Electronic Supplementary Material (ESI) for Chemical Communications.
This journal is © The Royal Society of Chemistry 2015

Pyridine Synthesis from Oximes and Alkynes via Rhodium (III) Catalysis: Cp* and Cp^t Provide Complementary Selectivity

Todd K. Hyster and Tomislav Rovis*

Department of Chemistry, Colorado State University, Fort Collins, CO 80523

Supporting Information

General Methods **S2**

General Procedure of Oxime Preparation and Characterization **S3**

General Procedure for Pyridine Synthesis **S4**

Characterization of New Compounds **S4**

General Procedure for Isoquinoline Synthesis and Characterization **S11**

Pyridine Mechanistic Experiments **S13**

Spectra **S16**

General Methods. All reactions were carried out in 1.5 dram sealed vials under an atmosphere of air with magnetic stirring in an aluminum-heating block without drying or degassing of the vial. ACS grade 2,2,2-triflouroethanol was purchased from Sigma Aldrich Chemical Company and used without further purification. Phenyl-1-propyne (**2a),** methylphenyl propiolate (**2d)**, di-phenyl acetylene (**2e)**, 1-and 5-decyne (**2g)**, 4-methyl-2-pentyne (**2i)**, were purchased Sigma-Aldrich Chemical Company and used without further purification. 1-methoxy-4-((4-(trifluoromethyl)phenyl)ethynyl)benzene,[1] (cyclopropylethynyl)-benzene,[2] and tert-butyl (3-phenylprop-2-yn-1-yl)carbamate,[3] was prepared via literature procedure. $[RhCp^*Cl_2]_2$,[4] di(*tert*-butyl)cyclopentadiene,[5] $[RhCp^tCl_2]_2$,[6] and $[RhCp^{CF3}Cl_2]_2$[7] were prepared via literature procedure. Column chromatography was performed on SiliCycle® Silica Flash® 40-63µm 60A. Thin Layer chromatography was performed on SiliCycle® 250 µm 60A plates. Visualization was accomplished with UV light (254 nm), $KMnO_4$, and CAM.

^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian 300 and 400 MHz spectrometers at ambient temperature. ^{1}H NMR data are reported as the following: chemical shift in parts per million (δ, ppm) from chloroform ($CHCl_3$) taken as 7.26 ppm, integration, multiplicity (s=singlet, d=doublet, t=triplet, q=quartet, m=multiplet, dd=doublet of doublets) and coupling constant (Hz). ^{13}C NMR are reported as the following: chemical shifts are reported in ppm from $CDCl_3$ taken as 77.0 ppm. Mass spectra were obtained on a Fisons VG Autospec. Infrared spectra (IR) were obtained on Bruker Tensor 27 FT-IR spectrometer. Regioselectivity was determined from nOe spectroscopy. Regiomeric ratios were determined by GC/MS, with absolute regiochemistry determined by NOESY, analogy to complementary substrates, or previously reported ^{1}H NMR.

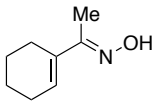
---

[1] Shirajawa, E.; Kitabata, T.; Otsuka, H.; Tsuchimoto, T. *Tetrahedron* **2005**, *61*, 9878.
[2] Ma, S.; He, Q. *Tetrahedron* **2006**, *62*, 2769.
[3] Chen, M.; Weng, Y.; Gua, M.; Zhang, H.; Lei, A. *Angew. Chem. Int. Ed.* **2008**, *47*, 2279.
[4] Fujita, K.; Takahashi, Y.; Owaki, M.; Yamamoto, K.; Yamaguchi, R. *Org. Lett.* **2004**, *6*, 2785.
[5] Venier, C. G.; Casserly, E. W. *J. Am. Chem. Soc.* **1990**, *112*, 2808.
[6] Qing-an, K.; Guo-xin, J. *Yingyong Huaxue* **2001**, *18*, 322.
[7] Gassman, P. G.; Mickelson, J. W.; Sowa, J. R. *J. Am. Chem. Soc.* **1992**, *114*, 6942.

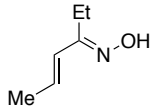
General procedure for synthesis of oximes:

All oximes were generated from the corresponding ketone or aldehyde. A 50 ml flask was charged with a stirbar, ketone or aldehyde (1 equiv), NH_2OH•HCl (1.2 equiv), NaOAc (1.2 equiv), and ethanol (.4 M). The flask was placed into an 80 °C oil bath and stirred until the reaction was complete as determined by TLC. The flask was removed from the oil bath and allowed to cool to room temperature. The solvent was removed *in vacuo*, and the residue was dissolved in CH_2Cl_2 and H_2O (4:1). The mixture was extracted with CH_2Cl_2 trice, washed with Na_2CO_3 twice. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified via silica gel column chromatography (2:1 Hex/EtOAc) to yield pure oxime as a mixture of isomers.

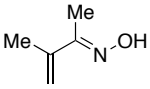
α,β Unsaturated Oxime Characterization



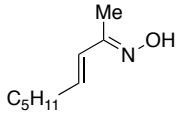
(*E*)-1-(cyclohex-1-en-1-yl)ethanone oxime (1a): ^{1}H (300 MHz, $CDCl_3$) δ 6.20 (m, 1H), 2.27-2.23 (comp m, 2H), 2.19-2.16 (comp m, 2H), 2.02 (s, 3H), 1.66-1.58 (comp m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 134.2, 130.2, 25.9, 24.3, 22.3, 21.9, 9.8.



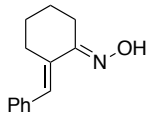
(3*E*,4*E*)-hex-4-en-3-one oxime (1b): Isolated as a 1:1 mixture of isomers. ^{1}H (400 MHz, $CDCl_3$) δ 6.08 (dd, *J* = 6.1, 1.4 Hz, 1H), 6.03 (d, *J* = 1.3 Hz, 1H), 2.54-2.46 (m, 2H), 2.42-2.34 (m, 2H), 1.91-1.88 (m, 3H), 1.87-1.81 (m, 5H), 1.13-1.02 (m, 7H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 132.0, 128.1, 124.7, 21.6, 19.2, 16.3, 15.8, 14.9, 8.4



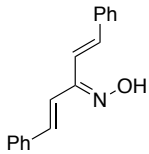
(*E*)-3-methylbut-3-en-2-one oxime (1c): ^{1}H (400 MHz, $CDCl_3$) δ 5.41 (t, *J* = 0.7 Hz, 1H), 5.31 (t, *J* = 1.2 Hz, 1H), 2.11 (s, 3H), 1.98 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 140.8, 117.5, 19.2, 10.1.



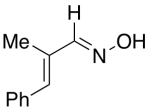
(2*E*,3*E*)-non-3-en-2-one oxime (1d): ^{1}H (400 MHz, $CDCl_3$) δ 6.07 (d, *J* = 0.8 Hz, 2H), 2.14 (q, *J* = 6.7 Hz, 2H), 1.97 (s, 3H), 1.41 (dt, *J* = 14.5, 7.2 Hz, 2H), 1.28-1.27 (m, 4H), 0.86 (t, *J* = 7.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 134.2, 124.5, 116.5, 30.2, 28.80, 28.75, 26.0, 19.9, 11.4, 7.0.



(1*E*,2*E*)-2-benzylidenecyclohexanone oxime (1e): ^{1}H (400 MHz, $CDCl_3$) δ 7.38-7.32 (m, 5H), 6.93 (s, 1H), 2.71-2.66 (m, 4H), 1.76-1.64 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 127.1, 125.5, 124.6, 26.4, 22.39, 22.28, 20.7.

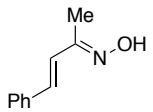


(1*E*,4*E*)-1,5-diphenylpenta-1,4-dien-3-one oxime (1f): ^{1}H (400 MHz, $CDCl_3$) δ 7.56-7.54 (m, 2H), 7.52-7.50 (m, 2H), 7.41-7.32 (m, 8H), 7.13 (d, *J* = 17.8 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 137.8, 136.3, 136.1, 135.4, 129.1, 128.76, 128.72, 128.63, 128.57, 127.36, 127.22, 127.0, 121.9, 116.7.

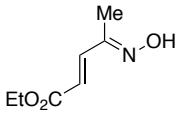


(1E,2E)-2-methyl-3-phenylacrylaldehyde oxime (1g): ^{1}H (400 MHz, $CDCl_3$) δ 8.10 (s, br, 1H), 7.84 (s, 1H), 7.27 (m, 5H), 6.62 (s, 1H), 2.03 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 136.7, 136.2, 131.7, 129.2,

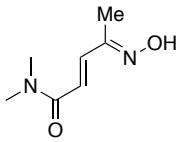
128.3, 127.6, 13.0.



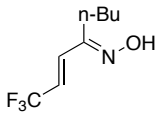
(2*E*,3*E*)-4-phenylbut-3-en-2-one oxime (1h): ^{1}H (400 MHz, $CDCl_3$) δ 7.47-7.45 (m, 2H), 7.34 (dd, *J* = 8.0, 6.6 Hz, 3H), 6.87 (d, *J* = 7.2 Hz, 2H), 2.15 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.7, 136.3, 133.4, 128.4, 127.5, 126.8, 125.7, 9.7.



(2*E*,4*E*)-ethyl 4-(hydroxyimino)pent-2-enoate (1i): ^{1}H (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 16.1 Hz, 1H), 6.13 (d, *J* = 16.1 Hz, 1H), 4.18 (q, *J* = 7.1 Hz, 2H), 1.97 (s, 3H), 1.24 (t, *J* = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 155.1, 141.4, 132.18, 132.08, 128.54, 128.42, 122.9, 60.8, 14.2, 9.6



(2*E*,4*E*)-4-(hydroxyimino)-*N*,*N*-dimethylpent-2-enamide (1j): ^{1}H (300 MHz, MeOH) δ 7.17 (dd, *J* = 15.7, 1.0 Hz, 1H), 6.82-6.77 (m, 1H), 3.18 (s, 3H), 3.02 (s, 3H), 2.02 (s, 3H).

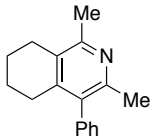


(2*E*,4*E*)-1,1,1-trifluorooct-2-en-4-one oxime (1k): Isolated as a 2.3:1 mixture of oximes isomers. ^{1}H (400 MHz, $CDCl_3$) δ 7.47 (dd, *J* = 16.6, 2.1 Hz, 1H minor), 6.76 (dd, *J* = 16.3, 2.0 Hz, 1H, major), 6.13 (dd, *J* = 16.6, 6.3 Hz, 1H, minor), 6.04 (dt, *J* = 17.8, 9.7 Hz, 1H, major), 2.53 (t, *J* = 7.8 Hz, 2H, major), 2.41 (t, *J* = 7.7 Hz, 2H, minor), 1.58-1.47 (m, 2H, major and minor), 1.39 (dt, *J* = 14.7, 7.2 Hz, 2H, major and minor), 0.94 (td, *J* = 7.3, 3.5 Hz, 3H, major and minor). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.9, 153.4, 134.41(q, major), 127.05, 126.87, 126.80, 124.94 (q, minor), 124.38, 124.24, 123.1, 122.8, 122.44, 122.40, 121.70, 121.55, 120.7, 120.3, 120.0, 119.6, 40.4, 39.1, 30.4, 28.9, 28.1, 23.9, 22.8, 22.3, 13.65, 13.60

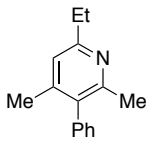
PYRIDINE

General Procedure:

A 1.5 dram vial was charged with a stirbar, free oxime (1 equiv), $[RhCp^*Cl_2]_2$ or $[RhCp^tCl_2]_2$ (2.5 mol %), and K_2CO_3 (2 equiv). TFE was added followed by alkyne (1.1 equiv). The reaction was sealed, warmed to 45 °C, and stirred until the reaction was complete as determined by TLC. Once complete the reaction was allowed to cool to room temperature and transferred to a 25 ml round bottom flask with excess CH_2Cl_2. Residual solvent was removed and the residue was purified via silica gel column chromatography.

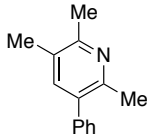


1,3-dimethyl-4-phenyl-5,6,7,8-tetrahydroisoquinoline (3a): This compound was previously characterized by Cheng and co-workers.[13] ^{1}H NMR is provided. (Cp* 2:1, 87%; Cp^t =1:4, 82%). ^{1}H (400 MHz, $CDCl_3$) δ 7.42-7.40 (m, 2H), 7.38-7.31 (m, 1H), 7.11 (dd, *J* = 8.2, 1.3 Hz, 2H), 2.66 (t, *J* = 6.5 Hz, 2H), 2.47 (s, 3H), 2.29 (t, *J* = 6.3 Hz, 2H), 2.19 (s, 3H), 1.78 (ddd, *J* = 6.6, 5.5, 5.3 Hz, 2H), 1.66-1.62 (m, 2H).

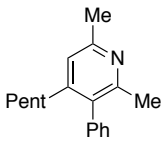


6-ethyl-3,4-dimethyl-2-phenylpyridine (3b): A 1.5 dram vial was charged with a stirbar, free oxime (1 equiv), $[RhCp^*Cl_2]_2$ or $[RhCp^tCl_2]_2$ (.025 mol %), and K_2CO_3 (2 equiv). TFE was added followed by alkyne (1.1 equiv). The reaction was sealed, warmed to 80 °C, and stirred until the reaction was

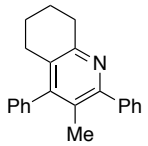
complete as determined by TLC. Once complete the reaction was allowed to cool to room temperature and transferred to a 25 ml round bottom flask with excess CH_2Cl_2. Residual solvent was removed and the residue was purified via silica gel column chromatography. Regioselectivity confirmed by analogy. (Cp* 1:1, 80%; Cp^t =4:1:, 83%). R_f = .18 (9:1 Hexanes/EtOAc); ^1H (400 MHz, $CDCl_3$) δ 7.48-7.41 (m, 4H, major), 7.39-7.35 (m, 4H, minor), 7.16 (d, *J* = 1.5 Hz, 1H, major), 7.16-7.14 (m, 1H, minor), 6.97 (s, 1H, minor), 6.93 (s, 1H, major), 2.81 (q, *J* = 7.6, 3H, major), 2.80 (q, *J* = 7.6, 3H, minor) 2.33 (s, 3H, minor), 2.26 (s, 3H, major), 2.18 (s, 3H, minor), 2.02 (s, 3H, major), 1.33 (t, *J* = 7.6 Hz, 3H, major), 1.32 (t, *J* = 7.6 Hz, 3H, minor). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 159.9, 158.0, 155.2, 146.8, 145.7, 141.5, 139.1, 134.2, 129.14, 129.08, 128.6, 128.0, 127.4, 127.0, 126.7, 121.9, 120.6, 31.03, 30.96, 23.4, 20.27, 20.15, 15.8, 14.27, 14.19. IR (thin film) 2969, 1592, 1462, 1071, 761, 702 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 212.1434; found 212.1432.



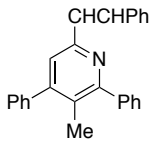
2,3,5-trimethyl-6-phenylpyridine (3c): Prepared using the general procedure. Pyridine **3b** was isolated as a viscous orange liquid. (Cp* 2:1, 87%; Cp^t =1:4, 85%). R_f = .10 (9:1 Hexanes/EtOAc); ^1H (400 MHz, $CDCl_3$) δ 7.50 (dd, *J* = 8.3, 1.4 Hz, 1H, minor), 7.45-7.41 (m, 3H, major), 7.38-7.36 (m, 1H, minor), 7.31 (dt, *J* = 6.5, 1.6 Hz, 2H, major), 7.28 (s, 1H), 2.54 (s, 3H, major), 2.52 (s, 1H, minor), 2.47 (s, 3H, major), 2.30 (s, 1H, minor), 2.29 (s, 3H, major), 2.27 (s, 1H, minor). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.4, 149.3, 137.5, 137.1, 136.1, 131.8, 127.1, 126.47, 126.41, 125.87, 125.68, 125.48, 124.9, 124.5, 20.0, 19.57, 19.48, 16.7, 16.06, 15.95. IR (thin film) 2966, 1553, 1431, 1073, 746 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 198.1277; found 198.1280.



2,6-dimethyl-4-pentyl-3-phenylpyridine (3d): Prepared using the general procedure. Pyridine **3b** was isolated as a viscous orange liquid. Regiochemistry determined by analogy. (Cp* 1:1.2, 92%; Cp^t =3.4:1, 93%). R_f = .15 (9:1 Hexanes/EtOAc); ^1H (400 MHz, $CDCl_3$) δ 7.44-7.39 (m, 3H), 7.38-7.33 (m, 2H), 7.15-7.12 (m, 2H), 6.92 (s, 1H), 2.54 (s, 3H), 2.29-2.24 (m, 2H), 2.23 (s, 3H), 1.44-1.35 (m, 6H), 1.20-1.11 (m, 5H), 0.79 (dd, *J* = 8.3, 5.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 152.9, 152.0, 148.5, 147.5, 136.2, 131.1, 126.8, 126.5, 125.8, 125.4, 124.8, 124.5, 119.6, 118.3, 30.7, 30.3, 28.9, 27.3, 21.6, 21.0, 19.9, 19.6, 11.39, 11.22. IR (thin film) 2928, 1592, 1458, 1008, 703 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 254.1903; found 254.1907.

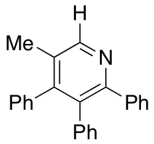


3-methyl-2,4-diphenyl-5,6,7,8-tetrahydroquinoline (3e): This compound was previously characterized by Cheng and co-workers.[8] Provided is a ^1H NMR. (Cp* 4:1, 75%; Cp^t =1:1, 70%). ^1H (400 MHz, $CDCl_3$) δ 7.51-7.35 (m, 8H), 7.16-7.13 (m, 2H), 3.01 (t, *J* = 6.4 Hz, 2H), 2.36 (t, *J* = 6.4 Hz, 2H), 1.91 (s, 3H), 1.89-1.86 (m, 2H), 1.72 (qd, *J* = 6.1, 2.6 Hz, 2H).

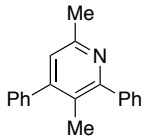


3-methyl-2,4-diphenyl-6-styrylpyridine (3f): Prepared using the general procedure. Pyridine **3b** was isolated as a viscous orange liquid. Regiochemistry determined by analogy (Cp* 3.5:1, 77%; Cp^t =1:3.4, 76%). . R_f = .15 (9:1 Hexanes/EtOAc); ^1H (400 MHz, $CDCl_3$) δ 7.67-7.05 (m, 18H), 2.46 (s, 3H, minor), 2.19 (s, 3H, major). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.6, 152.6, 151.2, 141.3, 140.1, 139.5, 136.87, 136.77, 133.8, 132.1, 130.2, 129.23, 129.18, 128.97, 128.94, 128.83, 128.70, 128.69, 128.63, 128.40, 128.36, 128.22,

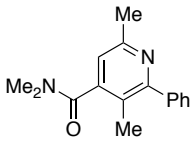
128.15, 128.04, 127.98, 127.96, 127.87, 127.84, 127.81, 127.29, 127.09, 127.04, 126.98, 126.91, 120.9, 120.3, 17.9. IR (thin film) 2925, 1579, 1449, 1074, 699 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 348.1747; found 348.1743.



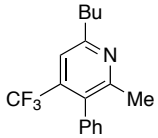
5-methyl-2,3,4-triphenylpyridine (3g): A 1.5 dram vial with a stir bar was charged with K_2CO_3 (0.11 mmol, 0.5 equiv), and $[RhCp^*Cl_2]_2$ (0.0055 mmol, 2.5 mol %). The 2,2,2 triflouroethanol (1.5 ml) was added followed by oxime (.24 mmol, 1.1 equiv) and alkyne (.22 mmol, 1 equiv). The vial was sealed and placed into a 80 °C heating block for 24 h. The reaction was concentrated *in vacuo*. The residue was dissolved in 1 ml of dichloromethane and loaded onto a neutral column of silica gel and eluted with a suitable solution of ethyl acetate and hexanes (typically 20:1 EtOAc/Hexanes with 1% Et_3N). Evaporation of solvent afforded the product. (45%); R_f = .60 (9:1 Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.46 (m, 3H), 7.39-7.35 (m, 6H), 7.17-7.16 (m, 4H), 7.03-7.00 (2H), 2.36 (s, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 149.3, 140.7, 138.09, 138.04, 134.6, 131.1, 129.7, 129.1, 127.7, 127.5, 127.2, 126.1, 17.7; IR (thin film) 1640, 1442, 1072, 760, 697 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 322.159; found 322.1597.



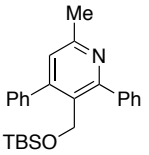
3,6-dimethyl-2,4-diphenylpyridine (3h): According to the general procedure, the desired pyridine was isolated as a yellow oil (Cp* 3.1:1, 91%; Cp^t =1:3.3, 90%). R_f = .25 (9:1 Hexanes/EtOAc); ^1H (400 MHz, $CDCl_3$) δ 7.54-7.35 (m, 11H, minor), 7.24-7.20 (m, 3H, major), 7.18-7.14 (m, 3H, major), 7.06-7.03 (m, 5H, major), 2.61 (s, 3H, major), 2.60 (s, 3H, minor), 2.39 (s, 3H, major), 2.14 (s, 3H, minor). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 156.25, 156.14, 154.8, 151.0, 149.1, 141.4, 140.1, 139.5, 138.5, 132.3, 130.47, 130.34, 129.21, 129.16, 129.05, 128.93, 128.7, 128.29, 128.21, 128.13, 127.97, 127.92, 127.80, 127.70, 127.68, 127.64, 127.1, 126.7, 125.1, 122.8, 121.7, 24.22, 24.12, 23.9, 17.5. IR (thin film) 1586, 1493, 1073, 700 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 260.1434; found 260.1438.



***N,N*,3,6-tetramethyl-2-phenylisonicotinamide (3i):** According to the general procedure, the desired pyridine was isolated as a yellow oil (Cp* 6.6:1, 72%; Cp^t =1:1, 74%). .; ^1H (400 MHz, $CDCl_3$) δ 7.47-7.45 (m, 5H), 6.98 (s, 1H), 3.16 (s, 3H), 2.92 (s, 3H), 2.59 (s, 3H), 2.20 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 159.3, 155.8, 146.0, 128.9, 128.2, 128.0, 123.2, 118.4, 38.2, 34.4, 30.0, 24.1, 16.0. IR (thin film) 1640, 1442, 1072, 760, 697 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 255.1492; found 255.1493.

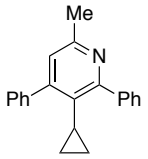


6-butyl-2-methyl-3-phenyl-4-(trifluoromethyl)pyridine (3j): According to the general procedure, the desired pyridine was isolated as a yellow oil (Cp* 10:1, 72%; Cp^t =1:1, 68%).;^1H (400 MHz, $CDCl_3$) δ 7.46-7.40 (m, 5H), 7.35 (s, 1H), 2.86 (t, *J* = 7.9 Hz, 2H), 2.36 (d, *J* = 1.6 Hz, 3H), 1.73 (dtd, *J* = 9.9, 7.8, 5.6 Hz, 2H), 1.41 (dd, *J* = 15.0, 7.4 Hz, 2H), 0.95 (t, *J* = 7.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 160.3, 140.1, 137.6 (q), 129.1, 128.25, 128.15, 125.3, 125.0, 117.22, 117.16, 37.9, 32.0, 22.5, 15.67, 15.64, 13.9. IR (thin film) 2961, 1593, 1445, 1251, 764 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 294.1467; found 294.1464.

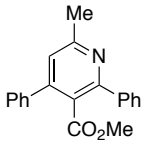


3-(((tert-butyldimethylsilyl)oxy)methyl)-6-methyl-2,4-diphenylpyridine (3k): According to the general procedure, the desired pyridine was isolated as a yellow oil (80%, 2.5:1); Rf = .78 (9:1

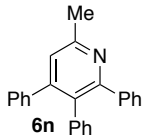
Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, CDCl3) δ 7.91 (dd, 1H, *J*=8.0 Hz, *J*=2.0 Hz), 7.72 (m, 2H), 7.65-7.60 (m, 4H), 7.45-7.21 (m, 5H), 4.80 (s, 2H), 4.66 (s, 2H), 4.49 (s, 2H), 2.85 (s, 3H), 2.83 (s, 3H), 2.82 (s, 3H), 1.07 (s, 9H, major), 1.03 (s, 9H, minor), .13 (s, 6H, minor). 0.00 (s, 6H, major); 13C NMR (100 MHz, CDCl3) δ 166.5, 162.7, 162.5, 158.3, 146.5, 145.1, 136.6, 135.8, 135.3, 135.1, 134.8, 134.1, 133.87, 133,83, 133.7, 133.5, 133.4, 133.2, 133.0, 132.7, 129.1, 128.6, 71.6, 67.9, 65.4, 31.8, 31.6, 30.2, 30.0, 29.8, 24.0, 0.5, 0.0; IR (thin film) 2927, 2360, 1588, 1252, 699 cm-1; HRMS (ESI) *m/e* calcd (M+H) 390.2248; found 390.2249.



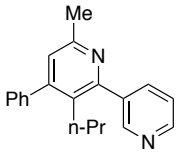
3-cyclopropyl-6-methyl-2,4-diphenylpyridine (3l): According to the general procedure, the desired pyridine was isolated as a yellow oil 81%, 4.4:1); R_f = .23 (19:1 Hexanes/EtOAc w/ 1% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 7.93-7.91 (m, 2H), 7.75-7.62 (m, 8H), 7.31 (s, 1H), 2.86 (s, 3H), 2.26-2.22 (m, 1H), 0.65-0.62 (m, 2H), 0.03-0.13 (m, 2H);); ^{13}C NMR (100 MHz, $CDCl_3$) δ 1604, 155.1, 152.3, 141.2, 139.9, 129.8, 128.9, 128.4, 127.5, 127.2, 127.0, 122.1, 23.7, 12.8, 9.9, 9.6; IR (thin film) 1586, 1493, 1072, 753, 700 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 286.159; found 286.1597.



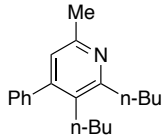
methyl 6-methyl-2,4-diphenylnicotinate (3m): According to the general procedure, the desired pyridine was isolated as a yellow oil (89%, 5:1); R_f = .15 (19:1 Hexanes/EtOAc w/ 1% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 7.53 (dd, *J* = 7.8, 1.7 Hz, 2H), 7.37-7.31 (m, 8H), 7.19 (s, 1H), 7.09 (s, 1H), 3.37 (s, 3H), 2.60 (s, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.3, 159.0, 156.4, 148.8, 139.8, 138.3, 128.99, 128.94, 128.84, 128.74, 128.64, 128.61, 128.53, 128.46, 128.34, 128.28, 128.21, 127.84, 127.76, 125.6, 122.32, 122.27, 52.1, 24.6; IR (thin film) 1730, 1587, 1266, 1107, 699 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 303.1259; found 303.1256.



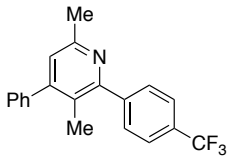
6-methyl-2,3,4-triphenylpyridine (3n): According to the general procedure, the desired pyridine was isolated as a white solid (89%); R_f = .35 (19:1 Hexanes/EtOAc w/ 1% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 7.27-7.25 (m, 3H), 7.21-7.17 (m, 6H), 7.08-7.02 (m, 5H), 6.85 (dd, *J* = 7.8, 1.7 Hz, 2H), 2.71 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 157.7, 156.7, 139.5, 137.7, 131.7, 131.4, 129.86, 129.82, 129.2, 127.8, 127.6, 127.25, 127.18, 126.4, 123.3, 24.2; IR (thin film) 1671, 1446, 1103, 749, 701 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 322.159; found 322.159.



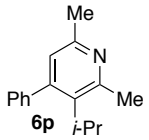
6-methyl-4-phenyl-3-propyl-2,3'-bipyridine (3o): According to the general procedure, the desired pyridine was isolated as a yellow oil. (66%, 2.5:1); R_f = .76 (9:1 Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 8.76 (s, 1H), 8.65 (d, *J* = 3.8 Hz, 1H), 7.85 (dt, *J* = 7.8, 1.8 Hz, 1H), 7.47-7.39 (m, 4H), 7.32 (dd, *J* = 7.9, 1.6 Hz, 2H), 7.04 (s, 1H), 2.60 (s, 3H), 2.55-2.51 (m, 2H), 1.13-1.07 (m, 2H), 0.50 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 189.6, 155.7, 155.0, 151.6, 149.4, 148.6, 139.7, 136.7, 131.0, 128.36, 128.31, 127.8, 124.3, 123.2, 30.7, 23.87, 23.67, 13.9; IR (thin film) 1671, 1446, 1103, 749, 701 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 289.1699; found 289.1696.



