

# Acceptorless dehydrogenation of 4-methylpiperidine by supported pincer-ligated iridium catalysts in continuous flow

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## Contents

<b>1) General experimental procedure</b>	<b>3</b>
<b>2) Synthesis of complex 3</b>	<b>3-4</b>
<b>3) Synthetic procedure for supported catalysts</b>	<b>4-5</b>
<b>4) General procedure for the acceptorless dehydrogenation of 4-methylpiperidine in a continuous flow reactor</b>	<b>5-8</b>
<b>5) Crystallography</b>	<b>8</b>
<b>6) NMR data</b>	<b>9-15</b>
<b>7) Calculation for the TON and TOF</b>	<b>16</b>
<b>8) References</b>	<b>16</b>

## 1. General experimental procedure

Al<sub>2</sub>O<sub>3</sub> and SiO<sub>2</sub> were calcined at 550 °C for 3 h in a gastight reactor equipped with valves to seal the samples in dry air during the calcination. After slow cooling of the calcined material, it was dried under high vacuum and stored in a nitrogen filled glovebox until use. Air or moisture sensitive materials were stored in a nitrogen filled glovebox. All experiments were carried out under an inert atmosphere using glove box, Schlenk or high vacuum line techniques unless otherwise noted. THF, hexane, benzene and toluene were distilled from Na/benzophenone under nitrogen. <sup>i</sup>PrOH was distilled from calcium hydride under nitrogen. All NMR spectra were recorded on Bruker Advance 400 MHz instrument and signals are reported in ppm. IR spectra were recorded on a Bruker Alpha II spectrometer. Elemental analysis was performed by Mikrolab Mikroanalytisches Laboratorium Kolbe. HRMS analysis were recorded on a Waters Xevo-G2 QTOF instrument. **1@SiO<sub>2</sub>-cal**,<sup>1</sup> **2@Al<sub>2</sub>O<sub>3</sub>-cal** and **2@Al<sub>2</sub>O<sub>3</sub>-uncal**<sup>2</sup> were synthesised according to previously reported procedures.

## 2. Synthesis of complex 3

**2.1. Dibenzyl-4,6-dihydroxyisophthalate:** 4,6-dihydroxyisophthalic acid (300 mg, 1.51 mmol, 1 equiv.) was dissolved in dry DMF (6 mL) to which was added benzyl bromide (0.38 mL, 3.2 mmol, 2.1 equiv.). After the solid was dissolved, potassium bicarbonate (198 mg, 1.98 mmol, 1.3 equiv.) was added and the mixture was left to stir overnight at ambient temperature. The reaction was quenched by addition of water after which the product was extracted using diethyl ether (3x50 mL) which was further washed with a mixture of ice and brine. The organic phase was collected and dried using magnesium sulphate. The solvent was removed under reduced pressure to obtain a white crystalline material (452 mg, 79% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 11.26 (s, 2H), 8.50 (s, 1H), 7.44-7.37 (m, 10H), 6.50 (s, 1H), 5.38 (s, 4H). <sup>13</sup>C NMR (101 MHz, CDCl<sub>3</sub>) δ 169.14, 167.29, 135.26, 134.32, 128.71, 128.56, 128.19, 105.81, 104.29, 66.99. IR: 3000 cm<sup>-1</sup> (w, very broad, O-H), 1676 cm<sup>-1</sup> (s, C=O).

**2.2. Dibenzyl-POCOP (L3):** Dibenzyl-4,6-dihydroxyisophthalate (300 mg, 0.8 mmol, 1 equiv.) and NaH (57 mg, 2.38 mmol, 3 eq.) were dissolved in THF and stirred at room temperature for 12 h under nitrogen. <sup>t</sup>Bu<sub>2</sub>PCl (0.53 mL, 2.78 mmol, 3.5 equiv.) was added with a syringe to the solution. The reaction mixture was heated at reflux for 2 h after which the solvent was evaporated. The residue was extracted with hexane and filtered through a pad of celite under inert conditions. The extract liquor was dried for 3 h at 80 °C, leaving a dense oily product which was around 98% pure and used in next step without further purification. <sup>1</sup>H

NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  8.95 (s, 1H), 8.35 (t,  $J$  = 6.4 Hz, 1H), 7.24-7.21 (m, 4H), 7.09-7.04 (m, 6H), 5.16 (s, 4H), 1.14 (d,  $J$  = 12.0 Hz, 36H). <sup>13</sup>C NMR (101 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  163.91, 137.27, 136.69, 128.30, 128.24, 113.95, 107.72, 65.90, 35.70 (d,  $J$  = 26.5 Hz), 29.85, 27.07 (d,  $J$  = 15.7 Hz) 2 carbons not visible. <sup>31</sup>P NMR (162 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  = 156.59 (s).

**2.3. [IrHCl(dibenzyl-POCOP)] (3a)** In a nitrogen-filled glovebox, ligand **L3** (250 mg, 0.37 mmol, 1 equiv.) was dissolved in 20 mL of toluene and transferred to a Schlenk flask. [Ir(COD)Cl]<sub>2</sub> (126 mg, 0.185 mmol, 0.5 equiv.) was added after which the reaction was refluxed overnight under nitrogen. The mixture was allowed to cool after which the solvent was removed in vacuum. The crude product was purified using column chromatography (silica gel 230-400 mesh, gradient hexane:DCM 1:1 to 0:1). The deep orange fraction was collected and evaporated which gave red-orange crystals (261 mg, 78% yield). <sup>1</sup>H NMR (400 MHz, C<sub>6</sub>D<sub>6</sub>):  $\delta$  8.92 (s, 1H), 7.21-7.19 (m, 4H), 7.09-7.02 (m, 6H), 5.22-5.14 (m, 4H), 1.22 (vt,  $J$  = 14.9 Hz, 18H), 1.16 (vt,  $J$  = 15.1 Hz, 18H) -40.49 (t,  $J$  = 12.7 Hz, 1H). <sup>13</sup>C NMR (101 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  168.79, 164.16, 136.64, 133.06, 128.53, 128.28, 110.44, 66.18, 42.92 (vt,  $J$  = 23.2 Hz), 39.31 (vt,  $J$  = 25.2 Hz), 27.15 (vt,  $J$  = 6.1 Hz) 27.04 (vt,  $J$  = 7.1 Hz) 2 carbons not visible. <sup>31</sup>P NMR (162 MHz, C<sub>6</sub>D<sub>6</sub>)  $\delta$  = 181.58 (s). IR: 1704 cm<sup>-1</sup> (s, C=O). Anal. calcd for C<sub>38</sub>H<sub>52</sub>ClIrO<sub>6</sub>P<sub>2</sub>: C, 51.03; H, 5.86. Found: C, 50.96; H, 5.88. HR-MS: calcd for C<sub>38</sub>H<sub>52</sub>ClIrO<sub>6</sub>P<sub>2</sub>: 892.2534. Found: 892.2554.

**2.4. [IrHCl(dicarboxylate-POCOP)] (3): 3a** (100 mg, 0.11 mmol) was charged into a Schlenk flask together with 10% Pd/C (50 mg) and suspended in 10 mL of THF:MeOH (1:1). The solution was degassed by three cycles of freeze-pump-thaw. The flask was filled with H<sub>2</sub> gas at -196 °C, and allowed to stir at room temperature for 4 h. The Pd/C was then removed by filtering the suspension over a pad of celite, after which the solution was evaporated giving a red-orange powder (64 mg, 81% yield). <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.54 (s, 1H), 1.43 (vt,  $J$  = 15.8 Hz, 18H), 1.42 (vt,  $J$  = 15.2 Hz, 18H), -40.80 (t,  $J$  = 12.9 Hz, 1H). <sup>13</sup>C NMR (101 MHz, THF-d<sub>8</sub>)  $\delta$  168.50, 164.87, 132.91, 124.93, 110.22, 43.01 (vt,  $J$  = 23.2 Hz), 39.38 (vt,  $J$  = 25.2 Hz), 26.91 (t,  $J$  = 6.6 Hz), 26.80 (t,  $J$  = 6.2 Hz). <sup>31</sup>P NMR (162 MHz, CDCl<sub>3</sub>)  $\delta$  185.13 (s). IR: 1680 cm<sup>-1</sup> (s, C=O). Anal. calcd for C<sub>24</sub>H<sub>40</sub>ClIrO<sub>6</sub>P<sub>2</sub>: C, 40.36; H, 5.65. Found: C, 40.12; H, 5.58. HR-MS: calcd for C<sub>24</sub>H<sub>40</sub>ClIrO<sub>6</sub>P<sub>2</sub>: 713.1673. Found: 713.1682.

