

Supporting Information

Palladium-Catalyzed Isoquinoline Synthesis by Tandem C–H Allylation and Oxidative Cyclization of Benzylamines with Allyl Acetate

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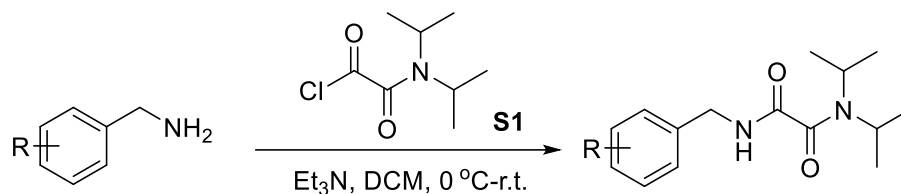
1.Reagents

Unless otherwise noted, all reagents were purchased from Acros, Alfa, Adamas and used without further purification. Column chromatography purifications were performed using 200–300 mesh silica gel.

2. Instruments

NMR spectra were recorded on Varian Inova-400 MHz, Inova-300 MHz, Bruker DRX-400 or Bruker DRX-500 instruments and calibrated using residual solvent peaks as internal reference. Multiplicities are recorded as: s = singlet, d = doublet, t = triplet, dd = doublet of doublets, m = multiplet. HRMS analysis were carried out using TOF-MS instrument with EI source.

3.Preparation of N, N–Diisopropylloxamoyl chloride S1



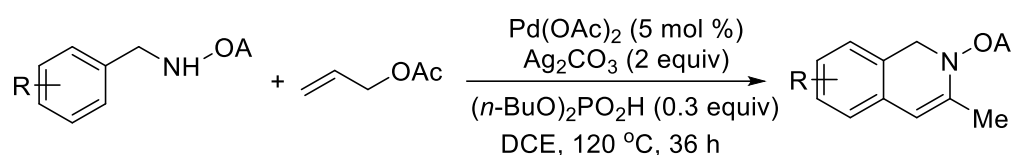
A solution of Diisopropylamine (7.01 mL, 50 mmol, 1.0 equiv) in CH₂Cl₂ (50 mL) was added dropwise to a solution of oxalyl chloride (6.44 mL, 75 mmol, 1.5 equiv) in CH₂Cl₂ (100 mL) at 0 °C, after stirring for 5 min, triethylamine (7.30 mL, 52.5 mmol, 1.05 equiv) was added dropwise. The solution was warmed to room temperature and stirred for 6 hours. The excess of oxalyl chloride and the solvent were removed under reduce pressure and CH₂Cl₂ (30 mL) was added and evaporated. This operation was performed twice to give S1 as a pale yellow solid. The crude product was used in the next step without any purification.

4. General procedures for the preparation of oxalamide substrates

A solution of amine (20 mmol, 1.0 equiv) in CH₂Cl₂ (40 mL) was added dropwise to a solution of N,N–Diisopropylloxamoyl chloride S1 (25 mmol, 1.25 equiv) in CH₂Cl₂ (50 mL) at 0 °C, after stirring for 5 min, triethylamine (2.92 ml, 21 mmol, 1.05 equiv) was added dropwise and then the mixture was stirred for 6 hours at room temperature

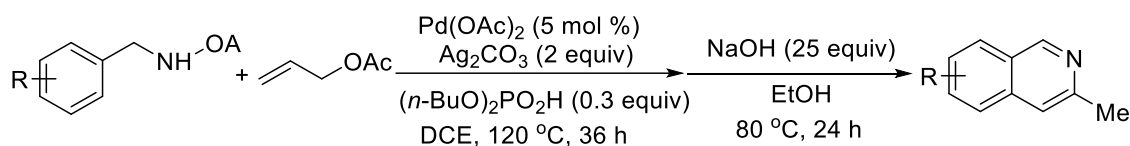
before quenched by water (50 mL). The organic layer was separated and the aqueous layer was extracted with CH₂Cl₂ (20 mL × 2). The combined organic phase was washed with brine (30 mL), and then dried over anhydrous Na₂SO₄. Evaporation and column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:5) to afford corresponding amide substrates as white solid or colourless liquid in >90% yield.

5. General procedures for constructing isoquinoline derivatives



A mixture of **1** (0.2 mmol), allyl acetate (0.4 mmol), Pd(OAc)₂ (2.25 mg, 5 mol%), Ag₂CO₃ (110 mg, 0.4 mmol), (*n*-BuO)₂PO₂H (12.6 mg, 0.06 mmol) and 0.6 mL DCE in a 15 mL sealed glass vial was heated at 120 °C in an oil bath under air with vigorous stirring for 36 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10 to 1:6) to give the corresponding product.

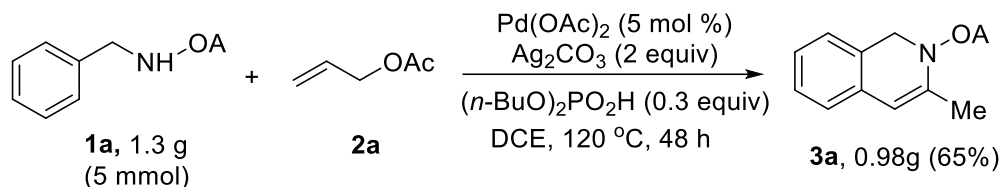
6. General procedures for the one-pot, two-step methods



A mixture of **1** (0.2 mmol), allyl acetate (0.4 mmol), Pd(OAc)₂ (2.25 mg, 5mol%), Ag₂CO₃ (110 mg, 0.4 mmol), (*n*-BuO)₂PO₂H (12.6 mg, 0.06 mmol) and 0.6 mL DCE in a 15 mL sealed glass vial was heated at 120 °C in an oil bath under air with vigorous stirring for 36 hours. Then NaOH (25 equiv) and ethanol solvent (2 mL) was added, the mixture was heated at 80 °C in an oil bath for 24 hours. The reaction mixture was cooled to room temperature, and diluted with H₂O. The organic layer was separated and the aqueous layer was extracted with EA. The combined organic phase was washed with brine, and then dried over anhydrous Na₂SO₄. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether =

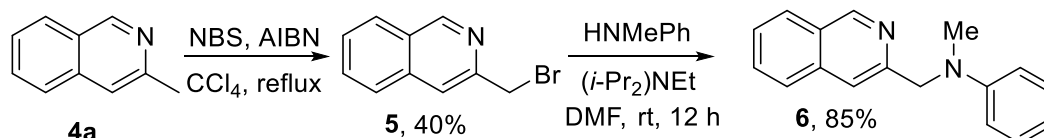
1:8 to 1:5) to give the corresponding product.

7. Gram scale reaction



A mixture of **1a** (5 mmol), allyl acetate (10 mmol), $\text{Pd}(\text{OAc})_2$ (56.1 mg, 5 mol%), Ag_2CO_3 (2.75 g, 10 mmol), $(n\text{-BuO})_2\text{PO}_2\text{H}$ (315 mg, 1.5 mmol) and 15 mL DCE in a 100 mL round-bottom flask was heated at 120 °C in an oil bath under air with vigorous stirring for 36 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:10) to give the corresponding product.

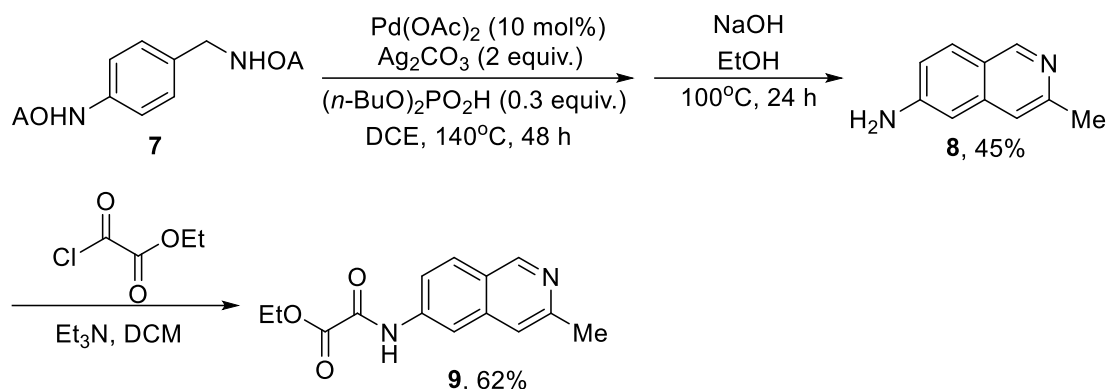
8. Further Transformation



A mixture of **4a** (57.2 mg, 0.4 mmol), NBS (143 mg, 0.8 mmol), AIBN (13.2 mg, 0.08 mmol) and 8 mL CCl_4 in a 25 mL round-bottom flask was heated at 80 °C in an oil bath under air with vigorous stirring for 12 hours. The reaction mixture was cooled to room temperature, and filtered through celite. The filtrate was washed with NaHCO_3 saturated solution and brine, and then dried over anhydrous Na_2SO_4 . The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:8) to give the corresponding product **5**.

A mixture of **5** (66 mg, 0.3 mmol), $(i\text{-Pr})_2\text{NEt}$ (58 mg, 0.45 mmol), N-methylaniline (0.36 mmol) and 1 mL DMF in a 15 mL sealed glass vial was heated at r.t. under air with vigorous stirring for 12 hours. The reaction mixture was diluted with H_2O and was extracted with DCM. The combined organic phase was washed with brine, and then dried over anhydrous Na_2SO_4 . The filtrate was concentrated in vacuo and purified by

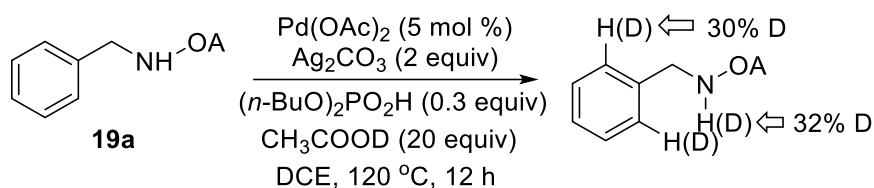
column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:5) to give the corresponding product **6**.



A mixture of **7** (0.2 mmol), allyl acetate (0.4 mmol), $\text{Pd}(\text{OAc})_2$ (4.5 mg, 10mol%), Ag_2CO_3 (110 mg, 0.4 mmol), $(n\text{-BuO})_2\text{PO}_2\text{H}$ (12.6 mg, 0.06 mmol) and 0.6 mL DCE in a 15 mL sealed glass vial was heated at 140°C in an oil bath under air with vigorous stirring for 36 hours. Then NaOH (50 equiv) and ethanol solvent (2 mL) was added, the mixture was heated at 100°C in an oil bath for 24 hours. The reaction mixture was cooled to room temperature, and diluted with H_2O . The organic layer was separated and the aqueous layer was extracted with EA. The combined organic phase was washed with brine, and then dried over anhydrous Na_2SO_4 . The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:5) to give the corresponding product **8** in 45% yield.

A solution of ethyl oxalyl monochloride (0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1 mL) was added dropwise to a solution of **8** (0.2 mmol, 1.0 equiv) and triethylamine (0.24 mmol, 1.2 equiv) in CH_2Cl_2 (1 mL) at 0°C and then the mixture was stirred for 6 hours at room temperature before quenched by water (2 mL). The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (2 mL \times 2). The combined organic phase was washed with brine (2 mL), and then dried over anhydrous Na_2SO_4 . Evaporation and column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:6) to afford corresponding substrate **9** in 62% yield.

9. Isotopic Labelling Studies

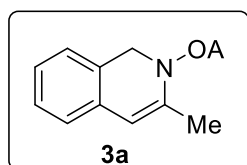


A mixture of **1** (0.2 mmol), Pd(OAc)_2 (2.25 mg, 5 mol%), Ag_2CO_3 (110 mg, 0.4 mmol), $(n\text{-BuO})_2\text{PO}_2\text{H}$ (12.6 mg, 0.06 mmol), deuterium acetate (20 equiv) and 0.6 mL DCE in a 15 mL sealed glass vial was heated at 120 °C in an oil bath under air with vigorous stirring for 12 hours. The reaction mixture was cooled to room temperature, and diluted with ethyl acetate and filtered through celite. The filtrate was concentrated in vacuo and purified by column chromatography on silica gel (Ethyl acetate/Petroleum ether = 1:5) to give the corresponding product.

10. Spectroscopic Data of All New Compounds

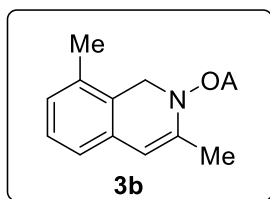
We thought product **3** have two chiral centers as well, one is chiral nitrogen, the other is axial chiral 1,2-dicarbonyl. Therefore, product **3** is a mixture of two isomers, and we did not calculate the value of dr^1 .

N,N-Diisopropyl-2-(3-methylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (**3a**)



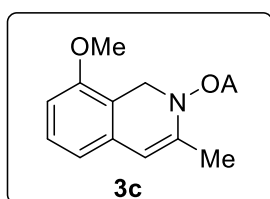
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as pale yellow solid, m.p. 86-88 °C; Yield: 42.6 mg, 71%; ^1H NMR (400 MHz, CDCl_3) δ 7.26-7.11 (m, 2.34H, ArH), 7.09-7.00 (m, 1.67H, ArH), 6.16 (s, 0.67H, CH), 6.08 (s, 0.33H, CH), 4.90 (s, 0.64H, CH_2), 4.53 (s, 1.36H, CH_2), 3.73-3.62 (m, 1H, CH), 3.55-3.40 (m, 1H, CH), 2.43 (s, 2H, CH_3), 2.23 (s, 1H, CH_3), 1.54 (d, J = 6.8 Hz, 4H, $2\times\text{CH}_3$), 1.45 (d, J = 6.8 Hz, 2H, $2\times\text{CH}_3$), 1.16 (d, J = 6.6 Hz, 2H, $2\times\text{CH}_3$), 1.10 (d, J = 6.6 Hz, 4H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.4, 164.2, 164.0, 163.9, 138.2, 134.7, 132.3, 131.8, 130.6, 130.1, 128.3, 127.8, 127.1, 126.9, 125.4, 124.6, 124.5, 124.4, 117.5, 116.6, 50.9, 50.7, 49.4, 46.0, 45.0, 21.3, 20.7, 20.4, 20.2, 20.2, 19.8. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{24}\text{N}_2\text{NaO}_2$ 323.1735; Found: 323.1752.

2-(3,8-Dimethylisoquinolin-2(1*H*)-yl)-*N,N*-diisopropyl-2-oxoacetamide (**3b**)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 45.9 mg, 73%; ^1H NMR (400 MHz, CDCl_3) δ 7.15-7.05 (m, 1H, ArH), 7.01-6.96 (m, 1H, ArH), 6.93-6.84 (m, 1H, ArH), 6.13 (s, 0.67H, CH), 6.04 (s, 0.33H, CH), 4.91 (s, 0.67H, CH_2), 4.58 (s, 1.33H, CH_2), 3.79-3.68 (m, 1H, CH), 3.56-3.42 (m, 1H, CH), 2.42 (s, 2H, CH_3), 2.32 (s, 1H, CH_3), 2.26 (s, 2H, CH_3), 2.22 (s, 1H, CH_3), 1.55 (d, $J = 6.8$ Hz, 4H, $2\times\text{CH}_3$), 1.45 (d, $J = 6.8$ Hz, 2H, $2\times\text{CH}_3$), 1.20 (d, $J = 6.6$ Hz, 2H, $2\times\text{CH}_3$), 1.12 (d, $J = 6.6$ Hz, 4H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.4, 164.3, 164.1, 163.9, 137.4, 133.9, 133.7, 132.4, 132.1, 131.7, 129.3, 129.1, 129.0, 129.0, 127.6, 127.2, 122.6, 122.3, 118.1, 116.9, 50.9, 50.8, 46.2, 46.0, 42.2, 21.1, 20.6, 20.3, 20.2, 20.1, 19.7, 18.8, 18.5. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_2$ 337.1892; Found: 337.1897.

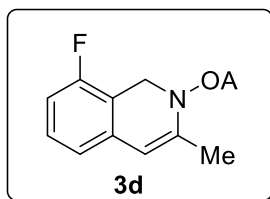
***N,N*-Diisopropyl-2-(8-methoxy-3-methylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (3c)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 46.9 mg, 71%; ^1H NMR (400 MHz, CDCl_3) δ 7.21-7.10 (m, 1H, ArH), 6.75-6.62 (m, 2H, ArH), 6.12 (s, 0.8H, CH), 6.02 (s, 0.2H, CH), 4.94 (s, 0.4H, CH_2), 4.63 (s, 1.6H, CH_2), 3.82 (s, 0.6H, CH_3O), 3.79 (s, 2.4H, CH_3O), 3.75-3.60 (m, 1H, CH), 3.54-3.42 (m, 1H, CH), 2.42 (s, 2.4H, CH_3), 2.22 (s, 0.6H, CH_3), 1.55 (d, $J = 6.8$ Hz, 4H, $2\times\text{CH}_3$), 1.45 (d, $J = 6.8$ Hz, 2H, $2\times\text{CH}_3$), 1.19 (d, $J = 6.6$ Hz, 2H, $2\times\text{CH}_3$), 1.08 (d, $J = 6.6$ Hz, 4H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 164.1, 154.1, 138.4, 133.5, 128.6, 118.2, 117.4, 117.3, 109.2, 55.3, 50.9, 46.0, 43.1, 20.2, 20.1, 19.5. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_3$ 353.1841; Found: 353.1842.

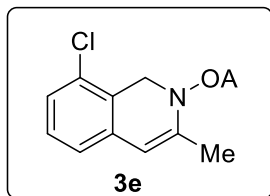
2-(8-Fluoro-3-methylisoquinolin-2(1*H*)-yl)-*N,N*-diisopropyl-2-oxoacetamide (3d)

The compound was purified by flash column chromatography (Ethyl acetate/Petroleum



ether = 1:10) to give the product as pale yellow solid, m.p. 114-116 °C; Yield: 44.5 mg, 70%; ^1H NMR (400 MHz, CDCl_3) δ 7.22-7.12 (m, 1H, ArH), 6.92-6.79 (m, 2H, ArH), 6.16 (s, 0.75H, CH), 6.06 (s, 0.25H, CH), 4.97 (s, 0.4H, CH_2), 4.63 (s, 1.6H, CH_2), 3.79-3.61 (m, 1H, CH), 3.55-3.44 (m, 1H, CH), 2.43 (s, 2.32H, CH_3), 2.22 (s, 0.68H, CH_3), 1.54 (d, $J = 6.8$ Hz, 4.6H, $2\times\text{CH}_3$), 1.44 (d, $J = 6.8$ Hz, 1.4H, $2\times\text{CH}_3$), 1.20 (d, $J = 6.6$ Hz, 1.4H, $2\times\text{CH}_3$), 1.11 (d, $J = 6.6$ Hz, 4.6H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.5, 164.0, 163.8, 163.7, 157.5 (d, $J = 245.0$ Hz), 139.4, 135.6, 134.5 (d, $J = 4.6$ Hz), 129.3 (d, $J = 8.3$ Hz), 128.8 (d, $J = 8.4$ Hz), 120.2 (d, $J = 3.0$ Hz), 120.0 (d, $J = 3.1$ Hz), 116.8 (d, $J = 3.4$ Hz), 116.6 (d, $J = 17.0$ Hz), 115.5 (d, $J = 3.2$ Hz), 114.1 (d, $J = 21.1$ Hz), 113.8 (d, $J = 21.4$ Hz), 51.0, 50.9, 46.1, 42.6, 42.5, 21.4, 20.4, 20.3, 20.1, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{23}\text{FN}_2\text{NaO}_2$ 341.1641; Found: 341.1649.

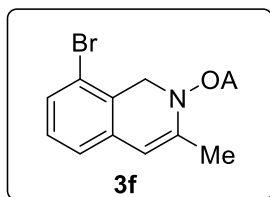
2-(8-Chloro-3-methylisoquinolin-2(1H)-yl)-N,N-diisopropyl-2-oxoacetamide (3e)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 49.4 mg, 74%; ^1H NMR (400 MHz, CDCl_3) δ 7.19-7.08 (m, 2H, ArH), 6.99-6.89 (m, 1H, ArH), 6.12 (s, 0.8H, CH), 6.02 (s, 0.2H, CH), 5.03 (s, 0.4H, CH_2), 4.72 (s, 1.6H, CH_2), 3.84-3.75 (m, 0.2H, CH), 3.73-3.62 (m, 0.8H, CH), 3.57-3.43 (m, 1H, CH), 2.43 (s, 2.4H, CH_3), 2.22 (s, 0.6H, CH_3), 1.55 (d, $J = 6.8$ Hz, 4.8H, $2\times\text{CH}_3$), 1.45 (d, $J = 6.8$ Hz, 1.2H, $2\times\text{CH}_3$), 1.22 (d, $J = 6.5$ Hz, 1.2H, $2\times\text{CH}_3$), 1.14 (d, $J = 6.6$ Hz, 4.8H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 163.7, 139.3, 134.2, 130.2, 129.0, 128.1, 127.5, 123.0, 116.9, 51.0, 46.3, 46.1, 20.5, 20.2, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{23}\text{ClN}_2\text{NaO}_2$ 357.1346; Found: 357.1360.

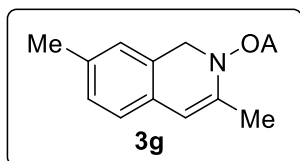
2-(8-Bromo-3-methylisoquinolin-2(1H)-yl)-N,N-diisopropyl-2-oxoacetamide (3f)

The compound was purified by flash column chromatography (Ethyl acetate/Petroleum



ether = 1:10) to give the product as colorless oil, Yield: 30.2 mg, 40%; ^1H NMR (400 MHz, CDCl_3) δ 7.33 (d, J = 8.0 Hz, 1H, ArH), 7.12-7.04 (m, 1H, ArH), 7.03-6.93 (m, 1H, ArH), 6.10 (s, 0.8H, CH), 6.01 (s, 0.2H, CH), 5.03 (s, 0.4H, CH_2), 4.72 (s, 1.6H, CH_2), 3.85-3.77 (m, 0.2H, CH), 3.74-3.64 (m, 0.8H, CH), 3.58-3.43 (m, 1H, CH), 2.43 (s, 2.4H, CH_3), 2.22 (s, 0.6H, CH_3), 1.56 (d, J = 6.8 Hz, 4.8H, $2\times\text{CH}_3$), 1.45 (d, J = 6.8 Hz, 1.2H, $2\times\text{CH}_3$), 1.23 (d, J = 6.6 Hz, 1.2H, $2\times\text{CH}_3$), 1.16 (d, J = 6.6 Hz, 4.8H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.7, 163.7, 139.3, 134.4, 130.7, 130.0, 129.4, 123.7, 120.2, 117.0, 51.1, 48.9, 46.1, 20.6, 20.2, 20.1. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{24}\text{BrN}_2\text{O}_2$ 379.1021; Found: 379.1011.

2-(3,7-Dimethylisoquinolin-2(1H)-yl)-N,N-diisopropyl-2-oxoacetamide (3g)

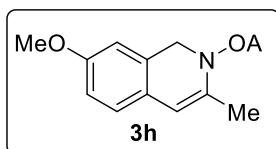


The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as pale yellow solid, m.p. 130-131 °C; Yield: 41.5 mg, 66%; ^1H NMR (400 MHz, CDCl_3) δ 7.07-6.90 (m, 2.33H, ArH), 6.89-

6.82 (m, 0.67H, ArH), 6.13 (s, 0.67H, CH), 6.05 (s, 0.33H, CH), 4.85 (s, 0.67H, CH_2), 4.49 (s, 1.33H, CH_2), 3.74-3.60 (m, 1H, CH), 3.55-3.39 (m, 1H, CH), 2.40 (s, 2H, CH_3), 2.33-2.29 (m, 3H, CH_3), 2.21 (s, 1H, CH_3), 1.55 (d, J = 6.8 Hz, 4H, $2\times\text{CH}_3$), 1.44 (d, J = 6.8 Hz, 2H, $2\times\text{CH}_3$), 1.15 (d, J = 6.6 Hz, 2H, $2\times\text{CH}_3$), 1.11 (d, J = 6.6 Hz, 4H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.4, 164.3, 164.1, 164.0, 137.1, 137.1, 136.9, 133.7, 130.7, 130.2, 129.6, 129.2, 128.8, 128.4, 126.2, 125.3, 124.5, 124.3, 117.5, 116.7, 50.8, 50.75, 49.5, 46.0, 46.0, 45.0, 21.4, 21.4, 21.2, 20.7, 20.4, 20.2, 20.1, 19.8. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_2$ 337.1892; Found: 337.1896.

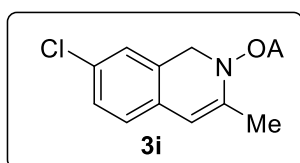
N,N-Diisopropyl-2-(7-methoxy-3-methylisoquinolin-2(1H)-yl)-2-oxoacetamide (3h)

The compound was purified by flash column chromatography (Ethyl acetate/Petroleum



ether = 1:10) to give the product as colorless oil, Yield: 40.3 mg, 61%; ^1H NMR (400 MHz, CDCl_3) δ 7.01-6.93 (m, 1H, ArH), 6.77-6.71 (m, 1.34H, ArH), 6.61-6.56 (m, 0.66H, ArH), 6.11 (s, 0.64H, CH), 6.04 (s, 0.36H, CH), 4.85 (s, 0.73H, CH_2), 4.49 (s, 1.27H, CH_2), 3.78 (s, 1.1H, CH_3O), 3.77 (s, 1.9H, CH_3O), 3.73-3.59 (m, 1H, CH), 3.54-3.39 (m, 1H, CH), 2.38 (s, 1.9H, CH_3), 2.20 (s, 1.1H, CH_3), 1.53 (d, $J = 6.8$ Hz, 3.8H, $2\times\text{CH}_3$), 1.44 (d, $J = 6.8$ Hz, 2.2H, $2\times\text{CH}_3$), 1.14 (d, $J = 6.6$ Hz, 2.2H, $2\times\text{CH}_3$), 1.11 (d, $J = 6.6$ Hz, 3.8H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.4, 164.3, 164.1, 164.0, 158.9, 158.7, 135.8, 132.3, 131.8, 125.8, 125.6, 125.4, 124.9, 117.3, 116.6, 113.2, 112.7, 111.3, 111.2, 55.5, 55.4, 50.9, 50.7, 49.5, 46.0, 46.0, 45.1, 21.1, 20.7, 20.4, 20.2, 19.9, 19.8. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_3$ 353.1841; Found: 353.1836.

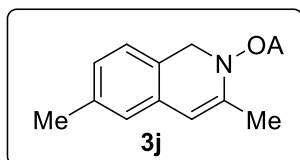
2-(7-Chloro-3-methylisoquinolin-2(1H)-yl)-N,N-diisopropyl-2-oxoacetamide (3i)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 36.7 mg, 55%; ^1H NMR (400 MHz, CDCl_3) δ 7.22-7.12 (m, 1.33H, ArH), 7.09-6.92 (m, 1.67H, ArH), 6.12 (s, 0.64H, CH), 6.03 (s, 0.36H, CH), 4.85 (s, 0.7H, CH_2), 4.49 (s, 1.3H, CH_2), 3.73-3.62 (m, 1H, CH), 3.56-3.40 (m, 1H, CH), 2.41 (s, 1.9H, CH_3), 2.21 (s, 1.1H, CH_3), 1.54 (d, $J = 6.8$ Hz, 3.8H, $2\times\text{CH}_3$), 1.44 (d, $J = 6.8$ Hz, 2.2H, $2\times\text{CH}_3$), 1.17 (d, $J = 6.6$ Hz, 2.2H, $2\times\text{CH}_3$), 1.13 (d, $J = 6.6$ Hz, 3.8H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 164.0, 163.8, 163.7, 138.8, 135.2, 132.5, 132.2, 132.1, 131.6, 130.8, 130.4, 128.3, 127.9, 125.7, 125.7, 125.5, 124.7, 116.6, 115.5, 50.8, 50.8, 49.0, 46.1, 46.1, 44.6, 21.2, 20.7, 20.3, 20.2, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{18}\text{H}_{23}\text{ClN}_2\text{NaO}_2$ 357.1346; Found: 357.1340.

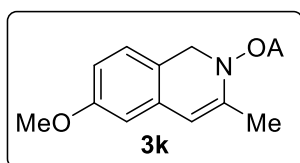
2-(3,6-Dimethylisoquinolin-2(1H)-yl)-N,N-diisopropyl-2-oxoacetamide (3j)

The compound was purified by flash column chromatography (Ethyl acetate/Petroleum



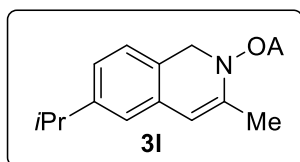
ether = 1:10) to give the product as colorless oil, Yield: 44.6 mg, 71%; ^1H NMR (400 MHz, CDCl_3) δ 7.06-7.01 (m, 0.3H, ArH), 6.98-6.87 (m, 2.4H, ArH), 6.84 (s, 0.3H, ArH), 6.11 (s, 0.7H, CH), 6.02 (s, 0.3H, CH), 4.85 (s, 0.6H, CH_2), 4.49 (s, 1.4H, CH_2), 3.73-3.62 (m, 1H, CH), 3.56-3.40 (m, 1H, CH), 2.41 (s, 2.1H, CH_3), 2.30 (s, 2H, CH_3), 2.29 (s, 1H, CH_3), 2.22 (s, 0.9H, CH_3), 1.54 (d, $J = 6.8$ Hz, 4.2H, $2\times\text{CH}_3$), 1.44 (d, $J = 6.8$ Hz, 1.8H, $2\times\text{CH}_3$), 1.16 (d, $J = 6.6$ Hz, 1.8H, $2\times\text{CH}_3$), 1.10 (d, $J = 6.6$ Hz, 4.2H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 164.3, 164.0, 163.9, 138.0, 137.9, 137.4, 134.5, 132.2, 131.7, 127.8, 127.7, 127.5, 127.2, 125.3, 125.0, 124.4, 117.6, 116.7, 50.9, 50.7, 49.2, 46.0, 44.8, 21.3, 20.7, 20.4, 20.2, 20.2, 19.8. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{26}\text{N}_2\text{NaO}_2$ 337.1892; Found: 337.1890.

***N,N*-Diisopropyl-2-(6-methoxy-3-methylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (3k)**



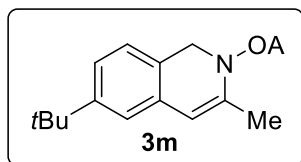
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 46.2 mg, 70%; ^1H NMR (400 MHz, CDCl_3) δ 7.07 (d, $J = 8.3$ Hz, 0.3H, ArH), 6.95 (d, $J = 8.2$ Hz, 0.7H, ArH), 6.73-6.56 (m, 2H, ArH), 6.11 (s, 0.7H, CH), 6.04 (s, 0.3H, CH), 4.83 (s, 0.57H, CH_2), 4.47 (s, 1.43H, CH_2), 3.79 (s, 2H, CH_3O), 3.77 (s, 1H, CH_3O), 3.73-3.63 (m, 1H, CH), 3.55-3.40 (m, 1H, CH), 2.42 (s, 2.1H, CH_3), 2.22 (s, 0.9H, CH_3), 1.54 (d, $J = 6.8$ Hz, 4.2H, $2\times\text{CH}_3$), 1.45 (d, $J = 6.8$ Hz, 1.8H, $2\times\text{CH}_3$), 1.17 (d, $J = 6.6$ Hz, 1.8H, $2\times\text{CH}_3$), 1.11 (d, $J = 6.6$ Hz, 4.2H, $2\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 164.2, 164.0, 163.8, 159.6, 159.3, 138.6, 135.1, 133.4, 132.9, 126.3, 125.4, 123.0, 122.5, 117.5, 116.6, 112.2, 112.1, 110.0, 55.4, 50.9, 50.7, 48.9, 46.0, 44.5, 21.3, 20.7, 20.4, 20.2, 19.8, 18.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{19}\text{H}_{27}\text{N}_2\text{O}_3$ 331.2022; Found: 331.2017.

***N,N*-Diisopropyl-2-(6-isopropyl-3-methylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (3l)**



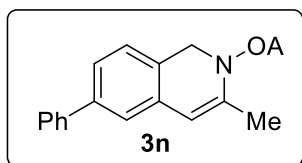
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 41.0 mg, 60%; ^1H NMR (400 MHz, CDCl_3) δ 7.10-6.87 (m, 3H, ArH), 6.14 (s, 0.66H, CH), 6.06 (s, 0.34H, CH), 4.86 (s, 0.66H, CH_2), 4.50 (s, 1.34H, CH_2), 3.76-3.63 (m, 1H, CH), 3.55-3.40 (m, 1H, CH), 2.92-2.80 (m, 1H, CH), 2.42 (s, 2H, CH_3), 2.22 (s, 1H, CH_3), 1.54 (d, $J = 6.8$ Hz, 4H, $2 \times \text{CH}_3$), 1.45 (d, $J = 6.8$ Hz, 2H, $2 \times \text{CH}_3$), 1.24-1.20 (m, 6H, $2 \times \text{CH}_3$), 1.17 (d, $J = 6.6$ Hz, 2H, $2 \times \text{CH}_3$), 1.11 (d, $J = 6.6$ Hz, 4H, $2 \times \text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 164.3, 164.1, 163.9, 149.1, 148.5, 138.0, 134.4, 132.2, 131.8, 128.1, 127.6, 125.3, 125.2, 125.0, 124.5, 122.7, 122.5, 117.7, 116.8, 50.9, 50.7, 49.2, 46.0, 44.9, 34.0, 24.1, 24.0, 21.3, 20.7, 20.3, 20.2, 20.2, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{21}\text{H}_{30}\text{N}_2\text{NaO}_2$ 365.2205; Found: 365.2200.

2-(6-(*tert*-Butyl)-3-methylisoquinolin-2(1*H*)-yl)-*N,N*-diisopropyl-2-oxoacetamide (3m)



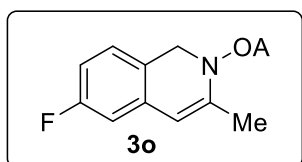
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 29.9 mg, 42%; ^1H NMR (400 MHz, CDCl_3) δ 7.21-7.14 (m, 1H, ArH), 7.11-7.04 (m, 1.33H, ArH), 6.96 (d, $J = 7.9$ Hz, 0.67H, ArH), 6.15 (s, 0.67H, CH), 6.08 (s, 0.33H, CH), 4.86 (s, 0.65H, CH_2), 4.50 (s, 1.35H, CH_2), 3.76-3.65 (m, 1H, CH), 3.56-3.40 (m, 1H, CH), 2.42 (s, 2H, CH_3), 2.22 (s, 1H, CH_3), 1.54 (d, $J = 6.8$ Hz, 4H, $2 \times \text{CH}_3$), 1.44 (d, $J = 6.8$ Hz, 2H, $2 \times \text{CH}_3$), 1.29 (s, 6H, $3 \times \text{CH}_3$), 1.28 (s, 3H, $3 \times \text{CH}_3$), 1.18 (d, $J = 6.6$ Hz, 2H, $2 \times \text{CH}_3$), 1.11 (d, $J = 6.6$ Hz, 4H, $2 \times \text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 164.3, 164.3, 164.1, 164.0, 151.4, 150.8, 137.9, 134.3, 131.9, 131.5, 127.2, 125.1, 124.2, 124.0, 123.9, 121.6, 121.5, 117.9, 117.0, 50.9, 50.7, 49.2, 46.0, 44.8, 34.7, 31.4, 31.2, 21.3, 20.7, 20.3, 20.2, 20.2, 19.7. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{22}\text{H}_{32}\text{N}_2\text{NaO}_2$ 379.2361; Found: 379.2370.

***N,N*-Diisopropyl-2-(3-methyl-6-phenylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (3n)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 45.9 mg, 61%; ¹H NMR (400 MHz, CDCl₃) δ 7.58-7.53 (m, 2H, ArH), 7.46-7.40 (m, 2H, ArH), 7.40-7.33 (m, 2H, ArH), 7.31-7.29 (m, 0.7H, ArH), 7.26-7.21 (m, 0.6H, ArH), 7.11 (d, *J* = 7.7 Hz, 0.7H, ArH), 6.23 (s, 0.66H, CH), 6.14 (s, 0.34H, CH), 4.95 (s, 0.66H, CH₂), 4.58 (s, 1.34H, CH₂), 3.78-3.68 (m, 1H, CH), 3.57-3.42 (m, 1H, CH), 2.46 (s, 2H, CH₃), 2.26 (s, 1H, CH₃), 1.56 (d, *J* = 6.8 Hz, 4H, 2×CH₃), 1.46 (d, *J* = 6.8 Hz, 2H, 2×CH₃), 1.19 (d, *J* = 6.6 Hz, 2H, 2×CH₃), 1.14 (d, *J* = 6.6 Hz, 4H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.4, 164.2, 164.0, 163.9, 141.4, 140.9, 140.9, 140.7, 138.6, 135.1, 132.7, 132.3, 131.0, 129.6, 129.0, 128.9, 128.8, 127.6, 127.4, 127.1, 125.9, 125.8, 125.6, 124.9, 123.3, 123.1, 117.5, 116.5, 50.9, 50.8, 49.2, 46.1, 44.8, 22.8, 21.3, 20.7, 20.4, 20.2, 19.8, 19.3. HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₂₄H₂₈N₂NaO₂ 399.2048; Found: 399.2047.

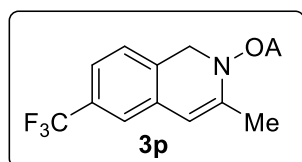
***N,N*-Diisopropyl-2-(6-fluoro-3-methylisoquinolin-2(1*H*)-yl)-2-oxoacetamide (3o)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 43.3 mg, 68%; ¹H NMR (400 MHz, CDCl₃) δ 7.14-7.07 (m, 0.33H, ArH), 7.03-6.95 (m, 0.67H, ArH), 6.86-6.71 (m, 2H, ArH), 6.11 (s, 0.67H, CH), 6.02 (s, 0.33H, CH), 4.85 (s, 0.66H, CH₂), 4.49 (s, 1.34H, CH₂), 3.73-3.62 (m, 1H, CH), 3.55-3.40 (m, 1H, CH), 2.42 (s, 2H, CH₃), 2.22 (s, 1H, CH₃), 1.53 (d, *J* = 6.8 Hz, 4H, 2×CH₃), 1.44 (d, *J* = 6.8 Hz, 2H, 2×CH₃), 1.18 (d, *J* = 6.6 Hz, 2H, 2×CH₃), 1.11 (d, *J* = 6.6 Hz, 4H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.3, 164.0, 163.9, 163.8, 162.7 (d, *J* = 232.0 Hz), 139.6, 136.1, 134.3, 134.2, 126.8 (d, *J* = 8.5 Hz), 125.8 (d, *J* = 8.6 Hz), 125.7 (d, *J* = 3.0 Hz), 116.7 (d, *J* = 2.4 Hz), 115.6 (d, *J* = 1.8 Hz), 113.7, 113.4, 113.2, 111.4 (d, *J* = 22.7 Hz), 111.1 (d, *J* = 22.9 Hz), 50.9, 50.8, 48.9, 46.1, 44.5, 21.3, 20.7, 20.3, 20.3, 20.2, 19.7. ¹⁹F NMR

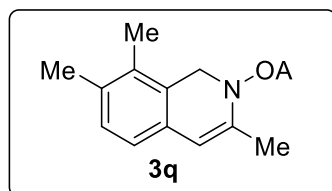
(376 MHz, CDCl₃) δ -114.0, -114.9. HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₁₈H₂₃FN₂NaO₂ 341.1641; Found: 341.1648.

