Pergamon

Tetrahedron Vol. 50, No. 13, pp. 3905-3914, 1994

0040-4020/94 $6.00+0.00

0040-4020(94)E0149-N

Synthetic Studies on the Key Component of the New Generation of Quinolonecarboxylic Acid, DU-6859. 2. Asymmetric Synthesis of (1*R*,2*S*)-2-Fluorocyclopropylamine

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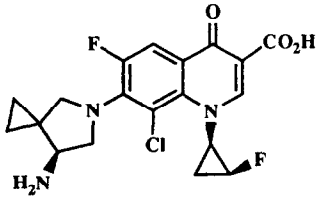
Key words: quinolonecarboxylic acid; (1*R*,2*S*)-2-fluorocyclopropylamine; (4*R*,5*S*)-2-diphenyl-3-vinyl-2-oxazolidinone; diastereoface-selective cyclopropanation; asymmetric synthesis

Abstract: *The title synthesis was achieved by featuring diastereoface-selective cyclopropanation of (4R,5S)-4,5-diphenyl-3-vinyl-2-oxazolidinone and its related compounds, the chiral conformationally rigid N-vinylcarbamates, with zinc-monofluorocarbenoid, followed by hydrogenolysis of the major addition products. The diastereoface-selectivity of the cyclopropanation could be explained by the most stable conformation of 3-vinyl-2-oxazolidinone derivatives and attack from the less hindered face of the conformer.*

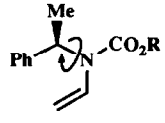
DU-6859 (**1**) was found as the new generation of quinolonecarboxylic acid exhibiting marked antibacterial activity and little side effects.[4] It has been disclosed that the pronounced characteristics of **1** are closely related with its (1*R*,2*S*)-2-fluorocyclopropylamine [(1*R*,2*S*)-**2**)] moiety.[5]

In the preceding paper,[6] it was reported that *dl*-**2** can be readily prepared from benzylamine derivatives by employing *cis*-selective cyclopropanation of *N*-benzyl-*N*-vinylcarbamates with zinc-monofluorocarbenoid. However, no asymmetric induction was achieved when *N*-[(*R*)-1-phenylethyl]-*N*-vinylcarbamates (**A**) derived from (*R*)-1-phenylethylamine were employed as the reaction substrates. Accordingly, the preparation of (1*R*, 2*S*)-**2** was accomplished by optical resolution of *dl*-**2** with *l*-menthyl chloroformate or less effectively by separation of diastereomeric (1*R*,2*S*)- and (1*S*,2*R*)-*N*-[(*R*)-1-phenylethyl]-2-fluorocyclopropylamine *p*-toluenesulfonate derived from **A**. Since it has been uncovered by means of NOE experiments that the vinyl

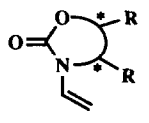


DU-6859 (**1**)

(1*R*,2*S*)-**2**



A



B

group of **A** is present in the vicinity of (*R*)-phenylethyl group, the unsuccessful asymmetric induction was explained by the conformational flexibility of chiral (*R*)-1-phenylethyl moiety.[6] Taking into accounts these results, we designed chiral cyclic carbamates (**B**) as the conformationally rigid substrates for cyclopropanation. If the vinyl group of **B** occupies the position close to the adjacent chiral center similarly to that of **A**, it is expected that the cyclopropanation of **B** can provide much better diastereoface-selectivity by the improved steric environment. We have now found that (4*R*,5*S*)-4,5-diphenyl-3-vinyl-2-oxazolidinone (**6a**) and its related compounds (**6b,c**) react with zinc-monofluorocarbenoid in a highly diastereoface-selective manner and that the major *cis*-adducts produced from **6a,c** can be readily elaborated to (1*R*,2*S*)-**2**.

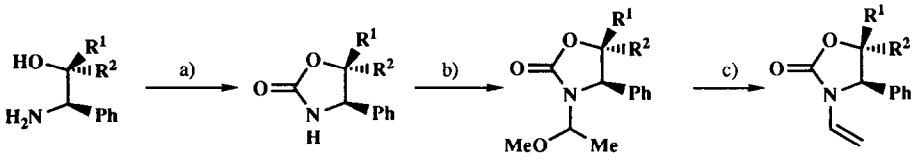
This report details a novel asymmetric synthesis of (1*R*,2*S*)-**2** featuring diastereoface-selective cyclopropanation of **6a,c** with zinc-monofluorocarbenoid.[7]

Results and discussion

1. Synthesis of 3-vinyl-2-oxazolidinones (6a-c), the substrates for cyclopropanation with zinc-monofluorocarbenoid

In order to assess the potential of 2-oxazolidinone moiety as a chiral auxiliary, three types of 3-vinyl-2-oxazolidinones (**6a-c**) were synthesized. As shown in **Scheme 1**, the synthesis of **6a-c** commenced with the (*R*)-2-phenylaminoethanols (**3a-c**) which were either commercially available (**3a,b**) or readily prepared (**3c**) by the reported method.[8] Thus, treatment of **3** with trichloromethyl chloroformate in the presence of triethylamine afforded the 2-oxazolidinones (**4**). These were allowed to react with 1,1-dimethoxyethane in the presence of a catalytic amount of *dl*-camphor-10-sulfonic acid (CSA), smoothly giving rise to the 3-(1-methoxyethyl)-2-oxazolidinones (**5**) as mixtures of the diastereomers. Heating **5** under a reduced pressure effected elimination of methanol[9] to yield **6**. While it has been reported that the enantiomers of **6a,b** can be prepared from the corresponding enantiomers of **3a,b** by employing chromium-carbene complex,[10] our synthetic route to **6** seems to be advantageous over that reported due to operational simplicity. Indeed, **6a** was synthesized from **3a** in 77% overall yield in a multi-gram scale without the use of chromatographic purification.

Scheme 1



3 4 5 6

a: R^1=Ph, R^2=H b: R^1=R^2=H c: R^1=R^2=Ph

a) $ClCO_2CCl_3$, Et_3N, **4a**, 97%; **4b**, 76%; **4c**, 99% b) $MeCH(OMe)_2$, cat. CSA, reflux c) 138-150 °C/ 1-16 mmHg: **6a**, 79%; **6b**, 56%; **6c**, 54% (2 steps)

2. Cyclopropanation of 3-vinyl-2-oxazolidinones (6a-c) with zinc-monofluorocarbenoid

With **6a-c** in hand, their cyclopropanations with zinc-monofluorocarbenoid were next examined. Considering its ready availability and chemical stability, **6a** was first selected as the substrate. Thus, treatments of **6a** with zinc-monofluorocarbenoid[11] generated from fluorodiiodomethane and diethylzinc gave (4*R*,5*S*)-3-(2-fluorocyclopropyl)-4,5-diphenyl-2-oxazolidinones (**7a-10a**) as a mixture of four possible diastereomers. The results collected by changing the reaction conditions are summarized in **Table 1**. The

ratios of **7a-10a** were definitely estimated by the ^{19}F-NMR spectra. Since the reactivity of **6a** was found to be lower than that of *N*-benzyl-*N*-vinylcarbamates employed in the preceding paper,[6] the reactions were carried out at higher reaction temperatures than those employed in the previous studies. Although the diastereoface-selectivity concerning the C_1-position of cyclopropane moiety [(**7a+8a**):(**9a+10a**) = 91:9] was high enough as expected, the chemical yield and *cis*-selectivity [(**7a+9a**):(**8a+10a**)] were found to be fairly low (44% and 54:46, respectively) (run 1). The low chemical yield was anticipated to be due to the decreased reactivity of **6a** by coordination of the carbonyl oxygen in the 2-oxazolidinone moiety to the zinc-carbenoid and short life time of the zinc-monofluorocarbenoid at room temperature in dichloromethane (CH_2Cl_2). It was recently reported that some sorts of ethers can coordinate with a zinc-carbenoid species as ligands to form stable complexes,[12] and that molecular sieves (MS) can be used in the presence of a Lewis acid.[13] Accordingly, in order to improve the chemical yield and *cis*-selectivity, effects of various ethers, MS, and reaction temperatures on the cyclopropanation were next studied.

