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Tuning the Peri Effect for Enantioselectivity: Asymmetric Hydrogenation of Unfunctionalized Olefins with the BIPI Ligands

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Abstract: The modular nature of the BIPI ligands allows for systematic optimization of each ligand region. The development of ligands optimized for asymmetric hydrogenation of the challenging unfunctionalized olefin substrate class is described. The naphthyl peri position, C-8, has been identified as a critical stereocontrol element in the design of these ligands. Highly enantioselective ligands suitable for hydrogenation of tri- and tetrasubstituted olefins are detailed.

Keywords: asymmetric hydrogenation; BIPI ligands; naphthalenes; peri position; unfunctionalized olefins

Asymmetric hydrogenation (AH) is a critical technology in the manufacture of pharmaceuticals, agrochemicals, fragrances, and many organic building blocks of commerce.[1] Significant advances have been realized in the years since the pioneering work of Kagan, Noyori, Knowles and others,[2] particularly for functionalized olefins in which a carbonyl group acts as a metal recognition element.[3] Unfunctionalized olefins, however, have remained a more challenging substrate class.

The BIPI ligands are a modular and electronically tunable ligand platform invented in the late 1990s[4] and designed for ready optimization to enable asymmetric transformations with differing electronic and steric requirements. Highly selective asymmetric hydrogenations of ene-ureas,[5] ene-carbamates, and enamides[6] with the rhodium complexes of a variety of these engineered ligands (Figure 1) have been achieved. The first applications of these systems to unfunctionalized olefins are described below.

Pfaltz et al.[7] and Buchwald et al.[8] have reported asymmetric hydrogenations of tri- and tetrasubstituted olefins with cationic iridium BAr^F and zirconocene catalysts, respectively. The Ir(COD)BAr^F complex of BIPI 153 was thus prepared and examined in the AH of tetrasubstituted olefin **1** (Scheme 1). Full conversion was obtained with 1 bar of H_2, yet a disappointing *er* of only 74:26 was observed. This established that the successful ligands for functionalized alkenes were unsuitable for the more diffcult substrate class. A systematic ligand optimization study was therefore initiated.

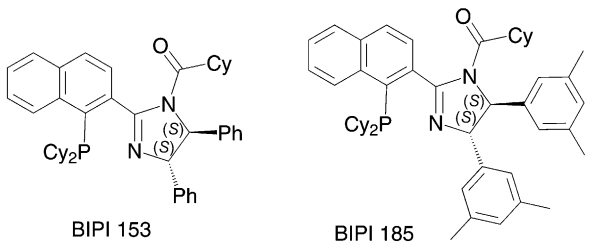
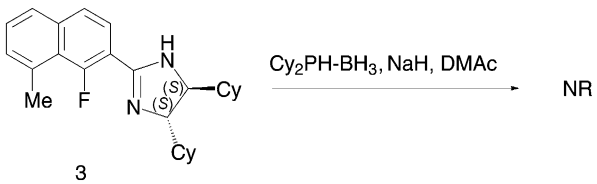


Figure 1. BIPI ligands for functionalized olefin AH.



Scheme 1. Failed S_NAr reaction.

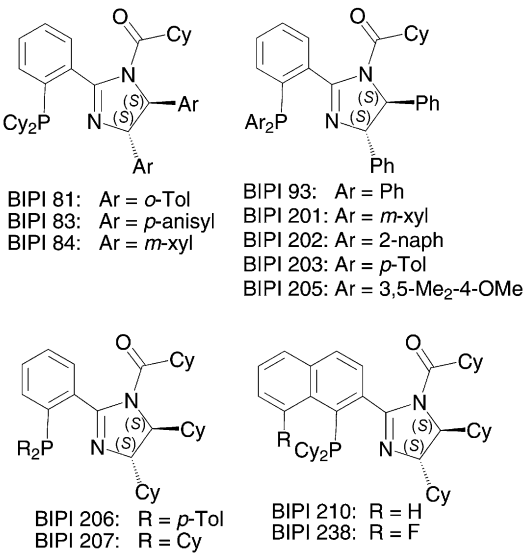
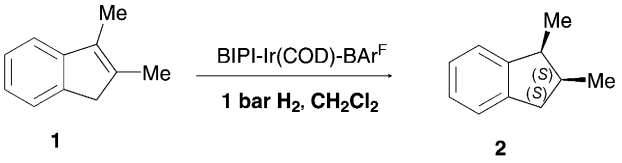


Figure 2. Ligands converted to cationic iridium BAr^F complexes.

A variety of structurally diverse BIPI ligands (Figure 2) were converted to their cationic iridium-(COD)BAr^F complexes, and all were purified by silica gel chromatography. Only *N*-acyl-containing ligands were chosen, as we have previously shown that all successful AH ligands require this functionality.[5,6,9] There are four subclasses of possible substitution patterns when either aryl or alkyl groups are chosen for the phosphorus and imidazoline substituents of the ligand. Examples of all four types were thus selected so that the different systems could be compared. Methanol, CH_2Cl_2 and toluene were examined as hydrogenation solvents for several of these complexes, and the highest conversions were consistently observed in CH_2Cl_2. Examination of these ligands in the asymmetric hydrogenation of dimethylindene **1** was then carried out under 1 bar of H_2 in CH_2Cl_2. The results for this screening set are shown in Table 1.

The complexes derived from ligands with dialkylphosphines and diarylimidazolines (BIPI 81, 83, and 84) showed low conversion, low selectivity, or both. Ligands with aryl groups on phosphorus and carbon (BIPI 93, 201–203, 205) all gave full conversion, yet the highest selectivity observed was 89:11 *er* (BIPI 93). Aryl *P*-substitution paired with *C*-alkyl groups (BIPI 206) gave full conversion yet a diminished *er* of 84:16. The fourth subclass, with alkyl substitution for both elements, proved to be optimum as long as small alkyl groups (Et, *i*-Pr) were avoided. BIPI 207, with a phenyl ligand core and cyclohexyl on phosphorus, provided product **2** with full conversion and 94:6 *er*. When the analogous naphthyl core ligand to BIPI 207, (BIPI 210), was examined, quantitative conversion with a slightly higher selectivity (95:5 *er*) was observed.

Table 1. AH of dimethylindene **1**.[a]



Ligand	% Conversion	*er* of **2**
BIPI 81	8	57:43
BIPI 83	100	65:35
BIPI 84	19	63:37
BIPI 93	100	89:11
BIPI 153	100	74:26
BIPI 201	100	77:23
BIPI 202	100	81:19
BIPI 203	100	85:15
BIPI 205	100	78:22
BIPI 206	100	84:16
BIPI 207	100	94:6
BIPI 210	100	95:5
BIPI 238	**100**	**98:2**

[a] Ir-COD-BAr^F complexes, CH_2Cl_2, 1 bar H_2, *dr* > 100:1.

Thus, the advantage of the naphthyl core ligands over the phenyl core, first observed in functionalized olefin hydrogenations, may also be in effect for the unfunctionalized substrates. For the former substrate class, strong evidence for the importance of the naphthyl peri proton (H-8) was gathered.[6] This may involve conformational restriction of the phosphine substituents leading to increased selectivity.

