Mannich Bases as Enone Precursors for Water-Mediated Efficient Synthesis of 2,3,6-Trisubstituted Pyridines and 5,6,7,8-Tetrahydroquinolines

Essam Hamied Ahmed Hanashalshahaby and Canan Unaleroglu*

Hacettepe University, Chemistry Department, 06800 Beytepe, Ankara Turkey

Supporting Information

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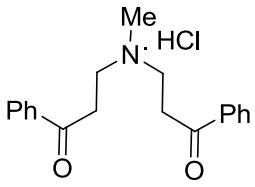
Active methylenes **4**{*1-7*} were purchased from commercial vendors and used without further purification. The ketonic Mannich bases **7**{*1*}, **7**{*2*} and **8** depicted in Scheme 2 have been synthesized according to the given literature and their melting points are convenient with literature.[1-3]

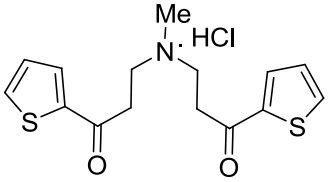
Synthesis of 3,3'-(methylazanediyl)bis(1-(furan-2-yl)propan-1-one) hydrochloride 7{*3*}: A mixture of 2-acetylfuran (5.51 mL, 0.05 mol), methylamine hydrochloride (1.69 g, 0.025), paraformaldehyde (1.50 g, 0.05 mol) in absolute ethanol (20 mL) was heated on a steam bath for 3 h. After completion the reaction, the reaction mixture was cooled to room temperature and then precipitated product was separated by filtration and crystallized in absolute ethanol. Yield: 72%, mp:193-195 ^{o}C. HRMS for free base (ESI): Calcd for $C_{15}H_{18}NO_4$ $[M+H]^+$: 276.1230, found: 276.1274.

Synthesis of 1-(1*H*-indol-3-yl)-3-morpholinopropan-1-one hydrochloride 1-(1*H*-indol-3-yl)-3-morpholinopropan-1-one hydrochloride 7{*4*}: A mixture of 3-acetylindole (3.98, 0.025 mole), morpholine hydrochloride (2.18 mL, 0.025), paraformaldehyde (0.75 g, 0.025 mol) in absolute ethanol (20 mL) was heated on a steam bath for 3 h. After completion the reaction, acetone (10 mL) was added to the mixture and was kept in the refrigerator over night and then precipitated product was separated by filtration and crystallized in absolute ethanol. Yield: 65%, mp: 229-230 ^{o}C. HRMS for free base (ESI): Calcd for $C_{15}H_{19}N_2O_2$ $[M+H]^+$: 259.1441, found: 259.1495.

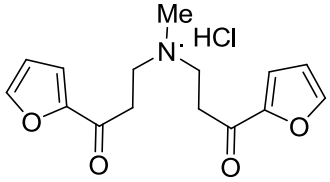
Scheme 1. Ketonic Mannich Bases **7**{*1-4*}, **8**



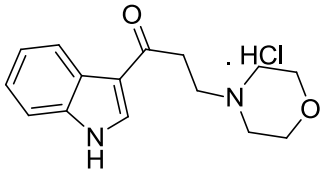
7{*1*}[1]



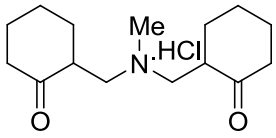
7{*2*}[2]



7{*3*}



7{*4*}



8[3]

General procedure for the synthesis of 2,3,6-trisubstituted pyridines 6{*1-6, 1*}: A mixture of diketo-base hydrochloride **7**{*1*} (0.22 g, 0.66 mmol), active methylene **4**{*1*} (0.045 mL, 0.44 mmol) and ammonium acetate (0.2 g, 2.6 mmol) in 3 mL of water was heated at 80 ºC for 2 hours. After completion the reaction (monitored by TLC), the reaction mixture was cooled to room temperature and 20 mL of water was added. The product was extracted with EtOAc (2x5 mL) and dried ($MgSO_4$). The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Silica gel, EtOAc-hexane, 1:6). All compounds were fully characterized by ^{1}H NMR, ^{13}C NMR and HRMS analysis.

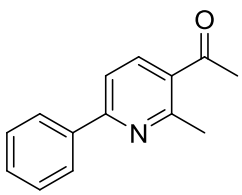
General procedure for the synthesis of 2,3,6-trisubstituted pyridines with K-10 catalysis 6{*2-6, 1-4*}: To the mixture of the diketo-base hydrochloride **7**{*1*} (0.22 g, 0.66 mmol), active methylene ketone **4**{*2*} (0.045 mL, 0.44 mmol) and ammonium acetate (0.2g, 2.6 mmol) in 3 mL of water was added K-10 (0.44 g) and heated on an oil bath with stirring at 80 ºC for 2 hours (monitored by TLC). The reaction mixture was cooled to room temperature and poured on 20 mL of water. The crude product was extracted with chloroform (2x25 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash

column chromatography (Silica gel, EtOAc-hexane, 1:6). All compounds were fully characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

Synthesis of 1-(2-Methyl-5,6,7,8-tetrahydroquinolin-3-yl)ethanone 9{*1*}: A mixture of 2,2'-(methylazanediyl)bis(methylene)dicyclohexanone hydrochloride **8** (0.2 g, 0.69 mmol), active methylene ketone **4**{*1*} (0.048 mL, 0.46 mmol) and ammonium acetate (0.2 g, 2.6 mmol) in 3 mL of water was heated on an oil bath with stirring at 80 ºC for 2 hours (monitored by TLC). The reaction mixture was cooled to room temperature and poured on 20 mL of water. The crude product was extracted with chloroform (2x25 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Silica gel, EtOAc-hexane, 1:6). The structure of **9**{*1*} was fully characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

General procedure for the synthesis of 5,6,7,8-tetrahydroquinolines in the presence of K-10 catalysis 9{*2-7*}: To the mixture of 2,2'-(methylazanediyl)bis(methylene)dicyclohexanone hydrochloride **8** (0.2 g, 0.69 mmol), active methylene ketone **4**{*2*} (0.048 mL, 0.46 mmol) and ammonium acetate (0.2 g, 2.6 mmol) in 3 mL of water was added K-10 (0.44 g) and heated on an oil bath with stirring at 80 ºC for 2 hours (monitored by TLC). The reaction mixture was cooled to room temperature and poured on 20 mL of water. The crude product was extracted with chloroform (2x25 mL) and dried over $MgSO_4$. The solvent was removed under reduced pressure and the residue was purified by flash column chromatography (Silica gel, EtOAc-hexane, 1:6). All compounds were fully characterized by ^{1}H NMR, ^{13}C NMR and HRMS.

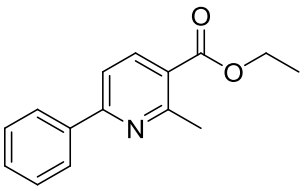
Experimental data for products 6{*1-4, 1-6*} and 9{*1-7*}



1-(2-Methyl-6-phenylpyridin-3-yl)ethanone 6{*1,1*}:
White solid; Yield: 98%, mp: 91-92 ^{o}C (lit[4] 92 ^{o}C); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.03-8.07 (m, 3H, ArH-PyrH), 7.64 (d, *J*= 8.0 Hz, 1H, PyrH), 7.44-7.50 (m, 3H, ArH), 2.83 (s, 3H, CH_3), 2.60 (s, 3H, $COCH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.0, 158.7, 158.6, 138.4, 138.0, 130.7, 129.7, 128.9,

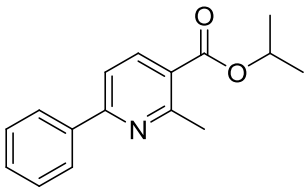
127.3, 117.3, 29.4, 25.4; HRMS (ESI): Calcd for $C_{14}H_{14}NO$ $[M+H]^+$: 212.1075, found: 212.1075. Spectroscopic data are in agreement with literature values.[5]

Ethyl 2-methyl-6-phenylnicotinate 6{*2,1*}:



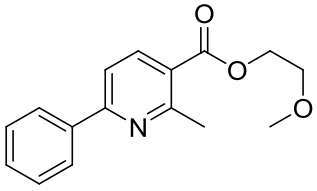
Pale yellow solid; Yield: 89%, mp: 54-56 ^oC; ^1H NMR (400 MHz, $CDCl_3$,) δ 8.26 (d, *J*= 8.2 Hz, 1H, PyrH), 8.06 (d, *J*= 8.0 Hz, 2H, ArH), 7.62 (d, *J*= 8.2 Hz, 1H, PyrH), 7.42-7.51 (m, 3H, ArH), 4.40 (q, *J*=7.1 Hz, 2H, CH_2CH_3), 2.91 (s, 3H, CH_3), 1.42 (t, *J*= 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 160.0, 159.1, 139.3, 138.5, 129.7, 128.8, 127.3, 123.7, 117.4, 61.1, 25.3, 14.3; HRMS (ESI): Calcd for $C_{15}H_{16}NO_2$ $[M+H]^+$: 242.1181, found: 242.1183. Spectroscopic data are in agreement with literature values.[5]

Isopropyl 2-methyl-6-phenylnicotinate 6{*3,1*}:



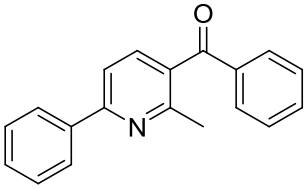
Colorless viscous oil; Yield: 66%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J*= 8.2 Hz, 1H, PyrH), 8.05 (d, *J*= 7.6 Hz, 2H, ArH), 7.61 (d, *J*= 8.2 Hz, 1H, PyrH), 7.41-7.50 (m, 3H, ArH), 5.24-5.30 (m, 1H, CH), 2.91 (s, 3H, CH_3), 1.39 (d, *J* =6.3 Hz, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 159.8, 159.0, 139.3, 138.6, 129.6, 128.8, 127.3, 124.1, 117.4, 68.7, 25.3, 22.0; HRMS (ESI): Calcd for $C_{16}H_{18}NO_2$ $[M+H]^+$: 256.1338, found: 256.1331.

2-Methoxyethyl 2-methyl-6-phenylnicotinate 6{*4,1*}:



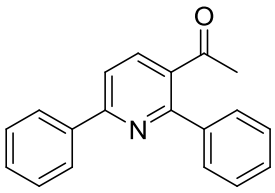
Yellow viscous oil; Yield: 93%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J*= 8.2 Hz, 1H, PyrH), 8.05 (d, *J*= 7.6 Hz, 2H, ArH), 7.61 (d, *J*= 8.2 Hz, 1H, PyrH), 7.41-7.50 (m, 3H, ArH), 4.48 (t, *J*= 4.7 Hz, 2H, CH_2), 3.73 (t, *J*= 4.7 Hz, 2H, CH_2), 3.43 (s, 3H, OCH_3), 2.92 (s, 3H, CH_3); ^{13}C NMR ($CDCl_3$, 100 MHz) δ 165.5, 160.1, 159.2, 139.5, 138.4, 129.7, 128.8, 127.3, 123.3, 117.4, 70.5, 64.1, 59.0, 25.3; HRMS (ESI): Calcd for $C_{16}H_{18}NO_3$ $[M+H]^+$: 272.1287, found: 272.1285.

(2-Methyl-6-phenylpyridin-3-yl)(phenyl)methanone 6a{*5,1*}:



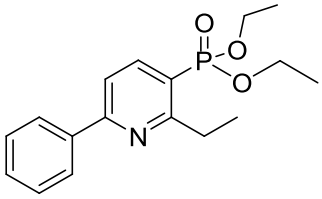
White solid; Yield: 57%, mp: 73-74 ^{o}C ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J*= 8.0 Hz, 2H, PyrH), 7.83(d, *J*= 8.0 Hz, 2H, PyrH), 7.72 (d, *J* =8.0 Hz, 1H, ArH), 7.61-7.65 (m, 2H, ArH), 7.43-7.52 (m, 5H, ArH), 2.63 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$); δ 197.2, 158.2, 157.0, 138.7, 137.4, 137.4, 133.6, 132.0, 130.0, 129.5, 128.9, 128.7, 127.2, 116.9, 23.9; HRMS (ESI): Calcd for $C_{19}H_{16}NO$ $[M+H]^+$: 274.1232, found: 274.1225**.**

1-(2,6-Diphenylpyridin-3-yl)ethanone 6b{*5,1*}:



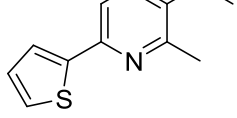
Colorless viscous oil; Yield: 9%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (d, *J*= 7.5 Hz, 2H, ArH), 7.96 (d, *J*= 8.1 Hz, 1H, PyrH), 7.79 (d, *J* =8.1 Hz, 1H, PyrH), 7.67-7.69 (m, 2H, ArH), 7.43-7.52 (m, 6H, ArH), 2.10 (s, 3H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.7, 158.2, 157.2, 140.0, 138.3, 137.5, 134.5, 129.8, 129.5, 129.4, 128.9, 128.7, 127.3, 118.2, 30.4; HRMS (ESI): Calcd for $C_{19}H_{16}NO$ $[M+H]^+$: 274.1232, found: 274.1225.

Diethyl 2-ethyl-6-phenylpyridin-3-ylphosphonate 6{*6,1*}:



Colorless viscous oil; Yield: 22%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.21 (dd, $^{3}J_{P,H}$=14.0 Hz, *J*= 8.1 Hz, 1H, PyrH), 8.07 (d, *J*= 8.0 Hz, 2H, ArH), 7.62 (d, *J*=8.1 Hz, 1H, ArH), 7.39-7.48 (m, 3H, ArH), 4.07-4.24 (m, 4H, $2OCH_2CH_3$), 3.14 (q, *J*= 7.4 Hz, 2H, CH_2CH_3), 1.30-1.42 (m, 9H, CH_2CH_3, $2OCH_2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.7 (d, $^{2}J_{P,C}$= 13.0 Hz), 159.2, 142.7 (d, $^{2}J_{P,C}$=9.6 Hz), 138.4, 129.5, 128.5, 127.1, 120.3 (d, $^{1}J_{P,C}$= 186.8 Hz), 116.3 (d, $^{3}J_{P,C}$= 11.5 Hz), 61.9 (d, $^{2}J_{P,C}$= 5.5 Hz), 30.1, 16.3 (d, $^{3}J_{P,C}$= 6.5 Hz), 13.4; HRMS (ESI): Calcd for $C_{17}H_{23}NO_3P$ $[M+H]^+$: 320.1416, found: 320.1413.

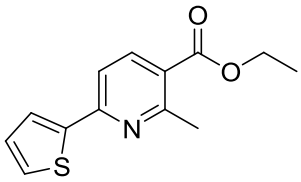
1-(2-Methyl-6-(thiophen-2-yl)pyridin-3-yl)ethanone 6{*1,2*}:



Colorless viscous oil; Yield: 74%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.0 (d, *J*= 8.2 Hz, 1H, PyrH), 7.66-7.68 (m, 1H, ThyH), 7.54 (d, *J*= 8.2 Hz, 1H, PyrH), 7.45-7.47 (m, 1H, ThyH), 7.12-7.15 (m, 1H, ThyH), 2.80 (s, 3H, CH_3), 2.60 (s, 3H, $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4, 159.1,

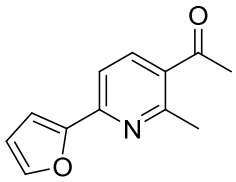
153.7, 144.0, 138.1, 130.2, 129.2, 128.3, 126.1, 115.5, 29.2, 25.3; HRMS (ESI): Calcd for $C_{12}H_{12}NOS$ $[M+H]^+$: 218.0640, found: 218.0632.

Ethyl 2-methyl-6-(thiophen-2-yl)nicotinate 6{*2,2*}:



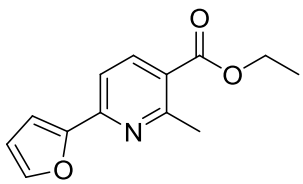
White solid; Yield: 82%, mp:58-59 ^oC (lit[7], 58^oC) ; ^1H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J*= 8.2 Hz, 1H, PyrH), 7.58(d, *J*= 3.7 Hz, 1H, ThyH), 7.44 (d, *J*= 8.2 Hz, 1H, PyrH), 7.37 (d, *J*= 5.0 Hz, 1H, ThyH), 7.05 (dd, *J*= 3.7 Hz, *J*= 5.0 Hz, 1H, ThyH), 4.30 (q, *J*= 7.1 Hz, 2H, CH_2CH_3), 2.78 (s, 3H, CH_3), 1.33 (t, *J*= 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 160.3, 154.1, 144.1, 139.3, 129.0, 128.2, 126.0, 123.2, 115.6, 61.1, 25.2, 14.3; HRMS (ESI): Calcd for $C_{13}H_{14}NO_2S$ $[M+H]^+$: 248.0745, found: 248.0739. Spectroscopic data are in agreement with literature values .[6]

1-(6-(Furan-2-yl)-2-methylpyridin-3-yl)ethanone 6{*1,3*}:



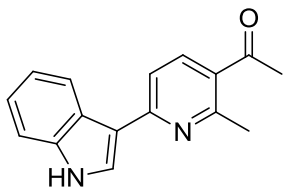
Colorless viscous oil; Yield: 80%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, *J*= 8.2 Hz, 1H, PyrH), 7.56-7.58 (m, 2H, FurH-PyrH), 7.17 (bs, 1H, FurH), 6.55 (bs, 1H, FurH), 2.80 (s, 3H, CH_3), 2.59 (s, 3H, $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.5, 159.0, 153.0, 150.3, 144.3, 138.1, 130.2, 115.3, 112.4, 110.8, 29.2, 25.3; HRMS (ESI): Calcd for $C_{12}H_{12}NO_2$ $[M+H]^+$: 202.0868, found: 202.0861.

