Highly Stereoselective Synthesis of Trifluoromethylated Compounds via Ester-Enolate [2,3]-Wittig and [3,3]-Ireland−Claisen Rearrangements

Tsutomu Konno, Hideki Umetani, and Tomoya Kitazume*

Department of Bioengineering, Tokyo Institute of Technology, Nagatsuta, Midori-ku, Yokohama, 226, Japan

Received July 2, 1996[⊗]

γ-Trifluoromethylated propargylic alcohols have been obtained in optically pure forms via effective enzymatic kinetic resolution and then converted into (*E*)- or (*Z*)-allylic alcohols. [2,3]-Wittig rearrangement of the corresponding [[γ-(trifluoromethyl)allyl]oxy]acetic acid methyl esters afforded α-hydroxy-β-(trifluoromethyl)-γ,δ-unsaturated carboxylic acid methyl esters in good yields. The rearrangement of (*Z*)-substrates proceeded in a highly stereoselective manner to give *anti*-isomers with *E* configuration at a newly created olefinic bond via complete chirality transfer. (*E*)-Substrates, however, showed relatively low stereoselectivities resulting in mixtures of *syn*- and *anti*-products. The trifluoromethylated allylic alcohols were also converted into the corresponding α-methoxyacetic acid γ-(trifluoromethyl)allyl esters and evaluated as substrates for [3,3]-Ireland−Claisen rearrangement. (*E*)-Substrates were efficiently transformed into *syn*-products while (*Z*)-substrates exhibited relatively low stereoselectivities. The two complementary methods provide facile routes to highly functionalized trifluoromethyl-containing molecules with a high degree of stereocontrol.

Trifluoromethyl substitution on organic molecules often confers significant changes in their chemical and physical properties, and therefore CF_3-containing materials have received considerable attention in recent years.[1] There are some established methods for the construction of single chiral centers with a CF_3 group,[2−7] while, to date, compounds with two contiguous stereocenters such as **1** (Scheme 1) are much more difficult to prepare both in diastereo- as well as in enantioselective manners.[8] It might be that application of such stereoselective reactions for nonfluorinated systems as the aldol reaction,[9] Diels−Alder reaction,[10] and ene reaction[11] would open new routes to our target compounds, even though this is not always reliable for fluorine-containing molecules. For example, α-CF_3-enolate **2**[12] and α-CF_3 aldehyde **3**,[13] which might be utilized in an aldol reaction as a nucleophile and an electrophile, respectively, are found to be difficult to handle due to defluorination and/or epimerization. Moreover, **2** is less nucleophilic than its nonfluorinated counterpart, presumably due to the electron deficiency of the carbon−carbon double bond due to the electron-withdrawing (CF_3) group (Scheme 1).

Sigmatropic rearrangement has become a powerful tool for the stereoselective construction of a new carbon−carbon bond.[14] In particular, [2,3]-Wittig[15] and [3,3]-Ireland−Claisen shifts[16] (eqs 1 and 2 in Scheme 2, respectively) have become indispensable synthetic methods because of their mild reaction conditions as well as

[⊗] Abstract published in *Advance ACS Abstracts,* December 15, 1996.

(1) (a) Liebman, J. F.; Greenberg, A.; Dolbier, W. R., Jr.; Eswarakrishnan, S. In *Fluorine-Containing Molecules; Structure, Reactivity, Synthesis*; VCH Publisher: New York, 1988. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; John Wiley & Sons: New York, 1990. (c) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha & Elsevier Biomedical: Tokyo, 1982. (d) Johno, M.; Itoh, K.; Lee, J.; Ouchi, Y.; Takezoe, H.; Fukuda, A.; Kitazume, T. *Jpn. J. Appl. Phys.* **1990**, *29*, 107. (e) Koden, M.; Shiomi, M.; Nakagawa, K.; Funada, F.; Awane, K.; Yamazaki, T.; Kitazume, T. *Jpn. J. Appl. Phys.* **1991**, *30*, 1300. (f) Doyle, T. R.; Vogol, O. *J. Am. Chem. Soc.* **1989**, *111*, 8510. (g) Walba, D. M.; Razavi, H. A.; Clark, N. A.; Parmar, D. S. *J. Am. Chem. Soc.* **1988**, *110*, 8686.

(2) (a) Ramachandran, P. V.; Teodorovic, A. V.; Brown, H. C. *Tetrahedron* **1993**, *49*, 1725. (b) Ramachandran, P. V.; Gong, B.; Teodorovic, A. V.; Brown, H. C. *Tetrahedron: Asym.* **1994**, *5*, 1061. (c) Ramachandran, P. V.; Teodorovic, A. V.; Gong, B.; Brown, H. C. *Tetrahedron: Asym.* **1994**, *5*, 1075.

(3) (a) Kitazume, T.; Yamazaki, T. In *Selective Fluorination in Organic and Bioorganic Chemistry*; ACS Symposium Series No. 456; Welch, J. T., Ed.; American Chemical Society: Washington, D.C., 1991. (b) Seebach, D.; Sutter, M. A.; Weher, R. H.; Züger, M. F. *Organic Syntheses*; Wiley; New York, 1990; Collect. Vol. VII, p 215. (c) Kitazume, T.; Sato, T.; Kobayashi, T.; Lin, J.-T. *J. Org. Chem.* **1986**, *51*, 1003. (d) Lin, J.-T.; Yamazaki, T.; Kitazume, T. *J. Org. Chem.* **1987**, *52*, 3211. (e) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Org. Chem.* **1993**, *58*, 4346.

(4) (a) Mikami, K.; Yajima, T.; Terada, M.; Uchimaru, T. *Tetrahedron Lett.* **1993**, *34*, 7591. (b) Mikami, K.; Yajima, T.; Terada, M.; Maruta, M. *Tetrahedron: Asym.* **1994**, *5*, 1087. (c) Mikami, K.; Yajima, T.; Takasaki, T.; Matsukawa, S.; Terada, M.; Uchimaru, T.; Maruta, M. *Tetrahedron* **1996**, *52*, 85.

(5) (a) Shinohara, N.; Haga, J.; Yamazaki, T.; Kitazume, T.; Nakamura, S. *J. Org. Chem.* **1995**, *60*. 4363. (b) Yamazaki, T.; Shinohara, N.; Kitazume, T.; Sato, S. *J. Org. Chem.* **1995**, *60*, 8140. (c) Yamazaki, T.; Haga, J.; Kitazume, T. *Chem. Lett.* **1991**, 2171. (d) Yamazaki, T.; Haga, J.; Kitazume, T. *Chem. Lett.* **1991**, 2175.

(6) (a) Yamazaki, T.; Ishikawa, N. *Chem. Lett.* **1985**, 889. (b) Yamazaki, T.; Ishikawa, N.; Iwatsubo, H.; Kitazume, T. *J. Chem. Soc., Chem. Commun.* **1987**, 1340.

(7) (a) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1994**, *35*, 3137. (b) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron: Asym.* **1994**, *5*, 961. (c) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169.

(8) These types of compounds have been synthesized by several groups thus far. (a) Morizawa, Y.; Yasuda, A.; Uchida, K. *Tetrahedron Lett.* **1986**, *27*, 1833. (b) Davis, F. A.; Vishwakarma, L. C.; Billmers, J. M.; Finn, J. *J. Org. Chem.* **1984**, *49*, 3241. (c) Hanamoto, T.; Fuchikami, T. *J. Org. Chem.* **1990**, *55*, 4969.

(9) (a) Evans, D. A.; Nelson, J. V.; Taber, T. R. *Top. Stereochem.* **1982**, *13*, 1. (b) Mukaiyama, T. *Org. React.* **1982**, *28*, 203. (c) Mukaiyama, T. *Pure. Appl. Chem.* **1983**, *55*, 1749. (d) Heathcock, C. H. In *Comprehensive Carbanion Chemistry*; Buncel, E., Durst, T., Eds.; Elsevier: Amsterdam, 1984; part B. (e) Evans, D. A. *Aldrichim. Acta* **1982**, *15*, 23. (f) Masamune, S.; Choy, W. *Aldrichim. Acta* **1982**, *15*, 47.

(10) (a) Bialecki, M.; Vogel, P. *Tetrahedron Lett.* **1994**, *35*, 5213. (b) Sevin, A.-F.; Vogel, P. *J. Org. Chem.* **1994**, *59*, 5920. (c) Myles, D. C.; Danishefsky, S. J. *J. Org. Chem.* **1990**, *55*, 1636.

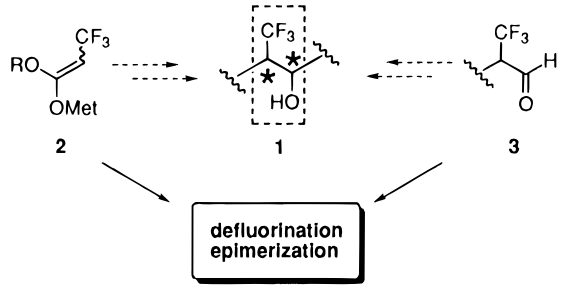
(11) (a) Mikami, K. In *Advances in Asymmetric Synthesis*, Hassner, A., Ed.; JAI: London, 1994; p 1. (b) Mikami, K.; Shimizu, M. *Chem. Rev.* **1992**, *92*, 1021. (c) Snider, B. B. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Ed.; Pergamon, Oxford, 1991; Vol. 2, p 527; Vol 5, p 1.

(12) (a) Yokozawa, T.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1984**, *25*, 3987. (b) Yokozawa, T.; Nakai, T.; Ishikawa, N. *Tetrahedron Lett.* **1984**, *25*, 3991.

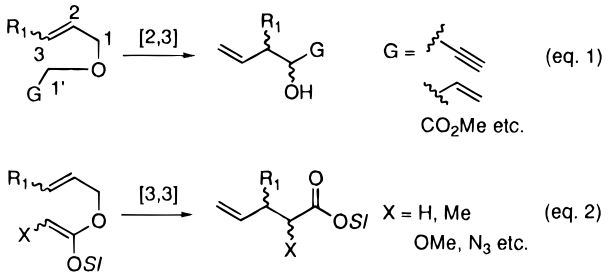
(13) (a) de Nanteuil, G. *Tetrahedron Lett.* **1991**, *32*, 2467. (b) Ojima, I. *J. Organomet. Chem.* **1985**, *279*, 203. (c) Konno, T.; Yamazaki, T.; Kitazume, T. *Tetrahedron* **1996**, *52*, 199.

S0022-3263(96)01246-7 CCC: $14.00

Scheme 1



Scheme 2



the predictable stereochemistry of the products. However, there are surprisingly few applications of these processes to CF_3-containing compounds,[17] possibly for the following reason.

If we apply the above rearrangements to the construction of **1**, we might encounter several difficulties. In the [2,3]-Wittig variant, allyl propargyl ether (G: CH≡C) and bisallyl ether (G: CH_2═CH) would be suitable substrates for our purpose (see eq 1 in Scheme 2) due to the high stereoselection in the nonfluorinated counterpart; however, there exists the following possible problem. Considering the high electron-withdrawing ability of a CF_3 group when introduced as R_1, proton abstraction by a strong base such as *n*-BuLi will proceed at the 1 position preferentially, causing the formation of a difluorodiene via the elimination of fluoride. Increasing the proton's acidity at the 1′ position would prevent this and might be realized by using an ester group as a migrating terminus. Thus the ester enolate [2,3]-Wittig rearrangement should be suitable. In the [3,3]-Ireland−Claisen rearrangement, on the other hand, the following two modes can be considered for the preparation of our desired compounds; (1) X = CF_3, R_1 = an alkoxy group, (2) X = an alkoxy group, R_1 = CF_3. However, the former is not a good choice because it involves the formation of α-CF_3 enolate[12] which, as described above, can easily undergo defluorination. The latter is therefore the substrate of choice. Moreover, employment of chiral secondary allylic alcohols in both reactions might result in the formation of desired chiral materials possessing two consecutive asymmetric centers with a hydroxyl (or equivalent) and a CF_3 group via [1,3]-chirality transfer. Herein, we describe the scope and limitations of the ester enolate [2,3]-Wittig variant of [[γ-(trifluoromethyl)allyl]-oxy]acetate derivatives and the [3,3]-Ireland−Claisen variant of α-methoxyacetic acid γ-(trifluoromethyl)allyl esters in detail, placing emphasis on the development of a new synthetic method for the construction of **1**.

