Supplementary Information

Asymmetric Catalytic Strecker Reaction of *N*-Phosphonyl Imine with Et_2AlCN using Amino Alcohols and BINOLs as Catalysts

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Contents

Experimental

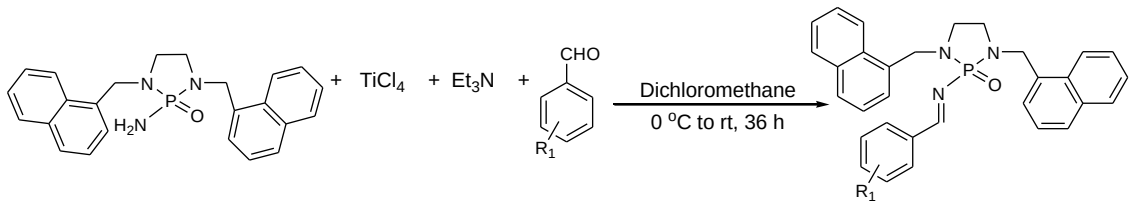
General information

All commercially available solvents, unless otherwise mentioned, were used without purification. THF was distilled from sodium/benzophenone ketyl. All the glassware used was dried overnight at 100 ^{o}C. All melting points are uncorrected. The NMR spectra were recorded at 500, 125, 202 MHz for ^{1}H, ^{13}C and ^{31}P respectively. Shifts are reported in ppm based on an internal TMS standard (for ^{1}H/$CDCl_3$) or on residual solvent peaks (for ^{13}C/$CDCl_3$). ^{31}P NMR spectra were referenced to external H_3PO_4 (0.00 ppm). Dry *i*-PrOH was obtained from Acros. Diethylaluminium cyanide (1.0 M solution in toluene) and Titanium (IV) chloride (1.0 M solution in dichloromethane) were obtained from Aldrich and used as obtained from commercial sources without any further purification. Flash chromatographic columns were carried out on silica gel 60, (230-400 mesh).

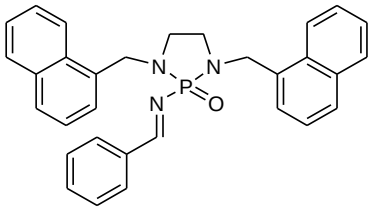
Typical procedure for the synthesis of achiral *N*-phosphonyl imine (1a-k)

In a dry vial, under inert gas protection, *N,N*-naphthalen-1-ylmethyl phosphoramide (1.0 equiv.) was taken and dissolved in dry dichloromethane. To the solution, corresponding aldehyde (1.5 equiv.) was added followed by the addition of triethylamine (3.0 equiv.). The reaction was cooled down to 0 ^{o}C and titanium (IV) chloride (1.0 M solution in DCM, 0.5 equiv.) was added to the reaction (Scheme 1). The reaction was allowed to stir at room temperature for 36 h and after that the mixture was loaded directly to silica gel. The reaction mixture was purified through column chromatography (Ethyl acetate: Hexane: 1% Et_3N). Pure product was obtained by eluting the reaction mixture with ethyl acetate: hexane: triethylamine (60:40:1mL) as white or pale yellow solid in all of the cases reported.

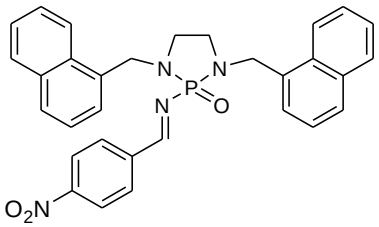
Scheme 1



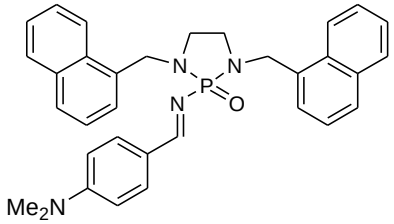
1a-1m



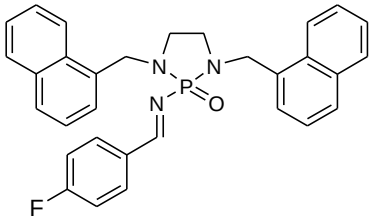
Compound 1a White solid; yield (0.172 g, 76%); mp 84-86 ^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.03 (d, *J* = 33.5 Hz, 1H), 8.28 (d, *J* = 9.0 Hz, 2H), 7.86-7.82 (m, 4H), 7.78 (d, *J* = 8.0 Hz, 2H), 7.53-7.46 (m, 9H), 7.42-7.39 (m, 2H), 4.67-4.64 (m, 2H), 4.55-4.52 (m, 2H), 3.13 (d, *J* = 9.5 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.5 (d, *J* = 7.0 Hz), 139.6, 135.8, 135.6 (2C), 133.7, 133.1, 132.7(2C), 132.6, 131.7 (2C), 129.9 (2C), 128.7 (2C), 128.4, 128.3, 126.7 (2C), 126.2, 125.7, 125.4, 125.0 (2C), 123.8, 120.5, 47.43, 47.40 (d, *J* = 7.3 Hz), 44.9, 42.3. ^{31}P NMR (202 MHz, $CDCl_3$) δ 24.2.



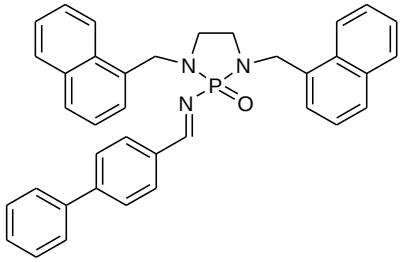
Compound 1b Pale yellow solid; Yield (0.230 g, 80%); mp 66-68 ^{0}C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.78 (d, *J* = 32.5 Hz, 1H), 8.27 (dd, *J* = 7.0, 1.5 Hz, 2H), 8.21 (d, *J* = 7.5 Hz, 2H), 8.08 (d, *J* = 9.0 Hz, 1H), 7.81-7.80 (m, 3H), 7.77 (d, *J* = 10.0 Hz, 2H), 7.51-7.44 (m, 6H), 7.39 (t, *J* = 7.0 Hz, 2H), 4.68-4.51 (m, 4H), 3.20 (d, *J* = 9.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 170.6 (d, *J* = 6.5 Hz), 150.1, 140.7 (d, *J* = 9.5 Hz), 133.7 (2C), 132.3 (d, *J* = 7.0 Hz, 2C), 131.7 (2C), 130.4, 130.3 (2C), 128.5 (d, *J* = 9.0 Hz, 2C), 127.0 (2C), 126.3 (2C), 125.8 (2C), 125.1 (2C), 124.2, 123.79 (2C), 123.73 (2C), 47.4 (d, *J* = 5.0 Hz, 2C), 45.1 (d, *J* = 10.0 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.1.