Efforts to incorporate a larger peri substituent on the naphthalene core were then undertaken. Fluoroimidazoline **3** with a methyl group at the peri position was prepared, yet the subsequent S_NAr reaction with the anion of dicyclohexylphosphine·borane failed (Scheme 1). The most likely explanation for this is the severe steric constraints imposed by 1,8-disubstituted naphthalenes.[10] The higher halogens (Cl, Br) suffered reduction by the phosphine·borane anion.

Reducing the size of the peri substituent to fluorine, however, gave a successful S_NAr reaction which, in turn, led to the 8-fluoro ligand BIPI 238. When the iridium complex of this ligand was screened against olefin **1**, full conversion with 98:2 *er* was obtained. The selectivity observed with BIPI 238 is the highest ever reported for this challenging substrate.

The synthetic limitations described above prevent a complete study of steric and electronic effects of the peri position in this ligand series. A fluorine electronic effect seems unlikely, though, in light of the reduced selectivity seen with less electron-donating *P*-substituents. Our current working hypothesis is thus steric in origin. Fluorine has a larger covalent radius[11] (~60 pm *vs.* 31 pm), than hydrogen, as well as a larger A value[12] (0.15 *vs.* 0.0). The steric de-

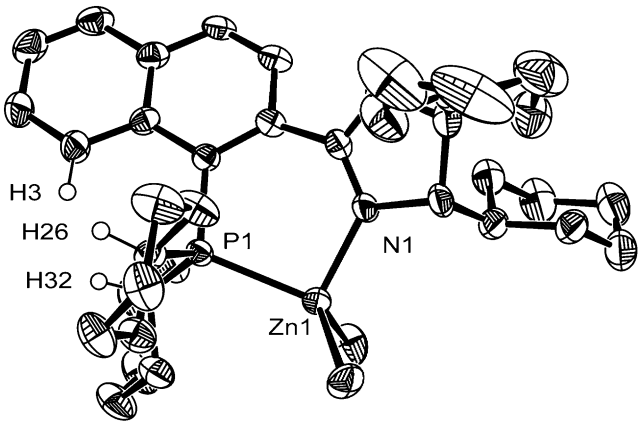


Figure 3. ORTEP diagram of the crystal structure of the zinc complex.

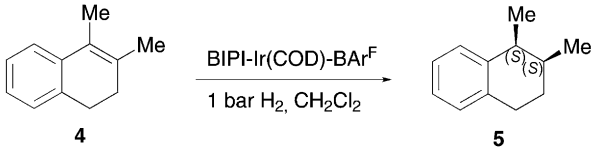
mands of this substituent may in effect be "magnified" by the unique interactions of 1,8-disubstituted naphthalenes. Insight into the sterics of these systems was gained through examination of the zinc complex precursor to BIPI 210. The crystal structure is shown in Figure 3.

The distances from the peri proton (H-3) to the two methine protons of the phosphine cyclohexyl rings (H-26, H-32) are only 1.997 and 2.151 Å, and the peri H–P distance is just 2.771 Å. All values are less than the sum of the van der Waals radii.

With several highly enantioselective catalysts in hand, additional unfunctionalized olefin substrates were then examined. Asymmetric hydrogenation of dimethyldihydronaphthalene **4** was studied, and the results are shown in Table 2.

Direct comparisons to the indene substrate **1** reveal that the dihydronaphthalene **4** is generally more difficult to hydrogenate enantioselectively. The *P*-aryl/*C*-aryl combination was again found to be the poorest ligand subclass. With substrate **4**, only the alkyl/alkyl substitution pattern led to full conversion with enantioselectivities above 90:10 *er*. The superiority of the 8-fluoro ligand BIPI 238 was again observed, providing the target with full conversion and 95:5 *er*. The less sterically demanding 8-H ligand, BIPI 210, furnished **5** in 93:7 *er*. In all cases, only a single diastereomer was observed.

Table 2. AH of dimethyldihydronaphthalene **4**.



4 **5**

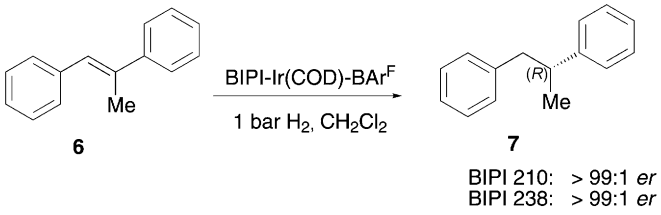
Ligand	% Conversion	*er* of **5**
BIPI 81	26	56:44
BIPI 83	100	54:46
BIPI 84	47	51:49
BIPI 93	89	67:33
BIPI 153	100	54:46
BIPI 201	100	55:45
BIPI 202	100	58:42
BIPI 203	100	65:35
BIPI 205	100	57:43
BIPI 206	100	87:13
BIPI 207	100	90:10
BIPI 210	100	93:7
BIPI 238	**100**	**95:5**

In comparison, the optimzed PHOX ligand gave **5** in 89:11 *er*,[7] although without complete conversion, while the best zirconocene catalyst[8] has been reported to give **5** in 96:4 *er*, yet this was carried out under almost 200 bar of H_2.

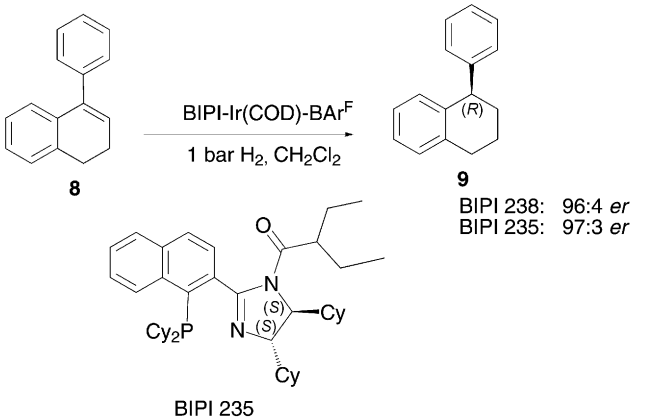
Two additional unfunctionalized olefin substrates were then studied, using a more reduced list of ligands. As shown in Scheme 2, treatment of (*E*)-α-methylstilbene **6** with the iridium complex of either BIPI 210 or BIPI 238 under 1 bar of H_2 gave adduct **7** in >99:1 *er*.

Reduction of phenyldihydronaphthalene **8** under 1 bar of H_2 with BIPI 238 (Scheme 3) gave adduct **9** in 96:4 *er*, while the branched, acyclic-amide ligand BIPI 235 provided the reduced product with an even higher selectivity of 97:3 *er*.

In summary, systematic optimization of the BIPI ligand platform has led to catalysts capable of asymmetric hydrogenation of unfunctionalized olefins with selectivities among the best reported for these difficult substrates. The importance of the naphthyl peri



Scheme 2. AH of trisubstituted olefin **6**.



Scheme 3. AH of olefin **8**.

position, first observed in the hydrogenation of functionalized olefins, has now been seen to operate for unfunctionalized olefins as well. By judicious choice of the ligand substituents, multiple classes of substrates can now be hydrogenated by these systems with excellent selectivity. Further applications of the naphthyl core BIPI ligands in olefin asymmetric hydrogenation are currently in progress.

