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Rapid Ketone Transfer Hydrogenation by Employing Simple, In Situ Prepared Iridium(I) Precatalysts Supported by "Non-N–H" P,N Ligands

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Abstract: The catalytic utility in ketone transfer hydrogenation (TH) of the preformed complexes $[Ir(cod)(\kappa^2\text{-}2\text{-}NMe_2\text{-}3\text{-}PiPr_2\text{-}indene)]^+X^-$ ($[\mathbf{2a}]^+X^-$; X: PF_6, BF_4, and OTf; cod: η^4-1,5-cyclooctadiene; OTf: trifluoromethanesulfonate), $[Ir(cod)(\kappa^2\text{-}1\text{-}PiPr_2\text{-}2\text{-}NMe_2\text{-}indene)]^+OTf^-$ ($[\mathbf{2b}]^+OTf^-$), $[Ir(cod)(\kappa^2\text{-}2\text{-}NMe_2\text{-}3\text{-}PiPr_2\text{-}indenide)]$ (**3**), and $[Ir(cod)(\kappa^2\text{-}o\text{-}tBu_2P\text{-}C_6H_4\text{-}NMe_2)]^+PF_6^-$ ($[\mathbf{4}]^+PF_6^-$), as well as of related mixtures prepared from $[\{IrCl(cod)\}_2]$ and various P,N-substituted indene or phenylene ligands, was examined. Whereas $[\mathbf{2a}]^+X^-$, $[\mathbf{2b}]^+OTf^-$, **3**, and related in situ prepared Ir catalysts derived from P,N-indenes proved to be generally effective in mediating the reduction of acetophenone to 1-phenylethanol in basic *i*PrOH at reflux (0.1 mol% Ir; 81–99% conversion) in a preliminary catalytic survey, the structurally related Ir catalysts prepared from $(o\text{-}R_2P\text{-}C_6H_4)NMe_2$ (R: Ph, *i*Pr, or *t*Bu) were observed to outperform the corresponding P,N-indene ligands under similar conditions. In the course of such studies, it was observed that alteration of the substituents at the donor fragments of the supporting P,N ligand had a pronounced influence on the catalytic performance of the derived catalysts, with ligands featuring bulky dialkylphosphino donors proving to be the most effective. Notably, the crystallographically characterized complex $[\mathbf{4}]^+PF_6^-$, either preformed or prepared in situ from a mixture of $[\{IrCl(cod)\}_2]$, $NaPF_6$, and $(o\text{-}tBu_2P\text{-}C_6H_4)NMe_2$, proved to be highly effective in mediating the catalytic transfer hydrogenation (TH) of ketones in basic *i*PrOH, with near quantitative conversions for a range of alkyl and/or aryl ketones and with very high turnover-frequency values (up to 230000 h^{-1} at >50% conversion); this thereby enabled the use of Ir loadings ranging from 0.1 to 0.004 mol%. Catalyst mixtures prepared from $[\{IrCl(cod)\}_2]$, $NaPF_6$, and the chiral (αS,αS)-1,1′-bis[α-(dimethylamino)benzyl]-(*R*,*R*)-2,2′-bis(dicyclohexylphosphino)-ferrocene (Cy-Mandyphos) ligand proved capable of mediating the asymmetric TH of aryl alkyl ketones, including that of the hindered substrate 2,2-dimethylpropiophenone with an efficiency (0.5 mol% Ir; 95% conversion, 95% *ee*) not documented previously in TH chemistry.

Keywords: asymmetric catalysis · homogeneous catalysis · iridium · ketones · transfer hydrogenation

Introduction

The catalytic transfer hydrogenation (TH) of ketones by employing *i*PrOH [Eq. (1)] or other H_2-donor solvents has emerged as a mild, convenient, environmentally friendly methodology for the synthesis of secondary alcohols that avoids the use of high H_2 pressures and stoichiometric reductants.[1] Among the numerous classes of metal complexes that have been shown to mediate the TH of ketones, precatalysts featuring an Ru–NH linkage are generally the most effective.[2] The high turnover frequency values (TOFs; in the very best cases, 10^6 h^{-1} at 50% conversion)[2c] and selectivities offered by such precatalysts are commonly attributed to the formation of $(H)Ru\text{–}NH_2R$ intermediates that can transfer H_2 to a ketone substrate in a bifunctional manner.[2–5] The catalytic utility in TH chemistry of Rh[6] and Ir[7] complexes that feature an M–NH functionality has also been demonstrated;[8] notably, Abdur-Rashid and coworkers[7a] have described the use of $IrH_3[(iPr_2P\text{-}C_2H_4)_2NH]$, which is among the most active of the previously reported Ir precatalysts for the TH of ketones in *i*PrOH, with a TOF of 43000 h^{-1} (at 50% conversion) for the reduction of acetophenone. Furthermore, the field of Rh- and Ir-mediated asymmetric ketone TH is dominated by precatalysts featuring an M–NH linkage, with chiral $[M(Cl)Cp^*(TsN\text{–}NH_2)]$ (Cp^*: $\eta^5\text{-}C_5Me_5$; Ts: toluene-4-sulfonyl) and related species,[8a–j] as well as alternative non-Cp* catalyst systems pre-

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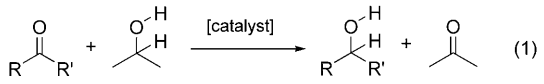
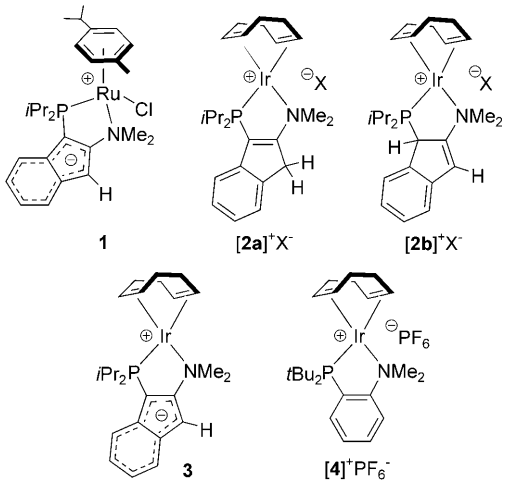
pared by using chiral tetradentate N–H ligands,[8k–o] being among the most effective.

