## Supporting Information

Unsymmetrical Ferrocenylethylamine-Derived Monophosphoramidites: Highly Efficient Chiral Ligands for Rh-Catalyzed Enantioselective Hydrogenation of Enamides and $\alpha$-Dehydroamino Acid Derivatives

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General Information: All reactions were conducted under a nitrogen or argon atmosphere unless otherwise noted. Anhydrous procedures were conducted using oven dried or flame dried glassware and standard syringe and cannula transfer techniques. Hydrogenation was performed in a stainless steel autoclave. Solvents were of reagent grade, dried and distilled before use following standard procedures. $\left(S_{c}, S_{a}\right)$-2b and $\left(S_{c}, R_{a}\right)$-2c were prepared from the corresponding ( $S$ )- $N$-methyl-1-phenylethylamine and chiral BINOL according a modified procedure. ${ }^{1}$ BINOL-based chlorophosphite 6 was synthesized according to the literature method. ${ }^{2}$ Enamides $\mathbf{7 a}-\mathbf{i}^{3}$ and $\alpha$-dehydroamino acid esters $\mathbf{9 a}-\mathbf{f}^{4}$ were known compounds which was synthesized according to the literature procedure. All other chemicals were obtained commercially. Optical rotations were recorded on a polarimeter at ambient temperature $(\mathrm{c}=\mathrm{g} / 100 \mathrm{~mL}) .{ }^{1} \mathrm{H},{ }^{13} \mathrm{C}$ and ${ }^{31} \mathrm{P}$ NMR spectra were recorded on a 400 MHz instrument using $\mathrm{CDCl}_{3}$ as the solvent. Enantiomeric excesses were determined by capillary GC analysis with a chiral column.

