Supporting Information for:

Highly Efficient Hydrogenation of Biomass-derived Levulinic Acid to γ-Valerolactone Catalyzed by Iridium Pincer Complexes

Wei Li, Jian-Hua Xie, Han Lin, Qi-Lin Zhou*
State Key Laboratory and Institute of Elemento-organic Chemistry, Nankai University
Tianjin 300071, China

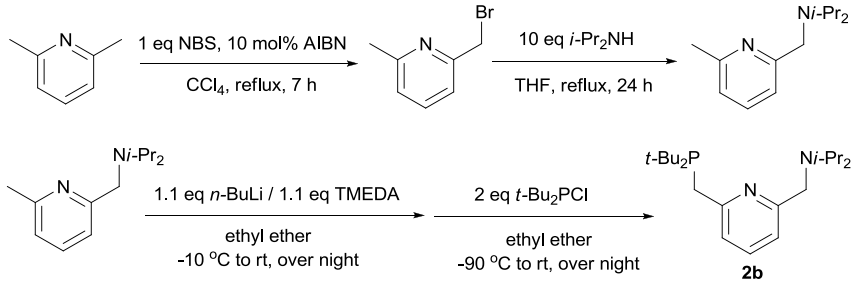
CONTENTS:

General: Unless otherwise noted, the manipulations which are sensitive to moisture or air were performed in an argon-filled glove box MBRAUN labstar or using standard Schlenk techniques. NMR spectra were recorded on a Bruker AV 400 spectrometer at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR) and 162 MHz (^{31}P NMR). Chemical shifts were reported in ppm down field from internal Me_4Si and external 85% H_3PO_4, respectively. Data are presented in the following space: chemical shift, multiplicity, coupling constant in hertz (Hz), and signal area integration in natural numbers. IR spectra were recorded on Nicolet Magna 560 FTIR Spectrometer. High-resolution mass spectra were recorded on an IonSpec FT-ICR mass spectrometer with ESI or MALDI resource. GC analyses were performed using a Hewlett Packard Model HP 6890 Series.

Hydrogen gas (99.999%) was purchased from Boc Gas Inc., Tianjin. All the solvents used for reactions were distilled under argon after drying over an appropriate drying agent. All the reagents were used as received. $[Ir(COE)_2Cl]_2$[1], *t*-Bu-PNP(**1a**)[2], *i*-Pr-PNP(**1b**)[3], Cy-PNP(**1c**)[4], Ph-PNP(**1d**)[5], PNN(**2a**)[6], NNN(**3a, 3b**)[7], PCP(**4**)[8], PONOP(**5**)[9], PPP(**7**)[10], (*t*-Bu-PNP)Ir$(H)_2$Cl(**8**)[11] were synthesized according to the literatures.

(A) Preparation and Analytical Data of Ligands 2b and 6

Synthesis of 2-(di-*tert*-butylphosphinomethyl)-6-(di-*iso*-propylaminomethyl) pyridine(2b)



2-(di-*iso*-propylamminomethyl)-6-methylpyridine

To a dry 250 mL round-bottom flask were added 2,6-dimethylpyridine(7.4 g, 68.8 mmol), NBS(12.2 g, 68.8 mmol) and CCl_4 (120 mL). The mixture was refluxed and AIBN (2,2'-Azobisisobutyronitrile) (0.2 g, 1.21 mmol) was added in every hour. After refluxing 7 h, the reaction mixture was cooled to room temperature and filtered. The filtrate was concentrated under vacuum and the residue was purified by column chromatography (200-300 mesh silica gel, petroleum ether/ethyl acetate 20:1) to afford 2-bromomethyl-6-methylpyridine (8.8 g, 68%) as a pink-red oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (t, *J* = 7.7 Hz, 1H), 7.25 (d, *J* = 7.7 Hz, 1H), 7.07 (d, *J* = 7.8 Hz, 1H), 4.52 (s, 2H), 2.56 (s, 3H).

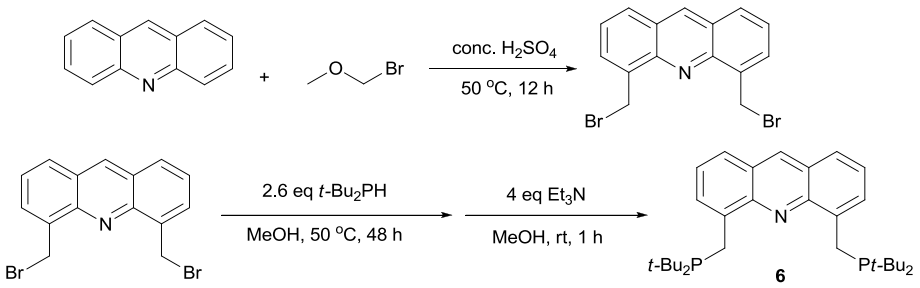
To a dry 250 mL round-bottom flask were added 2-bromomethyl-6-methyl-pyridine (8.3 g, 44.6 mmol), diisopropylamine (62 mL, 446 mmol) and THF (100 mL). The mixture was refluxed for 24 h and the solvent was removed under vacuum. The residue was dissolved in diethyl ether (250 mL) and washed with 10% aqueous KOH solution (2 × 50 mL). The ethereal solution was dried over anhydrous Na_2SO_4 and concentrated under vacuum. The residue was distilled under vacuum, yielding 2-(di-*iso*-propylamminomethyl)-6-methylpyridine (5.7 g, 62%) as a colorless oil, b.p.: 58 ℃ (0.3 mmHg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (t, *J* = 7.5 Hz, 1H), 7.45 (d, *J* = 7.6 Hz, 1H), 6.94 (d, *J* = 7.3 Hz, 1H), 3.76 (s, 2H), 3.03 (septet, *J* = 6.6 Hz, 2H), 2.52 (s, 3H), 1.02 (d, *J* = 6.6 Hz, 12H).

Synthesis of 2-(di-*tert*-butylphosphinomethyl)-6-(di-*iso*-propylamminomethyl)-pyridine (PNN) (2b)

To an oven-dried, argon flushed, 50 mL Schlenk flask equipped with an magnetic bar and a rubber septum was placed 2-(di-*iso*-propylamminomethyl)-6-methylpyridine (0.5 g, 2.42 mmol)), TMEDA(0.3 g, 2.72 mmol) and dry ether (20 mL). The solution was cooled to −10 ℃ and *n*-BuLi (2.72 mmol) in hexane was added with a syringe during 30 min. After stirring for another 30 minutes at −10 ℃ and overnight at room temperature, the mixture was added dropwise into a solution of di-*tert*-butylchlorophosphine (0.9 g, 4.84 mmol) in dry ether (20 mL) at −90 ℃. The reaction mixture was slowly warmed up to room temperature and stirred overnight.

