Supporting Information

for

Reusable and highly enantioselective water-soluble Ru(II)-Amm-Pheox catalyst for intramolecular cyclopropanation of diazo compounds

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Materials and general methods

All reactions were performed under air atmosphere unless otherwise noted. Diethyl ether (Et₂O) was purchased from Kanto Chemical Co., Inc. All reactions were monitored by thin layer chromatography (TLC), glass plates pre-coated with silica gel Merck KGaA 60 F254, layer thickness 0.2 mm. All the starting materials are commercially available and were used after purification. The products were visualized by irradiation with UV light or by treatment with a solution of phosphomolybdic acid or by treatment with a solution of p-anisaldehyde. Flash column chromatography was performed using silica gel (Merck, Art. No.7734). ¹H NMR and ¹³C NMR (500 MHz, 400 MHz) spectra were recorded on JEOL JNM-ECX500, JEOL JNM-ECS400 spectrometer. Chemical shifts are reported as δ values (ppm) relative to CDCl₃ (7.26 ppm). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet and b = broad. Optical rotations were performed
with a JASCO P-1030 polarimeter at the sodium D line (1.0 mL sample cell). DART mass (positive mode) analyses were performed on a LC-TOF JMS-T100LP. Infrared (IR) spectra were recorded on an FT/IR-4600 instrument (JASCO Co., Ltd., Tokyo, Japan). Enantiomeric excesses were determined by high-performance liquid chromatography (HPLC) analyses with a JASCO GULLIVER using Daicel CHIRALPAK or CHIRALCEL columns.

1. Analytical data for various diazo compounds

Allyl 2-diazoacetate\(^1\) (1a)

Yellow liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta \) 5.93 (ddt, \(J = 16.05, 10.32, 5.35\) Hz, 1H), 5.32 (dd, \(J = 17.20, 1.53\) Hz, 1H), 5.25 (dd, \(J = 10.32, 1.15\) Hz, 1H), 4.77 (brs, 1H), 4.68–4.64 (m, 2H) ppm.

Cinnamyl 2-diazoacetate\(^2\) (1b)

Yellow liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta \) 7.39 (d, \(J = 7.26\) Hz, 2H), 7.32 (t, \(J = 7.45\) Hz, 2H), 7.28–7.23 (m, 1H), 6.66 (d, \(J = 16.05\) Hz, 1H), 6.28 (dt, \(J = 16.05, 6.50\) Hz, 1H), 4.81 (dd, \(J = 6.50, 1.15\) Hz, 2H), 4.78 (brs, 1H) ppm.

\(\text{N-Benzyl-2-diazo-}\text{N-}(3\text{-methylbut-2-en-1-yl})\text{acetamide}\ tragedy (1e)

Yellow liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta \) 7.19–7.37 (m, 5H), 5.11 (brs, 1H), 4.93 (brs, 1H), 4.45 (brs, 2H), 3.78 (brs, 2H), 1.71 (s, 3H), 1.58 (s, 3H) ppm.

Methyl (\(E\))-4-(2-diazoacetoxo)but-2-enoate\(^4\) (1d)

Yellow liquid; \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta \) 6.95 (dt, \(J = 16.05, 4.59\) Hz, 1H), 6.02 (dt, \(J = 15.67, 1.91\) Hz, 1H), 4.83 (dd, \(J = 4.59, 1.91\) Hz, 2H), 4.83 (brs, 1H), 3.75 (s, 3H) ppm.
2-Cyclohexyldieneethan-1-ol

NaH in oil (132 mg, 5.5 mmol, 1.1 equiv) was washed by hexane, and THF was added (5 mL) at 0 °C. To a mixture was added triethyl phosphonoacetate (1.0 mL, 5 mmol, 1 equiv) and cyclohexanone in THF (5 mL). The mixture was stirred at 0 °C to rt for 8 h. The reaction mixture was quenched with NH₄Cl aq. (5 mL) and extracted with Et₂O. The organic layer was dried over Na₂SO₄, and concentrated under reduced pressure to give ethyl 2-cyclohexyldieneacetate as a colorless oil (93% yield, 783.8 mg, 4.7 mmol). This product was used for next reaction without further purification.

A solution of LiAlH₄ (353.7 mg, 9.3 mmol, 2 equiv) in Et₂O (5 mL) was added a solution of reactant (783.8 mg, 4.7 mmol, 1 equiv) in Et₂O (5 mL) at 0 °C. The mixture was stirred at 0 °C to rt for 2 h. The reaction mixture was quenched with H₂O and extracted with CH₂Cl₂. Purification was performed by silica gel column chromatography (Hex/EA = 9/1) to give 2-cyclohexyldieneethan-1-ol as a colorless oil (71% yield, 418.0 mg, 3.3 mmol). ¹H NMR (500 MHz, CDCl₃) δ 5.36 (t, J = 7.26 Hz, 1H), 4.14 (d, J = 7.26 Hz, 2H), 2.23–2.08 (m, 4H), 1.58–1.51 (m, 6H) ppm.