## General Procedure for the Synthesis of Chiral Ferrocenylethylamine-Derived

 Monophosphoramidites. To a solution of ferrocenylethylamine (5a-d) (10 mmol) and triethylamine ( 50 mmol ) in 100 mL of toluene was added dropwise a solution of BINOL-based chlorophosphite ( $3.8 \mathrm{~g}, 11 \mathrm{mmol}$ ) in 30 mL of toluene at $0^{\circ} \mathrm{C}$ under a $\mathrm{N}_{2}$ atmosphere during 30 minutes. The resulting mixture was standing at room temperature overnight. The precipitation was filtrated; the filtrate was collected and concentrated under reduced pressure. The residue was purified by column chromatography to give the crude product, which can be further purified by crystallizing from hexane/dichloromethane.$N$-methyl- $N$-[(R)-1-ferrocenylethyl]-(S)-1,1'-bi-2-naphthyl phosphoramidite
$\left(\boldsymbol{R}_{\boldsymbol{c}}, \boldsymbol{S}_{\boldsymbol{a}}\right)$-3a: orange solid; $[\alpha]^{20}{ }_{\mathrm{D}}+17.5\left(c 0.30, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 1.47$
$(\mathrm{d}, J=6.8 \mathrm{~Hz}, 3 \mathrm{H}), 2.00(\mathrm{~d}, J=5.6 \mathrm{~Hz}, 3 \mathrm{H}), 4.01(\mathrm{~s}, 4 \mathrm{H}), 4.13-4.15(\mathrm{~m}, 2 \mathrm{H}), 4.22(\mathrm{~s}, 1 \mathrm{H})$, $4.52(\mathrm{~s}, 1 \mathrm{H}), 4.69-4.73(\mathrm{q}, 1 \mathrm{H}), 7.13-7.97(\mathrm{~m}, 12 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\delta 18.4,26.7,52.2,52.6$, $67.7,67.9,68.8,69.4,69.8,77.4,77.7,78.0,89.9,122.7,123.1,124.6,125.2,125.4$, 126.7, 127.5, 127.7, 128.8, 129.0, 130.4, 130.9, 131.2, 132.0, 133.2, 133.5, 150.2, 150.9; ${ }^{31} \mathrm{P}$ NMR $\delta$ 148.0; HRMS (m/z) calcd. for $\mathrm{C}_{33} \mathrm{H}_{28} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}: 558.1279$, found 558.1254. $N$-methyl- $N$-[(R)-1-ferrocenylethyl]-(R)-1,1'-bi-2-naphthyl phosphoramidite $\left(\boldsymbol{R}_{\boldsymbol{c}}, \boldsymbol{R}_{\boldsymbol{a}}\right)$-3b: orange solid; $[\alpha]^{20}{ }_{\mathrm{D}}-128.3\left(\mathrm{c} 0.30, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ 1.63 (d, $J=7.2 \mathrm{~Hz}, 3 \mathrm{H}), 1.96(\mathrm{~d}, J=4.0 \mathrm{~Hz}, 3 \mathrm{H}), 4.10-4.14(\mathrm{~m}, 7 \mathrm{H}), 4.28(\mathrm{~s}, 1 \mathrm{H})$, 4.80-4.85 (q, 1H), 7.22-7.97 (m, 12H); ${ }^{13} \mathrm{C}$ NMR $\delta 19.4,26.6,53.0,53.5,67.7,67.8,68.9$, $69.0,69.5,77.4,77.7,78.0,90.3,122.7,122.8,123.3,124.6,125.2,125.4,126.7,127.6$, $127.7,128.9,129.0,130.6,130.9,131.3,132.0,133.3,133.5,150.3,150.8 ;{ }^{31} \mathrm{P}$ NMR $\delta$ 149.0; HRMS (m/z) calcd. for $\mathrm{C}_{33} \mathrm{H}_{28} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}$ : 558.1279, found 558.1250.
$N$-ethyl- $N$-[(R)-1-ferrocenylethyl]-(S)-1,1'-bi-2-naphthyl phosphoramidite $\left(\boldsymbol{R}_{\boldsymbol{c}}, \boldsymbol{S}_{\boldsymbol{a}}\right)$-3c: yellow solid; $[\alpha]^{20}{ }_{\mathrm{D}}-32.2\left(\mathrm{c} 0.30, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H} \mathrm{NMR}\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta$ $0.87-0.91(\mathrm{t}, 3 \mathrm{H}), 1.49(\mathrm{~d}, J=8.0 \mathrm{~Hz}, 3 \mathrm{H}), 2.61-2.77(\mathrm{~m}, 2 \mathrm{H}), 3.78(\mathrm{~s}, 4 \mathrm{H}), 4.00-4.11(\mathrm{t}$, $3 \mathrm{H}), 4.48-4.50(\mathrm{~m}, 2 \mathrm{H}), 7.20-7.97(\mathrm{~m}, 12 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\delta 19.3,20.7,37.9,38.0,51.5,51.8$, $67.6,68.9,69.3,70.4,77.5,77.8,78.1,90.9,122.9,125.3,125.4,127.6,127.7,128.9$, 129.0, 130.2, 130.9, 131.2, 132.1, 133.4, 133.6, 150.4, 150.4; ${ }^{31}$ P NMR $\delta 149.9$; HRMS $(\mathrm{m} / \mathrm{z})$ calcd. for $\mathrm{C}_{34} \mathrm{H}_{30} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}: 572.1436$, found 572.1457.

