Catalytic Asymmetric Hydrogenation of 2,3,5-Trisubstituted Pyrroles

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Supporting Information

General and Materials. All NMR spectra were measured with Bruker AVANCE 400 (9.4 T magnet) spectrometer. In ^{1}H NMR spectra, chemical shifts (ppm) referenced to internal tetramethylsilane (0.00 ppm, in $CDCl_3$) or residual solvent (7.15 ppm, in C_6D_6). In ^{13}C NMR spectra, chemical shifts (ppm) referenced to the carbon signal of the deuterated solvents (77.0 ppm in $CDCl_3$ or 128.0 ppm in C_6D_6). IR spectra were measured with JASCO FT/IR-4100. Elemental and high resolution mass (HRMS) analyses were performed by Service Centre of Elementary Analysis of Organic Compounds and Institute for Materials Chemistry and Engineering (ICME) in Kyushu University, respectively. Flash column chromatographies and medium-pressure liquid chromatographies (MPLC) were performed with silica gel 60 (230–400 mesh, Merck) and C.I.G. pre-packed column CPS-223L-1 (Kusano, Tokyo, Japan), respectively.

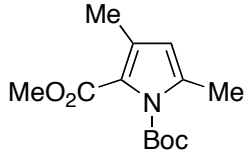
Acetonitrile (MeCN), ethyl acetate (EtOAc), 2-propanol (*i*-PrOH), and triethylamine (Et_3N) were dried with calcium hydride. Methanol (MeOH) was dried with $Mg(OMe)_2$. These solvents and reagents were distilled under nitrogen atmosphere. Tetrahydrofuran (THF) (HPLC grade, without inhibitor) was deoxidized by purging with nitrogen for 30 min and was dried with an alumina column system (GlassContour Co.). Ru(η^3-methallyl)$_2$(cod),[1] (*S*,*S*)-(*R*,*R*)-PhTRAP,[2] Methyl *N*-(*tert*-butoxycarbonyl)-pyrrole-2-carboxylate (**1a**),[3] were prepared according to literature procedures. All other materials were purchased and used without further purification.

Preparations of *N*-Boc Pyrroles 1.

General Procedure of *N*-Boc Protection of Pyrroles.

Under nitrogen atmosphere, $(Boc)_2O$ (2.40 g, 11 mmol) was added to a solution of a pyrrole (10 mmol) and DMAP (61 mg, 0.5 mmol) in dry MeCN (3.3 ml) at room temperature. The mixture was stirred until the pyrrole disappeared completely or the reaction mixture ceased evolving carbon dioxide (monitored by a bubbler tube). After water was added, the resulting mixture was extracted with EtOAc. The organic phase was washed with brine, dried with Na_2SO_4, and evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane) to give the desired *N*-Boc-pyrroles **1**.

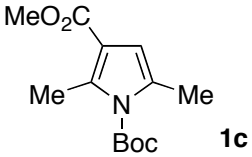
Methyl *N*-(*tert*-Butoxycarbonyl)-3,5-dimethylpyrrole-2-carboxylate (1b).



1b

The general procedure was followed with use of methyl 3,5-dimethylpyrrole-2-carboxylate[4] (1.25 g, 8.2 mmol). The reaction was conducted for 17 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1b** (1.47 g, 71% yield) as pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.56 (s, 9H), 2.20 (s, 3H), 2.32 (s, 3H), 3.82 (s, 3H), 5.77 (s, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 12.4, 14.0, 27.6, 51.3, 84.2, 113.0, 120.9, 130.9, 135.8, 149.7, 161.8; IR (neat) 2981, 1750, 1712, 1321, 1227, 1162, 1109 cm^{-1}; Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.70; H, 7.59; N, 5.57.

Methyl *N*-(*tert*-Butoxycarbonyl)-2,5-dimethylpyrrole-3-carboxylate (1c).



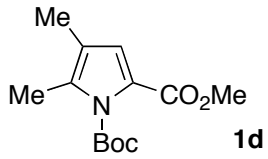
1c

Methyl 2,5-dimethylpyrrole-3-carboxylate[6] was prepared by the modified procedure reported by Roomi and MacDonald.[7]

Chloroacetone (4.0 ml, *d* 1.16 g/ml, 50 mmol) was added carefully to a mixture of methyl acetoacetate (5.4 ml, *d* 1.07 g/ml, 50 mmol), 28% NH_3 *aq.* (25 ml), and water (25 ml) at room temperature. After stirred for 17 h, the mixture was extracted five times with EtOAc. The combined organic phase was successively washed with 10% NaOH *aq.* and then with 5% HCl *aq.* The resulting solution was dried with Na_2SO_4 and then evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/2) to give the desired product (1.54 g, 20%) as pale yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.19 (s, 3H), 2.48 (s, 3H), 3.78 (s, 3H), 6.18 (d, J = 2.7 Hz, 1H), 7.70–8.30 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of the pyrrole prepared above (1.53 g, 10 mmol). The reaction was conducted for 9 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1c** (2.11 g, 83% yield) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.61(s, 9H), 2.34 (s, 3H), 2.71 (s, 3H), 3.79 (s, 3H), 6.22 (s, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 14.0, 15.8, 28.0, 51.0, 84.6, 110.8, 114.0, 130.2, 138.2, 149.9, 165.5; IR (nujor) 2979, 1750, 1713, 1335, 1278, 1214, 1171, 1151, 1068 cm^{-1}; Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.59; H, 7.57; N, 5.55.

Methyl *N*-(*tert*-Butoxycarbonyl)-4,5-dimethylpyrrole-2-carboxylate (1d).



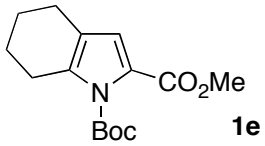
1d

Methyl 4,5-dimethylpyrrole-2-carboxylate was prepared by the modified procedure reported by Wallace.[8] Under nitrogen atmosphere, ethyl formate (14.5 ml, *d* 0.92 g/ml, 180 mmol) was added to a solution of 2-butanone (10.7 ml, *d* 0.81 g/ml, 120 mmol) in dry THF (14 ml) at 0°C. A solution of sodium *tert*-butoxide (13.8 g, 144 mmol) in dry THF (36 ml) was added dropwise to the mixture at 0°C for 2 h. After the mixture was stirred at room temperature for 18 h, the colorless precipitation was formed in the yellow solution. The precipitation was collected with filtration, washed with dry THF, and dried in vacuo to give sodium 2-methyl-3-oxobutanalate (12.2 g, 83%).

A solution of the precipitation (11.7 g, 96 mmol) in water (31 ml) was added to a mixture of methyl 2-(hydroxyimino)-3-oxobutanoate[9] (14.5 g, 100 mmol), 1,4-dioxane (29 ml), acetic acid (15 ml) and water (71 ml). Six portions of zinc powder (10.2 g, 160 mg-atoms) were added to the mixture at 60°C and intervals of 15 min. After stirred at 60°C for 15min and then at 80°C for 1.5 h, the resulting mixture was diluted with EtOAc, filtered through a Celite pad, and then extracted four times with EtOAc. The combined organic phase was dried with Na_2SO_4, and evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/10). The resulting crude product was recrystallized from EtOAc–hexane to give methyl 4,5-dimethylpyrrole-2-carboxylate (6.05 g, 41%) as colorless crystals: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 2.00 (s, 3H), 2.20 (s, 3H), 3.81 (s, 3H), 6.66 (d, J = 2.4 Hz, 1H), 8.48–8.78 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of the pyrrole prepared above (0.766 g, 5.0 mmol). The reaction was conducted for 14 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1d** (1.15 g, 91% yield) as colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.57 (s, 9H), 1.97 (s, 3H), 2.27 (s, 3H), 3.80 (s, 3H), 6.66 (s, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 10.8, 11.3, 27.5, 51.4, 84.4, 117.5, 121.1, 122.6, 133.2, 149.8, 161.0; IR (neat) 2981, 1749, 1714, 1370, 1315, 1219, 1151, 1087 cm^{-1}; Anal. Calcd for $C_{13}H_{19}NO_4$: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.83; H, 7.58; N, 5.47.

Methyl *N*-(*tert*-Butoxycarbonyl)-4,5,6,7-tetrahydroindole-2-carboxylate (1e).

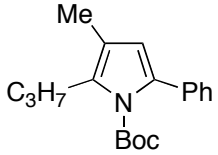


1e

The general procedure was followed with use of methyl 4,5,6,7-tetrahydroindole-2-carboxylate[5] (627 mg, 3.5 mmol). The reaction was conducted for 18 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1e** (901 mg, 92% yield) as a colorless solid: ^{1}H NMR (400

MHz, $CDCl_3$, TMS) δ 1.57 (s, 9H), 1.67–1.75 (m, 2H), 1.75–1.83 (m, 4H), 2.43 (t, *J* = 6.0 Hz, 2H), 2.73 (t, *J* = 6.2 Hz, 2H), 3.80 (s, 3H), 6.65 (s, 1H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 22.72, 22.73, 22.9, 23.9, 27.6, 51.5, 84.2, 119.9, 120.2, 123.3, 136.3, 149.3, 161.3; IR (neat) 1746, 1719, 1215 cm^{-1}; Anal. Calcd for $C_{15}H_{21}NO_4$: C, 64.50; H, 7.58; N, 5.01. Found: C, 64.25; H, 7.57; N, 5.02.

***N*-(*tert*-Butoxycarbonyl)-3-methyl-5-phenyl-2-propylpyrrole (1f).**



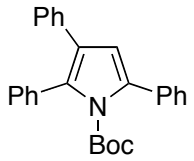
1f

Under nitrogen atmosphere, triethylamine (4.2 ml, *d* 0.726 g/ml, 30 mmol), 1-phenyl-2-buten-1-one (8.01 g, 55 mmol), and butyraldehyde (3.60 g, 50 mmol) were added to a solution of 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (2.70 g, 10 mmol) in EtOH (70 ml). After stirred at 80°C for 67 h, the reaction mixture was evaporated under reduced pressure. The residue was dissolved in EtOAc. The resulting solution was successively washed with 5% HCl *aq.*, with sat. $NaHCO_3$ *aq.*, and twice with water. The organic phase was dried with $MgSO_4$, and then evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/20) to give 3-methyl-1-phenyl-1,4-heptanedione (4.22 g, 39%) as yellow oil: ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 0.94 (t, *J* = 7.4 Hz, 3H), 1.18 (d, *J* = 7.24 Hz, 3H), 1.65 (sextet, *J* = 7.4 Hz, 2H), 2.59 (dt, *J* = 17.3, 7.4 Hz, 1H), 2.64 (dt, *J* = 17.3, 7.5 Hz, 1H), 2.92 (dd, *J* = 4.5, 17.9 Hz, 1H), 3.23 (ddq, *J* = 4.5, 8.9, 7.2 Hz, 1H), 3.55 (dd, *J* = 8.9, 17.9 Hz, 1H), 7.45 (t, *J* = 7.6 Hz, 2H), 7.56 (dt, *J* = 7.4, 1.2 Hz, 1H), 7.93–7.98 (m, 2H).

A solution of 3-methyl-1-phenyl-1,4-heptanedione (4.22 g, 19 mmol) and ammonium acetate (12.4 g, 160 mmol) in acetic acid (25 ml) was stirred under reflux for 16 h. After diluted with sat. $NaHCO_3$ *aq.*, the resulting mixture was extracted four times with EtOAc. The combined organic layer was dried with Na_2SO_4, and then evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/50) to give 3-methyl-5-phenyl-2-propylpyrrole (1.75 g, 45%) as yellow oil: ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 0.98 (t, *J* = 7.34 Hz, 3H), 1.63 (sextet, *J* = 7.5 Hz, 2H), 2.06 (s, 3H), 2.56 (t, *J* = 7.5 Hz, 2H), 6.29 (d, *J* = 2.8 Hz, 1H), 7.13 (t, *J* = 7.3 Hz, 1H), 7.32 (t, *J* = 7.8 Hz, 2H), 7.38–7.42 (m, 2H), 7.81–8.01 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of 3-methyl-5-phenyl-2-propylpyrrole (203 mg, 1.0 mmol). The reaction was conducted for 47 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/50) to give **1f** (78 mg, 26% yield) as pale yellow oil: ^1H NMR (400 MHz, $CDCl_3$, TMS) δ 0.96 (t, *J* = 7.4 Hz, 3H), 1.24 (s, 9H), 1.59 (sextet, *J* = 7.5 Hz, 2H), 2.02 (s, 3H), 2.77 (t, *J* = 7.5 Hz, 2H), 6.00 (s, 1H), 7.21–7.34 (m, 5H); ^{13}C {^1H} NMR (100 MHz, $CDCl_3$) δ 11.1, 13.9, 23.6, 27.3, 27.6, 83.0, 114.7, 118.0, 126.4, 127.7, 128.1, 133.1, 133.5, 135.4, 150.3; IR (neat) 2962, 1738, 1321, 1149 cm^{-1}; Anal. Calcd for $C_{19}H_{25}NO_2$: C, 76.22; H, 8.42; N, 4.68. Found: C, 76.33; H, 8.50; N, 4.58.

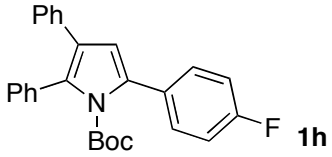
***N*-(*tert*-Butoxycarbonyl)-2,3,5-triphenylpyrrole (1g).**



1g

The general procedure was followed with use of 2,3,5-triphenylindole[10] (881 mg, 3.0 mmol). The reaction was conducted for 20 h. The crude product was purified with a MPLC (EtOAc/hexane = 1/5) to give **1g** (643 mg, 55% yield) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.13 (s, 9H), 6.48 (s, 1H), 7.09–7.19 (m, 5H), 7.29–7.47 (m, 10H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.0, 84.0, 112.7, 124.9, 126.0, 127.3, 127.7, 127.96, 127.99, 128.06, 128.12, 128.5, 130.9, 131.2, 133.4, 133.8, 135.1, 135.2, 149.7; IR (thin film) 1749, 1305, 1139 cm^{-1}; Anal. Calcd for $C_{27}H_{25}NO_2$: C, 82.00; H, 6.37; N, 3.54. Found: C, 82.11; H, 6.28; N, 3.54.

***N*-(*tert*-Butoxycarbonyl)-5-(4-fluorophenyl)-2,3-diphenylpyrrole (1h).**



1h

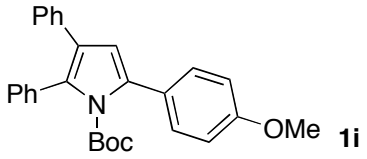
Under nitrogen atmosphere, benzaldehyde (1.09 g, 10 mmol) and triethylamine (630 mg, 6.2 mmol) were added to a solution of 1-(4-fluorophenyl)-3-phenyl-2-propen-1-one (2.49 g, 11 mmol) and 3-benzyl-5-(2-hydroxyethyl)-4-methylthiazolium chloride (545 mg, 2.0 mmol) in EtOH (5.0 ml). After stirred at 80°C for 48 h, the reaction mixture was evaporated under reduced pressure. The residue was dissolved in EtOAc. The resulting solution was successively washed with 5% HCl *aq.*, with sat. $NaHCO_3$ *aq.*, and with brine. The organic phase was dried with $MgSO_4$, and then evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give 4-(4-fluorophenyl)-1,2-diphenyl-1,4-butanedione (2.03 g, 59%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.26 (dd, J = 3.7, 17.9 Hz, 1H), 4.18 (dd, J = 10.1, 17.9 Hz, 1H), 5.31 (dd, J = 3.7, 10.1 Hz, 1H), 7.12 (t, J = 8.6 Hz, 2H), 7.21–7.34 (m, 5H), 7.40 (t, J = 7.6 Hz, 2H), 7.49 (t, J = 7.4 Hz, 1H), 7.98–8.05 (m, 4H).

The procedure for preparing 3-methyl-5-phenyl-2-propylpyrrole was followed with use of 4-(4-fluorophenyl)-1,2-diphenyl-1,4-butanedione (1.13 g, 3.4 mmol). The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give 5-(4-fluorophenyl)-2,3-diphenylpyrrole (929 mg, 87%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 6.63 (d, J = 2.9 Hz, 1H), 7.10 (t, J = 8.7 Hz, 2H), 7.19–7.42 (m, 10H), 7.48–7.54 (m, 2H), 8.30–8.38 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of 5-(4-fluorophenyl)-2,3-diphenylpyrrole (630 mg, 2.0 mmol). The reaction was conducted for 24 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1h** (676 mg, 81%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.13 (s, 9H), 6.44 (s, 1H), 7.06–7.21 (m, 7H), 7.31–7.37 (m, 5H), 7.60 (dd, J = 5.4, 8.7 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.1, 84.1, 112.9, 114.9 (d, J =

22 Hz), 125.0, 126.1, 127.7, 128.02, 128.08, 128.10, 129.9 (d, J = 3 Hz), 130.2 (d, J = 8 Hz), 130.8, 131.2, 133.4, 134.1, 134.9, 149.7, 162.2 (d, J = 247 Hz); IR (thin film) 1749, 1496, 1306, 1138 cm^{-1}; Anal. Calcd for $C_{27}H_{24}NO_2F$: C, 78.43; H, 5.85; N, 3.39. Found: C, 78.31; H, 5.95; N, 3.36.

***N*-(*tert*-Butoxycarbonyl)-5-(4-methoxyphenyl)-2,3-diphenylpyrrole (1i).**



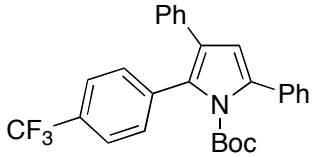
1i

The procedure for preparing 4-(4-fluorophenyl)-1,2-diphenyl-1,4-butanedione was followed with use of 1-(4-methoxyphenyl)-3-phenyl-2-propen-1-one (2.64 g, 11 mmol) and benzaldehyde (1.08 g, 10 mmol). The reaction was conducted for 48 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give 4-(4-methoxyphenyl)-1,2-diphenyl-1,4-butanedione (1.36 g, 39%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.27 (dd, J = 3.7, 17.8 Hz, 1H), 3.86 (s, 3H), 4.17 (dd, J = 10.1, 17.8 Hz, 1H), 5.32 (dd, J = 3.7, 10.1 Hz, 1H), 6.91 (d, J = 8.9 Hz, 2H), 7.22 (t, J = 7.2 Hz, 1H), 7.30 (t, J = 7.6 Hz, 2H), 7.34–7.43 (m, 4H), 7.49 (t, J = 7.4 Hz, 1H), 7.96 (d, J = 8.9 Hz, 2H), 8.01–8.06 (m, 2H).

The procedure for preparing 3-methyl-5-phenyl-2-propylpyrrole was followed with use of 4-(4-methoxyphenyl)-1,2-diphenyl-1,4-butanedione (902 mg, 2.6 mmol). The crude product was recrystallized from hexane to give 5-(4-methoxyphenyl)-2,3-diphenylpyrrole (560 g, 66%) as a colorless crystal: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.85 (s, 3H), 6.59 (d, J = 2.9 Hz, 1H), 6.95 (d, J = 8.8 Hz, 2H), 7.18–7.34 (m, 7H), 7.38–7.42 (m, 3H), 7.48 (d, J = 8.8 Hz, 2H), 8.27–8.37 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of 5-(4-methoxyphenyl)-2,3-diphenylpyrrole (540 mg, 1.7 mmol). The reaction was conducted for 24 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1i** (393 mg, 56%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.18 (s, 9H), 3.88 (s, 3H), 6.46 (s, 1H), 6.98 (d, J = 8.7 Hz, 2H), 7.13–7.25 (m, 5H), 7.35–7.40 (m, 5H), 7.42 (d, J = 8.7 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.1, 55.3, 83.8, 112.3, 113.4, 124.8, 125.9, 126.3, 127.6, 127.99, 128.04, 128.1, 129.8, 130.7, 130.8, 133.6, 135.0, 135.2, 149.9, 159.0; IR (thin film) 1748, 1496, 1305, 1250, 1135 cm^{-1}; Anal. Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 79.04; H, 6.45; N, 3.24.

***N*-(*tert*-Butoxycarbonyl)-2-[4-(trifluoromethyl)phenyl]-3,5-diphenylpyrrole (1j).**



1j

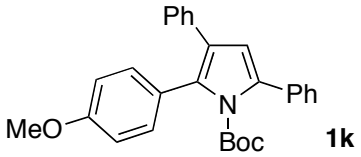
The procedure for preparing 4-(4-fluorophenyl)-1,2-diphenyl-1,4-butanedione was followed with use of 1,3-diphenyl-2-propen-1-one (11.5 g, 55 mmol) and 4-(trifluoromethyl)benzaldehyde (8.59 g, 49 mmol). The reaction was conducted for 89 h. The crude product was purified with a flash column chromatography

(EtOAc/hexane = 1/20) to give 2,4-diphenyl-1-[4-(trifluoromethyl)phenyl]-1,4-butanedione (18.2 g, 96%) as yellow viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.34 (dd, *J* = 3.5, 18.1 Hz, 1H), 4.23 (dd, *J* = 10.3, 18.1 Hz, 1H), 5.28 (dd, *J* = 3.5, 10.3 Hz, 1H), 7.23–7.36 (m, 5H), 7.46 (t, *J* = 7.7 Hz, 2H), 7.57 (t, *J* = 7.4 Hz, 1H), 7.67 (d, *J* = 8.2 Hz, 2H), 7.96–8.00 (m, 2H), 8.12 (d, *J* = 8.2 Hz, 2H).

The procedure for preparing 3-methyl-5-phenyl-2-propylpyrrole was followed with use of 2,4-diphenyl-1-[4-(trifluoromethyl)phenyl]-1,4-butanedione (18.2 g, 48 mmol). The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/20) to give 2-[4-(trifluoromethyl)phenyl]-3,5-diphenylpyrrole (11.5 g, 67%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 6.70 (d, *J* = 2.8 Hz, 1H), 7.23–7.31 (m, 2H), 7.33 (t, *J* = 7.5 Hz, 2H), 7.36–7.41 (m, 2H), 7.42 (t, *J* = 7.8 Hz, 2H), 7.48 (d, *J* = 8.2 Hz, 2H), 7.53–7.59 (m, 4H), 8.41–8.49 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of 2-[4-(trifluoromethyl)phenyl]-3,5-diphenylpyrrole (2.18 g, 6.0 mmol). The reaction was conducted for 21 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/20) to give **1j** (2.36 g, 85%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.13 (s, 9H), 6.46 (s, 1H), 7.10–7.23 (m, 5H), 7.32–7.48 (m, 7H), 7.60 (d, *J* = 8.1 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.0, 84.4, 113.3, 124.2 (q, *J* = 272 Hz), 124.9 (q, *J* = 4 Hz), 126.2, 126.4, 127.5, 128.0, 128.2, 128.3, 128.6, 129.46, 129.52 (q, *J* = 32 Hz), 131.1, 133.7, 134.6, 136.0, 137.2, 149.4; IR (thin film) 1750, 1325, 1136 cm^{-1}; Anal. Calcd for $C_{28}H_{24}NO_2F_3$: C, 72.56; H, 5.22; N, 3.02. Found: C, 72.57; H, 5.27; N, 3.06.

_N_-(_tert_-Butoxycarbonyl)-2-(4-methoxyphenyl)-3,5-diphenylpyrrole (1k).



1k

The procedure for preparing 4-(4-fluorophenyl)-1,2-diphenyl-1,4-butanedione was followed with use of 1,3-diphenyl-2-propen-1-one (2.29 g, 11.0 mmol) and 4-methoxybenzaldehyde (1.42 g, 10.4 mmol). The reaction was conducted for 72 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/5) to give 2,4-diphenyl-1-(4-methoxyphenyl)-1,4-butanedione (2.32 g, 65%) as yellow viscous oil: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.27 (dd, *J* = 3.8, 18.0 Hz, 1H), 3.81 (s, 3H), 4.20 (dd, *J* = 9.9, 18.0 Hz, 1H), 5.29 (dd, *J* = 3.8, 9.9 Hz, 1H), 6.87 (d, *J* = 8.9 Hz, 2H), 7.21 (t, *J* = 7.2 Hz, 1H), 7.30 (t, *J* = 7.6 Hz, 2H), 7.36 (d, *J* = 7.7 Hz, 2H), 7.44 (t, *J* = 7.8 Hz, 2H), 7.54 (t, *J* = 7.0 Hz, 1H), 7.98 (d, *J* = 8.2 Hz, 2H), 8.02 (d, *J* = 8.9 Hz, 2H).

