

Supporting Information

Visible-Light-Induced Cascade Radical Ring-Closure and Pyridylation for the Synthesis of Tetrahydrofurans

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Appendix I

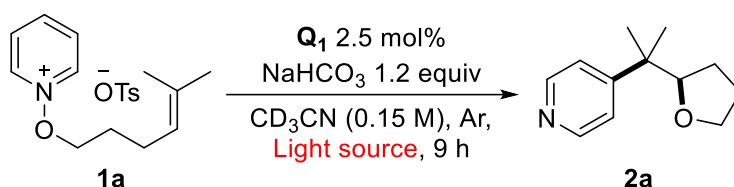
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I. General Methods and Materials.

Unless stated otherwise, reactions were performed in flame-dried glassware. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F²⁵⁴ plates and visualization on TLC was achieved by UV light (254 and 365 nm). Flash column chromatography was undertaken on silica gel (400-630 mesh) or a CombiFlash[®] R_f⁺ system with RediSep[®] R_f silica columns (230-400 mesh) using a proper eluent. ¹H NMR was recorded on Bruker Avance 400 MHz or Agilent Technologies DD2 600 MHz, and chemical shifts were quoted in parts per million (ppm) referenced to the appropriate solvent peak or 0.0 ppm for tetramethylsilane. The following abbreviations were used to describe peak splitting patterns when appropriate: br = broad, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublet, td = triplet of doublet, ddd = doublet of doublet of doublet. Coupling constants, *J*, were reported in hertz unit (Hz). ¹³C NMR was recorded on Bruker Avance 100 MHz or Agilent Technologies DD2 150 MHz and was fully decoupled by broad band proton decoupling. Chemical shifts were reported in ppm referenced to the centerline of a triplet at 77.0 ppm of CDCl₃. ¹⁹F NMR was recorded on Agilent Technologies DD2 (564 MHz). High-resolution mass spectra were obtained by using EI or FAB method from Korea Basic Science Institute (Daegu) or ESI from KAIST Research Analysis Center (Daejeon). Commercial grade reagents and solvents were used without further purification except as indicated below.

II. Control Experiments

Scheme S1. Light source screening

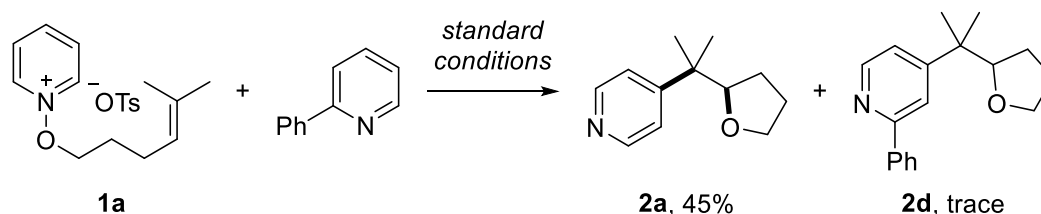


Entry	Light source	Result (NMR yield)
1	Green LED	No reaction, SM fully remained
2	Red LED	No reaction, SM fully remained
3	Blue LED	77%

Reactions were conducted in cap test tube (12 mL) sealed by assembled screw cap with hole and PTFE/silicone septa. 1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (**1a**) (36.3 mg, 0.10 mmol), 3-(diphenylphosphoryl)-6-methoxy-1-methylquinolin-2(1H)-one (**Q₁**) (1.0 mg, 0.0025 mmol), and NaHCO₃ (10.1 mg, 0.12 mmol) were combined in CH₃CN (0.67 mL) under argon atmosphere. The mixture was placed in the irradiation apparatus equipped with a blue LED. The resulting mixture was stirred at room temperature. After 9 hours, the reaction mixture was diluted and

filtered through a nylon syringe filter (pore size: 0.2 μm) with CH_2Cl_2 (10 mL). The yield of product was determined by ^1H NMR analysis using caffeine as an internal standard.

Scheme S2. Reaction with pyridine



Reaction was conducted in cap test tube (12 mL) sealed by assembled screw cap with hole and PTFE/silicone septa. 1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (**1a**) (36.3 mg, 0.10 mmol), 3-(diphenylphosphoryl)-6-methoxy-1-methylquinolin-2(1H)-one (**Q1**) (1.0 mg, 0.0025 mmol), NaHCO_3 (10.1 mg, 0.12 mmol), and 2-phenylpyridine (15.5 mg, 0.10 mmol) were combined in CD_3CN (0.67 mL) under argon atmosphere. The mixture was placed in the irradiation apparatus equipped with a blue LED. The resulting mixture was stirred at room temperature. The reaction mixture was monitored by TLC using ($\text{CH}_2\text{Cl}_2/\text{MeOH} = 15:1$) as the mobile phase. After 72 h, the reaction mixture was diluted and filtered through a nylon syringe filter (pore size: 0.2 μm) with CH_2Cl_2 (10 mL). The yield of product was determined by ^1H NMR analysis using caffeine as an internal standard. The yield of **2a** was determined to be 45% (0.045 mmol of **2a**).

Quantum yield measurements

Blue LED ($\lambda_{\text{max}} = 415 \text{ nm}$) was used for measurement of quantum yield.

Determination of the light intensity at 415 nm

According to the procedure of Yoon,^{S2} the photon flux of the LED ($\lambda_{\text{max}} = 415 \text{ nm}$) was determined by standard ferrioxalate actinometry. A 0.15 M solution of ferrioxalate was prepared by dissolving potassium ferrioxalate hydrate (0.737 g) in H_2SO_4 (10 mL of a 0.05 M solution). A buffered solution of 1,10-phenanthroline was prepared by dissolving 1,10-phenanthroline (5.0 mg) and sodium acetate (1.13 g) in H_2SO_4 (5.0 mL of a 0.5 M solution). Both solutions were stored in the dark. To determine the photon flux of the LED, the ferrioxalate solution (2.0 mL) was placed in a cuvette and irradiated for 45 seconds at $\lambda_{\text{max}} = 415 \text{ nm}$. After irradiation, the phenanthroline solution (0.35 mL) was added to the cuvette and the mixture was allowed to stir in the dark for 1 h to allow the ferrous ions to completely coordinate to the phenanthroline. The absorbance of the solution was measured at 510 nm. A non-irradiated sample was also prepared and the absorbance at 510 nm was measured. Conversion was

calculated using eq 1.

$$\text{mol of Fe}^{2+} = \frac{V \cdot \Delta A_{510 \text{ nm}}}{l \cdot \epsilon} = \frac{(0.00235 \text{ L}) \cdot (2.24)}{(1.00 \text{ cm}) \cdot (11,100 \frac{\text{L}}{\text{mol} \cdot \text{cm}})} = 4.74 \times 10^{-7} \text{ mol} \quad (1)$$

V is the total volume (0.00235 L) of the solution after addition of phenanthroline, ΔA is the difference in absorbance at 510 nm between the irradiated and non-irradiated solutions, l is the path length (1.00 cm), and ϵ is the molar absorptivity of the ferrioxalate actinometer at 510 nm (11,100 Lmol⁻¹cm⁻¹).^{S3} The photon flux can be calculated using eq 2.

$$\text{Photon flux} = \frac{\text{mol of Fe}^{2+}}{\Phi \cdot t \cdot f} = \frac{4.74 \times 10^{-7} \text{ mol}}{(1.12) \cdot (45 \text{ s}) \cdot (0.999)} = 9.41 \times 10^{-9} \text{ einstein/s} \quad (2)$$

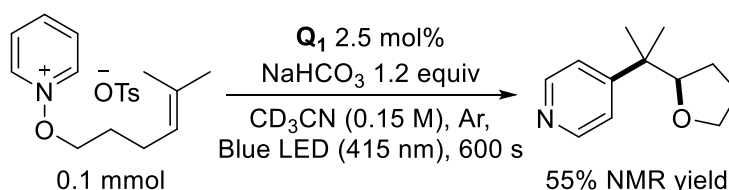
Where Φ is the quantum yield for the ferrioxalate actinometer (1.12 at $\lambda = 415 \text{ nm}$),^{S4} t is the irradiation time (45 s), and f is the fraction of light absorbed at 415 nm by the ferrioxalate actinometer. This value is calculated using eq 3 where $A_{415 \text{ nm}}$ is the absorbance of the ferrioxalate solution at 415 nm. An absorption spectrum gave an $A_{415 \text{ nm}}$ value of > 3, indicating that the fraction of absorbed light (f) is > 0.999.

$$f = 1 - 10^{-A_{415 \text{ nm}}} \quad (3)$$

The photon flux was thus calculated (average of three experiments) to be $9.41 \times 10^{-9} \text{ einstein s}^{-1}$

Determination of the reaction quantum yield.

Scheme S3.



The reaction mixture was stirred and irradiated by blue LED ($\lambda_{\text{max}} = 415 \text{ nm}$) for 600 s. After irradiation, the reaction mixture was passed through a celite plug. The yield of product was determined by ¹H NMR analysis using caffeine as an internal standard. The yield of **3a** was determined to be 55% ($55 \times 10^{-6} \text{ mol}$ of **3a**). The reaction quantum yield (Φ) was determined using eq 4 where the photon flux is $5.09 \times 10^{-9} \text{ einsteins s}^{-1}$ (determined by actinometry as described above), t is the reaction time (600 s) and f is the fraction of incident light absorbed by the catalyst, determined using eq 3. An absorption spectrum of the catalyst gave an absorbance value of 2.28 at 415 nm, indicating that the fraction of light absorbed by the photocatalyst (f) is 0.995.

$$\Phi = \frac{\text{mol of product}}{\text{flux} \cdot t \cdot f} \quad (4)$$

$$\Phi = \frac{55 \times 10^{-6} \text{ mol}}{9.41 \times 10^{-9} \text{ einstein s}^{-1} \cdot 600 \text{ s} \cdot 0.995} = 9.8$$

The reaction quantum yield (Φ) was calculated to be 9.8.

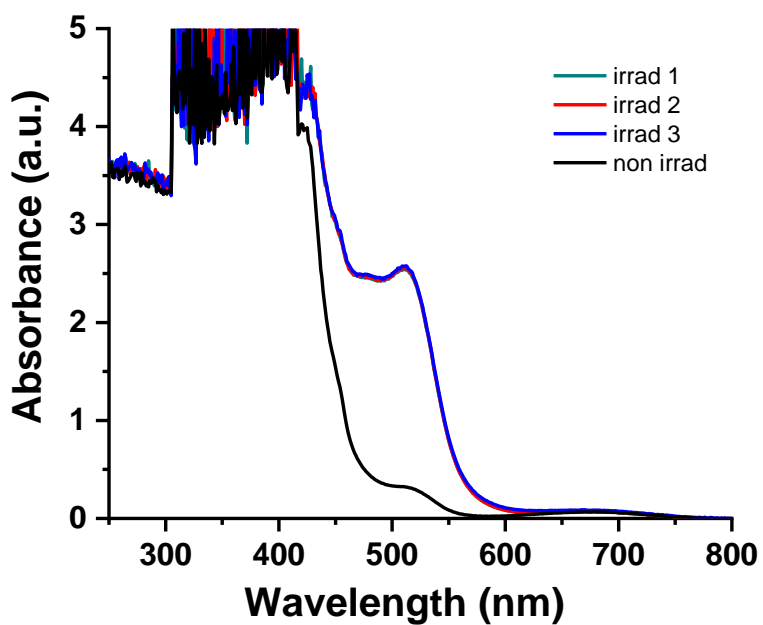


Figure S1. Three irradiation experiments and non-irradiation experiment absorption spectra

III. Absorption spectra

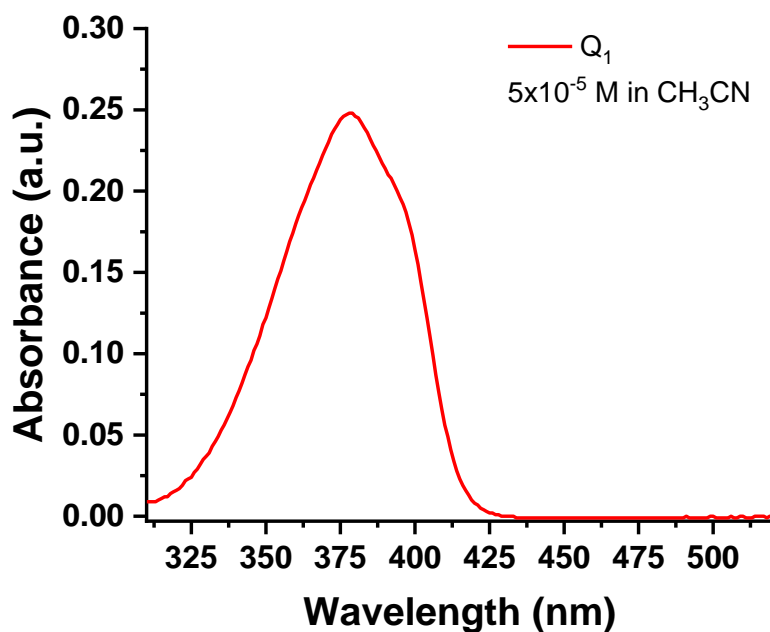


Figure S2. Absorption spectra of Q_1 . (5×10^{-5} M in acetonitrile). The wavelength of maximum absorbance is 378 nm. The tail wavelength was considered about 437 nm.

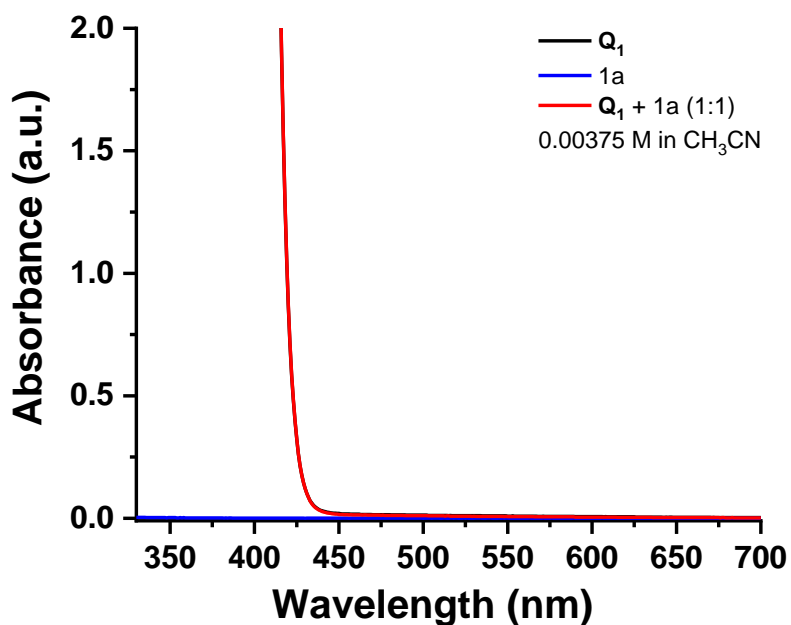


Figure S3. Absorption spectra of Q_1 , $1a$, and mixture of Q_1 and $1a$ (0.00375 M in acetonitrile).

IV. Stern–Volmer quenching experiment

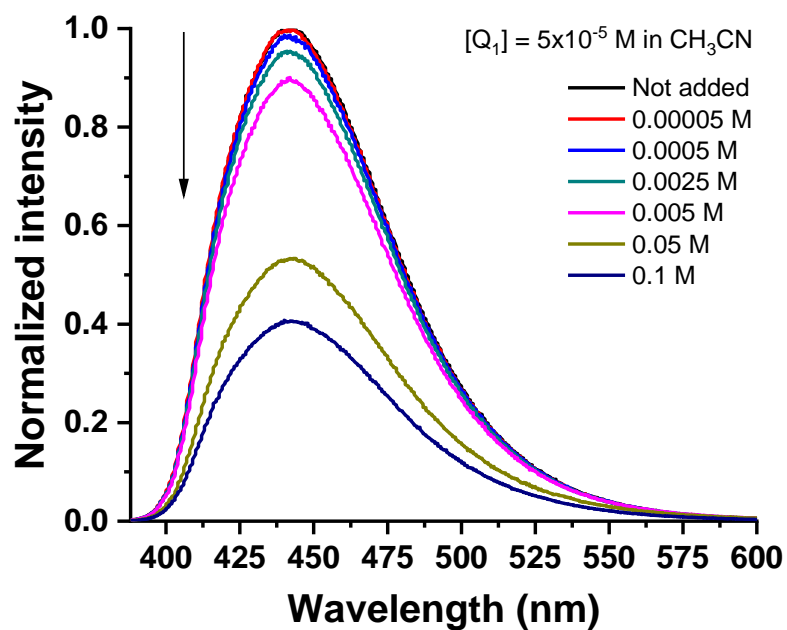


Figure S4. Quenching of the photoredox catalyst **Q₁** emission (5×10⁻⁵ M in acetonitrile) in the presence of increasing amounts of pyridinium salt (**1a**). Excitation wavelength : 378 nm, Bandwidth : Ex 3.0 nm, Em 3.0 nm

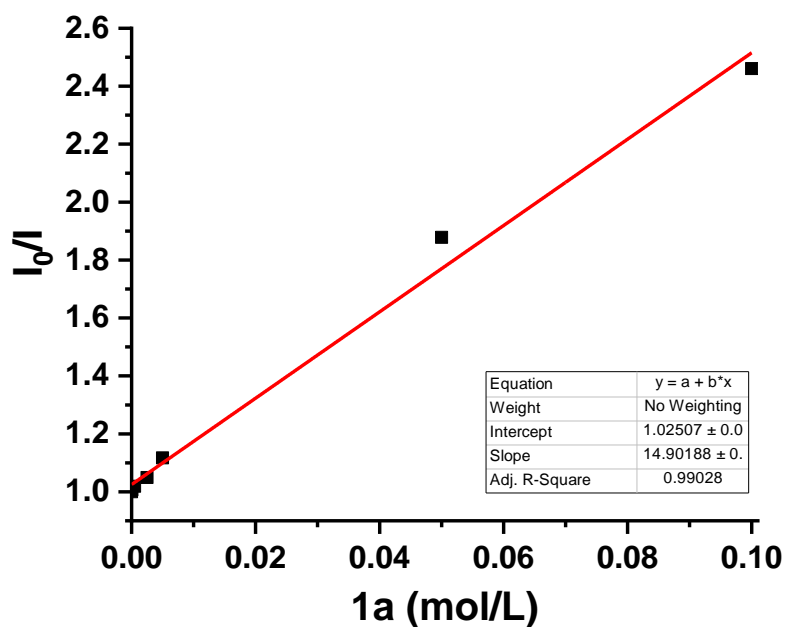


Figure S5. Stern-Volmer quenching plot.

V. Cyclic Voltammetry

Cyclic voltammetry was measured by a potentiostat (CH instrument, 600E) with conventional three electrode system (Reference electrode: Ag/Ag^+ , working electrode: Glassy carbon, counter electrode: Pt wire, Supporting electrolyte: 0.1 M NBu_4PF_6 CH_3CN) at 50 mV/sec of scan rate.

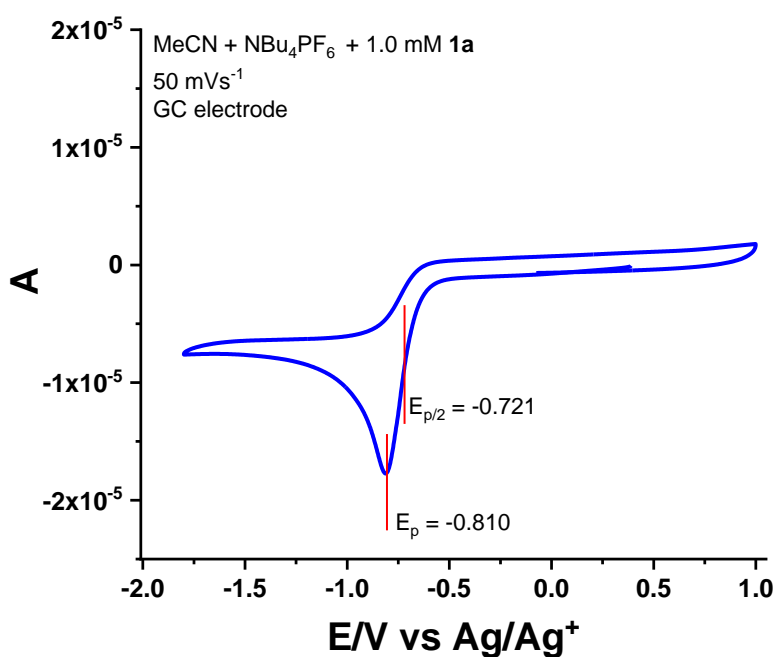


Figure S6. CV of **1a** (1 mM in CH_3CN)

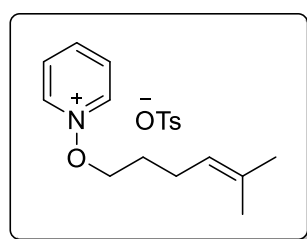
References

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- [S2] M. A. Cismesia, T. P. Yoon, *Chem. Sci.* **2015**, *6*, 5426.
- [S3] H. J. Kuhn, S. E. Braslavsky, R. Schmidt, *Pure Appl. Chem.* **2004**, *76*, 2105.
- [S4] E. E. Wegner, A. W. Adamson, *J. Am. Chem. Soc.* **1966**, *88*, 394.

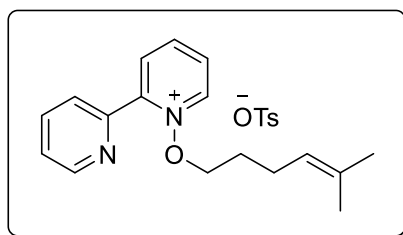
VI. Experimental Procedure and Compound Characterizations

General Procedure for *N*-alkenyloxypyridinium Salts (GP1)

Pyridine *N*-oxide (1 mmol) and appropriate alkyl tosylate (1.1 mmol) were stirred in CH₃CN (1.4 mL) for overnight at 80 °C. The reaction solvent was evaporated under reduced pressure. The product was recrystallized from CH₂Cl₂ (1 mL) and diethyl ether (100 mL) solution at 0 °C. A white solid product was obtained.

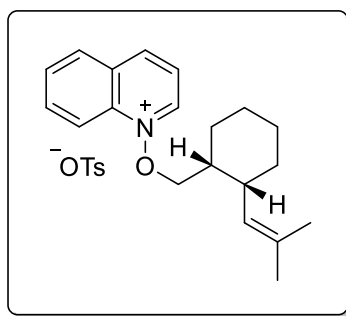


1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (1a). Prepared according to **GP1**. **1a** (265.3 mg; 73%) was obtained. White solid. ¹H NMR (600 MHz, Methylene Chloride-*d*₂) δ 9.41 (d, *J* = 6.3 Hz, 2H), 8.46 (t, *J* = 7.8 Hz, 1H), 8.18 (t, *J* = 7.1 Hz, 2H), 7.66 (d, *J* = 7.7 Hz, 2H), 7.11 (d, *J* = 7.7 Hz, 2H), 5.05 (t, *J* = 7.4 Hz, 1H), 4.58 (t, *J* = 6.6 Hz, 2H), 2.30 (s, 3H), 2.07 (q, *J* = 7.5 Hz, 2H), 1.75 (p, *J* = 7.1 Hz, 2H), 1.66 (s, 3H), 1.57 (s, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 145.2, 145.0, 141.9, 139.5, 133.5, 130.3, 128.9, 126.1, 122.7, 83.7, 28.0, 25.7, 24.0, 21.3, 17.8. HRMS (FAB) *m/z* calcd. For C₁₂H₁₈NO⁺ [M-OTs]⁺: 192.1383, found : 192.1389.

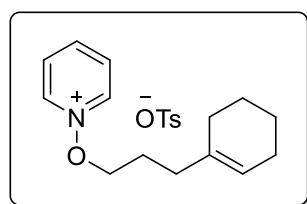


1-((5-methylhex-4-en-1-yl)oxy)-[2,2'-bipyridin]-1-ium 4-methylbenzenesulfonate (1h). Prepared according to **GP1**. **1h** (158.6 mg; 36%) was obtained. Yellow gum. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 9.89 (dd, *J* = 6.6, 1.3 Hz, 1H), 8.86 (ddd, *J* = 4.8, 1.8, 1.0 Hz, 1H), 8.57 (td, *J* = 7.8, 1.3 Hz, 1H), 8.43 (ddd, *J* = 7.7, 6.6, 2.0 Hz, 1H), 8.31 (dd, *J* = 7.9, 2.0 Hz, 1H), 8.06 (dt, *J* = 8.0, 1.1 Hz, 1H), 7.99 (td, *J* = 7.8, 1.7 Hz, 1H), 7.69 – 7.66 (m, 2H), 7.60 (ddd, *J* = 7.6, 4.8, 1.3 Hz, 1H), 7.16 – 7.12 (m, 2H), 4.92 (ddt, *J* = 7.1, 5.7, 1.5 Hz, 1H), 4.55 (t, *J* = 6.5 Hz, 2H), 2.34 (s, 3H), 1.90 (d, *J* = 7.5 Hz,

2H), 1.69 (dt, $J = 8.5, 6.5$ Hz, 2H), 1.64 (d, $J = 1.4$ Hz, 3H), 1.51 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 151.3, 150.5, 147.0, 145.6, 145.4, 144.3, 139.5, 138.0, 133.8, 131.3, 130.8, 129.0, 126.9, 126.4, 122.7, 84.8, 28.2, 25.9, 24.2, 21.5, 18.0. HRMS (FAB) m/z calcd. For $\text{C}_{17}\text{H}_{21}\text{N}_2\text{O}^+$ [M-OTs] $^+$: 269.1648, found : 269.1651.

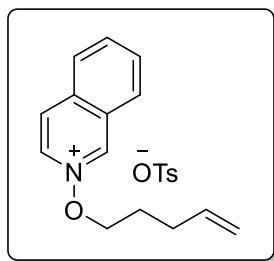


1-(((1R,2R)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)quinolin-1-ium 4-methylbenzenesulfonate (1o). Prepared according to **GP1**. **1o** (140.3 mg; 30%) was obtained. Pale yellow solid. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 10.21 (d, $J = 5.1$ Hz, 1H), 9.14 – 9.07 (m, 1H), 8.39 (d, $J = 8.2$ Hz, 1H), 8.36 – 8.28 (m, 2H), 8.17 (ddd, $J = 8.7, 7.0, 1.2$ Hz, 1H), 7.99 (t, $J = 7.6$ Hz, 1H), 7.69 (d, $J = 7.9$ Hz, 2H), 7.11 (d, $J = 7.7$ Hz, 2H), 5.45 (d, $J = 9.8$ Hz, 1H), 4.52 (dd, $J = 7.1, 2.2$ Hz, 2H), 2.90 (dq, $J = 8.6, 4.1$ Hz, 1H), 2.40 – 2.32 (m, 1H), 2.32 (s, 3H), 1.79 (dt, $J = 12.7, 3.8$ Hz, 1H), 1.75 (s, 3H), 1.72 (dt, $J = 13.1, 3.8$ Hz, 1H), 1.68 (s, 3H), 1.64 – 1.44 (m, 5H), 1.40 (qt, $J = 12.2, 9.5$ Hz, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 146.6, 146.3, 145.4, 139.4, 136.8, 136.6, 134.4, 131.4, 131.4, 131.0, 128.9, 126.4, 124.0, 123.6, 116.4, 87.1, 39.8, 34.5, 32.3, 26.5, 25.7, 24.8, 22.0, 21.5, 18.3. HRMS (FAB) m/z calcd. For $\text{C}_{20}\text{H}_{26}\text{NO}^+$ [M-OTs] $^+$: 296.2009, found : 296.2011.

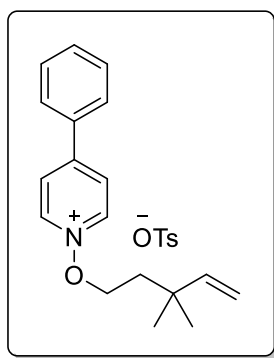


1-(3-(cyclohex-1-en-1-yl)propoxy)pyridin-1-ium 4-methylbenzenesulfonate (1u). Prepared according to **GP1**. **1u** (253.2 mg; 65%) was obtained. White solid. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 9.38 (d, $J = 6.3$ Hz, 2H), 8.47 (t, $J = 7.7$ Hz, 1H), 8.21 (t, $J = 7.1$ Hz, 2H), 7.67 (d, $J = 7.9$ Hz, 2H), 7.13 (d, $J = 7.8$ Hz, 2H), 5.43 (s, 1H), 4.65 (t, $J = 6.4$ Hz, 2H), 2.33 (s, 3H), 2.06 (t, $J = 7.8$ Hz, 2H), 1.97 (ddq, $J = 6.2, 4.2, 2.1$ Hz, 2H), 1.91 – 1.85 (m, 4H), 1.64 – 1.58 (m, 2H), 1.56 – 1.51 (m, 2H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 145.3, 145.2, 142.0, 139.6, 136.4, 130.5, 129.1,

126.3, 122.8, 84.3, 34.0, 28.6, 26.1, 25.7, 23.4, 23.0, 21.5. HRMS (FAB) m/z calcd. For $C_{14}H_{20}NO^+ [M-OTs]^-$: 218.1539, found : 218.1543.

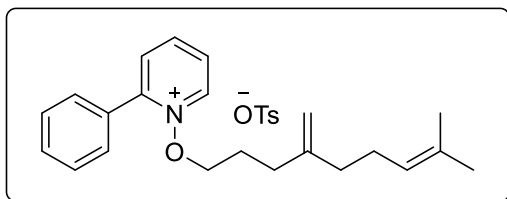


2-(pent-4-en-1-yloxy)isoquinolin-2-ium 4-methylbenzenesulfonate (1aa). Prepared according to **GP1**. **1aa** (273.7 mg; 71%) was obtained. White solid. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 10.98 (d, $J = 2.2$ Hz, 1H), 8.87 (dq, $J = 8.5, 1.0$ Hz, 1H), 8.55 (dd, $J = 7.2, 2.2$ Hz, 1H), 8.34 (dt, $J = 7.2, 0.6$ Hz, 1H), 8.19 – 8.14 (m, 2H), 8.02 (dt, $J = 8.3, 4.1$ Hz, 1H), 7.74 – 7.67 (m, 2H), 7.16 – 7.11 (m, 2H), 5.85 (ddt, $J = 16.9, 10.2, 6.6$ Hz, 1H), 5.11 (dq, $J = 17.1, 1.7$ Hz, 1H), 5.04 (ddt, $J = 10.2, 2.0, 1.3$ Hz, 1H), 4.86 (t, $J = 6.4$ Hz, 2H), 2.34 (s, 3H), 2.28 (dt, $J = 7.8, 6.4, 1.4$ Hz, 2H), 1.98 (dq, $J = 8.8, 6.5$ Hz, 2H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 146.5, 145.4, 139.6, 137.6, 137.5, 137.1, 132.3, 132.1, 132.0, 129.0, 128.8, 128.4, 127.9, 126.3, 116.1, 83.6, 29.9, 27.3, 21.5. HRMS (FAB) m/z calcd. For $C_{14}H_{16}NO^+ [M-OTs]^-$: 214.1226, found : 214.1235.

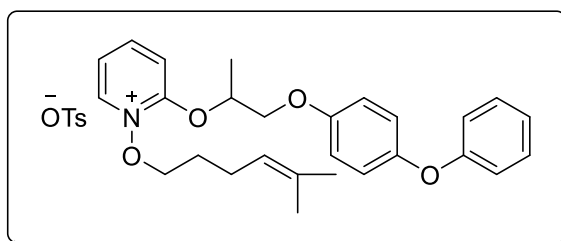


1-((3,3-dimethylpent-4-en-1-yl)oxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (1ac). Prepared according to **GP1**. **1ac** (356.0 mg; 81%) was obtained. White solid. 1H NMR (600 MHz, Methylene Chloride- d_2) δ 9.34 – 9.30 (m, 2H), 8.34 (d, $J = 7.0$ Hz, 2H), 7.81 – 7.77 (m, 2H), 7.73 – 7.69 (m, 2H), 7.61 – 7.56 (m, 1H), 7.53 (td, $J = 8.0, 2.7$ Hz, 2H), 7.12 (d, $J = 7.8$ Hz, 2H), 5.80 (ddd, $J = 17.8, 10.4, 1.7$ Hz, 1H), 5.00 (d, $J = 1.7$ Hz, 1H), 4.97 (dt, $J = 5.5, 1.2$ Hz, 1H), 4.63 (td, $J = 7.0, 2.8$ Hz, 2H), 2.30 (s, 3H), 1.83 (td, $J = 7.1, 2.2$ Hz, 2H), 1.05 (d, $J = 1.8$ Hz, 6H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 156.3, 147.1, 145.4, 141.8, 139.6, 133.9, 132.9, 130.3, 129.1, 128.6, 126.9,

126.4, 112.2, 82.1, 39.5, 36.1, 27.3, 21.5. HRMS (FAB) m/z calcd. For $C_{18}H_{22}NO^+ [M-OTs]^-$: 268.1696, found : 268.1698.

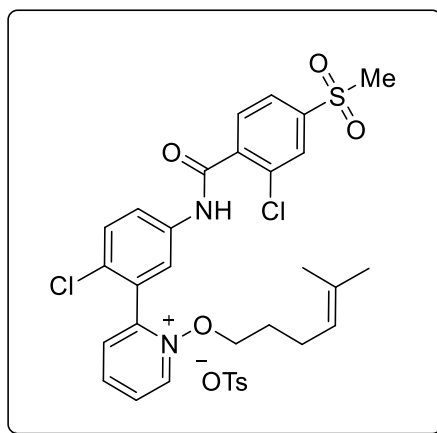


1-((8-methyl-4-methylenenon-7-en-1-yl)oxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (3c). Prepared according to **GP1**. **3c** (444.3 mg; 90%) was obtained. White solid. 1H NMR (600 MHz, Methylene Chloride- d_2) δ 9.74 – 9.68 (m, 1H), 8.62 (t, J = 7.1 Hz, 1H), 8.21 – 8.16 (m, 1H), 8.10 (d, J = 7.6 Hz, 1H), 7.74 (d, J = 6.8 Hz, 2H), 7.66 (dd, J = 8.0, 2.7 Hz, 2H), 7.64 – 7.61 (m, 1H), 7.60 – 7.55 (m, 2H), 7.10 (d, J = 7.0 Hz, 2H), 5.11 – 4.99 (m, 1H), 4.64 (s, 1H), 4.46 (s, 1H), 4.26 – 4.20 (m, 2H), 2.30 (s, 3H), 2.02 – 1.95 (m, 2H), 1.86 – 1.81 (m, 2H), 1.76 – 1.71 (m, 2H), 1.67 (s, 3H), 1.65 – 1.55 (m, 5H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 152.0, 148.0, 146.1, 145.2, 143.7, 139.2, 132.4, 131.9, 131.3, 130.4, 129.5, 129.3, 128.8, 128.4, 126.2, 124.2, 109.6, 83.2, 36.1, 31.7, 26.6, 25.8, 25.7, 21.3, 17.8. HRMS (FAB) m/z calcd. For $C_{22}H_{28}NO^+ [M-OTs]^-$: 322.2165, found : 322.2169.



1-((5-methylhex-4-en-1-yl)oxy)-2-((1-phenoxypentan-2-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (3e). Prepared according to **GP1**. **3e** (121.1 mg; 20%) was obtained. Colorless gum. 1H NMR (400 MHz, Methanol- d_4) δ 8.81 (dd, J = 6.8, 1.7 Hz, 1H), 8.41 (ddd, J = 9.1, 7.5, 1.8 Hz, 1H), 7.98 (dd, J = 9.0, 1.5 Hz, 1H), 7.76 – 7.69 (m, 4H), 7.56 – 7.47 (m, 1H), 7.32 – 7.23 (m, 2H), 7.22 – 7.16 (m, 4H), 7.07 – 6.99 (m, 1H), 6.90 (d, J = 1.8 Hz, 3H), 6.90 – 6.85 (m, 2H), 6.75 – 6.66 (m, 1H), 5.58 (pd, J = 6.5, 2.8 Hz, 1H), 5.09 (tp, J = 7.2, 1.4 Hz, 1H), 4.43 (t, J = 6.5 Hz, 2H), 4.35 (dd, J = 11.2, 2.5 Hz, 1H), 4.24 (dd, J = 11.1, 7.2 Hz, 1H), 2.32 (s, 6H), 2.11 (q, J = 7.0 Hz, 2H), 1.79 (p, J = 7.1 Hz, 2H), 1.65 (s, 3H), 1.64 (d, J = 6.4 Hz, 3H), 1.56 (s, 3H). ^{13}C NMR (100 MHz, Methanol- d_4) δ 159.5, 159.1, 155.6, 152.3, 148.0, 143.6, 141.5, 141.4, 133.8, 130.7 (d, J = 1.4 Hz), 129.8, 126.9, 123.9, 123.8, 121.7, 120.3, 118.7, 116.7, 115.4, 82.7, 81.7, 71.7, 29.0, 25.9, 24.9, 21.3,

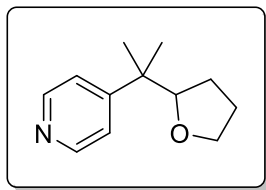
17.9, 16.2. HRMS (FAB) m/z calcd. For $C_{27}H_{32}NO_4^+ [M-OTs]^-$: 434.2326, found : 434.2334.



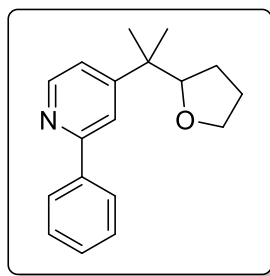
2-(2-chloro-5-(2-chloro-4-(methylsulfonyl)benzamido)phenyl)-1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (3f). Prepared according to **GP1**. **3f** (416.3 mg; 59%) was obtained. White solid. 1H NMR (400 MHz, Acetone- d_6) δ 10.96 (s, 1H), 9.69 (dd, J = 6.5, 1.3 Hz, 1H), 8.86 (td, J = 7.8, 1.3 Hz, 1H), 8.50 – 8.36 (m, 3H), 8.27 (dd, J = 8.9, 2.6 Hz, 1H), 8.00 (d, J = 1.7 Hz, 1H), 7.93 (dd, J = 8.0, 1.7 Hz, 1H), 7.85 (d, J = 8.0 Hz, 1H), 7.73 (d, J = 8.9 Hz, 1H), 7.54 (d, J = 8.2 Hz, 2H), 7.11 (d, J = 7.9 Hz, 2H), 5.00 – 4.86 (m, 1H), 4.72 – 4.41 (m, 2H), 3.20 (s, 3H), 2.31 (s, 3H), 1.76 (h, J = 7.4 Hz, 2H), 1.68 – 1.55 (m, 5H), 1.50 (s, 3H). ^{13}C NMR (100 MHz, Acetone- d_6) δ 165.19, 150.64, 146.71, 145.68, 144.51, 143.71, 141.41, 139.52, 139.43, 133.28, 132.81, 132.70, 131.20, 131.02, 130.79, 129.47, 129.11, 129.06, 128.31, 127.01, 126.71, 125.08, 123.62, 123.44, 84.44, 44.06, 28.64, 25.79, 24.34, 21.22, 17.80. HRMS (FAB) m/z calcd. For $C_{26}H_{27}Cl_2N_2O_4S^+ [M-OTs]^-$: 533.1063, found : 533.1072.

General Procedure for Visible-Light Induced Pyridylation (GP2)

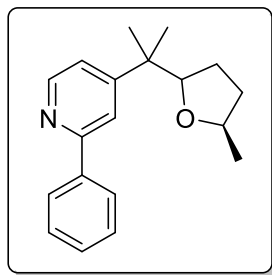
Reactions were conducted in cap test tube (12 mL) sealed by assembled screw cap with hole and PTFE/silicone septa. 1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (**1a**) (54.5 mg, 0.15 mmol), 3-(diphenylphosphoryl)-6-methoxy-1-methylquinolin-2(1H)-one (**Q1**) (1.5 mg, 0.00375 mmol), and $NaHCO_3$ (15.1 mg, 0.18 mmol) were combined in CH_3CN (1.0 mL) under argon atmosphere. The mixture was placed in the irradiation apparatus equipped with a blue LED. The resulting mixture was stirred at room temperature. The reaction mixture was monitored by TLC using ($CH_2Cl_2/MeOH$ = 15:1) as the mobile phase. After disappearance of starting material, the reaction mixture was diluted and filtered through a nylon syringe filter (pore size: 0.2 μm) with CH_2Cl_2 (10 mL). After removal of solvent, the residue was purified by flash chromatography on silica gel ($EtOAc/n$ -hexane = 1:2) to give the desired product compound **3a** (20.1 mg, 70%) as a pale yellow oil.



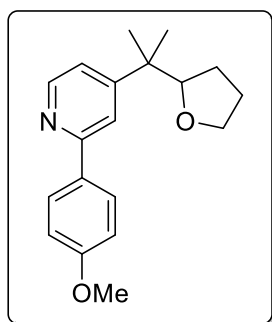
4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2a). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (54.5 mg, 0.15 mmol), compound **2a** (21.2 mg, 74%) was obtained. Pale yellow oil. ¹H NMR (600 MHz, Methylene Chloride-*d*₂) δ 8.46 (dd, *J* = 4.7, 1.5 Hz, 2H), 7.32 (dd, *J* = 4.7, 1.7 Hz, 2H), 3.90 (dd, *J* = 8.4, 6.5 Hz, 1H), 3.72 – 3.63 (m, 2H), 1.80 – 1.69 (m, 2H), 1.67 – 1.60 (m, 1H), 1.44 – 1.36 (m, 1H), 1.31 (s, 3H), 1.30 (s, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 156.8, 149.9, 122.9, 86.9, 69.0, 41.7, 27.6, 26.6, 24.9, 24.2. HRMS (EI) *m/z* calcd. For C₁₂H₁₇NO [M]⁺: 191.1310, found : 191.1311.



2-phenyl-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2b). Purified by flash chromatography on silica gel (Et₂O/*n*-hexane = 1:1.5). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (65.9 mg, 0.15 mmol), compound **2b** (29.3 mg, 73%) was obtained. Colorless oil. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.55 (dd, *J* = 5.3, 0.8 Hz, 1H), 8.03 – 7.98 (m, 2H), 7.81 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.50 – 7.44 (m, 2H), 7.43 – 7.38 (m, 1H), 7.29 (dd, *J* = 5.3, 1.8 Hz, 1H), 3.95 (dd, *J* = 8.6, 6.4 Hz, 1H), 3.74 – 3.68 (m, 2H), 1.80 – 1.72 (m, 2H), 1.69 – 1.62 (m, 1H), 1.48 – 1.40 (m, 1H), 1.37 (s, 3H), 1.36 (s, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 157.7, 157.3, 149.7, 140.5, 129.2, 127.5, 127.5, 121.6, 119.8, 87.0, 69.1, 42.0, 27.7, 26.7, 25.0, 24.4. HRMS (EI) *m/z* calcd. For C₁₈H₂₁NO [M]⁺: 267.1623, found : 267.1624.

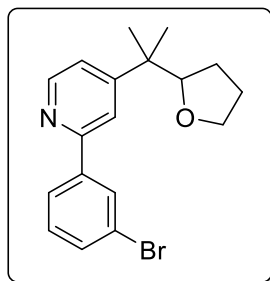


4-(2-((5R)-5-methyltetrahydrofuran-2-yl)propan-2-yl)-2-phenylpyridine (2c). d.r. 2.0:1. Purified by flash chromatography on silica gel ($\text{Et}_2\text{O}/n\text{-hexane} = 1:2.5$). Prepared according to **GP2**. From (*R*)-1-((6-methylhept-5-en-2-yl)oxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (68.0 mg, 0.15 mmol), compound **2c** (31.4 mg, 72%) was obtained. Colorless oil. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.56 (dd, $J = 5.3, 0.8$ Hz, 1H), 8.04 – 7.98 (m, 2H), 7.84 – 7.80 (m, 1H), 7.50 – 7.44 (m, 2H), 7.44 – 7.38 (m, 1H), 7.30 (dd, $J = 5.3, 1.8$ Hz, 1H), 4.12 (dd, $J = 9.0, 6.0$ Hz, 0.65H – major isomer), 3.97 (t, $J = 7.5$ Hz, 0.35H – minor isomer), 3.93 – 3.85 (m, 1H), 1.90 – 1.69 (m, 2H), 1.55 – 1.38 (m, 2H), 1.38 – 1.34 (m, 6H), 1.17 (d, $J = 6.1$ Hz, 1.95H – major isomer), 1.14 (d, $J = 6.0$ Hz, 1.05H – minor isomer). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 157.6, 157.3, 157.2, 149.7, 149.6, 140.6, 140.6, 129.2, 129.2, 129.1, 127.4, 127.4, 121.7, 121.7, 119.8, 119.8, 86.8, 86.6, 76.6, 75.9, 42.3, 41.7, 34.8, 33.5, 28.8, 27.5, 25.0, 24.5, 24.5, 21.5, 21.2. HRMS (EI) m/z calcd. For $\text{C}_{19}\text{H}_{23}\text{NO}$ $[\text{M}]^+$: 281.1780, found: 281.1781.

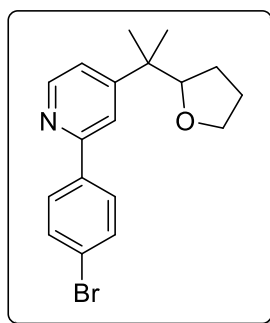


2-(4-methoxyphenyl)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2d). Purified by flash chromatography on silica gel ($\text{Et}_2\text{O}/n\text{-hexane} = 1:1.5$). Prepared according to **GP2**. From 2-(4-methoxyphenyl)-1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (70.4 mg, 0.15 mmol), compound **2d** (32.6 mg, 73%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.50 (dd, $J = 5.3, 0.8$ Hz, 1H), 7.96 (d, $J = 8.9$ Hz, 2H), 7.74 (dd, $J = 1.8, 0.8$ Hz, 1H), 7.23 (dd, $J = 5.3, 1.8$ Hz, 1H), 6.99 (d, $J = 8.9$ Hz, 2H), 3.98 – 3.92 (m, 1H), 3.85 (s, 3H), 3.73 – 3.68 (m, 2H), 1.81 – 1.72 (m, 2H), 1.69 – 1.63 (m, 1H), 1.47 – 1.40 (m, 1H), 1.36 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 160.9, 157.5, 157.0, 149.6, 133.1, 128.7, 120.9,

118.9, 114.5, 87.0, 69.1, 55.9, 41.9, 27.7, 26.7, 24.9, 24.5. HRMS (EI) m/z calcd. For $C_{19}H_{23}NO_2$ $[M]^+$: 297.1729, found : 297.1729.

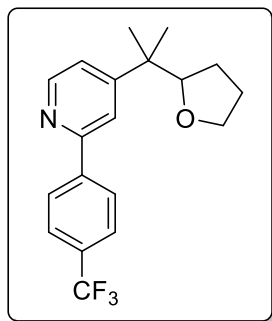


2-(3-bromophenyl)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2e). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 2-(3-bromophenyl)-1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (77.8 mg, 0.15 mmol), compound **2e** (45.7 mg, 88%) was obtained. Colorless gum. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.56 (dd, J = 5.2, 0.8 Hz, 1H), 8.19 (t, J = 1.8 Hz, 1H), 7.95 (ddd, J = 7.8, 1.7, 1.1 Hz, 1H), 7.78 (dd, J = 1.8, 0.8 Hz, 1H), 7.54 (ddd, J = 7.9, 2.0, 1.1 Hz, 1H), 7.35 (t, J = 7.9 Hz, 1H), 7.32 (dd, J = 5.2, 1.8 Hz, 1H), 3.98 – 3.91 (m, 1H), 3.73 – 3.67 (m, 2H), 1.85 – 1.72 (m, 2H), 1.71 – 1.60 (m, 1H), 1.47 – 1.39 (m, 1H), 1.37 (s, 3H), 1.36 (s, 3H). ^{13}C NMR (151 MHz, Methylene Chloride- d_2) δ 157.9, 155.7, 149.8, 142.7, 132.1, 130.7, 130.5, 126.1, 123.3, 122.2, 119.8, 86.9, 69.1, 42.0, 27.8, 26.7, 25.2, 24.3. HRMS (EI) m/z calcd. For $C_{18}H_{20}BrNO$ $[M]^+$: 345.0728, found : 345.0729.