Ethyl 6-(furan-2-yl)-2-methylnicotinate 6{*2,3*}:



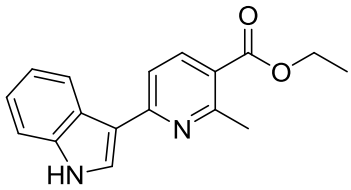
Colorless viscous oil; Yield: 60%; ^1H NMR (400 MHz, $CDCl_3$) δ 8.24 (d, *J*= 8.2 Hz, 1H, PyrH), 7.55-7.57 (m, 2H, FurH-PyH), 7.17 (d, *J*= 3.4 Hz, 1H, FurH), 6.54-6.56 (m, 1H, FurH), 4.38 (q, *J*= 7.1 Hz, 2H, CH_2CH_3), 2.87 (s, 3H, CH_3), 1.41 (t, *J*= 7.1 Hz, 3H, OCH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 160.3, 153.1, 150.7, 144.3, 139.3, 123.3, 115.5, 112.3, 110.7, 61.1, 25.2, 14.3; HRMS (ESI): Calcd for $C_{13}H_{14}NO_3$ $[M+H]^+$: 232.0974, found: 232.0966.

1-(6-(1*H*-indol-3-yl)-2-methylpyridin-3-yl)ethanone 6{*1,4*}:



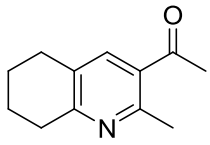
White solid; Yield: 77%, mp > 210 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.51 (bs, 1H, NH), 8.45-8.47 (m, 1H, IndolH), 8.04 (d, *J*= 8.2 Hz, 1H, PyrH), 7.91 (d, *J*= 2.8 Hz, 1H, NHCH), 7.61 (d, *J*= 8.2 Hz, 1H, PyrH), 7.42-7.46 (m, 1H, IndolH), 7.28- 7.31 (m, 3H, IndolH), 2.88 (s, 3H, CH_3), 2.62 (s, 3H, $COCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.6, 159.0, 156.8, 137.9, 136.9, 128.4, 125.8, 125.4, 122.9, 121.5, 121.4, 116.6, 111.5, 29.1, 25.7; HRMS (ESI): Calcd for $C_{16}H_{15}N_2O$ $[M+H]^+$: 251.1184, found: 251.1241.

Ethyl 6-(1*H*-indol-3-yl)-2-methylnicotinate 6{*2,4*}:



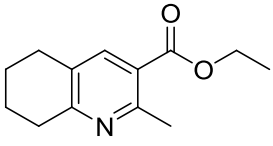
White solid; Yield: 54%, mp: 204-206 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.45-8.48 (m, 2H, IndolNH-ArH), 8.24 (d, *J*= 8.2 Hz, 1H, PyrH), 7.91 (d, *J*= 2.7 Hz, 1H, NHCH), 7.59 (d, *J*= 8.2 Hz, 1H, PyrH), 7.43-7.46 (m,1H, IndolH), 7.27-7.30 (m, 2H, IndolH), 4.39 (q, *J*= 7.1 Hz, 2H, CH_2CH_3), 2.94 (s, 3H, CH_3), 1.42 (t, *J*= 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.8, 160.1, 156.8, 139.0, 136.9, 125.9, 125.4, 122.9, 121.5, 121.4, 121.3, 116.9, 116.7, 111.5, 60.9, 25.3, 14.4; HRMS (ESI): Calcd for $C_{17}H_{17}N_2O_2$ $[M+H]^+$: 281.1290, found: 281.1343.

1-(2-Methyl-5,6,7,8-tetrahydroquinolin-3-yl)ethanone 9{*1*}:



White solid; Yield: 96%, mp: 52-53 ^{o}C, ; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (s, 1H, PyrH), 2.91 (t, *J*= 6.3 Hz, 2H, CH_2CH_2), 2.78 (t, *J*= 6.4 Hz, 2H, CH_2CH_2), 2.69 (s, 3H, CH_3), 2.56 (s, 3H, $COCH_3$) 1.88-1.95 (m, 2H, CH_2), 1.80-1.86 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1, 159.8, 155.0, 137.9, 130.0, 129.2, 32.6, 29.2, 28.2, 24.4, 22.8, 22.5. HRMS (ESI): Calcd for $C_{12}H_{16}NO$ $[M+H]^+$: 190.1232, found: 190.1234.

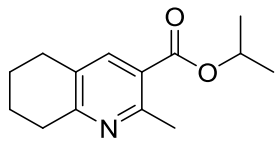
Ethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 9{*2*}:



Yellow viscous oil; Yield: 70%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 (s, 1H, PyrH), 4.35 (q, *J*= 7.1 Hz, 2H, CH_2CH_3), 2.91 (t, *J*= 6.3, 2H, CH_2CH_2), 2.81-2.75 (m, 5H, CH_2CH_2, CH_3), 1.87-1.90 (m, 2H, CH_2),

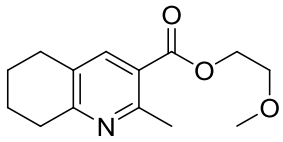
1.79-1.84 (m, 2H, CH_2), 1.40 (t, *J*= 7.1 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.6, 160.1, 156.5, 139.0, 129.2, 122.7, 60.8, 32.6, 28.1, 24.4, 22.7, 22.6, 14.3; HRMS (ESI): Calcd for $C_{13}H_{18}NO_2$ $[M+H]^+$: 220.1338, found: 220.1334.

Isopropyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 9{*3*}:



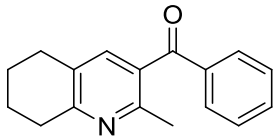
Colorless viscous oil; Yield: 44%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (s, 1H, PyrH), 5.21-5.27 (m, 1H, CH), 2.90 (t, *J*= 6.4 Hz, 2H, CH_2CH_2), 2.76-2.78 (m, 5H, CH_2CH_2, CH_3), 1.87-1.93 (m, 2H, CH_2), 1.78-1.84 (m, 2H, CH_2), 1.37 (d, *J*= 6.2 Hz, 6H, $2CH_3$); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 160.0, 156.3, 139.0, 129.4, 123.3, 68.5, 32.6, 28.1, 24.4, 22.9, 22.6, 22.0; HRMS (ESI) Calcd for: $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1494, found: 234.1508.

2-Methoxyethyl 2-methyl-5,6,7,8-tetrahydroquinoline-3-carboxylate 9{*4*}:



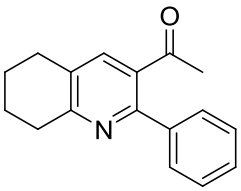
Yellow viscous oil; Yield: 65%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83 (s, 1H, PyrH), 4.37 (t, *J*= 4.7 Hz, 2H, OCH_2), 3.65 (t, *J*= 4.7 Hz, 2H, OCH_2), 3.35 (s, 3H, OCH_3), 2.83 (t, *J*= 6.3 Hz, 2H, CH_2CH_2), 2.67-2.69 (m, 5H, CH_2CH_2, CH_3), 1.79-1.86 (m, 2H, CH_2), 1.70-1.76 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 160.4, 156.6, 139.2, 129.4, 122.3, 70.4, 63.9, 59.0, 32.6, 28.1, 24.4, 22.8, 22.5; HRMS (ESI): Calcd for $C_{14}H_{20}NO_3$ $[M+H]^+$: 250.1443, found: 250.1457.

(2-Methyl-5,6,7,8-tetrahydroquinolin-3-yl)(phenyl)methanone 9a{*5*}:



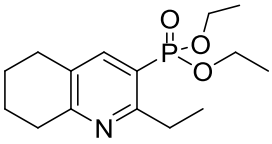
Yellow viscous oil; Yield: 51%, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79 (d, *J*= 7.2, Hz, 2H, ArH), 7.58-7.61 (m, 1H, ArH), 7.45-7.49 (m, 2H, ArH), 7.33 (s, 1H, PyrH), 2.96 (t, *J*= 6.2 Hz, 2H, CH_2 CH_2), 2.74 (t, *J*= 6.2 Hz, 2H, CH_2CH_2), 2.48 (s, 3H, CH_3), 1.90-1.95 (m, 2H, CH_2), 1.83-1.89 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 197.3, 158.8, 153.4, 137.4, 137.2, 133.4, 131.3, 129.9, 128.9, 128.6, 32.5, 28.2, 22.9, 22.9, 22.6; HRMS (ESI): Calcd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1388, found: 252.1395.

1-(2-Phenyl-5,6,7,8-tetrahydroquinolin-3-yl)ethanone 9b{*5*}:



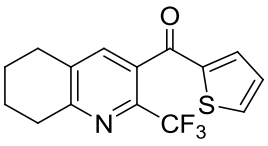
White solid; Yield: 8%; mp: 97-99 ^{o}C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (s, 1H, PyrH), 7.50-7.53 (m, 2H, ArH), 7.43-7.47 (m, 3H, ArH), 3.01 (t, *J*= 6.3 Hz, 2H, CH_2CH_2), 2.84 (t, *J*= 6.4 Hz, 2H, CH_2CH_2), 2.01 (s, 3H, CH_3), 1.91-1.98 (m, 2H, CH_2), 1.84-1.89 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.8, 159.6, 154.6, 140.1, 136.9, 133.8, 130.9, 129.1, 129.0, 128.7, 32.8, 30.3, 28.3, 22.9, 22.6; HRMS (ESI): Calcd for $C_{17}H_{18}NO$ $[M+H]^+$: 252.1388, found: 252.1395.

Diethyl 2-ethyl-5,6,7,8-tetrahydroquinolin-3-ylphosphonate 9{*6*}:



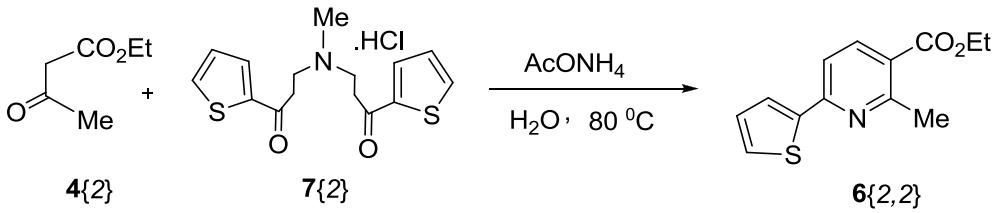
Colorless viscous oil; Yield: 15%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.33 (bs, 1H, PyrH), 4.12-4.20 (m, 2H, OCH_2CH_3), 4.04-4.11 (m, 2H, OCH_2CH_3), 3.20 (q, *J*= 7.4 Hz, 2H, CH_2CH_3), 3.14 (bs, 2H, CH_2), 2.76 (bs, 2H, CH_2), 1.77-1.79 (m, 4H, $2CH_2$), 1.34 (t, *J*= 7.1 Hz, 6H, $2OCH_2CH_3$), 1.29 (t, *J*= 7.4 Hz, 3H, CH_2CH_3); ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.0 (d, $^{2}J_{P,C}$= 15.0 Hz), 152.6, 152.0 (d, $^{2}J_{P,C}$= 11.2 Hz), 130.4 (d, $^{3}J_{P,C}$= 11.4 Hz), 120.5 (d, $^{1}J_{P,C}$= 179.7 Hz), 61.7 (d, $^{2}J_{P,C}$= 5.7 Hz), 31.1, 28.8 (d, $^{3}J_{P,C}$= 2.9 Hz), 27.0, 22.6, 21.7, 16.3 (d, $^{3}J_{P,C}$= 6.5 Hz), 15.1; Calcd for $C_{15}H_{25}NO_3P$ $[M+H]^+$: 298.1572, found: 298.1593.

Thiophen-2-yl(2-(trifluoromethyl)-5,6,7,8-tetrahydroquinolin-3-yl)methanone 9{*7*}:



Colorless viscous oil; Yield: 40%; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 (d, *J*= 4.9 Hz, 1H, ThyH), 7.49 (s, 1H, PyrH), 7.32 (d, *J*= 3.8 Hz, 1H, ThyH), 7.11 (m, 1H, ThyH), 3.04 (t, *J*= 6.1 Hz, 2H, CH_2CH_2), 2.87 (t, *J*= 6.3 Hz, 2H, CH_2CH_2), 1.95-2.01 (m, 2H, CH_2), 1.86-1.92 (m, 2H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.6, 159.4, 143.8, 141.6 (d, $^{2}J_{F,C}$= 34.3 Hz), 136.6, 135.8, 135.6, 135.2, 131.2, 128.2, 121.3 (d, $^{1}J_{F,C}$= 273.5 Hz), 32.3, 28.6, 22.6, 22.2; HRMS (ESI): Calcd for $C_{15}H_{13}F_3NOS$ $[M+H]^+$: 312.0670, found: 312.0676.

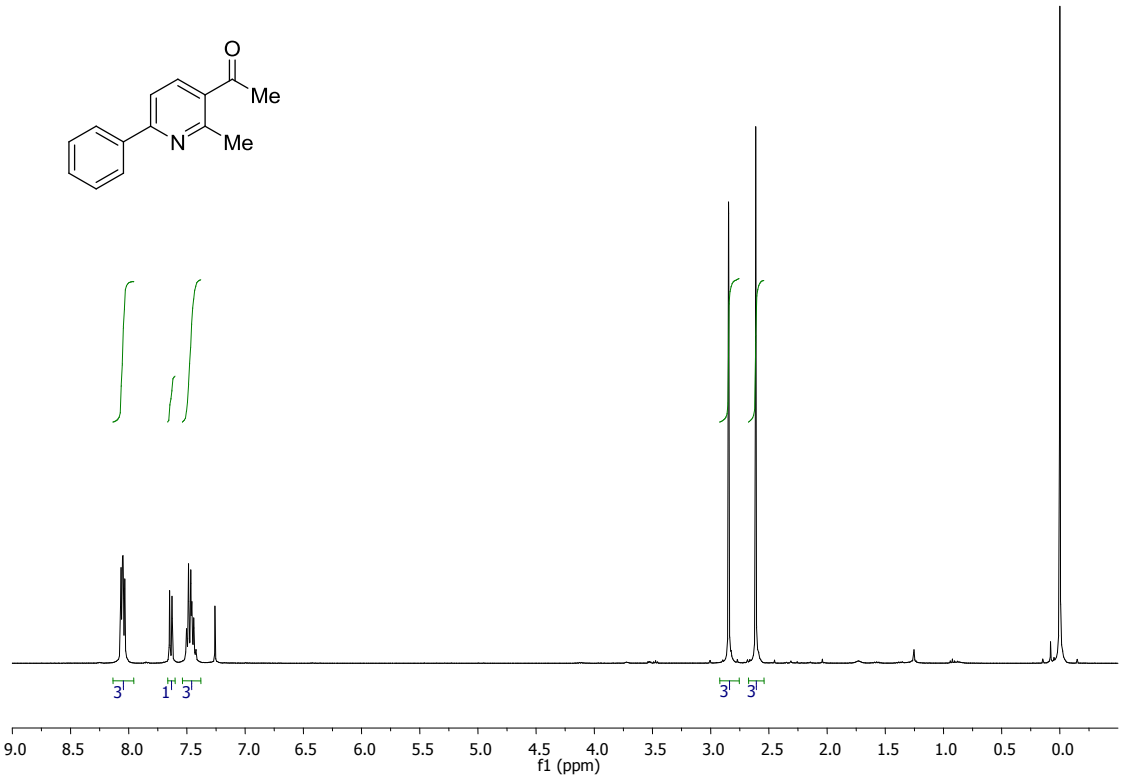
Table 1. Evaluation of Potential Catalysts[a]



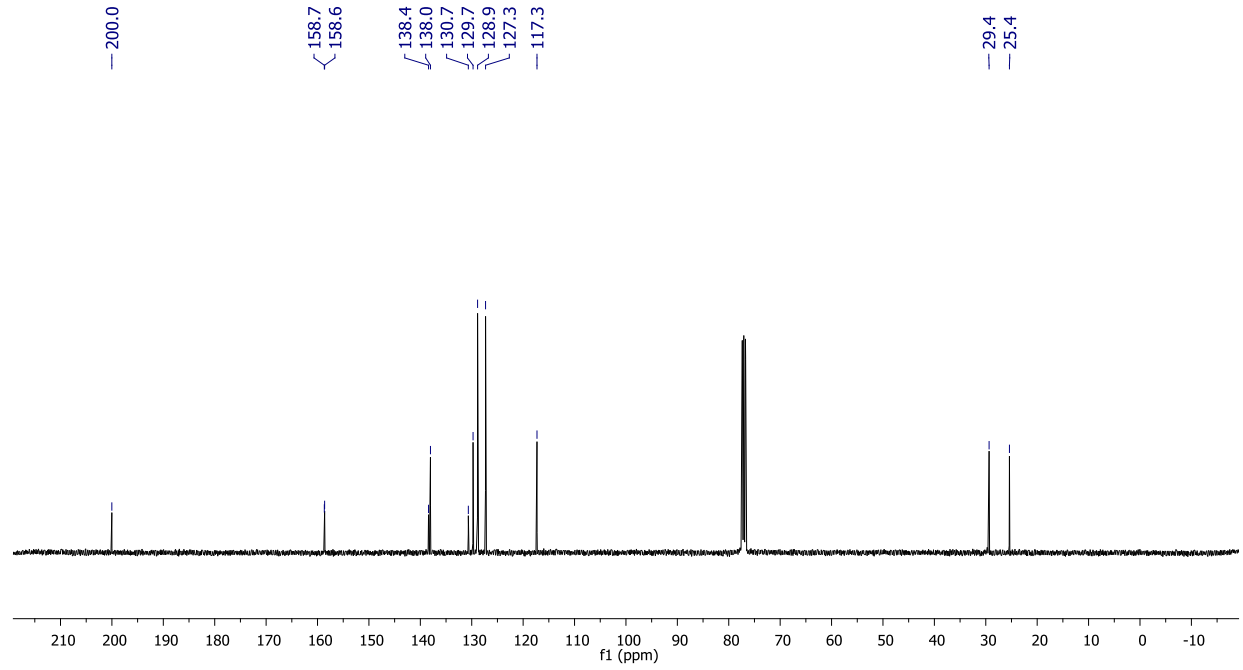
4{*2*} **7**{*2*} **6**{*2,2*}

Entry	Catalyst	Time(h)	Yield(%)[b]
1	CAN	2.0	26
2	$Cu(OTf)_2$	2.0	41
3	KSF	2.0	74
4	K-10	2.0	82
5	$Ce(OTf)_3$	2.0	46
6	AcOH	2.0	81[c]
7	without catalyst	2.0	42

