Supporting Information

Grignard-Mediated Rearrangement of Trifluoroacetyl from Dihdro-isoquinoline Enamides to Afford Tertiary Trifluoromethylcarbinols

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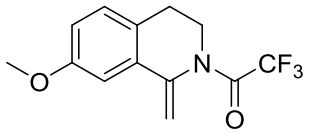
General Information

Unless otherwise noted, all reactions were performed under an atmosphere of nitrogen or argon. Dry tetrahydrofuran (THF), dichloromethane, and dimethylformamide (DMF) were obtained by passing these previously degassed solvents through activated alumina columns. All other reagents were used as received, unless stated otherwise. Reactions were monitored by thin layer chromatography (TLC) on precoated silica gel F254 plate (Merck, art. 5715) and column chromatography was performed using silica gel (Merck, mesh 230-400). Volatile solvents were removed under reduced pressure with a rotary evaporator. ^{1}H and ^{13}C NMR spectra were recorded with Bruker Avance spectrometers operating at 300 and 500 MHz for ^{1}H, 125 MHz for ^{13}C using $CDCl_3$ or other deuterated solvents. Chemical shifts were reported relative to the residual solvent signal (^{1}H NMR: $\delta = 7.26$ ($CDCl_3$); ^{13}C NMR: $\delta = 77.16$ ($CDCl_3$)). NMR data were reported as follows: chemical shift (multiplicity, coupling constants where applicable, number of hydrogens). Splitting is reported with the following symbols: s = singlet, bs = broad singlet, d = doublet, t = triplet, dd = doublet of doublets, ddd = doublet of doublet of doublets, dt = doublet of triplets, hept = heptet, m = multiplet. Melting points were determined in open capillaries using Optimelt apparatus. The IR spectra of compounds were recorded using Smiths FT-IR spectrometer (model: Identify IR). The ν_{max} values expressed in cm^{-1} for the main absorption bands. LC/MS analysis was performed on the Waters Acquity UPLC system with SQ Detector2 via electrospray ionization mode using a mixture of solvents as a mobile phase (Water + 0.1% HCOOH and CH_3CN + 0.1% HCOOH) and C18 column (Acquity UPLC BEH C18 1.7 μm). HRMS was measured with electron impact (EI) ionization or fast atom bombardment (FAB) ionization methods via double focusing mass analyzer (magnetic and electric fields) using JMS-700 (JEOL, Tokyo, Japan).

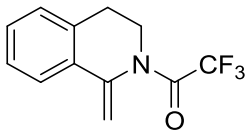
Preparation of Enamides

2,2,2-Trifluoro-1-(7-methoxy-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2a)



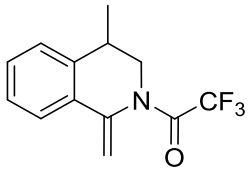
To a solution of 7-methoxy-1-methyl-3,4-dihydroisoquinoline[1] (**1a**, 100 mg, 0.57 mmol) in THF (1.0 mL) was added trifluoroacetic anhydride (TFAA) (0.20 mL, 1.4 mmol) followed by triethylamine (Et_3N) (0.20 mL, 1.4 mmol) at rt and the mixture was stirred at rt for 10 min. The reaction mixture was evaporated under vacuum to get crude mixture which was then purified on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford the title compound **2a** (182 mg, 0.67 mmol, 83%); TLC R_f = 0.85 (EtOAc/hexanes = 1/9); white solid; mp 71.9-74.1 °C; ^{1}H NMR (300 MHz, DMSO-d_6) δ 7.25 (d, J = 1.5 Hz, 1H), 7.13 (d, J = 8.5 Hz, 1H), 6.92 (dd, J = 8.4, 2.5 Hz, 1H), 6.07 (s, br, 1H), 5.34 (s, br, 1H), 3.95 (t, J = 5.3 Hz, 2H), 3.78 (s, 3H), 2.89 (t, J = 6.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 158.4, 155.5 (q, $^2J_{C\text{-}F}$ = 35.8 Hz), 141.1, 132.0, 130.1, 125.7, 116.5 (q, $^1J_{C\text{-}F}$ = 288.3 Hz), 115.6, 108.9, 108.7, 55.3, 44.7, 27.6; IR ν 3044, 3015, 2936, 1688, 1567, 1493, 1432, 1200, 1141, 1032, 913, 882, 798 cm^{-1}; LC/MS 272.0 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}F_3NO_2$ [M$^+$] 271.0820, found 271.0807.

2,2,2-Trifluoro-1-(1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2b)[2]



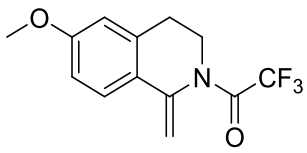
To a solution of 1-methyl-3,4-dihydroisoquinoline (**1b**, 200 mg, 1.38 mmol) in THF (2.0 mL) was added TFAA (0.29 mL, 2.07 mmol) followed by Et_3N (0.38 mL, 2.75 mmol) at 0 °C. The reaction mixture was stirred at rt for 1 h, quenched with H_2O and extracted with EtOAc (2 X 50 mL). The combined organic layers were dried over Na_2SO_4, evaporated under vacuum to get a crude mixture, which was then purified, on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2b** (241 mg, 0.99 mmol, 73%); TLC R_f = 0.88 (EtOAc/hexanes = 1/9); white solid; mp 54.3-56.5 °C (lit.[2] mp 55-56 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.59 (d, J = 6.3 Hz, 1H), 7.21-7.31 (m, 2H), 7.14 (d, J = 6.8 Hz, 1H), 5.77 (s, br, 1H), 5.34 (s, br, 1H), 4.05 (s, br, 2H), 3.01 (t, J = 5.9 Hz, 2H), 2.69 (t, J = 7.5 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.6 (q, $^2J_{C\text{-}F}$ = 34.9 Hz), 141.0, 137.2, 133.4, 131.1, 129.1, 126.9, 124.3, 116.5 (q, $^1J_{C\text{-}F}$ = 288.1 Hz), 108.6, 44.3, 28.5; IR ν 3124, 3010, 2951, 1679, 1634, 1434, 1357, 1137, 1043, 895, 770, cm^{-1}; LC/MS 242.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{12}H_{10}F_3NO$ [M$^+$] 241.0714, found 241.0728.

2,2,2-Trifluoro-1-(4-methyl-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2c)



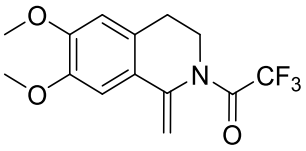
To a round-bottomed flask capped with a rubber septum were added 1,4-dimethyl-3,4-dihydroisoquinoline[3] (**1c**, 200 mg, 1.25 mmol) and a solution of Et_3N (152 mg, 1.51 mmol) in THF (3.0 mL). The mixture was cooled to 0 ℃ under stirring and a solution of TFAA (0.21 mL, 1.5 mmol) in THF (1.0 mL) was added dropwise. The reaction mixture was maintained at rt under stirring and a nitrogen atmosphere for 30 min. Afterwards, the reaction was diluted with EtOAc (10 mL) and washed with distilled water (10 mL). The organic phase was dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure to afford the crude mixture which was purified by silica gel column chromatography using EtOAc/hexane (1/4) as an eluent to afford **2c** (260 mg, 1.02 mmol, 81%); TLC R_f = 0.90 (EtOAc/hexanes = 1/9); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.58 (d, *J* = 7.56 Hz, 1H), 7.32 (t, *J* = 7.3 Hz, 1H), 7.27-7.21 (m, 2H), 5.74 (s, br, 1H), 5.31 (s, br, 1H), 4.02-3.96 (m, 1H), 3.94-3.89 (m, 1H), 3.15 (sextet, *J* = 6.69 Hz, 1H), 1.29 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 155.8 (q, $^2J_{C\text{-}F}$ = 36.3 Hz), 141.29, 138.8, 130.4, 129.3, 128.0, 126.9, 124.2, 116.6 (q, $^1J_{C\text{-}F}$ = 288.4 Hz), 108.0, 50.2, 33.3, 19.9; IR ν 2963, 1687, 1639, 1431, 1297, 1197, 1144, 1032, 965, 898, 770, 751 cm^{-1}; LC/MS 256.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}F_3NO$ [M$^+$] 255.0871, found 255.0865.

2,2,2-Trifluoro-1-(6-methoxy-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2d)



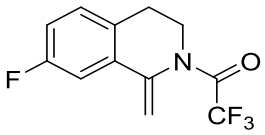
To a solution of 6-methoxy-1-methyl-3,4-dihydroisoquinoline (**1d**, 100 mg, 0.57 mmol) in THF (1.0 mL) was added TFAA (0.08 mL, 0.57 mmol) at 0 ºC. The reaction mixture was stirred at rt for 10 min, quenched with H_2O and extracted with EtOAc (2 x 50 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2d** (120 mg, 0.44 mmol, 78%); TLC R_f = 0.86 (EtOAc/hexanes = 1/9); white solid; mp 68.6-70.6 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.52 (d, *J* = 8.5 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 1H), 6.64 (s, 1H), 5.62 (s, br, 1H), 5.22 (s, br, 1H), 4.03 (s, br, 2H), 3.80 (s, 3H), 2.98 (t, *J* = 5.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.1, 155.6 (q, $^2J_{C\text{-}F}$ = 35.2 Hz), 140.6, 135.0, 125.7, 123.8, 116.5 (q, $^1J_{C\text{-}F}$ = 288.3 Hz), 113.4, 113.2, 106.4, 55.3, 44.2, 28.9; IR ν 3010, 2932, 2835, 1689, 1606, 1495, 1438, 1361, 1279, 1202, 1176, 1133 1037, 898, 877, 807 cm^{-1}; LC/MS 272.2 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}F_3NO_2$ [M$^+$] 271.0820, found 271.0831.

1-(6,7-Dimethoxy-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)-2,2,2-trifluoroethan-1-one (2e)[4]



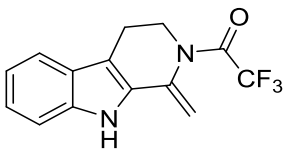
To a solution of 6,7-dimethoxy-1-methyl-3,4-dihydroisoquinoline (**1e**, 205 mg, 1.00 mmol) and pyridine (98.9 mg, 1.25 mmol) in CH_2Cl_2 (3.1 mL) was added dropwise TFAA (263 mg, 1.25 mmol) in CH_2Cl_2 (0.75 mL) at -50 ℃. The reaction mixture was stirred at -50 ℃ for 3 h, quenched with water (5 mL), and extracted with CH_2Cl_2 (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, concentrated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2e** (226 mg, 0.750 mmol, 75%); TLC R_f = 0.88 (EtOAc/hexanes = 1/9); slightly yellow solid; mp 81.5-83.1 ℃ (lit.[9] mp 80 ℃); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (s, 1H), 6.59 (s, 1H), 5.62 (s, br, 1H), 5.25 (s, br, 1H), 4.08-4.01 (m, 2H), 3.91 (s, 3H), 3.89 (s, 3H), 2.94 (t, J = 5.6 Hz, 2H); ^{13}C NMR (125 MHz, CDCl3) δ 155.6 (q, $^1J_{C\text{-}F}$ = 35.8 Hz), 150.1, 148.1, 126.3, 123.4, 116.5 (q, $^2J_{C\text{-}F}$ = 286.5 Hz), 111.1, 106.8, 106.6, 106.5, 56.0, 55.9, 44.6, 28.4; IR ν 3020, 2965, 2935, 1698, 1608, 1515, 1440, 1340, 1279, 1135 1037, 902, 810 cm^{-1}; LC/MS 302.1 [M + H$^+$].

2,2,2-Trifluoro-1-(7-fluoro-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2f)



To a solution of 7-Fluoro-1-methyl-3,4-dihydroisoquinoline (**1f**, 200 mg, 1.23 mmol) in THF (2.0 mL) was added Et_3N (0.43 mL, 3.06 mmol) followed by TFAA (0.26 mL, 1.84 mmol) at 0 ºC and stirred for 10 min at rt. The mixture was quenched with H_2O and extracted with EtOAc (2 x 200 mL). The combined organic layer was dried over Na_2SO_4 and concentrated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2f** (241 mg, 0.93 mmol, 76%); TLC R_f = 0.86 (EtOAc/hexanes = 1/9); white solid; mp 50.3-53.1 ℃; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.26-7.29 (m, 1H), 7.09-7.14 (m, 1H), 6.95-7.02 (m, 1H), 5.76 (s, br, 1H), 5.41 (s, br, 1H), 4.03 (s, br, 2H), 2.97 (t, J = 6.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.5 (d, $^1J_{C\text{-}F}$ = 245.0 Hz), 155.4 (q, $^2J_{C\text{-}F}$ = 34.9 Hz), 140.2, 132.6, 130.7, 129.1, 116.4 (d, $^2J_{C\text{-}F}$ = 21.1 Hz), 116.4 (q, $^2J_{C\text{-}F}$ = 288.2 Hz), 110.8 (d, $^2J_{C\text{-}F}$ = 23.2 Hz), 109.6, 44.3, 27.8; IR ν 3071, 3030, 2947, 1684, 1610, 1578, 1488, 1431, 1316, 1270, 1196, 1151, 931, 893, 752 cm^{-1}; LC/MS 260.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{12}H_9F_4NO$ [M$^+$] 259.0620, found 259.0624.

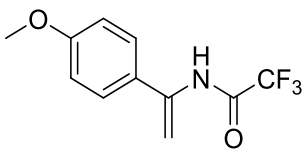
2,2,2-Trifluoro-1-(1-methylene-1,3,4,9-tetrahydro-2*H*-pyrido[3,4-*b*]indol-2-yl)ethan-1-one (2g)[5]



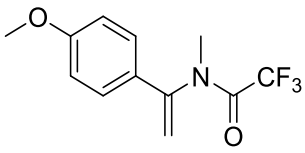
To a solution of 1-methyl-4,9-dihydro-3*H*-pyrido[3,4-*b*]indole[6] (**1g**, 100 mg, 0.54 mmol) in THF (1.0 mL) was added TFAA (0.12 mL, 0.81 mmol) followed by Et_3N (0.19 mL, 1.36 mmol) at 0 °C. The reaction mixture was stirred at rt for 30 min, quenched with H_2O, and extracted with EtOAc (2 x 100 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (2/1) as an eluent to afford **2g** (85 mg, 0.3 mmol, 56%); TLC R_f = 0.51 (EtOAc/hexanes = 2/1); white solid; mp 154.2-156.8 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.38 (s, br, 1H), 7.45 (d, *J* = 7.7 Hz, 1H), 7.29 (d, *J* = 8.0 Hz, 1H), 7.21 (t, *J* = 7.3 Hz, 1H), 7.10 (t, *J* = 7.7 Hz, 1H), 5.42 (s, br, 2H), 4.06-4.14 (m, 2H), 2.91 (s, br, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 136.9, 128.8, 126.5, 124.1 120.4, 119.1, (q, J_{C-F} = 286.3 Hz), 111.2, 103.9, 46.4, 22.2; IR ν 3329, 3243, 3101, 1700, 1633, 1559, 1418, 1334, 1184, 1120, 1067, 727 cm^{-1}; LC/MS 281.2 [M + H$^+$], 561.3 [2M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{14}H_{11}F_3N_2O$ [M$^+$] 280.0823, found 280.0832

2,2,2-Trifluoro-*N*-(1-(4-methoxyphenyl)vinyl)-*N*-methylacetamide (2h)[7]

[Step 1] To a solution of (*E*)-1-(4-methoxyphenyl)ethan-1-one oxime (500 mg, 3.03 mmol) and TFAA (0.51 mL, 3.63 mmol) in DMF (5.0 mL) was added Fe powder (507 mg, 9.08 mmol), and then the reaction was initiated by adding catalytic amount of TMSCl under nitrogen. The reaction mixture was stirred at rt for 4 h, quenched with H_2O, and extracted with EtOAc (2 x 150 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/3) as an eluent to afford 2,2,2-trifluoro-*N*-(1-(4-methoxyphenyl)vinyl)acetamide[8] (223 mg, 0.91 mmol, 30%); TLC R_f = 0.52 (EtOAc/hexanes = 2/8); white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.53 (s, 1H), 7.32 (d, *J* = 8.9 Hz, 1H), 6.91 (d, *J* = 8.1 Hz, 1H), 5.85 (s, 1H), 5.27 (s, 1H), 3.82 (s, 3H); LC/MS 246.1 [M + H$^+$].

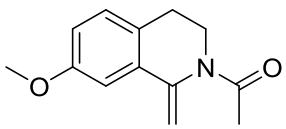


[Step 2] To a solution of above 2,2,2-trifluoro-*N*-(1-(4-methoxyphenyl)vinyl)acetamide (100 mg, 0.41 mmol) in THF (1.0 mL) was added NaH (24.4 mg, 0.61 mmol) at 0 °C. The mixture was stirred at 0 °C for 10 min and MeI (51μL, 0.80 mmol) was added. The reaction mixture was stirred at rt for 12 h, quenched with H_2O, and extracted with EtOAc (2 x 50 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2h** (38 mg, 0.15 mmol, 36%); TLC R_f



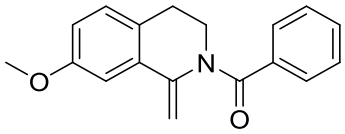
= 0.73 (EtOAc/hexanes = 2/8); white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.1 Hz, 2H), 6.91 (d, *J* = 8.1 Hz, 2H), 5.62 (s, 1H), 5.19 (s, 1H), 3.83 (s, 3H), 3.11 (s, 3H); LC/MS 260.3 [M + H^+].

1-(7-Methoxy-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)ethan-1-one (2i)



To a solution of 7-methoxy-1-methyl-3,4-dihydroisoquinoline (**1a**, 100 mg, 0.57 mmol) in THF (1.0 mL) was added Ac_2O (146 mg, 1.43 mmol) followed by Et_3N (0.19 mL, 1.43 mmol) at rt and stirred for 5 h. The reaction mixture was evaporated under vacuum to get a crude product which was then purified on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2i** (108 mg, 0.49 mmol, 87%); TLC R_f = 0.70 (EtOAc/hexanes = 1/9); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.15 (d, *J* = 2.7 Hz, 1H), 7.08 (d, *J* = 8.4 Hz, 1H), 7.86 (dd, *J* = 8.4, 2.7 Hz, 1H), 5.75 (s, 1H), 5.08 (s, br, 1H), 3.99 (t, *J* = 6.3 Hz, 2H), 3.85 (s, 3H), 2.86 (t, *J* = 6.3 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 203.5, 171.3, 157.8, 139.1, 132.9, 130.4, 117.1, 115.1, 100.0, 55.5, 42.3, 31.3, 29.8, 22.7; IR ν 3288, 2935, 2835, 1677, 1650, 1608, 1434, 1356, 1267, 1216, 1199, 1039, 728 cm^{-1}; LC/MS 217.8 [M + H^+]. HRMS (EI) *m*/*z* calcd for $C_{13}H_{15}NO_2$ [M^+] 217.1103, found 217.1091

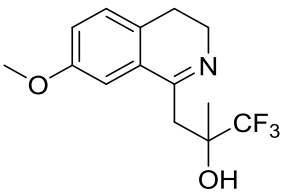
7-Methoxy-1-methylene-3,4-dihydroisoquinolin-2(1*H*)-yl)(phenyl)methanone (2j)



To a solution of 7-methoxy-1-methyl-3,4-dihydroisoquinoline (**1a**, 300 mg, 1.71 mmol) in THF (3.0 mL) was added Et_3N (0.59 mL, 4.28 mmol) followed by addition of benzoyl chloride (0.24 mL, 2.05 mmol) at 0 ºC and stirred at rt for 30 min. The reaction mixture was quenched with H_2O and extracted with EtOAc (2 x 50 mL). The organic layers were washed with H_2O and saturated NaCl (aq). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/4) as an eluent to afford **2j** (421 mg, 1.51 mmol, 88%); TLC R_f = 0.73 (EtOAc/hexanes = 1/9); yellow oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.45 (d, *J* = 7.8 Hz, 2H), 7.28-7.42 (m, 3H), 7.15 (d, *J* = 8.4 Hz, 1H), 7.08 (d, *J* = 2.1 Hz, 1H), 6.90 (dd, *J* = 8.4, 2.1 Hz, 1H), 5.42 (s, 1H), 5.55 (s, 1H), 4.13 (t, *J* = 6.0 Hz, 2H), 3.85 (s, 3H), 3.01 (t, *J* = 6.0 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.5, 42.8, 55.4, 107.4, 108.9, 115.1, 126.9, 127.9, 128.2, 129.9, 130.2, 132.2, 136.1, 142.9, 158.3, 169.9; IR ν 3055, 2930, 2833, 1719, 1633, 1571, 1490, 1445, 1382, 1291, 1218, 1036, 887, 788, 697 cm^{-1}; LC/MS 280.1 [M + H^+]; HRMS (EI) *m*/*z* calcd for $C_{18}H_{17}NO_2$ [M^+] 279.1259, found 279.1252

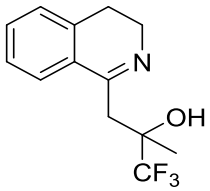
Synthesis of Trifluoromethylcarbinols

1,1,1-Trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4a)



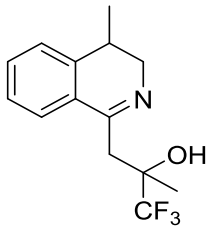
To a solution of **2a** (50.0 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in diethyl ether (0.09 mL, 0.27 mmol) at rt. The reaction mixture was stirred at rt for 10 min and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford the title compound **4a** (52 mg, 0.181 mmol, 98%); TLC R_f = 0.50 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, br, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 6.98-6.95 (m, 2H), 3.86 (s, 3H), 3.73-3.65 (m, 2H), 3.15 (d, *J* = 16.2 Hz, 1H), 2.82 (d, *J* = 16.5 Hz, 1H), 2.68 (t, *J* = 7.5 Hz, 2H), 1.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 24.8, 35.3, 46.1, 55.5, 73.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 110.9, 116.4, 124.7, 126.1 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.6, 129.4, 129.7, 158.7, 166.2; IR ν 3220, 2992, 2947, 2838, 1733, 1605, 1568, 1464, 1431, 1281, 1137, 1108, 1082 cm^{-1}; LC/MS 287.7 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{14}H_{16}F_3NO_2$ [M$^+$] 287.1133, found 287.1145

3-(3,4-Dihydroisoquinolin-1-yl)-1,1,1-trifluoro-2-methylpropan-2-ol (4b)



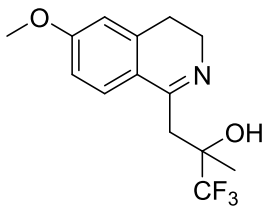
To a solution of **2b** (50.0 mg, 0.21 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in diethyl ether (0.10 mL, 0.31 mmol) at rt. The reaction mixture was stirred at rt for 10 min and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4b** (50 mg, 0.2 mmol, 94%); TLC R_f = 0.53 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.07 (s, br, 1H), 7.38-7.45 (m, 2H), 7.36 (d, *J* = 7.4 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 3.60-3.75 (m, 2H), 3.17 (d, *J* = 16.4 Hz, 1H), 2.81 (d, *J* = 16.4 Hz, 1H), 2.73 (t, *J* = 7.4 Hz, 2H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.8, 25.7, 35.3, 45.7, 73.5 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 124.7, 126.3 (q, $^1J_{C\text{-}F}$ = 284 Hz), 127.3, 127.9, 131.5, 137.4, 166.4; IR ν 3375, 3056, 2980, 2759, 1617, 1569, 1294, 1278, 1141, 1093, 865, 758 cm^{-1}; LC/MS 258.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{14}F_3NO$ [M$^+$] 257.1027, found 257.1034.

1,1,1-Trifluoro-2-methyl-3-(4-methyl-3,4-dihydroisoquinolin-1-yl)propan-2-ol (4c)



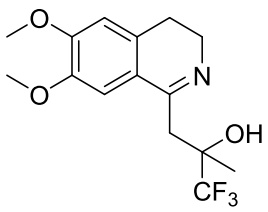
To solution of **2c** (200 mg, 0.78 mmol) in THF (5 mL) was added 3.0 M MeMgBr in Et_2O (0.39 mL, 1.17 mmol) at rt and stirred for 30 min. The reaction mixture was treated with sat. NH_4Cl (aq) solution and extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product obtained was purified through column chromatography using EtOAC/hexanes (1/3) as an eluent to afford **4c** (180 mg, 0.66 mmol, 85%); TLC R_f = 0.58 (EtOAc/hexanes = 2/8); white solid. mp 83.3-85.0 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.19 (s, br, 1H), 7.50-7.48 (m, 2H), 7.38-7.29 (m, 2H), 3.81-3.71 (s, 1H), 3.59-3.46 (s, 1H), 3.24-3.16 (m, 1H), 2.94-2.82 (m, 2H), 1.49 (s, 3H), 1.27 (dd, *J* = 7.0, 2.4 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 17.3, 17.5, 22.7, 22.9, 29.6, 29.7, 35.1, 35.2, 52.5, 52.6, 73.7 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 124.7, 124.7, 126.0, 126.1, 126.4 (q, $^1J_{C\text{-}F}$ = 284 Hz), 126.9, 127.0, 127.9, 127.9, 131.8, 142.3, 142.4, 166.2; IR ν 3067, 2846, 2777, 1618, 1570, 1464, 1276, 1137, 1089, 1015, 961, 748 cm^{-1}; LC/MS 272.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{14}H_{16}F_3NO$ [M$^+$] 271.1184, found 271.1183

1,1,1-Trifluoro-3-(6-methoxy-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4d)



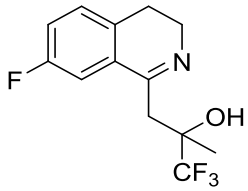
To a solution of **2d** (50.0 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in Et_2O (0.09 mL, 0.28 mmol) at rt and stirred for 10 min. The reaction mixture was quenched with saturated NH_4Cl (aq), extracted with EtOAc (2 x 25 mL), and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4d** (50 mg, 0.2 mmol, 96%); TLC R_f = 0.56 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (d, *J* = 8.5 Hz, 1H), 6.80 (d, *J* = 8.7 Hz, 1H), 6.72 (s, 1H), 3.84 (s, 3H), 3.62-3.69 (m, 2H), 3.10 (d, *J* = 16.2 Hz, 1H), 2.75 (d, *J* = 16.5 Hz, 1H), 2.70 (t, *J* = 7.3 Hz, 2H), 1.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.8, 26.3, 35.2, 45.5, 55.4, 73.5 (q, $^2J_{C\text{-}F}$ = 27.8 Hz), 112.2, 113.3, 122.4, 126.3 (q, $^1J_{C\text{-}F}$ = 284 Hz), 126.7, 139.8, 161.8, 165.9; IR ν 3390, 2952, 2765, 2580, 2244, 1604, 1568, 1315, 1251, 1137, 1093, 1026, 961, 726 cm^{-1}; LC/MS 287.9 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{14}H_{16}F_3NO_2$ [M$^+$] 287.1133, found 287.1127.

3-(6,7-Dimethoxy-3,4-dihydroisoquinolin-1-yl)-1,1,1-trifluoro-2-methylpropan-2-ol (4e)



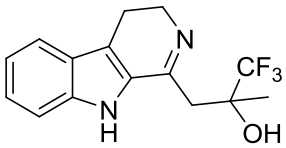
To solution of **2e** (205 mg, 0.68 mmol) in THF (5 mL) was added 3.0 M MeMgBr in Et_2O (0.33 mL, 0.99 mmol) at rt and stirred for 30 min. The reaction mixture was quenched with saturated NH_4Cl (aq) solution and extracted with EtOAc (2 X 20 mL). The organic layers were washed with water followed by saturated brine solution. The combined organic layers were dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude mixture was purified through column chromatography using EtOAC/hexanes (1/1) as an eluent to afford **4e** (180 mg, 0.57 mmol, 83%); TLC R_f = 0.60 (EtOAc/hexanes = 2/8); white solid; mp 107.2-109.0 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.23 (s, br, 1H), 6.92 (s, 1H), 6.72 (s, 1H), 3.94 (s, 3H), 3.93 (s, 3H), 3.74-3.58 (m, 1H), 3.15-3.09 (m, 1H), 2.79-2.73 (m, 1H), 2.67 (t, J = 7.65 Hz, 2H), 1.48 (s, 3H); ^{13}C NMR ($CDCl_3$, 125 MHz) δ 22.7, 25.4, 35.3, 45.6, 56.0, 56.3, 73.5 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 108.3, 110.5, 121.7, 126.3, (q, $^1J_{C\text{-}F}$ = 284 Hz), 131.4, 147.7, 151.6, 165.7.; IR ν 3095, 2973, 2781, 1608, 1567, 1465, 1363, 1268, 1211, 1140, 1093, 1031, 967, 865,784 cm^{-1}; LC/MS 318.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{15}H_{18}F_3NO_3$ [M$^+$] 317.1239, found 317.1237

1,1,1-Trifluoro-3-(7-fluoro-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4f)



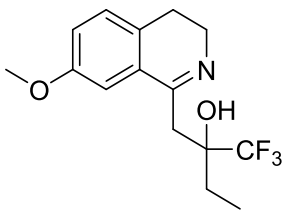
To a solution of **2f** (80.0 mg, 0.31 mmol) in THF (1.2 mL) was added 3.0 M MeMgBr in Et_2O (0.15 mL, 0.46 mmol) at rt and stirred for 15 min. The reaction mixture was quenched with NH_4Cl (aq) and extracted with EtOAc (2 X 100 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4f** (91 mg, 0.3 mmol, 86%); TLC R_f = 0.52 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.83 (s, br, 1H), 7.07-7.21 (m, 3H), 3.66-3.73 (m, 2H), 3.12 (d, J = 16.4 Hz, 1H), 2.76 (d, J = 16.4 Hz, 1H), 2.69 (t, J = 7.5 Hz, 2H), 1.46 (d, J = 0.5 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.8, 35.5, 45.9, 73.6 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 111.8 (d, J = 22.5 Hz), 118.2 (d, J = 21.1 Hz), 126.2 (q, $^1J_{C\text{-}F}$ = 284 Hz), 129.2 (d, J = 7.5 Hz), 129.9 (d, J = 6.5 Hz), 132.9 (d, J = 3.0 Hz), 161.7 (d, J = 244.4 Hz), 165.4; IR ν 3317, 2944, 1626, 1578, 1491, 1264, 1147, 1102, 1027, 887, 868,747 cm^{-1}; LC/MS 276.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{13}F_4NO$ [M$^+$] 275.0933, found 275.0929.

3-(4,9-Dihydro-3*H*-pyrido[3,4-*b*]indol-1-yl)-1,1,1-trifluoro-2-methylpropan-2-ol (4g)



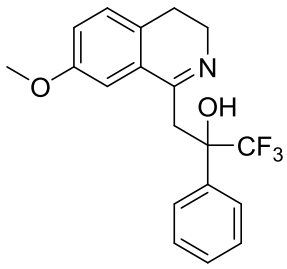
To a solution of **2g** (50 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in diethyl ether (0.18 mL, 0.53 mmol) at rt. The reaction mixture was stirred at same temperature for 10 min and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (25 mL x 2) and washed with H_2O. The combined organic layer was dried over Na_2SO_4 and evaporated under vacuum to get a crude product which was purified through silica gel column chromatography using EtOAc/hexanes (2/1) as an eluent to afford **4g** (42 mg, 0.14 mmol, 80%); TLC R_f = 0.3 (EtOAc/hexanes = 2/1); white solid; mp 144.1-146.8 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.40 (s, br, 1H), 7.60 (d, *J* = 7.9 Hz, 1H), 7.29 (d, *J* = 8.2 Hz, 1H), 7.21 (t, *J* = 7.1 Hz, 1H), 7.10 (t, *J* = 7.4 Hz, 1H), 5.42 (s, br, 2H), 4.06-4.14 (m, 2H), 2.91 (s, br, 2H); ^{13}C NMR (125 MHz, DMSO-d_6) δ 18.9, 21.5, 47.7, 73.2 (q, $^2J_{C\text{-}F}$ = 27.4 Hz), 112.9, 116.1, 120.2, 120.2, 124.6, 125.1, 126.9 (q, $^1J_{C\text{-}F}$ = 284.9 Hz), 129.1, 137.2, 159.1; IR ν 3405, 3105, 2959, 2720, 2510, 1602, 1543, 1369, 1281, 1134, 1092, 863, 727 cm^{-1}; LC/MS 297.11 [M + H$^+$], 593.3 [2M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{15}H_{15}F_3N_2O$ [M$^+$] 296.1136, found 296.1134

1,1,1-Trifluoro-2-((7-methoxy-3,4-dihydroisoquinolin-1-yl)methyl)butan-2-ol (4h)



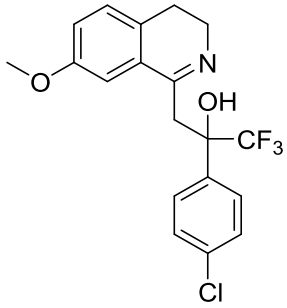
To a solution of compound **2a** (50.0 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M EtMgBr in diethyl ether (0.09 mL, 0.28 mmol) at rt. The reaction mixture was stirred at rt for 10 min and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford the title compound **4h** (52 mg, 0.2 mmol, 95%); TLC R_f = 0.53 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.24 (s, br, 1H), 7.15 (d, *J* = 8.1 Hz, 1H), 6.95-7.01 (m, 2H), 3.86 (s, 3H), 3.61-3.71 (m, 2H), 3.07 (d, *J* = 16.2 Hz, 1H), 2.82 (d, *J* = 16.2 Hz, 1H), 2.67 (t, *J* = 7.5 Hz, 2H), 1.86-1.95 (m, 1H), 1.59-1.78 (m, 1H), 1.06 (t, *J* = 7.2 Hz, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.5, 24.8, 28.4, 32.2, 46.0, 55.5, 75.7 (q, $^2J_{C\text{-}F}$ = 26.4 Hz), 111.1, 116.3, 124.7, 126.8 (q, $^1J_{C\text{-}F}$ = 286 Hz), 128.6, 129.4, 129.6, 130.2, 158.7, 166.8; IR ν 3125, 2939, 2836, 1607, 1571, 1461, 1428, 1281, 1262, 1139, 1108, 1044, 987, 814 cm^{-1}; LC/MS 302.0 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{15}H_{18}F_3NO_2$ [M$^+$] 301.1290, found 301.1292.