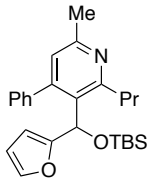
2,3-dibutyl-6-methyl-4-phenylpyridine (3p): According to the general procedure, the desired pyridine was isolated as a yellow oil. (65%); R_f = .76 (9:1 Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, $CDCl_3$) 7.34-7.28 (m, 3H), 7.18-7.16 (m, 2H), 6.72 (s, 1H), 2.76-2.72 (m, 2H), 2.42 (s, 3H), 2.42 (q, *J* = 2.7 Hz, 5H), 1.66-1.60 (m, 2H), 1.39 (dd, *J* = 15.0, 7.4 Hz, 2H), 1.24 (ddd, *J* = 13.7, 6.7, 3.5 Hz, 3H), 1.12-1.07 (m, 2H), 0.89 (t, *J* = 7.3 Hz, 3H), 0.66 (q, *J* = 6.7 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.4, 154.1, 150.5, 140.5, 130.0, 128.9, 128.43, 128.39, 128.21, 128.15, 128.02, 127.6, 127.3, 123.2, 122.1, 41.5, 35.2, 33.1, 32.80, 32.66, 28.0, 26.7, 23.9, 23.1, 22.8, 19.1, 14.02, 13.97, 13.53, 13.44. IR (thin film) 1671, 1446, 1103, 749, 701 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 282.2210 found 282.2216.



3,6-dimethyl-4-phenyl-2-(4-(trifluoromethyl)phenyl)pyridine (3q): According to the general procedure, the desired pyridine was isolated as a yellow oil (85%, 3.5:1); R_f = .76 (9:1 Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, $CDCl_3$) 7.64-7.56 (m, 3H), 7.39-7.32 (m, 4H), 7.28-7.25 (m, 2H), 6.99 (s, 1H), 2.51 (s, 3H), 2.05 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.6, 155.2, 151.4, 144.92, 144.91, 139.7, 132.6, 130.8, 129.66, 129.51, 129.07, 128.93, 128.67, 128.61, 128.38, 128.21, 127.94, 127.87, 127.84, 127.5, 126.4, 125.6, 125.25, 125.21, 125.17, 125.13, 125.10, 124.99, 124.96, 123.42, 123.32, 121.9, 24.0, 17.3. HRMS (ESI) *m/e* calcd (M+H) 328.1307 found 328.1308.



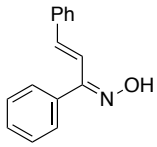
2-isopropyl-3,6-dimethyl-4-phenylpyridine (3r): According to the general procedure, the desired pyridine was isolated as an off white solid (73%, 10.8:1); R_f = .70 (9:1 Hexanes/EtOAc w/ 5% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 7.30 (m, 3H), 7.13 (dd, 2H, *J*=8.0 Hz, *J*=2.0 Hz), 6.69 (s, 1H), 3.11 (septet, 1H, *J*=7.6 Hz), 2.60 (s, 3H), 2.41 (s, 3H), 1.12 (d, 6H, *J*=7.2 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.3, 153.5, 150.5, 141.3, 135.2, 128.3, 127.9, 127.2, 122.5, 28.7, 24.3, 23.7, 21.4; IR (thin film) 2959, 1587, 1444, 1073, 777 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 226.159; found 226.1591.



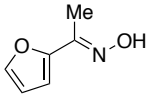
2-(((*tert*-butyldimethylsilyl)oxy)(furan-2-yl)methyl)-6-methyl-4-phenyl-3-propylpyridine (3s): According to the general procedure, the desired pyridine was isolated as a yellow oil (71%, 9:1); R_f = .4 (9:1 Hexanes/EtOAc); Regiochemistry assigned via analogy; ^1H (400 MHz, $CDCl_3$) δ 7.79-7.75 (m, 5H), 7.66 (s, 1H), 6.75 (dd, *J* = 3.2, 1.8 Hz, 1H), 6.59 (d, *J* = 3.2 Hz, 1H), 6.36 (s, 1H), 3.38-3.17 (m, 2H), 2.94 (s, 3H), 1.98 (s, 2H), 1.24 (t, *J* = 7.3 Hz, 3H), 1.19 (s, 7H), 0.10 (d, *J* = 35.8 Hz, 5H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.6, 162.5, 161.6, 147.0, 145.0, 134.6, 133.58, 133.55, 133.3, 126.9, 115.8, 111.8, 103.93, 103.92, 72.6, 43.3, 31.31, 31.16, 29.7, 28.8, 23.5, 19.9, 0.6, -0.0. IR (thin film) 1556, 1442, 1024, 753 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 422.2504; found 422.251.

Aryl Oxime Characterization

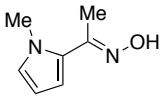
Aryl oximes **4a,**[8] **4b,**[8] **4c**,[9] **4j,**[8] **4e**,[10] **4f**[11], **4k**,[12] and **4l**[12] were prepared according to literature procedures.



(1*E*,2*E*)-chalcone oxime (4d): Prepared using the general procedure. Oxime **4d** was isolated as a single isomer. ^{1}H (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 16.6 Hz, 1H), 7.46-7.34 (m, 5H), 7.31-7.21 (m, 3H), 6.74 (d, *J* = 16.6 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 157.8, 139.7, 136.1, 134.7, 129.21, 129.17, 128.70, 128.68, 128.56, 128.42, 128.38, 128.33, 128.30, 127.5, 117.0



(*E*)-1-(furan-2-yl)ethanone oxime (4g): Prepared using the general procedure. Oxime **4g** was isolated as a single isomer. ^{1}H (400 MHz, $CDCl_3$) δ 7.46 (dd, *J* = 1.8, 0.7 Hz, 1H), 6.64 (dd, *J* = 3.4, 0.7 Hz, 1H), 6.44 (dd, *J* = 3.4, 1.8 Hz, 1H), 2.23 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.1, 147.4, 143.6, 111.2, 110.0, 11.1.

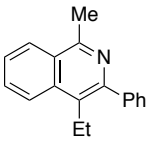


(*E*)-1-(1-methyl-1*H*-pyrrol-2-yl)ethanone oxime (4i): Prepared using the general procedure. Oxime **4i** was isolated as a single isomer. ^{1}H (400 MHz, $CDCl_3$) δ 6.65 (t, *J* = 2.2 Hz, 1H), 6.44 (dd, *J* = 3.8, 1.8 Hz, 1H), 6.11 (dd, *J* = 3.8, 2.6 Hz, 1H), 3.80 (s, 3H), 2.22 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 151.2, 128.5, 126.9, 112.5, 107.3, 37.9, 12.9.

ISOQUINOLINES:

General Procedure:

A 1.5 dram vial was charged with a stirbar, free oxime (1 equiv), $[RhCp^*Cl_2]_2$ or $[RhCp^tCl_2]_2$ (.00125 mol %), and K_2CO_3 (2 equiv). TFE was added followed by alkyne (1.1 equiv). The reaction was sealed, warmed to 45 °C, and stirred until the reaction was complete as determined by TLC. Once complete the reaction was allowed to cool to room temperature and transferred to a 25 ml round bottom flask with excess CH_2Cl_2. Residual solvent was removed and the residue was purified via silica gel column chromatography.

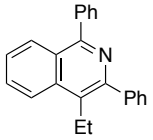


4-ethyl-1-methyl-3-phenylisoquinoline (5a): According to the general proceedure with the addition of 2 equiv. of $CF_3CO_3CH_2CF_3$, the desired

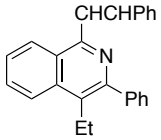
---

[8] Parthasarathy, K.; Cheng, C.–H. *J. Org. Chem.* **2009**, *74*, 9359.
[9] Cerniauskaite, D.; Gallienne, E.; Karciauskaite, H.; Farinha, A. S. F.; Rousseau, J.; Armand, S.; Tatibouet, A.; Sackus, A.; Rollin, P. *Tetrahedron Letters* **2009**, *50*, 3302.
[10] Cho, H.; Iwana, Y.; Sugimoto, K.; Mori, S.; Tokuyama, H. *J. Org. Chem.* **2010**, *75*, 627.
[11] Bosiak, M. J.; Krzeminski, M. P.; Jaisankar, P.; Zaidlewicz, M. *Tetrahedron Asymmetry* **2008**, *19*, 956.
[12] LaMattina, J. L.; Suleske, R. T. *Org. Synth.* **1986**, *64*, 19.

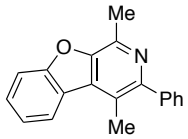
pyridine was isolated as an off white solid (94%, >10:1 rr). Cheng and coworkers previously prepared this compound.[13] Included is the ^{1}H NMR.



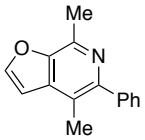
4-ethyl-1,3-diphenylisoquinoline (5b): According to the general proceedure, the desired pyridine was isolated as a yellow solid (86%, >15:1 rr). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 8.19-8.15 (m, 2H), 7.78-7.72 (m, 3H), 7.62 (dt, *J* = 8.1, 1.6 Hz, 2H), 7.58-7.46 (m, 6H), 7.45-7.40 (m, 1H), 3.13 (q, *J* = 7.5 Hz, 2H), 1.37 (t, *J* = 7.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.2, 151.1, 141.8, 139.9, 136.0, 130.29, 130.17, 130.07, 129.88, 129.4, 128.50, 128.41, 128.32, 128.26, 128.20, 128.15, 128.07, 127.4, 126.2, 125.9, 123.9, 21.9, 15.7 ; IR (thin film) cm^{-1}; HRMS (ESI) *m/e* calcd 309.1517 (M+) ; found 309.1522.



4-ethyl-3-phenyl-1-styrylisoquinoline (5c): According to the general proceedure, the desired pyridine was isolated as a yellow solid (87%, >10:1 rr). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 8.45 (d, *J* = 8.3 Hz, 1H), 8.12 (d, *J* = 8.4 Hz, 1H), 8.02 (d, *J* = 15.6 Hz, 1H), 7.95 (d, *J* = 15.6 Hz, 1H), 7.75 (ddd, *J* = 9.4, 6.0, 1.5 Hz, 1H), 7.69-7.61 (m, 5H), 7.54-7.37 (m, 5H), 7.34-7.29 (m, 2H), 3.08 (q, *J* = 7.5 Hz, 2H), 1.31 (dd, *J* = 9.6, 5.4 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.0, 151.3, 142.0, 137.2, 135.9, 135.6, 129.67, 129.55, 129.46, 129.38, 128.61, 128.42, 128.23, 128.01, 127.96, 127.45, 127.39, 127.32, 126.3, 125.9, 125.1, 124.2, 123.2, 21.9, 15.7. HRMS (ESI) *m/e* calcd 335.1674 (M+) ; found 335.1681.

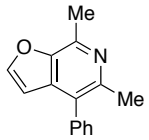


1,4-dimethyl-3-phenylbenzofuro[2,3-*c*]pyridine (5d): According to the general proceedure, the desired pyridine was isolated as a yellow solid (Cp* 2.1:1 92% / Cp^t 1:9.2 90%). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 7.59-7.51 (m, 4H), 7.49-7.44 (m, 1H), 7.40 (dt, *J* = 6.2, 1.7 Hz, 2H), 7.08 (td, *J* = 7.6, 0.9 Hz, 1H), 6.95 (ddd, *J* = 7.9, 1.3, 0.6 Hz, 1H), 2.86 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.8, 151.9, 149.5, 148.4, 140.9, 139.9, 137.4, 129.7, 129.35, 129.25, 128.99, 128.96, 128.94, 128.88, 128.81, 128.64, 128.32, 128.14, 127.9, 127.5, 123.8, 123.5, 123.17, 123.10, 123.02, 122.86, 122.70, 112.3, 112.0, 22.1, 18.6, 16.7. HRMS (ESI) *m/e* calcd 274.1226 (M+H) ; found 274.1228.

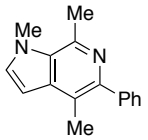


4,7-dimethyl-5-phenylfuro[2,3-*c*]pyridine (5e): According to the general proceedure, the desired pyridine was isolated as a yellow solid (88%, 2.7:1 rr). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 7.73 (d, *J* = 2.2 Hz, 1H), 7.52 (dd, *J* = 8.2, 1.3 Hz, 2H), 7.44 (dd, *J* = 8.2, 6.7 Hz, 2H), 7.38-7.36 (m, 1H), 6.82 (d, *J* = 2.2 Hz, 1H), 2.77 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 149.7, 147.5, 147.22, 147.09, 140.9, 140.5, 139.6, 134.4, 129.53, 129.49, 128.4, 128.1, 127.37, 127.28, 127.0, 121.1, 105.9, 105.5, 22.2, 18.48, 18.45, 16.2. HRMS (ESI) *m/e* calcd 224.107 (M+H) ; found 224.1067.

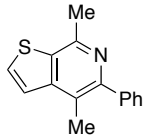
[13] Parthasarathy, K.; Jeganmohan, M.; Cheng, C–H. *Org. Lett.* **2008**, *10*, 325.



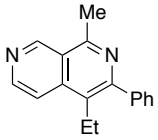
5,7-dimethyl-4-phenylfuro[2,3-*c*]pyridine (5e'): According to the general proceedure, the desired pyridine was isolated as a yellow solid (90%, 2.4:1 rr). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 7.64 (d, *J* = 2.1 Hz, 1H), 7.52-7.43 (m, 2H), 7.42-7.35 (m, 3H), 6.52 (d, *J* = 2.1 Hz, 1H), 2.77 (s, 3H), 2.52 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.8, 149.7, 149.2, 147.5, 147.21, 147.09, 140.9, 140.5, 139.6, 137.7, 134.4, 133.9, 129.61, 129.52, 129.49, 129.40, 128.52, 128.43, 128.1, 127.36, 127.27, 126.9, 121.0, 105.9, 105.5, 22.2, 18.5, 16.2. HRMS (ESI) *m/e* calcd 224.107 (M+H) ; found 224.1067.



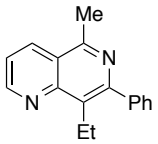
1,4,7-trimethyl-5-phenyl-1*H*-pyrrolo[2,3-*c*]pyridine (5f): According to the general proceedure, the desired pyridine was isolated as a yellow solid (Cp* 98% 4:1 / Cp^t 96% 1:2.1). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 7.48-7.42 (m, 2H), 7.41-7.35 (m, 3H), 7.01 (d, *J* = 3.0 Hz, 1H), 6.12 (d, *J* = 3.0 Hz, 1H), 4.06 (s, 3H), 2.98 (s, 3H), 2.48 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 142.3, 140.5, 138.7, 135.2, 133.6, 133.2, 131.0, 129.8, 128.2, 127.9, 126.90, 126.78, 126.1, 99.8, 99.5, 36.76, 36.74, 22.6, 21.7, 15.6. HRMS (ESI) *m/e* calcd 237.1386 (M+H) ; found 237.1381.



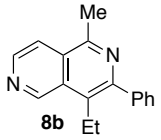
4,7-dimethyl-5-phenylthieno[2,3-*c*]pyridine (5g): According to the general proceedure, the desired pyridine was isolated as a yellow solid (Cp* 10:1 93% / Cp^t 1:2.5 95%). R_f = (2:1 Hexanes/EtOAc); ^{1}H (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 5.4 Hz, 1H), 7.46-7.44 (m, 2H), 7.38-7.36 (m, 4H), 7.31-7.29 (m, 1H), 2.74 (s, 3H), 2.45 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.1, 149.6, 145.9, 140.8, 134.0, 130.9, 129.69, 129.63, 128.5, 128.1, 127.4, 122.8, 122.1, 23.3, 16.6. HRMS (ESI) *m/e* calcd 240.0846 (M+H) ; found 240.0841.



6-ethyl-3-methyl-5-phenyl-1,4-naphthyridine (5h): According to the general procedure, the desired pyridine was isolated as an off white solid (73%, 10:1); R_f = .3 (19:1 Hexanes/EtOAc w/ 1% Et_3N); ^{1}H (400 MHz, $CDCl_3$) δ 9.61 (d, *J* = 1.0 Hz, 1H), 8.77 (d, *J* = 5.0 Hz, 1H), 7.83 (d, *J* = 5.8 Hz, 1H), 7.51-7.41 (m, 5H), 3.05 (s, 3H), 2.96 (q, *J* = 7.5 Hz, 2H), 1.24 (t, *J* = 7.5 Hz, 3H).; ^{13}C NMR (100 MHz, $CDCl_3$) δ ^{13}C NMR (126 MHz, $cdcl_3$) δ 157.06, 154.47, 151.61, 146.79, 140.88, 138.62, 128.98, 128.95, 128.34, 127.99, 127.66, 121.84, 116.77, 21.82, 21.81, 21.26, 15.56; IR (thin film) 1570, 1441, 1385, 720, 701 cm^{-1}; HRMS (ESI) *m/e* calcd (M+H) 249.1386; found 249.1392.



8-ethyl-5-methyl-7-phenyl-1,6-naphthyridine (5h'): ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.13 (dd, *J* = 4.2, 1.8 Hz, 1H), 8.46 (dd, *J* = 8.5, 1.8 Hz, 1H), 7.61 – 7.35 (m, 6H), 3.18 (q, *J* = 7.4 Hz, 2H), 2.97 (s, 3H), 1.27 (t, *J* = 7.4 Hz, 4H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 156.32, 154.21, 153.27, 150.04, 141.24, 134.11, 131.25, 129.12, 128.23, 127.70, 121.40, 121.37, 21.86, 20.97, 15.68.

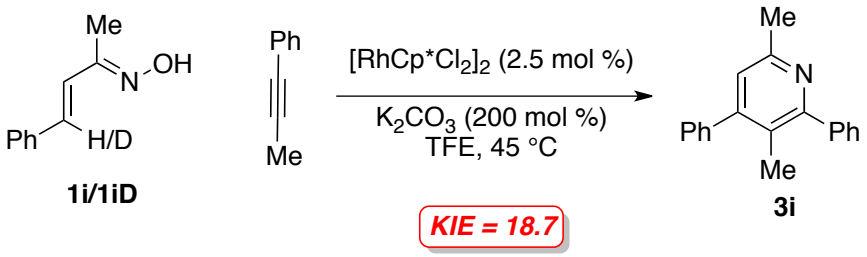


7-ethyl-4-methyl-6-phenyl-1,5-naphthyridine (5i): According to the general procedure, the desired pyridine was isolated as an off white solid (86%, 10:1); R_f = .3 (19:1 Hexanes/EtOAc w/ 1% Et_3N); ^1H (400 MHz, $CDCl_3$) δ 9.59 (s, 1H), 8.72 (d, 1H, *J*=6.0 Hz), 7.89 (dd, 1H, *J*=6.0 Hz, *J*=0.8 Hz), 7.52-7.42 (m, 5H), 3.10 (q, 2H, *J*=7.6 Hz), 2.96 (s, 3H), 1.32 (t, 3H. *J*=7.6 Hz); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 152.3, 149.8, 143.7, 140.7, 129.1, 128.2, 127.8, 117.9, 21.8, 20.9, 16.3.; IR (thin film) 2959, 1587, 1444, 1073, 777 cm^{-1}; HRMS (ESI) *m/e* calcd ($M+H_3$) 251.1543; found 251.1544.

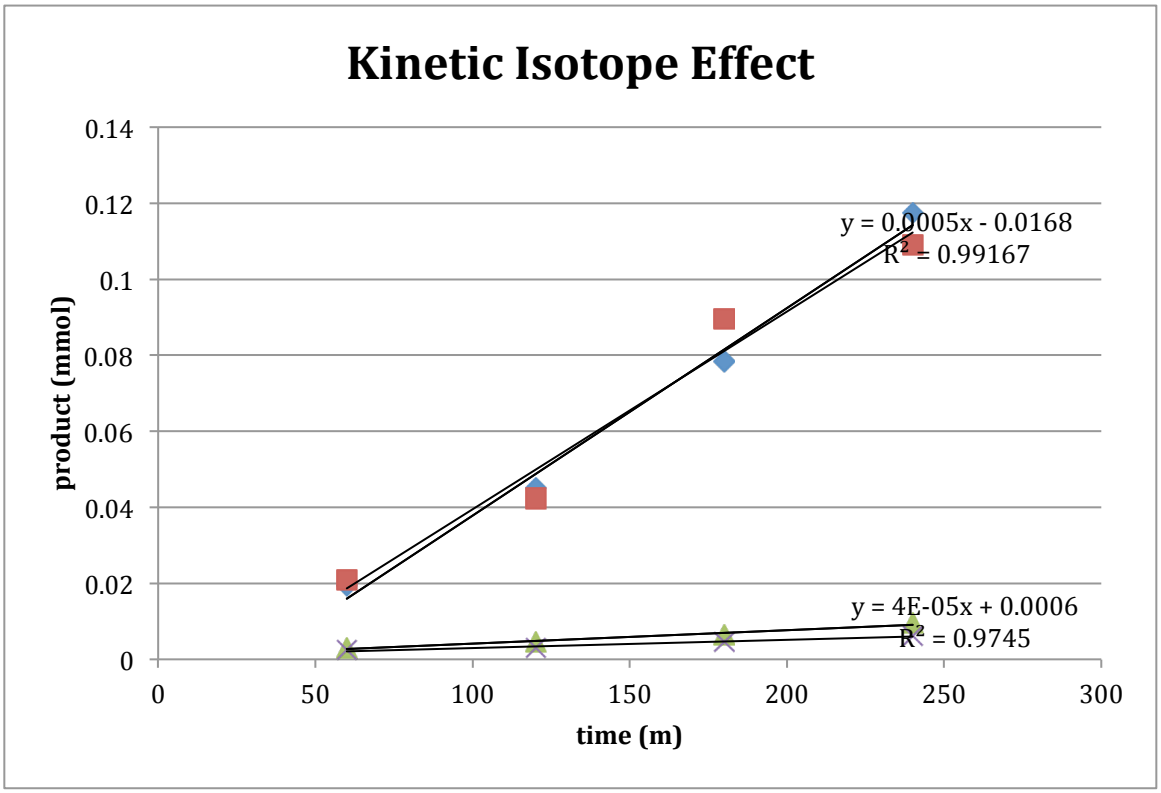
Internal Competition Experiment:

A one-dram vial with a stir bar was charged with amide (0.22 mmol, 1 equiv), $Cu(OAc)_2 \bullet H_2O$ (0.46 mmol, 210 mol %), and $[Cp^*RhCl_2]_2$ (0.0055 mmol, 2.5 mol) and 1.5 ml of *t*-amyl alcohol followed by the alkyne (0.275, 1.25 equiv). The vial was sealed and placed into a 110 °C heating block for 16 h. The reaction was allowed to cool and poured into a separatory funnel with excess dichloromethane and extracted twice with 10% NH_4OH in saturated NH_4Cl. The organic portion was extracted once with brine, dried over magnesium sulfate, and concentrated. The residue was dissolved in 1 ml of dichloromethane and loaded onto a column of silica gel and eluted with a suitable solution of ethyl acetate and hexanes (typically 1:4). Evaporation of solvent afforded the product.

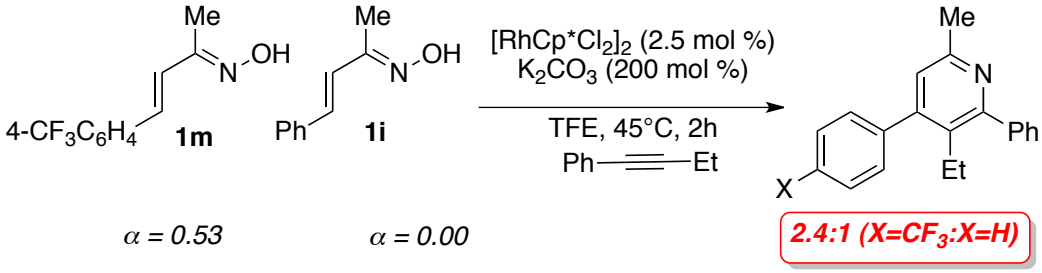
KIE Experiments:



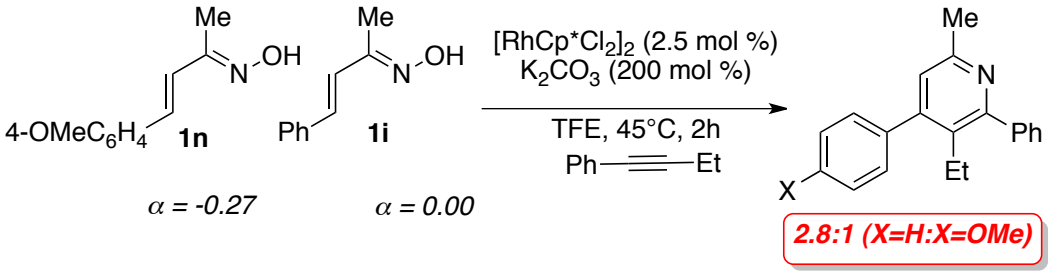
A 1.5 dram vial was charged with a stir-bar, (3E)-4-phenylbut-3-en-2-one oxime or D-(3E)-4-phenylbut-3-en-2-one oxime (.22 mmol), K_2CO_3 (.44 mmol), and 1,3,5 trimethoxy-benzene (.22 mmol). The vial was fitted with a septa and charged with 2,2,2-triflouroethanol (2.2 ml). 1-phenyl-1-butyne (.22 mmol) was added to the reaction solution and the vial was placed into an 45 °C heating block and stirred for 5 min. A separate vial was charged with $[RhCp^*Cl_2]_2$ (2.5 mol %) and .25 ml of 2,2,2-triflourorethanol to yield a bright yellow solution. This solution was added to the reaction vessel in the heating block. 0.1 ml aliquots were taken every 60 seconds for 4 minutes (after 60, 120, 180, 240 seconds), diluted with ethyl acetate and were interpreted using GC/MS. Aliquots were collected ever 4 min for D-(3E)-4-phenylbut-3-en-2-one oxime



Competition Experiments

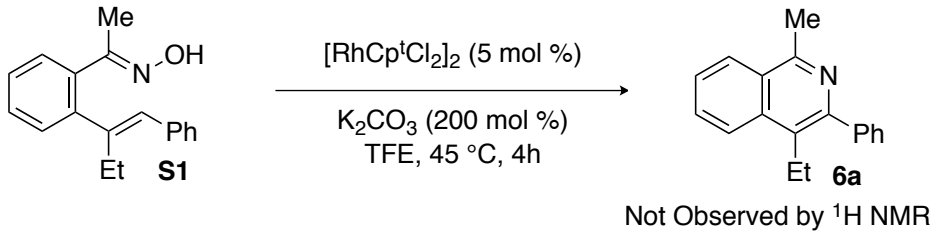


A 1.5 dram vial is charged with **1m** (.3 mmol), **1i** (.3 mmol), K_2CO_3 (200 mol %), 1,3,5 trimethoxybenzene (.3 mmol), and TFE (3 ml). 1-phenyl-1-butyne was added to this solution and the flask was sealed and placed into 45 °C aluminium heating block. After 2 hours the reaction was allowed to cool, and the reaction was interpreted by GC/MS.

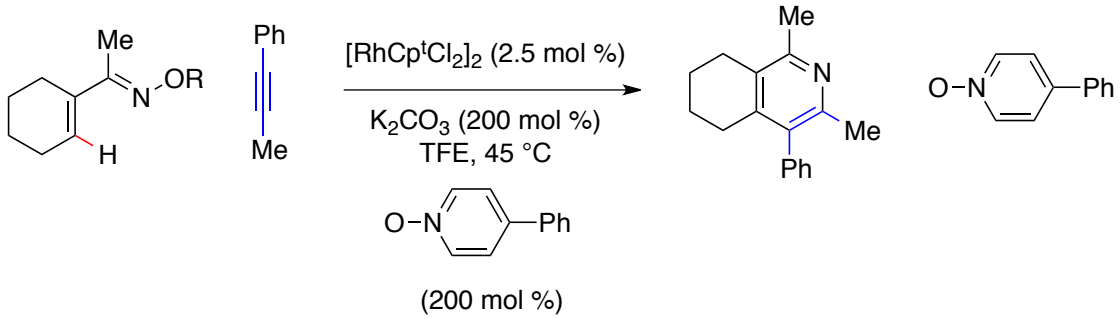


A 1.5 dram vial is charged with **1n** (.3 mmol), **1i** (.3 mmol), K_2CO_3 (200 mol %), 1,3,5 trimethoxybenzene (.3 mmol), and TFE (3 ml). 1-phenyl-1-butyne was added to this solution and the flask was sealed and placed into 45 °C aluminium heating block. After 2 hours the reaction was allowed to cool, and the reaction was interpreted by GC/MS.

