A THREE-STEP SYNTHESIS OF OPTICALLY ACTIVE
5-HALOMETHYL-2-OXAZOLIDINONES; ASYMMETRIC
DESYMMETRIZATION OF PROCHIRAL 1,3-DIHALO-2-PROPYL
CARbamates

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Abstract - Optically active 5-bromomethyl-2-oxazolidinones (2a and 3a) and 5-
chloromethyl-2-oxazolidinones (2b and 3b) were readily prepared from prochiral
1,3-dibromo-2-propanol (7a) and 1,3-dichloro-2-propanol (7b) by a three-step
sequence involving formation of carbamates (6a–c) followed by asymmetric
desymmetrization (up to 50% de) and debenzylation by anisole–methanesulfonic
acid system.

INTRODUCTION
The enantiopure 4-halomethyl-2-oxazolidinones (1a–b) and 5-halomethyl-2-oxazolidinones (2a–b and
3a–b) and their derivatives are useful chiral building blocks for organic syntheses (Figure 1).1 The
halomethyl groups in the oxazolidinones are able to convert to another functional groups such as alkyl
groups,2 alkenes,3 acetoxy groups,4 lactams,5 and silyl groups.6 Successful 4-methoxylation of the 5-
halomethyl-2-oxazolidinones (3a–b) can be also performed.7 The 4-halomethyl-2-oxazolidinones (1a–b)
are easily prepared from L-serine.2a On the contrary, suitable starting materials for preparation of 5-
halomethyl-2-oxazolidinones (2a–b and 3a–b) have not been available.8 For example, Danielmeier and
Steckhan reported syntheses of 2a–b and 3a–b starting from D-mannitol, L-ascorbic acid, and (R)-
and (S)-malic acid.9 The methods involve seven-step syntheses and complicated conversions of functional
groups in the optically active natural products.
We are investigating the asymmetric desymmetrization of σ-symmetric 1,3-difunctionalized 2-propanol...
derivatives. In a previous report, we described the asymmetric synthesis of a 4-hydroxymethyl-2-oxazolidinone from a serinol derivative and chloroformates. We present here the novel asymmetric synthesis of 5-halomethyl-2-oxazolidinones (2a–b and 3a–b) from optically active carbamates (6a–c).

The reaction involves cyclization of 6 (path A or B: asymmetric desymmetrization) forming the new chiral center at the 5-position of 4 and 5 (Scheme 1). We have also studied the reaction conditions that could remove N-1-phenylethyl and N-1-(1-naphthyl)ethyl groups from 4 and 5.

RESULTS AND DISCUSSION
Preparation of carbamates (6)
The carbamates (6a–c) were easily prepared by two methods. The prochiral alcohols, 1,3-dibromo-2-propanol (7a) and 1,3-dichloro-2-propanol (7b), reacted smoothly with (S)-(–)-1-phenylethyl isocyanate and (S)-(–)-1-(1-naphthyl)ethyl isocyanate in the presence of copper(I) chloride (CuCl) in DMF to give the carbamates (6a–c) in 56, 77, and 70% yields, respectively (Method I). In the second method, 6a–c were synthesized from (S)-(–)-1-phenylethylamine, (S)-(–)-1-(1-naphthyl)ethylamine, and 1,3-dihalo-2-propyl chloroformates prepared from 7a–b and triphosgene in the presence of pyridine and DMAP in the presence of pyridine and DMAP in

<table>
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<th>Entry</th>
<th>Method</th>
<th>Material</th>
<th>X</th>
<th>Ar</th>
<th>Product</th>
<th>Yield (%)</th>
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<td>Br</td>
<td>Ph</td>
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<td>56</td>
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</table>

*See text and EXPERIMENTAL section.*
methylene chloride (Method II). The yields (6a: 76%, 6b: 87%, and 6c: 91%) were better than those from Method I (Table 1).

**Cyclization of carbamate (6)**

The cyclization of 6a was carried out with various bases in THF or toluene at –78 °C (or –78 °C to room temperature) yielding 5-bromomethyl-2-oxazolidinone derivatives (4a and 5a). The results are summarized in Table 2. Each diastereomer was purified easily with silica gel column chromatography and each diastereomeric excess was determined by the isolated yields of 4 and 5. Although sodium hydride (NaH) was a good base to afford the oxazolidinones (4a and 5a) (95% yield), the reaction was slow at –78 °C and the diastereoselectivity was low (16% de, Entry 1). Then we tested the reaction with LDA, LHMDS, sodium bis(trimethylsilyl)amide (NaHMDS), and potassium bis(trimethylsilyl)amide (KHMDS) as a base in THF (Entries 2–5), some of which improved the reaction rate and the diastereo-

