Stereospecific Coupling of Boronic Esters with *N*-Heteroaromatic Compounds.

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Supporting Information

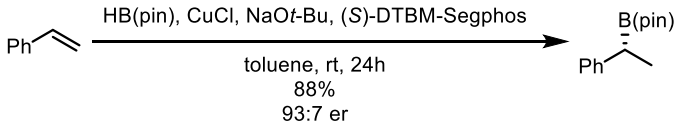
Table of Contents

1. General Information

All required fine chemicals were used directly without purification unless mentioned. All air- and water-sensitive reactions were carried out in flame-dried glassware under nitrogen atmosphere using standard Schlenk manifold technique. ^{1}H and ^{13}C Nuclear Magnetic Resonance (NMR) spectra were acquired at various field strengths as indicated, and were referenced to $CHCl_3$ (7.27 and 77.0 ppm for ^{1}H and ^{13}C respectively) or TMS (0.00 ppm for ^{1}H and ^{13}C). ^{1}H NMR coupling constants are reported in Hertz and refer to apparent multiplicities and not true coupling constants. Data are reported as follows: chemical shift, multiplicity (s = singlet, br s = broad singlet, d = doublet, t = triplet, q = quartet, qi = quintet, sx = sextet, sp = septet, m = multiplet, dd = doublet of doublets, etc.) and integration. ^{11}B-NMR spectra were recorded with complete proton decoupling. High resolution mass spectra were recorded using Electronic Ionization (EI), Electron Spray Ionization (ESI) or Chemical Ionization (CI). For CI, methane or NH_4OAc/MeOH was used. All IR data was obtained on a Perkin-Elmer Spectrum One FT-IR spectrometer. Optical rotations were obtained on a Perkin-Elmer 241MC polarimeter. Analytical TLC: aluminium backed plates pre-coated (0.25 mm) with Merck Silica Gel 60 F254. Compounds were visualized by exposure to UV-light or by dipping the plates in permanganate ($KMnO_4$) stain followed by heating. Flash column chromatography was performed using Merck Silica Gel 60 (40-63 μm). All mixed solvent eluents are reported as v/v solutions. Chiral HPLC was performed using Diacel Chiralpak IA, IB and IC columns (4.6 × 250 mm × 5 μm) fitted with the respective guards (4 × 10 mm), OD, OD-H and AD-H without guard and monitored by DAD (Diode Array Detector). Chiral GC was performed on Agilent Technologies 6890N Network GC system using a Supelco DM column (30 m × 2.5 mm). Solvents were purified by standard methods. TMEDA and $(iPr)_2NH$ were distilled over CaH_2. (–)-Sparteine was obtained from the commercially available sulfate pentahydrate salt (99%, Acros) and isolated according to literature procedure. The (–)-sparteine free base readily absorbs atmospheric carbon dioxide (CO_2) and should be stored under argon/nitrogen at −20 °C in a Schlenk tube. *sec*-BuLi was purchased from Acros. *n*-BuLi and *t*-BuLi were purchased from Sigma-Aldrich. The molarity of organolithium solutions was determined by titration using salicylaldehyde phenylhydrazone as an indicator.

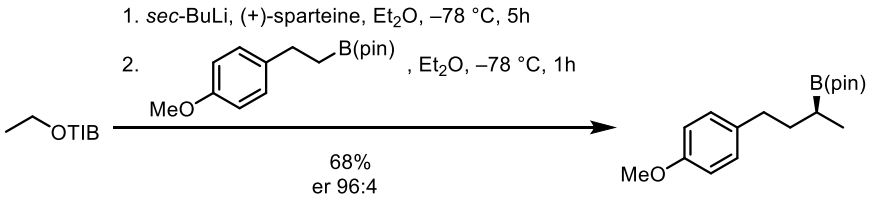
2. Preparation of boronic esters.

(*R*)-4,4,5,5-Tetramethyl-2-(1-phenylethyl)-1,3,2-dioxaborolane [(*R*)-8]



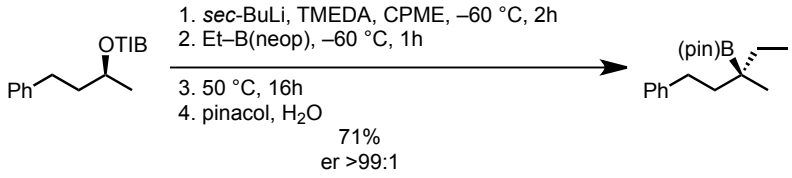
Prepared according to a literature procedure.[1]

(*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane [(*S*)-S1]



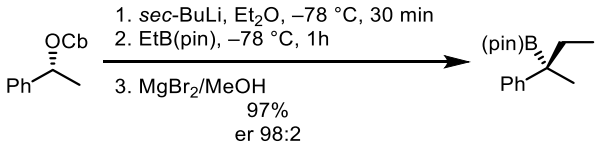
Prepared according to a literature procedure.[2]

(*S*)-4,4,5,5-Tetramethyl-2-(3-methyl-1-phenylpentan-3-yl)-1,3,2-dioxaborolane [(*S*)-S2]



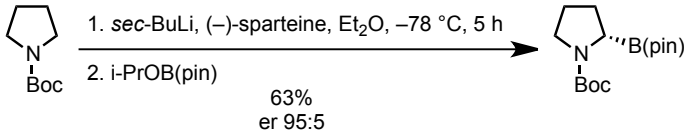
Prepared according to a literature procedure.[3]

(*R*)-4,4,5,5-Tetramethyl-2-(2-phenylbutan-2-yl)-1,3,2-dioxaborolane [(*R*)-S3]



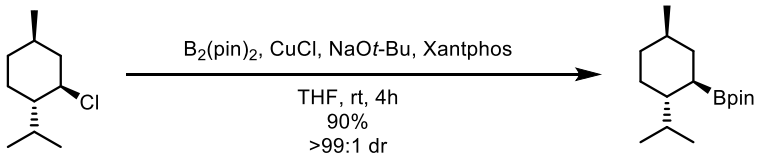
Prepared according to a literature procedure.[4]

(*S*)-*tert*-Butyl 2-(4,4,5,5-Tetramethyl-1,3,2-dioxaborolan-2-yl)pyrrolidine-1-carboxylate [(*S*)-S4]



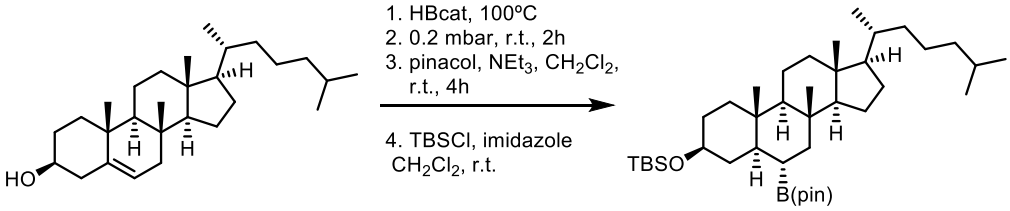
Prepared according to a literature procedure.[5]

***(1S, 2R, 5R)*-2-isopropyl-5-methylcyclohexyl boronic ester [S5]**



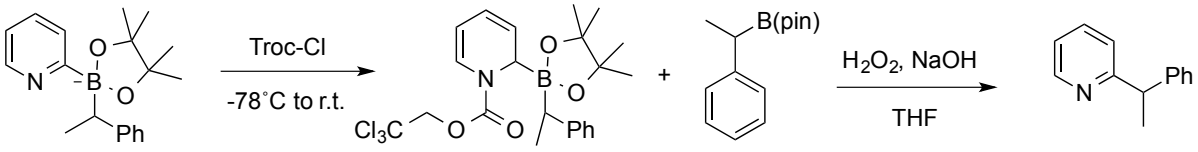
Prepared according to a literature procedure.[6]

***tert*-Butyl(((3*S*,5*R*,6*S*,8*R*,9*S*,10*S*,13*R*,14*S*,17*R*)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)-6-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)hexadecahydro-1H-cyclopenta[α]phenanthren-3-yl)oxy)dimethylsilane (S6)**



3. Optimization

Upon the borono-ate complex in THF at -78ºC (follow by ^{11}B NMR), Troc-Cl was added at that temperature and stirred under reaction conditions. The crude was diluted in Et_2O and H_2O was added, the layers were separated and the aqueous phase was extracted with Et_2O (x2). The volatiles were removed under vacuum and the residue was filtered over a pad of silica gel and rinse with hexane:EtOAc (8:2). The mixture was diluted in $CDCl_3$ and the ratio of starting material and product was analysed by ^1H NMR.



DHPyr **8** **23**

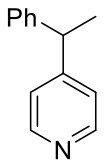
Entry	Activator	Equiv.	[M]/T (ºC)	DHPyr:8	Yield (%)[a]
1	Troc-Cl	1.1	0.15 M/-78 ºC→r.t	25:75	n.d.
2	Troc-Cl	1.5	0.15 M/-78 ºC→r.t	41:59	n.d.
3	Troc-Cl	2	0.15 M/-78 ºC→r.t	65:35	55
4[b]	Troc-Cl	2	0.15 M/-78 ºC→r.t	51:49	n.d.
5	Troc-Cl	2	0.15 M/-78 ºC→-40 ºC	49:51	n.d.
6	*p*-$NO_2C_6H_4OC(O)Cl$	2	0.15 M/-78 ºC→r.t	44:66	n.d.
7	MeOC(O)Cl	2	0.15 M/-78 ºC→r.t	50:50	n.d.
8	Troc-Cl	2	0.25 M/-78 ºC→r.t	86:14	68

[a] Isolated yield of **23** after oxidation. [b] Troc-Cl was added in THF (0.5 mL) dropwise. n.d.: not determined

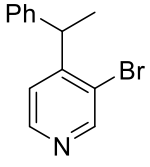
After the boron-ate complex formation, THF was removed under vacuum and dissolved in another solvent (CH_2Cl_2, $CHCl_3$, Et_2O, hexane, toluene) before Troc-Cl was added. In all cases, the reaction was less effective than THF.

4. Procedure and data analysis

4-(1-Phenylethyl)pyridine (15). *n*-BuLi (0.3 mL, 0.5 mmol, 1.6 M in hexane) was added by dropwise to a solution of 4-iodopyridine (102 mg, 0.5 mmol) in THF (2 mL) at -78 ºC over 20 minutes and the reaction mixture was stirred at -78 ºC for 2 hours.[7] A solution of **8** (90 mg, 0.4 mmol) in THF (0.5 mL) was added by dropwise and the mixture was stirred for 1 hour at -78 ºC. Troc-Cl (138 μl, 1 mmol) was added and the mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (9:1). The residue was evaporated, taken up in THF (2 mL) and cooled to 0 ºC. NaOH (1 mL, 2M) and H_2O_2 (1 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 8:2 to 7:3) gave **15** as a colourless oil (60 mg, 66%). **Rf** (Hexane:EtOAc = 1:1) = 0.45. **FT-IR (neat) υ** = IR 3062, 3027, 2970, 2876, 2932, 1595, 1494, 1451, 1413, 829, 699 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 8.50-8.48 (m, 2H), 7.34-7.28 (m, 2H), 7.25-7.17 (m, 3H), 7.15-7.13 (m, 2H), 4.12 (q, 1H, *J* = 7.2 Hz), 1.64 ppm (d, 3H, *J* = 7.2 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** 155.2, 149.6, 144.3, 128.6, 127.6, 126.6, 123.0, 44.2, 21.0 ppm. **GC-MS:** 184, 183, 182, 169, 168, 167, 139, 115, 105, 77, 51 *m/z*. **HRMS (EI)** calc. for $[M]^+$ $C_{13}H_{13}N$ 183.1048, found 183.1052. Experimental data match with the reported previously in the literature.[8]

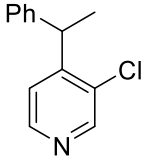


3-Bromo-(1-phenylehtyl)pyridine (16). A solution of (^{i}Pr)$_2$NH (70 μl, 0.5 mmol) in THF (1 mL, 0.5 M) was cooled to -78 ºC, treated with *n*-BuLi (0.33 mL, 1.6 M in hexane, 0.55 mmol) stirred at -78 ºC for 1 hour. A solution of 3-bromopyridine (47 μl, 0.5 mmol) in THF (0.5 mL) was added by dropwise and the mixture was stirred at -78 ºC for 30 minutes.[9] A solution of **8** (58 mg, 0.25 mmol) in THF (1 mL) was added and the miture was stirred for 2 hours at -78 ºC. Troc-Cl (138 μl, 1 mmol) was added and the mixture was stirred at -78 ºC for 12 hours and then allowed to warm to



room temperature overnight. The mixture was diluted with Et_2O and H_2O, the layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2), the combined organic layers were dried over $MgSO_4$, filtered and evaporated.and, the solvent was removed under vacuum. The residue was evaporated, taken up in THF (2 mL) and cooled to 0 ºC. NaOH (1 mL, 2M) and H_2O_2 (1 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1 to 8:2) gave **16** as a colorless oil (43 mg, 66%). **Rf** (hexanes:EtOAc, 7:3) = 0.6. **FT-IR (neat)** υ : 3090, 3063, 3029, 2972, 2933, 2876, 3063, 1579, 1496, 1451, 1398, 1089, 1019, 699 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 8.67 (s, 1H), 8.42 (d, 1H, *J* = 5.2 Hz), 7.34-7.29 (m, 2H), 7.26-7.20 (m, 3H), 7.13 (d, 1H, *J* = 5.2 Hz), 4.57 (q, 1H, *J* = 7.3 Hz), 1.62 (d, 3H, *J* = 7.3 Hz) ppm. **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 154.3, 151.9, 148.2, 142.8, 129.0, 127.8, 126.8, 123.7, 123.2, 43.3, 20.5 ppm. **GC-MS**: 263, 261, 248, 246, 182, 181, 166, 165, 152, 139, 105, 77, 51 *m/z*. **HRMS (EI)** calc. for $[M]^+$ $C_{13}H_{12}NBr$ 261.0153, found: 261.0147.

3-Chloro-4-(1-phenylehtyl)pyridine (17). 17 was obtained following the same experimental procedure reported for **16** but using 3-chloropyridine (47 μL, 0.5 mmol). Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1 to 8:2) gave **17** as a colorless oil (56 mg, 89%). **Rf** (hexane:EtOAc, 8:2) = 0.5. **FT-IR (neat) υ** = 3087, 3062, 3028, 2972, 2932, 2876, 2857, 1583, 1451, 1398, 1096, 1028, 837, 697 cm^{-1}. **^{1}H NMR (300 MHz, $CDCl_3$):** δ = 8.46 (brs, 1H), 8.35-8.30 (m, 1H), 7.32-7.06 (m, 6H), 4.53 (q, 1H, *J* = 7.5 Hz), 1.56 (d, 3H, *J* = 7.3 Hz). **^{13}C NMR (75 MHz, $CDCl_3$):** δ = 152.3, 149.5, 147.9, 142.9, 128.8, 127.7, 126.8, 126.8, 123.1, 40.7, 20.3 ppm. **GC-MS:** 219, 218, 217, 203, 204, 203, 202, 201, 182, 167, 166, 152, 140, 139, 105, 77 *m/z*. HRMS (EI) calc. for [M]+ $C_{13}H_{12}ClN$ 217.0658, found 217.0656.



(*R*)-3-Fluoro-4-(1-phenylehtyl)pyridine (18). 18 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (50 μL, 0.5 mmol) and (*R*)-**8** (93 mg, 0.4 mol) and carrying out the lithiation step at -60 ºC. Purification by flash chromatography on silica gel (hexanes:EtOAc, 19:1 to 8:2) gave **18** as a colorless oil (67 mg, 95%). $[\alpha]_D^{20}$ = (c 0.5, $CHCl_3$) + 14. **Rf** (hexanes: EtOAc, 8:2) = 0.35. **FT-IR (neat) υ:** 3060, 3029, 2973, 2931, 2880, 1601, 1490, 1452, 1415, 1244, 1196, 837, 699 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 8.30 (d, 1H, *J* = 1.9 Hz), 8.26 (d, 1H, *J* = 5.1 Hz), 7.28-7.23 (m, 2H), 7.20-7.16 (m, 3H), 7.08 (dd, 1H, *J* = 6.2, 5.0 Hz), 4.51 (q, 1H, *J* = 7.3 Hz), 1.59 ppm (d, 3H, *J* = 7.3 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 157.8 (d, *J* = 255.5 Hz), 145.8 (d, *J* = 5.1 Hz), 143.0, 141.8 (d, *J* = 12.1 Hz), 137.9 (d, *J* = 25.0 Hz), 128.6, 127.5, 126.8, 122.9 (d, *J* = 2.0 Hz), 37.3, 20.0. **^{19}F NMR (283 MHz)** δ = -132.0 ppm (d, *J* = 6.4 Hz). **GC-MS**: 202, 201, 182, 186, 185, 159, 133, 105, 92, 77, 63, 51 *m/z*. **HRMS (EI)** calc. for $[M]^+$ $C_{13}H_{12}NF$ 201.0954, found 201.0954. Resolution between the enantiomers was achieved using chiral HPLC system fitted with a Chiralpack IB column with guard as stationary phase with hexane:iPrOH (99:1) as the mobile phase at flow rate of 0.5 ml/min, 220 nm. t_{Rminor} = 19 min, t_{Rmajor} = 20 min, er = 98:2, es = 100%

3-Chloro-5-fluoro-4-(1-phenylethyl)pyridine (19). 19 was obtained following the same experimental procedure reported for **15** but using 3-chloro-5-fluoropyridine (65 mg, 0.5 mmol).[10] Purification by flash chromatography on silica gel (hexanes:EtOAc, 19:1 to 9:1) gave **19** as a colorless oil (91 mg, 97%). **Rf** (8:2, hexanes:EtOAc) = 0.7. **FT-IR (neat)** υ = 3060, 3028, 2974, 2940, 2882, 1405, 1260, 899, 881, 744, 696 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 8.37 (s, 1H), 8.23 (d, 1H, *J* = 1.7 Hz), 7.30-7.17 (m, 5H), 4.75 (q, 1H, *J* = 7.1 Hz), 1.72 (dd, 1H, *J* = 7.3, 1.6 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 158.3 (d, *J* = 259 Hz), 145.5 (d, *J* = 4.4 Hz), 141.2, 140.0 (d, *J* = 13.2 Hz), 137.1 (d, *J* = 24.6 Hz), 128.4, 127.2 (d, *J* = 2.1 Hz), 126.8, 38.0, 17.4 (d, *J* = 4.0 Hz). **^{19}F (283 MHz, $CDCl_3$)** δ = 125.6 ppm. **GC-MS:** 237, 236, 235, 222, 220, 200, 198, 185, 184, 170, 158, 157, 129, 105, 98, 79, 68, 57 *m/z*. **HRMS (EI)** calc. $[M]^+$ $C_{13}H_{11}ClFN$ 235.0564, found 235.0555.

***N,N*-diisopropyl-4-(1-phenylethyl)nicotinamide (20).** *n*-BuLi (0.9 mL, 1.6 M in hexane, 1.5 mmol) was added by dropwise to a solution of TMP (0.25 mL, 0.25 mmol) in DME (6 mL) at -50 ºC over 20 minutes and the reaction mixture was stirred at -78 ºC for 30 min.[11] A solution of amide (132 mg, 0.6 mmol) in DME (1 mL) was added and stirred for 20 minutes. A solution of **8** (165 mg, 0.8 mmol) in THF (3 mL) was added by dropwise and the mixture was stirred for 1.5 hour at -78 ºC. Troc-Cl (0.25 mL, 2 mmol) was added and the mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (7:3). The residue was evaporated, taken up in THF (2 mL) and cooled to 0 ºC. NaOH (1 mL, 2M) and H_2O_2 (1 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 3:2 to 1:1) gave **20** as a colourless oil (138 mg, 58%). **Rf** (hexanes:EtOAc, 6:4) = 0.2. **FT-IR (neat) υ** = 3024, 2970, 2931, 2879, 1629, 1586, 1440, 1339, 1030 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$, rotamers):** δ = 8.54 (d, 0.7H, *J* = 5.3 Hz, *major rot.*), 8.40 (d, 0.3H, *J* = 5.8 Hz, *minor rot.*), 8.34 (s, 0.3H, *minor rot.*), 8.31 (s, 0.7H, *major rot.*), 7.37-7.33 (m, 1H, *2 rot.*), 7.29-7.20 (m, 2H, *2 rot.*), 7.19-7.13 (m, 1H, *2 rot.*), 7.09-7.04 (m, 2H, *2 rot.*), 4.58 (q, 0.7H, *J* = 7.6 Hz, *major rot.*), 4.31 (q, 0.3H, *J* = 7.2 Hz, *minor rot.*), 3.73 (sept, 0.3H, *J* = 6.6 Hz, *minor rot.*), 3.54 (sept, 0.3H, *J* = 6.9Hz, *major rot.*), 3.57-3.25 (m, 1.4H, *major rot.*), 1.60-1.56 (m, 4.5H, *minor rot.*), 1.49 (d, 2.1H, *J* = 7.0 Hz, *major rot.*), 1.44 (d, 2.1H, *J* = 6.7 Hz, *major rot.*), 1.17 (d, 2.1H, *J* = 7.1 Hz, *major rot.*), 1.03 (d, 2.1H, *J* = 7.1 Hz, *major rot.*), 0.36 (d, 2.1H, *J* = 6.5 Hz, *major rot.*). **^{13}C NMR (100 MHz, $CDCl_3$, rotamers):** δ = 167.7 (*minor rot.*), 167.6 (*major rot.*), 153.2 (*minor rot.*), 152.2 (*major rot.*), 149.3 (*major rot.*), 149.2 (*minor rot.*), 145.6 (*major rot.*), 145.6 (*minor rot.*), 144.6 (*major rot.*), 143.1 (*minor rot.*), 134.3 (*major rot.*), 133.5 (*minor rot.*), 128.9 (*major rot.*), 128.6 (*minor rot.*), 127.7 (*major rot.*), 127.7 (*minor rot.*), 126.8 (*minor rot.*), 126.7 (*major rot.*), 123.2 (*minor rot.*), 122.9 (*major rot.*), 51.2 (*minor rot.*), 51.2 (*major rot.*), 46.3 (*minor rot.*), 46.2 (*major*

rot.), 40.4 (*major rot.*), 40.0 (*minor rot.*), 24.9 (minor *rot.*), 22.4 (major *rot.*), 21.0 (minor *rot.*), 20.9 (*major rot.*), 20.7 (*minor rot.*), 20.7 (*minor rot.*), 20.5 (*minor rot.*), 20.5 (*major rot.*), 20.5 (*major rot.)*, 19.7 (*major rot.*). **GC-MS:** 310, 309, 267, 210, 209, 195, 180, 167, 152, 139, 104, 77, 58. **HRMS (EI)** calc. for $[M]^+$ $C_{20}H_{26}N_2O$ 310.2045, found 310.2041.

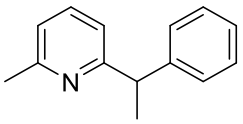
3-Methyl-4-(1-phenylethyl)pyridine (21). A solution of 4-bromo-3-methylpyridine (0.5 mL, 0.5 mmol) in THF (4 mL) was cooled to -78 ºC and *t*-BuLi (0.65 mL, 1 mmol) was added by dropwise. The mixture was stirred at –78 ºC for 30 minutes and a solution of **8** (60 mg, 0.26 mmol) in THF (0.7 mL) was added. The mixture was stirred at -78 ºC for 1 hour and then Troc-Cl (138 μL, 1 mmol) was added. The mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (9:1). The residue was evaporated, taken up in THF (1 mL) and cooled to 0 ºC. NaOH (1 mL, 2M) and H_2O_2 (1 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 7:3 to 6:4) gave **21** as a colourless oil (30 mg, 61%). **Rf** (hexanes:EtOAc, 8:2) = 0.2. **FT-IR (neat)** υ = 3061, 3025, 2968, 2929, 2874, 1591, 1493, 1450, 1404, 1028, 837, 670 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$):** 8.43 (d, 1H, *J* = 5.1 Hz), 8.35 (s, 1H), 7.31-7.28 (m, 2H), 7.23-7.19 (m, 1H), 7.18 (d, 1H, *J* = 5.2 Hz), 7.14 (m, 2H), 4.28 (q, 1H, *J* = 7.2 Hz), 2.21 (s, 3H), 1.62 (dd, 3H, *J* = 7.2, 1.1 Hz). **^{13}C NMR (125 MHz, $CDCl_3$):** 152.7, 150.8, 147.8, 144.2, 131.6, 128.5, 127.6, 126.4, 121.4, 40.8, 21.3, 16.4. **GC-MS:** 197, 183, 182, 181, 180, 167, 152, 139, 128, 119, 105, 91, 77, 65, 51 *m/z*. **HRMS (EI)** calc. for $[M+H]^+$ $C_{14}H_{16}N$ 198.1283, found 198.1279. Experimental data match with the reported in the literature.[12]

2-Chloro-4-(1-phenylethyl)pyridine (22). A solution of 4-bromo-2-chloropyridine (56 μl, 0.5 mmol) in Et_2O (2.5 mL) was cooled to -78 ºC and *n*-BuLi (0.31 mL, 0.5 mmol, 1.6 M) was added by dropwise.[13] The mixture was stirred at –78 ºC for 2 h and a solution of **8** (60 mg, 0.26 mmol) in THF (0.7 mL) was added. The mixture was stirred at -78 ºC for 1.5 hour and then Troc-Cl (138 μL, 1 mmol) was added. The mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (9:1). The residue was evaporated, taken up in THF (1 mL) and cooled to 0 ºC. NaOH (0.5 mL, 2M) and H_2O_2 (0.5 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1) gave **22** as a colourless oil (151 mg, 83%). **Rf** (hexanes:EtOAc) = 0.5. **FT-IR (neat) υ** = 3059, 3027, 2971, 2933, 2876, 1589, 1542, 1464, 1452, 1385, 1987, 1844, 698 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$):** δ = 8.26 (d, 1H, *J* = 5.2 Hz), 7.35-7.31 (m, 2H), 7.25 (tt, 1H, *J* = 7.3, 2.0 Hz), 7.19-7.17 (m, 3H), 7.05 (dd, 1H, *J* = 5.1, 1.4 Hz), 4.10 (q, 1H, *J* = 7.3 Hz), 1.64 (d, 3H, *J* = 7.4 Hz). **^{13}C NMR (125 MHz, $CDCl_3$)** δ = 158.8, 152.0, 149.8, 143.8, 129.0, 127.8 127.1, 123.5, 122.1, 44.3, 21.1. **GC-MS:** 219, 218, 217, 204, 203, 202, 182, 167, 166, 140, 139, 105, 77, 51 cm^{-1}. **HRMS (EI)** calc. for $[M]^+$ $C_{13}H_{12}ClN$ 217.0658, found 217.0659. Experimental data match with the reported in the literature.[14]

(*R*)-2-(1-Phenylethyl)pyridine (23). A solution of 2-bromopyridine (0.5 mL, 0.5 mmol) in THF (1 mL) was cooled to -78 ºC and *n*-BuLi (0.3 mL, 0.5 mmol, 1.6 M in hexane) was added by dropwise over 20 min.[15] The mixture was stirred at –78 ºC for 30 min and a solution of (*R*)-**8** (68 mg, 0.3 mmol) in THF (0.7 mL) was added. The mixture was stirred at -78 ºC for 1 hour and then Troc-Cl (138 μL, 1 mmol) was added. The mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was

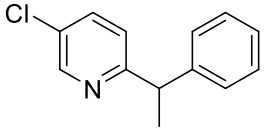
extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (9:1). The residue was evaporated, taken up in THF (1 mL) and cooled to 0 ºC. NaOH (0.5 mL, 2M) and H_2O_2 (0.5 mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1 to 8:2) gave **23** as a colourless oil (62 mg, 68%). **Rf** (hexane:EtOAc, 8:2) = 0.35. $[\alpha]_D^{20}$ = (c 0.4, cyclohexane) = -55. $[\alpha]_D^{20}$ = (c 2.8, cyclohexane) = +60 for the *S*-enantiomer.[16] **FT-IR (neat) υ** = 3061, 3026, 3005, 2969, 2930, 2873, 1589, 1472, 1432, 748 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$):** δ = 8.56 (d, 1H, *J* = 4.9 Hz), 7.57 (td, 1H, *J* = 8.0, 1.9 Hz), 7.32-7.30 (m, 4H), 7.21 (m, 1H), 7.13 (d, 1H, *J* = 7.9 Hz), 7.10 (dd, 1H, *J* = 7.6, 5.0 Hz), 4.31 (q, 1H, *J* = 7.2 Hz), 1.72 (d, 3H, *J* = 7.2 Hz). **^{13}C NMR (125 MHz, $CDCl_3$):** 165.0, 149.1, 145.1, 136.4, 128.5, 127.7, 126.6, 122.1, 121.2, 47.4, 20.7. **GC-MS:** 183, 182, 167, 139, 106, 78, 77, 51 cm^{-1}. **HRMS (ESI)** $[M+H]^+$ calc. for $C_{13}H_{14}N$ 184.1121, found 184.1118. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack AD-H column without guard as stationary phase with n-hexane:iPrOH (10% in hexanes) (99.5:0.5) as the mobile phase at flow rate of 1 $ml \cdot min^{-1}$,. tr_{minor} = 18.4 min, tr_{major} 19 min. e.r. = 97:3, es =100%.

2-Methyl-6-(1-phenylethyl)pyridine (24). A solution of 2-bromopyridine (2-methyl-6-bromopyridine (85 μL, 0.5 mmol)) in toluene:Et_2O (1.3 mL: 0.9 mL) was cooled to -95 ºC and *n*-BuLi (0.3 mL, 0.5 mmol, 1.6 M in hexane) was added by dropwise over 20 min.[15] The mixture was stirred at –78 ºC for 30 min and a solution of **8** (81 mg, 0.35 mmol) in THF (1 mL) was added. The mixture was stirred at -78 ºC for 1 hour and then Troc-Cl (138 μL, 1 mmol) was added. The mixture was allowed to warm to room temperature overnight. The crude was diluted with Et_2O and H_2O was added. The layers were separated and the aqueous phase was neutralized with saturated aqueous $NaHCO_3$ solution. The aqueous layer was extracted with Et_2O (x2) and the combined organic layers were dried over $MgSO_4$, filtered and evaporated. The residue was filtered over a short pad of silica gel eluting with hexane:EtOAc (9:1). The residue was evaporated, taken up in THF (1 mL) and cooled to 0 ºC. NaOH (0.5 mL, 2M) and H_2O_2 (0.5

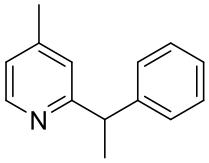


mL, 30%) were added and the mixture was stirred for 12 hours at room temperature. Et_2O was added, the layers were separated and the aqueous phase was acidified with aqueous HCl solution (1M) and extracted with Et_2O (x2). The aqueous phase was neutralized with saturated solution of $NaHCO_3$ and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$, filtered and evaporated. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1 to 8:2) gave **24** as a colourless oil (59 mg, 56% yield). **Rf** (hexanes:EtOAc, 8:2) = 0.5. **FT-IR (neat) υ** = 3061, 3026, 2928, 2966, 2871, 1588, 1575, 1452, 745, 698 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$):** δ = 7.43 (t, 1H, *J* = 7.6 Hz), 7.37-7.26 (m, 4H), 7.22-7.17 (m, 1H), 6.94 (d, 1H, *J* = 7.6 Hz), 6.86 (d, 1H, *J* = 7.6 Hz), 4.28 (q, 1H, *J* = 7.3 Hz), 2.54 (s, 3H), 1.68 ppm (d, 3H, *J* = 7.3 Hz). **^{13}C NMR (125 MHz):** 164.9, 157.8, 145.3, 136.8, 128.6, 128.0, 126.4, 120.9, 118.8, 47.7, 24.8, 21.2 ppm. **GC-MS** = 197, 196, 182, 181, 180, 167, 120, 93, 77, 65, 51 *m/z*. **HRMS (EI)** [M]+ for $C_{14}H_{15}N$ 197.1204, found 197.1201.

5-chloro-2-(phenyletyl)pyridine (25). 25 was obtained following the same experimental procedure reported for **24** but using 2-bromo-5-chloropyridine (80 mg, 0.5 mmol). Purification by flash chromatography on silica gel (toluene:dichloromethane, 8:2) gave **25** as a colorless oil (58 mg, 54%). **Rf** (hexanes:EtOAc, 8:2) = 0.7. **FT-IR (neat) υ:** 3063, 3027, 2969, 2929, 2869, 2851, 1577, 1494, 1468, 1453, 1375, 1111, 1013, 838, 758 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$):** δ = 8.54 (dd, 1H, *J* = 2.6, 0.7 Hz), 7.54 (dd, 1H, *J* = 8.4, 2.5 Hz), 7.33-7.27 (m, 4H), 7.22 (m, 1H), 7.08 (d, 1H, *J* = 8.4 Hz), 4.28 (q, 1H, *J* = 7.1 Hz), 1.70 (d, 3H, *J* = 7.1 Hz). **^{13}C NMR (125 MHz, $CDCl_3$):** δ = 163.2, 147.9, 144.6, 136.1, 129.5, 128.0, 127.6, 126.5, 122.9, 46.8, 20.7. **GC-MS:** 219, 218, 217, 216, 204, 203, 202, 201, 186, 167, 166, 152, 140, 113, 105, 91, 78, 51 *m/z*. **HRMS (EI) [**$M]^+$ for $C_{13}H_{12}NCl$ calc. 217.0658, found: 217.0651.



4-Methyl-2-(1-phenylethyl)pyridine (26). 26 was obtained following the same experimental procedure reported for **24** but using 2-bromo-4-methyhlpyridine (55 μl, 0.5 mmol). Purification by flash chromatography on silica gel (toluene:dichloromethane, 8:2) gave **26** as a colorless oil (19 mg, 47%). **Rf** (hexane:EtOAc, 8:2) 0.5. **FT-IR (neat) υ** = 3085, 3059, 3026, 2967, 2927, 2872, 1602, 1451, 826 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ = 8.40 (d, 1H, *J* = 5.2 Hz), 7.30-7.27 (m, 4H), 7.18 (m, 1H), 6.90 (d, 1H, *J* = 5.2 Hz), 6.92 (s, 1H), 4.24 (q, 1H, *J* = 7.3 Hz), 2.26 (s, 3H), 1.67 (d, 3H, *J* = 7.3 Hz). **^{13}C NMR (125 MHz, $CDCl_3$)**: δ = 164.8, 148.8,



147.4, 145.2, 128.4, 127.7, 126.2, 122.9, 122.3, 47.2, 21.1, 20.8. **GC-MS:** 183, 182, 167, 139, 106, 78, 77, 51 *m/z*. **HRMS (ESI)** $[M+H]^+$ for $C_{14}H_{15}N$ calc. 198.1277, found 198.1277. Experimental data match with the reported in the literature.[17]

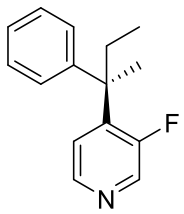
3-Fluoro-4-phenylpyridine (28). 28 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (140 μL, 1 mmol) and phenyl boronic ester (160 mg, 0.8 mmol) and carrying out the lithiation step at -60 ºC. Purification by flash chromatography on silica gel (hexanes:EtOAc, 19:1 to 8:2) gave **28** as a solid (110 mg, 82%). **Rf** (hexanes:EtOAc, 7:3) 0.45. **FT-IR (neat) υ** = 3063, 3028, 2955, 2929, 2862 1733, 1606, 1496, 1454, 1515, 1248, 1197, 754 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)**: δ = 8.53 (d, 1H, *J* = 2.5 Hz), 8.46 (dd, 1H, *J* = 4.9, 0.8 Hz), 7.62-7.58 (m, 2H), 7.51-7.44 (m, 3H), 7.39 (ddd, 1H, *J* = 6.8, 5.0, 0.4 Hz). **^{13}C NMR (500 MHz, $CDCl_3$):** δ = 165.5 (d, *J* = 165.5 Hz), 145.0 (d, *J* = 5.3 Hz), 139.0 (d, *J* = 25.7 Hz), 138.0, 136.1 (d, *J* = 11.2 Hz), 132.9, 129.2, 128.8, 124.2. **^{19}F NMR (283 MHz):** δ = -132.9. **HRMS (EI)** $[M]^+$ calc. for $C_{11}H_8NF$ 173.0641, found 173.0647. Experimental data (IR, ^{1}H and ^{13}C NMR) matched with reported in the literature.[18]

3-Fluoro-4-phenethylpyridine (29). 29 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (70 μL, 0.5 mmol) and **xx** (82 mg, 0.35 mmol) and carrying out the lithiation step at -60 ºC. Purification by flash chromatography on silica gel (hexanes:EtOAc, 8:2 to 7:3) gave **29** as a solid (67 mg, 96%). **Rf** (hexanes:EtOAc, 8:2) : 0.26. **FT-IR (neat) υ** = 3028, 3066, 2929, 1607, 1496, 1454, 1415, 1247, 1197, 836, 753, 699 cm^{-1}. **^{1}H NMR (400 MHz):** δ = 8.38 (d, 1H, *J* = 1.6 Hz), 8.27 (dd, 1H, *J* = 7.4, 0.7 Hz), 7.29 (dd, 2H, *J* = 7.4, 1.4 Hz), 7.21 (tt, 1H, *J* = 7.4, 2.1 Hz), 7.16 (d, 2H, *J* = 7.6, 1.4 Hz), 7.06 (dd, 1H, *J* = 6.3, 5.0 Hz), 3-01-2.91 (m, 4H). **^{13}C NMR (100 MHz):** 158.7 (d, *J* = 254.5 Hz), 145.7 (d, *J* = 5.2 Hz), 140.6, 138.0 (d, *J* = 25.1 Hz), 137.3 (d, *J* = 13.8 Hz), 128.7, 128.6, 126.6, 125.3 (d, *J* = 2.2 Hz), 35.5 (d, *J* = 1.1 Hz), 30.5 (d, *J* = 1.8 Hz). **^{19}F NMR (283 MHz)** = -133.2 (d, *J* = 6.5 Hz). **GC-MS**: 202, 201, 92, 91, 65 *m/z*. **HRMS (EI)** $[M]^+$ calc. for $C_{13}H_{12}NF$ calc. 201.0954, found 201.0953.

(*S*)-3-Fluoro-4-(4-(4-methoxyphenyl)butan-2-yl)pyridine (30). 30 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (45 μl, 0.5 mmol) and (*S*)-**S1** (102 mg, 0.35 mmol)

and carrying out the lithiation step at -60 ºC and the oxidation for 6 h. Purification by flash chromatography on silica gel (hexanes:EtOAc, 8:2 to 7:3) gave **30** as a solid (72 mg, 79%). $[\alpha]_D^{20}$ (c = 1.4, $CDCl_3$) = -49. **Rf** (hexanes:EtOAc, 7:3) = 0.4. **FT-IR (neat)** υ = 2963, 2931, 2859, 1768, 1610, 1512, 1458, 1415, 1245, 1178, 1037, 828, 721 cm^{-1}. **^{1}H NMR ($CDCl_3$, 400 MHz):** δ = 8.37 (d, 1H, *J* = 2.0 Hz), 8.34 (d, 1H, *J* = 5.0 Hz), 7.17 (dd, 1H, *J* = 6.3, 5.0 Hz), 7.05-7.03 (m, 2H), 6.83-6.79 (m, 2H), 3.78 (s, 3H), 3.10 (sext, 1H, *J* = 6.9 Hz), 2.52 (ddd, 1H, *J* = 13.8, 9.5, 6.9 Hz), 2.45 (ddd, 1H, *J* = 13.9, 9.5, 5.9 Hz), 1.99-1.82 (m, 2H), 1.29 (d, 3H, *J* = 7.0 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** δ = 158.5 (d, *J* = 254.3 Hz), 158.0, 146.1 (d, *J* = 5.1 Hz), 142.7 (d, *J* = 13.6 Hz), 138.2 (d, *J* = 26.2 Hz), 133.8, 129.4, 122.8 (d, *J* = 2.0 Hz), 114.0, 55.5, 38.5, 33.0, 32.3, 20.0 ppm. **^{19}F (283 MHz)** = -132.9 (d, *J* = 5.2 Hz). **GC-MS:** 260, 259, 258, 230, 229, 135, 134, 122, 121, 91, 78, 77, 65, 51 *m/z*. **HRMS (EI)** $[M]^+$ calc. for $C_{16}H_{18}NOF$ 259.1372, found 259.1367. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack IB column with guard as stationary phase with n-hexane:iPrOH (98.5:1.5) as the mobile phase at flow rate of 0.5 $ml \cdot min^{-1}$, λ = 220 nm. tr_{major} = 26 min, tr_{minor} = 29 min. e.r. = 96:4, es = 100%.

(*R*)-3-Fluoro-4-(2-phenylbutan-2-yl)pyridine (31). 31 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (45 μl, 0.5 mmol) and (*R*)-**S3** (102 mg, 0.35 mmol) and carrying out the lithiation step at -60 ºC and the oxidation for 10 h. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1) gave **31** as an oil (72 mg, 81%). **Rf** (hexane:EtOAc, 8:2) = 0.4**. FT-IR (neat)** υ = 3049, 3026, 2973, 2939, 2881, 1488, 1412, 1242, 1210, 829 cm^{-1}. $[\alpha]_D^{20}$ (c 1, $CHCl_3$) = + 8. **^{1}H NMR (500 MHz, $CDCl_3$):** 8.39 (dd, 1H, *J* = 5.1, 0.6 Hz), 8.26 (d, 1H, *J* = 3.6 Hz), 7.32 (dd, 1H, *J* = 7.0, 5.1 Hz), 7.30-7.26 (m, 2H), 7.20 (tt, 1H, *J* = 7.3, 1.3 Hz), 7.16-7.13 (m, 2H), 2.29 (dq, 1H, *J* = 13.5, 7.3 Hz), 2.12 (dq, 1H, *J* = 13.5, 7.3 Hz), 1.65 (s, 3H), 0.74 (t, 3H, *J* = 7.3 Hz). **^{13}C NMR (125 MHz):** 158.3 (d, *J* = 258.5 Hz), 146.9, 145.6 (d, *J* = 5.0 Hz), 144.6 (d, *J* = 9.0 Hz), 138.9 (d, *J* = 27.1 Hz), 128.2, 126.2 (d, *J* = 1.0 Hz), 126.1, 123.0 (d, *J* = 2.3 Hz), 45.2, 32.1, 25.1, 8.9 ppm. **^{19}F NMR (283 MHz) :** –123.1. **GC-MS** = 229, 201, 200, 185, 170, 152, 122, 103, 91, 77, 63, 51 *m/z*. **HRMS (EI)** [M]+ calc. for $C_{15}H_{16}NF$ 229.1267, found 229.1262. Resolution between the enantiomers was achieved using a reverse phase HPLC system fitted with a OJ-RH column without as stationary phase with MeCN:H_2O (75:35) as



the mobile phase at flow rate of 0.5 ml·min^{-1}, λ = 220 nm. tr_{minor} = 7.8 min, tr_{major} = 8.7 min. e.r. = 98:2, es = 100%.

(*S*)-3-Fluoro-4-(3-methyl-1-phenylpentan-3-yl)pyridine (32). 32 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (45 μl, 0.5 mmol) and (*S*)-**S2** (100 mg, 0.35 mmol) and carrying out the lithiation step at -60 ºC and the oxidation for 6 h. Purification by flash chromatography on silica gel (hexanes:EtOAc, 9:1) gave **32** as an oil (76 mg, 84%). **Rf** (hexane:EtOAc, 8:2) 0.55. $[\alpha]_D^{20}$ (c 1, $CHCl_3$) = -25. **FT-IR (neat) υ** = 3027, 2968, 2879, 2934, 1387, 1410, 1217, 834, 746 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$) :** 8.37 (d, 1H, *J* = 4.4 Hz), 8.35 (dd, 1H, *J* = 5.4, 0.9 Hz), 7.28-7.23 (m, 2H), 7.20-7.14 (m, 2H), 7.11-7.14 (m, 2H), 2.48 (dt, 1H, *J* = 14.2, 6.6 Hz), 2.30-2.17 (m, 2H), 1.99 (dqd, 1H, *J* = 15.0, 7.8, 1.3 Hz), 1.87 (dtd, 1H, *J* = 14.2, 6.7, 1.0 Hz), 1.67 (dq, 1H, *J* = 15.0, 7.5 Hz), 1.42 (s, 3H), 0,73 (t, 3H, *J* = 7.4 Hz). **^{13}C NMR (100 MHz, $CDCl_3$) :** 158.7 (d, *J* = 256.8 Hz), 145.7 (d, *J* = 4.7 Hz), 142.6 (d, *J* = 9.4 Hz), 142.2, 138.7 (d, *J* = 29.1 Hz), 128.4, 128.2, 125.8, 123.9 (d, *J* = 9.1 Hz), 42.5 (d, *J* = 4.2 Hz), 41.8 (d, *J* = 3.7 Hz), 33.2 (d, *J* = 3.3 Hz), 31.2, 23.0 (d, *J* = 2.0 Hz), 8.8 ppm. **^{19}F NMR (283 MHz):** -124.3 ppm. **GC-MS** = 257, 242, 228, 153, 152, 136, 124, 105, 104, 91, 77, 76, 65, 51 *m/z*. **HRMS (EI)** [M]+ calc. for $C_{17}H_{20}FN$ 257.1580, found 257.1592. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack IB column with guard as stationary phase with *n*-heptane:*i*PrOH (70:30) as the mobile phase at flow rate of 1 ml·min^{-1}, λ = 220 nm. tr_{major} = 5.6 min, tr_{minor} = 6.9 min. e.r. = 99:1, es = 100%.

(*S*)-*tert*-Butyl 2-(3-fluoropyridine-4-yl)pyrrolidine-1-carboxilate (33). 33 was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (45 μl, 0.5 mmol) and **S4** (100 mg, 0.35 mmol) and carrying out the lithiation step at -60 ºC and the oxidation for 6 h. Purification by flash chromatography on silica gel (hexanes:EtOAc, 6:4 to 4:6) gave **33** as an oil (63 mg, 69 %). **Rf** (hexane:EtOAc, 1:1) = 0.45. **FT-IR (neat) υ** = 2975, 2930, 2879, 1696, 1418, 1391, 1365, 1162 cm^{-1}. $[\alpha]_D^{20}$ (c 0.7, $CHCl_3$) = - 8.5. **^{1}H NMR (400 MHz, $CDCl_3$, rotamers):** 8.37 (brs, 1H), 8.34 (d, 1H, *J* = 4.3 Hz), 7.12-7.02 (m, 1H), 5.18 (m, 0.36H, *minor rot.*), 5.06-5.00 (m, 0.66H, *major rot.*), 3.65-3.50 (m, 2H), 2.44-2.31 (m, 1H), 1.94-1.78 (m, 3H), 1.45 (s, 3H, *minor rot.*), 1.20 (s, 3H, *major rot.*). **^{13}C NMR**

(125, $CDCl_3$, rotamers): 157.0 (d, *J* = 254 Hz), 154.3 (*minor rot.*), 154.0 (*minor rot.*), 145.7 (d, *J* = 4.9 Hz), 140.6 (d, *J* = 10.6 Hz, *major rot.*), 139.6 (d, *J* = 10.6 Hz, *minor rot.*), 137.9 (d, *J* = 24.2 Hz, *minor rot.*), 137.8 (d, *J* = 24.2 Hz, *major rot.*), 121.3, 80.0, 55.0 (*minor rot.*), 54.6 (*major rot.*), 47.2 (*minor rot.*), 46.9 (*major rot.*), 34.1 (*major rot.*), 32.9 (*minor rot.*), 28.4 (*minor rot.*), 28.1 (*major rot.*), 23.8 (*minor rot.*), 23.4 (*major rot.*). **^{19}F NMR (283 MHz):** 132.8 (brs, *1 rot., minor rot.*), 134 (d, *J* = 6.3 Hz, *1 rot., major rot.*). **GC-MS:** 211, 210, 193, 166, 165, 150, 138, 111, 70, 57 *m/z*. **HRMS (TOF)** $[M+H]^+$ $C_{14}H_{19}FN_2O_2$ calc. 267.1503, found 267.1516, $[M+Na]^+$ $C_{14}H_{19}FN_2NaO_2$ calc. 289.1321, found 289.1334. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack IA column with guard as stationary phase with n-hexane:iPrOH (99:1) as the mobile phase at flow rate of 0.7 ml·min^{-1}, λ = 220 nm. tr_{minor} = 9.4 min, tr_{major} = 10 min. e.r. = 98:2, es = 100%.

***(1S, 2R, 5R)*-2-isopropyl-5-methylcyclohexyl-3-fluoropyridine (34). 34** was obtained following the same experimental procedure reported for **16** but using 3-fluoropyridine (0.05 mL, 0.5 mmol) and **S5** (106 mg, 0.4 mmol) and carrying out the lithiation step at -60 ºC and the oxidation for 6 h. Purification by flash chromatography on silica gel (hexanes:EtOAc, 6:4 to 4:6) gave **35** as solid (67 mg, 72%). **Rf** (hexane:EtOAc, 8:2) = 0.46. $[\alpha]_D^{20}$ (c 1, $CHCl_3$) = -40. **FT-IR (neat) υ** = 2955, 2924, 2870, 1603, 1456, 1484, 1415, 1248, 1234, 830, 605 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** = 8.34 (d, 1H, *J* = 1.9 Hz), 8.29 (d, 1H, *J* = 5.2 Hz), 7.11 (t, 1H, *J* = 5.6 Hz), 2.88 (brs, 1H), 1.85-1.70 (m, 3H), 1.56-1.43 (m, 2H), 1.37 (dtd, 1H, *J* = 13.8, 7.0, 2.5 Hz), 1.26-0.96 (m, 3H), 0.89 (d, 3H, *J* = 6.8 Hz), 9.81 (d, 3H, *J* = 6.9 Hz), 9.67 (d, 3H, *J* = 6.9 Hz). **^{13}C NMR (125 MHz):** 158.1 (d, *J* = 252.7 Hz), 145.7 (d, *J* = 4.8 Hz), 141.7 (d, *J* = 12.6 Hz), 138.1 (d, *J* = 26.7 Hz), 122.5 (brs), 46.2, 43.1, 34.9, 12.9, 28.1, 24.4, 22.3, 21.4, 15.4. **^{19}F (283 MHz)** = -134.6 brs. **GC-MS** = 235, 192, 150, 135, 124, 111, 83, 69, 55 *m/z*. **HRMS (EI)** calc for $C_{15}H_{23}FN$ $[M+H]^+$ 236.1809, found 236.1808. dr (determined by ^{1}H NMR) >98:<2, ds = 100%.

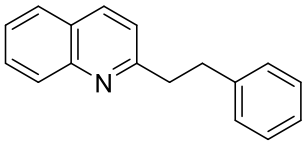
4-((3*S*,5*R*,6*S*,8*S*,9*S*,10*R*,13*R*,14*S*,17*R*)-3-((*tert*-Butyldimethylsilyl)oxy)-10,13-dimethyl-17-((*R*)-6-methylheptan-2-yl)hexadecahydro-1H-cyclopenta[α]phenanthren-6-yl)-3-fluoropyridine (35). 35 was obtained following the same experimental procedure reported for **23** but using **xx** (150 mg, 0.25 mmol). Purification by flash chromatography on silica gel (hexane:EtOAc, 20:1 to 9:1) gave **35** as colourless oil (105 mg, 72%). **Rf** (petroleum ether:EtOAc, 8:2) 0.75. $[\alpha]_D^{20}$ (c 2, $CHCl_3$) +15. **FT-IR (neat) υ** = 2931, 2853, 1470, 1414, 1382, 1098, 1082, 872, 838 cm^{-1}. **^{1}H NMR (400 MHz, C_6D_6)** = 8.36 (s, 0.25H, *minor rot.*), 8.35 (s, 0.75H, *major rot.*), 8.29 (d, 0.75H, *J* = 5.1 Hz, *major rot.*), 8.13 (d, 0.25H, *J* = 4.8 Hz, *minor rot.*), 6.68 (t, 0.75H, *J* = 5.7 Hz, *major rot.*), 6.23 (dd, 0.25H, *J* = 5.8, 5.2 Hz, *minor rot.*), 3.53 (tt, 0.25H, *J* = 10.4, 4.7 Hz, *minor rot.*), 3.38 (tt, 0.75H, *J* = 10.5, 5.6 Hz, *major rot.*), 2.97 (td, 0.75H, *J* = 12.0, 3.1 Hz, *major rot.*), 2.17 (td, 0.25H, *J*= 12.1, 3.2 Hz, *minor rot.*), 1.99-1.92 (m, 1H, *2 rot.*), 1.84-1.66 (m, 2H, *2 rot.*), 1.62-0.97 (m, 27H, *2 rot.*), 0.89-0.88 (m, 4H, *2 rot.*), 0.88-0.87 (m, 4H, *2 rot.*), 0.85 (s, 9H, *2 rot.*), 0.72 (s, 0.75H, *minor rot.*), 0.69 (s, 2.25H, major rot.), 0.62 (s, 0.75H, *minor rot.*), 0.58 (s, 2.25H, *major rot.*), -0.04 (s, 0.75H, *minor rot.*), -0.04 (s, 2.25H, *major rot.*), -0.10 (s, 0.75H, *minor rot.*), -0.11 (s, 2.25H, *major rot.*). **^{13}C NMR (125 MHz, C_6D_6) major rot.**: 158.0 (d, *J* = 252.5 Hz), 145.9 (d, *J* = 4.7 Hz), 140.5 (d, *J* = 13.5 Hz), 136.0 (d, *J* = 25.5 Hz), 121.2, 72.0, 56.6, 56.3, 54.3, 48.9, 42.6, 40.2, 39.6, 39.2, 37.2, 36.3, 35.9, 35.8, 35.1, 34.7, 34.8, 28.1, 27.9, 24.0, 24.0, 22.5, 22.3, 21.2, 18.6, 18.7, 12.7, 12.0, -4.8, -4.9. **^{19}F (283 MHz):** -129.2 (s, *minor rot.*), -134.1 (*J* = 55 Hz, *major rot.*). **HRMS (ESI)** $[M+H]^+$ calc. for $C_{38}H_{65}FNOSi$ 598.4814, found 598.4814. Confirmation of rotamers were performed by nOe studies.[19]

***(S)-tert*-butyl-2-(pyridine-2-yl)pyrolidine-1-carboxilate (36). 36** was obtained following the same experimental procedure reported for **23** but using **S4** (70 mg, 0.3 mmol). Purification by flash chromatography on silica gel (petrol ether:EtOAc, 7:3 to 6:4) gave **36** as solid (60 mg, 81%). **Rf** (hexane:EtOAc, 1:1) 0.3. $[\alpha]_D^{20}$ = (c 0.6, $CHCl_3$) -65. **FT-IR (neat) υ** = 2974, 2929, 2876, 1692, 1390, 1364, 1160, 1115 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$, rotamers):** 8,57-8.53 (m, 1H), 7.66-7.60 (m, 1H), 7.20-7.11 (m, 2H), 5.04-4.98 (m, 0.4H, *1 rot.*), 4.87 (dd, 0.6H, *J* = 9.0, 4.2 Hz, *1 rot.*), 2.43-2.34 (m, 0.6H, *1 rot.*), 2.34-2.28 (m, 0.4H,

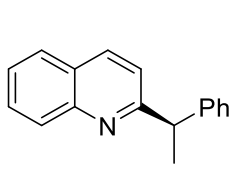
1 rot.), 2.10-2.04 (m, 0.4H, *1 rot.*), 2.03-1.97 (m, 0.6H, *1 rot.*), 1.90 (m, 2H), 1,47 (s, 3H, *1 rot.*), 1.21 (s, 6H, *1 rot.*) **^{13}C NMR (125 MHz, $CDCl_3$, rotamers):** 163.8, 154.5, 149.2 (*minor rot.*), 149.0 (*major rot.*), 136.4 (*minor rot.*), 136.2 (*major rot.*), 121.5, 120.1 (*minor rot.*), 119.6 (*major rot.*), 79.2, 62.9 (*major rot.*), 62.2 (*minor rot.*), 47.4 (*minor rot.*), 47.1 (*major rot.*), 34.3 (*major rot.*), 33.0 (*minor rot.*), 28.5 (*minor rot.*), 28.2 (*major rot.*), 23.8 (*minor rot.*), 23.2 (*major rot.*). **GC-MS:** 248, 192, 175, 147, 147, 130, 106, 78, 57 *m/z*. **HRMS (ESI)** $[M+H]^+$ calc. for $C_{14}H_{21}N_2O_2$ 249.1598, found 249.1603, calc. for $[M+Na]^+$ $C_{14}H_{20}N_2NaO_2$ 271.1417, found 271.1423. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (92:8) as the mobile phase at flow rate of 0.2 ml·min^{-1}, λ = 220 nm. tr_{major} = 26.7 min, tr_{major} = 37.9 min. e.r. = 98:2, es = 100%.