***N,N*-Diisopropyl-2-(3-methyl-6-(trifluoromethyl)isoquinolin-2(1*H*)-yl)-2-oxoacetamide (3p)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as pale yellow solid, m.p. 118-120 °C; Yield: 45.7 mg, 62%; ¹H NMR (400 MHz,) δ 7.40 (d, J = 7.9 Hz, 1H, ArH), 7.31 (s, 0.6H, ArH), 7.28-7.24 (m, 0.8H, ArH), 7.15 (d, J = 7.8 Hz, 0.6H, ArH), 6.18 (s, 0.6H, CH), 6.09 (s, 0.4H, CH), 4.93 (s, 0.7H, CH₂), 4.57 (s, 1.3H, CH₂), 3.76-3.64 (m, 1H, CH), 3.57-3.41 (m, 1H, CH), 2.44 (s, 1.8H, CH₃), 2.24 (s, 1.2H, CH₃), 1.54 (d, J = 6.8 Hz, 3.7H, 2×CH₃), 1.44 (d, J = 6.8 Hz, 2.3H, 2×CH₃), 1.19 (d, J = 6.6 Hz, 2.3H, 2×CH₃), 1.12 (d, J = 6.6 Hz, 3.7H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.2, 163.8, 163.6, 140.2, 136.6, 133.9, 133.4, 133.0, 132.5, 131.0, 130.4 (q, J = 48.6 Hz), 128.9, 125.8, 125.3, 124.9, 123.6 (q, J = 11.0 Hz), 122.3 (q, J = 284.2 Hz), 122.6, 121.2 (q, J = 10.1 Hz), 116.3, 115.1, 50.9, 50.9, 49.1, 46.1, 44.8, 21.3, 20.7, 20.3, 20.2, 19.7. ¹⁹F NMR (376 MHz, CDCl₃) δ -62.70, -62.72. HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₁₉H₂₃F₃N₂NaO₂ 391.1609; Found: 391.1606.

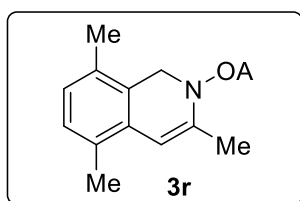
***N,N*-Diisopropyl-2-oxo-2-(3,7,8-trimethylisoquinolin-2(1*H*)-yl)acetamide (3q)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as white solid, m.p. 107-109 °C; Yield: 44.6 mg, 68%; ¹H NMR (400 MHz, CDCl₃) δ 7.03-6.94 (m, 1H, ArH), 6.85-6.75 (m, 1H, ArH), 6.11 (s, 0.67H, CH), 6.02 (s, 0.33H, CH), 4.94 (s, 0.6H, CH₂), 4.61 (s, 1.4H, CH₂), 3.79-3.66 (m, 1H, CH), 3.56-3.41 (m, 1H, CH), 2.41 (s, 2H, CH₃), 2.26 (s, 1H, CH₃), 2.25 (s, 2H, CH₃), 2.23 (s, 1H, CH₃), 2.20 (s, 1H, CH₃), 2.15 (s, 2H, CH₃), 1.55 (d, J = 6.8 Hz, 4H, 2×CH₃), 1.45 (d, J = 6.8 Hz,

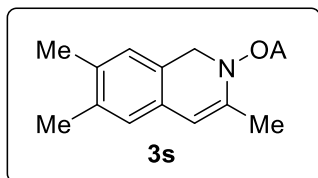
2H, 2×CH₃), 1.18 (d, *J* = 6.6 Hz, 2H, 2×CH₃), 1.10 (d, *J* = 6.6 Hz, 4H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.4, 164.2, 164.0, 163.9, 136.2, 136.0, 135.9, 132.7, 132.2, 130.9, 129.9, 129.5, 129.4, 129.0, 128.9, 128.6, 122.2, 121.9, 118.2, 117.2, 50.8, 50.6, 46.6, 45.9, 42.5, 20.9, 20.5, 20.4, 20.4, 20.2, 20.1, 19.8, 19.6, 14.6, 14.5. HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₂₉N₂O₂ 329.2229; Found: 329.2222.

***N,N*-Diisopropyl-2-oxo-2-(3,5,8-trimethylisoquinolin-2(1*H*)-yl)acetamide (3r)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 42.7 mg, 65%; ¹H NMR (400 MHz, CDCl₃) δ 6.97-6.86 (m, 2H, ArH), 6.27 (s, 0.7H, CH), 6.18 (s, 0.3H, CH), 4.87 (s, 0.6H, CH₂), 4.55 (s, 1.4H, CH₂), 3.79-3.66 (m, 1H, CH), 3.56-3.41 (m, 1H, CH), 2.45 (s, 2H, CH₃), 2.29 (s, 1H, CH₃), 2.28 (s, 2H, CH₃), 2.26 (s, 1H, CH₃), 2.24 (s, 1H, CH₃), 2.22 (s, 2H, CH₃), 1.54 (d, *J* = 6.8 Hz, 4.2H, 2×CH₃), 1.45 (d, *J* = 6.8 Hz, 1.8H, 2×CH₃), 1.18 (d, *J* = 6.6 Hz, 1.8H, 2×CH₃), 1.11 (d, *J* = 6.6 Hz, 4.2H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.4, 164.3, 164.0, 163.9, 137.1, 133.7, 131.1, 130.4, 130.1, 130.0, 129.8, 129.7, 129.5, 129.2, 129.1, 128.8, 128.7, 115.7, 114.4, 50.9, 50.8, 46.5, 46.0, 42.4, 21.4, 20.6, 20.3, 20.3, 20.2, 19.8, 18.7, 18.7, 18.4. HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₂₉N₂O₂ 329.2229; Found: 329.2227.

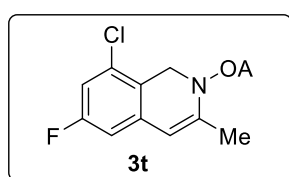
***N,N*-Diisopropyl-2-oxo-2-(3,6,7-trimethylisoquinolin-2(1*H*)-yl)acetamide (3s)**



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 43.9 mg, 67%; ¹H NMR (400 MHz, CDCl₃) δ 6.92 (s, 0.36H, ArH), 6.84 (s, 0.64H, ArH), 6.81-6.77 (m, 1H, ArH), 6.09 (s, 0.67H, CH), 6.01 (s, 0.33H, CH), 4.83 (s, 0.67H, CH₂), 4.46 (s, 1.33H, CH₂), 3.75-3.61 (m, 1H, CH), 3.56-3.39 (m, 1H, CH), 2.39 (s, 2H, CH₃), 2.21 (s, 6H, CH₃), 2.20 (s, 1H, CH₃), 1.55 (d, *J* = 6.8 Hz, 4H, 2×CH₃), 1.44 (d, *J* = 6.8 Hz, 2H, 2×CH₃), 1.15 (d, *J* = 6.6 Hz, 2H, 2×CH₃), 1.11 (d, *J*

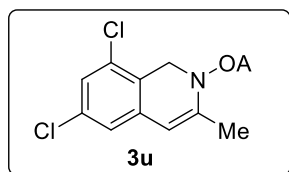
= 6.6 Hz, 4H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.4, 164.3, 164.1, 164.0, 137.0, 136.3, 135.8, 135.6, 135.4, 133.5, 129.9, 129.5, 128.2, 127.6, 126.7, 125.9, 125.8, 125.6, 117.5, 116.7, 50.8, 50.7, 49.1, 46.0, 45.9, 44.7, 21.2, 20.7, 20.4, 20.2, 20.0, 19.8, 19.6, 19.6, 19.6. HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₂₀H₂₉N₂O₂ 329.2229; Found: 329.2220.

2-(8-Chloro-6-fluoro-3-methylisoquinolin-2(1*H*)-yl)-*N,N*-diisopropyl-2-oxoacetamide (3t)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 28.1 mg, 40%; ¹H NMR (400 MHz, CDCl₃) δ 6.9-6.89 (m, 1H, ArH), 6.74-6.62 (m, 1H, ArH), 6.07 (s, 0.76H, CH), 5.97 (s, 0.24H, CH), 4.98 (s, 0.4H, CH₂), 4.68 (s, 1.6H, CH₂), 3.86-3.76 (m, 0.2H, CH), 3.75-3.61 (m, 0.8H, CH), 3.58-3.45 (m, 1H, CH), 2.44 (s, 2.3H, CH₃), 2.22 (s, 0.7H, CH₃), 1.55 (d, *J* = 6.8 Hz, 4.7H, 2×CH₃), 1.45 (d, *J* = 6.8 Hz, 1.3H, 2×CH₃), 1.24 (d, *J* = 7.1 Hz, 1.3H, 2×CH₃), 1.15 (d, *J* = 6.6 Hz, 4.7H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.6, 163.5, 162.0 (d, *J* = 248.8 Hz), 140.8, 135.5 (d, *J* = 9.2 Hz), 130.6 (d, *J* = 11.5 Hz), 123.9 (d, *J* = 3.3 Hz), 116.1 (d, *J* = 2.3 Hz), 114.5 (d, *J* = 25.3 Hz), 110.2 (d, *J* = 22.2 Hz), 51.1, 46.1, 45.9, 20.6, 20.3, 20.1. ¹⁹F NMR (376 MHz, CDCl₃) δ -112.2, -113.1. HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₈H₂₂ClFNaO₂ 375.1252; Found: 375.1246.

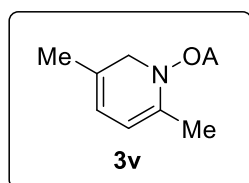
2-(6,8-Dichloro-3-methylisoquinolin-2(1*H*)-yl)-*N,N*-diisopropyl-2-oxoacetamide (3u)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 33.8 mg, 46%; ¹H NMR (400 MHz, CDCl₃) δ 7.20-7.16 (m, 1H, ArH), 6.97-6.89 (m, 1H, ArH), 6.05 (s, 0.8H, CH), 5.94 (s, 0.2H, CH), 4.97 (s, 0.4H, CH₂), 4.67 (s, 1.6H, CH₂), 3.85-

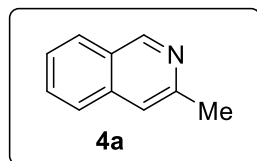
3.75 (m, 0.2H, CH), 3.73-3.62 (m, 0.8H, CH), 3.57-3.44 (m, 1H, CH), 2.44 (s, 2.4H, CH₃), 2.22 (s, 0.6H, CH₃), 1.54 (d, $J = 6.8$ Hz, 4.8H, 2×CH₃), 1.44 (d, $J = 6.7$ Hz, 1.2H, 2×CH₃), 1.23 (d, $J = 6.5$ Hz, 1.2H, 2×CH₃), 1.15 (d, $J = 6.6$ Hz, 4.8H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 164.5, 163.4, 140.9, 135.3, 134.2, 130.7, 127.0, 126.4, 123.1, 115.7, 51.1, 46.2, 46.0, 20.6, 20.4, 20.1. HRMS (ESI) m/z : [M + Na]⁺ Calcd for C₁₈H₂₂Cl₂N₂NaO₂ 391.0956; Found: 391.0970.

2-(3,6-Dimethylpyridin-1(2H)-yl)-N,N-diisopropyl-2-oxoacetamide (3v)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:10) to give the product as colorless oil, Yield: 15.8 mg, 30%; ¹H NMR (400 MHz, CDCl₃) δ 6.63 (s, 1H, CH), 5.97 (s, 1H, CH), 4.33 (s, 2H, CH₂), 3.82-3.71 (m, 1H, CH), 3.62-3.50 (m, 1H, CH), 2.03 (s, 3H, CH₃), 2.01 (s, 3H, CH₃), 1.54 (d, $J = 6.9$ Hz, 6H, 2×CH₃), 1.22 (d, $J = 6.6$ Hz, 6H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 171.0, 163.0, 162.6, 123.7, 118.3, 117.3, 62.8, 51.0, 46.3, 21.0, 20.7, 20.1. HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₅H₂₅N₂O₂ 265.1916; Found: 265.1920.

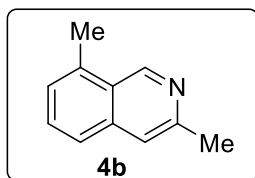
3-Methylisoquinoline (4a)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 18.0 mg, 63%; ¹H NMR (400 MHz, CDCl₃) δ 9.18 (s, 1H, ArH), 7.92 (d, $J = 8.2$ Hz, 1H, ArH), 7.72 (d, $J = 8.2$ Hz, 1H, ArH), 7.66-7.61 (m, 1H, ArH), 7.54-7.49 (m, 1H, ArH), 7.48 (s, 1H, ArH), 2.70 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 152.0, 151.7, 136.6, 130.3, 127.6, 126.9, 126.3, 126.0, 118.5, 24.3; HRMS (ESI) m/z : [M + H]⁺ Calcd for C₁₀H₁₀N 144.0813; Found: 144.0829.

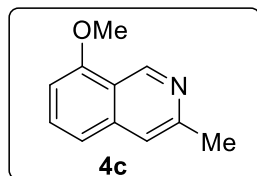
3,8-Dimethylisoquinoline (4b)

The compound was purified by flash column chromatography (Ethyl acetate/Petroleum



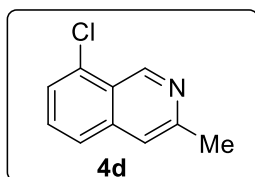
ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 19.1 mg, 61%; ^1H NMR (400 MHz, CDCl_3) δ 9.36 (s, 1H, ArH), 7.56 (d, J = 8.2 Hz, 1H, ArH), 7.53-7.48 (m, 1H, ArH), 7.46 (s, 1H, ArH), 7.29 (d, J = 6.8 Hz, 1H, ArH), 2.76 (s, 3H, CH_3), 2.70 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 151.5, 148.9, 137.0, 135.4, 130.2, 127.2, 126.0, 124.4, 119.0, 24.2, 18.5. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{12}\text{N}$ 158.0970; Found: 158.0967.

8-Methoxy-3-methylisoquinoline (4c)



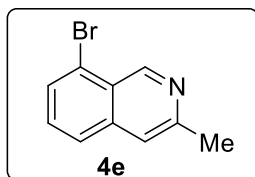
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 19.7 mg, 57%; ^1H NMR (400 MHz, CDCl_3) δ 9.52 (s, 1H, ArH), 7.52 (t, J = 8.0 Hz, 1H, ArH), 7.40 (s, 1H, ArH), 7.28-7.24 (m, 1H, ArH), 6.79 (d, J = 7.7 Hz, 1H, ArH), 4.01 (s, 3H, CH_3O), 2.68 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 156.7, 152.3, 147.2, 137.9, 131.0, 119.1, 118.1, 118.1, 104.3, 55.6, 24.3. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{12}\text{NO}$ 174.0919; Found: 174.0923.

8-Chloro-3-methylisoquinoline (4d)



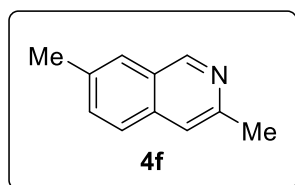
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 18.0 mg, 51%; ^1H NMR (400 MHz, CDCl_3) δ 9.18 (s, 1H, ArH), 7.93 (d, J = 8.2 Hz, 1H, ArH), 7.73 (d, J = 8.3 Hz, 1H, ArH), 7.67-7.62 (m, 1H, ArH), 7.52 (t, J = 7.5 Hz, 1H, ArH), 7.49 (s, 1H, ArH), 2.71 (s, 3H, CH_3). ^{13}C NMR (101 MHz, CDCl_3) δ 152.0, 151.7, 136.7, 130.4, 127.6, 127.0, 126.4, 126.0, 118.6, 24.3. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{10}\text{H}_9\text{ClN}$ 178.0424; Found: 178.0420.

8-Bromo-3-methylisoquinoline (4e)



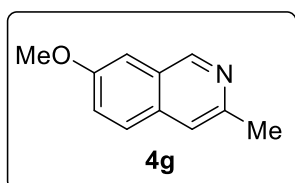
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 20.7 mg, 47%; ^1H NMR (400 MHz, CDCl_3) δ 9.18 (s, 1H, ArH), 7.93 (d, $J = 8.2$ Hz, 1H, ArH), 7.73 (d, $J = 8.3$ Hz, 1H, ArH), 7.66-7.61 (m, 1H, ArH), 7.54-7.50 (m, 1H, ArH), 7.48 (s, 1H, ArH), 2.70 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 152.0, 151.7, 136.7, 130.4, 127.6, 126.9, 126.4, 126.0, 118.6, 24.3. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{10}\text{H}_8\text{BrNNa}$ 243.9738; Found: 243.9733.

3,7-Dimethylisoquinoline (4f)



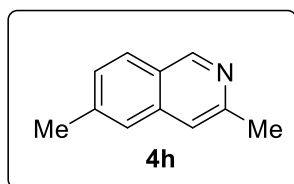
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 19.8 mg, 63%; ^1H NMR (400 MHz, CDCl_3) δ 9.10 (s, 1H, ArH), 7.60 (d, $J = 8.2$ Hz, 1H, ArH), 7.52-7.50 (m, 1H, ArH), 7.48 (s, 1H, ArH), 7.30 (d, $J = 6.8$ Hz, 1H, ArH), 2.71 (s, 3H, CH_3), 2.66 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 150.8, 150.1, 136.6, 135.2, 133.2, 127.1, 126.5, 125.9, 118.8, 23.7, 21.8. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{12}\text{N}$ 158.0970; Found: 158.0975.

7-Methoxy-3-methylisoquinoline (4g)



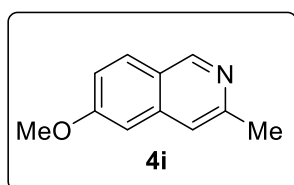
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 65-67 °C; Yield: 20.4 mg, 59%; ^1H NMR (400 MHz, CDCl_3) δ 9.07 (s, 1H, ArH), 7.62 (d, $J = 9.0$ Hz, 1H, ArH), 7.40 (s, 1H, ArH), 7.29 (dd, $J = 9.0, 2.5$ Hz, 1H, ArH), 7.17 (d, $J = 2.4$ Hz, 1H, ArH), 3.92 (s, 3H, CH_3O), 2.66 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 157.8, 150.5, 149.8, 132.4, 127.9, 127.6, 123.7, 118.5, 104.6, 55.5, 24.0. HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{11}\text{H}_{12}\text{NO}$ 174.0919; Found: 174.0922.

3,6-Dimethylisoquinoline (4h)



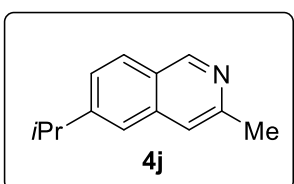
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 69-71 °C; Yield: 18.2 mg, 58%; ¹H NMR (400 MHz, CDCl₃) δ 9.10 (s, 1H, ArH), 7.81 (d, *J* = 8.4 Hz, 1H, ArH), 7.48 (s, 1H, ArH), 7.38 (s, 1H, ArH), 7.34 (dd, *J* = 8.4, 1.4 Hz, 1H, ArH), 2.67 (s, 3H, CH₃), 2.52 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 151.7, 151.6, 140.7, 137.0, 128.7, 127.4, 125.4, 124.9, 118.1, 24.3, 22.2. HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₂N 158.0970; Found: 158.0974.

6-Methoxy-3-methylisoquinoline (4i)



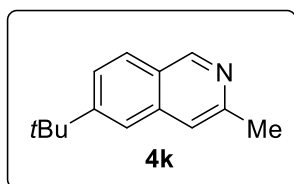
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 106-108 °C; Yield: 19.7 mg, 57%; ¹H NMR (400 MHz, CDCl₃) δ 9.02 (s, 1H, ArH), 7.80 (d, *J* = 8.9 Hz, 1H, ArH), 7.38 (s, 1H, ArH), 7.14 (dd, *J* = 8.9, 2.3 Hz, 1H, ArH), 6.96 (d, *J* = 2.1 Hz, 1H, ArH), 3.93 (s, 3H, CH₃O), 2.66 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 161.1, 152.2, 151.2, 138.6, 129.3, 122.8, 119.5, 117.9, 103.6, 55.5, 24.3. HRMS (ESI) *m/z*: [M + H]⁺ Calcd for C₁₁H₁₂NO 174.0919; Found: 174.0915.

6-Isopropyl-3-methylisoquinoline (4j)



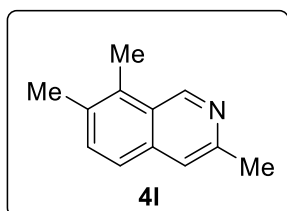
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 18.5 mg, 50%; ¹H NMR (400 MHz, CDCl₃) δ 9.10 (s, 1H, ArH), 7.84 (d, *J* = 8.5 Hz, 1H, ArH), 7.51 (s, 1H, ArH), 7.43-7.39 (m, 2H, ArH), 3.16-2.99 (m, 1H, ArH), 2.68 (s, 3H, CH₃), 1.33 (d, *J* = 6.9 Hz, 6H, 2×CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 151.7, 151.2, 137.2, 127.6, 126.6, 125.7, 122.2, 118.7, 34.6, 24.0, 23.7. HRMS (ESI) *m/z*: [M + Na]⁺ Calcd for C₁₃H₁₅NNa 208.1102; Found: 208.1099.

6-(*tert*-Butyl)-3-methylisoquinoline (4k)



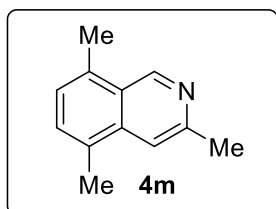
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 16.3 mg, 41%; ^1H NMR (400 MHz, CDCl_3) δ 9.10 (s, 1H, ArH), 7.86 (d, $J = 8.6$ Hz, 1H, ArH), 7.64 (s, 1H, ArH), 7.61 (dd, $J = 8.6, 1.8$ Hz, 1H, ArH), 7.45 (s, 1H, ArH), 2.68 (s, 3H, CH_3), 1.41 (s, 9H, $3\times\text{CH}_3$). ^{13}C NMR (100 MHz, CDCl_3) δ 154.4, 150.6, 150.6, 137.2, 127.4, 125.9, 125.2, 121.1, 119.4, 35.5, 31.1, 23.7). HRMS (ESI) m/z : $[\text{M} + \text{H}]^+$ Calcd for $\text{C}_{14}\text{H}_{18}\text{N}$ 200.1439; Found: 200.1443.

3,7,8-Trimethylisoquinoline (4l)



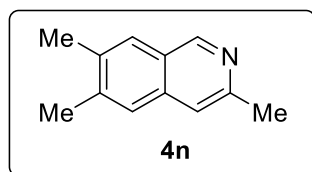
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 80-82 °C; Yield: 18.1 mg, 53%; ^1H NMR (400 MHz, CDCl_3) δ 9.39 (s, 1H, ArH), 7.47 (d, $J = 8.4$ Hz, 1H, ArH), 7.44-7.39 (m, 2H, ArH), 2.67 (s, 3H, CH_3), 2.65 (s, 3H, CH_3), 2.46 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 150.2, 148.5, 135.6, 133.8, 133.5, 132.2, 126.2, 123.7, 118.8, 24.0, 20.4, 13.9. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{NNa}$ 194.0946; Found: 194.0955.

3,5,8-Trimethylisoquinoline (4m)



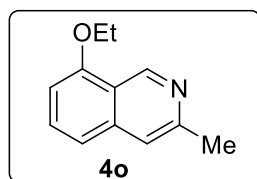
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 17.1 mg, 50%; ^1H NMR (400 MHz, CDCl_3) δ 9.33 (s, 1H, ArH), 7.57 (s, 1H, ArH), 7.33 (d, $J = 7.1$ Hz, 1H, ArH), 7.17 (d, $J = 7.1$ Hz, 1H, ArH), 2.73 (s, 3H, CH_3), 2.72 (s, 3H, CH_3), 2.59 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 151.4, 149.3, 136.3, 133.1, 130.9, 130.4, 126.7, 125.9, 115.6, 24.4, 18.5, 18.4. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{NNa}$ 194.0946; Found: 194.0951.

3,6,7-Timethyloisoquinoline (4n)



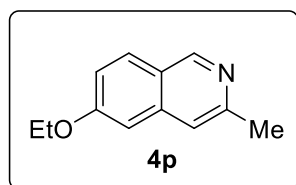
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 84-85 °C; Yield: 16.7 mg, 49%; ^1H NMR (400 MHz, CDCl_3) δ 9.04 (s, 1H, ArH), 7.65 (s, 1H, ArH), 7.47 (s, 1H, ArH), 7.35 (s, 1H, ArH), 2.66 (s, 3H, CH_3), 2.43 (s, 3H, CH_3), 2.42 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 150.8, 150.7, 140.9, 136.3, 135.7, 126.8, 126.1, 125.4, 117.8, 24.1, 20.7, 20.3. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{NNa}$ 194.0946; Found: 194.0953.

8-Ethoxy-3-methyloisoquinoline (4o)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as colorless oil, Yield: 22.4 mg, 60%; ^1H NMR (400 MHz, CDCl_3) δ 9.54 (s, 1H, ArH), 7.50 (t, J = 8.0 Hz, 1H, ArH), 7.39 (s, 1H, ArH), 7.24 (d, J = 8.3 Hz, 1H, ArH), 6.77 (d, J = 7.7 Hz, 1H, ArH), 4.22 (q, J = 7.0 Hz, 2H, CH_2O), 2.68 (s, 3H, CH_3), 1.55 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 156.0, 152.2, 147.4, 137.9, 131.0, 119.2, 118.0, 117.8, 105.0, 64.0, 24.3, 14.8. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{12}\text{H}_{13}\text{NNaO}$ 210.0895; Found: 210.0891.

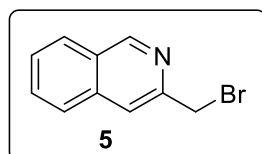
6-Ethoxy-3-methyloisoquinoline (4p)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8 to 1:5) to give the product as pale yellow solid, m.p. 89-90 °C; Yield: 20.2 mg, 54%; ^1H NMR (400 MHz, CDCl_3) δ 9.01 (s, 1H, ArH), 7.80 (d, J = 8.9 Hz, 1H, ArH), 7.35 (s, 1H, ArH), 7.13 (dd, J = 8.9, 2.4 Hz, 1H, ArH), 6.94 (d, J = 2.3 Hz, 1H, ArH), 4.15 (q, J = 7.0 Hz, 2H, CH_2O), 2.65 (s, 3H, CH_3), 1.49 (t, J = 7.0 Hz, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 160.4, 152.1, 151.1, 138.7, 129.3,

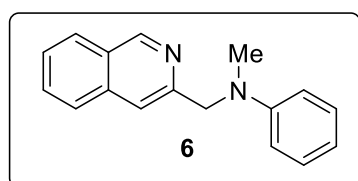
122.8, 119.7, 117.9, 104.2, 63.8, 24.3, 14.8. HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{12}H_{13}NNaO$ 210.0895; Found: 210.0887.

3-(Bromomethyl)isoquinoline (5)



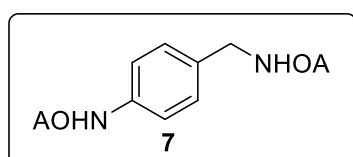
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:8) to give the product as white solid, m.p. 92-93 °C (lit. 90.5-92 °C)^[1]; Yield: 35.3 mg, 40%; ¹H NMR (400 MHz, DMSO) δ 9.41 (s, 1H), 8.23 (d, J = 8.2 Hz, 1H), 8.08 (s, 1H), 8.05 (d, J = 8.2 Hz, 1H), 7.92-7.87 (m, 1H), 7.82-7.77 (m, 1H), 4.97 (s, 2H). ¹³C NMR (100 MHz, DMSO) δ 152.6, 150.0, 135.5, 131.0, 128.0, 127.6, 127.4, 126.6, 119.8, 35.8. HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{10}H_8BrNNa$ 243.9738; Found: 243.9739.

N-(Isoquinolin-3-ylmethyl)-*N*-methylaniline (6)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:5) to give the product as colorless oil, Yield: 65.4 mg, 88%; ¹H NMR (400 MHz, CDCl₃) δ 9.26 (s, 1H, ArH), 7.97 (d, J = 8.1 Hz, 1H, ArH), 7.72 (d, J = 8.2 Hz, 1H, ArH), 7.67 – 7.62 (m, 1H, ArH), 7.58 – 7.53 (m, 1H, ArH), 7.50 (s, 1H, ArH), 7.26 – 7.21 (m, 2H, ArH), 6.79 (d, J = 8.1 Hz, 2H, ArH), 6.73 (t, J = 7.3 Hz, 1H, ArH), 4.82 (s, 2H, CH₂), 3.19 (s, 3H, CH₃). ¹³C NMR (100 MHz, CDCl₃) δ 152.7, 152.3, 149.5, 136.6, 130.6, 129.3, 127.8, 127.7, 126.9, 126.7, 116.7, 116.5, 112.3, 59.0, 39.1. HRMS (ESI) m/z : $[M + Na]^+$ Calcd for $C_{17}H_{16}N_2Na$ 271.1211; Found: 271.1207.

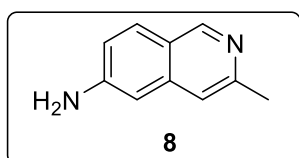
*N*¹-(4-(2-(diisopropylamino)-2-oxoacetamido)benzyl)-*N*²,*N*²-diisopropylloxalamide (7)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:5) to give the product as white solid, m.p. 127-128 °C;

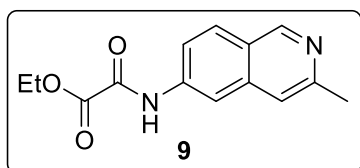
^1H NMR (400 MHz, CDCl_3) δ 9.45 (s, 1H, NH), 7.91 (t, $J = 6.3$ Hz, 1H, NH), 7.44 (d, $J = 8.5$ Hz, 2H, ArH), 7.23 (d, $J = 8.4$ Hz, 2H, ArH), 4.76-4.80 (m, 1H, NH), 4.68-4.62 (m, 1H CH), 4.38 (d, $J = 6.0$ Hz, 2H, CH_2), 3.59-3.46 (m, 2H, CH), 1.45 (d, $J = 6.8$ Hz, 6H, CH_3), 1.40 (d, $J = 6.8$ Hz, 6H, CH_3), 1.25 (dd, $J = 6.7, 4.2$ Hz, 12H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 163.87, 163.48, 163.22, 160.72, 136.85, 133.97, 128.87, 119.94, 50.14, 50.03, 46.84, 46.67, 42.96, 20.98, 20.21. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{23}\text{H}_{36}\text{N}_4\text{Na}$ 455.2634; Found: 455.2649.

3-methylisoquinolin-6-amine (8)



The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:5) to give the product as pale yellow oil, Yield: 14.1 mg, 45%; ^1H NMR (400 MHz, CDCl_3) δ 8.91 (s, 1H, ArH), 7.71 (d, $J = 8.7$ Hz, 1H, ArH), 7.20 (s, 1H, ArH), 6.91 (d, $J = 8.6$ Hz, 1H, ArH), 6.76 (s, 1H, ArH), 4.09 (s, 2H, NH_2), 2.61 (s, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 152.00, 151.21, 148.19, 138.85, 129.45, 121.89, 118.34, 116.84, 105.34, 24.34. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{10}\text{H}_{10}\text{N}_2\text{Na}$ 181.0742; Found: 181.0750.

ethyl 2-((3-methylisoquinolin-6-yl)amino)-2-oxoacetate (9)



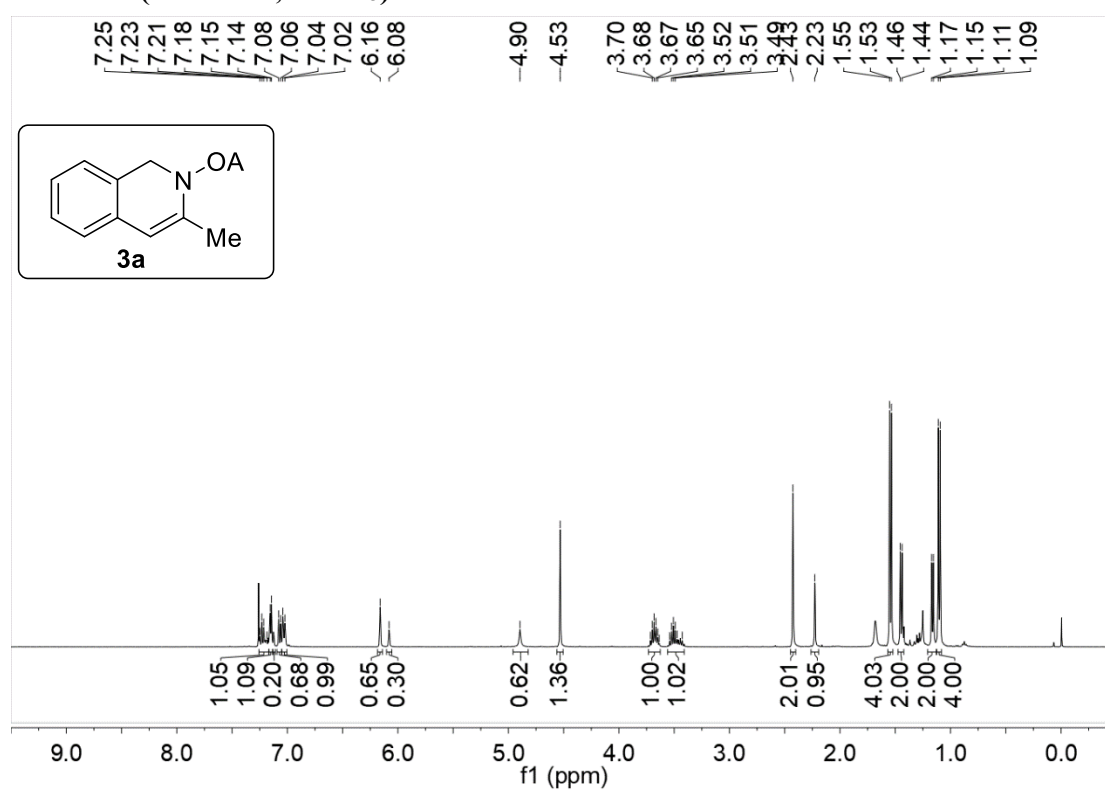
The compound was purified by flash column chromatography (Ethyl acetate/Petroleum ether = 1:6) to give the product as pale yellow oil, Yield: 32.0 mg, 62%; ^1H NMR (400 MHz, CDCl_3) δ 9.13 (s, 2H, ArH, NH), 8.32 (d, $J = 2.0$ Hz, 1H, ArH), 7.96 (d, $J = 8.8$ Hz, 1H, ArH), 7.58 (dd, $J = 8.8, 2.1$ Hz, 1H, ArH), 7.52 (s, 1H, ArH), 4.46 (q, $J = 7.1$ Hz, 2H, CH_2), 2.72 (s, 3H, CH_3), 1.46 (t, $J = 7.1$ Hz, 3H, CH_3). ^{13}C NMR (100 MHz, CDCl_3) δ 160.79, 154.40, 151.80, 150.70, 138.25, 137.89, 129.45, 124.44, 120.18, 119.25, 114.68, 64.23, 29.84, 14.15. HRMS (ESI) m/z : $[\text{M} + \text{Na}]^+$ Calcd for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{O}_3\text{Na}$ 281.0902; Found: 281.0911.

References

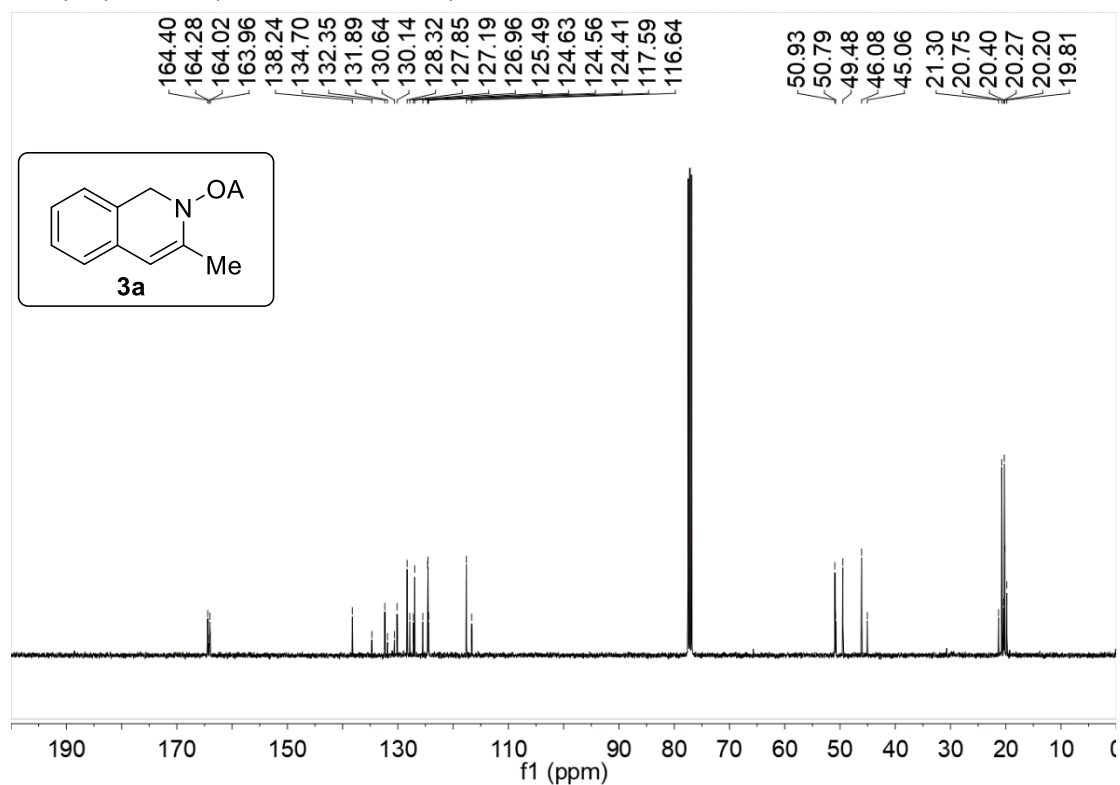
- [1] Wang, C.; Chen, C.; Zhang, J.; Han, J.; Wang, Q.; Guo, K.; Liu, P.; Guan, M.; Yao, Y.; Zhao, Y. Easily Accessible Auxiliary for Palladium-Catalyzed Intramolecular Amination of C(sp²)-H and C(sp³)-H Bonds at δ - and ϵ -Positions. *Angew. Chemie Int. Ed.* **2014**, *53*, 9884.