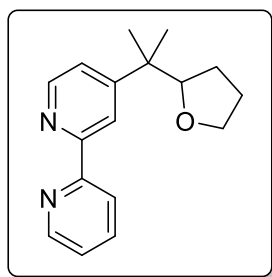


2-(4-bromophenyl)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2f). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 2-(4-bromophenyl)-1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (77.8 mg, 0.15 mmol), compound **2f** (43.1 mg, 83%) was obtained. Colorless gum. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.55 (dd, J = 5.3, 0.8 Hz, 1H), 7.95 – 7.88 (m, 2H), 7.79 (dd, J = 1.8, 0.8 Hz, 1H), 7.64 – 7.56 (m, 2H), 7.31 (dd, J = 5.3, 1.8 Hz, 1H), 3.98 – 3.90 (m, 1H), 3.74 – 3.66 (m, 2H), 1.85 – 1.71 (m, 2H), 1.71 – 1.61 (m, 1H), 1.47 – 1.38 (m, 1H), 1.37 (s, 3H), 1.35 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 157.9, 156.1, 149.8, 139.5, 132.2, 129.1, 123.5, 121.9, 119.5, 87.0,

69.1, 42.0, 27.8, 26.7, 25.2, 24.3. HRMS (EI) m/z calcd. For $C_{18}H_{20}BrNO$ $[M]^+$: 345.0728, found : 345.0726.

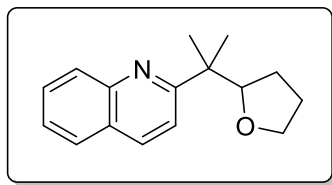


4-(2-(tetrahydrofuran-2-yl)propan-2-yl)-2-(4-(trifluoromethyl)phenyl)pyridine (2g). Purified by flash chromatography on silica gel (Et_2O/n -hexane = 1:2). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)-2-(4-(trifluoromethyl)phenyl)pyridin-1-ium 4-methylbenzenesulfonate (76.1 mg, 0.15 mmol), compound **2g** (36.7 mg, 73%) was obtained. Colorless oil. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.59 (dd, J = 5.3, 0.8 Hz, 1H), 8.15 (d, J = 8.0 Hz, 2H), 7.86 (dd, J = 1.8, 0.8 Hz, 1H), 7.73 (d, J = 8.2 Hz, 2H), 7.36 (dd, J = 5.2, 1.8 Hz, 1H), 3.98 – 3.92 (m, 1H), 3.74 – 3.67 (m, 2H), 1.84 – 1.73 (m, 2H), 1.70 – 1.61 (m, 1H), 1.48 – 1.40 (m, 1H), 1.38 (s, 3H), 1.37 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 158.1, 155.8, 150.0, 144.1, 130.8 (q, J_{C-F} = 32.3 Hz), 127.8, 126.1 (q, J_{C-F} = 3.9 Hz), 125.0 (q, J_{C-F} = 272.1 Hz), 122.5, 120.2, 87.0, 69.1, 42.0, 27.8, 26.7, 25.3, 24.2. HRMS (EI) m/z calcd. For $C_{19}H_{20}F_3NO$ $[M]^+$: 335.1497, found : 335.1498.

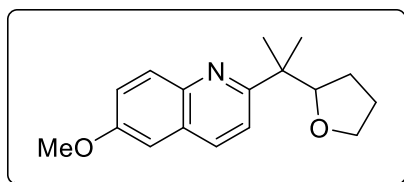


4-(2-(tetrahydrofuran-2-yl)propan-2-yl)-2,2'-bipyridine (2h). Purified by flash chromatography on alumina basic ($EtOAc/n$ -hexane = 1:4). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)-[2,2'-bipyridin]-1-ium 4-methylbenzenesulfonate (66.1 mg, 0.15 mmol), compound **2h** (22.9 mg, 57%) was obtained. Colorless gum. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.66 (ddd, J = 4.8, 1.8, 0.9 Hz, 1H), 8.55 (dd, J = 5.2, 0.8 Hz, 1H), 8.48 (dd, J = 2.0, 0.8 Hz, 1H), 8.42 (dt, J = 8.0, 1.1 Hz, 1H), 7.81 (ddd, J = 8.0, 7.5, 1.8 Hz, 1H), 7.38 (dd, J = 5.2, 2.0 Hz, 1H), 7.30 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 4.03 – 3.95 (m, 1H), 3.77 – 3.65 (m, 2H), 1.83 – 1.72 (m, 2H), 1.72 – 1.64 (m, 1H), 1.51 – 1.42 (m, 1H), 1.38 (s, 3H), 1.38 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 158.0, 157.1,

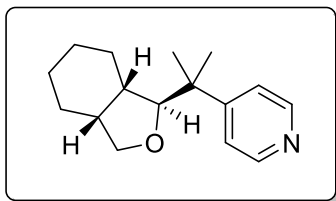
156.2, 149.6, 149.3, 137.3, 124.1, 123.1, 121.5, 119.8, 86.9, 69.1, 42.1, 27.7, 26.7, 24.9, 24.3. HRMS (EI) m/z calcd. For $C_{17}H_{20}N_2O$ $[M]^+$: 268.1576, found : 268.1578.



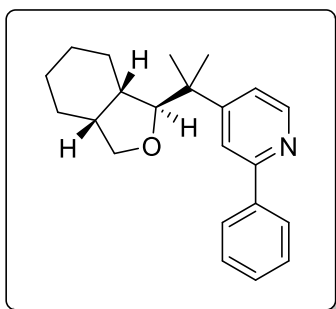
2-(2-(tetrahydrofuran-2-yl)propan-2-yl)quinolone (2i). Purified by flash chromatography on silica gel (Et_2O/n -hexane = 1:2). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)quinolin-1-ium 4-methylbenzenesulfonate (62.0 mg, 0.15 mmol), compound **2i** (18.4 mg, 51%) was obtained. Pale yellow oil. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.08 (dd, J = 8.7, 0.8 Hz, 1H), 8.00 (dd, J = 8.6, 1.1 Hz, 1H), 7.79 (dd, J = 8.1, 1.5 Hz, 1H), 7.67 (ddd, J = 8.5, 6.9, 1.5 Hz, 1H), 7.61 (d, J = 8.7 Hz, 1H), 7.49 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 4.25 – 4.19 (m, 1H), 3.73 – 3.63 (m, 2H), 1.82 – 1.73 (m, 2H), 1.67 – 1.57 (m, 2H), 1.47 (s, 3H), 1.44 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 167.4, 147.9, 135.8, 129.8, 129.4, 127.9, 127.2, 126.2, 120.6, 87.0, 69.0, 45.2, 27.5, 26.7, 24.3, 24.1. HRMS (EI) m/z calcd. For $C_{16}H_{19}NO$ $[M]^+$: 241.1467, found : 241.1465.



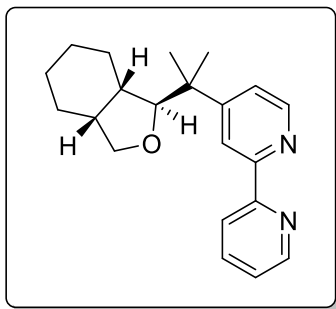
6-methoxy-2-(2-(tetrahydrofuran-2-yl)propan-2-yl)quinolone (2j). Purified by flash chromatography on silica gel (Et_2O/n -hexane = 1:1). Prepared according to **GP2**. From 6-methoxy-1-((5-methylhex-4-en-1-yl)oxy)quinolin-1-ium 4-methylbenzenesulfonate (66.5 mg, 0.15 mmol), compound **2j** (24.4 mg, 60%) was obtained. Pale yellow gum. 1H NMR (400 MHz, Methylene Chloride- d_2) δ 7.98 (dd, J = 8.7, 0.8 Hz, 1H), 7.88 (d, J = 9.2 Hz, 1H), 7.55 (d, J = 8.7 Hz, 1H), 7.30 (dd, J = 9.2, 2.8 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 4.22 – 4.16 (m, 1H), 3.91 (s, 3H), 3.73 – 3.62 (m, 2H), 1.82 – 1.71 (m, 2H), 1.67 – 1.56 (m, 2H), 1.45 (s, 3H), 1.41 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 164.8, 157.9, 143.9, 134.7, 131.2, 128.0, 121.9, 120.8, 105.5, 87.0, 68.9, 56.1, 44.9, 27.5, 26.7, 24.3, 24.1. HRMS (EI) m/z calcd. For $C_{17}H_{21}NO_2$ $[M]^+$: 271.1572, found : 241.1575.



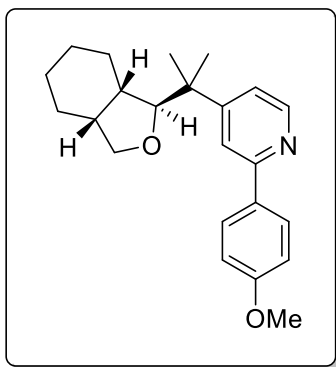
rel-4-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)pyridine (2k). Purified by flash chromatography on silica gel (Et₂O/*n*-hexane = 2:1). Prepared according to **GP2**. From 1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)pyridin-1-ium 4-methylbenzenesulfonate (62.6 mg, 0.15 mmol), compound **2k** (22.8 mg, 62%) was obtained. Colorless oil. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.46 (d, *J* = 6.3 Hz, 2H), 7.31 (d, *J* = 6.3 Hz, 2H), 3.76 (d, *J* = 5.3 Hz, 1H), 3.60 (dd, *J* = 7.9, 6.0 Hz, 1H), 3.52 (dd, *J* = 7.9, 6.6 Hz, 1H), 1.90 – 1.82 (m, 1H), 1.82 – 1.75 (m, 1H), 1.52 – 1.33 (m, 5H), 1.31 (s, 6H), 1.29 – 1.11 (m, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 156.6, 149.8, 122.9, 90.7, 72.3, 42.5, 39.4, 39.0, 28.8, 25.5, 25.0, 24.3, 23.6, 23.6. HRMS (EI) *m/z* calcd. For C₁₆H₂₃NO [M]⁺: 245.1780, found: 245.1776.



rel-4-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)-2-phenylpyridine (2l). Purified by flash chromatography on silica gel (Et₂O/*n*-hexane = 1:2). Prepared according to **GP2**. From 1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (74.0 mg, 0.15 mmol), compound **2l** (41.0 mg, 85%) was obtained. Colorless gum. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.56 (dd, *J* = 5.3, 0.8 Hz, 1H), 8.05 – 7.97 (m, 2H), 7.80 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.52 – 7.43 (m, 2H), 7.46 – 7.36 (m, 1H), 7.29 (dd, *J* = 5.3, 1.8 Hz, 1H), 3.84 (d, *J* = 5.4 Hz, 1H), 3.64 (dd, *J* = 7.9, 6.0 Hz, 1H), 3.56 (dd, *J* = 7.9, 6.7 Hz, 1H), 1.86 (dq, *J* = 24.7, 6.0 Hz, 2H), 1.57 – 1.37 (m, 5H), 1.38 (s, 6H), 1.33 – 1.18 (m, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 157.5, 157.3, 149.7, 140.6, 129.2, 129.1, 127.5, 121.6, 119.7, 90.9, 72.4, 42.7, 39.5, 39.1, 28.9, 25.6, 25.2, 24.4, 23.7, 23.6. HRMS (EI) *m/z* calcd. For C₂₂H₂₇NO [M]⁺: 321.2093, found: 321.2094.

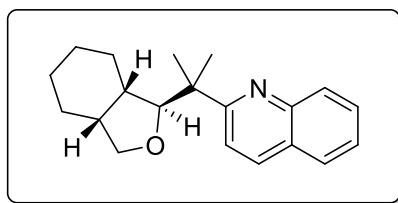


rel-4-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)-2,2'-bipyridine (2m). Purified by flash chromatography on alumina basic (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)-[2,2'-bipyridin]-1-ium 4-methylbenzenesulfonate (74.2 mg, 0.15 mmol), compound **2m** (28.0 mg, 58%) was obtained. Colorless gum. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.66 (ddd, *J* = 4.8, 1.9, 1.0 Hz, 1H), 8.54 (dd, *J* = 5.3, 0.8 Hz, 1H), 8.48 (dd, *J* = 2.0, 0.7 Hz, 1H), 8.42 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.81 (td, *J* = 7.7, 1.8 Hz, 1H), 7.37 (dd, *J* = 5.2, 2.0 Hz, 1H), 7.30 (ddd, *J* = 7.5, 4.8, 1.2 Hz, 1H), 3.85 (d, *J* = 5.3 Hz, 1H), 3.64 (dd, *J* = 7.9, 6.0 Hz, 1H), 3.55 (dd, *J* = 7.9, 6.8 Hz, 1H), 1.96 – 1.89 (m, 1H), 1.88 – 1.79 (m, 1H), 1.52 – 1.41 (m, 4H), 1.41 – 1.35 (m, 7H), 1.33 – 1.25 (m, 1H), 1.24 – 1.18 (m, 2H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 157.8, 157.1, 156.2, 149.6, 149.2, 137.3, 124.1, 123.2, 121.5, 119.7, 90.9, 72.3, 42.8, 39.5, 39.1, 28.9, 25.5, 25.1, 24.4, 23.7, 23.6. HRMS (EI) *m/z* calcd. For C₂₁H₂₆N₂O [M]⁺: 322.2045, found : 322.2044.

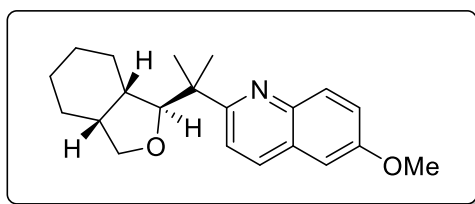


rel-2-(4-methoxyphenyl)-4-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)pyridine (2n). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 2-(4-methoxyphenyl)-1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)pyridin-1-ium 4-methylbenzenesulfonate (78.6 mg, 0.15 mmol), compound **2n** (35.3 mg, 67%) was obtained. Colorless oil. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.50 (dd, *J* = 5.3, 0.8 Hz, 1H), 8.00 – 7.92 (m, 2H), 7.72 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.22 (dd, *J* = 5.3, 1.8 Hz, 1H), 7.04 – 6.95 (m, 2H), 3.85 (s, 3H), 3.82 (d, *J* = 5.3 Hz, 1H), 3.63 (dd, *J* = 7.9, 6.0 Hz, 1H), 3.55 (dd, *J* = 7.9, 6.6 Hz, 1H), 1.94 – 1.75 (m, 2H), 1.52 – 1.37 (m, 5H), 1.36 (s, 6H), 1.33 – 1.25 (m, 1H), 1.24 –

1.15 (m, 2H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 161.0, 157.3, 157.0, 149.6, 133.1, 128.7, 120.9, 118.8, 114.5, 90.9, 72.4, 55.9, 42.7, 39.5, 39.1, 28.9, 25.6, 25.3, 24.3, 23.7, 23.6. HRMS (ESI) m/z calcd. For $\text{C}_{23}\text{H}_{29}\text{NO}_2$ $[\text{M}+\text{H}]^+$: 352.2271, found: 352.2273.

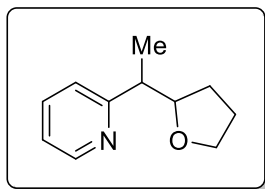


rel-2-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)quinolone (2o). Purified by flash chromatography on silica gel (acetone/*n*-hexane = 1:3). Prepared according to **GP2**. From 1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)quinolin-1-ium 4-methylbenzenesulfonate (70.1 mg, 0.15 mmol), compound **2o** (28.4 mg, 64%) was obtained. Pale yellow gum. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.07 (dd, J = 8.7, 0.8 Hz, 1H), 8.01 (d, J = 8.5 Hz, 1H), 7.79 (dd, J = 8.1, 1.5 Hz, 1H), 7.67 (ddd, J = 8.5, 6.8, 1.5 Hz, 1H), 7.59 (d, J = 8.7 Hz, 1H), 7.49 (ddd, J = 8.1, 6.9, 1.2 Hz, 1H), 4.11 (d, J = 5.7 Hz, 1H), 3.62 (dd, J = 7.9, 6.1 Hz, 1H), 3.54 (dd, J = 7.8, 6.6 Hz, 1H), 2.11 – 2.03 (m, 1H), 1.89 – 1.79 (m, 1H), 1.48 (s, 3H), 1.45 (s, 3H), 1.43 – 1.35 (m, 4H), 1.30 – 1.04 (m, 4H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 167.2, 147.9, 135.7, 129.9, 129.4, 127.9, 127.2, 126.3, 120.6, 90.7, 72.3, 46.0, 39.2, 39.2, 28.5, 25.7, 25.2, 23.8, 23.7, 23.7. HRMS (EI) m/z calcd. For $\text{C}_{20}\text{H}_{25}\text{NO}$ $[\text{M}]^+$: 295.1936, found: 295.1936.

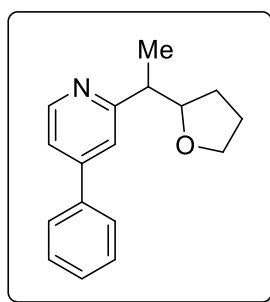


rel-6-methoxy-2-(2-((1S,3aR,7aS)-octahydroisobenzofuran-1-yl)propan-2-yl)quinolone (2p). Purified by flash chromatography on silica gel (acetone/*n*-hexane = 1:4). Prepared according to **GP2**. From 6-methoxy-1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)quinolin-1-ium 4-methylbenzenesulfonate (74.6 mg, 0.15 mmol), compound **2p** (32.7 mg, 67%) was obtained. Pale yellow gum. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 7.97 (dd, J = 8.7, 0.7 Hz, 1H), 7.90 (d, J = 9.2 Hz, 1H), 7.53 (d, J = 8.7 Hz, 1H), 7.31 (dd, J = 9.2, 2.8 Hz, 1H), 7.08 (d, J = 2.8 Hz, 1H), 4.08 (d, J = 5.6 Hz, 1H), 3.91 (s, 3H), 3.61 (dd, J = 7.8, 6.0 Hz, 1H), 3.53 (dd, J = 7.8, 6.5 Hz, 1H), 2.10 – 2.02 (m, 1H), 1.88 – 1.79 (m, 1H), 1.46 (s, 3H), 1.43 (s, 3H), 1.42 – 1.35 (m, 4H), 1.30 – 1.00 (m, 4H). ^{13}C NMR (151 MHz, Methylene Chloride- d_2) δ 164.6, 157.9, 143.9, 134.6, 131.2, 128.0, 121.9, 120.8, 105.5,

90.6, 72.3, 56.0, 45.6, 39.2, 39.1, 28.5, 25.7, 25.2, 23.8, 23.6, 23.6. HRMS (EI) m/z calcd. For $C_{21}H_{27}NO_2$ $[M]^+$: 325.2042, found : 325.2042.

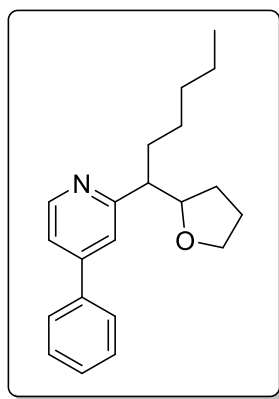


2-(1-(tetrahydrofuran-2-yl)ethyl)pyridine (2q). d.r. 2.7:1. Purified by flash chromatography on silica gel (acetone/*n*-hexane = 1:3). Prepared according to **GP2**. From (*E*)-1-(hex-4-en-1-yloxy)pyridin-1-ium 4-methylbenzenesulfonate (52.4 mg, 0.15 mmol), compound **2q** (18.3 mg, 69%) was obtained. Pale yellow oil. (major diastereomer). Pale yellow oil (minor diastereomer). 1H NMR (400 MHz, Methylene Chloride- d_2 , major diastereomer) δ 8.50 (ddd, J = 4.8, 1.9, 1.0 Hz, 1H), 7.59 (td, J = 7.7, 1.9 Hz, 1H), 7.18 (dt, J = 7.9, 1.1 Hz, 1H), 7.10 (ddd, J = 7.5, 4.8, 1.2 Hz, 1H), 4.05 (td, J = 8.4, 6.3 Hz, 1H), 3.75 (dtd, J = 8.3, 6.9, 0.5 Hz, 1H), 3.62 (dt, J = 8.2, 6.9 Hz, 1H), 2.88 (dq, J = 8.4, 7.0 Hz, 1H), 2.08 – 1.99 (m, 1H), 1.90 – 1.80 (m, 2H), 1.67 – 1.56 (m, 1H), 1.23 (d, J = 7.1 Hz, 3H). 1H NMR (400 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 8.49 (ddd, J = 5.0, 1.9, 1.0 Hz, 1H), 7.60 (td, J = 7.7, 1.8 Hz, 1H), 7.17 (dt, J = 7.8, 1.1 Hz, 1H), 7.15 – 7.07 (m, 1H), 4.08 – 3.98 (m, 1H), 3.79 (dt, J = 8.3, 6.7 Hz, 1H), 3.70 (dt, J = 8.3, 6.8 Hz, 1H), 2.89 (p, J = 7.1 Hz, 1H), 1.82 – 1.63 (m, 3H), 1.54 – 1.43 (m, 1H), 1.34 (d, J = 6.9 Hz, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , major diastereomer) δ 165.0, 149.5, 136.5, 123.2, 121.8, 83.6, 68.4, 47.9, 30.4, 26.3, 17.6. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 164.6, 149.6, 136.6, 123.2, 121.8, 83.6, 68.4, 47.6, 30.1, 26.4, 17.7. HRMS (EI, major diastereomer) m/z calcd. For $C_{11}H_{15}NO$ $[M]^+$: 177.1154, found : 177.1152. HRMS (EI, minor diastereomer) m/z calcd. For $C_{11}H_{15}NO$ $[M]^+$: 177.1154, found : 177.1151.



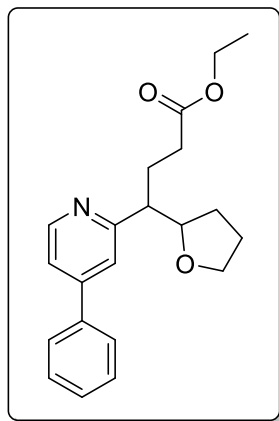
4-phenyl-2-(1-(tetrahydrofuran-2-yl)ethyl)pyridine (2r). d.r. 2.4:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2). Prepared according to **GP2**. From (*E*)-1-(hex-4-en-1-yloxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (63.8 mg, 0.15 mmol), compound **2r** (28.9 mg, 76%) was obtained. White solid (major diastereomer). Colorless oil (minor diastereomer). 1H NMR (400 MHz, Methylene Chloride- d_2 , major diastereomer) δ 8.55 (dd, J = 5.2, 0.8 Hz, 1H), 7.71 –

7.63 (m, 2H), 7.52 – 7.40 (m, 4H), 7.35 (dd, $J = 5.1, 1.8$ Hz, 1H), 4.12 (td, $J = 8.3, 6.3$ Hz, 1H), 3.77 (dt, $J = 8.2, 6.9$ Hz, 1H), 3.64 (dt, $J = 8.2, 6.8$ Hz, 1H), 2.97 (dq, $J = 8.3, 7.1$ Hz, 1H), 2.11 – 2.02 (m, 1H), 1.91 – 1.82 (m, 2H), 1.70 – 1.60 (m, 1H), 1.29 (d, $J = 7.0$ Hz, 3H). ^1H NMR (400 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 8.55 (dd, $J = 5.2, 0.8$ Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 – 7.40 (m, 4H), 7.36 (dd, $J = 5.2, 1.8$ Hz, 1H), 4.10 (td, $J = 7.6, 6.3$ Hz, 1H), 3.81 (dt, $J = 8.4, 6.6$ Hz, 1H), 3.76 – 3.69 (m, 1H), 3.02 – 2.93 (m, 1H), 1.84 – 1.70 (m, 3H), 1.58 – 1.50 (m, 1H), 1.40 (d, $J = 6.9$ Hz, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , major diastereomer) δ 165.6, 150.0, 148.8, 139.2, 129.5, 129.4, 127.6, 121.2, 119.9, 83.6, 68.4, 48.1, 30.4, 26.4, 17.7. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 165.2, 150.1, 148.9, 139.1, 129.6, 129.4, 127.6, 121.1, 119.9, 83.6, 68.5, 47.8, 30.1, 26.4, 17.8. HRMS (EI, major diastereomer) m/z calcd. For $\text{C}_{17}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 253.1467, found : 253.1466. HRMS (EI, minor diastereomer) m/z calcd. For $\text{C}_{17}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 253.1467, found : 253.1466.

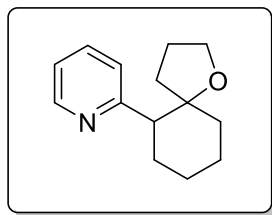


4-phenyl-2-(1-(tetrahydrofuran-2-yl)hexyl)pyridine (2s). d.r. 2.5:1. Purified by flash chromatography on silica gel (acetone/*n*-hexane = 1:5). Prepared according to **GP2**. From (*E*)-1-(dec-4-en-1-yloxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (72.2 mg, 0.15 mmol), compound **2s** (36.2 mg, 78%) was obtained. Yellow oil (major diastereomer). Yellow oil (minor diastereomer). ^1H NMR (400 MHz, Methylene Chloride- d_2 , major diastereomer) δ 8.56 (dd, $J = 5.1, 0.8$ Hz, 1H), 7.69 – 7.65 (m, 2H), 7.51 – 7.40 (m, 3H), 7.39 (dd, $J = 1.9, 0.8$ Hz, 1H), 7.35 (dd, $J = 5.2, 1.8$ Hz, 1H), 4.12 (td, $J = 8.2, 6.3$ Hz, 1H), 3.73 (dt, $J = 8.3, 6.9$ Hz, 1H), 3.61 (ddd, $J = 8.2, 7.3, 6.2$ Hz, 1H), 2.81 (ddd, $J = 10.9, 8.1, 3.9$ Hz, 1H), 2.11 – 2.03 (m, 1H), 1.90 – 1.78 (m, 3H), 1.69 – 1.60 (m, 2H), 1.29 – 1.02 (m, 6H), 0.81 (t, $J = 7.0$ Hz, 3H). ^1H NMR (400 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 8.56 (dd, $J = 4.7, 1.3$ Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 – 7.41 (m, 3H), 7.38 – 7.33 (m, 2H), 4.12 – 4.04 (m, 1H), 3.79 (dt, $J = 8.2, 6.8$ Hz, 1H), 3.71 (dt, $J = 8.2, 6.8$ Hz, 1H), 2.80 (ddd, $J = 10.6, 8.4, 3.8$ Hz, 1H), 2.02 – 1.93 (m, 1H), 1.91 – 1.80 (m, 1H), 1.80 – 1.72 (m, 2H), 1.67 – 1.59 (m, 1H), 1.52 – 1.42 (m, 1H), 1.28 – 1.07 (m, 6H), 0.82 (t, $J = 7.0$ Hz, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , major diastereomer) δ 164.4, 150.1, 148.4, 139.3, 129.5, 129.3, 127.6, 122.2, 119.8, 83.2, 68.2, 54.2, 32.5, 32.3, 30.7, 27.6, 26.3, 23.1, 14.4. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , minor

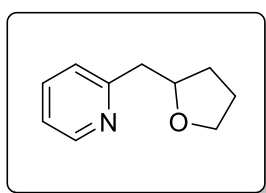
diastereomer) δ 163.9, 150.2, 148.6, 139.1, 129.6, 129.4, 127.6, 122.2, 119.8, 83.2, 68.3, 54.1, 32.7, 32.6, 30.3, 27.7, 26.2, 23.2, 14.4. HRMS (EI, major diastereomer) m/z calcd. For $C_{21}H_{27}NO$ $[M]^+$: 309.2093, found : 309.2091. HRMS (EI, minor diastereomer) m/z calcd. For $C_{21}H_{27}NO$ $[M]^+$: 309.2093, found : 309.2090.



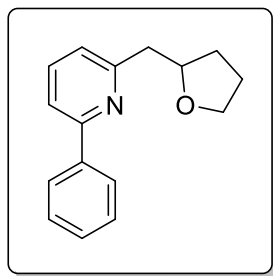
ethyl 4-(4-phenylpyridin-2-yl)-4-(tetrahydrofuran-2-yl)butanoate (2t). d.r. 2.5:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2). Prepared according to **GP2**. From (*E*)-1-((8-ethoxy-8-oxooct-4-en-1-yl)oxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (76.7 mg, 0.15 mmol), compound **2t** (35.6 mg, 70%) was obtained. Yellow oil (major diastereomer). Pale yellow oil (minor diastereomer). 1H NMR (400 MHz, Methylene Chloride- d_2 , major diastereomer) δ 8.58 (dd, J = 5.1, 0.9 Hz, 1H), 7.70 – 7.64 (m, 2H), 7.52 – 7.41 (m, 3H), 7.40 – 7.35 (m, 2H), 4.14 (td, J = 8.2, 6.4 Hz, 1H), 4.04 (q, J = 7.1 Hz, 2H), 3.78 – 3.71 (m, 1H), 3.65 – 3.58 (m, 1H), 2.89 – 2.81 (m, 1H), 2.17 – 1.99 (m, 5H), 1.89 – 1.80 (m, 2H), 1.72 – 1.64 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H). 1H NMR (400 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 8.57 (dd, J = 5.1, 0.9 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.53 – 7.41 (m, 3H), 7.40 – 7.35 (m, 2H), 4.13 (ddd, J = 8.5, 7.5, 6.4 Hz, 1H), 4.03 (q, J = 7.1 Hz, 2H), 3.84 – 3.78 (m, 1H), 3.73 (dt, J = 8.2, 6.8 Hz, 1H), 2.84 (ddd, J = 10.0, 8.3, 4.0 Hz, 1H), 2.36 – 2.26 (m, 1H), 2.21 – 2.08 (m, 3H), 1.82 – 1.73 (m, 2H), 1.70 – 1.63 (m, 1H), 1.53 – 1.42 (m, 1H), 1.18 (t, J = 7.1 Hz, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , major diastereomer) δ 173.7, 163.1, 150.3, 148.7, 139.0, 129.6, 129.4, 127.6, 122.5, 120.1, 82.8, 68.3, 60.7, 53.2, 32.6, 30.5, 27.3, 26.3, 14.6. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , minor diastereomer) δ 173.9, 162.7, 150.4, 148.9, 138.9, 129.6, 129.5, 127.6, 122.4, 120.1, 82.9, 68.4, 60.6, 53.1, 32.8, 30.3, 28.0, 26.2, 14.6. HRMS (EI, major diastereomer) m/z calcd. For $C_{21}H_{25}NO_3$ $[M]^+$: 339.1834, found : 339.1831. HRMS (EI, minor diastereomer) m/z calcd. For $C_{21}H_{25}NO_3$ $[M]^+$: 339.1834, found : 339.1833.



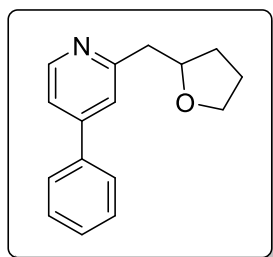
2-(1-oxaspiro[4.5]decan-6-yl)pyridine (2u). d.r. 2.0:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:7). Prepared according to **GP2**. From 1-(3-(cyclohex-1-en-1-yl)propoxy)pyridin-1-ium 4-methylbenzenesulfonate (58.4 mg, 0.15 mmol), compound **2u** (13.9 mg, 43%) was obtained. Colorless oil (major diastereomer). Colorless oil (minor diastereomer). ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 8.50 – 8.38 (m, 1H), 7.57 (td, J = 7.7, 1.9 Hz, 1H), 7.40 (dd, J = 8.1, 1.2 Hz, 1H), 7.10 (ddd, J = 7.4, 4.8, 1.2 Hz, 1H), 3.62 (td, J = 7.9, 6.6 Hz, 1H), 3.51 (td, J = 7.7, 4.9 Hz, 1H), 2.83 (dd, J = 13.0, 3.6 Hz, 1H), 2.02 (qd, J = 13.0, 3.7 Hz, 1H), 1.84 (ddd, J = 12.5, 8.6, 5.5 Hz, 1H), 1.82 – 1.75 (m, 2H), 1.72 (dt, J = 13.1, 3.8 Hz, 1H), 1.69 – 1.64 (m, 1H), 1.62 – 1.55 (m, 2H), 1.51 – 1.33 (m, 3H), 0.85 – 0.77 (m, 1H). ^1H NMR (600 MHz, Chloroform- d , minor diastereomer) δ 8.54 (d, J = 4.6 Hz, 1H), 7.56 – 7.52 (m, 1H), 7.29 (d, J = 7.8 Hz, 1H), 7.13 – 7.07 (m, 1H), 3.62 (q, J = 6.8 Hz, 1H), 3.12 (q, J = 6.8 Hz, 1H), 2.95 (dd, J = 12.5, 3.5 Hz, 1H), 2.14 – 2.07 (m, 1H), 1.99 (qd, J = 12.9, 3.5 Hz, 1H), 1.92 – 1.86 (m, 1H), 1.84 – 1.75 (m, 3H), 1.64 – 1.54 (m, 3H), 1.44 – 1.31 (m, 2H), 0.96 – 0.89 (m, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , major diastereomer) δ 164.3, 148.6, 136.0, 123.9, 121.7, 83.8, 68.3, 55.1, 39.1, 36.2, 30.0, 26.6, 26.1, 23.4. ^{13}C NMR (150 MHz, Chloroform- d , minor diastereomer) δ 162.2, 148.4, 135.0, 126.0, 121.1, 86.0, 67.3, 53.5, 40.2, 29.1, 29.1, 26.2, 25.7, 24.9. HRMS (EI, major diastereomer) m/z calcd. For $\text{C}_{14}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 217.1467, found : 217.1465. HRMS (EI, minor diastereomer) m/z calcd. For $\text{C}_{14}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 217.1467, found : 217.1464.



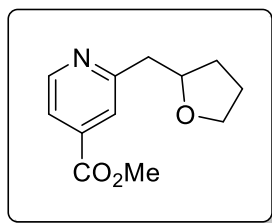
2-((tetrahydrofuran-2-yl)methyl)pyridine (2v). Purified by flash chromatography on silica gel (Acetone/*n*-hexane = 1:4). Prepared according to **GP2**. From 1-(pent-4-en-1-yloxy)pyridin-1-ium 4-methylbenzenesulfonate (50.3 mg, 0.15 mmol), compound **2v** (10.4 mg, 43%) was obtained. Colorless oil. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 8.5 (d, J = 4.9 Hz, 1H), 7.6 (tt, J = 7.7, 1.5 Hz, 1H), 7.2 (d, J = 7.7 Hz, 1H), 7.1 – 7.1 (m, 1H), 4.2 (p, J = 6.8 Hz, 1H), 3.8 (q, J = 7.3 Hz, 1H), 3.7 (q, J = 7.5 Hz, 1H), 2.9 (qd, J = 13.6, 6.5 Hz, 2H), 2.0 – 1.9 (m, 1H), 1.9 – 1.8 (m, 2H), 1.6 (dq, J = 12.1, 7.9 Hz, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 160.1, 149.6, 136.5, 124.2, 121.7, 79.3, 68.2, 44.8, 31.7, 26.1. HRMS (ESI) m/z calcd. For $\text{C}_{10}\text{H}_{13}\text{NO}$ $[\text{M}+\text{H}]^+$: 164.1070, found : 164.1061.



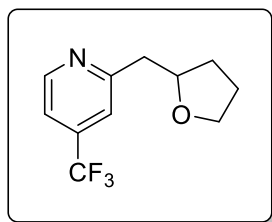
2-phenyl-6-((tetrahydrofuran-2-yl)methyl)pyridine (2w). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 1-(pent-4-en-1-yloxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (61.7 mg, 0.15 mmol), compound **2w** (12.5 mg, 35%) was obtained. Colorless oil. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 8.06 – 8.00 (m, 2H), 7.68 (t, J = 7.7 Hz, 1H), 7.59 (dd, J = 7.9, 0.9 Hz, 1H), 7.46 (dd, J = 8.3, 6.8 Hz, 2H), 7.43 – 7.38 (m, 1H), 7.17 (dd, J = 7.6, 0.9 Hz, 1H), 4.32 (p, J = 6.8 Hz, 1H), 3.87 (td, J = 7.9, 6.2 Hz, 1H), 3.70 (td, J = 8.0, 6.3 Hz, 1H), 3.07 (dd, J = 13.6, 7.2 Hz, 1H), 3.00 (dd, J = 13.6, 5.9 Hz, 1H), 2.03 (dddd, J = 11.8, 8.5, 6.5, 5.0 Hz, 1H), 1.96 – 1.83 (m, 2H), 1.69 (ddt, J = 12.1, 8.9, 7.4 Hz, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 159.9, 157.0, 140.2, 137.4, 129.3, 129.1, 127.4, 122.7, 118.3, 79.4, 68.3, 45.0, 31.8, 26.2. HRMS (EI) m/z calcd. For $\text{C}_{16}\text{H}_{17}\text{NO}$ $[\text{M}]^+$: 239.1310, found : 239.1311.



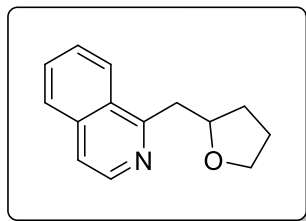
4-phenyl-2-((tetrahydrofuran-2-yl)methyl)pyridine (2x). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 2:1). Prepared according to **GP2**. From 1-(pent-4-en-1-yloxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (61.7 mg, 0.15 mmol), compound **2x** (20.1 mg, 56%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.54 (dd, J = 5.2, 0.8 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 – 7.41 (m, 4H), 7.37 (dd, J = 5.2, 1.9 Hz, 1H), 4.32 – 4.23 (m, 1H), 3.90 – 3.82 (m, 1H), 3.73 – 3.66 (m, 1H), 3.05 (dd, J = 13.6, 7.3 Hz, 1H), 2.99 (dd, J = 13.6, 5.7 Hz, 1H), 2.05 – 1.96 (m, 1H), 1.94 – 1.83 (m, 2H), 1.69 – 1.61 (m, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 160.7, 150.1, 148.9, 139.0, 129.6, 129.4, 127.6, 122.1, 119.8, 79.3, 68.3, 44.9, 31.7, 26.2. HRMS (EI) m/z calcd. For $\text{C}_{16}\text{H}_{17}\text{NO}$ $[\text{M}]^+$: 239.1310, found : 239.1307.



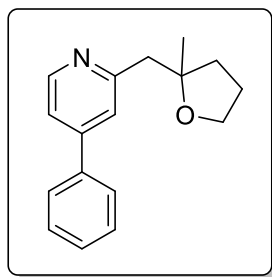
methyl 2-((tetrahydrofuran-2-yl)methyl)isonicotinate (2y). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:1). Prepared according to **GP2**. From 4-(methoxycarbonyl)-1-(pent-4-en-1-yloxy)pyridin-1-ium 4-methylbenzenesulfonate (59.0 mg, 0.15 mmol), compound **2y** (20.6 mg, 62%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Chloroform-*d*) δ 8.7 (ddt, $J = 3.9, 1.9, 1.0$ Hz, 1H), 7.8 (tt, $J = 2.2, 1.2$ Hz, 1H), 7.7 (dq, $J = 5.2, 1.7$ Hz, 1H), 4.3 (dtd, $J = 8.9, 7.3, 5.6$ Hz, 1H), 3.9 (dd, $J = 2.3, 1.5$ Hz, 3H), 3.9 – 3.8 (m, 1H), 3.8 – 3.7 (m, 1H), 3.1 – 3.0 (m, 2H), 2.1 – 1.9 (m, 1H), 2.0 – 1.7 (m, 2H), 1.7 – 1.5 (m, 1H). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.0, 160.7, 150.1, 137.7, 123.1, 120.6, 78.7, 68.1, 52.7, 44.3, 31.3, 25.7. HRMS (EI) m/z calcd. For $\text{C}_{12}\text{H}_{15}\text{NO}$ $[\text{M}]^+$: 221.1052, found: 221.1054.



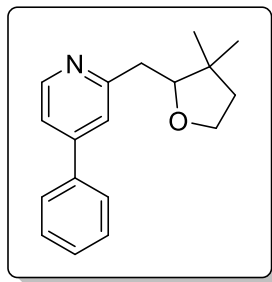
2-((tetrahydrofuran-2-yl)methyl)-4-(trifluoromethyl)pyridine (2z). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:2). Prepared according to **GP2**. From 1-(pent-4-en-1-yloxy)-4-(trifluoromethyl)pyridin-1-ium 4-methylbenzenesulfonate (60.5 mg, 0.15 mmol), compound **2z** (22.5 mg, 65%) was obtained. Colorless oil. ^1H NMR (600 MHz, Methylene Chloride-*d*₂) δ 8.70 (d, $J = 5.1$ Hz, 1H), 7.47 (s, 1H), 7.35 (d, $J = 5.1$ Hz, 1H), 4.24 (p, $J = 6.6$ Hz, 1H), 3.84 (qd, $J = 8.0, 7.3, 1.5$ Hz, 1H), 3.69 (qd, $J = 8.0, 7.2, 1.5$ Hz, 1H), 3.04 (d, $J = 6.4$ Hz, 2H), 2.01 (dddd, $J = 13.6, 8.2, 6.6, 3.5$ Hz, 1H), 1.94 – 1.80 (m, 2H), 1.66 – 1.56 (m, 1H). ^{13}C NMR (150 MHz, Methylene Chloride-*d*₂) δ 161.9, 150.7, 138.6 (q, $J = 33.8$ Hz), 123.7 (q, $J = 273.0$ Hz), 119.8 (q, $J = 3.7$ Hz), 117.3 (q, $J = 3.6$ Hz), 78.9, 68.4, 44.8, 31.8, 26.2. ^{19}F NMR (564 MHz, Methylene Chloride-*d*₂) δ -65.1. HRMS (EI) m/z calcd. For $\text{C}_{11}\text{H}_{12}\text{F}_3\text{NO}$ $[\text{M}]^+$: 231.0871, found: 231.0871.



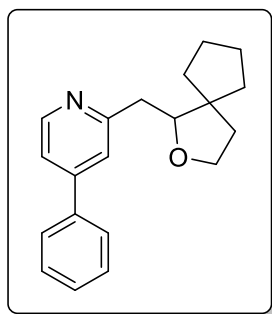
1-((tetrahydrofuran-2-yl)methyl)isoquinoline (2aa). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 2-(pent-4-en-1-yloxy)isoquinolin-2-ium 4-methylbenzenesulfonate (57.8 mg, 0.15 mmol), compound **2aa** (23.0 mg, 72%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.42 (d, J = 5.7 Hz, 1H), 8.23 (d, J = 8.4 Hz, 1H), 7.83 (d, J = 8.2 Hz, 1H), 7.68 (t, J = 7.5 Hz, 1H), 7.60 (t, J = 7.6 Hz, 1H), 7.53 (d, J = 5.7 Hz, 1H), 4.43 (p, J = 6.6 Hz, 1H), 3.88 (q, J = 7.2 Hz, 1H), 3.68 (q, J = 7.4 Hz, 1H), 3.61 (dd, J = 13.9, 6.7 Hz, 1H), 3.34 (dd, J = 13.9, 6.3 Hz, 1H), 2.02 (ddd, J = 14.1, 11.6, 5.5 Hz, 1H), 1.97 – 1.82 (m, 2H), 1.72 (dq, J = 11.5, 7.4 Hz, 1H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 160.0, 142.4, 136.7, 130.3, 128.1, 127.7, 127.5, 126.2, 119.8, 79.3, 68.3, 41.6, 31.9, 26.2. HRMS (EI) m/z calcd. For $\text{C}_{14}\text{H}_{15}\text{NO}$ $[\text{M}]^+$: 213.1154, found : 213.1156.



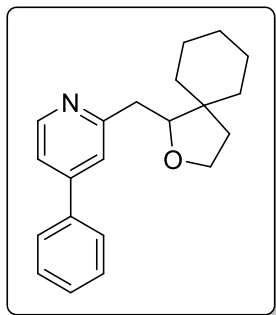
2-((2-methyltetrahydrofuran-2-yl)methyl)-4-phenylpyridine (2ab). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:4). Prepared according to **GP2**. From 1-((4-methylpent-4-en-1-yl)oxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (63.8 mg, 0.15 mmol), compound **2ab** (17.8 mg, 47%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Acetonitrile- d_3) δ 8.5 (dd, J = 5.3, 0.8 Hz, 1H), 7.8 – 7.7 (m, 2H), 7.6 (dd, J = 1.8, 0.8 Hz, 1H), 7.6 – 7.4 (m, 4H), 3.9 – 3.6 (m, 2H), 3.0 (s, 2H), 2.1 (ddd, J = 12.1, 8.4, 6.2 Hz, 1H), 2.0 – 1.9 (m, 1H), 1.8 (dddt, J = 12.1, 8.3, 7.2, 6.3 Hz, 1H), 1.6 (ddd, J = 12.0, 8.3, 6.4 Hz, 1H), 1.2 (s, 3H). ^{13}C NMR (150 MHz, Acetonitrile- d_3) δ 160.8, 150.1, 148.7, 139.3, 130.1, 130.0, 127.9, 123.6, 120.1, 83.4, 67.9, 49.4, 37.1, 26.9, 26.7. HRMS (EI) m/z calcd. For $\text{C}_{17}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 253.1467, found : 253.1464.



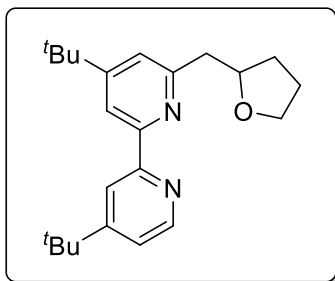
2-((3,3-dimethyltetrahydrofuran-2-yl)methyl)-4-phenylpyridine (2ac). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:3). Prepared according to **GP2**. From 1-((3,3-dimethylpent-4-en-1-yl)oxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (65.9 mg, 0.15 mmol), compound **2ac** (29.7 mg, 74%) was obtained. Pale yellow oil. ¹H NMR (600 MHz, Methylene Chloride-*d*₂) δ 8.55 (d, *J* = 5.2 Hz, 1H), 7.69 – 7.65 (m, 2H), 7.51 – 7.47 (m, 3H), 7.46 – 7.42 (m, 1H), 7.36 (dd, *J* = 5.1, 1.8 Hz, 1H), 3.90 – 3.82 (m, 2H), 3.73 (td, *J* = 8.7, 4.4 Hz, 1H), 2.93 (dd, *J* = 13.9, 2.9 Hz, 1H), 2.84 (dd, *J* = 13.8, 9.9 Hz, 1H), 1.85 – 1.74 (m, 2H), 1.10 (s, 3H), 1.05 (s, 3H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 161.5, 150.1, 148.8, 139.1, 129.5, 129.4, 127.6, 122.1, 119.7, 86.9, 65.8, 41.7, 41.1, 39.7, 25.6, 22.2. HRMS (EI) *m/z* calcd. For C₁₈H₂₁NO [M]⁺: 267.1623, found : 267.1623.