Results and Discussion

Preparation of Substrates for Ester-Enolate [2,3]-Wittig Rearrangement. Prior to the investigation of sigmatropic rearrangements, both reaction paths in eqs 1 and 2 (Scheme 2) require γ-trifluoromethylated allylic alcohols of specific stereochemistry. Thus, γ-trifluoromethylated propargylic alcohols[18] were chosen as starting materials because of their easy stereoselective transformation to both (*E*)- and (*Z*)-allylic alcohols. Furthermore, enzymatic kinetic resolution was selected for the induction of chirality based on its convenience and simultaneous obtention of both enantiomers. After several explorations of reaction conditions using *rac*-**4a** which was prepared according to the literature,[18f] we found that lipase (Novozym 435; *Candida antarctica*, immobilized) in hexane with vinyl acetate preferentially acetylates *S* alcohol (*E* value ≥ 100). Thus, this system allowed us to obtain the unreacted chiral alcohol, (*R*)-**4a**, with the *R* configuration (>99% ee, 45% yield) with 52% conversion. In this reaction, (*S*)-**5a** with 86% ee (47% yield) was also isolated, which was resolved by further enzymatic esterification using the same conditions (>99% ee, 85% yield). The absolute configuration of (*S*)-**5a** was assigned by its conversion into known diacetate (*R*)-**6**, followed by comparison of optical rotation values[19] (Scheme 3). On the other hand, (*R*)-**4b** (99% ee) in Scheme 4 was synthesized by the literature method.[17e,f] We have also attempted the enzymatic resolution of *rac*-**4c** by Lipase PL (*Alcaligenes sp.*; Meito Sangyo Co., Ltd., Japan), effectively affording (*S*)-alcohol (>99% ee, 45% yield) and (*R*)-acetate (81% ee, 51% yield) at 56% conversion (*E* value = 78).[20] The obtained chiral materials, along with racemic propargylic alcohols, were converted into the corresponding allylic alcohols by the method described in the literature,[18f] followed by etherification with bro-

(14) (a) Lutz, R. P. *Chem. Rev.* **1984**, *84*, 206. (b) Overman, L. E. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 579. (c) Ziegler, F. E. *Chem. Rev.* **1988**, *88*, 1423. (d) Bennett, G. B. *Synthesis* **1977**, 589. (e) Ziegler, F. E. *Acc. Chem. Res.* **1977**, *10*, 227.

(15) (a) Nakai, T.; Mikami, K. *Org. React.* **1994**, *46*, 105. (b) Marshall, J. A. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, Chapter 3. (c) Nakai, T.; Mikami, K. *Chem. Rev.* **1986**, *86*, 885. (d) Mikami, K.; Nakai, T. *Synthesis* **1991**, 594. (e) Brückner, R. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol 4, Chapter 4.6. (f) Nakai, T.; Mikami, K.; Sayo, N. *J. Synth. Org. Chem. Jpn.* **1983**, *41*, 100. (g) Hoffmann, R. W. *Angew. Chem., Int. Ed. Engl.* **1979**, *18*, 563.

(16) (a) Pereira, S.; Srebnik, M. *Aldrichim. Acta* **1993**, *26*, 17. (b) Wipf, P. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Oxford, 1991; Vol. 7, Chapter 7.2. (c) Ireland, R. E.; Norbeck, D. W.; Mandel, G. S.; Mandel, N. S. *J. Am. Chem. Soc.* **1985**, *107*, 3285. (d) Ireland, R. E.; Thaisrivongs, S.; Wilcox, C. S. *J. Am. Chem. Soc.* **1980**, *102*, 1155. (e) Rowley, M.; Tsukamoto, M.; Kishi, Y. *J. Am. Chem. Soc.* **1989**, *111*, 2735. (f) Abelman, M. M.; Funk, R. L.; Munger, J. D., Jr. *J. Am. Chem. Soc.* **1982**, *104*, 4030.

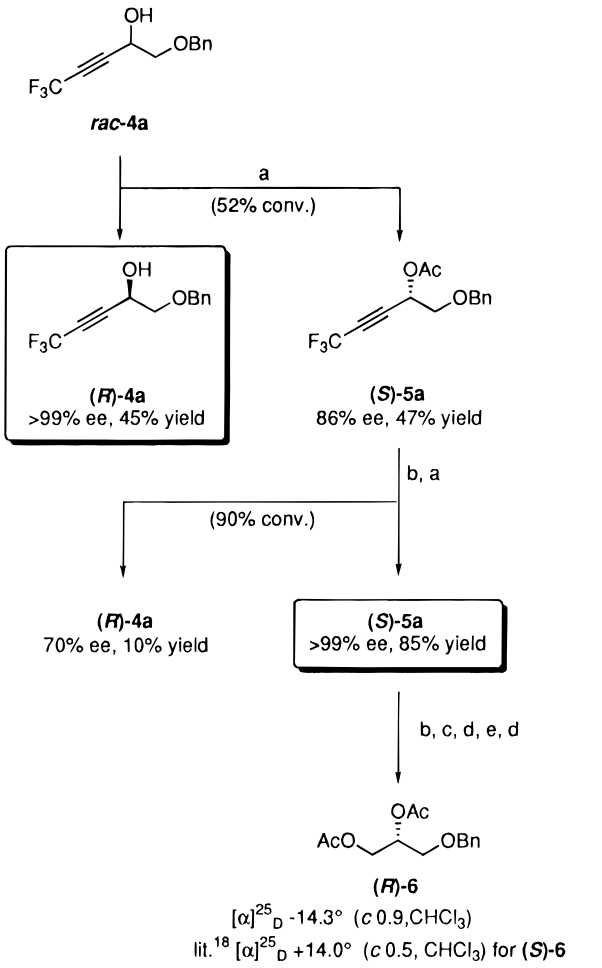
(17) There have been several reports concerning sigmatropic rearrangement of CF_3-containing molecules. (a) Hanzawa, Y.; Kawagoe, K.; Yamada, A.; Kobayashi, Y. *Tetrahedron Lett.* **1985**, *26*, 219. (b) see ref 12b.

(18) Propargyl alcohols with a CF_3 group have been synthesized from 3,3,3-trifluoropropyne. (a) Drakesmith, F. G.; Stewart, O. J.; Tarrant, P. *J. Org. Chem.* **1968**, *33*, 280. (b) Sibous, L.; Tipping, A. E. *J. Fluorine Chem.* **1993**, *62*, 39. (c) Ishihara, T.; Yamasaki, Y.; Ando, T. *Tetrahedron Lett.* **1985**, *26*, 79. (d) Burton, D. J.; Yang, Z.-Y.; Morken, P. A. *Tetrahedron* **1994**, *50*, 2993. Recently, we have reported the convenient as well as reliable method for the preparation of γ-trifluoromethylated propargylic alcohol. (e) Mizutani, K.; Yamazaki, T.; Kitazume, T. *J. Chem. Soc., Chem. Commun.* **1995**, 51. (f) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Org. Chem.* **1995**, *60*, 6046.

(19) Herradon, B.; Cueto, S.; Morcuende, A.; Valverde, S. *Tetrahedron: Asym.* **1993**, *4*, 845.

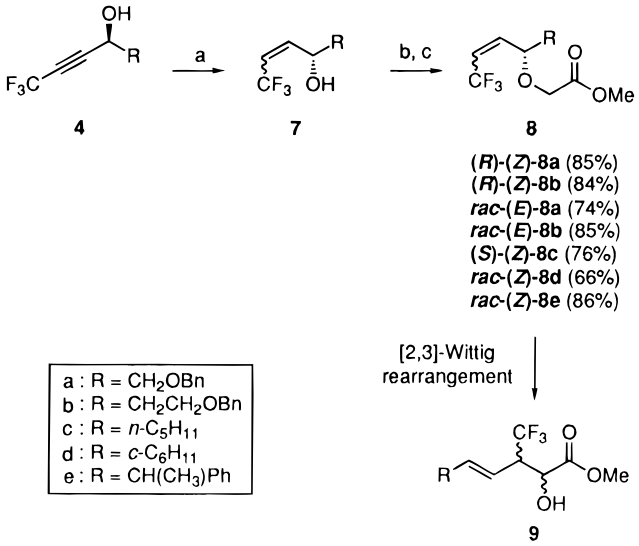
(20) The absolute configurations of (*S*)-**4c** was determined by its transformation into (2*S*)-hexane-1,2-diol. (1. Lindlar cat./H_2. 2. AcCl, Py. 3. O_3, then $(CH_3)_2S$. 4. $NaBH_4$/EtOH. 5. K_2CO_3/MeOH) and comparison of optical rotation value of subsequent diol to an authentic value. Hasegawa, J.; Ogura, M.; Tsuda, S.; Maemoto, S.; Kutsuki, H.; Ohashi, T. *Agric. Biol. Chem.* **1990**, *54*, 1819.

Scheme 3[a]



[a]Reagents: a) Novozym 435, vinyl acetate/hexane b) K_2CO_3/MeOH c) Lindlar cat., H_2/hexane d) AcCl, Py. e) i) O_3, then $(CH_3)_2S$ ii) $NaBH_4$

Scheme 4[a]



[a]Reagents: a) Lindlar cat. / H_2 or Red-Al b) $BrCH_2CO_2H$, NaH c) i) $(COCl)_2$, cat. DMF ii) MeOH, Py.

moacetic acid and esterification, giving substrates in high overall yields (Scheme 4).

Compounds (R = phenyl, furyl, (*E*)-PhCH=CH) could not be prepared such that the allylic hydrogen could be doubly activated by a CF_3 group and a substituent *R*. This might be due to decomposition via sequential abstraction of the allylic hydrogen by NaH and elimination of fluoride in the etherification step.

Table 1. [2,3]-Wittig Rearrangement of (*S*)-(*Z*)-8c[a]

entry	LDA (equiv)	additive	time (h)	yield (%)[b,c]
1	2	–	3	5 (87)[d]
2	2	HMPA	3	80 (12)
3	2	TMEDA	3	3 (68)
4	4	HMPA	3	62 (18)
5	2	HMPA	9	77 (6)
6	1.2	HMPA	<0.2	64[e] (trace)

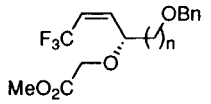
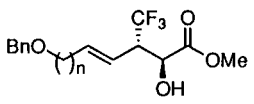
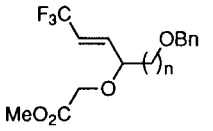
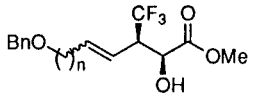
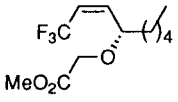
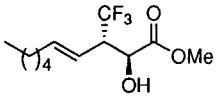
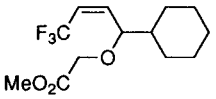
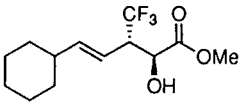
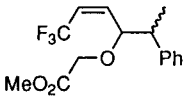
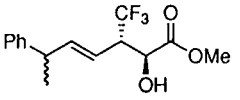
[a] All reactions were performed at −78 °C. [b] Determined by ^{19}F NMR. [c] Unless otherwise noted, in the parentheses, the combined yield of unknown compounds and recovered substrate was shown. [d] The yield of the recovered substrate in the parentheses. [e] Isolated yield.

Investigation of [2,3]-Wittig Rearrangement. With chiral substrates **8** in hand, we began to explore reaction conditions for the [2,3]-Wittig rearrangement. LDA was selected as a representative base and the reaction was performed with (*S*)-(*Z*)-**8c** at −78 °C in THF. As shown in Table 1, it was confirmed that the reaction does not proceed without HMPA and we recovered the starting material quantitatively (87% yield) (entry 1).[21] HMPA was the additive of choice rather than TMEDA (entry 2 vs 3). Employment of more than 2 equiv of LDA increased the amount of unknown products (entry 4), which might be difluorinated compounds because their ^{19}F NMR peaks appeared in the range of 80−85 ppm when hexafluorobenzene was used as an internal standard. On the other hand, the yield was independent of the reaction time (entry 2 vs 5). The order of addition made no difference; addition of the substrate into the mixture of LDA/HMPA/THF and the addition of LDA into the mixture of substrate/HMPA/THF gave the same result. After all, it was revealed that subjection of (*Z*)-α-(allyloxy)acetate (*S*)-(*Z*)-**8c** to 1.2 equiv of LDA in THF at −78 °C in the presence of HMPA as a cosolvent resulted in the rapid (<10 min) formation of α-hydroxy-*β*-(trifluoromethyl)-*γ*,*δ*-unsaturated ester *anti*-**9c** in 64% chemical yield, as the sole detectable isomer (entry 6). Moreover, in this case, the suppression of side products was observed. The obtained material was converted into the corresponding diol, followed by esterification using 2 equiv of MTPA-Cl. The ^{19}F NMR spectrum of this MTPA ester showed only one set of peaks (one doublet and two singlets), while in the racemic counterpart, two sets of peaks were observed in a ratio of 1:1, strongly suggesting that the rearranged product was in an optically pure form and that [1,3]-chirality transfer had occurred completely.