11. ¹H NMR and ¹³C NMR spectra

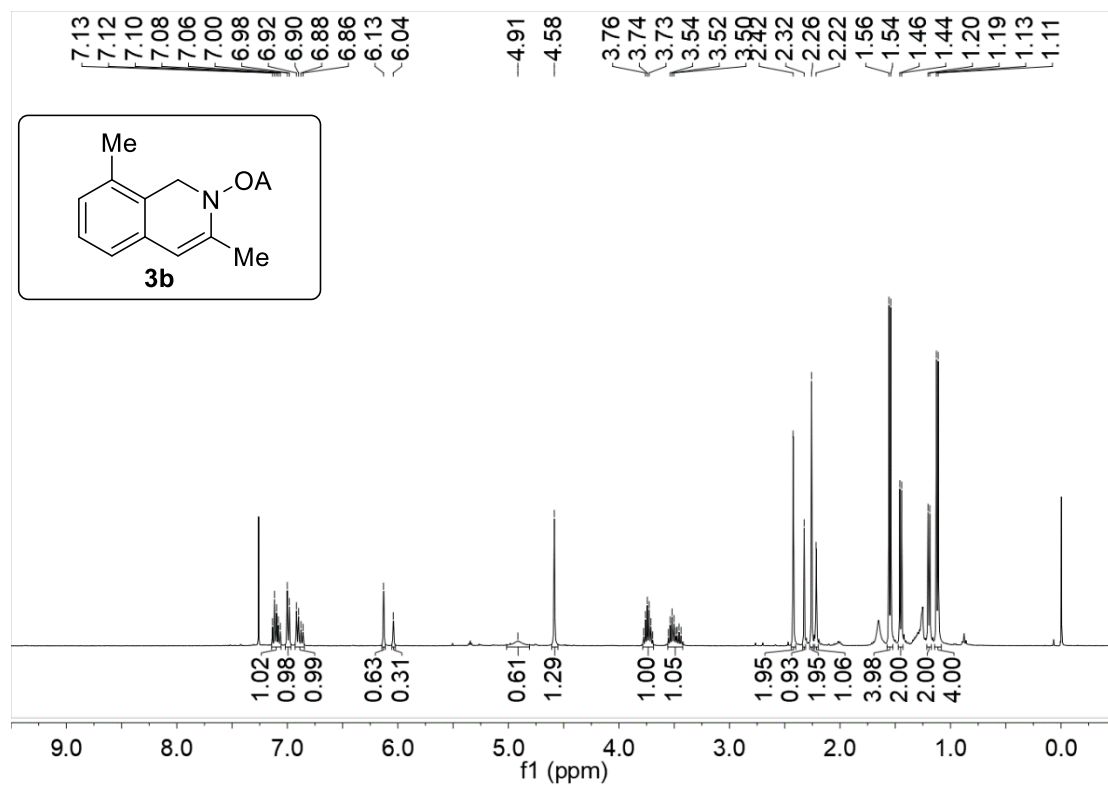
¹H NMR (400 MHz, CDCl₃) of 3a



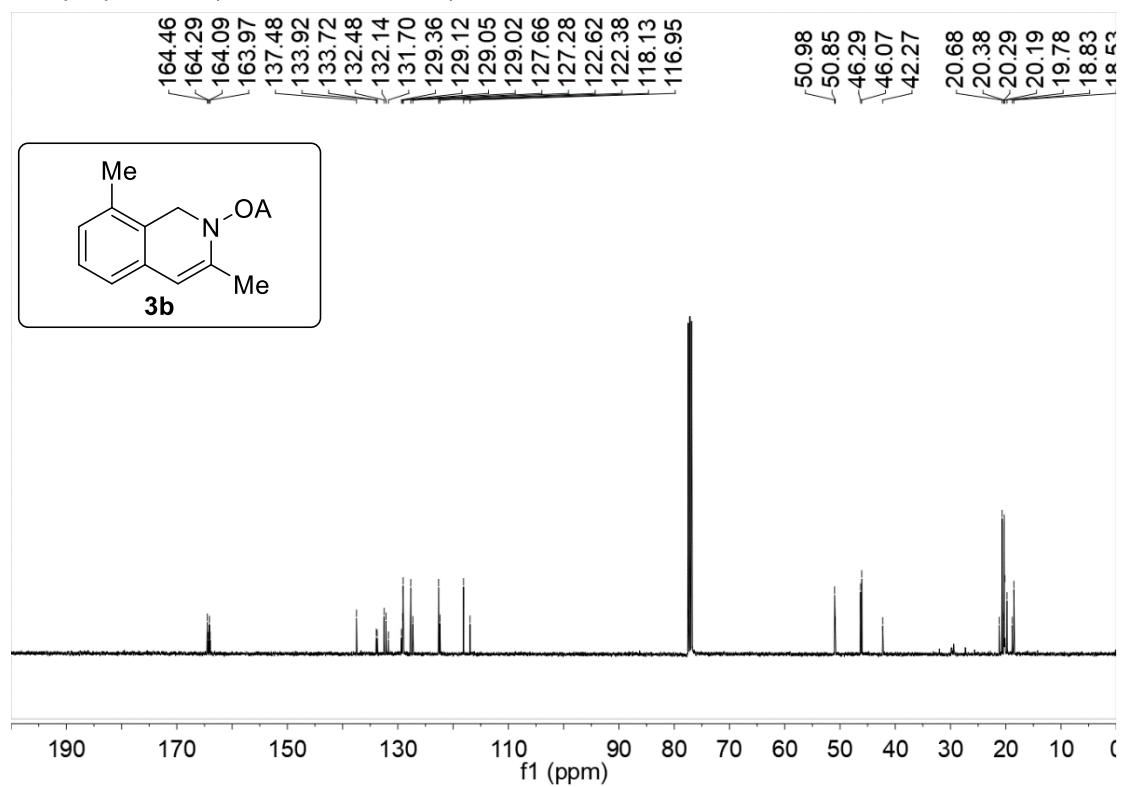
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **3a**



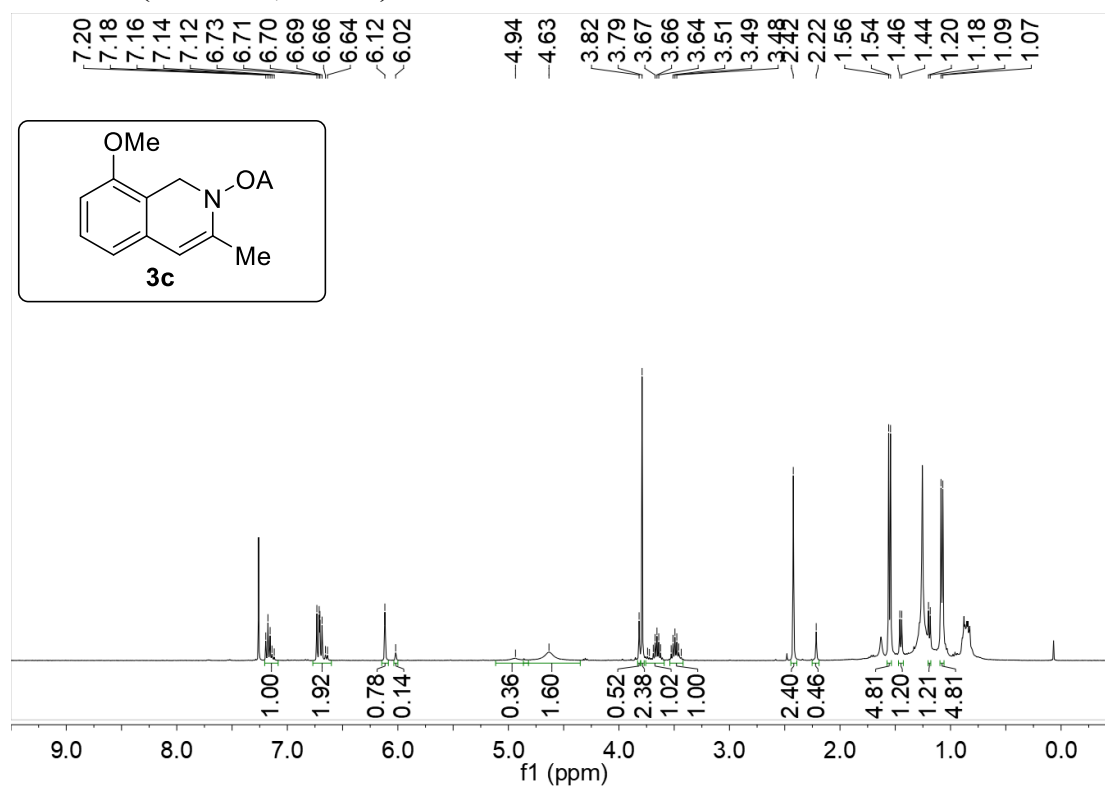
^1H NMR (400 MHz, CDCl_3) of **3b**



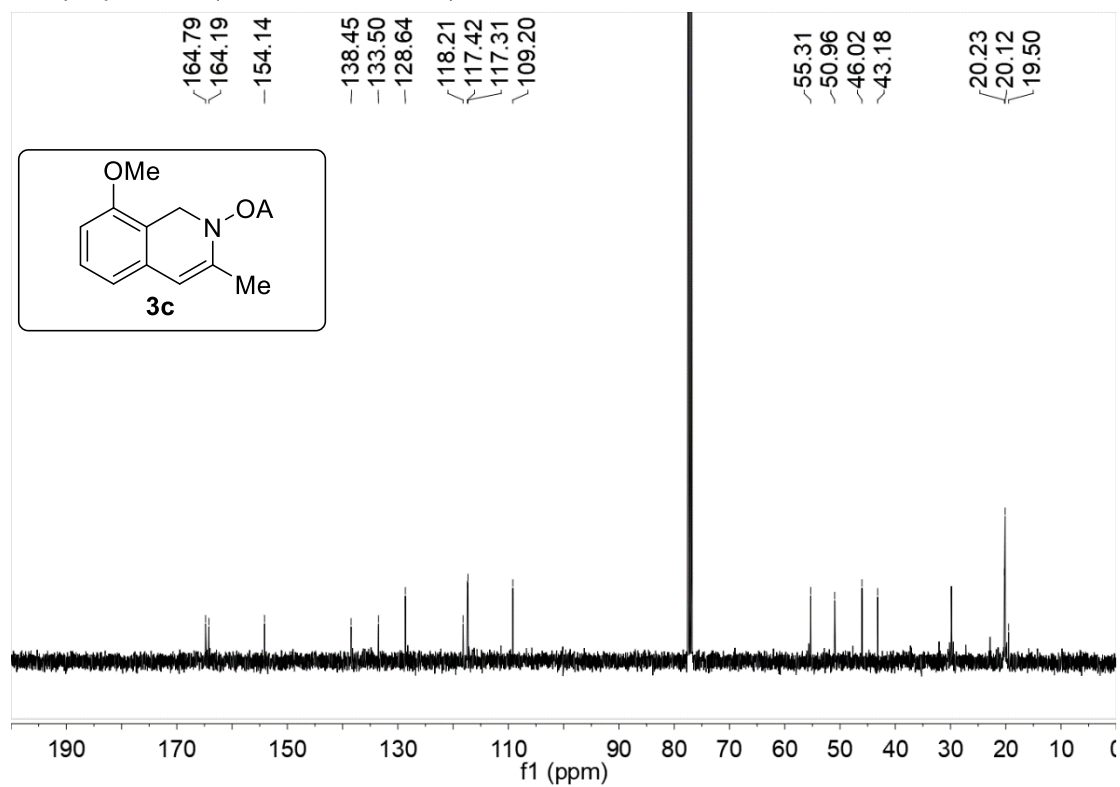
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **3b**



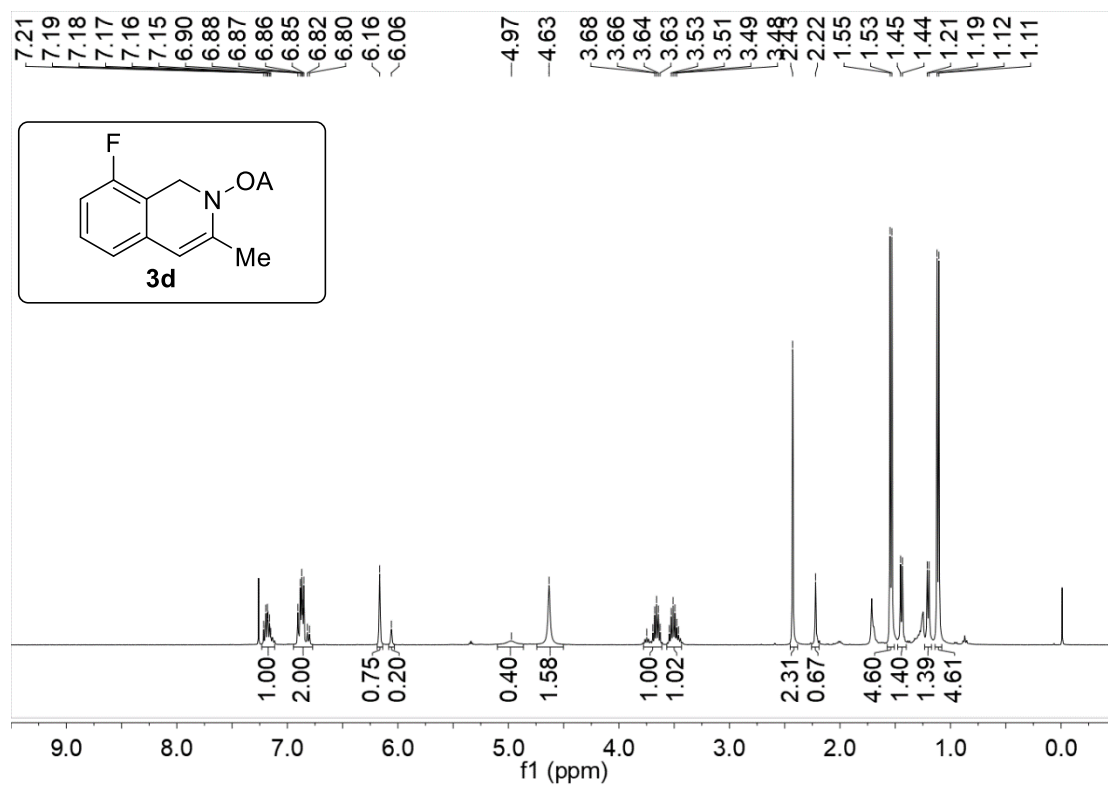
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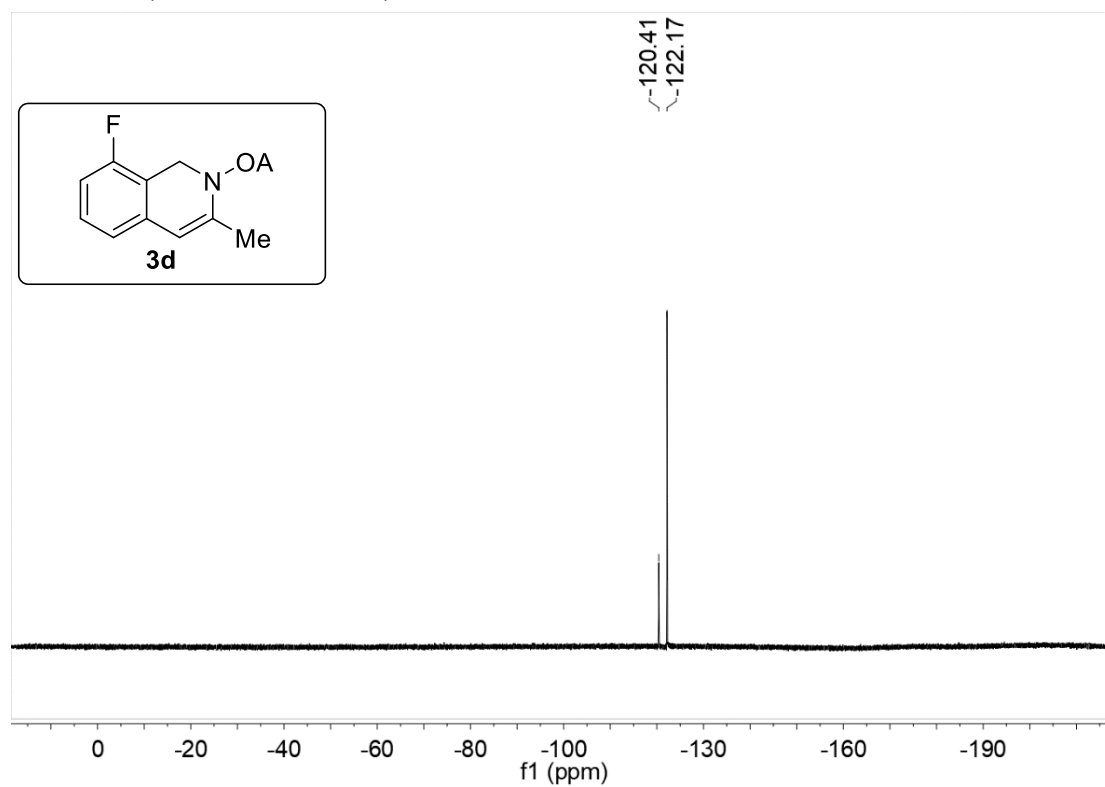
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 3c



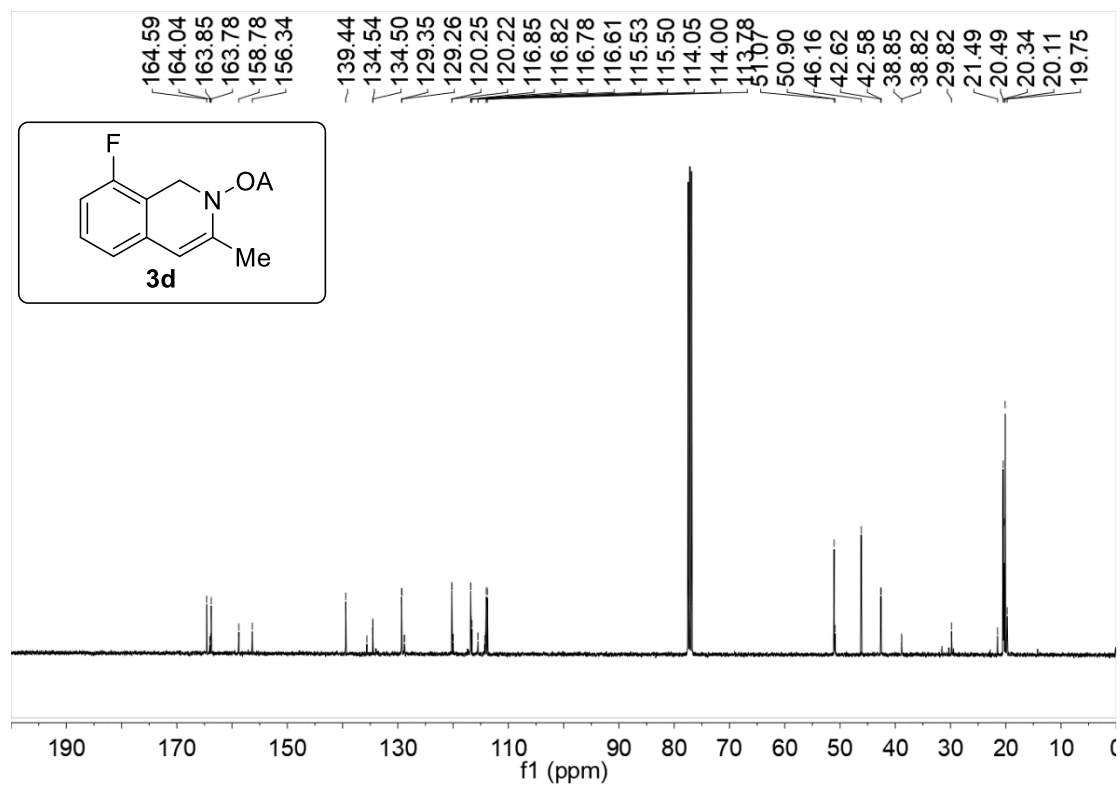
^1H NMR (400 MHz, CDCl_3) of 3d



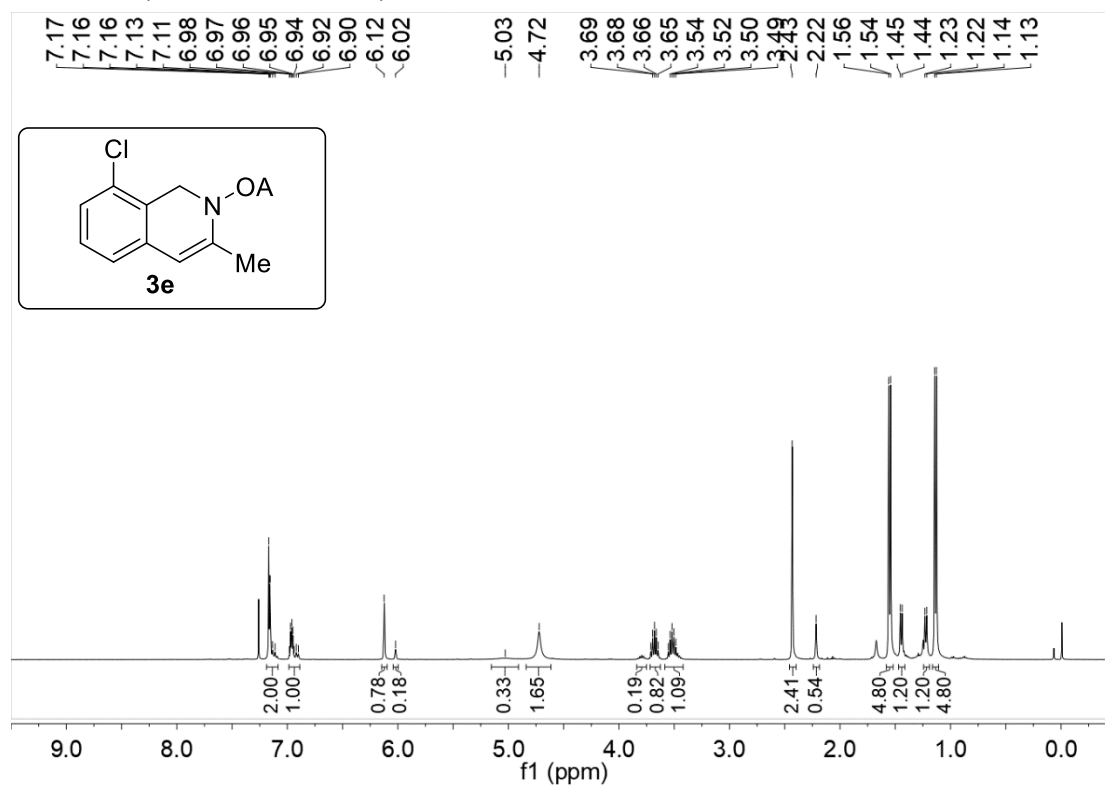
^{19}F NMR (376 MHz, CDCl_3) of 3d



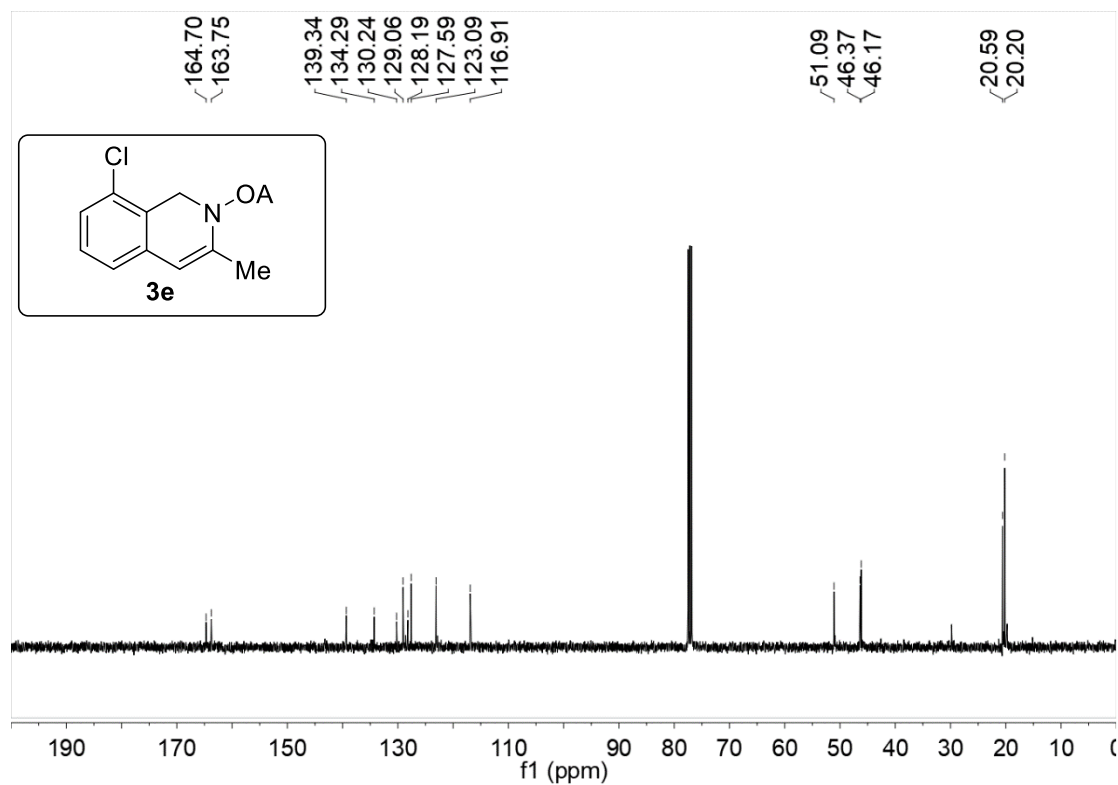
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 3d



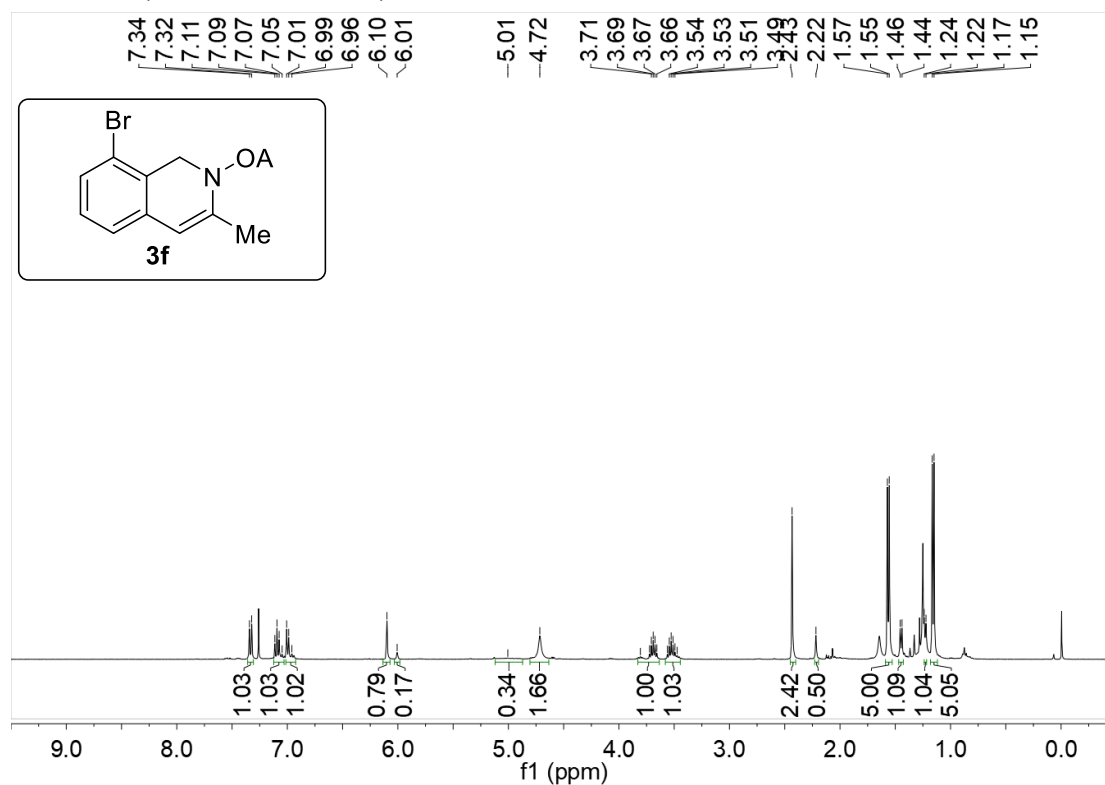
^1H NMR (400 MHz, CDCl_3) of **3e**



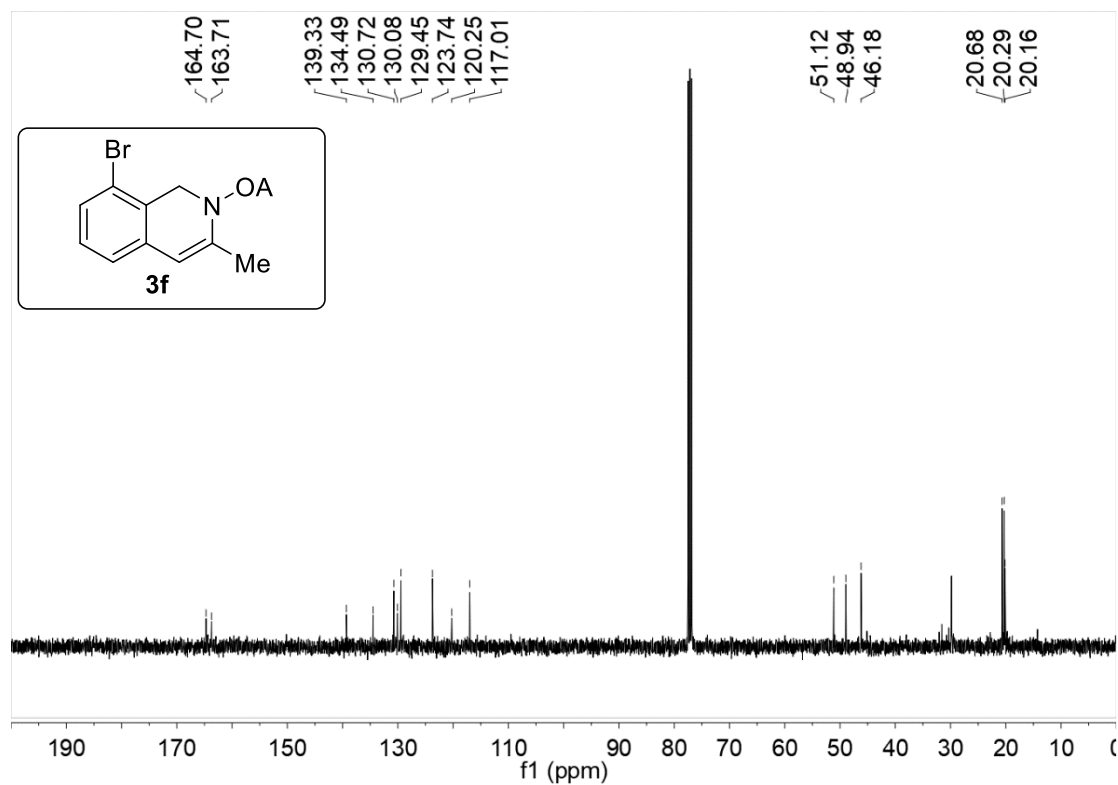
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **3e**



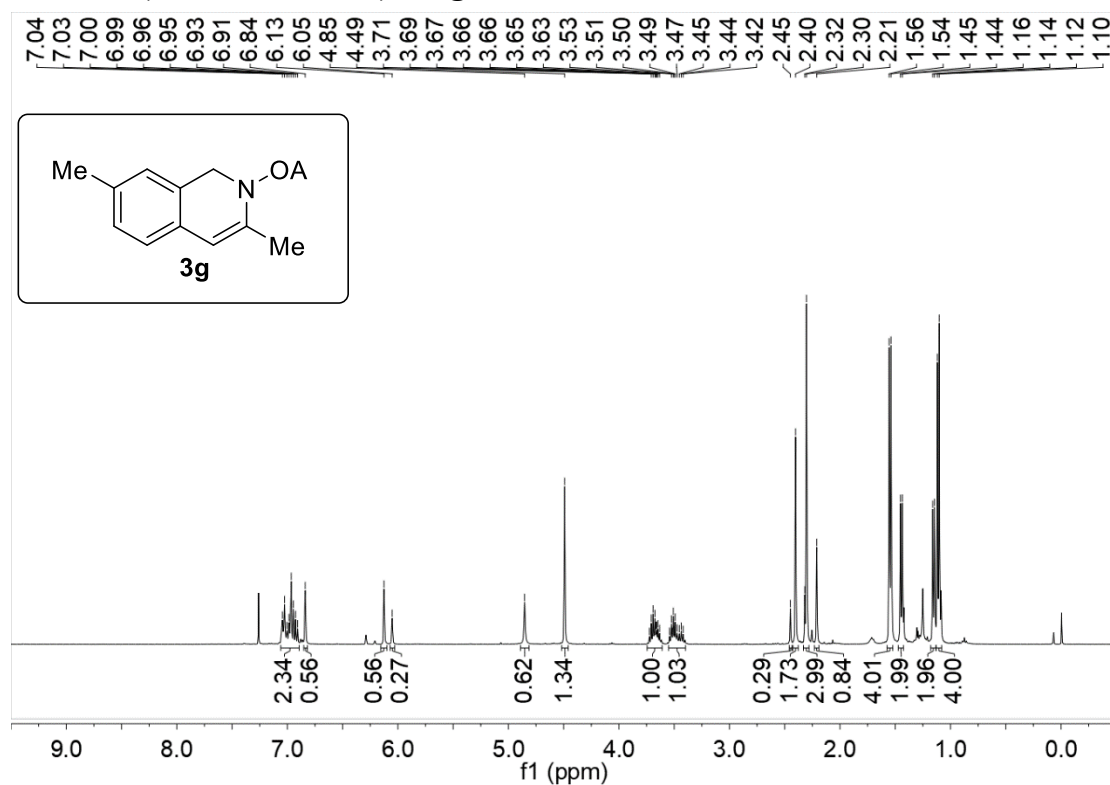
^1H NMR (400 MHz, CDCl_3) of **3f**



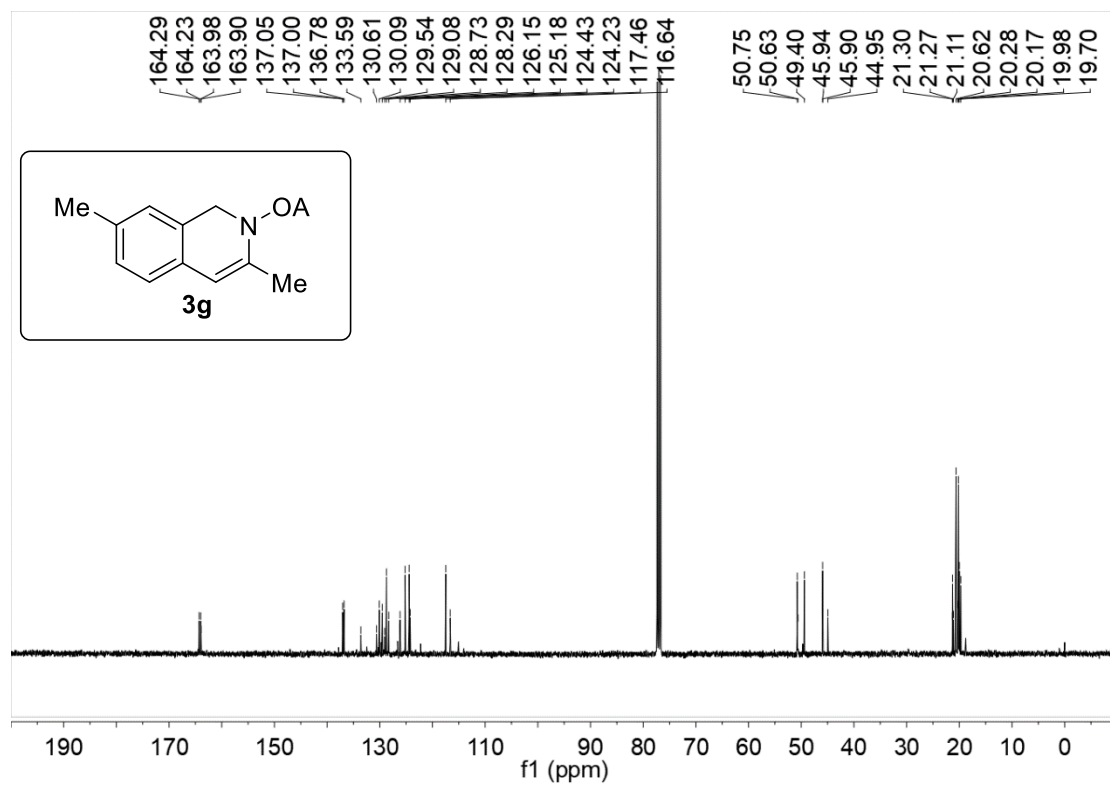
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **3f**



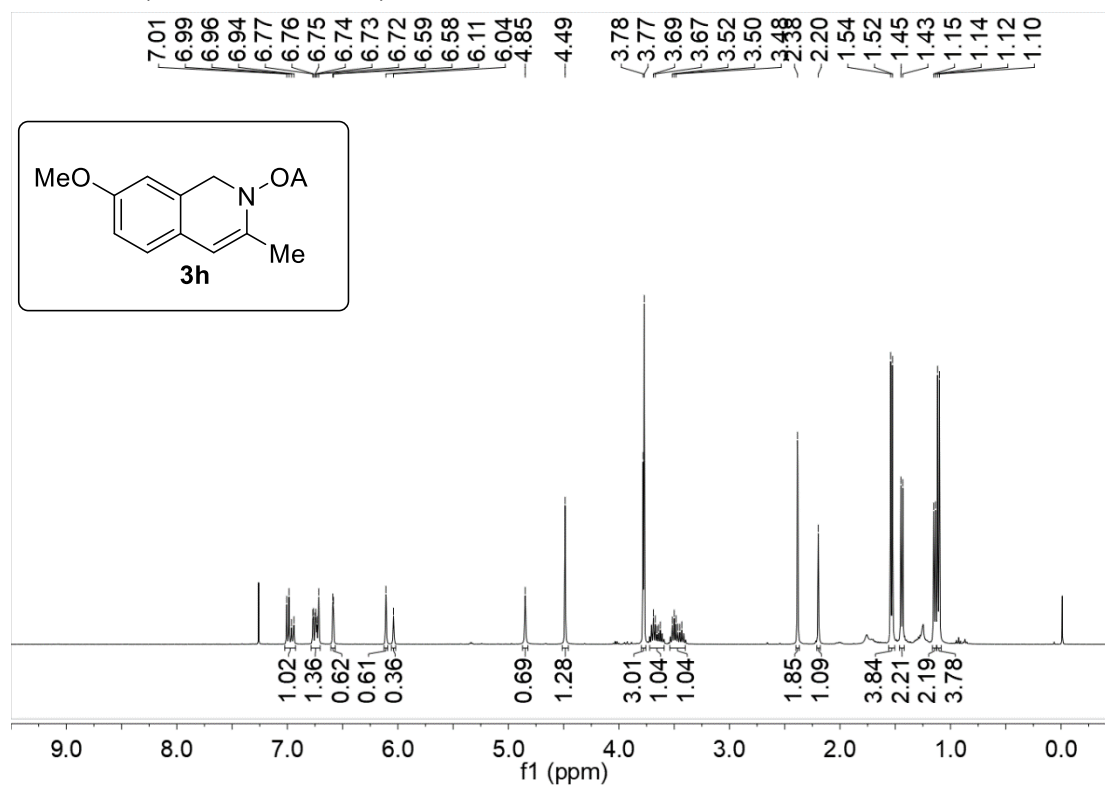
^1H NMR (400 MHz, CDCl_3) of **3g**



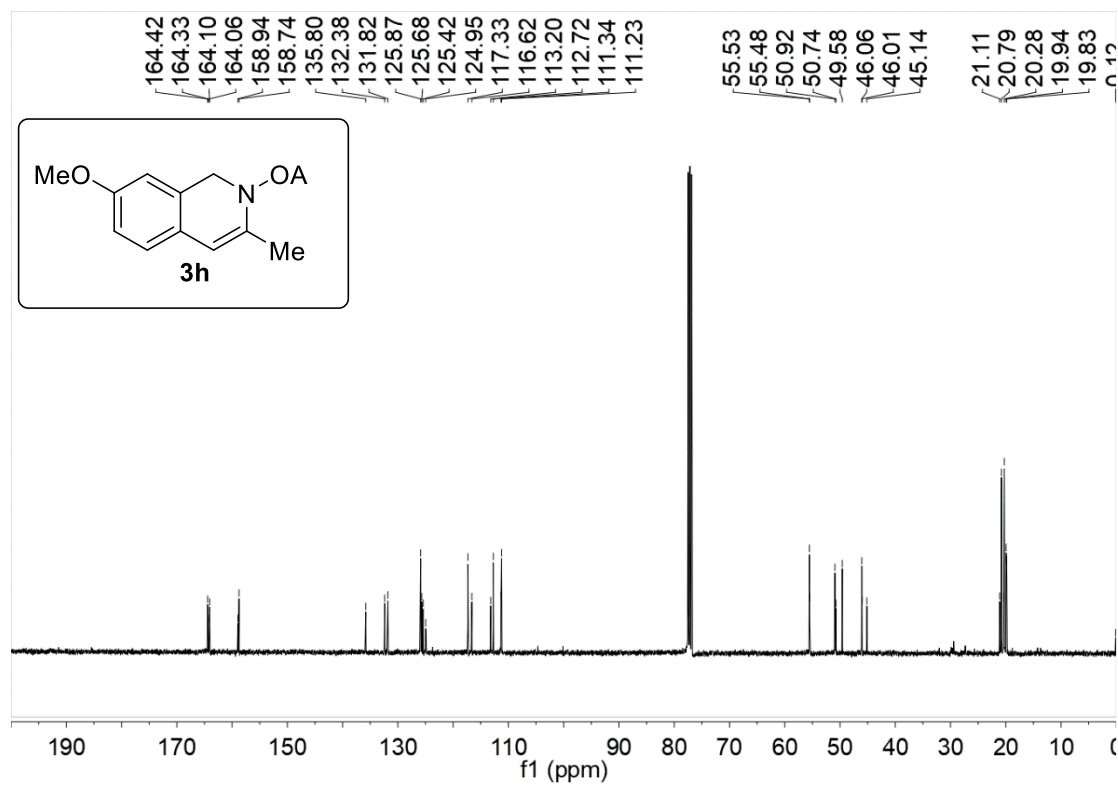
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **3g**