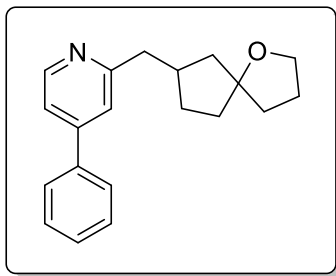
2-((2-oxaspiro[4.4]nonan-1-yl)methyl)-4-phenylpyridine (2ad). Purified by flash chromatography on silica gel (Et₂O/CH₂Cl₂ = 2:1). Prepared according to **GP2**. From 4-phenyl-1-(2-(1-vinylcyclopentyl)ethoxy)pyridin-1-ium 4-methylbenzenesulfonate (69.8 mg, 0.15 mmol), compound **2ad** (28.6 mg, 65%) was obtained. Pale yellow oil. ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.54 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 – 7.40 (m, 4H), 7.35 (dd, *J* = 5.2, 1.8 Hz, 1H), 4.08 (dd, *J* = 10.1, 2.9 Hz, 1H), 3.85 (ddd, *J* = 8.3, 7.7, 6.7 Hz, 1H), 3.74 (td, *J* = 8.2, 5.9 Hz, 1H), 2.96 (dd, *J* = 13.7, 2.8 Hz, 1H), 2.84 (dd, *J* = 13.7, 10.1 Hz, 1H), 1.92 – 1.79 (m, 2H), 1.78 – 1.57 (m, 8H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 161.5, 150.1, 148.8, 139.1, 129.5, 129.4, 127.6, 122.2, 119.7, 85.2, 66.4, 53.3, 40.8, 40.2, 36.8, 32.9, 25.4, 24.6. HRMS (EI) *m/z* calcd. For C₂₀H₂₃NO [M]⁺: 293.1780, found : 293.1778.



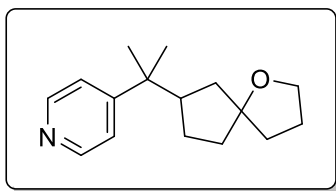
2-((2-oxaspiro[4.5]decan-1-yl)methyl)-4-phenylpyridine (2ae). Purified by flash chromatography on silica gel ($\text{Et}_2\text{O}/\text{CH}_2\text{Cl}_2 = 2:1$). Prepared according to **GP2**. From 4-phenyl-1-(2-(1-vinylcyclohexyl)ethoxy)pyridin-1-ium 4-methylbenzenesulfonate (71.9 mg, 0.15 mmol), compound **2ae** (29.1 mg, 63%) was obtained. Pale yellow oil. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.54 (dd, $J = 5.2, 0.8$ Hz, 1H), 7.69 – 7.64 (m, 2H), 7.52 – 7.40 (m, 4H), 7.35 (dd, $J = 5.2, 1.8$ Hz, 1H), 3.87 (td, $J = 8.3, 6.6$ Hz, 1H), 3.81 (dd, $J = 10.3, 2.7$ Hz, 1H), 3.70 (td, $J = 8.6, 5.8$ Hz, 1H), 2.94 (dd, $J = 13.7, 2.8$ Hz, 1H), 2.83 (dd, $J = 13.8, 10.3$ Hz, 1H), 2.06 – 1.97 (m, 1H), 1.71 – 1.36 (m, 11H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 161.7, 150.1, 148.8, 139.1, 129.5, 129.4, 127.6, 122.2, 119.7, 87.6, 66.0, 45.5, 39.6, 36.1, 35.8, 31.0, 27.1, 24.5, 23.6. HRMS (EI) m/z calcd. For $\text{C}_{21}\text{H}_{25}\text{NO}$ $[\text{M}]^+$: 307.1936, found : 307.1936.



4,4'-di-tert-butyl-6-((tetrahydrofuran-2-yl)methyl)-2,2'-bipyridine (2af). Purified by flash chromatography on alumina basic ($\text{EtOAc}/n\text{-hexane} = 1:19$). Prepared according to **GP2**. From 4,5'-di-tert-butyl-1-(pent-4-en-1-yloxy)-[2,2'-bipyridin]-1-ium 4-methylbenzenesulfonate (78.7 mg, 0.15 mmol), compound **2af** (24.8 mg, 47%) was obtained. Colorless gum. ^1H NMR (400 MHz, Methylene Chloride- d_2) δ 8.5 (dd, $J = 5.2, 0.8$ Hz, 1H), 8.5 (dd, $J = 2.0, 0.8$ Hz, 1H), 8.3 (d, $J = 1.8$ Hz, 1H), 7.3 (dd, $J = 5.2, 2.0$ Hz, 1H), 7.2 (d, $J = 1.8$ Hz, 1H), 4.4 (p, $J = 6.7$ Hz, 1H), 3.9 (ddd, $J = 8.3, 7.3, 6.1$ Hz, 1H), 3.7 (td, $J = 7.8, 6.4$ Hz, 1H), 3.1 (dd, $J = 13.6, 6.6$ Hz, 1H), 3.0 (dd, $J = 13.6, 6.4$ Hz, 1H), 2.0 (dddd, $J = 11.6, 8.4, 6.4, 5.1$ Hz, 1H), 2.0 – 1.8 (m, 2H), 1.7 (ddt, $J = 11.8, 8.8, 7.2$ Hz, 1H), 1.4 (s, 9H), 1.4 (s, 9H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 161.5, 161.2, 159.2, 157.3, 156.3, 149.4, 121.1 (d, $J = 2.9$ Hz), 118.6, 116.2, 79.5, 68.3, 45.0, 35.4, 35.4, 31.7, 31.0, 30.9, 26.2. HRMS (EI) m/z calcd. For $\text{C}_{23}\text{H}_{32}\text{N}_2\text{O}$ $[\text{M}]^+$: 352.2515, found : 352.2512.

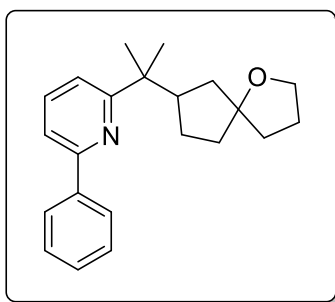


2-((1-oxaspiro[4.4]nonan-2-yl)methyl)-4-phenylpyridine (4a). d.r. 1:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:5). Prepared according to **GP2**. From 1-((4-methyleneoct-7-en-1-yl)oxy)-4-phenylpyridin-1-ium 4-methylbenzenesulfonate (44.2 mg, 0.15 mmol), compound **4a** (21.2 mg, 48%) was obtained. Colorless oil (diastereomer A). Colorless oil (diastereomer B). ¹H NMR (400 MHz, Methylene Chloride-*d*₂) δ 8.53 (dd, *J* = 5.2, 0.8 Hz, 1H), 7.68 – 7.64 (m, 2H), 7.52 – 7.40 (m, 3H), 7.37 (dd, *J* = 1.8, 0.8 Hz, 1H), 7.33 (dd, *J* = 5.2, 1.9 Hz, 1H), 3.82 – 3.66 (m, 2H), 2.89 (d, *J* = 7.5 Hz, 2H), 2.42 (dddd, *J* = 15.6, 8.8, 7.6, 1.1 Hz, 1H), 1.91 – 1.71 (m, 7H), 1.61 – 1.46 (m, 3H). ¹H NMR (400 MHz, Methylene Chloride-*d*₂, diastereomer B) δ 8.52 (dd, *J* = 5.2, 0.9 Hz, 1H), 7.68 – 7.64 (m, 2H), 7.52 – 7.40 (m, 3H), 7.38 (dd, *J* = 1.9, 0.8 Hz, 1H), 7.34 (dd, *J* = 5.2, 1.8 Hz, 1H), 3.81 – 3.61 (m, 2H), 2.95 – 2.75 (m, 2H), 2.58 (ddt, *J* = 10.1, 8.6, 7.4 Hz, 1H), 1.92 – 1.78 (m, 6H), 1.76 – 1.71 (m, 2H), 1.41 – 1.28 (m, 2H). ¹³C NMR (150 MHz, Methylene Chloride-*d*₂, diastereomer A) δ 162.9, 150.2, 148.8, 139.1, 129.6, 129.4, 127.5, 121.5, 119.4, 90.9, 67.1, 45.4, 45.2, 39.5, 38.5, 37.7, 31.6, 26.3. ¹³C NMR (150 MHz, Methylene Chloride-*d*₂) δ 162.8, 150.1, 148.8, 139.2, 129.6, 129.4, 127.5, 121.3, 119.5, 91.1, 66.9, 45.4, 45.2, 39.7, 38.4, 37.1, 31.6, 26.5. HRMS (EI, diastereomer A) *m/z* calcd. For C₂₀H₂₃NO [M]⁺: 293.1780, found : 293.1779. HRMS (EI, diastereomer B) *m/z* calcd. For C₂₀H₂₃NO [M]⁺: 293.1780, found : 293.1781.

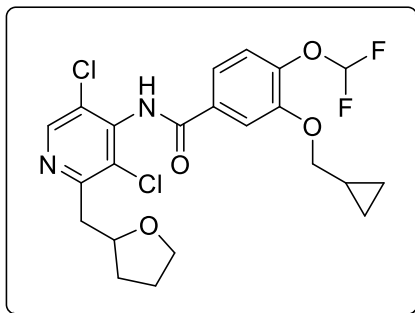


4-(2-(1-oxaspiro[4.4]nonan-7-yl)propan-2-yl)pyridine (4b). d.r. 1:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:1). Prepared according to **GP2**. From 1-((8-methyl-4-methylenenon-7-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (37.0 mg, 0.15 mmol), compound **4b** (19.5 mg, 53%) was obtained. Colorless oil (diastereomer A). Colorless oil (diastereomer B). ¹H NMR (600 MHz, Methylene Chloride-*d*₂, diastereomer A) δ 8.47 (s, 2H), 7.28 (d, *J* = 5.0 Hz, 2H), 3.68 (h, *J* = 8.2 Hz, 2H), 2.17 (p, *J* = 8.8 Hz, 1H), 1.89 – 1.78 (m, 2H), 1.75 – 1.66 (m, 3H), 1.52 – 1.38 (m, 5H), 1.28 (s, 3H), 1.27 (s, 3H). ¹H NMR (600 MHz, Methylene Chloride-*d*₂, diastereomer B)

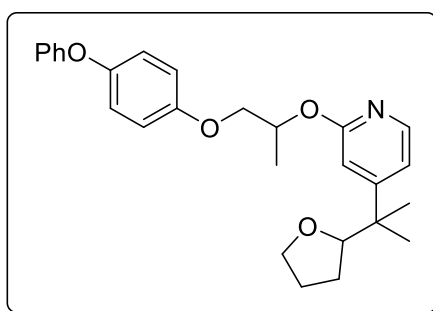
δ 8.46 (d, J = 5.1 Hz, 2H), 7.25 (d, J = 5.2 Hz, 2H), 3.68 (dq, J = 26.4, 7.6 Hz, 2H), 2.49 – 2.38 (m, 1H), 1.82 (p, J = 7.1 Hz, 2H), 1.74 – 1.64 (m, 3H), 1.61 – 1.52 (m, 3H), 1.34 – 1.24 (m, 8H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , diastereomer A) δ 160.1, 149.4, 122.3, 90.2, 67.0, 49.9, 40.6, 40.0, 38.5, 37.6, 26.6, 26.3, 25.2, 24.8. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , diastereomer B) δ 159.2, 150.0, 122.2, 90.8, 67.0, 49.8, 40.3, 39.7, 38.3, 36.5, 26.4, 25.2, 25.2. HRMS (EI, diastereomer A) m/z calcd. For $\text{C}_{16}\text{H}_{23}\text{NO}$ $[\text{M}]^+$: 245.1780, found : 245.1779. HRMS (EI, diastereomer B) m/z calcd. For $\text{C}_{16}\text{H}_{23}\text{NO}$ $[\text{M}]^+$: 245.1780, found : 245.1784.



2-(2-(1-oxaspiro[4.4]nonan-7-yl)propan-2-yl)-6-phenylpyridine (4c). d.r. 1:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:7). Prepared according to **GP2**. From 1-((8-methyl-4-methylenenon-7-en-1-yl)oxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (48.4 mg, 0.15 mmol), compound **4c** (28.8 mg, 60%) was obtained. Colorless oil (diastereomer A). Colorless oil (diastereomer B). ^1H NMR (600 MHz, Methylene Chloride- d_2 , diastereomer A) δ 8.55 (dd, J = 5.1, 2.3 Hz, 1H), 8.01 (d, J = 7.5 Hz, 2H), 7.71 (s, 1H), 7.50 – 7.45 (m, 2H), 7.41 (t, J = 7.5 Hz, 1H), 7.25 – 7.20 (m, 1H), 3.74 – 3.65 (m, 2H), 2.24 (p, J = 9.0 Hz, 1H), 1.84 (h, J = 6.3 Hz, 2H), 1.77 – 1.68 (m, 3H), 1.54 – 1.45 (m, 5H), 1.35 – 1.32 (m, 6H). ^1H NMR (600 MHz, Methylene Chloride- d_2 , diastereomer B) δ 8.55 (dd, J = 5.4, 2.4 Hz, 1H), 8.00 (d, J = 7.6 Hz, 2H), 7.72 (s, 1H), 7.47 (t, J = 7.7 Hz, 2H), 7.41 (t, J = 7.4 Hz, 1H), 7.25 – 7.20 (m, 1H), 3.69 (dq, J = 23.7, 7.2 Hz, 2H), 2.51 (p, J = 8.8 Hz, 1H), 1.82 (p, J = 7.3 Hz, 2H), 1.76 – 1.66 (m, 3H), 1.65 – 1.53 (m, 3H), 1.37 – 1.24 (m, 8H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , diastereomer A) δ 160.2, 157.5, 149.9, 140.6, 129.2, 127.5, 120.8, 118.8, 90.2, 67.0, 50.0, 40.6, 40.1, 38.5, 37.7, 26.6, 26.3, 25.3, 24.9. ^{13}C NMR (150 MHz, Methylene Chloride- d_2 , diastereomer B) δ 160.1, 157.5, 149.8, 140.6, 129.2, 129.1, 127.5, 120.9, 118.9, 90.8, 67.0, 49.8, 40.4, 40.0, 38.3, 36.6, 26.5, 26.4, 25.3, 25.3. HRMS (EI, diastereomer A) m/z calcd. For $\text{C}_{22}\text{H}_{27}\text{NO}$ $[\text{M}]^+$: 321.2093, found : 321.2092. HRMS (EI, diastereomer B) m/z calcd. For $\text{C}_{22}\text{H}_{27}\text{NO}$ $[\text{M}]^+$: 321.2093, found : 321.2095.

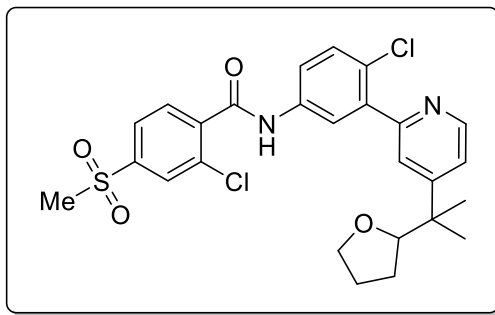


3-(cyclopropylmethoxy)-N-(3,5-dichloro-2-((tetrahydrofuran-2-yl)methyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (4d). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:3). Prepared according to **GP2**. From 3,5-dichloro-4-(3-(cyclopropylmethoxy)-4-(difluoromethoxy)benzamido)-1-(pent-4-en-1-yloxy)pyridin-1-ium 4-methylbenzenesulfonate (98.9 mg, 0.15 mmol), compound **4d** (59.2 mg, 81%) was obtained. Pale yellow oil. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 8.47 (s, 1H), 8.13 (s, 1H), 7.56 (d, J = 2.9 Hz, 1H), 7.49 (dd, J = 8.0, 2.8 Hz, 1H), 7.25 (d, J = 8.2 Hz, 1H), 6.76 (t, J = 75.1 Hz, 1H), 4.40 (p, J = 7.0 Hz, 1H), 3.96 (d, J = 6.9 Hz, 2H), 3.80 (q, J = 7.5 Hz, 1H), 3.61 (q, J = 7.5 Hz, 1H), 3.22 (dd, J = 14.4, 7.9 Hz, 1H), 3.03 (dd, J = 14.3, 5.2 Hz, 1H), 2.08 – 1.98 (m, 1H), 1.95 – 1.89 (m, 1H), 1.85 (dt, J = 12.8, 7.3 Hz, 1H), 1.66 (dq, J = 15.5, 8.4, 7.9 Hz, 1H), 1.32 (dq, J = 12.6, 5.9 Hz, 1H), 0.67 (d, J = 7.7 Hz, 2H), 0.37 (d, J = 5.0 Hz, 2H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 164.62, 157.10, 151.26, 147.51, 144.18, 140.48, 131.95, 129.31, 127.80, 122.40, 120.79, 116.60 (t, J = 260.0 Hz), 114.61, 77.92, 74.78, 68.29, 41.93, 31.87, 26.12, 10.50, 3.56. ^{19}F NMR (564 MHz, Methylene Chloride- d_2) δ -82.31 (d, J = 75.1 Hz). HRMS (EI) m/z calcd. For $\text{C}_{22}\text{H}_{22}\text{Cl}_2\text{F}_2\text{N}_2\text{O}_4$ $[\text{M}]^+$: 486.0925, found : 486.0922.



2-((1-(4-phenoxyphenoxy)propan-2-yl)oxy)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (4e). d.r. 1:1. Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 1:7). Prepared according to **GP2**. From 1-((5-methylhex-4-en-1-yl)oxy)-2-((1-(4-phenoxyphenoxy)propan-2-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (90.9 mg, 0.15 mmol), compound **4e** (28.6 mg, 44%) was obtained. Colorless oil. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 8.03 (d, J = 5.5 Hz, 1H), 7.30 (t, J = 7.7 Hz, 2H), 7.05 (t, J = 7.4 Hz, 1H), 6.98 – 6.92 (m, 7H), 6.75 (s, 1H), 5.56 (h, J = 6.1 Hz, 1H), 4.17 (dd,

$J = 10.0, 5.4$ Hz, 1H), 4.08 (dd, $J = 10.0, 4.6$ Hz, 1H), 3.90 (t, $J = 7.3$ Hz, 1H), 3.75 – 3.61 (m, 2H), 1.82 – 1.65 (m, 3H), 1.49 – 1.39 (m, 4H), 1.27 (d, $J = 3.1$ Hz, 6H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 164.01, 160.51, 159.10, 155.87, 150.87, 146.52, 130.18, 123.02, 121.28, 118.15, 116.63, 116.24, 110.12, 86.78, 71.73, 69.76, 69.03, 41.84, 27.65, 26.67, 24.55, 24.33, 17.32. HRMS (ESI) m/z calcd. For $\text{C}_{20}\text{H}_{25}\text{NO}$ $[\text{M}+\text{H}]^+$: 434.2326, found : 434.2327.



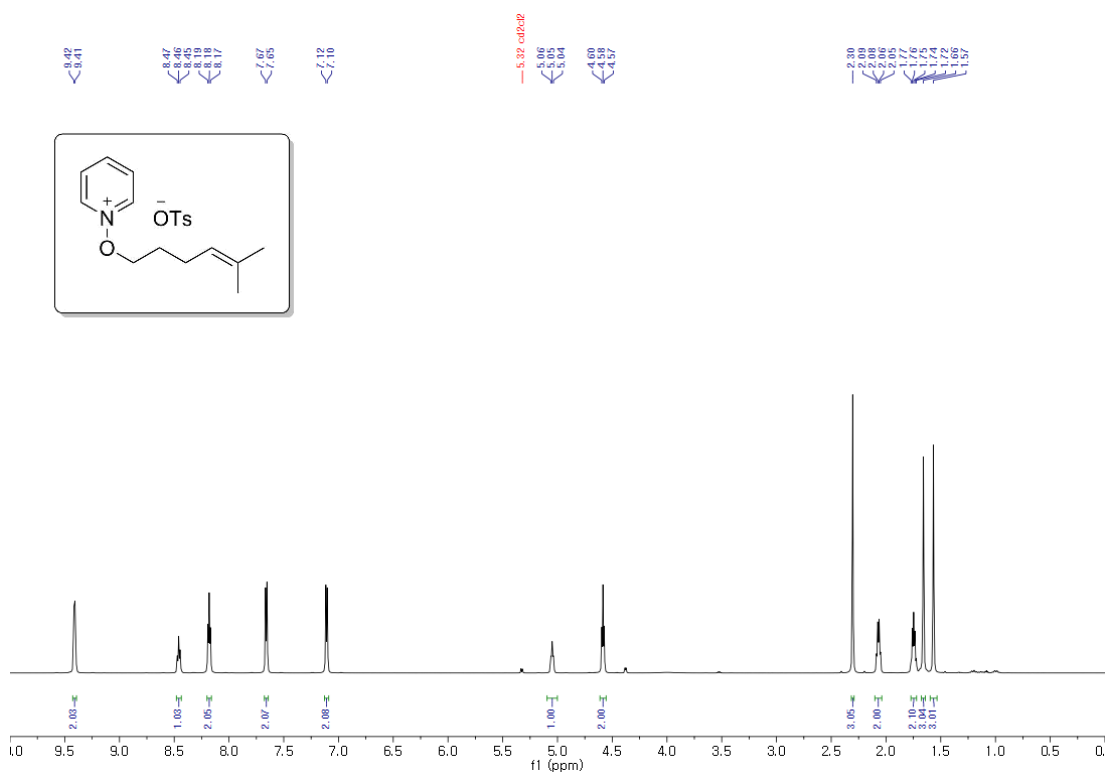
2-chloro-*N*-(4-chloro-3-(4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridin-2-yl)phenyl)-4-(methylsulfonyl)benzamide (4f). Purified by flash chromatography on silica gel (EtOAc/*n*-hexane = 2:1). Prepared according to **GP2**. From 2-(2-chloro-5-(2-chloro-4-(methylsulfonyl)benzamido)phenyl)-1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (105.8 mg, 0.15 mmol), compound **4f** (52.8 mg, 66%) was obtained. White Solid. ^1H NMR (600 MHz, Methylene Chloride- d_2) δ 10.55 (s, 1H), 8.16 (d, $J = 5.4$ Hz, 1H), 8.10 (dd, $J = 8.8, 2.6$ Hz, 1H), 7.83 (d, $J = 1.7$ Hz, 1H), 7.68 – 7.63 (m, 3H), 7.48 (d, $J = 8.7$ Hz, 1H), 7.46 (d, $J = 8.0$ Hz, 1H), 7.20 (dd, $J = 5.4, 1.8$ Hz, 1H), 3.85 (dd, $J = 8.4, 6.2$ Hz, 1H), 3.72 – 3.56 (m, 2H), 2.94 (s, 3H), 1.83 – 1.70 (m, 2H), 1.68 – 1.60 (m, 1H), 1.45 – 1.35 (m, 1H), 1.29 (s, 3H), 1.28 (s, 3H). ^{13}C NMR (150 MHz, Methylene Chloride- d_2) δ 164.6, 157.9, 155.7, 148.5, 143.1, 141.5, 139.6, 138.1, 132.6, 131.2, 130.2, 129.3, 127.5, 126.3, 124.9, 123.2, 122.0, 121.8, 86.6, 69.0, 44.8, 42.0, 27.7, 26.6, 25.0, 23.7. HRMS (EI) m/z calcd. For $\text{C}_{26}\text{H}_{26}\text{Cl}_2\text{N}_2\text{O}_4\text{S}$ $[\text{M}]^+$: 532.0990, found : 532.0986.

Appendix I

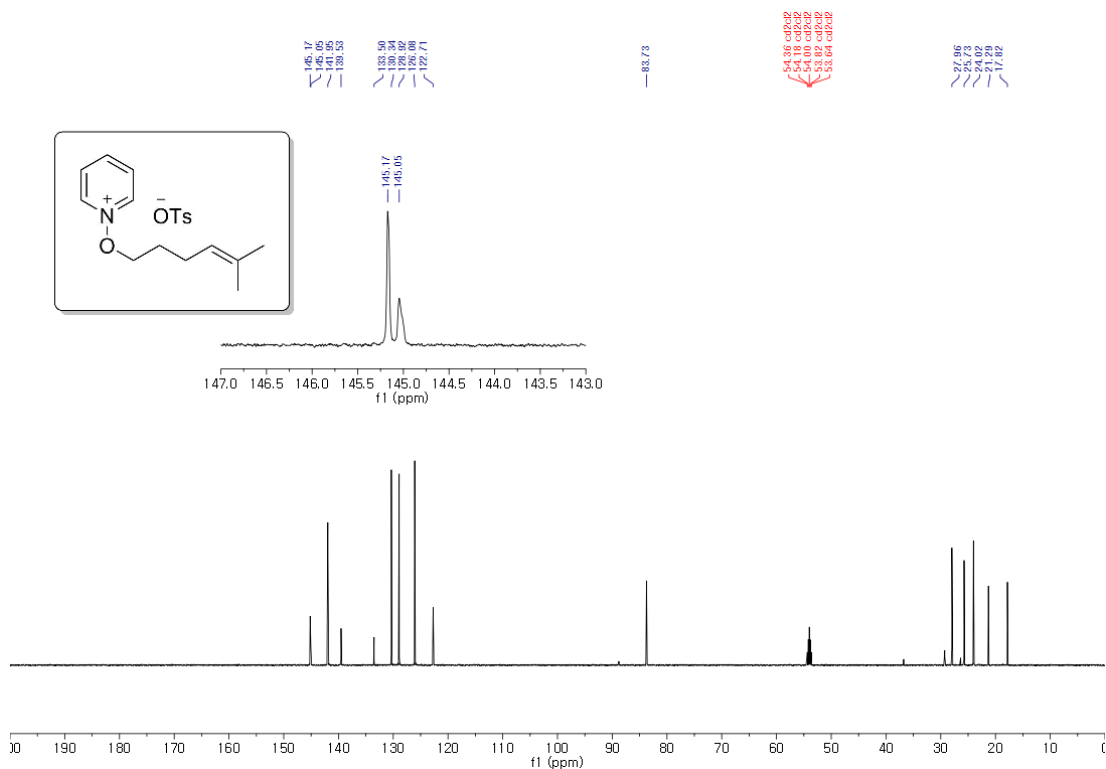
**Spectral Copies of ^1H , ^{13}C and ^{19}F NMR Data
Obtained in this Study**

1-((5-methylhex-4-en-1-yl)oxy)pyridin-1-ium 4-methylbenzenesulfonate (1a).

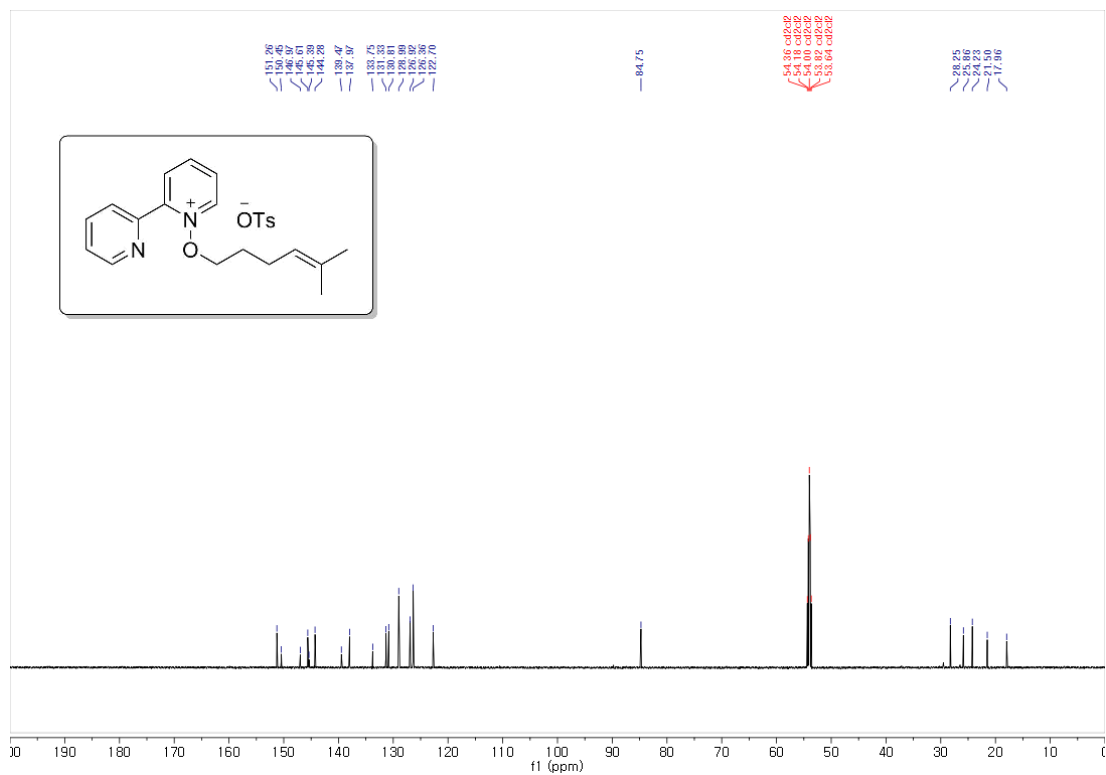
600 MHz, ^1H NMR in Methylene Chloride- d_2



150 MHz, ^{13}C NMR in Methylene Chloride- d_2



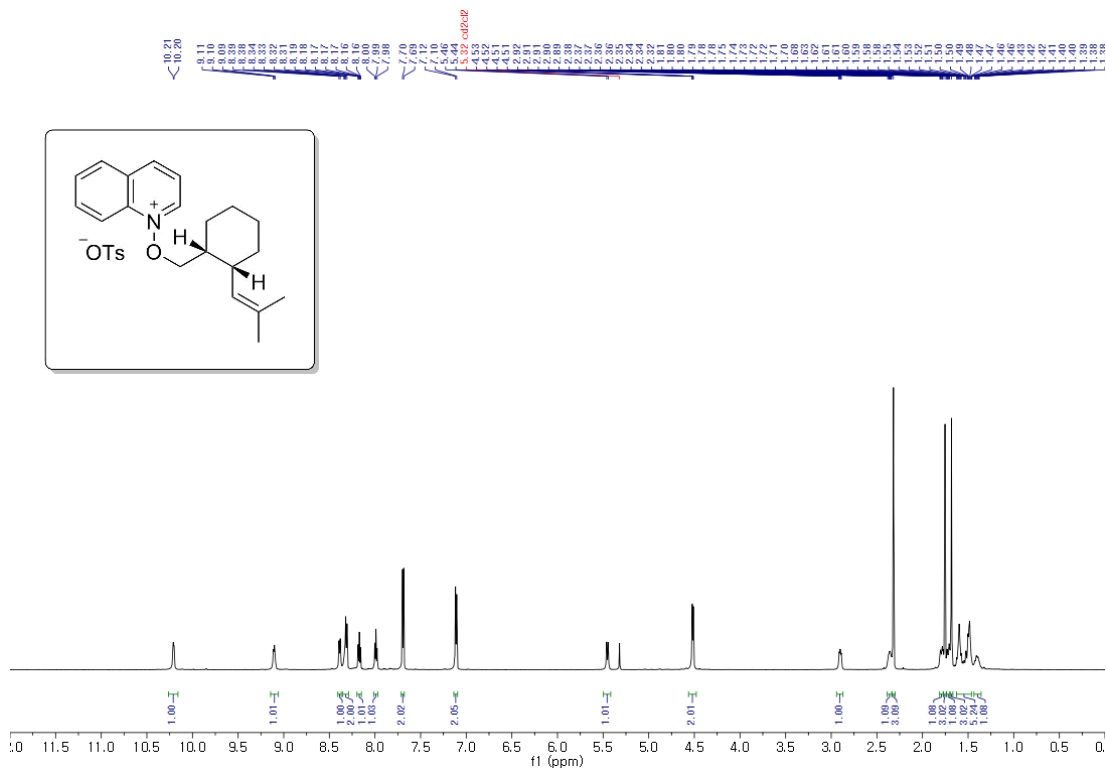
400 MHz, ^1H NMR in Methylene Chloride- d_2



**1-(((1*R*,2*R*)-2-(2-methylprop-1-en-1-yl)cyclohexyl)methoxy)quinolin-1-ium
methylbenzenesulfonate (1o).**

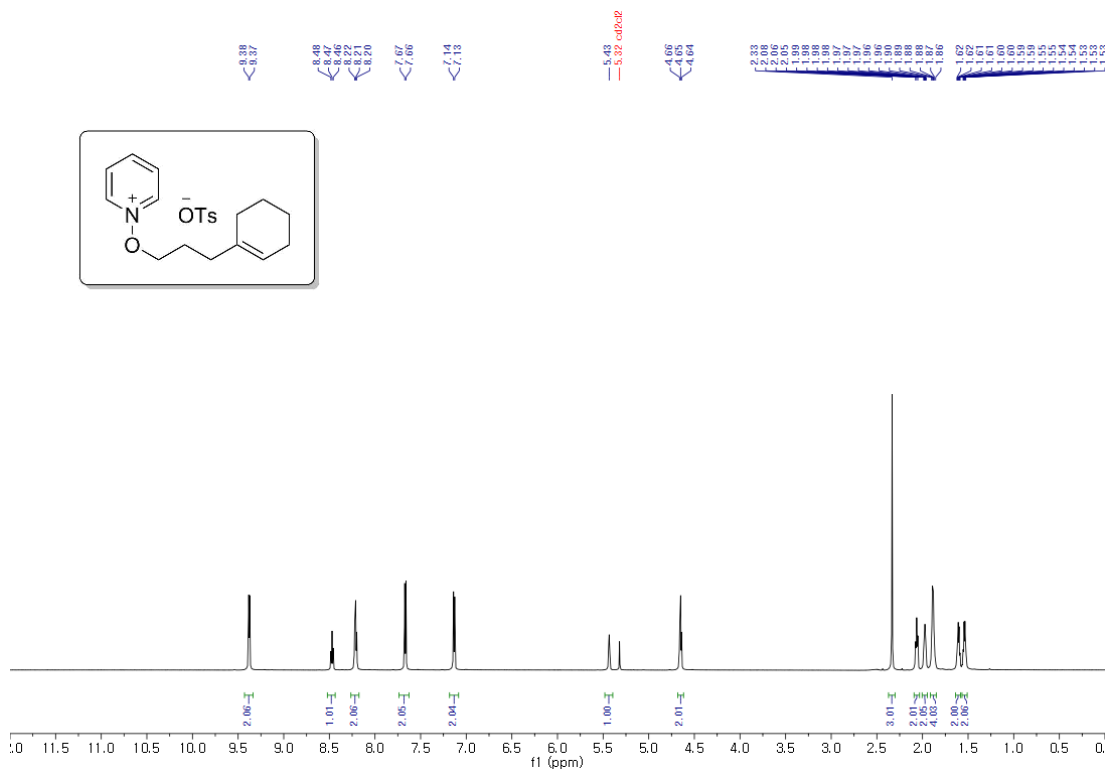
4-

600 MHz, ¹H NMR in Methylene Chloride-*d*₂

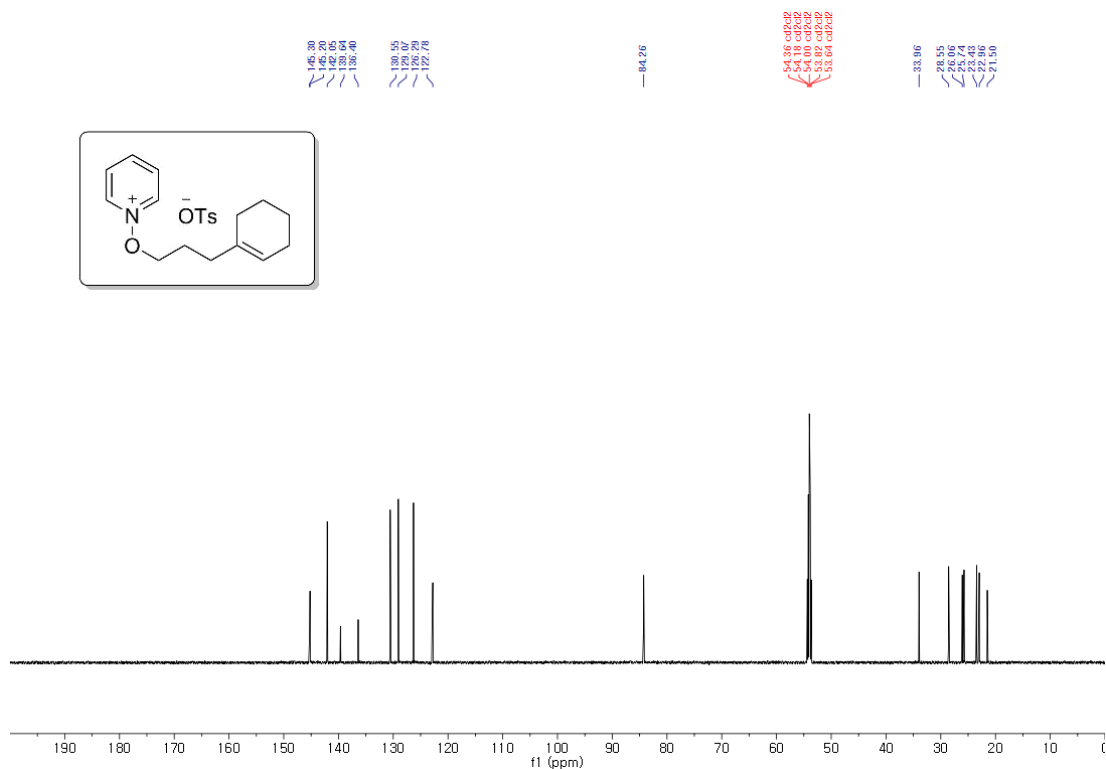


1-(3-(cyclohex-1-en-1-yl)propoxy)pyridin-1-ium 4-methylbenzenesulfonate (1u).

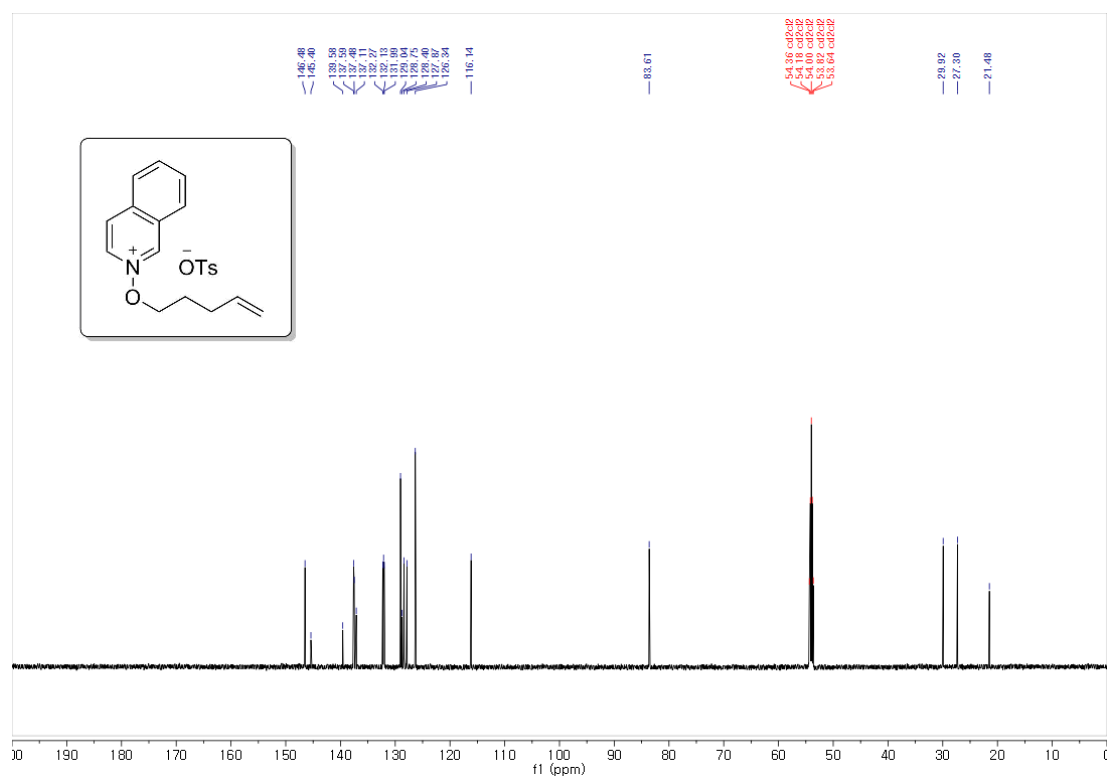
600 MHz, ^1H NMR in Methylene Chloride- d_2



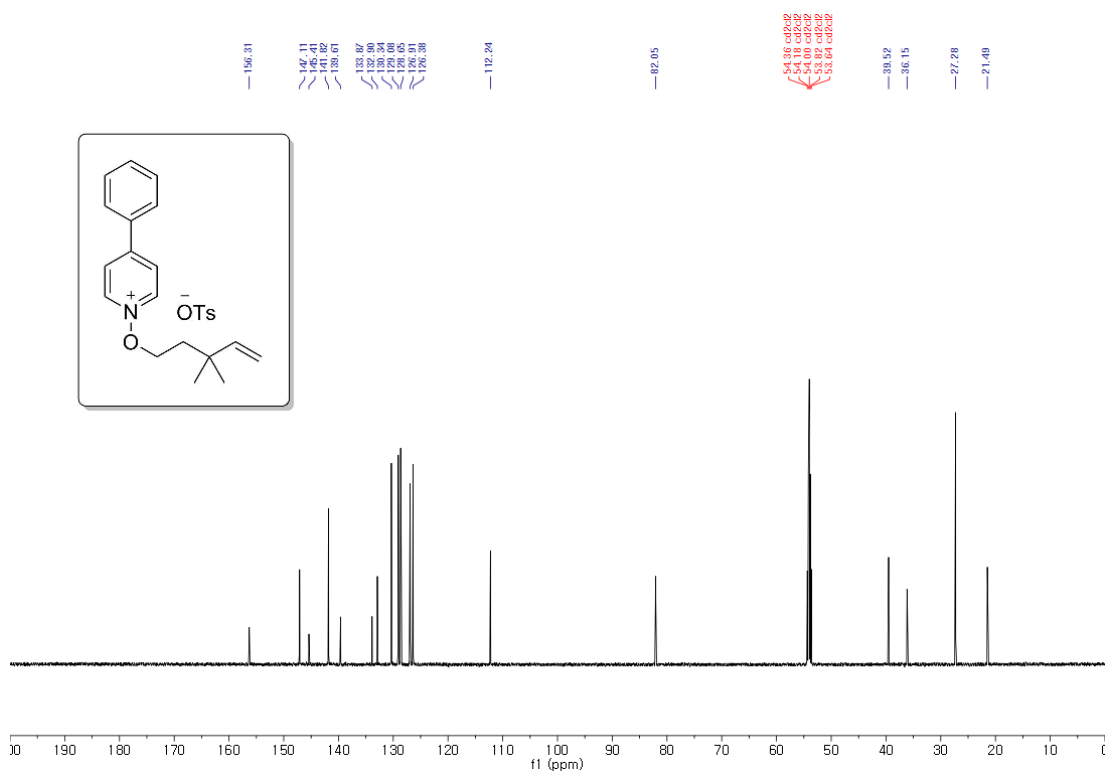
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



400 MHz, ^1H NMR in Methylene Chloride- d_2

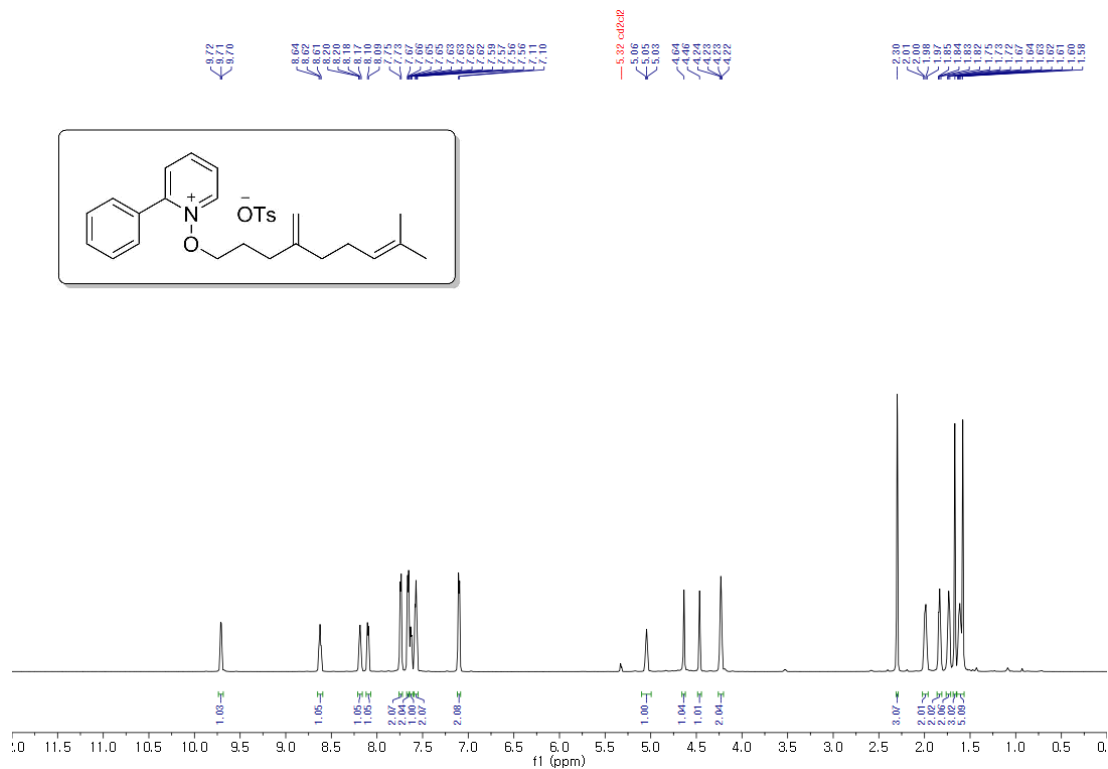


600 MHz, ^1H NMR in Methylene Chloride- d_2

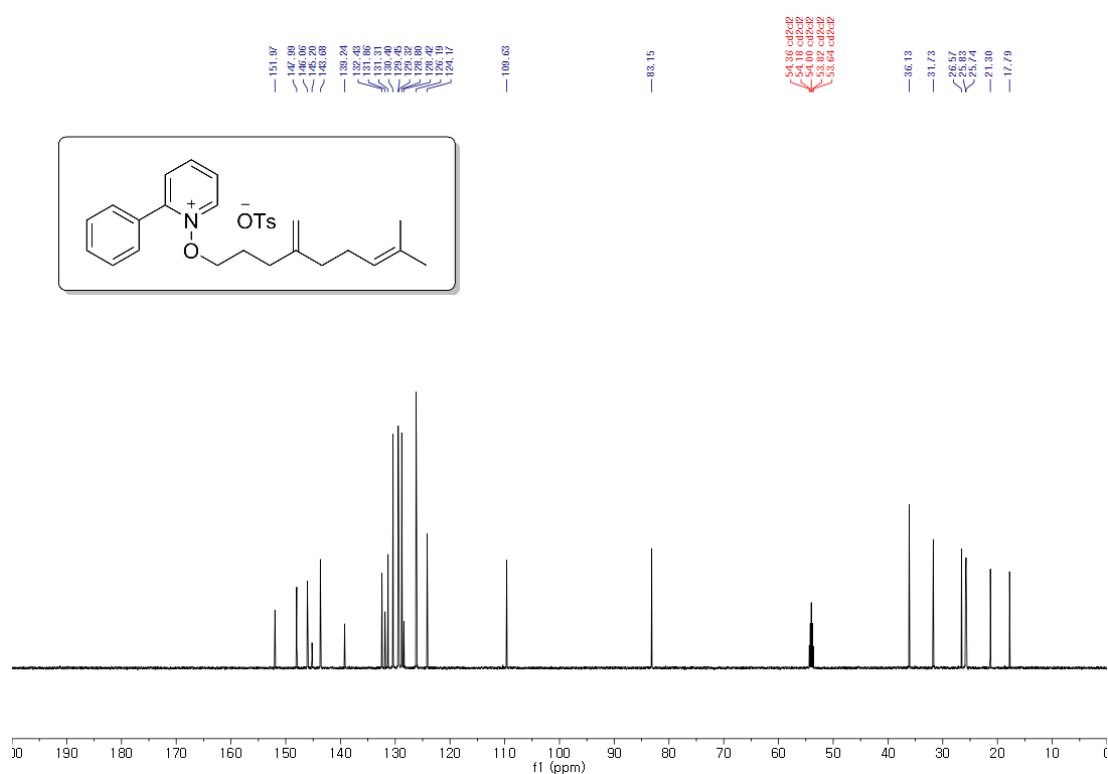


1-((8-methyl-4-methylenenon-7-en-1-yl)oxy)-2-phenylpyridin-1-ium 4-methylbenzenesulfonate (3c).