Under the same conditions, compounds **8a**−**e** were transformed into **9a**−**e**, respectively. The results are summarized in Table 2. As depicted in Table 2, no dependence of the stereoselectivity on the side chain R was observed for the *anti* isomers. Thus, when Z isomer was employed as a substrate, *anti* selectivity was not influenced by differences in the bulkiness of side chain R (entry 5 vs 6, 7) or by the existence or position of an oxygen atom in R which might coordinate to metal species (entries 1 and 2). A [2,3]-Wittig shift in (*Z*)-substrates

(21) It has been reported that the ester enolate [2,3]-Wittig rearrangement proceeded smoothly in the presence of HMPA. (a) Takahashi, O.; Sayo, T.; Mikami, K.; Nakai, T. *Chem. Lett.* **1986**, 1599. (b) Takahashi, O.; Maeda, T.; Mikami, K.; Nakai, T. *Chem. Lett.* **1986**, 1355.

Table 2. [2,3]-Wittig Rearrangement

Entry	Substrate	Product	Ds (*anti* : *syn*)[a, b]	Yield (%)[c]
				
1	(*R*)-(*Z*)-**8a** (n = 1)	***anti*-9a** (>98% ee)	>99:1	73
2	(*R*)-(*Z*)-**8b** (n = 2)	***anti*-9b** (>98% ee)	>99:1	78
		 ***syn*-(*E*)-9 or *syn*-(*Z*)-9** + ***anti*-9**		
3	***rac*-(*E*)-8a** (n = 1)		16:84[d]	61
4	***rac*-(*E*)-8b** (n = 2)		14:86[e]	46
5	 (*S*)-(*Z*)-**8c**	 ***anti*-9c** (>98% ee)	>99:1	64
6	 ***rac*-(*Z*)-8d**	 ***anti*-9d**	>99:1	75
7	 ***rac*-(*Z*)-8e**	 ***anti*-9e**	>99:1	85

a) Determined by ^{19}F NMR. b) Unless otherwise noted, *E* selection was obtained exclusively at the newly created olefinic bond. c) Isolated yield. d) The *syn* isomer consisted of *E* and *Z* forms in a ratio of 1:1 . e) The *syn* isomer consisted of *E* and *Z* forms in a ratio of 4:1 .

resulted in exclusive *E* selection at the newly created olefinic bond. In addition, complete transfer of chirality was achieved to obtain highly functionalized trifluoromethylated materials in enantiomerically pure forms. On the other hand, (*E*)-**8a** and **8b** rearranged to give *syn* isomers with lower diastereoselectivity (*syn*:*anti* = *ca.* 6:1). It should be noted that a large influence of the substituent R upon the olefinic configuration was observed, relative to the case of *Z* isomers, and that the *syn* isomer consisted of *E* and *Z* forms in a ratio of 4:1−1:1 (entry 3 vs 4). Generally, it has been reported that enolate [2,3]-Wittig rearrangement in the nonfluorinated system required several hours or more, and that the reaction sometimes was completely only with a raising of temperature.[22] In sharp contrast, the [2,3]-Wittig variant of **8** finished within 10 min even at −78 °C. The driving force for the accelerated rearrangement is probably the decrease of the LUMO energy level of the allylic portion due to the introduction of an electron-withdrawing (CF_3) group.[23]

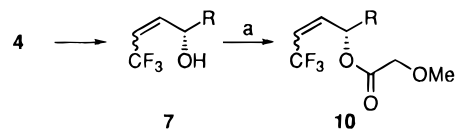
As described above, we have proved the utility of the ester-enolate [2,3]-Wittig rearrangement for the construction of our target structure **1** with a high degree of *anti* selectivity, from starting propargylic alcohols in only three steps. On the other hand, the corresponding *syn* isomers were obtained in about 70% de, which left a problem to be solved.

Examination of [3,3]-Ireland−Claisen Rearrangement. Next, we examined [3,3]-Ireland−Claisen rearrangement as an alternative approach to our target

(22) There have been reported the following reaction conditions. (a) (−78 °C, 22 h) Ender, D.; Backhaus, D.; Runsink, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 2098. (b) (−70 °C, 10 h then −70 → 0 °C) Takahashi, O.; Mikami, K.; Nakai, T. *Chem. Lett.* **1987**, 69. (c) (−35 °C, 2 d) Reetz, M. T.; Griebenow, N.; Goddard, R. *J. Chem. Soc., Chem. Commun.* **1995**, 1605. (d) (−78 °C, 40 min, then −40 °C, 2.7 h) Brückner, R. *Chem. Ber.* **1989**, *122*, 703. (e) (−78 °C, 2 h) Yokomatsu, T.; Yamagishi, T.; Shibuya, S. *Synlett* **1995**, 1035. (f) See ref 21.

(23) There have been some reports concerning an enhancement of the reaction rate and/or the reactivity due to the introduction of a CF_3 substituent. (a) Gassman, P. G.; Harrington, C. K. *J. Org. Chem.* **1990**, *55*, 1813. (b) Creary, X.; Sky, A. E.; Mehrsheikh-Mohammadi, M. E. *Tetrahedron Lett.* **1988**, *29*, 6839. (c) Yamazaki, T.; Hiraoka, S.; Kitazume, T. *J. Org. Chem.* **1994**, *59*, 5100.

Scheme 5[a]



7 10

a : R = CH_2OBn
b : R = CH_2CH_2OBn
c : R = *n*-C_5H_{11}
d : R = *c*-C_6H_{11}

(*R*)-(*Z*)-**10a** : 86%
rac-(*Z*)-**10b** : 88%
(*R*)-(*E*)-**10a** : 91%
rac-(*E*)-**10b** : 87%
(*S*)-(*Z*)-**10c** : 79%
(*S*)-(*E*)-**10c** : 77%
rac-(*Z*)-**10d** : 79%
rac-(*E*)-**10d** : 98%

[a]Reagents : a) $MeOCH_2COCl$, Py

Table 3. Optimization of [3,3]-Ireland−Claisen Rearrangement of (*S*)-(*Z*)-10c

entry[a]	base	method[b]	diastereoselectivity (*anti* (*E*:*Z*):*syn*)[c]	yield (%)[c]
1	LDA	A	96 (95:5):4	73
2	LDA	B	87 (91:9):13	49
3	LHMDS	A	93:7	quant
4	LHMDS	B	96:4	quant
5[d]	LHMDS	B	98 (74:26):2	64

[a] All reaction mixture was stirred at −78 °C for 30 min after the addition of substrate and TMSCl and was allowed to warm to room temperature. [b] Method A: TMSCl was added after the addition of the substrate. Method B: TMSCl was added prior to the addition of the substrate. [c] Determined by ^{19}F NMR using C_6F_6 as an internal standard. [d] TBSCl was employed instead of TMSCl.

molecule. The preparation of substrates for the [3,3]-variant was accomplished by the usual esterification of allylic alcohols with methoxyacetyl chloride (Scheme 5).

First of all, the influence of the base and silyl species used for trapping lithium enolates was investigated by using (*S*)-(*Z*)-**10c**.

Employment of LHMDS instead of LDA as a base increased the chemical yield (entry 1 vs 3 and entry 2 vs 4 in Table 3). When TMSCl was dropped into the enolate solution with LHMDS, a slight decrease in the stereoselectivity was observed relative to the internal trap method (entry 3 vs 4). On the other hand, a large decrease in both the selectivity and chemical yield was seen when substrate was added into the mixture of LDA and TMSCl. Moreover, the *anti* isomer with the *E* configuration at the newly created olefinic bond was obtained as a sole stereoisomer when using LHMDS as a base (entry 3 and 4), while *anti* isomer consisting of *E* and *Z* forms was produced when LDA was used (entry 1 and 2). It should be noted that treatment of lithium enolate with TBSCl instead of TMSCl resulted in decreasing stereoselectivity at the olefinic bond and yield, although a slight increase in the relative stereoselectivity was observed (entry 5). The best result was obtained when the substrate was added to the mixture of LHMDS and TMSCl, which was then stirred at −78 °C for 0.5 h and then allowed to warm to room temperature. After the usual workup, the resultant rearranged products were reduced with $LiAlH_4$ without purification. The optical purities of the obtained alcohols were determined by their conversion to the corresponding Mosher's esters.

As shown in Table 4, (*E*)- or (*Z*)-substrates provided *syn* or *anti* isomers, respectively. High diastereoselection as well as complete transfer of chirality was observed in both isomers; however, the diastereomeric excesses of *syn* isomers were a little higher than those of *anti* isomers, while the reverse phenomenon was observed in the [2,3]-Wittig rearrangement. Furthermore, the stereoselection at the newly created olefinic bond was slightly affected by the bulkiness of side chain R, and *E*:*Z* = 93:7 was obtained for R = cyclohexyl, which is considered to be the bulkiest substituent of those in Table 4 (entry 8). On the other hand, the diastereomeric excesses of *anti* isomers were a little lower than those of [2,3]-Wittig-rearranged products derived from (*Z*)-substrates.

As depicted in the previous section on the [2,3]-Wittig rearrangement, a similar phenomenon was observed for the reaction rate. Generally, it is known that the rearrangement is almost completed by heating the reaction mixture (50−80 °C), although Koreeda et al. have reported that an "anionic oxy-Ireland−Claisen shift", in which lithium enolate was not trapped by silyl species, was completed even at very low temperature due to an increase in the vinylic HOMO energy level.[24] In our system, the reaction might proceed efficiently even at room temperature because of the decrease of the LUMO energy level in the allylic group derived from a CF_3 moiety.

Clarification of the Stereochemistry. The relative stereochemistry was determined as outlined in Scheme 6. The stereostructure of *anti*-**9c** was confirmed after its conversion to cyclic acetal **13**. Thus, *anti*-**9c** was transformed into alcohol **12** by the method described in Scheme 6. Ozonolysis of **12** and the following reduction furnished the corresponding diol, which was treated with dimethoxypropane and a catalytic amount of PPTS to give acetonide **13**. Careful analysis of the ^1H NMR spectrum of **13** established the vicinal coupling constant between Ha and Hb to be 9.83 Hz, strongly suggesting its *anti* relative stereochemistry.

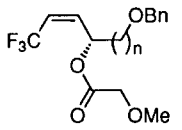
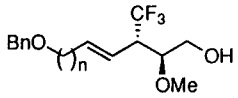
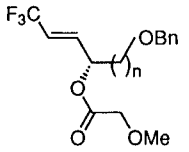
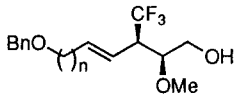
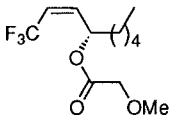
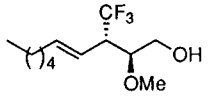
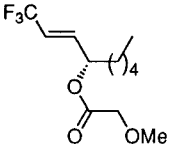
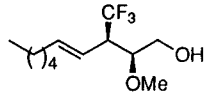
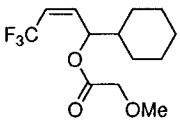
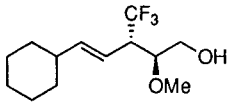
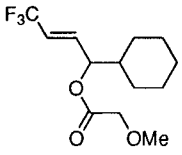
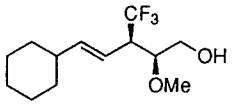
On the other hand, methylation of an α-hydroxyl group of *anti*-**9a**−**e** with Ag_2O/MeI was followed by reduction to give *anti*-**11a**−**e**, whose spectral data (except for **11e**) were consistent with those of the alcohols obtained via [3,3]-Ireland−Claisen rearrangement of (*Z*)-isomers **10a**−**d**. Ozonolysis of *anti*-**11a**−**e** and the reduction of the resultant aldehydes furnished the same materials **14**, indicating that the relative stereochemistry of [2,3]-Wittig- and [3,3]-Claisen-rearranged products derived from *Z* substrates was the same, i.e. *anti*. Furthermore, the chiral compounds possess the same absolute configuration by comparison of their optical rotation values.

