Electronic Supplementary Material (ESI) for Catalysis Science & Technology

Supplementary Data for

Development of the BIPI Ligands for Asymmetric Hydrogenation

Carl A. Busacca,*[a] Jon C. Lorenz, Anjan K. Saha, Sreedhar Cheekoori, Nizar Haddad, Diana Reeves, Heewon Lee, Zhibin Li, Sonia Rodriguez, and Chris H. Senanayake

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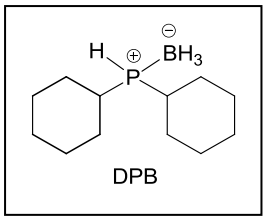
Contents:

General Experimental Comments

^{31}P and ^{19}F NMR chemical shifts were calibrated vs. external 85% H_3PO_4 (δ: 0.0 ppm) and neat C_6F_6 (δ: -162.3 ppm), respectively, contained in coaxial insert tubes (Wilmad WGS-5BL). ^{1}H and ^{13}C chemical shifts were calibrated vs. the deuterated solvent used. 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 ^{o}C, unless otherwise indicated. ^{1}H, ^{13}C, ^{19}F, and ^{31}P NMR spectra observe frequencies were ^{1}H: 600 or 500 MHz or 400 MHz; ^{13}C: 150 or 125 MHz; ^{19}F: 376 MHz; ^{31}P: 202 or 162 MHz. Where multiplicity is determined for ^{13}C 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 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. Once the dicyclohexylphosphine moiety is introduced into these compounds, hindered rotation is observed in all NMR spectra. This gives rise to complicated ^{1}H, ^{13}C, and even ^{31}P NMR spectra caused by the presence of rotamers. Some compounds show a ~ 1:1 mixture of rotamers, others show one major and one minor rotamer.

1-Fluoro-2-naphthaldehyde was prepared by a modification of the method of Schlosser *et al* [1] or purchased from Princeton Global Synthesis, New Jersey, USA. Imidazolines were usually prepared by a modification of the method of Fujioka *et al*.[2] Secondary phosphine boranes that were not commercially available were prepared as we have previously described.[3] The chiral diamines used in the ligand syntheses were purchased from DiaminoPharm, Toronto, Canada, and prepared by the stereoselective diaza-Cope rearrangements of Chin *et al*.[4]

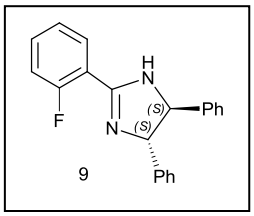
Accurate mass measurements were performed on a Time of Flight mass spectrometer (LC/MSD TOF) operating in a positive electrospray ionization mode with the capillary voltage of 3 kV. The mass spectrometer was tuned and calibrated using a tuning mix prior to sample analysis. Samples were introduced to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



DPB

Manufacture of Dicyclohexylphosphine Borane, DPB: [CAUTION! Dicyclohexylphosphine is a pyrophoric oil that burns spontaneously in air! It must be handled strictly under an inert atmosphere!] A 50 L reactor was inerted by three vacuum/N_2 cycles, and was then charged with 21.9 kg of 1M BH_3/THF (25L, 25.0 mol, 1.24 eq.) under N_2 pressure, and the batch was then cooled to 0.7 ^{o}C. A steel pressure cylinder containing 4.00 kg (20.17 mol, 1 eq.) of dicyclohexylphosphine was pressurized with N_2 and charged sub-surface to the cold borane solution over 25 minutes, causing the internal temperature to rise to 6.3 ^{o}C. The batch was then warmed to 23 ^{o}C over 10 minutes, aged 60 minutes at 23 ^{o}C, and then cooled to -1.6 ^{o}C over 40 minutes. 1.58 kg of methanol was then charged over 15 minutes, causing gas evolution for the first ~ 50% of the addition and an exotherm to 4.5 ^{o}C. The batch was aged 20 minutes at ~

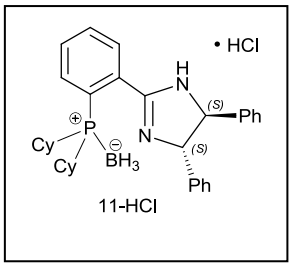
2 °C and the reactor was then configured for distillation. The batch was heated to 18 °C and volatiles were removed by distillation at 120 mm vacuum, collecting 17 L of distillate. 19 kg of 1N HCl was then charged to the batch over 10 minutes, followed by the addition of 36 L ethyl acetate. The batch was then warmed to 23 °C and agitation was stopped, giving two clear phases after ~ 20 minutes. The lower aqueous phase was then discharged to waste. The upper organic phase was then washed with 19 L 1N HCl, followed by 12 L of half-sat'd aq. NaCl, discharging the lower aqueous phase to waste each time. The reactor was then configured for distillation and volatiles were removed at 25 °C/90 mm to minimal stirrable volume, collecting 30 L of distillate. 16 L heptanes were then charged and distillation at 28 °C/90 mm was repeated to minimal stirrable volume. The distillation process was then repeated following a second 16 L charge of heptanes. 8.0 L heptanes were then charged and the batch was heated to 67 °C. The batch was then cooled linearly to 35 °C over 60 minutes, and 8.0 L of additional heptanes were charged. After 15 minutes, the resultant slurry was filtered with an Aurora filter under a vigorous flow of N_2. After 3h drying under maximum N_2 flow, the product was placed in a double polyethylene bag. 3.10 kg (72%) of dicyclohexylphosphine borane was obtained as a free-flowing, air-stable, white solid. M.p. 80 °C. δ_H (400 MHz, d_6-DMSO) 4.05 (1 H, dm, $^1J_{HP}$ 358), 1.76 (2 H, m), 1.68-1.52 (8 H, m), 1.47 (2 H, d, *J* 12.9), 1.20-0.96 (10 H, m), 0.14 (3 H, q, $^1J_{HB}$ 111). δ_C (100 MHz, d_6-DMSO) 28.7 (t, J_{CP} 2.9), 27.2 (d, $^1J_{CP}$ 33), 27.0 (t), 25.9 (t, J_{CP} 10.3), 25.7 (t, J_{CP} 12.2), 25.4 (t, J_{CP} 1.0). δ_P (162 MHz, d_6-DMSO) 13.9 ($^1J_{PB}$ 53).



9

Manufacture of BIPI 69, Part 1, Fluoroimidazoline 9: A 50 L reactor was charged with 2.00 kg (*S*,*S*)-diphenylethylenediamine (DPEDA, 9.42 mol, 1.0 eq.) and 2.40 kg fluoroimidate **12** (10.18 mol, 1.08 eq., Princeton Global Synthesis, New Jersey, USA). The reactor was then inerted by three vacuum/N_2 cycles, and was then charged with 12.0 L methanol. The batch was agitiated 60 minutes at 23 °C, then 60 minutes at 65 °C and then cooled to 40 °C and configured for distillation. The reactor was distilled to minmal stirrable volume at 100 mm vacuum. To the resultant slurry was then added 7.0 L EtOAc and the batch was cooled to 7 °C. 8.0 L 1.3N NaOH was then charged to the reactor via addition funnel over 15 minutes. The pH was determined to be 10. 2.0 L sat'd NaCl was then charged via adddition funnel. After 5 minutes, agitation was stopped and the phases allowed to separate. Both phases were then separated and saved. The lower aqueous phase was then returned to the reactor and 7.0 L EtOAc was charged. After 15 minutes, the lower aqueous phase was discarded to waste and the two organic phases were combined in the reactor. 8.0 L H_2O was charged and the mixture agitated for 15 minutes, before stopping agitation and discarding the lower aqueous phase to waste. The organic phase was then clarified by passage though a Celite pad in a Buchner filter, using 5.0 L EtOAc to wash the reactor walls into the filter. The clarified filtrate was then returned to the reactor, which was configured for distillation. Solvents were removed to minimal stirrable volume at 45 °C/90 mm, then 3.0 L heptanes was added to the resultant slurry. The batch was then heated to 50 °C, aged 15 minutes, and filtered warm through a large Buchner filter funnel. When the cake was largely de-liquored, the cake was washed with 3.0 L of 2:1 EtOAc: heptanes. The solids were then dried at 50 °C/40 mm

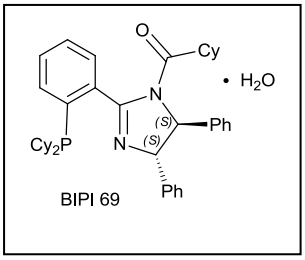
for six hours to give 1.62 kg of fluoroimidazoline **9** as a light yellow solid. The combined organic filtrates and washes were then returned to the reactor and concentrated to minimal stirrable volume by distillation for second crop recovery. The slurry thus obtained was then filtered and the cake washed and dried as described above to give 0.503 kg fluoroimidazoline **9** second crop as a light yellow solid. Both crops had >98A% purity by HPLC, 2.21 kg (71%). M.p. 118 ^{o}C; H_2O (KF): 0.33 %; $[\alpha]^{22}_{D}$ - 59 (c 0.24 in CH_2Cl_2); δ_H (400 MHz, d_6-DMSO) 8.00 (1 H, dt, *J* 1.8, 7.6), 7.70 (1 H, br s), 7.58 (1 H, m, 14 lines), 7.41-7.36 (5 H, m), 7.35-7.28 (7 H, m), 4.76 (3 H, s). δ_C (100 MHz, d_6-DMSO) 160.1 (s, $^{1}J_{CF}$ 252), 159.1 (s, J_{CF} 2.3), 144.1 (s), 132.4 (d, J_{CF} 8.6), 130.7 (d, J_{CF} 2.9), 128.5 (d), 127.1 (d), 126.4 (d), 124.5 (d, J_{CF} 3.3), 118.7 (s, J_{CF} 12), 116.3 (d, J_{CF} 22), 74.1 (d, br). δ_F (376 MHz, d_6-DMSO) - 111.8.



11-HCl

Manufacture of BIPI 69, Part 2, Imidazoline phosphineborane 11-HCl: A 25 L reactor was charged with 1.48 kg of dicyclohexylphosphine borane (6.98 mol, 2.2 eq.), then inerted by three vacuum/N_2 cycles. 4.0 L dry DMAc was then charged under N_2 pressure, and a vigorous nitrogen sweep of the reactor was then established. 279 g 60% NaH (6.98 mol, 2.2 eq.) was then charged in portions through the handway over 40 minutes [CAUTION! Flammable hydrogen gas evolution! Foaming!] causing immediate gas evolution and foaming. The batch was then aged 60 minutes at ~ 25 ^{o}C, then the N_2 sweep was stopped and the batch was cooled to 1 ^{o}C. The addition funnel was then charged with a solution of [1.00 kg (*S*,*S*)-fluoroimidazoline **9** (3.16 mol, 1.0 eq.) + 1.90 L dry DMAc]. This solution was then added dropwise to the cold batch over 30 minutes. The batch was then aged 12h at 23 ^{o}C, at which time HPLC showed the reaction was complete. 4.0 L MTBEwas then charged to the batch, and it was cooled to 2 ^{o}C. 4.0 L 5M NH4Cl was then added via adddition funnel over 20 minutes, giving a pH of 9.4. 2.5 L 4N HCl was then added via addition funnel over 30 minutes, giving a thick slurry of the HCl salt. 2.0 L MTBE was then charged to aid stirring. The system was then configured for filtration, and the batch was filtered through a Buchner funnel, using 4.0 L 0.4N HCl to transfer the slurry and wash the cake. The cake was then washed with 10 L H_2O, followed by 5.0 L MTBE. The damp filter cake was then returned to the reactor, 10 L MTBE was charged, and the resultant slurry agitated for 30 minutes at 23 ^{o}C. The batch was then filtered, washing the cake with 5.0 L MTBE. The solids were then dried at 50 ^{o}C/40 mm in a vacuum oven with a nitrogen breeze until the KF was < 5%, requiring 6 hours. A final slurry purification was then carried out. The solids were transferred to a 10 L reactor and 2.5 L THF was charged. The resultant mixture was agitated vigorously for 15 minutes, then filtered in a Buchner funnel under N_2 and dried on the frit to give 1.55 kg of **11-HCl** (90%) as a non-hygroscopic white solid. 98A% HPLC purity, and > 99.7% ee by chiral HPLC. M.p. 242 ^{o}C; $[\alpha]^{22}_{D}$ - 96 (c 0.24 in MeOH); δ_H (500 MHz, d_6-DMSO) 11.36 (2 H, s), 8.11-8.05 (2 H, m), 7.87 (2 H, m), 7.56 (4 H, m), 7.50-7.43 (6 H, m), 5.45 (2 H, br s), 2.59 (1 H, m), 2.28 (1 H, m), 1.98-1.85 (2 H, m), 1.83-1.60 (7 H, m), 1.55-1.02 (11 H, m), 0.75 (3 H, br s). δ_H (125 MHz, d_6-DMSO) 165.6 (s, $^{3}J_{CF}$ 2.3), 135.6 (s), 133.9 (d), 131.63 (d), 131.56 (d), 131.5 (d), 131.4 (d), 130.1 (s), 129.02 (d), 128.91 (d), 127.8 (d), 125.6 (s, $^{1}J_{CP}$ 40), 70.5 (d, br), 33.6 (d, $^{1}J_{CP}$ 33), 31.3 (d, $^{1}J_{CP}$ 34), 26.6 (t), 26.1 (t), 26.0 (t), 25.9 (t), 25.8 (t),

25.6 (t), 25.5 (t). δ_P (202 MHz, CD_2Cl_2) 29.76. HRMS [$C_{33}H_{42}BN_2P$ – HCl + H^+]: calculated 509.32624, observed 509.3273, difference = 2.077 ppm.