Mechanistic Experiments

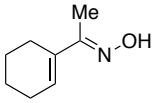


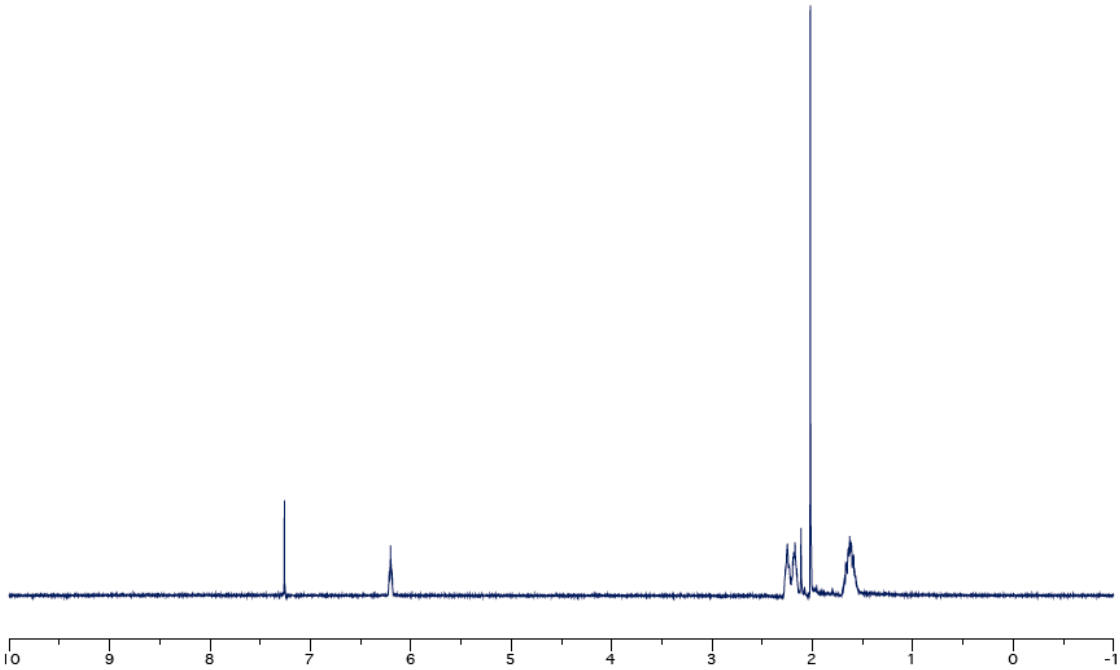
S1 was prepared as described by Cheng and coworkers,[13] and submitted to the standard reaction conditions, then concentrated *in vacuo*. None of the desired **6a** was observed.

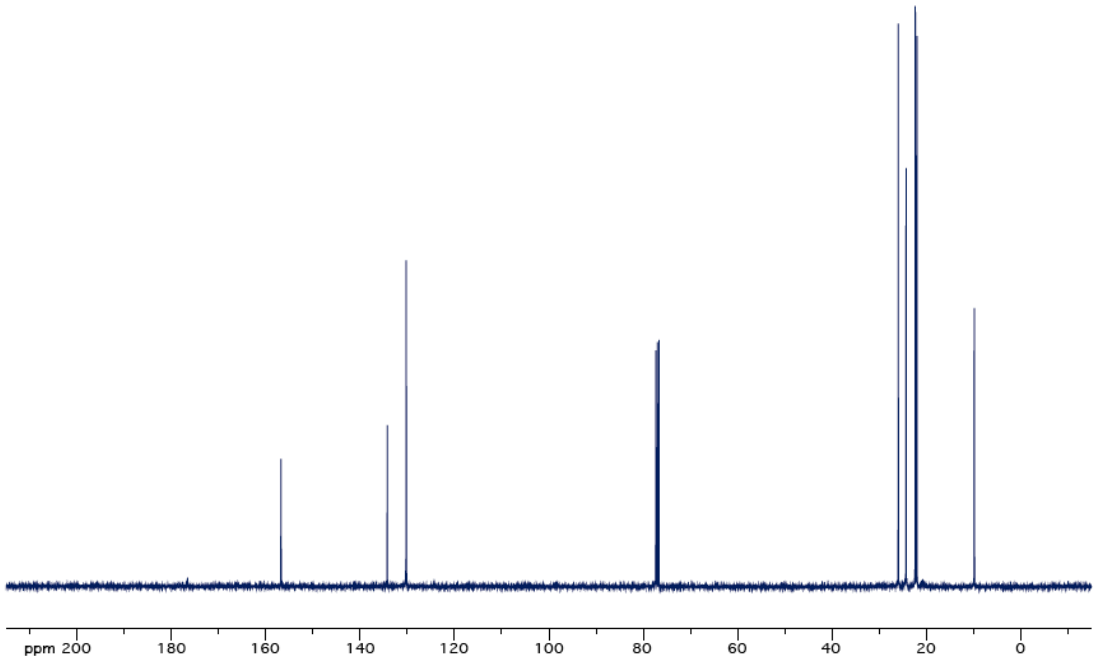


A 1.5 dram vial is charged with **1a** (.3 mmol), K_2CO_3 (200 mol %), 1,3,5 trimethoxybenzene (.3 mmol), and TFE (3 ml). 1-phenyl-1-butyne (100 mol %), and 4-phenyl pyridine *N-oxide* was added to this solution and the flask was sealed and placed into 45 °C aluminium heating block. After 4 hours the reaction was allowed to cool and was concentrated *in vacuo*. The crude NMR revealed product formation with no reduced pyridine *N-oxide.*