The determination of the absolute stereochemistry was carried out as described in Scheme 7. Reduction of *anti*-**9c** and hydrogenation under 10 atm afforded the corresponding diol **15**. This material was treated with $Pb(OAc)_4$ to give the aldehyde, which was further reduced with $LiAlH_4$ without purification. Conversion of **16** to the corresponding bromide was accomplished with CBr_4/PPh_3, followed by an S_N2 reaction by thiolate, affording the desired compound **17**.

On the other hand, reduction of **18**[6] and Swern oxidation of the resultant alcohol led to aldehyde **19** which underwent successive Wittig reaction and hydrogenation to furnish **17**. By comparison of optical rotation values of **17** and from the result described in Scheme 6, the absolute configurations of *anti*-**9a**−**c** and *anti*-**11a**,**c** were determined as (2*S*,3*R*). A significant decrease of the optical rotation value of **17** relative to that of *anti*-**9c** was

(24) Koreeda, M.; Luengo, J. I. *J. Am. Chem. Soc.* **1985**, *107*, 5572.

Table 4. [3,3]-Ireland−Claisen Rearrangement

Entry	Substrate	Product	Ds (*anti* : *syn*)[a, b]	Yield (%)[c]
1	 (*R*)-(*Z*)-**10a** (n=1)	 ***anti*-11a** (>98% ee)	97:3	68
2	***rac*-(*Z*)-10b** (n=2)	***anti*-11b**	98:2	81
3	 (*R*)-(*E*)-**10a** (n=1)	 ***syn*-11a** (>98% ee)	1:>99	59
4	***rac*-(*E*)-10b** (n=2)	***syn*-11b**	1:>99	61
5	 (*S*)-(*Z*)-**10c**	 ***anti*-11c** (>98% ee)	96:4	75
6	 (*S*)-(*E*)-**10c**	 ***syn*-11c** (>98% ee)	1:>99	67
7	 ***rac*-(*Z*)-10d**	 ***anti*-11d**	97:3	80
8	 ***rac*-(*E*)-10d**	 ***syn*-11d**	1:>99[d]	64

a) Determined by ^{19}F NMR. b) Unless otherwise noted, *E* isomers were obtained exclusively. b) Isolated yield.
c) The *syn* isomer consisted of *E* and *Z* forms in a ratio of 93:7.

observed because partial epimerization occurred in the oxidative cleavage of **15**.[25]

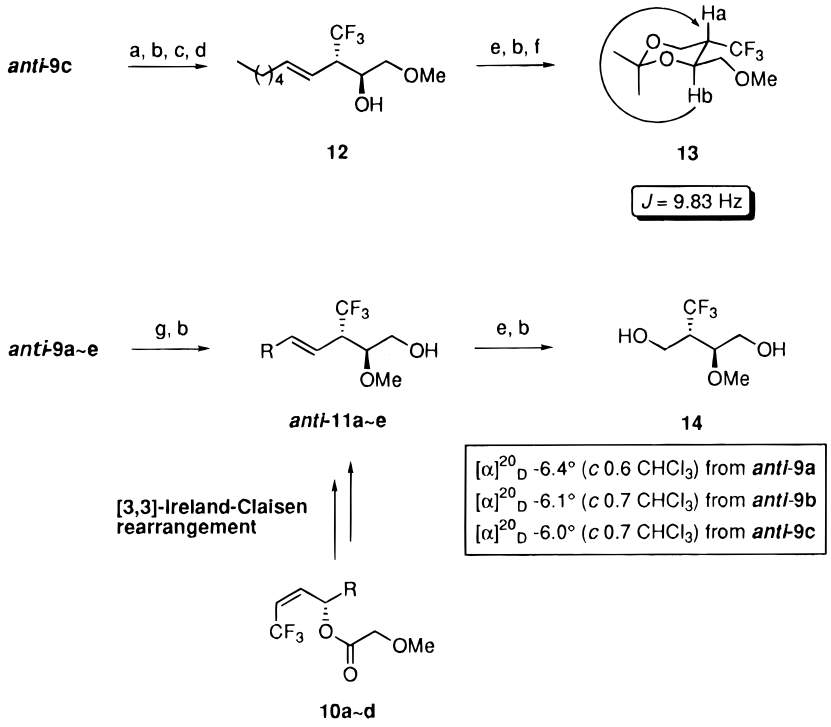
On the other hand, *syn*-**11c** was transformed into the enantiomeric **16** by the same method described above (Scheme 8). Moreover, ozonolysis of *syn*-**11a**−**c** and the following reduction provided the same compound **20** which is the diastereomer of **14**. From these results, the relative configuration of *syn*-**11a**−**c** was proven to be *syn*, and the absolute stereochemistry of *syn*-**11a** and **11c** were determined to be (2*S*,3*S*).

Mechanism. The mechanism of the [2,3]-Wittig rearrangement has been represented thus far by the postulate that the reaction proceeds via the five-membered envelopelike transition state suggested by Nakai,[13,26] Houk,[27] and Brückner.[28] Generally, it has been accepted that the stereoselective sense of the ester enolate [2,3]-Wittig shift is opposite to that of the reaction that involves an alkynyl group, an alkenyl group, and so on (except for a carbonyl moiety) as a migrating terminus. It is Houk's model at present that could explain not only the general trends of the stereoselectivities for bisallyl ether and/or allyl propargyl ether but also the exception of the enolate [2,3]-Wittig shift (Figure 1). Thus, in the

(25) It has already been reported that, in the preparation of α-CF_3 aldehyde, reaction under acidic condition gave optically active compound, whereas complete epimerization was observed even under such weakly basic condition as aqueous $NaHCO_3$, see ref 13c.

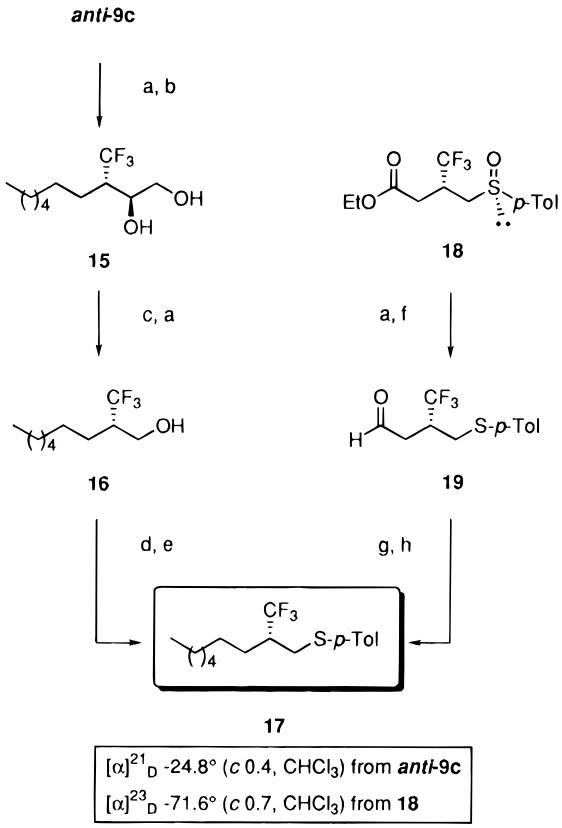
(26) Mikami, K.; Kimura, Y.; Kishi, N.; Nakai, T. *J. Org. Chem.* **1983**, *48*, 281.
(27) Wu, Y.-D.; Houk, K. N.; Marshall, J. A. *J. Org. Chem.* **1990**, *55*, 1421.
(28) (a) Priepke, H.; Brückner, R. *Chem. Ber.* **1990**, *123*, 153. (b) Brückner, R. *Chem. Ber.* **1989**, *122*, 703. (c) Priepke, H.; Brückner, R. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 278. (d) Scheuplein, S. W.; Kusche, A.; Brückner, R.; Harms, K. *Chem. Ber.* **1990**, *123*, 917.

Scheme 6[a]



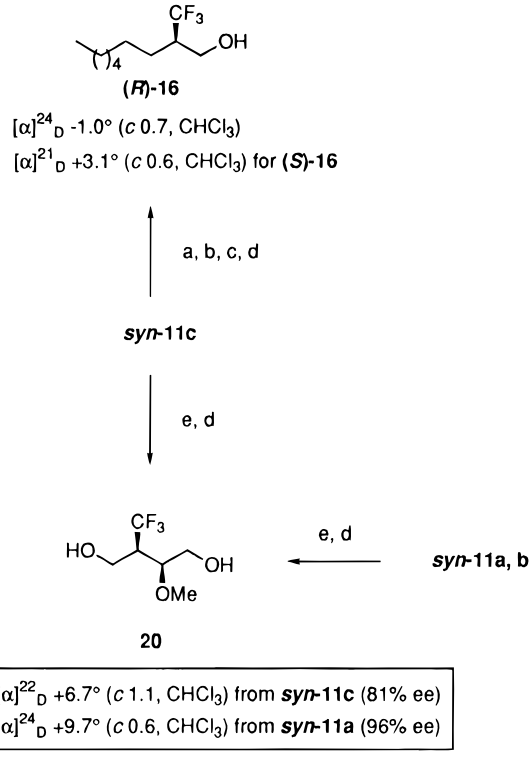
[a]Reagents: a) Ethyl vinyl ether, PPTS b) $LiAlH_4$ c) MeI, NaH d) TsOH, MeOH e) O_3 / MeOH then Me_2S f) $CH_3C(OCH_3)_2CH_3$, PPTS g) Ag_2O, MeI

Scheme 7[a]



[a]Reagents: a) $LiAlH_4$ b) Raney Ni, H_2, 10 atom c) $Pb(OAc)_4$ d) CBr_4, PPh_3 e) *p*Tol-S^-Na^+ f) $(COCl)_2$, DMSO, Et_3N g) $[n\text{-}C_5H_{11}P^+Ph_3]\ I^-$ h) Pd / C, H_2, 10 atom

Scheme 8[a]



[a]Reagents: a) Raney Ni, H_2, 10 atom b) BBr_3 c) $Pb(OAc)_4$ d) $LiAlH_4$ e) O_3 / MeOH, then Me_2S

"early" transition state calculated by Houk et al., the Hb−G(exo) distance is much shorter than the Ha−G(endo) distance. Accordingly, it is expected that the migrating terminus G might occupy the endo position. On the other hand, a negative charge develops at C1 in the transition state. Consequently, an endo π-acceptor substituent should stabilize the transition state, while an endo

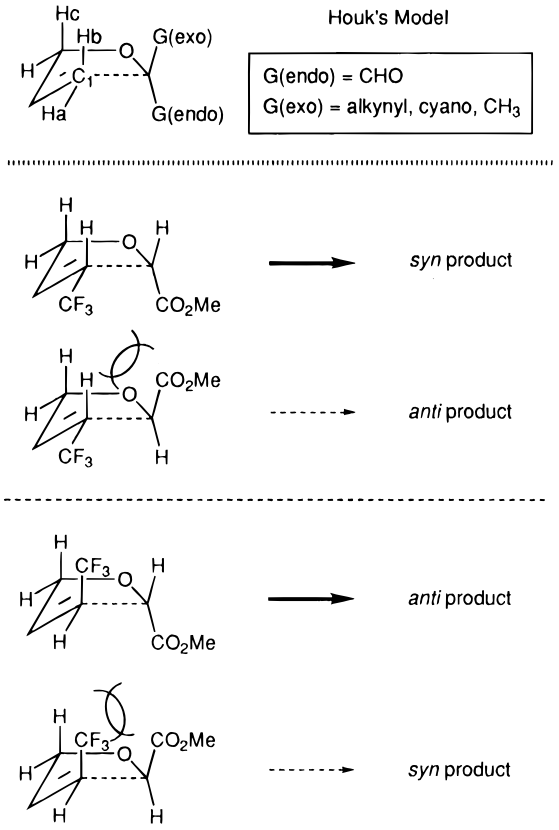


Figure 1.