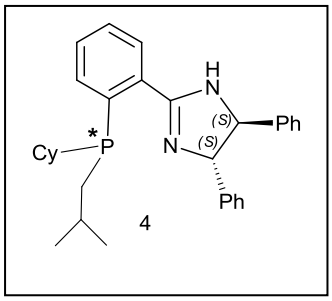
BIPI 69

Manufacture of BIPI 69, Part 3, BIPI 69 Hydrate: A 25 L reactor was charged with 1.44 kg **11-HCl** (2.64 mol, 1 eq.) and 0.952 kg DABCO (8.48 mol, 3.2 eq.). The reactor was then inerted by three vacuum/N_2 cycles. 13.0 L PhMe was then charged under N_2 pressure, and the batch was warmed to 60 ^oC. After 2h, HPLC showed the de-boronation was complete. The batch was then cooled to 23 ^oC, giving a slurry. This was then filtered through a Celite pad in a Buchner funnel, using 2 L PhMe to transfer the slurry and wash the pad. The filtrate was then transferred to a 50 L reactor, which was configured for distillation. Toluene was removed at 55 ^oC/70 mm to minimal stirrable volume, collecting 12 L. 32 L ethyl acetate was then charged via the addition funnel, followed by 11 L 0.5N HCl. The resultant mixture was agitated for 15 minutes, then 2.7 L sat'd NaCl was added. Agitation was then stopped and the phases were allowed to separate. The lower aqueous phase was then discarded to waste. The upper organic phase was then subjected to an in-line filtration through a Sparkler filter containing 1 kg of $MgSO_4$, returning the dried and clarified filtrate solution to the reactor. The reactor was then configured for distillation (24 ^oC/80 mm) to minimal stirrable volume, collecting 26 L of ethyl acetate. 9.0 L methylene chloride was then charged to the reactor, followed by 0.792 L triethylamine (5.68 mol, 2.2 eq.). The batch was then cooled to 4 ^oC, and then 0.380 L cyclohexanecarbonyl chloride (2.84 mol, 1.08 eq.) was then added over 15 minutes from a N_2-pressurized 1L flask. The batch was then warmed to 25 ^oC and aged for 60 minutes, at which time HPLC showed the acylation was complete. 0.10 L N,N,N'-trimethylethylenediamine was then charged at once from a N_2-pressurized 250 mL flask, and the mixture aged for 15 minutes. The reactor was then configured for distillation and volatiles were removed at 23 ^oC/200 mm, collecting 5 L of distillate. 36 L ethyl acetate was then charged to the reactor, followed by 10.8 L 0.5N HCl and 2.7 L sat'd NaCl. After 15 minutes, agitation was stopped and the phases were separated. The lower aqueous phase was discarded to waste. 10.8 L half-sat'd $NaCHCO_3$ and 2.7 L sat'd NaCl were then charged to the reactor. After 15 minutes, agitation was again stoped and the phases were allowed to separate. The lower aqueous phase was again discarded to waste, and the upper organic phase was filtered under N_2 through a pad of Celite in an Aurora filter. The clarified filtrate was then returned to the ethyl acetate-cleaned reactor. The reactor was then configured for distillation and ethyl acetate was removed at 40 ^oC/90 mm, collecting 26 L. 20 L *n*-propanol was then charged to the batch, then the reactor was again configured for distillation (60 ^oC/64 mm), collecting 15 L of distillate. The batch was then dropped to an inerted, tared, glass-lined vessel to determine the mass of the batch (7.74 kg), and KF (0.6%). The solution (close to the target of 17 wt%) was returned to the reactor under N_2 pressure, then the batch was heated to 50 ^oC. 0.64 kg H_2O was then added via addition funnel. Additional H_2O was then charged to give a final composition of 29% H_2O/*n*-propanol (w/w), requiring 1.92 kg. The batch was then aged 30 minutes at 50 ^oC. 100 g of BIPI 69 mnohydrate seed crystals were then

charged under N_2 pressure from a 500 mL flask as a slurry in 100 mL 1:1 H_2O: *n*-propanol. The batch was then cooled linearly to 23 °C over 60 minutes, causing a thick slurry to form. The batch was then aged 2 hours at 23 °C, then filtered under N_2 through an Aurora filter. The filter cake was then washed with 1.75 L of 2:1 *n*-propanol: H_2O. The cake was then dried in a vacuum oven at 83 °C/12 mm for 16 hours to give 1.21 kg of **BIPI 69 H_2O** (70%) as a free-flowing white solid. M.p. 178-179 °C; H_2O (KF): 2.2 wt%; 99.7% ee; δ_H (500 MHz, MeOH d_4, mixture of rotamers) 7.72 (2 H, m), 7.61 (2 H, m), 7.52 (3 H, m), 7.44 (4 H, m), 7.36 (3 H, m), 5.30 (1 H, s), 5.01 (1 H, d, *J* 6.5), 2.20 – 0.60 (33 H). δ_C (125 MHz, DMSO d_6, mixture of rotamers) 173.1 (s), 158.3 (s, br), 143.1 (s), 142.1 (s), 140.7 (s, br), 135.0 (s, br), 132.6 (d), 128.8 (d), 128.6 (d), 127.6 (d), 127.5 (d), 127.0 (s, br), 126.2 (s, br), 77.6 (d, br), 69.7 (d, br), 42.2 (d), 30.0 (t), 29.9 (t), 29.5 (t, br), 26.5 (t), 26.0 (t), 25.9 (t), 24.9 (t), 24.8 (t), 24.5 (t). δ_P (202 MHz, d_4-MeOH) -7.15. HRMS $(M+H)^+$ $C_{40}H_{50}N_2OP$: calculated 605.3655, observed 605.3655, difference = 0.0486 ppm.

Kilogram-Scale Asymmetric Hydrogenations: A 20 L autoclave was charged with solution of 3.0 kg olefin **3** (10.05 mol, 1.0 eq.) in 12 kg MeOH and the solution purged with N_2 for 30 min. The catalyst was formed separately in a 500 mL round bottom flask by the addition of 250 g N_2-degassed MeOH to 3.76 g (10.0 mmol, 0.001 eq.) of $Rh(NBD)_2BF_4$ and 5.38 g **BIPI 153-H_2O** (8.0 mmol, 0.0008 eq.) under Ar. The preformed catalyst mixture was then charged into the autoclave under N_2 pressure, and the lines flushed with MeOH. The autoclave was then pressurized to ~ 25 psi with N_2 and vented (3X), then filled to 100 psi H_2. A mass flow meter was then set at 70 psi and H_2 was automatically added to maintain this pressure throughout the reaction. After 17 h, HPLC analysis of an aliquot taken under pressure showed olefin **3** had been consumed. The vessel was then vented and the reaction mixture filtered through a pad of Celite, and the Celite pad was rinsed with 2.0 kg methanol. Chiral HPLC showed the optical purity of **2** was > 99.6% ee. The filtrate was used directly in the next synthetic step.

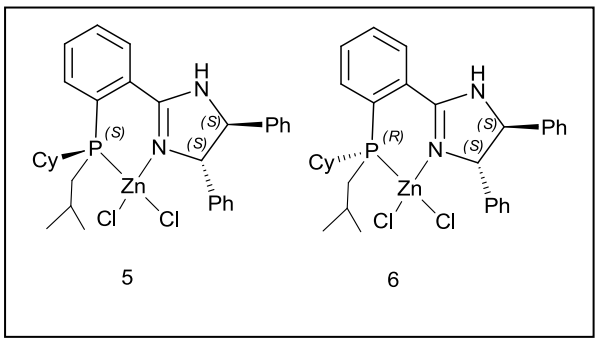
General Procedure. Lab-Scale Screening Asymmetric Hydrogenations: The hydrogenation screenings were conducted in the Argonaut Endeavor reactor system, equipped with eight parallel glass-lined reactors and polypropylene agitators; progress of the reactions was monitored continuously by hydrogen uptake. In a typical procedure, 1% $Rh(NBD)_2BF_4$ precatalyst and 1% ligand were first mixed in degassed MeOH under an Ar atmosphere at rt for 10 min and were then added to the substrate solution in MeOH. The reactors were then placed in the Endeavor, purged with nitrogen, presurized with H_2 to 100 psi, and then heated to 30 °C and stirred for 8-16h. Reverse phase HPLC and chiral HPLC were then performed on samples which had been filtered through apad of silica gel to remove the catalyst.



4

Optical Resolution *via* Zinc Complexes, BIPI 158 and BIPI 160: Part 1, Diastereomeric Phosphinoimidazolines 4: A 3-neck 100 mL flask was charged with 5.17 g cyclohexyl-i-butylphosphine borane (27.8 mmol, 2.22 eq.) and 16 mL dry DMAc. To the resulting solution, stirring under Ar at RT, was then added 1.10 g 60% NaH (27.8 mmol, 2.22 eq.) in portions, causing immediate gas evolution. After 30 minutes, the flask was placed in a cool water bath, then a solution of [3.97 g fluoroimidazoline **9** (12.5 mmol, 1 eq.) + 8.0 mL dry DMAc] was added via syringe over ~ 5 minutes, giving a yellow reaction mixture. The bath was then removed and the mixture allowed to warm to RT, giving an orange solution. After 14h at RT, the reaction mixture was poured into [50 cm^3 ice + 50 mL sat'd NH_4Cl], and the resulting mixture extracted with MTBE (2 X 100 mL). The combined organics were then washed with H_2O (1 X 150 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 9.0 g of a yellow oil. The oil was then partially dissolved in 50 mL boiling hexanes, then 3.0 mL MTBE was added, giving a clear solution. The solution was stirred under Ar as it cooled to RT, giving a slurry. After aging 2h at RT, the slurry was filtered and the solids dried on the frit to give 2.91 g of a light yellow powder. The filtrates were concentrated in vacuo to give an oil which was dissolved in 10 mL boiling hexanes, and again cooled to RT while stirring under Ar, giving a slurry. This slurry was then filtered and the solids dried on the frit to give an additional 0.84 g of the phosphine borane as a light yellow powder, for an overall yield of 3.75 g (7.77 mmol, 62%) of diastereomeric phosphineboranes.

The solids were then charged to a 3-neck 100 mL flask equipped with a direct Ar line, inert gas valve and septum was and 2.63 g DABCO (23.3 mmol, 3 eq.) and 35 mL toluene were then added, and Ar sparging beneath the solution surface was started. After 10 minutes, the flask was placed in a pre-equilibrated 60 ^oC oil bath and Ar sparging was stopped. After 2h under Ar at 60 ^oC, HPLC shows that the de-boronation is complete. Toluene was then removed under high vacuum, and 50 mL hexanes were added to the residue. The resultant mixture was stirred five minutes under Ar, then filtered under N_2 through a thin Celite pad. The filtrate was then concentrated in vacuo to give a yellow oil. The oil was then filtered through a pad of silica gel under N_2, eluting with ~ 150 mL EtOAc. The eluate was then concentrated in vacuo to give 3.8 g (~100%) of the free diastereomeric phosphinoimidazolines **4** as a pale yellow oil. These were immediately converted to the zinc complexes, as detailed below.



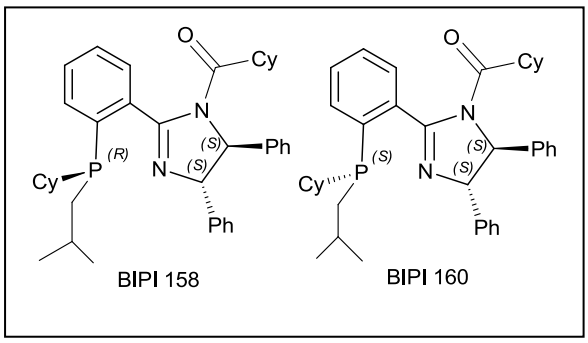
5 6

Part 2, Diastereomeric Zinc Complexes 5 and 6:

The crude phosphinoimidazolines **4** (taken as 7.77 mmol, 1 eq.) were then charged to a 3-neck 100 L flask and 20 mL THF was added via syringe. To the resulting solution, stirring under Ar at RT, was then added 15.5 mL 0.5M $ZnCl_2$/THF (7.75 mmol, 1 eq.) via syringe over ~ 3 minutes. After 1h at RT, the volatiles were removed in vacuo,

giving a white solid. ^{31}P NMR showed the two diastereomeric zinc complexes at -22.5 and -24.8 ppm (CD_2Cl_2). The solids were then fully dissolved in 150 mL boiling MeOH and allowed to cool to RT while standing, causing crystallization. The solids were then filtered and dried on the frit to give 1.00 g (21%) of a white crystalline solid, shown to be the pure -22.5 ppm diastereomer (complex #1, **5**). The filtrates were concentrated in vacuo and the residue was then dissolved in 12 mL boiling MeOH and allowed to cool to RT while standing, causing crystallization. The solids were then filtered and dried on the frit to give 1.40 g (30%) of the pure -24.8 ppm diastereomer (complex #2, **6**). Zn Complex # 1 (**5**): M.p. > 270 °C; $[\alpha]^{22}_D$ - 46 (c 0.13 in CH_2Cl_2); δ_H (500 MHz, CD_2Cl_2) 7.98 (1 H, m), 7.76-7.72 (2 H, m), 7.72-7.67 (1 H, m), 7.48-7.37 (8 H, m), 7.35 (2 H, m), 6.46 (1 H, br s), 5.54 (1 H, d, *J* 7.1), 4.96 (1 H, d, *J* 7.1), 2.33 (1 H, qt, *J* = 3, 13), 2.01 (2 H, t, *J* 6), 1.97-1.70 (7 H, m), 1.68-1.52 (2 H, m), 1.40-1.25 (2 H, m), 0.98 (6 H, t, *J* 7.4). δ_C (125 MHz, CD_2Cl_2) 165.0 (s, $^3J_{CP}$ 2.6), 133.7 (s), 132.8 (d, J_{CP} 4.2), 131.7 (d, J_{CP} 1.6), 131.5 (d), 131.4 (d), 131.3 (s), 129.9 (s, J_{CP} 17), 129.8 (d), 129.29 (s), 129.27 (d), 128.8 (d), 127.9 (d), 126.8 (d), 78.5 (d, J_{CP} 3.5), 67.9 (d, J_{CP} 1.3), 51.0 (s), 33.7 (d, J_{CP} 16), 31.2 (d, J_{CP} 11), 28.8 (t, J_{CP} 5.2), 28.3 (t, J_{CP} 4.9), 27.3 (t, J_{CP} 6.2), 27.2 (t, J_{CP} 7.3), 26.2 (t, J_{CP} 1.5), 26.0 (d), 25.2 (q, $^3J_{CP}$ 7.3), 25.0 (q, $^3J_{CP}$ 6.7). δ_P (202 MHz, CD_2Cl_2) - 22.5. HRMS [$C_{31}H_{37}N_2P + H^+$]: calculated 469.27781, observed 469.2781, difference = 0.6147 ppm.