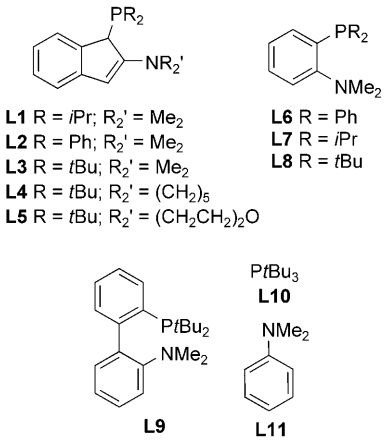


While progress in metal-mediated TH continues to be enabled through the study of precatalysts that exploit the now well-established ancillary-ligand "N–H effect", the identification of alternative ligation strategies that give rise to highly active and/or selective TH precatalysts represents a key step toward new and synthetically useful metal-mediated reactivity. In addition to advances that have been made in Ru-mediated TH chemistry,[9] (NHC)Ir complexes (NHC: *N*-heterocyclic carbene) have emerged as promising precatalysts for the TH of ketones.[10] For example, Crabtree, Faller, and co-workers[10h] have reported an Ir^{III} system of this type that is capable of mediating the nearly quantitative reduction of benzophenone with a TOF of 50000 h^{-1} (at 50% conversion). Notwithstanding such developments, (NHC)Ir complexes that exhibit a combination of high TOFs and high conversions for a broad range of ketone substrates at low catalyst loadings have yet to be reported, and only modest enantioselectivity has been achieved by the use of chiral (NHC)Ir precatalysts.[10d,g] Indeed, the quest is ongoing to identify alternative classes of simple and easily prepared "non-N–H" ancillary ligands to support Ir and other ketone-TH precatalysts that exhibit high efficiency and broad substrate scope.[11,12]

In this context, we have described recently the application of [RuCl(η^6-*p*-cymene)(κ^2-2-NMe_2-3-P*i*Pr_2-indenide)] (**1**, derived from **L1**; Schemes 1 and 2) as a precatalyst for the TH of ketones in *i*PrOH under basic conditions. Despite lacking an ancillary-ligand N–H functionality, complex **1** was shown to be among the most active ketone-TH precatalysts reported (for example, with a TOF of 180000 h^{-1} for acetophenone at 50% conversion).[9b] Encouraged by the catalytic abilities of **1**, and building on our previous studies of the related Ir complexes [Ir(cod)(κ^2-2-NMe_2-3-P*i*Pr_2-indene)]$^+X^-$ ([**2a**]$^+X^-$; cod: η^4-1,5-cyclooctadiene), [Ir(cod)(κ^2-1-P*i*Pr_2-2-NMe_2-indene)]$^+OTf^-$ ([**2b**]$^+OTf^-$; OTf: trifluoromethanesulfonate), and [Ir(cod)(κ^2-2-NMe_2-3-P*i*Pr_2-indenide)] (**3**) as precatalysts in the direct hydrogenation of alkenes,[13] we became interested in exploring the utility of [**2a**,**b**]$^+X^-$, **3**, and other (κ^2-*P*,*N*-ligand)Ir^I precatalysts (Scheme 1) in the TH of ketones; we report herein the results of these catalytic studies. Notably, in the course of these investigations, we discovered that the relatively simple complex [Ir(cod)(κ^2-*P*,*N*-**L8**)]$^+PF_6^-$ ([**4**]$^+PF_6^-$; **L8**: (*o*-*t*Bu_2P-C_6H_4)NMe_2), either preformed or prepared in situ from a mixture of [{IrCl(cod)}$_2$], $NaPF_6$, and **L8**, affords an unusually active Ir catalyst system for the TH of ketones in basic *i*PrOH, with nearly quantitative conversions for a range of alkyl and/or aryl ketones and with high TOFs (up to 230000 h^{-1} at >50% conversion); this enabled the use of remarkably low catalyst-to-substrate ratios (1:25000). Furthermore, catalyst mixtures prepared in situ from [{IrCl(cod)}$_2$], $NaPF_6$, and the structurally related chiral ancillary ligand Cy-Mandyphos (**L13**; Scheme 4)[14] proved capable of mediating the asymmetric TH of ketones, including that of the hindered substrate 2,2-dimethylpropiophenone with an efficiency (95% conversion, 95% *ee*) not documented previously in the literature.



Scheme 1. The structures of complexes **1**, [**2a**]$^+X^-$, [**2b**]$^+X^-$, **3**, and [**4**]$^+PF_6^-$.



Scheme 2. Achiral ligands employed in the transfer-hydrogenation studies.

Results and Discussion

The reduction of acetophenone (**K1**) in basic *i*PrOH at reflux was selected as a preliminary test reaction with which to assess the catalytic utility of the Ir cations [**2a**,**b**]$^+X^-$ and zwitterion **3** (0.1 mol%) in the TH of ketones (Table 1).[15] The preformed complexes [**2a**]$^+X^-$ (X: PF_6, BF_4, and OTf), [**2b**]$^+OTf^-$,[15b] and **3** each proved effective in mediating this transformation and provided very good TOFs (0.1 mol% Ir;

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Table 1. Preliminary screening of Ir complexes for the transfer hydrogenation of acetophenone (**K1**).[a]

Entry	Catalyst	t [h]	Conversion [%][b]	TOF [h^{-1}] (%)[c]
1	$[\mathbf{2a}]^+PF_6^-$	2	96	47000 (39)
2	$[\mathbf{2a}]^+BF_4^-$	2	98	42000 (35)
3	$[\mathbf{2a}]^+OTf^-$	2	93	36000 (30)
4	$[\mathbf{2b}]^+OTf^-$	3.25	99	48000 (40)
5	**3**	2	95	37000 (31)
6	Crabtree's[d]	2	29	n.d.

[a] Ir/ketone = 1:1000; 0.8 mmol scale; 0.1 M ketone; 82 °C; 1 mol% NaO*t*Bu in *i*PrOH. [b] On the basis of GC-FID data obtained at the stated time. [c] Determined at 30 s, with the corresponding % conversion given in parentheses. n.d.: not determined if the % conversion at 30 s was <25%. [d] $[Ir(cod)(PCy_3)(pyridine)]^+PF_6^-$; Cy: cyclohexyl.

36000–48000 h^{-1} measured at 30 s and 30–40% conversion)[15c] and high final conversions to 1-phenylethanol (93–99%; Table 1, entries 1–5). Poor results were obtained when using 0.1 mol% $[Ir(cod)(PCy_3)(pyridine)]^+PF_6^-$ (Cy: cyclohexyl; Table 1, entry 6) under similar conditions,[16] and negligible conversion was achieved by use of the Rh analogue of **3**.