Firstly, diethyl ether (Et_2O) and MS were separately used as an additive. The slightly better chemical yield of **7a-10a** was obtained by employing Et_2O as a solvent (run 2). Surprisingly, the use of MS4A as an additive gave better *cis*-selectivity (run 3). Based on these results, we next examined the combined uses of various ethers and MS4A. The more improved chemical yield was provided by using boiling Et_2O as a solvent

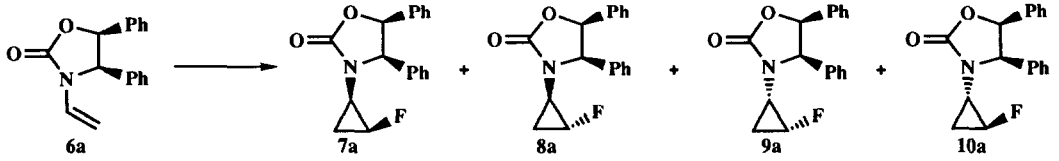
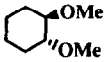
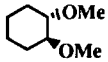


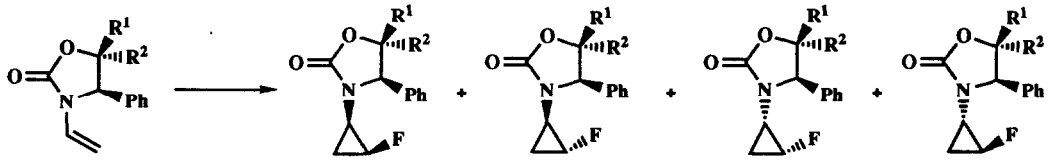
Table 1 Cycropropanation of **6a** with fluorodiiodomethane and diethylzinc[a]

Run	Conditions		Yield (%)[b]	Ratio[c]
	Additives	Temp.		**7a :8a:9a:10a**
1	none	rt	44 (88)	50 : 41 : 4 : 5
2	Et_2O	rt	50 (93)	51 : 36 : 6 : 7
3	MS4A	rt	52 (80)	60 : 28 : 7 : 5
4	Et_2O,[d] MS4A	reflux	69 (83)	50 : 41 : 4 : 5
5	Et_2O, MS4A	reflux	64 (87)	53 : 36 : 5 : 6
6	THF, MS4A	reflux	73 (85)	56 : 33 : 5 : 7
7	DME,[e] MS4A	reflux	68 (77)	63 : 27 : 5 : 5
8	DME, MS4A	reflux[f]	85 (94)	59 : 28 : 5 : 8
9	DME, MS4A	rt[f]	76 (83)	65 : 25 : 5 : 5
10	DEE,[g] MS4A	reflux	88 (92)	59 : 30 : 5 : 6
11	 MS4A	reflux	67 (84)	65 : 25 : 6 : 4
12	 MS4A	reflux	67 (84)	65 : 25 : 6 : 4

a) Otherwise noted, all the reactions were carried out in dichloromethane (CH_2Cl_2) by employing fluorodiiodomethane (3.0 eq.), diethylzinc (1.0 M solution in hexane, 3.0 eq.), ethers (3.0 eq.), and MS4A (equal weight to **6a**). b) The yields in parenthesis were corrected for the recovery of **6a**. c) Determined by the ^{19}F-NMR spectrum. d) Diethyl ether (Et_2O) was used as a solvent. e) 1,2-Dimethoxyethane. f) A 1.0 M solution of diethylzinc in CH_2Cl_2 was used. g) 1,2-Diethoxyethane.

(run 4). Interestingly, the similar result was obtained by employing 1.0 equivalent of Et_2O to the amounts of fluorodiiodomethane and diethylzinc in refluxing CH_2Cl_2 (run 5). The use of tetrahydrofran (THF) as a stronger ligand for the zinc-monofluorocarbenoid yielded desired **7a** with slightly higher *cis*-selectivity in a more improved yield (run 6). Following to Et_2O and THF, 1,2-dimethoxyethane (DME), 1,2-diethoxyethane (DEE), and (1*R*,2*R*)- and (1*S*,2*S*)-1,2-dimethoxycyclohexane were employed as bidentate ligands (runs 7-12). The best results in terms of chemical yield [88%, (run 10)] and *cis*-selectivity [(**7a**+**8a**):(**9a**+**10a**) = *ca.* 90:10 (runs 7-12); (**7a**+**9a**):(**8a**+**10a**) = 70:30 (runs 7,9,11,12)] were realized by the uses of these ethers as additives. In runs 8 and 10, **7a** was isolated in *ca.* 50% yield after separation by column chromatography. Enantiomeric (1*R*,2*R*)- and (1*S*,2*S*)-dimethoxycyclohexane were found not to give different effect on *cis*-selectivity of the reaction (runs 11 and 12).

With completion of studies using **6a**, we applied the established conditions to **6b,c** to explore the steric effect of the C_4-position of 2-oxazolidinone moiety. As expected, the conditions for cyclopropanation were found to be highly depend upon the structures of **6b,c**. Thus, as shown in **Table 2**, the reaction of **6b** smoothly proceeded even at lower temperature, and most bulky **6c** required 6.0 equivalents of the reagents in refluxing CH_2Cl_2. The ratios of the adducts (**7b,c**-**10b,c**) were similarly determined by the ^{19}F-NMR spectra. Although acyclic *N*-benzyl-*N*-vinylcarbamates carrying a bulky substituent adjacent to the nitrogen atom gave high *cis*-selectivity,[6] similar improvement could not be realized by the use of bulky **6c** bearing three phenyl groups at the $C_{4,5}$-positions of 2-oxazolidinone ring.



6 7 8 9 10

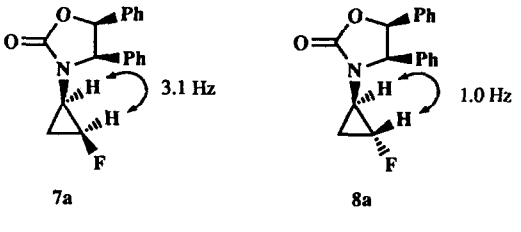
Table 2. Cyclopropanation of **6b,c** with fluorodiiodomethane and diethylzinc.

Run	Substrate	Conditions	Yield (%)[a]	Ratio[b] **7 : 8 : 9: 10**
1	**6b**: R^1=R^2=H	Et_2Zn, $CHFI_2$, DME (each 3.0 eq.), MS4A, CH_2Cl_2, -40→0 °C	80	59 : 27 : 9 : 4
2	**6c**: R^1=R^2=Ph	Et_2Zn, $CHFI_2$, DME (each 6.0 eq.), MS4A, CH_2Cl_2, 40 °C	67	49 : 26 : 15 : 9

a) Isolated yields. b) Determined by the ^{19}F-NMR spectrum.