### 3. Synthetic procedure for supported catalysts

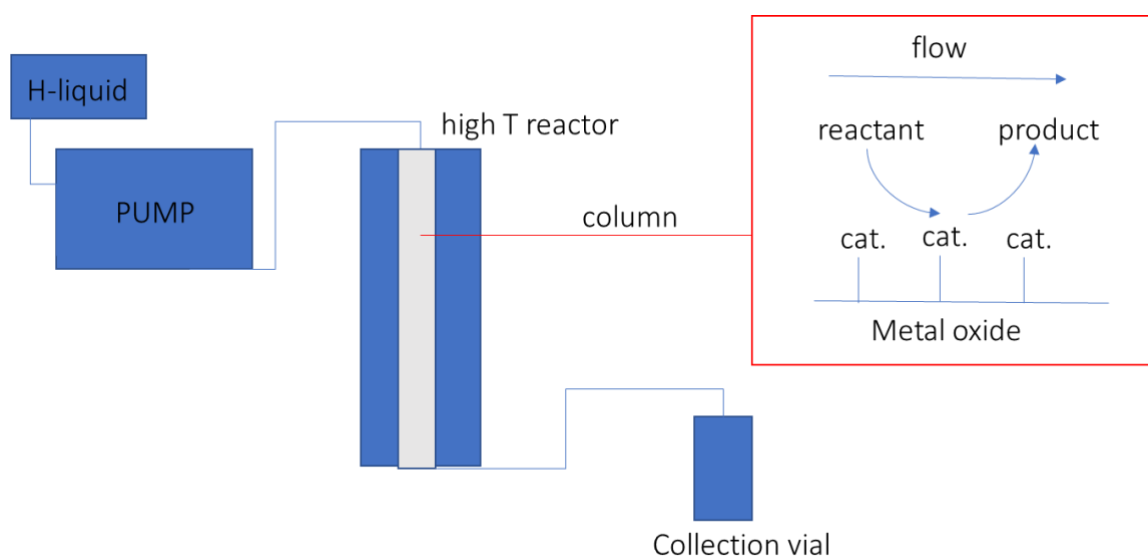
**4A. Procedure for 3@Al<sub>2</sub>O<sub>3</sub>-cal:** In a typical experiment, calcined alumina (1.6 g) was charged in a Straus flask inside the glove box. Complex **3** (0.020 g, 0.028 mmol), <sup>t</sup>BuOK (0.012 g, 0.112 mmol) and 12 ml of <sup>i</sup>PrOH were added, the flask was fully immersed into an oil bath

and heated at 100 °C for 2 h. The flask was brought to room temperature, the solution was decanted, and the solid residue was washed with *i*PrOH (2×4 mL) and dried in vacuum for 2 h. The pale orange solid was stored inside the glove box.

**4B. Procedure for 3@Al<sub>2</sub>O<sub>3</sub>-uncal:** The uncalcined alumina was kept in the oven at 135 °C overnight and stored inside the glove box. In a typical experiment, uncalcined alumina (1.6 g) was charged in a Straus flask inside the glove box. Complex **3** (0.020 g, 0.028 mmol), *t*BuOK (0.012 g, 0.112 mmol) and 12 mL of *i*PrOH were added, the flask was fully immersed into an oil bath and heated at 100 °C for 2 h. The flask was brought to room temperature, the solution was decanted, and the solid residue was washed with *i*PrOH (2×4 mL) and dried in vacuum for 2 h. The pale orange solid was stored inside the glove box.

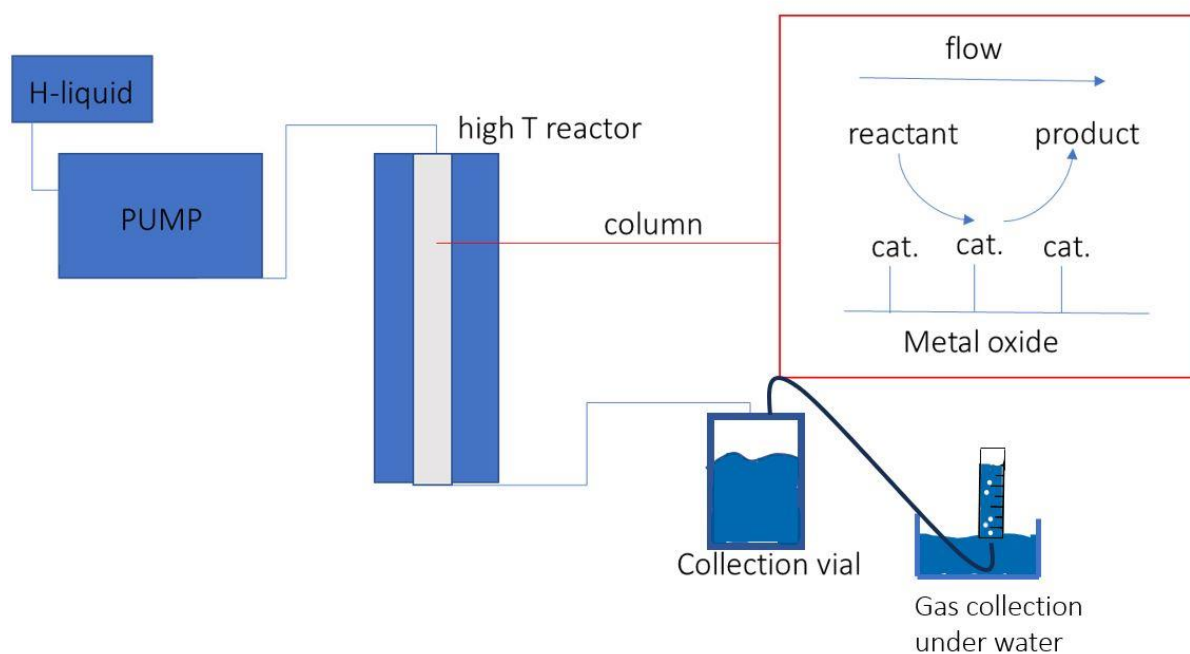
#### 4. General procedure for the acceptorless dehydrogenation of 4-methylpiperidine in a continuous flow reactor.

In a typical experiment, in a nitrogen atmosphere glovebox, the catalyst (5 mg of **1** on 0.150 g of SiO<sub>2</sub> or 5 mg of **2** on 0.400 g of calcined/uncalcined Al<sub>2</sub>O<sub>3</sub> or 5 mg of **3** on 0.400 g of calcined/uncalcined Al<sub>2</sub>O<sub>3</sub>) was placed inside a packed-bed tubular reactor (inner d = 5 mm, l = 200 mm), equipped with a porous metal plug at the outer end. The tubular reactor was sealed, taken out of the glovebox, placed inside an aluminium block heater and connected to a flask with substrate via an HPLC pump (Shimadzu LC-40D). The reactor was pre-heated to the specified temperatures and the flow of substrate was switched on. Cooling of an outlet tubing and collection flask was used to ensure that products of the reaction will not be partially evaporated by a hydrogen stream.