1,1,1-Trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)-2-phenylpropan-2-ol (4i)



To a solution of compound **2a** (50.0 mg, 0.18 mmol) in THF (1.0 mL) was added PhMgBr (0.28 mL, 0.28 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO4 and evaporated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford the title compound **4i** (41 mg, 0.12 mmol, 64%); TLC R_f = 0.57 (EtOAc/hexanes = 2/8); white solid; mp 74.3-75.2 ℃; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.2 Hz, 2H), 7.25-7.35 (m, 3H), 7.06 (d, *J* = 8.2 Hz, 1H), 7.02 (d, *J* = 2.3 Hz, 1H), 6.92 (dd, *J* = 8.2, 2.3 Hz, 1H), 3.83 (s, 3H), 3.42-3.55 (m, 4H), 2.32-2.58 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.7, 35.02, 45.9, 55.6, 76.6 (q, $^2J_{C\text{-}F}$ = 27.9 Hz), 110.9, 116.3, 125.3 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.1, 128.2, 128.6, 129.3, 129.7, 139.1, 158.7, 165.9; IR ν 3020, 2999, 2932, 2832, 1602, 1500, 1444, 1309, 1252, 1140, 1074, 1014, 963, 899, 841, 824 cm^{-1};LC/MS 350.1 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{19}H_{18}F_3NO_2$ [M$^+$] 349.1290, found 349.1297

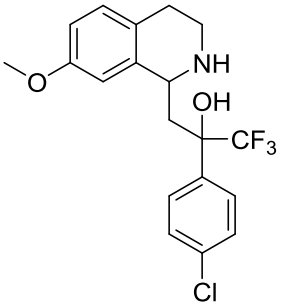
2-(4-Chlorophenyl)-1,1,1-trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)propan-2-ol (4j)



To a solution of compound **2a** (50 mg, 0.18 mmol) in THF (1.0 mL) was added 1.0 M 4-chlorophenylphenyl magnesium bromide in diethyl ether (0.28 mL, 0.28 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford unstable **4j** (43 mg, 0.1 mmol, 61%); TLC R_f = 0.55 (EtOAc/hexanes = 2/8); white solid; mp 104.9-105.8 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.59 (s, br, 1H), 7.58 (d, *J* = 8.2 Hz, 2H), 7.31 (d, *J* = 8.2 Hz, 2H), 7.10 (d, *J* = 8.2 Hz, 1H), 7.04 (s, 1H), 6.97 (d, *J* = 8.2 Hz, 1H), 3.88 (s, 3H), 3.53-3.60 (m, 2H), 3.43 (q, *J* = 16.4 Hz, 2H), 2.54-2.61 (m, 1H), 2.38-2.44 (m, 1H); IR ν 3314, 3117, 2942, 2831, 1608, 1499, 1244, 1154, 1091, 1033, 1011, 816 cm^{-1}; LC/MS 383.9 [M + H$^+$]; HRMS (FAB+) *m*/*z* calcd for $C_{19}H_{18}ClF_3NO_2$ [M + H$^+$] 384.0978, found 384.0992

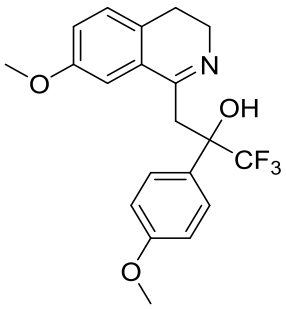
Note: Due to unstable nature of trifluoromethylcarbinols **4j, 4k and **4m** at rt, for the purpose of NMR confirmation these compounds were promptly reduced using $NaBH_4$ to obtain diastereomeric mixtures of stable 1,3-aminoalcohols in good yields.*

2-(4-Chlorophenyl)-1,1,1-trifluoro-3-(7-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-ol (5j)



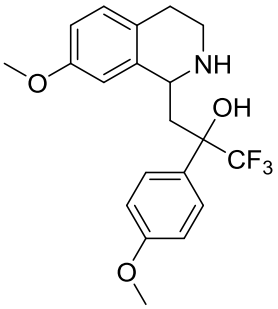
To a solution of **4d** (40 mg, 0.10 mmol) in MeOH (1.0 mL) was added $NaBH_4$ (10 mg, 0.26 mmol) and stirred at rt for 10 min. The reaction mixture was quenched with H_2O and the solvent was evaporated under vacuum. The crude mixture was extracted with EtOAc (2 x 25 mL) and washed with saturated NaCl (aq). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum. The crude mixture was purified on silica gel column chromatography using EtOAc/hexanes (1/1) as an eluent to afford **5j** (39 mg, 0.1 mmol, 98%); TLC R_f = 0.32 (EtOAc/hexanes = 1/1); white solid; mp 118.9-120.7 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.72 (d, *J* = 7.9 Hz, 0.5H), 7.52 (d, *J* = 7.9 Hz, 1.5H), 7.43 (d, *J* = 7.9 Hz, 0.5H), 7.29 (d, *J* = 7.9 Hz, 1.5H), 6.99 (d, *J* = 8.3 Hz, 1H), 6.73 (d, *J* = 8.3 Hz, 1H), 6.58 (s, 0.8H), 6.38 (s, 0.2H), 4.63 (d, *J* = 12.3 Hz, 1H), 3.78 (s, 3H), 3.04-3.15 (m, 2H), 2.67-2.71 (m, 2H), 2.37-2.54 (m, 1H), 2.03-2.17 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.6, 36.5, 37.4, 38.7, 51.7, 52.5, 55.4, 126.0, 126.2, 127.1, 128.2, 128.7, 128.7, 130.5, 133.9, 134.5, 137.6, 137.9, 139.5, 157.9; IR ν 3316, 2953, 2923, 2829, 1605, 1499, 1490, 1254, 1219, 1158, 1132, 1025, 898, 828, 663 cm^{-1}; LC/MS 385.9 [M + H$^+$]; HRMS (EI) *m*/*z* calcd for $C_{19}H_{19}ClF_3NO_2$ [M$^+$] 385.1056, found 385.1041

1,1,1-Trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)-2-(4-methoxyphenyl)propan-2-ol (4k)



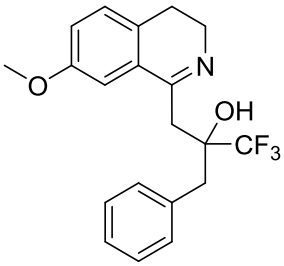
To a solution of compound **2a** (50 mg, 0.18 mmol) in THF (1.0 mL) was added 0.5 M 4-methoxyphenylmagnesium bromide in THF (0.55 mL, 0.28 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixuture which was purified through silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4k**. The isolated compound was highly unstable. Hence, it was directly used for the next step (46 mg, 0.1 mmol, 66%); TLC R_f = 0.49 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.55 (d, *J* = 8.5 Hz, 2H), 7.10 (d, *J* = 8.5 Hz, 1H), 7.05 (d, *J* = 2.5 Hz, 1H), 6.96 (d, *J* = 8.5, 2.5 Hz, 1H), 6.87 (d, *J* = 8.5 Hz, 2H), 3.88 (s, 3H), 3.81 (s, 3H), 3.53-3.61 (m, 2H), 3.47 (d, *J* = 16 Hz, 1H), 3.39 (d, *J* = 16 Hz, 1H), 2.54-2.60 (m, 1H), 2.38-2.45 (m, 1H); LC/MS 380.1 [M + H$^+$].

1,1,1-Trifluoro-3-(7-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)-2-(4-methoxyphenyl)propan-2-ol (5k)



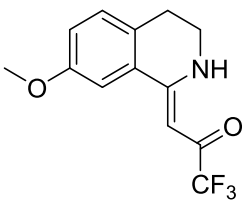
To a solution of **4e** (45 mg, 0.12 mmol) in MeOH (1.0 mL) was added $NaBH_4$ (6.7 mg, 0.2 mmol) at 0 ^oC. The reaction mixture was stirred at rt for 10 min and the solvent was evaporated under vacuum. The solid obtained was dissolved in H_2O and extracted with EtOAc (2 x 25 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/1) as an eluent to afford a diastereomeric mixture (50:50 based on LC/MS) of **5k** (38 mg, 0.099 mmol, 84%); TLC R_f = 0.26 (EtOAc/hexanes = 1/1); white solid; mp 125.7-126.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 7.51 (d, *J* = 8.3 Hz, 2H), 6.79 (d, *J* = 8.1 Hz, 1H), 6.86 (d, *J* = 8.3 Hz, 2H), 6.73 (d, *J* = 8.1 Hz, 1H), 6.61 (s, 1H), 4.64 (d, *J* = 12.4 Hz, 1H), 3.79 (s, 6H), 3.06-3.12 (m, 2H), 2.52-2.70 (m, 3H), 2.09-2.19 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.7, 37.3, 39.0, 52.5, 55.2, 55.4, 111.8, 112.7, 113.4, 126.0, 126.6 (q, $^1J_{C\text{-}F}$ = 286 Hz), 126.8, 130.4, 133.1, 138.3, 157.9, 159.2; ; IR ν 3303, 3012, 2943, 2843, 2024, 1607, 1496, 1457, 1251, 1162, 1139, 1031, 912, 884 cm^{-1}; LC/MS 381.9 [M + H^+]; HRMS (FAB+) *m*/*z* calcd for $C_{20}H_{23}ClF_3NO_3$ [M + H^+] 382.1630, found 382.1624

2-Benzyl-1,1,1-trifluoro-3-(7-methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)propan-2-ol (4l)



To a solution of compound **2a** (50 mg, 0.18 mmol) in THF (1.0 mL) was added 2.0 M benzylmagnesium chloride in THF (0.14 mL, 0.28 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4l** (48 mg, 0.1 mmol, 72%); TLC R_f = 0.55 (EtOAc/hexanes = 2/8); white solid; mp 50.2-51.5 °C; ^1H NMR (300 MHz, $CDCl_3$) δ 8.57 (s, br, 1H), 7.23-7.29 (m, 5H), 7.06 (d, *J* = 8.4 Hz, 1H), 6.90 (s, br, 2H), 3.81 (s, 3H), 3.49 (t, *J* = 6.8 Hz, 2H), 3.23 (d, *J* = 13.8 Hz, 1H), 3.03 (d, *J* = 16.4 Hz, 1H), 2.85 (d, *J* = 13.8 Hz, 1H), 2.60 (d, *J* = 16.4 Hz, 1H), 2.41-2.62 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 24.6, 31.9, 41.2, 45.8, 55.5, 76.3 (q, $^2J_{C\text{-}F}$ = 26.3 Hz), 111.2, 116.1, 126.5, (q, $^1J_{C\text{-}F}$ = 286 Hz), 126.9, 127.7, 128.5, 129.4, 129.5, 131.2, 135.5, 158.6, 166.6; IR ν 3085, 2951, 2835, 2165, 1631, 1573, 1413, 1430, 1281, 1162, 1110, 1043, 1010, 918, 865 cm^{-1}; LC/MS 364.0 [M + H^+]; HRMS (EI) *m*/*z* calcd for $C_{20}H_{20}F_3NO_2$ [M^+] 363.1446, found 363.1430

(Z)-1,1,1-trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1(2H)-ylidene)propan-2-one (3a)

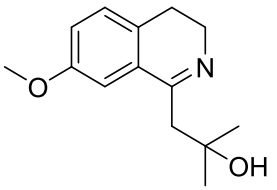


To a solution of **2a** (50 mg, 0.18 mmol) in THF (1.0 mL) was added *i*PrMgBr 1.3 M in THF (0.42 mL, 0.54 mmol) at rt and the reaction mixture was stirred for 30 min. The reaction mixture was treated with sat. NH_4Cl (aq) solution and extracted with EtOAc (2 x 20 mL). The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and the solvent was removed under reduced pressure. The crude product obtained was purified through column chromatography using EtOAC/hexanes (1/3) as an eluent to afford **3a** (44 mg, 0.16 mmol, 88%); TLC R_f = 0.5 (2:8 EtOAc/hexanes); slightly yellow solid. mp 114.6-116.1 ℃; ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.60 (s, 1H), 7.24 (d, *J* = 2.6 Hz, 1H), 7.22 (d, *J* = 8.4 Hz, 1H), 7.07 (dd, *J* = 8.4, 2.6 Hz, 1H), 5.94 (s, 1H), 3.89 (s, 3H), 3.61-3.57 (m, 2H), 2.94 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 176.3 (q, $^2J_{C\text{-}F}$ = 32.6 Hz), 162.3, 158.8, 129.4, 128.6, 128.5, 118.5, 117.8 (q, $^1J_{C\text{-}F}$ = 286.5 Hz), 111.2, 83.8, 55.6, 39.2, 26.8; IR ν 3184, 2916, 1588, 1564, 1489, 1278, 1231, 1117, 867 cm^{-1}; HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}F_3NO_2$ [M^+] 271.0820, found 271.0835.

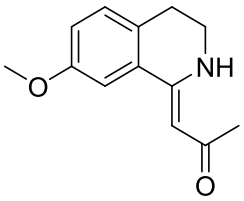
*In case of cyclopentyl and cyclohexyl magnesium bromides, **3a** was obtained in 76 and 72% yields, respectively.

1-(7-Methoxy-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4m)

(*Z*)-1-(7-Methoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene)propan-2-one (3b)



4m



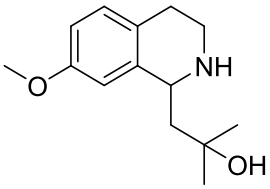
3b

To a solution of **2i** (50 mg, 0.23 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in diethyl ether (0.12 mL, 0.35 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (2 x 25 mL) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and concentrated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **4m** (30 mg, 0.1 mmol, 55%); TLC R_f = 0.52 (EtOAc/hexanes = 3/7); colorless oil; and **3b** (17.5 mg, 0.08 mmol, 35%); TLC R_f = 0.31 (EtOAc/hexanes = 3/7); yellow solid; mp 76.9-78.1 ℃; Unstable **4m** had a tendency to be transformed to DHIQ **1a** during purification. Basification of silica gel and running column chromatography expeditiously could overcome this conversion.

4m: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.13 (d, *J* = 8.1 Hz, 1H), 6.99 (d, *J* = 2.4 Hz, 1H), 7.94 (dd, *J* = 8.4, 2.4 Hz, 1H), 3.85 (s, 3H), 3.67-3.72 (m, 2H), 2.81 (s, 2H), 2.66 (t, *J* = 2.6 Hz, 1H), 1.34 (s, 6H); LC/MS 233.9 [M + H^+].

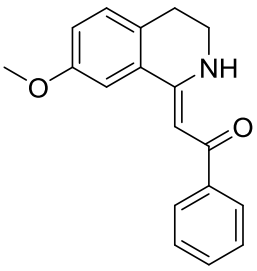
3b: ^{1}H NMR (500 MHz, $CDCl_3$) δ 11.25 (s, br, 1H), 7.21 (d, *J* = 8.1 Hz, 1H), 7.14 (d, *J* = 8.3 Hz, 1H), 6.97 (dd, *J* = 8.3, 2.6 Hz, 1H), 5.62 (s, 1H), 3.87 (s, 3H), 3.43-3.47 (m, 2H), 2.86 (t, *J* = 6.6 Hz, 2H), 2.18 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 29.4, 38.7, 55.4, 89.9, 110.4, 116.9, 128.9, 129.2, 129.9, 156.8, 158.5, 195.7; IR ν 3056, 2963, 2836, 1661, 1597, 1550, 1490, 1319, 1248, 1137, 1030, 979 cm^{-1}; LC/MS 218.1 [M + H^+]; HRMS (EI) *m/z* calcd for $C_{13}H_{15}NO_2$ [M^+] 217.1103, found 217.1120

1-(7-Methoxy-1,2,3,4-tetrahydroisoquinolin-1-yl)-2-methylpropan-2-ol (5m)



To a solution of **4m** (30 mg, 0.13 mmol) in MeOH (1.0 mL) was added $NaBH_4$ (6.7 mg, 0.2 mmol) at 0 °C. The reaction mixture was stirred at rt for 10 min and the solvent was evaporated under vacuum. The solid obtained was dissolved in H_2O and extracted with EtOAc (2 x 25 mL). The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified on silica gel column chromatography using EtOAc/hexanes (1/1) as an eluent to afford a diastereomeric mixture (50:50 based on LC/MS) of **5m** (26 mg, 0.11 mmol, 85%); TLC R_f = 0.25 (EtOAc/hexanes = 1/1); white solid; ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.98 (d, *J* = 8.1 Hz, 1H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.52 (s, 1H), 4.28 (d, *J* = 12.0 Hz, 1H), 3.78 (s, 3H), 3.19-3.08 (m, 2H), 2.68 (s, 2H), 1.99 (t, *J* = 13.0 Hz, 1H), 1.68-1.66 (m, 1H), 1.40 (s, 3H), 1.22 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 28.1, 28.4, 31.7, 37.9, 45.5, 52.9, 55.3, 70.4, 111.5, 112.3, 126.6, 130.4, 140.1, 157.8; IR ν 3279, 2961, 2916, 2832, 1608, 1500, 1420, 1249, 1146, 1120, 1037, 849, 771, 663 cm^{-1}; LC/MS 235.9 [M + H^+]; HRMS (EI) *m/z* calcd for $C_{14}H_{21}NO_2$ [M^+] 235.1572, found 235.1556

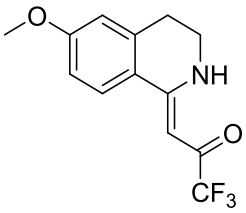
(*Z*)-2-(7-Methoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene)-1-phenylethan-1-one (3c)



To a solution of compound **2j** (50.0 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M MeMgBr in Et_2O (0.18 mL, 0.54 mmol) at rt. The reaction mixture was stirred at rt for 2 h and quenched with saturated NH_4Cl (aq). The mixture was extracted with EtOAc (25 mL x 2) and washed with H_2O. The combined organic layers were dried over Na_2SO_4 and evaporated under vacuum to get a crude mixture which was purified through silica gel column chromatography using EtOAc/hexanes (1/2) as an eluent to afford **3c** (29 mg, 0.1 mmol, 58%); TLC R_f = 0.36 (EtOAc/hexanes = 3/7); yellow oil; ^{1}H NMR (300

MHz, $CDCl_3$) δ 11.81 (s, br, 1H), 7.92-7.95 (m, 2H), 7.41-7.45 (m, 3H), 7.33 (d, *J* = 2.5 Hz, 1H), 7.17 (d, *J* = 8.3 Hz, 1H), 6.99 (dd, *J* = 8.3, 2.5 Hz, 1H), 6.29 (s, 1H), 3.87 (s, 3H), 3.50-3.56 (m, 2H), 2.89 (t, *J* = 6.6 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 188.8, 158.6, 158.4, 140.9, 130.5, 130.3, 129.2, 128.9, 128.2, 126.9, 116.8, 111.0, 86.9, 55.5, 38.9, 27.6; IR ν 3053, 2936, 2832, 1595, 1560, 1483, 1315, 1240, 1145, 1061, 1036, 863, 760 cm^{-1}; LC/MS 280.1 [M + H^+]; HRMS (EI) *m*/*z* calcd for $C_{18}H_{17}NO_2$ [M^+] 279.1259, found 279.1254.

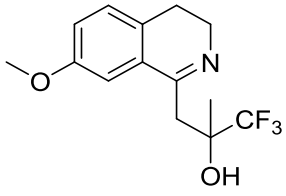
(*Z*)-1,1,1-Trifluoro-3-(6-methoxy-3,4-dihydroisoquinolin-1(2*H*)-ylidene)propan-2-one (3d)



To a solution of 6-methoxy-1-methyl-3,4-dihydroisoquinoline (**1d**, 1.0 g, 5.7 mmol) in THF (10 mL) was added TFAA (2.0 mL, 14 mmol) followed by Et_3N (2.40 mL, 17.1 mmol) at 0 ºC. The reaction mixture was stirred at rt for 20 min, quenched with H_2O and extracted with EtOAc (2 X 100 mL). The combined organic layer was dried over Na_2SO_4 and evaporated under vacuum to get a crude product which was purified through silica gel column chromatography using EtOAc/Hexanes (1/2) as an eluent to afford **3d**. Geometric isomerism was unambiguously determined based on the x-ray crystallography structure of **3d** (1.4 g, 5.2 mmol, 90%); TLC R_f = 0.31 (EtOAc/hexanes = 3/7); white solid; mp 167.4-168.5 ºC; ^{1}H NMR (300 MHz, $CDCl_3$) δ 11.52 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 6.86 (d, *J* = 8.8 Hz, 1H), 6.76 (s, 1H), 5.88 (s, 1H), 3.87 (s, 3H), 3.55-3.59 (s, 2H), 2.95 (t, *J* = 6.8 Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 27.9, 38.9, 55.5, 83.2, 113.3, 118.0 (q, $^1J_{C\text{-}F}$ = 286.5 Hz), 120.1, 128.4, 138.9, 162.4, 163.1, 175.4 (q, $^2J_{C\text{-}F}$ = 32.1 Hz); IR ν 3188, 2967, 2918, 1610, 1587, 1490, 1455, 1319, 1245, 1093, 1040, 855, 775 cm^{-1}; LC/MS 272.1 [M + H^+]; HRMS (EI) *m*/*z* calcd for $C_{13}H_{12}F_3NO_2$ [M^+] 271.0820, found 271.0829

One-Pot Synthesis of 4a

1,1,1-Trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4a)

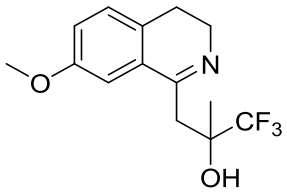


To a solution of a **1a** (50 mg, 0.28 mmol) in THF (3 mL) was added TFAA (0.04 mL, 0.31 mmol) at 0 ºC. The resulting mixture was stirred at rt for 10 min. TLC analysis showed the complete disappearance of starting material. The reaction mixture was then concentrated to remove THF to afford crude **2a** as a yellow oil. To a solution of crude **2a** in THF (3 mL) was added 3.0 M MeMgBr in diethyl ether (0.14 mL, 0.42 mmol) at rt. The resulting mixture was stirred at rt for 10 min. The reaction was quenched NH_4Cl (aq), water and then extracted with EtOAc (2 X 25 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The crude mixture was purified on silica gel column chromatography

using EtOAc/Hex (1/2) as an eluent to afford **4a** (51 mg, 0.18 mmol, 64%); TLC R_f = 0.50 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (s, br, 1H), 7.13 (d, *J* = 9.0 Hz, 1H), 6.99–6.92 (m, 2H), 3.83 (s, 3H), 3.79–3.56 (m, 3H), 3.13 (d, *J* = 16.4 Hz, 1H), 2.79 (d, *J* = 16.4 Hz, 1H), 2.66 (t, *J* = 7.5 Hz, 2H), 1.46 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 24.8, 35.3, 46.1, 55.5, 73.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 110.9, 116.4, 124.7, 126.1 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.6, 129.4, 129.7, 158.7, 166.2; 73.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 110.9, 116.4, 124.7, 126.1 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.6, 129.4, 129.7, 158.7, 166.2; LC/MS 287.7 [M + H^+].

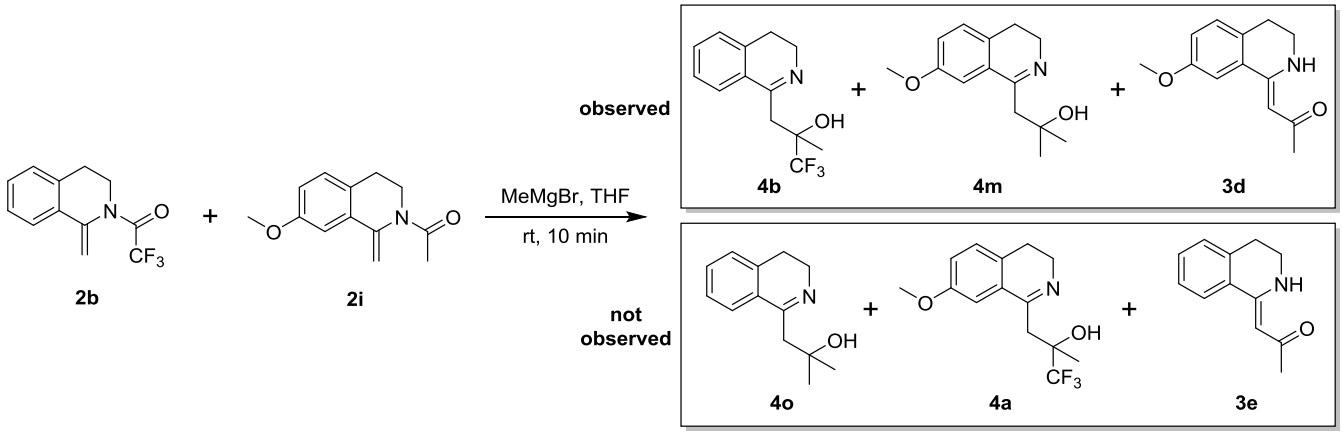
Alternate Procedure for the Synthesis of 4a

1,1,1-Trifluoro-3-(7-methoxy-3,4-dihydroisoquinolin-1-yl)-2-methylpropan-2-ol (4a)



To a solution of a **2a** (50 mg, 0.18 mmol) in THF (1.0 mL) was added 3.0 M MeLi in diethoxymethane (0.090 mL, 0.27mmol) at 0 ℃. The resulting mixture was stirred at rt for 1 h. The reaction was quenched with NH_4Cl (aq), water and then extracted with EtOAc (2 x 25 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The crude mixture was purified on silica gel column chromatography using EtOAc/Hex (1/2) as an eluent to afford **4a** (29 mg, 0.10 mmol, 57%); TLC R_f = 0.50 (EtOAc/hexanes = 2/8); colorless oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (s, br, 1H), 7.15 (d, *J* = 9.0 Hz, 1H), 6.98-6.95 (m, 2H), 3.86 (s, 3H), 3.73-3.65 (m, 2H), 3.15 (d, *J* = 16.2 Hz, 1H), 2.82 (d, *J* = 16.5 Hz, 1H), 2.68 (t, *J* = 7.5 Hz, 2H), 1.45 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 22.7, 24.8, 35.3, 46.1, 55.5, 73.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 110.9, 116.4, 124.7, 126.1 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.6, 129.4, 129.7, 158.7, 166.2; 73.6 (q, $^2J_{C\text{-}F}$ = 28 Hz), 110.9, 116.4, 124.7, 126.1 (q, $^1J_{C\text{-}F}$ = 284 Hz), 128.6, 129.4, 129.7, 158.7, 166.2; LC/MS 287.7 [M + H^+].

Crossover experiment



To a mixture of **2b** (50 mg, 0.21 mmol) and **2i** (45 mg, 0.21 mmol) in THF (3 mL) was added 3.0 M MeMgBr in diethyl ether (0.24 mL, 0.72 mmol) at rt. The resulting mixture was stirred at rt for 10 min. LC/MS analysis showed new peaks corresponding to **4b**, **4m**, and **3d** in addition to unreacted **2i**. There were no peaks matching with molecular weights of **4o**, **4a**, and **3e**. The reaction was quenched with NH_4Cl (aq) and then extracted with EtOAc (2 x 25 mL). The combined organic layers were dried over Na_2SO_4 and the solvent was removed under vacuum. The crude mixture was purified on silica gel column chromatography using EtOAc/Hex (1/2) as an eluent to afford **4b** (38 mg, 0.15 mmol, 72%), **4m** (5.0 mg, 0.021 mmol, 10%), **3d** (1.2 mg, 5.5 μmol, 3%), and recovered **2i** (28 mg, 0.13 mmol, 62%).

References

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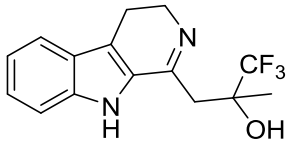
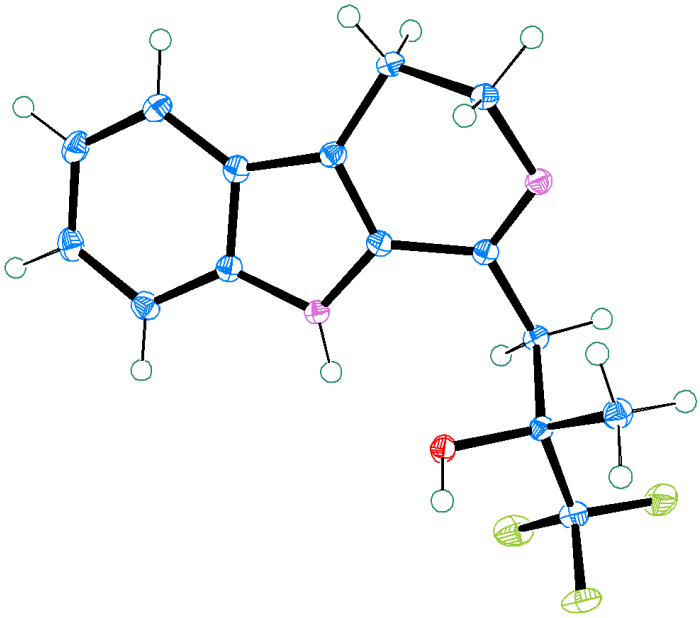
X-ray Crystallography Analysis of 4g

CCDC-1532366 contains the supplementary crystallographic data for **4g**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



4g

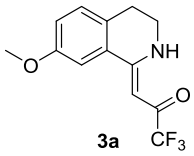


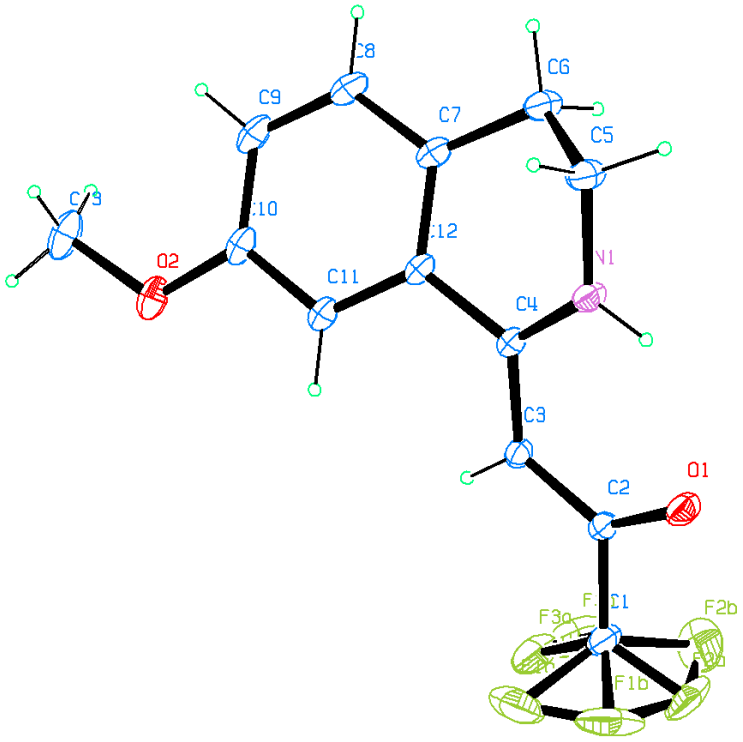
Crystal data and structure refinement for **4g**

Identification code	20150901lt_0m	
Empirical formula	C_{15} H_{15} F_3 N_2 O	
Formula weight	296.29	
Temperature	100(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/n	
Unit cell dimensions	a = 6.92630(10) Å	α = 90°.
	b = 8.72380(10) Å	β = 95.2920(10)°.
	c = 22.5349(4) Å	γ = 90°.
Volume	1355.84(3) $Å^3$	
Z	4	
Density (calculated)	1.452 Mg/m^3	
Absorption coefficient	0.120 mm^{-1}	
F(000)	616	
Crystal size	0.28 x 0.18 x 0.08 mm^3	
Theta range for data collection	1.82 to 26.00°	
Index ranges	-8<=h<=8, 0<=k<=10, 0<=l<=27	
Reflections collected	2669	
Independent reflections	2669 [R(int) = 0.0000]	
Completeness to theta = 26.00°	100.0 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9904 and 0.9671	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	2669 / 0 / 190	
Goodness-of-fit on F^2	1.067	
Final R indices [I>2sigma(I)]	R1 = 0.0347, wR2 = 0.0847	
R indices (all data)	R1 = 0.0382, wR2 = 0.0876	
Largest diff. peak and hole	0.398 and -0.482 e.$Å^{-3}$	

X-ray Crystallography Analysis of 3a

CCDC-1819355 contains the supplementary crystallographic data for **3a**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



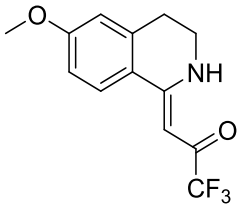


Crystal data and structure refinement for **3a.**

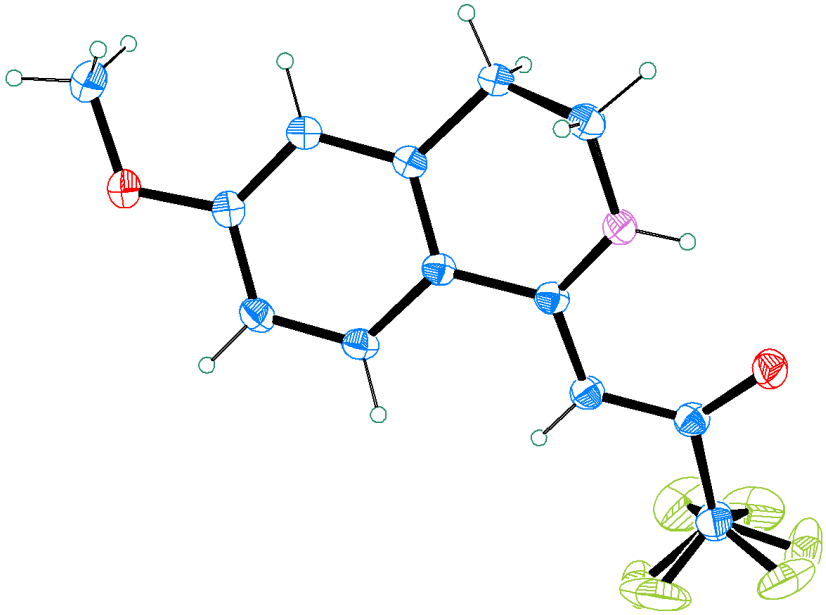
Identification code	20170922	
Empirical formula	C13 H12 F3 N O2	
Formula weight	271.24	
Temperature	296(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	C2/c	
Unit cell dimensions	a = 17.9537(9) Å	α= 90°.
	b = 7.1369(3) Å	β= 112.706(3)°.
	c = 21.8227(14) Å	γ = 90°.
Volume	2579.5(2) $Å^3$	
Z	8	
Density (calculated)	1.397 Mg/m^3	
Absorption coefficient	0.123 mm^{-1}	
F(000)	1120	
Crystal size	0.50 x 0.40 x 0.20 mm^3	
Theta range for data collection	2.51 to 29.89°.	
Index ranges	-24<=h<=22, -10<=k<=0, -30<=l<=21	
Reflections collected	3711	
Independent reflections	3711 [R(int) = 0.0000]	
Completeness to theta = 29.89°	99.7 %	
Absorption correction	None	
Max. and min. transmission	0.9758 and 0.9411	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3711 / 0 / 200	
Goodness-of-fit on F^2	1.027	
Final R indices [I>2sigma(I)]	R1 = 0.0596, wR2 = 0.1685	
R indices (all data)	R1 = 0.0842, wR2 = 0.1903	
Largest diff. peak and hole	0.257 and -0.205 $e.Å^{-3}$	

X-ray Crystallography Analysis of 3d

CCDC-1532365 contains the supplementary crystallographic data for **3d**. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.



