General Syntheses of Optically Active α-Trifluoromethylated Amines via Ring-Opening Reactions of *N*-Benzyl-2-trifluoromethylaziridine

Toshimasa Katagiri, Mikihiro Takahashi, Yasuyuki Fujiwara, Hideki Ihara, and Kenji Uneyama*

Department of Applied Chemistry, Faculty of Engineering, Okayama University, Tsushimanaka 3-1-1, Okayama 700-8530, Japan

Received February 3, 1999

Syntheses of optically active trifluoromethylated amines via ring-opening reactions of optically active *N*-benzyl-2-trifluoromethylaziridine were achieved. Proton-catalyzed ring-opening reactions of the 2-trifluoromethylaziridine proceeded very smoothly, while the compound was found to be inert toward nucleophiles; thus, the trifluoromethylaziridine itself cannot be ring-opened by nitrogen or carbon nucleophiles. The *N*-alkylated aziridinium ion of trifluoromethylaziridine was highly reactive to undergo smooth ring-opening by nitrogen and carbon nucleophiles.

Introduction

Selectively fluorinated organic compounds are very important, especially in the field of pharmaceuticals and agrochemicals.[1] To date, a large number of building blocks for further synthesis of such bioactive compounds have been proposed.[2] Although there has been recent general interest in the preparation and utilization of optically enriched and/or pure fluorinated building blocks,[3] there are very few optically active and synthetically usable fluorinated compounds which are commercially available, one exception being 2,3-epoxy-1,1,1-trifluoropropane (75% ee).[4,5] Therefore, further development of optically active (or if possible optically pure) fluorinated building blocks from this epoxide is worth studying.[6]

Aziridines are important intermediates for the syntheses of nitrogen-containing molecules, especially for amino acids,[7,8a] heterocycles,[7,8b] and alkaloids.[7,8c] Very recently, we have prepared optically pure *N*-benzyl-2-trifluoromethylaziridine from the trifluoromethylated epoxide in good yield.[9] However, studies on the reactivity of optically pure and racemic 2-trifluoromethylated aziridines have been very limited, although ring-opening reactions by an oxygen nucleophile,[9,10a] sulfur nucleophile,[10a] and halogens[10] have been reported. Thus, ring-opening reactions of the 2-trifluoromethylated aziridine by a nitrogen nucleophile and a carbon nucleophile remain to be studied.

We have reported the ring-opening reactions of the trifluoromethylated epoxide with carbanions to be difficult. Although the 2,3-epoxy-1,1,1-trifluoropropane was ring-opened smoothly by α-cyano carbanions generated from substituted acetonitriles, the compound was inert toward both the malonate carbanion and nitromethane carbanion.[11] Though the trifluoromethyl group of the epoxide should electronically activate the epoxide via its strong electron-withdrawing effect, the reaction should be prevented by electrostatic repulsion between lone pairs of fluorine on the trifluoromethyl group and the negative charge of nucleophiles. One would expect a similar situation in the ring-opening reactions of 2-trifluoromethylated aziridine.

We undertook the ring-opening reactions of 2-trifluoromethylaziridine **1** by halogen, chalcogen, nitrogen, and carbon nucleophiles, and the result of our systematic investigation is presented herein.

Results and Discussion

Acid-Promoted Ring-Opening Reactions of 2-Trifluoromethylaziridine 1. First, acid-promoted ring-opening reactions of optically active 2-trifluoromethylaziridine **1** were examined (Scheme 1). The acid-promoted reactions of racemate with Br*ϕ*nsted acids, such as

(1) (a) *Fluorine-containing Amino Acids Synthesis and Properties*; Kukhaŕ, V. P., Soloshonok, V. A., Eds.; John Wiley & Sons: New York, 1995. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley & Sons: New York, 1991.

(2) (a) *Chemistry of Organic Fluorine Compounds II*; Hudlicky, M., Pavlath, A. E., Eds.; American Chemical Society: Washington, DC, 1995. (b) Uneyama, K. *Yuki Gosei Kagaku Kyokaishi* **1991**, *49*, 612.

(3) (a) Yamazaki, T.; Kitazume, T. *Rev. Heteroatom Chem*. **1992**, *7*, 132. (b) Shinohara, N.; Yamazaki, T.; Kitazume, T. *Rev. Heteroatom Chem*. **1996**, *14*, 165.

(4) Furuhashi, K. In *Chirality in Industry*; Collins, A. N., Sheldrake, G. N., Crosby, J., Eds.; John Wiley & Sons: New York, 1992; p 167.

(5) Optically pure 2,3-epoxy-1,1,1-trifluoropropane and its synthon are also available in laboratory scales: (a) Bussche-Hunnefeld, C. von der; Cescato, C.; Seebach, D. *Chem. Ber*. **1992**, *125*, 2795. (b) Ramachandran, P. V.; Gong, B.; Brown, H. C. *J. Org. Chem*. **1995**, *60*, 41. (c) Shimizu, M.; Sugiyama, K.; Fujisawa, T. *Bull. Chem. Soc. Jpn*. **1996**, *69*, 2655. (d) Katagiri, T.; Obara, F. *Jpn. Kokai Tokkyo Koho* **1994**, Jp06−247953. (e) Vanhessche, K. P. M.; Sharpless, K. B. *Chem. Eur. J*. **1997**, *3*, 517.

(6) For a comprehensive review of 2,3-epoxy-1,1,1-trifluoropropane, see: Katagiri, T. In *Enantiocontrolled Synthesis of Fluoro-Organic Compounds, Stereochemical Challenges and Biomedical Targets*; Soloshonok, V. A., Ed.; John Wiley & Sons: New York, 1999; p 161.

(7) Tanner, D. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 599.

(8) (a) Dureault, A.; Tranchepain, I.; Depezay, J.-C. *J. Org. Chem*. **1989**, *54*, 5324. (b) Tanner, D.; He, H. M. *Tetrahedron* **1992**, *48*, 6079. (c) Hudlicky, T.; Luna, H.; Price, J. D.; Rulin, F. *J. Org. Chem*. **1990**, *55*, 4683.

(9) Katagiri, T.; Ihara, H.; Takahashi, M.; Kashino, S.; Furuhashi, K.; Uneyama, K. *Tetrahedron: Asymmetry* **1997**, *8*, 2933.

(10) (a) Karimova, N. M.; Teplenicheva, Yu. L.; Kolomiets, A. F.; Fokin, A. V. *Russ. Chem. Bull*. **1997**, *46*, 1136. (b) Rozhkov, I. N.; Karimova, N. M.; Ignatova, Yu. L.; Matveeva, A. G. *Russ. Chem. Bull*. **1994**, *43*, 258.

(11) Katagiri, T.; Akizuki, M.; Kuriyama, T.; Shinke, S.; Uneyama, K. *Chem. Lett*. **1997**, 549. Recently a Lewis acid bearing alkyl moiety was used for alkylation of 2,3-epoxy-1,1,1-trifluoropropane: Ooi, T.; Furuya, M.; Maruoka, K. *Chem. Lett*. **1998**, 817.