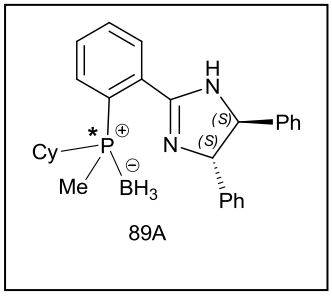
Zn Complex # 2 (**6**): M.p. 253 °C; $[\alpha]^{22}_D$ + 21 (c 0.19 in CH_2Cl_2); δ_H (500 MHz, CD_2Cl_2) 7.89 (1 H, m), 7.70-7.62 (3 H, m), 7.44-7.32 (8 H, m), 7.28 (2 H, m), 6.31 (1 H, s), 5.55 (1 H, d, *J* 8.3), 4.90 (1 H, d, *J* 8.4), 2.20-2.08 (2 H, m), 2.07-1.95 (4 H, m), 1.80 (2 H, dd, *J* 2.3, 13), 1.71 (1 H, d, *J* 12), 1.35-1.02 (5 H, m), 1.13 (6 H, dd, *J* 3, 6.3). δ_C (125 MHz, CD_2Cl_2) 165.2 (s, $^3J_{CP}$ 2.0), 141.7 (s), 141.0 (s), 134.0 (d), 132.6 (d), 131.8 (s), 131.7 (d, J_{CP} 1.8), 130.9 (d, J_{CP} 6.6), 129.8 (d), 129.4 (d), 129.3 (d), 129.0 (s, J_{CP} 17), 128.7 (d), 127.6 (d), 126.8 (d), 78.4 (d, J_{CP} 2.8), 68.2 (d, J_{CP} 1.2), 35.4 (d, J_{CP} 13), 29.1 (t, J_{CP} 1.5), 27.9 (t), 27.8 (t), 27.7 (t), 27.6 (t), 27.5 (t), 27.4 (t), 27.3 (t), 26.4 (d, J_{CP} 8), 26.3 (t, J_{CP} 1.4), 25.3 (q, $^3J_{CP}$ 9), 24.7 (q, $^3J_{CP}$ 9). δ_P (202 MHz, CD_2Cl_2) - 24.8. HRMS [$C_{31}H_{37}N_2P + H^+$]: calculated 469.27781, observed 469.2787, difference = 1.8933 ppm.



Part 3, BIPI 158 and 160: BIPI 158: 0.90 g of $ZnCl_2$ complex #1 (^{31}P – 22.5 ppm, 1.49 mmol, 1 eq.), and 30 mL CH_2Cl_2 were charged to a 100 mL 3-neck flask at RT under Ar. To this clear solution was then added 0.200 mL ethylenediamine (3.00 mmol, 2 eq.) via syringe, causing the instant formation of a thick suspension. After 10 minutes, the slurry was filtered under N_2, washing the solids with 5 mL additional CH_2Cl_2. The filtrate was then concentrated in vacuo to give 923 mg (~ 100%) of the free phosphinoimidazoline as a light yellow solid. This solid was then transferred to a 3-neck 50 mL flask equipped with a direct Ar line, inert gas valve and septum. 20 mL CH_2Cl_2 was then charged via syringe and slow Ar sparging beneath the solution surface was started. After 5 minutes, the flask was placed in an ice bath and 0.416 mL TEA (3.00 mmol, 2 eq.) was added via syringe, followed after 5 minutes by 0.235 mL cyclohexanecarbonyl chloride (1.49 mmol, 1 eq.). The ice bath was then removed and the mixture allowed to warm to RT. After 30 min. at RT, TLC shows

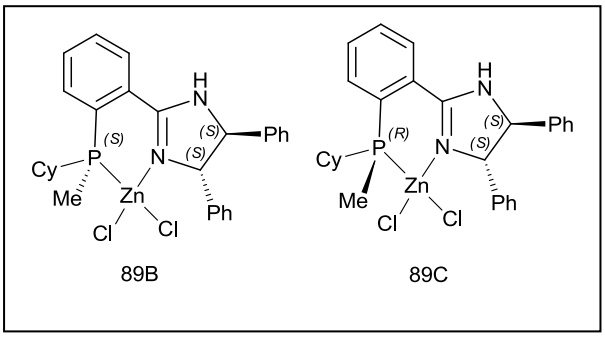
the reaction is complete to a non-polar spot. 0.15 mL N,N,N'-trimethylethylenediamine was then added to scavenge any uneacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 25 mL 0.5N HCl and 25 mL EtOAc. The organic phase was washed with 0.5N HCl (1 X 25 mL), sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 5:1 Hex: EtOAc and collecting only the center fractions. The pure fractions were then concentrated in vacuo, azeotroped with MTBE at the Rotovap (1 X 10 mL), and finally dried under high vacuum to give 0.690 g (80%) of **BIPI 158** as a white foam. δ_H (500 MHz, d_4-MeOH) 7.80 (1 H, br s), 7.76 (1 H, dd, *J* 2.7, 6.8), 7.59 (2 H, m), 7.53 (1 H, m), 7.50-7.34 (9 H, m), 5.30 (1 H, d, *J* 6.2), 5.06 (1 H, d, *J* 6.2), 2.07 (1 H, m), 1.88 (2 H, m), 1.81 (3 H, m), 1.72-1.57 (6 H, m), 1.46 (2 H, t, *J* 15), 1.31 (2 H, m), 1.24-1.09 (6 H, m), 1.02 (7 H, m), 0.90 (1 H, m), 0.58 (1 H, m). δ_C (125 MHz, d_4-MeOH) 176.2, 162.4, 143.9, 143.2, 141.6, 141.4, 139.0, 138.9, 132.8, 130.6, 130.14, 130.11, 130.1, 129.72, 129.65, 129.4, 129.2, 127.9, 79.4, 72.6, 44.8, 40.0, 31.6, 31.5, 30.7, 30.6, 30.0, 28.1, 28.0, 27.99, 27.92, 27.8, 27.7, 27.54, 27.53, 27.2, 26.6, 26.5, 26.2, 25.2, 25.1, 24.84, 24.77. δ_P (202 MHz, d_4-MeOH) - 26.3. HRMS [$C_{38}H_{47}N_2OP + H^+$]: calculated 579.35097, observed 579.3511, difference = 0.2131 ppm.

BIPI 160: 1.13g of $ZnCl_2$ complex #2 (^{31}P – 24.8 ppm, 1.87 mmol, 1 eq.), and 30 mL CH_2Cl_2 were charged to a 100 mL 3-neck flask at RT under Ar. To this clear solution was then added 0.251 mL ethylenediamine (3.78 mmol, 2 eq.) via syringe, causing the instant formation of a thick suspension. After 10 minutes, the slurry was filtered under N_2, washing the solids with 10 mL additional CH_2Cl_2. The filtrate was then concentrated in vacuo to give 1.1 g (~ 100%) of the free phosphinoimidazoline as a light yellow solid. This solid was then transferred to a 3-neck 50 mL flask equipped with a direct Ar line, inert gas valve and septum. 25 mL CH_2Cl_2 was then charged via syringe and slow Ar sparging beneath the solution surface was started. After 5 minutes, the flask was placed in an ice bath and 0.522 mL TEA (3.78 mmol, 2 eq.) was added via syringe, followed after 5 minutes by 0.295 mL cyclohexanecarbonyl chloride (1.87 mmol, 1 eq.). The ice bath was then removed and the mixture allowed to warm to RT. After 30 min. at RT, TLC shows the reaction is complete to a non-polar spot. 0.20 mL N,N,N'-trimethylethylenediamine was then added to scavenge any uneacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 25 mL 0.5N HCl and 25 mL EtOAc. The organic phase was washed with 0.5N HCl (1 X 25 mL), sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 4:1 Hex: EtOAc and collecting only the center fractions. The pure fractions were then concentrated in vacuo, azeotroped with MTBE at the Rotovap (3 X 20 mL), and finally dried under high vacuum to give 0.779 g (72%) of **BIPI 160** as a white foam. δ_H (500 MHz, d_4-MeOH) 8.80-8.70 (2 H, m), 7.68-7.50 (4 H, m), 7.50-7.24 (8 H, m), 5.36 (1 H, br s), 5.03 (1 H, d, *J* 6.0), 2.20-1.57 (12 H, m), 1.48 (2 H, m), 1.40-0.75 (16 H, m), 0.63 (1 H, m). δ_C (125 MHz, d_4-MeOH) 176.4, 161.9, 143.8, 143.0, 138.8, 132.8, 130.6, 130.2, 130.1, 129.9, 129.56, 129.51, 129.23, 129.21, 128.9, 127.9, 127.0, 79.8, 72.6, 72.0, 44.7, 39.4, 33.6, 31.6, 30.4, 28.0, 27.8, 27.7, 27.5, 27.2, 27.0, 26.6, 26.5, 26.2, 25.24, 25.18, 24.7. δ_P (202 MHz, d_4-MeOH) - 25.6. HRMS [$C_{38}H_{47}N_2OP + H^+$]: calculated 579.35097, observed 579.3522, difference = 2.1117 ppm.



89A

Optical Resolution *via* Zinc Complexes, BIPI 89 and BIPI 92: Part 1, Diastereomeric Phosphinoimidazoline Boranes 89A: A 250 mL 3-neck flask equipped with a direct Ar line, inert gas valve and septum was charged with 3.80 g cyclohexyl-methylphosphine borane (26.4 mmol, 2.2 eq.) and 16 mL dry DMAc, and Ar sparging beneath the solution surface was then started. After 10 minutes, the flask was placed in a cool water bath and 1.05 g 60% NaH (26.4 mmol, 2.22 eq.) was then added, causing immediate gas evolution and foaming. After 45 minutes, a solution of [3.77 g fluoroimidazoline **9** (11.9 mmol, 1 eq.) + 8.0 mL dry DMAc] was then added via syringe over ~ 5 minutes, giving a yellow reaction mixture. After 5 minutes, the bath was removed and the mixture allowed to warm to RT, at which time Ar sparging was stopped. After 16h at RT under Ar, the reaction mixture was poured into [50 cm^3 ice + 50 mL sat'd NH_4Cl], and the resultant mixture extracted with MTBE (2 X 75 mL). The combined organics were then washed with H_2O (1 X 150 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give an oil. The oil was then dissolved in 250 mL MTBE and transferred to a 3-neck 500 mL flask. To this solution, stirring under Ar at RT, was then added 6.0 mL 2M HCl/Et_2O (12.0 mmol, 1 eq.) dropwise via syringe over ~ 5 minutes, causing a thick slurry of the phosphineborane HCl salt to form. After 10 minutes, the slurry was filtered under N_2, washing the solid with ~ 100 mL MTBE, and drying under N_2 on the frit to give a solid which was then pulverized under MTBE on the frit and again filtered under N_2 to give 5.7 g (~ 100%) of the salt as a light yellow powder. These solids were then partitioned between 50 mL 1N NaOH and 200 mL 1: 1 (v/v) MTBE: EtOAc. The organic phase was then dried ($MgSO_4$), and the solvents removed in vacuo to give 5.60 g (~ 100%) of crude phosphinoimidazoline boranes **89A** as a light yellow oil, which was immediately converted to the diastereomeric zinc complexes.

