Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Supporting Information for:

Anion Effects to Deliver Enhanced Iridium Catalysts for Hydrogen Isotope Exchange Processes

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Contents

Experimental work

General Considerations

All reagents were obtained from commercial suppliers (Aldrich, Alfa Aesar or Strem) and used without further purification, unless otherwise stated. Purification was carried out according to standard laboratory methods,[1] as listed below:

- Tetrahydrofuran and 1,4-dioxane were dried by heating to reflux over sodium wire, using benzophenone ketyl as an indicator, and then distilled under nitrogen.
- Diethyl ether and toluene were obtained from a PureSolv SPS-400-5 Solvent Purification System, and deoxygenated by bubbling argon through for a minimum of thirty minutes.
- Ethanol, isopropyl acetate, diisopropyl ether, and cyclopentyl methyl ether were dried by heating to reflux over calcium chloride, and then distilled under argon.
- *Tert*-butyl methyl ether, dimethylformamide, and dimethyl carbonate were dried by heating to reflux over calcium sulfate, and then distilled under argon.
- Isopropyl alcohol and *tert*-amyl alcohol were dried by heating to reflux over calcium oxide, and then distilled under argon.
- Dimethylsulfoxide, 2-methyltetrahydrofuran, ethyl acetate, and dichloromethane were dried by heating to reflux over calcium hydride, and then distilled under argon.

Flash column chromatography was carried out using Prolabo silica gel (230-400 mesh).

IR spectra were obtained on a Shimadzu IRAffinity-1 Spectrophotometer machine.

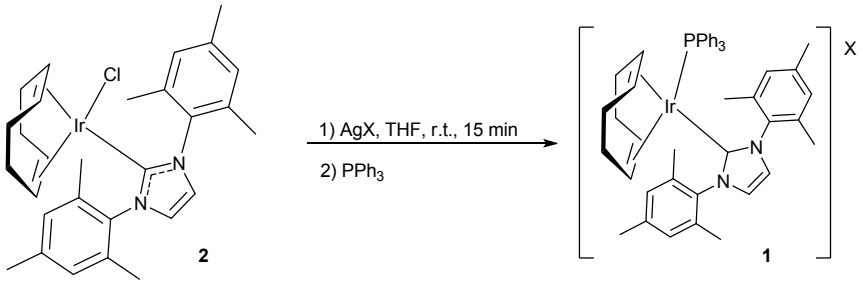
^{1}H, ^{13}C, ^{11}B, ^{19}F, and ^{31}P spectra were recorded on a Bruker DPX 400 spectrometer at 400 MHz, 100 MHz, 128 MHz, 376 MHz, and 162 MHz, respectively. Chemical shifts are reported in ppm. Coupling constants are reported in Hz and refer to H-H couplings, unless otherwise stated. Written accounts of ^{13}C DEPT-90° NMR spectra list methine (C-H) carbons only. Similarly, for ^{13}C DEPT-135° spectra, only negative (i.e. CH_2) carbon signals are detailed.

Mass spectrometry data were acquired at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

The cif files and xyz coordinates associated with X-ray crystal structures are provided separately from the current document and are available electronically.

General Procedures

General Procedure A – Preparation of Iridium (I) Complexes of the Type [(COD)Ir(IMes)(PPh$_3$)]X where X = BF$_4$, PF$_6$, or OTf



The yellow complex (COD)Ir(IMes)Cl, **2**, was dissolved in dry THF in a previously flame-dried round bottom flask, fitted with stopcock sidearm. After all solids had dissolved, the desired silver salt, AgX, was added, affording a yellow to opaque orange colour change on formation of a precipitate. The reaction mixture was stirred for 15 mins at r.t. before carrying out filtration through celite under Ar using the necessary flame-dried glassware. Addition of phosphine to the clear orange solution resulted in the immediate appearance of a bright red colour. After stirring the solution for the allotted reaction time at r.t. the solvent was expelled under reduced pressure. The red residue was redissolved in DCM (10 mL) and filtered through celite in air, washing the celite with DCM to remove the red colour. The clear red filtrate was concentrated *in vacuo* to reveal a red, oily solid. Addition of ethyl acetate (~5 mL) resulted in the precipitation of the product, **1**, as bright red solid, which was collected by filtration and washed with ethyl acetate and hexanes. The isolated catalyst was dried in a vacuum oven (40 ^{o}C, 0 bar) for 24 h before use.

Following *General Procedure A*, results for the syntheses of complexes **1a** – **1c** are reported as a) amount of **2**, b) volume of THF, c) amount of AgX, d) amount of PPh_3, e) reaction time, f) product yield, and g) method used to grow crystals for X-ray (applicable only to previously unpublished complexes, **1b** and **1c**).

General Procedure B for the Standard Hydrogen Isotope Exchange Procedure [2]

A three-necked round bottom flask was fitted with two stopcock side arms and a suba seal and flame-dried. To this flask was added the iridium(I) catalyst and substrate of choice under an argon atmosphere. The desired volume of dichloromethane was added, rinsing the inner walls of the flask. The suba seal was then replaced with a greased glass stopper. The solution was stirred whilst being cooled to -78 ^{o}C in a dry ice/acetone slurry. The flask was twice evacuated and flushed with Ar. Upon a third evacuation, an atmosphere of deuterium gas was introduced to the flask. After sealing the flask, the cold bath was removed and the flask heated in an oil bath to the desired temperature. NOTE: the glass stopper is physically restrained as the reaction mixture warms to room temperature. The reaction mixture was stirred for 1 h before removing excess deuterium and replacing with air. The yellow solution was washed with DCM and transferred to a single necked flask before removing the solvent under reduced pressure. The residue was filtered through a short plug of silica, eluting with a 1:1 mixture of ethyl acetate and hexanes. The solvent was evacuated again and the residue analysed directly by ^{1}H NMR. The level of deuterium incorporation in the substrate was determined by ^{1}H NMR. The integrals were calibrated against a peak corresponding to a position not expected to be labelled. **Equation 1** was then used to calculate the extent of labelling:

$$\%\ Deuteration = 100 - \left[\left(\frac{residual\ integral}{number\ of\ labelling\ sites}\right) x\ 100\right]$$

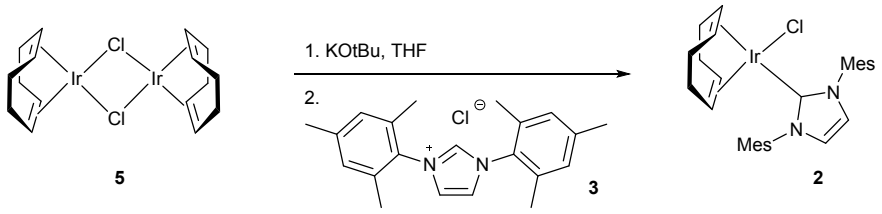
Equation 1

For example, in a substrate containing two possible positions of labelling, the percentage given refers to the level of D incorporation over the total number of positions, e.g. 92% deuterium

incorporation in the *ortho*-positions of acetophenone indicates 1.84D incorporation (see page S46 for an example of such a spectrum).

Synthesis of Iridium Complexes

Synthesis of Chloro(η^4–cycloocta–1,5–diene)(1,3-dimesitylimidazolin-2-ylidene) iridium(I), ***2*** [3]



Scheme S1

To a flame-dried Schlenk tube was added η^4-cycloocta-1,5-dieneiridium(I) chloride dimer, **5** (0.600 g, 0.893 mmol) and KO^{t}Bu (0.200 g, 1.786 mmol). After stirring the solid mixture under high vacuum for 10 mins, dry THF (10 mL) was added under an Ar atmosphere, and the resultant red-black solution stirred at r.t. for a further 10 mins. Subsequently, 1,3-dimesitylimidazolium chloride, **3** (0.609 g, 1.786 mmol) was added in one portion, causing a dark red to dark yellow colour change, and the reaction mixture stirred for 3 h. The THF was then removed *in vacuo* and the residue purified directly by flash column chromatography, eluting the yellow fraction with a 1:1 mixture EtOAc and petroleum ether. After removal of the solvent, the product was isolated as a bright yellow powder (1.029 g, 90%).

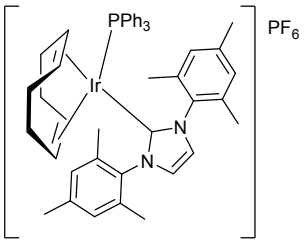
m.**p**.: decomposes at > 200 °C.

FTIR (neat): 3092, 3009, 2916, 2876, 1609, 1485 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 6.99-6.96 (2 x bs, 4H, ArH), 6.93 (s, 2H, olefinic CH), 4.14-4.10 (m, 2H, COD olefinic CH), 2.96-2.94 (m, 2H, COD olefinic CH), 2.34 (s, 12H, $ArCH_3$), 2.14 (s, 6H, $ArCH_3$), 1.74-1.59 (m, 4H, COD CH_2), 1.33-1.21 (m, 4H, COD CH_2)

^{13}C NMR (100 MHz, $CDCl_3$): δ 181.0, 138.8, 137.6, 136.3, 134.6, 133.0, 129.7, 128.3, 123.5, 82.8, 66.1, 51.6, 33.7, 29.2, 21.4, 19.9, 15.5.

Preparation of η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) hexafluorophosphate, ***1a*** [2]



1a

Following *General Procedure A*, results are: a) **2**, 0.700 g, 1.093 mmol, b) 15 mL of THF, c) $AgPF_6$, 0.276 g, 1.093 mmol, d) PPh_3, 0.287 g, 1.093 mmol, e) 1 h, f) 0.885 g, 80% yield, and g) X-ray crystals not required.

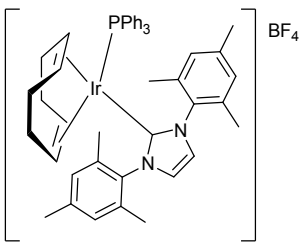
FTIR (CH_2Cl_2): 3040, 2995, 2319, 1631, 1495 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49-7.45 (m, 5H, ArH), 7.34-7.30 (m, 6H, ArH), 7.16-7.12 (m, 6H, ArH), 7.05 (s, 2H, ArH), 6.67 (s, 2H, olefinic CH), 4.41-4.40 (m, 2H, olefinic COD CH), 3.33 (m, 2H, COD CH), 2.37 (s, 6H, $ArCH_3$), 2.13 (s, 6H, $ArCH_3$), 1.78 (s, 6H, $ArCH_3$), 1.63-1.51 (m, 6H, COD CH_2), 1.49 (m, 2H, COD CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.5 (d, $^2J_{C\text{-}P}$ = 8.0 Hz), 139.2, 135.7, 135.2, 135.1, 134.6, 131.2, 130.7, 130.2, 129.7, 128.5, 126.4, 80.9, 80.0, 77.4, 31.4, 30.4, 21.2, 20.9, 18.9.

^{31}P NMR (162 MHz, $CDCl_3$): δ 16.3 (PPh_3), -144.3 (PF_6).

Preparation of η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) tetrafluoroborate, ***1b***



1b

Following *General Procedure A*, results are: a) **2**, 0.250 g, 0.390 mmol, b) 15 mL of THF, c) $AgBF_4$, 0.076 g, 0.390 mmol, d) PPh_3, 0.099 g, 0.390 mmol, e) 1 h, f) 0.298 g, 80% yield, and g) X-ray quality crystals were prepared by layering diethyl ether on top of a saturated DCM solution of the product, allowing the biphasic solvent system to mix for four days at r.t.

m.p.: Decomposes > 160 °C.

FTIR (neat): 3043, 2920, 2364, 1606, 1585, 1566, 1477, 1435, 1049 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (s, 2H, NCH=CHN), 7.48-7.44 (m, 3H, ArH), 7.34-7.29 (td, J = 7.8, 2.5 Hz, 6H, ArH), 7.15-7.10 (m, 6H, ArH), 7.04 (s, 2H, ArH), 6.66 (s, 2H, ArH), 4.40-4.38 (m, 2H, COD CH), 3.33-3.31 (m, 2H, COD CH), 2.36 (s, 6H, $ArCH_3$), 2.12 (s, 6H, $ArCH_3$), 1.77 (s, 6H, $ArCH_3$), 1.68-1.49 (m, 6H, COD CH_2), 1.32-1.27 (m, 2H, COD CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.1 (d, $^2J_{C\text{-}P}$ = 8.0 Hz), 139.1, 135.2, 135.1, 134.7, 134.3, 134.2, 130.7, 130.3, 129.8, 129.2, 128.1, 128.0, 126.4, 79.9, 79.8, 77.5, 31.4, 29.7, 20.7, 20.4, 18.5.

^{13}C DEPT-90° NMR (100 MHz, $CDCl_3$): δ 134.8, 134.7, 131.2, 130.3, 129.7, 128.6, 128.5, 126.9, 80.4, 80.3, 78.0.

^{13}C DEPT-135° NMR (100 MHz, $CDCl_3$): δ 31.9, 30.2.

^{31}P NMR (162 MHz, $CDCl_3$): δ 16.3 (PPh_3).

^{11}B NMR (128 MHz): δ -0.9 (BF_4).

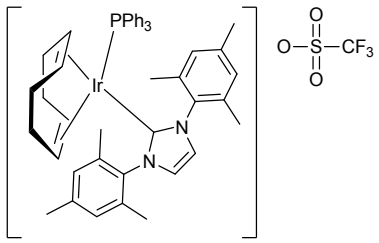
^{19}F NMR (376 MHz, $CDCl_3$): δ -153.8 (BF_4).

HRMS (positive ESI): m/z calc'd for $C_{29}H_{31}{}^{191}IrN_2$ $[M\text{-}BF_4\text{-}PPh_3\text{-}5H]^+$: 599.2166; found: 599.2168. No mass ion observed.

HRMS (negative ESI): m/z calc'd for $[BF_4]^-$: 87.0000; found: 87.0042.

X-Ray: see page S53 for details.

Preparation of η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) trifluoromethylsulfonate, ***1c***



1c

Following *General Procedure A*, results are: a) **2**, 0.500 g, 0.781 mmol, b) 20 mL of THF, c) AgOTf, 0.201 g, 0.781 mmol, d) PPh_3, 0.204 g, 0.781 mmol, e) 1 h, f) 0.545 g, 69% yield, and g) X-ray quality crystals were prepared by allowing diethyl ether to diffuse into a saturated DCM solution of the product at 4 °C overnight.

m.p.: Decomposes >170 °C.

FTIR (neat): 3174, 2951, 2924, 2887, 1477, 1437, 1381, 1267, 1140, 1032 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 (s, 2H, NCH=CHN), 7.49-7.45 (m, 3H, ArH), 7.34-7.28 (m, 6H, ArH), 7.16-7.11 (m, 6H, ArH), 7.05 (s, 2H, ArH), 6.67 (s, 2H, ArH), 4.31-4.38 (m, 2H, COD CH), 3.34-3.32 (m, 2H, COD CH), 2.37 (s, 6H, $ArCH_3$), 2.13 (s, 6H, $ArCH_3$), 1.77 (s, 6H, $ArCH_3$), 1.70-1.50 (m, 6H, COD CH_2), 1.33-1.25 (m, 2H, COD CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ 176.2 (d, $^3J_{C\text{-}P}$ = 8.0 Hz), 139.2, 135.2, 135.1, 134.7, 134.3, 134.2, 130.8, 130.2, 129.8, 129.2, 128.1, 128.0, 126.4, 80.0, 79.9, 77.5, 31.4, 29.7, 20.8, 20.4, 18.6.

^{13}C DEPT-135° NMR (100 MHz, $CDCl_3$): δ 31.9, 30.2.

^{31}P NMR (162 MHz, $CDCl_3$): δ 16.3 (PPh_3).

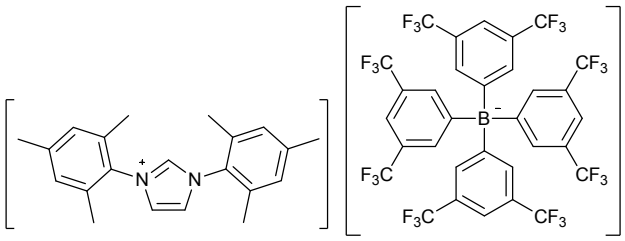
^{19}F NMR (376 MHz, $CDCl_3$): δ -78.0 (SO_3CF_3).

HRMS (positive ESI): m/z calc'd for $C_{29}H_{32}{}^{191}IrN_2$ $[M\text{-}SO_3CF_3\text{-}PPh_3\text{-}4H]^+$: 599.2166; found: 599.2169. No mass ion observed.

HRMS (negative ESI): m/z calc'd for $[SO_3CF_3]^-$: 148.9526; found: 148.9528.

X-Ray: see page S54 for details.

Preparation of N,N'- Dimesitylimidazolium tetrakis[(3,5-trifluoromethylphenyl)]borate, ***4*** *en route to* η^4*–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) tetrakis[(3,5-trifluoromethylphenyl)]borate,* ***1d***



4

N,*N*-Dimesitylimidazolium chloride, **3** (0.269 g, 0.789 mmol) and NaBArF (0.700 g, 0.789 mmol) were added to a 50 mL round bottom flask and dissolved in a 1:1 mixture of DCM and H_2O (10 mL:10 mL). The reaction mixture was stirred overnight, ensuring that the organic and aqueous phases stirred without a visual bilayer. The reaction mixture was subsequently transferred to a separating funnel and diluted with DCM (10 mL). The aqueous phase was washed with DCM (2 x 10 mL) and the combined organic phase washed with water (10 mL) then brine (10 mL). After drying the DCM layer over anhydrous sodium sulfate and filtering through a Büchner funnel, the solvent was removed *in vacuo* and the residue purified through a short plug of silica, eluting with DCM. Removal of the solvent *in vacuo* once more gave the desired product as a white solid (0.840 g, 92% yield). This process was repeated batch wise to obtain a stockpile of **4**, necessary for large scale synthesis of **1d** (*vide infra*).

X-ray quality crystals were grown by solution evaporation of a DCM solution of **4** at r.t. overnight.

m.p.: 135-136 ^oC.

FTIR (neat): 3156, 2994, 2968, 2928, 1609, 1545, 1479, 1352, 1273, 1115 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 8.11 (t, ^4J = 1.6 Hz, 1H, NCHN), 7.70-7.68 (m, 8H, ArH_{BArF}), 7.50 (s, 4H, ArH_{BArF}), 7.40 (d, $^4J_{H\text{-}H}$ = 1.6 Hz, 2H, NCH=CHN), 7.08 (s, 4H, ArH), 2.37 (s, 6H, $ArCH_3$), 2.04 (s, 12H, $ArCH_3$).

^{13}C NMR (100 MHz, $CDCl_3$): δ 161.8 (q, $^1J_{C\text{-}B}$ = 49.5 Hz), 143.1, 135.3, 134.8, 133.4, 130.4, 129.4-128.4 (unidentified multiplet), 125.0, 124.6 (q, $^1J_{C\text{-}F}$ = 270.7 Hz), 117.4, 21.0, 16.9.

^{11}B NMR (128 MHz, $CDCl_3$): δ -6.7 (BArF $B(Ar)_4$).