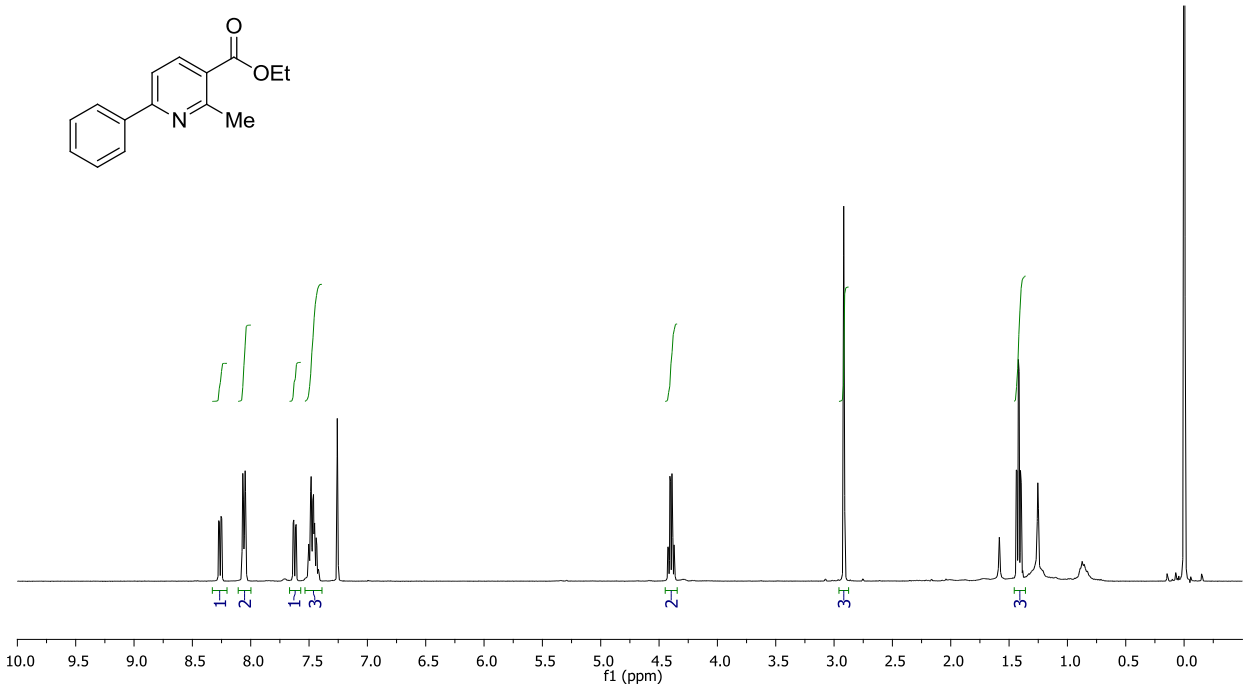
[a] All the reactions were performed with **4**{2} (1.0 mmol), **7**{*2*} (1.5 mmol), and NH_4OAc (4.4 mmol) in the presence of catalyst. [b] Isolated yield.[c] In AcOH.



^{1}H NMR spectrum of **6**{*1,1*}

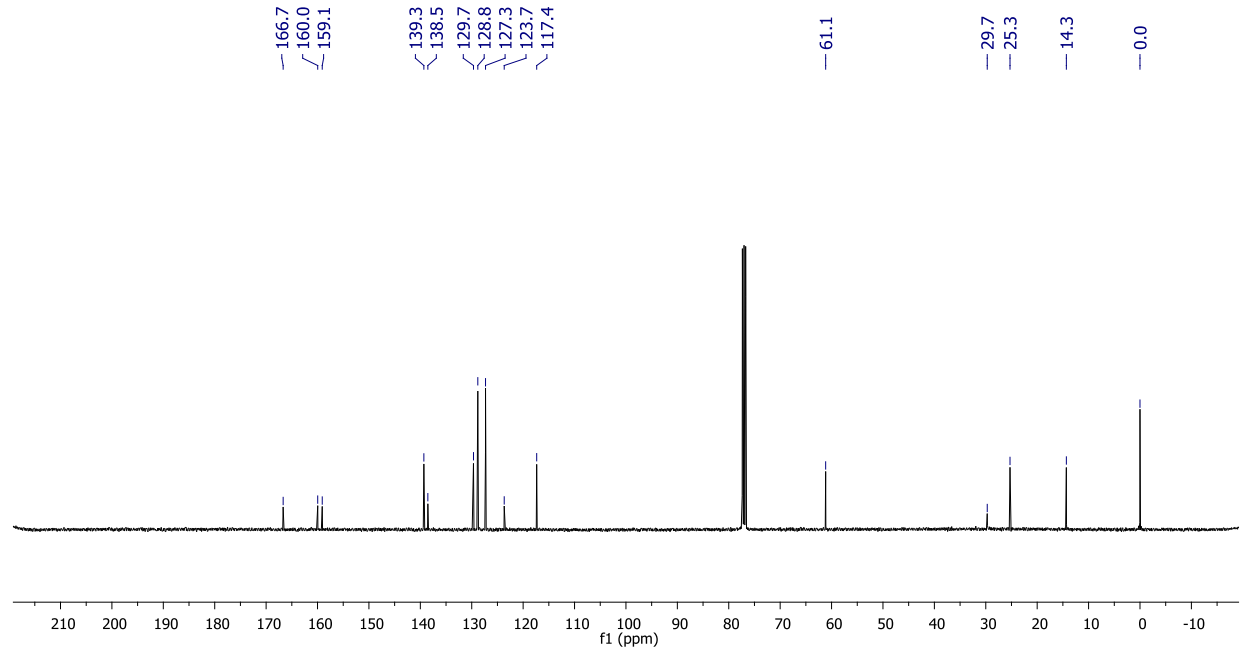


^{13}C NMR spectrum of **6**{*1,1*}



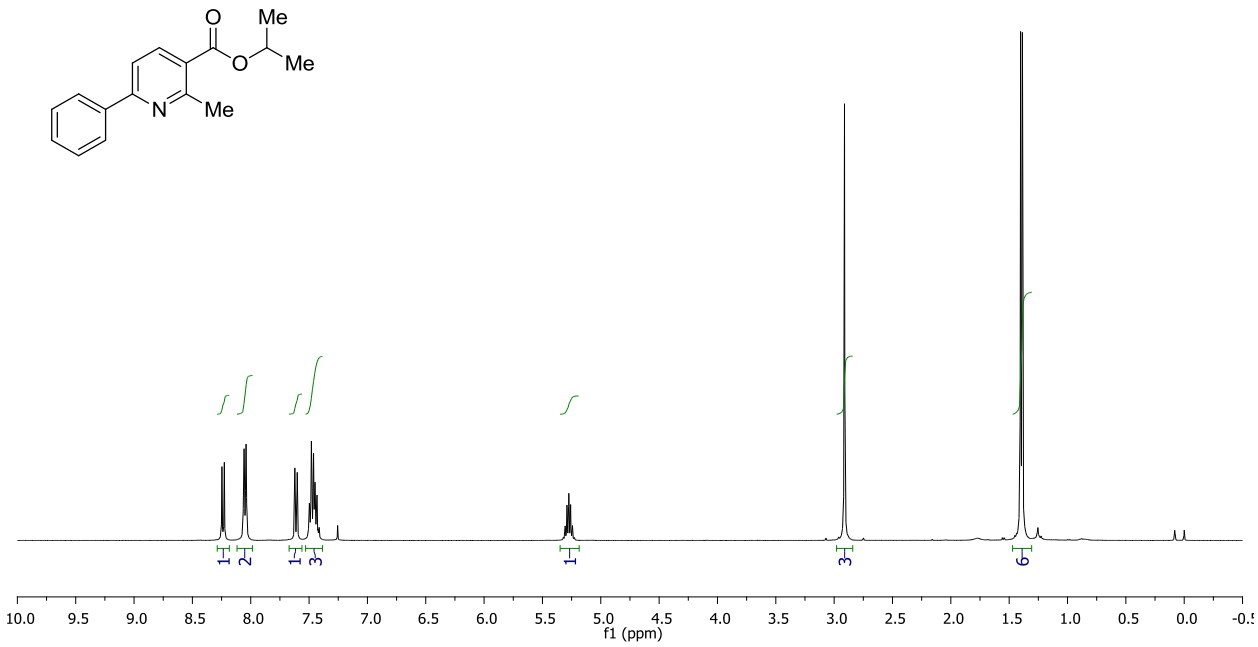
The peaks at 1.25 and 1.58 ppm due to residual solvent.

^{1}H NMR spectrum of **6**{*2,1*}

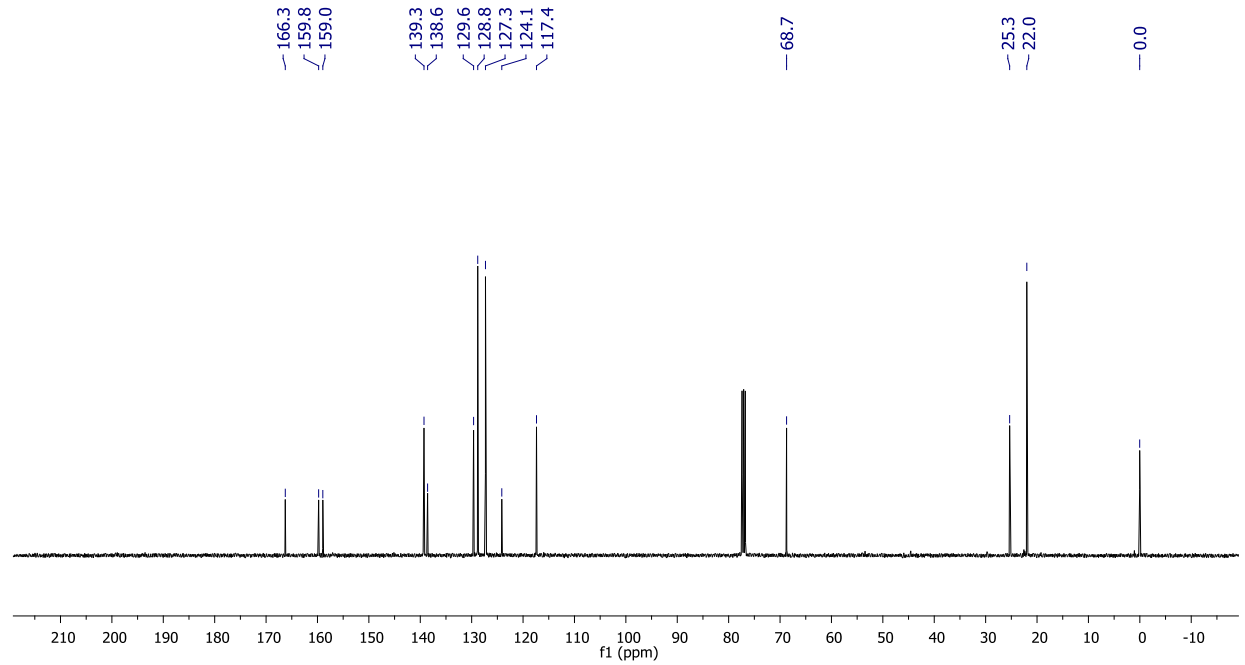


The peak at 29.7 ppm due to residual solvent.

