Supporting information

Asymmetric transfer hydrogenation (ATH) of ortho-hydroxyphenyl ketones; utilizing directing effects which optimize the asymmetric synthesis of challenging alcohols.

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**General procedures for the syntheses.**

Solvents and reagents for the synthesis of complexes and catalytic reactions were degassed prior to use and all reactions were carried out under either a nitrogen or argon atmosphere. Reactions were monitored by TLC using aluminum backed silica gel 60 (F254) plates, visualized using UV 254 nm and phosphomolybdic acid (PMA), potassium permanganate or vanillin dips as appropriate. Flash column chromatography was carried out routinely using 60 micrometer silica gel. Reagents were used as received from commercial sources unless otherwise stated. 1H NMR spectra were recorded on a Bruker DPX (300, 400 or 500 MHz) spectrometer. Chemical shifts are reported in δ units, parts per million relative to the singlet at 7.26 ppm for chloroform and 0.00 ppm for TMS. Coupling constants (J) are measured in Hertz. IR spectra were recorded on a Perkin-Elmer Spectrum One FT-IR Golden Gate. Mass spectra were recorded on a Bruker Esquire2000 or a Bruker MicroTOF mass spectrometer. Melting points were recorded on a Stuart Scientific SMP 1 instrument and are uncorrected. GC analysis was performed using a Hewlett Packard 5890. Dry solvents were purchased and used as received. HPLC analyses on a Hewlett-Packard 1050 instrument. Optical rotations were measured on an AA-1000 polarimeter. The details of the X-ray instrument are given in the X-ray crystallography section. A description of the sample preparation (i.e., solvent and method for crystal growth) and crystal measurement are given for each of the four crystal structures of $8c$, $8e$, $8g$, and $C$ (page S173-S174).
Synthesis and characterisation of reaction products 8a-8l.

2-Methoxyphenyl)(phenyl)methanol 8a.


To a solution of 2-bromoanisole (582 mg, 0.39 mL, 3.11 mmol) in THF (3 mL) at -78 °C was added a solution of n-butyllithium (1.13 mL, 2.5M in hexanes, 2.83 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which benzaldehyde (300 mg, 2.83 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-methoxyphenyl)(phenyl)methanol 8a as a colorless oil (542.6 mg, 2.54 mmol, 90%). δ_H (400 MHz, CDCl₃) 7.39-7.21 (7H, m, ArOH), 6.95-6.87 (2H, m, ArH), 6.05 (1H, d, J = 4.0, ArCHOH), 3.80 (3H, s, OCH₃), 3.01 (1H, s, ArCHOH) ppm; δ_C (100 MHz, CDCl₃) 156.8 (C), 143.3 (C), 132.0 (C), 128.0 (CH), 128.2 (CH), 127.9 (CH), 127.2 (CH), 126.6 (CH), 120.8 (CH), 110.8 (CH), 72.3 (CH), 55.4 (CH₃) ppm. Data matched that reported.

Enantiomeric excess and conversion were determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C) ketone 15.0 min, R isomer 33.9 min and S isomer 29.9 min.
ATH of (2- methoxyphenyl)(phenyl)methanone \(7a\) using \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst 2.

Catalyst \((R,R)-2\) (0.00187 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2- methoxyphenyl)(phenyl)methanone \(7a\) (40 mg, 0.187 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (9:1 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give \((S)-(2\text{-}methoxyphenyl)(phenyl)methanol \(8a\) (28.1 mg, 0.13 mmol, 69.6%; \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C); \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst: 81.4% conversion (HPLC calibration: 1:1 (2-methoxyphenyl)(phenyl)methanone : (2-methoxyphenyl)(phenyl)methanol gives 13.9:1 ratio of absorption at 254 nm); \([\alpha]_D^{24} -28.1 \text{ (c 1.405 in CHCl}_3\) 73.4% ee \((S)\) (lit. \([\alpha]_D^{20} +16.3 \text{ (c 0.62 in CHCl}_3\) 84% ee \((R)\)) Reference: Li, K.; Hu, N.; Luo, R.; Yuan, W.; Tang, W.; J. Org. Chem. 2013, 78, 6350 – 6355.

Formation of \(8a\) by methylation of \(8b\) (YZ219) to compare with ATH above (YZ198) to confirm configuration.

To a solution of asymmetric \((R)-2\text{-}(hydroxy(phenyl)methyl)phenol \(8b\) (200 mg, 1.0 mmol) in DMF (10 mL) was added potassium carbonate (165.6 mg, 1.2 mmol) and iodomethane (156 mg, 1.0 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on
silica eluted with 0-20% ethyl acetate in hexane to give asymmetric (R)-(2-methoxyphenyl)(phenyl)methanol 8a as a colorless oil (186.3 mg, 0.87 mmol, 87%). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.7 mL/min, T = 25°C): 77.4% ee (R configuration). It was shown that the product of ATH of 7b using the same catalyst (YZ157- see below) was of R configuration by comparison with the HPLC of the ATH product formed from 7a (YZ 198).

$^1$H NMR (400 MHz, CDCl$_3$) of 8a:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 8a:

HPLC of racemic (2-methoxyphenyl)(phenyl)methanol 8a:
HPLC of 8a after ATH of (2-methoxyphenyl)(phenyl)methanone 7a: 
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 81.4% conversion, 73.4% ee, S configuration).

HPLC of 8a after methylation of 2-(hydroxy(phenyl)methyl)phenol 8b (YZ219, 77.4% ee, R configuration):
(2-Methoxyphenyl)(phenyl)methanone 7a.

![Chemical structure of 7a](Image)

This compound has been reported and fully characterized.


To a solution of (2-methoxyphenyl)(phenyl)methanol 8a (300 mg, 1.40 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.8 g, 21 mmol). The reaction mixture was stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give the product 7a as a colorless oil (277.7 mg, 1.31 mmol, 93.5%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and KMnO₄; δ_H (400 MHz, CDCl₃) 7.83 (2H, d, J = 7.2, ArH), 7.57-7.54 (1H, m, ArH), 7.49-7.41 (3H, m, ArH), 7.37 (1H, d, J = 7.2, ArH), 7.06-6.99 (2H, m, ArH), 3.73 (3H, s, OCH₃) ppm; δ_C (100 MHz, CDCl₃) 196.5 (C), 157.4 (C), 137.8 (C), 132.9 (CH), 131.9 (CH), 129.8 (CH), 129.6 (CH), 128.9 (C), 128.2 (CH), 120.5 (CH), 111.5 (CH), 55.5 (CH₃) ppm. Data matched that reported.
$^1$H NMR (400 MHz, CDCl$_3$) of 7a:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 7a:
HPLC of (2-methoxyphenyl)(phenyl)methanone 7a:
2-(Hydroxy(phenyl)methyl)phenol 8b.

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
\text{C} & \quad \text{OH} \\
\end{align*}
\]

racemic: YZ158, Asymmetric: YZ157

This compound has been reported and fully characterized.


To a solution of 2-hydroxybenzophenone 7b (80 mg, 0.40 mmol) in MeOH (2 mL) was added sodium borohydride (32 mg, 0.82 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO₄, and the solvent was removed under vacuum to give 2-(hydroxy(phenyl)methyl)phenol 8b as a colorless oil (65 mg, 0.33 mmol, 80%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and KMnO₄; \( \delta_H \) (400 MHz, CDCl₃) 7.94 (1H, s, ArH), 7.37-7.18 (5H, m, ArH), 6.91-6.80 (3H, m, ArH), 6.00 (1H, s, CHOH), 3.05 (1H, s, CHOH) ppm; \( \delta_C \) (100 MHz, CDCl₃) 155.5 (C), 141.8 (C), 129.3 (CH), 128.8 (CH), 128.3 (CH), 126.9 (CH), 126.6 (C), 120.0 (CH), 117.3 (CH), 77.1 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion was determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 5.4 min, S isomer 13.1 min and R isomer 20.2 min.

Reduction of 7b to give (R)-8b using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (YZ157).

\[
\begin{align*}
\text{OH} & \quad \text{OH} \\
\text{C} & \quad \text{OH} \\
\end{align*}
\]

Catalyst (R,R)-2 (0.0020 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-hydroxybenzopenone 7b (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (1:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted
with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 25-100% ethyl acetate in hexane to give (R)-2-(hydroxy(phenyl)methyl)phenol 8b (32.6 mg, 0.16 mmol, 80.7%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]₀^26 -4.38 (c 0.65 in MeCN) 80% ee (R) (lit. [α]₀^20 -12.8 (c 1.2 in MeCN) 91% ee (R))


^1H NMR (400 MHz, CDCl₃) of 7b:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 7b:

HPLC of racemic 2-(hydroxy(phenyl)methyl)phenol 7b:
HPLC of 2-hydroxybenzophenone 7b:

\[ 7b \]

HPLC of 7a after ATH of 2-hydroxybenzophenone 7b:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 80% ee, R configuration)
2-(Hydroxy(2-methoxyphenyl)methyl)phenol 8c.

![Chemical structure]


This compound has been reported and fully characterized.


To a solution of 2-bromoanisole (935 mg, 0.62 mL, 5.0 mmol) in THF (5 mL) at -78 °C was added dropwise a solution of n-butyllithium (2 mL, 2.5M in hexanes, 5.0 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which salicylaldehyde (250 mg, 2.05 mmol) was added dropwise. The reaction mixture was stirred under anitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product 8c. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)phenol as a white solid (319 mg, 1.39 mmol, 67.7%).

TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; δ_H (400 MHz, CDCl₃) 8.31 (1H, s, ArOH), 7.35-7.31 (1H, m, ArH), 7.26-7.22 (1H, m, ArH), 6.97-6.92 (4H, m, ArH), 6.81 (2H, s, ArH), 6.21 (1H, s, ArCHOH), 4.09 (1H, s, ArCHOH), 3.91 (3H, s, OCH₃) ppm; δ_C (100 MHz, CDCl₃) 157.0 (C), 156.5 (C), 129.6 (CH), 129.3 (CH), 129.2 (C), 128.5 (CH), 128.0 (CH), 125.1 (C), 121.3 (CH), 119.7 (CH), 117.2 (CH), 110.8 (CH), 74.0 (CH), 55.6 (CH₃) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.8 mL/min, T = 25°C) ketone 9.8 min, R isomer 20.5 min and S isomer 22.5 min ([(R,R)-3C-tethered Ru(II)-TsDPEN catalyst); or R isomer 22.1 min and S isomer 24.4 min ([(R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst, (S,S)-Noyori Ru(II)-TsDPEN catalyst and (R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst).
ATH of (2-hydroxyphenyl)(2-methoxyphenyl)methanone 7c.

Catalyst (R,R)-2 (0.00175 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-hydroxyphenyl)(2-methoxyphenyl)methanone 7c (40 mg, 0.175 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched by saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product 8c. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (S)-(2-hydroxyphenyl)(2-methoxyphenyl)methanol 8c (29.1 mg, 0.13 mmol, 72%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.8 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D²⁵ -35.9 (c 1.0 in CHCl₃) 99.4% ee (S)

Crystal Structure of 8c: S configuration CCDC 1978884 (local code yz7).
Unit Cell Parameters: a 10.53840(10) b 10.63310(10) c 20.91760(10) P2₁2₁2₁

Crystal structure determination of [yz7]
Yz7 contains two crystallographically independent but chemically identical molecules in the asymmetric, there are eight molecules in the unit cell.
The OHs were located in a difference map and refined with distance restraints. The form H bonds tabulated below.

**Specified hydrogen bonds (with esds except fixed and riding H)**

<table>
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<tr>
<th>D-H</th>
<th>H...A</th>
<th>D...A</th>
<th>&lt;(DHA)</th>
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</thead>
<tbody>
<tr>
<td>0.84</td>
<td>1.82</td>
<td>2.6295(17)</td>
<td>162.1</td>
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<tr>
<td>0.84</td>
<td>2.12</td>
<td>2.7533(17)</td>
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<tr>
<td>0.84</td>
<td>1.81</td>
<td>2.6518(16)</td>
<td>175.2</td>
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<tr>
<td>0.84</td>
<td>2.00</td>
<td>2.6820(18)</td>
<td>137.2</td>
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</tbody>
</table>

O101-H101...O207_S1
O107-H10A...O114
O201-H201...O107_S2
O207-H20A...O201

Symmetry operators used to generate symmetry related atoms discussed in the above contacts was

$1$ 1.5-X,1-Y,0.5+Z
$2$ 0.5-X,1-Y,-0.5+Z

The Flack parameter and related Hooft y parameter are small with a small error so we can be reasonably confident with the assignment of the handedness of the crystal measured

Hooft y: -0.00(3)
Flack x: -0.01(4)

**Experimental**

Single crystals of C$_{14}$H$_{14}$O$_3$ were grown from DCM/Hexane in a small vial at room temperature. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimisation.


**Crystal Data** for C$_{14}$H$_{14}$O$_3$ (M=230.25 g/mol): orthorhombic, space group P2$_1$2$_1$2$_1$ (no. 19), $a = 10.53840(10)$ Å, $b = 10.63310(10)$ Å, $c = 20.91760(10)$ Å, $V = 2343.94(3)$ Å$^3$, $Z = 8$, $T = 150(2)$ K, μ(CuKα) = 0.744 mm$^{-1}$, $Dcalc = 1.305$ g/cm$^3$, 37252 reflections measured ($8.454^\circ \leq 2\Theta \leq 147.264^\circ$), 4693 unique ($R_{int} = 0.0255$, $R_{sigma} = 0.0111$) which were used in all calculations. The final $R_1$ was 0.0280 (I > 2σ(I)) and $wR_2$ was 0.0781 (all data).
Table 1 Crystal data and structure refinement for yz7.

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</thead>
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<tr>
<td>Empirical formula</td>
<td>C\textsubscript{14}H\textsubscript{14}O\textsubscript{3}</td>
</tr>
<tr>
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<td>Temperature/K</td>
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<td>Crystal system</td>
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<tr>
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</tr>
<tr>
<td>b/Å</td>
<td>10.63310(10)</td>
</tr>
<tr>
<td>c/Å</td>
<td>20.91760(10)</td>
</tr>
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<td>(\alpha/°)</td>
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<td>(\beta/°)</td>
<td>90</td>
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<td>(\gamma/°)</td>
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<tr>
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<td>(Z)</td>
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<tr>
<td>(\rho_{\text{calc}})/g/cm\textsuperscript{3}</td>
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</tr>
<tr>
<td>(\mu/\text{mm}^{-1})</td>
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<td>F(000)</td>
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<td>Crystal size/mm\textsuperscript{3}</td>
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</tr>
<tr>
<td>Radiation</td>
<td>CuK(\alpha) ((\lambda = 1.54184))</td>
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<td>2(\theta) range for data collection/°</td>
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<tr>
<td>Index ranges</td>
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<tr>
<td>Reflections collected</td>
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<tr>
<td>Independent reflections</td>
<td>4693 [(R_{\text{int}} = 0.0255, R_{\sigma} = 0.0111)]</td>
</tr>
<tr>
<td>Data/restraints/parameters</td>
<td>4693/0/313</td>
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<tr>
<td>Goodness-of-fit on (F^2)</td>
<td>1.053</td>
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<tr>
<td>Final R indexes [(I \geq 2\sigma (I))]</td>
<td>(R_1 = 0.0280, wR_2 = 0.0778)</td>
</tr>
<tr>
<td>Final R indexes [all data]</td>
<td>(R_1 = 0.0282, wR_2 = 0.0781)</td>
</tr>
<tr>
<td>Largest diff. peak/hole / e Å\textsuperscript{3}</td>
<td>0.21/-0.15</td>
</tr>
<tr>
<td>Flack parameter</td>
<td>-0.01(4)</td>
</tr>
</tbody>
</table>
$^1$H NMR (400 MHz, CDCl$_3$) of 8c:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 8c:
HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)phenol 8c:

Standard for comparison with reduction using \((R,R)\)-3C-tethered Ru(II)-TsDPEN catalyst: \(R\) isomer 20.5 min and \(S\) isomer 22.5 min.

Standard of racemate 8c for comparison with reduction using \((R,R)\)-benzyl-tethered Ru(II)-TsDPEN catalyst, \((S,S)\)-Noyori Ru(II)-TsDPEN catalyst and \((R,R)\)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: \(R\) isomer 22.1 min and \(S\) isomer 24.4 min.
HPLC after ATH of 2-(hydroxy(2-methoxyphenyl)methyl)phenone 7c:
Using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (after 72 hours, 100% conversion, 99.4% ee, S configuration).

Using (S,S)-Noyori Ru(II)-TsDPEN catalyst 6 (after 168 hours, 48.6% conversion, 73% ee, R configuration).
Using (R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst 4 (after 168 hours, 84% conversion, 92.6% ee, S configuration).

Using (R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst 5 (after 168 hours, 16% conversion, 30% ee, S configuration).
2-Hydroxyphenyl)(2-methoxyphenyl)methanone 7c.

This compound has been reported and fully characterized.


To a solution of 2-(hydroxy(2-methoxyphenyl)methyl)phenol 8c (300 mg, 1.30 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.7 g, 19.6 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: ethyl acetate) after this time indicated full conversion. The solids were removed by gravity filtration and the solid was washed with DCM. The combined solvent was removed to give the product 7c as a brown oil (204 mg, 0.89 mmol, 68.6%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; δH (400 MHz, CDCl₃) 12.17 (1H, s, OH), 7.48-7.47 (2H, m, ArH), 7.34-7.26 (2H, m, ArH), 7.08-7.03 (3H, m, ArH), 6.82-6.78 (1H, m, ArH), 3.78 (3H, s, OCH₃) ppm; δC (100 MHz, CDCl₃) 162.9 (C), 136.5 (CH), 133.8 (CH), 131.9 (CH), 128.8 (CH), 127.8 (C), 120.5 (CH), 120.0 (C), 118.7 (CH), 118.1 (CH), 111.4 (CH), 55.7 (CH₃) ppm. Data matched that reported.
$^1$H NMR (400 MHz, CDCl$_3$) of 7c:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 7c:
HPLC of (2-hydroxyphenyl)(2-methoxyphenyl)methanone 7c:
2-(Hydroxy(4-methoxyphenyl)methyl)phenol 8d.

\[
\text{racemic: YZ207, Asymmetric: YZ213}
\]

This compound has been reported and fully characterized.


To a solution of 4-bromoanisole (935 mg, 0.62 mL, 5.0 mmol) in THF (5 mL) at -78 °C was added dropwise a solution of n-butyllithium (2.0 mL, 2.5M in hexanes, 5.0 mmol. The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which salicylaldehyde (305 mg, 2.50 mmol) was added dropwise. The reaction mixture was stirred under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH\textsubscript{4}Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO\textsubscript{4}) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(4-methoxyphenyl)methyl)phenol 8d as a yellow oil (450 mg, 1.96 mmol, 78%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO\textsubscript{4}; \( \delta \text{H} \) (500 MHz, CDCl\textsubscript{3}) 8.02 (1H, s, ArOH), 7.32-7.17 (3H, m, ArH), 6.92-6.80 (5H, m, ArH), 5.98 (1H, s, ArCHOH), 3.80 (3H, s, OCH\textsubscript{3}), 2.83 (1H, s, ArCHOH) ppm; \( \delta \text{C} \) (125 MHz, CDCl\textsubscript{3}) 159.6 (C), 155.6 (C), 134.1 (C), 129.7 (CH), 129.5 (CH), 129.2 (CH), 128.3 (CH), 119.9 (CH), 117.3 (CH), 114.1 (CH), 77.0 (CH), 55.3 (CH\textsubscript{3}) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 6.4 min, \textit{R} isomer and \textit{S} isomer are 18.2 min and 22.5 min, configuration was assigned by analogy.
ATH of 2-(hydroxy(4-methoxyphenyl)methyl)phenone (YZ213).

Catalyst (R,R)-2 (0.00175 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-(hydroxy(4-methoxyphenyl)methyl)phenone 7d (40 mg, 0.175 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(4-methoxyphenyl)methyl)phenol 8d (8.4 mg, 0.037 mmol, 20.8%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). This reaction also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]₀²⁵ -43.2 (c 0.614 in CHCl₃) 63.8% ee.

¹H NMR (500 MHz, CDCl₃) of 8d:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8d:

HPLC of racemic 2-(hydroxy(4-methoxyphenyl)methyl)phenol 8d:
HPLC of 8d after ATH of 2-(hydroxy(4-methoxyphenyl)methyl)phenone 7d:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 63.8% ee).
(2-Hydroxyphenyl)(4-methoxyphenyl)methanone 7d.

This compound has been reported and fully characterized.