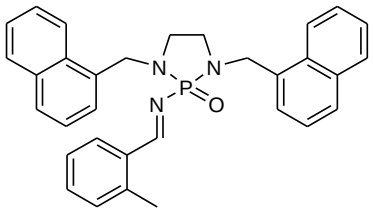
Compound 1c Off white solid ; Yield (0.190g, 82%); mp 78-80 ^{0}C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.99 (d, *J* = 33.5 Hz, 1H), 8.30 (d, *J* = 6.0 Hz, 2H), 7.83-7.75 (m, 6H), 7.52-7.37 (m, 8H), 6.73 (d, *J* = 9.0 Hz, 2H), 4.63-4.50 (m, 4H), 3.10 (s, 6H), 3.08-3.05 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.7 (d, *J* = 6.0 Hz), 153.7, 133.7 (2C), 133.2, 133.1, 132.2 (2C), 131.8 (d, *J* = 8.9 Hz, 2C), 128.3 (2C), 128.2 (2C), 126.7 (2C), 126.2 (2C), 125.7 (2C), 125.1 (2C), 124.1(2C), 111.1 (2C), 47.5 (d, *J* = 10.4 Hz, 2C), 45.0 (d, *J* = 10.4 Hz, 2C), 40.1 (2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 27.1.



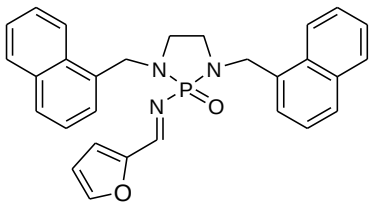
Compound 1d White foamy solid; Yield (0.214g, 82%); mp 68-70 ^{0}C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.87 (d, *J* = 32.9 Hz, 1H), 8.24 (dd, *J* = 8.9, 1.8 Hz, 2H), 7.83-7.76 (m, 6H), 7.52-7.46 (m, 6H), 7.41-7.38 (m, 2H), 7.15 (t, *J* = 8.5 Hz, 2H), 4.66-4.49 (m, 4H), 3.15-3.11 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.3 (d, *J* = 6.45 Hz), 166.8, 164.8, 133.8 (2C), 132.65 (d, *J* = 6.94 Hz, 2C), 132.18 (d, *J* = 8.9 Hz, 2C), 131.7 (2C), 128.5 (2C), 128.4 (2C), 126.8 (2C), 126.3 (2C), 125.8 (2C), 125.1 (2C), 123.9 (2C), 116.1, 115.9, 47.5 (d, *J* = 4.9 Hz, 2C), 45.0 (d, *J* = 10.4 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.1.



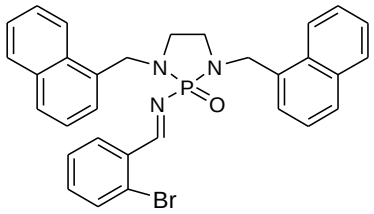
Compound 1e White solid; yield (0.301g, 76%); mp 71 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): 9.02 (d, *J* = 33 Hz, 1H), 8.28 (d, *J* = 8 Hz, 2H), 7.91 (d, *J* = 8.5 Hz, 2H), 7.84 (d, *J* = 8.0 Hz, 2H), 7.78 (d, *J* = 8.5 Hz, 2H), 7.71 (d, *J* = 8.5 Hz, 2H), 7.67 (d, *J* = 7.5, 2H), 7.54-7.39 (m, 11 H), 4.67 (dd, *J* = 7 Hz, 14.5 Hz, 2H), 4.55 (dd, *J* = 5 Hz, 15 Hz, 2H), 3.14 (d, *J* = 9.5 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$): 173.5 (d, *J* = 6.9 Hz), 145.9, 140.0, 134.8, 134.6, 133.8 (2C), 132.8 (d, *J* = 6.9 Hz), 131.8 (2C), 130.5 (2C), 128.9 (2C), 128.5 (2C), 128.4 (2C), 128.2, 127.4 (2C), 127.3 (2C), 126.8 (2C), 126.3 (2C), 125.8 (2C), 125.1 (2C), 123.9 (2C), 47.5 (d, *J* = 5 Hz, 2C), 45.0 (d, *J* = 10.4 Hz, 2C); ^{31}P NMR (200 MHz, $CDCl_3$): 26.4.



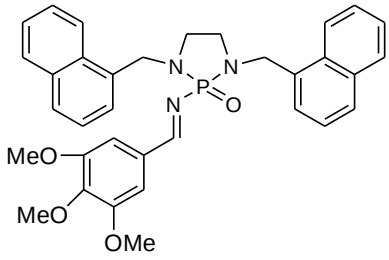
Compound 1f Pale yellow solid; Yield (0.284g, 82%); mp 62-64 ºC. ^{1}H NMR (500 MHz, $CDCl_3$): 9.62 (d, *J* = 33.5 Hz, 1H), 8.29 (d, *J* = 8.0 Hz, 2H), 7.82-7.76 (m, 6H), 7.53-7.38 (m, 10H), 4.69 (dd, *J* = 7.0 Hz, 15.0 Hz, 2H), 4.54 (dd, *J* = 5.0 Hz, 14.5 Hz, 2H), 3.08 (d, *J* = 10.0 Hz, 4H), 2.04 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$): 169.8 (d, *J* = 5.4 Hz), 134.7 (2C), 133.6 (2C), 132.8 (d, *J* = 7.3 Hz, 2C), 131.6 (2C), 128.3 (2C), 128.2 (2C), 128.0 (2C), 126.4, (2C), 126.2 (2C), 125.8 (2C), 125.1 (2C), 123.8 (2C), 120.4, 111.1, 47.3 (d, *J* = 4.5 Hz, 2C), 44.8 (d, *J* = 10.7, 2C), 14.0; ^{31}P NMR (202 MHz, $CDCl_3$): 25.8.



Compound 1g Yellow color solid; Yield (0.216 g, 90%), mp 68-70 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.85 (d, *J* = 34.2 Hz, 1H), 8.29 (d, *J* = 7.8Hz, 2H), 7.86-δ7.78 (m, 4H), δ7.71 (s, 1H), 7.57-7.41 (m, 8H), 7.07(d, *J* = 3.6Hz, 1H), 6.62-6.61(m, 1H), 4.71-4.64 (m, 2H), 4.56-4.49 (m, 2H), 3.22-3.09 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ161.2 (d, *J* = 5.9Hz), 152.1, 151.8, 147.4, 133.7 (2C), 132.6 (d, *J* = 7.3Hz), 131.7 (2C), 128.4 (d, *J* = 13.7Hz, 2C), 126.7 (2C), 126.3 (2C), 125.7 (2C), 125.1 (2C), 123.8 (2C), 121.2 (2C), 112.7 (2C), 47.2 (d, *J* = 5.0Hz, 2C), 44.8 (d, *J* =10.3Hz, 2C). ^{31}P NMR (202 MHz; $CDCl_3$) δ 26.4.