Experimental Section

General Remarks

^{1}H and ^{13}C NMR chemical shifts were calibrated *vs.* the deuterated solvent used. ^{1}H and ^{13}C NMR data in $CDCl_3$ were calibrated using 7.24 ppm and 77.0 ppm, C_6D_6 using 7.20 and 128.0 ppm, CD_2Cl_2 using 5.32 and 53.5 ppm, and DMSO-d_6 using 2.49 and 39.5 ppm. ^{11}B NMR chemical shifts are uncalibrated. All NMR spectra were collected on Bruker Avance spectrometers equipped with a 5 mm BBI probe (^{1}H, ^{13}C, ^{31}P) or a 5 mm QNP probe (^{19}F), each with z-gradient, at 30 °C, unless otherwise indicated. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra frequencies were ^{1}H: 600, 500 or 400 MHz; ^{13}C: 150, 125, or 100 MHz; ^{19}F: 471 or 376 MHz; ^{31}P: 202 or 162 MHz; ^{15}N: 51 MHz. Where multiplicity is determined for ^{13}C NMR data, any multiplicity listed first (s, d, t, q) refers to multiplicity *with respect to* ^{1}H. If coupling to other nuclei is present (^{19}F, ^{31}P, ^{11}B.), that coupling constant is listed *second*, and normally explicitly described. Boron is a quadrupolar nucleus with spin of 3/2. It therefore causes quadrupolar line broadening of attached nuclei, here ^{31}P and ^{1}H. This is seen in the spectra of all phosphine·borane starting materials and products.

Accurate mass measurements were performed on a time of flight mass spectrometer (LC/MSD TOF) operating in a positive electrospray ionization mode with the capillary voltage of 3 kV. The mass spectrometer was tuned and calibrated using a tuning mix prior to sample analysis. Samples were introduced to the mass spectrometer by flow injection using an HPLC system. All reagents were used as received unless stated otherwise.

All free secondary phosphines are pyrophoric and should be handled with great care. Dicyclohexylphosphine·borane and di-*tert*-butylphosphine·borane were purchased and used as received.

All of the deprotonations with NaH described below cause (***caution!***) gas evolution (H_2) and foaming to various degrees. It is therefore best to use an *oversize* flask or reactor to contain the foams that are generated.

BIPI 210, Part 1: Fluoronaphthylimidazoline

A 3-neck 2-L flask was charged with 1-fluoro-2-naphthaldehyde (31.0 g, 178 mmol, 1 equiv.), CH_2Cl_2 (700 mL), and crystalline (*S*,*S*)-1,2-dicyclohexylethylenediamine (40.0 g, 178 mmol, 1 equiv.) in the order given. The resulting yellow solution was stirred under argon at room temperature. After 3 h at room temprature, the flask was cooled in an ice bath, then NBS (33.1 g, 187 mmol, 1.05 equiv.) was added neat, at once. The mixture was then allowed to slowly warm to room temperature under argon. After 2 h at room temperature, 1 N NaOH (500 mL) was added, and the resulting mixture stirred vigorously. After ~5 min, the product began to precipitate from the organic phase. After 15 min, the 2-phase slurry was filtered. The filter cake was washed first with CH_2Cl_2 (~150 mL), then with H_2O (~500 mL). The resultant damp white solid was then dried on the frit under a flow of nitrogen for 4 h. As the crop 1 solids were drying, the original 2-phase filtrate was processed as follows: the phases were separated, and the organic phase washed with H_2O (1×700 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow solid. This solid was then suspended in MTBE (~200 mL) and the mixture heated to reflux. The slurry thus obtained was then filtered hot. The filter cake was then washed with MeOH (~100 mL) and air-dried on the frit to give 12.5 g of a light yellow powder. HPLC showed both crops were completely pure. KF of crop 1 after 4 h drying showed <1000 ppm H_2O, and 34.4 g of the fluoronaphthylimidazoline was obtained as a white powder. The combined yield of both crops was 46.9 g (70%); mp 197–199 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.13 (m, 2H), 7.83 (m, 1H), 7.62 (d, J = 9 Hz, 1H), 7.56 (m, 2H), 5.70 (br s, 1H), 1.81–1.65 (m, 10H), 1.41 (m, 2H), 1.31–1.00 (m, 10H); ^{13}C NMR (500 MHz, $CDCl_3$): δ = 157.8 (s, $^{3}J_{C,F}$ = 2 Hz), 157.0 (s, $^{1}J_{C,F}$ = 256 Hz), 135.7 (s, $J_{C,F}$ = 6 Hz), 127.9 (d), 127.5 (d, $J_{C,F}$ = 3 Hz), 126.7 (d, $J_{C,F}$ = 2 Hz), 126.6 (d, $J_{C,F}$ = 4 Hz), 123.6 (d, $J_{C,F}$ = 4 Hz), 123.5 (s, $J_{C,F}$ = 11 Hz), 121.1 (d, $J_{C,F}$ = 7 Hz), 112.7 (s, $J_{C,F}$ = 9 Hz), 73.6 (d), 64.1 (d), 43.4 (d), 28.9 (t), 28.6 (t), 26.7 (t), 26.4 (t), 26.3 (t); ^{19}F NMR (471 Hz, $CDCl_3$): δ = −123.8; HR-MS: m/z = 379.2553, calcd. for [$C_{25}H_{31}FN_2$ + H^+]: 379.2544 (error = 2.36 ppm).

BIPI 210, Part 2: S_NAr Reaction/Zinc Complex Formation

A 3-neck 2-L flask equipped with a direct argon line and septa was charged with (*S*,*S*)-fluoronaphthylimidazoline (50.0 g, 132 mmol, 1 equiv.), dicyclohexylphosphine·borane (33.6 g, 158 mmol, 1.2 equiv.) and anhydrous DMAc (300 mL) in the order given. Argon sparging beneath the surface of the white suspension was then started. After 15 min, the flask was placed in an ice bath, then 60% NaH (11.65 g, 290 mmol, 2.2 equiv.) was added in 2 portions, ~10 min apart, causing immediate gas evolution and foaming, and giving a yellow reaction mixture. After 15 min, the ice bath was removed and the mixture allowed to warm to room temperature. After 20 min at room temperature, argon sparging was stopped and the white suspension was stirred vigorously under argon. After stirring 14 h at room temperature, a dark red solution was present. HPLC showed that the starting material had been consumed, and ~6:1 ratio of product:de-boronated product was present. The reaction mixture was cautiously poured onto ice (500 cm^3) + saturated NH_4Cl (300 mL). The resulting mixture was then extracted with EtOAc (2×500 mL). The combined organics were then washed with H_2O (1×500 mL), dried ($MgSO_4$), and the solvents removed under vacuum to give a yellow foam. This foam was then dissolved in MTBE (750 mL) in a 2-L 3-neck flask. To this solution, stirring under argon at room temperature, was then added 4 N HCl/*p*-dioxane (33 mL, 132 mmol, 1 equiv.) dropwise *via* syringe over ~10 min, giving a thick slurry of the HCl salt. After 15 min, the slurry was filtered under N_2. The solids were