To a solution of 2-(hydroxy(4-methoxyphenyl)methyl)phenol 8d (360 mg, 1.57 mmol) in DCM (10 mL) at rt was added manganese dioxide (2.05 g, 23.6 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4: 1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and the solids were washed with DCM. The combined solvent was removed to give the product as a brown oil (98.7 mg, 0.43 mmol, 28%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; δH (500 MHz, CDCl₃) 11.96 (1H, s, OH), 7.73 (2H, d, J = 8.5, ArH), 7.64 (1H, dd, J = 8.0, 1.0, ArH), 7.51-7.48 (1H, m, ArH), 7.08 (1H, d, J = 8.5, ArH), 7.02-6.99 (2H, m, ArH), 6.88 (1H, t, J = 8.0, ArH), 3.90 (3H, s, OCH₃) ppm; δC (125 MHz, CDCl₃) 200.1 (C), 162.9 (C), 135.8 (CH), 132.3 (CH), 131.9 (CH), 130.4 (C), 119.4 (C), 118.5 (CH), 118.3 (C), 114.3 (CH), 113.7 (CH), 55.5 (CH₃) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 7d:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7d:
HPLC of (2-hydroxyphenyl)(4-methoxyphenyl)methanone 7d:

![HPLC chromatogram](image_url)

**Result Table**

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<th>Height [mV]</th>
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<th>Height [%]</th>
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<td>83.264</td>
<td>100.0</td>
<td>100.0</td>
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<td></td>
</tr>
</tbody>
</table>
2-(Tetrahydropyran-2-yloxy)phenyl bromide.

![Chemical structure](image)

This compound has been reported and fully characterized.


To a solution of 2-bromophenol (300 mg, 1.73 mmol) in DCM (6 mL) at rt was added dropwise 3, 4-dihydro-2H-pyran (291.5 mg, 3.47 mmol) and pyridinium p-toluenesulfonate (PPTS) (43.4 mg, 0.173 mmol). The reaction mixture was left stirring under the nitrogen atmosphere overnight. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-(tetrahydropyran-2-yloxy)phenyl bromide as a colorless oil (380 mg, 1.48 mmol, 85.5%). TLC: Rf ca 0.90 (9:1 hexane: EtOAc), strong UV and KMnO₄; δH (400 MHz, CDCl₃) 7.59 (1H, t, J = 7.6, ArH), 7.30-7.18 (2H, m, ArH), 6.92-6.89 (1H, m, ArH), 5.56 (1H, s, OCH₂), 3.96 (1H, t, J = 11.0, OCH₂CH₂), 3.67 (1H, d, J = 11.0, OCH₂CH₂), 2.17-2.12 (1H, m, CH₂), 2.05-2.02 (1H, m, CH₂), 1.96-1.89 (1H, m, CH₂), 1.81-1.66 (3H, m, CH₂) ppm; δC (100 MHz, CDCl₃) 153.4 (C), 133.3 (CH), 128.4 (CH), 122.8 (CH), 116.6 (CH), 113.1 (CBr), 96.7 (CHO), 61.8 (CH₂O), 30.2 (CH₂), 25.2 (CH₂), 18.3 (CH₂) ppm. Data matched that reported.
$^1$H NMR (400 MHz, CDCl$_3$) of 2-(Tetrahydropyran-2-ylxy)phenyl bromide:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 2-(Tetrahydropyran-2-ylxy)phenyl bromide:
(2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol.

This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (339.7 mg, 1.33 mmol) THF (1.6 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.48 mL, 2.5M in hexanes, 1.21 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 3 hours, after which 2-chlorobenzaldehyde (170 mg, 1.21 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: ethyl acetate). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a white solid (330 mg, 1.04 mmol, 85.7%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 87 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₈H₁₉ClNaO₃ 341.0911; Found 341.0915; 1.7 ppm error); νmax 3435 (br), 2948, 1484, 1389, 1240, 1026, 750 cm⁻¹; δH (500 MHz, CDCl₃) 7.59-7.57 (1H, m, ArH), 7.39-7.22 (4H, m, ArH), 7.17-7.12 (1H, m, ArH), 7.03-6.96 (2H, m, ArH), 6.53-6.50 (1H, m, ArCHOH), 5.26-5.25 (1H, m, OCH), 3.96-3.94 (1H, m, OCH₂CH₂), 3.63-3.58 (1H, m, OCH₂CH₂), 3.47-3.40 (1H, m, ArCHOH), 1.99-1.95 (1H, m, CH₂), 1.89-1.84 (1H, m, CH₂), 1.73-1.60 (4H, m, CH₂) ppm; δC (125 MHz, CDCl₃) 155.0 (C), 140.0 (C), 132.5 (C), 129.3 (CH), 129.1 (CH), 128.6 (CH), 128.4 (CH), 127.4 (CH), 126.9 (CH), 122.4 (C), 121.3 (CH), 116.1 (CH), 99.0 (CH), 67.7 (CH), 63.5 (CH₂), 30.7 (CH₂), 25.0 (CH₂), 19.7 (CH₂) ppm; m/z (ES-API+) 341.2 (M+ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

$^{13}$C NMR (125 MHz, CDCl$_3$) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
COSY (500 MHz, CDCl₃) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

HSQC (500 MHz, CDCl₃) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
HMBC (500 MHz, CDCl₃) of (2-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
2-((2-Chlorophenyl)(hydroxy)methyl)phenol 8e.

This compound is novel.

To a solution of (2-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (220 mg, 0.69 mmol) in EtOH (3.4 mL)/DCM (1.7mL) was added pyridinium p-Toluenesulfonate (PPTS) (26 mg, 0.10 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol 8e as a colorless oil (120.2 mg, 0.51 mmol, 74%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₃H₁₁ClNaO₂ 257.0335; Found 257.0340; 1.7 ppm error); νmax 3291 (br), 1587, 1488, 1234, 747 cm⁻¹; δH (500 MHz, CDCl₃) 7.42-7.40 (1H, m, ArH), 7.33-7.19 (4H, m, ArH), 6.94 (1H, t, J = 8.5, ArH), 6.82-6.78 (2H, m, ArH), 6.43 (1H, s, ArCHOH) ppm; δC (125 MHz, CDCl₃) 156.0 (C), 138.9 (C), 133.1 (C), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 128.1 (CH), 127.5 (CH), 124.6 (C), 120.1 (CH), 117.4 (CH), 73.8 (CH) ppm; m/z (ES-API+) 257.1 (M⁺ + 23, 100%). Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 11.6 min, S isomer 13.2 min, R isomer 16.9 min.

ATH of (2-chlorophenyl)(2-hydroxyphenyl)methanone) (YZ199, 385, 386, 387).

Catalyst (R,R)-2 (0.0017 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of (2-chlorophenyl)(2-hydroxyphenyl)methanone 7e (40 mg, 0.17 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1
hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol 8e (22.4 mg, 0.096 mmol, 55.5%); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6 mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D³¹ -47.7 (c 0.448 in CHCl₃) 93% ee (S)

Crystal structure determination of 8e:

Crystal structure: S configuration. CCDC 1978885 (local code yz8).

The asymmetric unit contains two diphenylmethanols, there are four molecules in the unit cell. The OHs were located in a difference map but refined with distance restraints. They form short contacts tabulated below

Specified hydrogen bonds (with esds except fixed and riding H)

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<th>D...A</th>
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Symmetry operators used to generate symmetry equivalent atoms in above contacts were

$1 -0.5+X,1.5-Y,1-Z$
The Flack parameter and related Hooft y parameter as a measure of the confidence we can have in the assignment of the handedness of the crystal measured were

Flack x: 0.006(3) Shelx 2018
Hooft y: -0.002(3) Olex 2

Which is small with a small error so we can be confident of the assignment of the handedness of the crystal measured.

**Experimental**

Single crystals of C$_{13}$H$_{11}$ClO$_2$ were grown from DCM/hexane in a small vial at room temperature. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least Squares minimisation.


**Crystal Data** for C$_{13}$H$_{11}$ClO$_2$ ($M_1=234.67$ g/mol): orthorhombic, space group P2$_1$2$_1$2$_1$ (no. 19), 

\[
a = 10.17811(5) \text{Å}, \quad b = 11.15611(4) \text{Å}, \quad c = 19.73742(9) \text{Å}, \quad V = 2241.148(17) \text{Å}^3, \quad Z = 8, \quad T = 150(2) \text{K}, \quad \mu(\text{CuKα}) = 2.864 \text{mm}^{-1}, \quad D_{\text{calc}} = 1.391 \text{g/cm}^3, \quad 34336 \text{ reflections measured (8.96° ≤ 2θ ≤ 147.308°)}, \quad 4512 \text{ unique (} R_{\text{int}} = 0.0320, \quad R_{\text{sigma}} = 0.0188) \text{ which were used in all calculations. The final } R_1 \text{ was 0.0271 (} I > 2\sigma(I)) \text{ and } wR_2 \text{ was 0.0703 (all data).} \]

**Table 1 Crystal data and structure refinement for yz8.**

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β/° 90
γ/° 90
Volume/Å³ 2241.148(17)
Z 8
ρ_c/cm³ 1.391
μ/mm⁻¹ 2.864
F(000) 976.0
Crystall size/mm³ 0.2 × 0.18 × 0.16 colourless block
Radiation CuKα (λ = 1.54184)
2θ range for data collection/° 8.96 to 147.308
Index ranges -12 ≤ h ≤ 10, -13 ≤ k ≤ 13, -24 ≤ l ≤ 24
Reflections collected 34336
Independent reflections 4512 [R_int = 0.0320, R_sigma = 0.0188]
Data/restraints/parameters 4512/0/293
Goodness-of-fit on F² 1.046
Final R indexes [I>=2σ(I)] R₁ = 0.0271, wR₂ = 0.0700
Final R indexes [all data] R₁ = 0.0274, wR₂ = 0.0703
Largest diff. peak/hole / e Å⁻³ 0.27/-0.33
Flack parameter 0.006(3)

¹H NMR (500 MHz, CDCl₃) of 8e:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8e:

COSY (500 MHz, CDCl$_3$) of 8e:
HSQC (500 MHz, CDCl$_3$) of 8e:

HMBC (500 MHz, CDCl$_3$) of 8e:
HPLC of racemic 2-((2-chlorophenyl)(hydroxy)methyl)phenol 8e:

HPLC of 8e after ATH of (2-chlorophenyl)(2-hydroxyphenyl)methanone 7e: 
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (after 72 hours, 100% conversion, 93% ee, S configuration).
(S,S)-Noyori Ru(II)-TsDPEN catalyst 6 (after 168 hours, 100% conversion, 89.2% ee, R configuration).

(R,R)-Benzyl-tethered Ru(II)-TsDPEN catalyst 4 (after 168 hours, 100% conversion, 91.2% ee, S configuration).
(R,R)-3C-Tethered, 4-methoxy-Ru(II)-TsDPEN catalyst 5 (after 168 hours, 100% conversion, 90.2% ee, S configuration).
(2-Chlorophenyl)(2-hydroxyphenyl)methanone 7e.

![Diagram of 7e](image)

This compound has been reported and fully characterized.


To a solution of 2-((2-chlorophenyl)(hydroxy)methyl)phenol 8e (120 mg, 0.51 mmol) in DCM (5 mL) at rt was added manganese dioxide (665 mg, 7.65 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The combined solvent was removed to give the product 7e as a colorless oil (40.1 mg, 0.17 mmol, 33.4%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; δₓ (400 MHz, CDCl₃) 11.95 (1H, s, OH), 7.54-7.29 (6H, m, ArH), 7.08 (1H, d, J = 8.4, ArH), 6.83 (1H, t, J = 8.0, ArH) ppm; δₓ (100 MHz, CDCl₃) 200.6 (C), 163.2 (C), 137.2 (CH), 136.2 (C), 133.5 (CH), 131.3 (CH), 131.0 (C), 130.1 (CH), 128.6 (CH), 126.8 (CH), 119.4 (C), 119.1 (CH), 118.4 (CH) ppm. Data matched that reported.

¹H NMR (400 MHz, CDCl₃) of 7e:
$^{13}$C NMR (100 MHz, CDCl$_3$) of 7e:

HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone 7e:
(4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol.

This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (431.9 mg, 1.69 mmol) THF) (2 mL at -78 °C was added a solution of n-butyllithium (0.61 mL, 2.5M in hexanes, 1.54 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 4-chlorobenzaldehyde (215.8 mg, 1.54 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a pale yellow solid (377 mg, 1.19 mmol, 77.2%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 90 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₈H₁₉ClNaO₃ 341.0903; Found 341.0899; -1.3 ppm error); v_max 3422 (br), 2931, 1485, 1385, 1238, 1027, 755 cm⁻¹; δ_H (500 MHz, CDCl₃) 7.31-7.20 (6H, m, ArH), 7.08 (1H, d, J = 8.0, ArH), 6.97 (1H, t, J = 7.5, ArH), 6.01 (1H, d, J = 5.5, ArCHOH), 5.35 (1H, t, J = 3.5, OCHO), 3.63-3.46 (2H, m, OCH₂CH₂), 3.19 (1H, d, J = 5.5, ArCHOH), 1.83-1.68 (3H, m, CH₃), 1.63-1.55 (2H, m, CH₂), 1.48-1.43 (1H, m, CH₂) ppm; δ_C (125 MHz, CDCl₃) 154.1 (C), 142.0 (C), 132.5 (C), 129.1 (CH), 128.2 (CH), 128.0 (CH), 122.0 (C), 115.0 (CH), 97.0 (CH), 71.7 (CH), 62.5 (CH₂), 30.4 (CH₂), 25.0 (CH₂), 19.0 (CH₂) ppm; m/z (ES-API+) 341.2 (M+ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

$^{13}$C NMR (125 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
COSY (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

![COSY spectrum](image)

HSQC (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

![HSQC spectrum](image)
HMBC (500 MHz, CDCl₃) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
2-((4-Chlorophenyl)(hydroxy)methyl)phenol 8f.

This compound has been reported and fully characterized.


To a solution of (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (375 mg, 1.18 mmol) in EtOH (5.9 mL)/DCM (3.0 mL) was added pyridinium \( p \)-toluenesulfonate (PPTS) (44.4 mg, 0.18 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((4-chlorophenyl)(hydroxy)methyl)phenol 8f as a colorless oil (120.1 mg, 0.51 mmol, 43.5%). TLC: \( R_f \) ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO\(_4\); \( \delta_H \) (400 MHz, CDCl\(_3\)) 7.51 (1H, s, ArOH), 7.33 (4H, s, ArH), 7.21 (1H, t, \( J = 7.2 \), ArH), 6.91-6.82 (3H, m, ArH), 6.00 (1H, s, ArCH\(_2\)OH), 2.84 (1H, s, ArCHOH) ppm; \( \delta_C \) (100 MHz, CDCl\(_3\)) 155.3 (C), 140.3 (C), 152.9 (C), 129.6 (CH), 128.9 (CH), 128.2 (CH), 126.7 (C), 120.1 (CH), 117.4 (CH), 76.2 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, \( T = 25^\circ\)C) ketone 5.4 min, \( R \) isomer and \( S \) isomer are 12.2 min and 13.8 min, configuration was assigned by analogy.

ATH of 2-((4-chlorophenyl)(hydroxy)methyl)phenol 7f (YZ208)

Catalyst (\( R<R \))-2 (0.0017 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-((4-chlorophenyl)(hydroxy)methyl)phenone 7f (40 mg, 0.17 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was
removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((4-chlorophenyl)(hydroxy)methyl)phenol 8f (24.5 mg, 0.10 mmol, 60.7%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D31 -40.3 (c 0.178 in CHCl3) 89% ee.

1H NMR (400 MHz, CDCl3) of 8f:

![NMR spectrum of 8f](image_url)
$^{13}$C NMR (100 MHz, CDCl$_3$) of **8f**:

HPLC of racemic 2-((4-chlorophenyl)(hydroxy)methyl)phenol **8f**:
HPLC of 8f after ATH of 2-((4-chlorophenyl)(hydroxy)methyl)phenone 7f:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 89% ee)
(4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone; via Weinreb reagent.

This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (210.9 mg, 0.824 mmol in THF (3 mL) at -78 °C was added a solution of n-butyllithium (0.30 mL, 2.5M in hexanes, 0.749 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 4-chloro-N-methoxy-N-methylbenzamide (149 mg, 0.749 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone as a colorless oil (82.0 mg, 0.259 mmol, 34.7%). TLC: Rf ca 0.60 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₈H₁₇ClNaO₃ 339.0756; Found 339.0758; 0.8 ppm error); νmax 3069, 2943, 2872, 1661, 1596, 1585, 1481, 1449, 1258, 1200, 956 cm⁻¹; δₘ (500 MHz, CDCl₃) 7.75 (1H, d, J = 8.6, ArH), 7.64 (1H, d, J = 8.6, ArH), 7.60-7.34 (3H, m, ArH), 7.17-7.03 (1H, m, ArH), 7.01-6.76 (1H, m, ArH), 5.46-4.62 (1H, m, OCH₂O), 4.25-3.80 (1H, m, OCH₂CH₂), 3.78-3.42 (1H, m, OCH₂CH₂), 2.03-1.79 (1H, m, CH₂), 1.67-1.31 (1H, m, CH₂), 1.29-1.09 (1H, m, CH₂) ppm; δc (125 MHz, CDCl₃) 154.9 (C), 138.9 (C), 137.1 (C), 136.6 (CH), 133.2 (CH), 130.7 (CH), 129.0 (C), 128.7 (CH), 121.6 (CH), 118.8 (CH), 118.9 (C), 115.1 (CH), 96.4 (CH), 61.6 (CH₂), 29.9 (CH₂), 24.9 (CH₂), 17.6 (CH₂) ppm; m/z (ES-API+) 339.2 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:
$^{13}$C NMR (125 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:

COSY (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:
HSQC (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:

![HSQC spectrum](image)

HMBC (500 MHz, CDCl$_3$) of (4-Chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone:

![HMBC spectrum](image)
(4-Chlorophenyl)(2-hydroxyphenyl)methanone 7f.

via oxidation; YZ205, from THP ether; YZ308

YZ205

YZ308

from Weinreb route.

This compound has been reported and fully characterized.


Via oxidation: To a solution of (4-chlorophenyl)(2-hydroxyphenyl)methanol (120 mg, 0.51 mmol) in DCM (5 mL) at rt was added manganese dioxide (665 mg, 7.65 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give (4-chlorophenyl)(2-hydroxyphenyl)methanone 7f as a yellow oil (55.8 mg, 0.24 mmol, 47%).

From Weinreb route: To a solution of (4-chlorophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (440.5 mg, 1.39 mmol) in EtOH (6.8 mL)/DCM (3.4 mL) was added pyridinium p-toluenesulfonate (PPTS) (52.5 mg, 0.209 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (4-chlorophenyl)(2-hydroxyphenyl)methanone 7f as a yellow oil (205.5 mg, 0.886 mmol, 63.5%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO4; δH (500 MHz, CDCl3) 11.88 (1H, s, OH), 7.64 (2H, d, J = 8.5, ArH), 7.57-7.45 (4H, m, ArH), 7.08 (1H, d, J = 8.3, ArH), 6.89 (1H, t, J = 7.9, ArH) ppm; δC (125 MHz, CDCl3) 200.2 (C), 163.2 (C), 138.4 (C), 136.6 (CH), 136.2 (C), 133.2 (CH), 130.7 (CH), 128.7 (CH), 118.8 (CH), 118.9 (C), 118.6 (CH) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 7f:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7f:
HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone 7f:

![HPLC graph and table]

**Result Table**

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</table>
(2-Chlorophenyl)(2-methoxyphenyl)methanol 8g.

This compound is novel.

