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Concise Syntheses of Nonracemic γ-Fluoroalkylated Allylic Alcohols and Amines Via an Enantiospecific Palladium-Catalyzed Allylic Substitution Reaction

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α-Fluoroalkylated allyl mesylates reacted with various carboxylates and amines in the presence of tetrakis(triphenylphosphine)palladium(0) catalyst to give the corresponding γ-fluoroalkylated (*E*)-allylic alcohol derivatives and amines, respectively, in excellent yields. In almost all cases, no other regio- and stereoisomers were produced. Application of this palladium-catalyzed allylic substitution reaction to various nonracemic mesylates afforded chiral γ-fluoroalkylated allylic alcohol derivatives and amines without any loss of enantiomeric excess through the reaction.

Introduction

The synthesis of regio- and stereoselective poly- or perfluoroalkylated molecules has become important in the field of phamaceutical research, owing to their unique physiological and biological properties imparted by a fluoroalkyl group.[1] In many cases, the substitution of an alkyl group by a poly- or perfluoroalkyl group results in increased metabolic stability and lipophilicity, which may improve pharmacokinetic properties of drug candidates.[2] Although much effort has been devoted to developing convenient and practical methods for the preparation of such poly- or perfluoroalkylated compounds,[3] the stereoselective synthesis of optically active compounds has received much less attention.[4]

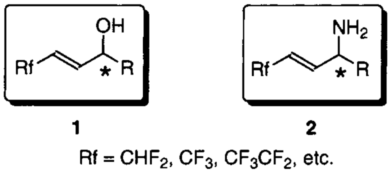

Figure 1. Optically active γ-fluoroalkylated allylic alcohols (**1**) and amines (**2**).

γ-Fluoroalkylated allylic alcohols **1**[5] and amines **2**, shown in Figure 1, are recognized as the most important synthetic intermediates for the preparation of structurally complex poly- or perfluoroalkylated molecules in organofluorine chemistry, and their syntheses in enantiomerically and geometrically pure forms should present significant challenges for the synthetic chemist.

Among several reported methods, the enzymatic kinetic resolution of the racemic propargyl alcohols **3**, followed by stereoselective reduction of the triple bond, is well-known as one of the most reliable synthetic methods to obtain both enantiomers of **1** with high optical purities (Scheme 1).[5] However, this method suffers from at least two serious disadvantages. First, the yields of the desired chiral alcohols are not more than 50%. Second, the enzyme has a high substrate-specificity, and a little structural change in the substrate sometimes prevents the reaction from proceeding and often results in a large decrease of enantioselectivity. On the other hand, an enantiospecific synthesis would have great advantages, such as the fact that the transformation can be carried out to completion (i.e., 100% maximum yield) and that a little structural change in the substrate does not necessarily influence the reaction.

In this contribution, we report the convenient synthesis of nonracemic γ-fluoroalkylated allylic alcohols **1** and amines **2** via an enantiospecific palladium-catalyzed

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(1) (a) McAtee, J. J.; Schinazi, R. F.; Liotta, D. C. *J. Org. Chem.* **1998**, *63*, 2161−2167. (b) *Fluorine-Containing Amino Acids: Synthesis and Properties*; Kukhar, V. P., Soloshonok, V. A., Eds.; Wiley & Sons: New York, 1995. (c) Resnati, G. *Tetrahedron* **1993**, *49*, 9385−9445. (d) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley & Sons: New York, 1991. (e) Bégué, J.-P.; Bonnet-Delpon, D. *Tetrahedron* **1991**, *47*, 3207−3258. (f) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123−3197.

(2) (a) Arnone, A.; Bernardi, R.; Blasco, F.; Cardillo, R.; Resnati, G.; Gerus, I. I.; Kukhar, V. P. *Tetrahedron* **1998**, *54*, 2809−2818. (b) Tan, L.; Chen, C.-Y.; Larsen, R. D.; Verhoeven, T. R.; Reider, P. J. *Tetrahedron Lett.* **1998**, *39*, 3961−3964.

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(4) Several general synthetic methods for the preparation of optically active poly- or perfluoroalkylated compounds have been reported. (a) Kumar, D. J. S.; Madhavan, S.; Ramachandran, P. V.; Brown, H. C. *Tetrahedron: Asymmetry* **2000**, *11*, 4629−4632. (b) Resnati, G.; Brabo, P. *Tetrahedron: Asymmetry* **1990**, *1*, 661−692. (c) Iseki, K. *Tetrahedron* **1998**, *54*, 13887−13914. (d) Matsutani, H.; Poras, H.; Kusumoto, T.; Hiyama, T. *Chem. Commun.* **1998**, 1259−1260.

(5) (a) Yamazaki, T.; Umetani, H.; Kitazume, T. *Tetrahedron Lett.* **1997**, *38*, 6705−6708. (b) Konno, T.; Kitazume, T. *Tetrahedron: Asymmetry* **1997**, *8*, 223−230. (c) Konno, T.; Umetani, H.; Kitazume, T. *J. Org. Chem.* **1997**, *62*, 137−150. (d) Konno, T.; Kitazume, T. *Chem. Commun.* **1996**, 2227−2228. (e) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Org. Chem.* **1995**, *60*, 6046−6056. (f) Konno, T.; Nakano, H.; Kitazume, T. *J. Fluorine Chem.* **1997**, *86*, 81−87. (g) Hanzawa, Y.; Kawagoe, K.; Yamada, A.; Kobayashi, Y. *Tetrahedron Lett.* **1985**, *26*, 219−222. (h) Kitazume, T.; Ishikawa, N. *J. Fluorine Chem.* **1985**, *29*, 431−444. (i) Hanzawa, Y.; Kawagoe, K.; Tanahashi, N.; Kobayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 4749−4752.

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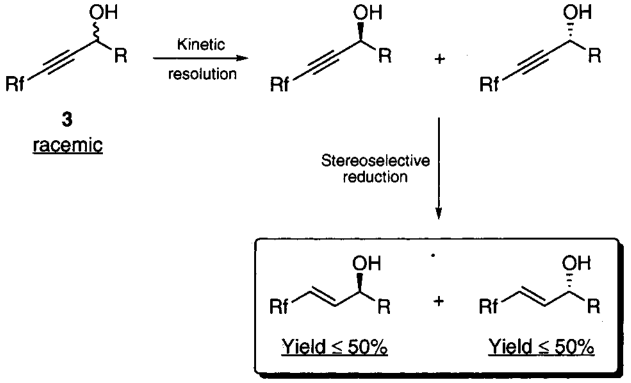
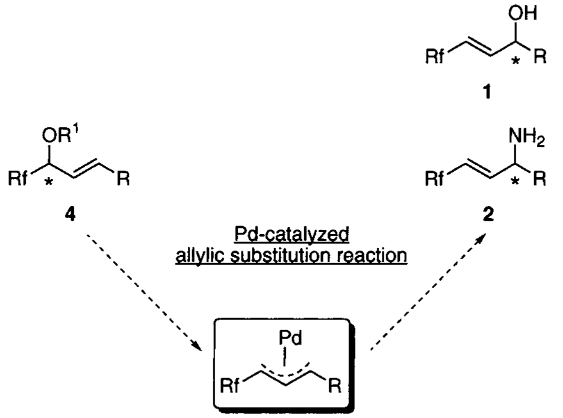
Scheme 1. Enzymatic Kinetic Resolution



Scheme 2. General Outline for the Synthesis of Chiral γ-Fluoroalkylated Allylic Alcohols (1) and Amines (2)



allylic substitution reaction of nonracemic α-fluoroalkylated allylic alcohol derivatives **4**, as described in Scheme 2.

Results and Discussion

Reaction of α-Fluoroalkylated Allyl Mesylates with Various Carboxylates. At first, we attempted the thermal allylic rearrangement using (α-trifluoromethyl)allyl benzoate **4c**, which was readily accessible from ethyl trifluoroacetate in three steps[6] (Scheme 3). Thus, **4c** was heated in refluxing THF but was recovered unchanged quantitatively (Table 1, entry 1). Even when the reaction was carried out in the presence of a catalytic amount of tetrakis(triphenylphosphine)palladium(0) (Pd(PPh$_3$)$_4$) at the reflux temperature of THF, no desired product was detected (entry 2). Next, we attempted the Pd-catalyzed reaction by using α-(trifluoromethyl)allyl mesylate **4d** as the starting material, which was prepared readily from ethyl trifluoroacetate in a manner similar to that for the preparation of **4c**. Thus, using 5 mol % Pd(PPh$_3$)$_4$ in THF at 0 °C, the starting material **4d** was completely consumed after 3 h, and the desired compound **5c** was formed as the sole product in 99% NMR yield without any formation of the α-product[7] (entry 3). We also examined the influence of the palladium catalyst upon this reaction, as shown in entries 4−9. The use of Pd$_2$(dba)$_3$ as the catalyst resulted in the complete suppression of the reaction (entry 4), while the use of triphenyl phosphite as the ligand afforded the desired allylic alcohol derivative **5c** in 86% yield together with a 12% yield of the diene **6c** (entry 5). The latter may be formed via the β-elimination of Pd−H from an intermediary π-allylpalladium complex.[8] When the reaction was carried out with the tributylphosphine or bis(diphenylphosphino)ethane (dppe) ligand, a large amount of the starting material remained unchanged (84−99% recovered, entries 6 and 8). On the other hand, the use of Bu$_3$P and dppe as ligands at room temperature for 14 h led to **5c** in 42% yield and to a mixture of **6c** (35% yield) and **5c** (4% yield), respectively (entries 7 and 9). As a result, triphenylphosphine was found to be the ligand of choice in the present reaction.