3d

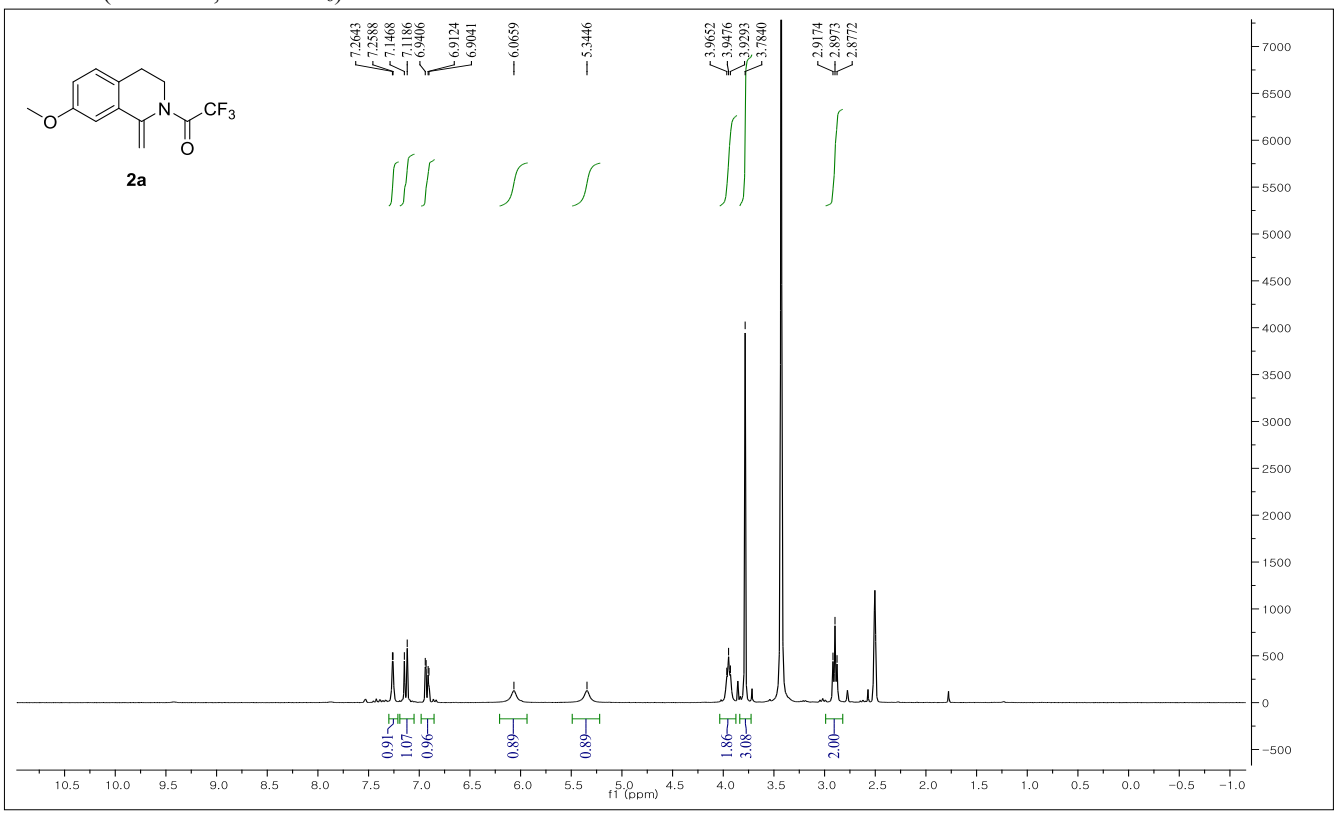


Crystal data and structure refinement for **3d**

Identification code	20150722_0m	
Empirical formula	C13 H12 F3 N O2	
Formula weight	271.24	
Temperature	296(1) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)/c	
Unit cell dimensions	a = 7.8606(2) Å	α = 90°
	b = 8.5158(2) Å	β = 98.771(1)°
	c = 18.6068(4) Å	γ = 90°
Volume	1230.96(5) $Å^3$	
Z	4	
Density (calculated)	1.464 Mg/m^3	
Absorption coefficient	0.129 mm^{-1}	
F(000)	560	
Crystal size	0.56 x 0.20 x 0.12 mm^3	
Theta range for data collection	2.21 to 28.28°	
Index ranges	-9<=h<=10, -11<=k<=10, -24<=l<=24	
Reflections collected	19921	
Independent reflections	3068 [R(int) = 0.0221]	
Completeness to theta = 28.28°	99.9 %	
Absorption correction	Multi-scan	
Max. and min. transmission	0.9847 and 0.9314	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3068 / 0 / 200	
Goodness-of-fit on F^2	1.029	
Final R indices [I>2sigma(I)]	R1 = 0.0439, wR2 = 0.1087	
R indices (all data)	R1 = 0.0581, wR2 = 0.1199	
Largest diff. peak and hole	0.147 and -0.242 e.$Å^{-3}$	

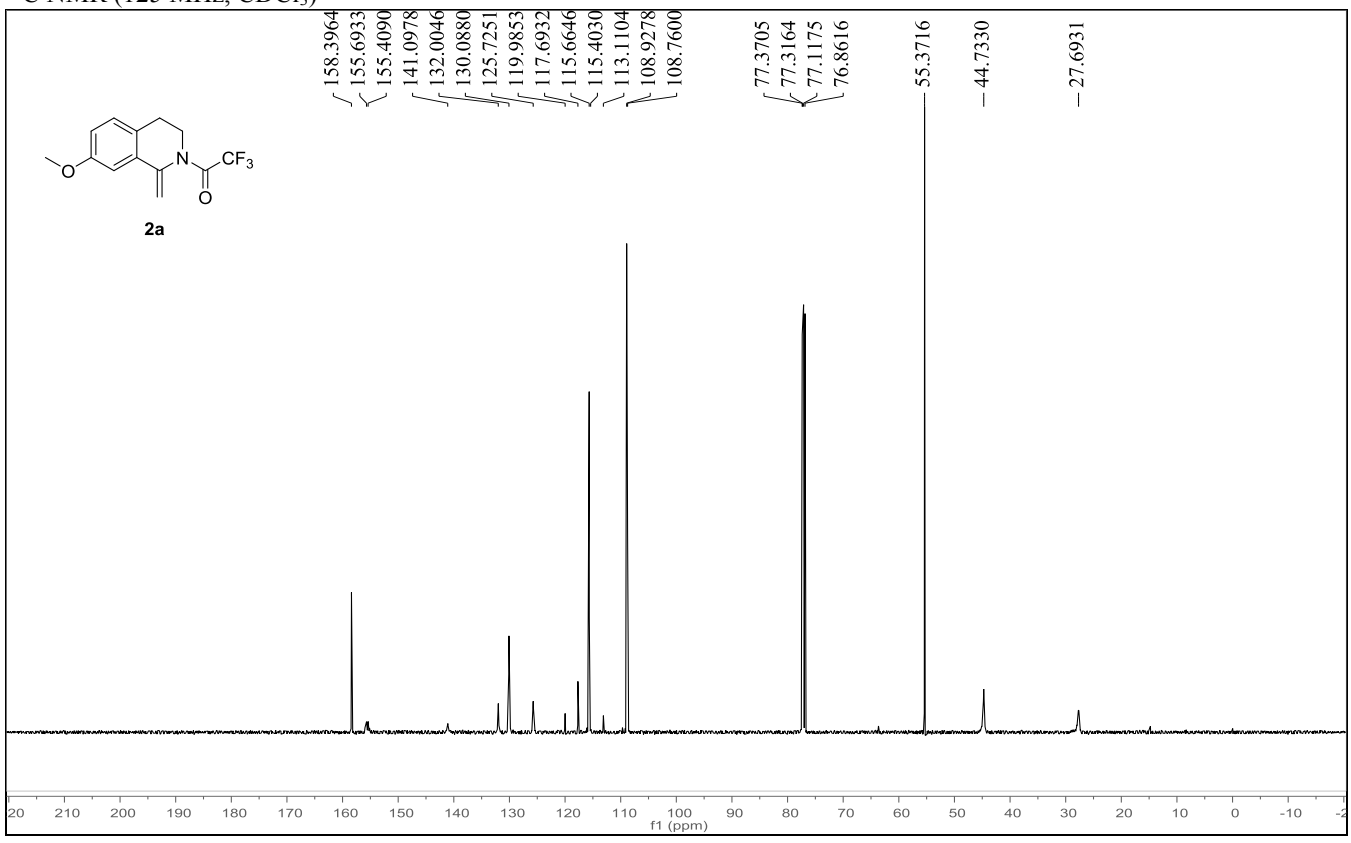
^{1}H & ^{13}C NMR Spectra

^{1}H NMR (300 MHz, DMSO-d_6)



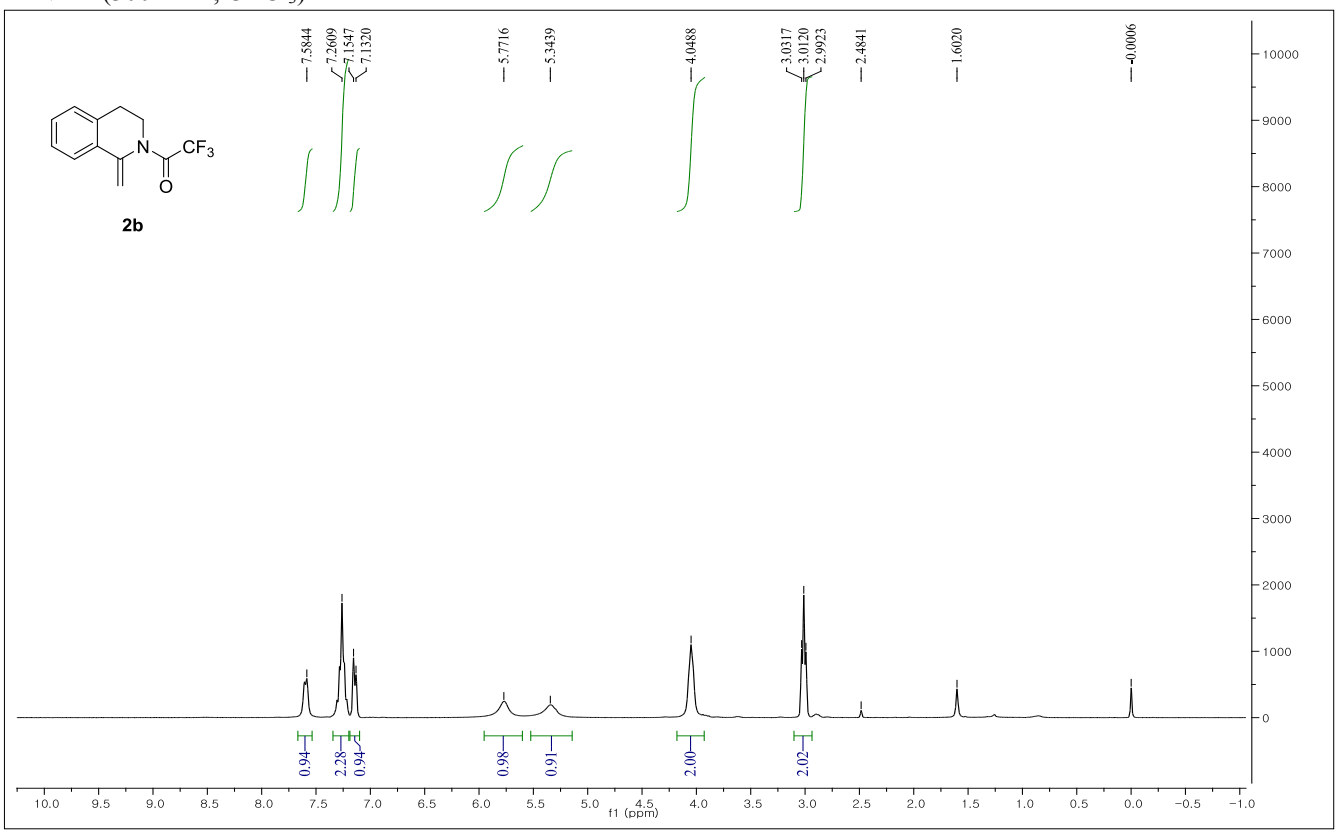
2a

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

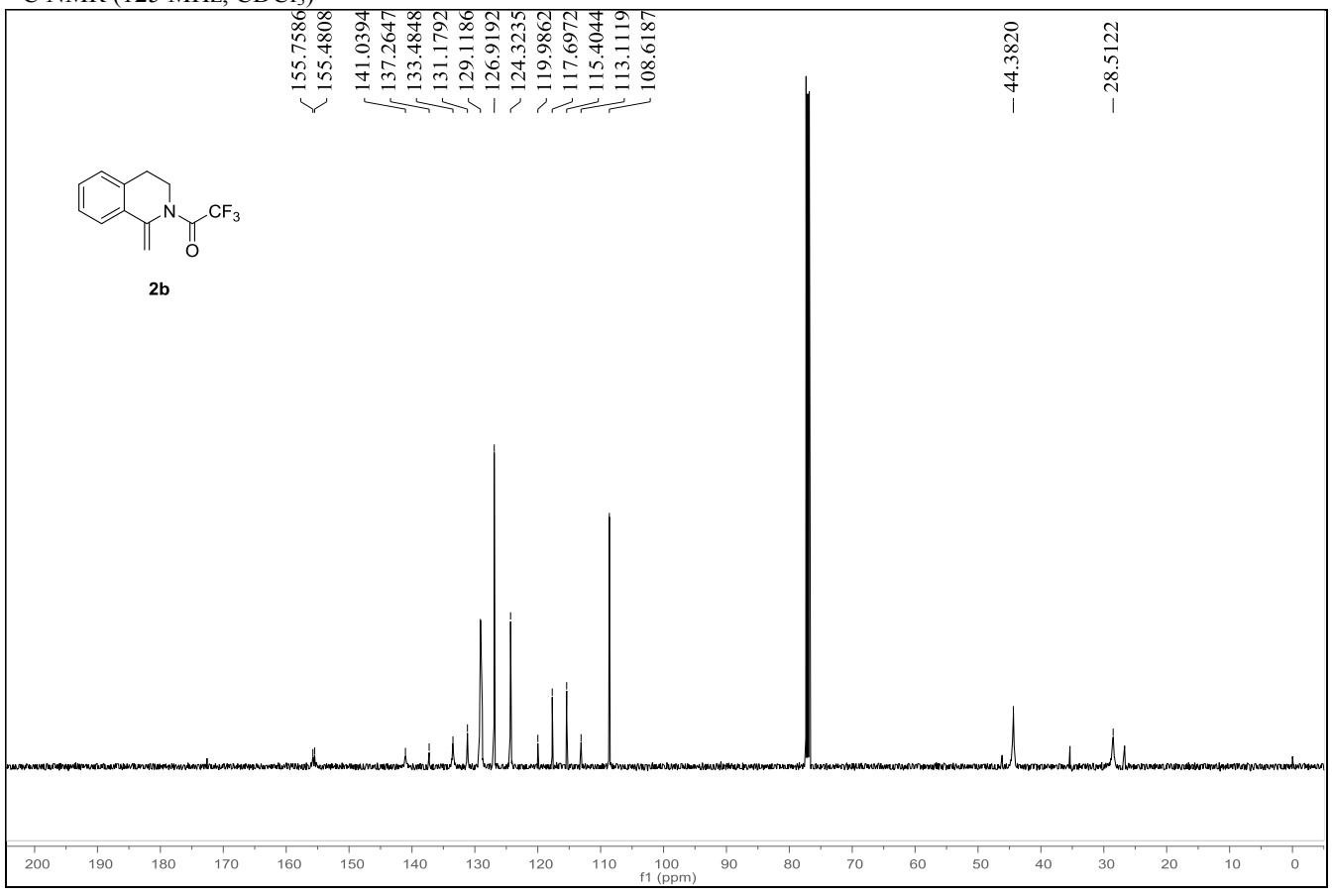


2a

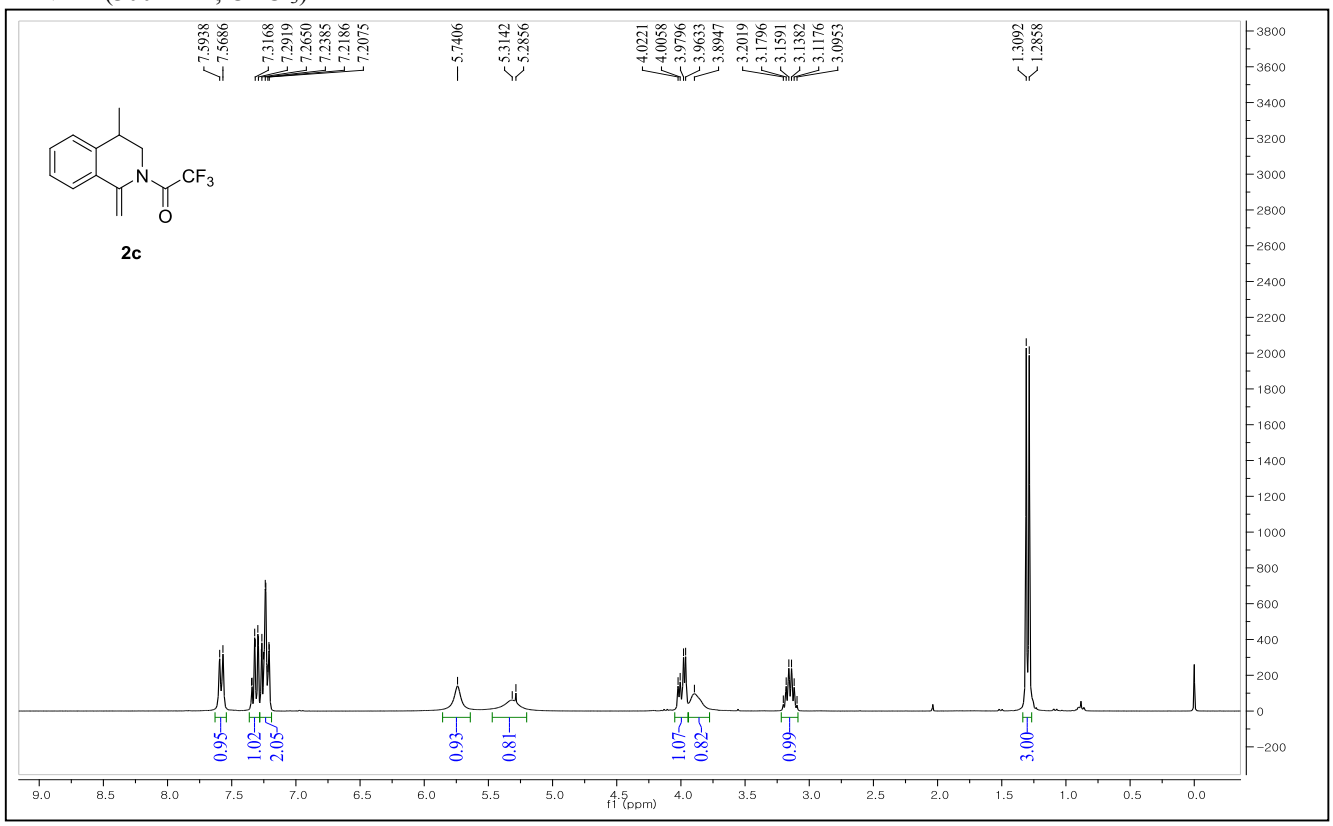
^{1}H NMR (300 MHz, $CDCl_3$)



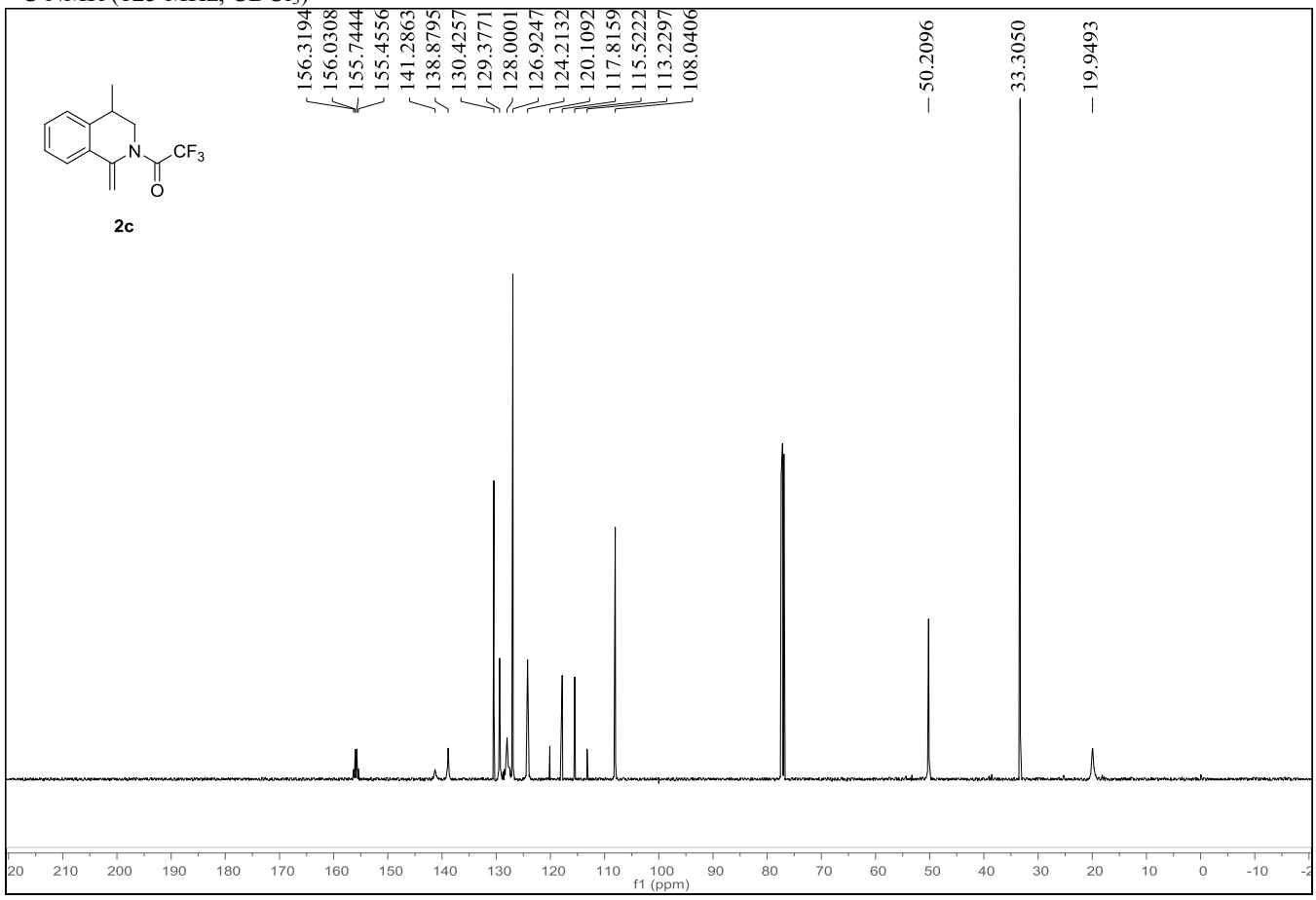
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)



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



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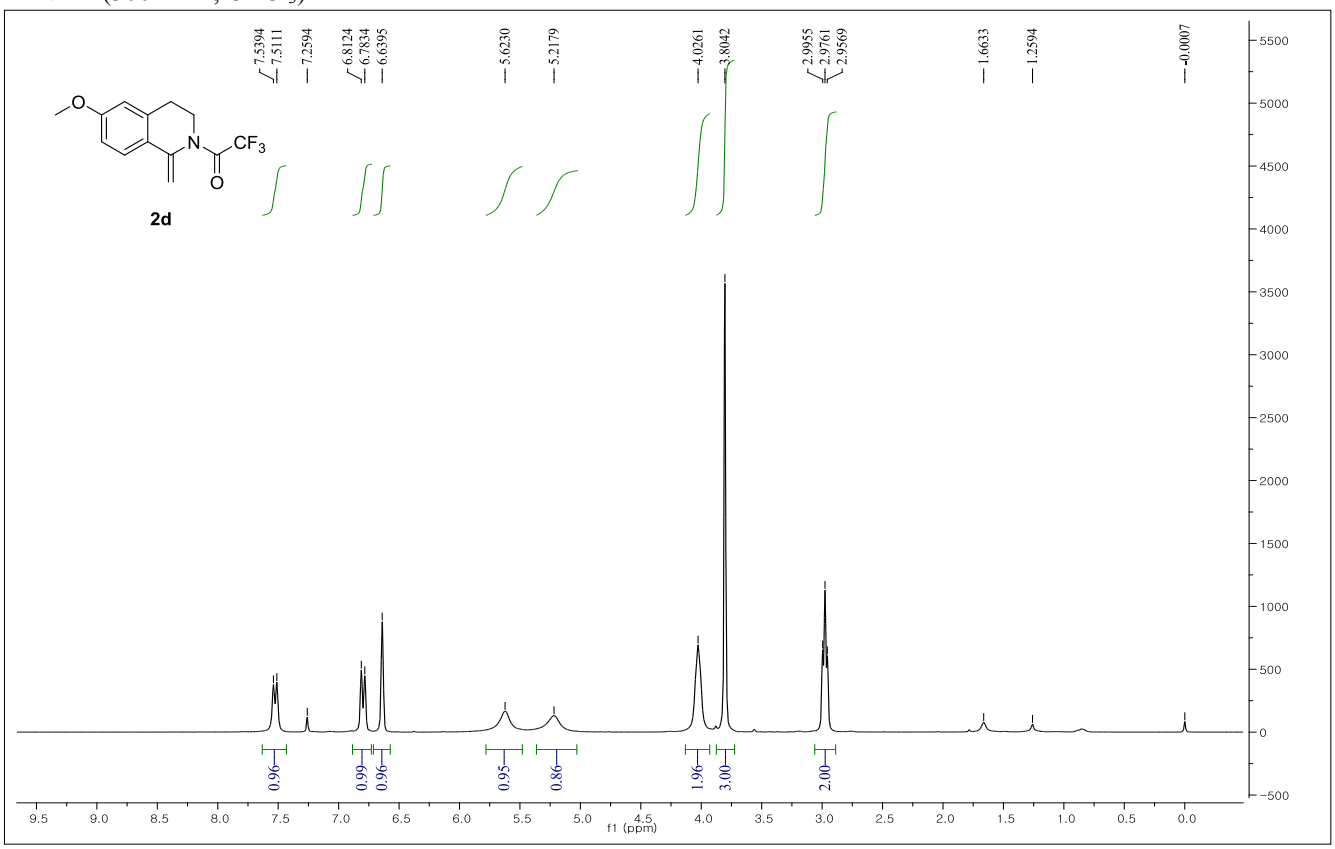

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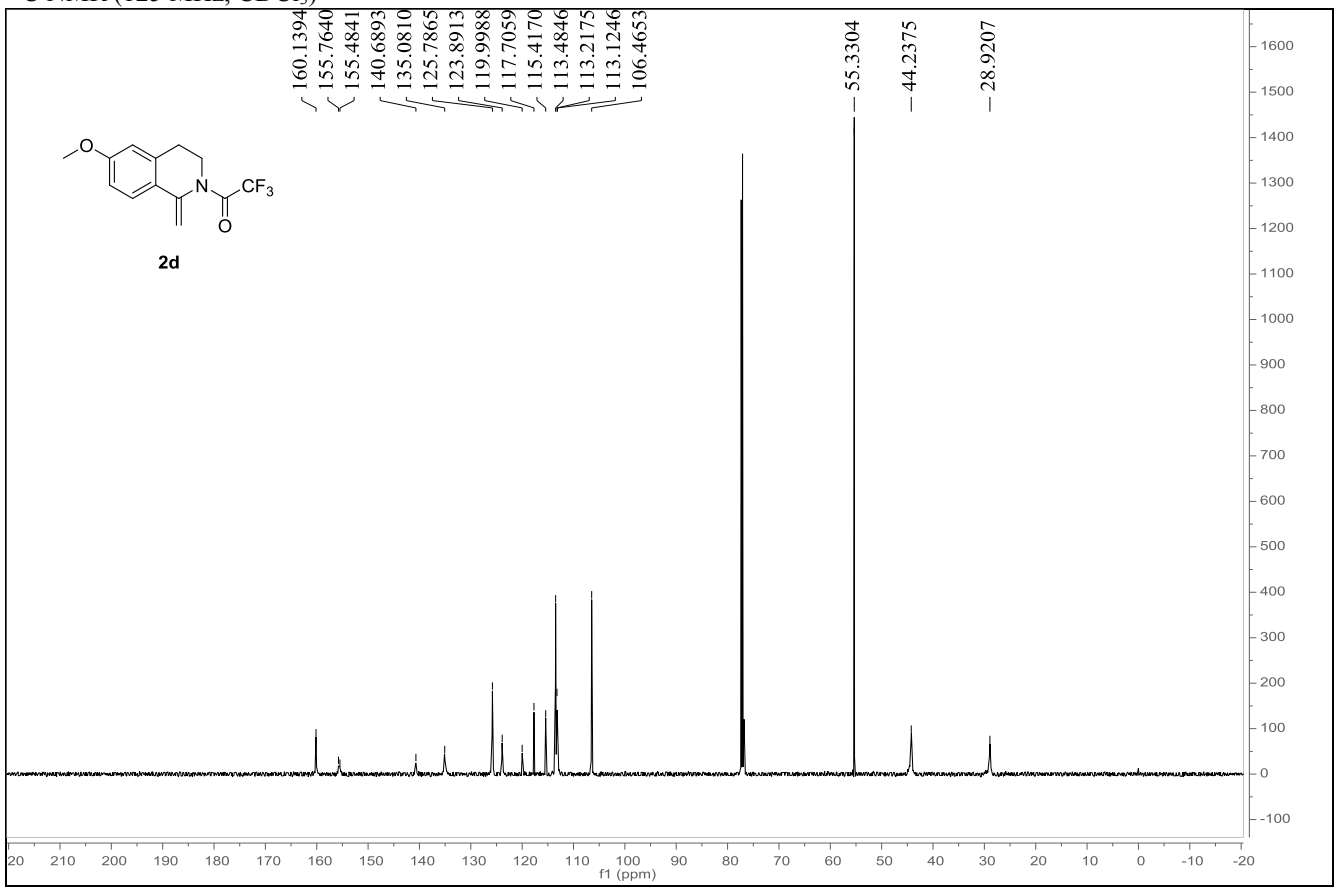