The two major adducts (**7a** and **8a**) produced from **6a** were readily separated from the two minor products (**9a** and **10a**) by column chromatography. In their ^{1}H-NMR spectra, the coupling constants between the C_1- and C_2-protons of cyclopropane moieties of **7a** and **8a** were found to be 3.1 and 1.0 Hz, respectively. Since *cis*-substituted cyclopropane derivative always exhibits a larger coupling constant than *trans*-substituted one, this spectral feature clearly suggests that **7a** and **8a** bear the *cis*- and *trans*-stereochemistries, respectively. Furthermore, the structures of **7a** and **8a** could be definitely established by successful synthesis of (1*R*,2*S*)-**2** from **11a** (*vide infra*) and X-ray diffraction analysis of **8a** (**Fig 1**).[14] The stereochemistries of **7b,c** and **8b,c** were tentatively assigned by comparing their ^{1}H-NMR and ^{19}F-NMR spectra with those of **7a** and **8a** and successful preparation of (1*R*,2*S*)-**2** from **7c**.

Fig 1



3. Mechanistic considerations

Hegedus et al. reported a highly diastereoface-selective coupling reaction of the enantiomer of **6a** with an acetoacetate anion using Pd(II) species.[10] They explained the observed stereoselectivity by chelation of the Pd(II) species with both the carbonyl oxygen and the π-electrons of vinyl group. If the zinc-monofluorocarbenoid similarly coordinates with the carbonyl oxygen of **6** in our reactions, the vinyl group would reduce its electron-donating ability, resulting in a rather low chemical yield. However, since the cyclopropanation of **6** gives an 88% chemical yield as the best result (**Table 1**, run 10), the remarkable diastereoface-selectivity [(**7**+**8**):(**9**+**10**) = max. 90:10] observed for **6** might be explained by the conformations of **6** themselves. In the conformers **C** and **D** of **6** shown in **Scheme 2**, the exocyclic olefin has a maximum conjugation with the lone pair of nitrogen. Since **C** has a severe steric interaction between the carbonyl oxygen and the vinyl proton (Ha), **D** is anticipated to be more favorable. Indeed, in the ^{1}H-NMR spectrum of **6a**, the NOE was observed between Ha and Hb of the 2-oxazolidinone ring (**Fig. 2**). Furthermore, the minimum energy conformations of **6a-c** (**Fig 3**) obtained by molecular mechanics calculation (CHARMm-QUANTA)[15] also indicated that **D** is the conformer of the lowest conformational energy. Accordingly, the diastereoface-selectivity should arise from the less hindered *si*-face attack of the zinc-monofluorocarbenoid.

Scheme 2

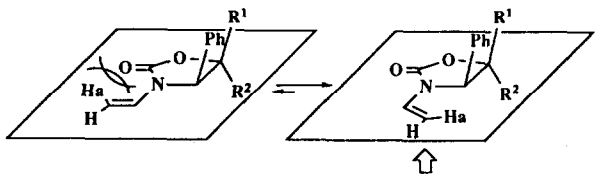


Fig 2

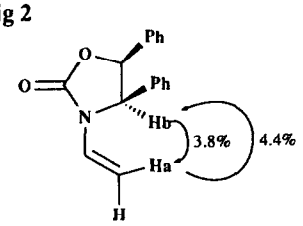
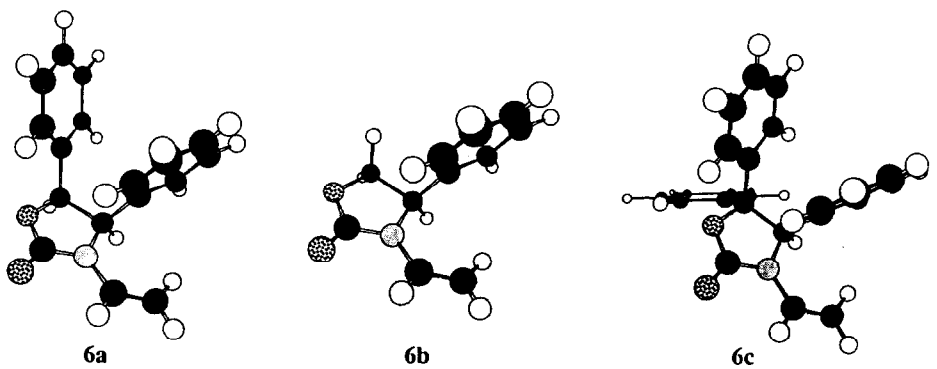
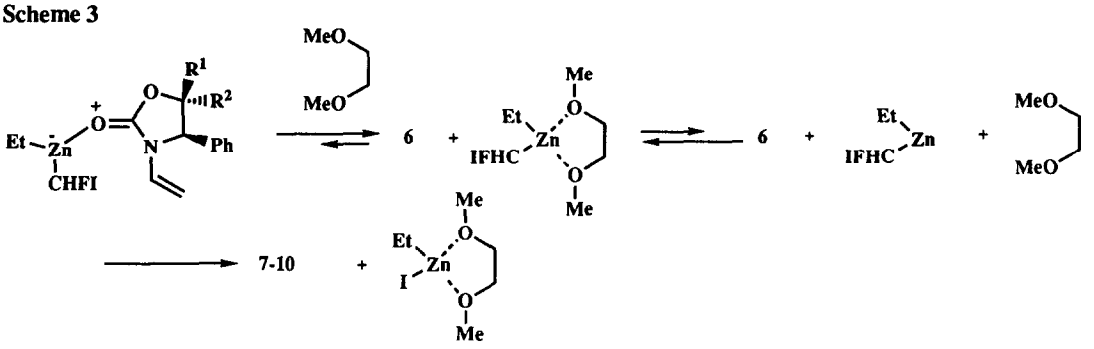


Fig. 3



The roles of bidentate ethers in the cyclopropanation may be the assistance on removal of zinc-carbenoid from the carbonyl oxygen in **6** and stabilization of the zinc-carbenoid by forming a stable complex.[12] Since the reactivity of zinc-carbenoid complexed with bidentate ethers obviously decreases, the cyclopropanation might proceed *via* dissociation of the complex. This speculation coincides well with the observation that the reactions in the presence of various ethers afford higher chemical yields at higher temperatures. The possible mechanism is shown in **Scheme 3**. Although the roles of MS4A remains unknown, the moderate *cis*-selectivity could be rationalized by the "bent" transition state model similar to that proposed previously.[6]