Scheme 3. Palladium-Catalyzed Allylic Substitution Reaction

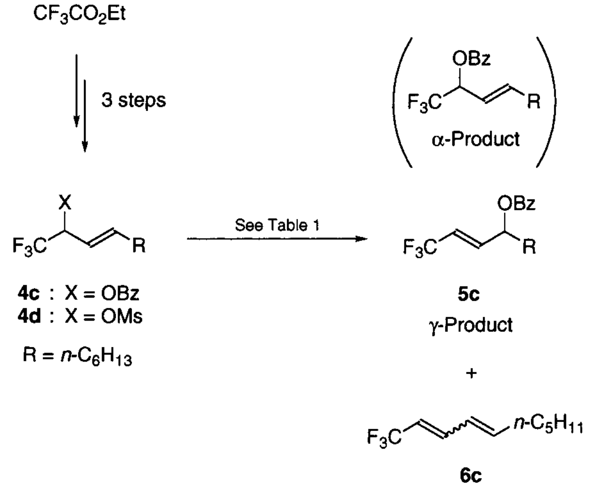


Table 1. Investigation of the Reaction Conditions for the Pd(0)-Catalyzed Allylic Substitution Reaction

entry[a]	catalyst	temp/°C	time/h	yield[b] (%) 5c	4c or 4d	6c (E:Z)
1[c]	none	reflux	3	0	99	0
2[c]	Pd(PPh$_3$)$_4$	reflux	3	0	99	0
3	Pd(PPh$_3$)$_4$	0	3	99	0	0
4	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$	0	3	0	99	0
5	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$ + 4(PhO)$_3$P	0	3	86	2	12 (100:0)
6	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$ + 4Bu$_3$P	0	3	16	84	0
7	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$ + 4Bu$_3$P	room	14	42	54	0
8	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$ + 2dppe	0	3	0	99	0
9	$^1/_2$Pd$_2$(dba)$_3$·CHCl$_3$ + 2dppe	room	14	4	51	35 (79:21)

[a] (α-Trifluoromethyl)allyl mesylate **4d** was employed as a starting material, unless otherwise noted. [b] Determined by ^{19}F NMR. [c] As the starting material, (α-trifluoromethyl)allyl benzoate **4c** was employed. Benzoic acid and triethylamine were not used.

Next, our attention was directed to the allylic substitution reactions of various types of mesylates **4**. The results

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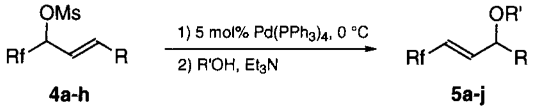
(6) (a) Ramachandran, P. V.; Teodorovic' A. V.; Gong, B.; Brown, H. C. *Tetrahderon: Asymmetry* **1994**, *5*, 1075−1086. (b) Ramachandran, P. V.; Gong, B.; Teodorovic, A. V.; Brown, H. C. *Tetrahderon: Asymmetry* **1994**, *5*, 1061−1074.

(7) The reaction of the trifluoromethylated π-allylpalladium complex with the carbanion derived from diethyl malonate has been reported. (a) Hanzawa, Y.; Ishizawa, S.; Ito, H.; Kobayashi, Y.; Taguchi, T. *J. Chem. Soc., Chem. Commun.* **1990**, 394−395. (b) Hanzawa, Y.; Ishizawa, S.; Kobayashi, Y. *Chem. Pharm. Bull.* **1988**, *36*, 4209−4212.

(8) Tsuji, J.; Yamakawa, T.; Kaito, M.; Manda, T. *Tetrahedron Lett.* **1978**, 2075−2078.

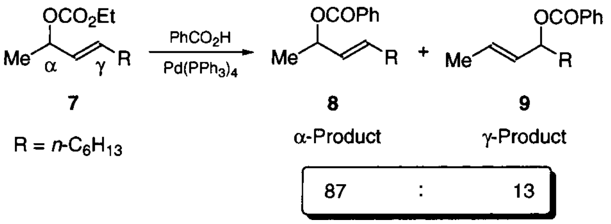
Table 2. Pd(0)-Catalyzed Reaction of Fluorinated Allyl Mesylate with Various Carboxylates



entry[a]	substrate	Rf	R	R′OH	product	yield[b,c] (%)
1	**4a**	CH_2F	n-C_6H_{13}	BzOH	**5a**	56[d]
2	**4b**	CHF_2	n-C_6H_{13}	BzOH	**5b**	89
3	**4d**	CF_3	n-C_6H_{13}	BzOH	**5c**	91
4	**4d**	CF_3	n-C_6H_{13}	CH_3CO_2H	**5d**	80
5	**4d**	CF_3	n-C_6H_{13}	$CH_2CH_2CO_2H$	**5e**	74
6	**4d**	CF_3	n-C_6H_{13}	$ClCH_2CO_2H$	**5f**	99
7	**4d**	CF_3	n-C_6H_{13}	$MeOCH_2CO_2H$	**5g**	96
8	**4e**	CF_3	$BnOCH_2$	BzOH	**5h**	93[e]
9	**4f**	CF_3	t-Bu	BzOH		0
10	**4g**	CF_3CF_2	n-C_6H_{13}	BzOH	**5i**	87
11	**4h**	$CF_3(CF_2)_2$	n-C_6H_{13}	BzOH	**5j**	99

[a] All reactions were performed at 0 °C by using 2 equiv each of Et_3N, carboxylic acid, and 5 mol % $Pd(PPh_3)_4$. [b] Isolated yields. [c] The (*E*)-isomer was produced exclusively in all cases, unless otherwise noted. [d] Two-step yield from a monofluoromethylated allylic alcohol. [e] The (*E*)- and (*Z*)-stereoisomers were obtained in a ratio of 94:6.

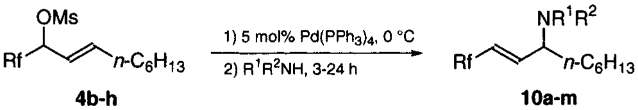
Scheme 4. Palladium-Catalyzed Substitution Reaction in the Non-fluorinated System



are summarized in Table 2. Monofluorinated mesylate **4a** (Rf = CH_2F) was too unstable to be purified by silica gel column chromatography and was used in the following allylic substitution reaction without any purification. Although the crude mesylate **4a** was employed as such for the Pd-catalyzed process, the desired allylic alcohol derivative **5a** was obtained in 56% yield in a two-step process as a single isomer (entry 1). As shown in entries 2, 3, 10, and 11, the Rf groups of **4** did not exert any influence on the regio- and stereochemical courses of the reaction, all of which led efficiently to γ-products with the (*E*) configuration. A variety of carboxylic acids such as benzoic acid, acetic acid, propionic acid, and chloro- and methoxyacetic acid participated nicely in the reaction, giving rise to the corresponding γ-products **5** exclusively (entries 3–7). It was found that differences in the R component of the side chain greatly affected the reaction. Thus, the stereoselectivity at the newly formed olefinic bond was slightly decreased when the benzyloxymethyl group was R (entry 8).[9] Furthermore, the *tert*-butyl group completely prevented the reaction from proceeding (entry 9).