600 MHz, ^1H NMR in Methylene Chloride- d_2



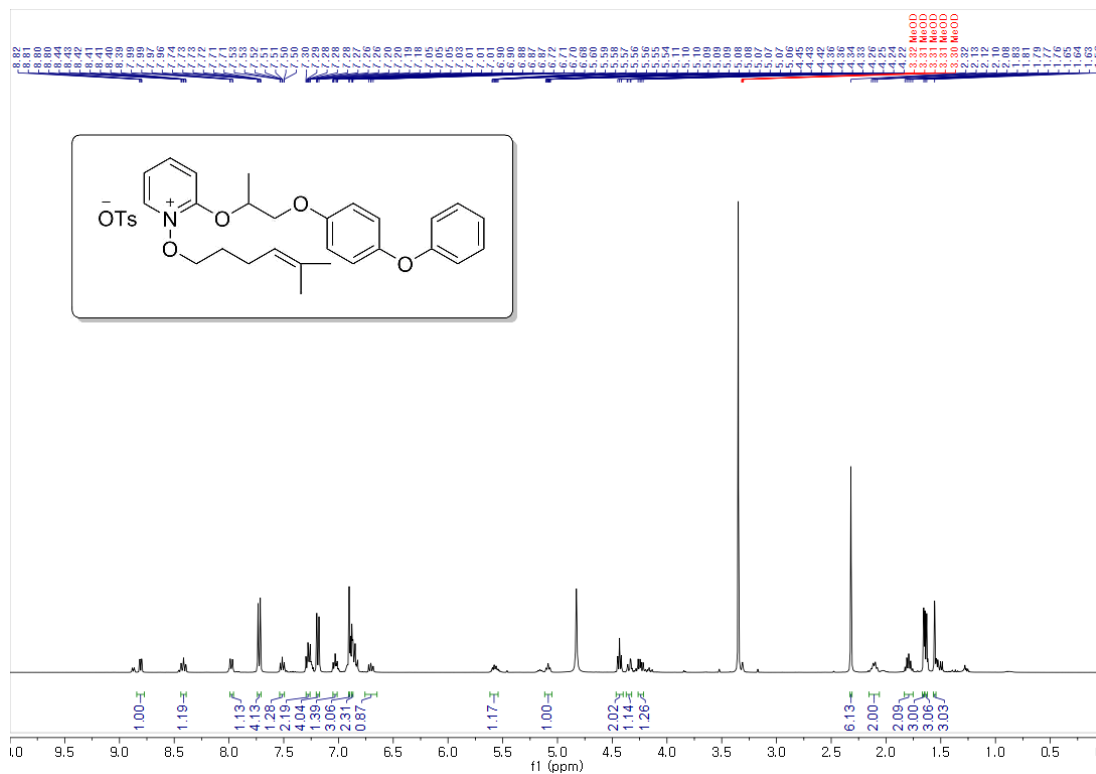
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



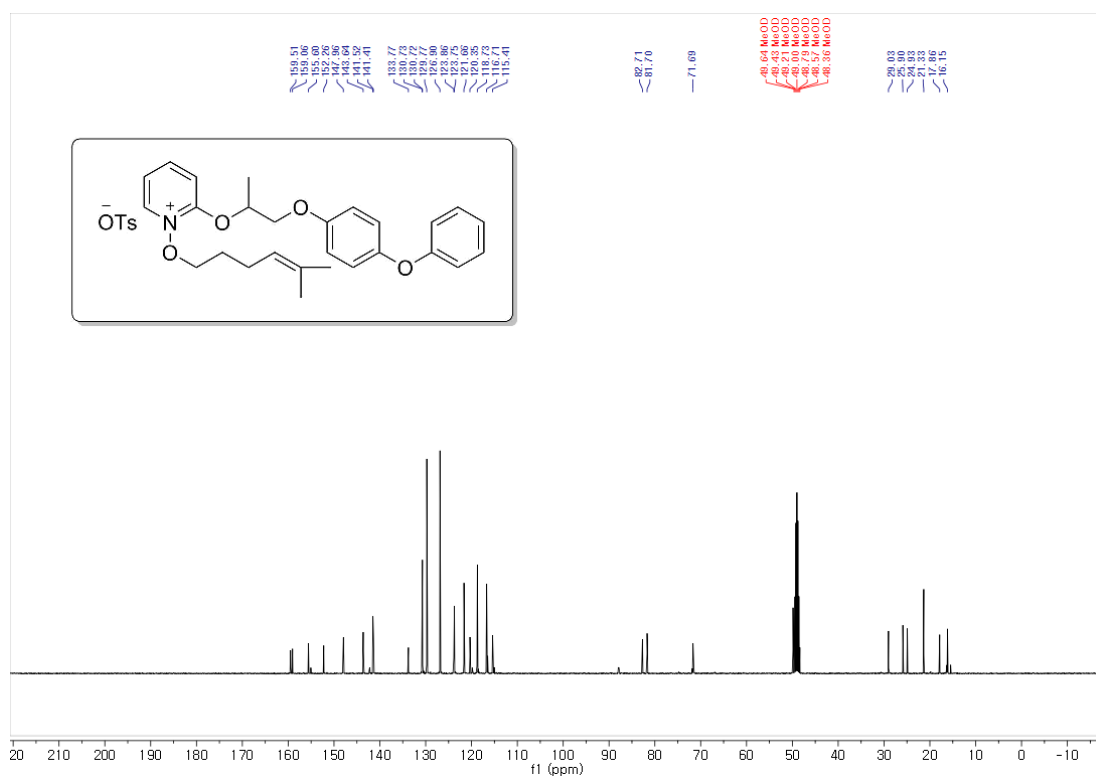
1-((5-methylhex-4-en-1-yl)oxy)-2-((1-phenoxypropan-2-yl)oxy)pyridin-1-ium methylbenzenesulfonate (3e).

4-

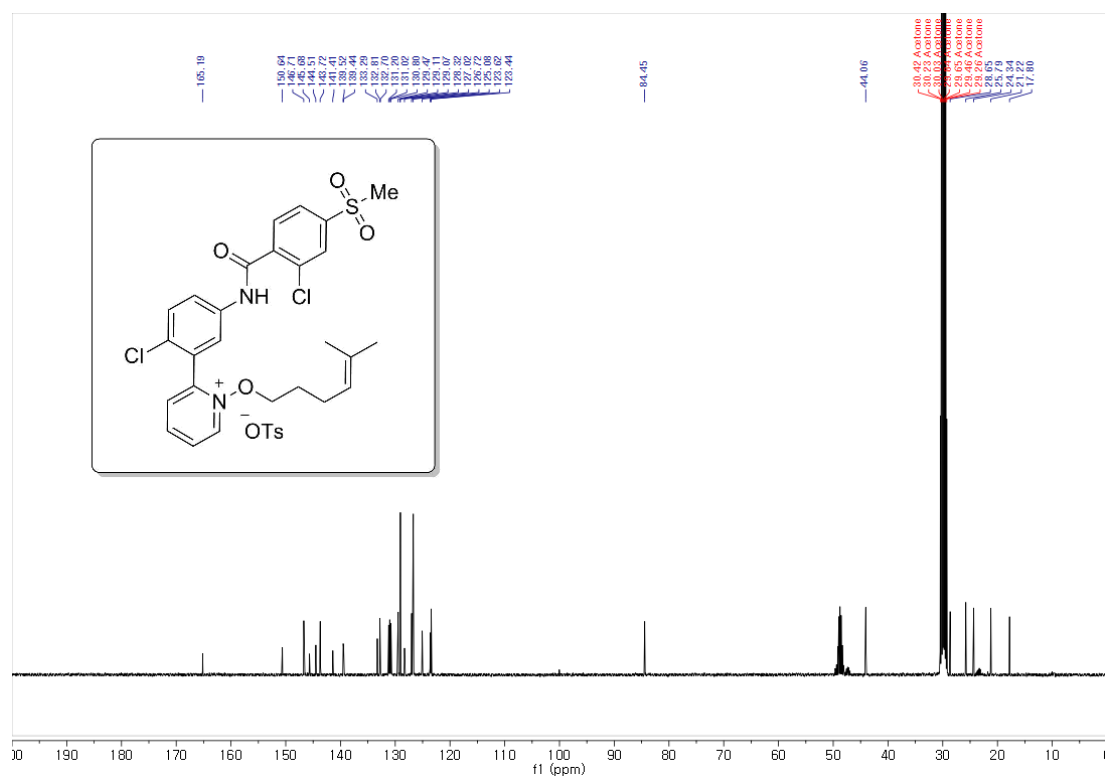
400 MHz, ^1H NMR in Methanol- d_4



100 MHz, ^{13}C NMR in Methanol- d_4

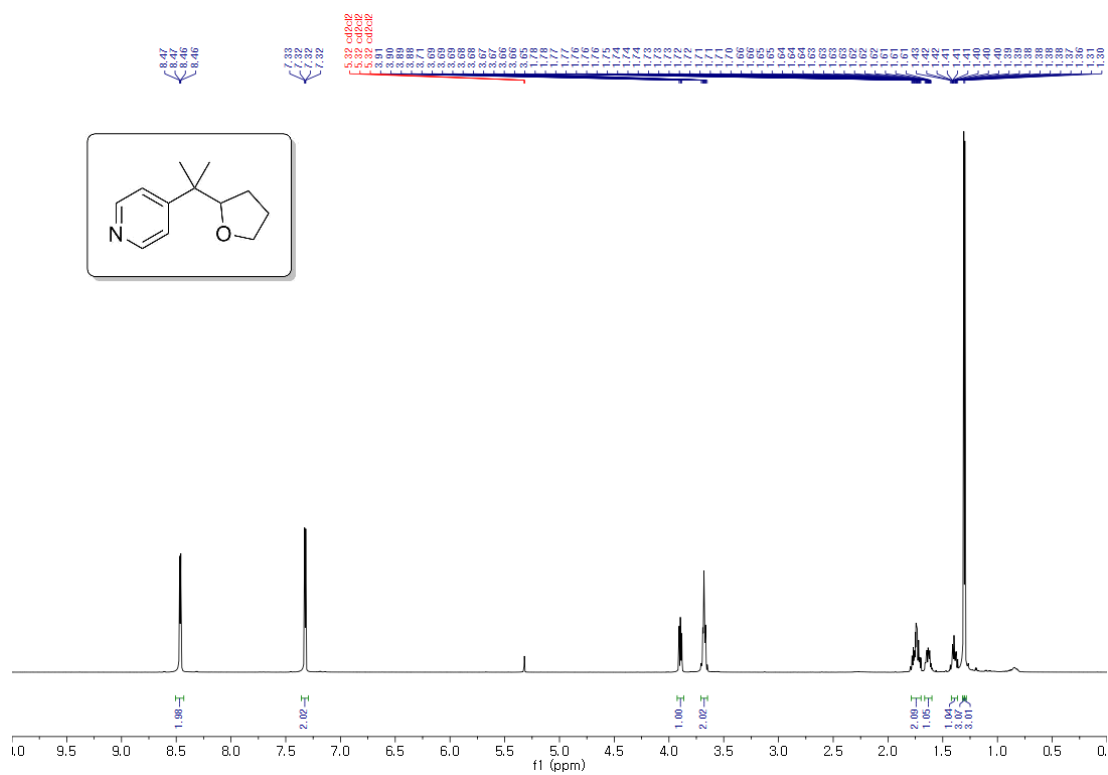


400 MHz, ^1H NMR in Acetone- d_6

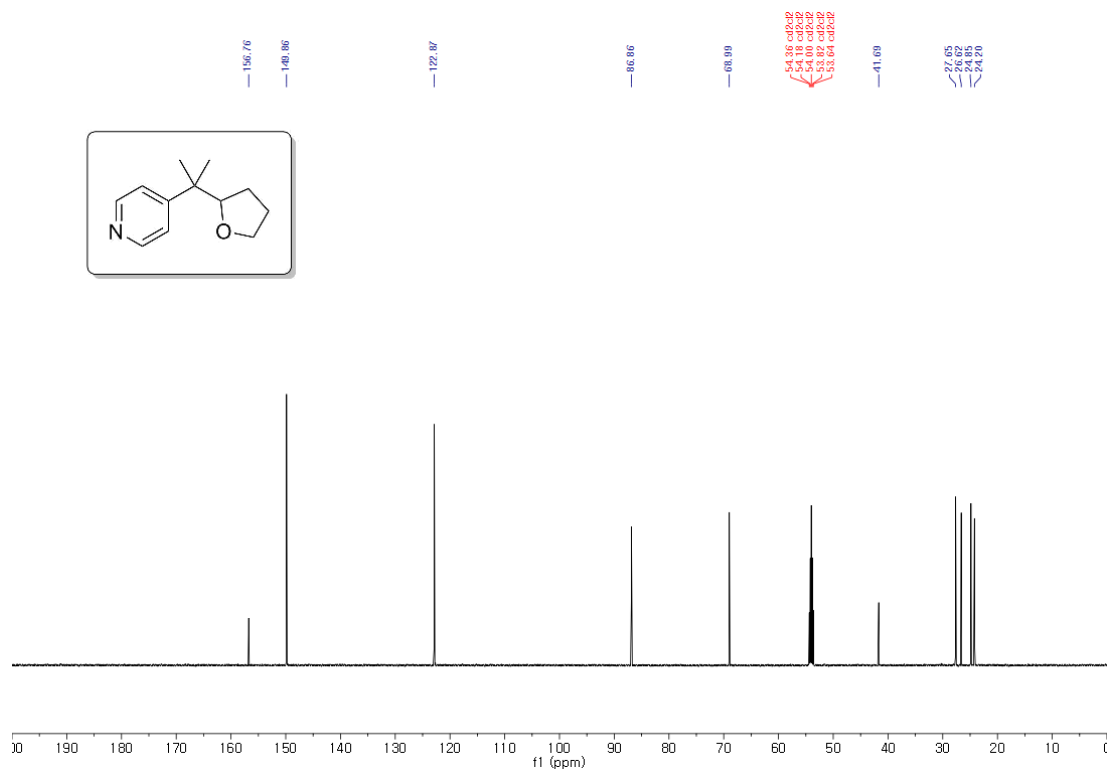


4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2a).

600 MHz, ^1H NMR in Methylene Chloride- d_2

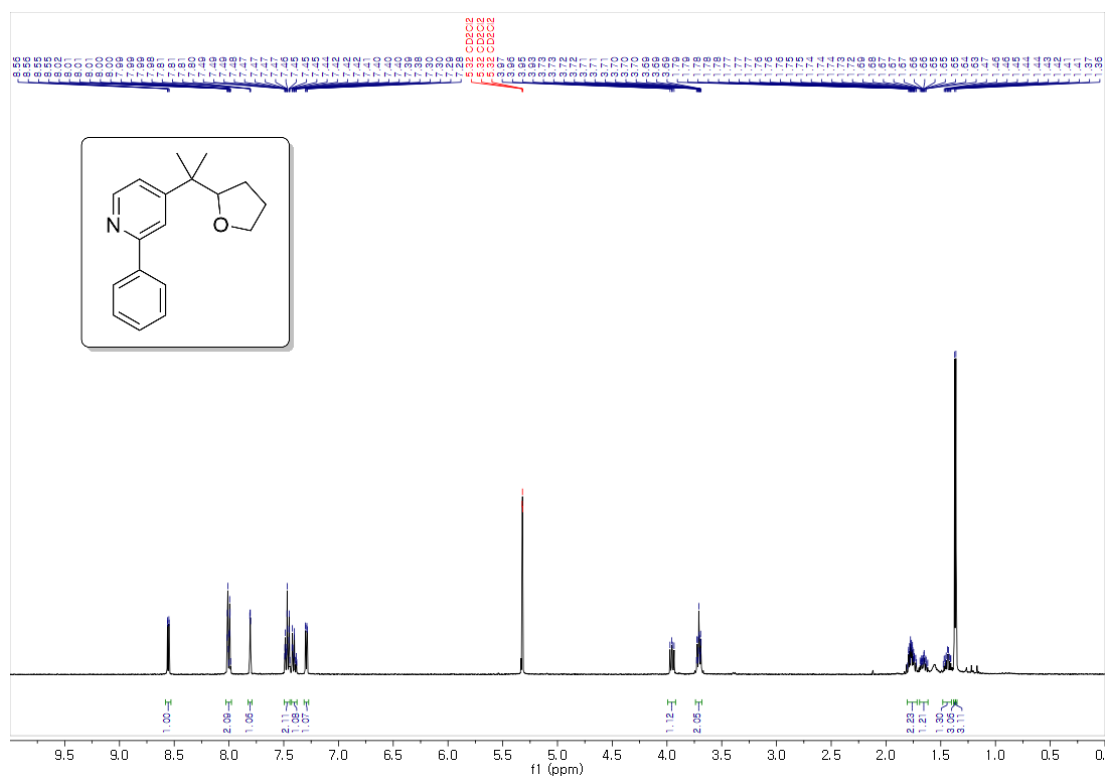


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

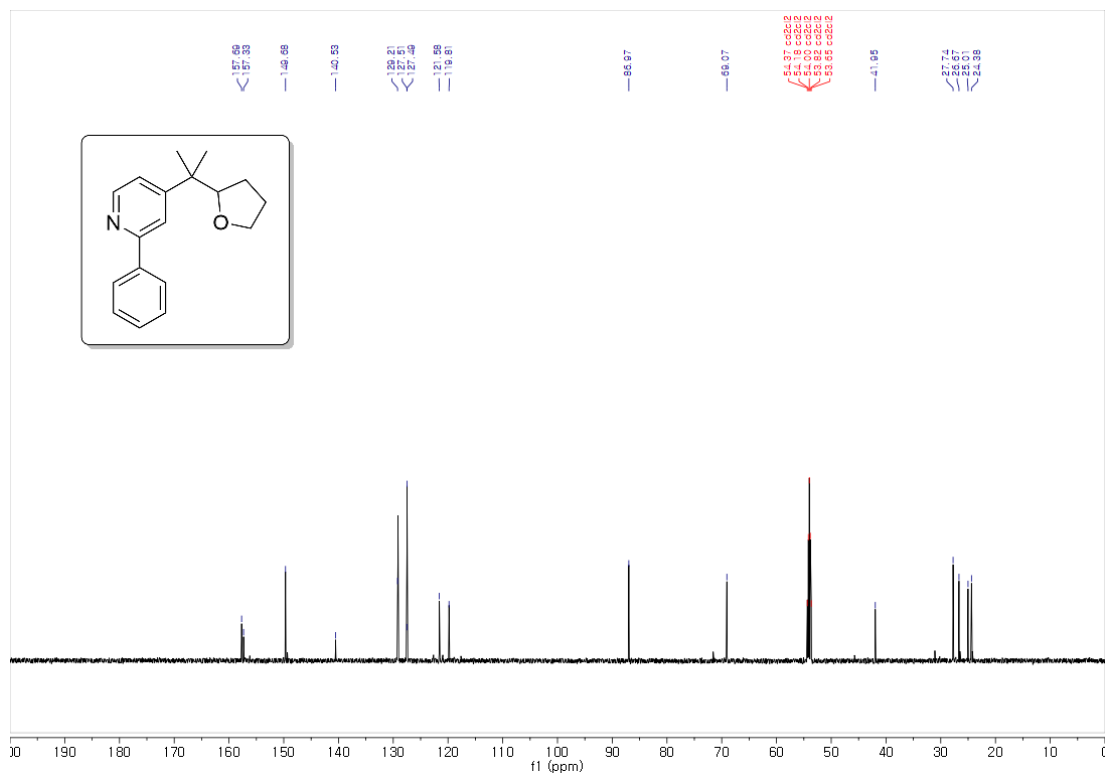


2-phenyl-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2b).

400 MHz, ^1H NMR in Methylene Chloride- d_2

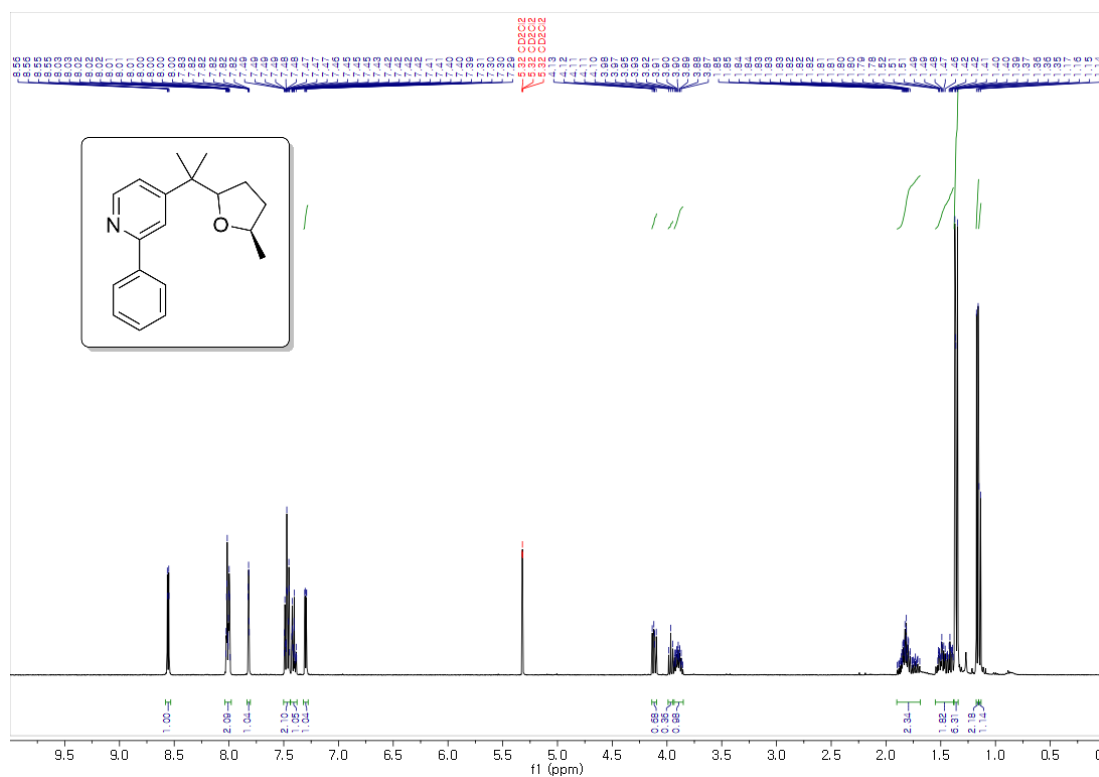


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

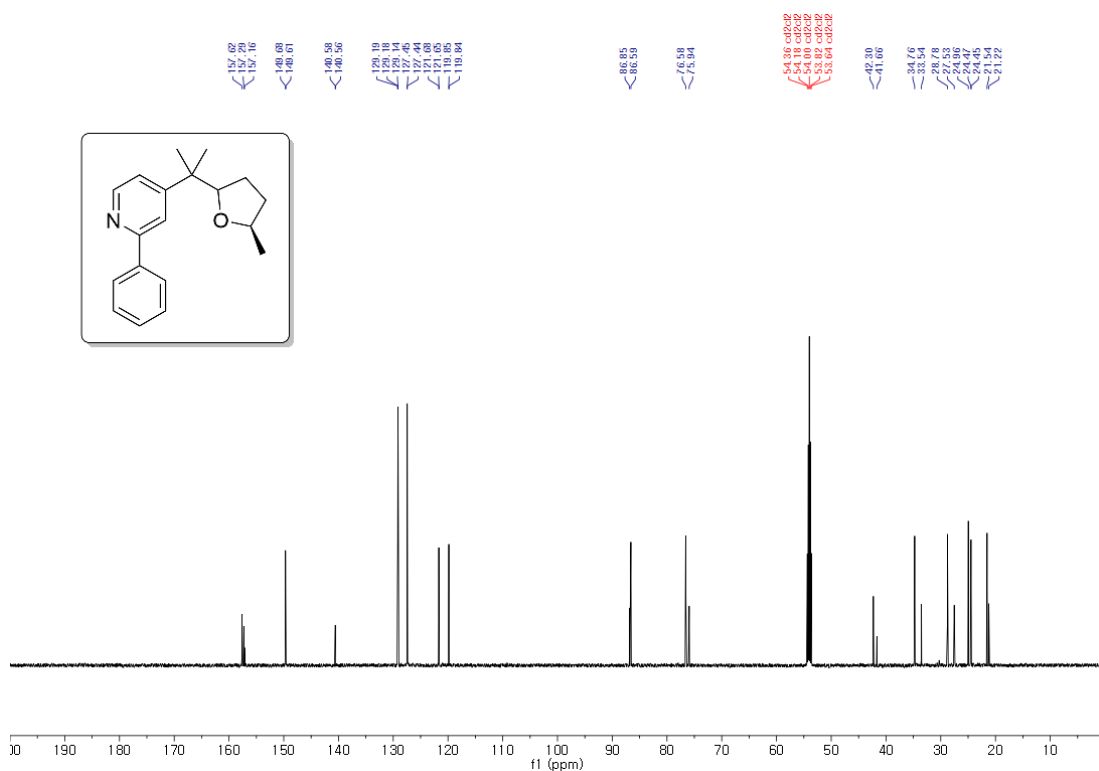


4-(2-((5*R*)-5-methyltetrahydrofuran-2-yl)propan-2-yl)-2-phenylpyridine (**2c**). d.r. 2.0:1.

400 MHz, ^1H NMR in Methylene Chloride- d_2

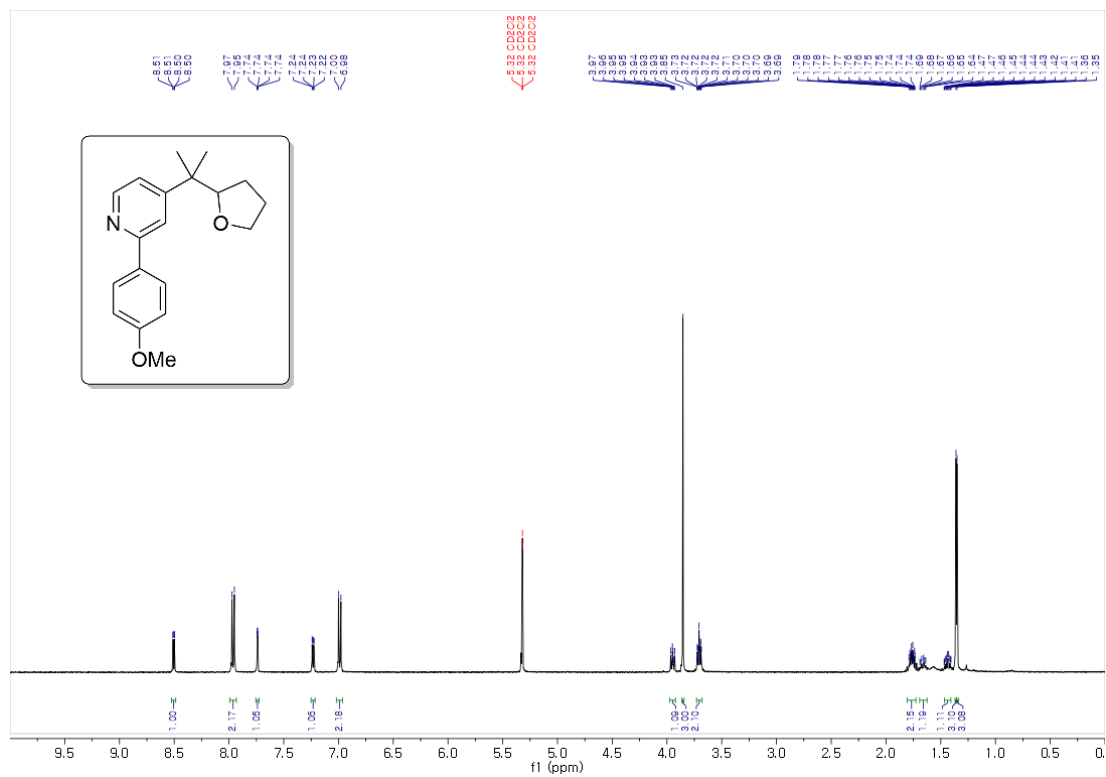


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

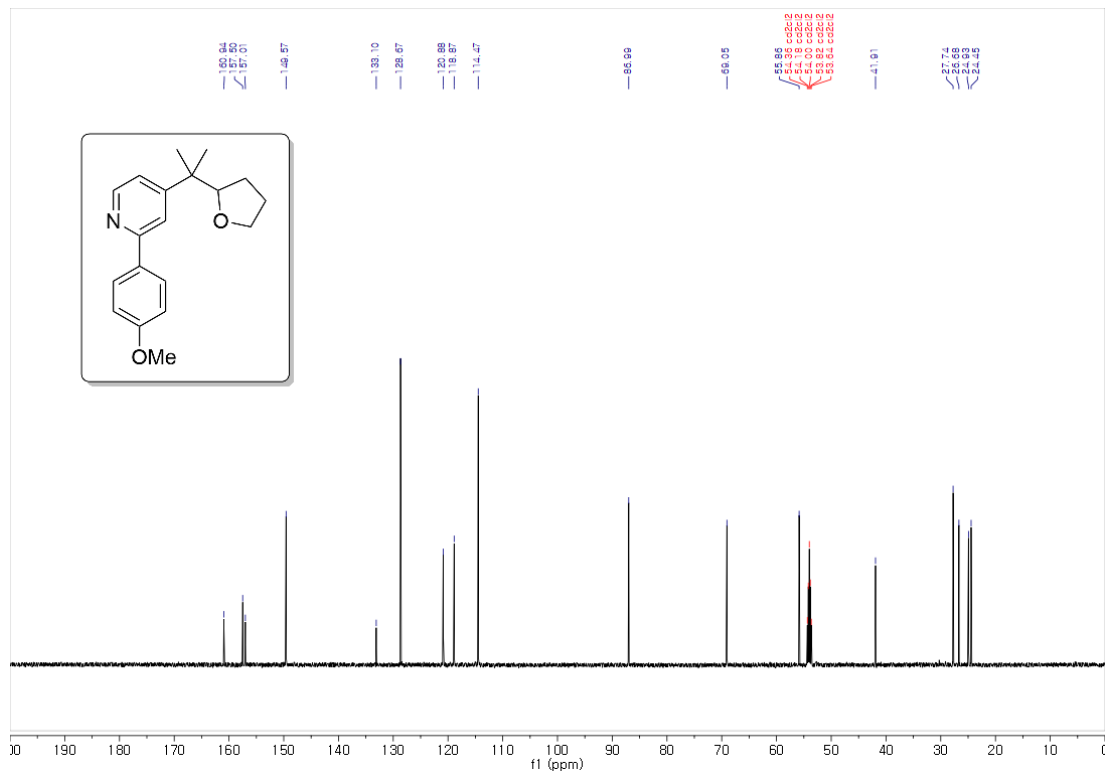


2-(4-methoxyphenyl)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (2d).

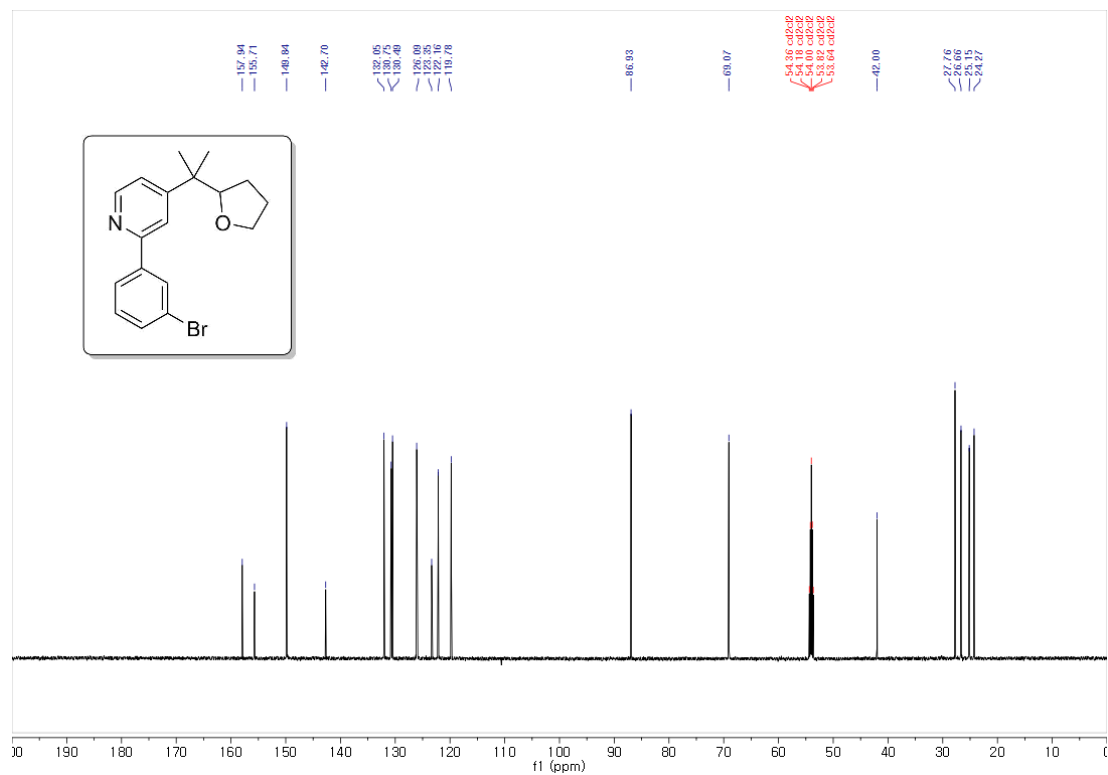
400 MHz, ^1H NMR in Methylene Chloride- d_2



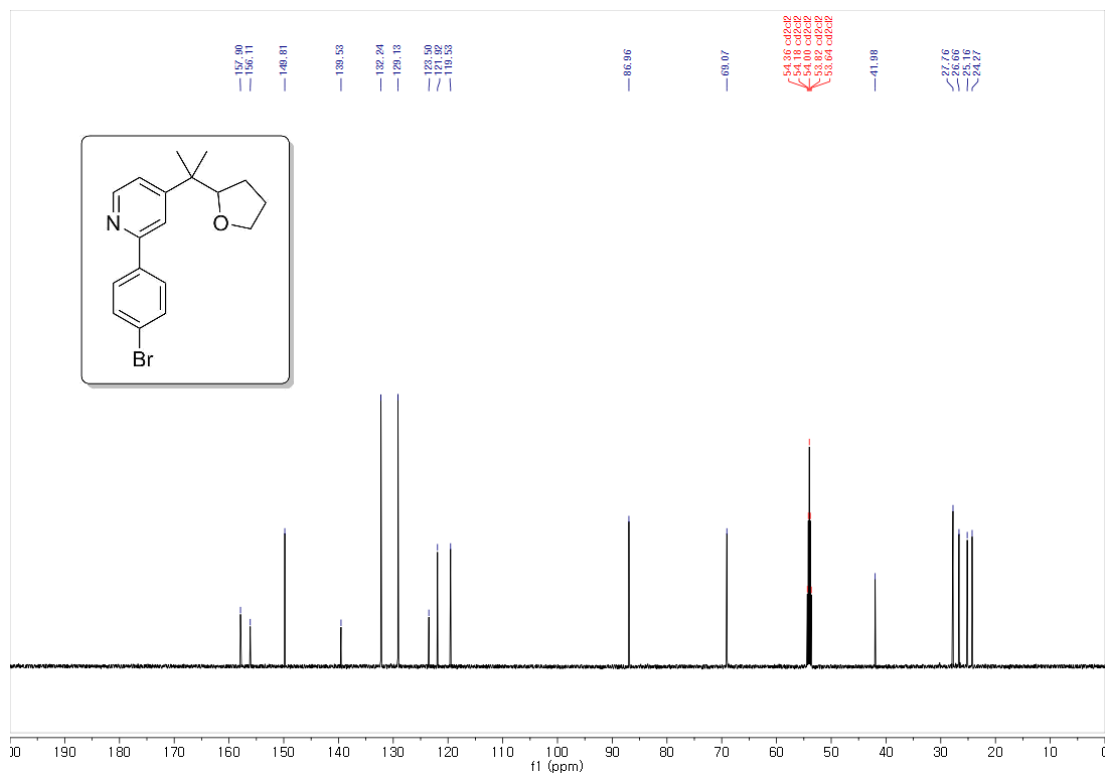
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



400 MHz, ^1H NMR in Methylene Chloride- d_2

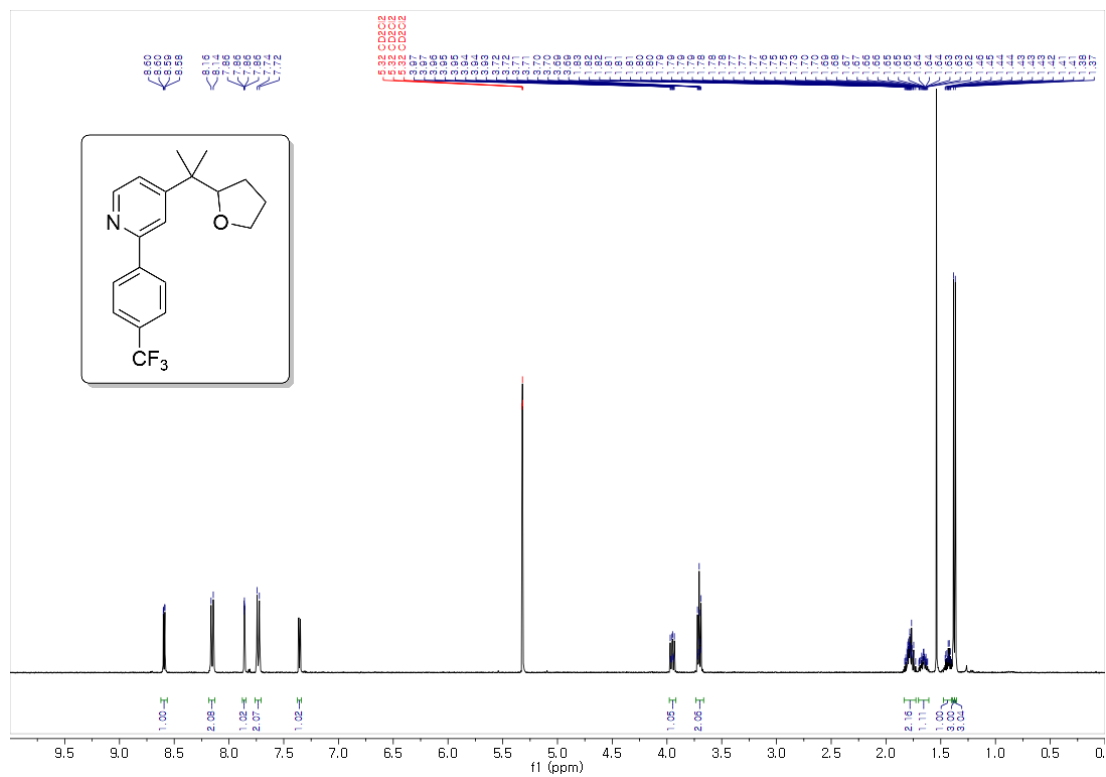


¹H NMR (400 MHz, Methylene Chloride-*d*₂)

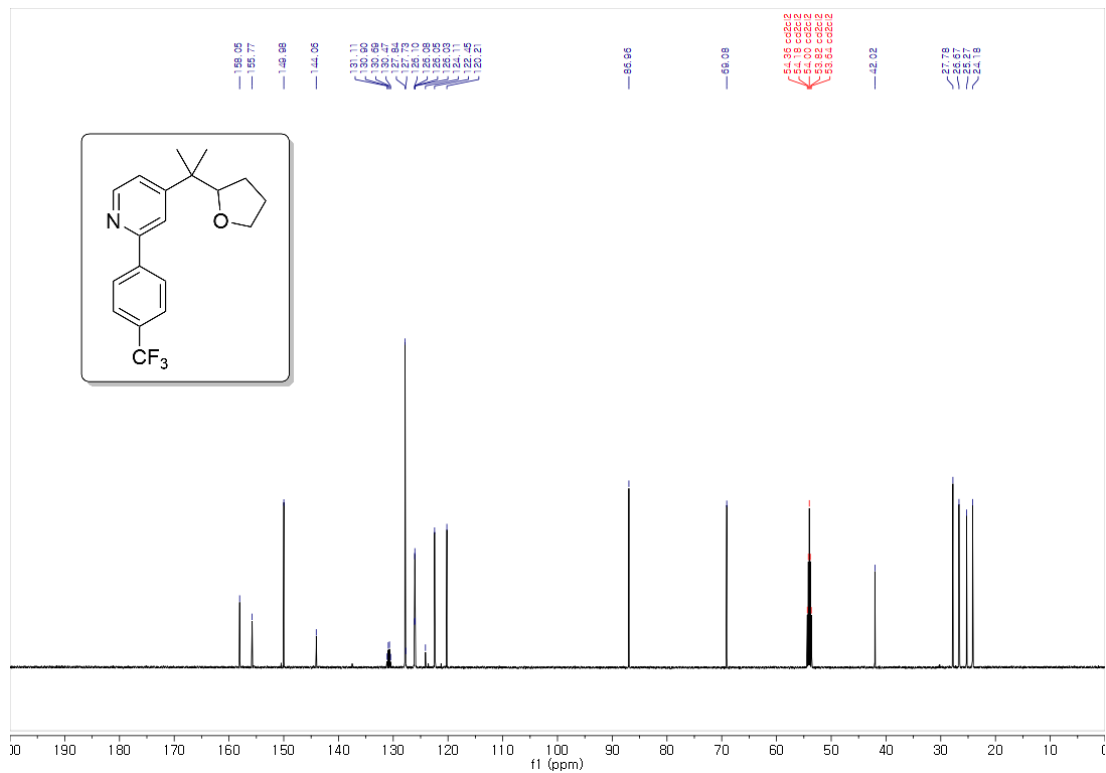


4-(2-(tetrahydrofuran-2-yl)propan-2-yl)-2-(4-(trifluoromethyl)phenyl)pyridine (2g).

400 MHz, ^1H NMR in Methylene Chloride- d_2

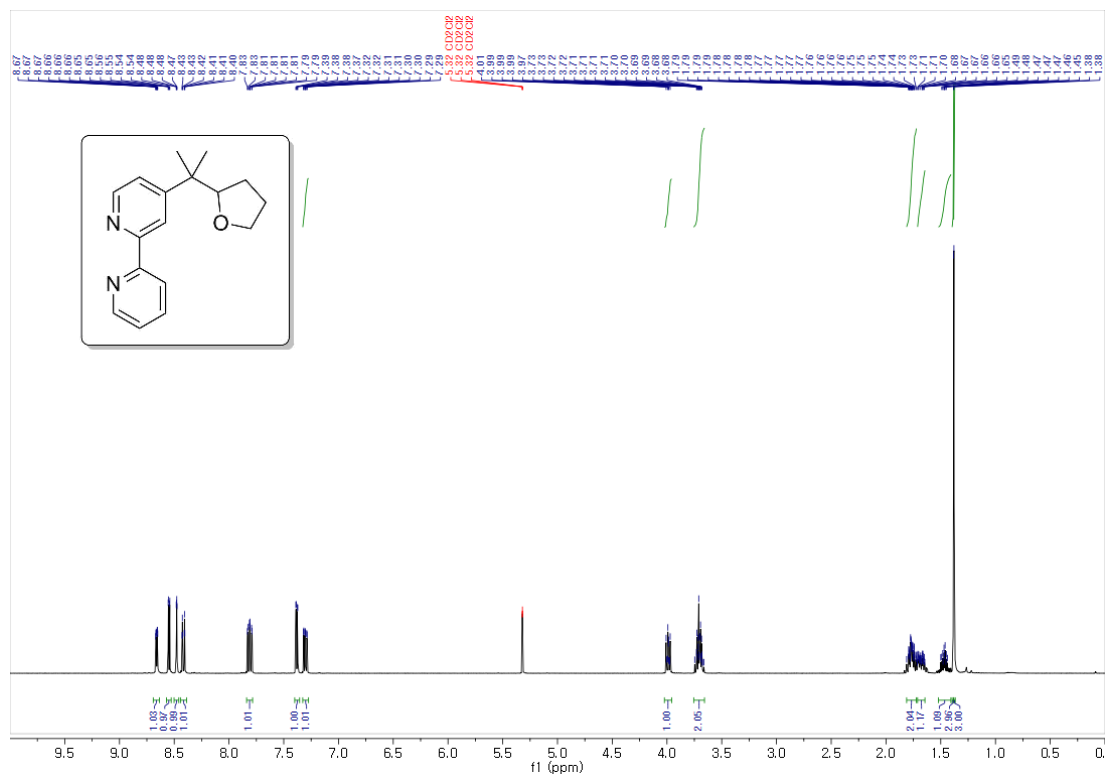


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

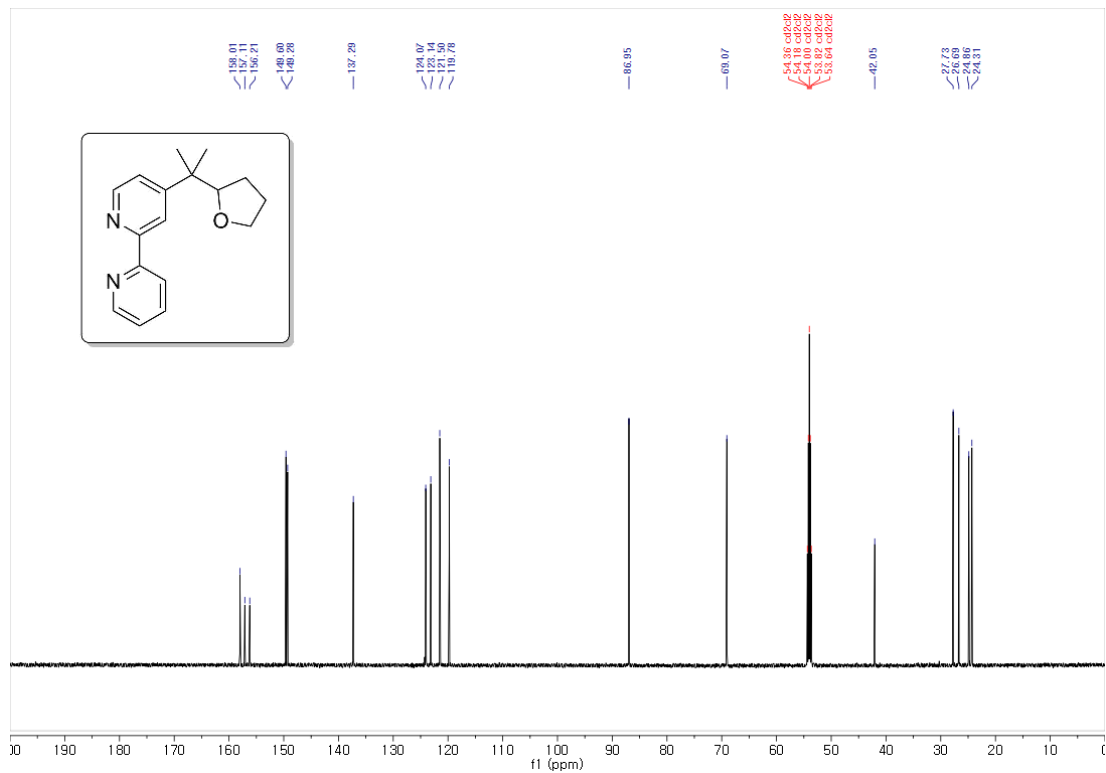


4-(2-(tetrahydrofuran-2-yl)propan-2-yl)-2,2'-bipyridine (2h).

