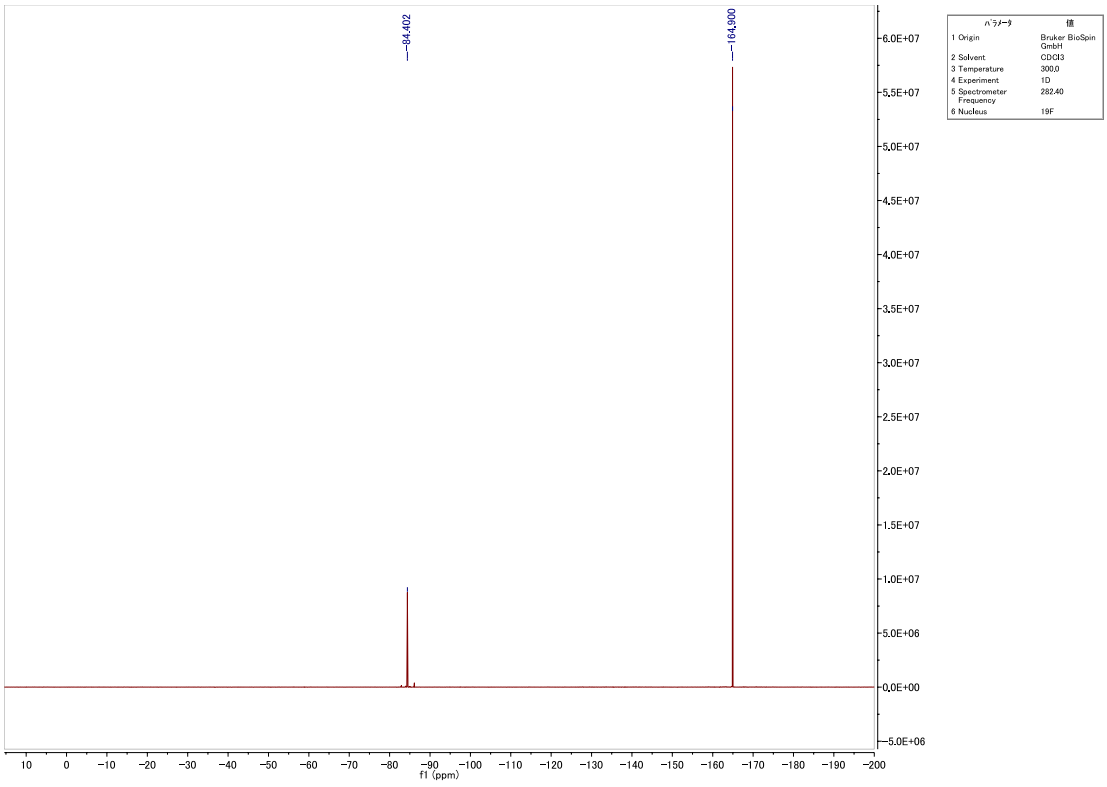
^{19}F NMR (283 MHz, CD_3OD) of **2j**



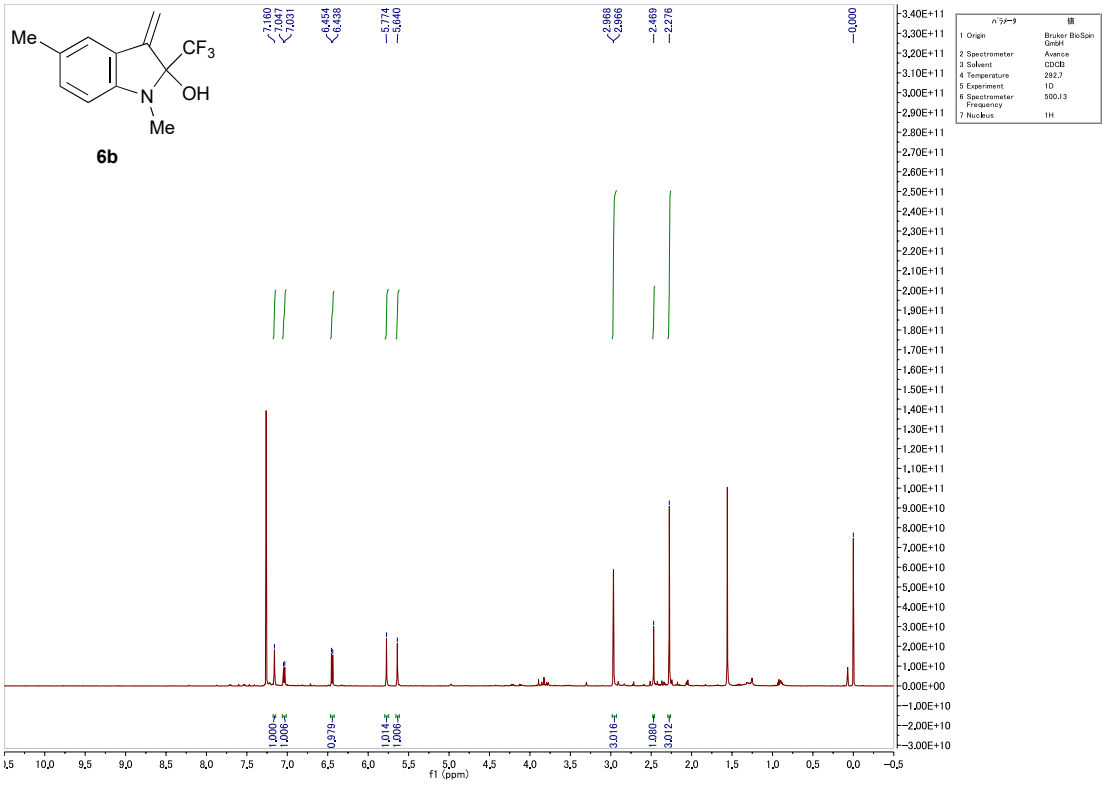
^{1}H NMR (500 MHz, $CDCl_3$) of **6a**



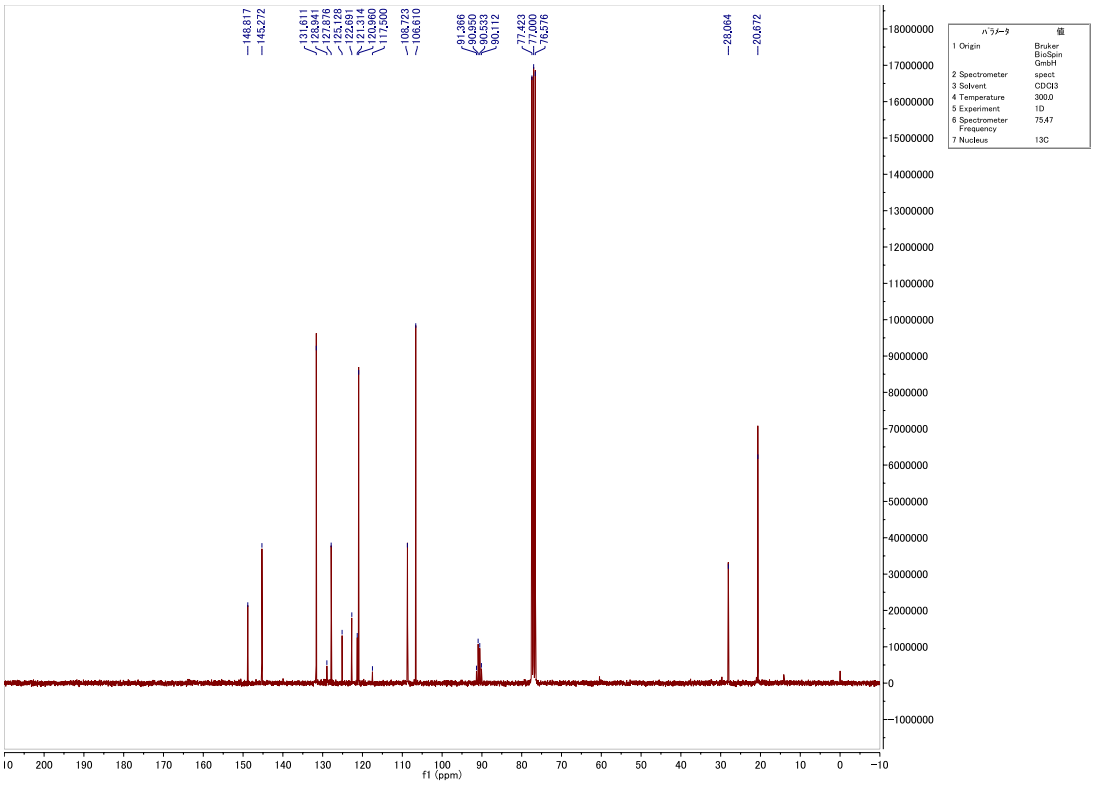
^{13}C NMR (100 MHz, $CDCl_3$) of **6a**