To this reaction mixture was added degassed water (15 mL) and the ether phase was separated under argon atmosphere. The aqueous phase was extracted with ether (2 × 10 mL). The combined ether solution was dried over anhydrous Na_2SO_4, filtered, and concentrated under vacuum. The residue was distilled under high vacuum (0.3 mmHg) to remove unreacted starting material, yielding PNN (0.6 g, 67%) as a pale-yellow oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 (t, *J* = 7.7 Hz, 1H), 7.32 (d, *J* = 7.6 Hz, 1H), 7.21 (d, *J* = 7.2 Hz, 1H), 3.66 (s, 2H), 3.01 – 2.91 (m, 4H), 1.06 (d, *J* = 11.0 Hz, 18H), 0.93 (d, *J* = 6.6 Hz, 12H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3 (s), 160.4 (d, *J* = 14.0 Hz), 136.3 (s), 121.4 (d, *J* = 10.3 Hz), 118.8 (s), 51.7 (s), 49.1 (s), 31.9 (d, *J* = 21.0 Hz), 31.7 (d, *J* = 23.4 Hz), 29.8 (d, *J* = 13.1 Hz), 20.9 (s). ^{31}P NMR (162 MHz, $CDCl_3$) δ 35.5 (s). HRMS (ESI) calcd for $C_{21}H_{40}N_2P^+$ ([M + H]$^+$):351.2924; Found: 351.2929.

Synthesis of 4,5-bis-(di-*tert*-butylphosphinomethyl)acridine(6)



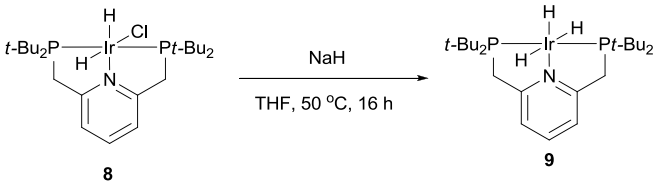
4,5-Bis(bromomethyl)acridine[12]

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.79 (s, 1H), 8.00 (d, *J* = 8.5 Hz, 2H), 7.94 (d, *J* = 6.7 Hz, 2H), 7.56 – 7.49 (m, 2H), 5.43 (s, 4H).

4,5-Bis-(di-*tert*-butylphosphinomethyl)acridine(6)

To an oven dried 100 mL Schlenk flask equipped with magnetic bar was added 4,5-bis(bromomethyl)acridine(1.0 g, 2.74 mmol), di-*tert*-butyl phosphine(1.1 g, 7.26 mmol)), and MeOH (20 mL). The flask was heated at 50 ℃ for 48 h with stirring. After cooling the reaction mixture, triethylamine (1.5 mL, 10.7 mmol) was added and the reaction mixture was stirred at room temperature for 1 h. The solvents were removed under reduced pressure. The residue was washed with ether (3 × 10 mL) and the ether solution was concentrated under reduced pressure to yield 4,5-bis-(di-*tert*-butylphosphinomethyl)acridine (**6**) (1.1 g, 80%) as a pale yellow solid. ^{1}H NMR (400 MHz, C_6D_6) δ 8.37 (s, 2H), 8.21 (s, 1H), 7.52 (d, *J* = 8.2 Hz, 2H), 7.32 (t, *J* = 7.5 Hz, 2H), 4.06 (s, 4H), 1.27 (d, *J* = 10.7 Hz, 36H). ^{13}C NMR (100 MHz, C_6D_6) δ 147.4 (d, *J* = 3.1 Hz), 141.5 (d, *J* = 13.4 Hz), 136.9 (s), 131.11 (d, *J* = 19.0 Hz), 125.8 (s), 125.8 (s), 32.2 (d, *J* = 23.7 Hz), 30.1(d, *J* = 13.8 Hz), 22.0 (d, *J* = 21.7 Hz). ^{31}P NMR (162 MHz, C_6D_6) δ 47.4 (s). HRMS (ESI) calcd for $C_{31}H_{48}NP_2^+$ ([M + H]$^+$):496.3256; Found: 496.3229.

(B) Preparation and Analytical Data of Catalyst 9



8 9

To a solution of **8** (125 mg, 200 μmol) in THF (6 mL), NaH (500 mg, 20 mmol) was added and the mixture was stirred at 50 °C for 16 h. The reaction mixture was filtered and the filtrate was concentrated in vacuo. Reprecipitation of the residue from THF/hexane gave a brown solid **9** (50 mg, 42 %). ^{1}H NMR (400 MHz, C_6D_6) δ 6.82 (t, *J* = 7.7 Hz, 1H), 6.50 (d, *J* = 7.7 Hz, 2H), 3.13 (s, 4H), 1.42 (t, *J* = 6.4 Hz, 36H), –10.12 (td, *J* = 15.3, 5.2 Hz, 2H), –19.78 (tt, *J* = 14.8, 4.8 Hz, 1H). ^{31}P NMR (162 MHz, C_6D_6) δ 88.0 (s). ^{1}H NMR (400 MHz, CD_2Cl_2) δ 7.36 (t, *J* = 7.6 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 2H), 3.41 (s, 4H), 1.32 (t, *J* = 6.4 Hz, 36H), –10.87 (td, *J* = 15.0, 5.0 Hz, 2H), –21.01 (tt, *J* = 14.0, 4.8 Hz, 1H). ^{13}C NMR (100 MHz, CD_2Cl_2) δ 163.5 (t, *J* = 3.6 Hz), 133.4 (s), 118.6 (t, *J* = 4.2 Hz), 42.8 (t, *J* = 9.9 Hz), 33.8 (t, *J* = 11.4 Hz), 29.8 (t, *J* = 2.9 Hz). ^{31}P NMR (162 MHz, CD_2Cl_2) δ 72.9 (s). HRMS (MALDI) calcd for $C_{23}H_{43}IrNP_2^+$ ($[M - 3H]^+$):588.2494; Found: 588.2489. IR (KBr, cm^{-1}) νIr–H 2107, 1754.

(C) General Procedure for Hydrogenation of LA to GVL

The catalyst was prepared in situ, S/C = 1000. $[Ir(COE)_2Cl]_2$(1.3 mg, 1.5 μmol), *t*-Bu-PNP (1.8 mg, 4.5 μmol) and degassed ethanol (2 mL) were added to a dry 10 mL Schlenk tube under argon atmosphere. The mixture was warmed up to 50 ℃ with stirring for 30 minutes gave a clear, reddish orange solution. The argon balloon was replaced with a hydrogen balloon and the reaction was stirred for 15 minutes to give the catalyst solution as a clear, colorless solution. This catalyst solution was transferred into a stainless autoclave equipped with a magnetic stirring bar under argon atmosphere. A degassed solution of LA (348 mg, 3 mmol), KOH (85% purity) (230 mg, 3.5 mmol) and ethanol (2 mL) was transferred into the autoclave by a syringe. The autoclave was tightened and flushed with hydrogen three times and was finally charged with hydrogen to 50 atm. The reaction mixture was magnetically stirred (1250 rpm) under hydrogen at 100 °C for 15 h. The autoclave was cooled to room temperature and the pressure was released. The reaction mixture was acidified to pH 3~4 and stirred for 20 minutes. After adding γ-butyrolactone (GBL) as a an internal standard, an aliquot portion of the mixture was taken and filtered through a short silica column and submitted to analysis of yield of GVL by GC (Agilent HP-5, 30 m × 0.32 mm × 0.25 μm) using a flame ionization detector (FID) operating at 250 ℃. Injector temperature was set at 230 °C. The carrier gas was nitrogen with a flow rate of 1.0 mL/min. The following temperature program was used in the analysis: 80 ℃ (8 min) – 10 ℃/min – 250 ℃ (10 min).