400 MHz, ^1H NMR in Methylene Chloride- d_2

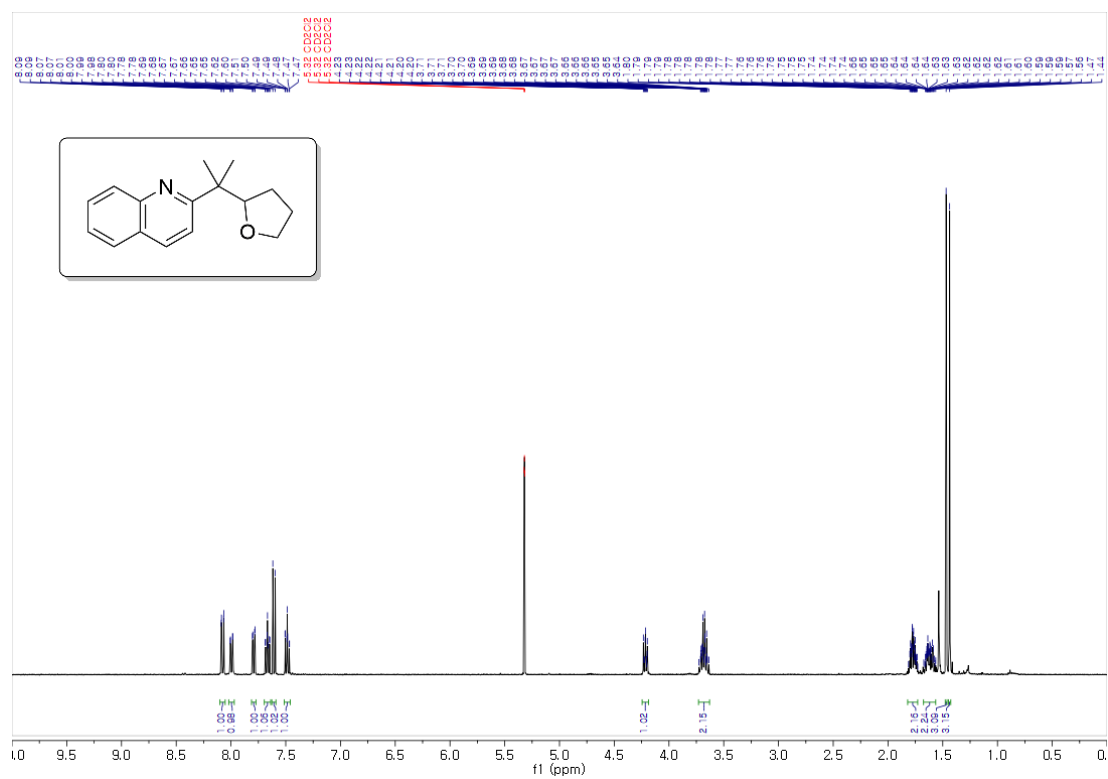


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

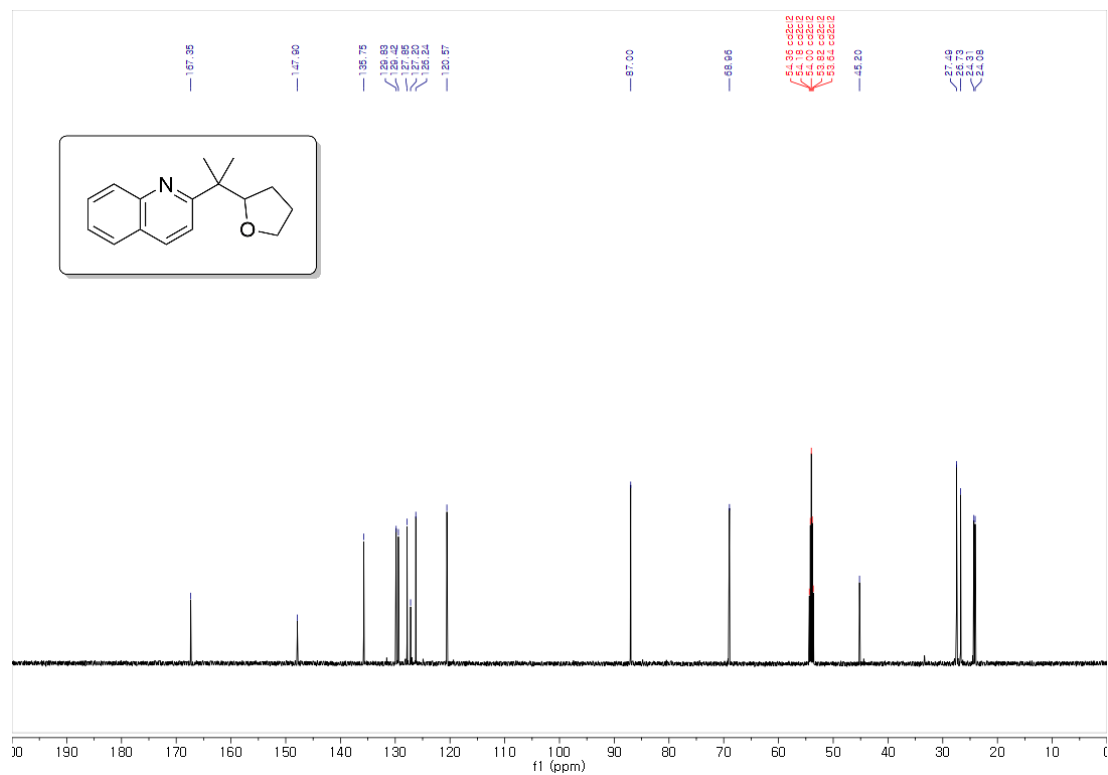


2-(2-(tetrahydrofuran-2-yl)propan-2-yl)quinolone (2i).

400 MHz, ^1H NMR in Methylene Chloride- d_2

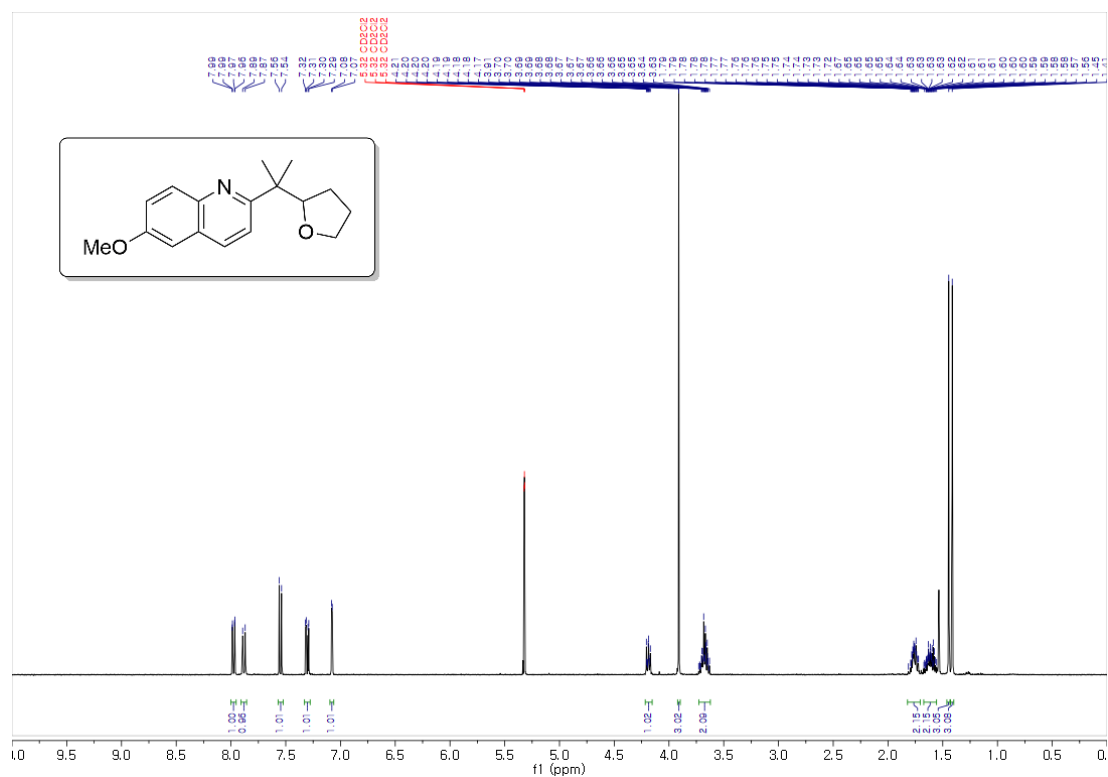


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

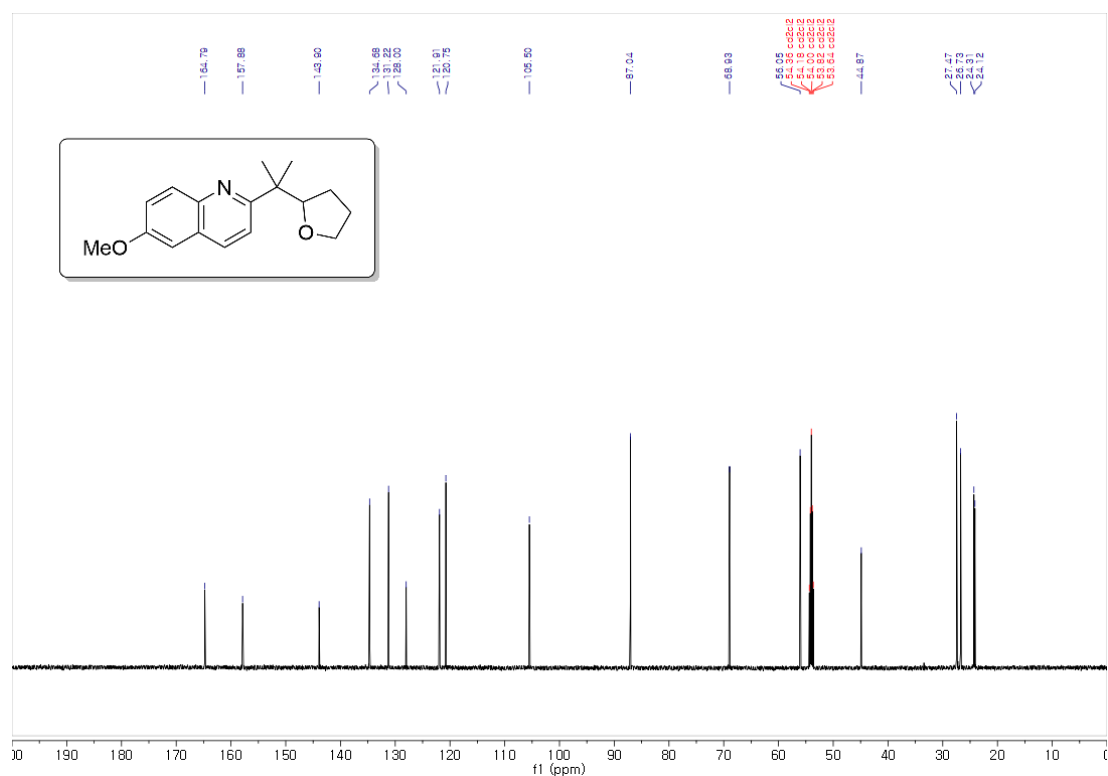


6-methoxy-2-(2-(tetrahydrofuran-2-yl)propan-2-yl)quinolone (2j).

400 MHz, ^1H NMR in Methylene Chloride- d_2

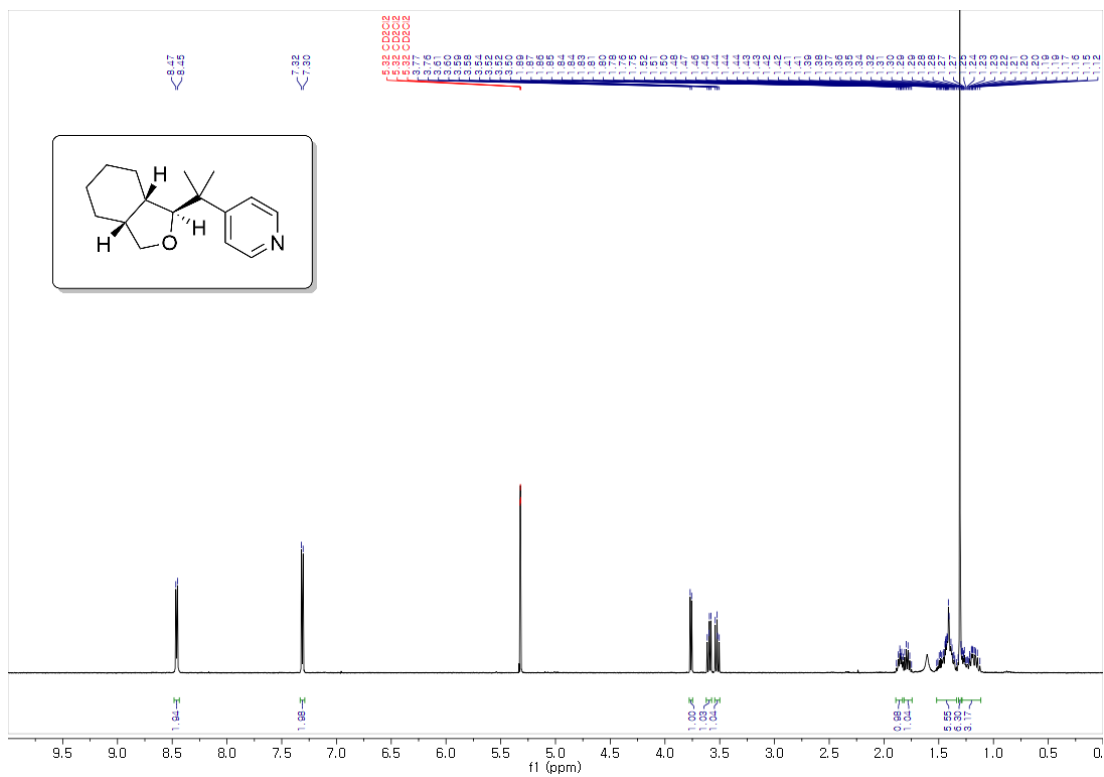


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

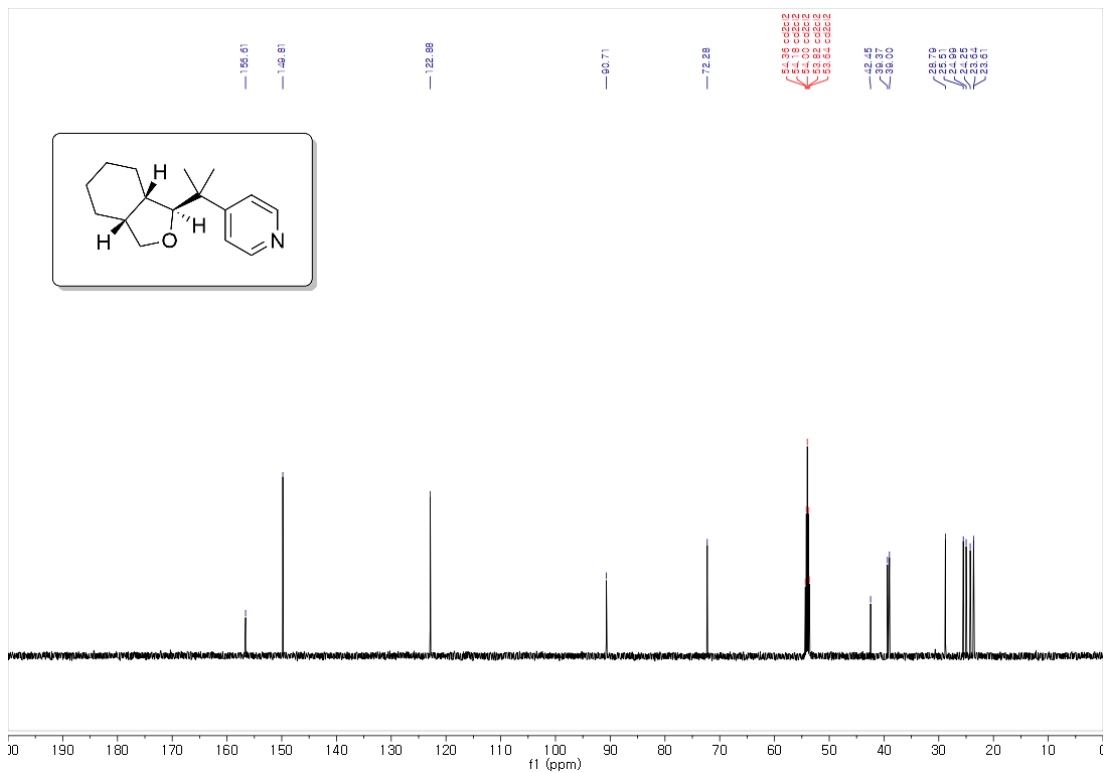


***rel*-4-(2-((1*S*,3*aR*,7*aS*)-octahydroisobenzofuran-1-yl)propan-2-yl)pyridine (2k).**

400 MHz, ^1H NMR in Methylene Chloride- d_2

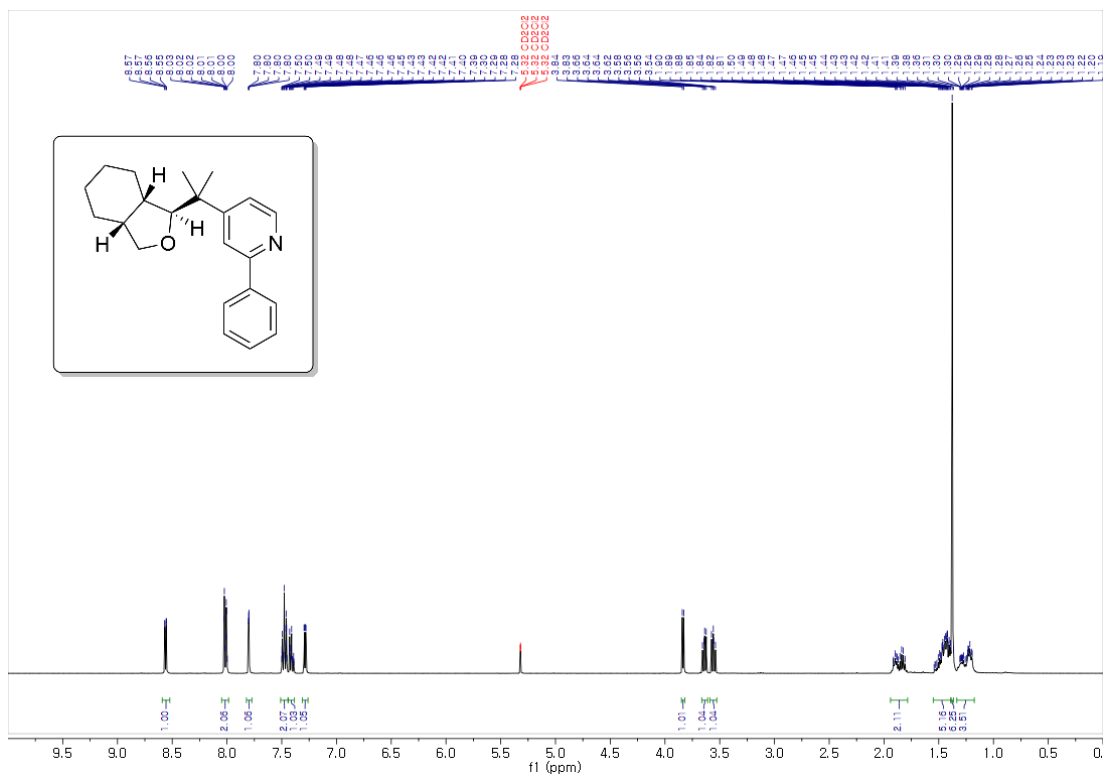


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

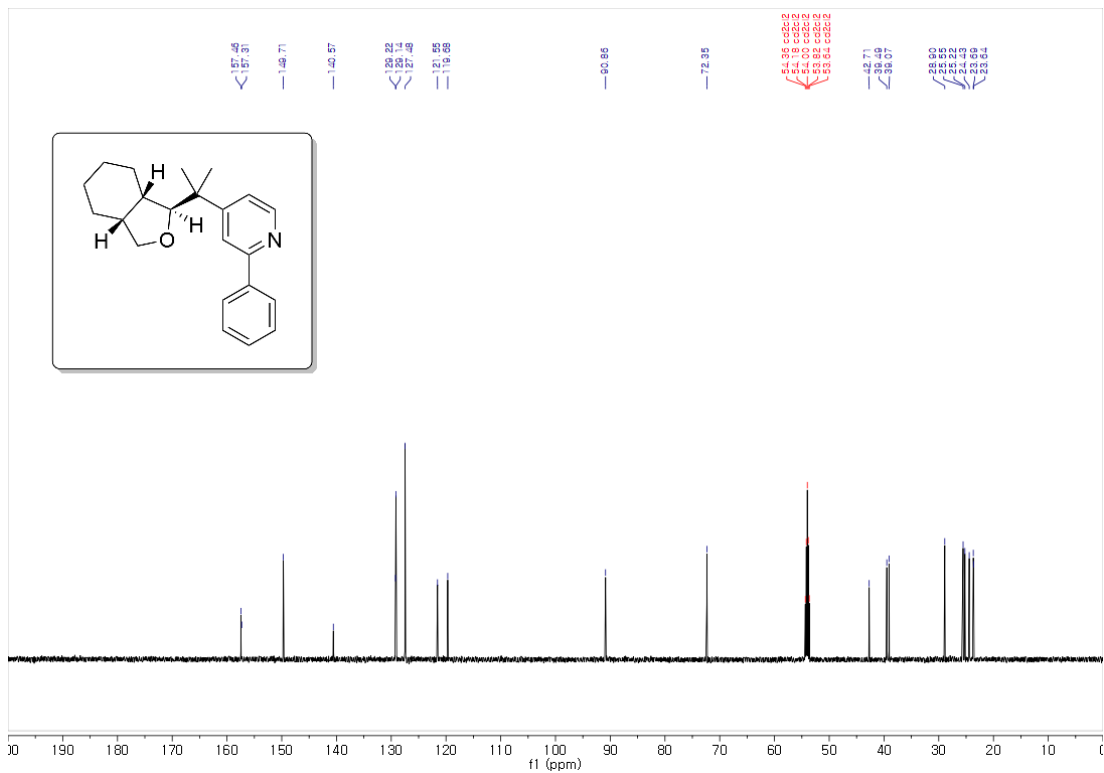


***rel*-4-(2-((1*S*,3*aR*,7*aS*)-octahydroisobenzofuran-1-yl)propan-2-yl)-2-phenylpyridine (2l).**

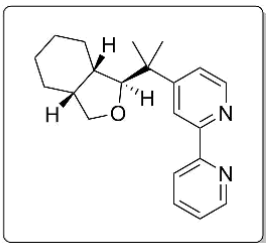
400 MHz, ^1H NMR in Methylene Chloride- d_2



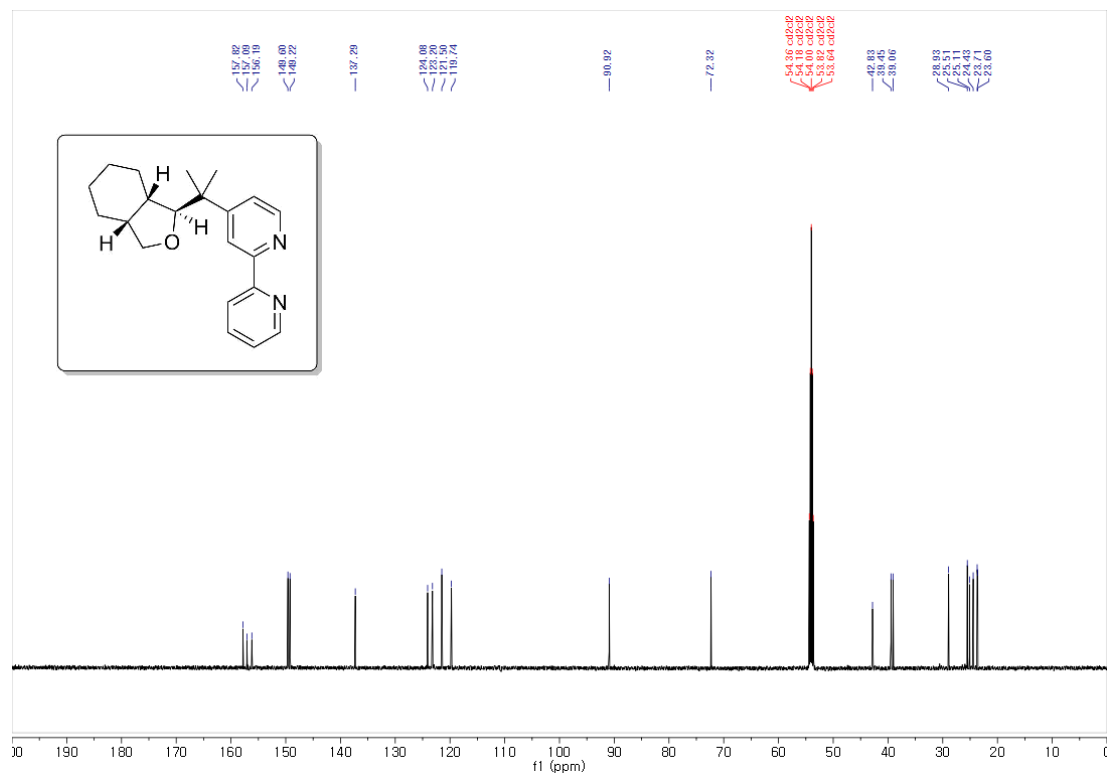
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



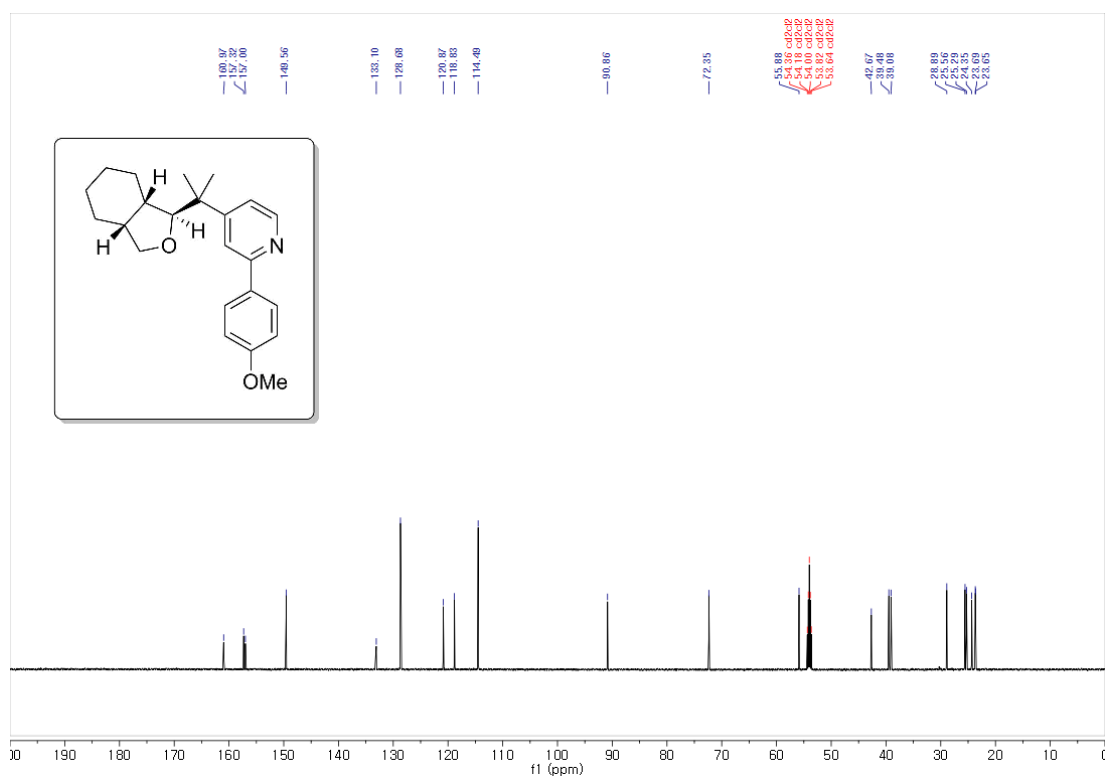
400 MHz, ^1H NMR in Methylene Chloride- d_2



The chemical structure shows a bicyclic system consisting of a cyclohexane ring fused to a tetrahydropyran ring. The tetrahydropyran ring has a methyl group at the 2-position and a 2-pyridyl group at the 3-position. Stereochemistry is indicated with wedges and dashes: the methyl group at C2 is dashed, and the 2-pyridyl group at C3 is wedged. The cyclohexane ring has two hydrogens at the bridgehead carbons, one wedged and one dashed.

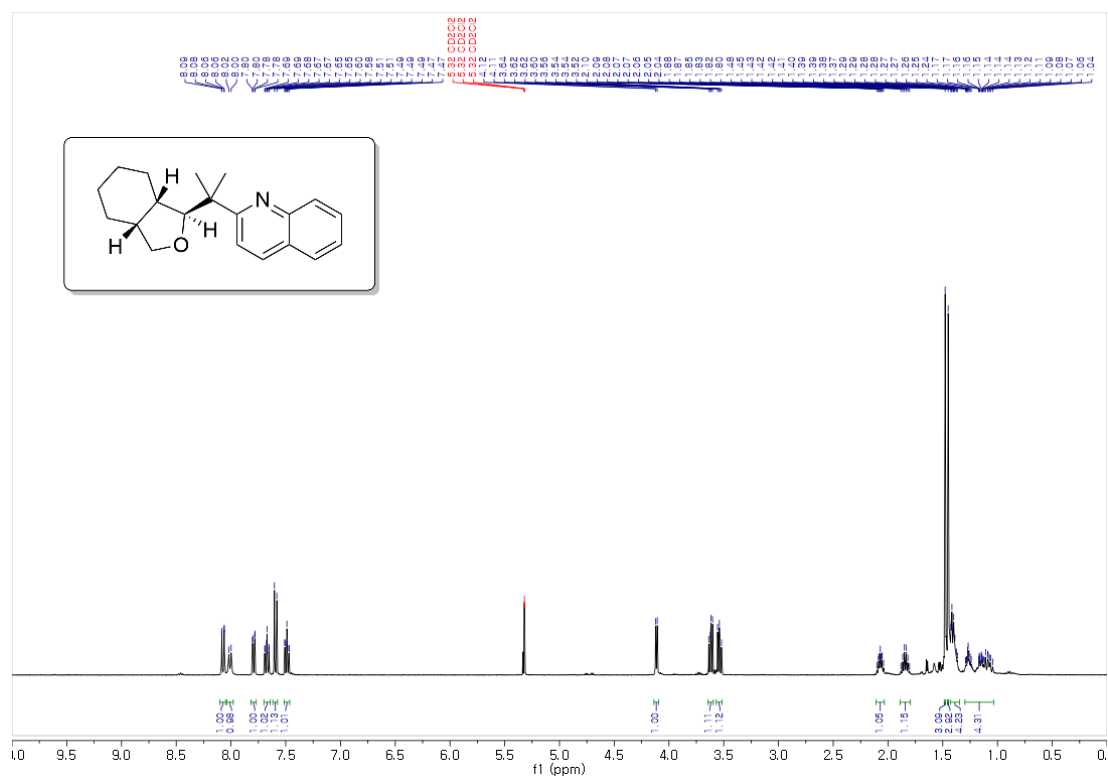


400 MHz, ^1H NMR in Methylene Chloride- d_2

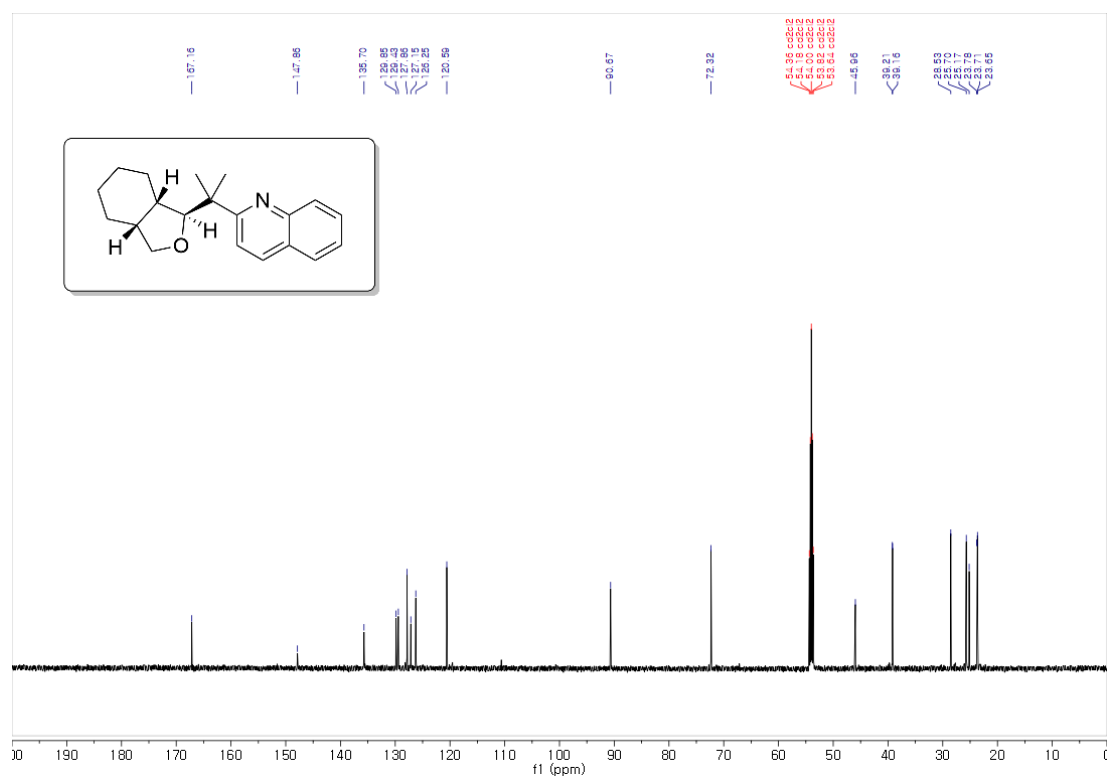


***rel*-2-(2-((1*S*,3*aR*,7*aS*)-octahydroisobenzofuran-1-yl)propan-2-yl)quinolone (2o).**

400 MHz, ^1H NMR in Methylene Chloride- d_2

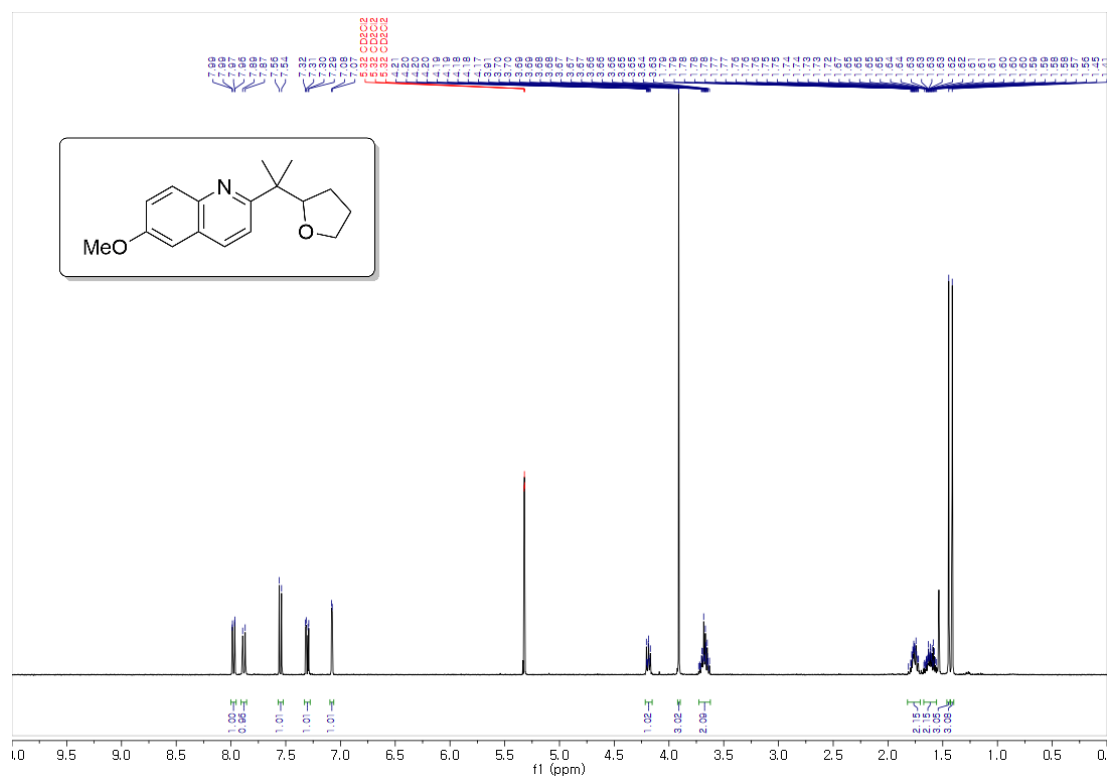


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

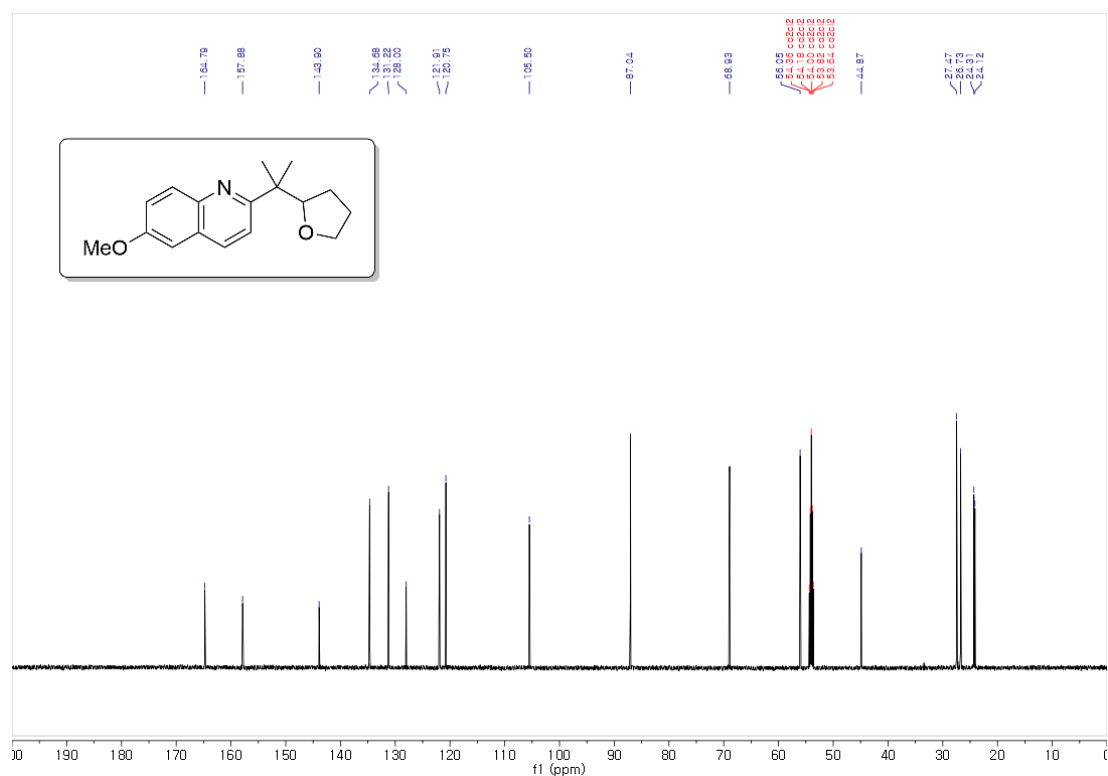


***rel*-6-methoxy-2-((1*S*,3*aR*,7*aS*)-octahydroisobenzofuran-1-yl)propan-2-yl)quinolone (2p).**

400 MHz, ^1H NMR in Methylene Chloride- d_2

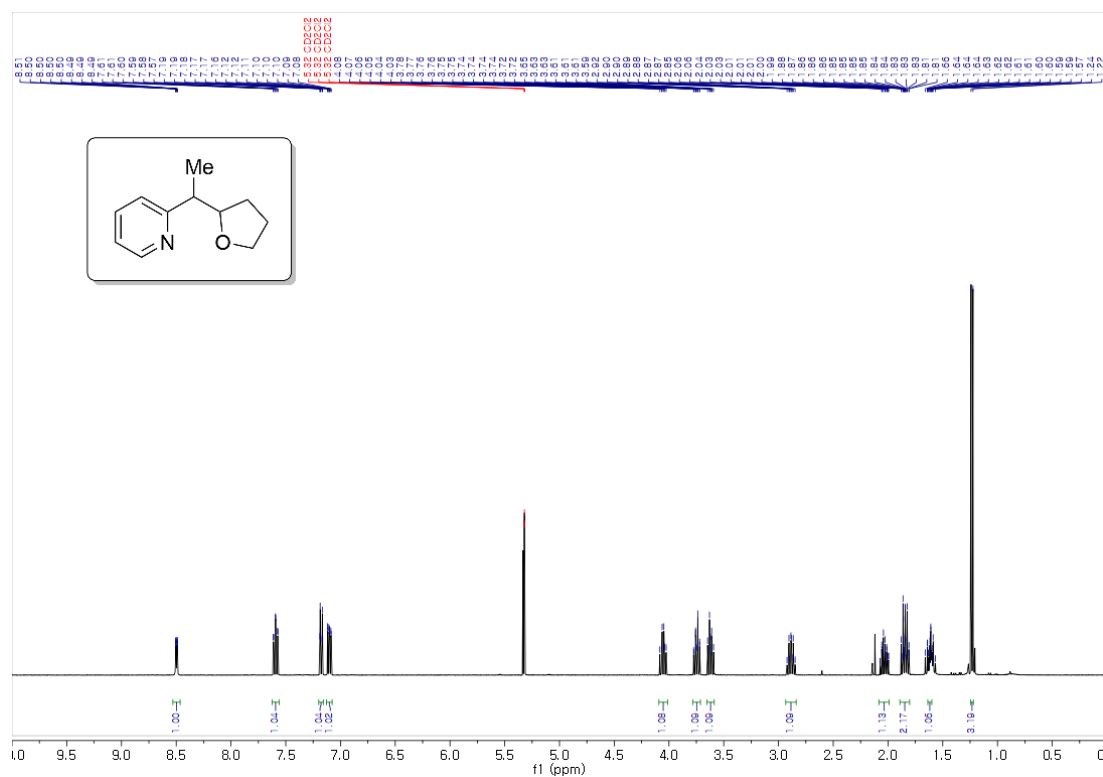


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

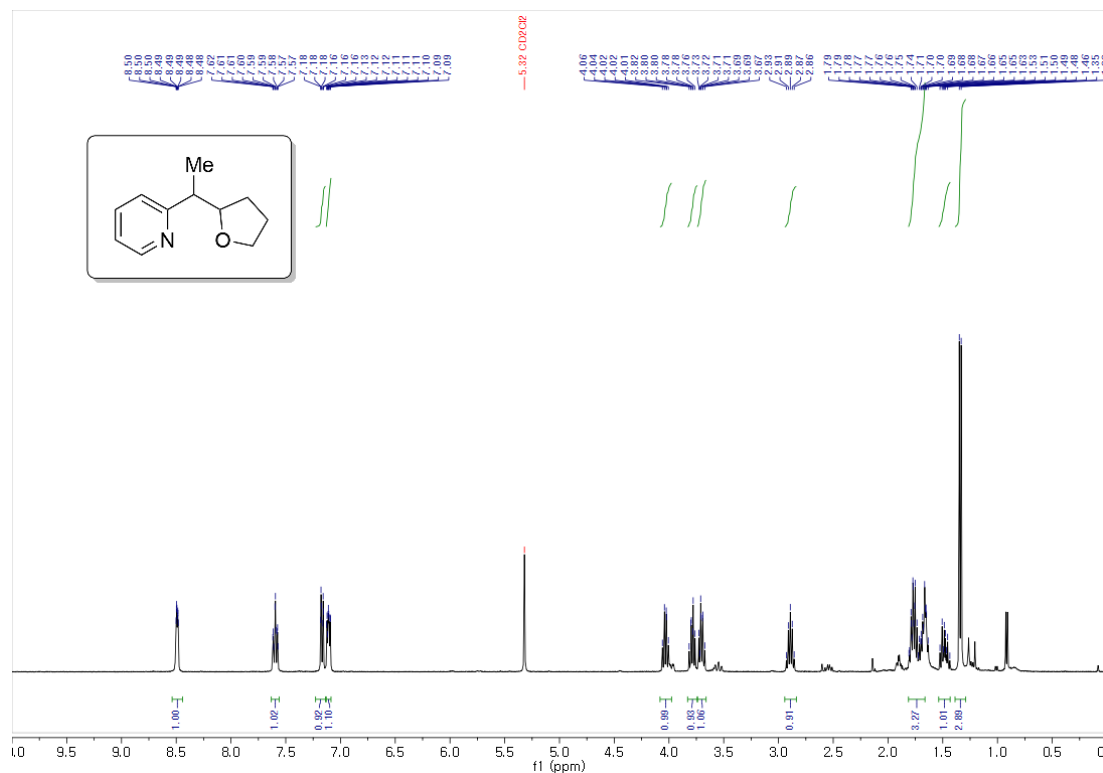


2-(1-(tetrahydrofuran-2-yl)ethyl)pyridine (2q).

