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Asymmetric electrochemical oxidation of 1,2-diols, aminoalcohols and aminoaldehydes in the presence of chiral copper catalyst

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Abstract—Asymmetric oxidation of 1,2-diols, aminoalcohols and aminoaldehydes in the presence of copper(II) triflate and (R,R)-Ph-BOX, was accomplished by electrochemical method using Br⁻ as a mediator. This oxidation was applicable to kinetic resolution of racemic cis-cycloalkane-1,2-diols, aminoalcohols and aminoaldehydes to afford optically active compounds with good to high enantioselectivity.

Key words: Asymmetric electrochemical oxidation; Copper complex; 1,2-Diol; α-Ketoalcohol; Aminoalcohol; Aminoaldehyde

1. Introduction

Selective oxidation of hydroxyl group to carbonyl group is a basic and important organic reaction. It was reported in 1974 that 1,2-diols are selectively oxidized to the corresponding α-ketoalcohols by utilizing a stoichiometric amount of dibutyltin oxide (Bu₂SnO) which forms dibutylstannylenes followed by brominolysis.¹ From the standpoint of green chemistry, we have reported efficient oxidation of 1,2-diols A by electrochemical method using a catalytic amount of Bu₂SnO and Br⁻ ion to afford α-ketoalcohols B in high yield without 1,2-diketones C (Eq. 1).²

\[
\begin{align*}
\text{R} & \quad \text{OH} \quad \text{OH} \\
\text{R} & \quad \text{O} \quad \text{R} \\
\text{A} & \quad \xrightarrow{[e]} \quad \text{Bu}_2\text{SnO} \ (0.05 \text{ equiv}) \quad \text{Et}_4\text{NBr} \ (0.2 \text{ equiv}) \quad \text{MeOH} \\
\text{R} & \quad \text{OH} \\
\text{B} & \quad \text{R} \quad \text{O} \\
\text{R} & \quad \text{O} \\
\text{C} & \quad \text{R} \\
\text{up to 96\% yield} & \quad \text{~0\%} \\
\end{align*}
\]

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More recently, we reported the first catalytic asymmetric oxidation of 1,2-diols A’ to afford the corresponding optically active \( \alpha \)-ketoalcohols B’ in high enantioselectivity,\(^3\) which is based on recognition of the diol-moiety by copper(II) ion associated with \((R,R)\)-Ph-BOX complex\(^4\) to form the activated intermediates D’ followed by oxidation with NBS (Eq. 2). So far, to the best of our knowledge, catalytic asymmetric oxidation of A’ to B’ has not been known except for two examples using semi-catalytic amount of chiral dioxiranes\(^5\) or chiral hypervalent iodine.\(^6\)

In continuing the study, we succeeded in kinetic resolution of A’ by electrochemical oxidation. The concept we used in the asymmetric electrochemical oxidation of A’ to optically active \( \alpha \)-ketoalcohols B’ is schematically represented in Scheme 1. Complex D’ consisting diols A’ and chiral copper catalyst Cu-L* was easily deprotonated by cathodically generated MeO\(^-\) to afford alkoxide anions E’, which reacted with anodically generated Br\(^-\) to form O-brominated intermediates F’. MeO\(^-\) removed HBr from F’ to afford B’ and regenerate Cu-L*. Although a mechanism for this oxidation is similar to that of the oxidation with NBS,\(^3\) this electrochemical method is effective for some diols that NBS could not oxidize. In addition, this method is applicable to the asymmetric oxidation of aminoalcohols G’ and aminoaldehydes H’ to the corresponding optically active aminooesters.
2. Results and discussion

2.1 Accelerating effect based on recognition of the diol-moiety under the electrochemical oxidation condition

First, we tried electrochemical oxidation of phenylcyclohexane-cis-1,2-diol (cis-1) as a model compound to check for accelerating effect based on recognition of cis-1 with the Cu(II)-(R,R)-Ph-BOX complex. The electrochemical oxidation of cis-1 in the presence of Cu(OTf)$_2$ and (R,R)-Ph-BOX predominantly afforded mono-oxidized product 2 (36% yield). However, the oxidation did not proceed in the absence of Cu(OTf)$_2$ and (R,R)-Ph-BOX (Eq. 3). These results suggest that cis-1 might be recognized by the Cu(II)-(R,R)-Ph-BOX complex under this oxidation condition.
2.2 Effects of electrolytes and solvents on asymmetric oxidation

Next, we investigated electrolytes and solvents for the electrochemical oxidation applicable to kinetic resolution of cis-1 (Eq. 4). The results are summarized in Table 1. A procedure for asymmetric electrochemical oxidation of cis-1 is as follows; Anodic oxidation of 1 was carried out using platinum electrodes (2 x 1 cm²) in an undivided beaker-type cell containing 0.5 mmol of 1, 1.0 equiv of electrolyte, 0.1 equiv of Cu(OTf)₂, 0.1 equiv of (R,R)-Ph-BOX, and solvent (5 mL). After passing through 2.0 F/mol of electricity at constant current (50 mA) at 0°C and usual workup, optically active α-ketoalcohol (S)-2 was obtained in 36% yield with moderate selectivity (s) value of 8 (Table 1, entry 1).⁶⁻⁹ Comparable result was obtained by use of CuBr₂ instead of Cu(OTf)₂ (entries 1 and 2). Among solvents tested, methanol was most suitable for this reaction (entries 1, 3, and 4). Although the counter cation of electrolytes had little effect on both yield and selectivity for the electrochemical reaction, Et₄NBr was slightly better than other bromide salts (entries 1 and 5-7). On the other hand, use of either Et₄NCl or Et₄NI did not yield the oxidation product (entries 8 and 9).
Asymmetric electrochemical oxidation of several \textit{cis}-cycloalkane-1,2-diols

Asymmetric electrochemical oxidation of several \textit{cis}-cycloalkane-1,2-diol derivatives 3-8 are summarized in Table 2 (Eq. 5).\textsuperscript{10} The $s$ values of (\textit{S})-9-11 varied significantly depending on the ring size (entries 1-3 in Table 2 and entry 1 in Table 1). That is, the larger the ring size, the better $s$ value obtained. R substituent also influenced the $s$ value (entries 4–6). Compound 8 with a cyclohexyl group was asymmetrically oxidized to afford (\textit{S})-14 in higher selectivity ($s=11$, entry 6) than (\textit{S})-12 with a benzyl group ($s=2$, entry 6) and (\textit{S})-13 with an isopropyl group ($s=9$, entry 5).
2.4 Oxidative kinetic resolution of piperidine-3,4-diols