π-donor should destabilize the transition state. Therefore, an alkynyl group, a cyano group and so on might occupy the exo position, while a formyl group might occupy the endo position. Then, in the ester-enolate [2,3]-Wittig rearrangement, (*E*)-substrate (Ha = H, Hb ≠ H) might give *syn* isomer, while (*Z*)-substrate (Ha ≠ H, Hb = H) might produce *anti* isomer.[29] In the present study, the hypothesis is applicable. Considering the bulkiness of a CF_3 group,[30] it is highly possible that in the transition state derived from (*Z*)-substrates, a CO_2Me group might occupy the endo position which is antiperiplanar to a CF_3 group. This would be because the endo occupation is considered to be doubly favorable from the viewpoint of the steric as well as electrostatic interaction. Thus, a CO_2Me group might not occupy the exo position due to the large gauche repulsion with a CF_3 group and no stabilization of the negative charge at C1. Therefore, the (*Z*)-isomer gives *anti* product in a highly stereoselective manner. In the transition state derived from (*E*)-substrates, on the other hand, the bulkiness of a CF_3 group might result in the destabilization of its endo positioning due to severe gauche repulsion between a CF_3 and a CO_2Me group, leading to the decrease in *syn* stereoselection. In addition, it is deduced that the Hb−CHO(exo) gauche repulsion is larger than the 1,3-diaxial interaction between a substituent R (Hc = R) and Hb from the experimental result obtained with the *syn-Z* product.[31,32]

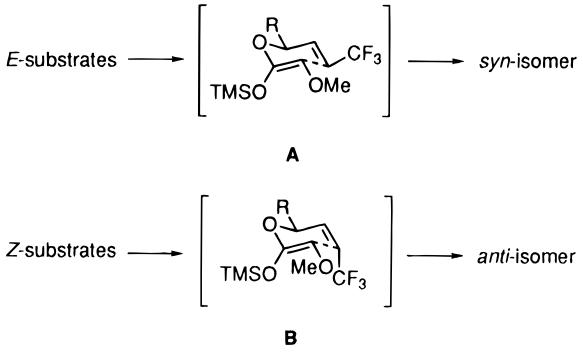


Figure 2.

Concerning the mechanism for the [3,3]-Ireland−Claisen variant, on the other hand, the postulate suggested for hydrocarbon chemistry is applicable to our system. Thus, it might be unambiguous that this rearrangement proceeded via a six-membered transition state in which a lithium atom coordinates to an oxygen atom of a methoxy group to afford (*Z*)-ketene silyl acetal preferentially (Figure 2).[33] In the six-membered transition state **A** or **B** derived from *E* or *Z* isomer, a CF_3 group, considered to be sterically similar to an isopropyl group,[30] might occupy the equatorial or axial position, respectively. The bulkiness of a CF_3 group might result in the destabilization of transition state **B** due to 1,3-diaxial interaction between the CF_3 group and hydrogen atom, causing a decrease of *anti* stereoselectivity.

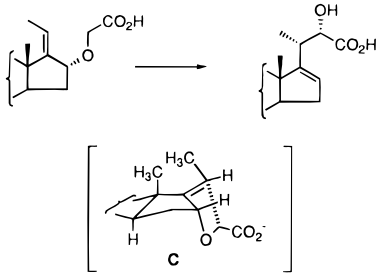
Summary

In conclusion, we have investigated ester-enolate [2,3]-Wittig and [3,3]-Ireland−Claisen rearrangements of various types of substrates, including chiral materials obtained by extremely effective enzymatic kinetic resolution. As described above, it was revealed that the [2,3]-Wittig shift is effective for the preparation of *anti* isomers in

(29) In the enolate [2,3]-Wittig rearrangement without transition metal species, high *syn* selection using *E*-substrate (low *anti* selection using *Z*-substrate) has been reported. For example, see the following reference. Uchikawa, M.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 4581. There have been several examples that ester-enolate [2,3]-Wittig shift of *Z* substrate showed high *anti* stereoselection. See ref 28.

(30) Bott, G.; Field, L. G.; Sternhell, S. *J. Am. Chem. Soc.* **1980**, *102*, 5618.

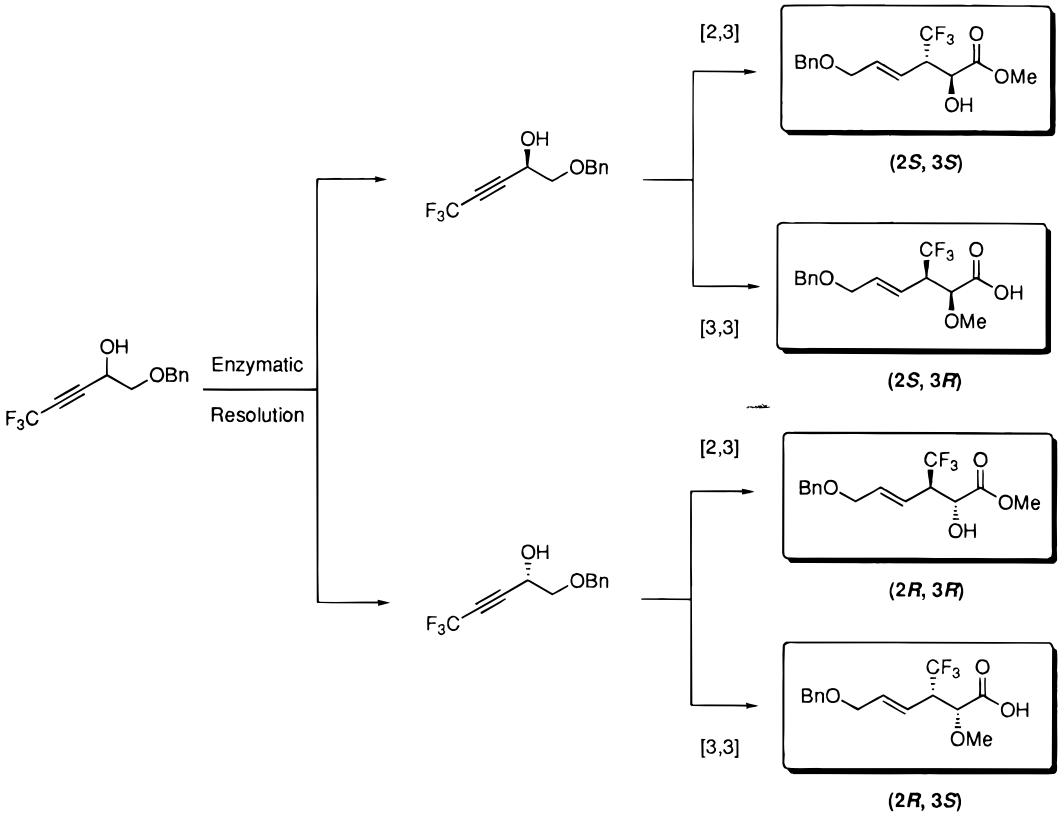
(31) Koreeda et al. have been reported that the following substrate gave *anti* isomer in a highly stereoselective fashion. The unusual selectivity has been explained by the envelope-like transition state **C** suggested by Rautenstrauch (Koreeda, M.; Ricca, D. *J. Org. Chem.* **1986**, *51*, 4090.)



(32) We have already performed *ab initio* calculation (3-21G full optimization) of the transition state derived from CF_3-containing (*E*)- or (*Z*)-substrate. It was supposed that HMPA employed as a cosolvent might be a scavenger for lithium cation. Therefore, the transition state without this cation was calculated which is different from Houk's one. As a result, (*Z*)-substrate affords *anti* product in a highly stereoselective manner, while (*E*)-substrate also provides *anti* isomer stereoselectively. Furthermore, surprisingly, the second stable TS derived from (*E*)-isomer is the one which might produce *anti* isomer possessing *Z* configuration at the newly created olefinic bond.

(33) (a) Burke, S. D.; Fobare, W. F.; Pacofsky, G. J. *J. Org. Chem.* **1983**, *48*, 5221. (b) Gould, T. J.; Balestra, M.; Wittman, M. D.; Gary, J. A.; Rossano, L. T.; Kallmerten, J. *J. Org. Chem.* **1987**, *52*, 3889. (c) Kallmerten, J.; Gould, T. J. *Tetrahedron Lett.* **1983**, *24*, 5177. (d) Bartlett, P. A.; Tanzella, D.; Barstow, J. F. *J. Org. Chem.* **1982**, *47*, 3941.

Scheme 9



optically as well as diastereomerically pure forms, while this transformation furnishes lower selectivity in the formation of the corresponding *syn* isomers. On the other hand, the [3,3]-Ireland−Claisen shift was found to play a complementary role and furnishes the structurally equivalent **11** as a single product. Thus, these processes enable us to provide all stereoisomers of very useful synthetic intermediates which possess a variety of chemically distinguishable functionalities (an allylic alcohol, a hydroxyl, and a carboxyl moiety) (Scheme 9).

Experimental Section

General.[18f] Gas liquid chromatography (GLC) was performed using Silicone GE XE-60 or ULBON HR-20M on Chromosorb W, 30 m × 3 mm. NMR patterns of minor isomers are the same as those of major one, with an exception of signals indicated.

General Procedure for Enzymatic Transesterification. To a 0.17 M solution of a racemic propargylic alcohol *rac*-**4** (4.03 mmol) in *n*-hexane (24 mL) were added vinyl acetate (8.10 mL, 97.4 mmol) and an enzyme, and the whole was stirred at 30 °C for 24 h. After removal of the residue by filtration and concentration of this solution, separation by silica gel column chromatography afforded an optically active alcohol and an ester. The enantiomeric excess was determined by capillary GC after derivatization into the corresponding MTPA esters.

(3*R*)-4-(Benzyloxy)-1-(trifluoromethyl)-1-butyn-3-ol ((*R*)-4a). Yield: 45% (0.445 g, 1.82 mmol). Novozym 435 (0.984 g, 6888 PLU; Novo Nordisk, Denmark) was employed as an enzyme. Physical properties of this compound were the same as the ones described in the literature[18f] except for the optical rotation. $[\alpha]^{27}_D = -2.4$ (*c* 1.0, $CHCl_3$) (>99% ee).

(3*S*)-3-Acetoxy-4-(benzyloxy)-1-(trifluoromethyl)-1-butyne ((*S*)-5a). Yield: 47% (0.545 g, 1.90 mmol). ^{1}H NMR ($CDCl_3$) δ 2.14 (3 H, s), 3.71 (1 H, dd, J = 4.88, 10.74 Hz), 3.74 (1 H, dd, J = 6.11, 10.74 Hz), 4.58 (1 H, d, J = 12.21 Hz), 4.63 (1 H, d, J = 12.20 Hz), 5.60−5.66 (1 H, m), 7.20−7.40 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 20.45, 61.58 (q, J = 2.7 Hz), 69.58 (q, J = 1.4 Hz), 73.32, 82.26 (q, J = 6.6 Hz), 113.63 (q, J = 257.9 Hz), 127.66, 127.96, 128.45, 137.05, 169.25. ^{19}F NMR ($CDCl_3$) δ 110.863 (s). IR (neat) ν 3067, 3035, 2940, 2869, 2282, 1756. $[\alpha]^{28}_D = +40.9$ (*c* 1.2, $CHCl_3$) (86% ee). Anal. Calcd for $C_{14}H_{13}O_3F_3$: C, 58.74; H, 4.58. Found: C, 58.36; H, 4.80.

(3*S*)-1-(Trifluoromethyl)-1-octyn-3-ol ((*S*)-4c). Yield: 45% (0.353 g, 1.82 mmol). Lipase PL (0.548 g, 49320 U; *Alcaligenes* sp. Meito Sangyo Co., Lid., Japan) was employed as an enzyme. Physical properties of this compound were the same as the ones described in the literature[18f] except for the optical rotation. $[\alpha]^{14}_D = -4.1$ (*c* 0.8, $CHCl_3$) (>99% ee).

(3*R*)-3-Acetoxy-1-(trifluoromethyl)-1-octyne. Yield: 51% (0.484 g, 2.05 mmol). ^{1}H NMR ($CDCl_3$) δ 0.90 (3 H, t, J = 6.84 Hz), 1.30−1.50 (6 H, m), 1.70−1.90 (2 H, m), 2.11 (3 H, s), 5.86 (1 H, tq, J = 2.93, 5.86 Hz). ^{13}C NMR ($CDCl_3$) δ 13.80, 20.61, 22.32, 24.34, 31.05, 33.62, 62.48, 72.09 (q, J = 53.0 Hz), 84.66 (q, J = 6.4 Hz), 113.83 (q, J = 257.6 Hz), 169.53. ^{19}F NMR ($CDCl_3$) δ 11.14 (d, J = 3.05 Hz). IR (neat) ν 2950, 2934, 2864, 2274, 1753. $[\alpha]^{15}_D = +50.8$ (*c* 0.7, $CHCl_3$) (81% ee).