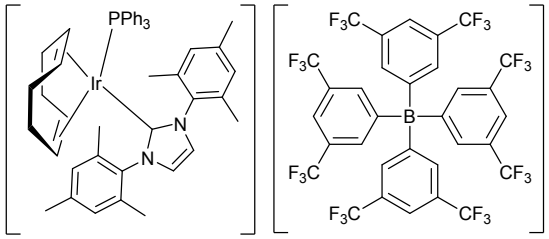
^{19}F NMR (376 MHz, $CDCl_3$): -62.4 (BArF $ArCF_3$)

HRMS (positive ESI): m/z calc'd for $C_{21}H_{25}N_2$ $[M\text{-}BArF]^+$: 305.2012; found: 305.2012 $[M\text{-}BArF]^+$.

HRMS (negative ESI): m/z calc'd for [$C_{32}H_{12}BF_{24}$, $BArF]^-$: 863.0660; found: 863.0621.

X-Ray: see page S55 for details.

Preparation of η⁴–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) tetrakis[(3,5-trifluoromethylphenyl)]borate, ***1d***



1d

To a flame-dried round bottom flask fitted with stopcock sidearm was added η⁴-cycloocta-1,5-dieneiridium(I) chloride dimer, **5** (0.544 g, 0.81 mmol), and dry THF (5 mL). After all solids had dissolved, triphenylphosphine (0.426 g, 1.62 mmol) was added in one portion, causing an orange to yellow colour change. Having allowed the reaction mixture to stir at r.t. for 15 mins, the BArF salt, **4** (1.894 g, 1.62 mmol), was added in one portion and allowed to dissolve completely. After a further 5 mins stirring, KO^{t}Bu (0.273 g, 2.43 mmol) was added in one portion, causing an immediate yellow to bright red, then black, colour change. The reaction mixture was stirred for 1 h at r.t. before the THF was removed *in vacuo*. The red-black residue was dissolved in DCM and purified directly through a short plug of silica, eluting the bright red fraction with DCM. The combined fractions were concentrated under reduced pressure to reveal a red, oily solid, which was triturated with pentane to give the product as a grainy red solid (1.86 g, 67% yield).

X-ray quality crystals were prepared by layering hexane on top of a saturated THF solution of the product, allowing the biphasic solvent system to mix for one week at r.t.

m.p.: Decomposes >156 ^{o}C.

FTIR (neat): 3024, 2978, 1610, 1539, 1479, 1467, 1426, 1352, 1271, 1187 cm^{-1}.

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.74-7.73 (m, 8H, ArH_{BArF}), 7.53 (bs, 4H, ArH_{BArF}), 7.46-7.42 (m, 3H, ArH), 7.32-7.27 (overlapping s and m, 8H, ArH + NCH=CHN), 7.16-7.11 (m, 6H, ArH), 7.05 (s, 2H, ArH), 6.69 (s, 2H, ArH), 4.40-4.37 (m, 2H, COD CH), 3.38-3.36 (m, 2H, COD CH), 2.36 (s, 6H, $ArCH_3$), 2.11 (s, 6H, $ArCH_3$), 1.77 (s, 6H, $ArCH_3$), 1.71-1.48 (m, 6H, COD CH_2), 1.33-1.27 (m, 2H, COD CH_2).

^{13}C NMR (100 MHz, $CDCl_3$): δ 178.0 (d, $^{3}J_{C\text{-}P}$ = 10.0 Hz), 161.8 (q, $^{1}J_{C\text{-}B}$ = 50.0 Hz), 140.1, 135.4, 135.1, 134.8, 134.7, 131.3, 131.2, 130.7, 130.4, 129.8, 129.0, 128.7, 128.5, 124.5 (q, $^{1}J_{C\text{-}F}$ = 270.0 Hz), 117.4, 80.5, 80.4, 78.5, 31.8, 21.1, 20.7, 18.9.

^{13}C DEPT-135^{o} NMR (100 MHz, $CDCl_3$): δ 31.8, 30.1.

^{31}P NMR (162 MHz, $CDCl_3$): δ 16.4 (PPh_3).

^{19}F NMR (376 MHz, $CDCl_3$): δ -62.5 (BArF $ArCF_3$).

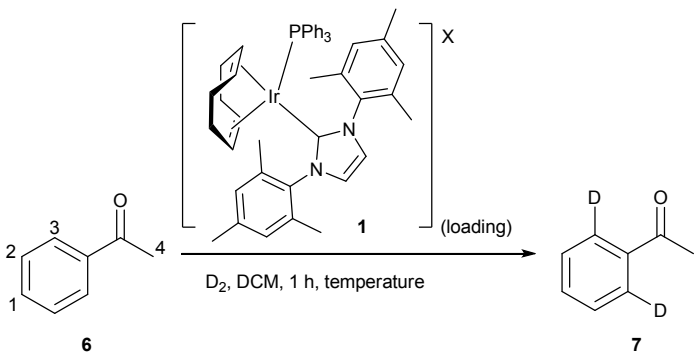
^{11}B NMR (128 MHz, $CDCl_3$): δ -6.60 (BArF $B(Ar_4)$).

HRMS (positive ESI): m/z calc'd for $C_{29}H_{32}{}^{191}IrN_2$ $[M\text{-}BArF\text{-}PPh_3\text{-}4H]^+$: 599.2166; found: 599.2168. No mass ion observed.

HRMS (negative ESI): m/z calc'd for $[C_{32}H_{12}BF_{24}, BArF]^-$: 863.0660; found: 863.0632.

X-Ray: see page S56 for details.

Assessment of Counterion Effects on Catalyst Efficiency



Scheme 2 (from main manuscript)

Data for unlabeled acetophenone, ***6***:

^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, ^3J = 7.5 Hz, 2H, CH^3), 7.47 (t, ^3J = 7.4 Hz, 1H, CH^1), 7.35 (t, ^3J = 7.4 Hz, 2H, CH^2), 2.62 (s, 3H, CH^4).

Incorporation expected at δ 7.95.

Determined against integral at δ 2.62.

Scheme 2 (main manuscript) represents assessment of five different catalyst loadings (0.0, 0.5, 1.0, 3.0, and 5.0 mol%) at 25 °C. Each point on a graph is representative of an average of two independent runs for that particular set of reaction conditions. Results are referenced as *Scheme Number, Catalyst Loading, Counterion, Run Number* for each line (BF_4, PF_6, OTf, and BArF).

Following *General Procedure B*, results are reported as a) amount of acetophenone, **6**, b) amount of catalyst **1a**, **b**, **c**, or **d**, c) reaction temperature, and d) level of deuterium incorporation.

Scheme 2, 0.0 mol% , Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) no catalyst, c) 25 °C, and d) 0%.

Scheme 2, 0.0 mol% , Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) no catalyst, c) 25 °C, and d) 0%.

Scheme 2, 0.5 mol% , BF_4, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 1.0 mg, 0.001 mmol, 0.5 mol %, c) 25 ^oC, and d) 36%.

Scheme 2, 0.5 mol% , BF_4, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 1.0 mg, 0.001 mmol, 0.5 mol %, c) 25 ^oC, and d) 38%.

Scheme 2, 1.0 mol% , BF_4, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 2.0 mg, 0.002 mmol, 1.0 mol %, c) 25 ^oC, and d) 58%.

Scheme 2, 1.0 mol% , BF_4, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 2.0 mg, 0.002 mmol, 1.0 mol %, c) 25 ^oC, and d) 66%.

Scheme 2, 3.0 mol% , BF_4, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 6.2 mg, 0.006 mmol, 3.0 mol %, c) 25 ^oC, and d) 92%.

Scheme 2, 3.0 mol% , BF_4, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 6.2 mg, 0.006 mmol, 3.0 mol %, c) 25 ^oC, and d) 97%.

Scheme 2, *5.0 mol% , BF_4, Run 1*

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 9.5 mg, 0.010 mmol, 5.0 mol %, c) 25 ^oC, and d) 87%.

Scheme 2, 5.0 mol% , BF_4, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1b**, 9.5 mg, 0.010 mmol, 5.0 mol %, c) 25 ^oC, and d) 97%.

Scheme 2, *0.5 mol% , PF_6, Run 1*

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 1.1 mg, 0.001 mmol, 0.5 mol %, c) 25 ^oC, and d) 60%.

Scheme 2, 0.5 mol% , PF_6, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 1.1 mg, 0.001 mmol, 0.5 mol %, c) 25 ^oC, and d) 59%.

Scheme 2, 1.0 mol% , PF_6, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 2.2 mg, 0.002 mmol, 1.0 mol %, c) 25 ^oC, and d) 77%.

Scheme 2, 1.0 mol% , PF_6, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 2.2 mg, 0.002 mmol, 1.0 mol %, c) 25 ^oC, and d) 79%.

Scheme 2, 3.0 mol% , PF_6, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 6.5 mg, 0.006 mmol, 3.0 mol %, c) 25 ^oC, and d) 97%.

Scheme 2, 3.0 mol% , PF_6, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 6.5 mg, 0.006 mmol, 3.0 mol %, c) 25 ^oC, and d) 98%.

Scheme 2, 5.0 mol% , PF_6, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 10.8 mg, 0.010 mmol, 5.0 mol %, c) 25 ^oC, and d) 97%.

Scheme 2, 5.0 mol% , PF_6, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1a**, 10.8 mg, 0.010 mmol, 5.0 mol %, c) 25 ^oC, and d) 98%.

Scheme 2, 0.5 mol% , OTf, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 1.1 mg, 0.001 mmol, 0.5 mol %, c) 25 ^{o}C, and d) 68%.

Scheme 2, 0.5 mol% , OTf, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 1.1 mg, 0.001 mmol, 0.5 mol %, c) 25 ^{o}C, and d) 79%.

Scheme 2, 1.0 mol% , OTf, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 2.2 mg, 0.002 mmol, 1.0 mol %, c) 25 ^{o}C, and d) 86%.

Scheme 2, 1.0 mol% , OTf, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 2.2 mg, 0.002 mmol, 1.0 mol %, c) 25 ^{o}C, and d) 94%.

Scheme 2, 3.0 mol% , OTf, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 6.6 mg, 0.006 mmol, 3.0 mol %, c) 25 ^{o}C, and d) 96%.

Scheme 2, 3.0 mol% , OTf, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 6.6 mg, 0.006 mmol, 3.0 mol %, c) 25 ^{o}C, and d) 96%.

Scheme 2, 5.0 mol% , OTf, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 10.9 mg, 0.010 mmol, 5.0 mol %, c) 25 ^{o}C, and d) 96%.

Scheme 2, 5.0 mol% , OTf, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1c**, 10.9 mg, 0.010 mmol, 5.0 mol %, c) 25 ^{o}C, and d) 97%.

Scheme 2, 0.5 mol% , BArF, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 1.9 mg, 0.001 mmol, 0.5 mol %, c) 25 ^{o}C, and d) 71%.

Scheme 2, 0.5 mol% , BArF, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 1.9 mg, 0.001 mmol, 0.5 mol %, c) 25 ^{o}C, and d) 79%.

Scheme 2, 1.0 mol% , BArF, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 3.7 mg, 0.002 mmol, 1.0 mol %, c) 25 ^{o}C, and d) 89%.

Scheme 2, 1.0 mol% , BArF, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 3.7 mg, 0.002 mmol, 1.0 mol %, c) 25 ^{o}C, and d) 86%

Scheme 2, 3.0 mol% , BArF, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 11.1 mg, 0.006 mmol, 3.0 mol %, c) 25 ^{o}C, and d) 98%.

Scheme 2, 3.0 mol% , BArF, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 11.1 mg, 0.006 mmol, 3.0 mol %, c) 25 ^{o}C, and d) 96%.

Scheme 2, 5.0 mol% , BArF, Run 1

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 18.3 mg, 0.010 mmol, 5.0 mol %, c) 25 ^{o}C, and d) 97%.

Scheme 2, 5.0 mol% , BArF, Run 2

a) acetophenone, **6**, 0.026 g, 0.215 mmol, b) complex **1d**, 18.3 mg, 0.010 mmol, 5.0 mol %, c) 25 ^{o}C, and d) 98%.

Counterion Influence on Ether and Carbonate Solvent Scope

Figure 3 (main manuscript) represents assessment of catalysts **1a** and **1d** in various ether and carbonate solvents. Each bar on a graph is representative of an average of two independent runs for that particular set of reaction conditions. Reactions were run using *General Procedure B*, and are shown in detail below in **Table S1**.

Table S1

Entry[a]	Solvent	Catalyst[b]	% Deuteration		Average % Deuteration
			Run 1	Run 2	
1	dioxane	**1a**	93	94	94
2	dioxane	**1d**	94	95	95
3	MTBE	**1a**	90	92	91
4	MTBE	**1d**	97	97	97
5	Et_2O	**1a**	94	93	94
6	Et_2O	**1d**	96	98	97
7	2-MeTHF	**1a**	95	94	95
8	2-MeTHF	**1d**	96	94	95
9	$^{i}Pr_2O$	**1a**	78	66	72
10	$^{i}Pr_2O$	**1d**	98	98	98
11	CPME	**1a**	66	64	65
12	CPME	**1d**	96	98	97
13	THF	**1a**	38	48	43
14	THF	**1d**	92	88	90
15	dimethyl carbonate	**1a**	72	88	80
16	dimethyl carbonate	**1d**	92	92	92

[a]Conditions: 2.5mL solvent, 0.215 mmol **6**, 1 h, 25ºC, 5 mol% [Ir]

[b]Mass of **1a** per reaction = 10.8 mg; mass of **1d** per reaction = 18.3 mg

Counterion Influence on Alcohol, Ester, Chlorinated, and Aromatic Solvent Scope

Figure 4 (main manuscript) represents assessment of catalysts **1a** and **1d** in various additional solvents. Each bar on a graph is representative of an average of two independent runs for that particular set of reaction conditions. Reactions were run using *General Procedure B*, and are shown in detail below in **Table S2**. This also includes results of labelling reactions using DMSO and DMF as the solvent (not shown in main manuscript). For these two solvents, reactions were run with catalyst **1d** only.

Table S2

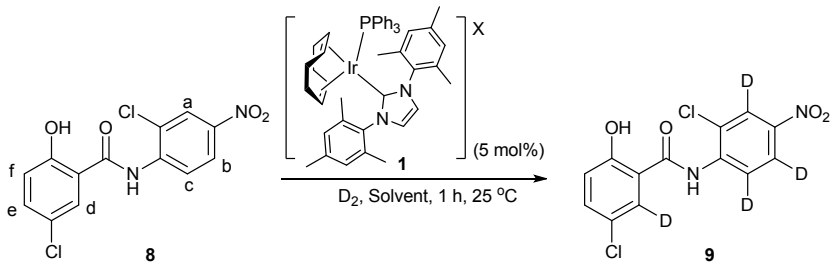
Entry[a]	Solvent	Catalyst[b]	% Deuteration		Average % Deuteration
			Run 1	Run 2	
1	EtOH	**1a**	31	28	30
2	EtOH	**1d**	37	37	37
3	IPA	**1a**	28	36	32
4	IPA	**1d**	40	46	43
5	^{t}AmOH	**1a**	65	76	71
6	^{t}AmOH	**1d**	88	75	82
7	EtOAc	**1a**	56	68	62
8	EtOAc	**1d**	86	80	83
9	^{i}PrOAc	**1a**	84	80	82
10	^{i}PrOAc	**1d**	97	93	95
11	DCM	**1a**	97	97	97
12	DCM	**1d**	96	96	96
13	DCE	**1a**	95	97	96
14	DCE	**1d**	99	97	98
15	Toluene	**1a**	57	44	51
16	Toluene	**1d**	90	92	91
17	DMSO	**1a**	-	-	-
18	DMSO	**1d**	4	8	6
19	DMF	**1a**	-	-	-
20	DMF	**1d**	3	0	2

[a]Conditions: 2.5mL solvent, 0.215 mmol **6**, 1 h, 25ºC, 5 mol% [Ir]

[b]Mass of **1a** per reaction = 10.8 mg; mass of **1d** per reaction = 18.3 mg

Improved Deuterium Labelling of Niclosamide

From **Table 2** (main manuscript).



Data for unlabeled Niclosamide, ***8***:

^{1}H NMR (400 MHz, DMSO): δ 11.47 (s, 1H, OH), 8.82 (d, ^3J = 9.2 Hz, 1H, CH^c), 8.43 (d, ^4J = 2.8 Hz, 1H, CH^a), 8.30 (dd, J = 9.2 Hz, ^4J = 2.7 Hz, 1H, CH^b), 7.97 (d, ^4J = 2.8 Hz, 1H, CH^d), 7.55 (dd, ^3J = 8.7 Hz, ^4J = 2.8 Hz, 1H, CH^e), 7.10 (d, ^3J = 8.7 Hz, 1H, CH^f).

Incorporation expected at δ 8.82, 8.43, 8.30 and 7.97.

Determined against integral at δ 7.55.

NOTE: The reactions involving Niclosamide were run in accordance with *General Procedure B* but with a modified work-up. On completion, the reaction mixture was concentrated *in vacuo* and the product triturated with acetone. The product was collected as a white solid *via* filtration. Deuterium incorporations are delineated in **Table S3**.