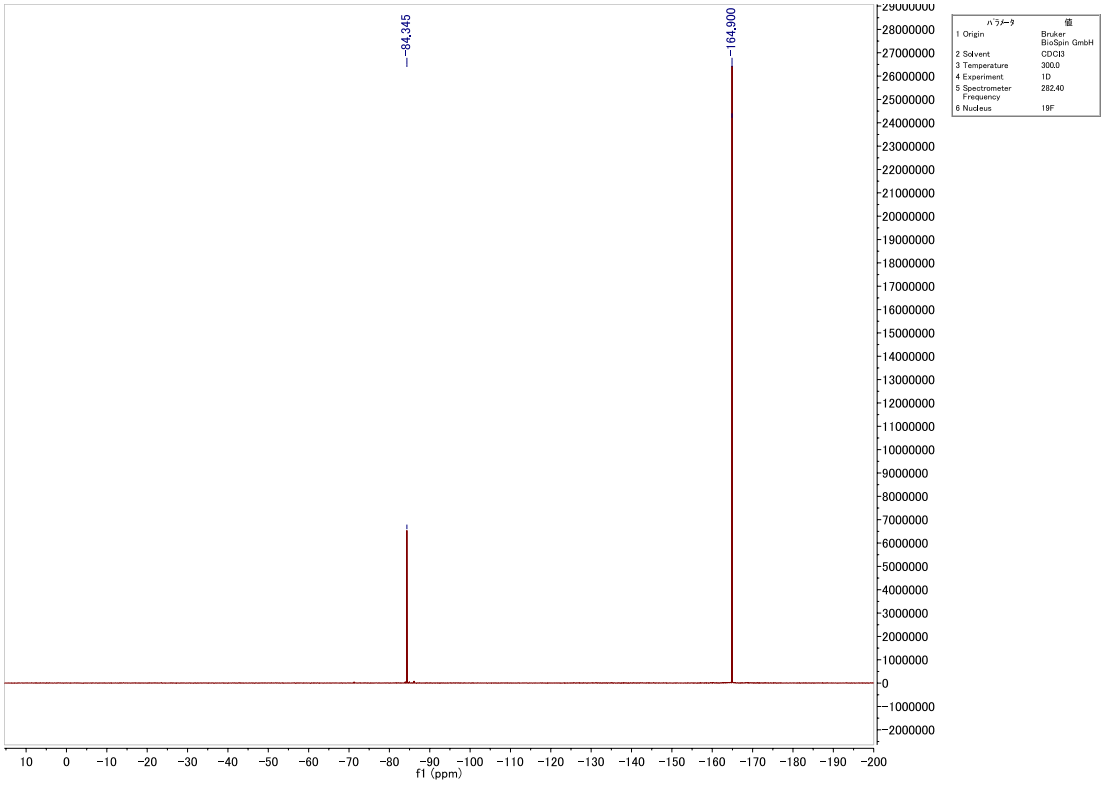
^{19}F NMR (283 MHz, $CDCl_3$) of **6a**