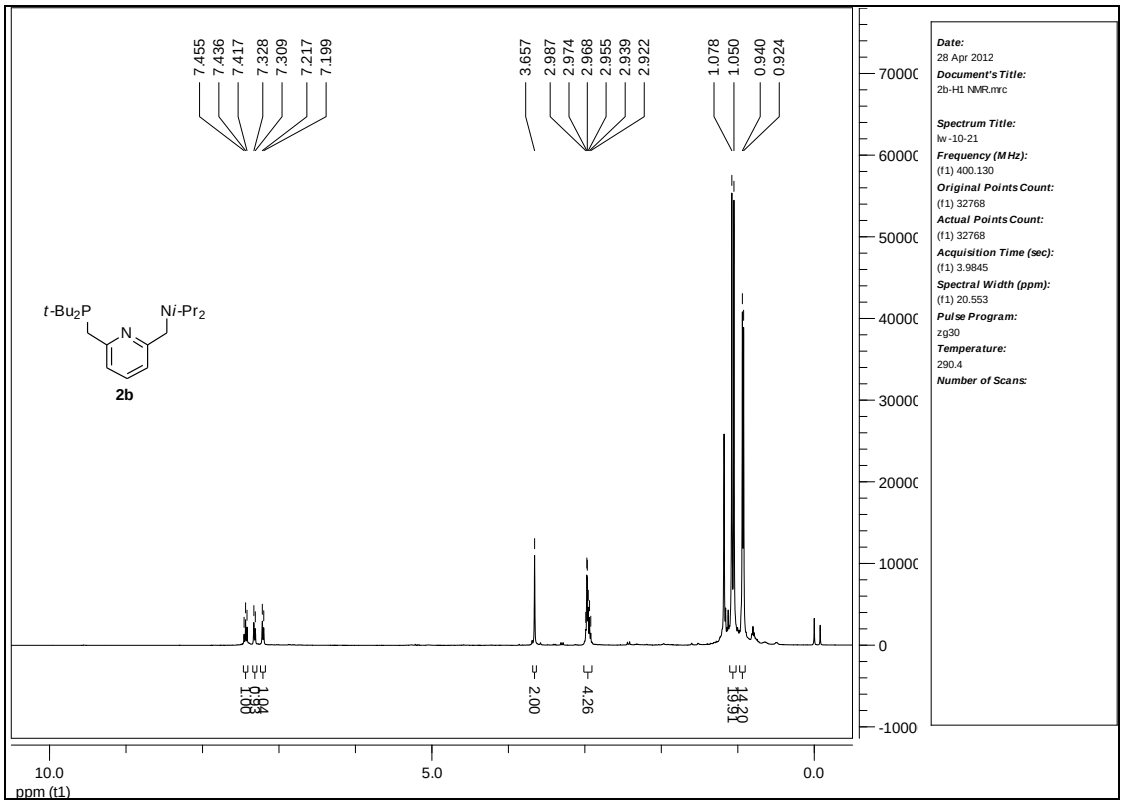
(*t*-Bu-PNP)IrH$_3$ (9), S/C = 100,000. The catalyst (*t*-Bu-PNP)IrH$_3$ (**9**) (1.7 mg, 3

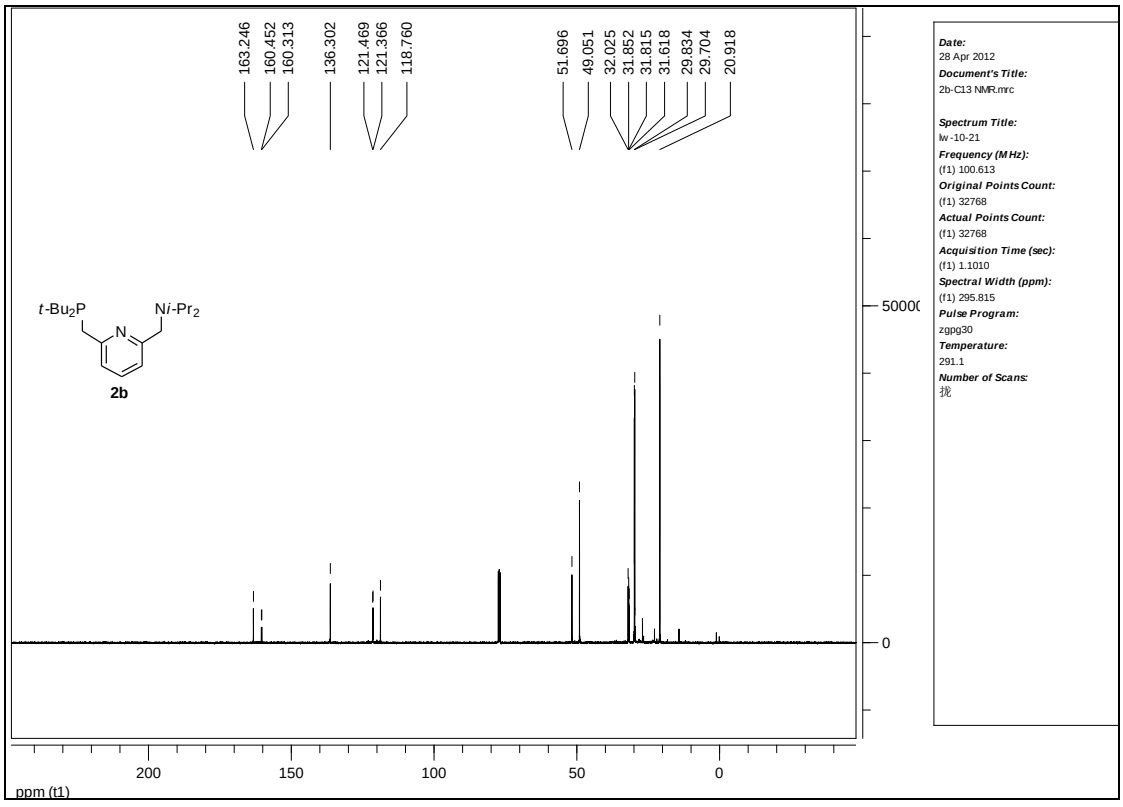
μmol) was dissolved in 3 mL degassed ethanol. One mL of the solution was transferred into a stainless autoclave equipped with a magnetic stirring bar under argon atmosphere. A degassed solution of LA (11.0 g, 94.7 mmol), KOH (85% purity) (9.0 g, 136.6 mmol) and ethanol (35 mL) was transferred into the autoclave by a syringe. The autoclave was tightened and flushed with hydrogen three times and was finally charged with hydrogen to 100 atm. The reaction mixture was magnetically stirred (1250 rpm) under hydrogen at 100 ^{o}C for 48 h. The autoclave was cooled to room temperature and the pressure was released. The reaction mixture was acidified to pH 3~4 and stirred for one hour. Then γ-butyrolactone (GBL) was added as a an internal standard and an aliquot of the mixture was filtered through a short silica column and submitted to the analyse of the yield of GVL by GC.