Related catalyst mixtures prepared in situ from $[\{IrCl(cod)\}_2]$ and 1-P*i*Pr_2-2-NMe_2-indene (**L1**; Scheme 2) were also found to be reasonably effective under analogous conditions (34000 h^{-1} at 28% conversion; Table 2, entry 1). On the basis of these preliminary findings, we proceeded to investigate the influence of donor-fragment substitution on the catalyst's performance by examining acetophenone TH mediated by mixtures of $[\{Ir(cod)Cl\}_2]$ and alternative P,N-indene ligands (Scheme 2). While the PPh_2 variant (**L2**; Table 2, entry 2) proved inferior to **L1**, the closely related P*t*Bu_2 derivative (**L3**) gave rise to a significantly more active catalyst system and, thereby, allowed the near quantitative reduction of acetophenone in only 0.25 h (59000 h^{-1} at 49% conversion; Table 2, entry 3). Despite the apparent reactivity advantages of employing a bulky P*t*Bu_2 substituent in this family of P,N-indene ligands, further elaboration of the N-donor fragment proved deleterious (**L4** and **L5**; Table 2, entries 4 and 5, respectively).

Table 2. Transfer hydrogenation of acetophenone (**K1**) by employing $[\{IrCl(cod)\}_2]$ and various ligands.[a]

Entry	Ligand (L)	t [h]	Conversion [%][b]	TOF [h^{-1}] (%)[c]
1	**L1**	2	81	34000 (28)
2	**L2**	2	54	n.d.
3	**L3**	0.25	98	59000 (49)
4	**L4**	2	57	n.d.
5	**L5**	2	39	n.d.
6	**L6**	2	84	n.d.
7	**L7**	2	96	42000 (35)
8[d]	**L8**	0.25	94	100000 (43)
9[e]	**L8**	0.25	96	150000 (63)
10	**L9**	2	4	n.d.
11	**L10**	2	21	n.d.
12	**L10/L11**	2	14	n.d.
13	2 PPh_3	2	43	n.d.

[a] Ir/L/ketone = 1:1:1000; 0.8 mmol scale; 0.1 M ketone; 82 °C; 1 mol% NaO*t*Bu in *i*PrOH. [b] On the basis of GC-FID data obtained at the stated time. [c] Determined at 30 s, with the corresponding % conversion given in parentheses. n.d.: not determined if the % conversion at 30 s is <25%. [d] Ir/L/ketone = 1:1:2000. [e] With $NaPF_6$; Ir/L/$NaPF_6$/ketone = 1:1:1.1:2000.

We have observed previously that the cationic κ^2-*P,N*-indene complexes $[\mathbf{2a,b}]^+X^-$ can be transformed under basic conditions into the corresponding zwitterionic κ^2-*P,N*-indenide complex **3** upon loss of HX.[13] We became interested in determining whether the anionic nature of P,N-indenide ligands formed in situ from **L1** (as in **3**) or **L3** might play a role in facilitating the observed ketone-TH chemistry mediated by mixtures of $[\{IrCl(cod)Cl\}_2]$ and these P,N-indenes in basic *i*PrOH (Table 2, entries 1 and 3). Toward this end, the catalytic utility of the structurally related phenylene P,N ligands (*o*-R_2P-C_6H_4)NMe_2 (R: Ph, **L6**; R: *i*Pr, **L7**; R: *t*Bu, **L8**; Table 2, entries 6–8, respectively) was evaluated.[17] Interestingly, **L6**–**L8** were observed to outperform the corresponding P,N-indene ligand in the Ir-mediated TH of acetophenone under similar conditions, with mixtures of $[\{Ir(cod)Cl\}_2]$, $NaPF_6$, and **L8** affording a particularly active Ir catalyst system (96%, 0.25 h, 0.05 mol% Ir; TOF = 150000 h^{-1} at 63% conversion; Table 2, entry 9).[15c] Conversely, *t*Bu-DavePhos (**L9**; Scheme 2; Table 2, entry 10), *t*Bu_3P (**L10**; Table 2, entry 11), 1:1 mixtures of *t*Bu_3P/$PhNMe_2$ (**L10/L11**; Table 2, entry 12), and PPh_3 (2 equiv; Table 2, entry 13)[12] proved ineffective in supporting similarly active catalyst systems when used in place of **L8**, as did mixtures of **L8** with either $[\{RhCl(cod)\}_2]$, $[\{IrCl_2Cp^*\}_2]$, $[\{RhCl_2Cp^*\}_2]$, $[RuCl_2(PPh_3)_3]$, or $[\{RuCl_2(p\text{-cymene})\}_2]$ (0.1 mol% M, <10%, 0.25 h).

Intrigued by the remarkable activity of $[\{IrCl(cod)\}_2]$/$NaPF_6$/**L8** mixtures in mediating the catalytic TH of acetophenone, we examined the reduction of other ketones in basic *i*PrOH at reflux (Table 3, Scheme 3). This in situ prepared catalyst mixture proved very effective for the TH of a range of substituted acetophenones (**K1**–**K5**) and benzophenones (**K7**–**K9**), as well as other aryl alkyl (**K12** and **K14**) and dialkyl (**K15** and **K16**) ketones. In the case of cyclohexanone (**K15**), high conversions were achieved in relatively short reaction times by the use of 0.01 mol% Ir (>99%, 0.33 h; Table 3, entry 19) and even 0.004 mol% Ir (95%, 1.5 h; Table 3, entry 20). In preliminary studies, imines and aldehydes were resistant to reduction under our standard reaction conditions.

