Dynamic Kinetic Resolution Utilizing 2-Oxoimidazolidine-4-carboxylate as a Chiral Auxiliary: Stereoselective Alkylation of α-Bromo Amides with Malonic Ester Enolates

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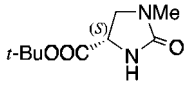
Stereoselective carbon−carbon bond formation by dynamic kinetic resolution using *tert*-butyl (4*S*)-1-methyl-2-oxoimidazolidine-4-carboxylate (**1**) as a chiral auxiliary was developed. Reaction of a diastereomeric mixture of *tert*-butyl (4*S*)-3-[(2*RS*)-2-bromoacyl]-1-methyl-2-oxoimidazolidine-4-carboxylates (**2**) with a malonic ester enolate in HMPA predominantly afforded *tert*-butyl (4*S*)-3-[(2*R*)-2-alkyl-3,3-bis(alkoxycarbonyl)propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-**8**] in good yields. The stereoselectivity of this reaction was in accordance with our working hypothesis based on the conformational analysis of **2** and elucidated the unique characteristics of **1** as a novel chiral auxiliary for dynamic kinetic resolution. The alkylated products (*S*,*R*)-**8e**,**j**,**k** were easily converted to chiral α-alkyl succinic acid derivatives and chiral *β*-amino acid derivatives, both of which have been known as key building blocks for the syntheses of a variety of biologically active compounds.

Dynamic kinetic resolution has been recognized as an effective synthetic method for the preparation of enantiomerically enriched compounds because racemic substrates can be transformed to optically pure products in 100% yield in theory.[1] Moreover, a novel type of dynamic kinetic resolution, in which a diastereomeric mixture of a chirally labile α-halo amides or α-halo esters having a chiral auxiliary is employed as a substrate, has recently received much attention as a new category of asymmetric synthesis.[2]

In our synthetic studies on ACE inhibitors, we noticed a new dynamic kinetic resolution process in which the reaction of a diastereomeric mixture of *tert*-butyl (4*S*)-3-[(2*RS*)-2-bromoacyl]-1-methyl-2-oxoimidazolidine-4-carboxylate (**2**) with a variety of L-α-amino acid esters gave one diastereomer in greater than 50% yield.[3] Furthermore, as part of general studies on dynamic kinetic resolution through stereoselective nucleophilic substitution reaction using (4*S*)-2-oxoimidazolidine-4-carboxylate (**1**) as a chiral auxiliary, we have reported the reaction of **2** with an amine in the presence of a base.[2a,b] The reaction proceeded by stereospecific SN2 substitution incorporated with rapid interconversion between a couple of diastereomeric substrates, resulting in the predominant formation of optically active amination products. Through easy removal of **1**, this procedure provides a practical synthesis of a range of optically active α-amino acids. These results revealed not only the potency of **1** as a novel chiral auxiliary but also the possibility of a new effective transformation process of synthetically accessible racemic α-halo acids (**3**) to useful chiral synthons. Thus we expected that an extension of this novel methodology by employing various nucleophiles would enable the efficient syntheses of a wide variety of useful optically active α-substituted carboxylic acid derivatives (**5**) (Scheme 1).



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In a previous paper, we proposed a working hypothesis on the stereoselectivity for the reaction of *tert*-butyl (4*S*)-3-[(2*RS*)-2-bromopropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate (**2a**) with a nucleophile, based on the conformational analysis of **2a** (Scheme 2).[2b] According to this hypothesis, (*S*,*R*)-**2a** would be more reactive for a nucleophile than (*S*,*S*)-**2a** because the reaction site of (*S*,*S*)-**2a** was supposed to be shielded by the sterically hindered *tert*-butyl ester group. In the amination reaction, however, the stereochemistry of the product was completely opposite to that expected in this hypothesis.

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(1) (a) Noyori, R.; Tokunaga, M.; Kitamura, M. *Bull. Chem. Soc. Jpn.* **1995**, *68*, 36. (b) Ward, R. S. *Tetrahedron: Asymmetry* **1995**, *6*, 1475. (c) Stecher, H.; Faber, K. *Synthesis* **1997**, 1. (d) Noyori, R.; Ikeda, T.; Ohkuma, T.; Widhalm, M.; Kitamura, M.; Takaya, H.; Akutagawa, S.; Sayo, N.; Saito, T.; Taketomi, T.; Kumobayashi, H. *J. Am. Chem. Soc.* **1989**, *111*, 9134. (e) Kitamura, M.; Ohkuma, T.; Tokunaga, M.; Noyori, R. *Tetrahedron: Asymmetry* **1990**, *1*, 1. (f) Kitamura, M.; Tokunaga, M.; Noyori, R. *J. Am. Chem. Soc.* **1993**, *115*, 144. (g) Kitamura, M.; Tokunaga, M.; Noyori, R. *Tetrahedron* **1993**, *49*, 1853. (h) Hayashi, T.; Konishi, M.; Fukushima, M.; Kanehira, K.; Hioki, T.; Kumada, M. *J. Org. Chem.* **1983**, *48*, 2195. (i) Stürmer, R. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 59. (j) Tai, A.; Watanabe, H.; Harada, T. *Bull. Chem. Soc. Jpn.* **1979**, *52*, 1468. (k) Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1320. (l) Inagaki, M.; Hiratake, J.; Nishioka, T.; Oda, J. *J. Am. Chem. Soc.* **1991**, *113*, 9360. (m) Fülling, G.; Sih, C. J. *J. Am. Chem. Soc.* **1987**, *109*, 2845. (n) Gu, R.; Lee, I.; Sih, C. J. *Tetrahedron Lett.* **1992**, *33*, 1953. (o) Matteson, D. S.; Man, H. W. *J. Org. Chem.* **1994**, *59*, 5734.

(2) (a) Nunami, K.; Kubota, H.; Kubo, A. *Tetrahedron Lett.* **1994**, *35*, 8639. (b) Kubota, H.; Kubo, A.; Takahashi, M.; Shimizu, R.; Da-te, T.; Okamura, K.; Nunami, K. *J. Org. Chem.* **1995**, *60*, 6776. (c) Kubo, A.; Kubota, H.; Takahashi, M.; Nunami, K. *Tetrahedron Lett.* **1996**, *37*, 4957. (d) Koh, K.; Ben, R. N.; Durst, T. *Tetrahedron Lett.* **1993**, *34*, 4473. (e) Koh, K.; Durst, T. *J. Org. Chem.* **1994**, *59*, 4683. (f) O'Meara, J. A.; Jung, M.; Durst, T. *Tetrahedron Lett.* **1995**, *36*, 2559. (g) Ward, R. S.; Pelter, A.; Goubet, D.; Pritchard, M. C. *Tetrahedron: Asymmetry* **1995**, *6*, 93. (h) Ward, R. S.; Pelter, A.; Goubet, D.; Pritchard, M. C. *Tetrahedron: Asymmetry* **1995**, *6*, 469. (i) Caddick, S.; Jenkins, K. *Tetrahedron Lett.* **1996**, *37*, 1301.

(3) Hayashi, K.; Nunami, K.; Kato, J.; Yoneda, N.; Kubo, M.; Ochiai, T.; Ishida, R. *J. Med. Chem.* **1989**, *32*, 289.

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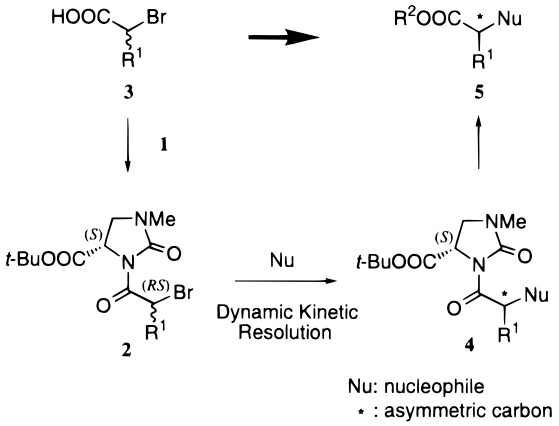
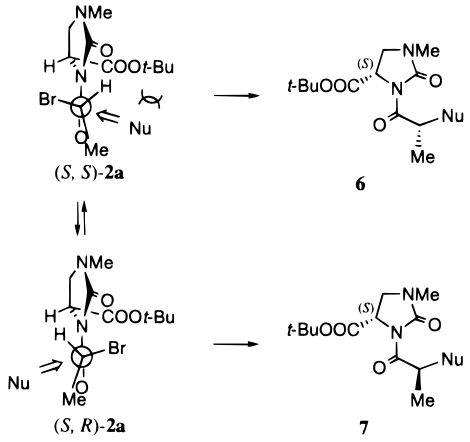
Scheme 1. Asymmetric Transformation of Racemic α-Halo Acids by Dynamic Kinetic Resolution



Scheme 2



Primary and secondary amines reacted with (*S*,*S*)-**2a** selectively, and the dynamic kinetic resolution resulted in the predominant formation of **6** (Nu = NR^3R^4). We speculated that this stereoselectivity is based on the unique transition state in which an interaction between an amine and the ester moiety of (*S*,*S*)-**2a** accelerated the formation of **6**.[2b] This speculation prompted us to investigate the reaction of **2a** with a nucleophile having no capability for the interaction with the ester moiety in the transition state. Such a nucleophile was supposed to react with (*S*,*R*)-**2a** stereoselectively to afford **7**, according to our initial working hypothesis.