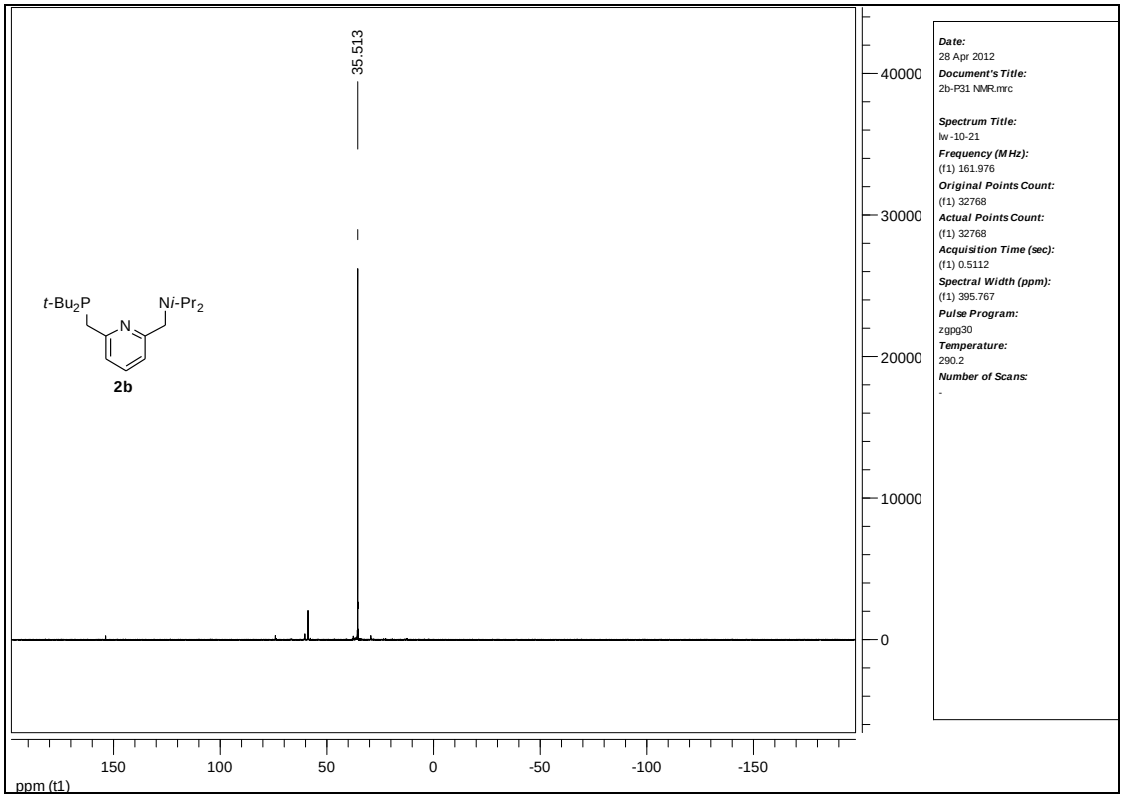
References

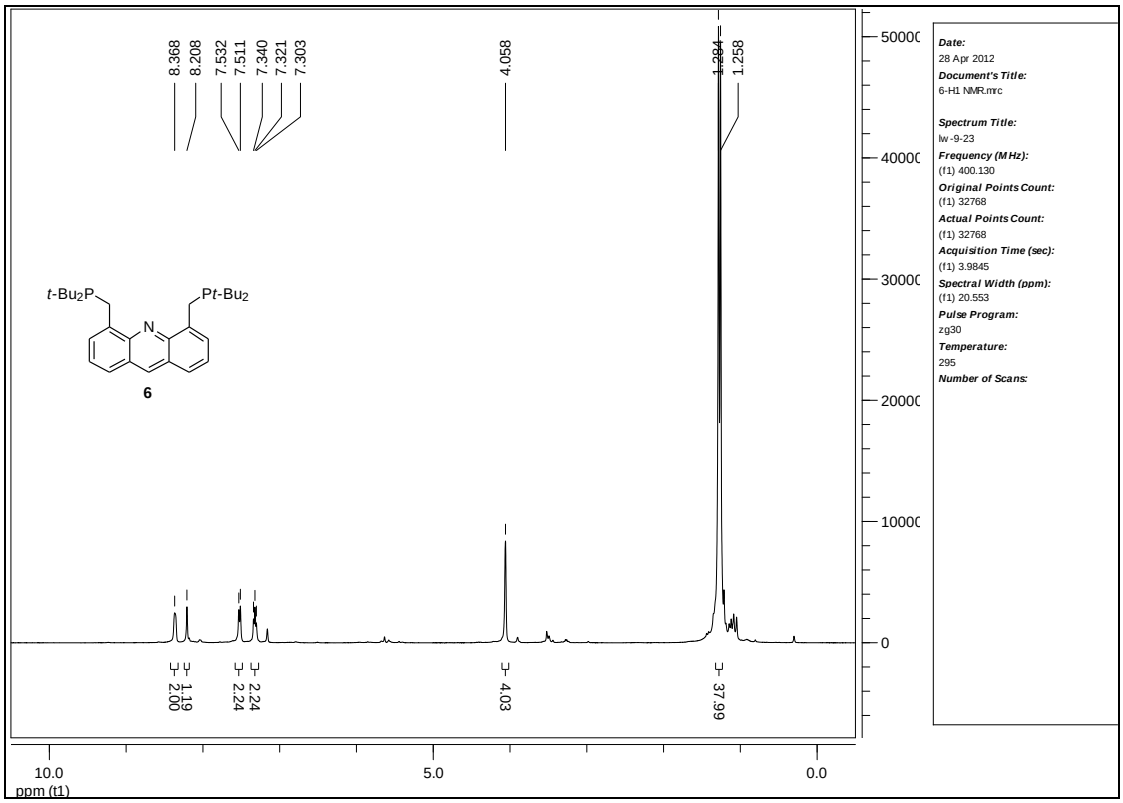
1 J. L. Herde, J. C. Lambert and C. V. Senoff, *Inorg. Synth.*, 1974, **15**, 18-20.
2 D. Hermann, M. Gandelman, H. Rozenberg, L. J. W. Shimon and D. Milstein, *Organometallics*, 2002, **21**, 812-818.
3 W. P. Leung, Q. W. Y. Ip, S. Y.Wong and T. C.W. Mak, *Organometallics*, 2003, ***22***, 4604-4609.
4 H. Katayama, C. Wada, K. Taniguchi and F. Ozawa, *Organometallics*, 2002, **21**, 3285-3291.
5 N. Rahmouni, J. A. Osborn, A. De Cian, J. Fischer and A. Ezzamarty, *Organometallics*, 1998, **17**, 2470-2476.
6 J. Zhang, G. Leitus, Y. Ben-David and D. Milstein, *J. Am. Chem. Soc.*, 2005, **127**, 10840-10841.
7 A. N. Vedernikov, P. Wu, J. C. Huffman and K. G. Caulton, *Inorg. Chim. Acta.*, 2002, **330**, 103-110.
8 D. G. Gusev, M. Madott, F. M. Dolgushin, K. A. Lyssenko and M. Y. Antipin, *Organometallics*, 2000, **19**, 1734-1739.
9 W. H. Bernskoetter, S. K. Hanson, S. K. Buzak, Z. Davis, P. S. White, R. Swartz, K. I. Goldberg and M. Brookhart, *J. Am. Chem. Soc.*, 2009, **131**, 8603-8613.
10 W. Hewertson and H. R. Watson, *J. Chem. Soc.*, 1962, **12**, 1490-1494.
11 R. Tanaka, M. Yamashita and K. Nozaki, *J. Am. Chem. Soc.*, 2009, **131**, 14168-14169.
12 J. Chiron and J. P. Galy, *Synlett*, 2003, **15**, 2349-2350.