In an effort to support our view that $[\{IrCl(cod)\}_2]$/$NaPF_6$/**L8** mixtures give rise to $[Ir(cod)(\kappa^2\text{-}P,N\text{-}\mathbf{L8})]^+PF_6^-$ ($[\mathbf{4}]^+PF_6^-$) as the precatalyst in these reactions, we sought to evaluate the catalytic utility of isolated $[\mathbf{4}]^+PF_6^-$; this compound was prepared as an analytically pure solid in 64% isolated yield. The solution NMR characterization of $[\mathbf{4}]^+PF_6^-$ as a traditional square-planar $[Ir(cod)(\kappa^2\text{-}P,N\text{-ligand})]^+X^-$ complex is entirely consistent with the crystallographically determined structure; an ORTEP[18] diagram of $[\mathbf{4}]^+PF_6^-$ is presented in Figure 1. Gratifyingly, the catalytic performance of $[\mathbf{4}]^+PF_6^-$ mirrored that of the $[\{IrCl(cod)\}_2]$/$NaPF_6$/**L8** mixture (Table 3); the TH of acetophenone (**K1**) with $[\mathbf{4}]^+PF_6^-$ (Table 3, entry 3) proceeded with a TOF of

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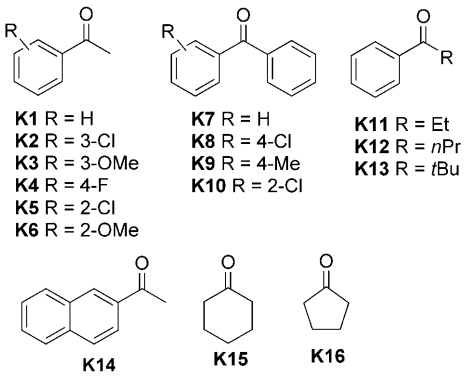
Table 3. Scope of ketone transfer hydrogenation with [{IrCl(cod)}$_2$], **L8**, and $NaPF_6$, or with [**4**]$^+PF_6^-$.[a]

Entry	Ketone	Ir/ketone	t [min]	Conversion [%][b]
1[c]	**K1**	1:2000	15	96
2[c]	**K1**	1:4000	60	96
3[d]	**K1**	1:2000	15	97
4[c]	**K2**	1:2000	15	98
5[d]	**K2**	1:2000	15	99
6[c]	**K3**	1:2000	15	95
7[d]	**K3**	1:2000	15	97
8[c]	**K4**	1:2000	15	93
9[c]	**K5**	1:1000	5	>99[e]
10[d]	**K6**	1:1000	5	99
11[c]	**K7**	1:2000	40	90
12[c]	**K8**	1:2000	15	94
13[c]	**K9**	1:2000	120	91
14[d]	**K10**	1:1000	60	87
15[c]	**K12**	1:2000	30	79
16[d]	**K12**	1:2000	30	83
17[c]	**K14**	1:2000	15	96
18[c]	**K15**	1:2000	15	>99
19[c]	**K15**	1:10000	20	>99
20[c]	**K15**	1:25000	90	95
21[d]	**K15**	1:10000	10	99
22[c]	**K16**	1:2000	15	98

[a] Ir/**L8**/$NaPF_6$ = 1:1:1.1; 0.8 mmol scale; 0.1 M ketone; 82 °C; 1 mol% NaO*t*Bu in *i*PrOH. [b] On the basis of GC-FID data obtained at the stated time. [c] With [{IrCl(cod)}$_2$], **L8**, and $NaPF_6$. [d] With [**4**]$^+PF_6^-$. [e] When the reaction was conducted on a 2.0 mmol scale, the corresponding secondary alcohol was isolated in 95% yield.



Scheme 3. Ketones employed in the transfer-hydrogenation studies.

230000 h^{-1} (measured at 20 seconds and 63% conversion).[15c] The demonstrated ability of [{IrCl(cod)}$_2$]/$NaPF_6$/**L8** (or, alternatively, [**4**]$^+PF_6^-$) to mediate the rapid reduction of such a structurally diverse set of ketones with high conversions and routinely low catalyst loadings (0.004–0.1 mol% Ir) is noteworthy. These results serve to establish **L8** and other appropriately substituted simple P,N ligands as a useful class of ancillary ligands in metal-mediated ketone-TH chemistry.

Having succeeded in establishing the utility of simple P,N ligands such as **L8** in the Ir-mediated TH of ketones, we sought to develop asymmetric variants of this reaction by employing structurally related chiral ancillary ligands. Given the pairing of a bulky PR_2 fragment with an NMe_2 donor, as

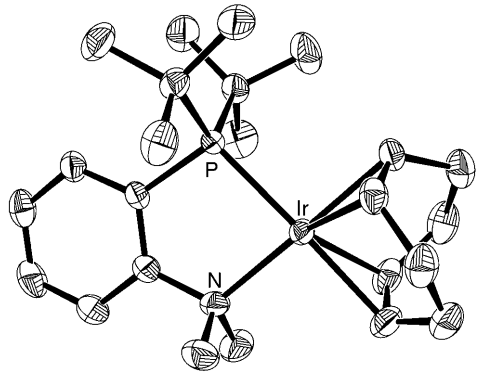
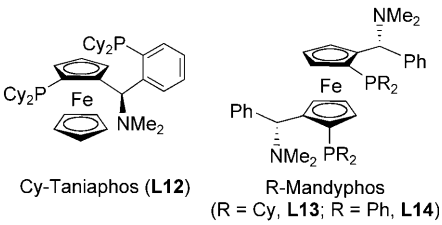


Figure 1. ORTEP diagram for [**4**]$^+PF_6^-$. The hydrogen atoms and the PF_6^- anion have been omitted for clarity. Selected bond lengths: Ir–P 2.3212(6), Ir–N 2.184(2), Ir–alkene 2.118(3) and 2.166(2) (*trans* to N), 2.168(3) and 2.228(3) Å (*trans* to P).

featured in **L8**, we identified commercially available Cy-Taniaphos (**L12**; Scheme 4) and Cy-Mandyphos (**L13**) as attractive ligand candidates for asymmetric-TH experiments



Scheme 4. Chiral ligands employed in the asymmetric transfer-hydrogenation studies.

in basic *i*PrOH. In a preliminary survey, good conversion (94%, 4.5 h) and enantioselectivity (72% *ee*) were achieved when Cy-Mandyphos was employed for the TH of acetophenone (**K1**) at 40 °C by using catalyst mixtures comprising [{IrCl(cod)}$_2$]/$NaPF_6$/**L13** (1.0 mol% Ir; Table 4, entry 1). Al-

Table 4. Asymmetric transfer hydrogenation of ketones by employing [{IrCl(cod)}$_2$], Cy-Mandyphos (**L13**), and $NaPF_6$.[a]

Entry	Ketone	t [h]	Conversion [%][b]	Enantiomer ratio (*ee*)[b]
1	**K1**	4.5	94	86:14 (72, *S*)[c]
2[d]	**K1**	24	81	85:15 (70)
3	**K2**	3	95	79.5:20.5 (59)
4	**K4**	22	94	84:16 (68)
5	**K5**	2.5	98	61:39 (22)
6	**K11**	14	86	89:11 (78)
7	**K12**	28	87	90.5:9.5 (81)
8	**K13**	2	95	96.5:3.5 (93)
9[e]	**K13**	12	95	97.5:2.5 (95)
10[d]	**K13**	24	56	97.5:2.5 (95)

[a] Ir/**L13**/$NaPF_6$/ketone = 1:1:1.1:100; 0.4 mmol; 0.1 M ketone; 40 °C; 5 mol% NaO*t*Bu in *i*PrOH. [b] On the basis of chiral GC-FID data at the stated time. [c] Absolute configuration assignment made by comparison to literature data; see the Experimental Section. [d] Reaction conducted at 30 °C. [e] Ir/**L13**/$NaPF_6$/ketone = 1:1:1.1:200.