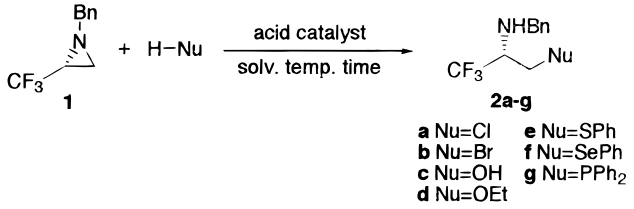
10.1021/jo990207e CCC: $18.00
Published on Web 09/08/1999

Table 1. Acid-Promoted Ring-Opening Reactions of 1

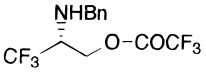
								enantiomeric excess (% ee)	
entry	HNu	acid catalyst	solvent	temp (°C)	time (h)	product	yield[e] (%)	aziridine **1**	product **2**
1	HCl[a]		water	rt	10	**2a**	94	94	94
2	HBr[a]		water	rt	10	**2b**	93	94	94
3	H_2O	CF_3CO_2H[c]	THF	rt	48	**2c**	64	*f*	*f*
4	H_2O	H_2SO_4[c]		rt	10	**2c**	98	>99	>99
5	EtOH	H_2SO_4[c]		rt	10	**2d**	88	83	83
6	PhSH[a]	CF_3SO_3H[d]		90	3	**2e**	85	92	*f*
7	PhSH[a]			90	3	**2e**	40	92	*f*
8	PhSeH[b]	CF_3SO_3H[d]	CH_2Cl_2	rt	10	**2f**	97	92	92
9	PhSeH[b]		CH_2Cl_2	40	10	**2f**	87	92	*f*
10	Ph_2PH[b]	CF_3SO_3H[d]	CH_2Cl_2	rt	10	**2g**	85	83	*f*

[a] Used 20 equiv. [b] Used 1.2 equiv. [c] Used 2 equiv. [d] Used 1.1 equiv. [e] Isolated yield. [f] Not determined.

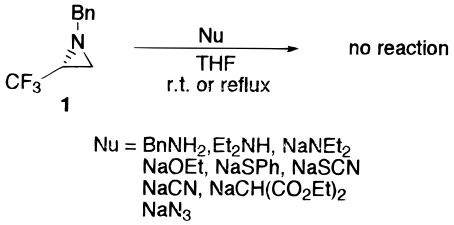
Scheme 1



Scheme 2



Scheme 3



thioacetic acid, hydrogen halide, sulfuric acid, *p*-toluenesulfonic acid, and picric acid, have been reported by Karimova's group.[10] In our present study, ring-opening reactions by Brϕnsted acids as well as acid-catalyzed ring-opening reactions in the presence of nucleophiles were studied. Results of the ring-opening reactions of the optically active aziridines are summarized in Table 1. These acid-promoted ring-opening reactions proceeded very smoothly in a manner similar to that of the reported cases of nonfluorinated aziridines.[12] The reactions proceeded regiospecifically to give β-cleaved products in good yields. Haloamines **2a** and **2b** were obtained in good yields without byproducts in water. Amino alcohol **2c** was synthesized in 64% yield (entry 3) via ring-opening reaction of aziridine **1** with CF_3CO_2H followed by the hydrolysis of trifluoroacetate **3** (Scheme 2); thus, an alternative method was developed. The optically pure amino alcohol **2c** was synthesized quantitatively (entry 4) by the ring-opening reaction of optically pure aziridine **1** with dilute H_2SO_4**.** Sulfuric acid-catalyzed ring-opening by EtOH also provided amino ether **2d** in 88% yield (entry 5). The ring-opening reaction with PhSH promoted by H_2SO_4 gave not only amino sulfide **2e** but also amino alcohol **2c** as a byproduct. Trifluoromethanesulfonic acid was found to be a useful acid catalyst for the preparation of amino sulfide **2e**. Although the ring-opening by PhSH without an acid catalyst gave **2e** as a sole product in 40% yield along with 50% recovery of **1** (entry 7), the reaction of PhSH with 1.2 equiv of CF_3SO_3H catalyst gave 85% yield of the ring-opened product (entry 6). It is noted that the acidities of PhSH and PhSeH were great enough to promote ring-opening reactions (entries 7 and 9) and that, in contrast, NaSPh was unable to ring-open aziridine **1** (Scheme 3). On reacting aziridine **1** with CF_3SO_3H as an acid catalyst, the PhSeH nucleophile gave **2f** in 97% yield (entry 8). The reaction of Ph_2PH with aziridine **1** in the presence of a CF_3SO_3H catalyst gave **2g** in 85% yield.

As summarized in Table 1, β-amino halides **2a** and **2b**, β-amino alcohol **2c**, β-amino ether **2d**, β-amino sulfide **2e**, and β-amino selenide **2f**, whose stereochemistries are totally retained, are available by the acid-promoted ring-opening reactions. However, this method is not applicable for the preparation of diamino compounds because unlike aziridine **1**, the basic nitrogen atom of acyclic amine nucleophiles is protonated and unreactive under acidic conditions.

It is of particular importance to note that aziridine **1** was inert toward any nucleophiles under neutral or basic conditions. Some aziridines having an electron-withdrawing group on nitrogen are known to be reactive toward negatively charged nucleophiles such as NaSPh,[13a] NaN_3,[13b] and Ph_3CLi.[13c] However, aziridine **1** did not react with even highly nucleophilic NaN_3 or NaSCN, and all attempts toward nucleophilic ring-openings were unsuccessful; that is, the aziridine **1** was completely recovered in these reactions (Scheme 3).

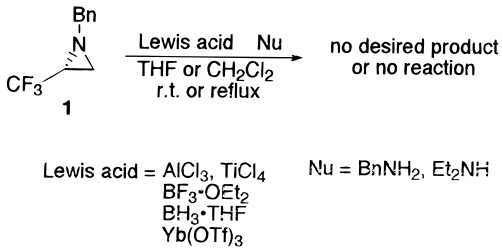
Of course, some epoxides and aziridines, especially those containing electron-withdrawing groups, are known to be reactive toward nucleophiles.[6,11,13] Preliminary MO calculations of the trifluoromethylated aziridines **1** predicted higher reactivity of the fluorinated aziridine to nucleophiles due to a higher positive charge on its methylene carbon, a much more polar β-carbon−nitrogen bond, and a much lower LUMO level,[14] compared with

(12) (a) Wade, T. M. *J. Org. Chem.* **1980**, *45*, 5328. (b) Takeuchi, H.; Koyama, K. *J. Chem. Soc., Perkin Trans. 2* **1981**, 121.

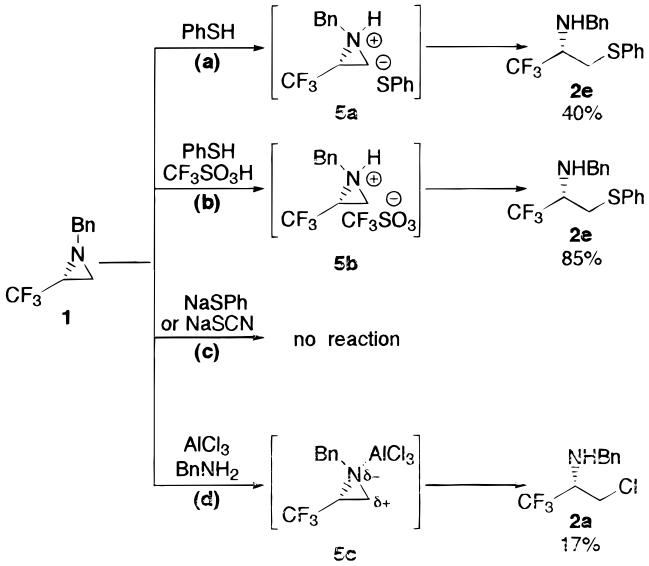
(13) (a) Mall, T.; Stamm, H. *Chem. Ber.* **1988**, *121*, 1353. (b) Guthrie, R. D.; Williams, G. J. *J. Chem. Soc., Perkin Trans. 1* **1976**, 801. (c) Hassner, A.; Kascheres, A. *Tetrahedron Lett.* **1970**, 4623.