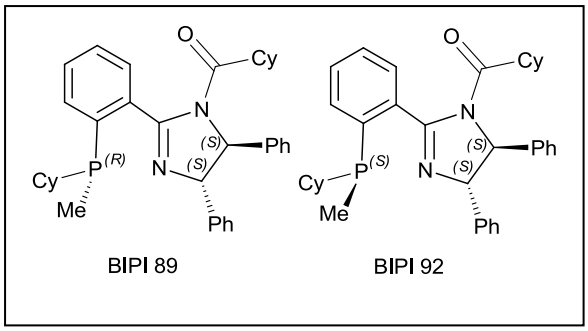


89B 89C

Part 2, Diastereomeric Zinc Complexes 89B and 89C: 5.60 g of the crude phosphinoimidazoline boranes **89A** (11.9 mmol, 1 eq.) and 4.01 g DABCO (35.7 mmol, 3 eq.) were charged to a 250 mL flask equipped with a direct Ar line, inert gas valve, and septum. 40 mL toluene was then added and Ar spearging beneath the solution surface was then started. After 10 minutes, the flask was placed in a pre-equilibrated 60 °C oil bath and Ar sparging was stopped. After 2h at 60 °C under Ar, HPLC showed the de-boronation was complete. The reaction mixture was then cooled to RT and toluene was removed under high vacuum. The reidual oil was then triturated with 20 mL MTBE causing some precipitate to form, which was filtered off under N_2 and discarded. The filtrate was then concentrated in vacuo and filtered through a short column of silica gel under N_2 pressure eluting with ~ 400 mL EtOAc. The eluates were then concentrated in vacuo to give 4.2 g (~ 84%) of the free phosphinoimidazolines as a pale yellow oil. To this oil was then added 25 mL THF and the solution transferred to a 100 mL flask under Ar. 20 mL of 0.5M $ZnCl_2$/THF (10.0 mmol, 1 eq.)

was then added via syringe. The resulting solution was then stirred at RT for 60 minutes, then the volatiles were removed in vacuo to give an oil. ^{31}P NMR showed the two diastereomeric zinc complexes at – 29.65 and – 31.24 ppm (CD_2Cl_2). This oil was then fully dissolved in 20 mL methanol at RT, causing a thick precipitate to form after stirring for ~ 5 minutes. The resultant slurry was then filtered and dried on the frit to give 1.7 g of a white powder. NMR showed a 10: 1 ratio of diastereomers, so this solid was slurried in 50 mL hot methanol, and then filtered warm and dried on the frit to give 1.20 g (42%) of a white powder, zinc complex # 1 (**89B**, ^{31}P –31.24 ppm), as a single diastereomer. All filtrates and triturates were then combined and concentrated in vacuo to give a white solid. This solid was then fully dissolved in 150 mL boiling 1:1 MeOH: H_2O and allowed to cool to RT while standing, causing crystallization. The resultant slurry was then filtered and the solids then dissolved in 40 mL of 2: 1 (v/v) $CHCl_3$: MeCN and dried ($MgSO_4$), and the solvents removed in vacuo to give 2.1 g of a white solid. This solid was then fully dissolved in 60 mL boiling methanol and allowed to cool to RT while standing, causing crystallization. The slurry thus obtained was then filtered and dried on the frit to give 0.62 g (20%) of zinc complex # 2 (**89C**) as a single diastereomer. The methanol filtrates were then concentrated in vacuo and the residue recrystallized from 20 mL boiling methanol and allowed to again cool to RT while standing, causing crystallization. The slurry thus obtained was then filtered and the solids air-dried on the frit to give 0.49 g (18%) of **89C** as a second crop, also diastereomrically pure by NMR, overall yield of **89C** was 1.11 g, 38% (**89C**, ^{31}P –29.65 ppm). Data for zinc complex # 1 (**89B**): M.p. > 270 °C; $[\alpha]^{22}_D$ - 21 (c 0.08 in CH_2Cl_2); δ_H (500 MHz, CD_2Cl_2) 7.88 (1 H, m), 7.75-7.63 (3 H, m), 7.43-7.28 (10 H, m), 6.20 (1 H, br s), 5.66 (1 H, d, *J* 7.5), 4.93 (1 H, d, *J* 7.5), 1.93 (1 H, m), 1.83 (1 H, m), 1.73 (1 H, m), 1.70 (1 H, d, *J* 5.1), 1.45-1.19 (5 H, m). δ_C (125 MHz, CD_2Cl_2) 165.0 (s), 141.7 (s), 141.1 (s), 133.4 (d), 133.0 (d, J_{CP} 4.2), 131.9 (d), 131.8 (s), 130.6 (d, J_{CP} 4.2), 129.9 (d), 129.4 (d), 129.3 (d), 128.8 (d), 127.5 (d), 126.8 (d), 78.1 (d, J_{CP} 3.0), 68.1 (d), 37.3 (d, J_{CP} 15.5), 28.3 (t, J_{CP} 3.1), 28.0 (t, J_{CP} 2.2), 27.2 (t, J_{CP} 2.9), 27.1 (t, J_{CP} 2.4), 26.2 (t), 3.5 (q, $^1J_{CP}$ 16). δ_P (202 MHz, CD_2Cl_2) - 31.24. HRMS [$C_{28}H_{31}N_2P + H^+$]: calculated 427.23086, observed 427.2302, difference = 1.548 ppm.

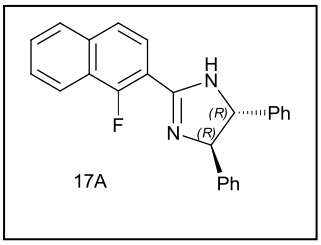
Data for zinc complex # 2 (**89C**): M.p. 128 °C; $[\alpha]^{22}_D$ - 8.6 (c 0.77 in CH_2Cl_2); δ_H (500 MHz, CD_2Cl_2) 7.94 (1 H, m), 7.75-7.69 (2 H, m), 7.50-7.23 (11 H, m), 6.47 (1 H, br s), 5.66 (1 H, d, *J* 7.7), 4.96 (1 H, d, *J* 7.8), 1.97 (1 H, m), 1.86 (2 H, m), 1.77 (1 H, m), 1.72 (3 H, d, *J* 5.1), 1.61 (1 H, m), 1.47-1.24 (6 H, m). δ_C (125 MHz, CD_2Cl_2) 165.2 (s, $^3J_{CP}$ = 2.0 Hz). δ_P (202 MHz, CD_2Cl_2) - 29.65. HRMS $(M+H)^+$ $C_{25}H_{20}FN_2$: calculated 367.1605, observed 367.1619, difference = 3.8035 ppm.



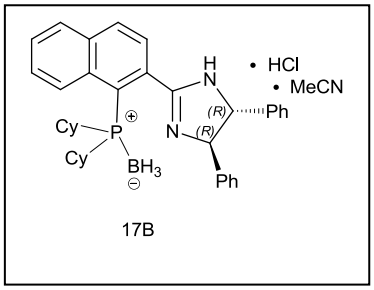
Part 3, BIPI 89 and BIPI 92: 1.00 g of $ZnCl_2$ complex #1 (**89B**, 1.78 mmol, 1 eq.), and 20 mL CH_2Cl_2 were charged to a 50 mL 3-neck flask at RT under Ar, giving a solution. To this clear solution was then added 0.239 mL ethylenediamine (3.56 mmol, 2 eq.) via syringe, causing the instant formation of a thick suspension. After 10 minutes, the slurry was filtered under N_2, washing the solids with ~ 15 mL additional CH_2Cl_2. The filtrate was then concentrated in vacuo to give 880 mg (~ 100%) of the free phosphimo imidazoline as a light yellow solid. This solid was then transferred to a 3-neck 25 mL flask equipped with a direct Ar line, inert gas valve and septum. 10 mL CH_2Cl_2 was then charged via syringe and slow Ar sparging beneath the solution surface was started. After 5 minutes, the flask was placed in an ice bath and 0.497 mL TEA (3.56 mmol, 2 eq.) was added via syringe, followed after 5 minutes by 0.281 mL cyclohexanecarbonyl chloride (1.78 mmol, 1 eq.). The ice bath was then removed and the mixture allowed to warm to RT. After 30 min. at RT, TLC shows the reaction is complete to a non-polar spot. 0.20 mL N,N,N'-trimethylethylenediamine was then added to scavenge any uneacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 25 mL 0.5N HCl and 25 mL EtOAc. The organic phase was washed with 0.5N HCl (1 X 25 mL), sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a pale yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 4:1 Hex: EtOAc and collecting only the center fractions. The pure fractions were then concentrated in vacuo, azeotroped with MTBE at the Rotovap (2 X 25 mL), and finally dried under high vacuum to give 0.80 g (84%) of **BIPI 89** as a white foam. δ_H (500 MHz, d_4-MeOH) δ_H: 7.74 (1 H, m), 7.63-7.52 (5 H, m), 7.48-7.41 (5 H, m), 7.40-7.34 (3 H, m), 5.36 (1 H, d, *J* 5.0), 5.04 (1 H, d, *J* 5.0), 2.03 (1 H, br s), 1.88-1.70 (5 H, m), 1.69-1.55 (4 H, m), 1.52-1.46 (2 H, m), 1.33 (3 H, d, *J* 3.7), 1.28-0.95 (7 H, m), 0.92-0.58 (2 H, m). δ_C (125 MHz, d_4-MeOH) 176.2, 161.6, 143.3, 142.6, 140.8, 140.5, 139.3, 139.2, 132.0, 130.5, 130.1, 130.0, 129.6, 129.0, 128.4, 126.7, 79.4, 71.6, 44.5, 39.9, 30.9, 30.8, 29.2, 27.8, 27.7, 27.63, 27.56, 27.3, 26.5, 26.2, 25.9. δ_P (202 MHz, d_4-MeOH) – 34.0. HRMS [$C_{35}H_{41}N_2OP + H^+$]: calculated 537.30402, observed 537.3047, difference = 1.2538 ppm.

0.50 g of $ZnCl_2$ complex #2 (**89C**, 0.89 mmol, 1 eq.), and 10 mL CH_2Cl_2 were charged to a 25 mL 3-neck flask at RT under Ar, giving a solution. To this clear solution was then added 0.170 mL ethylenediamine (1.78 mmol, 2 eq.) via syringe, causing the instant formation of a thick suspension. After 30 minutes, the slurry was filtered under N_2, washing the solids with ~ 15 mL additional CH_2Cl_2. The filtrate was then concentrated in vacuo to give 475 mg (~ 100%) of the free phosphimo imidazoline as a light yellow solid. This solid was then transferred to a 3-neck 25 mL flask equipped with a direct Ar line, inert gas valve and septum. 5.0 mL CH_2Cl_2 was then charged via syringe and slow Ar sparging beneath the solution surface was started. After 5 minutes, the flask was placed in an ice bath and 0.250 mL TEA (1.8 mmol, 2 eq.) was added via syringe, followed after 5 minutes by 0.140 mL cyclohexanecarbonyl chloride (0.89 mmol, 1 eq.). The ice

bath was then removed and the mixture allowed to warm to RT. After 30 min. at RT, TLC shows the reaction is complete to a non-polar spot. 0.10 mL N,N,N'-trimethylethylenediamine was then added to scavenge any uneacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 15 mL 0.5N HCl and 15 mL EtOAc. The organic phase was washed with 0.5N HCl (1 X 15 mL), sat'd $NaHCO_3$ (1 X 15 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a pale yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 3:1 Hex: EtOAc and collecting only the center fractions. The pure fractions were then concentrated in vacuo, azeotroped with MTBE at the Rotovap (2 X 20 mL), and finally dried under high vacuum to give 0.42 g (88%) of **BIPI 92** as a white foam. δ_H (500 MHz, d_4-MeOH) 7.79 (1 H, dd, *J* 2.6, 7.2), 7.70-7.59 (3 H, m), 7.56 (1 H, m), 7.50-7.44 (6 H, m), 7.42-7.34 (3 H, m), 5.31 (1 H, d, *J* 6.3), 5.03 (1 H, d, *J* 6.3), 2.08 (1 H, m), 1.99-1.82 (3 H, m), 1.78-1.53 (5 H, m), 1.51-1.42 (2 H, m), 1.42-1.34 (1 H, m), 1.33 (3 H, br s), 1.30-1.20 (3 H, m), 1.20-1.09 (3 H, m), 1.03 (1 H, qt, *J* 3.6, 13), 0.86 (1 H, m), 0.59 (1 H, m). δ_C (125 MHz, d_4-MeOH) 176.5, 143.7, 143.1, 140.9, 140.6, 140.1, 140.0, 132.1, 132.0, 131.0, 130.2, 130.1, 130.07, 129.8, 129.2, 129.1, 128.1, 127.6, 79.3, 72.5, 44.6, 31.3, 31.2, 30.8, 29.9, 29.8, 27.80, 27.77, 27.7, 27.54, 27.53, 27.2, 26.6, 26.5, 26.2. δ_P (202 MHz, d_4-MeOH) – 34.2. HRMS [$C_{35}H_{41}N_2OP + H^+$]: calculated 537.30402, observed 537.3035, difference = 0.9796 ppm.