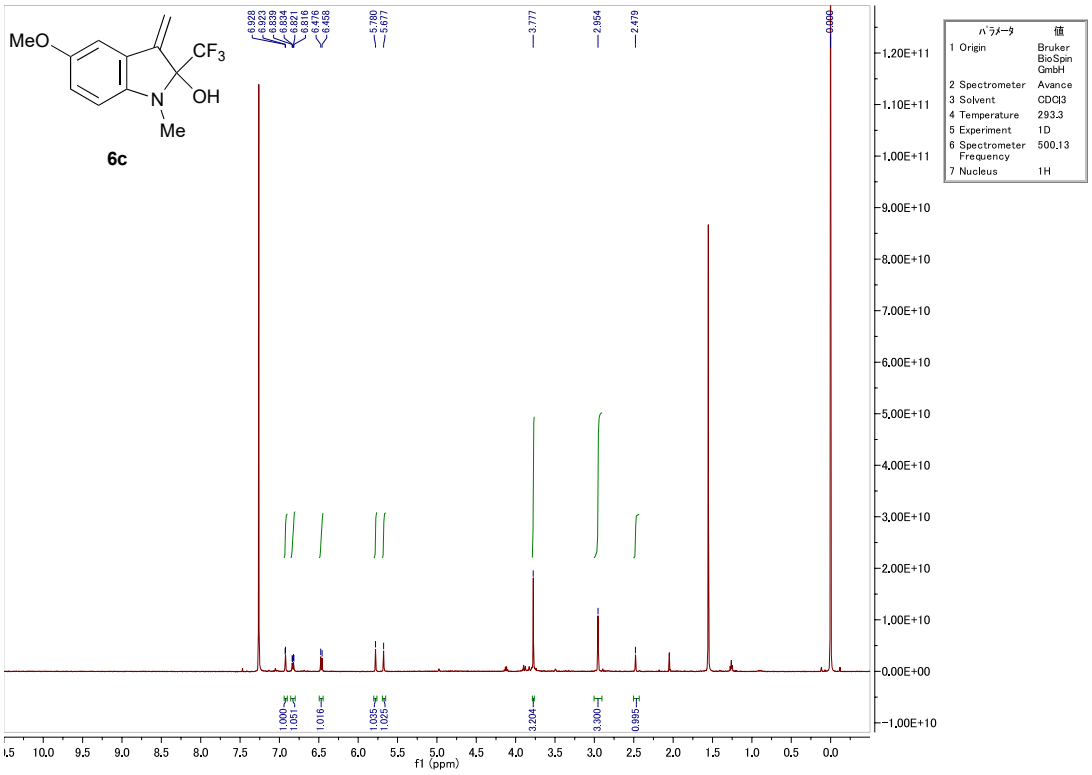
^{1}H NMR (500 MHz, $CDCl_3$) of **6b**



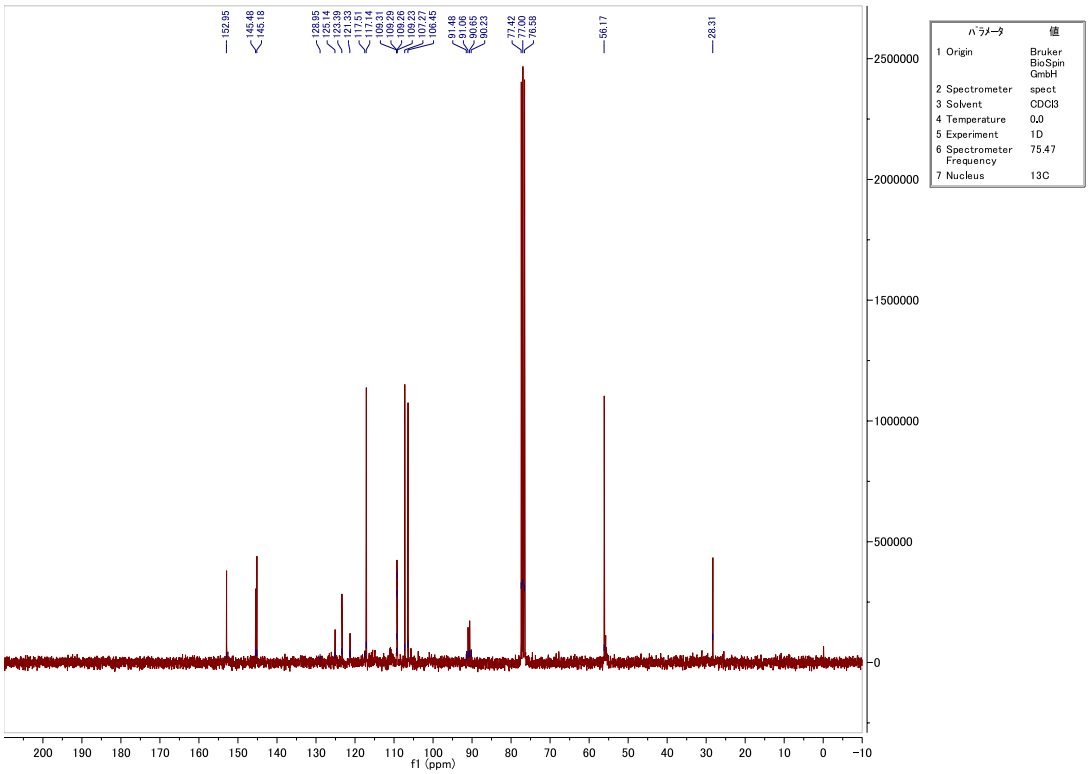
^{13}C NMR (75 MHz, $CDCl_3$) of **6b**



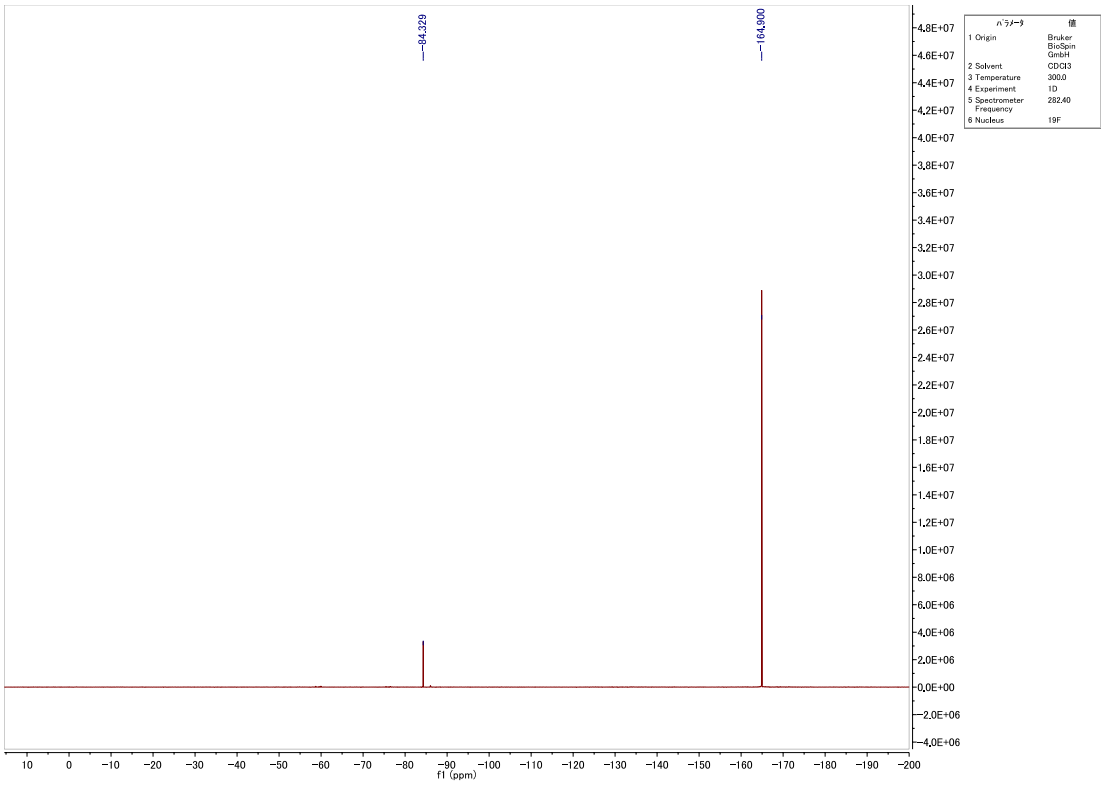
^{19}F NMR (283 MHz, $CDCl_3$) of **6b**