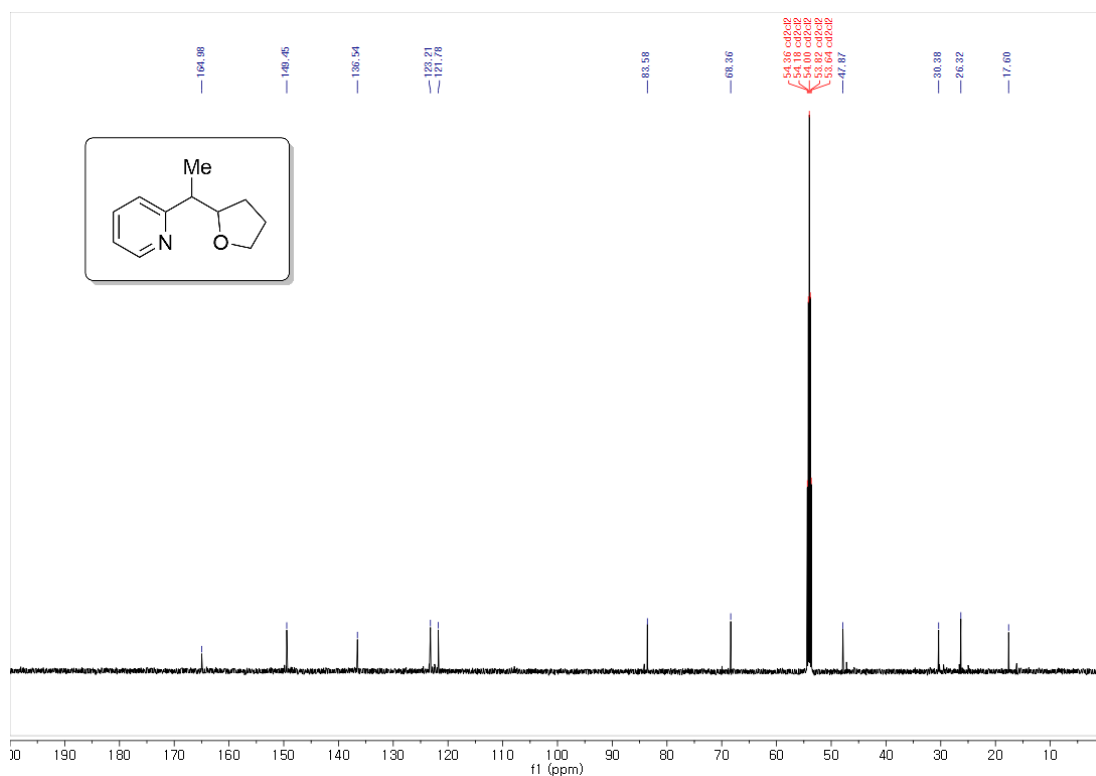
400 MHz, ^1H NMR in Methylene Chloride- d_2 , major diastereomer



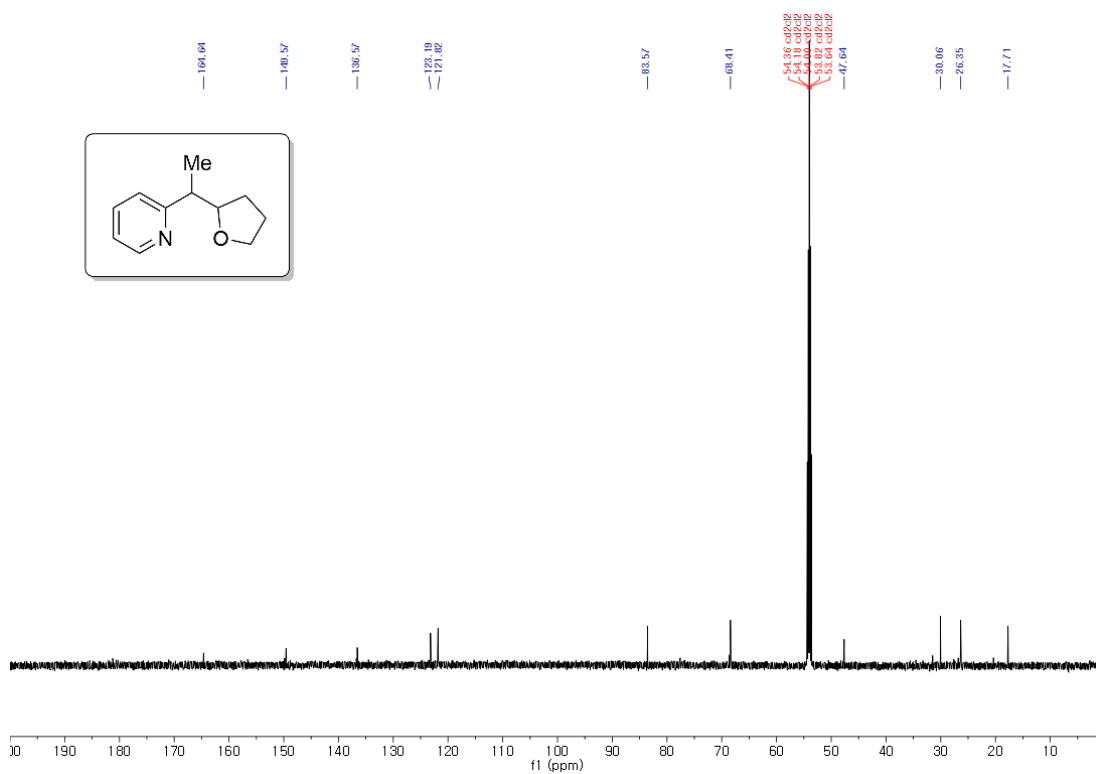
400 MHz, ^1H NMR in Methylene Chloride- d_2 , minor diastereomer



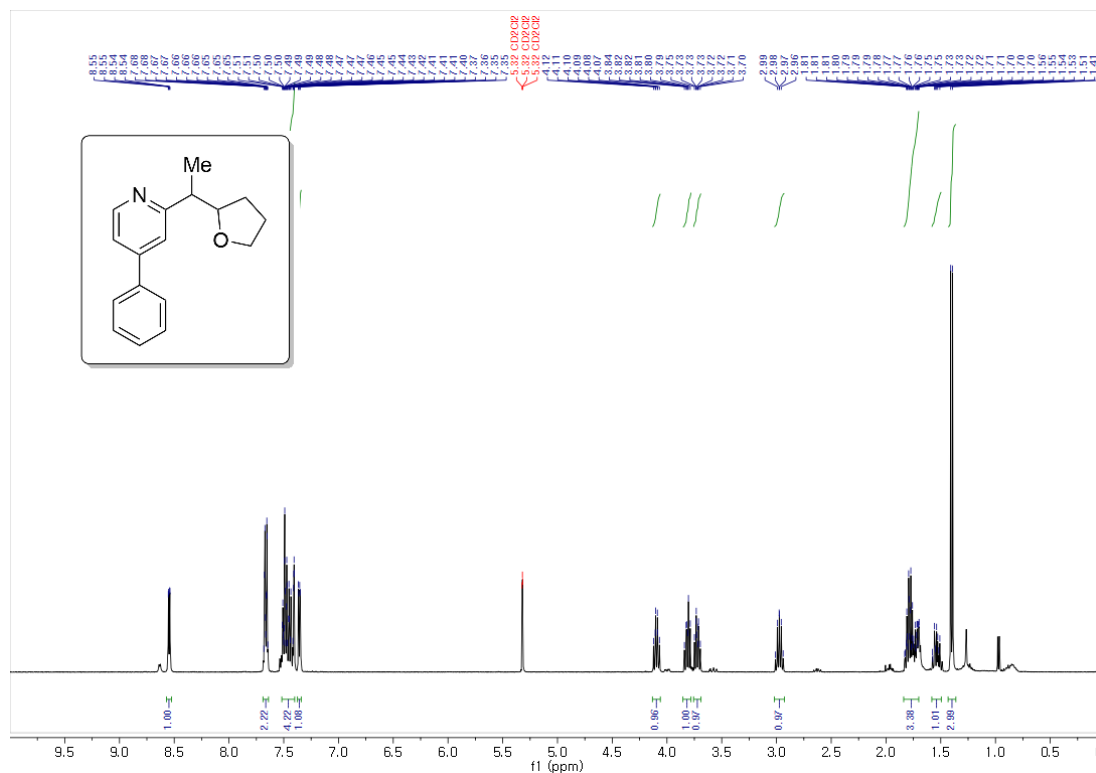
150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , major diastereomer



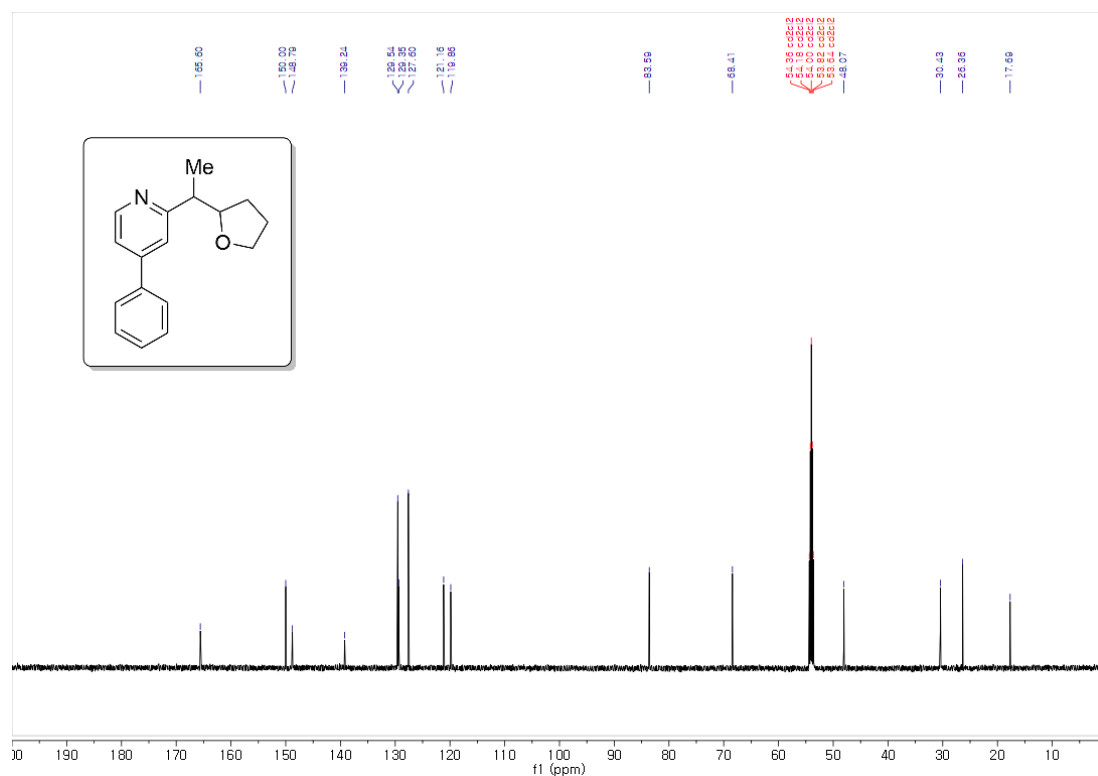
150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , minor diastereomer



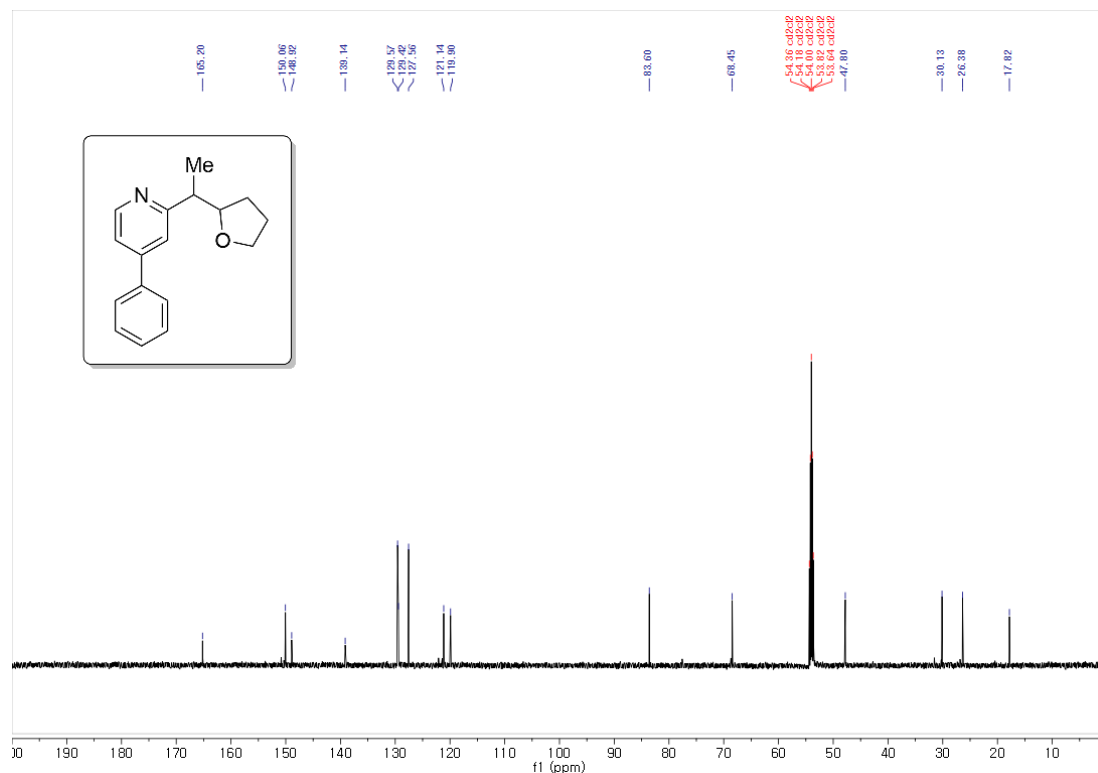
400 MHz, ¹H NMR in Methylene Chloride-*d*₂, major diastereomer



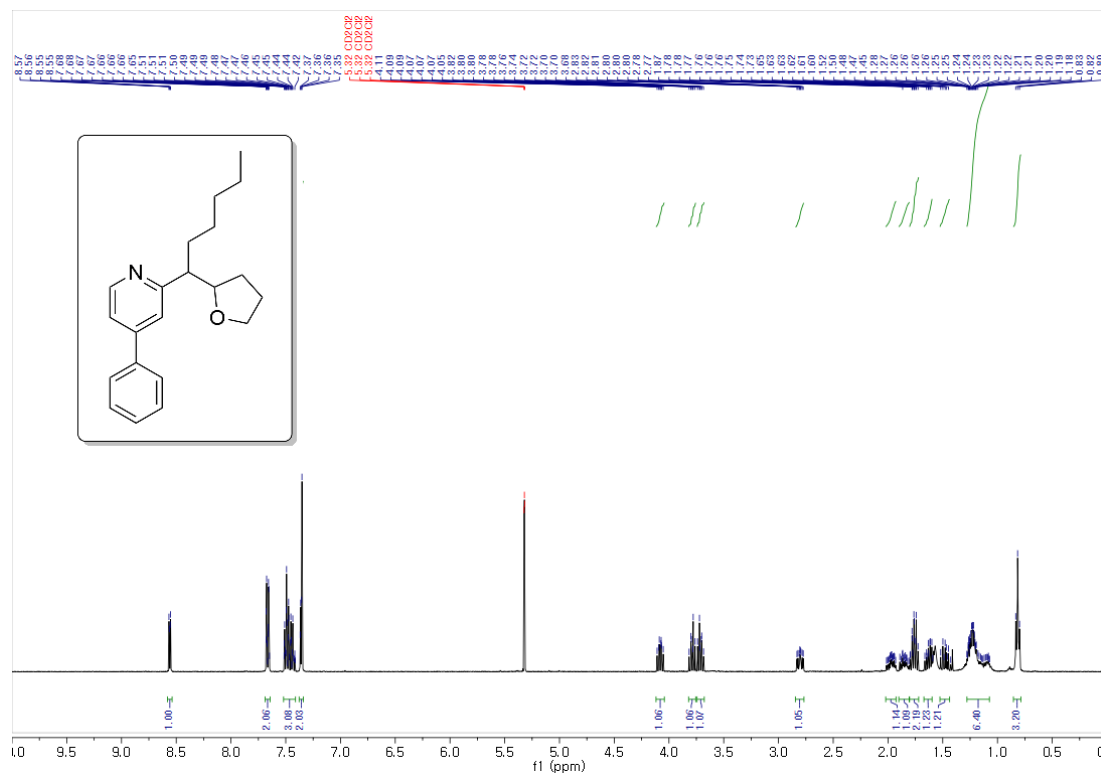
150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , major diastereomer



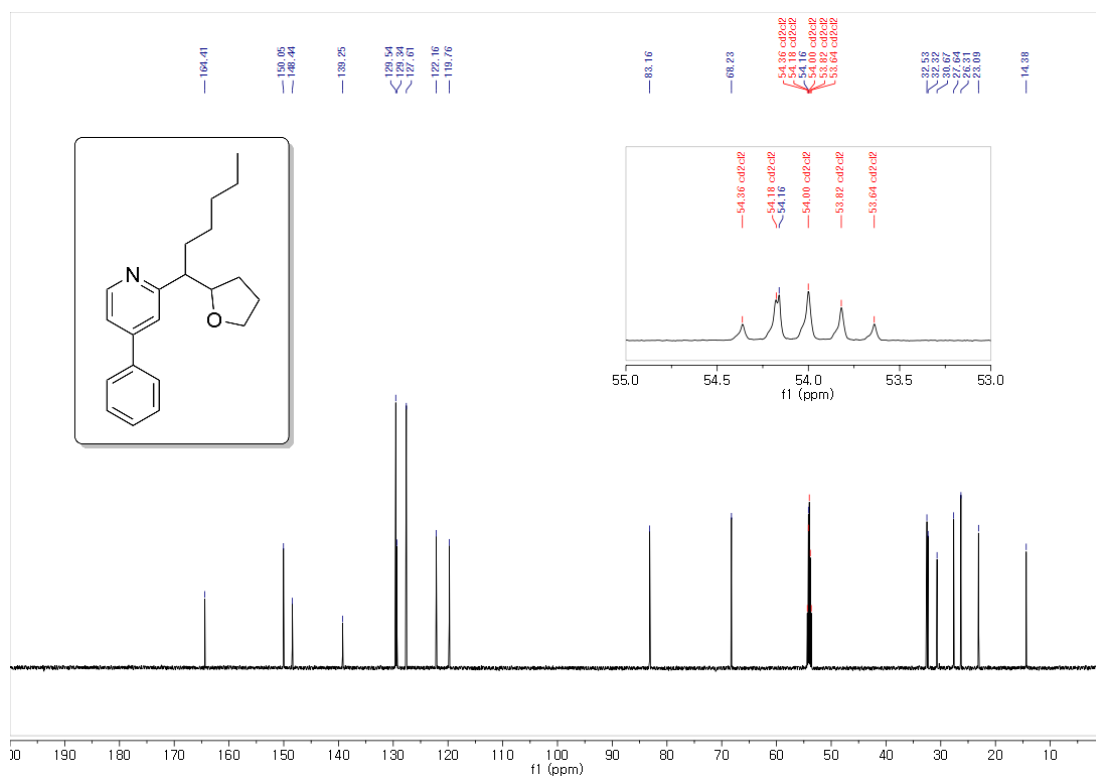
150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , minor diastereomer



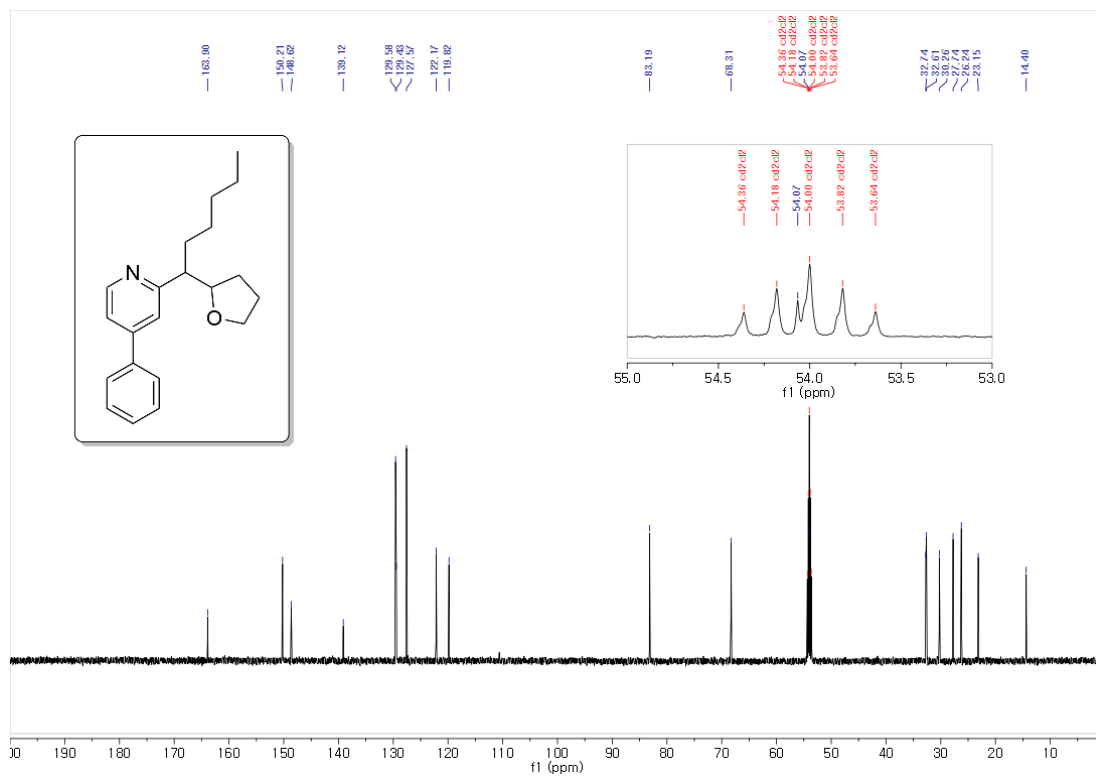
400 MHz, ¹H NMR in Methylene Chloride-*d*₂, major diastereomer



150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , major diastereomer

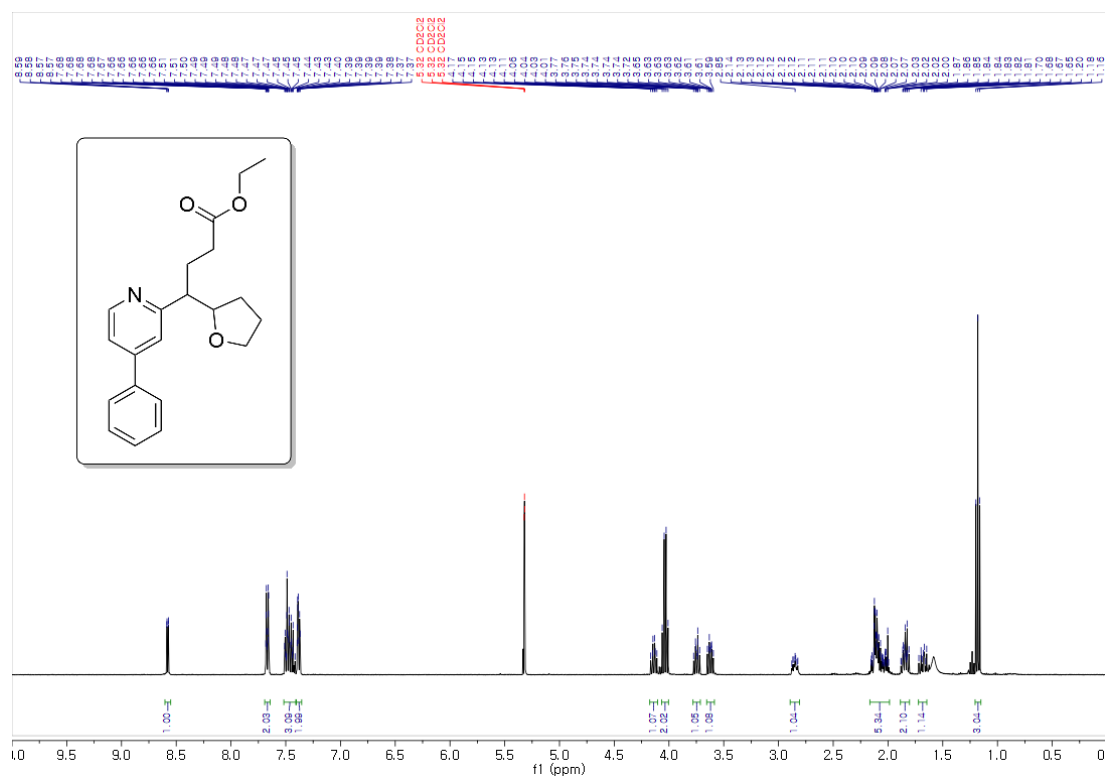


150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , minor diastereomer

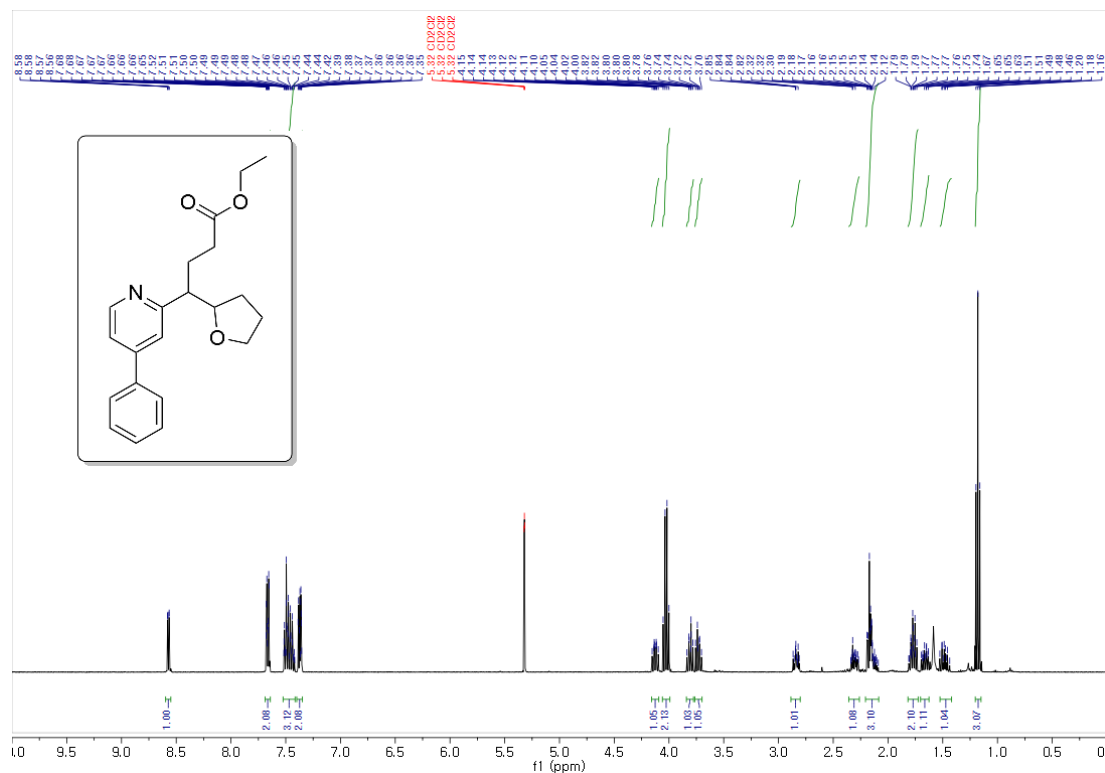


ethyl 4-(4-phenylpyridin-2-yl)-4-(tetrahydrofuran-2-yl)butanoate (2t).

400 MHz, ^1H NMR in Methylene Chloride- d_2 , major diastereomer



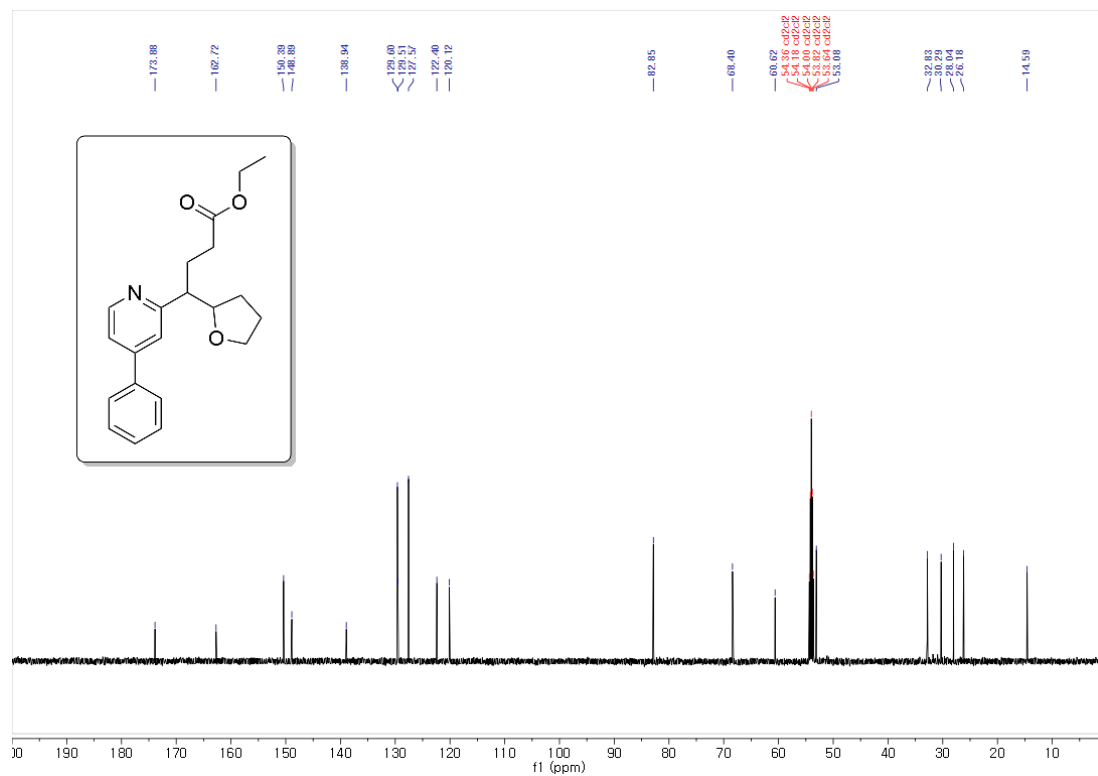
400 MHz, ^1H NMR in Methylene Chloride- d_2 , minor diastereomer



150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , major diastereomer

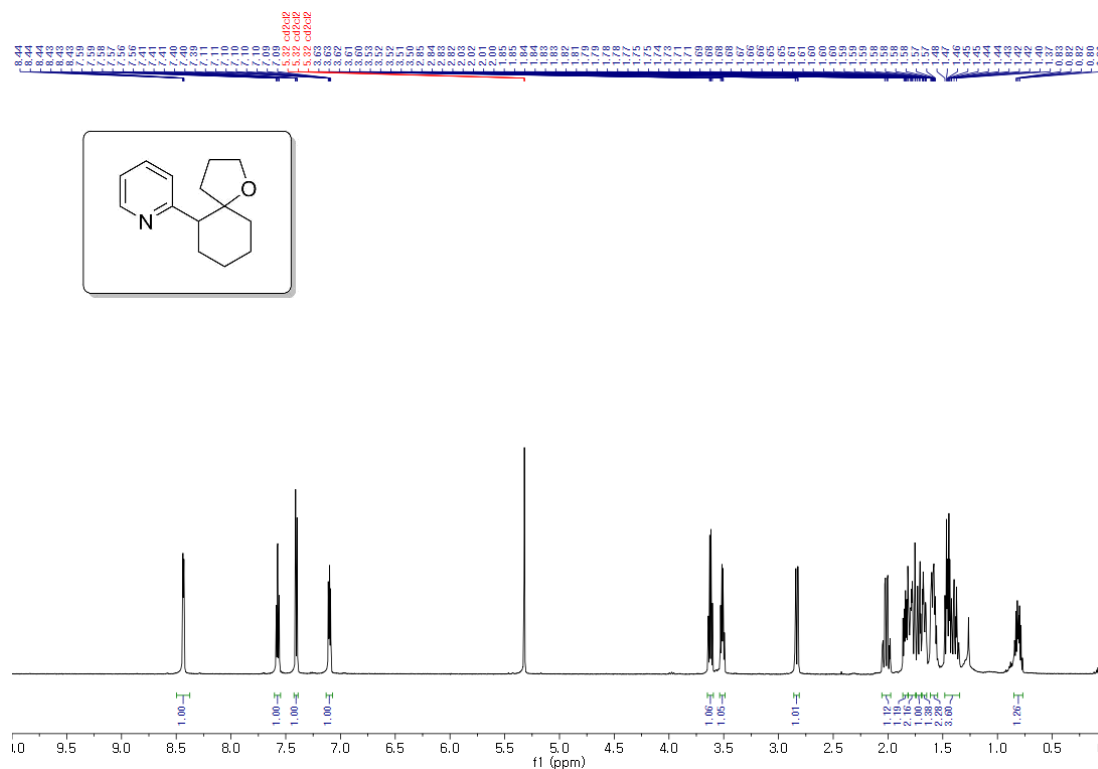


150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , minor diastereomer

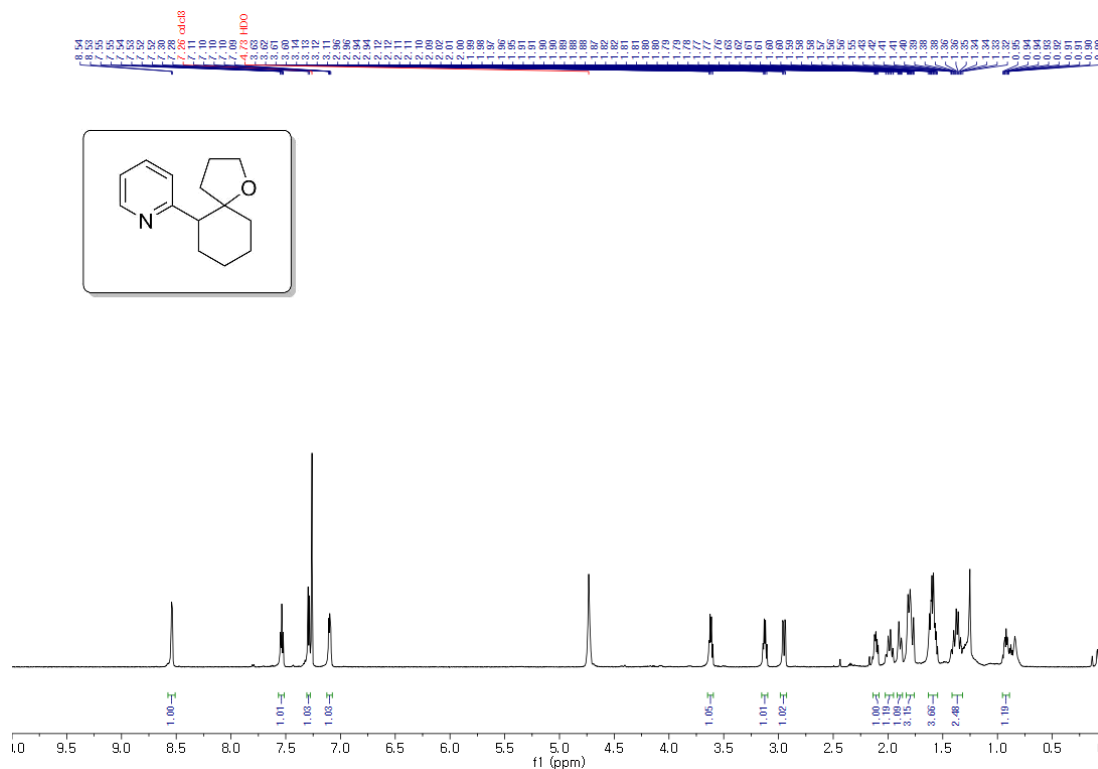


2-(1-oxaspiro[4.5]decan-6-yl)pyridine (2u).

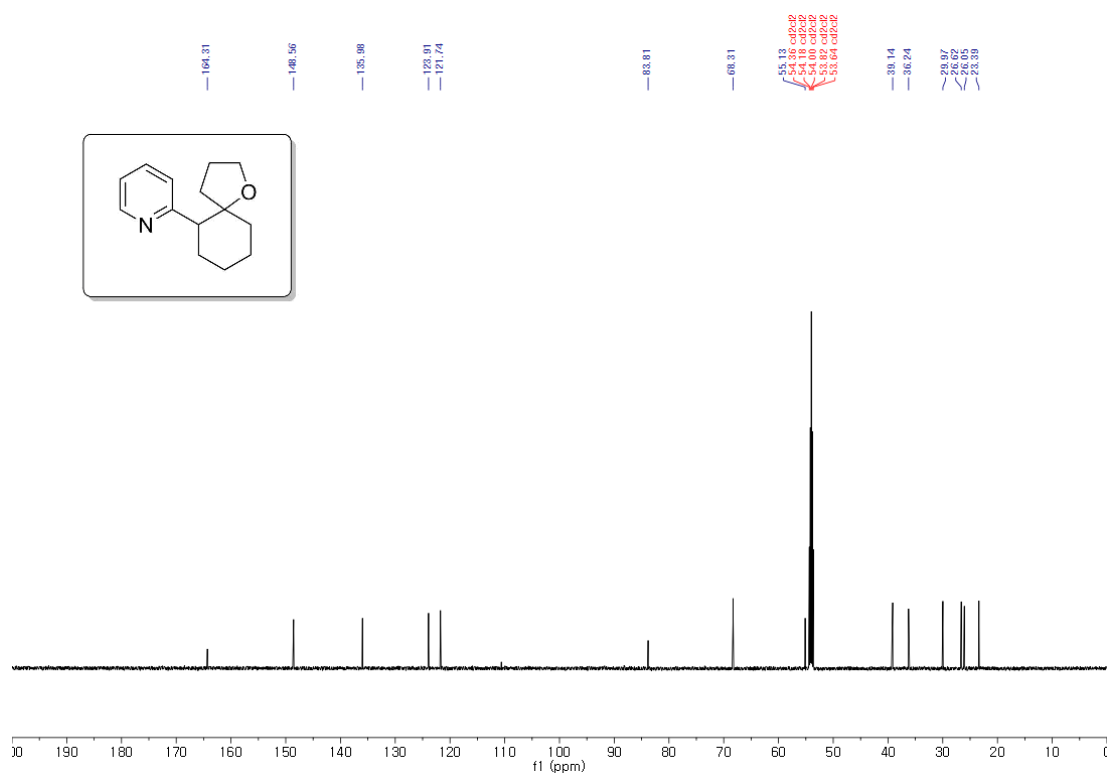
600 MHz, ^1H NMR in Methylene Chloride- d_2 , major diastereomer



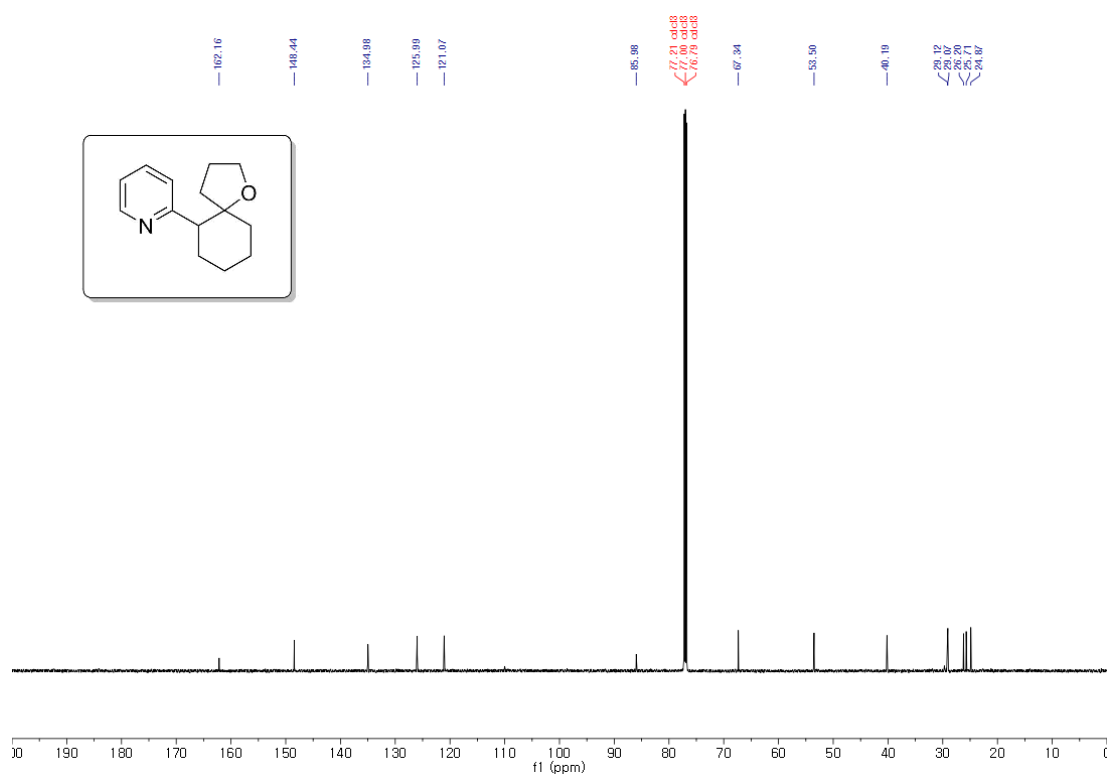
600 MHz, ^1H NMR in Chloroform- d , minor diastereomer



150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , major diastereomer

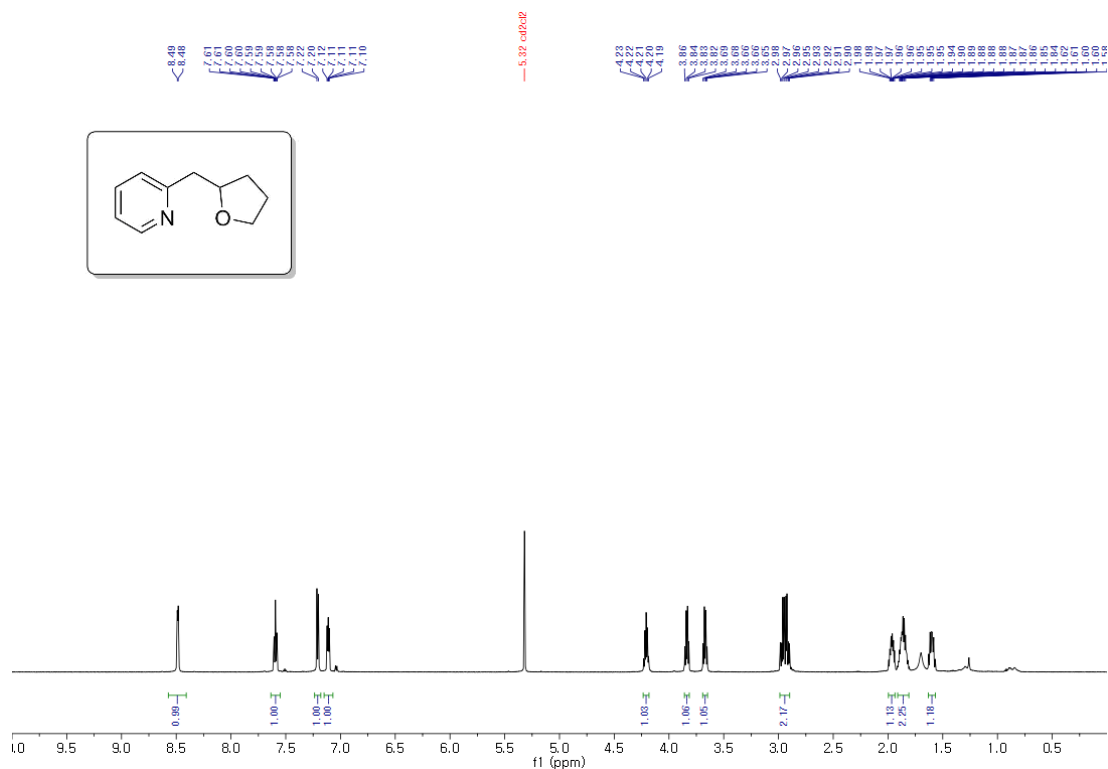


150 MHz, ^{13}C NMR in Chloroform- d , minor diastereomer

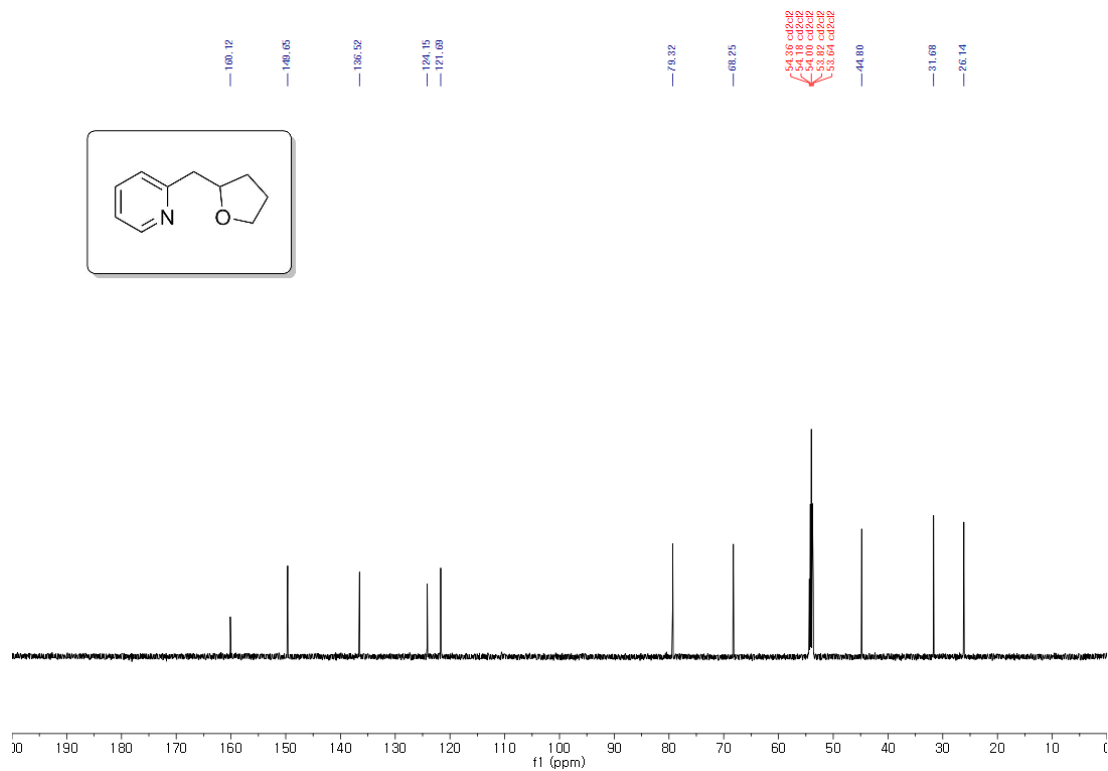


2-(((tetrahydrofuran-2-yl)methyl)pyridine (2v).