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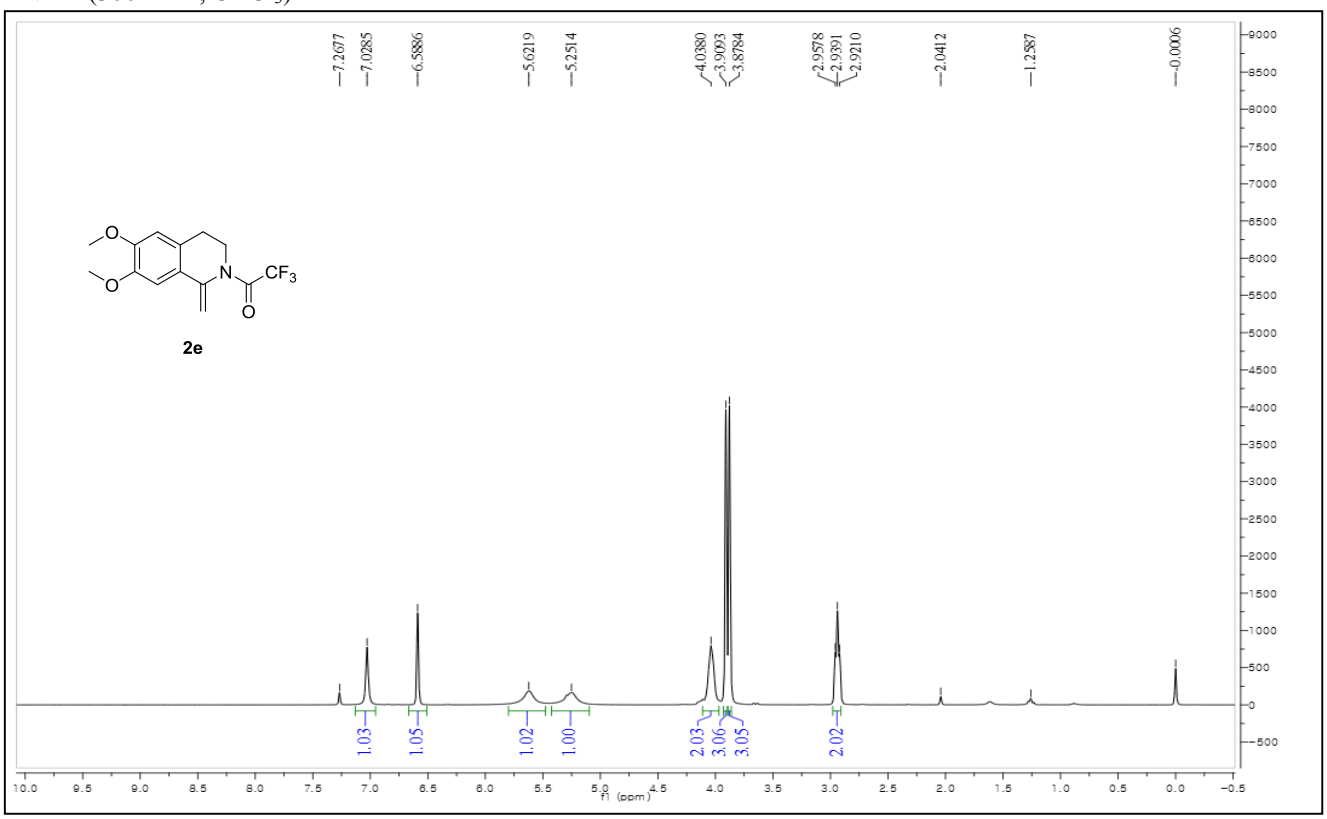

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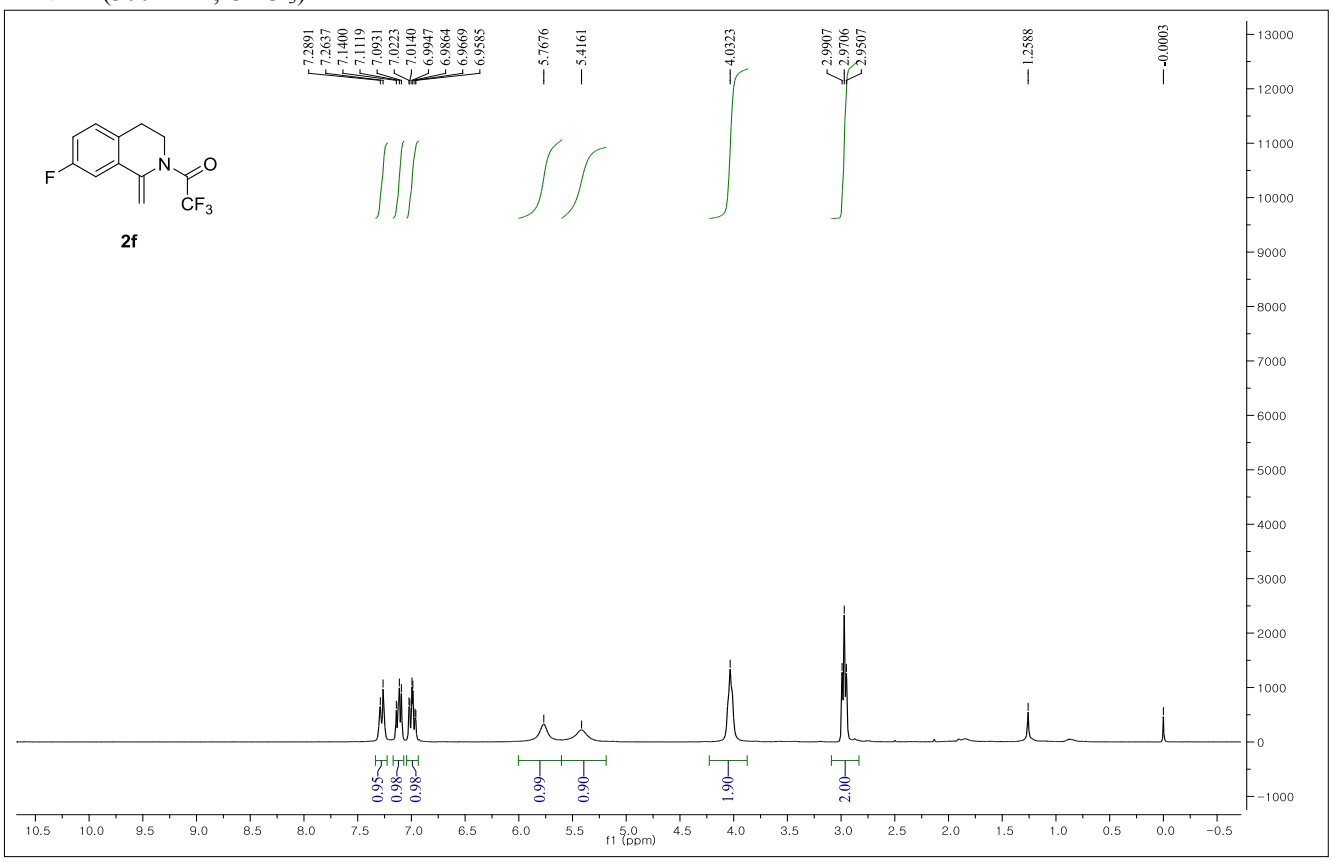

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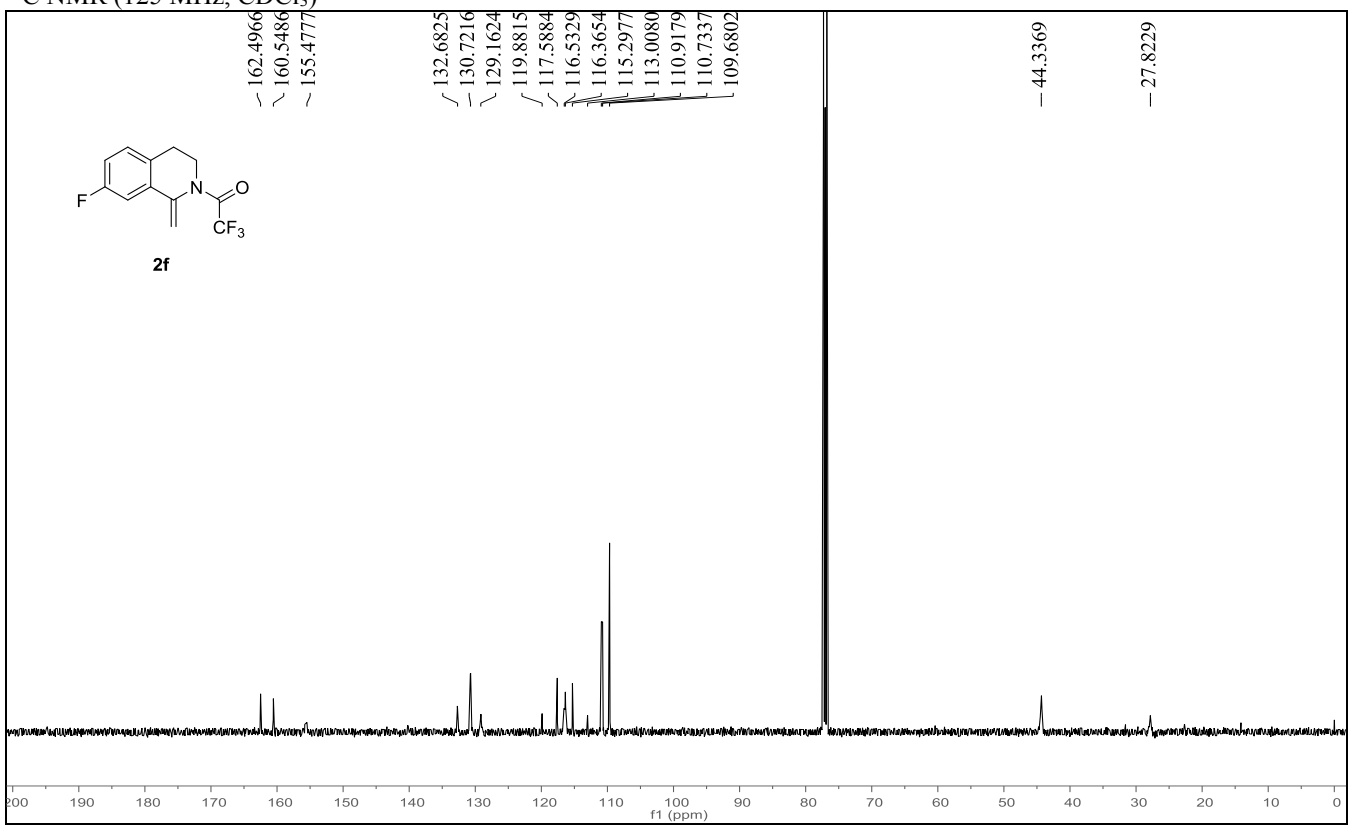

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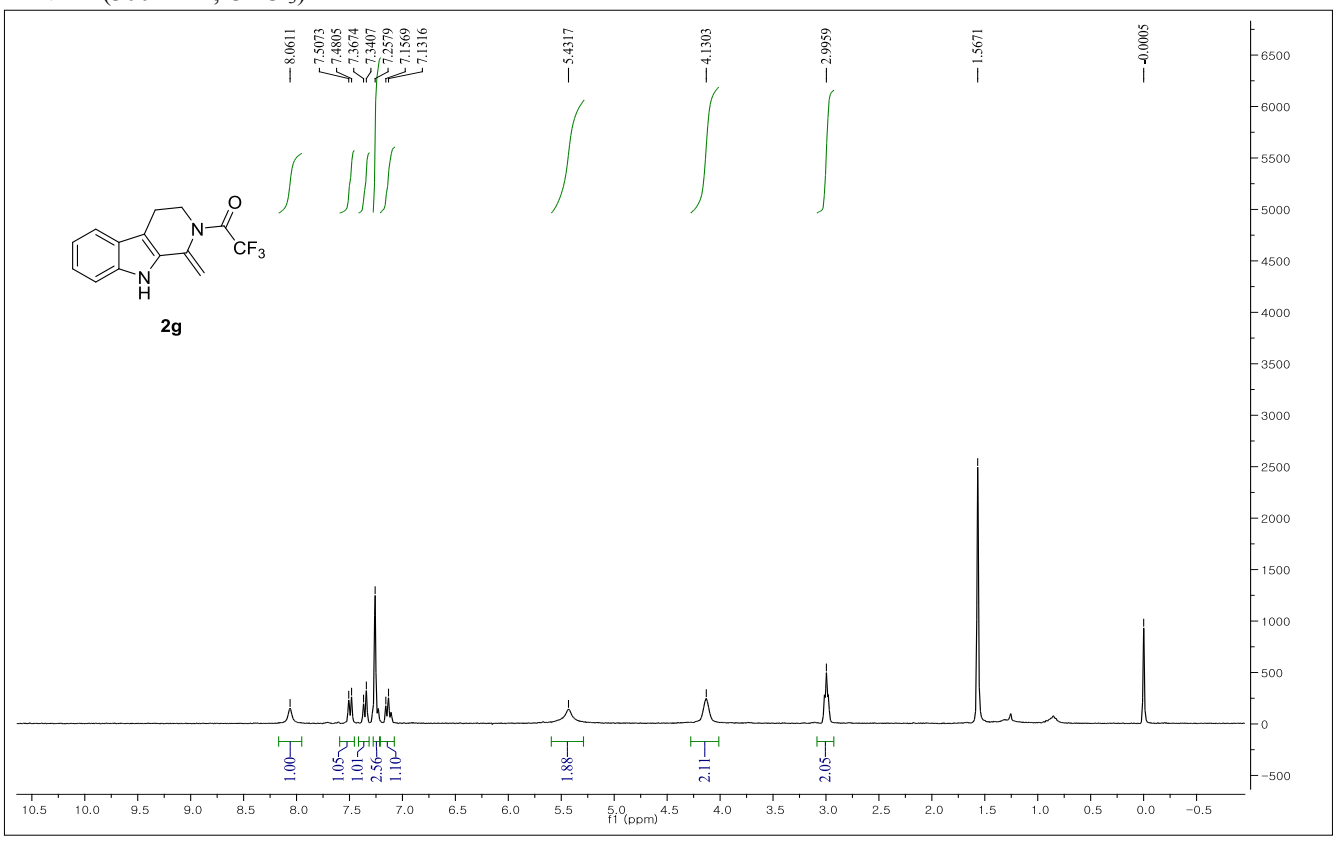

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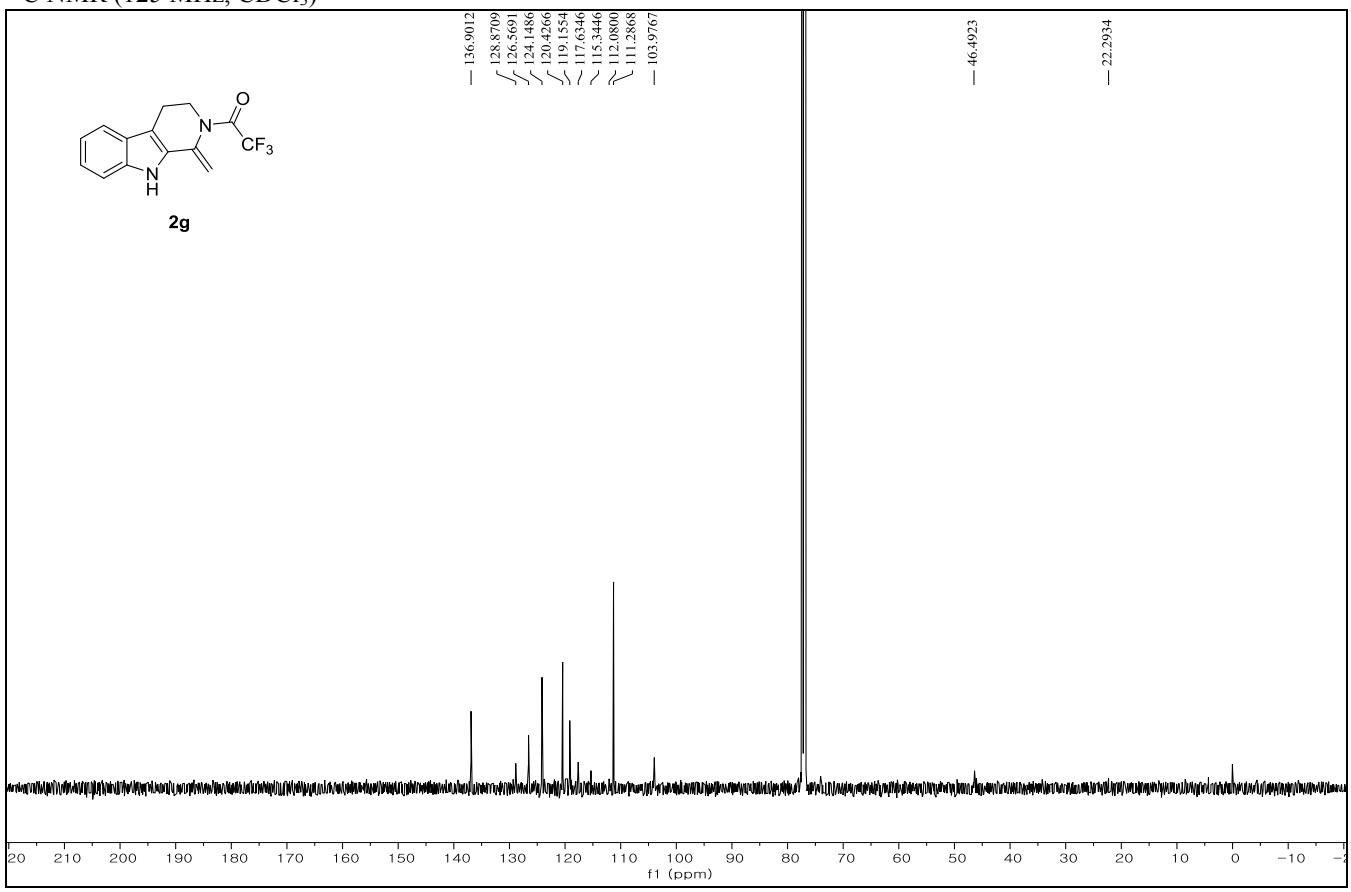

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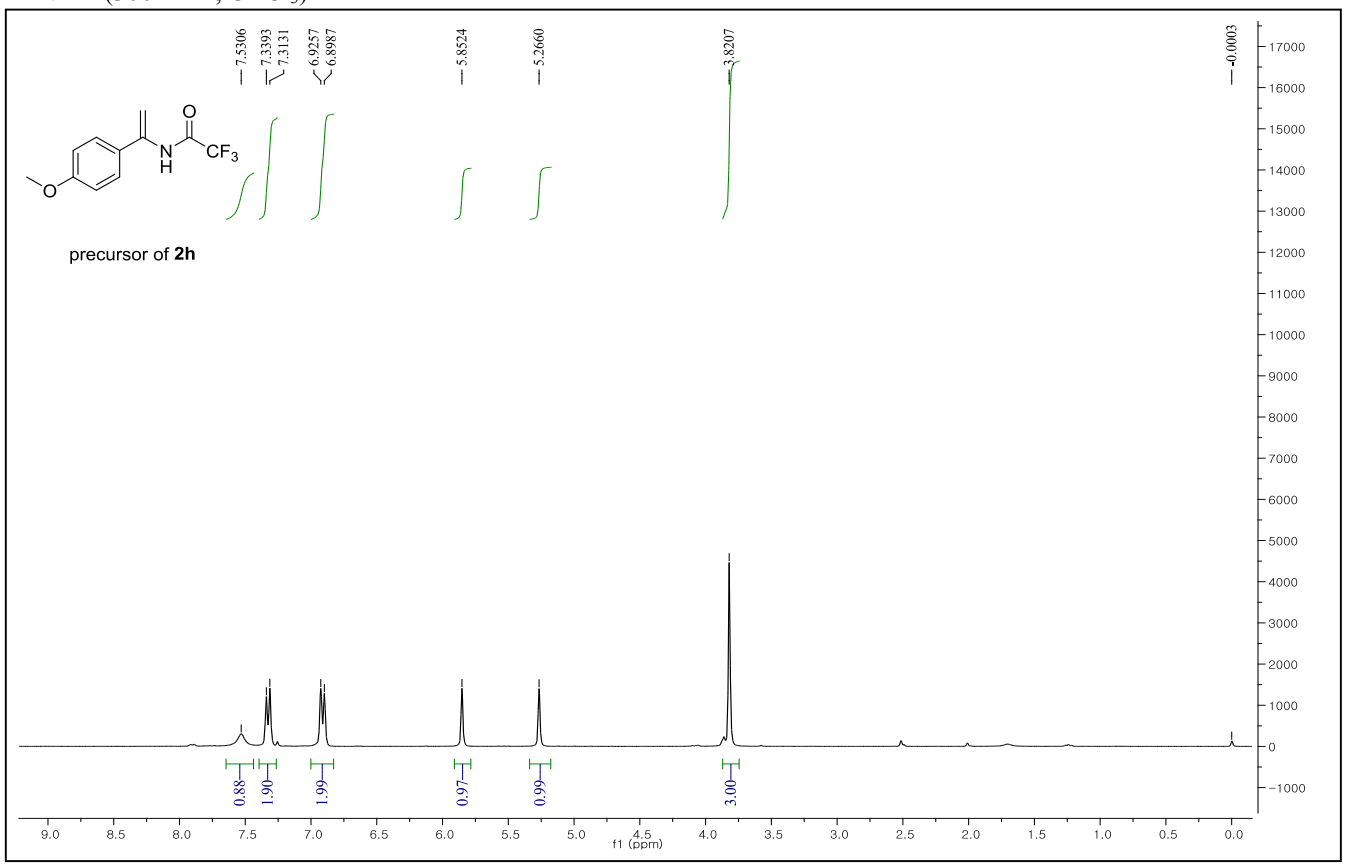

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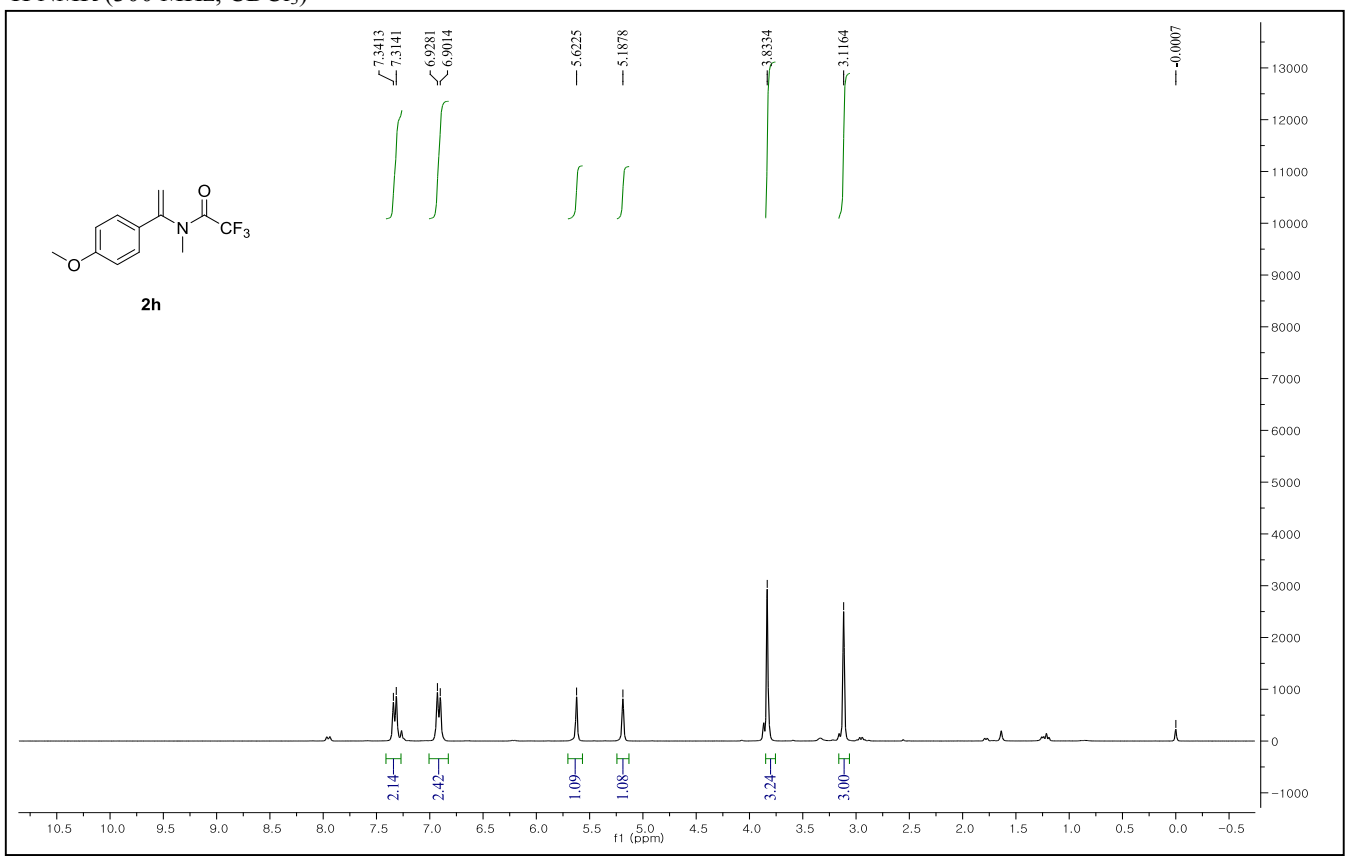

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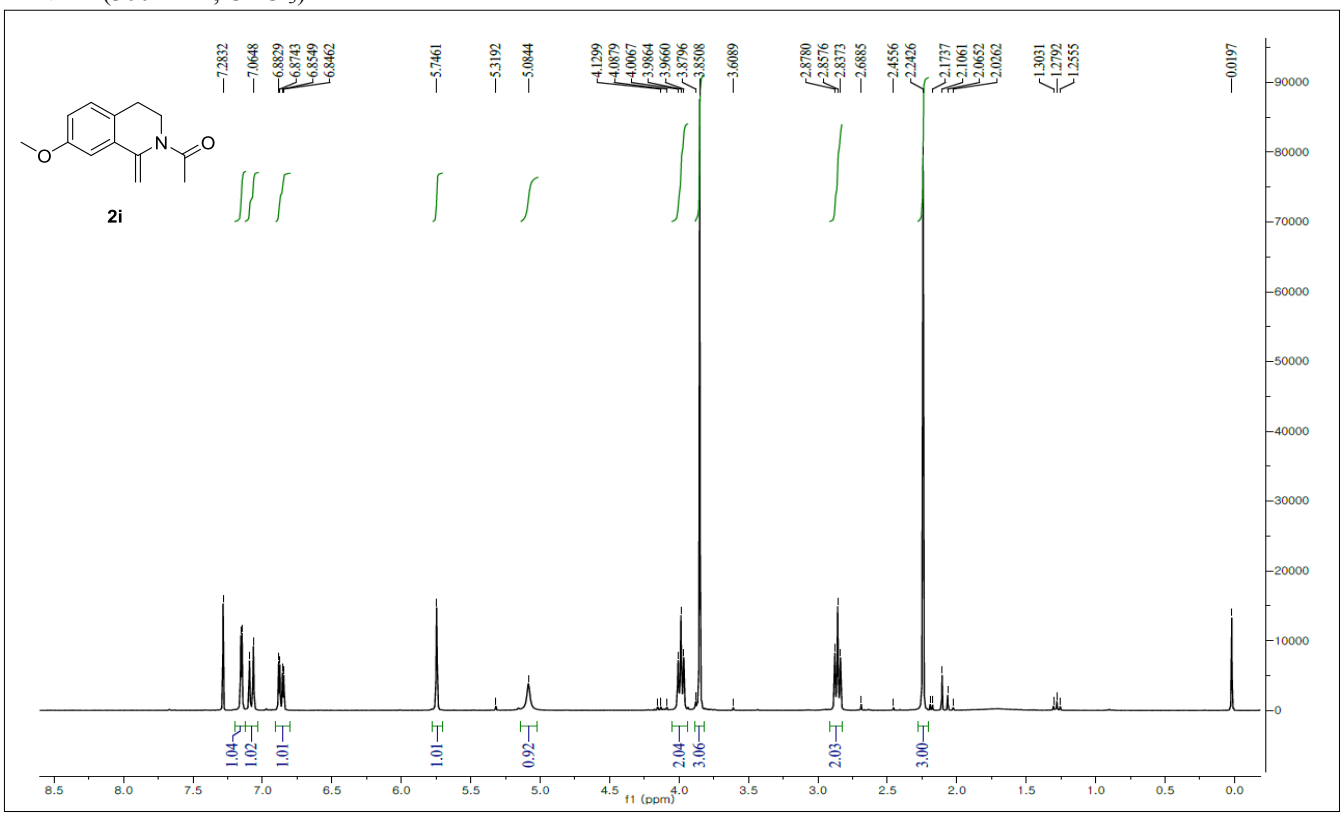

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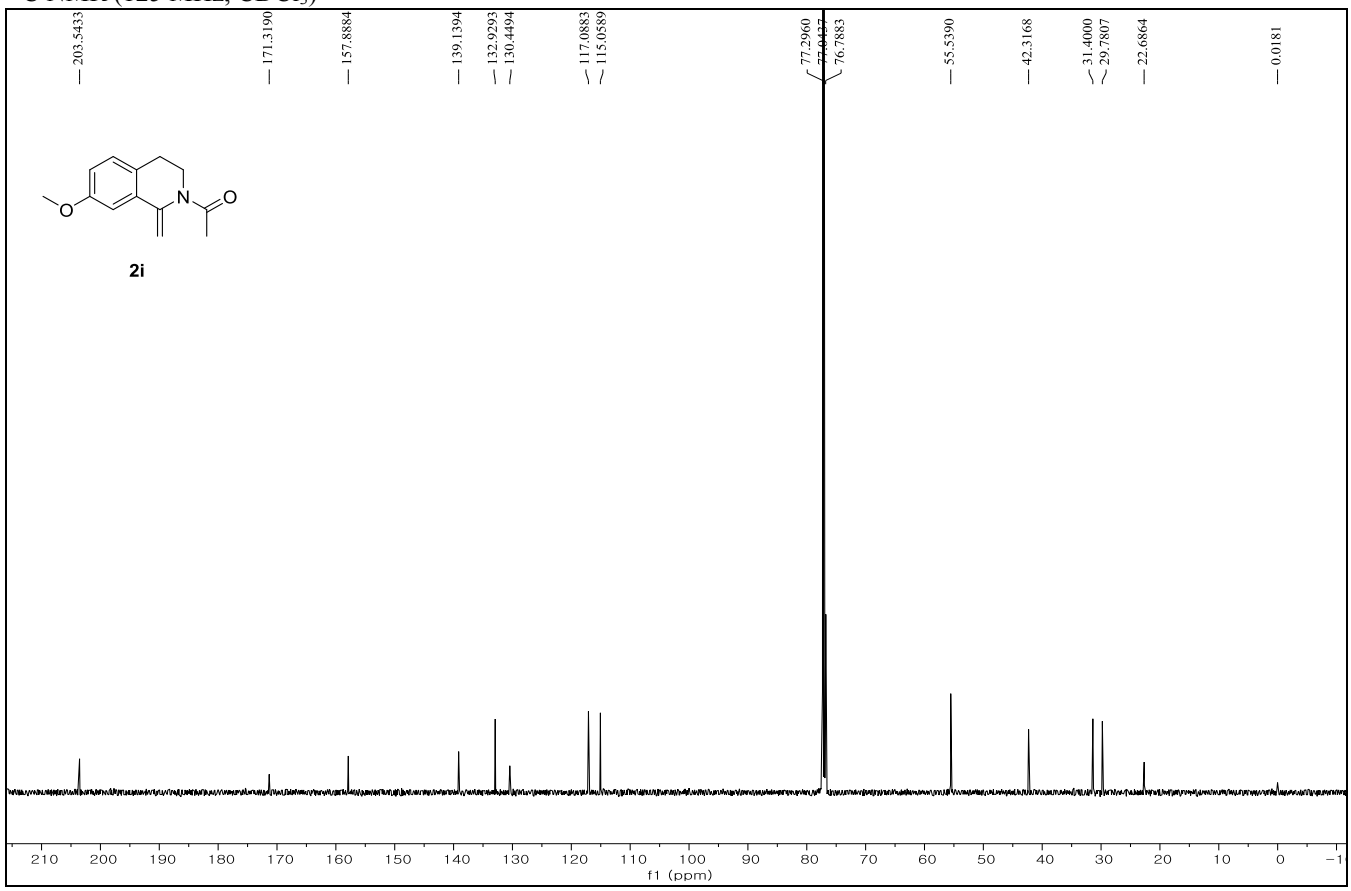

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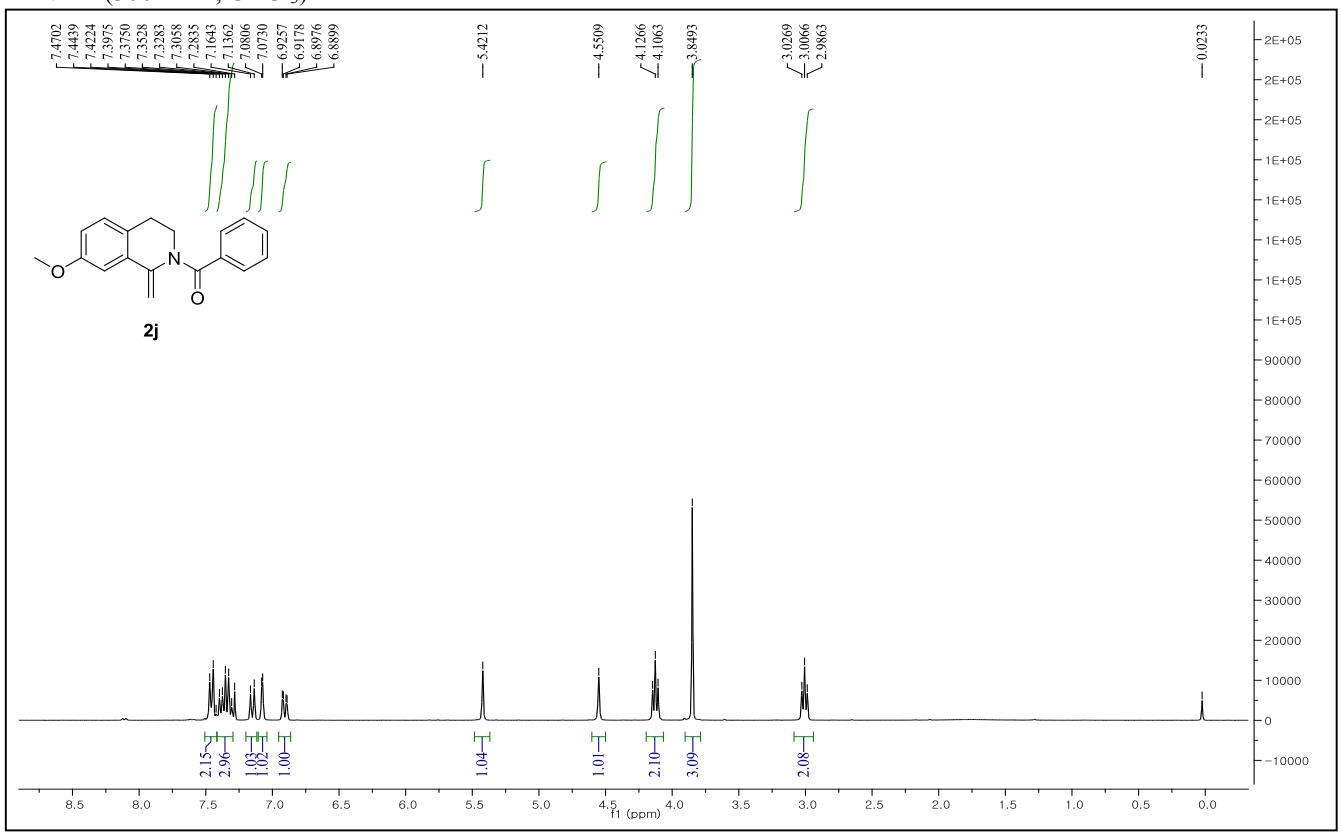