To a solution of 2-bromoanisole (840 mg, 0.560 mL, 4.52 mmol) in THF (3.5 mL) at -78 °C was added dropwise a solution of n-butyllithium (1.8 mL, 2.5M in hexanes, 4.5 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-chlorobenzaldehyde (250 mg, 1.79 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-methoxyphenyl)methanol 7g as a colorless oil (300 mg, 1.21 mmol, 68%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₄H₁₃ClNaO₂ 271.0499; Found 271.0496; -1.1 ppm error); νmax 3406 (br), 3065, 2937, 2836, 1600, 1489, 1239, 1023, 749 cm⁻¹; δH (500 MHz, CDCl₃) 7.59 (1H, d, J = 7.5, ArH), 7.37-7.23 (4H, m, ArH), 6.98-6.88 (3H, m, ArH), 6.46 (1H, d, J = 4.0, ArCHOH), 3.88 (3H, s, OCH₃), 3.10 (1H, d, J = 4.0, ArCHOH) ppm; δC (125 MHz, CDCl₃) 157.1 (C), 139.9 (C), 132.9 (C), 130.4 (C), 129.4 (CH), 129.1 (CH), 128.6 (CH), 128.5 (C), 127.8 (CH), 126.8 (CH), 120.7 (CH), 110.6 (CH), 68.6 (CH), 55.5 (CH₃) ppm; m/z (ES-API+) 271.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane: iPrOH 95:5, 0.8 mL/min, T = 25°C) ketone 24.2 min, R isomer 15.8 min and S isomer 12.9 min.
ATH of (2-chlorophenyl)(2-methoxyphenyl)methanone 7g (YZ172)

Catalyst \((R,R)-2\) (0.00162 mmol, 1 mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-chlorophenyl)(2-methoxyphenyl)methanone \(7g\) (40 mg, 0.162 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 168 hours, the reaction was quenched by saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-chlorophenyl)(2-methoxyphenyl)methanol \(8g\) (35.1 mg, 0.141 mmol, 87%; \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C); \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst: 98% conversion (HPLC calibration: 1:1 (2-chlorophenyl)(2-methoxyphenyl)methanone: (2-chlorophenyl)(2-methoxyphenyl)methanol gives 12.7:1 absorption at 254 nm); \([\alpha]_D^{25}\) -20.2 (c 0.875 in CHCl\(_3\)) 85.8% ee (S).

Crystal structure determination of \(8g\) CCDC 1978883 [local code yz6]
The asymmetric unit contains five crystallographically independent but chemically identical molecules in the asymmetric unit of yz6, ten in the unit cell. The chlorobenzene ring of molecule Cl31-C317 was disordered over two closely related positions. The occupancy of the two components was linked to a free variable which refine to 78:22. The minor component was refined isotropically. An AFIX 66 restraint and several SIMU and RIGU restraints were used to give the thermal parameters of the minor disordered component sensible thermal parameters. The OHs were located in a difference map but refined with positional restraints. They form short contacts tabulated below.

Specified hydrogen bonds (with esds except fixed and riding H)

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Symmetry elements used to generate symmetry equivalent atoms in above contacts $1 -1+X,+Y,+Z$

The Flack parameter as a measure of the confidence we can have in the assignment of the refined stereochemistry is

Flack x: 0.002(5) Shelxl 2018
Hooft y: -0.005(6) Olex2

This is low with a low error so we can be confident in the assignment of the crystal measured (caution here as the all the crystals examined were twinned and the data is a little weak)

Note All crystals measured were rather poor and twinned. The data used here was from the main twin component of the best sample (strongest diffracting, least twinned) as no suitable twin refinement could be found.

Experimental

Single crystals of $C_{14}H_{13}ClO_2$ [yz6] were grown from DCM/hexane in a small vial at room temperature. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero) equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution


Crystal Data for \( \text{C}_{14}\text{H}_{13}\text{ClO}_2 \) (\( M = 248.69 \) g/mol): monoclinic, space group \( \text{P2}_1 \) (no. 4), \( a = 11.49164(17) \) Å, \( b = 21.8268(3) \) Å, \( c = 13.18932(16) \) Å, \( \beta = 108.4101(14)^\circ \), \( V = 3138.91(7) \) Å\(^3\), \( Z = 10 \), \( T = 150(2) \) K, \( \mu(\text{CuK} \alpha) = 2.585 \) mm\(^{-1}\), \( D_{\text{calc}} = 1.316 \) g/cm\(^3\), 56916 reflections measured (7.064\(^\circ\) \( \leq 2\Theta \leq 147.322^\circ\)), 12126 unique (\( R_{\text{int}} = 0.0679 \), \( R_{\text{sigma}} = 0.0587 \)) which were used in all calculations. The final \( R_1 \) was 0.0312 (I > 2\( \sigma(I) \)) and \( wR_2 \) was 0.0604 (all data).

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$^1$H NMR (500 MHz, CDCl$_3$) of 8g:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 8g:
COSY (500 MHz, CDCl₃) of 8g:

![COSY spectrum image](image)

HSQC (500 MHz, CDCl₃) of 8g:

![HSQC spectrum image](image)
HMBC (500 MHz, CDCl₃) of 8g:

![HMBC spectrum](image)

HPLC of racemic (2-chlorophenyl)(2-methoxyphenyl)methanol 8g:

![HPLC chromatogram](image)

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HPLC of 8g after ATH of (2-chlorophenyl)(2-methoxyphenyl) methanone 7g:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 98% conversion, 85.8% ee, S configuration)
This compound is novel.

To a solution of (2-chlorophenyl)(2-methoxyphenyl)methanol 8g (100 mg, 0.40 mmol) in DCM (3 mL) at rt was added manganese dioxide (521.4 mg, 6.0 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: ethyl acetate) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The solvent was removed to give the product 7g as a white solid (69 mg, 0.28 mmol, 69%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C_{14}H_{11}ClNaO₂ 269.0342; Found 269.0340; -0.8 ppm error); \( \nu_{\text{max}} \) 3067, 2995, 2940, 2838, 1643, 1591, 1482, 1434, 1307, 1250, 1153, 930, 770, 754 cm⁻¹; \( \delta_{\text{H}} \) (500 MHz, CDCl₃) 7.56 (1H, dd, \( J = 8.0, 1.5 \), ArH), 7.42-7.39 (1H, m, ArH), 7.32-7.15 (4H, m, ArH), 6.93 (1H, t, \( J = 7.5 \), ArH), 6.84 (1H, d, \( J = 8.5 \), ArH), 3.54 (3H, s, OCH₃) ppm; \( \delta_{\text{C}} \) (125 MHz, CDCl₃) 194.7 (C), 159.2 (C), 140.6 (C), 134.2 (CH), 131.5 (CH), 131.4 (C), 131.0 (CH), 129.8 (CH), 129.5 (CH), 127.8 (C), 126.5 (CH), 120.7 (CH), 111.9 (CH), 55.8 (CH₃) ppm; m/z (ES-API+) 269.1 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of 7g:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7g:
COSY (500 MHz, CDCl₃) of 7g:

HSQC (500 MHz, CDCl₃) of 7g:
HMBC (500 MHz, CDCl₃) of 7g:

HPLC of (2-Chlorophenyl)(2-methoxyphenyl)methanone 7g:
This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (2.58g, 10.1 mmol) THF (12 mL) at -78 °C was added dropwise a solution of n-butyllithium (3.67 mL, 2.5M in hexanes, 9.18 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 3 hours, after which 2-bromobenzaldehyde (1.70 g, 9.18 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol as a white solid (2.45 g, 6.77 mmol, 73.7%). TLC: Rf ca 0.30 (9:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 104.2 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₈H₁₉BrNaO₃ 385.0411; Found 385.0410; -0.3 ppm error); νmax 3381 (br), 2947, 2927, 2860, 1483, 1384, 1229, 1202, 751 cm⁻¹; δH (500 MHz, CDCl₃) 7.63-7.50 (2H, m, ArH), 7.41-7.21 (3H, m, ArH), 7.20-7.10 (2H, m, ArH), 7.05-6.93 (2H, m, ArH), 6.48-6.45 (1H, m, ArCHOH), 5.25-5.24 (1H, m, OCH₂), 4.00-3.95 (1H, m, OCH₂), 3.69-3.52 (1H, m, OCH₂), 3.53-3.33 (1H, m, ArCHOH), 2.07-1.91 (1H, m, CH₂), 1.91-1.78 (1H, m, CH₂), 1.75-1.59 (4H, m, CH₂) ppm; δC (125 MHz, CDCl₃) 155.1 (C), 141.7 (C), 132.5 (C), 132.6 (CH), 129.1 (CH), 128.9 (CH), 128.7 (CH), 127.5 (CH), 127.4 (CH), 123.3 (C), 122.5 (CH), 116.1 (CH), 99.1 (CH), 70.0 (CH), 63.5 (CH₂), 30.8 (CH₂), 25.1 (CH₂), 19.7 (CH₂) ppm; m/z (ES-API+) 385.1 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

$^{13}$C NMR (125 MHz, CDCl$_3$) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
COSY (500 MHz, CDCl₃) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:

HSQC (500 MHz, CDCl₃) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
HMBC (500 MHz, CDCl₃) of (2-Bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol:
2-((2-Bromophenyl)(hydroxy)methyl)phenol 8h.

This compound is novel.

To a solution of (2-bromophenyl)(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (2.45 g, 6.77 mmol) in EtOH (34 mL)/DCM (17.5 mL) was added pyridinium p-Toluenesulfonate (PPTS) (256 mg, 1.02 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: EtOAc). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-Bromophenyl)(hydroxy)methyl)phenol 8h as a colorless oil (1.27 g, 4.57 mmol, 67.5%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₃H₁₁BrNaO₂ 300.9834; Found 300.9835; 0.1 ppm error); ν max 3229 (br), 1602, 1453, 1403, 1304, 1279, 1009, 711 cm⁻¹; δH (500 MHz, CDCl₃) 7.95 (1H, m, ArH), 7.61 (1H, dd, J = 8.0, 1.0, ArH), 7.40-7.30 (2H, m, ArH), 7.24-7.19 (2H, m, ArH), 7.07-6.87 (1H, m, ArH), 6.91-6.63 (2H, m, ArH), 6.42 (1H, d, J = 3.7, ArCHOH), 3.24 (1H, d, J = 3.8, ArCHOH) ppm; δC (125 MHz, CDCl₃) 156.0 (C), 140.6 (C), 133.1 (CH), 130.0 (CH), 129.6 (CH), 129.6 (CH), 128.2 (CH), 128.2 (CH), 124.9 (C), 123.3 (C), 120.1 (CH), 117.4 (CH), 75.8 (CH) ppm; m/z (ES-API+) 301.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 15.1 min, R isomer 17.9 min, S isomer 20.2 min.

ATH of (2-bromophenyl)(2-hydroxyphenyl)methanone (Y390, YZ394) 7h:
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (12.6 mg, 0.0203 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 2.52 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of (2-bromophenyl)(2-hydroxyphenyl)methanone (559.2 mg, 2.03 mmol) in DCM (3.97 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was
added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-chlorophenyl)(hydroxy)methyl)phenol 8h (290 mg, 1.04 mmol, 51.5%). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C): 100% conversion; [α]D -162.8 (c 0.390 in CHCl₃) 99% ee (S)

1H NMR (500 MHz, CDCl₃) of 8h:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8h:

COSY (500 MHz, CDCl$_3$) of 8h:
HSQC (500 MHz, CDCl₃) of 8h:

HMBC (500 MHz, CDCl₃) of 8h:
HPLC of racemic 2-((2-bromophenyl)(hydroxy)methyl)phenol 8h:

HPLC of 8h after ATH of (2-bromophenyl)(2-hydroxyphenyl)methanone 7hL
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 99% ee, S configuration)
2-Bromophenyl)(2-hydroxyphenyl)methanone 7h.

This compound has been reported but not fully characterized.


To a solution of 2-((2-bromophenyl)(hydroxy)methyl)phenol 8h (1.53 g, 5.50 mmol) in DCM (55 mL) at rt was added manganese dioxide (7.17 g, 82.5 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and washed with DCM. The combined solvent was removed to give the product 7h as a brown oil (559.2 mg, 2.03 mmol, 36.8%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₃H₉BrNaO₂ 298.9682; Found 298.9678; -1.3 ppm error); νmax 3229 (br), 3055, 2927, 1626, 1482, 1428, 1260, 1240, 752 cm⁻¹; δH (500 MHz, CDCl₃) 11.93 (1H, s, OH), 7.68-7.65 (1H, m, ArH), 7.56-7.50 (1H, m, ArH), 7.46-7.32 (3H, m, ArH), 7.24-7.20 (1H, m, ArH), 7.09-7.06 (1H, m, ArH), 6.84-6.81 (1H, m, ArH) ppm; δC (125 MHz, CDCl₃) 201.3 (C), 163.3 (C), 139.4 (C), 137.2 (CH), 133.6 (CH), 133.2 (CH), 131.3 (CH), 131.0 (C), 128.5 (CH), 127.3 (CH), 119.2 (C), 119.1 (CH), 118.4 (CH) ppm; m/z (ES-API+) 299.0 (M⁺ + 23, 100%). Data matched that reported.
$^{1}H$ NMR (500 MHz, CDCl$_3$) of 7h:

$^{13}C$ NMR (125 MHz, CDCl$_3$) of 7h:
COSY (500 MHz, CDCl$_3$) of 7h:

[Image of COSY spectrum]

HSQC (500 MHz, CDCl$_3$) of 7h:

[Image of HSQC spectrum]
HMBC (500 MHz, CDCl₃) of 7h:

HPLC of (2-chlorophenyl)(2-methoxyphenyl)methanone 7h
2-(Hydroxy(naphthalen-1-yl)methyl)phenol 8i.

This compound is novel.

To a solution of 1-bromonaphthalene (849 mg, 4.10 mmol) in THF (4.3 mL) at rt was added magnesium (98.4 mg, 4.10 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 30 minutes and heated to reflux on a hot plate for 1 hour, after which a solution of salicylaldehyde (200 mg, 1.64 mmol) in THF (1.8 mL) was added dropwise at 0 °C. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). DCM (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with DCM (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 2-(hydroxy(naphthalen-1-yl)methyl)phenol 8i as a colorless oil (355 mg, 1.42 mmol, 86.6%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₇H₁₄NaO₂ 273.0886; Found 273.0886; 0.2 ppm error; νmax (500 MHz, CDCl₃) 7.89-7.83 (2H, m, ArH), 7.70-7.42 (2H, m, ArH), 7.31-7.16 (3H, m, ArH), 7.04-6.95 (1H, m, ArH), 6.78-6.63 (1H, m, ArH), 6.58-6.33 (3H, m, ArH + ArCHOH), 2.79 (1H, s, ArCHOH) ppm; δC (125 MHz, CDCl₃) 155.9 (C), 136.6 (C), 134.1 (C), 130.9 (C), 129.5 (CH), 129.4 (CH), 129.0 (CH), 128.5 (CH), 126.6 (CH), 125.9 (CH), 125.9 (CH), 125.9 (CH), 125.9 (CH), 125.5 (CH), 124.1 (CH), 120.1 (CH), 117.2 (CH), 74.4 (CH) ppm; m/z (ES-API+) 273.4 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 6.3 min, R and S isomer 19.5 min and 33.2 min, configuration was assigned by analogy.

ATH of 2-(hydroxy(naphthalen-1-yl)methyl)phenone 7i (YZ258).
Catalyst \((R,R)\)-3C-tethered Ru(II)-TsDPEN catalyst 2 (0.99 mg, 0.00161 mmol, 1 mol\%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of 2-(hydroxy(naphthalen-1-yl)methyl)phenone 7i (40 mg, 0.161 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (9:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to 2-(hydroxy(naphthalen-1-yl)methyl)phenol (23 mg, 0.092 mmol, 57%; \((R,R)\)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C); \((R,R)\)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; \([\alpha]_D^{25}\) -150 (c 0.115 in CHCl\(_3\)) 97.2% ee

\(^1\)H NMR (500 MHz, CDCl\(_3\)) of 8i:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8i:

COSY (500 MHz, CDCl$_3$) of 8i:
HSQC (500 MHz, CDCl₃) of 8i:

HMBC (500 MHz, CDCl₃) of 8i:
HPLC of racemic 2-(hydroxy(naphthalen-1-yl)methyl)phenol 8i

HPLC of 8i after ATH of 2-(hydroxy(naphthalen-1-yl)methyl)phenone 7i:
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 97.2% ee).
2-Hydroxyphenyl)(naphthalen-1-yl)methanone 7i.

This compound has been reported and fully characterized.


To a solution of 2-(hydroxy(naphthalen-1-yl)methyl)phenol 8i (320.4 mg, 1.28 mmol) in DCM (10 mL) at rt was added manganese dioxide (1.67 g, 19.2 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The combined solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-hydroxyphenyl)(naphthalen-1-yl)methanone 7i as a yellow oil (100.9 mg, 0.207 mmol, 31.7%). TLC: Rf ca 0.50 (9:1 hexane: EtOAc), strong UV and KMnO4; δH (500 MHz, CDCl3) 12.06 (1H, s, ArOH), 7.73 (1H, dd, J = 7.2, 1.9, ArH), 7.66-7.61 (2H, m, ArH), 7.29-7.21 (5H, m, ArH), 7.05-6.97 (1H, m, ArH), 6.82 (1H, d, J = 8.4, ArH), 6.48 (1H, t, J = 7.6, ArH) ppm; δc (125 MHz, CDCl3) 203.7 (C), 163.4 (C), 137.0 (CH), 135.6 (C), 134.0 (CH), 133.6 (C), 130.9 (CH), 130.4 (C), 128.5 (CH), 127.3 (CH), 126.6 (CH), 126.4 (CH), 125.3 (CH), 124.5 (CH), 120.5 (C), 118.9 (CH), 118.4 (CH) ppm.
$^1$H NMR (500 MHz, CDCl$_3$) of 7i:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7i:
HPLC of (2-hydroxyphenyl)(naphthalen-1-yl)methanone 7i:
Furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol 8j.

This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (591.4 mg, 2.31 mmol) in THF (3 mL) at -78 °C was added a solution of n-butyllithium (0.84 mL, 2.5M in hexanes, 2.10 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which furfural (202 mg, 2.10 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (9:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol 8j as a yellow oil (481.8 mg, 1.76 mmol, 84.4%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+) [M+Na]+, Calcd for C₁₆H₁₈NaO₄ 297.1094; Found 297.1097; 1.2 ppm error); νₓₜₐₓ 3422 (br), 3120, 2940, 2882, 1600, 1484, 1450, 1235, 1024, 960 cm⁻¹; δₗ₉ (500 MHz, CDCl₃) 7.34-7.12 (3H, m, ArH + C₄H₃O), 7.05 (1H, t, J = 8.8, ArH), 6.92 (1H, t, J = 7.5, ArH), 6.26-6.12 (1H, m, C₄H₃O), 6.06-5.93 (2H, m, C₄H₃O + ArCHOH), 5.39-5.18 (1H, m, ArOCHO), 3.73-3.61 (1H, m, OCH₂CH₂), 3.59-3.36 (1H, m, OCH₂CH₂), 3.13-2.97 (1H, m, ArCHOH), 1.83-1.34 (6H, m, CH₂) ppm; δcx (125 MHz, CDCl₃) 155.9 (C), 154.4 (C), 142.0 (CH), 130.2 (C), 129.2 (CH), 127.8 (CH), 122.0 (CH), 115.0 (CH), 110.2 (CH), 106.7 (CH), 97.0 (CH), 99.0 (CH), 62.3 (CH₂), 30.4 (CH₂), 25.1 (CH₂), 18.9 (CH₂) ppm; m/z (ES-API+) 297.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 21.7 and 23.0 min, R and S isomer 30.8, 37.3 min and 33.9, 41.1 min, configuration was assigned by analogy.
Catalyst \((R,R)-2\) (0.00147 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (40 mg, 0.147 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (9:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol \(8j\) (15.7 mg, 0.0573 mmol, 39%); \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C); \((R,R)-3C\)-tethered Ru(II)-TsDPEN catalyst: 100% conversion; \([\alpha]_D^{23}\) -11.3 (c 0.785 in CHCl\(_3\)) 66.8% ee and 81.4% ee.

\(^1\)H NMR (500 MHz, CDCl\(_3\)) of \(8j\):

![NMR spectrum of 8j](image)
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8j:

COSY (500 MHz, CDCl$_3$) of 8j:
HSQC (500 MHz, CDCl₃) of 8j:

HMBC (500 MHz, CDCl₃) of 8j:
HPLC of racemic furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol 8j:

\[
\text{HPLC of } 8j \text{ after ATH of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7j:}
\]

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 66.8% ee and 81.4% ee).
Furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7j.

This compound is novel.