2-Cyclohexyldieneethyl 2-diazoacetate (1c)

Bromoacetyl bromide (0.85 mL, 9.93 mmol, 3 equiv) was slowly added to a stirred solution of 2-cyclohexyldieneethan-1-ol (418 mg, 3.31 mmol, 1 equiv) and K₂CO₃ in CH₂Cl₂ (15 mL). The mixture was stirred at 0 °C to rt for 1 h. The reaction mixture was quenched with H₂O and extracted with CH₂Cl₂. Purification was performed by silica gel column chromatography to give 2-cyclohexyldieneethyl 2-bromoacetate (85% yield, 696.4 mg, 2.81 mmol).
To a solution of 2-cyclohexylideneethyl 2-bromoacetate (696.0 mg, 2.81 mmol, 1 equiv) and N,N'-ditosylhydrazine (1.4 g, 4.21 mmol, 1.5 equiv) were dissolved in THF (8.5 mL) and cooled down to 0 °C for 30 min. The reaction mixture was quenched with NaHCO₃ aq. and extracted with Et₂O, the organic layer was dried over NaSO₄ and evaporated to give the crude product. Purification was performed by column chromatography (Hex/EA = 50/1, Hex/CH₂Cl₂ = 4/1) to give 2-cyclohexylideneethyl 2-diazoacetate as a yellow oil (187.4 mg, 34% yield, 0.96 mmol). This yield was determined by ¹H NMR, because desired product was not purified completely by column chromatography. ¹H NMR (500 MHz, CDCl₃) δ 5.29 (t, J = 7.26 Hz, 1H), 4.74 (brs, 1H), 4.67 (d, J = 7.26 Hz, 2H), 2.09–2.23 (m, 4H), 1.50–1.58 (m, 6H) ppm. IR (neat) ν 2930, 2109, 1695 cm⁻¹. HRMS (DART) calcd for C₁₀H₁₅N₂O₂ [M+H]⁺: 195.1133 found: 195.1132.

2. Typical procedure for the synthesis of trans-allylic diazo-Weinreb amide derivatives

According to the Fukuyama method, O-methylhydroxylamine hydrochloride was added to a solution of trans-allylic bromide and K₂CO₃ in CH₃CN, the reaction mixture was stirred at room temperature until the reaction was completed. After the evaporation of the solvent, the residue was used for the next step without further purification. K₂CO₃ and bromoacetyl bromide were added to the residue at 0 °C. The reaction mixture was stirred for 15 min and then the reaction was quenched with H₂O and extracted with CH₂Cl₂. The organic layer was washed with brine and dried over Na₂SO₄. After the evaporation of the solvent, the residue was used for the next step without further purification. The resulting bromoacetate was dissolved in THF. N,N'-ditosylhydrazine and DBU were added dropwise at 0 °C and the reaction was stirred for 10 min. The reaction was quenched by the addition of saturated solution of NaHCO₃ and extracted with diethyl ether. The organic layer was washed with brine, dried over Na₂SO₄ and evaporated to give crude trans-allylic diazo-Weinreb amide derivatives that were purified by column chromatography to give the desired products.
3. Analytical data for various trans-allylic diazo-Weinreb amide derivatives products

Data for compounds 1f–h were already reported. 5

\[(E)-2\text{-Diazo-N-methoxy-N-[3-(3-nitrophenyl)allyl]acetamide (1g)}\]

Yellow liquid; IR: \(\nu = 2984, 1715 \text{ cm}^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 3.70 \text{ (s, 3H), 4.39 \text{ (dd, } J = 1.15 \text{ Hz, } J = 6.31 \text{ Hz, 2H), 5.37 \text{ (s, 1H), 6.34–6.40 (m, 1H), 6.63 (d, } J = 16.05 \text{ Hz, 1H), 7.47 (t, } J = 16.05 \text{ Hz, 1H), 7.66 (d, } J = 7.64 \text{ Hz, 1H), 8.07 (d, } J = 8.03 \text{ Hz, 1H), 8.21 \text{ (s, 1H) ppm.}\)

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 46.9, 48.7, 62.6, 121.2, 122.5, 127.0, 129.6, 131.4, 132.4, 138.3, 148.7, 168.8 \text{ ppm. HRMS (DART) } m/z \text{ calcd for } C_{12}H_{14}N_4O_3 [M+H]^+ 262.1066 \text{ found: 262.1062.}\)

\[(E)-2\text{-Diazo-N-[3-(2-fluorophenyl)allyl]-N-methoxyacetamide (1n)}\]

Yellow liquid; IR: \(\nu = 2954, 1719 \text{ cm}^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 3.68 \text{ (s, 3H), 4.37 \text{ (dd, } J = 1.53, J = 6.05 \text{ Hz, 2H), 5.36 \text{ (s, 1H), 6.27–6.33 (m, 1H), 6.73 (d, } J = 16.05 \text{ Hz, 1H), 6.99–7.03 (m, 1H), 7.17–7.22 (m, 1H), 7.42 (t, } J = 17.20 \text{ Hz, 1H) ppm.}\)