![Table 2 Intramolecular cyclization of carbamates (6)\(^a\)](image)

<table>
<thead>
<tr>
<th>Entry</th>
<th>Carbamate</th>
<th>Base</th>
<th>Solvent</th>
<th>Reaction Time (h)</th>
<th>Yield (%)</th>
<th>de of 4 (%) (^b)</th>
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<td>LDA</td>
<td>THF</td>
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<td>LHMDS</td>
<td>THF</td>
<td>5</td>
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<td>32</td>
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<tr>
<td>4</td>
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<td>5</td>
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<td>5</td>
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<td>0</td>
</tr>
<tr>
<td>11</td>
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<td>NaHMDS</td>
<td>THF</td>
<td>5</td>
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<td>26</td>
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<tr>
<td>12</td>
<td>6b</td>
<td>MeMgBr</td>
<td>THF</td>
<td>5</td>
<td>28</td>
<td>14</td>
</tr>
<tr>
<td>13</td>
<td>6c</td>
<td>NaHMDS</td>
<td>THF</td>
<td>5</td>
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<td>MeMgBr</td>
<td>THF</td>
<td>5</td>
<td>69</td>
<td>23</td>
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</table>

\(^a\) The reactions were carried out in the presence of 1 equiv. of bases for 5 h at –78 °C except Entries 1 and 7.  
\(^b\) Based on isolated yield. \(^c\) This reaction was carried out overnight at –78 °C to rt.
selectivity of the reaction. Exchange of the solvent to toluene decreased the yield and diastereoselectivity (Entry 6). Next we carried out the reaction with methylmagnesium halides and tert-butylmagnesium chloride. The cyclization proceeded smoothly with methylmagnesium halides (Entries 7–9), however, failed with tert-butylmagnesium chloride (Entry 10). The best yield and the best diastereoselectivity of the major product (4a) were given by the use of methylmagnesium bromide (MeMgBr) (Entry 9). The cyclization of 6b (X; Cl, Entries 11 and 12) gave 4b in lower yield and in less diastereoselectivity than that of the carbamate (6a) (Entries 4 and 9). Since the cyclization of carbamate (6a) gave the oxazolidinone (4a) in moderate diastereoselectivity, the reaction of N-(1-naphthyl)ethylcarbamate (6c) possessing more bulky group on the N-substituent was investigated. Using NaHMDS and MeMgBr, the reaction afforded the oxazolidinone (4c) in 38 and 50% de, respectively (Entries 13 and 14). The diastereomeric excesses of these reactions were somewhat higher than those of reaction of carbamate (6a).

**Debenzylation of 4**

We investigated the debenzylation of the oxazolidinones (4a and 4b) at first by the Birch reduction. Treatment of 4a with one equivalent of lithium metal in liquid ammonia for 30 min at −78 °C, afforded (S)-N-allyl-1-phenylethylamine (8) in 11% yield and 4a was recovered in 47% yield (Scheme 2). However, 5-bromomethyl-2-oxazolidinone (2a) was not formed. The reaction mechanism for the formation of 8 from 4a would be followed; debromination from bromomethyl group of 4a occurred faster than removal of N-1-phenylethyl group and then the oxazolidinone ring was cleaved followed by decarboxylation. In the case of 4b, a similar result was obtained.

![Scheme 2](image)
Thus, we screened the debenzylating reagents including 10% Pd/C with hydrogen or cyclohexene,
hydrogen bromide in acetic acid, formic acid, and trifluoromethanesulfonic acid. We found that
the anisole–methanesulfonic acid system, which has been used for removal of \( O \)-benzyl group, was the
most effective reagent for removal of the \( N \)-1-phenylethyl and \( N \)-1-(1-naphthyl)ethyl groups of
oxazolidinones (4a–c and 5a–c) (Table 3). The yields of bromides (2a; 69% and 3a; 77%) from 4a and 5a were lower than those of chlorides (2b; 86% and 3b; 82%) from 4b and 5b. The removal of
\( N \)-1-(1-naphthyl)ethyl groups from 4c and 5c proceeded quantitatively leading to 2a and 3a, respectively.
Absolute configurations of 2a–b and 3a–b were determined in comparison with reported data.