To evaluate the effect of an Rf group on the reaction, we examined the reaction of a nonfluorinated counterpart (Scheme 4). Ethyl carbonate **7** was employed as the starting ester because the corresponding allyl mesylate was so thermally labile that it could not be obtained. **7** was treated with 5 mol % $Pd(PPh_3)_4$ and 2 equiv of benzoic acid at room temperature for 24 h. HPLC analysis of the reaction mixture indicated that a large amount of **7** remained unchanged and that the α- and γ-products, **8** and **9**, were obtained in only 16% combined yield in a ratio of 87:13, respectively. It should be emphasized that the α-product was obtained preferentially instead of the γ-product. This result is totally different from the results of the reaction of the fluorinated substrates **4**.[10]

Table 3. Pd(0)-Catalyzed Reaction of Fluorinated Allyl Mesylate with Various Amines



entry[a]	substrate	Rf	R^1R^2NH	product	yield[b,c] (%)
1	**4b**	CHF_2	$BnNH_2$	**10a**	88
2[d]	**4d**	CF_3	$BnNH_2$		0
3	**4d**	CF_3	$BnNH_2$	**10b**	96
4	**4d**	CF_3	allylamine	**10c**	81
5	**4d**	CF_3	$PhNH_2$	**10d**	99
6	**4d**	CF_3	p-$NO_2C_6H_4NH_2$	**10e**	99
7[e]	**4d**	CF_3	$EtOOCCH_2NH_2{\cdot}HCl$	**10f**	90
8	**4d**	CF_3	$Me_2NH{\cdot}HCl$	**10g**	92
9	**4d**	CF_3	Bn_2NH	**10h**	70
10	**4d**	CF_3	$EtOOCCH_2NHBn$	**10i**	88
11	**4d**	CF_3	$EtOOCCH_2CH_2NHBn$	**10j**	95
12	**4d**	CF_3	cyclohexylamine	**10k**	83
13	**4g**	CF_3CF_2	$BnNH_2$	**10l**	99
14	**4h**	$CF_3(CF_2)_2$	$BnNH_2$	**10m**	99

[a] All reactions were performed at room temperature for 3 h by using 2 equiv of both the amine and 5 mol % $Pd(PPh_3)_4$, unless otherwise noted. [b] Isolated yields. [c] The (*E*)-isomer was produced exclusively. [d] The reaction was carried out in the absence of $Pd(PPh_3)_4$. [e] Stirred for 24 h.

Reaction of α-Fluorolalkylated Allyl Mesylates with Various Amines. We also investigated the Pd-catalyzed allylic substitution reaction of **4** with various amines. The results are summarized in Table 3. As shown in entries 1, 3, 13, and 14, various fluoroalkylated mesylates **4** gave the corresponding allylamines **10** in excellent yields, indicating that using different Rf groups did not affect the present reaction at all. The fact that the reaction did not proceed at all in the absence of the palladium catalyst (entry 2) strongly suggests that the direct S_N2' reaction of the allyl mesylate with amine does not occur. The primary amines, such as benzylamine and allylamine, could participate nicely in the reaction to give the corresponding γ-trifluoromethylated allylamine derivatives **10b** and **10c** in 96 and 81% yields, respectively (entries 3 and 4). The reaction with less-nucleophilic amines, such as aniline and *p*-nitroaniline, also proceeded smoothly to afford the corresponding allylamines **10d** and **10e** quantitatively (entries 5 and 6). Free glycine ethyl ester or dimethylamine, which was generated in situ by treating its hydrochloride salt with an equimolar amount of triethylamine, reacted efficiently with the mesylate **4d** in the presence of the Pd(0) catalyst to produce **10f** and **10g** in excellent yields (entries 7 and 8). As shown in entries 8–12, various secondary and cyclic amines could also be employed for the present reaction, leading to

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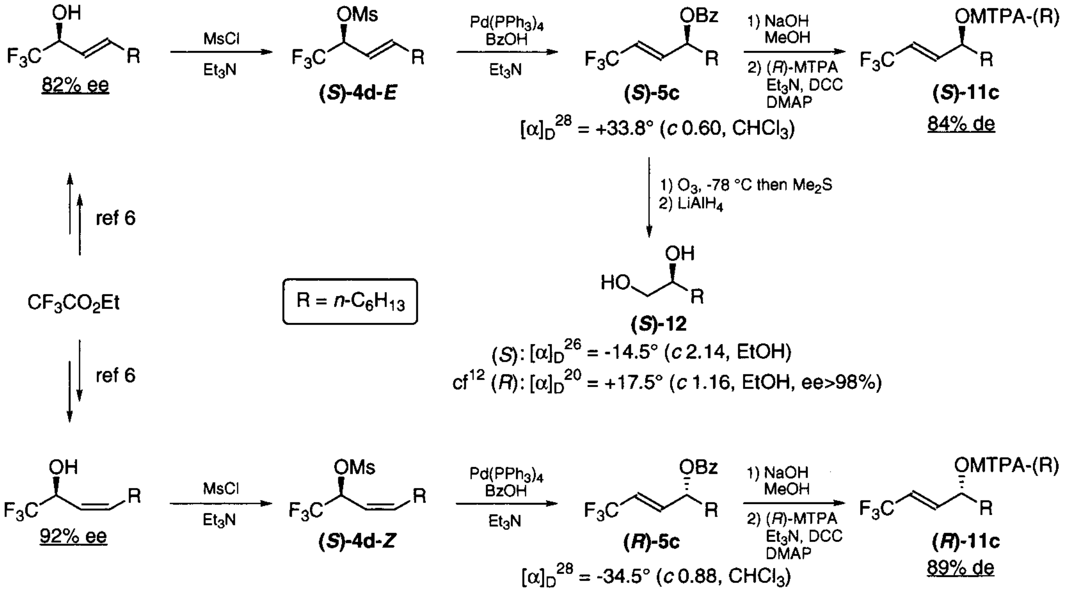
(9) The effect that the side chain has on the regioselectivity in the allylic substitution reaction has been reported. Kaffit, M. E.; Fu, Z.; Procter, M. J.; Wilson, A. M.; Dasse, O. A.; Hirosawa, C. *Pure Appl. Chem.* **1998**, *70*, 1083–1090.

(10) The regioselectivity in the palladium-catalyzed allylic substitution reaction in the nonfluorinated system has been discussed in detail. (a) Frost, C. G.; Howarth, J.; Williams, J. M. *Tetrahedron: Asymmetry* **1992**, *3*, 1089–1122. (b) Keinan, E.; Sahai, M. *J. Chem. Soc., Chem. Commun.* **1984**, 648–650.

Scheme 5. Synthesis of Optically Active γ-Trifluoromethylated Allylic Alcohol Derivatives and Their Stereochemical Assignments



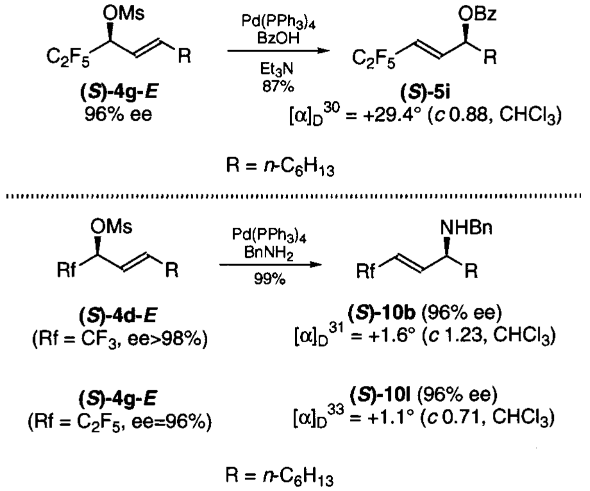
satisfactory results. In all cases, the newly formed olefinic bonds were of the E configuration; no product with (*Z*) configuration was detected. Furthermore, the regioisomer α-product could not be observed.

Preparation of Nonracemic Allylic Alcohol and Amine Derivatives. The synthesis of nonracemic γ-fluoroalkylated allylic alcohol derivatives **5** was undertaken as outlined in Scheme 5. Thus, on treating the nonracemic (*E*)-substrate **(*S*)-4d-*E***[6] (82% ee) with benzoic acid and triethylamine under the same conditions as described above, the optically active product **(*S*)-5c** was obtained in 91% yield. The ester **(*S*)-5c**, after hydrolysis, was converted into the MTPA ester **(*S*)-11c**,[11] whose diastereomeric excess was determined to be 84% by gas chromatography. This result clearly indicates that the reaction proceeds without any loss of enantiomeric excess throughout the reaction. Similarly, the reaction of the nonracemic (*Z*)-substrate **(*S*)-4d-*Z*** (92% ee) was conducted under the same reaction conditions, leading to the corresponding nonracemic allylic alcohol derivative ***(R)*-5c** in 88% yield. This ester was transformed into the MTPA ester **(*R*)-11c**, whose diastereomeric excess was determined to be 89% by gas chromatography. This fact indicates that even the reaction of the (*Z*)-substrate takes place in an enantiospecific fashion.