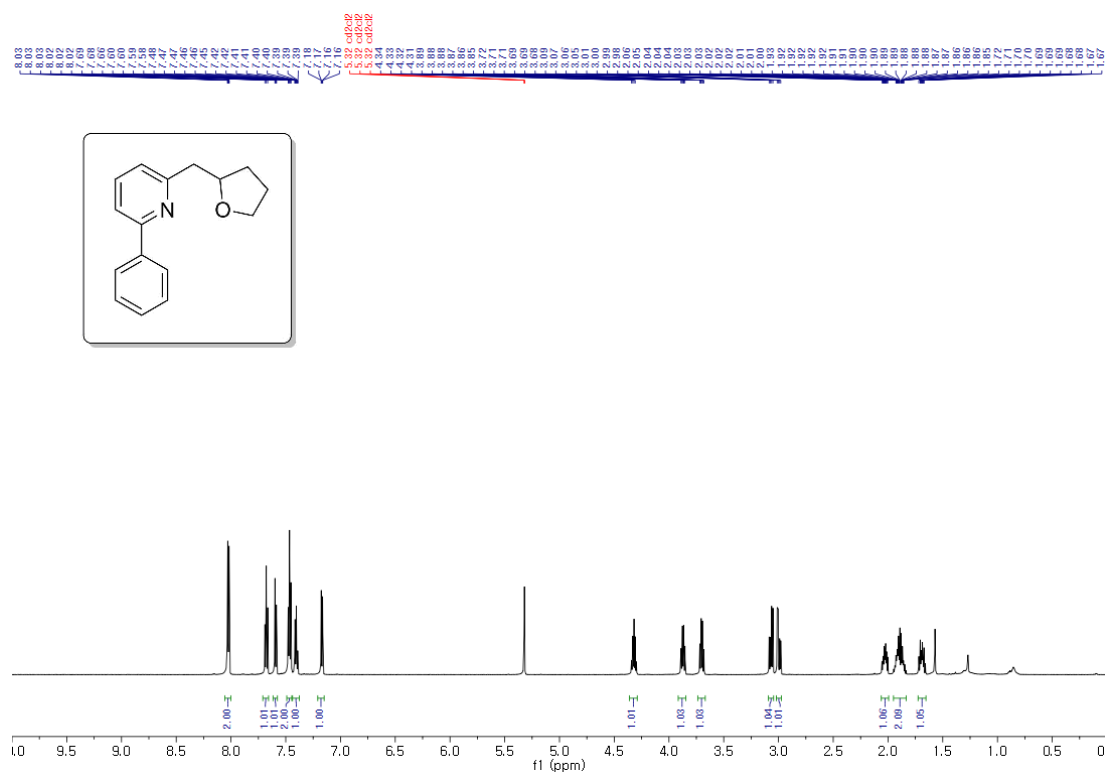
600 MHz, ^1H NMR in Methylene Chloride- d_2



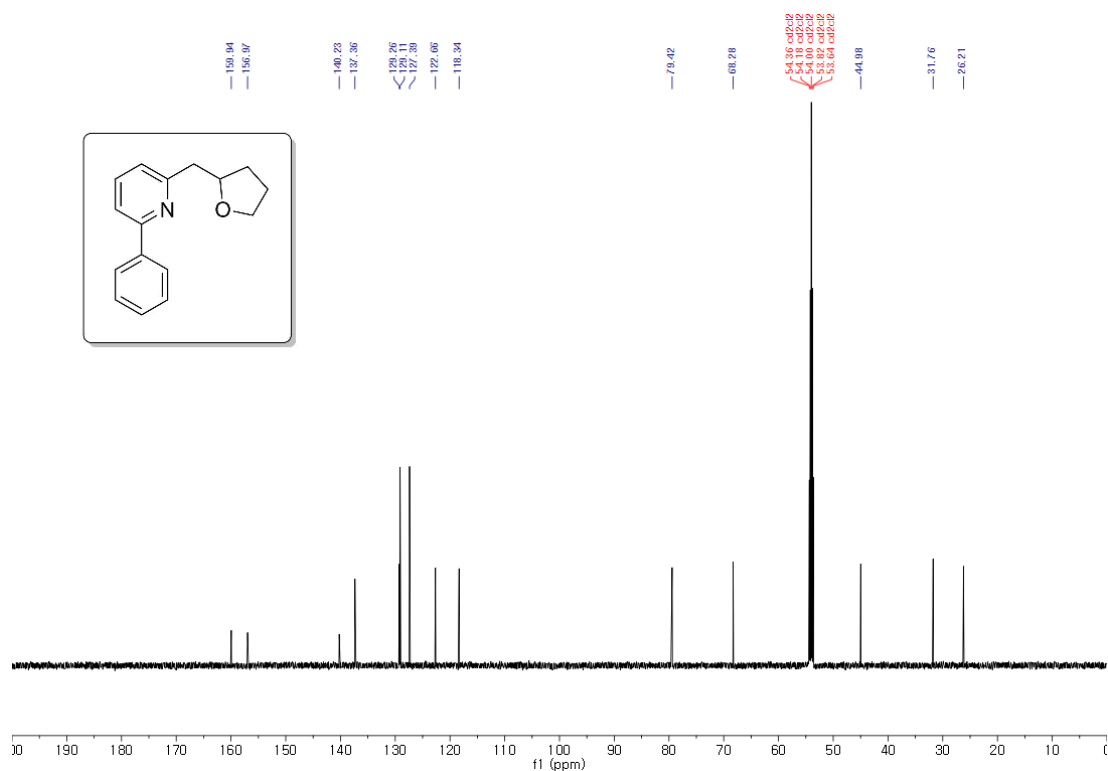
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



600 MHz, ^1H NMR in Methylene Chloride- d_2

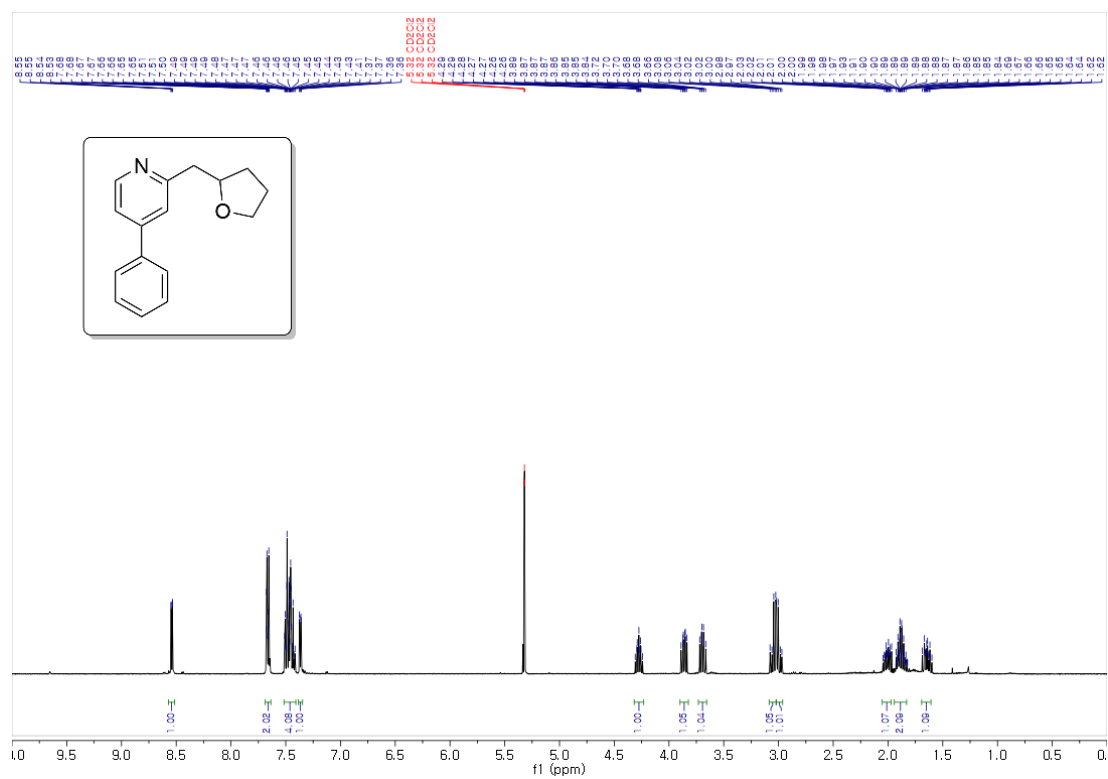


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

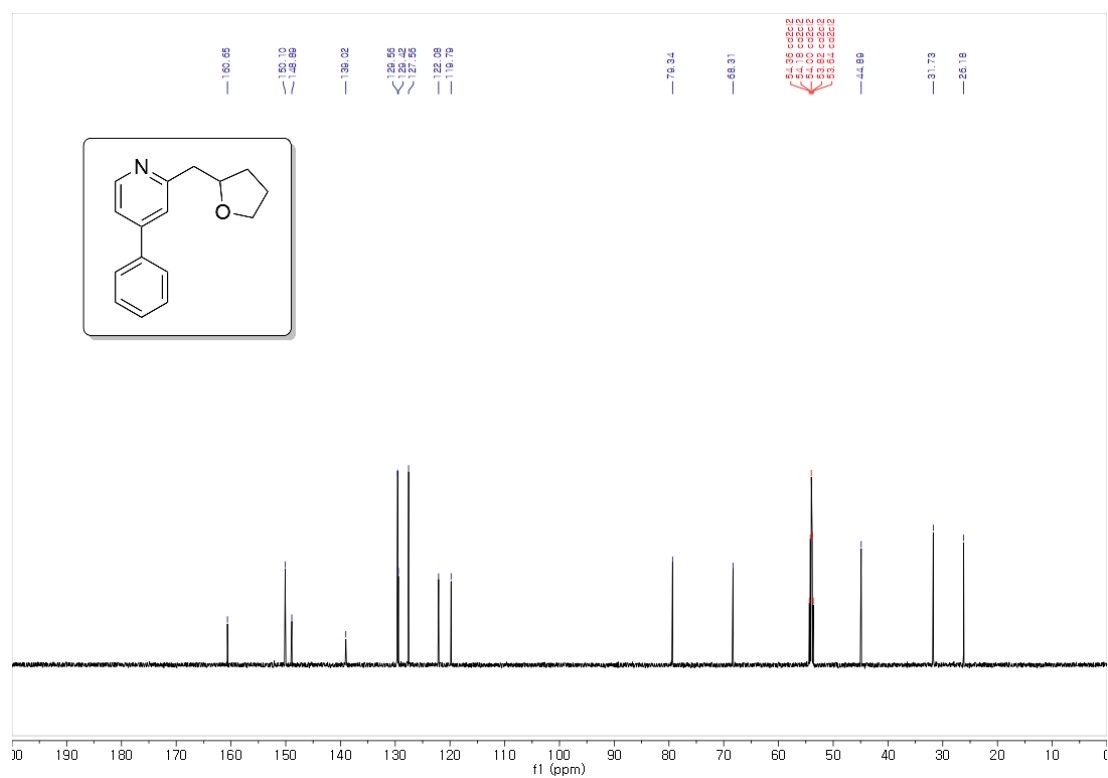


4-phenyl-2-((tetrahydrofuran-2-yl)methyl)pyridine (2x).

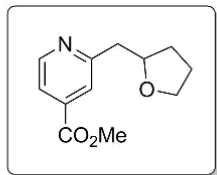
400 MHz, ^1H NMR in Methylene Chloride- d_2



150 MHz, ^{13}C NMR in Methylene Chloride- d_2



400 MHz, ^1H NMR in Chloroform-*d*



Chemical structure of the compound is shown in the inset:

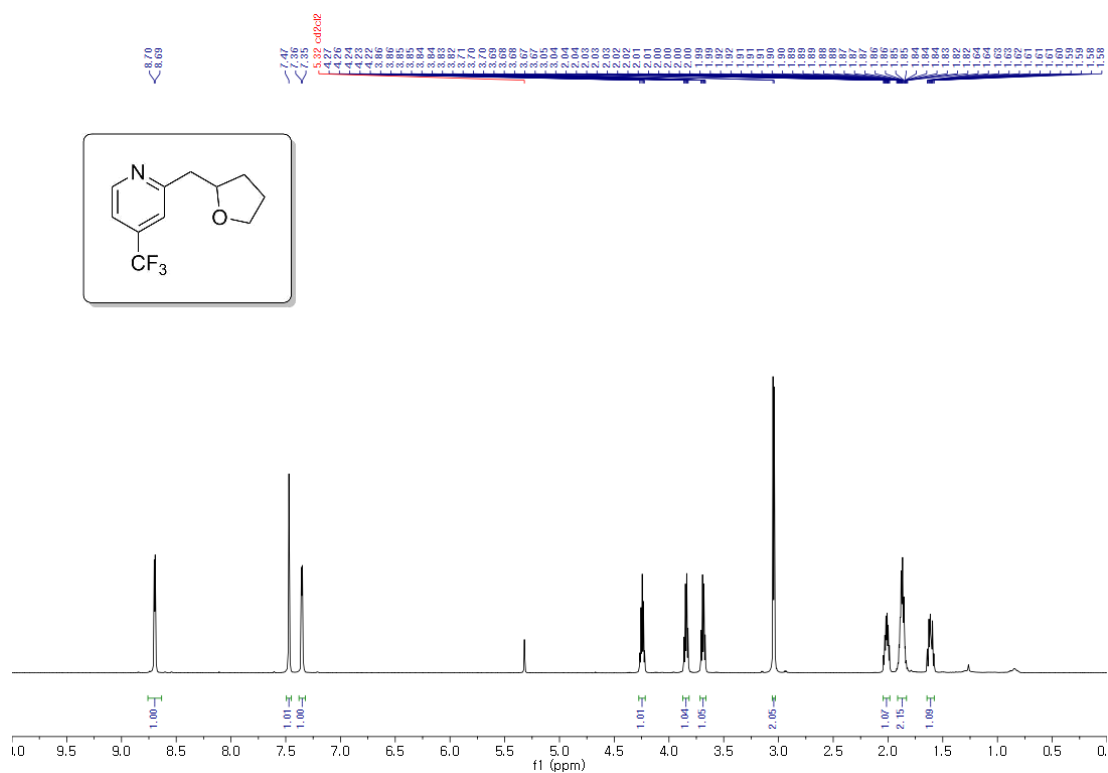
COC(=O)c1ccc(CCN2CCCC2O)cn1

The ¹³C NMR spectrum (f1 (ppm)) displays the following peaks (ppm):

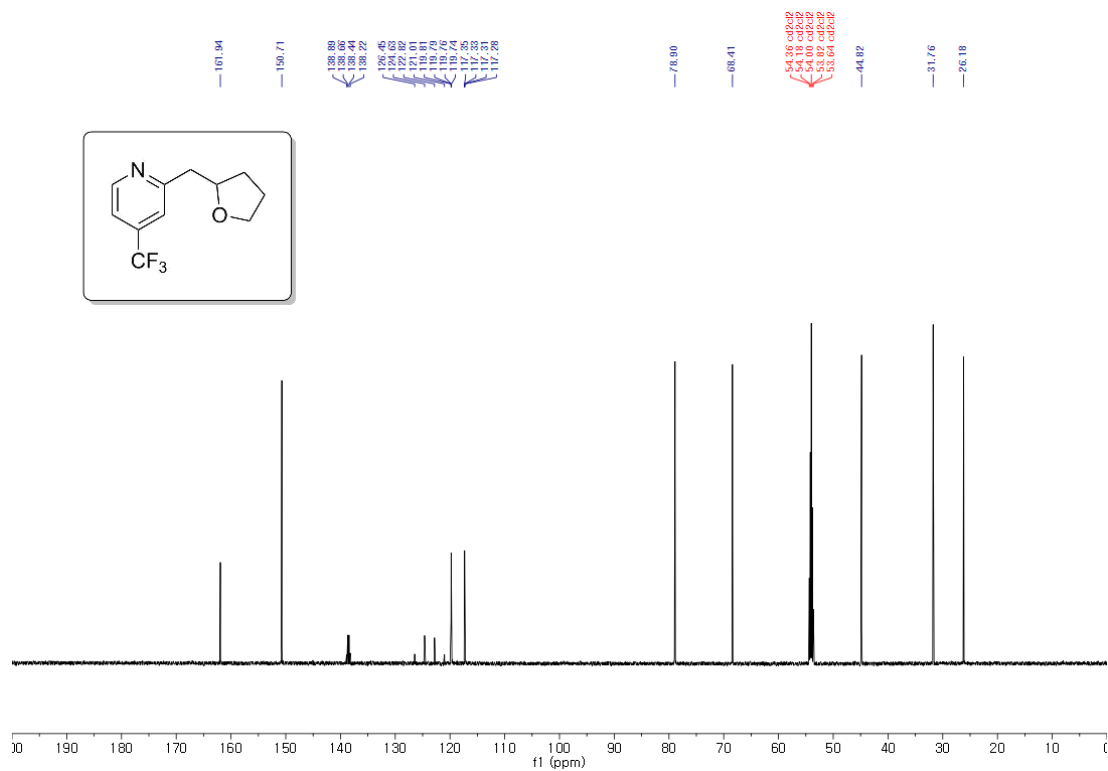
- 165.96
- 160.66
- 150.12
- 137.70
- 123.06
- 120.64
- 78.70
- 78.48
- 78.26
- 77.96
- 77.64
- 77.32
- 68.13
- 52.73
- 44.33
- 31.32
- 25.72

2-(((tetrahydrofuran-2-yl)methyl)-4-(trifluoromethyl)pyridine (2z).

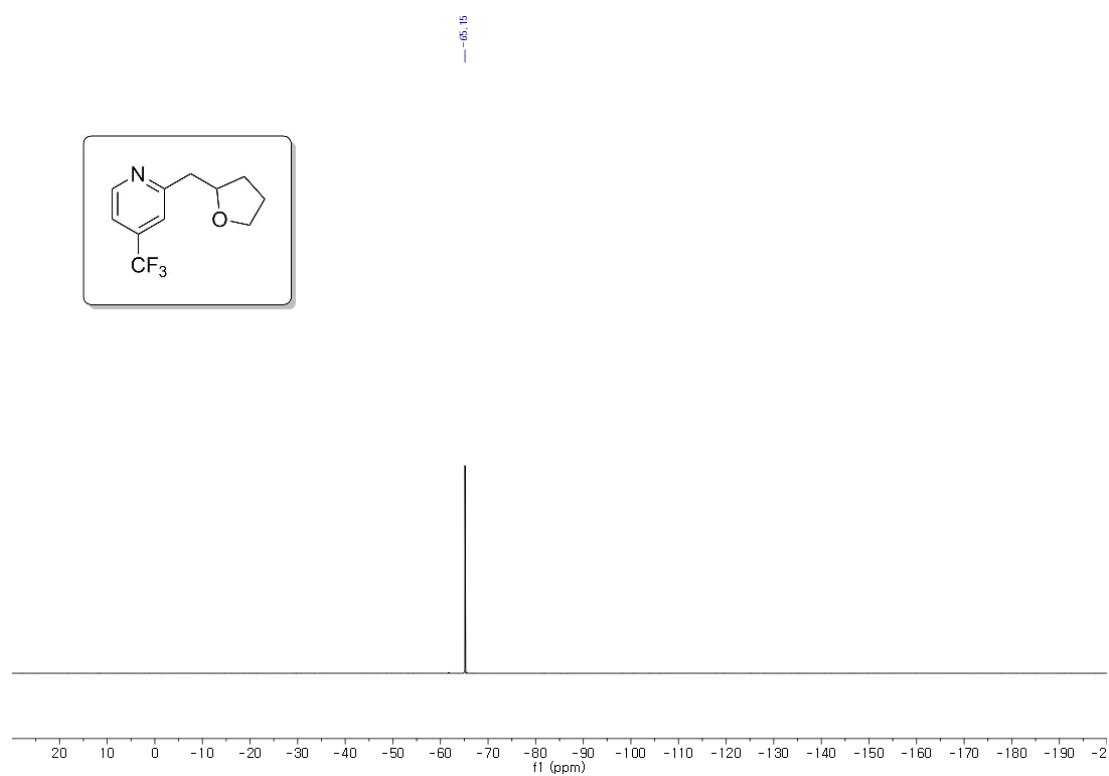
¹H NMR (600 MHz, Methylene Chloride-*d*₂)



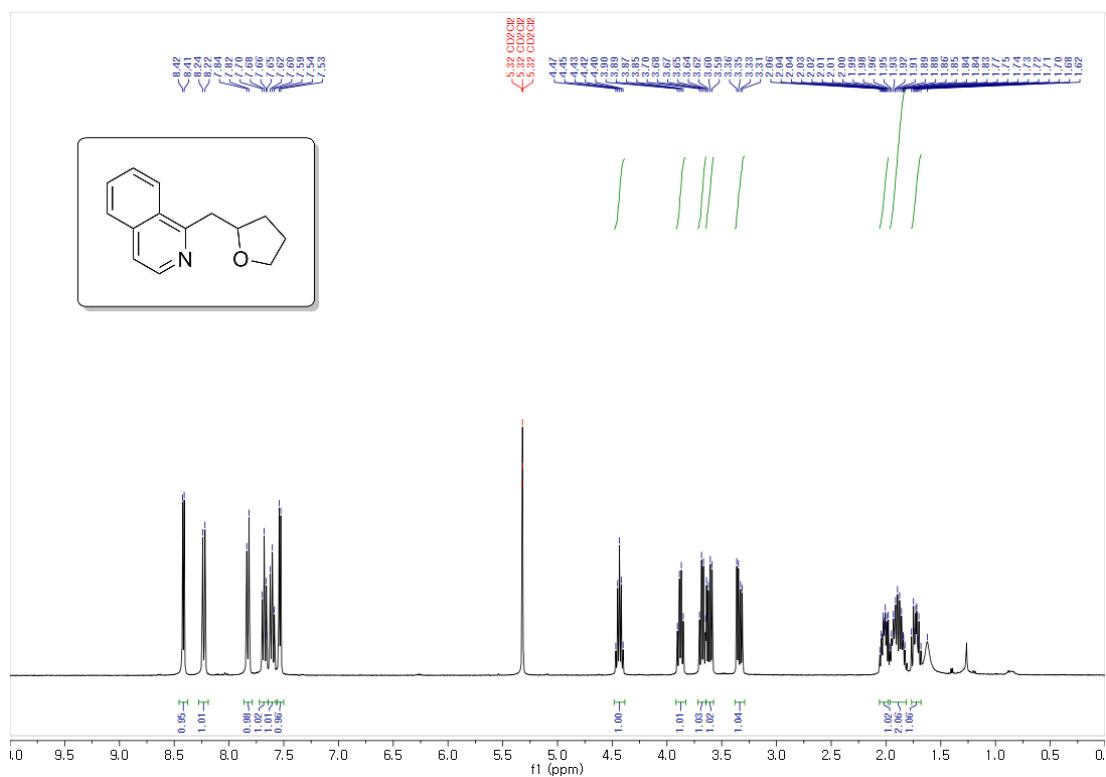
¹³C NMR (150 MHz, Methylene Chloride-*d*₂)



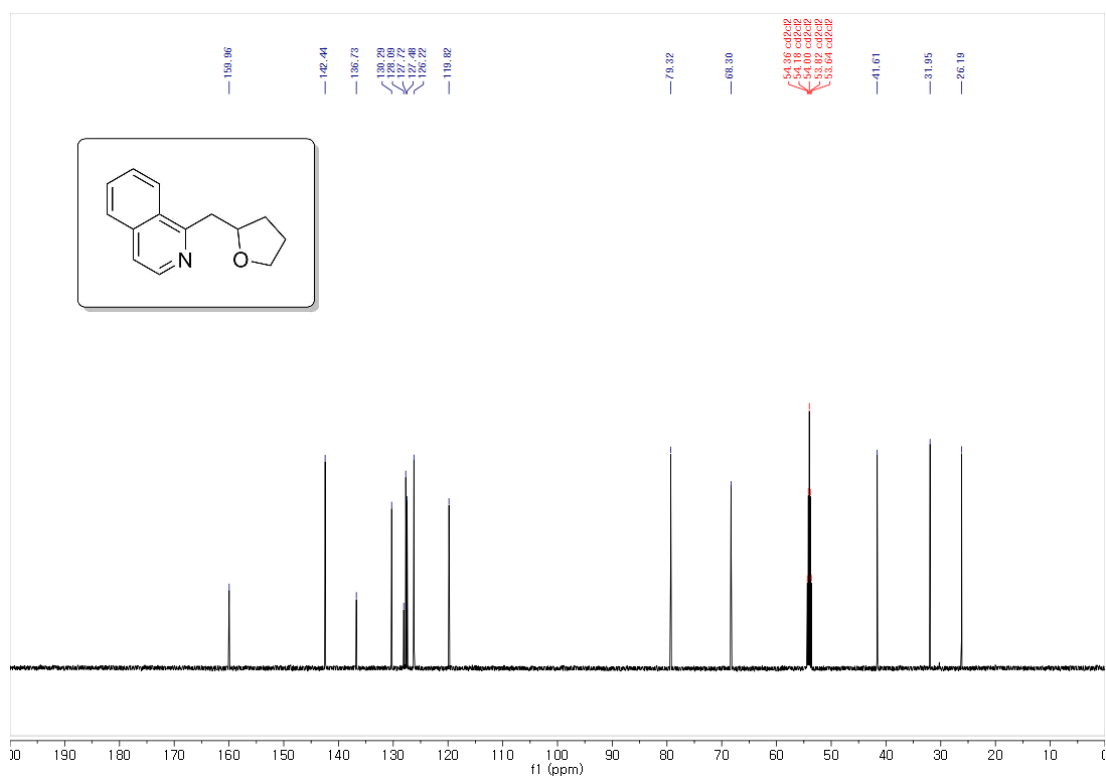
^{19}F NMR (564 MHz, Methylene Chloride- d_2)



400 MHz, ^1H NMR in Methylene Chloride- d_2

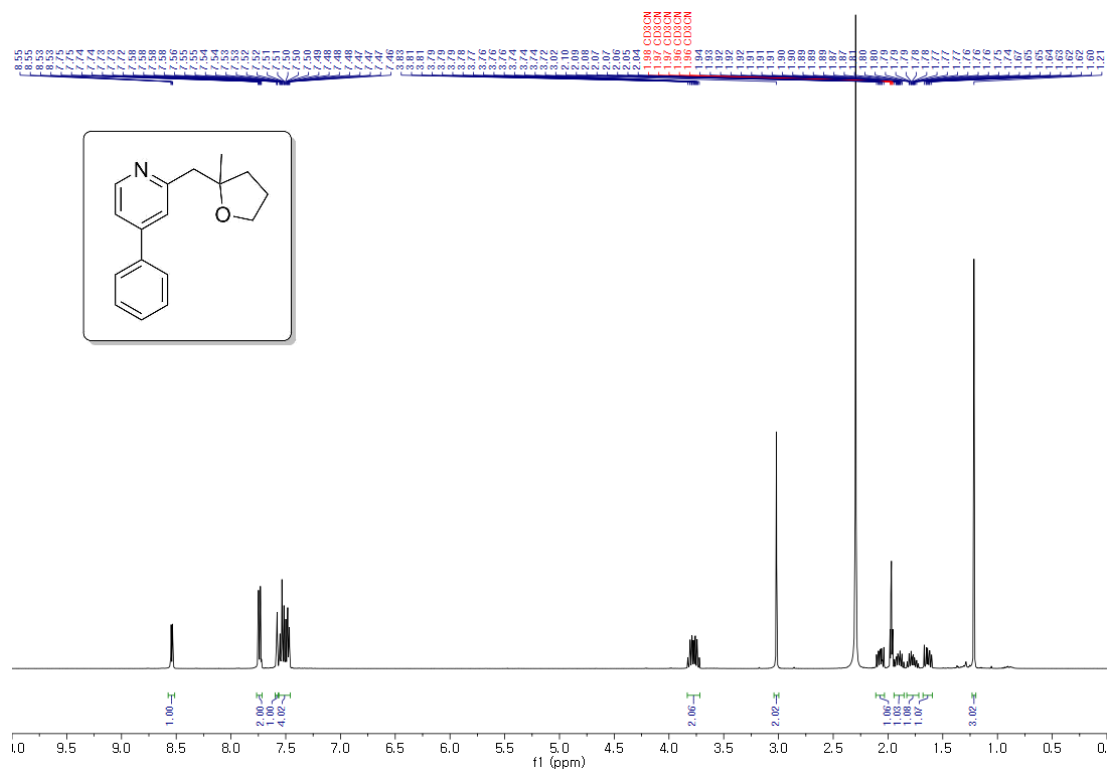


150 MHz, ^{13}C NMR in Methylene Chloride- d_2

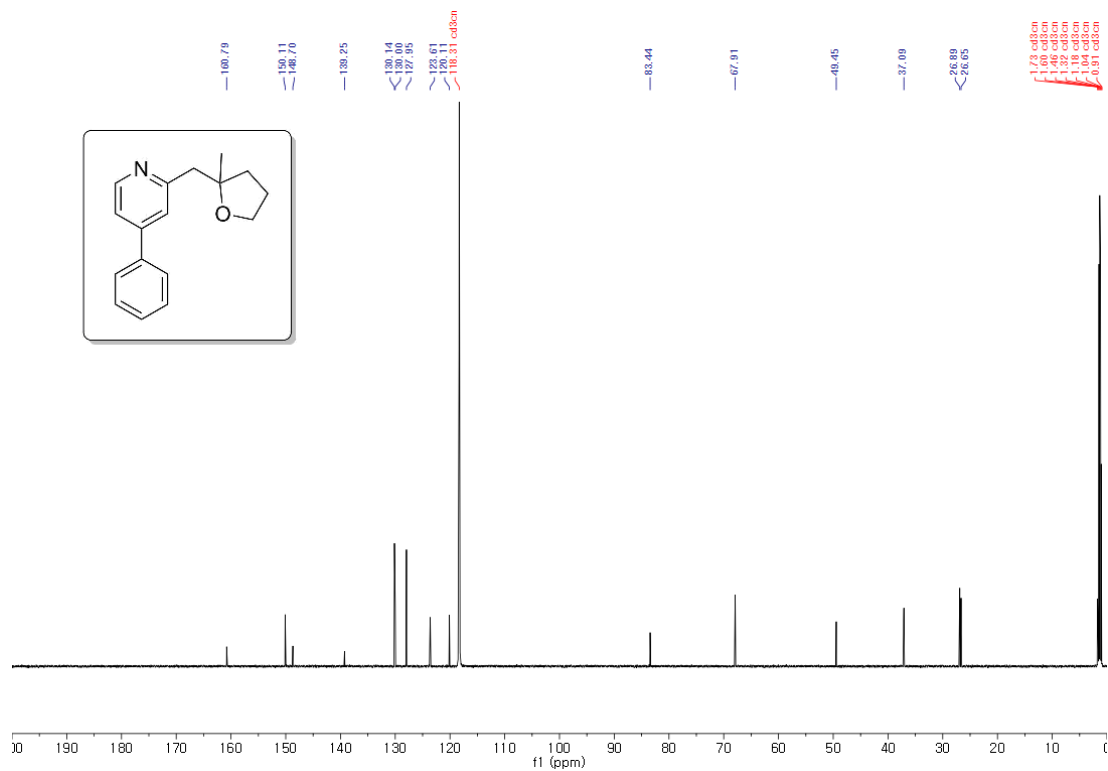


2-((2-methyltetrahydrofuran-2-yl)methyl)-4-phenylpyridine (2ab).

400 MHz, ^1H NMR in Acetonitrile- d_3

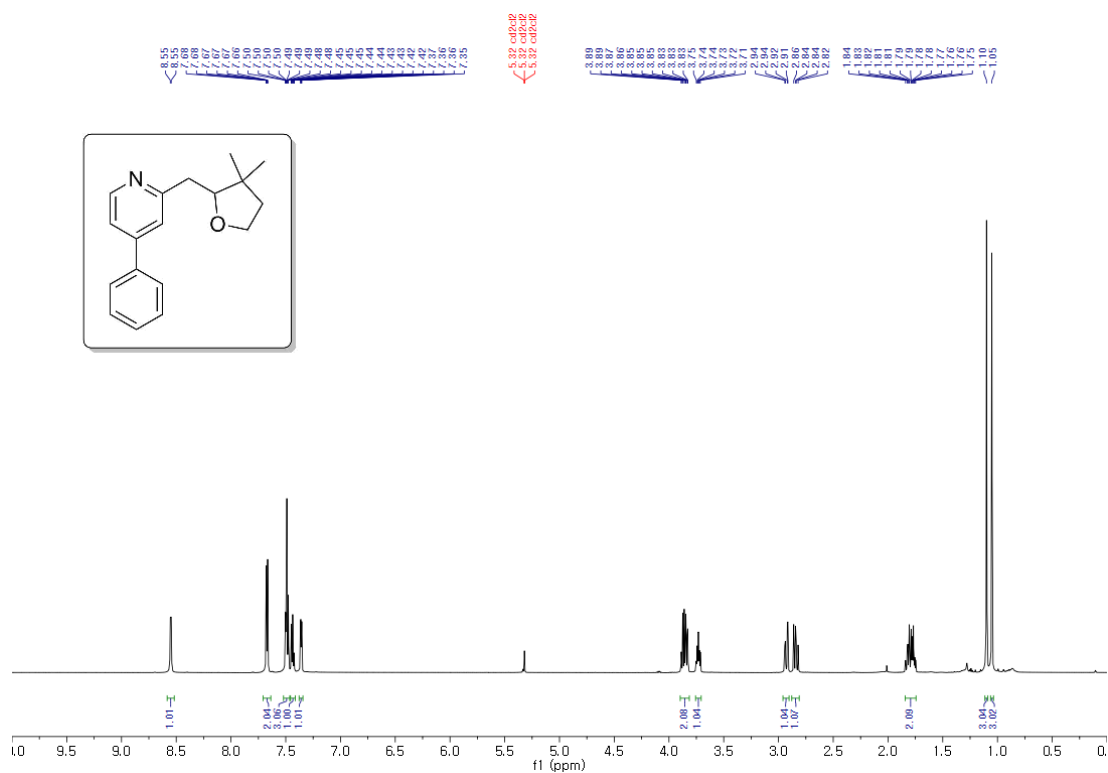


150 MHz, ^{13}C NMR in Acetonitrile- d_3

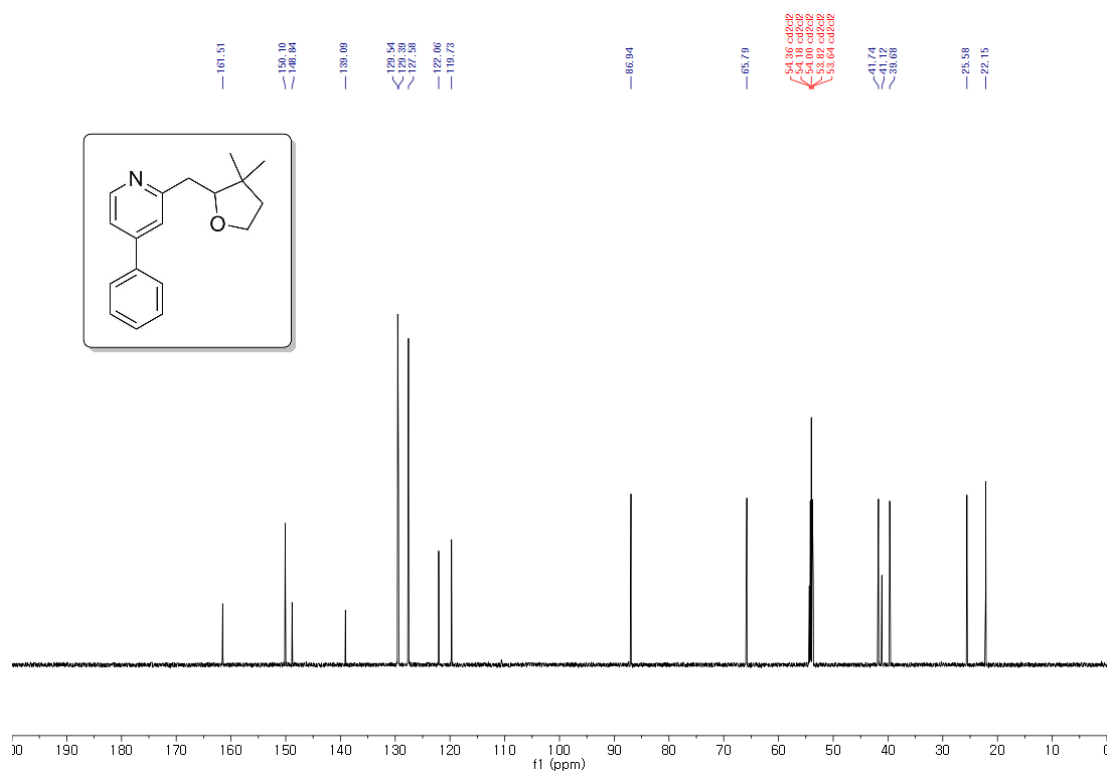


2-((3,3-dimethyltetrahydrofuran-2-yl)methyl)-4-phenylpyridine (2ac).

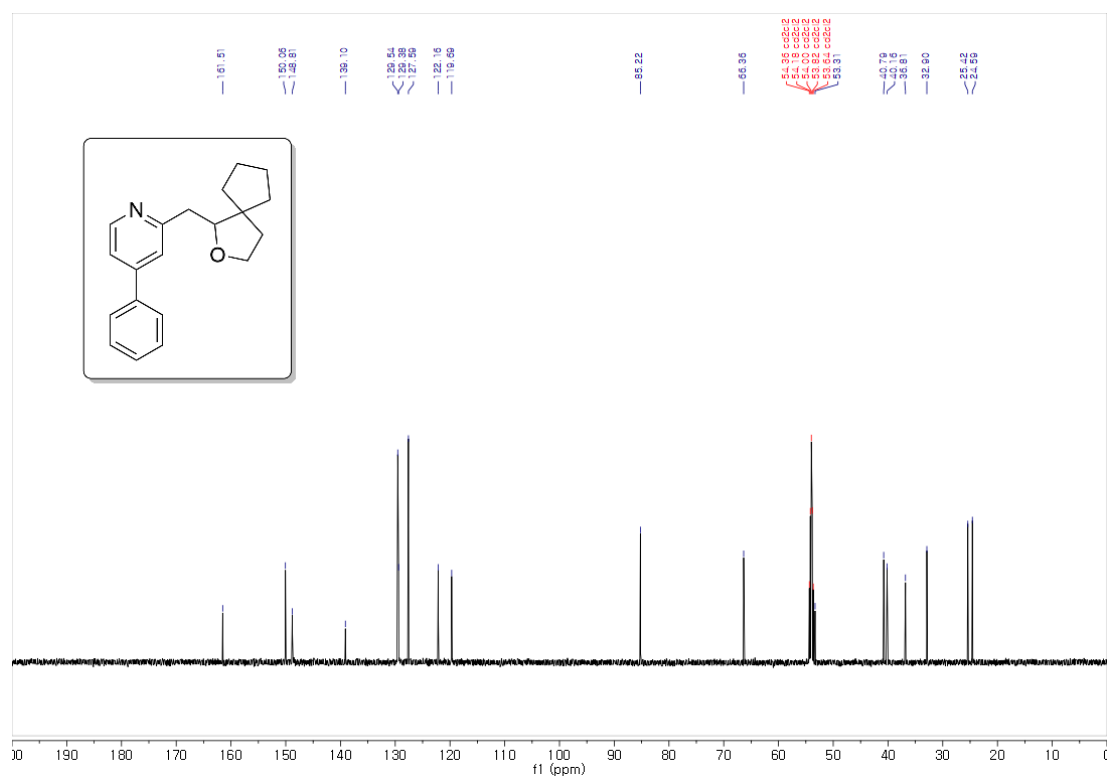
600 MHz, ^1H NMR in Methylene Chloride- d_2



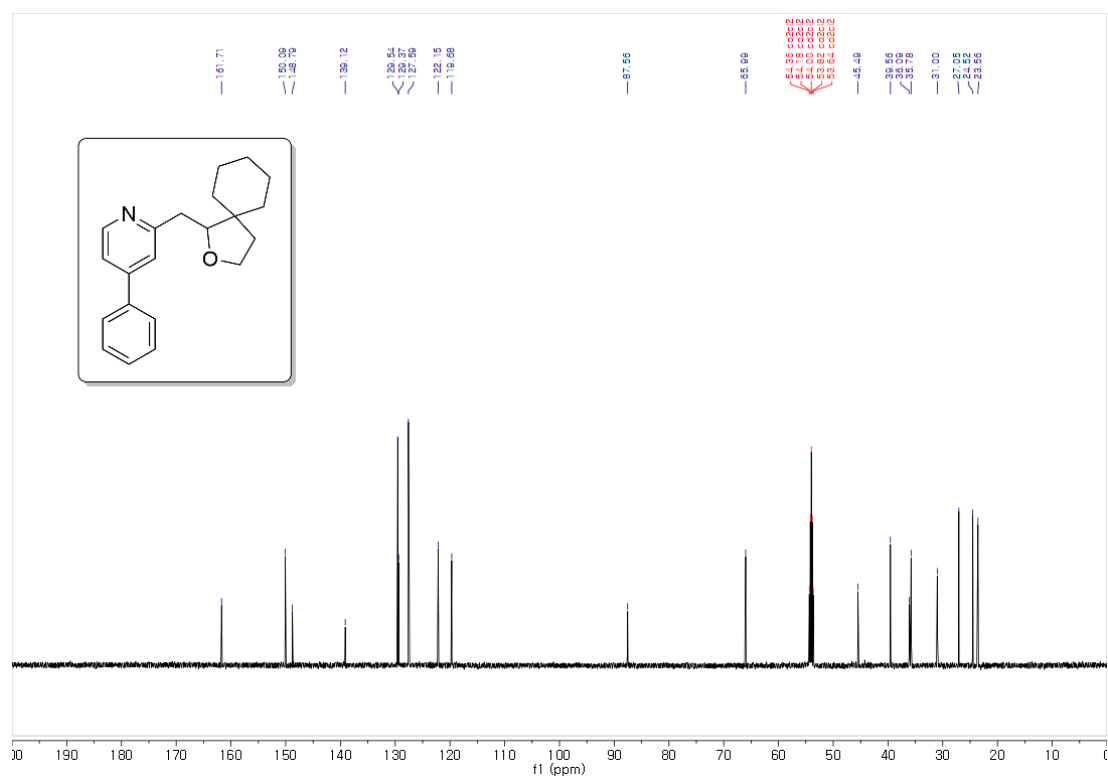
150 MHz, ^{13}C NMR in Methylene Chloride- d_2



400 MHz, ^1H NMR in Methylene Chloride- d_2

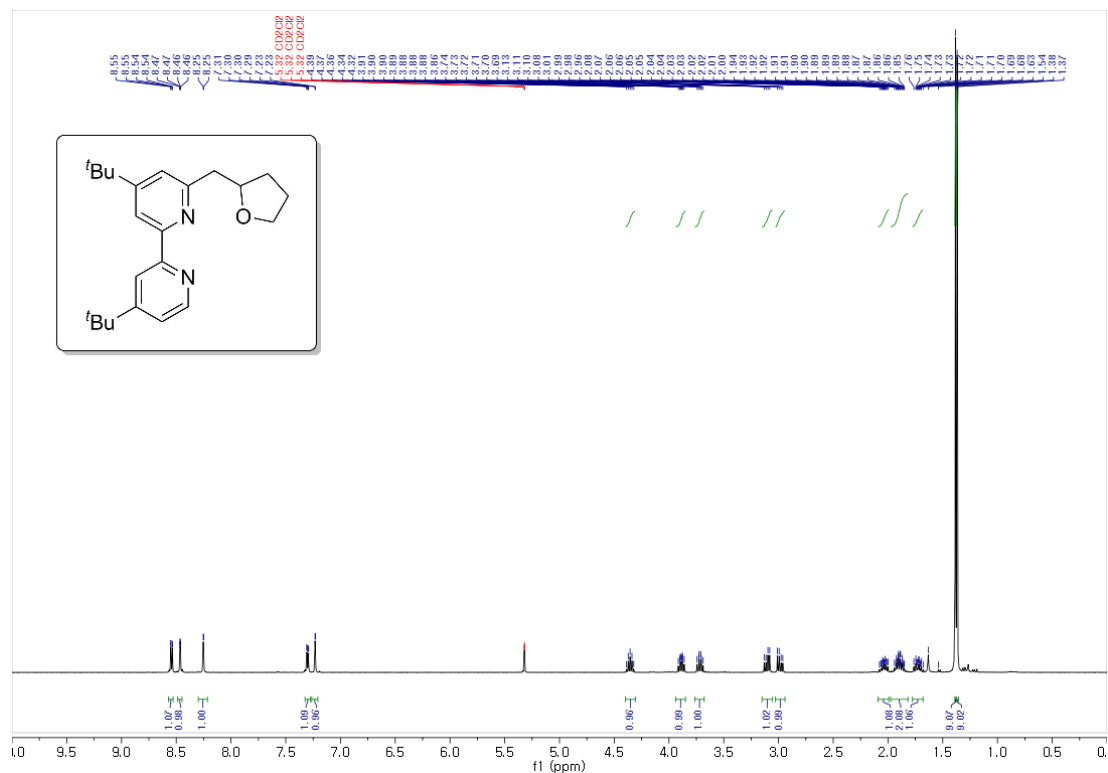


400 MHz, ^1H NMR in Methylene Chloride- d_2

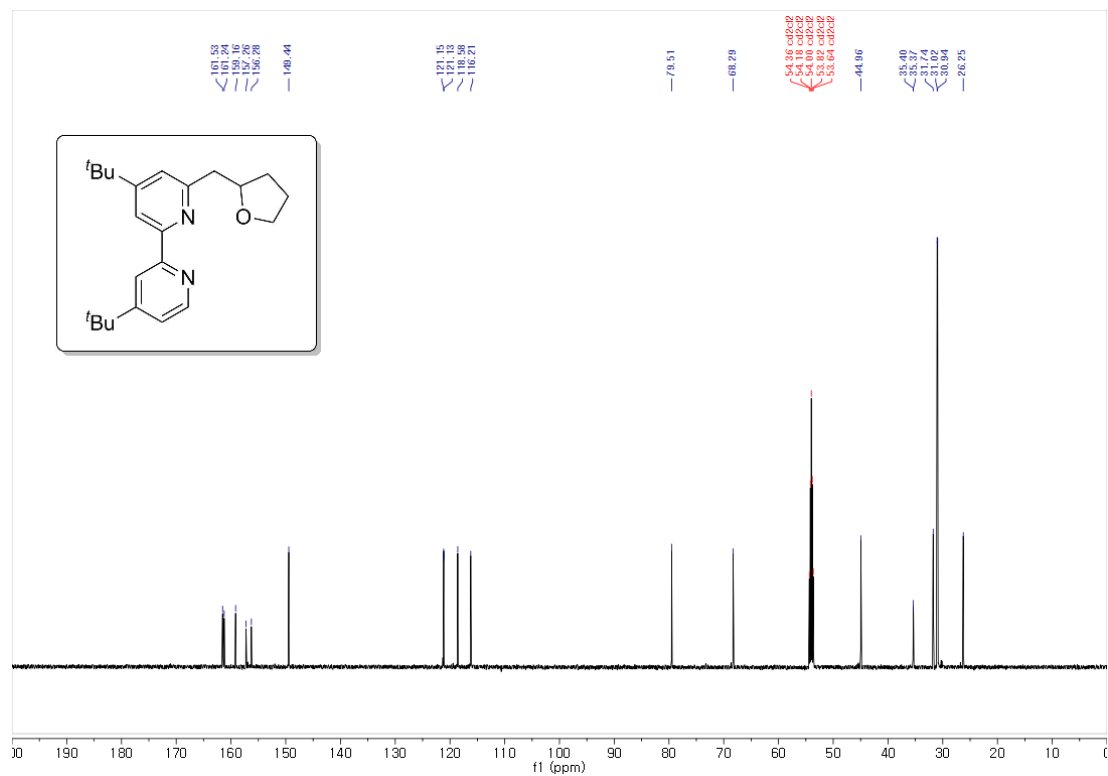


4,4'-di-tert-butyl-6-((tetrahydrofuran-2-yl)methyl)-2,2'-bipyridine (2af).