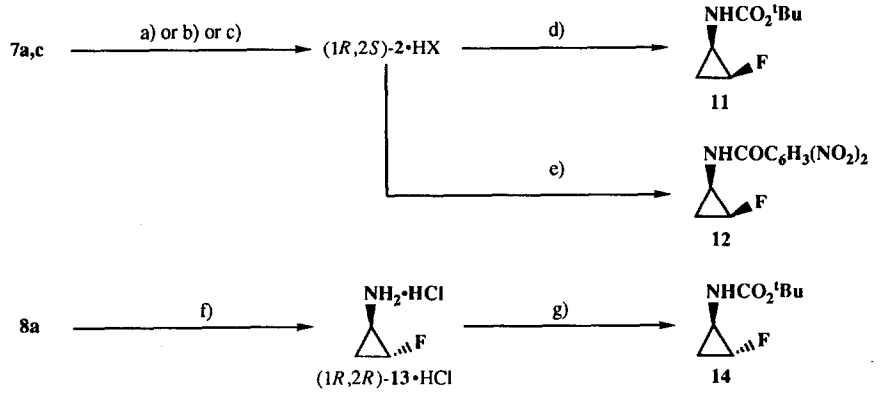
Scheme 3



4. Synthesis of (1*R*, 2*S*)-2 and its (1*R*, 2*R*)-isomer [(1*R*, 2*S*)-13]

As shown in **Scheme 4**, elaborations of **7a,c** to (1*R*,2*S*)-**2** were effected in a single step. Thus, reductive removal of the 2-oxazolidinone moiety from **7a** was readily achieved by hydrogenolysis in acetic acid in the presence of 10% palladium on charcoal, affording (1*R*,2*S*)-**2**•HCl, mp 154-156 °C (decomp.) and $[\alpha]_D^{20}$ -20.6° (*c* 0.781, EtOH) [*lit.*[6] mp 153-157 °C, $[\alpha]_D^{20}$ -19.0° (*c* 0.738, EtOH)], after treatment with a methanolic hydrogen chloride. In a similar manner, (1*R*,2*S*)-**2**•TsOH, mp 178-179 °C (decomp.) and $[\alpha]_D^{20}$ -10.7° (*c* 1.08, MeOH) [*lit.*[6] mp 168.5-170.5 °C (decomp) and $[\alpha]_D^{20}$ -8.9° (*c* 0.699, MeOH)], was also produced by

Scheme 4



a) H_2 (3 kg/ cm^2), 10% Pd-C, AcOH; HCl-MeOH for **7a**, 87% (1*R*,2*S*)-**2**•HCl b) H_2 (3 kg/ cm^2), 10% Pd-C, AcOH; TsOH-MeOH for **7a**, 90% (1*R*,2*S*)-**2**•TsOH c) H_2 (10 kg/cm^2), 20% $Pd(OH)_2$-C, TsOH, AcOH for **7c**, 74% (1*R*,2*S*)-**2**•TsOH d) $(Boc)_2O$, Et_3N, CH_2Cl_2, 64% e) 3,5-$(NO_2)_2C_6H_3COCl$, Et_3N, THF f) H_2 (3 kg/ cm^2), 10% Pd-C, AcOH; HCl-MeOH, 65% g) $(Boc)_2O$, Et_3N, CH_2Cl_2, 44%.

hydrogenolysis of **7a** followed by treatment with *p*-toluenesulfonic acid (TsOH) or by hydrogenolysis of **7c** in the presence of TsOH. Further identification of (1*R*,2*S*)-**2** was achieved by transforming (1*R*,2*S*)-**2**•HCl tc *t*-butyl *N*-[(1*R*,2*S*)-2-fluorocyclopropyl]carbamate (**11**), mp 77.5-78.5 °C and $[\alpha]_D^{25}$ -66.5° (*c* 0.840, $CHCl_3$), [*lit.*[4b], mp 63 °C and $[\alpha]_D$ -60.27° (*c* 0.740, $CHCl_3$) for **11**; mp 73 °C and $[\alpha]_D$ +65.57° (*c* 0.610, $CHCl_3$) for the enantiomer of **11**]. The optical purity of (1*R*,2*S*)-**2** was determined as 98% ee by converting (1*R*,2*S*)-**2**•TsOH to *N*-[(1*R*,2*S*)-2-fluorocyclopropyl]-3,5-dinitrobenzamide (**12**) followed by chiral HPLC analysis.[16] Similarly, hydrogenation of **8a** followed by treatment with a methanolic solution of hydrogen chloride gave (1*R*,2*R*)-2-fluorocyclopropylamine hydrochloride (**13**•HCl), mp 131-134°C (decomp.) and $[\alpha]_D^{20}$ -14.2° (*c* 0.604, EtOH). This was similarly derivated to *t*-butyl *N*-[(1*R*,2*R*)-2-fluorocyclopropyl)carbamate (**14**), mp 59.5-61 °C and $[\alpha]_D^{25}$ -23.9° (*c* 0.999, $CHCl_3$). In contrast with **7a,c**, and **8a**, all the attempts to deprotect **7b** by hydrogenolysis, acidic and basic hydrolysis, and so on, met with failure.

Conclusion

As mentioned above, we have succeeded in exploring a novel asymmetric synthesis of (1*R*,2*S*)-2-fluorocyclopropylamine [(1*R*,2*S*)-**2**] by employing diastereoface-selective cyclopropanation of the rationally designed, chiral, and conformationally rigid 3-vinyl-2-oxazolidinones (**6**) with zinc-monofluorocarbenoid.

Experimental

General. All melting points were determined with a Yanagimoto MP-21 melting point apparatus and were uncorrected. Optical rotations were measured with a Horiba SEPA-200 autodigital polarimeter. Infrared (IR) spectra were recorded on a JASCO A-202 spectrometer. ^{1}H-NMR spectra were measured with a Hitachi R-90H (90 MHz), a Brucker AM 200 (200 MHz), and a Brucker AM 400 (400 MHz) spectrometer. The chemical shifts are expressed in ppm downfield from tetramethylsilane, using tetramethylsilane (δ = 0) or residual chloroform (δ = 7.25) as an internal standard. Splitting patterns are indicated as s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet; br, broad signal. ^{19}F-NMR spectra were measured with Brucker AM 200 (188 MHz) spectrometer. The chemical shifts are expressed in ppm downfield from trichlorofluoromethane, using trichlorofluoromethane (δ = 0) as an internal standard. Mass spectra were taken with a Hitachi RMU-6MG mass spectrometer. FAB mass spectra were taken with a JEOL JMS-AX505W mass spectrometer. Unless otherwise noted, all experiments were carried out under an atmosphere of dry argon using anhydrous solvents. Especially, diethyl ether, tetrahydrofuran, 1,2-dimethoxyethane, and 1,2-diethoxyethane were distilled from sodium benzophenone ketyl. For thin layer chromatographic (TLC) analyses, Merck precoated TLC plates (silica gel 60 F254, 0.25 mm, Art 5715) were used. The following abbreviations were used: tetrahydrofuran (THF), diethyl ether (Et_2O), ethyl acetate (AcOEt), ethanol (EtOH), methanol (MeOH), chloroform ($CHCl_3$), dichloromethane (CH_2Cl_2), 1,2-diethoxyethane (DEE), 1,2-dimethoxyethane (DME), triethylamine (Et_3N), *dl*-camphor-10-sulfonic acid (CSA), diethylzinc (Et_2Zn). Fluorodiiodomethane was prepared by the reported method.[17]

(4*R*,5*S*)-4,5-Diphenyl-2-oxazolidinone (4a) To a stirred suspension of commercially available **3a** (10.0 g, 47 mmol) and Et_3N (14.4 ml, 0.10 mol) in CH_2Cl_2 (100 ml) was added dropwise trichloromethyl chloroformate (3.0 ml, 25 mmol) at 0 °C, and the mixture was stirred for 1 h at the same temperature. After concentration *in vacuo*, the residue was poured into water to precipitate crystals. The crystals were collected by filtration, successively washed with 10% HCl and H_2O, and dried at 50-60 °C for 3 h *in vacuo* to afford **8a** as colorless crystals (10.9 g, 97%), mp 232.5-233.5 °C (recrystallized from toluene) and $[\alpha]_D^{20}$ +60.6° (*c* 0.858, MeOH). IR ($CHCl_3$): 3580, 1765, 1540 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 5.20 (d, 1H, J = 8.0 Hz, NC*H*Ph), 5.85 (br, 1H, NH), 5.96 (d, 1H, J = 8.0 Hz, OC*H*Ph), 6.8-7.6 (m, 10H, Phx2). MS (m/z): 239 (M^+), 108, 107. *Anal.* Calcd for $C_{15}H_{13}NO_2$: C, 75.30; H, 5.48; N, 5.86. Found: C, 75.09; H, 5.38; N, 5.86.