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 46.8, 49.4, 62.7, 115.7, 115.9, 124.2, 126.3, 127.6, 129.2, 159.3, 161.3, 168.7 \text{ ppm. HRMS (DART) } m/z \text{ calcd for } C_{12}H_{13}FN_3O [M+H]^+ 236.1199 \text{ found 236.1192.}\)

Data for compound 1o were already reported. 5

\[(E)-2\text{-Diazo-N-methoxy-N-[3-(naphthalen-1-yl)allyl]acetamide (1p)}\]

Yellow liquid; IR: \(\nu = 2967, 1694 \text{ cm}^{-1}\). \(^1\)H NMR (500 MHz, CDCl\(_3\)): \(\delta = 4.84 \text{ (d, } J = 6.5 \text{ Hz, 2H), 5.38 \text{ (s, 1H), 6.23–6.29 (m, 1H), 7.35 (d, } J = 15.67 \text{ Hz, 1H), 7.43 (t, } J = 15.29 \text{ Hz, 1H), 7.47–7.35 (m, 1H), 7.58 (d, } J = 7.26 \text{ Hz, 1H), 7.77 (d, } J = 8.41 \text{ Hz, 1H), 7.84 (d, } J = 8.03 \text{ Hz, 1H), 8.1(d, } J = 8.41 \text{ Hz, 1H) ppm.}\)

\(^{13}\)C NMR (125 MHz, CDCl\(_3\)): \(\delta = 46.8, 49.6, 62.9, 123.8, 124.1, 125.7, 125.9, 126.2, 126.8, 128.3, 128.6, 131.2, 131.2, 133.7, 134.3, 168.8 \text{ ppm. HRMS (DART) } m/z \text{ calcd for } C_{16}H_{17}N_3O [M+H]^+ 268.1450, \text{ found 268.1453.}\)

Data for compounds 1q–s were already reported. 5
4. Typical procedures for intramolecular cyclopropanation reactions of various trans-allylic diazo-Weinreb amide derivatives using Ru(II)-Amm-Pheox as a catalyst

To a solution of Ru(II)-Amm-Pheox catalyst (0.003 mmol) in H2O (1.00 mL), a solution of diazo Weinreb amide (1 mmol) in ether (1.00 mL) was added at room temperature. The progress of the reaction was monitored by TLC. After the reaction was completed, the two layers were separated and the aqueous layer was washed 3 times with ether. The collected ether layers were evaporated and the residue was purified using column chromatography on silica gel (Hex/EtOAc = 10:1) to give the desired product. The enantiomeric excesses of products were determined by HPLC analysis.

5. Analytical data for products

(1S,5R)-3-Oxabicyclo[3.1.0]hexan-2-one\(^1\) (2a)

Colorless liquid; \([\alpha]\)\(^{26}\)_D = –54.4 (c = 0.2, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 4.36 (dd, \(J = 9.17, 4.97\) Hz, 1H), 4.28 (brd, \(J = 9.17\) Hz, 1H), 2.27–2.20 (m, 1H), 2.10–2.05 (m, 1H), 1.30–1.25 (m, 1H), 0.91–0.86 (m, 1H) ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 220 nm, eluent: Hex/IPA = 7/3, Flow rate = 1.2 mL/min, tR = 18.5 min (major product), tR = 17.7 min (minor product).

(1S,5R,6R)-6-Phenyl-3-oxabicyclo[3.1.0]hexan-2-one\(^2\) (2b)

White Solid; \([\alpha]\)\(^{26}\)_D = –102.7 (c = 1.0, CHCl\(_3\)). \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 7.31 (t, \(J = 7.64\) Hz, 2H), 7.25 (t, \(J = 7.26\) Hz, 1H), 7.06 (d, \(J = 6.88\) Hz, 2H), 4.47 (dd, \(J = 9.56, 4.97\) Hz, 1H), 4.41 (d, \(J = 9.56\) Hz, 1H), 2.55–2.51 (m, 1H), 2.36–2.31 (m, 2H) ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK OJ-H), UV detector 230 nm, eluent: Hex/IPA = 4/1, Flow rate = 1.0 mL/min, tR = 20.4 min (major product), tR = 23.6 min (minor product).
**Methyl (1R,5R,6R)-2-oxo-3-oxabicyclo[3.1.0]hexane-6-carboxylate (2d)**

White solid; [α]$_{D}^{28}$ = −52.4 (c = 0.3, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) δ 4.44 (dd, J = 9.94, 4.59 Hz, 1H), 4.32 (d, J = 9.94 Hz, 1H), 3.74 (s, 3H), 2.73–2.69 (m, 1H), 2.59 (dd, J = 6.50, 2.68 Hz, 1H), 2.00 (t, J = 3.06 Hz, 1H) ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK IC), UV detector 220 nm, eluent: Hex/IPA = 7/3 (product was dissolved by CH$_2$Cl$_2$). Flow rate = 1.2 mL/min, tR = 83.8 min (major product), tR = 76.1 min (minor product).