To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol 8j (554 mg, 2.02 mmol) in DCM (20 mL) at rt was added manganese dioxide (2.63 g, 30.3 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The solvent was removed to give furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7 as a yellow solid (402.4 mg, 1.48 mmol, 73.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 74 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₆H₁₆NaO₄ 295.0939; Found 295.0941; 0.5 ppm error; νₘₐₓ 2944, 2885, 1642, 1595, 1460, 1304, 1235, 1115, 1016, 948 cm⁻¹; Major diastereomer: δ_H (500 MHz, CDCl₃) 7.62 (1H, s, ArH), 7.45-7.40 (2H, m, ArH), 7.12-7.01 (3H, m, ArH + C₄H₃O), 6.55-6.54 (1H, m, C₄H₃O), 5.45 (1H, s, OCHO), 3.94-3.71 (1H, m, OCH₂CH₂), 3.72-3.42 (1H, m, OCH₂CH₂), 1.64-1.47 (6H, m, CH₂) ppm; Minor diastereomer: δ_H (500 MHz, CDCl₃) 8.31 (1H, d, J = 9.4, ArH), 7.76 (1H, s, ArH), 7.53 (1H, t, J = 7.8, ArH), 7.27-7.26 (2H, m, ArH + C₄H₃O), 6.98 (1H, t, J = 7.6, C₄H₃O), 6.67-6.66 (1H, m, C₄H₃O), 4.11-3.92 (1H, m, OCHO), 3.70-3.48 (2H, m, OCH₂CH₂), 2.10-1.95 (1H, m, CH₂), 1.94-1.81 (2H, m, CH₂), 1.80-1.67 (3H, m, CH₂) ppm; Major diastereomer: δ_C (125 MHz, CDCl₃) 163.4 (C), 155.0 (C), 153.3 (C), 136.1 (CH), 132.2 (CH), 129.3 (CH), 128.9 (C), 121.3 (CH), 119.6 (CH), 115.6 (CH), 112.2 (CH), 96.7 (CH), 61.7 (CH₂), 30.0 (CH₂), 25.1 (CH₂), 18.0 (CH₂) ppm; Minor diastereomer: δ_C (125 MHz, CDCl₃) 163.4 (C), 155.0 (C), 153.3 (C), 136.1 (CH), 131.5 (CH), 129.3 (CH), 128.9 (C), 121.0 (CH), 119.0 (CH), 118.5 (CH), 112.5 (CH), 96.7 (CH), 61.7 (CH₂), 30.0 (CH₂), 25.1 (CH₂), 17.97 (CH₂) ppm; m/z (ES-API+) 295.2 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) 7j Major diastereomer:

![Major Diastereomer NMR](image1)

7j Minor diastereomer:

![Minor Diastereomer NMR](image2)
$^{13}$C NMR (125 MHz, CDCl$_3$) of 7j:

COSY (500 MHz, CDCl$_3$) of 7j:
HSQC (500 MHz, CDCl$_3$) of 7j:

HMBC (500 MHz, CDCl$_3$) of 7j:
HPLC of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7:

![HPLC graph and table]

**Result Table**

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2-(Furan-2-yl(hydroxy)methyl)phenol 8k.

Asymmetric: YZ297

YZ266: attempt

YZ293: attempt

This compound is novel.

YZ266: To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanol (457 mg, 1.67 mmol) in EtOH (8.6 mL)/DCM (4.3 mL) was added pyridinium p-toluenesulfonate (PPTS) (62.8 mg, 0.25 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane but NMR indicated the product had decomposed.

YZ293: To a solution of furan-2-yl(2-hydroxyphenyl)methanone (115.5 mg, 0.614 mmol) in MeOH (2.8 mL) was added sodium borohydride (46.7 mg, 1.228 mmol). The reaction was stirred for 4 hours. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO₄, filtered, and the solvent was removed under vacuum to give the product. NMR indicated the product was significantly decomposed but HPLC was obtained and showed two peaks sufficient for location of products.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 1.0 mL/min, λ= 210 nm, T = 25°C) ketone 6.6 min, R and S isomers 22.7 min and 24.0 min, configuration was assigned by analogy.
ATH of furan-2-yl(2-hydroxyphenyl)methanone 7k.

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (0.00213 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone 7k (40 mg, 0.213 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (4:1 hexane: ethyl acetate).

After 168 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane but the product was decomposed. The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 74.6% conversion and 0.8% ee

YZ293 (HPLC of racemic 2-(furan-2-yl(hydroxy)methyl)phenol) 8k:

![Graph and table image]
HPLC of 8k after ATH of furan-2-yl(2-hydroxyphenyl)methanone 7k, after 168 hours, 74.6% conversion, 0.8% ee).
Furan-2-yl(2-hydroxyphenyl)methanone 7k.

This compound is novel.

To a solution of furan-2-yl(2-((tetrahydro-2H-pyran-2-yl)oxy)phenyl)methanone (350 mg, 1.29 mmol) in EtOH (6.5 mL)/DCM (3.25mL) was added Pyridinium p-Toluenesulfonate (PPTS) (48.7 mg, 0.194 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-25% ethyl acetate in hexane to give furan-2-yl(2-hydroxyphenyl)methanone 7k as a yellow oil (198.5 mg, 1.06 mmol, 82.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₁H₈NaO₃ 211.0362; Found 21.0366; 1.6 ppm error); ν max 3135, 2961, 1621, 1587, 1558, 1459, 1220, 955, 750 cm⁻¹; δH (500 MHz, CDCl₃) 12.09 (1H, s, OH), 8.28 (1H, d, J = 9.4, ArH), 7.74 (1H, s, ArH), 7.59-7.44 (1H, m, ArH), 7.40 (1H, d, J = 3.6, ArH), 7.04 (1H, d, J = 8.4, C₄H₃O), 6.96 (1H, t, J = 7.6, C₄H₃O), 6.64 (1H, dd, J = 3.5, 1.6, C₄H₃O) ppm; δC (125 MHz, CDCl₃) 184.9 (C), 163.4 (C), 152.0 (C), 147.2 (CH), 136.1 (CH), 131.5 (CH), 121.0 (CH), 119.0 (CH), 118.7 (C), 118.5 (CH), 112.5 (CH), 23.8 (CH) ppm; m/z (ES-API+) 211.1 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of 7k:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7k:
COSY (500 MHz, CDCl$_3$) of 7k:

![COSY spectrum of 7k](image1)

HSQC (500 MHz, CDCl$_3$) of 7k:

![HSQC spectrum of 7k](image2)
HMBC (500 MHz, CDCl₃) of 7k:

HPLC of furan-2-yl(2-hydroxyphenyl)methanone 7k:
To a solution of (2-hydroxyphenyl)(2-methoxyphenyl)methanone 7c (200 mg, 0.88 mmol) in DMF (8.8 mL) was added potassium carbonate (146 mg, 1.06 mmol) and iodomethane (137 mg, 0.88 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-ethoxyphenyl)(2-methoxyphenyl)methanone 7l as a white solid (112.6 mg, 0.44 mmol, 50%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₆H₁₆NaO₃ 279.0989; Found 279.0992; 0.9 ppm error; ν max 3073.83, 2980.82, 1650.68, 1596.45, 1484.84, 1307.50, 1247.35, 749.51 cm⁻¹; δ H (500 MHz, CDCl₃) 7.63-7.61 (1H, m, ArH), 7.47-7.40 (3H, m, ArH), 7.02-6.96 (2H, m, ArH), 6.91-6.85 (2H, m, ArH), 3.86-3.82 (2H, m, OCH₂CH₃), 3.66 (1H, s, OCH₃), 0.94 (3H, t, J = 7.0, OCH₂CH₃) ppm; δ C (125 MHz, CDCl₃) 195.6 (C), 158.2 (C), 157.9 (C), 132.8 (CH), 132.1 (CH), 131.2 (C), 130.4 (CH), 130.3 (C), 129.9 (CH), 120.4 (CH), 120.3 (CH), 112.2 (CH), 111.3 (CH), 63.9 (CH₂), 55.7 (CH₃), 14.1 (CH₃) ppm; m/z (ES-API+) 279.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 31.9 min, R isomer 18.5 min, S isomer 19.7 min.
$^1$H NMR (500 MHz, CDCl$_3$) of 7l:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7l:
COSY (500 MHz, CDCl₃) of 7l:

HSQC (500 MHz, CDCl₃) of 7l:
HMBC (500 MHz, CDCl₃) of 7l:

HPLC of (2-ethoxyphenyl)(2-methoxyphenyl)methanone 7l:

Signal 1: MWD1 B, Sig=254,4 Ref=off

Peak RetTime Type Width Area Height Area %
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Totals: 5615.63525  153.83638
(2-Ethoxyphenyl)(2-methoxyphenyl)methanol 8l.

This compound is novel.

To a solution of racemic 2-(hydroxyl-(2-methoxyphenyl)methyl)phenol 8c (230 mg, 1.0 mmol) in DMF (10 mL) was added potassium carbonate (165.6 mg, 1.2 mmol) and iodoethane (156 mg, 1.0 mmol) at rt. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give racemic (2-ethoxyphenyl)(2-methoxyphenyl)methanol 8l as a colorless oil (69.6 mg, 0.27 mmol, 27%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found [M+Na]+, Calcd for C₁₆H₁₈NaO₃ 281.1151; Found 281.1148; -1.1 ppm error; ν_max 3441 (br), 3034, 2977, 1600, 1488, 1237, 1026, 748 cm⁻¹; δH (500 MHz, CDCl₃) 7.31 (1H, dd, J = 7.6, 1.6, ArH), 7.29-7.18 (3H, m, ArH), 7.06-6.76 (4H, m, ArH), 6.34 (1H, d, J = 5.7, ArCHOH), 4.24-3.93 (2H, m, OCH₂CH₃), 3.82 (3H, s, OCH₃), 3.63 (1H, d, J = 5.8, ArCHOH), 1.38 (3H, t, J = 7.0, OCH₂CH₃) ppm; δC (125 MHz, CDCl₃) 156.7, 156.2, 131.1 (C), 128.4 (CH), 128.3 (CH), 128.0 (CH), 127.8 (CH), 120.5 (CH), 120.4 (CH), 111.4 (CH), 110.5 (CH), 67.8 (CH), 63.7 (CH₂), 55.4 (CH₃), 14.9 (CH₃) ppm; m/z (ES-API+) 281.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C) ketone 31.9 min, R isomer 18.5 min, S isomer 19.7 min.

ATH of (2-ethoxyphenyl)(2-methoxyphenyl)methanone 7l (YZ236).

Catalyst (R,R)-2 (0.0020 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-ethoxyphenyl)(2-methoxyphenyl)methanone 7l (40 mg, 0.156 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC
(4:1 hexane: ethyl acetate). After 168 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 25-100% ethyl acetate in hexane to give 2-(hydroxy(phenyl)methyl)phenol 8l (5.6 mg, 0.022 mmol, 13.9%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 0.5 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 52% conversion (HPLC calibration: 1:1 furan-2-yl(2-hydroxyphenyl)methanone : 2-(furan-2-yl(hydroxy)methyl)phenol gives 8.6:1 absorption at 254 nm) and 13.4% ee; R configuration.

Ethylation of 8c (YZ237, 384): To a solution of asymmetric 2-(hydroxy(2-methoxyphenyl)methyl)phenol 8c (92.7 mg, 0.403 mmol, 99.4% ee) in DMF (4.0 mL) was added potassium carbonate (66.8 mg, 0.484 mmol) and iodoethane (62.9 mg, 0.403 mmol) at rt. The mixture was stirred under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give asymmetric (2-ethoxyphenyl)(2-methoxyphenyl)methanol 8l as a colorless oil (59.7 mg, 0.231 mmol, 57.4%). [α]₀⁺²⁴ -10.3 (c 0.924 in CHCl₃) 97% ee (R).
\(^1\)H NMR (500 MHz, CDCl\(_3\)) of 8l:

\(^13\)C NMR (125 MHz, CDCl\(_3\)) of 8l:
COSY (500 MHz, CDCl₃) of 8l:

![COSY spectrum](image)

HSQC (500 MHz, CDCl₃) of 8l:

![HSQC spectrum](image)
HMBC (500 MHz, CDCl₃) of 8l:

HPLC of racemic (2-ethoxyphenyl)(2-methoxyphenyl)methanol 8l:

Signal 1: MWD1 B, Sig=254,4 Ref=off

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HPLC of **8l** after ATH of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l**: 

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 52% conversion, 13.4% ee, *R* configuration).

HPLC of **8l** after ATH of (2-ethoxyphenyl)(2-methoxyphenyl)methanone **7l**: 

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 52% conversion, 13.4% ee, *R* configuration).

**Signal 1: MWD1 B, Sig=254,4 Ref=off**

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**Totals :**

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HPLC of **8l** (97% ee, *R* configuration) by ethylation of **8c** (YZ237).

**Signal 1: MWD1 B, Sig=254,4 Ref=off**

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**Totals :**

1826.23808 75.38667
N-(2-Benzoylphenyl)acetamide 7m.

This compound has been reported and fully characterized.


To a solution of (2-aminophenyl)(phenyl)methanone 7s (150 mg, 0.76 mmol) in DCM (3.8 mL) at 0°C was added pyridine (360 mg, 4.56 mmol) and acetyl chloride (71.6 mg, 0.91 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (5:1 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-40% ethyl acetate in hexane to give N-(2-benzoylphenyl)acetamide 7m as a yellow oil (154.1 mg, 0.65 mmol, 85%). TLC: Rf ca 0.40 (5:1 hexane: EtOAc), strong UV and KMnO₄; δ₉ (500 MHz, CDCl₃) 10.82 (1H, s, NH), 8.63 (1H, d, J = 8.4, ArH), 7.73 (2H, d, J = 7.3, ArH), 7.65-7.41 (5H, m, ArH), 7.08 (1H, t, J = 7.5, ArH), 2.23 (3H, s, CH₃) ppm; δ₁₃ (125 MHz, CDCl₃) 199.8 (C), 169.2 (C), 140.5 (C), 134.3 (CH), 133.6 (CH), 132.5 (CH), 129.92 (CH), 128.4 (CH), 123.2 (C), 122.1 (CH), 121.5 (CH), 25.3 (CH₃) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 7m:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7m:
HPLC of N-(2-benzoylphenyl)acetamide 7m:

![HPLC chromatogram]

Signal 1: MWD1 A, Sig=250,4 Ref=off

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Totals : 7533.63086 289.03574
Synthesis and characterisation of reaction products 8m-8s

N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide 8m.

This compound is novel.

To a solution of (2-aminophenyl)(phenyl)methanone 7m (100 mg, 0.42 mmol) in MeOH (3 mL) was added sodium borohydride (32 mg, 0.84 mmol). The reaction was stirred for 4 hours. TLC (9:1 hexane:EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO₄, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol 8m as a yellow oil (40.6 mg, 0.168 mmol, 40.3%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₅H₁₅NNaO₂ 264.0997; Found 264.0995; -0.9 ppm error; νmax 3294 (br), 3061, 3029, 2927, 1664, 1587, 1522, 1493, 1303, 697 cm⁻¹; δH (500 MHz, CDCl₃) 8.39 (1H, s, NH), 8.01 (1H, d, J = 8.0, ArH), 7.37-7.27 (6H, m, ArH), 7.14-7.08 (2H, m, ArH), 6.92 (1H, d, J = 3.0, ArCHOH), 3.07 (1H, d, J = 3.0, OH), 1.96 (3H, s, CH₃) ppm; δC (125 MHz, CDCl₃) 168.6 (C), 141.3 (C), 136.6 (C), 132.3 (C), 129.0 (CH), 129.0 (CH), 128.7 (CH), 127.8 (CH), 126.0 (CH), 124.3 (CH), 113.6 (CH), 75.5 (CH), 29.7 (CH), 24.4 (CH₃) ppm; m/z (ES-API+) 264.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 16.6 min, R and S isomers 22.4 min and 25.0 min, configuration was assigned by analogy.

(ATH of N-(2-benzoylphenyl)acetamide 7m (YZ230).

Catalyst (R,R)-2 (0.0023 mmol, 1mol%) was added to the FA: TEA (5:2 azeotrophic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-benzoylphenyl)acetamide 7m (40 mg, 0.167 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (9:1 hexane:
EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide 8m (24.6 mg, 0.102 mmol, 60.9%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 95% conversion (HPLC calibration: 1:1 N-(2-benzoylphenyl)acetamide : N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide gives 1.4:1 absorption at 254 nm); [α]D²⁴ -35.01 (c 0.692 in CHCl₃) 61.4% ee.

¹H NMR (500 MHz, CDCl₃) of 8m:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8m:

COSY (500 MHz, CDCl$_3$) of 8m:
HSQC (500 MHz, CDCl$_3$) of 8m:

HMBC (500 MHz, CDCl$_3$) of 8m:
HPLC of racemic N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide 8m:

![HPLC graph]

Signal 1: MWD1 A, Sig=250.4 Ref=off

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Totals: 3.71036e4 543.49591

HPLC of 8m after ATH of N-(2-benzoylphenyl)acetamide 7m:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 95% conversion, 61.4% ee)

![HPLC graph]

Signal 1: MWD1 A, Sig=250.4 Ref=off

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Totals: 8044.58179 144.10958
1-Acetylbenzo[b]azet-2(1H)-one.

![Chemical Structure](image)

This compound has been reported but not fully characterized.


To a solution of 2-acetamidobenzoic acid (358 mg, 2.00 mmol) in THF (16 mL) at 0 °C was added CDI (324 mg, 2.00 mmol) and stirred under a nitrogen atmosphere for 2 hours. To a solution of N, O-dimethylhydroxylamine hydrochloride (195 mg, 2.00 mmol) in THF (4 mL) at rt was added triethylamine (202 mg, 2.00 mmol) and stirred under a nitrogen atmosphere for 2 hours. Then the two reaction mixture was combined and left to stir under a nitrogen atmosphere overnight. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The mixture was quenched by saturated NaHCO$_3$ solution (20 mL), EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO$_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give 1-acetylbenzo[b]azet-2(1H)-one as a white solid (138.5 mg, 0.860 mmol, 43%). TLC: Rf ca 0.20 (9:1 hexane: EtOAc), strong UV and KMnO$_4$; Mp: 173 °C; HRMS: (found (ESI+): [M+Na]$^+$, Calcd for C$_9$H$_7$NNaO$_2$ 184.0371; Found 184.0369; -1.3 ppm error; $\nu_{\text{max}}$ 3070, 2930, 1778, 1752, 1643, 1604, 1470, 1264, 1051, 997, 960 cm$^{-1}$; $\delta_H$ (500 MHz, CDCl$_3$) 8.18 (1H, d, $J = 7.9$, ArH), 7.79 (1H, t, $J = 7.7$, ArH), 7.64–7.40 (2H, m, ArH), 2.37 (3H, s, COCH$_3$) ppm; $\delta_C$ (125 MHz, CDCl$_3$) 160.2 (C), 159.7 (C), 146.4 (C), 136.6 (CH), 128.5 (CH), 128.2 (CH), 128.4 (CH), 116.6 (C), 21.4 (CH$_3$) ppm; m/z (ES-API+) did not show molecular ion.
$^1$H NMR (500 MHz, CDCl$_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:
COSY (500 MHz, CDCl$_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:

HSQC (500 MHz, CDCl$_3$) of 1-Acetylbenzo[b]azet-2(1H)-one:
HMBC (500 MHz, CDCl₃) of 1-Acetylbenzo[b]azet-2(1H)-one:
N-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide.

![Chemical Structure]

This compound is novel.

To a solution of 2-(2-bromophenoxy)tetrahydro-2H-pyran (270 mg, 1.05 mmol) in THF (2.1 mL) at -78 °C was added a solution of n-butyllithium (0.53 mL, 2.5M in hexanes, 1.05 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 1-acetylbenzo[b]azet-2(1H)-one (254.3 mg, 1.58 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N-(2-((tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide as a white solid (157.4 mg, 0.464 mmol, 44%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 113 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₂₀H₂₁NNaO₄ 362.1367; Found 362.1363; -1.2 ppm error); νmax 2953, 2926, 2883, 1628, 1596, 1581, 1514, 1288, 1118, 956 cm⁻¹; δH (500 MHz, CDCl₃) 11.38 (1H, s, NH), 8.72 (1H, d, J = 8.4, ArH), 7.58-7.39 (3H, m, ArH), 7.36 (1H, dd, J = 7.5, 1.5, ArH), 7.24 (1H, d, J = 8.4, ArH), 7.10 (1H, t, J = 7.4, ArH), 7.00 (1H, t, J = 7.6, ArH), 5.38 (1H, s, OCHO), 3.68 (1H, td, J = 11.2, 2.1, OCH₂CH₂), 3.54 (1H, d, J = 11.2, OCH₂CH₂), 2.27 (3H, s, COCH₃), 1.59-1.51 (2H, m, CH₂), 1.44-1.31 (3H, m, CH₂), 1.31-1.17 (1H, m, CH₂) ppm; δC (125 MHz, CDCl₃) 200.8 (C), 169.5 (C), 154.4 (C), 140.6 (C), 134.7 (CH), 134.2 (CH), 132.2 (CH), 129.9 (C), 128.9 (CH), 123.5 (C), 122.0 (CH), 121.5 (CH), 120.5 (CH), 115.1 (CH), 96.5 (CH), 61.7 (CH₂), 29.9 (CH₂), 25.6 (CH₃), 25.0 (CH₂), 17.7 (CH₂) ppm; m/z (ES-API+) 362.2 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:

$^{13}$C NMR (125 MHz, CDCl$_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:
COSY (500 MHz, CDCl$_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:

HSQC (500 MHz, CDCl$_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:
HMBC (500 MHz, CDCl$_3$) of N-(2-(2-((Tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide:
N-(2-(2-Hydroxybenzoyl)phenyl)acetamide 7n.

