Supporting Information

Subtle Effects of Ligand Backbone on the Efficiency of Iron-diphos Catalysed Cross-Coupling Reactions

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General considerations

Unless otherwise stated, all manipulations were carried out under a dry N_2 or argon atmosphere using standard Schlenk line and glove-box techniques. Toluene, *n*-hexane, diethyl ether, dichloromethane and tetrahydrofuran were purified by means of a Grubbs type solvent system and deoxygenated by sparging with N_2 for approximately 30 minutes. Deuterated chloroform ($CDCl_3$) were stirred with CaH_2 overnight, distilled, deoxygenated by three freeze-pump-thaw cycles and stored over 4 Å molecular sieves. Water was deoxygenated by sparging with N_2. NMR spectra were acquired on Jeol ECP (Eclipse) 300, Jeol ECS 300, Varian 400-MR, Jeol ECS 400 and Varian VNMRS500 spectrometers. Chemical shifts are referenced relative to high frequency of residual solvent (^1H and ^{13}C), and 85% H_3PO_4 (^{31}P). Elemental analyses were carried out by the Microanalytical Laboratory at the University of Bristol. Mass spectrometry was carried out by the Mass Spectrometry Service at the University of Bristol. All other reagents were used as received from Sigma-Aldrich, Acros or Strem Chemicals.

3,4-bis(diphenylphosphino)thiophene (L_{1a}). 3,4-dibromothiophene (4.90 g, 20.3 mmol) was stirred in diethyl ether (20 mL) and the mixture was cooled to -78 °C. *n*-BuLi (7.05 mL, 1.6 M in hexane, 40.1 mmol) was slowly added and the mixture was stirred for 4 h at -78 °C ensuring the temperature did not change. PPh_2Cl (7.05 mL, 41.0 mmol) was then added dropwise and the mixture stirred at ambient temperature for 10 min. The salts were removed by extraction with CH_2Cl_2 (20 mL) and distilled water (20 mL) under air and the organic layer was concentrated under reduced pressure. The title compounds can be separated and purified by column chromatography on silica gel (1:1 CH_2Cl_2: hexane), or more commonly by distillation. Side products *n*-$BuPPh_2$ and 3-diphenylphosphino-4-bromothiophene could be removed at 180 °C (0.5 Torr), and 200 °C at (0.5 Torr) respectfully. The product $\mathbf{L_{1a}}$ was distilled at 240 °C (0.5 Torr) as a colourless oil which was an air-stable glassy solid at ambient temperatures. 4.79 g (52 % yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 2) and ^{31}P (Fig 3) NMR spectra indicate >95% purity. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (m, 20H), 6.96 (t, *J* = 2.2 Hz, 2H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 141.7 (dd, *J* = 9.5, 7.5 Hz), 136.2 (t, *J* = 2.4 Hz), 133.6 (t, *J* = 10.2 Hz), 132.3, 128.5, 128.3 (t, *J* = 3.7 Hz). **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$) δ -22.7. **HR-MS (EI)** *m/z* calculated for $C_{28}H_{22}P_2S$ $[M]^{\cdot+}$ = 452.0917; obs.: 452.0916.

(2-(trimethylsilyl)thiophene-3,4-diyl)bis(diphenylphosphine) ($L_{1a'}$). *n*-BuLi (1.6 M in hexane, 0.24 mL, 0.38 mmol) was slowly added to a solution of $\mathbf{L_{1a}}$ (0.16 mg, 0.35 mmol) in THF (2-5 mL) at 0 °C. The mixture was stirred for 5 min, and then TMSCl (0.053 mL, 0.42 mmol) was added. The volatile products were removed in vacuo and the residue was then dissolved in CH_2Cl_2 and passed through a short plug of silica gel to purify. 0.228 g (83% yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 5) and ^{31}P (Fig 6) NMR spectra indicate >95% purity. **^{1}H NMR** (500 MHz, $CDCl_3$) δ 7.39 (dddd, *J* = 7.9, 7.3, 1.5, 0.6 Hz, 4H), 7.28 (dd, *J* = 1.5, 0.5 Hz, 1H), 7.21-6.99 (m, 12H), 6.89-6.80 (m, 4H), 0.46 (d, *J* = 1.2 Hz, 9H). **^{13}C{^{1}H} NMR** (126 MHz, $CDCl_3$) δ 144.3 (q), 140.8 (d, *J* = 5.9 Hz), 138.4 (d, *J* = 12.5 Hz), 134.0 (d, *J* = 10.7 Hz), 133.1 (d, Ph, *J* = 19.5 Hz), 132.5 (dd, Ph, *J* = 17.8, 3.7 Hz), 1.4. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$) δ -20.55 (d, *J* = 5.0 Hz), -27.0 (d, *J* = 5.2 Hz). **HR-MS (EI)** *m/z* calculated for $C_{31}H_{302}P_2SSi$ $[M]^{\cdot+}$ = 524.1313; obs.: 524.1306.

3,4-bis(di-*o*-tolylphosphinyl)thiophene (L_{1b}) See preparation of $\mathbf{L_{1a}}$. Lithium chloride was removed by extraction with CH_2Cl_2 and distilled water under air. Low boiling fractions (butyldiphenylphosphine and (4-bromothiophen-3-yl)di-o-tolylphosphine) were removed by heating to 190 °C in a Kugelrohr apparatus (0.5 Torr). The title compound sublimed (in the Kugelrohr apparatus) at 200 °C (0.5 Torr) to afford a white crystalline solid. 0.56 g (53 % yield). **^{1}H NMR** (400 MHz $CDCl_3$): δ 7.20 (b, *J* = 7.4, 1.2 Hz, 4H), 7.17-7.10 (m b, 4H), 7.02 (b, *J* = 6.9 Hz, 4H), 6.84 (b, *J*=2.0 Hz, 2H, TP), 6.83-6.74 (b, 4H), 2.26 (s, 12H). **^{13}C{^{1}H}** NMR (126 MHz, $CDCl_3$) δ 142.3 (q, t, *J* = 13.4 Hz), 140.5 (q, m), 135.4 (q, t, *J* = 4.0 Hz), 133.0, 132.5 (TP), 129.9 (t, *J* = 2.5 Hz), 128.5, 125.8, 21.1 (t, *J* = 10.9 Hz, *o*-tolyl-CH_3). **^{31}P{^{1}H}** NMR (160 MHz, $CDCl_3$) δ -37.4. **HR-MS (EI)** *m/z* calculated for $C_{32}H_{30}P_2S$ $[M]^{\cdot+}$ = 508.1539; obs.: 508.1543. **Anal.** Found (calcd. for $C_{32}H_{30}P_2S$): C, 75.61 (75.57), H, 6.00 (5.95).

3,4-bis(bis(3,5-dimethylphenyl)phosphinyl)thiophene (L_{1c}). See preparation of $\mathbf{L_{1a}}$. Lithium chloride was removed by extraction with CH_2Cl_2 and distilled water under air. The residue was purified by flash chromatography on silica gel under air, 1:9 CH_2Cl_2: hexane eluted the butyldiphenylphosphine and (4-bromothiophen-3-yl)bis(3,5-dimethylphenyl)phosphine and the title compound was eluted using CH_2Cl_2 to afford a white foam. 0.72 g (58 % yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 9) and ^{31}P (Fig 10) NMR spectra indicate >95% purity. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.00 (t, *J* = 2.2 Hz, 2H), 6.90-6.86 (m, 4H), 6.86-6.82 (m, 8H), 2.20 (m, 24H). **^{13}C{^{1}H} NMR** (101 MHz, $CDCl_3$) δ 137.4 (t, *J* = 3.8 Hz), 136.8 (t, *J* = 3.1 Hz), 131.9, 131.3 (t, *J* = 10.3 Hz), 130.2, 21.3. **^{31}P{^{1}H} NMR** (162 MHz, $CDCl_3$) δ -23.0. **HR-MS (EI)** *m/z* calculated for $C_{36}H_{38}P_2S$ $[M]^{\cdot+}$ = 564.2170; obs.: 564.2178.