This electrochemical method, interestingly, was applicable to kinetic resolution of some piperidine-3,4-diols 15, 18, and 22 (Eqs. 6-8), which were not oxidized with NBS. The electrochemical oxidation of 15 afforded optically active ketoalcohol (R)-17 and (3S,4R)-15 in 49% ee and 41% ee, respectively, while 16 was not obtained (Eq. 6). The loss in the total yield (82%) in the reaction of 15 might be explained by instability of 3-ketopiperidines under the oxidative conditions. In fact, the oxidation of 18 afforded (3S,4S)-18 in moderate enantioselectivity along with a small amount of further oxidized products 20 and 21 instead of 19 (Eq. 7). On the other hand, oxidation of 22 gave (R)-23 and (3S,4R)-22 with little loss in the total yield (Eq. 8).
2.5 Oxidative kinetic resolution of racemic aminoalcohols and aminoaldehydes

Kinetic resolution of some racemic aminoalcohols 24-27 by electrochemical oxidation was tested (Eq. 9). The results are summarized in Table 3. In the oxidation of
*racemic*-N-benzoylpiperidinemethanol (24),\(^{13}\) optically active \(\alpha\)-aminoester (\(R\))-28 was obtained with low yield but good enantioselectivity (6\% yield, 71\% ee) after passing through 5 F/mol\(^{14}\) of electricity (entry 1). The oxidation of *racemic* N-benzyolated cyclic and acyclic aminoalcohols 25-27 afforded the corresponding (\(R\))-aminoesters (\(R\))-29-31 (entries 2-4) with low electron efficiencies.

![Chemical structure](image)

**Table 3.** Electrochemical oxidation of *racemic* aminoalcohols 24-27

<table>
<thead>
<tr>
<th>entry</th>
<th><em>racemic</em>-aminoalcohols</th>
<th>(F/\text{mol})</th>
<th>product ((R)-28-31)</th>
<th>yield (%)</th>
<th>recovered ((S)-24-27)</th>
<th>yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>5</td>
<td>((R)-28)</td>
<td>6 [71]</td>
<td>((S)-24)</td>
<td>85 [2]</td>
</tr>
<tr>
<td>2</td>
<td>25</td>
<td>3</td>
<td>((R)-29)</td>
<td>27 [70]</td>
<td>((S)-25)</td>
<td>50 [15]</td>
</tr>
<tr>
<td>3</td>
<td>26</td>
<td>5</td>
<td>((R)-30)</td>
<td>27 [59]</td>
<td>((S)-26)</td>
<td>60 [6]</td>
</tr>
<tr>
<td>4</td>
<td>27</td>
<td>10</td>
<td>((R)-31)</td>
<td>13 [22]</td>
<td>((S)-27)</td>
<td>88 [0]</td>
</tr>
</tbody>
</table>

Since further improvement of the electron efficiency and yield was difficult, we
tried oxidative kinetic resolution of *racemic* N-benzoylaminealdehyde (32-35) (Eq. 10), which might be intermediates for the oxidation of aminoalcohols to amino esters. The results are shown in Table 4. The oxidation of 32 proceeded more efficiently than that of aminoalcohol 24 to afford (R)-28 with improved yield and good enantioselectivity after passing through 2.5 F/mol$^{14}$ of electricity (entry 1). Also, the oxidation of several aminoaldehydes (33-35) proceeded to afford (R)-29-31 with improved yields and good enantioselectivities (entries 2-4).

\[
\begin{align*}
\text{racemic-32-35} & \stackrel{-[e]}{\text{Pt electrodes, rt}} \\
& \text{El}_{4}NBBr (1.0 \text{ equiv}) \\
& \text{MeOH} \\
& \text{Cu(OTf)$_2$ (0.1 equiv)} \\
& (R,R)-\text{Ph-BOX} (0.1 \text{ equiv}) \\
\rightarrow & \text{33} \\
& \text{34} \\
& \text{35} \\
\end{align*}
\]

\[\text{CHO} \quad \text{N} \quad \text{Bz} \quad \text{R}^3 \quad \text{R}^4 \quad \text{CHO} \quad \text{N} \quad \text{Bz} \quad \text{R}^3 \quad \text{R}^4 \quad \text{COOMe} \quad \text{CHO} \quad \text{N} \quad \text{Bz} \quad \text{R}^3 \quad \text{R}^4 \]

\[\text{(R)-28-31} + \text{(S)-32-35}\]

**Table 4.** Electrochemical oxidation of *racemic* aminoaldehydes 32-35

<table>
<thead>
<tr>
<th>entry</th>
<th>racemic-aminoaldehydes</th>
<th>F/mol</th>
<th>(R)-aminoesters yield (%)</th>
<th>(S)-aminoaldehydes yield (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>32</td>
<td>2.5</td>
<td>19</td>
<td>66</td>
</tr>
<tr>
<td></td>
<td>33</td>
<td>2</td>
<td>43</td>
<td>34</td>
</tr>
<tr>
<td>3</td>
<td>34</td>
<td>1.5</td>
<td>50</td>
<td>18</td>
</tr>
<tr>
<td>4</td>
<td>35</td>
<td>1.5</td>
<td>18</td>
<td>65</td>
</tr>
</tbody>
</table>

$^a$ Determined after transformation of (S)-32-35 to (S)-24-27, respectively.
2.6 Oxidation potentials

Oxidation potentials of materials used in these oxidations are shown in Table 5. The most oxidizable species was Br\textsuperscript{-}, while Cu(OTf)\textsubscript{2} was hardly oxidizable (entries 1 and 2). Although oxidation potential of (\textit{R},\textit{R})-Ph-BOX was moderate, Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex was stable under the oxidative conditions (entries 3 and 4). Diol \textit{cis}-\textbf{1} formed a complex with Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX which was more oxidizable (entries 5 and 6). Similar tendencies were observed for aminoalcohol \textbf{24} and aminoaldehyde \textbf{32}(entries 9-12). On the other hand, such negative shifts were not observed in the oxidation potentials of ketoalcohol \textbf{2} and aminoester \textbf{28} (entries 7, 8, 13, and 14). Among these complexes, \textit{cis}-\textbf{1}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX and \textbf{32}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complexes had the lowest oxidation potentials (entries 6 and 12).