## $N$-benzyl- $N$-[(R)-1-ferrocenylethyl]-(S)-1,1'-bi-2-naphthyl phosphoramidite

 $\left(\boldsymbol{R}_{c}, \boldsymbol{S}_{\boldsymbol{a}}\right)$-3d: yellow solid; $[\alpha]^{20}{ }_{\mathrm{D}}$-32.2 (c $\left.0.30, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 1.20$ $(\mathrm{d}, 3 \mathrm{H}), 1.27-1.30(\mathrm{~m}, 2 \mathrm{H}), 3.84(\mathrm{~s}, 4 \mathrm{H}), 4.10(\mathrm{~s}, 1 \mathrm{H}), 4.13(\mathrm{~s}, 1 \mathrm{H}), 4.19(\mathrm{~s}, 1 \mathrm{H}), 4.47(\mathrm{~s}$, $1 \mathrm{H}), 4.53-4.57(\mathrm{q}, 1 \mathrm{H}), 7.18-8.00(\mathrm{~m}, 17 \mathrm{H}) ;{ }^{13} \mathrm{C}$ NMR $\delta 14.9,21.2,23.4,32.3,47.0,47.1$,$52.6,52.9,67.9,68.2,69.0,69.3,70.2,77.4,77.7,78.1,89.8,122.6,122.9,125.3,125.5$, $126.8,127.3,127.6,127.7,128.5,128.7,128.8,129.0,130.5,130.9,131.3,132.1,133.3$, 133.5, 142.1, 150.1, $150.7 ;{ }^{31} \mathrm{P}$ NMR $\delta$ 146.5; HRMS (m/z) calcd. for $\mathrm{C}_{39} \mathrm{H}_{32} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}$ : 634.1593, found 634.1578.

## $N$-methyl- $N$ - $\{(\boldsymbol{R})$-1-[(R)-2-methylferrocenyl]ethyl $\}$-(S)-1,1'-bi-2-naphthyl

phosphoramidite $\left(\boldsymbol{R}_{c}, \boldsymbol{R}_{p}, \boldsymbol{S}_{a}\right)$-3e: orange solid; $[\alpha]^{20}{ }_{\mathrm{D}}+44.8\left(c \quad 0.17, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 1.60(\mathrm{~d}, J=7.6 \mathrm{~Hz}, 3 \mathrm{H}), 1.92(\mathrm{~d}, J=3.6 \mathrm{~Hz}, 3 \mathrm{H}), 2.24(\mathrm{~s}, 3 \mathrm{H})$, 4.06-4.10 (m, 7H), 4,81-4.89 (m, 1H), 6.90-7.96 (m, 12H); ${ }^{13} \mathrm{C}$ NMR 814.7, 19.3, 26.4, $51.4,51.9,66.0,67.4,70.1,70.8,77.4,77.7,78.2,83.7,122.7,123.1,125.1,125.4,126.6$, $127.6,127.7,128.8,129.0,130.5,130.9,131.2,132.0,133.1,133.5,150.3,150.4 ;{ }^{31} \mathrm{P}$ NMR $\delta$ 149.5; $\mathrm{HRMS}(\mathrm{m} / \mathrm{z})$ calcd. for $\mathrm{C}_{34} \mathrm{H}_{30} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}: 572.1436$, found 572.1407.