(4-bromothiophen-3-yl)diphenylphosphine. 3,4-dibromothiophene (3.05 g, 12.6 mmol) was stirred in diethyl ether (15 mL) and the mixture was cooled to -78 °C. *n*-BuLi (1.6M in hexane, 7.1 mL, 11.4 mmol) was added dropwise and the mixture was stirred for 2 h at -78 °C. Occasionally at this point the lithiothiophene salts precipitated. PPh_2Cl (2.26 mL, 12.6 mmol) was then added dropwise and the mixture was stirred at ambient temperature for 10 mins. Distilled water and CH_2Cl_2 were added (20 mL) and the organic layer was removed and concentrated under reduced pressure. Depending on the purity shown by *in situ* ^{31}P NMR the mixture could be worked up with very little purification. In this case the mixture was passed through a plug of silica gel (1:1 CH_2Cl_2:hexane), and the volatiles components were removed to afford a white powder. 3.6 g (82% yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 12) and ^{31}P (Fig 13) NMR spectra indicate >95% purity. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43-7.27 (m, 10H), 6.66 (dt, *J* = 3.3, 0.8 Hz, 2H). **^{13}C{^{1}H}** NMR

(126 MHz, $CDCl_3$) δ 138.2 (d, q, *J* = 13.8 Hz), 136.0 (d, *J* = 9.4 Hz), 133.8 (d, *J* = 20.2 Hz), 131.3 (d, *J* = 1.2 Hz), 129.2 (s, *p*-Ph), 128.7 (d, Ph, *J* = 7.3 Hz), 124.6 (d, *J* = 3.1 Hz), 115.7 (d, *J* = 31.9 Hz). **$^{31}P\{^1H\}$** NMR (162 MHz, $CDCl_3$) δ -16.5. **HR-MS (EI)** *m/z* calculated for $C_{16}H_{12}BrPS$ $[M]^{\cdot+}$ = 345.9581; obs.: 345.9590.

(4-(di-*o*-tolylphosphinyl)thiophen-3-yl)diphenylphosphine (L_{1d}). (4-bromothiophen-3-yl)diphenylphosphine (0.30 g, 0.86 mmol) was stirred in diethyl ether (5 mL) and the mixture was cooled to -78 °C. *n*-BuLi (0.54 mL, 1.6M in hexane, 0.86 mmol) was added dropwise and the mixture was stirred for 1 h at -78 °C. P(*o*-tolyl)$_2$Cl (0.22 g, 0.86 mmol) was dissolved in CH_2Cl_2 (1 mL) and then added dropwise. The mixture was stirred at ambient temperature for 10 mins. Distilled water and CH_2Cl_2 were added (5 mL) and the organic layer was removed and concentrated under reduced pressure. The mixture was purified by column chromatography on silica gel (1:4 CH_2Cl_2:hexane), and the volatiles components could be removed to afford a white solid. 193 mg (46% yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 15) and ^{31}P (Fig 16) NMR spectra indicate >95% purity. **^1H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.23 (m, 10H, Ph), 7.22 – 7.17 (m, 2H), 7.15 – 7.10 (m, 2H, *o*-tolyl), 7.01 (b, *J* = 7.4Hz, 2H, *o*-tolyl), 6.96 (td, *J* = 2.9, 1.6 Hz, 1H, TP), 6.83 (td, *J* = 2.8, 1.4Hz, 1H, TP), 6.75(m b, 2H, *o*-tolyl) 2.26 (s, 6H). **$^{13}C\{^1H\}$** NMR (100 MHz, $CDCl_3$) δ 142.3 (q, d, *J* = 26.7 Hz), 142.0 (q, dd, *J* = 32.9, 14.8 Hz), 140.1 (q, dd, *J* = 32.1, 14.1 Hz), 137.1 (q, dd, *J* = 10.1, 2.9 Hz), 135.2 (q, dd, *J* = 10.5, 2.5 Hz), 133.6 (q, d, *J* = 19.8 Hz, Ph), 133.1 (d, *J* = 1.2 Hz, *o*-tolyl), 132.7 (dd, *J* = 6.0, 4.0 Hz, TP), 132.1 (dd, *J* = 6.2, 3.5 Hz, TP), 129.9 (d, *J* = 4.9 Hz, *o*-tolyl), 128.5 (d, *J* = 2.1 Hz, *o*-tolyl), 128.2 (d, *J* = 6.9 Hz, Ph), 125.8 (*o*-tolyl), 21.1 (d, *J* = 21.7 Hz, *o*-tolyl-CH_3). **$^{31}P\{^1H\}$ NMR** (160 MHz, $CDCl_3$) δ -21.9 (d, *J* = 89.5 Hz, Ph), -38.24 (d, *J* = 89.3 Hz, *o*-tolyl). **HR-MS (EI)** *m/z* calculated for $C_{30}H_{26}P_2S$ $[M]^{\cdot+}$ = 480.1230; obs.: 480.1218.

thiophene-2,3-diylbis(diphenylphosphine) (L_{2a}). See preparation of **L_{1a}**. Low boiling fractions (butyldiphenylphosphine and (3-bromothiophen-2-yl)diphenylphosphine) were removed by heating to 270 °C in a Kugelrohr apparatus (0.5 Torr) and the title compound was separated and purified by column chromatography on silica gel (1:1 CH_2Cl_2:hexane) to afford a powdery white solid. 19.8 g (45% yield). **^1H NMR** (400 MHz, $CDCl_3$) δ 7.48 (dd, *J* = 5.0, 1.1 Hz, 1H), 7.33-7.20 (m, 20H), 6.84 (ddd, *J* = 5.0, 2.2, 0.9 Hz, 1H). **$^{13}C\{^1H\}$** (126 MHz, $CDCl_3$) δ 146.3 (dd, *J* = 34.2 Hz, 25.2 Hz), 144.8 (dd, *J* = 25.8 Hz, *J* = 11.8 Hz), 137.6 (Ph, dd, *J* = 9.5, 2.5 Hz), 137.2 (dd, *J* = 8.4, 2.4 Hz), 133.5 (d, *J* = 1.8 Hz), 133.4 (t, *J* = 1.7 Hz), 133.2 (d, *J* = 1.6 Hz), 133.1 (d, *J* = 4.5 Hz), 131.2 (d, *J* = 2.4 Hz), 128.8, 128.4, 128.3 (d, *J* = 6.6 Hz). **$^{31}P\{^1H\}$ NMR** (202 MHz, $CDCl_3$) δ -25.0 (d, *J* = 111.3 Hz), -26.1 (d, *J* = 111.3 Hz). **HR-MS (EI)** *m/z* calculated for $C_{28}H_{22}P_2S$ $[M]^{\cdot+}$ = 452.0917; obs.: 452.0898. **Anal.** Found (calcd. for $C_{28}H_{22}P_2S$): C, 74.22 (74.32) H, 4.98 (4.90).

(5-(trimethylsilyl)thiophene-2,3-diyl)bis(diphenylphosphine) ($L_{2a'}$). *n*-BuLi (0.55 mL, 1.6 M in hexane, 0.88 mmol) was slowly added to a solution of **L_{2a}** (0.40 mg, 0.88 mmol) in THF (2-5 mL) at 0 °C. The mixture was stirred for 5 min, and then TMSCl (0.22 mL, 1.8 mmol) was added. The volatile products were removed in vacuo and the residue was then dissolved in CH_2Cl_2 and passed through a short plug of silica gel to purify. Product afforded as a white powder. 0.35 g (76% yield). Satisfactory elemental analyses were not obtained although ^{13}C (Fig 19) and ^{31}P (Fig 20) NMR spectra indicate >95% purity. **^1H NMR** (500 MHz, $CDCl_3$) δ 7.36-7.19 (m, 20H), 6.95 (dd, *J*=2.3, 0.8 Hz, 1H), 0.20 (s, 9H). **$^{13}C\{^1H\}$** NMR (126 MHz, $CDCl_3$) δ 151.3 (d, *J*=25.8 Hz), 151.0 (d, *J*=25.8 Hz), 147.3 (d, *J*=1.9 Hz), 145.4 (dd, *J*=26.0, 12.3 Hz), 139.4 (m), 138.0 (dd, *J*=9.7, 2.5 Hz), 137.5 (dd, *J*=8.5, 2.5 Hz), 133.6 (p-ddd, *J*=20.3, 18.6, 1.8 Hz), 128.8 (Ph), 128.5-128.01 (Ph, m), 0.05.