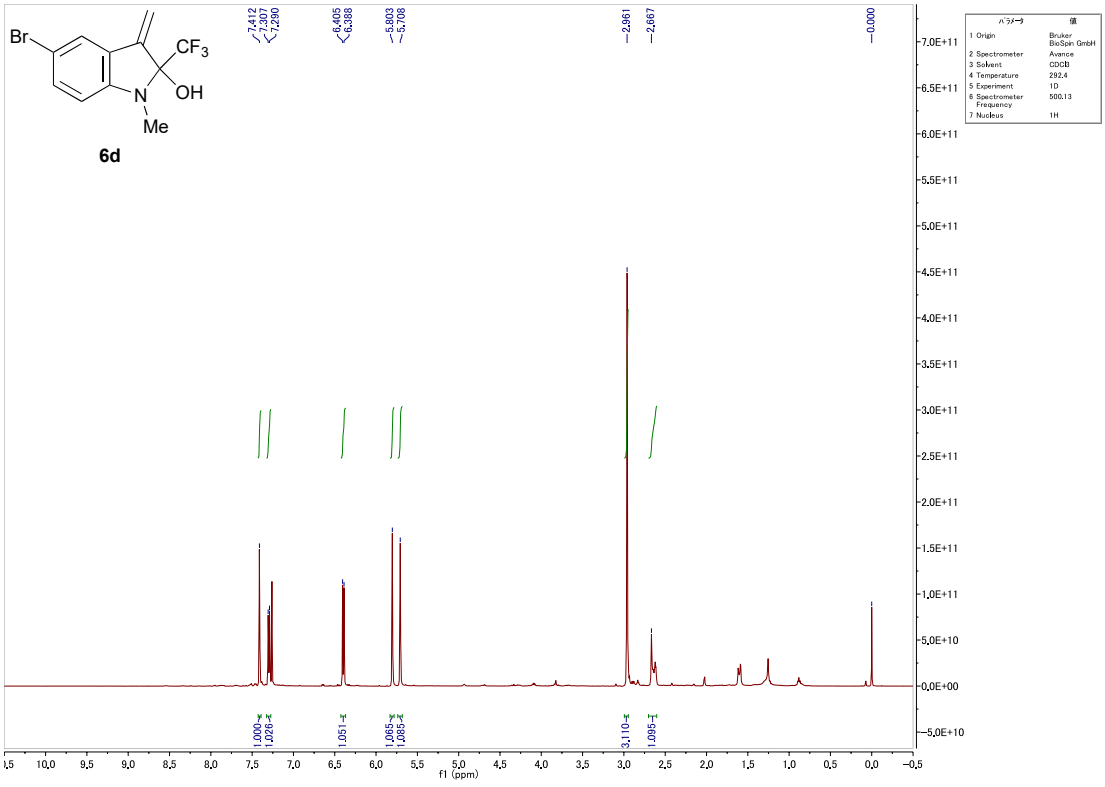
^{1}H NMR (400 MHz, $CDCl_3$) of **6c**



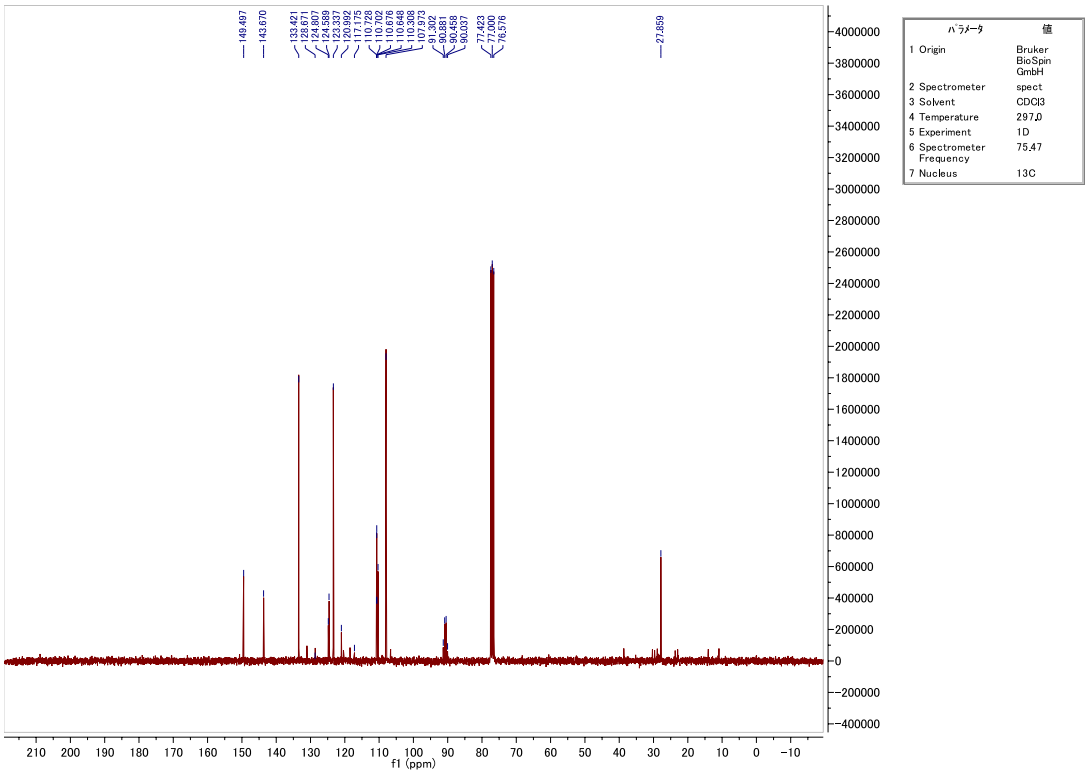
^{13}C NMR (75 MHz, $CDCl_3$) of **6c**



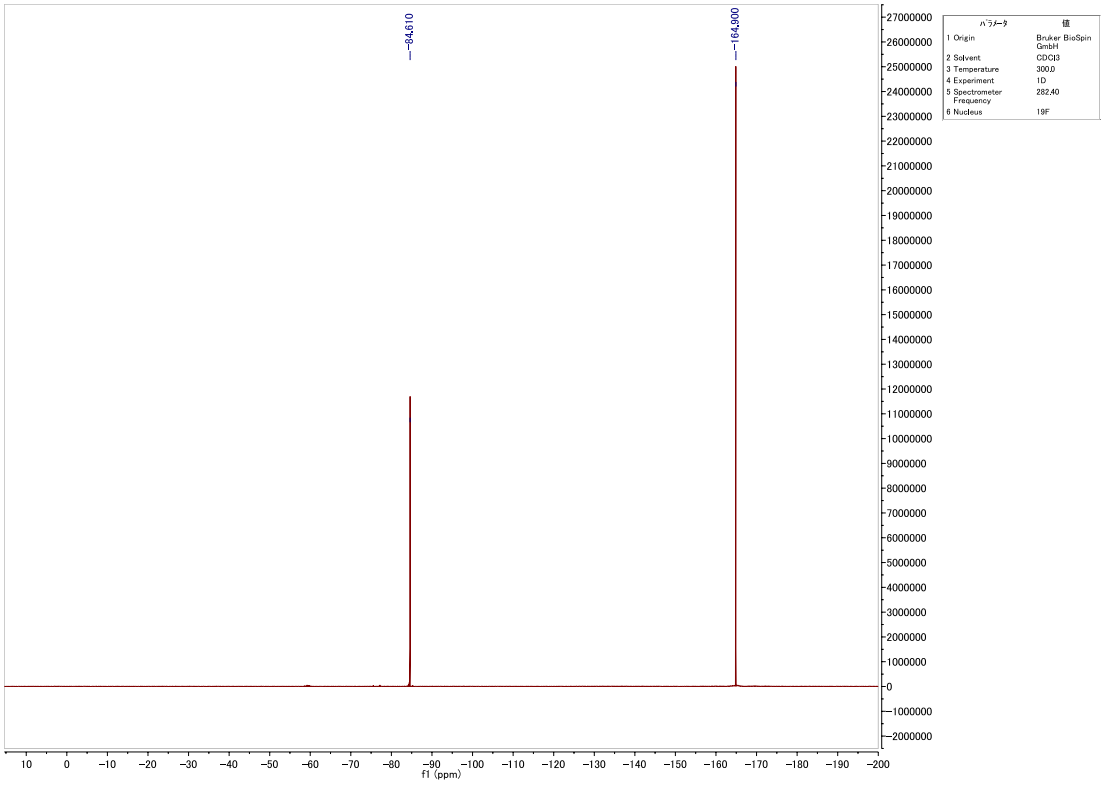
^{19}F NMR (283 MHz, $CDCl_3$) of **6c**