(4*R*)-4-Phenyl-2-oxazolidinone (4b) To a stirred solution of commercially available **3b** (2.0 g, 15 mmol) and Et_3N (4.0 ml, 29 mmol) in CH_2Cl_2 (15 ml) was added dropwise trichloromethyl chloroformate (0.9 ml, 7.3 mmol) at 0°C. After stirring for 1 h, the mixture was diluted with CH_2Cl_2, successively washed with a saturated solution of citric acid and brine, and dried (Na_2SO_4). After filtration, the filtrate was concentrated *in vacuo* to afford **4b** as colorless crystals (1.80 g, 76%), mp 132-134 °C (recrystallized from hexane-AcOEt) and $[\alpha]_D^{20}$ -57.7° (*c* 1.083, $CHCl_3$). [for the enantiomer of **4b**, *lit.*[18] mp 132-133 °C and $[\alpha]_D^{20}$ +49.5° (*c* 2.1, $CHCl_3$)] IR (KBr): 3256, 1744, 1708, 1404, 1238, 1026, 698 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 4.19 (dd, 1H, J = 7.2 and 8.7 Hz, C*H*H-CHPh), 4.74 (t, 1H, J = 8.7 Hz, CH*H*CHPh), 4.86 (dd, 1H, J = 7.2 and 8.7 Hz, CH_2CHPh), 5.85 (br s, 1H, NH), 7.34-7.42 (m, 5H, Ph). MS (m/z): 163 (M^+), 133, 104 (base peak), 91, 77, 51.

(4*R*)-4,5,5-Triphenyl-2-oxazolidinone (4c) a) Preparation of (*R*)-2-amino-1,1,2-triphenylethanol: This was prepared from (*R*)-methyl phenylglycinate according to the reported method.[8] The compound obtained showed mp 126-127 °C (recrystallized from EtOH) and $[\alpha]_D^{20}$ +233° (*c* 1.05, $CHCl_3$). [*lit.*[8] $[\alpha]_D^{20}$ +235° (*c* 0.995, $CHCl_3$)].

b) Preparation **4c**: To a stirred mixture of (*R*)-2-amino-1,1,2-triphenylethanol (1.47 g, 4.7 mmol) and Et_3N (1.42 ml, 10 mmol) in CH_2Cl_2 (20 ml) was added dropwise trichloromethyl chloroformate (0.3 ml, 2.4 mmol) at 0 °C. After stirring for 1 h at the same temperature, a small portion of H_2O was added to the mixture. The mixture was concentrated *in vacuo*, diluted with AcOEt, washed with brine, then dried (Na_2SO_4). After filtration, the filtrate was concentrated *in vacuo* to yield **4c** as colorless crystals (1.60 g, 99%), mp 247-248 °C (recrystallized from AcOEt) and $[\alpha]_D^{20}$ +203° (*c* 0.998, $CHCl_3$). IR ($CHCl_3$): 3460, 1760, 1440 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 5.62 (s, 1H, CHPh), 6.06 (br s, 1H, NH), 6.9-7.8 (m, 15H, Phx3). MS (m/z): 316 (M^+), 270, 183 (base peak), 105, 51. *Anal.* Calcd for $C_{21}H_{17}NO_2$: C, 79.98; H, 5.43; N, 4.44. Found.: C, 79.69; H, 5.31; N, 4.34.

(4*R*,5*S*)-3-(1-Methoxyethyl)-4,5-diphenyl-2-oxazolidinone (5a) A mixture of **4a** (10.9 g, 45 mmol) and CSA (500 mg, 2.2 mmol) in 1,1-dimethoxyethane (150 ml) was heated at reflux for 3 days. The mixture was partitioned between Et_2O and an aqueous saturated solution of $NaHCO_3$, and the aqueous phase was further extracted with Et_2O. The organic phases were combined, washed with brine, dried ($MgSO_4$) and concentrated *in vacuo* to give crude **5a** as a 2:1 diastereomeric mixture (14.1 g, quantitative yield). This compound was used for next step without purification. IR ($CHCl_3$): 3000, 1750, 1410, 1100, 1055 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.96 (d, 3Hx2/3, J = 6.2 Hz, *Me*CH), 1.46 (d, 3Hx1/3, J = 6.2 Hz, *Me*CH), 3.25 (s, 3Hx1/3, OMe), 3.46 (s, 3Hx2/3, OMe), 5.0-6.1 (m, 3H, MeOC*H*N, NC*H*Ph, OC*H*Ph), 6.6-7.5 (m, 10H, Phx2). MS (m/z): 297 (M^+), 238, 222, 165, 59 (base peak).

(4*R*)-3-(1-Methoxyethyl)-4-phenyl-2-oxazolidinone (5b) To 1,1-dimethoxyethane (50 ml) was added **4b** (3.26 g, 20 mmol) and CSA (0.93 g, 4.0 mmol), then the mixture was heated at 50 °C for 24 h. After cooling, the mixture was washed successively with water and brine, and dried (Na_2SO_4). After filtration, the filtrate was concentrated *in vacuo* to give **5b** as a 2:1 diastereomeric mixture (4.4 g, quantitative yield). This mixture was used for the next step without purification. IR (KBr): 3040, 3004, 1738, 1404, 1208, 1096, 702 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.88 (d, 3Hx2/3, J = 5.6 Hz, CH*Me*), 1.42 (d, 3Hx1/3, J = 5.6 Hz, CH*Me*), 3.15 (s, 3Hx1/3, OMe), 3.56 (s, 3Hx2/3, OMe), 4.17 (dd, 1Hx2/3, J = 5.6 and 8.7 Hz, C*H*H-CHPh), 4.21 (dd, 1Hx1/3, J = 5.6 and 8.7 Hz, C*H*H-CHPh), 4.62 (t, 1Hx1/3, J = 8.7 Hz, CH*H*-CHPh), 4.66 (t, 1Hx2/3, J = 8.7 Hz, CH*H*-CHPh), 4.88 (dd, 1Hx2/3, J = 5.6 and 8.7 Hz, CH_2-C*H*Ph), 4.89 (dd, 1Hx1/3, J = 6.4 and 8.7 Hz, CHH-C*H*Ph), 5.12 (q, 1Hx1/3, J = 5.6 Hz, NC*H*OMe), 5.25 (q, 1Hx2/3, J = 5.6 Hz, NC*H*OMe), 7.3-7.4 (m, 5H, Ph). MS (m/z): 221 (M^+), 206, 190 (base peak), 104, 91, 59.