Considering the synthetic utility and the mechanistic interest of this new methodology, we focused our attention on the carbon nucleophile which enables the carbon−carbon bond formation. Malonic ester enolates were selected as suitable carbon nucleophiles because they have soft nucleophilicity sufficient for an alkylation reaction and have appropriate basicity to cause rapid epimerization at the asymmetric carbon attached to the bromo substituent of **2**, which is essential to achieve the dynamic kinetic resolution but not to racemize the asymmetric carbon of 2-oxoimidazolidine ring of **2**.

In this paper, we report the first example of highly stereoselective carbon−carbon bond formation by chiral auxiliary based dynamic kinetic resolution of α-halo acid,[4] which can be applied to the synthesis of a variety of optically active α-alkyl succinic acid derivatives and optically active α- or *β*-alkyl *β*-amino acid derivatives, both of which have been noticed as key building blocks for the syntheses of biologically active compounds.

Scheme 3

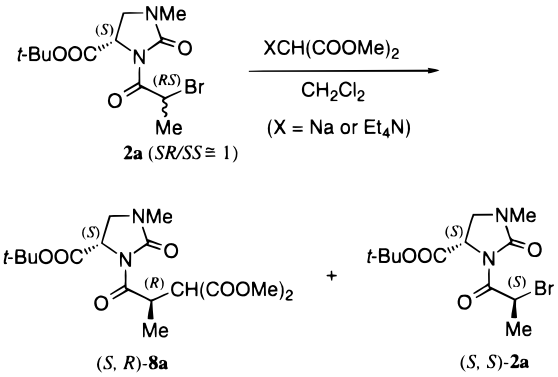


Table 1. Reaction of 2a with Malonic Ester Enolate in CH_2Cl_2

		8a		2a	
run	time	*SR* :*SS* [c]	yield [d] (%)	*SS*:*SR* [c]	yield [d] (%)
1[a]	90 h	93:7	31	70:30	62
2[b]	20 min	97:3	15	59:41	84
3[b]	1 h	89:11	40	78:22	57
4[b]	3 h	76:24	63	99:1	33

[a] The reaction was carried out with 3 equiv of sodium dimethyl malonate at 25 °C. [b] The reaction was performed using 3 equiv of tetraethylammonium dimethyl malonate at 4 °C. [c] Determined by HPLC analysis. [d] Isolated yield.

Results and Discussion

Kinetic Resolution. In order to confirm the difference of the reaction rate between the diastereomeric substrates in the reaction with malonic ester enolate, the kinetic resolution of **2a** was examined. The reaction of a diastereomeric mixture of **2a** with malonic ester enolate was performed in CH_2Cl_2 since the chirality of **2a** and the alkylated products was supposed to be completely preserved in CH_2Cl_2 (Scheme 3).[5]

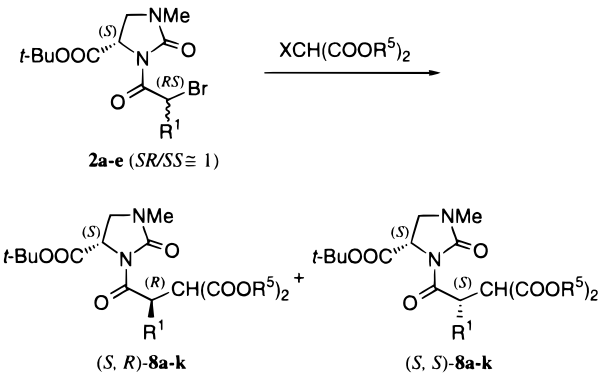
When **2a** was treated with 3 equiv of sodium dimethyl malonate, an easily accessible enolate, in CH_2Cl_2 at 25 °C, the alkylation reaction proceeded resulting in the formation of **8a**. After 90 h, HPLC analysis of the isolated products revealed that (*S*,*R*)-**8a**[6] of 86% de was obtained in 31% yield, while (*S*,*S*)-**2a** of 40% de was recovered in 62% yield (Table 1, run 1). Though this result indicated that efficient kinetic resolution actually proceeded as expected, the reaction rate of (*S*,*R*)-**2a** with sodium enolate was very slow, and it was probably because of its poor solubility in CH_2Cl_2 that other reaction conditions were examined. Consequently, the ammonium enolate of malonic ester was found to react easily

(4) A part of this work has been reported in previous communication: Kubo, A.; Takahashi, M.; Kubota, H.; Nunami, K. *Tetrahedron Lett.* **1995**, *36*, 6251.

(5) Kubota, H.; Kubo, A.; Nunami, K. *Tetrahedron Lett.* **1994**, *35*, 3107.

(6) The designation of (*R*)-configuration of (*S*,*R*)-**8a** is a consequence of a change in substituent priority assignments. Since the reaction is assumed to proceed with inversion of the asymmetric carbon attached to the bromo substituent of **2a**, (*S*,*R*)-**8a** is derived from (*S*,*R*)-**2a**.

Scheme 4



with **2a** in CH_2Cl_2. The reaction of **2a** with 3 equiv of tetraethylammonium dimethyl malonate, which was prepared from Et_4NCl and freshly prepared sodium dimethyl malonate, in CH_2Cl_2 at 4 °C for 20 min, proceeded stereoselectively to afford (*S*,*R*)-**8a** of 94% de in 15% yield (run 2). When the reaction was allowed to continue for 3 h, (*S*,*S*)-**2a** of 98% de was recovered in 33% yield (run 4). The stereochemistry of (*S*,*R*)-**8a** was confirmed by X-ray crystallographic analysis.[7] These results apparently showed that **1** works as an efficient chiral auxiliary for kinetic resolution of **2a** with a carbon nucleophile as well as with an amine,[5] and malonic ester enolate reacted with (*S*,*R*)-**2a** more rapidly than with (*S*,*S*)-**2a**. It was noteworthy that the stereoselectivity of this reaction completely accorded with our working hypothesis in which (*S*,*R*)-**2a** would be more reactive than (*S*,*S*)-**2a** due to the steric effect of the chiral auxiliary, unless there were any attractive intermolecular interactions between **1** and a nucleophile.

Dynamic Kinetic Resolution. The satisfactory results of kinetic resolution prompted us to examine the dynamic kinetic resolution (Scheme 4). As a rapid interconversion between the substrates is essential to achieve efficient dynamic kinetic resolution, we performed the reaction in several kinds of polar solvents, which were verified to accelerate epimerization at the asymmetric carbon attached to the bromo substituent of **2a** in the presence of a base.[2a] The reaction of **2a** with 3 equiv of sodium dimethyl malonate in polar solvents such as DMF, DMSO, *N*-methyl-2-pyrrolidinone (NMP), and HMPA at 25 °C resulted in the predominant formation of (*S*,*R*)-**8a** in accordance with the stereochemistry of the kinetic resolution (Table 2, entries 1−4). The stereoselectivity was greatly affected by a solvent. The best result was observed in both yield and stereoselectivity by using HMPA, in which it was ascertained that the epimerization of **2a** was extremely fast (entry 4). Besides, even though each isolated product, (*S*,*R*)- or (*S*,*S*)-**8a**, was treated again with 3 equiv of sodium dimethyl malonate in HMPA at 25 °C for 3 h, the products were completely recovered without any epimerization. These results apparently indicated that (*S*,*R*)-**8a** was predominantly afforded not by the thermodynamic stability of the product but by the dynamic kinetic resolution of **2a**. Reduction of the reaction temperature did not change the stereoselectivity significantly (entry 5). Moreover, addition of a base such as Et_3N also scarcely affected the yield or the stereoselectivity, revealing that a malonic ester enolate acts not only as a nucleophile but also as an effective base for the epimerization of **2a** as expected (entry 6). Slightly diminished stereoselectivity was observed by changing the counter cation of malonic ester enolate from sodium to lithium or potassium (entries 7 and 8).

Next, the effect of the ester moiety of malonic esters on stereoselectivity was examined. The bulkiness of the alkyl ester group scarcely influenced the stereoselectivity of the reaction with **2a** (entries 4 and 9−11). On the other hand, sodium dibenzyl malonate increased the stereoselectivity affording (*S*,*R*)-**8e** of 88% de in 82% yield (entry 12). Variations of R^1 on the substrates[8] gave satisfactory yields and stereoselectivity, except for **2e** which was accompanied by a side reaction (entries 13−18). Among them, the reaction of **2c** having a bulky substituent with sodium dibenzyl malonate gave (*S*,*R*)-**8k** of 90% de in 79% yield (entry 18). The stereochemistry of (*S*,*R*)-**8d** and (*S*,*R*)-**8g** was confirmed by X-ray crystallographic analysis,[7] and that of other major products was assumed to have the same (*S*,*R*) configuration by the analogy with **8a**, **8d**, and **8g**.