then pulverized under MTBE on the frit and re-filtered under N_2. After ~30 min, 88 g (~100%) of crude, dry, phosphineborane imidazoline HCl salt was obtained as a light yellow powder. A 3-neck 2-L flask equipped with a direct argon line, reflux condenser and septum with thermocouple was charged with free base (*S*,*S*)-imidazolinephosphine·borane [82.7 g, 0.145 mol, from 88 g HCl salt after partitioning between 0.5 N NaOH and EtOAc and drying ($MgSO_4$)] and 190 proof ethanol (450 mL). Argon sparging beneath the yellow solution surface was then started. After 10 min, argon sparging was stopped, and the mixture heated to gentle reflux under argon. After 45 min at reflux, HPLC showed that the de-boronation was complete to a longer-retention time peak. The mixture was then cooled to room temperature while sparging with argon and the solvents were then removed under vacuum. The residual yellow semi-solid was then dissolved in THF (500 mL) which had been de-oxygenated by sparging vigorously with N_2 for 30 min prior to use, and placed in a 3-neck 2-L flask equipped with a direct argon line, inert gas valve, septum with thermocouple, and a graduated 250 mL addition funnel. Argon sparging beneath the yellow solution surface was then started. After 10 min, 1 M $ZnCl_2/Et_2O$ (145 mL, 0.145 mol, 1 equiv.) was charged to the addition funnel *via* cannula under N_2 pressure. While continuing to sparge with argon, this solution was then added dropwise over ~10 min to the well-stirred reaction mixture, causing an exotherm from 22.4 °C to 25.3 °C. When ~60% of the $ZnCl_2$ solution had been added, the reaction mixture converted from a clear yellow solution to a white suspension. After 20 min, the volatiles were removed under vacuum. To the residue, in a round-bottom flask, was then added *i*-PrOH (200 mL) and the mixture heated to reflux under argon. A clear solution was never obtained, though crystallization occurred in a slurry-to-slurry conversion. After 10 min at reflux, the mixture was cooled to room temperature and the resultant slurry filtered under a vigorous flow of N_2 in a medium-fritted filter funnel, washing the filter cake with additional *i*-PrOH (~50 mL). After 20 min drying on the frit, 73.4 g (73%) of the phosphinoimidazoline·zinc chloride complex was obtained as a dense, white powder, which crystallized as the mono-*i*-PrOH solvate; mp >250 °C. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.48 (br s, 1H), 8.37 (d, J = 8 Hz, 1H), 8.20 (d, J = 8 Hz, 1H), 8.08 (d, J = 8 Hz, 1H), 7.73 (m, 1H), 7.69 (m, 2H), 4.34 (d, J = 4 Hz, 1H), 4.08 (br s, 1H), 3.78 (m, 1H), 3.60 (m, 1H), 3.50 (m, 1H), 2.96 (br s, 1H), 2.63 (m, 1H), 2.12 (m, 1H), 2.04 (m, 1H), 1.89–1.07 (m, 42H), 1.04 (d, J = 6 Hz, 6H), 1.02–0.73 (m, 3H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 165.9 (s), 136.1 (s, $^1J_{C,P}$ = 21 Hz), 134.7 (s, $J_{C,P}$ = 4 Hz), 133.6 (s), 131.5 (d), 129.2 (d), 127.6 (d, $J_{C,P}$ = 4 Hz), 127.2 (d), 126.9 (d), 71.4 (d), 67.0 (t), 62.0 (d), 61.1 (d), 41.9 (d, $^1J_{C,P}$ = 49 Hz), 35.1 (d, $J_{C,P}$ = 4 Hz), 34.4 (d), 31.4 (t), 31.3 (t), 30.6 (t), 29.3 (t), 28.0 (t), 27.9 (t), 27.7 (t), 27.4 (t), 26.45 (t), 26.38 (t), 26.27 (t), 26.25 (t), 26.16 (t), 26.12 (t), 26.04 (t), 26.00 (t), 25.74 (t), 25.66 (t), 25.63 (t), 25.5 (q), 25.4 (t), 25.2 (t), 25.1 (t); ^{31}P NMR (202 MHz, DMSO-d_6): δ = −8.94; HR-MS: m/z = 557.4014, calcd. for [$C_{37}H_{53}N_2P$ + H^+]: 557.4019 (error = 0.92 ppm).

The crystal structure data for the complex have been deposited with the Cambridge Crystallographic Database (CCDC 915865). These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

BIPI 210 Part 3: Decomplexation

A 3-neck 100-mL flask equipped with a direct argon line, inert gas valve and septum was charged with the phosphinoimidazoline·zinc chloride complex *i*-PrOH solvate (1.00 g, 1.33 mmol, 1 equiv.), and CH_2Cl_2 (15 mL). Argon sparging beneath the colorless solution surface was then started. After 10 min, ethylenediamine (0.178 mL, 2.66 mmol, 2 equiv.) was added at once *via* syringe, causing immediate formation of a white precipitate. After 15 min, the reaction mixture was filtered under a vigorous flow of N_2 through a thin Celite pad in a medium-fritted filter funnel into a 100-mL 1-neck flask, washing the pad with CH_2Cl_2 (~5 mL). The solvents were then removed under vacuum, and the residual solids dried under high vacuum to give 0.75 g (~100%) of the free phosphinoimidazoline product as a light yellow foam which was used without further purification.

BIPI 210 Part 4: Acylation

The free phosphinoimidazoline described above was dissolved in CH_2Cl_2 (10 mL) and transferred to a 3-neck 50-mL flask. The solution was then cooled under argon to ~2 °C in an ice bath. TEA (0.37 mL, 2.66 mmol, 2 equiv.) was then added *via* syringe, followed after 5 min by CyCOCl (0.18 mL, 1.33 mmol, 1 equiv.). After a further 5 min, the ice bath was removed. After 30 min at room temperature, *N*,*N*,*N*′-trimethylethylenediamine (0.10 mL) was added to scavenge any unreacted acid chloride. The volatiles were then removed under vacuum. The residue was partitioned between EtOAc (20 mL) and 0.5 N HCl (20 mL) and the phases were separated. The organic phase was then washed with saturatedd $NaHCO_3$ (1 × 20 mL), dried ($MgSO_4$), and the solvents removed under vacuum to give a light yellow foam. This material was then chromatographed on silica gel under N_2 pressure, eluting with 6:1 hexane: EtOAc, and capping fractions as soon as they were collected to prevent any oxidation. The active fractions were then combined and concentrated under high vacuum to give 0.656 g BIPI 210 (74%) as a light yellow foam. ***Note:*** Hindered rotation in these ligands coupled with many conformations of the five cyclohexyl rings leads to extreme line broadening in all nuclei, with peak doubling and broad envelopes of resonances observed, even with highly purified materials. This NMR behavior has been noted previously (*Org. Lett.* **2008**, *10*, 341, see the Supporting Information). ^{1}H NMR (500 MHz, C_6D_6): δ = 8.41 (br m, 1H), 7.64–7.47 (m, 3H), 7.38 (t, J = 7 Hz, 1H), 7.21 (t, J = 7 Hz, 1H), 4.56 (br m, 1H), 3.87 (br m, 1H), 2.71–0.16 (m, 55H); ^{13}C NMR (125 MHz, C_6D_6): δ = 174.2 (s), 159.0 (s), 144.5 (s), 137.1 (s), 136.6 (s), 134.6 (s), 134.3 (s), 130.7 (d), 130.2 (d), 127.8 (d), 127.2 (d), 127.1 (d), 127.0 (d), 74.1 (d), 73.4 (d), 65.9 (d), 65.3 (d), 43.5 (d), 43.1 (d), 38.1 (d), 38.0 (d), 37.2 (d), 37.1 (d), 35.0 (t), 34.8 (t), 34.2 (t), 34.0 (t), 33.9 (t), 31.4 (t), 31.3 (t), 30.4 (t), 30.1 (t), 29.8 (t), 29.5 (t), 28.2 (t), 28.0 (t), 27.4 (t), 27.3 (t), 27.2 (t), 27.1 (t), 26.9 (t), 26.2 (t), 26.0 (t), 25.7 (t); ^{31}P NMR (202 MHz, C_6D_6): δ = −0.53 (minor), −4.43 (major); HR-MS: m/z = 667.4759, calcd. for [$C_{44}H_{63}N_2OP$ + H^+]: 667.4751 (error = 1.2 ppm).