Table S3

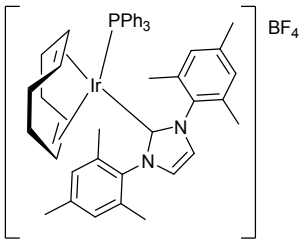
Entry[a]	Solvent	Catalyst[b]	% Deuteration								Average % Deuteration			
			Run 1				Run 2							
1	DCM	**1a**	a: 67	b: 50	c: 30	d: 70	a: 65	b: 55	c: 52	d: 62	a: 66	b: 53	c: 41	d: 66
2	DCM	**1d**	a: 68	b: 53	c: 17	d: 70	a: 74	b: 60	c: 19	d: 76	a: 71	b: 57	c: 18	d: 73
3	2-MeTHF	**1a**	a: 48	b: 9	c: 4	d: 98	a: 53	b: 13	c: 4	d: 97	a: 51	b: 11	c: 4	d: 98
4	2-MeTHF	**1d**	a: 96	b: 97	c: 73	d: 96	a: 97	b: 95	c: 56	d: 96	a: 97	b: 96	c: 65	d: 96

[a]Conditions: 1.25 mL solvent, 0.1075 mmol **8**, 1 h, 25ºC, 5 mol% [Ir]

[b]Mass of **1a** per reaction = 5.4 mg; mass of **1d** per reaction = 9.1 mg; mass of **8** per reaction = 34.0 mg

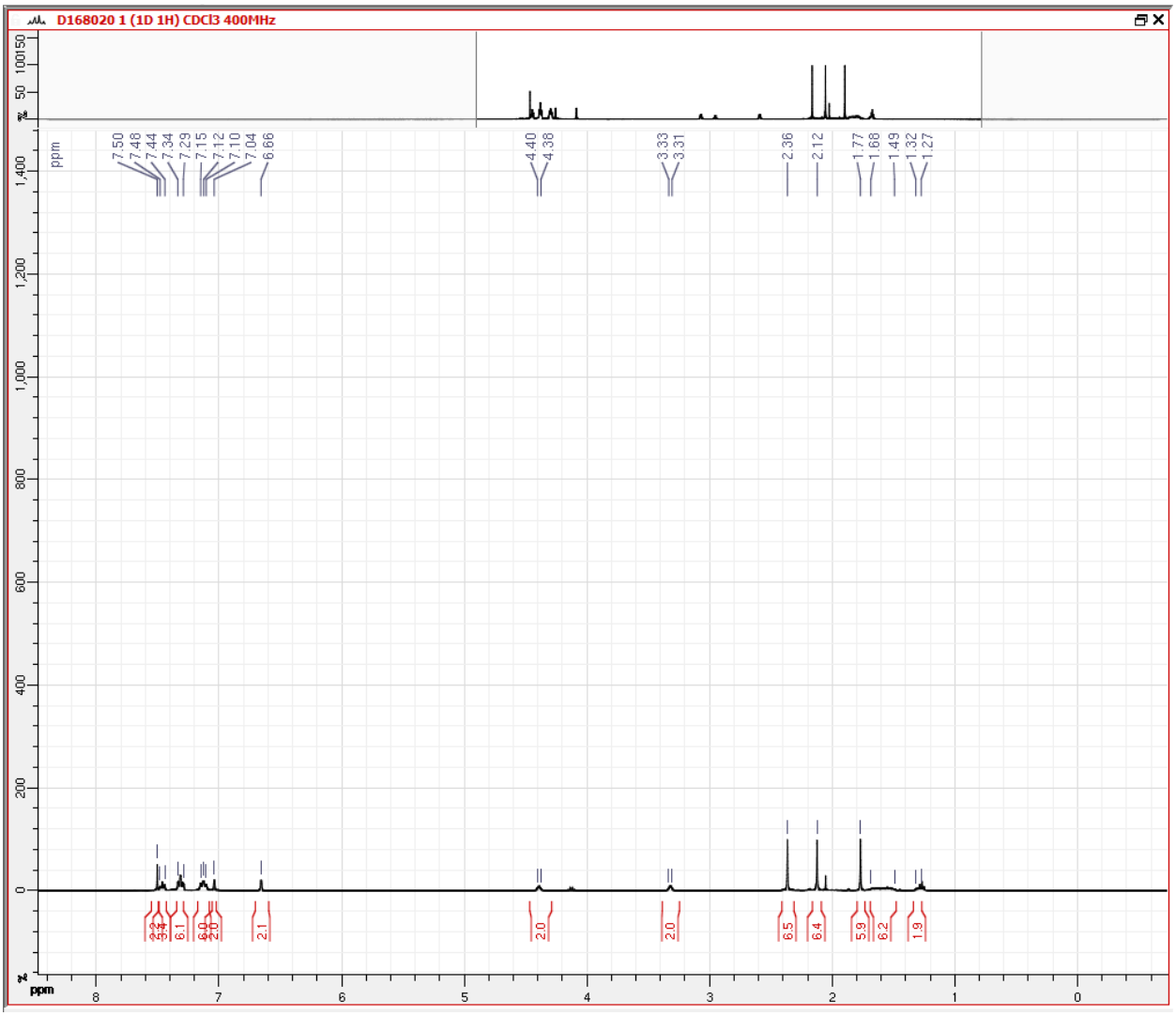
Spectra for Novel Compounds

η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) tetrafluoroborate, ***1b***

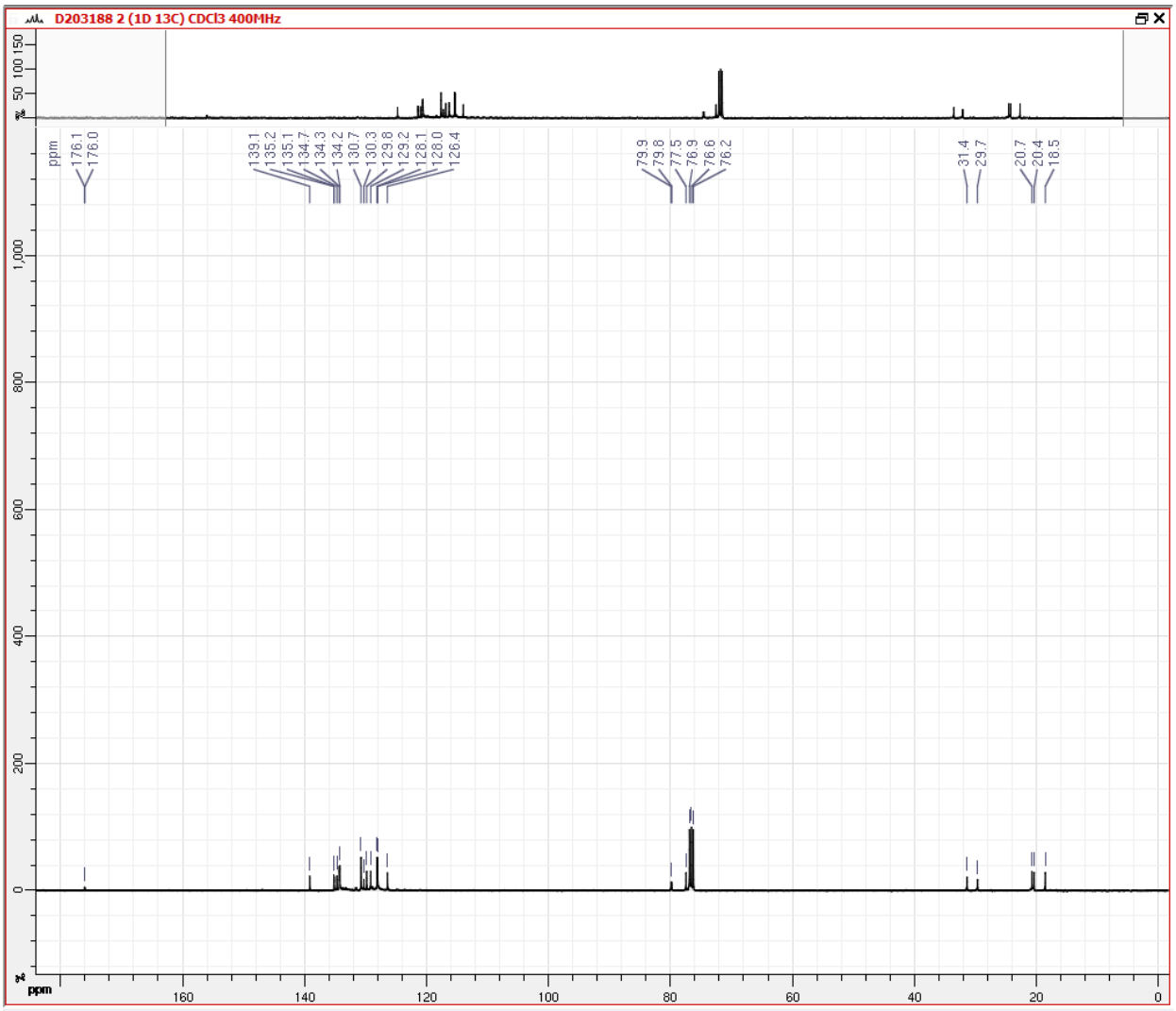


1b

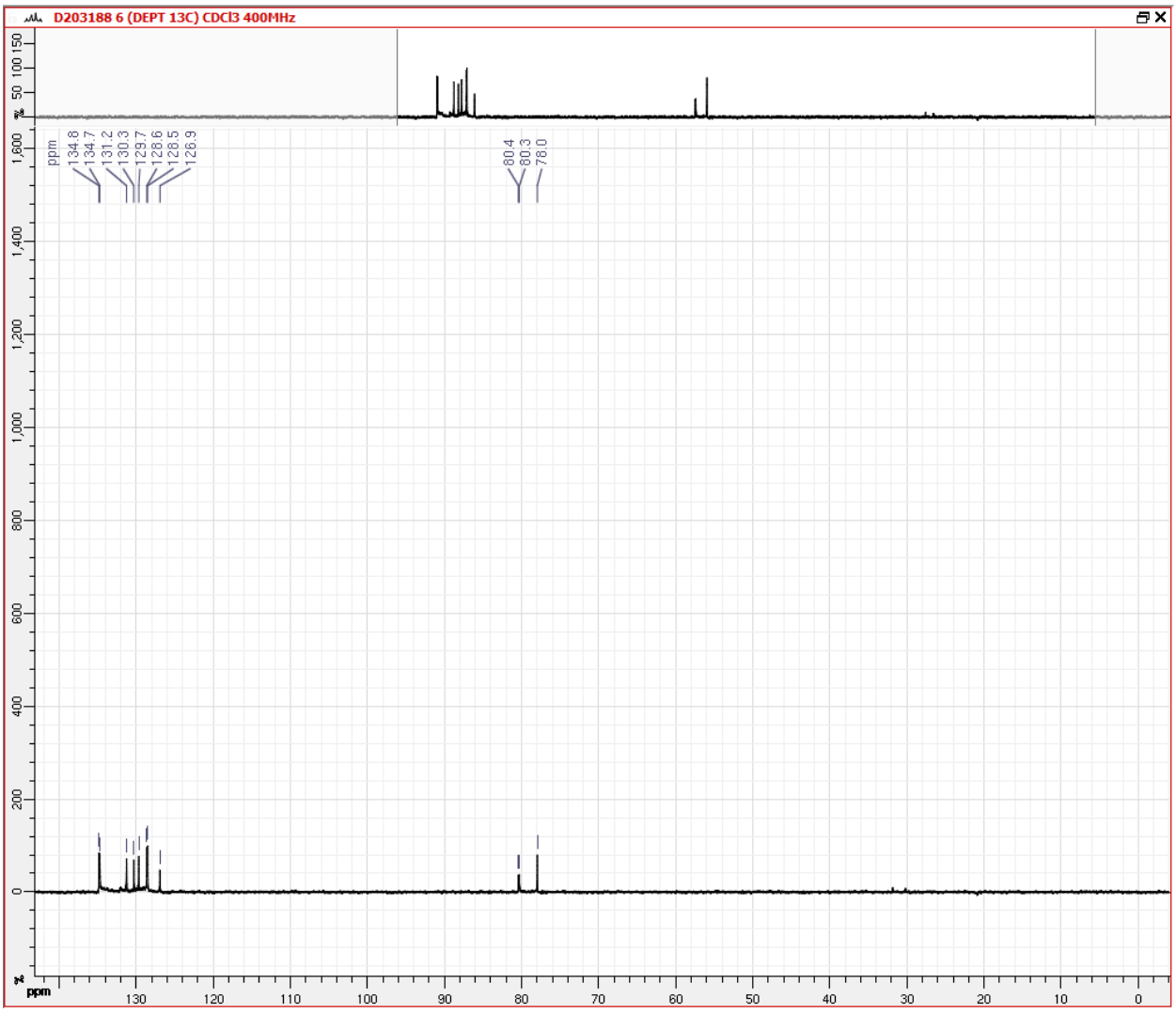
^{1}H NMR (400 MHz, $CDCl_3$):



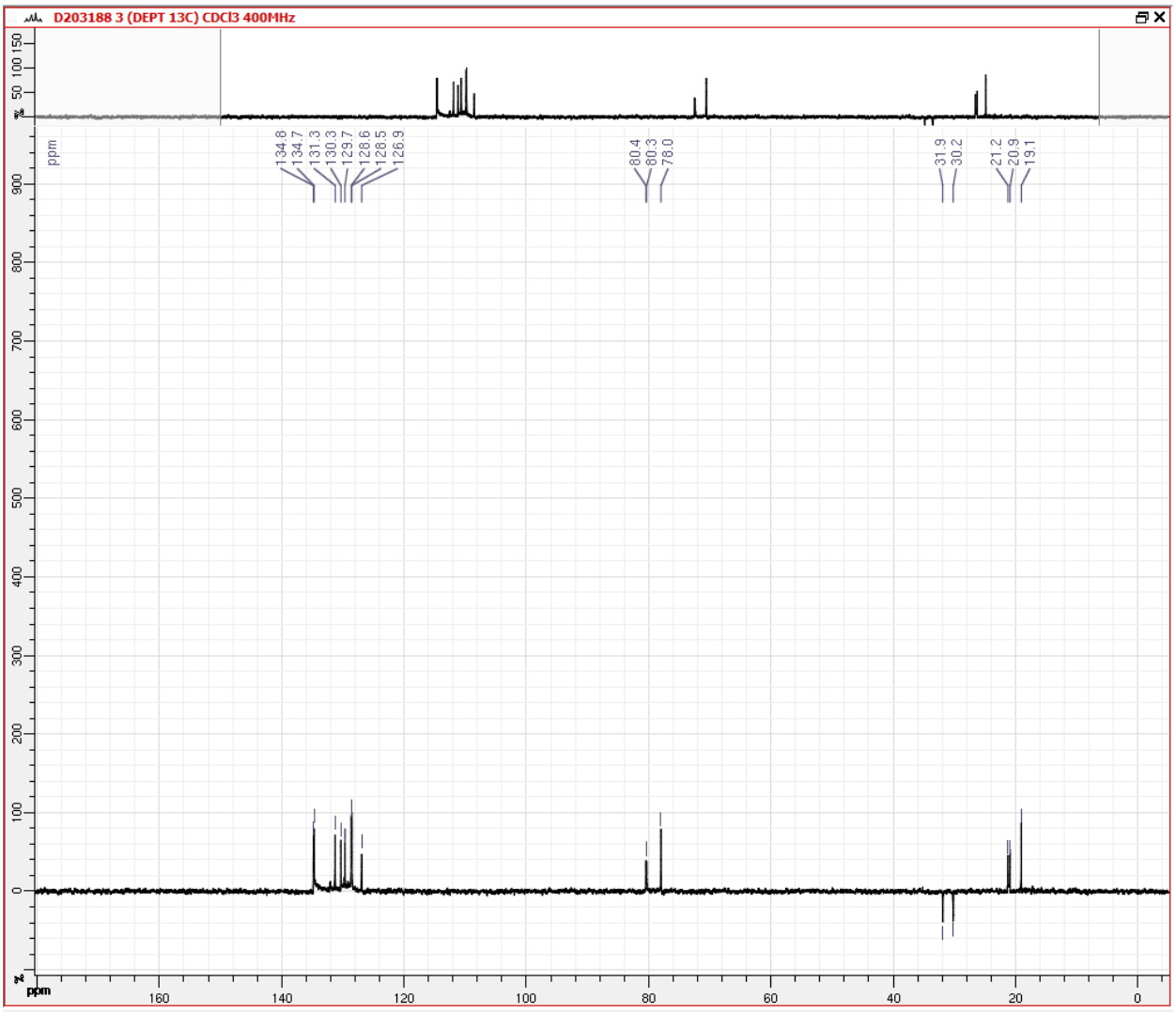
^{13}C NMR (100 MHz, $CDCl_3$):



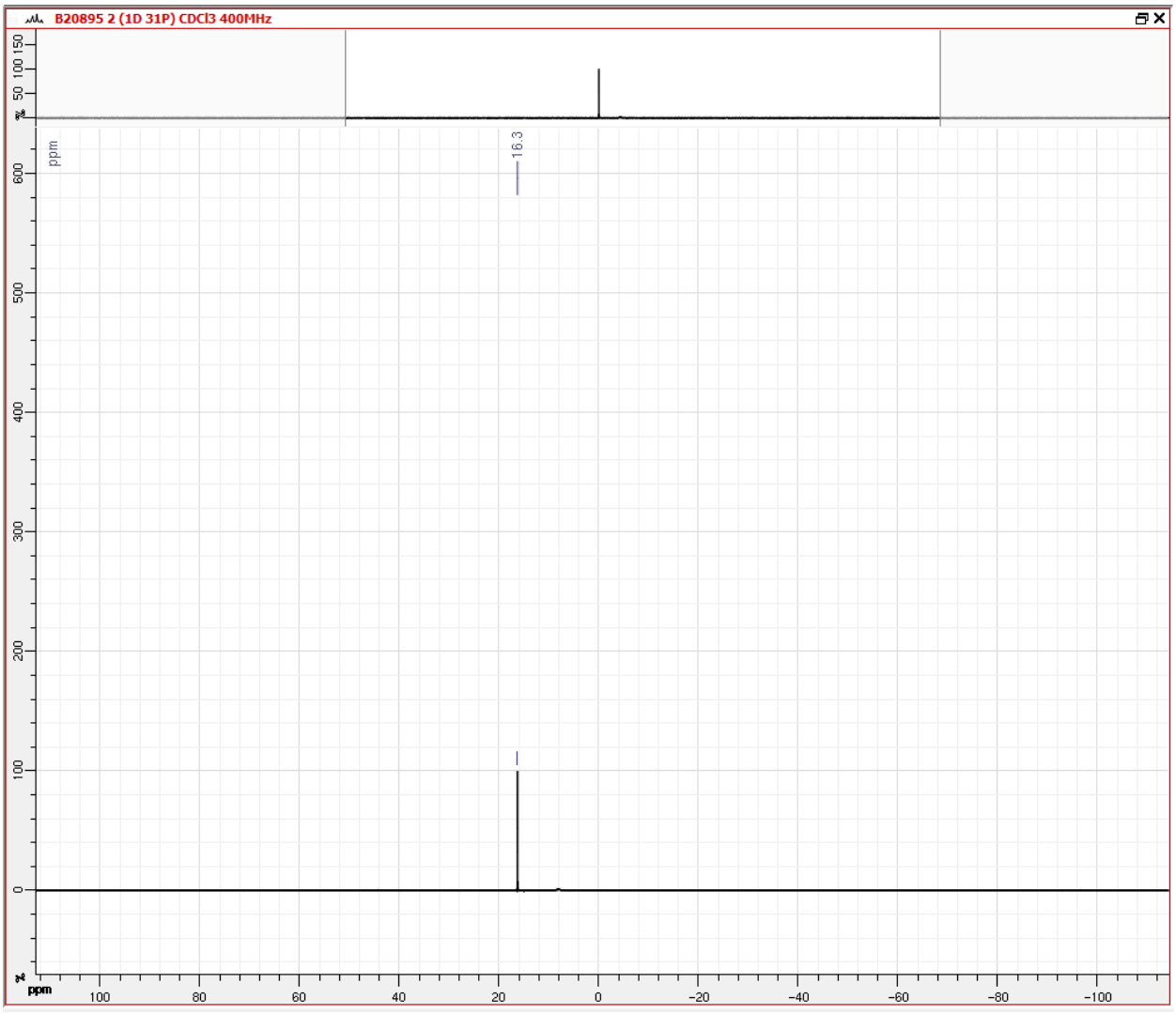
^{13}C DEPT-90° NMR (100 MHz, $CDCl_3$):



^{13}C DEPT-135° NMR (100 MHz, $CDCl_3$):



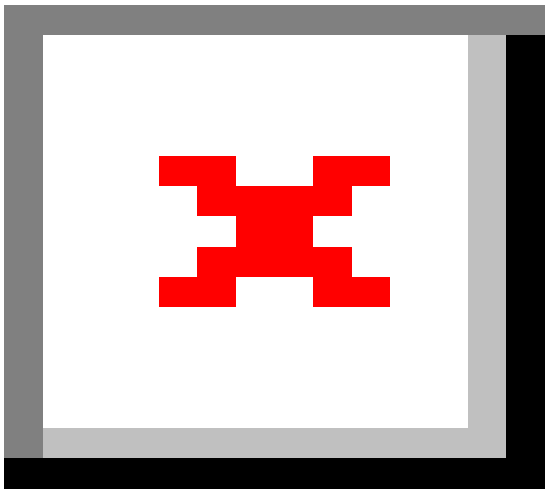
^{31}P NMR (162 MHz, $CDCl_3$):