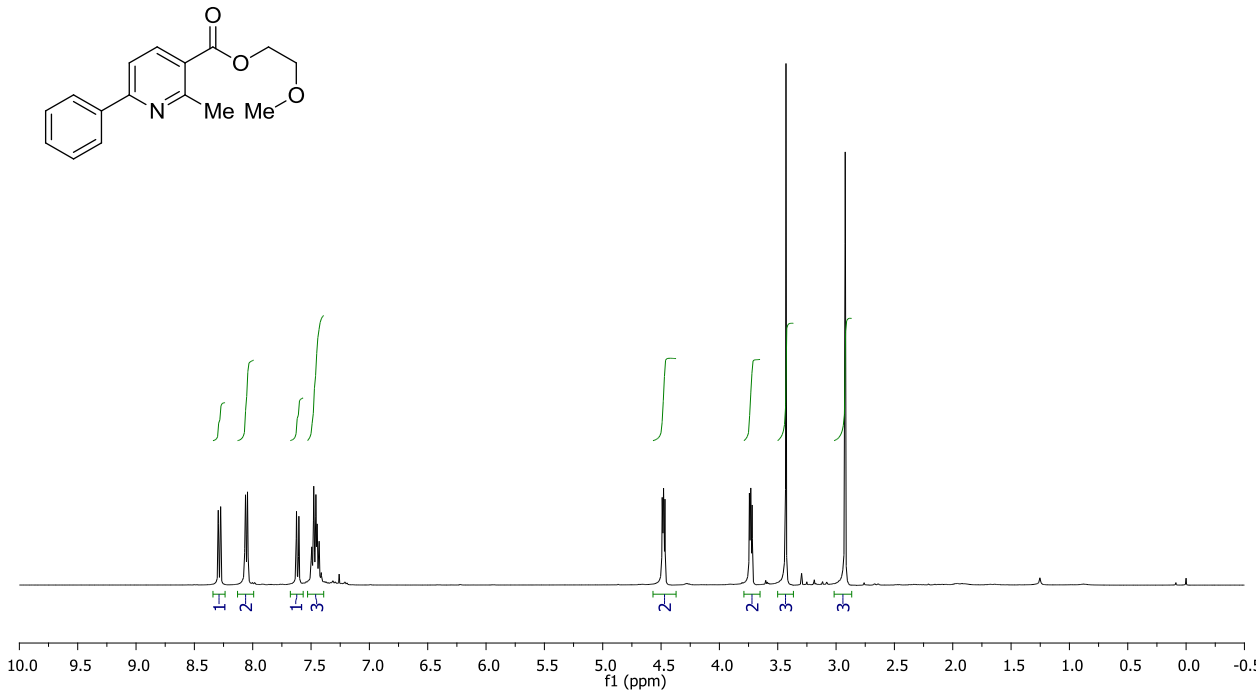
^{13}C NMR spectrum of **6**{*2,1*}



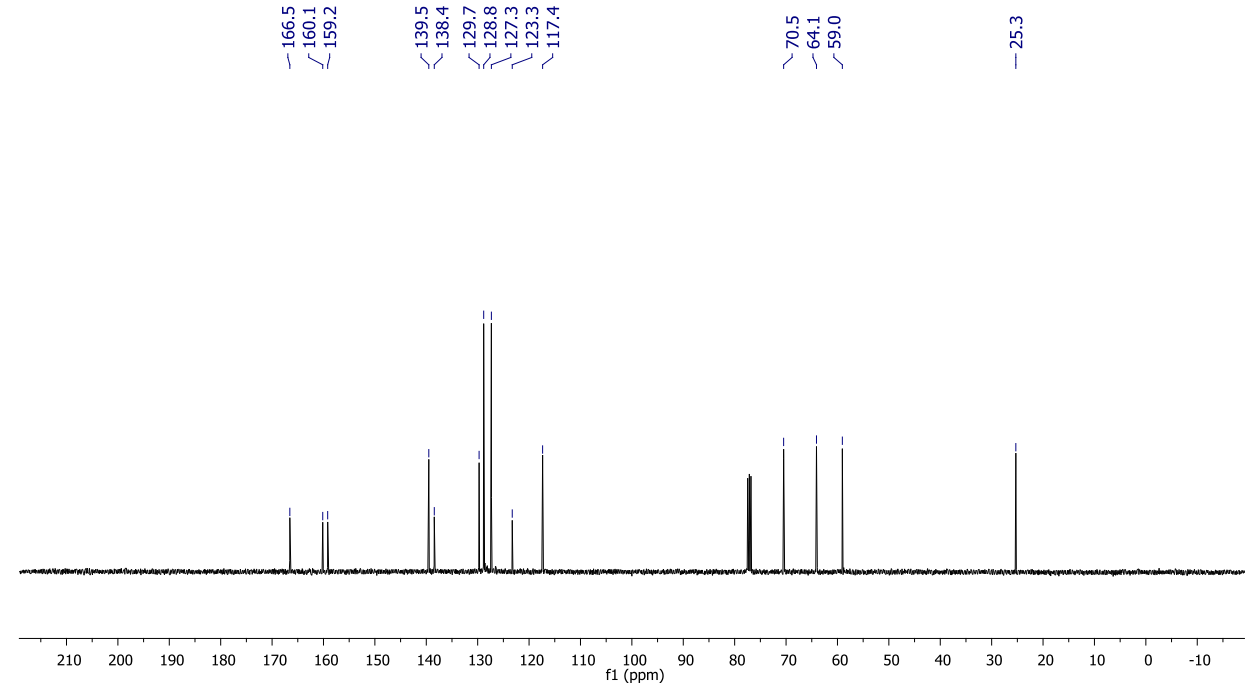
^{1}H NMR spectrum of **6**{*3,1*}



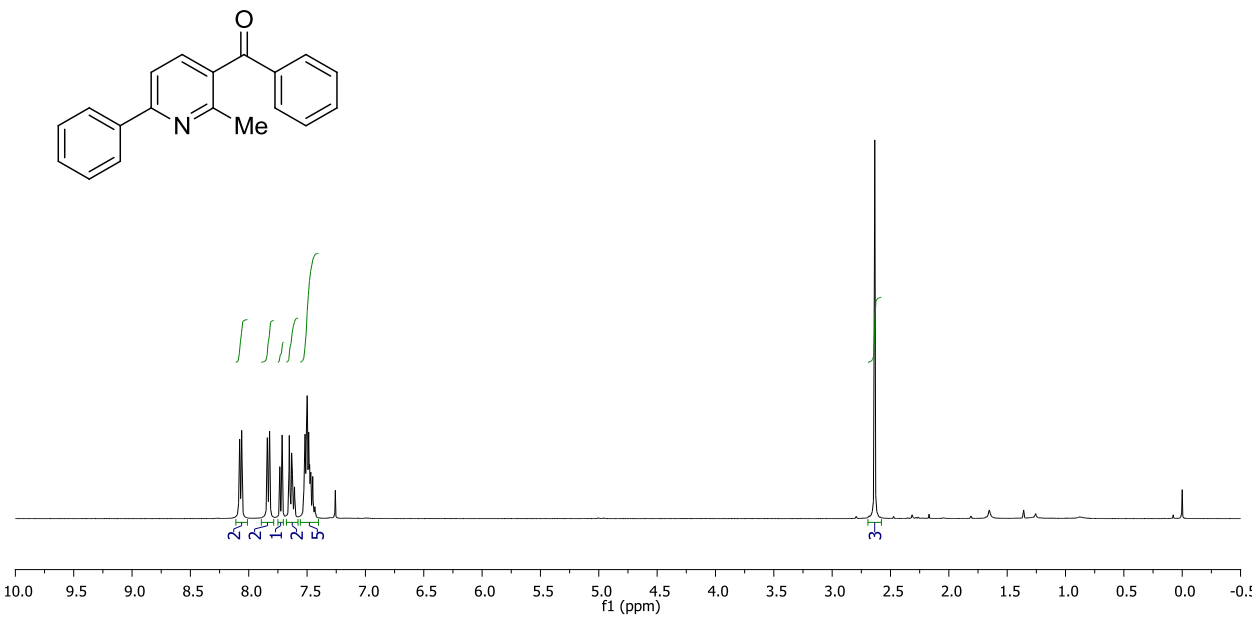
^{13}C NMR spectrum of **6**{*3,1*}



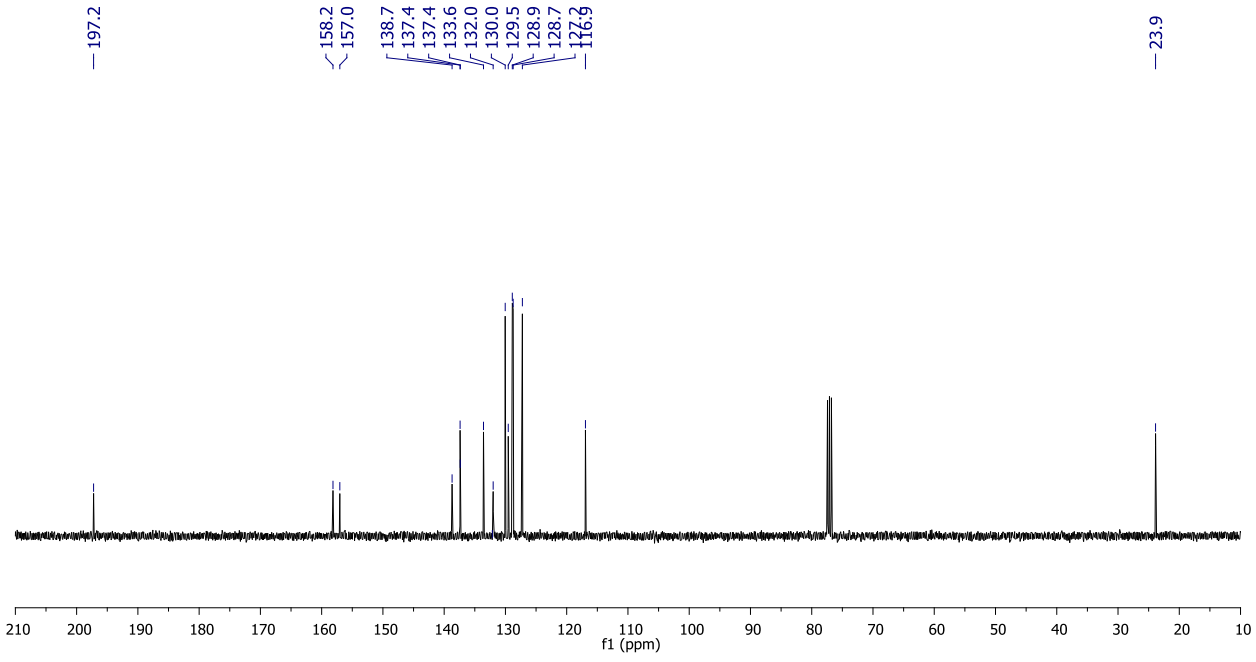
^{1}H NMR spectrum of **6**{*4,1*}



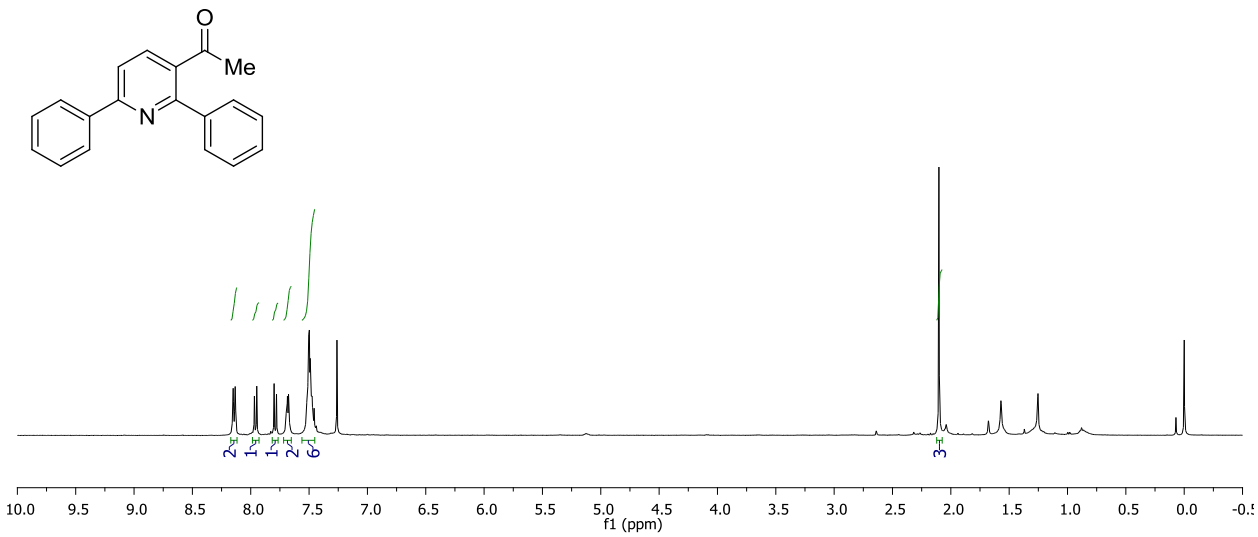
^{13}C NMR spectrum of **6**{*4,1*}



^{1}H NMR spectrum of **6a**{*5,1*}

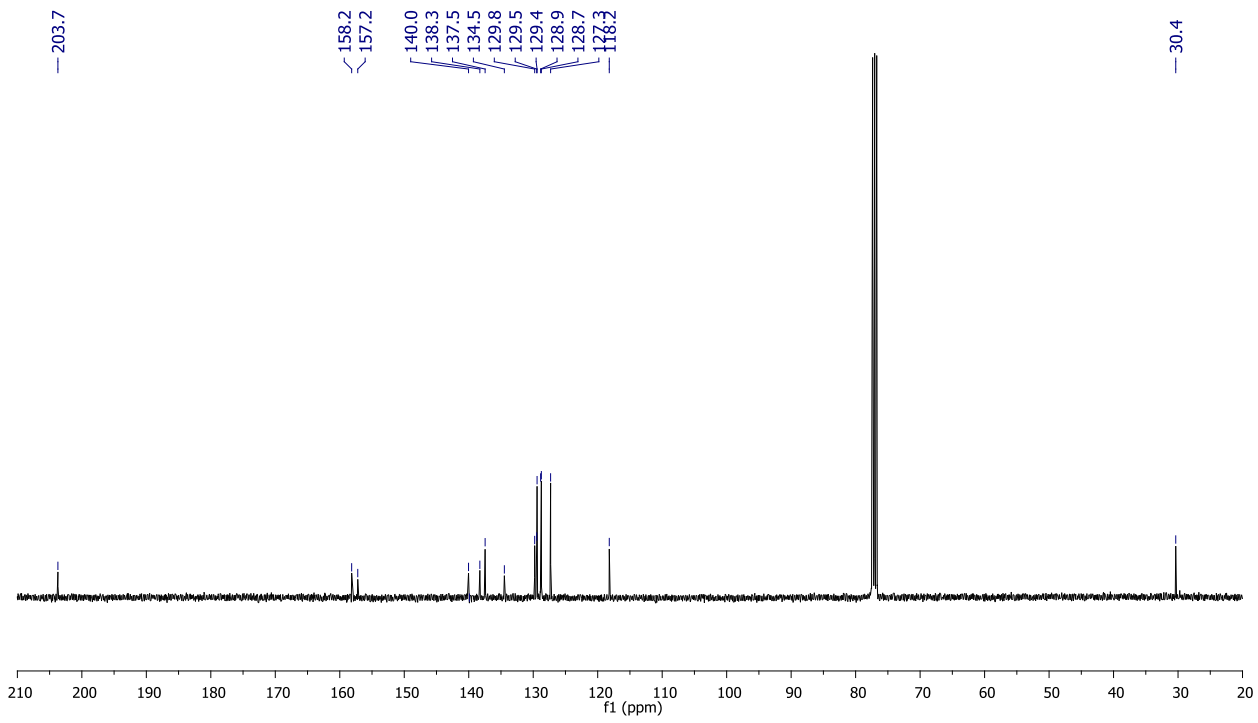


^{13}C NMR spectrum of **6a**{*5,1*}

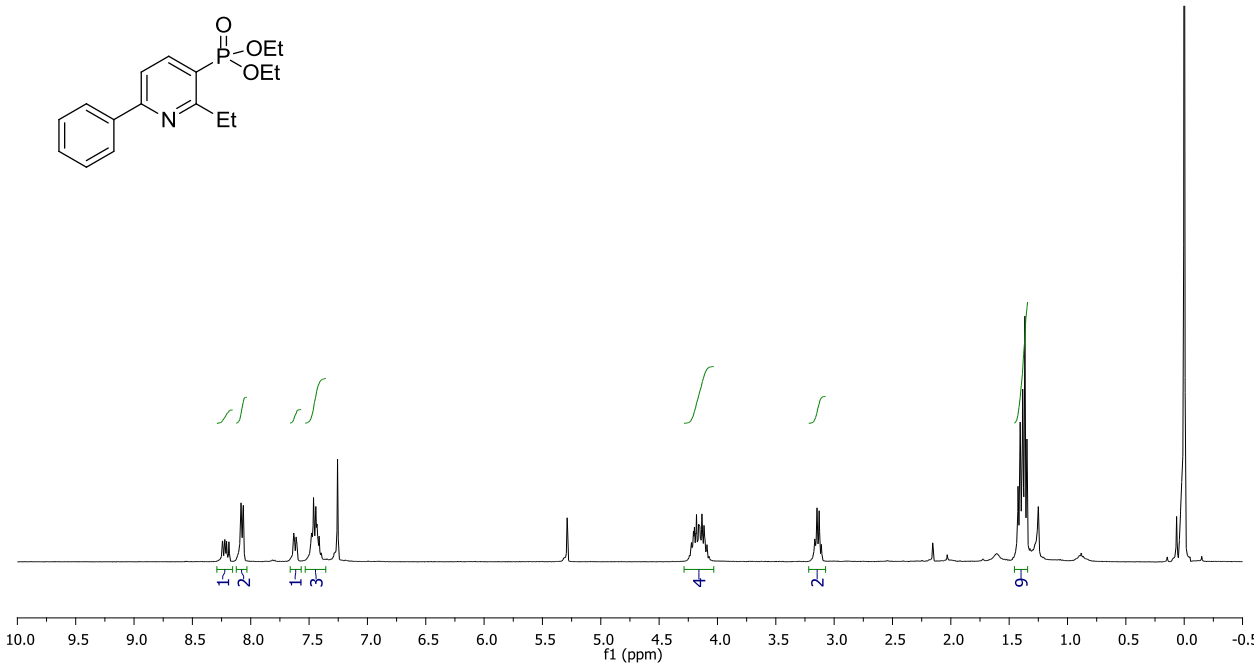


The peaks between 0.8-1.5 ppm due to residual solvent.