Transformation of the Alkylated Products to Chiral Synthons. We investigated the transformation of the asymmetrically alkylated products to synthetically and/or biologically useful compounds. Benzyl ester derivative (*S*,*R*)-**8e** was hydrogenated to afford dicarboxylic acid (*S*,*R*)-**9a**. Decarboxylation of (*S*,*R*)-**9a** by heating at 100 °C in DMSO for 1 h occurred easily, and thus obtained (*S*,*R*)-**10a** was methylated with (trimethylsilyl)-diazomethane ($TMSCHN_2$)[9] in a good yield. The chiral auxiliary of (*S*,*R*)-**11a** was removed by treatment with 1 equiv of NaOMe in MeOH at rt for 2 h to afford dimethyl (2*R*)-2-methylsuccinate [(*R*)-**12a**)] (Scheme 5). The optical purity of (*R*)-**12a** was confirmed by comparison of its optical rotation value ($[\alpha]^{25}_D$ +4.8) with that in the literature ($[\alpha]^{20}_D$ +4.8).[10] Alkylated products (*S*,*R*)-**8j**,**k** were converted to corresponding dimethyl 2-alkylsuccinates (*R*)-**12b**,**c**, respectively, in the same procedure. The optically active α-alkyl succinic acid derivatives are key building blocks for the synthesis of a variety of biologically active compounds.[11]

Conversion of carboxylic acid **10** to each type of the optically active α- or *β*-substituted *β*-amino acid derivatives,[12] which are also noticeable synthetic intermediates, was investigated (Scheme 6). As a typical example, Curtius rearrangement of (*S*,*R*)-**10a** using diphenylphosphoryl azide (DPPA)[13] followed by treatment with benzyl alcohol and removal of the chiral auxiliary with NaOMe afforded methyl (2*R*)-3-[((benzyloxy)carbonyl)amino]-2-methylpropionate [(*R*)-**14**]. On the other hand, *tert*-butyl (3*R*)-3-[((benzyloxy)carbonyl)amino]butanoate [(*R*)-**17**] was synthesized by Curtius rearrangement of (*R*)-**16**, which

(7) The author has deposited atomic coordinates for this structure with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, U.K.

(8) The syntheses of the substrates **2a**−**e** were previously reported.[2b,3]

(9) Aoyama, T.; Shioiri, T. *Chem. Pharm. Bull.* **1981**, *29*, 3249.

(10) Rossi, R.; Diversi, P.; Ingrosso, G. *Gazz. Chim. Ital.* **1968**, *98*, 1391.

(11) (a) Gordon, J. J.; Devlin, J. P.; East, A. J.; Ollis, W. D.; Sutherland, I. O.; Wright, D. E.; Ninet, L. *J. Chem. Soc., Perkin Trans. 1* **1975**, 819. (b) Reich, R.; Thompson, E. W.; Iwamoto, Y.; Martin, G. R.; Deason, J. R.; Fuller, G. C.; Miskin, R. *Cancer Res.* **1988**, *48*, 3307. (c) Umezawa, H.; Aoyagi, T.; Tanaka, T.; Suda, H.; Okuyama, A.; Naganawa, H.; Hamada, M.; Takeuchi, T. *J. Antibiot.* **1985**, *38*, 1629.

(12) (a) Cole, D. C. *Tetrahedron* **1994**, *50*, 9517. (b) Juarist, E.; Quintana, D.; Escalante, J. *Aldrichimica Acta*. **1994**, *27*, 3.

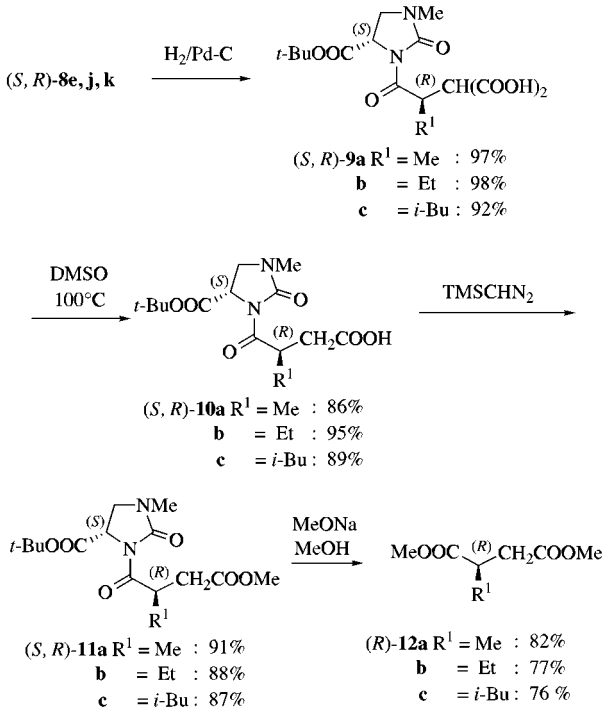
(13) (a) Ninomiya, K.; Shioiri, T.; Yamada, S. *Tetrahedron* **1974**, *30*, 2151. (b) Ninomiya, K.; Shioiri, T.; Yamada, S. *Chem. Pharm. Bull.* **1974**, *22*, 1398.

Table 2. Reaction of Bromides 2a−e with Malonic Ester Enolate in a Polar Solvent

entry[a]	substrate	solvent	time(h)	X	R^1	R^5	product	(*S*, *R*):(*S*, *S*) [b]	yield(%) [c]
1	**2a**	DMF	24	Na	Me	Me	**8a**	68:32	77
2	**2a**	DMSO	3	Na	Me	Me	**8a**	69:31	97
3	**2a**	NMP	3	Na	Me	Me	**8a**	87:13	90
4	**2a**	HMPA	3	Na	Me	Me	**8a**	88:12	92
5 [d]	**2a**	HMPA	24	Na	Me	Me	**8a**	89:11	91
6 [e]	**2a**	HMPA	3	Na	Me	Me	**8a**	88:12	90
7	**2a**	HMPA	24	Li	Me	Me	**8a**	76:24	79
8	**2a**	HMPA	3	K	Me	Me	**8a**	84:16	85
9	**2a**	HMPA	12	Na	Me	Et	**8b**	91:9	86
10	**2a**	HMPA	12	Na	Me	*i*-Pr	**8c**	90:10	93
11	**2a**	HMPA	12	Na	Me	*t*-Bu	**8d**	89:11	73
12	**2a**	HMPA	12	Na	Me	Bn	**8e**	94:6	82
13	**2b**	HMPA	24	Na	Et	Me	**8f**	90:10	89
14	**2c**	HMPA	48	Na	*i*-Bu	Me	**8g**	94:6	81
15	**2d**	HMPA	24	Na	$(CH_2)_2Ph$	Me	**8h**	93:7	85
16	**2e**	HMPA	24	Na	CH_2Ph	Me	**8i**	96:4	45[f]
17	**2b**	HMPA	24	Na	Et	Bn	**8j**	94:6	80
18	**2c**	HMPA	48	Na	*i*-Bu	Bn	**8k**	95:5	79

[a] The reaction was carried out with 3 equiv of freshly prepared malonic ester enolate at 25 °C. [b] Determined by HPLC analysis. [c] Isolated yield. [d] The reaction was performed at 4 °C. [e] 1 equiv of Et_3N was added. [f] Elimination of HBr from the substrate **2e** occurred as a side reaction.

Scheme 5



was easily prepared by chemoselective hydrolysis of the imide moiety of (*S*,*R*)-**15**.[14]

(14) To confirm the optical purities of (*R*)-**14** and (*R*)-**17**, both compounds were converted to *β*-amino acids, (2*R*)-3-amino-2-methylpropanoic acid {$[\alpha]^{23}_D$ −14.0 (*c* 0.42, H_2O) [lit.[15a] $[\alpha]^{17}_D$ −14.2 (*c* 0.42, H_2O)]} and (3*R*)-3-aminobutanoic acid {$[\alpha]^{23}_D$ −38.1 (*c* 0.48, H_2O) [lit.[15b] $[\alpha]^{18}_D$ +38.8 (*c* 0.48, H_2O) for the antipode]}, respectively.

(15) (a) Balenović, K.; Bregant, N. *Tetrahedron* **1959**, *5*, 44. (b) Balenović, K.; Cerar, D.; Fuks, Z. *J. Chem. Soc.* **1952**, 3316.