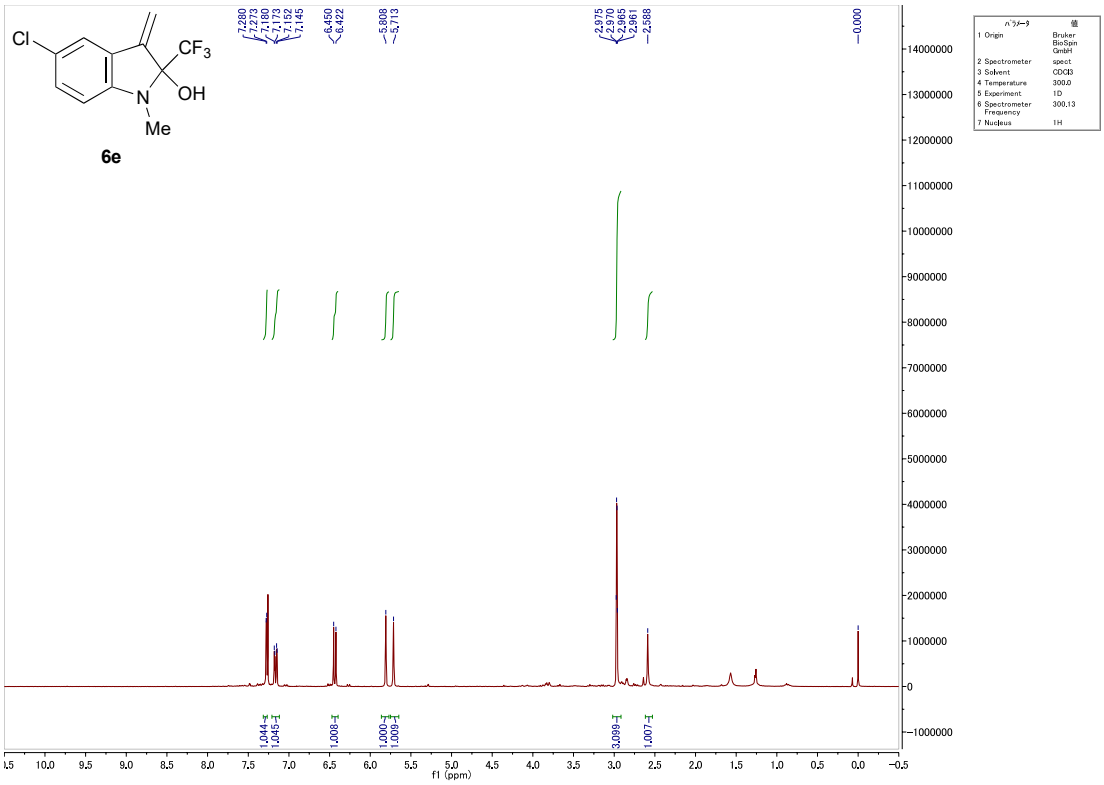
^{1}H NMR (400 MHz, $CDCl_3$) of **6d**



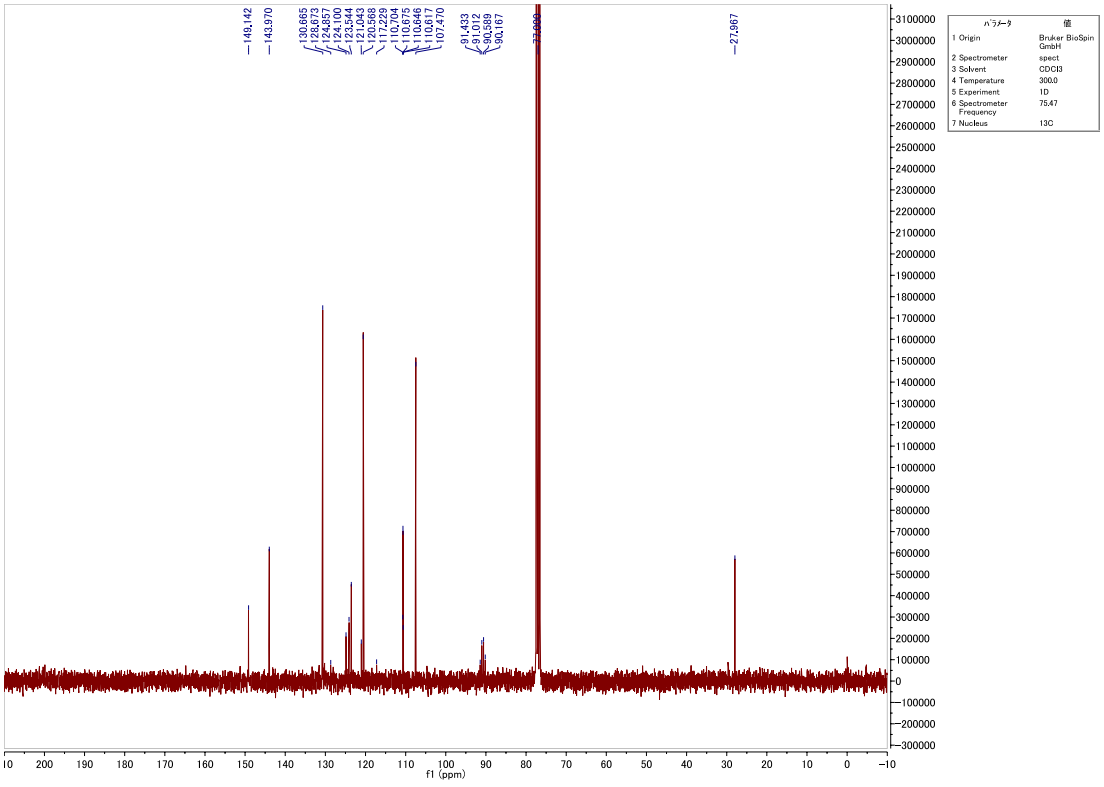
^{13}C NMR (75 MHz, $CDCl_3$) of **6d**



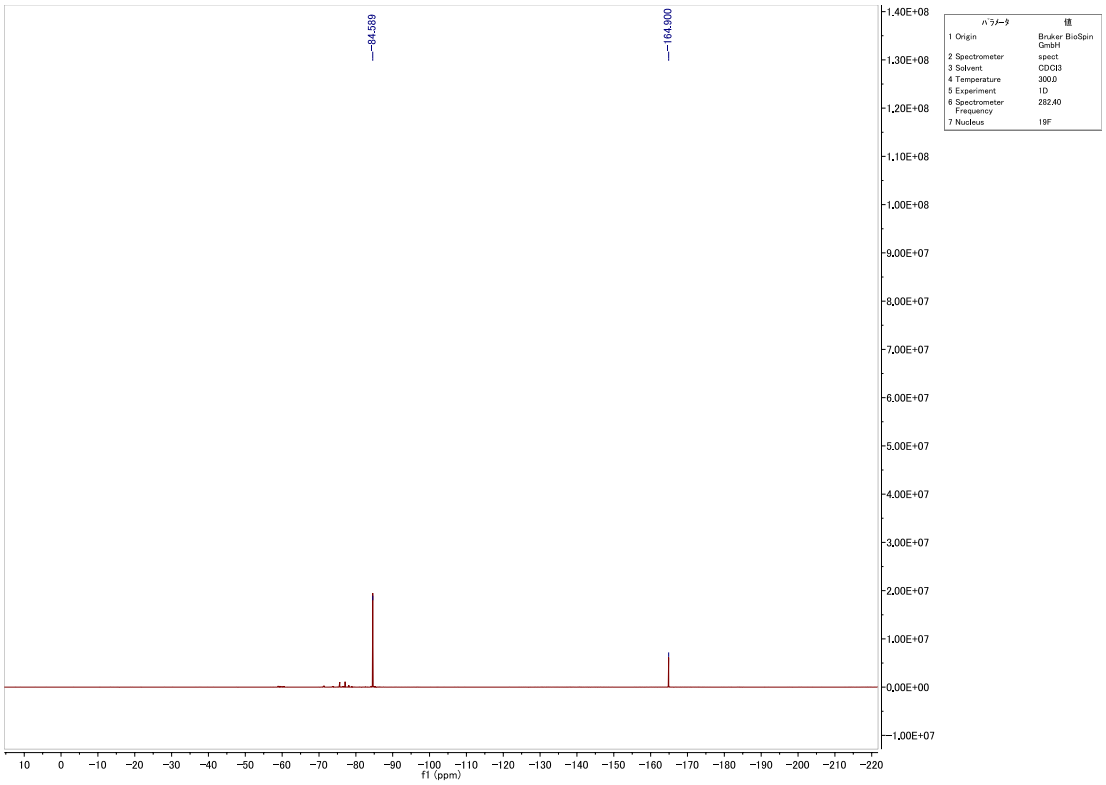
^{19}F NMR (283 MHz, $CDCl_3$) of **6d**