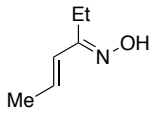
Oxime 1a

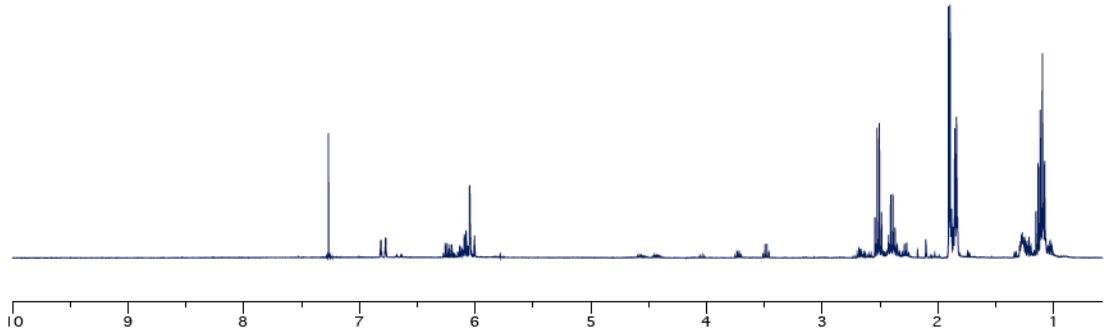


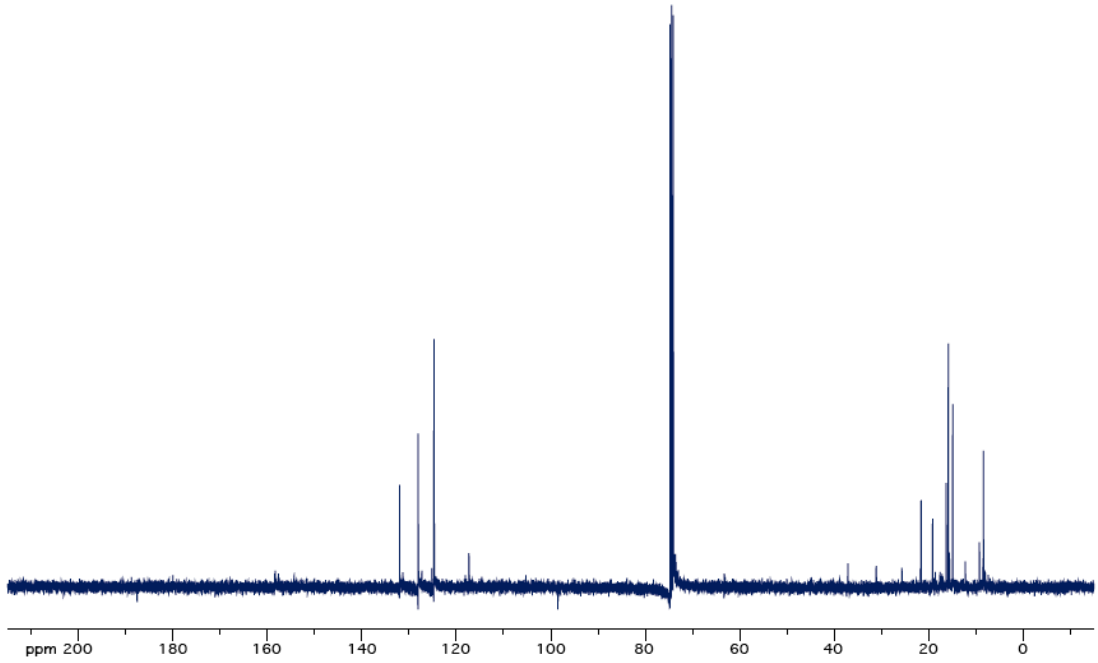




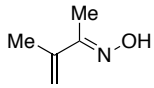
Oxime 1b

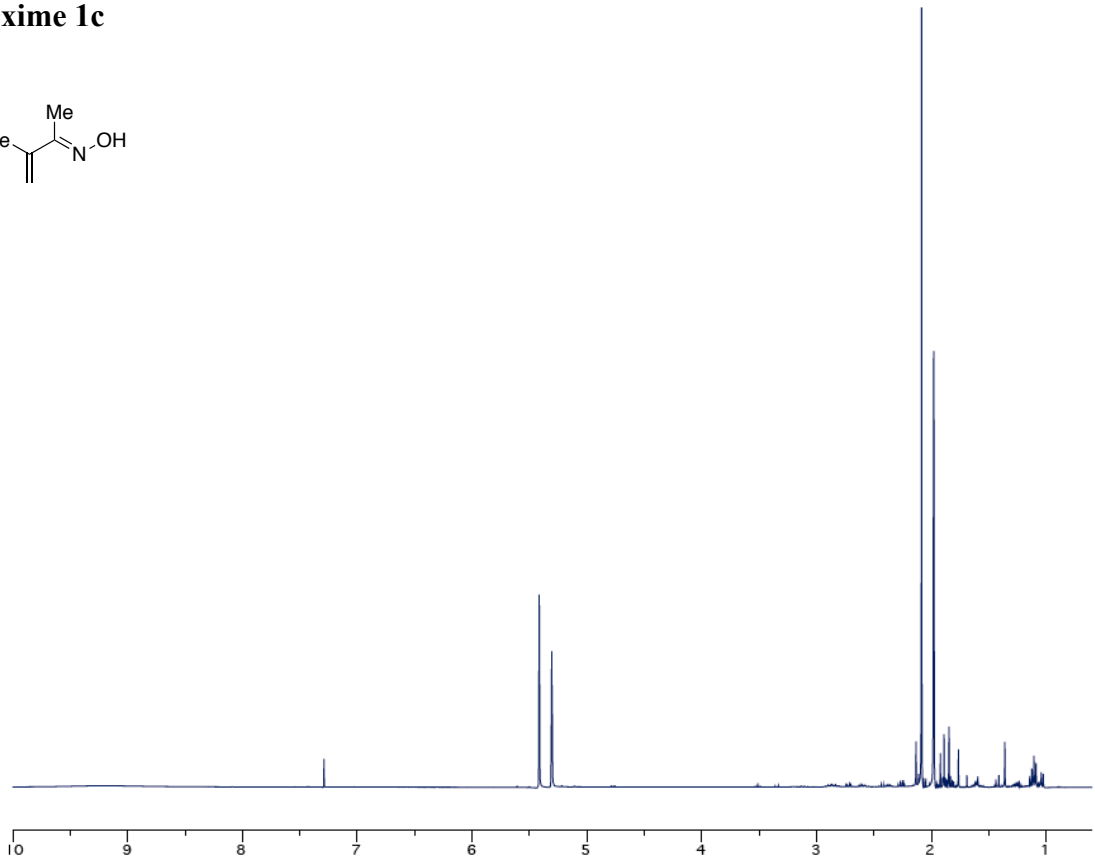


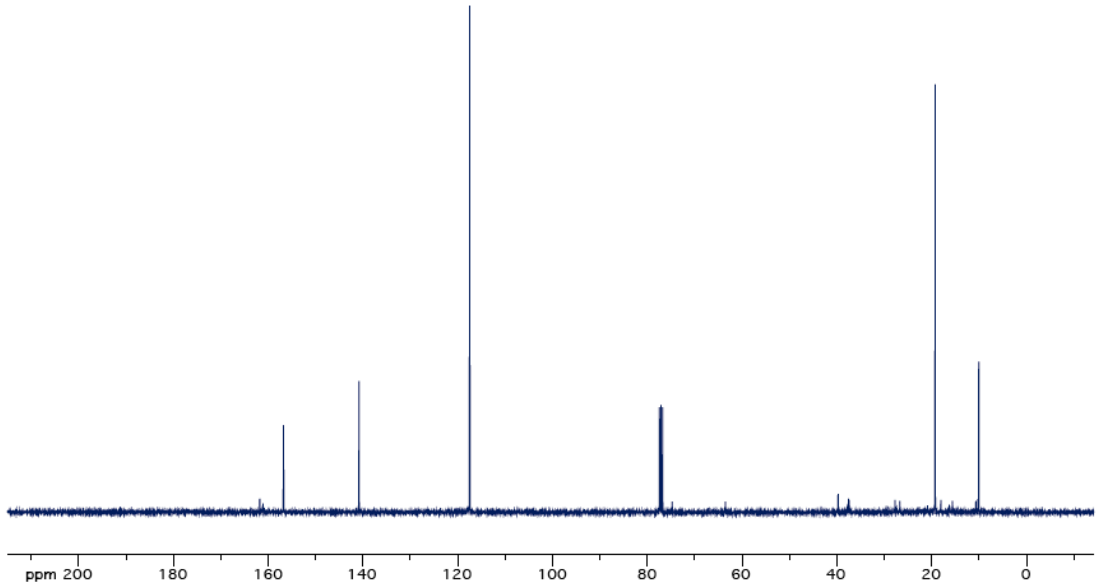




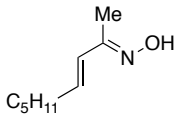
Oxime 1c

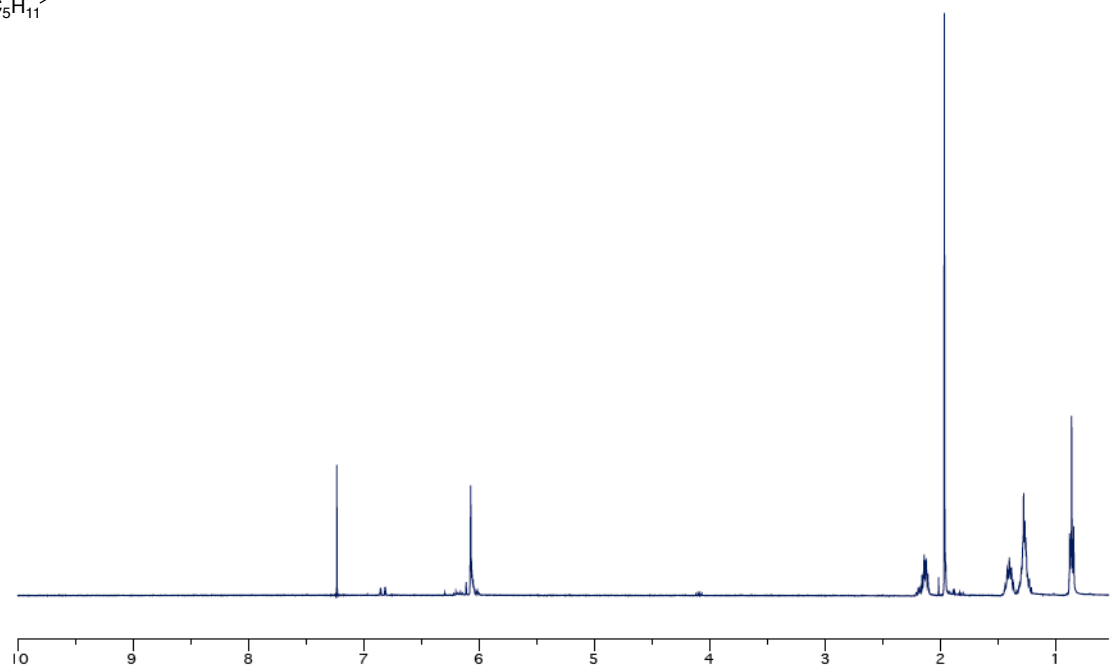


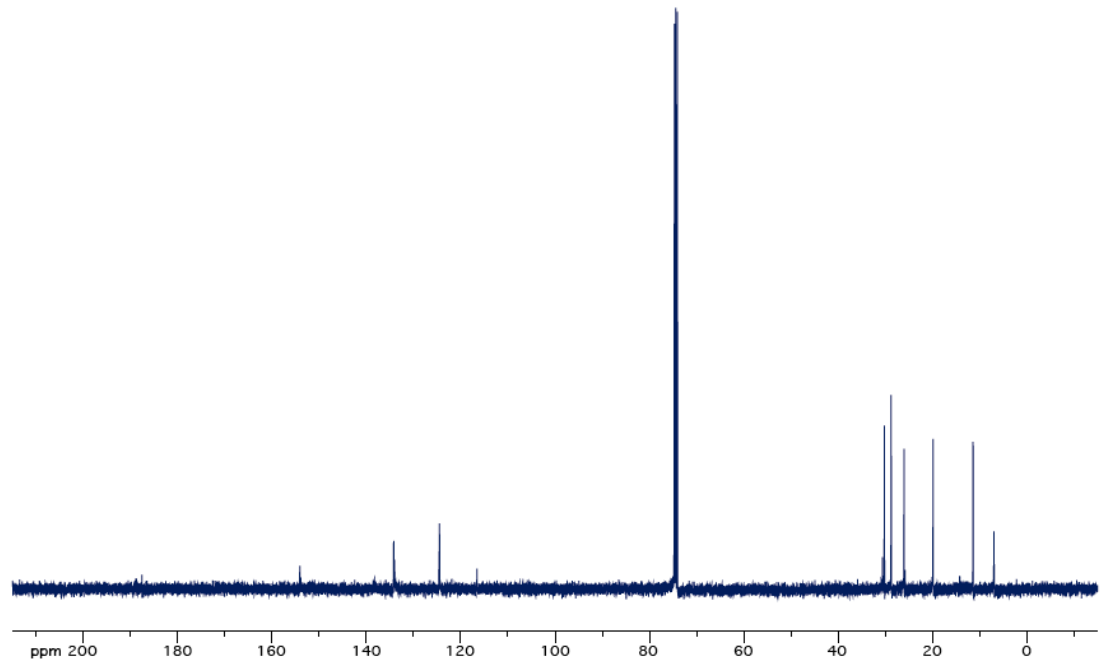




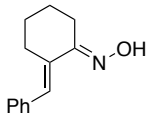
Oxime 1d

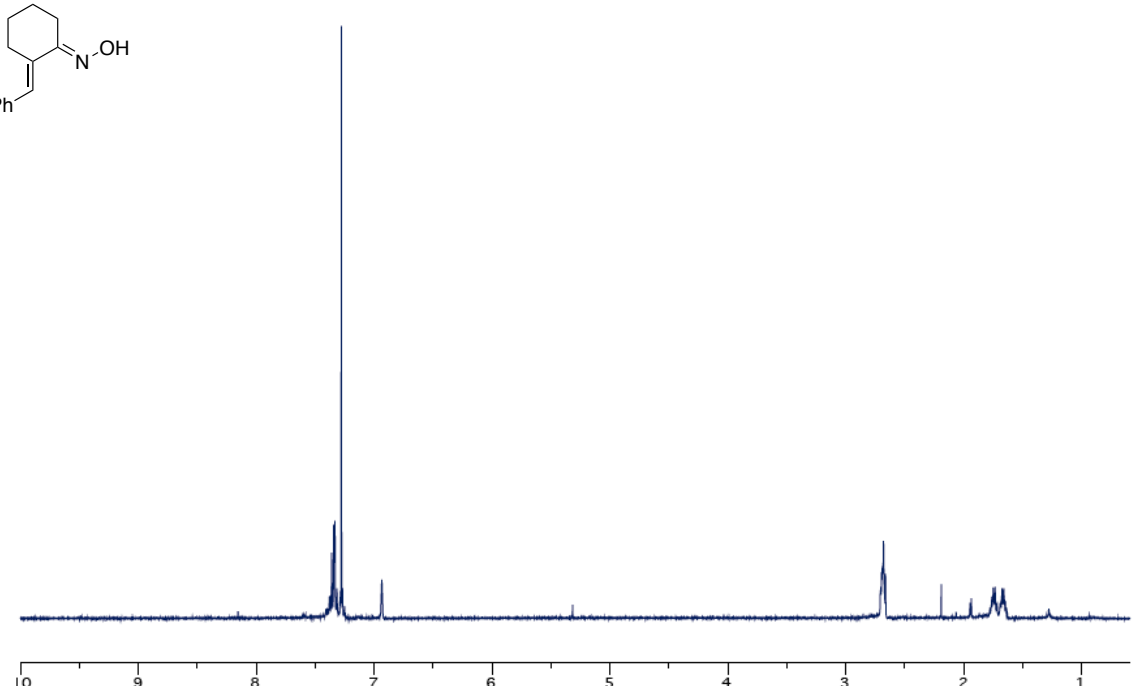

Me
N
OH
C5H11

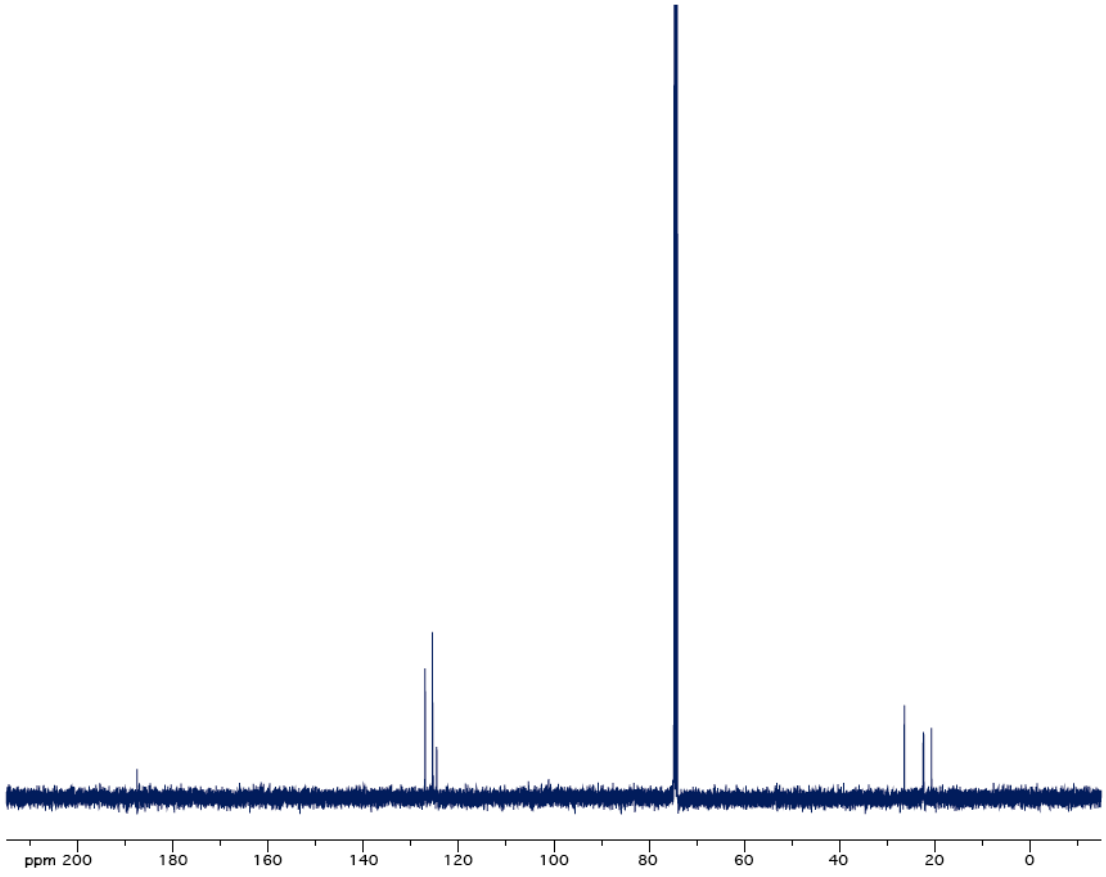

10
9
8
7
6
5
4
3
2
1


ppm 200
180
160
140
120
100
80
60
40
20
0

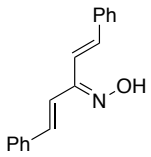
Oxime 1e

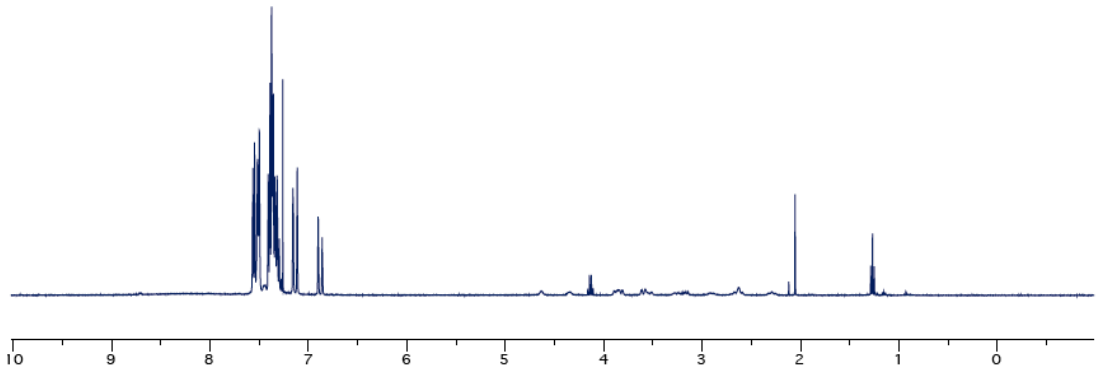


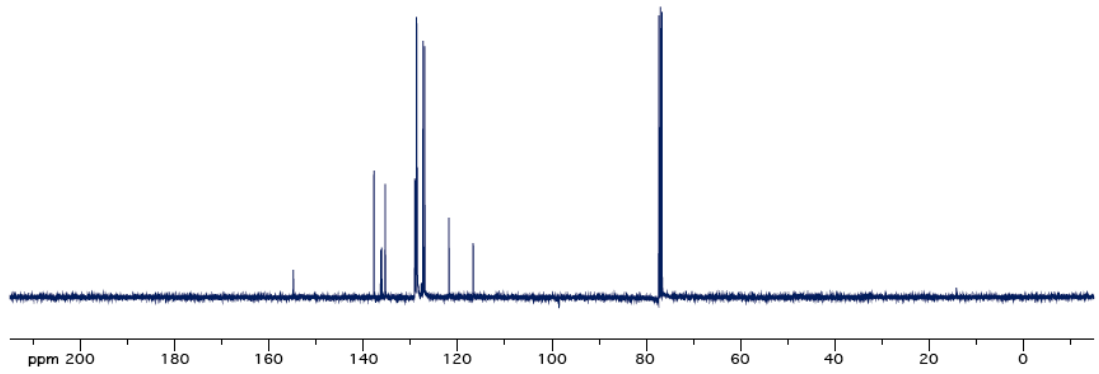




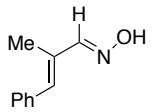
Oxime 1f

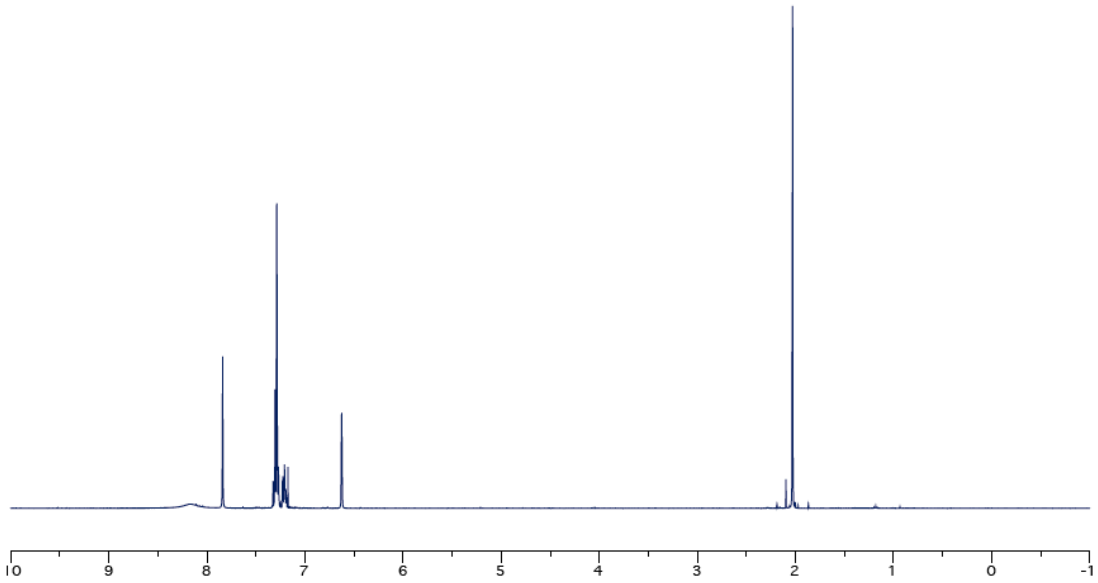


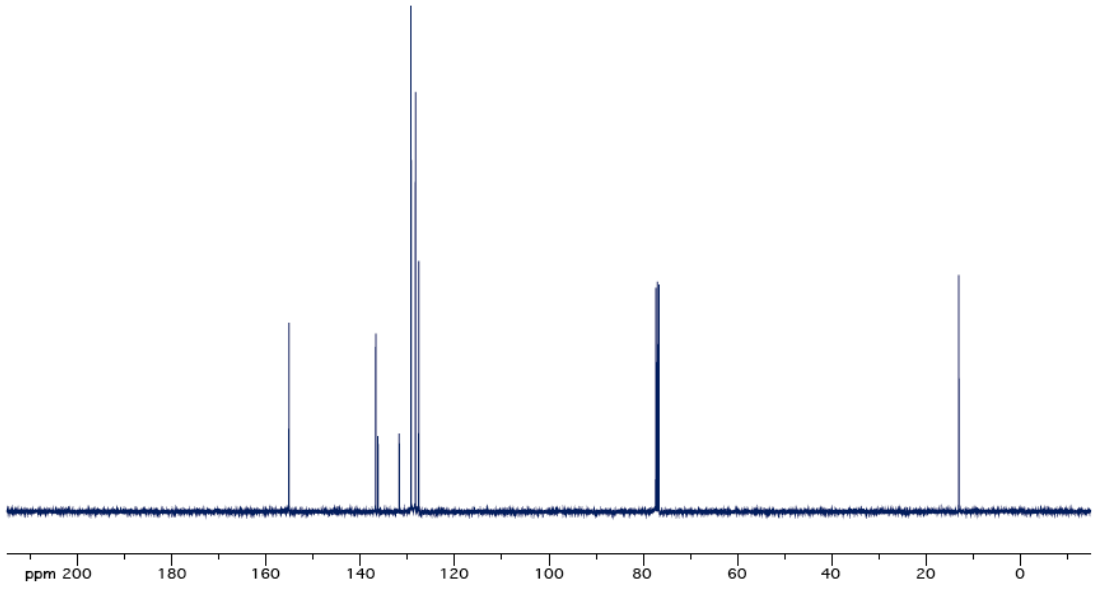




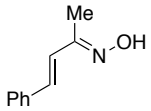
Oxime 1g

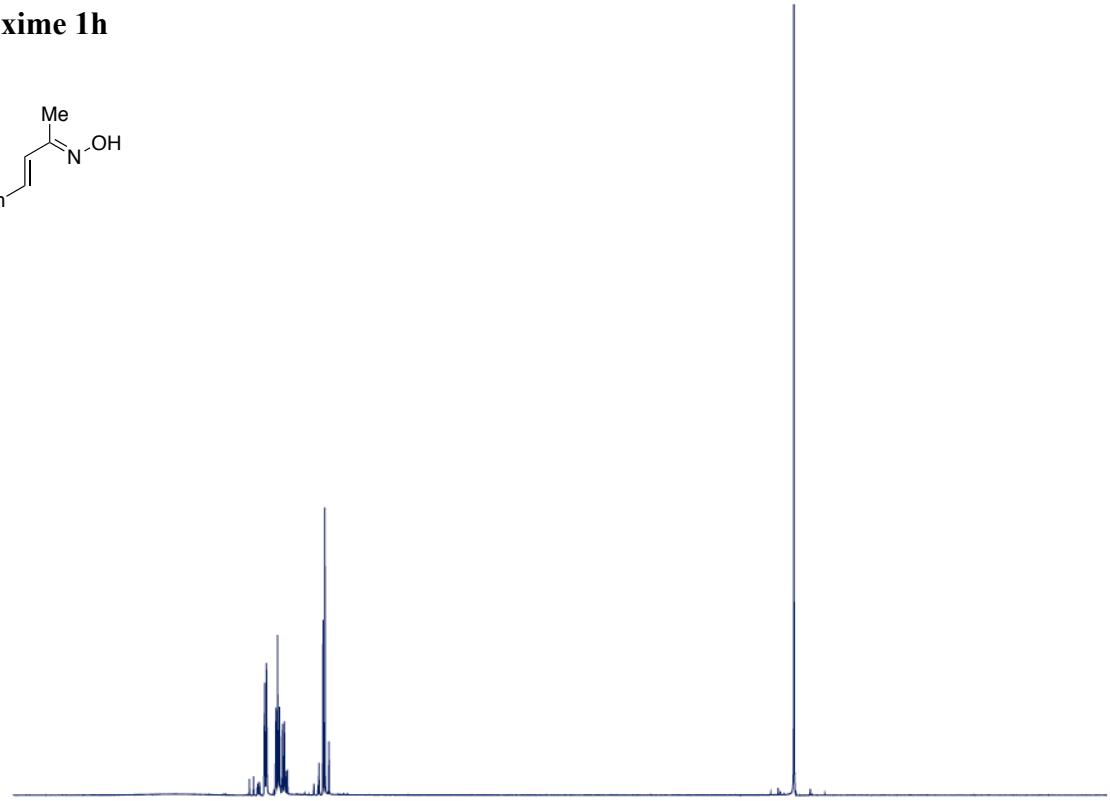

H
Me
N
OH
Ph

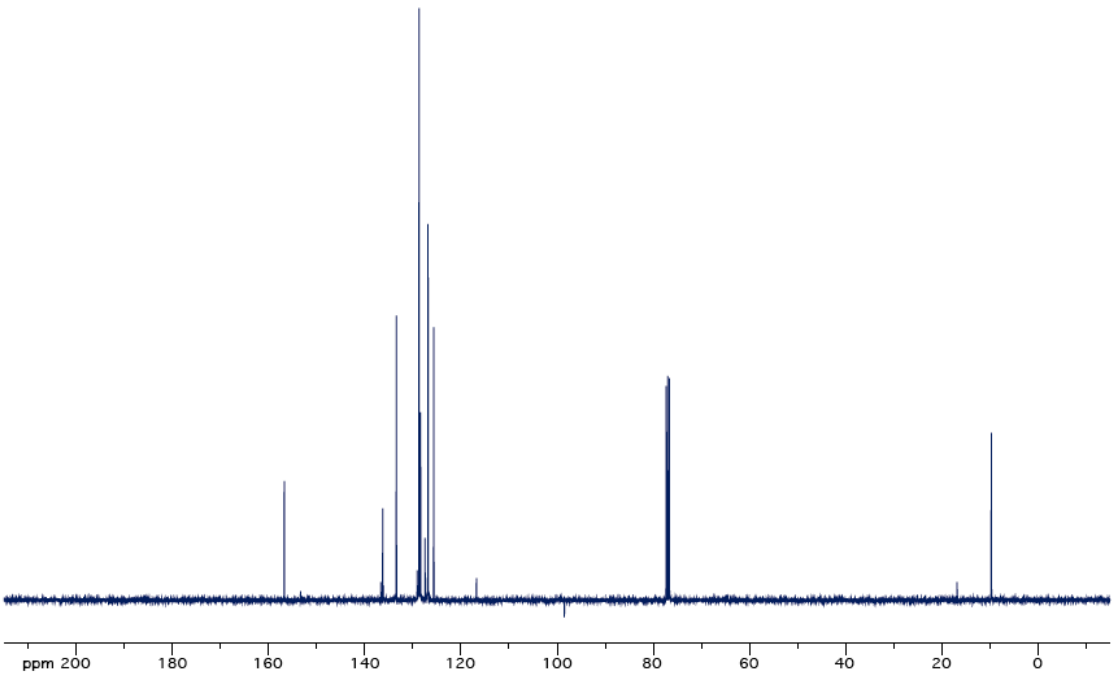

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

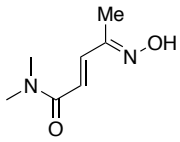
Oxime 1h

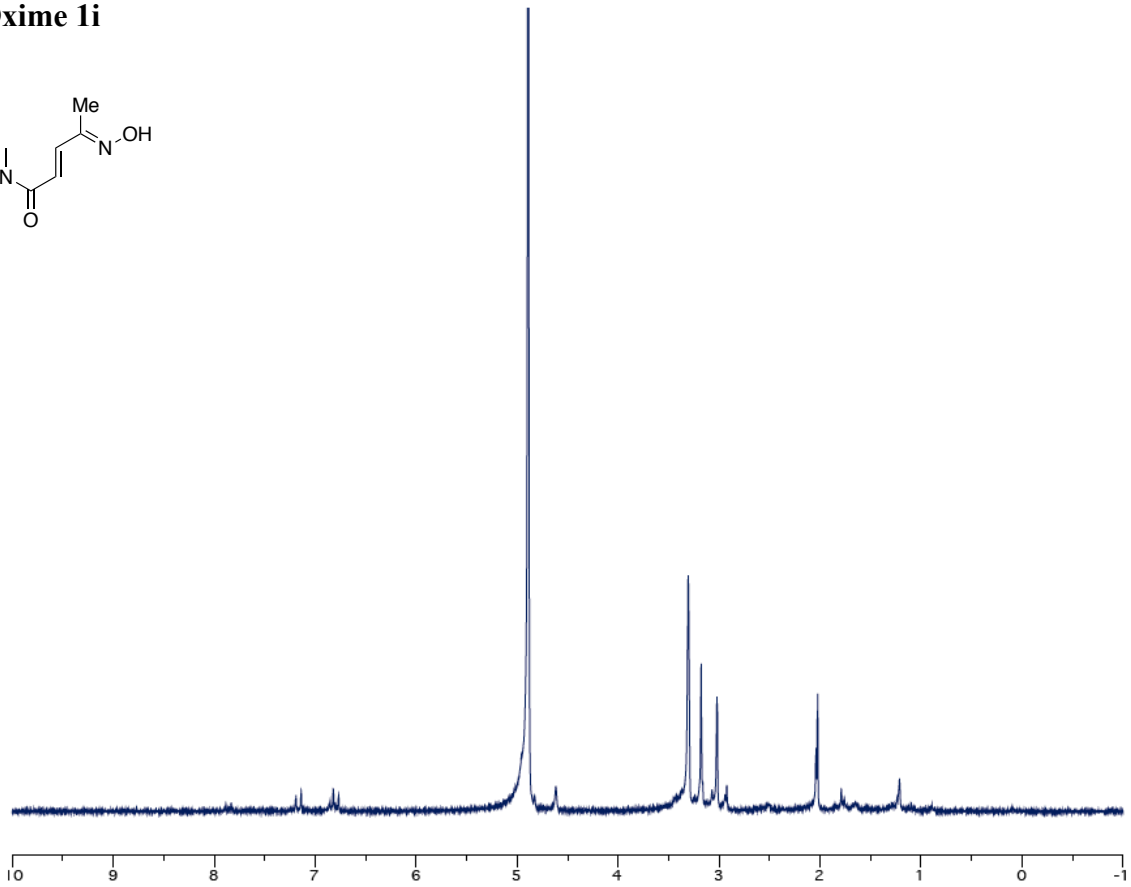




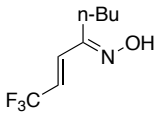


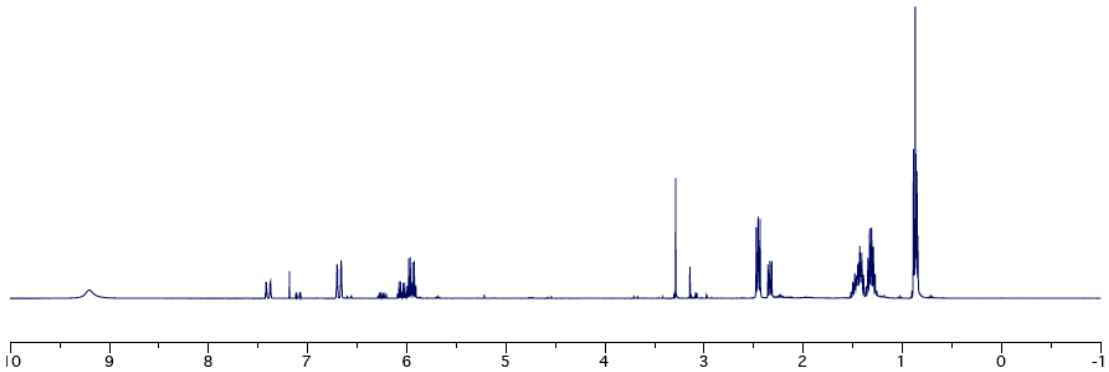
Oxime 1i

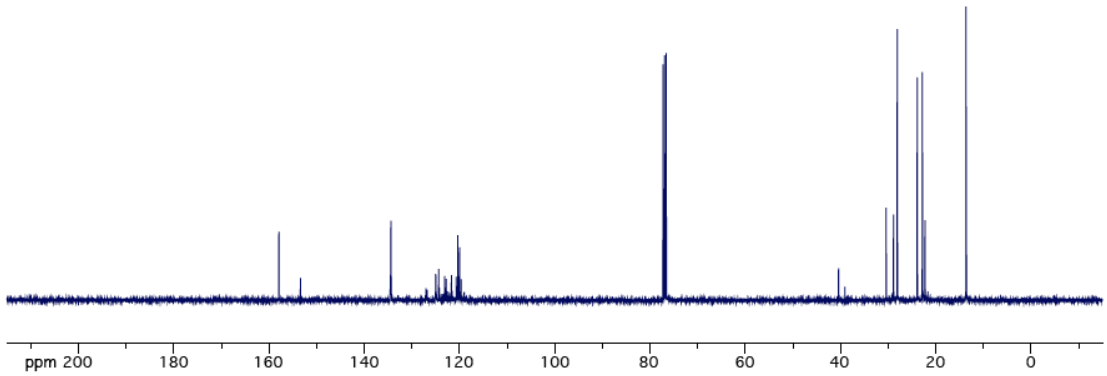




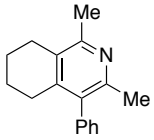
Oxime 1j

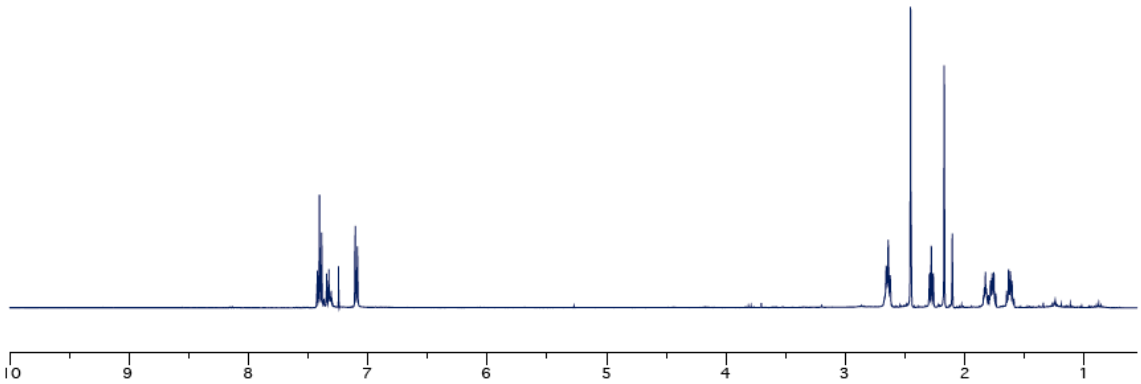