(14) The PM3 level molecular geometry optimization calculation done by MacSpartan Plus showed that the positive charge on the methylene carbon of *N*-benzyl-2-trifluoromethylaziridine is 0.15, while that of *N*-benzyl-2-methylaziridine is 0.04 and that of 2,3-epoxy-1,1,1-trifluoropropane is 0.09. Subtraction of the charge between the methylene carbon and nitrogen of *N*-benzyl-2-trifluoromethylaziridine is 0.59, while that of *N*-benzyl-2-methylaziridine is 0.52 and that of 2,3-epoxy-1,1,1-trifluoropropane is 0.32. The LUMO level of *N*-benzyl-2-trifluoromethylaziridine is −0.002 eV, while that of *N*-benzyl-2-methylaziridine is +0.298 eV and that of 2,3-epoxy-1,1,1-trifluoropropane is +0.699 eV.

Scheme 4



Scheme 5



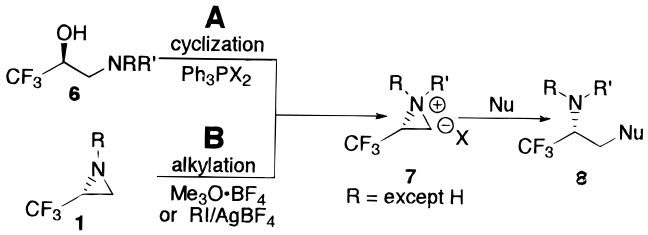
nonfluorinated methylaziridine and 2,3-epoxy-1,1,1-trifluoropropane. Thus, we initially considered 2-trifluoromethylated aziridine (**1**) would be somewhat reactive toward nucleophiles; however, this was contrary to the present experimental results.

In contrast, ring-opening reactions of the trifluoromethylated epoxide proceeded quite smoothly. 2,3-Epoxy-1,1,1-trifluoropropane reacted vigorously with alkoxides to form polymers,[15] with amines to yield trifluoromethylated amino alcohols,[9] and with cyano-stabilized carbanions to make γ-cyanohydrins.[11] On the other hand, the epoxide was inert toward malonate and nitro group stabilized carbanions.

To obtain optically active trifluoromethylated diamines, Lewis acid-catalyzed ring-openings of aziridine **1** by amines were examined. An aluminum chloride[16] catalyzed reaction of aziridine **1** with $BnNH_2$ provided an appreciable amount (17%) of amino halide **2a**, although no aminated product was obtained**.** Moreover, the reactions with BF_3•OEt_2, $TiCl_4$, BH_3•THF, and $Yb(OTf)_3$[17] resulted in the complete recovery of aziridine **1** (Scheme 4). These results might be due to the low coordinating ability of the lone pair on the nitrogen atom of 2-trifluoromethylaziridine **1** toward Lewis acids.

Ring-Opening Reactions via Aziridinium Salts 5a−c. Scheme 5 summarizes the ring-opening reactions of 2-trifluoromethylaziridine **1**. In the first route (a), aziridinium salt **5a** is generated by an acidic reagent and

Scheme 6



reacts with the conjugate anion species to give ring-opening product **2e**. The reaction was remarkably accelerated by an acid catalyst (route b). The trials of nucleophile-promoted reactions have resulted in the only recovery of aziridine **1** (route c). In the final route (d), coordination of Lewis acid is the criterion for the reaction. It is clear that the generation of highly reactive aziridinium salts such as **5a**,**b**, or Lewis acid-coordinated amine **5c**, is essential for the ring-opening reactions. Thus, quaternary aziridinium salts **7** generated by cyclization of tertiary amino alcohol or alkylation of the nitrogen of aziridine **1** (Scheme 6) should be highly reactive.

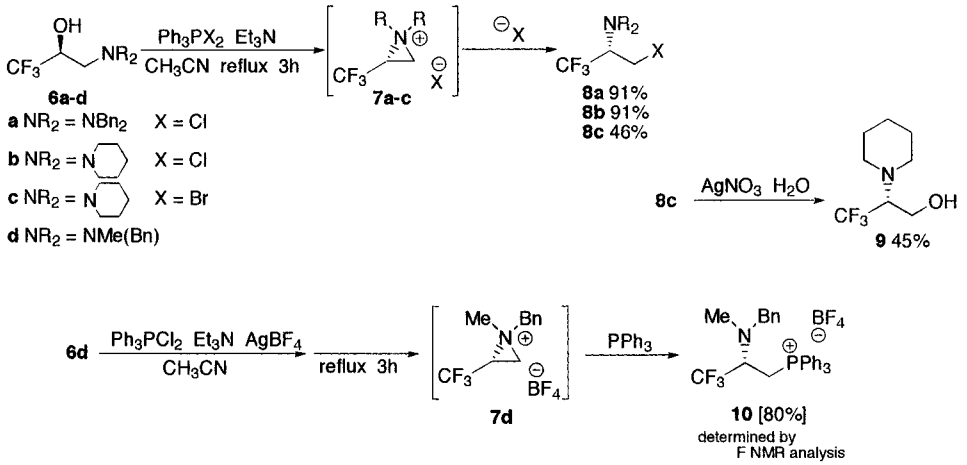
Preparation (Method A) of Quaternary Aziridinium Salts 7a−d. We at first attempted a preparation of aziridinium salts **7a−c** by cyclization of tertiary amino alcohols **6a−c** (prepared from 2,3-epoxy-1,1,1-trifluoropropane and secondary amines) with a method similar to that for preparing aziridine **1** (Scheme 7).[9] The reaction gave amino halides **8a−c** in 46−91% yield. The reaction **6** → **8** proceeded via aziridinium salts **7a−c**, which suffer successive nucleophilic attack of counteranion (Cl^- or Br^-), resulting in the production of haloamines **8a−c**. Hydrolysis of optically pure haloamine **8c** by $AgNO_3$ gave optically pure (>99% ee) amino alcohol **9** in 45% yield. Stereochemical inversion throughout this amino alcohol synthesis implies the intermediacy of the aziridinium salt. The nucleophilic substitution on the α-carbon to the trifluoromethyl group proceeded in a perfect S_N2 manner.[9] Also, it is known that the generation of a nonfluorinated aziridinium salt by cyclization of tertiary amino alcohol proceeds via an S_N2 reaction.[18]

To avoid nucleophilic attack by the counteranion of aziridinium ion, exchange of the counteranion from Cl^- to BF_4^- by an excess amount of $AgBF_4$ in situ was examined. As a result, the exchange of counteranion prevented ring-opening by the chloride anion. However, ring-opening of **7d** by PPh_3, which came from an excess of Ph_3PCl_2, occurred to give **10** in 80% yield (determined by ^{19}F NMR).

Preparation (Method B) and Reactions of Quaternary Aziridinium Salts 7d−f. Judging from the successful transformation of **6d** to **10** (Scheme 7), aziridinium species having a nonreactive counteranion such as BF_4^- would be required for introduction of a nitrogen or carbon nucleophile at the β-position of aziridine **1**. In view of this, methylation of the nitrogen atom of aziridine **1** appears useful for this purpose and was achieved by two methods: methylation with MeI−$AgBF_4$ and methylation with Me_3O^+•BF_4^- (Scheme 8). Generation of an active methylating reagent such as [$Me^+BF_4^-$] by MeI with $AgBF_4$ and its reaction at 0 °C in CH_3NO_2 were

(15) Umezawa, J.; Hagiwara, T.; Narita, T.; Furuhashi, K.; Nohira, H. *Polym. J.* **1994**, *26*, 715.
(16) Coleman, G. H.; Callen, J. E. *J. Am. Chem. Soc.* **1946**, *68*, 2006.
(17) Meguro, M.; Asao, N.; Yamamoto, Y. *Tetrahedron Lett.* **1994**, *35*, 7395.
(18) (a) De Sousa, S. E.; O'Brien, P. *Tetrahedron Lett.* **1997**, *38*, 4885. (b) De Sousa, S. E.; O'Brien, P.; Poumellec, P. *Tetrahedron: Asymmetry* **1997**, *8*, 2613.