(4*R*)-3-(1-Methoxyethyl)-4,5,5-triphenyl-2-oxazolidinone (5c) A mixture of **4c** (1.0 g, 3.2 mmol) and CSA (74 mg, 0.32 mmol) in 1,1-dimethoxyethane (20 ml) was heated at reflux for 45 h. After cooling, the mixture was partitioned between Et_2O and a saturated solution of $NaHCO_3$, the aqueous phase was further extracted with Et_2O. The organic phases were combined, washed with brine, and dried ($MgSO_4$). After filtration, the filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography on silica gel (hexane-AcOEt, 5:1) to afford **5c** as a 3:1 diastereomeric mixture (978 mg, 86%). This was used for the next step without separation of the diastereomers. IR (KBr): 2992, 1744, 1412, 748, 700 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.91 (d, 3Hx3/4, J = 6.3 Hz, CH*Me*), 1.29 (d, 3Hx1/4, J = 6.3 Hz, CH*Me*), 2.72 (s, 3Hx3/4, OMe), 3.05 (s, 3Hx1/4, OMe), 4.14 (q, 1Hx1/4, J = 6.3 Hz, C*H*Me), 5.22 (q, 1Hx1/4, J = 6.3 Hz, C*H*Me), 5.53 (s, 1Hx1/4, C*H*Ph), 5.60 (s, 1Hx3/4, C*H*Ph), 6.8-8.0 (m, 15H, Phx3). MS (FAB, m/z): 374 (M^++1), 342, 298, 256, 183, 59.

(4*R*,5*S*)-4,5-Diphenyl-3-vinyl-2-oxazolidinone (6a) A crude sample of **5a** (14.2 g) was heated at 150 °C for 0.5 h under a reduced pressure (15 mmHg). The material solidified was distilled under a reduced pressure to give **6a** as a colorless solid (9.69 g, 78%), bp 175-180 °C (2 mmHg, bath temp.), mp 170-171 °C (recrystallized from hexane-AcOEt), and $[\alpha]_D^{20}$ +21.7° (*c* 0.775, $CHCl_3$). [*lit.*[10] $[\alpha]_D^{20}$ -22.1° (*c* 1.99, $CHCl_3$) for the enantiomer of **6a**]. IR ($CHCl_3$): 1760, 1640, 1540, 1382, 1364 cm^{-1}. ^{1}H-NMR (C_6D_6): 3.88 (dd, 1H, J = 1.0 and 16.0 Hz, *Z*-C*H*=CHN, spin saturation at δ = 4.42, NOE: 3.8%), 4.10 (dd, 1H, J = 1.0 and 9.2 Hz, *E*-C*H*=CHN, spin saturation at δ = 3.88, NOE; 13.4%), 4.42 (d, 1H, J = 8.1 Hz, NC*H*Ph, spin saturation at δ = 3.88, NOE; 4.4%), 5.08 (d, 1H, J = 8.1 Hz, OC*H*Ph, spin saturation at δ = 4.42, NOE: 7.6%), 6.50-6.9 (m, 10H, Phx2), 7.13 (dd, 1H, J = 9.2 and 16.0 Hz NC*H*=CH_2). MS (m/z): 265 (M^+), 180, 131, 132, 104 (base peak). *Anal.* Calcd for $C_{17}H_{15}NO_2$: C, 76.96; H; 5.70; N, 5.28. Found: C, 76.80; H, 5.65; N, 5.25.

(4*R*)-4-Phenyl-3-vinyl-2-oxazolidinone (6b) A crude sample of **5b** (4.40 g, 20 mmol) was distilled under a reduced pressure to afford **6b** as a colorless solid (2.1g, 56%), bp 150 °C (1 mmHg, bath temp.), mp 40.5-41.5 °C, and $[\alpha]_D^{20}$ -117° (*c* 1.03, CH_2Cl_2). [*lit.*[10] $[\alpha]_D^{20}$ +113° (*c* 1.25, CH_2Cl_2) for the enantiomer of **6b**]. IR (KBr): 1758, 1644, 1402, 1230, 702 cm^{-1}. ^{1}H-NMR (C_6D_6): 3.35 (dd, 1H, J = 5.6 and 8.7 Hz, C*H*HCHPh), 3.68 (br t, 1H, J = 8.7 Hz, CH*H*CHPh), 3.83 (d, 1H, J = 15.9 Hz, *Z*-C*H*=CHN), 4.01 (d, 1H, J = 9.5 Hz, *E*-C*H*=CHN), 4.05-4.08 (br, 1H, CH_2C*H*Ph), 6.71-7.02 (m, 6H, Ph and NC*H*=CH_2). MS (m/z): 189 (M^+), 146, 130, 104 (base peak), 91, 77, 54. *Anal.* Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40. Found: C, 69.79; H, 5.86; N, 7.36.

(4*R*)-4,5,5-Triphenyl-3-vinyl-2-oxazolidinone (6c) To a crude sample of **5c** (113 mg, 0.30 mmol) was added a solution of NH_4Cl (3.4 mg, 0.06 mmol)) in methanol (0.1 ml), and the mixture was concentrated *in vacuo* to give a homogeneous solid. This was heated at 138 °C for 2 h under a reduced pressure (16 mmHg). After cooling, the mixture was partitioned between AcOEt and brine, and the organic phase separated was dried (Na_2SO_4). After filtration, the filtrate was concentrated *in vacuo* to give a residue, which was purified by column chromatography on silica gel (CH_2Cl_2-AcOEt, 5:1) to afford **6c** as a colorless solid (68 mg, 66%) and recovered starting **5c** (29 mg, 26%). The compound **6c** showed mp 220-222 °C (recrystallized from AcOEt-hexane) and $[\alpha]_D^{20}$ +314° (*c* 1.01 $CHCl_3$). IR (KBr): 1752, 1642, 1388, 698 cm^{-1}. ^{1}H-NMR (C_6D_6): 4.03 (d, 1H, J = 9.5 Hz, *E*-C*H*=CHN), 4.03 (d, 1H, J = 15.9 Hz, *Z*-C*H*=CHN), 5.48 (s, 1H, C*H*Ph), 6.67-7.5 (m, 16H, Phx3 and NC*H*=CH_2). MS (m/z): 341 (M^+), 297, 256, 183, 131, 104 (base peak), 59. *Anal.* Calcd for $C_{23}H_{19}NO_2 \cdot 1/4H_2O$: C, 79.86; H; 5.68; N, 4.05. Found: C, 79.78; H, 5.58; N, 3.91.