**Methyl (1R,5S,6S)-2-oxo-3-oxabicyclo[3.1.0]hexane-6-carboxylate (2e)**

White solid; [α]$_{D}^{28}$ = −25.8 (c = 1.0, CHCl$_3$). $^1$H NMR (500 MHz, CDCl$_3$) δ 7.22–7.34 (m, 5H), 4.50 (d, J = 14.52 Hz, 1H), 4.15 (d, J = 14.52 Hz, 1H), 3.37 (dd, J = 11.08, 6.88 Hz, 1H), 2.99 (d, J = 11.08 Hz, 1H), 1.83 (dd, J = 6.50, 1.91 Hz, 1H), 1.56 (t, J = 6.50 Hz, 1H), 1.08 (s, 3H), 0.94 (s, 3H) ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK OJ-H), UV detector 254 nm, eluent: Hex/IPA = 30/1, Flow rate = 1.0 mL/min, tR = 12.7 min (major product), tR = 15.6 min (minor product).
(1S,5R,6R)-3-Methoxy-6-phenyl-3-azabicyclo[3.1.0]hexane-2-one (2f)

Yellow liquid; $[\alpha]_D^{28} = -53.6$ (c = 1.5, CHCl$_3$).

Spectral data of this compound were already reported. $^5$

(1S,5R,6R)-6-(2-Methylphenyl)-3-methoxy-3-azabicyclo[3.1.0]hexane-2-one (2h)

Yellow liquid; $[\alpha]_D^{27} = -37.8$ (c = 1, CHCl$_3$).

Spectral data of this compound were already reported. $^5$

(1S,5R,6R)-6-(3-Methylphenyl)-3-methoxy-3-azabicyclo[3.1.0]hexane-2-one (2i)

Yellow liquid; $[\alpha]_D^{27} = -35.3$ (c = 1, CHCl$_3$).

Spectral data of this compound were already reported. $^5$

(1S,5R,6R)-6-(4-Methylphenyl)-3-methoxy-3-aza-bicyclo[3.1.0]hexane-2-one (2j)

Yellow liquid; $[\alpha]_D^{25} = -34.2$ (c = 0.5, CHCl$_3$). Spectral data of this compound were already reported. $^5$

(2-Chlorophenyl)-3-methoxy-3-azabicyclo[3.1.0]hexane-2-one (2k)

Yellow liquid; $[\alpha]_D^{26} = -54.9$ (c = 1, CHCl$_3$).

Spectral data of this compound were already reported. $^5$
(3-Chlorophenyl)-3-methoxy-3-azabicyclo[3.1.0]hexan-2-one (2l)

Yellow liquid; $[\alpha]_{D}^{29} = -43.8$ (c = 1, CHCl$_3$).

Spectral data of this compound were already reported.

(1S,5R,6R)-6-(4-Chlorophenyl)-3-methoxy-3-azabicyclo[3.1.0] hexane-2-one (2m)

Yellow liquid; $[\alpha]_{D}^{25} = -57.0$ (c = 0.64, CHCl$_3$).

Spectral data of this compound were already reported.

(1S,5R,6R)-3-Methoxy-6-(3-nitrophenyl)-3 azabicyclo[3.1.0] hexan-2-one (2g) 

White solid; IR: $\nu$ = 2937, 1719 cm$^{-1}$. $[\alpha]_{D}^{25} = -41.2$ (c = 1, CHCl$_3$).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 2.17–2.21 (m, 2H), 2.28 (t, $J$ = 6.50 Hz, 1H), 3.69 (d, $J$ = 9.56 Hz, 1H), 3.77 (s, 3H), 3.89–3.93 (m, 1H), 7.40 (d, $J$ = 7.64 Hz, 1H), 7.64 (t, $J$ = 15.67 Hz, 1H), 7.89 (s, 1H), 8.07 ppm. $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 19.3, 27.4, 29.4, 47.7, 62.4, 120.8, 122.0, 129.7, 132.5, 140.5, 148.5, 168.3 ppm. HRMS (DART) m/z calcd for C$_{12}$H$_{12}$N$_2$O$_4$ [M+H]$^+$ 284.0797, found 284.0796.

(1S,5R)-6-(2-Fluorophenyl)-3-methoxy-3-azabicyclo[3.1.0]hexan-2-one (2n)

Yellow liquid; IR: $\nu$ = 2983, 1711 cm$^{-1}$. $[\alpha]_{D}^{25} = -53.0$ (c = 0.8, CHCl$_3$).

$^1$H NMR (500 MHz, CDCl$_3$): $\delta$ = 2.09–2.13 (m, 1H), 2.19–2.21 (m, 1H), 2.32 (t, $J$ = 6.88 Hz, 1H), 3.69 (dd, $J$ = 1.15 Hz, $J$ = 9.75 Hz, 1H), 3.84–3.87 (m, 1H), 6.89 (t, $J$ = 15.29 Hz, 1H), 7.00–7.06 (m, 2H), 7.16–7.21 (m, 1H) ppm. $^{13}$C NMR (125 MHz, CDCl$_3$): $\delta$ = 18.2, 24.0, 25.4, 47.8, 62.3, 124.3, 125.3, 126.8, 128.5, 136.8, 169.1 ppm. HRMS (DART) m/z calcd for C$_{12}$H$_{12}$FNO$_2$ [M+H]$^+$ 222.0930, found 222.0938.
(1S,5R,6R)-6-(2,4-dichlorophenyl)-3-methoxy-3-azabicyclo[3.1.0]hexan-2-one (2o)