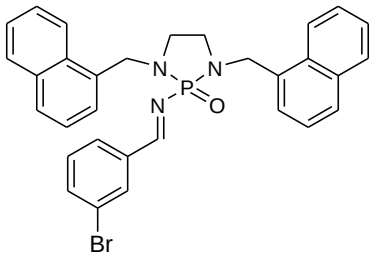


Compound 1h Pale yellow solid; Yield (0.362g, 79%); mp 54-56 ºC. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.32 (d, *J* = 32.5 Hz, 1H), 8.27 (d, *J* = 8.5 Hz, 2H), 8.15-8.13 (m, 1H), 7.83 (d, *J* = 8.25 Hz, 2H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.62-7.60 (m,1H), 7.54-7.44 (m, 6H), 7.42-7.36 (m, 4H), 4.71 (dd, *J* = 7.0 Hz, 15.0 Hz, 2H), 4.56 (dd, *J* = 5.0 Hz, 14.5 Hz, 2H), 3.12 (d, *J* = 10.0 Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.4 (d, *J* = 5.4 Hz), 134.23, 133.9, 133.8, 133.4, 132.6 (d, *J* = 7.0 Hz, 2C), 131.7 (2C), 129.6, (2C), 128.4 (d, 11.2 Hz, 2C), 127.6 (2C), 127.5 (2C), 126.6 (2C), 126.4 (2C), 125.8 (2C), 125.1 (2C), 123.8 (2C), 47.5 (d, *J* = 4.5 Hz, 2C), 44.9 (d, *J* = 10.7 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.0

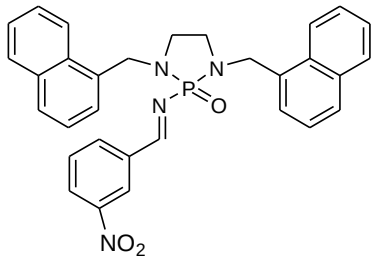


Compound 1i White foamy solid, Yield (0.210g, 91%), mp 60-62 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 33.0 Hz, 1H), 8.29 (d, *J* = 9.3 Hz, 2H), 7.89-7.79 (m, 4H), 7.56-7.41 (m, 8H), 7.05 (s, 2H), 4.72-4.53 (m, 4H), 3.98 (s, 3H), 3.94 (s, 6H), 3.17- 3.13 (m, 4H). ^{13}C NMR

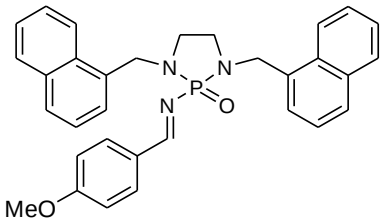
(125 MHz, $CDCl_3$) δ 173.1, 153.6, 142.7, 134.1 (2C), 133.07 (d, *J* = 6.9 Hz, 2C), 132.0 (2C), 131.5, 131.1, 128.8 (2C), 128.7 (2C), 127.2 (2C), 126.6 (2C), 126.0 (2C), 125.4 (2C), 124.2 (2C), 107.2 (2C), 61.3, 56.5 (2C), 47.8 (d, *J* = 4.6 Hz, 2C), 45.3 (d, *J* = 10.6 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.7.



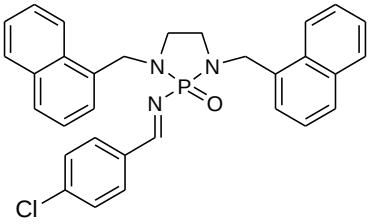
Compound 1j Pale yellow color solid; Yield (0.138g, 87%), mp 70-72^{o}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.80 (d, *J* =32.7Hz, 1H), 8.26 (d, *J* =7.5Hz, 2H), 7.95 (s, 1H), 7.86-7.78 (m, 4H), 7.72-7.62 (m, 2H), 7.55-7.32 (m, 9H), 4.71-4.64 (m, 2H), 4.57-4.51 (m, 2H), 3.18 (d, *J* =9.6Hz, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ172.4 (d, *J* = 6.5Hz), 138.1, 137.7 (2C), 136.0 (2C), 134.0 (2C), 132.8 (d, *J* = 6.5Hz, 2C), 132.0 (d, *J* = 4.6Hz, 2C), 130.5, 129.4 (2C), 128.7 (2C), 127.2 (2C), 126.6 (2C), 126.1 (2C), 125.4 (2C), 124.1 (2C), 47.7 (d, *J* = 4.6Hz, 2C), δ 44.8 (d, *J* =10.9Hz, 2C). ^{31}P NMR (202 MHz; $CDCl_3$) δ 25.6.



Compound 1k White solid, Yield (0.214g, 81%); mp 64-66 ^{0}C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.30 (d, *J* = 33.0 Hz, 1H), 8.32-8.25 (m, 2H), 8.12-8.07 (m, 1H), 7.88-7.56 (m, 5H), 7.59-7.38 (m, 10H), 4.72-4.49 (m, 4H), 3.13-2.92 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 171.5 (d, *J* = 5.7 Hz), 148.2, 137.1 (d, *J* = 8.9 Hz), 135.5, 133.7 (d, *J* = 6.8 Hz), 132.3, 131.7, 129.7, 128.5 (2C), 128.6 (2C), 127.0 (2C), 126.9 (2C), 126.5 (2C), 126.3 (2C), 125.8 (2C), 125.1 (2C), 123.77 (2C), 123.71, 47.6 (d, *J* = 4.8 Hz, 2C), 45.1 (d, *J* = 10.9 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.2



Compound 1l White solid, yield (0.198g, 87%); mp 64-66 ^{0}C ; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.98 (d, *J* = 33.3 Hz, 1H), 8.31 (d, *J* = 8.4 Hz, 2H), 7.88-7.79 (m, 6H), 7.57-7.41 (m, 8H), 7.02 (d, *J* = 8.7 Hz, 2H), 4.71-4.53 (m, 4H), 3.92 (s, 3H), 3.13 (d, *J* = 9.6 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 173.4 (d, *J* = 6.52 Hz), 164.1 (2C), 134.1 (2C), 133.16 (d, *J* = 7.4 Hz, 2C), 132.4 (2C), 132.1 (2C), 128.7 (2C), 128.6 (2C), 127.0 (2C), 126.6 (2C), 126.0 (2C), 125.4 (2C), 124.2 (2C), 114.4 (2C), 55.8, 47.8 (d, *J* = 4.7 Hz, 2C), 45.3 (d, *J* = 10.6 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.8