BIPI 210 Iridium Complex

A 3-neck 100-mL flask equipped with a direct argon line, inert gas valve and septum was charged with (*S*,*S*)-BIPI 210 (0.395 g, 0.592 mmol, 1 equiv., weighed in glovebox), $[Ir(COD)Cl]_2$ (0.216 g, 0.326 mmol, 0.55 equiv., 1.1 Ir equiv., weighed in glovebox), and dry CH_2Cl_2 (17 mL) was then added *via* syringe. Slow argon sparging beneath the surface of the red solution was started immediately. After 5 min, $NaBAr^F$ (0.571 g, 0.650 mmol, 1.1 equiv.) was added at once. After 30 min at room temperature, TLC (CH_2Cl_2) of an aliquot showed the expected very non-polar red spot for the anion-exchanged BAr^F complex. The volatiles were then removed under vacuum and the residue chromatographed on silica gel under N_2 pressure eluting with 3:1 CH_2Cl_2:hexane, collecting only the center fractions, to give 0.90 g (83%) of the BIPI 210 iridium BAr^F complex as a red foam. ***Note:*** Hindered rotation in these ligands coupled with different conformations of the five cyclohexyl rings leads to extreme line broadening in all nuclei, peak doubling or trebling, and broad envelopes of resonances observed, even with *highly* purified materials. In addition, there is quadrupolar line broadening caused by abundant ^{191}Ir and ^{193}Ir (both spin 3/2). This NMR behavior has been noted previously (*Org. Lett*. **2008**, *10*, 341, see the Supporting Information). ^1H NMR (500 MHz, CD_2Cl_2): $\delta = 7.77$ (s, 9H), 7.61 (s, 5H), 7.37 (m, 6H), 5.11–3.77 (m, 2H), 2.84–0.35 (m, 63H); ^{13}C NMR (125 MHz, CD_2Cl_2): $\delta = 176.0$ (s), 162.2 (s, $^2J_{C,F} = 50$ Hz), 149.8 (d), 135.2 (d), 129.3 (s, qq, *C*-B, $^4J_{C,F} = 3$ Hz, $^1J_{C,B} = 32$ Hz), 125.0 (s, *C*-F, $^1J_{C,F} = 270$ Hz), 117.8 (d, 5 lines, $J = 4$ Hz), 93.5 (d, $J = 9$ Hz), 86.4 (d, $J = 13$ Hz), 70.2 (d), 67.6 (d), 66.8 (d), 63.4 (d), 44.7 (d), 44.3 (d), 42.2 (d), 39.2 (d, $J_{C,P} = 23$ Hz), 37.3 (d, $J_{C,P} = 4$ Hz), 32.5 (d, $J_{C,P} = 27$ Hz), 31.4 (t), 30.8 (t), 30.1 (t), 29.9 (t), 29.7 (t), 29.5 (t), 29.3 (t), 29.2 (t), 29.1 (t), 28.3 (t), 27.2–25.3 [broad baseline below 17 lines, all (t)]; ^{31}P NMR (202 MHz, CD_2Cl_2): $\delta = 55.5$ (major isomer); HR-MS: $m/z = 943.5173$, calcd. for $[C_{50}H_{75}IrN_2OP]$: 943.5241 (error = 7.2 ppm).

BIPI 238, Part 1: 1,8-Difluoro-2-naphthaldehyde

To a 250-mL three-neck flask with magnetic stirring bar, rubber septum, and low temperature thermometer, was charged with 1,8-dibromonaphthalene (2.84 g, 10 mmol, 1 equiv.). The reaction flask was evacuated and then refilled with N_2 (3×). Anhydrous THF (50 mL) was then added *via* syringe. The reaction mixture was cooled to −78 °C by a dry ice/acetone bath. 1.6 M *n*BuLi/hexane (20 mL, 32 mmol, 3.2 equiv.) was added dropwise *via* syringe, keeping the internal temperature below −68 °C. After the addition was complete, the reaction mixture was further stirred for 1 h at −75 °C. NFSI (9.45 g, 30 mmol, 3 equiv.) was then dissolved in anhydrous THF (25 mL), and the resultant solution was added to the reaction mixture *via* syringe, keeping the internal temperature below −50 °C. Without removal of the cooling bath, the reaction mixture was allowed to warm up overnight and stirred for another 4 h at room temperature the following day. The reaction mixture was then filtered to remove insoluble by-products. A sample from the filtrate was checked by GC-MS, which showed the desired 1,8-difluoronaphthalene as the major component. The filtrate was carefully concentrated (~20 °C/100 mm) by rotary evaporation (***caution!*** the product is volatile!), and purified by chromatography on silica gel with pentane as eluent. The major fraction was again carefully concentrated to give 8.5 g of a pale pink solution, which contained about 1.1 g 1,8-difluoronaphthalene (~67%) by NMR assay. Complete removal of solvent was avoided because of the volatility of the desired compound, and the solution was used directly in the subsequent step. ^1H NMR (400 MHz, $CDCl_3$): $\delta = 7.59$ (H-4, dd, $J = 0.8$, 8.0 Hz, 2H), 7.39 (H-3, tt, $J = 2.4$, 8.0 Hz, 2H), 7.13 (H-2, m, 12 lines, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 157.6$ (s, C-1, $^1J_{C,F} = 259$ Hz, $^3J_{C,F} = 12$ Hz), 137.3 (s, C-4a, $^{3,3}J_{C,F} = 3$, 3 Hz), 126.7 (d, C-3, $^{3,5}J_{C,F} = 3$, 3 Hz), 123.4 (d, C-4, $^{4,4}J_{C,F} = 4$, 4 Hz), 114.4 (s, C-8a, $^{2,2}J_{C,F} = 12$, 12 Hz), 111.2 (d, C-2, $^{2,4}J_{C,F} = 10$, 13 Hz); ^{19}F NMR (471 MHz, $CDCl_3$): $\delta = -115.8$. GC-MS: 164 (M^+), 144, 123.

