Supporting information

Room Temperature and Solvent-Free Iridium-Catalyzed Selective Alkylation of Anilines with Alcohols

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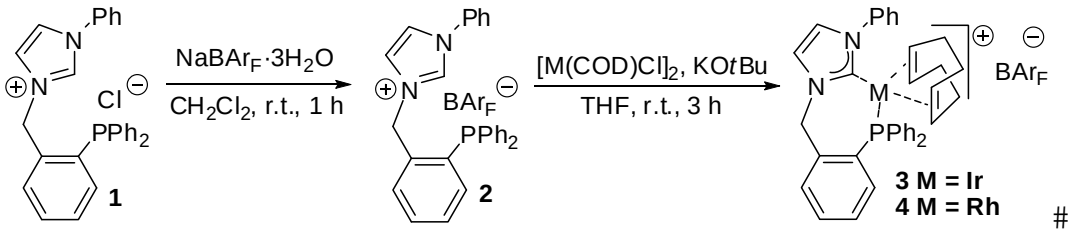
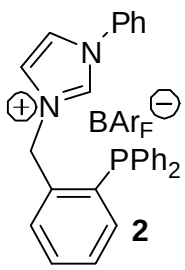
General methods

All reactions were conducted under dry Argon atmosphere using magnetic stirring.
DCM was freshly distilled from CaH_2 under nitrogen. Diglyme was freshly distilled from $LiAlH_4$ under reduced pressure. Toluene, DIPE, THF, DME, and dioxane were freshly distilled from sodium-benzophenone under nitrogen.
KO*t*Bu was bought from Sigma-Aldrich as sublimed grade, 99.99% trace metals basis. The 3-(2-aminophenyl)propanol was synthesized according to the literature.[1] The 1-Naphthylmethanol and 2-naphthylmethanol were prepared by reduction of the corresponding acid by $LiAlH_4$. Dapsone was bought from Sigma-Aldrich and used as received.
Except reagents mentioned above, all commercial reagents (amines and alcohols) were purified by vacuum distillation before using.
Chromatographic separations were performed on Kiesel gel 60 H silica gel (particle size: 0.063-0.100 mm). Thin layer chromatography (TLC) was performed on aluminum plates coated with Kieselgel 60 (0.20 mm, UV254) and visualized under ultraviolet light (ν = 254 nm), or by staining with ethanolic nihydrin (2,2-dihydroxyindane-1,3-dione) and heating.
^{1}H NMR spectra were recorded at 500 MHz in $CDCl_3$ and referenced internally to the residual $CHCl_3$ peak (7.26 ppm). ^{13}C NMR spectra were recorded at 75 MHz in $CDCl_3$ and referenced to the central peak of $CDCl_3$ (77.0 ppm). ^{31}P NMR spectra were spectra were recorded at 121 MHz in $CDCl_3$ and referenced to external H_3PO_4. Chemical shifts are reported in ppm (δ scale). Coupling constants, *J*, are reported in Hertz.
IR spectra were measured using a Perkin Elmer FT-IR apparatus
High resolution mass spectrometric (HRMS) data were obtained using a Bruker microTOF-Q II instrument operating at ambient temperatures, using a sample concentration of approximately 1 ppm.

The synthesis of Ir and Rh complexes



Imidazolium salt **1** (3 mmol) was dissolved in DCM (15 mL). $NaBAr_F \cdot 3H_2O$ (3.3 mmol) was added in one portion and the solution was stirred at r.t. for 1h. After the reaction was completed by TLC, the solution was dried under vacuum and the residual was purified by flash chromatographic on silica gel with CH_2Cl_2 as the eluent to afford BAr_F salt **2** as clear oil.

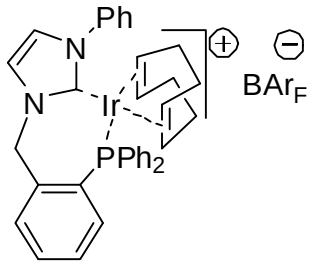


Clear oil, (yield = 83 %), (R_f = 0.40 (tailing), in DCM).
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.97 (s, 1H), 7.73-7.68 (m, 8H), 7.57-7.38 (m, 11H), 7.36-7-04 (m, 12H), 7.01-6.98 (m, 1H), 6.96-6.90 (m, 2H), 5.61 (s, 1H).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 161.6 (q, *J* = 49.8), 137.6 (d, *J* = 15.5), 136.0, 134.0-134.5 (br), 134.3, 133.5, 133.3, 133.0, 132.4-132.2 (m), 131.6 (d, J =11.9), 131.3, (d, *J* = 3.8), 130.8, 130.7, 130.0, 129.8, 129.6-129.4 (m), 129.1, 128.8-128.2 (m), 126.3, 122.8, 122.7, 121.7, 121.6, 119.1, 117.7-117.3 (m), 53.7 (d, *J* = 21.6).

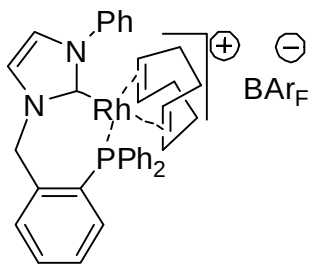
^{31}P NMR ($CDCl_3$, 121 MHz): δ -17.6.
IR (neat, cm^{-1}): 1353, 1272, 1112, 886, 681.
HRMS (ESI) m/z = 419.1820, calcd for $C_{28}H_{24}N_2P$ [M- BAr_F]$^+$ = 419.1672.

BAr_F salt **2** (3 mmol) was co-evaporated with dry toluene (3 × 20 mL) and dissolved in dry THF (30 mL) under Ar. $[M(COD)Cl]_2$ (M = Ir or Rh)(1.5 mmol) and KO*t*Bu (3.15 mmol) were added. The atmosphere in the flask was evacuated and replenished with Ar three times. The mixture was stirred at r.t. for 3h. After the reaction was completed by TLC, the solution was dried under vacuum and the residual was purified by flash chromatographic on silica gel with CH_2Cl_2 : pentane (2 : 1) as the eluent to afford iridium complex **3** as red solid or rhodium complex **4** as yellow solid.

CCDC 902840 (iridium complex **3**) and 902841 (rhodium complex **4**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif

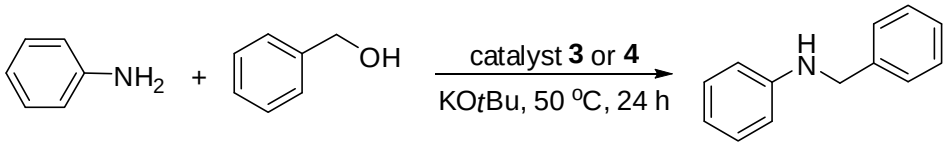


Red solid, (yield = 84%), (R_f = 0.50 (tailing), in DCM/pentane 3/1).
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.83-7.71 (m, 8H), 7.59-7.38 (m, 15H), 7.36-7.23 (m, 5H), 7.22-7.15 (m, 3H), 7.09-6.99 (m, 3H), 6.73-6.64 (m, 2H), 4.99-4.87 (m, 1H), 4.82-4.70 (m, 1H), 4.27-4.16 (m, 1H), 3.95-3.84 (m, 1H), 3.49-3.29 (m, 1H), 2.37-1.97 (m, 5H), 1.73-1.34 (m, 3H).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 169.2 (q, *J* = 10.5), 161.7, 141.0, 140.8, 139.2, 137.7, 134.8 (br), 132.3, 132.2, 132.0, 131.9, 131.8, 131.2-131.0 (m), 130.7, 130.2-129.9 (m), 129.7-129.4 (m), 129.2-129.0 (m), 128.9-128.6 (m), 128.4-128.2 (m), 128.1, 126.3, 124.0, 123.5, 122.7, 120.6, 119.1, 117.9-117.2 (m), 89.3 (d, *J* = 10.0), 85.5 (d, *J* = 13.3), 79.6, 79.2, 55.5 (d, *J* = 7.5), 34.5, 33.9, 33.8, 28.2, 27.9.
^{31}P NMR ($CDCl_3$, 121 MHz): δ 6.1.
IR (neat, cm^{-1}): 1353, 1273, 1118, 885, 681.
HRMS (ESI) m/z = 719.2333, calcd for $C_{36}H_{35}IrN_2P$ [M- BAr_F]$^+$ = 719.2167.



Yellow solid, (yield = 86%), (R_f = 0.50 (tailing), in DCM/pentane 3/1).
^{1}H NMR ($CDCl_3$, 500 MHz): δ 7.79-7.69 (m, 8H), 7.54-7.27 (m, 18H), 7.27-7.18 (m, 5H), 7.09-7.04 (m, 1H), 7.02-6.95 (m, 2H), 6.81-6.76 (m, 2H), 5.07-4.94 (m, 2H), 4.55-4.45 (m, 1H), 4.41-4.32 (m, 1H), 3.83-3.67 (m, 1H), 2.59-2.28 (m, 5H), 2.18-2.06 (m, 1H), 2.00-1.67 (m, 2H).
^{13}C NMR ($CDCl_3$, 75 MHz): δ 173.2 (dd, $J = 50.0_{Rh,C}, 15.9_{P,C}$), 161.7 (q, *J* = 50.5), 141.3, 141.1, 138.7, 137.9, 134.8 (br), 132.3 (d, J = 2.3), 132.1, 132.0, 131.8, 131.7, 131.6, 131.0, 130.8, 130.7 (d, *J* = 2.2), 130.2,130.0, 129.9, 129.8, 129.6-129.4 (m), 129.2-128.9 (m), 128.8, 128.7-128.6 (m), 128.4-128.2 (m), 124.0, 123.5, 122.7, 120.7, 119.1, 117.6-117.2 (m), 99.3 (m), 96.6 (m), 93.7 (d, *J* = 8.7), 92.0 (d, *J* = 7.9), 55.8 (d, *J* = 10.4), 33.3, 32.9 (d, *J* = 3.3), 30.9, 28.0, 27.4.
^{31}P NMR ($CDCl_3$, 121 MHz): δ 13.5 (d, *J* = 151.7).
IR (neat, cm^{-1}): 1353, 1273, 1117, 886, 681.
HRMS (ESI) m/z = 629.1772, calcd for $C_{36}H_{35}N_2PRh$ [M- BAr_F]$^+$ = 629.1593.

Table S1. N-Alkylation of aniline with benzyl alcohol under different conditions[a]



Entry	Catalyst	Catalyst loading (mol%)	Solvent	Solvent Volume (mL)	KO*t*Bu (mol%)	Conv[b] (%)
1	**3**	1.0	THF	1.0	100	77
2	**3**	1.0	DIPE[c]	1.0	100	82
3	**3**	1.0	dioxane	1.0	100	34
4	**3**	1.0	toluene	1.0	100	70
5	**4**	1.0	toluene	1.0	100	81
6	**3**	1.0	DME	1.0	100	99
7	**4**	1.0	DME	1.0	100	68
8	**3**	1.0	diglyme	1.0	100	99
9	**4**	0.5	Toluene	1.0	100	80
10	**4**	0.5	diglyme	1.0	100	92
11	**3**	0.5	DME	1.0	100	97
12	**3**	0.5	diglyme	1.0	100	99
13	**3**	0.5	diglyme	0.5	100	99
14	**3**	0.5	diglyme	0.25	100	99
15	**3**	0.5	diglyme	0.25	50	99
16	**3**	0.5	diglyme	0.25	40	78
17	**3**	0.5	diglyme	0.25	0	0

[a] Reaction conditions: 0.5 mmol aniline, 0.55 mmol benzyl alcohol, iridium catalyst **3** or rhodium **4**, KO*t*Bu, solvent, 50 °C, 24 h. [b] Conversion was calculated by ^{1}H NMR spectroscopy, based on unreacted aniline. [c] DIPE = diisopropyl ether.

General procedure for alkylation of amine with alcohols

Diglyme as solvent

Method A (When both aniline derivatives and alcohols are liquids)

A Microwave vial (5 mL, tapered style) with a magnetic stirring bar was charged with iridium catalyst **3** (0.5-1.5 mol%) and KO*t*Bu (0.25 mmol). Under an argon atmosphere, aniline (0.5 mmol) and benzyl alcohol (0.55 mmol) were dissolved in diglyme (0.25 mL) and the solution was added. Next, the vial was sealed with a speta (PTFE-faced silicone septa) and the mixture was stirred either 24 h at 50 °C or 48 h at room temperature. The reaction mixture was then quenched by addition of saturated aqueous NH_4Cl solution. The organic phase was extracted three times with 20 mL of chloroform. The combined organic phases were over $MgSO_4$. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

Method B (When either aniline derivatives or alcohols is solid)

A Microwave vial (5 mL, tapered style) with a magnetic stirring bar was charged with iridium catalyst **3** (0.5-1.5 mol%), KO*t*Bu (0.25 mmol) and the solid reagent . Under an argon atmosphere, the other liquid reagent was dissolved in diglyme (0.25 mL) and the solution was added. Next, the vial was sealed with a speta (PTFE-faced silicone septa) and the mixture was stirred either 24 h at 50 ^{o}C or 48 h at room temperature. The reaction mixture was then quenched by addition of saturated aqueous NH_4Cl solution. The organic phase was extracted three times with 20 mL of chloroform. The combined organic phases were over $MgSO_4$. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

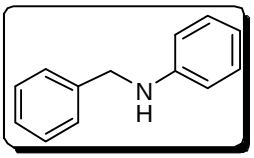
Solvent free condition

Method A (When both aniline derivatives and alcohols are liquid)

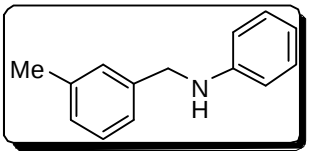
A Microwave vial (5 mL, tapered style) with a magnetic stirring bar was charged with iridium catalyst **3** (0.5-1.0 mol%) and KO*t*Bu (0.5 mmol). Under an argon atmosphere, aniline (1.0 mmol) was added followed by addition of benzyl alcohol (1.1 mmol). Next, the vial was sealed with a speta (PTFE-faced silicone septa) and the mixture was stirred either 24 h at 50 ^{o}C or 48 h at room temperature. The reaction mixture was then quenched by addition of saturated aqueous NH_4Cl solution. The organic phase was extracted three times with 20 mL of chloroform. The combined organic phases were over $MgSO_4$. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.

Method B (When either aniline derivatives or alcohols is solid)

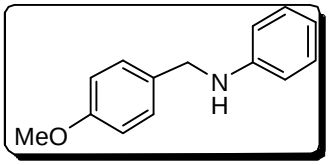
A Microwave vial (5 mL, tapered style) with a magnetic stirring bar was charged with iridium catalyst **3** (0.5-1.0 mol%), KO*t*Bu (0.5 mmol) and the solid reagent . Under an argon atmosphere, the other liquid reagent was added. Next, the vial was sealed with a speta (PTFE-faced silicone septa) and the mixture was stirred either 24 h at 50 ^{o}C or 48 h at room temperature. The reaction mixture was then quenched by addition of saturated aqueous NH_4Cl solution. The organic phase was extracted three times with 20 mL of chloroform. The combined organic phases were over $MgSO_4$. Solvent was evaporated under vacuum and the residue was further purified by column chromatography.



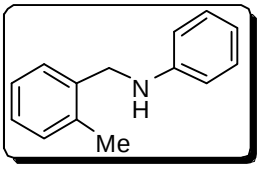
Spectral data match those previously reported.[2]



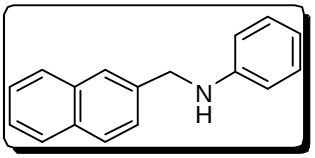
Spectral data match those previously reported.[3]



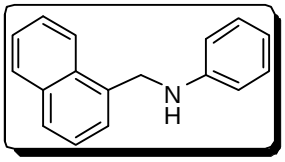
Spectral data match those previously reported.[4]



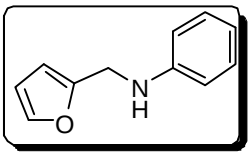
Spectral data match those previously reported.[5]



Spectral data match those previously reported.[6]



Spectral data match those previously reported.[7]



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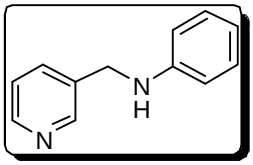
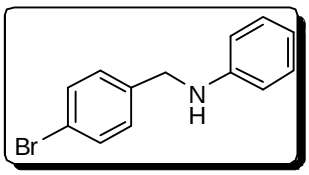


Spectral data match those previously reported.[8]



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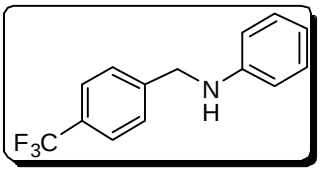

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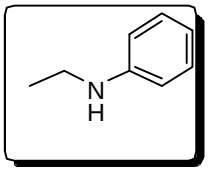
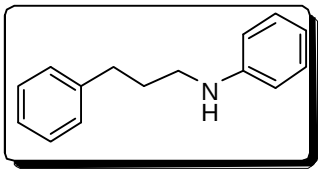


Spectral data match those previously reported.[9]



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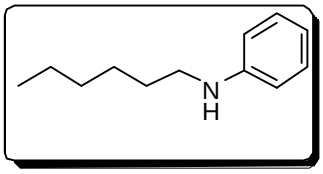
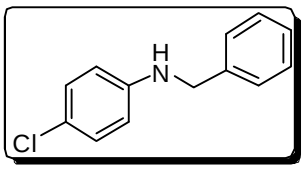


Spectral data match those previously reported.[6]



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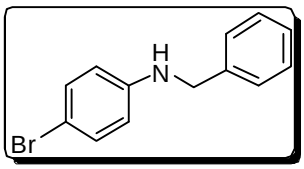

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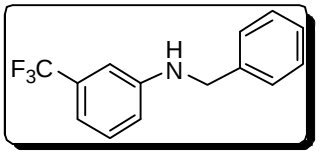
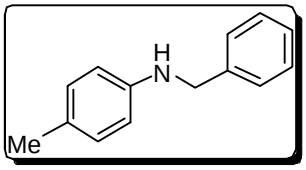


Spectral data match those previously reported.[11]



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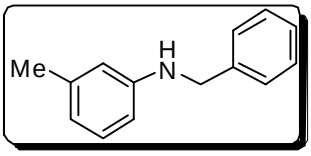

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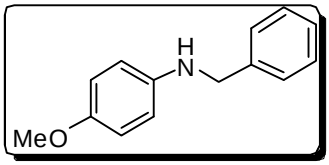

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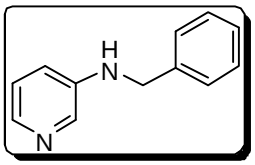

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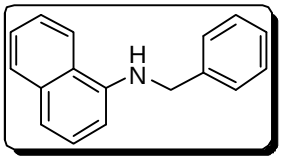

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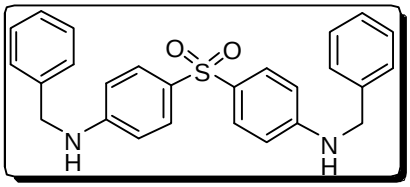

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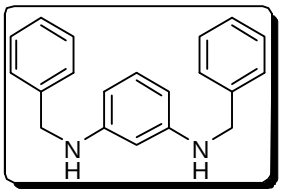
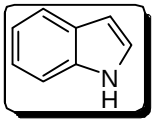
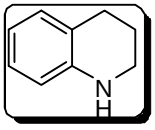


Spectral data match those previously reported.[13]

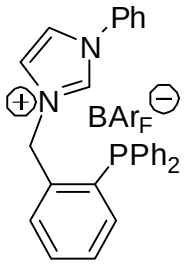


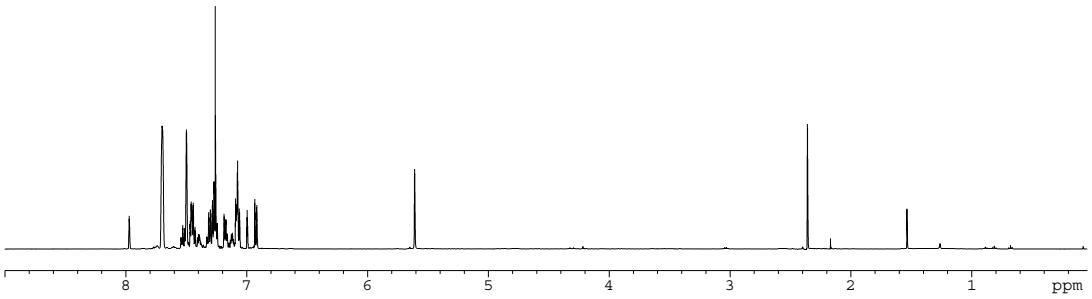
Spectral data match those previously reported.[14]

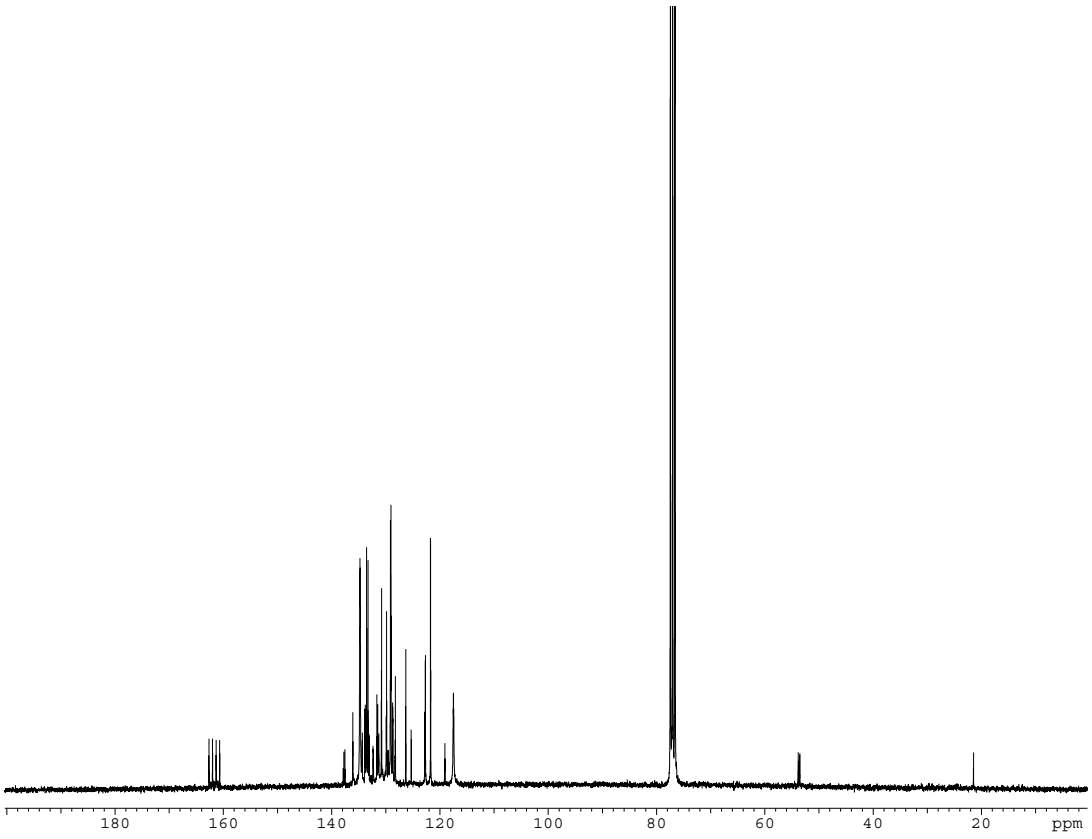


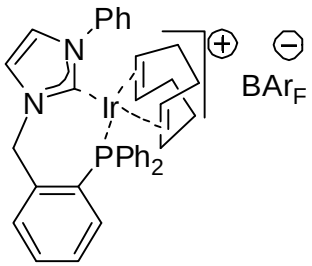
Spectral data match those previously reported.[14]

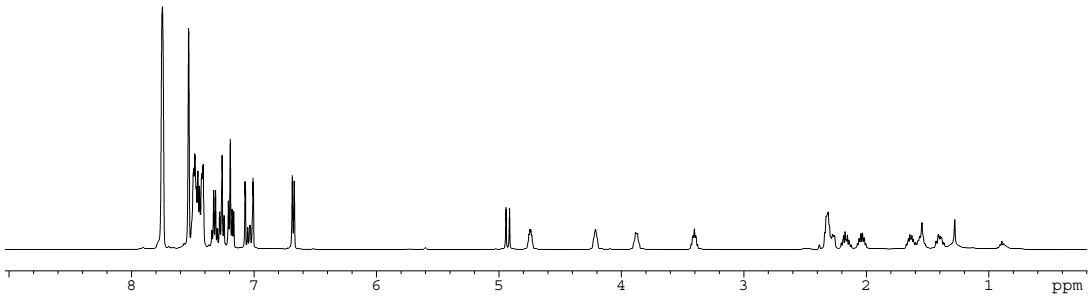
Spectra of new compounds

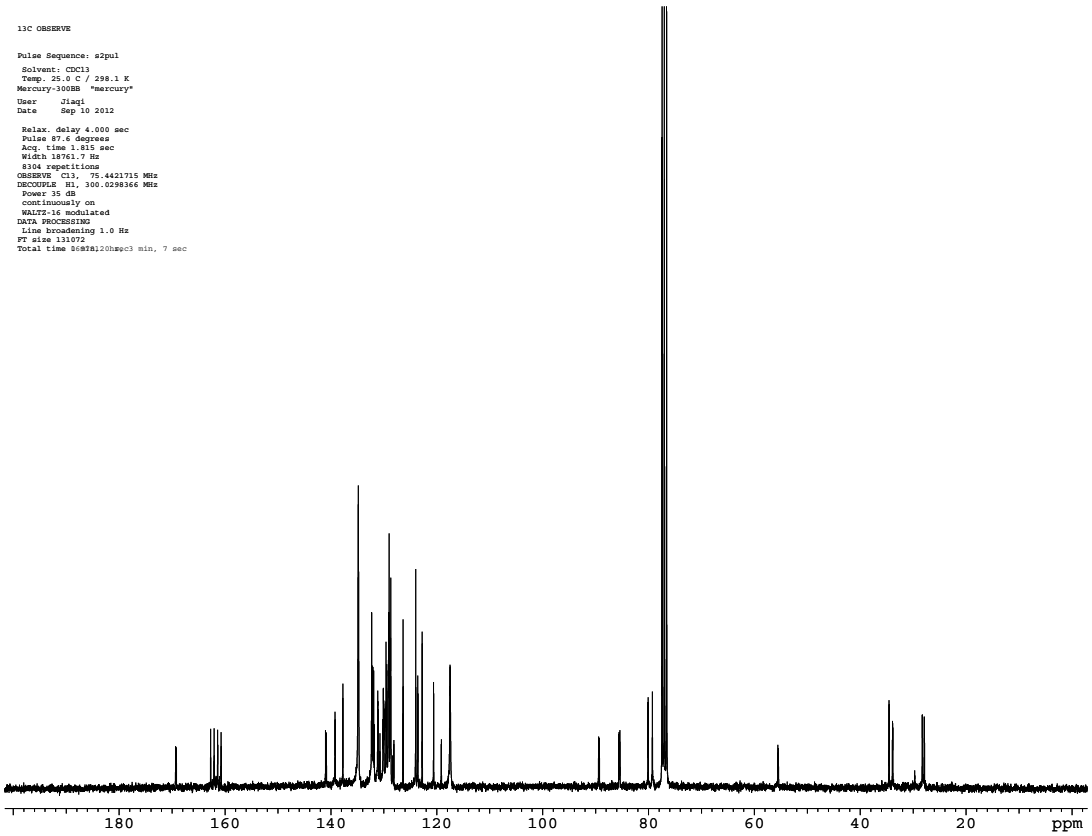


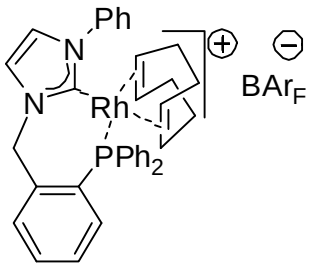


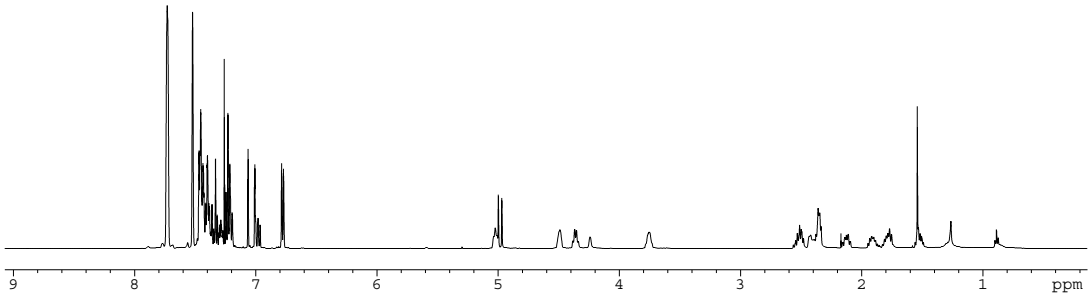


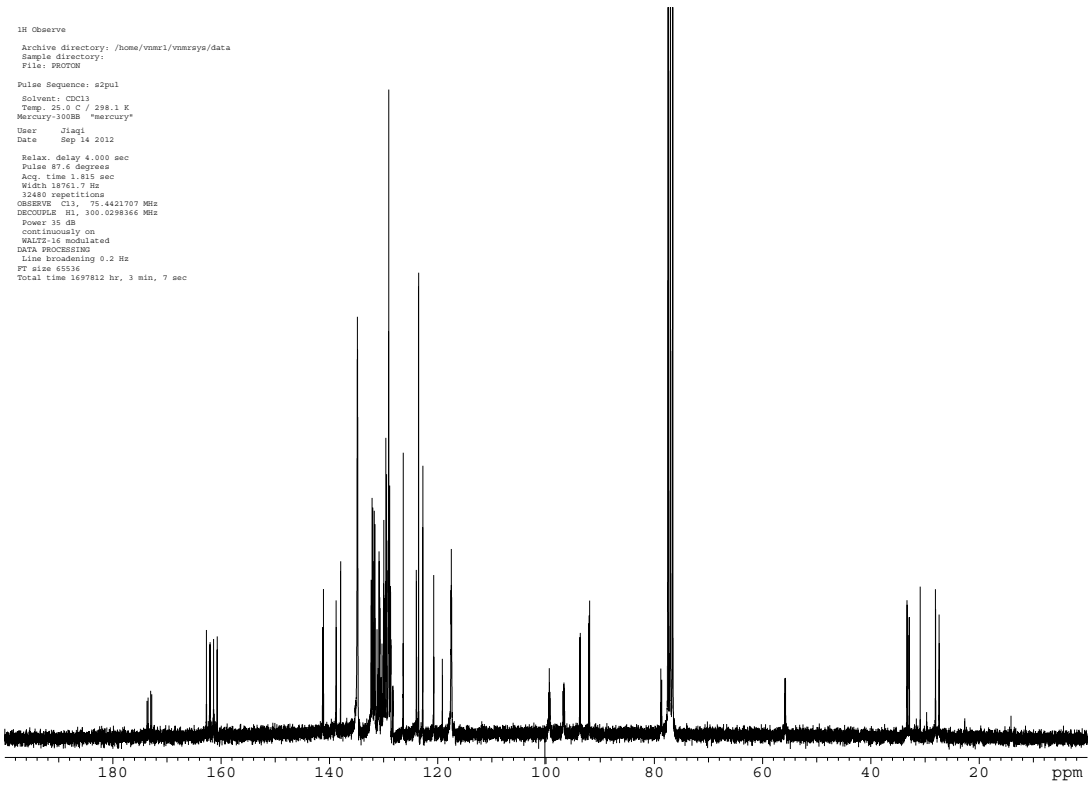

Ph
N
N
Ir
PPh2
BArF


8
7
6
5
4
3
2
1
ppm


13C OBSERVE
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BE "mercury"
User Jiaqi
Date Sep 10 2012
Relax. delay 4.000 sec
Pulse 87.6 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
8304 repetitions
OBSERVE C13, 75.4421715 MHz
DECOUPLE H1, 300.0298366 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 86878.120hrs3 min, 7 sec
180
160
140
120
100
80
60
40
20
ppm


Ph
N
N
Rh
PPh2
BArF


9
8
7
6
5
4
3
2
1
ppm


1H Observe
Archive directory: /home/vmmr1/vmmrsys/data
Sample directory:
File: PROTON
Pulse Sequence: s2pul
Solvent: CDCl3
Temp. 25.0 C / 298.1 K
Mercury-300BB "mercury"
User Jlaqi
Date Sep 14 2012
Relax. delay 4.000 sec
Pulse 87.6 degrees
Acq. time 1.815 sec
Width 18761.7 Hz
32480 repetitions
OBSERVE C13, 75.4421707 MHz
DECOUPLE H1, 300.0298366 MHz
Power 35 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1697812 hr, 3 min, 7 sec
180
160
140
120
100
80
60
40
20
ppm

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[14] ^{1}H NMR was available on the Sigma-Aldrich Library.