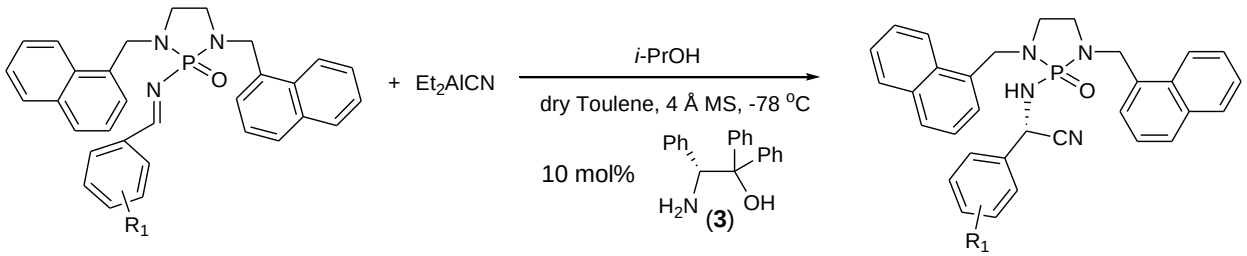


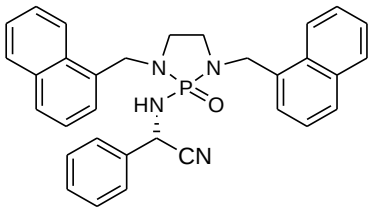
Compound 1m White foamy solid; Yield (0.186g, 87%); mp 60-62 ^{0}C; ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.84 (d, *J* = 33.0 Hz, 1H), 8.25-8.22 (m, 2H), 7.84-7.69 (m, 6H), 7.52-7.37 (m, 10H), 4.68-4.48 (m, 4H), 3.15-2.89 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 172.5 (d, *J* = 6.6 Hz), 139.5, 134.6, 134.2, 134.0 (2C), 132.8 (d, *J* = 6.9 Hz), 131.9 (2C), 131.3 (2C), 129.3 (2C), 128.7 (2C), 128.7 (2C), 127.1 (2C), 126.5 (2C), 126.0 (2C), 125.3 (2C), 124.0 (2C), 47.6 (d, *J* = 4.9 Hz, 2C), 45.2 (d, *J* = 10.9 Hz, 2C). ^{31}P NMR (202 MHz, $CDCl_3$) δ 26.0.

Typical procedure for the synthesis of *N*-phosphonyl substituted α-aminonitrile

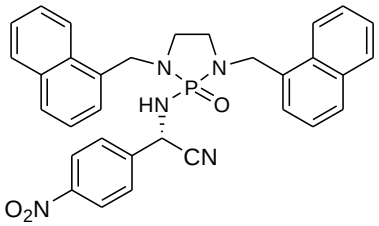
In a dry vial, under inert gas protection, 4 Å MS and the chiral amino alcohol/substituted-BINOL (**3**) was loaded followed by the addition of dry toluene. A turbid solution was obtained in which diethylaluminium cyanide (**2**) (1.0 M solution in toluene, 1.50 equiv.) was added followed by the addition of *i*-PrOH (1.0 equiv.). The solution slowly became clear on stirring at room temperature for 15 min. After 15 min, the reaction was brought to -78 ^{o}C and stirred for 30 min followed by the addition of achiral *N*-phosphonyl imine (1.0 equiv.) pre-dissolved in 3 mL of toluene (Scheme 2). The reaction mixture was constantly monitored by TLC and allowed to stir for 5 h before it was quenched by adding 0.05 M hydrochloric acid followed by the addition of 10 mL ethylacetate and 10 mL water. The solution was filtered off through celite and organic layer was separated and dried over anhydrous sodium sulfate. Sodium sulfate was filtered off and the organic layer was evaporated to obtain the desired product as pale yellow solid which on washing with hexanes afforded the pure product as white solid without any further purification in all the cases reported. For determining the enantioselectivity as well as the absolute configuration, the product was hydrolysed using MeOH/HCl followed by the *t*-Boc protection of the free amine using *t*-Boc anhydride (Scheme 4).

Scheme 2

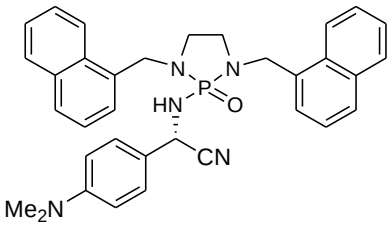




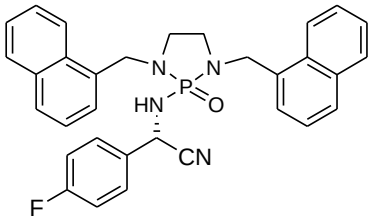
Compound 3a White solid; yield (0.246 g, 92%); mp 112-114 ^{o}C; $[\alpha]_D^{24}$ = + 2.52 (c 1.0, $CHCl_3$) ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, *J* = 9.5 Hz, 2H), 8.15 (d, *J* = 7.5 Hz, 2H), 7.86 (t, *J* = 7.0 Hz, 2H), 7.80 (d, *J* = 8.0 Hz, 2H), 7.51-7.45 (m, 5H), 7.44-7.39 (m, 4H), 7.35-7.34 (m, 2H), 5.42 (t, *J* = 9.0 Hz, 1H), 4.65-4.55 (m, 4H), 3.44 (t, *J* = 9.5 Hz, 1H), 3.05-3.01 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.36, 135.31, 133.8, 133.7, 132.37, 132.31, 131.6 (d, *J* = 8.0 Hz, 2C), 128.6 (d, *J* = 7.3 Hz, 2C), 128.5, 128.4, 128.3, 126.7, 126.6, 126.5, 126.4, 126.3, 125.9, 125.8, 125.24, 125.20, 123.4, 123.3 (2C), 119.98, 119.92, 47.5, 46.8 (d, *J* = 7.3 Hz), 44.6 (d, *J* = 7.8 Hz), 44.0, 43.9. ^{31}P NMR (202 MHz, $CDCl_3$) δ 21.9. HRMS (ESI): m/z calcd for $C_{32}H_{30}N_4OP$, 517.2152; found, 517.2156. Ee: 98% {retention time = 6.32 (minor), 6.74 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.