<table>
<thead>
<tr>
<th>entry</th>
<th>material</th>
<th>oxidation potential (V)\textsuperscript{a}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Et\textsubscript{4}NBr</td>
<td>1.15</td>
</tr>
<tr>
<td>2</td>
<td>Cu(OTf)\textsubscript{2}</td>
<td>&gt;3.0</td>
</tr>
<tr>
<td>3</td>
<td>(\textit{R},\textit{R})-Ph-BOX</td>
<td>2.07</td>
</tr>
<tr>
<td>4</td>
<td>Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>&gt;3.0</td>
</tr>
<tr>
<td>5</td>
<td>diol \textit{cis}-\textbf{1}</td>
<td>2.10</td>
</tr>
<tr>
<td>6</td>
<td>\textit{cis}-\textbf{1}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>1.80</td>
</tr>
<tr>
<td>7</td>
<td>ketoalcohol \textbf{2}</td>
<td>2.20</td>
</tr>
<tr>
<td>8</td>
<td>\textbf{2}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>2.35</td>
</tr>
<tr>
<td>9</td>
<td>aminoalcohol \textbf{24}</td>
<td>2.20</td>
</tr>
<tr>
<td>10</td>
<td>\textbf{24}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>2.10</td>
</tr>
<tr>
<td>11</td>
<td>aminoaldehyde \textbf{32}</td>
<td>2.10</td>
</tr>
<tr>
<td>12</td>
<td>\textbf{32}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>1.75</td>
</tr>
<tr>
<td>13</td>
<td>aminoester \textbf{28}</td>
<td>2.32</td>
</tr>
<tr>
<td>14</td>
<td>\textbf{28}-Cu(OTf)\textsubscript{2}-(\textit{R},\textit{R})-Ph-BOX complex</td>
<td>2.65</td>
</tr>
</tbody>
</table>

\textsuperscript{a}V vs. Ag/AgNO\textsubscript{3}
2.7 Reaction mechanism for the asymmetric electrochemical oxidation of aminoalcohols and aminoaldehydes

On the basis of oxidation potentials described above, mechanisms for asymmetric electrochemical oxidation of aminoalcohols $G'$ and aminoaldehydes $H'$ are presented in Schemes 2 and 3, respectively. The electrochemical oxidation of $G'$ and $H'$ might proceed in similar manner to that of diols as shown in Scheme 1. Anodically generated $\text{Br}^+$ and cathodically generated $2\text{MeO}^-$ react with complexes $I'$ and/or $M'$ to afford corresponding optically active esters $P'$. 

Scheme 2
The stereochemical courses for kinetic resolution of cis-1 and 32 catalyzed by Cu(II)-(R,R)-Ph-BOX are shown in Schemes 4 and 5. Although the activated intermediates (R,R)-1-complex and (S)-32-complex might be formed more easily than (S,S)-1-complex and (R)-32-complex, MeO⁻ as a base predominantly approaches the less crowded intermediate (S,S)-1-complex and (R)-32-complex to afford (S)-2 and (R)-28.
Scheme 4. Plausible stereochemical course for kinetic resolution of cis-1.

Scheme 5. Plausible stereochemical course for kinetic resolution of racemic-32 in MeOH.
3. Conclusion

In conclusion, this article describes an efficient procedure for the kinetic resolution of racemic cis-cycloalkane-1,2-diols, aminoalcohols and aminoaldehydes in the presence of copper(II) triflate and (R,R)-Ph-BOX by electrochemical oxidation. Further study to improve the enantioselectivity is underway.

4. Experimental Section

4.1 General

Electrochemical reactions were carried out by using DC Power Supply (GP 050-2) of Takasago Seisakusho, Inc. HPLC analyses were achieved by using a LC-10AT VP and a SPD-10A VP of Shimadzu Seisakusho Inc. Specific rotations were measured with Jasco DIP-1000. $^1$H and $^{13}$CNMR spectra were measured at 300 (or 400) and 75 (or 100) MHz on a Varian Gemini 300 spectrometer (or JEOL JNM-AL 400) with TMS as an internal standard. All melting points were measured on MICRO MELTING POINT APPARATUS (Yanaco) and are uncorrected. IR spectra were obtained on a Shimadzu FTIR-8100A. Mass spectra were obtained on a JEOL JMS-DX 303 instrument.

(R,R)-Ph-BOX, Cu(OTf)$_2$, Me$_4$NBr, Et$_4$NBr, n-Pr$_4$NBr, n-Bu$_4$NBr, Et$_4$NCl, and Et$_4$NI were commercially available.

4.2 Measurement of oxidation potentials

BAS CV-50W was used as a voltametric analyzer. A solution of substrate (0.1 mmol) in MeCN (10 mL) containing 0.1 M Et$_4$NBF$_4$ was measured. Reference electrode was Ag/AgNO$_3$ in saturated aqueous KCl, a working electrode was a glassy carbon, and a counter electrode was a platinum wire. Scan rate was 100 mV/s.
4.3 Preparation of cis-cycloalkane-1,2-diols 3-8

4% OsO₄ (0.098 mmol) was added to a stirring solution of 1-phenylcyclohexene (32 mmol, 5.0 g) and 50% N-methylmorpholine-Ν-oxide (35.4 mmol) in THF-acetone-H₂O (1:1:1, 180 mL) at 0°C. After stirring for 16 h, sat. NaHSO₃ aqueous (120 mL) was added the resulting mixture and the solution stirred for 1 h. The solution was evaporated in vacuo to give residue, which was then dissolved in AcOEt. The organic portion was extracted with AcOEt and dried over MgSO₄. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (hexane/AcOEt =5/1) to afford 1 (93 % yield).

4.4 Asymmetric electrochemical oxidation of 1: a typical procedure

Under an aerobic atmosphere, into an undivided electrolysis cell equipped with a platinum anode and cathode (1 cm x 2 cm) was added a solution of Cu(OTf)₂ (18.1 mg, 0.05 mmol) and (R,R)-Ph-BOX (16.7 mg, 0.05 mmol) in MeOH (5 mL). This solution was stirred for 10 min. Into the solution were added 1-phenylcyclohexane-cis-1,2-diol (1, 96.1 mg, 0.5 mmol), tetraethylammonium bromide (105.1 mg, 0.5 mmol), and 2 F/mol of electricity was passed at a constant rate of 50 mA (terminal voltage; ca. 10 V) through the solution as it was cooled with ice-water. The solvent was evaporated in vacuo to give residue, which was then dissolved in AcOEt. The solution was poured into sat. aqueous Na₂S₂O₃ (5 mL). The organic portion was extracted with AcOEt (10 mL x 3) and dried over MgSO₄. The resulting solution was concentrated in vacuo. The residue was purified by silica gel column chromatography (n-hexane:AcOEt =10 : 1) to afford (S)-2-hydroxy-2-phenylcyclohexanone (2) as a white solid and recovered
(1R,2R)-1-phenylcyclohexane-cis-1,2-diol (1) as a white solid.

4.4.1.1 (S)-2-Hydroxy-2-phenylcyclohexanone (2)
White solid; mp 74°C; \([\alpha]_D^{29} +119.3\) (c=1.2, CHCl₃, 67% ee); IR (neat) v 3474, 2944, 2867, 1717, 1451, 1101 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 1.62-1.95 (m, 4H), 2.00-2.10 (m, 1H), 2.38-2.60 (m, 2H), 2.95-3.05 (m, 1H), 4.50 (s, 1H), 7.26-7.42 (m, 5H); HR-EI (M⁺) calcd for C₁₂H₁₄O₂ 190.0994 found 190.0972.
The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmϕ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 15 min for (R)-2 and 19 min for (S)-2].