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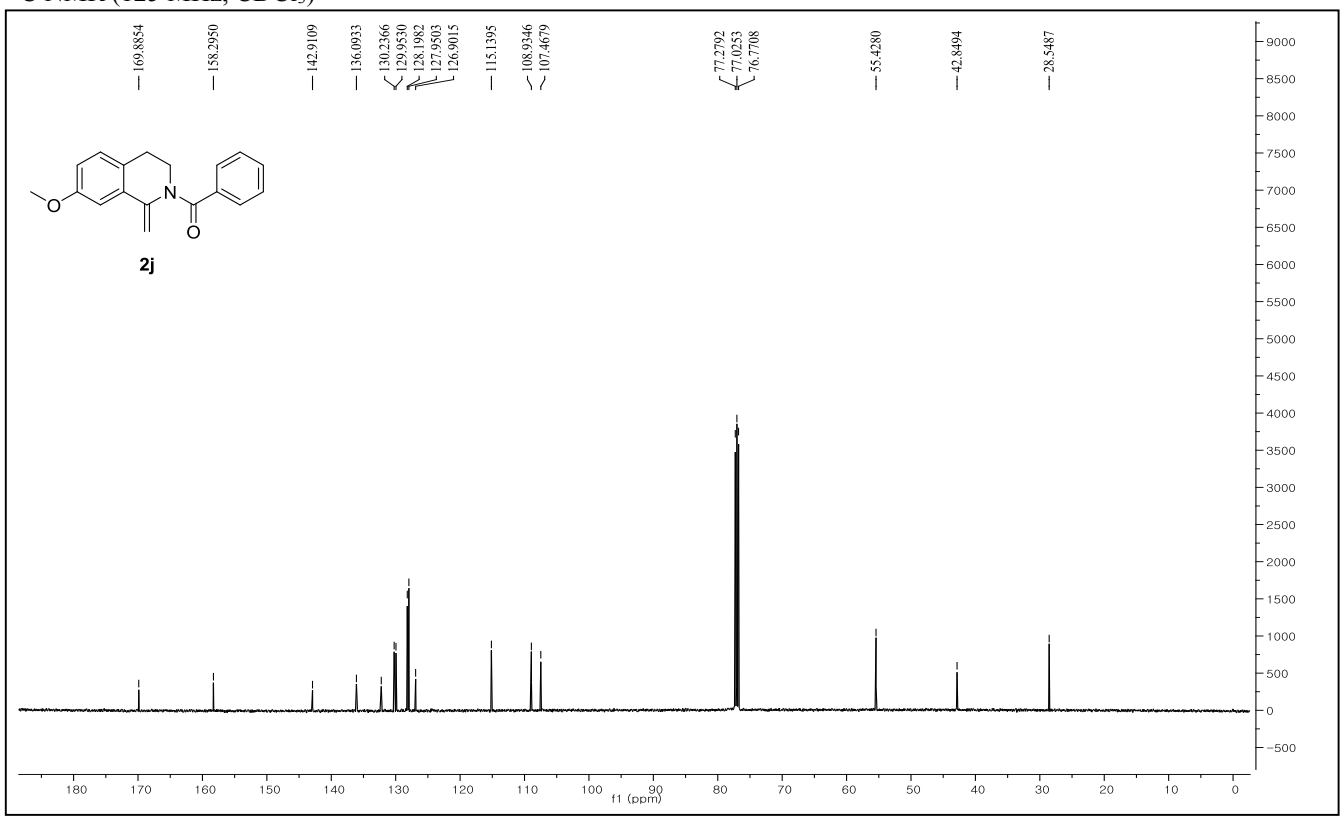

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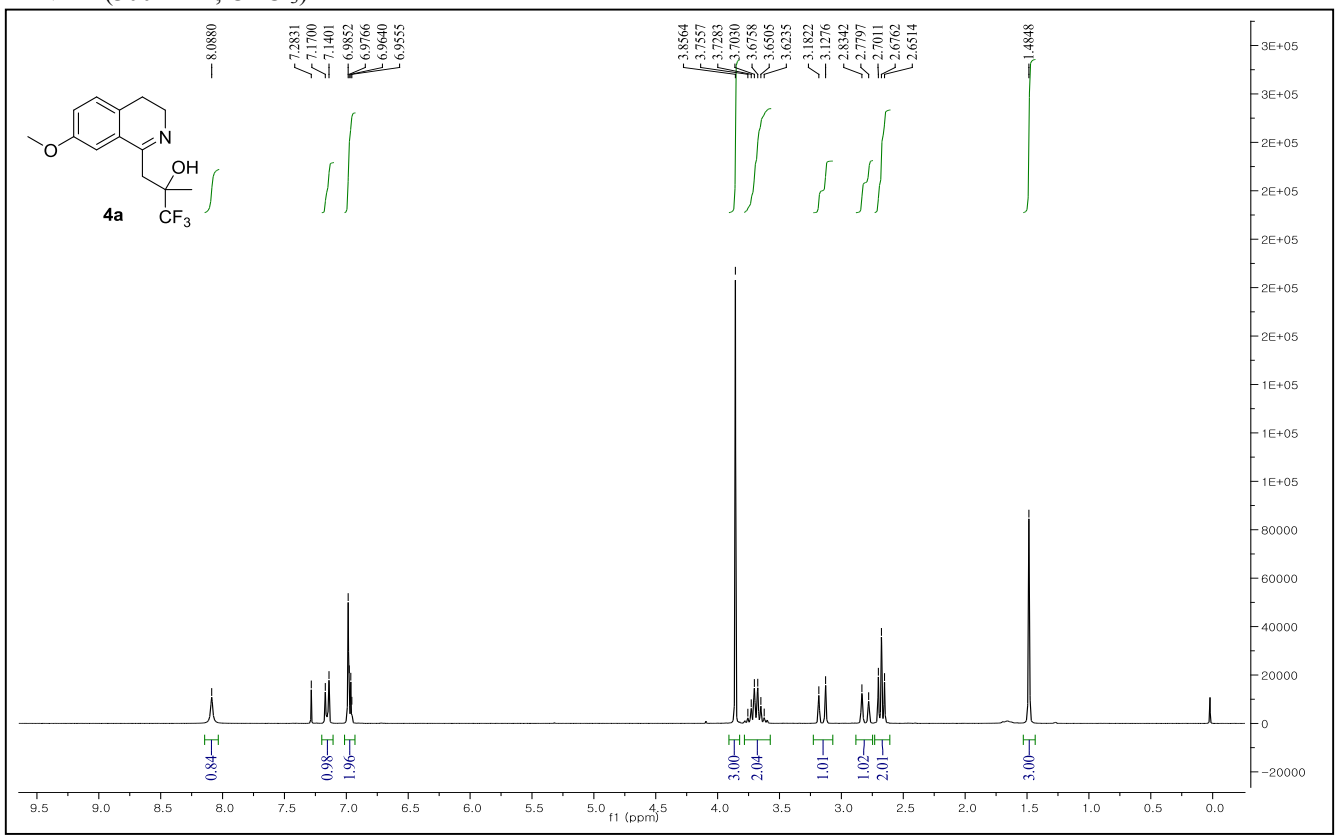

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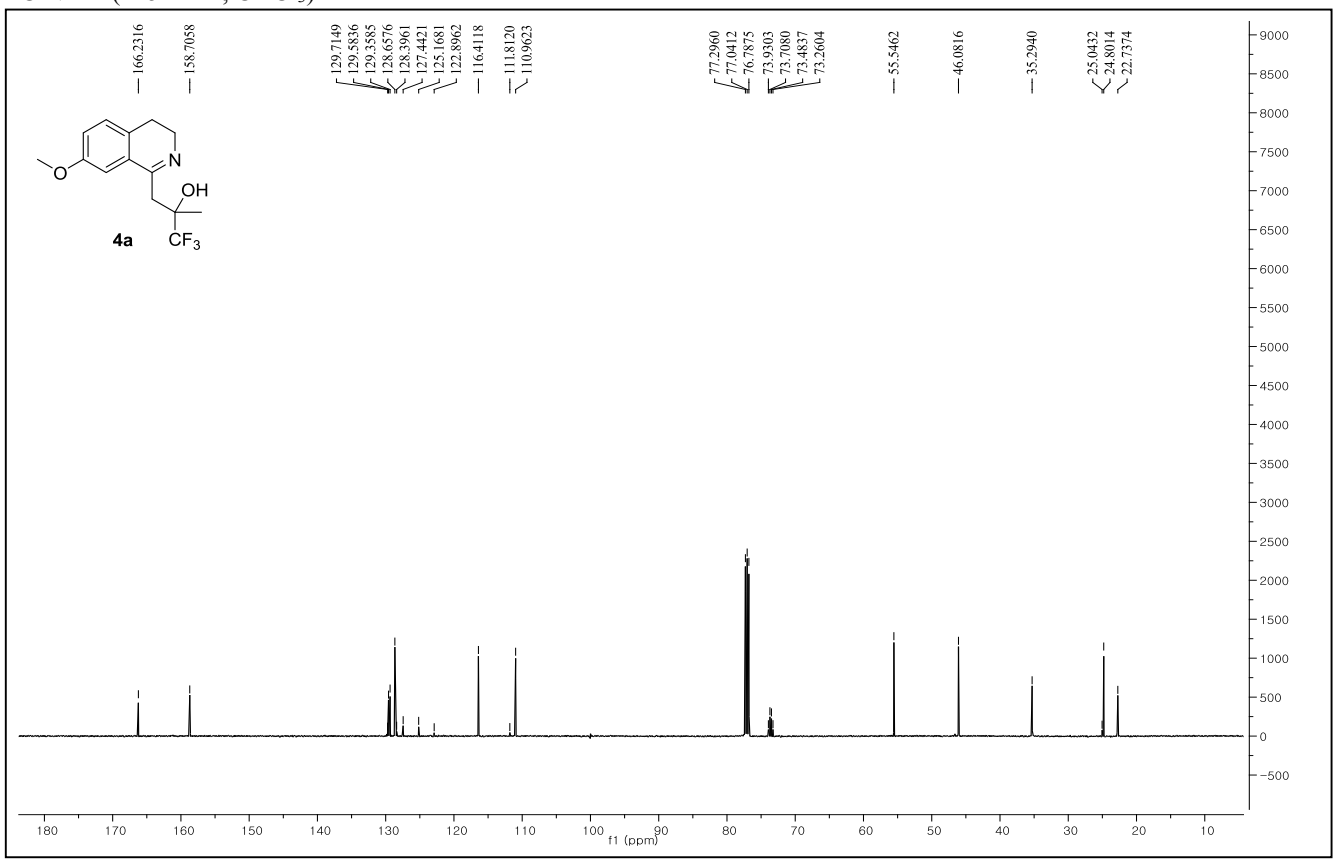

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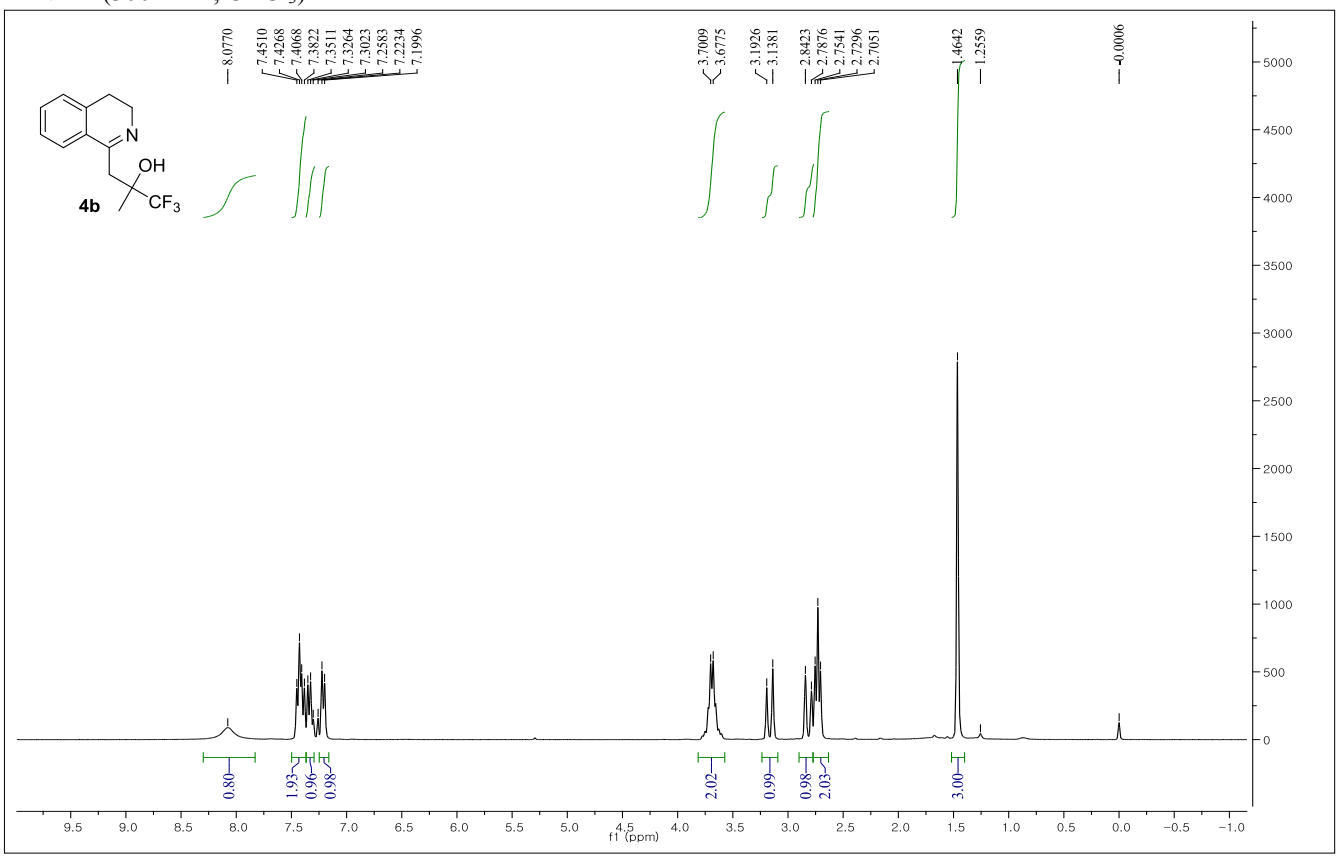

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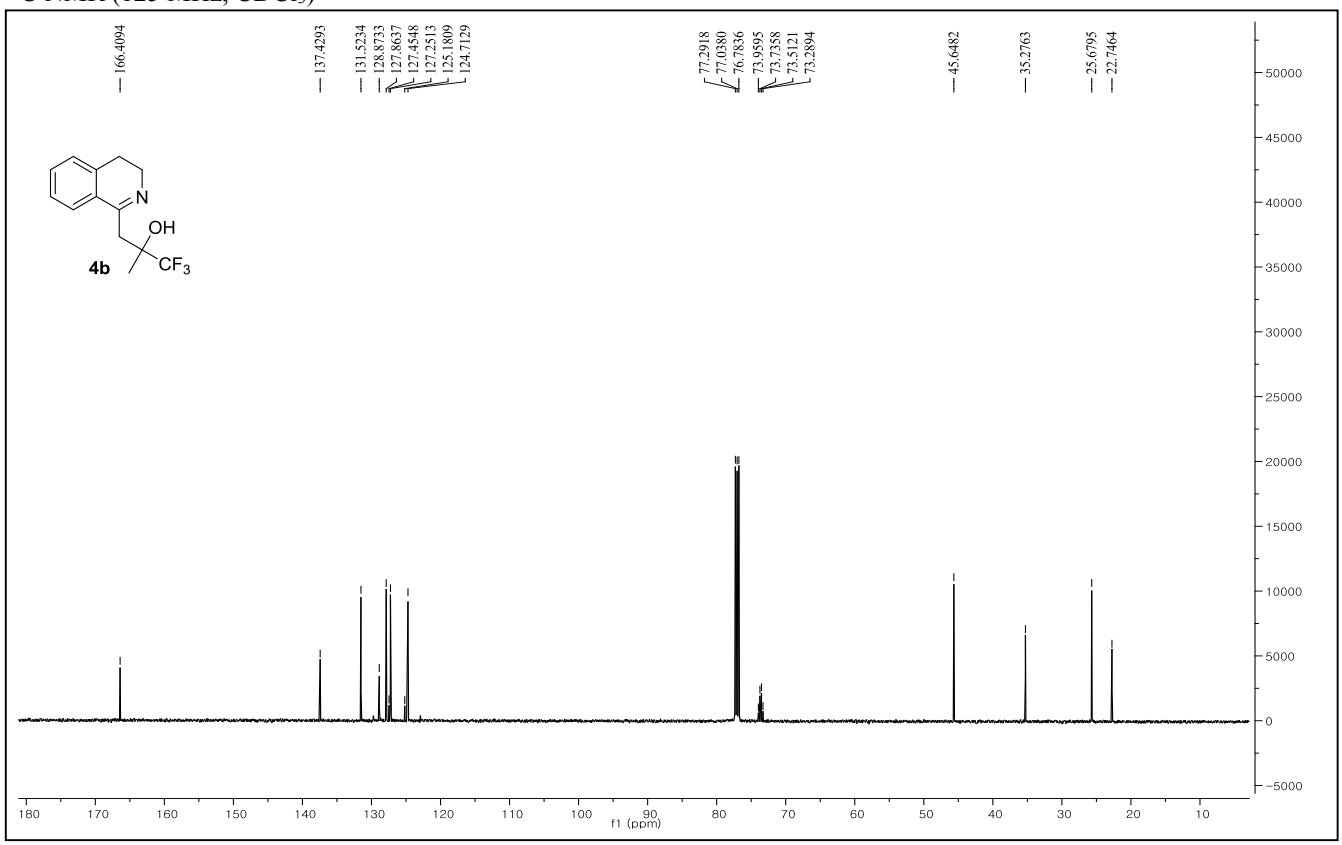

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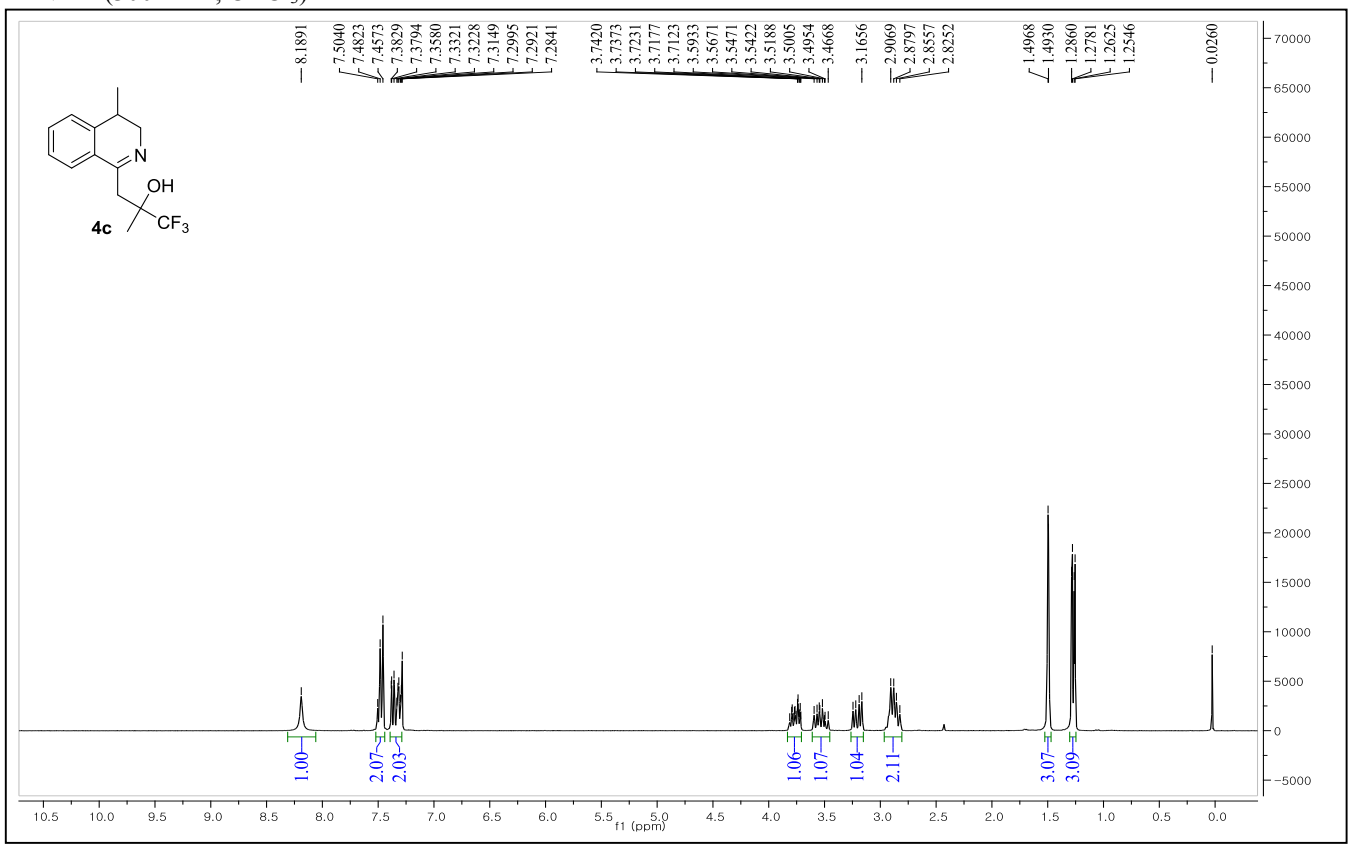

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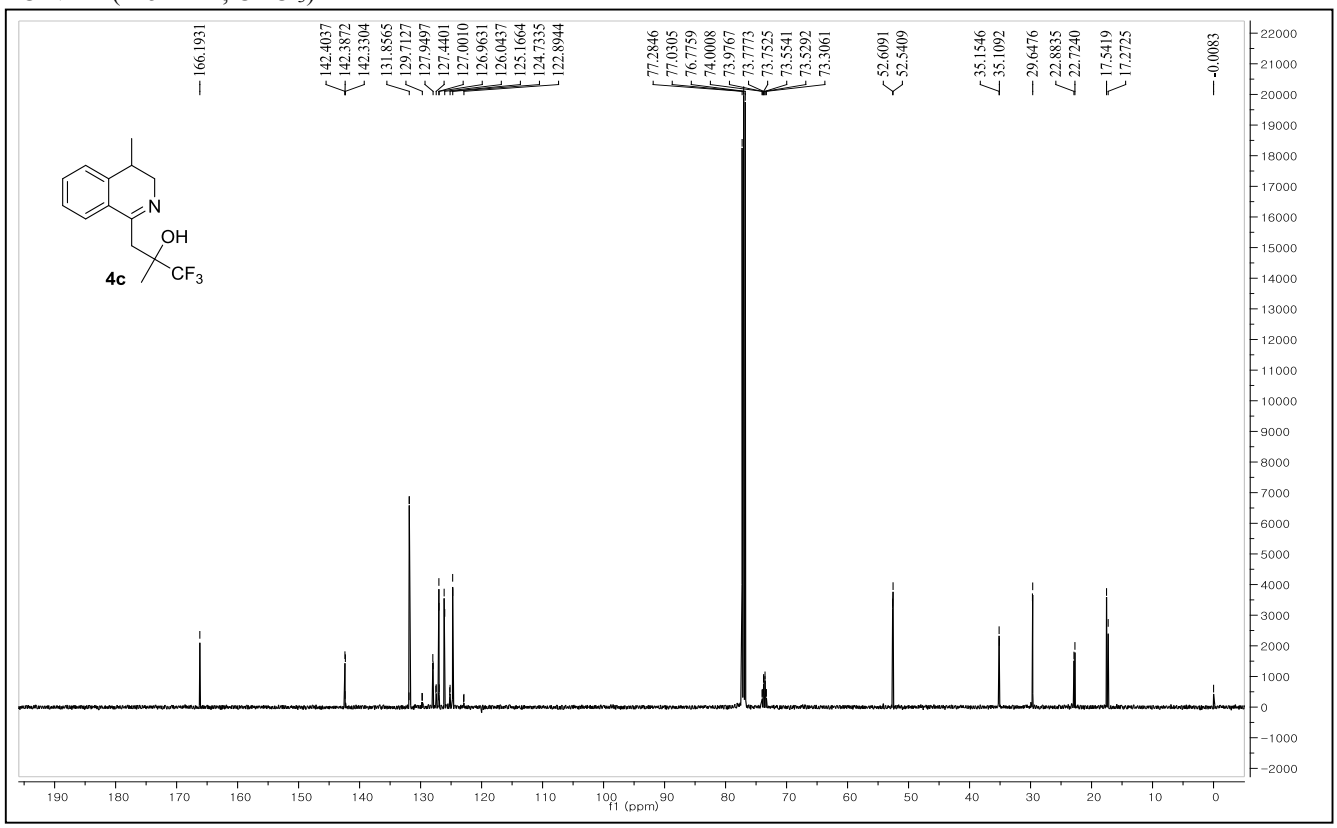

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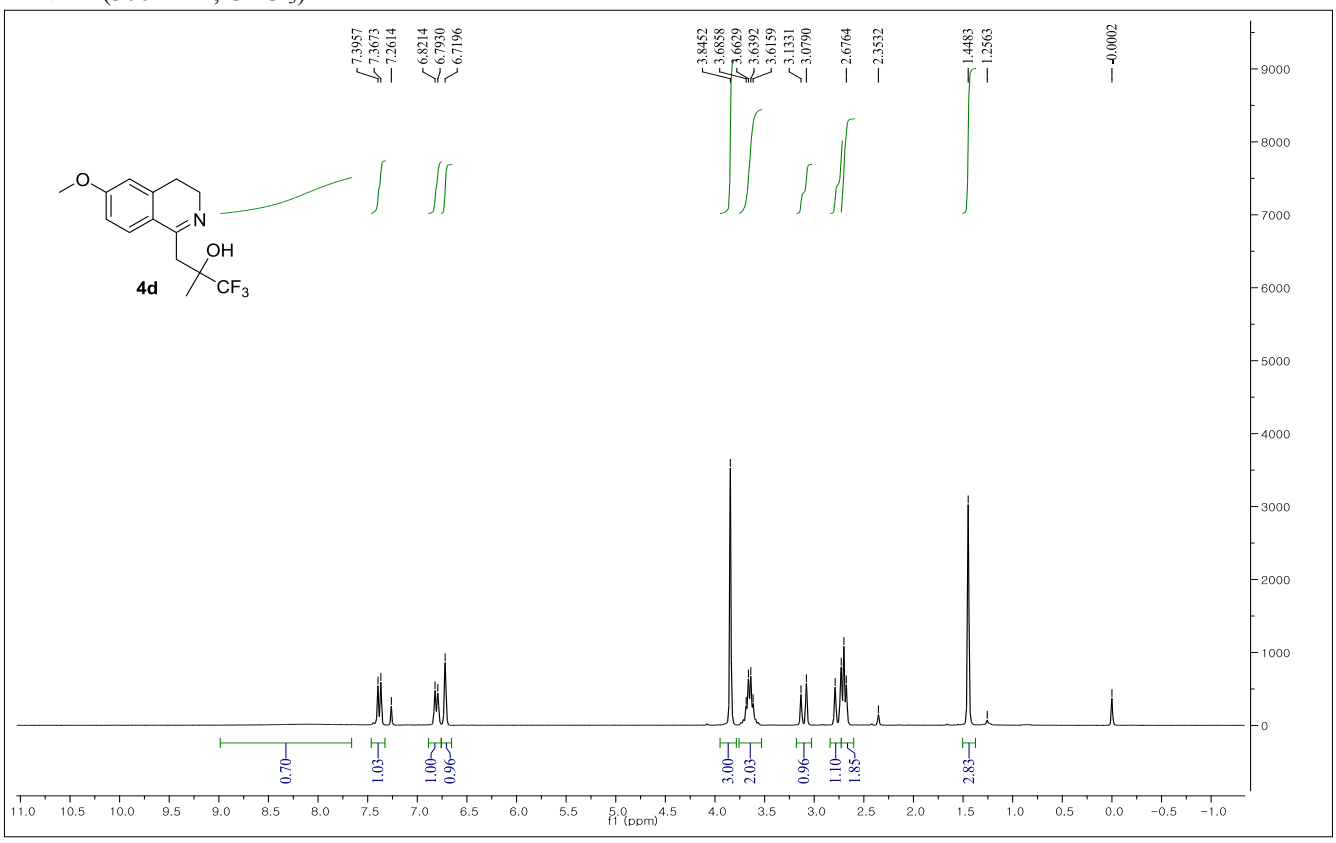
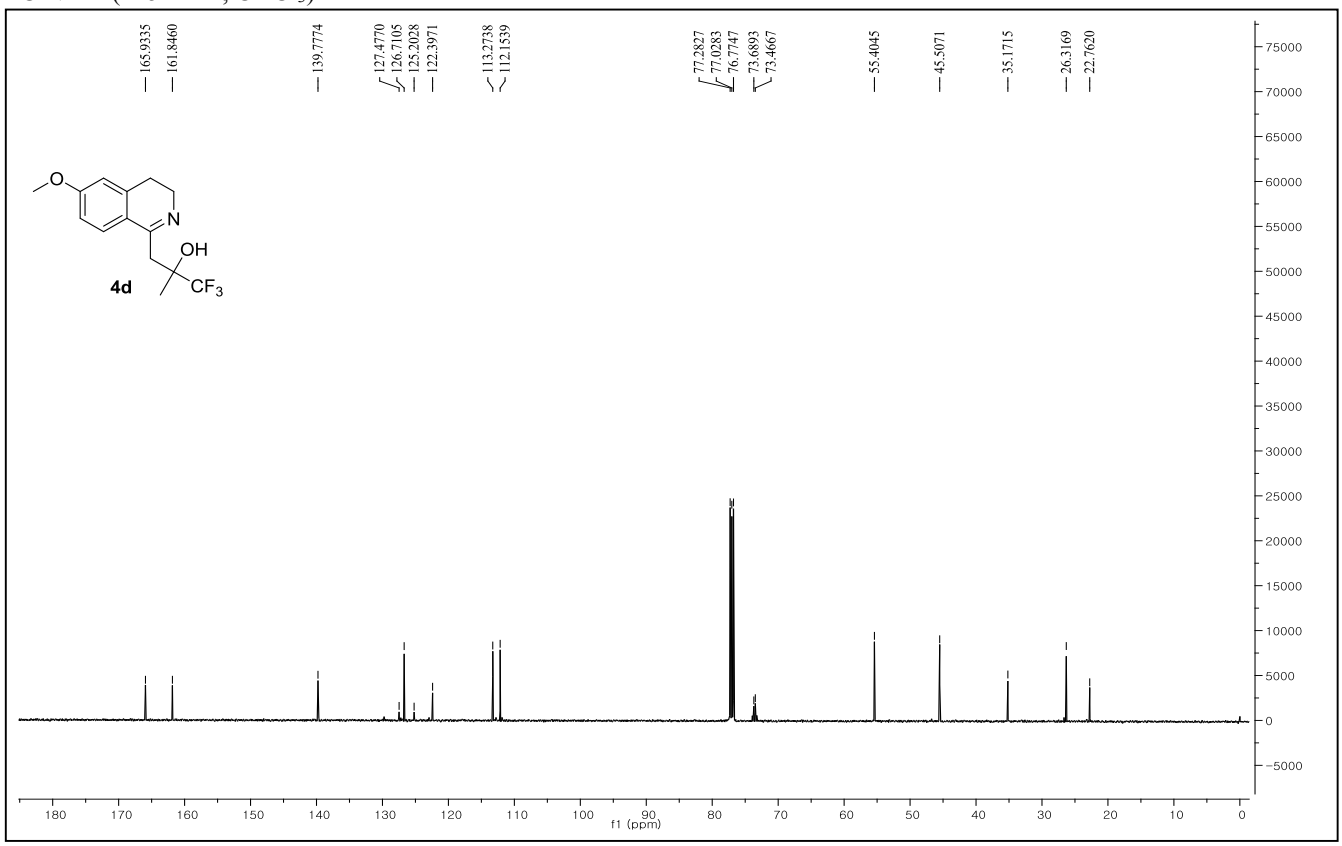
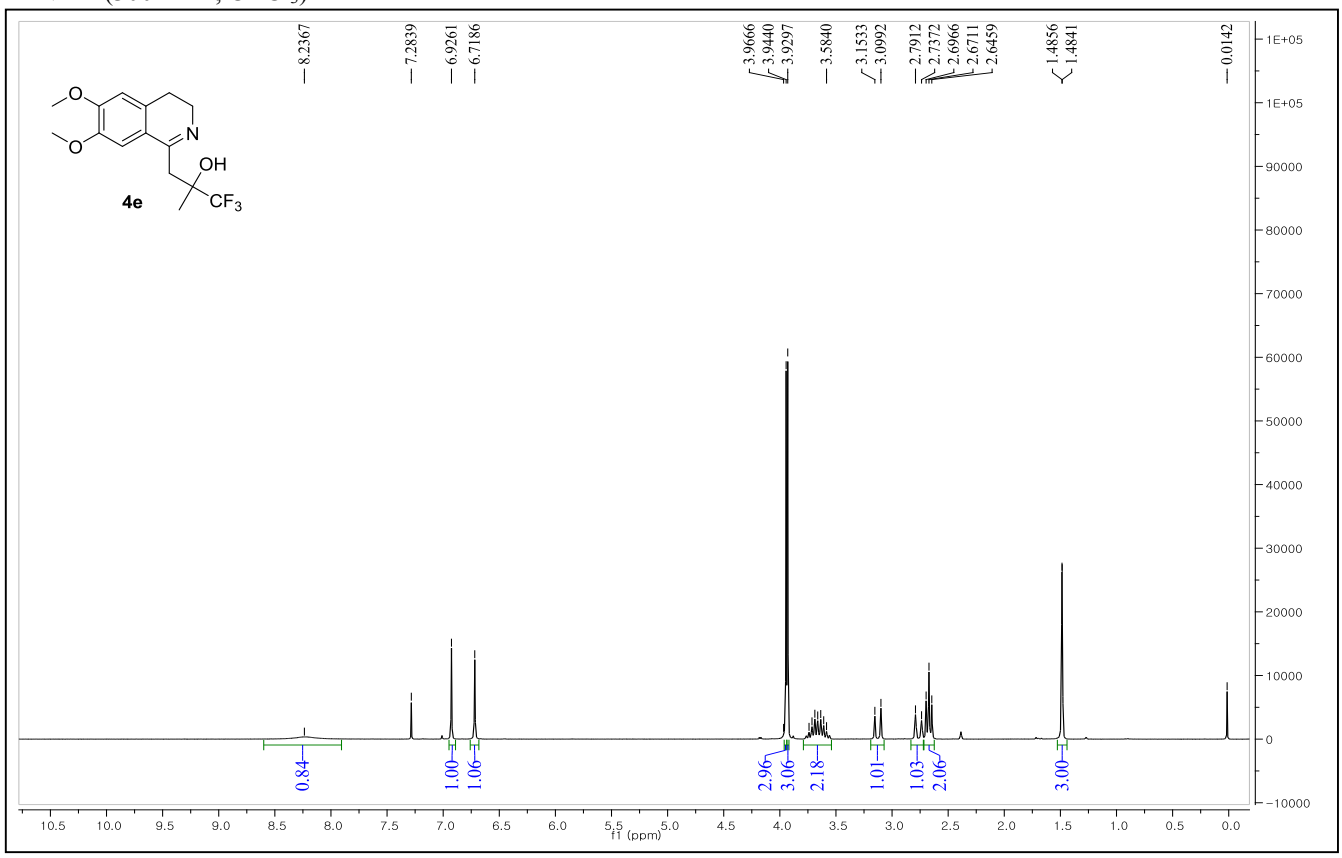