Scheme 7



Scheme 8

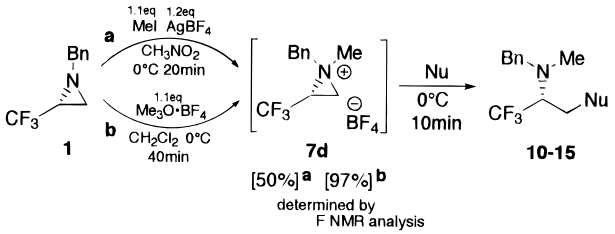
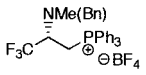
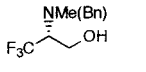
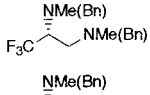
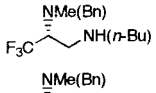
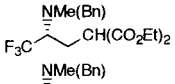
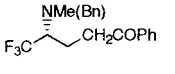


Table 2. Ring-Opening Reactions of 7d[b]

entry	Nu	product		yield[a][%]
1	PPh_3	**10**		96
2	H_2O	**11**		82
3	(Bn)MeNH	**12**		94
4	*n*-$BuNH_2$	**13**		74
5	$NaCH(CO_2Et)_2$	**14**		92
6	$LiCH_2COPh$	**15**		56

[a] Isolated yield. [b] Aziridinium salt **7a** was generated with method a (using $Me_3O{\cdot}BF_4$).

examined. ^{19}F NMR analysis revealed the in situ formation of aziridinium salt **7d** in 50% yield. Alternatively, the reaction of **1** with $Me_3O{\cdot}BF_4$ (Meerwein's reagent) at 0 °C in CH_2Cl_2 proceeded very cleanly and gave **7d** almost quantitatively (determined by ^{19}F NMR). Table 2 summarizes the results of ring-opening reactions of the aziridinium salt **7d** by various nucleophiles. Aziridinium salt **7d** reacted with nucleophiles including nitrogen (entries 3 and 4) and carbon (entries 5 and 6) nucleophiles immediately and gave products **10**−**15**, respectively. It is clear that methylation of **1** is very effective in promoting reaction of **1** with nearly any nucleophile.

A series of ^{19}F NMR spectra (Figure 1) clearly reveal the formation of the aziridinium salt **7d**. Although isolation of **7d** as a crystal has been attempted, suitable crystals have not been isolated.

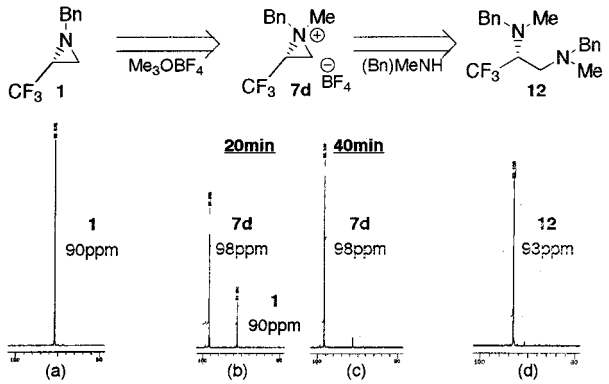
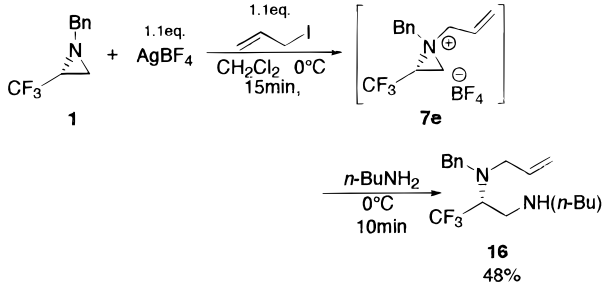


Figure 1. 188 MHz ^{19}F NMR charts: (a) aziridine **1**, (b) after 20 min, (c) after 40 min, (d) ring-opening product, diamine **12**.

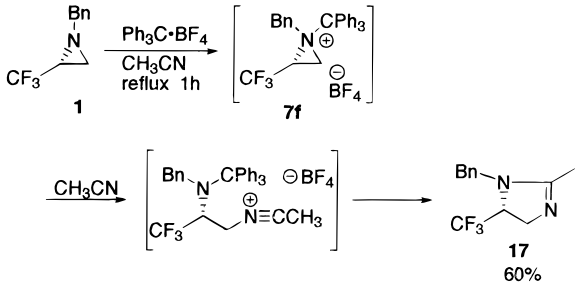
Scheme 9



Although *N*-methylation is useful for ring-opening, it is not a good choice as a protective group because of the associated difficulty in deprotection. Therefore, *N*-allylation and *N*-tritylation of aziridine **1** were examined. To prepare practically usable *N*-protected compounds, allyl iodide was allowed to react with aziridine **1** in the presence of $AgBF_4$ at 0 °C in CH_2Cl_2 (Scheme 9). The generated aziridinium salt was then quenched with *n*-$BuNH_2$, resulting in the production of **16** in 48% yield. The reaction needs appropriate choice of a reaction solvent. The reaction in CH_2Cl_2 gave **7e** in a moderate yield; the same reaction in THF, CH_3NO_2, or CH_3CN solvent resulted in the recovery of aziridine **1**. To avoid recovery of aziridine **1** in this reaction, an excess of allyl cation·BF_4^- species was used for complete conversion of aziridine **1** to the salt **7e**. However, these conditions resulted only in a lower yield of product **16**.

As a much easier group for deprotection, the trityl group was selected. Tritylation of aziridine **1** by

Scheme 10



$Ph_3C{\cdot}BF_4$ at 90 °C in CH_3CN gave imidazoline **17** in 60% yield. The aziridinium salt **7f** underwent a Ritter type reaction with CH_3CN, and subsequent cyclization produced imidazoline **17** (Scheme 10).

Conclusion

In summary, we have achieved the synthesis of optically active trifluoromethylated amines bearing functional groups via ring-opening reactions of optically active *N*-benzyl-2-trifluoromethylaziridine (**1**). The proton-catalyzed ring-opening reactions of the aziridine **1** were efficient, affording halogen- and chalcogen-functionalized trifluoromethylated amines **2**. However, the aziridine itself was found to be inert toward nucleophiles, and so could not be ring-opened by nitrogen or carbon nucleophiles. When the aziridine **1** was *N*-alkylated to the highly reactive aziridinium ion, smooth ring-opening by nitrogen and carbon nucleophiles was achieved. Since the optically active 2-trifluoromethylated aziridines are prepared from commercially available (*S*)-2,3-epoxy-1,1,1-trifluoropropane (75% ee), the present ring-opening reactions provide a general route to the synthesis of optically active 3-substituted-1,1,1-trifluoro-2-propylamines. These trifluoromethylamines are a promising ligand for asymmetric reactions, the utilization of which is now under active investigation in our laboratory.