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though the use of Cy-Taniaphos under similar conditions afforded good conversions, poor enantioselectivity (< 50 % *ee*) was achieved. In keeping with the inferior performance of catalysts prepared from the PPh_2-substituted ligand **L6** relative to those featuring the $PtBu_2$ variant **L8** (see above), Ph-Mandyphos (**L14**, Scheme 4) displayed poor activity and selectivity for the reduction of acetophenone under analogous conditions (29 % conversion, 37 % *ee*, 4.5 h).

While $[\{IrCl(cod)\}_2]$/$NaPF_6$/**L13** (1.0 mol % Ir) proved capable of reducing other aryl alkyl ketones under relatively mild conditions (Table 4), this catalyst mixture was found to be particularly effective for the reduction of the sterically encumbered substrate 2,2-dimethylpropiophenone (**K13**), with excellent conversion (95 %, 2 h) and enantioselectivity (93 % *ee*; Table 4, entry 8). Whereas lowering of the reaction temperature from 40 to 30 °C decreased the extent of reduction without providing any gain in enantioselectivity (Table 4, entries 2 and 10), enhanced enantioselectivity was achieved by reducing the catalyst loading to 0.5 mol % Ir (95 % conversion, 12 h, 95 % *ee*; Table 4, entry 9). To the best of our knowledge, the metal-catalyzed asymmetric TH of **K13** with such efficiency has not documented in the literature. This result highlights the utility of employing Ir in combination with this class of ligands in addressing challenging asymmetric-TH chemistry. Indeed, the efficient Ru-catalyzed hydrogenation of **K13** by use of dihydrogen gas has been reported only recently.[19]

Conclusion

The catalytic utility in ketone TH of Ir complexes supported by various P,N-substituted indene, indenide, or phenylene ligands was evaluated. In a preliminary catalytic survey the cationic and formally zwitterionic complexes $[\mathbf{2a},\mathbf{b}]^+X^-$ and **3**, as well as related in situ prepared Ir catalysts derived from P,N-indenes, were found to be generally effective in mediating the reduction of acetophenone to 1-phenylethanol in basic *i*PrOH at reflux. Although the catalytic performance of these Ir complexes proved inferior to that of the highly active zwitterionic Ru species **1**,[9b] the related Ir complex $[\mathbf{4}]^+PF_6^-$ supported by the rather simple ancillary ligand (o-tBu_2P-C_6H_4)NMe_2 (**L8**) exhibited remarkable activity that rivals that of **1**. Notably, $[\mathbf{4}]^+PF_6^-$ is a rare example of a ketone-TH catalyst system that exhibits TOF values of $10^5\ h^{-1}$ and also provides high conversions for a diversity of simple ketone substrates at low catalyst loadings (0.004–0.1 mol % Ir). In addition, the outstanding catalytic performance of $[\mathbf{4}]^+PF_6^-$ was mirrored by in situ prepared catalyst mixtures that were formed conveniently by the combination of $[\{IrCl(cod)\}_2]$, $NaPF_6$, and **L8**. In the course of these catalytic studies, it was observed that alteration of the substituents at the donor fragments of the supporting P,N ligands had a pronounced influence on the catalytic performance of the derived catalysts, with ligands featuring bulky dialkylphosphino donors proving to be the most effective. Based on these observations, chiral catalysts prepared in situ from commercially available $[\{IrCl(cod)\}_2]$, $NaPF_6$, and the PCy_2-substituted chiral ligand Cy-Mandyphos (**L13**) proved capable of mediating the asymmetric TH of ketones, including that of the hindered substrate 2,2-dimethylpropiophenone with unprecedented efficiency (95 % conversion, 95 % *ee*). Collectively, these results demonstrate that appropriately constructed simple P,N ligands represent an effective class of often-overlooked "non-N–H" ancillary ligands in metal-mediated ketone-TH chemistry. Encouraged by these preliminary findings, we are currently exploring the utility of **L8** and related P,N ligands in a variety of metal-mediated synthetic applications and will report on the results of these investigations in due course.