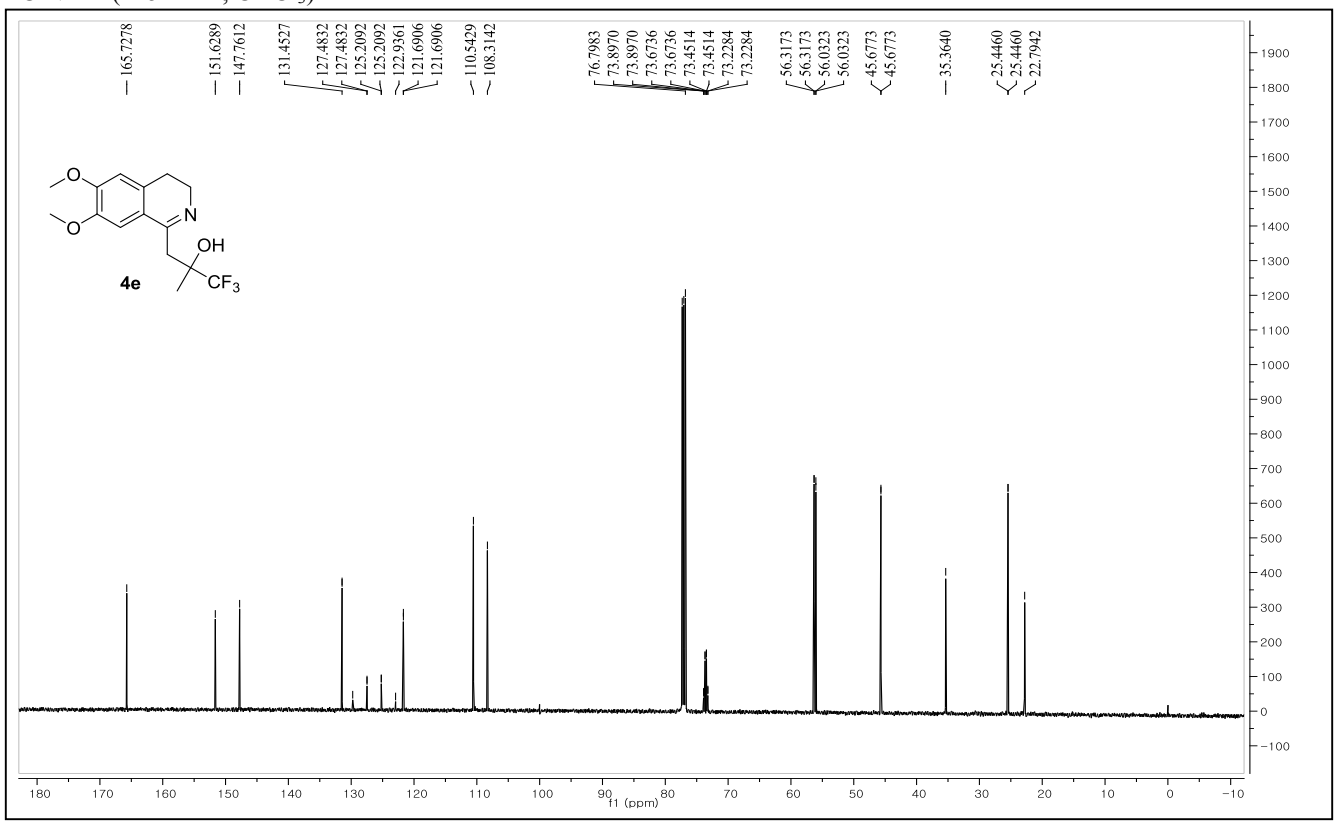
^{13}C NMR (125 MHz, $CDCl_3$)



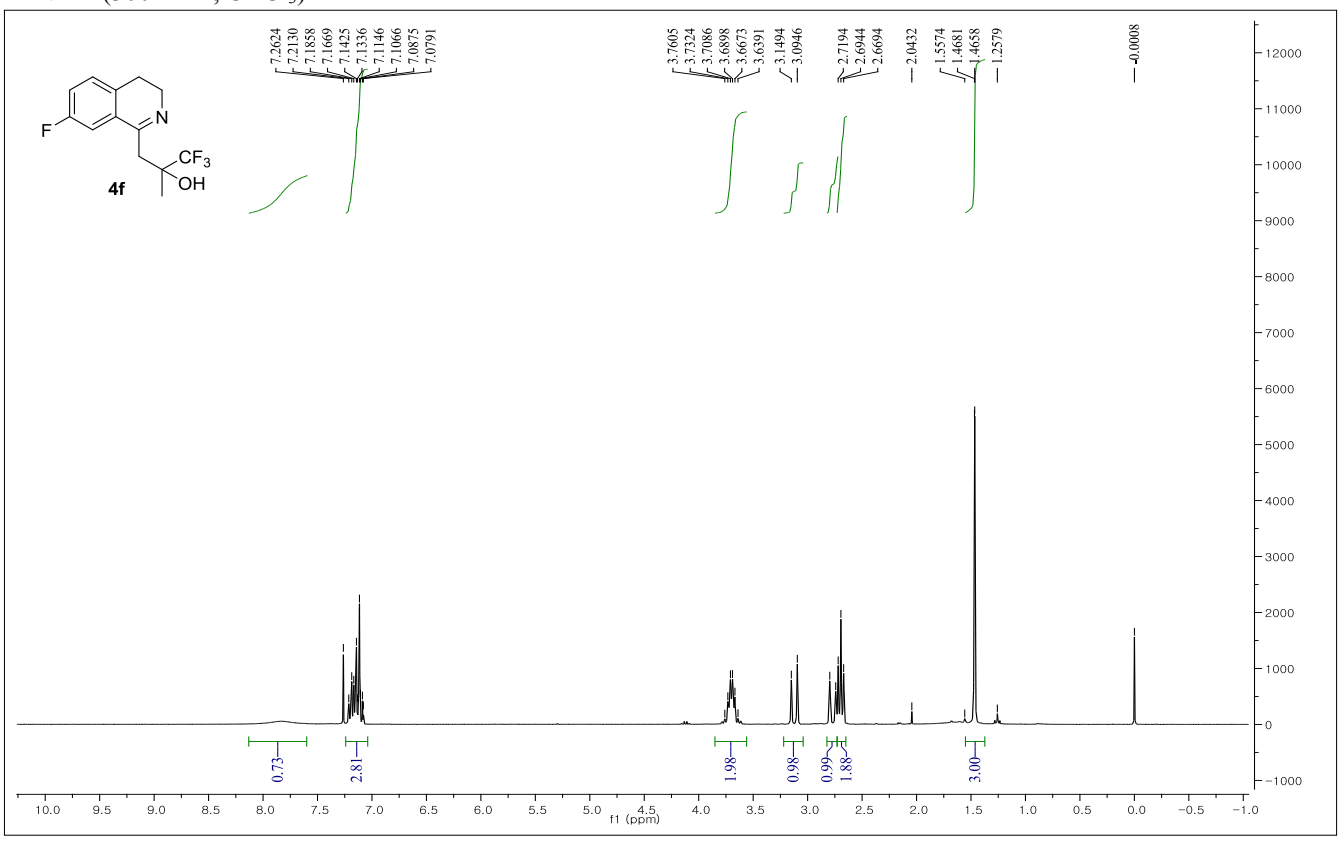
^{1}H NMR (300 MHz, $CDCl_3$)



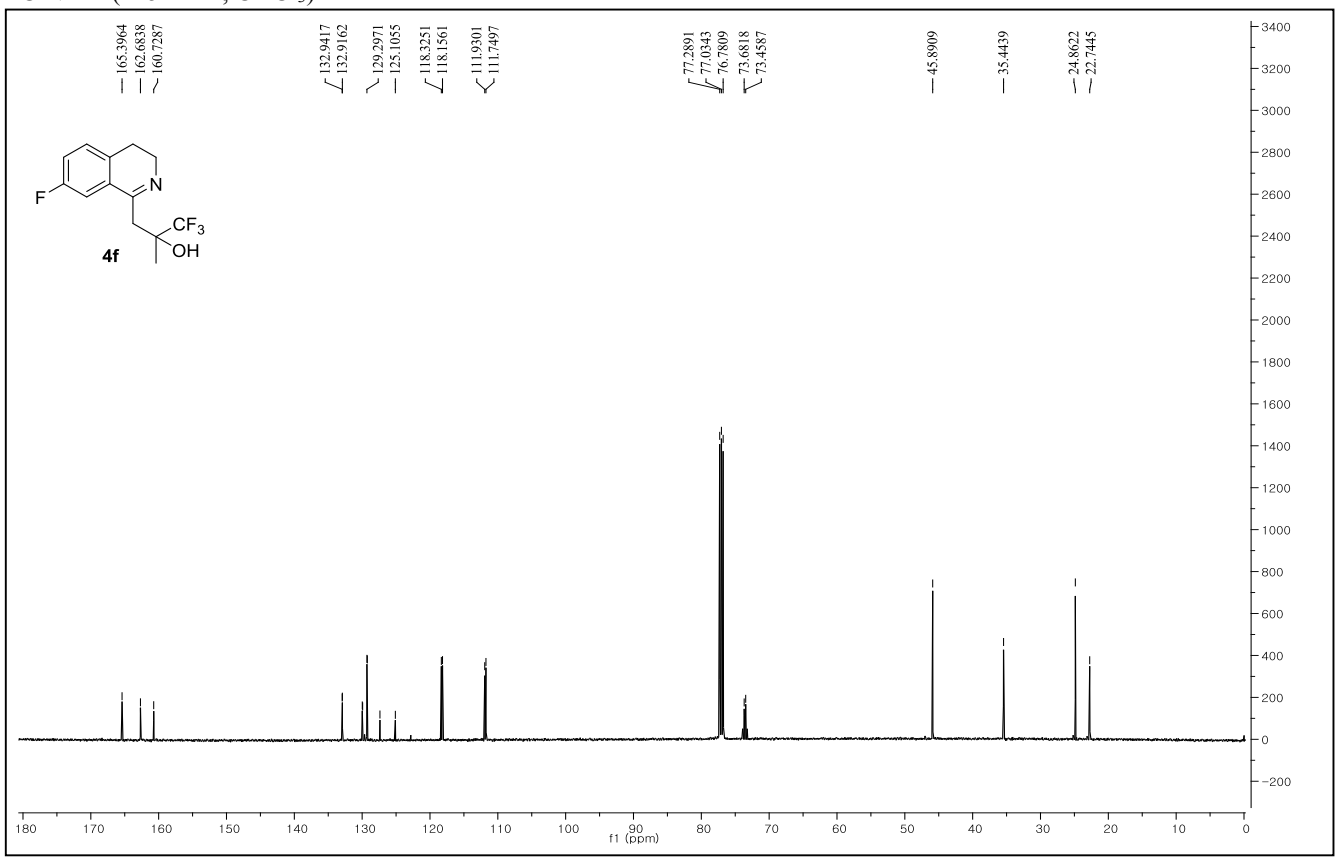
^{13}C NMR (125 MHz, $CDCl_3$)



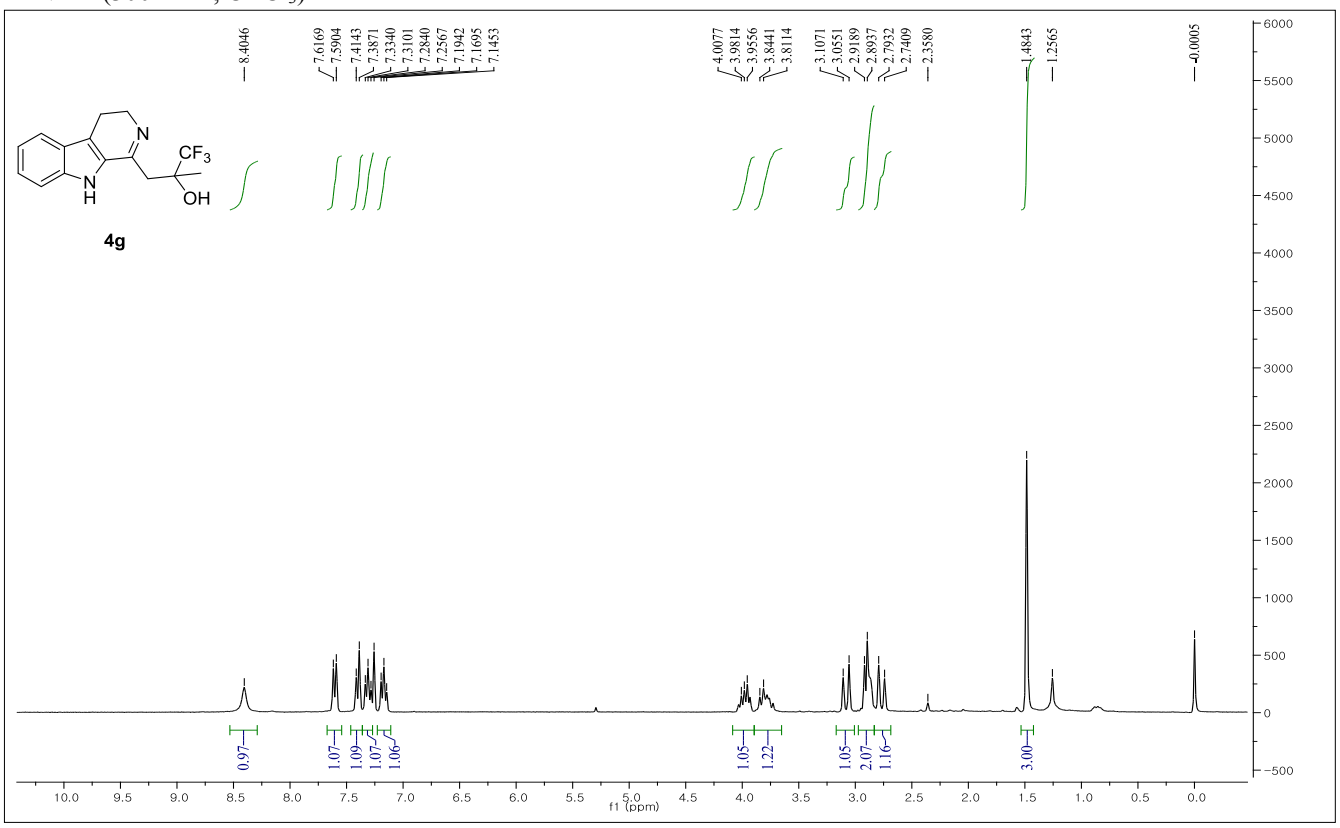
^{1}H NMR (300 MHz, $CDCl_3$)



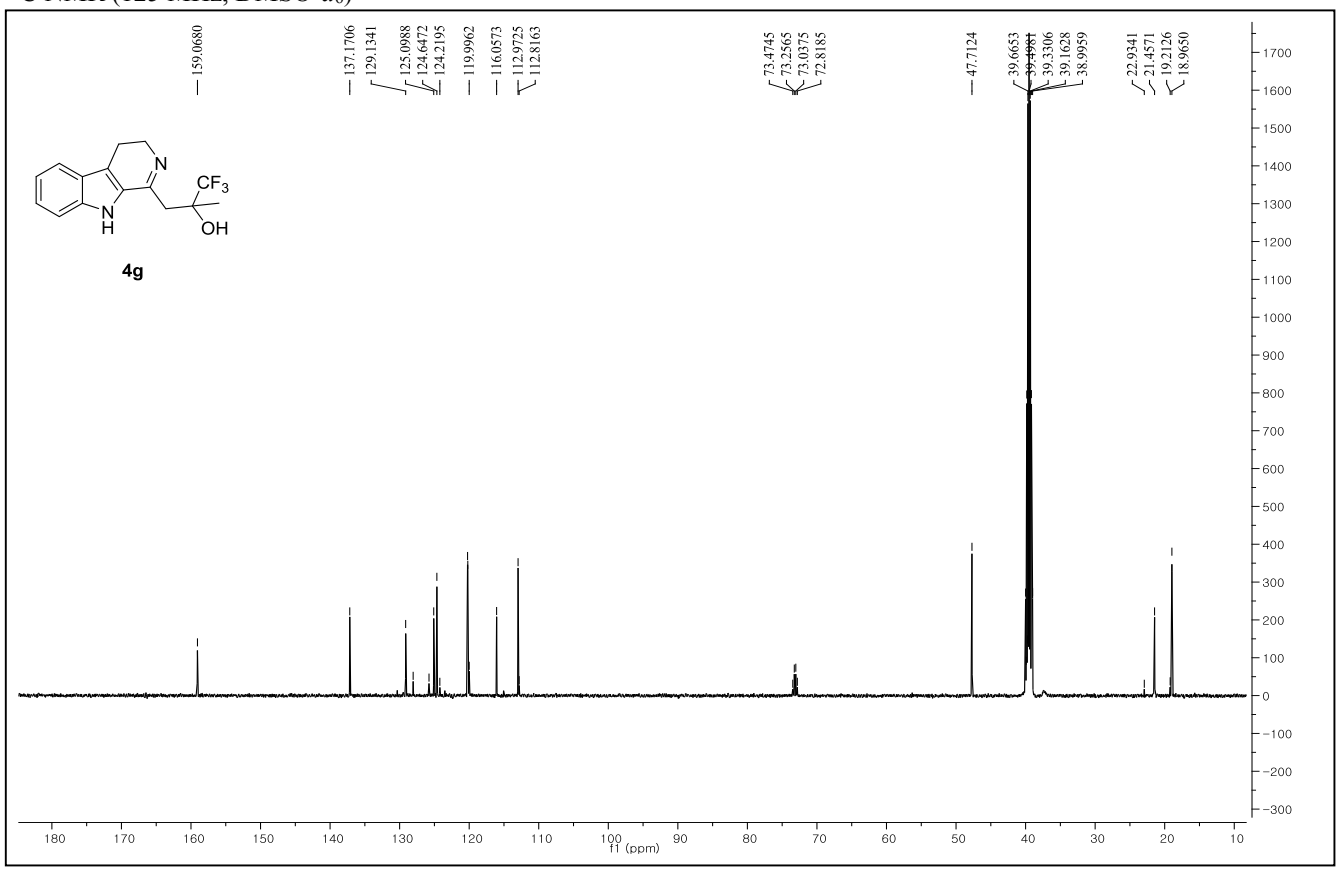
^{13}C NMR (125 MHz, $CDCl_3$)



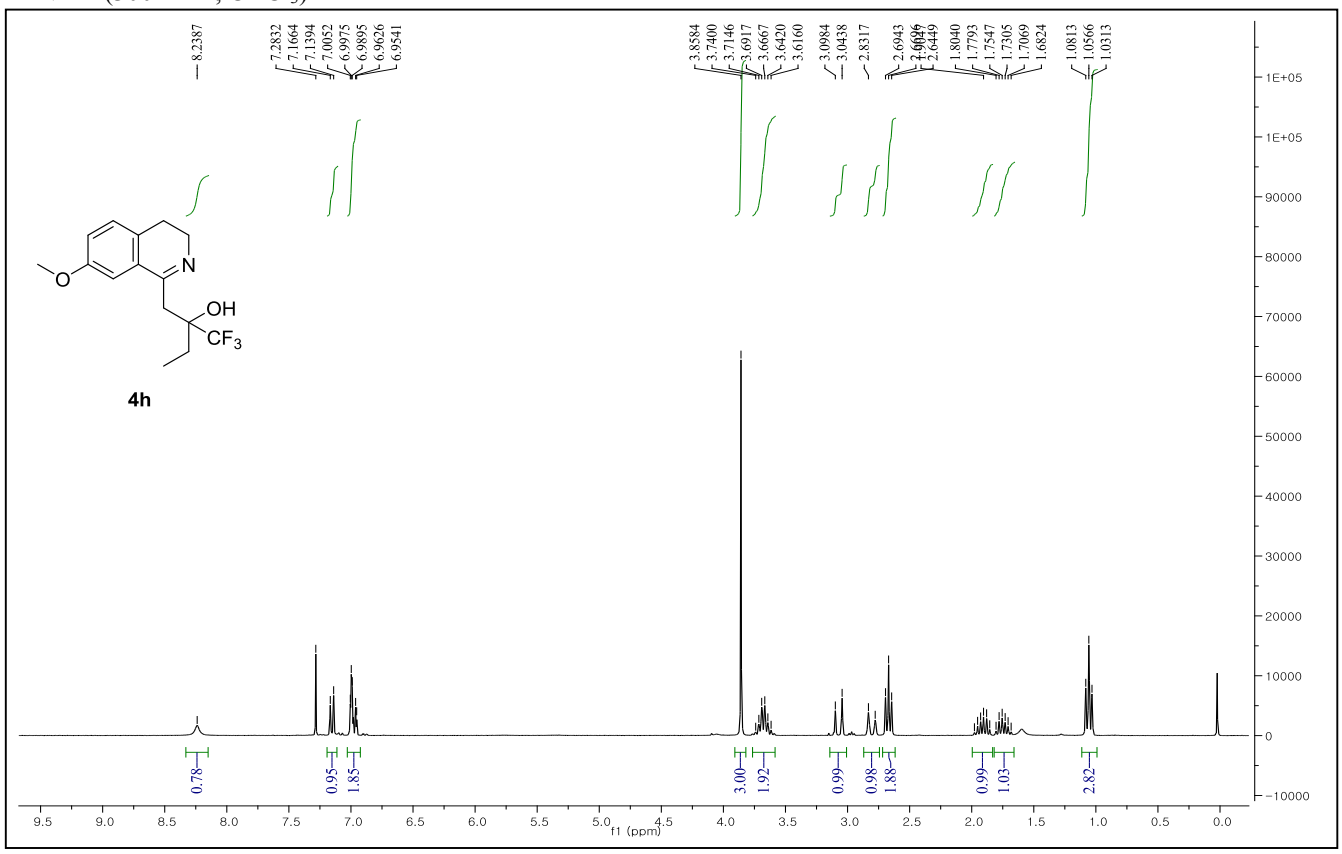
^{1}H NMR (300 MHz, $CDCl_3$)



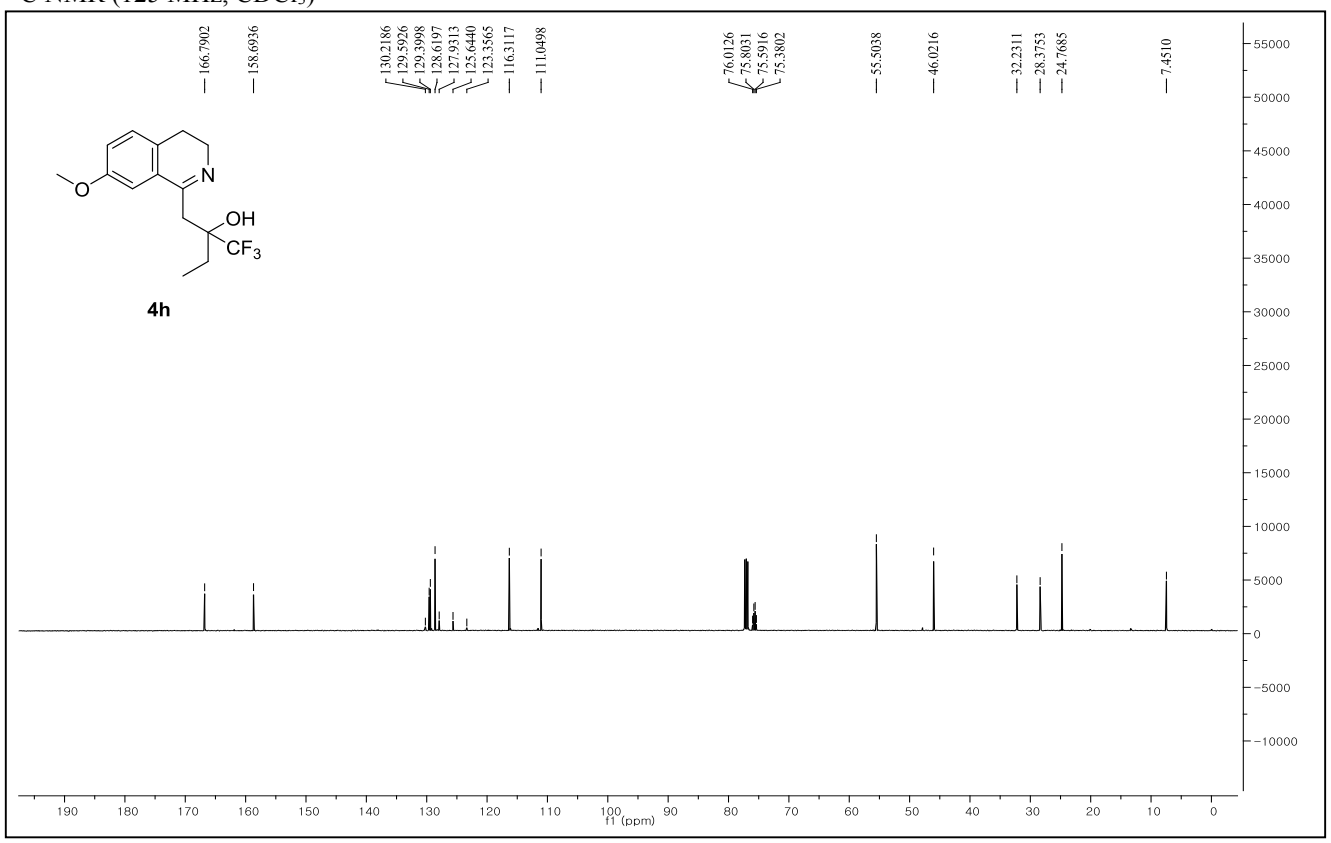
^{13}C NMR (125 MHz, DMSO-d_6)



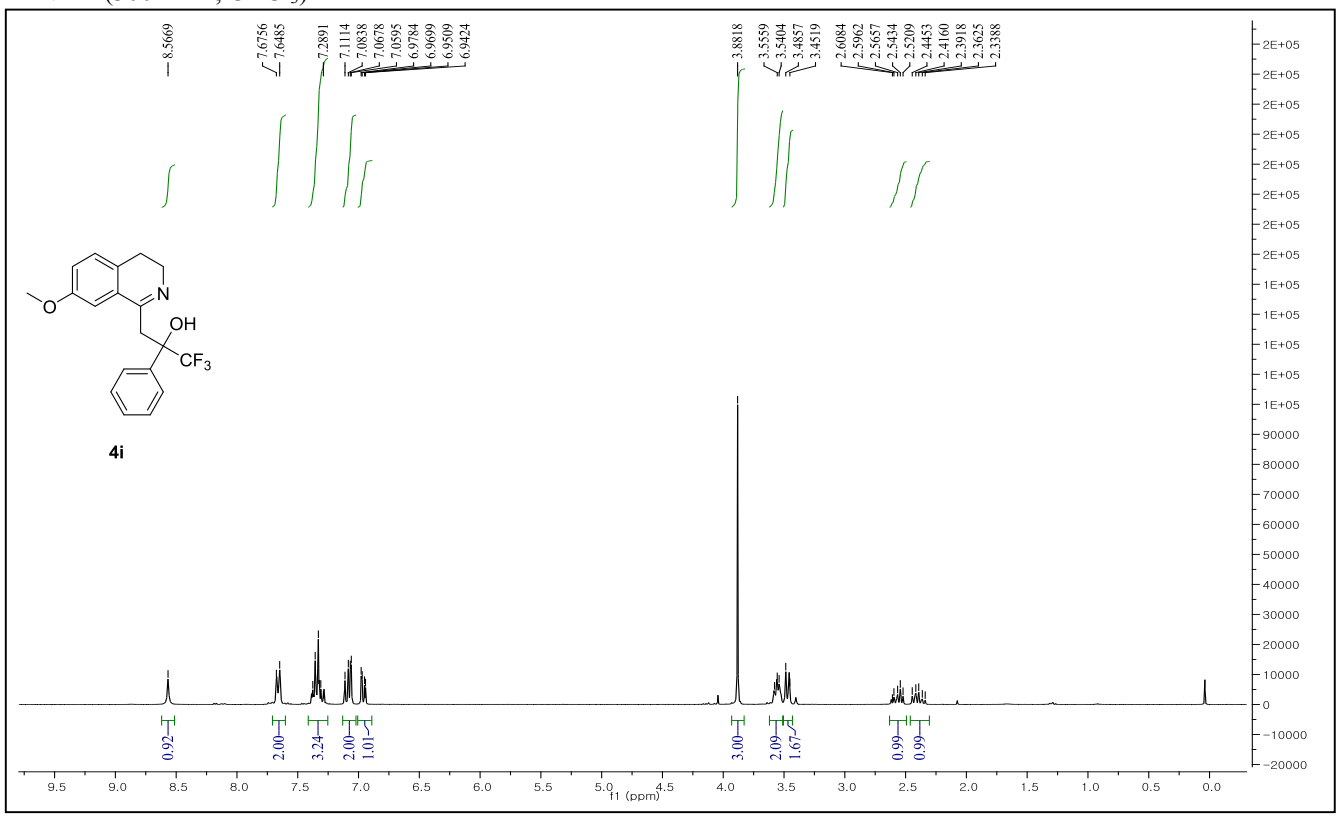
^{1}H NMR (300 MHz, $CDCl_3$)



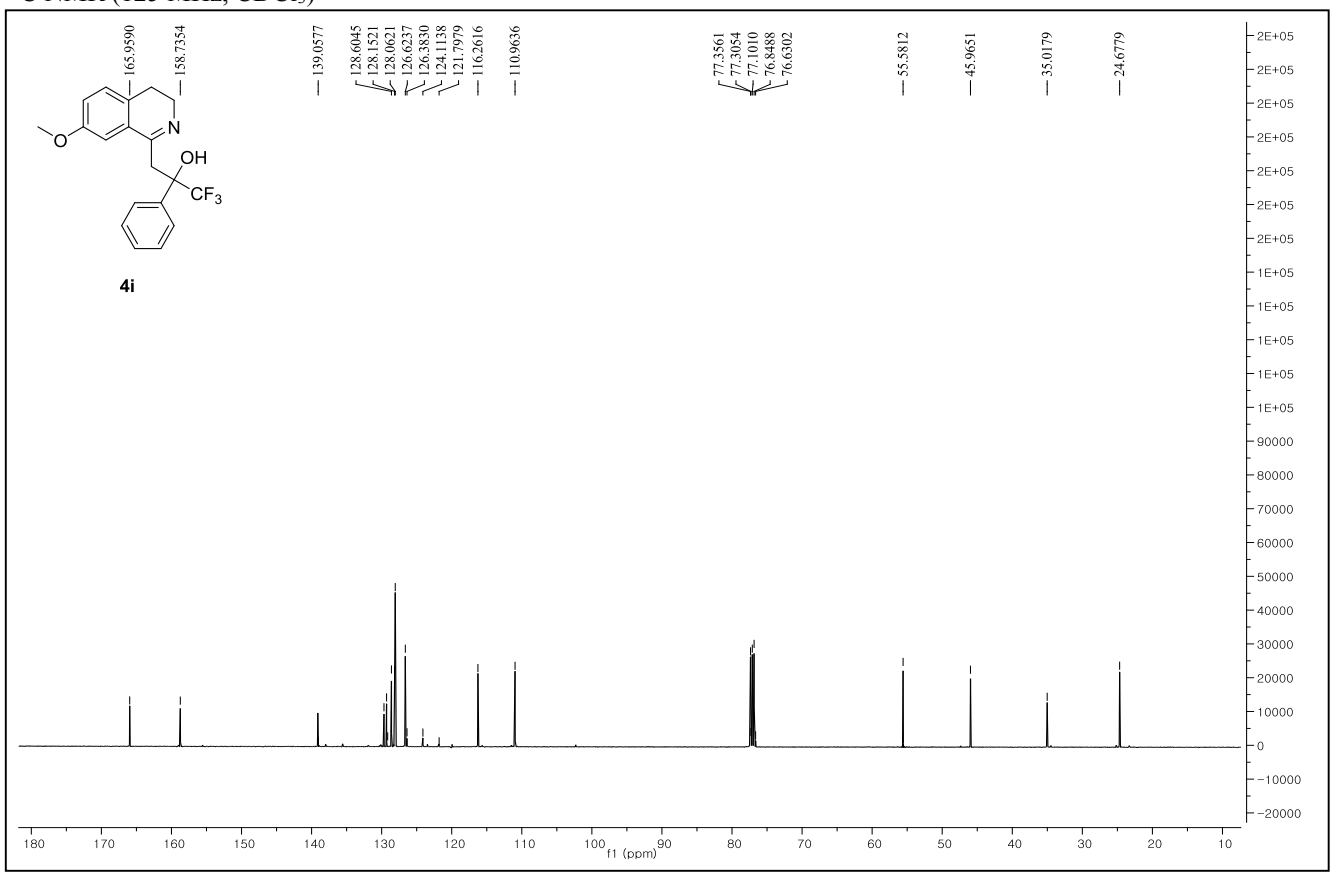
^{13}C NMR (125 MHz, $CDCl_3$)