n-Bu
N
OH
F3C


10
9
8
7
6
5
4
3
2
1
0
-1

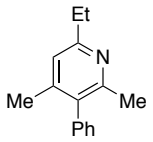

ppm 200
180
160
140
120
100
80
60
40
20
0

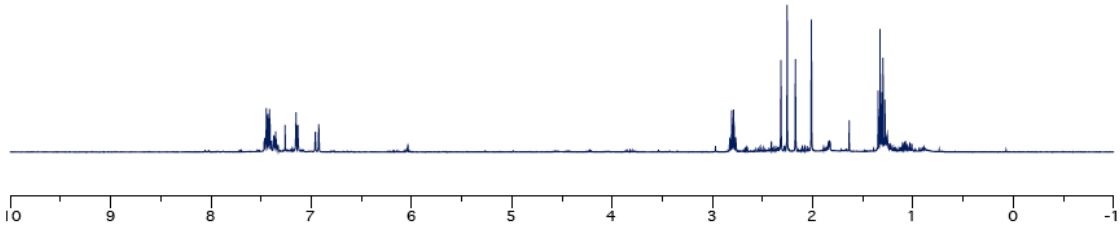
Pyridine 3a

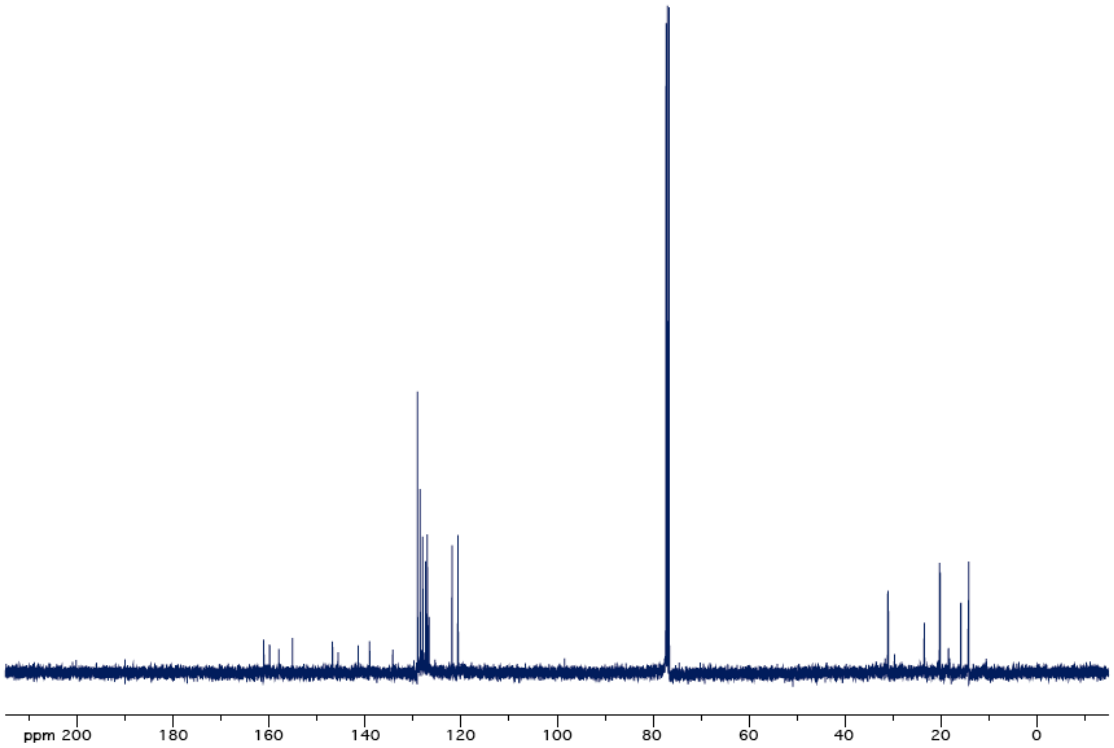




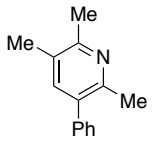
Pyridine 3b

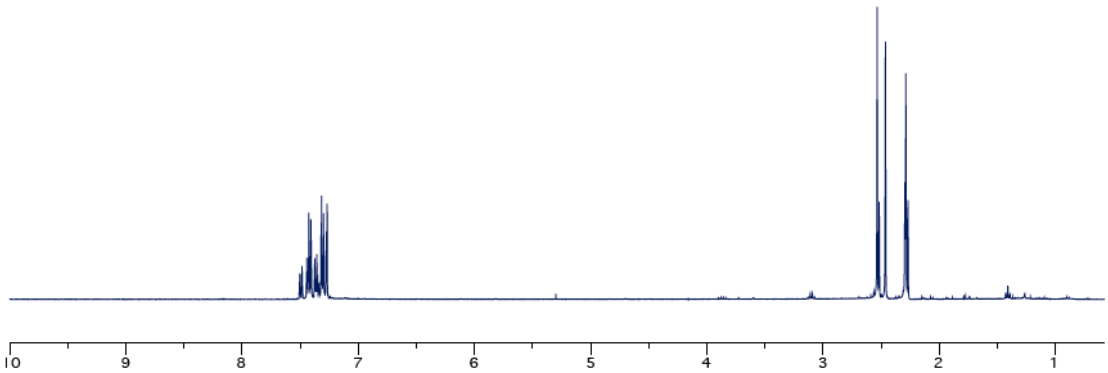

Et
N
Me
Me
Ph

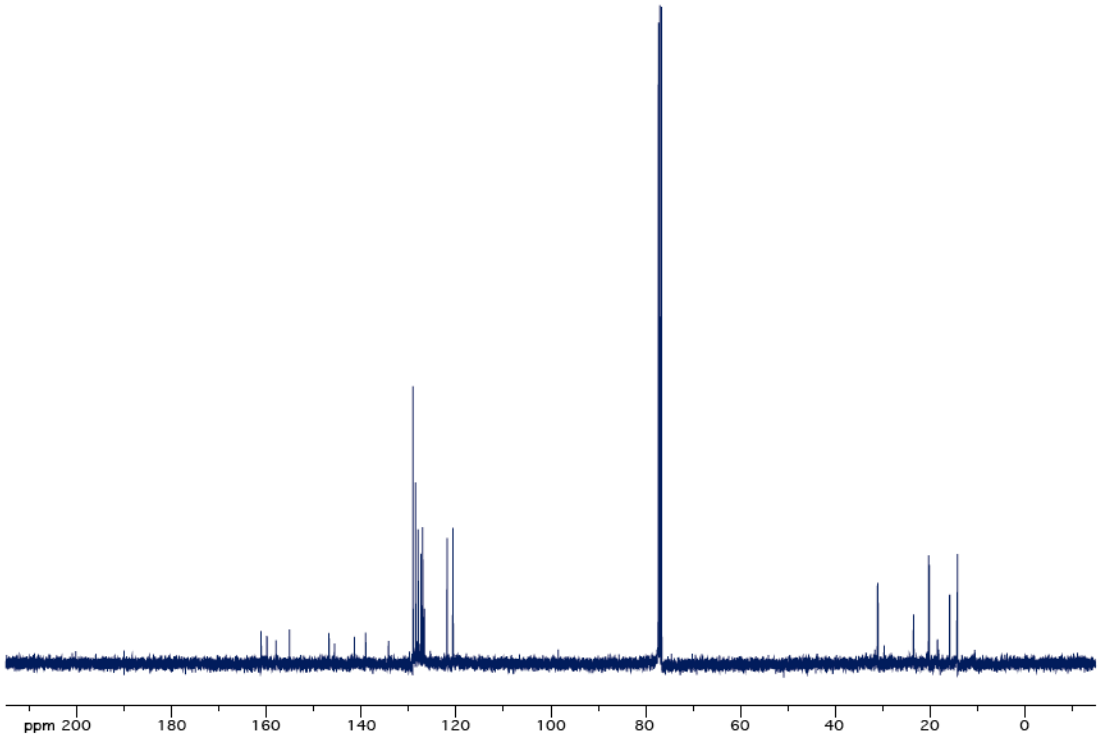

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

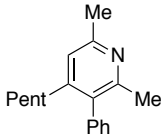
Pyridine 3c

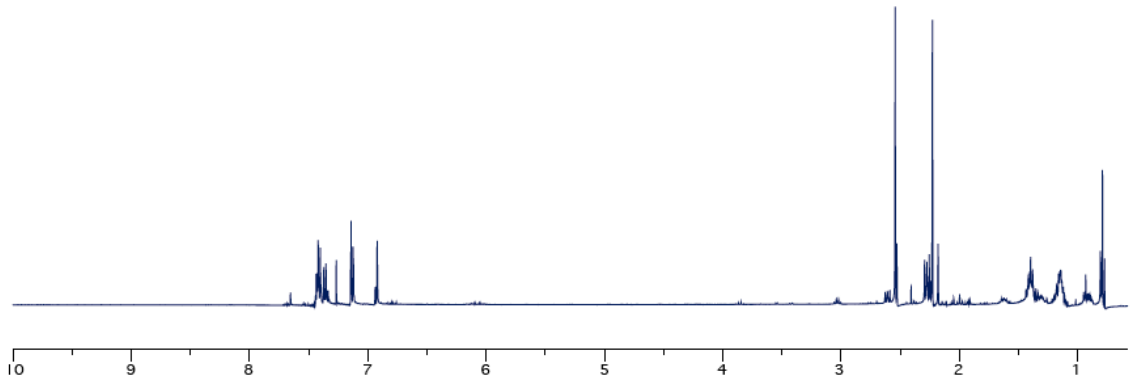

Me
Me
N
Me
Ph

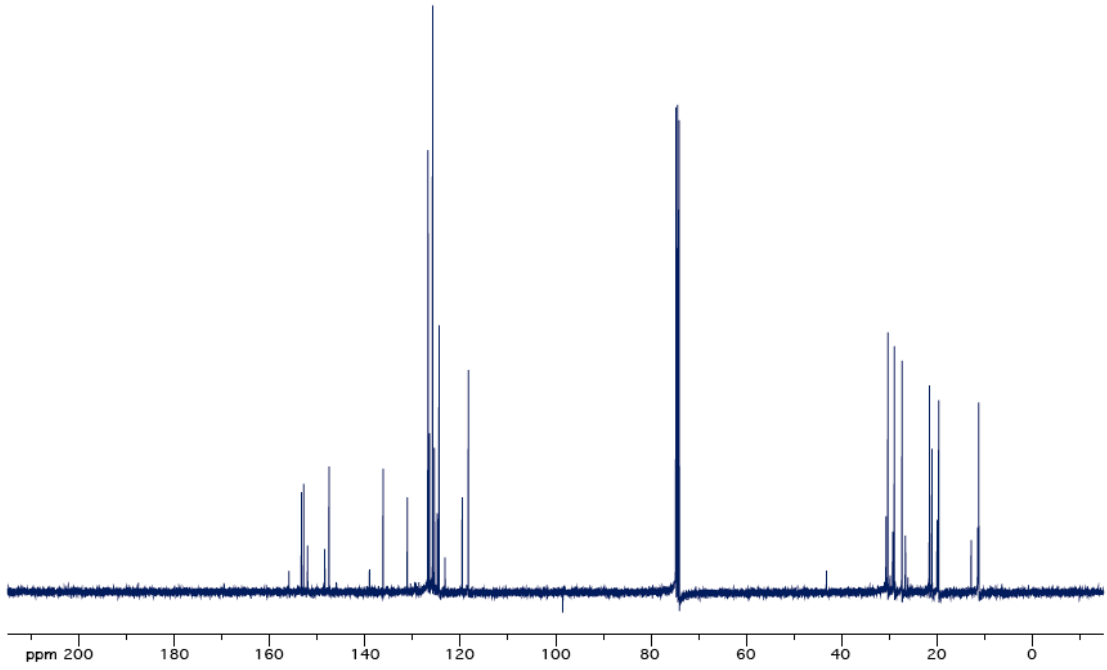

10
9
8
7
6
5
4
3
2
1


ppm 200
180
160
140
120
100
80
60
40
20
0

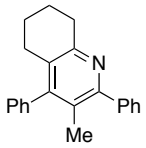
Pyridine 4d

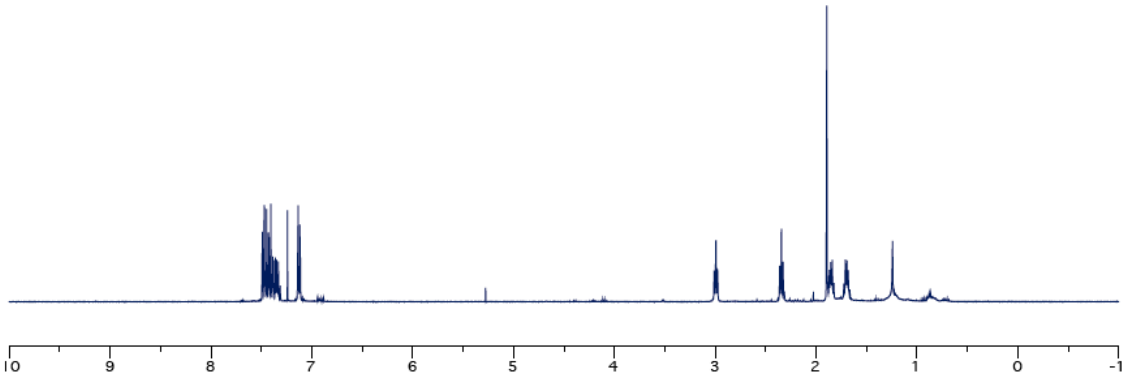

Me
N
Pent
Me
Ph


10
9
8
7
6
5
4
3
2
1

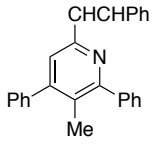

ppm 200
180
160
140
120
100
80
60
40
20
0

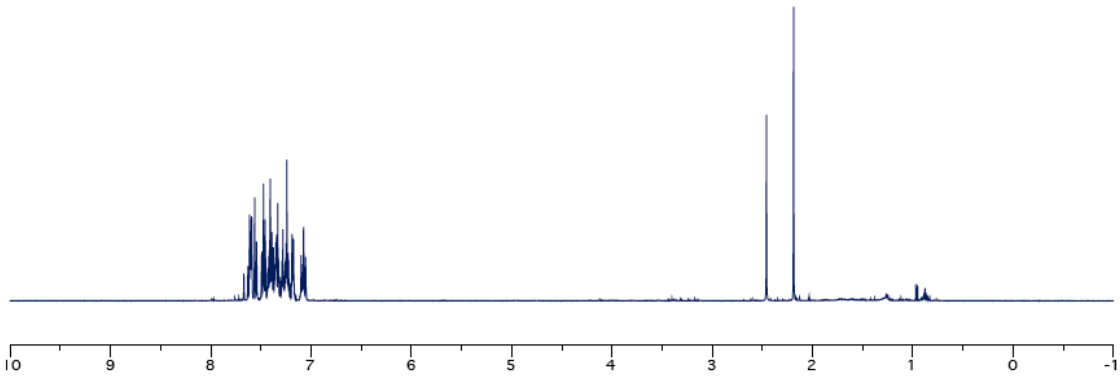
Pyridine 3e

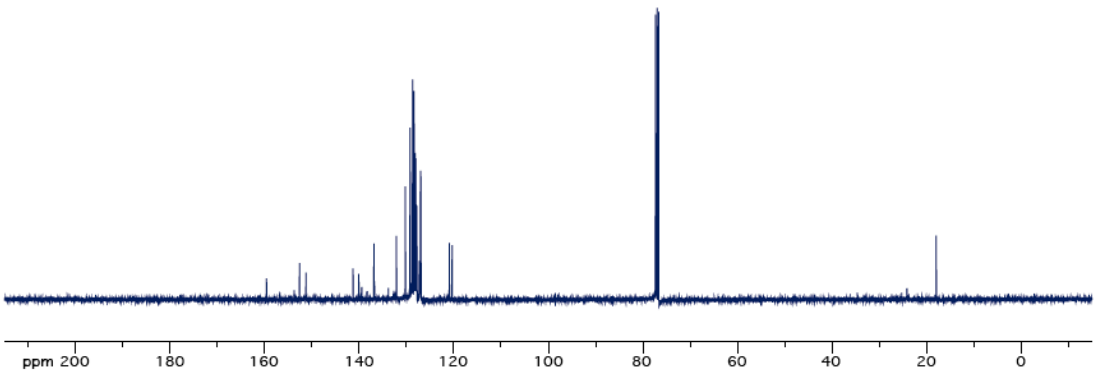




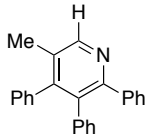
Pyridine 3f

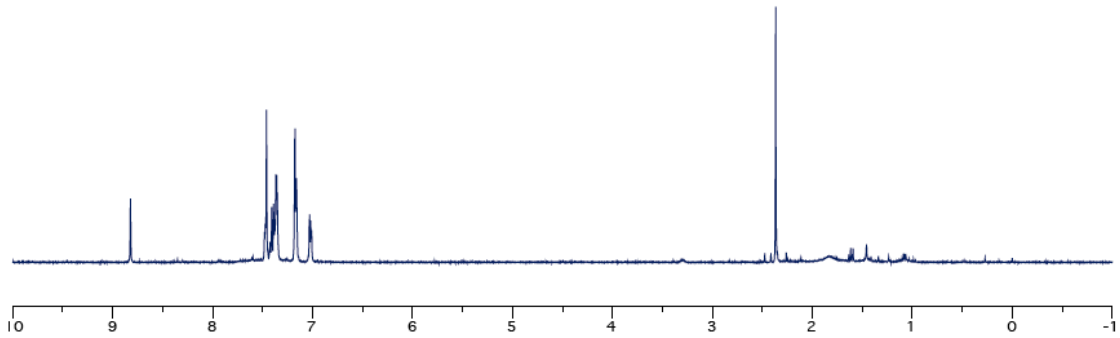

CHCHPh
N
Ph
Ph
Me

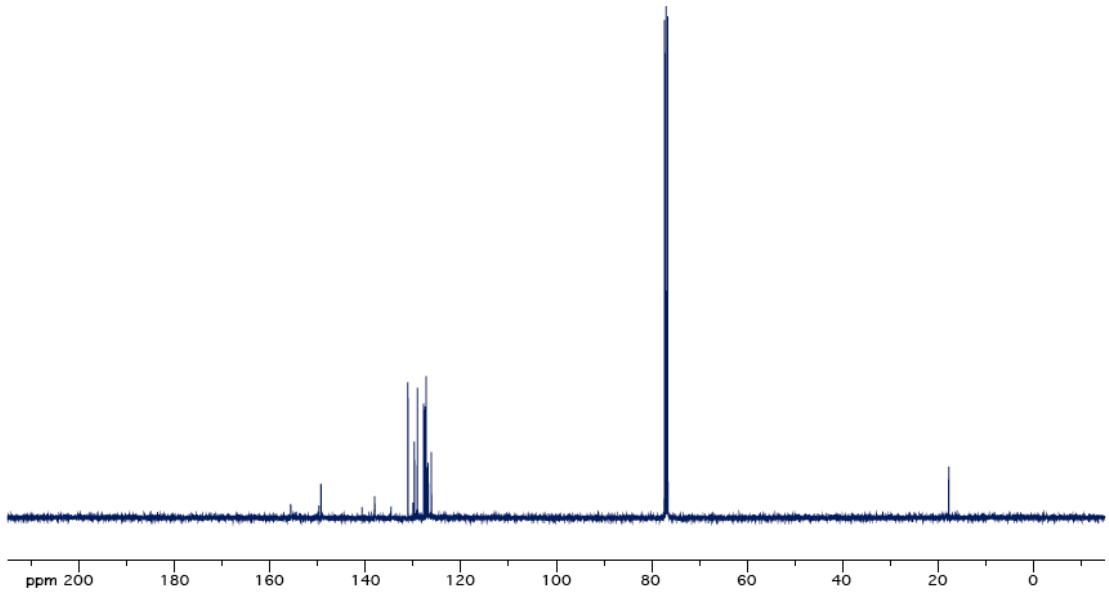

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

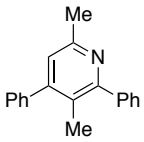
Pyridine 3g

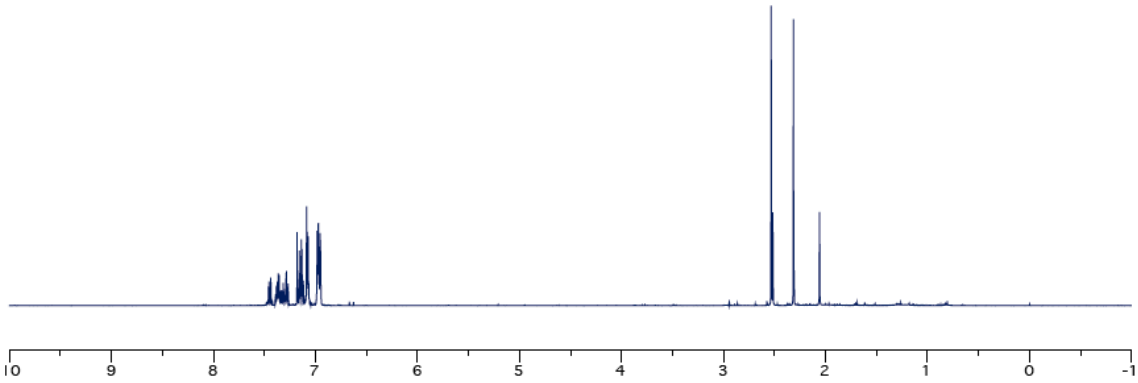

H
Me
N
Ph
Ph
Ph

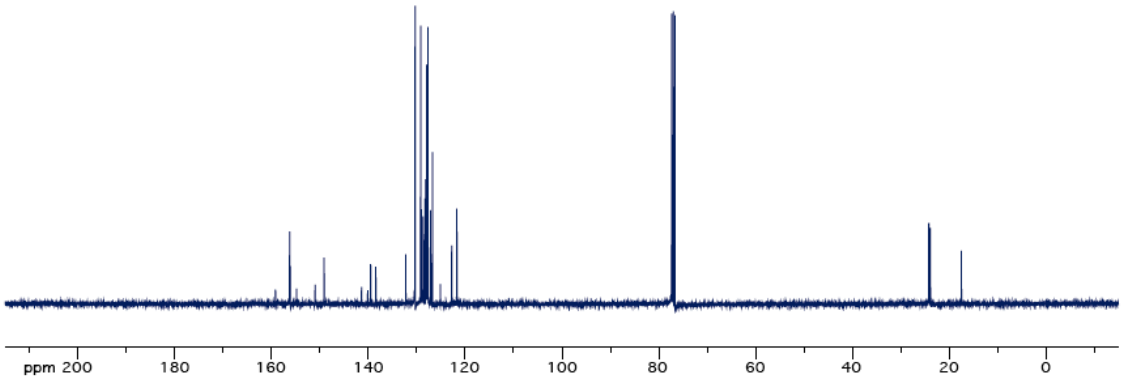

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

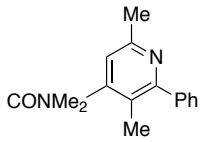