$^{31}P\{^{1}H\}$ NMR (200 MHz, $CDCl_3$) δ -23.5 (d, *J*=110.3 Hz), -24.9 (d, *J*=111.6 Hz). **HR-MS (EI)** *m/z* calculated for $C_{31}H_{30}P_2SSi$ $[M]^{\cdot+}$ = 524.1313; obs.: 524.1304.

$FeCl_2(L_{1a})_2$

Acetone was dried by stirring over $MgSO_4$ for 2 hours. $FeCl_2$ (21 mg, 0.17 mmol) was suspended in acetone (1 mL) with stirring and **L_{1a}** (157 mg, 0.35 mmol) was added. The mixture was stirred overnight and the solid collected by Buchner filtration and washed with diethyl ether (2-3 mL) to afford a pale yellow powdery solid. 100 mg (59% yield). **HR-MS (ESI)** *m/z* calculated for $C_{56}H_{44}ClFeP_4S_2$ $[M\text{-}Cl]^+$ = 995.0869; obs.: 995.0870. **Anal.** Found (calcd. for $C_{56}H_{44}Cl_2FeP_4S_2$): C, 65.72 (65.19) H, 4.46 (4.30).

Catalysis general procedures.

This proceedure was adapted from work by Bedford and coworkers.[2]

The arylating reagent, in this case di-*p*-tolyl zinc, was formed beforehand by addition of *p*-tolyl magnesium bromide (19 mL) to $ZnCl_2$ (1.3 g) in THF (19 mL).

The catalyst precurser complexes were formed *in situ* by combination of the required ligand (10 mol%) and $FeCl_2$ (5 mol%) in a Schlenk flask in a glove box. The preformed di-*p*-tolyl zinc solution was then added to the complex and the mixture heated to 45 °C with stirring in a Carousel. After 10 minutes 4-methoxybenzyl bromide or chloride (1 eq.) was added along with the internal standard (1,3,5-trimethoxybenzene) and the mixture was stirred for 4 hours. For some of the catalytic runs the benzyl halide was made up as a standard solution with 1,3,5-trimethoxybenzene (in toluene) and both species added to the catalysis mixture – the presence of the internal standard had no effect on the catalysis. The reaction was quenched with H_2O (5 mL) and 1 mL of 1.0M HCl was added. The organic components were extracted with CH_2Cl_2 (2x10 mL), dried over $MgSO_4$ and filtered. The mixture was dried in vacuo and the residue was dissolved in $CDCl_3$. The conversion to coupled products was determined by ^1H NMR spectroscopy by integration of the benzylic methylene resonance for the starting material and the product (single 90 ° pulse for ^1H spectra). Quantities of the two homocoupled products were ascertained in the same fashion by integration of the methylene regions.

Reaction profiles were obtained by setting up the catalysis in the fashion detailed above. The reaction was sampled periodically by removing an aliquot of the reaction mixture and quenching with a 0.2 M HCl solution, before extracting the organic phases with CH_2Cl_2, drying ($MgSO_4$), and removing the volatile components under reduced pressure. The residue was redissolved in $CDCl_3$ and the conversions determined by ^1H NMR.

NMR Spectra of Ligands

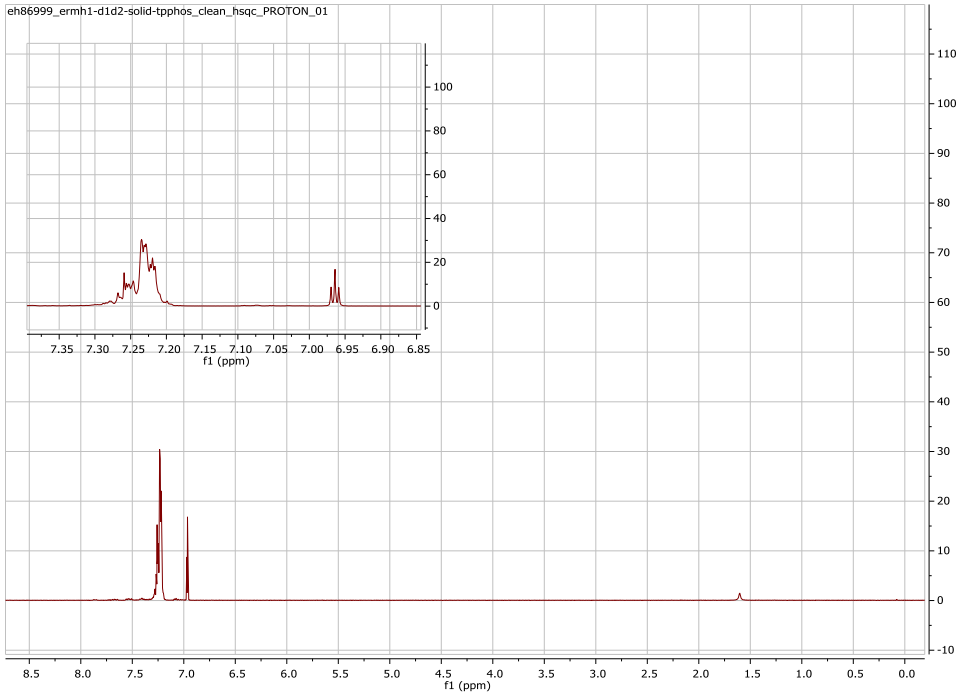

Figure 1 - ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{1a}}$

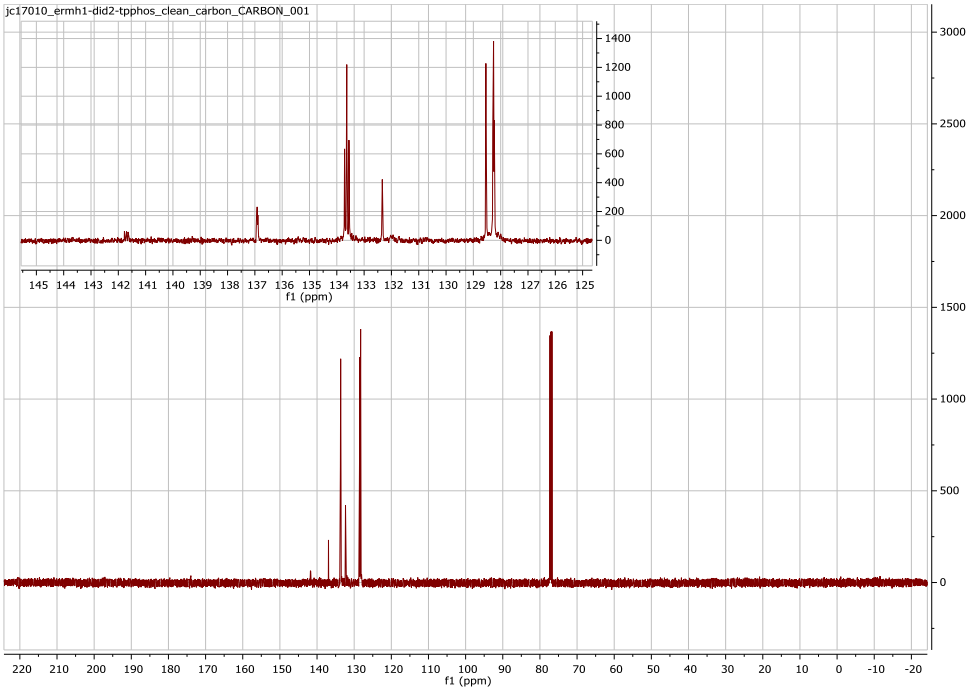

Figure 2 - ^{13}C NMR Spectrum of ligand $\boldsymbol{L_{1a}}$

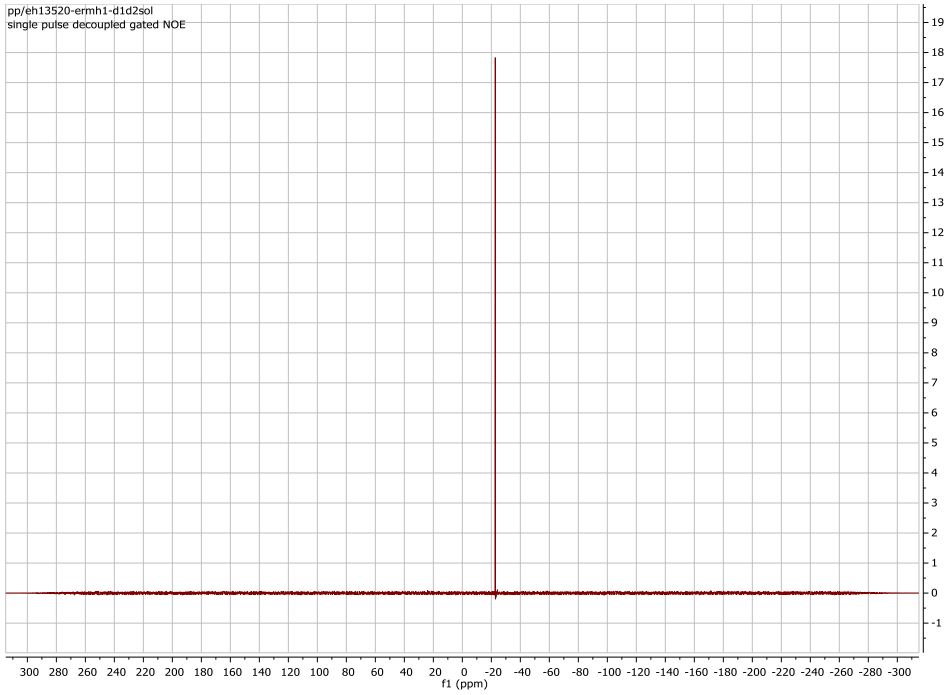

Figure 3 - ^{31}P NMR Spectrum of ligand $\boldsymbol{L_{1a}}$

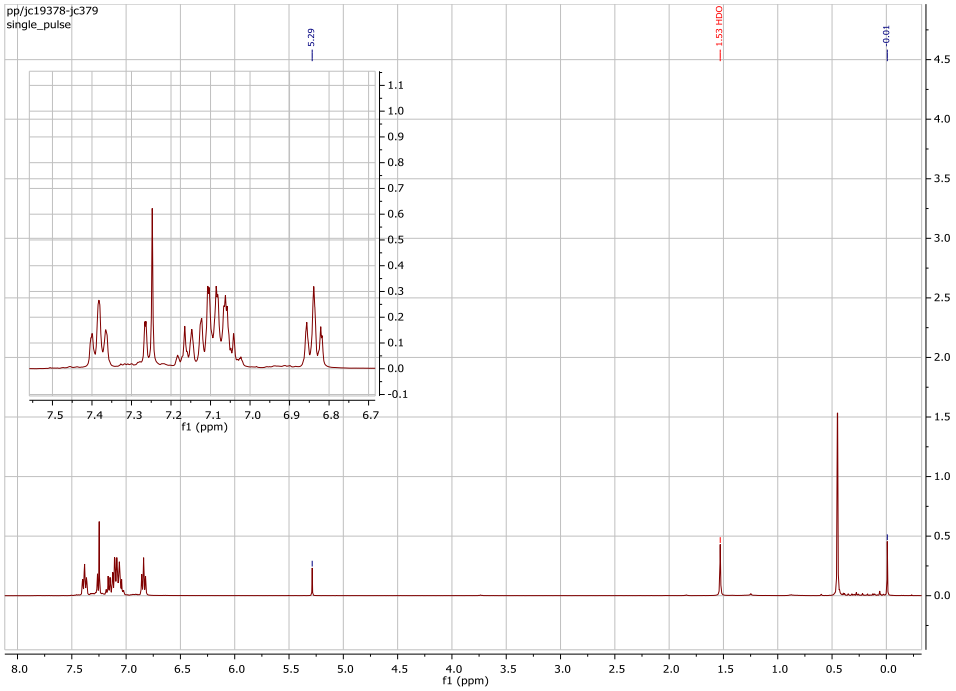

Figure 4 - ^{1}H NMR Spectrum ligand $\boldsymbol{L_{1a'}}$

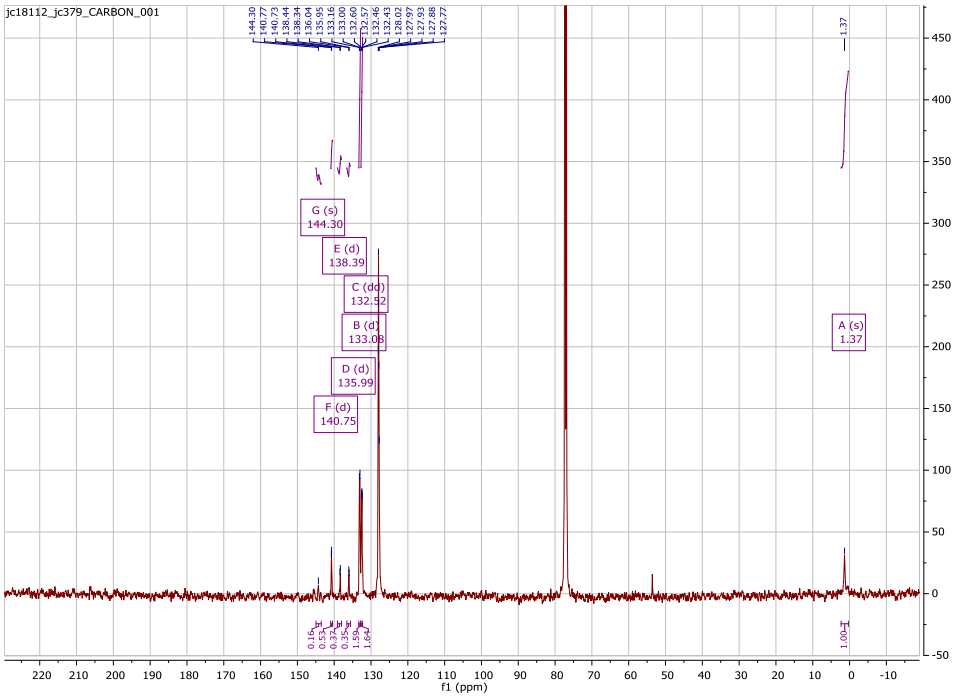

Figure 5 - ^{13}C NMR Spectrum of ligand $\boldsymbol{L_{1a}}$,

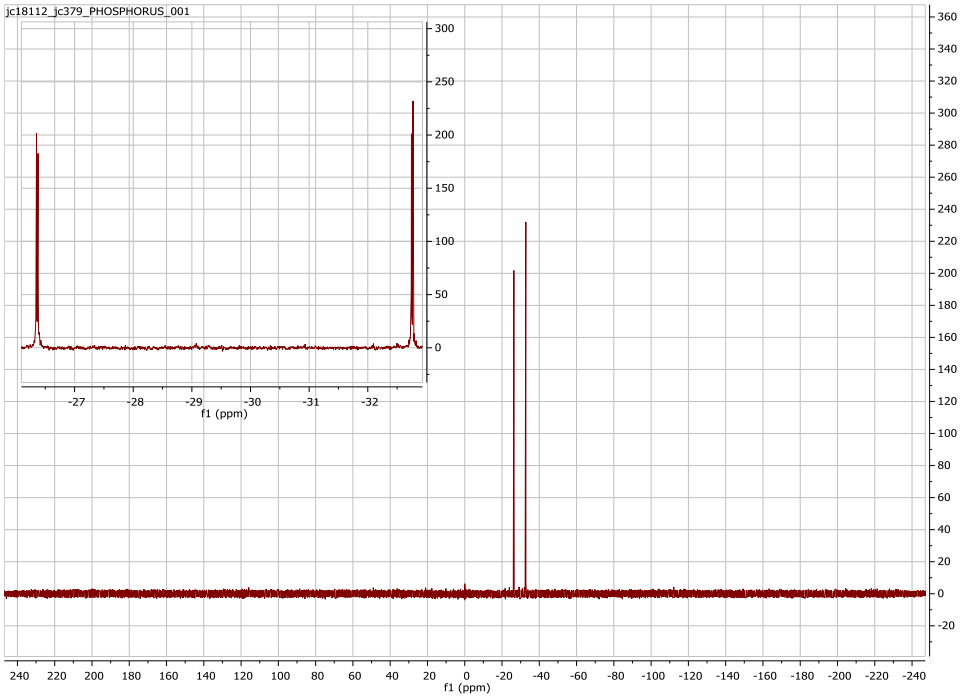

Figure 6 - ^{31}P NMR Spectrum of ligand $\boldsymbol{L_{1a}}$,

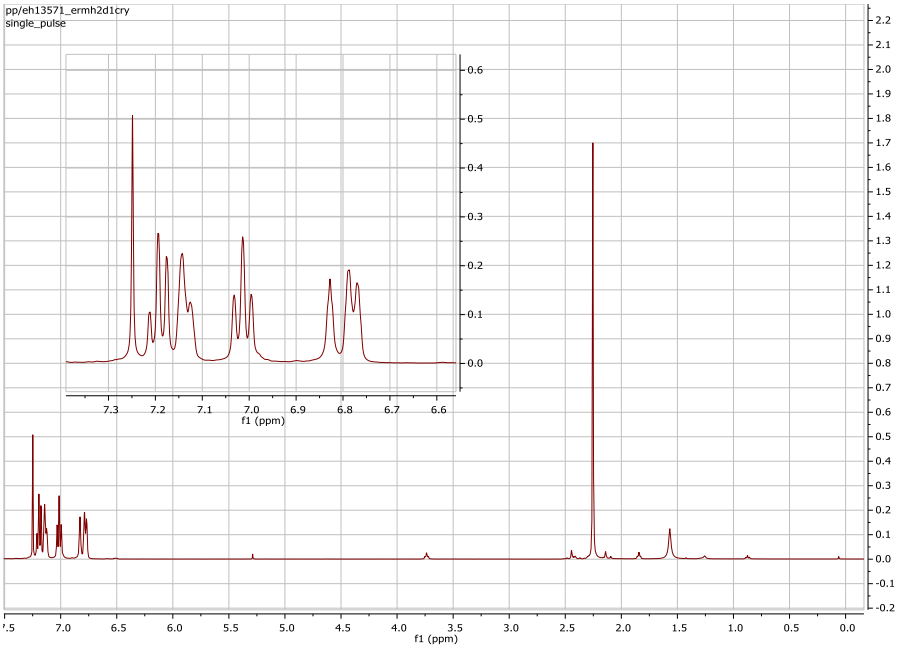

Figure 7 - ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{1b}}$

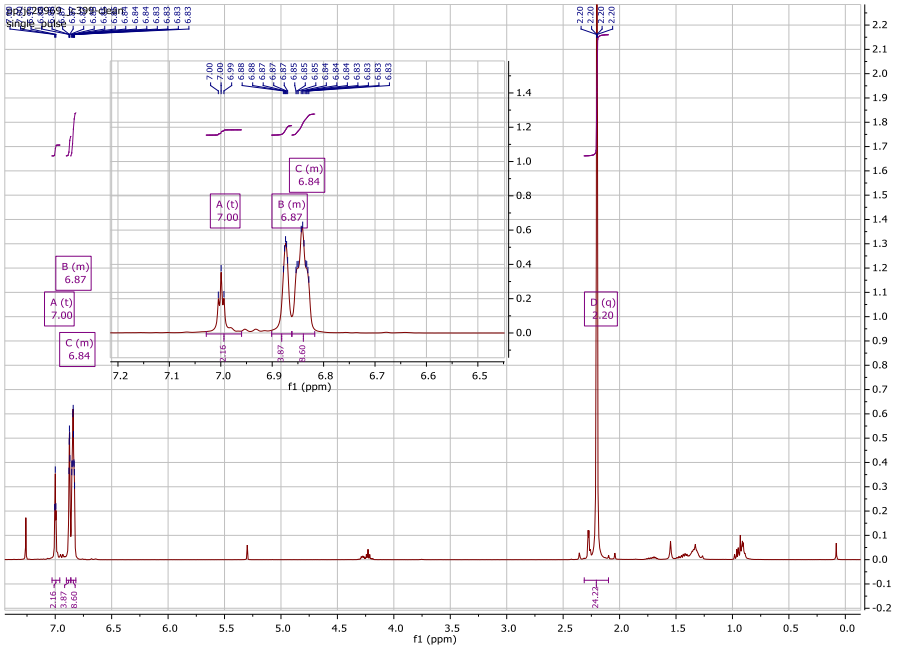

Figure 8 - ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{1c}}$

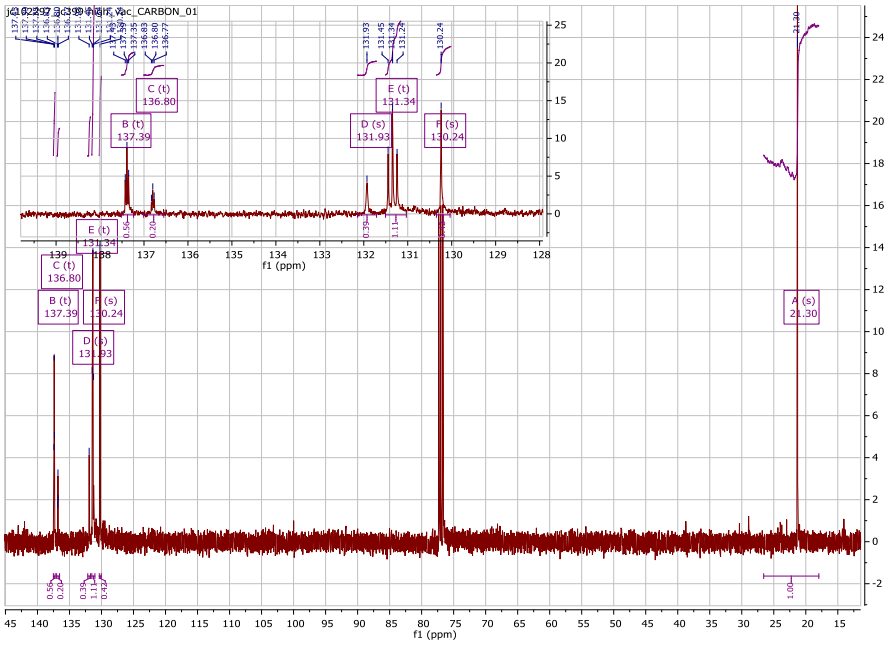

Figure 9 - ^{13}C NMR Spectrum of ligand $\boldsymbol{L_{1c}}$

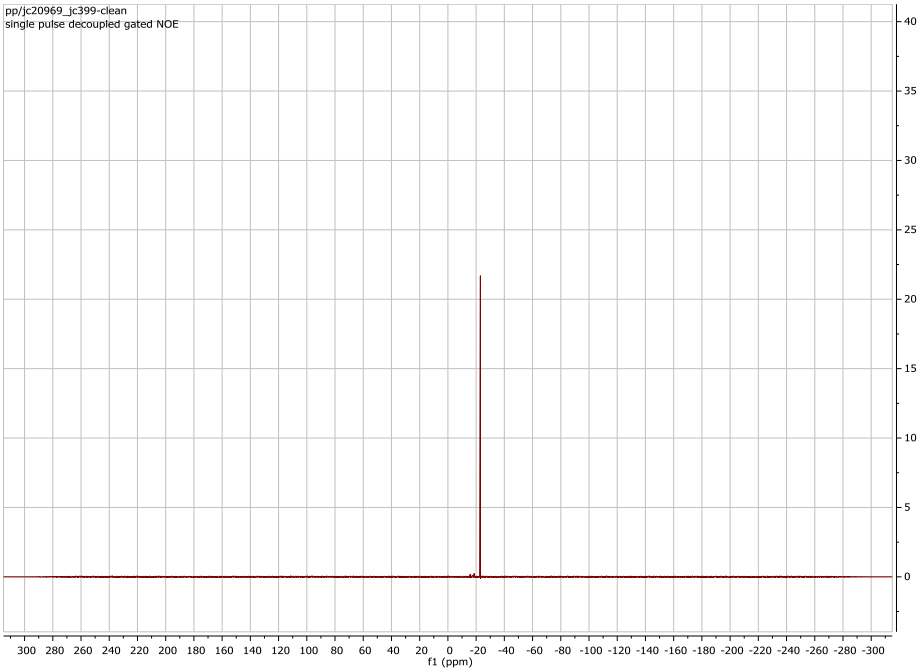

Figure 10 - ^{31}P NMR Spectrum of ligand $\boldsymbol{L_{1c}}$

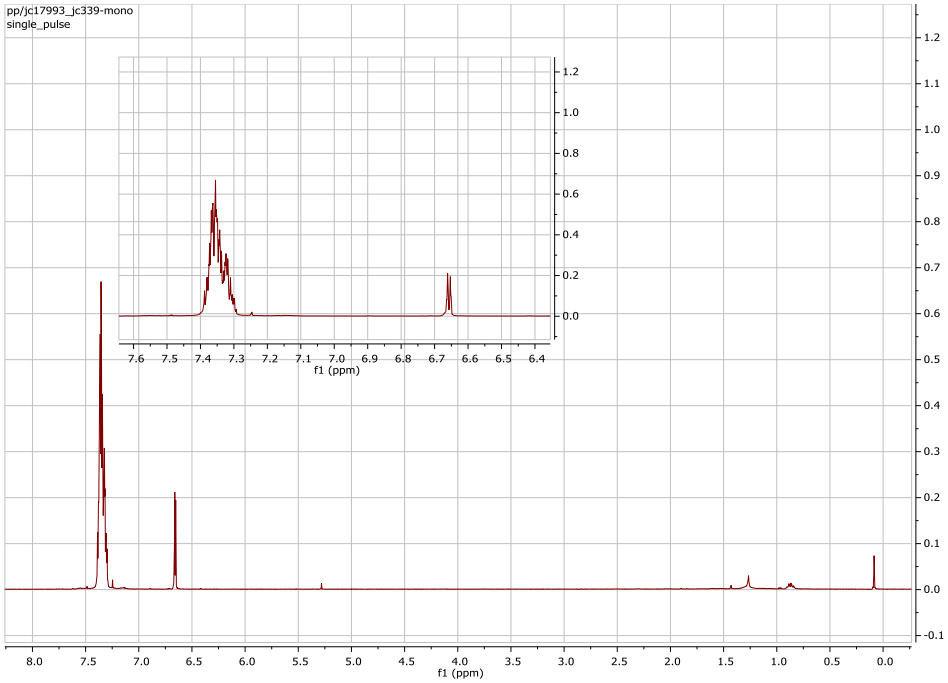

Figure 11 – ^{1}H NMR Spectrum of ***(4-bromothiophen-3-yl)diphenylphosphine***

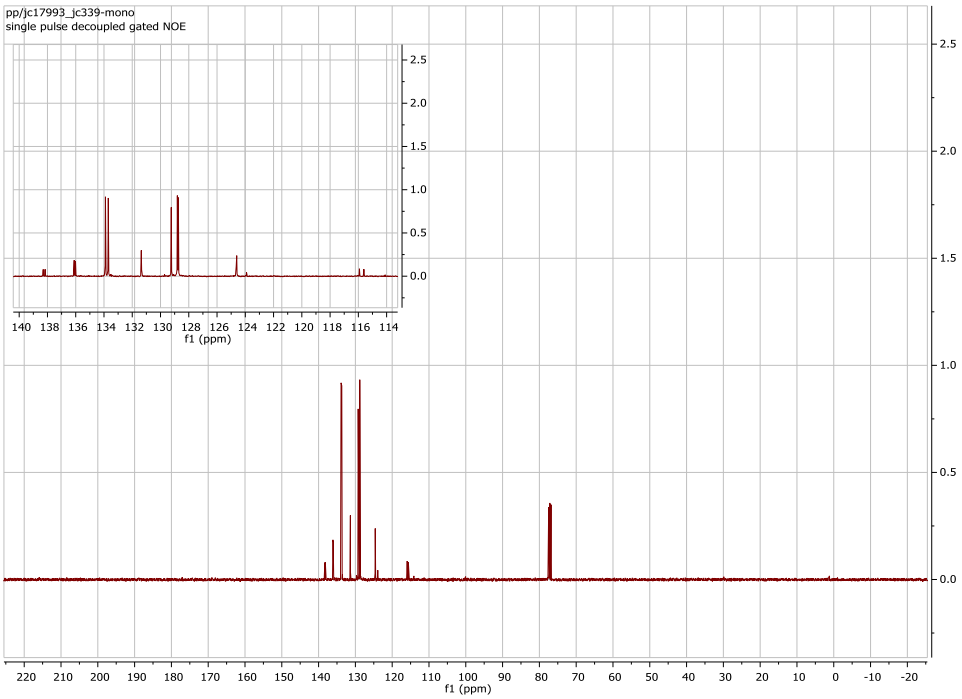

Figure 12 - ^{13}C NMR Spectrum of ***(4-bromothiophen-3-yl)diphenylphosphine***