4.4.1.2 (1R,2R)-1-Phenylcyclohexane-cis-1,2-diol (1)¹⁵
White solid; mp 90°C (lit.¹⁵ mp 121-122°C); \([\alpha]_D^{25} -3.7\) (c=1.2, EtOH, 41% ee); ¹H NMR (300MHz, CDCl₃) δ 1.35-1.95 (m, 9H), 2.62 (s, 1H), 3.92-4.04 (m, 1H), 7.22-7.28 (m, 1H), 7.38 (t, \(J=7.8\)Hz, 2H), 7.51 (d, \(J=7.2\)Hz, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6mm ϕ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210nm, 10 min for (1S,2S)-1 and 13 min for (1R,2R)-1].

4.4.2.1 (S)-2-Hydroxy-2-phenylcyclopentanone (9)
Light-yellow oil (lit.¹⁶ for racemate, mp 67°C); \([\alpha]_D^{18} +57.4\) (c=1.9, CHCl₃, 38% ee); ¹H NMR (300MHz, CDCl₃) δ 1.79-1.94 (m, 1H), 2.00-2.16 (m, 1H), 2.16-2.31 (m, 1H), 2.40-2.58 (m, 3H), 2.88 (s, 1H), 7.27-7.46 (m, 5H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmϕ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 16 min for (R)-9 and 20 min for (S)-9].
4.4.2.2 (1R,2R)-1-Phenylcyclopentane-cis-1,2-diol (3) (lit.\textsuperscript{17} for racemate)

White solid; mp 62-63°C; $[\alpha]_D^{29}$ -7.2 (c=3.2, CHCl\textsubscript{3}, 22% ee); IR (neat) ν 3400, 2967, 1447, 1092, 758, 700 cm\textsuperscript{-1}; $^1$H NMR (300MHz, CDCl\textsubscript{3}) δ 1.60-1.86 (m, 2H), 1.86-2.16 (m, 4H), 2.30 (br s, 1H), 2.80 (br s, 1H), 4.22 (t, $J$=7.5Hz, 1H), 7.15-7.28 (m, 1H), 7.33 (t, $J$=7.5Hz, 2H), 7.45 (d, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 15 min for (1S,2S)-3 and 19 min for (1R,2R)-3].

4.4.3.1 (S)-2-Hydroxy-2-phenylcycloheptanone (10) (lit.\textsuperscript{18} for racemate)

Light-yellow oil; $[\alpha]_D^{29}$ +123.4 (c=1.7, CHCl\textsubscript{3}, 64% ee); $^1$H NMR (300MHz, CDCl\textsubscript{3}) δ 1.22-1.68 (m, 3H), 1.83-2.10 (m, 3H), 2.22-2.40 (m, 2H), 2.40-2.55 (m, 1H), 2.75-2.88 (m, 1H), 4.58 (s, 1H), 7.25-7.40 (m, 3H), 7.40-7.50 (m, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 20 min for (S)-10 and 30 min for (R)-10].

4.4.3.2 (1R,2R)-1-Phenylcycloheptane-cis-1,2-diol (4)

White solid; mp 99-100°C; $[\alpha]_D^{28}$ -1.9 (c=1.0, CHCl\textsubscript{3}, 85% ee); IR (neat) ν 3400, 3023, 2930, 1460, 1019 cm\textsuperscript{-1}; $^1$H NMR (400MHz, CDCl\textsubscript{3}) δ 1.40-1.78 (m, 7H), 1.78-2.15 (m, 4H), 2.90 (s, 1H), 4.00 (d, $J$=10.4Hz, 1H), 7.22-7.32 (m, 1H), 7.32-7.47 (m, 2H), 7.47-7.64 (m, 2H); $^{13}$C NMR (100MHz, CDCl\textsubscript{3}) δ 20.0, 22.7, 26.6, 29.8, 39.1, 77.5, 78.9, 124.8, 126.9, 128.5, 148.3; HR-EI (M\textsuperscript{+}) calcd for C\textsubscript{13}H\textsubscript{18}O\textsubscript{2} 206.1307 found 206.1300. The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 11 min for (1S,2S)-4 and 13 min for (1R,2R)-4].
4.4.4.1 (S)-2-Hydroxy-2-phenylcyclooctanone (II)

Colorless oil; $[\alpha]_D^{29} +177.7$ (c=2.0, CHCl$_3$, 80% ee); IR (neat) ν 3467, 2930, 2859, 1701, 1698, 1466, 1447, 1364, 1127 cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$) δ 0.96-1.12 (m, 1H), 1.35-1.62 (m, 2H), 1.62-2.04 (m, 5H), 2.04-2.16 (m, 1H), 2.16-2.28 (m, 1H), 2.70-2.88 (m, 1H), 2.88-3.02 (m, 1H), 4.81 (s, 1H), 7.25-7.40 (m, 3H), 7.48 (d, $J=6.9$Hz, 2H); $^{13}$C NMR (100MHz, CDCl$_3$) δ 22.6, 24.2, 25.3, 30.1, 31.3, 36.0, 81.0, 126.0, 127.9, 128.5, 141.4, 216.6; HR-EI (M$^+$) calcd for C$_{14}$H$_{18}$O$_2$ 218.1307 found 218.1302. The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 20 min for (S)-II and 28 min for (R)-II].

4.4.4.2 (1R,2R)-1-Phenylcyclooctane-cis-1,2-diol (5)

White solid; mp 46-47°C; $[\alpha]_D^{29} -8.3$ (c=1.2, CHCl$_3$, 80% ee); IR (neat) ν 3400, 2923, 1601, 1447, 1028, 702 cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$) δ 1.20-1.92 (m, 11H), 2.00-2.15 (m, 1H), 2.24-2.40 (m, 1H), 2.98 (s, 1H), 4.40 (dd, $J=3.0$Hz, 8.7Hz, 1H), 7.22-7.32 (m, 1H), 7.39 (t, $J=7.8$Hz, 2H), 7.54 (d, $J=6.9$Hz, 2H); $^{13}$C NMR (100MHz, CDCl$_3$) δ 21.3, 24.2, 26.8, 28.1, 30.8, 36.5, 75.6, 78.3, 125.4, 127.0, 128.4, 146.4; HR-EI (M$^+$) calcd for C$_{14}$H$_{20}$O$_2$ 220.1554 found 220.1454. The ee was determined by DAICEL Chiralpak AS (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 7 min for (1S, 2S)-5 and 13 min for (1R, 2R)-5].