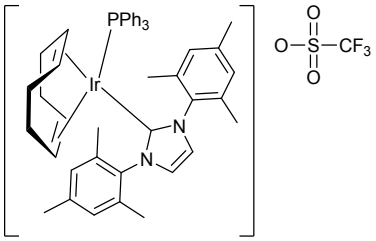
^{11}B NMR (128 MHz):

^{19}F NMR (376 MHz, $CDCl_3$):

FTIR (neat):



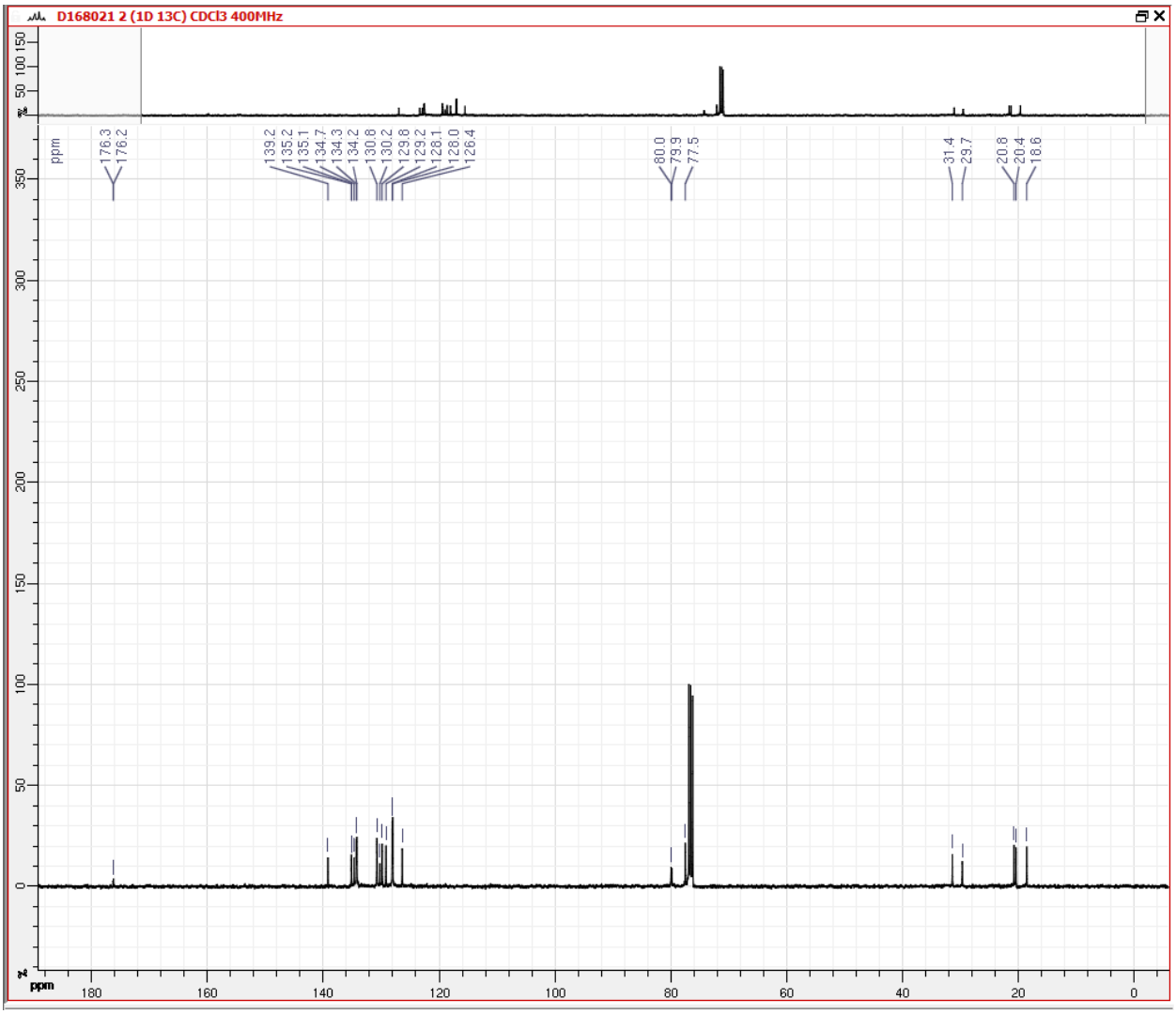
η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) trifluoromethylsulfonate, ***1c***



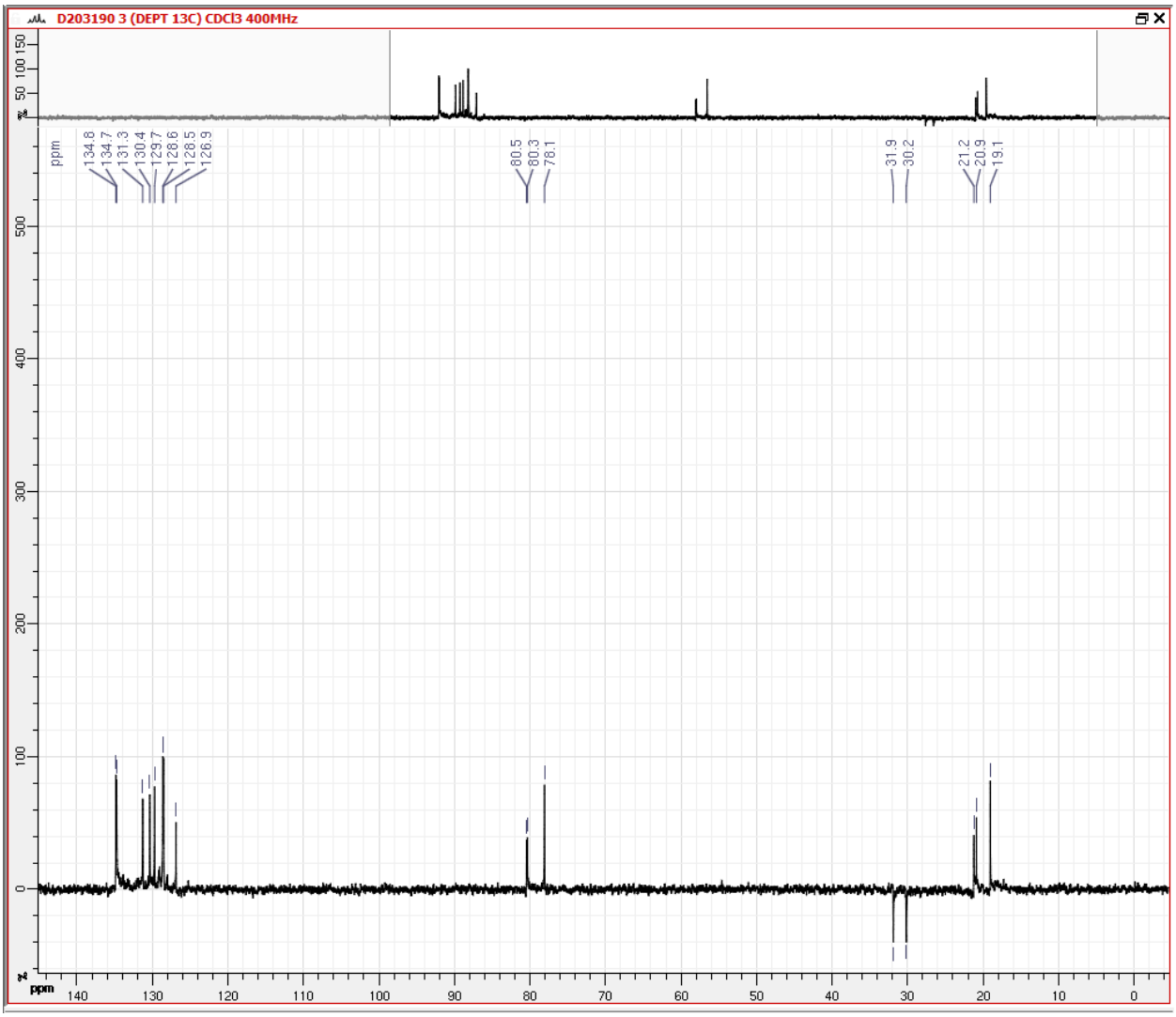
1c

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

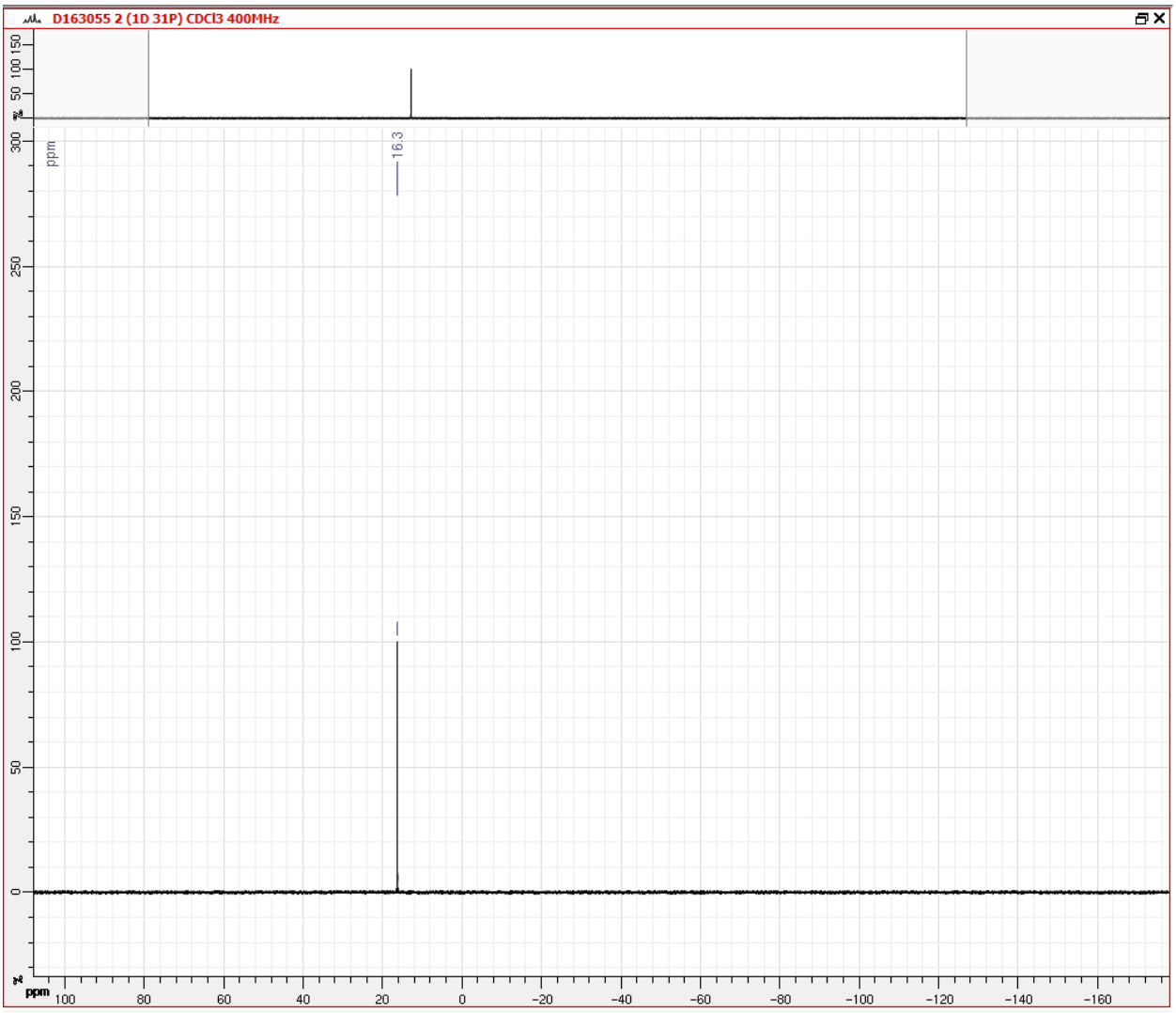
^{13}C NMR (100 MHz, $CDCl_3$):



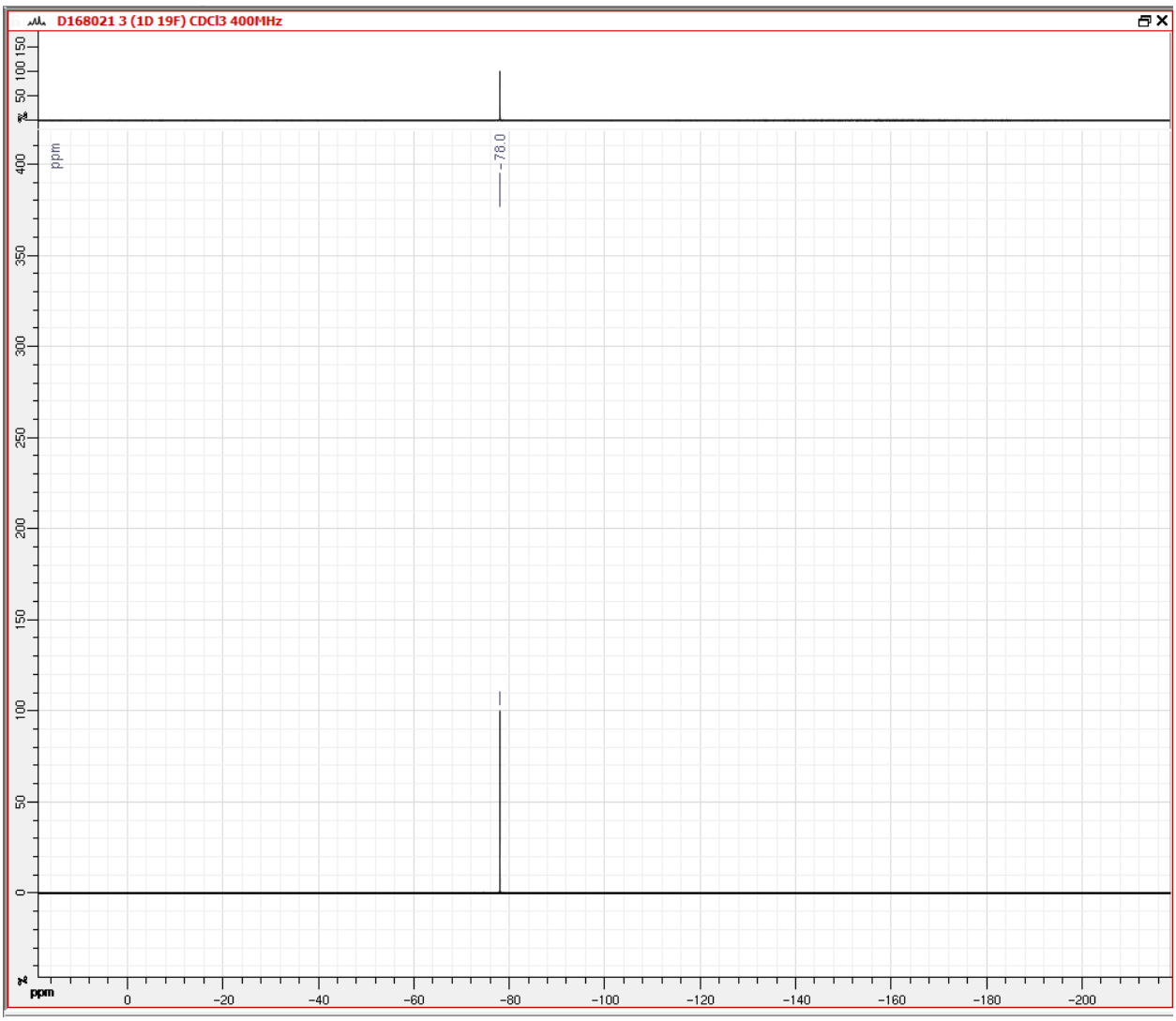
^{13}C DEPT-135° NMR (100 MHz, $CDCl_3$):



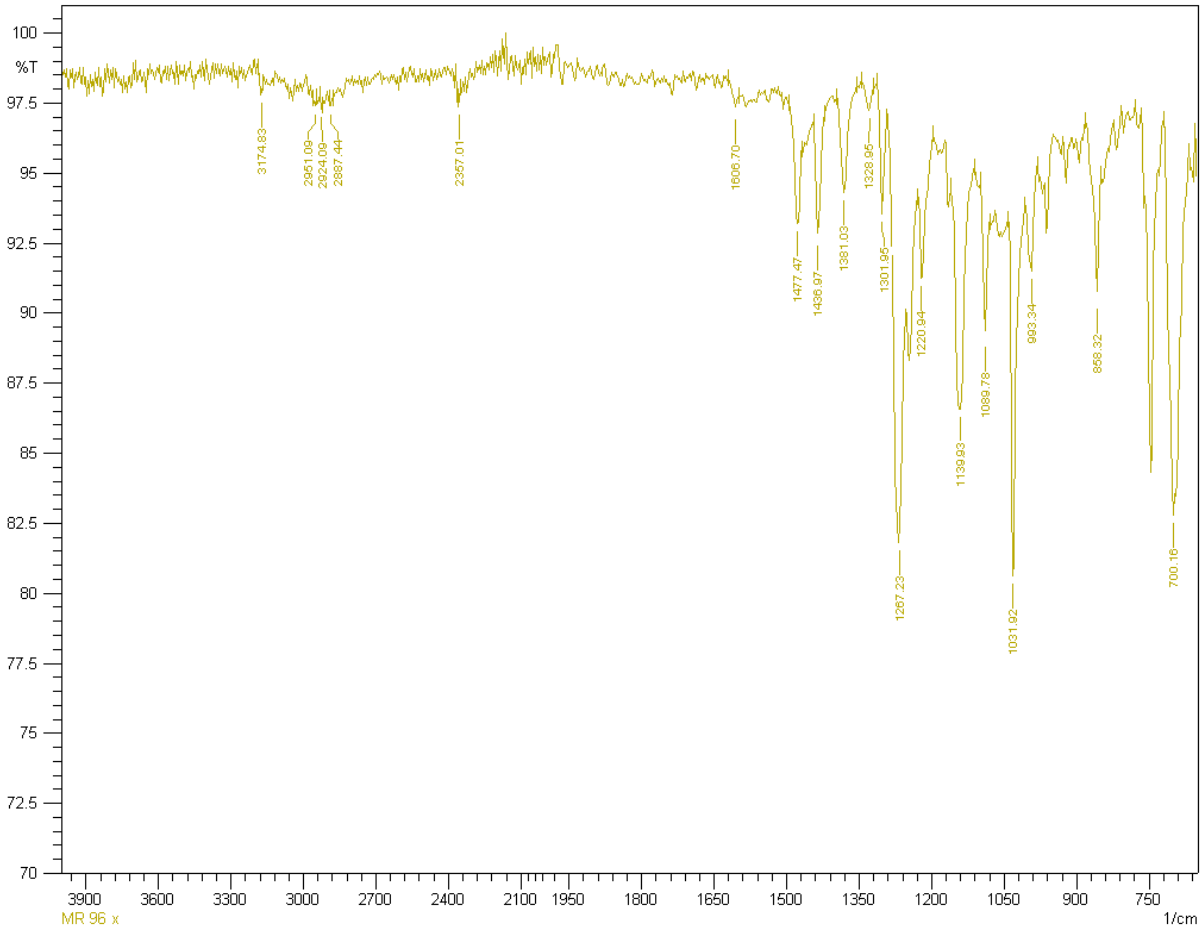
^{31}P NMR (162 MHz, $CDCl_3$):