This compound is novel.

To a solution of N-(2-(2-((tetrahydro-2H-pyran-2-yl)oxy)benzoyl)phenyl)acetamide (151.5 mg, 0.450 mmol) in EtOH (2.28 mL)/DCM (1.14 mL) was added pyridinium p-toluenesulfonate (PPTS) (16.9 mg, 0.0675 mmol) at rt. The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n as a yellow solid (84.1 mg, 0.330 mmol, 73.8%). TLC: Rf ca 0.60 (3:2 hexane: EtOAc), strong UV and KMnO₄; Mp: 101 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₅H₁₃NNaO₃ 278.0783; Found 278.0788; 1.5 ppm error; νₘₐₓ 3257 (br), 3050, 1665, 1623, 1604, 1578, 1515, 1481, 1443, 1292, 1283, 1118, 933 cm⁻¹; δₜ (500 MHz, CDCl₃) 11.54, (1H, s, NH), 9.38 (1H, s, OH), 8.41 (1H, d, J = 8.3, ArH), 7.58-7.45 (4H, m, ArH), 7.17 (1H, t, J=7.6, ArH), 7.08 (1H, d, J = 8.3, ArH), 6.89 (1H, t, J = 7.6, ArH), 2.18 (1H, s, COCH₃) ppm; δc (125 MHz, CDCl₃) 202.3 (C), 168.7 (C), 163.3 (C), 138.1 (C), 136.9 (CH), 133.9 (CH), 133.2 (CH), 131 7 (CH), 125.6 (C), 122.9 (CH), 122.6 (CH), 119.8 (C), 118.9 (CH), 118.6 (CH), 25.0 (CH₃) ppm; m/z (ES-API+) 278.2 (M⁺ + 23, 100%).
$^{1}H$ NMR (500 MHz, CDCl$_3$) of 7n:

$^{13}C$ NMR (125 MHz, CDCl$_3$) of 7n:
COSY (500 MHz, CDCl$_3$) of 7n:

HSQC (500 MHz, CDCl$_3$) of 7n:
HMBC (500 MHz, CDCl$_3$) of 7n:

HPLC of N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n:
N-(2-(Hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide 8n.

This compound is novel.

To a solution of N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n (84.1 mg, 0.330 mmol) in MeOH (2 mL) was added sodium borohydride (25.1 mg, 0.660 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO₄, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-100% ethyl acetate in hexane to give N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide 8n as a colorless oil (4.20 mg, 0.0163 mmol, 4.96%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₅H₁₅NNaO₃ 280.0945; Found 280.0944; -0.3 ppm error; νmax 3236 (br), 3064, 2922, 2852, 1730, 1665, 1587, 1482, 1370, 1243, 1037, 966 cm⁻¹; δH (500 MHz, CDCl₃) 8.36 (2H, d, J = 16.1, NH + ArOH), 7.78 (1H, d, J = 8.0, ArH), 7.32 (1H, t, J = 8.3, ArH), 7.19-7.11 (3H, m, ArH), 6.90 (1H, d, J = 8.1, ArH), 6.83-6.67 (2H, m, ArH), 6.10 (1H, s, ArCHOH), 4.73 (1H, s, ArCHOH) 2.01 (3H, s, COCH₃) ppm; δC (125 MHz, CDCl₃) 170.1 (C), 155.3 (C), 135.8 (C), 132.8 (C), 129.4 (CH), 129.2 (CH), 129.1 (CH), 127.9 (CH), 125.7 (CH), 125.2 (C), 124.3 (CH), 120.2 (CH), 116.9 (CH), 74.2 (CH), 24.1 (CH₃) ppm; m/z (ES-API+) 280.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane: iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 25.3 min, R and S isomer 33.9 min and 41.6 min, configuration was assigned by analogy.

ATH of N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n (YZ359)

Catalyst (R,R)-2 (0.00157 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n (40 mg, 0.157 mmol) in DCM (0.25 mL)
was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (1:1 hexane: EtOAc). After 72 hours, the reaction was quenched using saturated NaHCO$_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO$_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-100% ethyl acetate in hexane to give N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide 8n (30.3 mg, 0.118 mmol, 75.2%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [$\alpha$]$_D^{24}$ -82 (c 0.995 in CHCl$_3$) 93.6% ee.

$^1$H NMR (500 MHz, CDCl$_3$) of 8n:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8n:

COSY (500 MHz, CDCl$_3$) of 8n:
HSQC (500 MHz, CDCl₃) of 8n:

HMBC (500 MHz, CDCl₃) of 8n:
HPLC of racemic N-(2-(hydroxy(2-hydroxyphenyl)methyl)phenyl)acetamide 8n:

HPLC of 8n after ATH of N-(2-(2-hydroxybenzoyl)phenyl)acetamide 7n: (R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 93.6% ee).
(2-Aminophenyl)[2-methoxyphenyl]methanone.

![Chemical Structure](image)

This compound has been reported and fully characterized.


To a solution of 2-bromoanisole (1.189 g, 6.36 mmol) in THF (6.36 mL) at rt was added magnesium (152.6 mg, 6.36 mmol). The reaction mixture was stirred under a nitrogen atmosphere at rt for 30 minutes and then heated to reflux on a hot plate for 1 hour. After cooling down to 0°C, a solution of 2-aminobenzonitrile (250 mg, 2.12 mmol) in THF (6.36 mL) was added dropwise and the reaction mixture was left stirring under the nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (4.24 mL, 2.0 M, 8.48 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. The reaction was followed by TLC (4:1 hexane:EtOAc). The mixture was quenched by saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-aminophenyl)[2-methoxyphenyl]methanone as a yellow solid (90.8 mg, 0.400 mmol, 19.5%). TLC: Rf ca 0.30 (4:1 hexane:EtOAc), strong UV and KMN₄; δₘₕ (400 MHz, CDCl₃) 7.47-7.35 (1H, m, ArH), 7.29-7.21 (3H, m, ArH), 7.06-6.96 (2H, m, ArH), 6.69 (1H, d, J = 8.1, ArH), 6.52 (1H, t, J = 8.0, ArH), 6.42 (2H, s, NH₂), 3.76 (3H, s, OCH₃) ppm; δ (100 MHz, CDCl₃) 198.9 (C), 156.4 (C), 151.0 (C), 135.0 (CH), 134.6 (CH), 130.7 (CH), 130.3 (C), 128.5 (CH), 120.4 (CH), 118.6 (C), 116.8 (CH), 115.5 (CH), 111.3 (CH), 55.9 (CH₃). Data matched that reported. Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 90:10, 1.0 mL/min, T = 25°C) ketone 49.4 min, R and S isomer 30.5 min and 56.9 min, configuration is not known.
$^1$H NMR (400 MHz, CDCl$_3$) of (2-Aminophenyl)(2-methoxyphenyl)methanone:

$^{13}$C NMR (100 MHz, CDCl$_3$) of (2-Aminophenyl)(2-methoxyphenyl)methanone:
HPLC of (2-aminophenyl)(2-methoxyphenyl)methanone:

![HPLC graph and result table]

**Result Table**

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N-(2-(2-Methoxybenzoyl)phenyl)acetamide 7o.

This compound has been reported and fully characterized.


To a solution of (2-aminophenyl)(2-methoxyphenyl)methanone (293.6 mg, 1.29 mmol) in DCM (6.5 mL) at 0°C was added pyridine (611.5 mg, 7.74 mmol) and acetyl chloride (121.8 mg, 1.55 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (7:3 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-60% ethyl acetate in hexane to give N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o as a white solid (229.6 mg, 0.854 mmol, 66%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and KMnO₄; δ_H (500 MHz, CDCl₃) 11.59 (1H, s, NH), 8.74 (1H, d, J = 8.4, ArH), 7.57-7.51 (1H, m, ArH), 7.50-7.40 (2H, m, ArH), 7.30-7.24 (1H, m, ArH), 7.05 (1H, t, J = 7.4, ArH), 7.02-6.96 (2H, m, ArH), 3.75 (3H, s, CH₂), 2.27 (3H, s, COCH₃) ppm; δ_C (125 MHz, CDCl₃) 200.6 (C), 196.6 (C), 158.8 (C), 141.4 (C), 135.1 (CH), 134.6 (CH), 132.0 (CH), 129.1 (CH), 122.6 (C), 122.0 (CH), 120.5 (CH), 111.4 (CH), 55.7 (CH₃), 25.6 (CH₃) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 7o:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7o:
HPLC of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o:
N-(2-(Hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide 8o.

This compound is novel.

To a solution of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o (139.6 mg, 0.519 mmol) in MeOH (3.7 mL) was added sodium borohydride (39.5 mg, 1.04 mmol). The reaction was stirred for 4 hours. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 ml), dried with MgSO₄, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(Hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide 8o as a white solid (121.7 mg, 0.449 mmol, 86.5%). TLC: Rf ca 0.20 (3:2 hexane: EtOAc), strong UV and KMnO₄; Mp: 167.3 °C; HRMS: (found (ESI+): \([\text{M+Na}^+]\), Calcd for C\text{\textsubscript{16}}H\text{\textsubscript{17}}NNaO\text{\textsubscript{2}} 294.1104; Found 294.1101; -1.2 ppm error; ν\text{\textsubscript{max}} 3373, 1672, 1591, 1535, 1447, 1290, 1036, 1016, 784, 756 cm\textsuperscript{-1}; δ\textsubscript{H} (500 MHz, CDCl\textsubscript{3}) 9.01 (1H, s, NH), 8.15 (1H, d, J = 8.0, ArH), 7.32 (2H, t, J = 7.7, ArH), 7.07-6.89 (5H, m, ArH), 6.09 (1H, d, J = 4.8, ArCHOH), 3.90 (3H, s, OCH\textsubscript{3}), 3.85 (1H, d, J = 5.0, OH), 2.07 (3H, s, COCH\textsubscript{3}) ppm; δ\textsubscript{C} (125 MHz, CDCl\textsubscript{3}) 168.4 (C), 156.9 (C), 137.3 (C), 130.1 (C), 129.4 (CH), 128.9 (C), 128.6 (CH), 128.2 (CH), 128.2 (CH), 124.0 (CH), 122.8 (CH), 121.3 (CH), 110.8 (CH), 72.8 (CH\textsubscript{3}), 55.6 (CH\textsubscript{3}) ppm; m/z (ES-API+) 294.2 (M\textsuperscript{+} + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 22.1 min, R and S isomers 40.4 min and 60.8 min, configuration was assigned by analogy.

ATH of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o (YZ317).

Catalyst (R,R)-2 (0.00149 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o (40 mg, 0.149 mmol) in DCM (0.25 mL)
was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (3:2 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO$_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO$_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(2-methoxyphenyl)methyl)phenyl)acetamide $8o$ (13.4 mg, 0.0494 mmol, 33.3%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 50% conversion; $[\alpha]_D$ +37.4 (c 0.0147 in CHCl$_3$) 59.4% ee. The conversion was established by NMR of the crude reduction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) of $8o$:

![NMR Spectrum](image-url)
$^{13}$C NMR (125 MHz, CDCl₃) of 8o:

COSY (500 MHz, CDCl₃) of 8o:
HSQC (500 MHz, CDCl₃) of 8o:

HMBC (500 MHz, CDCl₃) of 8o:
HPLC of racemic N-(2-(hydroxy(phenyl)methyl)phenyl)acetamide 8o:

\[
\text{HPLC of} \ 8o \ \text{after ATH of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7o:}
\]

\[(R,R)-3C-tethered \text{Ru(II)-TsDPEN catalyst (after 168 hours, 50% conversion, 59.4% ee)}\]
(2-Aminophenyl)(4-methoxyphenyl)methanone.

This compound has been reported and fully characterized.


To a solution of 4-bromoanisole (2.128 g, 12.3 mmol) in THF (12.3 mL) at rt was added magnesium (295.2 mg, 12.3 mmol). The reaction mixture was stirred under a nitrogen atmosphere at rt for 30 minutes and then heated to reflux on a hot plate for 1 hour. After cooling down to 0°C, a solution of 2-aminobenzonitrile (500 mg, 4.10 mmol) in THF (12.3 mL) was added dropwise and the reaction mixture was left stirring under the nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (8.20 mL, 2.0 M, 16.4 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give (2-aminophenyl)(4-methoxyphenyl)methanone as a yellow solid (414 mg, 1.82 mmol, 44.5%). TLC: Rf ca. 0.50 (4:1 hexane: EtOAc), strong UV and KMnO₄; δ_H (500 MHz, CDCl₃) 7.68 (2H, d, J = 8.8, ArH), 7.52-7.36 (1H, m, ArH), 7.31-7.21 (1H, m, ArH), 6.95 (2H, d, J = 8.8, ArH), 6.77-6.73 (1H, m, ArH), 6.63 (1H, t, J = 7.5, ArH), 5.85 (2H, s, NH₂), 3.88 (3H, s, OCH₃) ppm; δ_C (125 MHz, CDCl₃) 197.8 (C), 162.3 (C), 150.4 (C), 134.0 (CH), 133.7 (CH), 132.3 (C), 131.8 (CH), 119.0 (C), 117.0 (CH), 115.6 (CH), 113.4 (CH), 55.5 (CH₃). Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of (2-Aminophenyl)(4-methoxyphenyl)methanone:

$^{13}$C NMR (125 MHz, CDCl$_3$) of (2-Aminophenyl)(4-methoxyphenyl)methanone:
N-(2-(4-Methoxybenzoyl)phenyl)acetamide 7p.

This compound has been reported and fully characterized.


To a solution of (2-aminophenyl)(4-methoxyphenyl)methanone (476.8 mg, 2.10 mmol) in DCM (10.6 mL) at 0°C was added pyridine (995.4 mg, 12.6 mmol) and acetyl chloride (197.8 mg, 2.52 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (7:3 hexane: EtOAc). The mixture was quenched by 2M HCl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-60% ethyl acetate in hexane to give N-(2-(4-methoxybenzoyl)phenyl)acetamide 7p as a white solid (407 mg, 1.51 mmol, 72%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and KMnO₄; δH (500 MHz, CDCl₃) 10.52 (1H, s, NH), 8.56 (1H, d, J = 8.2, ArH), 7.74 (2H, d, J = 8.8, ArH), 7.55 (2H, t, J = 8.0, ArH), 7.09 (1H, t, J = 7.6, ArH), 6.97 (2H, d, J = 8.8, ArH), 3.90 (3H, s, OCH₃), 2.20 (3H, s, COCH₃) ppm; δC (125 MHz, CDCl₃) 198.0 (C), 169.1 (C), 163.5 (C), 139.8 (C), 133.7 (CH), 132.7 (CH), 132.8 (CH), 130.9 (C), 124.3 (C), 122.1 (CH), 121.8 (CH), 1213.7 (CH), 55.6 (CH₃), 25.2 (CH₃) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 7p:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7p:
HPLC of N-(2-(2-methoxybenzoyl)phenyl)acetamide 7p:
N-(2-(Hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide 8p.

This compound is novel.

To a solution of N-(2-(4-methoxybenzoyl)phenyl)acetamide (139.6 mg, 0.519 mmol) in MeOH (3.7 mL) was added sodium borohydride (39.5 mg, 1.04 mmol). The reaction was stirred for 4 hours. TLC (3:2 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 ml), dried with MgSO₄, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide 8p as a colorless oil (95.7 mg, 0.353 mmol, 68%). TLC: Rf ca 0.20 (3:2 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₁₆H₁₇NNaO₃ 294.1102; Found 294.1101; -0.4 ppm error; ν_{max} 3266 (br), 2998, 2958, 2836, 1633, 1610, 1509, 1368, 1244, 1029, 966 cm⁻¹; δ₉ (500 MHz, CDCl₃) 8.47 (1H, s, NH), 8.02 (1H, d, J = 8.1, ArH), 7.32 (1H, t, J = 8.4, ArH), 7.27-7.15 (2H, m, ArH), 7.14-7.02 (2H, m, ArH), 6.87 (2H, d, J = 8.7, ArH), 5.87 (1H, s, ArCHOH), 3.80 (3H, s, OCH₃), 3.06 (1H, s, OH), 1.97 (3H, s, COCH₃) ppm; δ₁₃ (125 MHz, CDCl₃) 168.6 (C), 159.2 (C), 136.6 (C), 134.2 (CH), 133.4 (C), 132.3 (C), 128.8 (CH), 128.7 (CH), 127.5 (CH), 124.2 (CH), 123.4 (CH), 114.0 (CH), 75.2 (CH), 55.3 (CH₃), 24.5 (CH₃) ppm; m/z (ES-API+) 294.2 (M⁺ + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 31.1 min, R and S isomers 39.4 min and 45.1 min, configuration was assigned by analogy.

ATH of N-(2-(4-methoxybenzoyl)phenyl)acetamide 7p (YZ329).

Catalyst (R,R)-2 (0.00149 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N-(2-(4-methoxybenzoyl)phenyl)acetamide 7p (40 mg, 0.149 mmol) in DCM (0.25 mL)
was added. The reaction mixture was stirred under a nitrogen atmosphere, followed by TLC (3:2 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO$_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO$_4$) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-80% ethyl acetate in hexane to give N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide (4.50 mg, 0.0166 mmol, 11.2%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IG, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 28.2% conversion; $[\alpha]_{D}^{24} -13.2$ (c 0.0340 in CHCl$_3$) 53.6% ee. The conversion was established by NMR of the crude reduction mixture.

$^1$H NMR (500 MHz, CDCl$_3$) of 8p:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8p:

COSY (500 MHz, CDCl$_3$) of 8p:
HSQC (500 MHz, CDCl$_3$) of 8p:

HMBC (500 MHz, CDCl$_3$) of 8p:
HPLC of racemic N-(2-(hydroxy(4-methoxyphenyl)methyl)phenyl)acetamide 8p:

HPLC of 8p after ATH of N-(2-(4-methoxybenzoyl)phenyl)acetamide 7p: (R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 28.2% conversion, 53.6% ee).
N,N-Diisopropylbenzamide.

This compound has been reported and fully characterized.


To a solution of benzoyl chloride (421.5 mg, 3.0 mmo) in THF (10 mL) at 0 °C was added dropwise diisopropylamine (454.5 mg, 4.5 mmol) and Et3N (606 mg, 6.0 mmol). The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH4Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were washed with 1M HCl solution (2 ×20 mL), 1M Na2CO3 solution (20 mL) and brine (20 mL), dried (MgSO4) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N,N-Diisopropylbenzamide as a white solid (552 mg, 2.69 mmol, 89.8%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO4; δH (500 MHz, CDCl3) 7.37-7.26 (5H, m, ArH), 3.83-3.53 (2H, m, NCH), 1.52-1.15 (12H, m, CH3) ppm; δC (125 MHz, CDCl3) 171.0 (C), 139.0 (C), 128.6 (CH), 128.5 (CH), 125.6 (CH), 20.7 (CH3) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of N,N-Diisopropylbenzamide:

$^{13}$C NMR (125 MHz, CDCl$_3$) of N,N-Diisopropylbenzamide:
Note on synthesis of 7q.

Substrate 7q was prepared by the addition of anion A to aldehyde B, followed by TBS removal and oxidation. An X-ray crystallographic structure of the initial adduct formed between A and B however revealed it to be the product C of TBS migration from the phenolic to the secondary alkyl hydroxyl group (Figure S1).

**Figure S1.** A). Formation of the precursor to 7q results in TBS migration to form C. B). X-ray crystallographic structure of C.

Ketone 7q and alcohol 8q exhibited interesting rotameric properties, reflecting the likely out-of-plane conformation of the amide group, as evidenced by the peaks in their $^1$H-NMR structures (Figure S2). Compound 7q had two NCH resonances in the 1H-NMR spectrum (as did 7r), reflecting the stereochemical non-equivalence of its isopropyl groups, whereas 8q exhibited two major and two minor NCH peaks in the 1H-NMR spectrum, i.e. corresponding to the NCH of each isopropyl of the two diastereomers.