Experimental Section

General Procedure. The chemical shifts of ^{19}F NMR (188 MHz) are reported in δ (ppm) values relative to C_6F_6. For the quantitative analysis, 1,3-bis(trifluoromethyl)benzene was used as an internal standard for ^{19}F NMR. Optical rotation was measured in a cell with 50 mm length and 1 mL capacity. Enantiomeric excesses were determined by HPLC (equipped with a chiral column, Daicel Chiralcel OJ) or GC (equipped with a chiral column, CP-Cyclodex-β-256M) analysis.

(*R*)-2-(*N*-Benzylamino)-3-chloro-1,1,1-trifluoropropane (2a). 2-Trifluoromethylaziridine **1** (0.102 g, 0.51 mmol, 94% ee) was added to an aqueous solution of hydrochloric acid (35% aqueous, 0.9 mL, 10 mmol) at 0 °C. After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 5:1) to give colorless oily product **2a** (0.114 g, 0.48 mmol, 94% yield, 94% ee) [enantiomeric excess determined by HPLC (hexane:2-propanol = 200:1)]: $[\alpha]^{29}_D = +28.5°$ (*c* 1.55, $CHCl_3$); IR (neat) 3400 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.9 (br, 1H), 3.4 (ddq, 1H, $^3J_{HH} = 6$, $^3J_{HH} = 4$, $^3J_{HF} = 7$), 3.7 (dd, 1H, $^2J_{HH} = 12$, $^3J_{HH} = 6$), 3.8 (dd, 1H, $^2J_{HH} = 12$, $^3J_{HH} = 4$), 3.9 (d, 1H, $^2J_{HH} = 13$), 4.0 (d, 1H, $^2J_{HH} = 13$), 7.3−7.4 (m, 5H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 41.5, 51.7, 59.2 (q, $^2J_{CF} = 28$), 125.3 (q, $^1J_{CF} = 284$), 127.5, 128.3, 128.5, 138.8. ^{19}F NMR (188 MHz, $CDCl_3$) δ 88.7 (d, $^3J_{HF} = 7$); EI MS *m*/*z* (relative intensity) 239 (M^+, 2), 237 (M^+, 5). Anal. Calcd for $C_{10}H_{11}ClF_3N$: C, 50.54; H, 4.67; N, 5.89. Found: C, 50.21; H, 4.76; N, 5.94.

(*R*)-2-(*N*-Benzylamino)-3-bromo-1,1,1-trifluoropropane (2b). Trifluoromethylaziridine **1** (0.099 g, 0.49 mmol, 94% ee) was added to an aqueous solution of hydrobromic acid (48% aqueous, 1.1 mL, 10 mmol) at 0 °C. After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 5:1) to give colorless oily product **2b** (0.128 g, 0.45 mmol, 93% yield, 94% ee) [enantiomeric excess determined by HPLC (hexane:2-propanol = 200:1)]: $[\alpha]^{26}_D = +15.4°$ (*c* 1.48, $CHCl_3$); IR (neat) 3368 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.8 (br, 1H), 3.4 (m, 2H), 3.6 (m, 1H) 3.9 (d, 1H, $^2J_{HH} = 13$), 4.0 (d, 1H, $^2J_{HH} = 13$), 7.3−7.4 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 88.9 (d, $^3J_{HF} = 6$); EI MS *m*/*z* (relative intensity) 283 (M^+, 4), 281 (M^+, 4), 214 (13), 212 (13), 188 (20), 154 (85), 91 (100). Anal. Calcd for $C_{10}H_{11}BrF_3N$: C, 42.58; H, 3.93; N, 4.97. Found: C, 42.62; H, 3.89; N, 4.92.

(*R*)-2-(*N*-Benzylamino)-3,3,3-trifluoro-1-propanol (2c). To a solution of trifluoromethylaziridine **1** (0.136 g, 0.68 mmol, >99% ee) in water (2 mL) was added H_2SO_4 (0.04 mL, 0.72 mmol). After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with AcOEt, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 3:1) to give the colorless crystal **2c** (0.145 g, 0.66 mmol, 98% yield, >99% ee) [enantiomeric excess determined by HPLC (hexane:2-propanol = 200:1)]: $[\alpha]^{25}_D = +60.3°$ (*c* 1.26, $CHCl_3$); IR (Nujol) 3292, 3120 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.7 (br, 2H), 3.2 (ddq, 1H, $^3J_{HH} = 8$, $^3J_{HH} = 4$, $^3J_{HF} = 8$), 3.6 (dd, 1H, $^2J_{HH} = 11$, $^3J_{HH} = 8$), 3.8 (dd, 1H, $^2J_{HH} = 12$, $^3J_{HH} = 4$), 3.9 (d, 1H, $^2J_{HH} = 13$), 4.1 (d, 1H, $^2J_{HH} = 13$), 7.3−7.4 (m, 5H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 51.7, 59.0, 59.7 (q, $^2J_{CF} = 27$), 126.1 (q, $^1J_{CF} = 285$), 127.5, 128.2, 128.6, 138.9; ^{19}F NMR (188 MHz, $CDCl_3$) δ 88.9 (d, $^3J_{HF} = 7$); EI MS *m*/*z* (relative intensity) 219 (M^+, 2). Anal. Calcd for $C_{10}H_{12}F_3NO$: C, 54.79; H, 5.52; N, 6.39. Found: C, 54.87; H, 5.63; N, 6.39.

(*R*)-2-(*N*-Benzylamino)-3-ethoxy-1,1,1-trifluoropropane (2d). H_2SO_4 (0.05 mL, 0.90 mmol) was added to a solution of trifluoromethylaziridine **1** (0.172 g, 0.86 mmol, 83% ee) in EtOH (2 mL). After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 5:1) to give the colorless oily product **2d** (0.185 g, 0.75 mmol, 88% yield, 83% ee) [enantiomeric excess determined by HPLC (hexane:2-propanol = 400:1)]: $[\alpha]^{25}_D = +21.4°$ (*c* 2.27, $CHCl_3$); IR (neat) 3368 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.2 (t, 3H, $^3J_{HH} = 7$), 2.0 (s, 1H), 3.3 (ddq, 1H, $^3J_{HH} = 7$, $^3J_{HH} = 4$, $^3J_{HF} = 7$), 3.5 (q, 2H, $^3J_{HH} = 7$), 3.5 (dd, 1H, $^2J_{HH} = 10$, $^3J_{HH} = 7$), 3.6 (dd, 1H, $^2J_{HH} = 10$, $^3J_{HH} = 4$), 3.9 (d, 1H, $^2J_{HH} = 14$), 4.0 (d, 1H, $^2J_{HH} = 14$), 7.3−7.4 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 88.7 (d, $^3J_{HF} = 8$); EI MS *m*/*z* (relative intensity) 247 (M^+, trace). Anal. Calcd for $C_{12}H_{16}F_3NO$: C, 58.29; H, 6.52; N, 5.66. Found: C, 58.23; H, 6.56; N, 5.87.