Yellow liquid; \([\alpha]_D^{27} = -25.3\) (c = 1, CHCl₃).
Spectral data of this compound were already reported.⁵

(1S,5R)-3-Methoxy-6-(naphthalen-1-yl)-3-azabicyclo[3.1.0]hexan-2-one (2p)⁶

Yellow liquid; IR: ν = 2926, 1689 cm⁻¹. \([\alpha]_D^{26} = -48\) (c = 1, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ = 2.18–2.21 (m, 1H), 2.24–2.27 (m, 1H), 2.63 (t, J = 6.88 Hz, 1H), 3.82 (s, 3H), 3.84 (d, J = 1.15 Hz, 1H), 3.95–3.98 (m, 1H), 3.98 (d, J = 6.88 Hz, 1H), 7.27 (d, J = 7.26 Hz, 1H), 7.38 (t, J = 15.67 Hz, 1H), 7.52 (t, J = 14.91 Hz, 1H), 7.58 (t, J = 15.29 Hz, 1H), 7.77 (d, J = 8.03 Hz, 1H), 7.86 (d, J = 7.64, 1H), 8.24 (d, J = 8.41 Hz, 1H). ¹³C NMR (125 MHz, CDCl₃): δ = 17.0, 24.9, 28.3, 47.8, 62.3, 123.9, 124.5, 125.3, 126.2, 126.7, 128.2, 128.8, 132.8, 133.2, 133.7, 169.6 ppm. HRMS (DART) m/z calcd for C₁₆H₁₅NO₂ [M+H]+ 253.1103, found 253.1107.

(1S,5R,6R)-3-Methoxy-1-methyl-6-phenyl-3-azabicyclo[3.1.0]hexane-2-one (2q)

Yellow liquid; \([\alpha]_D^{28} = -19.5\) (c = 0.94, CHCl₃).
Spectral data of this compound were already reported.⁵

(1S,5R,6R)-3-Methoxy-6-((E)-prop-1-en-1-yl)-3-azabicyclo[3.1.0]hexan-2-one (2r)

Yellow liquid; \([\alpha]_D^{26} = -27.6\) (c = 0.82, CHCl₃).
Spectral data of this compound were already reported.⁵

(1S,5R,6R)-3-Methoxy-6-propyl-3-azabicyclo[3.1.0]hexan-2-one (2s)

Yellow liquid; \([\alpha]_D^{26} = -32.3\) (c = 1, CHCl₃).
Spectral data of this compound were already reported.⁵
(1S,2R,3R)-N-Benzyl-2-(hydroxymethyl)-3-phenylcyclopropane-1-carboxamide (3)

Benzyamine (23 µL, 0.218 mmol, 0.218 mmol, 1.16 equiv) was dissolved in dry THF (0.5 mL), cooled to –15 °C, and DIBAL-H (200 µL, 0.218 mmol, 1.16 equiv) was injected. After the mixture was stirred for 20 min, the solution was allowed to warm to 30 °C and left to react for 3 h. Then, it was cooled at –5 °C, and a solution of 2d (32.7 mg, 0.188 mmol, 1 equiv) in THF (1 mL) was added with stirring for 10 min. After 20 h at room temperature, the reaction was quenched with water and 4N HCl, and the product was extracted three times with Et2O. The combined organic phase was washed with NaHCO3 aq., then dried Na2SO4, filtered and concentrated. The residue was purified by flash column chromatography with Hexane/EtOAc to give product 3 as white solid (44% yield, 95% ee, 16.0 mg, 0.056 mmol). [α]D23 = –104.5 (c 0.8, CHCl3). 1H NMR (500 MHz, CDCl3) δ 7.33 (dd, J = 7.64, 7.26 Hz, 2H), 7.29–7.23 (m, 5H), 7.19 (t, J = 7.26 Hz, 1H), 7.09 (d, J = 6.88 Hz, 2H), 6.20 (s, 1H), 4.49 (dd, J = 14.52, 5.73 Hz, 1H), 4.43 (dd, J = 14.52, 5.73 Hz, 1H), 4.12 (dd, J = 12.13, 3.63 Hz, 1H), 3.95 (dd, J = 12.13, 7.26 Hz, 1H), 2.90 (s, 1H), 2.79 (t, J = 5.73 Hz, 1H), 1.98–1.90 (m, 1H), 1.79 (dd, J = 8.79, 4.97 Hz, 1H) ppm. 13C NMR (125MHz, CDCl3) δ 171.72, 140.15, 137.91, 128.93, 128.68, 127.94, 127.82, 126.66, 126.26, 59.79, 44.18, 32.01, 31.09, 28.26 ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 5/1, flow late = 1.0 mL/min, tR = 11.3 min (minor product), tR = 13.4 min (major product). IR (neat) ν 3307, 3063, 3029, 1639, 1544, 1028 cm⁻¹. HRMS (DART) calcd for C18H20N1O2 [M+H]+: 282.1493 found: 282.1494.