A 3-neck 100-mL flask equipped with an inert gas valve and septum with thermocouple was evacuated/argon filled (2×), then it was charged with dry THF (9.0 mL) *via* syringe, and the solution cooled to −78 °C under argon. Once equilibrated, 1.4 M *s*BuLi/cyclohexane (3.70 mL, 5.19 mmol, 1.1 equiv.) was added dropwise *via* syringe over 10 min while maintaining the internal temperature below −60 °C, giving a yellow reaction mixture. After aging for 15 min, a solution of 1,8-difluoronaphthalene (0.773 g, 4.71 mmol, 1 equiv.) + pentane (6.0 mL) was added dropwise *via* syringe over ~5 min, giving a dark green reaction mixture. The resultant mixture was then aged for 3 h at −78 °C, at which point an orange reaction mixture was present. Dry DMF (0.45 mL, 5.75 mmol, 1.2 equiv.) was then added dropwise *via* syringe over ~5 min. After 5 min, the −78 °C bath was replaced with a 0 °C bath. After 15 min at ~0 °C, TLC (hexane) showed clean conversion to a significantly more polar, brilliantly blue-fluorescing spot. The reaction was quenched at 0 °C by the slow addition of 0.5 N HCl (10 mL), then H_2O (15 mL) and MTBE (25 mL) were added. The phases were then separated and the aqueous phase re-extracted with MTBE (1×50 mL). The combined organics were then dried washed with H_2O (1×25 mL), dried ($MgSO_4$), and the solvents removed under vacuum to give an orange solid. This material was then fully dissolved in boiling cyclohexane (~6 mL) and allowed to cool to room temperature while standing, causing crystallization. The slurry thus obtained was then filtered, using a small amount of cyclohexane to transfer the slurry and wash the cake. After air-drying on the frit ~10 min, 0.420 g (46% first crop recrystallized yield) of 1,8-difluoro-2-naphthaldehyde was obtained as a yellow, crystalline solid. The filtrates were concentrated to give an orange solid, which was then chromatographed on silica gel eluting with 10:1 hexane:EtOAc to give a further 0.20 of the aldehyde as a yellow solid. The combined yield was 0.62 g (69%); mp 86–87 °C. ^1H NMR (500 MHz, C_6D_6): $\delta = 10.28$ (s, H-9, $J_{H,F} = 0.7$ Hz, 1H), 7.71 (dd, H-3, $J = 6$, 9 Hz, 1H), 6.93 (m, H-4 + H-5, 2H), 6.82 (ddd, H-6, $J = 5$, 8, 8 Hz, 1H), 6.67 (ddd, H-7, $J = 0.8$, 8, 12 Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6): $\delta = 185.7$ (d, C-9, $^3J_{C,F} = 10$ Hz), 162.3 (s, C-1, $^3J_{C,F} = 2$ Hz, $^1J_{C,F} = 272$ Hz), 159.0 (s, C-8, $^3J_{C,F} = 1.4$ Hz, $^1J_{C,F} = 260$ Hz), 140.1 (s, C-4a, $^{3,3}J_{C,F} = 2$, 4 Hz), 130.2 (d, C-6, $^{5,3}J_{C,F} = 2$, 8 Hz), 124.4 (d, C-4, $^{4,4}J_{C,F} = 3$, 5 Hz), 124.1 (d, C-5, $^{5,3}J_{C,F} = 3$, 5 Hz), 123.7 (d, C-3, $^{3,5}J_{C,F} = 2$, 2 Hz), 120.9 (s, C-2, $^{4,2}J_{C,F} = 2$, 6 Hz), 114.4 (s, C-8a, $^{2,2}J_{C,F} = 12$, 12 Hz), 112.7 (d, C-7, $^{4,2}J_{C,F} = 2$, 20 Hz); ^{19}F NMR (470 MHz, $CDCl_3$): $\delta = -112.7$ (F-8, $J_{F,F} = 66$ Hz), −123.6

(F-1, $J_{F,F}=66$ Hz); HR-MS: $m/z=210.0724$, calcd. for $C_{11}H_6F_2O+NH_4^+$]: 210.0725 (error = 0.46 ppm).

BIPI 238, Part 2: Difluoronaphthylimidazoline

A 3-neck 50-mL flask was charged with 1,8-difluoro-2-naphthaldehyde (0.60 g, 3.12 mmol, 1 equiv.), CH_2Cl_2 (12 mL), and crystalline (*S*,*S*)-1,2-dicyclohexylethylenediamine (0.701 g, 3.12 mmol, 1 equiv.) in the order given. The resulting yellow solution was stirred under argon at room temperature. After 2.5 h at room temperature, the flask was cooled in an ice bath, then NBS (0.58 g, 3.28 mmol, 1.05 equiv.) was added neat, at once. After 15 min at ~2 °C, the ice bath was replaced by a cool water bath. After 2 h at room temperature, 1 N NaOH (25 mL) was added, and the resulting mixture stirred vigorously, causing a precipitate to form. After 15 min, the slurry was filtered, washing the solids with H_2O (1 × 25 mL). The solids were then pulverized on the frit under hexane (~25 mL), then filtered and air-dried on the frit for 60 min to give 1.2 g of a yellow powder. This solid was then fully dissolved in boiling *n*-heptane (60 mL) and allowed to cool to room temperature while standing, causing crystallization. The resultant slurry was then filtered, and the solids air-dried on the frit to give 0.687 g (55% 1st crop recrystallized yield) of the difluoronaphthylimidazoline as a fluffy, light yellow solid; mp 183–184 °C. ^{1}H NMR (500 MHz, C_6D_6): δ = 8.59 (dd, H-3, $J=7$, 8 Hz, 1 H), 7.17 (dd, H-4, $J=2.1$, 8 Hz, 1 H), 7.04 (dd, H-5, $J=1.6$, 8 Hz, 1 H), 6.85 (ddd, H-6, $J=5$, 8, 13 Hz, 1 H), 6.77 (dd, H-7, $J=$ 8, 12 Hz, 1 H), 5.48 (br s, N-H, 1 H), 3.85 (br s, H-10, 1 H), 3.21 (br s, H-11, 1 H), 2.04 (br s, 1 H), 1.89–1.47 (m, 10 H), 1.46–0.75 (m, 11 H); ^{13}C NMR (125 MHz, C_6D_6): δ = 158.2 (s, C-8, $^3J_{C,F}=2$ Hz, $^1J_{C,F}=254$ Hz), 157.1 (s, C-9, $^3J_{C,F}=2$ Hz), 156.1 (s, C-1, $^3J_{C,F}=2$ Hz, $^1J_{C,F}=256$ Hz), 138.0 (s, C-4a, $^{3,3}J_{C,F}=2.5$, 4 Hz), 128.9 (d, C-3, $^{5,3}J_{C,F}=1.6$, 3.5 Hz), 128.2 (d, C-6,), 123.5 (d, C-5, $^{4,4}J_{C,F}=3$, 4.5 Hz), 123.4 (d, C-4, $^{4,4}J_{C,F}=3$, 4 Hz), 115.1 (s, C-2, $^{4,2}J_{C,F}=2$, 9 Hz), 114.2 (s, C-8a, $^{3,3}J_{C,F}=11$, 14 Hz), 111.9 (d, C-7, $^{4,2}J_{C,F}=1.6$, 21 Hz), 74.2 (d, C-11), 64.3 (d, C-10), 44.2 (d), 43.5 (d), 29.7 (t), 29.3 (t), 29.1 (t), 28.4 (t), 27.1 (t), 26.8 (t), 26.4 (t), 26.3 (t); ^{19}F NMR (470 MHz, $CDCl_3$): δ = −114.7 (F-8, $J_{F,F}=69$ Hz), −117.2 (F-1, $J_{F,F}=69$ Hz); HR-MS; $m/z=397.2445$, calcd. for $[C_{25}H_{30}F_2N_2+H^+]$: 397.2450.

