**Supporting Information:**

Bifunctional Ferrocene-Based Squaramide-Phosphine as an Organocatalyst for Highly Enantioselective Intramolecular Morita–Baylis–Hillman Reaction

Xiaorui Zhang, Pengfei Ma, Dongxu Zhang, Yang Lei, Shengyong Zhang, Ru Jiang*, Weiping Chen*

I. General considerations

All commercially obtained reagents and solvents were used without further purification. Compound \((RC,S_{Fe})-2\) and substrates aldehydes \(4\) were prepared according to published procedures.\(^{[1,2]}\) Optical rotations were measured on a Perkin-Elmer 343 polarimeter. \(^1\)H (400 MHz), \(^{13}\)C (100.6 MHz) and \(^{31}\)P (162 MHz) NMR spectra were recorded on a Bruker Avance-400 spectrometer with an internal deuterium lock. Chemical shifts are quoted as parts per million and referenced to CHCl\(_3\) (δH 7.26) and or CDCl\(_3\) (δC 77.0, central line of triplet). \(^{13}\)C and \(^{31}\)P NMR spectra were recorded with broadband proton decoupling. Coupling constants (\(J\)) are quoted in Hertz. High-Resolution Mass Spectroscopy (HRMS) was carried out on a VARIAX FT-ICR MS. High performance liquid chromatography (HPLC) was performed on DIONEX SUMMT with MANAGEMENT system using Daicel Chiralcel OD-H, Chiralpak AS-H or Chiralpak AD-H column.

II. Preparation of phosphine-squaramide \((RC,S_{Fe})-1\)

1. \((RC,S_{Fe})-1\)-(Diphenylphosphino)-2-[(1-amino)ethyl]ferrocene \([RC,S_{Fe}] -2\):

A solution of \((RC,S_{Fe})-PPFA\) (2.21 g, 5 mmol) in Ac\(_2\)O (20 mL) was heated to 100 °C under
nitrogen condition, and the mixture was stirred for 2 h at 100 °C. After cooling to room temperature, the orange reaction mixture was concentrated in vacuo to give acetate. The acetate could be used in the next step without purification. To the solution of acetate in 80 mL mixture of MeOH and THF (1:1) was added aqueous ammonia (20 mL), the reaction was stirred at 60 °C for 24 h. After cooling to room temperature, the mixture was quenched by the addition of ice water. The red-brown solution was extracted with ether, the organic phase was dried over Na₂SO₄, and the solvent was removed under reduced pressure. The residue was purified by chromatography to the product (1.45 g, 70%). Yellow crystals; mp 132.4-132.9 °C; [α]₂⁵D -407.2 (c = 0.25, CH₂Cl₂); ¹H NMR (500 Hz, CDCl₃) δ 7.57-7.50 (m, 2H), 7.40-7.35 (m, 3H), 7.28-7.24 (m, 5H), 4.44 (s, 1H), 4.29-4.26 (m, 1H), 4.24-4.17 (m, 1H), 4.02 (s, 5H), 3.78-3.75 (m, 1H), 1.45 (d, J = 6.5 Hz, 3H).

2. Phosphine-squaramide (Rᵥ₅Sᵥ₅)-1:

Amine (Rᵥ₅Sᵥ₅)-2 (413.3 mg, 1.0 mmol) in CH₂Cl₂ (8 mL) was added dropwise into a solution of diethyl squarate 3 (204.2 mg, 1.2 mmol) in CH₂Cl₂ (8 mL) at room temperature under an inert atmosphere, and the corresponding mixture was stirring under reflux for 24h (monitoring by TLC). The solvent was removed under reduced pressure and the residue was purified by column chromatography (petroleum ether/ethyl acetate 4:1) to afford the desired product as yellow amorphous solid (94% yield), m.p. 90.5-91.5 °C. [α]₀²⁵D = -298.1 (c 0.25, CH₂Cl₂). ¹H NMR (400 MHz, DMSO): major conformer: δ 8.31 (d, J = 9.21 Hz, 1H), 6.98-7.48 (m, 10H), 5.46 (m, 1H), 4.60 (m, 2H), 4.25 (m, 2H), 4.07 (s, 5H), 3.64 (br. s, 1H), 3.39 (q, J = 6.8 Hz, 1H), 1.60 (d, J = 6.78 Hz, 3H), 1.19 (t, J = 6.78 Hz, 3H); minor conformer: 8.62 (d, J = 9.34 Hz, 0.45H), 6.98-7.48 (m, 10H), 4.95 (m, 1H), 4.56 (m, 2H), 4.42 (m, 2H), 4.06 (s, 5H), 4.03 (q, J = 6.8 Hz, 1H), 3.65 (br. s, 1H), 1.63 (d, J = 6.78 Hz, 3H), 1.43 (t, J = 6.8 Hz, 3H). ¹³C NMR (100 MHz, DMSO): mixture of two conformers: δ 188.89, 188.66, 181.77, 181.61, 175.82, 175.68, 170.38, 170.12, 139.36, 137.09, 136.99, 135.34, 135.19, 135.12, 134.98, 132.73, 132.54, 132.30, 132.11, 129.75,
III. General procedure for the asymmetric intramolecular MBH reaction

(RC,SFc)-1 (21.5 mg, 0.04 mmol) was added to a solution of aldehyde 4 (0.20 mmol) in CH2Cl2 (1.0 mL) at 25 °C under an inert atmosphere. The mixture was stirred at the same temperature. After the reaction was completed (monitoring by TLC), the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel to afford the intramolecular MBH adduct 5. The ee was determined by HPLC analysis using chiral column, and the absolute configuration was determined by comparison of specific rotation with that of a literature report.[3,4]

References

IV. NMR and HRMS spectra for \((R, S)\)-1

(1) NMR spectra in DMSO

\(\text{① } \text{\textsuperscript{1}H NMR (25 °C)}\)

\(\text{② } \text{\textsuperscript{31}P NMR (25 °C)}\)
7. $^{31}$P NMR (70 °C)

NMR spectra in CDCl$_3$

2. $^1$H NMR (25 °C)
(2) $^{31}$P NMR (25°C)

(3) NMR spectra in CD$_2$Cl$_2$

(1) $^1$H NMR (25°C)
② \(^{31}\text{P NMR (25 °C)}\)

![31P NMR spectrum](image)

(4) NMR spectra in CD\(_3\)OD

① \(^{1}\text{H NMR (25 °C)}\)

![1H NMR spectrum](image)
V. \textsuperscript{1}H NMR and ee determination for the MBH Products

(1) (S)-(6-Hydroxycyclohex-1-enyl) (phenyl) methanone 5a

\textsuperscript{1}H NMR (400 MHz, CDCl\textsubscript{3}): \( \delta \) 7.66-7.64 (m, 2H), 7.53 (t, \( J = 7.4 \) Hz, 1H), 7.43 (t, \( J = 7.5 \) Hz, 2H), 6.73 (t, \( J = 3.9 \) Hz, 1H), 4.74 (d, \( J = 2.2 \) Hz, 1H), 3.51 (d, \( J = 1.9 \) Hz, 1H), 2.38-2.21 (m, 2H), 1.97-1.82 (m, 3H), 1.69-1.65 (m, 1H).
HPLC analysis (Daicel CHIRALPAK OD-H column, λ=254 nm, eluent: n-hexane/i-propanol=94/6, flow rate: 0.6 mL/min): t_R=19.8 min (minor), 22.7 min (major).

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(2) (S)-(6-Hydroxycyclohex-1-enyl) (4-nitrophenyl) methanone 5b

$^1$H NMR (400 MHz, CDCl$_3$) δ 8.30 (d, $J = 8.6$ Hz, 2H), 7.79 (d, $J = 8.6$ Hz, 2H), 6.72 (d, $J = 3.6$ Hz, 1H), 4.78 (s, 1H), 3.24 (s, 1H), 2.41-2.24 (m, 2H), 1.94-1.86 (m, 3H), 1.1.69-1.64 (m, 1H).

HPLC analysis (Daicel CHIRALPAK AS-H column, $\lambda = 254$ nm, eluent: $n$-hexane/i-propanol = 90/10, flow rate: 0.9mL/min): $t_R = 24.2$ min (minor), 67.9 min (major).
(3) (S)-(4-Fluorophenyl) (6-hydroxycyclohex-1-enyl) methanone 5c

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.72-7.69 (m, 2H), 7.12 (dd, $J$ = 11.9, 5.2 Hz, 2H), 6.69 (t, $J$ = 3.9 Hz, 1H), 4.72 (s, 1H), 3.43 (d, $J$ = 2.2 Hz, 1H), 2.39-2.22 (m, 2H), 1.95-1.83 (m, 3H), 1.68-1.65 (m, 1H).

HPLC analysis (Daicel CHIRALPAK AD-H column, $\lambda$=254 nm, eluent: n-hexane/i-propanol = 90/10, flow rate: 0.8 mL/min): $t_R$ = 14.6 min (major), 16.4 min (minor).
(4) (S)-(4-Bromophenyl) (6-hydroxycyclohex-l-enyl)methanone 5d

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.60 (dd, $J = 8.7, 2.0$ Hz, 2H), 7.40 (dd, $J = 8.7, 2.0$ Hz, 2H), 6.68 (t, $J = 3.9$ Hz, 1H), 4.72 (s, 1H), 3.42 (d, $J = 2.2$ Hz, 1H), 2.33-2.25 (m, 2H), 1.94-1.82 (m, 3H), 1.67-1.63 (m, 1H).
HPLC analysis (Daicel CHIRALPAK AD-H column, \( \lambda = 254 \) nm, eluent: \( n \)-hexane/i-propanol=90/10, flow rate: 1.0 mL/min): \( t_R = 14.4 \) min (major), 17.0 min (minor).

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(5) (S)-(4-Chlorophenyl) (6-hydroxycyclohex-1-enyl)methanone 5e

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.62 (d, $J = 8.4$ Hz, 2H), 7.43 (d, $J = 8.4$ Hz, 2H), 6.70 (t, $J = 3.9$ Hz, 1H), 4.73 (s, 1H), 3.40 (d, $J = 2.0$ Hz, 1H), 2.34-2.25 (dd, $J = 30.1$, 7.0 Hz, 2H), 1.92-1.84 (m, 3H), 1.68-1.65 (m, 1H).

HPLC analysis (Daicel CHIRALPAK AD-H column, $\lambda=254$ nm, eluent: $n$-hexane/i-propanol=90/10, flow rate: 1.0 mL/min): $t_R=13.7$ min (major), 15.9 min (minor);
(6) (S)-(6-Hydroxycyclohex-1-yl) (4-(trifluoromethyl) phenyl) methanone 5f

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.74-7.68 (m, 4H), 6.71 (t, $J$ = 3.8 Hz, 1H), 4.76 (s, 1H), 3.64-3.37 (m, 1H), 2.40-2.21 (m, 2H), 1.97-1.81 (m, 3H), 1.69-1.62 (m, 1H).

HPLC analysis (Daicel CHIRALPAK AS-H column, $\lambda$ = 254 nm, eluent: $n$-hexane/i-propanol = 90/10, flow rate: 1.0 mL/min): $t_R$ = 5.8 min (minor), 8.7 min (major);
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(7) (S)-(3-Bromophenyl) (6-hydroxycyclohex-1-enyl)methanone 5g

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.76 (t, J = 1.6 Hz, 1H), 7.66 (d, J = 8.0 Hz, 1H), 7.57 (d, J = 7.7 Hz, 1H), 7.31 (t, J = 7.8 Hz, 1H), 6.72 (t, J = 3.9 Hz, 1H), 4.72 (s, 1H), 3.39 (s, 1H), 2.38-2.27 (m, 2H), 1.94-1.82 (m, 3H), 1.67-1.63 (m, 1H).
HPLC analysis (Daicel CHIRALPAK AD-H column, λ=254 nm, eluent: n-hexane/i-propanol=90/10, flowrate: 0.8 mL/min): t_R=14.9 min (major), 17.1 min (minor).
(8) (S)-(3-Chlorophenyl) (6-hydroxycyclohex-1-enyl)methanone 5h

$^1$H NMR (400 MHz, CDCl$_3$) δ 7.62 (s, 1H), 7.51 (s, 2H), 7.40 (d, $J = 7.5$ Hz, 1H), 6.73 (s, 1H), 4.73 (s, 1H), 3.33 (s, 1H), 2.35 (d, $J = 27.2$ Hz, 2H), 1.86 (s, 3H), 1.66 (s, 1H).

HPLC analysis (Daicel CHIRALPAK AD-H column, $\lambda = 254$ nm, eluent: $n$-hexane/$i$-propanol = 90/10, flow rate: 1.0 mL/min): $t_R=11.2$ min (major), 12.5 min (minor).
### HPLC Analysis

1H NMR (400 MHz, CDCl₃) δ 8.16 (s, 1H), 7.92 (m, 3H), 7.77 (d, J = 8.5 Hz, 1H), 7.61-7.54 (m, 2H), 6.80 (t, J = 3.9 Hz, 1H), 4.80 (s, 1H), 3.54 (d, J = 1.6 Hz, 1H), 2.42-2.26 (m, 2H), 2.03-1.88 (m, 3H), 1.72-1.65 (m, 1H).

HPLC analysis (Daicel CHIRALPAK OD-H column, λ=254 nm, eluent: n-hexane/i-propanol=95/5, flow rate: 1.0 mL/min): tᵣ=13.9 min (minor), 17.3 min (major).
(10) (S)-(6-Hydroxycyclohex-1-enyl) (4-tolyl)methanone 5j

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.95 (d, $J = 8.1$ Hz, 2H), 7.25 (d, $J = 7.9$ Hz, 2H), 6.70 (t, $J = 3.9$ Hz, 1H), 4.72 (d, $J = 1.7$ Hz, 1H), 3.57 (d, $J = 1.7$ Hz, 1H), 2.41 (s, 3H), 2.34-2.22 (m, 2H), 1.94-1.82 (m, 3H), 1.70-1.63 (m, 1H).
HPLC analysis (Daicel CHIRALPAK AD-H column, λ=254 nm, eluent: n-hexane/i-propanol=90/10, flow rate: 1.0 mL/min): t_R=13.9 min (minor), 15.1 min (major).

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(11) (S)-(6-Hydroxycyclohex-1-enyl) (4-methoxyphenyl)methanone 5k

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.71 (d, $J = 7.3$ Hz, 2H), 6.93 (d, $J = 7.3$ Hz, 2H), 6.65 (d, $J = 2.8$ Hz, 1H), 4.69 (s, 1H), 3.87 (s, 3H), 3.59 (s, 1H), 2.36 (dd, $J = 41.9, 19.0$ Hz, 2H), 1.94 – 1.85 (m, 3H), 1.67 (d, $J = 14.5$ Hz, 1H).

HPLC analysis (Daicel CHIRALPAK AS-H column, $\lambda = 254$ nm, eluent: $n$-hexane/i-propanol = 90/10, flow rate: 1.0 mL/min): $t_R = 19.1$ min (minor), 60.4 min (major).
(12) (S)-(2-Bromophenyl) (6-hydroxycyclohex-1-enyl)methanone \( 51 \)

\(^1\)H NMR (400 MHz, CDCl\(_3\)) \( \delta \) 7.60 (dd, \( J = 7.9, 1.0 \) Hz, 1H), 7.39-7.24 (m, 3H), 6.60 (t, \( J = 4.0 \) Hz, 1H), 4.80 (s, 1H), 3.32 (d, \( J = 2.3 \) Hz, 1H), 2.34-2.17 (m, 2H), 1.93-1.81 (m, 3H), 1.68-1.62 (m, 1H).

HPLC analysis (Daicel CHIRALPAK AS-H column, \( \lambda =254 \) nm, eluent: \( n \)-hexane/\( i \)-propanol=90/10, flow rate: 1.0 mL/min): \( t_R =8.8 \) min (minor), 20.8 min (major).
(13) (S)-(2-Chlorophenyl) (6-hydroxycyclohex-1-enyl)methanone 5m

$^1$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.40 (ddd, $J = 21.8, 15.8, 7.7$ Hz, 4H), 6.61 (s, 1H), 4.80 (s, 1H), 3.35 (s, 1H), 2.34-2.17 (m, 2H), 1.95-1.80 (m, 3H), 1.68-1.62 (m, 1H).
HPLC analysis (Daicel CHIRALPAK OD-H column, λ = 254 nm, eluent: n-hexane/i-propanol = 90/10, flow rate: 0.8 mL/min): t_R=9.2 min (minor), 14.9 min (major).

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