## $N$-methyl- $N$-\{(R)-1-[(R)-2-methylferrocenyl]ethyl $\}-(\boldsymbol{R})$-1,1’-bi-2-naphthyl

 phosphoramidite $\left(\boldsymbol{R}_{c}, \boldsymbol{R}_{p}, \boldsymbol{R}_{a}\right)$-3f: orange power; $[\alpha]^{20}{ }_{\mathrm{D}}-291\left(c \quad 0.20, \mathrm{CHCl}_{3}\right) ;{ }^{1} \mathrm{H}$ NMR $\left(400 \mathrm{MHz}, \mathrm{CDCl}_{3}\right) \delta 1.72(\mathrm{~d}, J=6.8 \mathrm{~Hz}, 3 \mathrm{H}), 1.82(\mathrm{~d}, J=3.2 \mathrm{~Hz}, 3 \mathrm{H}), 2.07(\mathrm{~s}, 3 \mathrm{H})$, 3.95-4.07 (m, 7H), 4.93-5.01(m, 1H), 7.21-7.45(m, 8H), 7.87-7.95 (m, 4H); ${ }^{13} \mathrm{C}$ NMR $\delta$ $14.5,19.2,25.9,52.0,52.5,65.8,67.5,70.0,71.0,77.4,77.7,78.0,84.1,87.2,122.6$, 122.7, 125.2, 125.4, 126.7, 127.6, 127.7, 128.9, 129.0, 130.6, 130.8, 131.3, 132.0, 133.3, 133.5, 150.2, 150.4; ${ }^{31} \mathrm{P}$ NMR $\delta$ 149.9; HRMS (m/z) calcd. for $\mathrm{C}_{34} \mathrm{H}_{30} \mathrm{FeNO}_{2} \mathrm{P}+\mathrm{H}$ : 572.1436, found 572.1445.General Procedure for Asymmetric Hydrogenation. In a nitrogen-filled glovebox, a stainless steel autoclave was charged with $\mathrm{Rh}(\mathrm{COD})_{2} \mathrm{BF}_{4}\left(2.0 \mathrm{mg}, 0.5 \times 10^{-2} \mathrm{mmol}\right)$ and monophosphoramidite ligand $3\left(1.1 \times 10^{-2} \mathrm{mmol}\right)$ in 1.5 mL of a degassed solvent. After stirring for 10 min at room temperature. A substrate $(0.5 \mathrm{mmol})$ in 1.5 mL of same
solvents was added to the reaction mixture, and then the hydrogenation was performed at room temperature under 10 bar of $\mathrm{H}_{2}$ pressure for 20 hours. The reaction mixture was passed through a short silica gel column to remove the catalyst. After evaporation of the solvent, the crude reaction mixture was subjected for GC to determine the conversion and enantiomeric excesses.

## Determination of Enantiomeric Excesses for $N$-Acetyl-1-Arylalkylamine 8a-8i:

 Chiral Capillary GC Column. Chiral Select-1000 column (dimensions $30 \mathrm{~m} \times 0.25 \mathrm{~mm}$ (i.d.)). Carrier gas: $\mathrm{N}_{2}$. The racemic products were obtained by hydrogenation of substrates with an achiral catalyst prepared from $\mathrm{PPh}_{3}$ and $\mathrm{Rh}(\mathrm{COD})_{2} \mathrm{BF}_{4} .{ }^{5}$ The following are the retention times for the racemic products.$N$-Acetyl-1-phenylethylamine (8a): (capillary GC, Chiral Select-1000 column, $130^{\circ} \mathrm{C}$, $15 \mathrm{psi})(S) \mathrm{t}_{1}=16.74,(R) \mathrm{t}_{2}=17.64 ; N$-Acetyl-1-[(4-trifluoromethyl)phenyl]ethylamine (8b): (capillary GC, Chiral Select-1000 column, $\left.150^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=9.50$, $(R) \mathrm{t}_{2}=10.27 ; N$-Acetyl-1-(4-chlorophenyl)ethylamine (8c): (capillary GC, Chiral Select-1000 column, $\left.150^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=24.18,(R) \mathrm{t}_{2}=24.82 ; N$-Acetyl-1-(4-bromophenyl)ethylamine (8d): (capillary GC, Chiral Select-1000 column, $150^{\circ} \mathrm{C}, 15$ $\mathrm{psi})(S) \mathrm{t}_{1}=41.87,(R) \mathrm{t}_{2}=44.35 ; N$-Acetyl-1-(4-methylphenyl)ethylamine (8e): (capillary GC, Chiral Select-1000 column, $\left.130^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=28.49,(R) \mathrm{t}_{2}=30.86$; $N$-Acetyl-1-(4-methoxyphenyl)ethylamine (8f): (capillary GC, Chiral Select-1000 column, $\left.140^{\circ} \mathrm{C}, \quad 15 \mathrm{psi}\right) \quad(S) \quad \mathrm{t}_{1}=44.16, \quad(R) \quad \mathrm{t}_{2} \quad=25.73$; $N$-Acetyl-1-(3-methoxyphenyl)ethylamine (8g): (capillary GC, Chiral Select-1000 column, $\left.140^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=34.85,(R) \mathrm{t}_{2}=37.23 ; N$-Acetyl-1-phenylpropylamine (8h): (capillary GC, Chiral Select- 1000 column, $\left.130^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=20.74,(R) \mathrm{t}_{2}=$
23.05; $N$-Acetyl-1-phenylbuthylamine (8i): (capillary GC, Chiral Select-1000 column, $\left.110^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(S) \mathrm{t}_{1}=138.11,(R) \mathrm{t}_{2}=147.24$.