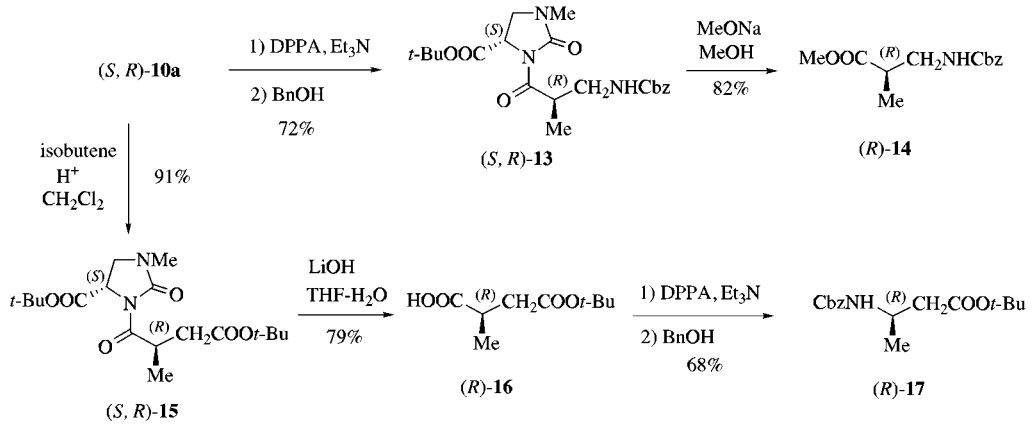
Conclusion

We have developed highly stereoselective carbon−carbon bond formation by dynamic kinetic resolution of α-bromo carboxylic acid using *tert*-butyl (4*S*)-1-methyl-2-oxoimidazolidine-4-carboxylate (**1**) as a chiral auxiliary. The reaction of the diastereomeric mixture of **2** with malonic ester enolates in HMPA predominantly afforded (*S*,*R*)-**8** in good yields. This reaction was revealed to consist of the stereoselective substitution reaction incorporated with a rapid interconversion between the substrates according to our working hypothesis. In this system, a malonic ester enolate acts not only as an appropriate nucleophile but also as a base for the epimerization of **2**. Stereoselectivity of this alkylation accorded to our working hypothesis and was opposite to that of amination of **2** (Scheme 7). These results demonstrated the unique character of **1** as a chiral auxiliary for dynamic kinetic resolution. The ester moiety of **2** would exist as a sterically hindered shielding group in the reaction with an anionic nucleophile such as a malonic ester enolate. On the other hand, the same ester moiety is supposed to serve as a directing group in the amination reaction by interacting with an amine in the transition state.[2b] Further, a new methodology for an efficient synthesis of a variety of chiral α-alkyl succinic acid derivatives and optically active α- or *β*-alkyl *β*-amino acid derivatives was developed by decarboxylation of the alkylated products (*S*,*R*)-**8**, followed by the removal of the chiral auxiliary without racemization. Efforts to further expand the utility of this methodology are in progress in this laboratory.

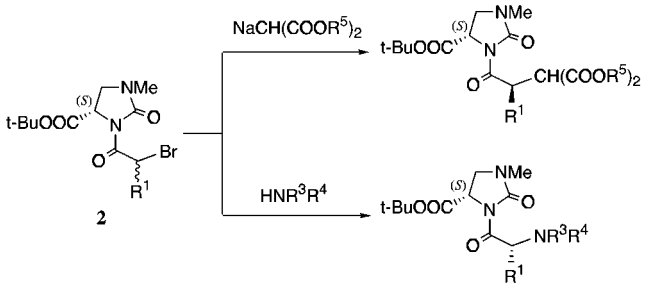
Experimental Section

General. Melting points are uncorrected. ^1H NMR spectra were recorded at 200 MHz with TMS as an internal standard. HPLC analyses were performed with a C_{18} column (4.6 × 150

Scheme 6



Scheme 7



mm) using a H_2O-CH_3CN solvent system as eluent. Column chromatography was performed on silica gel (70−230 mesh). Preparative TLC was performed on silica gel precoated glass plates. All reactions with air- and moisture-sensitive compounds were conducted in oven-dried glassware under an atmosphere of dry nitrogen.

Reaction of Bromide 2a with Tetraethylammonium Dimethyl Malonate (Kinetic Resolution, Table 1, Run 3). Sodium hydride (107 mg, 4.46 mmol) was added portionwise to a solution of dimethyl malonate (591 mg, 4.47 mmol) in CH_2Cl_2 (10 mL) at 4 °C. After the solution was stirred at 25 °C for 1 h, Et_4NCl (741 mg, 4.47 mmol) was added to the above mixture. Stirring was continued for 30 min at 25 °C, and then **2a** (500 mg, 1.49 mmol) was added to the solution at 4 °C. After stirring was continued for 1 h at the same temperature, the reaction mixture was diluted with AcOEt and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was chromatographed on silica gel eluting with hexane−AcOEt (2:1) to give a diastereomeric mixture of **8a** (231 mg, 40%), and a diastereomeric mixture of **2a** (284 mg, 57%) was recovered. The mixture of **8a** was separated by preparative TLC [hexane−AcOEt (2:1)] to afford (*S*,*R*)-**8a** (R_f 0.45) and (*S*,*S*)-**8a** (R_f 0.38), each as colorless needles.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis(methoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8a]**: colorless needles, mp 139−140 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −43.2 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.26 (3H, d, J = 7.0 Hz), 1.45 (9H, s), 2.89 (3H, s), 3.31 (1H, dd, J = 4.0, 9.6 Hz), 3.64−3.76 (1H, m), 3.66 (3H, s), 3.76 (3H, s), 3.82 (1H, d, J = 11.2 Hz), 4.46−4.59 (1H, m), 4.65 (1H, dd, J = 4.0, 10.3 Hz); IR (KBr) 1750, 1728, 1681 cm^{-1}; SIMS m/z 387 (M^+ + 1), 331, 187, 127 (base). Anal. Calcd for $C_{17}H_{26}N_2O_8$: C, 52.84; H, 6.78; N, 7.25. Found: C, 52.75; H, 6.69; N, 7.23.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis(methoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8a]**: colorless needles, mp 89−90 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −57.4 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.21 (3H, d, J = 7.0 Hz), 1.47 (9H, s), 2.91 (3H, s), 3.30 (1H, dd, J = 4.2, 9.6 Hz), 3.67 (1H, dd, J = 9.6, 10.1 Hz), 3.70 (3H, s), 3.75 (3H, s), 3.87 (1H, d, J = 10.5 Hz), 4.50−4.65 (2H, m); IR (KBr) 1760, 1740, 1672 cm^{-1}; SIMS m/z 387 (M^+ + 1), 331, 187, 127 (base). Anal. Calcd for $C_{17}H_{26}N_2O_8$: C, 52.84; H, 6.78; N, 7.25. Found: C, 52.60; H, 6.62; N, 7.19.

Typical Procedure for the Reaction of Bromide 2 with Sodium Dialkyl Malonate (Dynamic Kinetic Resolution). *tert*-Butyl (4*S*)-3-[3,3-Bis(ethoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8b and (*S*,*S*)-8b]. Sodium hydride (321 mg, 13.4 mmol) was added portionwise to a solution of diethyl malonate (2.15 g, 13.4 mmol) in HMPA (10 mL) at 0 °C. Stirring was continued for 1 h at 25 °C, and then **2a** (1.50 g, 4.47 mmol) was added to the solution at 0 °C. After stirring was continued for 12 h at 25 °C, the reaction mixture was diluted with AcOEt and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The residue was purified by column chromatography on silica gel eluting with hexane−AcOEt (2:1) to give a diastereomeric mixture of **8b** (1.59 g, 86%). The diastereomers were separated by preparative TLC [hexane−AcOEt (2:1)] to afford (*S*,*R*)-**8b** (R_f 0.60) and (*S*,*S*)-**8b** (R_f 0.52), each as colorless needles. **(*S*,*R*)-8b**: mp 83−84 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −44.9 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.14−1.31 (9H, m), 1.45 (9H, s), 2.89 (3H, s), 3.30 (1H, dd, J = 4.0, 9.6 Hz), 3.69 (1H, dd, J = 9.6, 10.4 Hz), 3.88 (1H, d, J = 11.2 Hz), 4.04−4.30 (4H, m), 4.45−4.58 (1H, m), 4.65 (1H, dd, J = 4.0, 10.4 Hz); IR (KBr) 1749, 1733, 1673 cm^{-1}; SIMS m/z 415 (M^+ + 1), 359, 215, 187, 141 (base). Anal. Calcd for $C_{19}H_{30}N_2O_8$: C, 55.06; H, 7.30; N, 6.76. Found: C, 54.84; H, 7.04; N, 6.73. **(*S*,*S*)-8b**: mp 114−115 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −61.6 (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.14−1.30 (9H, m), 1.46 (9H, s), 2.90 (3H, s), 3.29 (1H, dd, J = 4.3, 9.6 Hz), 3.66 (1H, dd, J = 9.7, 10.0 Hz), 3.83 (1H, d, J = 10.4 Hz), 4.10−4.26 (4H, m), 4.49−4.64 (2H, m); IR (KBr) 1755, 1745, 1730, 1677 cm^{-1}; SIMS m/z 415 (M^+ + 1), 359, 215, 187, 141 (base). Anal. Calcd for $C_{19}H_{30}N_2O_8$: C, 55.06; H, 7.30; N, 6.76. Found: C, 55.16; H, 7.19; N, 6.74.