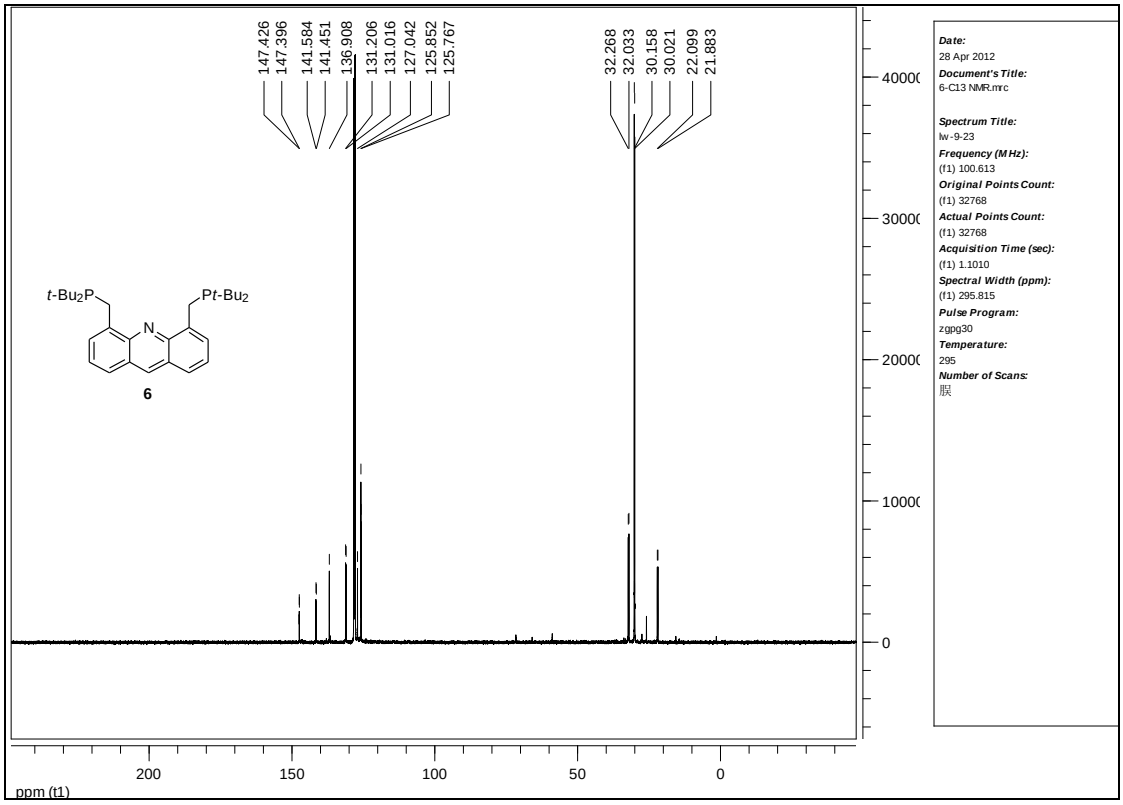
(D) ^{1}H, ^{13}C and ^{31}P NMR Spectra