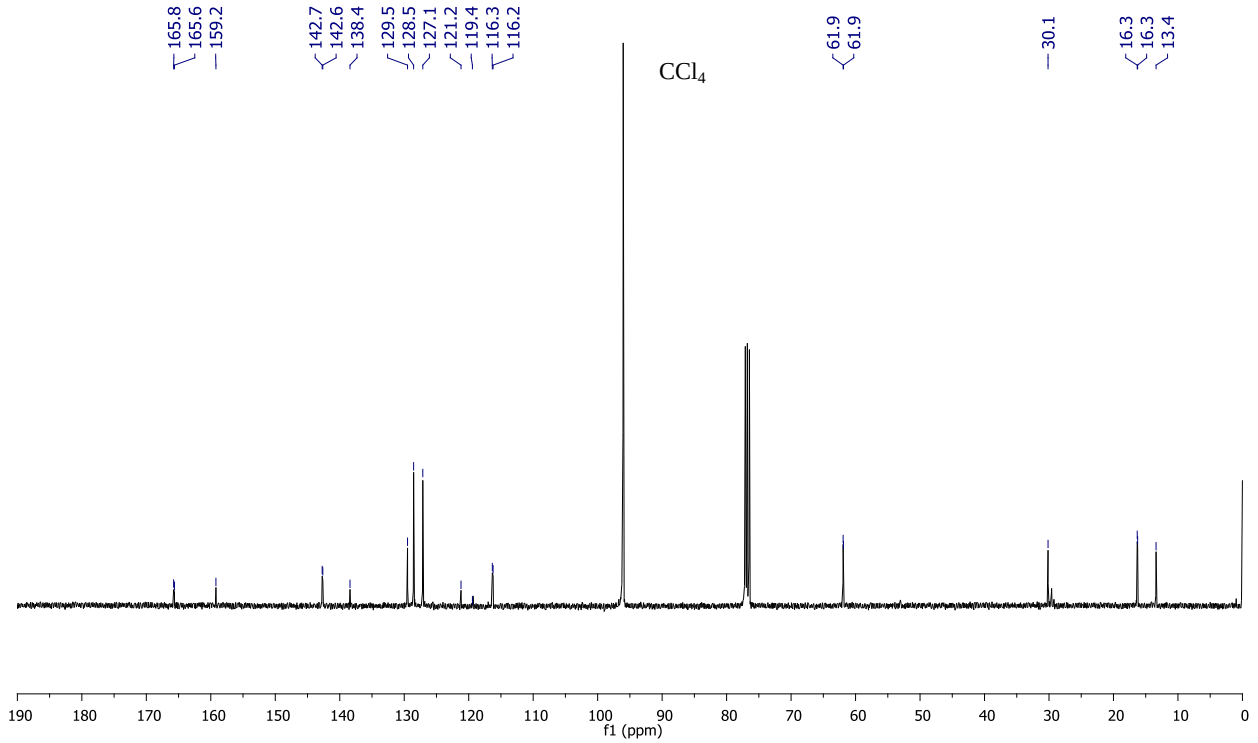
^{1}H NMR spectrum of **6b**{*5,1*}



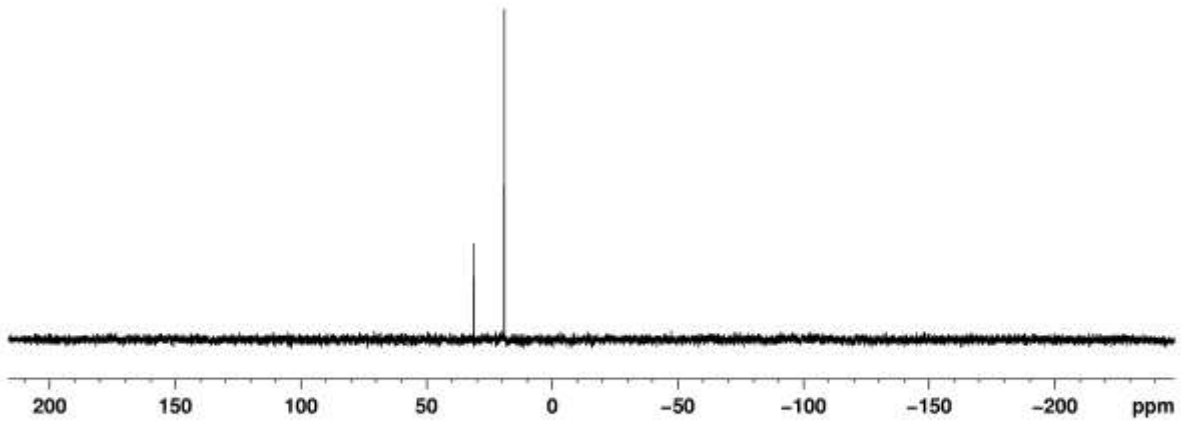
^{13}C NMR spectrum of **6b**{*5,1*}



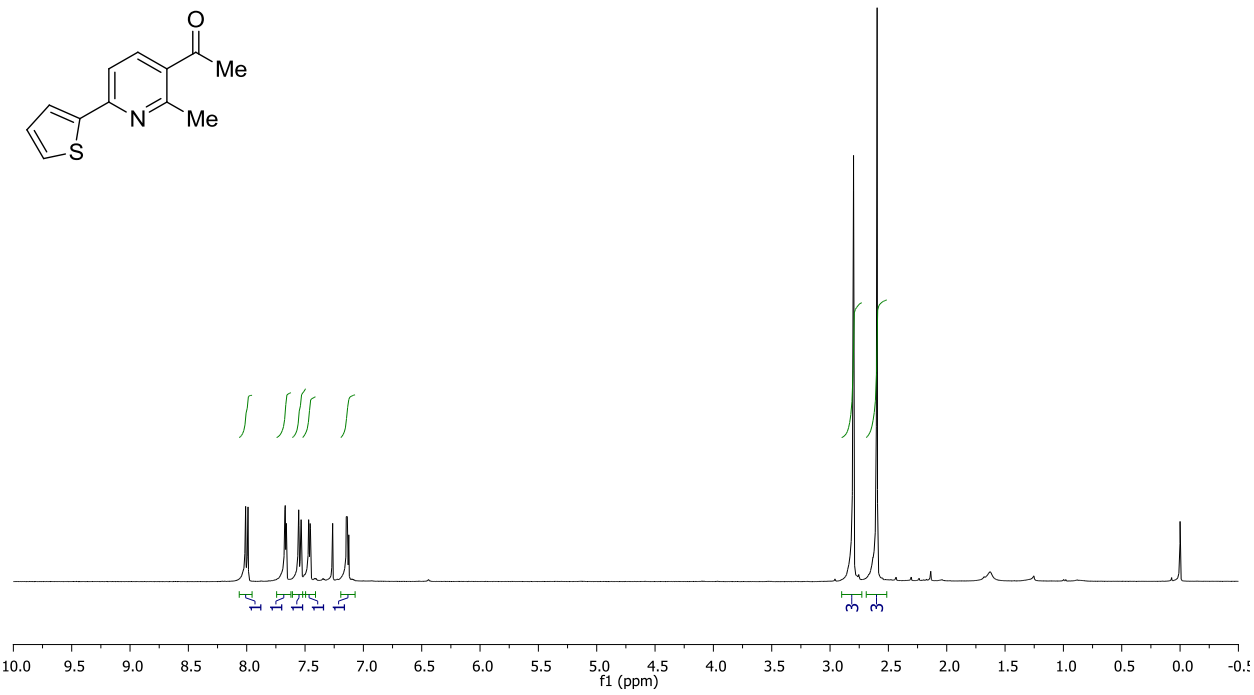
^{1}H NMR spectrum of **6**{*6,1*}



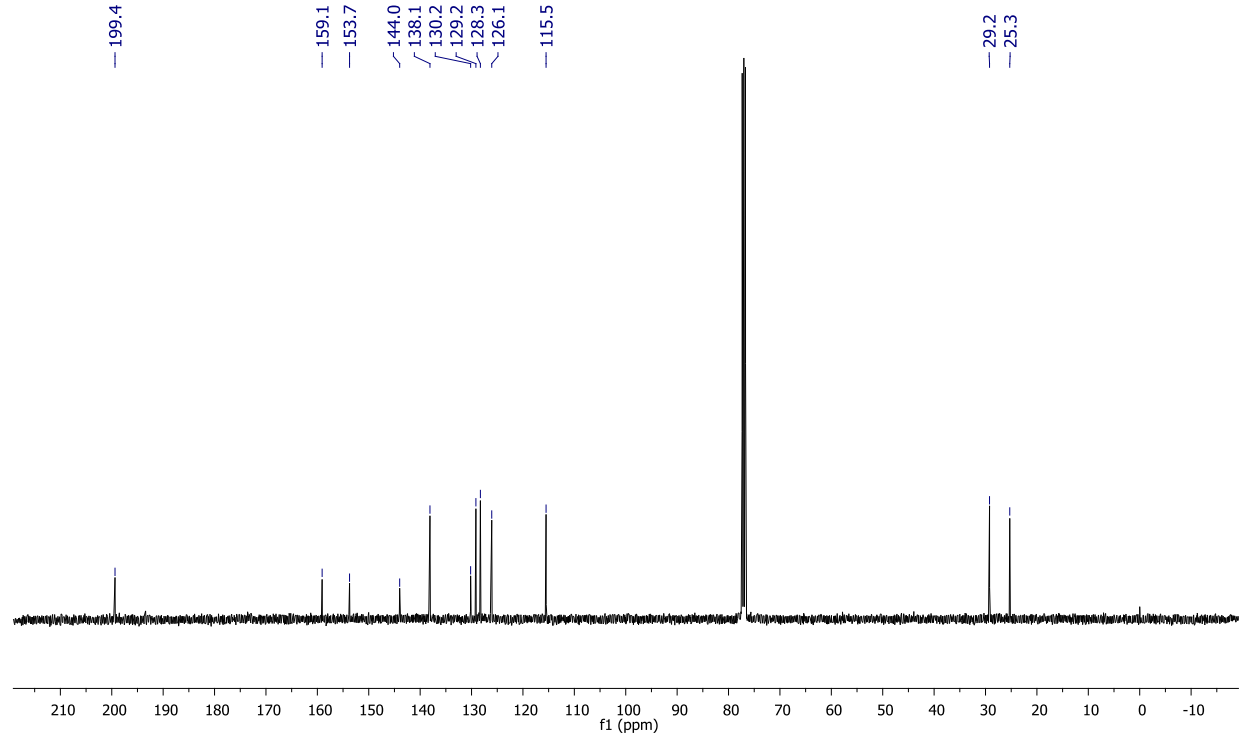
^{13}C NMR spectrum of **6**{*6,1*}



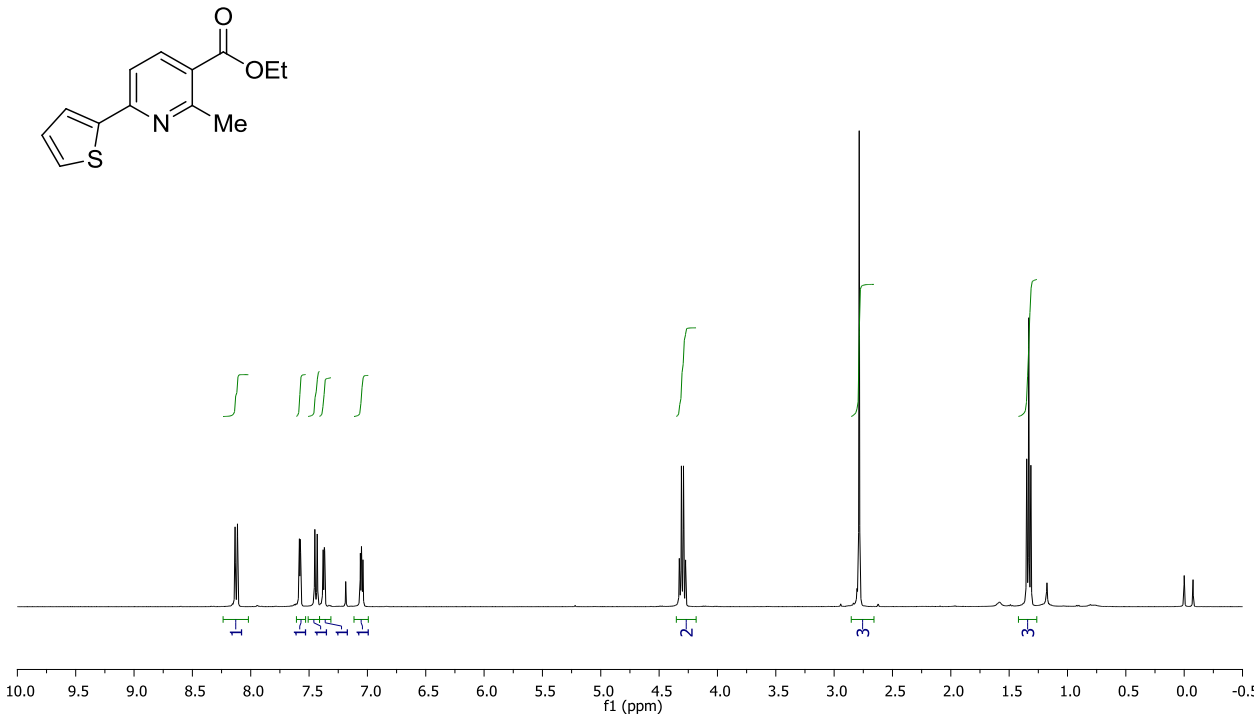
^{31}P NMR spectrum of **6**{*6,1*}



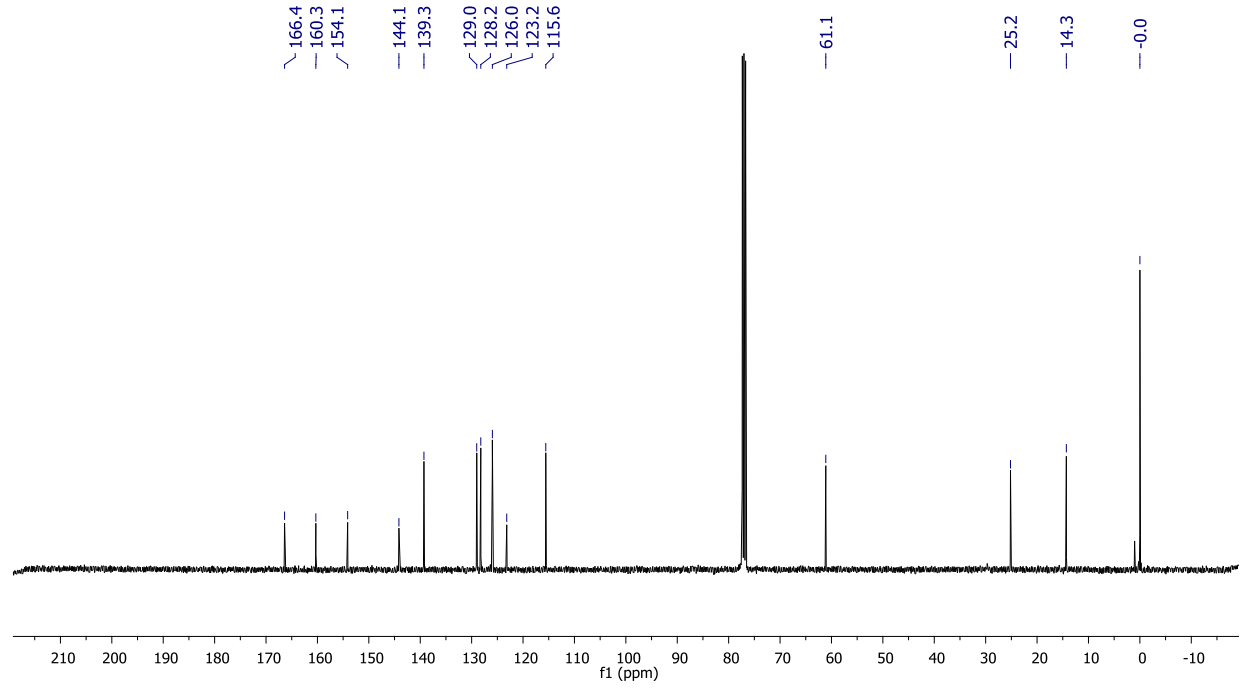
^{1}H NMR spectrum of **6**{*1,2*}



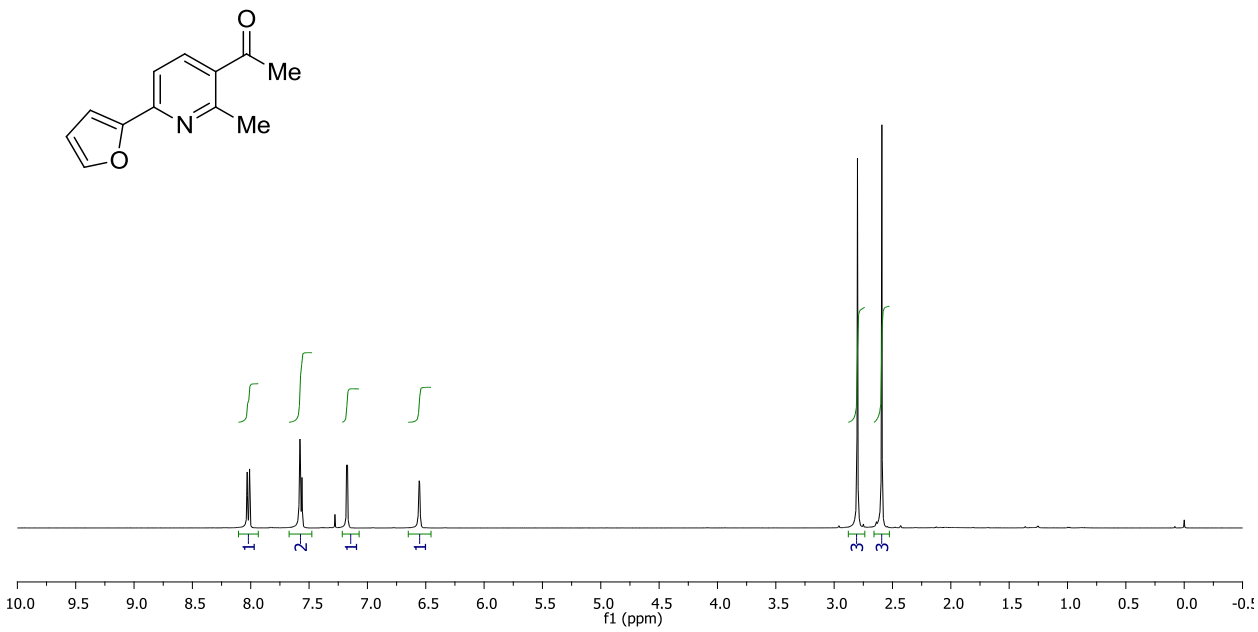
^{13}C NMR spectrum of **6**{*1,2*}



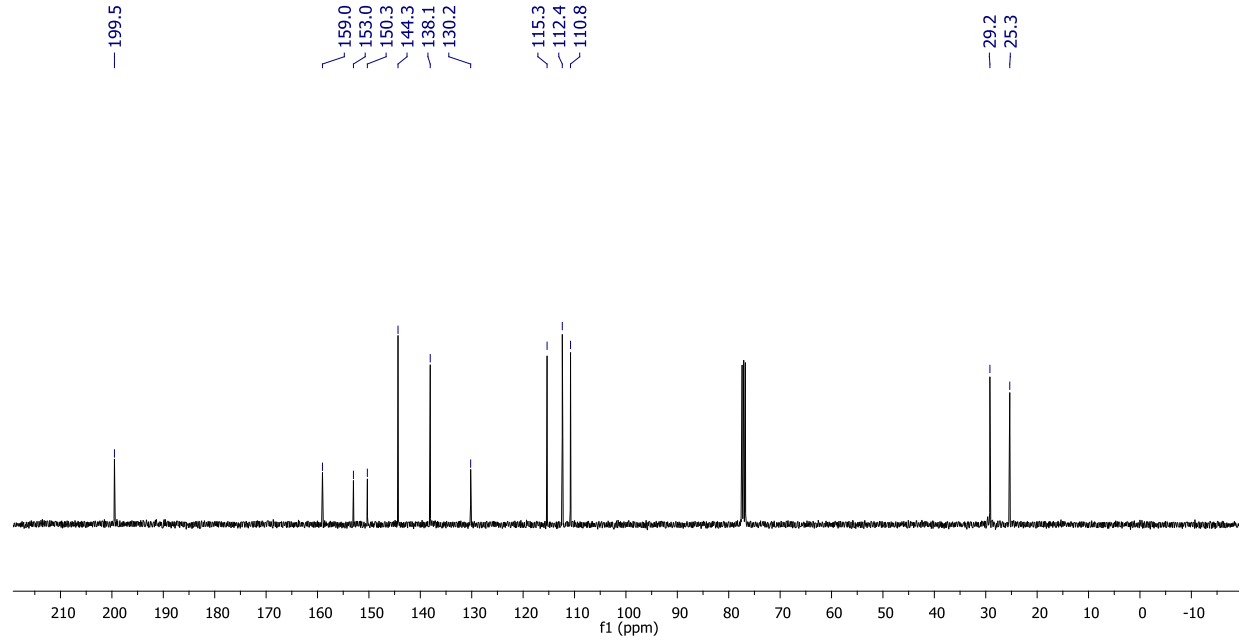
^{1}H NMR spectrum of **6**{*2,2*}