The stereochemical assignment of **(*S*)-** or **(*R*)-5c** was made as follows. The ozonolysis of **5c** obtained from **(*S*)-4d-*E*** produced the crude α-alkoxy aldehyde, which was immediately reduced by an excess amount of lithium aluminum hydride to give the known compound **(*S*)-12**. The comparison of the observed optical rotation of **(*S*)-12** with its literature value[12] made it possible to determine the absolute configuration of **5c** from **(*S*)-4d-*E*** as *S*. On the other hand, the optical rotation of **5c** obtained from **(*S*)-4d-*Z*** was opposite to that of the (*S*)-enantiomer, **(*S*)-5c**, indicating that its absolute configuration was *R*.

The chiral mesylate possessing a pentafluoroethyl group, **(*S*)-4g-*E***, could also be converted into the corresponding nonracemic allylic alcohol derivative **(*S*)-5i** in 87% yield, as shown in Scheme 6.

Scheme 6. Synthesis of Chiral γ-Fluoroalkylated Allylic Alcohol and Amine Derivatives



In a similar way, nonracemic γ-trifluoromethylated and γ-pentafluoroethylated allylic amine derivatives **(*S*)-10b** and **(*S*)-10l** could be obtained in 99% yields with high enantiomeric excesses (96% ee), which were measured by HPLC using a chiral column (DAICEL, CHIRALPAK AD). This fact indicates that the reaction of the mesylate with amine also proceeds without any loss of enantiomeric excess throughout the reaction. To the best of our knowledge, this is the first example of the synthesis of nonracemic allylamines having a fluoroalkylated group at the γ-position.

Mechanism. The proposed mechanism for the present reaction is outlined in Scheme 7. Thus, when the Pd complex coordinates on the face of the olefin distal to the mesyloxy group, the Pd species displaces the mesylate with inversion to give a π-allyl complex **13**. The carboxylate nucleophile attacks **13** on the face opposite to that occupied by Pd. The double inversion results in a net retention for these processes.[13] In this case, the Pd moiety might be closer to the Rf group than to the R because of

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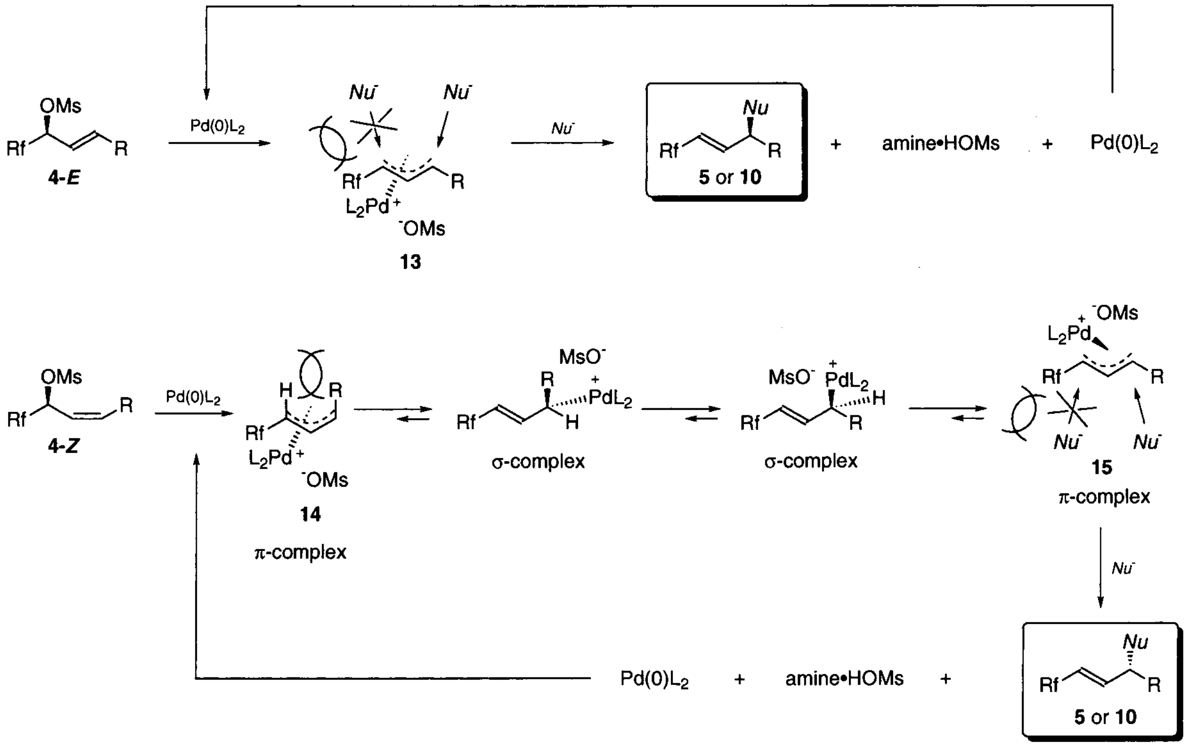
[11] Dale, J. A.; Dull, D. L.; Mosher, H. S. *J. Org. Chem.* **1969**, *34*, 2543–2549.

[12] Moussou, P.; Archelas, A.; Furstoss, R. *Tetrahedron* **1998**, *54*, 1563–1572.

Scheme 7. Mechanism of the Palladium-Catalyzed Allylic Substitution Reactions



the electron-withdrawing effect of the Rf group.[14] Therefore, the nucleophile attacks preferentially at the less-hindered γ-carbon to give the γ-fluoroalkylated allylic alcohol or amine derivatives **5** or **10**.

On the other hand, oxidative addition of Pd(0) to the (*Z*)-substrate **4-*Z*** generates the π-allylpalladium complex **14**, which is less stable than **15** because of ^{1,3}A strain.[15] Therefore, **14** could be converted into **15** via $\pi-\sigma-\pi$ equilibrium[16] with inversion. The attack of the nucleophile occurs with inversion, as mentioned for the (*E*)-substrate. Thus, the reaction of the (*Z*)-substrate involves three inversion processes, resulting in a net inversion.

Conclusions

In summary, we have described the reaction of α-fluoroalkylated allylic mesylates **4** with various carboxylates and amines in the presence of a palladium catalyst to give the corresponding γ-fluoroalkylated allylic alcohol (**5**) and amine (**10**) derivatives in excellent yields. Only γ-products with (*E*) stereochemistry were obtained in these reactions. Moreover, the reaction using nonracemic substrates afforded the corresponding nonracemic products without any loss of enantiomeric excess.

Experimental Section

General Methods. NMR spectra were recorded with 500 and 300 MHz spectrometers. A JEOL JNM-EX90A (84.21 MHz) FT-NMR spectrometer was used to obtain ^{19}F NMR spectra in $CDCl_3$ solution with an internal standard of trichlorofluoromethane. High-resolution mass spectra (HRMS) were taken on a Hitachi M-80B mass spectrometer by electron impact (EI) or chemical ionization (CI) methods. Gas–liquid chromatography (GLC) was performed on a Shimazdu GC-7AG chromatograph equipped with a flame ionization detector and nitrogen carrier gas using a Shimazdu capillary column (HiCap CBP-5-M25-025, 25 m × 0.2 mm). High-performance liquid chromatography (HPLC) was carried out on a Shimazdu LC-3A chromatograph equipped with a UV detector using a chiral column (CHIRALPAK AD, DAICEL CHEMICAL IND. Ltd., 0.46 cm ∅ × 25 cm).

Typical Procedure for the Preparation of Allyl Mesylates 4. To a solution of α-fluoroalkylated allylic alcohol[6] (1 mmol) and methansulfonyl chloride (1.2 mmol) in CH_2Cl_2 (5 mL) was added dropwise triethylamine (1.2 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and was stirred for several hours. Then, the reaction mixture was poured into saturated NH_4Cl(aq) and extracted three times with CH_2Cl_2. The combined organic layers were washed with water, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The crude materials were purified by silica gel column chromatography to give the corresponding allyl mesylate in over 90% yield. Monofluorinated allyl mesylate **4a** could not be isolated because of thermal instability; therefore, the crude mixture was used for the next reaction without purification.

1-(Difluoromethyl)-(2*E*)-nonenyl Methanesulfonate (4b): ^{1}H NMR ($CDCl_3$) δ 0.85 (t, J = 6.60 Hz, 3H), 1.20–1.42 (m, 8H), 2.05–2.15 (m, 2H), 3.02 (s, 3H), 5.04 (ddt, J = 3.45, 8.25, 10.80 Hz, 1H), 5.49 (dd, J = 8.25, 15.30 Hz, 1H), 5.77 (dt, J = 3.45, 54.90 Hz, 1H), 6.07 (dt, J = 6.60, 15.30 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.96, 22.47, 28.24, 28.64, 31.48, 32.31, 39.29, 79.62 (t, J = 26.74 Hz), 112.84 (t, J = 246.61 Hz), 118.75, 142.81; ^{19}F NMR ($CDCl_3$) δ −130.31 (ddd, J = 10.80, 54.90, 288.25 Hz, 1F), −126.33 (ddd, J = 10.80, 54.90, 288.25 Hz, 1F); IR (neat) 1670, 1366 cm^{-1}.