**Figure S2.** Diastereomers formed by 7q and 8q.
This compound is novel.

To a solution of N,N-diisopropylbenzamide (205 mg, 1.00 mmol) in THF (2 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.400 mL, 2.5M in hexanes, 1.00 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-((tert-butyldimethylsilyl)oxy)benzaldehyde (354 mg, 1.50 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-((2-(tert-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-N,N-diisopropylbenzamide as a white solid (283.3 mg, 0.642 mmol, 64.2%). Then to a solution of 2-((2-(tert-butyldimethylsilyl)oxy)phenyl)(hydroxy)methyl)-N,N-diisopropylbenzamide (280 mg, 0.635 mmol) in THF (10 mL) was added a solution of tetra-n-butylammonium fluoride (TBAF) (0.95 mL, 1.0M in THF, 0.95 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere and followed by TLC (4:1 hexane: ethyl acetate). Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q as a white solid (129 mg, 0.394 mmol, 62.1%). TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₂₀H₂₅NNaO₃ 350.1727; Found 350.1727; -0.1 ppm error); v max 3244 (br), 2969, 2932, 1589, 1485, 1454, 1370, 1345, 1232, 1030, 751 cm⁻¹; Major diastereomer: δH (500 MHz, CDCl₃) 8.97 (1H, s, ArOH), 7.31-7.20 (5H, m, ArH), 6.84-6.81 (3H, m, ArH), 5.97 (1H, s, ArCHOH), 5.68 (1H, s, ArCHOH), 4.01-3.96 (1H, m, N[CH(CH₃)₂]₂), 3.64-3.59 (1H, m, N[CH(CH₃)₂]₂), 1.65-1.55 (7H, m, N[CH(CH₃)₂]₂), 1.31-1.13 (5H, m, N[CH(CH₃)₂]₂) ppm; Minor diastereomer: δH (500 MHz, CDCl₃) 9.86 (1H, s, ArOH), 7.43-7.38 (2H, m, ArH), 7.34-7.29 (2H, m, ArH), 7.09 (1H, t, J = 7.5, ArH), 7.04-7.03 (1H, m, ArH), 6.99 (1H, d, J = 8.2, ArH), 6.69 (1H, t, J = 7.5, ArH), 6.02 (1H, s, ArH).
ArCHOH), 3.86-3.81 (3H, m, N(CH(CH$_3$)$_2$)$_2$), 1.19-1.14 (6H, m, N(CH(CH$_3$)$_2$)$_2$), 0.83-0.82 (3H, m, N(CH(CH$_3$)$_2$)$_2$ ppm; Major diastereomer: $\delta$ (125 MHz, CDCl$_3$) 172.1 (C), 157.2 (C), 140.0 (C), 137.3 (C), 129.6 (CH), 129.3 (CH), 128.7 (CH), 128.2 (CH), 126.6 (CH), 125.0 (CH), 123.3 (C), 119.5 (CH), 117.7 (CH), 75.7 (CH), 51.7 (CH), 46.5 (CH), 21.1 (CH$_3$), 20.8 (CH$_3$), 20.3 (CH$_3$), 20.1 (CH$_3$) ppm; Minor diastereomer: $\delta$ (125 MHz, CDCl$_3$) 172.1 (C), 156.6 (C), 140.6 (C), 136.2 (C), 131.1 (CH), 129.9 (CH), 128.8 (CH), 128.0 (CH), 127.8 (CH), 127.1 (C), 126.4 (CH), 119.3 (CH), 117.4 (CH), 75.8 (CH), 51.4 (CH), 46.6 (CH), 20.8 (CH$_3$), 20.6 (CH$_3$), 20.4 (CH$_3$), 19.9 (CH$_3$) ppm; m/z (ES-API+) 350.2 (M$^+ + 23$, 100%).

X-ray crystallographic structure of C (page S173, CCDC 1978886, local code yz9) revealed TBS migration from the phenolic to the secondary alkyl hydroxyl group to give C.

Unit Cell Parameters: a 12.84169(9) b 10.91697(5) c 18.56931(10) P21/n

solid state structure of yz9 with only key atoms labelled and thermal ellipsoids drawn at 50% probability level

Crystal structure determination of C [yz9]
The asymmetric unit contains the silyl ether, there are four molecules in the unit cell (two of each enantiomer)
The OH was located in a difference map but refined with distance constraints. It form an H bond with a neighbouring amide carbonyl tabulated below
D-H H...A D...A <(DHA)
0.84 1.87 2.7042(10) 171.1 O22-H22...O8_1

Symmetry operator used to generate symmetry equivalent atom discussed in above contact was $1$
1.5-X,-0.5+Y,1.5-Z

Experimental

Single crystals of C_{26}H_{39}NO_{3}Si [yz9] were grown from DCM/hexane in a small vial at room
temperature. A suitable crystal was selected and mounted on a glass fibre with Fomblin oil and
placed on a Rigaku Oxford Diffraction SuperNova diffractometer with a duel source (Cu at zero)
equipped with an AtlasS2 CCD area detector. The crystal was kept at 150(2) K during data
collection. Using Olex2 [1], the structure was solved with the ShelXT [2] structure solution
program using Intrinsic Phasing and refined with the ShelXL [3] refinement package using Least
Squares minimisation.


Crystal Data for C_{26}H_{39}NO_{3}Si ($M$=441.67 g/mol): monoclinic, space group P2_{1}/n (no. 14), $a$ =
12.84169(9) Å, $b$ = 10.91697(5) Å, $c$ = 18.56931(10) Å, $\beta$ = 90.7611(5)°, $V$ = 2603.05(3) Å$^3$, $Z$ =
4, $T$ = 150(2) K, $\mu$(CuKα) = 0.986 mm$^{-1}$, $D_{calc}$ = 1.127 g/cm$^3$, 27378 reflections measured (8.32° ≤
2Θ ≤ 147.258°), 5240 unique ($R_{int}$ = 0.0250, $R_{sigma}$ = 0.0270) which were used in all calculations.
The final $R_1$ was 0.0329 (I > 2σ(I)) and $wR_2$ was 0.0864 (all data).

Table 1 Crystal data and structure refinement for yz9.

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Enantiomeric excess and conversion were determined by HPLC analysis (Chiralpak IA, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 23.9 min, \( \text{R} \) and \( \text{S} \) isomer 26.1 min and 29.3 min, configuration is not known.

ATH of \( \text{7q} \) using \((\text{R},\text{R})\)-3C-tethered Ru(II)-TsDPEN catalyst \( 2 \) (YZ251).

Catalyst \((\text{R},\text{R})\)-\( 2 \) (0.00123 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide \( \text{7q} \) (40 mg, 0.123 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: ethyl acetate). After 72 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide \( \text{8q} \) (18.3 mg, 0.056 mmol, 45.5%; \((\text{R},\text{R})\)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6 mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C); \((\text{R},\text{R})\)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [\( \alpha \)]\(_D^{26}\) -57.5 (c 0.366 in CHCl\(_3\)) 86.8% ee
$^1$H NMR (500 MHz, CDCl$_3$) of 8q:

Major diastereomer:

Minor diastereomer:
$^{13}$C NMR (125 MHz, CDCl₃) of 8q:

COSY (500 MHz, CDCl₃) of 8q:
HSQC (500 MHz, CDCl$_3$) of 8q:

HMBC (500 MHz, CDCl$_3$) of 8q:
HPLC of racemic 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q:

![HPLC graph]

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Totals: 3.25530e4 440.44977

HPLC of 8q after ATH of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide 7q:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 72 hours, 100% conversion, 86.8% ee)

![HPLC graph]

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Totals: 7916.77686 93.06989
2-(2-Hydroxybenzoyl)-N,N-diisopropylbenzamide 7q.

This compound is novel.

To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q (119 mg, 0.36 mmol) in DCM (2.5 mL) at rt was added manganese dioxide (474 mg, 5.46 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (7:3 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and wash with DCM. The combined solvent was removed to give the product 7q as a yellow oil (56.2 mg, 0.173 mmol, 47.5%). TLC: Rf ca 0.40 (7:3 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₂₀H₂₃NNaO₃ 348.1561; Found 348.1570; 2.5 ppm error; ν max 3052, 2971, 2933, 1624, 1485, 1445, 1370, 1340 cm⁻¹; δH (500 MHz, CDCl₃) 11.95 (1H, s, ArOH), 7.52-7.43 (5H, m, ArH), 7.36 (1H, d, J = 7.5, ArH), 7.02 (1H, d, J = 8.3, ArH), 6.84 (1H, t, J = 7.5, ArH), 3.88-3.84 (1H, m, N[CH(CH₃)₂]₂), 3.48-3.42 (1H, m, N[CH(CH₃)₂]₂), 1.64-1.60 (1H, m, N[CH(CH₃)₂]₂), 1.41-1.40 (5H, m, N[CH(CH₃)₂]₂), 1.20-1.19 (6H, m, N[CH(CH₃)₂]₂) ppm; δC (125 MHz, CDCl₃) 201.8 (C), 169.1 (C), 163.1 (C), 129.2 (C), 136.6 (CH), 136.2 (C), 134.0 (CH), 130.5 (CH), 129.1 (CH), 127.6 (CH), 126.1 (CH), 119.7 (C), 118.9 (CH), 118.0 (CH), 51.4 (CH), 45.9 (CH), 20.5 (CH₃), 20.2 (CH₃) ppm; m/z (ES-API+) 348.3 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of 7q:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7q:
COSY (500 MHz, CDCl₃) of 7q:

HSQC (500 MHz, CDCl₃) of 7q:
HMBC (500 MHz, CDCl$_3$) of 7q:

HPLC of 2-(2-hydroxybenzoyl)-N,N-diisopropylbenzamide 7q:

Signal 2: MWD1 C, Sig=210,4 Ref=off

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Totals: 1.37298e4 294.90503
2-(Hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r.

This compound is novel.

YZ216 (racemic): To a solution of N,N-diisopropylbenzamide (200 mg, 0.976 mmol) in THF (2 mL) at -78 °C was added dropwise a solution of n-butyllithium (0.400 mL, 2.5M in hexanes, 0.976 mmol). The reaction mixture was then stirred under a nitrogen atmosphere for 2-3 hours, after which 2-methoxybenzaldehyde (199 mg, 1.46 mmol) was added dropwise. The reaction mixture was left stirring under the nitrogen atmosphere and allowed to warm to rt. The reaction was followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by saturated NH₄Cl solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r as a white solid (263 mg, 0.771 mmol, 79%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 81 °C; HRMS: (found (ESI+): [M+Na]+, Calcd for C₂₁H₂₇NNaO₃ 364.1886; Found 364.1883; -0.8 ppm error; νmax 3387 (br), 2968, 2872, 1595, 1463, 1442, 1371, 1237 cm⁻¹; δH (500 MHz, CDCl₃) 7.77-7.57 (1H, m, ArH), 7.39-7.07 (5H, m, ArH), 6.96-6.75 (2H, m, ArH), 6.08 (1H, s, ArCHOH), 4.52 (1H, s, ArCHOH), 4.02-3.97 (1H, m, N(CH(CH₃)₂)₂), 3.65 (1H, s, N(CH(CH₃)₂)₂), 3.61 (3H, s, OCH₃), 1.63-1.56 (4H, m, N(CH(CH₃)₂)₂), 1.49-1.44 (2H, m, N(CH(CH₃)₂)₂),
1.24-1.16 (5H, m, N\(\text{CH(CH}_3\text{)}_2\)), 1.06 (1H, d, \(J = 6.6\), N\(\text{CH(CH}_3\text{)}_2\)) ppm; \(\delta\)C (125 MHz, CDCl\(_3\)) 172.0 (C), 155.9 (C), 142.0 (C), 137.9 (C), 131.6 (CH), 129.3 (C), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.0 (CH), 126.3 (CH), 124.5 (CH), 120.7 (CH), 110.0 (CH), 73.7 (CH), 68.0 (CH), 62.2 (CH\(_3\)), 55.1 (CH\(_3\)), 51.5 (CH\(_3\)), 46.2 (CH\(_3\)), 20.4 (CH\(_3\)) ppm; m/z (ES-API+) 263.1 (M\(^+\) + 23, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, \(T = 25^\circ\)C) ketone 39.2 min, \(R\) and \(S\) isomer 43.1 min and 46.1 min, configuration was assigned by analogy.

ATH of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide 7r (YZ241)

\((R,R)-3\text{C-tethered Ru(II)-TsDPEN catalyst (0.74 mg, 0.00168 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide 7r (40 mg, 0.12 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (4:1 hexane: EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. The solvent was removed to give the crude product. Crude NMR indicated there was only about 20% conversion. The reaction was also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, \(T = 25^\circ\)C); \((R,R)-3\text{C-tethered Ru(II)-TsDPEN catalyst: 20% conversion and 11.9% ee.}\)

Racemic, by methylation (YZ360): To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q (113.6 mg, 0.347 mmol) in DMF (3.5 mL) was added potassium carbonate (57.4 mg, 0.416 mmol) and iodomethane (49.3 mg, 0.347 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r as a white solid (47.8 mg, 0.140 mmol, 40.3%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO\(_4\); Mp: 81 °C; HRMS: [found (ESI+): [M+Na]+, Calcd for C\(_{21}\)H\(_{27}\)NNaO\(_3\) 364.1886; Found 364.1883; -0.8 ppm error; \(v_{\text{max}}\) 3387 (br), 2968, 2872, 1595, 1463, 1442, 1371, 1237 cm\(^{-1}\); \(\delta\)H (500 MHz, CDCl\(_3\)) 7.77-7.57 (1H, m, ArH), 7.39-7.07 (5H, m, ArH), 6.96-6.75 (2H, m, ArH), 6.08 (1H, s, ArCHOH), 4.52 (1H, s, ArCHOH), 4.02-3.97 (1H, s, N\[\text{CH(CH}_3\text{)}_2\]), 3.65 (1H, s, N\[\text{CH(CH}_3\text{)}_2\]), 3.61 (3H, s, OCH\(_3\)), 1.63-1.56 (4H, m,
N[CH(CH$_3$)$_2$)$_2$], 1.49-1.44 (2H, m, N[CH(CH$_3$)$_2$)$_2$], 1.24-1.16 (5H, m, N[CH(CH$_3$)$_2$)$_2$], 1.06 (1H, d, J = 6.6, N[CH(CH$_3$)$_2$)$_2$] ppm; $\delta$C (125 MHz, CDCl$_3$) 172.0 (C), 155.9 (C), 142.0 (C), 137.0 (C), 131.6 (CH), 129.3 (C), 128.9 (CH), 128.3 (CH), 127.9 (CH), 127.0 (CH), 126.3 (CH), 124.5 (CH), 120.7 (CH), 110.0 (CH), 73.7 (CH), 68.0 (CH), 62.2 (CH$_3$), 55.1 (CH$_3$), 51.5 (CH$_3$), 46.2 (CH$_3$), 20.4 (CH$_3$) ppm; m/z (ES-API+) 263.1 (M$^+$ + 23, 100%).

Racemic, by methylation (YZ360) and asymmetric, by methylation (YZ363,YZ370): Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.5 mL/min, T = 25°C) ketone 39.2 min, R and S isomer 49.2 min and 53.8 min, configuration was assigned by analogy.

Asymmetric, by methylation (YZ363,YZ370): To a solution of 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide $8q$ (69.4 mg, 0.212 mmol) in DMF (2 mL) was added potassium carbonate (35.1 mg, 0.254 mmol) and iodomethane (30.1 mg, 0.212 mmol) at rt. The reaction mixture was left stirring under the nitrogen atmosphere overnight. TLC (4:1 hexane:EtOAc) after this time indicated full conversion. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide $8r$ as a white solid (48.8 mg, 0.143 mmol, 67.4%). ($R,R$)-3C-tethered Ru(II)-TsDPEN catalyst: $[\alpha]_b^{24}$ -110.9 (c 0.815 in CHCl$_3$) 86.8% ee
$^1$H NMR (500 MHz, CDCl$_3$) of 8r:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 8r:
COSY (500 MHz, CDCl₃) of 8r:

![COSY spectrum of 8r](image)

HSQC (500 MHz, CDCl₃) of 8r:

![HSQC spectrum of 8r](image)
HMBC (500 MHz, CDCl$_3$) of $8r$:

HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide $8r$ (YZ216):

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HPLC after ATH of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide 7r (YZ241): 
(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 20% conversion, 11.9% ee).

Signal 2: MWD1 C, Sig=210,4 Ref=off

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Totals: 1.56706e4 209.07749
HPLC of racemic 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r (after methylation of racemic 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8q, YZ360).

HPLC after methylation of asymmetric 2-(hydroxy(2-hydroxyphenyl)methyl)-N,N-diisopropylbenzamide 8c (YZ363; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst, 86.8% ee).
N,N-Diisopropyl-2-(2-methoxybenzoyl)benzamide 7r.

This compound is novel.

To a solution of 2-(hydroxy(2-methoxyphenyl)methyl)-N,N-diisopropylbenzamide 8r (100 mg, 0.29 mmol) in DCM (1 mL) at rt was added pyridinium chlorochromate (95 mg, 0.44 mmol). The reaction mixture was left to stir under a nitrogen atmosphere overnight. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. The solids were removed by gravity filtration and was washed with DCM. The combined solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide 8r as a colorless oil (28.1 mg, 0.08 mmol, 28%).

TLC: Rf ca 0.20 (4:1 hexane: EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+Na]+, Calcd for C₂₁H₂₅NNaO₃ 362.1729; Found 362.1727; -0.6 ppm error; vₘₐₓ 2970, 2933, 1624, 1597, 1434, 1339, 1243 cm⁻¹; δₜₜ (500 MHz, CDCl₃) 7.50-7.40 (4H, m, ArH), 7.31-7.26 (2H, m, ArH), 6.99 (1H, t, J = 7.4, ArH), 6.94 (1H, d, J = 8.7, ArH), 3.74-3.71 (1H, m, N(CH(CH₃)₂)₂), 3.68 (3H, s, OCH₃), 3.48-3.46 (1H, m, N(CH(CH₃)₂)₂), 1.55 (6H, d, J = 6.8, N(CH(CH₃)₂)₂), 1.17-1.10 (6H, m, N(CH(CH₃)₂)₂) ppm; δc (125 MHz, CDCl₃) 196.0 (C), 170.0 (C), 157.9 (C), 139.3 (C), 136.2 (C), 132.6 (CH), 131.8 (CH), 131.1 (CH), 130.7 (CH), 128.6 (C), 127.5 (CH), 126.3 (CH), 120.5 (CH), 111.5 (CH), 55.6 (CH), 51.0 (CH), 45.6 (CH₃), 23.9 (CH₃), 20.8 (CH₃), 20.4 (CH₃) ppm; m/z (ES-API+) 362.3 (M⁺ + 23, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of 7r:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 7r:
COSY (500 MHz, CDCl₃) of 7r:

HSQC (500 MHz, CDCl₃) of 7r:
HMBC (500 MHz, CDCl₃) of 7r:

HPLC of N,N-diisopropyl-2-(2-methoxybenzoyl)benzamide 7r:

Signal 2: MWD1 C, Sig=210,4 Ref=off

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Totals:

|        | \text{3.14424e5} | 2680.12549 |
(2-Aminophenyl)(phenyl)methanone 7s.

This compound has been reported and fully characterized.


To a solution of 2-aminobenzonitrile (250 mg, 2.12 mmol) in THF (2.5 mL) was added phenyl magnesium bromide (2.12 mL, 3.0 M in diethyl ether, 6.36 mmol) dropwise at 0°C and the reaction was stirred under a nitrogen atmosphere for 12 hours and allowed to warm to rt. After cooling down to 0°C, HCl solution (6.36 mL, 2.0 M, 12.7 mmol) was added dropwise and the mixture was stirred at rt for another 12 hours. TLC (9:1 hexane: EtOAc) after this time indicated full conversion. The mixture was basified to pH = 9 with 10% NaOH solution and extracted with EtOAc (20 mL × 3). The combined organic layers were then washed with brine (20 mL) and dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanone 7s as a yellow solid (99.1 mg, 0.50 mmol, 23.8%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and KMnO₄; δH (400 MHz, CDCl₃) 7.65 (2H, d, J = 6.0, ArH), 7.53-7.44 (3H, m, ArH), 7.31-7.26 (2H, m, ArH), 6.75 (1H, d, J = 8.4, ArH), 6.60 (1H, t, J = 7.6, ArH), 6.09 (2H, s, NH₂) ppm; δC (100 MHz, CDCl₃) 150.9 (C), 134.6 (CH), 134.3 (CH), 131.1 (CH), 129.1 (CH), 128.1 (CH), 117.0 (CH), 115.5 (CH). Data matched that reported.
$^1$H NMR (400 MHz, CDCl$_3$) of 7s:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 7s:
HPLC of (2-aminophenyl)(phenyl)methanone 7s:
(2-Aminophenyl)(phenyl)methanol 8s.

\[
\begin{align*}
\text{NH}_2 \text{OH} & \quad \text{NH}_2 \text{O} \\
\text{Ar} & \quad \text{Ar} \\
\text{NaBH}_4 & \quad \text{MeOH} \\
\end{align*}
\]

This compound has been reported and fully characterized.