Determination of Stereochemistry of (*S*)-5a. A solution of (*S*)-**5a** (0.95 g, 3.32 mmol) and K_2CO_3 (2.29 g, 16.6 mmol) in methanol (15 mL) was stirred at room temperature for 1 h and then evaporated in *vacuo*. After complete removal of methanol, the crude oil was diluted with ether and the whole was washed with water and brine, dried over anhydrous $MgSO_4$, and then evaporated. The resulting materials were purified by silica gel column chromatography to furnish the propargyl alcohol, which was converted into the corresponding allylic alcohol by the same method as described in the literature.[18] To a solution of the obtained allylic alcohol and acetyl chloride (0.22 mL, 3.16 mmol) in CH_2Cl_2 (10 mL) was added pyridine (0.25 mL, 3.16 mL) at 0 °C, and then the whole was allowed to warm to room temperature and stirred for 2 h. The reaction was quenched with 3 N aqueous HCl, and the mixture was extracted with CH_2Cl_2. The organic layer was washed with water, dried over anhydrous $MgSO_4$, and then evaporated to give crude materials which were treated with ozone at −78 °C in methanol for 30 min. Dimethyl sulfide (1.0 mL) was added to the reaction mixture, and the whole was stirred at that temperature for 30 min and then allowed to warm to room temperature and stirred for 30 min. After

removal of solvent, the obtained crude materials were immediately reduced with $NaBH_4$ (0.076 g, 2.0 mmol) in ethanol (5 mL) (rt, 30 min). Usual workup gave the crude materials which were purified by silica gel column chromatography to afford the alcohol which was acetylated by the usual method (AcCl, 0.102 mL, 1.43 mmol; pyridine, 0.116 mL, 1.43 mmol) to give the desired compound (0.25 g, 0.95 mmol).

(2*R*)-1,2-Diacetoxy-3-(benzyloxy)propane ((*R*)-6). Yield: 29%. Physical properties of this compound were the same as the ones described in the literature[19] except for the optical rotation. $[\alpha]^{25}_D = -14.3$ (*c* 0.9, $CHCl_3$).

Determination of Stereochemistry of (*S*)-4c. Chiral propargyl alcohol (*S*)-**4c** (0.68 g, 3.51 mmol) was converted into (*S*)-2-acetoxyheptan-1-ol (0.23 g, 1.45 mmol) by the same method as described in the determination of stereochemistry of (*S*)-**5a** (1. Partial hydrogenation by Lindlar cat./H_2. 2. Acetylation. 3. Ozonolysis. 4. Reduction by $NaBH_4$). A solution of the obtained alcohol and K_2CO_3 (0.629 g, 4.55 mmol) in methanol (10 mL) was stirred at room temperature for 30 min, and usual workup gave the diol (0.12 g, 0.91 mmol). (*S*)-1,2-Heptanediol. Yield: 26%. Physical properties of this compound were the same as the ones described in the literature[20] except for the optical rotation. $[\alpha]^{15}_D = -11.9$ (*c* 0.8, MeOH).

General Procedure of the Preparation for Substrates of [2,3]-Wittig Rearrangement. To a suspension of NaH (ca. 0.16 g, 4 mmol) in THF (10 mL) was added dropwise a solution of allylic alcohol (2 mmol) in THF (5 mL) at 0 °C which was prepared from the corresponding propargyl alcohol by the same method as described in the literature,[18f] and the mixture was stirred for 10 min. To this was added a solution of bromoacetic acid (0.278 g, 2 mmol) in THF (5 mL) at 0 °C. The reaction mixture was stirred overnight at room temperature and poured into ice-cooled water. The organic layer was extracted with 1 N aqueous NaOH three times, the combined aqueous layers were acidified with 3 N HCl, and the whole was extracted with ether three times. The organic solution was dried over anhydrous $MgSO_4$, and then evaporated. To a solution of crude carboxylic acid in CH_2Cl_2 (10 mL) were added $(COCl)_2$ (0.349 mL, 4.0 mmol) and a catalytic amount of DMF (two drops) at 0 °C, and the mixture was stirred overnight at ambient temperature. The solvent and an excess amount of $(COCl_2)$ were removed under reduced pressure, to this were added CH_2Cl_2 (10 mL), MeOH (1 mL), and pyridine (0.34 mL, 4.19 mmol) at 0 °C, and the reaction mixture was stirred overnight at room temperature, poured into 3 N aqueous HCl, and extracted with CH_2Cl_2 three times. The organic extracts were dried over anhydrous $MgSO_4$ and evaporated. The residue was purified by silica gel column chromatography to afford the ester.

(4*R*)-Methyl (*Z*)-6-(Trifluoromethyl)-3-oxa-4-[(benzyloxy)methyl]-5-hexenoate ((*R*)-(*Z*)-8a). Yield: 85%. R_f = 0.34 (hexane:CH_2Cl_2 = 1:3). ^{1}H NMR ($CDCl_3$) δ 3.62 (1 H, dd, J = 4.15, 10.74 Hz), 3.65 (1 H, dd, J = 5.38, 10.50 Hz), 3.74 (3 H, s), 4.12 (1 H, d, J = 16.60 Hz), 4.18 (1 H, d, J = 16.61 Hz), 4.57 (1 H, d, J = 12.21 Hz), 4.60 (1 H, d, J = 12.20 Hz), 4.6−4.7 (1 H, m), 5.84 (1 H, ddq, J = 0.98, 7.57, 11.96 Hz), 6.05 (1 H, dd, J = 9.52, 11.96 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 51.64, 66.35, 71.92, 73.25, 75.03, 121.57 (q, J = 34.2 Hz), 122.44 (q, J = 272.2 Hz), 127.46, 127.54, 128.22, 137.69, 139.07 (q, J = 5.1 Hz), 170.26. ^{19}F NMR ($CDCl_3$) δ 103.98 (d, J = 9.16 Hz). IR (neat) ν 3065, 3033, 3006, 2925, 2916, 2863, 1758, 1676. $[\alpha]^{16}_D = -36.7$ (*c* 0.8, $CHCl_3$). Anal. Calcd for $C_{15}H_{17}O_4F_3$: C, 56.60; H, 5.38. Found: C, 56.44; H, 5.61.

Methyl (*E*)-6-(Trifluoromethyl)-3-oxa-4-[(benzyloxy)methyl]-5-hexenoate (*rac*-(*E*)-8a). Yield: 74%. ^{1}H NMR ($CDCl_3$) δ 3.58 (1 H, dd, J = 4.52, 10.14 Hz), 3.63 (1 H, dd, J = 6.23, 10.13 Hz), 3.73 (3 H, s), 4.18 (1 H, d, J = 16.36 Hz), 4.25 (1 H, d, J = 16.36 Hz), 4.2−4.3 (1 H, m), 4.55 (1 H, d, J = 12.21 Hz), 4.58 (1 H, d, J = 11.96 Hz), 6.00 (1 H, ddq, J = 1.57, 6.47, 15.75 Hz), 6.35 (1 H, ddq, J = 2.06, 5.37, 15.87 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 51.68, 66.99, 71.79, 73.34, 77.82, 120.60 (q, J = 34.1 Hz), 122.72 (q, J = 269.4 Hz), 127.55, 127.69, 128.32, 137.56, 136.63 (q, J = 6.2 Hz) 170.35. ^{19}F NMR ($CDCl_3$) δ 97.42 (d, J = 6.10 Hz). IR (neat) ν 3066, 3032, 2956, 2910, 2865, 1757, 1685.

(4*R*)-Methyl (*Z*)-6-(Trifluoromethyl)-3-oxa-4-[2-(benzyloxy)ethyl]-5-hexenoate ((*R*)-(*Z*)-8b). Yield: 84%. R_f = 0.25 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 1.85 (1 H, ddt, J = 5.86, 7.08, 13.43 Hz), 2.00 (1 H, ddt, J = 5.86, 8.06, 13.92 Hz), 3.59 (1 H, dt, J = 6.11, 9.77 Hz), 3.66 (1 H, ddd, J = 5.86, 7.57, 9.52 Hz), 3.73 (3 H, s), 3.98 (1 H, d, J = 16.11 Hz), 4.06 (1 H, d, J = 16.36 Hz), 4.48 (1 H, d, J = 11.96 Hz), 4.52 (1 H, d, J = 11.72 Hz), 4.54−4.60 (1 H, m), 5.79 (1 H, ddq, J = 0.73, 8.79, 11.72 Hz), 5.95 (1 H, dd, J = 9.77, 11.72 Hz). ^{13}C NMR ($CDCl_3$) δ 35.14, 51.68, 65.69, 66.10, 72.77, 73.04, 120.69 (q, J = 34.4 Hz), 122.57 (q, J = 272.9 Hz), 127.41, 127.51, 128.23, 138.30, 141.97 (q, J = 4.7 Hz), 170.31. ^{19}F NMR ($CDCl_3$) δ 104.28 (d, J = 7.63 Hz). IR (neat) ν 2957, 2867, 1750. $[\alpha]^{15}_D = -17.7$ (*c* 0.7, $CHCl_3$). HRMS calcd for $C_{16}H_{19}O_4F_3$ 332.1235. Found 332.1240.

Methyl (*E*)-6-(Trifluoromethyl)-3-oxa-4-[2-(benzyloxy)ethyl]-5-hexenoate (*rac*-(*E*)-8b). Yield: 85%. R_f = 0.21 (hexane:EtOAc = 3:1). ^{1}H NMR ($CDCl_3$) δ 1.86 (1 H, ddt, J = 5.12, 7.82, 13.97 Hz), 1.96 (1 H, dddd, J = 5.13, 5.96, 8.06, 12.94 Hz), 3.55 (1 H, dt, J = 5.61, 9.52 Hz), 3.68 (1 H, ddd, J = 4.63, 7.56, 9.27 Hz), 3.74 (3 H, s), 4.60 (1 H, d, J = 16.11 Hz), 4.10 (1 H, d, J = 16.11 Hz), 4.13−4.19 (1 H, m), 4.48 (1 H, d, J = 11.72 Hz), 5.85 (1 H, ddq, J = 1.22, 6.34, 15.86 Hz), 6.29 (1 H, ddq, J = 1.95, 6.35, 15.87 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 35.00, 51.76, 65.57, 72.96, 76.34, 119.80 (q, J = 34.0 Hz), 122.67 (q, J = 269.7 Hz), 127.60, 127.68, 128.32, 138.14, 139.29 (q, J = 6.0 Hz). ^{19}F NMR ($CDCl_3$) δ 97.55 (d, J = 6.11 Hz). IR (neat) ν 3089, 3066, 3032, 2955, 2926, 2865, 1751, 1684. HRMS calcd for $C_{12}H_{19}O_3F_3$ 332.1235. Found 332.1237.

(4*S*)-Methyl (*Z*)-6-(Trifluoromethyl)-3-oxa-4-pentyl-5-hexenoate ((*S*)-(*Z*)-8c). Yield: 76%. R_f = 0.47 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 6.96 Hz), 1.3−1.8 (8 H, m), 3.75 (3 H, s), 4.01 (1 H, d, J = 16.36 Hz), 4.08 (1 H, d, J = 16.36 Hz), 5.79 (1 H, dq, J = 8.47, 11.97 Hz), 5.89 (1 H, dd, J = 9.76, 11.96 Hz). ^{13}C NMR ($CDCl_3$) δ 13.83, 22.37, 24.38, 31.49, 34.87, 51.64, 65.94, 75.68, 120.73 (q, J = 34.2 Hz), 122.62 (q, J = 272.1 Hz), 142.48 (q, J = 5.4 Hz), 170.44. ^{19}F NMR ($CDCl_3$) δ 104.40 (d, J = 9.15 Hz). IR (neat) ν 2958, 2935, 2863, 1760, 1671. $[\alpha]^{14}_D = -33.2$ (*c* 0.7, $CHCl_3$). HRMS calcd for $C_{12}H_{19}O_3F_3$ 268.1286. Found 268.1293.