(1*S*)-1-(Trifluoromethyl)-(2*E*)-nonenyl Methanesulfonate ((*S*)-4d-*E*): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 5.10 Hz, 3H), 1.20–1.50 (m, 8H), 2.10–2.20 (m, 2H), 3.08 (s, 3H), 5.24 (dq, J = 8.20, 6.30 Hz, 1H), 5.54 (dd, J = 8.20, 15.45 Hz, 1H), 6.17 (dt, J = 15.45, 6.50 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.94,

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22.46, 28.08, 28.58, 31.45, 32.22, 39.45, 77.80 (q, J = 34.12 Hz), 117.78, 122.25 (q, J = 279.94 Hz), 144.10; ^{19}F NMR ($CDCl_3$) δ −77.38 (d, J = 6.30 Hz, 3F); IR (neat) 1670, 1373 cm^{-1}; $[\alpha]^{20}_{D}$ +38.9 (*c* 0.82, $CHCl_3$) (82% ee); HRMS *m/z*: (M^+) calcd for $C_{11}H_{19}F_3O_3S$, 288.1007; found, 288.0990; Anal. Calcd for $C_{11}H_{19}F_3O_3S$: C, 45.82; H, 6.64. Found: C, 45.47; H, 6.59.

(1*S*)-1-(Trifluoromethyl)-(2*Z*)-nonenyl Methanesulfonate ((*S*)-4d-*Z*): ^{1}H NMR ($CDCl_3$) δ 0.89 (t, J = 6.50 Hz, 3H), 1.20−1.50 (m, 8H), 2.13−2.30 (m, 2H), 3.08 (s, 3H), 5.45 (m, 1H), 5.64 (dq, J = 9.50, 6.00 Hz, 1H), 6.05 (dt, J = 11.00, 7.50 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.97, 22.51, 28.08, 28.80, 28.82, 31.52, 39.46, 72.74 (q, J = 34.92 Hz), 117.24, 122.46 (q, J = 280.82 Hz), 143.01; ^{19}F NMR ($CDCl_3$) δ −77.22 (d, J = 6.00 Hz, 3F); IR (neat) 1659, 1373 cm^{-1}; $[\alpha]^{25}_{D}$ −34.2 (*c* 0.95, $CHCl_3$) (92% ee).

4-Benzyloxy-1-(trifluoromethyl)-(2*E*)-butenyl Methanesulfonate (4e): ^{1}H NMR ($CDCl_3$) δ 3.10 (s, 3H), 4.11 (d, J = 3.75 Hz, 2H), 4.55 (s, 2H), 5.33 (quint., J = 7.00 Hz, 1H), 5.89 (dd, J = 7.00, 15.75 H, 1H), 6.25 (dt, J = 15.75, 3.75 Hz, 1H), 7.28−7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 39.40, 68.53, 72.72, 76.78 (q, J = 34.91 Hz), 118.77, 122.18 (q, J = 280.84 Hz), 127.72, 127.86, 128.47, 137.58, 138.49; ^{19}F NMR ($CDCl_3$) δ −77.17 (d, J = 7.00 Hz); IR (neat) 1690, 1315 cm^{-1}.

(1*S*)-1-(Pentafluoroethyl)-(2*E*)-nonenyl Methanesulfonate ((*S*)-4 g): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.50 Hz, 3H), 1.20−1.34 (m, 6H), 1.38−1.45 (m, 2H), 2.16 (q, J = 6.82 Hz, 2H), 3.06 (s, 3H), 5.34 (q, J = 10.00 Hz, 1H), 5.56 (dd, J = 10.00, 15.50 Hz, 1H), 6.17 (dt, J = 15.50, 6.82 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.95, 22.50, 28.14, 28.61, 31.49, 32.29, 39.66, 77.66 (dd, J = 17.51, 27.98 Hz), 110.0−114.0 (m), 117.53, 118.40 (tq, J = 35.07, 286.70 Hz), 144.68; ^{19}F NMR ($CDCl_3$) δ −124.13 (m, 2F), −81.66 (s, 3F); IR (neat) 1670, 1373 cm^{-1}; $[\alpha]^{22}_{D}$ +27.4 (*c* 0.82, $CHCl_3$) (96% ee); Anal. Calcd for $C_{12}H_{19}F_5O_3S$: C, 42.60; H, 5.66. Found: C, 42.57; H, 5.60.

1-(Heptafluoropropyl)-(2*E*)-nonenyl Methanesulfonate (4h): ^{1}H NMR ($CDCl_3$) δ 0.81 (t, J = 6.50 Hz, 3H), 1.15−1.27 (m, 6H), 1.30−1.40 (m, 2H), 2.06−2.14 (m, 2H), 2.99 (s, 3H), 5.34 (q, J = 9.25 Hz, 1H), 5.51 (dd, J = 9.25, 15.00 Hz, 1H), 6.12 (dt, J = 15.00, 7.00 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.96, 22.50, 28.16, 28.62, 31.50, 32.32, 39.76, 77.67 (dd, J = 24.20, 28.65 Hz), 117.55, 106−120 (m), 144.82; ^{19}F NMR ($CDCl_3$) δ −125.90 to (approx.) −125.30 (m, 2F), −121.30 to (approx.) −120.70 (m, 2F), −81.29 (t, J = 9.25 Hz, 3F); IR (neat) 1670, 1373 cm^{-1}; Anal. Calcd for $C_{13}H_{19}F_7O_3S$: C, 40.21; H, 4.93. Found: C, 40.72; H, 5.02.

Typical Procedure for the Synthesis of γ-Fluoroalkylated Allylic Alcohol Derivatives 5. To a solution of Pd(PPh_3)$_4$ (5 mol %, 58 mg) in THF (2 mL) was added α-fluoroalkylated allyl mesylate **4** (1 mmol) at 0 °C. After stirring the reaction mixture at that temperature for 10 min, 2 equiv each of carboxylic acid and triethylamine were added to the mixture, followed by stirring at 0 °C for 3 h. The reaction was quenched with saturated NH_4Cl(aq) and extracted with ethyl acetate three times. The combined organic layers were washed with brine, dried over anhydrous Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography to give the corresponding γ-fluoroalkylated allyl ester **5** in 74−99% yield.

1-(3-Fluoro-(1*E*)-propenyl)heptyl Benzoate (5a): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 7.00 Hz, 3H) 1.20−1.47 (m, 8H), 1.69−1.87 (m, 2H), 4.87 (dd, J = 5.50, 47.51 Hz, 2H), 5.50 (m, 1H), 5.85−6.00 (m, 2H), 7.40−7.60 (m, 3H), 8.00−8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 14.01, 22.54, 25.02, 29.02, 31.65, 34.34, 73.97, 82.43 (d, J = 164.12 Hz), 126.72 (d, J = 16.79 Hz), 128.35, 129.57, 130.36, 132.60 (d, J = 11.93 Hz), 132.94, 165.76; ^{19}F NMR ($CDCl_3$) δ −215.10 (dt, J = 7.74, 47.51 Hz, 1F); IR (neat) 1720 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{17}H_{23}FO_2$, 278.1682; found, 278.1678.

1-(3,3-Difluoro-(1*E*)-propenyl)heptyl Benzoate (5b): ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.90 Hz, 3H), 1.20−1.50 (m, 8H), 1.70−1.90 (m, 2H), 5.55 (m, 1H), 5.80 (m, 1H), 6.10 (dt, J = 5.25, 55.50 Hz, 1H), 6.17 (ddt, J = 15.90, 5.25, 3.00 Hz, 1H), 7.43−7.50 (m, 2H), 7.55 (m, 1H), 8.05−8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.96, 22.48, 24.85, 28.93, 31.55, 33.97, 72.75, 114.18 (t, J = 233.22 Hz), 123.91 (t, J = 24.27 Hz), 128.40, 129.57, 129.92, 133.123, 136.92 (t, J = 10.94 Hz), 165.54; ^{19}F NMR ($CDCl_3$) δ −112.80 to (approx.) −112.670 (m, 1F), −112.00 to (approx.) −111.80 (m, 1F). IR (neat): 1720 cm^{-1}; HRMS *m/z* (M^+) calcd for for $C_{17}H_{22}F_2O_2$, 296.1588; found, 296.1591; Anal. Calcd for $C_{17}H_{22}F_2O_2$: C, 68.90; H, 7.48. Found: C, 68.60; H, 7.60.