BIPI 238, Part 3: S_NAr Reaction/De-Boronation

A 3-neck 25-mL flask equipped with a direct argon line, inert gas valve and septum was charged with (*S*,*S*)-difluoronaphthylimidazoline (0.656 g, 1.65 mmol, 1 equiv.), dicyclohexylphosphine·borane (0.420 g, 1.97 mmol, 1.2 equiv.) and anhydrous DMAc (5.0 mL) in the order given. Argon sparging beneath the surface of the thick yellow suspension was then started. After 15 min, the flask was placed in an ice bath, then 60% NaH (0.145 g, 3.62 mmol, 2.2 equi.v) was added at once, causing immediate gas evolution and foaming, and giving a yellow reaction mixture. After 5 min, the ice bath was removed and the mixture allowed to warm to room temperature, at which point it was a wine-red color. After 4 h at room temperature, HPLC (@ 230 nm) showed 96% conversion to a peak with significantly longer retention time than the difluoride starting material. The reaction mixture was cautiously poured onto ice (25 cm^3) + saturated NH_4Cl (25 mL). The resulting mixture was then extracted with EtOAc (2 × 25 mL). The combined organics were then washed with H_2O (2 × 50 mL), dried ($MgSO_4$), and the solvents removed under vacuum to give a yellow oil. This oil was then fully dissolved in MTBE (25 mL) and transferred to a 100-mL 3-neck flask equipped with direct argon line, inert gas valve and septum. To this solution, stirring under argon at room temperature, was then added 4 N HCl/*p*-dioxane (0.41 mL, 1.65 mmol, 1 equiv.) dropwise via syringe over ~3 min, giving a thick slurry of the HCl salt. After 15 min, the slurry was filtered under N_2. The solids were then pulverized under MTBE on the frit and re-filtered under N_2. After ~15 min, 0.98 g (~95%) of the dry HCl salt was obtained as a non-hygroscopic, pale yellow powder. NMR showed it was a mixture of the phosphine·borane and the free phosphine, so the mixture was then fully de-protected as follows: A 3-neck 100-mL flask equpped with a direct argon line, reflux condenser with inert gas valve and septum was charged with absolute EtOH (40 mL) and argon sparging beneath the solution surface was started. After 15 min, the crude phosphine borane·HCl salt (0.75 g, ~1.20 mmol, 1 equiv.) was added, and the flask was placed in a pre-equilibrated 78 °C oil bath. Argon sparging was then stopped, H_2O was flowed through the condenser, and the light yellow solution was heated at gentle reflux under argon. After 60 min at reflux, HPLC showed complete conversion to a later-eluting peak. TLC (basic alumina, EtOAc) showed conversion to a much slower-moving spot. The reaction mixture was cooled, and then the volatiles were removed under vacuum. The residue was then azeotroped with PhMe at the Rotovap (1 × 50 mL) and finally dried under high vacuum to give 0.65 g of a yellow solid. This solid was then partitioned between EtOAc (50 mL) and saturated $NaHCO_3$ (50 mL). The phases were separated and the organic phase was dried ($MgSO_4$), and the solvents removed under vacuum. The residue was then chromatographed under N_2 pressure on basic alumina (Activity I), eluting with EtOAc and capping fractions as soon as they were collected to prevent oxidation. After concentration under vacuum, the residue was azeotroped with cyclohexane (1 × 20 mL) at the Rotovap, to give a yellow foam. This material was then fully dissolved in 2.0 mL boiling MeOH and allowed to cool to room temperature while standing under argon, causing crystallization. After 30 min at room temperature, the slurry was filtered under N_2 to give 530 mg (69%, 0.83 mmol) of the free phosphinoimidazoline as a pale yellow solid, which crystallized as the bis-methanol solvate; mp 101–102 °C. ^{1}H NMR (500 MHz, C_6D_6): δ = 7.72 (dd, H-3, $J=3$, 8 Hz, 1 H), 7.50 (d, H-5, $J=8$ Hz, 1 H), 7.26 (dd, H-5, $J=1$, 8 Hz, 1 H), 7.00 (ddd, H-7, $J=1.3$, 7.5, 7.5 Hz, 1 H), 6.96 (m, H-6, 1 H), 5.05 (br s, N-H, 1 H), 3.98 (br s, H-10, 1 H), 3.35 (br s, H-11, 1 H), 3.08 (s, H-14, 6 H), 2.57 (m, H-15 + H-16, 2 H), 2.34–0.80 (m, 42 H); ^{13}C NMR (125 MHz, C_6D_6): δ = 165.6 (s, C-9, $^3J_{C,P}=9$ Hz), 160.2 (s, C-8, $^1J_{C,F}=252$ Hz), 146.6 (s), 136.9 (s, C-4a, $J=5$ Hz), 130.7 (d, C-4), 128.9 (d, C-3, $^3J_{C,P}=11$ Hz, $^5J_{C,F}=1$ Hz), 126.6 (d, C-7, $^3J_{C,F}=9$ Hz), 126.4 (d, C-5, $J=$ 3 Hz), 125.2 (s), 113.3 (d, C-7, $^2J_{C,F}=25$ Hz), 77.3 (d, C-10), 65.7 (d, C-11), 50.4 (q, C-14), 44.7 (d, C-12/13), 43.4 (d, C-12/13), 36.64 (d, C-15, $^1J_{C,P}=54$ Hz, $J_{CF}=29$ Hz), 36.63 (d, C-16, $^1J_{C,P}=52$ Hz, $J_{C,F}=2$ Hz); ***note:*** all t's (CH_2's) follow, yet *J* values cannot be determined: 34.2 (t), 33.9 (t), 33.6 (t), 33.4 (t), 32.0 (t), 31.9 (t), 31.7 (t), 31.6 (t), 30.8 (t), 30.4 (t), 29.9 (t), 27.9 (t), 27.8 (t), 27.75 (t), 27.70 (t), 27.66 (t), 27.63

(t), 27.57 (t), 27.55 (t), 27.5 (t, br), 27.20 (t), 27.19 (t), 26.99 (t), 26.98 (t); ^{19}F NMR (376 MHz, C_6D_6): δ = −109.31; ^{31}P NMR (202 MHz, C_6D_6): δ = 10.74. HR-MS: *m/z* = 575.3936, calcd. for $[C_{37}H_{52}FN_2P+H^+]$: 575.3925 (error = 1.9 ppm).