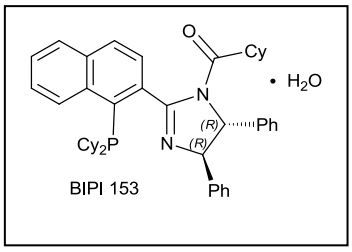
Synthesis of (*R*,*R*)-BIPI 153: (The synthesis of BIPI 153 has been previously described (*Org. Lett*. **2008**, *10*, 341). What follows here is a modified, larger-scale synthesis, with crystallization of the intermediate imidazoline phosphineborane HCl salt). **Part 1, Fluoroimidazoline 17A:** A 3L flask was charged with 50.0 g 1-fluoro-2-naphthaldehyde (288 mmol, 1 eq., Princeton Global Synthesis, New Jersey, USA) and 1.5 L CH_2Cl_2. After stirring for five minutes at RT under Ar, 64.0 g (*R*,*R*)-diamine (DPEDA, 302 mmol, 1.05 eq.) was added at once. The resultant mixture was stirred 1h at RT under Ar, then cooled in a cool water bath. 53.8 g NBS (302 mmol, 1.05 eq.) was then added neat, at once. After 2h, TLC shows the reaction is complete to a polar product. 1L 1N NaOH was then added, and the mixture agitated vigorously for 10 minutes, then the phases were separated. The lower organic phase was concentrated in vacuo, giving a thick orange oil. 500 mL hexanes were added, and the mixture was heated to reflux, giving a slurry. The slurry was agitated vigorously while cooling to RT. At RT the slurry was filtered, washing the solids with ~ 150 mL hexanes, and air-drying on the frit for ~ 15 minutes to give 102 g of (*R*,*R*)-fluoroimidazoline **17A** (97%) as a nearly colorless solid, which was then ground to a powder with a mortar and pestle. M.p. 128 °C; $[\alpha]^{22}_D$ - 8.6 (c 0.77 in CH_2Cl_2); δ_H (500 MHz, $CDCl_3$) 8.19 (1 H, t, *J* 7.8), 8.04 (1 H, d, *J* 7.2), 7.76 (1 H, d, *J* 7.1), 7.57 (1 H, d, *J* 8.7), 7.49 (2 H, m), 7.27-7.21 (8 H, m), 7.17 (2 H, m), 4.85 (2 H, s). δ_C (125 MHz, $CDCl_3$) 159.5 (s, $^1J_{CF}$ 2), 157.4 (s, $^1J_{CF}$ 258), 143.3 (s), 135.9 (s, J_{CF} 5.5), 128.6 (d), 128.1 (d), 127.4 (d), 126.7 (d, J_{CF} 1.3), 126.5 (d), 126.4 (d, J_{CF} 3.2), 123.8 (d, J_{CF} 3.8), 123.4 (s, J_{CF} 17.5), 121.1 (d, J_{CF} 6.6), 112.0 (s, J_{CF} 9.1), 74.4 (d). δ_F (376 MHz, $CDCl_3$) -118.34 (d, J_{FH} 7.0). HRMS $(M+H)^+$ $C_{25}H_{20}FN_2$: calculated 367.1605, observed 367.1619, difference = 3.8035 ppm. Anal. Calcd for $C_{25}H_{19}FN_2$: C, 81.94; H, 5.23; N, 7.64. Found C, 81.63; H, 5.24; N, 7.75.



17B

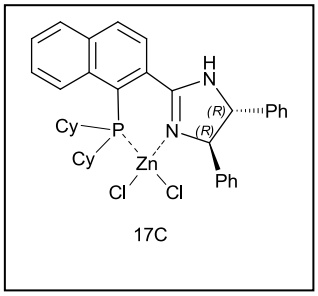
Part 2, Imidazoline Phosphineborane HCl Salt 17B: A 4-neck 1L flask equipped with direct Ar line, inert gas valve, septum with thermocouple and a 45/50 center joint was charged with 36.6 g (*R*,*R*)-fluoroimidazoline **17A** (100 mmol, 1 eq.) and 25.5 g dicyclohexylphosphine borane (120 mmol, 1.2 eq.). 300 mL anhydrous DMAc was then charged via cannula under N_2 pressure. Ar sparging beneath the solution surface was then started and the flask was placed in an ice bath. After 15 minutes, the sparge line was raised above the solution surface, then 8.80 g 60% NaH (220 mmol, 2.2 eq.) was added in portions over ~ 20 minutes to the vigorously stirred reaction mixture, causing immediate gas evolution and foaming (CAUTION!), and giving a dark red reaction mixture. The internal temperature rose to a maximum of 17 ^{o}C during the addition. 10 minutes after the NaH addition was complete, the ice bath was removed and the mixture allowed to warm to RT. After 20 minutes at RT, gas evolution had largely ceased, so the Ar sparge line was lowered again beneath the solution surface. After 2h at RT, HPLC shows the reaction is complete. The reaction mixture was then poured into [200 cm^3 ice + 300 mL 5M NH_4Cl], giving a slurry. To this slurry was then added 100 mL sat'd NaCl + 500 mL EtOAc and the mixture was stirred well for 5 minutes. The phases were then separated and the aq. phase was re-extracted with EtOAc (1 X 500 mL). The combined organics were then washed with [500 mL H_2O + 100 mL sat'd NaCl], dried ($MgSO_4$), and the solvent was removed in vacuo. The residual yellow semi-solid was then dissolved in ~ 400 mL MTBE, and this solution was transferred to a 3-neck 2L flask with inert gas valve, septum and a graduated 125 mL addition funnel. To this solution, stirring under Ar at RT, was then added 25 mL 4N HCl/*p*-dioxane (100 mmol, 1 eq.) dropwise via addition funnel over ~ 15 minutes, causing a thick slurry to form. 300 mL additional MTBE was then added to aid stirring. The mixture was agitated well for 10 minutes and was then filtered through a medium-fritted filter funnel under a vigorous flow of N_2, using additional MTBE to transfer the slurry and wash the cake. After the initial de-liquoring of the cake, the solids were pulverized under MTBE on the frit and again filtered under a vigorous flow of N_2. After 30 minutes drying, the crude product HCl salt was obtained as a light yellow powder. This powder was then transferred to a 500 mL flask with a stir bar and 50 mL MeCN was added. The resultant mixture was then heated to reflux under Ar. When ~ 80% of the material had dissolved, crystalline material began to deposit, giving a thick slurry after ~ 1 minute. 100 mL additional MeCN was added to aid stirring, and the well-agitated slurry was then cooled to RT under Ar. The slurry thus obtained was then filtered through a medium-fritted filter funnel under a vigorous flow of N_2 to give, after drying under N_2 ~ 60 minutes, 39 g (61% 1st crop recrystallized yield) of **17B** was obtained as a white powder. ^{1}H NMR showed that it crystallized as the mono-acetonitrile solvate. M.p. 270 °C; $[\alpha]^{22}_{D}$ + 127 (c 0.17 in MeOH); δ_H (500 MHz, DMSO-d_6) 11.2 (2 H, s), 8.39 (1 H, d, *J* 8.1), 8.28 (1 H, d, *J* 8.4), 8.16 (1 H, d, *J* 7.8), 7.91 (1 H, dd, *J* 2.8, 8.4), 7.92 (1 H, t, *J* 7.3), 7.75 (1 H, t, *J* 7.6), 7.70 (4 H, d, *J* 7.1), 7.56-7.45 (6 H, m), 5.38 (2 H, s), 3.35 (2 H, br s), 2.72 (1 H, m), 2.64 (1 H, m), 2.22-2.10 (2 H, m), 2.09 (3 H, s), 1.84 (1 H, br d, *J* 12), 1.79 (1 H, br d, *J* 10), 1.65-1.35 (9 H, m), 1.20-0.85 (9 H, m). δ_C (125 MHz, DMSO-d_6) 167.0 (s, $^3J_{CP}$ 8), 139.1 (s), 134.34 (s), 134.29 (s), 134.25 (s), 134.1 (s), 134.0 (s), 133.6 (s), 133.3 (s), 131.5 (d), 129.7 (d), 129.05 (d), 129.03

(d), 128.1 (d), 128.0 (d), 127.52 (d, J_{CP} 3.6), 127.1 (d), 124.3 (d, J_{CP} 10), 118.0 (s, $CH_3\underline{C}N$), 70.0 (d), 35.2 (d, J_{CP} 12), 35.0 (d, J_{CP} 12.4), 33.2 (t), 33.0 (t), 32.9 (t), 32.7 (t), 29.7 (t, J_{CP} 8), 29.6 (t, J_{CP} 10), 26.3 (t), 26.25 (t, J_{CP} 2.5), 26.20 (t), 25.8 (t), 25.5 (t), 1.1 (q, $\underline{C}H_3CN$). δ_P (202 MHz, DMSO-d_6) 3.12. HRMS [$C_{37}H_{41}N_2P + H^+$]: calculated 545.30911, observed 545.3091, difference = 0.0214 ppm.



Part 3, (*R*,*R*)-BIPI 153 H_2O: 6.36 g of (*R*,*R*)-phosphineborane imidazoline HCl salt **17B** (10.0 mmol, 1 eq.) was charged to a 3-neck 250 mL flask equipped with a direct Ar line, inert gas valve, and septum with thermocouple. 70 mL PhMe was then added and Ar sparging beneath the solution surface was then started. After 10 minutes, 4.49 g DABCO (40.0 mmol, 4 eq.) was added. After 5 minutes, Ar sparging was stopped and the flask placed in a pre-equilibrated 65 °C oil bath under Ar. After 1h, TLC (1:1 Hex: EtOAc) and HPLC show the reaction is complete. The reaction mixture was then cooled to RT and Ar sparging was re-started. 100 mL 0.5N HCl was then added at once, and the 2-phase mixture agitated vigorously. After 15 minutes, the mixture was transferred to a separatory funnel and the phases were separated. The upper organic phase was then dried ($MgSO_4$) and the solvents removed in vacuo to give a sticky yellow foam. This crude material (assumed to be 10.0 mmol, 1 eq.) was then dissolved in 70 mL CH_2Cl_2 and transferred to a 3-neck 250 mL flask equippped with a direct Ar line, inert gas valve and septum, and Ar sparging was started immediately and maintained throughout. The flask was then placed in an ice bath and 4.18 mL TEA (30.0 mmol, 3 eq.) was added, followed after 5 minutes by 1.41 mL cyclohexanecarbonyl chloride (10.5 mmol, 1.05 eq.), added dropwise via syringe over ~ five minutes. After five minutes, the ice bath was removed and the mixture allowed to warm to RT. After 20 minutes, TLC (4:1 Hex: EtOAc) shows clean conversion to a very non-polar spot. 0.50 mL N,N,N'-trimethylethylenediamine was then added to scavenge any unreacted acid chloride. After 5 minutes, the volatiles were removed in vacuo. The residue was partitioned between 100 mL EtOAc and 100 mL 0.5N HCl. The phases were then separated and the organic phase then washed with sat's $NaHCO_3$ (1 X 100 ml), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow foam. This foam was then chromatographed on silica gel under N_2 pressure eluting with 5:1 Hex: EtOAc, collecting only the center fractions. The solvents were then removed in vacuo to give 6.0 g of a colorless foam. This foam was then dissolved in 100 mL of Ar-degassed MeOH and placed in a 3-neck 250 mL flask again equipped with a direct Ar line, inert gas valve and septum, and Ar sparging was immediately started and maintained throughout. To the resulting solution, stirring at RT, was then added H_2O dropwise until the first presistent cloudiness was observed, requiring ~ 15 mL. After ~ 30 minutes, nucleation occurred, rapidly giving a slurry of white solid. The slurry was aged 30 minutes at RT, then 30 minutes in an ice bath, and it was then filtered under N_2, washing the cake with a small amount of MeOH and drying on the frit to give 5.20 g (79% over 2 steps + crystallization) of **(*R*,*R*)-BIPI 153 H_2O** as a white crystalline solid. M.p. 120 °C; δ_H (500 MHz, CD_3OD) (1:1 rotameric mixture) 8.33 (1 H, d, *J* 8.4), 8.08 (1 H, d, *J* 6.1), 8.04 - 7.95 (2 H, m), 7.73 (1 H, d, *J* 6.9), 7.65 -7.35 (11 H, m), 5.42 (0.5 H, d, *J* 6.2), 5.25 (0.5 H, d, *J* 5.7) 5.17 (0.5 H, d, *J* 5.3),

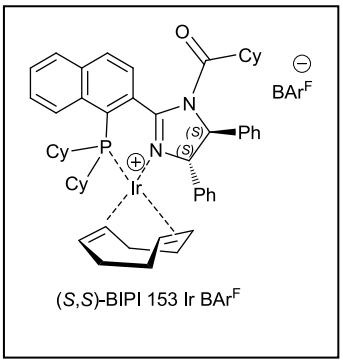
5.07 (0.5 H, d, *J* 5.9), 2.72-2.50 (2 H, m), 2.32 – 2.11 (2 H, m), 2.02-0.50 (29 H, m). δ_C (125 MHz, CD_3OD) 175.9, 144.5, 143.6, 137.0, 135.4 (br), 131.6, 130.8, 130.7, 130.4, 130.2, 129.9, 129.7, 129.63, 129.55, 129.39, 129.35, 129.2, 129.1, 128.52, 128.46, 127.9, 127.8, 127.6, 127.2, 127.1, 126.8 (d, J_{CP} 10.3), 81.4 (br), 80.6 (br), 72.9 (d), 72.0 (d, br), 45.5, 45.1, 39.1, 39.0, 38.5, 38.4, 37.8, 37.7, 36.0, 35.9, 35.8, 35.7, 34.6 (br), 34.4 (br), 32.2, 32.1, 31.7, 31.6 (br), 30.9, 30.2, 29.4, 28.3 (br), 28.1 (br), 28.03, 27.97, 27.6, 27.54, 27.49, 27.4, 26.9, 26.7, 26.6, 26.43, 26.37, 26.1. δ_P (202 MHz, CD_3OD) 2.90, 0.95. HRMS $(M+H)^+$ $C_{44}H_{52}N_2OP$: calculated 655.3811, observed 655.3812, difference = 0.0311 ppm. Chiral HPLC: Chiralpak IA, 5 μm packing, 4.6 X 250 mm, 25 °C, 90: 10 heptane: $CHCl_3$ (stabilized w/ 0.75% EtOH), 2.0 mL/minute, 3 μL injection, 250 nm. (*R,R*)-isomer retention time 3.71 min., (*S,S*)-isomer retention time 4.69 min., sample observed to be > 99.6 % ee (*R,R*).