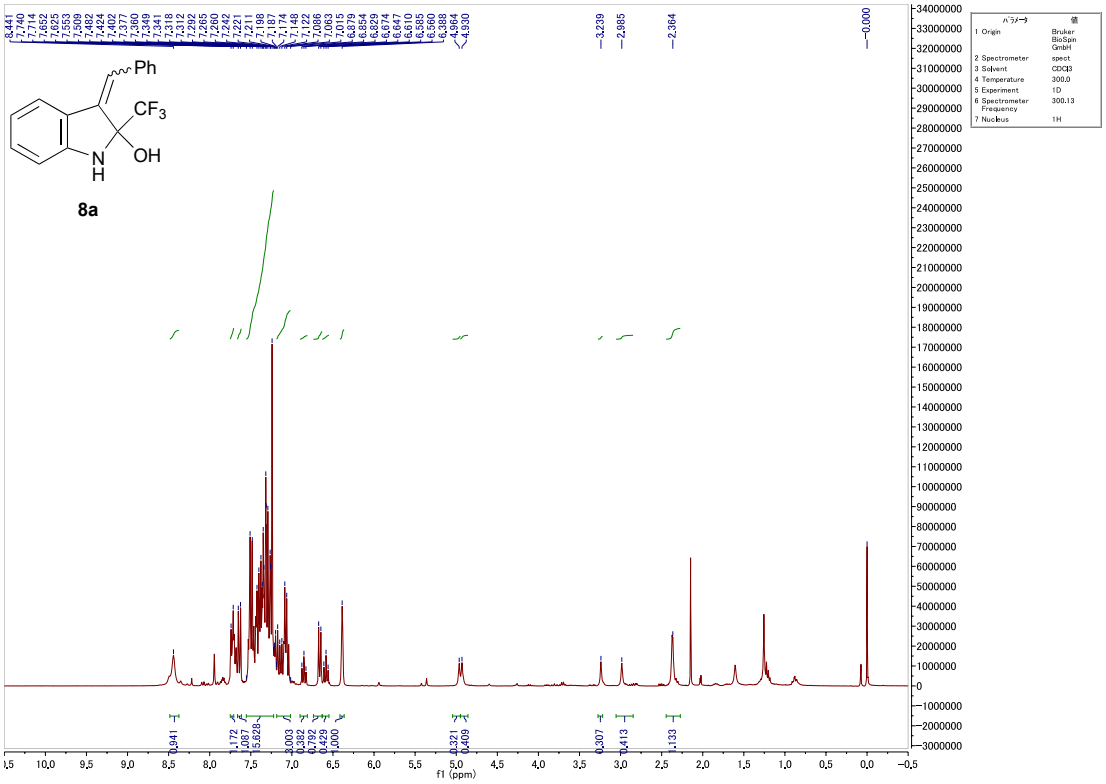
^{1}H NMR (300 MHz, $CDCl_3$) of **6e**



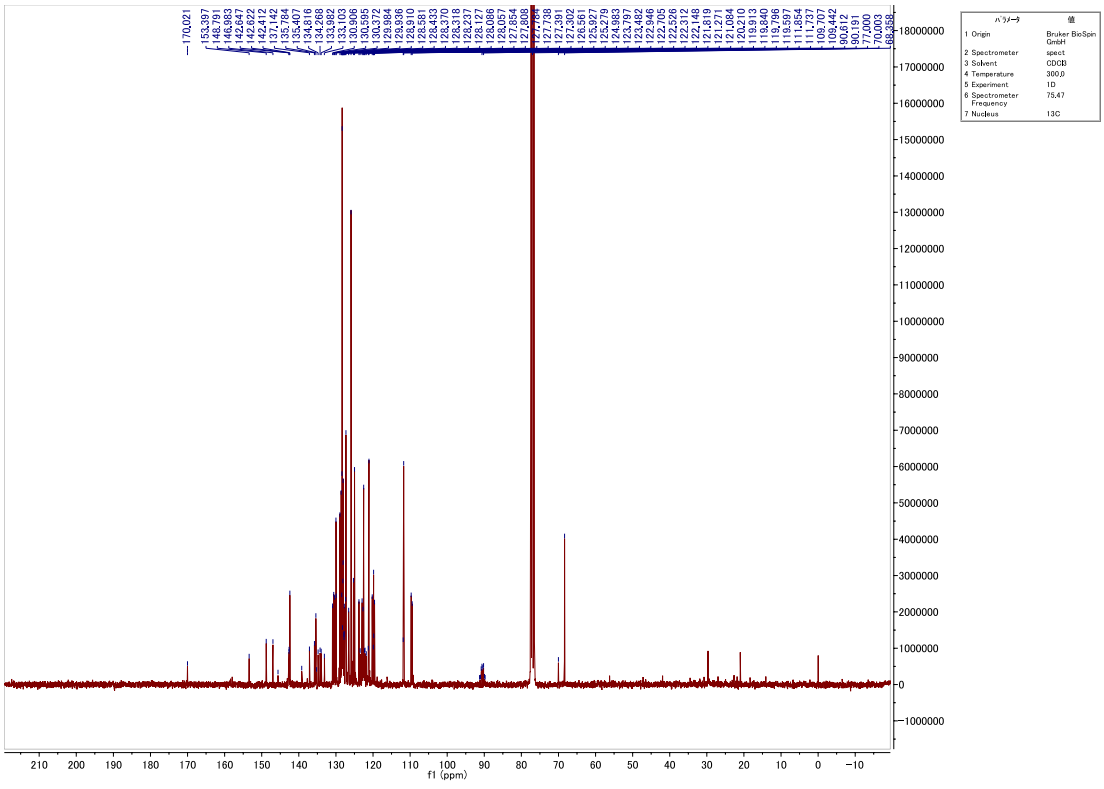
^{13}C NMR (75 MHz, $CDCl_3$) of **6e**



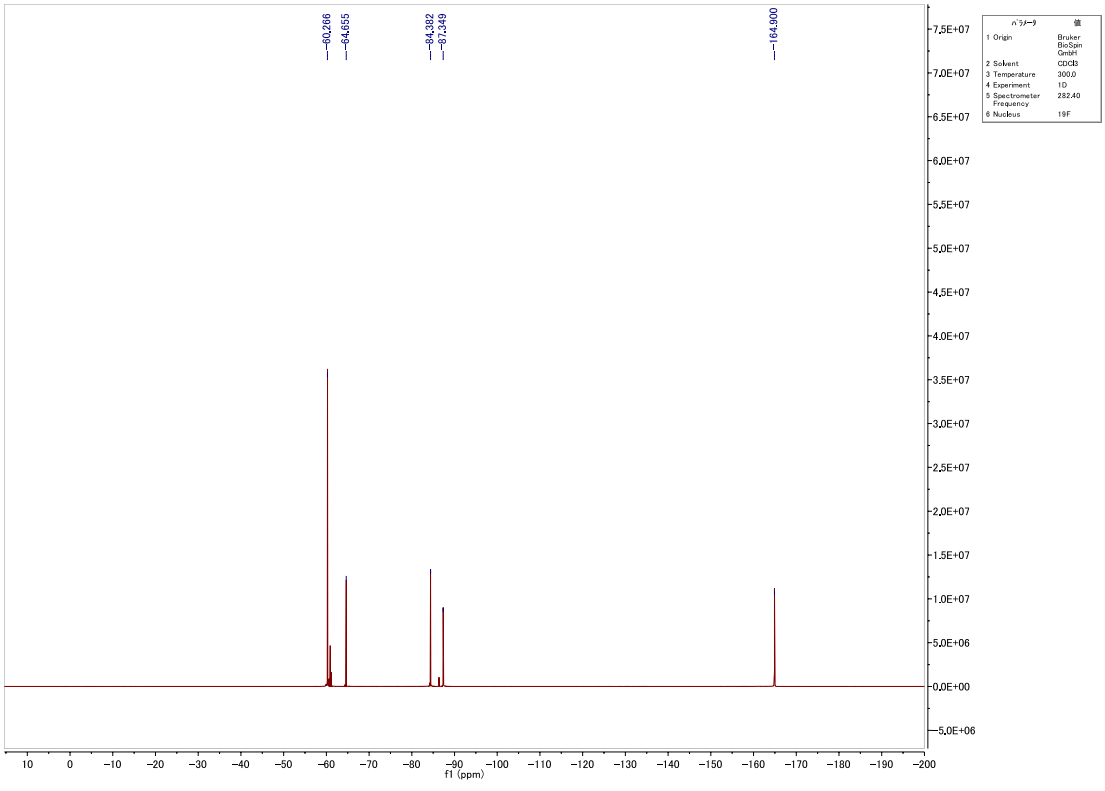
^{19}F NMR (283 MHz, $CDCl_3$) of **6e**