Determination of Enantiomeric Excesses for $\alpha$-Amino Acid Esters 10a-10f: Chiral Capillary GC Column. CP-Chiralsil-L-Val column ( $25 \mathrm{~m} \times 0.25 \mathrm{~mm} \times 0.12 \mu \mathrm{~m}$ ). Carrier gas: $\mathrm{N}_{2}$. The racemic products were obtained by hydrogenation of substrates with an achiral catalyst prepared from $\mathrm{PPh}_{3}$ and $\mathrm{Rh}(\mathrm{COD})_{2} \mathrm{BF}_{4}{ }^{6}$ The following are the retention times for the racemic products.

Methyl 2-Acetamido-3-phenylpropanoate (10a): (capillary GC, CP-Chiralsil-L-Val column, $\left.\quad 160^{\circ} \mathrm{C}, \quad 15 \mathrm{psi}\right) \quad(R) \quad \mathrm{t}_{1}=7.23, \quad(S) \quad \mathrm{t}_{2}=8.43 ; \quad$ Methyl 2-Acetamido-3-(4-methoxyphenyl)propanoate (10b): (capillary GC, CP-Chiralsil-L-Val column, $\left.160^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(R) \mathrm{t}_{1}=21.23$, ( $S$ ) $\mathrm{t}_{2}=23.48$; Methyl 2-Acetamido-3-(2-methoxyphenyl)propanoate (10c): (capillary GC, CP-Chiralsil-L-Val column, $\left.160^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(R) \mathrm{t}_{1}=15.95$, $(S) \mathrm{t}_{2}=17.65$; Methyl 2-Acetamido-3-(4-chlorophenyl)propanoate (10d): (capillary GC, CP-Chiralsil-L-Val column, $\left.\quad 160^{\circ} \mathrm{C}, \quad 15 \mathrm{psi}\right) \quad(R) \quad \mathrm{t}_{1}=18.23, \quad(S) \quad \mathrm{t}_{2}=20.09 ; \quad$ Methyl 2-Acetamido-3-(2-chlorophenyl)propanoate (10e): (capillary GC, CP-Chiralsil-L-Val column, $\left.\quad 160^{\circ} \mathrm{C}, \quad 15 \mathrm{psi}\right) \quad(R) \quad \mathrm{t}_{1}=15.34, \quad(S) \quad \mathrm{t}_{2}=17.05 ; \quad$ Ethyl

2-Acetamido-3-phenylpropanoate (10f): (capillary GC, CP-Chiralsil-L-Val column, $\left.160^{\circ} \mathrm{C}, 15 \mathrm{psi}\right)(R) \mathrm{t}_{1}=21.08,(S) \mathrm{t}_{2}=24.49$.

## References

1. Peña, D.; Minnaard, A. J.; de Vries, J. G.; Feringa, B. L. J. Am. Chem. Soc. 2002, 124, 14552.
2. Franciò, G.; Arena, C. G.; Faraone, F.; Graiff, C.; Lanfranchi, M.; Tiripicchio, A. Eur. J. Inorg. Chem. 1999, 1219.
3. (a) van den Berg, M.; Minnaard, A. J.; Schudde, E. P.; van Esch, J.; de Vries, J. G.; Feringa, B. L. J. Am. Chem. Soc. 2000, 122, 11539. (b) Burk, M. J.; Casy, G.; Johnson, N. B. J. Org. Chem. 1998, 63, 6084.
4. Blott, A. H. Org. Syn., coll. Vol. 1950, 1.
5. Burk, M. J.; Feaster, J. E.; Nugent, W. A.; Harlow, R. L. J. Am. Chem. Soc. 1993, 115, 10125.
6. Burk, M. J.; Wang, Y. M.; Lee, J. R. J. Am. Chem. Soc. 1996, 118, 5142.
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