(1*S*)-1-(Trifluoro-(1*E*)-propenyl)heptyl Benzoate ((*S*)-5c): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.31 Hz, 3H), 1.20−1.50 (m, 8H), 1.75−1.90 (m, 2H), 5.60−5.70 (m, 1H), 5.87 (ddq, J = 1.50, 15.75, 6.00 Hz, 1H), 6.44 (ddq, J = 5.10, 15.75, 2.10 Hz, 1H), 7.45−7.52 (m, 2H), 7.55−7.65 (m, 1H), 8.05−8.10 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 13.94, 22.46, 24.79, 28.89, 31.51, 33.82, 72.07, 119.03 (q, J = 34.71 Hz), 122.74 (q, J = 268.44 Hz), 128.46, 129.60, 129.69, 133.26, 138.24 (q, J = 5.72 Hz), 165.40; ^{19}F NMR ($CDCl_3$) δ −64.77 (d, J = 6.00 Hz, 3F); IR (neat): 1724 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{17}H_{21}F_3O_2$, 314.1494; found, 314.1489; $[\alpha]^{28}_{D}$ +33.8 (*c* 0.60, $CHCl_3$) (84% de); Anal. Calcd for $C_{17}H_{21}F_3O_2$: C, 64.96; H, 6.73. Found: C, 64.91; H, 6.80.

1-(Trifluoro-(1*E*)-propenyl)heptyl Acetate (5d): ^{1}H NMR ($CDCl_3$) δ 0.82 (t, J = 6.50 Hz, 3H), 1.15−1.28 (m, 8H), 1.50−1.65 (m, 2H), 2.04 (s, 3H), 5.05−5.35 (m, 1H), 5.72 (ddq, J = 1.00, 16.00, 6.50 Hz, 1H), 6.25 (ddq, J = 5.50, 16.00, 1.50 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.93, 20.90, 22.44, 24.69, 28.84, 31.50, 33.67, 71.60, 119.03 (q, J = 34.08 Hz), 122.72 (q, J = 269.75 Hz), 138.09 (q, J = 6.29 Hz), 169.92; ^{19}F NMR ($CDCl_3$) δ −64.87 (d, J = 6.50 Hz). IR (neat) 1747 cm^{-1}.

1-(Trifluoro-(1*E*)-propenyl)heptyl Propionate (5e): ^{1}H NMR ($CDCl_3$) δ 0.81 (t, J = 7.00 Hz, 3H), 1.10 (t, J = 7.50 Hz, 3H), 1.15−1.30 (m, 8H), 1.50−1.65 (m, 2H), 2.31 (q, J = 7.50 Hz, 2H), 5.27 (m, 1H), 5.71 (ddq, J = 1.00, 15.50, 6.25 Hz, 1H), 6.25 (ddq, J = 5.00, 15.50, 2.00 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 9.10, 13.93, 22.44, 24.69, 27.55, 28.84, 31.50, 33.70, 71.34, 118.90 (q, J = 34.46 Hz), 122.74 (q, J = 269.37 Hz), 138.25 (q, J = 6.16 Hz), 173.35; ^{19}F NMR ($CDCl_3$) δ −64.82 (d, J = 6.25 Hz); IR (neat) 1744 cm^{-1}. HRMS *m/z* (M^+) calcd for $C_{13}H_{21}F_3O_2$, 266.1494; found, 266.1475.

1-(Trifluoro-(1*E*)-propenyl)heptyl Chloroacetate (5f): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.31 Hz, 3H), 1.20−1.40 (m, 8H), 1.70−1.80 (m, 2H), 4.09 (s, 2H), 5.35−5.50 (m, 1H), 5.75−5.90 (m, 1H), 6.25−6.40 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 13.95, 22.46, 24.61, 28.80, 31.49, 33.59, 40.71, 73.66, 119.88 (q, J = 34.46 Hz), 122.57 (q, J = 269.75 Hz), 137.11 (q, J = 6.29 Hz), 166.36; ^{19}F NMR ($CDCl_3$) δ −65.00 (d, J = 6.64 Hz, 3F); IR (neat) 1763 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{12}H_{18}ClF_3O_2$, 286.0947; found, 286.0927; Anal. Calcd for $C_{12}H_{18}ClF_3O_2$: C, 50.27; H, 6.33. Found: C, 50.87; H, 6.54.

1-(Trifluoro-(1*E*)-propenyl)heptyl Methoxyacetate (5g): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.60 Hz, 3H), 1.20−1.40 (m, 8H), 1.65−1.80 (m, 2H), 3.46 (s, 3H), 4.07 (s, 2H), 5.40−5.55 (m, 1H), 5.81 (ddq, J = 1.50, 15.90, 6.30 Hz, 1H), 6.32 (ddq, J = 5.70, 15.90, 1.80 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 13.89, 22.41, 24.65, 28.77, 31.46, 33.62, 59.32, 69.62, 72.14, 119.54 (q, J = 34.68 Hz), 122. 59 (q, J = 269.25 Hz), 137.56 (q, J = 6.16 Hz), 169.25; ^{19}F NMR ($CDCl_3$) δ −64.96 (d, J = 6.30 Hz, 3F); IR (neat) 1763 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{13}H_{21}F_3O_3$, 282.1443; found, 282.1446; Anal. Calcd for $C_{13}H_{21}F_3O_3$: C, 55.31; H, 7.50. Found: C, 54.98; H, 7.60.

1-(Benzyloxymethyl)-4,4,4-trifluoro-(2*E*)-butenyl Benzoate (5h): ^{1}H NMR ($CDCl_3$) δ 3.71 (dd, J = 5.00, 10.75 Hz, 1H), 3.76 (dd, J = 6.50, 10.75 Hz, 1H), 4.57 (d, J = 12.00 Hz, 1H), 4.63 (d, J = 12.00 Hz, 1H), 5.81−5.88 (m, 1H), 5.96 (ddq, J = 1.50, 16.00, 6.00 Hz, 1H) 6.53 (ddq, J = 4.50, 16.00, 2.00 Hz, 1H), 7.25−7.35 (m, 5H), 7.45−7.51 (m, 2H), 7.57−7.63 (m, 1H), 8.05−8.12 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 70.26, 70.86, 73.34, 120.34 (q, J = 34.50 Hz), 122.65 (q, J = 268.92 Hz), 125.86, 127.66, 127.89, 128.46, 128.52, 129.79, 133.48, 135.50 (q, J = 6.21 Hz), 137.46, 165.27; ^{19}F NMR ($CDCl_3$) δ −64.92 (d, J = 6.00 Hz, 3F); IR (neat) 1724 cm^{-1}; HRMS *m/z* (M^+) calcd for $C_{19}H_{17}F_3O_3$, 350.1130; found, 350.1137.

(1*S*)-1-(3,3,4,4,4-Pentafluoro-(1*E*)-butenyl)heptyl Benzoate ((*S*)-5i): ^{1}H NMR ($CDCl_3$) δ 0.80 (t, J = 6.50 Hz, 3H), 1.15−1.40 (m, 8H), 1.65−1.80 (m, 2H), 5.50−5.65 (m, 1H), 5.77 (dt, J = 15.50, 12.00 Hz, 1H), 6.35−6.45 (m, 1H), 7.40 (t, J = 7.50 Hz, 2H), 7.53 (t, J = 7.50 Hz, 1H), 8.00 (d, J = 7.50 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 13.98, 22.50, 24.76, 28.93, 31.55, 33.88, 72.42, 117.42 (t, J = 23.64 Hz), 120˜140 (m), 128.52, 129.65, 129.74, 133.32, 140.53 (t, J = 8.44 Hz), 165.42; ^{19}F NMR (CDCl$_3$) δ −116.18 (d, J = 11.02 Hz, 2F), −85.71 (s, 3F); IR (neat) 1724 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{18}H_{21}F_5O_2$, 364.1462; found, 364.1466; $[\alpha]^{30}_D$ +29.4 (*c* 0.88, CHCl$_3$).