Pyridine 3h

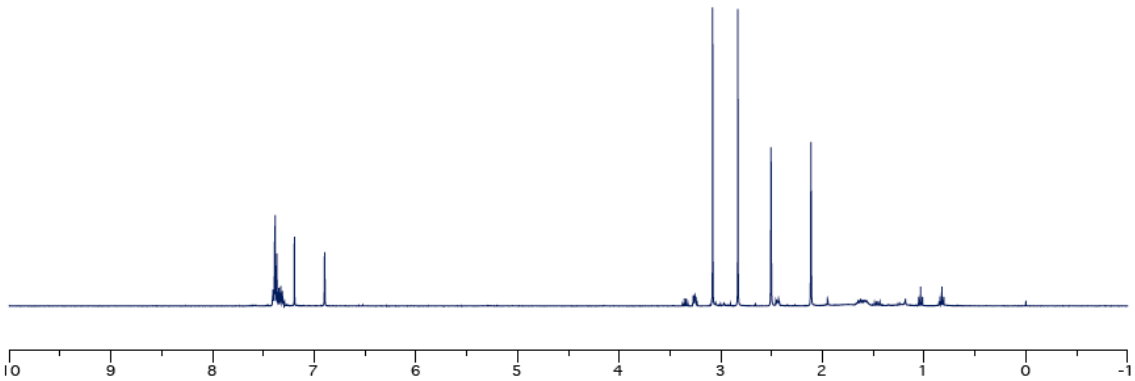

Me
N
Ph
Ph
Me

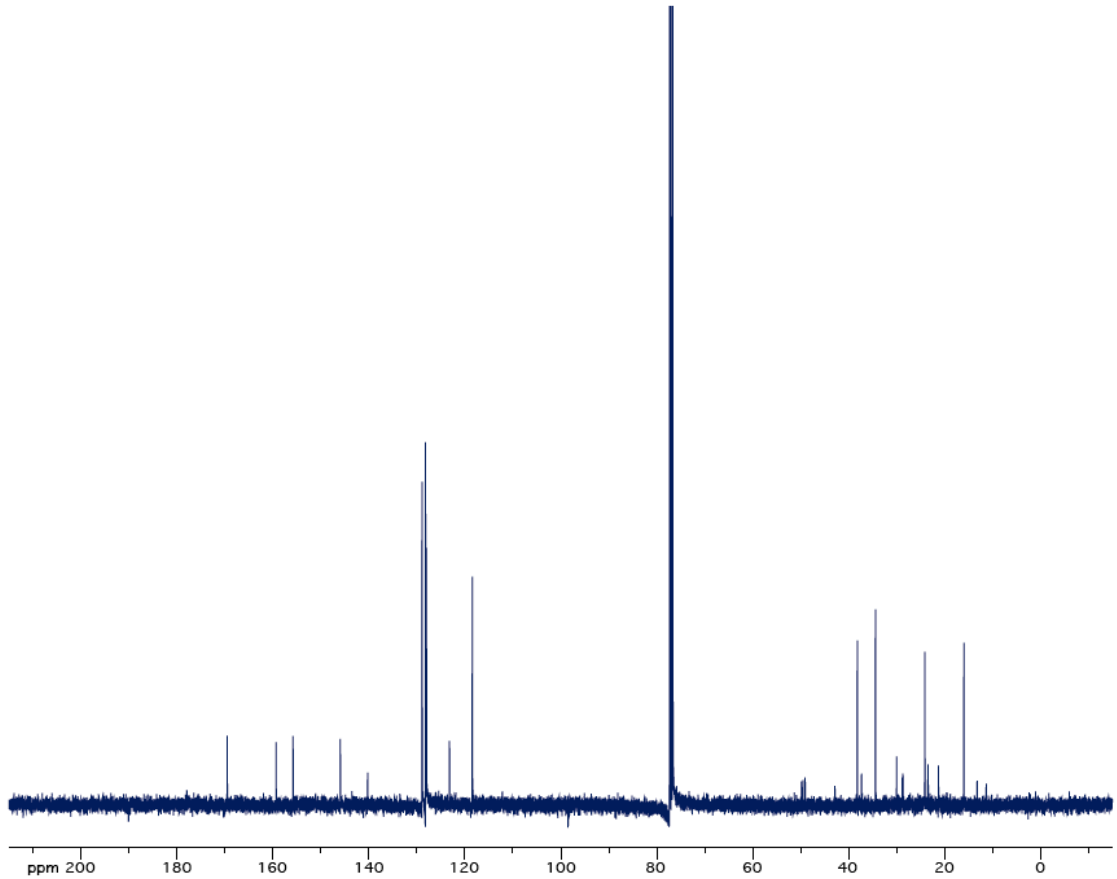

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

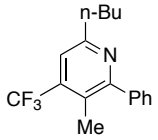
Pyridine 3i

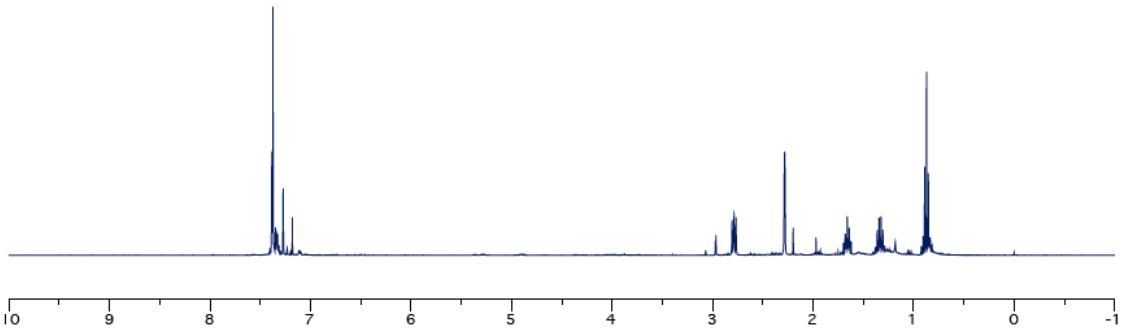

Me
N
CONMe2
Ph
Me

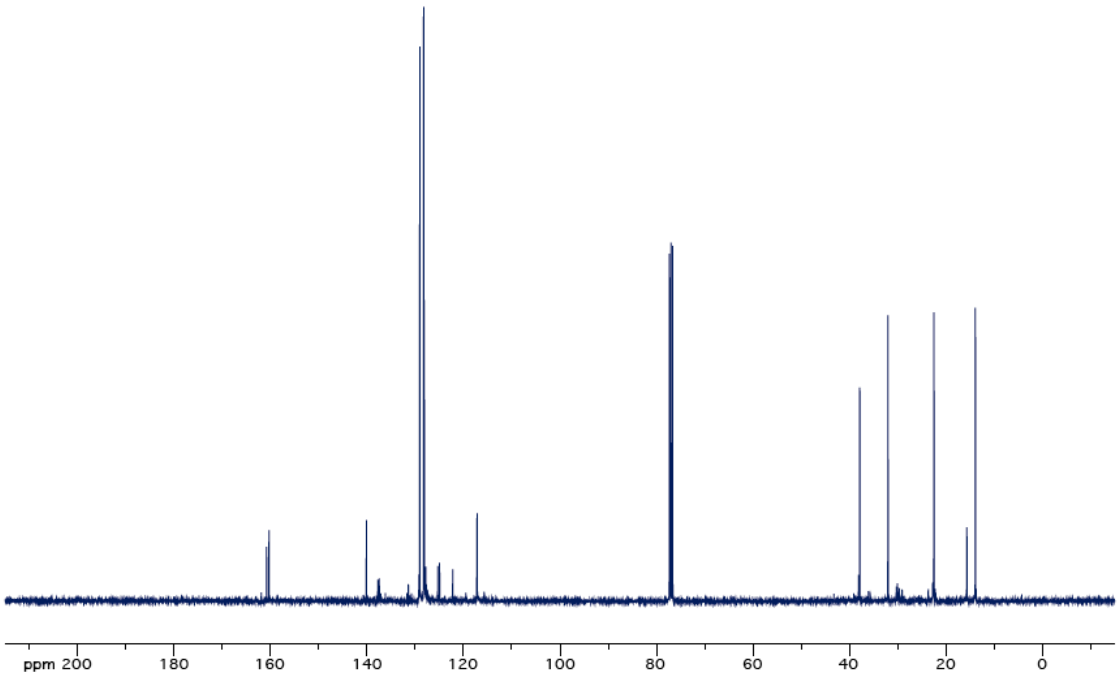

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

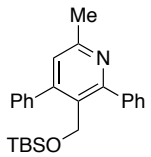
Pyridine 3j

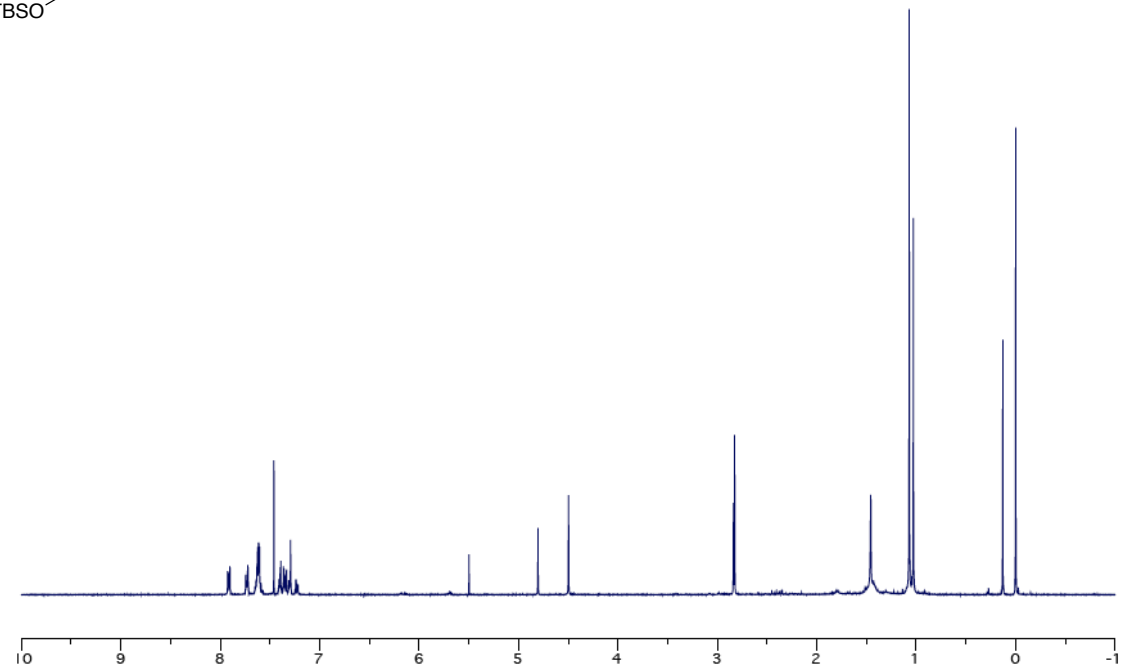

n-Bu
N
CF3
Ph
Me

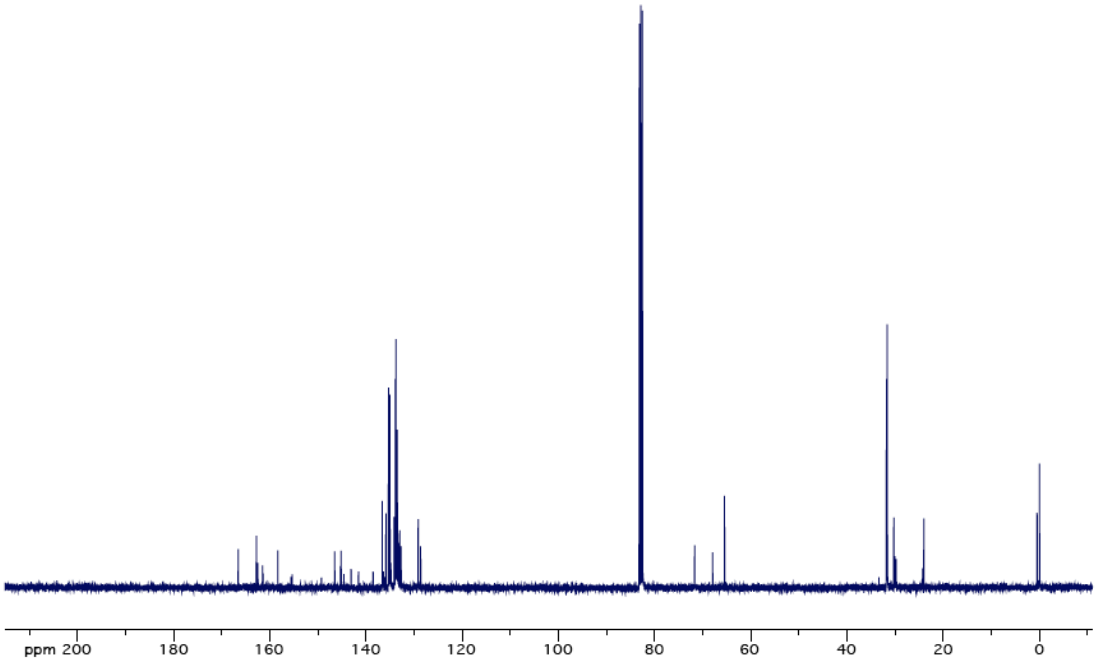

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

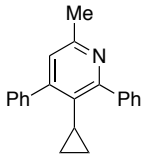
Pyridine 3k

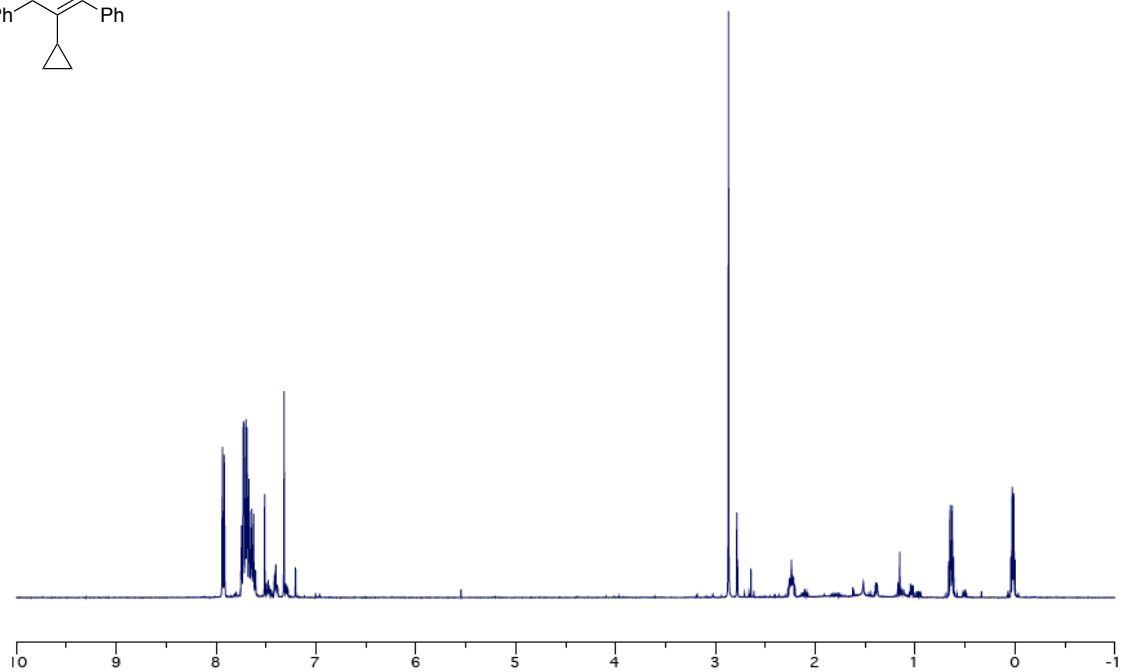

Me
N
Ph
Ph
TBSO

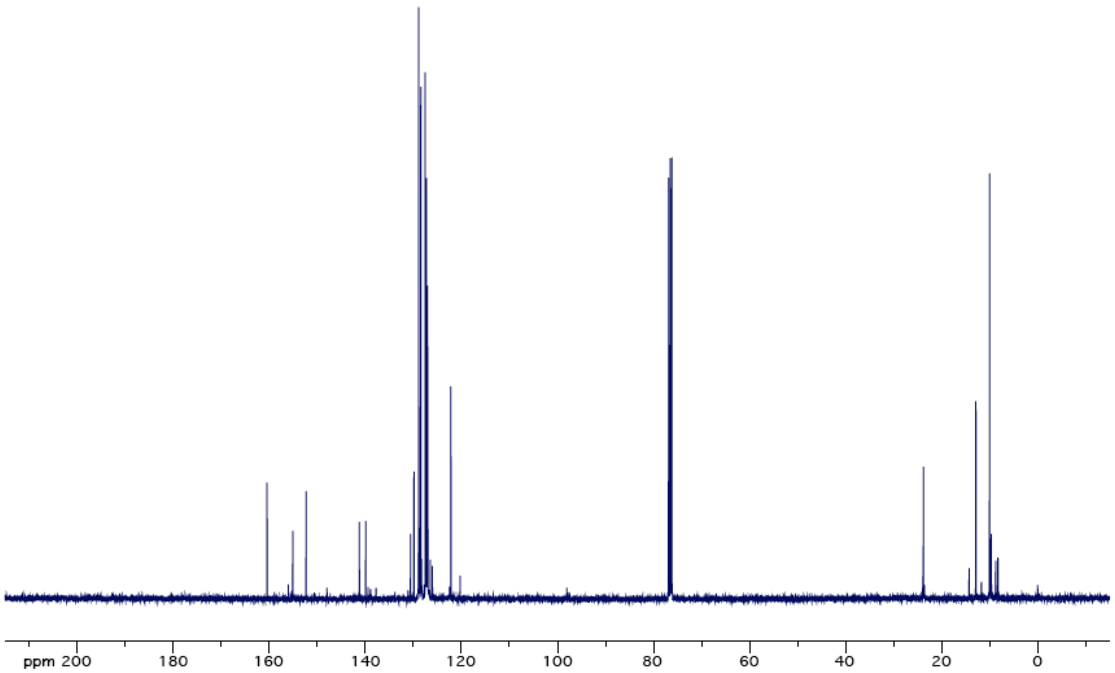

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

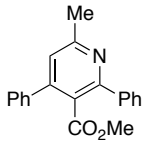
Pyridine 3l

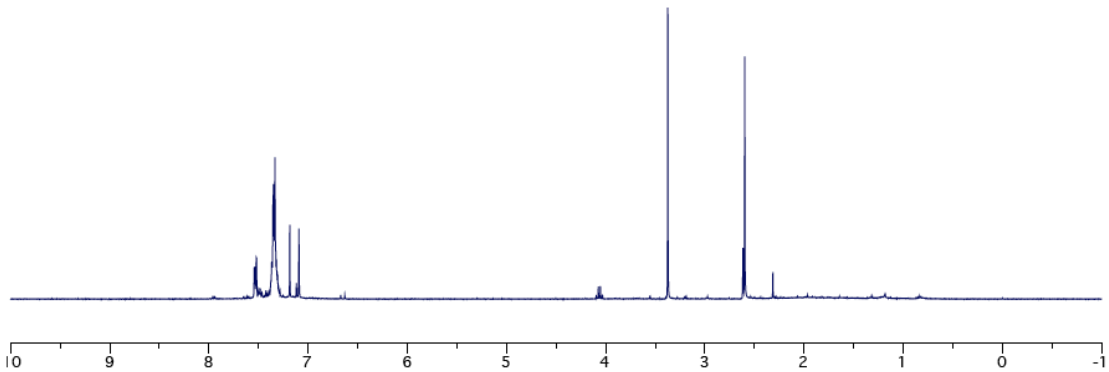

Me
N
Ph
Ph

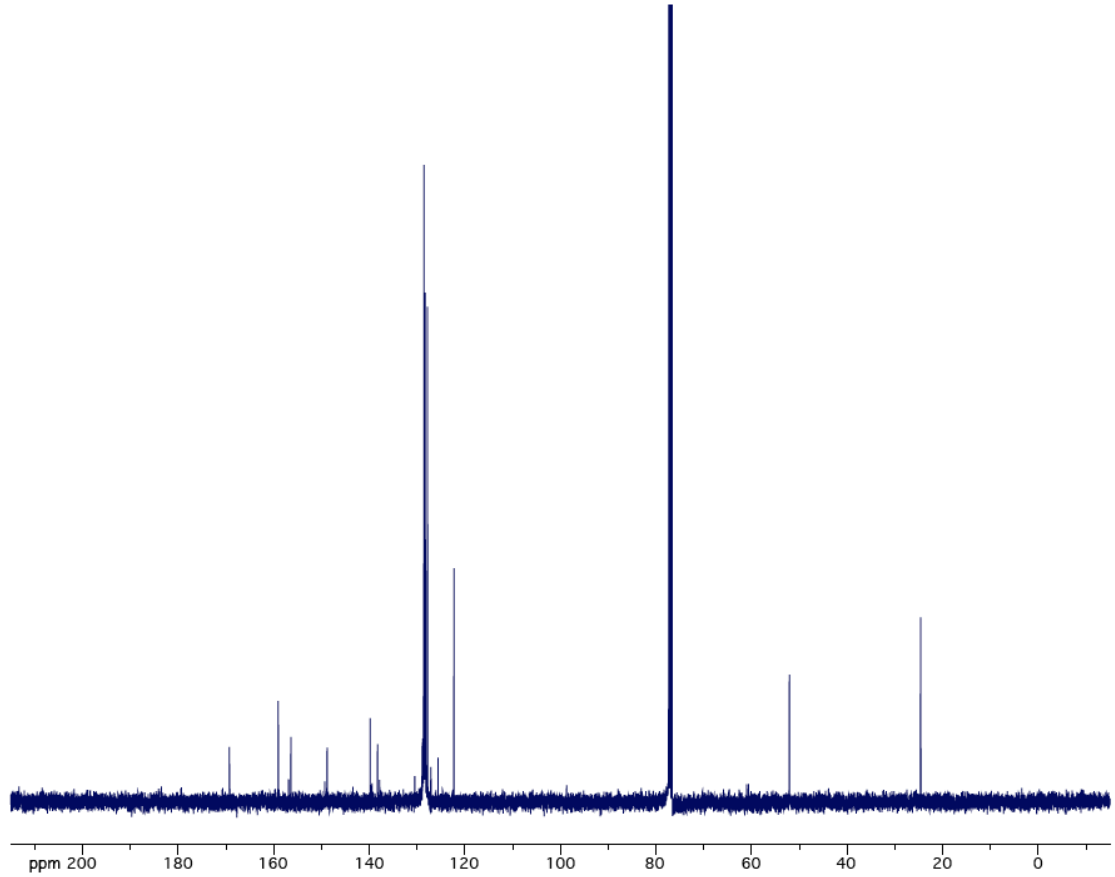

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

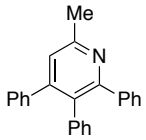
Pyridine 3m

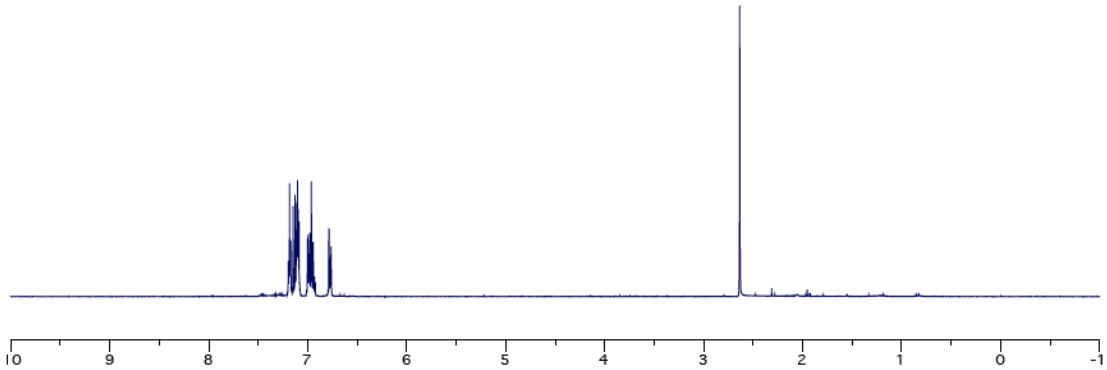

Me
N
Ph
Ph
CO2Me

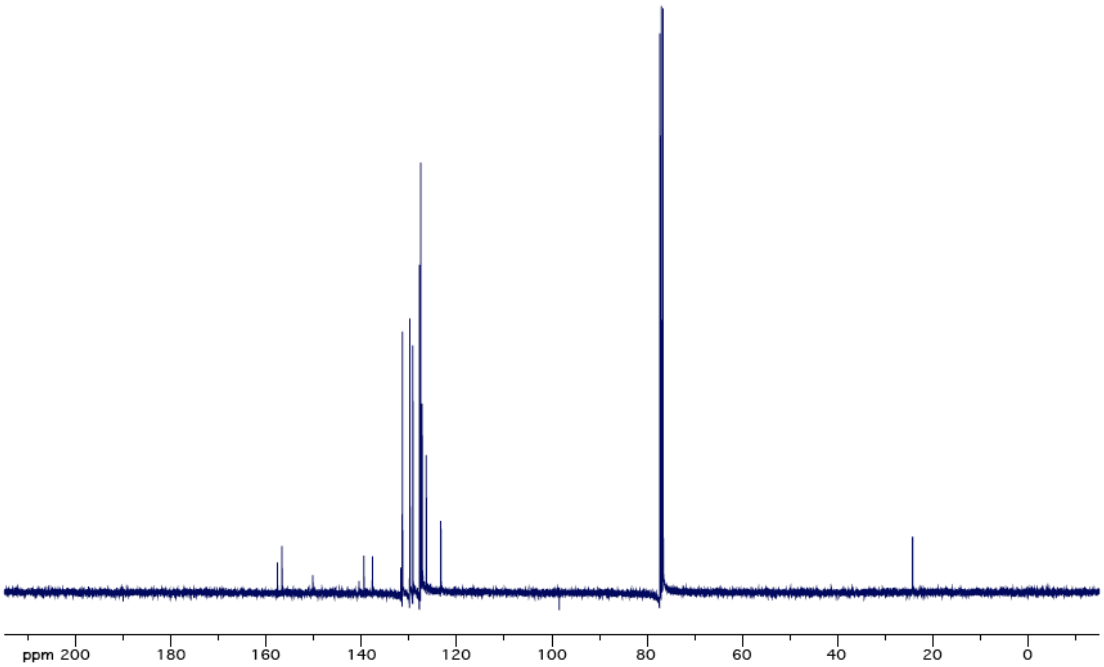

10
9
8
7
6
5
4
3
2
1
0
-1


ppm 200
180
160
140
120
100
80
60
40
20
0

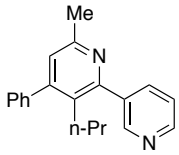
Pyridine 3n

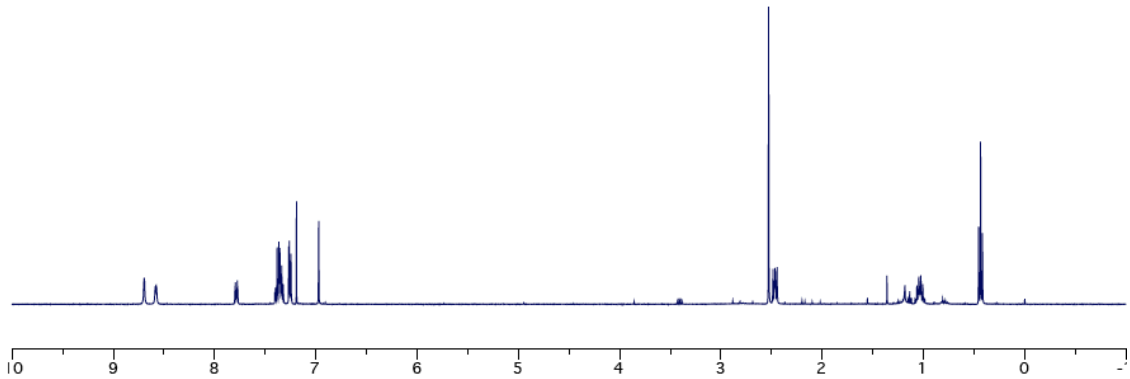

Me
N
Ph
Ph
Ph

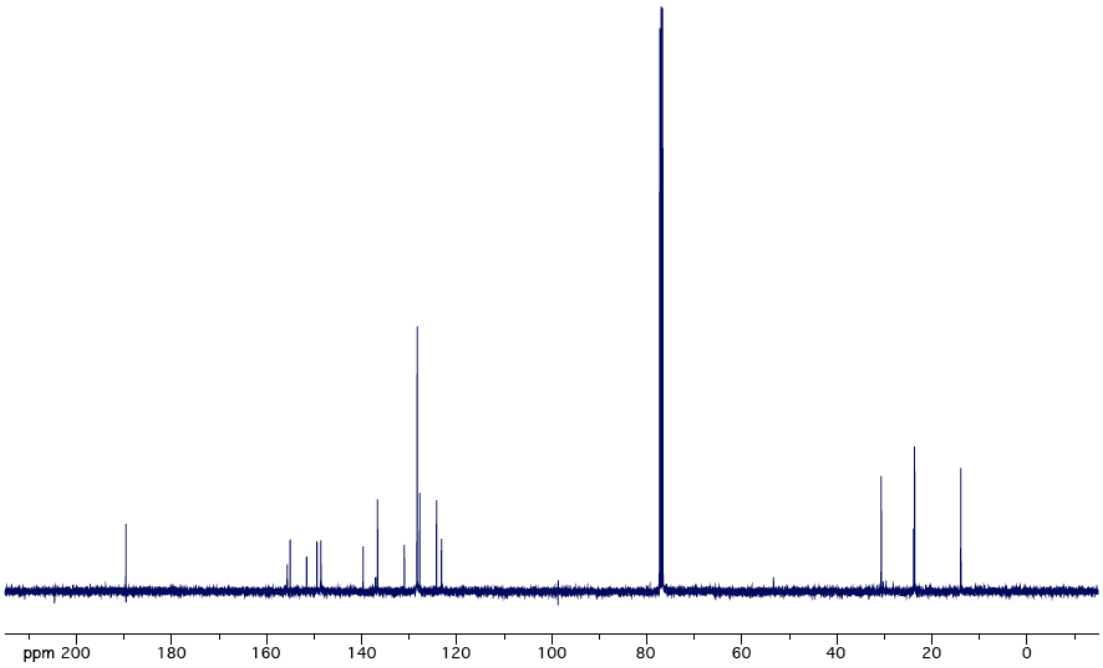

10
9
8
7
6
5
4
3
2
1
0
-1