^{19}F NMR (376 MHz, $CDCl_3$):



FTIR (neat):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87.5
85
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80
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75
72.5
70
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2951.09
2924.09
2887.44
2357.01
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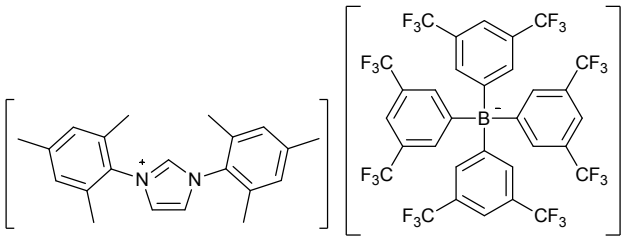
1477.47
1436.97
1381.03
1328.95
1301.95
1267.23
1220.94
1139.93
1089.78
1031.92
993.34
858.32
700.16
3900
3600
3300
3000
2700
2400
2100
1950
1800
1650
1500
1350
1200
1050
900
750
1/cm
MR 96 x

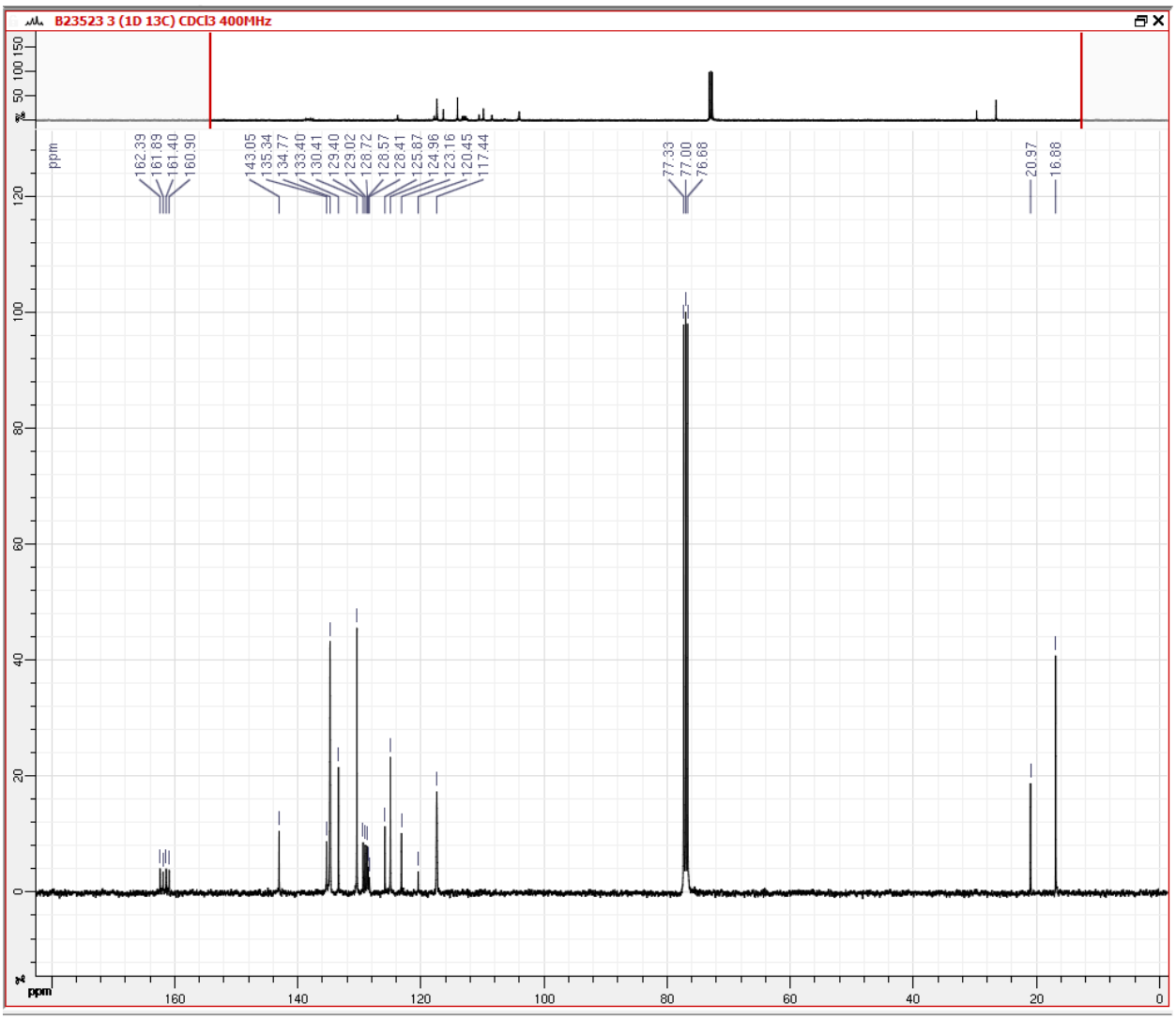
N,N'- Dimesitylimidazolium tetrakis[(3,5-trifluoromethylphenyl)]borate, ***4***



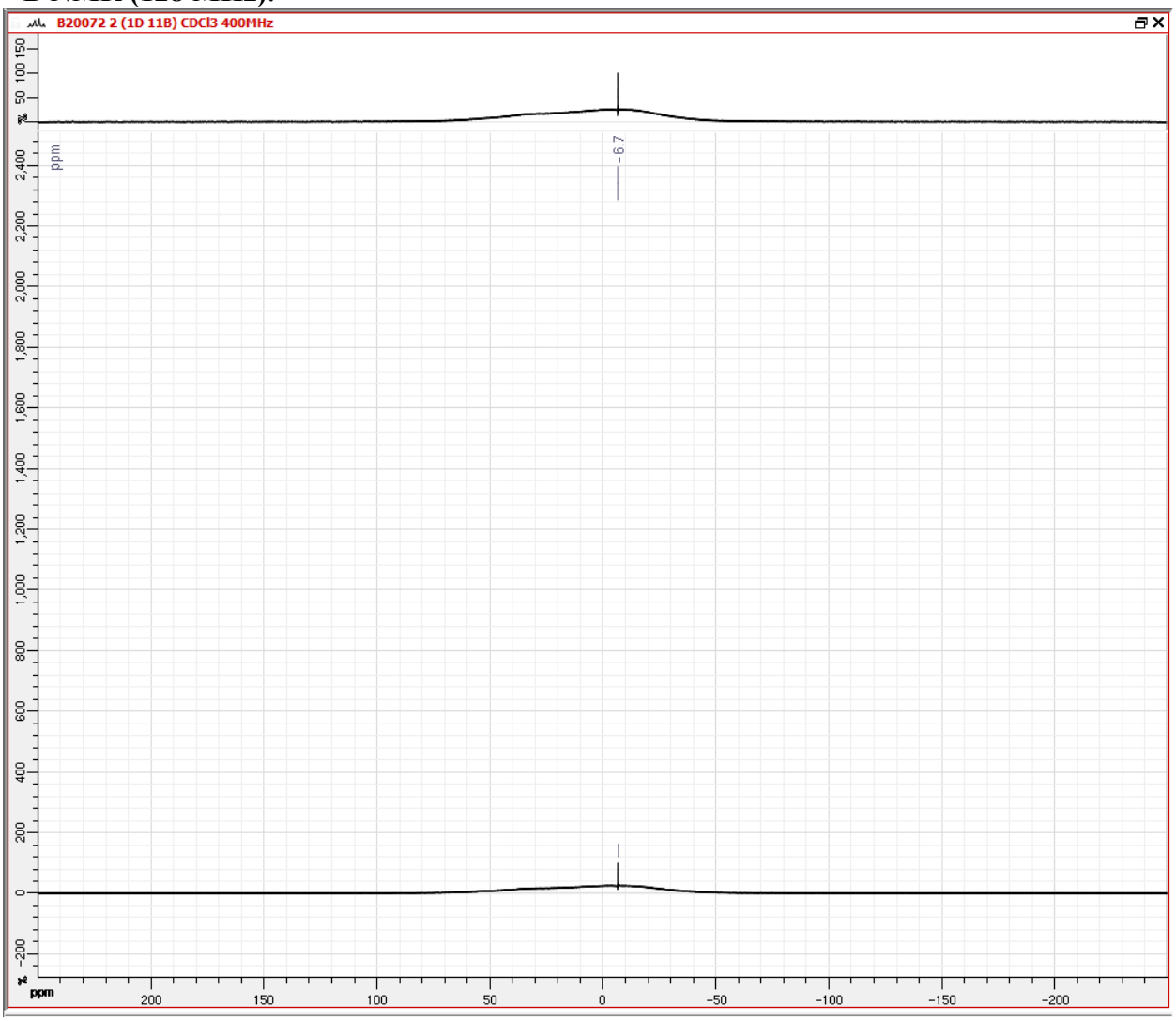
4

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

^{13}C NMR (100 MHz, $CDCl_3$):

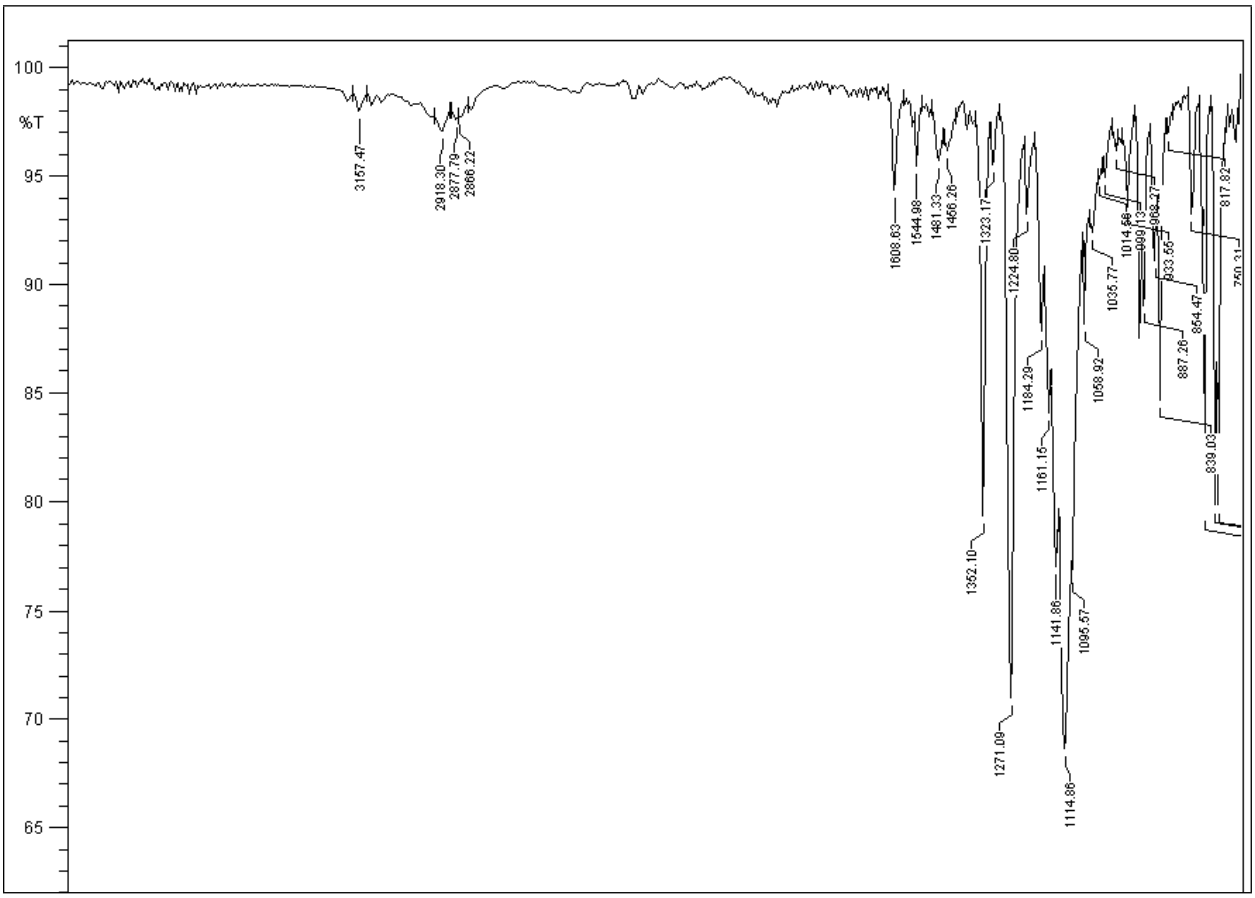


^{11}B NMR (128 MHz):



^{19}F NMR (376 MHz, $CDCl_3$):

FTIR (neat):


100
%T
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90
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80
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70
65
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2877.79
2866.22
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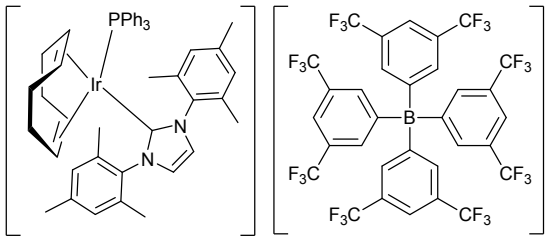
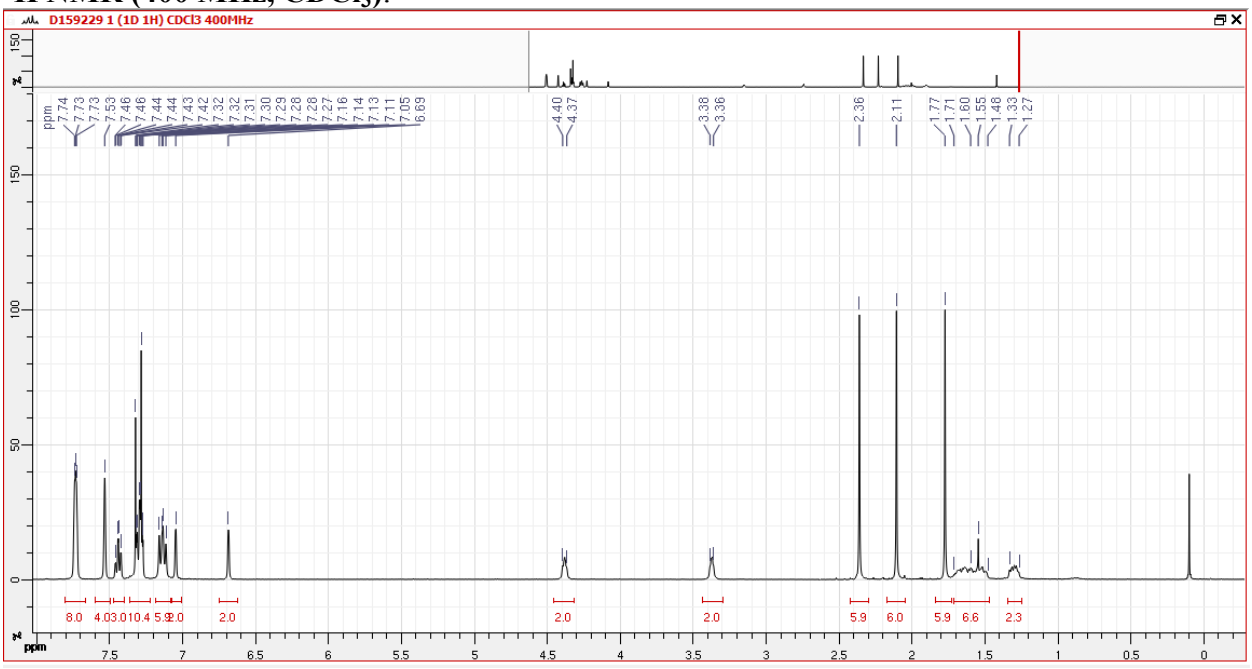
1481.33
1456.26
1323.17
1224.80
1184.29
1161.15
1352.10
1141.86
1271.09
1114.86
1095.57
1058.92
1035.77
1014.68
998.13
908.27
887.26
864.47
839.03
833.55
817.82
750.31

η^4–Cycloocta-1,5-diene(1,3-dimesitylimidazoline-2-ylidene) (triphenylphosphine)iridium(I) tetrakis[(3,5-trifluoromethylphenyl)]borate, ***1d***