Compound 3b Pale yellow solid; Yield (0.174g, 96%); mp 138-140 ^{o}C; $[\alpha]_D^{25}$ = +5.7^{o} (c 1.4, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): 8.21 (d, *J* = 11.5 Hz, 1H), 8.06 (d, *J* = 10.0 Hz, 1H), 7.99 (d, *J* = 8.5 Hz, 2 H), 7.86 (d, *J* = 7.5 Hz, 2H), 7.78 (t, *J* = 8.0 Hz, 2H), 7.52-7.44 (m, 6 H), 7.42-7.26 (m, 4H), 5.47 (t, *J* = 9.5 Hz, 1H), 4.70-4.54 (m, 4H), 3.54 (t, *J* = 9.5 Hz, 1H), 3.21-3.09 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): 148.0, 141.7 (d, *J* = 7.0 Hz), 133.8, 133.7, 132.1 (d, *J* = 7.0 Hz), 131.6, 131.3, 128.8 (2C), 128.7, 128.4, 127.5 (2C), 126.8 (2C), 126.5 (2C), 126.4 (2C), 126.0 (d, *J* = 7.5 Hz), 125.7, 125.2 (d, *J* = 6.5 Hz, 2C), 124.2 (2C), 123.2, 122.9, 118.8 (d, *J* = 5.4 Hz), 47.0 (d, *J* = 2 Hz), 46.1 (d, *J* = 5.9 Hz), 45.0 (d, *J* = 4.5 Hz), 44.5 (d, *J* = 6.0Hz); ^{31}P NMR (202 MHz, $CDCl_3$): 22.4. Ee: 93% {retention time = 6.49 (minor) and 6.96 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

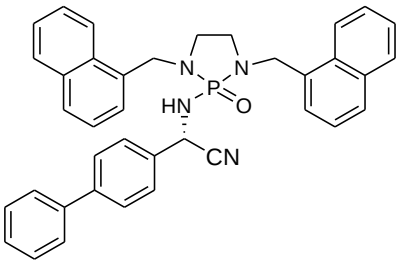


Compound 3c Off white solid; Yield (0.158g, 97%); mp 146-148 ^{o}C; $[\alpha]_D^{25}$ = + 8.2^{o} (c 1.7, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): 8.21-8.16 (m, 2H), 7.88-7.85 (m, 2H), 7.80-7.78 (m, 2 H), 7.51-7.48 (m, 6H), 7.42 (t, *J* = 7.0 Hz 2H), 7.25-7.23 (m, 2 H), 6.63-6.61 (m, 2H), 5.28 (t, *J* = 9.5 Hz, 1H), 4.65-4.54 (m, 4H), 3.30 (t, *J* =10.5 Hz, 1H), 3.09-3.10 (m, 4H),2.93 (s, 6H). ^{13}C NMR (125 MHz, $CDCl_3$) 151.1, 134.0 (d, *J* = 8.5 Hz), 132.8 (d, *J* = 9.5 Hz), 131.9 (d, *J* = 6.5 Hz), 128.9 (2C), 128.8 (2C), 128.6 (2C), 128.5 (2C), 127.9 (2C), 126.7 (2C), 126.6 (2C), 126.1 (2C), 126.0 (2C), 125.5 (d, *J* = 6.0 Hz, 2C), 123.7, 112.6, 47.3, 46.9 (d, *J* = 2 Hz), 46.4 (d, *J* = 5.9 Hz), 44.9 (d, *J* = 6.0Hz), 44.2 (d, *J* = 5.0 Hz), 40.5 (2C); ^{31}P NMR (202 MHz, $CDCl_3$): 21.9. Ee: 96% {retention time = 6.49 (minor) and 6.97 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

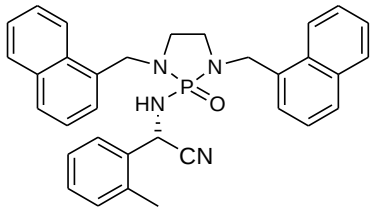


Compound 3d Off-white solid, Yield (0.172g, 95%); mp: 126-128 ^{0}C, $[\alpha]_D^{24}$ = + 7.0 (c 0.8, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (dd, *J* = 9.2, 27.2 Hz, 2H), 7.82 (dd, *J* = 8.0, 36.0 Hz, 4H), 7.51-7.44 (m, 6H), 7.40 (q, *J* = 8.2 Hz, 2H), 7.33 (q, *J* = 5.1 Hz, 2H), 6.95 (t, *J* = 8.5 Hz, 2H), 5.36 (t, *J* = 9.0 Hz, 1H), 4.67-4.52 (m, 4H), 3.82 (q, *J* = 9.8 Hz, 1H, NH), 3.12-3.02 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.9, 161.9, 133.8 (d, *J* = 8.9 Hz, 2C), 132.3 (d, *J* = 2.5 Hz), 132.2, 131.5 (d, *J* = 9.9 Hz), 131.2, 128.7 (d, *J* = 6.9 Hz, 2C), 128.6 (2C), 128.5, 128.4, 126.7, 126.4 (d, *J* = 12.4 Hz, 2C), 126.3, 125.9 (d, *J* = 9.9 Hz, 2C), 125.2 (d, *J* = 3.9 Hz, 2C), 123.3 (d, *J* = 12.9 Hz, 2C), 119.7 (d, *J* = 3.5 Hz), 116.14 (d, *J* = 21.8 Hz, 2C), 46.84 (d, *J* = 3.9 Hz), 46.82, 46.1 (d, *J* = 4.9 Hz), 44.8 (d, *J* = 12.4 Hz), 44.0 (d, *J* = 13.4 Hz). ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.1. HRMS (ESI): m/z calcd for $C_{32}H_{28}FN_4OPNa$, 557.1877; found, 557.1884.

Ee: 94% {retention time = 6.49 (minor) and 7.17 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

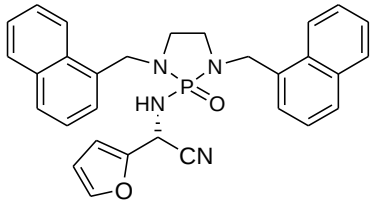


Compound 3e White solid; yield (0.187g, 94%); mp 158-160 ºC; $[\alpha]_D^{25}$ = + 6.0 (c 1.0, $CHCl_3$). ^{1}H NMR (300 MHz, $CDCl_3$): 8.18 (t, *J* = 9.6 Hz, 2H), 7.88-7.78 (m, 4H), 7.55-7.41 (m, 17H), 5.44 (t, *J* = 11.4 Hz, 1H), 4.71-4.50 (m, 4H), 3.64 (t, *J* = 9.9 Hz, 1H), 3.06 (d, *J* = 11.4 Hz, 4H); ^{13}C NMR (75 MHz, $CDCl_3$): 142.5, 140.1, 134.5 (d, *J* = 7.5 Hz), 134.1 (d, *J* = 4.3 Hz), 132.6 (d, *J* = 6.8 Hz), 131.9 (d, *J* = 4.3 Hz), 129.1 (2C), 128.9 (d, *J* = 4.0 Hz, 2C), 128.8 (2C), 128.7 (2C), 128.2 (2C), 128.1, 127.4 (d, *J* = 1.4 Hz, 2C), 126.9 (2C), 126.7 (2C), 126.6 (d, *J* = 2.8 Hz, 2C), 126.1 (d, *J* = 6.0 Hz, 2C), 125.5 (2C), 123.6 (d, *J* = 3.8 Hz, 2C), 120.1 (d, *J* = 4.0 Hz), 47.5, 47.0 (d, *J* = 5.0 Hz), 46.4 (d, *J* = 4.8 Hz), 44.9 (d, *J* = 12.3 Hz), 44.3 (d, *J* = 13.4Hz); ^{31}P NMR (202 MHz, $CDCl_3$): 22.6. Ee: 99% {retention time = 6.75 (minor) and 7.05 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