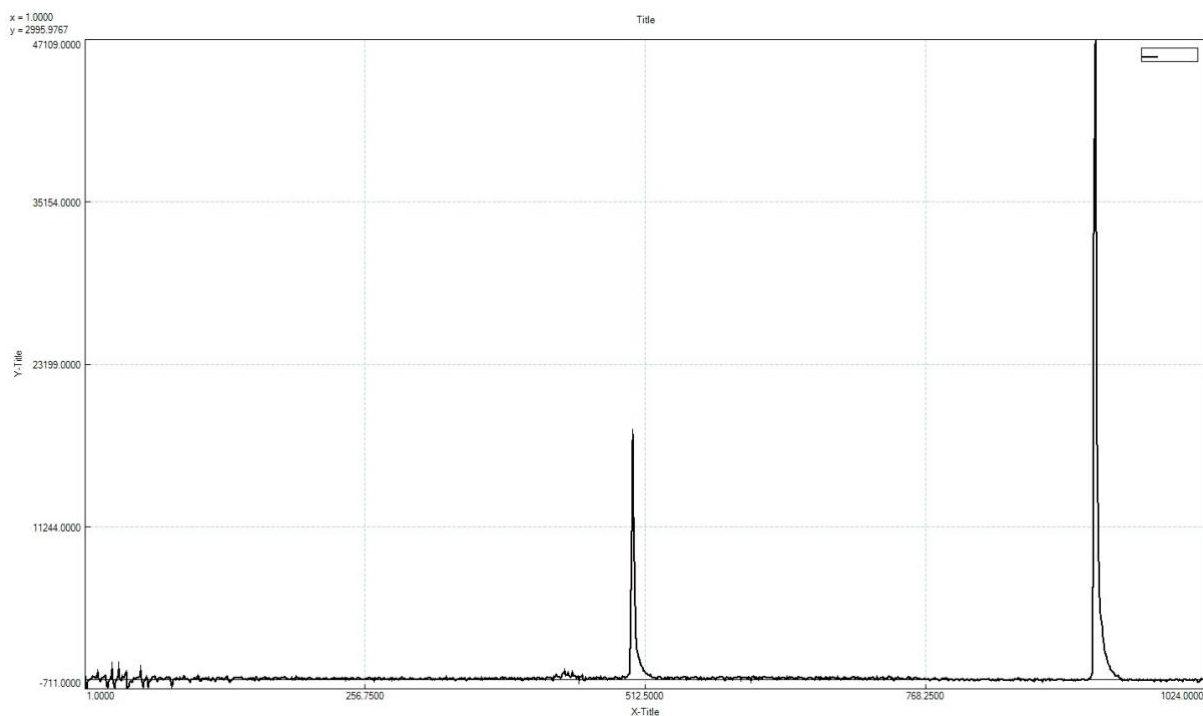


**Figure S1.** Pictorial diagram of the continuous-flow reactor system.

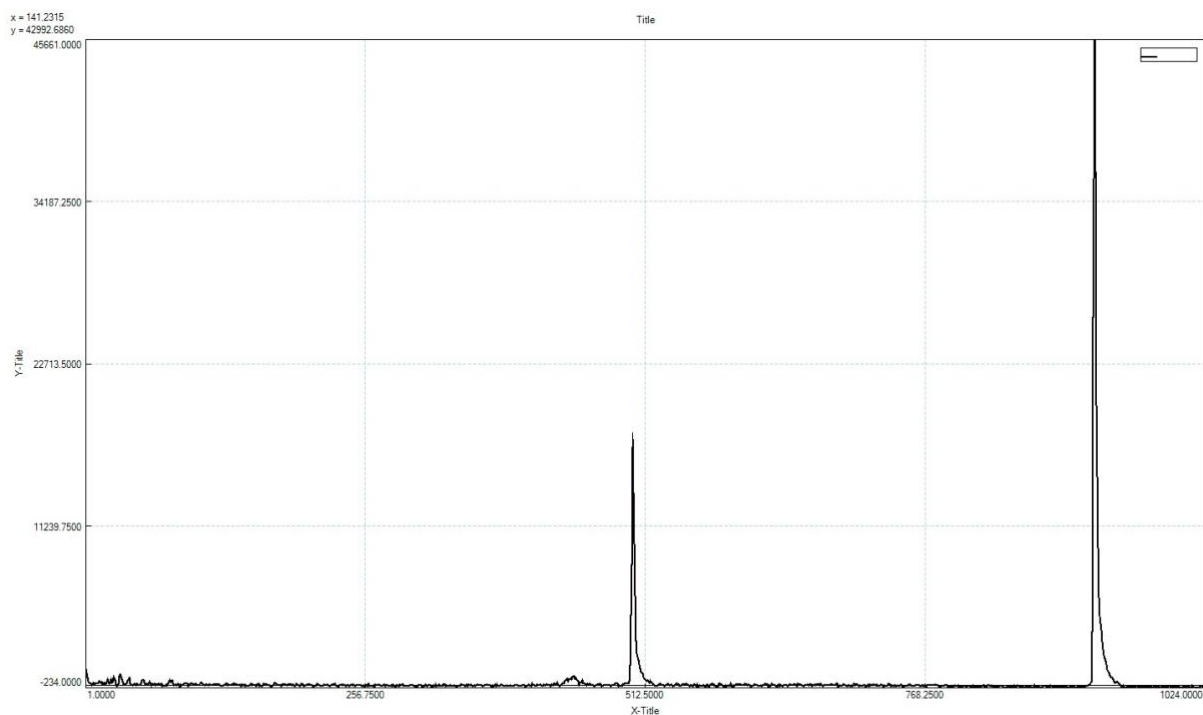
For the quantitative and qualitative analysis of hydrogen produced, the whole flow system was fitted to ensure that there was no gas leak. The organic contents were collected into a vial and the remaining hydrogen gas was collected by the inverted burette method under water (**Figure S2**). The collected hydrogen gas was analysed by Raman spectroscopy (**Figure S3**) and compared against pure hydrogen gas from commercial source (**Figure S4**).



**Figure S2.** Pictorial diagram of the continuous flow system modified for gas collection.



**Figure S3.** Raman spectrum of hydrogen from flow reactor.



**Figure S4.** Raman spectrum of pure hydrogen gas from commercial source.

The produced hydrogen was quantified by comparing the flow rate of hydrogen with the yields of dehydrogenated products calculated from the NMR spectra of the corresponding organic fractions.

**Flow reaction condition for quantitative analysis of H<sub>2</sub>**

Catalyst = **1**@SiO<sub>2</sub>, temperature = 350 °C, flow rate = 0.025 mL/min.

H<sub>2</sub> collected over 1 h = 103.4 mL = 4.61 mmol

Quantities of dehydrogenated products (calculated by NMR analysis):

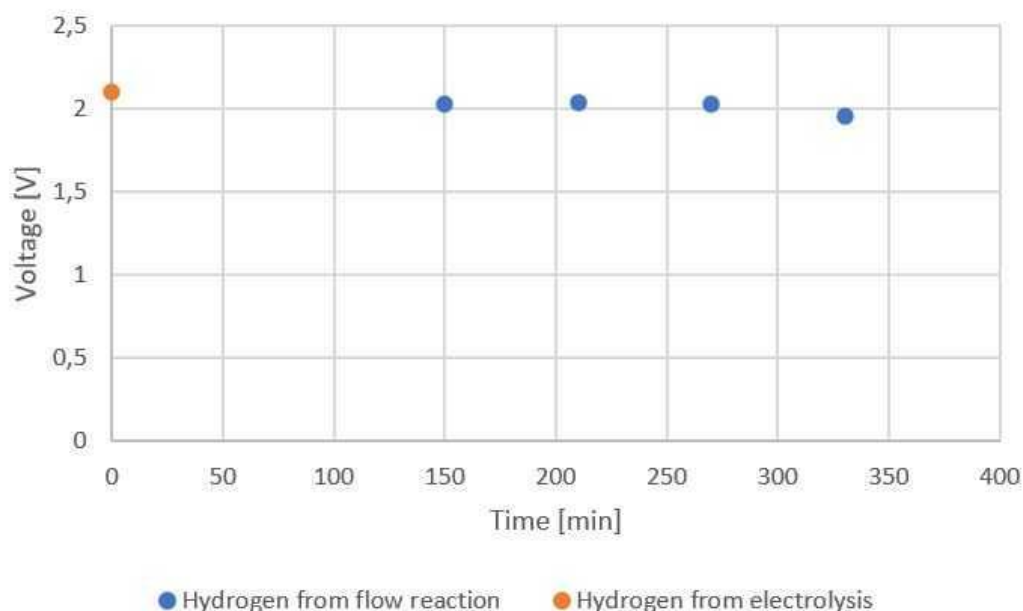
P1 = 29.6 % = 4.25 mmol, P2 = <1 % = negligible, P3 = 2.4 % = 0.37 mmol

Expected amount of H<sub>2</sub> formed = 5.35 mmol

% of H<sub>2</sub> collected = 86%.