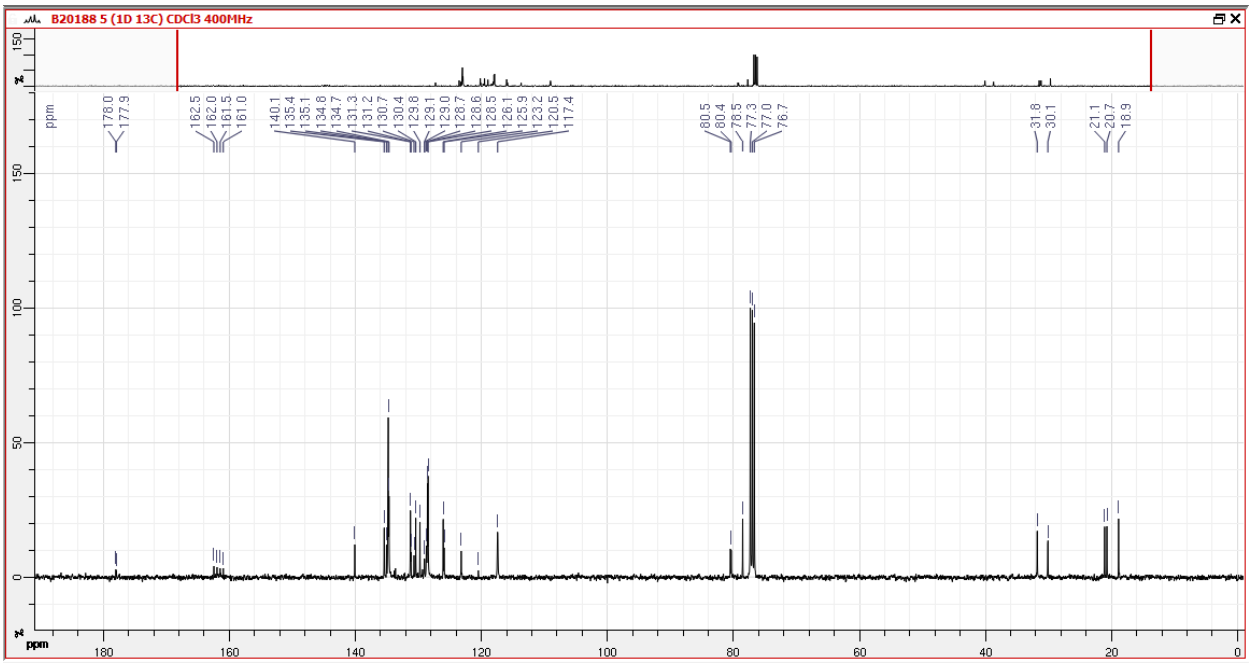


1d

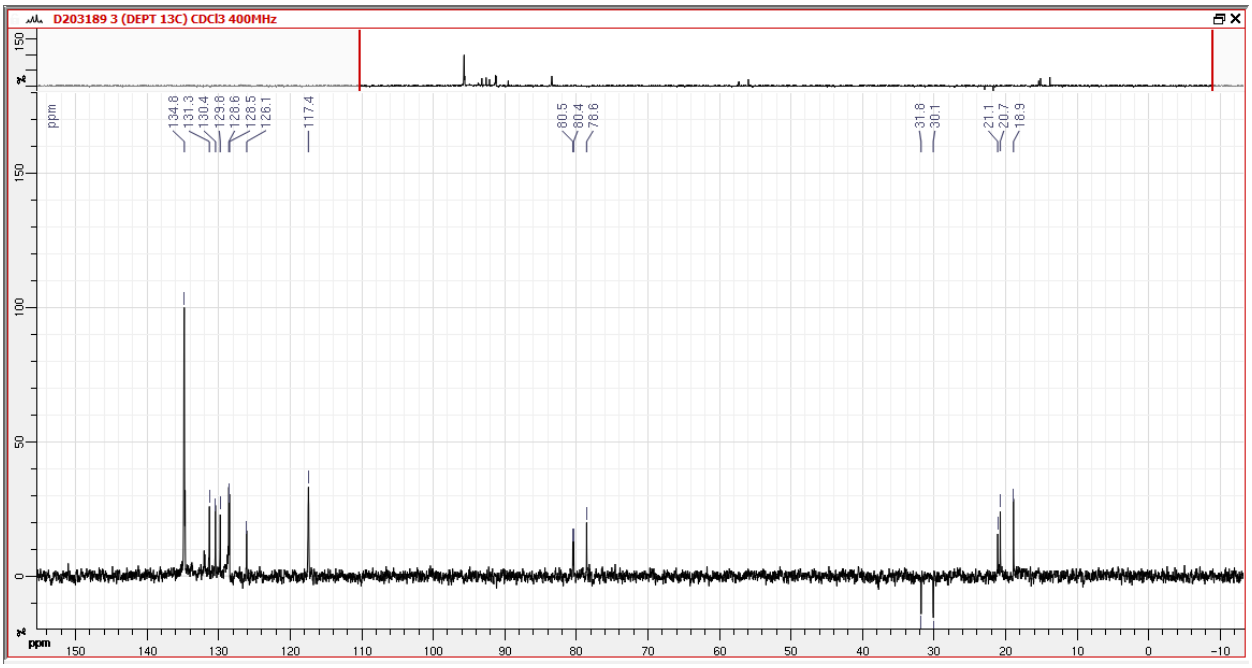
^{1}H NMR (400 MHz, $CDCl_3$):



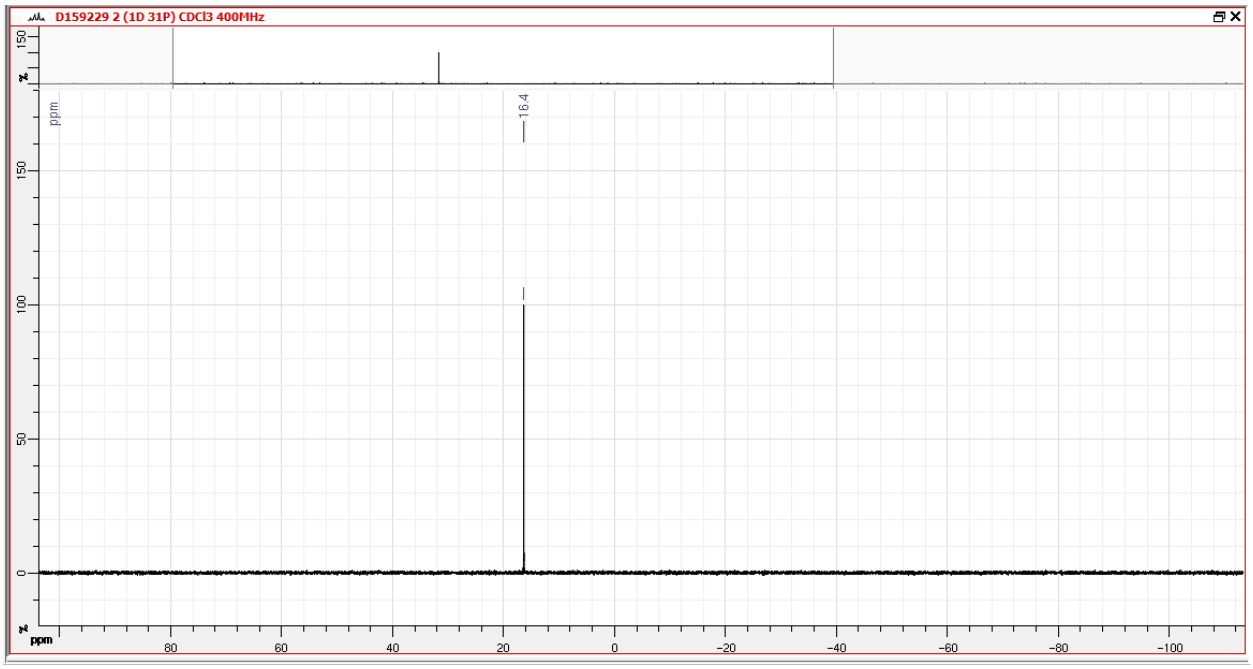
^{13}C NMR (100 MHz, $CDCl_3$):



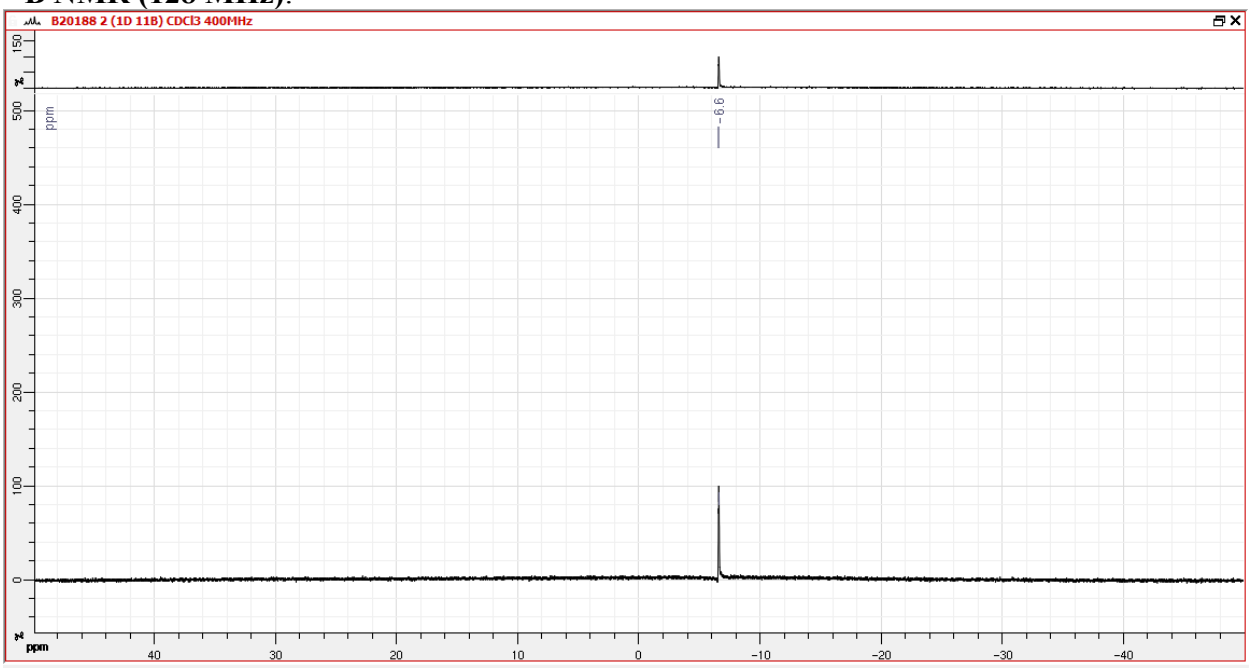
^{13}C DEPT-135º NMR (100 MHz, $CDCl_3$):



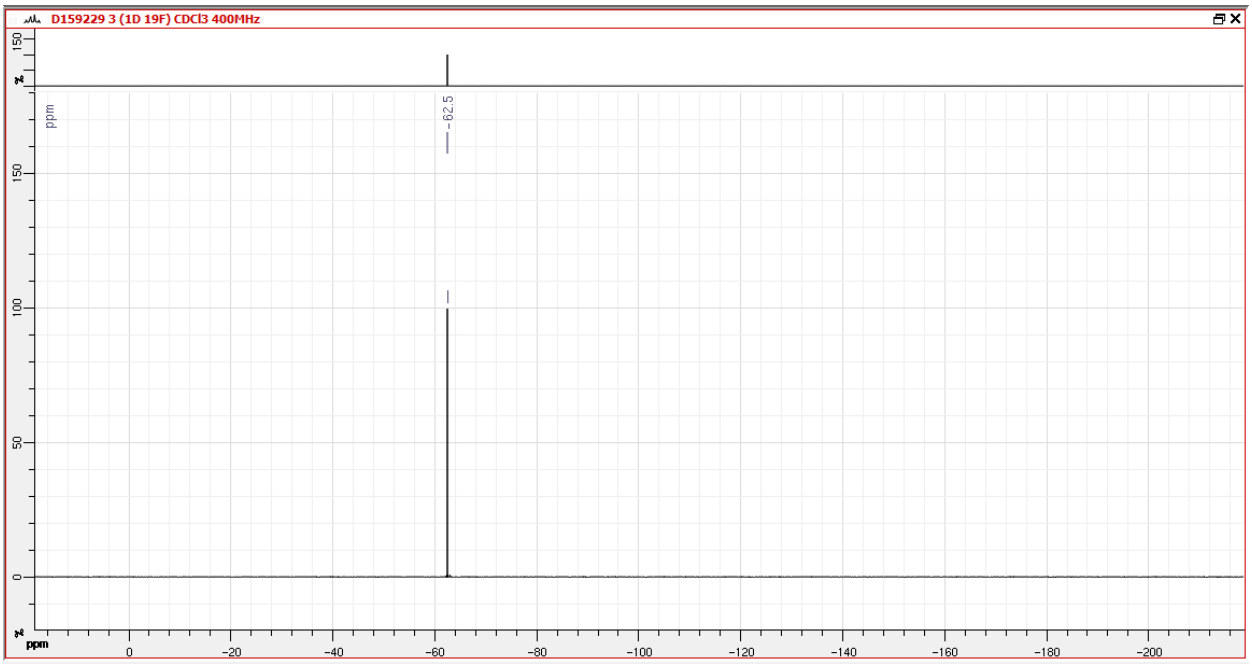
^{31}P NMR (162 MHz, $CDCl_3$):



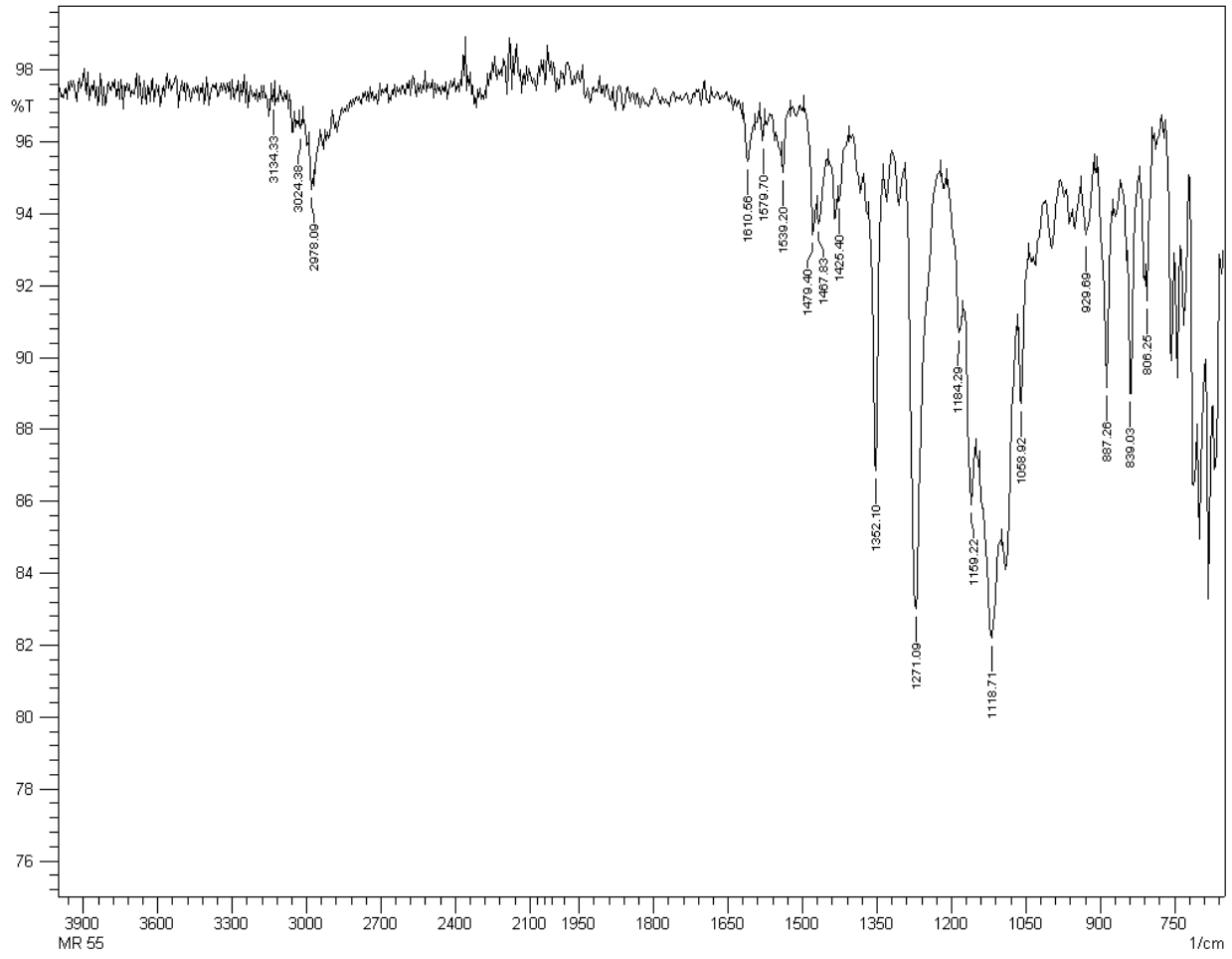
^{11}B NMR (128 MHz):



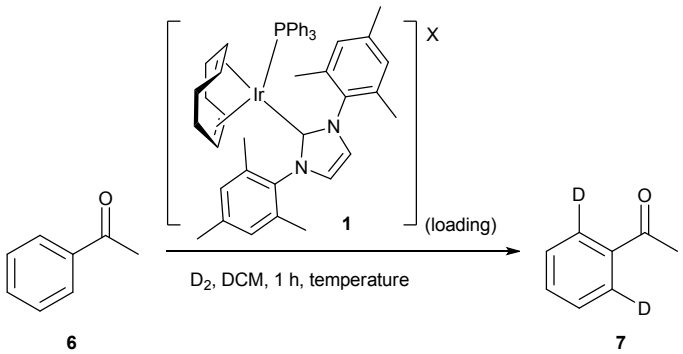
^{19}F NMR (376 MHz, $CDCl_3$):



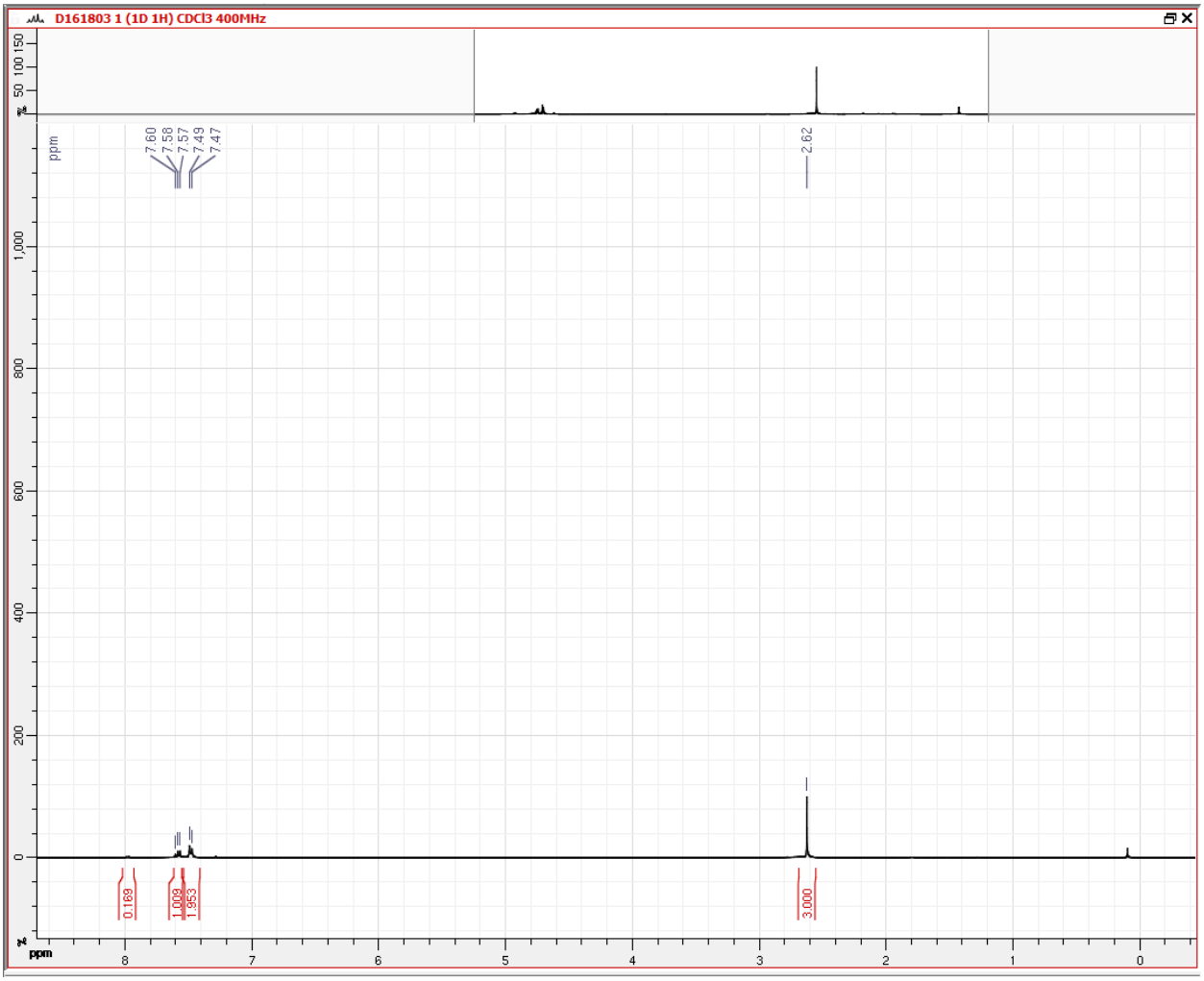
FTIR (neat):