Experimental Section

General considerations: All manipulations were conducted in the absence of oxygen and water under an atmosphere of dinitrogen, either by use of standard Schlenk methods or within an mBraun glovebox apparatus, by utilizing glassware that was oven dried (130 °C) and evacuated while hot prior to use. Celite (Aldrich) was oven dried (130 °C) for 5 d and then evacuated for 24 h prior to use. The nondeuterated solvents diethyl ether, dichloromethane, tetrahydrofuran (THF), pentane, and hexane were deoxygenated and dried by sparging with dinitrogen gas, followed by passage through a double-column solvent-purification system purchased from mBraun Inc. Diethyl ether, dichloromethane, and tetrahydrofuran were purified over two alumina-packed columns, while pentane and hexane were purified over one alumina-packed column and one column packed with copper-Q5 reactant. Purification of *i*PrOH (Aldrich, anhydrous 99.5 %) was achieved by sparging with dinitrogen over a period of 0.25 h, followed by storage over 4 Å sieves (approximately 10 g per 100 mL of *i*PrOH) for a minimum of 24 h. All solvents used within the glovebox were stored over activated 4 Å molecular sieves. $CDCl_3$ (Aldrich) was degassed by using 3 repeated freeze–pump–thaw cycles, dried over CaH_2 for 7 d, distilled in vacuo, and stored over 4 Å molecular sieves for 24 h prior to use. All ketone substrates were obtained from commercial sources in high purity; solid ketones were dried in vacuo for a minimum of 12 h prior to use, while liquid ketones were degassed by use of 3 repeated freeze–pump–thaw cycles. In the cases of acetophenone, cyclohexanone, and cyclopentanone, the ketones were dried over CaH_2 for a minimum of 12 h and distilled before degassing. *o*-Bromo-*N*,*N*-dimethylaniline (Alfa Aesar), *N*,*N*-dimethylaniline (**L11**, Alfa Aesar), *n*BuLi (2.9 M in hexanes, Alfa Aesar), $ClPPh_2$ (Aldrich), $ClPiPr_2$ (Aldrich), $ClPtBu_2$ (Aldrich), and $PtBu_3$ (**L10**, Strem) were used as received. $[\{IrCl(cod)\}_2]$, $[\{RhCl(cod)\}_2]$, $[\{IrCl_2Cp^*\}_2]$, $[\{RhCl_2Cp^*\}_2]$, $[RuCl_2(PPh_3)_3]$, $[\{RuCl_2(p\text{-cymene})\}_2]$, *t*Bu-DavePhos (**L9**), Cy-Taniaphos (**L12**), Cy-Mandyphos (**L13**), Ph-Mandyphos (**L14**), and Crabtree's catalyst (all obtained from Strem), as well as $NaPF_6$ (Aldrich) and NaO*t*Bu (Aldrich), were dried in vacuo for a minimum of 12 h prior to use. While ligands 1-P*i*Pr_2-2-NMe_2-indene (**L1**) and 1-PPh_2-2-NMe_2-indene (**L2**) were prepared by employing published procedures,[20] these ligands are now commercially available from Strem Chemicals Inc. The preparation of (o-Ph_2P-C_6H_4)NMe_2 (**L6**),[21] $[Ir(cod)(\kappa^2\text{-}2\text{-}NMe_2\text{-}3\text{-}PiPr_2\text{-indene})]^+X^-$ ($[\mathbf{2a}]^+X^-$),[13] $[Ir(cod)(\kappa^2\text{-}1\text{-}PiPr_2\text{-}2\text{-}NMe_2\text{-indene})]^+OTf^-$ ($[\mathbf{2b}]^+OTf^-$),[13] and $[Ir(cod)(\kappa^2\text{-}2\text{-}NMe_2\text{-}3\text{-}PiPr_2\text{-indenide})]$ (**3**)[13] has been reported previously. The 2-NR_2-indenes[22] used in the preparation of 1/3-P*t*Bu_2-2-NMe_2-indene (**L3**), 1/3-P*t*Bu_2-2-piperidyl-indene (**L4**), and 1/3-P*t*Bu_2-2-morpholino-indene (**L5**) were prepared according to literature procedures. ^1H, ^{13}C, and ^{31}P NMR characterization data were collected at 300 K on a Bruker AV-500 spectrometer operating at 500.1, 125.8, and 202.5 MHz, respectively, with chemical shifts reported in parts per million downfield of $SiMe_4$ for ^1H and ^{13}C data or of 85 % H_3PO_4 in D_2O for ^{31}P data. ^1H and ^{13}C NMR chemical shift assignments are based on data obtained from ^{13}C-DEPT, ^1H–^1H COSY, ^1H–^{13}C HSQC, and ^1H–^{13}C HMBC

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NMR experiments. In some cases, fewer than expected independent ^{13}C NMR resonances were observed, despite prolonged data-acquisition times. Elemental analyses were performed by Canadian Microanalytical Service Ltd., Delta, BC, Canada.

Synthesis of 1/3-P*t*Bu$_2$-2-NMe$_2$-indene (L3), 1/3-P*t*Bu$_2$-2-piperidyl-indene (L4), and 1/3-P*t*Bu$_2$-2-morpholino-indene (L5): These P,N-substituted indenes were prepared from the corresponding 2-aminoindenes by using synthetic methods directly analogous to those employed in the preparation of the closely related indenes 1-P*i*Pr$_2$-2-NMe$_2$-indene (**L1**) and 1-PPh$_2$-2-NMe$_2$-indene (**L2**),[20] with the exception that extended reaction times (up to 6 d) at ambient temperatures were required to obtain optimal yields. The propensity of isomerically pure **L1** and **L2** to form a mixture of allylic (1-PR$_2$-2-NR$_2$-indene) and vinylic (3-PR$_2$–2-NR$_2$-indene) isomers upon standing in solution has been well-documented;[20b] similarly, **L3**–**L5** were obtained as varying mixtures of allylic and vinylic isomers: **L3**: 48% yield; $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 51.6$ (allylic), 14.6 ppm (vinylic); **L4**: 47% yield; $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 55.3$ (allylic), 15.7 ppm (vinylic); **L5**: 35% yield; $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 53.2$ (allylic), 14.9 ppm (vinylic). Given that [Ir(cod)(κ^2-1-P*i*Pr$_2$-2-NMe$_2$-indene)]$^+$OTf$^-$ ([**2b**]$^+$OTf$^-$) has been shown to isomerize rapidly to [**2a**]$^+$OTf$^-$ under basic conditions,[13] such as those employed in the catalytic experiments detailed herein, and that a similar performance has been observed for [**2a**]$^+$OTf$^-$ and [**2b**]$^+$OTf$^-$ in head-to-head acetophenone-transfer-hydrogenation experiments, it appears that the isomeric form of the ancillary P,N-indene ligand backbone has minimal influence over the performance of the derived catalyst complexes. As such, for simplicity, only the allylic forms of **L3**–**L5** are represented and discussed in the text.