2-Phenylquinoline (37). Following the procedure for the synthesis of **39** using 2-bromoquinoline (104 mg, 0.5 mmol) and phenylboronic ester x (60 mg, 0.3 mmol) but running the oxidation for 14 hours at room temperature flash chromatography (hexanes:EtOAc, 9:1) gave **37** as an oil (45 mg, 73%). **Rf** (hexanes:EtOAc, 7:3) = 0.7. **FT-IR (neat) υ** = 3059, 2957, 2925, 2860, 1597, 1508, 1491, 830 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.24 (d, 1H, *J* = 8.5 Hz), 8.21-8.15 (m, 3H), 7.89 (d, 1H, *J* = 8.7 Hz), 7.84 (d, 1H, *J* = 8.4 Hz), 7.73 (ddd, 1H, *J* = 8.5, 7.0, 1.5 Hz), 7.54 (m, 3H), 7.47 (tt, 1H, *J* = 7.0, 1.4 Hz). **^{13}C NMR (100 MHz, $CDCl_3$) δ** = 157.4, 148.3, 139.7, 136.8, 129.7, 129.6, 129.3, 128.8, 127.6, 127.4, 127.2, 126.3, 119.0 ppm. **GC-MS** = 205, 204, 175, 102, 88, 76, 51 *m/z*. **HRMS (EI)** $[M]^+$ calc for $C_{15}H_{11}N$ 205.0891, found: 205.0900. Experimental data match with reported in the literature.[20]

2-Phenethylquinoline (38). Following the procedure for the synthesis of **39** using 2-bromoquinoline (104 mg, 0.5 mmol) and ethylphenylboronic ester (73 mg, 0.3 mmol but running the oxidation for 10 hours at room temperature flash chromatography (hexanes:EtOAc, 8:2) gave **38** as an oil (64 mg, 91%). **Rf** (hexanes:EtOAc, 7:3) = 0.7. **FT-IR (neat) υ** = 3059, 3028, 2947, 2924, 2855, 1617, 1598. 1560, 1501, 1452, 1426, 821 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.08 (d, 1H, *J* = 8.7 Hz), 8.05 (d, 1H, *J* = 8.5 Hz), 7.78 (dd, 1H, *J* = 8.2, 1.2 Hz), 7.70 (ddd, 1H, *J* = 8.2, 6.8, 1.4 Hz), 7.50 (ddd, 1H, *J* = 8.2, 7.0, 1.2 Hz), 7.31-7.18 (m, 6H), 3.31 (m, 2H), 3.17 (m, 2H). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 161.8, 148.0, 141.5, 136.2, 129.4, 128.9, 128.5, 128.4, 127.5, 126.8, 126.0, 125.8, 121.5, 41.1, 35.9 ppm. HRMS (EI) $[M]^+$ calcd for $C_{17}H_{15}N$ 233.1204, found: 233.1212. Experimental data match with reported in the literature.[21]



(*R*)-2-(1-Phenylethyl)quinoline (39). *n*-BuLi (0.35 mL, 0.55 mmol, 1.6 M in hexanes) was added by dropwise to a solution of 2-bromoquinoline (104 mg, 0.50 mmol) in Et_2O (1.5 mL) at -100 ºC during 30 minutes. The reaction mixture was stirred for 2 hours and then warmed to -65ºC.[22] The mixture was cooled to -78 ºC and then a solution of the boronic ester **(*S*)-8** (70 mg, 0.3 mmol) in THF (0.5 mL) was added. The mixture was stirred for 1.5 hours at the same temperature, Troc-Cl (115 μl, 1 mmol) was added and the mixture was slowly allowed to warm to room temperature overnight. Et_2O and H_2O were added and the layers were separated. The aqueous layer was washed with saturated $NaHCO_3$ solution and extracted with Et_2O (x 3). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was filtered over a pad of silica gel rinsing with hexanes:EtOAc (7:3). The solvent was removed under vacuum and the crude was dissolved in THF (2 mL) and cooled to 0 ºC. NaOH (1 mL, 2M) and H_2O_2 (0.5 mL, 30%) were added and the mixture was stirred overnight at room temperature. The crude was diluted with Et_2O and the layers were separated. The aqueous layer was acidified with HCl (1M) aqueous solution and the layers were separated. The aqueous phase was neutralized with saturated $NaHCO_3$ aqueous solution and extracted with Et_2O (x 2). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by flash chromatography (hexanes:EtOAc, 19:1 to 9:1) to give **39** as an oil (100 mg, 87%). **Rf** (hexanes:EtOAc, 8:2) = 0.5. $[\alpha]_D^{20}$ = (c = 0.5, $CHCl_3$) = + 8. **FT-IR (neat) υ** = 3058, 2954, 2923, 2855, 1585, 1563, 1497, 1421, 1294, 1135, 1094 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** δ



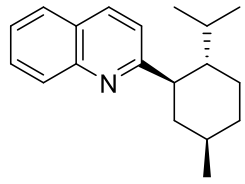
= 8.15 (d, 1H, *J* = 8.6 Hz), 7.99 (d, 1H, *J* = 8.6 Hz), 7.75 (d, 1H, *J* = 8.2 Hz), 7.70 (ddd, 1H, *J* = 8.2, 6.9, 1.2 Hz), 7.49 (ddd, 1H, *J* = 7.9, 6.9, 1.2 Hz), 7.37-7.32 (m, 2H), 7.32-7.28 (m, 2H), 7.21 (tt, 1H, *J* = 7.2, 1.2 Hz), 7.19 (d, 1H, *J* = 8.6 Hz, overlap.), 4.50 (q, 1H, *J* = 7.2 Hz), 1.80 (d, 3H, *J* = 7.2 Hz). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 165.2, 147.7, 144.7, 136.3, 129.3, 129.3, 128.7, 127.8, 127.4, 126.9, 126.4, 125.9, 120.7, 48.1, 20.4 ppm. **GC-MS:** 234, 233, 232, 218, 217, 156, 129, 128, 108, 95, 77, 51 *m/z*. **HRMS (EI)** calc. for $[M]^+$ $C_{17}H_{15}N$ 233.1204, found: 233.1212. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with *n*-hexane:iPrOH (98:2) as the mobile phase at flow rate of 0.5 ml·min^{-1}. tr_{minor} = 12 min, tr_{major} = 19 min. e.r. = 97:3, es = 100%.

(*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)quinoline (40). Following the procedure for the synthesis of **39** using 2-bromoquinoline (104 mg, 0.5 mmol) and boronic ester *S1* (87 mg, 0.3 mmol) but running the oxidation for 10 hours at room temperature flash chromatography (hexanes:EtOAc, 8:2) gave **40** as an oil (76 mg, 88%). $[\alpha]_D^{20}$ (c 1, $CHCl_3$) = +6.0. **Rf** (hexanes:EtOAc, 7:3) = 0.77. **FT-IR (neat)** υ = 3061, 2993, 1958, 2930, 2863, 2834, 1611, 1601, 1511, 1244, 1177, 1037, 829 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** δ = 8.09 (d, 1H, *J* = 8.4 Hz), 8.08 (d, 1H, *J* = 8.4 Hz), 7.79 (dd, 1H, *J* = 8.4, 1.2 Hz), 7.69 (ddd, 1H, *J* = 8.4, 7.0, 1.2 Hz), 7.49 (ddd, 1H, *J* = 8.2, 7.1, 1.5 Hz), 7.31 (d, 1H, *J* = 8.4 Hz), 7.07 (m, 2H), 6.80 (m, 2H), 3.77 (s, 3H), 3.19-3.09 (m, 1H), 2.59 (ddd, 1H, *J* = 13.5, 10.3, 6.2 Hz), 2.49 (ddd, 1H, *J* = 13.5, 10.2, 5.6 Hz), 2.17 (dddd, 1H, *J* = 13.5, 10.2, 8.1, 5.6 Hz), 1.99 (ddt, 1H, *J* = 13.4, 10.3, 6.4 Hz), 1.41 (d, 3H, *J* = 7.0 Hz). **^{13}C NMR (100 MHz, $CDCl_3$)** δ = 166.8, 157.9, 148.1, 136.6, 134.7, 129.4, 129.3, 127.7, 127.2, 125.9, 119.9, 113.9, 55.4, 42.7, 39.2, 33.2, 21.1 ppm. **GC-MS** = 207, 157, 156, 134, 119, 91, 77, 65, 51 *m/z*. **HRMS (ESI)** $[M+H]^+$ for $C_{20}H_{22}NO$ calc. 292.1696, found 292.1708. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (97:3) as the mobile phase at flow rate of 0.7 ml·min^{-1}, λ = 220 nm. Tr_{minor} = 13 min, tr_{major} = 18 min. e.r. = 96:4, es = 100%.

***(S)-tert*-Butyl 2-(2-quinolinyl)pyrrolidine-1-carboxilate (41).** Following the procedure for the synthesis of **39** using 2-bromoquinoline (52 mg, 0.25 mmol) and boronic ester x (45 mg, 0.15 mmol) but running the oxidation for 10

hours at room temperature flash chromatography (hexanes:EtOAc, 8:2to 7:3) gave **41** as an oil (36 mg, 81%). **Rf** (hexanes:EtOAc, 7:3) = 0.4. $[\alpha]_D^{20}$ (c 1.0, $CHCl_3$) = -21. **FT-IR (neat) υ** = 2966, 2931, 2874, 1693, 1391, 1365, 1258, 1158, 1114, 1090, 1017, 795 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$, broad signals due to rotamers)** δ = 8.11 (d, 0.7H, *J* = 8.5, overlap), 8.10-8.08 (m, 0.3H, overlap), 8.03 (d, 1H, *J* = 8.5 Hz), 7.80 (d, 0.7H, *J* = 7.9 Hz, overlap), 7.79-7.75 (m, 0.3 H, overlap), 7.69 (t, 0.7 H, *J* = 7.5 Hz, overlap), 7.67-7.63 (m, 0.3 H, overlap), 7.51 (t, 0.7 H, *J* = 7.7 Hz, overlap), 7.49-7.44 (m, 0.3H, overlap), 7.33 (d, 1H, *J* = 8.3 Hz), 5.16 (brs, 0.3H), 5.03 (dd, 0.7H, *J* = 5.3, 0.7 Hz), 3.72 (t, 1.4H, *J* = 6.6 Hz), 3.66-3.58 (m, 0.6H), 2.52-2.35 (m, 1H), 2.16-1.88 (m, 3H), 1.46 (s, 3H), 1.11 (s, 6H). **^{13}C NMR (100 MHz, $CDCl_3$, broad signals due to the rotamers)** δ =164.3 (*major rot.*), 163.4 (*minor rot.*), 154.6 *(major rot.*), 154.6 (*minor rot.*), 147.5 (*major rot.*), 147.8 (*minor rot.*), 136.5 (*2 rot.*), 129.5 (*major rot.*), 129.2 (*minor rot.*), 128.9 (*major rot.*), 129.1 (*minor rot.*), 127.5 (*major rot.*), 127.0 (*minor rot.*), 125.9 (*major rot.*), 125 (*minor rot.*), 118.1 (*major rot.*), 117.1 (*minor rot.*), 79.4 (*2 rot.*), 63.6 (*major rot.*), 62.9 (*minor rot.*), 47.5 (*minor rot.*), 47.3 (*major rot.*), 34.7 (*major rot.*), 33.3 (*minor rot.*), 28.5 (*minor rot.*), 28.1 (*major rot.*), 23.9 (*minor rot.*), 23.6 (*major rot*.). **GC-MS** = 299, 298, 243, 242, 225, 226, 197, 182, 181, 180, 156, 142, 129, 128, 101, 57 *m/z*. **HRMS (ESI)** $[M+H]^+$ for $C_{18}H_{23}N_2O_2$ calc. 299.1754, found 299.1752. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (96:4) as the mobile phase at flow rate of 0.7 ml·min^{-1}, λ = 215 nm. Tr_{minor} = 5 min, tr_{major} = 10 min. e.r. = 98:2, es = 100%.

***2-(1S, 2R, 5R)*-2-isopropyl-5-methylcyclohexylquinoline (42).** Following the procedure for the synthesis of **39** using 2-bromoquinoline (104 mg, 0.5 mmol) and boronic ester **S5** (80 mg, 0.3 mmol) but running the oxidation for 15 hours at room temperature flash chromatography (hexanes:EtOAc, 9:1) gave **42** as an solid (80 mg, 81%). **Rf** (hex:EtOAc, 8:2) = 0.72. $[\alpha]_D^{20}$ (c 0.1, $CHCl_3$) = -70. **FT-IR υ** = 3057, 2953, 2921, 2869, 2854, 1601, 1503, 1455, 827 cm^{-1}. **^{1}H RMN (500 MHz, $CDCl_3$):** 8.05 (d, 1H, *J* = 8.4 Hz), 8.03 (d, 1H, *J* = 8.4 Hz), 7.75 (dd, 1H, *J* = 8.1, 6.2 Hz), 7.65 (dd, 1H, *J* = 8.1, 1.2 Hz), 7.46 (ddd, 1H, *J* = 8.1, 7.1, 1.1 Hz), 7.28 (d, 1H, *J* = 8.7 Hz), 2.91 (td, 1H, *J* = 11.7, 3.4 Hz), 1.92-1.73 (m, 4H), 1.36-1.03 (m, 5H), 0.90 (d, 3H, *J* = 6.3 Hz), 0.80 (d, 3H, *J* = 7.1 Hz), 0.72 (d, 3H, *J* = 6.8 Hz). **^{13}C NMR (125 MHz) δ** = 166.3, 148.0, 136.1, 129.1, 129.0, 127.4, 126.9, 125.5, 120.0,



50.9, 46.6, 35.1, 28.3, 24.6, 22.5, 21.4, 15.7. **GC-MS** = 276, 252, 224, 210, 196, 180, 170, 156, 143, 128, 115, 102, 77, 55 *m/z*. **HRMS (ESI)** for $C_{19}H_{26}N$ $[M+H]^+$ calc. 268.2060, found 268.2060.

(*R*)-4-(1-Phenylethyl)quinoline (43). Follow the same procedure and the same amounts as the 2-bromoquinoline using 4-bromoquinoline (104 mg, 0.5 mmol) and boronic ester **(*R*)-8** (70 mg, 0.3 mmol). The residue was purified by flash chromatography (hexanes:EtOAc, 19:1 to 9:1) to afford **43** as a white oil (96 mg, 82%). **Rf** (hexanes:EtOAc, 7:3) = 0.8. $[\alpha]_D^{20}$ (c 1, $CHCl_3$) +29. **FT-IR (neat)** υ : 3059, 3027, 2970, 2932, 2875, 1590, 1567, 1507, 1494, 1451, 852, 776, 757, 699 cm^{-1}. **^{1}H NMR (400 MHz):** δ = 8.89 (d, 1H, *J* = 4.8 Hz), 8.11 (d, 1H, *J* = 8.6 Hz), 8.04 (d, 1H, *J* = 8.9 Hz), 7.66 (ddd, 1H, *J* = 8.4, 6.9, 1.5 Hz), 7.48 (ddd, 1H, *J* = 8.4, 6.9, 1.5 Hz), 7.32 (d, 1H, *J* = 4.8 Hz, *overlapp*), 7.31-7.26 (m, 2H, *overlapp*), 7.23-7.18 (m, 3H), 4.92 (q, 1H, *J* = 7.1 Hz), 1.77 (d, 3H, *J* = 7.1 Hz). **^{13}C NMR (100 MHz):** 150.3, 148.3, 144.8, 130.3, 128.3, 128.9. 128.7, 127.5, 127.1, 126.5, 126.4, 123.8, 119.2, 40.2, 21.9 ppm. GC-MS: 234, 233, 232, 219, 218, 217, 204, 189, 154, 128, 115, 108, 101, 94, 77 *m/z*. **HRMS (EI)** $[M]^+$ calc. for $C_{17}N_{15}N$ 233.1204, found 233.1207. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (98:2) as the mobile phase at flow rate of 0.5 ml·mi-1,. tr_{minor} = 24 min, tr_{major} 38 min. e.r. = 97:3, es =100%.

(*S*)-4-(4-(4-methoxyphenyl)butan-2-yl)quinoline (44). Follow the procedure for the synthesis of **39** using 4-bromoquinoline (104 mg, 0.5 mmol) and boronic ester **S1** (87 mg, 0.3 mmol). The oxidation was running for 10 h. After the work-up, the residue was purified by flash chromatography (hexanes:EtOAc, 8:2) to afford **44** as a colorless oil (61 mg, 70%). **Rf** (hexanes:EtOAc, 7:3) = 0.42. $[\alpha]_D^{20}$ = +90. **FT-IR (neat) υ**: 2964, 2922, 2854, 1511, 1261, 1094, 1035, 816, 801 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$):** 8.87 (brs, 1H), 8.13 (d, 1H, *J* = 8.4 Hz), 7.95 (d, 1H, *J* = 8.6 Hz), 7.70 (ddd, 1H, *J* = 8.4, 6.9, 1.1 Hz), 7.52 (ddd, 1H, *J* = 8.4, 6.9, 1.1 Hz), 7.04 (m, 2H), 6.81 (m, 2H), 3.79 (s, 3H), 3.60 (sx, 1H, *J* = 7.1 Hz), 2.62 (ddd, 1H, *J* = 14.0, 9.2, 6.5 Hz), 2.54 (ddd, 1H, *J* = 14.0, 9.0, 6.5 Hz), 2.12 (ddd, 1H, *J* = 13.6, 9.4, 6.7 Hz), 1.98 (ddd, 1H, *J* = 13.0, 9.0, 6.7 Hz), 1.41 (d, 3H, *J* = 7.0 Hz). **^{13}C NMR (100 MHz, $CDCl_3$):** 157.8, 153.5, 150.2, 148.4, 133.8, 130.3, 129.3, 128.9, 132.2, 123.0, 117.7, 113.8,

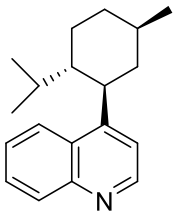
55.8, 39.2, 32.8, 32.7, 21.1. **GC-MS** = 292, 291, 290, 281, 262, 261, 207, 157, 156, 135, 134, 121, 91, 78, 77, 65, 51 *m/z*. **HRMS (EI)** $[M]^+$ calc. for $C_{20}H_{21}NO$ 291.1623, found 291.1627. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (99:1) as the mobile phase at flow rate of 1 ml·min^{-1},. Tr_{major} = 25.4 min, tr_{minor} = 30.4 min. es = 100%.

(*R*)-4-(2-phenyl)butan-2-ylquinoline (46). Follow the procedure for the synthesis of **43** using 4-bromoquinoline (51 mg, 0.25 mmol) and boronic ester **S3** (49 mg, 0.15 mmol). The intermediate was passed through a short pad of silica gel eluting with hexane:EtOAx, 9:1. The solvent was evaporated and the residue was submitted to the oxidation (16 hours at room temperature). After usual work-up, the residue was purified by flash chromatography (hexanes:EtOAc, 8:2 to 7:3) to afford **46** as a colourless oil (12 mg, 32%). **Rf** (hexane:EtOAc, 7:3) 0.5. $[\alpha]_D^{20}$ (c 0.4, $CHCl_3$) +18. **FT-IR (neat) υ:** 3087, 3060, 3030, 2969, 2926, 2854, 2877, 1509 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)**: 8.93 (d, 1H, *J* = 4.4 Hz), 8.11 (d, 1H, *J* = 8.2 Hz), 7.60 (d, 1H, *J* = 4.6 Hz), 7.54 (ddd, 1H, *J* = 8.1, 6.9, 1.1 Hz), 7.48 (d, 1H, *J* = 8.7 Hz), 7.24 (d, 2H, *J* = 8.0 Hz), 7.19-7.14 (m, 4H), 2.47 (dq, 1H, *J* = 14.8, 7.3 Hz), 2.30 (dq, 1H, *J* = 14.6, 7.3 Hz), 1.75 (s, 3H), 0.61 (t, 3H, *J* = 7.3 Hz). **^{13}C MMR (125 MHz, $CDCl_3$):** 154.0, 149.6, 149.2, 149.0, 130.2, 128.5, 128.4, 126.9, 126.9, 126.3, 126.0, 125.3, 120.0, 47.4, 33.4, 28.5, 9.1. **GC-MS:** 261, 232, 154, 108, 77 *m/z*. **HRMS (EI)** $[M]^+$ calc. for $C_{19}H_{19}N$ 261.1517, found 261.1509. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (99:1) as the mobile phase at flow rate of 1 ml·min^{-1},. tr_{minor} = 50.0 min, tr_{minor} = 64.2 min. e.r. = 98:2, es = 100%.

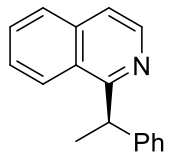
***(S)-tert*-Butyl 2-(4-quinolinyl)pyrrolidine-1-carboxilate (45).** Follow the procedure for the synthesis of **39** using 4-bromoquinoline (104 mg, 0.5 mmol) and boronic ester x (89 mg, 0.3 mmol). The oxidation was running for 12 h. After the work-up, the residue was purified by flash chromatography (hexanes:EtOAc, 7:3 to 6:4) to afford **45** as colourless oil. (mg, 62%). $[\alpha]_D^{20}$ = **^{1}H NMR (400 MHz, $CDCl_3$, rotamers):** 8.84 (d, 1H, J = 3.2 Hz), 8.16-8.10 (m, 1H), 8.00 (d, 1H, *J* = 8.0 Hz), 7.75-7.56 (m, 1H), 7.59-7.53 (m, 1H), 7.20-7.14 (m, 1H), 5.70 (d, 0.4H, J = 8.4 Hz), 5.56 (d, 0.6H, *J* = 7.6 Hz), 3.81-3.56 (m, 2H), 2.58-2.44 (m, 1H), 1.99-1.82 (m, 3H), 1.48 (s, 3H), 1.11 (s, 6H). **^{13}C NMR (125 MHz, $CDCl_3$, rotamers):** 163.8 (*major rot.*), 162.6 (*minor rot.*), 154.6 *(minor rot.*), 154.5 (*major rot.*),

149.2, 148.9, 136.5, 136.5, 121.6, 121.5, 120.1 (*minor rot.*), 119.7 (*major rot.*), 79.3, 62.8 (*major rot.*), 62.1 (*minor rot.*), 47.4 (*minor rot.*), 47.1 (*major rot.*), 34.3 (*major rot.*), 30.(*minor rot.*), 29.5 (*minor rot.*), 28.2 (*major rot.*), 23.8 (*minor rot.*), 23.2 (*major rot.*). Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (94:6), as the mobile phase at flow rate of 1 ml·min^{-1}, λ = 280 nm. tr_{minor} = 10.0 min, tr_{major} = 13.6 min. e.r. = 98:2, es = 100%.

4-[*(1S, 2R, 5R)*-2-isopropyl-5-methylcyclohexyl]quinoline (47). Following the procedure for the synthesis of **39** using 4-bromoquinoline (104 mg, 0.5 mmol) and boronic ester **S5** (80 mg, 0.3 mmol) but running the oxidation for 8 hours at room temperature flash chromatography (hexanes:EtOAc, 9:1) gave **47** as an white solid (58 mg, 73%). **Rf** (hexanes:EtOAc, 7:3) = 0.6. $[\alpha]_D^{20}$ = (c 1, $CHCl_3$) = -60. **FT-IR (neat) υ** = 2953, 2923, 2868, 1586, 1568, 1507, 1455, 758 cm^{-1}. **^{1}H NMR (400 MHz, $CDCl_3$)** : 8.84 (d, 1H, *J* = 4.7 Hz), 8.15 (d, 1H, *J* = 8.6 Hz), 8.11 (d, 1H, *J* = 8.4 Hz), 7.68 (t, 1H, *J* = 7.6 Hz), 7.53 (t, 1H, *J* = 7.8 Hz), 7.27 (d, 1H, *J* = 4.7 Hz), 3.38 (td, 1H, *J* = 11.7, 3.1 Hz), 1.93-1.82 (m, 3H), 1.75 (tt, 1H, *J* = 11.5, 2.5 Hz), 1.65-1.54 (m, 1H), 1.51-1.44 (m, 1H), 1.33-1.24 (m, 1H), 0.88 (d, 3H, *J* = 6.5 Hz), 0.81 (d, 3H, *J* = 6.9 Hz), 0.61 (d, 3H, *J* = 7.0 Hz). **^{13}C NMR (100 MHz, $CDCl_3$)** = 153.0, 150.4, 148.9, 130.7, 129.1, 127.7, 126.4, 122.8, 118.0, 46.7, 45.3, 40.9, 35.3, 33.6, 27.7, 24.8, 22.5, 21.7, 16.7. **GC-MS** = 268, 267, 252, 224, 180, 167, 156, 143, 130, 115, 81, 69, 55 *m/z*. **HRMS (EI)** $[M]^+$ for $C_{19}H_{25}N$ calc. 267.1987, found 267.1978.



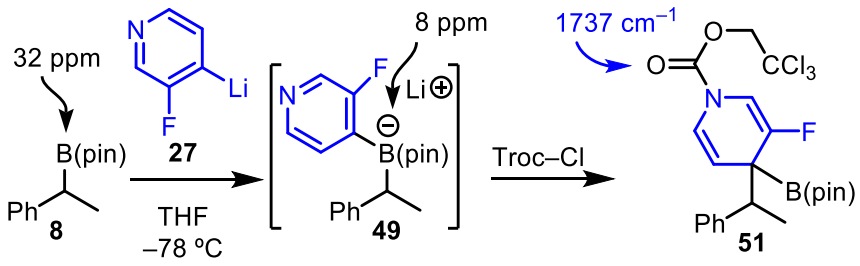
(*R*)1-(1-Phyenylethyl)isoquinoline (48). *n*-BuLi (0.25 mL, 0.4 mmol, 1.6M in hexane) was dropwise added to a solution of isoquinoline (128 mg, 0.5 mmol) in toluene:Et_2O (3:2, 0.25M) at -100ºC during 20 minutes.[23] A solution of boronic ester **(*R*)-8** (81 mg, 0.35 mmol) in THF (0.35 mL) was dropwise added and the reaction mixture was stirred for 1 hour and 30 minutes at -78ºC. Troc-Cl (1 mmol, 131 μl) was slowly added at -78ºC and stirred overnight to reach ambient temperature. The crude was dissolved in Et_2O and H_2O was added, the layers were separated and the aqueous phase was extracted with E_2O. The aqueous phase was neutralized with a saturated $NaHCO_3$ solution and extracted again with Et_2O. The combiened organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was dissolved in THF (2 mL) and a aqueous solution of NaOH (2 M, 1mL) and H_2O_2 (30%, 0.5



mL) were added. The reaction mixture was stirred for 12 hours at ambient temperature before Et_2O was added. The layers were separated and the aqueous phase was acidified with aqueous HCl (1M) solution and extracted with Et_2O. Then, the aqueous solution was neutralized with saturated aqueous $NaHCO_3$ solution and extracted with Et_2O. The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. The residue was purified by flash chromatography (hexanes:EtOAc, 8:2) to afford **48** a pale solid (51%). **Rf** (hexane:EtOAc, 8:2) 0.3. $[\alpha]_D^{20}$ (c 1, $CHCl_3$) +29. **FT-IR (neat) υ :** 3051, 3025, 2969, 2927, 2865, 1561, 822, 745, 700 cm^{-1}. **^{1}H NMR (400 MHz):** δ =8.57 (d, 1H, *J* = 5.9 Hz), 8.17 (d, 1H, *J* = 8.4 Hz), 7.79 (ddd, 1H, *J* = 8.3, 7.1, 1.3 Hz), 7.54 (d, 1H, *J* = 5.8 Hz), 7.48 (ddd, 1H, *J* = 8.3, 7.1, 1.3 Hz), 7.31 (dd, 1H, *J* = 7.8, 1.6 Hz), 7.24 (t, 2H, *J* = 7.8 Hz), 7.14 (tt, 1H, *J* = 7.3, 1.8 Hz) 5.08 (q, 1H, *J* = 7.0 Hz), 1.84 ppm (d, 3H, *J* = 7.0 Hz). **^{13}C NMR (100 MHz):** 162.9, 145.9, 141.7, 136.4, 129.5, 128.5, 127.5, 127.4, 127.0, 126.8, 126.1, 125.3, 119.5, 43.2, 21.8 ppm. **GC-MS:** 233, 232, 218, 217, 156, 129, 108, 77 *m/z*. **HRMS (EI)** [M]+ calc. for C17H15N 233.1204, found 233.1205. Resolution between the enantiomers was achieved using a chiral HPLC system fitted with a Chiralpack OD-H column without guard as stationary phase with n-hexane:iPrOH (94:6), as the mobile phase at flow rate of 1 $ml \cdot min^{-1}$, λ = 280 nm. tr_{minor} = 10.0 min, tr_{major} = 13.6 min. e.r. = 98:2, es = 100%.

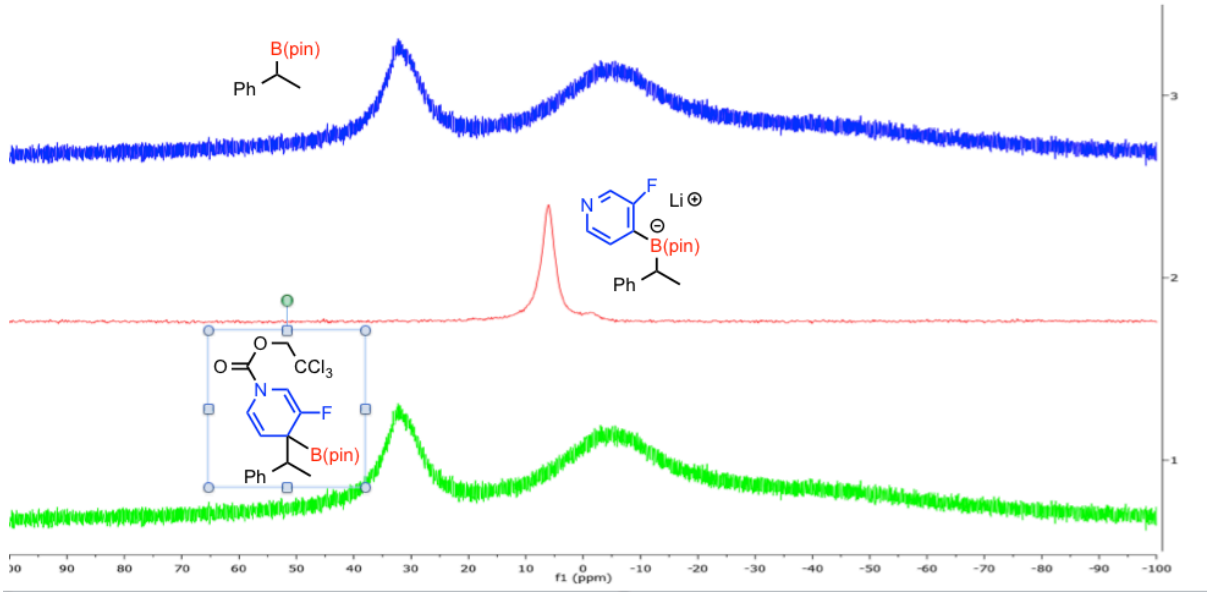
5. ^{11}B NMR studies

The following reaction was followed by React-IR.



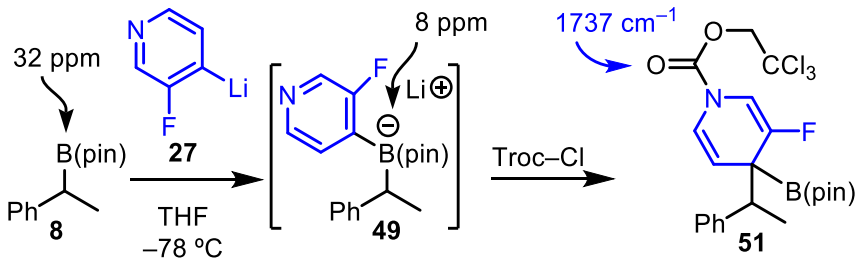
Experimental procedure:

A dry schlenck tube equipped with a stirring bar was charged with *i*-Pr$_2$NH (0.14 mL, 1.2 mmol, 1.2 equiv.) and THF (2 mL), cooled to –78 ºC and *n*-BuLi (0.6 mL, 1.1 mmol, 1.1 equiv., 1.6 M in hexane) was added by dropwise. The mixture was stirred at –78 ºC for 1 h and 3-fluoropyridine (0.09 mL, 1 mmol, 1 equiv.) was added as a solution in THF (0.5 mL). The mixture was stirred for 2 h at –78 ºC and then **8** (190 mg, 1 mmol, 0.8 equiv.) was added as a solution in THF (1 mL) by slow dropwise at –78 ºC. An aliquot (0.1 mL) was removed form the reaction mixture and put into a dry NMR tube. ^{11}B NMR spectroscopy analysis of the sample confirmed the complete formation of **49**; ^{11}B NMR (96 MHz, THF) δ c.a. 8 ppm.[24] Troc-Cl (0.24 mL, 2 mmol, 2 equiv.) was added by slow dropwise at –78 ºC. The mixture was allowed to warm to room temperature overnight. An aliquot (0.1 mL) was removed form the reaction mixture and put into a dry NMR tube. ^{11}B NMR spectroscopy analysis of the sample confirmed the complete formation of **51**; ^{11}B NMR (96 MHz, THF) δ c.a. 32 ppm. Et$_2$O and H$_2$O were added to the reaction mixture at -78ºC and warmed to ambient temperature. The layers were separated and the aqueous phase was extracted with Et$_2$O (x 2). The combined organic layers were dried over MgSO$_4$ and the solvent was removed under vacuum. ^{1}H NMR spectroscopy analysis of the crude revealed complete formation of **51**.


B(pin)
Ph
F
N
Li
B(pin)
Ph
O
O
CCl3
N
F
B(pin)
Ph
3
2
1
f1 (ppm)

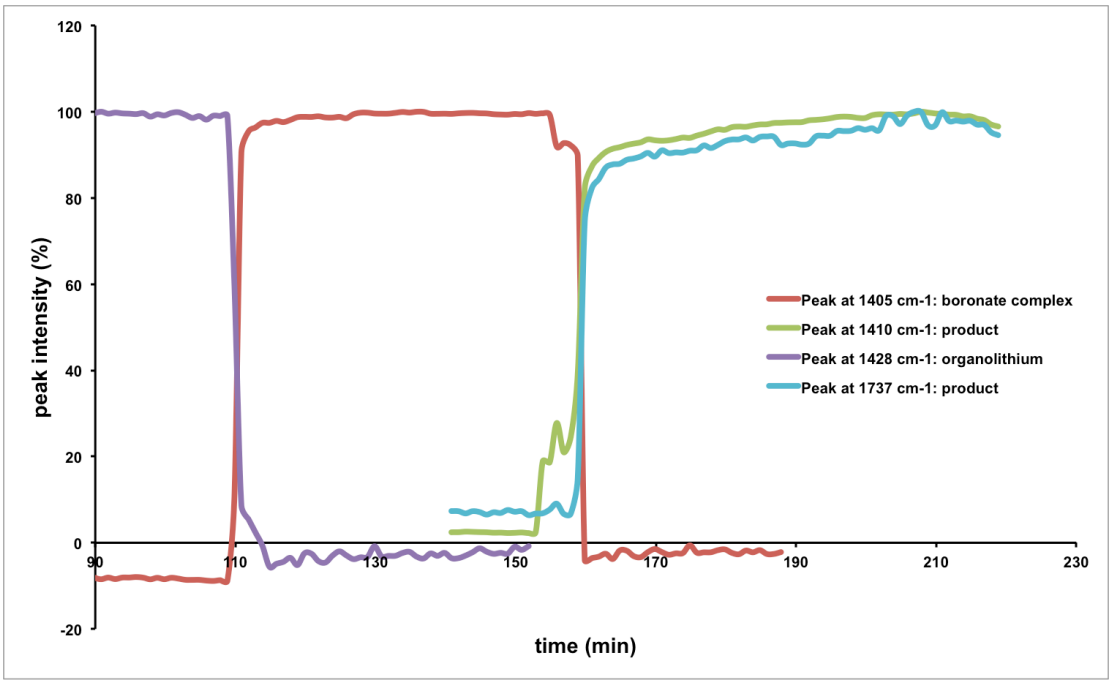
6. React-IR studies

The following reaction was followed by React-IR.



Experimental procedure:

A three-necks round bottomed flask equipped with a stirring bar was connected to the React-IR probe, evacuated and refilled with N_2 (x 3). The flask was charged with THF (2 mL), cooled to –78 ºC and the background spectrum was acquired. *i*-Pr_2NH (0.14 mL, 1.2 mmol, 1.2 equiv.) was added and *n*-BuLi (0.6 mL, 1.1 mmol, 1.1 equiv., 1.6 M in hexane) was added by dropwise. The mixture was stirred at –78 ºC for 1 h and 3-fluoropyridine (0.09 mL, 1 mmol, 1 equiv.) was added as a solution in THF (0.5 mL). The mixture was stirred for 2 h at –78 ºC and then the React-IR acquisition was started. *We selected the peak at 1428 cm^{-1} to follow the organolithium* **27**. **8** (190 mg, 1 mmol, 0.8 equiv.) was added as a solution in THF (1 mL) by slow dropwise at –78 ºC (a slow addition is essential in order to avoid line broadening due to T variation) and this immediately resulted in the disappearance of the peak at 1428 cm^{-1} and the appearance of a new peak at 1405 cm^{-1}. *We selected the peak at 1405 cm^{-1} to follow the boronate complex* **49** [^{11}B NMR spectroscopy analysis confirmed the complete formation of **49**; ^{11}B NMR (96 MHz, THF) δ c.a. 8 ppm]. Troc-Cl (0.24 mL, 2 mmol, 2 equiv.) was added by slow dropwise at –78 ºC. This immediately resulted in the disappearance of the peak at 1405 cm^{-1} and the appearance of two peaks at 1410 cm^{-1} and 1737 cm^{-1} indicating essentially instantaneous formation of **51**. The mixture was stirred at –78 ºC for an additional 3 h and no changes in the React-IR spectra were observed. Et_2O and H_2O were added to the reaction mixture at -78ºC and warmed to ambient temperature. The layers were separated and the aqueous phase was extracted with Et_2O (x 2). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under vacuum. ^{1}H NMR spectroscopy analysis of the crude revealed complete formation of **51**.



The peak intensity has been normalized.

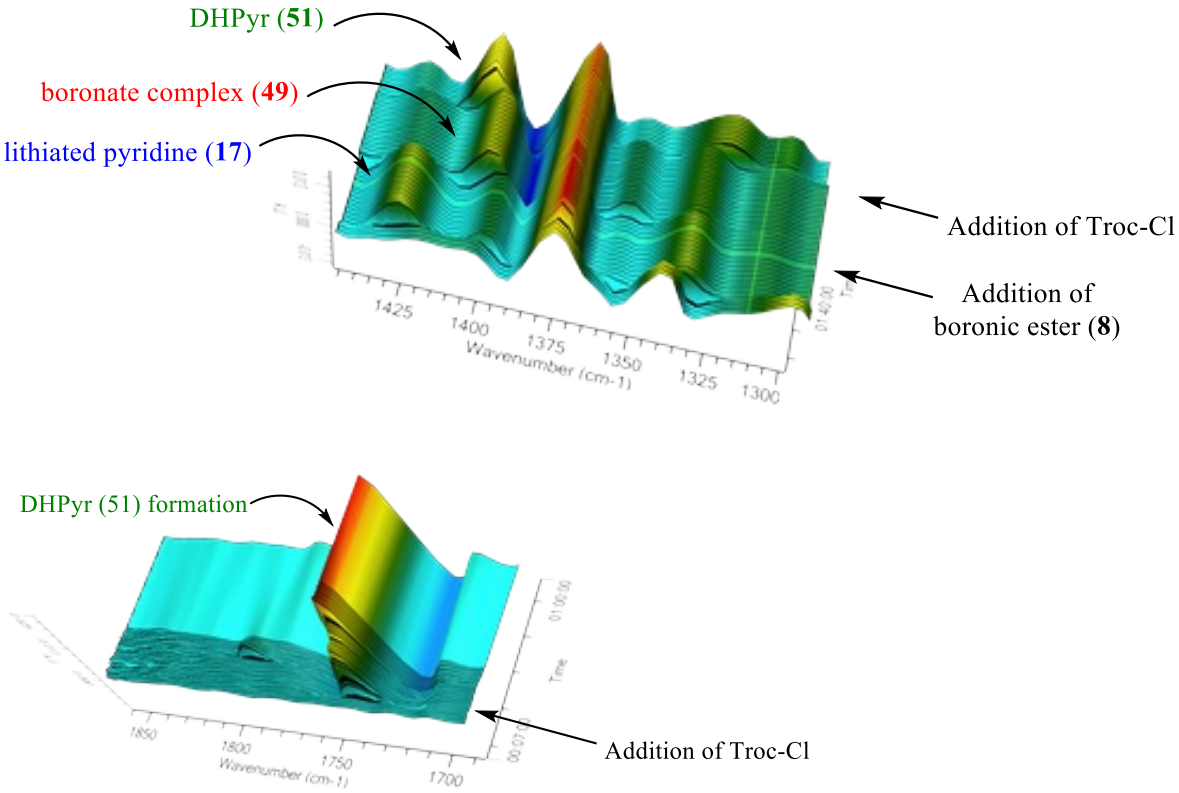
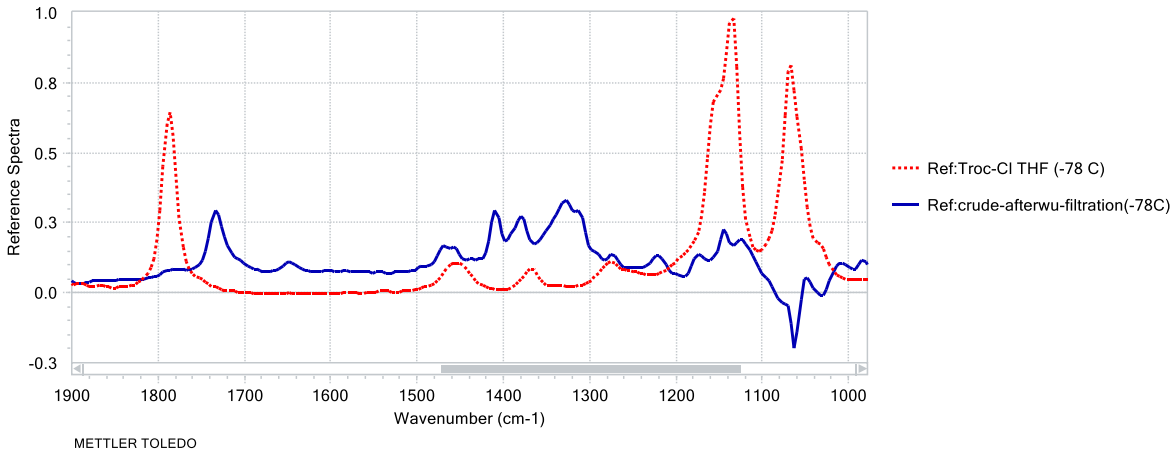
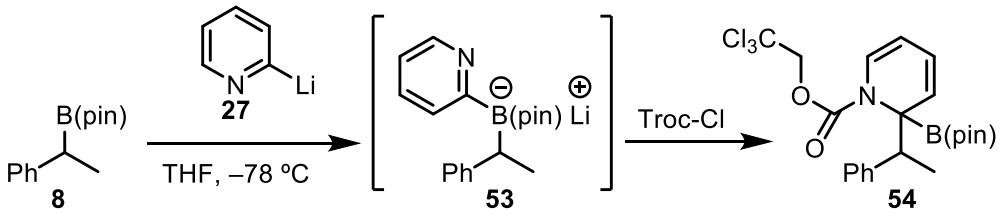


Figure **1**: React-IR trace of the reaction of the lithiated pyridine **27** with boronic ester **8** leading to formation of the boronate complex **49** and subsequent reaction with Troc-Cl with formation of dihydropyridine **51**.

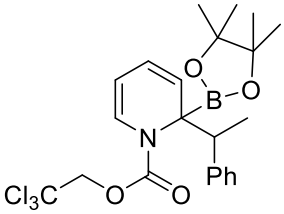
Even though an excess of Troc-Cl (2.0 equiv.) was added to **49** we were unable to detect the Troc-Cl C=O peak (1786 cm^{-1}; THF solution at –78 ºC). We believe this is because of fast reaction of Troc-Cl with the *i*-Pr_2NH present in the reaction. This reaction produces *i*-Pr_2N-Troc that is expected to show a C=O peak similar to **51**. The peak at 1737 cm^{-1} was confirmed to belong to **51** by React-IR analysis of a solution in THF at –78 ºC following work-up and silica gel filtration of the reaction crude (^{1}H NMR analysis confirmed the quantitative presence of **51** in the sample).



51 proved unstable under normal flash column chromatography and we could not obtain an analytically pure sample. However we succeeded in obtaining a pure sample of the C-2-dihydropyridine **54**. IR analysis of **54** confirmed the presence of the C=O peak at 1703 cm^{-1}.

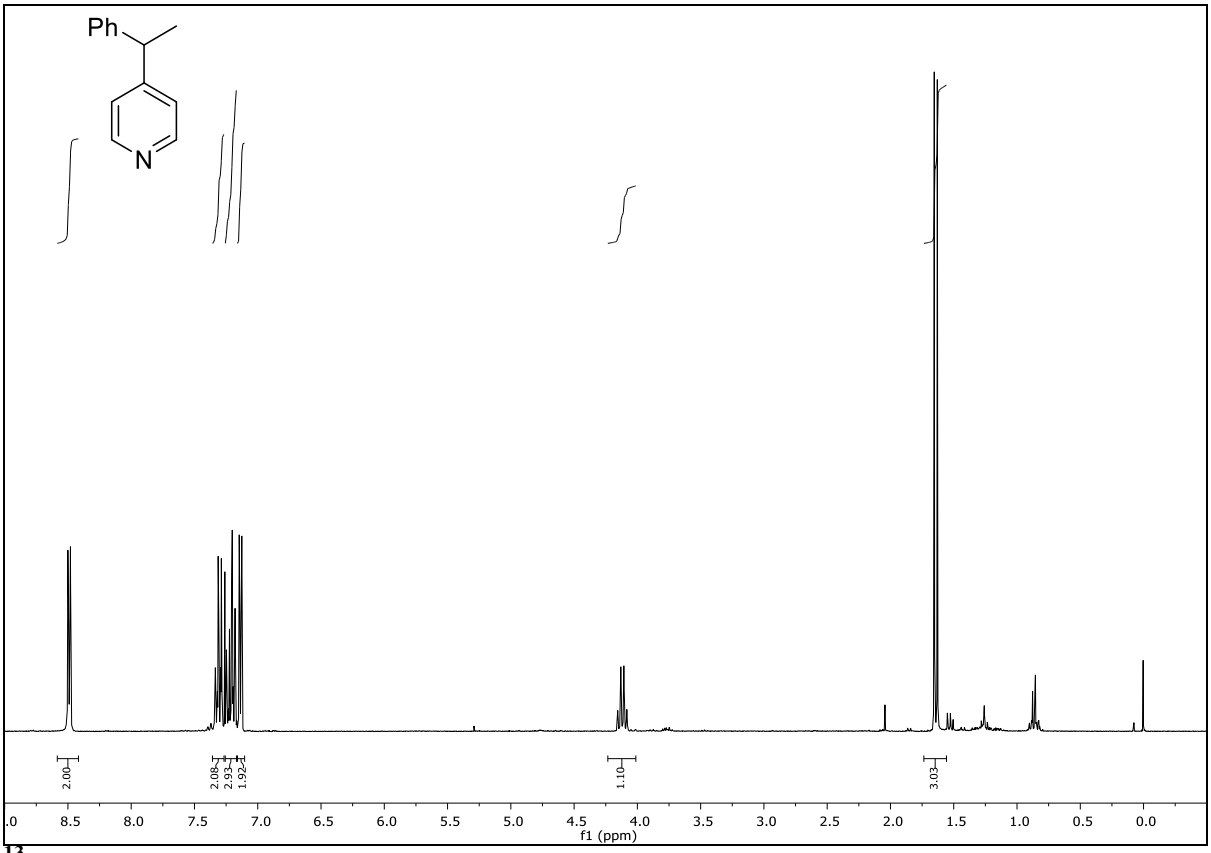


Dihydropyridine (54) . It was isolated by silica gel flash chromatography (hexane:EtOAc, 19:1 to 18:2) to give a colourless oil as an mixture of diastereoisomers, dr 1:1. (**Rf** (hexanes:EtOAc, 8:2) 0.7. **FT-IR (neat) υ** : 2974, 2927, 1703, 1392, 1329, 1267, 1144, 718 cm^{-1}. **^{1}H**

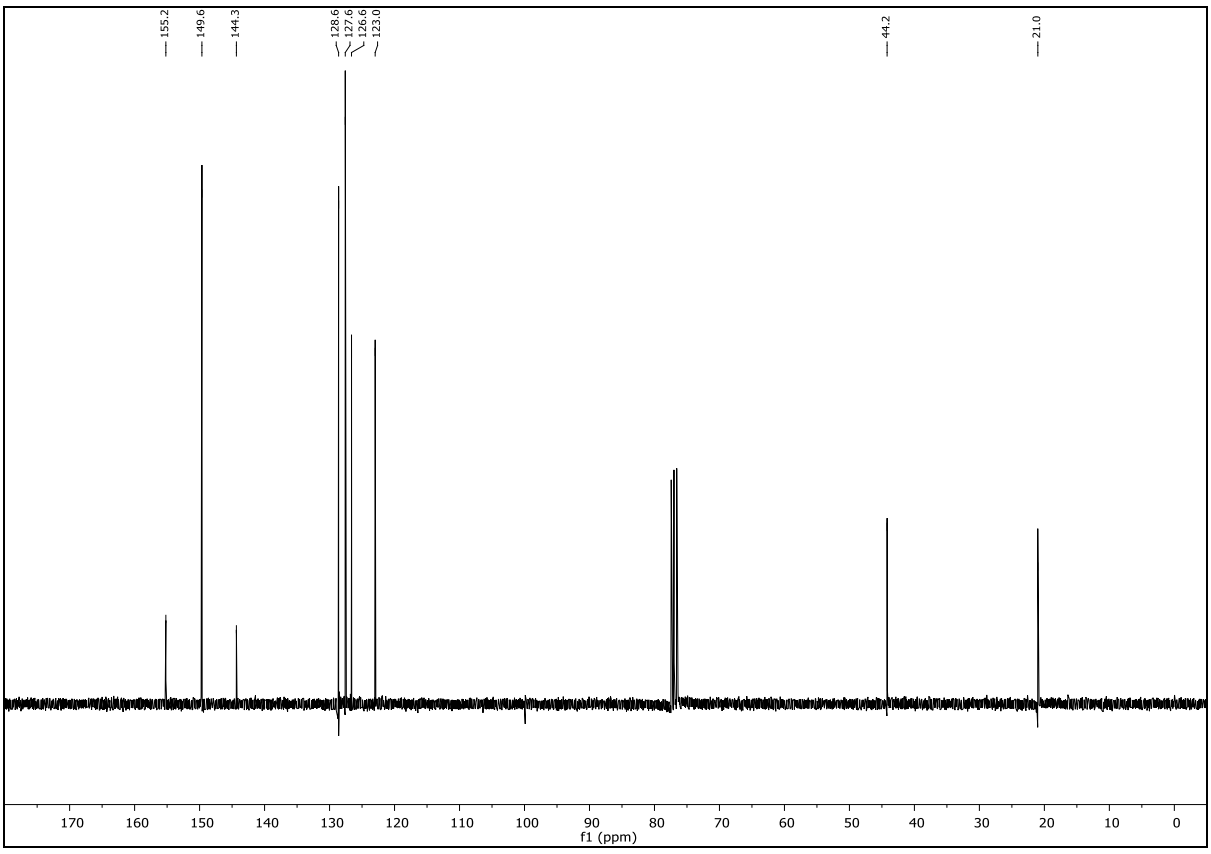


NMR (500 MHz, $CDCl_3$): 7.43 (d, 2H, *J* = 7.2 Hz, *2 diast.*), 7.27-7.25 (m, 4H, *2 diast.*), 7.21-.14 (m, 4H, *2 diast.*), 6.64 (d, 1H, *J* = 7.7 Hz, *1 diast.*, *diast. A*), 6.00 (dd, 1H, *J* = 7.8, 0.8 Hz, *1 diast.*, *diast. B*), 5.91 (dd, 1H, *J* = 9.6, 5.6 Hz, *1 diast.*, *diast. A*), 5.87 (dd, 1H, *J* = 10.0, 5.7 Hz, *1 diast.*, diast. B), 5.48 (dd, 1H, *J* = 9.9, 0.9 Hz, *1 diast.*, *diast. B*), 5.28 (m, 1H, *1 diast.*, *diast. A*), 4.96 (d, 1H, *J* = 11.9 Hz, *1 diast.*), 4.68 (m, 1H, *1 diast.*, diast. B), 4.87 (s, 1H, *1 diast.*), 4.67 (d, 1H, *J* = 11.8 Hz, *1 diast.*), 4.46 (s, 1H, *1 diast.*), 3.52 (q, 1H, *J* = 7.3, *1 diast.*), 3.27 (q, 1H, *J* = 7.2 Hz, *1 diast.*), 1.49 (d, 3H, *J* = 7.3 Hz, *1 diast.*), 1.42 (d, 3H, *J* = 7.3 Hz, *1 diast.*), 1.32 (s, 3H, *1 diast.*), 1.30 (s, 3H, *1 diast.*), 1.27 (s, 3H, *1 diast.*), 1.25 (s, 3H, *1 diast.*). **^{13}C NMR (125 MHz, $CDCl_3$):** 153.5 (*1 diast.*), 153.2 (*1 diast.*), 143.5 (*1 diast.*), 142.8 (*1 diast.*), 129.8 (*2 diast.*), 129.1 (*2 diast.*), 127.3 (*2 diast.*), 126.5 (*1 diast.*), 126.3 (*1 diast.*), 126.2 (*2 diast.*), 123.1 (*1 diast.*), 123.8 (*1 diast.*), 122.0 (*1 diast.*), 121.2 (*1 diast.*), 119.9 (*1 diast.*), 107.1 (*1 diast.*), 106.0 (*1 diast.*), 94.9 (*1 diast.*), 94.7 (*1 diast.*), 83.8 (*2 diast.*), 83.3 (*2 diast.*), 77.1 (*1 diast.*), 75.6 (*2 diast.*), 45.1 (*1 diast.*), 42.4 (*1 diast.*), 25.0 (*1 diast.*), 24.9 (*1 diast.*), 24.6 (*1 diast.*), 24.5 (*1 diast.*), 15.3 (*1 diast.*), 14.4 (*1 diast.*). **HRMS (EI)** $[M+Na]^+$ calc. for $C_{22}H_{27}BCl_3NNaO_4$ 508.0995, found 508.1004.