<table>
<thead>
<tr>
<th>Table 3</th>
<th>Debenzylation of the oxazolidinones (4a–c and 5a–c)(^a)</th>
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<tr>
<td>Entry</td>
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</tr>
<tr>
<td>5</td>
<td>5b</td>
</tr>
<tr>
<td>6</td>
<td>5c</td>
</tr>
</tbody>
</table>

\(^a\) The mixture of oxazolidinones and methanesulfonic acid in anisole was stirred at 50 °C.

\(^b\) Not trail to isolate. However, the TLC indicated the formation of the side products in every case.

To confirm the reaction mechanism, we isolated two anisole derivatives (9a\(^{22}\); 56% and 10a\(^{22}\); 18%) as side products from debenzylation of 4b (Table 3, Entry 2). The reaction of 4c gave two anisole derivatives (9b; 77% and 10b; 19%) as side products (Entry 3). The respective total yields of the anisole derivatives (74% and 96% in Entries 2 and 3) agreed well with the yields of the products (2b; 77% and 2c; 97%). We transformed 10a with treatment of trimethylsilyl iodide\(^{23}\) to a phenol (10c) to ascertain the optical purity of 10a. The phenol (10c) was racemate checked by HPLC analysis using a chiral column. This fact indicated clearly that this debenzylation proceeds via a benzylic cation.\(^{24}\) Oxazolidinones (2a–b and 3a–b) were converted to \( N \)-benzoyl-2-oxazolidinones (11a–b and 12a–b) (Scheme 3),\(^{25}\) and then we confirmed the optical purities to be greater than 95% ee by HPLC analysis.

In conclusion, an efficient three-step synthesis of optically active 5-halomethyl-2-oxazolidinones (2 and

![Scheme 3](image)

Reagents and conditions: (a) PhCOCl, DMAP, THF, 0 °C to rt.
3) has been achieved from prochiral 1,3-dihalo-2-propanols. The characteristic feature of this method is selective cyclization of chiral carbamates containing diastereotopic groups in the molecule and selective debenzylation by anisole–methanesulfonic acid system.

EXPERIMENTAL
Melting points were measured with Yanaco MP-3 apparatus and are uncorrected. Optical rotations were determined on a JASCO DIP-140 polarimeter. IR spectra were recorded on a Hitachi 215 spectrophotometer. NMR spectra were obtained with a JEOL JNM-GX400 (1H-NMR: 400 MHz and 13C-NMR: 100 MHz) spectrometer in CDCl3 using tetramethylsilane as an internal standard and J values are given in Hz. MS and high-resolution MS (HR-MS) were taken on a JEOL JMS-DX302 spectrometer. Column chromatography was performed with Merck silica gel 60 (230–400 mesh). Analytical TLC was performed on plates pre-coated with 0.25 mm layer of silica gel 60 F254 (Merck). The ampoules of isocyanates were purchased from Tokyo Kasei and opened just before use. All metal amides and Grignard reagents were purchased from Aldrich.

Preparation of the carbamates.
Method A.12 (S)-(–)-1-Phenylethyl isocyanate (1.02 g, 6.79 mmol) was added to a mixture of 7a (1.48 g, 6.79 mmol) and copper(I) chloride (672 mg, 6.79 mmol) in DMF (34 mL) at rt, and the mixture was stirred for 2.5 h at rt. The reaction mixture was poured into 10% hydrochloric acid and extracted with ether. The organic extracts were combined, washed once with water and once with saturated aqueous sodium chloride, dried with magnesium sulfate and concentrated in vacuo. The residue was chromatographed on silica gel (hexane:ethyl acetate = 12:1) to give 6a (1.39 g, 56%). According to this procedure, we synthesized 6b (77%) and 6c (70%).

Method B.14 Pyridine (4.80 g, 60 mmol) was added dropwise to a mixture of 7a (4.40 g, 20.2 mmol) and triphosgene (2.00 g, 6.74 mmol) in methylene chloride (50 mL) at 0 °C. After being stirred for 2 h at rt, the mixture was cooled to 0 °C, and (S)-(–)-1-phenylethylamine (2.45 g, 20.2 mmol), pyridine (1.60 g, 20 mmol) and catalytic amount of DMAP (74 mg, 0.61 mmol) were added. The resulting mixture was stirred overnight at rt. The reaction mixture was poured into saturated aqueous ammonium chloride and extracted with ether. The organic extracts were subjected to the same work-up as used for the Method A. The residue was chromatographed on silica gel (hexane:ethyl acetate = 12:1) to give the carbamate (6a) as white solid (5.61 g, 76%). According to the Method B, we synthesized 6b (87%) and 6c (91%) from (S)-(–)-1-phenylethylamine and (S)-(–)-1-(1-naphthyl)ethylamine, respectively.