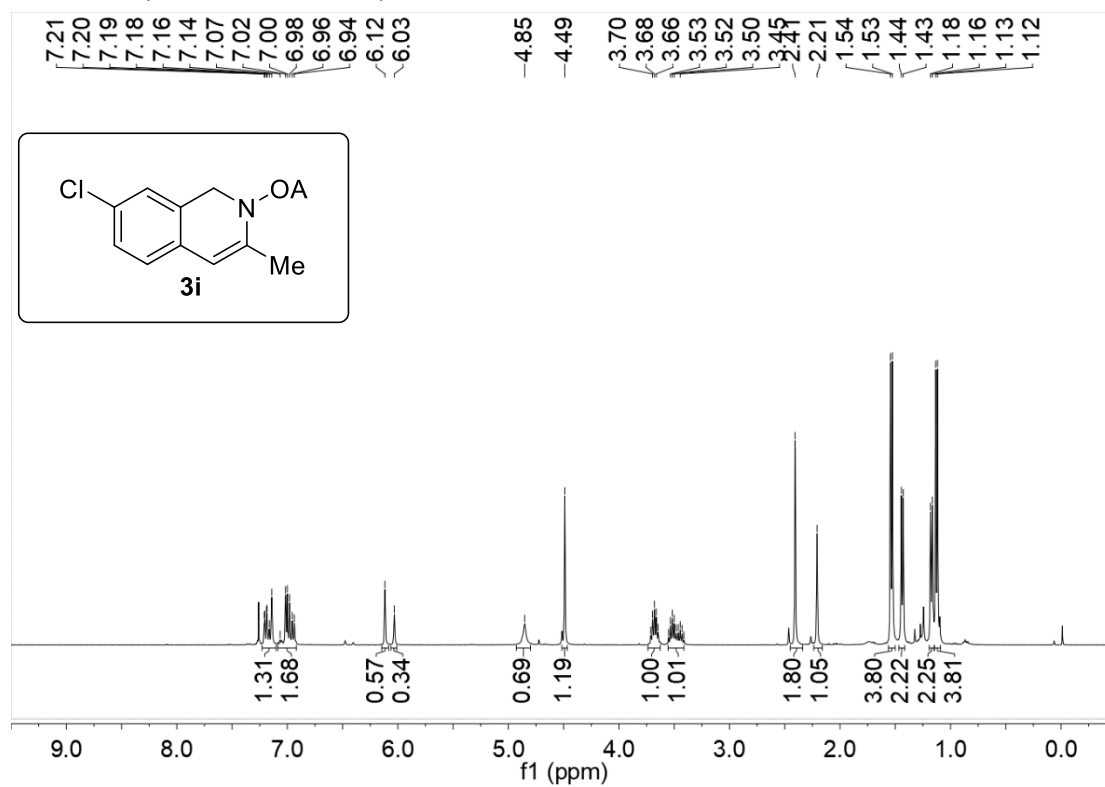
^1H NMR (400 MHz, CDCl_3) of 3h



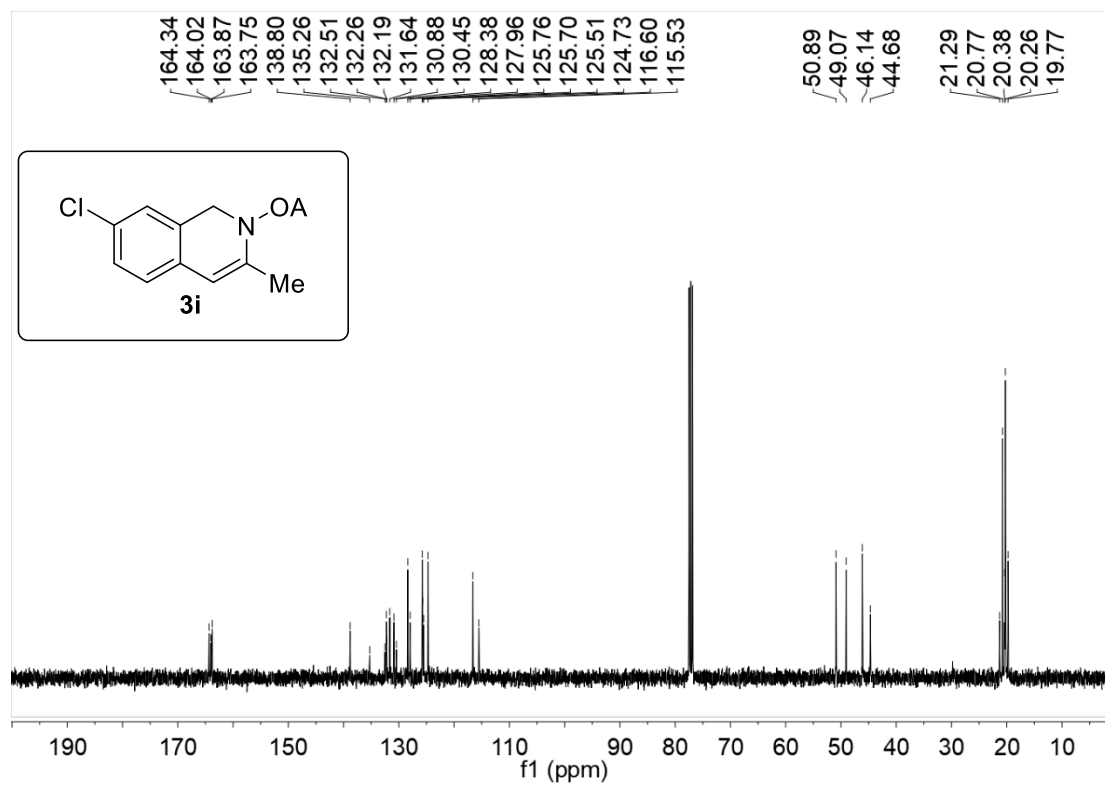
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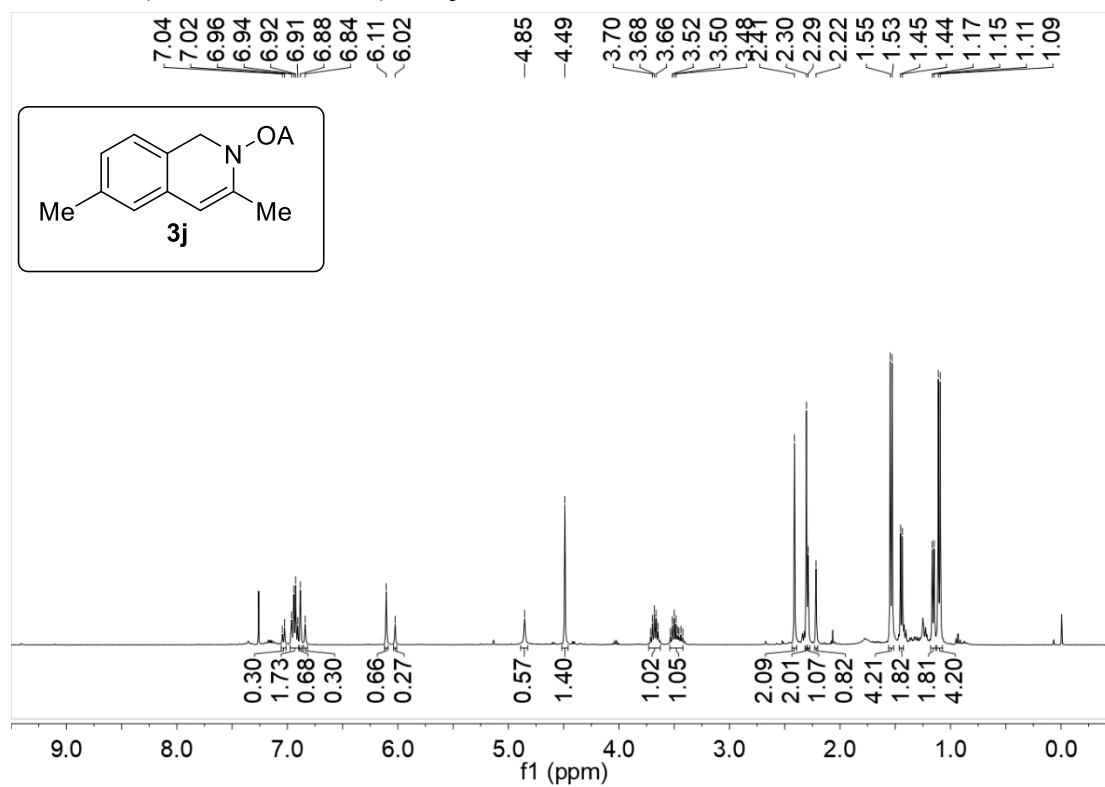
^1H NMR (400 MHz, CDCl_3) of **3i**



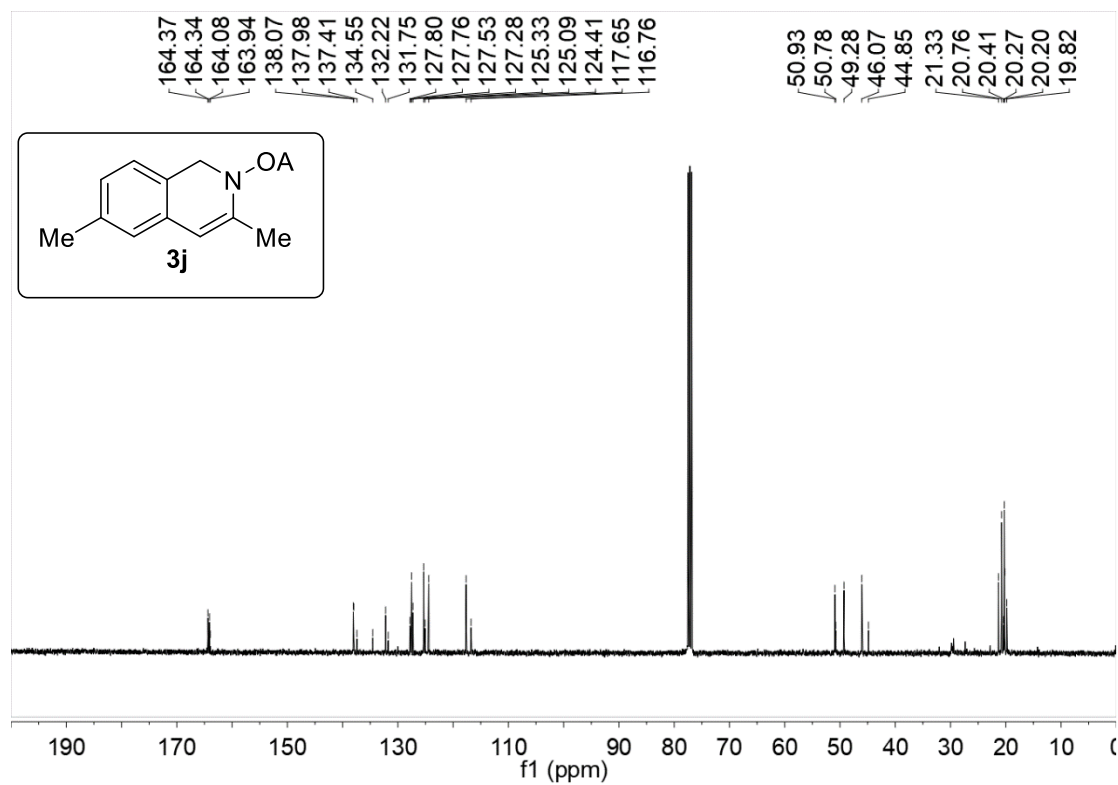
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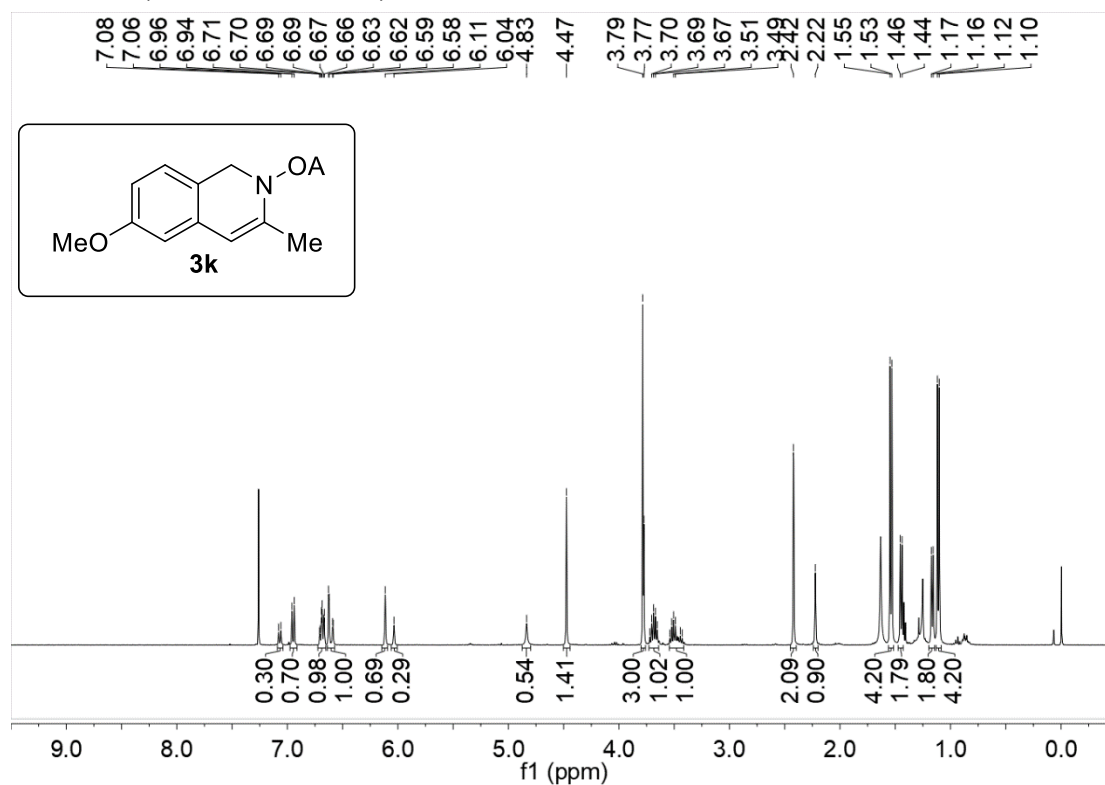
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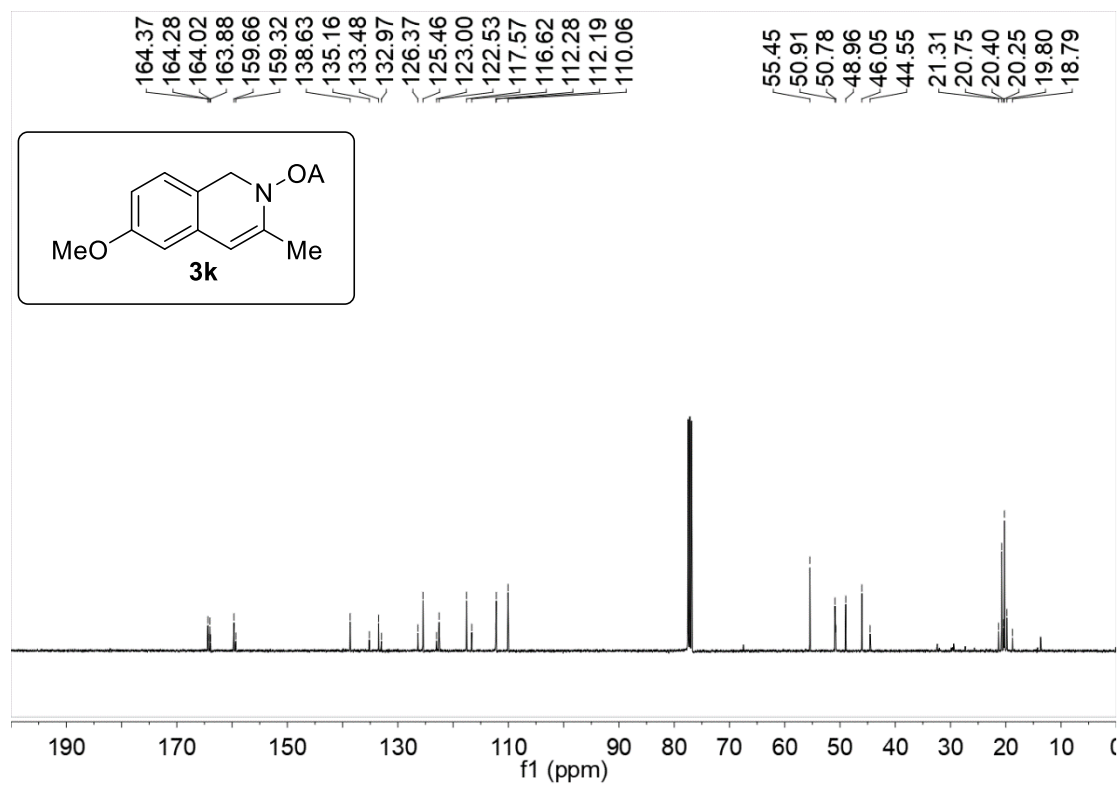
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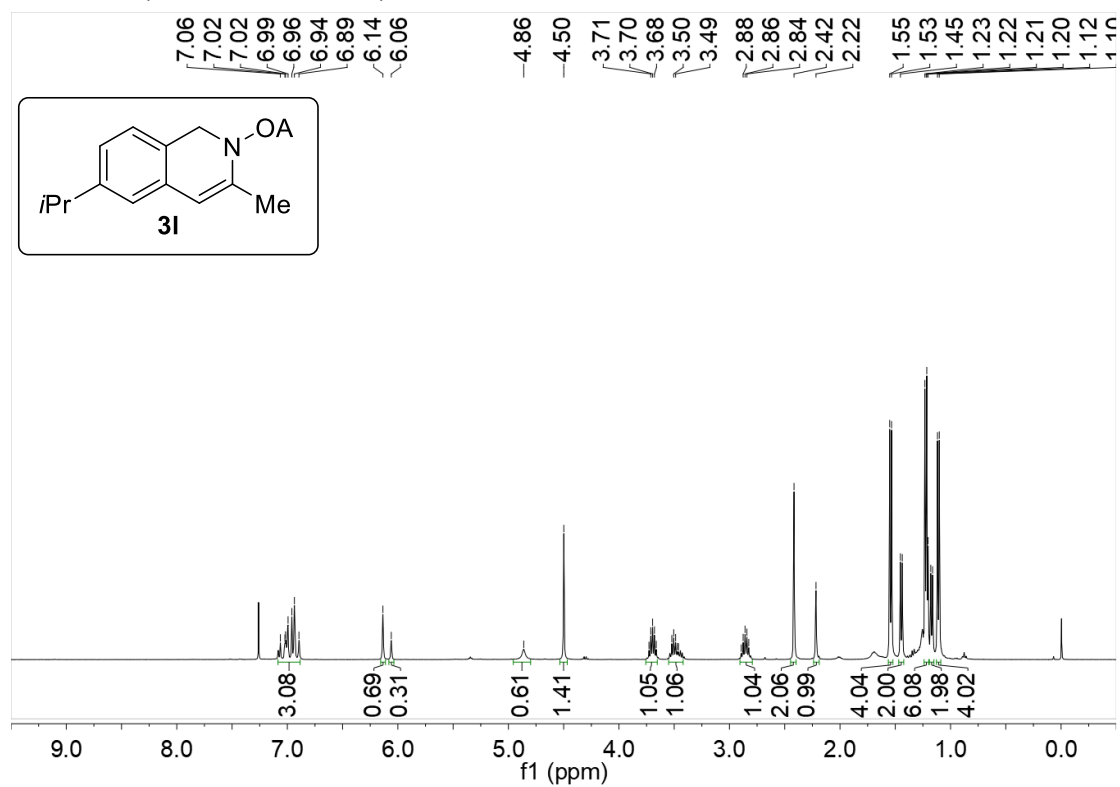
^1H NMR (400 MHz, CDCl_3) of 3k



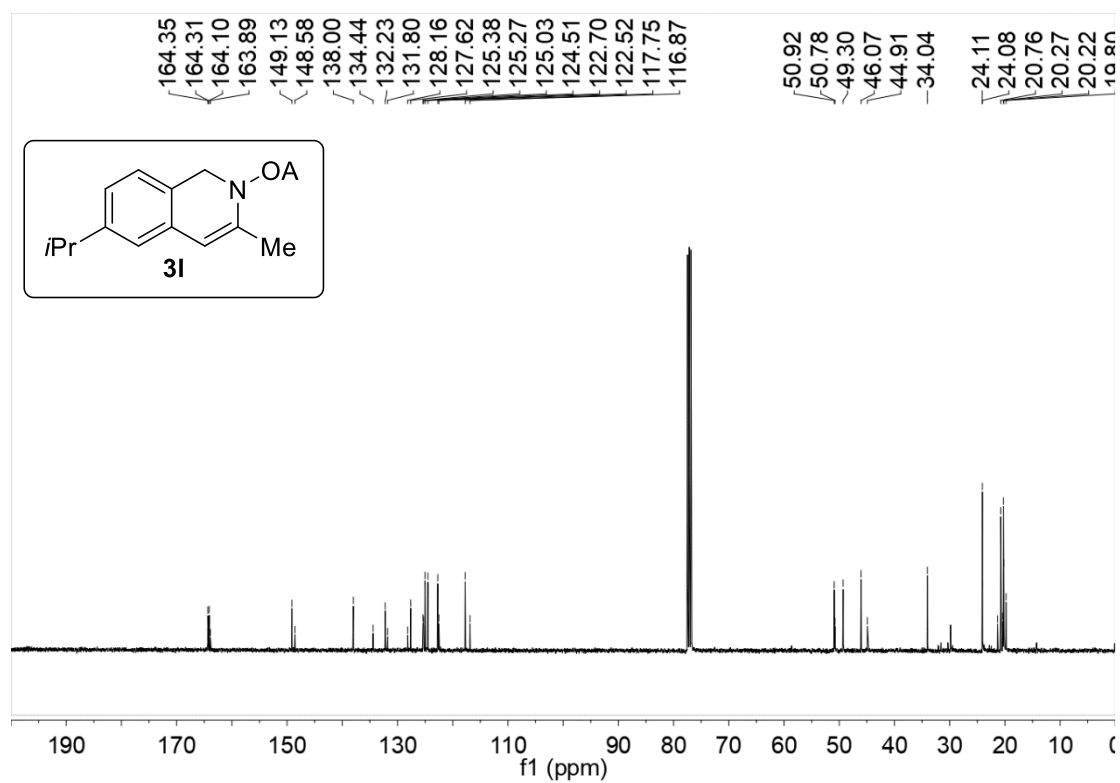
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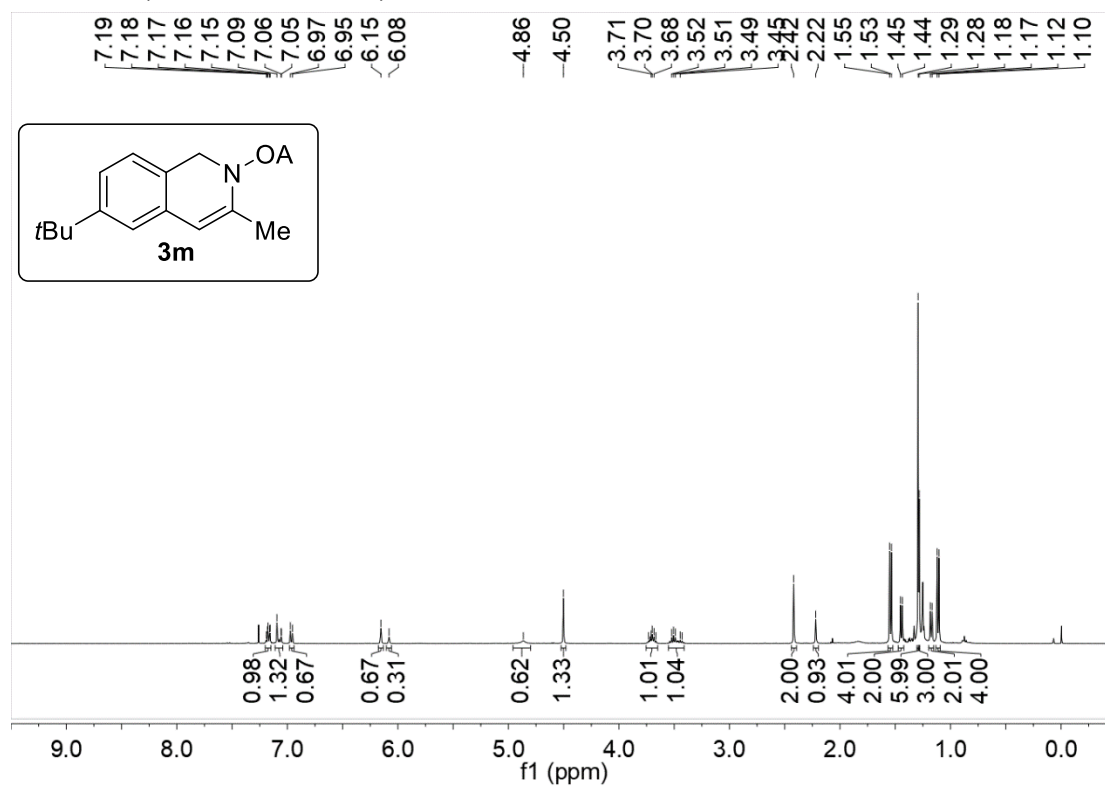
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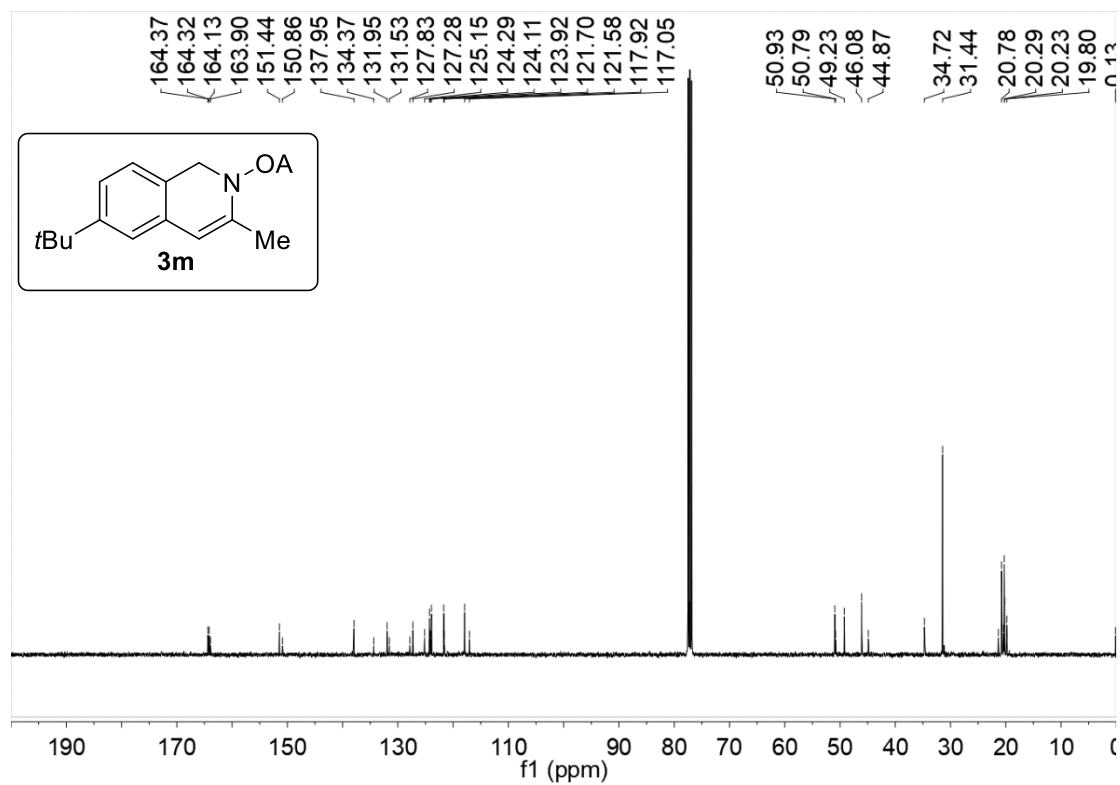
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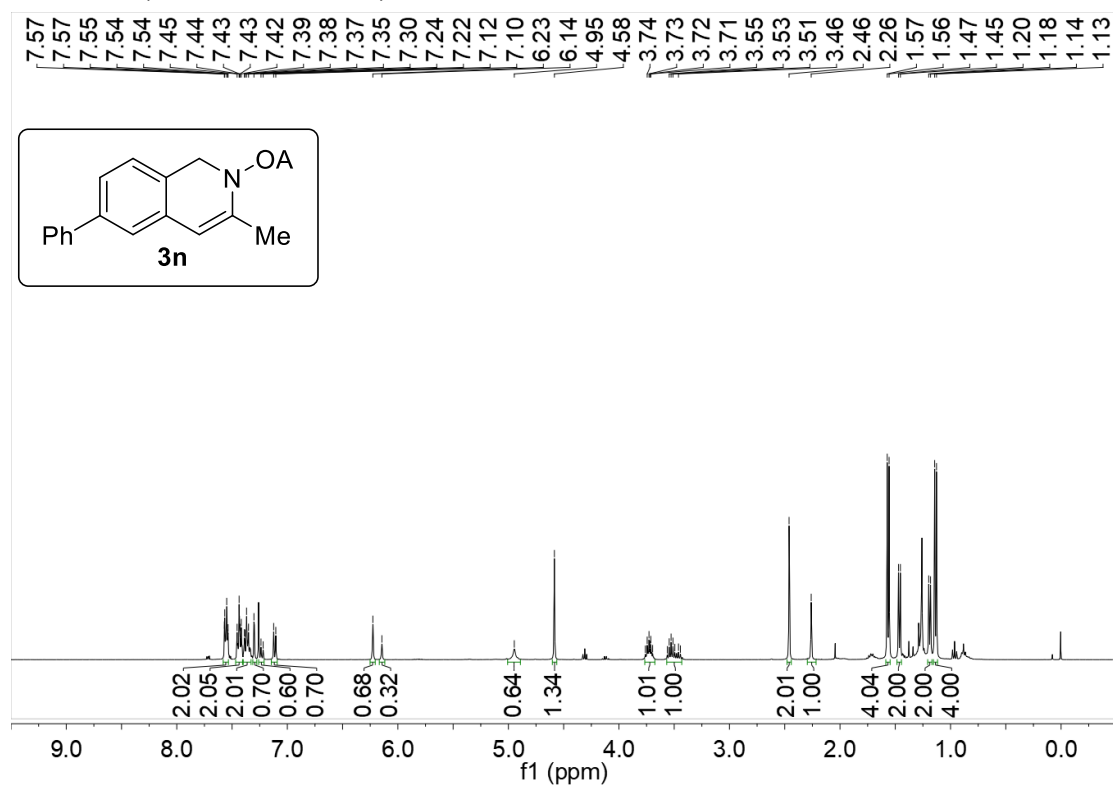
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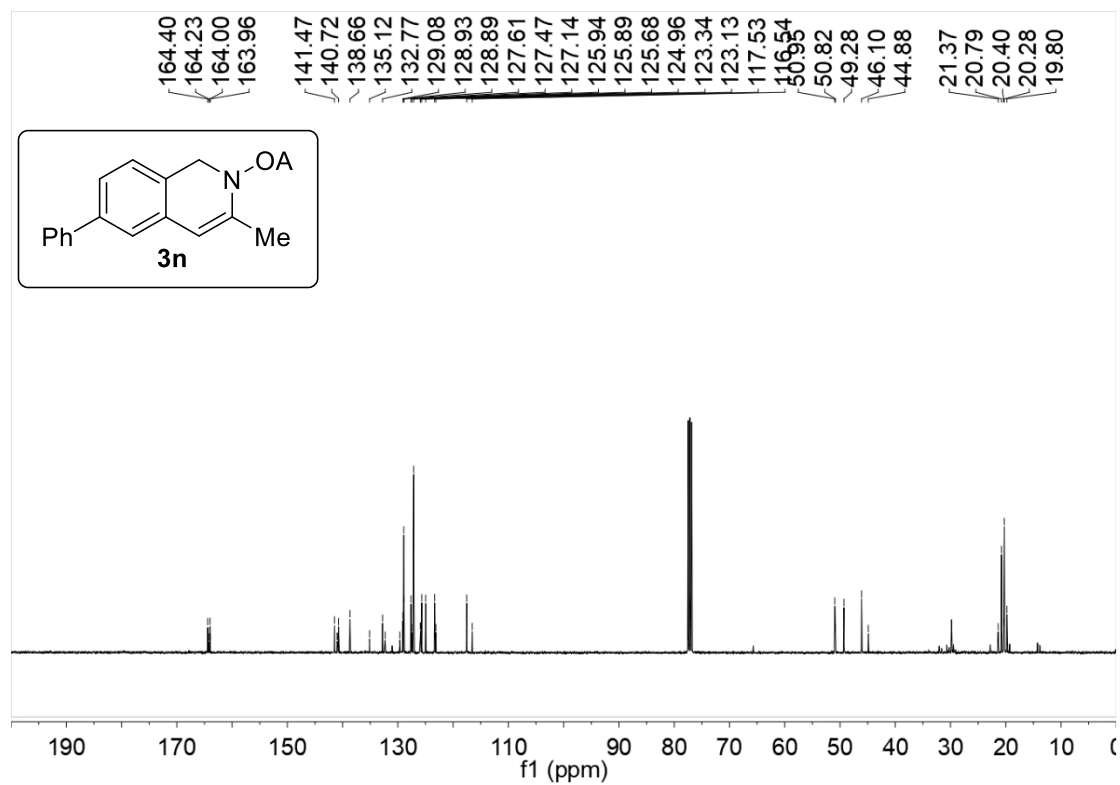
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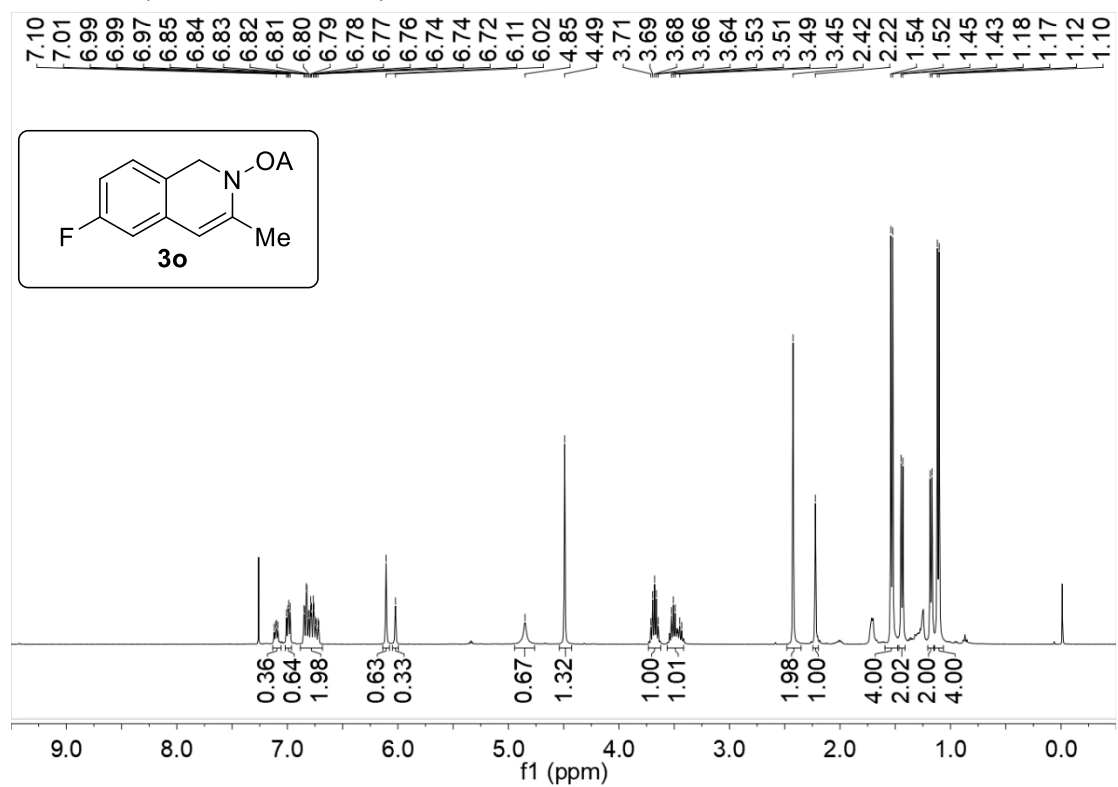
^1H NMR (400 MHz, CDCl_3) of 3n



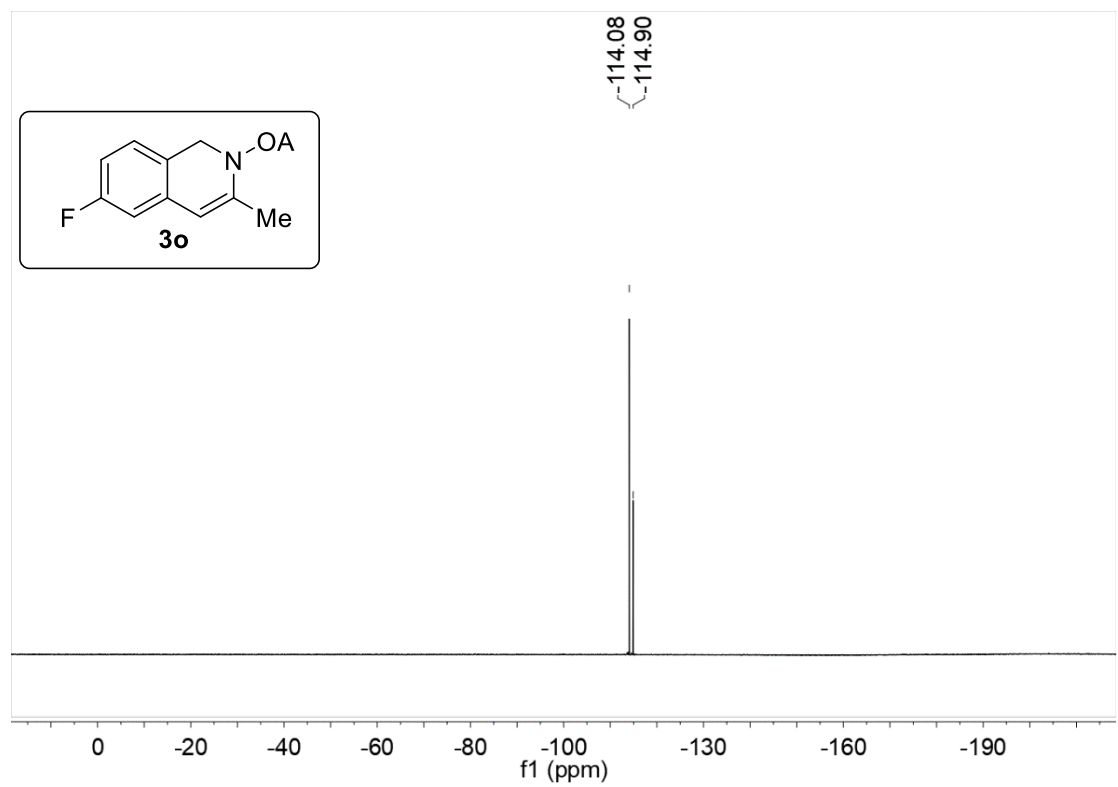
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 3n