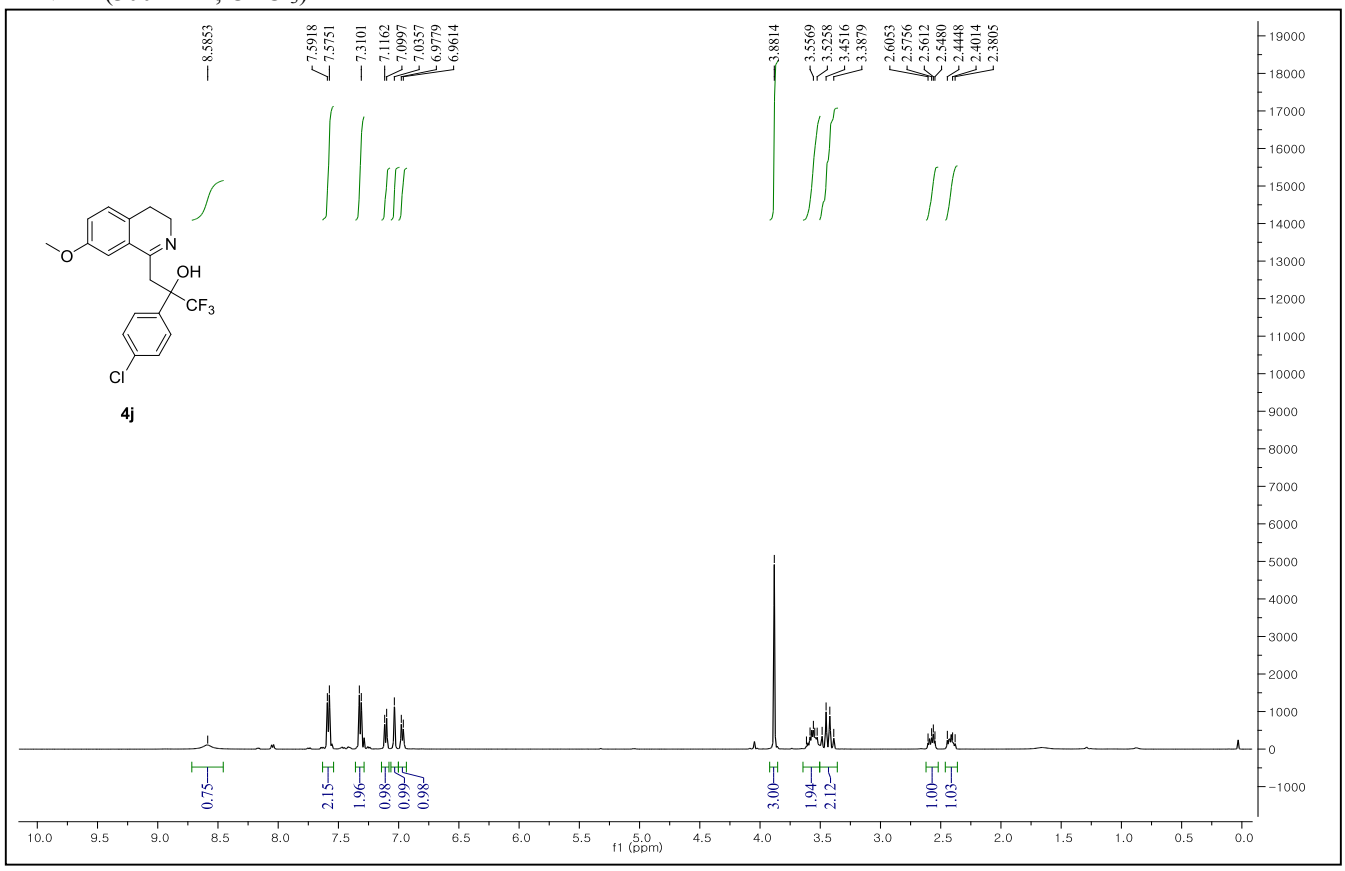
^{1}H NMR (300 MHz, $CDCl_3$)



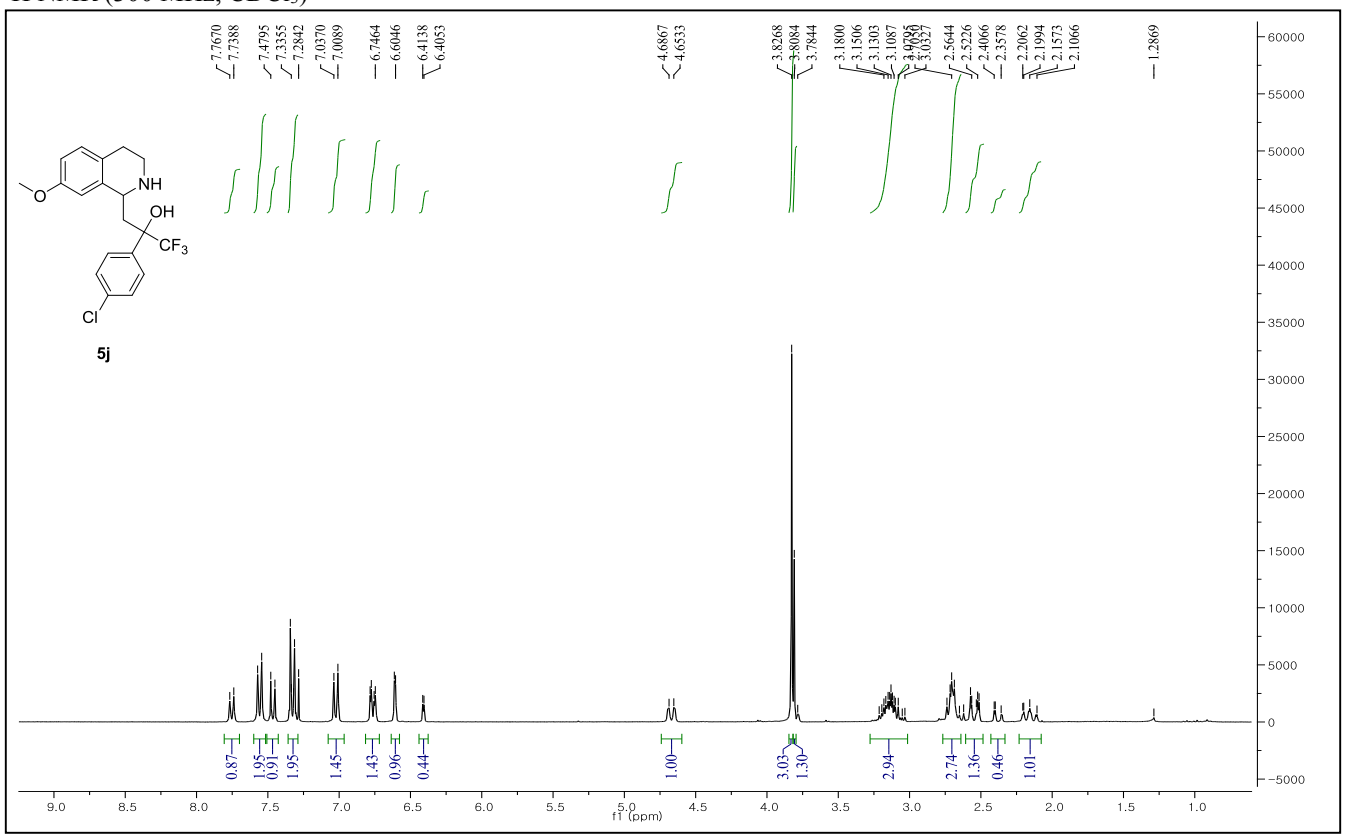
^{13}C NMR (125 MHz, $CDCl_3$)



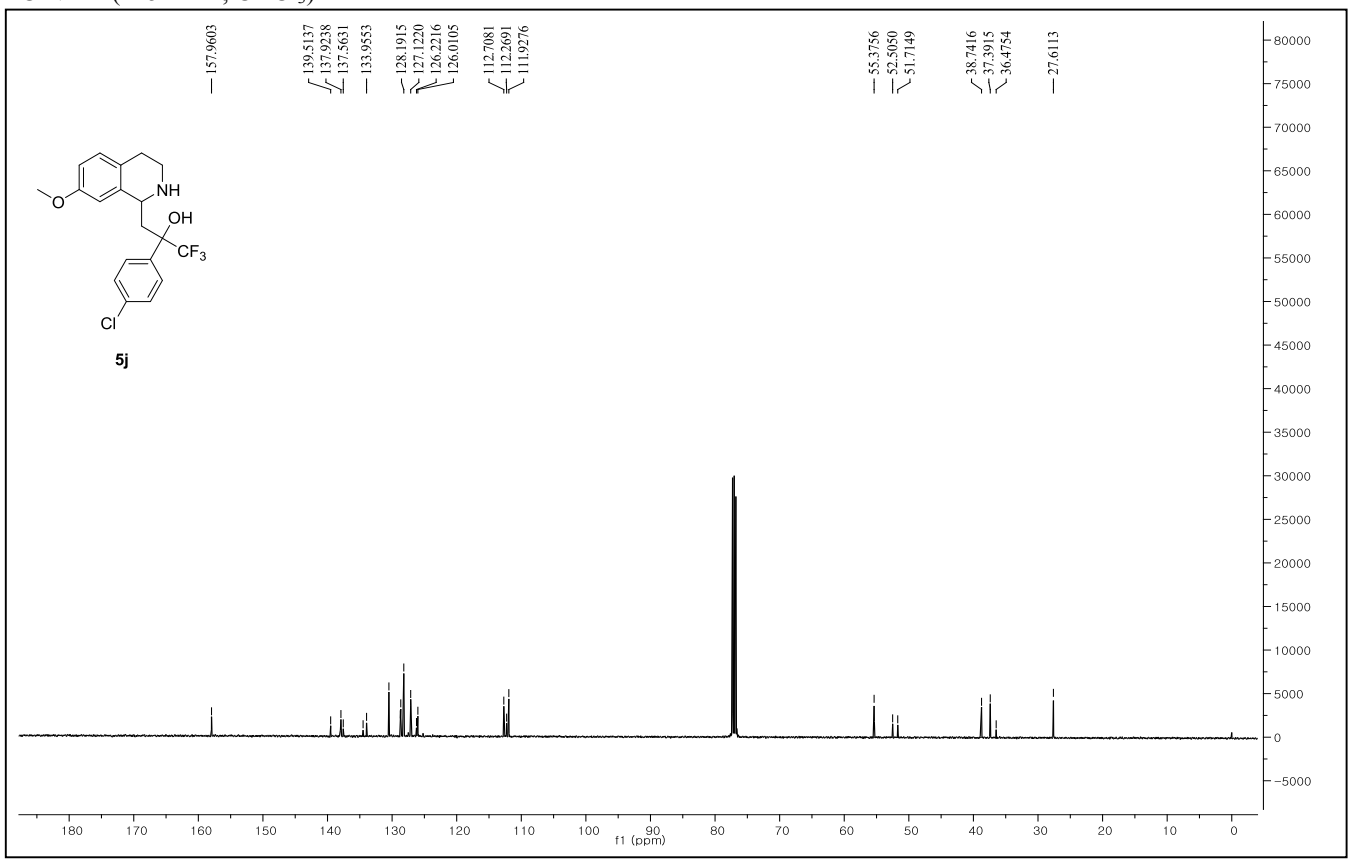
^{1}H NMR (300 MHz, $CDCl_3$)



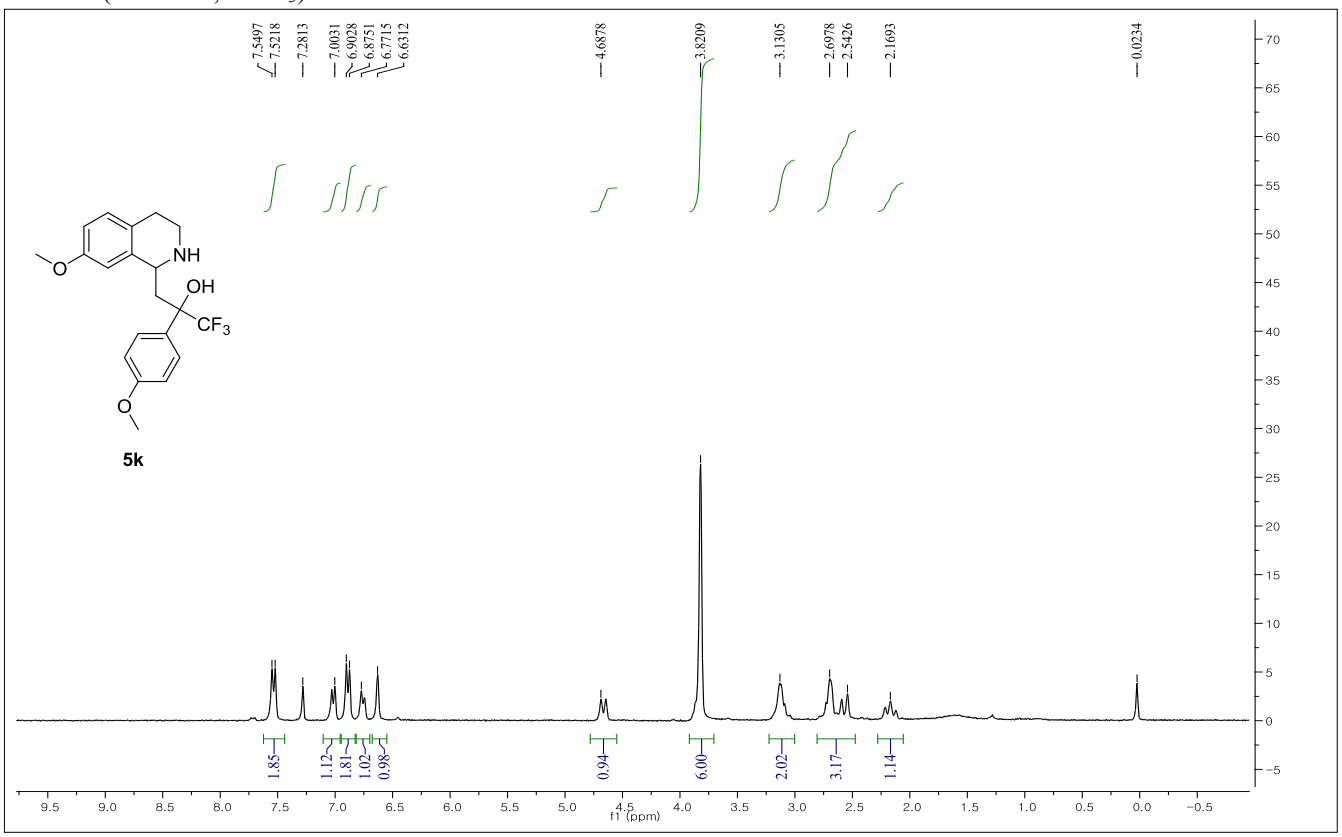
^{1}H NMR (300 MHz, $CDCl_3$)



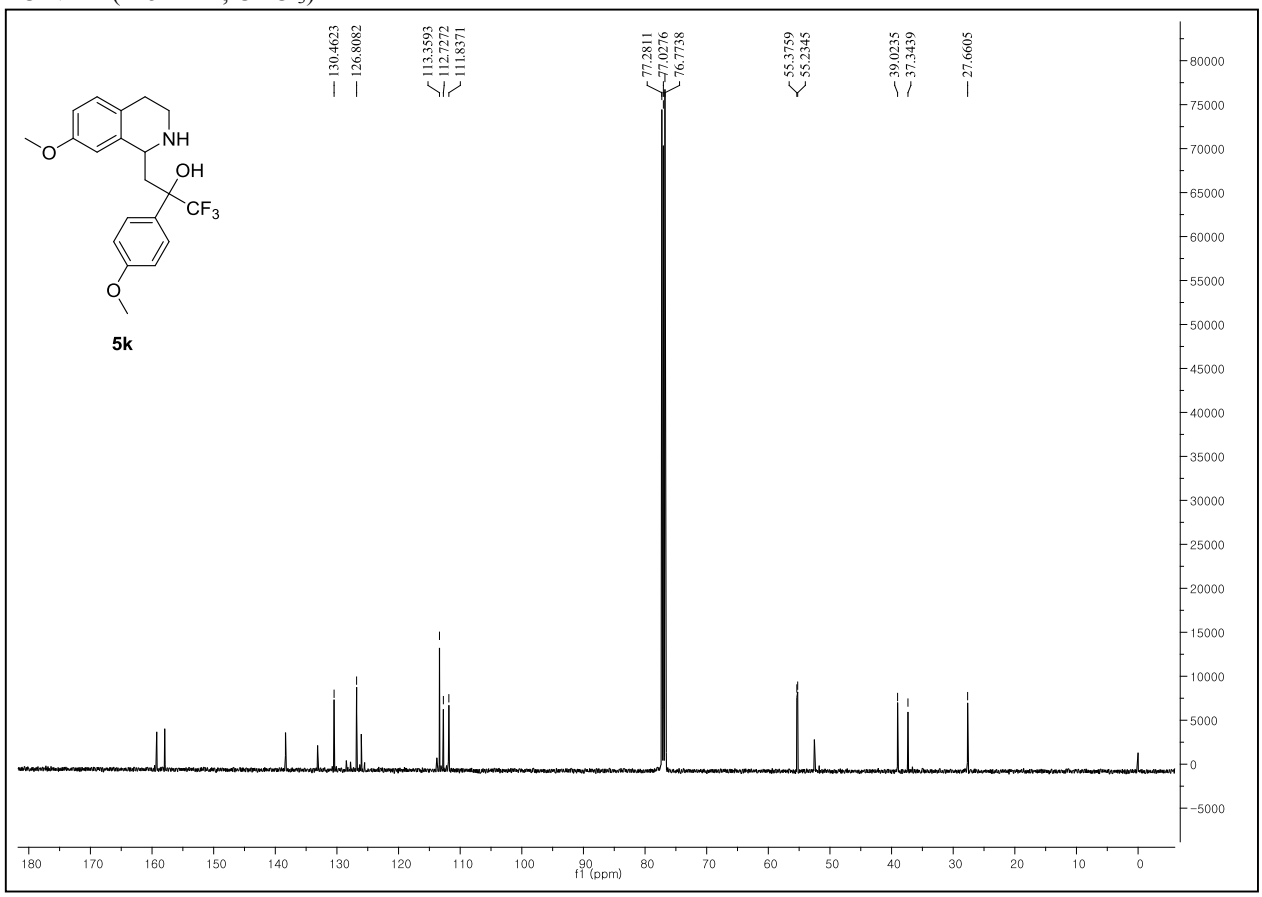
^{13}C NMR (125 MHz, $CDCl_3$)



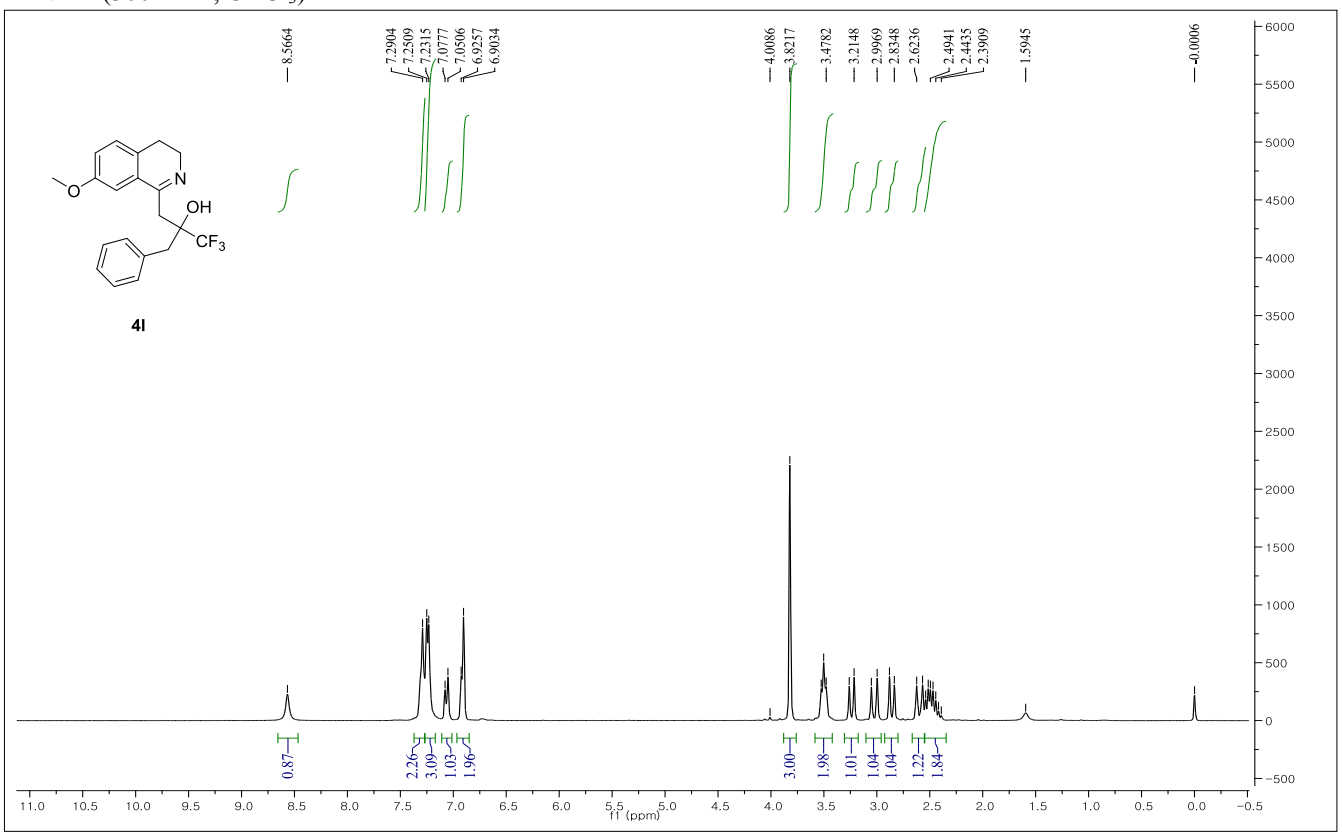
^{1}H NMR (300 MHz, $CDCl_3$)



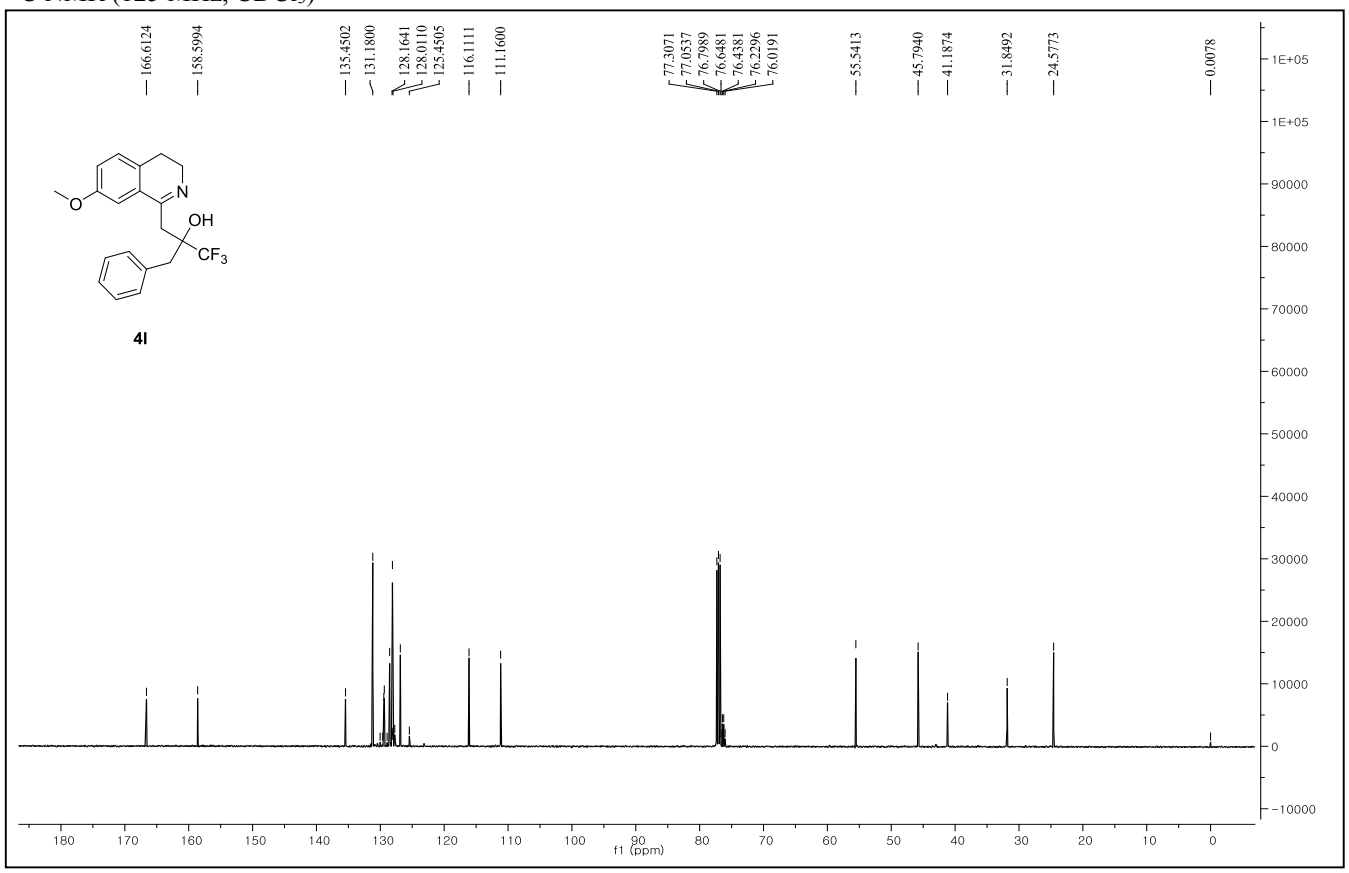
^{13}C NMR (125 MHz, $CDCl_3$)



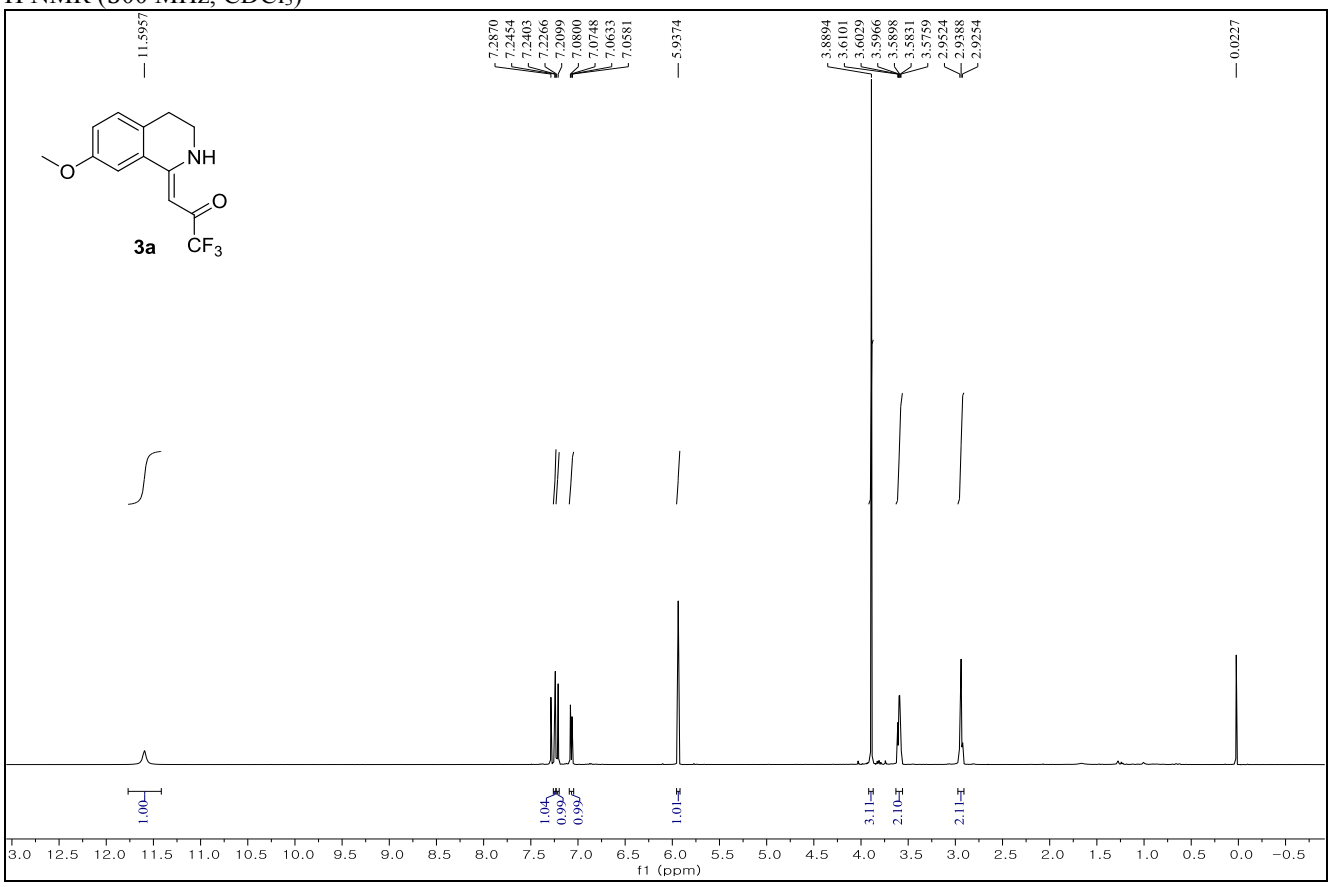
^{1}H NMR (300 MHz, $CDCl_3$)



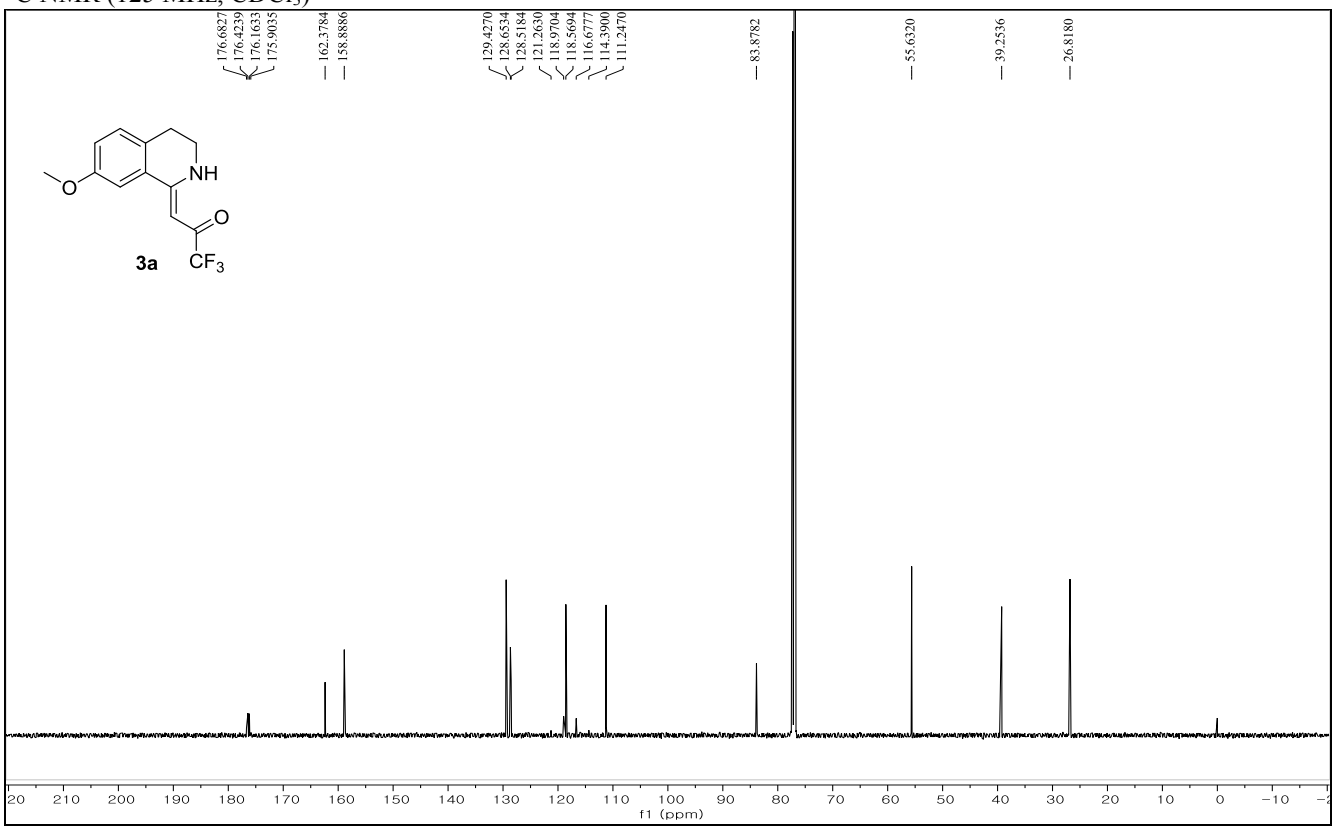
^{13}C NMR (125 MHz, $CDCl_3$)