4.4.5.1 (S)-2-Hydroxy-2-benzylcyclohexanone (12)$^{19}$

White solid; mp 55°C; $[\alpha]_D^{29} +6.3$ (c=1.7, CHCl$_3$, 5% ee); $^1$H NMR (300MHz, CDCl$_3$) δ 1.60-1.80 (m, 2H), 1.80-1.95 (m, 2H), 2.14-2.47 (m, 2H), 2.50-2.60 (m, 1H), 2.70 (dt,
$J$=6.0Hz, 13.5Hz, 1H), 2.97 (d, $J$=13.7Hz, 1H), 3.14 (d, $J$=13.7Hz, 1H), 3.85 (s, 1H), 7.18-7.36 (m, 5H). The ee was determined by DAICEL Chiralpak AD (4.6 mmφ, 250 mm) [$n$-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 254 nm, 9 min for (S)-12 and 11 min for (R)-12].

4.4.5.2 (1R,2R)-1-Benzylcyclohexane-cis-1,2-diol (6)

White solid; mp 103-104°C (lit.20 for racemate, mp 107-108°C); $[\alpha]_D^{29}$ -0.3 (c=1.0, CHCl₃, 47% ee); IR (neat) ν 3404, 2938 cm⁻¹; $^1$H NMR (300MHz, CDCl₃) δ 1.16-1.92 (m, 8H), 2.85 (d, $J$=13.5Hz, 2H), 2.95 (d, $J$=13.5Hz, 2H), 3.40-3.50 (m, 1H), 7.20-7.35 (m, 5H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [$n$-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (1S,2S)-6 and 11 min for (1R,2R)-6].

4.4.6.1 (S)-2-Hydroxy-2-isopropylcyclohexanone (13) (lit.21 for racemate)

Colorless oil; $[\alpha]_D^{29}$ +44.1 (c=0.4, CHCl₃, 75% ee); $^1$H NMR (300MHz, CDCl₃) δ 0.70 (d, $J$=6.9Hz, 3H), 1.01 (d, $J$=6.6Hz, 3H), 1.55-1.80 (m, 4H), 2.06-2.18 (m, 1H), 2.18-2.32 (m, 1H), 2.32-2.43 (m, 1H), 2.43-2.53 (m, 2H), 3.81 (s, 1H). The ee was determined by DAICEL Chiralpak AS (4.6 mmφ, 250 mm) [$n$-hexane/isopropanol (80/1) (v/v), 1.0 mL/min, detection at 210 nm, 6.5 min for (S)-13 and 7.5 min for (R)-13].

4.4.6.2 (1R,2R)-1-Isopropylcyclohexane-cis-1,2-diol (7)

White solid; mp 91-92°C; IR (neat) ν 3400, 2940, 1449, 1071 cm⁻¹; $^1$H NMR (300MHz, CDCl₃) δ 0.91 (d, $J$=7.5Hz, 3H), 0.94 (d, $J$=7.5Hz, 3H), 1.12-1.30 (m, 3H), 1.40-1.80
(m, 7H), 2.08 (sep, J=7.1Hz, 1H), 3.66 (dd, J=4.2Hz, 9.0Hz, 1H); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta$ 16.2, 17.6, 20.6, 23.6, 28.0, 30.6, 32.8, 71.0, 75.4; HR-EI (M$^+$) calcd for C$_9$H$_{18}O$_2 158.1307 found 158.1267. The ee of the 1-isopropylcyclohexane-cis-1,2-diol (7) was determined by HPLC of the corresponding 2-phenylcarbamoylated compound 7' by usual method.

4.4.6.3 (1R,2R)-1-Hydroxy-1-isopropyl-2-phenylcarbamoyloxycyclohexane (7')
Light-yellow oil; $[\alpha]_D^{27}$ +1.8 (c=1.0, CHCl$_3$, 25% ee); IR (neat) ν 3300, 2942, 2867, 1707, 1601, 1545, 1231, 1061 cm$^{-1}$; $^1$H NMR (300MHz, CDCl$_3$) $\delta$ 0.92 (d, J=7.2Hz, 3H), 0.96 (d, J=7.2Hz, 3H), 1.22-1.41 (m, 2H), 1.41-2.00 (m, 8H), 4.91 (dd, J=5.1Hz, 10.2Hz, 1H), 6.75 (s, 1H), 7.07 (t, J=6.9Hz, 1H), 7.22-7.45 (m, 4H); $^{13}$C NMR (100MHz, CDCl$_3$) $\delta$ 16.1, 17.5, 20.3, 23.7, 27.5, 28.5, 33.7, 75.2, 25.3, 118.5, 123.4, 129.0, 137.9, 152.8; HR-EI (M$^+$) calcd for C$_{16}$H$_{23}$NO$_3$ 277.1678 found 277.1677. The ee was determined by DAICEL Chiralpak AS (4.6 mmφ, 250 mm) [$n$-hexane/isopropanol (50/1) (v/v), 1.0 mL/min, detection at 254 nm, 16 min for (1S, 2S)-7' and 19 min for (1R, 2R)-7'].

4.4.7.1 (S)-2-Hydroxy-2-cyclohexylcyclohexanone (14))
Light-yellow oil (lit.$^{21}$ for racemate, mp 46-46.5°C); $[\alpha]_D^{29}$ +91.9 (c=1.2, CHCl$_3$, 81% ee); $^1$H NMR (300MHz, CDCl$_3$) $\delta$ 1.00-1.48 (m, 7H), 1.55-2.06 (m, 8H), 2.06-2.18 (m, 1H), 2.36-2.57 (m, 3H), 3.85 (s, 1H). The ee was determined by DAICEL Chiralpak AD (4.6 mmφ, 250 mm) [$n$-hexane/isopropanol (40/1) (v/v), 1.0 mL/min, detection at 210 nm, 8 min for (S)-14 and 11 min for (R)-14].
4.4.7.2 (1R,2R)-1-Cyclohexylcyclohexane-cis-1,2-diol (8)
White solid; mp 109-110°C; IR (neat) ν 3400, 2928, 1445, 1075 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 0.95-1.90 (m, 21H), 3.60-3.70 (m, 1H); ¹³C NMR (100MHz, CDCl₃) δ 20.8, 23.7, 26.7, 26.9, 27.8, 29.5, 30.6, 43.6, 70.7, 75.2; HR-EI (M⁺) calcd for C₁₂H₂₂O₃ 198.16208 found 198.1582. The ee of the 1-cyclohexylcyclohexane-cis-1,2-diol (8) was determined by HPLC of the corresponding 2-phenylcarbamoylated compound 8’. 

4.4.7.3 (1R,2R)-1-Hydroxy-1-cyclohexyl-2-phenylcarbamoyloxycyclohexane (8’)
White solid; mp 125°C; [α]D²⁹ +3.5 (c=2.5, CHCl₃, 18% ee); IR (neat) ν 3308, 2938, 2855, 1736, 1608, 1549, 1447, 1325, 1237 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 0.90-1.90 (m, 20H), 4.89 (dd, J=4.8Hz, 10.2Hz, 1H), 6.76 (s, 1H), 7.07 (t, J=7.2Hz, 1H) 7.28-7.43 (m, 4H); ¹³C NMR (100MHz, CDCl₃) δ 20.5, 23.7, 26.1, 26.6, 26.8, 26.9, 27.4, 27.7, 30.2, 44.6, 75.0, 75.1, 118.5, 123.4, 129.1, 137.9, 152.7; HR-EI (M⁺) calcd for C₁₉H₂₇NO₃ 317.1991 found 317.2000. The ee was determined by DAICEL Chiralpak AD (4.6 mmφ, 250 mm) [n-hexane/isopropanol (10/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (1R,2R)-8’ and 12 min for (1S,2S)-8’]. 