17C

Zinc Complex 17C: 74.4 g of amorphous HCl salt **17B** (~ 125 mmol, 1 eq.) was partitioned between 250 mL 1N NaOH and 200 mL IPAc, and the aqueous phase was re-extracted with IPAc (1 X 250 mL). The combined organic phases were then washed with half-sat'd NaCl (1 X 400 mL), dried ($MgSO_4$), and the solvents removed in vacuo give 67 g of crude phosphineborane imidazoline free base (~ 120 mmol, 1 eq.) as a light yellow powder. This solid was then charged to a 4-neck 1L flask equipped with direct Ar line, inert gas valve, septum with thermocouple, and a 45/50 center joint. 40.8 g DABCO (360 mmol, 3 eq.) was then added, followed by 300 mL toluene. Ar sparging beneath the solution surface was then started. After 15 minutes, the Ar sparge was stopped, and the flask was heated to 50 °C under Ar. After 1h, HPLC showed the de-boronation was complete. The toluene was then removed under high vacuum at < 30 °C to give an oil. 300 mL MTBE was added to this oil and the mixture was agitated vigorously at RT under Ar, giving a slurry. This slurry was then filtered under N_2 through a short pad of Celite. The filtrate was then concentrated in vacuo to give a yellow solid. This solid was then dissolved in EtOAc and filtered through a broad pad of silica gel under weak N_2 pressure, collecting ~ 1.5 L of eluate. This solution was then concentrated in vacuo to give 79 g of a yellow solid. This solid was then charged to a clean 3-neck 2L flask equipped with a direct Ar line, inert gas valve, 250 mL graduated addition funnel, and septum. 400 mL THF was then added via cannula under N_2 pressure, and slow Ar sparging beneath the slurry surface was then started. After agitating ~ 10 minutes, a clear solution was formed. The flask was then placed in a cool water bath and the addition funnel was then charged with 240 mL 0.5M $ZnCl_2$/THF (120 mmol, 1 eq.). This solution was then added over ~ 5 minutes, giving a yellow solution. After 1h at RT, the volatiles were removed in vacuo to give a yellow foam. This foam was then charged to a 1L flask under Ar. 50 mL methanol was then added and the resulting well-agitated slurry was then heated to reflux. Additional methanol was then added at reflux until a clear solution was obtained, requiring a total of 200 mL. The solution thus obtained was then allowed to cool to RT under Ar while standing, causing crystallization. After 1h at RT, the slurry was filtered under N_2 and the solids dried on the frit to give 49.2 g (60% overall yield) of **17C** as light yellow crystals. M.p.

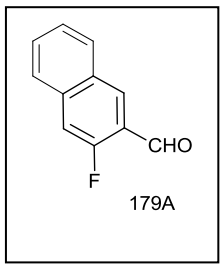
260 °C. $[\alpha]^{22}_{D}$ - 54 (c 0.35, CH_2Cl_2); δ_H (400 MHz, CD_2Cl_2) 7.98 (1 H, d, *J* 8.6), 8.17 (1 H, d, *J* 8.6), 8.02 (1 H, d, *J* 8.0), 7.94 (1 H, dd, *J* 3.7, 8.6), 7.78 (1 H, dt, *J* 1.5, 6.8), 7.73 (1 H, dt, *J* 1.1, 7.3), 7.49-7.36 (8 H, m), 7.33-7.29 (2 H, m), 6.33 (1 H, s), 5.68 (1 H, d, *J* 9.0), 5.00 (1 H, d, *J* 9.0), 3.43 (1 H, d, *J* 5.2), 3.01 (1 H, qt, *J* 2.7, 12.3), 2.75 (1 H, m), 2.32 (1 H, br d, *J* 14), 2.06-1.95 (3 H, m), 1.95-1.80 (3 H, m), 1.78-1.60 (4 H, m), 1.56-1.18 (6 H, m), 1.11 (1 H, m), 0.89 (1 H, br d, *J* 14). δ_C (125 MHz, CD_2Cl_2) 166.4 (s), 141.5 (s), 140.8 (s), 136.4 (s, J_{CP} 3.3), 135.0 (s, J_{CP} 0.8), 135.0 (s, J_{CP} 12), 133.6 (d, J_{CP} 2.1), 130.0 (d), 129.7 (d), 129.2 (d), 129.1 (d), 128.9 (d), 128.7 (d), 128.6 (d), 127.8 (d), 127.5 (d, J_{CP} 1.6), 126.9 (d), 126.8 (s, J_{CP} 7.1), 126.4 (s, J_{CP} 8.2), 78.2 (d, J_{CP} 3.0), 68.2 (d, J_{CP} 1.3), 36.2 (d, $^1J_{CP}$ 12.2), 35.8 (d, $^1J_{CP}$ 12.2), 31.9 (t, J_{CP} 14.5), 30.3 (t, J_{CP} 4.6), 30.3 (t, J_{CP} 1.8), 27.5 (t, J_{CP} 5.5), 27.4 (t, J_{CP} 2.3), 27.34 (t, J_{CP} 1.1), 27.25 (t), 27.1 (t), 26.1 (t, J_{CP} 1.5), 25.9 (t, J_{CP} 1.6). δ_P (162 MHz, CD_2Cl_2) - 12.5. HRMS.



(*S*,*S*)-BIPI 153 Ir BAr^F

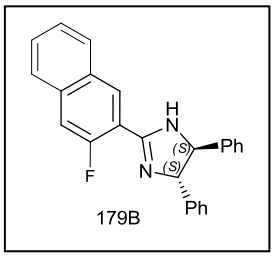
Synthesis of (*S*,*S*)-BIPI 153 Iridium-BAr^F Complex: A 3-neck 100 mL flask equipped with a direct Ar line, inert gas valve and septum was charged with 39 mL CH_2Cl_2. Slow Ar sparging beneath the solution surface was then started. After 10 minutes, 0.367 g $[Ir(COD)Cl]_2$ (0.546 mmol, 0.55 eq., 1.10 Ir eq., weighed in Glovebox) was then added at once, giving a bright orange solution. After 10 minutes, 0.673 g (*S*,*S*)-**BIPI 153 H_2O** (1.00 mmol, 1 eq., weighed in Glovebox) was then added at once to the vigorously stirred mixture, giving immediately a dark red solution which converted to a light orange solution within ~ 20 seconds. After 20 minutes, TLC (CH_2Cl_2) of an aliquot shows the ligand has been consumed. 0.971 g $NaBAr^F$ (1.10 mmol, 1.1 eq.) was then added neat, at once, to the vigorously stirred reaction mixture, causing the rapid formation of a dark red reaction mixture again. After 1h at RT, the volatiles were removed in vacuo and the residue chromatographed on silica gel under N_2 pressure eluting with 2: 1 CH_2Cl_2: Hex and collecting only the center fractions, to give a red oil. This oil was then azeotroped with MTBE (1 X 50 mL) at the Rotovap and finally dried under high vacuum to give 1.091 g (60%) of (*S*,*S*)-**BIPI 153-Ir-BAr^F** as a red foam. δ_H (500 MHz, d_4-MeOH) 8.30 (1 H, d, *J* 4.7), 8.15 (1 H, d, *J* 8.2), 8.08 (1 H, m), 7.95 (1 H, d, *J* 6.9), 7.79 (3 H, m), 7.67-7.50 (26 H, m), 5.76 (1 H, br s), 5.25 (1 H, br s), 2.57-0.75 (41 H, m). δ_C (125 MHz, d_4-MeOH): (NOTE: This complex contains 25 spin ½ nuclei with the capacity to couple to ^{13}C. In addition, there is a quadruploar nucleus (Ir) that causes line broadening of all spectra, and as previously noted,[5] conformational restriction leads to several rotamers as well. Since couplings cannot generally be distinguished from the presence of two resonances (or rotamers) with similar chemical shifts in this complex, the ^{13}C resonances are simply listed with their proton multiplicity): 163.6 (s), 163.2 (s), 162.8 (s), 162.4 (s), 136.0 (d), 131.2 (d), 130.9 (d), 130.8 (d), 130.75 (s), 130.72 (s), 130.70 (s), 130.50 (s), 130.47 (s), 130.45 (s), 129.7 (s), 129.2 (s), 128.6 (d), 128.3 (d), 127.0 (s), 126.7 (d), 124.8 (s), 122.7 (s), 118.66 (d), 118.63 (d), 118.60 (d), 92.6 (s), 78.3 (d), 69.3 (d), 46.3 (d), 33.1 (s), 29.1 (t), 27.9 (t), 27.8 (t), 27.6 (t), 27.3 (d), 27.0 (t), 26.7 (t), 26.4 (t), 26.3 (t), 25.7 (t). δ_P (202 MHz, d_4-MeOH) 17.9. δ_F (376 MHz, d_4-MeOH) - 64.3. δ_B (160

MHz, d_4-MeOH) - 6.74. HRMS [$C_{52}H_{63}N_2OPIr$ + MeCN]: calculated 996.45674, observed 996.4599, difference = 3.1651 ppm.



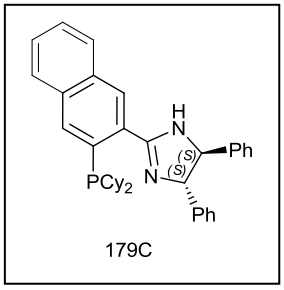
179A

Synthesis of BIPI 179, Part 1, Aldehyde 179A: A 4-neck 500 mL flask was fitted with a thermocouple, 125 mL addition funnel, inert gas valve, and direct Ar line. The flask was charged with 23.0 g 2-fluoronaphthalene (157 mmol, 1 eq.). The flask was then evacuated/Ar filled (3 X), then 150 mL dry THF was added via syringe through the addition funnel. The Ar line was then inserted beneath the solution surface and Ar flow was started. The mixture was then cooled in a -78 ^{o}C bath under Ar. When the internal temperature reached - 60 ^{o}C, the Ar sparging was stopped. The addition funnel was then charged with 100 mL 1.6M *n*-BuLi/hexanes (160 mmol, 1.03 eq.). This solution was then added dropwise over ~ 25 minutes, maintaining the internal temperature < - 55 ^{o}C, giving a green solution. The mixture was maintained at ~ - 70 ^{o}C for 6 hours, then 12.2 mL dry DMF (157 mmol, 1 eq.) was added dropwise via syringe over ~ 10 minutes, causing the internal temperature to rise to - 58 ^{o}C. 10 minutes after completion of the DMF addition, the cold bath was removed, and the mixture allowed to warm to RT. The green color discharged between -30 ^{o}C and 0 ^{o}C. When mixture reached ~ 18 ^{o}C, 150 mL H_2O added via the addition funnel. After stirring overnight at RT, the phases were separated, and the lower aqueous phase was extracted with MTBE (1 X 150 mL). The combined organics were then washed with H_2O (1 X 200 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 30 g of a yellow oil. The oil was chromatographed on silica gel eluting first with hexane to elute unreacted aldehyde (6.5 g white solid). Then column was then eluted with 20: 1 and 10: 1 Hex: EtOAc, collecting 15.5 g of light yellow solid. The 15.5 g of solid was then triturated with ~ 25 mL *n*-heptane, filtered, and air-dried to give 7.5 g of a light yellow solid, and all filtrates were saved. The 7.5 g solid from the middle spot was recrystallized from ~ 40 mL boiling heptane, and allowed to cool while standing, giving 5.00 g of white needles obtained, m.p. 87-89 ^{o}C. Detailed NMR analyses (*Mag. Res. Chem*. **2010**, *48*, 74) show that this solid is the 2-fluoro-3-naphthaldehyde **179A**, 26% yield based on recovered starting material. All of the mother liquors and filtrates were then combined and chromatographed on a 330 g Silicycle silica gel catridge (Combiflash), eluting linearly from 10% CH_2Cl_2/Hex to 60% CH_2Cl_2/Hex over 6 column volumes, at 85 mL/min. Pure fractions of the upper, desired spot (first to elute) were then concentrated in vacuo to give 6.80 g (35% based on recovered starting material) of 2-fluoro-1-naphthaldehyde **19** as a white, crystalline solid. Data for aldehyde **179A**: M.p. 63.5-64.5 ^{o}C. δ_H (600 MHz, $CDCl_3$) 10.44 (1 H, s), 8.41 (1 H, d, *J* 7.0), 7.96 (1 H, d, *J* 8.3), 7.81 (1 H, d, *J* 8.3), 7.62 (1 H, t, *J* 7.1), 7.52 (1 H, d, *J* 11), 7.51 (1 H, t, *J* 7.4). δ_C (150 MHz, $CDCl_3$) 187.5 (d, $^3J_{CF}$ 5), 160.1 (s, $^1J_{CF}$ 255), 136.9 (s, $^3J_{CF}$ 10), 131.9 (d, $^3J_{CF}$ 3), 129.9 (d, $^5J_{CF}$ 1), 129.7 (d, $^5J_{CF}$ 1), 129.6 (s, $^4J_{CF}$ 1), 127.2 (d, $^4J_{CF}$ 5), 126.3 (d, $^6J_{CF}$ 3), 124.1 (d, $^2J_{CF}$ 13), 112.2 (d, $^2J_{CF}$ 20). δ_F ($CDCl_3$, 376 MHz) -122.93 (dd, J_{FC} 7.0, 11.6). HRMS [$C_{11}H_7FO + H^+$]: calculated 175.05646, observed 175.0550, difference = 8.3790 ppm.