### Fuel cell test

The quality of the hydrogen produced in the flow reaction was tested by feeding it to a fuel cell and the output voltage was monitored. The H<sub>2</sub> from flow reactor was able to maintain the voltage for 6 h. The output voltage with H<sub>2</sub> produced from flow reaction was same as with the H<sub>2</sub> produced by electrolysis.



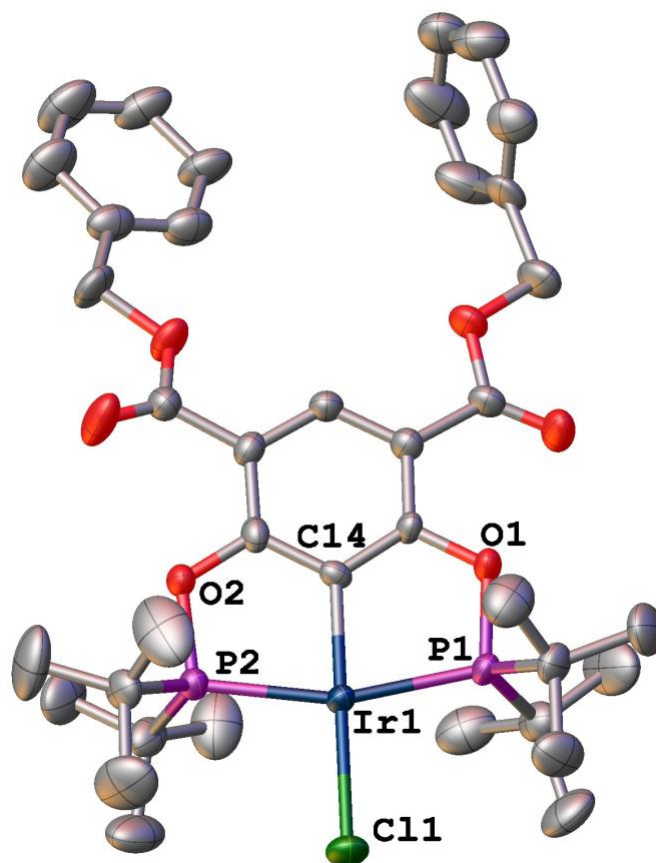
**Figure S5.** Comparison of output voltage of fuel cell utilizing H<sub>2</sub> from flow reaction and H<sub>2</sub> from electrolysis.

## 5. Crystallography

Crystals of complex **3a** suitable for single crystal X-ray analysis were grown by vapour diffusion of hexane to a saturated solution of **3a** in benzene. The X-ray diffraction intensity data were collected using an Oxford diffraction Excalibur 3 diffractometer,<sup>3</sup> using  $\omega$ -scans and Mo K $\alpha$  ( $\lambda = 0.71073 \text{ \AA}$ ) radiation. The crystals were thin needles which had severe twinning. After mounting multiple samples, the best dataset was selected and used. Crysalispro RED program<sup>4</sup> was used to extract and integrate the data. Structure solution was done by intrinsic



phasing method with ShelXT,<sup>5</sup> and the structure was refined by full matrix least square calculations on  $F^2$  with ShelXL.<sup>6</sup> The structure graphics was generated using the Olex2 program.<sup>7</sup> The CCDC deposition number of the XRD data of complex **3a** is 2270316.



**Figure S5.** XRD structure of complex **3a** (hydrogen atoms and minor components of disordered atoms are omitted for clarity). Selected bond length: C14–Ir1 2.023(7), P2–Ir1 2.293(2), P1–Ir1 2.286(2), C11–Ir1 2.388(2), P1–O1 1.670(5), P2–O2 1.663(5). Selected bond angles: P2–Ir1–C14 80.7(2), P1–Ir1–C14 80.1(2), P1–Ir1–C11 99.65 (8), P1–Ir1–C11 99.03 (8), C14–Ir1–C11 172.6, P1–Ir1–P2 160.63(7).

## 6. NMR data

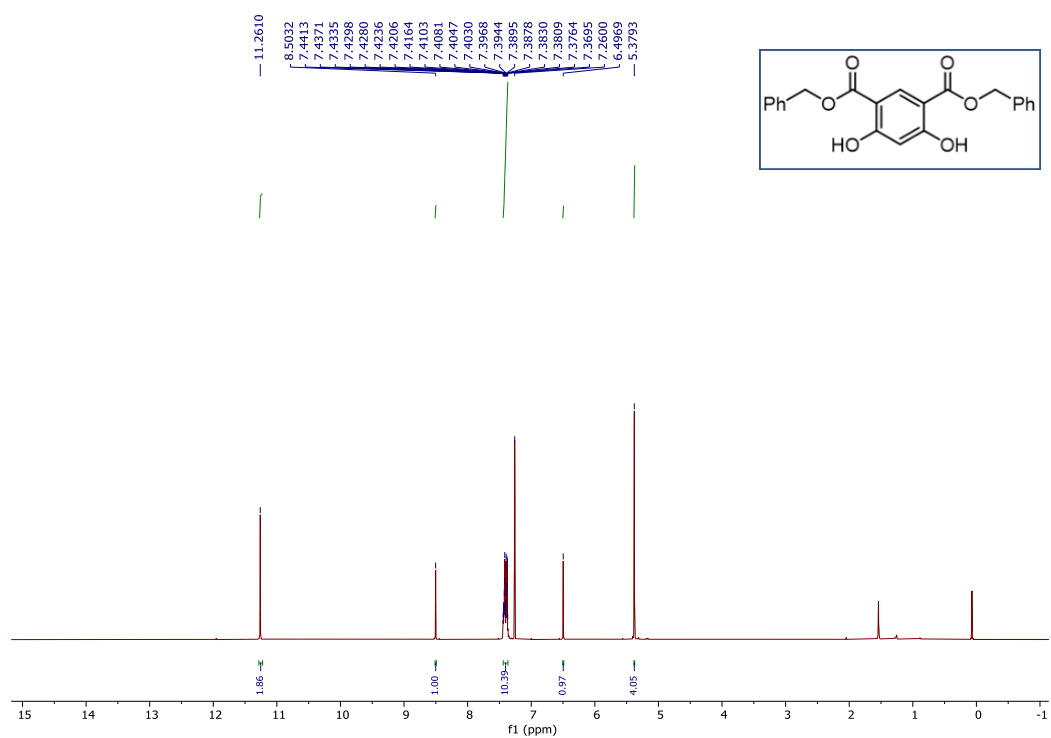


Figure S6. <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of the dibenzyl-4,6-dihydroxyisophthalate.