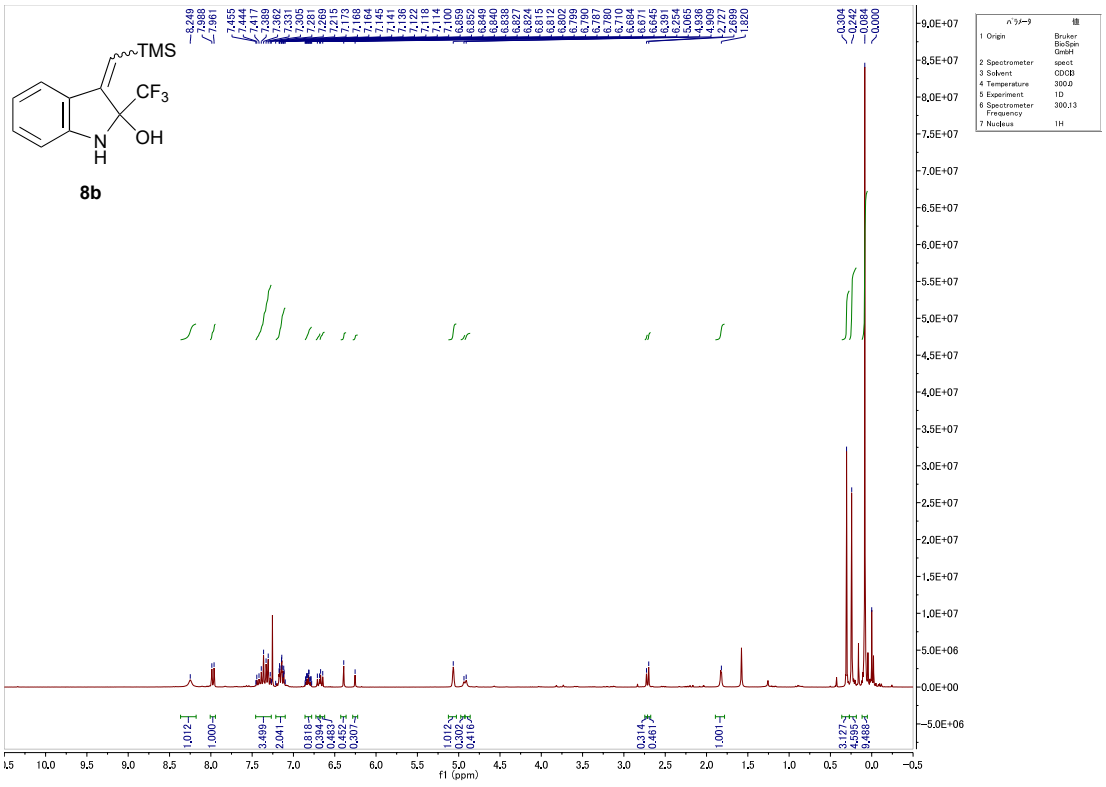
^{1}H NMR (300 MHz, $CDCl_3$) of **8a**



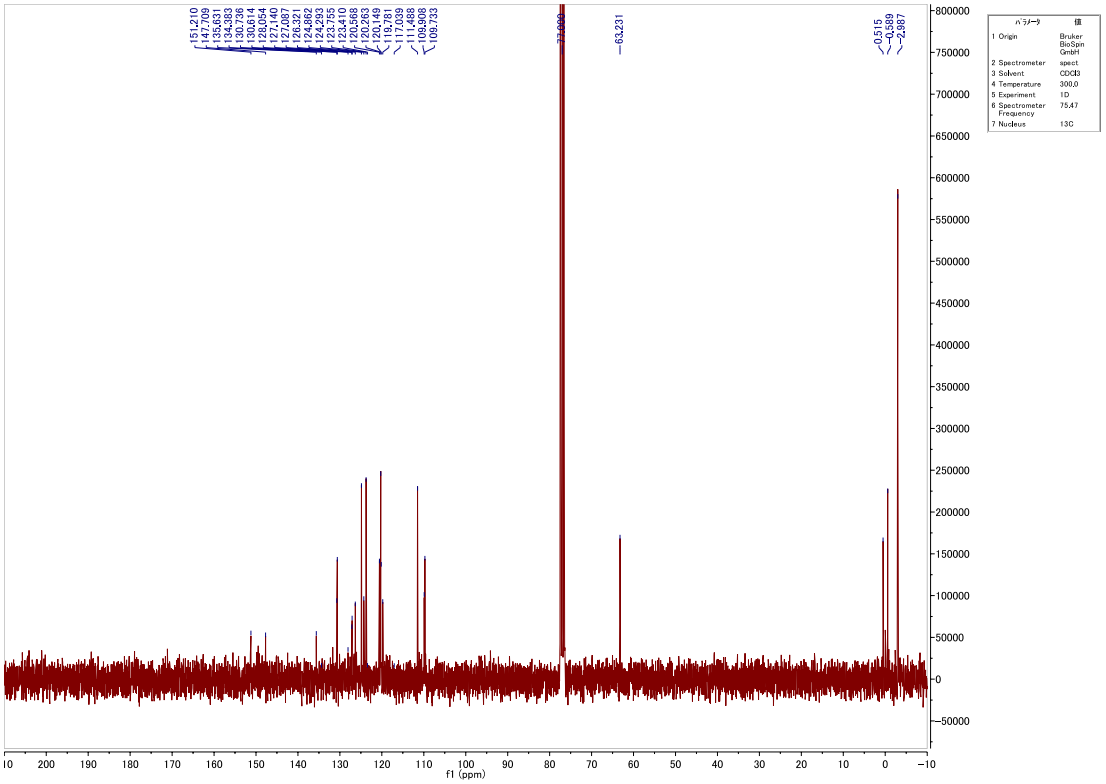
^{13}C NMR (75 MHz, $CDCl_3$) of **8a**



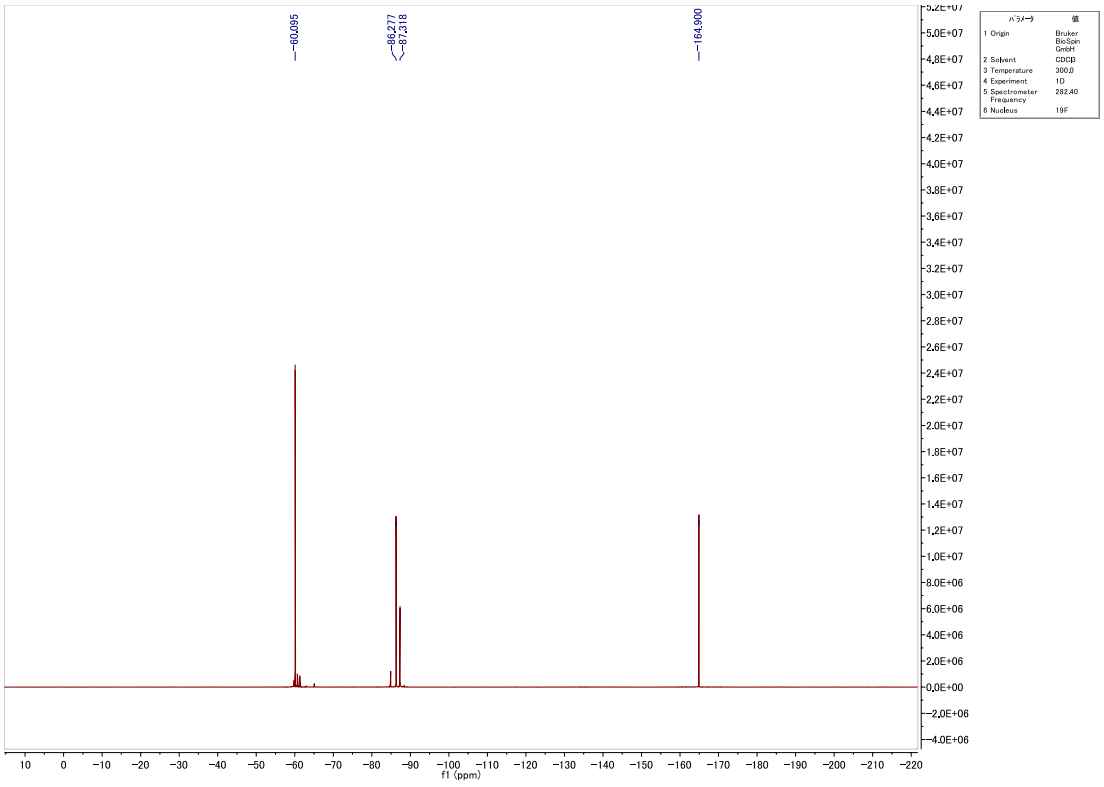
^{19}F NMR (283 MHz, $CDCl_3$) of **8a**