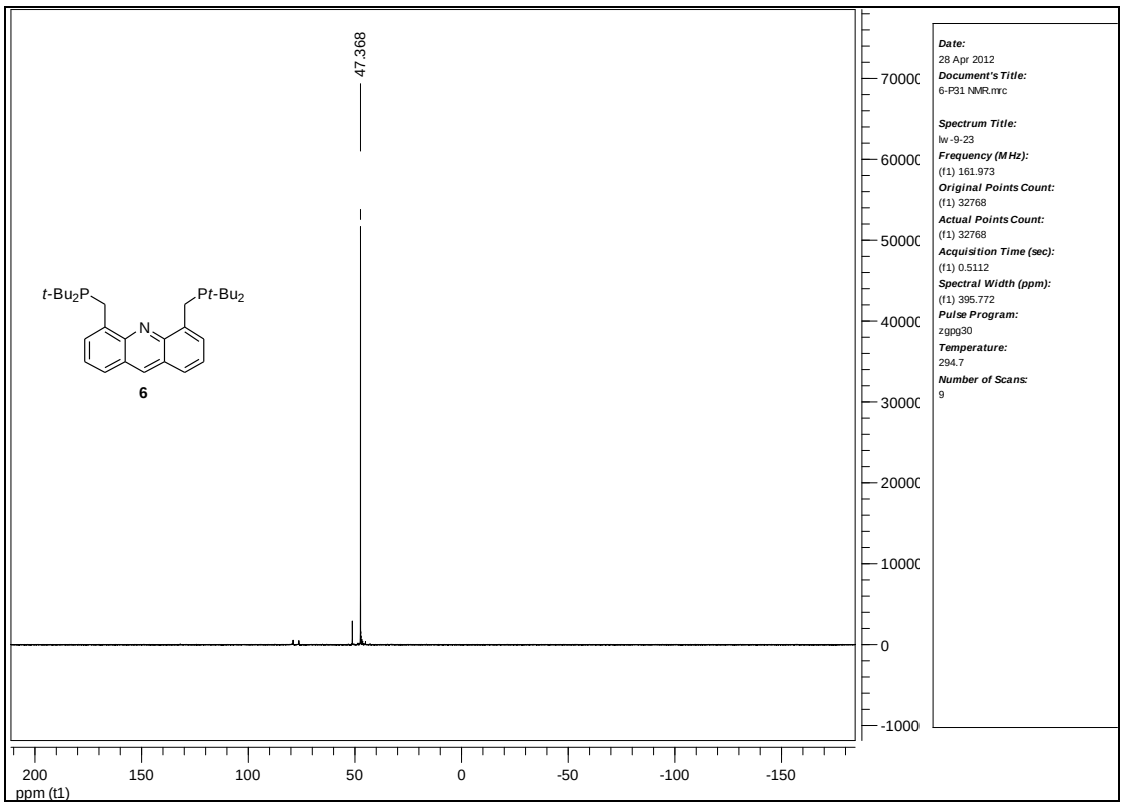


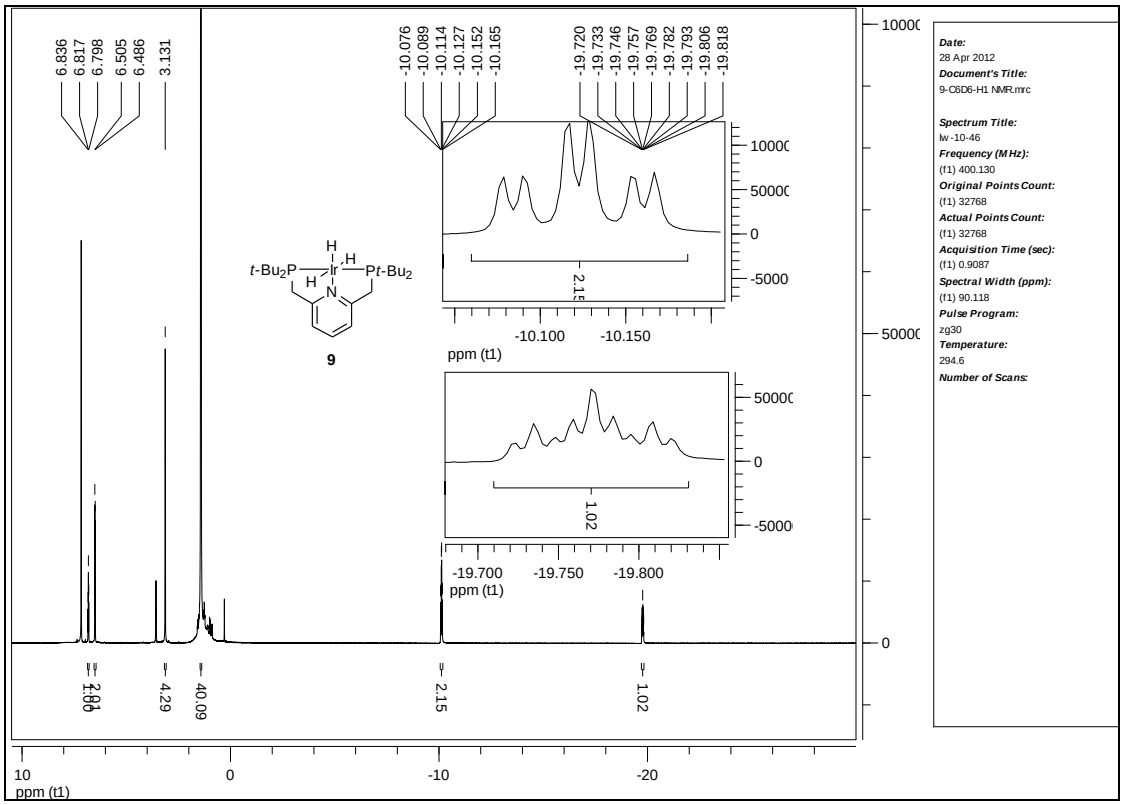


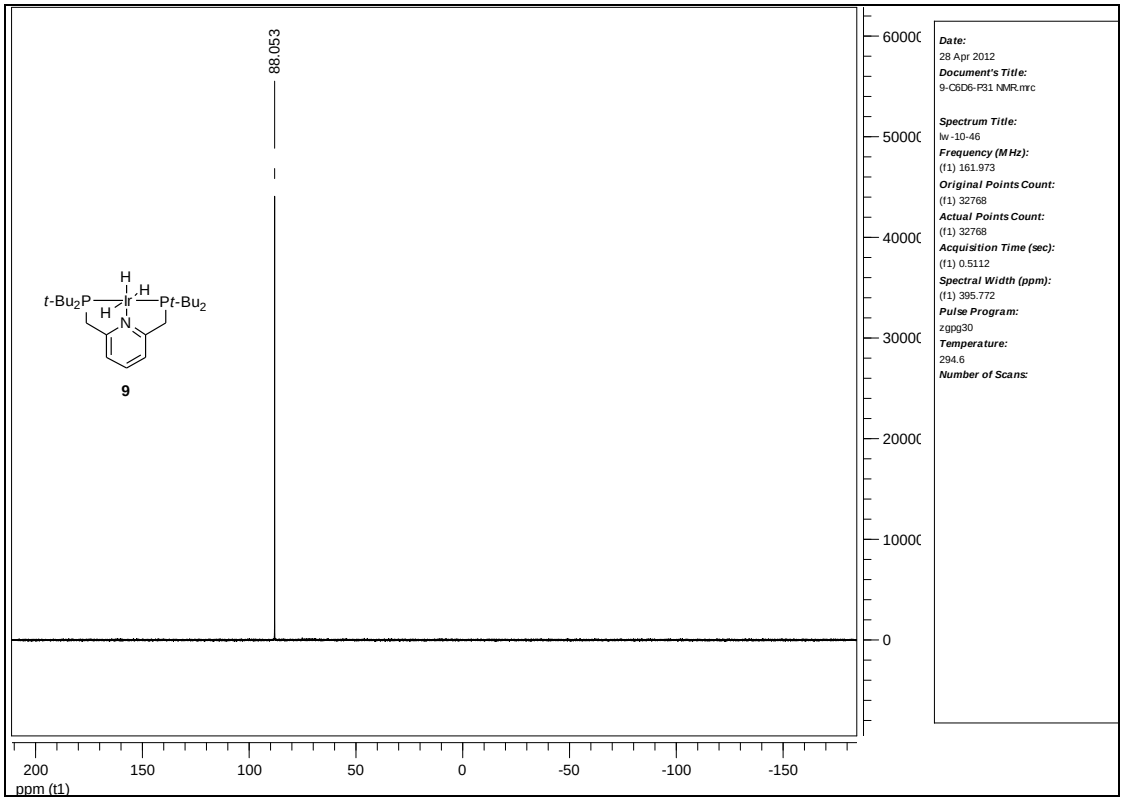

35.513
t-Bu2P
Ni-Pr2
N
2b
40000
30000
20000
10000
0
150
100
50
0
-50
-100
-150
ppm (t1)
Date:
28 Apr 2012
Document's Title:
2b-P31 NMR.mrc
Spectrum Title:
lw -10-21
Frequency (MHz):
(f1) 161.976
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 0.5112
Spectral Width (ppm):
(f1) 395.767
Pulse Program:
zgpg30
Temperature:
290.2
Number of Scans:
-