Methyl (*Z*)-6-(Trifluoromethyl)-3-oxa-4-cyclohexyl-5-hexenoate (*rac*-(*Z*)-8d). Yield: 66%. R_f = 0.60 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 0.9−2.1 (11 H, m), 3.73 (3 H, s), 3.98 (1 H, d, J = 16.36 Hz), 4.07 (1 H, d, J = 16.60 Hz), 4.05−4.10 (1 H, m), 5.7−5.9 (2 H, m). ^{13}C NMR ($CDCl_3$) δ 25.73, 25.86, 26.24, 28.24, 28.64, 42.03, 51.49, 65.76, 79.60, 121.69 (q, J = 33.9 Hz), 122.58 (q, J = 272.0 Hz), 140.99 (q, J = 4.8 Hz), 170.47. ^{19}F NMR ($CDCl_3$) δ 104.83 (d, J = 7.63 Hz). IR (neat) ν 3004, 2932, 2856, 1760, 1670. HRMS calcd for $C_{13}H_{19}O_3F_3$ 280.1286. Found 280.1258.

Methyl (*Z*)-6-(Trifluoromethyl)-3-oxa-4-(1-phenylethyl)-5-hexenoate (*rac*-(*Z*)-8e). Yield: 86%. R_f = 0.32 (hexane:CH_2Cl_2 = 1:1). Diastereoselectivity = 89:11. IR (neat) ν 3063, 3031, 2970, 2915, 2851, 1758, 1671. HRMS calcd for $C_{15}H_{17}O_3F_3$ 302.1130. Found 302.1158. (Major isomer) ^{1}H NMR ($CDCl_3$) δ 1.42 (3 H, d, J = 7.08 Hz), 3.00 (1 H, quint, J = 6.96 Hz), 3.73 (3 H, s), 3.98 (1 H, d, J = 16.60 Hz), 4.09 (1 H, d, J = 16.36 Hz), 4.4−4.5 (1 H, m), 5.66 (1 H, ddq, J = 0.74, 8.54, 11.96 Hz), 5.78 (1 H, dd, J = 10.26, 11.97 Hz), 7.1−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 16.56, 44.73, 51.54, 65.95, 79.28, 121.16 (q, J = 34.0 Hz), 122.46 (q, J = 272.0 Hz), 126.70, 128.03, 128.08, 141.84, 140.10 (q, J = 5.0 Hz), 170.37. ^{19}F NMR ($CDCl_3$) δ 104.36 (d, J = 7.63 Hz). (Minor isomer) ^{1}H NMR ($CDCl_3$) δ 1.31 (3 H, d, J = 7.32 Hz), 2.92 (1 H, quint, J = 7.24 Hz), 3.67 (3 H, s), 3.88 (1 H, d, J = 16.36 Hz), 3.99 (1 H, d, J = 16.60 Hz), 4.50−4.55 (1 H, m). ^{13}C NMR ($CDCl_3$) δ 17.67, 44.39, 66.07, 79.37, 121.53 (q, J = 34.2 Hz), 126.53, 127.88, 128.26, 142.16, 140.98 (q, J = 4.9 Hz) 170.24. ^{19}F NMR ($CDCl_3$) δ 104.64 (d, J = 7.63 Hz).

General Method for [2,3]-Wittig Rearrangement. To a solution of diisopropylamine (0.622 mmol, 0.093 mL) in THF (5 mL) was added a 1.6 M solution of *n*-BuLi in hexane (0.622 mmol, 0.41 mL) at −78 °C, HMPA (0.34 mL, 1.95 mmol) was added, and the resulting clear solution was stirred for 30 min at that temperature. To this was added a solution of ester

(0.331 mmol) in THF (2 mL), and the mixture was stirred at that temperature for 10 min. At this point, the ester disappeared completely (monitored by TLC). Then the reaction mixture was poured into ice-cooled 3 N aqueous HCl and extracted with ethyl acetate. The organic layer was dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. After a purification of silica gel column chromatography, the hydroxy ester was obtained.

(2*S*,3*S*)-Methyl 6-(Benzyloxy)-3-(trifluoromethyl)-2-hydroxy-4(*E*)-hexenoate (*anti*-9a). Yield: 73%. ^{1}H NMR ($CDCl_3$) δ 2.99 (1 H, d, J = 5.37 Hz), 3.27 (1 H, dquint, J = 1.96, 9.04 Hz), 3.82 (3 H, s), 3.97−4.07 (2 H, m), 4.48 (2 H, s), 4.66 (1 H, dd, J = 1.95, 5.13 Hz), 5.77 (1 H, dd, J = 9.28, 15.63 Hz), 5.85 (1 H, dd, J = 5.13, 15.87 Hz), 7.20−7.40 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 50.02 (q, J = 27.1 Hz), 53.23, 69.15 (q, J = 2.5 Hz), 69.47, 71.91, 120.21 (q, J = 2.5 Hz), 125.54 (q, J = 280.6 Hz), 127.71, 127.73, 128.41, 136.00, 137.82, 172.58. ^{19}F NMR ($CDCl_3$) δ 93.43 (d, J = 7.63 Hz). IR (neat) ν 3500, 3150, 3100, 3050, 3000, 2956, 2860, 1746. $[\alpha]^{17}_D$ = +10.1 (*c* 0.3, $CHCl_3$).

(2*S,3*R**)-Methyl 6-(Benzyloxy)-3-(trifluoromethyl)-2-hydroxy-4(*E*)-hexenoate (*syn*-9a).** Yield: 61% (A small amount of unidentified compounds was included, which could not be separated from the desired ester). IR (neat) ν 3458, 3090, 3070, 3032, 2956, 2861, 1747. ^{1}H NMR ($CDCl_3$) δ 3.00 (1 H, s), 3.33 (1 H, dquint, J = 3.42, 8.91 Hz), 3.82 (1 H, m), 3.83 (3 H, s), 4.06 (1 H, m), 4.07 (1 H, m), 4.52 (2 H, m), 5.84 (1 H, ddt, J = 1.34, 9.16, 15.38 Hz), 5.99 (1 H, dt, J = 5.50, 15.63 Hz), 7.27−7.38 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 50.62 (q, J = 25.7 Hz), 53.00, 69.58, 70.04 (q, J = 2.0 Hz), 72.31, 122.34 (q, J = 2.5 Hz), 124.99 (q, J = 269.2 Hz), 126.95, 127.73, 127.79, 135.07, 137.81, 172.50. ^{19}F NMR ($CDCl_3$) δ 93.55 (d, J = 9.16 Hz) (for *anti*-*E* isomer) 95.59 (d, J = 7.63 Hz) (for syn-*E* isomer) 95.64 (d, J = 7.62 Hz) (for *syn*-*Z* isomer).

(2*S*,3*S*)-Methyl 7-(Benzyloxy)-3-(trifluoromethyl)-2-hydroxyl-4(*E*)-heptenoate (*anti*-9b). Yield: 78%. R_f = 0.08 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 2.3−2.5 (2 H, m), 3.18 (1 H, dquint, J = 1.95, 9.28 Hz), 3.49 (1 H, dt, J = 6.60, 12.94 Hz), 3.50 (1 H, dt, J = 6.35, 12.70 Hz), 3.76, (3 H, s), 4.4−4.5 (2 H, m), 4.5−4.6 (1 H, m), 5.79 (1 H, dt, J = 6.96, 15.63 Hz), 5.56 (1 H, dd, J = 9.64, 15.38 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 32.97, 50.32 (q, J = 27.0 Hz), 53.03, 69.3 (q, J = 1.8 Hz), 72.87, 119.18 (q, J = 2.2 Hz), 125.68 (q, J = 280.2 Hz), 127.59, 128.34, 136.86, 138.15, 172.59. ^{19}F NMR ($CDCl_3$) δ 93.33 (d, J = 9.15 Hz). IR (neat) ν 3032, 2956, 2929, 2861, 1747. $[\alpha]^{17}_D$ = +11.9 (*c* 0.7, $CHCl_3$). HRMS calcd for $C_{16}H_{19}O_4F_3$ 332.1235. Found 332.1239.

(2*S,3*R**)-Methyl 7-(Benzyloxy)-3-(trifluoromethyl)-2-hydroxyl-4(*E*)-heptenoate (*syn*-9b).** Yield: 46% (A small amount of unidentified compounds was included, which could not be separated from the desired ester). ^{1}H NMR ($CDCl_3$) δ 2,42 (2 H, dq, J = 1.46, 6.59 Hz), 3.25 (1 H, dquint, J = 3.66, 8.79 Hz), 3.40−3.70 (1 H, m), 3.54 (2 H, J = 7.05 Hz), 3.81 (3 H, s), 4.32 (1 H, d, J = 3.42 Hz), 4.51 (2 H, s), 5.57−5.64 (1 H, m), 5.89 (1 H, dt, J = 7.08, 15.62 Hz). ^{13}C NMR ($CDCl_3$) δ 32.91, 51.14 (q, J = 26.0 Hz), 52.85, 69.12, 70.15 (q, J = 2.1 Hz), 72.87, 121.28 (q, J = 2.6 Hz), 125.48 (q, J = 281.2 Hz), 127.60, 127.70, 128.35, 134.23, 136.01, 172.57. ^{19}F NMR ($CDCl_3$) δ 95.40 (d, J = 10.68 Hz), 95.42 (d, J = 9.16 Hz) (for *E*- or *Z*-isomer). IR (neat) ν 3482, 3090, 3070, 3032, 2956, 2980, 2961, 1748.

(2*S*,3*S*)-Methyl 3-(Trifluoromethyl)-2-hydroxyl-4(*E*)-decenoate (*anti*-9c). Yield: 64%. R_f = 0.25 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 7.08 Hz), 1.2−1.4 (6 H, m), 2.0−2.1 (2 H, m), 2.96 (1 H, d, J = 5.38 Hz), 3.16 (1 H, dquint, J = 1.95, 9.28 Hz), 3.81 (3 H, s), 4.6−4.65 (1 H, m), 5.4−5.5 (1 H, m), 5.70 (1 H, dt, J = 6.84, 15.38 Hz). ^{13}C NMR ($CDCl_3$) δ 13.95, 22.37, 28.46, 31.05, 32.48, 50.36 (q, J = 26.9 Hz), 53.04, 69.38 (q, J = 2.5 Hz), 117.05 (q, J = 2.4 Hz), 125.77 (q, J = 280.5 Hz), 140.63, 172.75. ^{19}F NMR ($CDCl_3$) δ 93.21 (d, J = 9.16 Hz). IR (neat) ν 3495, 2958, 2930, 2874, 2859, 1743. $[\alpha]^{14}_D$ = +17.9 (*c* 0.6, $CHCl_3$). HRMS calcd for $C_{12}H_{19}O_3F_3$ 268.1286. Found 268.1297.

(2*S,3*S**)-Methyl 5-Cyclohexyl-3-(trifluoromethyl)-2-hydroxyl-4(*E*)-pentenoate (*anti*-9d).** Yield: 75%. R_f = 0.22 (hexane:CH_2Cl_2 = 1:1). ^{1}H NMR ($CDCl_3$) δ 0.9−2.0 (11 H, m), 2.94 (1 H, d, J = 5.37 Hz), 3.12 (1 H, dquint, J = 2.20, 9.28 Hz), 3.80 (3 H, s), 4.63 (1 H, dd, J = 1.95, 5.61 Hz), 5.41 (1 H, ddd, J = 1.22, 9.76, 15.62 Hz), 5.63 (1 H, dd, J = 6.84, 15.63 Hz). ^{13}C NMR ($CDCl_3$) δ 25.09, 25.72, 25.94, 32.45, 32.48, 40.66, 50.43 (q, J = 26.9 Hz), 53.00, 69.56 (q, J = 2.4 Hz), 114.74 (q, J = 2.4 Hz), 125.78 (q, J = 280.7 Hz). ^{19}F NMR ($CDCl_3$) δ 93.30 (d, J = 9.16 Hz). IR (neat) ν 3501, 2928, 2854, 1746. HRMS calcd for $C_{13}H_{19}O_3F_3$ 280.1286. Found 280.1287.