1-(3,3,4,4,5,5,5-Heptafluoro-(1*E*)-pentenyl)heptyl Benzoate (5j): ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.60 Hz, 3H), 1.25−1.50 (m, 8H), 1.75−1.85 (m, 2H), 5.60−5.70 (m, 1H), 5.86 (dt, J = 12.60, 16.05 Hz, 1H), 6.48 (ddt, J = 5.10, 16.05, 2.40 Hz, 1H), 7.45−7.50 (m, 2H), 7.55−7.65 (m, 1H), 8.05−8.10 (m, 2H); ^{13}C NMR (CDCl$_3$) δ 13.92, 22.44, 24.69, 28.88, 31.50, 33.83, 72.38, 117.45 (t, J = 23.77 Hz), 120˜140 (m) 128.46, 129.58, 129.69, 133.25, 140.55 (t, J = 8.68 Hz) 165.36; ^{19}F NMR (CDCl$_3$) δ −128.28 (s, 2F), −113.51 (m, 2F), −80.87 (t, J = 11.02 Hz, 3F); IR (neat) 1728 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{19}H_{21}F_7O_2$, 414.1430; found, 414.1408; Anal. Calcd for $C_{19}H_{21}F_7O_2$: C, 55.07; H, 5.11. Found: C, 55.32; H, 5.21.

Typical Procedure for the Synthesis of γ-Fluoroalkylated Allylic Amines 10. To a solution of Pd(PPh$_3$)$_4$ (5 mol %) in THF (2 mL) was added the α-fluoroalkylated allyl mesylate **4** at 0 °C. After the reaction mixture was stirred for 5 min, 2 equiv of amine was added at 0 °C, and the reaction mixture was warmed to room temperature and then stirred for 3−24 h. The reaction was quenched with saturated NH$_4$Cl(aq), extracted three times with ethyl acetate, dried over anhydrous Na$_2$SO$_4$, and concentrated in vacuo. The crude material was purified by silica gel column chromatography (ethyl acetate/hexane 1:3) to give the corresponding γ-fluoroalkylated allylamine **10**.

***N*-Benzyl-1-(3,3-difluoro-(1*E*)-propenyl)heptylamine (10a):** ^{1}H NMR (CDCl$_3$) δ 0.87 (t, J = 6.50 Hz, 3H), 1.20−1.35 (m, 8H), 1.35−1.60 (m, 3H), 3.13 (q, J = 7.25 Hz, 1H), 3.63 (d, J = 13.25 Hz, 1H), 3.80 (d, J = 13.25 Hz, 1H), 5.75 (ddt, J = 5.75, 15.75, 8.00 Hz, 1H), 5.90 (ddt, J = 7.25, 15.75, 3.50 Hz, 1H), 6.09 (dt, J = 5.75, 56.01 Hz, 1H), 7.23−7.35 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.04, 22.57, 25.63, 29.21, 31.69, 35.35, 51.36, 58.96, 115.03 (t, J = 233.74 Hz), 124.23 (t, J = 24.12 Hz), 127.00, 128.10, 128.44, 140.22, 142.22 (t, J = 11.23 Hz); ^{19}F NMR (CDCl$_3$) δ −110.46 (dd, J = 56.01, 8.00 Hz, 2F); IR (neat) 1678 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{17}H_{25}F_2N$, 281.1955; found, 281.1955.

(1*S*)-*N*-Benzyl-1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylamine ((*S*)-10b): ^{1}H NMR (CDCl$_3$) δ 0.80 (t, J = 6.75 Hz, 3H), 1.10−1.20 (m, 10H), 1.40 (m, 1H), 3.08 (q, J = 7.17 Hz, 1H), 3.56 (d, J = 13.00 Hz, 1H), 3.72 (d, J = 13.00 Hz, 1H), 5.69 (dq, J = 15.65, 6.33 Hz, 1H), 6.14 (ddq, J = 15.65, 7.17, 2.00 Hz, 1H), 7.20 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 13.97, 22.51, 25.50, 29.12, 31.61, 35.10, 51.32, 58.37, 119.12 (q, J = 33,45 Hz), 123.00 (q, J = 268.87 Hz), 127.02, 128.01, 128.48, 139.99, 142.87 (q, J = 6.29 Hz); ^{19}F NMR (CDCl$_3$) δ −64.27 (d, J = 6.33 Hz, 3F); IR (neat) 1678 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{17}H_{24}F_3N$, 299.1861; found, 299.1875; $[\alpha]^{31}_D$ +1.6 (*c* 1.23, CHCl$_3$, 96% ee). The retention time in HPLC (hexane only, 0.7 mL/min) is as follows: (*R*) isomer, 9.4 min; (*S*) isomer, 9.8 min.

***N*-Allyl-1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylamine (10c):** ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.75 Hz, 3H), 1.27−1.61 (m, 11H), 3.11−3.21 (m, 2H), 3.25−3.29 (m, 1H), 5.11−5.20 (m, 2H), 5.74 (dq, J = 15.75, 6.50 Hz, 1H), 5.83−5.91 (m, 1H), 6.18 (ddq, J = 15.75, 8.00, 2.00 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 14.00, 22.34, 25.60, 29.17, 31.64, 34.99, 49.75, 58.51, 116.53, 119.53 (q, J = 33.58 Hz), 122.92 (q, J = 269.13 Hz), 136.03, 142.35 (q, J = 5.53 Hz); ^{19}F NMR (CDCl$_3$) δ −64.40 (d, J = 6.50 Hz, 3F); IR (neat) 1678 cm^{-1}; HRMS *m/z* (M$^+$ + H) calcd for $C_{13}H_{23}F_3N$, 250.1783; found, 250.1774.

***N*-{1-(3,3,3-Trifluoro-(1*E*)-propenyl)heptyl}aniline (10d):** ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.75 Hz, 3H), 1.20−1.50 (m, 10H), 3.60 (s, 1H), 3.90 (s, 1H), 5.78−5.86 (m, 1H), 6.37 (ddq, J = 15.82, 6.81, 2.08 Hz, 1H), 6.55 (d, J = 7.68 Hz, 2H), 6.72 (t, J = 7.68 Hz, 1H), 7.17 (t, J = 7.68 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 14.0, 22.55, 25.84, 29.08, 31.63, 35.37, 54.06, 117.84, 118.49 (q, J = 33.83 Hz), 118.90, 122.20, 123.28 (q, J = 269.76 Hz), 124.35, 141.78 (q, J = 5.78 Hz); ^{19}F NMR (CDCl$_3$) δ −64.10 (d, J = 4.37 Hz, 3F); IR (neat) 1605 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{16}H_{22}F_3N$, 285.1704; found, 285.1660.

***N*-{1-(3,3,3-Trifluoro-(1*E*)-propenyl)heptyl}-*p*-nitroaniline (10e):** ^{1}H NMR (CDCl$_3$) δ 0.89 (t, J = 6.75 Hz, 3H), 1.26−1.78 (m, 10H), 4.0−4.1 (m, 1H), 4.56 (d, J = 6.50 Hz, 1H), 5.78 (ddq, J = 1.00, 15.88, 6.50 Hz, 1H), 6.36 (dq, J = 15.88, 2.25 Hz, 1H), 6.52 (d, J = 9.00 Hz, 2H), 8.10 (d, J = 9.00 Hz, 2H); ^{13}C NMR (CDCl$_3$) δ 13.95, 22.48, 25.73, 28.90, 31.52, 35.04, 53.71, 116.63, 119.20 (q, J = 34.02 Hz), 122.84 (q, J = 269.57 Hz), 126.36, 138.61, 139.89 (q, J = 5.87 Hz), 152.04; ^{19}F NMR (CDCl$_3$) δ −64.16 (d, J = 6.50 Hz, 3F); IR (neat) 1600 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{16}H_{21}F_3N_2O_2$, 330.1555; found, 330.1559.

Ethyl-2-{1-(3,3,3-trifluoro-(1*E*)-propenyl)heptyl}aminoacetate (10f): ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.50 Hz, 3H), 1.26−1.59 (m, 13H), 1.78 (s, 1H), 3.13 (dt, J = 7.25, 6.50 Hz, 1H), 3.28 (d, J = 7.25 Hz, 1H), 3.37 (d, J = 7.25 Hz, 1H), 4.19 (q, J = 7.20 Hz, 2H), 5.76 (dq, J = 15.50, 7.00, Hz, 1H), 6.15 (ddq, J = 15.50, 7.25, 2.00 Hz, 1H); ^{13}C NMR (CDCl$_3$) δ 13.99, 14.13, 22.53, 25.53, 29.15, 31.61, 35.14, 48.50, 59.16, 60.90, 119.51 (q, J = 33.60 Hz), 122.84 (q, J = 269.18 Hz), 142.28 (q, J = 6.06 Hz), 172.43; ^{19}F NMR (CDCl$_3$) δ −64.03 (d, J = 7.00 Hz, 3F); IR (neat) 1740 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{14}H_{24}F_3NO_2$, 295.1759; found, 295.1753.