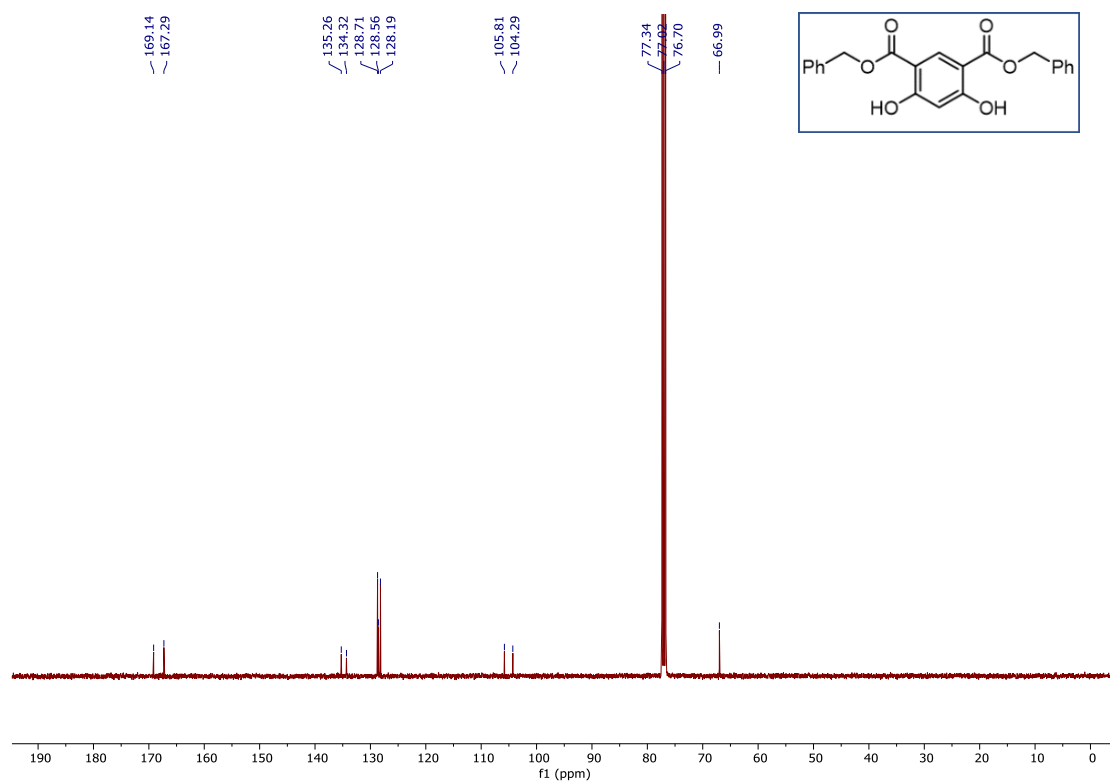
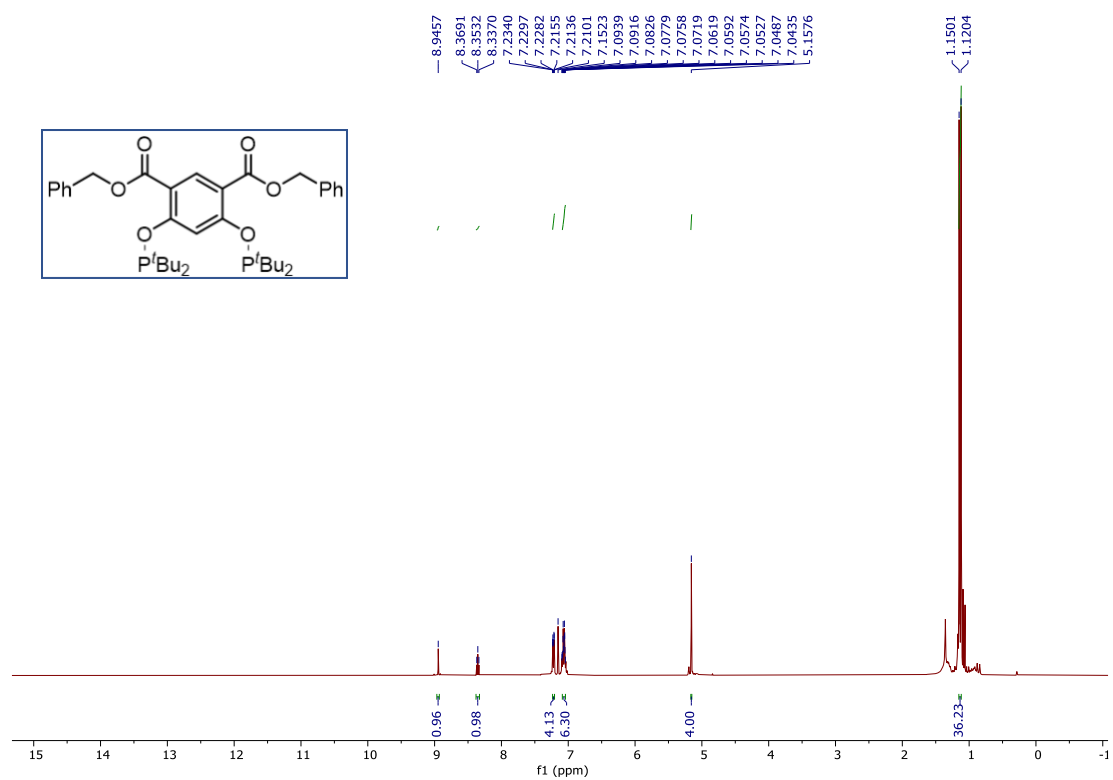
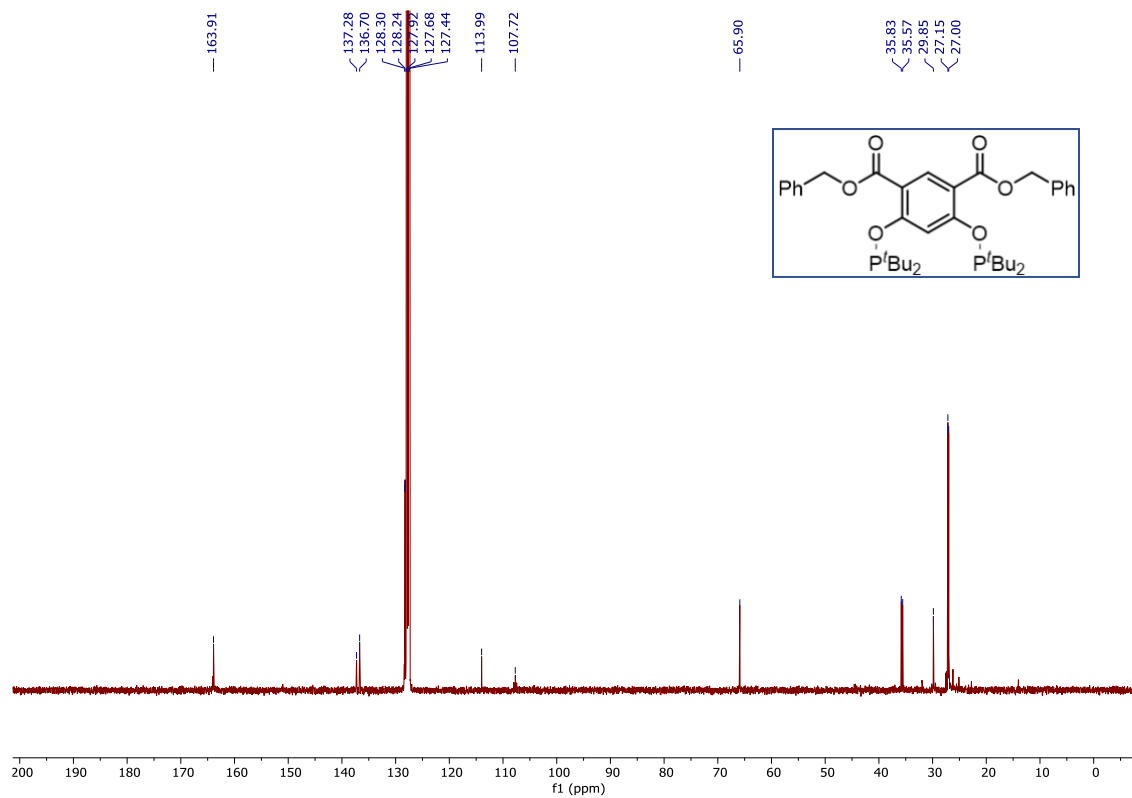