179B

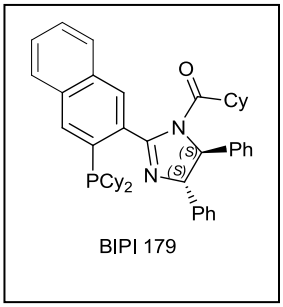
Synthesis of BIPI 179, Part 2, Fluoroimidazoline 179B: A 3-neck 125 mL flask was charged with 3.33 g fluoroaldehyde **179A** (19.1 mmol, 1 eq.), 4.24 g (*S,S*)-diamine (20.0 mmol, 1.05 eq.), and 125 mL CH_2Cl_2 in the order given. The resulting pale yellow solution was stirred at RT under Ar. After 1h at RT, the mixture was cooled to ~ 5 ^{o}C, then 3.56 g NBS (20.0 mmol, 1.05 eq.) was added neat, at once. After 5 min., the bath was removed, and the batch allowed to warm to RT. After 1.5h, HPLC shows the reaction is complete. 50 mL 1N NaOH was then added, and the mixture stirred vigorously for ~ 5 minutes. The phases were then separated, and the aqueous phase was re-extracted with CH_2Cl_2 (1 X 50 mL). The combined organics were then washed with H_2O (1 X 100 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 8.0 g of a yellow solid. This solid was then recrystallized from ~ 25 mL boiling EtOAc and allowed to cool to RT while standing, causing a crystalline mass to form. The resultant slurry was filtered, and the solids air-dried on the frit to give 3.2 g of fluoroimidazoline **179B** as a white solid (46 % first crop yield). All of the filtrates were combined, and the volatiles were removed in vacuo. The residue was then dissolved in ~ 25 mL boiling *n*-heptane, and allowed to cool to RT while standing, causing crystallization. The crystals thus formed were then filtered and air-dried on the frit to give a further 1.7 g of **179B** as a white solid. The combined recrystallized yield was 4.9 g (70%). M.p. 157 ^{o}C; $[\alpha]^{22}_{D}$ + 39 (c 0.22 in CH_2Cl_2); δ_H (400 MHz, $CDCl_3$) 8.85 (1 H, d, *J* 7.7), 7.92 (1 H, d, *J* 8.2), 7.80 (1 H, d, *J* 8.2), 7.59-7.52 (2 H, m), 7.48 (1 H, dt, *J* 1.0, 7.7), 7.40-7.26 (10 H, m), 6.09 (1 H, br s), 4.96 (2 H, s). δ_C (100 MHz, $CDCl_3$) 159.6 (s, J_{CF} 2.5), 158.3 (s, $^{1}J_{CF}$ 248), 143.4 (s), 135.0 (s, J_{CF} 10.1), 132.4 (d, J_{CF} 4.0), 130.1 (s), 128.9 (d), 128.7 (d), 128.3 (d), 127.6 (d), 126.8 (d, J_{CF} 5.0), 126.6 (d), 126.0 (d, J_{CF} 2.3), 112.1 (d), 111.9 (d), (line broadening eliminates the two aliphatic d's). δ_F (376 MHz, $CDCl_3$) – 117.84. HRMS [$C_{25}H_{19}FN_2$ + H^+]: calculated 367.1616, observed 367.1620, difference = 1.0877 ppm.



179C

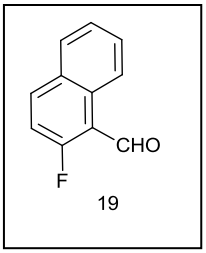
Synthesis of BIPI 179, Part 3, Phosphinoimidazoline 179C: A 3-neck 50 mL flask with direct Ar line, inert gas valve, and septum was charged with 10 mL dry DMAc. Ar sparging was then started. After 20 min., flask placed in a cool water bath. To this solution was then added [1.50 g (*S,S*)-F-imidazoline **179B** (4.09 mmol, 1 eq.) + 1.06 gdicyclohexylphosphine borane (4.50 mmol, 1.1 eq.) + 630 mg 60% NaH (8.59 mmol, 2.1 eq.)] at once, causing immediate gas evolution and foaming and giving a bright yellow reaction mixture. After ~ 30 min., gas evolution had mostly ceased. Ar sparging was then stopped, the bath was removed, and the reaction mixture stirred under Ar at RT, giving a thin, dark yellow slurry, which gave way to a green slurry after 1.5h. After 23h at RT, HPLC at 220 nm (abs. maximum of pdt.) shows 97% completion. The mixture was stirred 1 h additional, and then poured into ~ 25 mL 5M NH_4Cl, and extracted with MTBE (2 X 25 mL). The combined organic phases were then washed with H_2O (1 X 50 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow, sticky oil. 1.38 g DABCO (12.3 mmol, 3 eq.) was then added to the yellow oil, followed by 25 mL PhMe. The resultant yellow solution was then placed in a pre-

equilibrated 50 °C oil bath under Ar. After 4h, HPLC shows < 2% of the intermediate phosphineborane remains. The volatiles were then removed in vacuo. The residual material was then dissolved in EtOAc and filtered through a short column of silica gel, eluting with ~ 100 mL EtOAc. The eluates were then concentrated in vacuo to give 2.4 g (~ 100%) of free phosphinoimidazoline **179C** as a yellow oil which was used immediately.



BIPI 179

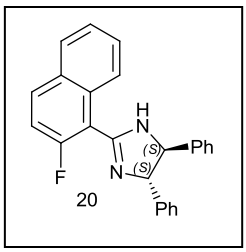
Synthesis of BIPI 179, Part 4, Ligand BIPI 179: A flask was charged with 1.41 g phosphinoimidazoline **179C** (2.59 mmol, 1 eq.) and 15 mL CH_2Cl_2. The resilting solution was cooled to ~ 5 °C under Ar, then 0.722 mL TEA (5.18 mmol, 2 eq.) was added via syringe. After 5 min., 0.346 mL acid chloride (2.59 mmol, 1 eq.) was added via syringe. The bath was then removed, and the mixture allowed to warm to RT. After 1h, TLC shows the reaction is complete to a non-polar spot. 0.25 mL N,N,N"-trimethylethylenediamine was then added via syringe to scavenge any unreacted acid chloride. After 15 min., the volatiles were removed in vacuo. The residue thus obtained was then partitioned between 25 mL EtOAc + 25 mL 0.5N HCl. The organic phase was then washed with 0.5 N HCl (1 X 25 mL), sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 4:1 Hex: EtOAc, and collecting only the center clean fractions, to give a colorless oil. The oil was then azeotroped with MTBE (1 X 25 mL) at the Rotovap, and finally dried under high vacuum to give 1.20 g of **BIPI 179** (71%) as a white, fluffy solid. ^{1}H NMR (500 MHz, d_4-MeOH) δ: 7.89 (m, 1H), . ,). ^{13}C NMR (125 MHz, d_4-MeOH) δ: 165.2 (s, $^3J_{CP}$ = 2.0 Hz),. ^{31}P NMR (202 MHz, d_4-MeOH) δ: - 24.8. . HRMS [$C_{44}H_{51}N_2OP + H^+$]: calculated 655.38227, observed 655.3831, difference = 1.2562 ppm.



19

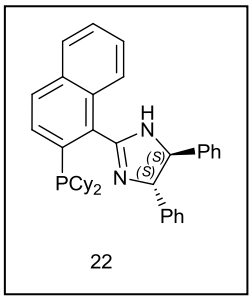
Synthesis of BIPI 180, Part 1, Aldehyde 19: A 4-neck 500 mL flask was fitted with a thermocouple, 125 mL addition funnel, inert gas valve, and direct Ar line. The flask was charged with 23.0 g 2-fluoronaphthalene (157 mmol, 1 eq.). The flask was then evacuated/Ar filled (3 X), then 150 mL dry THF was added via syringe through the addition funnel. The Ar line was then inserted beneath the solution surface and Ar flow was started. The mixture was then cooled in a -78 °C bath under Ar. When the internal temperature reached - 60 °C, the Ar sparging was stopped. The addition funnel was then charged with 100 mL 1.6M *n*-BuLi/hexanes (160 mmol, 1.03 eq.). This solution was then added dropwise over ~ 25 minutes, maintaining the internal temperature < - 55 °C, giving a green solution. The mixture was maintained at ~ - 70 °C for 6 hours, then 12.2 mL dry DMF (157 mmol, 1 eq.) was added dropwise via syringe over ~ 10 minutes, causing the internal temperature to rise to - 58 °C. 10 minutes after completion of the DMF addition, the cold bath was removed, and the mixture allowed to warm to RT. The green color discharged between -30 °C and 0 °C. When mixture reached ~ 18 °C,

150 mL H_2O added via the addition funnel. After stirring overnight at RT, the phases were separated, and the lower aqueous phase was extracted with MTBE (1 X 150 mL). The combined organics were then washed with H_2O (1 X 200 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 30 g of a yellow oil. The oil was chromatographed on silica gel eluting first with hexane to elute unreacted aldehyde (6.5 g white solid). Then column was then eluted with 20: 1 and 10: 1 Hex: EtOAc, collecting 15.5 g of light yellow solid. The 15.5 g of solid was then triturated with ~ 25 mL *n*-heptane, filtered, and air-dried to give 7.5 g of a light yellow solid, and all filtrates were saved. The 7.5 g solid from the middle spot was recrystallized from ~ 40 mL boiling heptane, and allowed to cool while standing, giving 5.00 g of white needles obtained, m.p. 87-89 ^{o}C. Detailed NMR analyses (*Mag. Res. Chem*. **2010**, *48*, 74) show that this solid is the 2-fluoro-3-naphthaldehyde **179A**, 26% yield based on recovered starting material. All of the mother liquors and filtrates were then combined and chromatographed on a 330 g Silicycle silica gel catridge (Combiflash), eluting linearly from 10% CH_2Cl_2/Hex to 60% CH_2Cl_2/Hex over 6 column volumes, at 85 mL/min. Pure fractions of the upper, desired spot (first to elute) were then concentrated in vacuo to give 6.80 g (35% based on recovered starting material) of 2-fluoro-1-naphthaldehyde **19** as a white, crystalline solid, m.p. 63.5-64.5 ^{o}C. Data for aldehyde **19**: δ_H (600 MHz, $CDCl_3$) 10.82 (1 H, s), 9.27 (1 H, d, *J* = 8.7), 8.10 (1 H, d, *J* 9), 7.85 (1 H, d, *J* 8.3), 7.70 (1 H, dd, *J* 7.6, 8.7), 7.55 (1 H, dd, *J* 7.6, 8.3), 7.30 (1 H, d, *J* 9). δ_C (150 MHz, $CDCl_3$) 189.0 (d, $^3J_{CF}$ 13), 167.0 (s, $^1J_{CF}$ 262), 138.0 (d, $^3J_{CF}$ 11), 130.8 (s, $^3J_{CF}$ 2), 130.5 (s), 130.2 (d), 128.4 (d), 126.2 (d, $^6J_{CF}$ 2), 125.5 (d, $^4J_{CF}$ 6), 116.5 (s), 115.7 (d, $^2J_{CF}$ 26). δ_F (376 MHz, $CDCl_3$) - 115.4 (dd, J_{FC} 5.6, 10.7). HRMS [$C_{11}H_7FO + H^+$]: calculated 175.05646, observed 175.0576, difference = 6.4734 ppm.



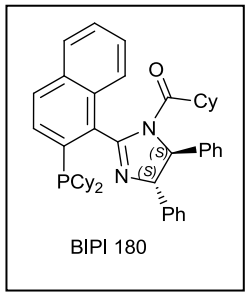
Synthesis of BIPI 180, Part 2, Fluoroimidazoline 20: A 3-neck 125 mL flask was charged with 1.67 g fluoroaldehyde **19** (9.55 mmol, 1 eq.), 2.12 g (*S,S*)-DPEDA (10.0 mmol, 1.05 eq.), and 60 mL CH_2Cl_2 in the order given. The resulting pale yellow solution was stirred at RT under Ar. After 1h at RT, the mixture was cooled to ~ 5 ^{o}C, then 1.78 g NBS (10.0 mmol, 1.05 eq.) was added neat, at once. After 5 min., the cold bath was removed, and the mixture allowed to warm to RT. After 3h, HPLC shows the reaction is complete. 50 mL 1N NaOH was then added, and the mixture stirred vigorously for ~ 5 minutes. The phases were then separated, and the aqueous phase re-extracted with CH_2Cl_2 (1 X 50 mL). The combined organics were then washed with H_2O (1 X 100 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 5.0 g of a yellow oil. 25 mL heptane was added, and the mixture heated to reflux, causing a solid to form. To this suspension was then added EtOAc until a clear solution was just obtianed at reflux (~25 mL EtOAc added). The resultant solution was then allowed to cool to RT while standing, causing crystallization. The slurry obtained was then filtered, and the solids air-dried on the frit to give 1.9 g (54% 1st crop recrystallized yield) of fluoroimidazoline **20** as a white solid. M.p. 163 ^{o}C; $[\alpha]^{22}_D$ - 96 (c 0.24 in CH_2Cl_2); δ_H (400 MHz, $CDCl_3$) 8.53 (1 H, d, *J* 8.2), 7.89 (1 H, dd, *J* 5.5, 9.0), 7.83 (1 H, d, *J* 8.1), 7.57 (1 H, t, *J* 7.2), 7.47 (1 H, dt, *J* 1.1, 8.5), 7.40-7.23 (11 H, m), 5.61 (1 H, br s), 5.00 (2 H, s). δ_C (100 MHz, $CDCl_3$) 158.5 (s, $^1J_{CF}$ 249), 158.2 (s), 143.3 (s), 132.3 (d, J_{CF} 10), 130.5 (s), 128.7 (d), 128.1 (d), 127.9 (d), 127.5 (d), 126.6 (d), 125.6 (d, J_{CF} = 6.0 Hz), 125.5

(d, J_{CF} 2.2), 75.1 (d, br). δ_F (376 MHz, $CDCl_3$) -112.48. HRMS [$C_{25}H_{19}FN_2 + H^+$]: calculated 367.1616, observed 367.1616, difference = 0.0018 ppm.