((1S,2R,3R)-2-(Methoxyamino)methyl)-3-(p-tolyl)cyclopropyl)(phenyl)methanone (4) ⁶

To a solution of 2f (85.0 mg, 0.42 mmol) in dry THF (2.0 mL) was slowly added a solution of PhMgBr (0.28 mL, 1.5 equiv, 3 M in THF) at 0 °C. The resulting mixture
was stirred for 30 min at 0 °C followed by addition of H₂O (2.0 mL). The product was extracted with CH₂Cl₂ (10 mL). The organic phase was separated and dried with Na₂SO₄. The solvent was removed and the residue was purified by column chromatography on silica gel eluted with Hex/EA = 5/1 to give the desired cyclopropane 4 as a sole stereoisomer (37% yield, 98% ee, 43.8 mg, 0.16 mmol). [α]²²º = −89.8 (c 1.2, CHCl₃). ¹H NMR (500 MHz, CDCl₃) δ 8.01 (d, J = 7.26 Hz, 2H), 7.54 (dd, J = 7.64, 7.26 Hz, 1H), 7.45 (dd, J = 8.03, 7.26 Hz, 2H), 7.29 (dd, J = 7.64, 7.26 Hz), 7.22–7.16 (m, 3H), 3.36 (s, 3H), 3.34 (dd, J = 13.76, 5.35 Hz, 1H), 3.18 (dd, J = 13.76, 8.41 Hz, 1H), 3.06 (dd, J = 9.17, 5.35 Hz, 1H), 2.98–2.89 (m, 1H), 2.35–2.30 (m, 1H) ppm. ¹³C NMR (125MHz, CDCl₃) 197.26, 140.18, 138.42, 132.92, 128.64, 128.60, 128.23, 126.65, 126.52, 61.71, 48.31, 33.34, 32.25, 31.15 ppm. The ee value was determined by chiral HPLC analysis. Column (CHIRALPAK IC-3), UV detector 254 nm, eluent: Hex/IPA = 9/1, Flow rate = 0.5 mL/min, tR = 28.8 min (minor product), tR = 31.4 min (major product). IR (neat) ν 3030, 2934, 1666 cm⁻¹. HRMS (DART) calcd for C₁₈H₂₉N₁O₂ [M+H]⁺: 282.1494 found: 282.1494.
6. Solubility of catalyst

- **Ru(II)-Pheox**

Ru(II)-Pheox (2.5 mg) was dissolved in H$_2$O (6 mL) and Et$_2$O (6 mL). Ru(II)-Pheox was partially dissolved in water phase. The Et$_2$O phase was separated, and no catalyst was observed after removal of the solvent. The water phase was filtered to remove insoluble solid and the water was removed under reduced pressure to give Ru(II)-Pheox (0.3 mg) in 12% recovered yield.

- **Ru(II)-Amm-Pheox**

Ru(II)-Amm-Pheox (2.5 mg) was dissolved in H$_2$O (6 mL) and Et$_2$O (6 mL). Ru(II)-Amm-Pheox almost completely dissolved in water phase. The Et$_2$O phase was separated, and no catalyst was observed after removal of the solvent. The water phase was filtered and the water was removed under reduced pressure to give Ru(II)-Amm-Pheox (1.9 mg) in 76% recovered yield.

Based on these results, we expected that the Ru(II)-Amm-Pheox has more high solubility in water than Ru(II)-Pheox.
7. Solvent screening

Table S1. Solvent screening$^a$

| Entry | cat.  | Solvent            | Time [h] | Yield [\%]$^b$ | ee [\%]$^c$ |
|-------|-------|--------------------|----------|-----------------|-------------|
| 1     | cat. 1| CH$_2$Cl$_2$       | 1 min    | 92              | 90          |
| 2     | cat. 2| CH$_2$Cl$_2$       | 1 min    | 96              | 94          |
| 3     | cat. 2| H$_2$O/Benzene     | 24       | 31              | 75          |
| 4     | cat. 2| H$_2$O/Toluene     | 24       | 47              | 65          |
| 5     | cat. 2| H$_2$O/Cyclohexane | 24       | 37              | 67          |
| 6     | cat. 2| H$_2$O/Heptane     | 24       | 42              | 75          |
| 7     | cat. 2| H$_2$O/CHCl$_3$    | 10       | 76              | 88          |
| 8     | cat. 2| H$_2$O/CH$_2$Cl$_2$ | 4        | 81              | 89          |
| 9     | cat. 2| H$_2$O/ DCE        | 4        | 69              | 93          |
| 10    | cat. 2| H$_2$O/DIPE        | 3        | 97              | 85          |
| 11    | cat. 2| H$_2$O/Et$_2$O     | 1        | 99              | 99          |

$^a$Reaction conditions: (3 mol %) of the cat. 2 was dissolved in water (1 mL) and a solution of diazo compound 1f in the selected organic solvent (1 mL) was added. The reaction was stirred for the mentioned time at room temperature. $^b$Isolated yield. $^c$Determined by chiral HPLC analysis. DCE = 1,2-dichloroethane, DIPE = diisopropyl ether, Et$_2$O = diethyl ether.
8. Reaction mechanism