1,3-Dibromo-2-propyl (S)-(1-phenylethyl)carbamate (6a). White needles, mp 72–73 °C (ethyl acetate). 1H-NMR (CDCl3) δ: 1.51 (3 H, d, J = 7.0, Me), 3.55–3.68 (4 H, m, 2 x CH 2Br), 4.83 (1 H, m, MeCHPh), 5.02 (1 H, m, OCH), 5.13 (1 H, br m, NH), 7.43 (5 H, m, Ph). 13C-NMR (CDCl3) δ: 22.2 (q, Me), 31.9 (t, 2 x CH2Br), 50.8 (d, MeCHPh), 71.2 (d, OCH), 125.8, 127.4, 128.6 (3 d, Ph), 142.9 (s, Ph), 153.9 (s, C=O). IR (CHCl3) cm⁻¹: 1720 (C=O). MS (El) m/z: 367 (M⁺), 365 (M⁺), 363 (M⁺), 352, 350, 348, 164, 120, 105. [α]D23 –35.7° (c 2.1, CHCl3). Anal. Calcd for C13H15NO2Br2: C, 39.48; H, 4.14; N,
3.84. Found: C, 39.92; H, 4.16; N, 3.87.

1,3-Dichloro-2-propyl (S)-N-(1-phenylethyl)carbamate (6b). White needles, mp 69–72 °C (ethyl acetate). 1H-NMR (CDCl3) δ 1.51 (3 H, d, J = 7.0, Me), 3.73 (2 H, d, J = 4.4, CH2Cl), 3.83 (1 H, m, MeCPh), 5.07–5.11 (2 H, m, OCH and NH), 7.43 (5 H, m, Ph). 13C-NMR (CDCl3) δ: 22.2 (q, Me), 32.6 (t, CH2Cl), 50.7 (d, MeCPh), 71.9 (d, OCH), 125.8, 127.3, 128.5 (3 d, Ph), 143.0 (s, Ph), 153.9 (s, C=O). IR (CHCl3) cm–1: 1725 (C=O). MS (EI) m/z: 279 (M+), 277 (M+), 275 (M+), 264, 262, 260, 164, 105. [α]D23 –42.8° (c 2.4, CHCl3). Anal. Calcd for C12H15NO3Cl2: C, 52.19; H, 5.47; N, 5.07. Found: C, 52.30; H, 5.47; N, 5.05.

1,3-Dibromo-2-propyl (S)-N-[1-(1-naphthyl)ethyl]carbamate (6c). White solid, mp 84–86 °C (ethyl acetate). 1H-NMR (CDCl3) δ: 1.68 (3 H, d, J = 7.0, Me), 3.56–3.71 (4 H, m, 2 x CH2Br), 5.07 (1 H, m, MeCPh), 5.20 (1 H, br m, NH), 5.65 (1 H, m, Ar), 7.44–7.58 (4 H, m, Ar), 7.80 (1 H, d, J = 8.4, Ar), 7.88 (1 H, d, J = 7.3, Ar), 8.10 (1 H, d, J = 8.4, Ar). IR (CHCl3) cm–1: 1725 (C=O). MS (EI) m/z: 417 (M+), 415 (M+), 413 (M+), 214, 170, 155, 127. [α]D23 –4.1° (c 2.1, CHCl3). Anal. Calcd for C16H17NO2Br2: C, 46.29; H, 4.13; N, 3.37. Found: C, 46.48; H, 4.16; N, 3.38.

Cyclization of the carbamates.

Typical procedure. Methylmagnesium bromide (3.0 mmol/mL solution in ether, 0.83 mL, 2.50 mmol) was added dropwise to a stirred solution of 6a (700 mg, 1.92 mmol) in THF (30 mL) at –78 °C. The mixture was stirred for 5 h at this temperature and saturated aqueous ammonium chloride solution was added. After being warmed to rt, the mixture was extracted with methylene chloride. The organic extracts were combined, dried with magnesium sulfate, and concentrated in vacuo. The residue was chromatographed on silica gel (hexane:ethyl acetate = 4:1) to give 4a (336 mg, 62%) and 5a (130 mg, 24%). The other results are shown in Table 2.