(*R*)-2-(*N*-Benzylamino)-1,1,1-trifluoro-3-phenylthiopropane (2e). CF_3SO_3H (0.028 mL, 0.32 mmol) was added to a solution of trifluoromethylaziridine **1** (0.059 g, 0.29 mmol, 92% ee) in PhSH (0.6 mL, 5.84 mmol). After being stirred for 3 h at 90 °C, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:CH_2Cl_2 = 10:1) to give the colorless oily product **2e** (0.077 g, 0.25 mmol, 85% yield): $[\alpha]^{29}_D = +124.9°$ (*c* 2.65, $CHCl_3$); IR (neat) 3368 cm^{-1}; ^1H NMR (200 MHz, $CDCl_3$) δ 1.8 (s, 1H), 2.9 (ddq, 1H, $^2J_{HH} = 13$, $^3J_{HH} = 10$, $^4J_{HF} = 2$), 3.2 (ddq, 1H, $^3J_{HH} = 10$, $^3J_{HH}$

= 3, $^3J_{HF}$ = 7), 3.3 (ddq, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 3, $^4J_{HF}$ = 2), 3.8 (d, 1H, $^2J_{HH}$ = 13), 4.0 (d, 1H, $^2J_{HH}$ = 13), 7.2−7.3 (m, 10H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 34.0, 52.6, 57.7 (q, $^2J_{CF}$ = 28), 126.2 (q, $^1J_{CF}$ = 284), 127.0, 127.3, 128.4, 128.5, 129.2, 130.3, 134.4, 139.1; ^{19}F NMR (188 MHz, $CDCl_3$) δ 87.4 (d, $^3J_{HF}$ = 7); EI MS *m*/*z* (relative intensity) 311 (M^+, 18). Anal. Calcd for $C_{16}H_{16}F_3NS$: C, 61.72; H, 5.18; N, 4.50. Found: C, 61.86; H, 5.20; N, 4.80.

(*R*)-2-(*N*-Benzylamino)-1,1,1-trifluoro-3-phenylselenopropane (2f). CF_3SO_3H (0.032 mL, 0.36 mmol) was added to a solution of trifluoromethylaziridine **1** (0.066 g, 0.33 mmol, 92% ee) and PhSeH (0.042 mL, 0.40 mmol) in CH_2Cl_2 (1 mL). After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:CH_2Cl_2 = 10:1) to give the yellow liquid **2f** (0.116 g, 0.32 mmol, 97% yield, 92% ee) [enantiomeric excess determined by HPLC (hexane:2-propanol = 400:1)]: $[\alpha]^{25}_D$ = +122.7° (*c* 1.94, $CHCl_3$); IR (neat) 3360 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.8 (s, 1H), 3.0 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 11), 3.2 (dd, 1H, $^2J_{HH}$ = 14, $^3J_{HH}$ = 3), 3.3 (ddq, 1H, $^3J_{HH}$ = 11, $^3J_{HH}$ = 3, $^3J_{HF}$ = 7), 3.8 (d, 1H, $^2J_{HH}$ = 13), 4.0 (d, 1H, $^2J_{HH}$ = 13), 7.3−7.4 (m, 8H), 7.5 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 27.2, 52.3, 58.5 (q, $^2J_{CF}$ = 28), 126.2 (q, $^1J_{CF}$ = 288), 127.3, 127.6, 128.3, 128.4, 129.0, 129.3, 133.1, 139.1; ^{19}F NMR (188 MHz, $CDCl_3$) δ 87.5 (d, $^3J_{HF}$ = 6); EI MS *m*/*z* (relative intensity) 359 (M^+, trace). Anal. Calcd for $C_{16}H_{16}F_3NSe$: C, 53.64; H, 4.50; N, 3.91. Found: C, 53.66; H, 4.57; N, 4.11.

(*R*)-2-(*N*-Benzylamino)-1,1,1-trifluoro-3-diphenylphosphinopropane (2g). CF_3SO_3H (0.017 mL, 0.19 mmol) was added to a solution of trifluoromethylaziridine **1** (0.039 g, 0.19 mmol, 83% ee) and PPh_2H (0.049 g, 0.26 mmol) in CH_2Cl_2 (0.5 mL). After being stirred for 10 h at room temperature, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:CH_2Cl_2 = 10:1) to give the colorless oily product **2g** (0.057 g, 0.16 mmol, 85% yield): $[\alpha]^{25}_D$ = +45.5° (*c* 0.31, $CHCl_3$); IR (neat) 3368 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.7 (s, 1H), 2.2 (ddq, 1H, $^2J_{HH}$ = 14, $^3J_{HH}$ = 11, $^4J_{HF}$ = 2), 2.5 (ddq, 1H, $^2J_{HH}$ = 14, $^3J_{HH}$ = 3, $^4J_{HF}$ = 2), 3.1 (ddq, 1H, $^3J_{HH}$ = 11, $^3J_{HH}$ = 3, $^3J_{HF}$ = 7), 3.8 (d, 1H, $^2J_{HH}$ = 13), 4.0 (d, 1H, $^2J_{HH}$ = 13), 7.2−7.4 (m, 15H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 86.5 (d, $^3J_{HF}$ = 6). Anal. Calcd for $C_{22}H_{21}F_3NP$: C, 68.21; H, 5.46; N, 3.62. Found: C, 68.04; H, 5.70; N, 3.69.

(*R*)-2-(*N*,*N*-Dibenzylamino)-3-chloro-1,1,1-trifluoropropane (8a). Et_3N (2.2 mL, 15.9 mmol) was added dropwise to a solution of (*S*)-3-(*N*,*N*-dibenzylamino)-1,1,1-trifluoro-2-propanol (**6a**) (0.490 g, 1.59 mmol) and PPh_3Cl_2 (1.324 g, 3.97 mmol) in 5 mL of CH_3CN under nitrogen atmosphere at 0 °C. The reaction mixture was stirred for 3 h at reflux condition. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:AcOEt = 3:1) to give the white solid **8a** (0.474 g, 1.45 mmol, 91% yield): $[\alpha]^{24}_D$ = +6.8° (*c* 1.71, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 3.5 (m, 1H), 3.8 (m, 2H), 3.8 (d, 2H, $^2J_{HH}$ = 14), 4.0 (d, 2H, $^2J_{HH}$ = 14), 7.3−7.5 (m, 10H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.8 (d, $^3J_{HF}$ = 7); EI MS *m*/*z* (relative intensity) 329 (M^+, 2), 327 (M^+, 7). Anal. Calcd for $C_{17}H_{17}ClF_3N$: C, 62.29; H, 5.23; N, 4.27. Found: C, 62.47; H, 5.38; N, 4.42.

(*R*)-3-Chloro-2-piperidino-1,1,1-trifluoropropane (8b). Et_3N (1.8 mL, 12.9 mmol) was added dropwise to a solution of (*S*)-3-piperidino-1,1,1-trifluoro-2-propanol (**6b**) (0.253 g, 1.28 mmol) and PPh_3Cl_2 (1.066 g, 3.20 mmol) in 3 mL of CH_3CN under nitrogen atmosphere at 0 °C. The reaction mixture was stirred for 3 h at reflux condition. After filtration, the filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography (hexane:ether = 3:1) to give the colorless oily product **8b** (0.251 g, 1.17 mmol, 91% yield): $[\alpha]^{25}_D$ = +54.79° (*c* 1.03, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.5 (m, 6H), 2.8 (m, 4H), 3.3 (tq, 1H, $^3J_{HH}$ = 7, $^3J_{HF}$ = 8), 3.7 (d, 2H, $^3J_{HH}$ = 7); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 24.4, 26.7, 38.9, 50.7, 68.0 (q, $^2J_{CF}$ = 26), 125.8 (q, $^1J_{CF}$ = 291); ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.0 (d, $^3J_{HF}$ = 8); EI MS *m*/*z* (relative intensity) 217 (M^+, 6), 215 (M^+, 18). Anal. Calcd for $C_8H_{13}ClF_3N$: C, 44.56; H, 6.08; N, 6.50. Found: C, 44.66; H, 5.92; N, 6.28.