To a solution of (2-aminophenyl)(phenyl)methanone 7s (100 mg, 0.51 mmol) in MeOH (3 mL) was added sodium borohydride (96.9 mg, 2.55 mmol). The reaction was stirred for 4 hours. TLC (9:1 hexane:EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 mL), dried with MgSO₄, and the solvent was removed under vacuum to give crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol 8s as a yellow oil (40.6 mg, 0.20 mmol, 40.2%). TLC: Rf ca 0.30 (9:1 hexane:EtOAc), strong UV and KMnO₄; \(\delta_H\) (500 MHz, CDCl₃) 7.41-7.30 (5H, m, ArH), 7.15-7.11 (1H, m, ArH), 7.05 (1H, d, \(J = 7.5\), ArH), 6.77-6.74 (1H, m, ArH), 6.69 (1H, d, \(J = 8.0\), ArH), 5.87 (1H, s, ArCHOH), 3.97 (2H, s, NH₂), 2.61 (1H, s, ArCHOH) ppm; \(\delta_C\) (125 MHz, CDCl₃) 144.9 (C), 141.9 (C), 129.0 (CH), 128.7 (CH), 128.5 (CH), 127.7 (CH), 127.5 (C), 126.6 (CH), 118.4 (CH), 117.0 (CH), 75.0 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 23.3 min, \(R\) isomer 36.0 min and \(S\) isomer 29.3 min.

ATH of (2-aminophenyl)(phenyl)methanone 7s (YZ221):

Catalyst \((R,R)-2\) (0.0023 mmol, 1mol%) was added to the FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was stirred under a nitrogen atmosphere for 10-15 minutes; after which a solution of (2-aminophenyl)(phenyl)methanone 7s (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere, followed by TLC (9:1
hexane: EtOAc). After 168 hours, the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give (2-aminophenyl)(phenyl)methanol 8s (15.2 mg, 0.076 mmol, 37.6%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC (Chiralcel ODH, 30 cm x 6 mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 91% conversion (HPLC calibration: 1:1 (2-aminophenyl)(phenyl)methanone : (2-aminophenyl)(phenyl)methanol gives 6.04:1 absorption at 254 nm); [α]D²⁵ -13.6 (c 0.022 in MeOH) 46.2% ee (R) (lit. [α]D²⁰ +43.7 (c 1.0 in MeOH) 87% ee (S)) Reference: Mannam, S.; Sekar, G. Tetrahedron: Asymmetry, 2009, 20, 497-502.

¹H NMR (500 MHz, CDCl₃) of 8s:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 8s:

HPLC of racemic (2-aminophenyl)(phenyl)methanol 8s:
HPLC of 8s after ATH of (2-aminophenyl)(phenyl)methanone 7s:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 168 hours, 91% conversion, 46.2% ee, R configuration).
Synthesis and characterisation of compounds 9-15.

Note on reaction not illustrated in paper: Imine A was prepared from 2’-hydroxyacetophenone in 93% yield and was converted to the racemic amine B using sodium borohydride (Figure S2). However in attempts at ATH with catalyst (R,R)-2 using FA/TEA/DCM the hydrolysis of B was the major reaction. The alternative use of ammonium formate in DCM, at 70 °C (sealed tube) as reported by Mangion et al. (reference 10 in main paper) was used in order to avoid hydrolysis, but the major product was the dimer C rather than the desired amine B.

![Figure S2. Attempted reduction of imine from 2’-hydroxyacetophenone.](image)

2’-Hydroxyacetophenone imine A.

This compound has been reported and fully characterized.


2’-Hydroxyacetophenone (250 mg, 1.84 mmol) was dissolved in ammonia (1.32 mL, 7N in MeOH, 9.2 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. TLC (1: 1 hexane: EtOAc) after this time indicated full conversion. The solvent was removed to give the product A as a yellow solid (231.2 mg, 1.71 mmol, 93%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 140 °C; δH (500 MHz, CDCl₃) 15.14 (1H, s, ArOH), 9.18 (1H, s, NH), 7.50 (1H, dd, J = 8.0, 1.2, ArH), 7.43-7.30 (1H, m, ArH), 6.97 (1H, d, J = 8.2, ArH), 6.81 (1H, t, J = 7.5, ArH), 2.49 (3H, s, CH₃) ppm; δC (125 MHz, CDCl₃) 133.4 (CH), 129.0 (CH), 118.5 (C), 117.6 (CH), 26.2 (CH₃) ppm. Data matched that reported.
$^1$H NMR (500 MHz, CDCl$_3$) of 2'-Hydroxyacetophenone imine A:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 2'-Hydroxyacetophenone imine A:
HPLC of 2'-hydroxyacetophenone imine A:

![HPLC Graph]

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2-(1-Aminoethyl)phenol B.

\[
\begin{align*}
\text{racemic: YZ83. Asymmetric: YZ85, YZ97, YZ106}
\end{align*}
\]

This compound has been reported and fully characterized.


To a solution of 2'-hydroxyacetophenone \( A \) (40 mg, 0.296 mmol) in MeOH (1 mL) was added sodium borohydride (22.5 mg, 0.592 mmol). The reaction was stirred for 4 hours. TLC (1: 1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 x 20ml), dried with MgSO\(_4\), and the solvent was removed under vacuum to give 2-(1-aminoethyl)phenol \( B \) as a white solid (40.6 mg, 0.296 mmol, 88.9%). \( \delta \)\(_H\) (400 MHz, CDCl\(_3\)) 7.20-7.13 (1H, m, ArH), 6.97 (1H, d, \( J = 7.3 \), ArH), 6.84 (1H, d, \( J = 8.3 \), ArH), 6.78 (1H, t, \( J = 7.2 \), ArH), 4.33 (1H, q, \( J = 6.8 \), CH\(_2\)N\(_2\)), 1.48 (3H, d, \( J = 6.6 \), CH\(_3\)) ppm; \( \delta \)\(_C\) (100 MHz, CDCl\(_3\)) 157.6 (C), 128.5 (CH), 128.1 (C), 127.2 (CH), 119.0 (CH), 117.2 (CH), 51.7 (CH), 23.9 (CH\(_3\)) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) ketone 21.8 min, \( R \) and \( S \) isomers 13.1 min and 16.6 min, configuration is not known.

Attempt ATH in FA/TEA of 2'-Hydroxyacetophenone imine \( A \) (YZ85).

Catalyst \((R,R)\)-2 (0.00296 mmol, 1mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was left to stir under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2'-Hydroxyacetophenone imine \( A \) (40 mg, 0.296 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirred under a nitrogen atmosphere overnight. The reaction was followed by TLC (19:1 DCM: MeOH). Then the reaction was quenched using saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. However, NMR indicated there is no product present. The starting material was hydrolysed.
Attempt ATH in water of A using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 and formation of C (YZ97 and YZ106).

2'-Hydroxyacetophenone imine A (40 mg, 0.296 mmol), ammonium formate (74.6 mg, 1.184 mmol) and (R,R)-3C-tethered Ru(II)-TsDPEN catalyst (0.92 mg, 0.00148 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. Dry DCM (1.5 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated NaHCO₃ solution (20 mL). After which EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO4) and filtered. NMR indicated there was no product present. m/z (ES-API+) 258.3 (M⁺ + 1, 100%) indicated the product was the dimer C.

³¹H NMR (400 MHz, CDCl₃) amine B:
\[ ^{13}\text{C NMR (100 MHz, CDCl}_3\text{) of amine B:} \]

Phenyl 2-phenylacetate.

This compound has been reported and fully characterized.


To a solution of phenol (227 mg, 2.42 mmol) and pyridine (190.8 mg, 2.415 mmol) in dry DCM (5 mL) was added dropwise 2-phenylacetyl chloride (250 mg, 1.61 mmol). The reaction mixture was stirred under a nitrogen atmosphere overnight. TLC (9:1 hexane:EtOAc) after this time indicated full conversion. After 17 hours, distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO\textsubscript{4}, and the solvent was removed under vacuum to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-20% ethyl acetate in hexane to give phenyl 2-phenylacetate as a white solid (308 mg, 1.45 mmol,
89.8%). TLC: Rf ca 0.50 (9:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 43 °C; δₜ (400 MHz, CDCl₃) 7.40-7.32 (7H, m, ArH), 7.26-7.21 (1H, m, ArH), 7.08 (2H, d, J = 7.6, ArH), 3.87 (2H, s, CH₂) ppm; δₖ (100 MHz, CDCl₃) 170.0 (C), 150.8 (C), 133.5 (C), 129.4 (CH), 129.3 (CH), 128.8 (CH), 127.4 (CH), 125.9 (CH), 121.5 (CH), 41.5 (CH₂) ppm. Data matched that reported.

¹H NMR (400 MHz, CDCl₃) of phenyl 2-phenylacetate:
$^{13}$C NMR (100 MHz, CDCl$_3$) of phenyl 2-phenylacetate:
1-(2-Hydroxyphenyl)-2-phenylethan-1-one.

This compound has been reported and fully characterized.


Phenyl 2-phenylacetate (300 mg, 1.42 mmol) was mixed with aluminium chloride (378 mg, 2.84 mmol) and the mixture heated on a hot plate at 100°C for 1.5 hr. Then the mixture was cooled in an ice bath and decomposed with 2M HCl solution. Chloroform was added and the organic layer was separated. The aqueous layer was extracted with CHCl₃ (3 × 20 mL). The combined organic layer was washed with water (3 × 20 mL), 2M NaOH solution (3 × 20 mL) and water (3 × 20 mL), successively, dried (MgSO₄) and filtered. Solvent was removed to give the crude product. The reaction was followed by TLC (9:1 hexane: ethyl acetate). The product was isolated via flash chromatography on silica eluted with 0-10% ethyl acetate in hexane to give 1-(2-hydroxyphenyl)-2-phenylethan-1-one as a white solid (153.2 mg, 0.72 mmol, 51.1%). TLC: Rf ca 0.40 (9:1 hexane: EtOAc), strong UV and KMnO₄; δH (400 MHz, CDCl₃) 12.22 (1H, s, OH), 7.88 (1H, d, J = 8.0, ArH), 7.47 (1H, t, J = 7.6, ArH), 7.37-7.26 (5H, m, ArH), 7.00 (1H, d, J = 8.4, ArH), 6.90 (1H, t, J = 7.6, ArH), 4.31 (2H, s, CH₂) ppm; δC (100 MHz, CDCl₃) 203.9 (C), 136.6 (CH), 133.9 (C), 130.4 (CH), 129.4 (CH), 128.8 (CH), 127.2 (CH), 119.0 (CH), 118.7 (CH), 45.2 (CH₂) ppm. The data matched that reported.
$^1$H NMR (400 MHz, CDCl$_3$) of 1-(2-hydroxyphenyl)-2-phenylethan-1-one:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 1-(2-hydroxyphenyl)-2-phenylethan-1-one:
2-(1-Imino-2-phenylethyl)phenol 9.

\[
\begin{array}{c}
\text{NH} \\
\text{OH}
\end{array}
\begin{array}{c}
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\begin{array}{c}
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This compound has been reported but not fully characterized.


1-(2-Hydroxyphenyl)-2-phenylethan-1-one (50 mg, 0.71 mmol) was dissolved in ammonia (1.72 mL, 7N in MeOH, 12.1 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product 9 as a yellow solid (104.8 mg, 0.50 mmol, 70.3%).

TLC: Rf ca 0.30 (9:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 97 °C; HRMS: (found (ESI+): [M+H]+, Calcd for C₁₄H₁₄NO 212.1066; Found 212.1070; 1.9 ppm error); \(\nu\)max 3353, 2922, 2852, 1604, 1518, 1473, 1251, 855, 740 cm⁻¹; \(\delta\)H (500 MHz, CDCl₃) 15.19 (1H, s, OH), 9.10 (1H, s, NH), 7.69-7.67 (1H, m, ArH), 7.43 (2H, t, \(J = 7.3\), ArH), 7.41-7.31 (2H, m, ArH), 7.21 (2H, d, \(J = 7.0\), ArH), 7.02 (1H, d, \(J = 8.5\), ArH), 6.86 (1H, t, \(J = 7.5\), ArH), 4.15 (2H, s, CH₂) ppm; \(\delta\)C (125 MHz, CDCl₃) 179.0 (C), 163.2 (C), 133.2 (CH), 133.2 (C), 130.4 (CH), 129.4 (CH), 129.3 (CH), 127.9 (CH), 118.6 (CH), 118.5 (C), 117.7 (CH), 42.5 (CH₂) ppm; m/z (ES-API+) 212.2 (M+ + 1, 100%).
$^1$H NMR (500 MHz, CDCl$_3$) of 9:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 9:
COSY (500 MHz, CDCl₃) of 9:

![COSY spectrum of 9]

HSQC (500 MHz, CDCl₃) of 9:

![HSQC spectrum of 9]
HMBC (500 MHz, CDCl₃) of 9:

HPLC of 2-(1-imino-2-phenylethyl)phenol 9:
1-(2-Aminophenyl)-2-phenylethan-1-ol 12.

racemic: YZ99. Asymmetric: YZ107, YZ114, YZ121, YZ123, YZ131

This compound is novel.

To a solution of 2-(1-imino-2-phenylethyl)phenol 9 (50 mg, 0.237 mmol) in MeOH (1 mL) was added sodium borohydride (18.1 mg, 0.474 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane:EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 x 20ml), dried with MgSO₄, and the solvent was removed under vacuum to give 1-(2-aminophenyl)-2-phenylethan-1-ol 12 as a yellow oil (39 mg, 0.18 mmol, 78%). TLC: Rf ca 0.20 (1:1 hexane:EtOAc), strong UV and KMnO₄; HRMS: (found (ESI+): [M+H]+, Calcd for C₁₄H₁₆NO 214.1227; Found 214.1226; -0.2 ppm error); ν max 3369, 3300, 3026, 2921, 1585, 1490, 1254, 1030, 751, 698 cm⁻¹; δ H (500 MHz, CDCl₃) 7.36 (2H, t, J = 7.5, ArH), 7.29-7.22 (3H, m, ArH), 7.19-7.16 (1H, m, ArH), 6.96 (1H, d, J = 7.0, ArH), 6.89 (1H, d, J = 8.5, ArH), 6.78 (1H, t, J = 7.5, ArH), 4.33 (1H, dd, J = 10.5, 5.0, CHNH₂), 3.11-3.07 (1H, m, CH₂), 2.98-2.93 (1H, m, CH₂) ppm; δ c (125 MHz, CDCl₃) 157.7 (C), 138.0 (C), 129.3 (CH), 128.8 (CH), 128.7 (CH), 127.8 (CH), 126.9 (CH), 126.8 (C), 119.1 (CH), 117.4 (CH), 58.0 (CH), 43.2 (CH₂) ppm; m/z (ES-API+) 214.2 (M⁺ + 1, 100%).

Enantiomeric excess andconversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane: iPrOH 9:1, 1.0 mL/min, T = 25°C) ketone 22.5 min, R isomer and S isomers 17.9 min and 20.5 min, configuration assigned by analogy with reported reduction.

ATH of 2-(1-imino-2-phenylethyl)phenol 9 (YZ107, 114.121.123.131).
(MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 50%-100% ethyl acetate in hexane to give 1-(2-aminophenyl)-2-phenylethan-1-ol 12 (18.7 mg, 0.088 mmol, 46%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction also by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 9:1, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D²⁴ -27.4 (c 0.0502 in CHCl₃) 84% ee; (S,S)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion, 85% ee; (S,S)-Noyori Ru(II)-TsDPEN catalyst: 100% conversion, 31.8% ee; (R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: 100% conversion, 92% ee; (R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst: 100% conversion, 93.2% ee.

¹H NMR (500 MHz, CDCl₃) of 12:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 12:

COSY (500 MHz, CDCl$_3$) of 12:
HSQC (500 MHz, CDCl₃) of 12:

HMBC (500 MHz, CDCl₃) of 12:
HPLC of racemic 1-(2-aminophenyl)-2-phenylethan-1-ol 12:

HPLC of 12 after ATH of 2-(1-imino-2-phenylethyl)phenol 9:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (after 24 hours, 100% conversion, 84% ee).
(S,S)-3C-tethered Ru(II)-TsDPEN catalyst 2 (after 24 hours, 100% conversion, 85% ee).

(S,S)-Noyori Ru(II)-TsDPEN catalyst 6 (after 24 hours, 100% conversion, 31.8% ee).
(R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst 5 (after 24 hours, 100% conversion, 92% ee).

(R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst 4 (after 24 hours, 100% conversion, 93.2% ee).
2-(Imino(phenyl)methyl)phenol 10.

This compound has been reported and fully characterized.


2-Hydroxybenzophenone (400 mg, 2.02 mmol) was dissolved in ammonia (1.45 mL, 7N in MeOH, 10.1 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. Then the solvent was removed to give the product 10 as a yellow solid (279.6 mg, 1.42 mmol, 70%). TLC: Rf ca 0.40 (1:1 hexane: EtOAc), strong UV and KMnO₄; δ_H (400 MHz, CDCl₃) 12.04 (1H, s, OH), 9.33 (1H, s, NH), 7.50-7.34 (6H, m, ArH), 7.21 (1H, d, J = 7.6, ArH), 7.06 (1H, d, J = 8.4, ArH), 6.74 (1H, t, J = 7.2, ArH) ppm; δ_C (100 MHz, CDCl₃) 181.4 (C), 163.6 (C), 139.2 (C), 133.5 (CH), 132.2 (CH), 129.9 (CH), 128.7 (CH), 127.2 (CH), 118.4 (CH), 117.9 (CH) ppm; m/z (ES-API+) 198.2 (M⁺ + 1, 100%). Data matched that reported.

_H NMR (400 MHz, CDCl₃) of 10:
$^{13}$C NMR (400 MHz, CDCl$_3$) of 10:

HPLC of 2-(imino(phenyl)methyl)phenol 10:
2-(Amino(phenyl)methyl)phenol 13.

![Chemical Structure Image]

This compound has been reported and fully characterized.


To a solution of 2-(imino(phenyl)methyl)phenol 10 (80 mg, 0.41 mmol) in MeOH (2 mL) was added sodium borohydride (32 mg, 0.82 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane:EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 ml), dried with MgSO₄, and the solvent was removed under vacuum to give the 2-(amino(phenyl)methyl)phenol 13 as a white solid (60.1 mg, 0.30 mmol, 74.4%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and KMnO₄; δH (400 MHz, CDCl₃) 7.38-7.26 (5H, m, ArH), 7.16 (1H, t, J = 7.0, ArH), 6.90 (1H, d, J = 8.0, ArH), 6.80-6.71 (2H, m, ArH), 5.32 (1H, s, CH₂NH₂) ppm; δC (100 MHz, CDCl₃) 157.9 (C), 143.2 (C), 129.0 (CH), 128.6 (CH), 127.8 (CH), 127.0 (CH), 126.3 (C), 119.1 (CH), 117.4 (CH), 60.0 (CH) ppm; m/z (ES-API+) 120.2 (M⁺ + 1, 100%). Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 7:3, 0.7 mL/min, T = 25°C) ketone 8.02 min, R isomer 20.7 min and S isomer 13.5 min.

ATH of 2-(1-imino-2-phenylethyl)phenol (YZ154, 156, 159, 160, 163).

Attempted ATH of 10 using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 in FA/TEA (YZ154). Catalyst (R,R)-2 (0.002 mmol, 1 mol%) was added to FA: TEA (5:2 azeotropic mixture, 0.18 mL) at rt and the mixture was left to stir under a nitrogen inert atmosphere for 10-15 minutes; after which a solution of 2-(1-imino-2-phenylethyl)phenol 13 (40 mg, 0.20 mmol) in DCM (0.25 mL) was added. The reaction mixture was stirrer under a nitrogen atmosphere overnight. The reaction was
followed by TLC (1:1 hexane: EtOAc). Then the reaction was quenched using saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. However, NMR indicated there were both alcohol and imine present.

ATH of 13 using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 in water (YZ156, 159, 160, 163).

2-(1-Imino-2-phenylethyl)phenol 10 (40 mg, 0.20 mmol), ammonium formate (50.4 mg, 0.80 mmol) and catalyst (R,R)-2 (0.0010 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. DCM (1 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated NaHCO₃ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 50%-100% ethyl acetate in hexane to give 2-(amino(phenyl)methyl)phenol 13 (8.3 mg, 0.042 mmol, 20.5%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 7:3, 0.7 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D -2.41 (c 0.0415 in CHCl₃) 75.2% ee (R). Product is highly coloured. (lit. [α]D +109.2 (c 0.60 in CHCl₃) 96% ee (S)) Reference: Wang, Y.-Q.; Yu, C.-B.; Wang, D.-W.; Wang, X.-B.; Zhou, Y.-G. Org. Lett. 2018, 10, 2071-2074; (S,S)-Noyori Ru(II)-TsDPEN catalyst: no conversion; (R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst: no conversion; (R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst: no conversion.
$^1$H NMR (400 MHz, CDCl$_3$) of 13:

$^{13}$C NMR (100 MHz, CDCl$_3$) of 13:
HPLC of racemic 2-(amino(phenyl)methyl)phenol 13:

HPLC of 13 after ATH of 2-(1-imino-2-phenylethyl)phenol 10:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 100% conversion, 75.2% ee, R configuration)
(S,S)-Noyori Ru(II)-TsDPEN catalyst (no conversion).