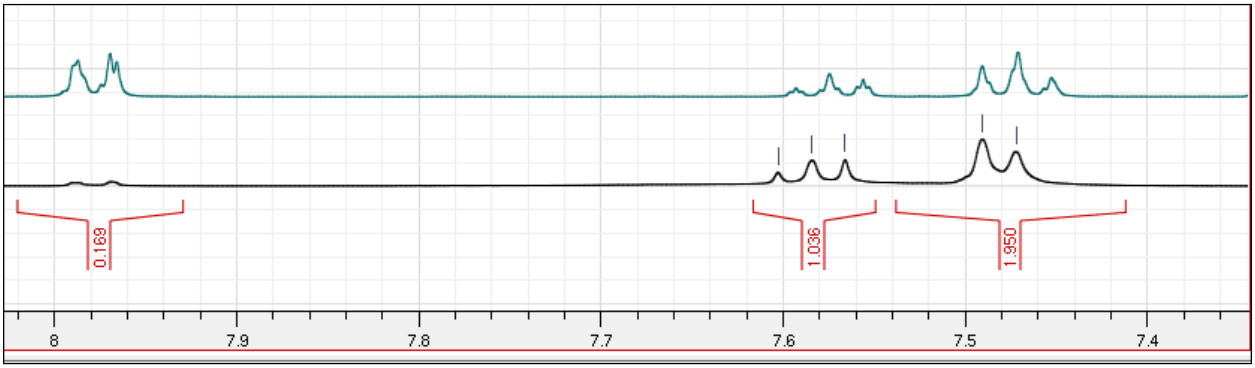


*Example Spectrum for Deuterated Acetophenone, **7***

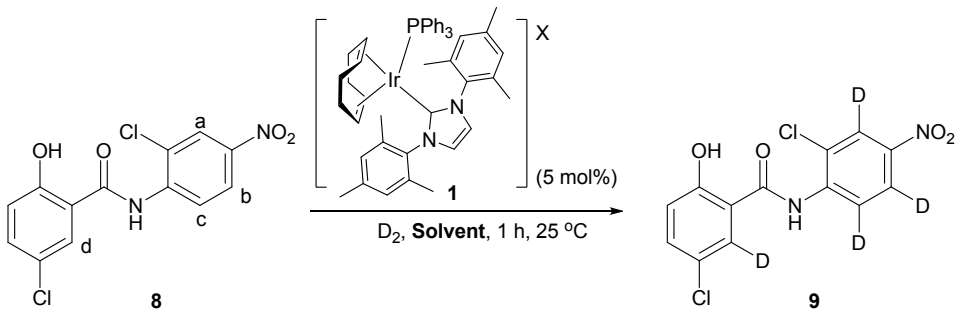


The spectrum below represents 92% deuterium incorporation. The zoomed in view shows the deuterated product, **7** (black), *versus* the unlabelled substrate, **6** (green).

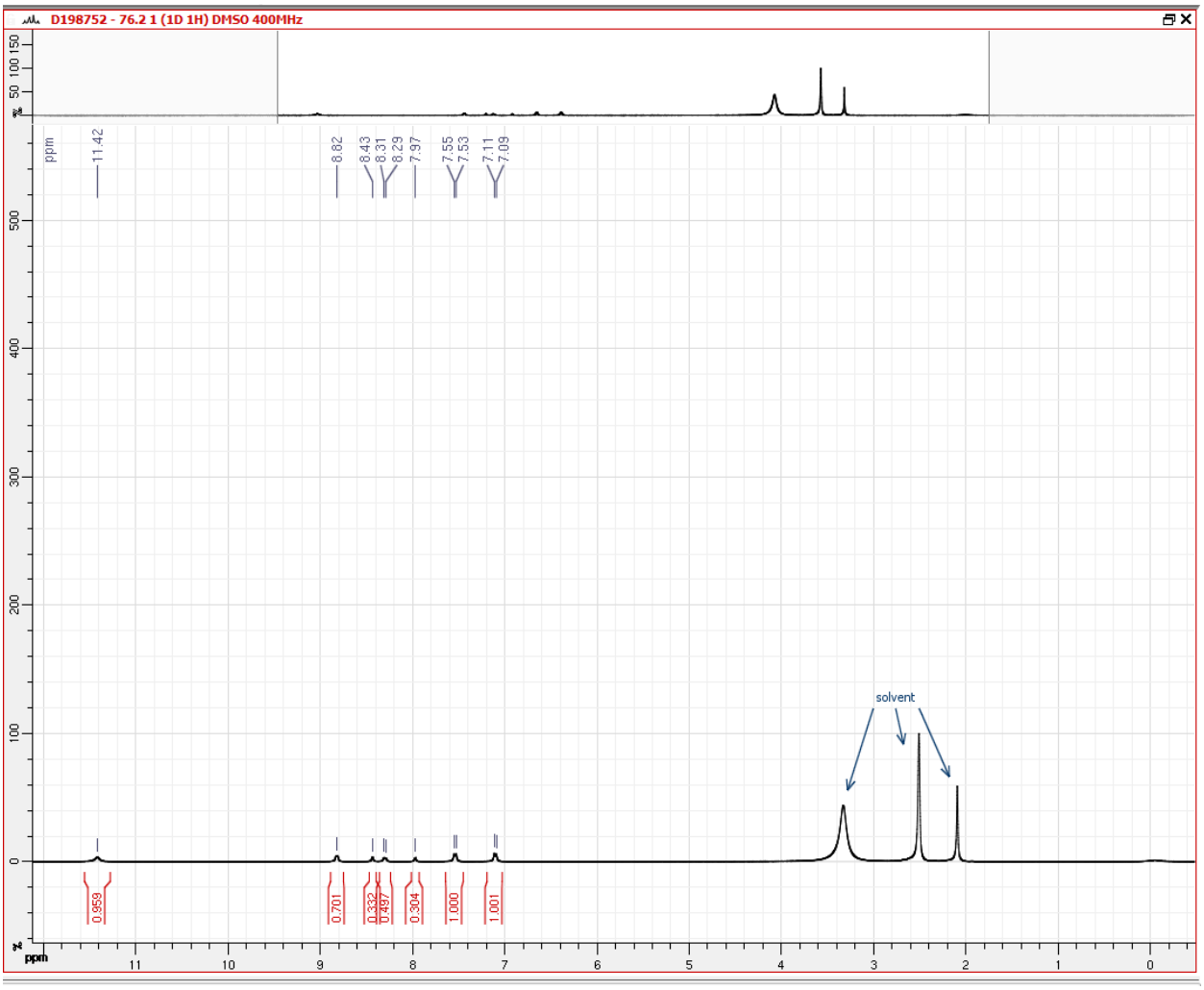


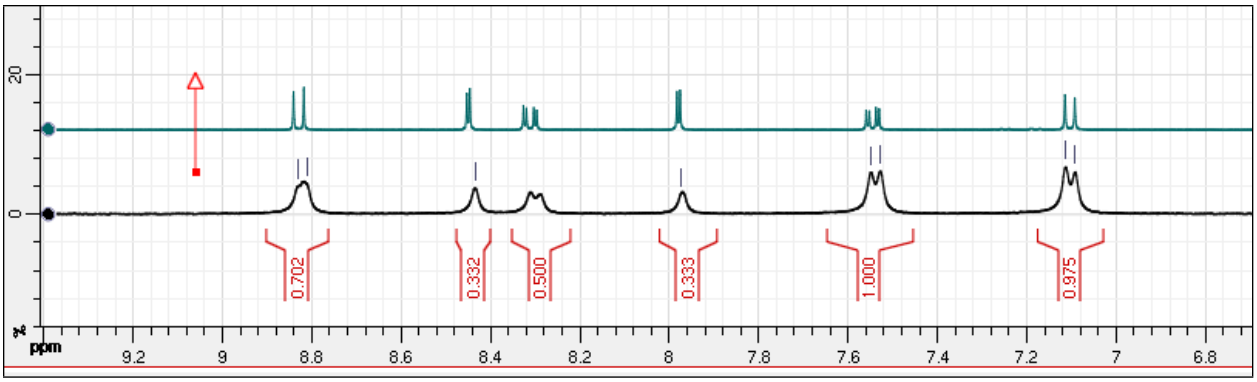


Example Spectra for Deuterated Niclosamide, ***9***

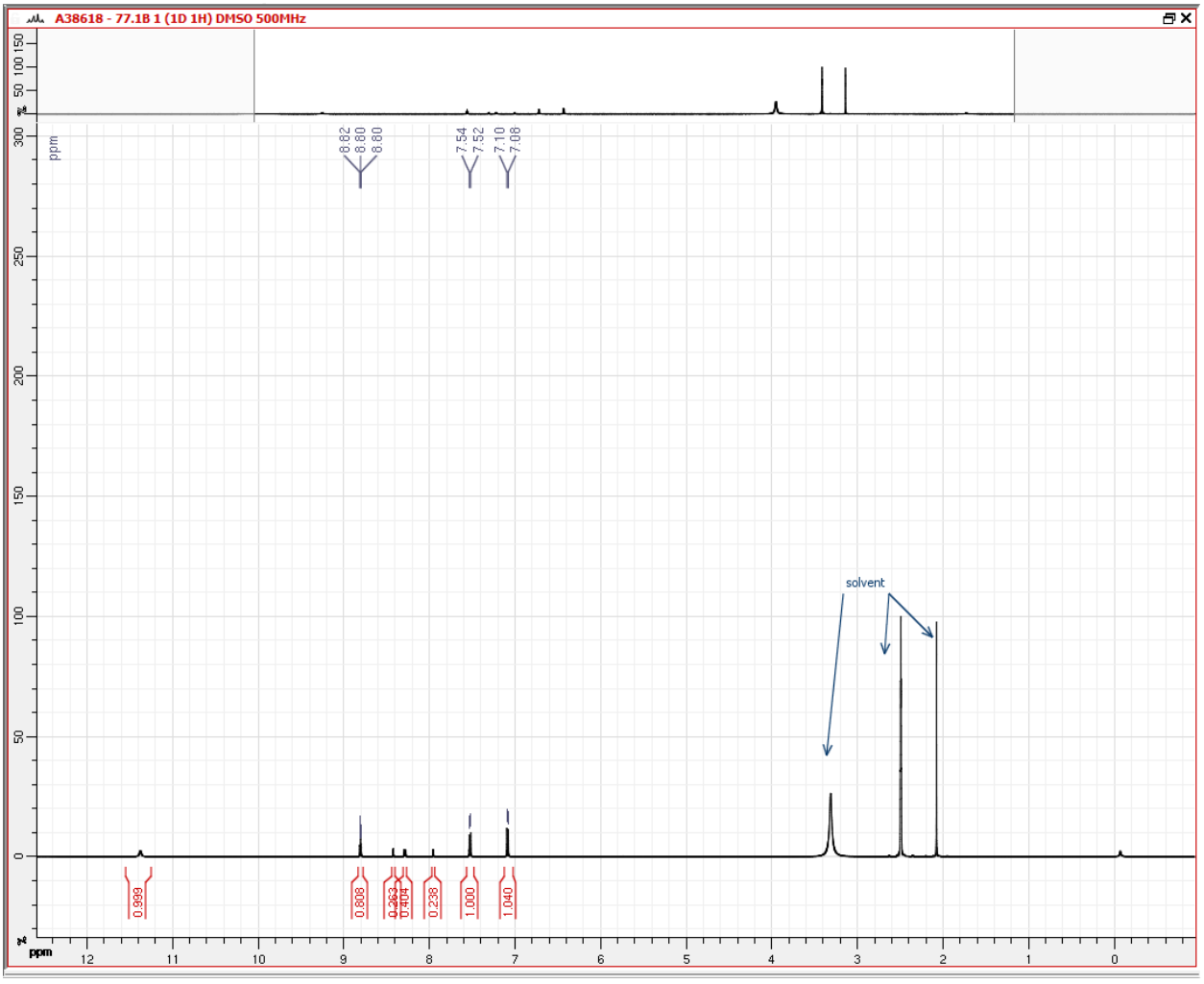


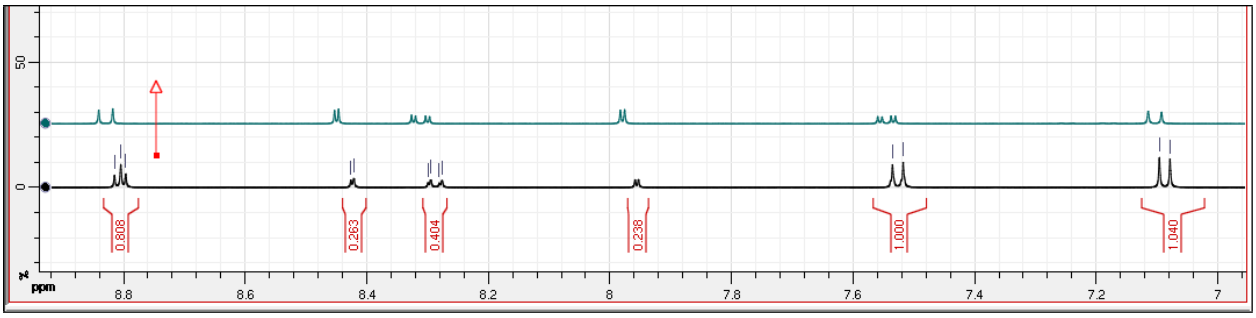
From **Table S3**, **Entry 1**, **Run 1**:



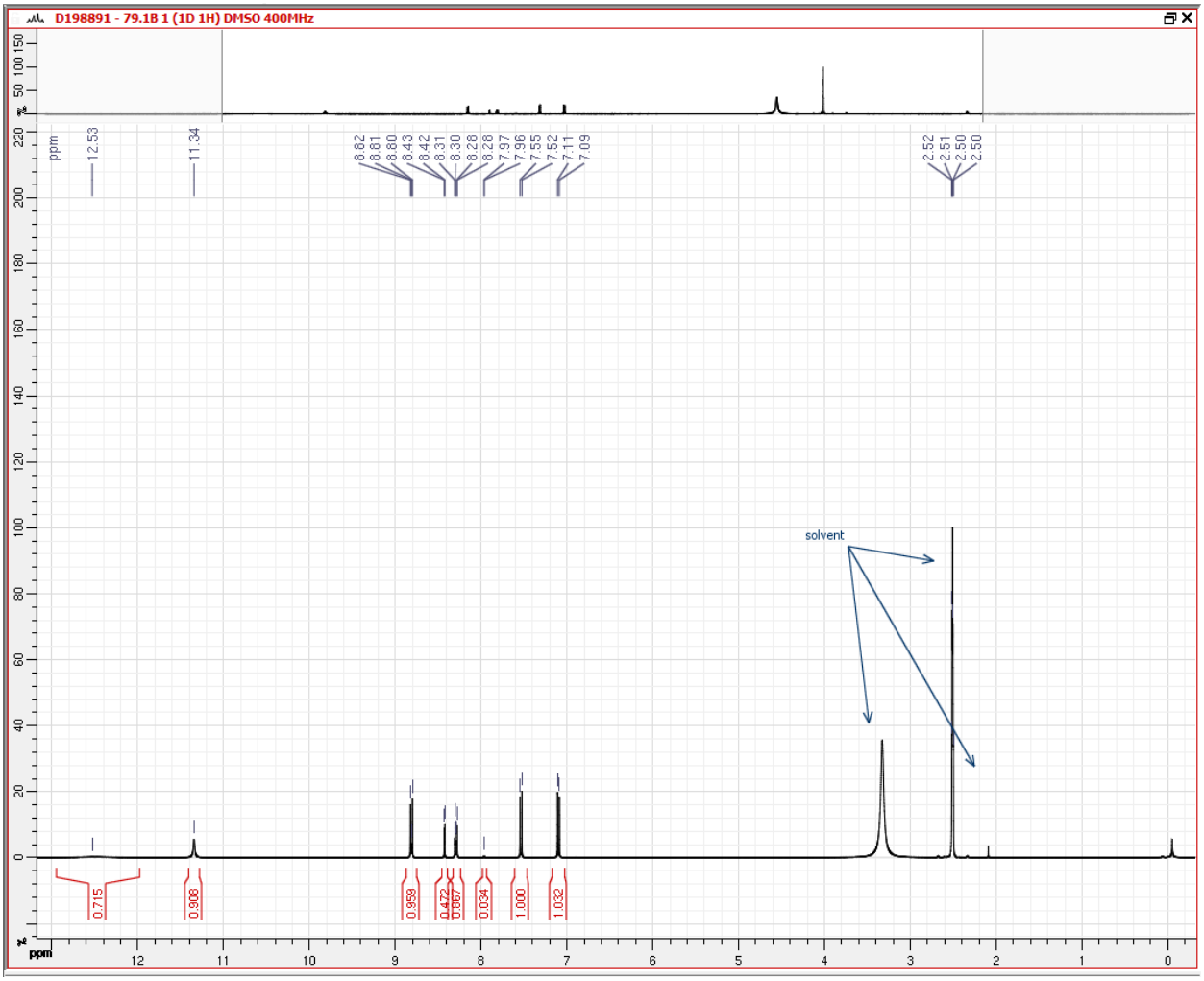


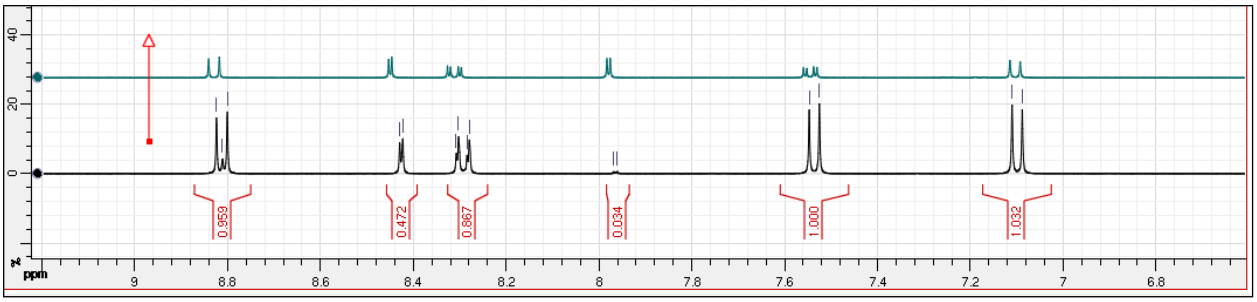
From **Table S3**, **Entry 2**, **Run 2**:



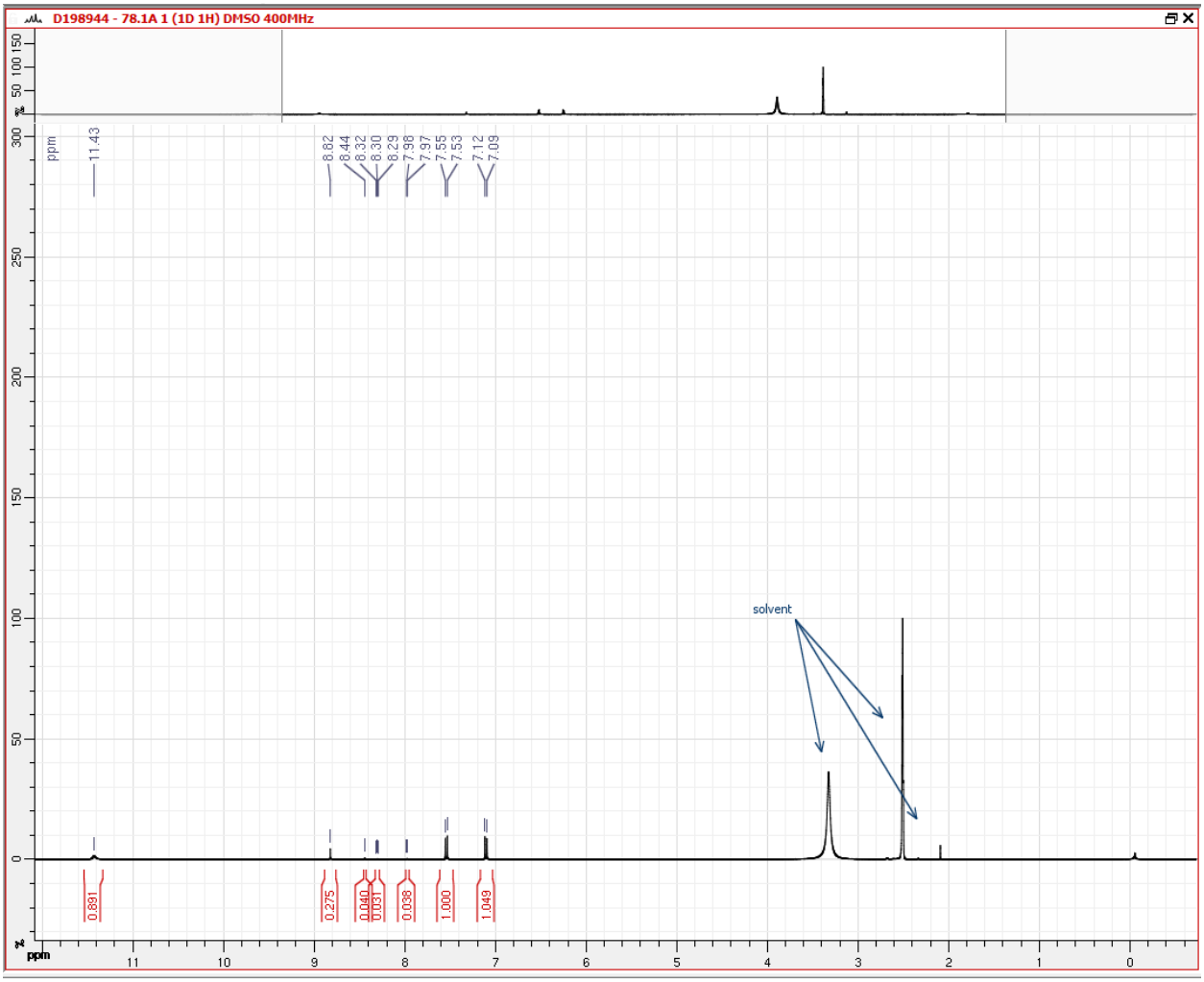


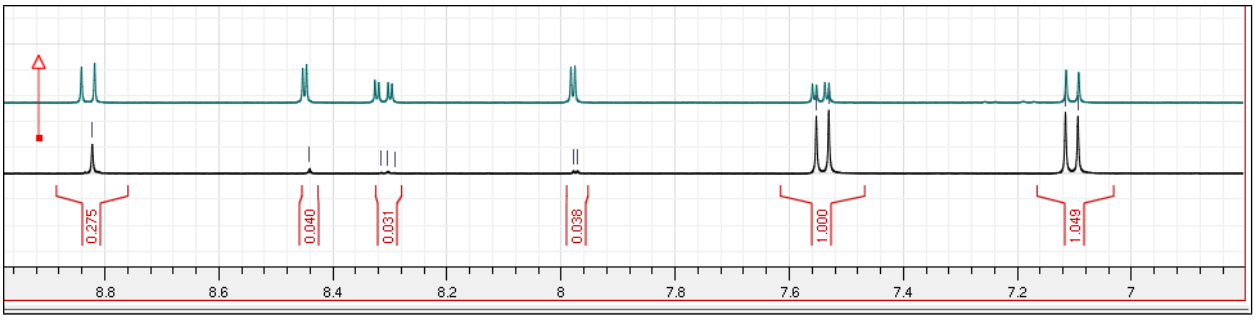
From **Table S3**, **Entry 3**, **Run 2**:





From **Table S3**, **Entry 4**, **Run 1**:




0.275
0.040
0.031
0.038
1.000
1.049
8.8
8.6
8.4
8.2
8
7.8
7.6
7.4
7.2
7

Crystal Structure Determination

Single-crystal diffraction data were measured using Oxford Diffraction instruments. The structures were refined to convergence against F^2 using all independent reflections and the full-matrix least-squares method using the program SHELXL-97.[4] For structure **1b**, disorder in one of the two independent BF_4 ion sites required restraints to be applied to both bond lengths and thermal parameters of this fragment. Similar restraints were required to model disorder of the CF_3 groups of the $[B(C_8H_3F_6)_3]$ ions in structures **1d** and **4**. Selected crystallographic parameters are given in **Table S4** and full details are given in the deposited cif files. CCDC reference numbers CCDC 1001847 – CCDC 1001850 contain the supplementary crystallographic data for this paper. This data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table S4 Selected crystallographic data and refinement parameters.

Compound	**1b**	**1c**	**1d**	**4**
Formula	$[C_{47}H_{51}IrN_2P]$ $[BF_4]$	$[C_{47}H_{51}IrN_2P]$ $[SO_3CF_3]$	$[C_{47}H_{51}IrN_2P]$ $[C_{32}H_{12}BF_{24}]$	$[C_{21}H_{25}N_2]$ $[C_{32}H_{12}BF_{24}]$
M_r (g mol^{-1})	953.88	1016.14	1730.29	626.34
Crystal system	Monoclinic	Triclinic	Triclinic	Monoclinic
Space group	$P2_1/c$	P-1	P-1	$P2_1/c$
Temperature (K)	123(2)	123(2)	123(2)	153(2)
a (Å)	15.5996(2)	17.2768(4)	12.5160(3)	20.4198(5)
b (Å)	20.3256(3)	17.2947(3)	14.3186(4)	11.9065(2)
c (Å)	20.7522(2)	17.8826(4)	20.839(5)	23.6916(5)
α (°)		109.210(2)	84.989(2)	
β (°)	91.354(1)	106.118(2)	77.642(2)	114.629(3)
γ (°)		109.130(2)	84.507(2)	
V/Å^3	8264.82(17)	4299.26(16)	3627.04(16)	5236.07(19)
Z	8	4	2	4
Wavelength (Å)	0.71073	0.71073	0.71073	1.5418
Measured reflections	41947	59686	30422	21350
Unique reflections	18942	2084	15718	10263
R_{int}	0.0292	0.0272	0.0721	0.0193
Observed rflns [$I > 2\sigma(I)$]	12570	17431	12008	8411
μ (mm^{-1})	3.323	3.249	1.971	1.308
No. of parameters	1037	1075	1009	794
2θmax (°)	55.0	58.0	55.78	146.34
R [on *F*, obs rflns only]	0.0323	0.0293	0.0472	0.0598
wR [on F^2, all data]	0.0700	0.0714	0.1165	0.1708
GoF	1.038	1.032	0.987	1.167
Largest diff. peak/hole/e Å^{-3}	1.080/–0.669	2.598/-1.182	1.955/-2.081	0.773/-0.466

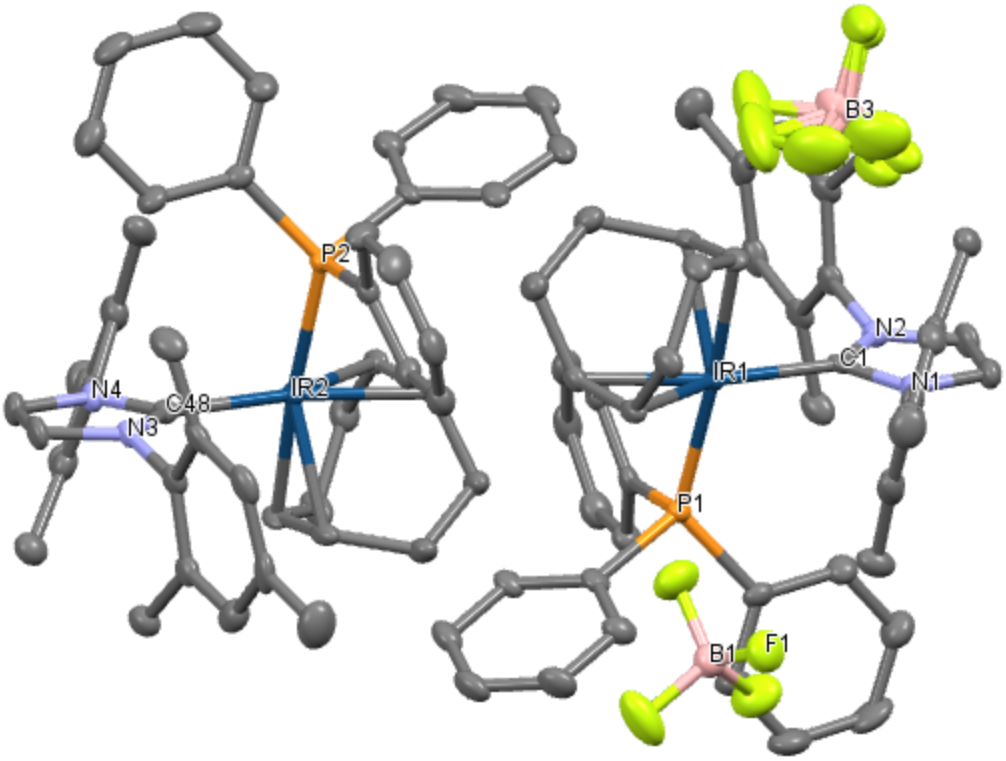


Fig. **S1** Asymmetric unit for complex **1b** as determined by X-ray crystallography. Selected bond lengths (Å): IR1-C1 2.061; IR1-P1 2.358; IR2-C48 2.063; IR2-P2 2.363.

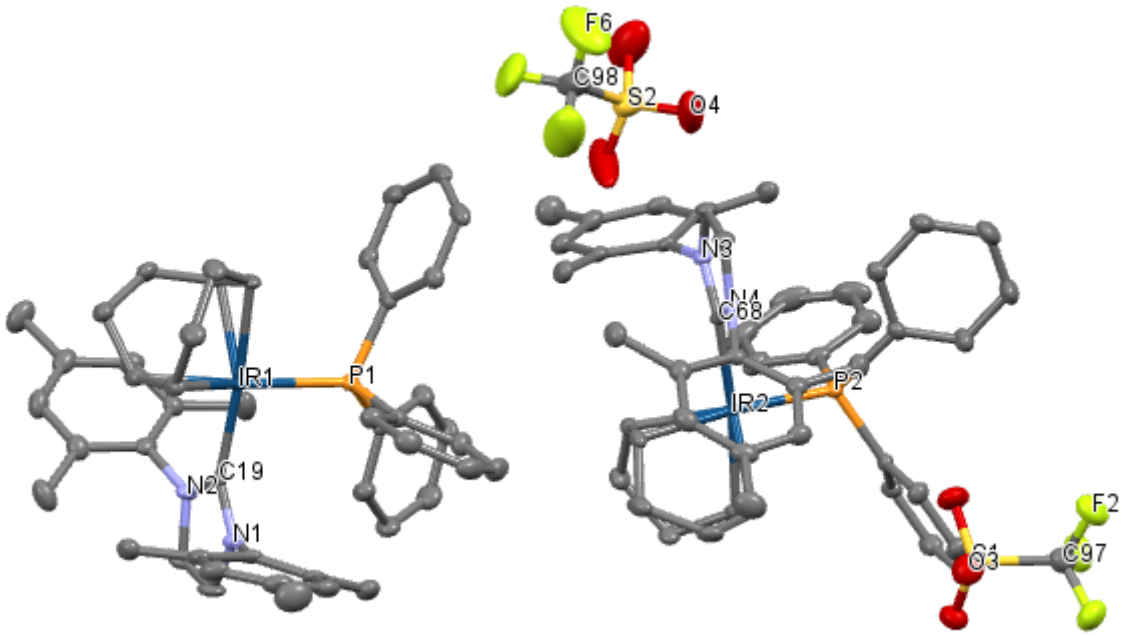


Fig. **S2** Asymmetric unit for complex **1c** as determined by X-ray crystallography. Selected bond lengths (Å): IR1-C19 2.063; IR1-P1 2.354; IR2-C68 2.070; IR2-P2 2.355.

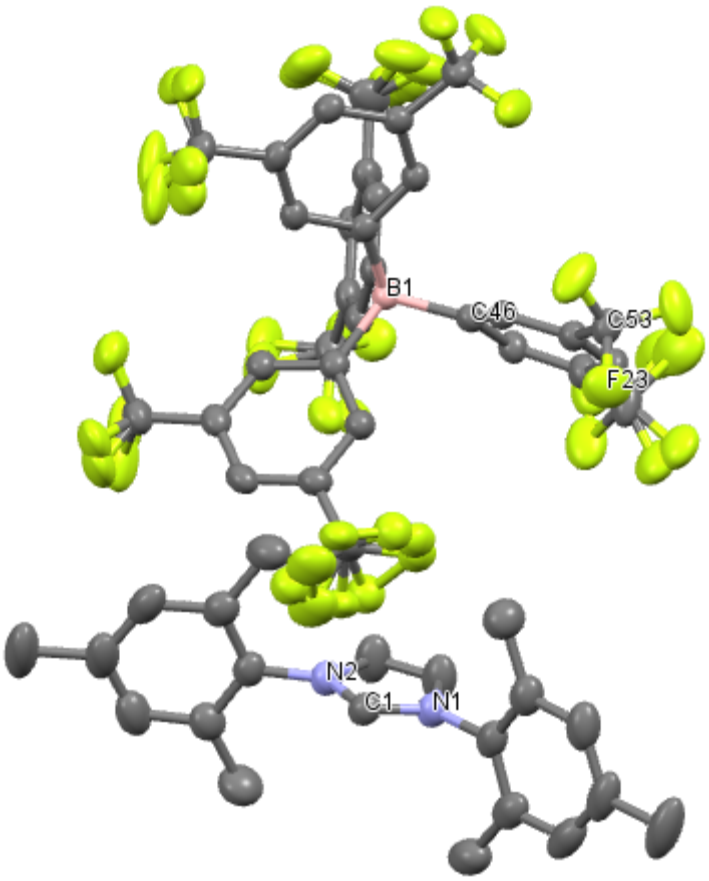


Fig. **S3** Asymmetric unit for imidazolium salt **4** as determined by X-ray crystallography. Selected bond lengths (Å): C1-N1 1.326; B1-C46 1.644.

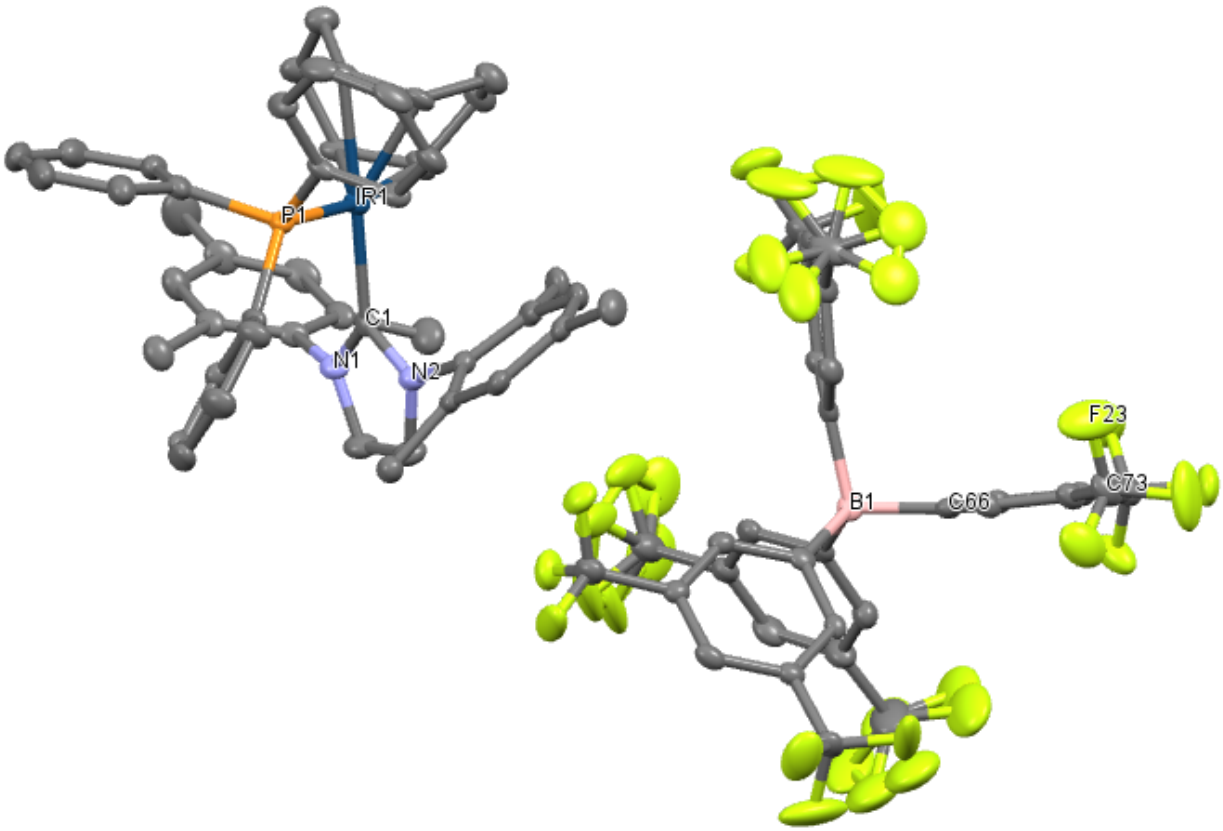


Fig. **S4** Asymmetric unit for complex **1d** as determined by X-ray crystallography. Selected bond lengths (Å): IR1-C1 2.078; IR-P1 2.336; B1-C66 1.654.

References

1. W. L. F. Armarego and C. Chai, In *Purification of Laboratory Chemicals*, Butterworth-Heinemann, Oxford, UK, 2012.
2. J. A. Brown, S. Irvine, A. R. Kennedy, W. J. Kerr, S. Andersson and G. N. Nilsson, *Chem. Commun.*, 2008, 1115.
3. S. Leuthaußer, D. Schwarz and H. Plenio, *Chem. Eur. J.*, 2007, **13**, 7195.
4. G. M. Sheldrick, *Acta Crystallogr. A*, 2008, **64**, 112.