Physical properties of the new compounds are as follows.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis((isopropyloxy)carbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8c]**: colorless needles, mp 93−94 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −42.6 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.16−1.28 (15H, m), 1.45 (9H, s), 2.89 (3H, s), 3.30 (1H, dd, J = 4.0, 9.6 Hz), 3.69 (1H, dd, J = 9.6, 10.3 Hz), 3.83 (1H, d, J = 11.2 Hz), 4.42−4.58 (1H, m), 4.65 (1H, dd, J = 4.0, 10.3 Hz) , 4.87−5.14 (2H, m); IR (KBr) 1752, 1735, 1674 cm^{-1}; SIMS m/z 443 (M^+ + 1), 387, 201, 159, 145 (base), 99. Anal. Calcd for $C_{21}H_{34}N_2O_8$: C, 57.00; H, 7.74; N, 6.33. Found: C, 56.74; H, 7.48; N, 6.31.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis((isopropyloxy)carbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8c]**: colorless needles, mp 72−73 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −58.7 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.18−1.27 (15H, m), 1.46 (9H, s), 2.90 (3H, s), 3.30 (1H, dd, J = 4.4, 9.6 Hz), 3.66 (1H, dd, J = 9.6, 10.0 Hz), 3.78 (1H, d, J = 10.5 Hz), 4.46−4.62 (2H, m), 4.90−5.13 (2H, m); IR (KBr) 1741, 1732, 1680 cm^{-1}; SIMS m/z 443 (M^+ + 1), 387, 201, 159, 145 (base), 99. Anal. Calcd for $C_{21}H_{34}N_2O_8$: C, 57.00; H, 7.74; N, 6.33. Found: C, 56.72; H, 7.45; N, 6.35.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis(*tert*-butoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8d]**: colorless needles, mp 144−145 °C (Et_2O/hexane); $[\alpha]^{27}_D$ −39.7 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.24 (3H, d, J = 7.0 Hz), 1.40 (9H, s), 1.45 (9H, s), 1.47 (9H, s), 2.88 (3H, s), 3.29 (1H, dd, J = 3.8, 9.6 Hz), 3.63−3.74 (2H, m), 4.31−4.48 (1H, m), 4.66 (1H, dd, J = 3.8, 10.3 Hz); IR (KBr) 1743, 1721, 1681 cm^{-1}; SIMS m/z 471 (M^+ + 1), 415, 359, 303, 145, 99, 57 (base). Anal. Calcd for $C_{23}H_{38}N_2O_8$: C, 58.71; H, 8.14; N, 5.95. Found: C, 58.33; H, 7.81, N, 6.00.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis(*tert*-butoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8d]**: colorless needles, mp 114−115 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −61.6 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.18 (3H, d, J = 7.1 Hz), 1.42 (9H, s), 1.46 (18H, s), 2.89 (3H, s), 3.29 (1H, dd, J = 4.0, 9.5 Hz), 3.61−3.71 (2H, m), 4.35−4.55 (2H, m); IR (KBr) 1745, 1722, 1676 cm^{-1}; SIMS m/z 471 (M^+ + 1), 415, 359, 303 (base), 145, 99, 57. Anal. Calcd for $C_{23}H_{38}N_2O_8$: C, 58.71; H, 8.14; N, 5.95. Found: C, 58.35; H, 7.82; N, 6.02.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis((benzyloxy)carbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8e]**: colorless needles, mp 115−116 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −50.7 (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.23 (3H, d, J = 7.0 Hz), 1.44 (9H, s), 2.86 (3H, s), 3.23 (1H, dd, J = 4.0, 9.6 Hz), 3.54 (1H, dd, J = 9.6, 10.3 Hz), 4.01 (1H, d, J = 11.1 Hz), 4.49−4.67 (2H, m), 4.99, 5.13 (2H, ABq, J = 12.3 Hz), 5.12, 5.19 (2H, ABq, J = 12.2 Hz), 7.19−7.35 (10H, m); IR (KBr) 1742, 1679 cm^{-1}; SIMS m/z 539 (M^+ + 1), 483, 235, 145, 91 (base). Anal. Calcd for $C_{29}H_{34}N_2O_8$: C, 64.67; H, 6.36; N, 5.20. Found: C, 64.52; H, 6.37; N, 5.23.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis((benzyloxy)carbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8e]**: colorless oil; $[\alpha]^{25}_D$ −37.7 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.19 (3H, d, J = 7.0 Hz), 1.45 (9H, s), 2.89 (3H, s), 3.29 (1H, dd, J = 4.4, 9.6 Hz), 3.66 (1H, dd, J = 9.6, 10.0 Hz), 3.98 (1H, d, J = 10.4 Hz), 4.49−4.67 (2H, m), 5.04−5.19 (4H, m), 7.15−7.35 (10H, m); IR (film) 1738, 1678 cm^{-1}; SIMS m/z 539 (M^+ + 1), 483, 235, 145, 91 (base). Anal. Calcd for $C_{29}H_{34}N_2O_8$: C, 64.67; H, 6.36; N, 5.20. Found: C, 64.37; H, 6.41; N, 5.22.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis(methoxycarbonyl)-2-ethylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8f]**: colorless needles, mp 115−116 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −43.7 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.97 (3H, t, J = 7.5 Hz), 1.47 (9H, s), 1.57−1.98 (2H, m), 2.89 (3H, s), 3.28 (1H, dd, J = 4.7, 9.5 Hz), 3.64−3.76 (1H, m), 3.67 (3H, s), 3.75 (3H, s), 3.98 (1H, d, J = 11.1 Hz), 4.62−4.73 (2H, m); IR (KBr) 1737, 1680 cm^{-1}; SIMS m/z 401 (M^+ + 1), 345, 201, 173, 141 (base), 99. Anal. Calcd for $C_{18}H_{28}N_2O_8$: C, 53.99; H, 7.05; N, 7.00. Found: C, 53.72; H, 6.91; N, 6.90.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis(methoxycarbonyl)-2-ethylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8f]**: colorless oil; $[\alpha]^{25}_D$ −69.1 (*c* 1.02, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.86 (3H, t, J = 7.5 Hz), 1.47 (9H, s), 1.53−1.92 (2H, m), 2.91 (3H, s), 3.28 (1H, dd, J = 4.1, 9.6 Hz), 3.61−3.70 (1H, m), 3.71 (3H, s), 3.74 (3H, s), 3.96 (1H, d, J = 10.4 Hz), 4.54 (1H, dd, J = 4.1, 10.2 Hz), 4.62−4.74 (1H, m); IR (film) 1737, 1676 cm^{-1}; SIMS m/z 401 (M^+ + 1), 345, 201 (base), 173, 141, 99. Anal. Calcd for $C_{18}H_{28}N_2O_8$: C, 53.99; H, 7.05; N, 7.00. Found: C, 53.71; H, 7.14; N, 6.73.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis(methoxycarbonyl)-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8g]**: colorless prisms, mp 120−121 °C (Et_2O/hexane); $[\alpha]^{23}_D$ −67.8 (*c* 0.99, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.89−0.97 (6H, m), 1.14−1.40 (1H, m), 1.46 (9H, s), 1.60−1.77 (2H, m), 2.90 (3H, s), 3.28 (1H, dd, J = 5.1, 9.5 Hz), 3.64−3.73 (1H, m), 3.67 (3H, s), 3.75 (3H, s), 3.81 (1H, d, J = 9.8 Hz), 4.65 (1H, dd, J = 5.1, 10.4 Hz), 4.78−4.89 (1H, m); IR (KBr) 1746, 1727, 1673 cm^{-1}; SIMS m/z 429 (M^+ + 1), 373, 229, 169, 99 (base). Anal. Calcd for $C_{20}H_{32}N_2O_8$: C, 56.06; H, 7.53; N, 6.54. Found: C, 56.21; H, 7.44; N, 6.45.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis(methoxycarbonyl)-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8g]**: colorless oil; $[\alpha]^{25}_D$ −73.2 (*c* 0.52, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.86−0.92 (6H, m), 1.15−1.45 (1H, m), 1.47 (9H, s), 1.60−1.85 (2H, m), 2.91 (3H, s), 3.27 (1H, dd, J = 4.0, 9.6 Hz), 3.62−3.72 (1H, m), 3.73 (6H, s), 3.89 (1H, d, J = 8.0 Hz), 4.55 (1H, dd, J = 4.0, 10.1 Hz), 4.71−4.80 (1H, m); IR (film) 1737, 1680 cm^{-1}; SIMS m/z 429 (M^+ + 1), 373, 229 (base), 169, 99. Anal. Calcd for $C_{20}H_{32}N_2O_8$: C, 56.06; H, 7.53; N, 6.54. Found: C, 55.78; H, 7.79; N, 6.45.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis(methoxycarbonyl)-2-(2-phenylethyl)-propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8h]**: colorless needles, mp 119−120 °C (Et_2O/hexane); $[\alpha]^{24}_D$ +4.2 (*c* 0.50, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.47 (9H, s), 1.79−2.12 (2H, m), 2.54−2.85 (2H, m), 2.90 (3H, s), 3.30 (1H, dd, J = 4.5, 9.6 Hz), 3.65−3.75 (1H, m), 3.69 (3H, s), 3.75 (3H, s), 4.06 (1H, d, J = 11.0 Hz), 4.69 (1H, dd, J = 4.5, 10.5 Hz), 4.77−4.88 (1H, m), 7.11−7.29 (5H, m); IR (KBr) 1747, 1674 cm^{-1}; SIMS m/z 477 (M^+ + 1), 421, 245, 91 (base). Anal. Calcd for $C_{24}H_{32}N_2O_8$: C, 60.49; H, 6.77; N, 5.88. Found: C, 60.28; H, 6.86; N, 5.63.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis(methoxycarbonyl)-2-(2-phenylethyl)-propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8h]**: colorless oil; $[\alpha]^{25}_D$ −60.3 (*c* 0.68, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.46 (9H, s), 1.90−2.10 (2H, m), 2.48−2.74 (2H, m), 2.89 (3H, s), 3.23 (1H, dd, J = 4.1, 9.6 Hz), 3.54 (1H, dd, J = 9.6, 10.1 Hz), 3.72 (3H, s), 3.74 (3H, s), 4.01 (1H, d, J = 9.8 Hz), 4.34 (1H, dd, J = 4.1, 10.1 Hz), 7.11−7.26 (5H, m); IR (film) 1737, 1676 cm^{-1}; SIMS m/z 477 (M^+ + 1), 421, 245 (base). Anal. Calcd for $C_{24}H_{32}N_2O_8$: C, 60.49; H, 6.77; N, 5.88. Found: C, 60.20; H, 6.92; N, 5.73.

***tert*-Butyl (4*S*)-3-[(2*R*)-2-benzyl-3,3-bis(methoxycarbonyl)propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8i]**: colorless oil; $[\alpha]^{25}_D$ −15.9 (*c* 0.54, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.46 (9H, s), 2.84−2.96 (1H, m), 2.93 (3H, s), 3.25−3.36 (2H, m), 3.29 (3H, s), 3.67 (3H, s), 3.68−3.81 (2H, m), 4.69 (1H, dd, J = 4.1, 10.3 Hz), 4.91−5.02 (1H, m), 7.13−7.42 (5H, m); IR (film) 1738, 1680 cm^{-1}; SIMS m/z 463 (M^+ + 1), 407, 171 (base), 99. Anal. Calcd for $C_{23}H_{30}N_2O_8$: C, 59.73; H, 6.54; N, 6.06. Found: C, 59.57; H, 6.44; N, 6.25.

***tert*-Butyl (4*S*)-3-[(2*S*)-2-benzyl-3,3-bis(methoxycarbonyl)propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8i]**: colorless needles, mp 110−111 °C (Et_2O/hexane); $[\alpha]^{24}_D$ −104.3 (*c* 0.52, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.45 (9H, s), 2.76 (3H, s), 2.83−3.04 (2H, m), 3.13 (1H, dd, J = 3.7, 9.5 Hz), 3.28 (1H, dd, J = 9.5, 9.8 Hz), 3.64 (3H, s), 3.70 (3H, s), 3.92 (1H, d, J = 9.2 Hz), 4.27 (1H, dd, J = 3.7, 9.8 Hz), 5.01−5.13 (1H, m), 7.16−7.26 (5H, m); IR (KBr) 1735, 1682, 1668 cm^{-1}; SIMS m/z 463 (M^+ + 1), 407, 203 (base), 171.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis((benzyloxy)carbonyl)-2-ethylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8j]**: colorless needles, mp 106−107 °C (Et_2O/hexane); $[\alpha]^{23}_D$ −53.1 (*c* 0.54, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.93 (3H, t, J = 7.5 Hz), 1.45 (9H, s), 1.54−2.05 (2H, m), 2.85 (3H, s), 3.21 (1H, dd, J = 4.6, 9.5 Hz), 3.52 (1H, dd, J = 9.5, 10.4 Hz), 4.07 (1H, d, J = 11.0 Hz), 4.49 (1H, dd, J = 4.6, 10.4 Hz), 4.66−4.77 (1H, m), 4.96−5.21 (4H, m), 7.14−7.32 (10H, m); IR (KBr) 1751, 1732, 1726, 1676 cm^{-1}; SIMS m/z 553 (M^+ + 1), 497, 235, 91 (base). Anal. Calcd for $C_{30}H_{36}N_2O_8$: C, 65.20; H, 6.57; N, 5.07. Found: C, 64.98; H, 6.64; N, 4.95.

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis((benzyloxy)carbonyl)-2-ethylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8j]**: colorless oil; $[\alpha]^{25}_D$ −44.8 (*c* 0.50, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.83 (3H, t, J = 7.5 Hz), 1.44 (9H, s), 1.53−1.83 (2H, m), 2.89 (3H, s), 3.28 (1H, dd, J = 4.3, 9.6 Hz), 3.65 (1H, dd, J = 9.6, 10.1 Hz), 4.06 (1H, d, J = 10.4 Hz), 4.53 (1H, dd, J = 4.2, 10.1 Hz), 4.66−4.79 (1H, m), 5.04−5.13 (4H, m), 7.26−7.28 (10H, m); IR (film) 1737, 1674 cm^{-1}; SIMS m/z 553 (M^+ + 1), 497, 235, 91 (base). Anal. Calcd for $C_{30}H_{36}N_2O_8$: C, 65.20; H, 6.57; N, 5.07. Found: C, 64.90; H, 6.71; N, 5.13.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-bis((benzyloxy)carbonyl)-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-8k]**: colorless oil; $[\alpha]^{23}_D$ −47.9 (*c* 0.65, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.82−0.87 (6H, m), 1.25−1.44 (1H, m), 1.44 (9H, s), 1.58−1.76 (2H, m), 2.84 (3H, s), 3.18 (1H, dd, J = 5.1, 9.5 Hz), 3.44 (1H, dd, J = 9.5, 10.4 Hz), 3.89 (1H, d, J = 9.6 Hz), 4.45 (1H, dd, J = 5.1, 10.4 Hz), 4.79−4.91 (1H, m), 4.99−5.21 (4H, m), 7.21−7.33 (10H, m); IR (film) 1737, 1680 cm^{-1}; SIMS m/z 581 (M^+ + 1), 525, 235, 91 (base).

***tert*-Butyl (4*S*)-3-[(2*S*)-3,3-bis((benzyloxy)carbonyl)-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*S*)-8k]**: colorless oil; $[\alpha]^{23}_D$ −45.6 (*c* 1.23, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.78−0.83 (6H, m), 1.26−1.75 (3H, m), 1.44 (9H, s), 2.88 (3H, s), 3.26 (1H, dd, J = 4.2, 9.6 Hz), 3.64 (1H, dd, J = 9.6, 10.2 Hz), 3.97 (1H, d, J = 8.2 Hz), 4.53 (1H, dd, J = 4.2, 10.2 Hz), 4.74−4.84 (1H, m), 5.05−5.21 (4H, m), 7.28−7.29 (10H, m); IR (film) 1736, 1676 cm^{-1}; SIMS m/z 581 (M^+ + 1), 525, 235, 91 (base). Anal. Calcd for $C_{32}H_{40}N_2O_8$: C, 66.19; H, 6.94; N, 4.82. Found: C, 65.81; H, 6.99; N, 4.61.

Preparation of Dimethyl (2*R*)-2-Alkylsuccinate [(*R*)-12a−c]. ***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-Dicarboxy-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-9a].** A solution of (*S*,*R*)-**8e** (3.30 g, 6.13 mmol) in MeOH (100 mL) was hydrogenolyzed in the presence of palladium on carbon (300 mg) under atmospheric pressure at rt for 3 h. After the catalyst was filtered off, the filtrate was concentrated to dryness in *vacuo*. The resulting crystals were triturated with Et_2O to afford (*S*,*R*)-**9a** (2.19 g, 97%) as colorless needles: mp 157−158 °C dec; $[\alpha]^{25}_D$ −37.3 (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.35 (3H, d, J = 7.1 Hz), 1.46 (9H, s), 2.91 (3H, s), 3.34 (1H, dd, J = 4.0, 9.8 Hz), 3.72−3.88 (2H, m), 4.52−4.63 (1H, m), 4.70 (1H, dd, J = 4.0, 10.4 Hz), 5.21 (2H, br) ; IR (KBr) 3498, 1756, 1735, 1720, 1689 cm^{-1}; SIMS m/z 359 (M^+ + 1), 303, 145 (base), 99. Anal. Calcd for $C_{15}H_{22}N_2O_8$: C, 50.28; H, 6.19; N, 7.82. Found: C, 49.97; H, 6.38; N, 7.71.

***tert*-Butyl (4*S*)-3-[(2*R*)-3-Carboxy-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-10a].** A solution of (*S*,*R*)-**9a** (1.70 g, 4.74 mmol) in DMSO (10 mL) was stirred at 100 °C for 1 h. After being cooled, the reaction mixture was diluted with AcOEt and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The resulting crystals were triturated with Et_2O to afford (*S*,*R*)-**10a** (1.28 g, 86%) as colorless needles: mp 124−125 °C; $[\alpha]^{25}_D$ −88.7 (*c* 1.00, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.27 (3H, d, J = 7.0 Hz), 1.46 (9H, s), 2.41 (1H, dd, J = 4.6, 17.2 Hz), 2.89 (3H, s), 2.93 (1H, dd, J = 10.1, 17.2 Hz), 3.31 (1H, dd, J = 4.1, 9.6 Hz), 3.71 (1H, dd, J = 9.6, 10.4 Hz), 4.14−4.32 (1H, m), 4.67 (1H, dd, J = 4.1, 10.4 Hz), 8.95 (1H, br); IR (KBr) 1751, 1734, 1718, 1688 cm^{-1}; SIMS m/z 315 (M^+ + 1), 259, 241, 145 (base), 99. Anal. Calcd for $C_{14}H_{22}N_2O_6$: C, 53.49; H, 7.05; N, 8.91. Found: C, 53.21; H, 6.92; N, 8.84.

***tert*-Butyl (4*S*)-3-[(2*R*)-3-(Methoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-11a].** (Trimethylsilyl)diazomethane (2 M solution in hexane, 1.53 mL, 3.06 mmol) was added dropwise to a solution of (*S*,*R*)-**10a** (786 mg, 2.50 mmol) in toluene (10 mL)−MeOH (5 mL) at rt. After stirring was continued for 1 h, the reaction mixture was concentrated in *vacuo*. The resulting residue was chromatographed on silica gel eluting with hexane−AcOEt (3:2) to give (*S*,*R*)-**11a** (743 mg, 91%) as colorless needles: mp 102−103 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −88.2 (*c* 1.01, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.26 (3H, d, J = 7.0 Hz), 1.46 (9H, s), 2.38 (1H, dd, J = 4.7, 16.9 Hz), 2.88 (3H, s), 2.92 (1H, dd, J = 10.3, 16.9 Hz), 3.30 (1H, dd, J = 4.1, 9.6 Hz), 3.63 (3H, s), 3.68 (1H, dd, J = 9.6, 10.4 Hz), 4.17−4.35 (1H, m), 4.66 (1H, dd, J = 4.1, 10.4 Hz); IR (KBr) 1752, 1740, 1729, 1721, 1678 cm^{-1}; SIMS m/z 329 (M^+ + 1), 273, 145, 129 (base), 99. Anal. Calcd for $C_{15}H_{24}N_2O_6$: C, 54.87; H, 7.37; N, 8.53. Found: C, 54.67; H, 7.18; N, 8.49.

Dimethyl (2*R*)-2-Methylsuccinate [(*R*)-12a]. To a solution of (*S*,*R*)-**11a** (329 mg, 1.00 mmol) in MeOH (3 mL) was added MeONa (55 mg, 1.02 mmol) at 0 °C under stirring. After stirring was continued for 2 h at rt, the reaction mixture was diluted with AcOEt and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The resulting residue was chromatographed on silica gel eluting with hexane−AcOEt (10:1) to give (*R*)-**12a** (131 mg, 82%) as a colorless oil: $[\alpha]^{25}_D$ +4.8 (*c* 2.90, $CHCl_3$) [lit.[10] $[\alpha]^{20}_D$ +4.8 (*c* 2.9, $CHCl_3$)]; ^{1}H NMR ($CDCl_3$) δ 1.22 (3H, d, J = 7.1 Hz), 2.41 (1H, dd, J = 6.0, 16.3 Hz), 2.75 (1H, dd, J = 8.0, 16.3 Hz), 2.84−3.02 (1H, m), 3.68 (3H, s), 3.70 (3H, s); IR (film), 1738 cm^{-1}; SIMS m/z 161 (M^+ + 1), 129 (base).

Compounds (*R*)-**12b** and (*R*)-**12c** were prepared similarly. The yields and physical data are as follows.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-Dicarboxy-2-ethylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-9b]**: yield 98%; colorless needles, mp 164−165 °C dec (Et_2O); $[\alpha]^{23}_D$ −37.8 (*c* 0.50, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.06 (3H, t, J = 7.5 Hz), 1.47 (9H, s), 1.65−1.98 (2H, m), 2.92 (3H, s), 3.34 (1H, dd, J = 4.4, 9.8 Hz), 3.77 (1H, dd, J = 9.8, 10.1 Hz), 3.91 (1H, d, J = 7.3 Hz), 4.65−4.77 (1H, m), 5.54 (2H, br); IR (KBr) 3223, 1741, 1715, 1646 cm^{-1}; SIMS m/z 373 (M^+ + 1), 317, 145 (base), 99. Anal. Calcd for $C_{16}H_{24}N_2O_8$: C, 51.61; H, 6.50; N, 7.52. Found: C, 51.38; H, 6.74; N, 7.41.

***tert*-Butyl (4*S*)-3-[(2*R*)-3,3-dicarboxy-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-9c]**: yield 92%; colorless needles, mp 160−161 °C dec (Et_2O); $[\alpha]^{25}_D$ −39.6 (*c* 0.53, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.96 (6H, t, J = 5.9 Hz), 1.47 (9H, s), 1.48−1.75 (3H, m), 2.93 (3H, s), 3.35 (1H, dd, J = 4.4, 9.8 Hz), 3.73−3.85 (2H, m), 4.71 (1H, dd, J = 4.4, 10.4 Hz), 4.85−4.93 (1H, m), 8.30 (2H, br); IR (KBr) 3267, 1754, 1711, 1646 cm^{-1}; SIMS m/z 401 (M^+ + 1), 345, 145 (base), 99, 57. Anal. Calcd for $C_{18}H_{28}N_2O_8$: C, 53.99; H, 7.05; N, 7.00. Found: C, 53.77; H, 7.24; N, 6.95.

***tert*-Butyl (4*S*)-3-[(2*R*)-3-carboxy-2-ethylpropionyl]-1-methyl-2-oxoimida-zolidine-4-carboxylate [(*S*,*R*)-10b]**: yield 95%; colorless needles, mp 128−129 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −76.6 (*c* 0.52, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.00 (3H, t, J = 7.4 Hz), 1.46 (9H, s), 1.50−1.91 (2H, m), 2.49 (1H, dd, J = 4.1, 17.0 Hz), 2.69 (3H, s), 2.89 (1H, dd, J = 10.4, 17.0 Hz), 3.30 (1H, dd, J = 4.4, 9.6 Hz), 3.70 (1H, dd, J = 9.6, 10.4 Hz), 4.13−4.20 (1H, m), 4.67 (1H, dd, J = 4.4, 10.4 Hz); IR (KBr) 1741, 1697, 1692 cm^{-1}; SIMS m/z 329 (M^+ + 1), 273, 255, 145 (base), 99. Anal. Calcd for $C_{15}H_{24}N_2O_6$: C, 54.87; H, 7.37; N, 8.53. Found: C, 54.68; H, 7.54; N, 8.75.

***tert*-Butyl (4*S*)-3-[(2*R*)-3-carboxy-2-isobutylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-10c]**: yield 89%; colorless needles, mp 108−109 °C (Et_2O); $[\alpha]^{25}_D$ −74.5 (*c* 0.51, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.93−0.98 (6H, m), 1.25−1.70 (3H, m), 1.46 (9H, s), 2.52 (1H, dd, J = 4.3, 16.8 Hz), 2.81 (1H, dd, J = 9.8, 16.8 Hz), 2.89 (3H, s), 3.30 (1H, dd, J = 4.4, 9.6 Hz), 3.69 (1H, dd, J = 9.6, 10.4 Hz), 4.26−4.41 (1H, m), 4.67 (1H, dd, J = 4.4, 10.4 Hz); IR (KBr) 1742, 1698, 1665 cm^{-1}; SIMS m/z 357 (M^+ + 1), 301, 145 (base), 99. Anal. Calcd for $C_{17}H_{28}N_2O_6$: C, 57.29; H, 7.92; N, 7.86. Found: C, 57.41; H, 7.89; N, 7.66.

***tert*-Butyl (4*S*)-3-[(2*R*)-2-ethyl-3-(methoxycarbonyl)-propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-11b]**: yield 88%; colorless needles, mp 96−97 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −77.7 (*c* 0.57, MeOH); ^{1}H NMR ($CDCl_3$) δ 1.00 (3H, t, J = 7.4 Hz), 1.46 (9H, s), 1.52−1.89 (2H, m), 2.45 (1H, dd, J = 4.2, 17.0 Hz), 2.81−2.94 (1H, m), 2.88 (3H, s), 3.28 (1H, dd, J = 4.4, 9.6 Hz), 3.61−3.72 (1H, m), 3.62 (3H, s), 4.17−4.31 (1H, m), 4.67 (1H, dd, J = 4.4, 10.4 Hz); IR (KBr) 1732, 1672 cm^{-1}; SIMS m/z 343 (M^+ + 1), 287, 143 (base).

***tert*-Butyl (4*S*)-3-[(2*R*)-2-isobutyl-3-(methoxycarbonyl)propionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S*,*R*)-11c]**: yield 87%; colorless needles, mp 101−102 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −75.9 (*c* 0.56, MeOH); ^{1}H NMR ($CDCl_3$) δ 0.93−0.97 (6H, m), 1.22−1.46 (1H, m), 1.46 (9H, s), 1.61−1.75 (2H, m), 2.48 (1H, dd, J = 4.3, 16.9Hz), 2.79 (1H, dd, J = 10.6, 16.9Hz), 2.89 (3H, s), 3.28 (1H, dd, J = 4.5, 9.5 Hz), 3.62−3.72 (1H, m), 3.63 (3H, s), 4.32−4.47 (1H, m), 4.66 (1H, dd, J = 4.5, 10.4 Hz); IR (KBr) 1731, 1680 cm^{-1}; SIMS m/z 371 (M^+ + 1), 315, 171 (base). Anal. Calcd for $C_{18}H_{30}N_2O_6$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.12; H, 8.14; N, 7.45.