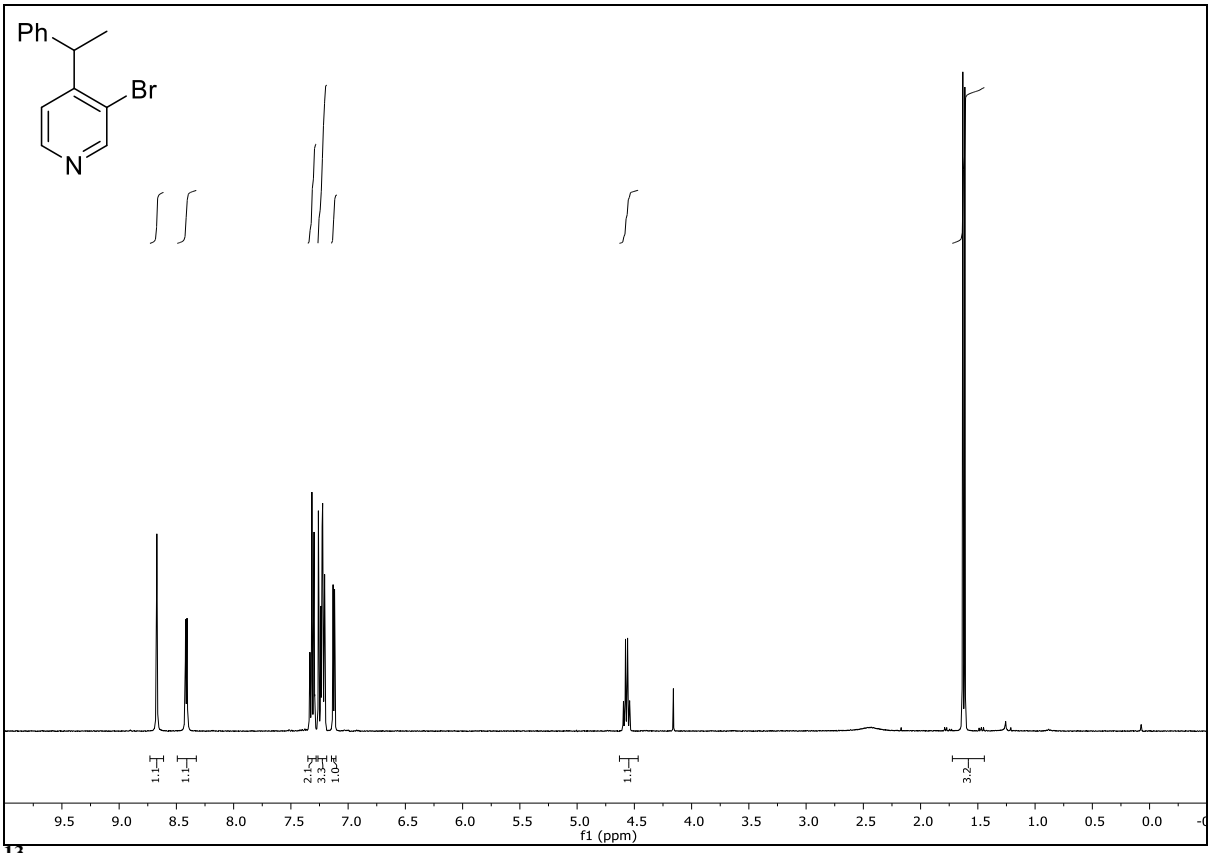
^{1}H NMR (400 MHz, $CDCl_3$) for 4-(1-phenylethyl)pyridine (15)



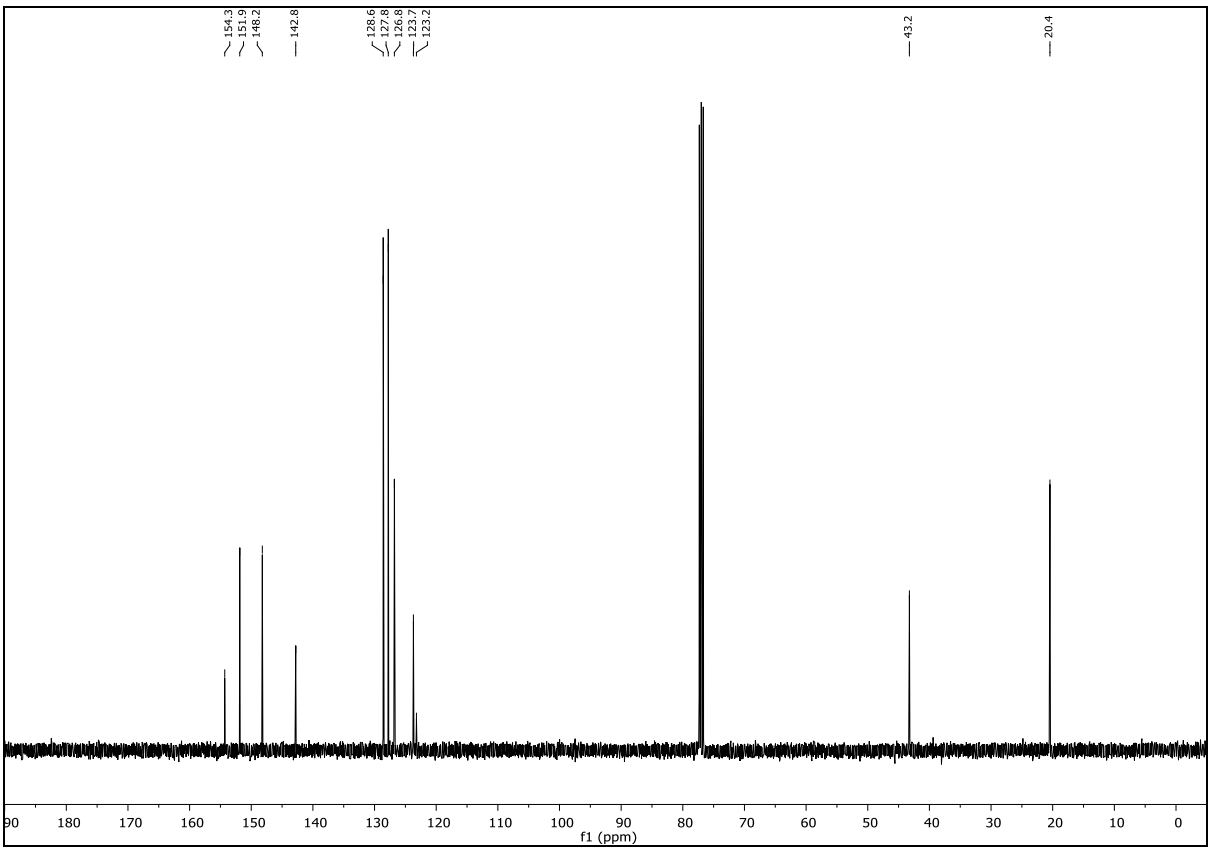
^{13}C NMR (100 MHz, $CDCl_3$) for 4-(1-phenylethyl)pyridine (15)



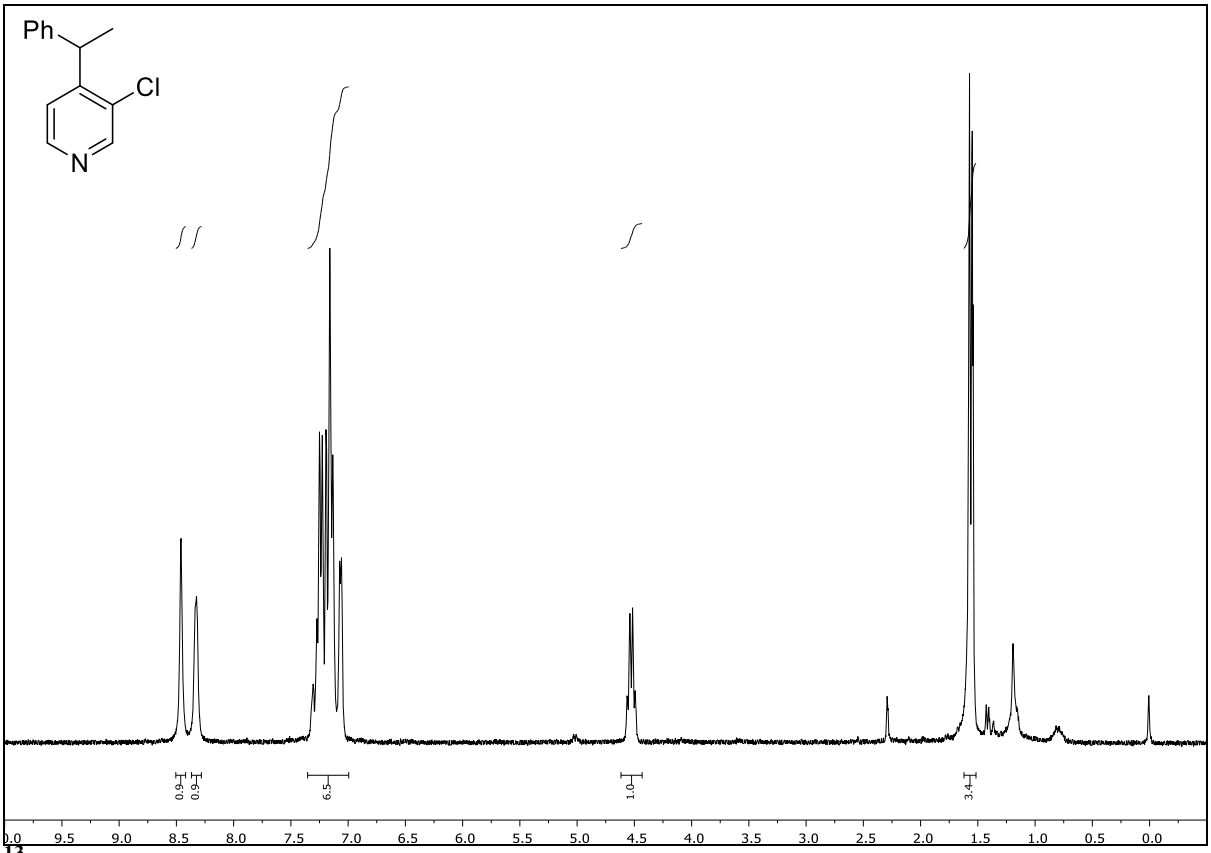
^{1}H NMR (400 MHz, $CDCl_3$) for 3-bromo-(1-phenylehtyl)pyridine (16)



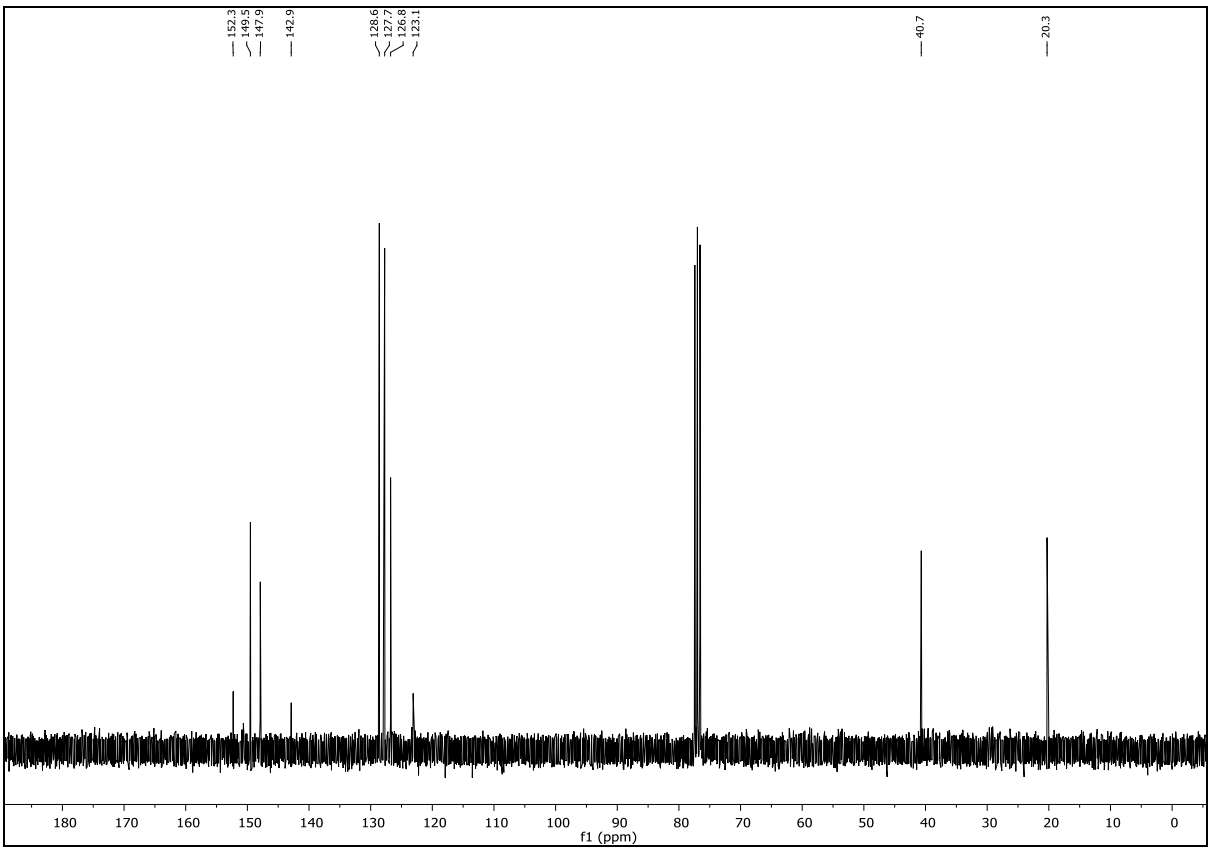
^{13}C NMR (100 MHz, $CDCl_3$) for 3-bromo-(1-phenylehtyl)pyridine (16)



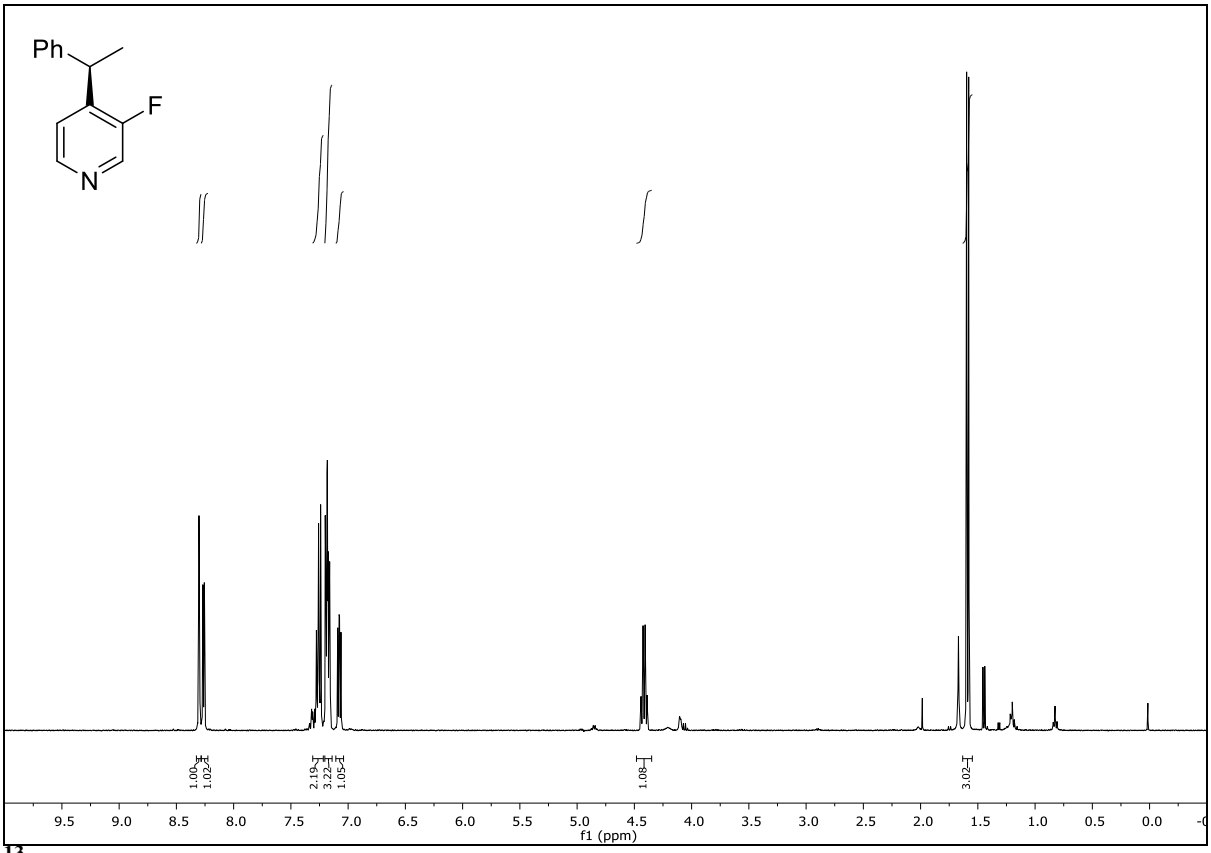
^{1}H NMR (300 MHz, $CDCl_3$) for 3-chloro-4-(1-phenylehtyl)pyridine (17)



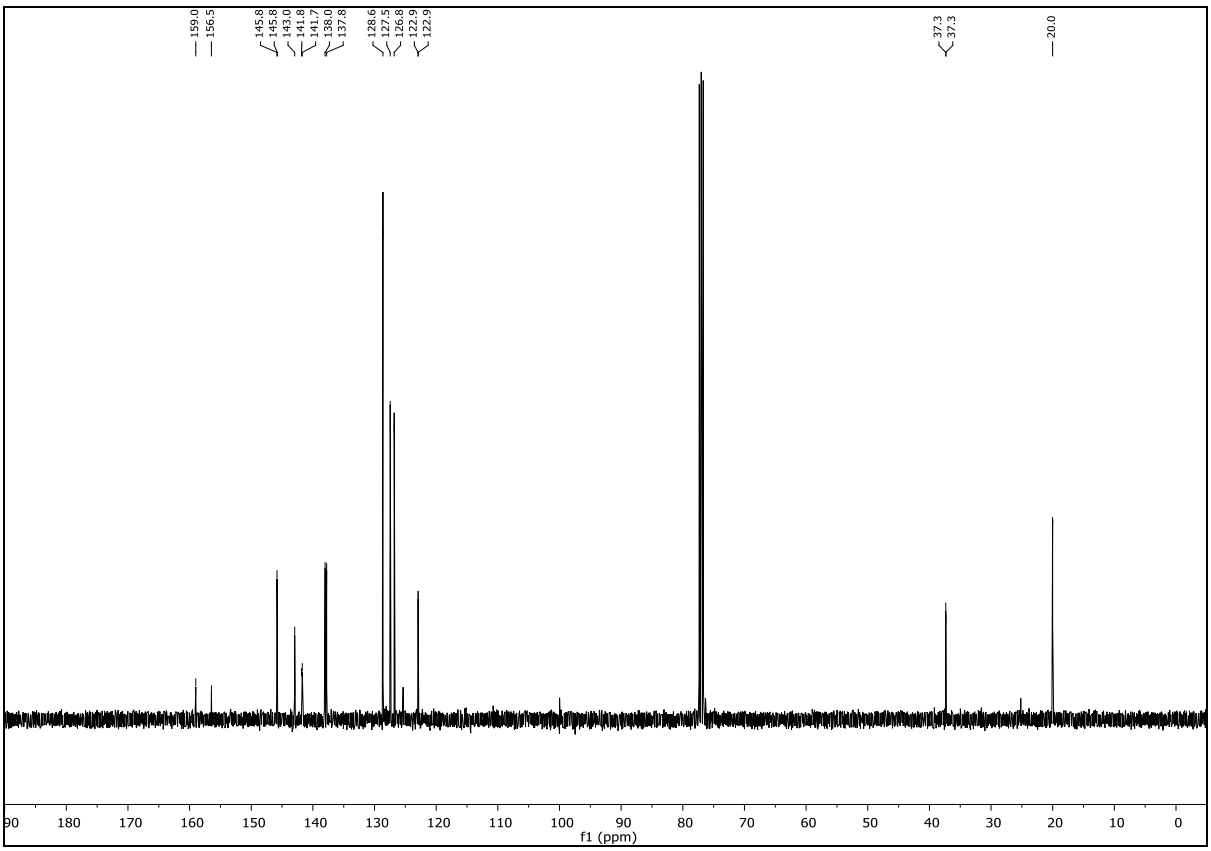
^{13}C NMR (75 MHz, $CDCl_3$) for 3-chloro-4-(1-phenylehtyl)pyridine (17)



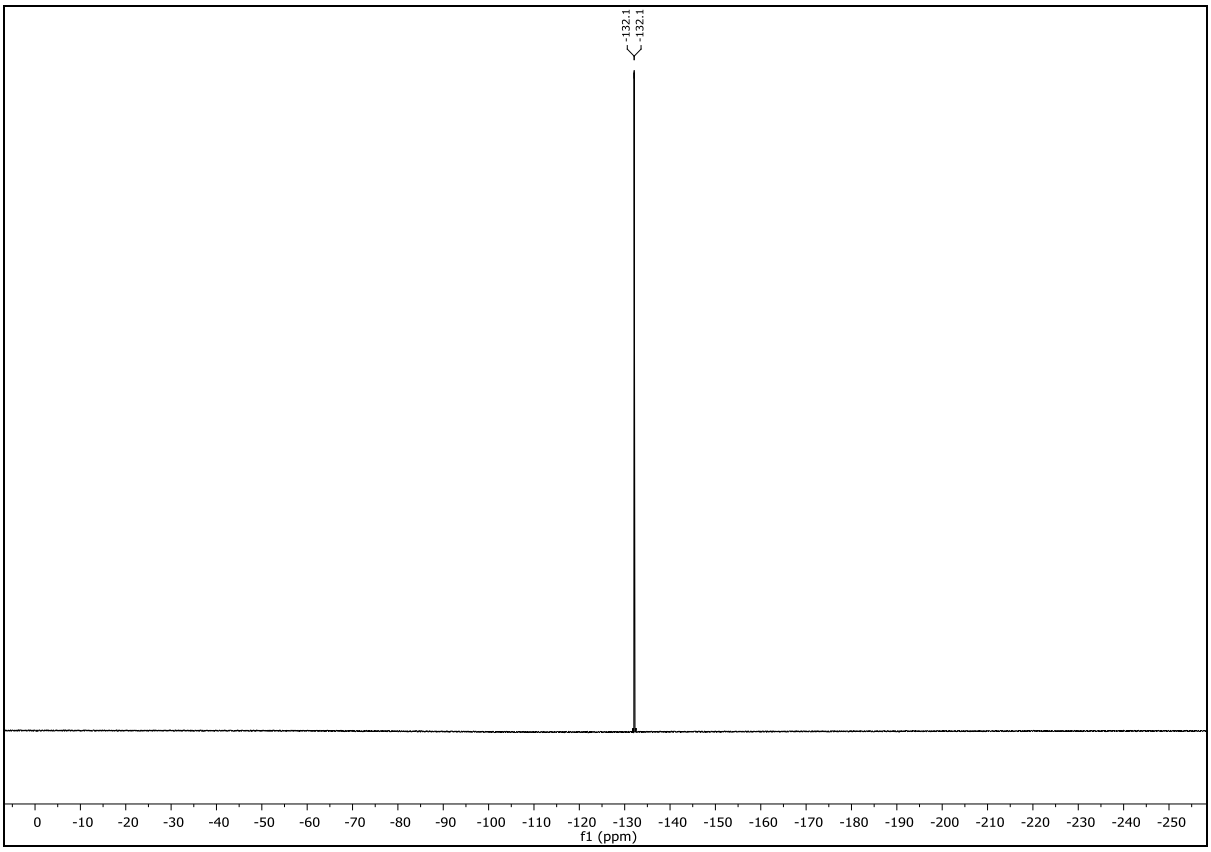
^{1}H NMR (400 MHz, $CDCl_3$) for (*R*)-3-fluoro-4-(1-phenylehtyl)pyridine (18)

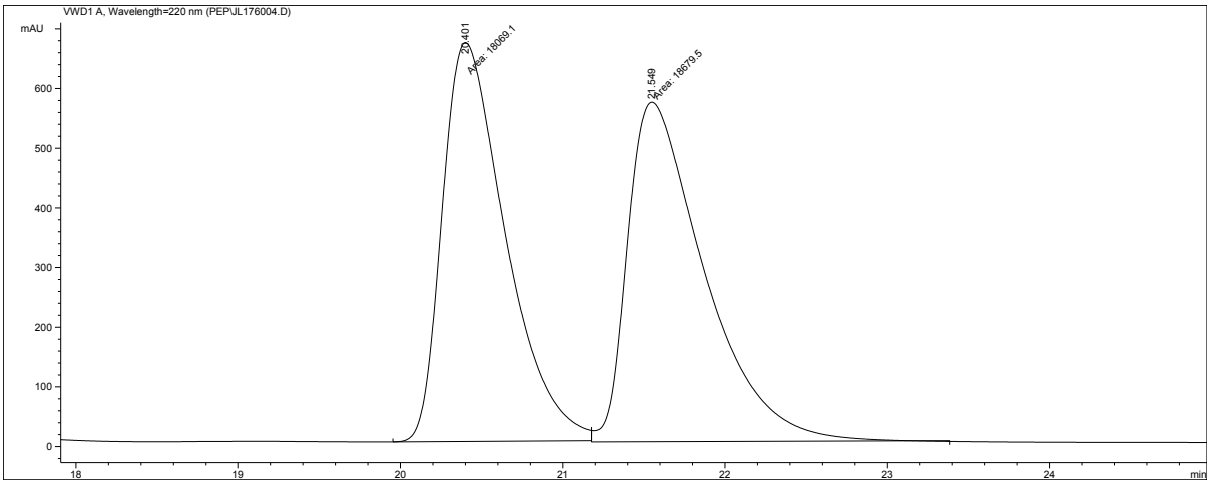


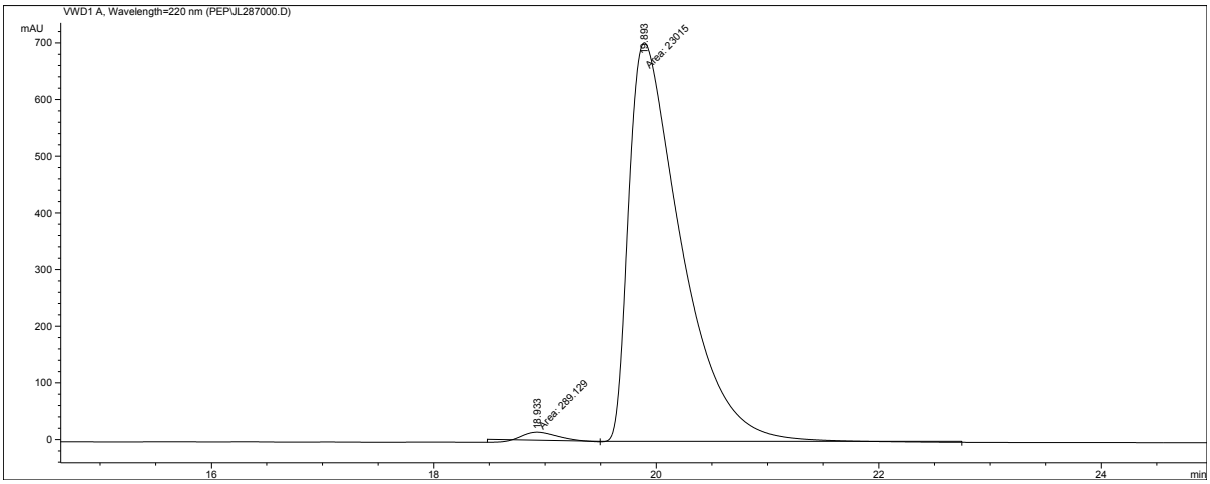
^{13}C NMR (100 MHz, $CDCl_3$) for (*R*)-3-fluoro-4-(1-phenylehtyl)pyridine (18)



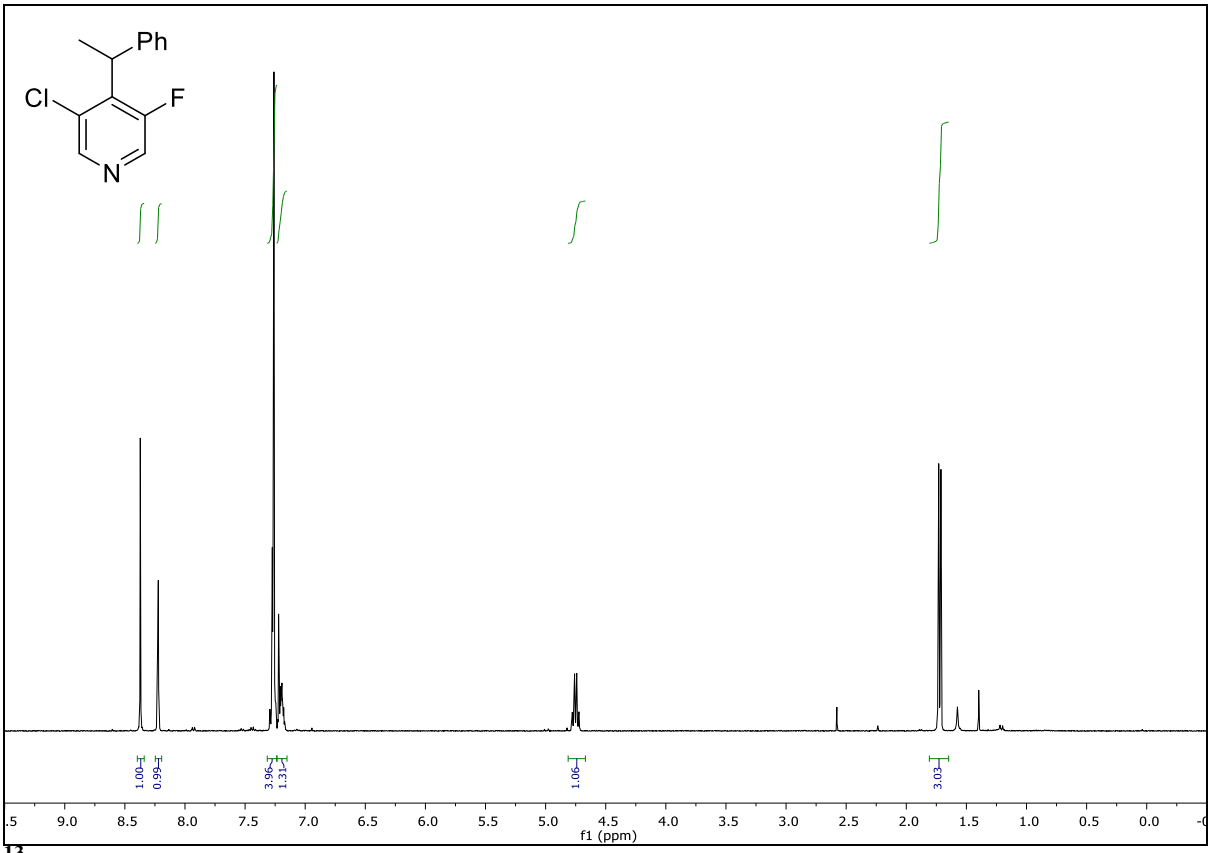
^{19}F NMR (283 MHz, $CDCl_3$) for (*R*)-3-fluoro-4-(1-phenylehtyl)pyridine (19)



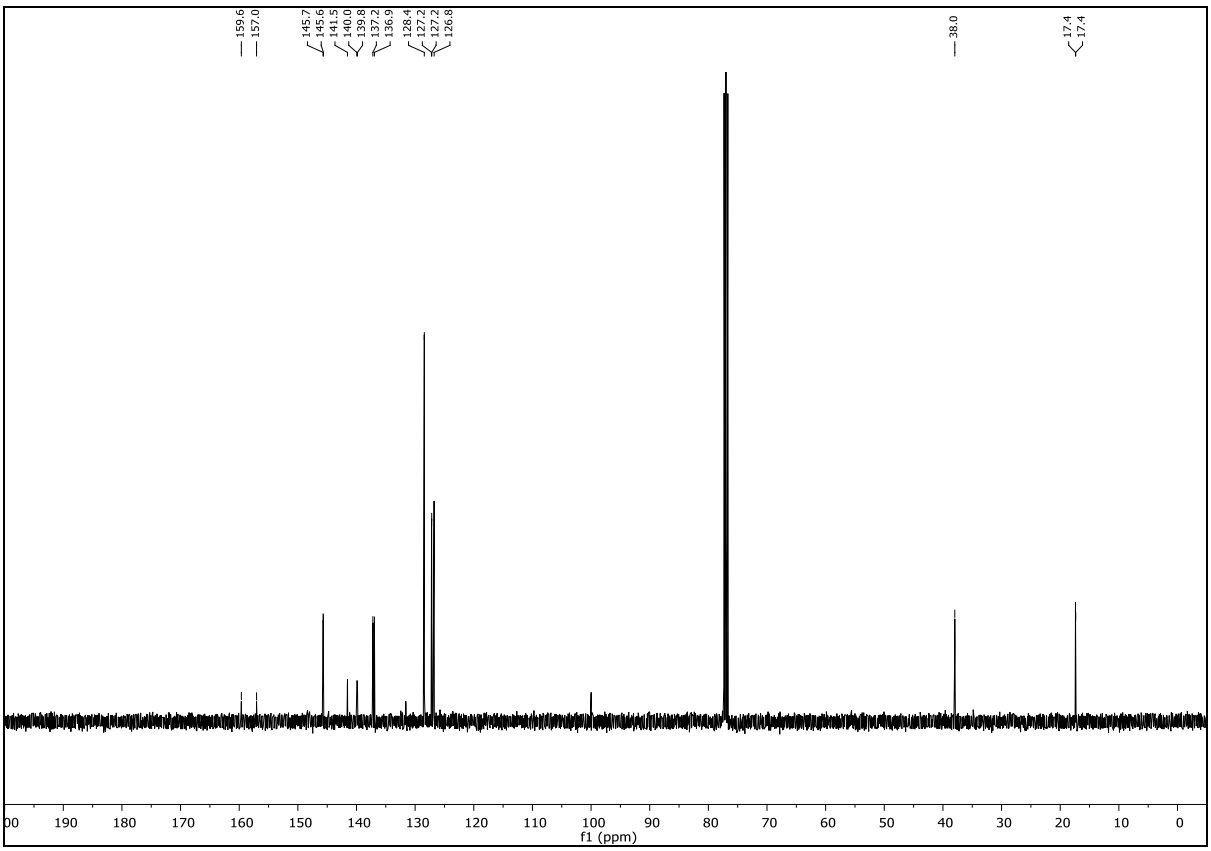

VWD1 A, Wavelength=220 nm (PEP\JL176004.D)
mAU
600
500
400
300
200
100
0
20.401
Area: 18069.1
21.549
Area: 18679.5
18
19
20
21
22
23
24
min


VWD1 A, Wavelength=220 nm (PEP\JL287000.D)
mAU
700
600
500
400
300
200
100
0
18.933
Area: 289.129
19.893
Area: 23015
16
18
20
22
24
min

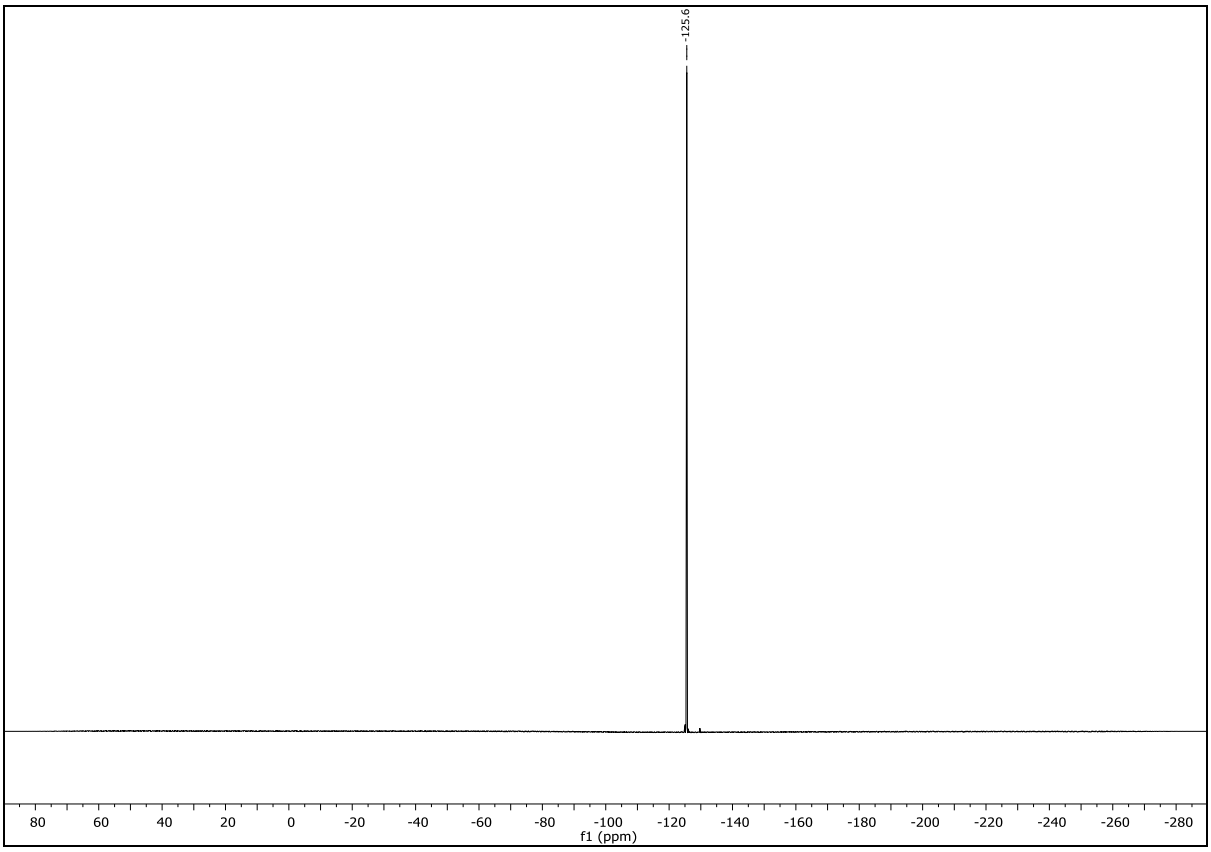
^{1}H NMR (400 MHz, $CDCl_3$) 3-Chloro-5-fluoro-4-(1-phenylethyl)pyridine.



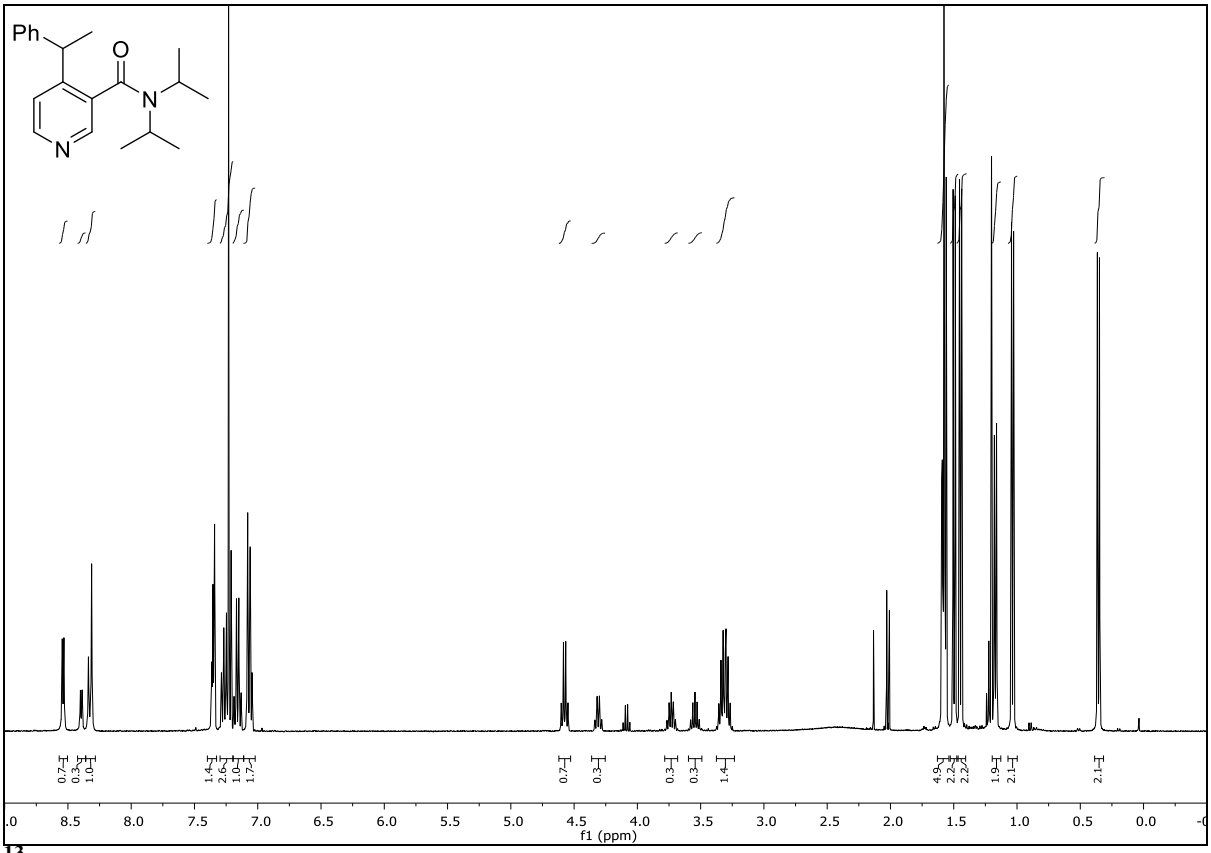
^{13}C NMR (100 MHz, $CDCl_3$) 3-Chloro-5-fluoro-4-(1-phenylethyl)pyridine.



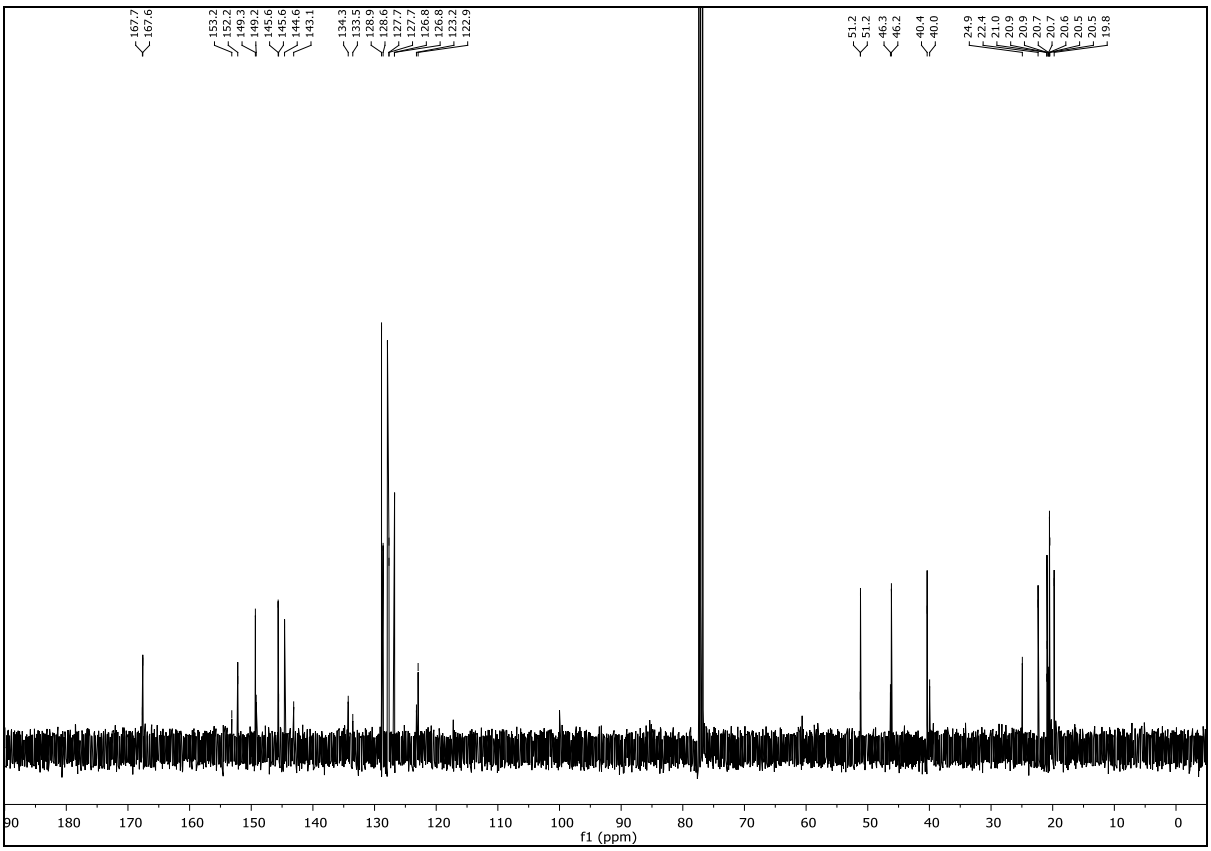
^{19}F NMR (283 MHz, $CDCl_3$) 3-chloro-5-fluoro-4-(1-phenylethyl)pyridine



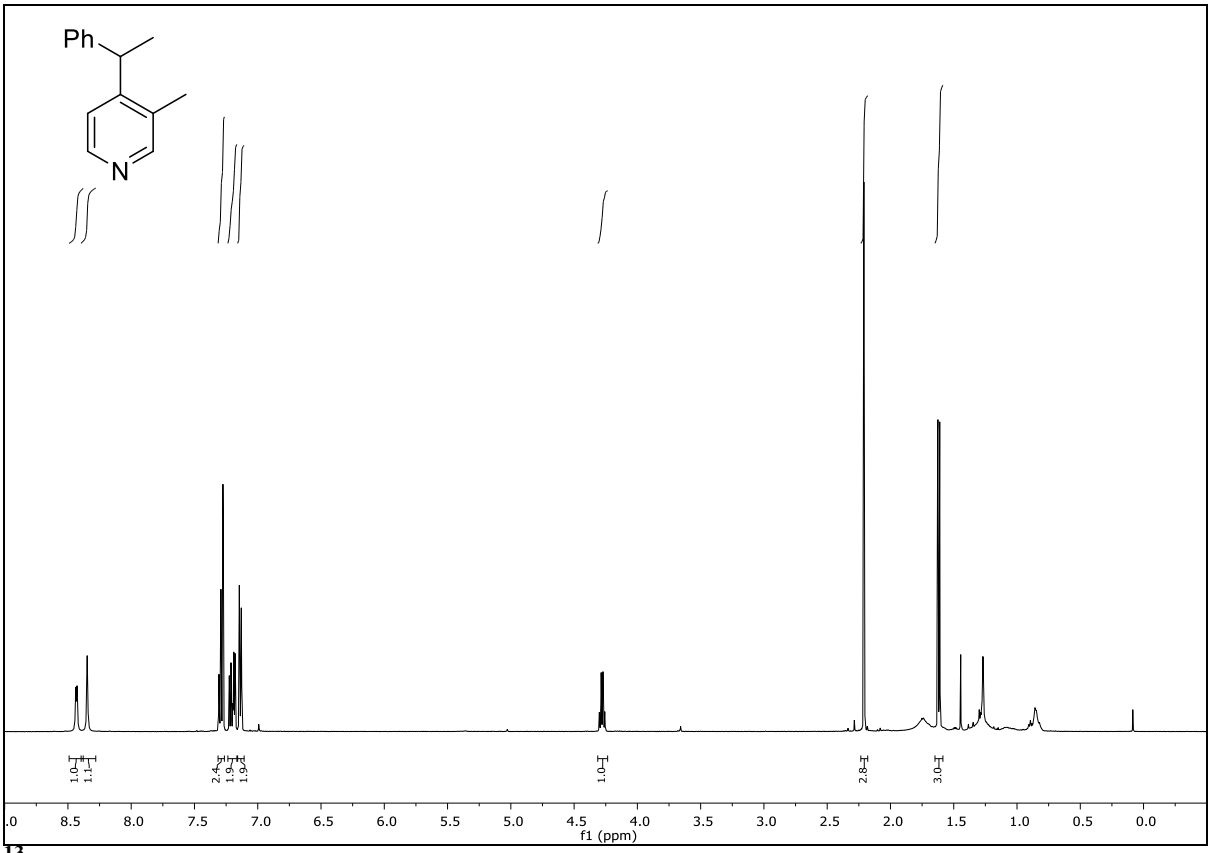
^{1}H NMR (400 MHz, $CDCl_3$) for N,N-diisopropyl-4-(1-phenylethyl)nicotinamide (20)



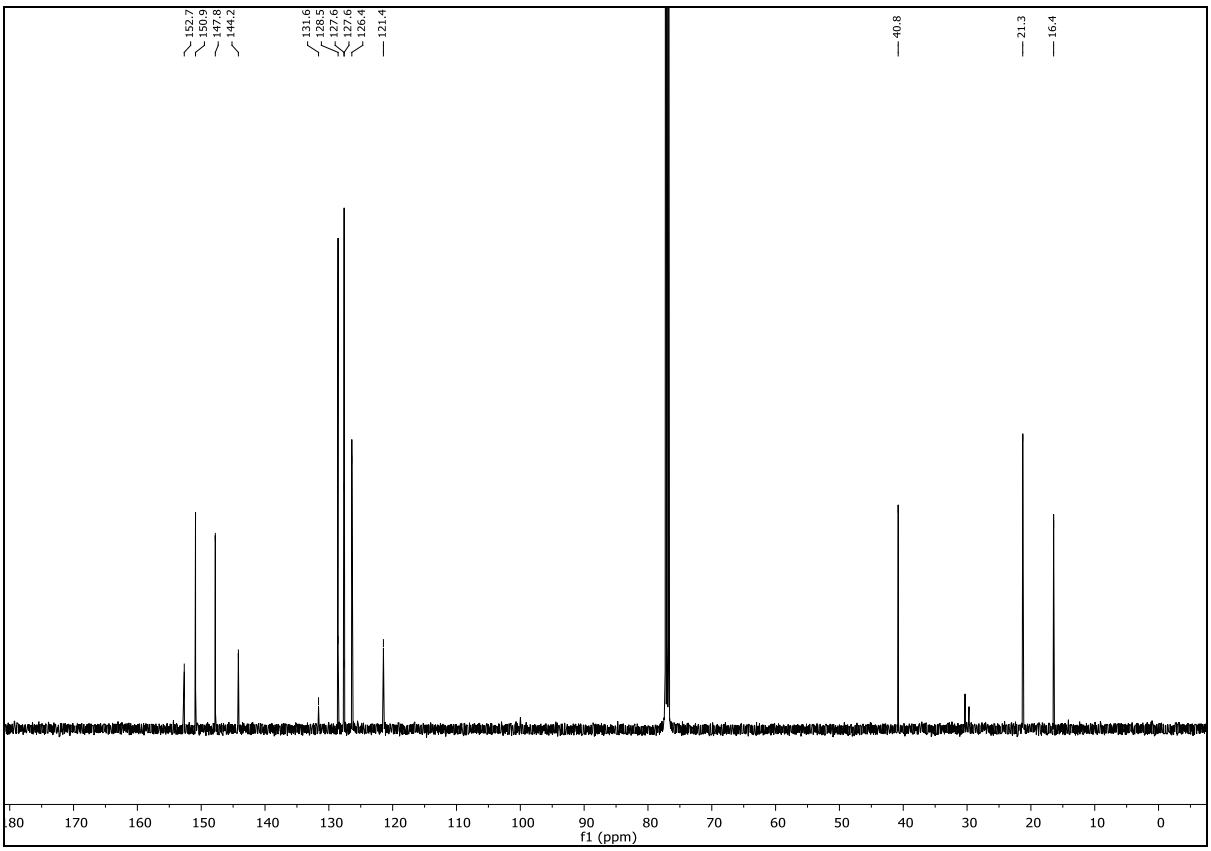
^{13}C NMR (100 MHz, $CDCl_3$) for N,N-diisopropyl-4-(1-phenylethyl)nicotinamide (20)



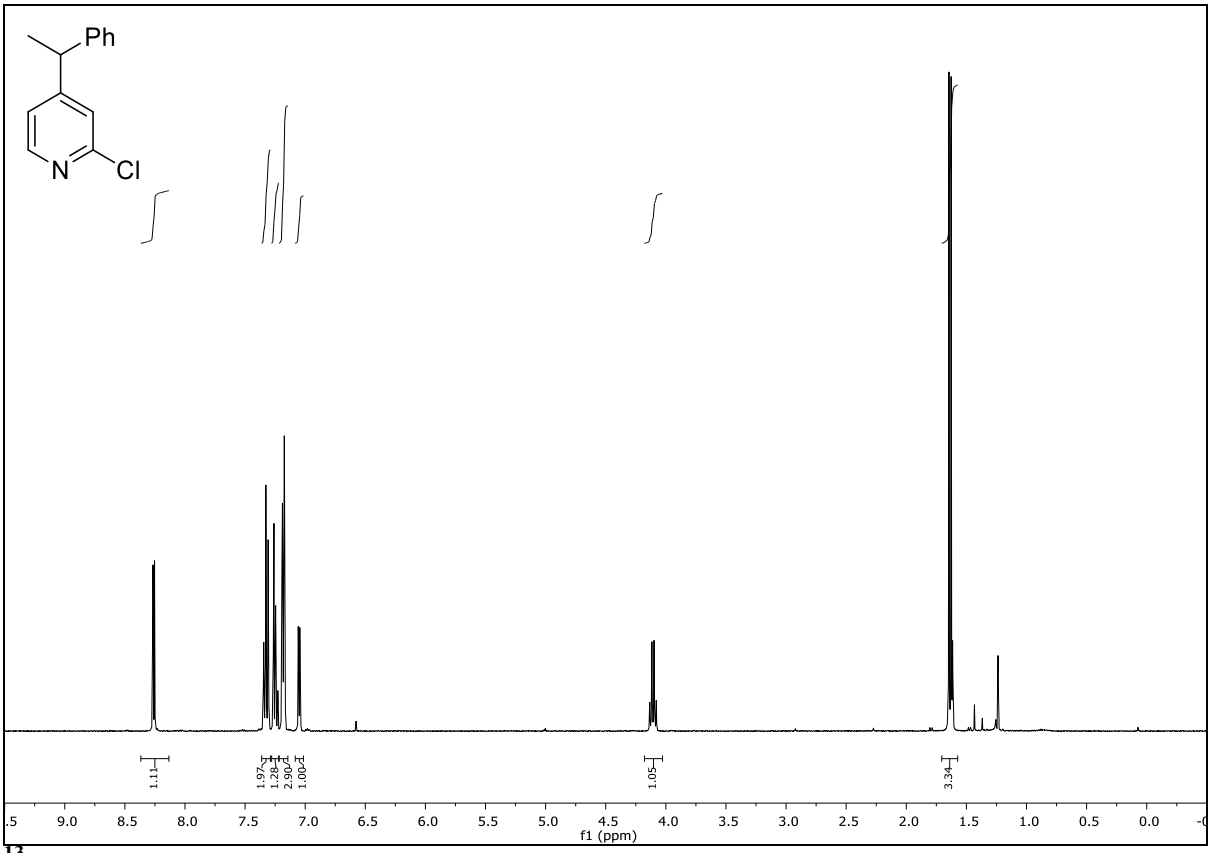
^{1}H NMR (400 MHz, $CDCl_3$) for 3-Methyl-4-(1-phenylethyl)pyridine (21)



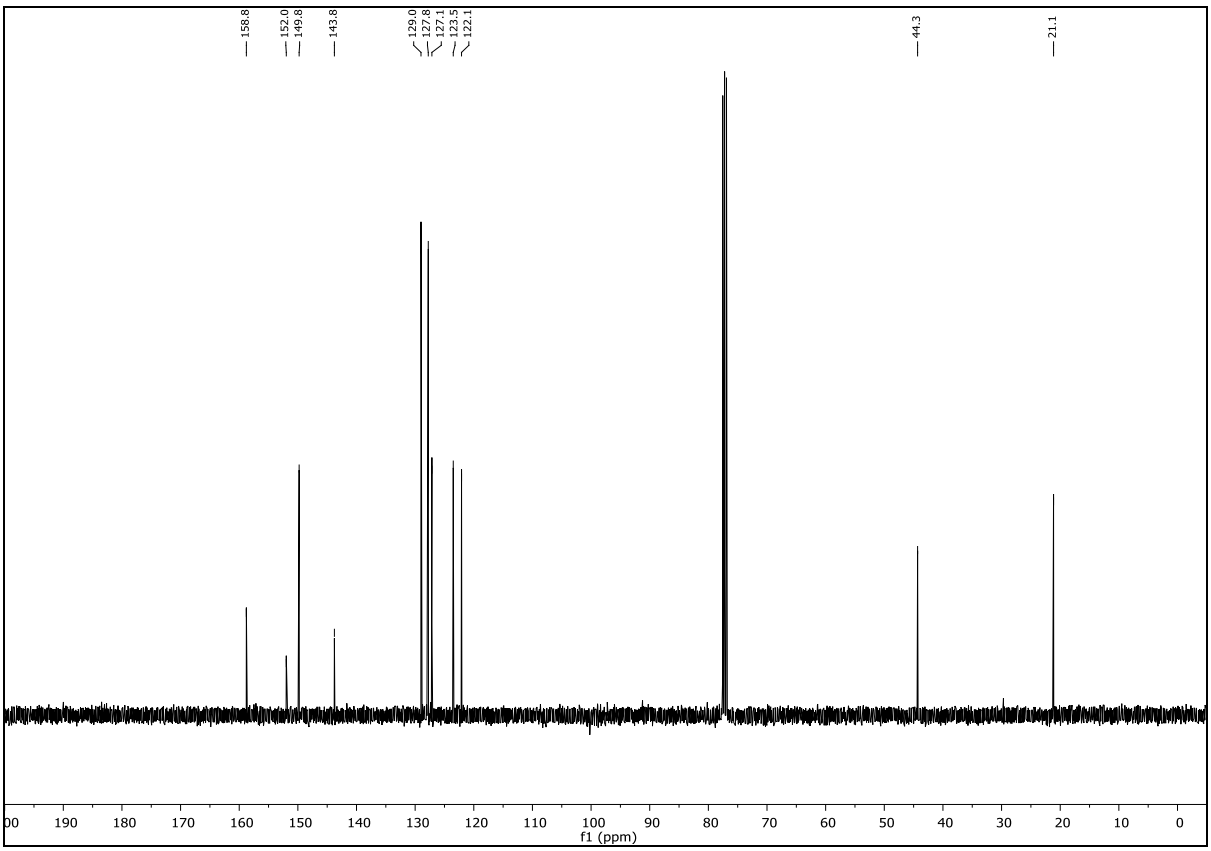
^{13}C NMR (125 MHz, $CDCl_3$) for 3-Methyl-4-(1-phenylethyl)pyridine (21)



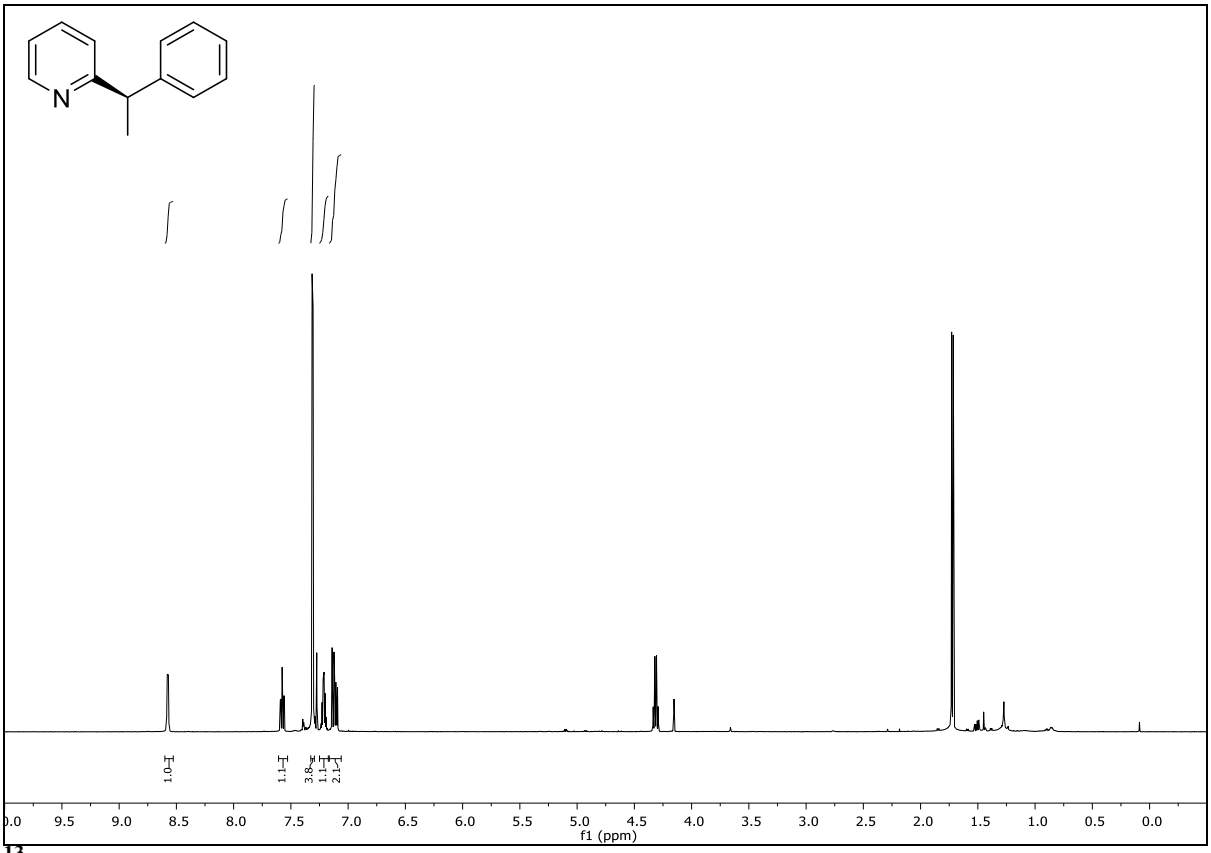
^{1}H NMR (500 MHz, $CDCl_3$) for 2-Chloro-4-(1-phenylethyl)pyridine (22)



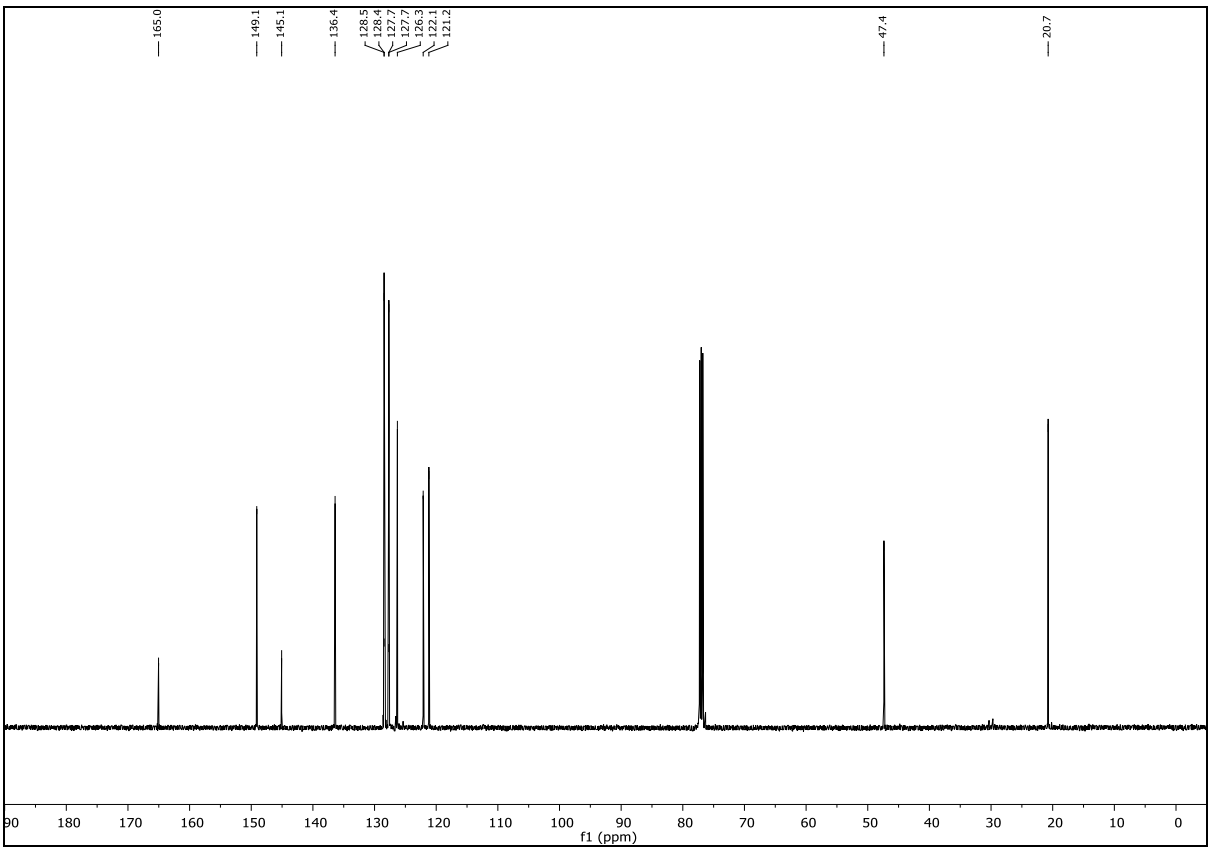
^{13}C NMR (125 MHz, $CDCl_3$) for 2-Chloro-4-(1-phenylethyl)pyridine (22)

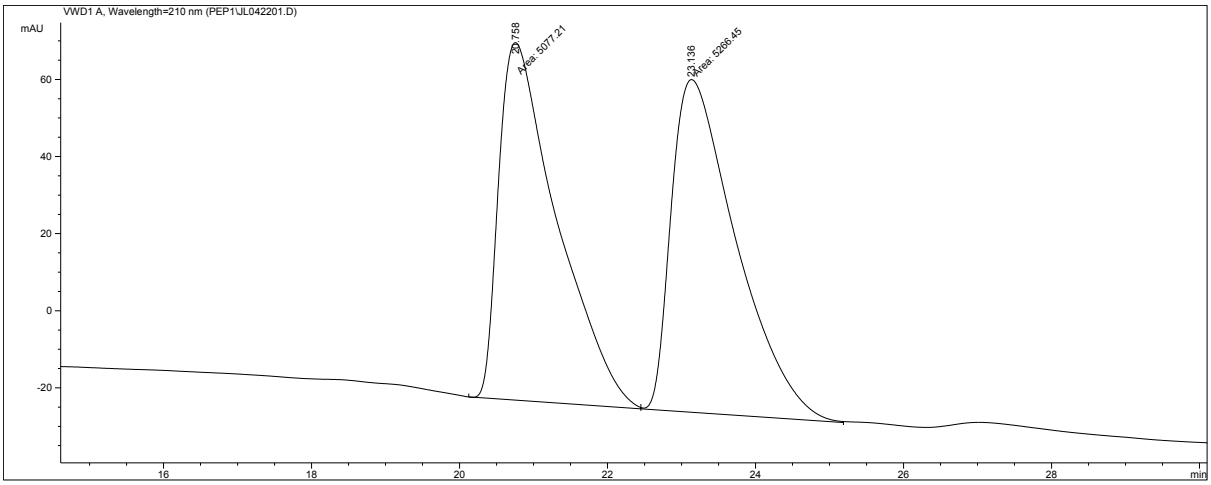


^{1}H NMR (400MHz, $CDCl_3$) of (*R*)-2-(1-phenylethyl)pyridine (23)



^{13}C NMR (125MHz, $CDCl_3$) of (*R*)-2-(1-Phenylethyl)pyridine (23)




VWD1 A, Wavelength=210 nm (PEP1\JL042201.D)
mAU
60
40
20
0
-20
20.758
Area: 5077.21
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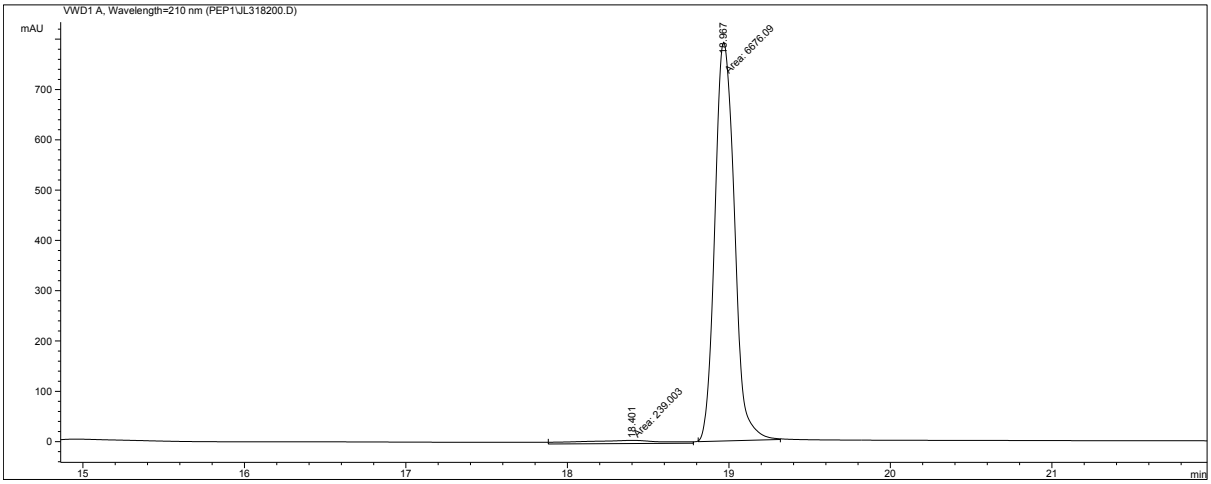
Area: 5266.45
16
18
20
22
24
26
28
min


VWD1 A, Wavelength=210 nm (PEP1\JL318200.D)
mAU
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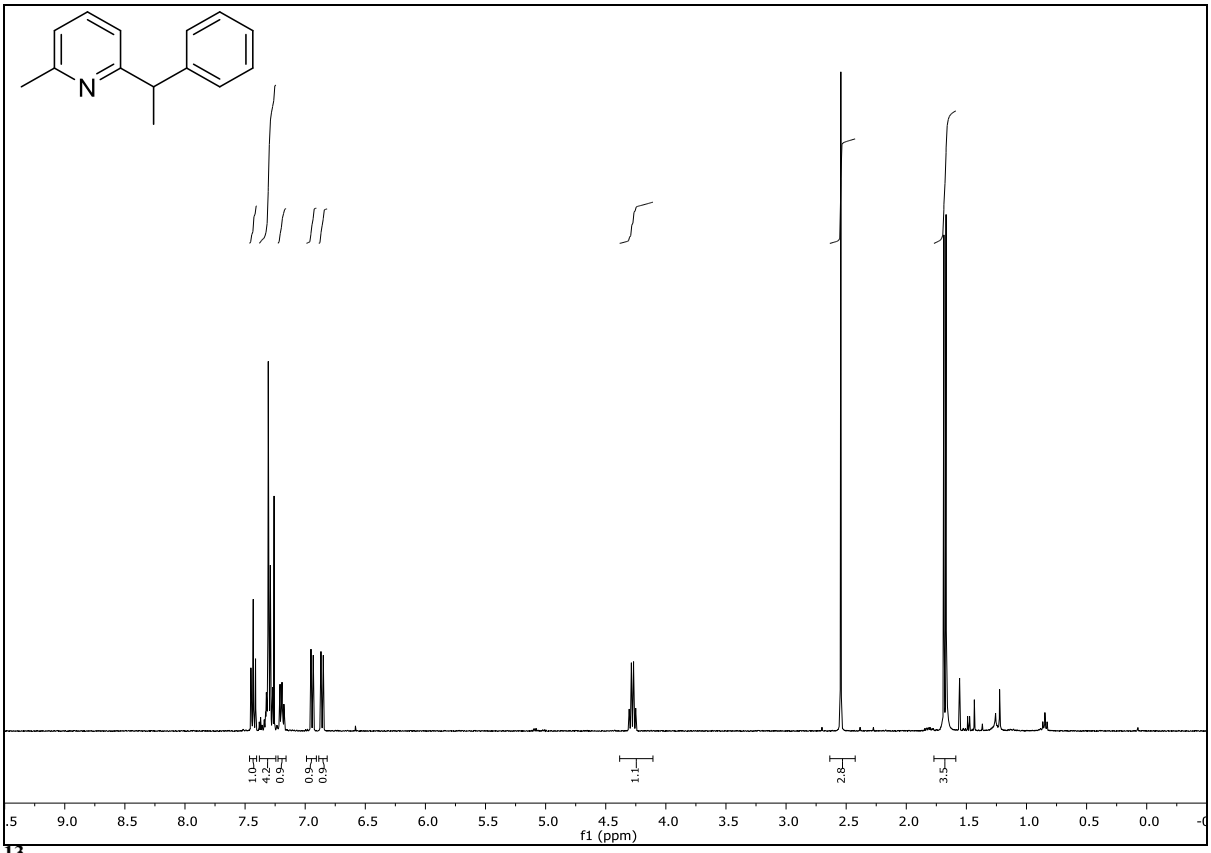
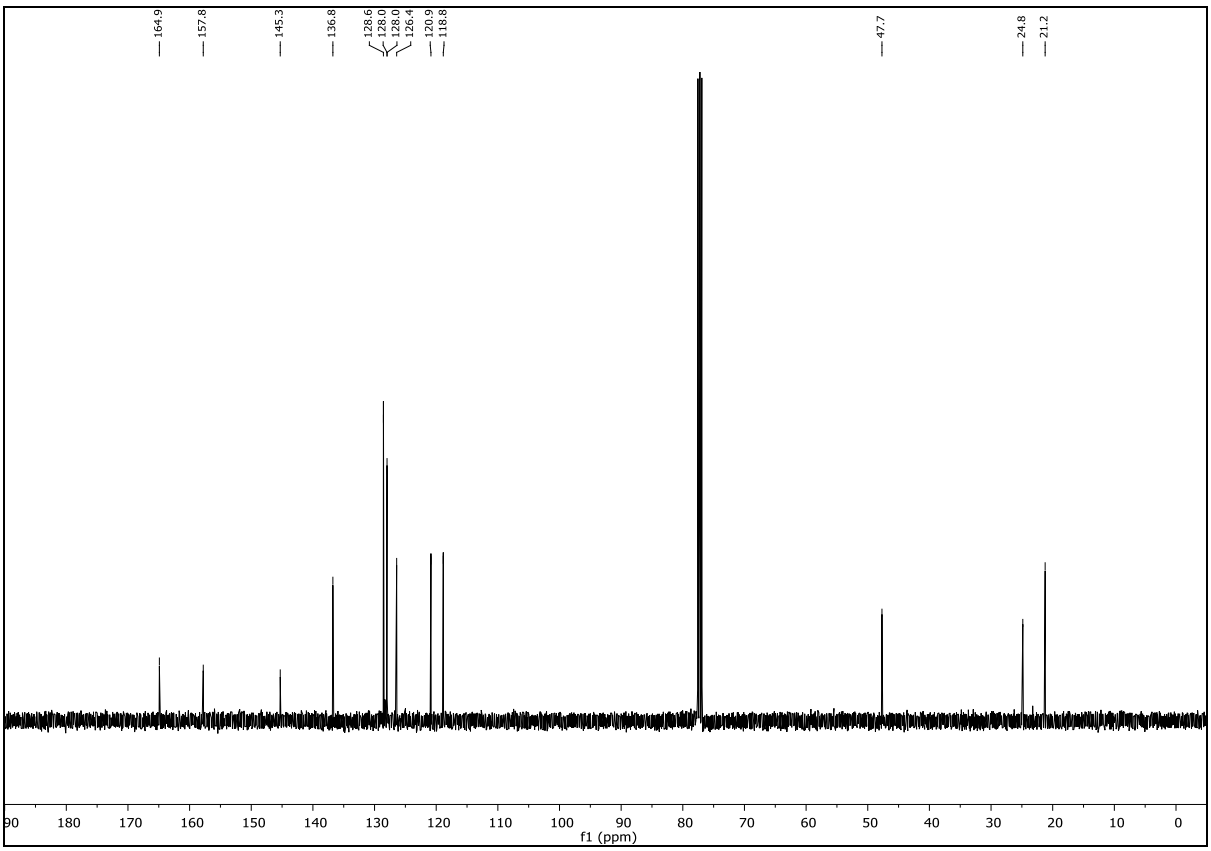
600
500
400
300
200
100
0
18.967
Area: 6676.09
18.401
Area: 239.003
15
16
17
18
19
20
21
min

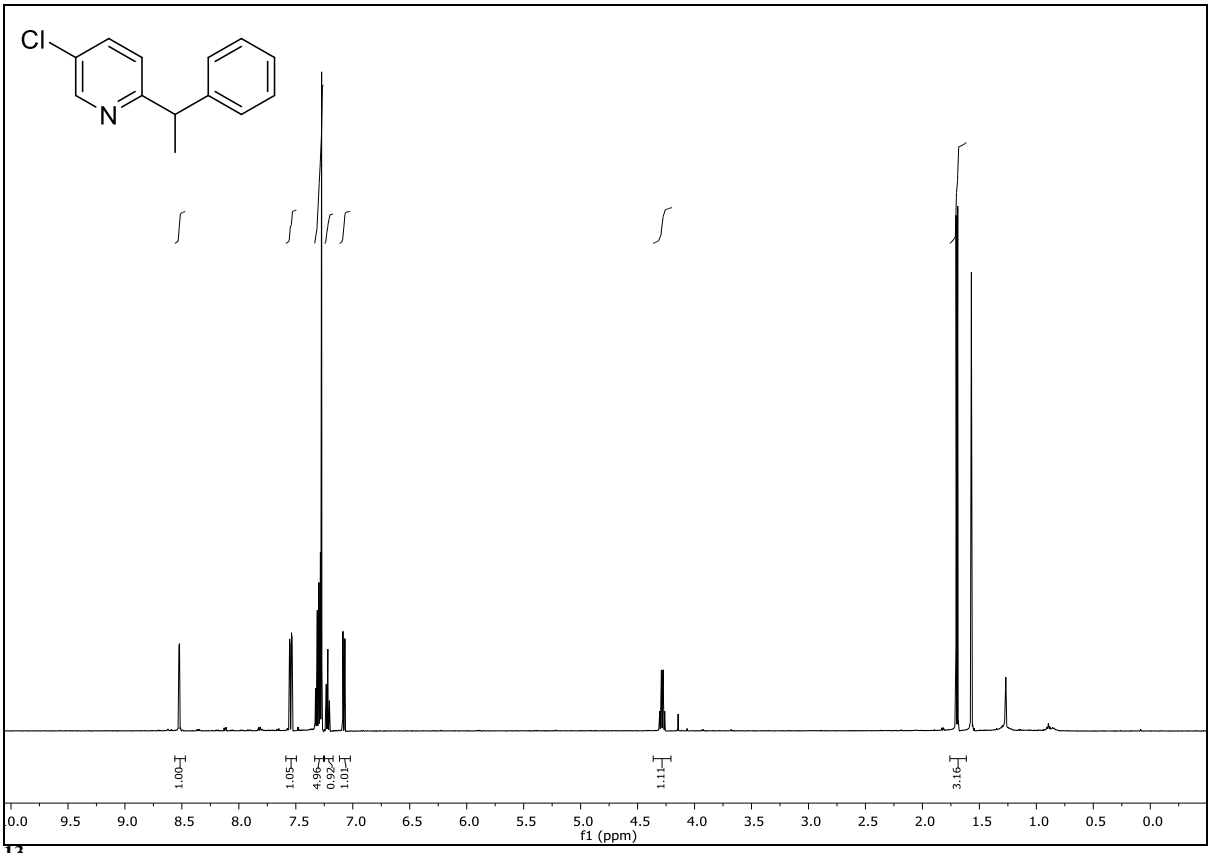
^{1}H NMR (500MHz, $CDCl_3$) of 2-methyl-6-(1-phenylethyl)pyridine (24)



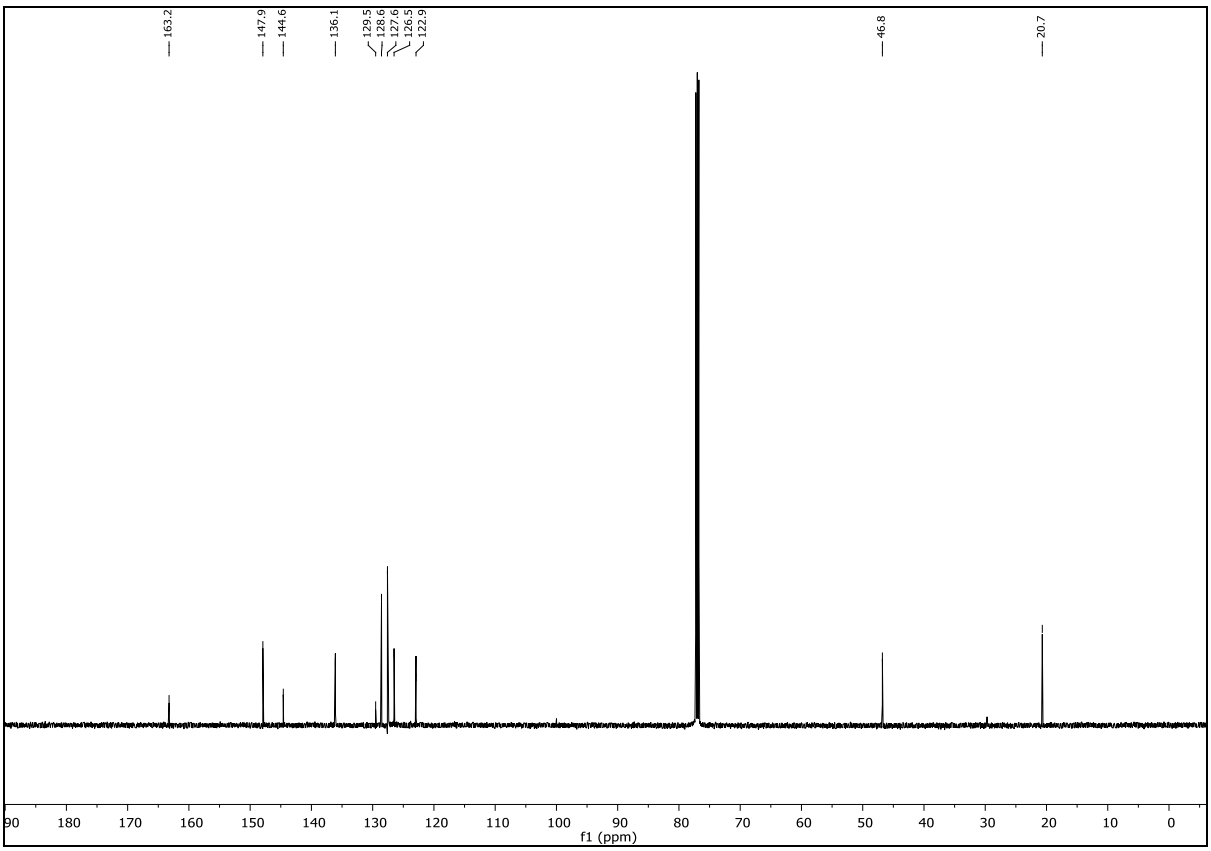
^{13}C NMR (125MHz, $CDCl_3$) of 2-methyl-6-(1-phenylethyl)pyridine (24)



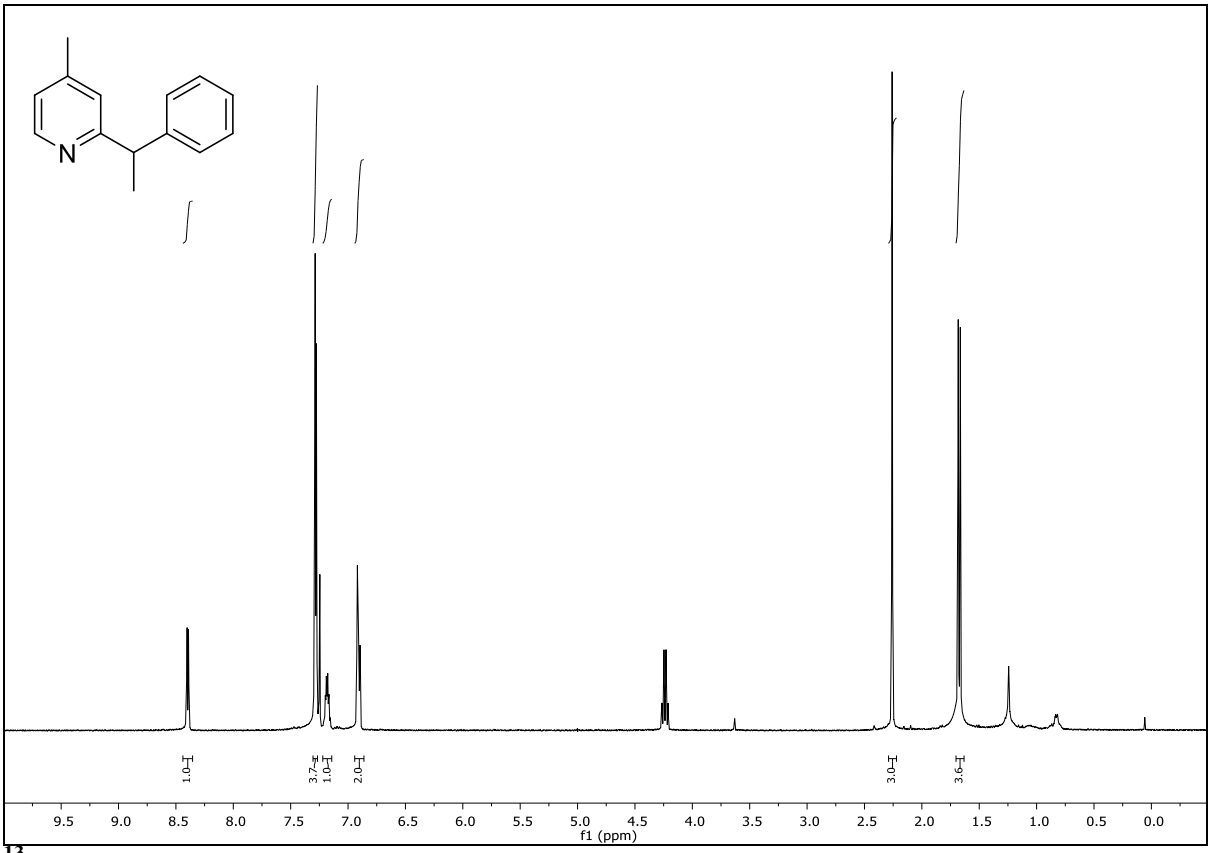
^{1}H NMR (500MHz, $CDCl_3$) of 3-chloro-6-(1-phenylethyl)pyridine (25)



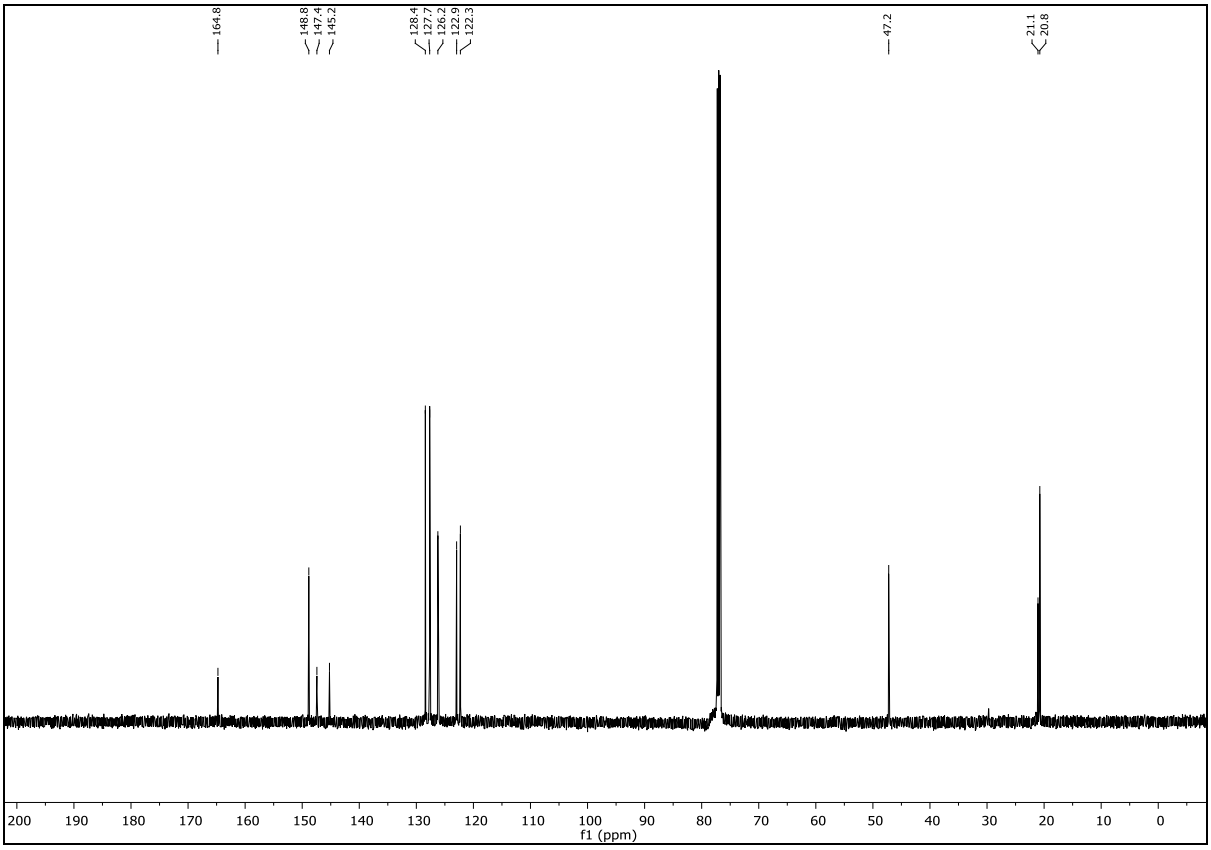
^{13}C NMR (125MHz, $CDCl_3$) of 3-chloro-6-(1-phenylethyl)pyridine (25)



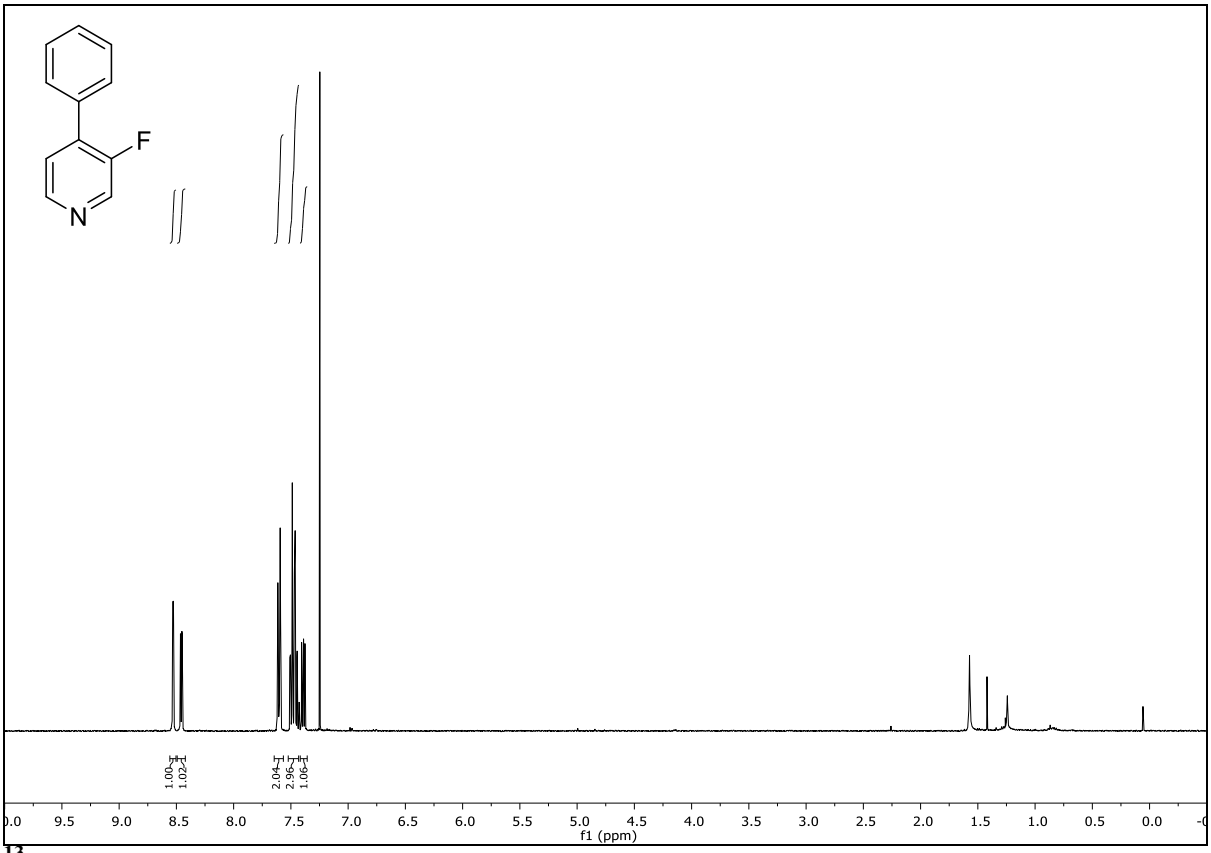
^{1}H NMR (400MHz, $CDCl_3$) of 4-methyl-2-(1-phenylethyl)pyridine (26)



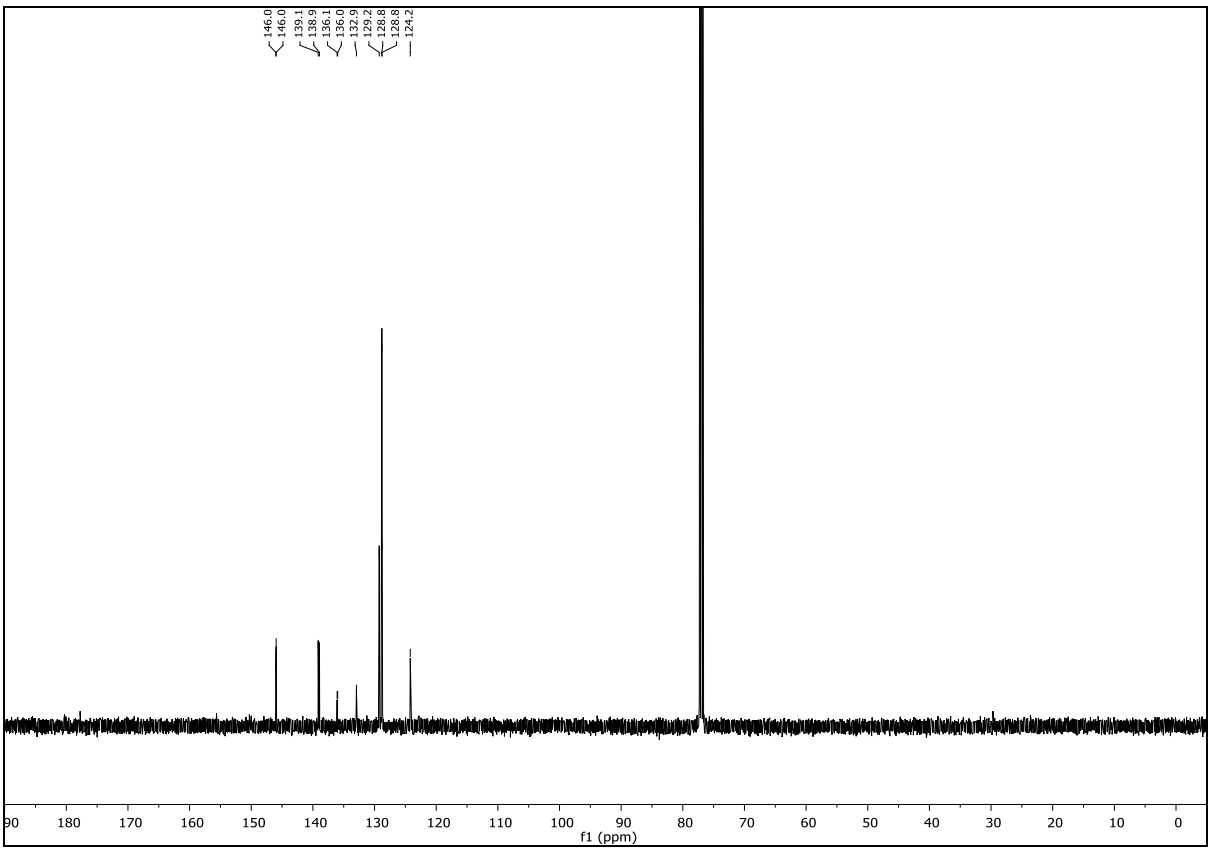
^{13}C NMR (125MHz, $CDCl_3$) of 4-methyl-2-(1-phenylethyl)pyridine (26)



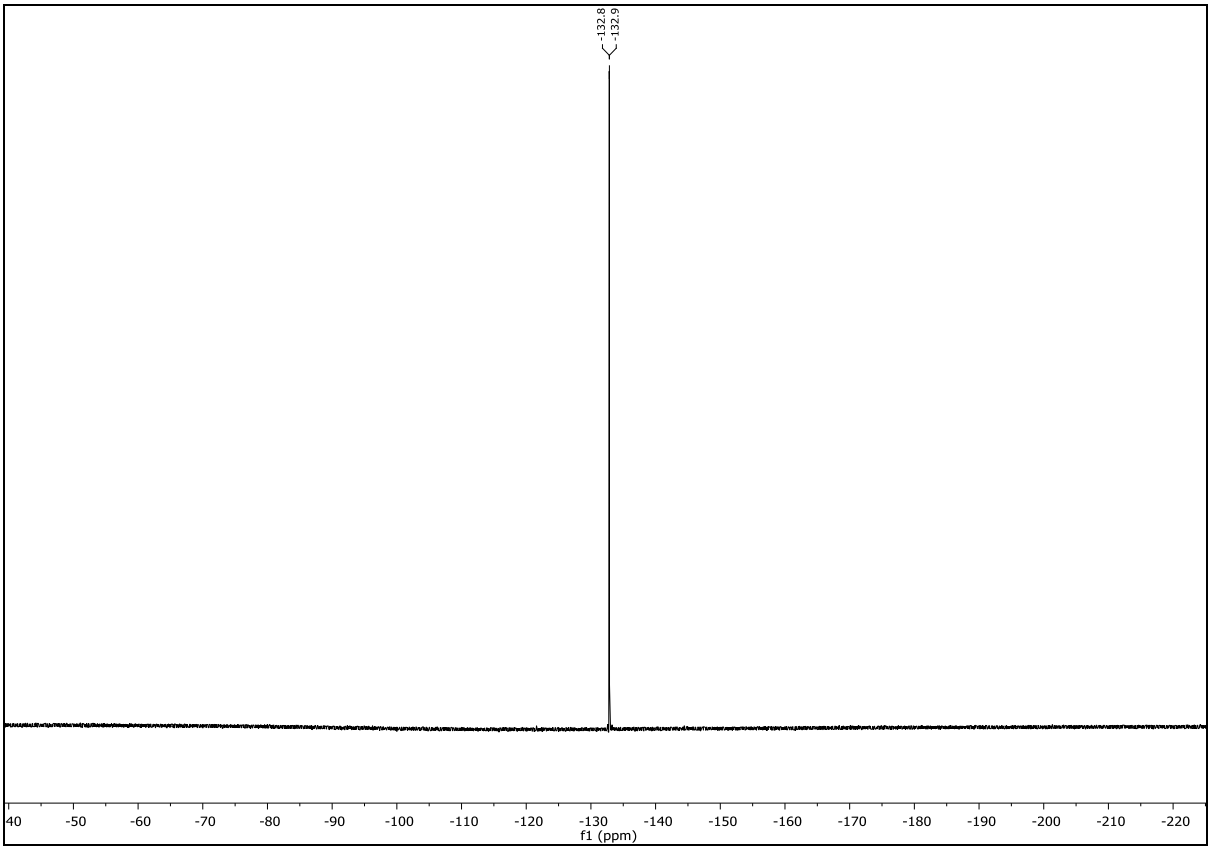
^{1}H NMR (400 MHz, $CDCl_3$) of 3-Fluoro-4-phenylpyridine (28)



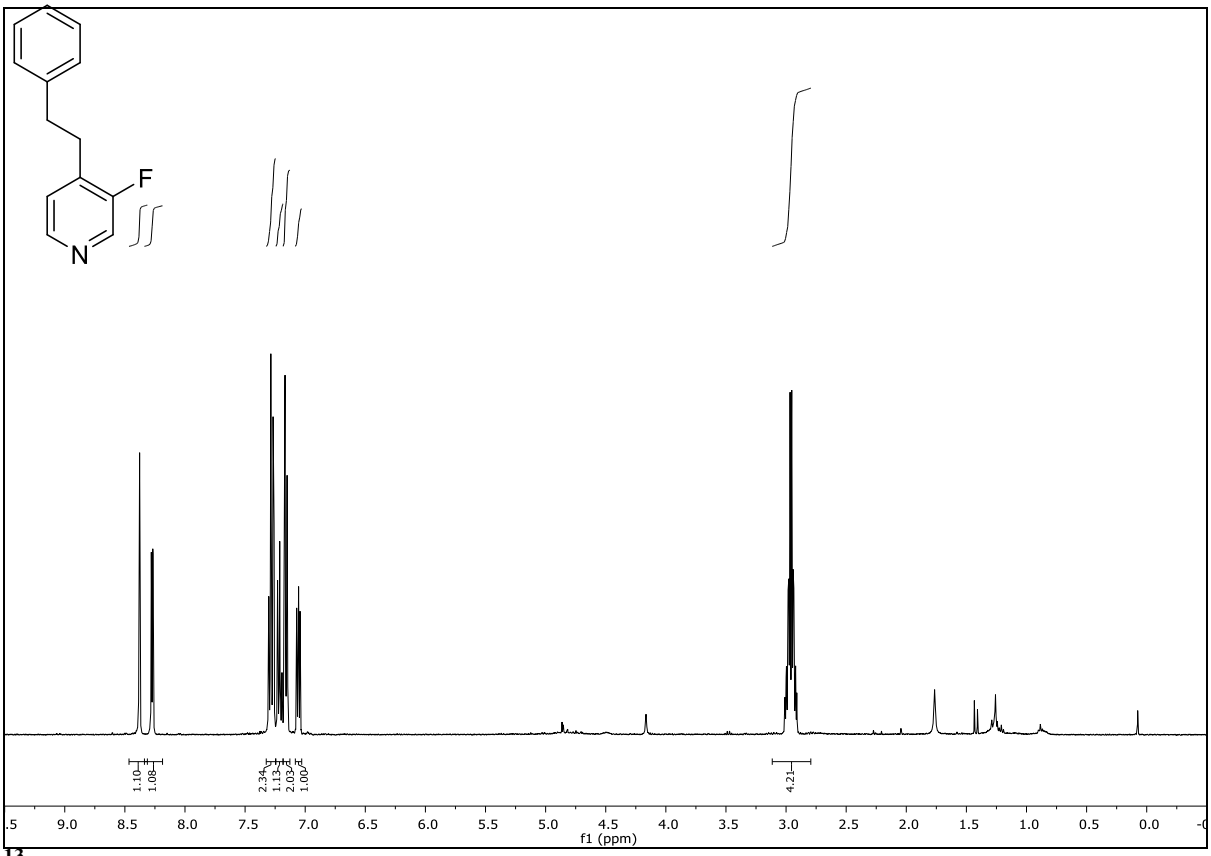
^{13}C NMR (500 MHz, $CDCl_3$) of 3-Fluoro-4-phenylpyridine (28)



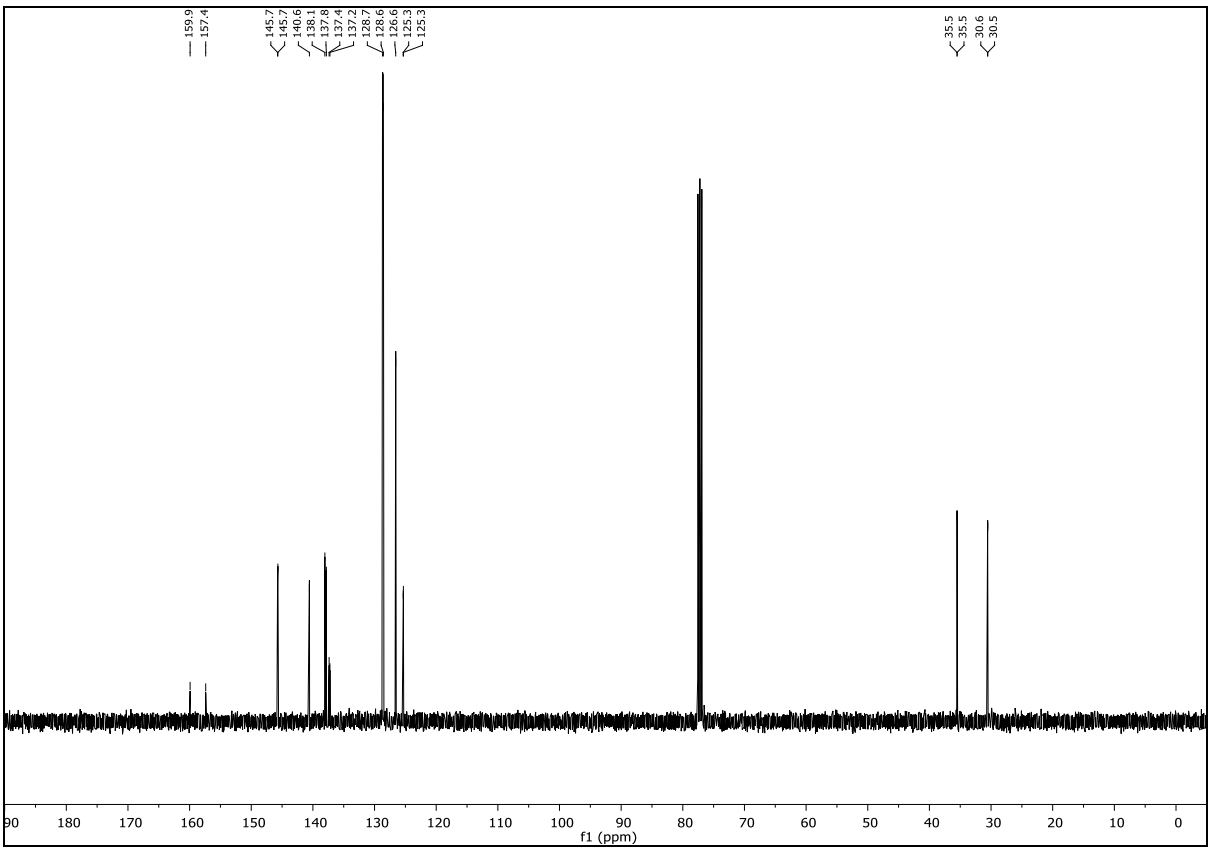
^{19}F NMR (283 MHz) of 3-Fluoro-4-phenylpyridine (28)



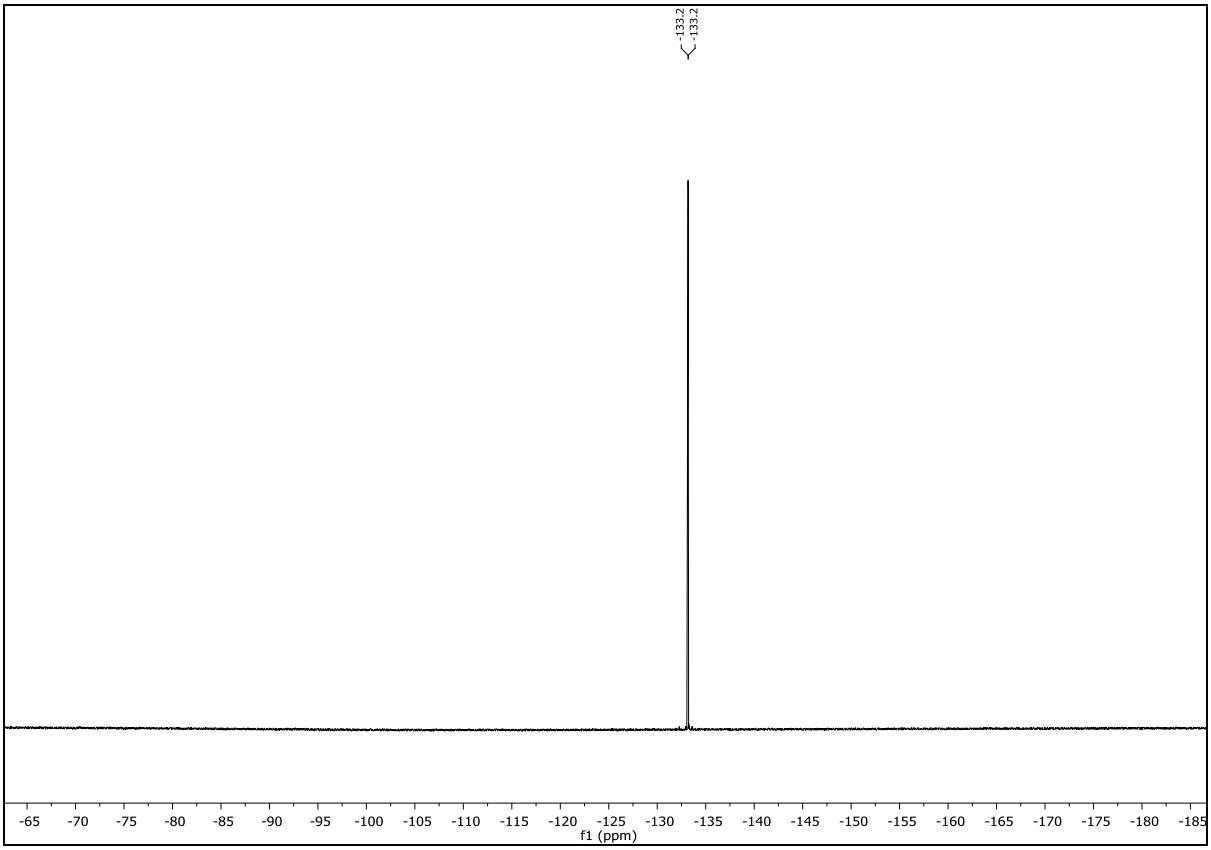
^{1}H NMR (400 MHz, $CDCl_3$) of 3-Fluoro-4-phenethylpyridine (29)



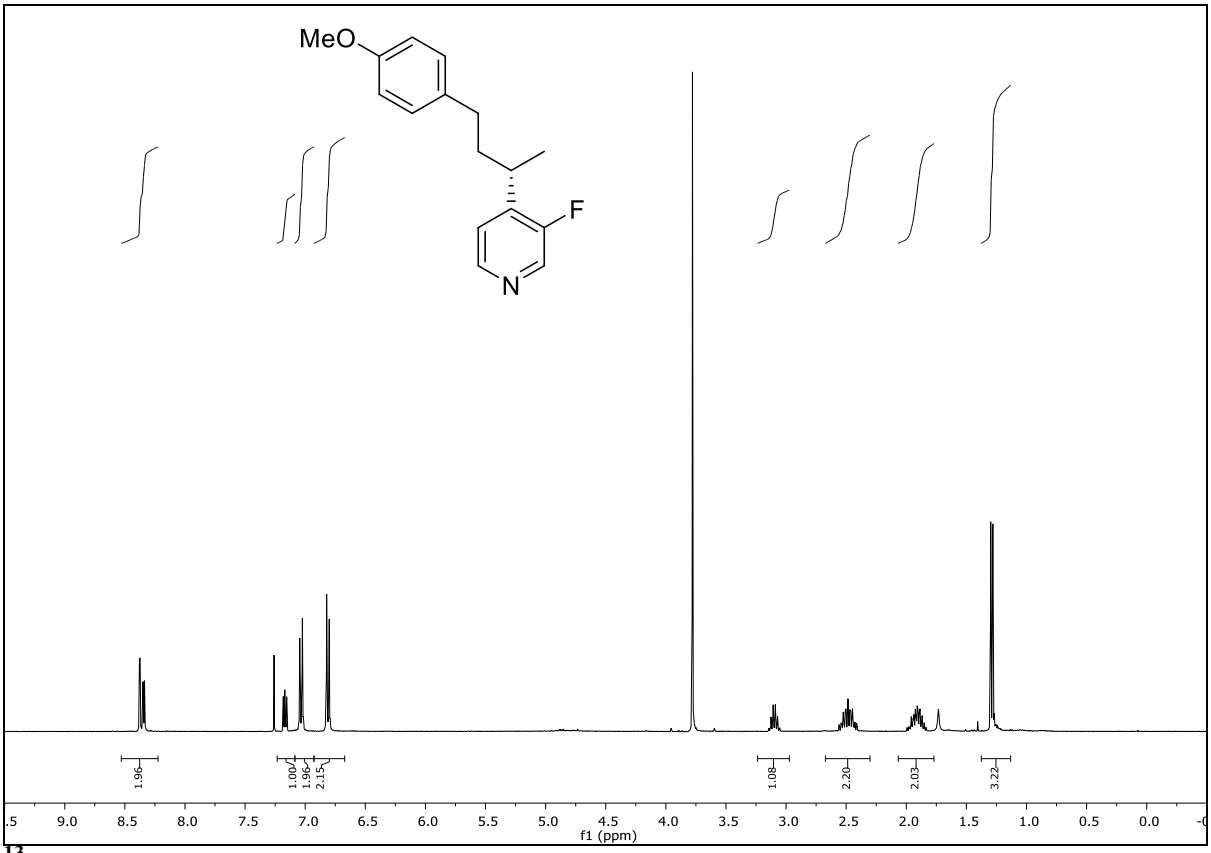
^{13}C NMR (100 MHz, $CDCl_3$) of 3-Fluoro-4-phenethylpyridine (29)



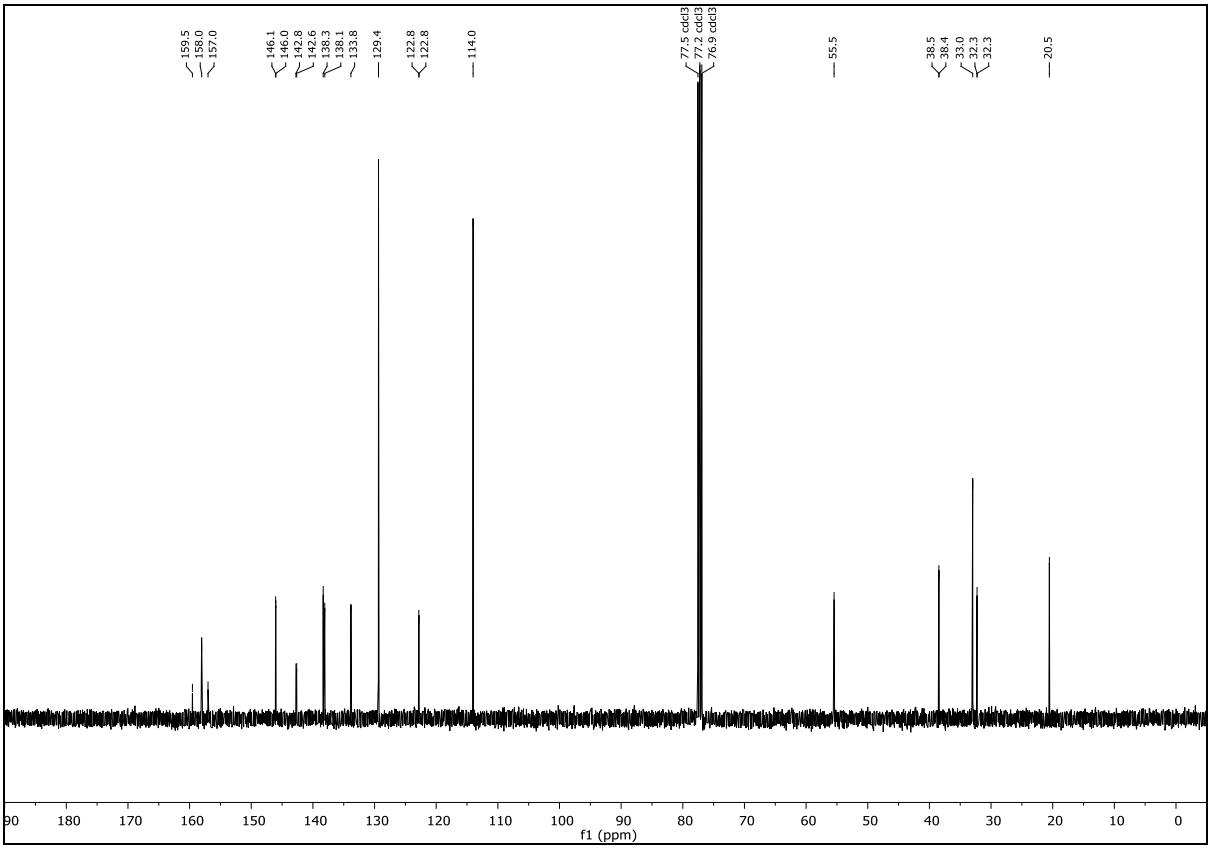
^{19}F NMR (283 MHz) of 3-fluoro-4-phenethylpyridine (29)



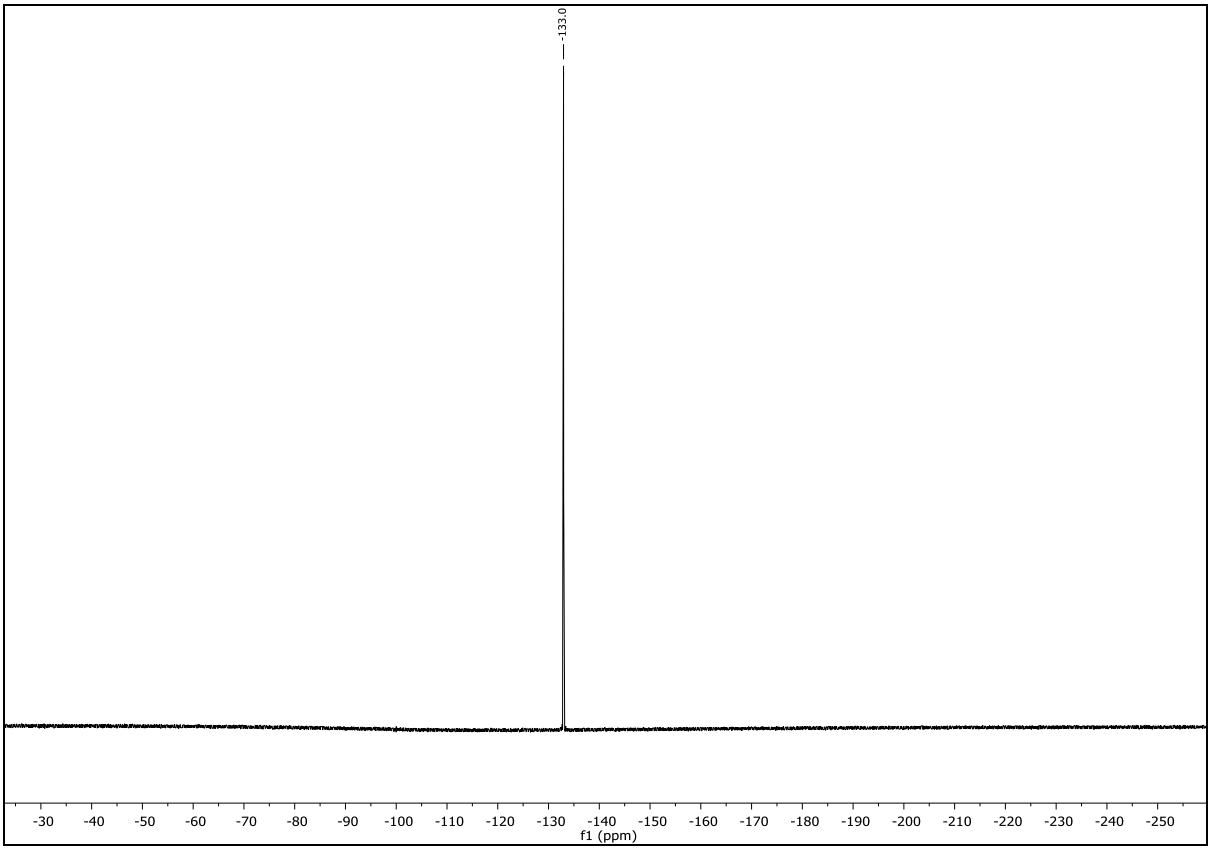
^{1}H NMR (400 MHz) of (*S*)-3-Fluoro-4-(4-(4-methoxyphenyl)butan-2-yl)pyridine (30)

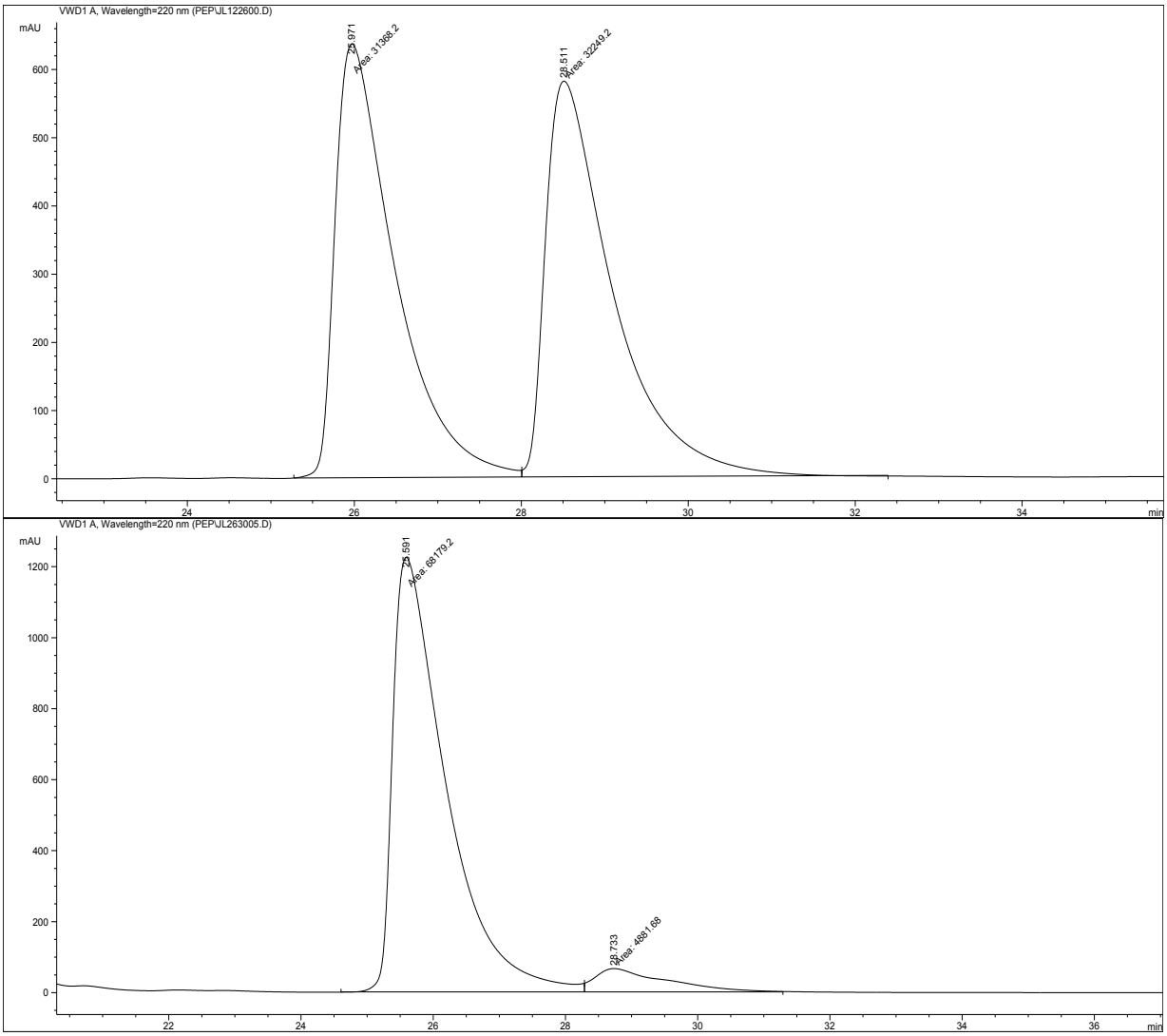


^{13}C NMR (100 MHz) of (S)-3-Fluoro-4-(4-(4-methoxyphenyl)butan-2-yl)pyridine (30)

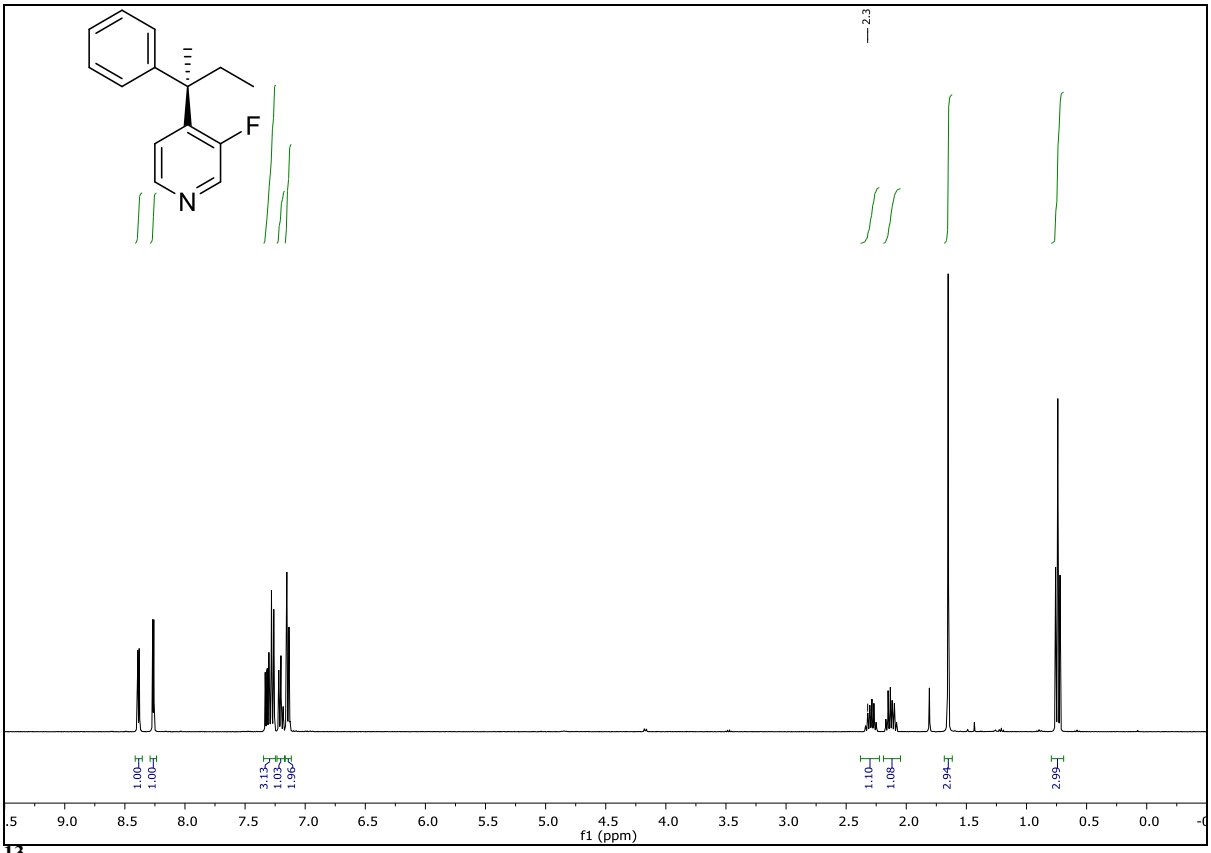


^{19}F (283 MHz) of (*S*)-3-fluoro-4-(4-(4-methoxyphenyl)butan-2-yl)pyridine (30)

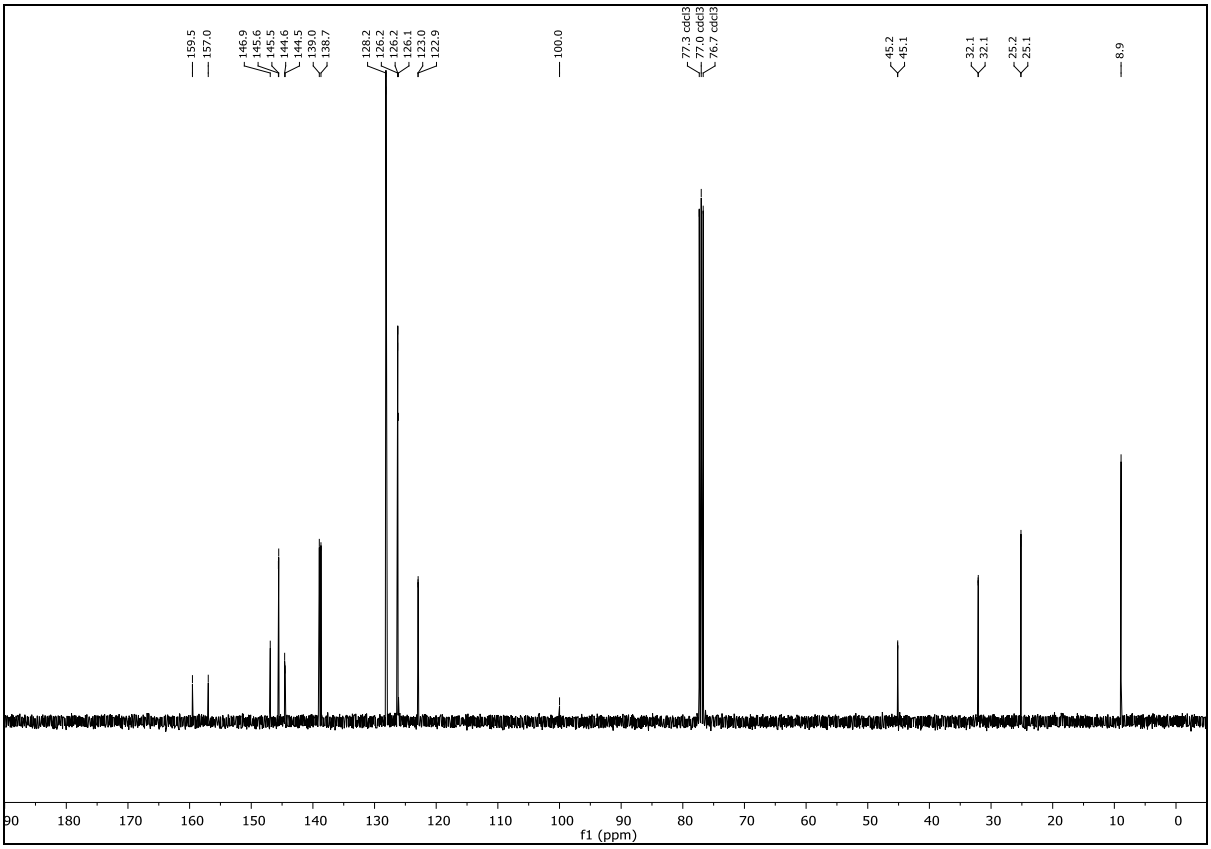



VWD1 A, Wavelength=220 nm (PEP\JL122600.D)
mAU
25.971
Area: 31368.2
28.511
Area: 32249.2
min
VWD1 A, Wavelength=220 nm (PEP\JL263005.D)
mAU
25.591
Area: 68179.2
28.733
Area: 4681.68
min

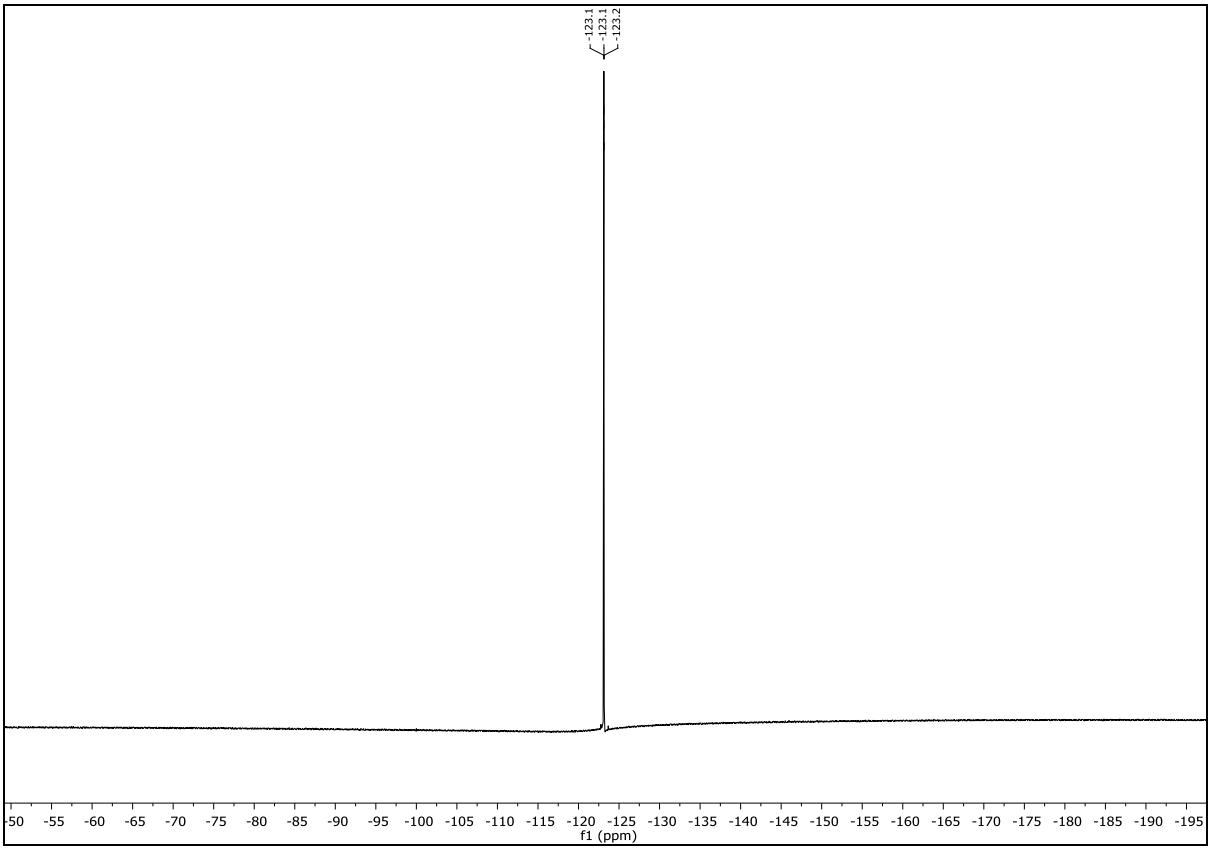
^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-3-Fluoro-4-(2-phenylbutan-2-yl)pyridine (31)

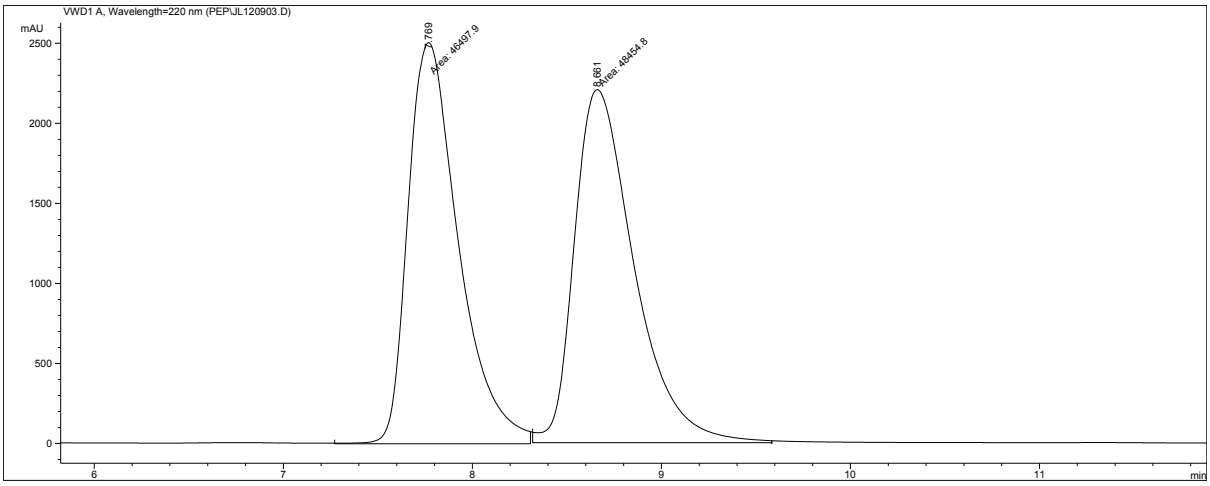


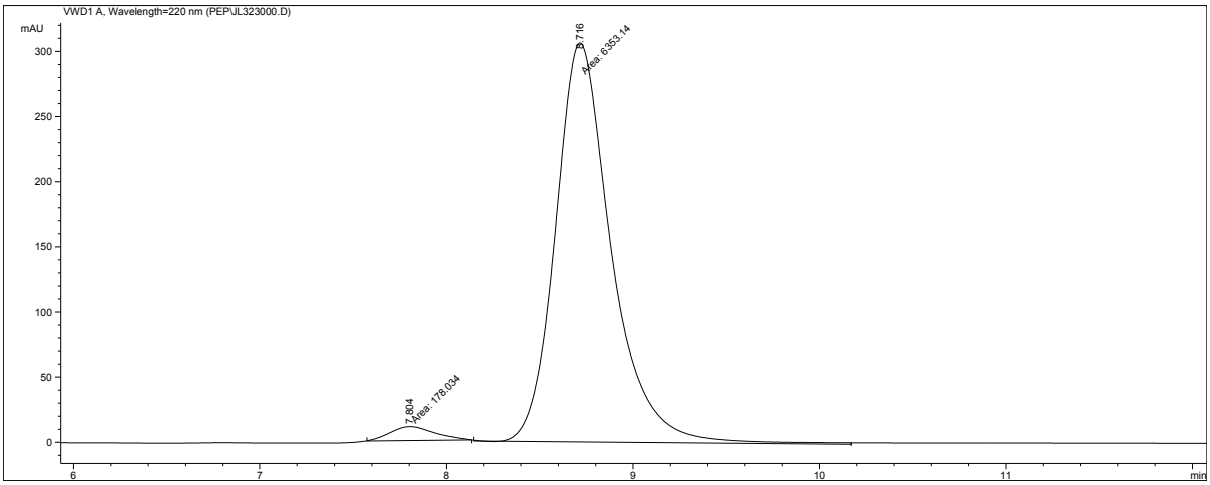
^{13}C NMR (125 MHz, $CDCl_3$) of (*R*)-3-fluoro-4-(2-phenylbutan-2-yl)pyridine (31)



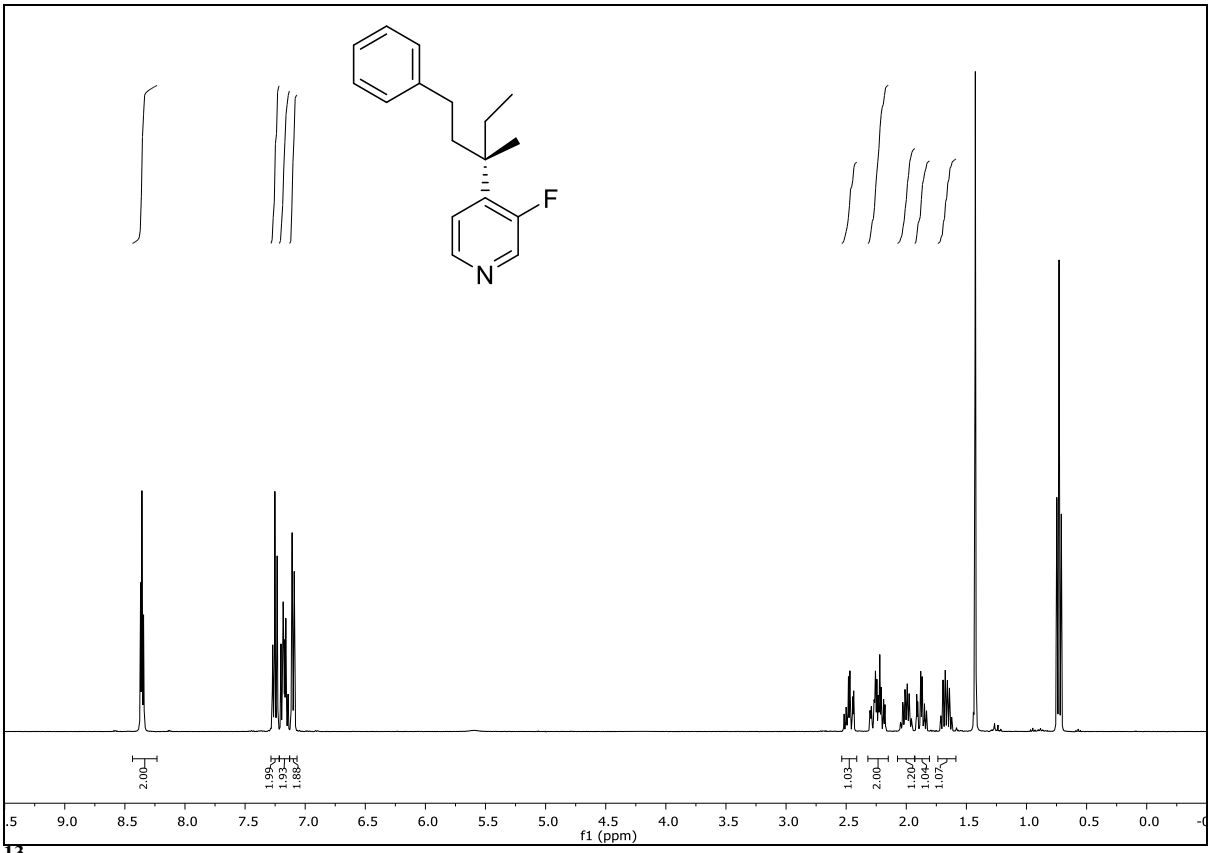
^{19}F NMR (283 MHz) of (*R*)3-Fluoro-4-(2-phenylbutan-2-yl)pyridine (31)



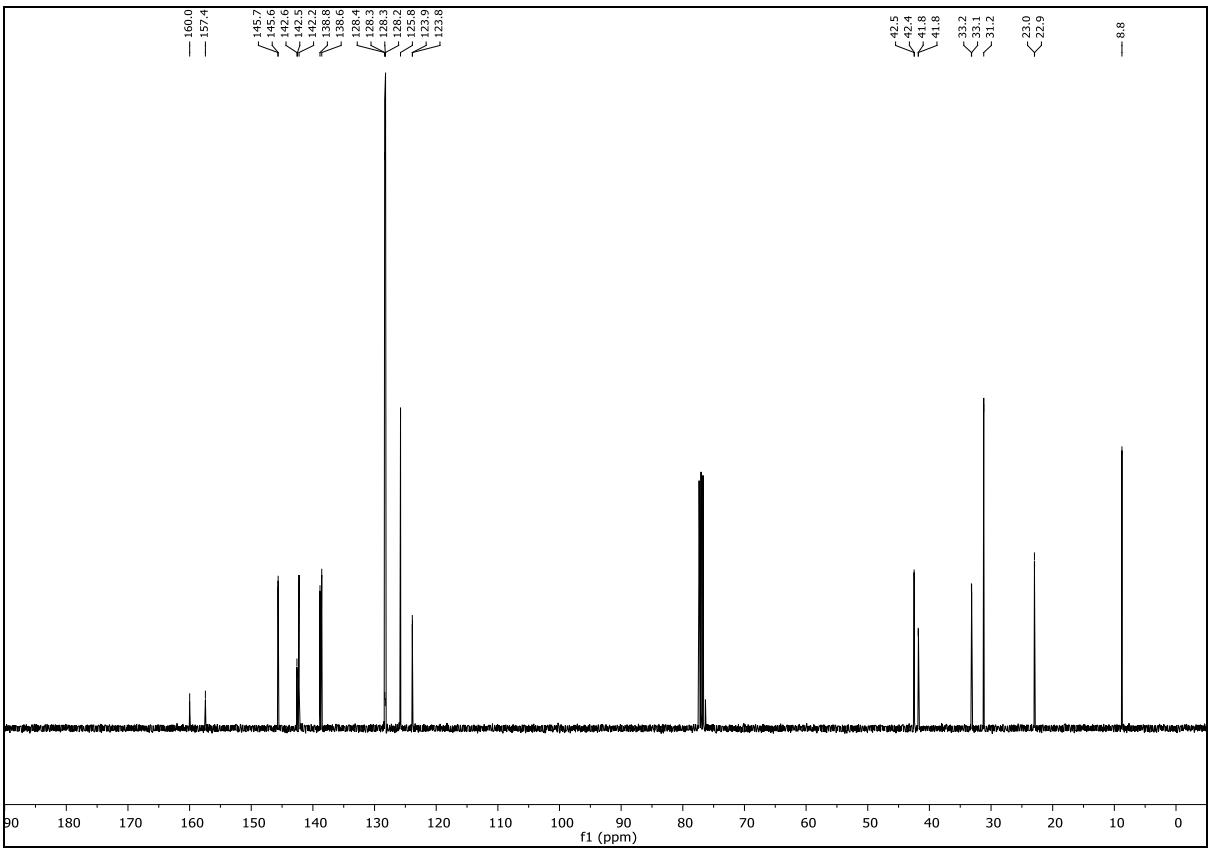

VWD1 A, Wavelength=220 nm (PEP\JL120903.D)
mAU
2500
2000
1500
1000
500
0
7.769
Area: 45497.9
8.661
Area: 49454.8
6
7
8
9
10
11
min


VWD1 A, Wavelength=220 nm (PEP\JL323000.D)
mAU
300
250
200
150
100
50
0
7.804
Area: 178.034
8.716
Area: 6353.14
6
7
8
9
10
11
min

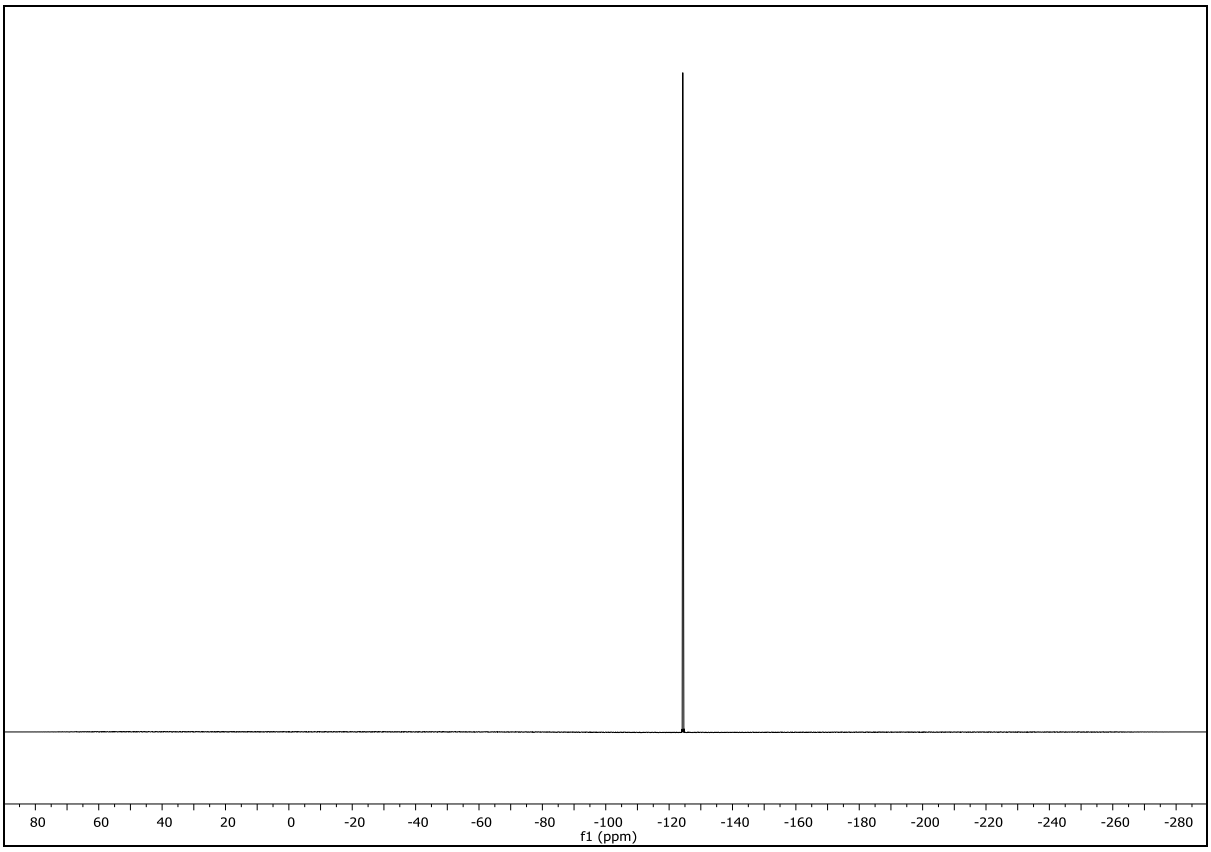
^{1}H NMR (400 MHz) of (*S*)-3-Fluoro-4-(3-methyl-1-phenylpentan-3-yl)pyridine (32)

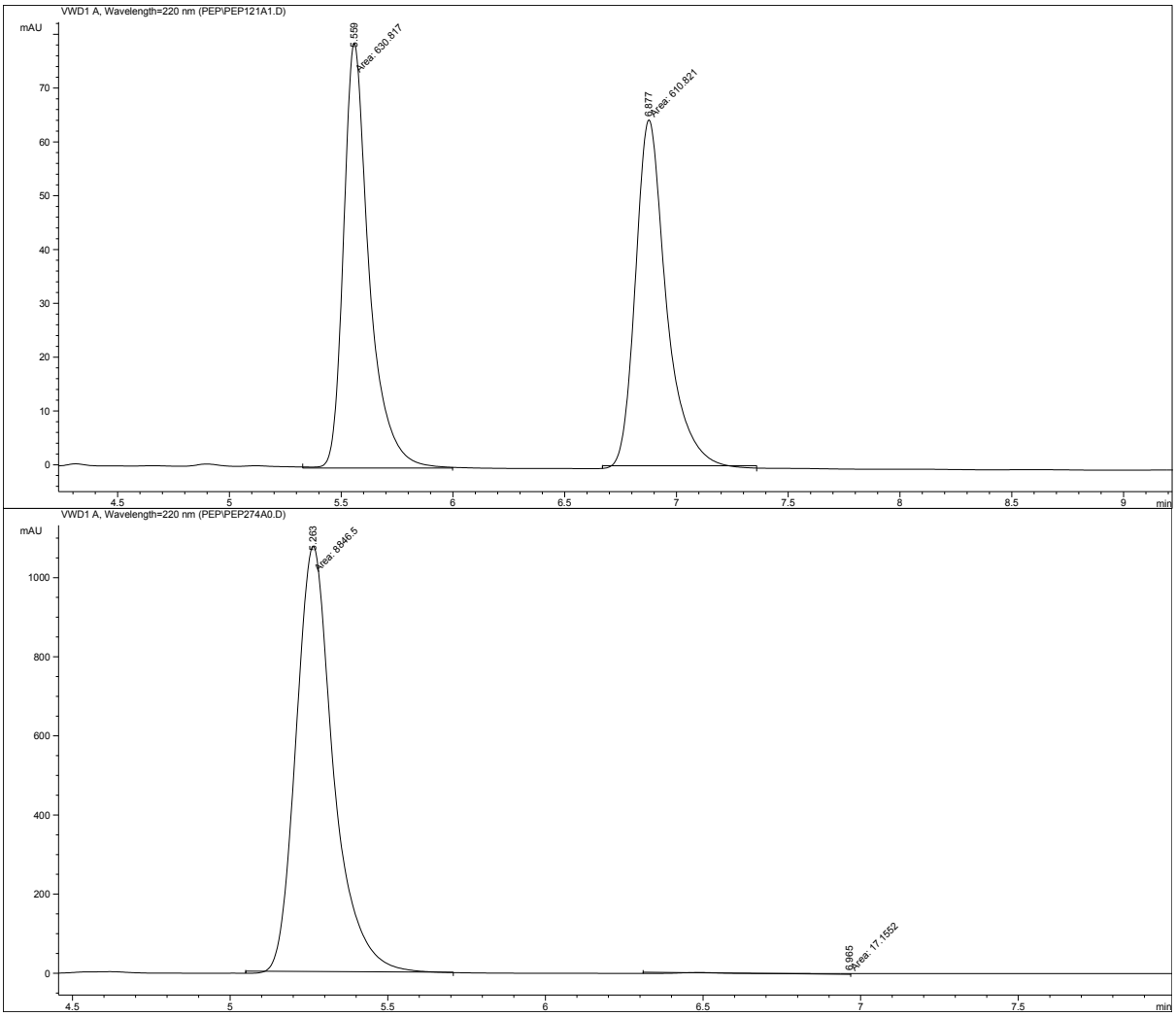


^{13}C NMR (100 MHz) of (*S*)-3-Fluoro-4-(3-methyl-1-phenylpentan-3-yl)pyridine (32)

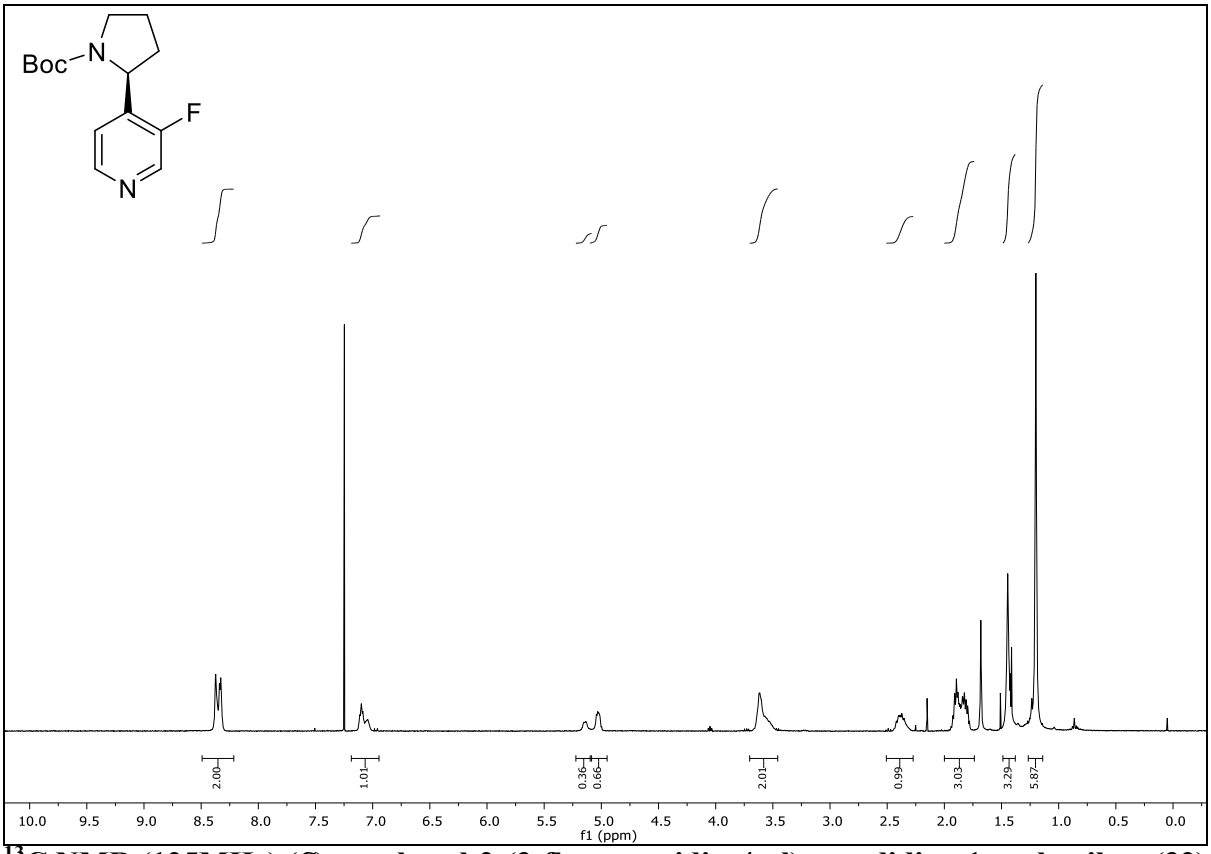


^{19}F NMR (283 MHz) of (*S*)-3-Fluoro-4-(3-methyl-1-phenylpentan-3-yl)pyridine (31)

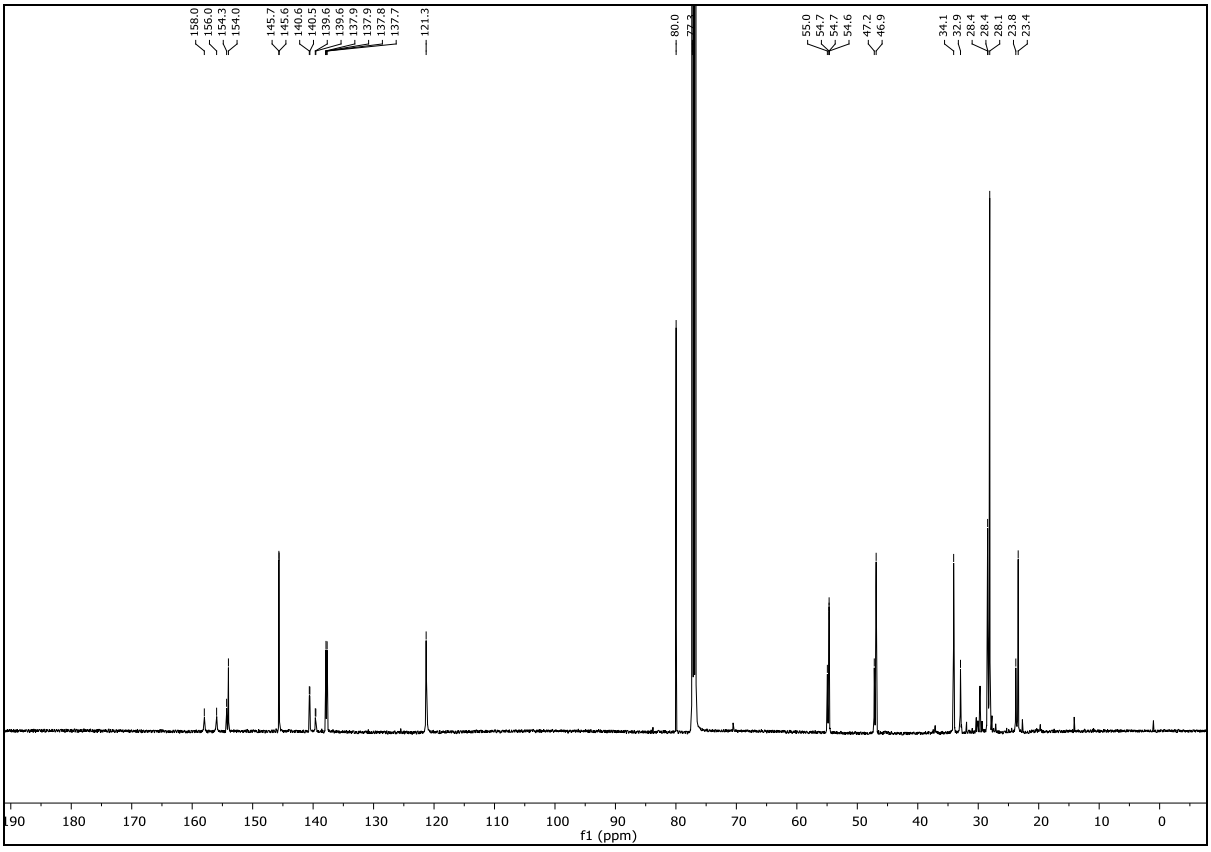



VWD1 A, Wavelength=220 nm (PEP\PEP121A1.D)
mAU
5.559
Area: 630.817
8.877
Area: 610.821
min
VWD1 A, Wavelength=220 nm (PEP\PEP274A0.D)
mAU
5.263
Area: 8846.5
6.965
Area: 17.1552
min

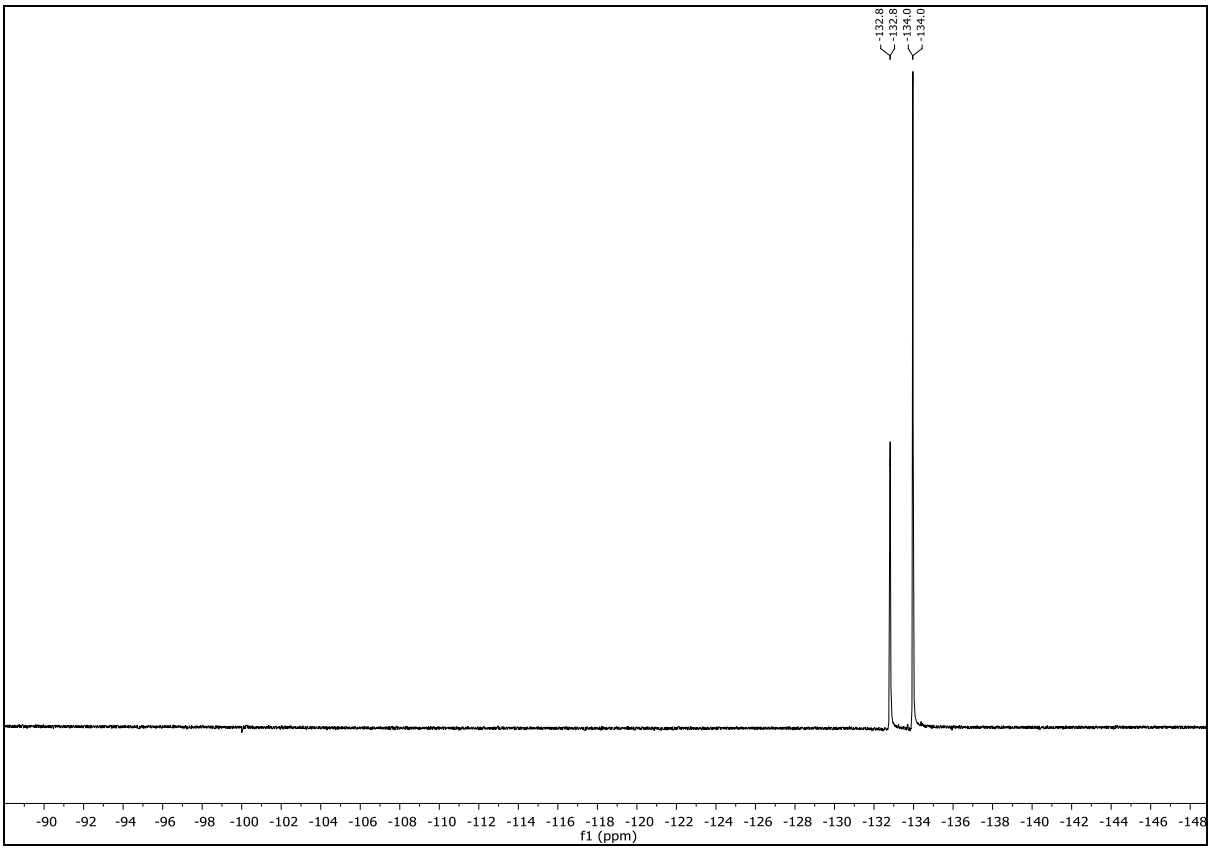
^{1}H NMR (400 MHz) (*S*)-tert-butyl-2-(3-fluoropyridin-4-yl)pyrrolidine-1-carboxilate (32)

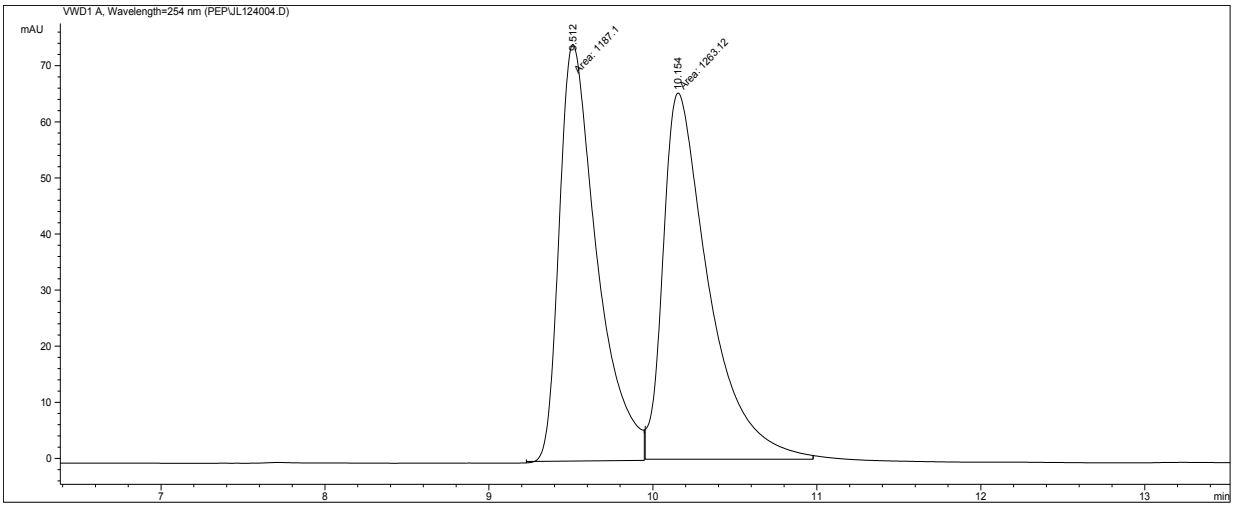


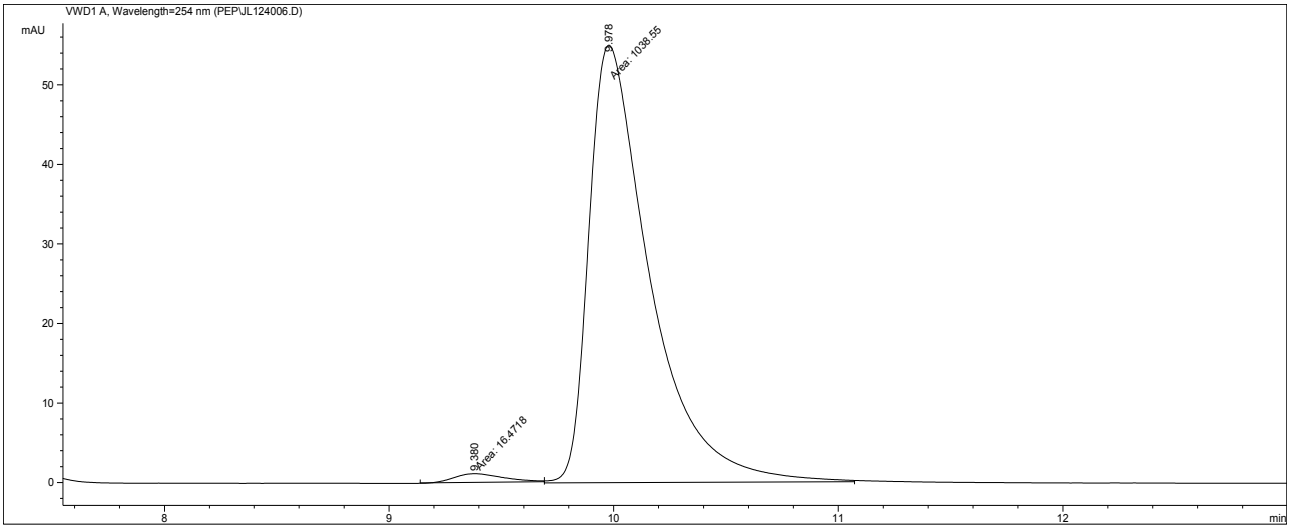
^{13}C NMR (125MHz) (*S*)-tert-butyl-2-(3-fluoropyridin-4-yl)pyrrolidine-1-carboxilate (32)



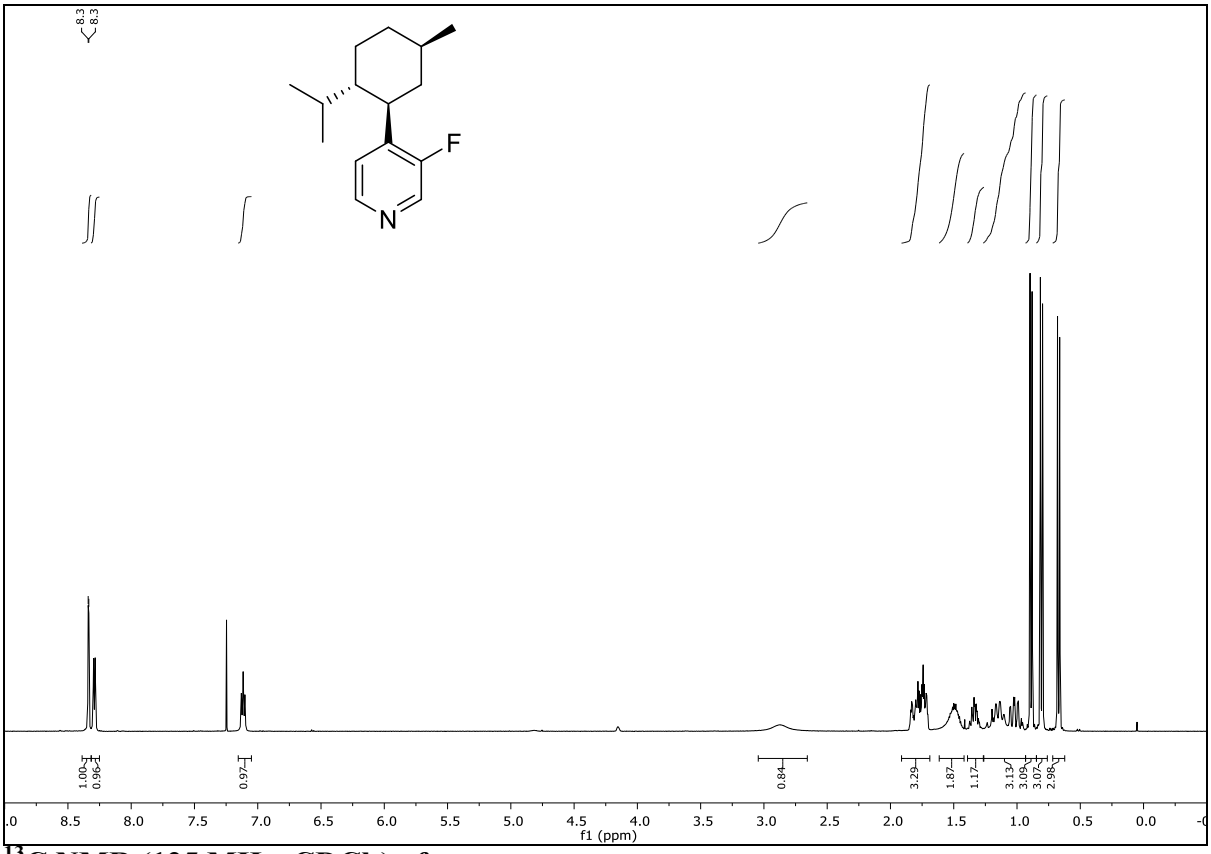
^{19}F NMR (283 MHz) (*S*)-tert-butyl-2-(3-fluoropyridin-4-yl)pyrrolidine-1-carboxilate (32)



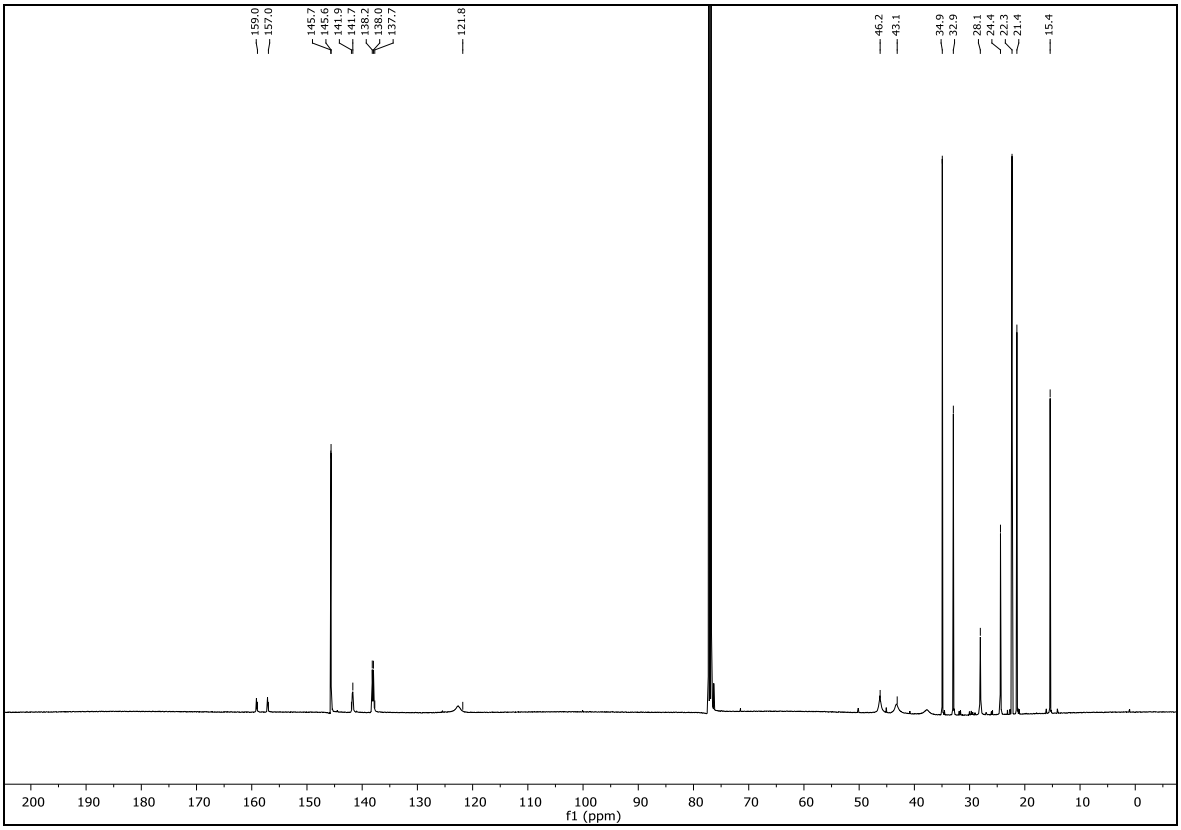

VWD1 A, Wavelength=254 nm (PEP\JL124004.D)
mAU
9.512
Area: 1187.1
10.154
Area: 1263.12
min


VWD1 A, Wavelength=254 nm (PEP\JL124006.D)
mAU
9.978
Area: 1038.55
9.380
Area: 16.4718
min

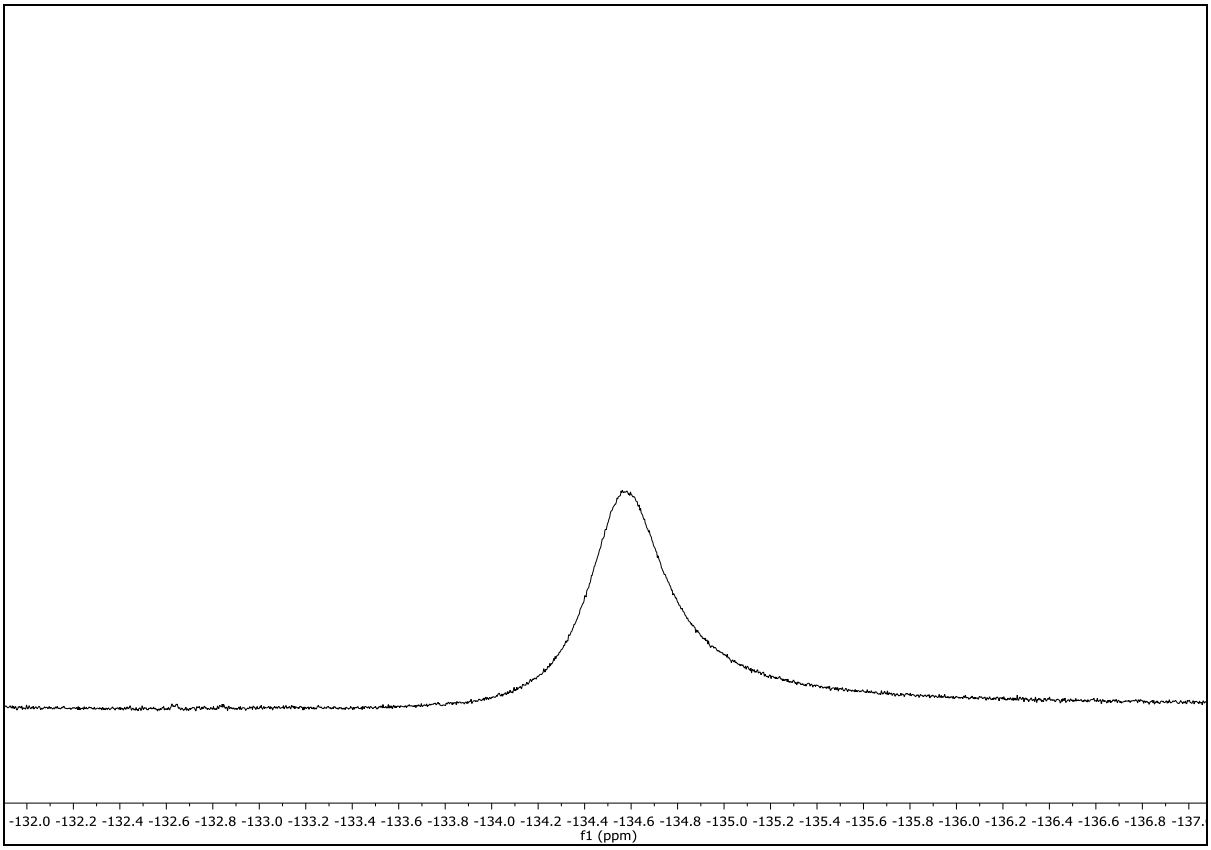
^{1}H NMR (500 MHz, $CDCl_3$) of 34



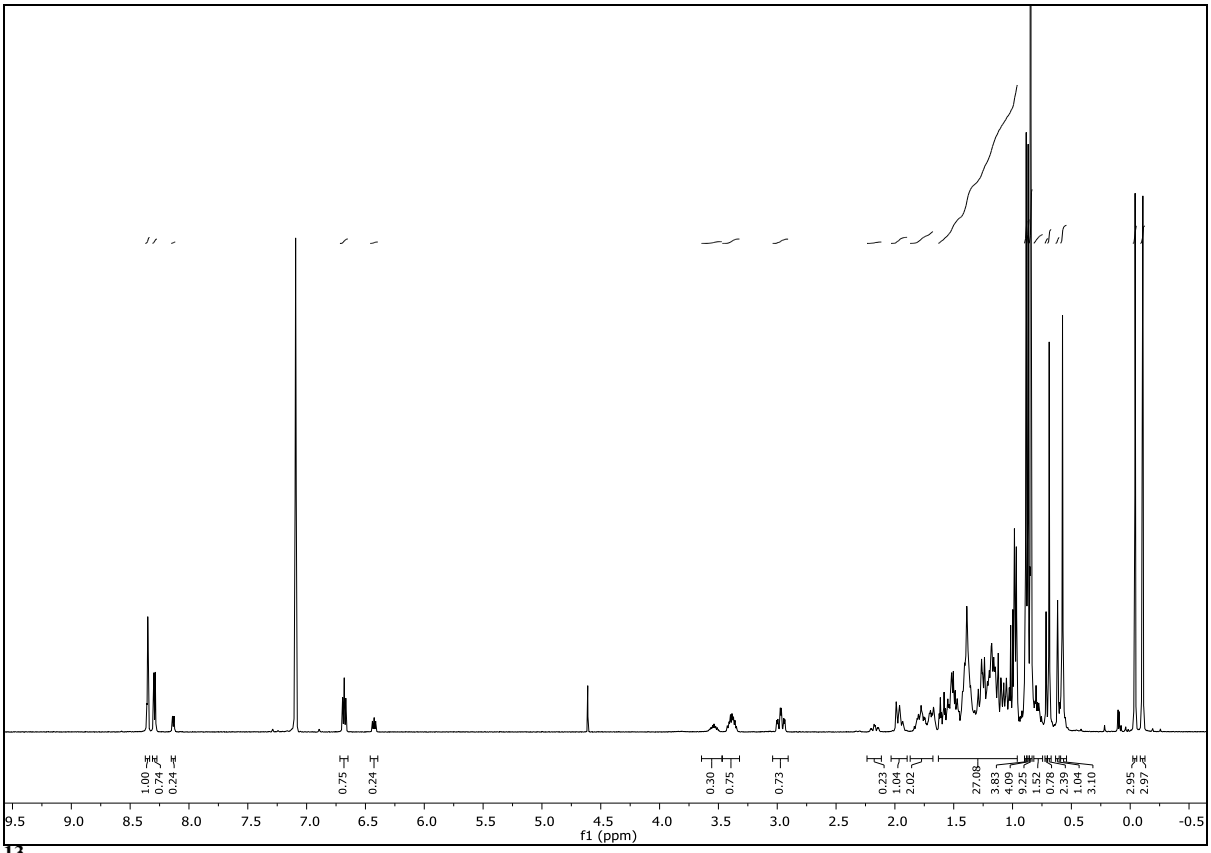
^{13}C NMR (125 MHz, $CDCl_3$) of 34



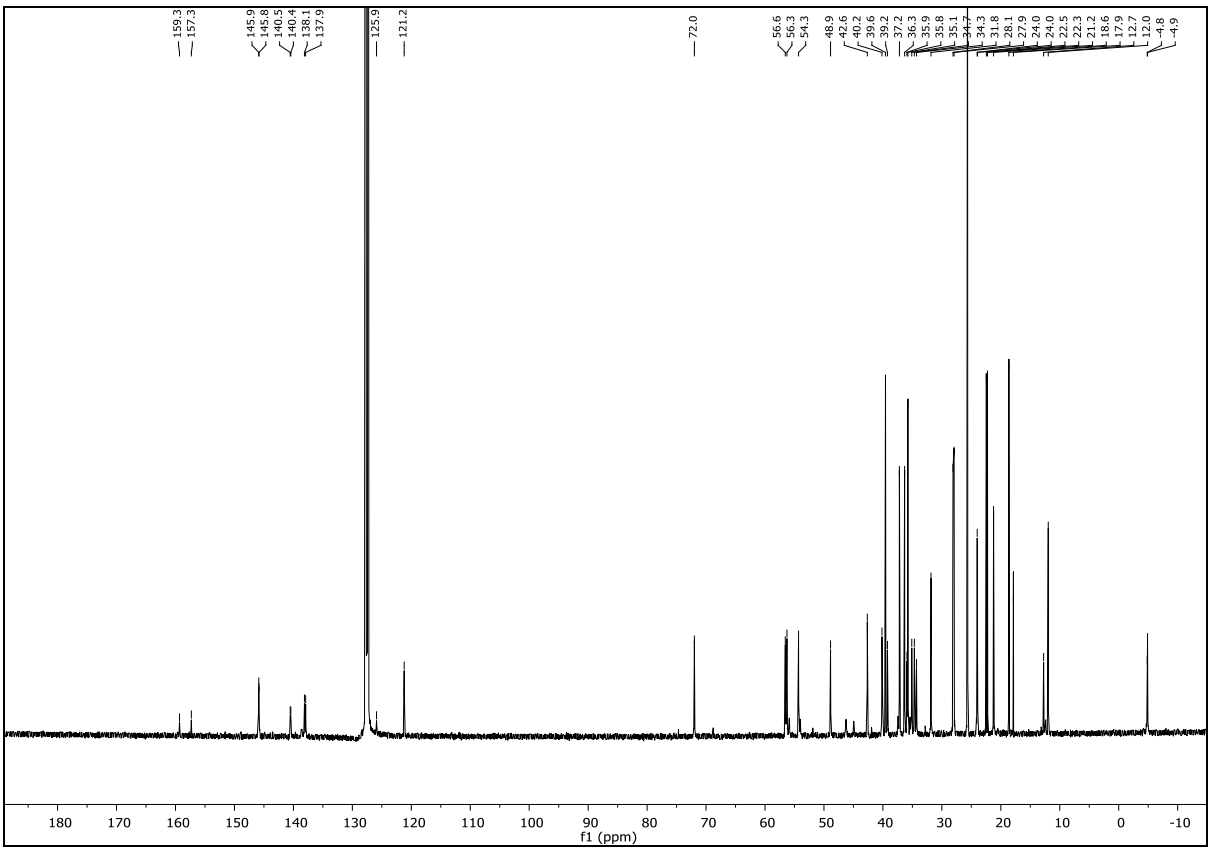
^{19}F NMR (283 MHz) of 34



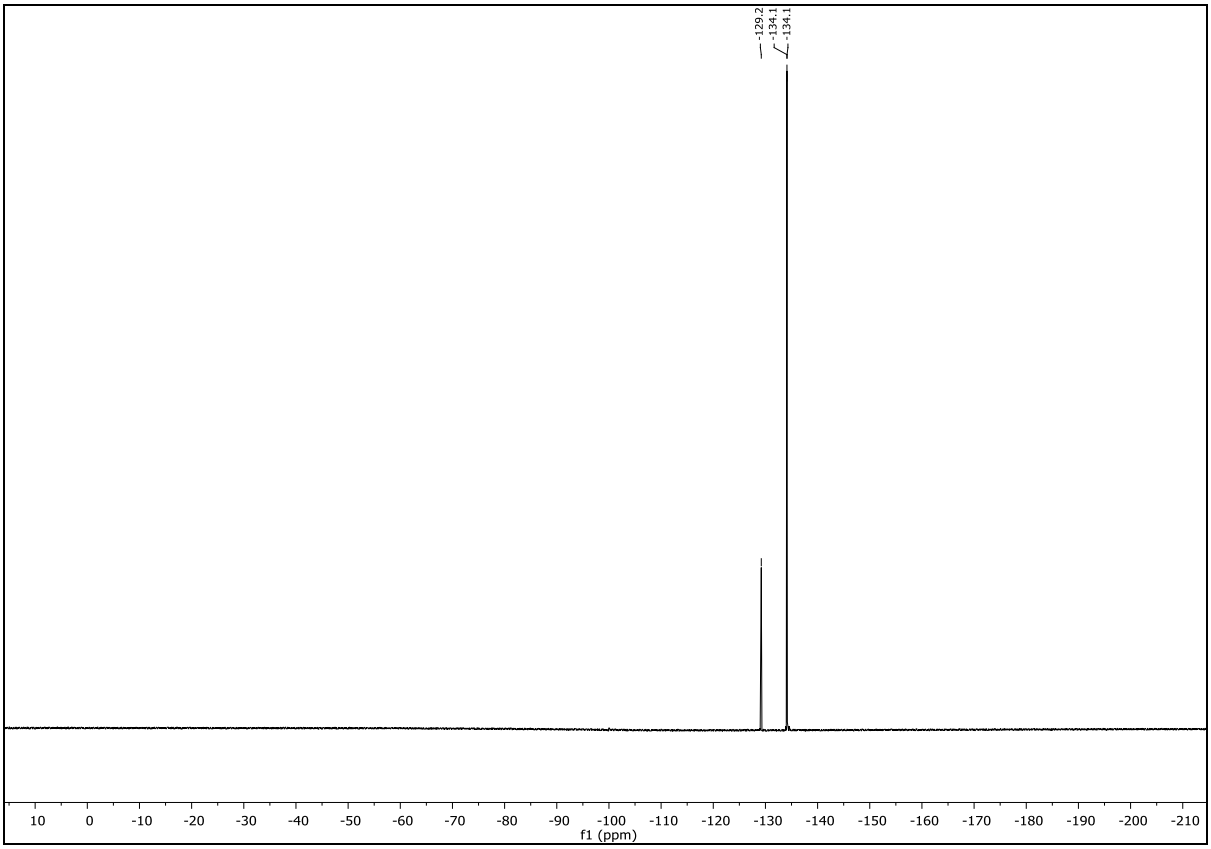
^{1}H NMR (400 MHz, C_6D_6) of 35

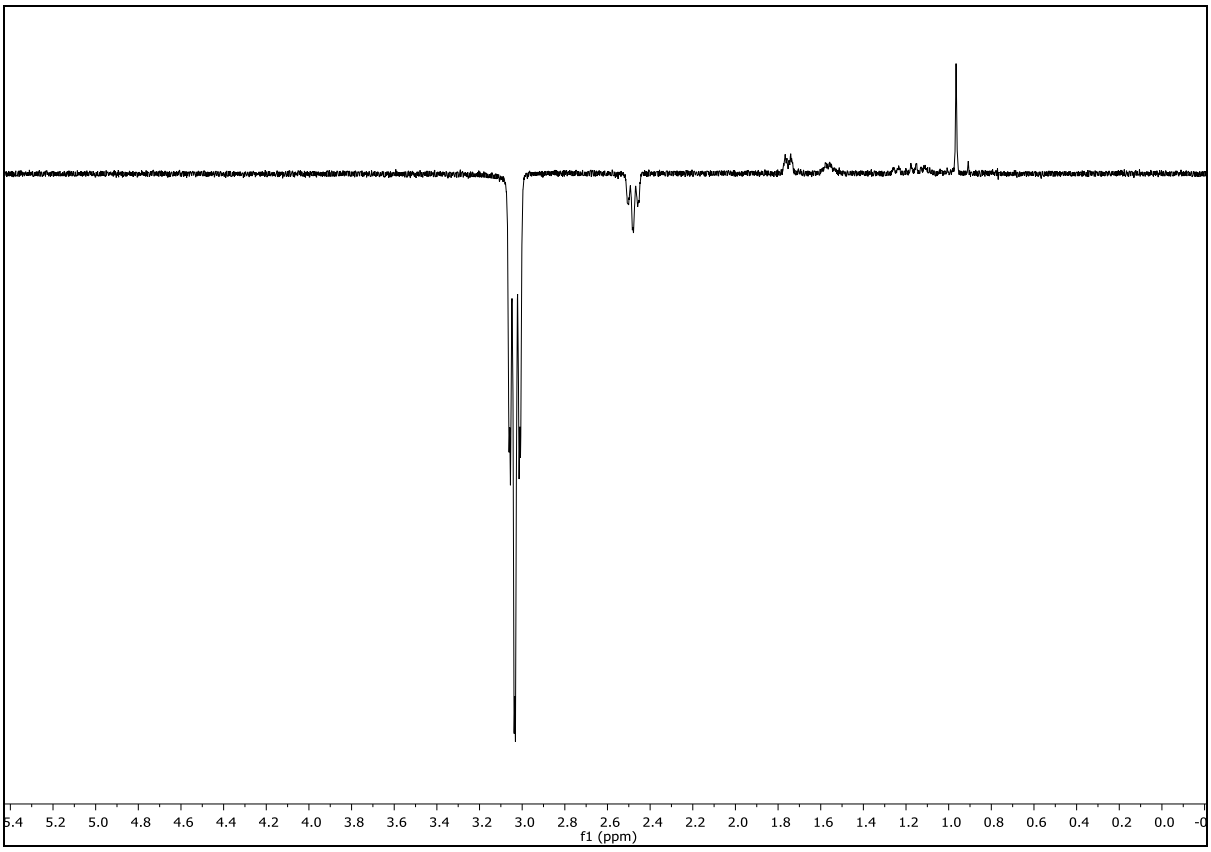


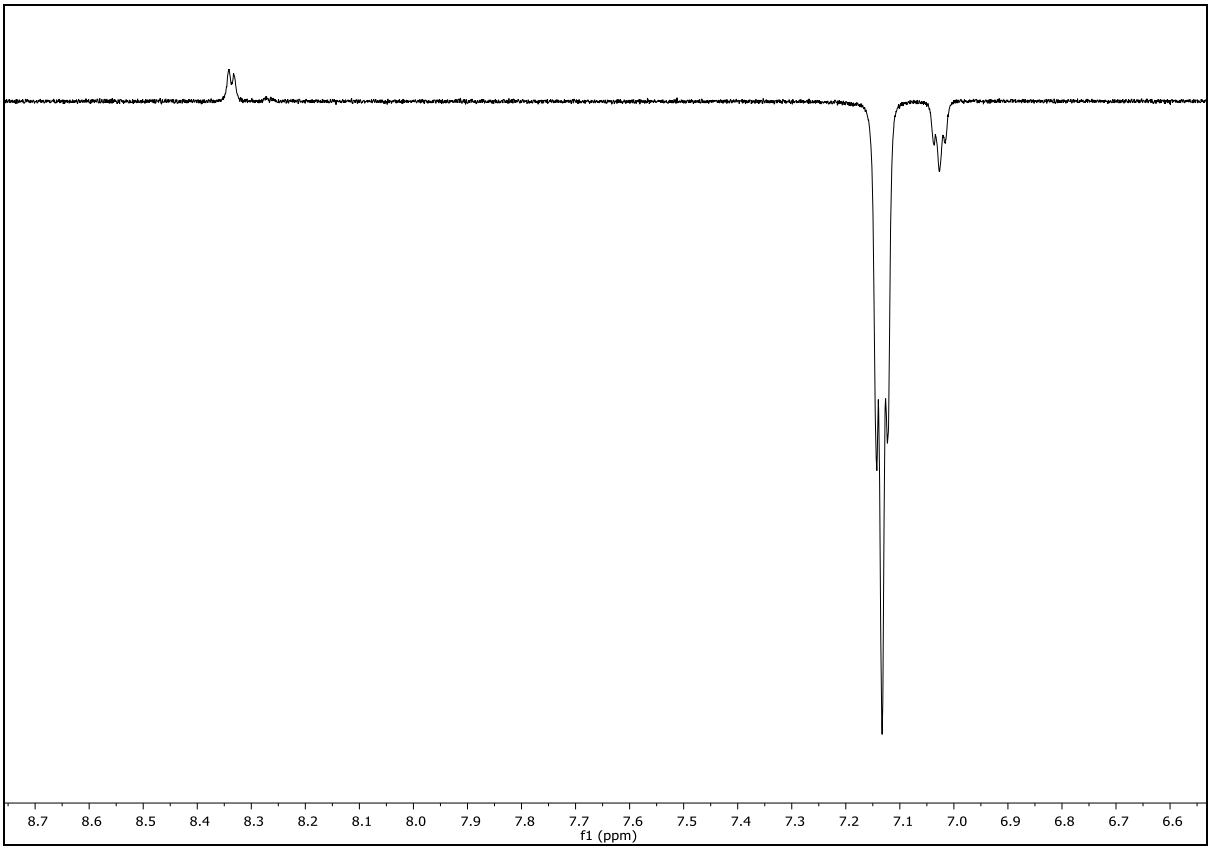
^{13}C NMR (125 MHz, $CDCl_3$) of 34



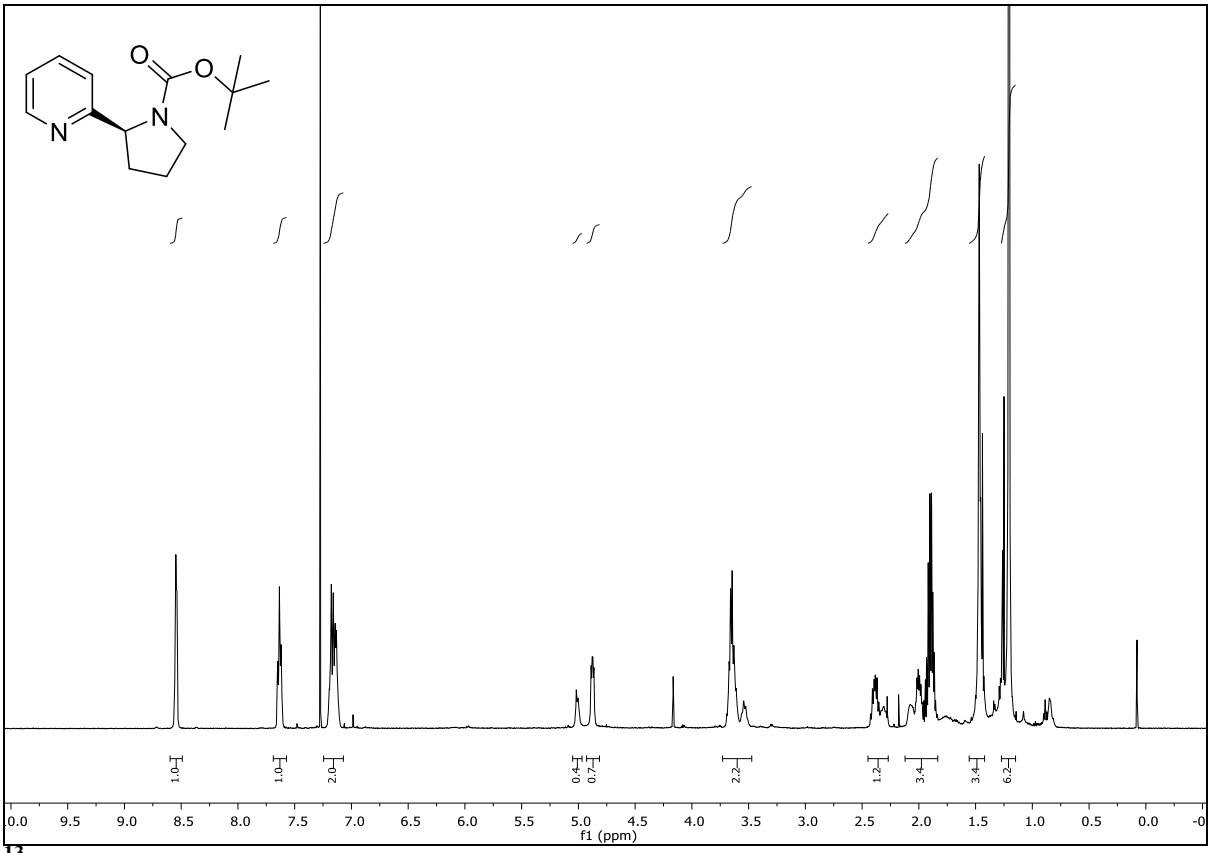
^{19}F NMR (283 MHz) of 34



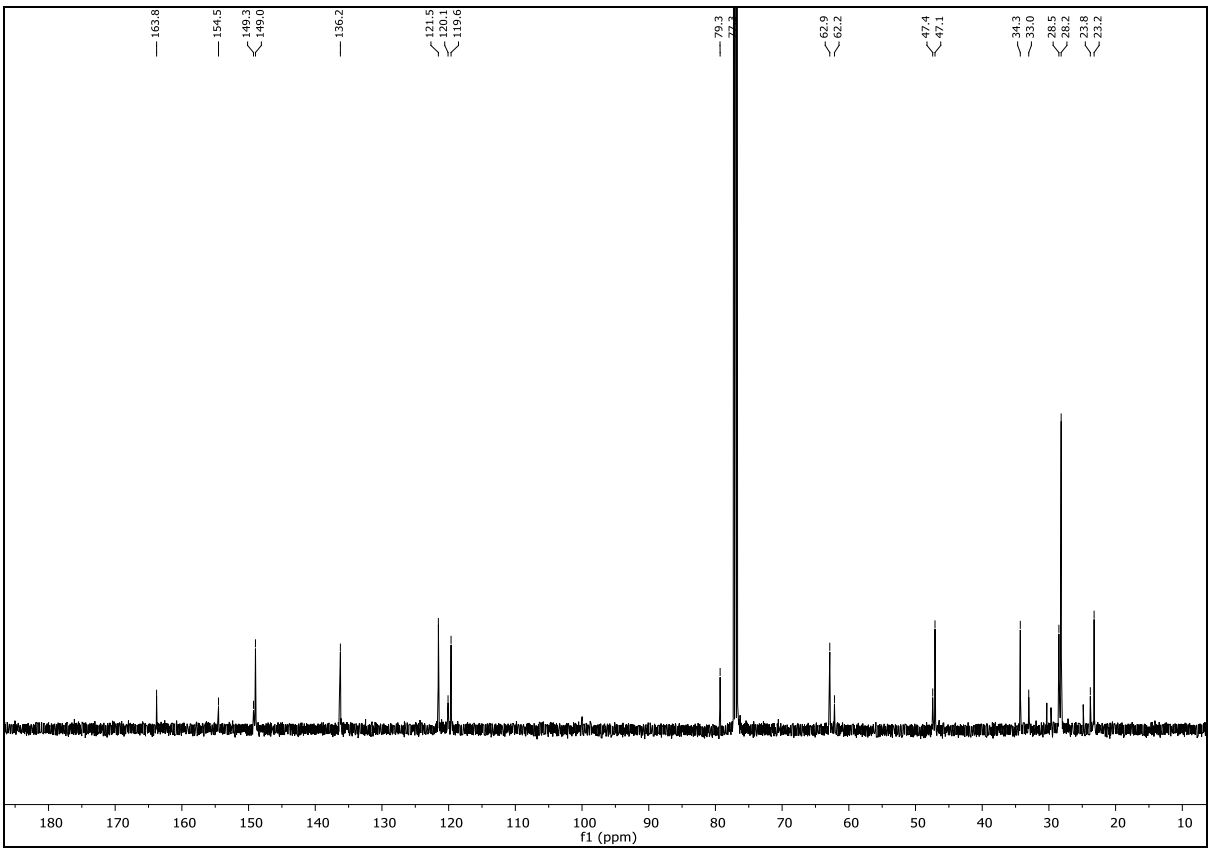

5.4 5.2 5.0 4.8 4.6 4.4 4.2 4.0 3.8 3.6 3.4 3.2 3.0 2.8 2.6 2.4 2.2 2.0 1.8 1.6 1.4 1.2 1.0 0.8 0.6 0.4 0.2 0.0
f1 (ppm)

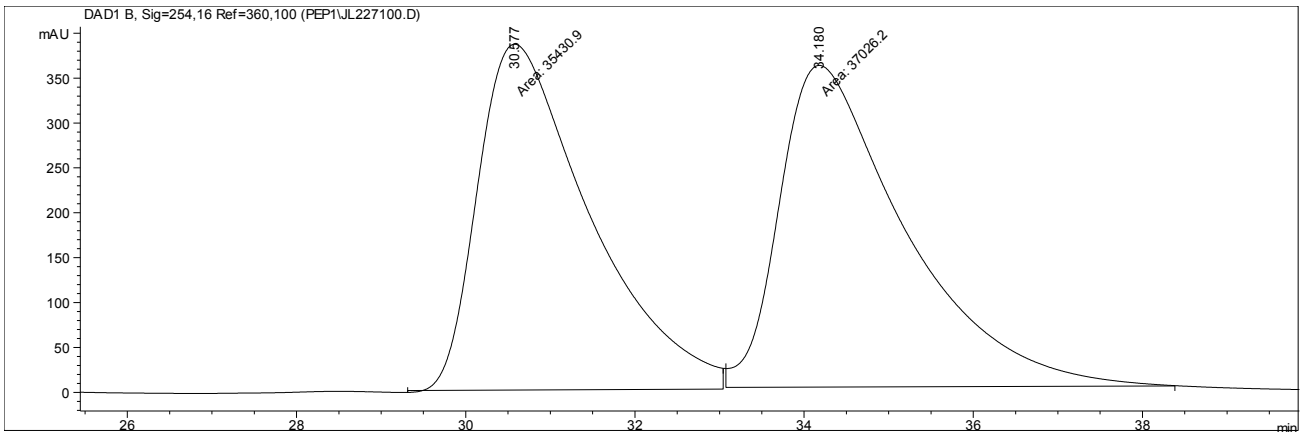

8.7 8.6 8.5 8.4 8.3 8.2 8.1 8.0 7.9 7.8 7.7 7.6 7.5 7.4 7.3 7.2 7.1 7.0 6.9 6.8 6.7 6.6
f1 (ppm)

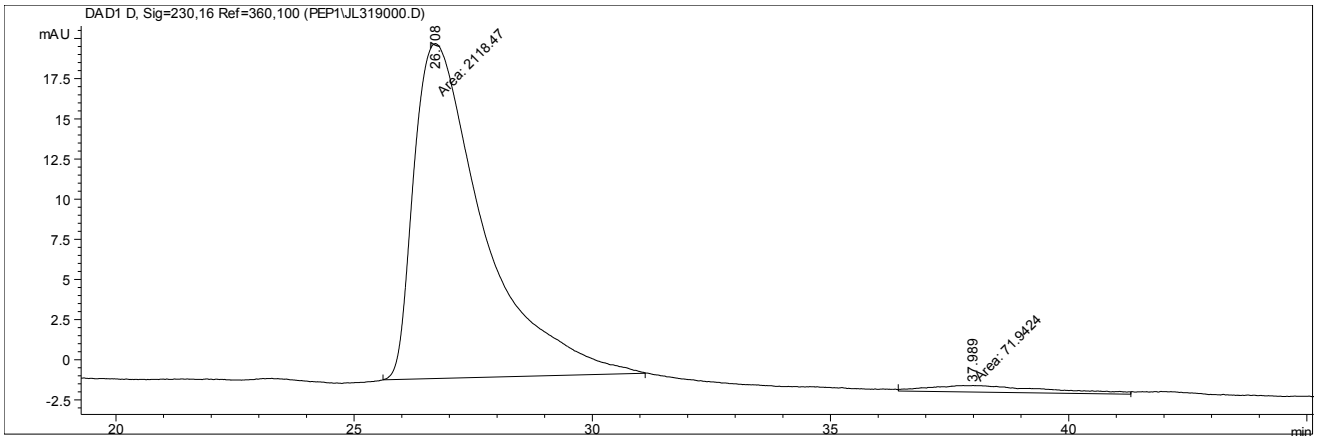
^{1}H NMR (500MHz) of *(S)-tert*-butyl-2-(pyridine-2-yl)pyrolidine-1-carboxilate (36)



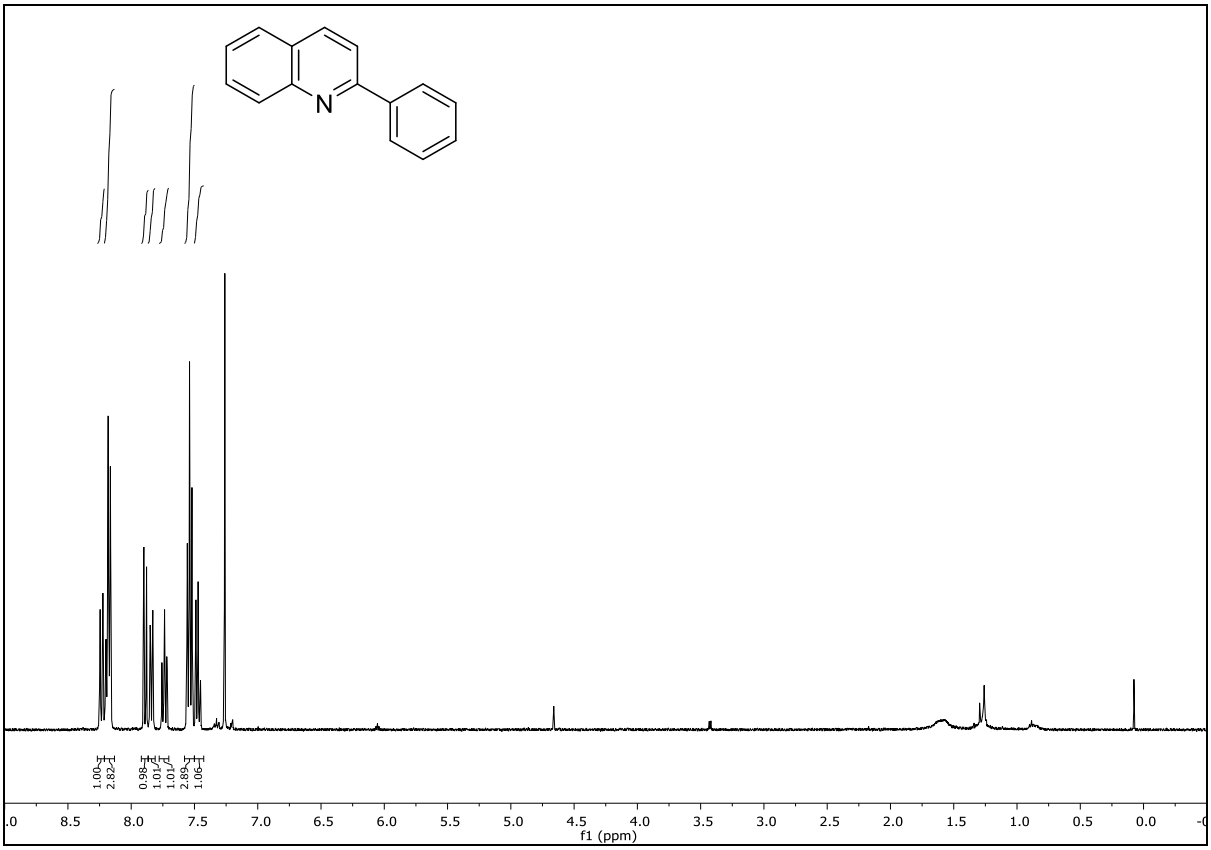
^{13}C NMR (125MHz) of (S)-*tert*-butyl-2-(pyridine-2-yl)pyrolidine-1-carboxilate (36)



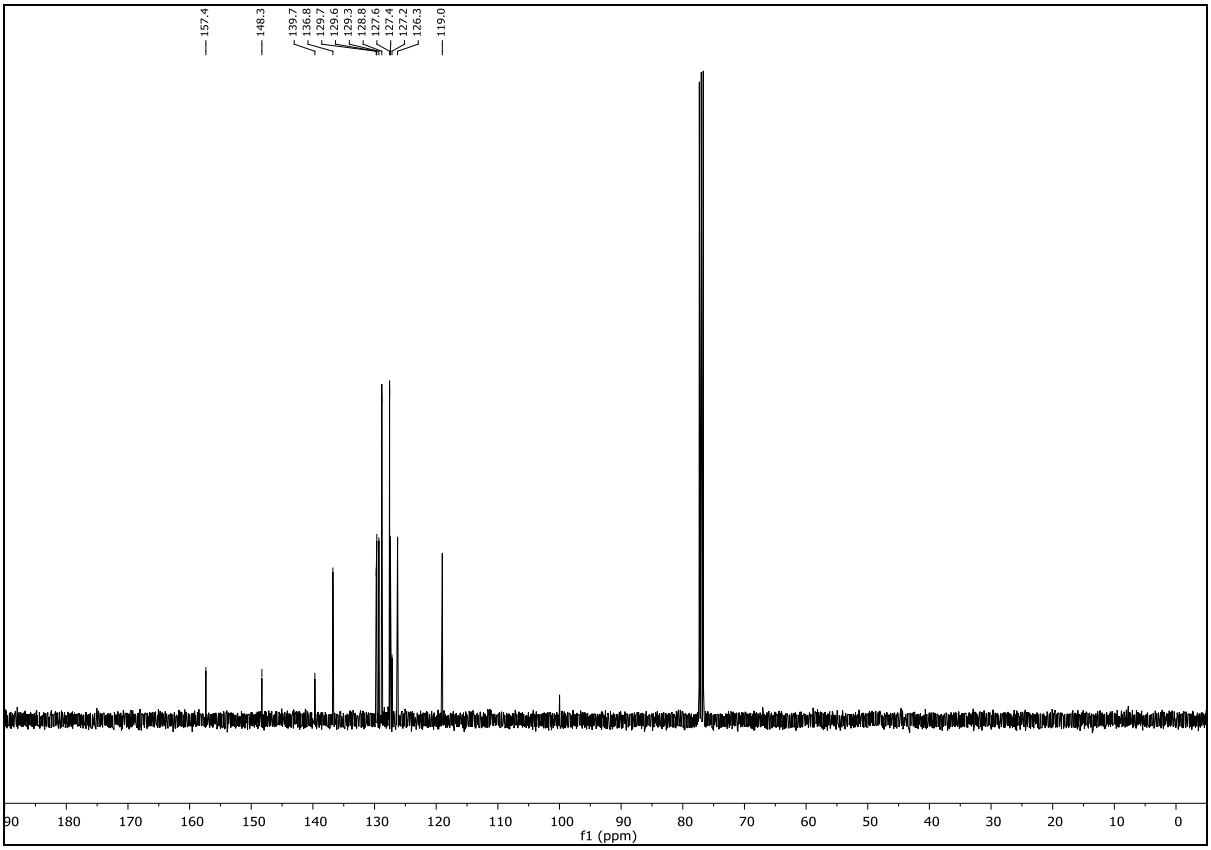

DAD1 B, Sig=254,16 Ref=360,100 (PEP1\JL227100.D)
mAU
30.377
Area: 35430.9
34.180
Area: 37026.2
min


DAD1 D, Sig=230,16 Ref=360,100 (PEP1\JL319000.D)
mAU
26.708
Area: 2118.47
37.989
Area: 71.9424
min

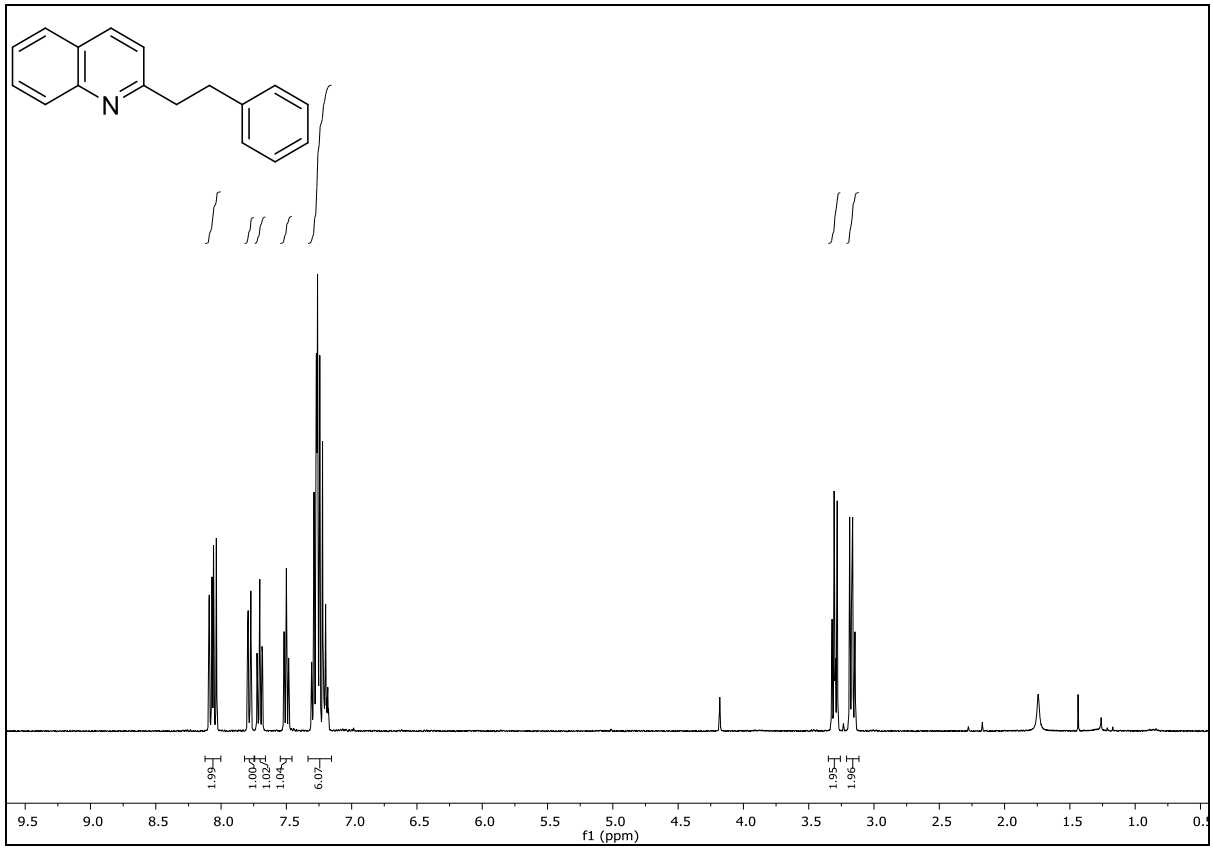
^{1}H NMR (400 MHz, $CDCl_3$) for 2-phenylquinoline (37)



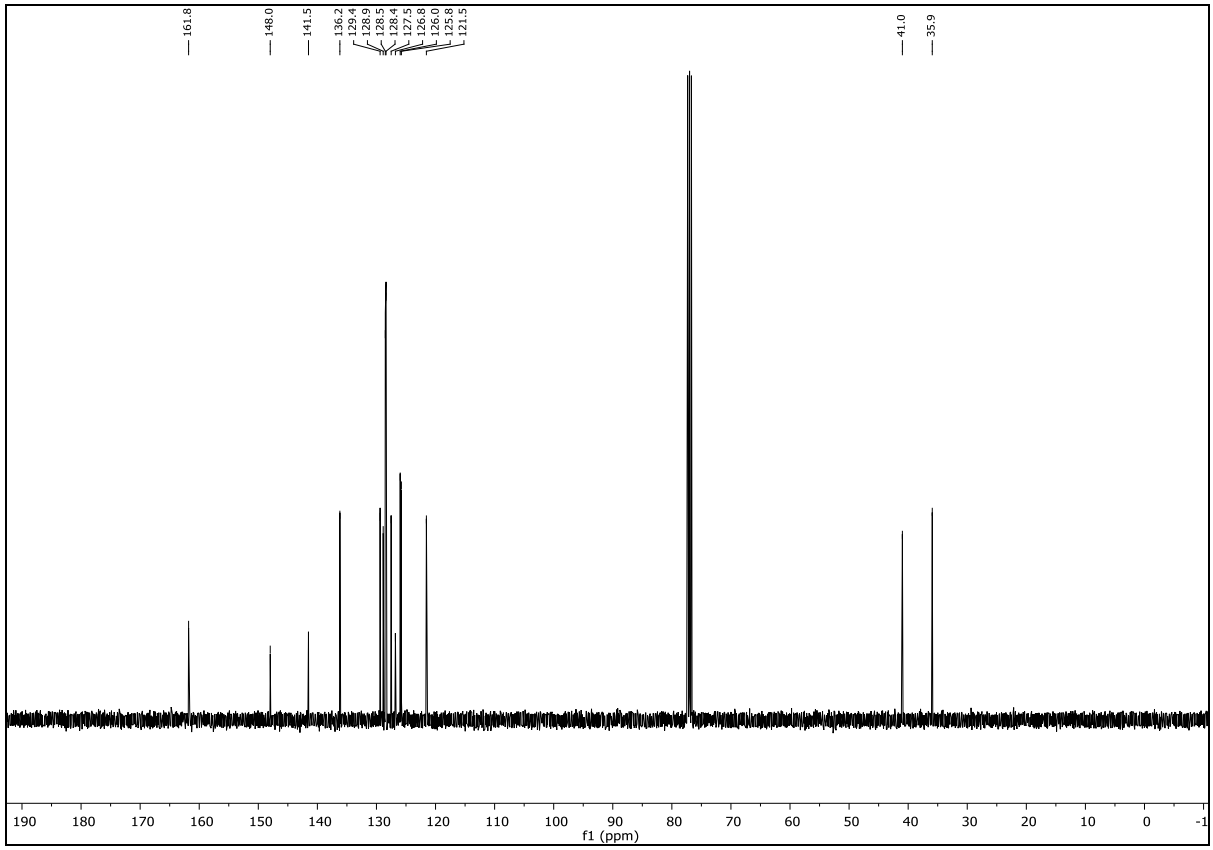
^{13}C NMR (100 MHz, $CDCl_3$) for 2-phenylquinoline (37)



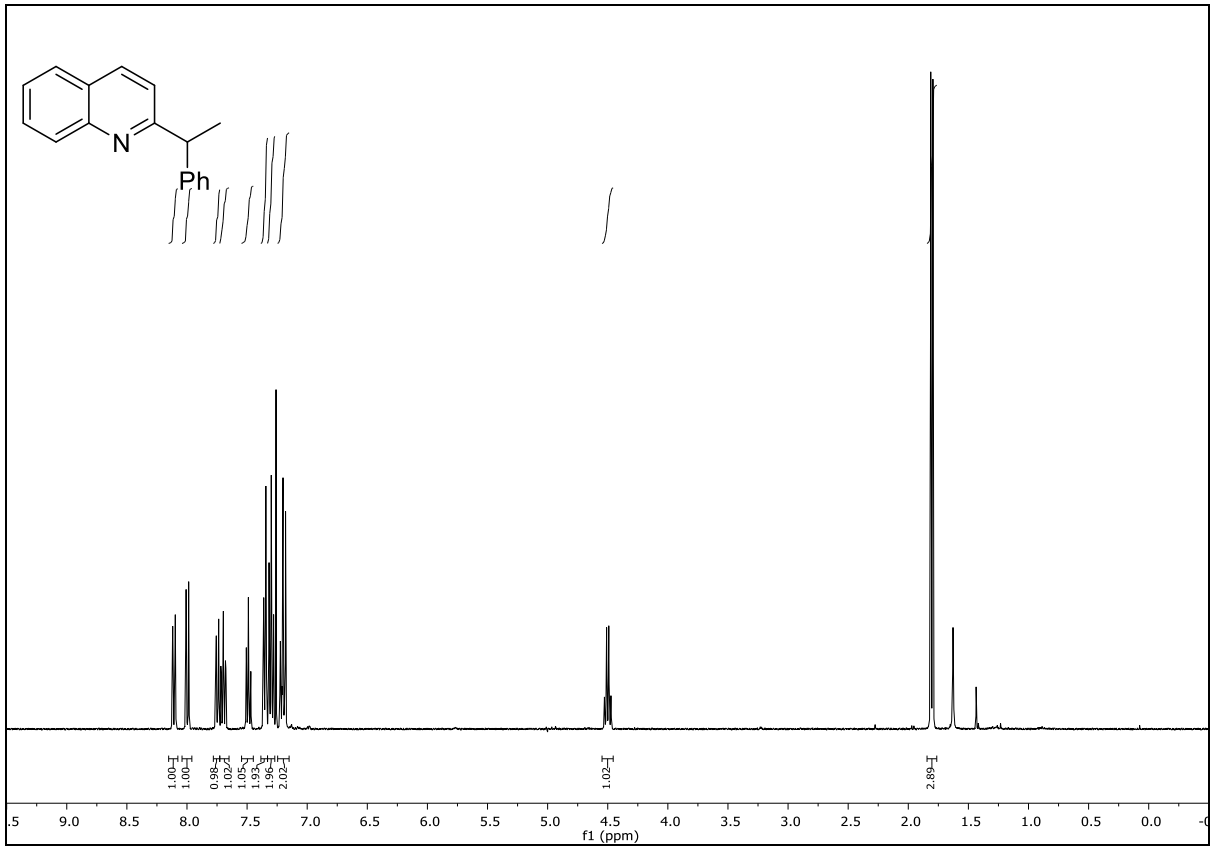
^{1}H NMR (400 MHz, $CDCl_3$) for 2-(2-phenylethyl)quinoline (38)



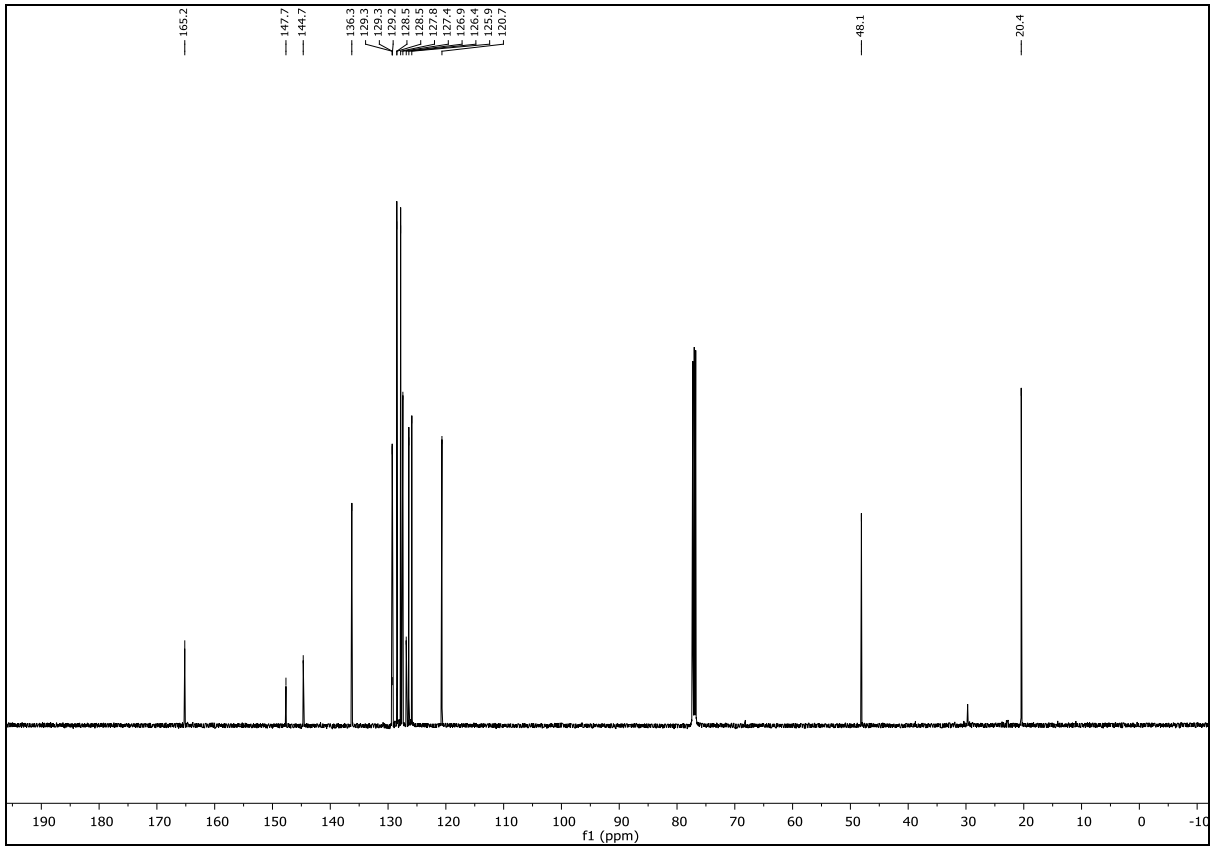
^{13}C NMR (100 MHz, $CDCl_3$) for 2-(2-phenylethyl)quinoline (38)

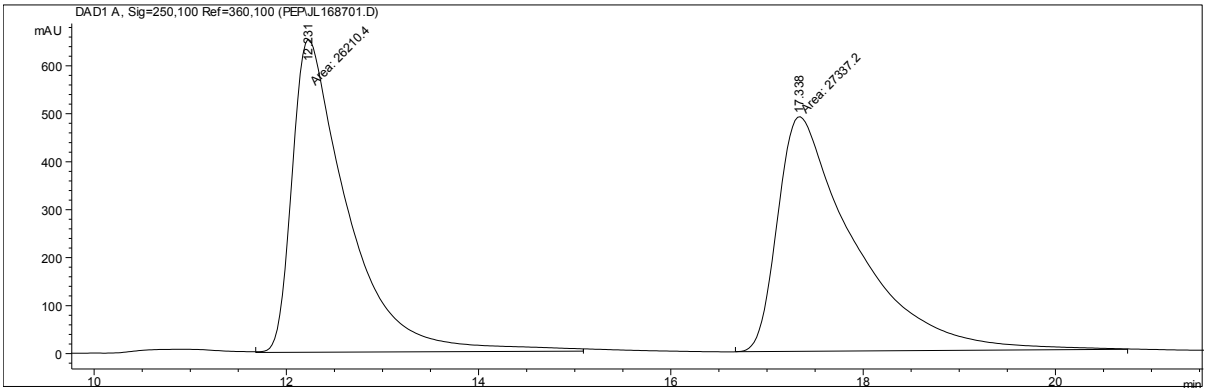


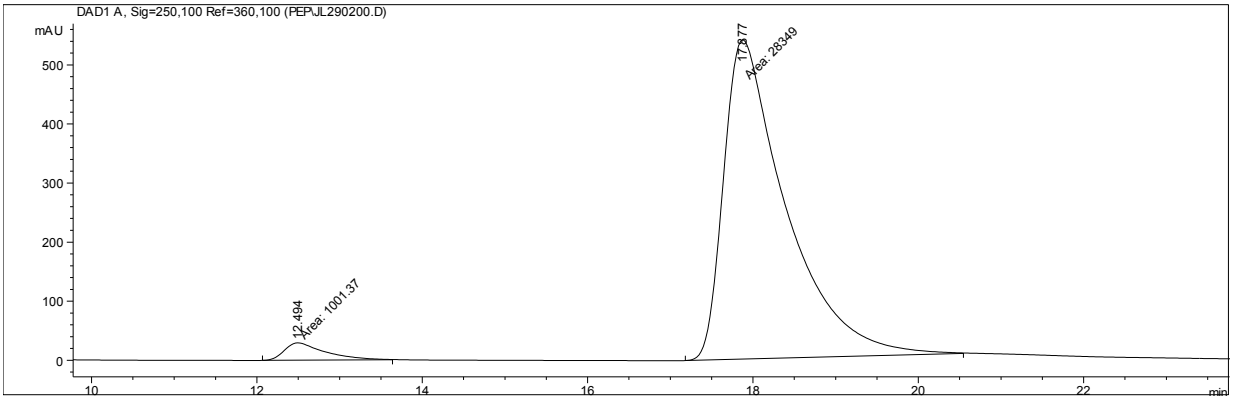
^{1}H NMR (400 MHz, $CDCl_3$) for (*R*)-2-(1-Phenylethyl)quinoline



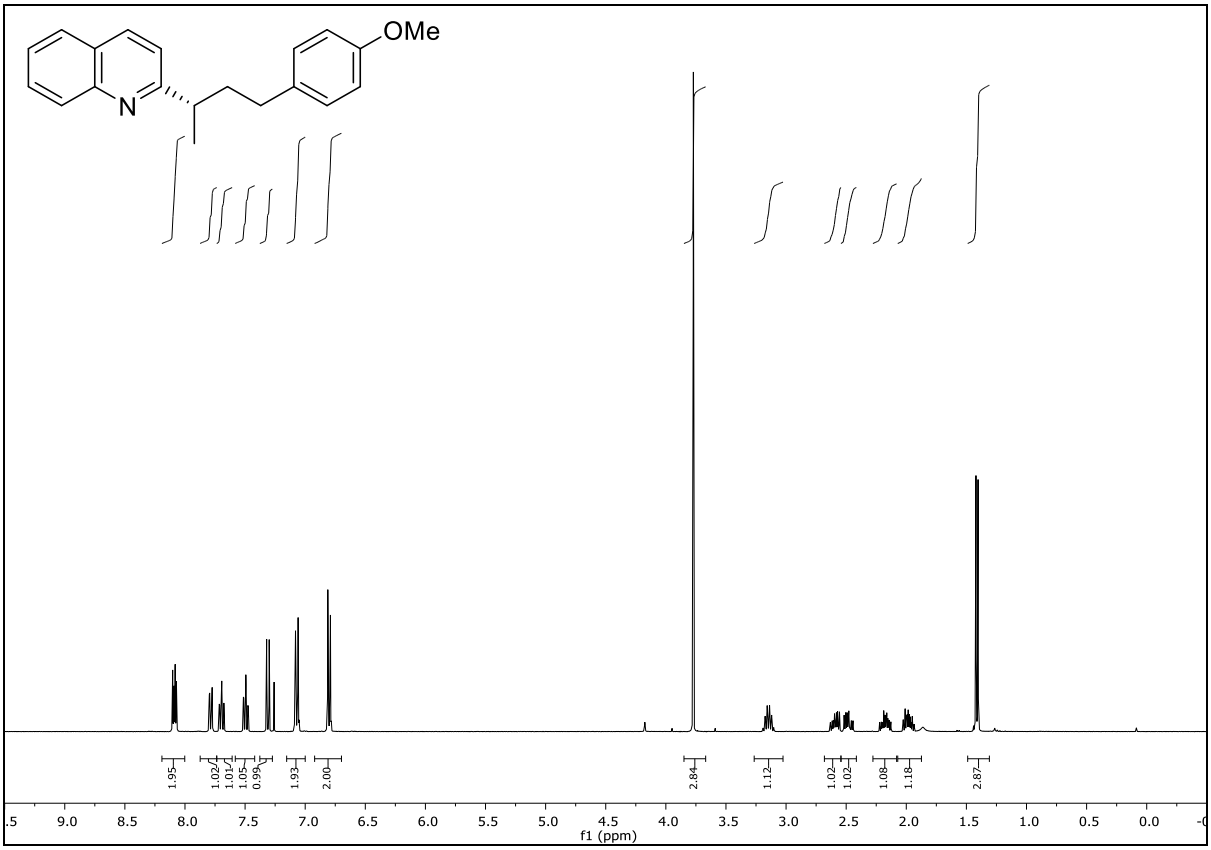
^{13}C NMR (100 MHz, $CDCl_3$) for (*R*)-2-(1-Phenylethyl)quinoline



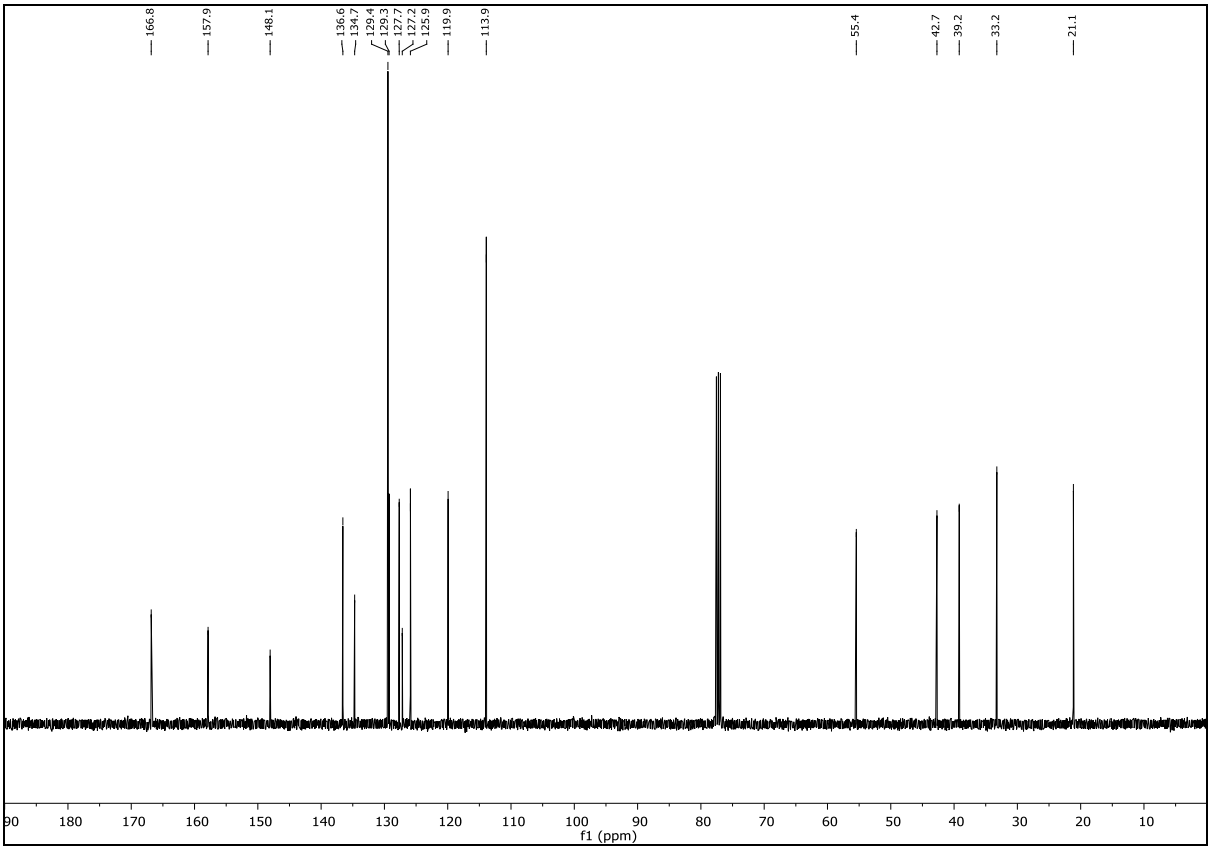

DAD1 A, Sig=250,100 Ref=360,100 (PEP\JL168701.D)
mAU
600
500
400
300
200
100
0
12.231
Area: 26210.4
17.38
Area: 27337.2
10
12
14
16
18
20
min

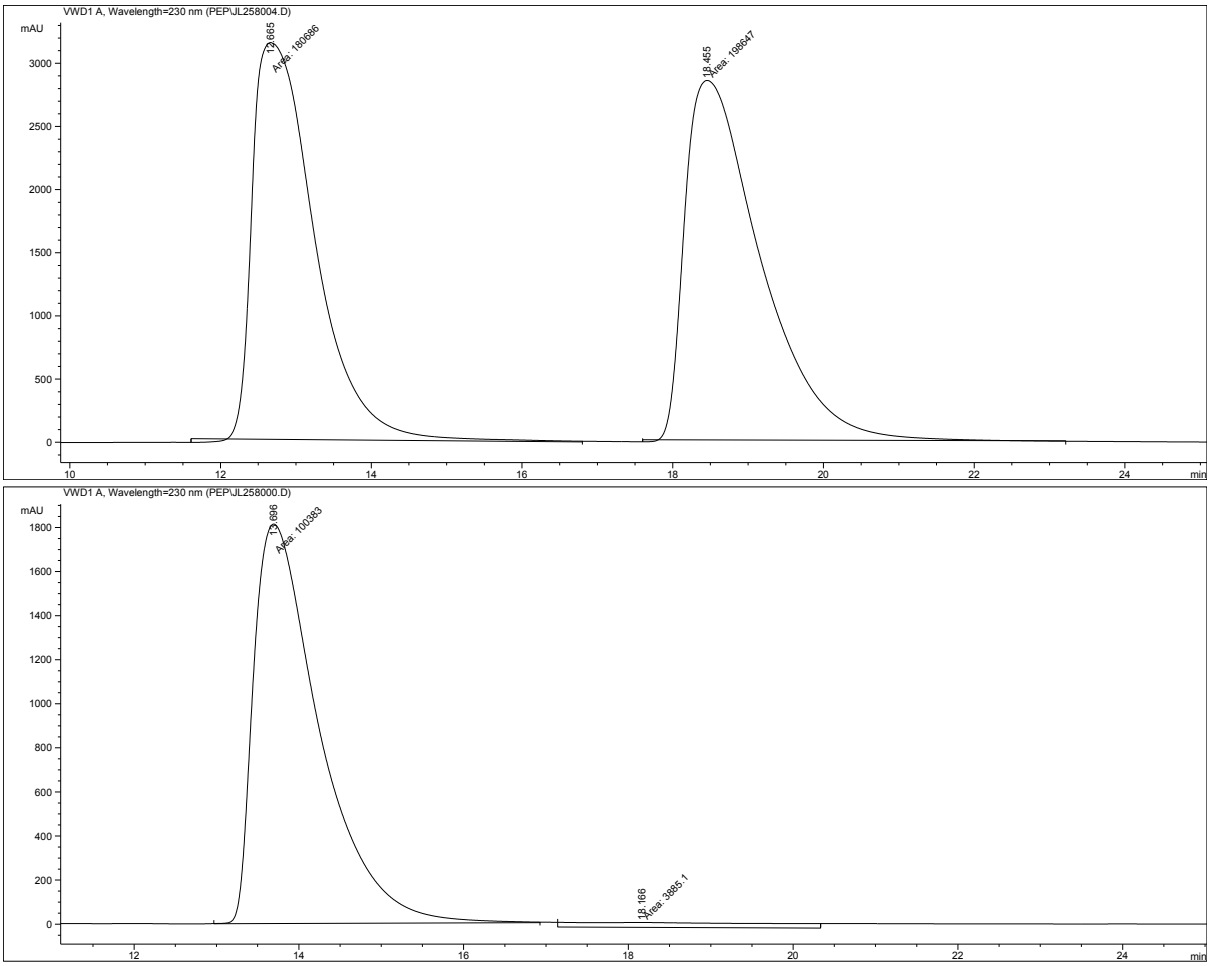

DAD1 A, Sig=250,100 Ref=360,100 (PEP\JL290200.D)
mAU
500
400
300
200
100
0
12.494
Area: 1001.37
17.877
Area: 28349
10
12
14
16
18
20
22
min

^{11}H NMR (400 MHz, $CDCl_3$) for (*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)quinoline (40)

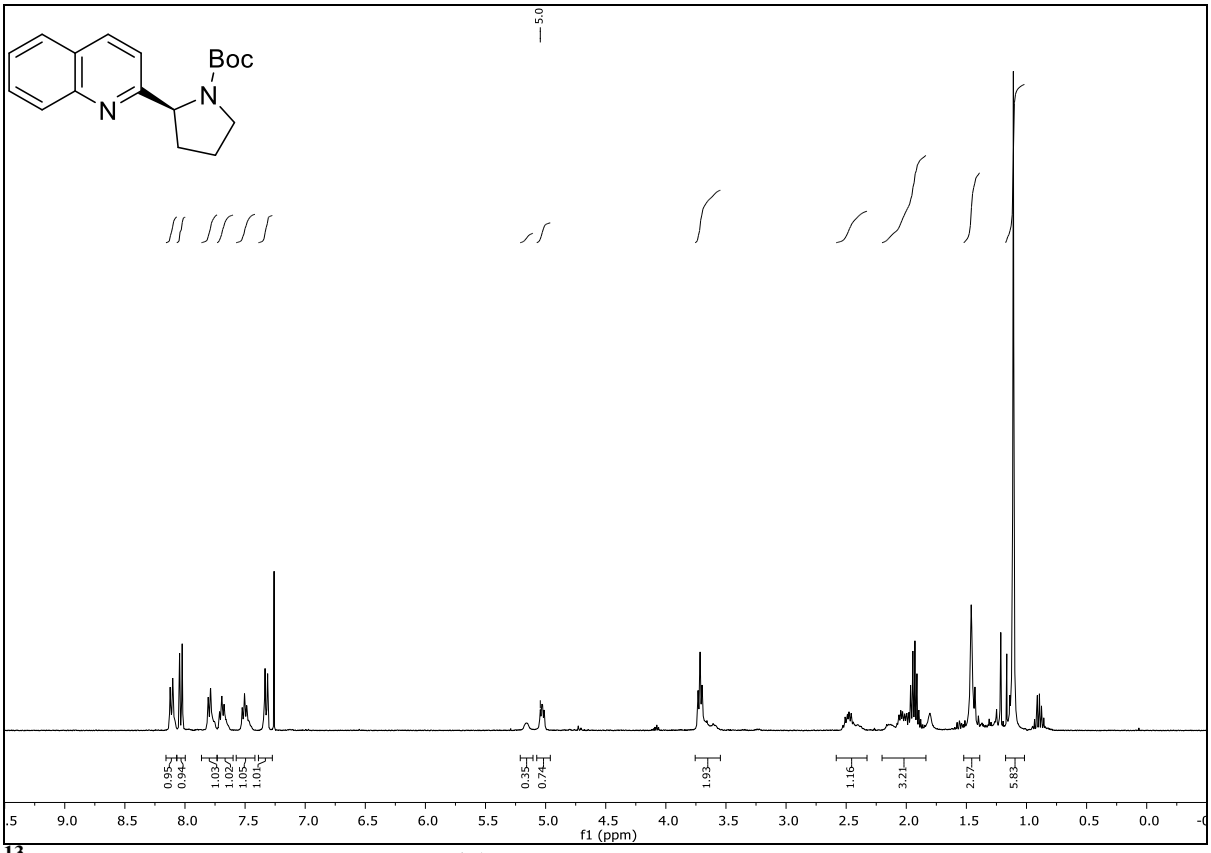


^{13}C NMR (100 MHz, $CDCl_3$) for (*S*)-2-(4-(4-methoxyphenyl)butan-2-yl)quinoline (40)

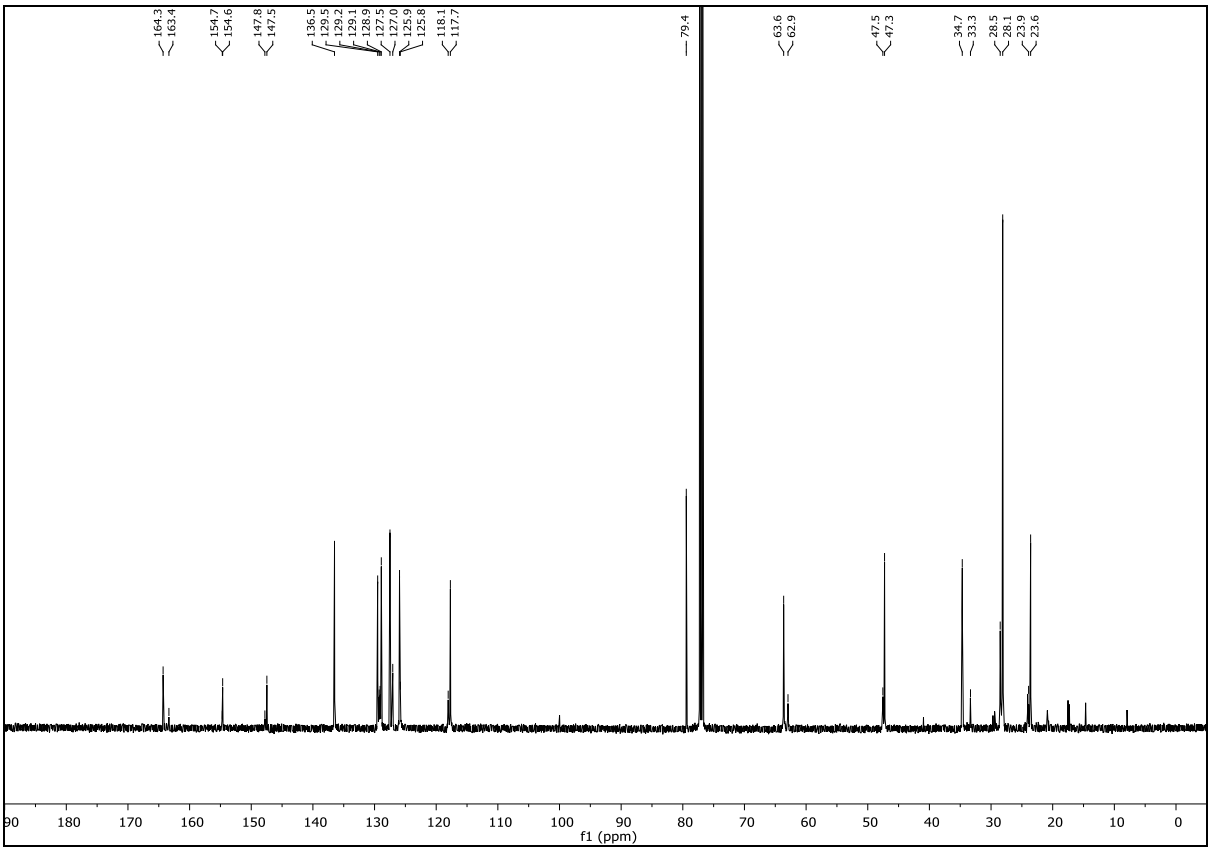


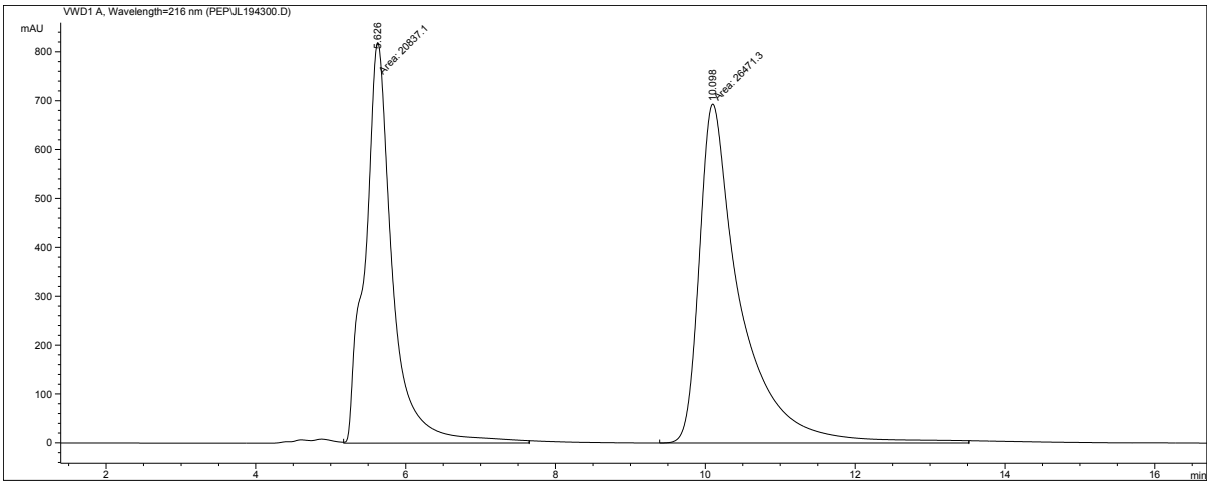

VWD1 A, Wavelength=230 nm (PEP\JL258004.D)
mAU
3000
2500
2000
1500
1000
500
0
12.665
Area: 180686
18.455
Area: 196647
10
12
14
16
18
20
22
24
min
VWD1 A, Wavelength=230 nm (PEP\JL258000.D)
mAU
1800
1600
1400
1200
1000
800
600
400
200
0
12.696
Area: 100383
18.166
Area: 3885.1
12
14
16
18
20
22
24
min

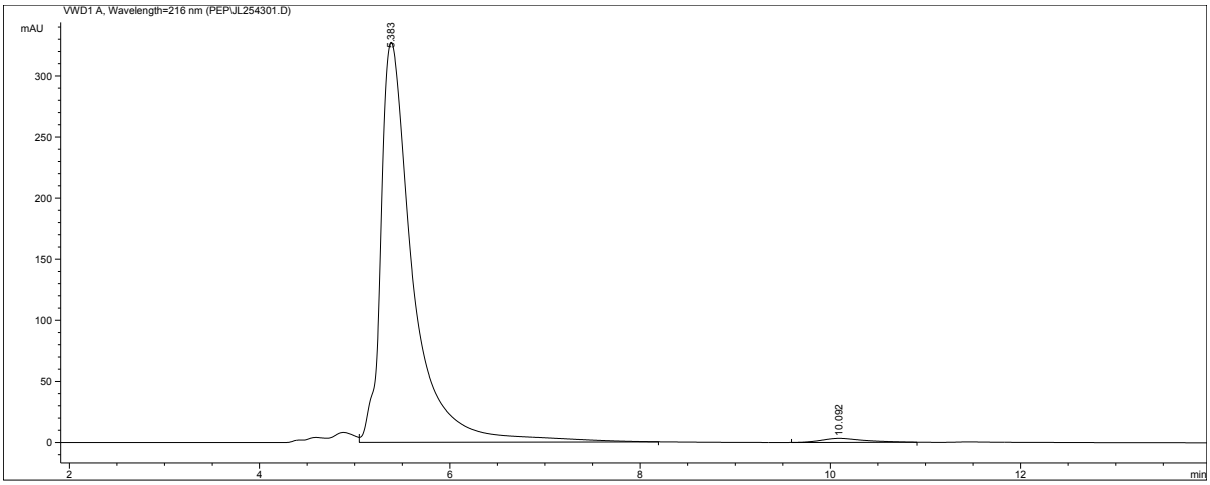
^{1}H NMR (400 MHz, $CDCl_3$) for *(S)-tert*-Butyl 2-(2-quinolinyl)pyrrolidine-1-carboxylate (41)



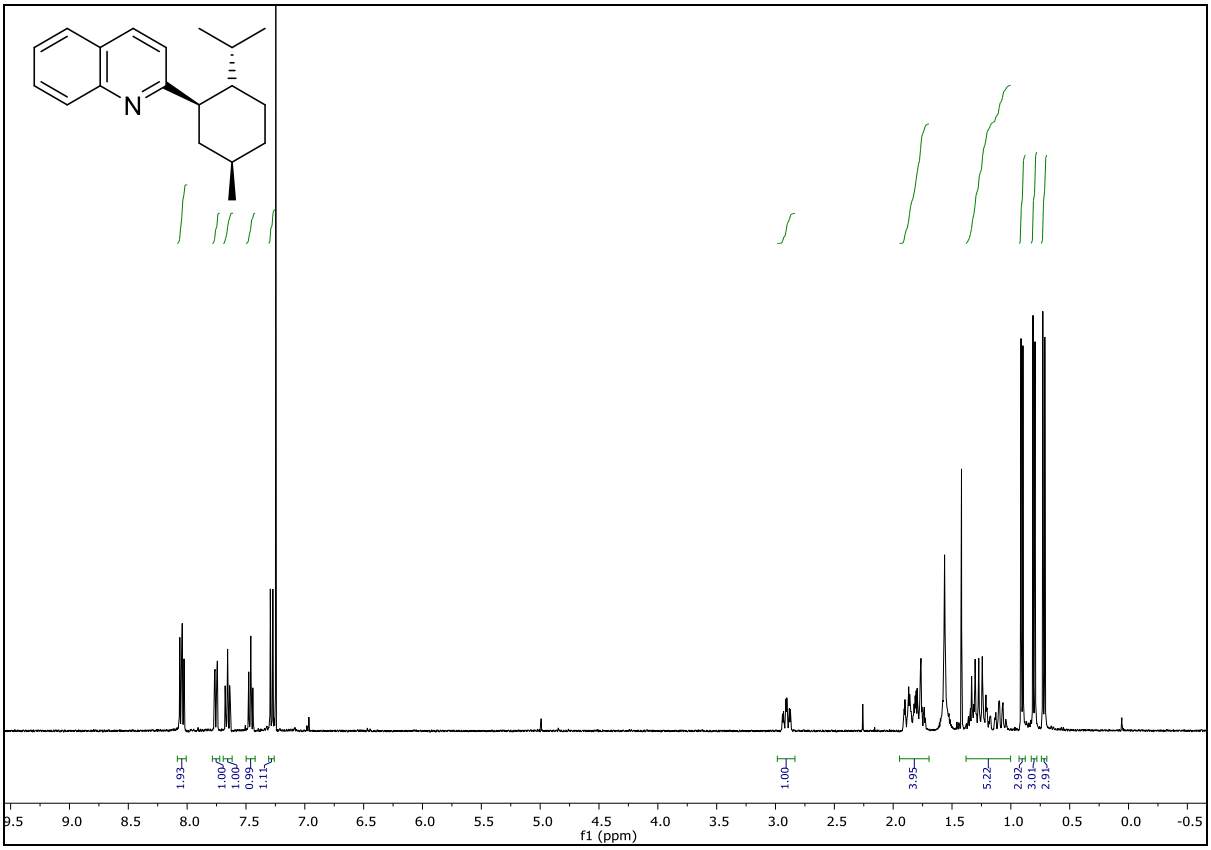
^{13}C NMR (100 MHz, $CDCl_3$) for *(S)-tert*-Butyl 2-(2-quinolinyl)pyrrolidine-1-carboxylate



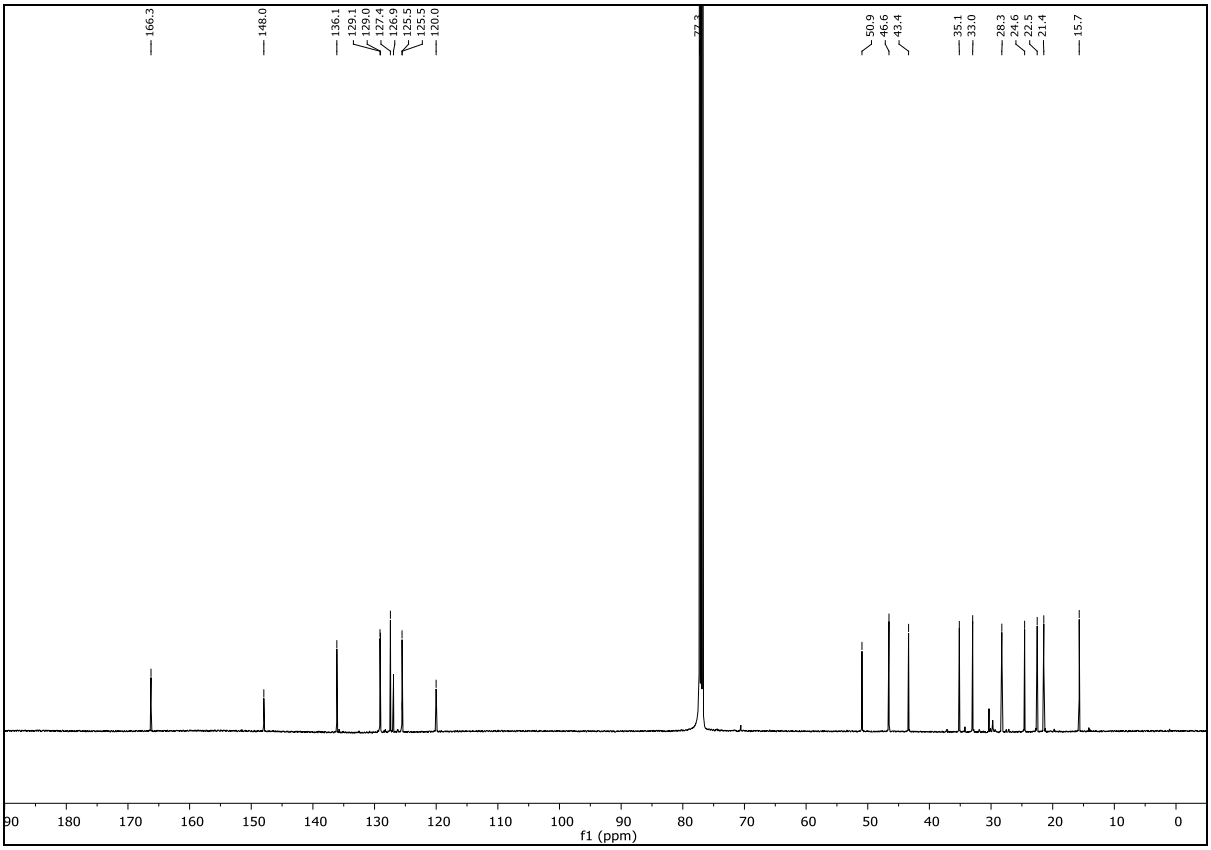

VWD1 A, Wavelength=216 nm (PEP\JL194300.D)
mAU
5.626
Area 20837.1
10.098
Area 26471.3
min


VWD1 A, Wavelength=216 nm (PEP\JL254301.D)
mAU
5.383
10.092
min

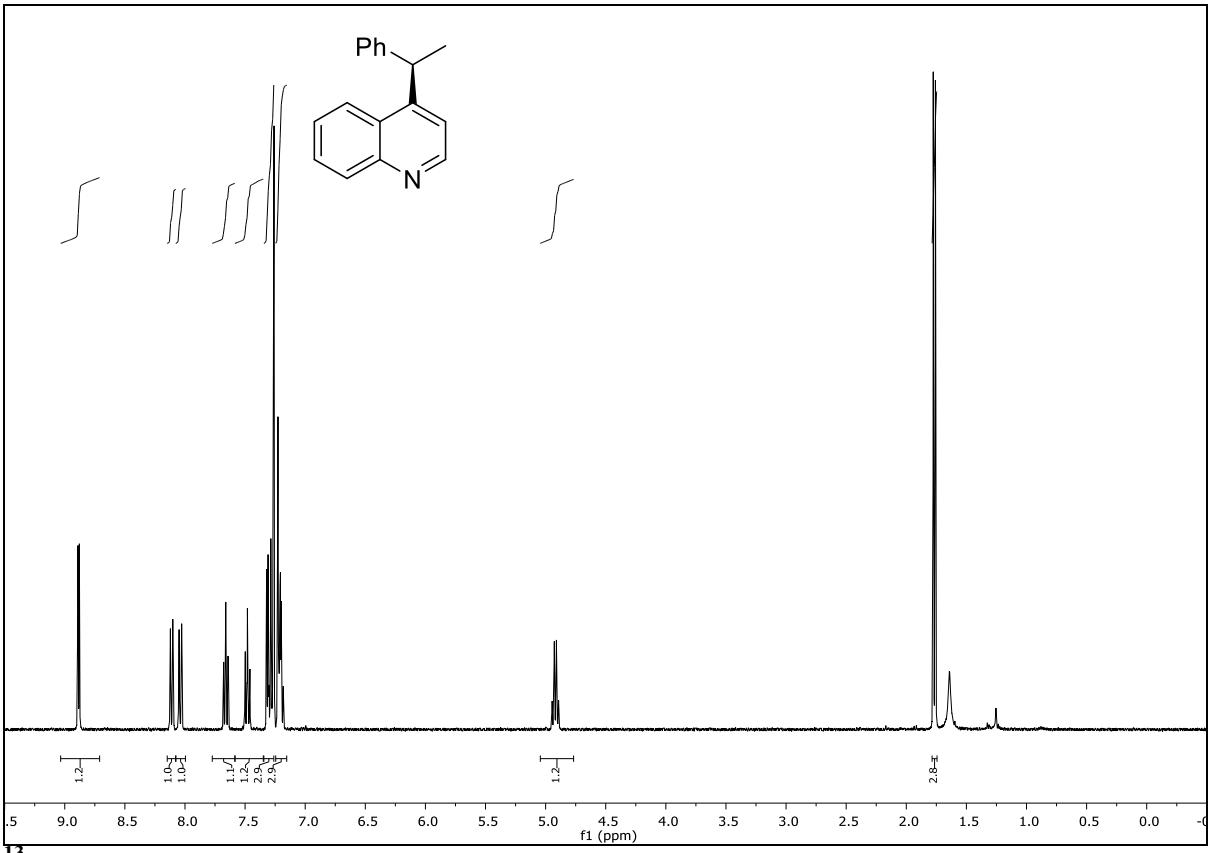
^{1}H NMR (400 MHz, $CDCl_3$) for 42



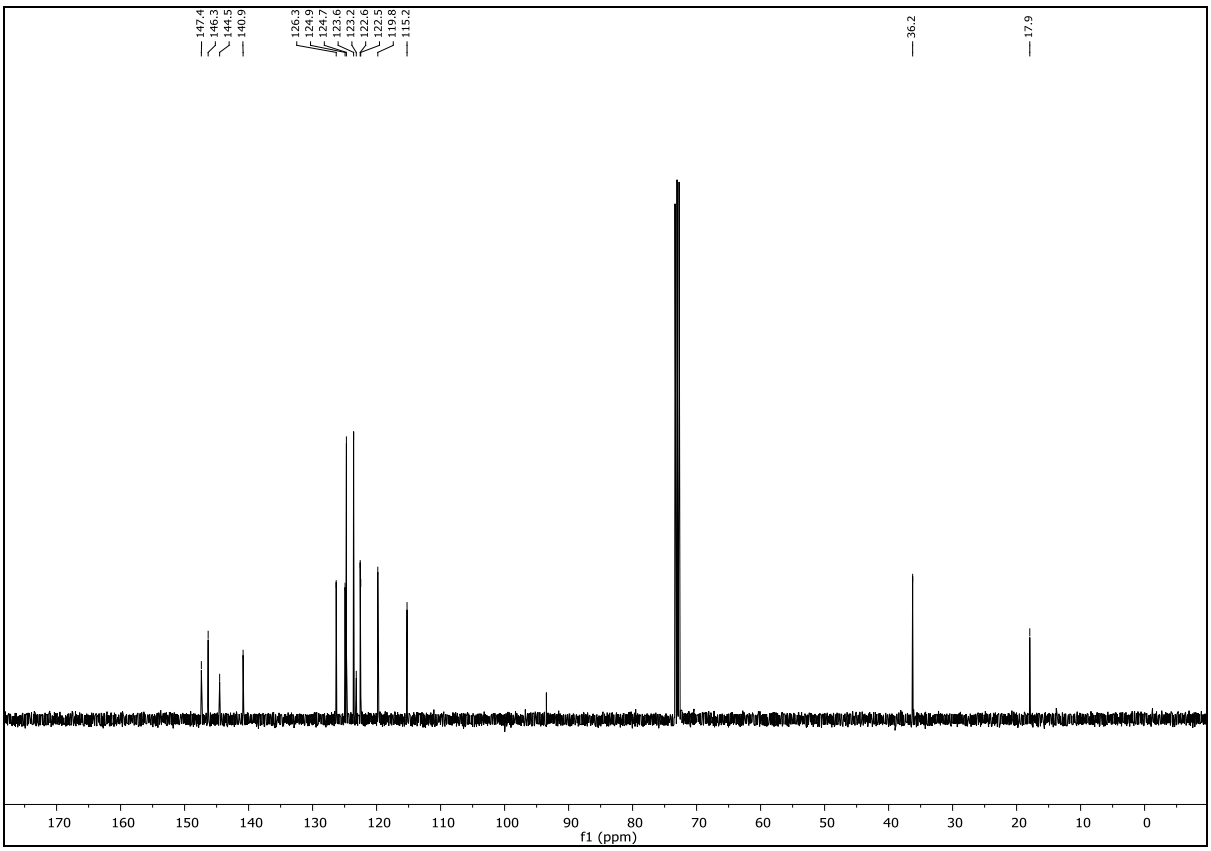
^{13}C NMR (125 MHz, $CDCl_3$) for 42

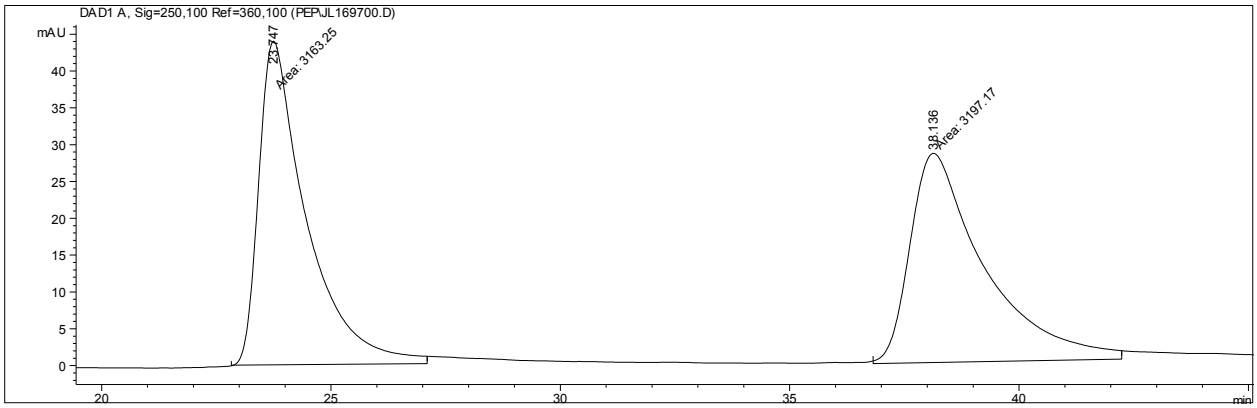


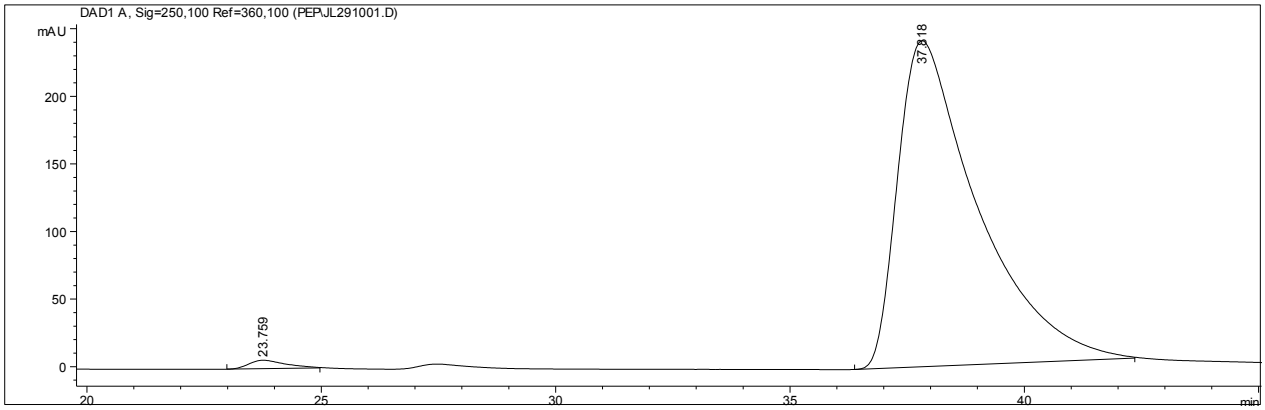
^{1}H NMR (400 MHz, $CDCl_3$) of (*R*)4-(1-phenylethyl)quinoline (43).