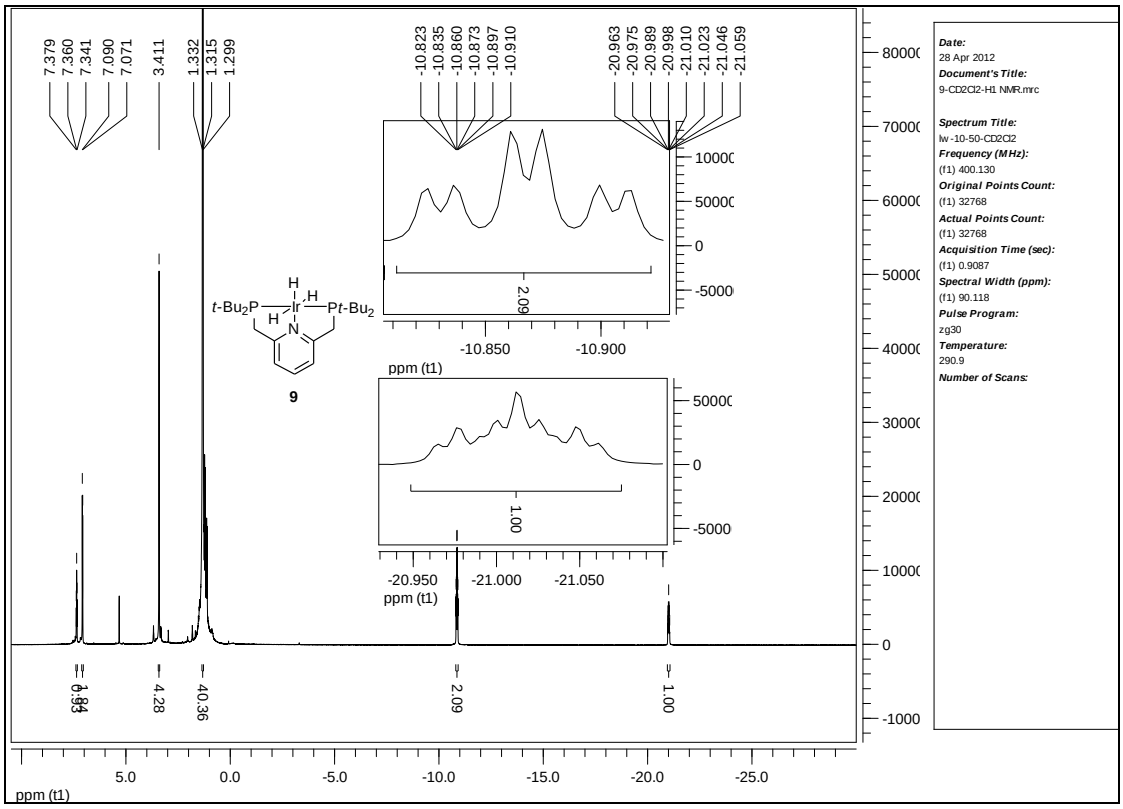

8.368
8.208
7.532
7.511
7.340
7.321
7.303
4.058
1.284
1.258
t-Bu2P
Pt-Bu2
N
6
1.19
2.00
2.24
2.24
4.03
37.99
50000
40000
30000
20000
10000
0
10.0
5.0
0.0
ppm (t1)
Date:
28 Apr 2012
Document's Title:
6-H1 NMR.mrc
Spectrum Title:
lw -9-23
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 3.9845
Spectral Width (ppm):
(f1) 20.553
Pulse Program:
zg30
Temperature:
295
Number of Scans:

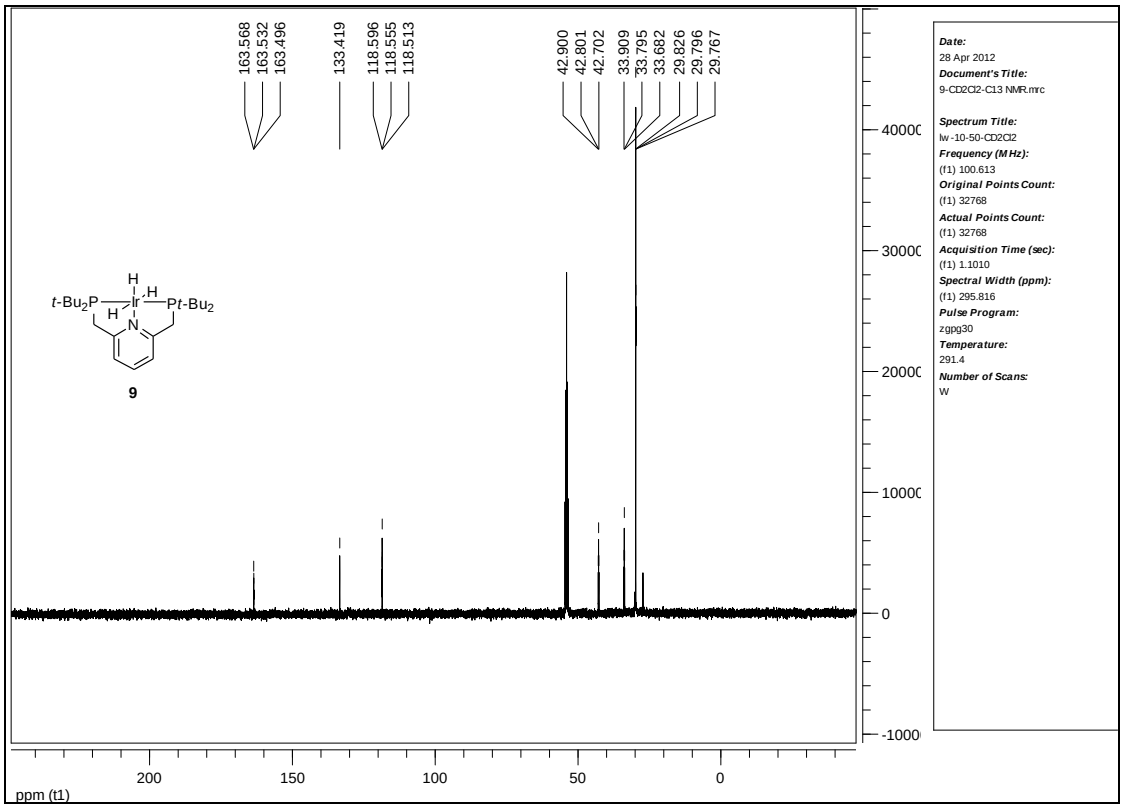

147.426
147.396
141.584
141.451
136.908
131.206
131.016
127.042
125.852
125.767
32.268
32.033
30.158
30.021
22.099
21.883
t-Bu2P
Pt-Bu2
N
6
4000
3000
2000
1000
0
200
150
100
50
0
ppm (t1)
Date:
28 Apr 2012
Document's Title:
6-C13 NMR.mrc
Spectrum Title:
lw-9-23
Frequency (MHz):
(f1) 100.613
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.1010
Spectral Width (ppm):
(f1) 295.815
Pulse Program:
zgpg30
Temperature:
295
Number of Scans:
膜