(R,R)-3C-tethered, 4-methoxy-Ru(II)-TsDPEN catalyst (no conversion).
(R,R)-benzyl-tethered Ru(II)-TsDPEN catalyst (no conversion).
**Compound name:** 2-(Imino(2-methoxyphenyl)methyl)phenol 11.

![ChemAxon](image)

This compound is novel.

(2-Hydroxyphenyl)(2-methoxyphenyl)methanone (114 mg, 0.50 mmol) was dissolved in ammonia (1.2 mL, 7N in MeOH, 8.5 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product 11 as a brown solid (98.4 mg, 0.43 mmol, 86.7%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; Mp: 95 °C; HRMS: (found [ESI+]: [M+Na]+, Calcd for C_{14}H_{14}NO_{2} 228.1017; Found 228.1019; 0.1 ppm error); ν\textsubscript{max} 2937, 2838, 1602, 1490, 1281, 1023, 902 cm\textsuperscript{-1}; δ\textsubscript{H} (500 MHz, CDCl\textsubscript{3}) 14.70 (1H, s, OH), 9.37 (1H, s, NH), 7.45 (1H, t, J = 7.5, ArH), 7.32 (1H, t, J = 7.0, ArH), 7.21 (1H, d, J = 7.5, ArH), 7.06-7.00 (4H, m, ArH), 6.69 (1H, t, J = 7.5, ArH), 3.77 (3H, s, OCH\textsubscript{3}) ppm; δ\textsubscript{C} (125 MHz, CDCl\textsubscript{3}) 179.1 (C), 163.3 (C), 155.8 (C), 133.1 (CH), 131.8 (CH), 130.9 (CH), 128.7 (CH), 127.8 (C), 120.6 (CH), 119.1 (C), 118.1 (CH), 117.6 (CH), 111.3 (CH), 55.6 (CH\textsubscript{3}) ppm; m/z (ES-API+) 228.3 (M\textsuperscript{+} + 1, 100%).

\textsuperscript{1}H NMR (500 MHz, CDCl\textsubscript{3}) of 11:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 11:

COSY (500 MHz, CDCl$_3$) of 11:
HSQC (500 MHz, CDCl$_3$) of \textbf{11}:

HMBC (500 MHz, CDCl$_3$) of \textbf{11}:
HPLC of 2-(imino(2-methoxyphenyl)methyl)phenol 11:

![HPLC graph and table]

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2-(Amino(2-methoxyphenyl)methyl)phenol.

This compound is novel.

Racemic: To a solution of 2-(imino(2-methoxyphenyl)methyl)phenol 11 (98 mg, 0.43 mmol) in MeOH (2 mL) was added sodium borohydride (33 mg, 0.86 mmol). The reaction was stirred for 4 hours. TLC (1:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO$_4$, and the solvent was removed under vacuum to give 2-(amino(2-methoxyphenyl)methyl)phenol as a brown oil (48 mg, 0.21 mmol, 48.5%). TLC: Rf ca 0.20 (1:1 hexane: EtOAc), strong UV and KMnO$_4$; HRMS: (found (ESI+): [M+Na]$^+$, Calcd for C$_{14}$H$_{16}$NO$_2$ 230.1174; Found 230.1176; 0.8 ppm error); $\nu_{\text{max}}$ 3375, 2926, 2852, 1732, 1585, 1487, 1237, 1021, 748 cm$^{-1}$; $\delta_H$ (500 MHz, CDCl$_3$) 7.31-7.28 (1H, m, ArH), 7.19-7.16 (1H, m, ArH), 6.95-6.90 (4H, m, ArH), 6.73-6.71 (2H, m, NH$_2$), 5.57 (1H, s, CH), 3.85 (3H, s, OCH$_3$) ppm; $\delta_C$ (125 MHz, CDCl$_3$) 158.5 (C), 157.0 (C), 130.3 (C), 129.0 (CH), 128.8 (CH), 128.8 (CH), 128.4 (CH), 125.6 (C), 121.0 (CH), 118.9 (CH), 117.2 (CH), 110.8 (CH), 55.4 (CH$_3$) ppm; m/z (ES-API+) 230.3 (M$^+$ + 1, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak ADH, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.5 mL/min, T = 25°C) imine 17.6 min, $R$ and $S$ isomers 18.4 min and 20.0 min, configuration is not known.

Attempted reduction of 2-(imino(2-methoxyphenyl)methyl)phenol 11 (YZ192).

2-(Imino(2-methoxyphenyl)methyl)phenol 11 (40 mg, 0.176 mmol), ammonium formate (44.4 mg, 0.704 mmol) and catalyst (0.00088 mmol, 0.5 mol%) were added to a sealed tube and stirred under a nitrogen atmosphere for 10 minutes. DCM (0.88 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated NaHCO$_3$ solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO$_4$) and filtered. The solvent was removed. The reaction also followed by HPLC analysis (Chiralpak
ADH, 30 cm x 6mm column, hexane: iPrOH 9:1, 0.5 mL/min, T = 25°C). NMR and HPLC indicated no product present.

$^1$H NMR (500 MHz, CDCl$_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 2-(Amino(2-methoxyphenyl)methyl)phenol:
COSY (500 MHz, CDCl₃) of 2-(Amino(2-methoxyphenyl)methyl)phenol:

HSQC (500 MHz, CDCl₃) of 2-(Amino(2-methoxyphenyl)methyl)phenol:
HMBC (500 MHz, CDCl₃) of 2-(Amino(2-methoxyphenyl)methyl)phenol:

HPLC of racemic 2-(imino(2-methoxyphenyl)methyl)phenol of 2-(Amino(2-methoxyphenyl)methyl)phenol:
HPLC after ATH of 2-(imino(2-methoxyphenyl)methyl)phenol:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (no conversion).
2-((2-Chlorophenyl)(imino)methyl)phenol.

This compound is novel.

(2-Chlorophenyl)(2-hydroxyphenyl)methanone (156.4 mg, 0.674 mmol) was dissolved in ammonia (1.64 mL, 7N in MeOH, 11.46 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product as a brown oil (76.7 mg, 0.332 mmol, 49.3%). TLC: Rf ca 0.50 (4:1 hexane: EtOAc), strong UV and KMnO$_4$; HRMS: (found (ESI+): [M+H]+, Calcd for C$_{13}$H$_{11}$ClNO 232.0522; Found 232.0524; 0.8 ppm error); $\nu_{\text{max}}$ 3061 (br), 1626, 1590, 1473, 1445, 1241, 935 cm$^{-1}$; $\delta_{\text{H}}$ (500 MHz, CDCl$_3$) 11.97 (1H, s, OH), 7.45 (3H, m, ArH), 7.45-7.34 (2H, m, ArH), 7.32-7.28 (1H, m, ArH), 7.13-7.05 (1H, m, ArH), 6.94-6.74 (1H, m, ArH) ppm; $\delta_{\text{C}}$ (125 MHz, CDCl$_3$) 200.6 (C), 163.2 (C), 137.4 (C), 137.2 (CH), 133.5 (CH), 131.3 (CH), 130.9 (C), 130.1 (CH), 128.6 (CH), 126.8 (CH), 119.4 (C), 119.1 (CH), 118.4 (CH) ppm; m/z (ES-API+) 232.3 (M$^+$ + 1, 100%).

$^1$H NMR (500 MHz, CDCl$_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:
$^{13}$C NMR (125 MHz, CDCl$_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:

COSY (500 MHz, CDCl$_3$) 2-((2-Chlorophenyl)(imino)methyl)phenol:
HSQC (500 MHz, CDCl₃) 2-((2-Chlorophenyl)(imino)methyl)phenol:
HPLC of 2-((2-chlorophenyl)(imino)methyl)phenol:

![HPLC graph](image)

### Result Table

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2-(Amino(2-chlorophenyl)methyl)phenol 14.

\[
\begin{array}{c}
\text{Cl} \quad \text{NN}_2 \quad \text{OH} \\
\text{Cl} \quad \text{NH} \quad \text{OH} \\
\end{array}
\]

racemic: YZ292. Asymmetric: YZ315

This compound is novel.

To a solution of 2-((2-chlorophenyl)(imino)methyl)phenol (70.8 mg, 0.306 mmol) in MeOH (1.4 mL) was added sodium borohydride (23.3 mg, 0.612 mmol). The reaction was stirred for 4 hours. TLC (4:1 hexane: EtOAc) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20 ml), dried with MgSO\(_4\), and the solvent was removed under vacuum to give 2-(amino(2-chlorophenyl)methyl)phenol 14 as a yellow oil (20.2 mg, 0.0867 mmol, 28.3%). TLC: Rf ca 0.40 (4:1 hexane: EtOAc), strong UV and KMnO\(_4\); HRMS: (found (ESI+): [M+H]+, Calcd for C\(_{13}\)H\(_{13}\)ClNO 234.0674; Found 234.0680; 2.7 ppm error); \(\nu_{\text{max}}\) 3060, 3039, 2955, 2924, 2844, 1592, 1242, 1009, 823 cm\(^{-1}\); \(\delta_{\text{H}}\) (500 MHz, CDCl\(_3\)) 7.84 (1H, s, OH), 7.34-7.08 (6H, m, ArH), 6.94-6.83 (1H, m, ArH), 6.72-6.88 (1H, m, ArH), 6.52-6.36 (1H, m, CH) ppm; \(\delta_{\text{C}}\) (125 MHz, CDCl\(_3\)) 156.0 (C), 149.9 (C), 133.1 (C), 130.0 (CH), 129.8 (CH), 129.7 (CH), 129.6 (CH), 129.2 (CH), 128.1 (CH), 127.5 (CH), 124.6 (C), 120.1 (CH), 117.6 (CH) ppm; m/z (ES-API+) 234.2 (M\(^+\) + 1, 100%).

Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane: iPrOH 95:5, 1.0 mL/min, T = 25°C) imine 13.2 min, \(R\) and \(S\) isomers 19.6 min and 23.4 min, configuration was assigned by analogy.

ATH of 2-((2-chlorophenyl)(imino)methyl)phenol using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (YZ315).

2-((2-Chlorophenyl)(imino)methyl)phenol (40 mg, 0.173 mmol), ammonium formate (44 mg, 0.692 mmol) and catalyst (R,R)-2 (0.00085 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. DCM (0.87 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched by saturated NaHCO\(_3\) solution (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO\(_4\)) and filtered. Solvent was removed to give the product 14 (27.4 mg, 0.118 mmol, 67.9%). The
reaction also followed by HPLC analysis (Chiralpak IA, 30 cm x 6mm column, hexane: iPrOH 95:5, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst: 100% conversion; [α]D 27 -101 (c 0.048 in CHCl₃) 97.4% ee.

1H NMR (500 MHz, CDCl₃) of 14b:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 14:

COSY (500 MHz, CDCl$_3$) of 14:
HSQC (500 MHz, CDCl₃) of 14:

HMBC (500 MHz, CDCl₃) of 14:
HPLC of racemic 2-(amino(2-chlorophenyl)methyl)phenol 14:

![HPLC graph](image)

**Result Table (Uncal - C:\Clarity\WORK\DATA\ye zheng\YE292 IA 1.0 ppm 9505 hex IPA run one 050919 - U-PAD2 - 1)**

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HPLC of 14 after ATH of 2-(imino(2-methoxyphenyl)methyl)phenol:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 100% conversion, 97.4% ee).

![HPLC graph](image)

**Result Table (Uncal - C:\Clarity\WORK\DATA\ye zheng\YE315 IA 1.0 ppm 9505 hex IPA run one 020919 - U-PAD2 - 1)**

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2-((4-Chlorophenyl)(imino)methyl)phenol.

This compound has been reported and fully characterized.


(4-Chlorophenyl)(2-hydroxyphenyl)methanone (160 mg, 0.69 mmol) was dissolved in ammonia (1.68 mL, 7N in MeOH, 11.7 mmol) and the mixture was stirred under a nitrogen atmosphere overnight. The solvent was removed to give the product as a dark yellow oil (81.6 mg, 0.353 mmol, 51.2%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO₄; δH (500 MHz, CDCl₃) 14.46 (1H, s, ArOH), 9.36 (1H, s, NH), 7.47 (2H, d, J = 8.4, ArH), 7.42-7.29 (3H, m, ArH), 7.14 (1H, dd, J = 8.0, 1.4, ArH), 7.05 (1H, t, J = 8.3, ArH), 6.75 (1H, t, J = 7.3, ArH) ppm; δC (125 MHz, CDCl₃) 180.3 (C), 163.3 (C), 137.6 (C), 136.1 (C), 133.7 (CH), 131.9 (CH), 129.1 (CH), 128.6 (CH), 118.4 (CH), 118.2 (C), 117.9 (CH) ppm. Data matched that reported.

1H NMR (500 MHz, CDCl₃) of 2-((4-Chlorophenyl)(imino)methyl)phenol.
$^{13}$C NMR (125 MHz, CDCl$_3$) of 2-((4-Chlorophenyl)(imino)methyl)phenol.

HPLC of 2-((4-chlorophenyl)(imino)methyl)phenol:
2-(Amino(4-chlorophenyl)methyl)phenol 15.

This compound has been reported and fully characterized.


To a solution of 2-((4-chlorophenyl)(imino)methyl)phenol (81.6 mg, 0.353 mmol) in MeOH (1.6 mL) was added sodium borohydride (26.8 mg, 0.706 mmol). The reaction was stirred for 4 hours. TLC (99:1 DCM: MeOH) after this time indicated full conversion. Distilled water (20 mL) was added, and the mixture was extracted with EtOAc (3 × 20ml), dried with MgSO_4_, and the solvent was removed under vacuum to give 2-(amino(4-chlorophenyl)methyl)phenol 15 as a yellow oil (74.7 mg, 0.321 mmol, 90.8%).

TLC: Rf ca 0.20 (99:1 DCM: MeOH), strong UV and KMnO_4_; δ_H (500 MHz, CDCl_3) 7.32 (4H, s, ArH), 7.19-7.11 (1H, m, ArH), 6.88 (1H, d, J = 8.0, ArH), 6.79-6.72 (2H, m, ArH), 5.30 (1H, s, ArCHNH_2) ppm; δ_C (125 MHz, CDCl_3) 157.7 (C), 141.6 (C), 133.6 (C), 129.1 (CH), 128.4 (CH), 128.3 (CH), 125.8 (C), 119.3 (CH), 117. (CH), 59.5 (CH) ppm. Data matched that reported.

Enantiomeric excess and conversion determined by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 80:20, 1.0 mL/min, T = 25°C) imine 8.86 min, S isomer 12.3 min and R isomer 15.3 min.

ATH of 2-((4-Chlorophenyl)(imino)methyl)phenol (YZ312) using (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (YZ312).

Ammonium formate (43.6 mg, 0.692 mmol) and (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2 (0.54 mg, 0.000865 mmol, 0.5 mol%) were added into a sealed tube and left to stir under a nitrogen atmosphere for 10 minutes. 2-((4-chlorophenyl)(imino)methyl)phenol (40 mg, 0.173 mmol) with DCM (0.87 mL) was degassed with nitrogen then added under nitrogen to the tube. The mixture was heated to 70 °C on a hot plate and stirred under a nitrogen atmosphere overnight. Then the reaction was quenched using saturated NaHCO_3_ solution (20 mL). EtOAc (20 mL) was added and
the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL) and the combined organic layers were dried (MgSO₄) and filtered. The solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to 2-(amino(4-chlorophenyl)methyl)phenol 15 (15.6 mg, 0.0670 mmol, 38.7%; (R,R)-3C-tethered Ru(II)-TsDPEN catalyst example). The reaction was also followed by HPLC analysis (Chiralcel ODH, 30 cm x 6mm column, hexane:iPrOH 80:20, 1.0 mL/min, T = 25°C); (R,R)-3C-tethered Ru(II)-TsDPEN catalyst 2: 78.7% conversion; [α]D24 -20.4 (c 0.0147 in CHCl₃) 82.2% ee (R) (lit. [α]D24 +99.1 (c 4.06 in CHCl₃) 93% ee (S)) Reference: Nguyen, T. B.; Wang, Q.; Gueritte, F. Chem.- Eur. J. 2011, 17, 9576 – 9580.

1H NMR (500 MHz, CDCl₃) of 15:
$^{13}$C NMR (125 MHz, CDCl$_3$) of 15:

HPLC of racemic 2-(amino(4-chlorophenyl)methyl)phenol 15:
HPLC after ATH of 2-((4-chlorophenyl)(imino)methyl)phenol:

(R,R)-3C-tethered Ru(II)-TsDPEN catalyst (after 24 hours, 78.7% conversion, 82.2% ee, R configuration).
Synthesis and characterisation of reaction product 18.

2-[[1,1'-Biphenyl]-2-yl(hydroxy)methyl]phenol 18.

![Chemical structure of 2-[[1,1'-Biphenyl]-2-yl(hydroxy)methyl]phenol 18.

This compound is novel.

Racemic 18: A round-bottom flask was charged with 2-[[2-bromophenyl](hydroxy)methyl]phenol 8h (100 mg, 0.360 mmol), potassium phenyltrifluoroborate (79.5 mg, 0.720 mmol), sodium carbonate (76.3 mg, 0.720 mmol), Pd(OAc)$_2$ (1.62 mg, 0.00720 mmol) and H$_2$O-PEG (2.16:2.16 g). The reaction mixture was heated to 80 °C on a hot plate and left stirring under the nitrogen atmosphere overnight, followed by TLC (4:1 hexane: EtOAc). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 × 20 mL), and the combined organic layers were dried (MgSO$_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-[[1,1'-biphenyl]-2-yl(hydroxy)methyl]phenol 18 as a colorless oil (50.7 mg, 0.184 mmol, 51.1%). TLC: Rf ca 0.30 (4:1 hexane: EtOAc), strong UV and KMnO$_4$; HRMS: (found (ESI+): [M+Na]+, Calcd for C$_{19}$H$_{16}$NaO$_2$ 299.1044; Found 299.1043; -0.5 ppm error); $\nu_{\text{max}}$ 3298 (br), 3058, 3054, 1478, 1455, 1235, 994, 701 cm$^{-1}$; $\delta_H$ (500 MHz, CDCl$_3$) 8.18 (1H, s, ArOH), 7.57-7.48 (1H, m, ArH), 7.43-7.36 (5H,
Enantiomeric excess and conversion determined by HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) R isomer 16.4 min, S isomer 12.8 min.

Asymmetric 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol 18 (YZ418): A round-bottom flask was charged with (S)-2-((2-bromophenyl)(hydroxy)methyl)phenol (286 mg, 1.03 mmol), potassium phenyltrifluoroborate (228 mg, 1.24 mmol), sodium carbonate (218 mg, 2.06 mmol), Pd(OAc)$_2$ (4.62 mg, 0.0206 mmol) and H$_2$O-PEG (6.18:6.18 g). The reaction mixture was heated to 80 °C on a hot plate and left stirring under the nitrogen atmosphere overnight, followed by TLC (4:1 hexane:EtOAc). The mixture was quenched by distilled water (20 mL). EtOAc (20 mL) was added and the organic layer was separated. The aqueous layer was extracted with EtOAc (3 x 20 mL), and the combined organic layers were dried (MgSO$_4$) and filtered. Solvent was removed to give the crude product. The product was isolated via flash chromatography on silica eluted with 0-50% ethyl acetate in hexane to give 2-([1,1'-biphenyl]-2-yl(hydroxy)methyl)phenol 18 as a colorless oil (147.6 mg, 0.535 mmol, 52%). HPLC analysis (Chiralpak IC, 30 cm x 6mm column, hexane:iPrOH 95:5, 0.8 mL/min, T = 25°C) indicated 96% ee ($R$).
$^1$H NMR (500 MHz, CDCl$_3$) of 18:

$^{13}$C NMR (125 MHz, CDCl$_3$) of 18:
COSY (500 MHz, CDCl₃) of 18:

HSQC (500 MHz, CDCl₃) of 18:
HMBC (500 MHz, CDCl₃) of 18:

HPLC of racemic 2-[[1,1'-biphenyl]-2-yl(hydroxy)methyl]phenol 18:
HPLC of asymmetric 2-[[1,1′-biphenyl]-2-yl(hydroxy)methyl]phenol (96% ee, R configuration) 18: