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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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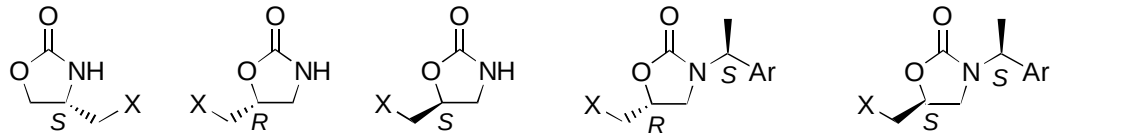
Abstract - Optically active 5-bromomethyl-2-oxazolidinones (**2a** and **3a**) and 5-chloromethyl-2-oxazolidinones (**2b** and **3b**) were readily prepared from prochiral 1,3-dibromo-2-propanol (**7a**) and 1,3-dichloro-2-propanol (**7b**) by a three-step sequence involving formation of carbamates (**6a**–**c**) 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,3a] 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



1a X = I
1b X = Br

2a X = Br
2b X = Cl

3a X = Br
3b X = Cl

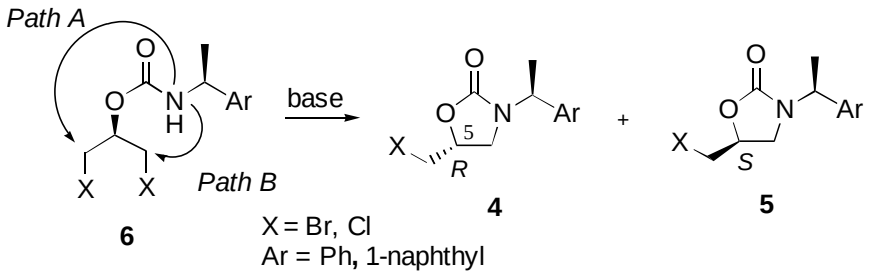
4a X = Br, Ar = Ph
4b X = Cl, Ar = Ph
4c X = Br, Ar = 1-naphthyl

5a X = Br, Ar = Ph
5b X = Cl, Ar = Ph
5c X = Br, Ar = 1-naphthyl

Figure 1

derivatives. In a previous report,[10] 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** (Scheme1). We have also studied the reaction conditions that could remove *N*-1-phenylethyl and *N*-1-(1-naphthyl)-ethyl groups from **4** and **5**.[11]



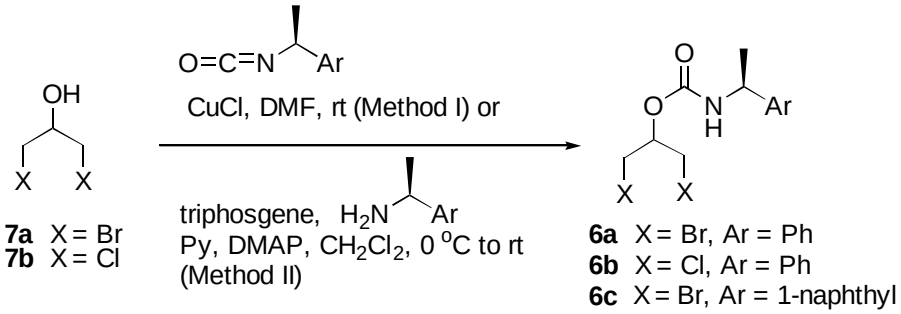
Scheme 1

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)[12] 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[13] prepared from **7a–b** and triphosgene[14] in the presence of pyridine and DMAP in

Table 1 Synthesis of the carbamates (**6a–c**)



Entry	Method[a]	Material	X	Ar	Product	Yield (%)
1	I	**7a**	Br	Ph	**6a**	56
2	I	**7b**	Cl	Ph	**6b**	77
3	I	**7a**	Br	1-naphthyl	**6c**	70
4	II	**7a**	Br	Ph	**6a**	76
5	II	**7b**	Cl	Ph	**6b**	87
6	II	**7a**	Br	1-naphthyl	**6c**	91

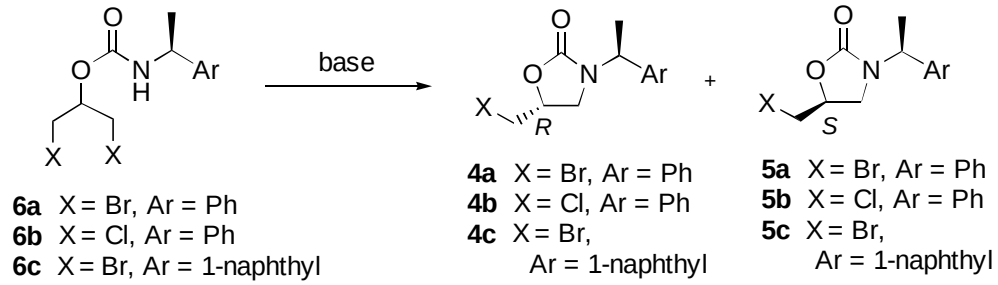
[a]See text and EXPERIMENTAL section.

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]



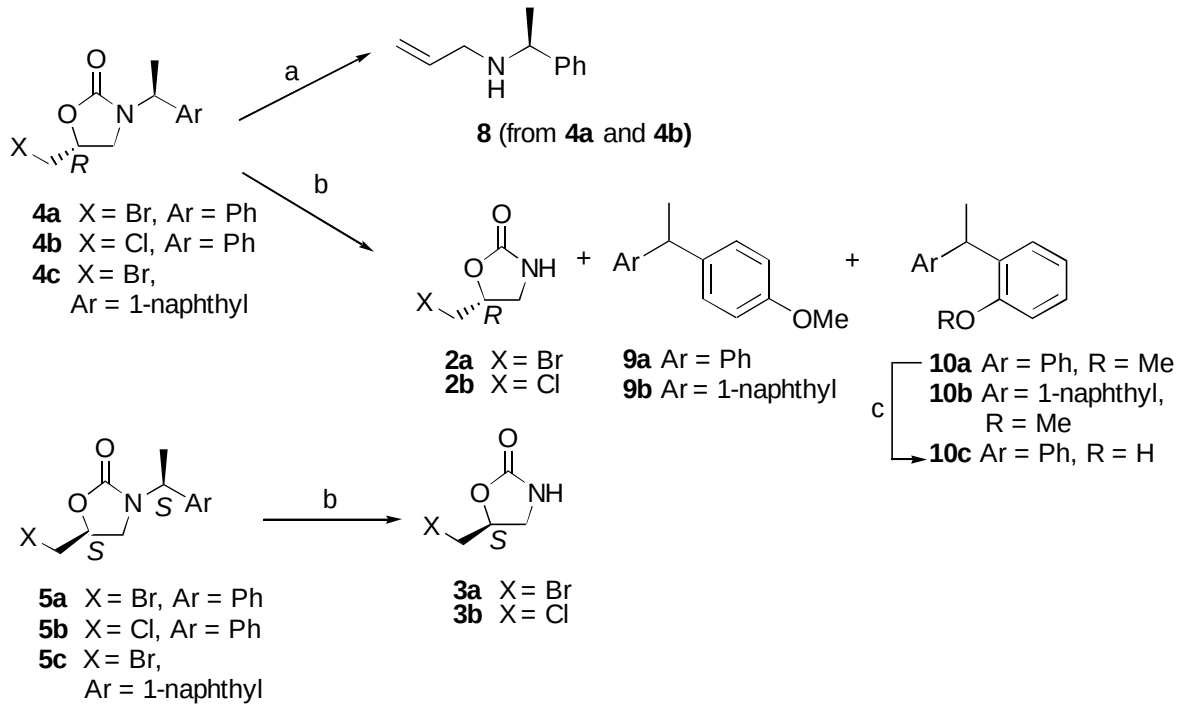
Entry	Carbamate	Base	Solvent	Reaction Time (h)	Yield (%)		
					4	**5**	de of **4** (%)[b]
1[c]	**6a**	NaH	THF	15	55	40	16
2	**6a**	LDA	THF	5	45	27	24
3	**6a**	LHMDS	THF	5	33	32	2
4	**6a**	NaHMDS	THF	5	52	27	32
5	**6a**	KHMDS	THF	5	49	33	20
6	**6a**	KHMDS	toluene	5	23	18	12
7	**6a**	MeMgI	THF	5	25	16	22
8	**6a**	MeMgCl	THF	5	52	30	26
9	**6a**	MeMgBr	THF	5	63	25	44
10	**6a**	^{t}BuMgCl	THF	5	0	0	-
11	**6b**	NaHMDS	THF	5	43	26	24
12	**6b**	MeMgBr	THF	5	28	14	34
13	**6c**	NaHMDS	THF	5	49	22	38
14	**6c**	MeMgBr	THF	5	69	23	50

[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**)[15] 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[16] followed by decarboxylation. In the case of **4b**, a similar result was obtained.



Reagents and conditions: (a) Li, NH_3, *t*-BuOH, THF, -60 °C; (b) anisole, MsOH, 50 °C; (c) TMSI, CH_2Cl_2, rt.

Scheme 2

Thus, we screened the debenzylating reagents including 10% Pd/C with hydrogen or cyclohexene,[17] hydrogen bromide in acetic acid,[18] formic acid,[19] and trifluoromethanesulfonic acid.[20] We found that the anisole–methanesulfonic acid system,[21] 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.[9]

Table 3 Debenzylation of the oxazolidinones (**4a–c** and **5a–c**)[a]

Entry	Oxazolidinones	Reaction time (h)	Products (yield, %)	Side products (yield, %)
1	**4a**	5	**2a** (69)	N.T.[b]
2	**4b**	8	**2b** (77)	**9a** (56), **10a** (18)
3	**4c**	8	**2a** (97)	**9b** (77), **10b** (19)
4	**5a**	5	**3a** (69)	N.T.
5	**5b**	8	**3b** (82)	N.T.
6	**5c**	8	**3a** (100)	N.T.

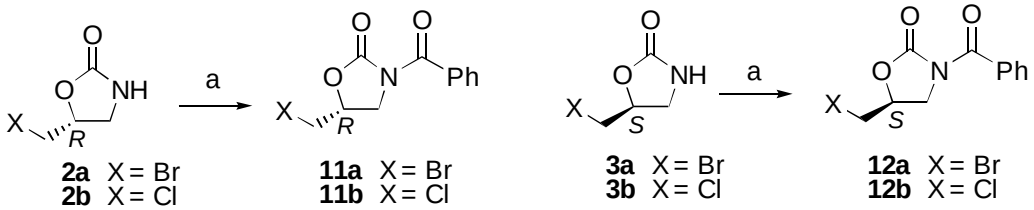
[a] The mixture of oxazolidinones and methanesulfonic acid in anisole was stirred at 50 °C.

[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



2a X = Br **2b** X = Cl — **11a** X = Br **11b** X = Cl — **3a** X = Br **3b** X = Cl — **12a** X = Br **12b** X = Cl

Reagents and conditions: (a) PhCOCl, DMAP, THF, 0 °C to rt.

Scheme 3

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 (^{1}H-NMR: 400 MHz and ^{13}C-NMR: 100 MHz) spectrometer in $CDCl_3$ 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 F_{254} (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*)-*N*-(1-phenylethyl)carbamate (6a). White needles, mp 72–73 °C (ethyl acetate). ^{1}H-NMR ($CDCl_3$) 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, Me*CH*Ph), 5.02 (1 H, m, OCH), 5.13 (1 H, br m, NH), 7.43 (5 H, m, Ph). ^{13}C-NMR ($CDCl_3$) δ: 22.2 (q, Me), 31.9 (t, 2 x CH_2Br), 50.8 (d, Me*C*HPh), 71.2 (d, OCH), 125.8, 127.4, 128.6 (3 d, Ph), 142.9 (s, Ph), 153.9 (s, C=O). IR ($CHCl_3$) cm^{-1}: 1720 (C=O). MS (EI) *m/z*: 367 (M^+), 365 (M^+), 363 (M^+), 352, 350, 348, 164, 120, 105. $[\alpha]_D^{23}$ –35.7° (*c* 2.1, $CHCl_3$). *Anal*. Calcd for $C_{12}H_{15}NO_2Br_2$: 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). ^{1}H-NMR ($CDCl_3$) δ 1.51 (3 H, d, *J* = 7.0, Me), 3.73 (2 H, d, *J* = 4.4, CH_2Cl), 3.78 (2 H, d, *J* = 4.4, CH_2Cl), 4.83 (1 H, m, MeC*H*Ph), 5.07–5.11 (2 H, m, OCH and NH), 7.43 (5 H, m, Ph). ^{13}C-NMR ($CDCl_3$) δ: 22.2 (q, Me), 32.6 (t, CH_2Cl), 50.7 (d, Me*C*HPh), 71.9 (d, OCH), 125.8, 127.3, 128.5 (3 d, Ph), 143.0 (s, Ph), 153.9 (s, C=O). IR ($CHCl_3$) cm^{-1}: 1725 (C=O). MS (EI) *m/z*: 279 (M^+), 277 (M^+), 275 (M^+), 264, 262, 260, 164, 105. $[\alpha]_D^{23}$ –42.8° (*c* 2.4, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{15}NO_3Cl_2$: 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). ^{1}H-NMR ($CDCl_3$) δ: 1.68 (3 H, d, *J* = 7.0, Me), 3.56–3.71 (4 H, m, 2 x CH_2Br), 5.07 (1 H, m, MeC*H*Ar), 5.20 (1 H, br m, NH), 5.65 (1 H, m, OCH), 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 ($CHCl_3$) cm^{-1}: 1725 (C=O). MS (EI) *m/z*: 417 (M^+), 415 (M^+), 413 (M^+), 214, 170, 155, 127. $[\alpha]_D^{23}$ –4.1° (*c* 2.1, $CHCl_3$). *Anal.* Calcd for $C_{16}H_{17}NO_2Br_2$: 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.

(5*R*,1'*S*)-5-Bromomethyl-3-(1'-phenylethyl)-2-oxazolidinone (4a). White needles, mp 95–97 °C (ethyl acetate). ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3 H, d, *J* = 7.0, Me), 2.99 (1 H, dd, *J* = 8.9, 6.1 Hz, NC*H*H), 3.29 (1 H, dd, *J* = 10.6, 7.7, BrC*H*H), 3.44 (1 H, dd, *J* = 10.6, 4.0, BrCH*H*), 3.62 (1 H, t, *J* = 8.9, NCH*H*), 4.68 (1 H, m, OCH), 5.22 (1 H, q, *J* = 7.0, MeC*H*Ph), 7.35 (5 H, m, Ph). ^{13}C-NMR ($CDCl_3$) δ: 16.2 (q, Me), 32.6 (t, NCH_2), 44.1 (t, CH_2Br), 51.4 (d, Me*C*HPh), 71.4 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 138.9 (s, Ph), 156.4 (s, C=O). IR ($CHCl_3$) cm^{-1}: 1780 (C=O). MS (EI) *m/z*: 285 (M^+), 283 (M^+), 270, 268, 204, 105. $[\alpha]_D^{23}$ –33.1° (*c* 1.4, $CHCl_3$). *Anal* Calcd for $C_{12}H_{14}NO_2Br$: C, 50.72; H, 4.97; N, 4.93. Found: C, 51.00; H, 4.98; N, 4.85.

(5*S*,1'*S*)-5-Bromomethyl-3-(1'-phenylethyl)-2-oxazolidinone (5a). A colorless oil. ^{1}H-NMR ($CDCl_3$) δ:1.62 (3 H, d, *J* = 7.0, Me), 3.28 (1 H, t, *J* = 8.9, NC*H*H), 3.36 (1 H, dd, *J* = 8.9, 5.7, NCH*H*), 3.47 (1 H, dd, *J* = 10.6, 7.0, BrC*H*H), 3.54 (1 H, dd, *J* = 10.6, 3.7, BrCH*H*), 4.60 (1 H, m, OCH), 5.23 (1 H, q, *J* = 7.0, MeC*H*Ph), 7.34 (5 H, m, Ph). ^{13}C-NMR ($CDCl_3$) δ: 16.1 (q, Me), 33.2 (t, NCH_2), 44.1 (t, CH_2Br), 51.4 (d, Me*C*HPh), 70.9 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 139.0 (s, Ph), 156.4 (s, C=O). IR (neat) cm^{-1}: 1750 (C=O). MS (EI) *m/z*: 285 (M^+), 283 (M^+), 270, 268, 204, 105. $[\alpha]_D^{23}$ –32.2° (*c* 1.6, $CHCl_3$). *Anal*. Calcd for $C_{12}H_{14}NO_2Br$: C, 50.72; H, 4.97; N, 4.93. Found: C, 51.01; H, 4.98; N, 4.85.

(5*R*,1'*S*)-5-Chloromethyl-3-(1'-phenylethyl)-2-oxazolidinone (4b). White prisms, mp 68–70 °C (ethyl

acetate). ^{1}H-NMR ($CDCl_3$) δ: 1.59 (3 H, d, *J* = 7.0, Me), 3.04 (1 H, dd, *J* = 9.2, 5.9, NC*H*H), 3.48 (1 H, dd, *J* = 11.5, 6.8, ClC*H*H), 3.59 (1 H, dd, *J* = 11.5, 4.2, ClCH*H*), 3.62 (1 H, t, *J* = 9.2, NCH*H*), 4.69 (1 H, m, OCH), 5.23 (1 H, q, *J* = 7.0, MeC*H*Ph), 7.36 (5 H, m, Ph). ^{13}C-NMR ($CDCl_3$) δ: 16.2 (q, Me), 43.1 (t, NCH_2), 44.6 (t, CH_2Br), 51.4 (d, Me*C*HPh), 71.5 (d, OCH), 126.9, 127.9, 128.6 (3 d, Ph), 139.0 (s, Ph), 156.5 (s, C=O). IR ($CHCl_3$) cm^{-1}: 1750 (C=O). MS (EI) *m/z*: 241 (M^+), 239 (M^+), 226, 224, 204, 105. $[\alpha]_D^{23}$ –57.3° (*c* 1.5, $CHCl_3$). *Anal.* Calcd for $C_{12}H_{14}NO_2Cl$: C, 60.13; H, 5.89; N, 5.84. Found: C, 60.47; H, 6.07; N, 5.59.

(5*S*,1'*S*)-5-Chloromethyl-3-(1'-phenylethyl)-2-oxazolidinone (5b). A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.60 (3 H, d, *J* = 7.0, Me), 3.27 (1 H, t, *J* = 8.8, NC*H*H), 3.40 (1 H, dd, *J* = 8.8, 5.5, NCH*H*), 3.66 (2 H, m, $ClCH_2$), 4.62 (1 H, m, OCH), 5.23 (1 H, q, *J* = 7.0, MeC*H*Ph), 7.35 (5 H, m, Ph). IR ($CHCl_3$) cm^{-1}: 1750 (C=O). MS (EI) *m/z*: 241 (M^+), 239 (M^+), 226, 224, 204, 105. $[\alpha]_D^{23}$ –32.2° (*c* 1.6, $CHCl_3$). *Anal* Calcd for $C_{12}H_{14}NO_2Cl$: C, 60.13; H, 5.89; N, 5.84. Found: C, 59.85; H, 5.98; N, 5.69.

(5*R*,1'*S*)-5-Bromomethyl-3-[1'-(1''-naphthyl)ethyl]-2-oxazolidinone (4c). White needles, mp 105–106 °C (ethyl acetate). ^{1}H-NMR ($CDCl_3$) δ: 1.74 (3 H, d, *J* = 7.0, Me), 2.53 (1 H, dd, *J* = 9.2, 5.1, NC*H*H), 2.97 (1 H, dd, *J* = 10.6, 8.1, BrC*H*H), 3.23 (1 H, dd, *J* = 10.6, 4.4, BrCH*H*), 3.55 (1 H, t, *J* = 9.2, NC*H*H), 4.61 (1 H, m, OCH), 5.92 (1 H, q, *J* = 7.0, MeC*H*Ar), 7.43 (4 H, m, Ar), 7.88 (2 H, m, Ar), 8.12 (1 H, d, *J* = 8.8, Ar). IR ($CHCl_3$) cm^{-1}: 1750 (C=O). MS (EI) *m/z*: 335 (M^+), 333 (M^+), 320, 318, 254, 155. $[\alpha]_D^{23}$ –6.3° (*c* 2.0, $CHCl_3$). *Anal*. Calcd for $C_{16}H_{16}NO_2Br$: C, 57.50; H, 4.83; N, 4.19. Found: C, 57.67; H, 4.86; N, 4.14.

(5*S*,1'*S*)-5-Bromomethyl-3-[1'-(1''-naphthyl)ethyl]-2-oxazolidinone (5c). A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.75 (3 H, d, *J* = 7.0, Me), 2.84 (1 H, t, *J* = 9.2, NC*H*H), 3.28 (1 H, dd, *J* = 9.2, 6.2, NCH*H*), 3.47 (2 H, d, *J* = 4.4, $BrCH_2$), 4.45 (1 H, m, OCH), 5.93 (1 H, q, *J* = 7.0, MeC*H*Ar), 7.53 (4 H, m, Ar), 7.87 (2 H, m, Ar), 8.15 (1 H, d, *J* = 8.8, Ar). IR ($CHCl_3$) cm^{-1}: 1750 (C=O). MS (EI) *m/z*: 335 (M^+), 333 (M^+), 320 (26), 318 (26), 254 (48), 155 (100). $[\alpha]_D^{23}$ –26.7° (*c* 2.1, $CHCl_3$). *Anal*. Calcd for $C_{16}H_{16}NO_2Br$: 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 literature;[4] 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 literature[15] clearly showed the formation of **8**: $[\alpha]_D^{31}$ –47.0° (*c* 0.08, $CHCl_3$) [lit.,[15a] $[\alpha]_D^{20}$ –46° (*c* 0.66, EtOH); for (*R*)-enantiomer, lit.,[15b] $[\alpha]_D^{20}$ +49.3° (*c* 1.12, CH_2Cl_2)].

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 *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 each filtrate from the hexane-suspension in the reaction of **4b** and **4c** was concentrated *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**.

(*R*)-5-Bromomethyl-2-oxazolidinone (2a). $[\alpha]_D^{23}$ –2.6° (*c* 1.0, $CHCl_3$) [lit.,[9] –2.6° (*c* 3.2, CH_2Cl_2)].

(*S*)-5-Bromomethyl-2-oxazolidinone (3a). $[\alpha]_D^{23}$ +3.0° (*c* 0.9, $CHCl_3$) [lit.,[9] +2.8° (*c* 3.2, CH_2Cl_2)].

(*RS*)-1-(4-Methoxyphenyl)-1-phenylethane (9a).[22] A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.61 (3 H, d, *J* = 7.3, *Me*CH), 3.78 (3 H, s, OMe), 4.10 (1 H, q, *J* = 7.33, MeC*H*), 6.82 (2 H, d, *J* = 8.8, *Ar*OMe), 7.13 (2 H, d, *J* = 8.6, *Ar*OMe), 7.17–7.27 (5 H, m, Ar). IR (neat) cm^{-1}: 1520 (Ar), 1250 (ArOMe). MS (EI) *m/z*: 212 (M^+), 197, 182, 165, 153. *Anal*. Calcd $C_{15}H_{16}O$: C, 84.9; H, 7.60. Found: C, 84.77. H, 7.69.

(*RS*)-1-(2-Methoxyphenyl)-1-phenylethane (10a).[22] A colorless oil. ^{1}H-NMR ($CDCl_3$) δ: 1.57 (3 H, d, *J* = 7.3 Hz, CH*Me*), 3.77 (3 H, s, OMe), 4.57 (1 H, q, *J* = 7.3, MeC*H*), 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, 181, 165, 152.