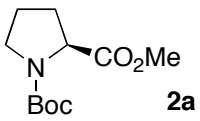
The procedure for preparing 3-methyl-5-phenyl-2-propylpyrrole was followed with use of 2,4-diphenyl-1-(4-methoxyphenyl)-1,4-butanedione (2.32 g, 6.7 mmol). The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give 2-(4-methoxyphenyl)-3,5-diphenylpyrrole (1.94 g, 88%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 3.82 (s, 3H), 6.69 (s, 1H), 6.88 (d, *J* = 8.6 Hz, 2H), 7.17–7.57 (m, 12H), 8.30–8.40 (br, 1H).

The general procedure of *N*-Boc protection was followed with use of 2-(4-methoxyphenyl)-3,5-diphenylpyrrole (251 mg, 0.77 mmol). The reaction was conducted for 24 h. The crude product was purified with a flash column chromatography (EtOAc/hexane = 1/10) to give **1k** (246 mg, 75%) as a colorless solid: ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.15 (s, 9H), 3.83 (s, 3H), 6.47 (s, 1H), 6.89 (d, J = 8.7 Hz, 2H), 7.09–7.21 (m, 5H), 7.24–7.35 (m, 3H), 7.35–7.46 (m, 4H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.1, 55.2, 83.9, 112.5, 113.5, 124.8, 125.5, 125.9, 127.2, 127.97, 128.04, 128.06, 128.3, 131.2, 132.2, 134.0, 134.9, 135.2, 149.8, 159.2; IR (thin film) 2979, 1748, 1510, 1489, 1305, 1248, 1139 cm^{-1}; Anal. Calcd for $C_{28}H_{27}NO_3$: C, 79.03; H, 6.40; N, 3.29. Found: C, 78.86; H, 6.66; N, 3.24.

Asymmetric Hydrogenation of Pyrroles (1).

General Procedure. Under nitrogen atmosphere, dry EtOAc (1.0 ml) and dry Et_3N (5.1 mg, 50 μmol) was added to a mixture of Ru(η^3-methallyl)$_2$(cod) (1.6 mg, 5.0 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (4.4 mg, 5.5 μmol). After stirred at room temperature for 10 min, the mixture was transferred through cannula into a pyrrole **1** (0.20 mmol) in a test tube. The test tube was inserted into a nitrogen-filled stainless steel autoclave, and the autoclave was sealed immediately. Hydrogen gas was introduced into the autoclave until the pressure gauge indicated over 50 atm, and then the pressure was carefully released to 1 atm. This procedure was repeated twice, and finally the inside of the autoclave was pressurized with hydrogen to 50 atm. After the mixture was stirred at 80°C for 24 h, the autoclave was allowed to cool to room temperature. Excess hydrogen was released carefully, and then the resulting reaction mixture was evaporated under reduced pressure. The residue was analyzed with ^{1}H NMR in order to determine its composition, and then purified with a MPLC (EtOAc/hexane) after passed through a short silica gel column.

Methyl (*S*)-*N*-(*tert*-Butoxycarbonyl)pyrrolidine-2-carboxylate (2a) (eq 1).

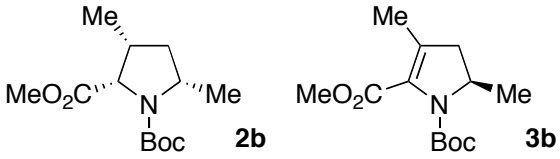


2a

Under nitrogen atmosphere, dry *i*-PrOH (1.0 ml) and dry Et_3N (5.1 mg, 50 μmol) was added mixture of Ru(η^3-methallyl)$_2$(cod) (1.6 mg, 5.0 μmol) and (*S*,*S*)-(*R*,*R*)-PhTRAP (4.4 mg, 5.5 μmol). After stirred at room temperature for 10 min, the mixture was transferred through cannula into a mixture of pyrrole **1a** in a test tube. The mixture was treated with 50 atm of hydrogen gas along the general procedure. The residue was purified with a short silica gel column (EtOAc/hexane = 1/2) to give the desired compound **2a** (113 mg, 92%) as colorless oil: $[\alpha]_D^{27}$ = –48.9 (*c* 0.364, MeOH), lit.[11] $[\alpha]_D$ = –61.5 (*c* 0.34, MeOH); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.41 and 1.46 (a pair of s, 9H), 1.79–2.02 (m, 3H), 2.12–2.29 (m, 1H), 3.35–3.60 (m, 2H), 3.72 (s, 3H), 4.22 and 4.33 (a pair of dd, J = 4.2, 8.5 Hz and J = 3.2, 8.5 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 23.7 and 24.3 (a pair of s), 28.3 and 28.4 (a pair of s), 30.9 and 29.9 (a pair of s), 46.3 and 46.5 (a pair of s), 51.9 and 52.1 (a pair of s), 59.1 and 58.7 (a pair of s), 79.83 and 79.78 (a pair of s), 153.8 and 154.4 (a pair of s), 173.7 and 173.5 (a pair of s).

The enantiomeric excess of **2a** was determined to be 79% ee by capillary GC analysis with Chirasil-DEX CB (0.25 mm $\phi \times$ 25 m, df = 0.25 μm): N_2, 33 cm/sec flow, at 120°C, (*R*) t_1 = 32.8 min, (*S*) t_2 = 34.0 min.

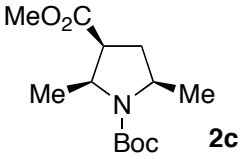
Methyl (–)-*N*-(*tert*-Butoxycarbonyl)-3,5-dimethylpyrrolidine-2-carboxylate (2b) and Methyl (–)-*N*-(*tert*-Butoxycarbonyl)-3,5-dimethyl-4,5-dihydropyrrole-2-carboxylate (3b) (Table 1, entry 1).



The general procedure was followed with use of pyrrole **1b** (52.2 mg, 0.21 mmol). The crude product was purified with a MPLC (EtOAc/hexane = 1/2) after passed through a short silica gel column (EtOAc/hexane = 1/3) to give **2b** (27.1 mg, 52%) as colorless oil and **3b** (21.7 mg, 42%) as colorless oil. (–)-**2b**: $[\alpha]_D^{27}$ = –9.5 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.97 (d, *J* = 6.9 Hz, 3H), 1.37–1.52 (m, 13H), 2.15 (dt, *J* = 13.0, 6.7 Hz, 1H), 2.31–2.45 (br m, 1H), 3.72 (s, 3H), 3.69–3.88 (br m, 1H), 4.29 and 4.40 (a pair of d, *J* = 8.5 Hz and *J* = 8.4 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 14.83 and 14.75 (a pair of s), 20.1 and 21.2 (a pair of s), 28.37 and 28.45 (a pair of s), 35.2 and 35.0 (a pair of s), 40.8 and 41.4 (a pair of s), 51.46 and 51.50 (a pair of s), 54.0 and 54.2 (a pair of s), 64.9 and 64.4 (a pair of s), 79.6 and 79.7 (a pair of s), 153.5 and 154.5 (a pair of s), 172.7; IR (neat) 2972, 1746, 1698, 1391, 1177 cm^{-1}; Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.78; H, 8.90; N, 5.37. (–)-**3b**: $[\alpha]_D^{27}$ = –66.1 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.25 (d, *J* = 6.5 Hz, 3H), 1.44 (s, 9H), 1.88 (s, 3H), 1.92 (d, *J* = 17.2 Hz, 1H), 2.98 (ddq, *J* = 9.3, 17.2, 1.6 Hz, 1H), 3.81 (s, 3H), 4.23–4.33 (m, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 13.7, 21.8, 28.2, 42.7, 51.6, 54.7, 80.6, 128.0, 128.6, 152.9, 163.5; IR (neat) 2978, 1731, 1703, 1394, 1368, 1295, 1171 cm^{-1}; HRMS (FAB) Calcd for $C_{13}H_{22}NO_4$: 256.1549. Found: *m*/*z* = 256.1531 $(M+H)^+$.

The enantiomeric excesses of (–)-**2b** and (–)-**3b** were determined to be 11% ee and 75% ee by capillary GC analysis with Chirasil-DEX CB (0.25 mm $\phi \times$ 25 m, df = 0.25 μm): N_2, 33 cm/sec flow, at 110°C. **2b**: (+) t_1 = 62.2 min, (–) t_2 = 65.0 min. **3b**: (–) t_1 = 87.1 min, (+) t_2 = 91.2 min.

Methyl (–)-*N*-(*tert*-Butoxycarbonyl)-2,5-dimethylpyrrolidine-3-carboxylate (2c) (Table 1, entry 2).



The general procedure was followed with use of pyrrole **1c** (50.9 mg, 0.20 mmol). The crude product was purified with a MPLC (EtOAc/hexane = 1/3) after passed through a short silica gel column (EtOAc/hexane = 1/3) to give **2c** (46.8 mg, 91%) as colorless oil: $[\alpha]_D^{26}$ = –0.94 (*c* 1.06, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.06 (d, *J* = 6.6 Hz, 3H), 1.34 (br d, *J* = 5.7 Hz, 3H), 1.46 (s, 9H), 2.02 (br q, *J* = 11.3 Hz, 1H), 2.24 (dt, *J* = 13.8, 7.1 Hz, 1H), 3.02 (dt, *J* = 12.9, 7.4 Hz), 3.70 (s, 3H), 3.65–3.82 (br m, 1H),

4.10–4.42 (br m, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 17.4 (br s), 22.2 and 22.9 (a pair of br s), 28.5, 33.5 and 34.1 (a pair of br s), 46.0 (br s), 51.8, 52.7, 55.0, 79.3, 154.0 (br s), 171.9; IR (neat) 2975, 1742, 1688, 1389, 1303, 1257, 1176 cm^{-1}; Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.78; H, 9.04; N, 5.48.

The relative configuration of **2c** was determined as follows. All peaks in the above ^{1}H NMR spectrum were assigned with the ^{1}H–^{1}H COSY spectrum as shown in Figure S-1 (a). The ^{1}H{^{1}H}-NOE experiment of **2c** was summarized in Figure S-1 (b), indicating that the configuration is all-cis.

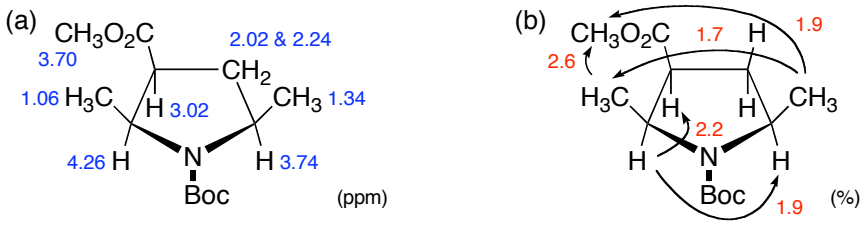
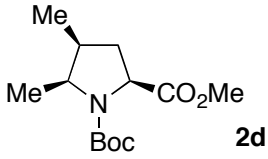


Figure S-1. Assignment of relative configuration of **2c**.

The enantiomeric excess of (–)-**2c** was determined to be 74% ee by HPLC analysis with Chiralcel OJ-H (4.6 mm ϕ × 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 230 nm detection, (–) t_1 = 11.4 min, (+) t_2 = 12.6 min.

Methyl (–)-*N*-(*tert*-Butoxycarbonyl)-4,5-dimethylpyrrolidine-2-carboxylate (2d) (Table 1, entry 3).



2d

The general procedure was followed with use of pyrrole **1d** (52.1 mg, 0.21 mmol). The crude product was purified with a MPLC (EtOAc/hexane = 1/3) after passed through a short silica gel column (EtOAc/hexane = 1/3) to give **2d** (45.1 mg, 85%) as colorless oil: $[\alpha]_D^{27}$ = –38.6 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.98 (d, *J* = 6.3 Hz, 3H), 1.13 and 1.10 (a pair of d, *J* = 6.7 Hz and *J* = 6.8 Hz, 3H), 1.40 and 1.46 (a pair of s, 9H), 1.54–1.71 (br m, 1H), 2.21–2.36 (m, 2H), 3.72 (s, 3H), 3.98 (a pair of quint, *J* = 6.7 Hz and *J* = 6.6 Hz, 1H), 4.15 and 4.21 (a pair of dd, *J* = 7.1, 10.1 Hz and *J* = 7.5, 9.9 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 13.8 and 13.9 (a pair of s), 14.0 and 14.5 (a pair of s), 28.3 and 28.4 (a pair of s), 35.7 and 36.3 (a pair of s), 36.1 and 35.3 (a pair of s), 51.8 and 52.0 (a pair of s), 56.7 and 56.9 (a pair of s), 59.4 and 58.9 (a pair of s), 79.65 and 79.60 (a pair of s), 153.2 and 154.0 (a pair of s), 174.0 and 173.7 (a pair of s); IR (neat) 2975, 1755, 1699, 1391, 1256, 1176, 1127 cm^{-1}; Anal. Calcd for $C_{13}H_{23}NO_4$: C, 60.68; H, 9.01; N, 5.44. Found: C, 60.64; H, 8.95; N, 5.42.

The relative configuration of **2d** was determined as follows. All peaks in the above ^{1}H NMR spectrum were assigned with the ^{1}H–^{1}H COSY spectrum as shown in Figure S-2 (a). The ^{1}H{^{1}H}-NOE experiment of **2d** was summarized in Figure S-2 (b), indicating that the configuration is all-cis.

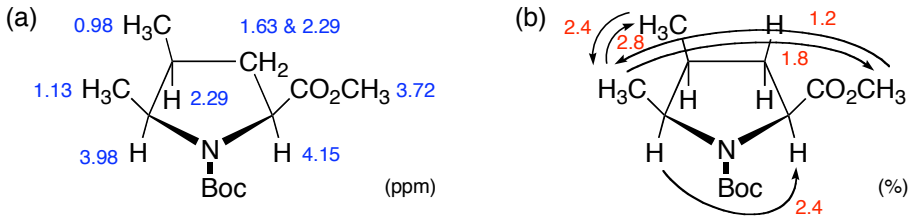
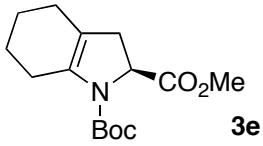


Figure S-2. Assignment of relative configuration of **2d**.

The enantiomeric excess of (–)-**2d** was determined to be 96% ee by capillary GC analysis with Chirasil-DEX CB (0.25 mm ϕ × 25 m, df = 0.25 μm): N_2, 33 cm/sec flow, at 130°C, (+) t_1 = 29.1 min, (–) t_2 = 31.0 min.

Methyl (*S*)-*N*-(*tert*-Butoxycarbonyl)-2,3,4,5,6,7-hexahydroindole-2-carboxylate (3e) (Table 1, entry 4).

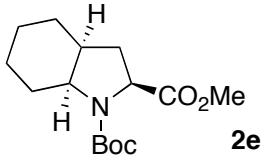


3e

The general procedure was followed with use of pyrrole **1e** (56.0 mg, 0.20 mmol). The crude product was purified with a MPLC (EtOAc/hexane = 1/3) after passed through a short silica gel column (EtOAc/hexane = 1/3) to give **3e** (39.2 mg, 70%) as a colorless solid and **2e** (4.6 mg, 8%). (–)-**3e**: $[\alpha]_D^{29}$ = –94.5 (*c* 1.02, $CHCl_3$); ^{1}H NMR (400 MHz, C_6D_6) δ 1.27–1.47 (m, 4H), 1.41 (s, 9H), 1.57–1.74 (m, 2H), 2.21 (br d, *J* = 15.5 Hz, 1H), 2.42 (br t, *J* = 13.7 Hz, 1H), 2.60–3.00 (br, 2H), 3.37 (s, 3H), 4.30–4.95 (br, 1H); ^{13}C {^{1}H} NMR (100 MHz, C_6D_6) δ 22.5, 23.0 (br s), 24.7, 25.1 (br s), 28.4, 36.4 (br s), 51.5, 59.4, 79.7 (br s), 112.7 (br s), 137.0 (br s), 151.6 (br s), 172.7; IR (thin film) 2933, 1759, 1715, 1686, 1402, 1150 cm^{-1}; Anal. Calcd for $C_{15}H_{23}NO_4$: C, 64.03; H, 8.24; N, 4.98. Found: C, 63.93; H, 8.18; N, 4.93.

The enantiomeric excess of (–)-**3e** was determined to be 95% ee by capillary GC analysis with Chirasil-DEX CB (0.25 mm ϕ × 25 m, df = 0.25 μm): N_2, 33 cm/sec flow, at 160°C, (*S*) t_1 = 33.3 min, (*R*) t_2 = 36.0 min. The diastereomeric and enantiomeric excesses of **2e** were determined to be 89% de, 91% ee (major), and 44% ee (minor) by capillary GC analysis with Chirasil-DEX CB (0.25 mm ϕ × 25 m, df = 0.25 μm): N_2, 33 cm/sec flow, at 150°C. Major diastereomer: (2*R*, 3a*R*, 7a*R*) t_1 = 47.4 min, (2*S*, 3a*S*, 7a*S*) t_2 = 49.7 min. Minor diastereomer: t_1 = 46.1 min, t_2 = 53.2 min.

The stereochemistry was assigned by the specific rotation of methyl *N*-(*tert*-butoxycarbonyl)-octahydroindole-2-carboxylate **2e**[12] derived from the hydrogenation product (–)-**3e**.



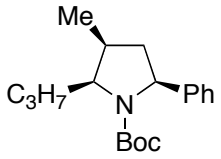
2e

Under nitrogen atmosphere, a mixture of (–)-**3e** (95% ee, 45.4 mg, 0.16 mmol) and 5% palladium on carbon (34 mg) was dissolved in dry MeOH in a test tube. The test tube was inserted into a nitrogen-filled

stainless steel autoclave, and the autoclave was sealed immediately. Hydrogen gas was introduced into the autoclave until the pressure gauge indicated over 50 atm, and then the pressure was carefully released to 1 atm. The inside of the autoclave was pressurized with hydrogen to 50 atm. The reaction mixture was vigorously stirred at room temperature for 24 h. The resulting suspension was filtered through a Celite pad and evaporated under reduced pressure. The residue was purified with a flash column chromatography (EtOAc/hexane = 1/4) to give **2e** (38.2 mg, 84%) as colorless oil: $[\alpha]^{25}_{D} = -36.8$ (*c* 1.02, $CHCl_3$), lit.[12] $[\alpha]_D^{22} = -32.7$ (*c* 1.21, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.08–1.52 (m, 4H), 1.40 and 1.45 (a pair of s, 9H), 1.54–1.75 (m, 3H), 1.91–2.18 (m, 3H), 2.23–2.37 (m, 1H), 3.67–3.87 (m, 1H), 3.73 (s, 3H), 4.19 and 4.26 (dd, *J* = 7.9, 9.7 Hz and *J* = 7.7, 10.1 Hz, 1H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 20.6 and 20.5 (a pair of s), 23.7 and 23.8 (a pair of s), 25.8 and 25.9 (a pair of s), 27.5 and 27.9 (a pair of s), 28.3 and 28.5 (a pair of s), 32.5 and 31.7 (a pair of s), 36.4 and 37.1 (a pair of s), 51.9 and 52.1 (a pair of s), 57.1 and 57.4 (a pair of s), 59.3 and 58.8 (a pair of s), 79.64 and 79.55 (a pair of s), 153.3 and 154.0 (a pair of s), 174.1 and 173.9 (a pair of s).

The specific rotation indicated the absolute configuration of (–)-**3e** to be *S*.

(–)-*N*-(*tert*-Butoxycarbonyl)-3-methyl-5-phenyl-2-propylpyrrolidine (2f) (Table 1, entry 5).

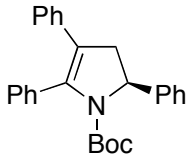


2f

The general procedure was followed with use of pyrrole **1f** (62 mg, 0.21 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/10) to give **2f** (60 mg, 96%) as colorless oil: $[\alpha]_D^{25} = -43.0$ (*c* 0.97, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 0.92–1.66 (m, 20H), 2.21–2.41 (m, 2H), 3.88–4.09 (br, 1H), 4.50–4.95 (br, 1H), 7.15–7.22 (m, 3H), 7.28 (t, *J* = 7.5 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 14.2, 14.6, 20.3 (br s), 28.1 (br s), 33.5 (br s), 36.4 (br s), 42.7 and 42.0 (a pair of br s), 61.2 (br s), 62.6 and 62.2 (a pair of br s), 78.9 (br s), 125.4 (br s), 126.2, 128.1 (br s), 145.5 and 144.9 (a pair of br s), 155.3 (br s); IR (neat) 2959, 1697, 1384, 1169 cm^{-1}; Anal. Calcd for $C_{19}H_{29}NO_2$: C, 75.21; H, 9.63; N, 4.62. Found: C, 75.29; H, 9.70; N, 4.58.

The enantiomeric excess of (–)-**2f** was determined to be 93% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 220 nm detection, (–) t_1 = 7.7 min, (+) t_2 = 8.8 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-2,3,5-triphenyl-4,5-dihydropyrrole (3g) (Table 1, entry 6).

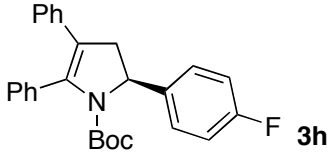


3g

The general procedure was followed with use of pyrrole **1g** (80.1 mg, 0.20 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/3) to give **3g** (80.6 mg, >99%) as a colorless solid: $[\alpha]_D^{28}$ = –300.8 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.08 (s, 9H), 2.71 (dd, *J* = 2.4, 15.6 Hz, 1H), 3.89 (dd, *J* = 10.5, 15.6 Hz, 1H), 5.43 (dd, *J* = 2.4, 10.5 Hz, 1H), 6.91–6.95 (m, 2H), 7.02–7.12 (m, 3H), 7.26 (t, *J* = 7.3 Hz, 1H), 7.30–7.38 (m, 7H), 7.46 (d, *J* = 7.5 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.8, 41.8, 61.5, 80.2, 119.0, 125.5, 126.0, 127.1, 127.2, 127.8, 127.9, 128.2, 128.7, 129.0, 134.6, 136.0, 137.8, 144.3, 152.7; IR (thin film) 2977, 1692, 1387, 1366, 1167 cm^{-1}; HRMS (FAB) Calcd for $C_{27}H_{27}NO_2$: 397.2042. Found: *m*/*z* = 397.2031 M^+.

The enantiomeric excess of (*S*)-**3g** was determined to be 99.7% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 254 nm detection, (+) t_1 = 11.0 min, (–) t_2 = 17.2 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-5-(4-fluorophenyl)-2,3-diphenyl-4,5-dihydropyrrole (3h) (Table 1 entry 7).

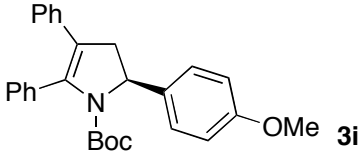


3h

The general procedure was followed with use of pyrrole **1h** (82.4 mg, 0.20 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/3) to give **3h** (82.0 mg, 99%) as a colorless solid: $[\alpha]_D^{25}$ = –207.5 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.08 (s, 9H), 2.67 (dd, *J* = 2.3, 15.7 Hz, 1H), 3.87 (dd, *J* = 10.5, 15.7 Hz, 1H), 5.41 (dd, *J* = 2.3, 10.5 Hz, 1H), 6.91–6.95 (m, 2H), 7.01–7.12 (m, 5H), 7.28–7.34 (m, 5H), 7.46 (dd, *J* = 5.4, 8.5 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.7, 41.7, 60.8, 80.3, 115.4 (d, *J* = 21 Hz), 118.9, 126.1, 127.0, 127.1 (d, *J* = 8 Hz), 127.8, 127.9, 128.2, 128.9, 134.4, 135.8, 137.6, 140.1 (d, *J* = 3 Hz), 152.7, 162.0 (d, *J* = 245 Hz); IR (thin film) 2975, 1509, 1692, 1388, 1157 cm^{-1}; Anal. Calcd for $C_{27}H_{26}NO_2F$: C, 78.05; H, 6.31; N, 3.37. Found: C, 78.14; H, 6.40; N, 3.37.

The enantiomeric excess of (*S*)-**3h** was determined to be 99.3% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 306 nm detection, (+) t_1 = 8.9 min, (–) t_2 = 13.8 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-5-(4-methoxyphenyl)-2,3-diphenyl-4,5-dihydropyrrole (3i) (Table 1 entry 8).