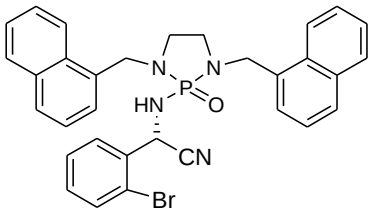


Compound 3f White solid, Yield (0.152g, 93%); mp 204-206 ^{0}C, $[\alpha]_D^{24}$ = + 3.50 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.31 (d, *J* = 7.2 Hz, 1H), 8.18 (d, *J* = 8.0 Hz, 1H), 7.88-7.78 (d, *J* = 7.8 Hz, 7H), 7.50-7.26 (m, 10H), 5.56 (t, *J* = 9.8 Hz, 1H), 4.46-4.14 (m, 4H), 3.52 (t, *J* = 10.0 Hz, 1H, NH), 3.04-2.96 (m, 4H), 2.41 (s, 3H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.6, 133.7 (d, *J* = 4.9 Hz), 132.3, 131.7 (d, *J* = 6.9 Hz), 131.4 (2C), 129.4 (2C), 128.6 (2C), 128.4 (d, *J* = 5.4 Hz, 2C), 128.2, 126.9 (d, *J* = 7.5 Hz, 2C), 126.6 (2C), 126.4 (d, *J* = 20.8 Hz, 2C), 126.3 (d, *J* = 4.9 Hz, 2C), 125.8, 125.1 (d, *J* = 9.0 Hz, 2C), 123.6, 123.4, 123.3, 46.9 (d, *J* = 4.9 Hz),

46.6 (d, *J* = 4.9 Hz), 46.3 (d, *J* = 2.5 Hz), 44.3 (t, *J* = 2.9 Hz), 43.9 (d, *J* = 3.0 Hz), 19.0. ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.3. Ee: 96% {retention time = 6.23 (minor) and 6.83 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

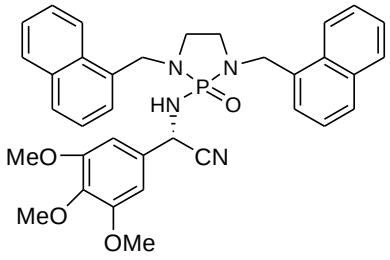


Compound 3g White solid; yield (0.165g, 94%), mp 148-150 ^{o}C $[\alpha]_D^{25}$ + 1.74 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.25(d, *J* = 8.5Hz, 1H), 8.19-8.17 (m, 1H), 7.88-7.84 (m, 2H), 7.79 (t, *J* = 7.0Hz, 2H), 7.55-7.47 (m, 6H), 7.43-7.39 (m, 2H), 7.37-7.36 (m, 1H), 6.46-6.45 (m, 1H), 6.35-6.34(m, 1H), 5.60(t, *J* = 9.5Hz, 1H), 4.65-4.53 (m, 4H), 3.62 (t, *J* = 10.0Hz, 1H), 3.03-2.93 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 147.5 (d, *J* = 6.4Hz), 143.8, 133.8 (d, *J* = 7.8Hz), 132.3, 131.7 (d, *J* = 7.3Hz), 128.7, 128.4, 126.9, 126.5 (d, *J* = 13.4Hz), 125.9 (d, *J* = 7.8Hz), 125.2 (d, *J* = 5.9Hz), 123.4 (d, *J* = 9.3Hz), 117.9 (d, *J* = 4.4Hz), 46.6 (d, *J* = 5.0Hz), 46.1 (d, *J* = 5.3Hz), 44.4 (d, *J* = 12.8Hz), 43.9 (d, *J* = 13.3Hz), 41.9 (d, *J* = 1.0Hz). ^{31}P NMR (202 MHz; $CDCl_3$) δ 21.6. HRMS (ESI): m/z calcd for $C_{30}H_{27}N_4O_2PNa$, 529.1764; found, 529.1761. Ee: 95% {retention time = 6.55 (minor) and 6.83 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system)}.

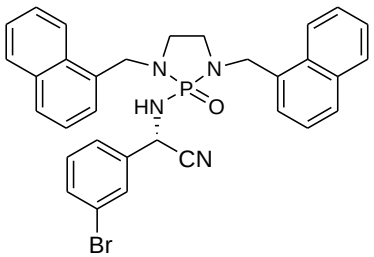


COMPOUND 3h White solid; Yield (0.146g, 92%); mp 128-130 ^{o}C; $[\alpha]_D^{25}$ = +7.7^{o} (c 1.1, $CHCl_3$). ^{1}H NMR (500 MHz, $CDCl_3$): 8.19 (d, *J* = 8.5 Hz, 1H), 8.11 (d, *J* = 8.0 Hz, 1H), 7.85 (d, *J* = 7.5 Hz, 2 H), 7.77 (d, *J* = 8.0 Hz, 2H), 7.60-7.57 (m, 2H), 7.54-7.37 (m, 8 H), 7.33-7.30 (m, 1H), 7.21-7.18 (m, 1H), 5.77 (t, *J* = 9.5 Hz, 1H), 4.64 (dd, *J* = 6.5 Hz, 14.5 Hz, 1H), 4.57 (t, *J* = 6 Hz, 2H), 4.36 (dd, *J* = 6.5 Hz, 15 Hz, 1H), 3.88 (t, *J* = 10 Hz, 1H), 3.03-2.94 (m, 4H); ^{13}C NMR (125 MHz, $CDCl_3$): 135.0 (d, *J* = 5.0 Hz), 133.8 (d, *J* = 8.9 Hz, 2C), 132.4, 132.3 (d, *J* = 3.4 Hz),