(*RS*)-1-(4-Methoxyphenyl)-1-(1-naphthyl)ethane (9b). White solid, mp 70–71 °C (hexane). ^{1}H-NMR ($CDCl_3$) δ: 1.74 (3 H, d, *J* = 7.0, *Me*CH), 3.75 (3 H, s, OMe), 4.88 (1 H, q, *J* = 7.0, MeC*H*), 6.80 (2 H, d, *J* = 8.6, *Ar*OMe), 7.14 (2 H, d, *J* = 8.6, *Ar*OMe), 7.39–7.47 (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-Methoxyphenyl)-1-(1-naphthyl)ethane (10b). Amorphous solid. ^{1}H-NMR ($CDCl_3$) δ: 1.67 (3 H, d, *J* = 7.0, *Me*CH), 3.88 (3 H, s, OMe), 5.32 (1 H, q, *J* = 7.0 Hz, MeC*H*), 6.77 (1 H, m, Ar), 6.88–6.93 (2 H, m, Ar), 7.12–7.14 (1 H, m, Ar), 7.38–7.47 (4 H, m, Ar), 7.72 (1 H, m, Ar), 7.89 (1 H, m, Ar), 8.01 (1 H, m, Ar). IR (neat) cm^{-1}: 1495 (Ar), 1245 (ArOMe). HR-MS *m/z*: 262.1355 (Calcd for $C_{15}H_{16}O$: 262.1358). MS (EI) *m/z*: 262 (M^+), 247, 231, 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 *in vacuo*. The residue was chromatographed on silica gel (hexane:ethyl acetate = 9:1) to give **10c** as a colorless oil (50 mg, 64%). ^{1}H-NMR ($CDCl_3$) δ: 1.63 (3 H, d, *J* = 1.6, Me), 4.37 (1 H, q, *J* = 7.3 ArC*H*), 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° (*c* 3.3, $CHCl_3$) [lit.,[9] –18.7° (*c* 3.2 CH_2Cl_2)].

(*S*)-5-Chloromethyl-2-oxazolidinone (3b). $[\alpha]_D^{23}$ +20.0° (*c* 2.4, $CHCl_3$) [lit.,[9] +19.1° (*c* 3.3, CH_2Cl_2)].

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.[25] 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 ($CHCl_3$) cm^{-1}: 1790 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.64 (2 H, d, *J* = 5.1, CH_2Br), 4.05 (1 H, dd, *J* = 11.4, 5.9, NC*H*H), 4.31 (1 H, dd, *J* = 11.4, 8.4, NCH*H*), 4.90 (1 H, m, OCH), 7.42–7.67 (5 H, m, Ar). HR-MS *m/z*: 282.9841 (Calcd for $C_{11}H_{10}NO_3Br$: 282.9844). MS (EI) *m/z*: 285 (M^+), 283 (M^+), 105, 77. $[\alpha]_D^{30}$ +9.4° (*c* 0.8, $CHCl_3$).

(*R*)-*N*-Benzoyl-5-chloromethyl-2-oxazolidinone (11b). White solid, mp 93–94 °C (ethyl acetate). IR ($CHCl_3$) cm^{-1}: 1800 (C=O). ^{1}H-NMR ($CDCl_3$) δ: 3.77–3.87 (2 H, m, CH_2Cl), 4.11 (1 H, dd, *J* = 11.4, 5.9, NC*H*H), 4.31 (1 H, dd, *J* = 11.4, 8.8, NCH*H*), 4.94 (1 H, m, OCH), 7.42–7.67 (5 H, m, Ar). HR-MS *m/z*: 239.0349 (Calcd for $C_{11}H_{10}NO_3Cl$: 239.0350). MS (EI) *m/z*: 241 (M^+), 239 (M^+), 105, 77. $[\alpha]_D^{28}$ –4.6° (*c* 0.4, $CHCl_3$).

(*S*)-*N*-Benzoyl-5-bromomethyl-2-oxazolidinone (12a). HR-MS *m/z*: 282.9842 (Calcd for $C_{11}H_{10}NO_3Br$: 282.9844). $[\alpha]_D^{31}$ –9.6° (*c* 1.0, $CHCl_3$). 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 $C_{11}H_{10}NO_3Cl$: 239.0350). $[\alpha]_D^{31}$ +4.6° (*c* 0.4, $CHCl_3$). 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 ϕ); 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 ϕ); 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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