Synthesis of (*o*-R$_2$P-C$_6$H$_4$)NMe$_2$ (R: *i*Pr, L7; R: *t*Bu, L8): The analogous compound in which R is Ph (**L6**) has been reported.[21] *n*BuLi (625 μL, 1.8 mmol) was added to a glass vial containing *o*-bromo-*N*,*N*-dimethylaniline (218 μL, 1.5 mmol) in Et_2O (3 mL, precooled to −35 °C). After the reaction mixture had been maintained for 0.5 h at −35 °C and an additional 0.25 h at room temperature, the resulting yellow precipitate was isolated by removing the solvent by pipette. This was followed by washing of the remaining solid with cold hexanes (2×2 mL), after which the volatile materials were removed in vacuo. The resulting solid was dissolved in THF (3 mL), and ClP*i*Pr$_2$ (238 μL, 1.5 mmol) was added dropwise. The mixture was stirred magnetically at room temperature overnight (ca. 18 h). The solvent and volatile materials were then removed in vacuo. The resulting mixture was dissolved in CH_2Cl_2 and filtered through a celite plug. Removal of the CH_2Cl_2 in vacuo yielded **L7** as a pale yellow oil (0.11 g, 0.47 mmol, 31% yield); ^1H NMR ($CDCl_3$): $\delta =$ 7.37 (m, 1H, Ar-H), 7.31 (m, 1H, Ar-H), 7.17 (m, 1H, Ar-H), 7.09 (m, 1H, Ar-H), 2.77 (s, 6H, N(CH_3)$_2$), 2.07 (m, 2H, P(CH(CH$_3$)$_2$)$_2$), 1.15 (dd, $^3J_{PH} = 14.2$, $^3J_{HH} = 7.0$ Hz, 6H, P(CH(CH_3CH$_3$)$_2$), 0.94 ppm (dd, $^3J_{PH} =$ 11.5, $^3J_{HH} = 7.0$ Hz, 6H, P(CH(CH$_3$$CH_3$)$_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta =$ 160.1 (d, $J_{PC} = 18.6$ Hz), 133.0 (d, $J_{PC} = 3.3$ Hz), 131.8 (d, $J_{PC} = 17.4$ Hz), 129.5, 123.2, 119.7 (d, $J_{PC} = 4.7$ Hz), 45.8 (d, $^4J_{PC} = 5.2$ Hz, N(CH_3)$_2$), 23.6 (d, $^1J_{PC} = 13.9$ Hz, P(CH(CH$_3$)$_2$)$_2$), 20.1 (d, $^2J_{PC} = 18.6$ Hz, P(CH-(CH_3CH$_3$)$_2$), 19.3 ppm (d, $^2J_{PC} = 10.5$ Hz, P(CH(CH$_3$$CH_3$)$_2$); $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 3.5$ ppm.

Compound **L8** was prepared in a similar manner by using *o*-bromo-*N*,*N*-dimethylaniline (288 μL, 2.0 mmol) and *n*BuLi (759 μL, 2.20 mmol), with the exception that the resulting solid was dissolved in Et_2O (6 mL; rather than 3 mL of THF), ClP*t*Bu$_2$ (392 μL, 2.0 mmol) was used in place of ClP*i*Pr$_2$, and the mixture was stirred at room temperature for 6 d at which point no further conversion of the chlorophosphane was observed (by ^{31}P NMR spectroscopy). **L8** was isolated as a beige powder (0.204 g, 0.78 mmol, 39% yield); ^1H NMR ($CDCl_3$): $\delta = 7.70$ (m, 1H, Ar-H), 7.32 (m, 1H, Ar-H), 7.21 (m, 1H, Ar-H), 7.06 (m, 1H, Ar-H), 2.76 (s, 6H, N-(CH_3)$_2$), 1.21 ppm (d, 18H, $^3J_{PC} = 11.5$ Hz, P(C(CH_3)$_3$)$_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 161.0$ (d, $J_{PC} = 21.7$ Hz), 136.2 (d, $J_{PC} = 3.7$ Hz), 133.6 (d, $J_{PC} = 22.9$ Hz), 129.8, 122.7, 120.4 (d, $J_{PC} = 3.7$ Hz), 46.0 (d, $^4J_{PC} = 4.3$ Hz, N(CH_3)$_2$), 32.1 (d, $^1J_{PC} = 24.7$ Hz, P(C(CH$_3$)$_3$)$_2$), 30.7 ppm (d, $^2J_{PC} =$ 15.4 Hz, P(C(CH_3)$_3$)$_2$); $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta = 17.6$ ppm.

Synthesis of [Ir(cod)(κ^2-*P*,*N*-L8)]$^+$PF$_6^-$ ([4]$^+$PF$_6^-$): [{IrCl(cod)}$_2$] (0.067 g, 0.20 mmol), **L8** (0.053 g, 0.20 mmol), $NaPF_6$ (0.034 g, 0.20 mmol), and CH_2Cl_2 (8 mL) were added to a glass vial. The resulting mixture was stirred magnetically at room temperature for 24 h, after which the solvent was removed in vacuo. The residue was then taken up in CH_2Cl_2 (5 mL) and filtered through a plug of silica. The solvent was removed in vacuo and the residue was washed with pentane (2×2 mL). The product was then dried in vacuo to yield [**4**]$^+$PF$_6^-$ as an orange solid (0.091 g, 0.13 mmol, 64% yield); ^1H NMR ($CDCl_3$): $\delta = 7.97$ (m, 1H, Ar-H), 7.91 (m, 1H, Ar-H), 7.73 (m, 1H, Ar-H), 7.47, (m, 1H, Ar-H), 4.70–4.62 (m, 4H, cod), 3.31 (s, 6H, N(CH_3)$_2$), 2.33–2.27 (m, 4H, cod), 1.85–1.80 (m, 4H, cod), 1.41 ppm (d, $^3J_{PH} = 14.5$ Hz, 18H, P(C(CH_3)$_3$)$_2$); $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta = 163.1$, 134.7, 128.7 (d, $J_{PC} = 5.0$ Hz), 123.4 (d, $J_{PC} = 8.8$ Hz), 89.4 (d, $J_{PC} = 11.3$ Hz, cod), 62.2 (cod), 53.6 (N(CH_3)$_2$), 32.9 (d, $J_{PC} = 2.5$ Hz, cod), 30.7 (d, $J_{PC} = 3.8$ Hz, P(C(CH_3)$_3$)$_2$), 29.7 (P(C-(CH$_3$)$_3$)$_2$), 29.3 ppm (d, $J_{PC=}2.5$ Hz, cod); $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta =$ 52.8 ppm; elemental analysis calcd (%) for $C_{24}H_{40}Ir_1N_1P_2F_6$: C 40.56, H 5.67, N 1.97; found: C 40.21, H 5.54, N 1.89. A single crystal of [**4**]$^+$PF$_6^-$ suitable for single-crystal X-ray diffraction was obtained from vapor diffusion of diethyl ether into a concentrated solution of [**4**]$^+$PF$_6^-$ in dichloromethane.

Typical procedure for the catalytic transfer hydrogenation of ketones: A mixture of [{IrCl(cod)}$_2$] (3.9 mg, 0.0058 mmol), **L8** (3.2 mg, 0.0119 mmol), and $NaPF_6$ (2.1 mg, 0.0125 mmol) was vigorously stirred in THF (4.000 mL) for approximately 1 h before an aliquot (139 μL, 0.4 μmol) was delivered to a Schlenk flask by use of an Eppendorf pipette. The solvent within the Schlenk flask was then removed in vacuo, and ketone (0.8 mmol), followed by *i*PrOH (6 mL), was subsequently added to the residue within the Schlenk flask. The solution was then heated at 82 °C for 10 min, at which point a 0.004 M solution of NaO*t*Bu in *i*PrOH (2 mL) was added to the Schlenk flask (Ir/**L8**/$NaPF_6$/NaO*t*Bu/ketone 1:1:1.1:20:2000; [ketone] = 0.1 M), which resulted in rapid reduction of the ketone. Reactions were sampled by removing an aliquot (0.25–1 mL) of the reaction mixture with a syringe and immediately filtering it through a plug of silica. Conversions were determined by use of GC-FID, and the identities of the hydrogenation products were confirmed by use of ^1H NMR methods or by comparison to authentic samples. All reported data represent the average of a minimum of two catalytic runs.

Typical procedure for the catalytic asymmetric transfer hydrogenation of ketones: [{IrCl(cod)}$_2$] (7.1 mg, 0.011 mmol), Cy-Mandyphos (18.0 mg, 0.021 mmol), and $NaPF_6$ (4.1 mg, 0.024 mmol) were vigorously stirred in THF (4.000 mL) for approximately 1 h before an aliquot (379 μL, 0.002 mmol) was delivered to a Schlenk flask by use of an Eppendorf pipette. The solvent within the Schlenk flask was then removed in vacuo, and ketone (0.4 mmol), followed by *i*PrOH (2 mL), was subsequently added to the residue within the Schlenk flask. The solution was then heated at 40 °C for 10 min, at which point a 0.04 M solution of NaO*t*Bu in *i*PrOH (2 mL) was added to the Schlenk flask (Ir/Cy-Mandyphos (**L13**)/$NaPF_6$/NaO*t*Bu/ketone 1:1:1.1:10:200; [ketone] = 0.1 M). Conversions and enantiomeric ratios were determined by use of chiral GC-FID (Astec CHIRALDEX G-TA 30 m×0.25 mm for all substrates with exception of 2′-chloroacetophenone for which a Supelco Beta-Dex 120 30 m×0.25 mm column was employed), and the identities of the hydrogenation products were confirmed by use of ^1H NMR methods or by comparison to authentic samples. The *S*-absolute configuration assigned to the major enantiomer of 1-phenylethanol formed in the reduction of **K1** was determined by comparison to literature data.[23] Retention times for substrates and products were as follows. Acetophenone (**K1**; 100 °C; 20 psi): 11.0 min; 1-phenylethanol: $t_1 = 11.6$ min; $t_2 = 12.4$ min. 3-Chloroacetophenone (**K2**; 145 °C; 12 psi): 8.3 min; 1-(*m*-chlorophenyl)ethanol: $t_1 = 13.8$ min; $t_2 =$ 14.8 min. 4-Fluoroacetophenone (**K4**; 110 °C; 17 psi): 6.8 min; 1-(*p*-fluorophenyl)ethanol: $t_1 = 9.7$ min; $t_2 = 10.3$ min. 2′-Chloroacetophenone (**K5**; 145 °C; 12 psi): 8.0 min; 1-(*o*-chlorophenyl)ethanol: $t_1 = 10.3$ min; $t_2 =$ 10.8 min. Propiophenone (**K11**; 110 °C; 17 psi): 10.6 min; 1-phenylpropan-1-ol: $t_1 = 12.7$ min; $t_2 = 13.1$ min. *n*-Butyrophenone (**K12**; 125 °C; 8 psi): 18.0 min; 1-phenylbutan-1-ol: $t_1 = 21.7$ min; $t_2 = 22.5$ min. 2,2-Dimethylpropiophenone (**K13**; 125 °C; 8 psi): 14.5 min; 2,2-dimethyl-1-phenylpropanol: $t_1 = 20.8$ min; $t_2 = 21.5$. All reported data represent the average of a minimum of two catalytic runs.

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Crystallographic solution and refinement details: Crystallographic data for $[4]^+PF_6^-$ were collected on a Bruker PLATFORM/SMART 1000 CCD diffractometer by using graphite-monochromated Mo Kα ($\lambda = 0.71073$ Å) radiation and by employing a sample that was mounted in inert oil and transferred to a cold gas stream on the diffractometer (193(±2) K). Programs for diffractometer operation, data collection, data reduction, and absorption correction (including SAINT and SADABS) were supplied by Bruker. The structure of $[4]^+PF_6^-$ was solved by use of direct methods and refined by use of full-matrix least-squares procedures (on F^2) with R_1 based on $F_o^2 \geq 2\sigma(F_o^2)$ and wR_2 based on $F_o^2 \geq -3\sigma(F_o^2)$. Anisotropic displacement parameters were employed throughout for the non-H atoms. All H atoms were added at calculated positions and refined by use of a riding model employing isotropic displacement parameters based on the isotropic displacement parameter of the attached atom. Selected crystal data for $[4]^+PF_6^-$: empirical formula $C_{24}H_{40}F_6Ir_1N_1P_2$; crystal size $0.31 \times 0.25 \times 0.17$ mm monoclinic; space group $P2(1)/c$; $a = 9.7092(7)$, $b = 16.0329(12)$, $c = 17.0851(13)$ Å; $\alpha = 90$, $\beta = 96.7480(10)$, $\gamma = 90°$; $V = 2641.2(3)$ Å^3; $Z = 4$; $\mu = 5.232$ mm^{-1}; ϕ range for data collection 1.75–27.51°; limiting indices $-12 \leq h \leq 12$, $-20 \leq k \leq 20$, $-22 \leq l \leq 22$; 22776 reflections measured; 6062 unique reflections ($R_{int} = 0.0228$); completeness 99.6%; max. and min. transmission 0.4699 and 0.2938; data/restraints/parameters 6062/0/307; goodness of fit on F^2 1.035; final R indices with $I > 2\sigma(I)$: $R1 = 0.0200$, $wR2 = 0.0496$; final R indices (all data): $R1 = 0.0230$, $wR2 = 0.0509$; largest diff. peak and hole 1.145 and -0.363 e Å^3. CCDC-683381 contains 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.

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