(*R*)-3-Bromo-2-piperidino-1,1,1-trifluoropropane (8c). Et_3N (4 mL, 28.0 mmol) was added dropwise to a solution of (*S*)-3-piperidino-1,1,1-trifluoro-2-propanol (**6c**) (1.1 g, 5.4 mmol, >99% ee) and PPh_3Br_2 (3.6 g, 8.5 mmol) in 30 mL of CH_3CN under nitrogen atmosphere at 0 °C. The reaction mixture was stirred for 3 h at reflux condition. After filtration, the filtrate was concentrated under reduced pressure. The mixture of **8c** and (*S*)-2-bromo-3-piperidino-1,1,1-trifluoropropane (87:13 by ^{19}F NMR analysis, 0.16 g, 53% yield) was obtained as a yellow liquid by column chromatography on silica gel and distillation (9 mmHg, 80 °C). The compound was found to be optically pure (>99% ee) [enantiomeric excess determined by GC]: $[\alpha]^{24}_D$ = +47.3° (*c* 2.35, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.5 (m, 6H), 2.7 (m, 2H), 2.8 (m, 2H), 3.3 (tq, 1H, $^3J_{HH}$ = 8, $^3J_{HF}$ = 8), 3.5 (d, 2H, $^3J_{HH}$ = 8); ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.1 (d, $^3J_{HF}$ = 8); EI MS *m*/*z* (relative intensity) 261 (M^+, 8), 259 (M^+, 8). Anal. Calcd for $C_8H_{13}BrF_3N$: C, 36.94; H, 5.04; N, 5.39. Found: C, 36.59; H, 4.91; N, 5.29.

(*R*)-2-Piperidino-3,3,3-trifluoro-1-propanol (9). The mixture of **8c** and (*S*)-2-bromo-3-piperidino-1,1,1-trifluoropropane (87:13 by ^{19}F NMR analysis, 0.48 g, 1.8 mmol) was added to a solution of $AgNO_3$ (0.50 g, 2.9 mmol) and potassium carbonate (0.79 g, 5.7 mmol) in THF (1 mL) and water (6 mL). The reaction mixture was stirred for 4 h at reflux condition and 12 h at room temperature. After extraction by ether and removal of solvent under reduced pressure, product **9** (0.16 g, 0.83 mmol, 45% yield) was obtained by column chromatography on silica gel and distillation (15 mmHg, 100 °C). The compound was found to be optically pure (>99% ee) [enantiomeric excess determined by GC]: $[\alpha]^{24}_D$ = +35.8° (*c* 4.84, $CHCl_3$); IR (KBr) 3460 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.5 (m, 6H), 2.6 (m, 2H), 3.0 (m, 2H), 3.2 (tq, 1H, $^3J_{HH}$ = 8, $^3J_{HF}$ = 8), 3.6 (d, 2H, $^3J_{HH}$ = 8); ^{19}F NMR (188 MHz, $CDCl_3$) δ 95.1 (d, $^3J_{HF}$ = 8); EI MS *m*/*z* (relative intensity) 197 (M^+, 8). Anal. Calcd for $C_8H_{14}F_3NO$: C, 48.73; H, 7.16; N, 7.10. Found: C, 49.04; H, 6.98; N, 6.99.

(*R*)-[2-(*N*-Benzyl-*N*-methylamino)-3,3,3-trifluoropropyl]triphenylphosphonium Tetrafluoroborate (10). Trifluoromethylaziridine **1** (0.099 g, 0.49 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.085 g, 0.57 mmol) in 1 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 20 min at 0 °C, a solution of PPh_3 (0.156 g, 0.59 mmol) in CH_2Cl_2 (0.5 mL) was added. After 10 min, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with AcOEt, and the combined organic phase was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was washed by hexane to give the white solid product **10** (0.266 g, 0.47 mmol, 96% yield): $[\alpha]^{25}_D$ = +23.2° (*c* 0.40, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.4 (s, 3H), 3.2 (tq, 1H, *J* = 14, $^4J_{HF}$ = 2), 3.5 (m, 1H), 3.6 (d, 1H, $^2J_{HH}$ = 14), 3.8 (d, 1H, $^2J_{HH}$ = 14), 4.2 (ddd, 1H, *J* = 16, *J* = 12, *J* = 10), 6.6 (m, 2H), 7.1−7.3 (m, 4H), 7.6−7.8 (m, 14H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 94.9 (d, 3F, $^3J_{HF}$ = 5), 9.6 (d, 4F, *J* = 10). Anal. Calcd for $C_{29}H_{28}BF_7NP$: C, 61.61; H, 4.99; N, 2.48. Found: C, 61.29; H, 5.01; N, 2.69.

(*R*)-2-(*N*-Benzyl-*N*-methylamino)-3,3,3-trifluoro-1-propanol (11). Trifluoromethylaziridine **1** (0.112 g, 0.56 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.092 g, 0.62 mmol) in 1 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 40 min at 0 °C, water (0.2 mL) was added. After 10 min, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 10:1) to give colorless oily product **11** (0.107 g, 0.46 mmol, 82% yield): $[\alpha]^{25}_D$ = +34.0° (*c* 0.74, $CHCl_3$); IR (neat) 3464 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.4 (s, 3H), 2.5 (br, 1H), 3.4 (tq, 1H, $^3J_{HH}$ = 8, $^3J_{HF}$ = 7), 3.7 (d, 2H, $^3J_{HH}$

= 8), 3.8 (d, 1H, $^2J_{HH}$ = 13), 4.0 (d, 1H, $^2J_{HH}$ = 13), 7.3−7.4 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 95.0 (d, $^3J_{HF}$ = 8); EI MS *m/z* (relative intensity) 233 (M^+, 3). Anal. Calcd for $C_{11}H_{14}F_3NO$: C, 56.65; H, 6.05; N, 6.01. Found: C, 56.41; H, 6.07; N, 5.98.

(*R*)-2,3-Bis(*N*-Benzyl-*N*-methylamino)-1,1,1-trifluoropropane (12). Trifluoromethylaziridine **1** (0.164 g, 0.82 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.131 g, 0.89 mmol) in 1.5 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 40 min at 0 °C, (Bn)MeNH (0.2 mL) was added. After 10 min, the mixture was poured into water. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 5:1) to give the colorless oily product **12** (0.258 g, 0.77 mmol, 94% yield): $[\alpha]^{25}_D$ = +4.8° (*c* 1.25, $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.3 (s, 3H), 2.4 (s, 3H), 2.6 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 4), 2.9 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 9), 3.4 (ddq, 1H, $^3J_{HH}$ = 4, $^3J_{HH}$ = 9, $^3J_{HF}$ = 8), 3.6 (d, 1H, $^2J_{HH}$ = 14), 3.6 (d, 1H, $^2J_{HH}$ = 14), 3.9 (d, 1H, $^2J_{HH}$ = 14), 4.0 (d, 1H, $^2J_{HH}$ = 14), 7.3−7.4 (m, 10H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 37.3, 42.3, 53.9, 59.4, 61.9 (q, $^2J_{CF}$ = 24), 62.7, 127.1, 127.2 (q, $^1J_{CF}$ = 291), 128.2, 128.3, 128.6, 129.0, 138.8, 139.4; ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.1 (d, $^3J_{HF}$ = 9); EI MS *m/z* (relative intensity) 336 (M^+, trace). Anal. Calcd for $C_{19}H_{23}F_3N_2$: C, 67.84; H, 6.89; N, 8.33. Found: C, 67.87; H, 7.14; N, 8.65.