(5R,1'S)-5-Bromomethyl-3-(1'-phenylethyl)-2-oxazolidinone (4a). White needles, mp 95–97 °C (ethyl acetate). 1H-NMR (CDCl3) δ: 1.59 (3 H, d, J = 7.0, Me), 2.99 (1 H, dd, J = 8.9, 6.1 Hz, NC6H), 3.56–3.71 (4 H, m, 2 x CH2Br), 3.29 (1 H, dd, J = 8.9, 6.1 Hz, BrC6H), 3.44 (1 H, dd, J = 10.6, 4.0, BrCH2), 3.62 (1 H, t, J = 8.9, NCH3), 4.68 (1 H, m, OCH), 5.22 (1 H, q, J = 7.0, MeC6H), 7.35 (5 H, m, Ph). 13C-NMR (CDCl3) δ: 16.2 (q, Me), 32.6 (t, NCH2), 44.1 (t, CH2Br), 51.4 (d, MeCPh), 71.4 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 138.9 (s, Ph), 156.4 (s, C=O). IR (CHCl3) cm–1: 1780 (C=O). MS (EI) m/z: 285 (M+), 283 (M+), 270, 268, 204, 105. [α]D23 –33.1° (c 1.4, CHCl3). Anal. Calcd for C12H14NO2Br: C, 50.72; H, 4.97; N, 4.93. Found: C, 51.00; H, 4.98; N, 4.85.

(5S,1'S)-5-Bromomethyl-3-(1'-phenylethyl)-2-oxazolidinone (5a). A colorless oil. 1H-NMR (CDCl3) δ: 1.62 (3 H, d, J = 7.0, Me), 3.28 (1 H, t, J = 8.9, NCH3), 3.36 (1 H, dd, J = 8.9, 5.7, NCH3), 3.47 (1 H, dd, J = 10.6, 7.0, BrC6H), 3.54 (1 H, dd, J = 10.6, 3.7, BrCH2), 4.60 (1 H, m, OCH), 5.23 (1 H, q, J = 7.0, MeC6H), 7.34 (5 H, m, Ph). 13C-NMR (CDCl3) δ: 16.1 (q, Me), 33.2 (t, NCH2), 44.1 (t, CH2Br), 51.4 (d, MeCPh), 70.9 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 138.9 (s, Ph), 156.4 (s, C=O). IR (neat) cm–1: 1780 (C=O). MS (EI) m/z: 285 (M+), 283 (M+), 270, 268, 204, 105. [α]D23 –32.2° (c 1.6, CHCl3). Anal. Calcd for C12H14NO2Br: C, 50.72; H, 4.97; N, 4.93. Found: C, 51.01; H, 4.98; N, 4.85.

(5R,1'S)-5-Chloromethyl-3-(1'-phenylethyl)-2-oxazolidinone (4b). White prisms, mp 68–70 °C (ethyl acetate).
acetate). 1H-NMR (CDCl₃) δ: 1.59 (3 H, d, J = 7.0, Me), 3.04 (1 H, dd, J = 9.2, 5.9, NCHH), 3.48 (1 H, dd, J = 9.2, 4.2, CH₂C), 3.59 (1 H, dd, J = 11.5, 6.8, ClCH₂H), 3.62 (1 H, d, J = 9.2, NCHH), 4.69 (1 H, m, OCH), 5.23 (1 H, q, J = 7.0, MeC₃H₇Ph), 7.36 (5 H, m, Ph). 13C-NMR (CDCl₃) δ: 16.2 (q, Me), 43.1 (t, NCH₂), 44.6 (t, CH₂Br), 71.5 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 139.0 (s, Ph), 156.5 (s, C=O). IR (CHCl₃) cm⁻¹: 1750 (C=O). MS (EI) m/z: 241 (M⁺), 239 (M⁺), 226, 224, 204, 105. [α]D²⁰ –57.3° (c 1.5, CHCl₃). Anal. Calcd for C₁₂H₁₄NO₂Cl: C, 60.13; H, 5.89; N, 5.84. Found: C, 60.47; H, 6.07; N, 5.59.

(5S,1'S)-5-Chloromethyl-3-(1'-phenylethyl)-2-oxazolidinone (5b). A colorless oil. 1H-NMR (CDCl₃) δ: 1.60 (3 H, d, J = 7.0, Me), 3.27 (1 H, t, J = 8.8, NC₃H), 3.40 (1 H, dd, J = 8.8, 5.5, NCH₂H), 3.66 (2 H, m, ClCH₂), 4.62 (1 H, m, OCH), 5.23 (1 H, q, J = 7.0, MeC₃H₇Ph), 7.35 (5 H, m, Ph). IR (CHCl₃) cm⁻¹: 1750 (C=O). MS (EI) m/z: 241 (M⁺), 239 (M⁺), 226, 224, 204, 105. [α]D²³ –32.2° (c 1.6, CHCl₃). Anal. Calcd for C₁₂H₁₄NO₂Cl: C, 60.13; H, 5.89; N, 5.84. Found: C, 59.85; H, 5.98; N, 5.69.