Dimethyl (2*R*)-2-ethylsuccinate [(*R*)-12b]: yield 77%; colorless oil; $[\alpha]^{22}_D$ +13.0 (*c* 1.23, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.92 (3H, t, J = 7.5 Hz), 1.52−1.76 (2H, m), 2.36−2.52 (1H, m), 2.67−2.88 (2H, m), 3.68 (3H, s), 3.71 (3H, s); IR (film) 1739 cm^{-1}; SIMS m/z 175 (M^+ + 1), 101 (base).

Dimethyl (2*R*)-2-isobutylsuccinate [(*R*)-12c]: yield 76%; colorless oil; $[\alpha]^{22}_D$ +20.9 (*c* 1.11, $CHCl_3$); ^{1}H NMR ($CDCl_3$) δ 0.88−0.94 (6H, m), 1.20−1.36 (1H, m), 1.47−1.68 (2H, m), 2.42 (1H, dd, J = 5.0, 16.4Hz), 2.70 (1H, dd, J = 9.3, 16.4Hz), 2.84−2.98 (1H, m), 3.67 (3H, s), 3.70 (3H, s); IR (film) 1740 cm^{-1}; SIMS m/z 203 (M^+ + 1), 55 (base).

***tert*-Butyl (4*S*)-3-[(2*R*)-3-(((Benzyloxy)carbonyl)amino)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-car-**

boxylate [(*S,R*)-13]. To a solution of (*S,R*)-**10a** (1.00 g, 3.18 mmol) and Et_3N (0.442 mL, 3.18 mmol) in toluene (10 mL) was added diphenylphosphoryl azide (875 mg, 3.18 mmol). After being stirred at 80 °C for 1 h, benzyl alcohol (378 mg, 3.50 mmol) was added to the mixture, and stirring was continued for 12 h at the same temperature. After being cooled, the mixture was diluted with AcOEt, washed with water, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography eluting with $CHCl_3$−AcOEt (10:1) to give (*S,R*)-**13** (960 mg, 72%) as a colorless needles: mp 103−104 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −83.4 (*c* 1.09, MeOH); ^1H NMR ($CDCl_3$) δ 1.24 (3H, d, J = 7.0 Hz), 1.46 (9H, s), 2.87 (3H, s), 3.29 (1H, dd, J = 4.2, 9.6 Hz), 3.57−3.68 (2H, m), 3.63 (1H, dd, J = 9.6, 10.3 Hz), 3.95−4.08 (1H, m), 4.61 (1H, dd, J = 4.2, 10.3 Hz), 5.07 (2H, s), 5.20 (1H, br), 7.29−7.34 (5H, m); IR (KBr) 1734, 1705, 1686 cm^{-1}; SIMS *m/z* 420 ($M^+ + 1$), 364, 320, 145, 91 (base). Anal. Calcd for $C_{21}H_{29}N_3O_6$: C, 60.13; H, 6.97; N, 10.02. Found: C, 59.92; H, 6.95; N, 9.99.

Methyl (2*R*)-3-[((Benzyloxy)carbonyl)amino]-2-methylpropionate [(*R*)-14]. To a solution of (*S,R*)-**13** (200 mg, 0.48 mmol) in MeOH (2 mL) was added MeONa (26 mg, 0.48 mmol) at 0 °C under stirring. After stirring was continued for 2 h at 25 °C, the reaction mixture was diluted with AcOEt and water. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The resulting residue was chromatographed on silica gel eluting with hexane−AcOEt (4:1) to give (*R*)-**14** (98 mg, 82%) as colorless oil: $[\alpha]^{23}_D$ −31.9 (*c* 1.05, MeOH); ^1H NMR ($CDCl_3$) δ 1.18 (3H, d, J = 7.2 Hz), 2.63−2.82 (1H, m), 3.23−3.48 (2H, m), 3.68 (3H, s), 5.09 (2H, s), 5.18 (1H, br), 7.30−7.37 (5H, m); IR (film) 1730 cm^{-1}; SIMS *m/z* 252 ($M^+ + 1$), 208, 91 (base). Anal. Calcd for $C_{13}H_{17}NO_4$: C, 62.14; H, 6.82; N, 5.57. Found: C, 61.92; H, 7.10; N, 5.85.

***tert*-Butyl (4*S*)-3-[(2*R*)-3-(*tert*-Butoxycarbonyl)-2-methylpropionyl]-1-methyl-2-oxoimidazolidine-4-carboxylate [(*S,R*)-15].** To a solution of (*S,R*)-**10a** (500 mg, 1.59 mmol) in CH_2Cl_2 (5 mL) were added liquid isobutene (5 mL) and a drop of H_2SO_4 at −40 °C. The resulting solution was kept in a pressure bottle at rt for 12 h. The mixture was cooled to −40 °C, poured into saturated aqueous $NaHCO_3$, and the organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo*. The resulting residue was chromatographed on silica gel eluting with hexane−AcOEt (2:1) to give (*S,R*)-**15** (538 mg, 91%) as colorless needles: mp 87−88 °C (Et_2O/hexane); $[\alpha]^{25}_D$ −81.0 (*c* 0.52, MeOH); ^1H NMR ($CDCl_3$) δ 1.23 (3H, d, J = 7.0 Hz), 1.40 (9H, s), 1.46 (9H, s), 2.29 (1H, dd, J = 4.5, 16.9 Hz), 2.78−2.92 (1H, m), 2.88 (3H, s), 3.29 (1H, dd, J = 3.9, 9.6 Hz), 3.66 (1H, dd, J = 9.6, 10.4 Hz), 4.12−4.31 (1H, m), 4.67 (1H, dd, J = 3.9, 10.4 Hz); IR (KBr) 1751, 1733, 1681 cm^{-1}; SIMS *m/z* 371($M^+ + 1$), 315, 259 (base), 145. Anal. Calcd for $C_{18}H_{30}N_2O_6$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.04; H, 7.99; N, 7.58.

***tert*-Butyl (3*R*)-3-Carboxybutanoate [(*R*)-16].** To a solution of (*S,R*)-**15** (741 mg, 2.00 mmol) in THF (10 mL) and water (5 mL) was added $LiOH \cdot H_2O$ (126 mg, 3.00 mmol) at 0 °C. After stirring was continued for 3 h at rt, the reaction mixture was diluted with Et_2O and water. The aqueous layer was acidified with citric acid and extracted with AcOEt. The organic layer was washed with brine, dried over $MgSO_4$, and concentrated in *vacuo* to afford (*R*)-**16** (296 mg, 79%) as colorless solid: mp 58−59 °C; $[\alpha]^{22}_D$ +3.0 (*c* 0.64, MeOH); ^1H NMR ($CDCl_3$) δ 1.24 (3H, d, J = 7.1 Hz), 1.44 (9H, s), 2.37 (1H, dd, J = 5.8, 16.4 Hz), 2.65 (1H, dd, J = 8.1, 16.4 Hz), 2.82−2.95 (1H, m), 3.53 (1H, br); IR (KBr) 1723, 1705 cm^{-1}; SIMS *m/z* 189 ($M^+ + 1$), 133 (base), 115. Anal. Calcd for $C_9H_{16}O_4$: C, 57.43; H, 8.57. Found: C, 57.71; H, 8.34.

***tert*-Butyl (3*R*)-3-[((Benzyloxy)carbonyl)amino]butanoate [(*R*)-17].** To a solution of (*R*)-**16** (200 mg, 1.06 mmol) and Et_3N (0.148 mL, 1.06 mmol) in toluene (4 mL) was added diphenylphosphoryl azide (292 mg, 1.06 mmol). After being stirred at 80 °C for 1 h, benzyl alcohol (126 mg, 1.17 mmol) was added to the mixture, and stirring was continued for 14 h at the same temperature. After being cooled, the mixture was diluted with AcOEt, washed with water, saturated $NaHCO_3$, and brine, dried over $MgSO_4$, and evaporated. The residue was purified by silica gel column chromatography eluting with $CHCl_3$−AcOEt (15:1) to give (*R*)-**17** (212 mg, 68%) as a colorless oil: $[\alpha]^{22}_D$ +16.2 (*c* 1.02, $CHCl_3$); ^1H NMR ($CDCl_3$) δ 1.23 (3H, d, J = 6.7 Hz), 1.44 (9H, s), 2.46 (2H, d, J = 5.7 Hz), 4.01−4.14 (1H, m), 5.10 (2H, s), 5.23 (1H, br), 7.29−7.37 (5H, m) ; IR (film) 1724 cm^{-1}; SIMS *m/z* 294 ($M^+ + 1$), 238, 194, 91 (base). Anal. Calcd for $C_{16}H_{23}NO_4$: C, 65.51; H, 7.90; N, 4.77. Found: C, 65.20; H, 8.14; N, 5.01.

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Supporting Information Available: ^1H NMR spectra of compounds lacking analyses and HPLC conditions for **8a**−**k** (8 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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