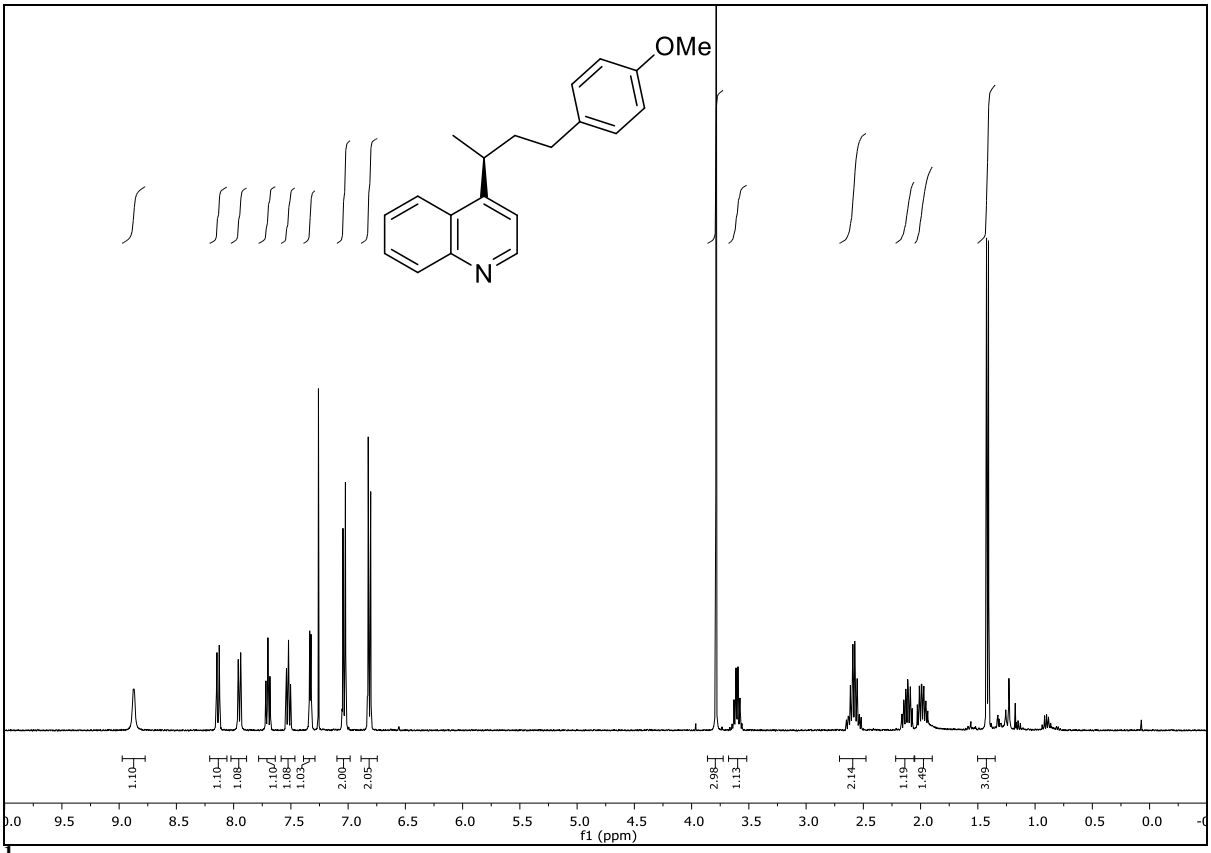
^{13}C NMR (100 MHz, $CDCl_3$) of (R)-4-(1-phenylethyl)quinoline (43)



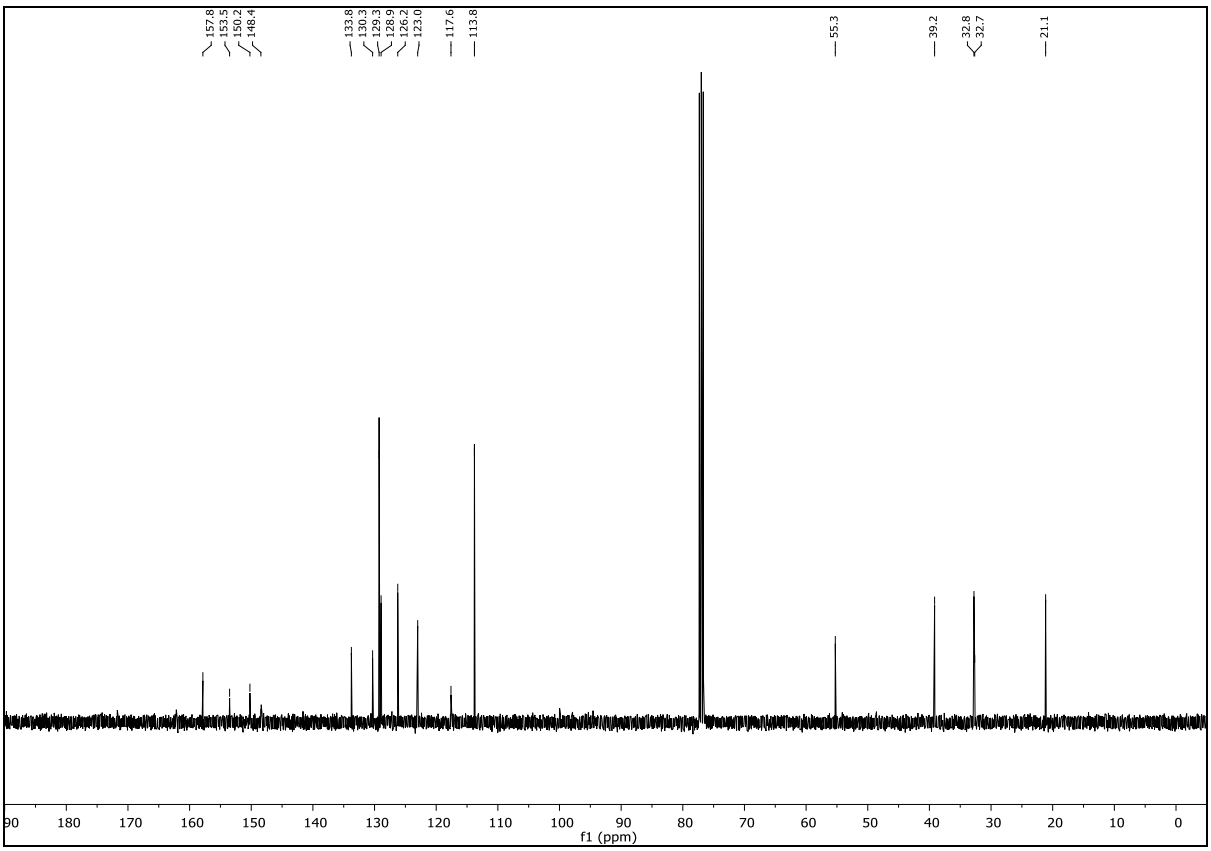

DAD1 A, Sig=250,100 Ref=360,100 (PEP\JL169700.D)
mAU
23.747
Area: 3163.25
38.136
Area: 3197.17
min

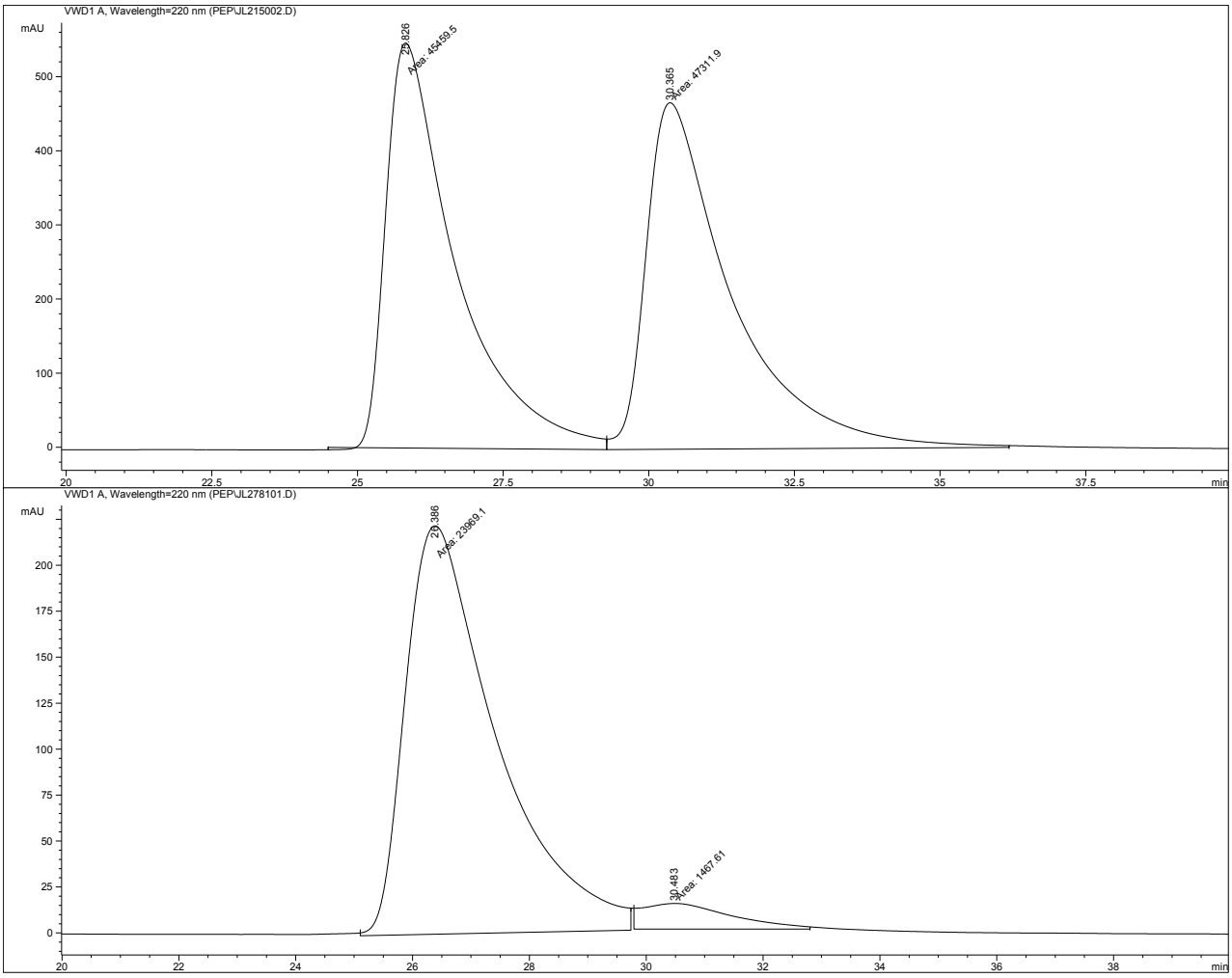

DAD1 A, Sig=250,100 Ref=360,100 (PEP\JL291001.D)
mAU
37.918
23.759
min

^{1}H NMR (400 MHz, $CDCl_3$) of (*S*)-4-(4-methoxy-1-phenylethyl)quinoline (44).

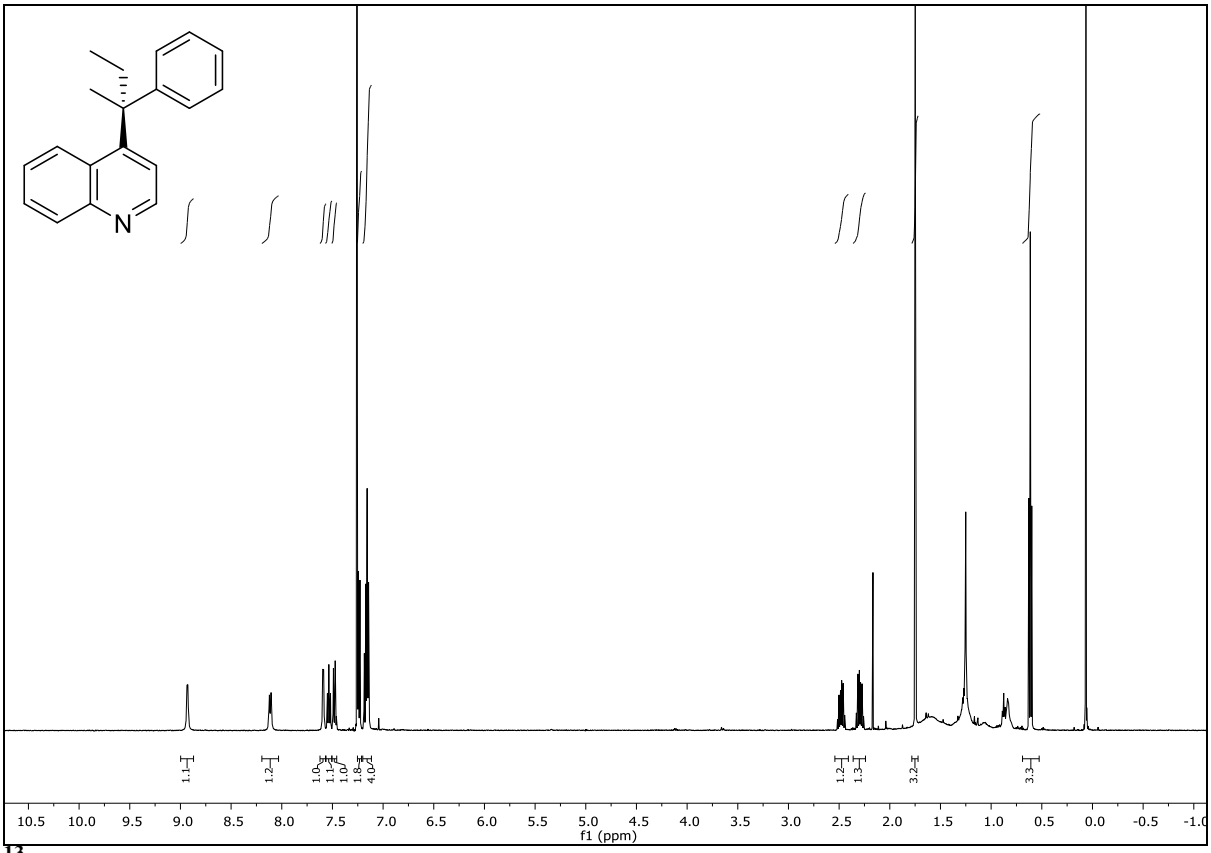


^{1}H NMR (400 MHz, $CDCl_3$) of (*S*)-4-(4-methoxy-1-phenylethyl)quinoline (44)

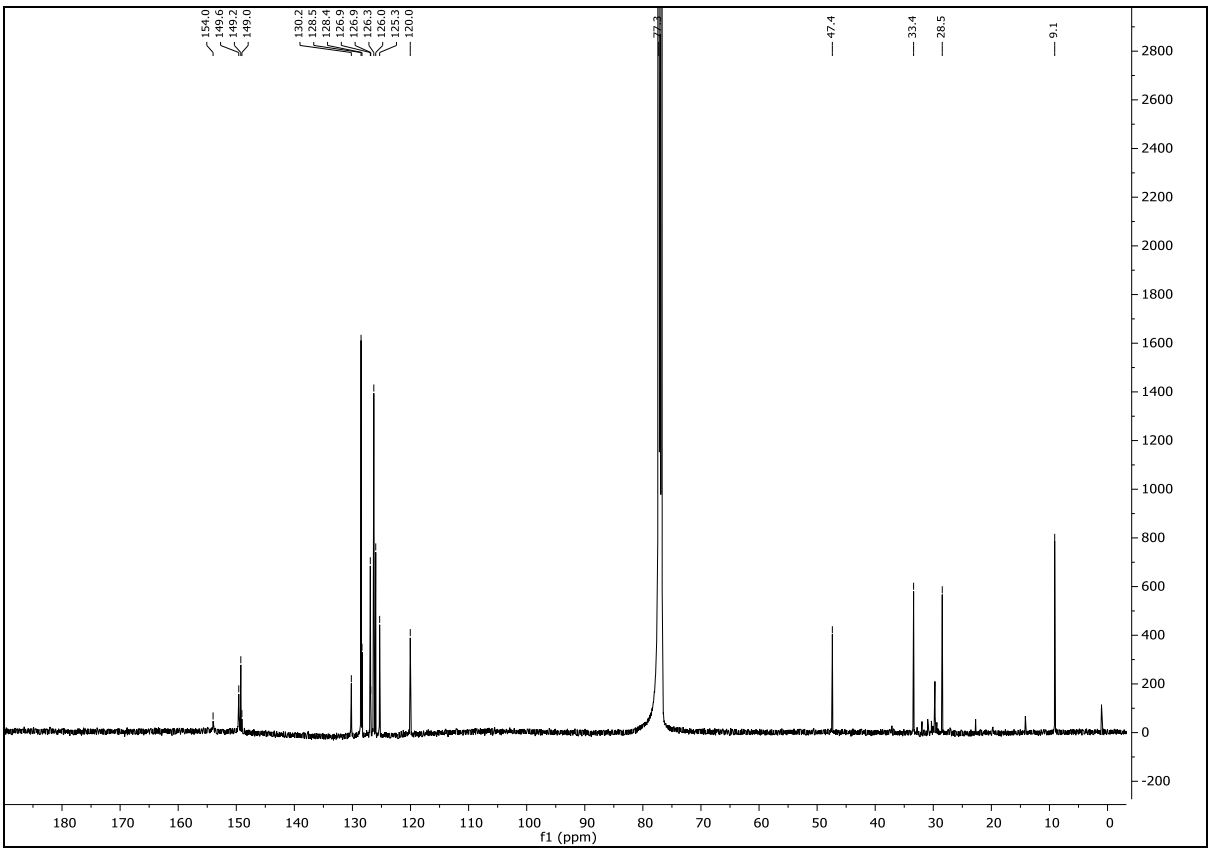


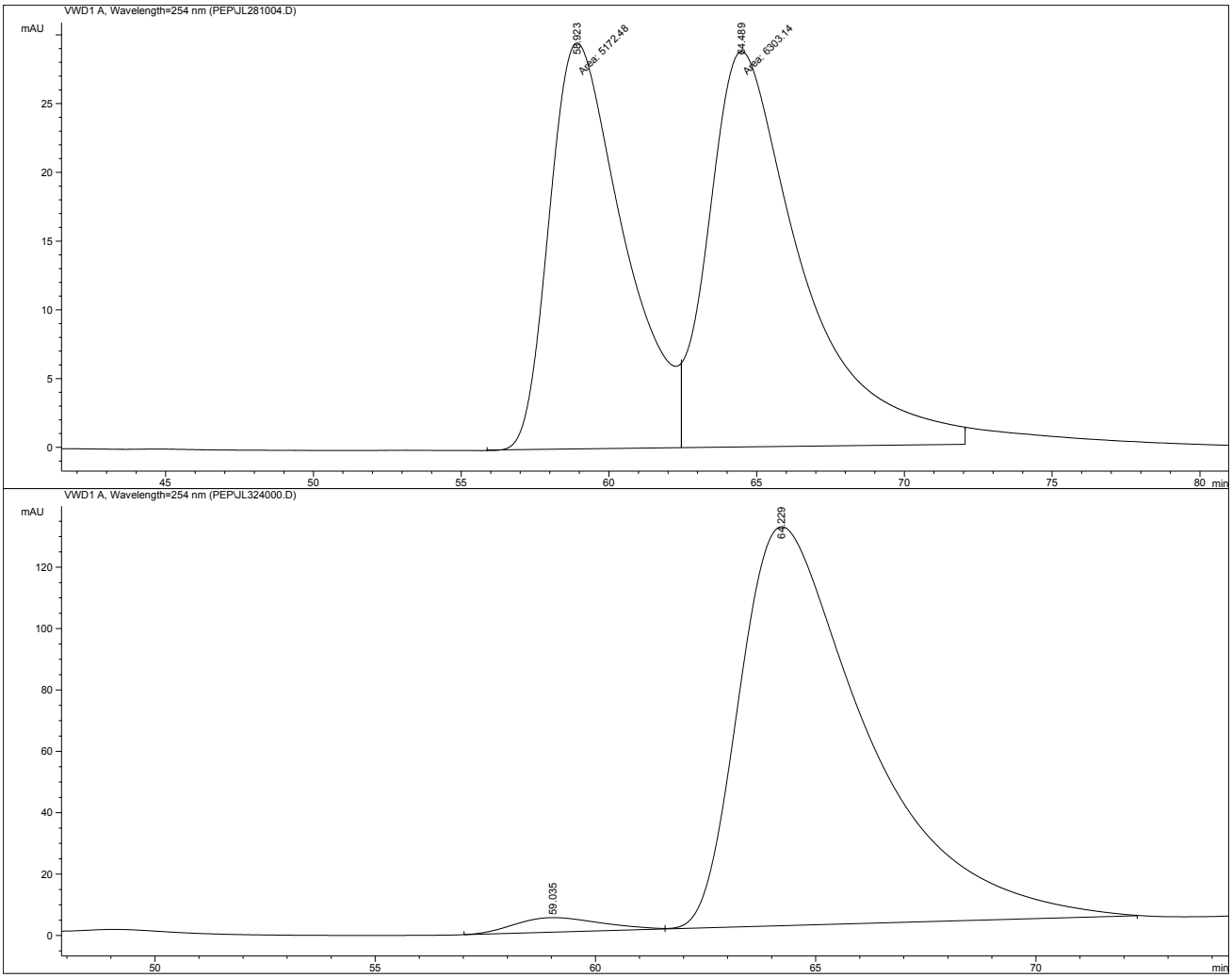

VWD1 A, Wavelength=220 nm (PEPJL215002.D)
mAU
25.826
Area: 45459.5
30.365
Area: 47311.9
min
VWD1 A, Wavelength=220 nm (PEPJL278101.D)
mAU
25.386
Area: 23969.1
30.483
Area: 1457.61
min

^{1}H NMR (500 MHz, $CDCl_3$) of (*R*)-4-(2-phenylbutan-2-yl)quinoline (46).

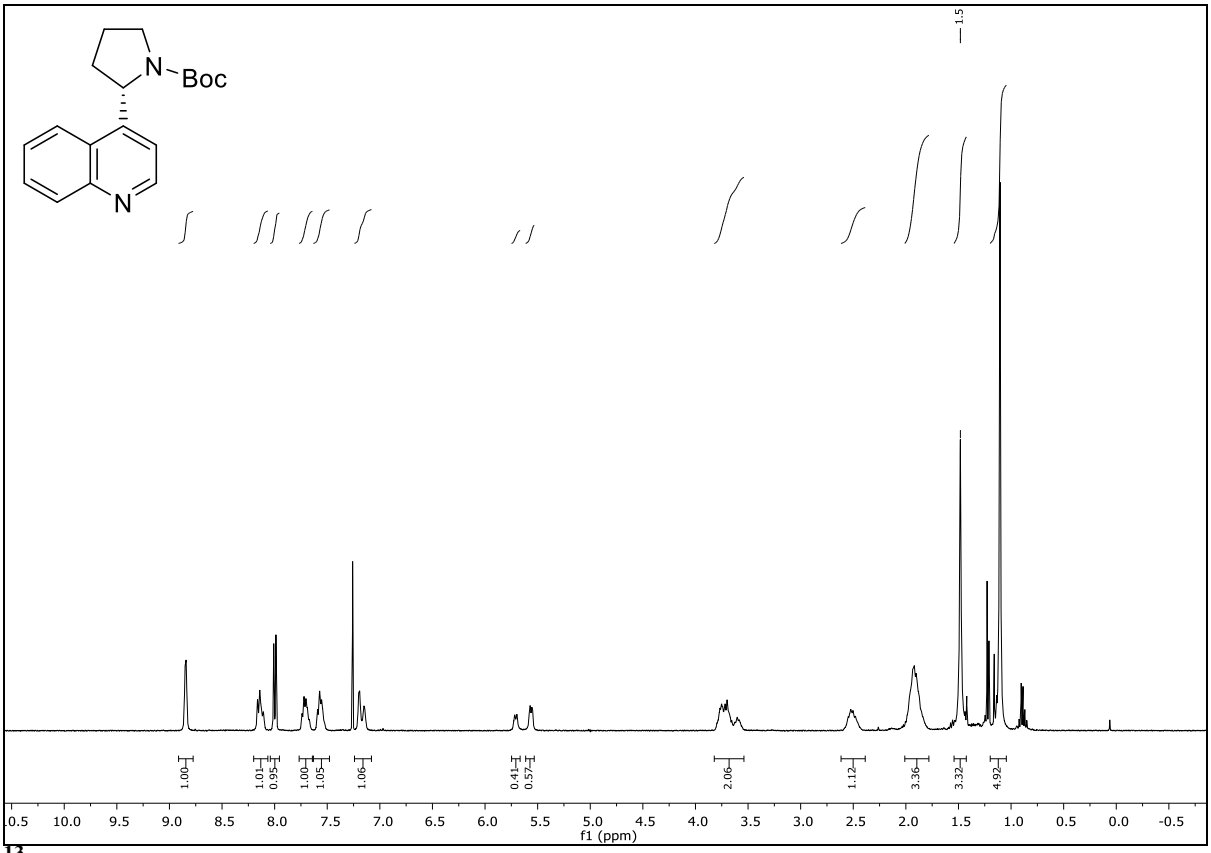


^{13}C NMR (125 MHz, $CDCl_3$) of (*R*)-4-(2-phenylbutan-2-yl)pyridine (46).

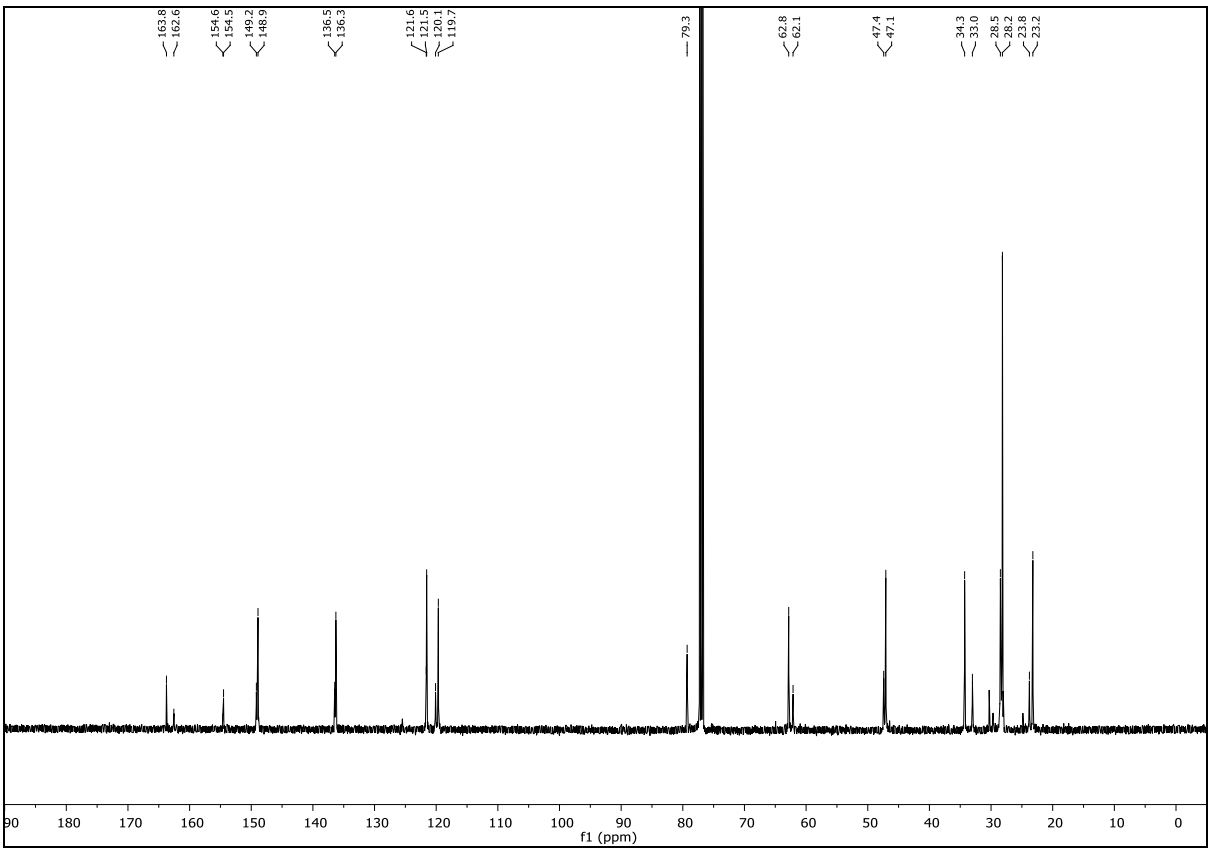


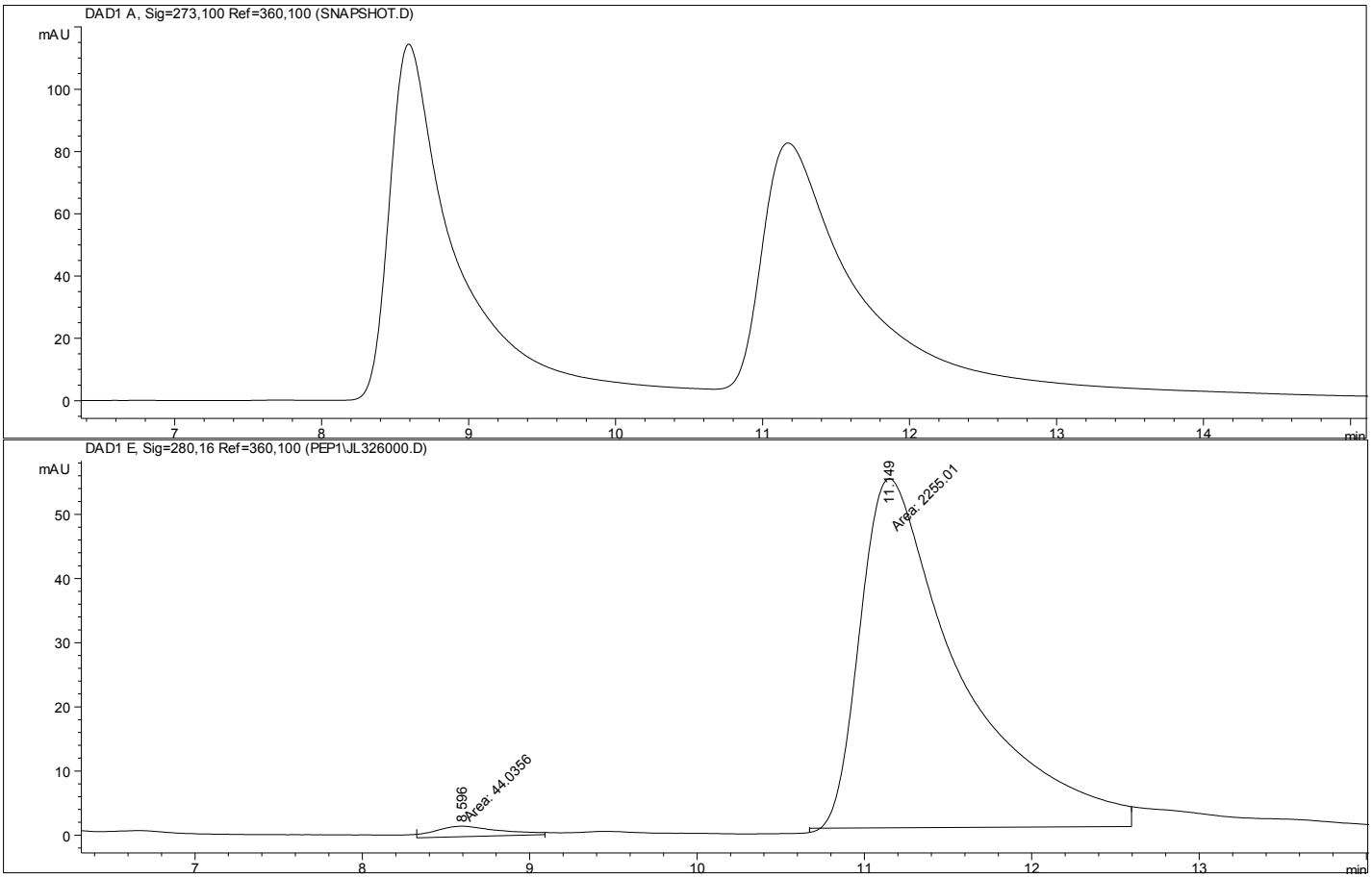

VWD1 A, Wavelength=254 nm (PEP\JL281004.D)
mAU
59.923
Area: 5172.48
64.489
Area: 6303.14
min
VWD1 A, Wavelength=254 nm (PEP\JL324000.D)
mAU
64.229
59.035
min

^{1}H NMR (500 MHz, $CDCl_3$) of *tert*-Butyl 2-(4-quinolinyl)pyrrolidine-1-carboxilate (45)

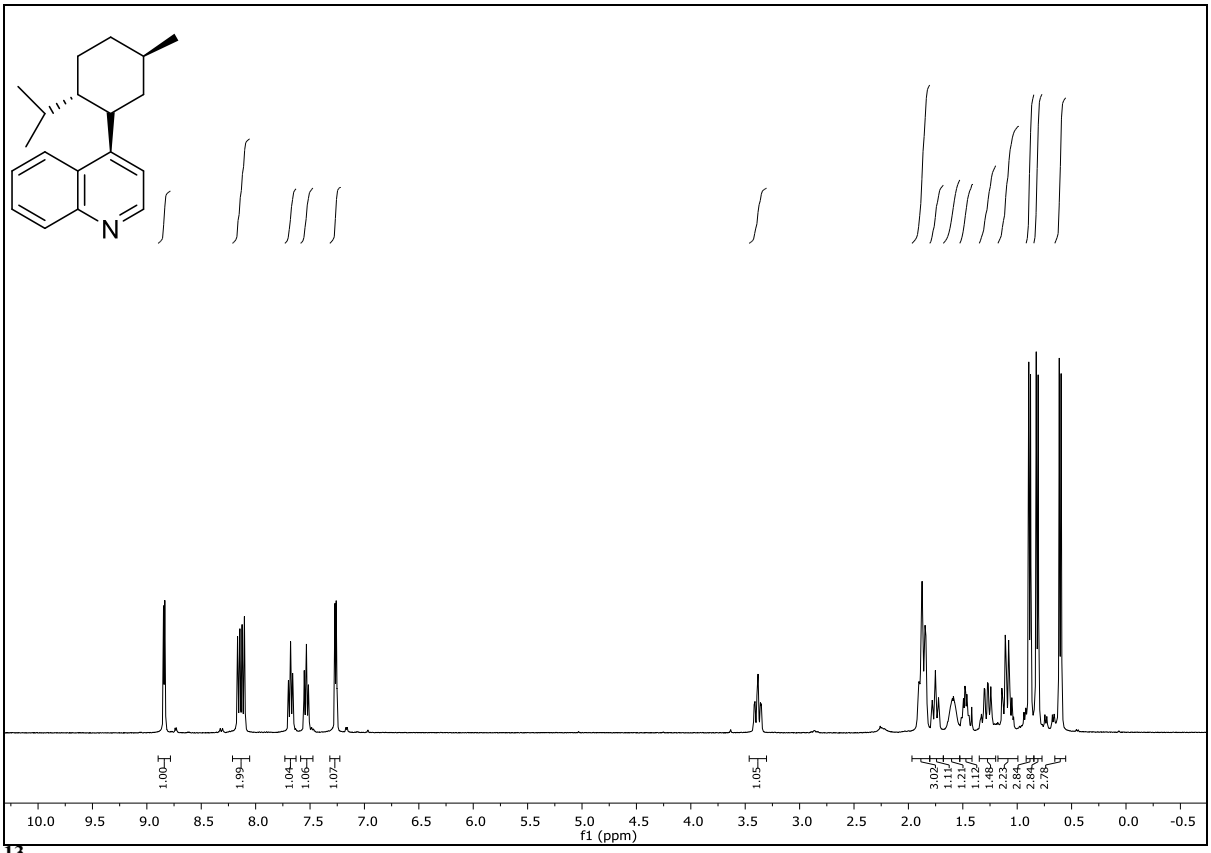


^{13}C NMR (125 MHz, $CDCl_3$) of *tert*-Butyl 2-(4-quinolinyl)pyrrolidine-1-carboxilate.

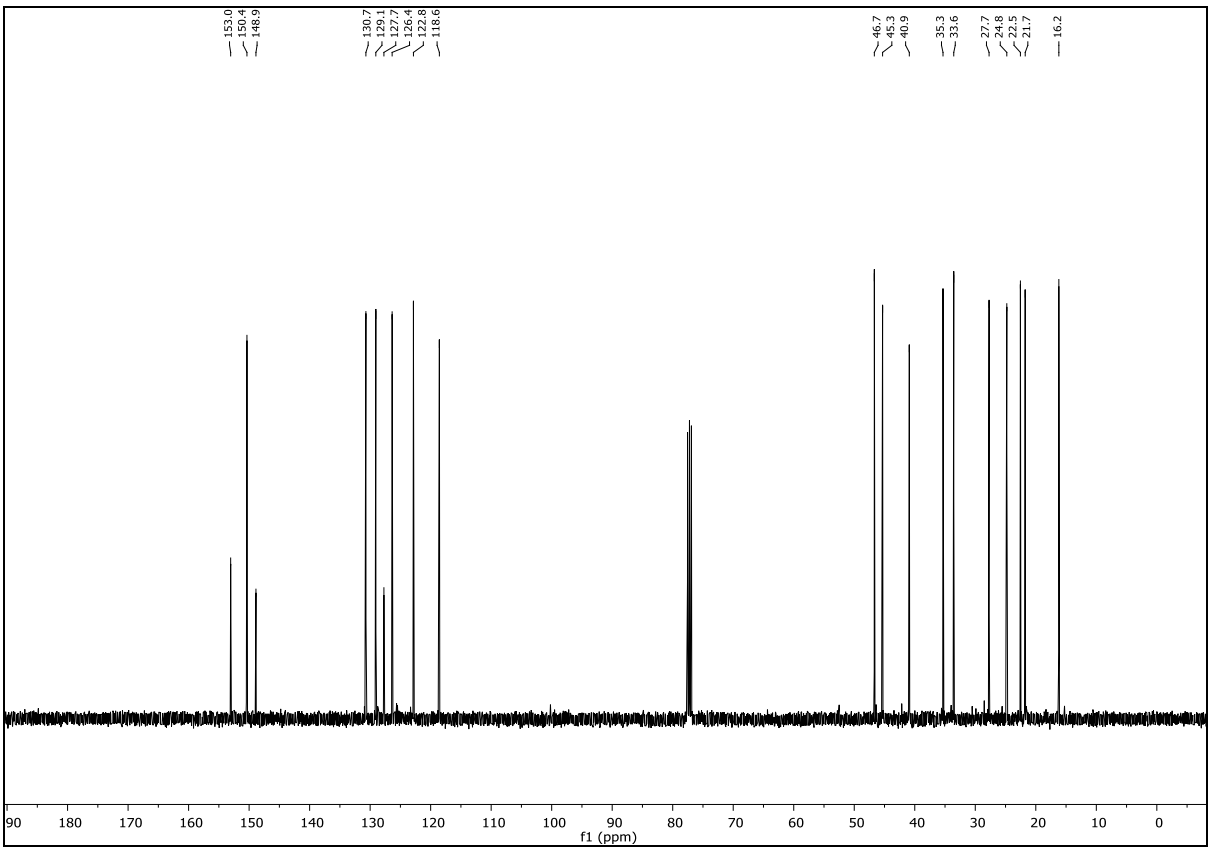



DAD1 A, Sig=273,100 Ref=360,100 (SNAPSHOT.D)
mAU
100
80
60
40
20
0
7
8
9
10
11
12
13
14
min
DAD1 E, Sig=280,16 Ref=360,100 (PEP1\JL326000.D)
mAU
50
40
30
20
10
0
8.596
Area: 44.0356
11.149
Area: 2255.01
7
8
9
10
11
12
13
min

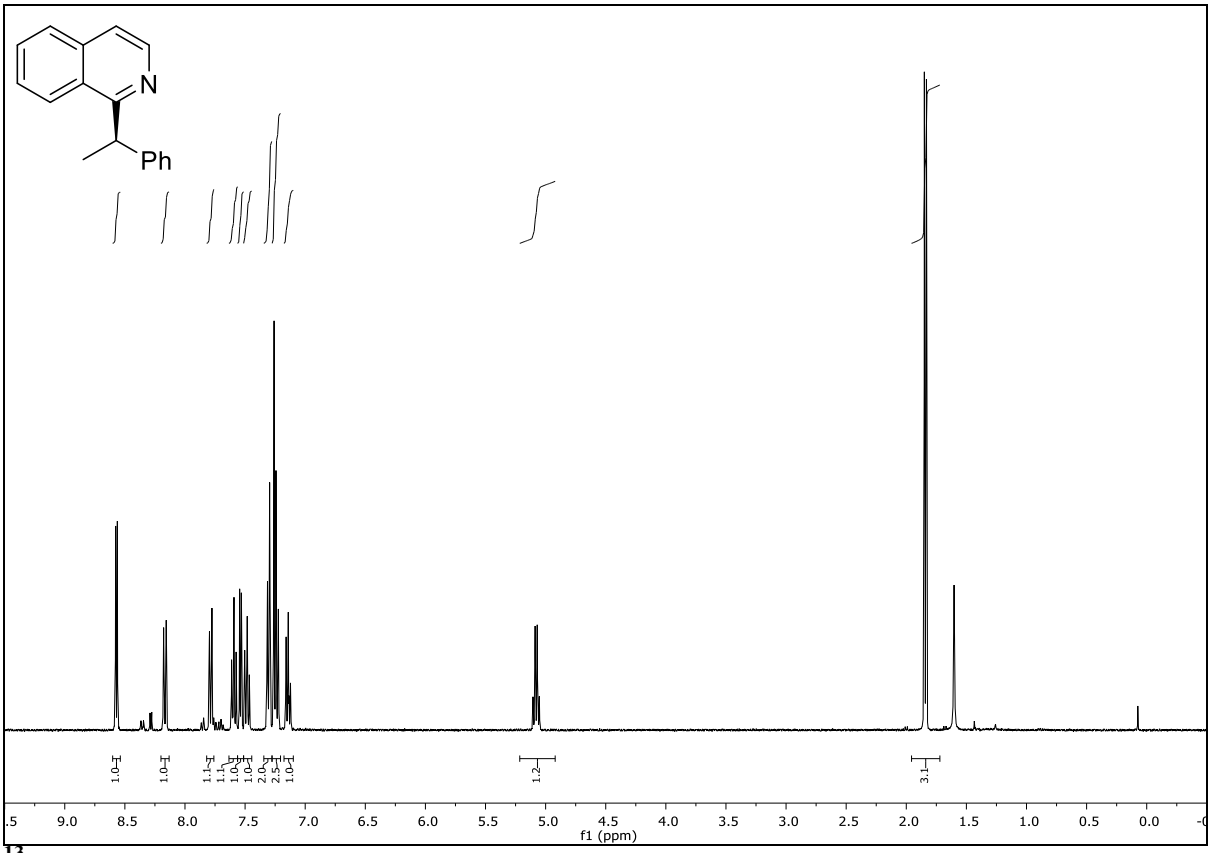
^{1}H NMR (500 MHz, $CDCl_3$) of 47



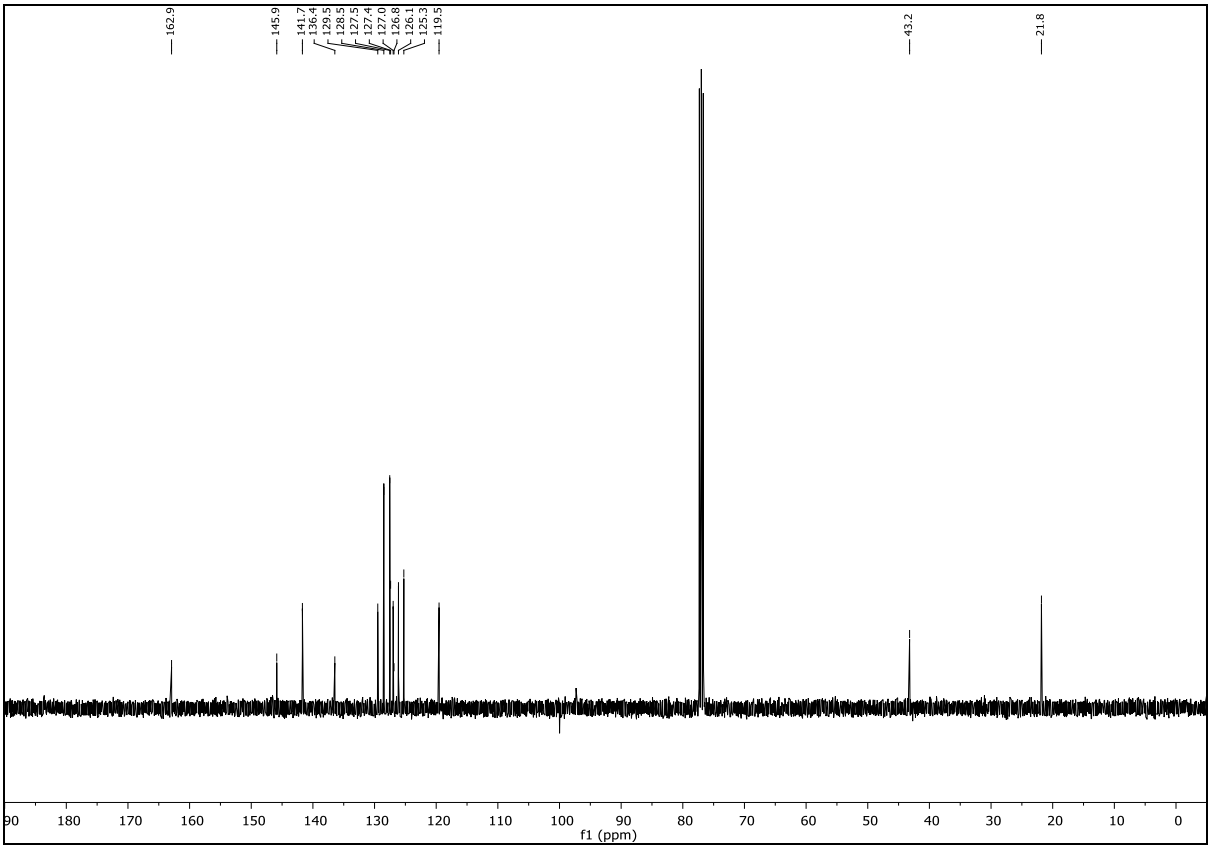
^{13}C NMR (125 MHz, $CDCl_3$) of 47



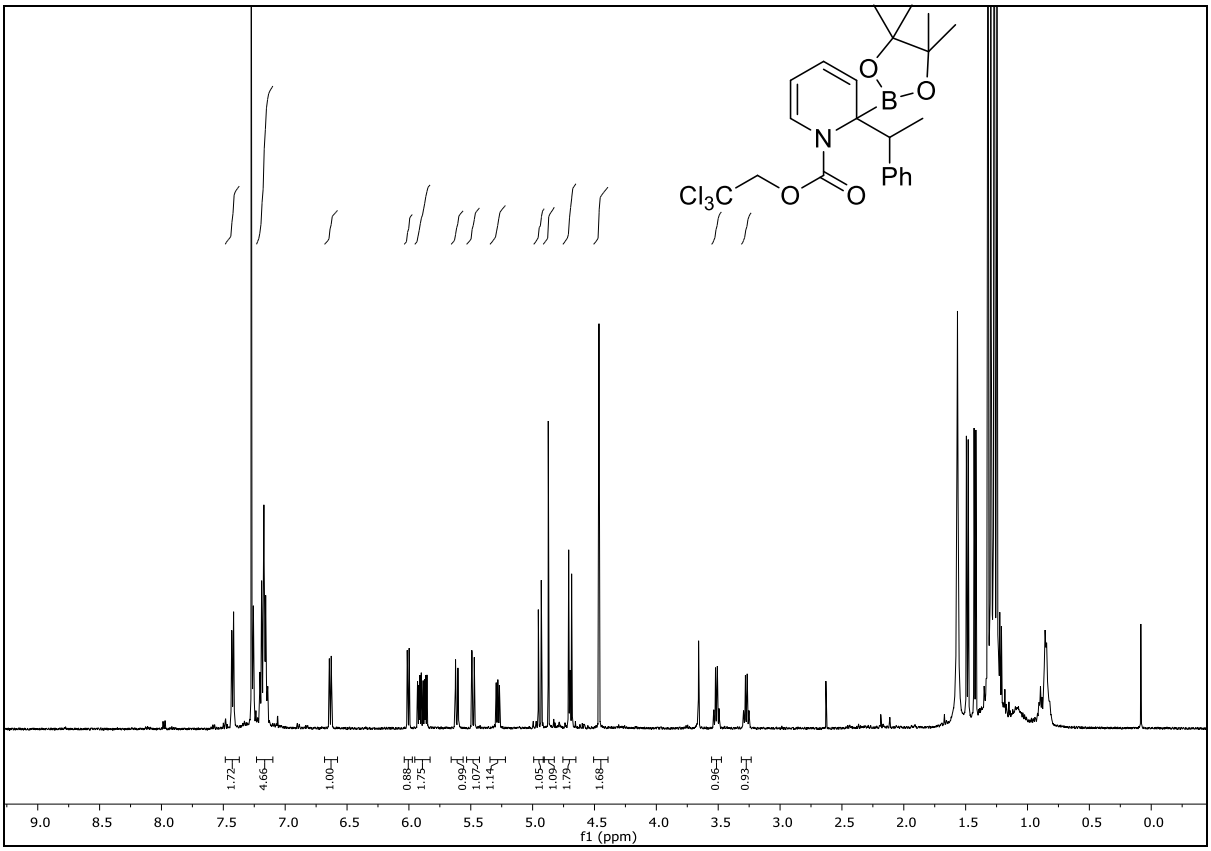
^{1}H NMR (400 MHz, CDCl3) of (R)-1-(1-Phyenylethyl)isoquinoline (48)



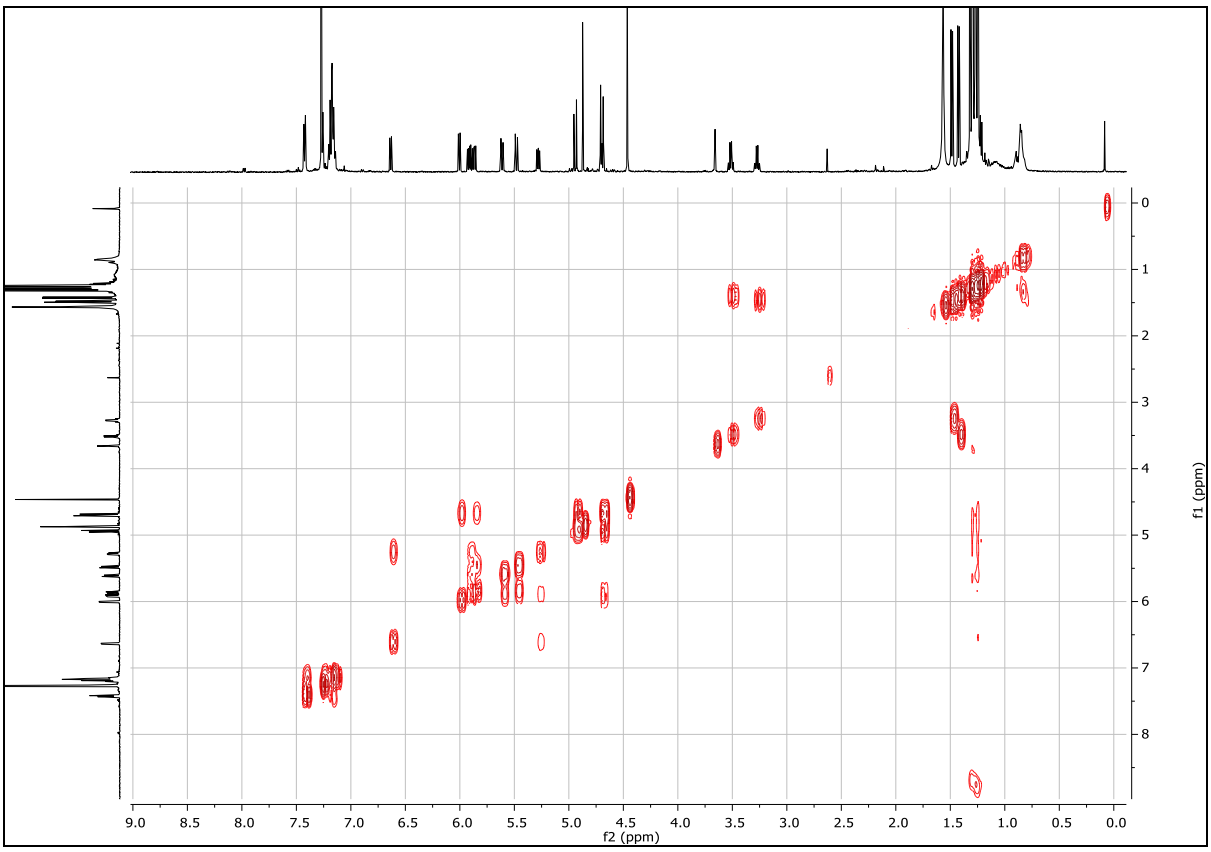
^{13}C NMR (125 MHz, $CDCl_3$) of (R)-1-(1-Phyenylethyl)isoquinoline (48)



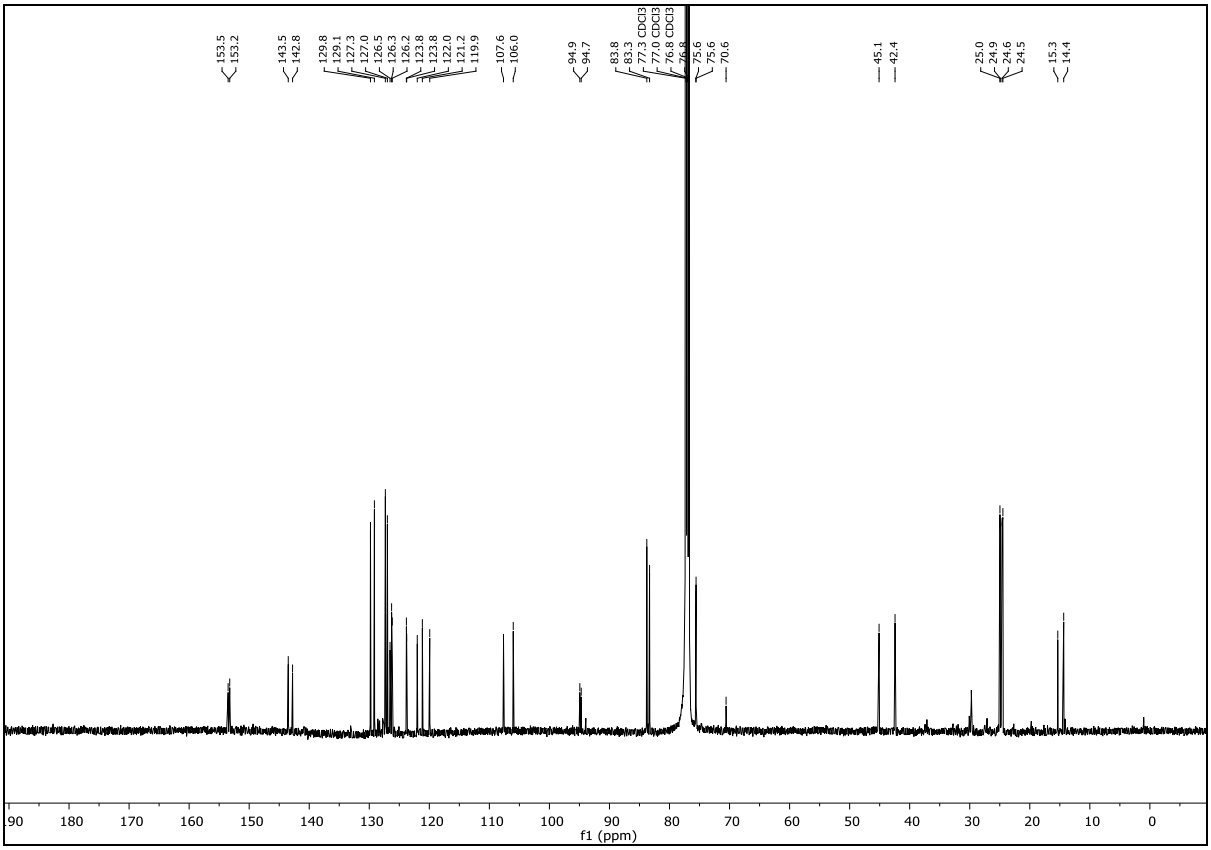
^{1}H NMR (500 MHz, $CDCl_3$) of DHPyr (mixture of diastereoisomers)



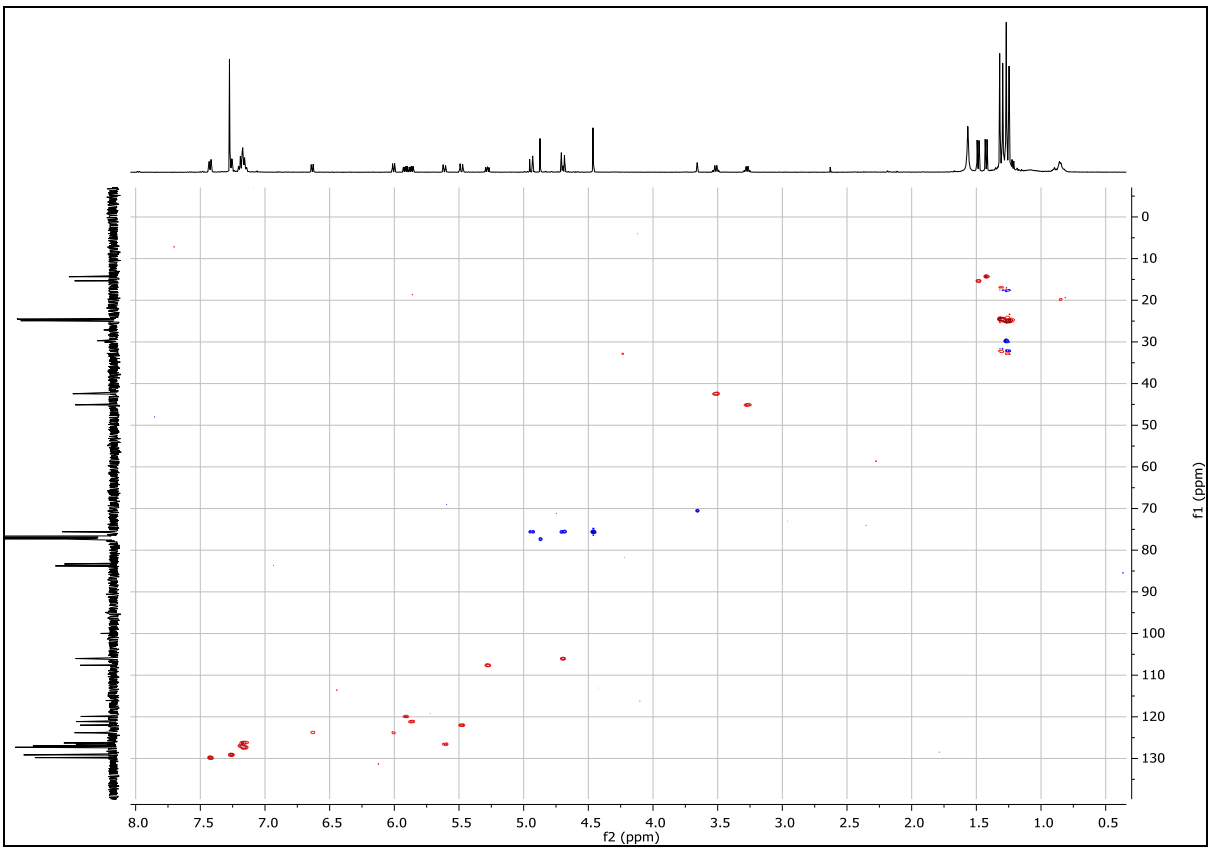
COSY (500 Mhz, $CDCl_3$) (mixture of diastereoisomers)



^{13}C NMR (125 MHz, $CDCl_3$) of x (mixture of diastereoisomers)



HSQC NMR (500 MHz, $CDCl_3$) of x (mixture of diastereoisomers)



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[24] For a discussion of ^{11}B NMR chemical shifts, see: (a) B. Wrackmeyer *Annu. Rep. NMR Spectrosc.*, **1988**, *20*, 61. (b) S. Hermanek *Chem. Rev.* **1992** *92*, 325.