Typical procedure for the cyclopropanation of 6a with zinc-fluorocarbenoid (Table 1, run 10) To a stirred mixture of **6a** (50 mg, 0.19 mmol), DEE (80 μl, 0.56 mmol), and MS4A (50 mg) in CH_2Cl_2 (1.0 ml) was added Et_2Zn (1.0 M hexane solution, 0.56 ml, 0.56 mmol) at room temperature. After stirring for 10 min at the same temperature, a solution of $CHFI_2$ (180 mg, 0.63 mmol) in CH_2Cl_2 (0.5 ml) was added dropwise to the mixture at 40 °C. After stirring for 24 h at the same temperature, a saturated solution of NH_4Cl was added to the mixture to quench the reaction, and the mixture was extracted with CH_2Cl_2. The organic extracts were combined, washed with brine, and dried (Na_2SO_4). After filtration, the filtrate was concentrated *in vacuo* to give crude products. ^{19}F-NMR ($CDCl_3$): -209.17 (dddd, 30/100F, J = 11.9, 16.0, 27.9, and 61.9 Hz, **8a**), -211.51 (dddd, 6/100F, J = 12.4, 14.7, 27.5, and 61.9 Hz, **10a**), -223.98 (ddd, 59/100F, J = 15.1, 24.2, and 63.7 Hz, **7a**), -228.49 (ddd, 5/100F, J = 15.2, 25.7, and 63.7 Hz, **9a**). This crude product was subjected to column chromatography on silica gel (CH_2Cl_2-AcOEt, 80:1), affording the starting **6a** (2.1 mg, 4.2%), **7a** (29.0 mg, 51 %) and an unseparatable mixture of **8a-10a** (20.2 mg, 36%). Pure **8a** was obtained by recrystallization of the mixture of **8a-10a** from hexane-AcOEt. **7a**: mp 173-177.5 °C (decomp.) (recrystallized from hexane-AcOEt) and $[\alpha]_D^{20}$ +73.6° (*c* 0.451, $CHCl_3$). IR ($CHCl_3$): 1760, 1540, 1410 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.88-1.09 (m, 2H, FCHC*H*$_2$), 2.63-2.67 (m, 1H, NC*H*CHF), 4.74 (dddd, 1H, J = 3.1, 4.8, 6.0, and 63.7 Hz, FCH), 4.93 (d, 1H, J = 7.8 Hz, NC*H*Ph), 5.89 (d, 1H, J = 7.8 Hz, OC*H*Ph), 6.9-7.15 (m, 10H, Phx2). ^{19}F-NMR ($CDCl_3$): -223.98 (ddd, J = 15.1, 24.2, and 63.7 Hz). MS (m/z): 298 (M^++1), 253, 206, 180 (base peak). *Anal.* Calcd for $C_{18}H_{16}FNO_2$: C, 72.71; H, 5.42; N, 4.71. Found: C, 72.46; H, 5.35; N, 4.66. **8a**: mp 171-173.5 °C (decomp.) (recrystallized from hexane-AcOEt) and $[\alpha]_D^{20}$ +55.4° (*c* 0.523, $CHCl_3$). IR ($CHCl_3$): 1760, 1540, 1410 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.98-1.28 (m, 2H, FCHC*H*$_2$), 2.83 (dddd, 1H, J = 1.0, 5.4, 9.4, and 16.0 Hz, NC*H*CHF), 4.81 (d, 1H, J = 8.0 Hz, NC*H*Ph), 4.87 (dddd, 1H, J = 1.0, 3.4, 6.9, and 61.9 Hz, CHF), 5.77 (d, 1H, J = 8.0 Hz, OC*H*Ph), 6.87-7.18 (m, 10H, Phx2). ^{19}F-NMR: -209.17 (dddd, J = 11.9, 16.0, 27.9, and 61.9 Hz). MS (m/z); 298 (M^++1), 253, 206, 180 (base peak). *Anal.* Calcd for $C_{18}H_{16}FNO_2$: C, 72.71; H, 5.42; N, 4.71. Found: C, 72.57; H, 5.34; N, 4.68.

(4*R*)-3-(2-Fluorocyclopropyl)-4-phenyl-2-oxazolidinone (7b-10b) (Table 2, run 1) To a stirred mixture of **7b** (300 mg, 1.6 mmol) and MS4A (300 mg) in CH_2Cl_2 (10 ml) was added DME (0.48 ml, 4.8 mmol) and neat Et_2Zn (600 mg, 4.9 mmol) at room temperature. After cooling to -40 °C, $CHFI_2$ (1.4 g, 4.8 mmol) was added to the mixture. The mixture was allowed to warm to room temperature, and stirred for 15 h under the same temperature. The mixture was diluted with a saturated solution of NH_4Cl, and extracted with CH_2Cl_2. The organic extracts were combined, washed with brine, dried (Na_2SO_4), then filtered. The filtrate was concentrated *in vacuo* to give a residue, which was subjected to column chromatography on silica gel (hexane-AcOEt, 4:1→2:1) to give a mixture of **7b-10b** as a caramel, (281 mg, 80 %). ^{19}F-NMR ($CDCl_3$): -209.44 (dddd, 27/100F, J = 12.2, 15.5, 28.2, and 61.6 Hz, **8b**), -211.51 (dddd, 9/100F, J = 12.2, 15.1, 27.2, and 61.6 Hz, **10b**), -223.27 (ddd, 59/100F, J = 15.1, 24.9, and 64.0 Hz, **7b**), -227.75 (ddd, 4/100F, J = 15.5, 25.4, and 64.0 Hz, **9b**). The major product (**7b**) was obtained as a colorless syrup by preparative HPLC [TSK gel ODS-80Tm (20 mmϕ x 250 mm), CH_3CN:H_2O = 4:6]. **7b**: $[\alpha]_D^{20}$ -44.2° (*c* 1.08, $CHCl_3$). IR (neat): 1758, 1414, 1040, 768, 704 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.88-0.98 (m, 1H, FCHC*H*H), 1.05 (dddd, 1H, J = 2.9, 5.9, 8.8, and 24.9 Hz, FCHCH*H*) 2.43 (br td, 1H, J = 4.5 and 5.9 Hz, NC*H*CHF), 4.20 (dd, 1H, 4.9 and 8.8 Hz, OC*H*HCHPh), 4.66 (t, 1H, J = 8.8 Hz, OCH*H*CHPh), 4.65 (dm, 1H, J = 64.0 Hz, CHF), 4.74 (dd, 1H, J = 4.9 and 8.8 Hz, C*H*Ph), 7.33-7.45 (m, 5H, Ph). ^{19}F-NMR ($CDCl_3$): -223.27 (ddd, J = 15.1, 24.9, and 64.0 Hz). MS (m/z): 221 (M^+), 189, 144, 112, 104 (base peak), 91, 77. HRMS. Calcd for $C_{12}H_{12}FNO_2$: 221.0852. Found: 221.0850.