Figure S1. Plausible reaction mechanism in water/Et₂O.
9. X-ray analysis

Figure S2. Thermal ellipsoid plot for 2g structure
10. NMR spectral data
### 11. HPLC spectral data

#### Table 1: HPLC Data

| Entry | RT [min] | Area   | Area % |
|-------|----------|--------|--------|
| 1     | 16.9     | 137031 | 49.23  |
| 2     | 18.2     | 141308 | 50.768 |

#### Table 2: HPLC Data

| Entry | RT [min] | Area   | Area % |
|-------|----------|--------|--------|
| 1     | 17.7     | 296341 | 6.18   |
| 2     | 18.5     | 449408 | 93.81  |
| PEAK | RT [min] | area    | area %  |
|------|---------|---------|---------|
| 1    | 20.4    | 16209356| 50.38   |
| 2    | 22.8    | 15964206| 49.619  |

| entry | RT [min] | area    | area %  |
|-------|---------|---------|---------|
| 1     | 20.4    | 17907788| 96.34   |
| 2     | 23.6    | 679258  | 3.654   |
| entry | RT [min] | area     | area %   |
|-------|---------|----------|----------|
| 1     | 19.4    | 597989   | 50.42    |
| 2     | 23.0    | 587829   | 49.57    |

| entry | RT [min] | area     | area %   |
|-------|---------|----------|----------|
| 1     | 20.2    | 815328   | 98.33    |
| 2     | 24.8    | 13819    | 1.66     |
| entry | RT [min] | area    | area %  |
|-------|----------|---------|---------|
| 1     | 12.7     | 996097  | 50.14   |
| 2     | 15.6     | 990498  | 49.85   |

| entry | RT [min] | area    | area %  |
|-------|----------|---------|---------|
| 1     | 12.7     | 3332812 | 71.68   |
| 2     | 15.6     | 1316145 | 28.31   |
| entry | RT [min] | area   | area % |
|-------|----------|--------|--------|
| 1     | 67.9     | 4019087| 50.34  |
| 2     | 77.0     | 3963716| 49.65  |

| entry | RT [min] | area   | area % |
|-------|----------|--------|--------|
| 1     | 76.1     | 39197  | 1.98   |
| 2     | 83.8     | 1940744| 98.02  |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 30.50   | 45256405 | 50.47  |
| 2     | 33.75   | 44404766 | 49.53  |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 30.21   | 21412045 | 95.34  |
| 2     | 33.68   | 1044654  | 4.65   |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 30.17   | 31355247 | 97.52  |
| 2     | 33.79   | 796566   | 2.48   |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 30.10   | 19008278 | 93.99  |
| 2     | 33.46   | 1215067  | 6.01   |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 29.57   | 29252529 | 98.05   |
| 2     | 33.08   | 581720   | 1.95    |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 30.90   | 16956096 | 99.16   |
| 2     | 34.80   | 142997   | 0.84    |
| entry | tR[min] | area     | area %    |
|-------|---------|----------|-----------|
| 1     | 30.45   | 4737061  | 87.43     |
| 2     | 33.64   | 680996   | 12.57     |

| entry | tR[min] | area     | area %    |
|-------|---------|----------|-----------|
| 1     | 30.60   | 8643353  | 82.73     |
| 2     | 33.35   | 1803675  | 17.27     |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 26.98   | 367747   | 84.38   |
| 2     | 29.47   | 68039    | 15.62   |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 27.31   | 985736   | 87.57   |
| 2     | 29.93   | 139961   | 12.43   |
| entry | tR[min] | area    | area % |
|-------|---------|---------|--------|
| 1     | 29.87   | 45848193| 93.925 |
| 2     | 33.40   | 2965173 | 6.075  |

| entry | tR[min] | area    | area % |
|-------|---------|---------|--------|
| 1     | 28.59   | 38042337| 94.68  |
| 2     | 31.98   | 2137036 | 5.31   |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 29.29   | 37492806 | 97.21  |
| 2     | 32.75   | 1075112  | 2.79   |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 29.56   | 29761003 | 92.53  |
| 2     | 32.89   | 2401935  | 7.47   |
| entry | tR[min] | area      | area %  |
|-------|---------|-----------|---------|
| 1     | 30.90   | 16956096  | 99.17   |
| 2     | 34.80   | 142997    | 0.83    |

| entry | tR[min] | area      | area %  |
|-------|---------|-----------|---------|
| 1     | 30.90   | 16956096  | 99.17   |
| 2     | 34.80   | 142997    | 0.83    |
| entry | tR[min] | area       | area %  |
|-------|---------|------------|---------|
| 1     | 31.58   | 49236765   | 99.61   |
| 2     | 35.89   | 456987     | 0.39    |

| entry | tR[min] | area       | area %  |
|-------|---------|------------|---------|
| 1     | 31.42   | 29461318   | 98.50   |
| 2     | 35.47   | 447790     | 1.50    |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 31.45   | 31761845 | 97.40   |
| 2     | 35.47   | 846789   | 2.60    |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 32.42   | 35202200 | 95.76   |
| 2     | 36.63   | 1557696  | 4.23    |
| entry | tR [min] | area     | area %   |
|-------|----------|----------|----------|
| 1     | 32.89    | 58005665 | 94.79    |
| 2     | 37.42    | 3191079  | 5.21     |