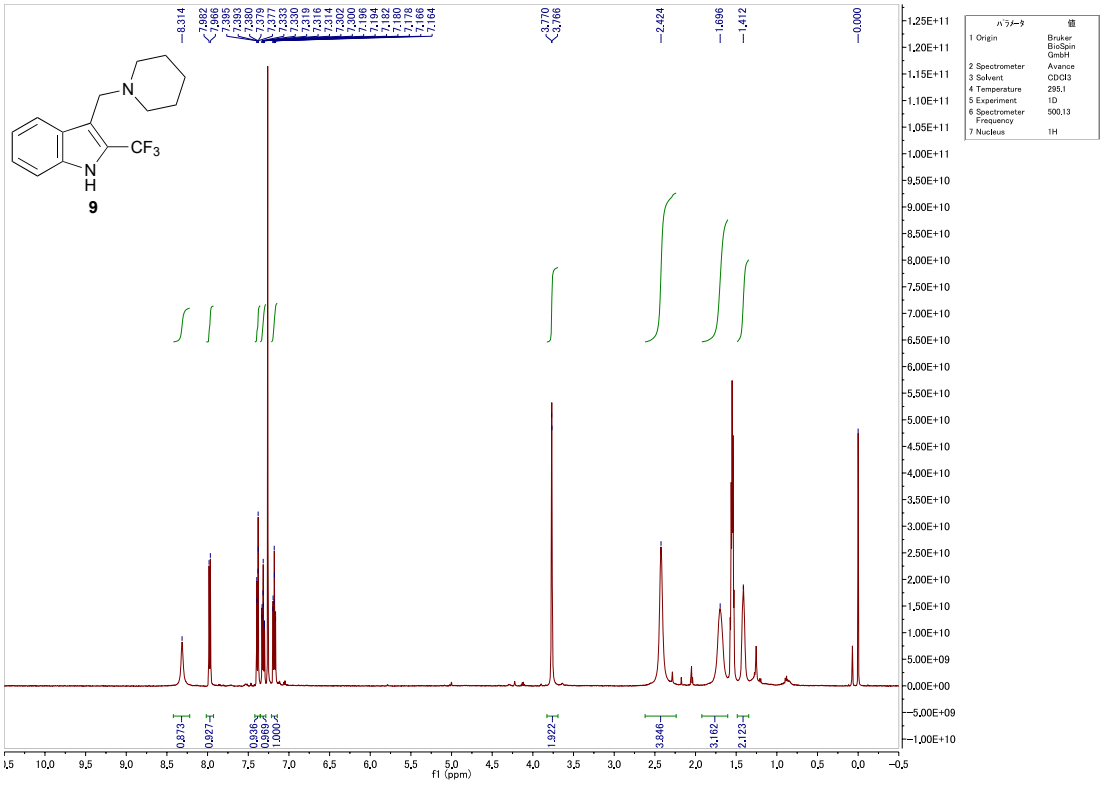
^{1}H NMR (300 MHz, $CDCl_3$) of **8b**



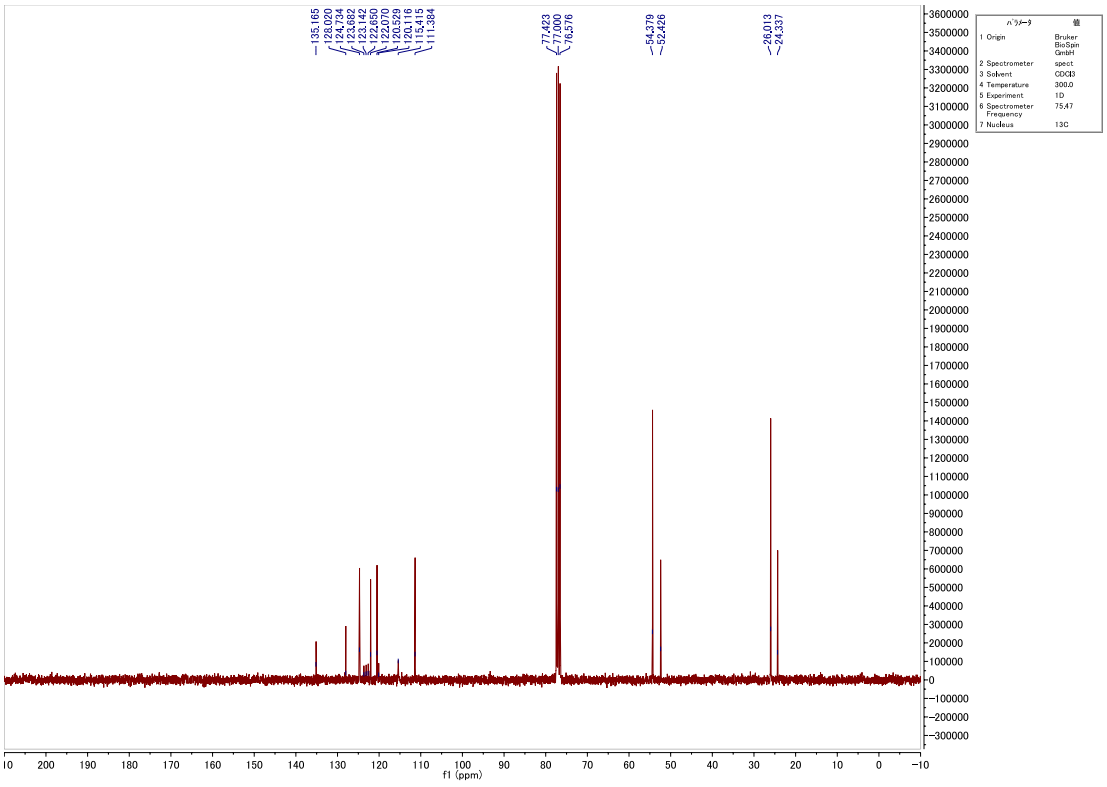
^{13}C NMR (75 MHz, $CDCl_3$) of **8b**



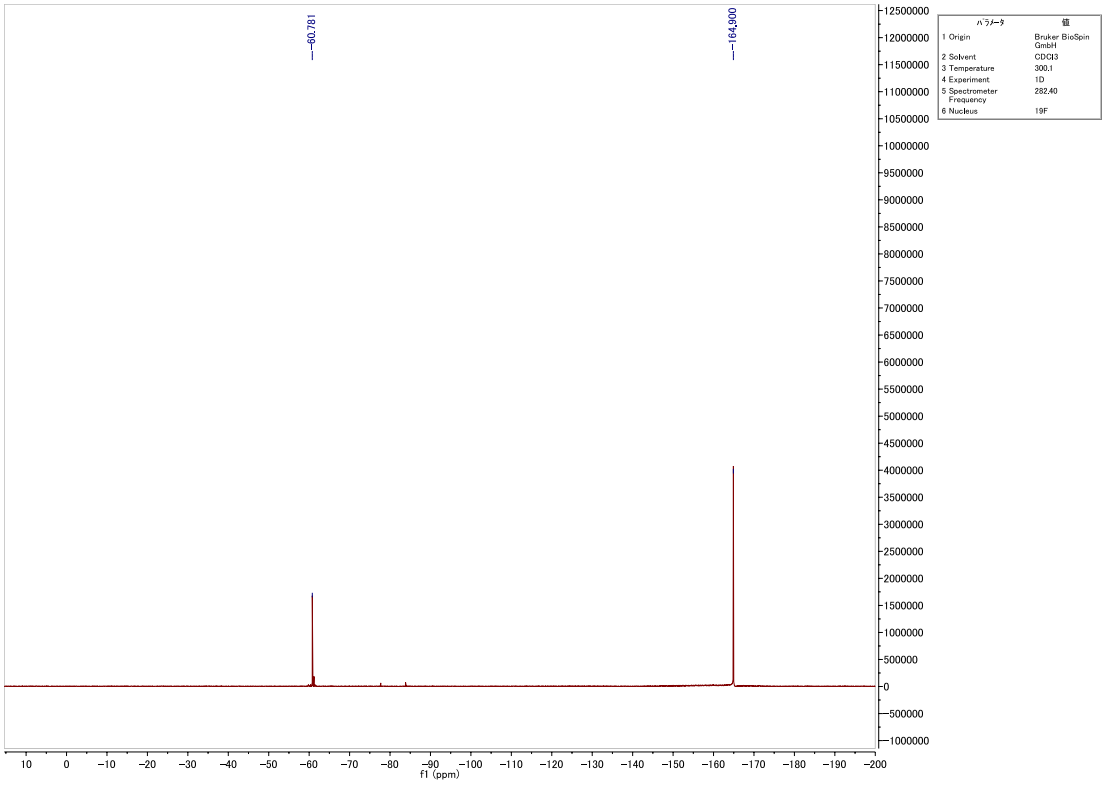
^{19}F NMR (283 MHz, $CDCl_3$) of **8b**



^{1}H NMR (500 MHz, $CDCl_3$) of **9**



^{13}C NMR (75 MHz, $CDCl_3$) of **9**



^{19}F NMR (283 MHz, $CDCl_3$) of **9**