22

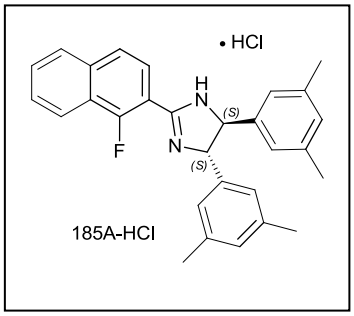
Synthesis of BIPI 180, Part 3, Phosphinoimidazoline 22: A 3-neck 25 mL flask was equipped with a direct Ar line, inert gas valve, and septum. 8.00 mL dry DMAc was then added via syringe, and Ar sparging (bubbling) beneath the solution surface was then started. After 20 min., the flask was placed in a cool water bath. To the flask was then added [1.00 g (*S*,*S*)-Fluoroimidazoline **20** (2.73 mmol, 1 eq.), 0.707 g dicyclohexylphosphine borane (3.00 mmol, 1.1 eq.) + 0.420 g 60% NaH (5.73 mmol, 2.1 eq.)] at once. Ar sparging was maintained, and a dark blue-green reaction mixture was formed. After 24 h at RT, the reaction mixture was poured into 30 mL 5M NH_4Cl, and extracted with MTBE (2 X 30 mL). The combined organics were then washed with H_2O (1 X 50 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give 2.1 g of a yellow foam. 1.12 g DABCO (10 mmol, ~ 3 eq.) was added to the foam, followed by 12 mL PhMe. The resultant mixture was then placed in a pre-equilibrated 50 °C oil bath under Ar. After 3h, the volatiles were removed in vacuo. The residue was then chromatographed on silica gel under N_2 pressure eluting with 2:1 Hex: EtOAc to give 1.26 g (~85% overall) of the intermediate phosphinoimidazoline **22** as a pale yellow foam which was used immediately.



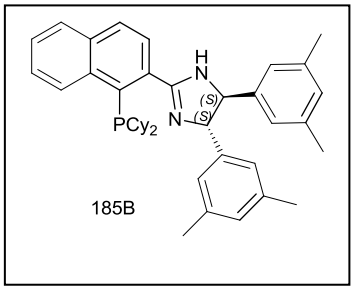
BIPI 180

Synthesis of BIPI 180, Part 4, Ligand BIPI 180: A flask was charged with 1.26 g phosphinoimidazoline **22** (2.32 mmol, 1 eq.) and 10 mL CH_2Cl_2. The resulting solution was cooled to ~ 5 °C under Ar, then 0.65 mL TEA (4.64 mmol, 2 eq.) was added via syringe. After 5 min., 0.310 mL cyclohexanecarbonyl chloride (2.32 mmol, 1 eq.) was added via syringe. After 5 min., the bath was removed, and the mixture allowed to warm to RT. After 45 min. at RT, TLC shows the reaction is complete to a non-polar spot. 0.10 mL N,N,N'-trimethylethylenediamine was then added to scavenge any uneacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 25 mL 0.5N HCl and 50 mL EtOAc. The organic phase was washed with 0.5N HCl (1 X 25 mL), sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a pale yellow foam. The foam was then chromatographed on silica gel under N_2 pressure eluting with 4:1 Hex: EtOAc and collecting only the center fractions. The pure fractions were then concentrated in vacuo, azeotroped with MTBE at the Rotovap (2 X 25 mL), and finally dried under high vacuum to give 0.96 g (62%) of **BIPI 180** as a white foam. δ_H (500 MHz, d_4-MeOH) 7.78 (1 H, d, *J* 8.3), 7.75-7.68 (4 H, m), 7.58 (1 H, d, *J* 7.6), 7.37 (2 H, m), 7.25 (4 H, m), 7.19 (4 H, m), 5.20 (1 H, d, *J* 7.7), 5.03 (1 H, d, *J* 7.3), 2.10 (1 H, br s), 1.90-1.75 (4 H, m), 1.68 (2 H, m), 1.57-1.35 (8 H, m), 1.35-0.66 (15 H, m), 0.63 (2 H, m), 0.40 (1 H, br d). δ_C (125 MHz, d_4-MeOH) 176.2, 144.1, 143.0, 134.9 (J_{CP} 0.9), 132.7 (J_{CP} 8.5), 130.2, 130.1, 129.8 (J_{CP} 2.7), 129.5, 129.2, 128.9, 128.8, 128.2, 128.15, 128.10, 126.1 (J_{CP} 2.5), 80.5, 72.6, 45.0, 37.4, 37.3, 32.3, 32.1, 32.0, 31.9, 31.7, 30.6, 30.1,

28.6, 28.5, 28.4, 28.3, 27.83, 27.82, 27.8, 27.7, 27.5, 27.2, 26.42, 26.38, 26.0. δ_P (202 MHz, d_4-MeOH) - 7.25. HRMS [$C_{44}H_1FN_2OP + H^+$]: calculated 655.38227, observed 655.3841, difference = 2.7820 ppm.

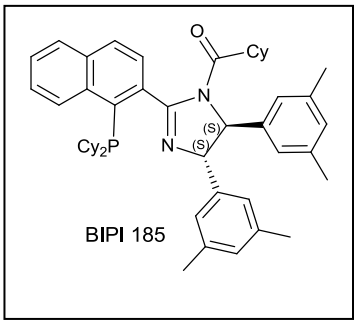


Synthesis of BIPI 185, Part 1, Fluoroimidazoline 185A-HCl: 0.60 g (*S,S*)-bis-(*m*-xyl)-ethylenediamine phosphate salt was partitioned between 25 mL CH_2Cl_2 and 25 mL 1N NaOH, then the aqueous phase was re-extracted with CH_2Cl_2 (2 X 25 mL). The combined organics were then dried ($MgSO_4$), and the solvents removed in vacuo to give 0.370 g (1.38 mmol, 1 eq.) of the free base diamine as a nearly colorless oil. To this oil was then added 0.24 g fluoro-naphthaldehyde **17** (1.38 mmol, 1 eq.) and 8.0 mL CH_2Cl_2. The resulting solution was stirred 2h at RT under Ar, and then cooled in an ice bath. To the reaction mixture was then added 0.258 g NBS (1.45 mmol, 1.05 eq.) neat, at once. The reaction mixture was left in the ice bath and allowed to slowly warm to RT overnight. After stirring overnight, 20 mL 1N NaOH added, the mixture stirred vigorously ~ 5 min., then the phases were separated, and the aqueous phase re-extracted with CH_2Cl_2 (1 X 20 mL). The combined organics were then washed with H_2O (1 X 50 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow oil. This oil was then dissolved in ~ 25 mL MTBE. To this solution, stirring under Ar at RT, was then added 0.70 mL 2M HCl/Et_2O (1.4 mmol, 1 eq.) dropwise via syringe, causing a thick slurry of the HCl salt to form. The slurry was stirred ~ 5 min., then filtered under N_2, washing the solids well with MTBE to give 300 mg (47%) of **185A-HCl** as an off-white solid. M.p. 161 ^oC; $[\alpha]^{22}_D$ - 52 (c 0.10, MeOH); δ_H (500 MHz, d_6-DMSO) 11.5 (2 H, s), 8.32 (1 H, d, *J* 8.3), 8.20 (1 H, d, *J* 8.2), 8.11-8.05 (2 H, m), 7.90 (1 H, t, *J* 7.0), 7.84 (1 H, t, *J* 7.3), 7.15-7.07 (6 H, m), 5.24 (2 H, s), 2.51 (1 H, m), 2.33 (12 H, s). δ_C (100 MHz, d_6-DMSO) 160.0 (s), 157.5 (s, $^1J_{CF}$ 266), 138.7 (s), 138.3 (s), 136.9 (s, J_{CF} 5.9), 130.6 (d), 130.3 (d), 128.5 (d), 128.0 (d, J_{CF} 2.1), 124.8 (d, J_{CF} 3.0), 124.65 (d), 124.57 (d), 122.0 (s, J_{CF} 15.4), 121.4 (d, J_{CP} 6.0), 105.6 (s, J_{CP} 9.4), 68.9 (d), 20.9 (q). δ_F (376 MHz, d_6-DMSO) - 114.52. HRMS [$C_{29}H_{27}FN_2 + H^+$]: calculated 423.2242, observed 423.2247, difference = 1.791 ppm.



Synthesis of BIPI 185, Part 2, Phosphinoimidazoline 185B: 300 mg of **185A-HCl** was suspended in 25 mL 2N NaOH and extracted with CH_2Cl_2 (2 X 25 mL). The combined organics were then dried ($MgSO_4$), and the solvents removed in vacuo to give 0.257 g of the free base fluoroimidazoline **185A**, which was used immediately in the following step. A 3-neck 15 mL flask equipped with direct Ar line, inert gas valve and septum was charged with 0.257 g (*S,S*)-fluoroimidazoline **185A** (0.608 mmol, 1 eq.), 0.155 g dicyclohexylphosphine borane (0.729 mmol, 1.2 eq.), and 2.5 mL dry DMAc. Ar sparging beneath the yellow solution surface was then started. After 15 min., 53 mg 60% NaH (1.33 mmol, 2.2 eq.) was added quickly, while maintaining Ar sparging. Immediate gas evolution was noted, with formation of a yellow-orange solution. After 15 min. at RT, Ar sparging was stopped. The resultant orange solution was then stirred at RT under Ar. After 18h, a yellow solution was

present, and HPLC indicated the reaction was complete. The reaction mixture was then quenched with 10 mL 5M NH_4Cl, and then extracted with MTBE (2 X 20 mL). The combined organics were then washed with H_2O (1 X 40 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow oil. To this oil was then added 0.35 g DABCO (3 mmol, ~ 5 eq.) and 5.0 mL PhMe. The resulting mixture was then placed in a pre-equilibrated 50 ^oC oil bath under Ar. After 2h, HPLC showed de-boronation was complete. The reaction mixture was then cooled to RT, and the volatiles were removed in vacuo. The residue was then chromatographed on silica gel under N_2 pressure eluting with EtOAc to give 150 mg of **185B** (0.25 mmol, 41% over 2 steps) as a light yellow solid, which was used immediately.



Synthesis of BIPI 185, Part 3, Ligand BIPI 185:.

150 mg of the phosphinoimidazoline **185B** (0.25 mmol, 1 eq.), 2.0 mL CH_2Cl_2, and 0.07 mL TEA (0.50 mmol, 2 eq.) were charged to a 15 mL flask. To this yellow solution, stirring under Ar at RT, was then added 0.033 mL acid chloride (0.25 mmol, 1 eq.) via syringe. After 2h, 0.05 mL *N,N,N'*-trimethylethylenediamine added to scavenge any unreacted acid chloride. After 5 min., the volatiles were removed in vacuo. The residue was then partitioned between 25 mL EtOAc + 25 mL 0.5N HCl. The organic phase was then washed with sat'd $NaHCO_3$ (1 X 25 mL), dried ($MgSO_4$), and the solvents removed in vacuo to give a yellow foam. This foam was then chromatographed on silica gel under N_2 pressure eluting with 6:1 Hex: EtOAc and collecting only the center fractions, to give an oil. This oil was then azeotroped with MTBE (2 X 10 mL) at the Rotovap, and finally dried under high vacuum to give 0.110 g (62 %) of **BIPI 185** as a white foam. δ_H (500 MHz, d_4-MeOH) 8.22 (1 H, d, *J* 8.4), 8.00 (2 H, m), 7.66 (2 H, m), 7.56 (2 H, m), 7.52 (0.6 H, dd, *J* 2.6, 8.4), 7.32 (1 H, s), 7.07 (1 H, s), 7.04 (2 H, s), 6.95 (1 H, s), 5.36 (0.45 H, d, *J* 5.2), 5.15 (0.55 H, d, *J* 6.2), 5.09 (0.55 H, d, *J* 6.1), 4.98 (0.45 H, d, *J* 5.0), 2.60 (2 H, m), 2.43 (3 H, s), 2.39 (6 H, s), 2.38 (3 H, s), 2.30-0.91 (30 H, m), 0.64 (1 H, m). δ_C (125 MHz, d_4-MeOH) 176.0, 144.4, 143.4, 124.9, 140.5, 140.0, 139.9, 139.4, 139.2, 136.88, 136.83, 136.70, 136.66, 135.2, 131.4, 130.9, 130.8, 130.7, 130.6, 130.55, 130.53, 128.4, 127.8, 127.7, 127.5, 127.4, 127.3, 127.2, 127.0, 126.9, 126.62, 126.58, 126.54, 126.50, 125.4, 124.8, 81.6, 80.8, 72.9, 71.6, 45.3, 44.9, 39.0, 38.9, 38.3, 38.2, 37.83, 37.78, 37.72, 37.67, 36.1, 35.9, 35.7, 34.8, 34.6, 34.1, 33.9, 32.1, 32.0, 31.9, 31.8, 31.7, 31.6, 31.1, 30.8, 30.0, 29.3, 28.2, 28.1, 28.06, 28.0, 27.9, 27.5, 27.44, 27.38, 27.25, 27.21, 26.7, 26.62, 26.57, 26.34, 26.31, 26.0. δ_P (202 MHz, d_4-MeOH) 0.6, - 0.7. HRMS [$C_{48}H_{59}N_2OP + H^+$]: calculated 711.44487, observed 711.4468, difference = 2.7029 ppm.

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