Run 2 after keeping the water phase which contains the catalyst in the refrigerator for 5 months.

| entry | tR [min] | area     | area %   |
|-------|----------|----------|----------|
| 1     | 30.25    | 7184688  | 84.18    |
| 2     | 33.56    | 1349575  | 15.82    |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 57.18   | 23931962 | 50.39   |
| 2     | 69.03   | 23559879 | 49.61   |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 56.05   | 44528683 | 97.61   |
| 2     | 68.85   | 1089492  | 2.39    |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 49.24   | 54674636 | 50.45  |
| 2     | 60.87   | 53699095 | 49.55  |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 49.55   | 37895724 | 98.65  |
| 2     | 62.19   | 515166   | 1.34   |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 36.85   | 11709831 | 50.26   |
| 2     | 48.56   | 11584762 | 49.74   |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 34.91   | 61559416 | 93.53   |
| 2     | 47.02   | 4254625  | 6.47    |
| entry | tR [min] | area    | area %  |
|-------|----------|---------|---------|
| 1     | 32.25    | 3138136 | 50.36   |
| 2     | 35.81    | 3093540 | 49.64   |

| entry | tR [min] | area    | area %  |
|-------|----------|---------|---------|
| 1     | 30.94    | 10590639| 93.16   |
| 2     | 35.35    | 777500  | 6.83    |
| entry | tR[min] | area      | area % |
|-------|---------|-----------|--------|
| 1     | 59.61   | 20018088  | 49.68  |
| 2     | 70.94   | 20273120  | 50.32  |

| entry | tR[min] | area      | area % |
|-------|---------|-----------|--------|
| 1     | 62.16   | 1071692   | 5.24   |
| 2     | 71.85   | 19381762  | 94.76  |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 57.53   | 76070646 | 49.94  |
| 2     | 70.45   | 76242002 | 50.06  |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 54.52   | 85496013 | 96.95  |
| 2     | 69.84   | 2686559  | 3.04   |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 29.46   | 36252165 | 51.23  |
| 2     | 32.27   | 34515533 | 48.77  |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 29.57   | 32849913 | 95.53  |
| 2     | 33.12   | 1535069  | 4.47   |
| entry | tR[min] | area    | area % |
|-------|--------|---------|--------|
| 1     | 13.95  | 21116277| 49.34  |
| 2     | 16.43  | 21679616| 50.65  |

| entry | tR[min] | area    | area % |
|-------|--------|---------|--------|
| 1     | 14.00  | 16537511| 96.98  |
| 2     | 16.63  | 513845  | 3.02   |
| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 37.50   | 13316778 | 49.35  |
| 2     | 40.15   | 13669404 | 50.65  |

| entry | tR[min] | area     | area % |
|-------|---------|----------|--------|
| 1     | 37.33   | 13151247 | 97.98  |
| 2     | 40.31   | 270389   | 2.02   |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 74.37   | 63405199 | 49.15   |
| 2     | 77.91   | 65598546 | 50.85   |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 73.25   | 1243073  | 2.40    |
| 2     | 76.13   | 50644713 | 97.60   |
| entry | tR[min] | area    | area %  |
|-------|---------|---------|---------|
| 1     | 16.82   | 7849172 | 50.60   |
| 2     | 18.22   | 7885385 | 49.40   |

| entry | tR[min] | area    | area %  |
|-------|---------|---------|---------|
| 1     | 15.90   | 5221816 | 89.54   |
| 2     | 17.36   | 610287  | 10.46   |
| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 7.57    | 8296203  | 50.73   |
| 2     | 8.30    | 8058874  | 49.27   |

| entry | tR[min] | area     | area %  |
|-------|---------|----------|---------|
| 1     | 7.71    | 12038739 | 94.77   |
| 2     | 8.51    | 664794   | 5.23    |
| entry | tR[min] | area       | area % |
|-------|---------|------------|--------|
| 1     | 42.32   | 18562087   | 50.88  |
| 2     | 49.61   | 17921631   | 49.12  |

| entry | tR[min] | area       | area % |
|-------|---------|------------|--------|
| 1     | 42.23   | 3234054    | 94.86  |
| 2     | 49.20   | 175230     | 5.14   |
| entry | tR [min] | area  | area %  |
|-------|---------|-------|---------|
| 1     | 11.35   | 601642| 50.06   |
| 2     | 13.48   | 600040| 49.58   |

| entry | tR [min] | area  | area %  |
|-------|---------|-------|---------|
| 1     | 11.31   | 10074 | 2.08    |
| 2     | 13.40   | 474020| 97.91   |
| entry | tR [min] | area     | area % |
|-------|----------|----------|--------|
| 1     | 46.40    | 1527824  | 46.60  |
| 2     | 50.45    | 1750380  | 53.39  |

| entry | tR [min] | area     | area % |
|-------|----------|----------|--------|
| 1     | 41.80    | 72701    | 1.18   |
| 2     | 48.43    | 6060994  | 98.85  |
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