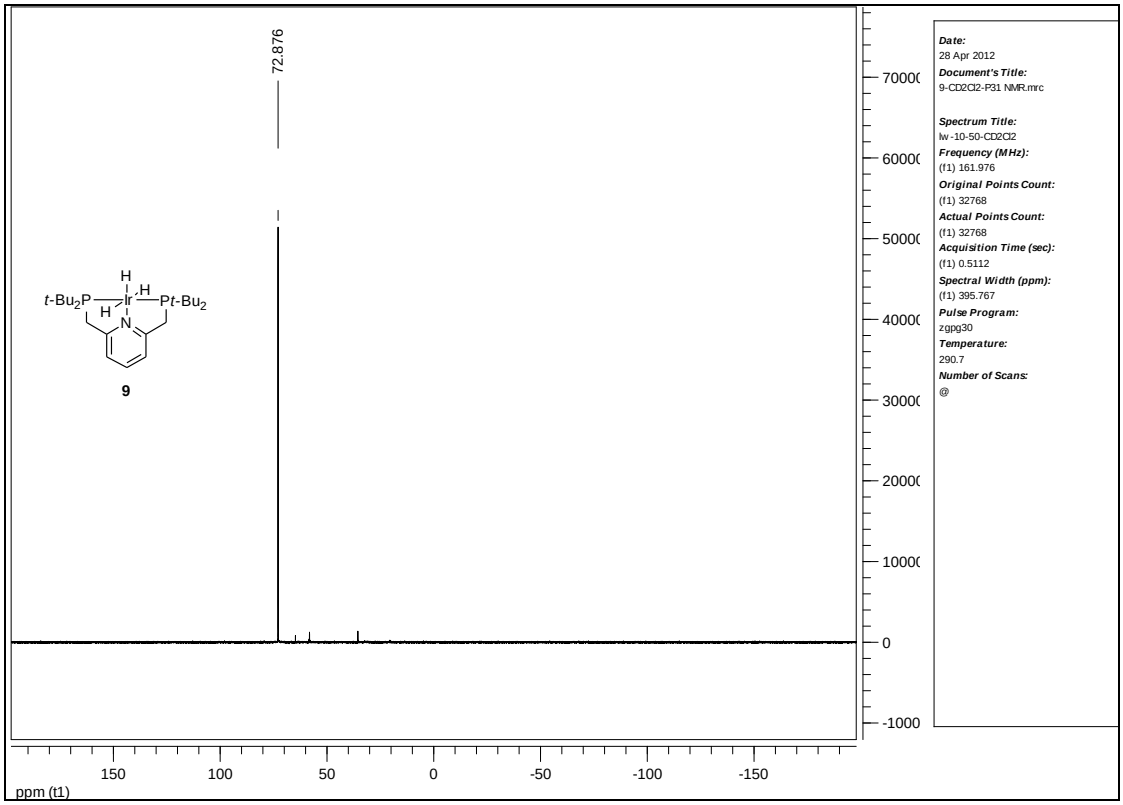

47.368
t-Bu2P
Pt-Bu2
N
6
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
150
100
50
0
-50
-100
-150
ppm (t1)
Date:
28 Apr 2012
Document's Title:
6-P31 NMR.mrc
Spectrum Title:
lw-9-23
Frequency (MHz):
(f1) 161.973
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 0.5112
Spectral Width (ppm):
(f1) 395.772
Pulse Program:
zgpg30
Temperature:
294.7
Number of Scans:
9


6.836
6.817
6.798
6.505
6.486
3.131
-10.076
-10.089
-10.114
-10.127
-10.152
-10.165
-19.720
-19.733
-19.746
-19.757
-19.769
-19.782
-19.793
-19.806
-19.818
t-Bu2P
Ir
Pt-Bu2
H
N
9
ppm (t1)
-10.100
-10.150
-19.700
-19.750
-19.800
2.15
1.02
2.01
1.00
4.29
40.09
10
0
-10
-20
Date:
28 Apr 2012
Document's Title:
9-C6D6-H1 NMR.mrc
Spectrum Title:
lw-10-46
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 0.9087
Spectral Width (ppm):
(f1) 90.118
Pulse Program:
zg30
Temperature:
294.6
Number of Scans:


88.53
t-Bu2P
Ir
Pt-Bu2
H
N
9
200
150
100
50
0
-50
-100
-150
ppm (t1)
Date:
28 Apr 2012
Document's Title:
9-C6D6-P31 NMR.mrc
Spectrum Title:
lw-10-46
Frequency (MHz):
(f1) 161.973
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 0.5112
Spectral Width (ppm):
(f1) 395.772
Pulse Program:
zgpg30
Temperature:
294.6
Number of Scans:


7.379
7.360
7.341
7.090
7.071
3.411
1.332
1.315
1.299
-10.823
-10.835
-10.860
-10.873
-10.897
-10.910
-20.963
-20.975
-20.989
-20.998
-21.010
-21.023
-21.046
-21.059
t-Bu2P
Ir
H
Pt-Bu2
N
9
2.09
1.00
-10.850
-10.900
-20.950
-21.000
-21.050
ppm (t1)
1.84
4.28
4.36
2.09
1.00
5.0
0.0
-5.0
-10.0
-15.0
-20.0
-25.0
Date:
28 Apr 2012
Document's Title:
9-CD2Cl2-H1 NMR.mrc
Spectrum Title:
lw -10-50-CD2Cl2
Frequency (MHz):
(f1) 400.130
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 0.9087
Spectral Width (ppm):
(f1) 90.118
Pulse Program:
zg30
Temperature:
290.9
Number of Scans:


163.568
163.532
163.496
133.419
118.596
118.555
118.513
42.900
42.801
42.702
33.909
33.795
33.682
29.826
29.796
29.767
t-Bu2P
Ir
H
Pt-Bu2
N
9
200
150
100
50
0
ppm (t1)
Date:
28 Apr 2012
Document's Title:
9-CD2Cl2-C13 NMR.mrc
Spectrum Title:
lw -10-50-CD2Cl2
Frequency (MHz):
(f1) 100.613
Original Points Count:
(f1) 32768
Actual Points Count:
(f1) 32768
Acquisition Time (sec):
(f1) 1.1010
Spectral Width (ppm):
(f1) 295.816
Pulse Program:
zgpg30
Temperature:
291.4
Number of Scans:
W



(E) Representative chromatogram of GVL derived from LA

Sample Info : HP-5, 230/80(8)-10-250(10)/250 , N2=1.0 mL/min