(4*R*)-3-(2-fluorocyclopropyl)-4,5,5-triphenyl-2-oxazolidinones (7c-10c) (Table 2, run 2) To a stirred mixture of **6c** (62.7 mg, 0.18 mmol) and MS4A (71 mg) in CH_2Cl_2 (10 ml) was added DME (57 ml, 0.55 mmol) and neat Et_2Zn (70 mg, 0.57 mmol) at room temperature. After warming to 40 °C, $CHFI_2$ (160 mg, 0.56 mmol) was added to the stirred mixture. After stirring for 6 h at the same temperature, further amounts of Et_2Zn (70 mg, 0.57 mmol) and $CHFI_2$ (160 mg, 0.56 mmol) were added to the mixture, and the mixture was stirred for 15 h. After cooling, the mixture was diluted with 1 N HCl and extracted with CH_2Cl_2. The organic extracts were combined, washed with brine, dried (Na_2SO_4), then filtered. The filtrate was concentrated *in vacuo* to give a residue, which was subjected to column chromatography on silica gel (hexane-AcOEt, 4:1) to afford a mixture of **7c-10c** as a solid (46.3 mg, 68%). ^{19}F-NMR ($CDCl_3$): -209.54 (dddd, 26/100F, J = 12.2, 16.0, 28.2, and 61.6 Hz, **8c**), -211.90 (dddd, 15/100F, J = 12.2, 14.6, 26.8, and 61.6 Hz, **10c**), -223.46 (ddd, 49/100F, J = 15.1, 24.0, and 63.5 Hz, **7c**), -228.01 (ddd, 9/100F, J = 14.6, 23.5, and 64.0 Hz, **9c**). This mixture was subjected to column chromatography on silica gel (hexane-AcOEt, 4:1) to afford pure **7c** as a colorless solid, mp 228-229 °C (recrystallized from AcOEt-hexane) and $[\alpha]_D^{20}$ +160° (*c* 1.04, $CHCl_3$). IR (KBr): 2928, 1752, 1452, 1406, 698 cm^{-1}. ^{1}H-NMR ($CDCl_3$): 0.88-1.00 (m, 2H, FCHC*H*$_2$), 2.50 (br td, 1H, J = 4.8 and 9.5 Hz, NC*H*CHF), 4.65 (dm, 1H, J = 63.5 Hz, CHF), 5.37 (s, 1H, CHPh), 6.97-7.60 (m, 15H, Phx3). ^{19}F-NMR ($CDCl_3$): -223.46 (ddd, J = 15.1, 24.3, and 63.5 Hz). MS (m/z): 374 (M^++1), 329, 256 (base peak), 165, 117 105, 77, 59. *Anal.* Calcd for $C_{24}H_{20}FNO_2$: C, 77.19; H, 5.40; N, 3.75; F, 5.09. Found: C, 77.03; H, 5.17; N, 3.76; F, 4.77.

(1*R*,2*S*)-2-Fluorocyclopropylamine Hydrochloride [(1*R*,2*S*)-2•HCl] A mixture of **7a** (118 mg, 0.40 mmol) and 10% Pd-C (50 mg) in AcOH (3 ml) was stirred for 3 h at room temperature under a hydrogen atmosphere (pressure of 3 kg/cm^2). After filtration, the filtrate was diluted with a methanolic solution of hydrogen chloride (5 M solution, 3 ml) and concentrated *in vacuo*. The residue was recrystallized from EtOH-Et_2O to give (1*R*,2*S*)-2•HCl (38.8 mg, 87%) as colorless crystals, mp 154-156 °C (decomp.) and $[\alpha]_D^{20}$ -20.6° (*c* 0.781, EtOH) [*lit.*[6] mp 153-157°C (decomp.) and $[\alpha]_D$ -19.0° (*c* 0.738, EtOH)]. *IR and ^{1}H-NMR spectra of this* sample were identical with those of an authentic sample.[6]

(1*R*,2*S*)-2-Fluorocyclopropylammonium *p*-Toluenesulfonate [(1*R*,2*S*)-2•TsOH] A mixture of **7a** (168 mg, 0.57 mmol) and 10% palladium on charcoal (80 mg) in AcOH (4 ml) was stirred for 3 h at room temperature under a hydrogen atmosphere (pressure of 3-3.5 kg/cm^2). After filtration, a solution of anhydrous *p*-toluenesulfonic acid (97 mg, 0.56 mmol) in MeOH (1 ml) was added, then

the mixture was concentrated *in vacuo*. The residue was triturated with Et_2O to afford (1*R*,2*S*)-2•TsOH as colorless crystals (126 mg, 90%).
This compound [(1*R*,2*S*)-2•TsOH] was also prepared from **7c**. A mixture of **7c** (20.5 mg, 0.055 mmol), *p*-toluenesulfonic acid hydrate (10.5 mg, 0.055 mmol), and 20% palladium hydroxide on charcoal (10 mg) in AcOH (1 ml) was stirred for 20 h at room temperature under a hydrogen atmosphere (pressure of 10 kg/ cm^2). After filtration, the mixture was concentrated *in vacuo* to give a residue, which was triturated with $CHCl_3$ to yield (1*R*,2*S*)-2•TsOH (9.8 mg, 74%). The optical purities of two sorts of (1*R*,2*S*)-2•TsOH were determined both as 98% ee by the same method as described in preceding paper.[6] A sample of (1*R*,2*S*)-2•TsOH recrystallized from toluene-EtOH showed mp 178-179 °C (decomp.) and $[\alpha]_D^{20}$ -10.7° (*c* 1.08, MeOH). [*lit.*[6] 168.5-170.5 °C (decomp.) and $[\alpha]_D^{20}$ -8.9° (*c* 0.699, MeOH)] All the spectral data were identical with those of an authentic sample.[6]

***t*-Butyl *N*-[(1*R*,2*S*)-2-Fluorocyclopropyl]carbamate (11)** To a stirred suspension of (1*R*,2*S*)-2•HCl (8.7 mg, 78 μmol) and di-*t*-butyl dicarbonate (34 mg, 0.16 mmol) in CH_2Cl_2 (0.2 ml) was added Et_3N (16 μl, 0.114 mmol) at 0 °C, and the mixture was stirred at the same temperature for 2 h. The mixture was partitioned between Et_2O and H_2O, and the aqueous phase was further extracted with Et_2O. All the organic extracts were combined, washed with brine, dried ($MgSO_4$), then concentrated *in vacuo*. The residue was subjected to column chromatography on silica gel (hexane-Et_2O, 2:1) to afford **11** as colorless crystals (8.7 mg, 64%), mp 77.5-78.5 °C (recrystallized from hexane) and $[\alpha]_D^{25}$ -66.5° (*c* 0.840, $CHCl_3$) [*lit.*[4b] mp 63 °C and $[\alpha]_D$ -60.27° (*c* 0.740, $CHCl_3$)]. ^{1}H-NMR spectrum of this sample was identical with that of an authentic racemic sample.[6]

(1*R*,2*R*)-2-Fluorocyclopropylamine Hydrochloride [(1*R*,2*R*)-13•HCl] A mixture of **8a** (87.5 mg, 0.30 mmol) and 10% Pd-C (30 mg) in AcOH (2 ml) was stirred for 3 h at room temperature under a hydrogen atmosphere (pressure of 3 kg/cm^2). After filtration, the mixture was diluted with a methanolic solution of hydrogen chloride (5 M solution, 3 ml), and concentrated *in vacuo*. The residue was recrystallized from EtOH-Et_2O to give (1*R*,2*R*)-13•HCl as colorless crystals (21.3 mg, 65%), mp 131-134 °C (decomp.) and $[\alpha]_D^{20}$ -14.2° (*c* 0.604, EtOH). ^{1}H-NMR spectrum of this sample was identical with that of an authentic racemic (1*R**,2*R**)-13•HCl.[6]

***t*-Butyl *N*-[(1*R*,2*R*)-2-Fluorocyclopropyl]carbamate (14)** Treatment of (1*R*,2*R*)-13•HCl (8.9 mg, 80 μmol) in the same manner as described for the preparation of **11** from (1*R*,2*S*)-2•HCl gave **14** as colorless crystals (6.2 mg, 44%) after purification by column chromatography, mp 59.5-61 °C (recrystallized from hexane) and $[\alpha]_D^{25}$ -23.9° (*c* 0.999, $CHCl_3$). ^{1}H-NMR spectrum of this sample was identical with that of an authentic racemic sample.[6]

References and Notes

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(*Received in Japan* 10 *December* 1993; *accepted* 31 *January* 1994)