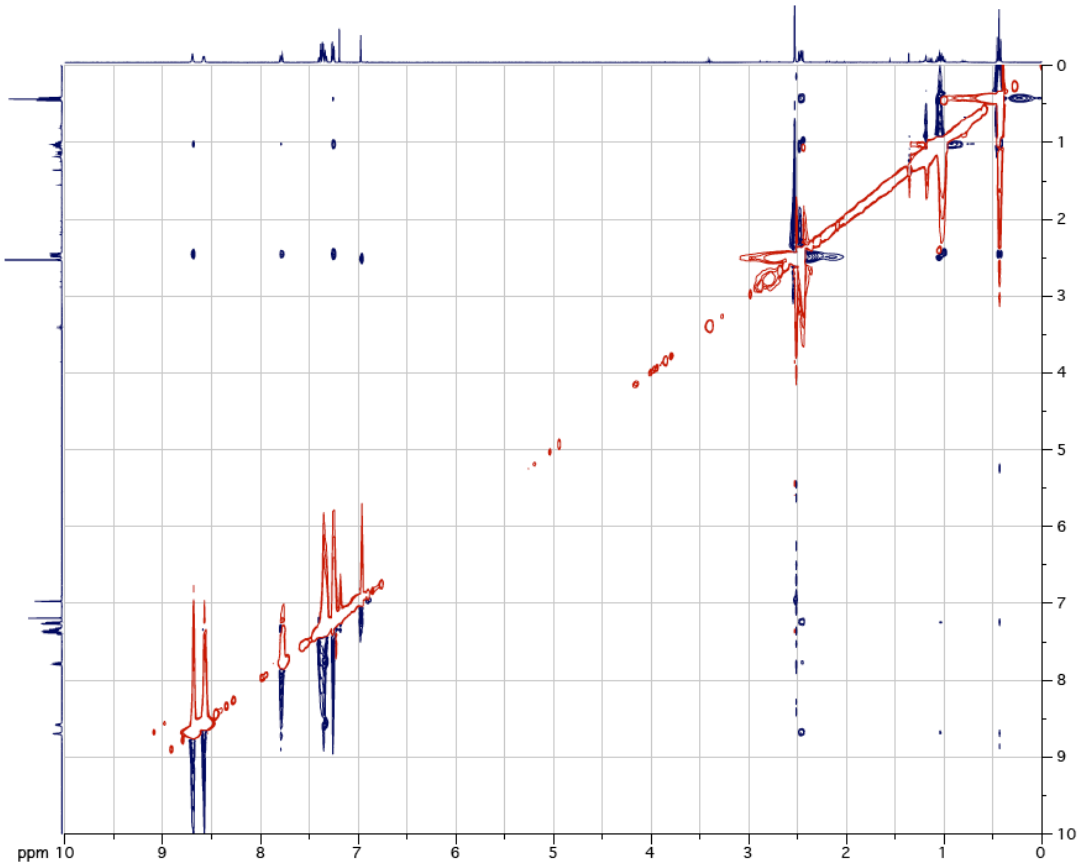

ppm 200
180
160
140
120
100
80
60
40
20
0

Pyridine 3o

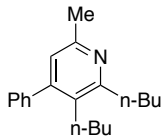

Me
N
Ph
n-Pr
N

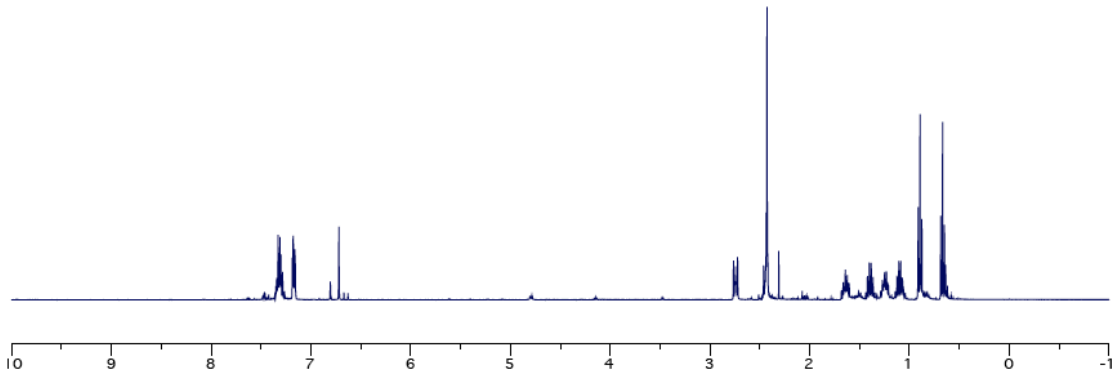

10
9
8
7
6
5
4
3
2
1
0

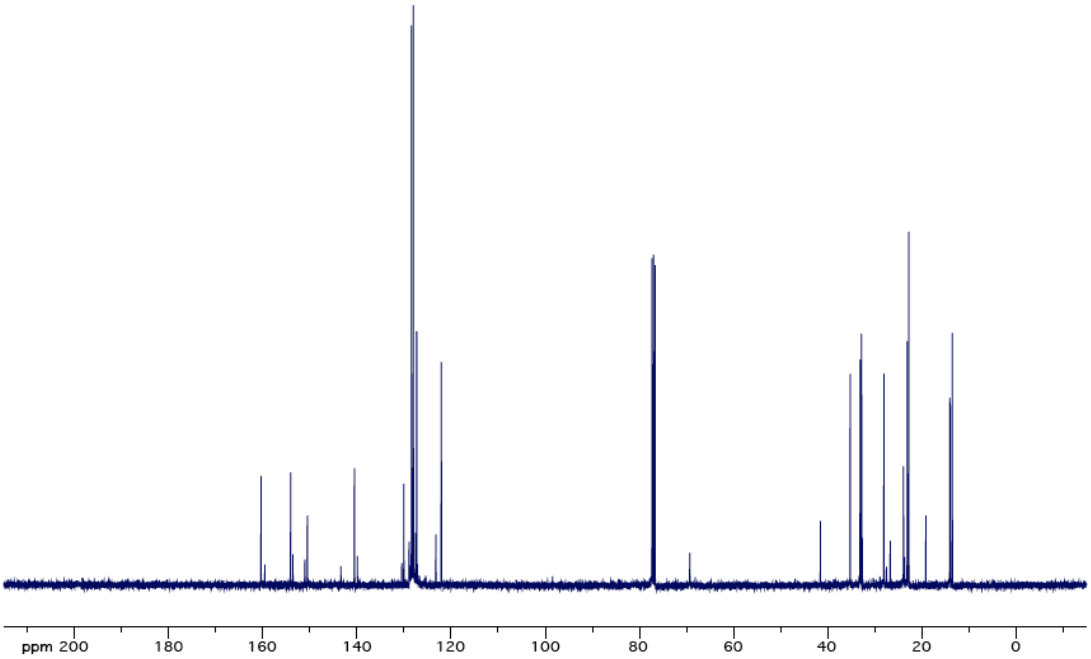

ppm 200
180
160
140
120
100
80
60
40
20
0


ppm 10
9
8
7
6
5
4
3
2
1
0
0
1
2
3
4
5
6
7
8
9
10

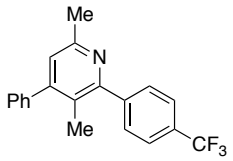
Pyridine 3p

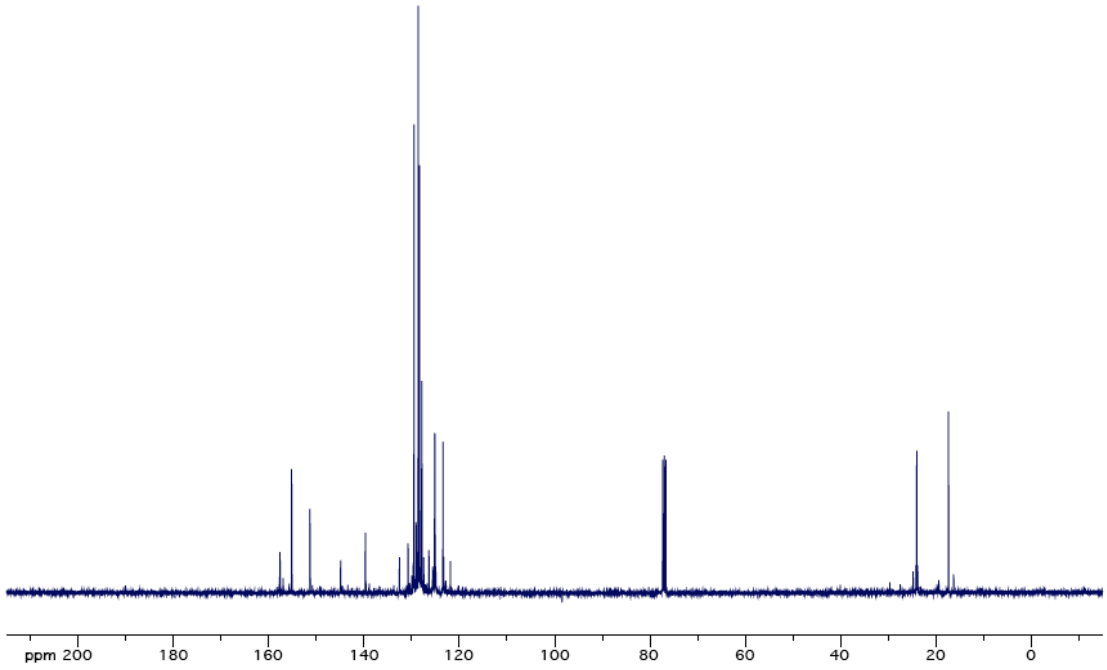




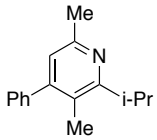


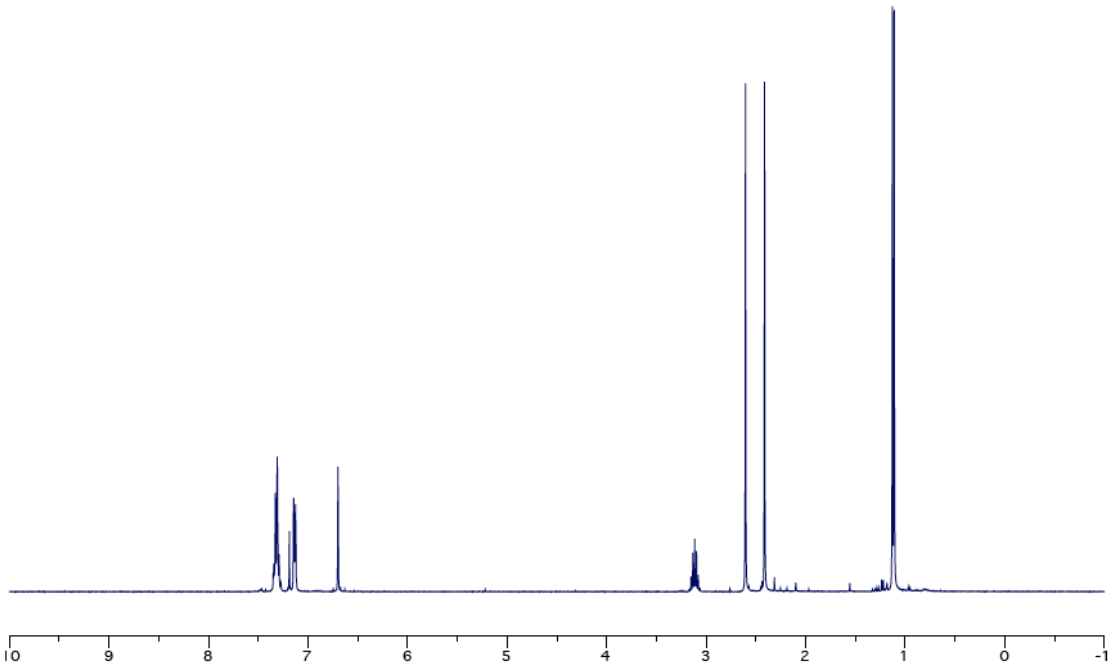
Pyridine 3q

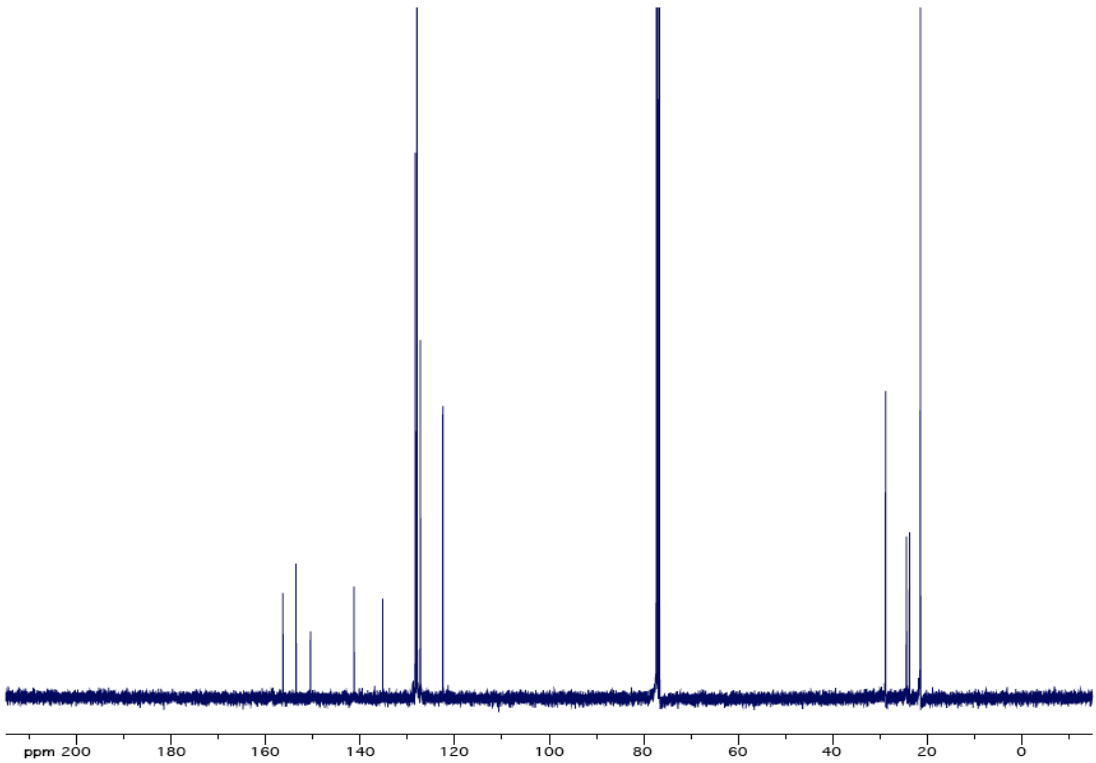

Me
N
Ph
Me
CF3

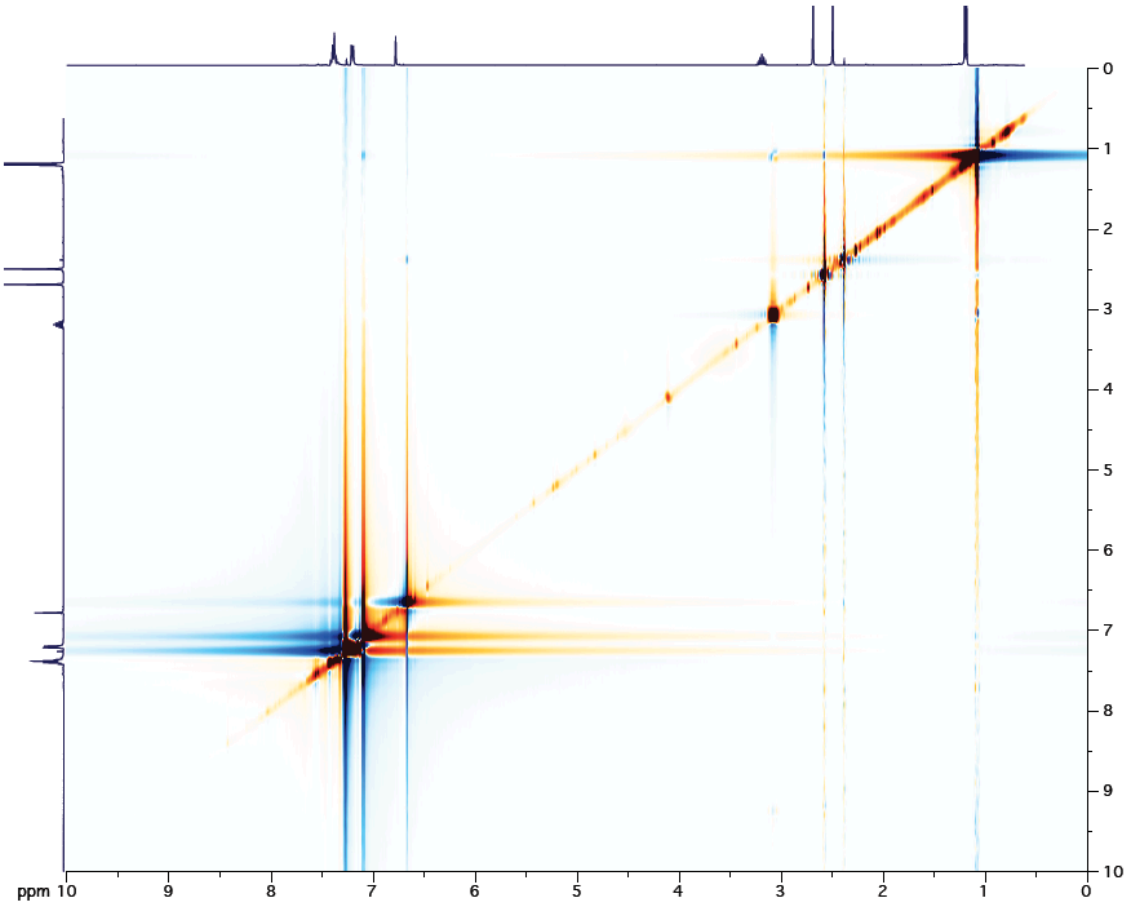

ppm 200
180
160
140
120
100
80
60
40
20
0

Pyridine 3r

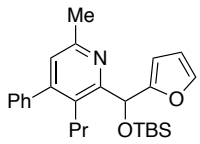

Me
N
Ph
i-Pr
Me

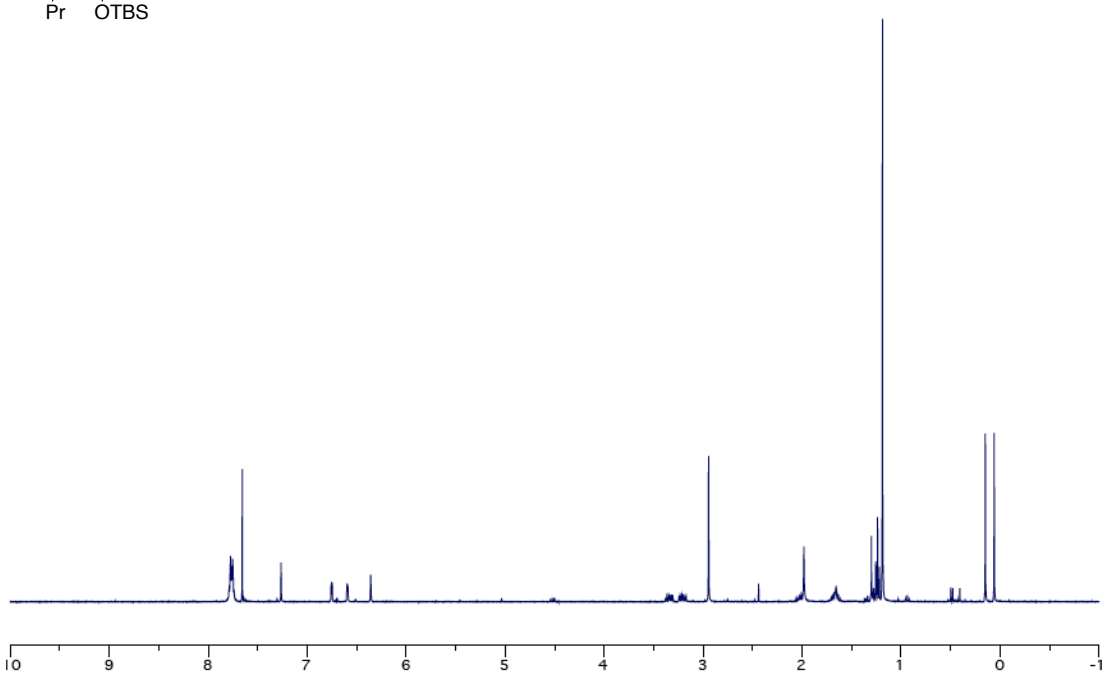

10
9
8
7
6
5
4
3
2
1
0
-1

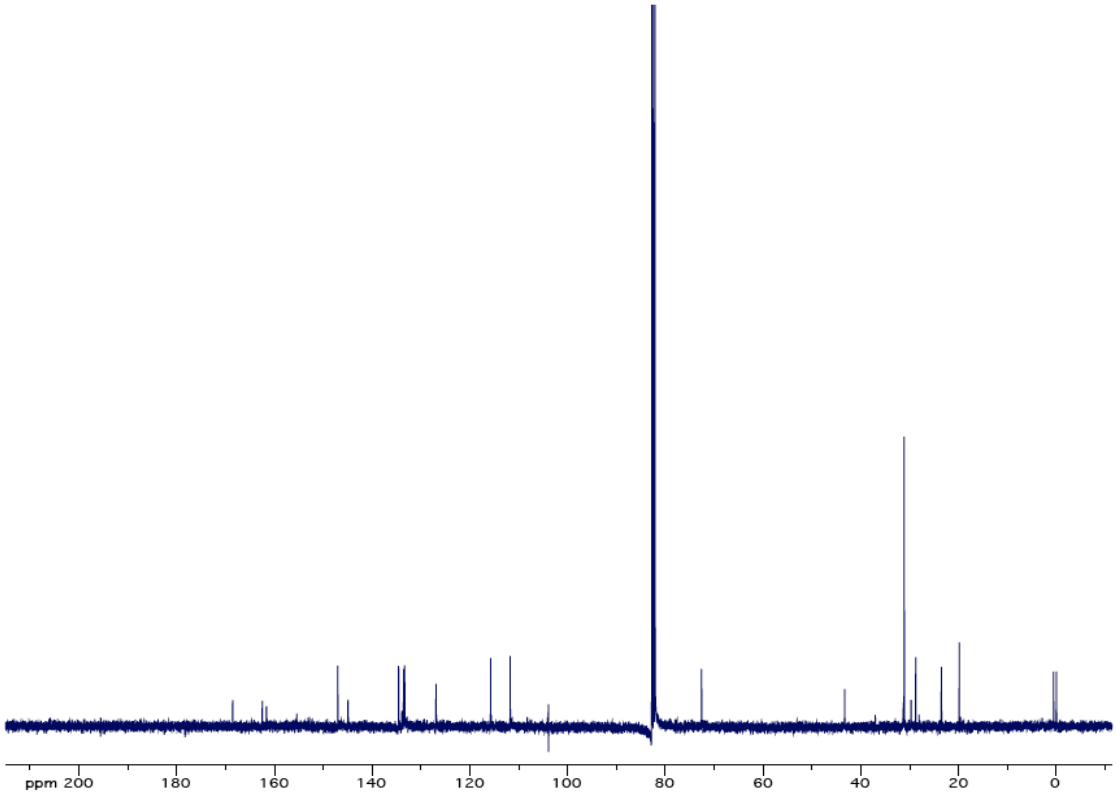

ppm 200
180
160
140
120
100
80
60
40
20
0


ppm 10
9
8
7
6
5
4
3
2
1
0
0
1
2
3
4
5
6
7
8
9
10

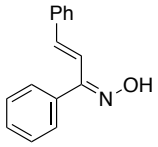
Pyridine 3s

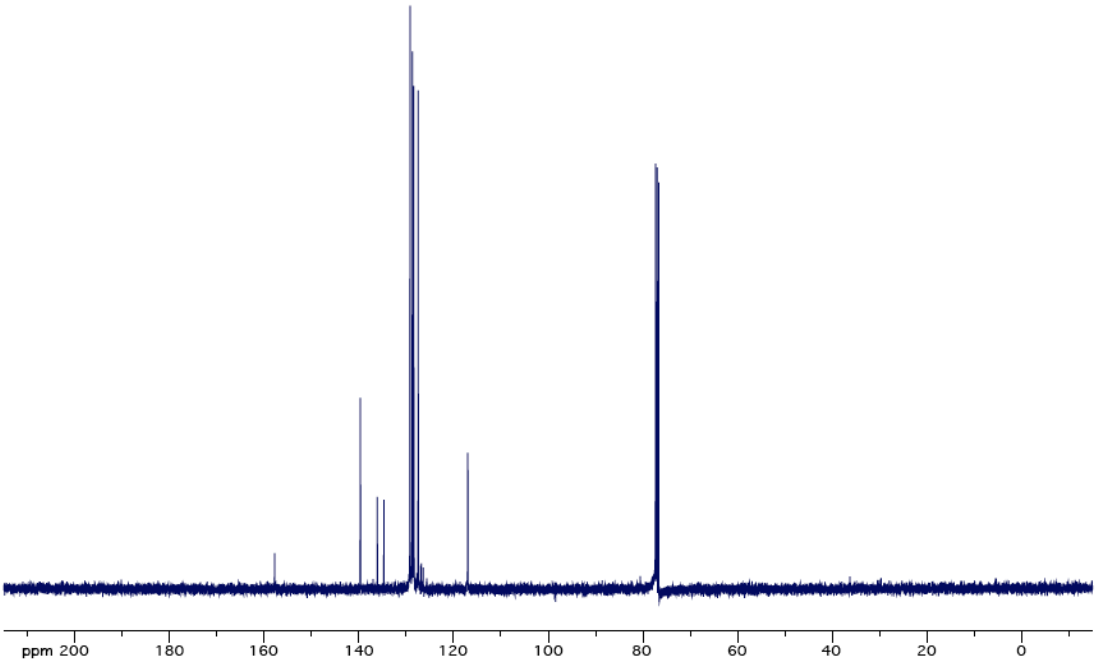




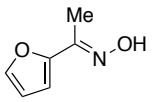


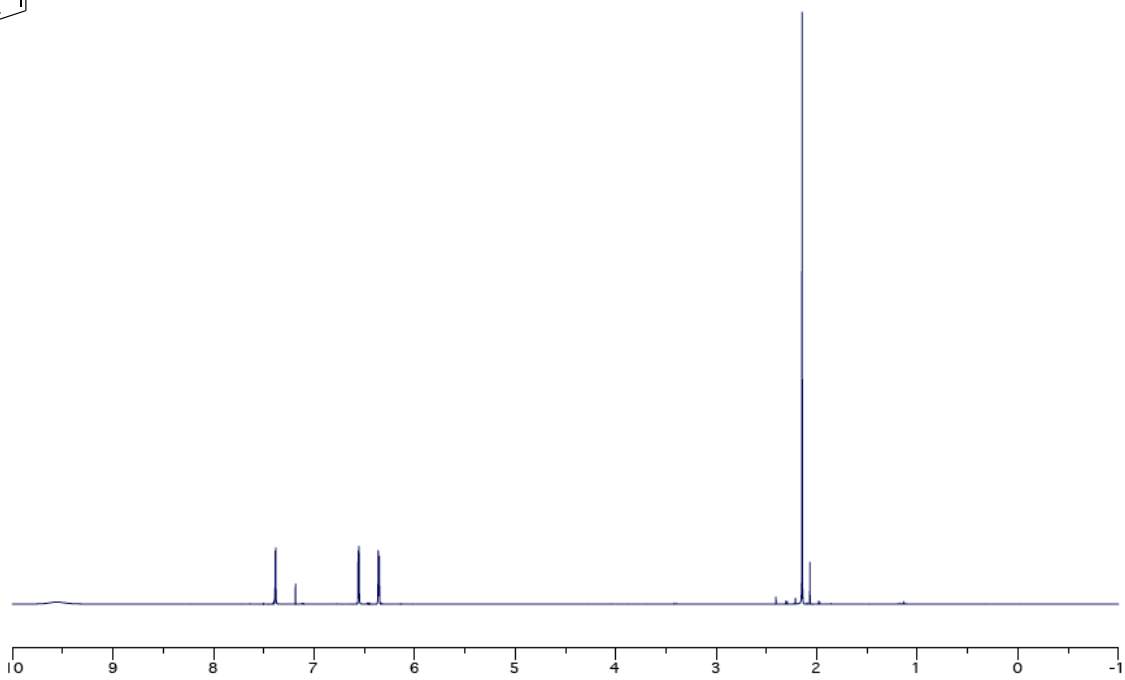
Aryl Oxime 4d

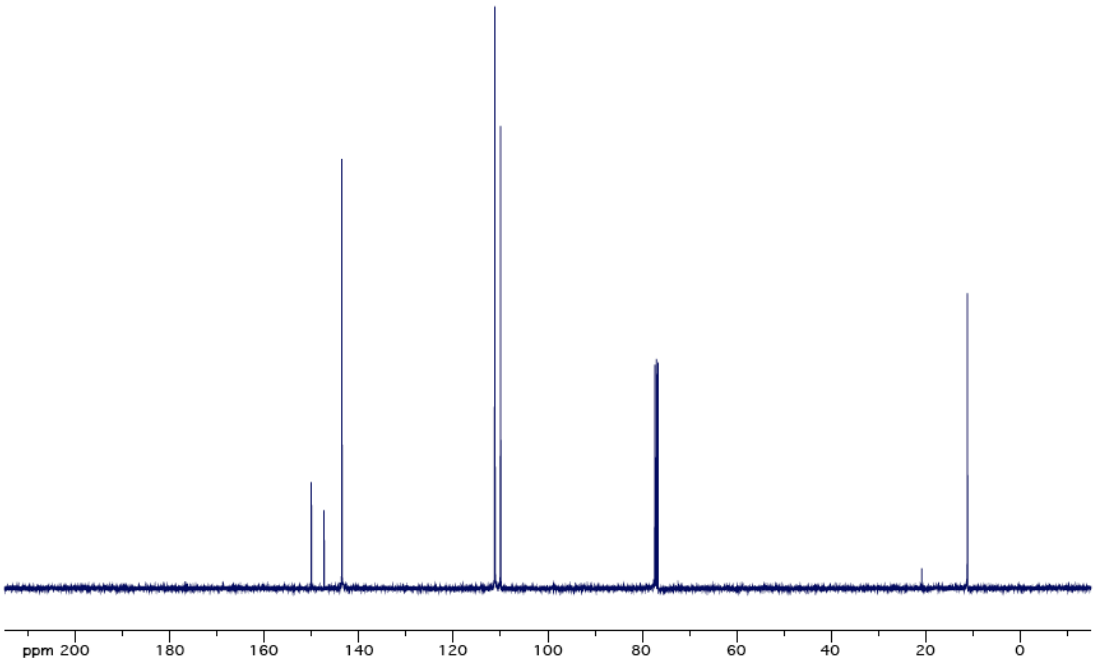

Ph
N
OH


ppm 200
180
160
140
120
100
80
60
40
20
0

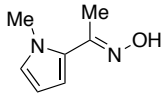
Oxime 4g

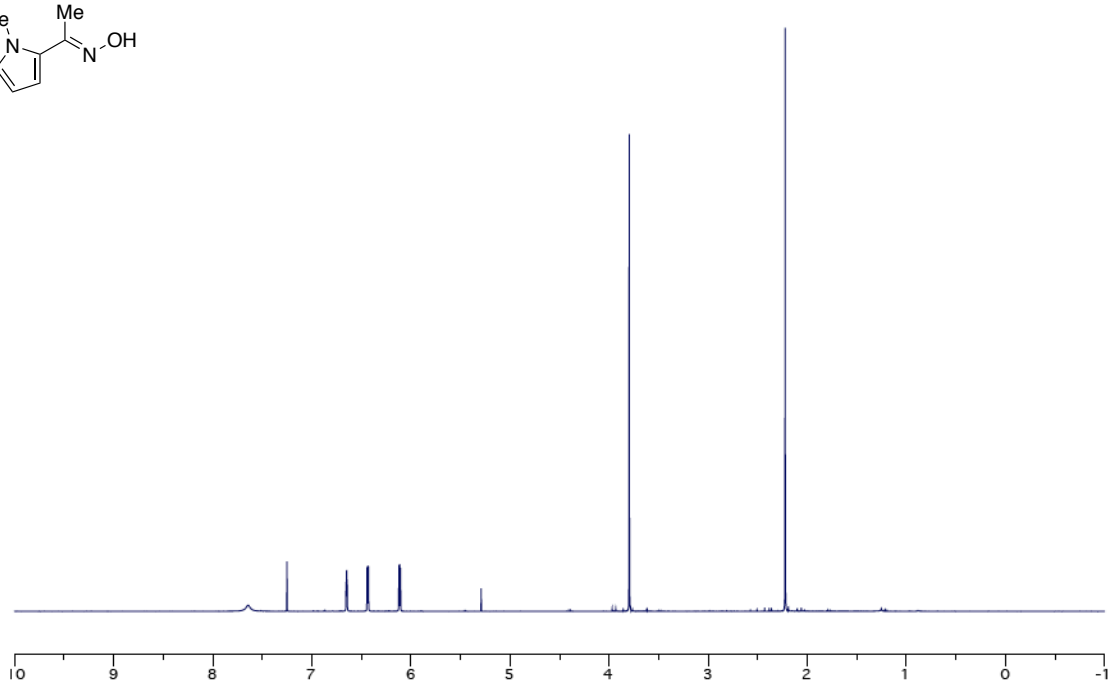


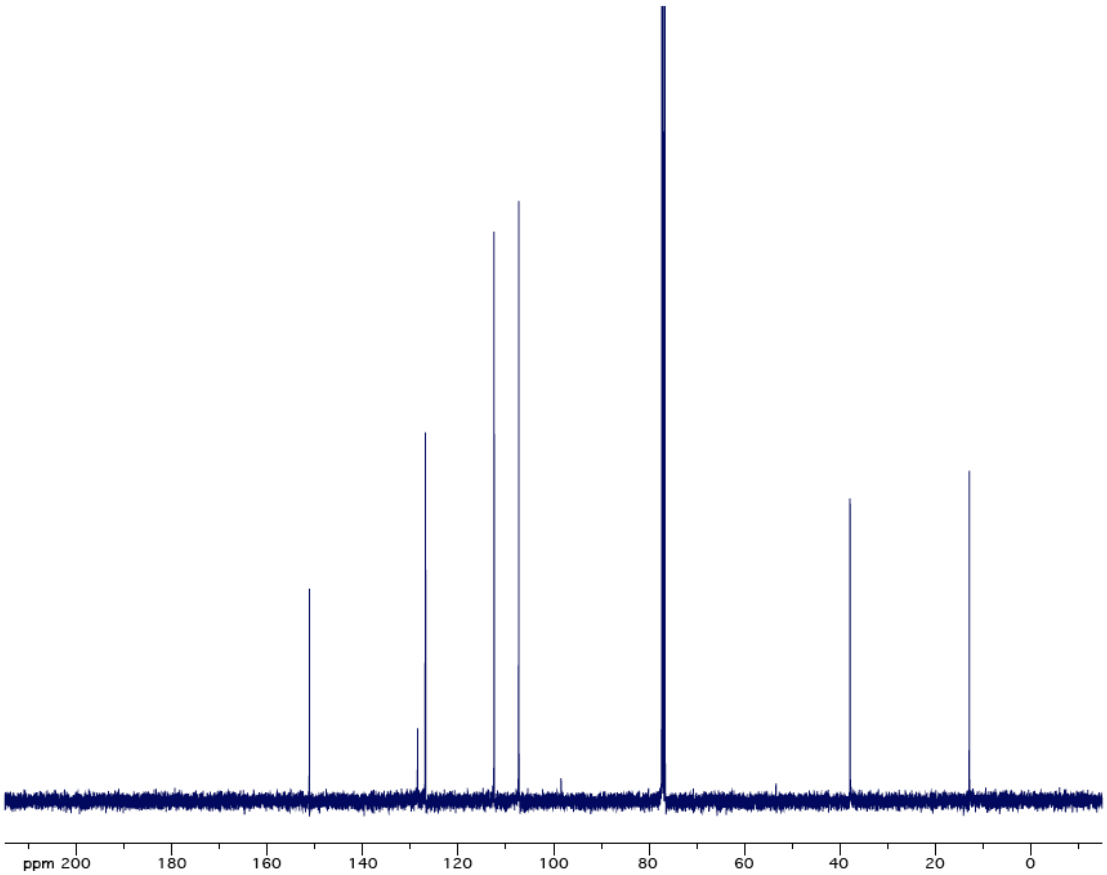




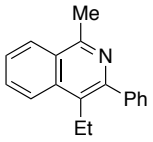