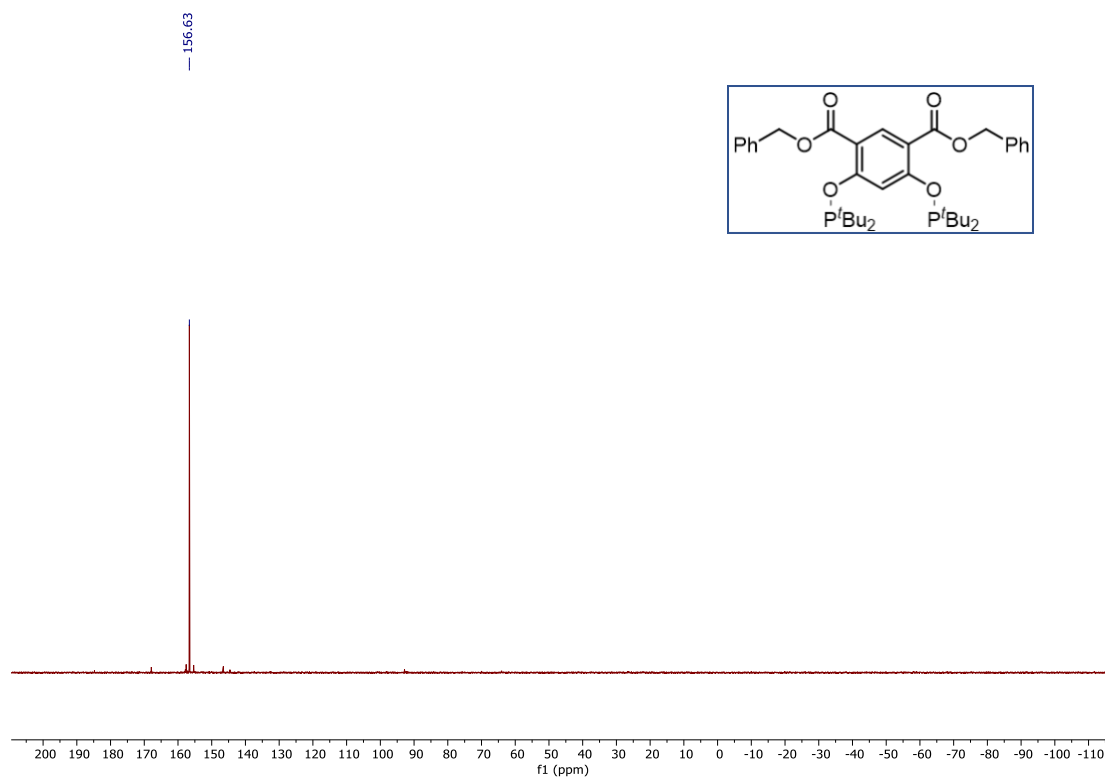
Figure S7. <sup>13</sup>C NMR spectrum (101 MHz, CDCl<sub>3</sub>) of the dibenzyl-4,6-dihydroxyisophthalate.



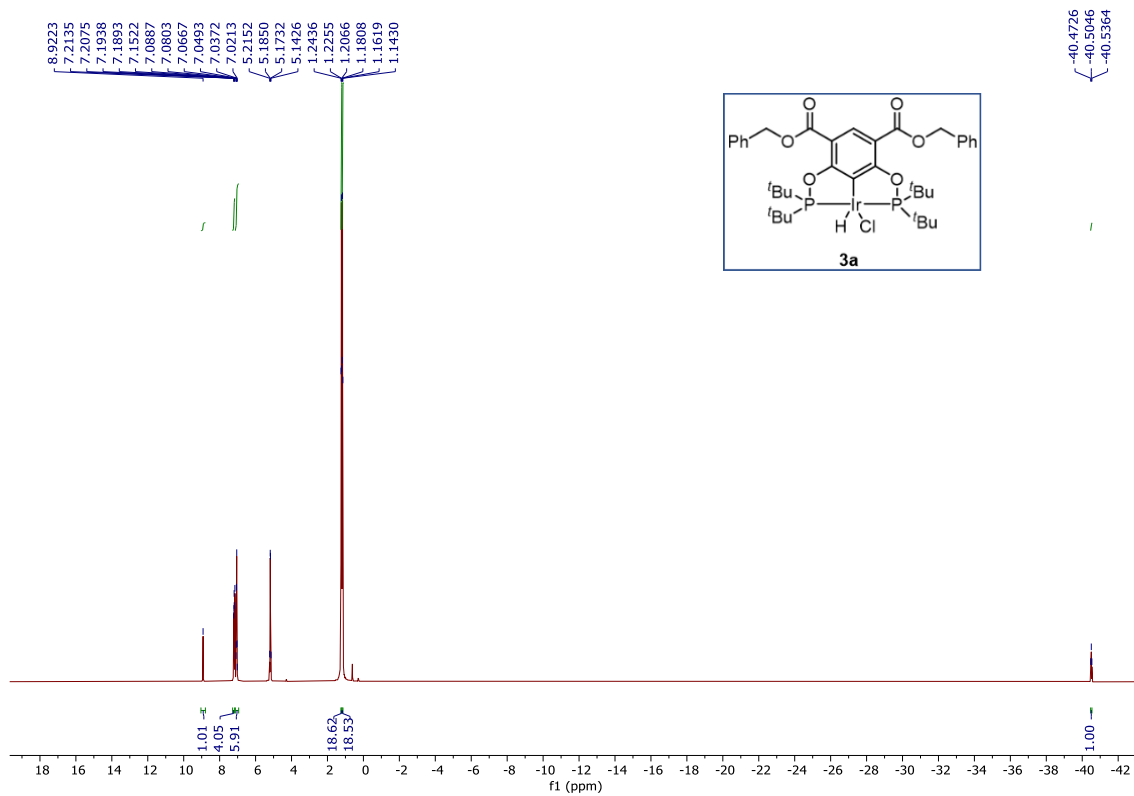
**Figure S8.** <sup>1</sup>H NMR spectrum (400 MHz, C<sub>6</sub>D<sub>6</sub>) of the dibenzyl-POCOP (L3).



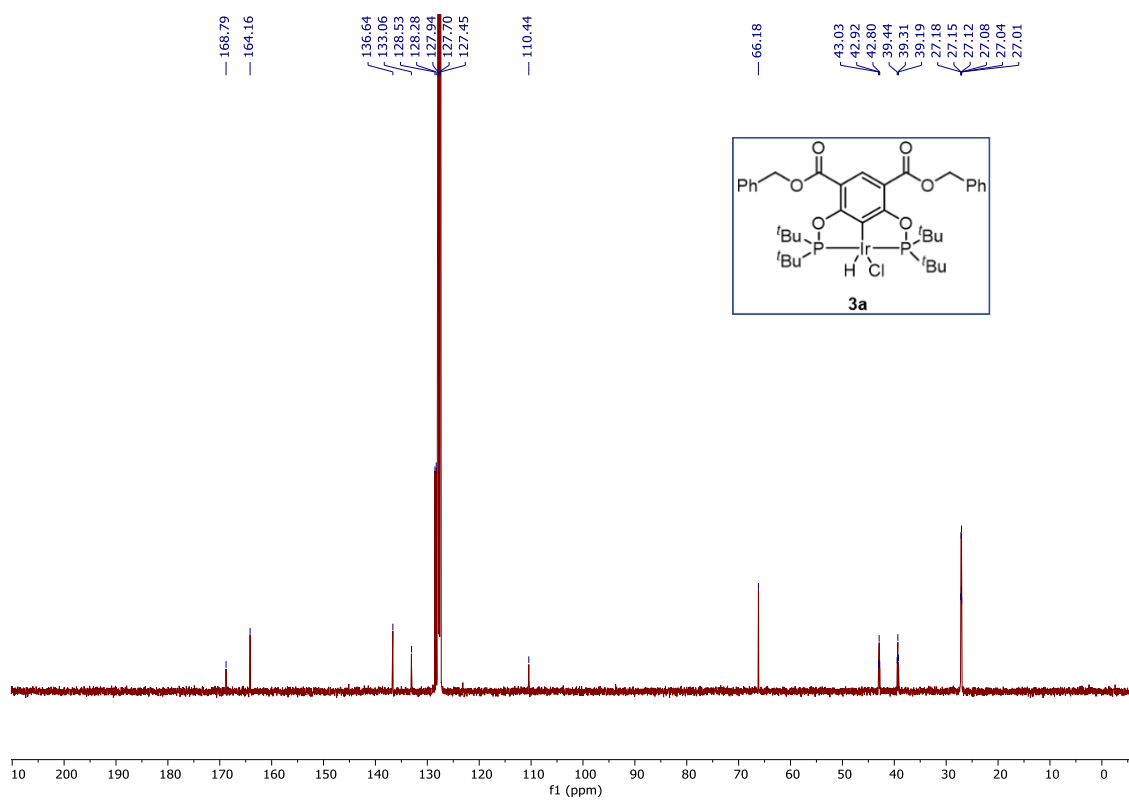
**Figure S9.** <sup>13</sup>C NMR spectrum (101 MHz, C<sub>6</sub>D<sub>6</sub>) of the dibenzyl-POCOP (L3).