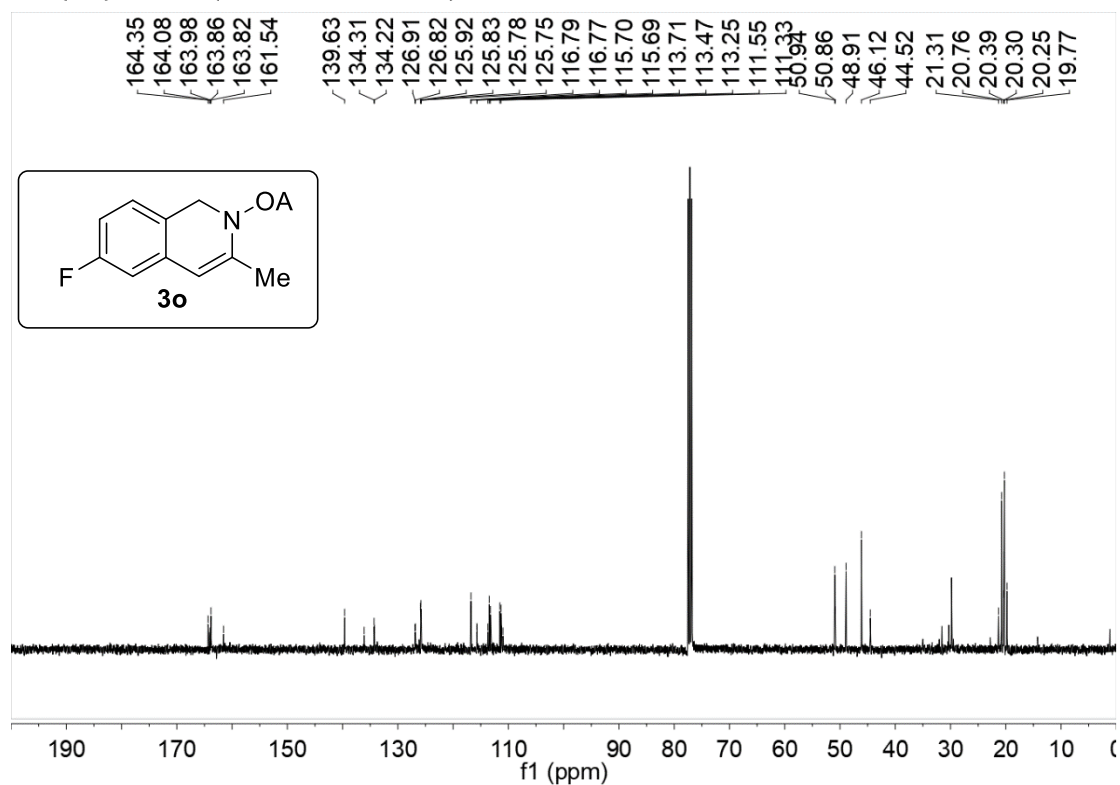
¹H NMR (400 MHz, CDCl₃) of 3o



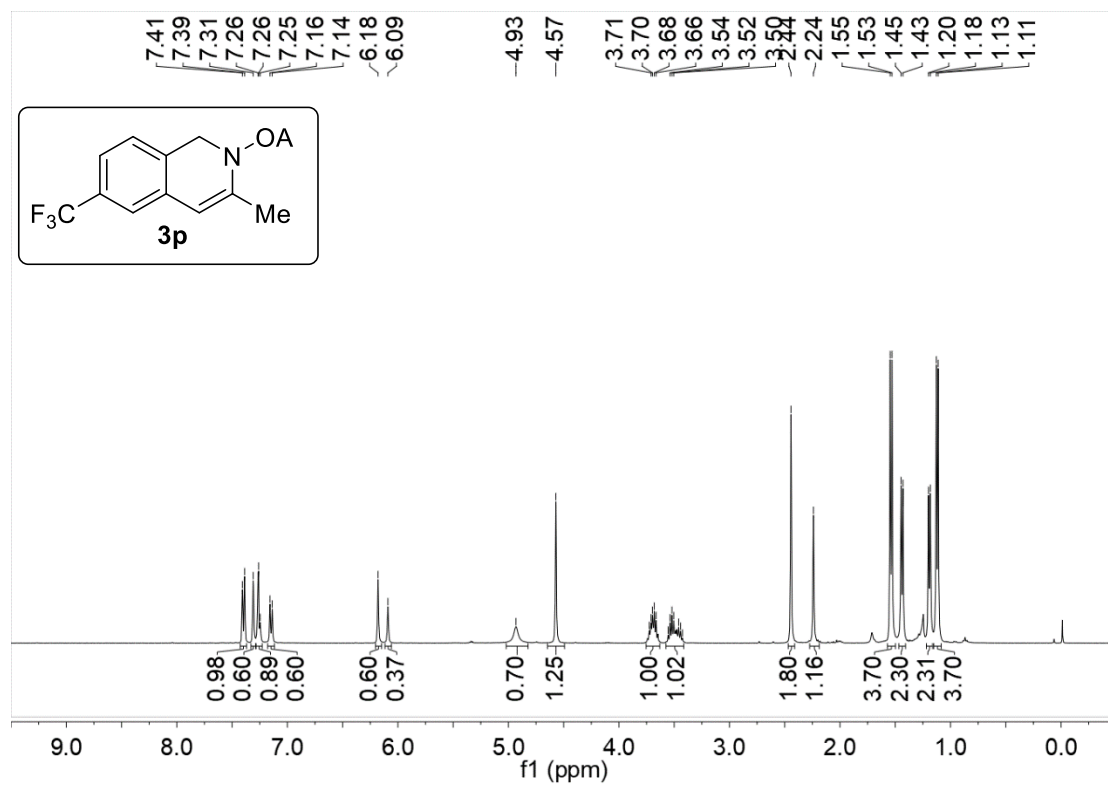
¹⁹F NMR (376 MHz, CDCl₃) of 3o



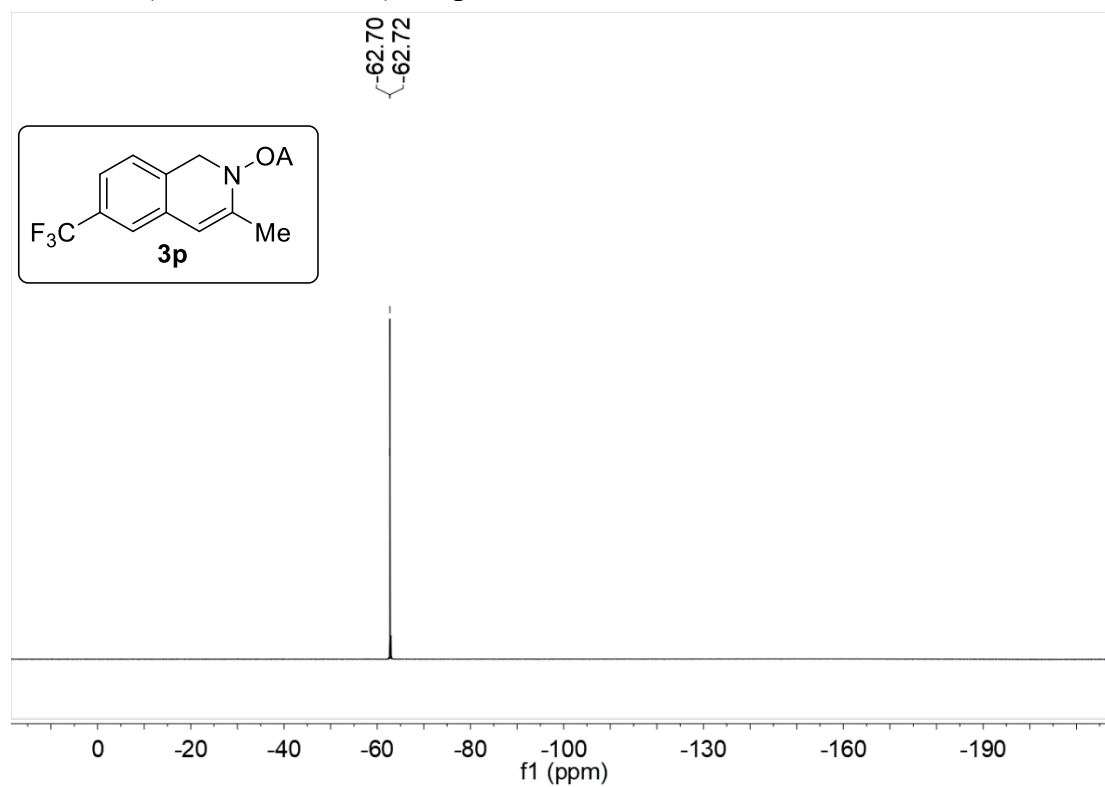
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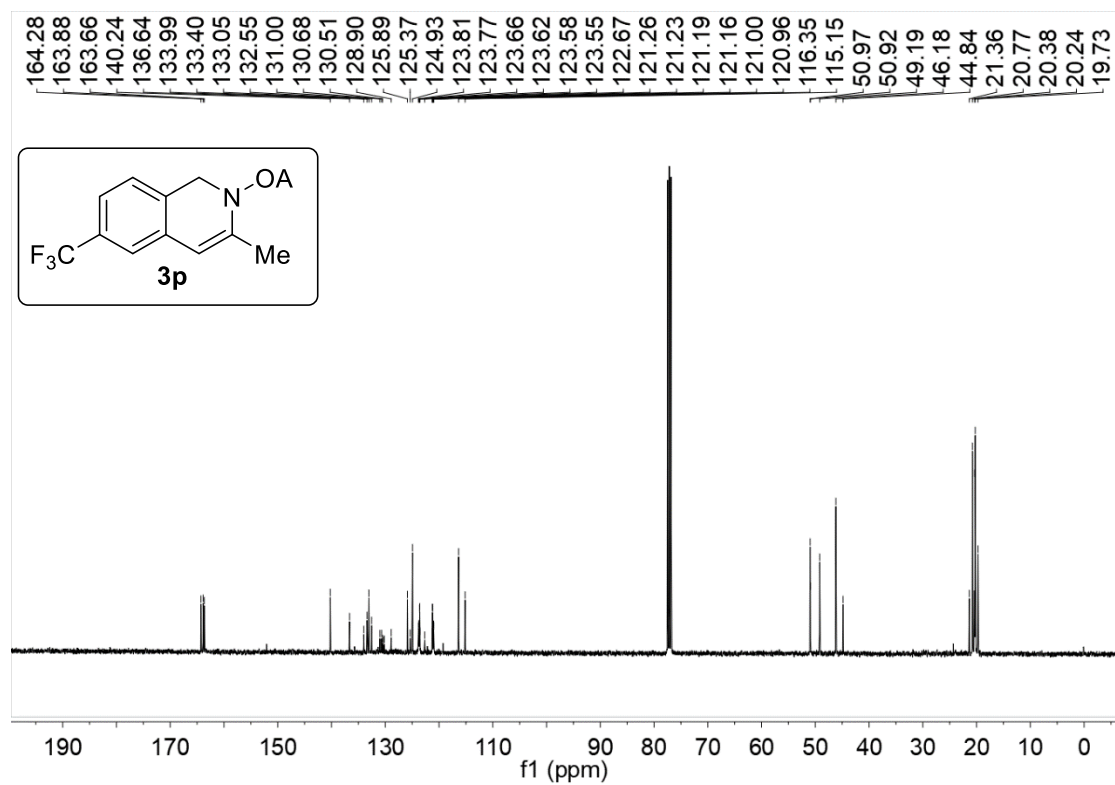
^1H NMR (400 MHz, CDCl_3) of **3p**



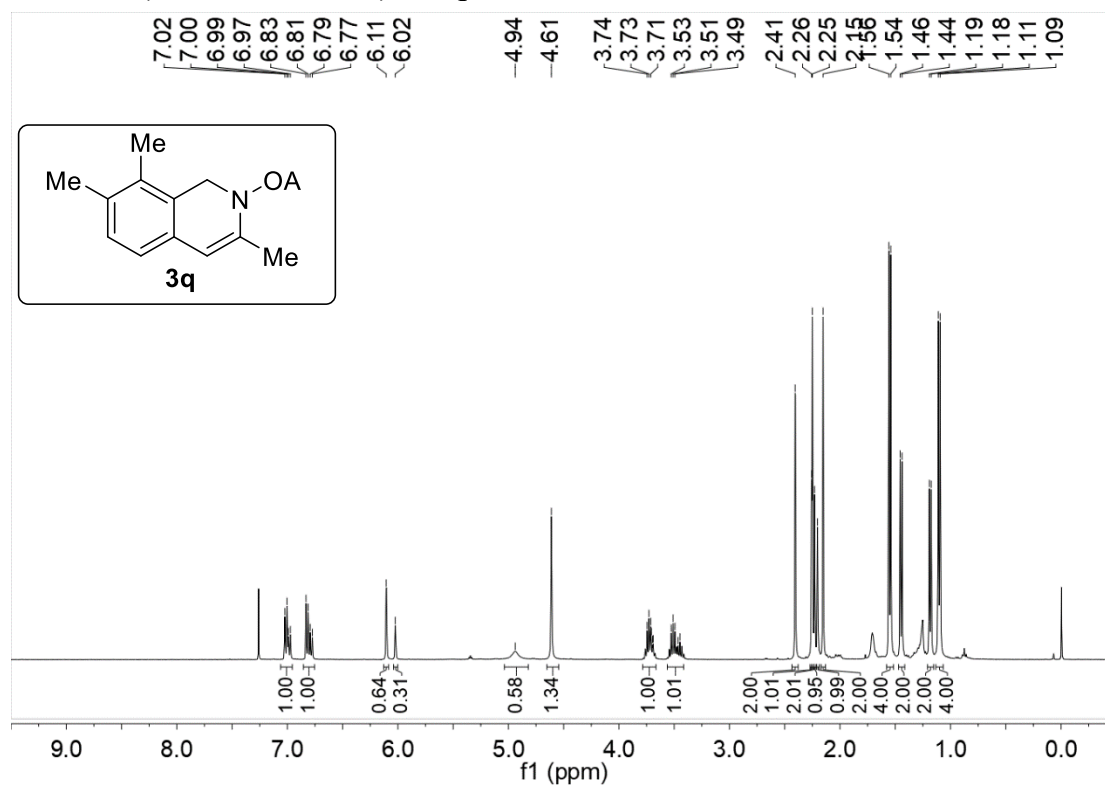
^{19}F NMR (376 MHz, CDCl_3) of 3p



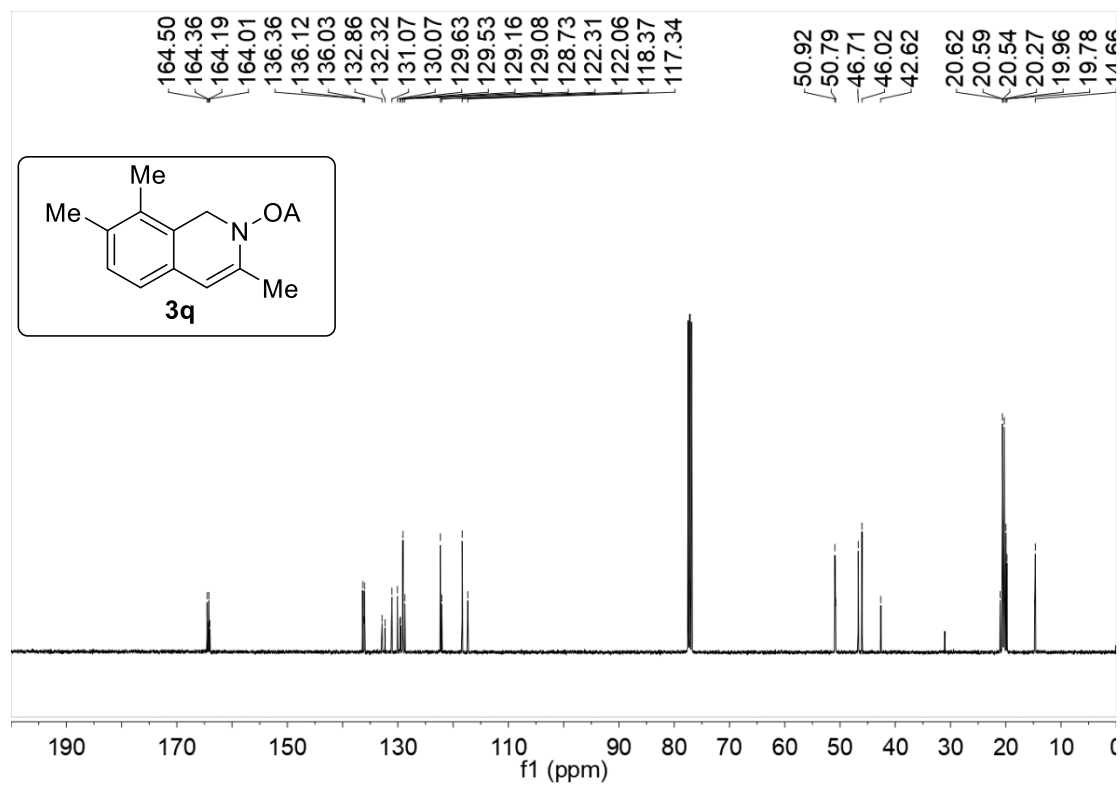
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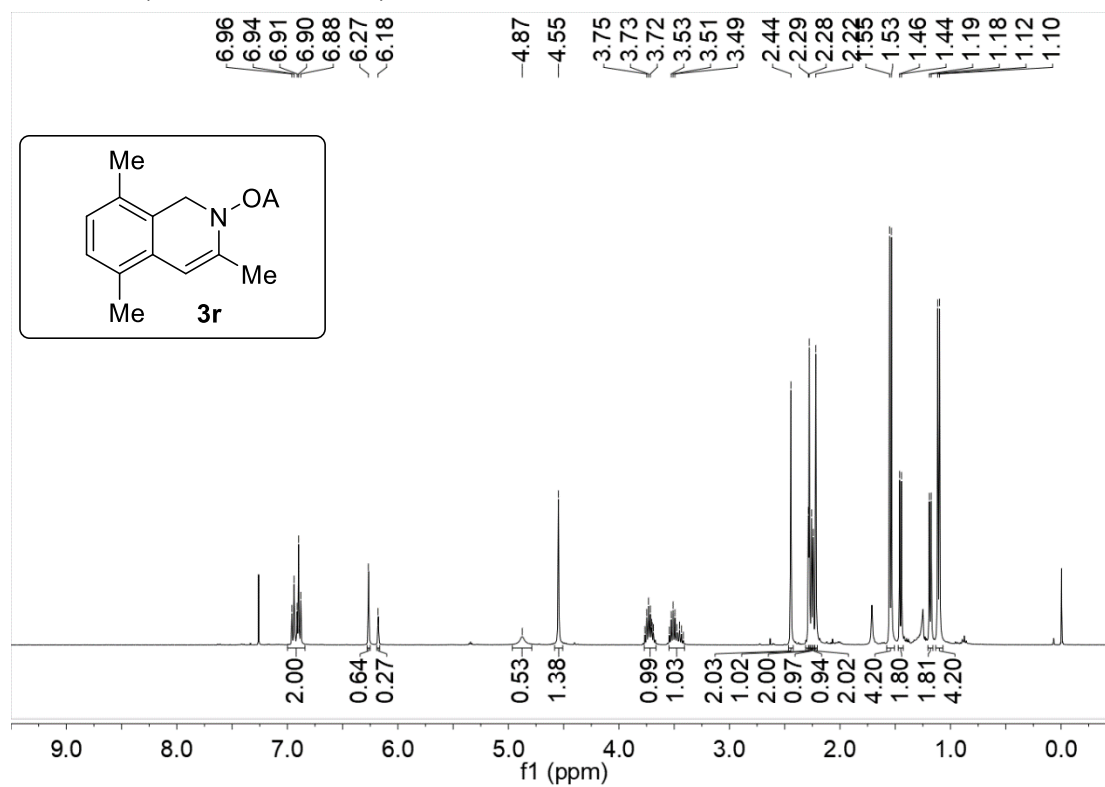
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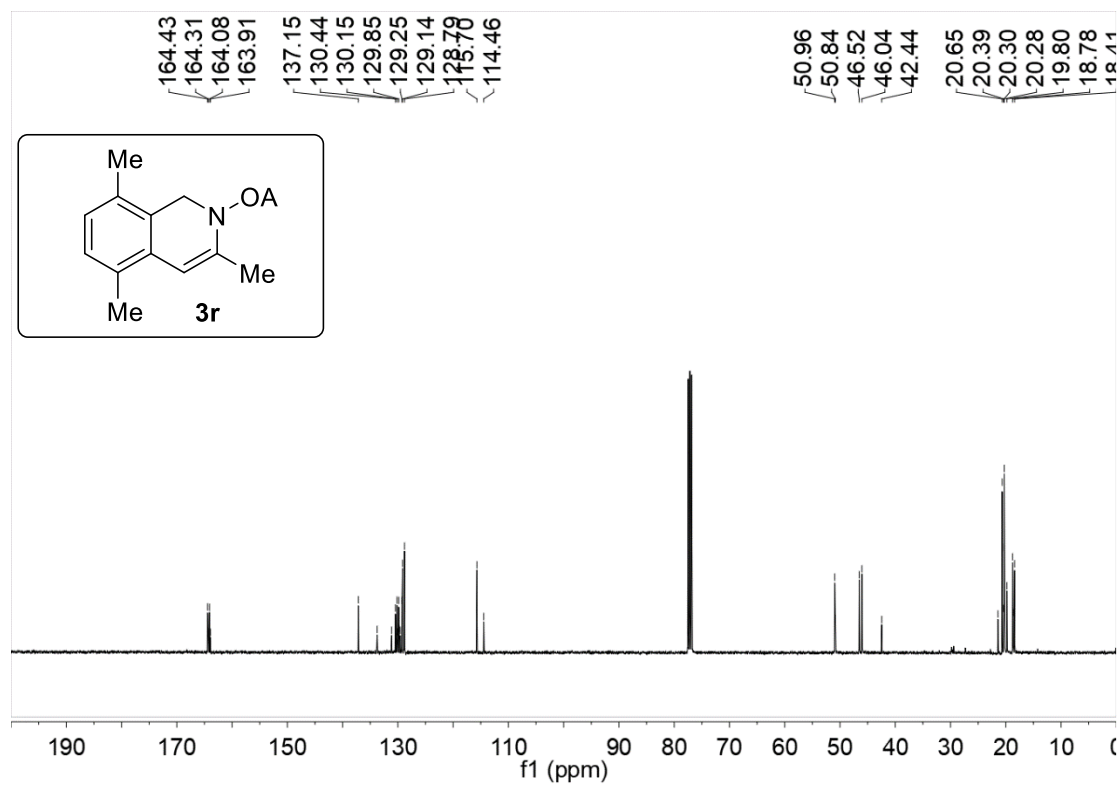
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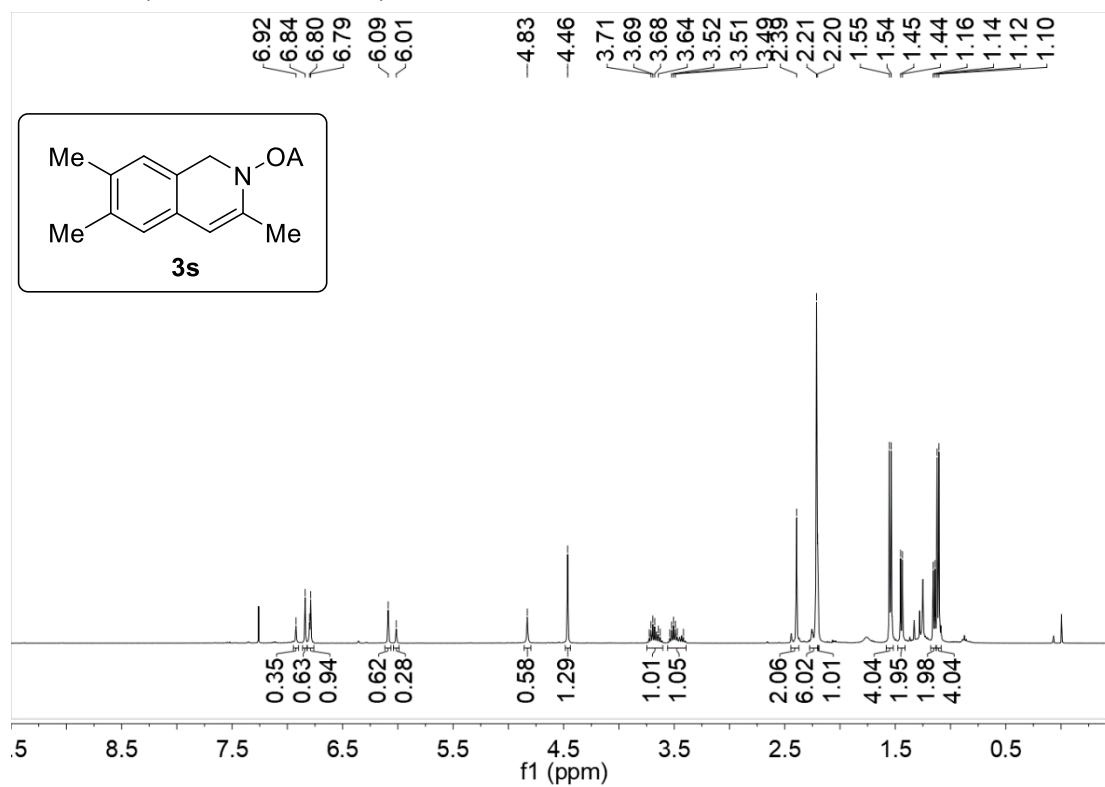
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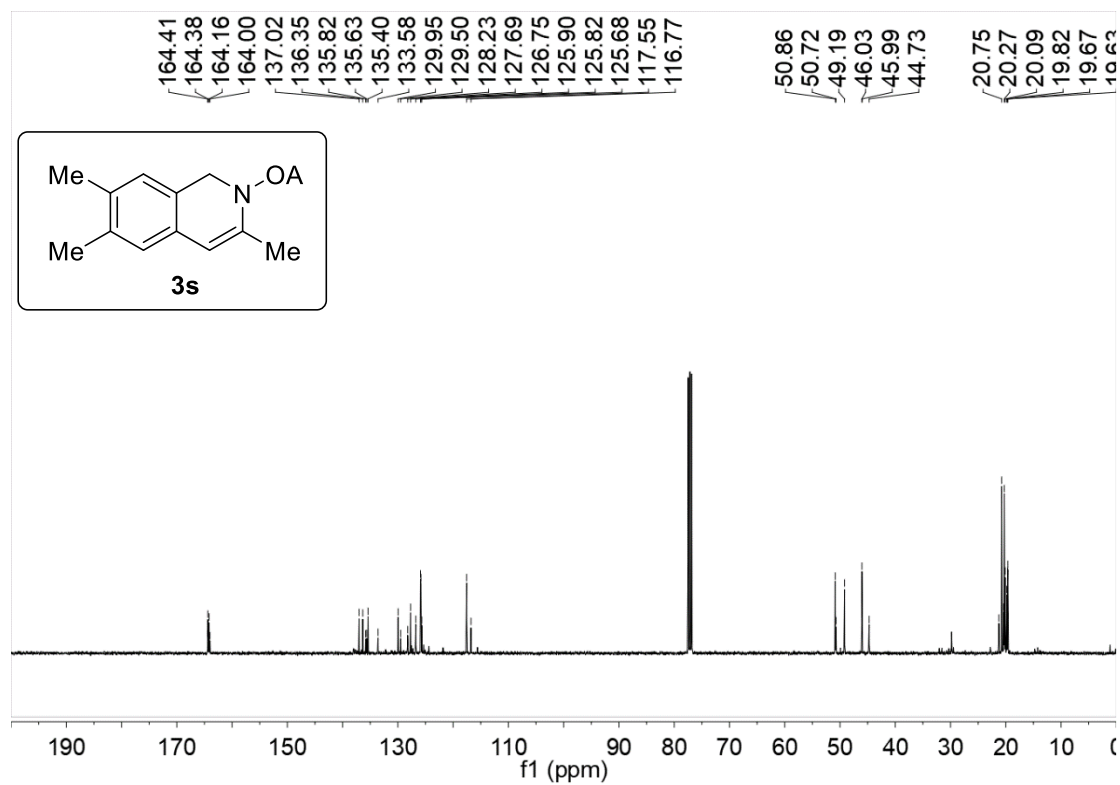
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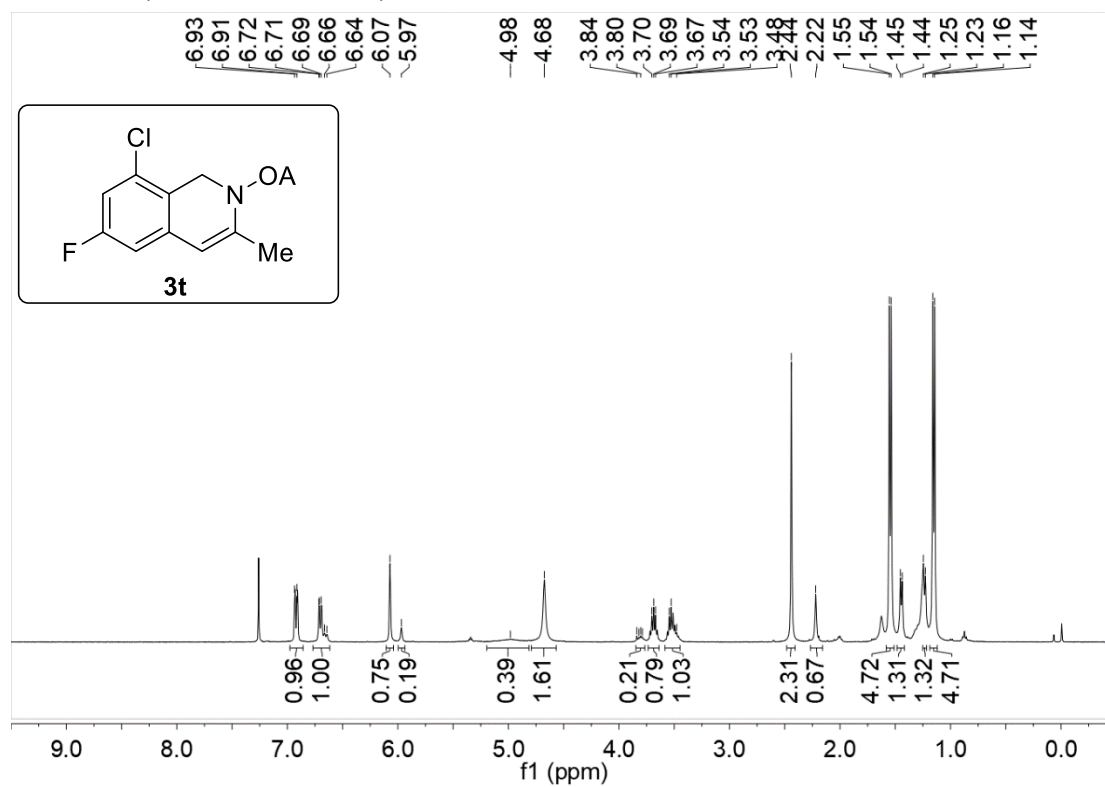
^1H NMR (400 MHz, CDCl_3) of **3s**



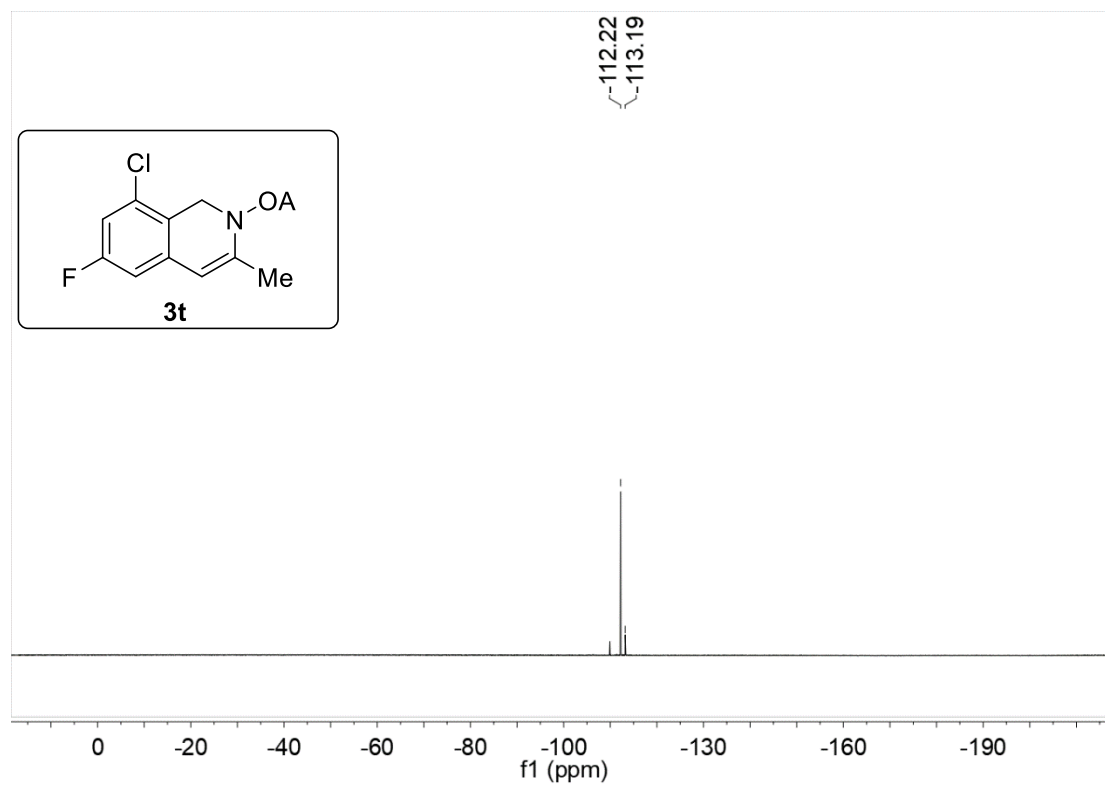
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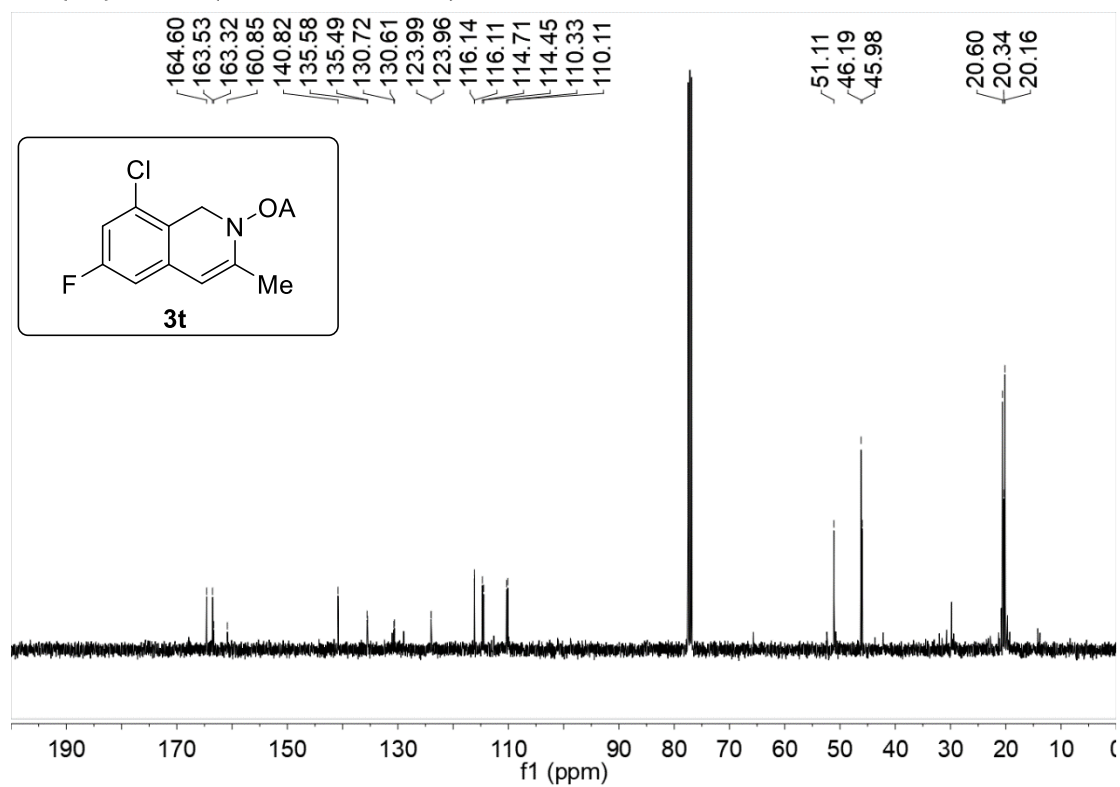
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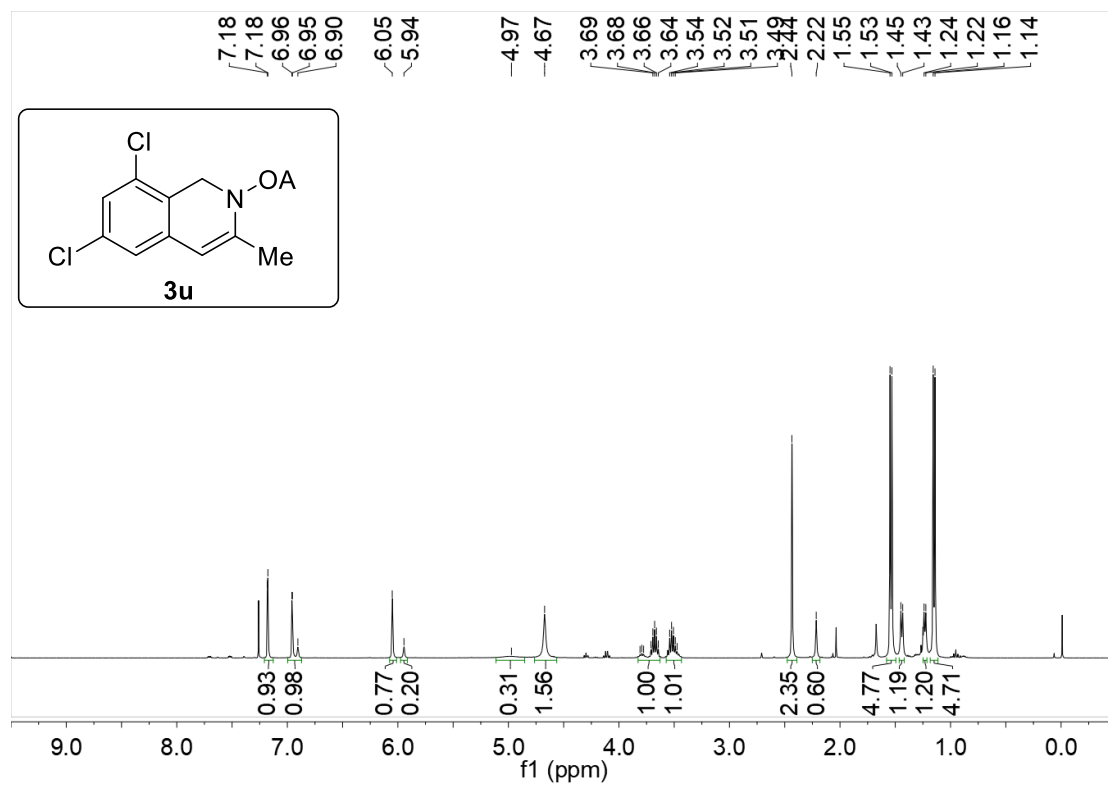
¹⁹F NMR (376 MHz, CDCl₃) of 3t