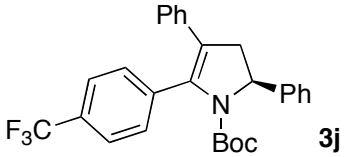
3i

The general procedure was followed with use of pyrrole **1i** (86.2 mg, 0.2026 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/3) to give **3i** (82.9 mg, 96%) as a colorless solid: $[\alpha]_D^{26}$ = –230.4 (*c* 1.01, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.08 (s, 9H), 2.68 (dd, *J* = 2.2,

15.6 Hz, 1H), 3.78 (s, 3H), 3.85 (dd, J = 10.3, 15.6 Hz, 1H), 5.38 (dd, J = 2.2, 10.3 Hz, 1H), 6.89 (d, J = 8.6 Hz, 2H), 6.91–6.95 (m, 2H), 7.01–7.11 (m, 3H), 7.27–7.33 (m, 5H), 7.39 (d, J = 8.6 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.8, 41.7, 55.2, 61.0, 80.1, 114.0, 119.1, 125.9, 126.7, 127.0, 127.7, 127.8, 128.1, 128.9, 134.6, 136.0, 136.5, 137.6, 152.7, 158.7; IR (thin film) 2974, 1691, 1513, 1388, 1248, 1173 cm^{-1}; Anal. Calcd for $C_{28}H_{29}NO_3$: C, 78.66; H, 6.84; N, 3.28. Found: C, 78.76; H, 6.89; N, 3.30.

The enantiomeric excess of (*S*)-**3i** was determined to be 98% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 2% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 305 nm detection, (+) t_1 = 11.7 min, (–) t_2 = 18.0 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-2-[4-(trifluoromethyl)phenyl]-3,5-diphenyl-4,5-dihydropyrrole (3j) (Table 1 entry 9).

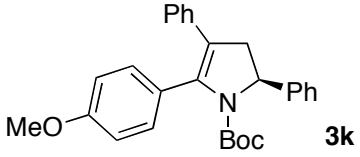


3j

The general procedure was followed with use of pyrrole **1j** (92.7 mg, 0.20 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/5) to give **3j** (93.4 mg, >99%) as a colorless solid: $[\alpha]_D^{26}$ = –232.5 (*c* 1.00, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.09 (s, 9H), 2.75 (dd, J = 2.4, 15.9 Hz, 1H), 3.89 (dd, J = 10.5, 15.9 Hz, 1H), 5.43 (dd, J = 2.4, 10.5 Hz, 1H), 6.90–6.98 (m, 2H), 7.06–7.15 (m, 3H), 7.24–7.31 (m, 1H), 7.34 (t, J = 7.5 Hz, 2H), 7.41–7.47 (m, 4H), 7.58 (d, J = 8.1 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.8, 42.1, 61.6, 80.7, 121.0, 124.1 (q, J = 272 Hz), 125.0 (q, J = 4 Hz), 125.4, 126.6, 127.2, 127.4, 128.1, 128.8, 129.4, 129.7 (q, J = 32 Hz), 135.3, 136.1, 138.3, 144.0, 152.7; IR (thin film) 2978, 1698, 1378, 1327, 1165 cm^{-1}; Anal. Calcd for $C_{28}H_{26}NO_2F_3$: C, 72.24; H, 5.63; N, 3.01. Found: C, 72.13; H, 5.69; N, 3.01.

The enantiomeric excess of (*S*)-**3j** was determined to be 99.6% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 306 nm detection, (+) t_1 = 8.3 min, (–) t_2 = 9.3 min.

(–)-*N*-(*tert*-Butoxycarbonyl)-2-(4-methoxyphenyl)-3,5-diphenyl-4,5-dihydropyrrole (3k) (Table 1 entry 10).



3k

The general procedure was followed with use of pyrrole **1k** (84.8 mg, 0.20 mmol). The crude product was purified with a short silica gel column (EtOAc/hexane = 1/5) to give **3k** (82.3 mg, 97%) as a colorless solid: $[\alpha]_D^{25}$ = –238.0 (*c* 0.99, $CHCl_3$); ^{1}H NMR (400 MHz, $CDCl_3$, TMS) δ 1.12 (s, 9H), 2.69 (dd, J = 2.4, 15.5 Hz, 1H), 3.83 (s, 3H), 3.85 (dd, J = 10.5, 15.5 Hz, 1H), 5.40 (dd, J = 2.4, 10.5 Hz, 1H), 6.87 (d, J = 8.7

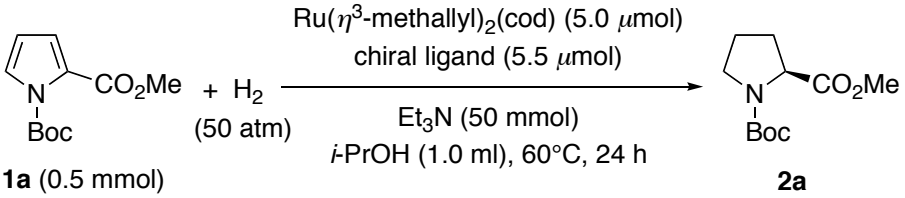
Hz, 2H), 6.93–6.97 (m, 2H), 7.04 (t, J = 7.2 Hz, 1H), 7.10 (t, J = 7.3 Hz, 2H), 7.23–7.28 (m, 3H), 7.35 (t, J = 7.6 Hz, 2H), 7.44 (d, J = 7.3 Hz, 2H); ^{13}C {^{1}H} NMR (100 MHz, $CDCl_3$) δ 27.9, 41.7, 55.2, 61.4, 80.1, 113.6, 118.4, 125.5, 125.9, 126.8, 127.0, 127.1, 127.9, 128.6, 130.2, 136.2, 137.6, 144.4, 152.7, 159.2; IR (thin film) 2974, 1690, 1387, 1247, 1173 cm^{-1}; HRMS (FAB) Calcd for $C_{28}H_{29}NO_3$: 427.2147. Found: m/z = 427.2181 M^+.

The enantiomeric excess of (*S*)-**3k** was determined to be 99.2% ee by HPLC analysis with Chiralpak AD-H (4.6 mm ϕ × 250 mm): 4% 2-propanol in hexane, 0.5 ml/min flow, at 35°C, UV 305 nm detection, (+) t_1 = 12.7 min, (–) t_2 = 16.3 min.

Evaluation of Various Chiral Ligands on the Asymmetric Hydrogenation of 1a. (note 15)

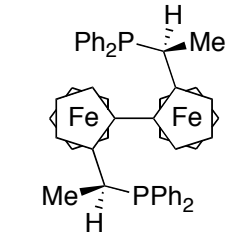
Asymmetric induction of each chiral ligand was evaluated by following the procedure for eq 1. Chiral ligands (5.5 mmol) were used in place of (*S*,*S*)-(*R*,*R*)-PhTRAP. The result of the ligand screening was summarized in Table S-1.

Table S-1. Screening of Chiral Ligands.

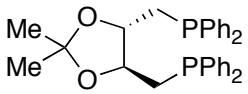


1a (0.5 mmol) **2a**

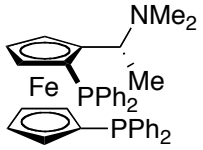
entry	ligand	convn, %	ee, %	entry	ligand	convn, %	ee, %
1	(*S*,*S*)-(*R*,*R*)-PhTRAP	100	79 (*S*)	9	**L2**	100	2 (*R*)
2	(2*S*,3*S*)-DIOP	100	1 (*S*)	10	**L3**	35	3 (*R*)
3	(*R*)-(*S*)-BPPFA	100	0	11	**L4**	100	2 (*R*)
4	(*R*)-PHANEPHOS	100	0	12	**L5**	7	3 (*R*)
5	(2*S*,3*S*)-CHIRAPHOS	100	0	13	**L6**	0	–
6	(*R*)-BINAP	57	1 (*S*)	14	**L7**	7	1 (*S*)
7	(*R*,*R*)-Me-DuPHOS	48	39 (*S*)	15	**L8**	34	2 (*S*)
8	**L1**	5	3 (*S*)				



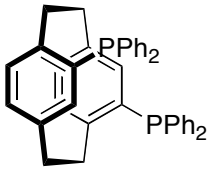
(*S*,*S*)-(*R*,*R*)-PhTRAP



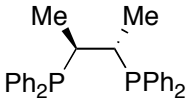
(2*S*,3*S*)-DIOP



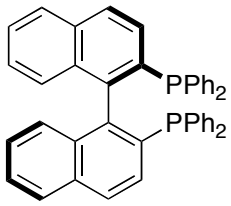
(*R*)-(*S*)-BPPFA



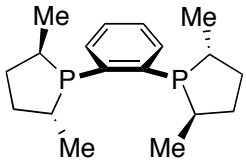
(*R*)-PHANEPHOS



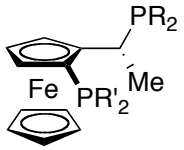
(2*S*,3*S*)-CHIRAPHOS



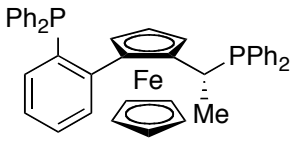
(*R*)-BINAP



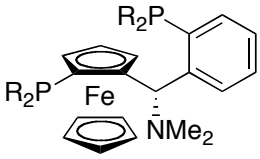
(*R*,*R*)-Me-DuPHOS



L1: R = R' = *c*-C_6H_{11}
L2: R = *c*-C_6H_{11}, R' = Ph
L3: R = *t*-Bu, R' = Ph
L4: R = 3,5-$Me_2C_6H_3$-, R' = Ph



L5



L6: R = Ph
L7: R = *c*-C_6H_{11}
L8: R = 3,5-Me_2-4-$MeOC_6H_2$

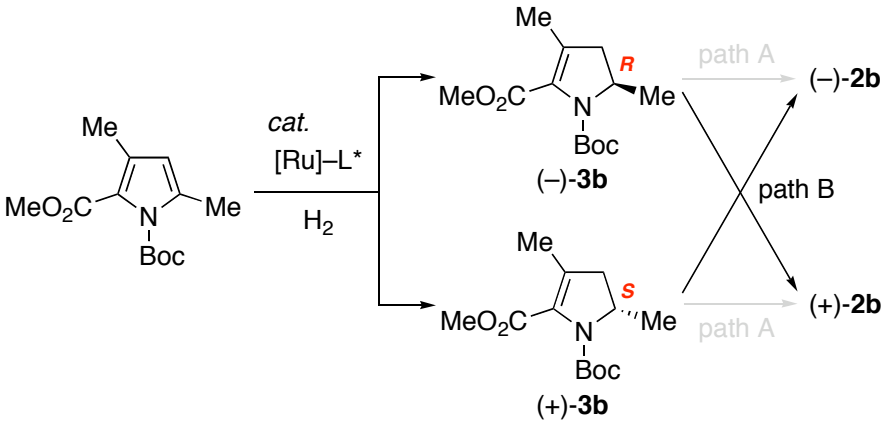
Estimation of the Enantioselelctivity in the Transformation of 1b into 3b. (note 15)

The net enantioselectivity was estimated as follows. Compositions of **1b**, **2b**, and **3b** in the reaction mixtures at 6 and 24 h were calculated from eq 2 and summarized in Table S-2. The stereoselectivity in the first transformation of **1b** into **3b** would equal $\{(a+c)–(b+d)\}/\{(a+c)+(b+d)\}\times100$ = 41% ee (–) (average) when (–)-**3b** was presumed to give (–)-**2b** through the second hydrogenation (path A, Scheme S-1). Alternatively, it would be $\{(a+d)–(b+c)\}/\{(a+d)+(b+c)\} \times 100$ = 28% ee (–) (average) when (–)-**2b** was obtained from (+)-**3b** (path B). In the former case, the enantiomeric excess of **2b** must be close to 41% ee (–) as the fully hydrogenated product increased. The ee value of **2b**, however, got away from 41% ee (–) over time according to our observation. Consequently, the formation of **2b** from **3b** proceeded through path B. The virtual stereoselectivity of the first step was estimated to be 28% ee (–).

Table S-2. Compositions of each compound.

	composition, %[a]				
time	**1b**	(–)-**3b** (*a*)	(+)-**3b** (*b*)	(–)-**2b** (*c*)	(+)-**2b** (*d*)
6 h	27	38.7	13.3	13.2	7.8
24 h	0	40.3	5.7	30.0	24.0

[a] Compositions of each compound were determined by ^{1}H NMR spectra of the reaction mixture.



Scheme S-1. Two possible pathways to the formation of **2b**.

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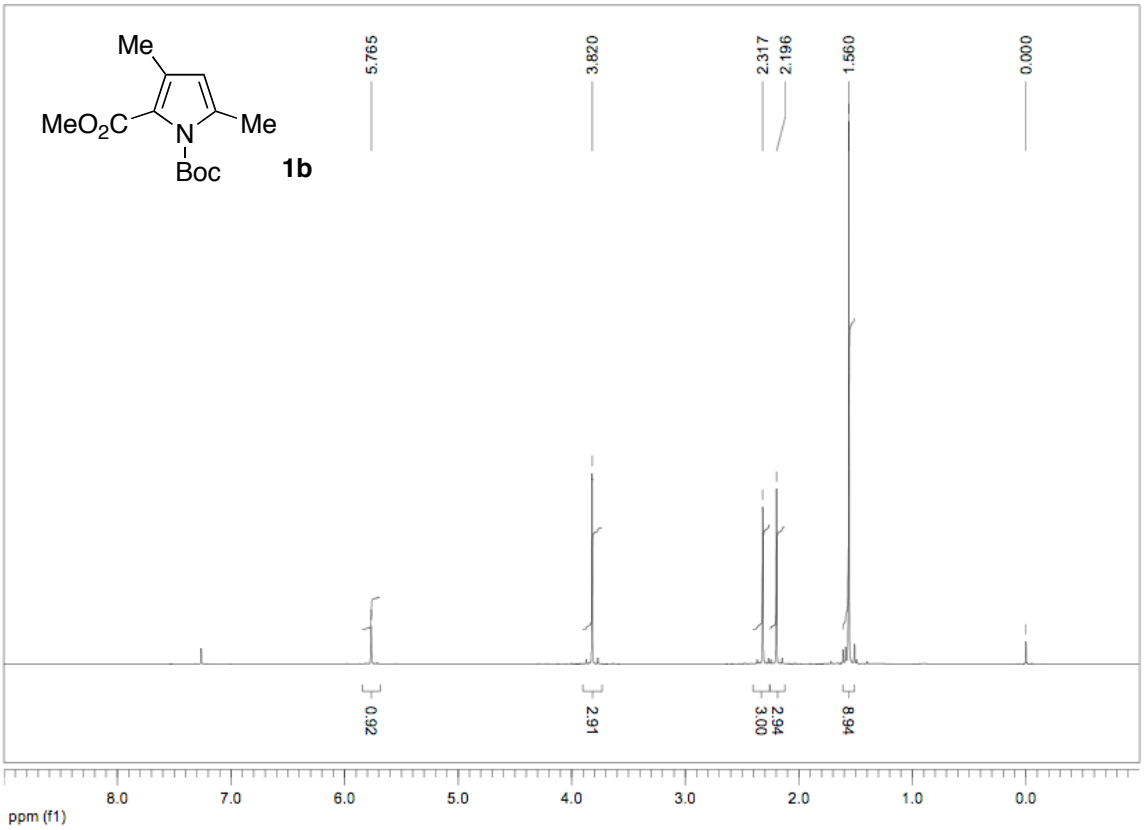

Figure S-3. ^{1}H NMR spectrum of **1b**.

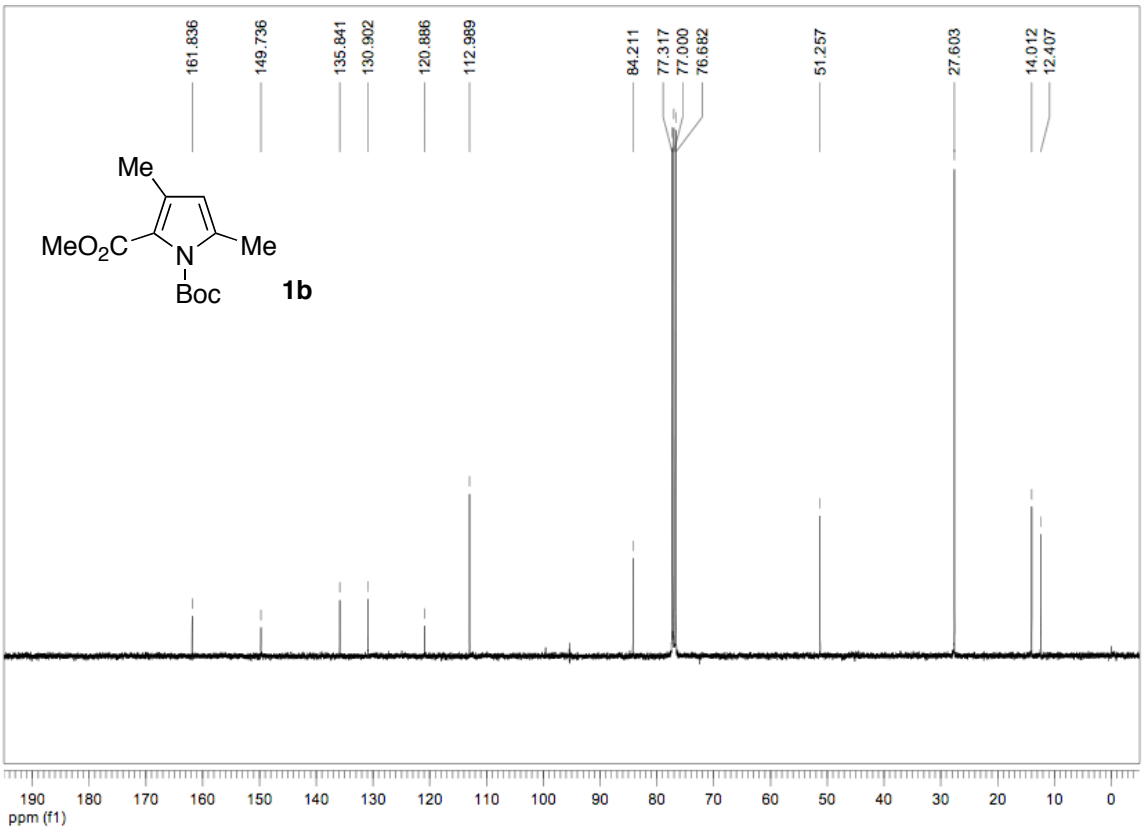

Figure S-4. ^{13}C {^{1}H} NMR spectrum of **1b**.

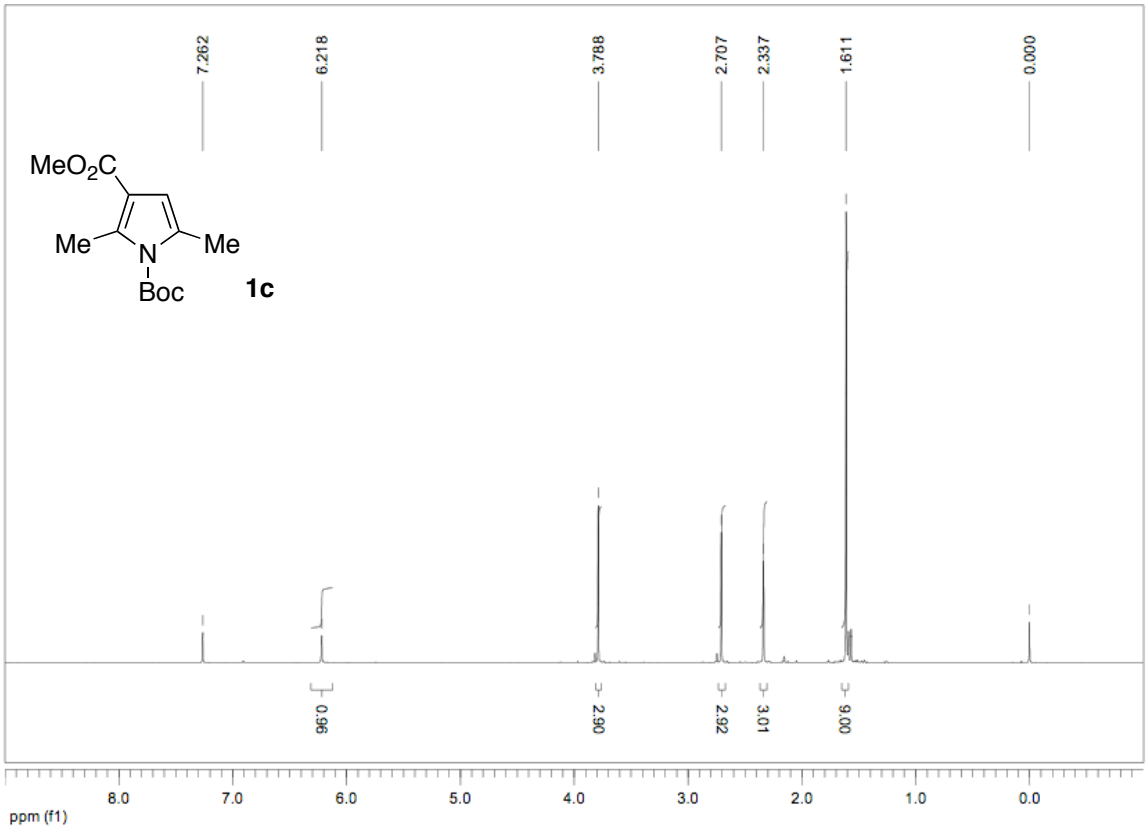

Figure S-5. ^{1}H NMR spectrum of **1c**.

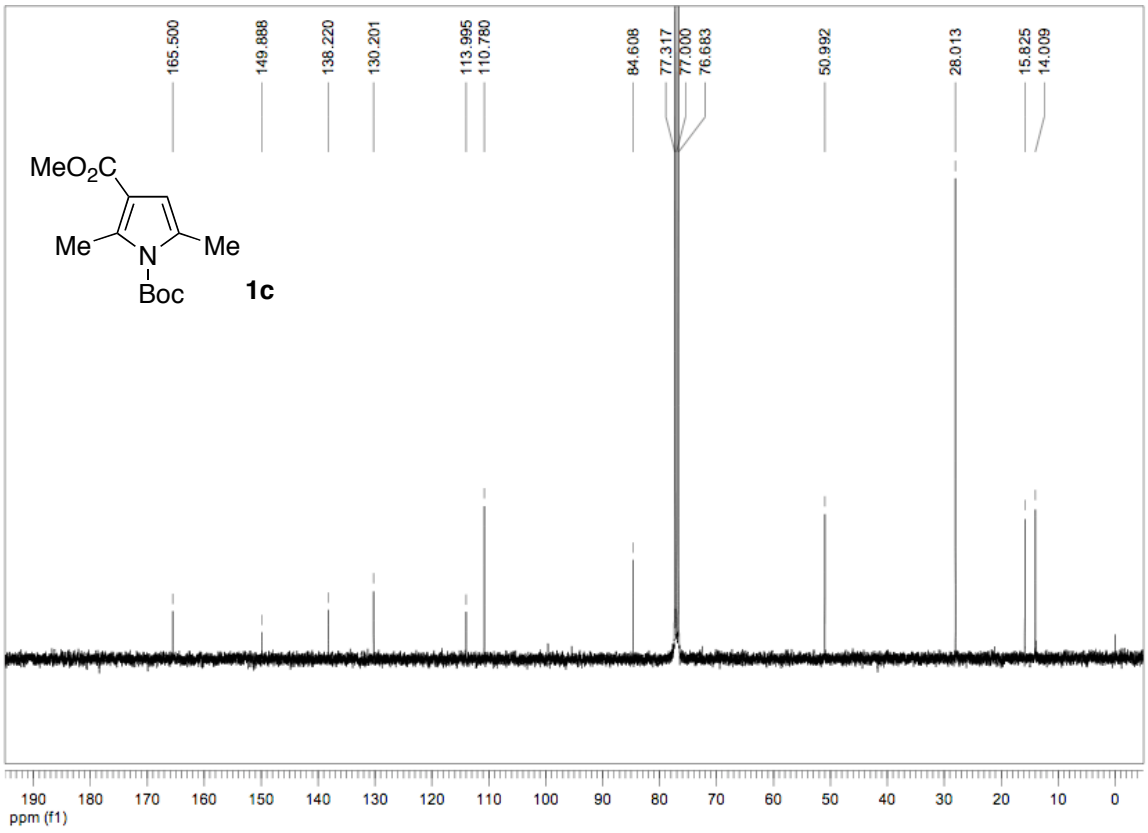

Figure S-6. ^{13}C {^{1}H} NMR spectrum of **1c**.

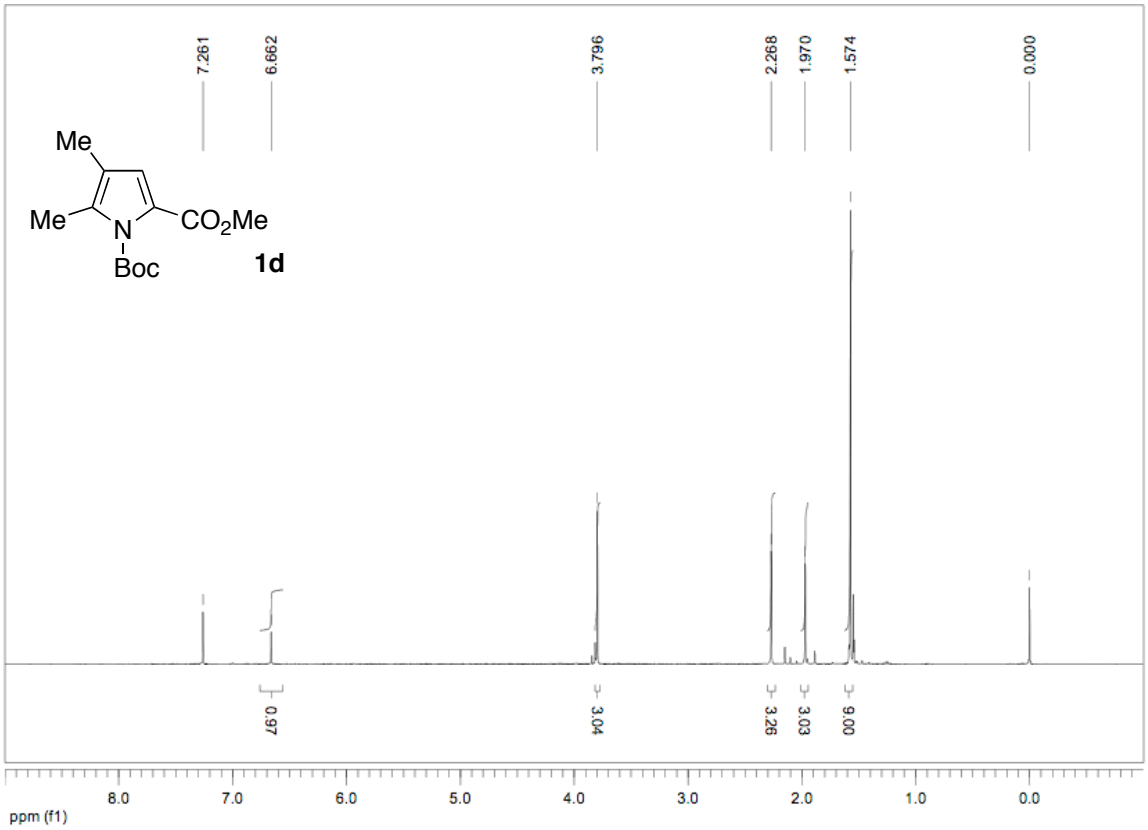

Figure S-7. ^{1}H NMR spectrum of **1d**.

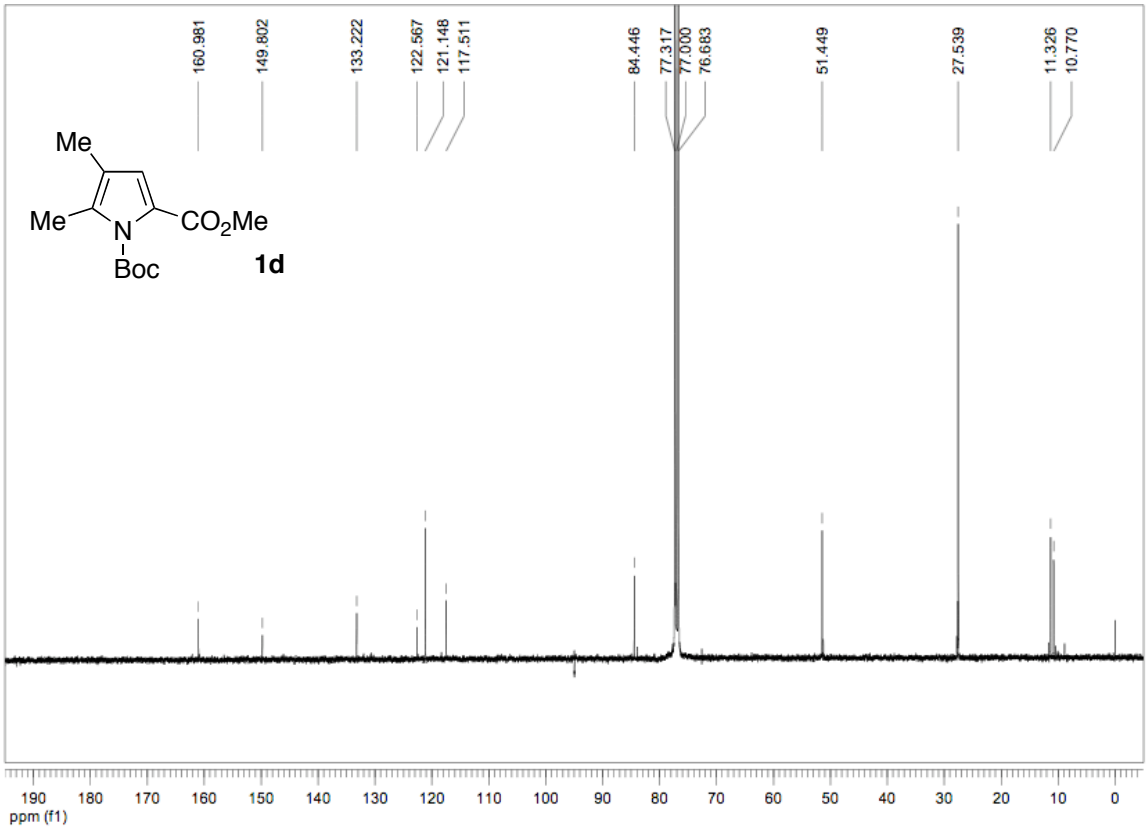

Figure S-8. ^{13}C {^{1}H} NMR spectrum of **1d**.

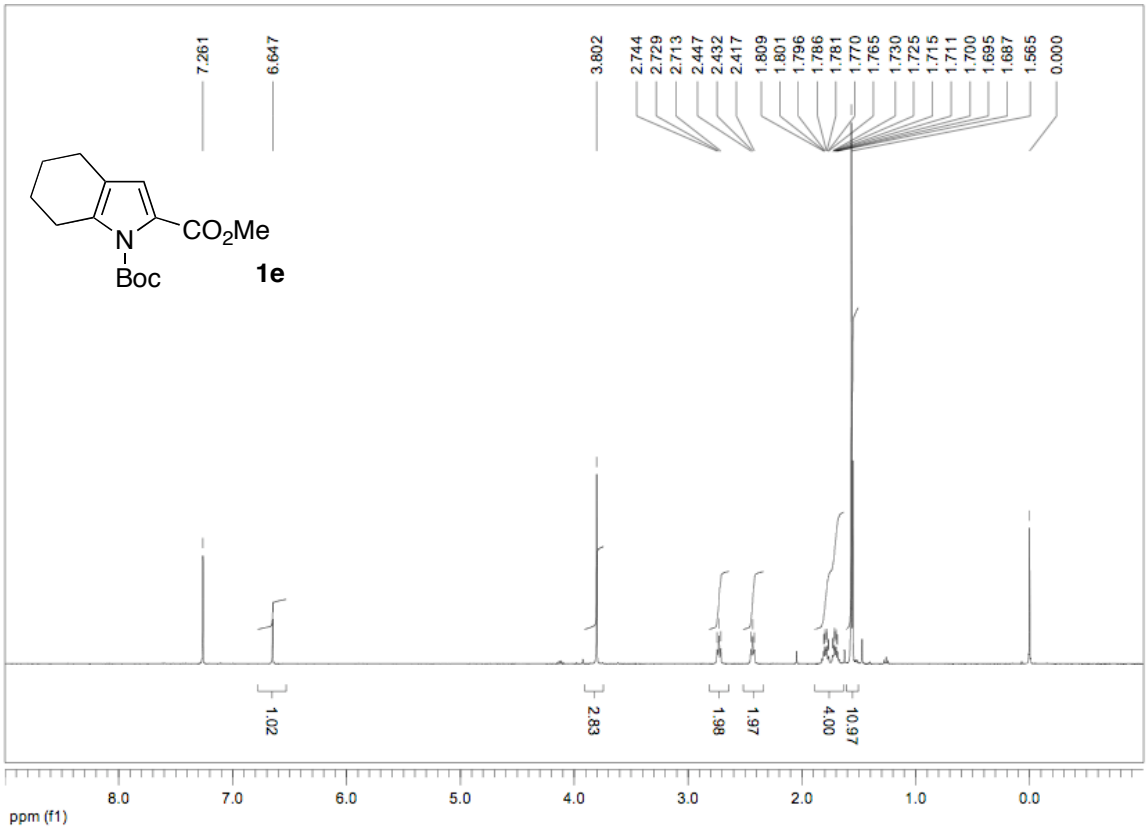

Figure S-9. ^{1}H NMR spectrum of **1e**.

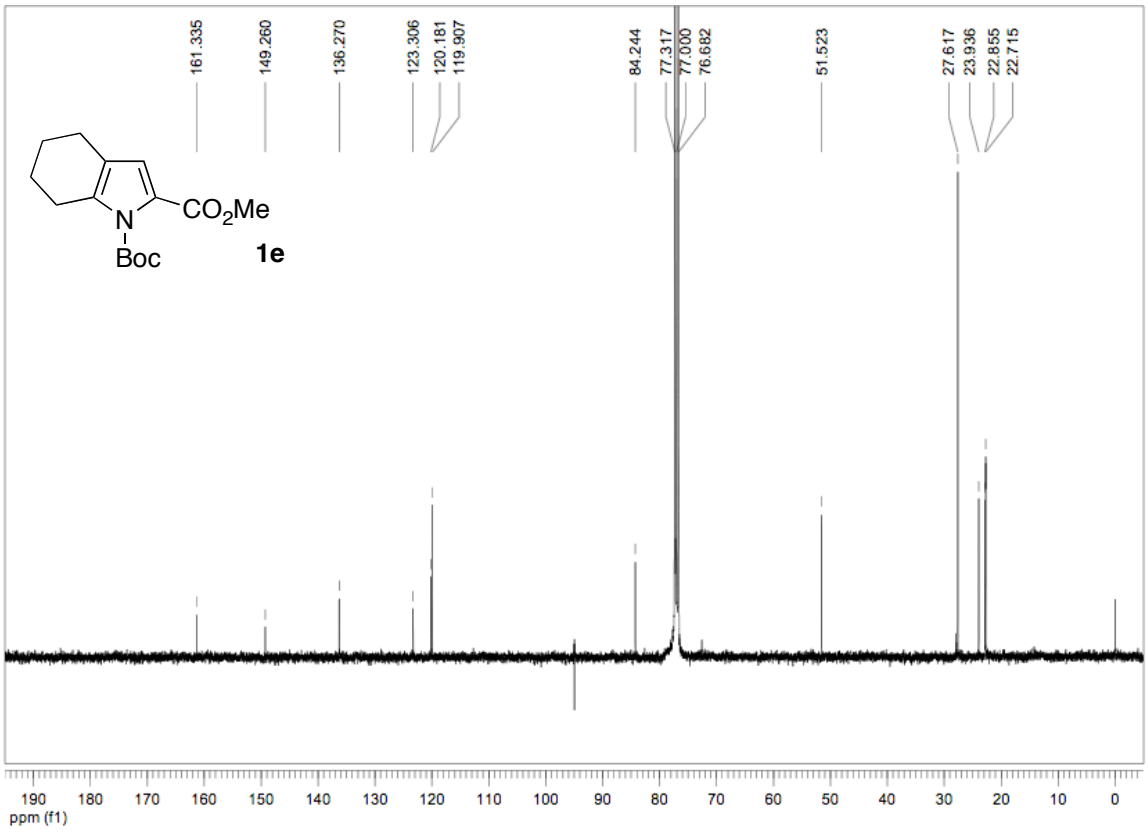

Figure S-10. ^{13}C {^{1}H} NMR spectrum of **1e**.

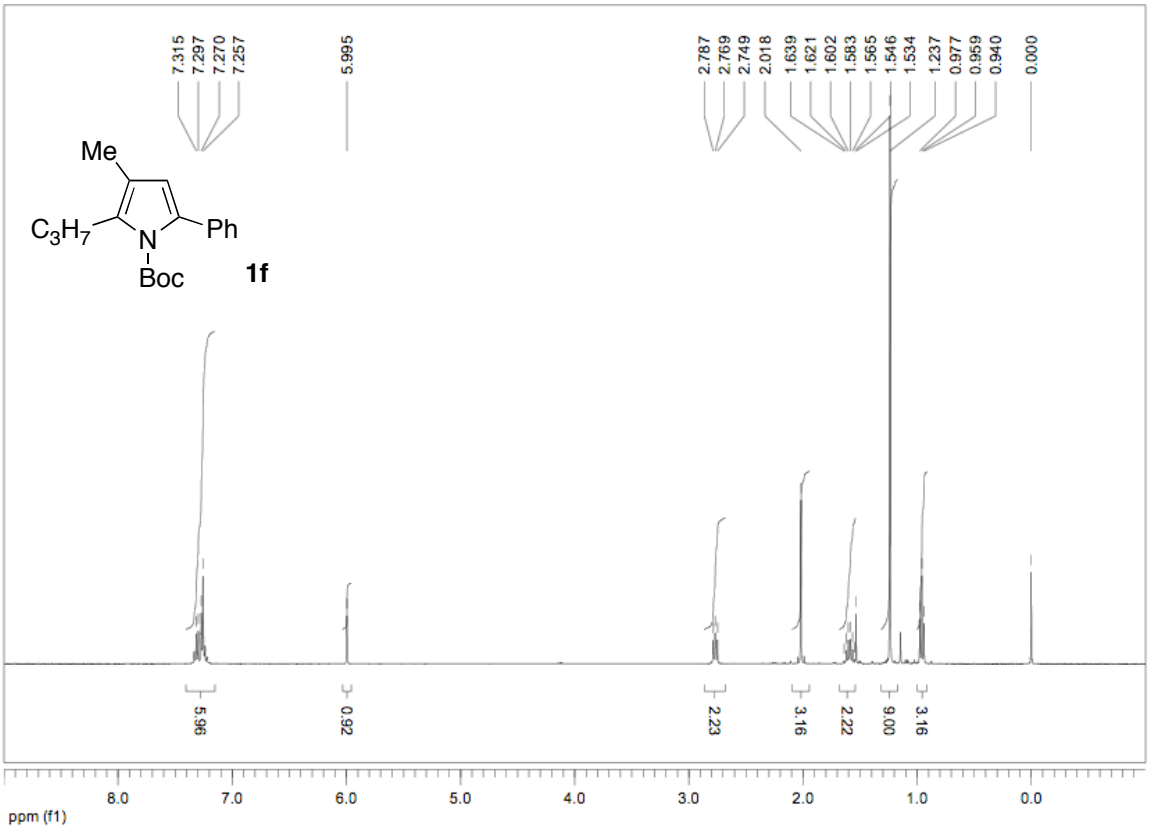

Figure S-11. ^{1}H NMR spectrum of **1f**.

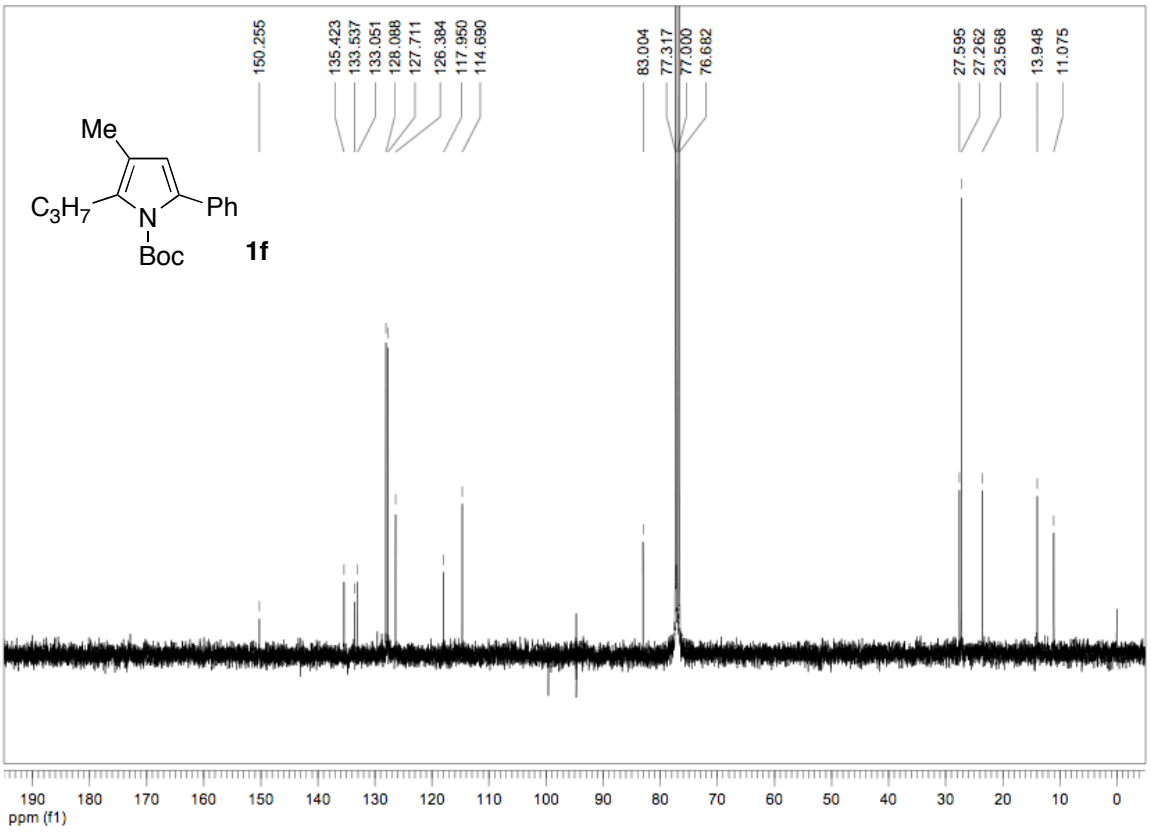

Figure S-12. ^{13}C {^{1}H} NMR spectrum of **1f**.

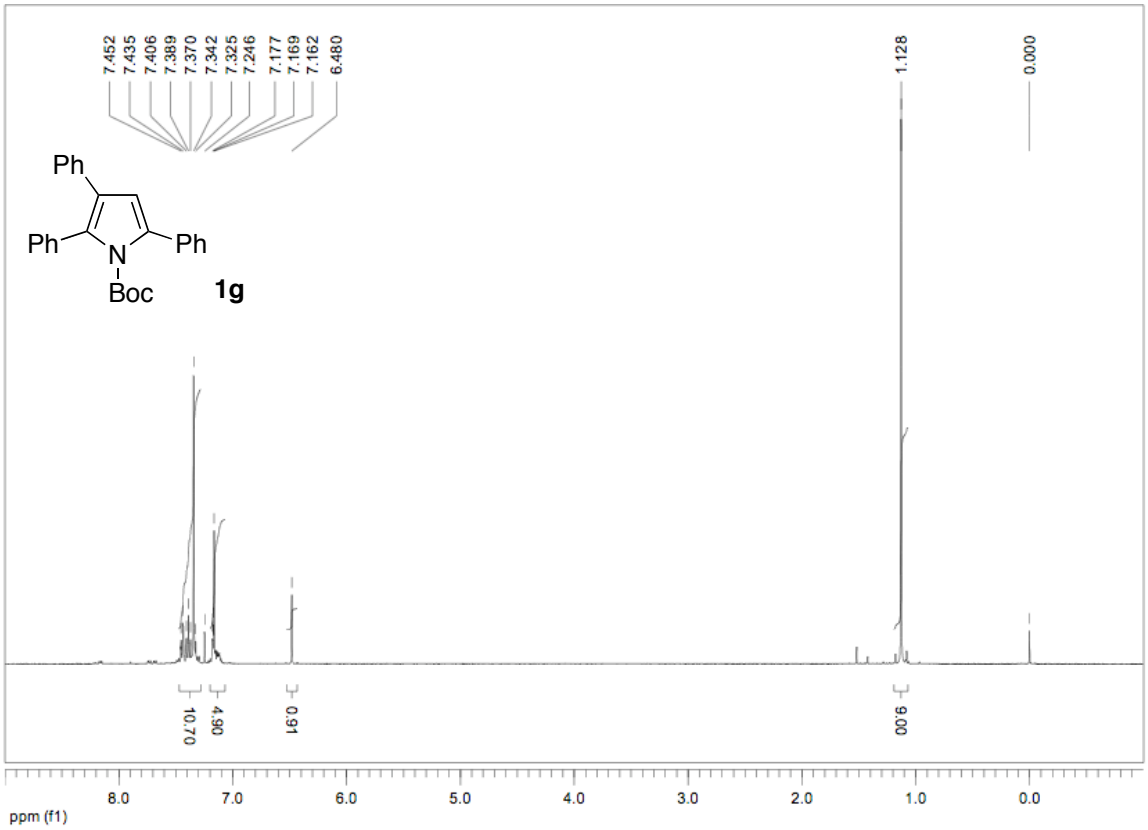

Figure S-13. ^{1}H NMR spectrum of **1g**.

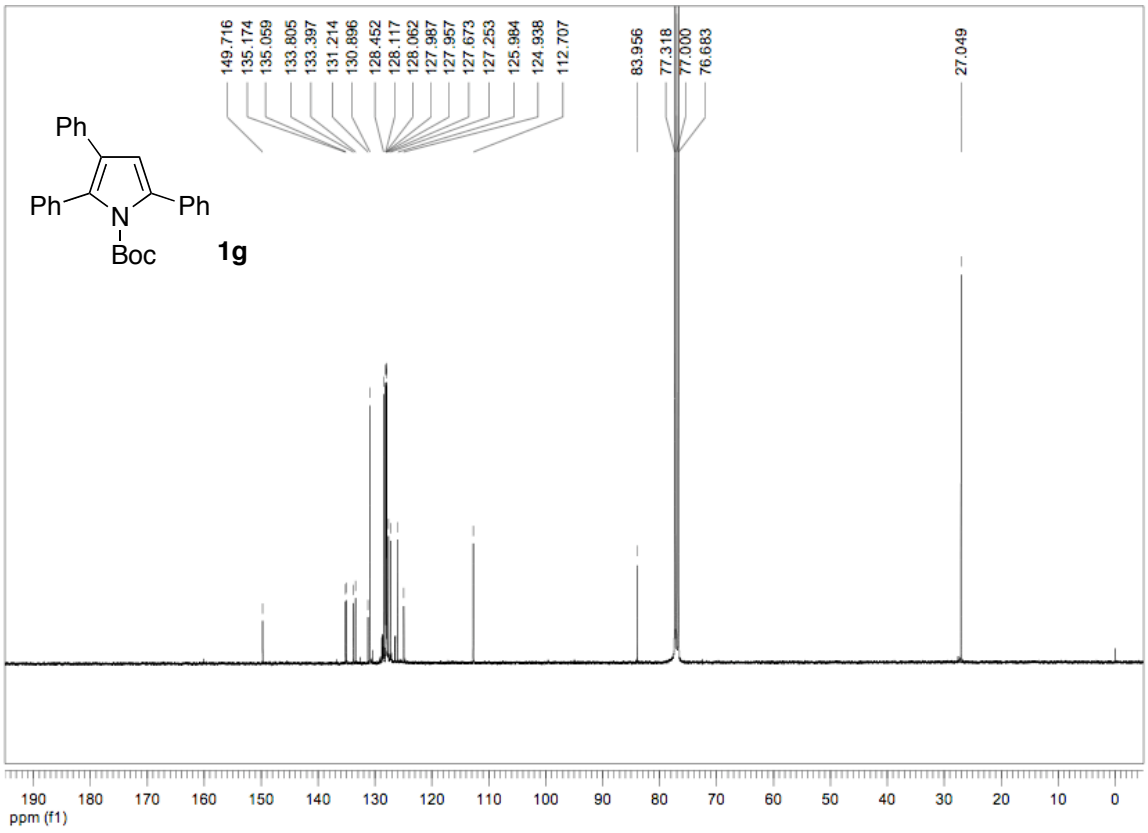

Figure S-14. ^{13}C {^{1}H} NMR spectrum of **1g**.

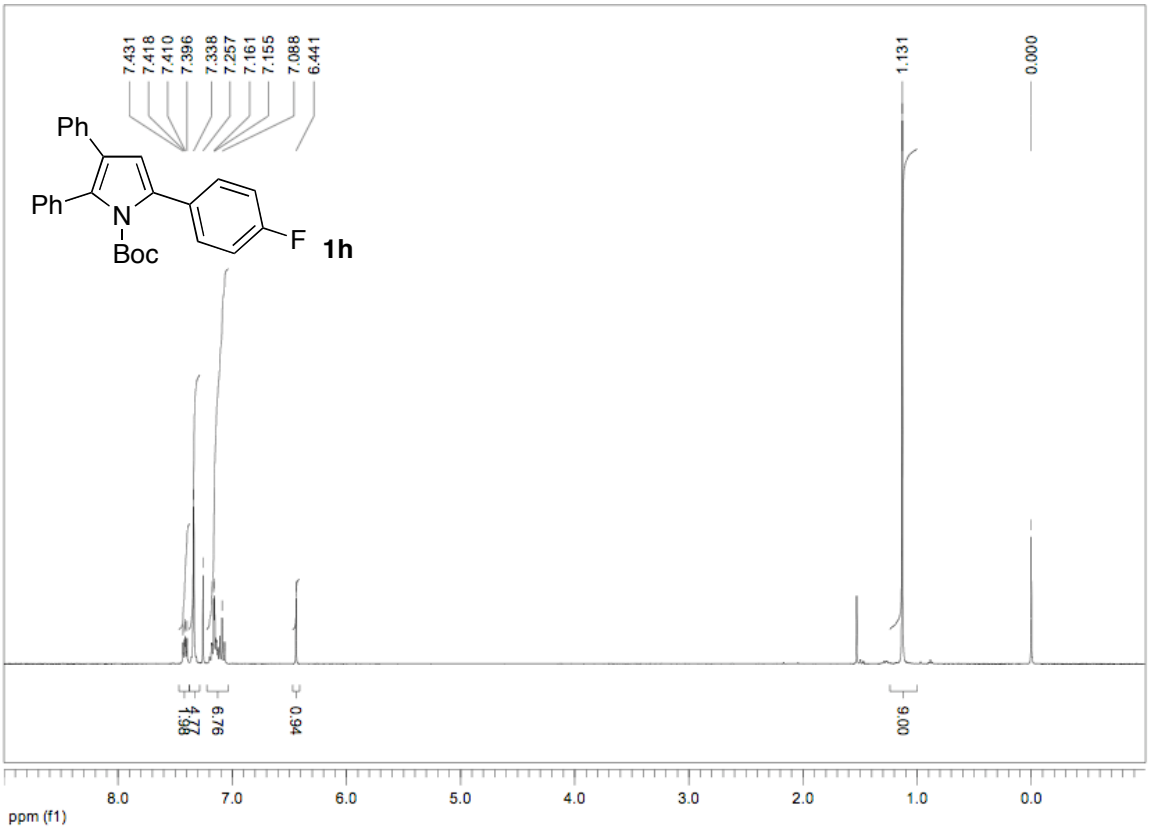

Figure S-15. ^{1}H NMR spectrum of **1h**.

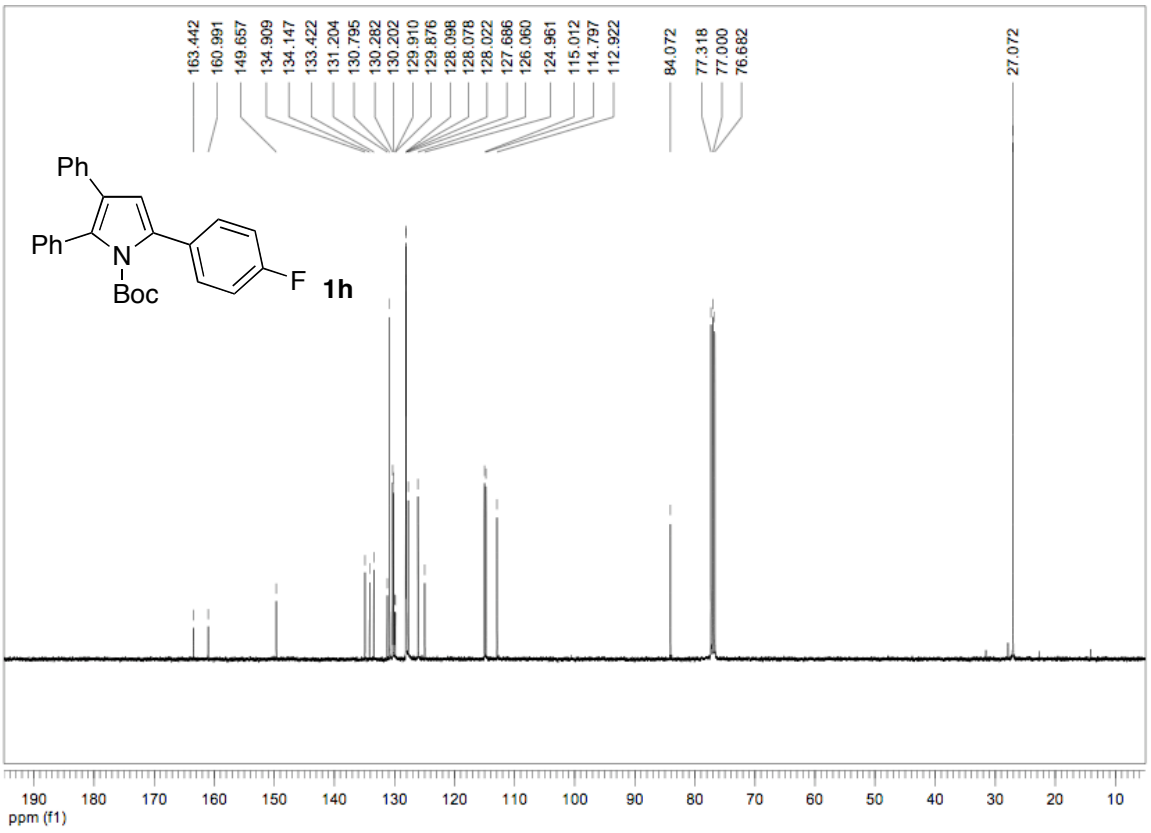

Figure S-16. ^{13}C {^{1}H} NMR spectrum of **1h**.

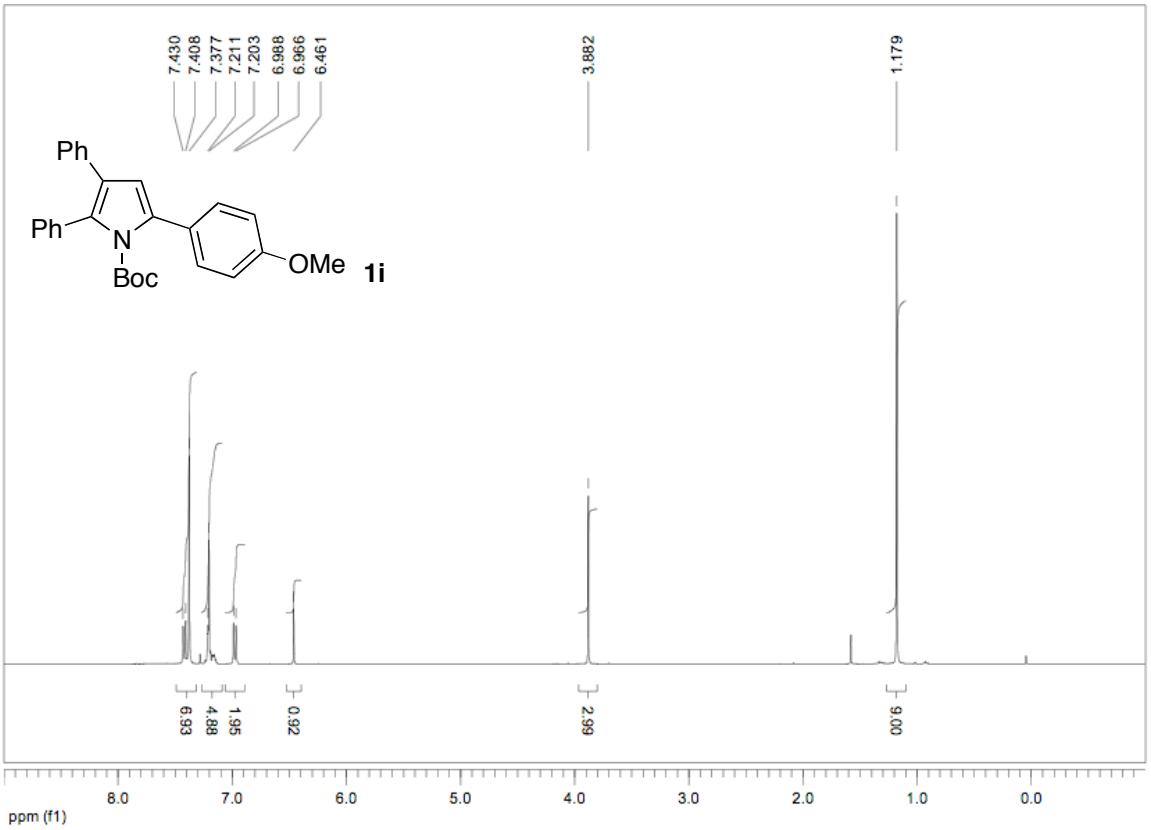

Figure S-17. ^{1}H NMR spectrum of **1i**.

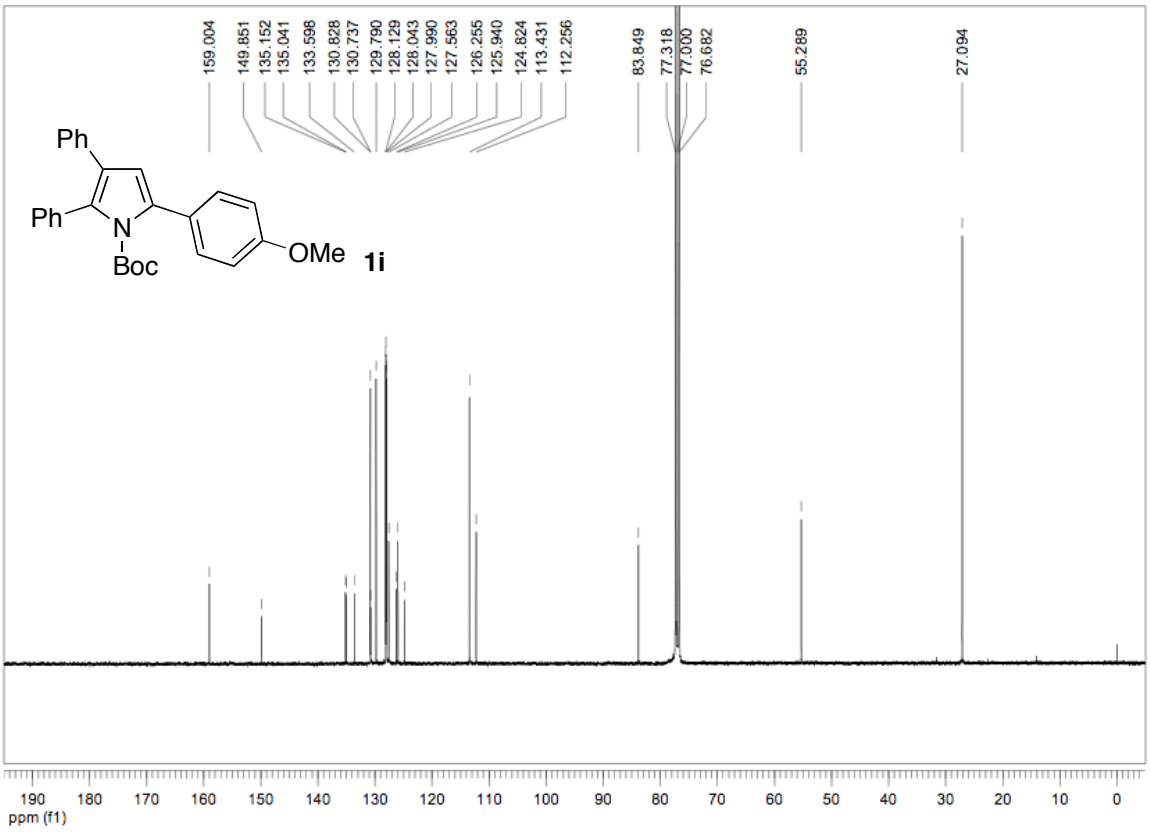

Figure S-18. ^{13}C {^{1}H} NMR spectrum of **1i**.

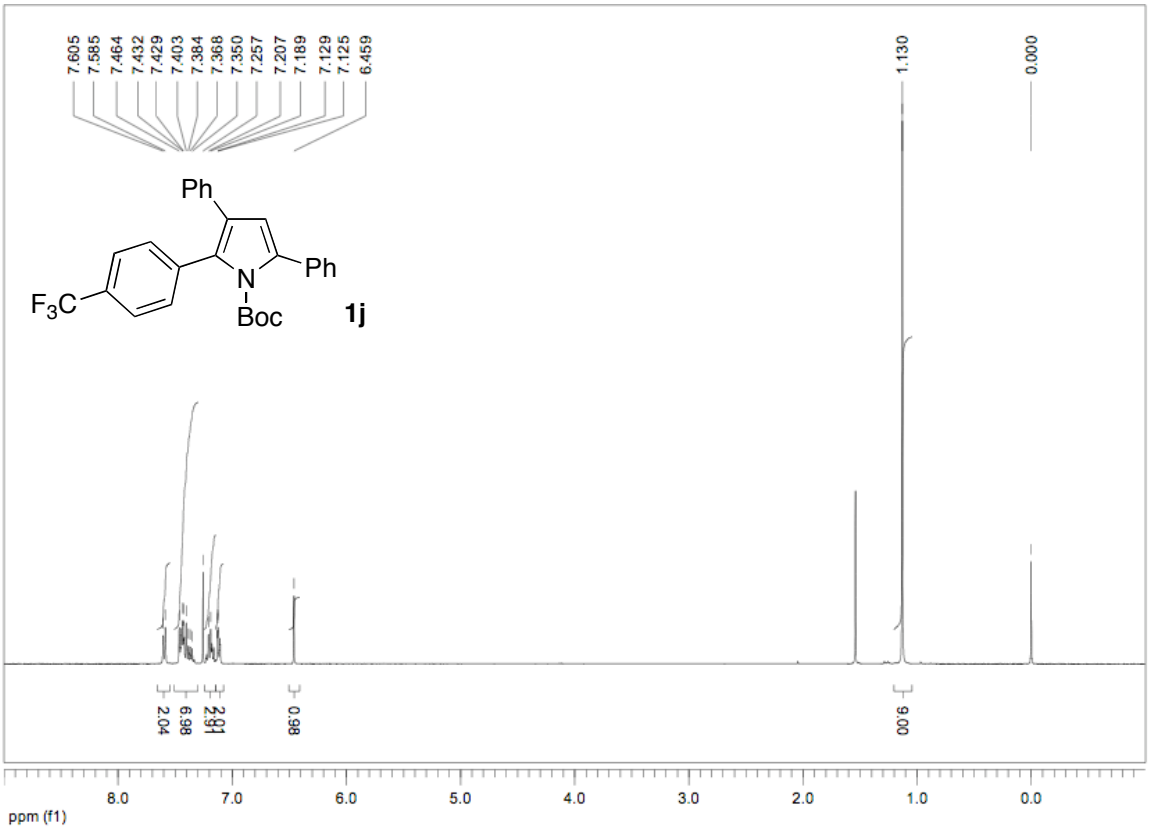

Figure S-19. ^{1}H NMR spectrum of **1j**.

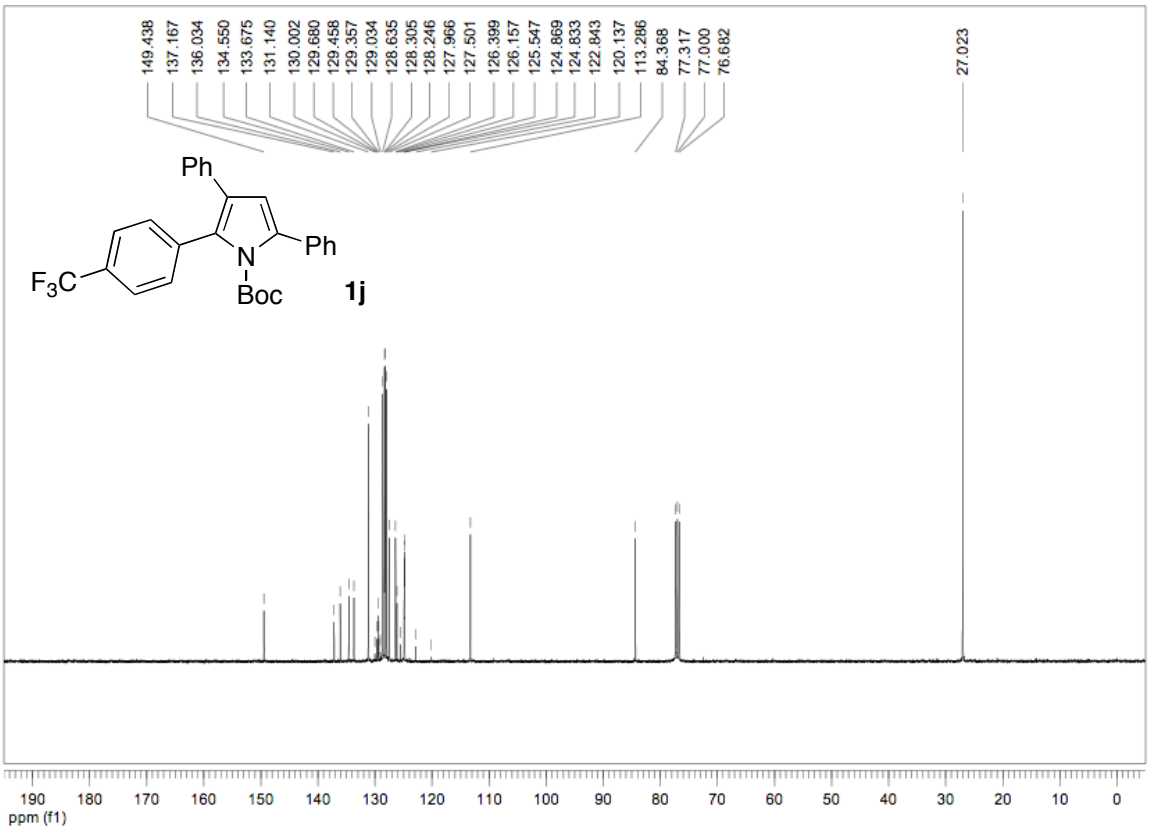

Figure S-20. ^{13}C {^{1}H} NMR spectrum of **1j**.

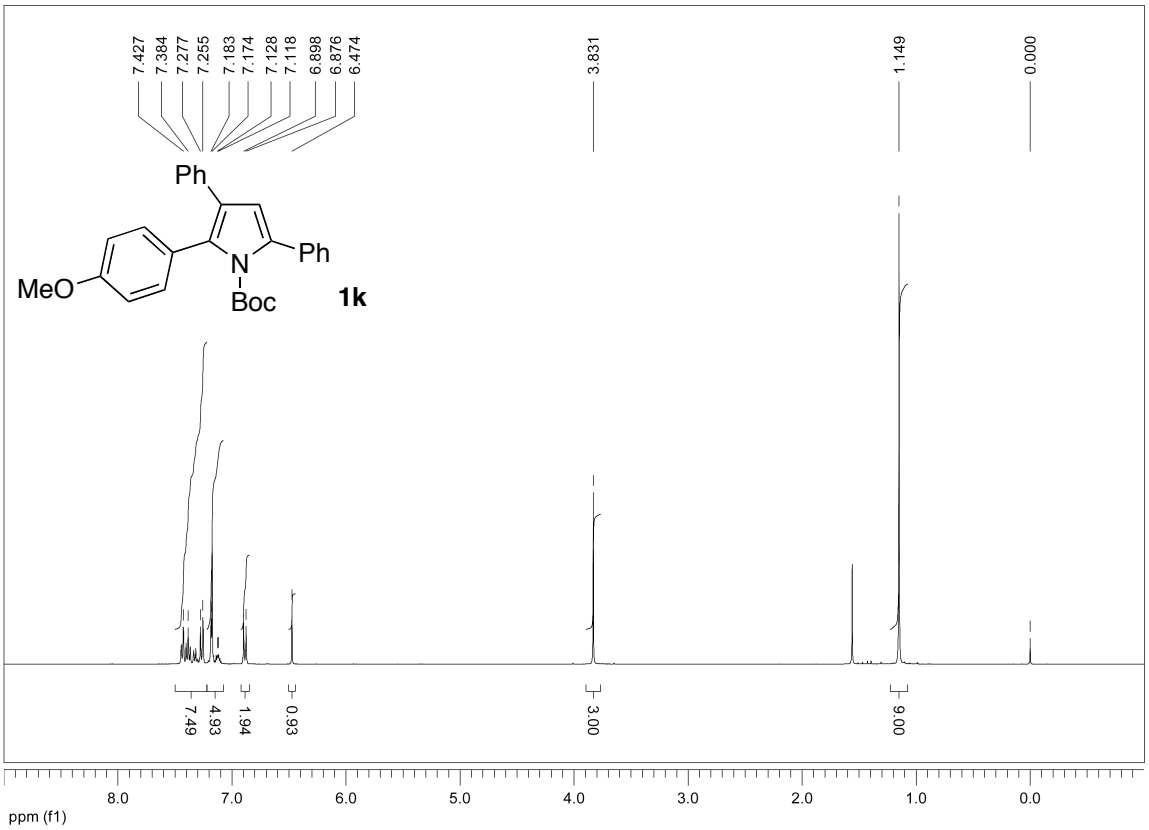

Figure S-21. ^{1}H NMR spectrum of **1k**.

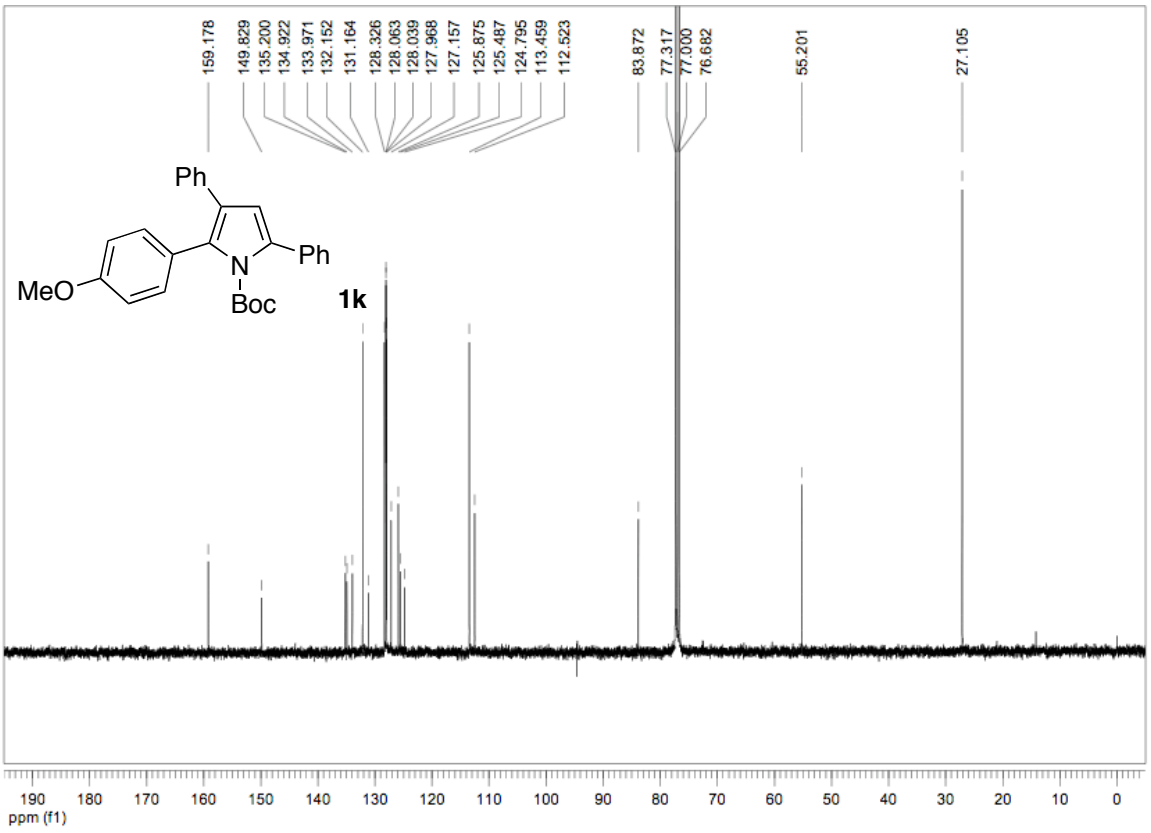

Figure S-22. ^{13}C {^{1}H} NMR spectrum of **1k**.

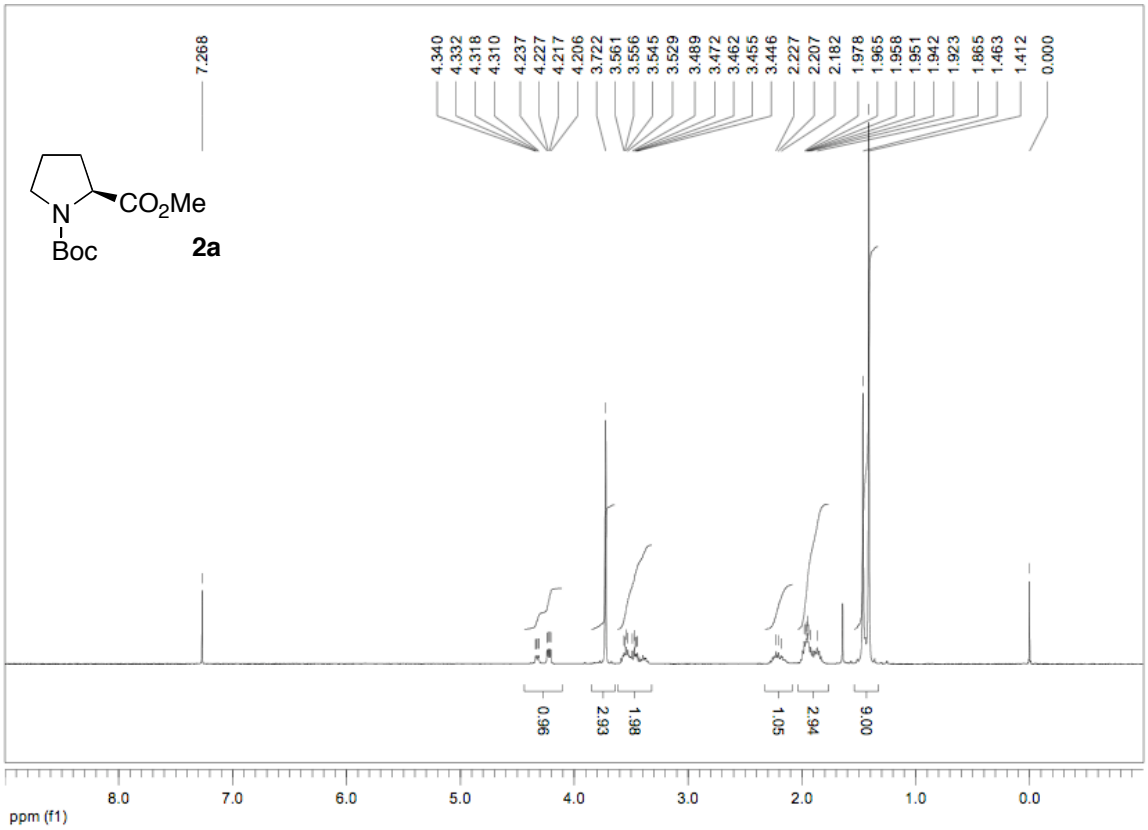

Figure S-23. ^{1}H NMR spectrum of **2a**.

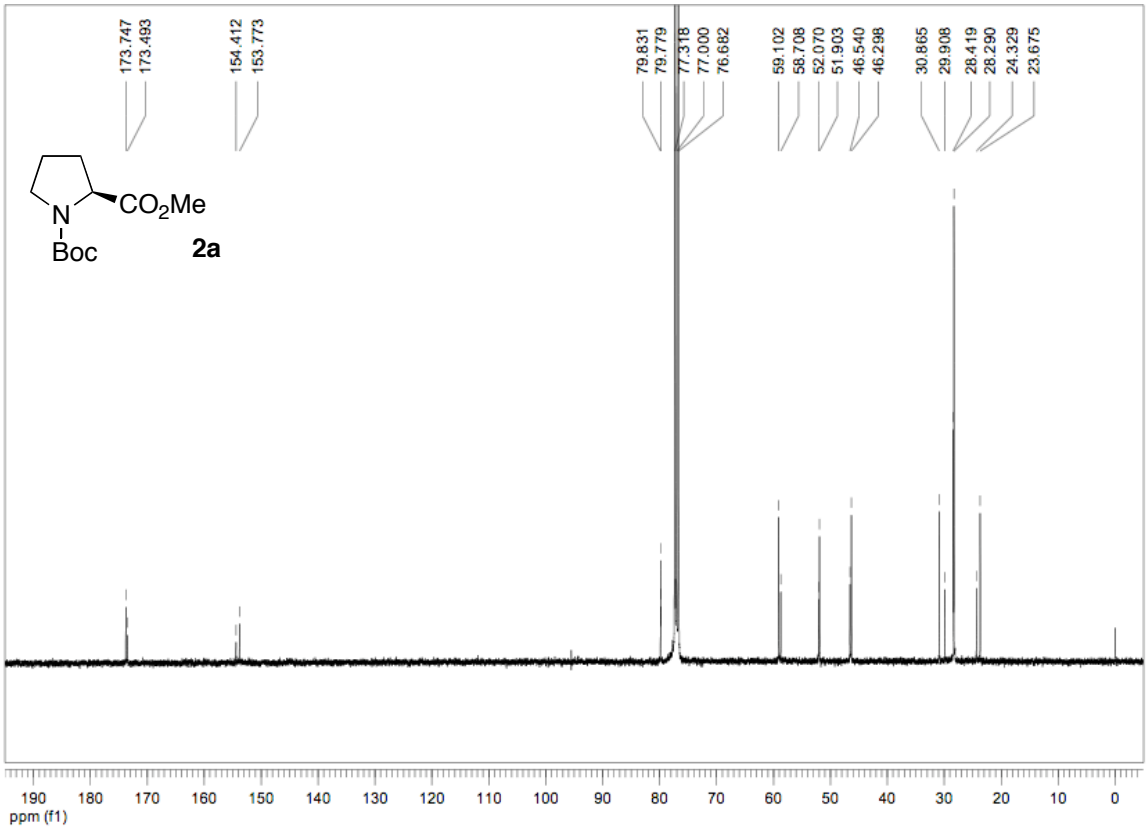

Figure S-24. ^{13}C {^{1}H} NMR spectrum of **2a**.

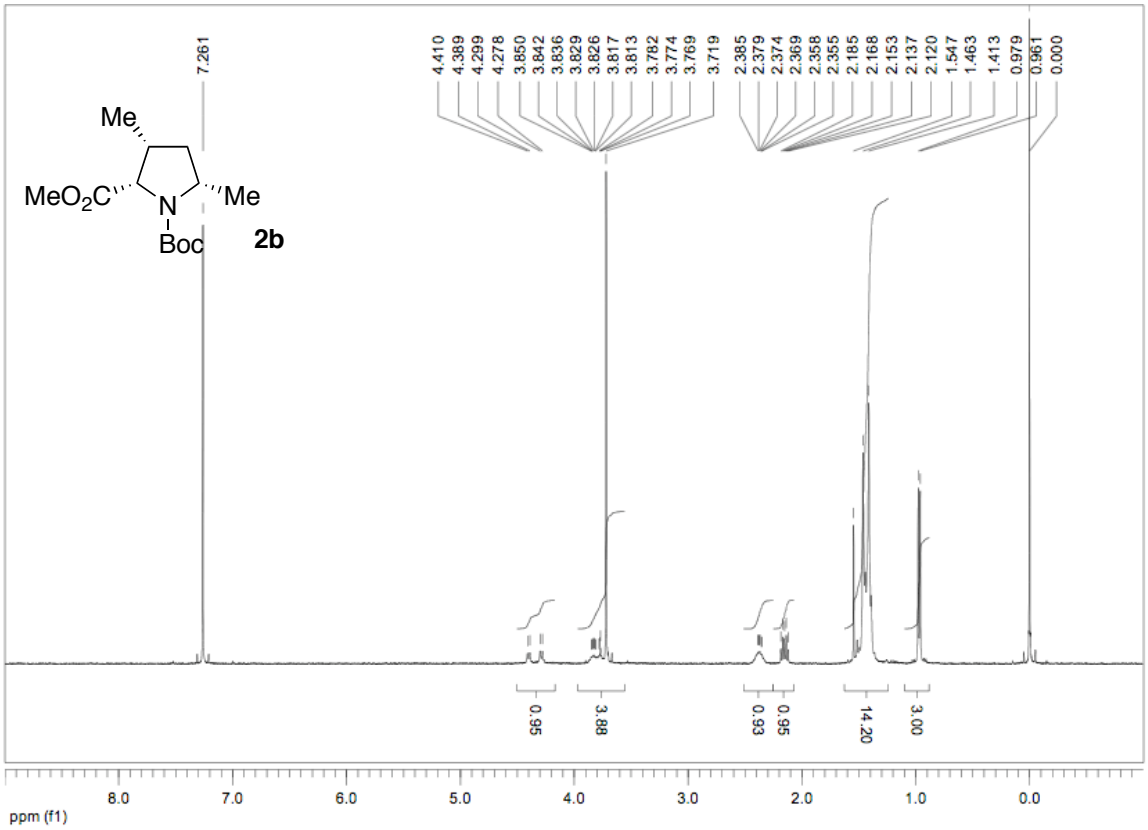

Figure S-25. ^{1}H NMR spectrum of **2b**.

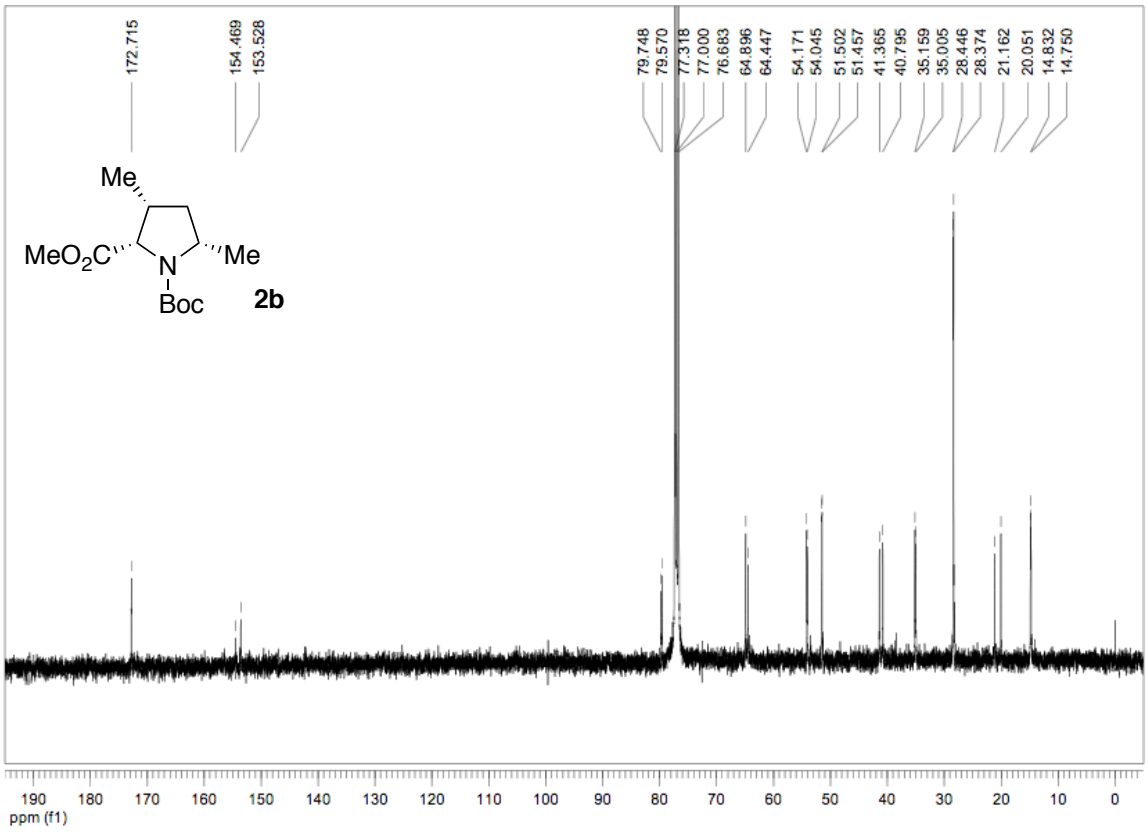

Figure S-26. ^{13}C {^{1}H} NMR spectrum of **2b**.

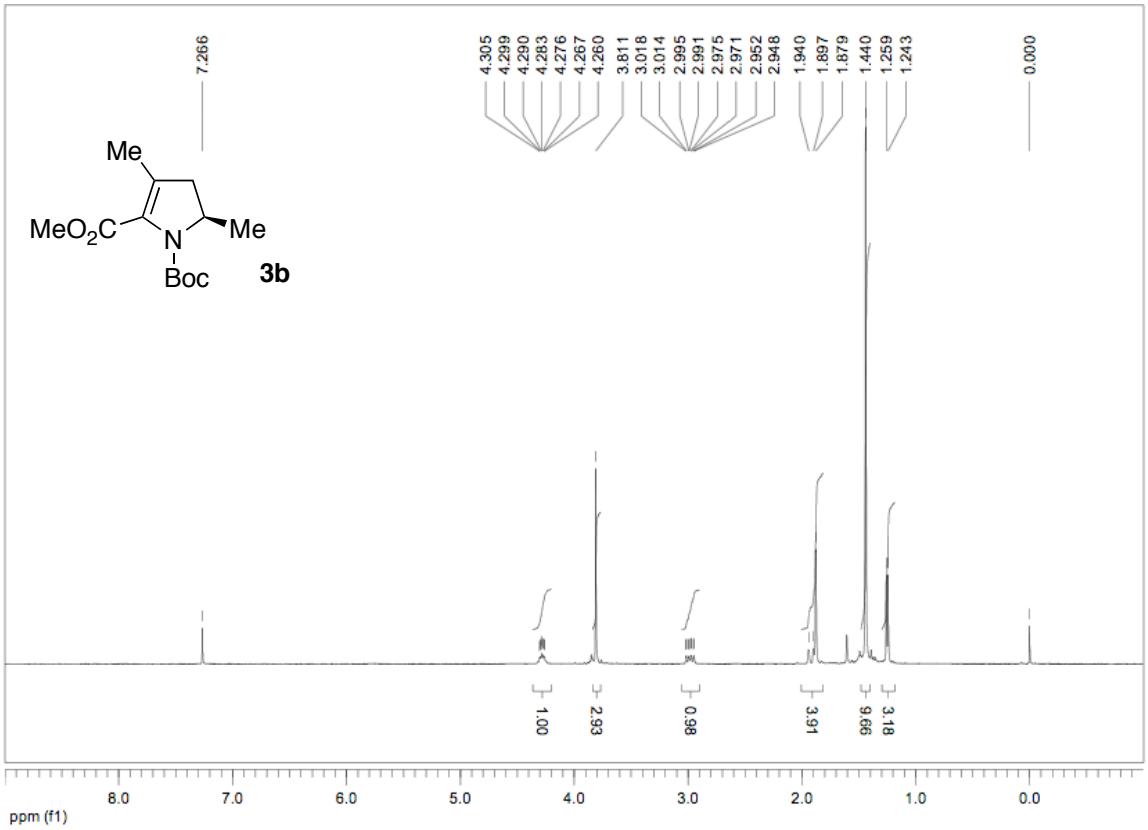

Figure S-27. ^{1}H NMR spectrum of **3b**.

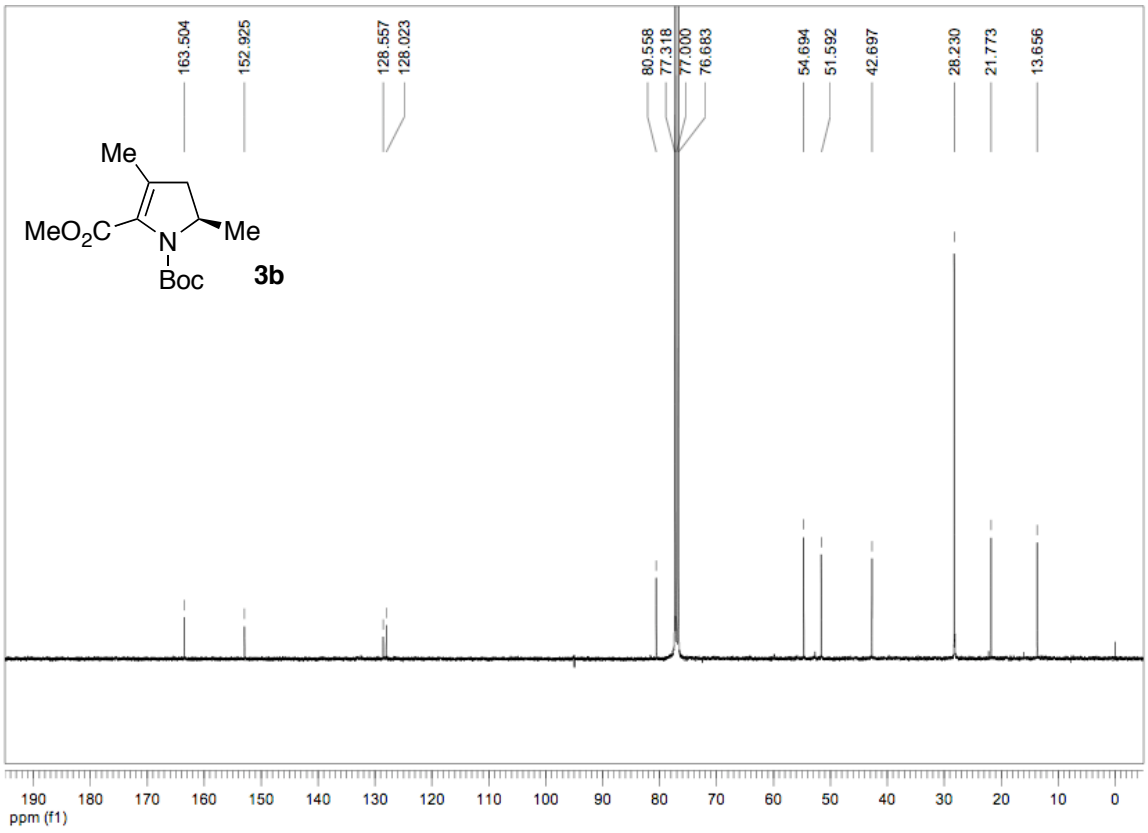

Figure S-28. ^{13}C {^{1}H} NMR spectrum of **3b**.

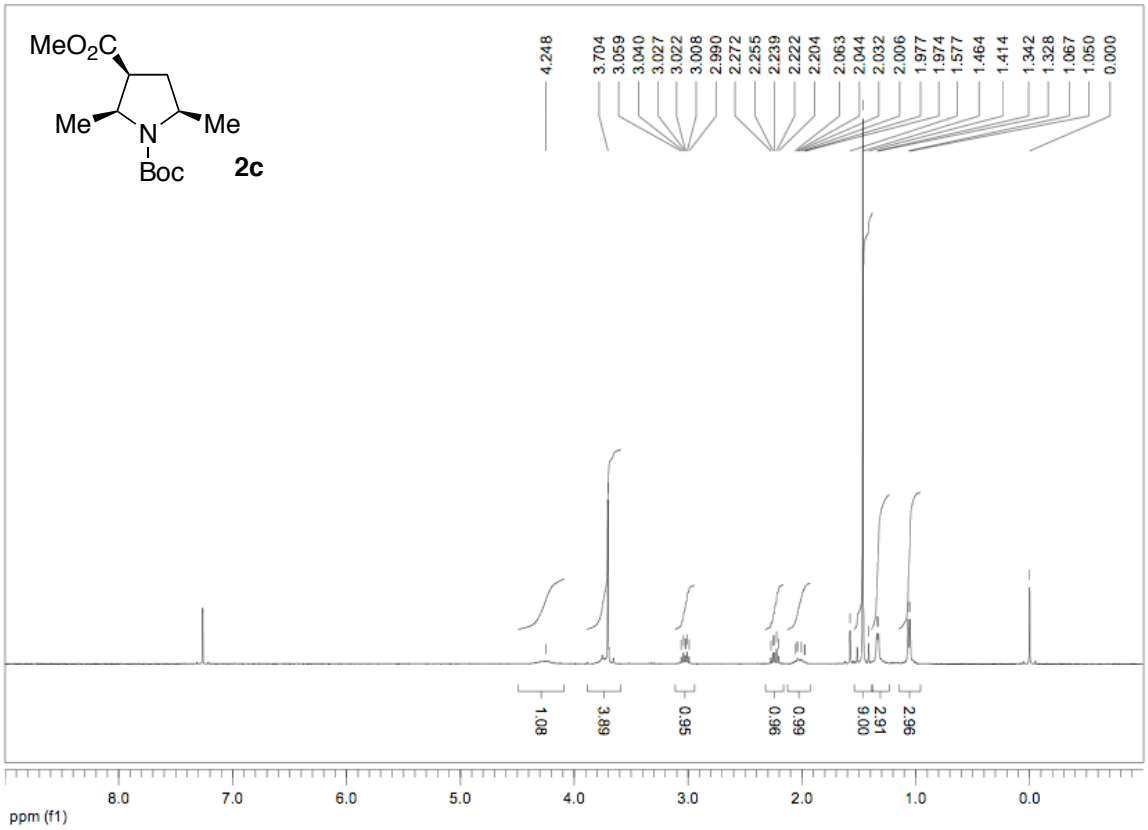

Figure S-29. ^{1}H NMR spectrum of **2c**.

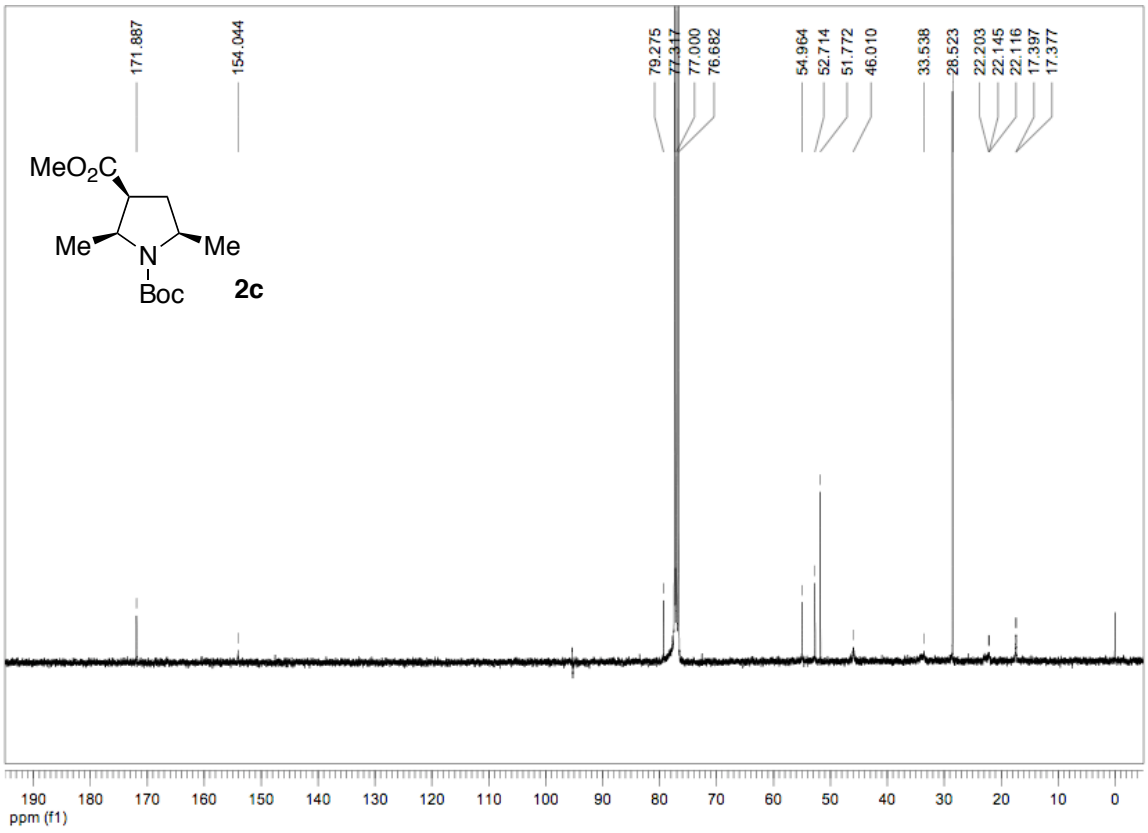

Figure S-30. ^{13}C {^{1}H} NMR spectrum of **2c**.