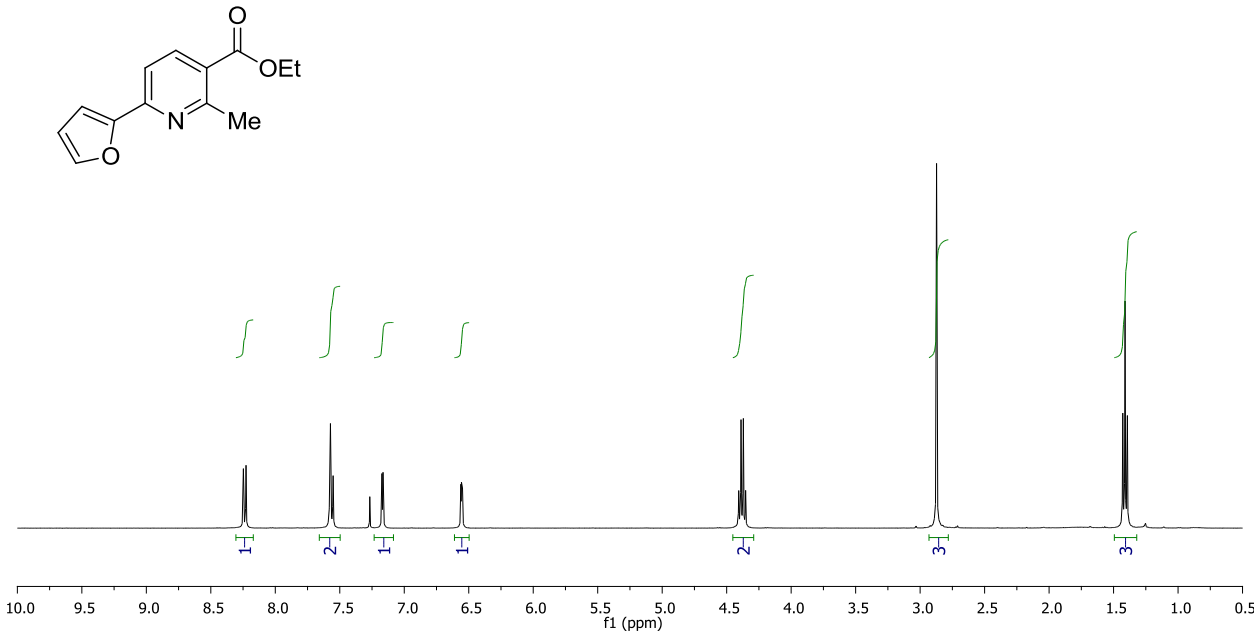
^{13}C NMR spectrum of **6**{*2,2*}



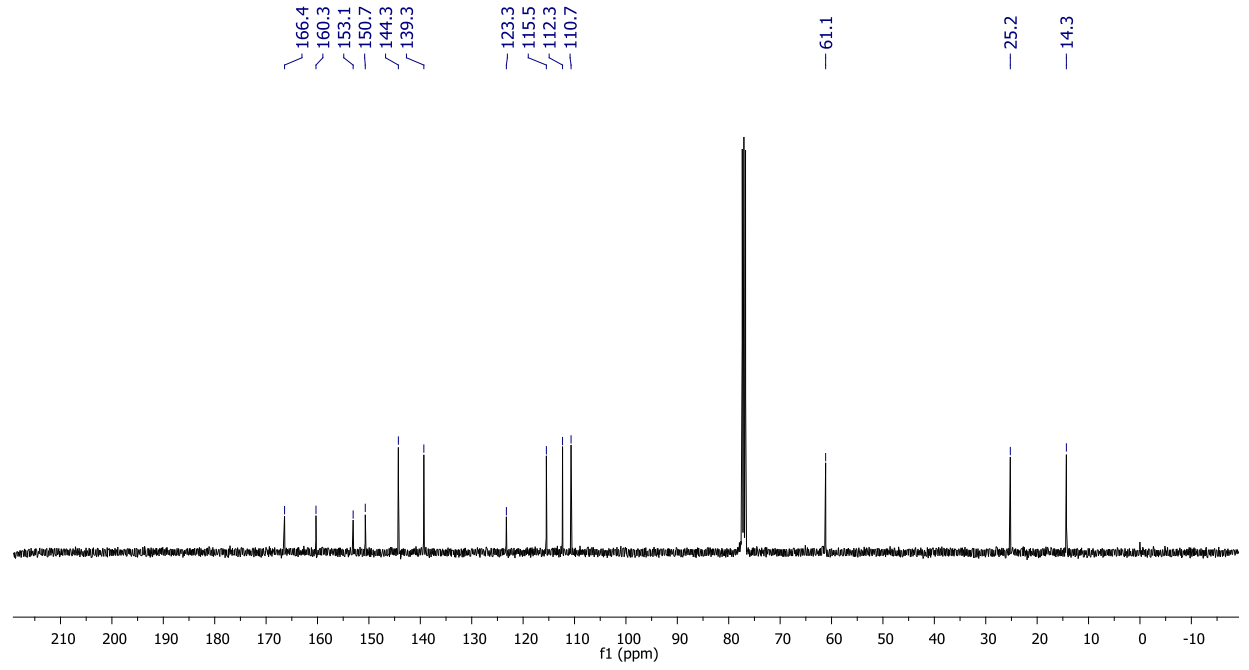
^{1}H NMR spectrum of **6**{*1,3*}



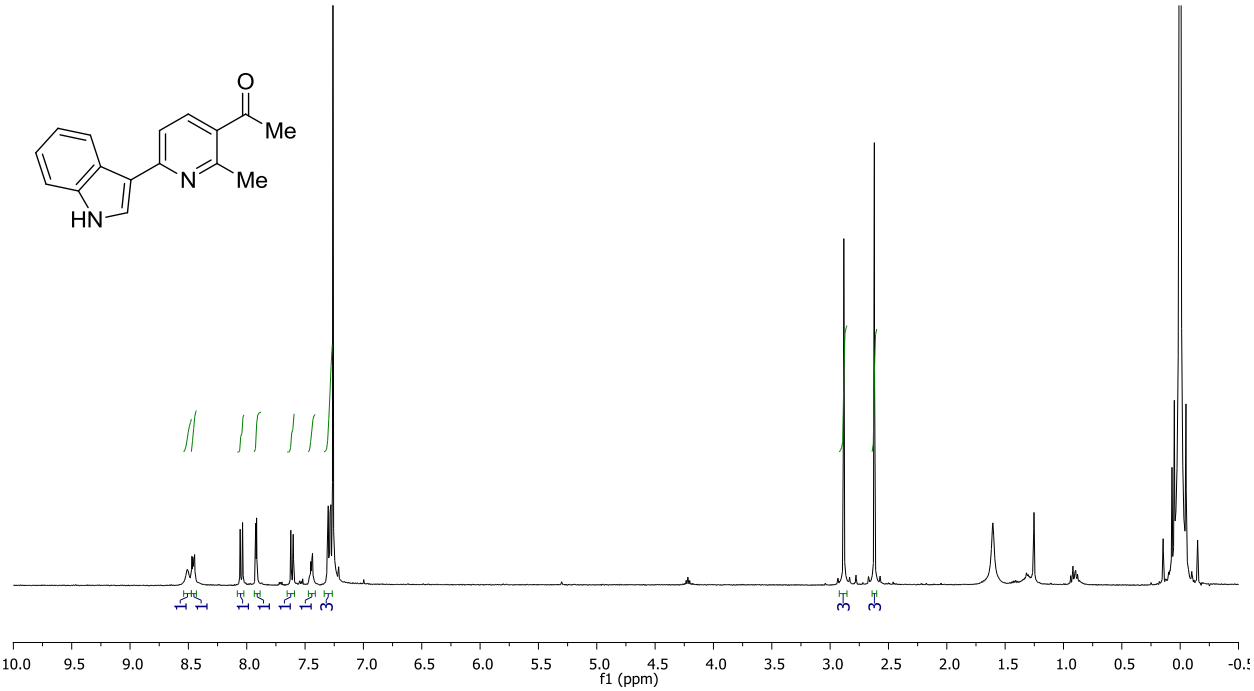
^{13}C NMR spectrum of **6**{*1,3*}



^{1}H NMR spectrum of **6**{*2,3*}

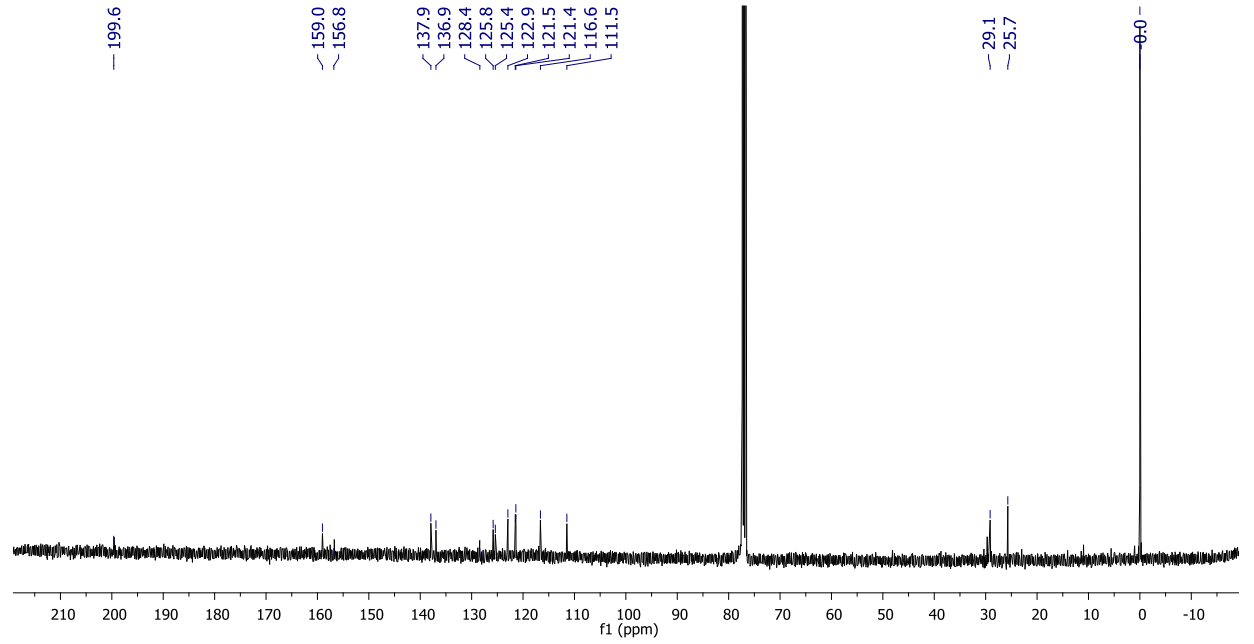


^{13}C NMR spectrum of **6**{*2,3*}

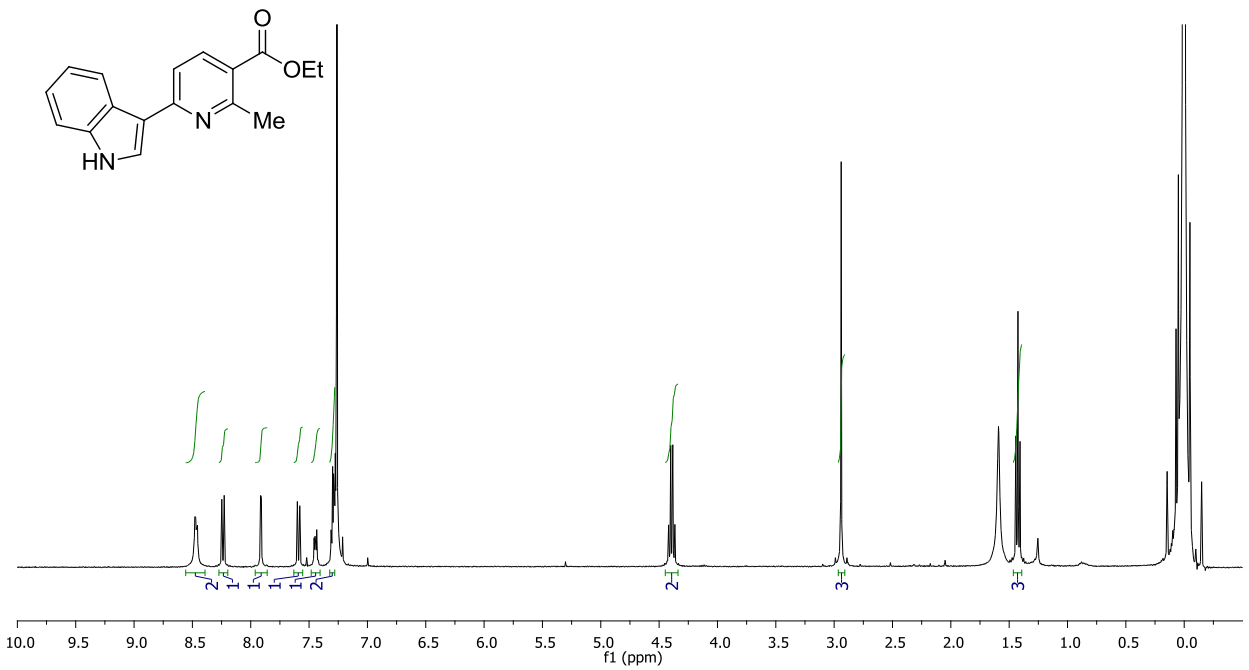


The peaks between 0.8-1.7 ppm due to residual solvent.

^{1}H NMR spectrum of **6**{*1,4*}

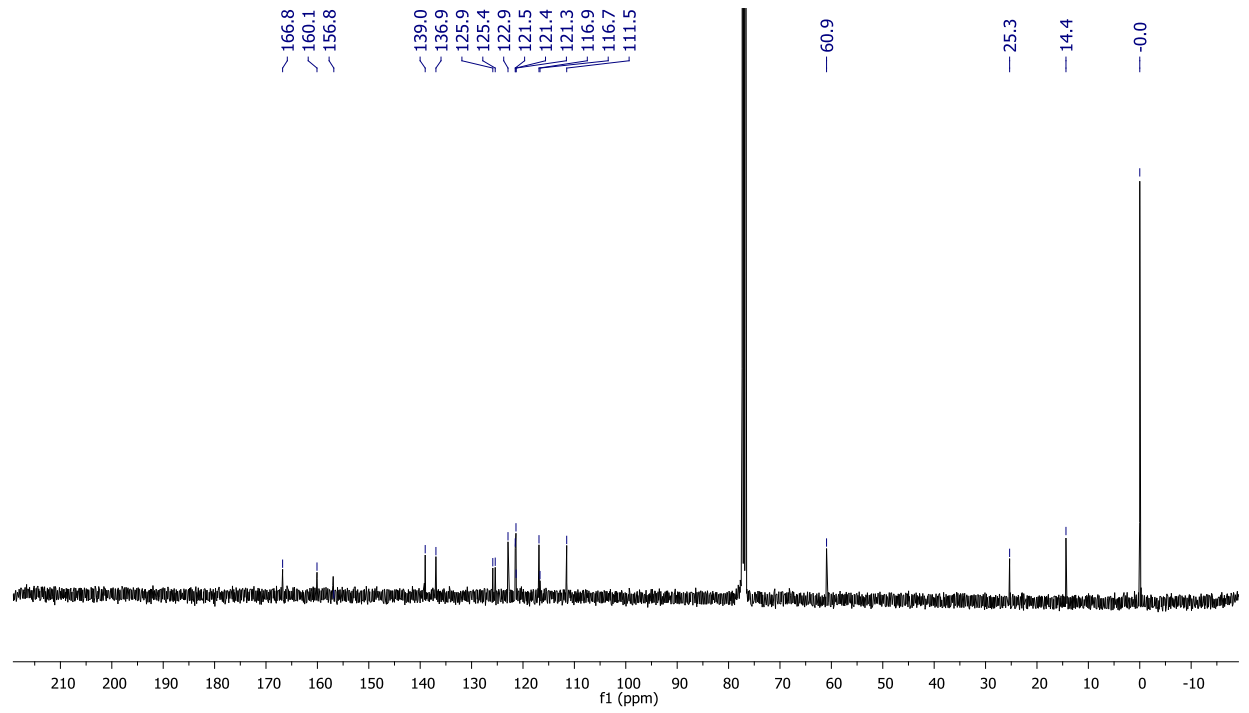


^{13}C NMR spectrum of **6**{*1,4*}

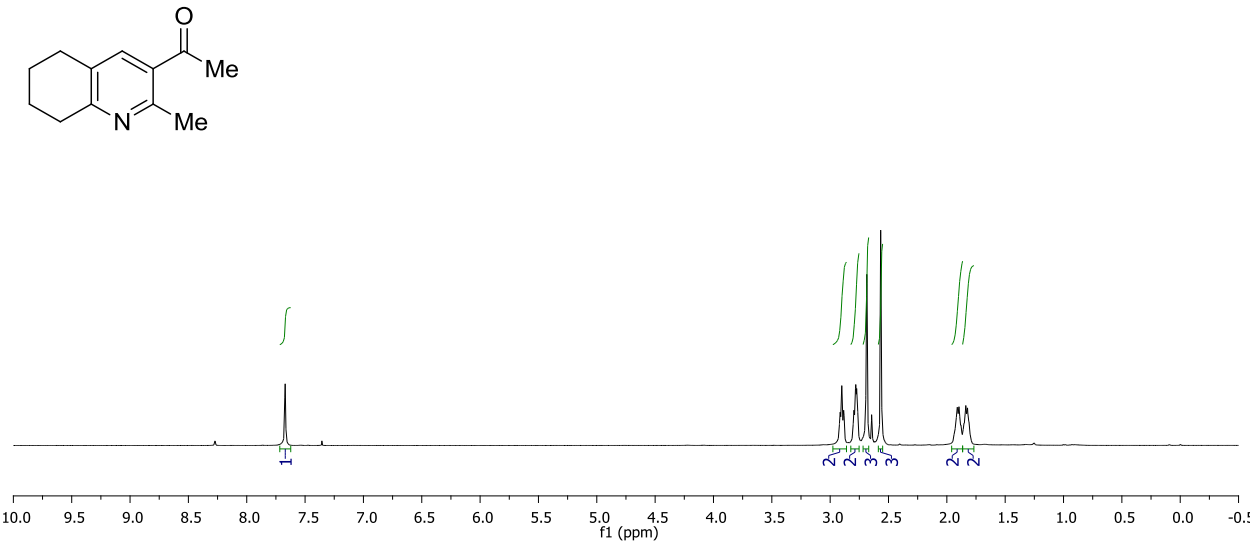


The peak at 1.59 ppm due to residual solvent.

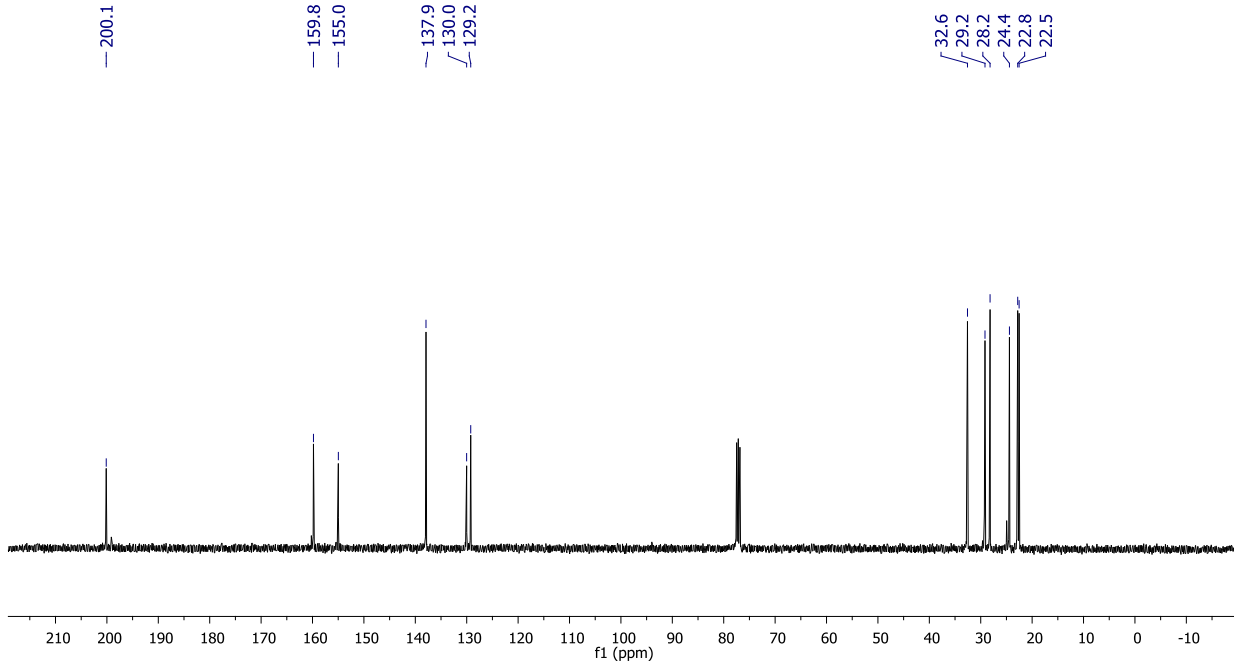
^{1}H NMR spectrum of **6**{*2,4*}



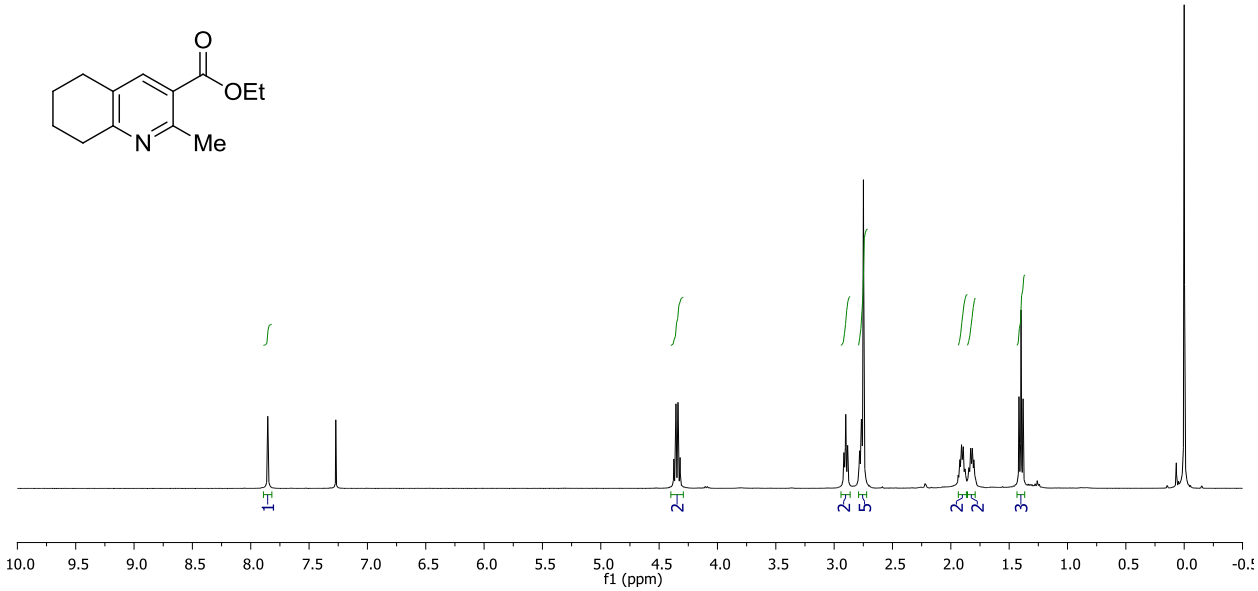
^{13}C NMR spectrum of **6**{*2,4*}



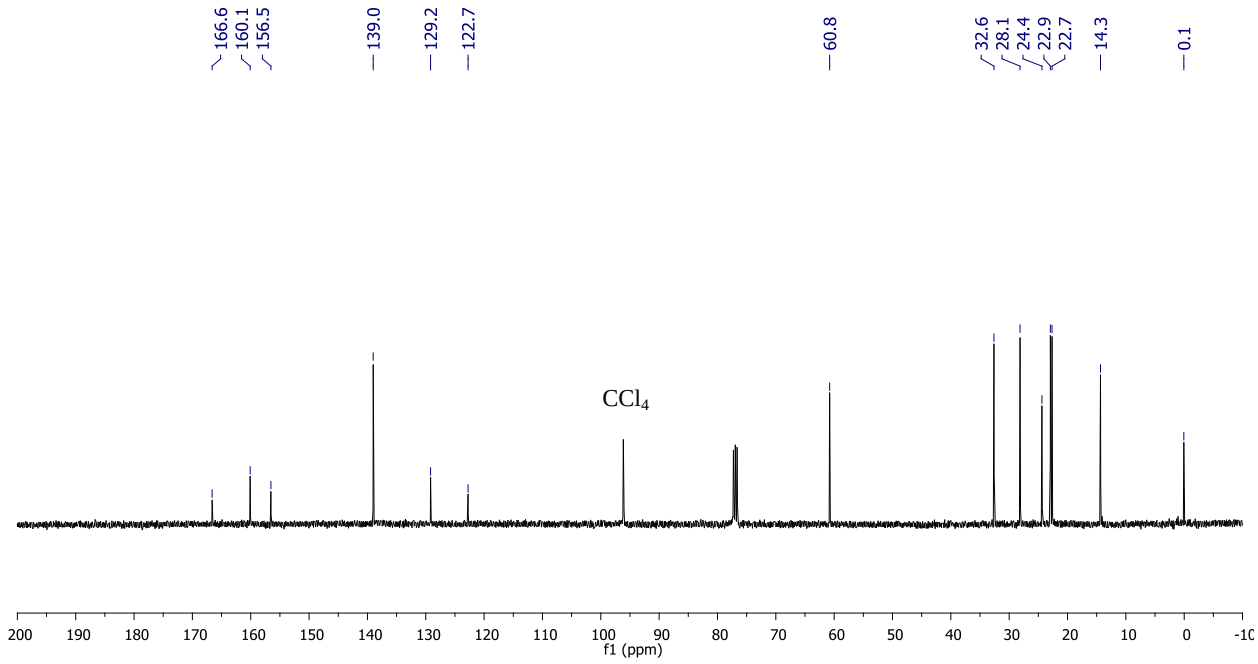
^{1}H NMR spectrum of **9**{*1*}



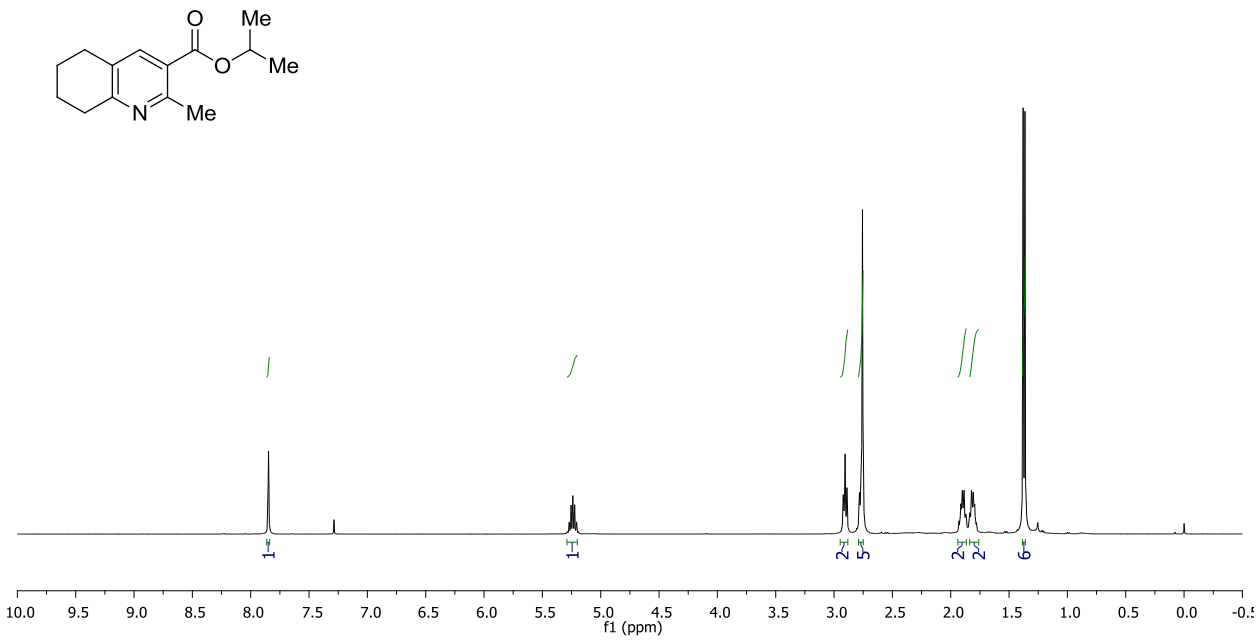
^{13}C NMR spectrum of **9**{*1*}



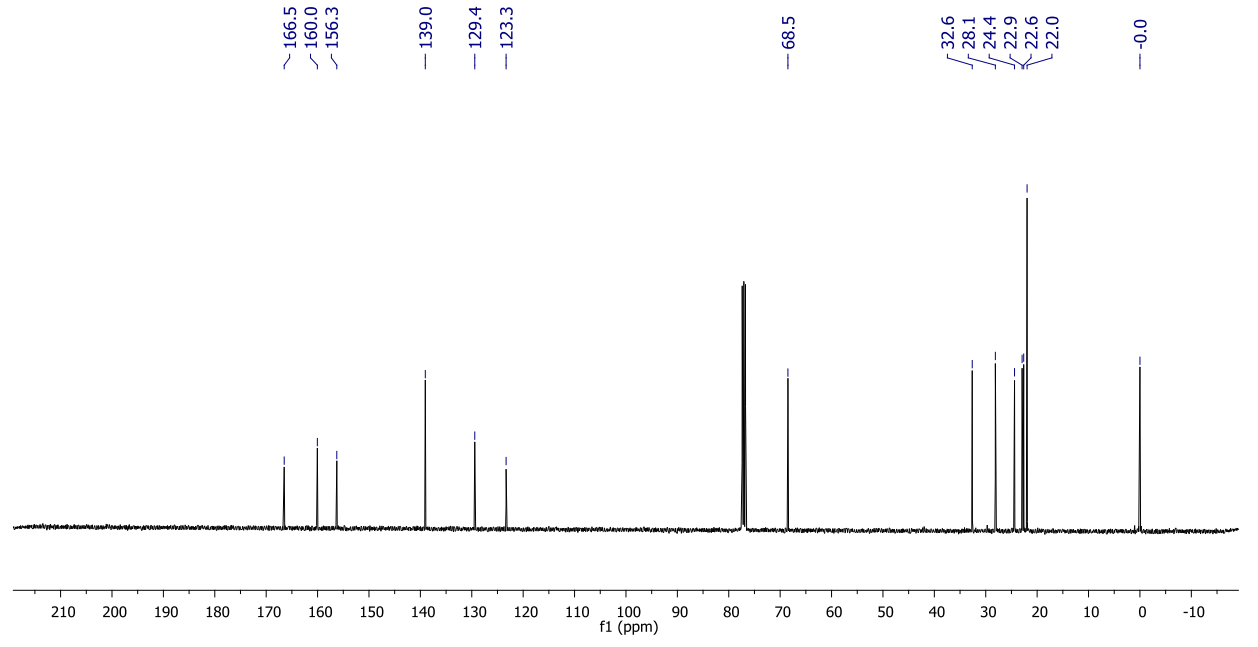
^{1}H NMR spectrum of **9**{*2*}



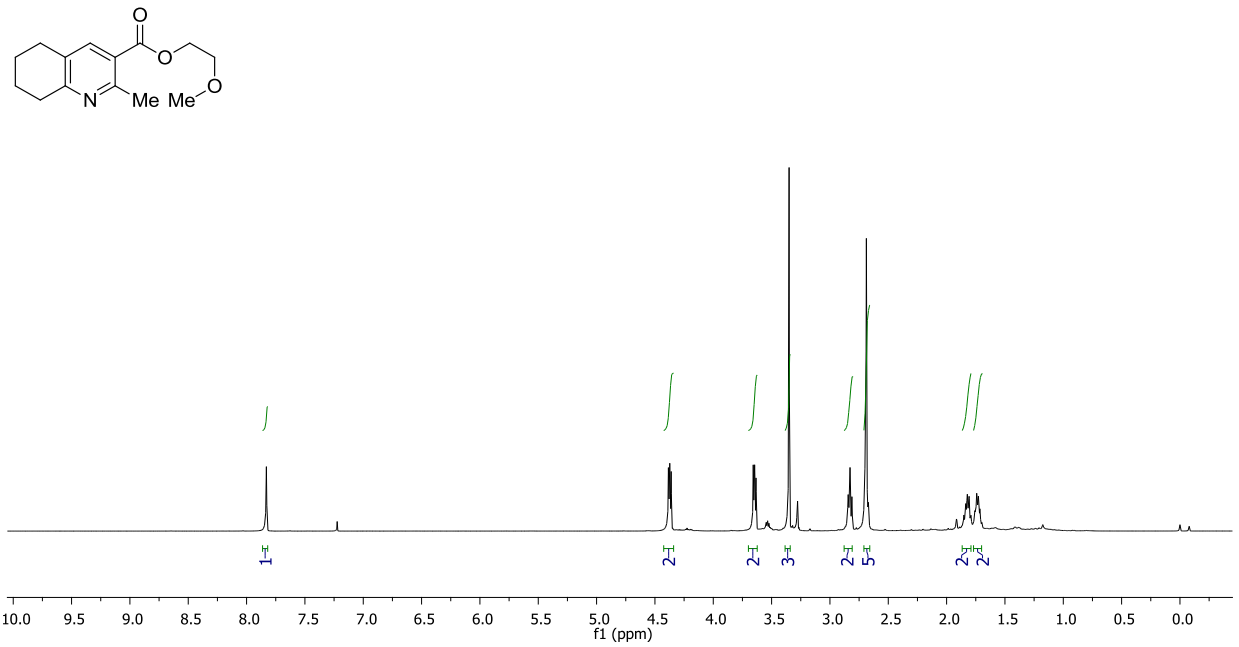
^{13}C NMR spectrum of **9**{*2*}



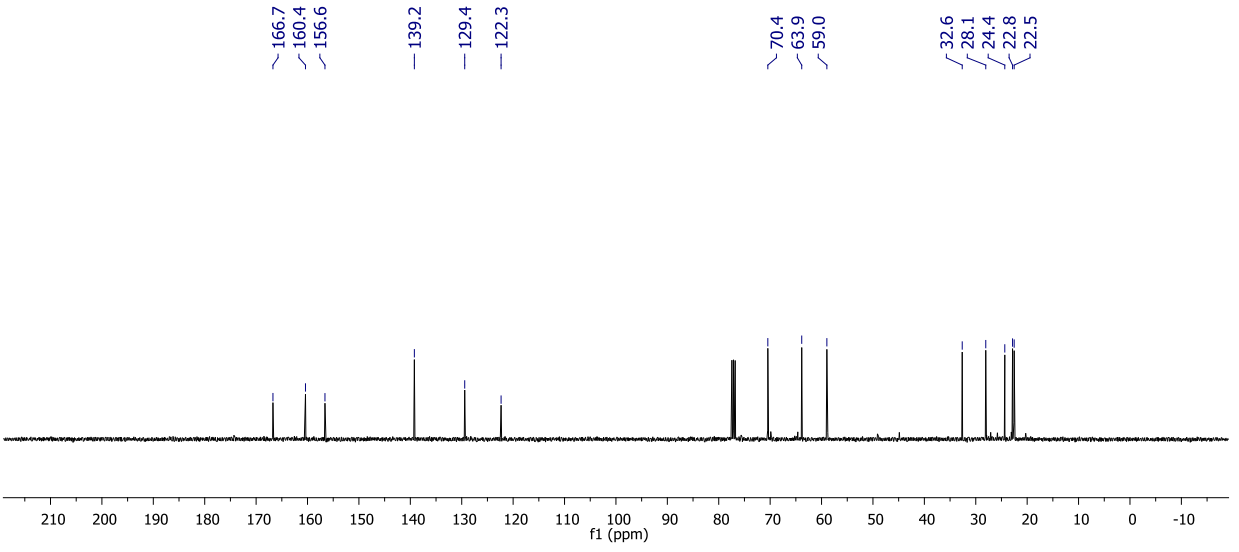
^{1}H NMR spectrum of **9**{*3*}



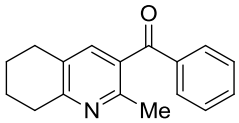
^{13}C NMR spectrum of **9**{*3*}

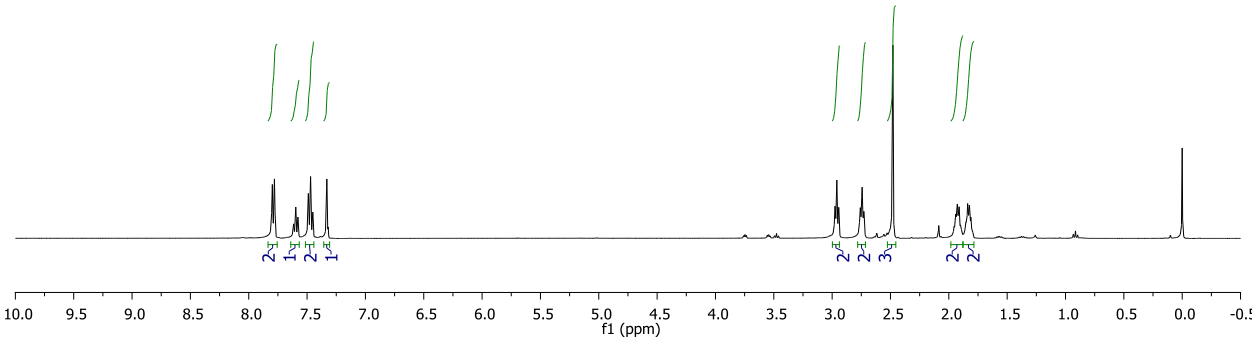


^{1}H NMR spectrum of **9**{*4*}

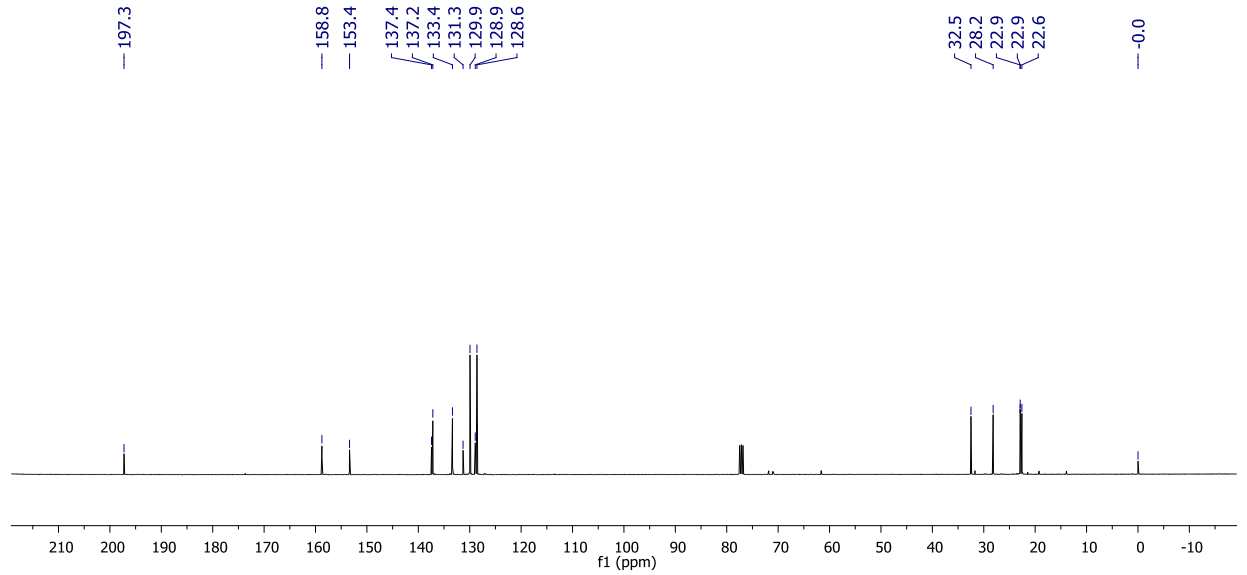


^{13}C NMR spectrum of **9**{*4*}

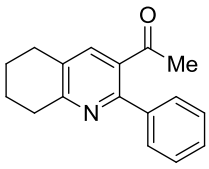


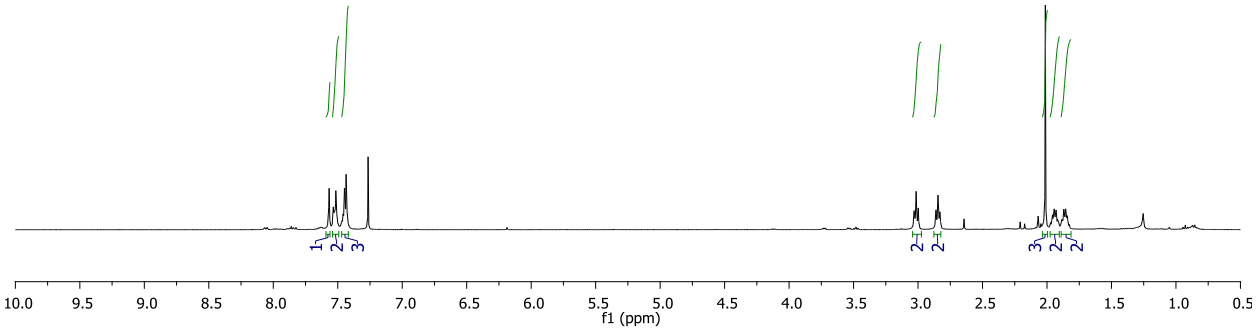


^{1}H NMR spectrum of **9a**{*5*}



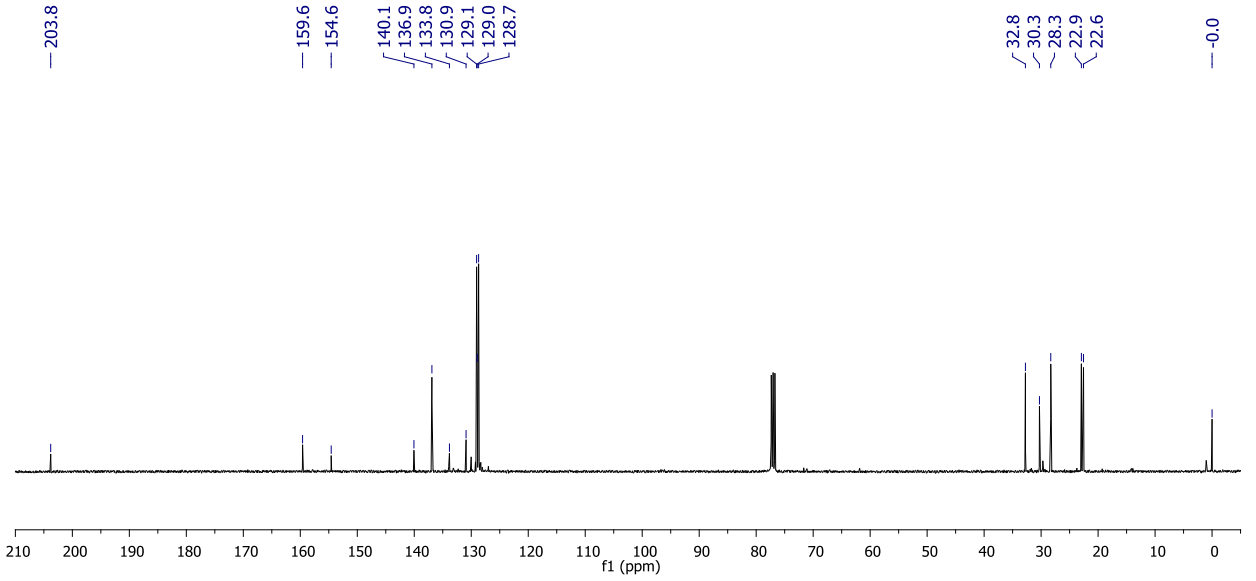
^{13}C NMR spectrum of **9a**{*5*}



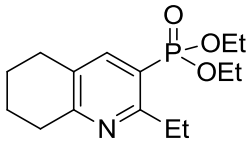


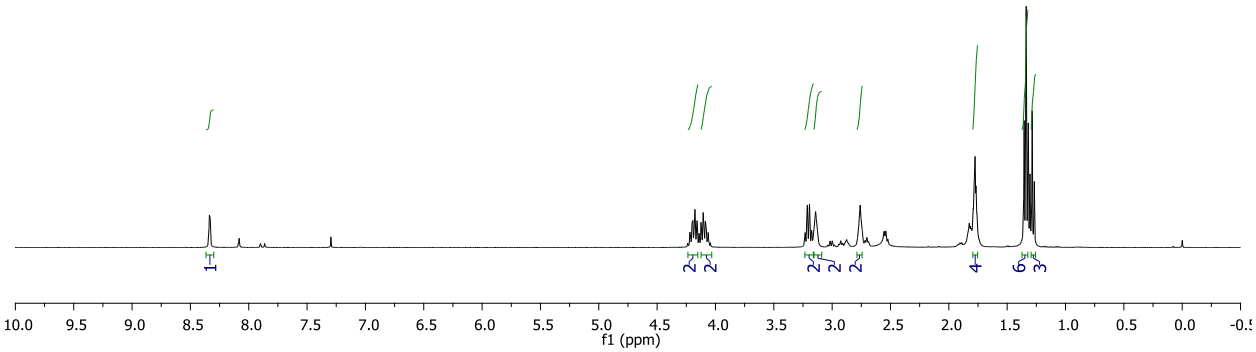
The peaks between 0.8-1.4 ppm due to residual solvent.

^{1}H NMR spectrum of **9b**{*5*}

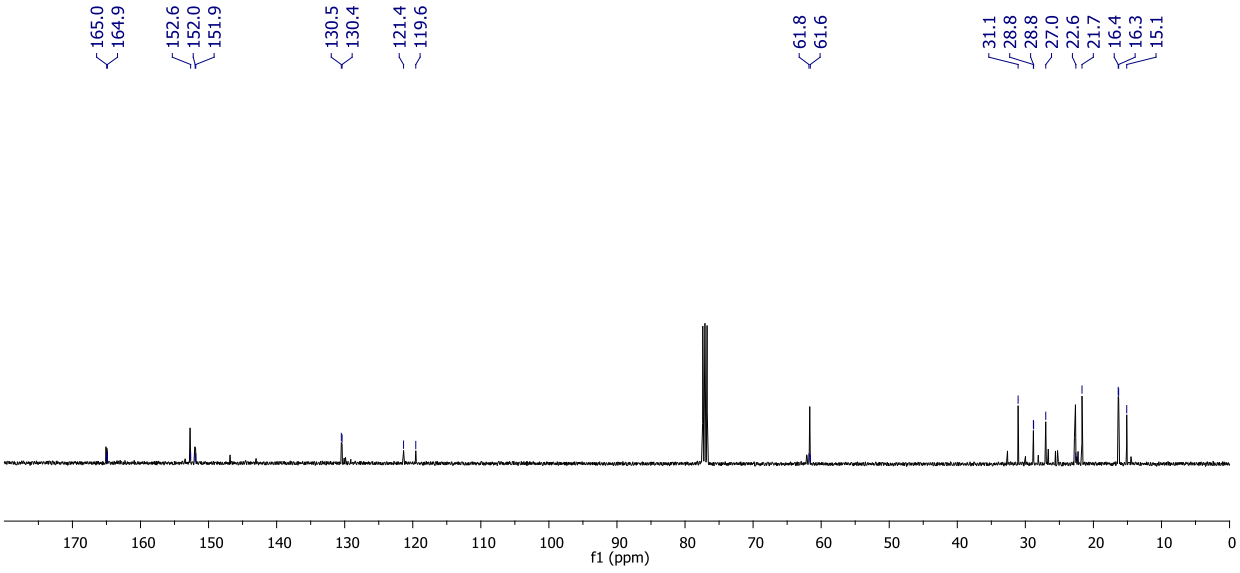


^{13}C NMR spectrum of **9b**{*5*}

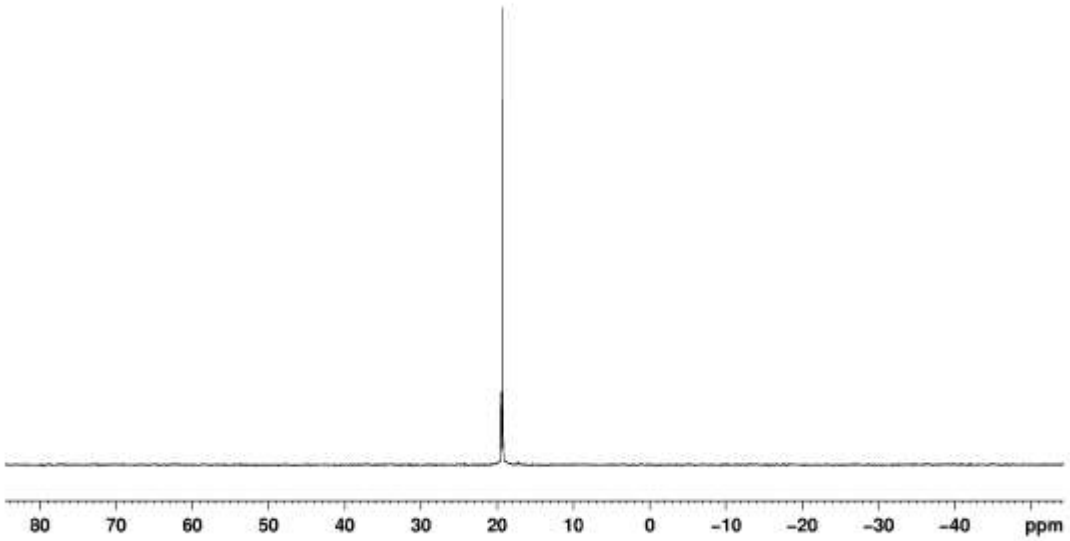




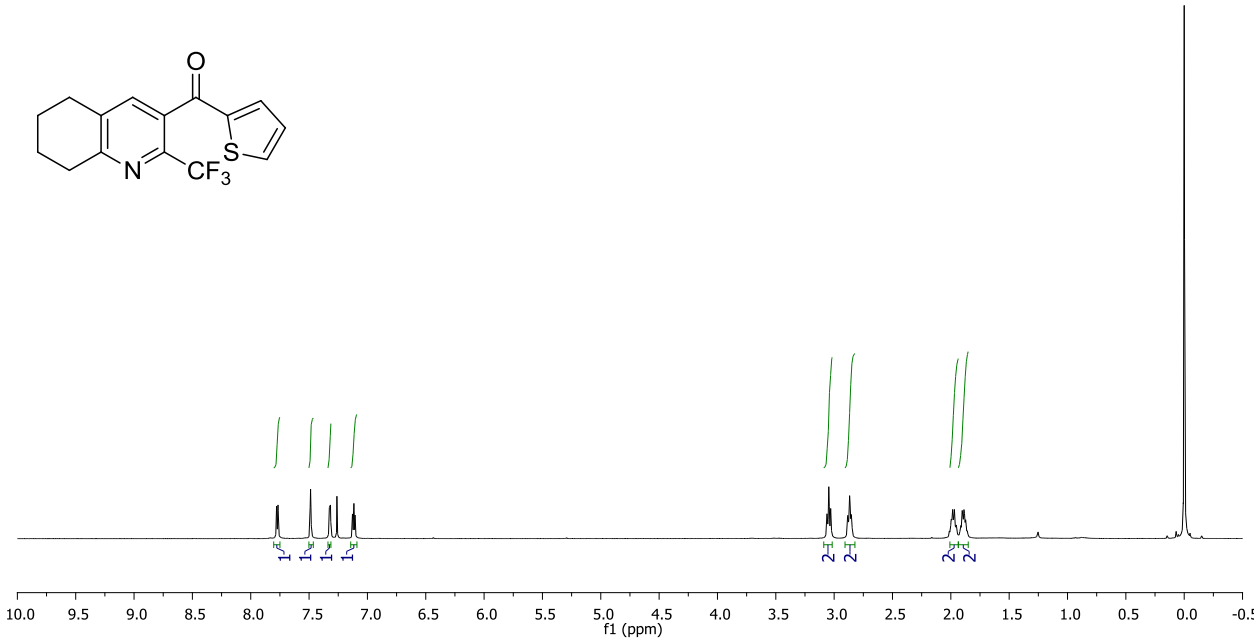
^{1}H NMR spectrum of **9**{*6*}



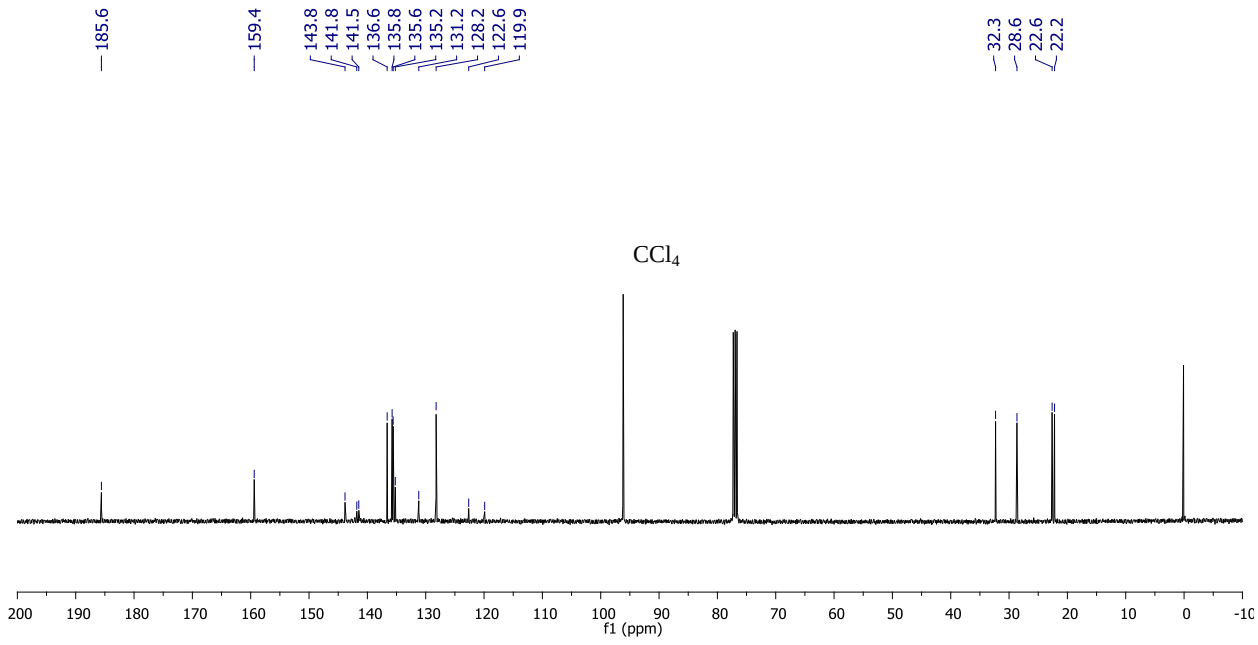
^{13}C NMR spectrum of **9**{*6*}



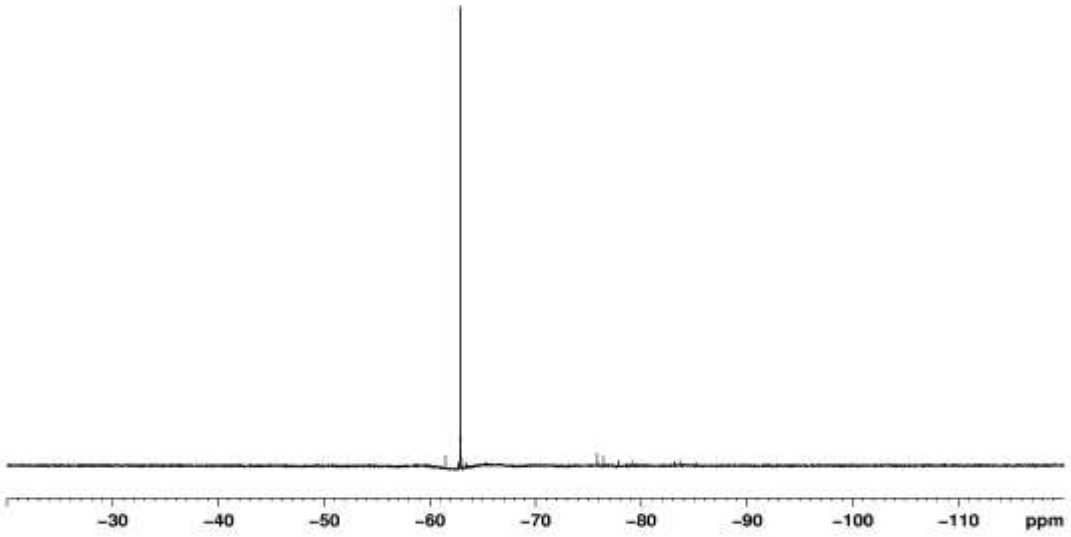
^{31}P NMR spectrum of **9**{*6*}



^{1}H NMR spectrum of **9**{*7*}



^{13}C NMR spectrum of **9**{*7*}



^{19}F NMR spectrum of **9**{*7*}

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