(5R,1'S)-5-Bromomethyl-3-[1'-(1''-naphthyl)ethyl]-2-oxazolidinone (4c). White needles, mp 105–106 °C (ethyl acetate). 1H-NMR (CDCl₃) δ: 1.74 (3 H, d, J = 7.0, Me), 2.53 (1 H, t, J = 9.2, 6.1, BrCH₂H), 2.97 (1 H, dd, J = 10.6, 4.4, BrCH₂H), 3.23 (1 H, d, J = 10.6, MeC₃H₇Ar), 7.43 (4 H, m, Ar), 7.88 (2 H, m, Ar), 8.12 (1 H, d, J = 8.8, Ar). IR (CHCl₃) cm⁻¹: 1750 (C=O). MS (EI) m/z: 335 (M⁺), 333 (M⁺), 320, 318, 254, 155. [α]D²³ –6.3° (c 2.0, CHCl₃). Anal. Calcd for C₁₆H₁₆NO₂Br: C, 57.50; H, 4.83; N, 4.19. Found: C, 57.67; H, 4.86; N, 4.14.

(5S,1'S)-5-Bromomethyl-3-[1'-(1''-naphthyl)ethyl]-2-oxazolidinone (5c). A colorless oil. 1H-NMR (CDCl₃) δ: 1.75 (3 H, d, J = 7.0, Me), 2.84 (1 H, t, J = 9.2, NCHH), 3.28 (1 H, dd, J = 9.2, 6.2, NCHH), 3.47 (2 H, d, J = 4.4, BrCH₂), 4.45 (1 H, m, OCH), 5.93 (1 H, q, J = 7.0, MeCHAr), 7.53 (4 H, m, Ar), 7.87 (2 H, m, Ar), 8.15 (1 H, d, J = 8.8, Ar). IR (CHCl₃) cm⁻¹: 1750 (C=O). MS (EI) m/z: 335 (M⁺), 333 (M⁺), 320, 318, 254, 155 (100). [α]D²³ –26.7° (c 2.1, CHCl₃). Anal. Calcd for C₁₆H₁₆NO₂Br: C, 57.50; H, 4.83; N, 4.19. Found: C, 57.38; H, 4.87; N, 3.98.

Typical procedure for Birch reduction of the oxazolidinones (4a and 4b). Birch reduction of 4a was carried out according to the literature⁴; a mixture of lithium metal (7.4 mg, 1.1 mmol) in anhydrous ammonia (4 mL) was stirred at –60 °C, and then a solution of 4a (100 mg, 0.35 mmol) in THF/tert-butyl alcohol (10:1, 2 mL) was added all at once. After 30 min stirring, the reaction was quenched by addition of solid ammonium chloride (59 mg, 1.1 mmol). Ammonia was allowed to evaporate and the volatiles were removed in vacuo. The residue was dissolved in ethyl acetate and washed with water. The organic solution was dried with magnesium sulfate, filtered, and concentrated in vacuo. The residue was chromatographed on silica gel (methylene chloride:methanol = 19:1) to give 8 (6.2 mg, 11%) and 4a (47.0 mg) was recovered. Comparison of the spectrum data with the literature¹⁵ clearly showed the formation of 8: [α]D³¹ –47.0° (c 0.08, CHCl₃) [lit.,¹⁵a [α]D²⁰ –46° (c 0.66, EtOH); for (R)-enantiomer, lit.,¹⁵b [α]D²⁰ +49.3° (c 1.12, CH₂Cl₂)].

According to the procedure described above, we confirmed the formation of 8 (7.5 mg, 11%) from 4b (100 mg, 0.42 mmol), and 4b (31.0 mg) was recovered.
Typical procedure for debenzylation of the oxazolidinones by anisole–methanesulfonic acid. Methanesulfonic acid (801 mg, 8.34 mmol) was added to a solution of 4a (229 mg, 0.807 mmol) in anisole (472 mg, 4.36 mmol), and the mixture was stirred for 5 h at 50 °C (bath temperature). The reaction mixture was poured into saturated aqueous sodium hydrogen carbonate and extracted with ethyl acetate. The extracts were combined, dried with magnesium sulfate, filtered, and concentrated \( \text{in vacuo} \). The residue was suspended with hexane and filtered. The solid was chromatographed on silica gel (ethyl acetate) to give 2a as colorless solid (99.6 mg, 69%). The other results are shown in Table 3. The filtrate from the hexane-suspension in the reaction of 4b and 4c was concentrated \( \text{in vacuo} \), and the each residue was purified with preparative TLC (hexane:toluene = 3:7) to afford 9a and 10a from 4b, and 9b and 10b from 4c.