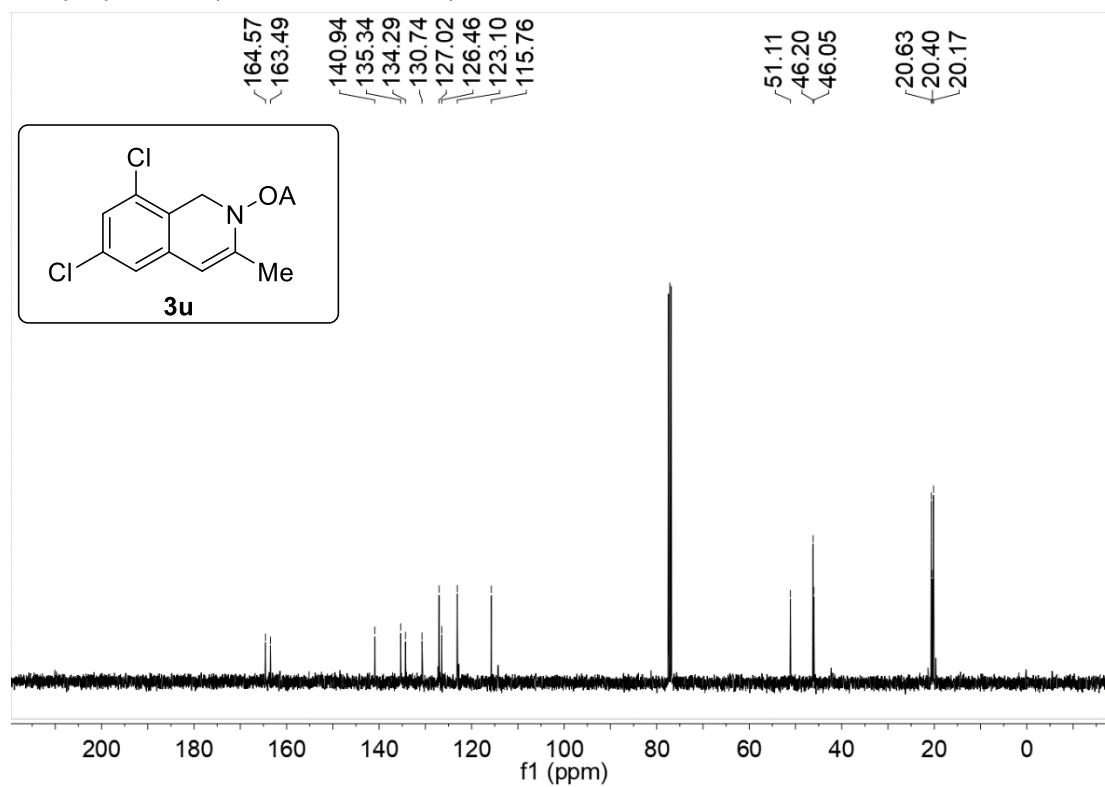
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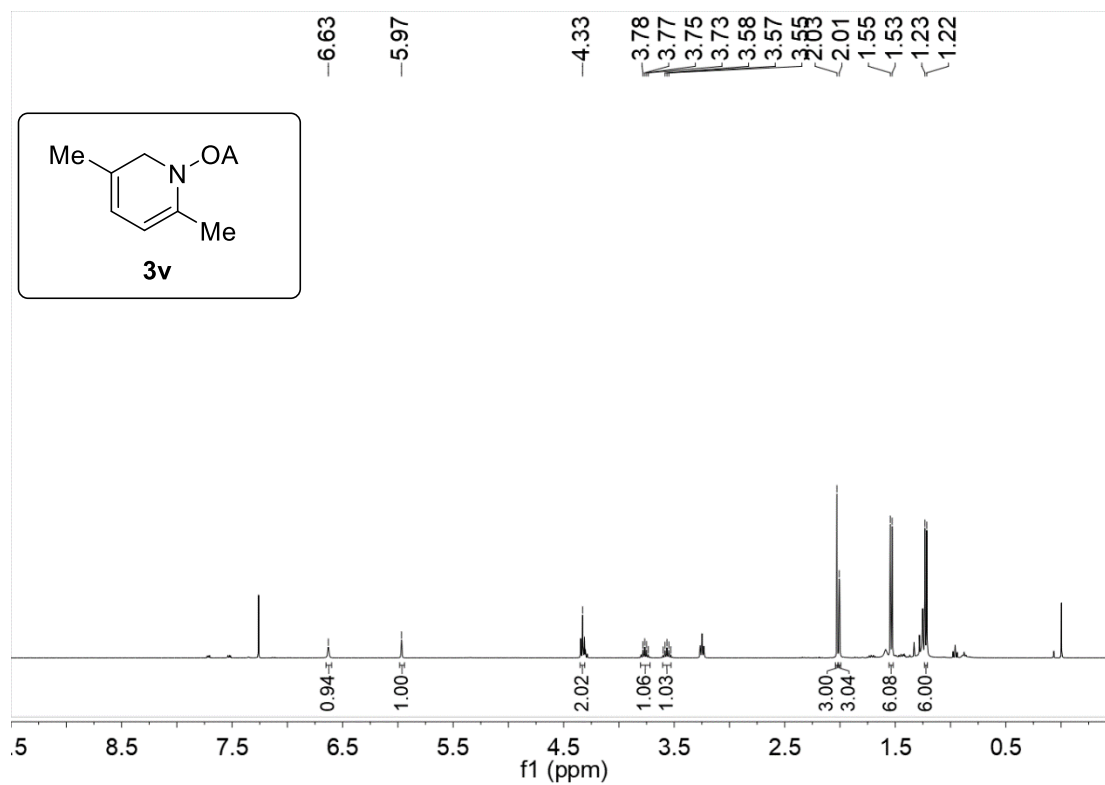
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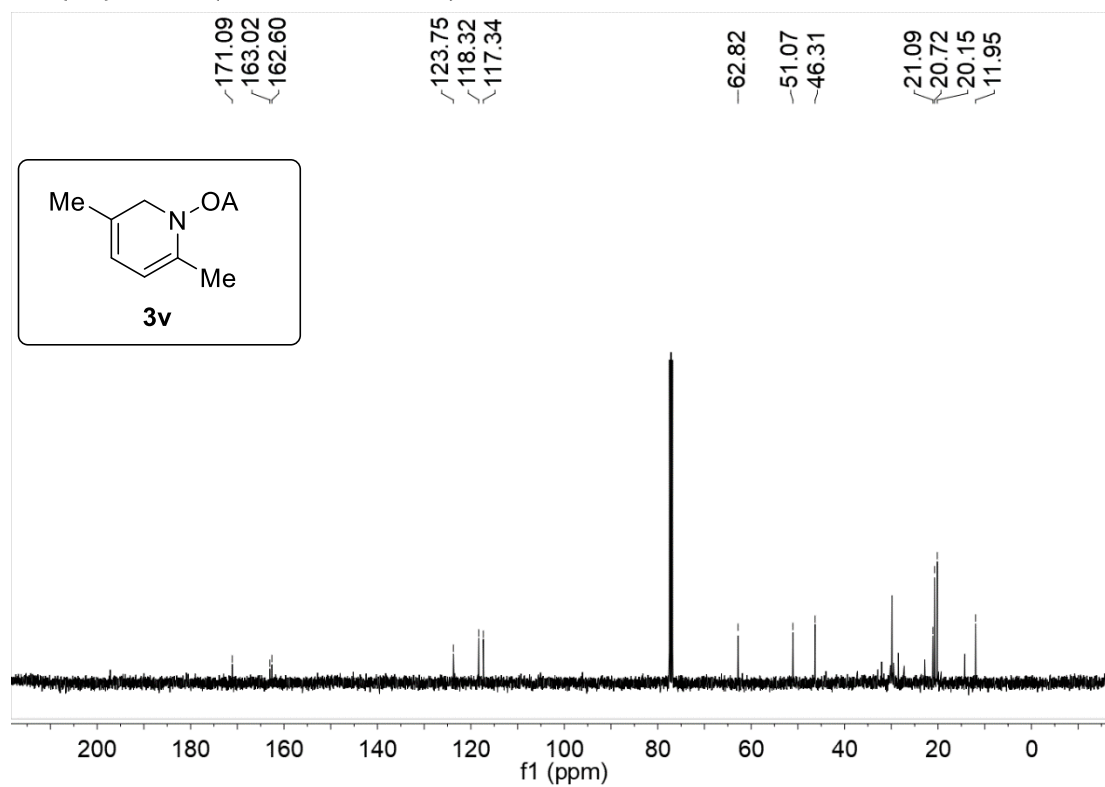
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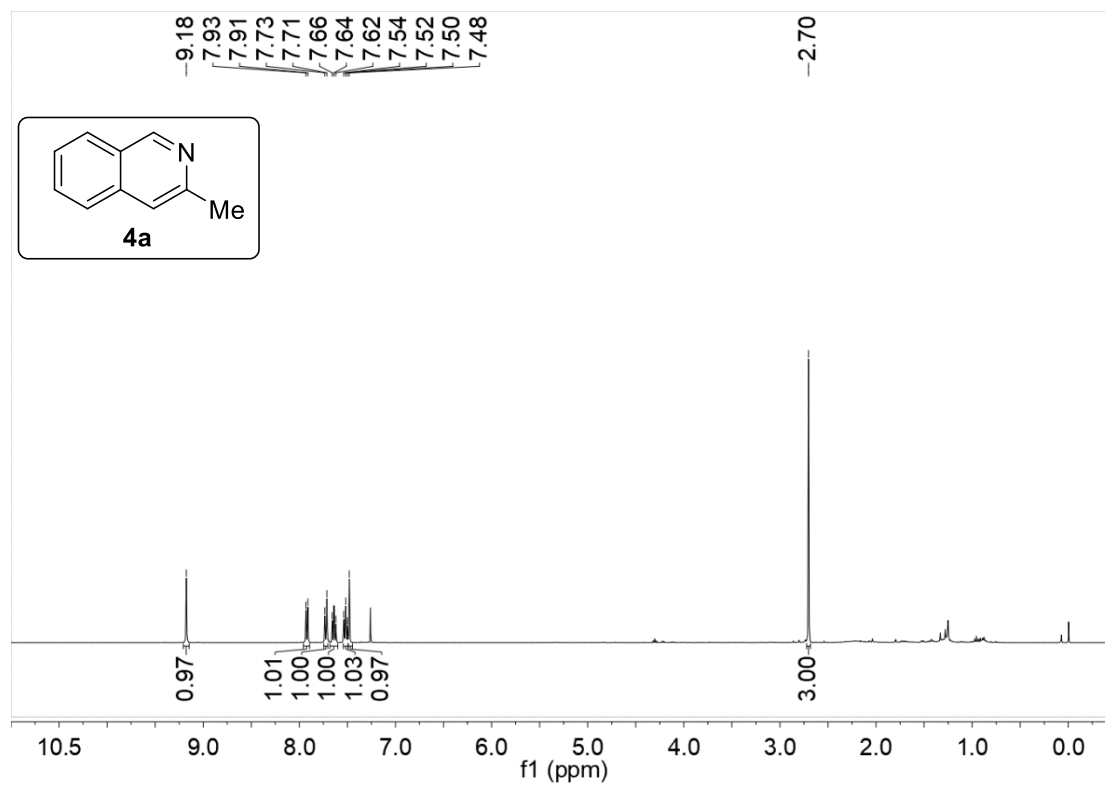
^1H NMR (400 MHz, CDCl_3) of **3v**



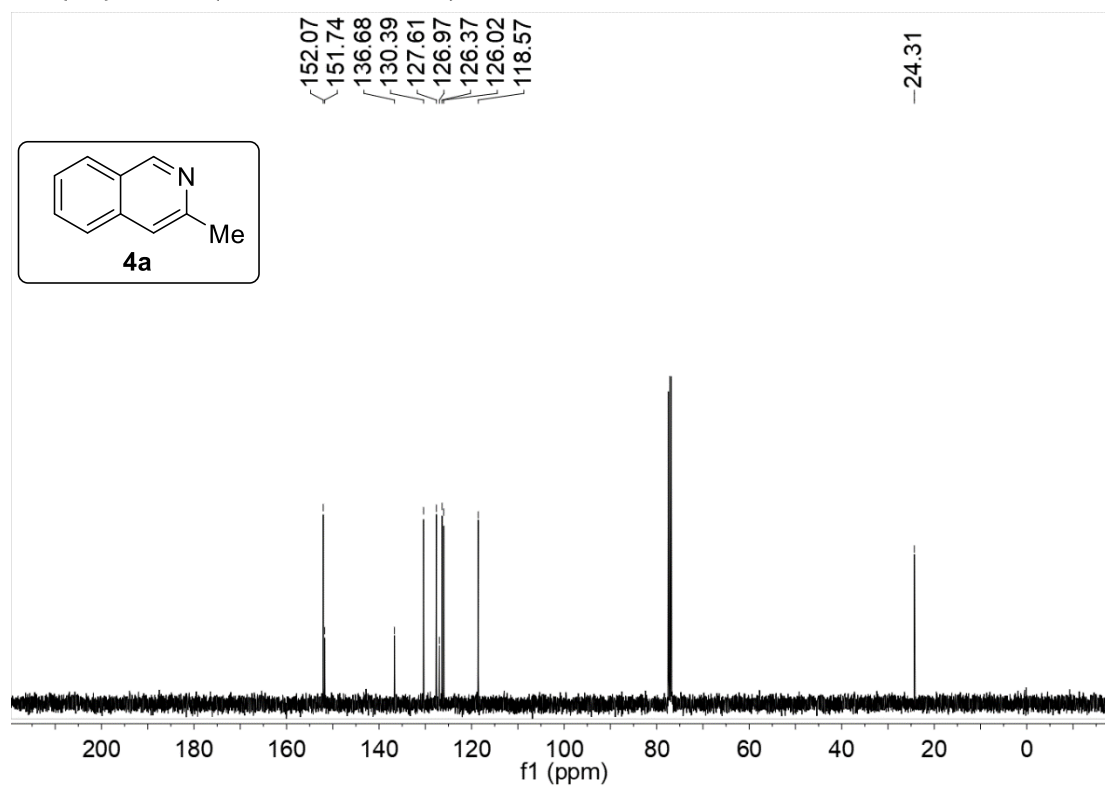
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 3v



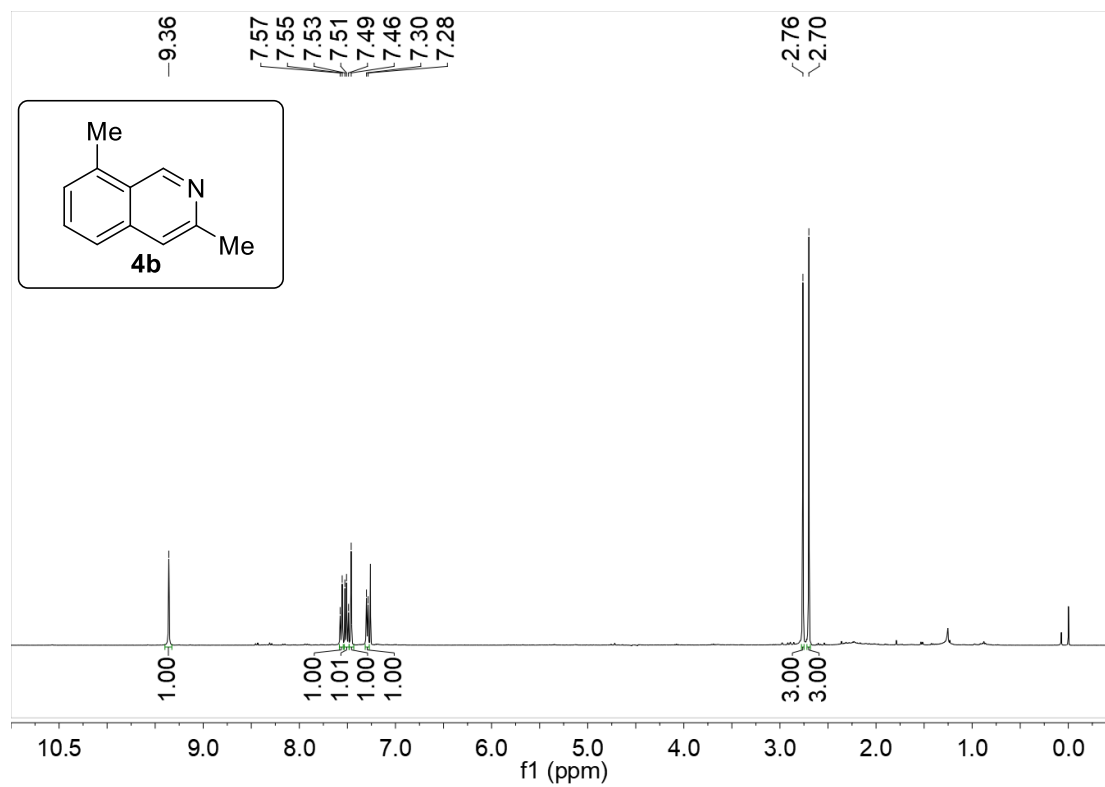
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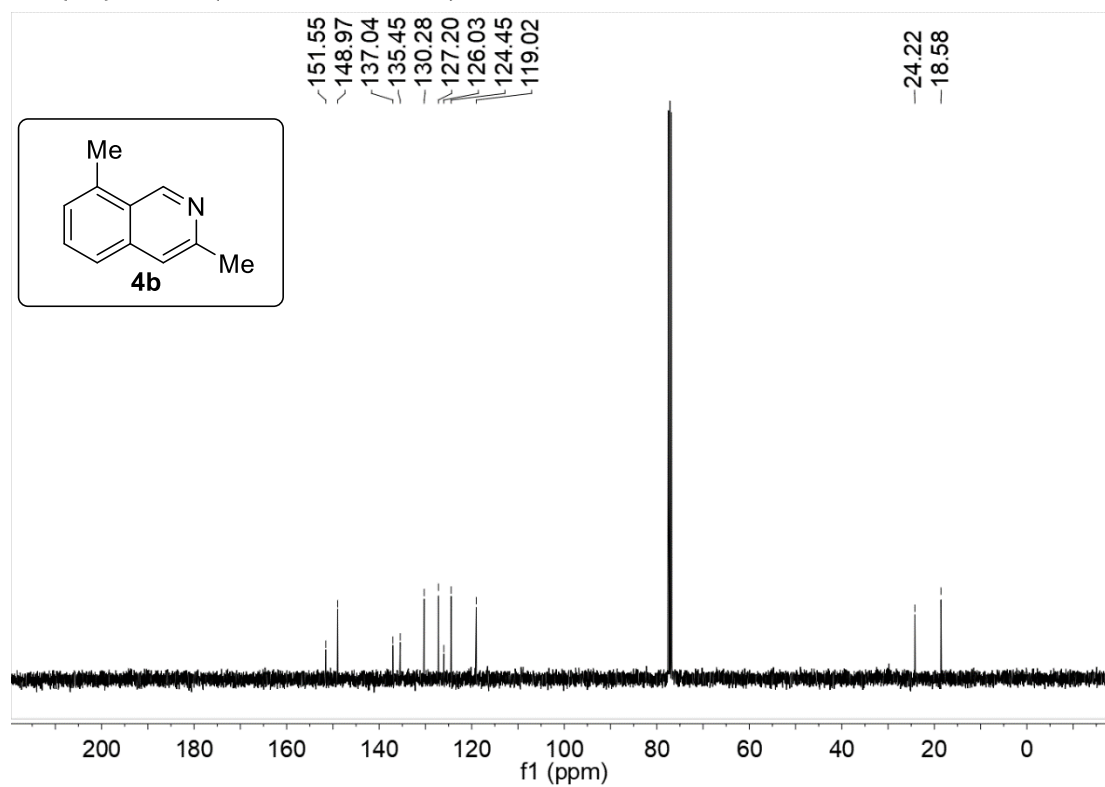
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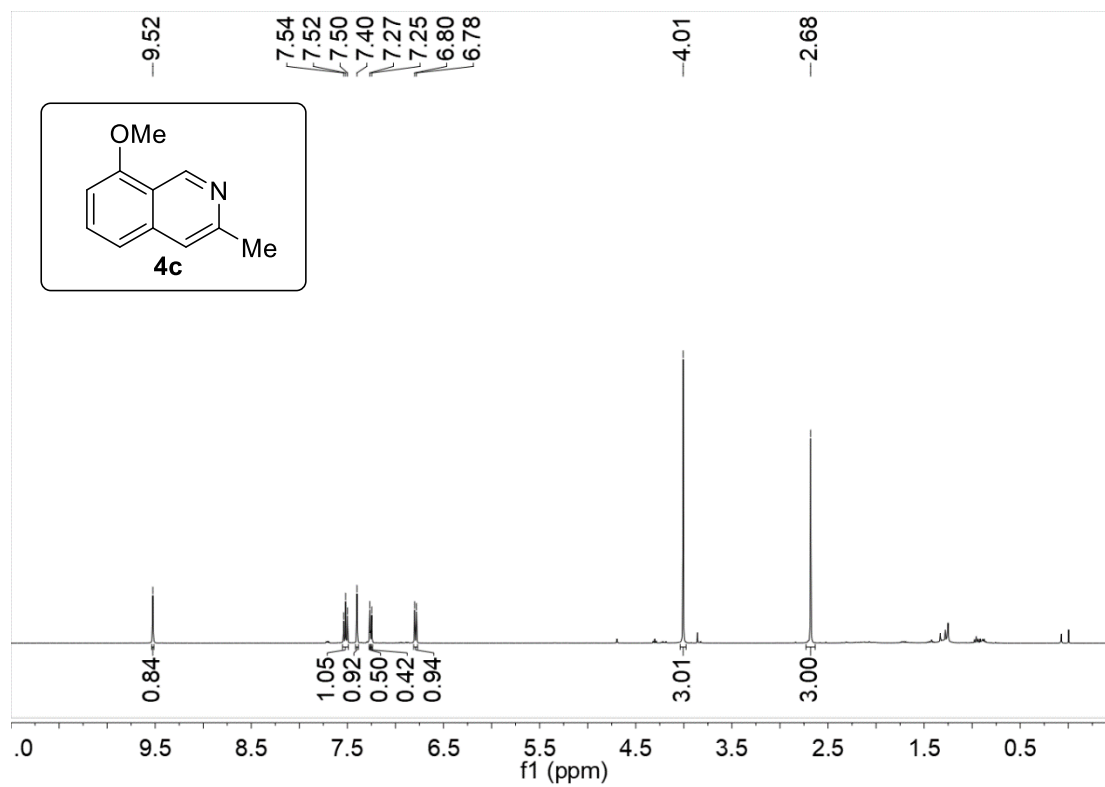
^1H NMR (400 MHz, CDCl_3) of 4b



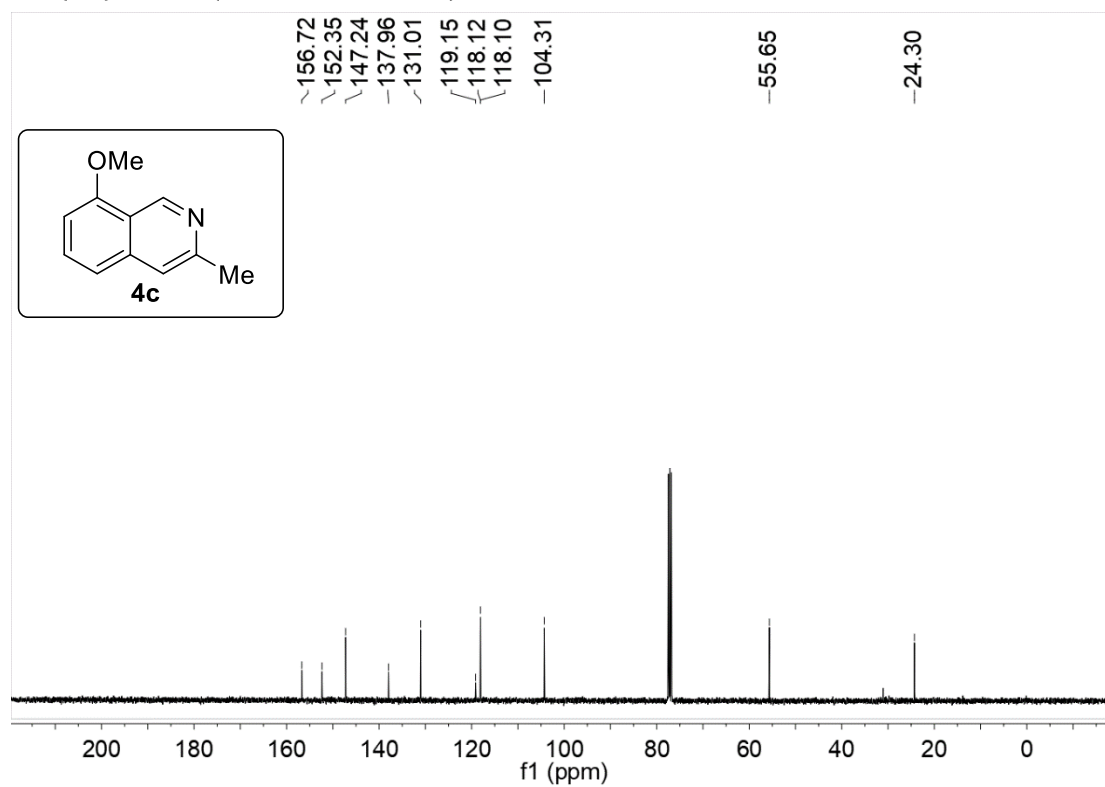
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4b



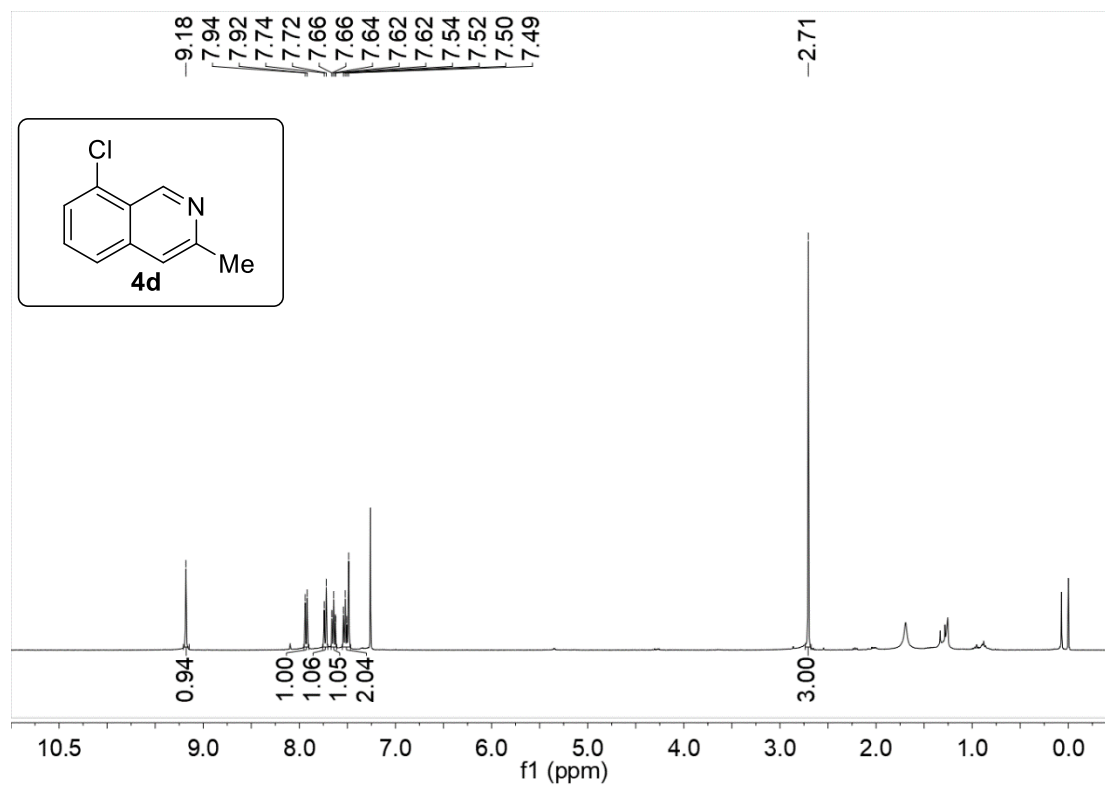
^1H NMR (400 MHz, CDCl_3) of 4c



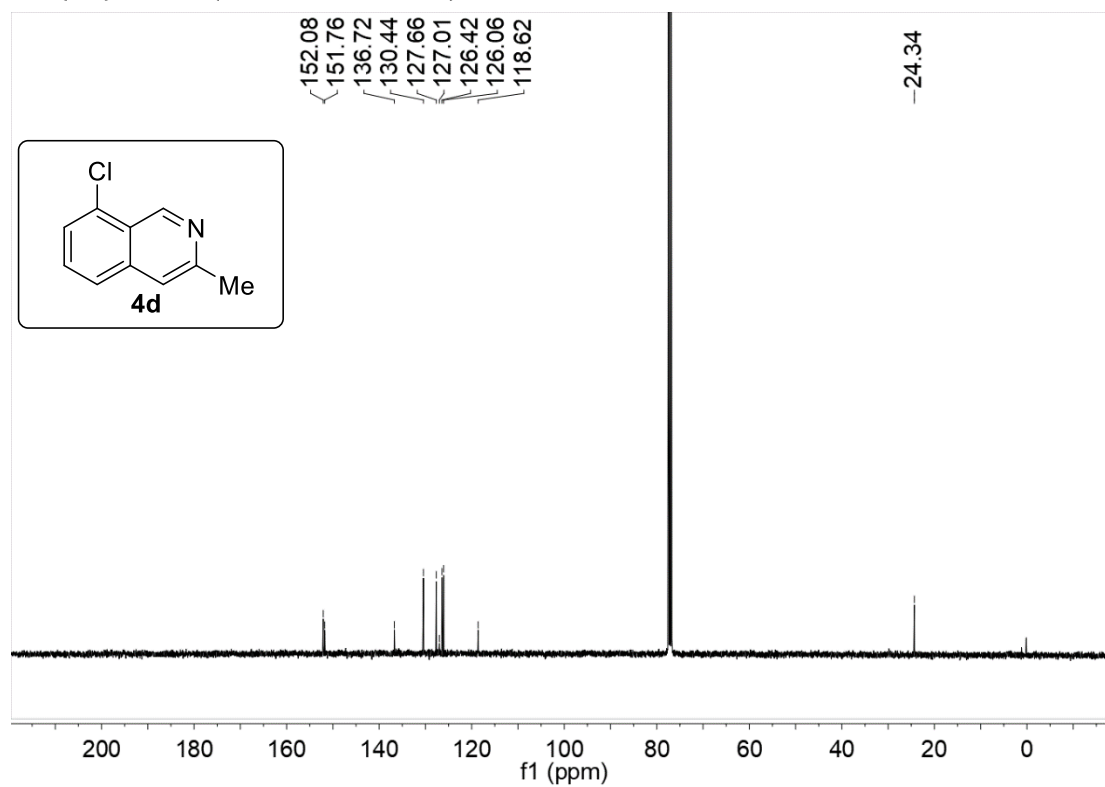
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4c



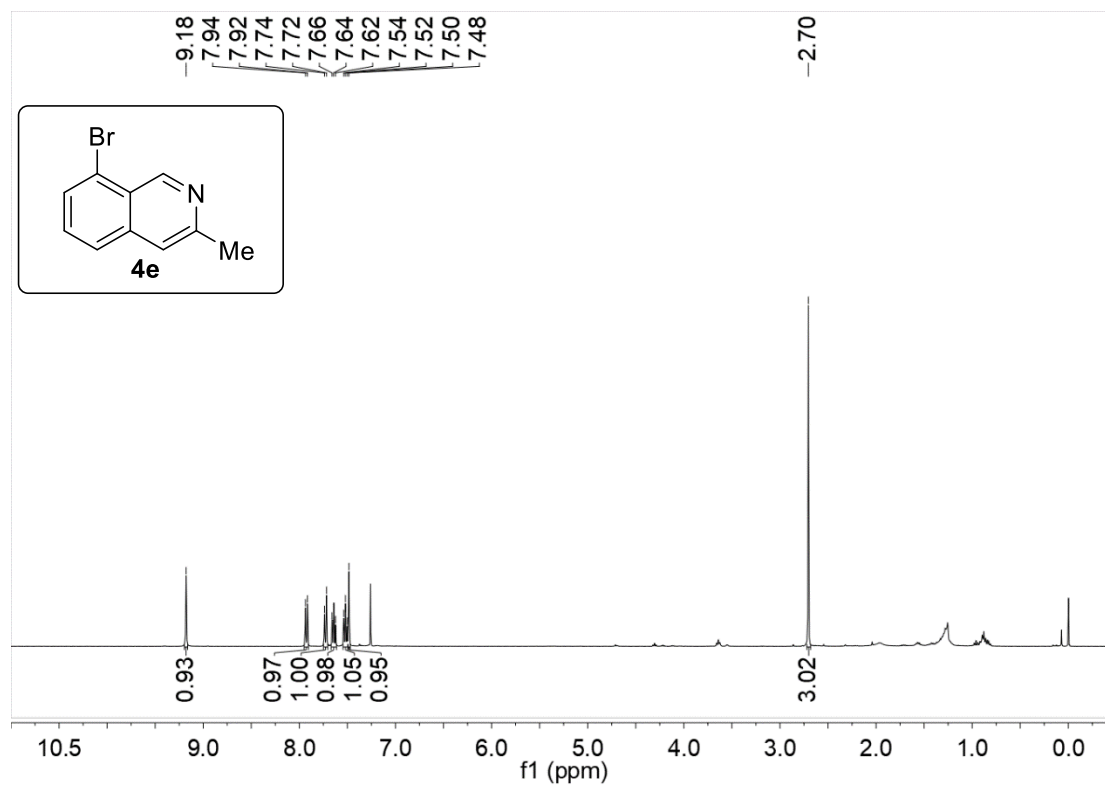
^1H NMR (400 MHz, CDCl_3) of 4d



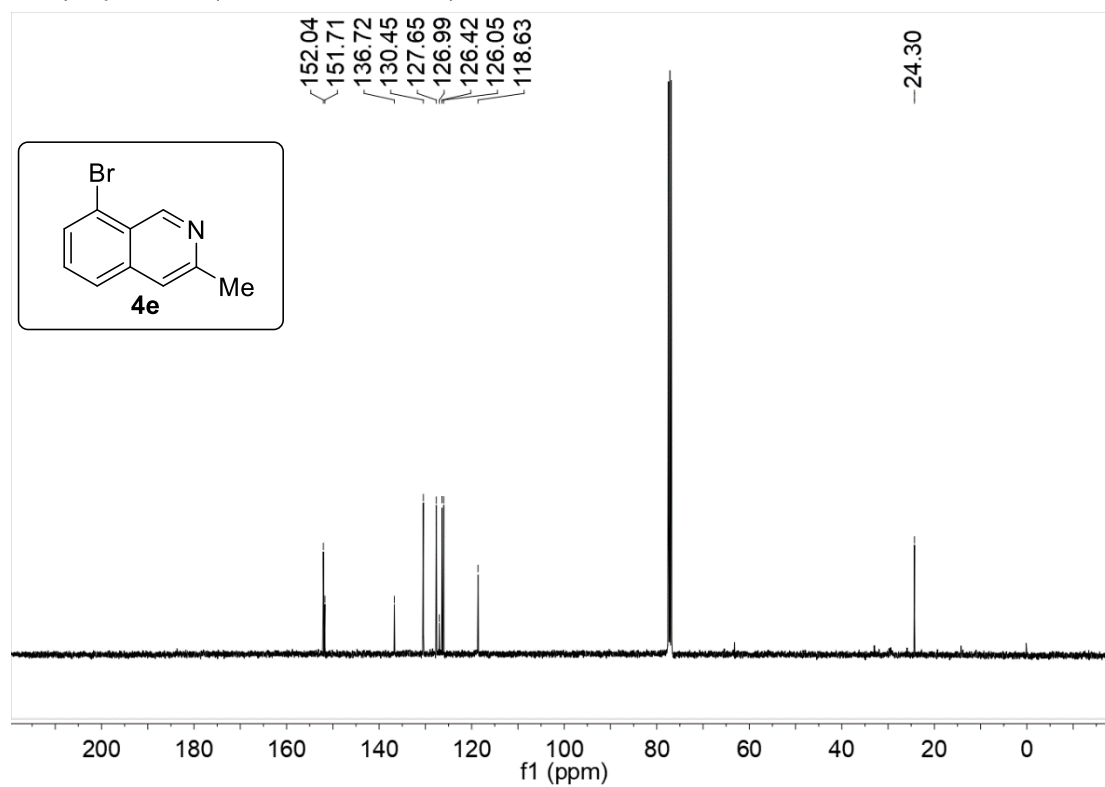
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4d



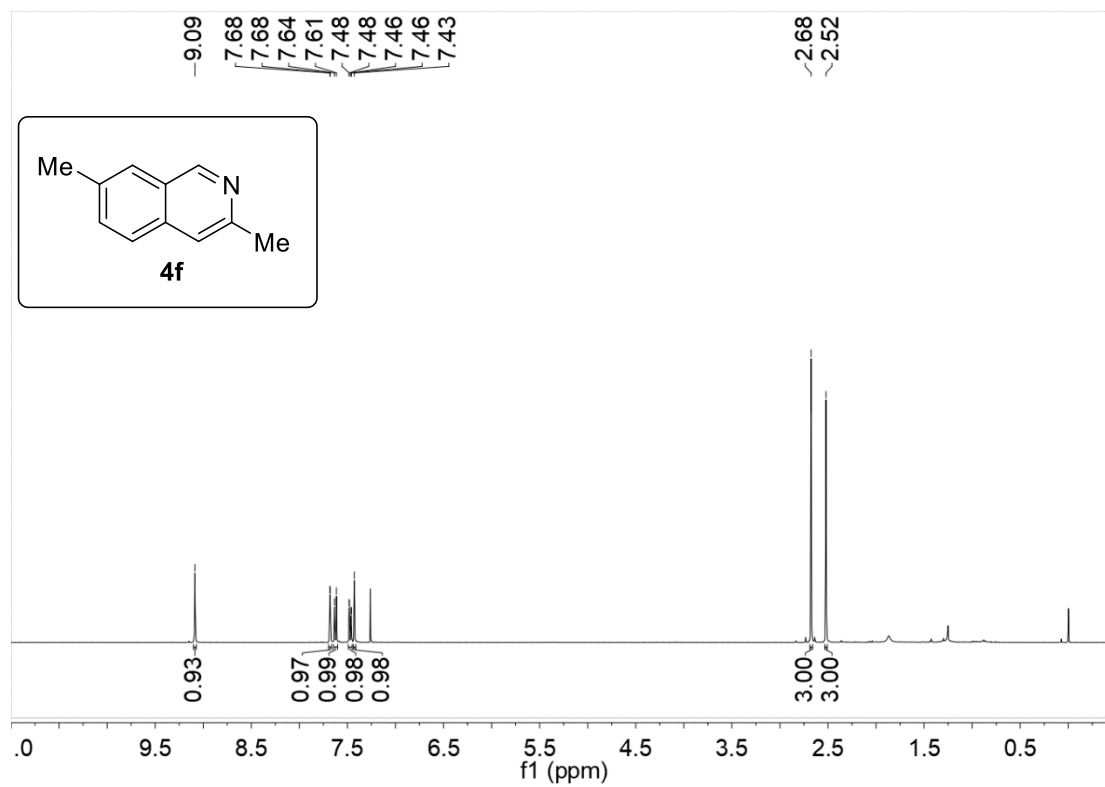
^1H NMR (400 MHz, CDCl_3) of 4e



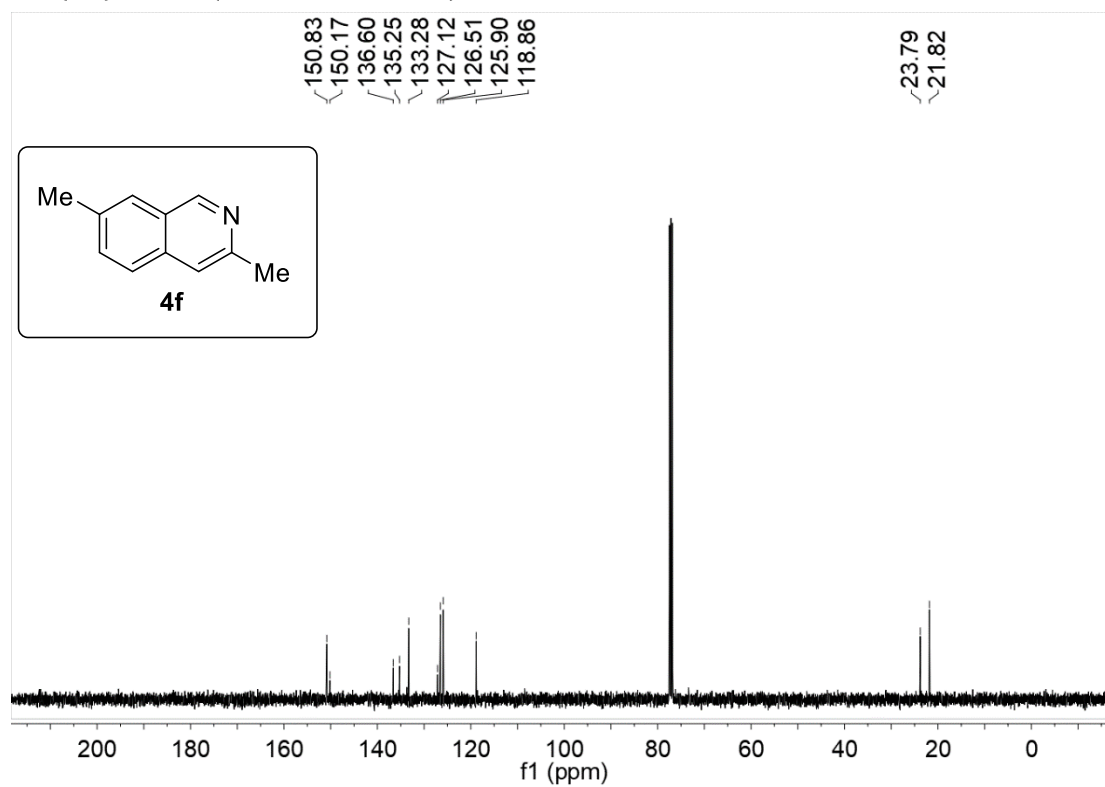
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4e



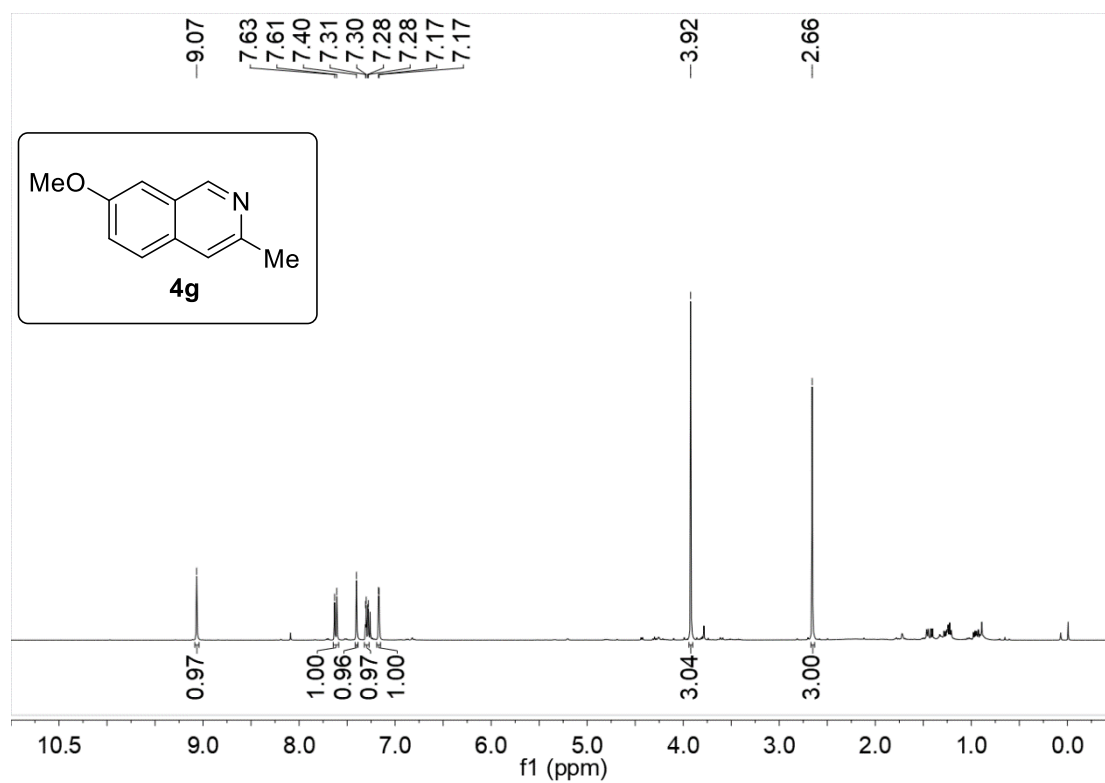
^1H NMR (400 MHz, CDCl_3) of 4f



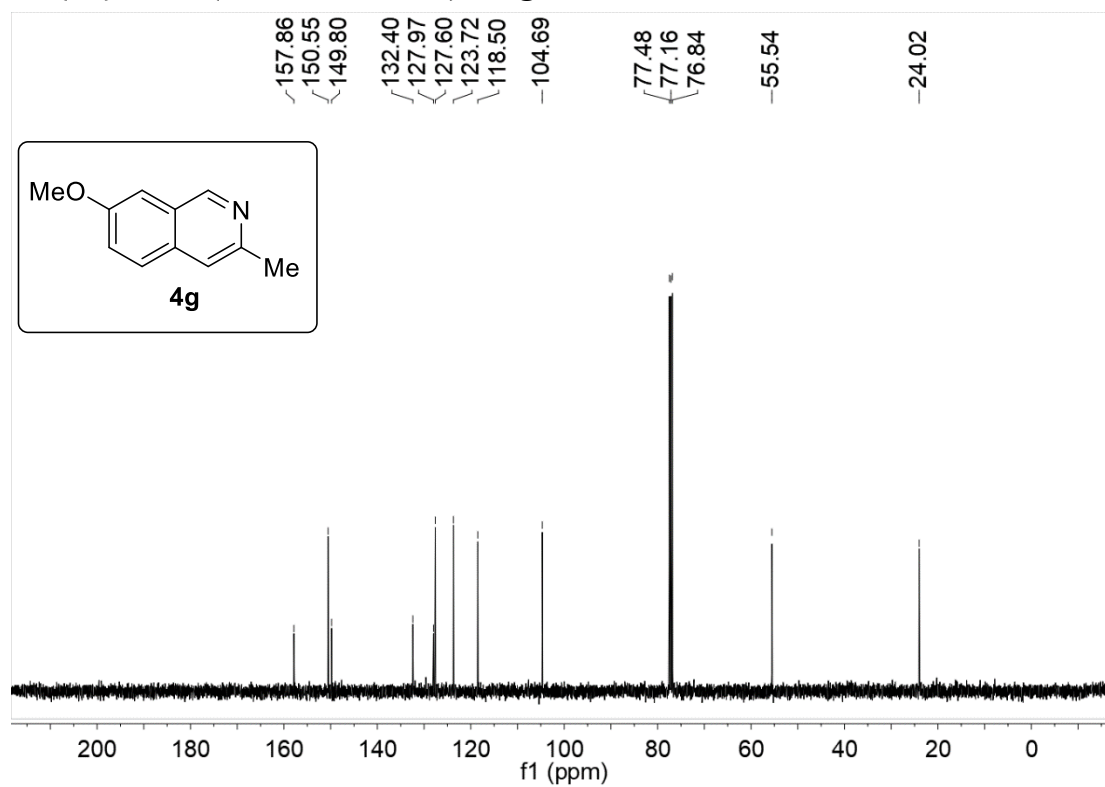
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4f



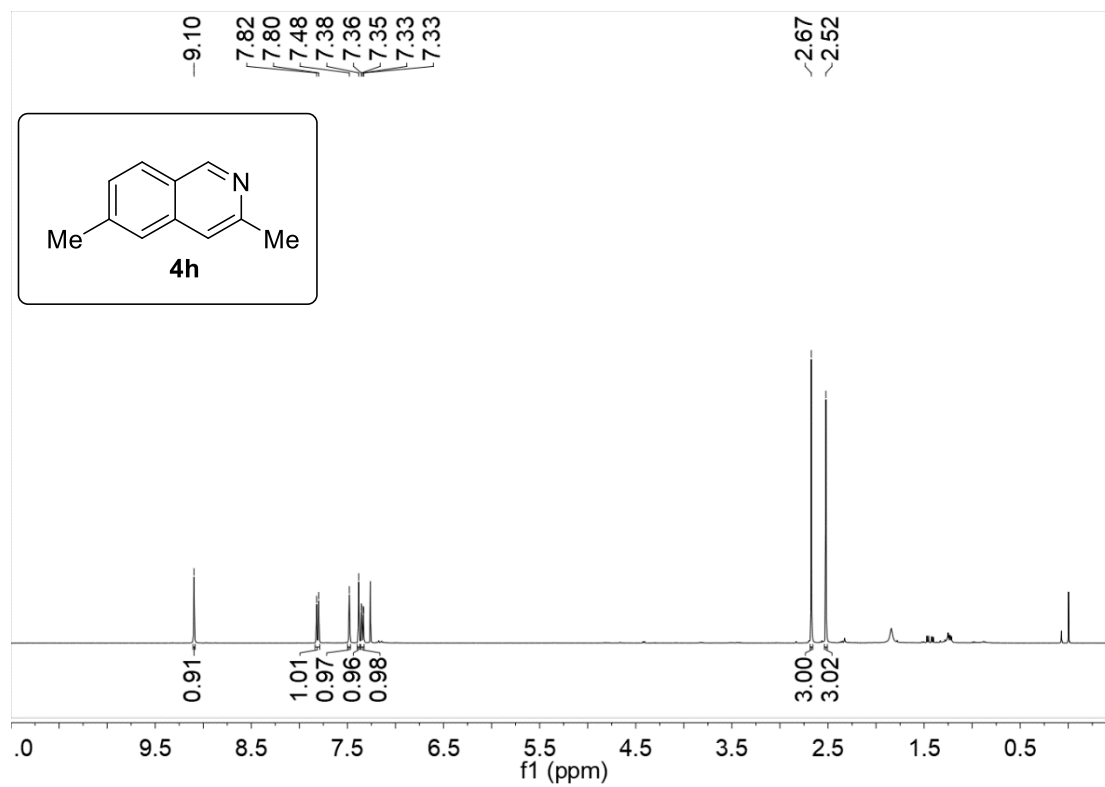
^1H NMR (400 MHz, CDCl_3) of 4g



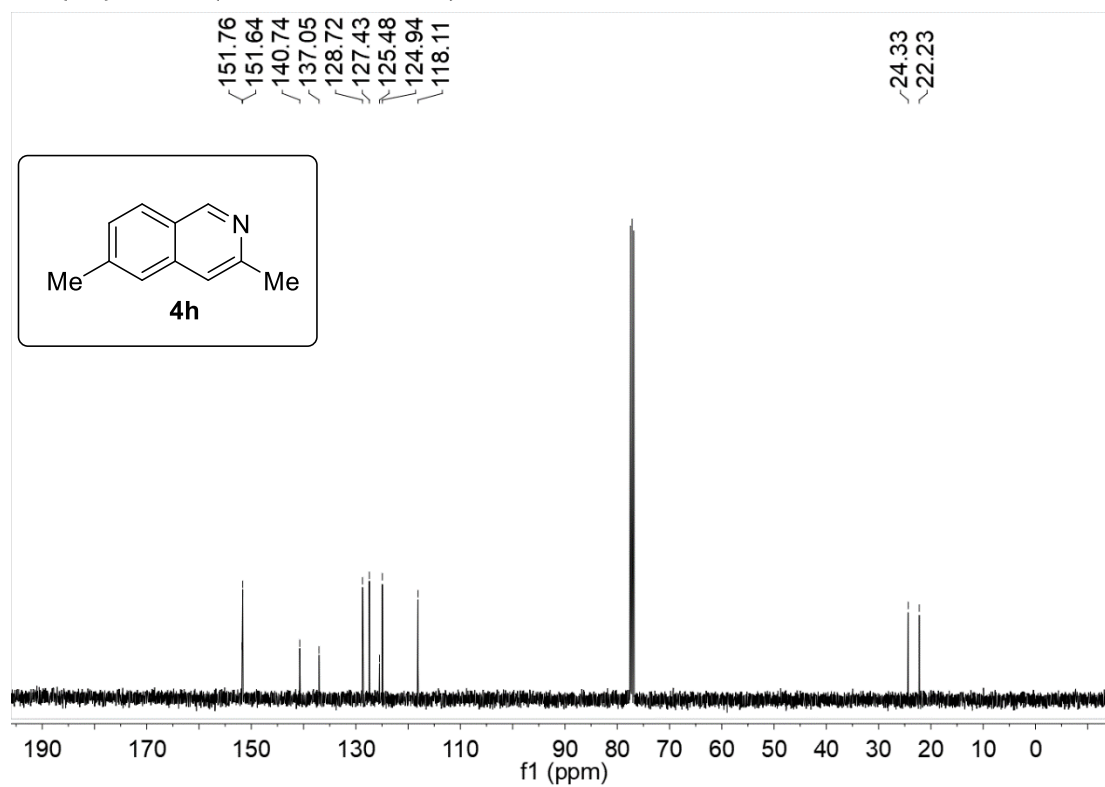
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4g



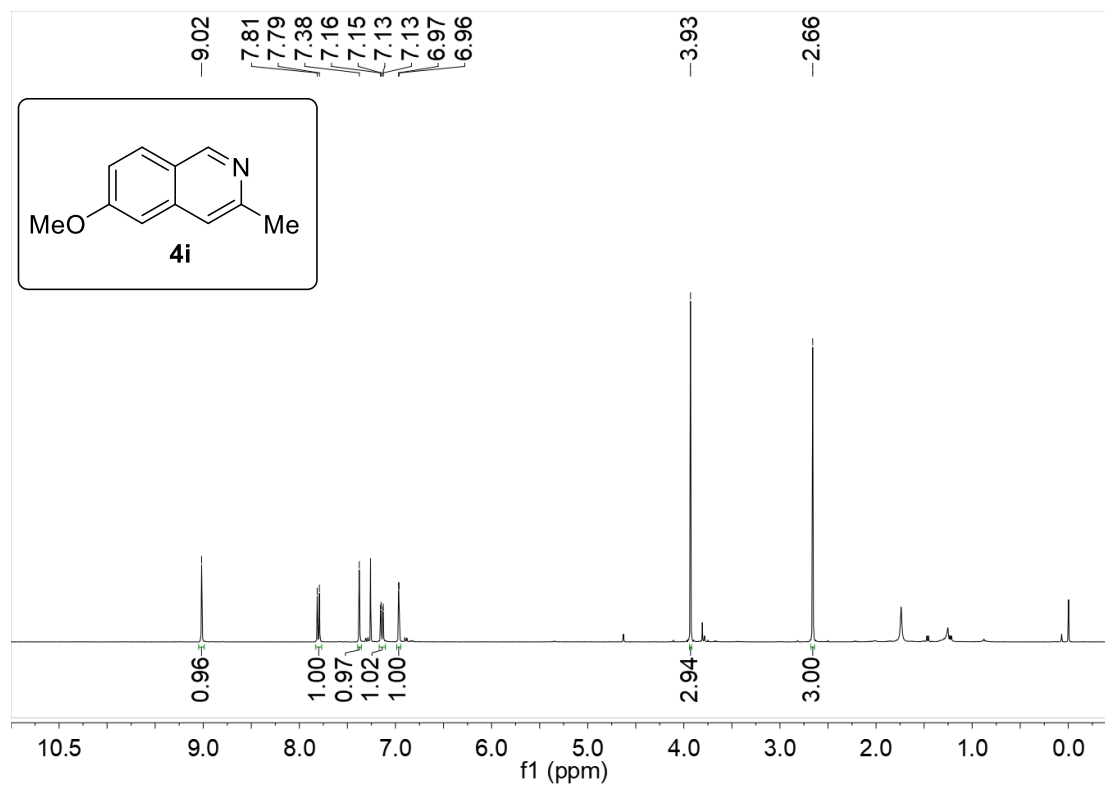
^1H NMR (400 MHz, CDCl_3) of 4h



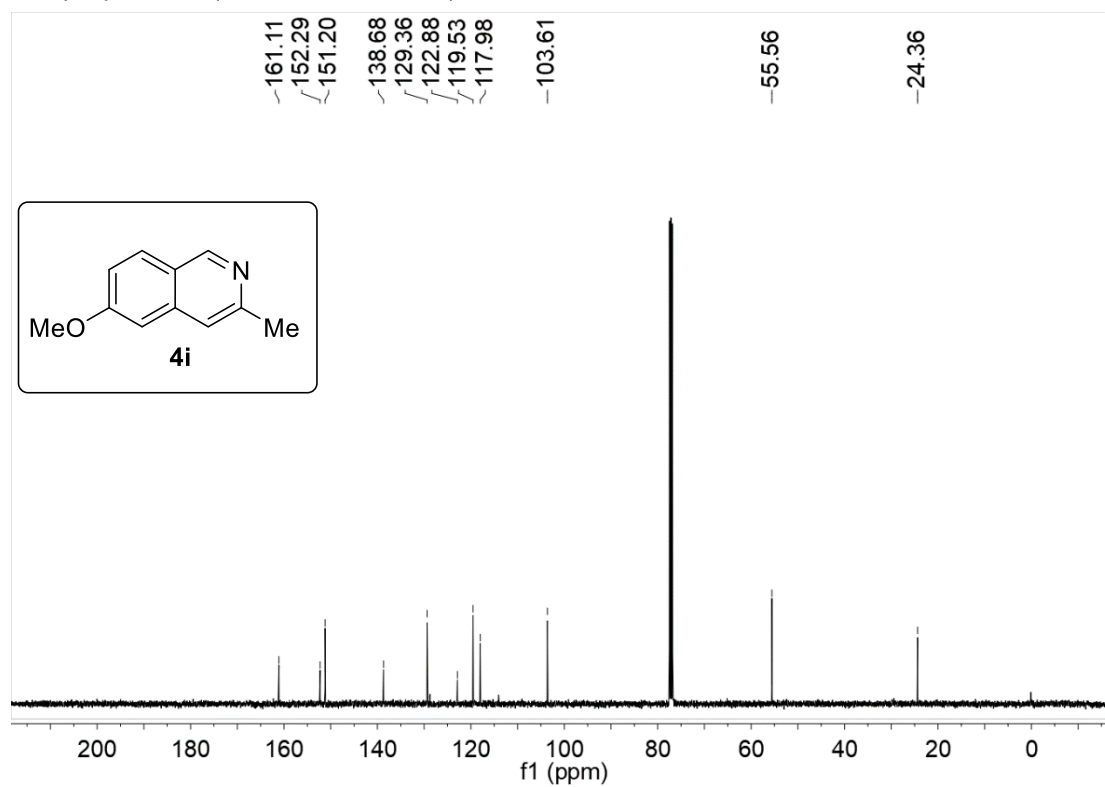
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4h



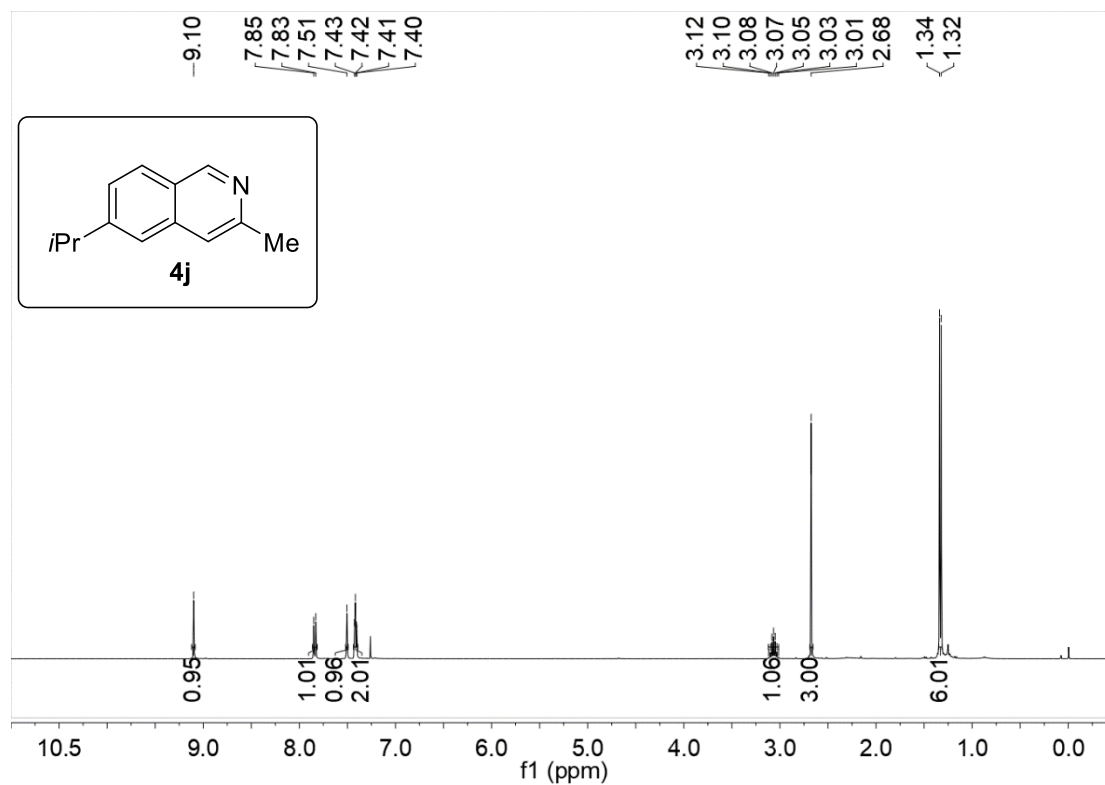
^1H NMR (400 MHz, CDCl_3) of 4i



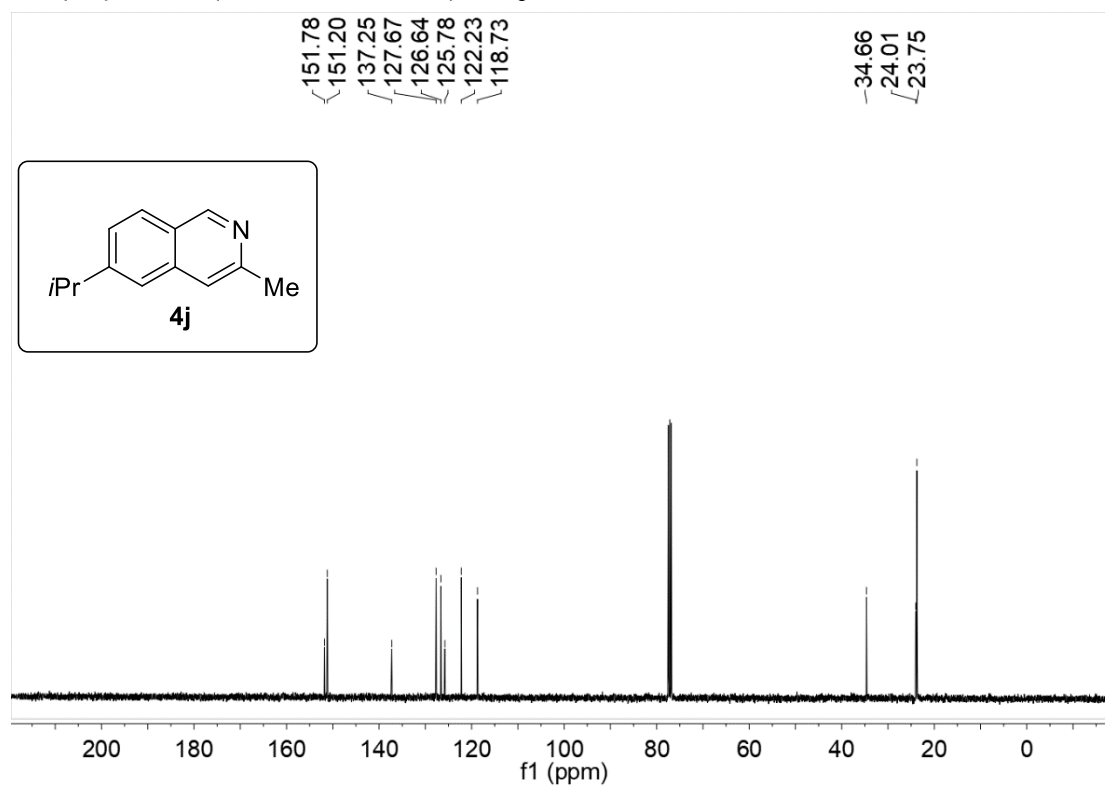
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4i



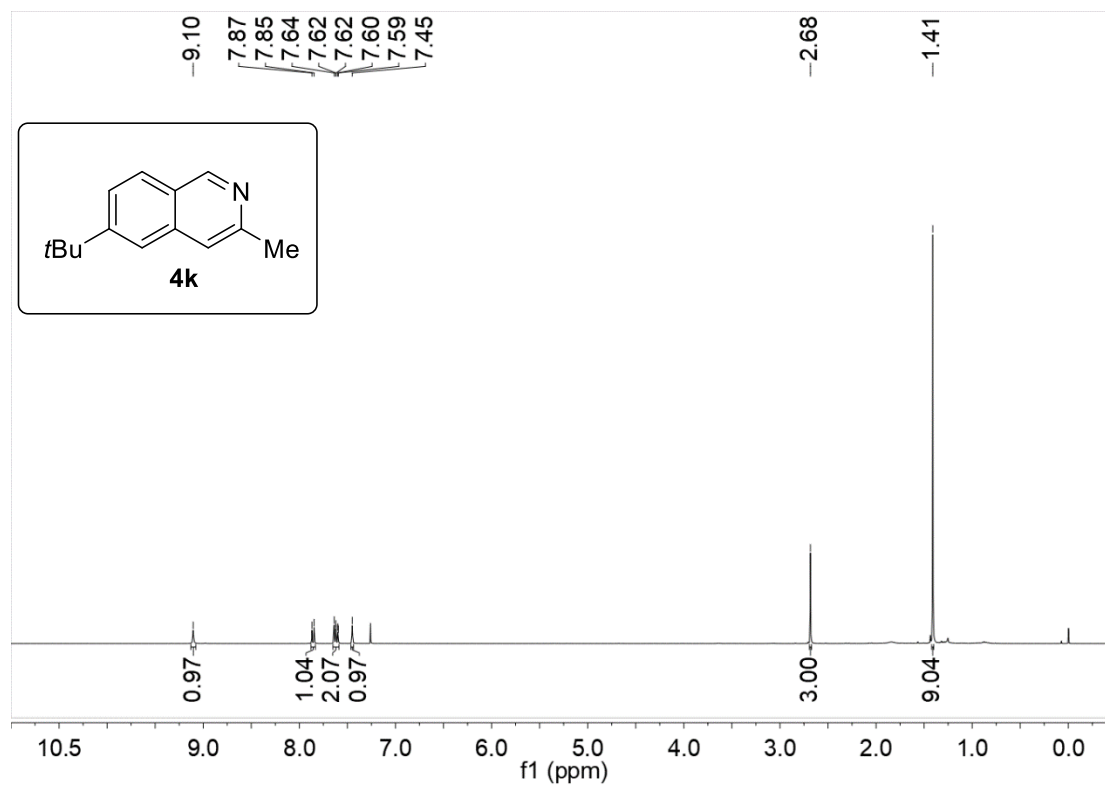
^1H NMR (400 MHz, CDCl_3) of 4j



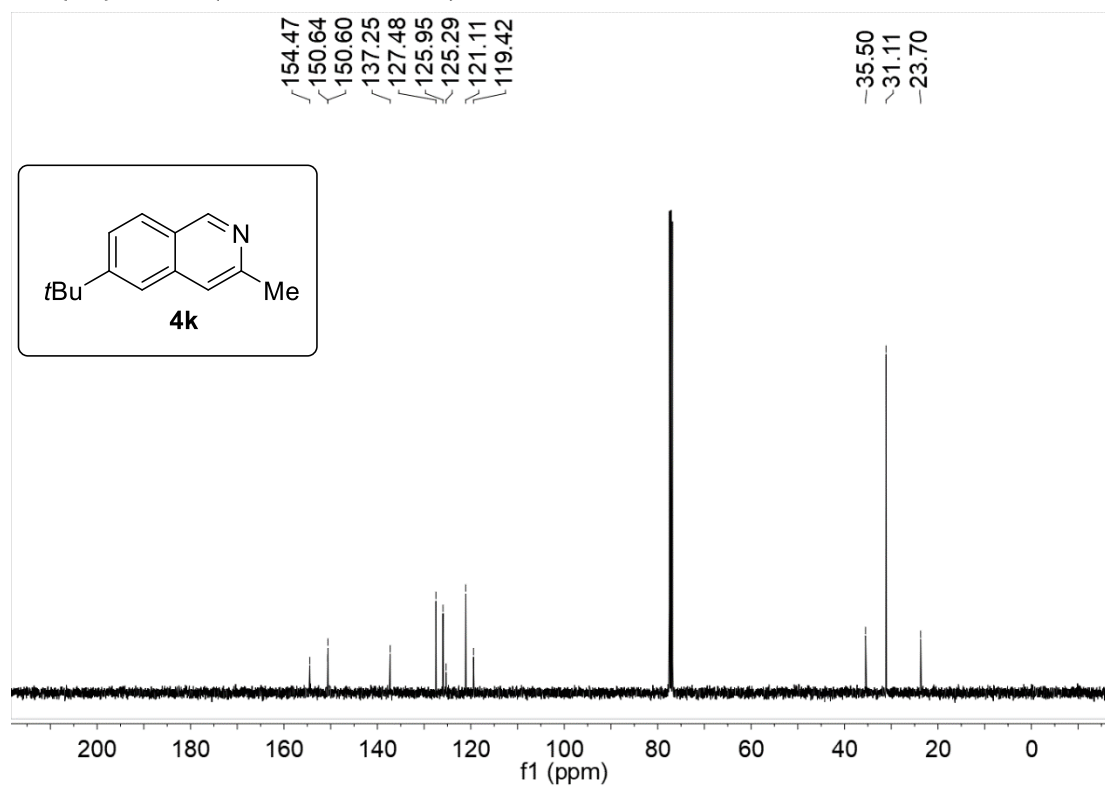
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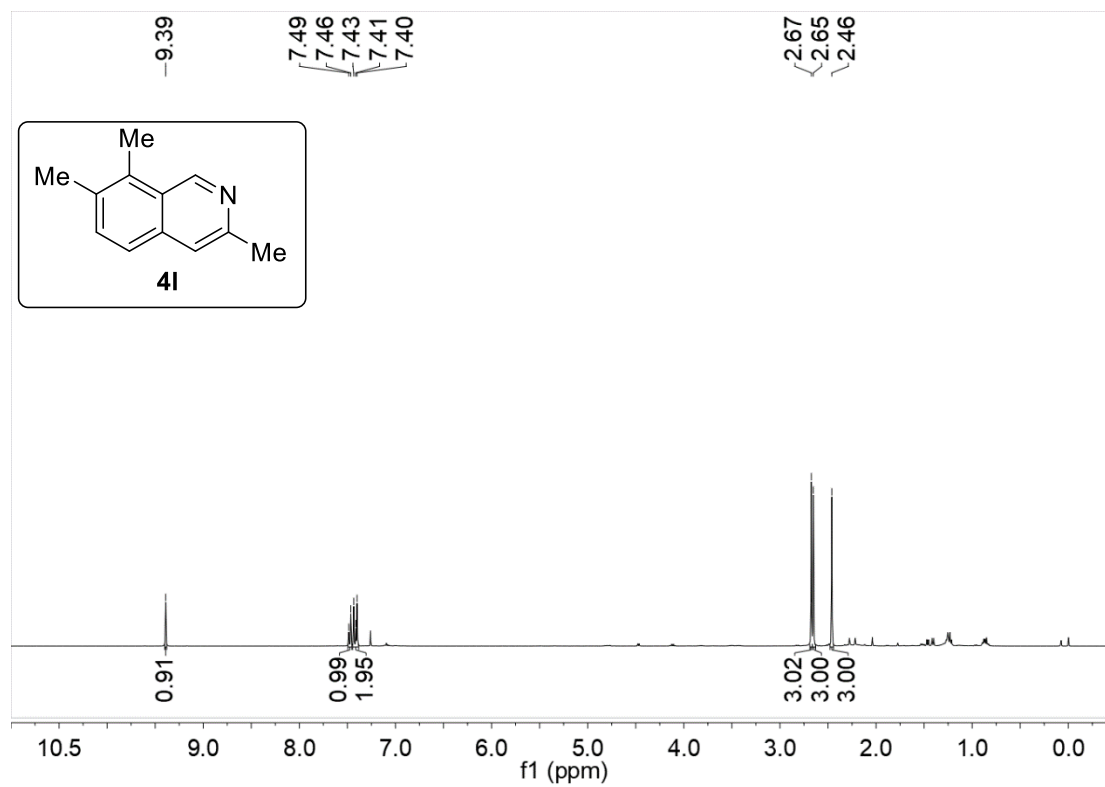
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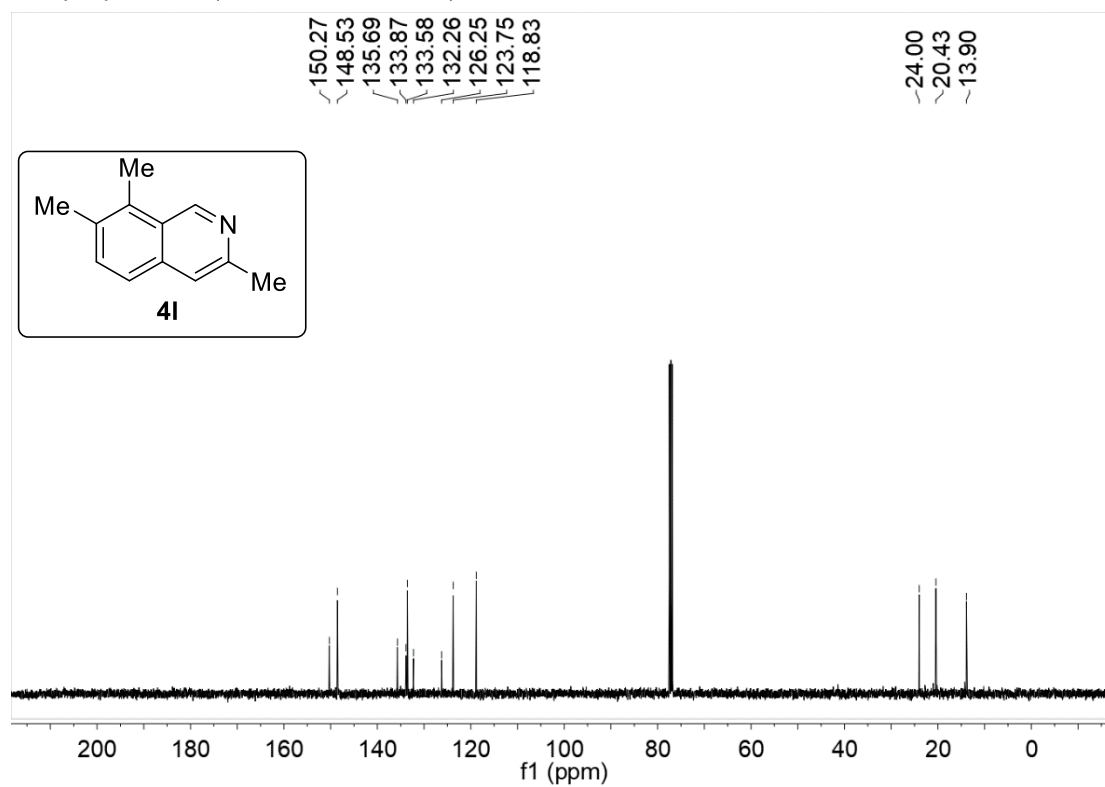
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4k



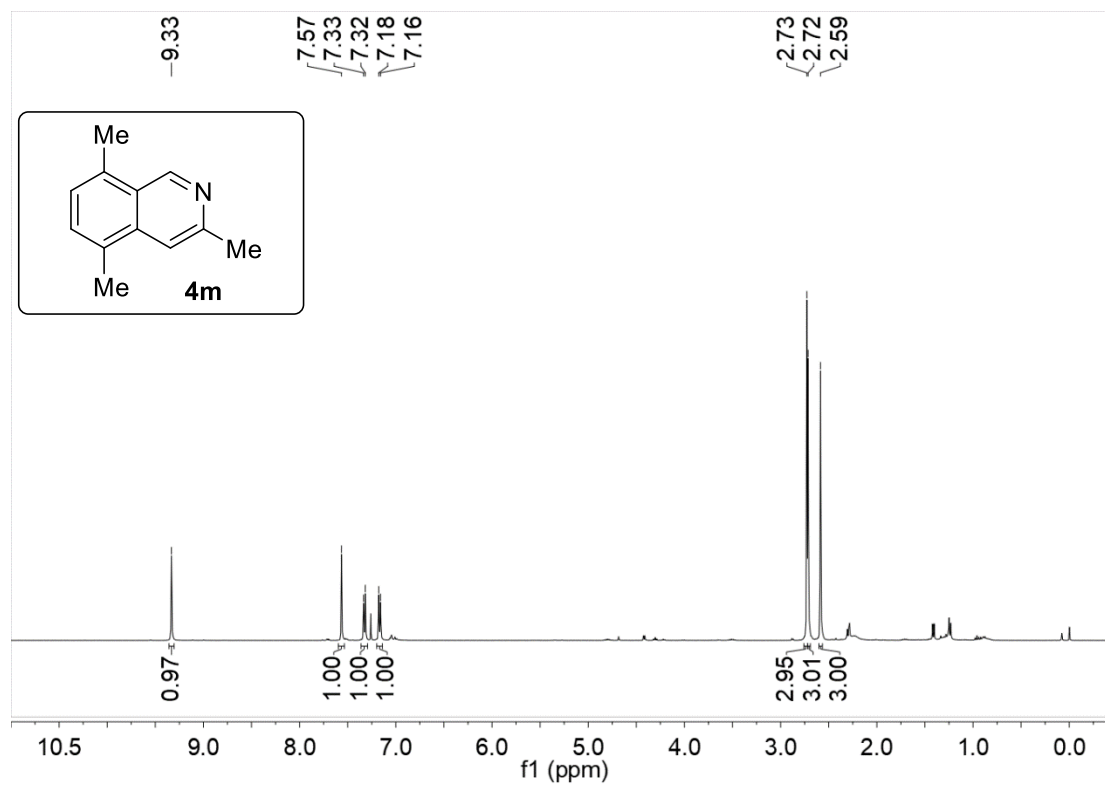
^1H NMR (400 MHz, CDCl_3) of 4l



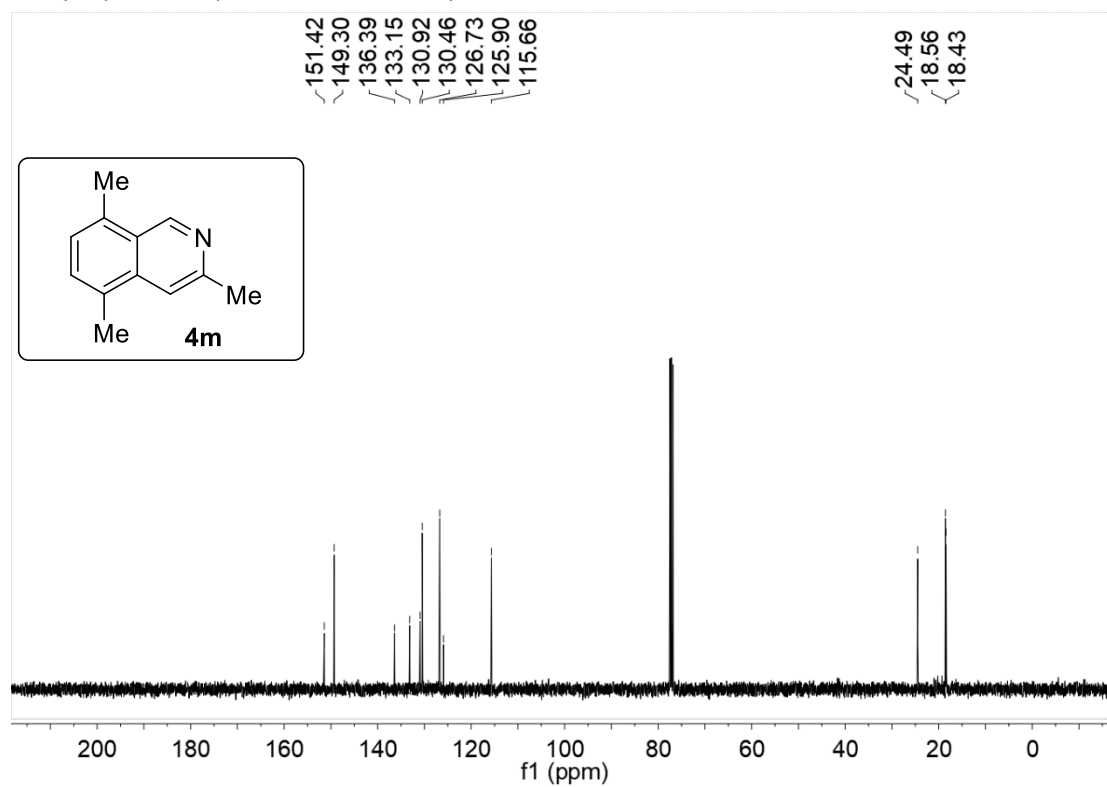
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 4l