Oxime 4i

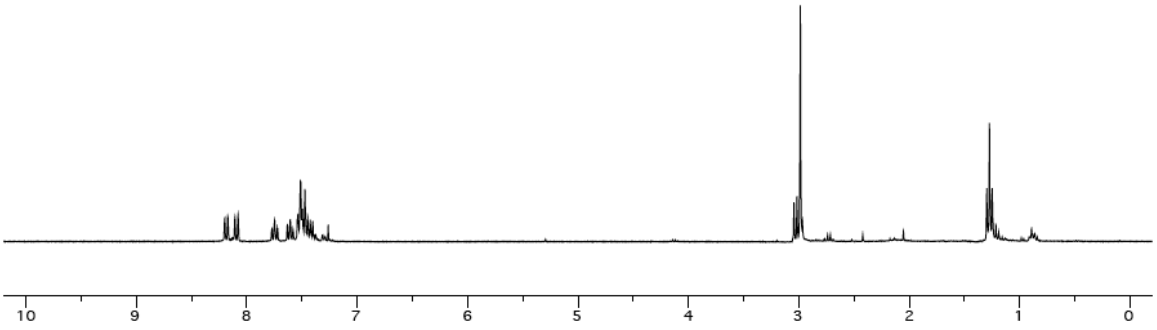

Me
Me
N
N
OH


10
9
8
7
6
5
4
3
2
1
0
-1

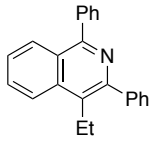

ppm 200
180
160
140
120
100
80
60
40
20
0

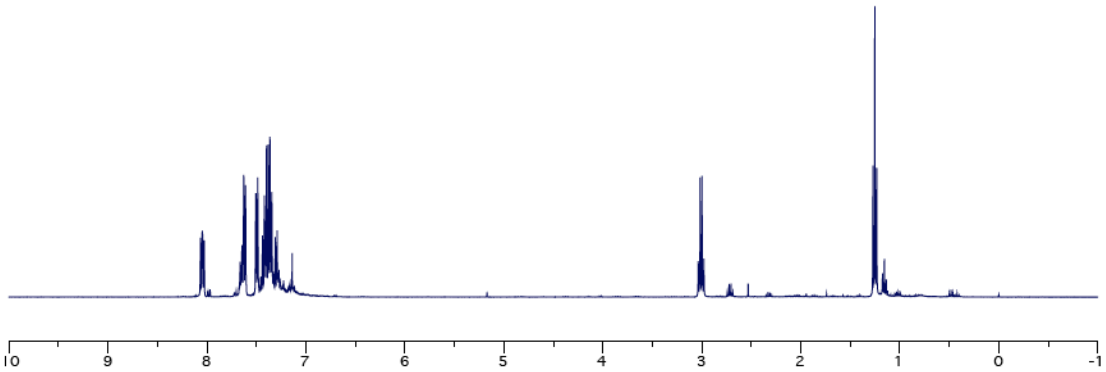
Isoquinoline 5a

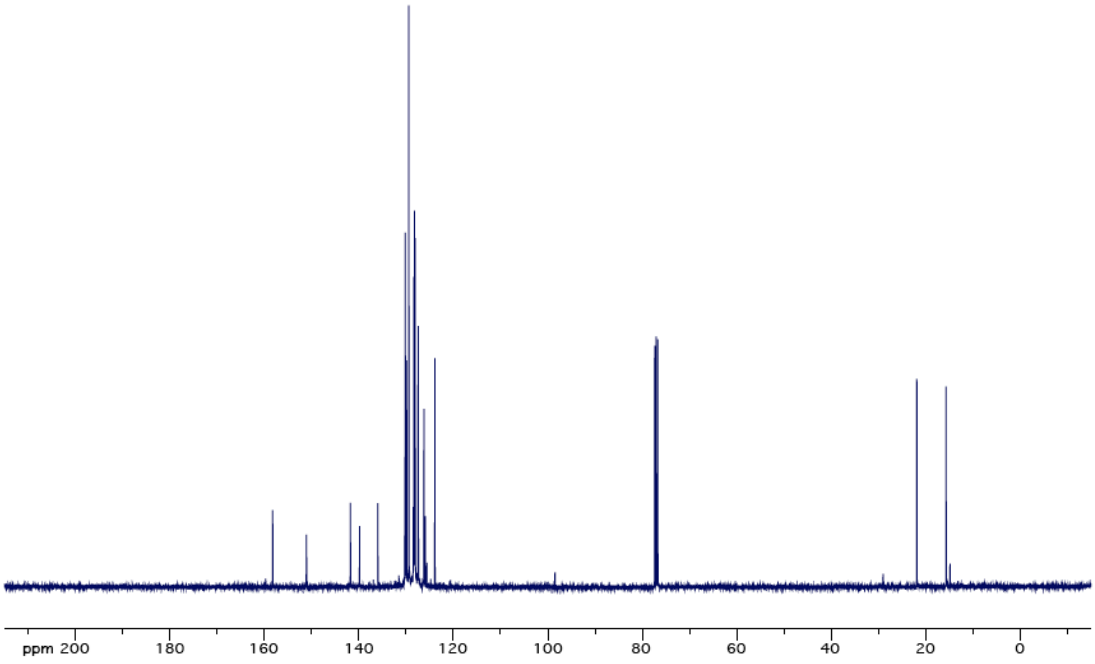




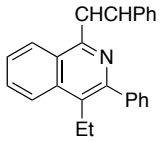
Isoquinoline 5b

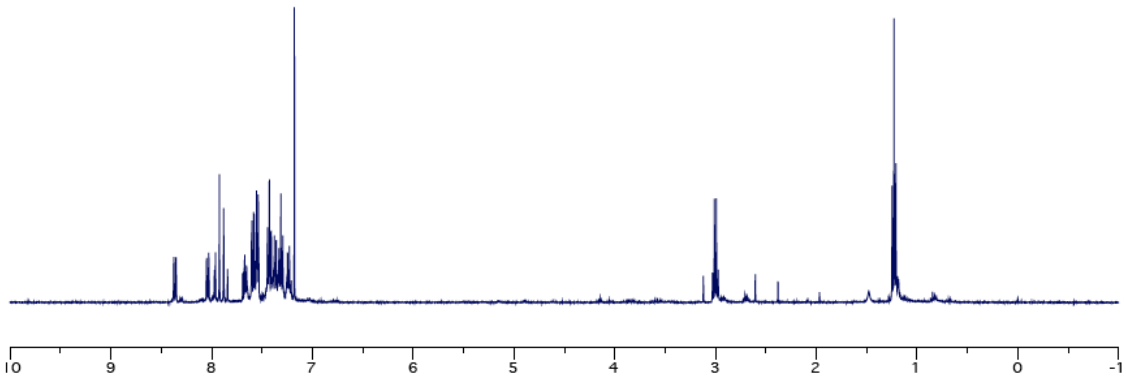


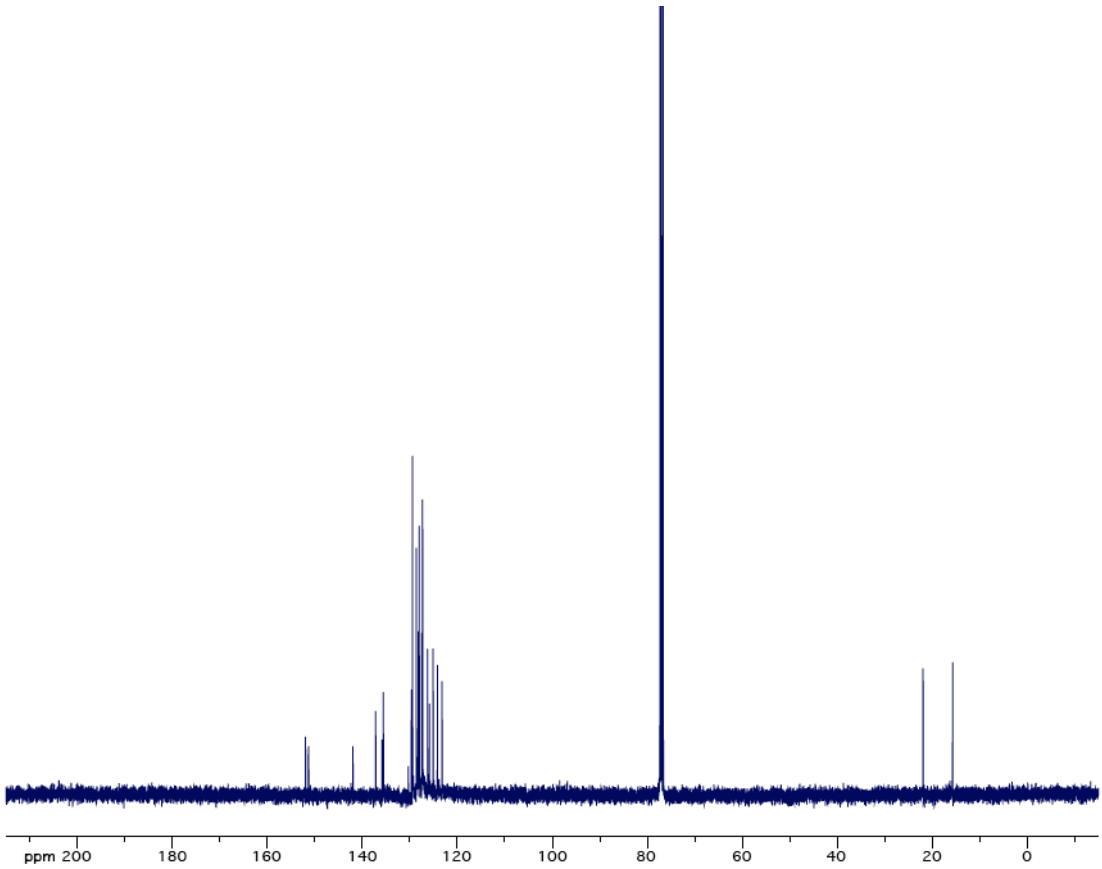




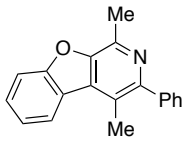
Isoquinoline 5c

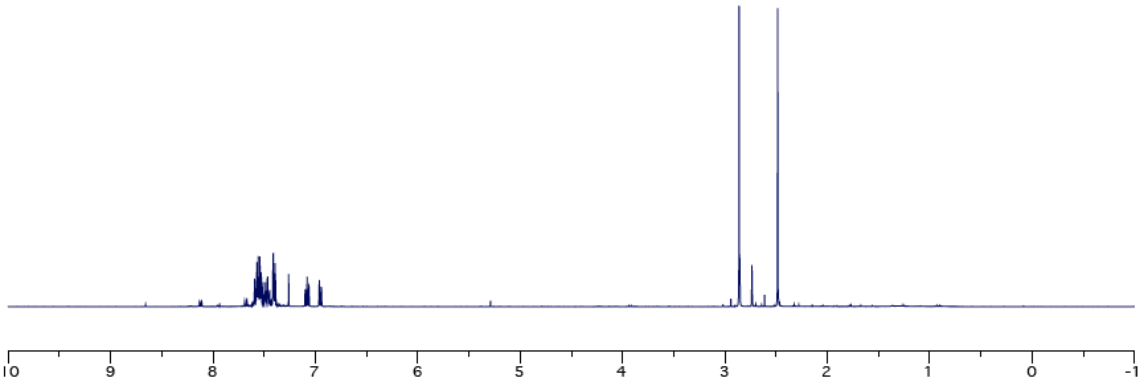


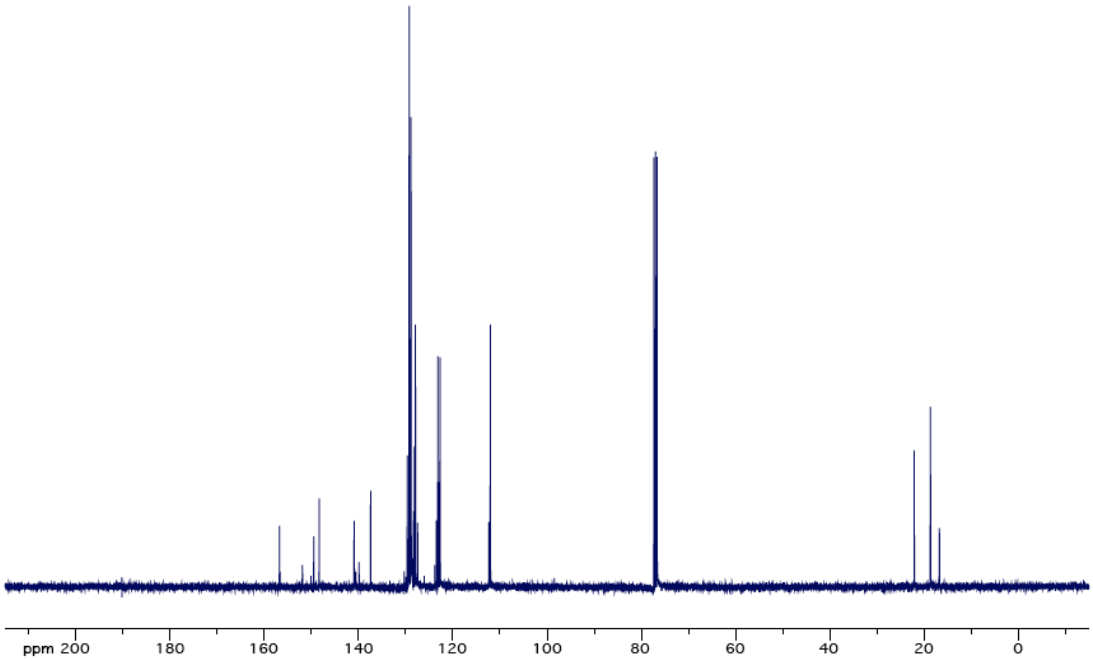




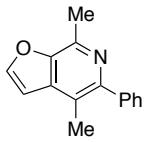
Isoquinoline 5d

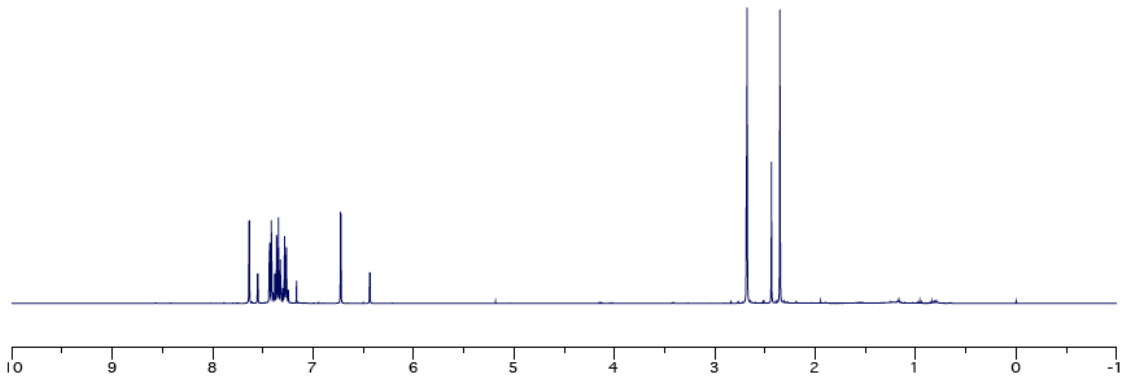


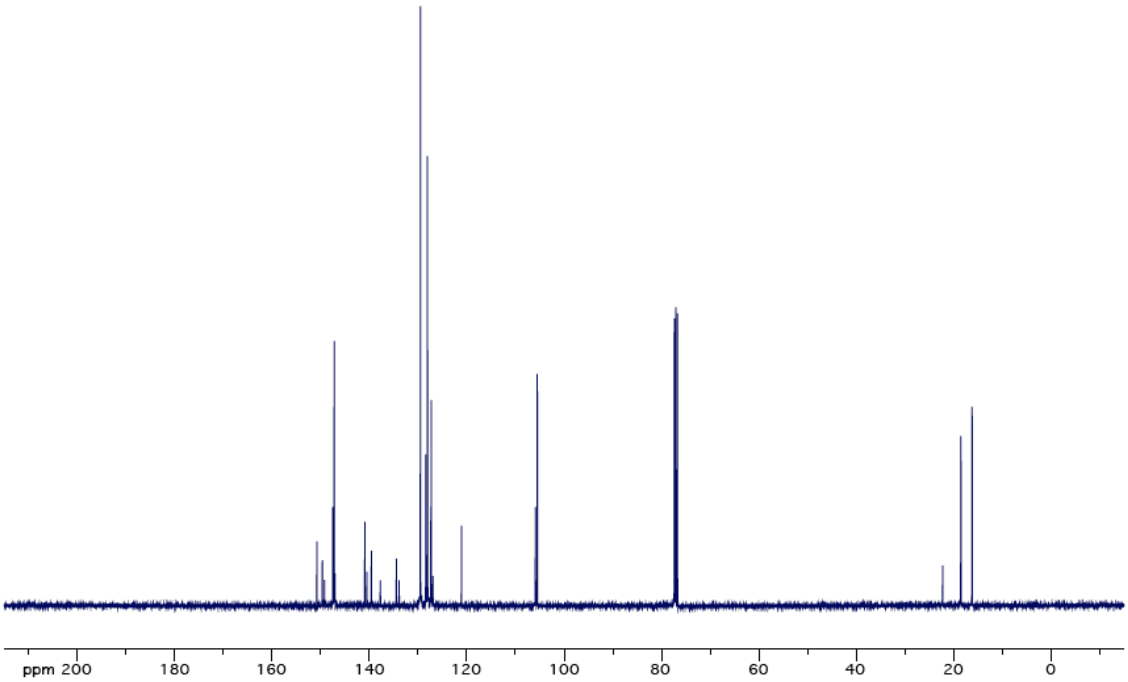




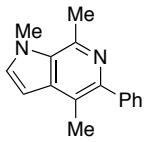
Isoquinoline 5e

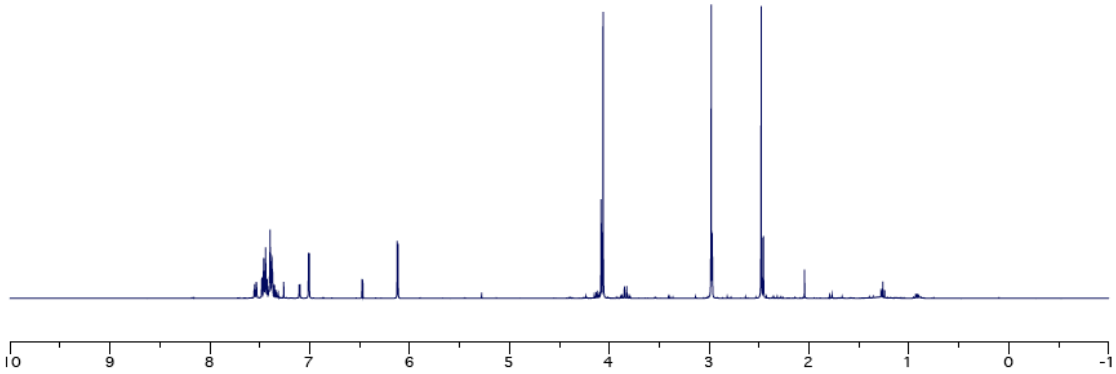


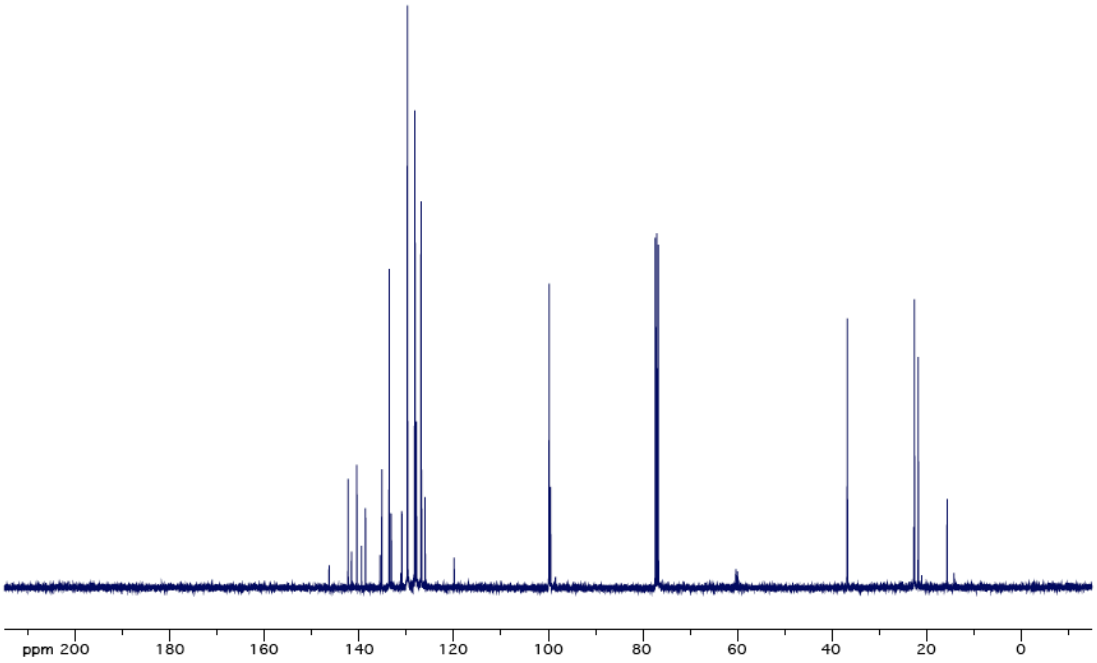




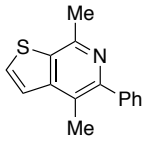
Isoquoinoline 5f

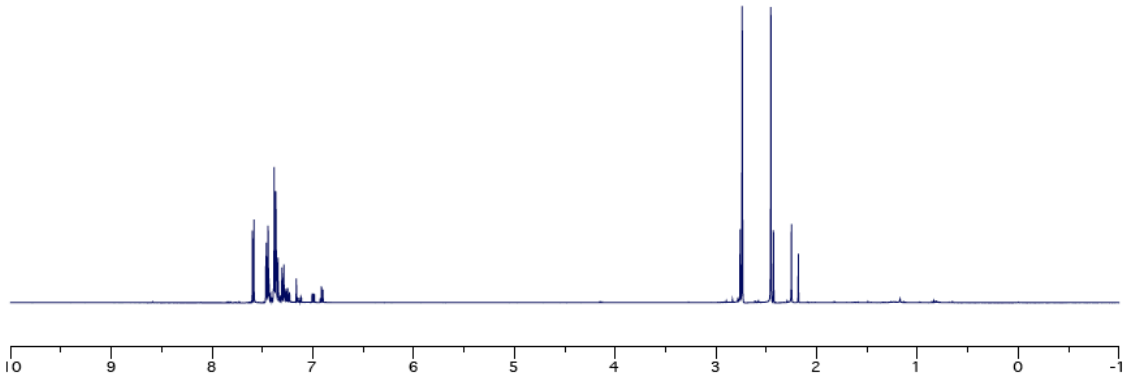


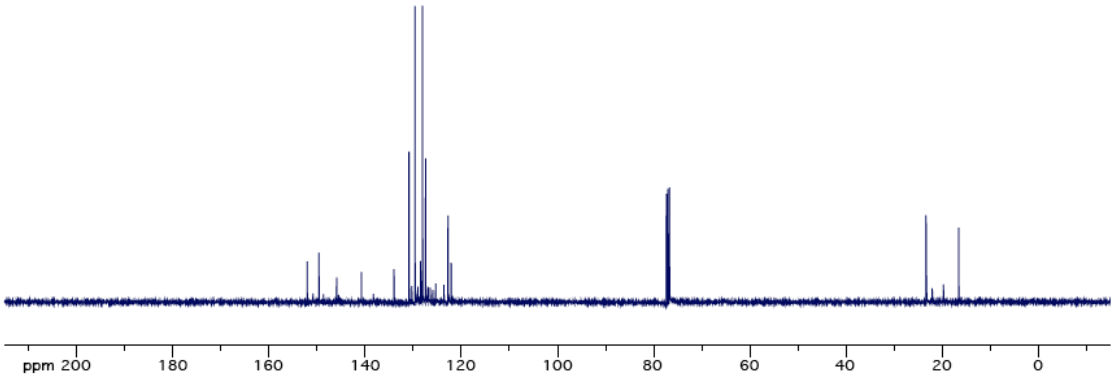




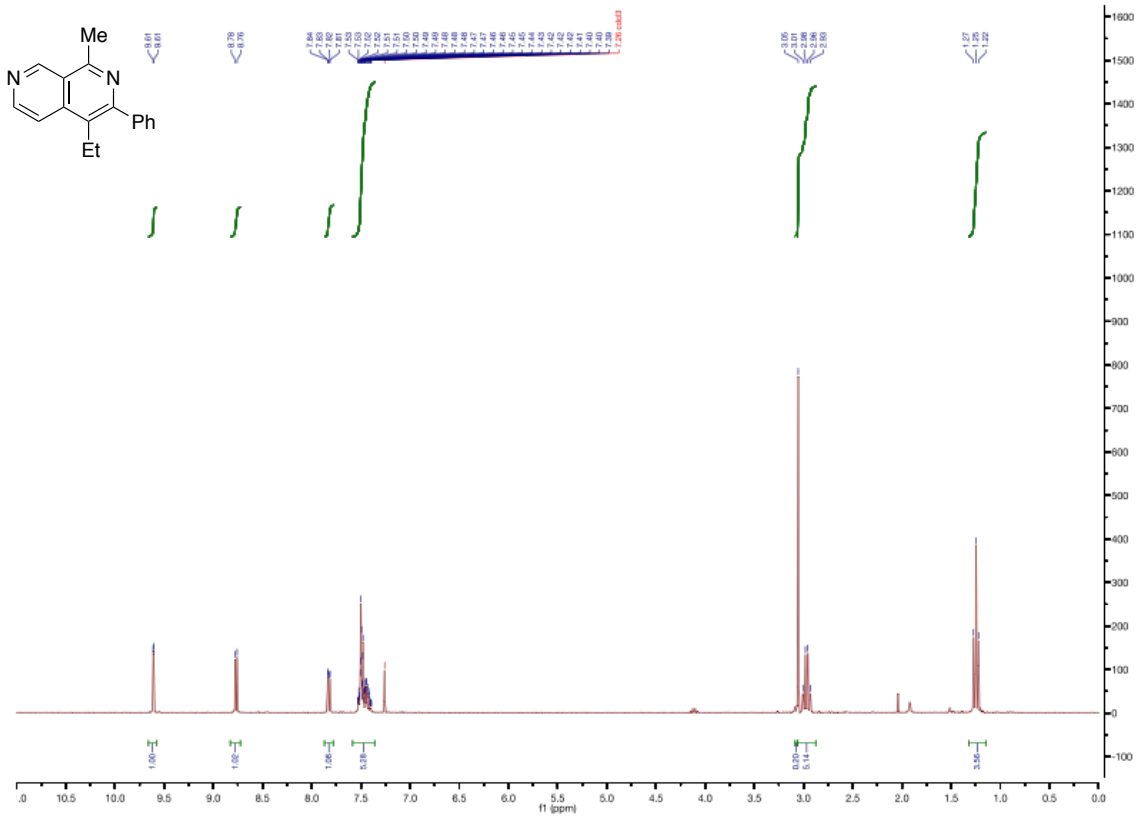
Isoqiunoline 5g

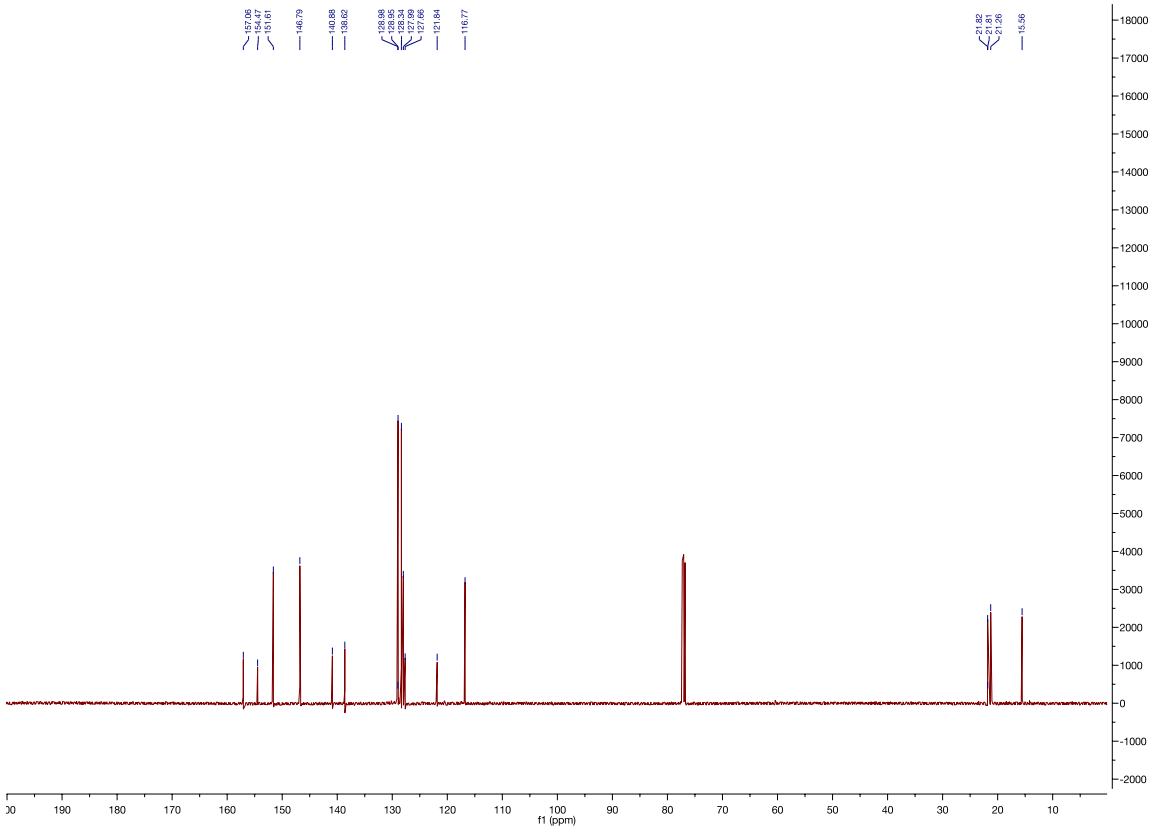




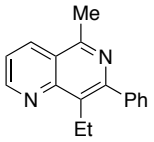


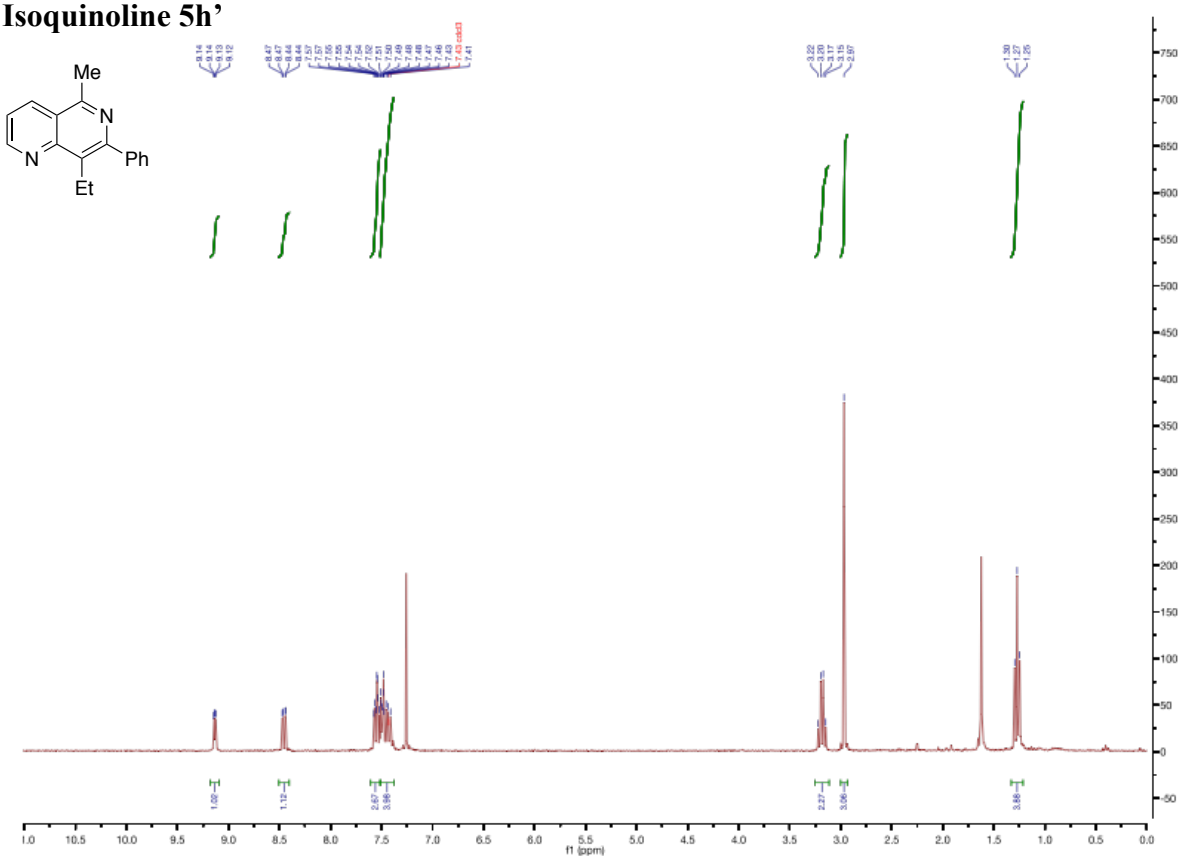
Isoquinoline 5h

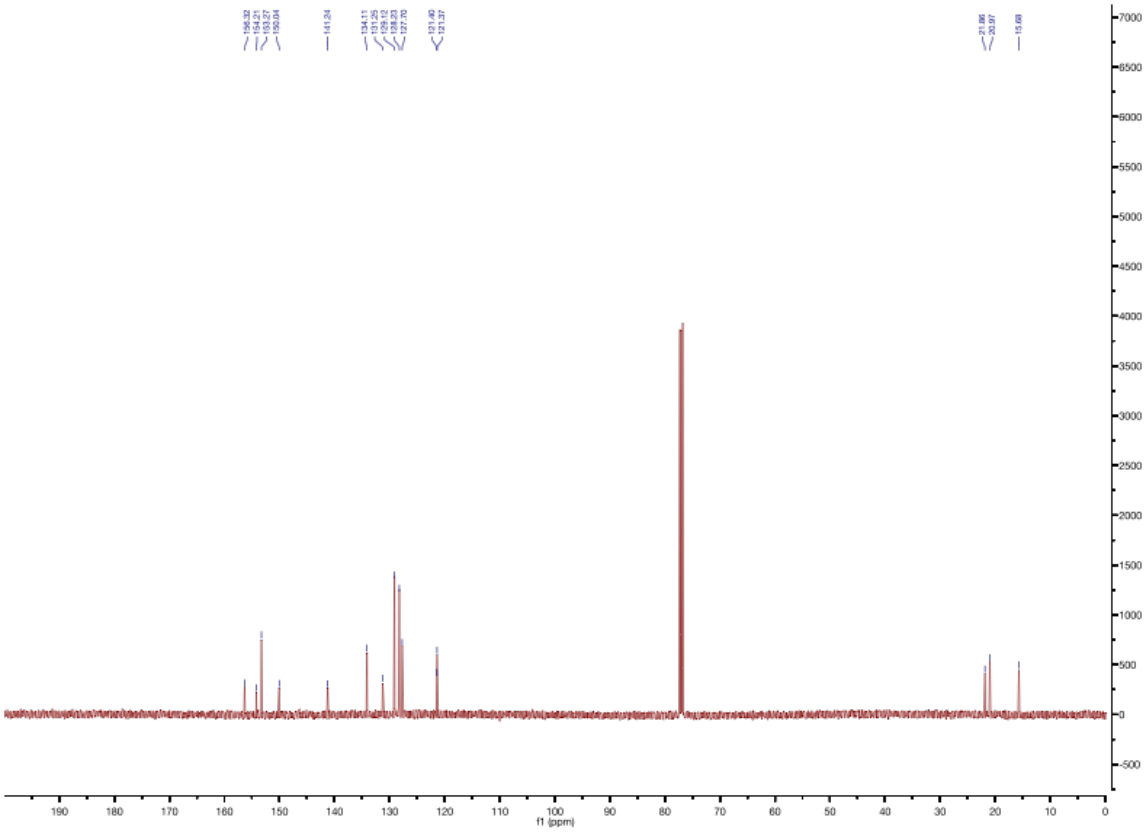




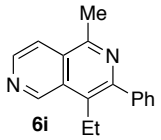
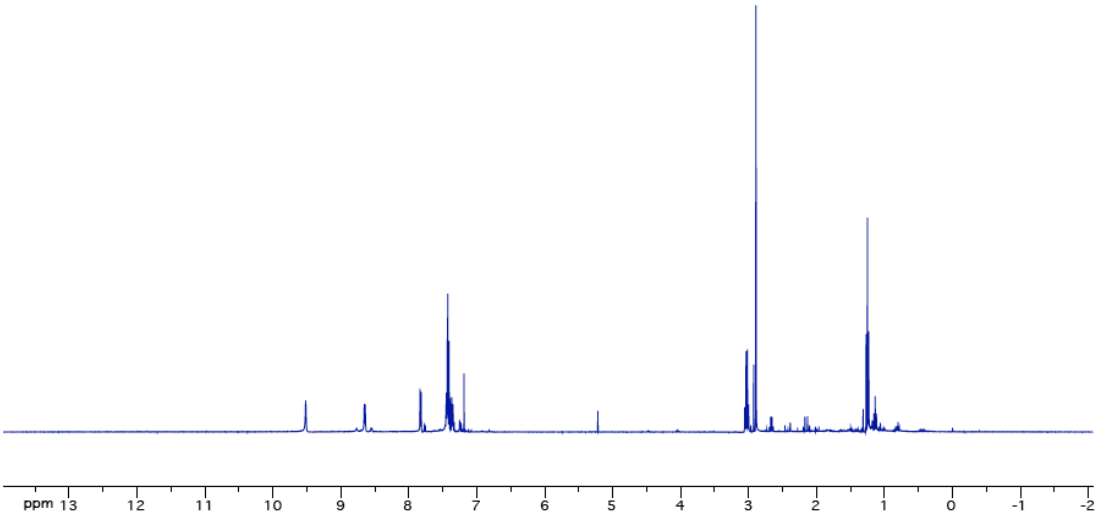
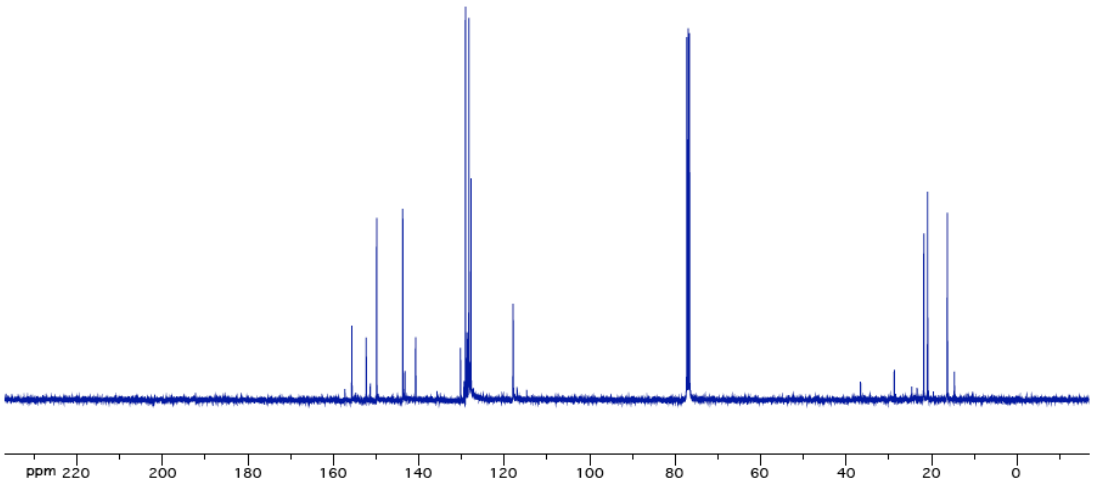
Isoquinoline 5h'







Isoquinoline 5i



6i