4.4.8.1 N-(p-Tolylsulfonyl)piperidine-(3S,4R)-diol (15)
White solid; mp 112°C (lit.²² for racemate, mp 138-140°C); [α]D²² −7.1 (c=1.0, CHCl₃, 41% ee); IR (neat) ν 3350, 2926, 2872, 2359, 1929, 1732, 1661, 1599 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 1.77-1.95 (m, 2H), 2.08-2.18 (m, 1H), 2.18-2.36 (m, 1H), 2.44 (s, 3H), 2.94-3.10 (m, 3H), 3.10-3.23 (m, 1H), 3.70-3.82 (m, 1H), 3.82-3.94 (m, 1H), 7.33 (d, J=8.1Hz, 2H), 7.65 (d, J=8.1Hz, 2H); ¹³C NMR (100MHz, CDCl₃) δ 21.5, 29.2, 41.9,
42.0, 67.4, 67.7, 127.6, 129.8, 143.8; HR-EI (M⁺) calcd for C₁₂H₁₇NO₄S 271.0878 found 271.0876. The ee was determined by DAICEL Chiralcel OD-H (4.6 mmφ, 250 mm) [n-hexane/ethanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 12 min for (3R,4S)-15 and 16 min for (3S,4R)-15].

4.4.8.2 (3R)-Hydroxy-N-(p-tolylsulfonyl)piperidine-4-one (17)
Colorless solid; mp 114°C; [α]_D^{19} +1.1 (c=0.75, CHCl₃, 49% ee); IR (neat) ν 3350, 2926, 2857, 1732, 1345 cm⁻¹; ¹H NMR (300MHz, CDCl₃) δ 2.30-2.43 (m, 1H), 2.44 (s, 3H), 2.50-2.90 (m, 3H), 3.53 (br s, 1H), 4.10-4.25 (m, 1H), 4.28-4.45 (m, 2H), 7.35 (d, J=10.4Hz, 2H), 7.69 (d, J=10.4Hz, 2H); ¹³C NMR (100MHz, CDCl₃) δ 21.5, 38.7, 46.5, 52.5, 72.5, 100.6, 127.4, 127.7, 130.0, 133.5, 144.3; HR-EI (M⁺) calcd for C₁₂H₁₅NO₄S 269.0722 found 269.0719. The ee was determined by DAICEL Chiralcel OJ (4.6 mmφ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (3S)-17 and 11 min for (3R)-17].

4.4.9.1 N-(t-Butoxycarbonyl)-3-phenylpiperidine-(3S,4S)-diol (18)
Colorless solid; mp 101-103°C; [α]_D^{22} -10.1 (c=0.2, CHCl₃, 55% ee); IR (neat) ν 3350, 2976, 2926, 2957, 2855, 1750, 1694, 1671, 1466, 1377, 1167 cm⁻¹; ¹H NMR (400MHz, CDCl₃) δ 1.48 (s, 9H), 1.85-2.10 (m, 3H), 2.70-2.87 (m, 1H), 2.90-3.08 (m, 2H), 3.80-4.30 (m, 3H), 7.28 (t, J=7.6Hz, 1H), 7.38 (t, J=7.6Hz, 2H), 7.47 (d, J=7.6Hz, 2H); ¹³C NMR (100MHz, CDCl₃) δ 28.4, 37.9, 40.0, 44.4, 70.9, 74.3, 79.9, 125.0, 127.4, 128.6, 144.8, 154.8; HR-EI (M⁺) calcd for C₁₆H₂₃NO₄ 293.1627 found 293.1616. The ee was determined by DAICEL Chiralcel OJ (4.6 mmφ, 250 mm) [n-hexane/ethanol (15/1) (v/v), 1.0 mL/min, detection at 210 nm, 9 min for (3S,4S)-18 and 11 min for
4.4.9.2 *N-*(t-Butoxycarbonyl)*-*N-*(3-oxo-3-phenylpropyl)*formamide (20)

Colorless oil; IR (neat) \( \nu = 2978, 2932, 2359, 2344, 1740, 1686, 1342, 1149 \) cm\(^{-1}\); \(^1\)H NMR (300MHz, CDCl\(_3\)) \( \delta = 1.53 \) (s, 9H), 3.25 (t, \( J=7.5 \)Hz, 2H), 4.05 (t, \( J=7.5 \)Hz, 2H), 7.40-7.50 (m, 2H), 7.50-7.64 (m, 1H), 7.90-8.00 (m, 2H), 9.19 (s, 1H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \( \delta = 28.0, 29.7, 36.6, 36.9, 84.4, 128.1, 128.7, 133.3, 136.5, 163.0, 197.7; \) HR-EI (M\(^+\)) calcd for C\(_{15}\)H\(_{19}\)NO\(_4\) 277.1314 found 277.1292.

4.4.9.3 *N-*(t-Butoxycarbonyl)*-*N-*(3-oxo-3-phenylpropyl)*glycine methyl ester (21)

Colorless oil; IR (neat) \( \nu = 2976, 2359, 1752, 1705, 1682, 1367, 1213, 1169 \) cm\(^{-1}\); \(^1\)H NMR (400MHz, CDCl\(_3\)) \( \delta = 1.41 \) and 1.47 (2s, 9H), 3.25-3.45 (m, 2H), 3.60-3.80 (m, 5H), 4.07 (d, \( J=14.4 \)Hz, 2H), 7.40-7.55 (m, 2H), 7.50-7.65 (m, 1H), 7.97 (d, \( J=8.0 \)Hz, 2H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \( \delta = 28.2, 38.0, 44.4, 51.2, 51.9, 80.4, 128.1, 128.6, 133.2, 136.7, 155.2, 170.9, 199.2; \) HR-EI (M\(^+\)) calcd for C\(_{17}\)H\(_{23}\)NO\(_5\) 321.1576 found 321.1571.