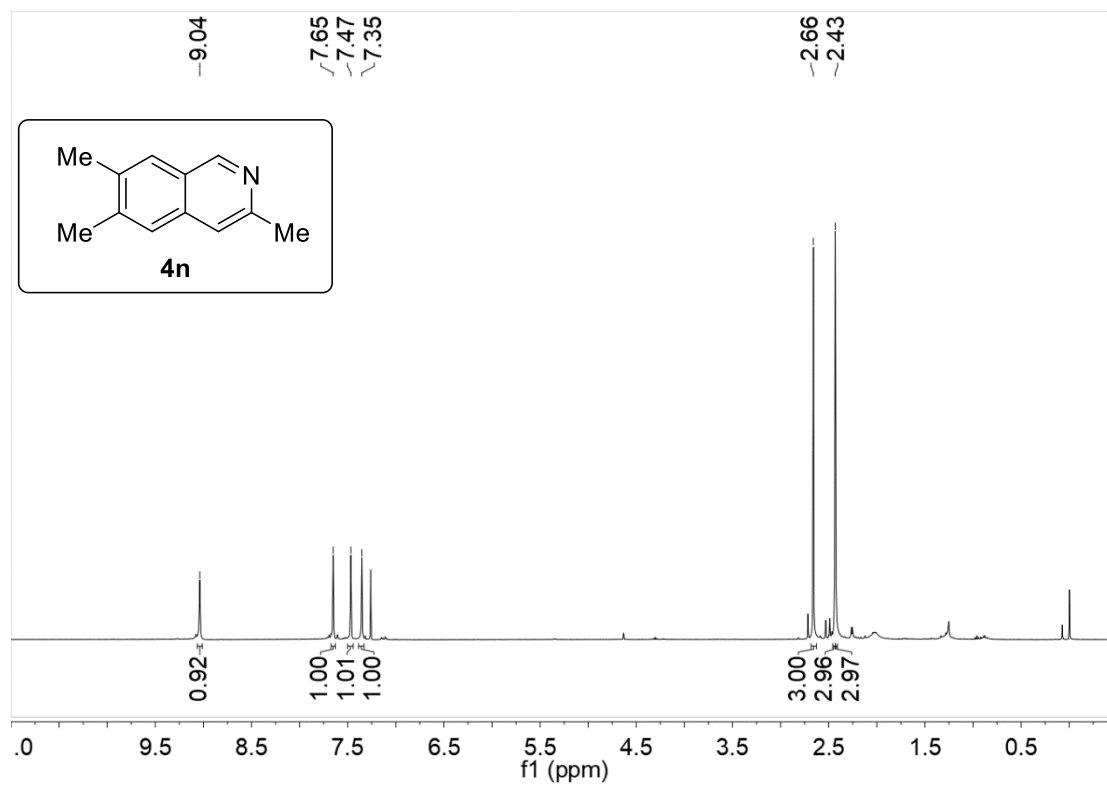
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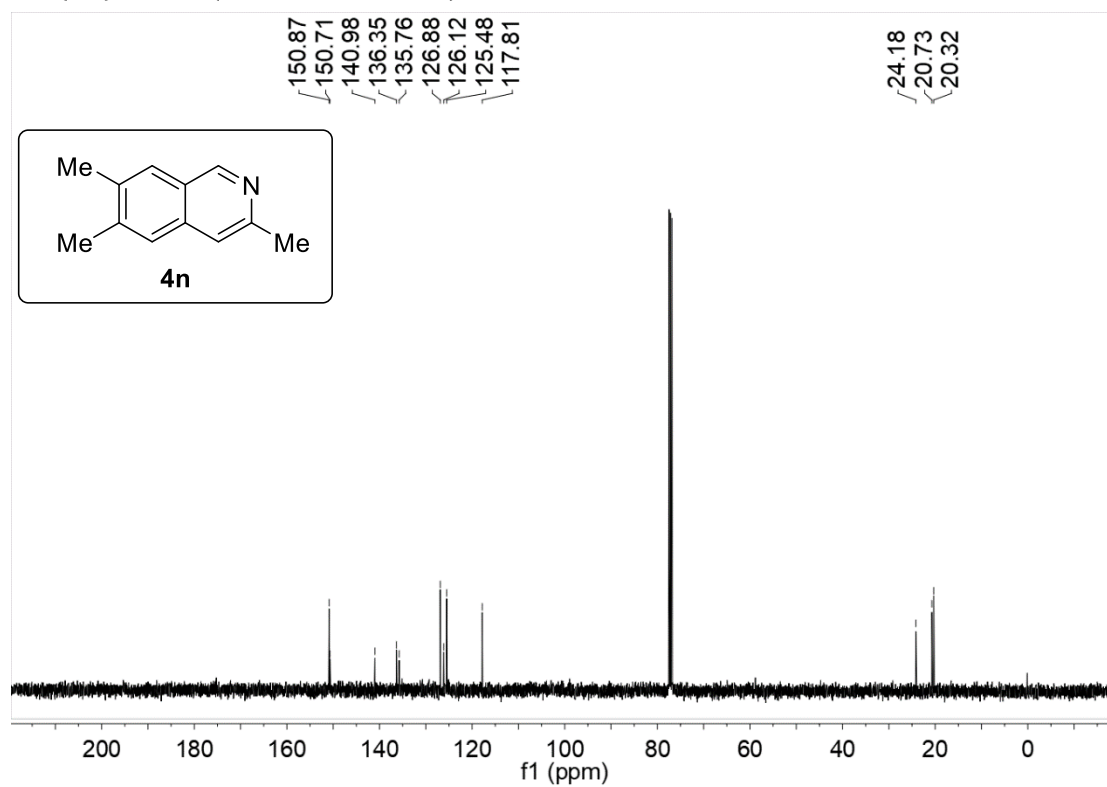
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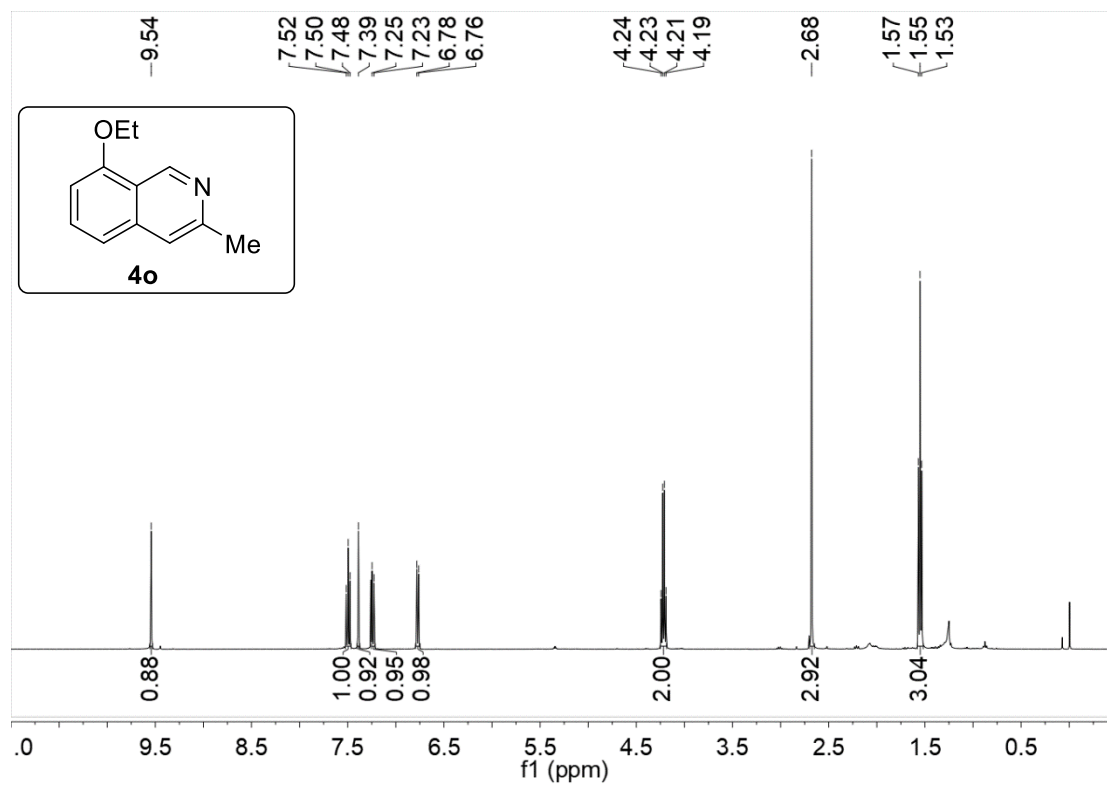
^1H NMR (400 MHz, CDCl_3) of 4n



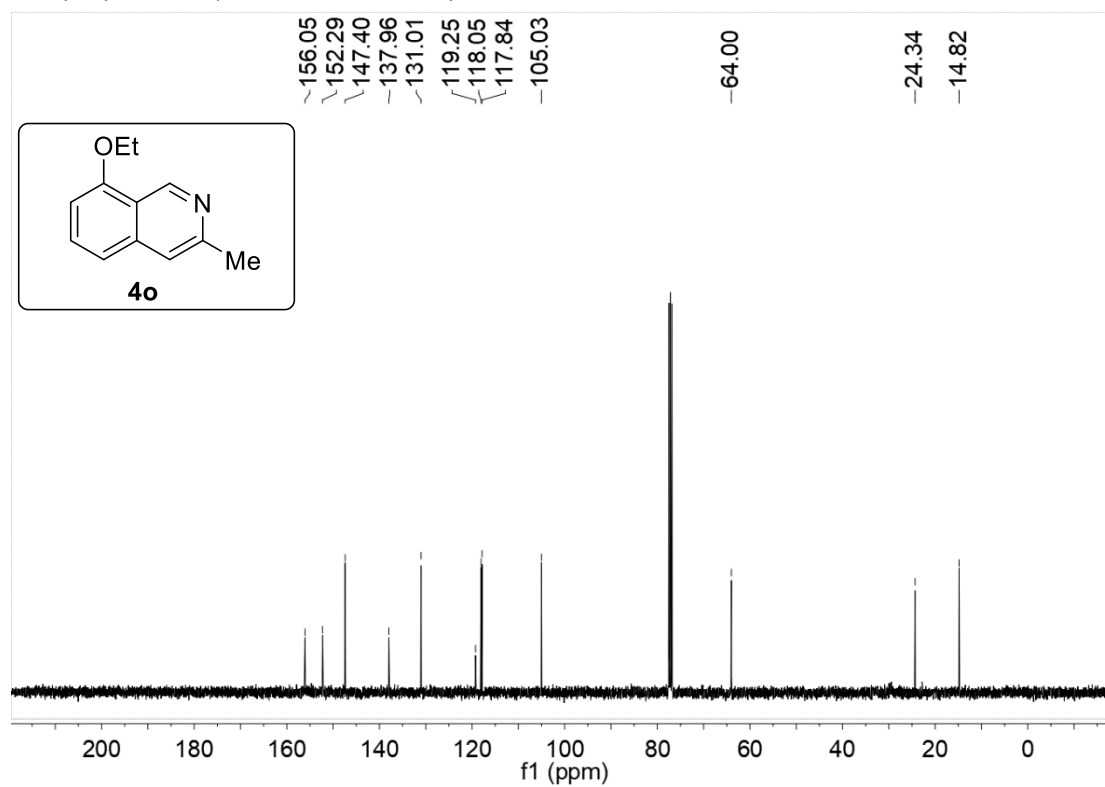
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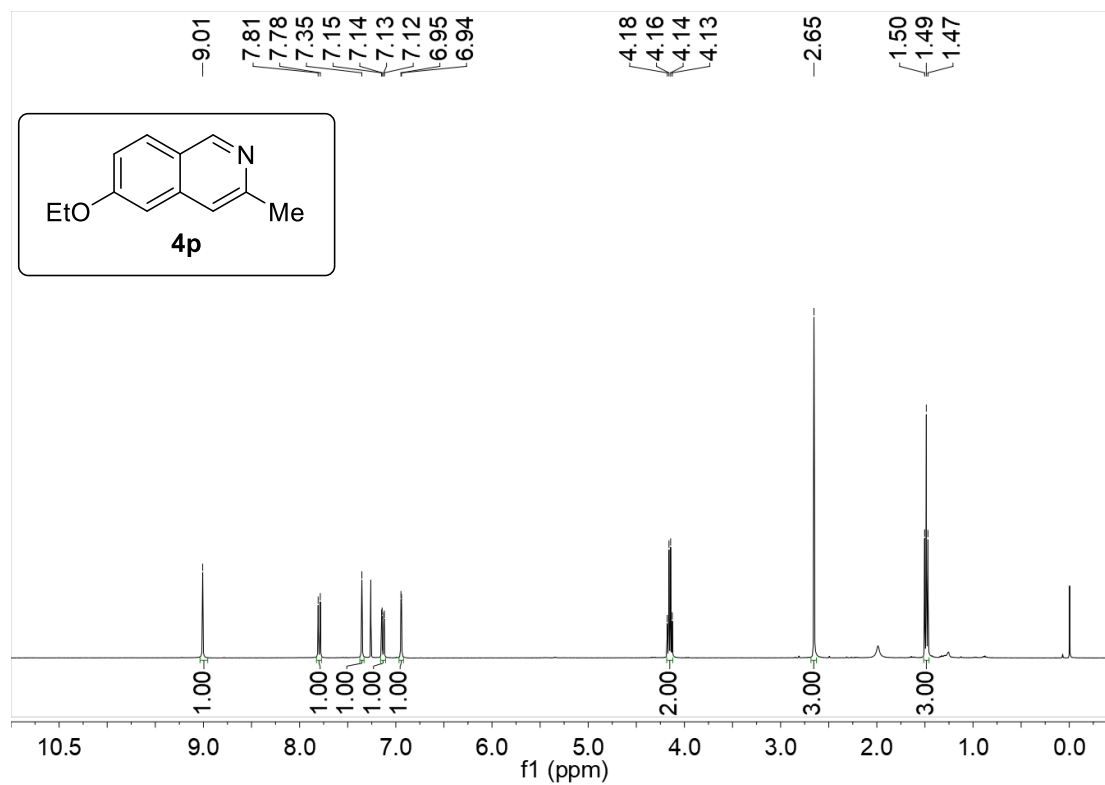
^1H NMR (400 MHz, CDCl_3) of 4o



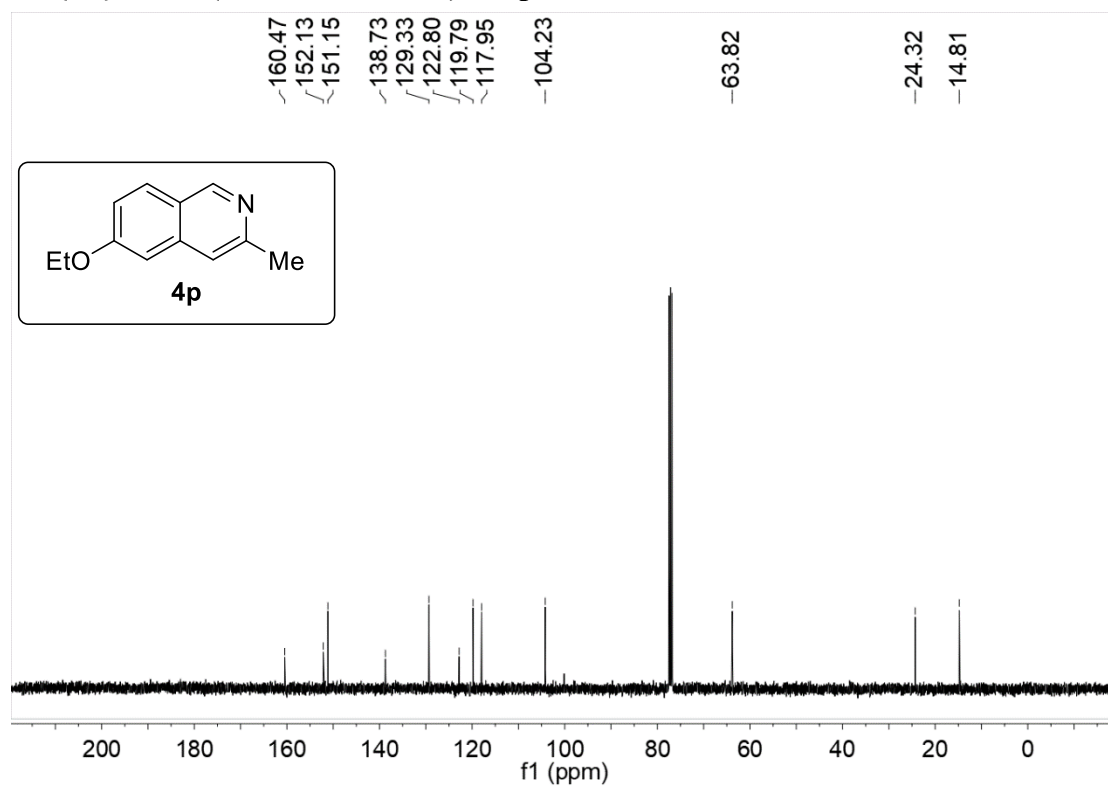
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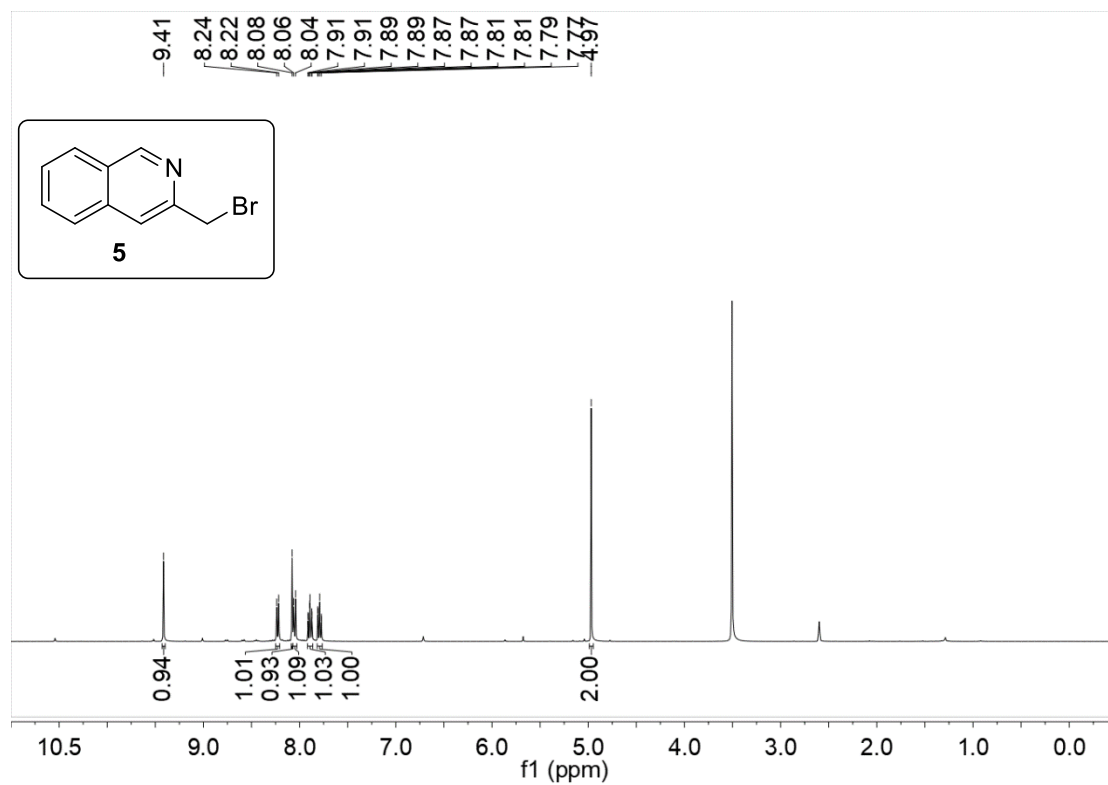
^1H NMR (400 MHz, CDCl_3) of 4p



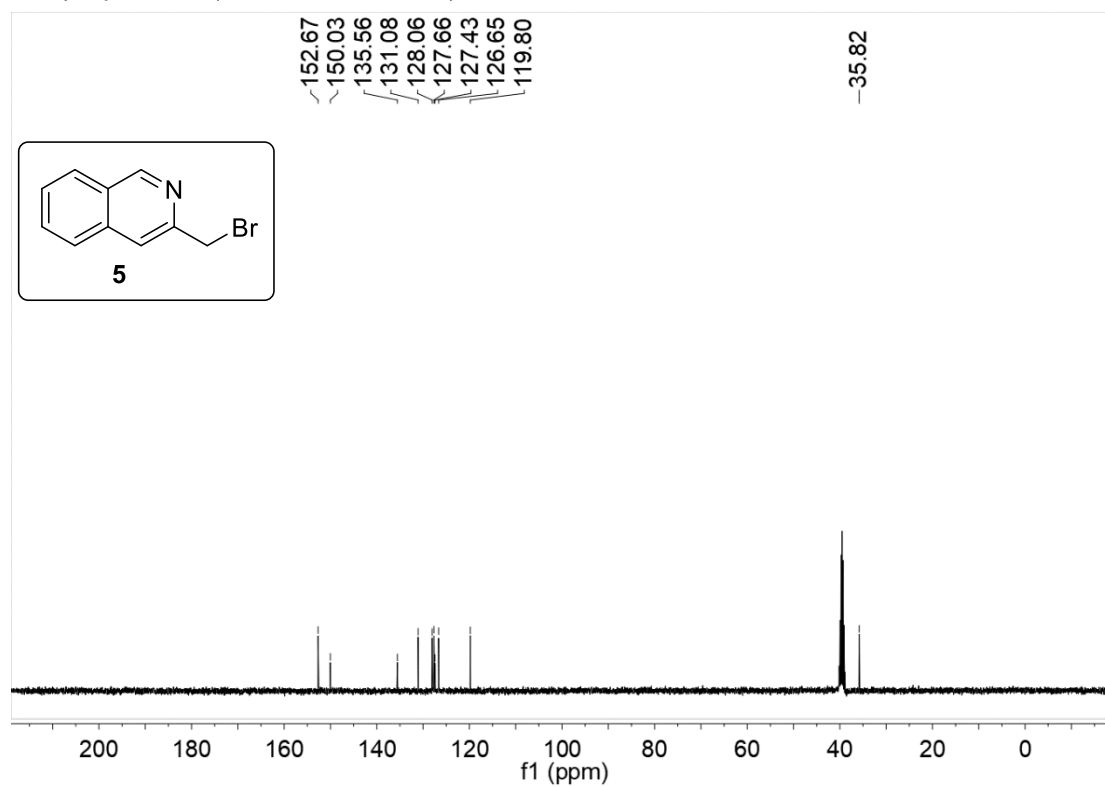
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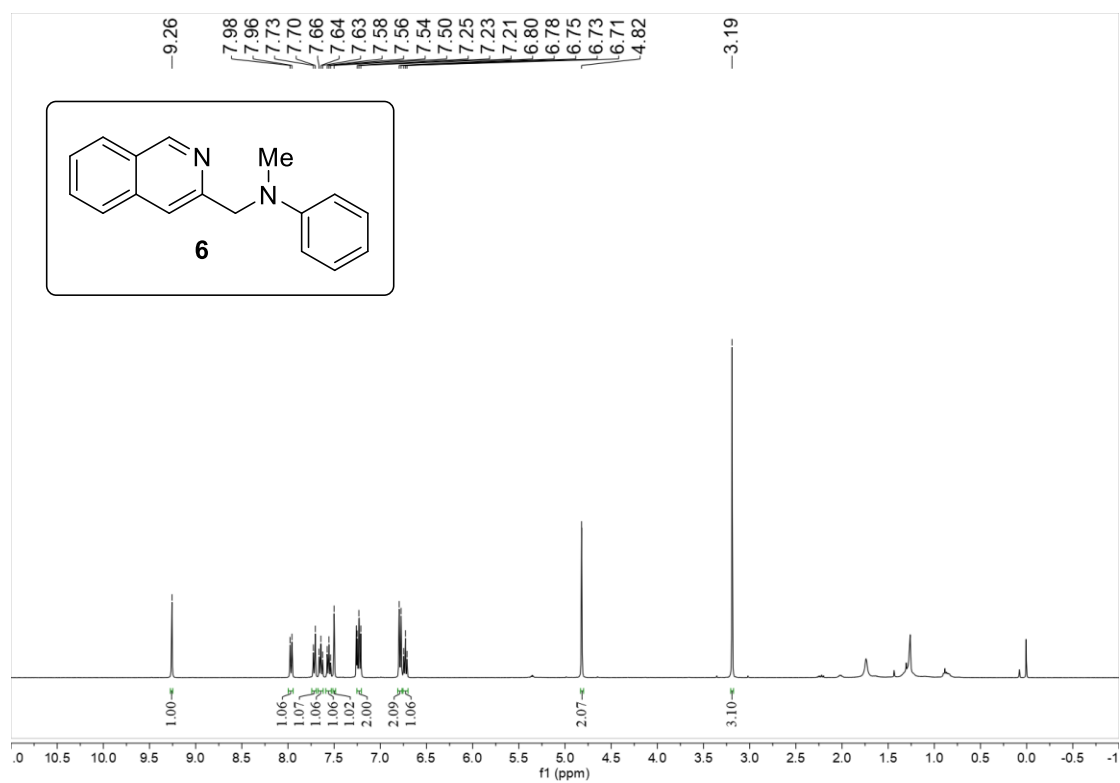
^1H NMR (400 MHz, CDCl_3) of 5



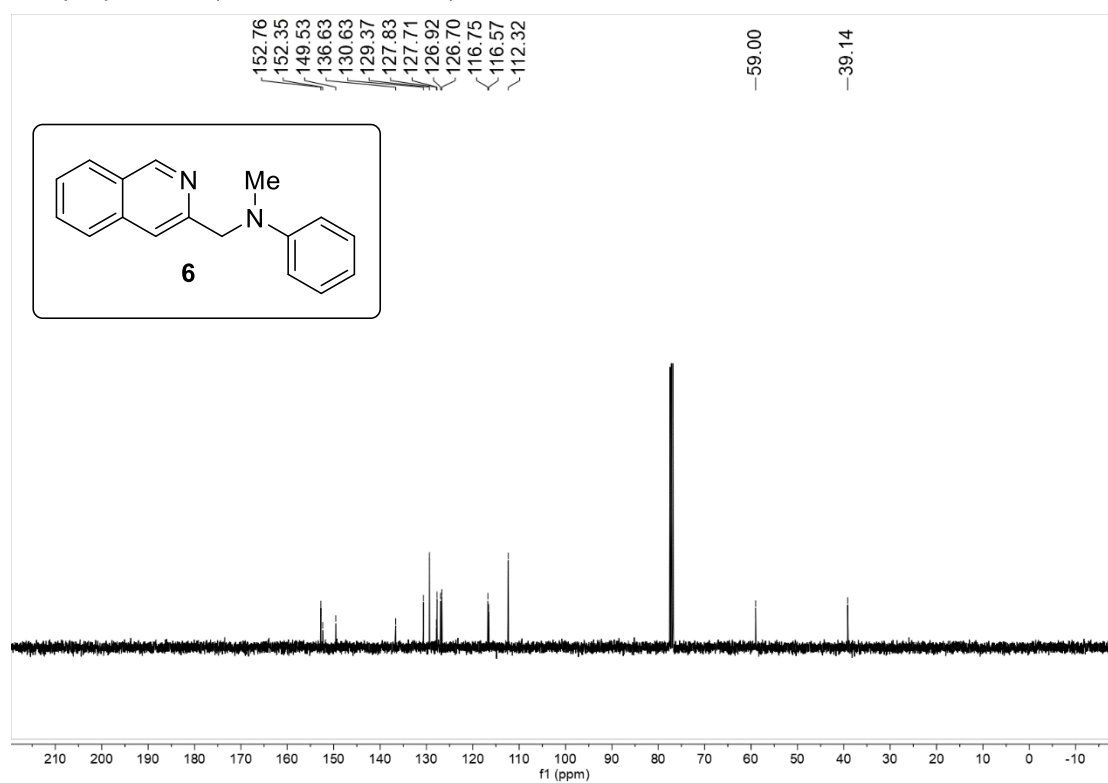
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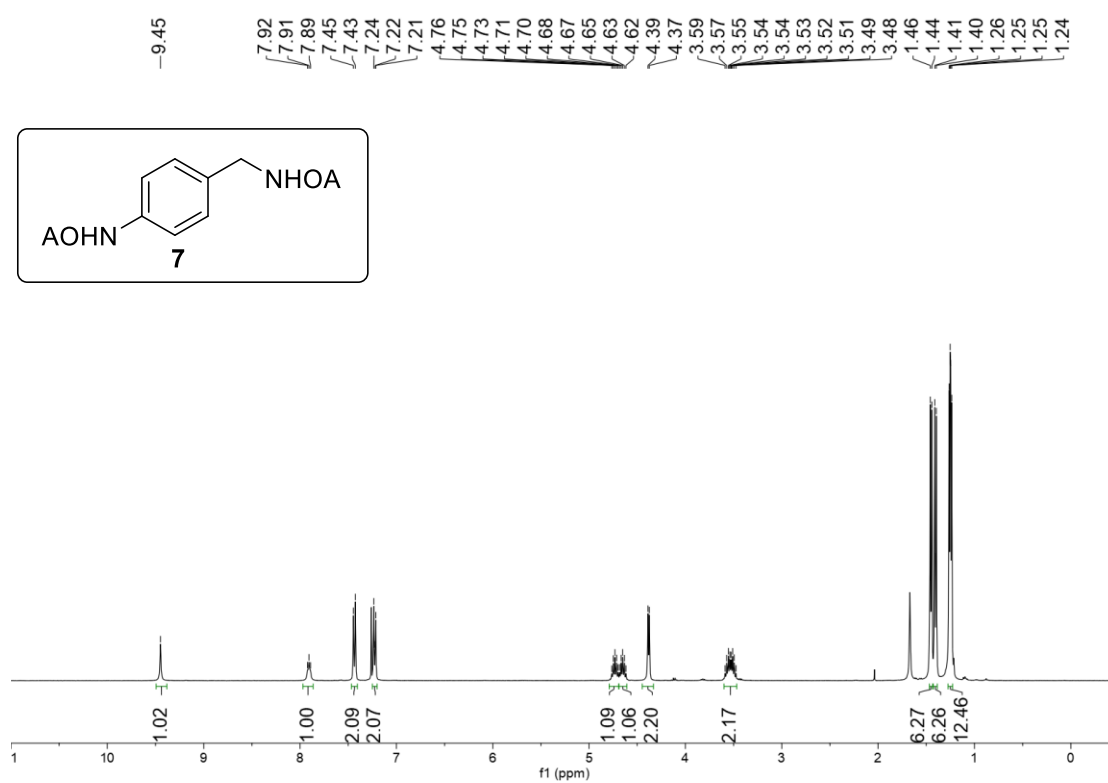
^1H NMR (400 MHz, CDCl_3) of 6



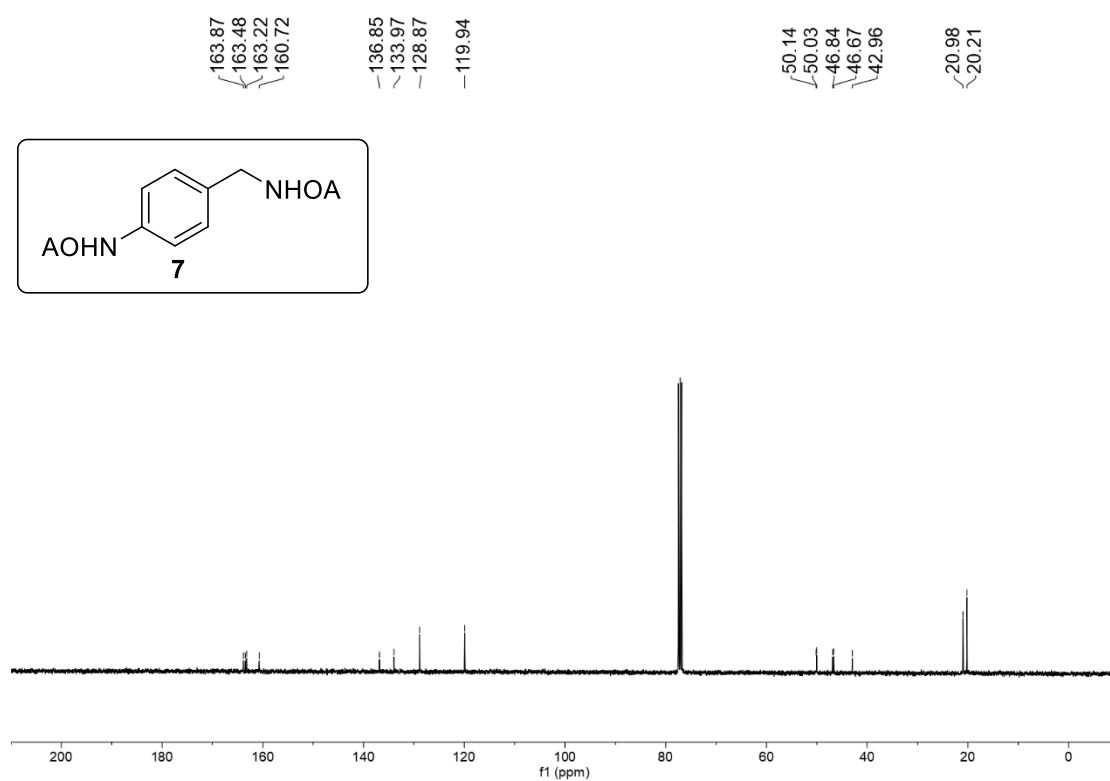
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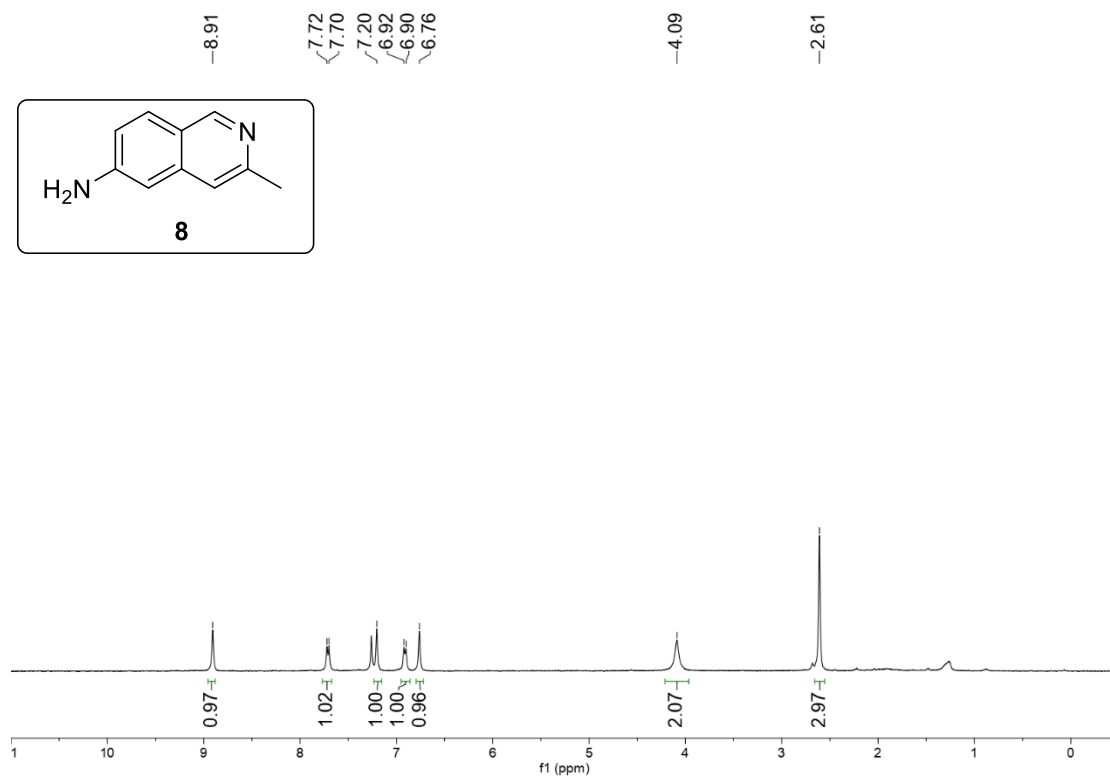
^1H NMR (400 MHz, CDCl_3) of 7



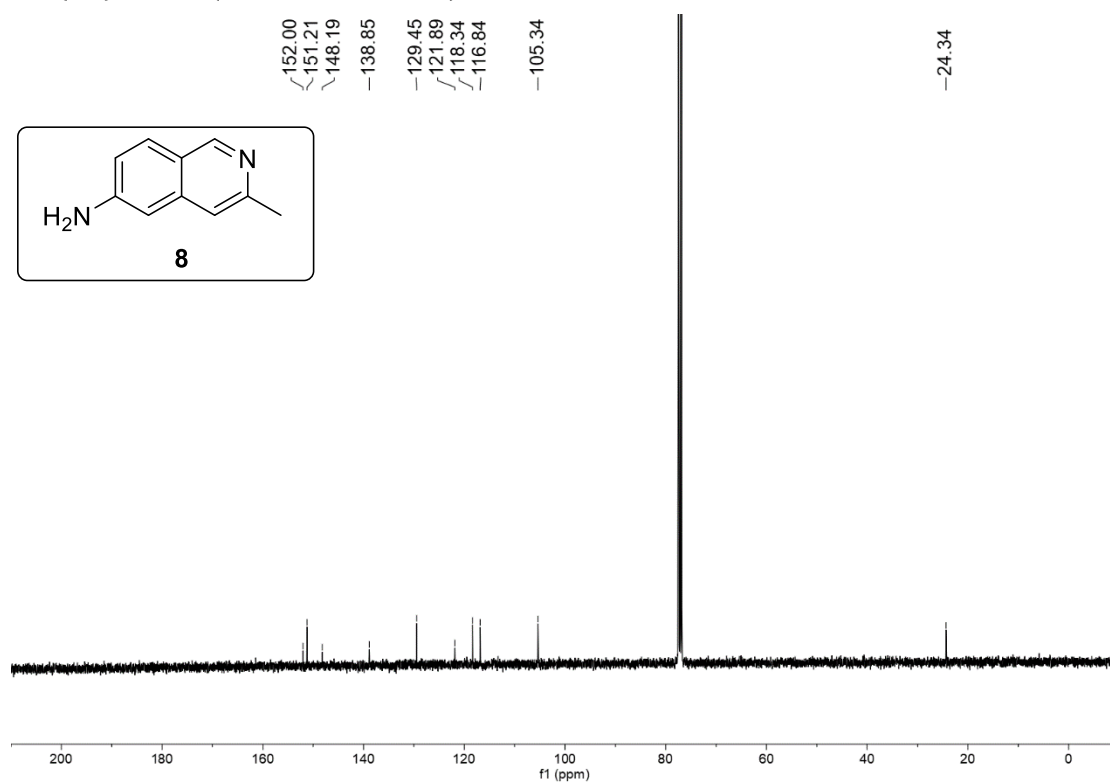
$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of 7



^1H NMR (400 MHz, CDCl_3) of 8



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **8**



^1H NMR (400 MHz, CDCl_3) of **9**



$^{13}\text{C}\{^1\text{H}\}$ NMR (100 MHz, CDCl_3) of **9**