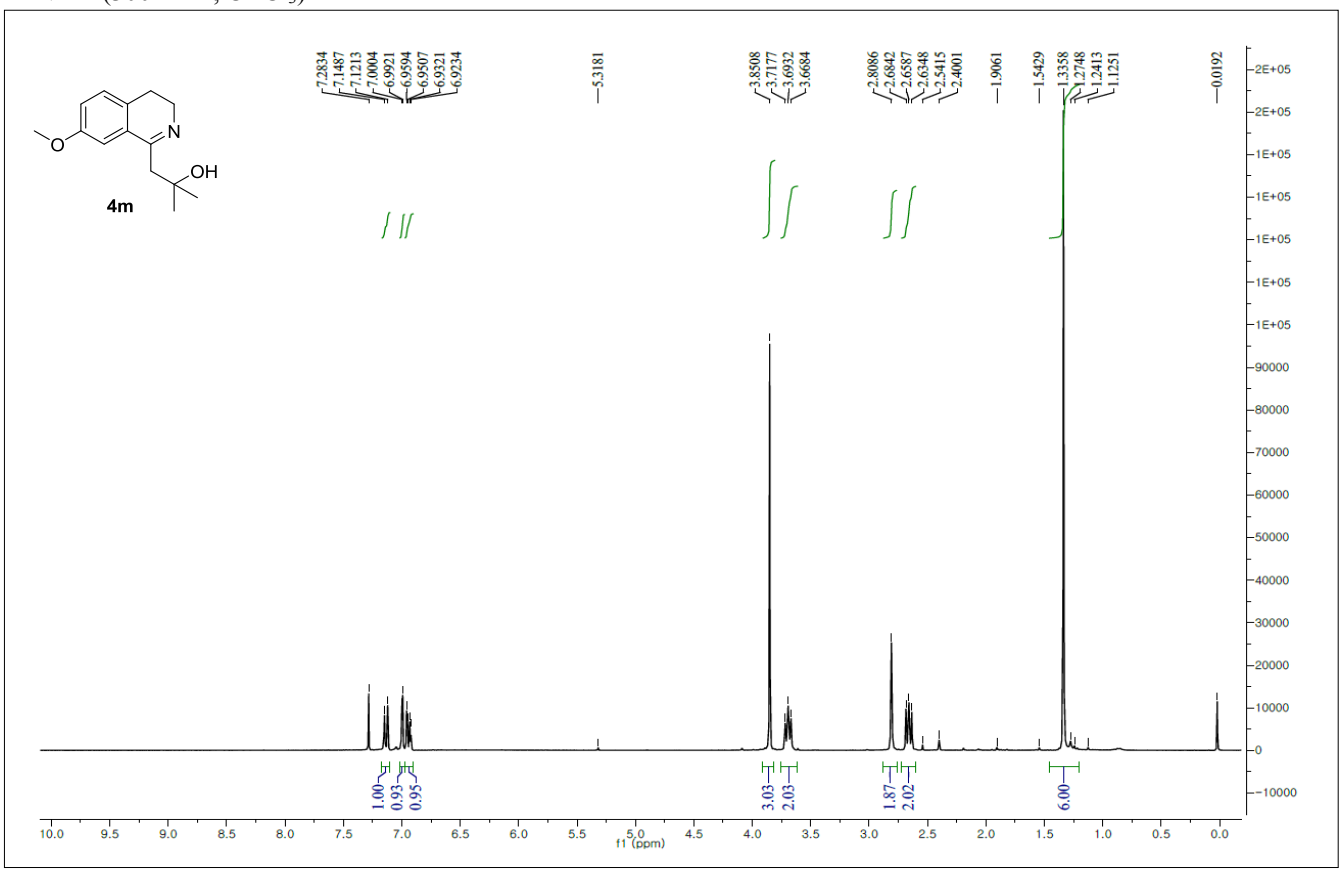
^{1}H NMR (500 MHz, $CDCl_3$)



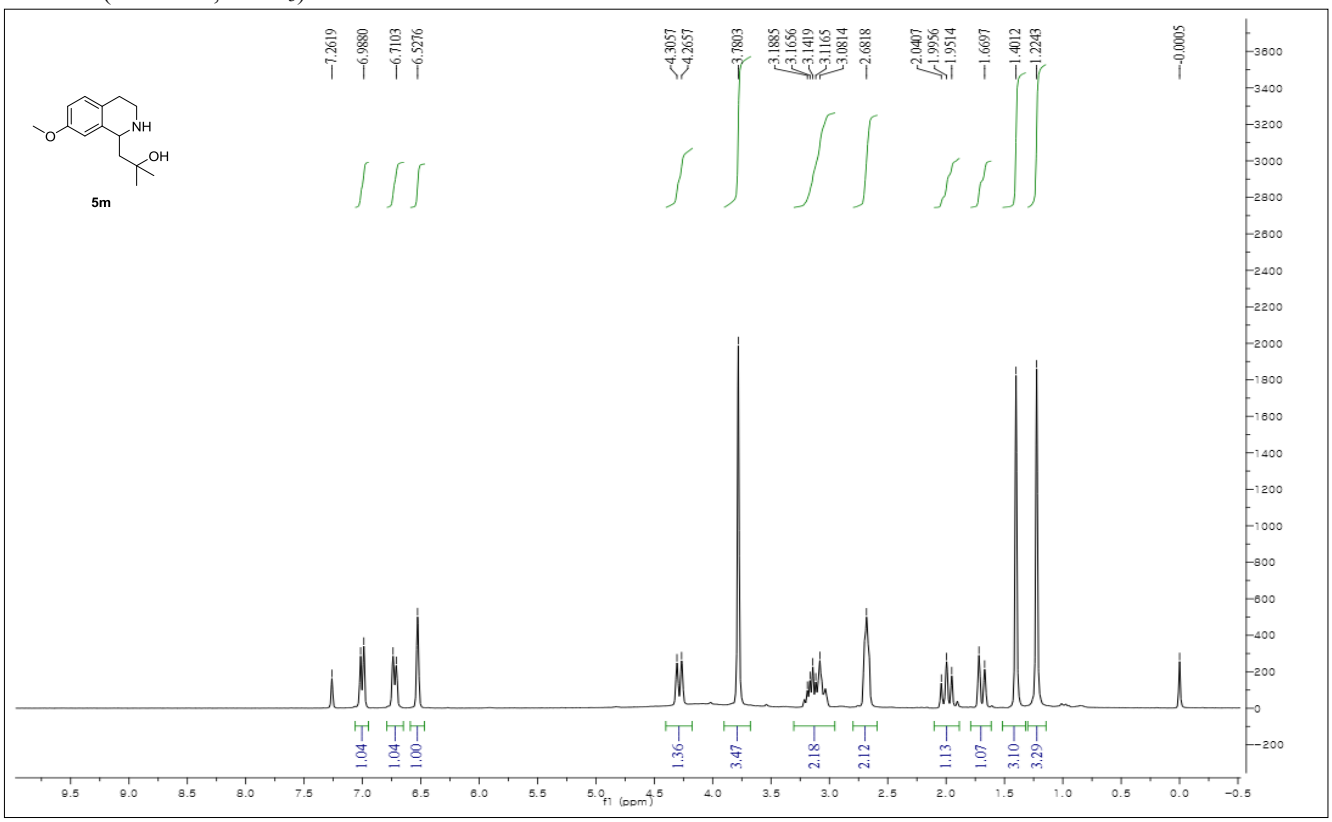
^{13}C NMR (125 MHz, $CDCl_3$)



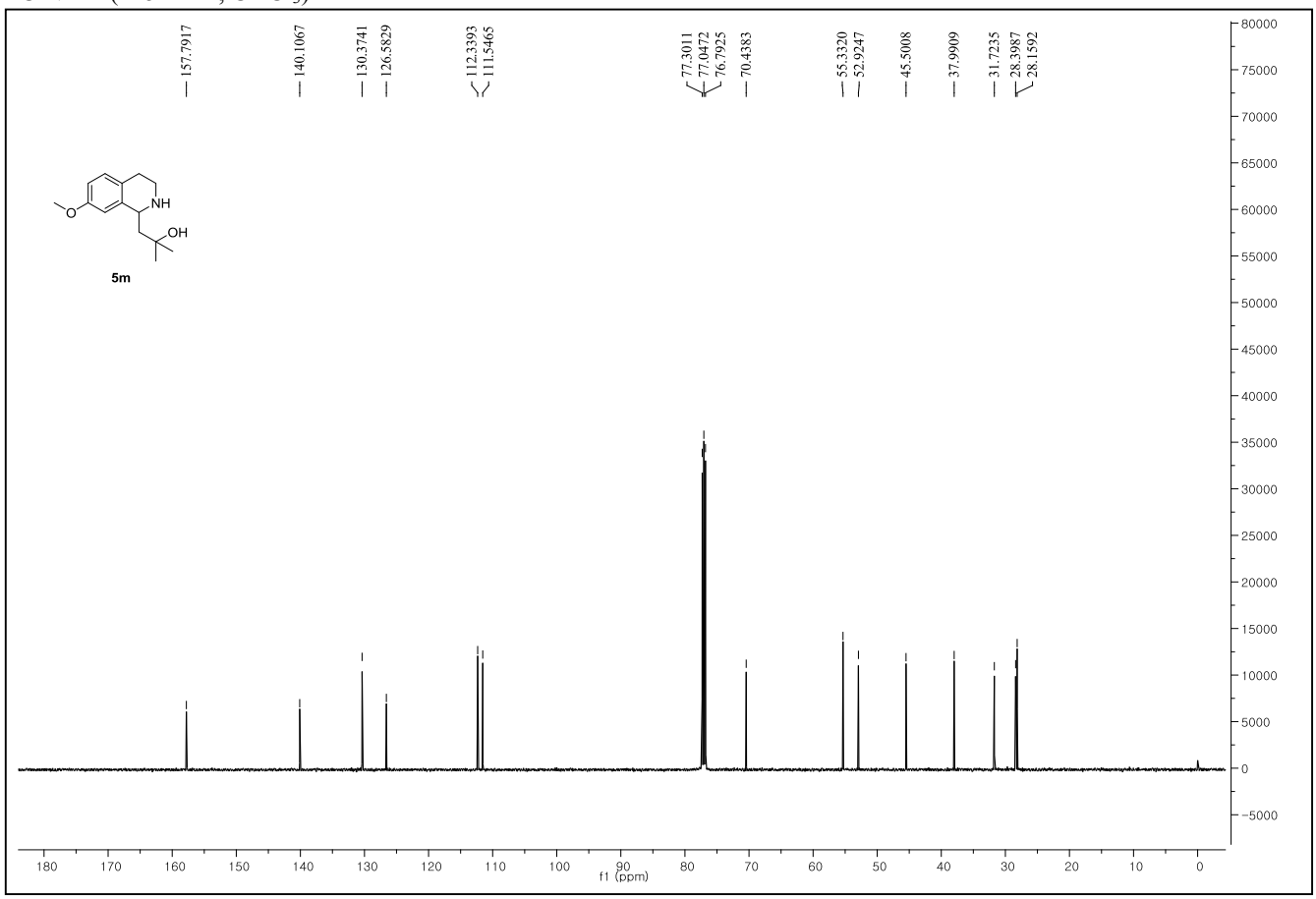
^{1}H NMR (300 MHz, $CDCl_3$)



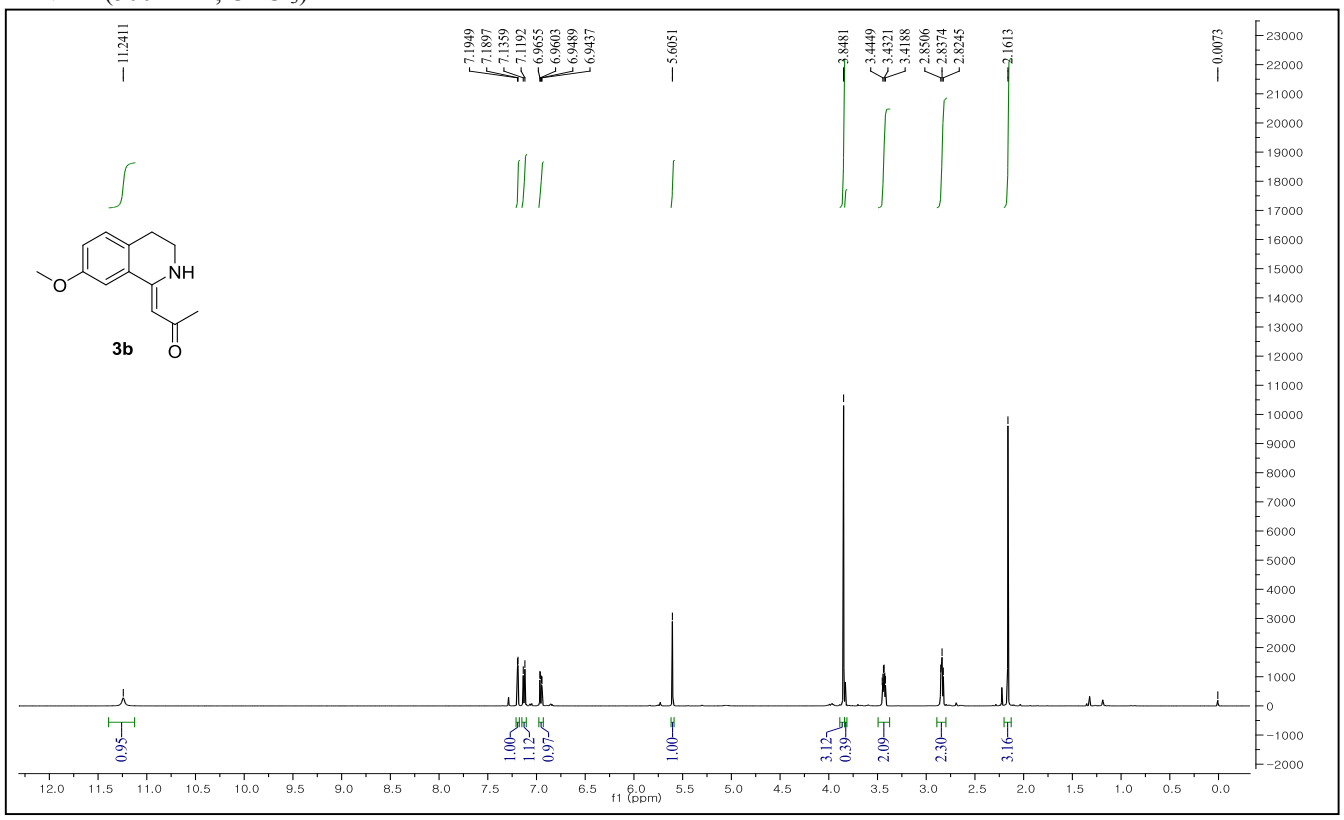
^{1}H NMR (300 MHz, $CDCl_3$)



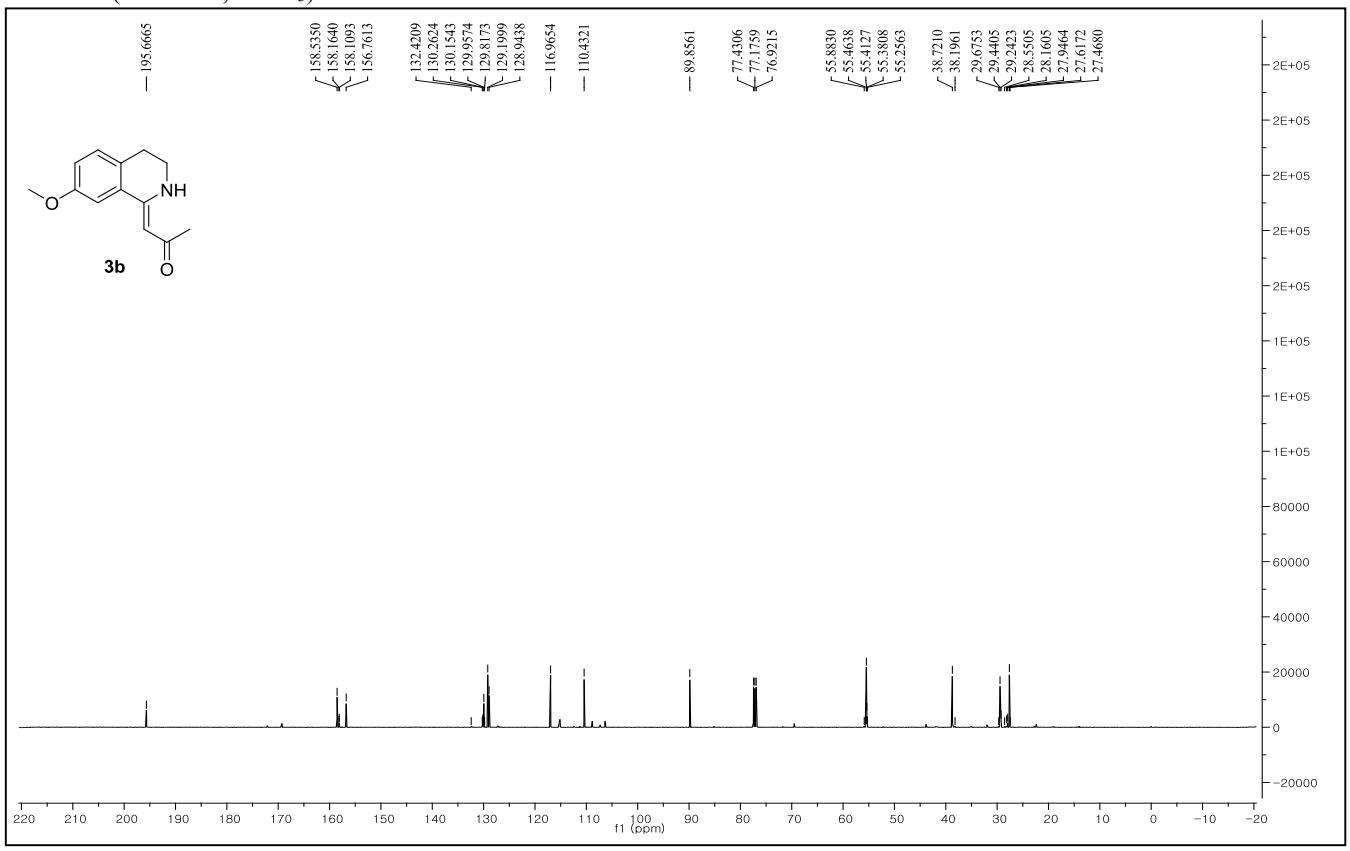
^{13}C NMR (125 MHz, $CDCl_3$)



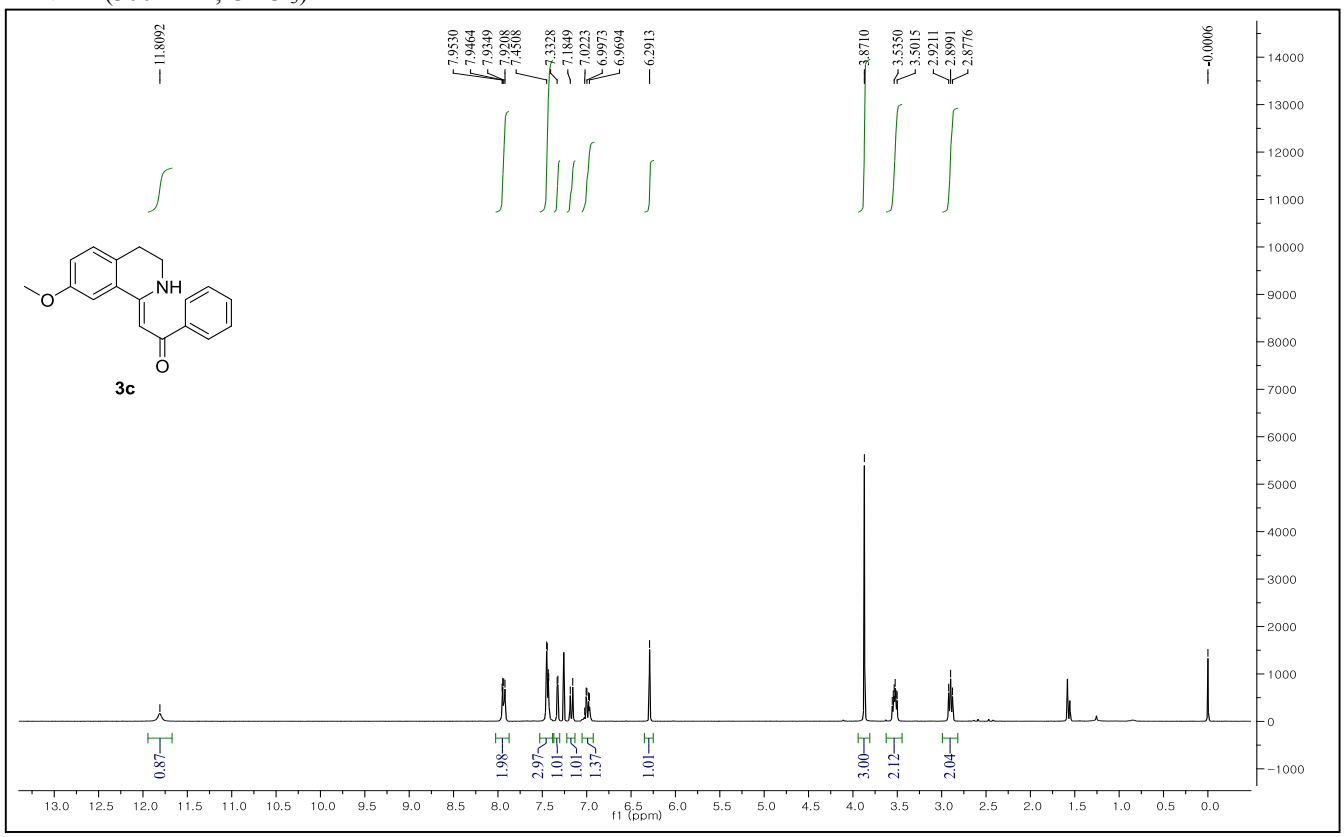
^{1}H NMR (500 MHz, $CDCl_3$)



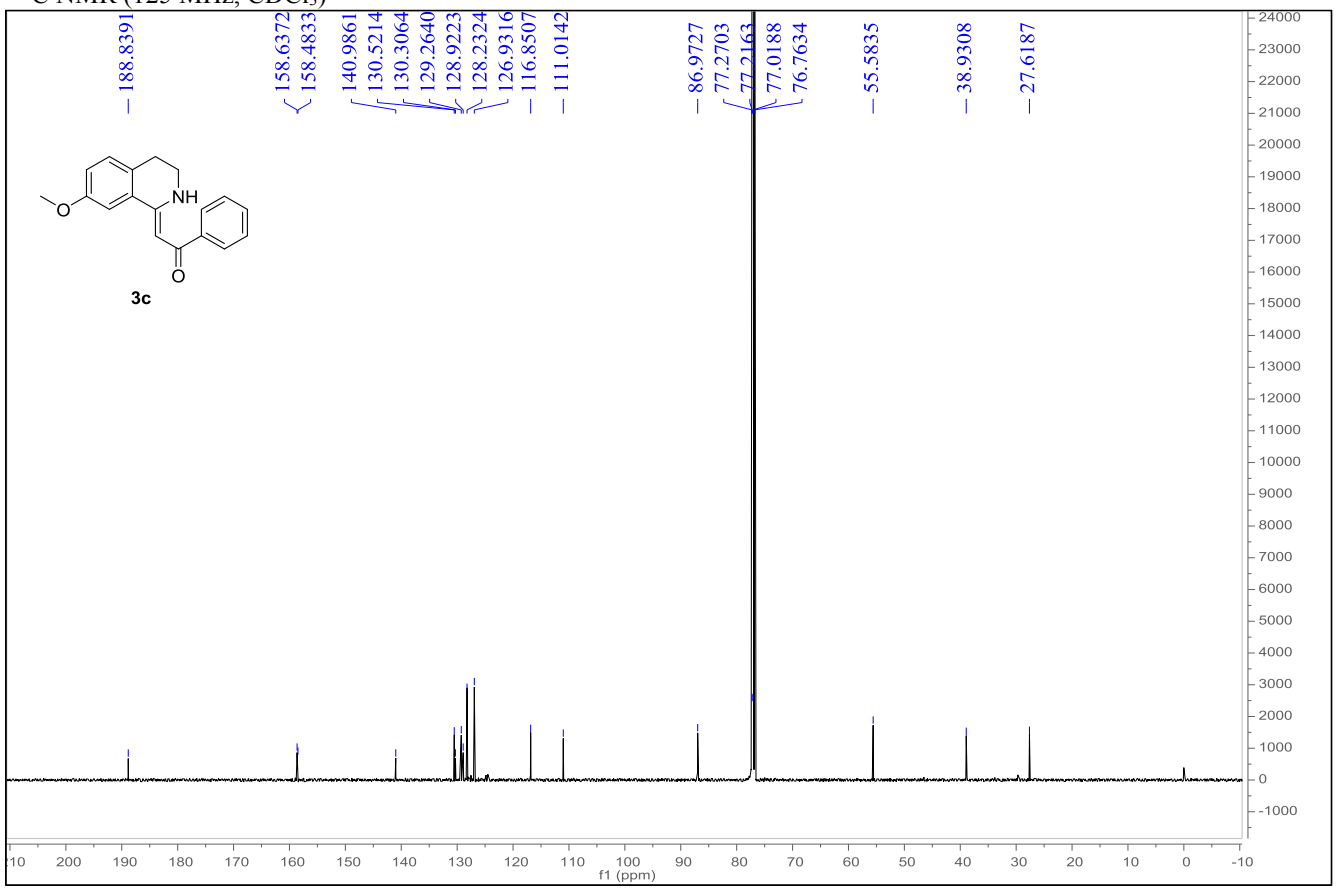
^{13}C NMR (125 MHz, $CDCl_3$)



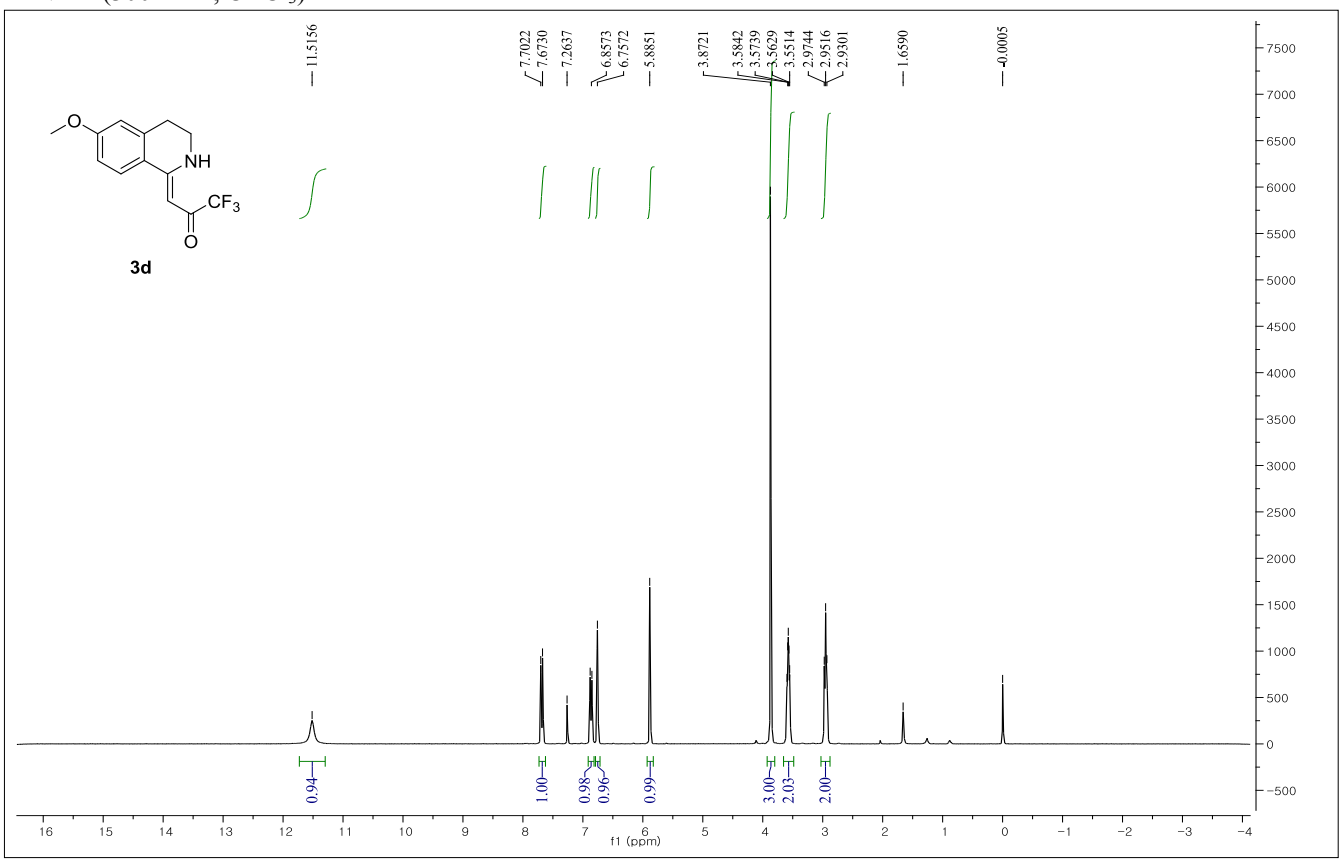
^{1}H NMR (300 MHz, $CDCl_3$)



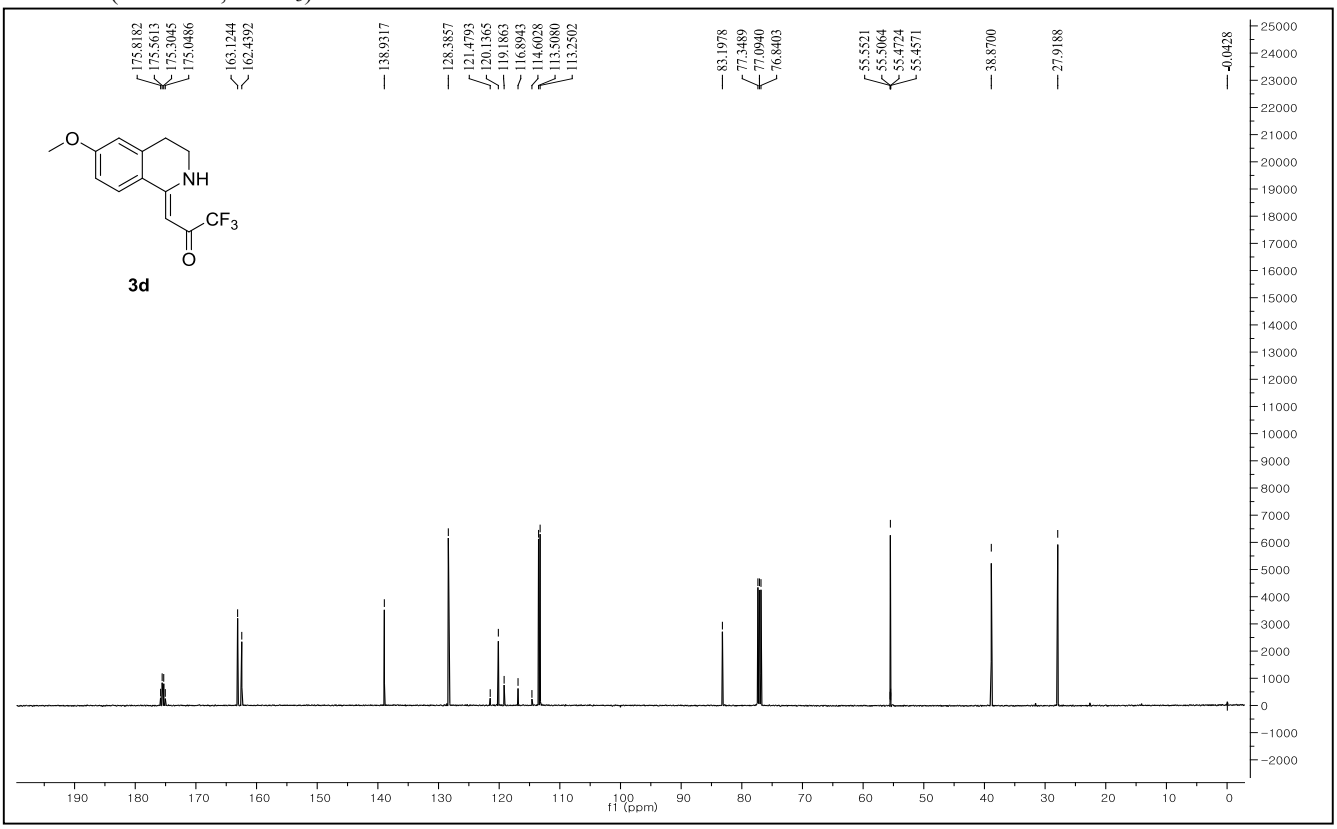
^{13}C NMR (125 MHz, $CDCl_3$)



^{1}H NMR (300 MHz, $CDCl_3$)



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



LC/MS of Crossover Experiment