4.4.10.1 *R*-3-Ethyl-3-hydroxy-*N-*(p-tolylsulfonyl)*piperidine-4-one (23)

White solid; mp 85-87°C; \([\alpha]_D^{27} = -11.2 \) (c=1.0, CHCl\(_3\), 31% ee); IR (neat) \( \nu = 2855, 1718, 1339, 1157 \) cm\(^{-1}\); \(^1\)H NMR (400MHz, CDCl\(_3\)) \( \delta = 0.87 \) (t, \( J=11.6 \)Hz, 1H), 2.00-2.15 (m, 1H), 2.31 (d, \( J=11.6 \)Hz, 1H), 2.40-2.62 (m, 2H), 2.43 (s, 3H), 2.82-2.97 (m, 1H), 3.72 (s, 1H, -OH), 4.03 (dd, \( J=2.8 \)Hz, \( J=12.0 \)Hz, 1H), 4.08-4.20 (m, 1H), 7.34 (d, \( J=8.4 \)Hz, 2H), 7.65 (d, \( J=8.4 \)Hz, 2H); \(^{13}\)C NMR (100MHz, CDCl\(_3\)) \( \delta = 6.6, 21.5, 29.5, 37.3, 46.9, 55.8, 78.0, 127.4, 129.9, 133.1, 144.2, 209.9; \) HR-EI (M\(^+\)) calcd for C\(_{14}\)H\(_{18}\)NO\(_4\)S 297.1035 found 297.1022. The ee was determined by DAICEL.
Chiralcel OD-H (4.6 mmφ, 250 mm)  [n-hexane/ethanol (20/1) (v/v), 1.0 mL/min, detection at 210 nm, 18 min for (3S)-23 and 19 min for (3R)-23].

4.4.10.2 N-(p-Tolylsulfonyl)-3-ethylpiperidine-(3S,4R)-diol (22)

White solid; mp 98-102°C; [α]D^28 +3.6 (c=0.6, CHCl₃, 39% ee); IR (neat) ν 2967, 1464, 1335, 1163 cm⁻¹; ^1H NMR (400MHz, CDCl₃) δ 0.94 (t, J=7.6Hz, 3H), 1.58-1.80 (m, 2H), 1.70-1.82 (m, 1H), 1.88-2.00 (m, 1H), 2.00-2.40 (m, 2H, -OH), 2.44 (s, 3H), 2.71 (d, J=11.6Hz, 1H), 2.70-2.82 (m, 1H), 3.11 (d, J=11.6Hz, 1H), 3.18-3.30 (m 1H), 3.35-3.45 (m, 1H), 7.34 (d, J=8.0Hz, 2H), 7.64 (d, J=8.0Hz, 2H); ^13C NMR (100MHz, CDCl₃) δ 7.0, 21.5, 27.7, 29.5, 43.2, 51.0, 70.5, 71.8, 127.6, 129.8, 132.9, 143.8; HR-EI (M⁺) calcd for C₁₄H₂₁NO₄S 299.1191 found 299.1181. The ee was determined by DAICEL Chiralcel OD-H (4.6 mmφ, 250 mm)  [n-hexane/ethanol (10/1) (v/v), 1.0mL/min, detection at 210 nm, 19 min for (3R,4S)-22 and 23 min for (3S,4R)-22].

4.5 A typical procedure for preparation of racemic aminoalcohols

Sodium tetrahydroborate (120 mmol, 4.54 g) and calcium chloride (60 mmol, 6.66 g) was added to a stirred solution of racemic N-benzoylalanine methyl ester (racemic-30, 30 mmol, 6.22 g) in THF-MeOH (4:1, 150 mL) at 0°C. The reaction mixture was stirred for 12 h. Water (50 mL) was added to the resulting mixture and the solution stirred for 15 min. The solution was evaporated in vacuo to give a residue, which was then dissolved in AcOEt. The organic portion was extracted with AcOEt and dried over MgSO₄. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (n-hexane/AcOEt =1/1) to afford 26 (85 % yield).
4.6 A typical procedure for preparation of racemic aminoaldehydes

To a solution of N-Benzoyl-2-(hydroxymethyl)piperidine (racemic-24, 10 mmol, 2.19 g) and TEMPO (1 mmol, 156 mg) in CH2Cl2 (10 mL) was added PhI(OAc)2 (11 mmol, 3.54 g). The reaction mixture was stirred for 1 h, then quenched with sat. aqueous Na2S2O3 (5 mL). The organic portion was extracted with CH2Cl2 and dried over MgSO4. The resulting solution was concentrated in vacuo. The residue was chromatographed on silica gel (n-hexane/AcOEt =2/1) to afford 32 (73 % yield).

4.6.1 N-Benzoyl-2-piperidinecarbaldehyde (32)23
Colorless oil; 1H-NMR (300MHz, CDCl3) δ 1.30-1.90 (m, 5H), 2.16-2.20 (m, 1H), 3.02-3.21 (m, 1H), 3.60-3.80 (m, 1H), 5.30 (s, 1H), 7.43 (m, 5H), 9.66 (s, 1H).

4.6.2 N-Benzoyl-2-pyrrolidinecarbaldehyde (33)23
Colorless oil; 1H-NMR (300MHz, CDCl3) δ 1.81-2.30 (m, 4H), 3.50-3.70 (m, 2H), 4.64-4.75 (m, 1H), 7.30-7.45 (m, 3H), 7.50-7.80 (m, 2H), 9.69 (s, 1H).

4.6.3 N-(1-Formylethyl)benzamide (34)24
Colorless oil; 1H-NMR (300MHz, CDCl3) δ 1.51 (d, J=7.5Hz, 3H), 4.70-4.81 (m, 1H), 6.83 (br s, 1H), 7.32-7.58 (m, 3H), 7.81-7.86 (m, 2H), 9.66 (s, 1H).

4.6.4 N-(1-Formyl-2-methylpropyl)benzamide (35)
White solid; mp 68-70°C; IR (neat) ν 3320, 2967, 1732, 1647, 1536, 1314 cm⁻¹; 1H-NMR (300MHz, CDCl3) δ 1.07 (d, J=6.9Hz, 3H), 1.09 (d, J=6.9Hz, 3H), 2.40-2.52 (m, 1H), 4.82-4.89 (m, 1H), 6.73 (br s, 1H), 7.44-7.59 (m, 3H), 7.83 (d, J=6.9Hz, 2H),
9.77 (s, 1H); 13C NMR (100MHz, CDCl$_3$) δ 17.9, 19.0, 24.4, 63.6, 127.1, 128.6, 131.8, 140.0, 167.6, 199.8; HR-EI (M$^+$) calcd for C$_{12}$H$_{15}$NO$_2$ 205.1103 found 205.1098.

4.7 Asymmetric electrochemical oxidation of aminoalcohols

The oxidation were carried out according to a typical experimental procedure for the oxidation of 1.

4.7.1.1 N-Benzoyl-(2R)-(methoxycarbonyl)piperidine (28) (lit.$^{23}$ for racemate)

Colorless oil; [α]$_D^{26}$ +51.0 (c=0.40, CHCl$_3$, 87% ee); $^1$H-NMR (300MHz, CDCl$_3$) δ 1.25-1.82 (m, 5H) 2.26-2.40 (m, 1H), 3.18-3.30 (m, 1H), 3.60-3.70 (m, 1H), 3.79 (s, 3H), 5.50-5.58 (m, 1H), 7.42 (m, 5H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmφ, 250 mm) $[n$-hexane/isopropanol (30/1) (v/v), 1.0 mL/min, detection at 254 nm, 25 min for (R)-28 and 27 min for (S)-28].