(RS)-1-(4-Methoxyphenyl)-1-phenylethane (9a). A colorless oil. \( ^1H\)-NMR (CDCl\(_3\)) \( \delta \): 1.74 (3 H, d, \( J = 7.0 \) Hz, CHMe), 3.77 (3 H, s, OMe), 4.57 (1 H, q, \( J = 7.3 \) MeCH), 6.83–6.92 (2 H, m, Ar), 7.13–7.26 (7 H, m, Ar). IR (neat) cm\(^{-1}\): 1495 (Ar), 1245 (ArOMe). HR-MS \( m/z \): 212.1202 (Calcd for C\(_{15}\)H\(_{16}\)O: 212.1202). MS (EI) \( m/z \): 212 (M\(^+\)), 197, 182, 165, 152.

(RS)-1-(2-Methoxyphenyl)-1-phenylethane (10a). A colorless oil. \( ^1H\)-NMR (CDCl\(_3\)) \( \delta \): 1.67 (3 H, d, \( J = 7.0 \) Hz, CHMe), 3.88 (3 H, s, OMe), 4.57 (1 H, q, \( J = 7.3 \) MeCH), 6.88–6.93 (2 H, m, Ar), 7.12–7.14 (1 H, m, Ar), 7.38–7.47 (4 H, m, Ph-H), 7.73 (1 H, d, \( J = 8.06 \) Naph-H), 7.82–7.85 (1 H, m, Naph-H), 8.03 (1 H, m, Naph-H). IR (CHCl\(_3\)) cm\(^{-1}\): 1510 (Ar), 1250 (ArOMe). HR-MS \( m/z \): 262.1355 (Calcd for C\(_{15}\)H\(_{16}\)O: 262.1358). MS (EI) \( m/z \): 262 (M\(^+\)), 247, 232, 215, 202.

(RS)-1-(2-Hydroxyphenyl)-1-(1-phenyl)ethane (10c). Trimethylsilyl iodide \( ^{23} \) (0.16 mL, 0.80 mmol) was added dropwise to a mixture of 10a (84 mg, 0.40 mmol) in dichloromethane (0.4 mL) and the mixture was stirred for 24 h at rt. The reaction was quenched with methanol (0.064 mL) and diluted with ethyl acetate. The mixture was washed with 10% aqueous sodium thiosulfate and dried with magnesium sulfate, filtered and concentrated \( \text{in vacuo} \). The residue was chromatographed on silica gel (hexane:ethyl acetate = 9:1) to give 10c as a colorless oil (50 mg, 64%). \( ^1H\)-NMR (CDCl\(_3\)) \( \delta \): 1.63 (3 H, d, \( J = 1.6 \) Me), 4.37 (1 H, q, \( J = 7.3 \) ArCH), 4.58 (1 H, s, OH), 6.75 (1 H, dt, \( J = 7.3, 1.1 \) Ar), 6.94 (1 H, dt, \( J = 7.3, 1.1 \) Ar), 7.12 (1 H, dt, \( J = 7.3, 1.8 \) Ar), 7.19–7.32 (6 H, m, Ar). IR (neat) cm\(^{-1}\): 3550 (OH), 1460, 765, 710.
HR-MS m/z: 198.1046 (Calcd for C_{14}H_{14}O: 198.1045). MS (EI) m/z: 198 (M+), 183, 165.

(R)-5-Chloromethyl-2-oxazolidinone (2b). \([\alpha]_D^{23} -20.4^\circ (c 3.3, \text{CHCl}_3) \) [lit.,\(^9\) -18.7\(^\circ\) (c 3.2 CH2Cl2)].

(S)-5-Chloromethyl-2-oxazolidinone (3b). \([\alpha]_D^{23} +20.0^\circ (c 2.4, \text{CHCl}_3) \) [lit.,\(^9\) +19.1\(^\circ\) (c 3.3, CH2Cl2)].

Typical procedure for N-benzoylation of the oxazolidinones (2a–b and 3a–b).

Benzoic anhydride (48.9 mg, 0.21 mmol) was added to a mixture of 2a (19 mg, 0.11 mmol), triethylamine (0.014 mL, 0.11 mmol) and catalytic amount of DMAP in THF (0.038 mL) at 0 °C. After stirred for 15 h at rt, the mixture was diluted with ethyl acetate, and the extract was washed with saturated aqueous ammonium chloride, dried with magnesium sulfate filtered and concentrated in vacuo. The residue was chromatographed on silica gel (hexane:ethyl acetate = 4:1) to give 11a as a colorless solid (27 mg, 90%).