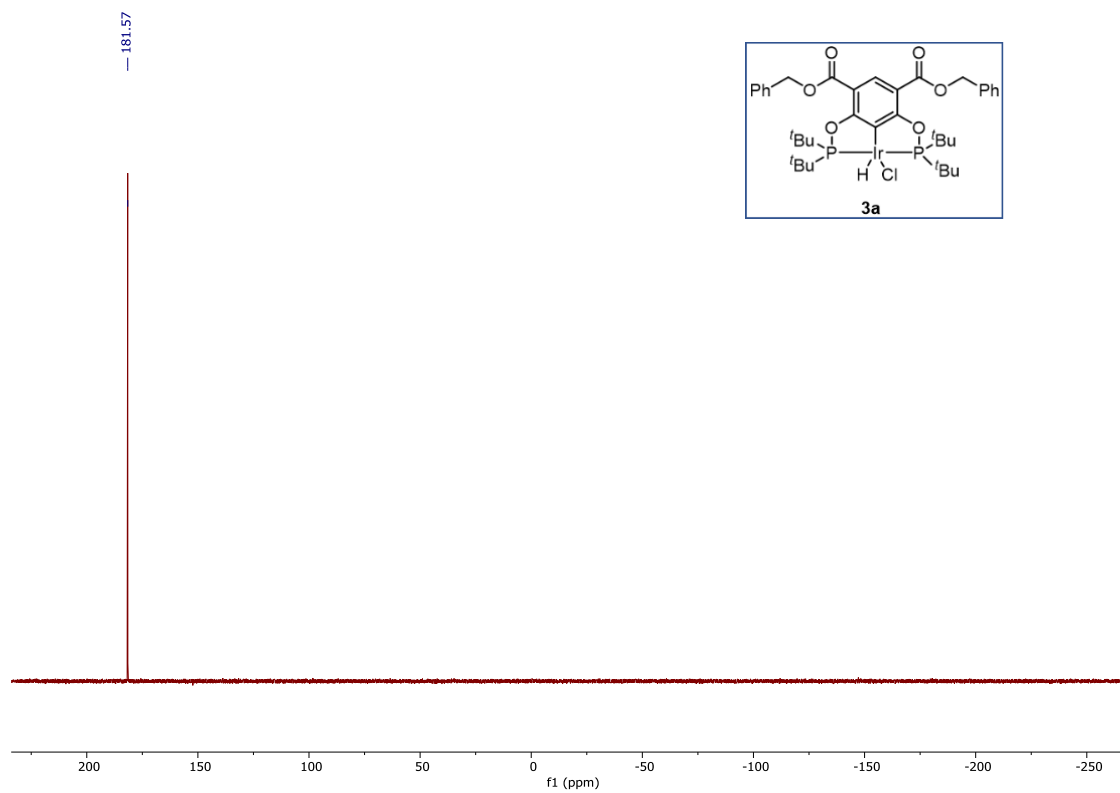
**Figure S10.**  $^{31}\text{P}$  NMR spectrum (162 MHz,  $\text{C}_6\text{D}_6$ ) of the dibenzyl-POCOP (**L3**).



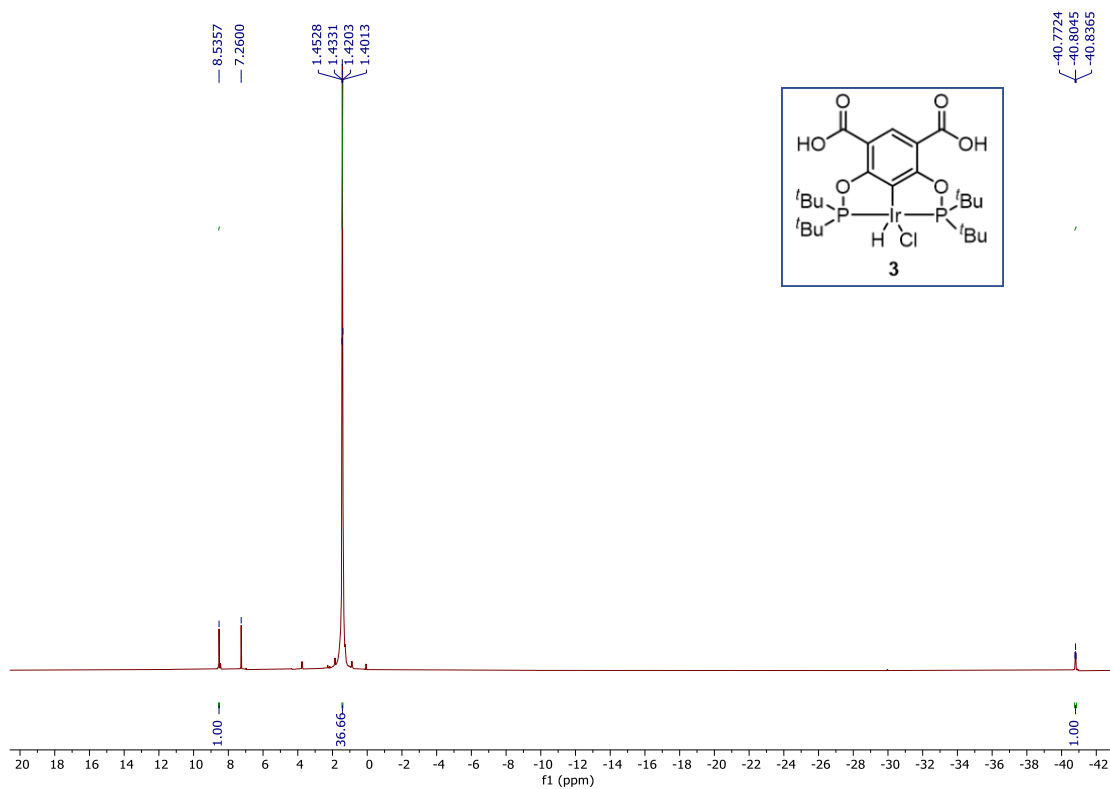
**Figure S11.**  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{C}_6\text{D}_6$ ) of the  $[\text{IrHCl}(\text{dibenzyl-POCOP})]$  (**3a**).



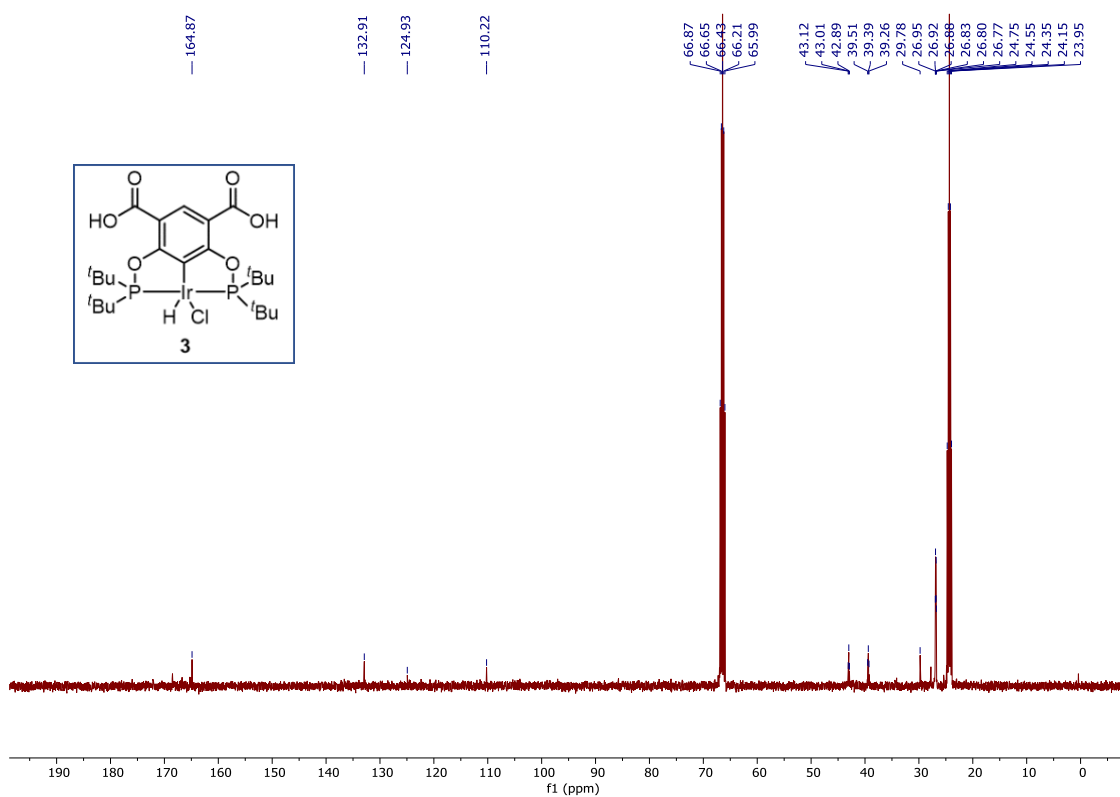
**Figure S12.** <sup>13</sup>C NMR spectrum (101 MHz, C<sub>6</sub>D<sub>6</sub>) of the [IrHCl(dibenzyl-POCOP)] (**3a**).