4.7.1.2 N-Benzoyl-(2S)-(hydroxymethyl)piperidine (24)$^{4c}$

White solid; mp 89-92°C (lit.$^{25}$ for racemate, mp 93-95°C); [α]$_D^{26}$ -7.1 (c=2.0, CHCl$_3$, 12% ee); $^1$H-NMR (300MHz, CDCl$_3$) δ 1.40-1.90(m, 6H) 2.80-3.20 (m, 2H), 3.50-3.80 (m, 1H), 3.96 (dd, J=9.9, 10.5Hz, 1H), 4.85 (br s, 1H), 7.41 (m, 5H). The ee was determined by DAICEL Chiralcel OD-H (4.6 mmφ, 250 mm) $[n$-hexane/isopropanol (30/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (S)-24 and 34 min for (R)-24].

4.7.2.1 N-Benzoyl-(2R)-methoxycarbonylpyrrolidine (N-Benzoyl-D-proline methyl ester) (29)

White solid; mp 69-72°C (lit.$^{26}$ for L-form, mp 89-90°C); [α]$_D^{21}$ +83.7 (c=0.5, CHCl$_3$,
86% ee); $^1$H-NMR (300MHz, CDCl$_3$) $\delta$ 1.80-2.11 (m, 3H), 2.14-2.40 (m, 1H), 3.50-3.60 (m, 1H), 3.62-3.71 (m, 1H), 3.78 (s, 3H), 4.66-4.70 (m, 1H), 7.30-7.45 (3H), 7.50-7.60 (m, 2H). The ee was determined by DAICEL Chiralpak AD (4.6 mmφ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (R)-29 and 39 min for (S)-29].

4.7.2.2 N-Benzoyl-(2S)-hydroxymethylpyrrolidine (25)$^{27}$
Colorless oil; $[\alpha]_D^{19}$ -21.1 (c=1.6, CHCl$_3$, 15% ee); $^1$H-NMR (300MHz, CDCl$_3$) $\delta$ 1.57-1.95 (m, 4H) 2.12-2.25 (m, 1H), 3.42-3.58 (m, 2H), 3.70-3.83 (m, 2H), 4.37-4.46 (m, 1H), 4.90-4.98 (m, 1H), 7.38-7.55 (m, 5H). The ee was obtained by DAICEL Chiralpak AD (4.6 mmφ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 30 min for (R)-25 and 36 min for (S)-25].

4.7.3.1 Methyl (2R)-(N-benzoyl)aminopropionate (N-Benzoyl-D-alanine methyl ester) (30)
Colorless oil (lit.$^{28}$ for L-form, mp 52-53$^o$C); $[\alpha]_D^{23}$ -23.3 (c=1.4, CHCl$_3$, 59% ee) [lit.$^{28}$ for L-form, $[\alpha]_D^{23}$ +38.6 (c=2.9, CHCl$_3$)]; $^1$H-NMR (300MHz, CDCl$_3$) $\delta$ 1.53 (d, $J$=6.9Hz, 3H), 3.80 (s, 3H), 4.75-4.83 (m, 1H), 6.74 (br s, 1H), 7.41-7.55 (m, 3H), 7.80-7.85 (m, 2H). The ee was obtained by DAICEL Chiralcel OJ-H (4.6 mmφ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 220 nm, 16 min for (R)-30 and 17 min for (S)-30].

4.7.3.2 (2S)-(N-Benzoyl)aminopropan-1-ol (26)$^{29}$
White solid; mp 110-112$^o$C (lit.$^{29}$ mp 132-133$^o$C); $[\alpha]_D^{26}$ -1.0 (c=0.9, CHCl$_3$, 18% ee);
1H-NMR (300MHz, CDCl3) δ 1.28 (d, J=6.6Hz, 3H), 2.40-2.83 (br s, 1H), 3.60-3.68 (m, 1H), 3.72-3.80 (m, 1H), 4.322-4.35 (m, 1H), 6.44 (br s, 1H), 7.30-7.56 (m, 3H), 7.70-7.88 (m, 2H). The ee was determined by DAICEL Chiralcel OJ-H (4.6 mmϕ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 220 nm, 8.3 min for (S)-26 and 9.6 min for (R)-26].

4.7.4.1 Methyl (2R)-(N-benzoyl)amino-3-methylbutyrate (N-Benzoyl-D-valine methyl ester) (31)

White solid; mp 94-96°C (lit.30 for racemic form, mp 86°C); [α]D20 -33.5 (c=0.5, CHCl3, 64% ee); 1H-NMR (300MHz, CDCl3) δ 0.99 (d, J=7.2Hz, 3H), 1.03 (d, J=7.2Hz, 3H), 2.22-2.35 (m, 1H), 3.78 (s, 3H), 4.78-4.82 (m, 1H), 6.62 (m, 1H), 7.43-7.56 (m, 3H), 7.82 (d, J=6.6Hz, 2H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmϕ, 250 mm) [n-hexane/isopropanol (50/1) (v/v), 1.0 mL/min, detection at 254 nm, 15 min for (R)-31 and 20 min for (S)-31].

4.7.4.2 (2S)-(N-Benzoyl)amino-3-methylbutan-1-ol (27)31

White solid; mp 84-85°C (lit.31 mp 99°C); [α]D27 -4.5 (c=1.0, CHCl3, 12% ee); 1H-NMR (300MHz, CDCl3) δ 1.00 (d, J=6.9Hz, 3H) 1.02 (d, J=6.9Hz, 3H), 1.95-2.06 (m, 1H), 2.90-3.22 (br s, 1H), 3.75-3.78 (m, 2H), 3.89-3.98 (m, 1H), 6.48 (br s, 1H), 7.39-7.56 (m, 3H), 7.77 (d, J=6.9Hz, 2H). The ee was obtained by DAICEL Chiralcel OD-H (4.6 mmϕ, 250 mm) [n-hexane/isopropanol (20/1) (v/v), 1.0 mL/min, detection at 254 nm, 13 min for (S)-27 and 22 min for (R)-27].

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References and notes
8. The absolute stereoconfiguration of recovered (R,R)-1 was determined by comparing with specific rotation of authentic sample.9
10. Absolute stereoconfigurations of (R,R)-3-8 shown in Eq. 5 and Table 2 were deduced on the basis of that of (R,R)-1ap.
11. Absolute stereoconfigurations of 15, 17, 18, 22, and 23 shown in Eqs. 6-8 were deduced on the basis of that of (R,R)-1.
13. *Racemic* N-benzylxycarbonylpiperidinemethanol$^k$ was hardly oxidized under the reaction conditions.