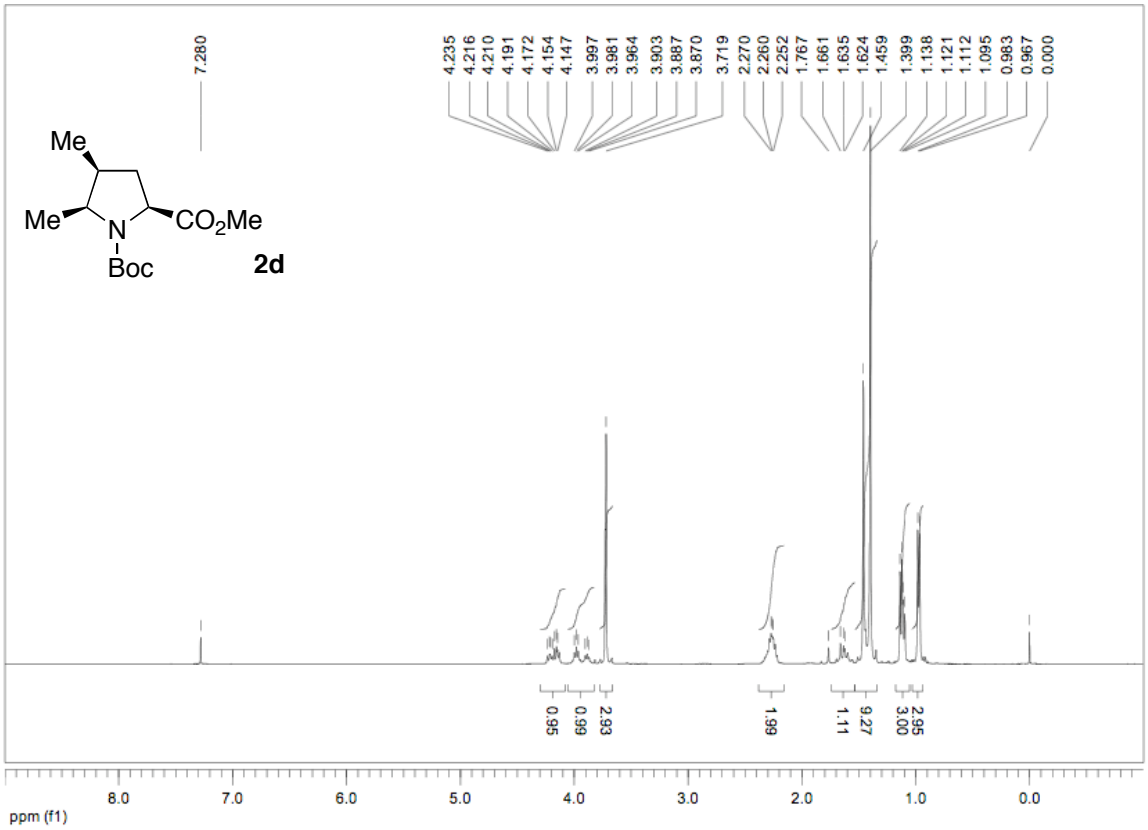

Figure S-31. ^{1}H NMR spectrum of **2d**.

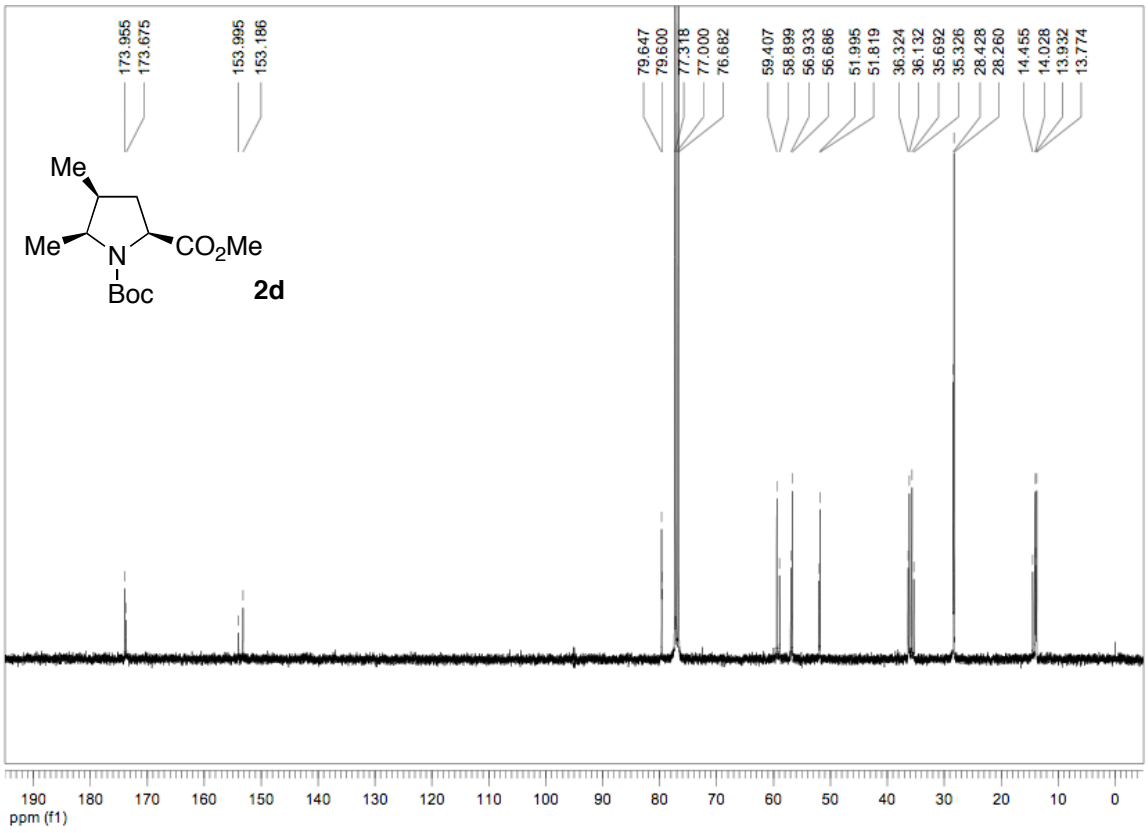

Figure S-32. ^{13}C {^{1}H} NMR spectrum of **2d**.

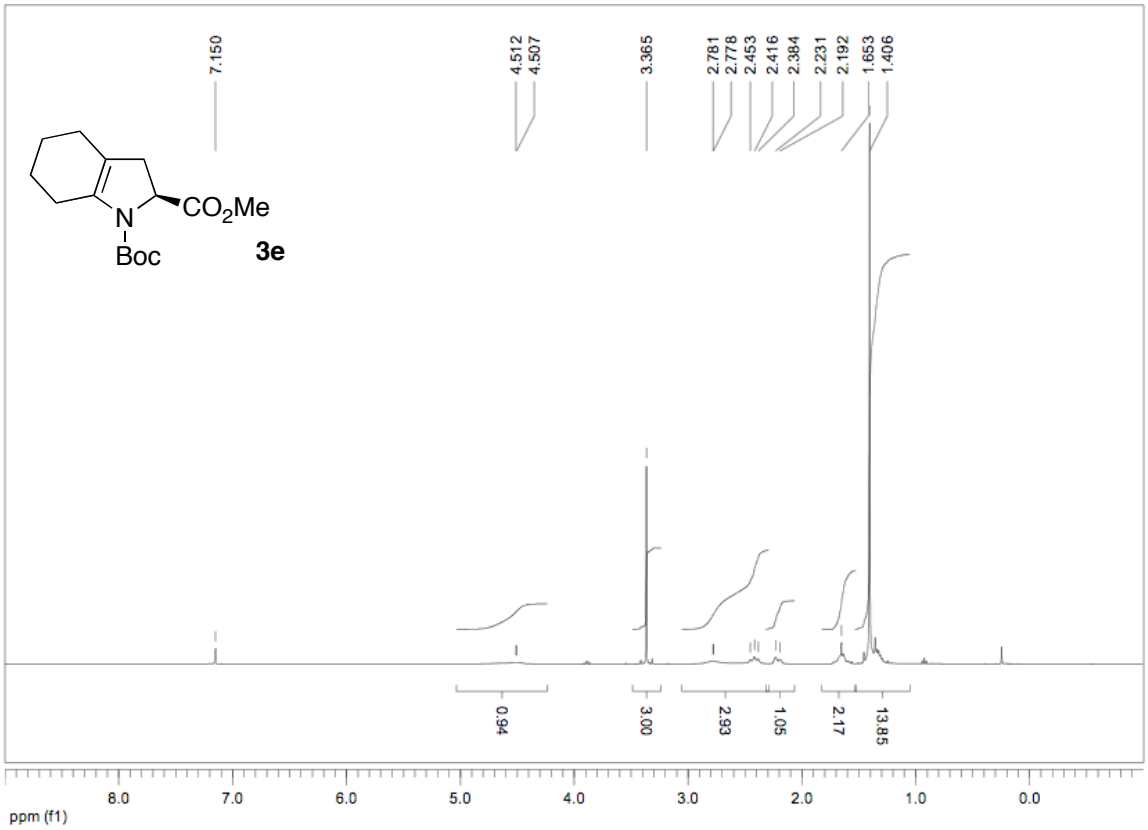

Figure S-33. ^{1}H NMR spectrum of **3e**.

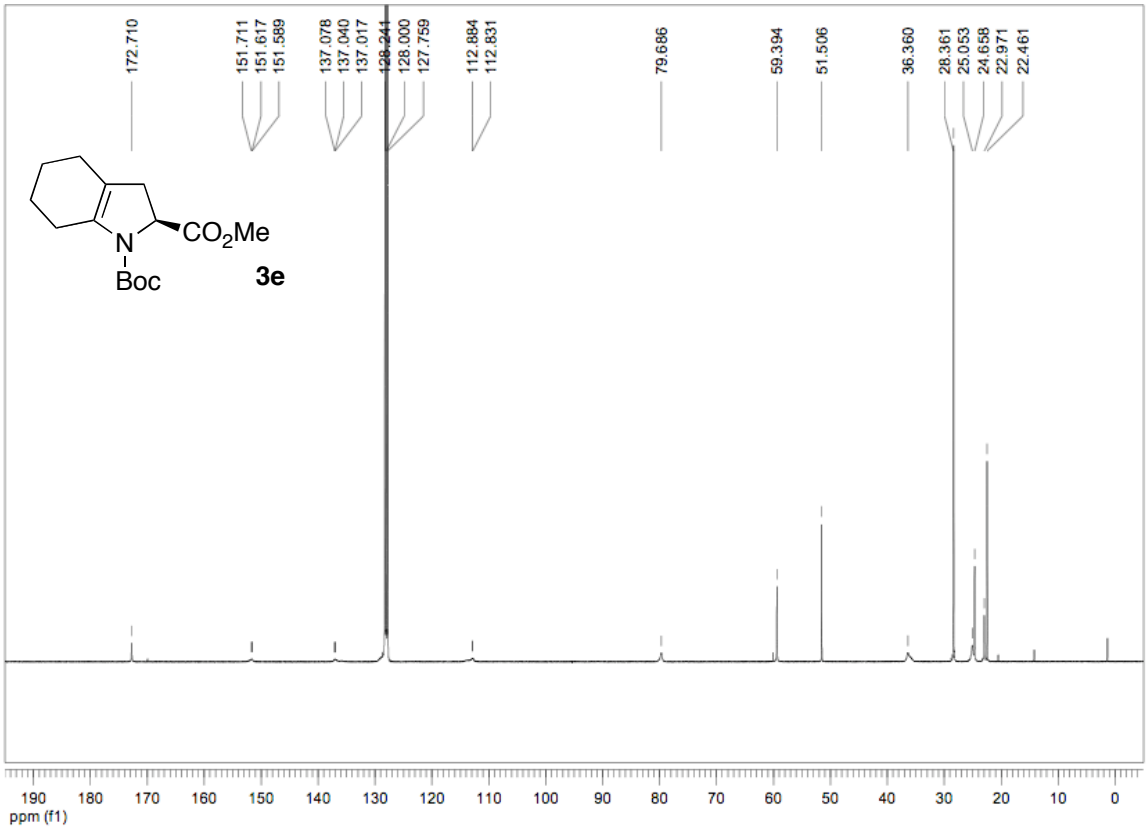

Figure S-34. ^{13}C {^{1}H} NMR spectrum of **3e**.

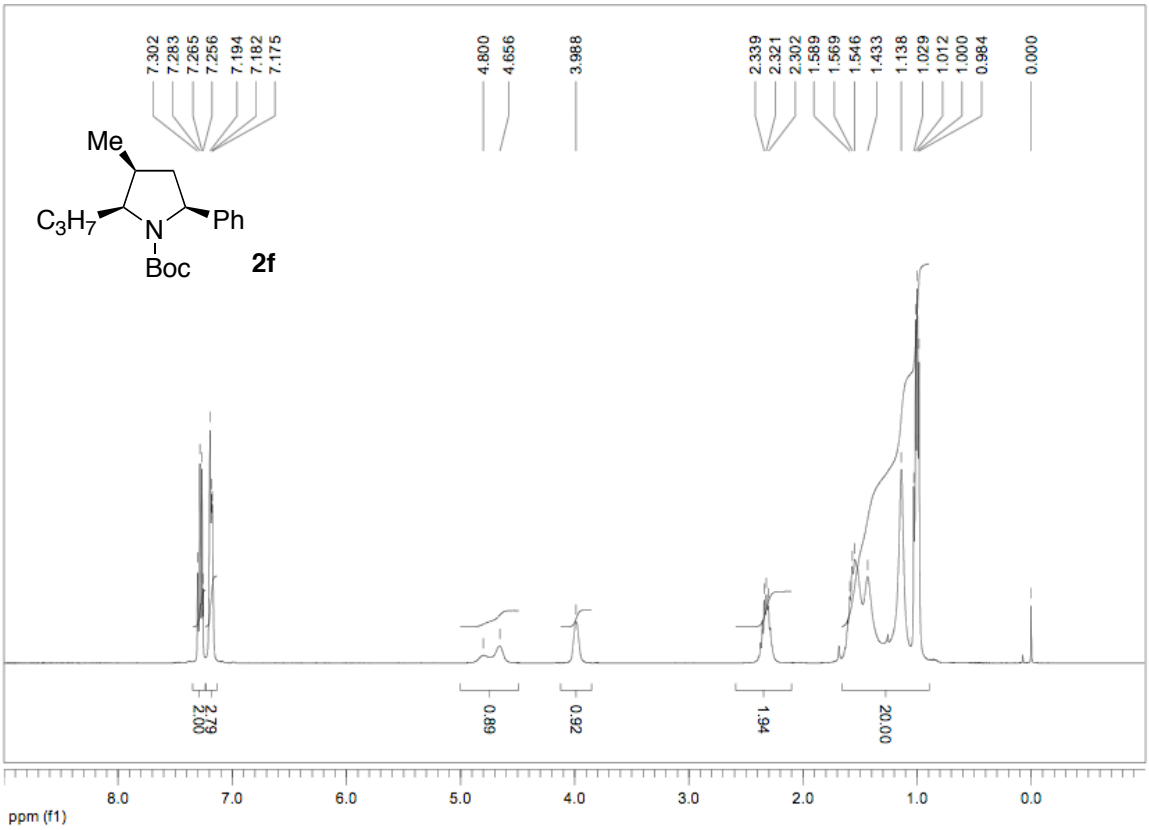

Figure S-35. ^{1}H NMR spectrum of **2f**.

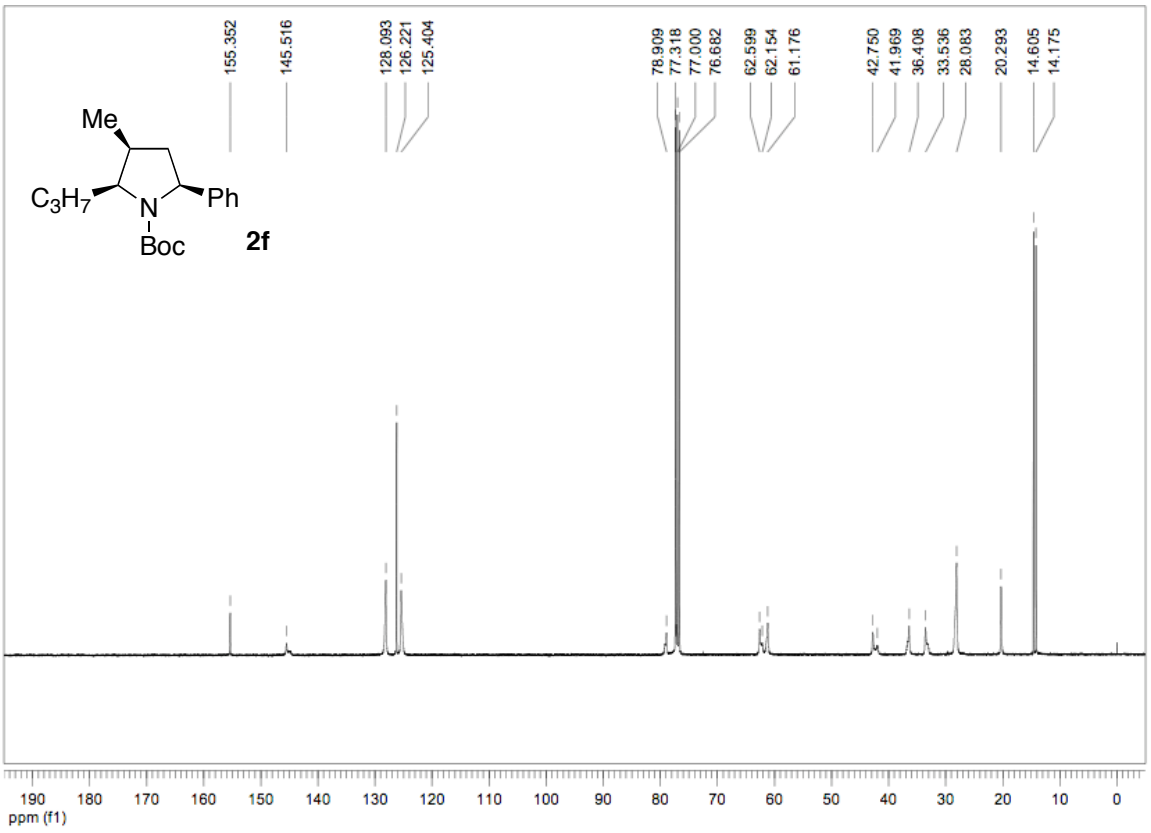

Figure S-36. ^{13}C {^{1}H} NMR spectrum of **2f**.

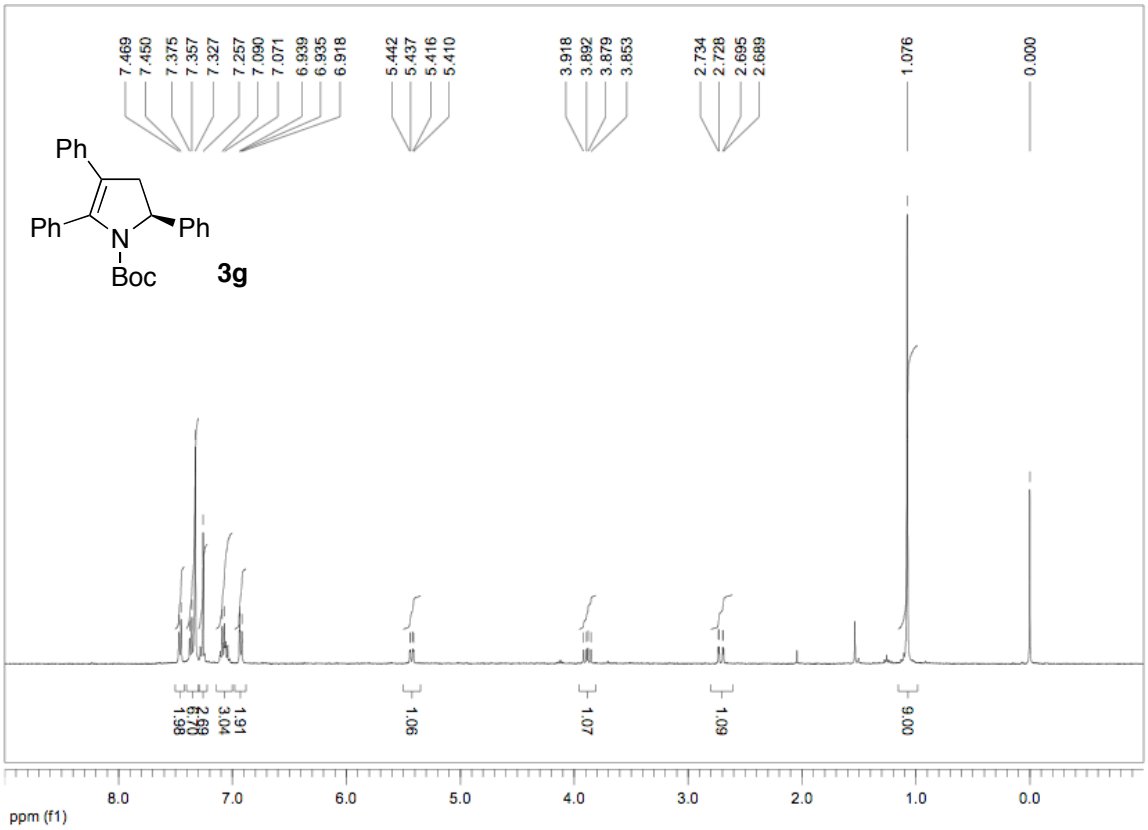

Figure S-37. ^{1}H NMR spectrum of **3g**.

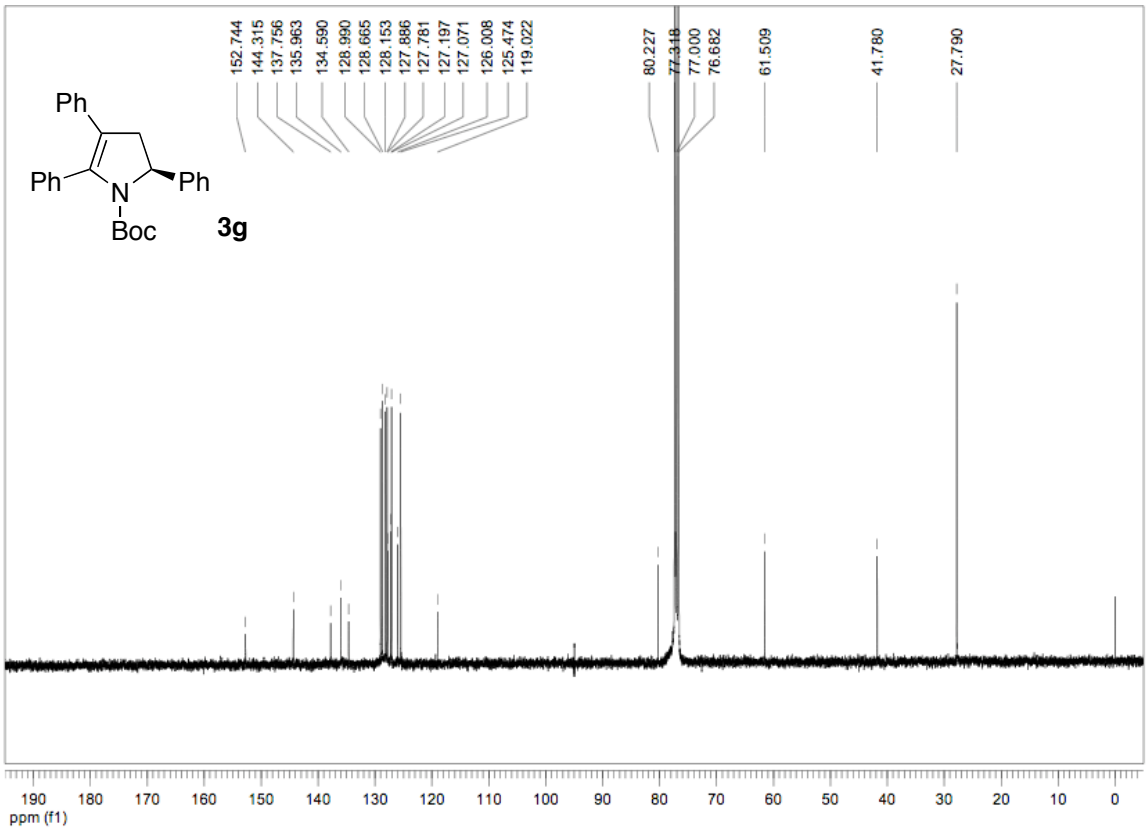

Figure S-38. ^{13}C {^{1}H} NMR spectrum of **3g**.