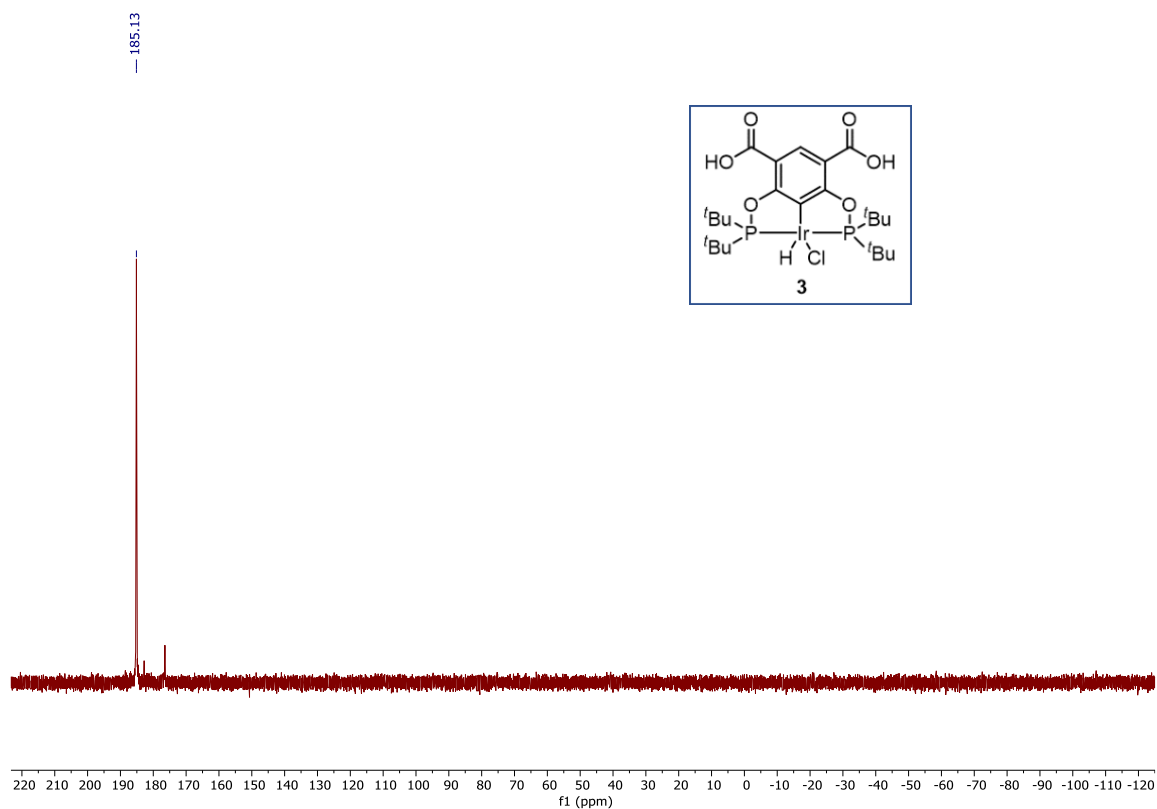
**Figure S13.** <sup>31</sup>P NMR spectrum (162 MHz, C<sub>6</sub>D<sub>6</sub>) of the [IrHCl(dibenzyl-POCOP)] (**3a**).



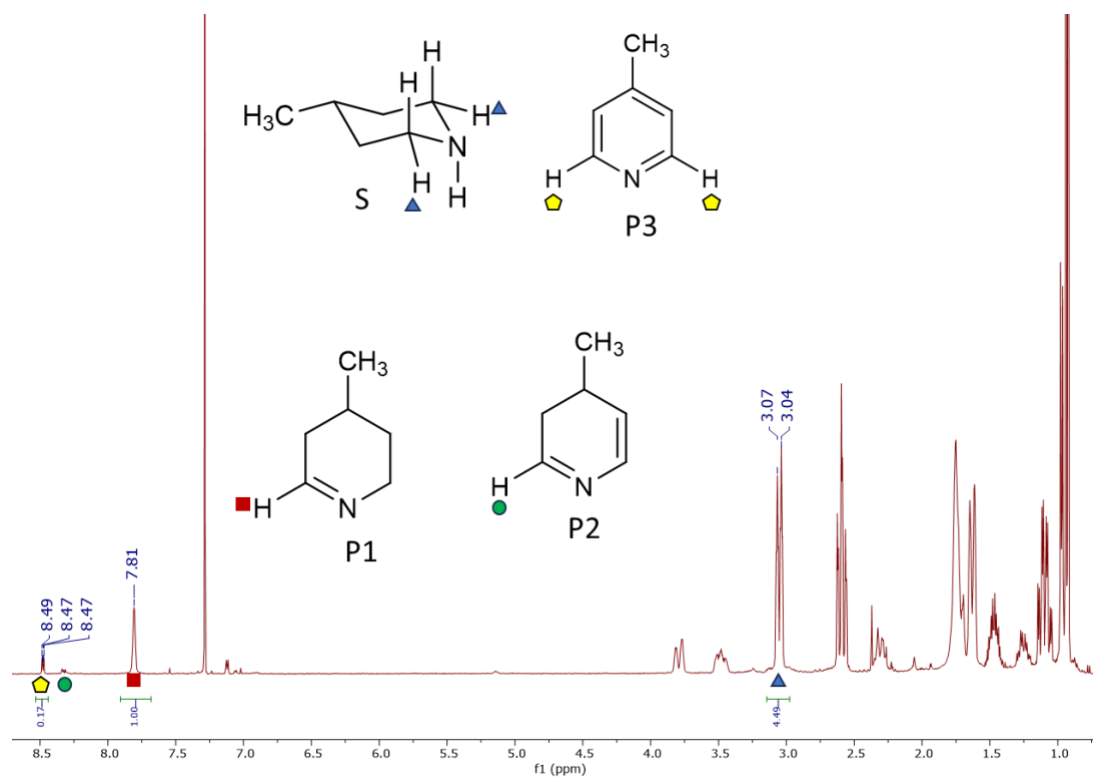
**Figure S14.** <sup>1</sup>H NMR spectrum (400 MHz, CDCl<sub>3</sub>) of the [IrHCl(dicarboxylate-POCOP)] (**3**).



**Figure S15.** <sup>13</sup>C NMR spectrum (101 MHz, THF-*d*<sub>8</sub>) of the [IrHCl(dicarboxylate-POCOP)] (**3**).



**Figure S16.**  $^{31}\text{P}$  NMR spectrum (162 MHz,  $\text{CDCl}_3$ ) of the  $[\text{IrHCl}(\text{dicarboxylate-POCOP})]$  (**3**).



**Figure S17.** Representative  $^1\text{H}$  NMR spectrum (400 MHz,  $\text{CDCl}_3$ ) of fractions collected from the flow reactor.

## 7. Calculation for the TON and TOF

Each hour a fraction of products was collected and weighed and, from a small sample of this, the molar fractions of substrate and products 1 (major) and 3 (minor) was determined using  $^1\text{H}$  NMR spectroscopy.

The total amount of substance (in moles) in the collected fractions was calculated as:

(mass of the liquid in each fraction)/[sum of (molar fraction x molecular weight for each substance)]

The total amount of  $\text{H}_2$  (in moles) was then given by:

The total amount of substance x [molar fraction of major product + 3(molar fraction of minor product)]

Major product: 4-methyl-2,3,4,5-tetrahydropyridine

Minor product: 4-methylpyridine

**TON** = (moles of  $\text{H}_2$ )/(moles of catalyst)

**TOF** = TON per unit time (usually 1 h)

## 8. References

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