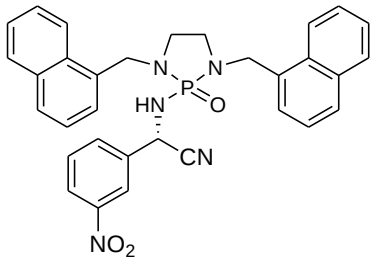
132.2, 131.6 (d, *J* = 6.4 Hz), 130.9 (s, 2C), 129.3 (s, 2C), 128.6 (d, *J* = 1.4 Hz, 2C), 128.4 (t, *J* = 3.0 Hz, 2C), 126.5 (d, *J* = 4.9 Hz, 2C), 126.3 (s, 2C), 125.8 (d, *J* = 5.4 Hz, 2C), 125.2 (d, *J* = 9.9 Hz, 2C), 123.4 (d, *J* = 5.5 Hz, 2C), 122.6, 118.8 (d, *J* = 5.4 Hz), 47.8 (d, *J* = 2 Hz), 46.4 (t, *J* = 5.9 Hz, 2C), 44.2 (dd, *J* = 6.0Hz, 12.9 Hz, 2C); ^{31}P NMR (202 MHz, $CDCl_3$): 22.1. HRMS (ESI): m/z calcd for $C_{32}H_{29}BrN_4OP$, 595.1257; found, 595.1253. Ee: 97% (retention time = 6.49 (minor) and 6.95 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).



Compound 3i white solid, yield (0.182, 90%), mp 210-212 ^{0}C, $[\alpha]_D^{24}$ = + 3.82; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22-8.12 (m, 2H), 7.87-7.78 (m, 4H), 7.52-7.39 (m, 8H), 6.63 (s, 2H), 5.44 (t, *J* = 9.3 Hz, 1H), 4.72-4.62 (m, 4H), 3.79 (s, 3H), 3.65 (s, 6H), 3.45 (t, *J* = 9.9 Hz, 1H, NH), 3.14-3.06 (m, 4H). ^{13}C NMR (75 MHz, $CDCl_3$) δ 153.9, 138.8, 134.0 (2C), 132.6, 132.5 (d, *J* = 2.8 Hz), 132.4, 131.8 (2C), 131.0 (d, *J* = 6.3 Hz), 128.9 (2C), 128.7 (d, *J* = 4.6 Hz, 2C), 126.7 (d, *J* = 7.2 Hz, 2C), 126.4, 126.2 (2C), 126.1, 125.5 (d, *J* = 4.3 Hz, 2C), 123.5 (d, *J* = 8.8 Hz, 2C), 120.2, 103.8 (2C), 61.1, 56.3 (2C), 47.9, 46.9 (d, *J* = 4.6 Hz), 46.4 (d, *J* = 7.4 Hz), 44.9 (d, *J* = 12.3 Hz), 44.4 (d, *J* = 12.8 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ 22.7. Ee: 95% (retention time = 6.32 (minor) and 6.81 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

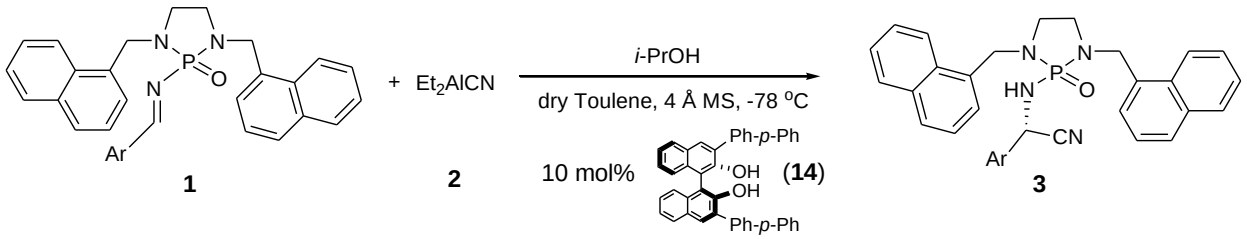


Compound 3j Colorless solid; yield (0.132g, 92%), mp 146-148 ^{o}C, $[\alpha]_D^{25}$ = + 2.10, (c = 0.5, $CDCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21-8.18 (m, 1H), 8.14-8.11 (m, 1H), 7.88-7.84 (m, 2H), 7.81-7.78 (m, 2H), 7.52-7.39 (m, 10H), 7.30-7.29 (m, 1H), 7.16-7.13 (m, 1H), 5.34(t, *J* = 9.0Hz, 1H), 4.67-4.53 (m, 4H), 3.56 (t, *J* = 9.5Hz, 1H), 3.11-3.02 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 137.4 (d, *J* = 6.4Hz), 133.8 (d, *J* = 7.8Hz), 132.4, 132.2 (d, *J* = 6.4Hz), 131.6 (d, *J* = 7.8Hz), 130.7, 129.7, 128.7, 128.6 (d, *J* = 12.5Hz), 128.4, 126.8, 126.5, 126.4 (d, *J* = 7.3Hz),, 125.9 (d, *J* = 10.8Hz), 125.3 (d, *J* = 2.0Hz), 125.2, 123.3, 123.2, 123.2, 119.4 (d, *J* = 3.4Hz), 46.9, 46.9 (d, *J* = 4.4Hz), 46.1 (d, *J* = 5.3Hz), 44.8 (d, *J* = 12.3Hz), 44.1 (d, *J* = 13.2Hz) ^{31}P NMR (202 MHz; $CDCl_3$) δ 21.9. Ee: 97% (retention time = 6.03 (minor) and 6.82 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).



Compound 3k White foamy solid, Yield (0.122g, 89%); mp 180-182 ^{0}C, $[\alpha]_D^{24}$ = + 3.30 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 (d, *J* = 8.2 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 7.86-7.83 (m, 2H), 7.79-7.76 (m, 2H), 7.54-7.29 (m, 10H), 7.13-7.05 (m, 2H), 5.64 (t, *J* = 9.8 Hz, 1H), 4.66-4.39 (m, 4H), 3.95 (t, *J* = 10.0 Hz, 1H, NH), 2.99 (d, *J* = 10.7 Hz, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 133.72 (d, *J* = 1.5 Hz), 133.44 (d, *J* = 4.9 Hz), 132.7, 132.3 (d, *J* = 6.9 Hz), 132.2 (d, *J* = 7.4 Hz), 131.6 (d, *J* = 6.9 Hz), 130.6 (d, *J* = 32.3 Hz, 2C), 129.1 (2C), 128.6 (2C), 128.4 (d, *J* = 5.4 Hz, 2C), 127.8 (2C), 126.4 (2C), 126.3 (d, *J* = 20.8 Hz, 2C), 125.8 (d, *J* = 4.9 Hz, 2C), 125.2 (d, *J* = 9.4 Hz, 2C), 123.3 (d, *J* = 7.9 Hz, 2C), 118.8 (d, *J* = 5.5 Hz), 46.4 (d, *J* = 4.9 Hz), 46.2 (d, *J* = 4.9 Hz), 45.6 (d, *J* = 2.5 Hz), 44.2 (d, *J* = 2.9 Hz), 44.1 (d, *J* = 2.9 Hz). ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.3. Ee: 96% (retention time = 6.36 (minor) and 6.83 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