(R)-N-Benzoyl-5-bromomethyl-2-oxazolidinone (11a). White prisms, mp 98–99 °C (ethyl acetate). IR (CHCl3) cm\(^{-1}\): 1790 (C=O). \(^1\)H-NMR (CDCl\(_3\)) \(\delta\): 3.64 (2 H, d, \(J = 5.1\), CH2Br), 4.05 (1 H, dd, \(J = 11.4, 5.9\), NCHH), 4.31 (1 H, dd, \(J = 11.4, 8.4\), NCHH), 4.90 (1 H, m, OCH), 7.42–7.67 (5 H, m, Ar). HR-MS m/z: 282.9841 (Calcd for C\(_{11}\)H\(_{10}\)NO\(_3\)Br: 282.9844). MS (EI) m/z: 285 (M\(^+\)), 283 (M\(^+\)), 105, 77. \([\alpha]_D^{30} +9.4^\circ (c 0.8, \text{CHCl}_3)\).

(R)-N-Benzoyl-5-chloromethyl-2-oxazolidinone (11b). White solid, mp 93–94 °C (ethyl acetate). IR (CHCl3) cm\(^{-1}\): 1800 (C=O). \(^1\)H-NMR (CDCl\(_3\)) \(\delta\): 3.77–3.87 (2 H, m, CH2Cl), 4.11 (1 H, dd, \(J = 11.4, 5.9\), NCHH), 4.31 (1 H, dd, \(J = 11.4, 8.8\), NCHH), 4.94 (1 H, m, OCH), 7.42–7.67 (5 H, m, Ar). HR-MS m/z: 239.0349 (Calcd for C\(_{11}\)H\(_{10}\)NO\(_3\)Cl: 239.0350). MS (EI) m/z: 241 (M\(^+\)), 239 (M\(^+\)), 105, 77. \([\alpha]_D^{31} +4.6^\circ (c 0.4, \text{CHCl}_3)\). The other spectral data were identical with those of 11a.

(S)-N-Benzoyl-5-bromomethyl-2-oxazolidinone (12a). HR-MS m/z: 282.9842 (Calcd for C\(_{11}\)H\(_{10}\)NO\(_3\)Br: 282.9844). \([\alpha]_D^{31} -9.6^\circ (c 1.0, \text{CHCl}_3)\). The other spectral data were identical with those of 11a.

(S)-N-Benzoyl-5-chloromethyl-2-oxazolidinone (12b). HR-MS m/z: 239.0347 (Calcd for C\(_{11}\)H\(_{10}\)NO\(_3\)Cl: 239.0350). \([\alpha]_D^{31} +4.6^\circ (c 0.4, \text{CHCl}_3)\). The other spectral data were identical with those of 11b.

Determination of the optically purity.

HPLC analysis of 11a, 12a, 11b, and 12b. Column, Daisel Chiralcel OD (25 cm x 0.46 cm \(\phi\)); eluent, hexane:2-propanol = 4:1; flow-rate, 1.0 mL/min; detection, UV (254 nm); retention time, 11a: 35.2 min, 12a: 28.1 min, 11b: 35.1 min, and 12b: 31.8 min.

HPLC analysis of 10c. Column, Daisel Chiralpak AD (25 cm x 0.46 cm \(\phi\)); eluent, hexane:2-propanol = 9:1; flow-rate, 0.5 mL/min; detection, UV (254 nm); retention time, 12.3 min and 13.5 min.

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REFERENCES AND NOTES

11. *N*-Benzyl and *N*-1-phenylethyl groups in some 2-oxazolidinones are commonly removed by Birch reduction without decomposition of 2-oxazolidinone ring. No other method of debenzylation of *N*-1-phenylethyl-2-oxazolidinones is well known. The efficiency of debenzylation of the 2-oxazolidinones depends greatly on their 4- and 5-substituents.
28. Recently Davies et al. reported that a variety of hydrogenolysis conditions for debenzylation of their N-(1-phenylethyl)-2-oxazolidinone derivative possessing a lactone proved ineffective. Birch reduction could remove the benzyl group; however, the lactone was also reduced. See: S. G. Davies, G. D. Smyth, and A. M. Chippindale, *J. Chem. Soc., Perkin Trans. 1*, 1999, 3089.