BIPI 238, Part 4: Acylation

The phosphinoimidazoline bis-methanol solvate (0.500 g, 0.78 mmol, 1 equiv.) described above was azeotroped with THF (2×20 mL) at the Rotovap to remove the methanol that had co-crystallized. The resultant yellow oil was then transferred to a 3-neck 50-mL flask equipped with a direct argon line, inert gas valve and septum. CH_2Cl_2 (12 mL) was then added and slow arfon sparging beneath the solution surface was then started. After 10 min, the flask was placed in an ice bath, then TEA (0.219 mL, 1.57 mmol, 2 equiv,) was added *via* syringe, followed after 2 min by cyclohexanecarbonyl chloride (0.105 mL, 0.78 mmol, 1 equiv.), added dropwise *via* microsyringe over ~2 min. The ice bath was then removed and the mixture allowed to warm to room temperature. After 5 min at room temperature, TLC (7:1 hexane:EtOAc) showed the reaction was complete to a non-polar spot. *N*,*N*,*N*′-Trimethylethylenediamine (0.10 mL) was then added *via* syringe to scavenge any unreacted acid chloride. After 5 min, the volatiles were removed under vacuum and the residue partitioned between 0.5 N HCl (30 mL) and EtOAc (30 mL). The organic phase was then washed with saturated $NaHCO_3$ (1×30 mL), dried ($MgSO_4$), and the solvents removed under vacuum to give a yellow foam. This material was then chromatograhed under N_2 on silica gel eluting with 7:1 hexane:EtOAc. The pure fractions were collected, and they were capped as soon as they were collected to prevent oxidation. After concentration under vacuum, the residue was azeotroped with cyclohexane at the Rotovap, and finally dried under high vacuum to give 0.487 g (91%) of BIPI 238 as a light yellow foam. ***Note:*** Hindered rotation in these ligands coupled with numerous conformations of the five cyclohexyl rings leads to extreme line broadening in all nuclei, with peak doubling and broad envelopes of resonances observed, even with highly purified materials. This NMR behavior has been described previously (*Org. Lett*. **2008**, *10*, 341, see the Supporting Information). ^{1}H NMR (500 MHz, C_6D_6): δ = 7.56 (dd, *J* = 2.5, 8 Hz, 1 H), 7.45 (br s, 1 H), 7.25 (d, *J* = 8 Hz, 1 H), 7.00 (m, 1 H), 6.93 (m, 1 H), 4.55 (br s, 1 H), 3.90 (br s, 1 H), 2.75–0.40 (m, 55 H); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 159.7 (s, C-8, $^1J_{C,F}$ = 250 Hz), 146.6 (s), 129.9 (d), 129.6 (d), 128.2 (d), 126.4 (d), 125.8 (d), 113.0 (d, C-7, $^2J_{C,F}$ = 25 Hz), 73.5 (d), 65.2 (d), 43.2 (d), 42.7 (d), 37.7 (d), 37.6 (d), 37.5 (d), 36.7, 33.5, 31.1, 30.3, 29.5, 29.2, 27.3, 27.2, 27.1, 26.8, 26.7, 26.6, 25.7; ^{19}F NMR (471 MHz, DMSO-d_6): δ = −107.73, −109.30; ^{31}P NMR (162 MHz, DMSO-d_6): δ = 14.97, 10.13; HR-MS: *m/z* = 685.4621, calcd. for $[C_{44}H_{62}FN_2OP+H^+]$: 685.4657 (error = 5.2 ppm).

BIPI 238 Iridium Complex

A 3-neck 50-mL flask equipped with a direct argon line, inert gas valve and septum was charged with CH_2Cl_2 (15 mL). Slow argon sparging beneath the solution surface was then started. After 10 min, $[Ir(COD)Cl]_2$ (0.145 g, 0.216 mmol, 0.55 equiv., 1.10 Ir equiv., weighed in glovebox) was then added at once, giving a bright orange solution. After 10 min, (*S*,*S*)-BIPI 238 (0.269 g, 0.393 mmol, 1 equiv., weighed in glovebox) was then added at once to the vigorously stirred mixture, giving immediately a dark red solution. After 20 min, TLC (10:1 hexane:EtOAc) of an aliquot of the mixture showed a small amount of free ligand remains and there is a major polar spot. After 1.5 h at room temperature, TLC shows some ligand still remains, so an additional 25 mg of the iridium dimer was added. After a further 30 min, $NaBAr^F$ (0.382 g, 0.433 mmol, 1.1 equiv.) was added neat, at once, to the vigorously stirred reaction mixture. After 30 min, TLC (CH_2Cl_2) shows the reaction is complete to a very non-polar spot. The volatiles were then removed under vacuum to give a red foam. This foam was then chromatographed on silica gel under N_2 eluting with 1:1 CH_2Cl_2:cyclohexane and collecting only the center, pure fractions to give a semi-solid. This material was then azeotroped with MTBE (1×40 mL) at the Rotovap and finally dried under high vacuum to give 0.53 g (73%) of the iridium complex as a red foam. ***Note:*** Hindered rotation in these ligands coupled with different conformations of the five cyclohexyl rings leads to extreme line broadening in all nuclei, peak doubling or trebling, and broad envelopes of resonances observed, even with *highly* purified materials. In addition, there is quadrupolar line broadening caused by abundant ^{191}Ir and ^{193}Ir (both spin 3/2). This NMR behavior has been noted previously (*Org. Lett*. **2008**, *10*, 341, see the Supporting Information). ^{1}H NMR (500 MHz, CD_2Cl_2): δ = 8.22–7.22 (br m, 5 H), 7.64 (s, 11 H), 7.47 (s, 5 H), 5.01–2.49 (br m, 3 H), 2.45–0.17 (br m, 60 H); ^{13}C NMR (125 MHz, CD_2Cl_2): δ = 162.3 (s, *C*-CF_3, $^2J_{C,F}$ = 50 Hz), 135.4 (d), 129.4 (s, qq, *C*-B, $^4J_{C,F}$ = 3 Hz, $^1J_{C,B}$ = 32 Hz), 125.1 (s, $^1J_{C,F}$ = 272 Hz), 118.0 (d, 5 lines, *J* = 4 Hz), 63.71 (d, br), 32.1–24.5 (br baseline resonances); ^{19}F NMR (376 MHz, CD_2Cl_2): δ = −62.86; ^{31}P NMR (202 MHz, CD_2Cl_2): δ = 40.77, 23.13; HR-MS: *m/z* = 985.5083, calcd. for $[C_{52}H_{74}IrN_2OP]$: 985.5147 (error = 6.5 ppm).

General Procedure. Lab-Scale Screening Asymmetric Hydrogenations

To a vial were added 29 mg (0.15 mmol) *trans*-α-methylstilbene **6**, 5.5 mg (0.003 mmol) of Ir-(BIPI-238)(COD)BAr^F and 0.5 mL of degassed CH_2Cl_2 in the glovebox. The vial was inserted into a HEL CAT 24 autoclave reactor. The autoclave was then closed and transferred out of the glovebox. The reactor was first purged with N_2 (3×) and then cooled down to 0 °C followed by a hydrogen purge (3×). The autoclave was then pressurized to 1 bar H_2 and stirred at 0 °C for 20 h. The reactor was then vented, purged with N_2, and warmed to room temperature. The% conversion and% *ee* of **7** were then determined by chiral HPLC.

Enantioselectivity Determinations

2: Chiral GC, Astec Chiraldex B-PH @ 90 °C, isothermal; the retention times of the enantiomers are 14.07 min and 14.35 min.

5: Chiral GC, Astec Chiraldex B-PH @ 120 °C, isothermal; the retention times of the enantiomers are 10.64 min and 10.96 min.

7: Chiral HPLC, Chiralpak OJ-3, 99:1 heptane:EtOH, 25 °C, 1.0 mL min^{-1}.; The retention times of the enantiomers are 2.15 min and 3.20 min.

9: Chiral GC, Astec Chiraldex B-PH @ 150 °C, isothermal; the retention times of the enantiomers are 25.28 min and 26.81 min.

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