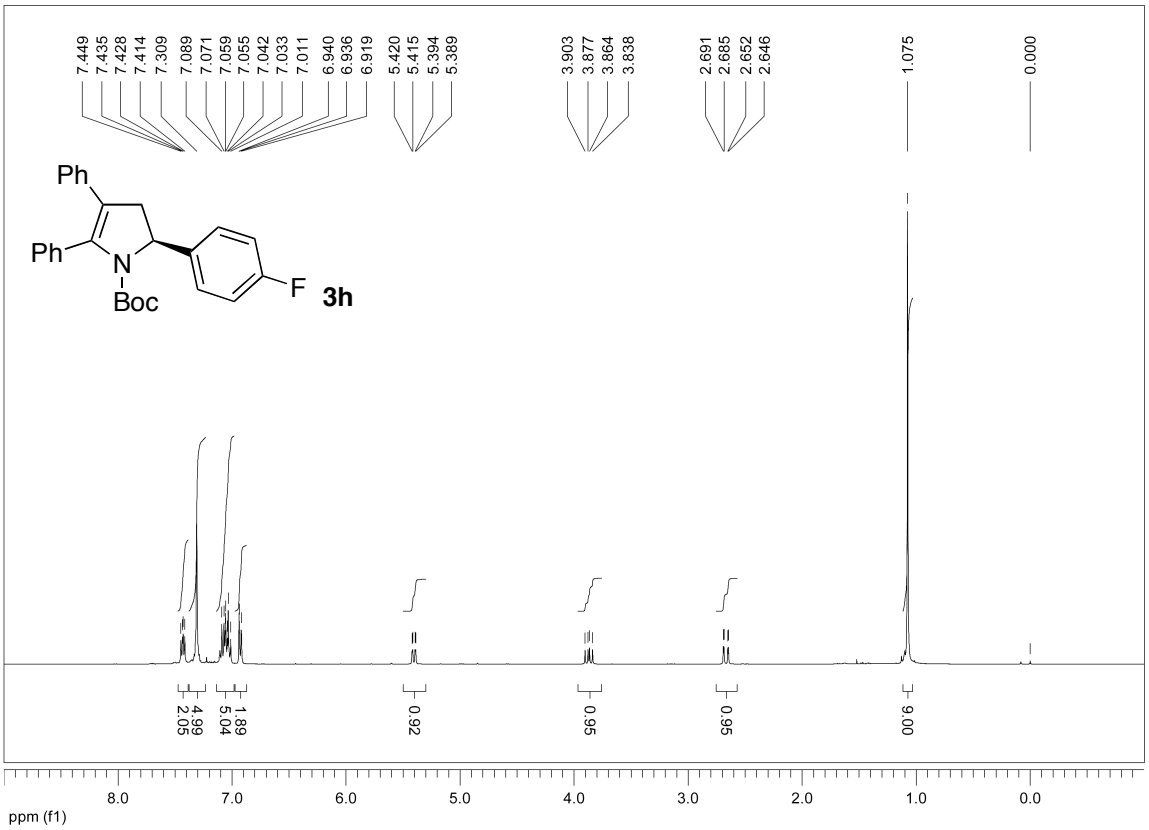

Figure S-39. ^{1}H NMR spectrum of **3h**.

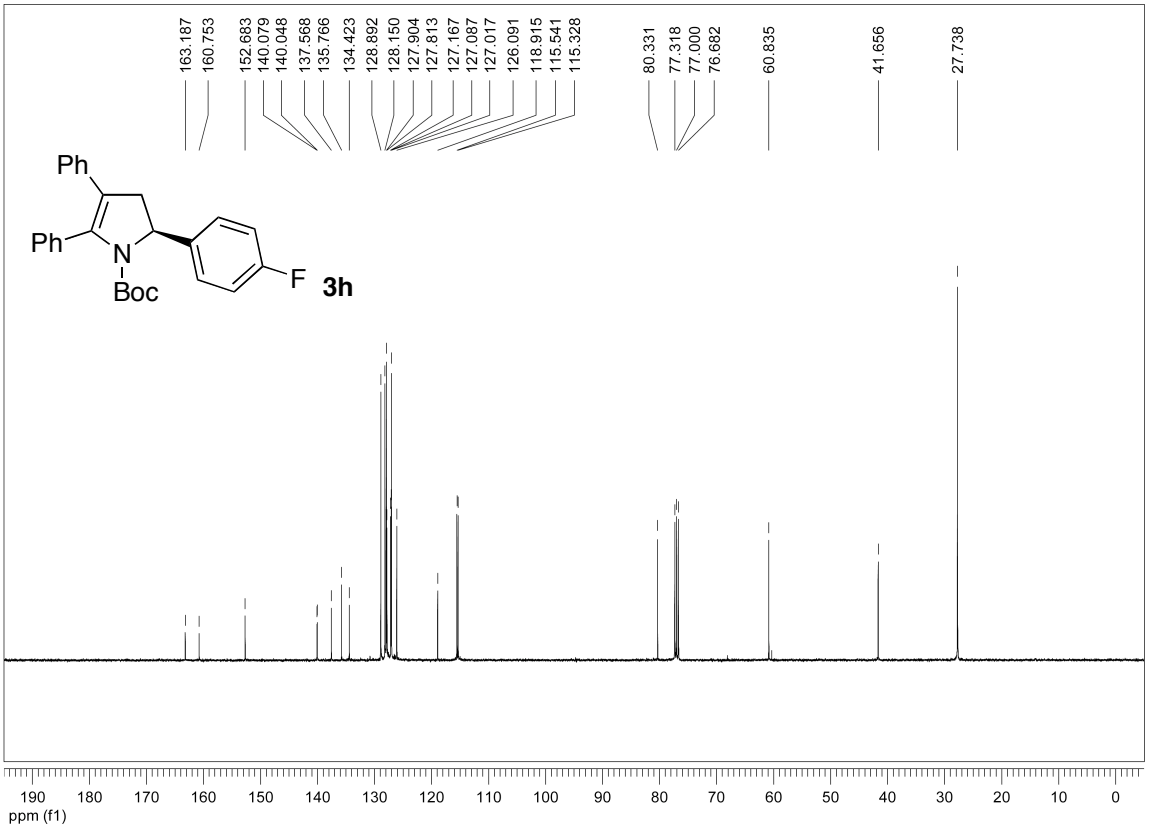

Figure S-40. ^{13}C {^{1}H} NMR spectrum of **3h**.

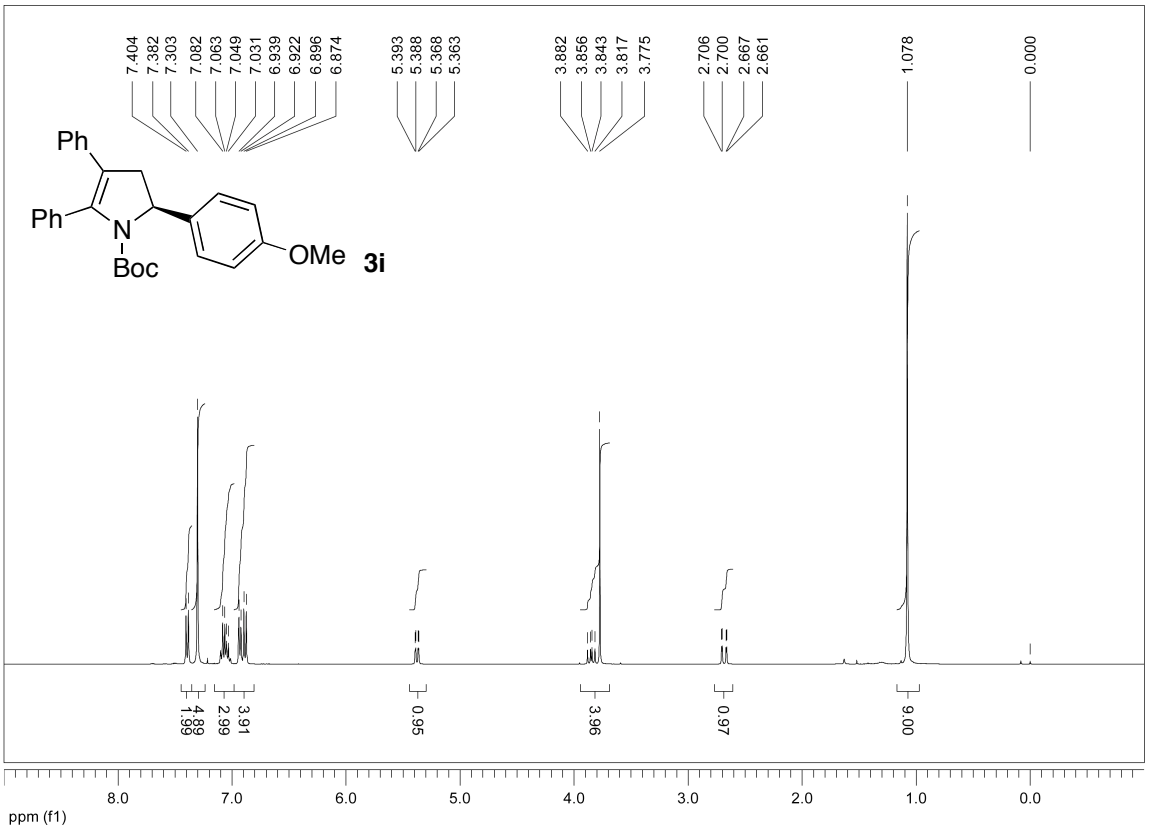

Figure S-41. ^{1}H NMR spectrum of **3i**.

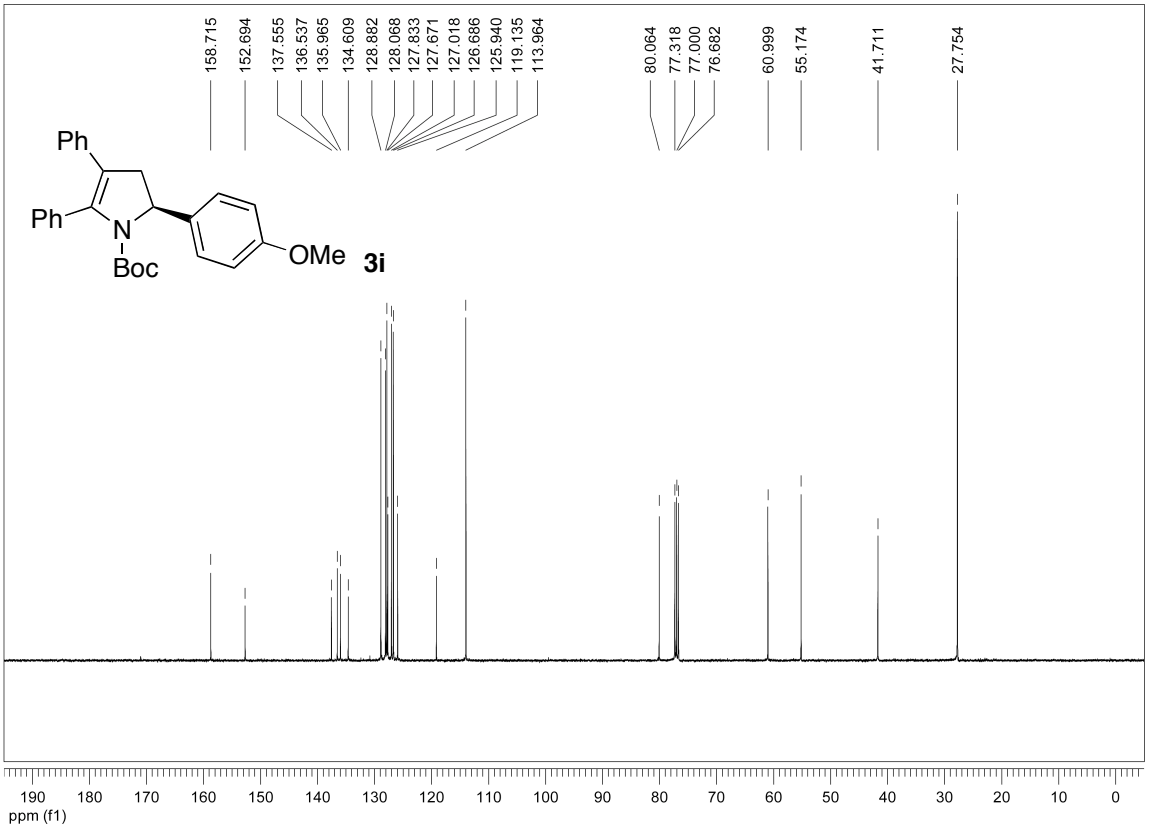

Figure S-42. ^{13}C {^{1}H} NMR spectrum of **3i**.

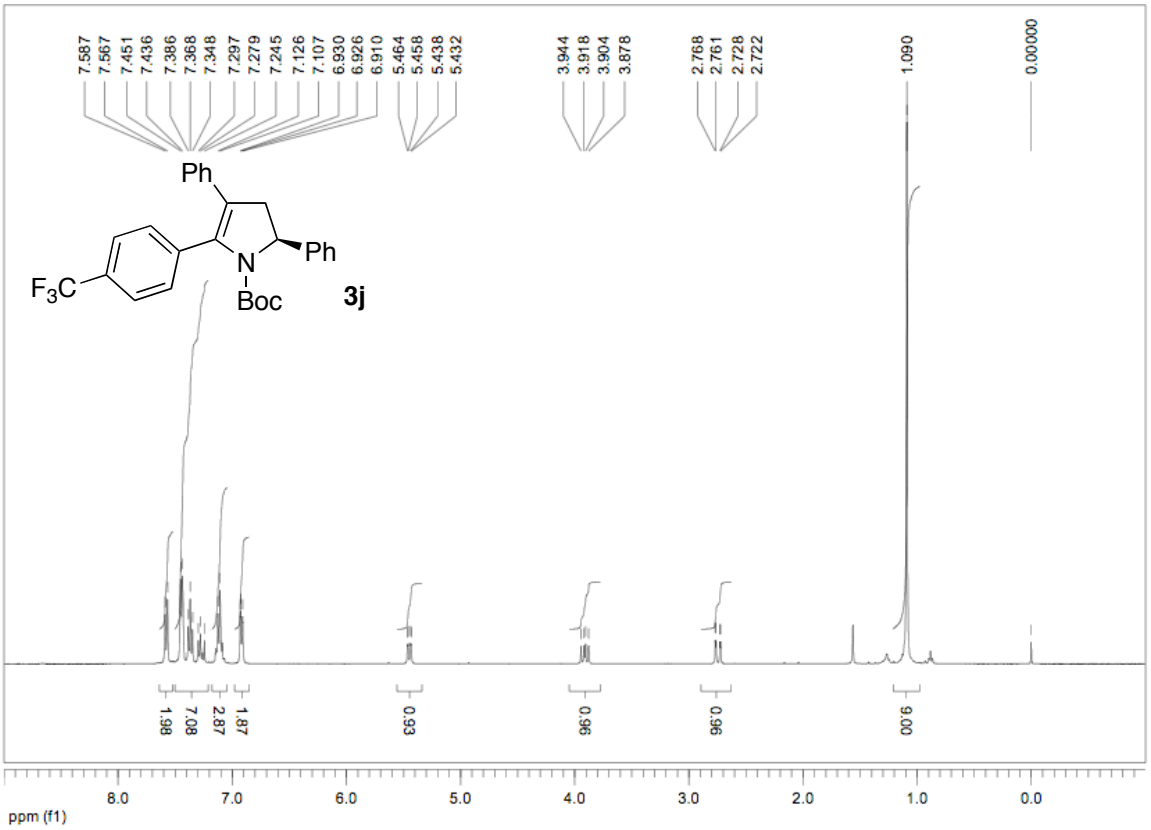

Figure S-43. ^{1}H NMR spectrum of **3j**.

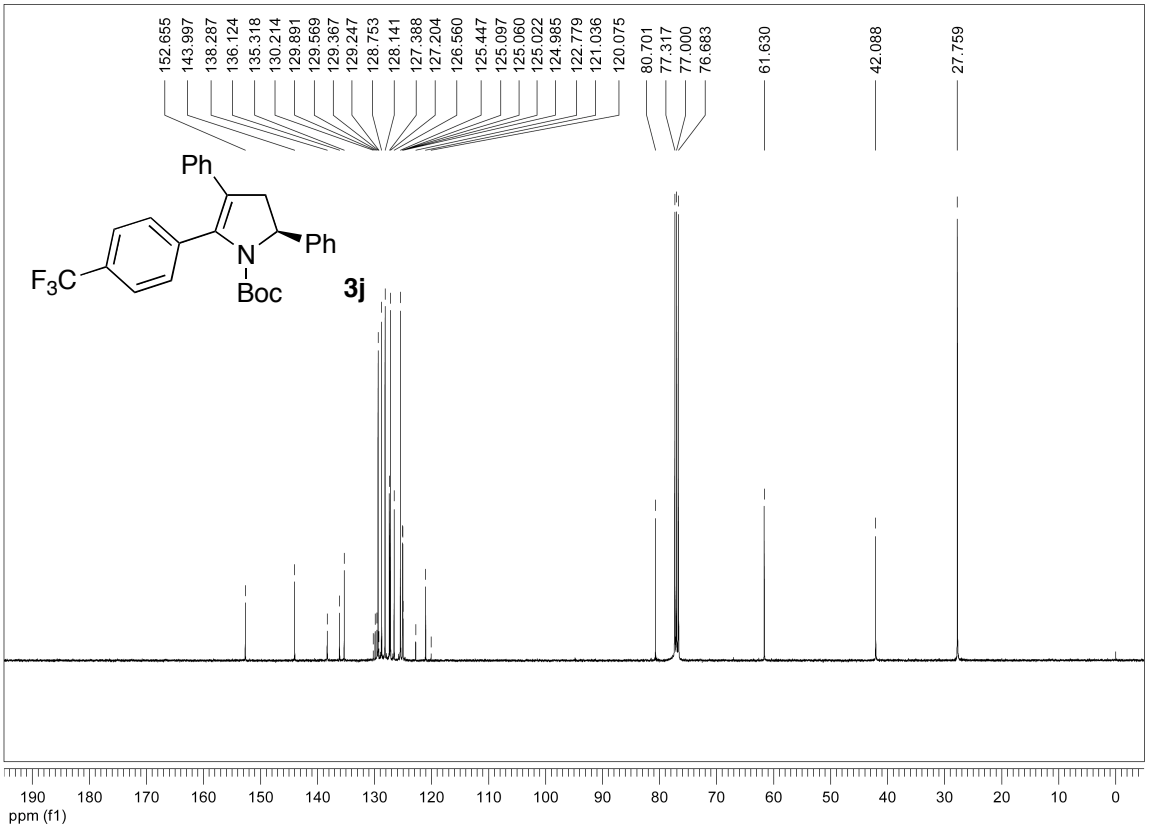

Figure S-44. ^{13}C {^{1}H} NMR spectrum of **3j**.

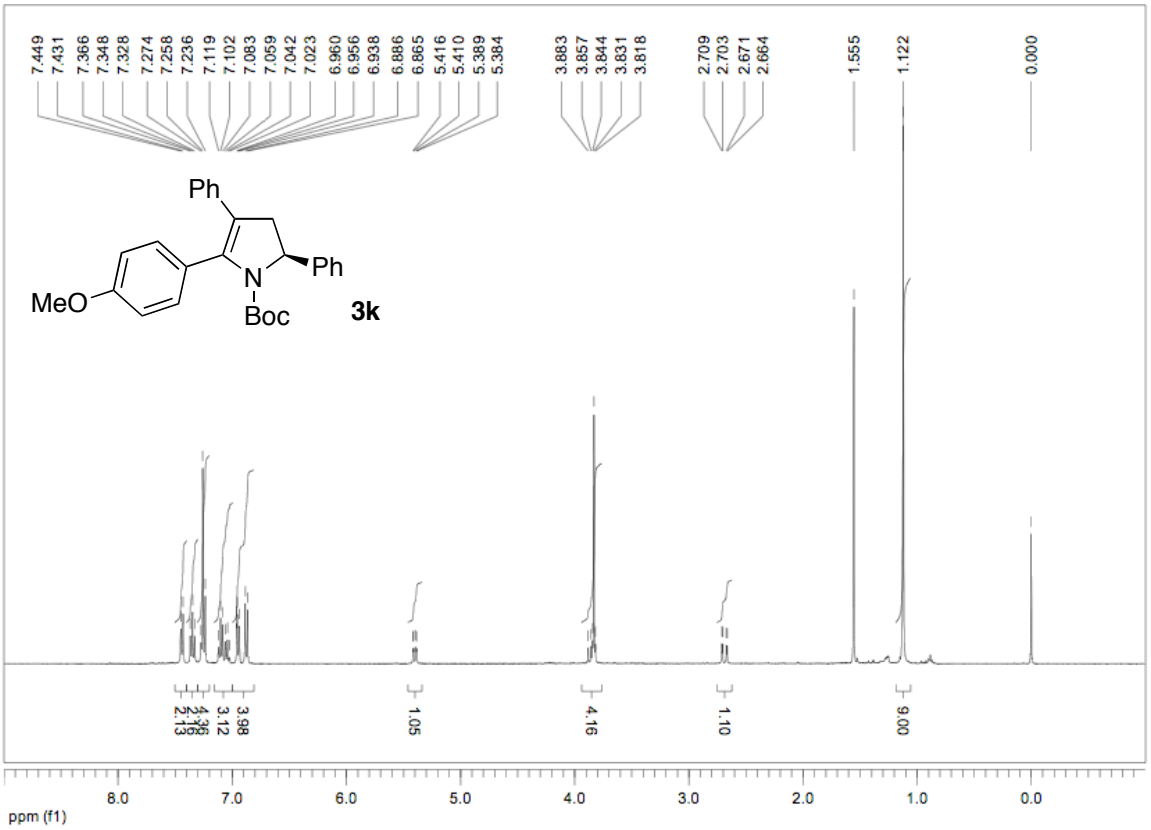

Figure S-45. ^{1}H NMR spectrum of **3k**.

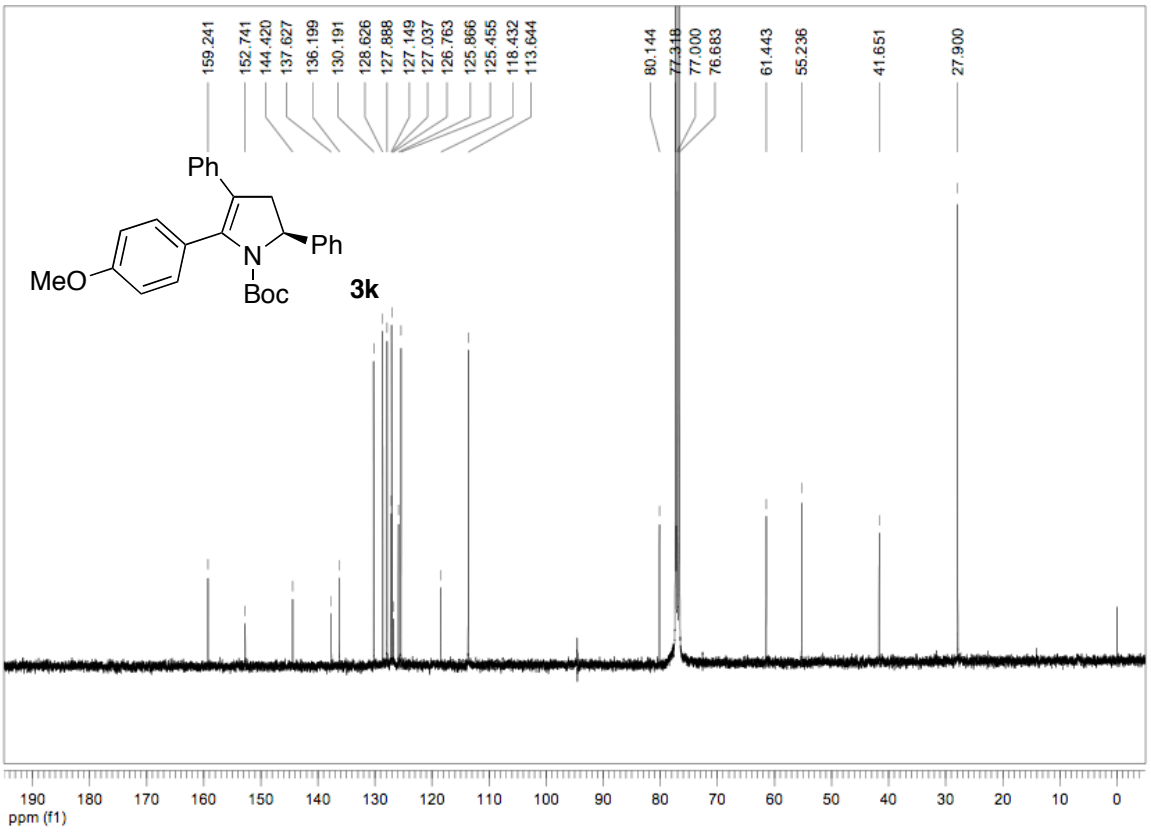

Figure S-46. ^{13}C {^{1}H} NMR spectrum of **3k**.