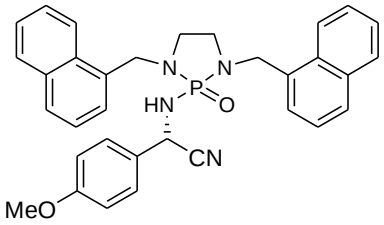
Scheme 3



Compound 3a White solid, Yield (0.041g, 97%); Ee: 99% (retention time = 6.68 (minor) and 7.00 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

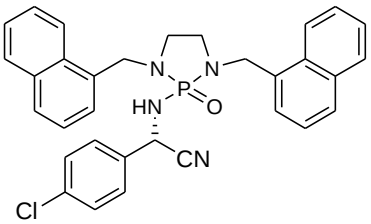
Compound 3f White solid, Yield (0.056g, 94%); Ee: 94% (retention time = 6.42 (minor) and 6.88 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Compound 3h White solid, Yield (0.039g, 94%); Ee: 97% (retention time = 6.50 (minor) and 6.88 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).



Compound 3l White solid, Yield (0.56g, 95%); mp 182-184 ^{0}C, $[\alpha]_D^{24}$ = + 1.45 (c 1.1, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23-8.19 (m, 1H), 8.16-8.14 (m, 1H), 7.89-7.84 (m, 2H), 7.80-7.78 (m, 2H), 7.52-7.47 (m, 6H), 7.43-7.39 (m, 2H), 7.32-7.28 (m, 2H), 6.83-6.79 (m, 2H), 5.34 (t, *J* = 8.7 Hz, 1H), 4.66-4.52 (m, 4H), 3.75 (s, 3H), 3.50 (t, *J* = 9.6 Hz, 1H, NH), 3.09-3.00 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 160.2, 133.8 (d, *J* = 8.4 Hz), 132.4 (d, *J* = 6.5 Hz), 131.6 (d, *J* = 8.4 Hz, 2C), 128.7 (2C), 128.6 (2C), 128.5 (2C), 128.3 (2C), 128.0 (2C), 127.5 (d, *J* = 6.4 Hz), 126.6, 126.4, 126.3, 125.9 (2C), 125.8 (2C), 125.2 (d, *J* = 4.0 Hz), 123.4 (d, *J* = 7.5 Hz), 120.1(d, *J* = 4.0 Hz), 114.5 (2C), 55.3, 46.9, 46.7 (d, *J* = 4.5 Hz), 46.1 (d, *J* = 5.4 Hz), 44.7 (d, *J* = 11.9 Hz), 44.0 (d, *J* = 12.9 Hz). ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.5. HRMS (ESI): m/z calcd

for $C_{33}H_{31}N_4O_2PNa$, 569.2077; found, 569.2070. Ee: 95% (retention time = 6.17 (minor) and 6.66 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

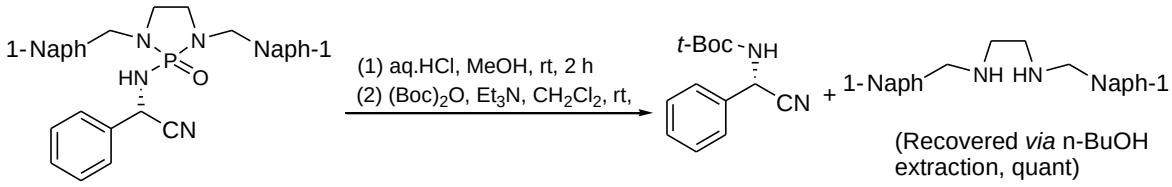


Compound 3m Pale yellow color solid, Yield (0.048g, 98%); mp 134-136 ^{0}C, $[\alpha]_D^{24}$ = + 8.60 (c 0.6, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (dd, *J* = 8.3, 23.4 Hz, 2H), 7.86 (d, *J* = 7.8 Hz, 2H), 7.78 (d, *J* = 8.1 Hz, 2H), 7.51-7.45 (m, 6H), 7.40 (q, *J* = 7.8 Hz, 2H), 7.28-7.22 (m, 4H), 5.35 (t, *J* = 9.0 Hz, 1H), 4.66-4.51 (m, 4H), 3.77 (bs, 1H, NH), 3.12-3.03 (m, 4H). ^{13}C NMR (125 MHz, $CDCl_3$) δ 135.2, 133.85, 133.81, 133.7, 132.27, 132.25, 132.21, 131.5 (d, *J* = 9.9 Hz), 129.3 (2C), 128.7 (d, *J* = 4.9 Hz, 2C), 128.5 (d, *J* = 17.9 Hz, 2C), 127.9 (2C), 126.7, 126.4 (d, *J* = 9.9 Hz, 2C), 126.3, 125.9 (d, *J* = 8.4 Hz, 2C), 125.3 (d, *J* = 2.9 Hz, 2C), 123.2 (d, *J* = 14.4 Hz, 2C), 119.5 (d, *J* = 3.5 Hz), 46.9, 46.8 (d, *J* = 4.5 Hz), 46.1 (d, *J* = 5.4 Hz), 44.8 (d, *J* = 11.9 Hz), 44.1 (d, *J* = 13.4 Hz). ^{31}P NMR (202 MHz, $CDCl_3$) δ 22.6. HRMS (ESI): m/z calcd for $C_{32}H_{29}ClN_4OP$, 551.1761; found, 551.1768. Ee: 98% (retention time = 6.86 (minor) and 7.32 (major), flow rate = 0.60 ml/min, OD-H chiral column (7:3 hexane:IPA solvent system).

Absolute Configuration Determination

The absolute configuration for this asymmetric induction was determined by converting a product (**3a**) to an authentic sample.[2] In this conversion, **3a** was subjected to deprotection with 2.0 M aq. HCl at r.t. in methanol followed by *in situ* *t*-Boc protection by treating with $(t\text{-Boc})_2O$ in the presence of Et_3N to give product **5** (Scheme 3). The optical rotation of this product was confirmed to be consistent with that of the known sample with *S* configuration. During this transformation, the cleaved N^1, N^2-bis(naphthalen-1-ylmethyl)ethane-1,2-diamine (**6**) was extracted with *n*-butanol from the acidic mixture prior to *t*-Boc protection to give a quantitative yield. $[\alpha]^{24}_D$ -1.97 (c = 0.8, CHCl3) {Literature value $[\alpha]^{24}_D$ -1.82 (c = 1.1, CHCl3)}. N-Protected ligands in Figure 1 gave opposite configuration to that from free NH_2-ligands due to anti arrangement of the protection groups on their nitrogens.

Scheme 4



4a **15** **16**