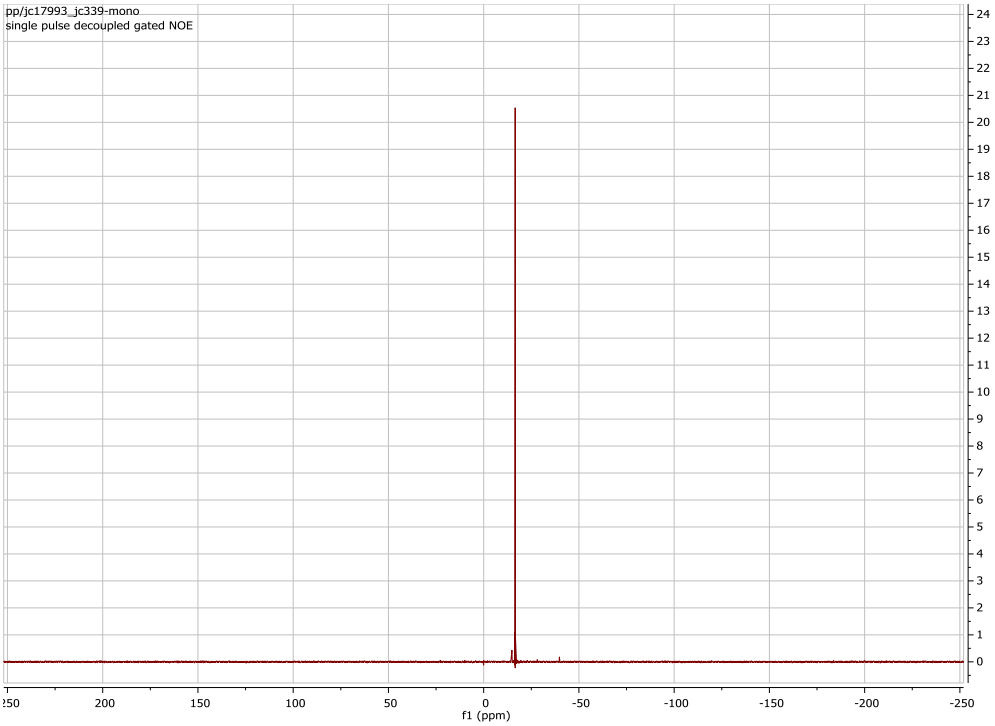

Figure 13 - ^{31}P NMR Spectrum of ***(4-bromothiophen-3-yl)diphenylphosphine***

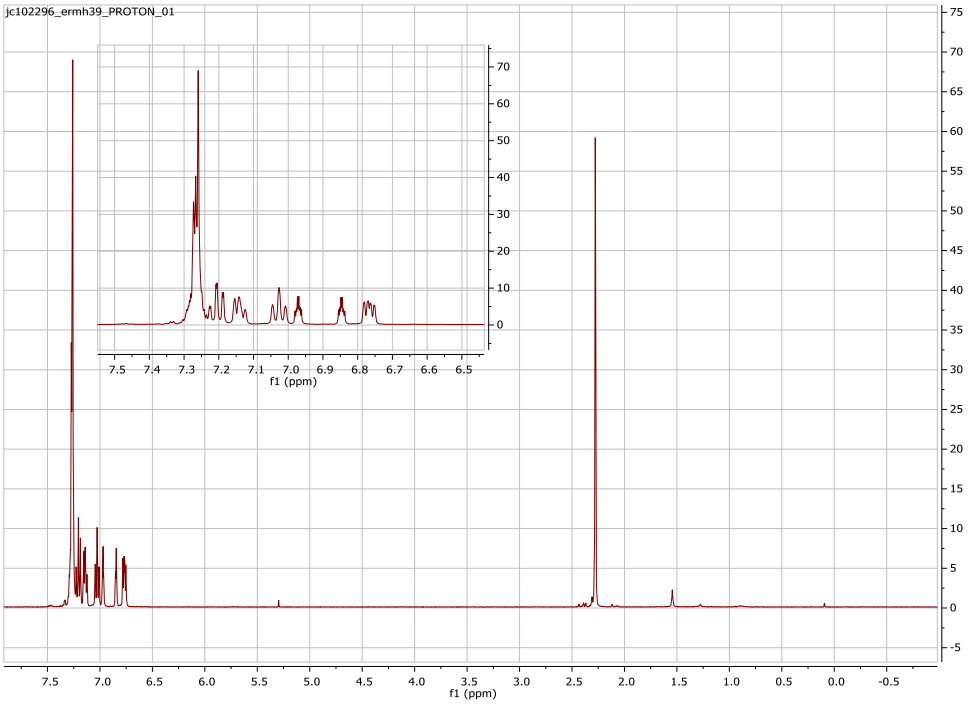

Figure 14 - ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{1d}}$

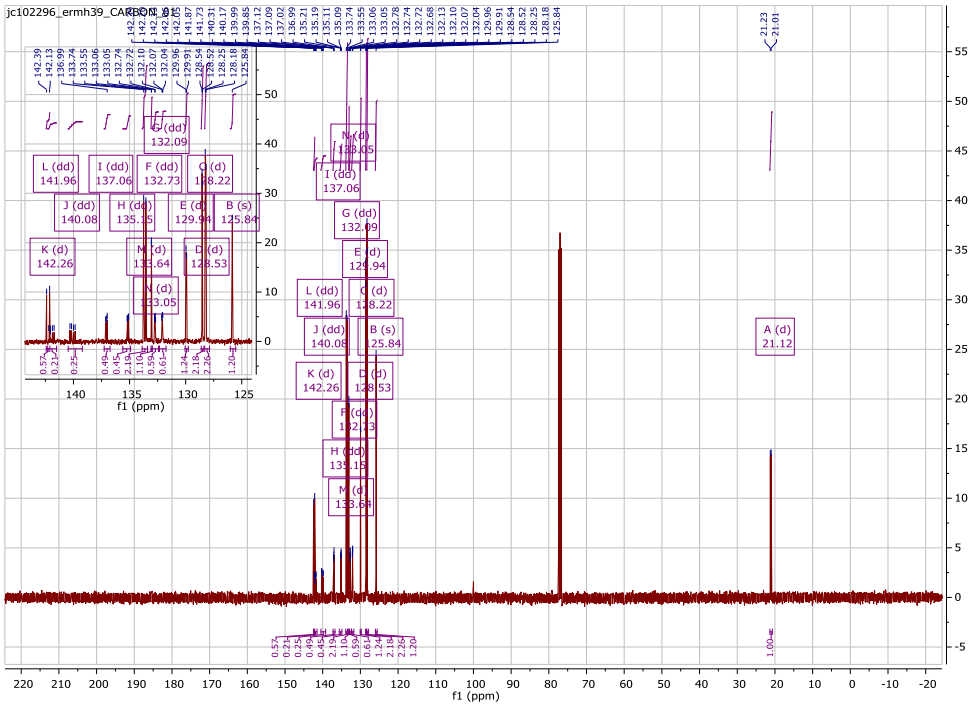

Figure 15 - ^{13}C NMR Spectrum of ligand ***L*** $_{1d}$

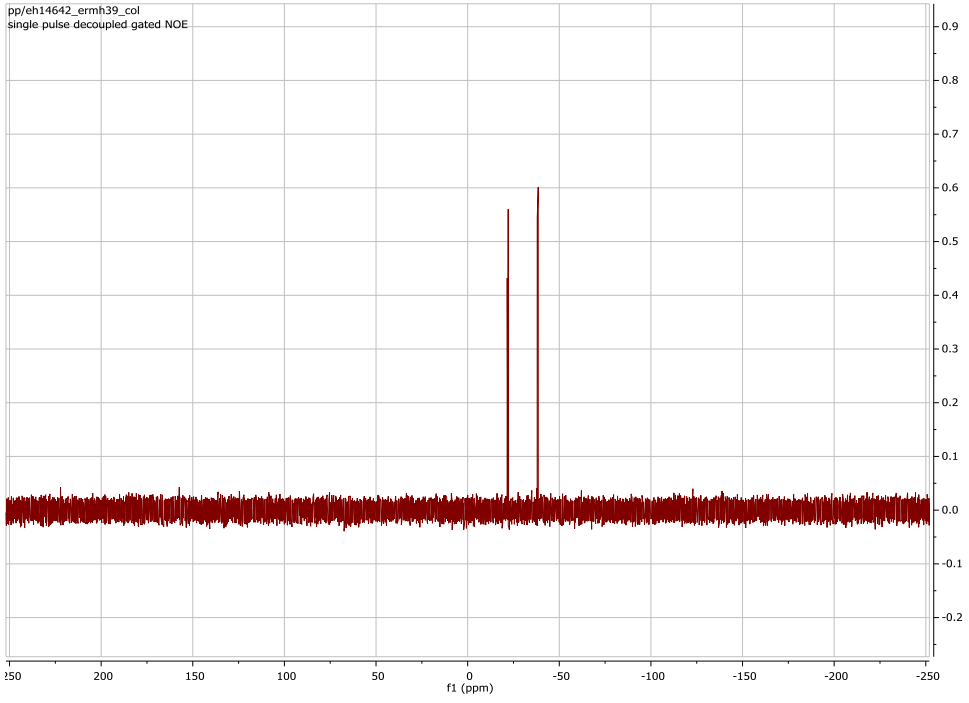

Figure 16 - ^{31}P NMR Spectrum of ligand ***L*** $_{1d}$

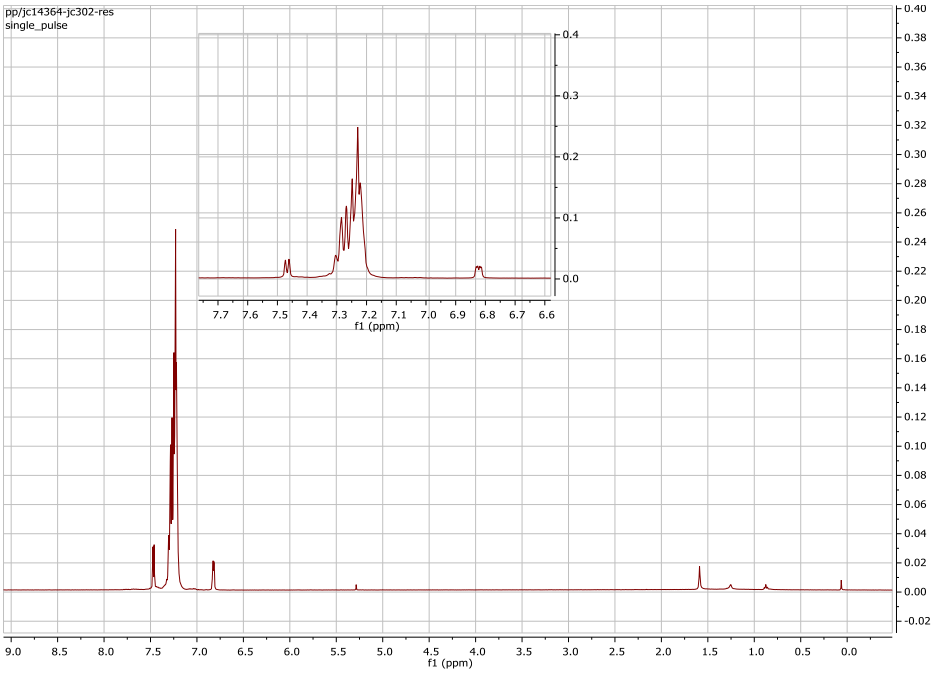

Figure 17 – ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{2a}}$

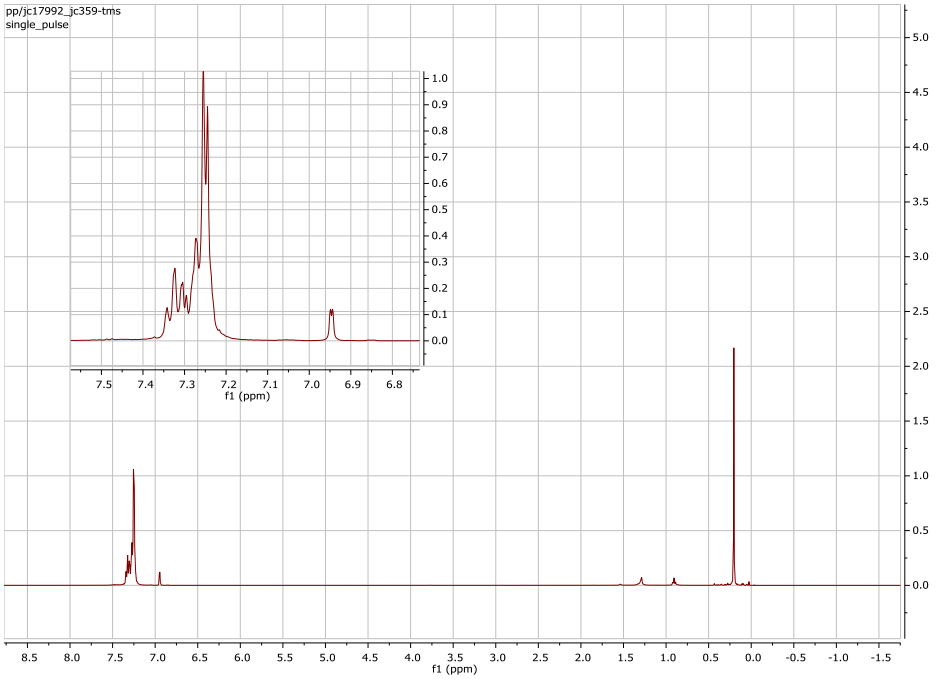

Figure 18 - ^{1}H NMR Spectrum of ligand $\boldsymbol{L_{2a}}$.

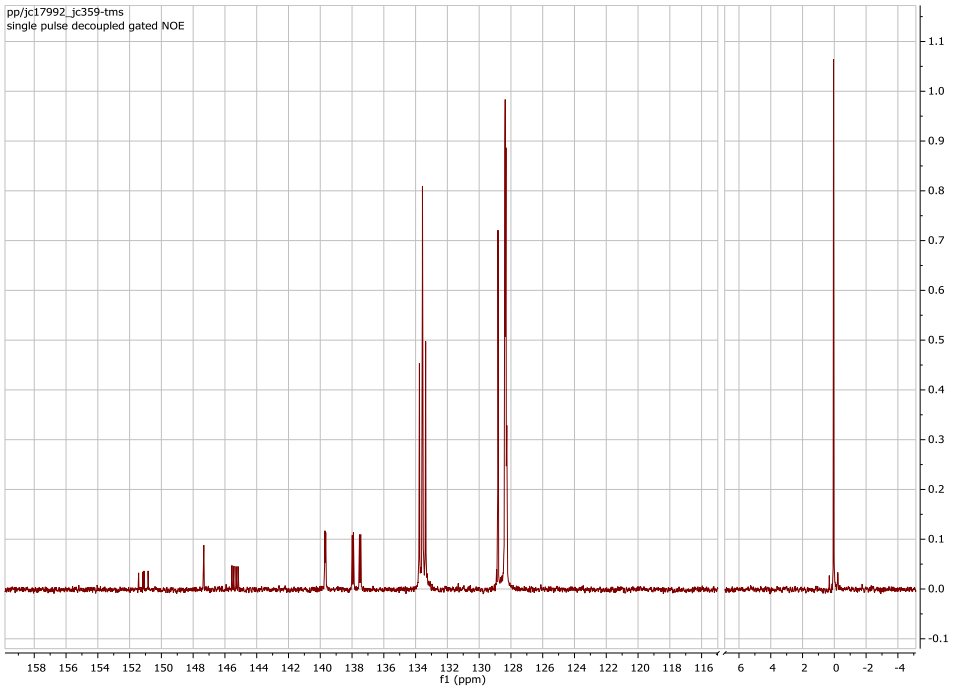

Figure 19 - ^{13}C NMR Spectrum of ligand $\boldsymbol{L_{2a}}$,

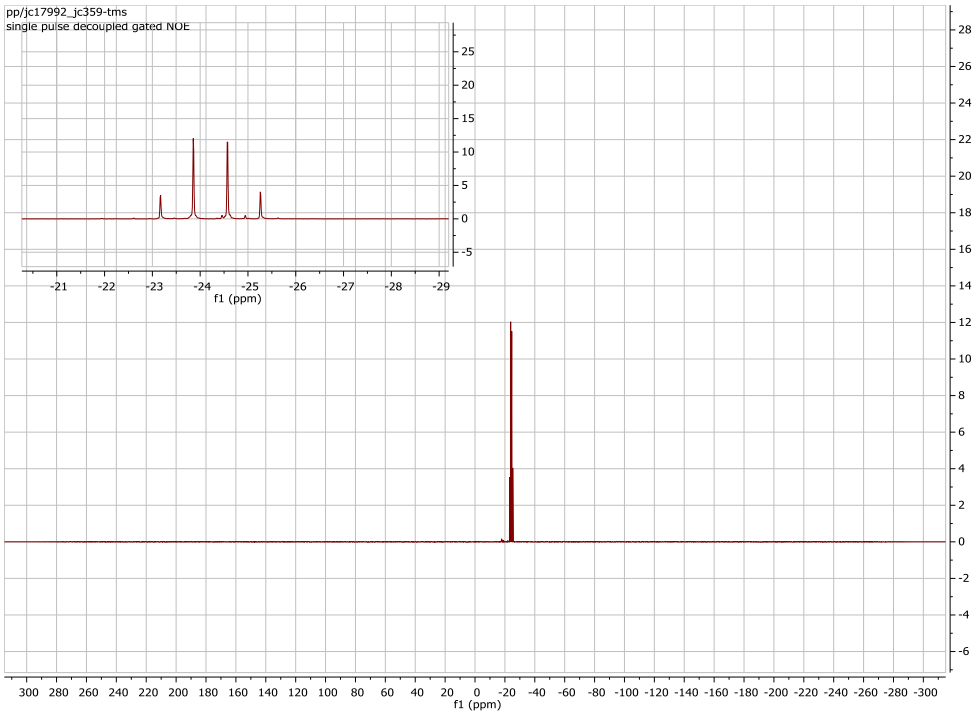

Figure 20 - ^{31}P NMR Spectrum of ligand $\boldsymbol{L_{2a}}$,

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