***N*,*N*-Dimethyl-1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylamine (10g):** ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.50 Hz, 3H), 1.20−1.35 (m, 8H), 1.40−1.50 (m, 1H), 1.63−1.68 (m, 1H), 2.25 (s, 6H), 2.81−2.85 (m, 1H), 5.70 (dq, J = 15.88, 6.35 Hz, 1H), 6.25−6.31 (m, 1H); ^{13}C NMR (CDCl$_3$) δ 14.38, 22.59, 26.01, 29.28, 31.68, 31.70, 41.50, 65.98, 120.73 (q, J = 33.45 Hz), 122.71 (q, J = 268.01 Hz), 139.37 (q, J = 5.68 Hz); ^{19}F NMR (CDCl$_3$) δ −64.01 (t, J = 6.35 Hz, 3F); IR (neat) 1678 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{12}H_{22}F_3N$, 237.1704; found, 237.1683.

***N*,*N*-Dibenzyl-1-(3,3,3-trifluoro-(1*E*)-propenyl)heptylamine (10h):** ^{1}H NMR (CDCl$_3$) δ 0.87 (t, J = 6.75 Hz, 3H), 1.20−1.80 (m, 10H), 3.10−3.20 (m, 1H), 3.38 (d, J = 13.75 Hz, 2H), 3.81 (d, J = 13.75 Hz, 2H), 5.64 (dq, J = 15.80, 6.31 Hz, 1H), 6.30−6.40 (m, 1H), 7.20−7.30 (m, 2H), 7.30−7.40 (m, 8H); ^{13}C NMR (CDCl$_3$) δ 14.06, 22.62, 26.20, 29.10, 31.07, 31.71, 53.63, 58.40, 120.74 (q, J = 33.07 Hz), 126.98, 127.10 (q, J = 306.35 Hz), 128.31, 128.56, 138.86 (q, J = 5.78 Hz), 139.62; ^{19}F NMR (CDCl$_3$) δ −64.14 (d, J = 6.31 Hz, 3F); IR (neat) 1674 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{24}H_{30}F_3N$, 389.2330; found, 389.2336.

Ethyl *N*-Benzyl-2-{1-(3,3,3-trifluoro-(1*E*)-propenyl)heptyl}aminoacetate (10i): ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.75 Hz, 3H), 1.20−1.50 (m, 12H), 1.60−1.75 (m, 1H), 3.24 (d, J = 13.50 Hz, 1H), 3.29 (q, J = 7.30 Hz, 1H), 3.35 (d, J = 13.50 Hz, 1H), 3.68 (d, J = 13.50 Hz, 1H), 3.87 (d, J = 13.50 Hz, 1H), 4.13 (q, J = 7.00 Hz, 2H), 5.73 (dq, J = 15.50, 6.00 Hz, 1H), 6.25−6.35 (m, 1H), 7.20−7.40 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.04, 22.59, 26.00, 29.14, 31.42, 31.70, 50.99, 54.93, 60.47, 60.82, 120.38 (q, J = 33.24 Hz), 122.86 (q, J = 269.52 Hz), 127.19, 128.34, 128.70, 138.88, 139.60 (q, J = 5.78 Hz), 171.73; ^{19}F NMR (CDCl$_3$) δ −64.31 (d, J = 6.00 Hz, 3F); IR (neat) 1736 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{21}H_{30}F_3N$, 385.2229; found, 385.2233.

Ethyl *N*-Benzyl-3-{1-(3,3,3-trifluoro-(1*E*)-propenyl)heptyl}aminopropionate (10j): ^{1}H NMR (CDCl$_3$) δ 0.79 (t, J = 7.00 Hz, 3H), 1.12−1.23 (m, 11H), 1.37 (m, 1H), 1.53−1.58 (m, 1H), 2.31−2.41 (m, 2H), 2.60 (dt, J = 13.00, 6.50 Hz, 1H), 2.91 (dt, J = 13.00, 7.50 Hz, 1H), 2.95−3.05 (m, 1H), 3.36 (d, J = 14.00 Hz, 1H), 3.71 (d, J = 14.00 Hz, 1H), 4.04 (m, 2H), 5.57 (dq, J = 15.80, 6.30 Hz, 1H), 6.21−6.27 (m, 1H), 7.15−7.25 (m, 5H); ^{13}C NMR (CDCl$_3$) δ 14.03, 14.50, 22.59, 26.25, 29.08, 31.19, 31.73, 34.84, 45.55, 54.70, 60.03, 60.38, 120.50 (q, J = 33.62 Hz), 122.83 (q, J = 269.69 Hz), 127.02, 128.27, 128.52, 138.89 (q, J = 5.01 Hz), 139.50, 172.40; ^{19}F NMR (CDCl$_3$) δ −64.18 (d, J = 6.30 Hz, 3F); IR (neat) 1736 cm^{-1}; HRMS *m/z* (M$^+$) calcd for $C_{22}H_{32}F_3NO_2$, 399.2385; found, 399.2393.

1-(3,3,3-Trifluoro-(1*E*)-propenyl)heptylcyclohexyamine (10k): ^{1}H NMR (CDCl$_3$) δ 0.88 (t, J = 6.75 Hz, 3H), 1.22−1.31 (m, 10H), 1.35−1.50 (m, 3H), 1.51−1.70 (m, 5H), 2.39−2.41 (m, 2H), 2.48−2.50 (m, 2H), 2.80−2.84 (m, 1H), 5.67

(dq, J = 15.57, 6.33 Hz, 1H), 6.30 (ddq, J = 15.57, 8.50, 2.0 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 14.03, 22.59, 24.63, 26.27, 26.32, 29.27, 31.23, 31.69, 50.56, 66.39, 122.16 (q, J = 32.19 Hz), 122.84 (q, J = 269.89 Hz), 140.16 (q, J = 4.78 Hz); ^{19}F NMR ($CDCl_3$) δ −64.19 (d, J = 6.33 Hz, 3F); IR (neat) 1739 cm^{-1}.

(1*S*)-*N*-Benzyl-1-(3,3,4,4,4-pentafluoro-(1*E*)-butenyl)-heptylamine ((*S*)-10l): ^{1}H NMR ($CDCl_3$) δ 0.88 (t, J = 6.50 Hz, 3H), 1.20−1.35 (m, 8H), 1.45−1.55 (m, 3H), 3.20 (q, J = 7.25 Hz, 1H), 3.63 (d, J = 13.25 1H), 3.80 (d, J = 13.25 Hz, 1H), 5.74 (dt, J = 15.75, 12.00 Hz, 1H), 6.26 (ddt, J = 15.75, 7.25, 2.00 Hz, 1H), 7.24−7.36 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.01, 22.52, 25.50, 29.13, 31.64, 35.11, 51.29, 58.75, 110.00−125.00 (m), 117.63 (t, J = 24.00 Hz), 127.13, 128.09, 128.49, 131.95−132.13 (m), 139.83, 145.10−145.20 (m); ^{19}F NMR ($CDCl_3$) δ −85.84 (s, 3F), −115.63 (d, J = 12.00 Hz, 2F); IR (neat) 1739 cm^{-1}; HRMS m/z (M^{+}) calcd for $C_{18}H_{24}F_5N$, 349.1829; found, 349.1824; $[\alpha]^{33}_{D}$ +1.1 (c 0.71, $CHCl_3$, 96% ee). The retention time in HPLC (hexane only, 0.7 mL/min) is as follows: (*R*)-isomer, 8.0 min; (*S*)-isomer, 8.5 min; Anal. Calcd for $C_{18}H_{24}F_5N$: C, 61.88; H, 6.92; N, 4.01. Found: C, 61.89; H, 7.07; N, 3.71.

***N*-Benzyl-1-(3,3,4,4,5,5,5-heptafluoro-(1*E*)-pentenyl)-heptylamine (10m):** ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6.50 Hz, 3H), 1.20−1.35 (m, 8H), 1.40−1.60 (m, 3H), 3.20 (q, J = 7.50 Hz, 1H), 3.62 (d, J = 13.25 Hz, 1H), 3.79 (d, J = 13.25 Hz, 1H), 5.76 (dt, J = 15.75, 12.00 Hz, 1H), 6.25 (ddt, J = 15.75, 7.50, 2.00 Hz, 1H), 7.23−7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 14.01, 22.53, 25.52, 29.16, 31.65, 35.24, 51.33, 58.80, 110−120 (m), 117.49 (t, J = 23.09 Hz), 127.10, 128.06, 128.49, 133.66, 133.82, 140.02, 145.47 (t, J = 8.35 Hz); ^{19}F NMR ($CDCl_3$) δ −128.25 (s, 2F), −113.20 to (approx.) −112.50 (m, 2F), −80.82 (t, J = 8.83 Hz, 3F); IR (neat) 1670 cm^{-1}.

Supporting Information Available: NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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