400 MHz, ¹H NMR in Methylene Chloride-*d*₂

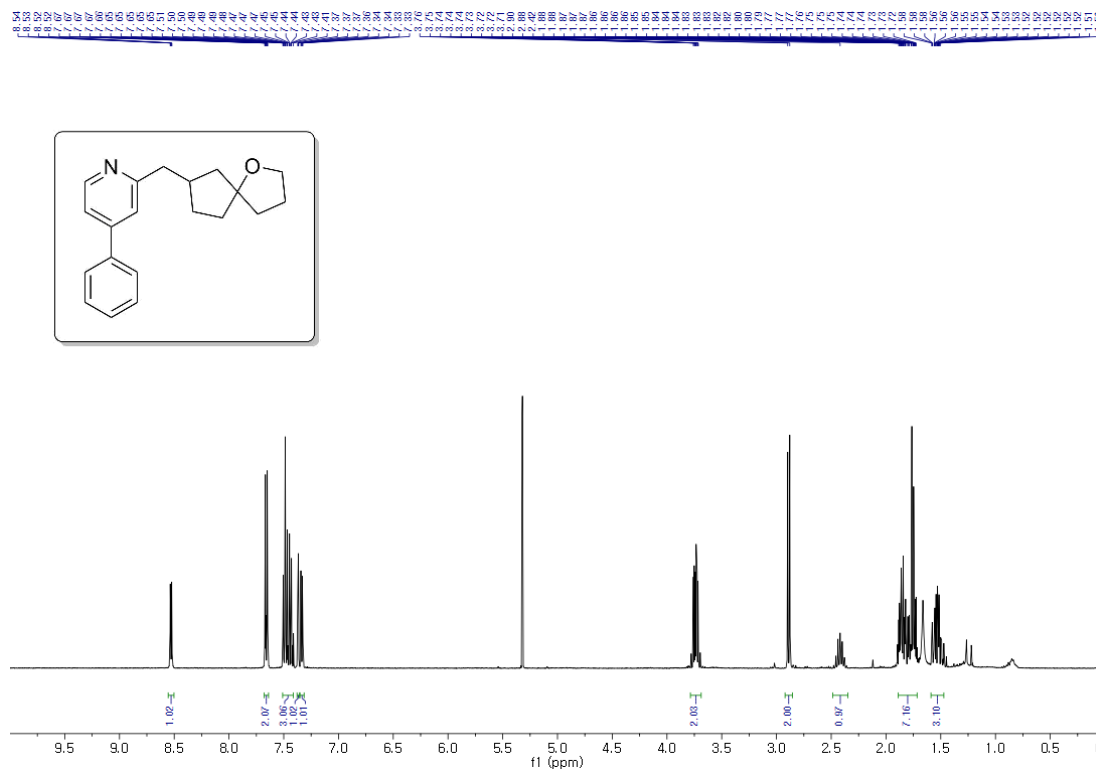


150 MHz, ¹³C NMR in Methylene Chloride-*d*₂

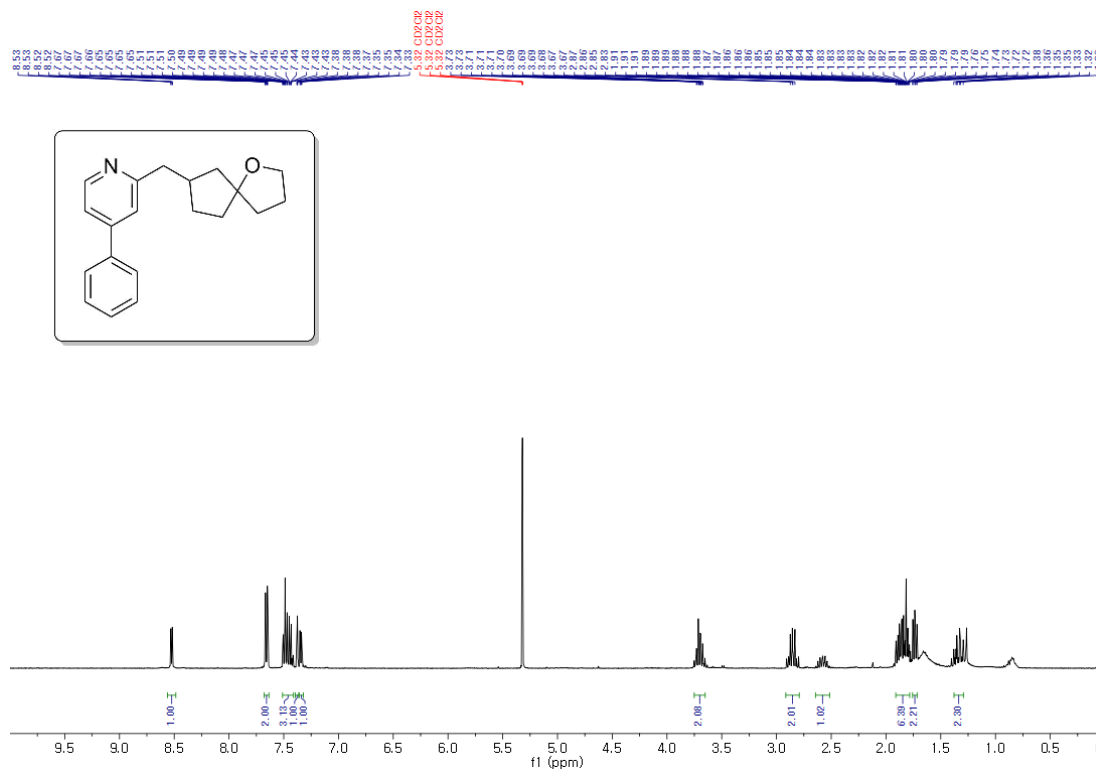


2-((1-oxaspiro[4.4]nonan-2-yl)methyl)-4-phenylpyridine (4a).

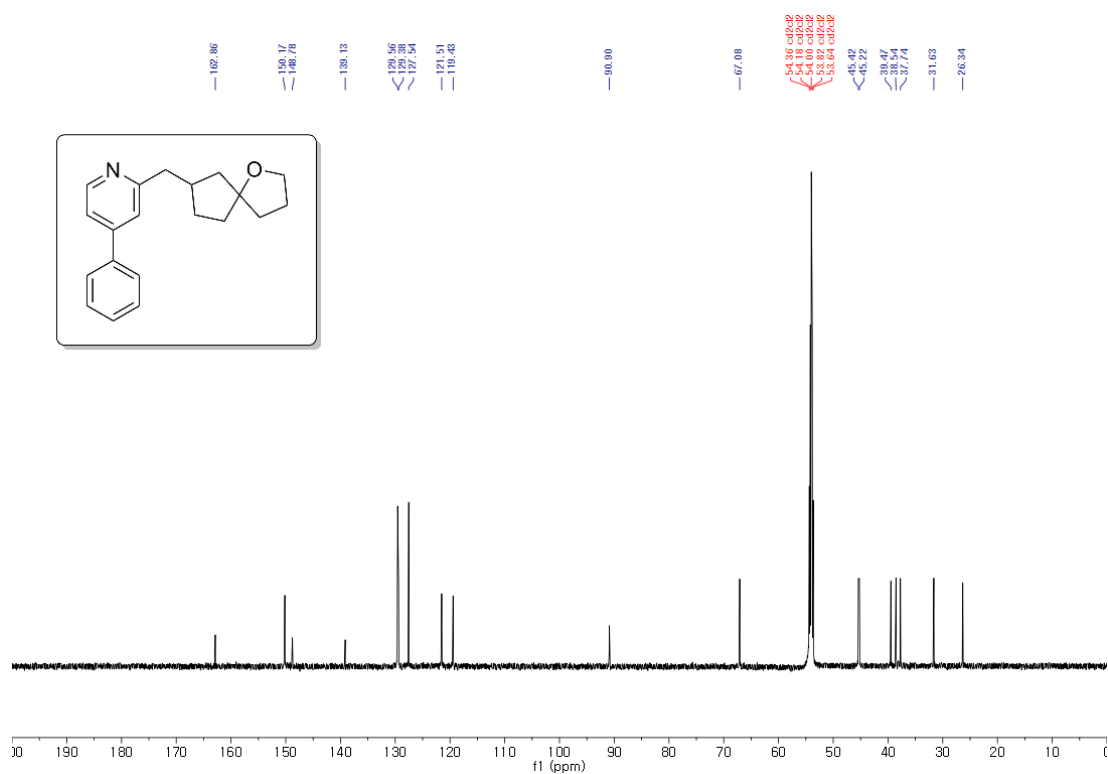
400 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer A



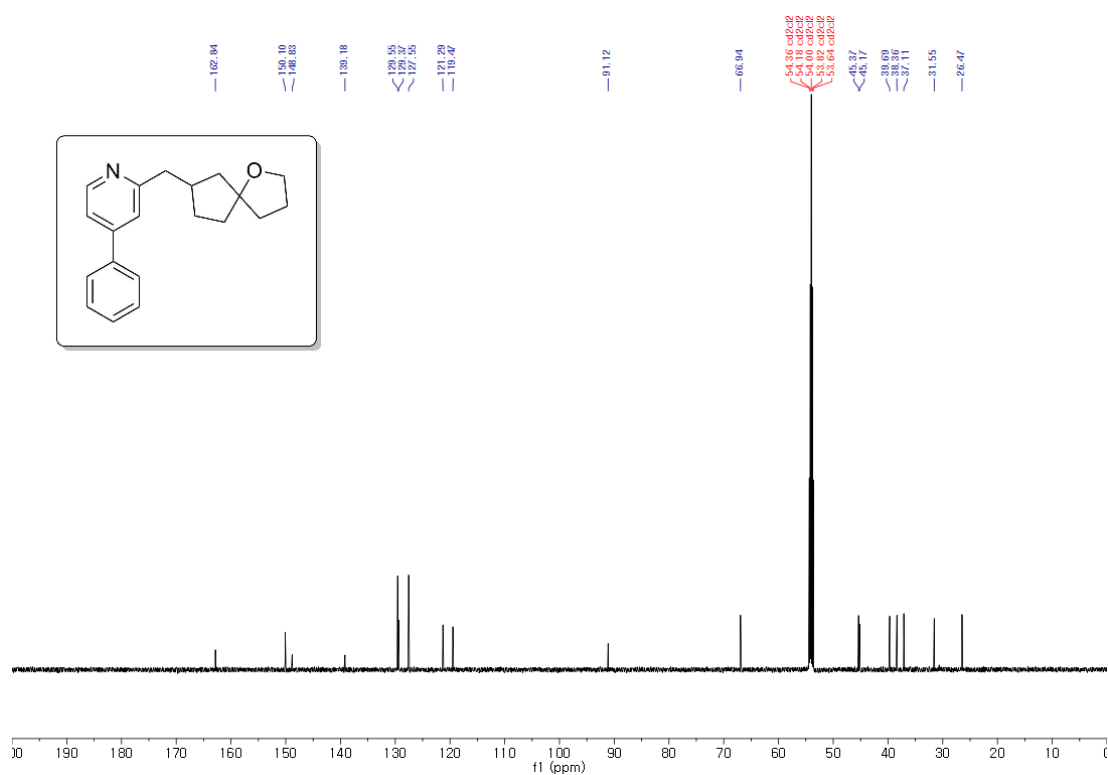
400 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer B



150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer A

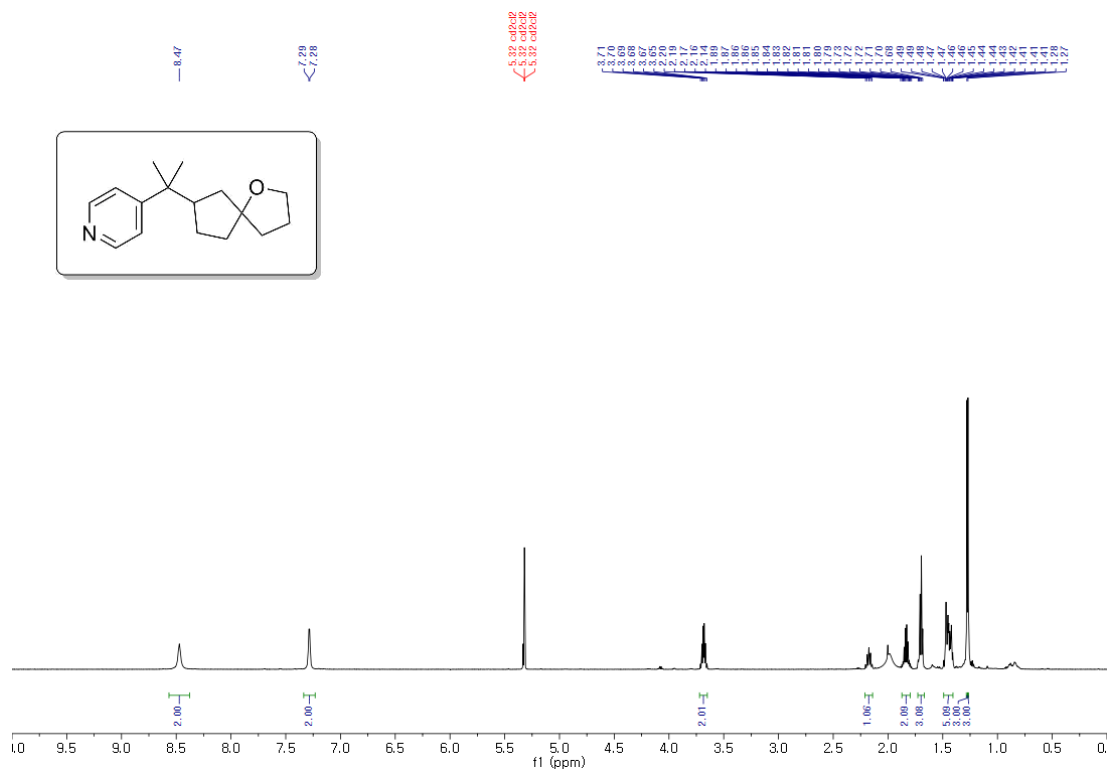


150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer B

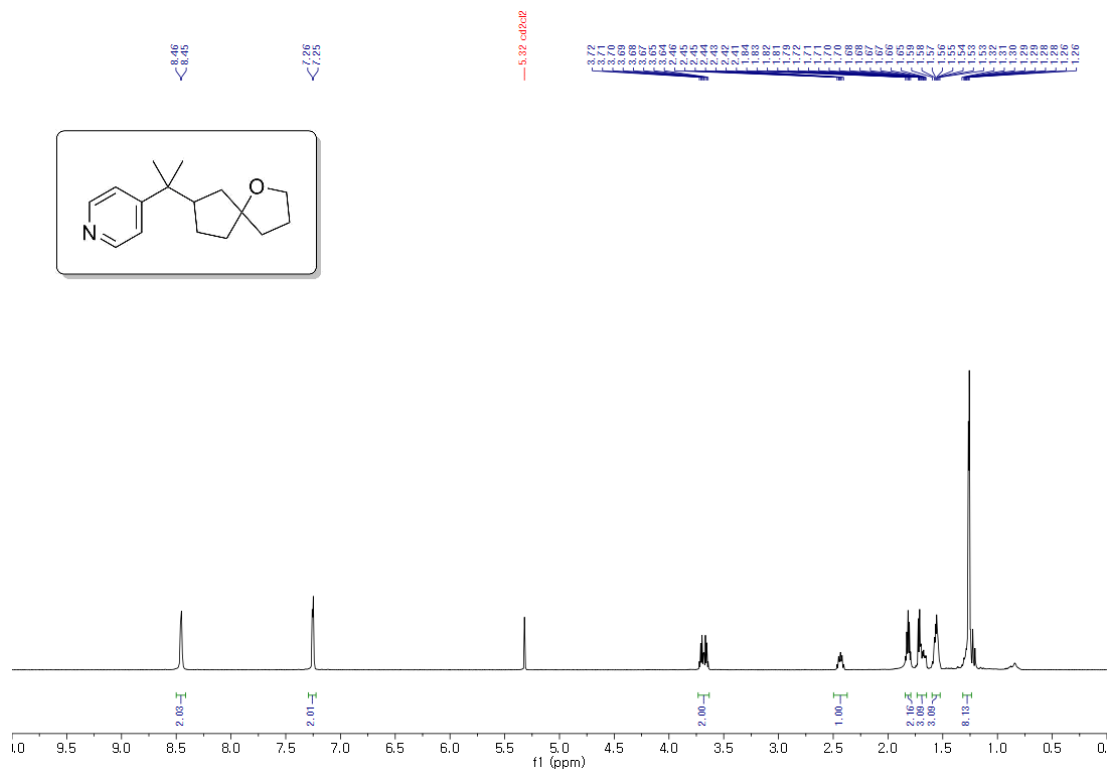


4-(2-(1-oxaspiro[4.4]nonan-7-yl)propan-2-yl)pyridine (4b).

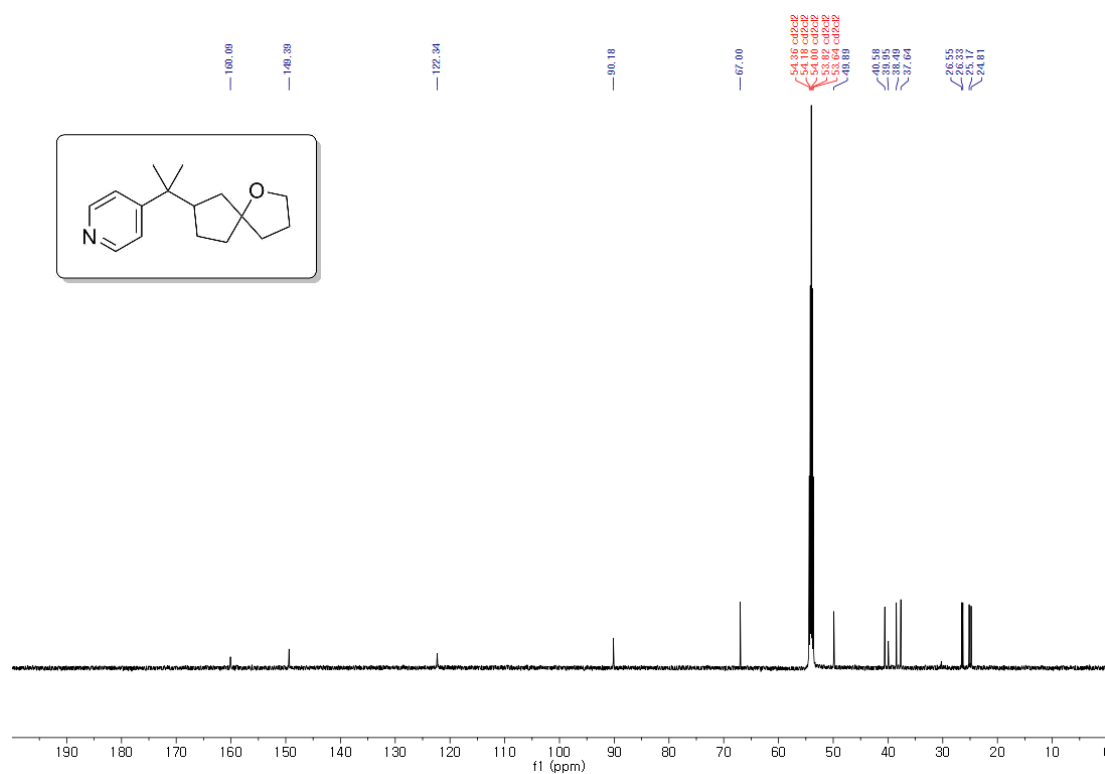
600 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer A



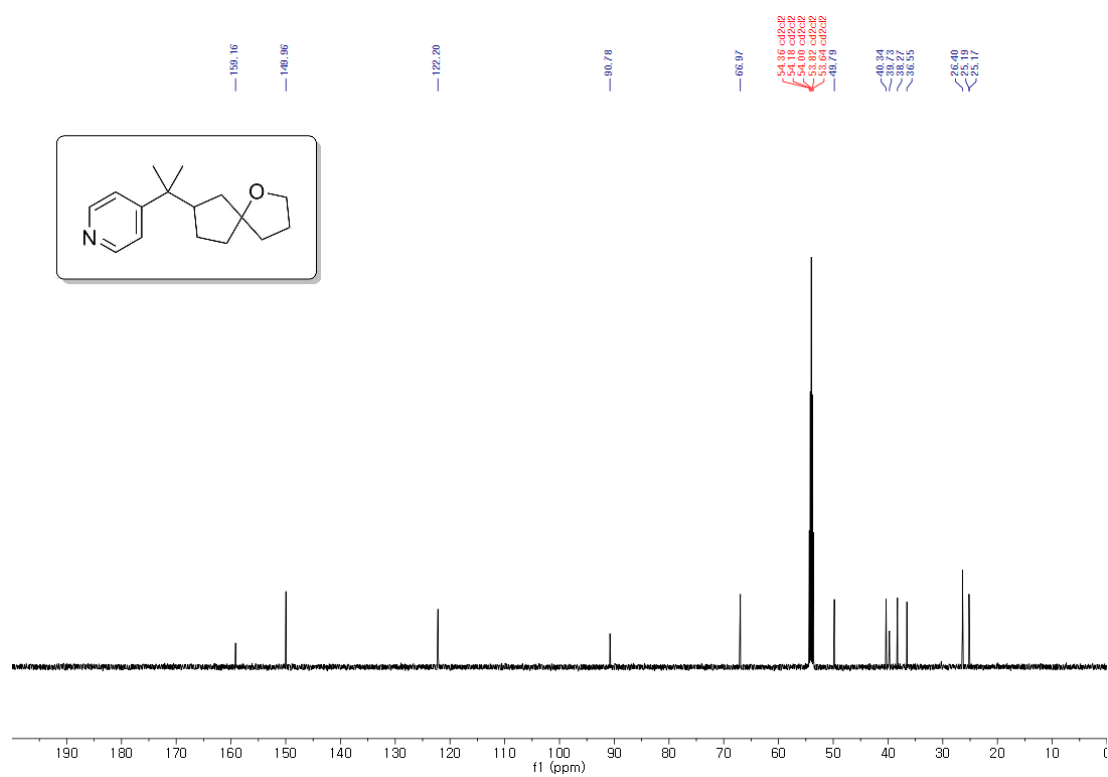
600 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer B



150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer A

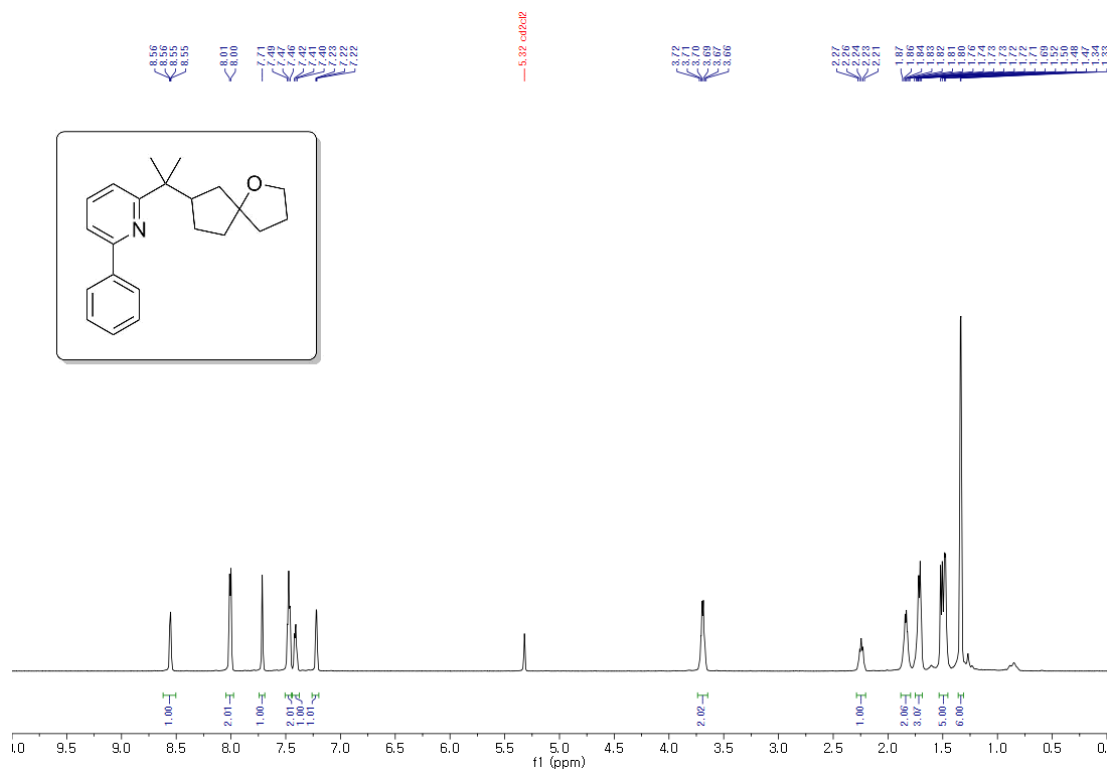


150 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer B

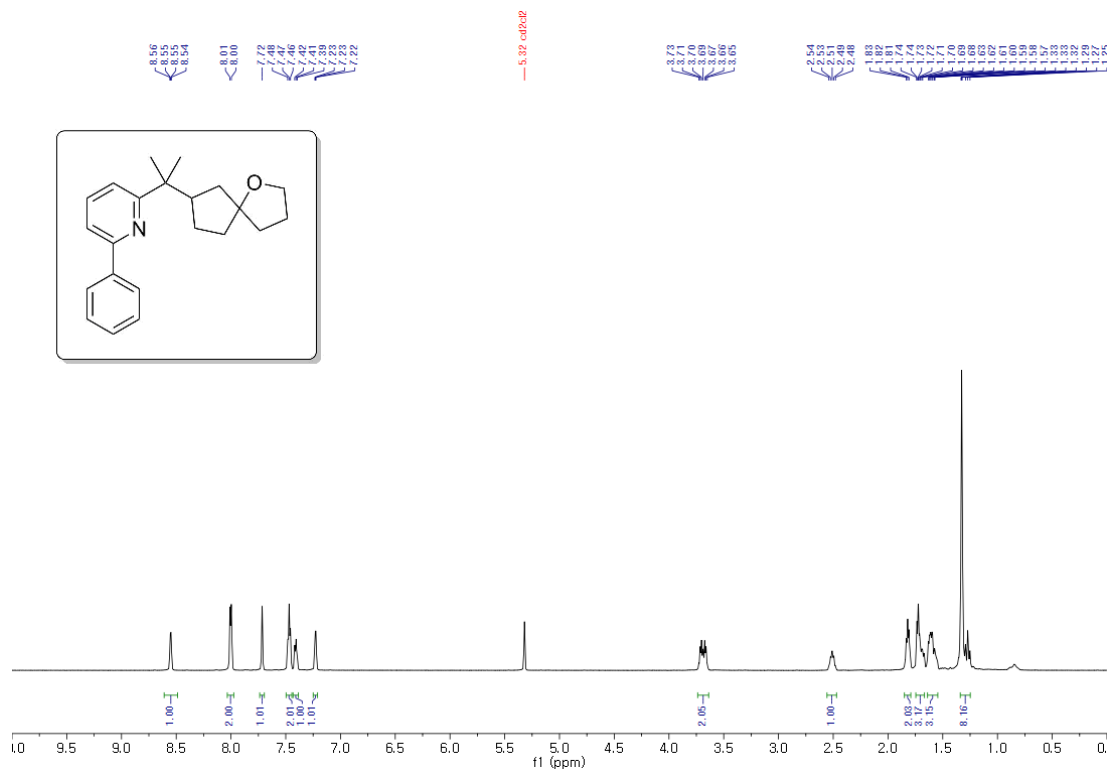


2-(2-(1-oxaspiro[4.4]nonan-7-yl)propan-2-yl)-6-phenylpyridine (4c).

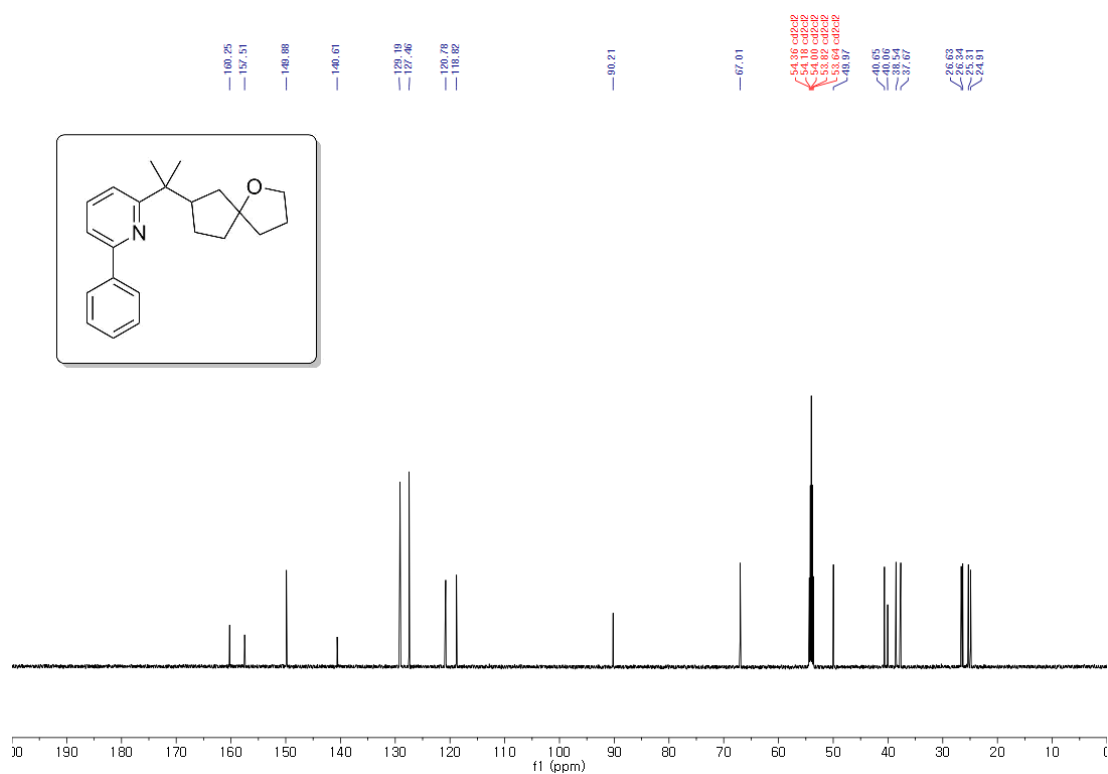
600 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer A



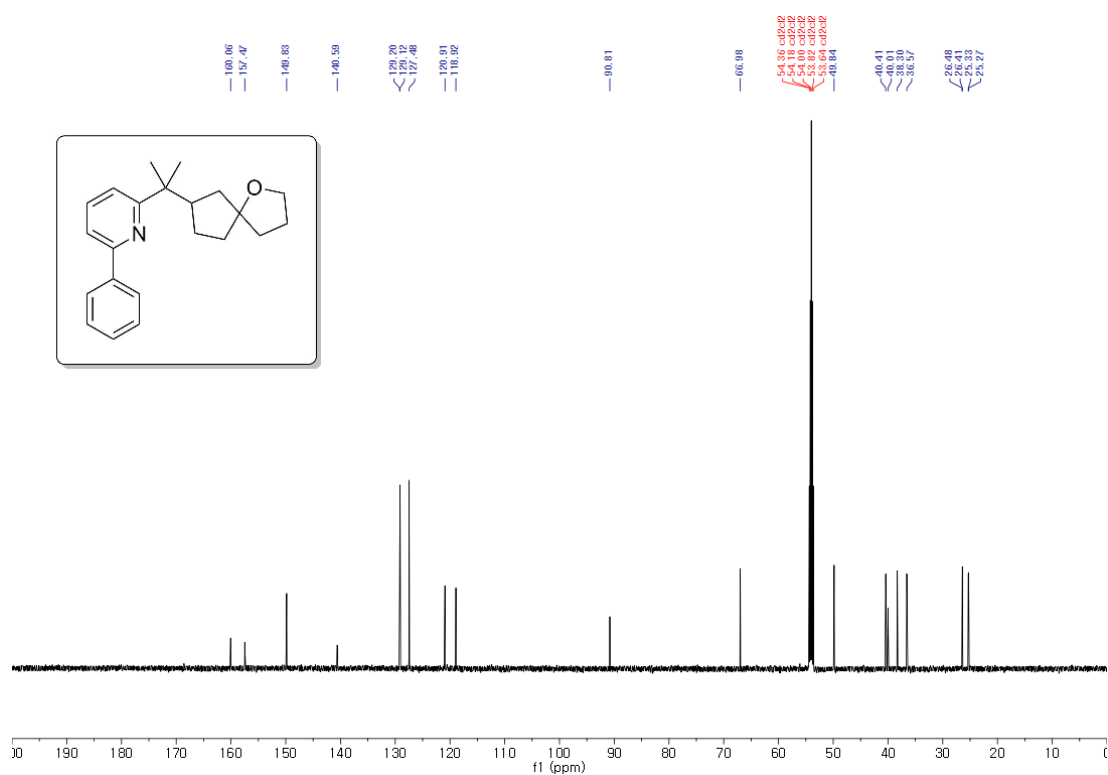
600 MHz, ^1H NMR in Methylene Chloride- d_2 , diastereomer B



600 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer A

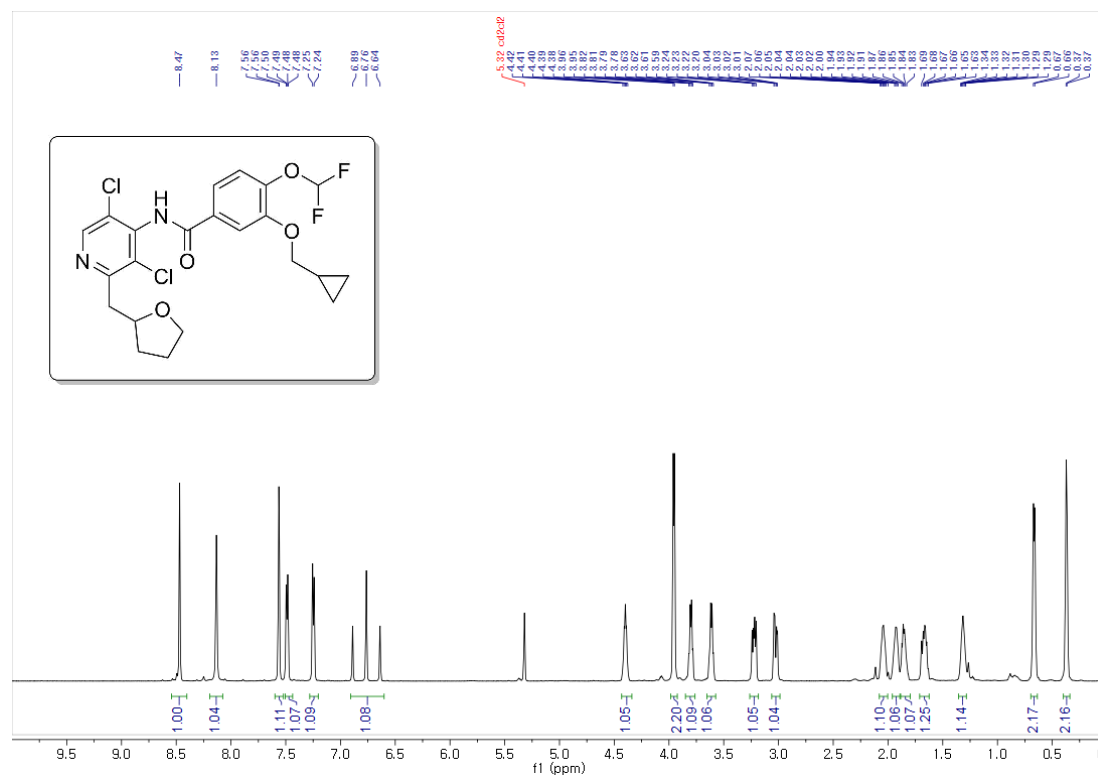


600 MHz, ^{13}C NMR in Methylene Chloride- d_2 , diastereomer B

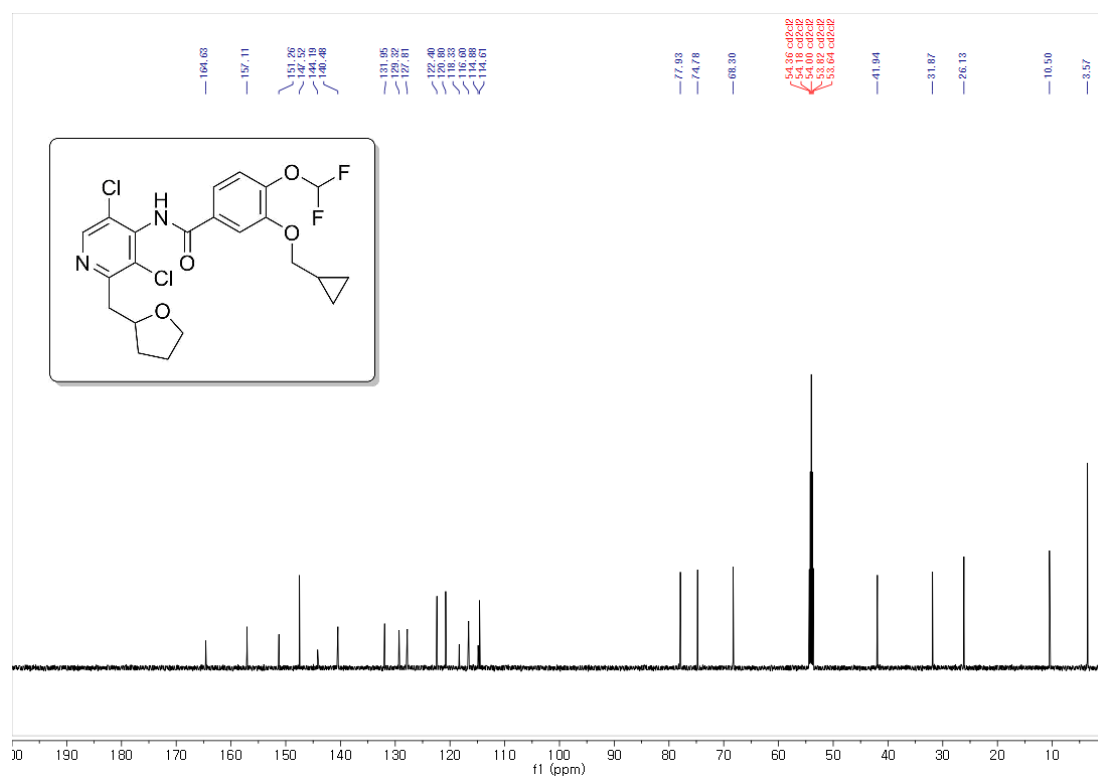


3-(cyclopropylmethoxy)-N-(3,5-dichloro-2-((tetrahydrofuran-2-yl)methyl)pyridin-4-yl)-4-(difluoromethoxy)benzamide (4d).

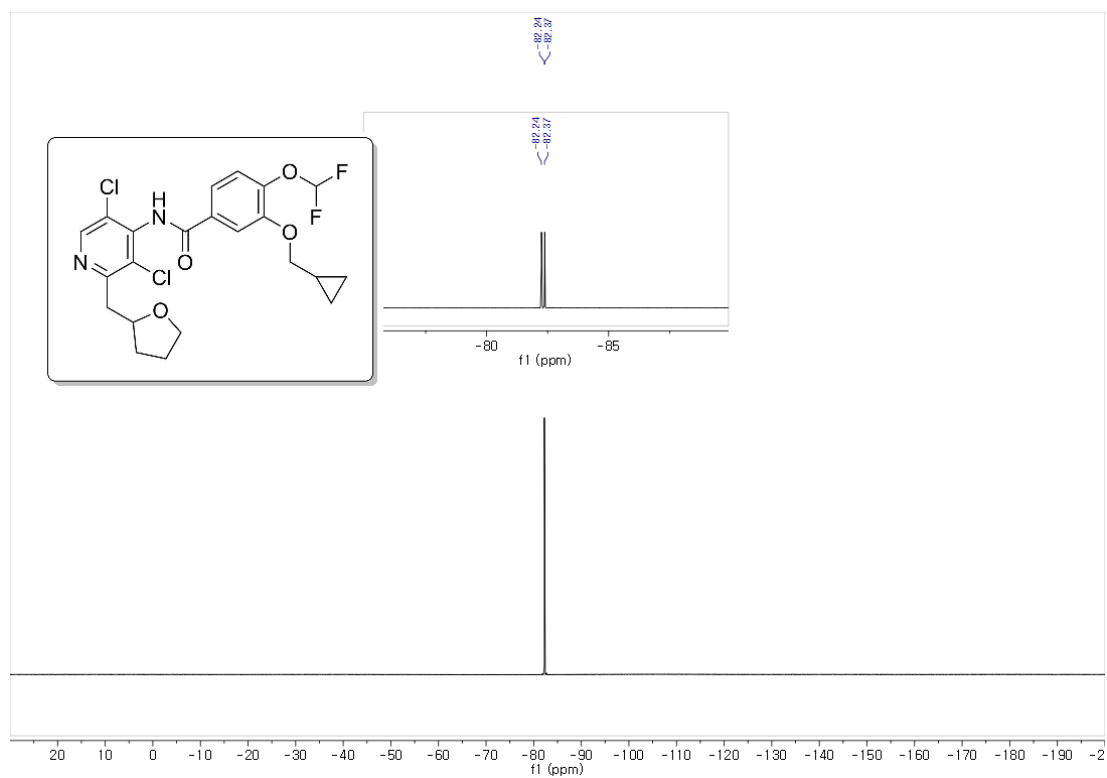
600 MHz, ^1H NMR in Methylene Chloride- d_2



150 MHz, ^{13}C NMR in Methylene Chloride- d_2

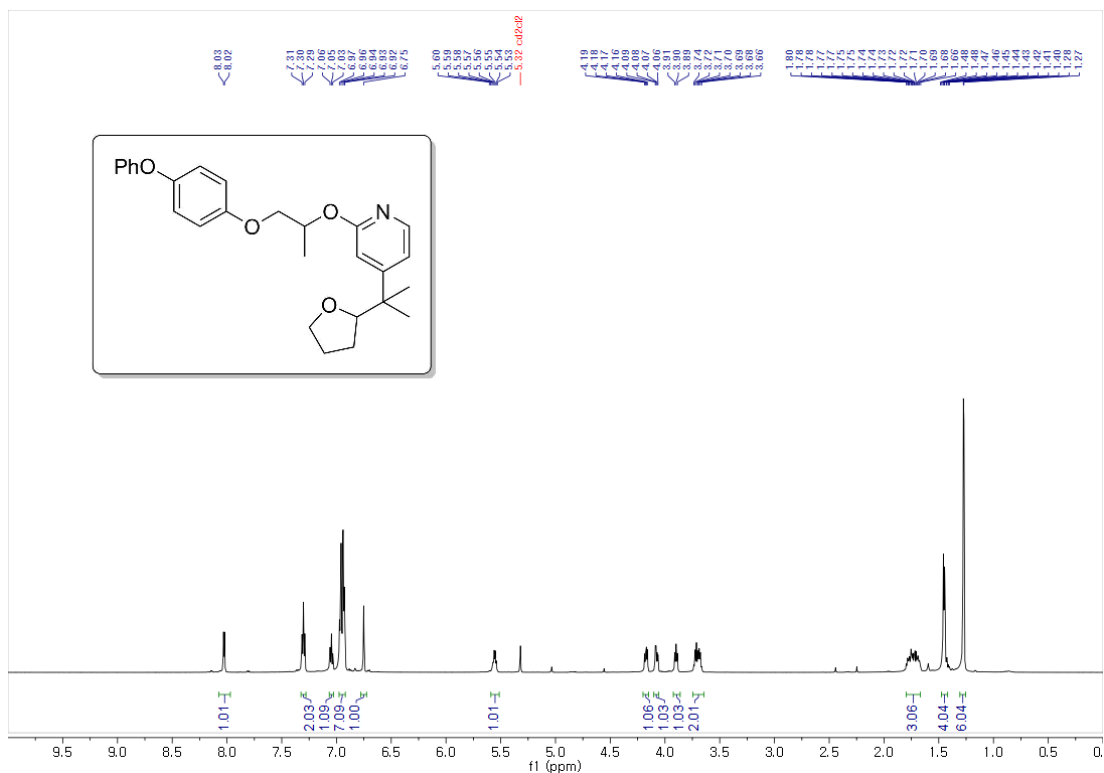


564 MHz, ^{19}F NMR in Methylene Chloride- d_2

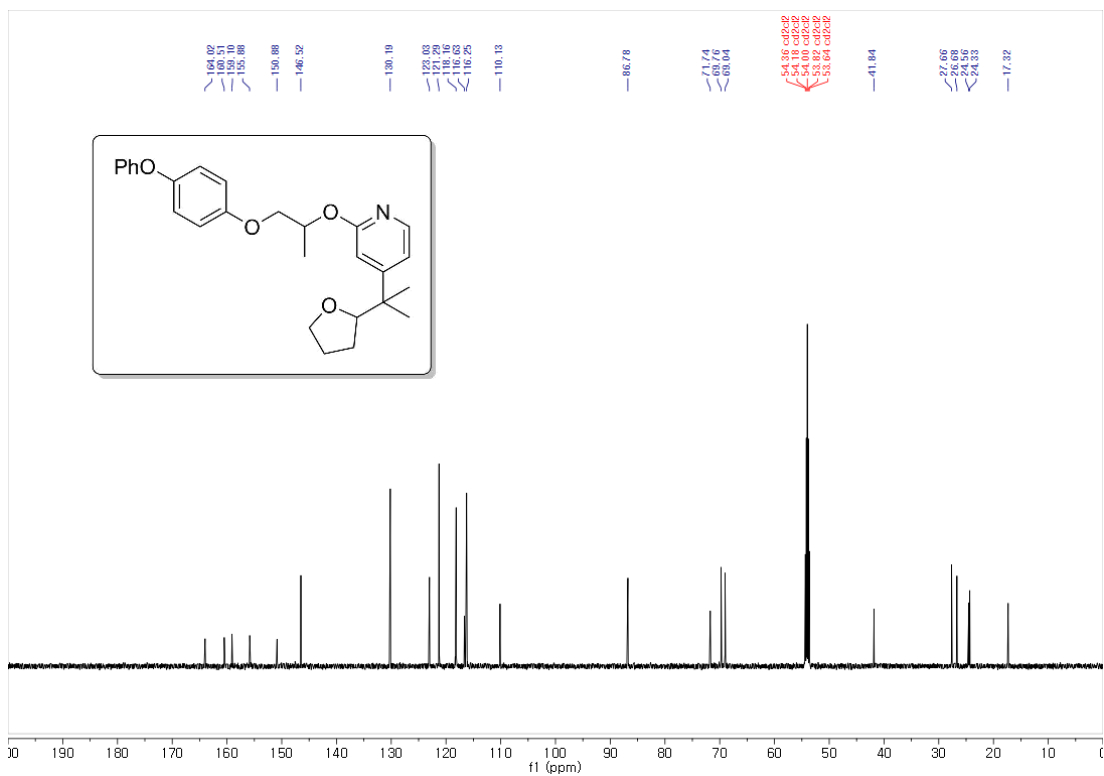


2-((1-(4-phenoxyphenoxy)propan-2-yl)oxy)-4-(2-(tetrahydrofuran-2-yl)propan-2-yl)pyridine (4e).

600 MHz, ^1H NMR in Methylene Chloride- d_2



150 MHz, ^{13}C NMR in Methylene Chloride- d_2



600 MHz, ^1H NMR in Methylene Chloride- d_2