(*R*)-2-(*N*-Benzyl-*N*-methylamino)-3-(*N*-butylamino)-1,1,1-trifluoropropane (13). Trifluoromethylaziridine **1** (0.036 g, 0.18 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.030 g, 0.20 mmol) in 0.3 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 40 min at 0 °C, *n*-$BuNH_2$ (0.3 mL) was added in one portion. After 10 min, the mixture was poured into water. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 5:1) to give the colorless oily product **13** (0.038 g, 0.13 mmol, 74% yield): $[\alpha]^{25}_D$ = +16.2° (*c* 1.45, $CHCl_3$); IR (neat) 3332 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.9 (m, 3H), 1.4 (m, 4H), 1.6 (s, 1H), 2.4 (br, 3H), 2.6 (m, 2H), 2.8 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 4), 2.9 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 10), 3.4 (ddq, 1H, $^3J_{HH}$ = 4, $^3J_{HH}$ = 10, $^3J_{HF}$ = 8), 3.8 (d, 1H, $^2J_{HH}$ = 14), 4.0 (d, 1H, $^2J_{HH}$ = 14), 7.3 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 94.4 (d, $^3J_{HF}$ = 8); EI MS *m/z* (relative intensity) 288 (M^+, trace). Anal. Calcd for $C_{15}H_{23}F_3N_2$: C, 62.48; H, 8.04; N, 9.71. Found: C, 62.45; H, 8.20; N, 9.67.

(*R*)-Diethyl [2-(*N*-Benzyl-*N*-methylamino)-3,3,3-trifluoropropyl]malonate (14). Trifluoromethylaziridine **1** (0.041 g, 0.20 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.034 g, 0.23 mmol) in 0.5 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 40 min at 0 °C, $NaCH(CO_2Et)_2$ (0.46 mL, 0.3 mmol, 0.65 M solution in THF) was added. After 10 min, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 3:1) to give the colorless oily product **14** (0.069 g, 0.18 mmol, 92% yield): $[\alpha]^{24}_D$ = +28.5° (*c* 1.10, $CHCl_3$); IR (neat) 1736 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 1.3 (m, 6H), 2.2 (m, 2H), 2.3 (s, 3H), 3.3 (m, 1H), 3.8 (m, 3H), 4.2 (m, 4H), 7.3 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.7 (d, $^3J_{HF}$ = 7); EI MS *m/z* (relative intensity) 375 (M^+, trace). Anal. Calcd for $C_{18}H_{24}F_3NO_4$: C, 57.59; H, 6.44; N, 3.73. Found: C, 57.35; H, 6.30; N, 3.56.

(*R*)-4-(*N*-Benzyl-*N*-methylamino)-1-phenyl-3,3,3-trifluoropentan-1-one (15). Trifluoromethylaziridine **1** (0.113 g, 0.56 mmol, 83% ee) was added to a solution of Me_3OBF_4 (0.089 g, 0.60 mmol) in 0.75 mL of CH_2Cl_2 under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 40 min at 0 °C, $LiCH_2COPh$ (1.2 mL, 0.85 mmol, 0.71 M solution in THF) was added at −40 °C. After 10 min, the mixture was poured into saturated aqueous $NaHCO_3$. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 10:1) to give the yellow liquid **15** (0.105 g, 0.31 mmol, 56% yield): $[\alpha]^{23}_D$ = +34.5° (*c* 0.89, $CHCl_3$); IR (neat) 1690 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.0 (q, 2H, $^3J_{HH}$ = 7), 2.3 (s, 3H), 3.1 (t, 2H, $^3J_{HH}$ = 7), 3.2 (tq, 1H, $^3J_{HH}$ = 7, $^3J_{HF}$ = 8), 3.7 (d, 1H, $^2J_{HH}$ = 14), 3.8 (d, 1H, $^2J_{HH}$ = 14), 7.1 (s, 5H), 7.4−7.6 (m, 3H), 7.9 (m, 2H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 93.5 (br); EI MS *m/z* (relative intensity) 335 (M^+, trace). Anal. Calcd for $C_{19}H_{20}F_3NO$: C, 68.05; H, 6.01; N, 4.18. Found: C, 67.69; H, 6.09; N, 4.15.

(*R*)-2-(*N*-Allyl-*N*-benzylamino)-3-(*N*-butylamino)-1,1,1-trifluoropropane (16). A solution of allyl iodide (0.108 g, 0.64 mmol) in 0.5 mL of CH_2Cl_2 was added to a mixture of trifluoromethylaziridine **1** (0.103 g, 0.51 mmol, 83% ee) and $AgBF_4$ (0.109 g, 0.54 mmol) and CH_2Cl_2 (0.5 mL) under nitrogen atmosphere at 0 °C. After the reaction mixture was stirred for 15 min at 0 °C, *n*-$BuNH_2$ (0.5 mL) was added in one portion. After 10 min, the mixture was poured into water. The product was extracted with ether, and the combined organic phase was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography (hexane:ether = 10:1) to give the colorless oily product **16** (0.077 g, 0.24 mmol, 48% yield): $[\alpha]^{24}_D$ = +16.1° (*c* 2.08, $CHCl_3$); IR (neat) 3036 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 0.9 (t, 3H, $^3J_{HH}$ = 7), 1.4 (m, 5H), 2.4 (m, 2H), 2.7 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 4), 2.9 (dd, 1H, $^2J_{HH}$ = 13, $^3J_{HH}$ = 10), 3.2 (m, 1H), 3.5 (m, 2H), 3.7 (d, 1H, $^2J_{HH}$ = 14), 4.0 (d, 1H, $^2J_{HH}$ = 14), 5.2 (m, 2H), 5.8 (m, 1H), 7.3 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 94.3 (d, $^3J_{HF}$ = 9); EI MS *m/z* (relative intensity) 315 (M^+, 1). Anal. Calcd for $C_{17}H_{25}F_3N_2$: C, 64.95; H, 8.01; N, 8.91. Found: C, 64.80; H, 8.18; N, 8.88.

(*R*)-1-*N*-Benzyl-2-methyl-5-trifluoromethyl-2-imidazoline (17). Trifluoromethylaziridine **1** (0.139 g, 0.69 mmol, 83% ee) was added to a solution of Ph_3CBF_4 (0.234 g, 0.71 mmol) in 2.5 mL of CH_3CN under nitrogen atmosphere. After being stirred for 1 h at reflux condition, the reaction mixture was quenched with water. The solvent was removed under reduced pressure. The residue was poured into saturated aqueous NH_4Cl and extracted with ether. Next the product was extracted with AcOEt under basic condition. The AcOEt extract was dried over $MgSO_4$. The solvent was removed under reduced pressure, and the residue was purified by distillation to give white solid **17** (0.108 g, 0.41 mmol, 60% yield): $[\alpha]^{25}_D$ = +130.9° (*c* 0.45, $CHCl_3$); IR (Nujol) 1640 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 2.0 (s, 3H), 3.8 (m, 3H), 4.3 (d, 1H, $^2J_{HH}$ = 17), 4.6 (d, 1H, $^2J_{HH}$ = 17), 7.1−7.4 (m, 5H); ^{19}F NMR (188 MHz, $CDCl_3$) δ 86.1 (br); EI MS *m/z* (relative intensity) 242 (63). Anal. Calcd for $C_{12}H_{13}F_3N_2$: C, 59.50; H, 5.41; N, 11.56. Found: C, 59.24; H, 5.44; N, 11.42.

Acknowledgment. We are grateful to the Ministry of Education, Science, Sports and Culture for financial support (Grant No. 09305058 and Priority Areas No. 706) and the SC-NMR Laboratory of Okayama University for ^{19}F NMR analysis.

JO990207E