(2*S,3*S**)-Methyl 3-(Trifluoromethyl)-2-hydroxyl-6-phenyl-4(*E*)-heptenoate (*anti*-9e).** Yield: 85%. R_f = 0.17 (hexane:CH_2Cl_2 = 1:1). Diastereoselectivity = 88:12. IR (neat) ν 3504, 3084, 3029, 2965, 2933, 2876, 1744. HRMS calcd for $C_{15}H_{17}O_3F_3$ 302.1130. Found 302.1111. (Major isomer) ^{1}H NMR ($CDCl_3$) δ 1.36 (3 H, d, J = 7.08 Hz), 2.99 (1 H, d, J = 5.12 Hz), 3.18 (1 H, dquint, J = 2.04, 9.28 Hz), 3.48 (1 H, quint, J = 6.59 Hz), 3.60 (3 H, s), 4.6−4.65 (1 H, m), 5.54 (1 H, ddd, J = 1.22, 9.77, 15.63 Hz), 5.84 (1 H, dd, J = 7.20, 15.50 Hz), 7.1−7.3 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 20.41, 42.32, 50.31 (q, J = 27.2 Hz), 52.89, 69.31 (q, J = 2.5 Hz), 116.03 (q, J = 2.4 Hz), 125.70 (q, J = 280.5 Hz), 126.33, 127.03, 128.46, 144.94, 144.46, 172.54. ^{19}F NMR ($CDCl_3$) δ 93.43 (d, J = 9.41 Hz). (Minor isomer) ^{1}H NMR ($CDCl_3$) δ 1.34 (3 H, d, J = 7.08 Hz), 3.04 (1 H, d, J = 5.13 Hz), 3.71 (3 H, s), 4.64−4.7 (1 H, m), 5.58 (1 H, ddd, J = 1.59, 9.64, 15.87 Hz), 5.89 (1 H, dd, J = 6.10, 15.87 Hz). ^{13}C NMR ($CDCl_3$) δ 20.32, 41.97, 50.38 (q, J = 27.0 Hz), 52.97, 69.36 (q, J = 1.9 Hz), 115.82 (q, J = 2.5 Hz), 126.37, 127.10, 144.54. ^{19}F NMR ($CDCl_3$) δ 93.45 (d, J = 10.82 Hz).

General Procedure of the Preparation for 3-(trifluoromethyl)allyl Ester Derivatives. To a solution of allylic alcohol (1 mmol) in dry CH_2Cl_2 (5 mL) was added methoxyacetyl chloride (0.14 mL, 1.5 mmol) and pyridine (0.12 mL, 1.5 mmol) at 0 °C. The resulting solution was allowed to warm to room temperature and then stirred at that temperature for 2 h. 1 N HCl was added to the reaction mixture, which was extracted with CH_2Cl_2, washed with water, dried over anhydrous $MgSO_4$, and evaporated in *vacuo*. The crude materials were purified by silica gel column chromatography, affording the ester.

(1′*R*)-3′-(Trifluoromethyl)-1′-[(benzyloxy)methyl]-(*Z*)-2′-propenyl 2-Methoxyacetate ((*R*)-(*Z*)-10a). Yield: 86%. ^{1}H NMR ($CDCl_3$) δ 3.44 (3 H, s), 3.64−3.66 (2 H, m), 4.04 (1 H, d, J = 16.60 Hz), 4.08 (1 H, d, J = 16.60 Hz), 4.52 (1 H, d, J = 11.96 Hz), 4.59 (1 H, d, J = 12.2 Hz), 5.77 (1 H, dq, J = 8.55, 10.50 Hz), 6.0−6.1 (2 H, m), 7.3−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 59.16, 69.11, 69.42, 70.55, 73.05, 120.75 (q, J = 34.8 Hz), 122.24 (q, J = 271.8 Hz), 127.50, 127.71, 128.28, 136.43 (q, J = 5.1 Hz), 132.32, 169.16. ^{19}F NMR ($CDCl_3$) δ 102.72 (d, J = 9.15 Hz). IR (neat) ν 3090, 3064, 3033, 2996, 2932, 2869, 1760, 1688. $[\alpha]^{27}_D$ = −16.4 (*c* 1.3, $CHCl_3$). Anal. Calcd for $C_{15}H_{17}O_4F_3$: C, 56.60; H, 5.38. Found: C, 56.63; H, 5.55.

3′-(Trifluoromethyl)-1′-[2″-(Benzyloxy)ethyl]-(*Z*)-2′-propenyl 2-Methoxyacetate (*rac*-(*Z*)-10b). Yield: 88%. ^{1}H NMR ($CDCl_3$) δ 1.8−2.1 (2 H, m), 3.40 (3 H, s), 3.53 (2 H, t, J = 6.34 Hz), 3.94 (1 H, d, J = 16.60 Hz), 3.98 (1 H, d, J = 16.61 Hz), 4.44 (1 H, d, J = 11.96 Hz), 4.51 (1 H, d, J = 11.97 Hz), 5.68 (1 H, dq, J = 8.54, 10.74 Hz), 5.93−5.99 (2 H, m), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 34.26, 59.16, 65.32, 68.16 (q, J = 1.5 Hz) 69.46, 72.82, 119.29 (q, J = 34.9 Hz), 122.37 (q, J = 271.7 Hz), 127.51, 127.56, 128.25, 137.94, 139.37 (q, J = 5.0 Hz), 169.13. ^{19}F NMR ($CDCl_3$) δ 102.86 (d, J = 7.63 Hz). IR (neat) ν 3089, 3064, 3032, 2993, 2931, 2867, 1760, 1688. Anal. Calcd for $C_{16}H_{19}O_4F_3$: C, 57.83; H, 5.76. Found: C, 57.98; H, 5.98.

(1′*R*)-3′-(Trifluoromethyl)-1′-[(benzyloxy)methyl]-(*E*)-2′-propenyl 2-Methoxyacetate ((*R*)-(*E*)-10a). Yield: 91%. ^{1}H NMR ($CDCl_3$) δ 3.46 (3 H, s), 3.60−3.64 (2 H, m), 4.10 (2 H, s), 4.53 (1 H, d, J = 11.96 Hz), 4.58 (1 H, J = 12.21 Hz), 5.66−5.72 (1 H, m), 5.89 (1 H, ddq, J = 1.71, 6.35, 15.87 Hz), 6.40 (1 H, ddq, J = 1.95, 5.13, 15.87 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 59.02, 69.26, 29.81, 70.52, 73.00, 120.39 (q, J = 34.3 Hz) 122.41 (q, J = 269.7 Hz) 127.45, 127.69, 128.25, 134.77 (q, J = 6.5 Hz) 137.20, 169.00. ^{19}F NMR ($CDCl_3$) δ 97.15 (d, J = 6.11 Hz). $[\alpha]^{28}_D$ = +11.7 (*c* 0.9, $CHCl_3$) (98% ee).

IR (neat) ν 3060, 3050, 3033, 2934, 2868, 1762, 1686. Anal. Calcd for $C_{15}H_{17}O_4F_3$: C, 56.60; H, 5.38. Found: C, 56.48; H, 5.58.

3′-(Trifluoromethyl)-1′-[2″-(benzyloxy)ethyl]-(*E*)-2′-propenyl 2-Methoxyacetate (*rac*-(*E*)-10b). Yield: 87%. ^{1}H NMR ($CDCl_3$) δ 1.97 (1 H, ddq, J = 5.86, 11.96, 14.40 Hz), 2.01 (1 H, ddq, J = 5.62, 7.57, 14.41 Hz), 3.42 (3 H, s), 3.51 (2 H, t, J = 5.85 Hz), 3.99 (1 H, d, J = 16.36 Hz), 4.02 (1 H, d, J = 16.35 Hz), 4.46 (1 H, d, J = 11.72 Hz), 4.49 (1 H, d, J = 11.72 Hz), 5.68 (1 H, qq, J = 1.95, 5.62 Hz), 5.81 (1 H, ddq, J = 1.46, 6.34, 15.87 Hz), 6.35 (1 H, ddq, J = 1.95, 5.86, 15.87 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 33.84, 59.21, 65.21, 69.48, 69.74, 73.01, 119.50 (q, J = 34.3 Hz), 122.56 (q, J = 269.6 Hz), 127.64, 127.68, 128.32, 137.44 (q, J = 6.4 Hz), 169.08. ^{19}F NMR ($CDCl_3$) δ 97.26 (d, J = 6.10 Hz). IR (neat) ν 3050, 3032, 2931, 2867, 1759, 1686. Anal. Calcd for $C_{16}H_{19}O_4F_3$: C, 57.83; H, 5.76. Found: C, 58.11; H, 5.99.

(1′*R*)-3′-(Trifluoromethyl)-1′-pentyl-(*Z*)-2′-propenyl 2-Methoxyacetate ((*S*)-(*Z*)-10c). Yield: 79%. ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 6.83 Hz), 1.2−1.8 (8 H, m), 3.45 (3 H, m), 4.01 (1 H, d, J = 16.36 Hz), 4.05 (1 H, d, J = 16.61 Hz), 5.68 (1 H, ddq, J = 1.22, 8.55, 11.97 Hz), 5.78−5.83 (1 H, m), 5.91 (1 H, dd, J = 9.03, 11.96 Hz). ^{13}C NMR ($CDCl_3$) δ 13.82, 22.33, 24.28, 31.24, 34.19, 59.30, 69.67, 70.51, 119.40 (q, J = 34.7 Hz), 122.42 (q, J = 271.5 Hz), 139.61 (q, J = 4.9 Hz), 169.29. ^{19}F NMR ($CDCl_3$) δ 102.90 (d, J = 9.50 Hz). IR (neat) ν 2950, 2935, 2900, 2850, 1762, 1677. $[\alpha]^{28}_D$ = −6.4 (*c* 1.0, $CHCl_3$). Anal. Calcd for $C_{12}H_{19}O_3F_3$: C, 53.73; H, 7.14. Found: C, 53.77; H, 7.35.

(1′*R*)-3′-(Trifluoromethyl)-1′-pentyl-(*E*)-2′-propenyl 2-Methoxyacetate ((*S*)-(*E*)-10c). Yield: 77%. ^{1}H NMR ($CDCl_3$) δ 0.8−0.9 (3 H, m), 1.2−1.4 (6 H, m), 1.6−1.8 (2 H, m), 3.46 (3 H, s), 4.05 (1 H, d, J = 16.36 Hz), 4.09 (1 H, d, J = 16.36 Hz), 5.46−5.50 (1 H, m), 5.81 (1 H, ddq, J = 1.71, 6.34, 15.62 Hz), 6.32 (1 H, ddq, J = 2.20, 5.61 15.87 Hz). ^{13}C NMR ($CDCl_3$) δ 13.73, 22.28, 24.32, 31.22, 33.54, 59.22, 69.54, 72.07, 119.44 (q, J = 269.4 Hz), 137.57 (q, J = 6.4 Hz), 169.22. ^{19}F NMR ($CDCl_3$) δ 97.30 (d, J = 6.10 Hz). IR (neat) ν 2960, 2935, 2810, 1751. $[\alpha]^{28}_D$ = +2.7 (*c* 0.9, $CHCl_3$) (100% ee). Anal. Calcd for $C_{12}H_{19}O_3F_3$: C, 53.73; H, 7.14. Found: C, 53.38; H, 7.36.

3′-(Trifluoromethyl)-1′-cyclohexyl-(*Z*)-2′-propenyl 2-Methoxyacetate (*rac*-(*Z*)-10d). Yield: 79%. ^{1}H NMR ($CDCl_3$) δ 0.9−1.8 (11 H, m), 3.44 (3 H, s), 4.01 (1 H, d, J = 16.60 Hz), 4.05 (1 H, d, J = 16.36 Hz), 5.60−5.67 (1 H, m), 5.72 (1 H, ddq, J = 0.73, 8.55, 12.33 Hz), 5.87 (1 H, dd, J = 9.27, 12.09 Hz). ^{13}C NMR ($CDCl_3$) δ 25.67, 25.76, 25.99, 27.94, 28.18, 41.66, 59.29, 69.59, 73.71 (q, J = 1.5 Hz), 120.41 (q, J = 34.7 Hz), 122.35 (q, J = 271.9 Hz), 137.93 (q, J = 5.1 Hz). ^{19}F NMR ($CDCl_3$) δ 103.11 (d, J = 9.16 Hz). IR (neat) ν 3010, 3000, 2932, 2856, 1762, 1676. Anal. Calcd for $C_{13}H_{19}O_3F_3$: C, 55.71; H, 6.83. Found: C, 56.44; H, 7.31.

3′-(Trifluoromethyl)-1′-cyclohexyl-(*E*)-2′-propenyl 2-Methoxyacetate (*rac*-(*E*)-10d). Yield: 98%. ^{1}H NMR ($CDCl_3$) δ 0.9−1.8 (11 H, m), 3.46 (3 H, s), 4.06 (1 H, d, J = 16.36 Hz), 4.10 (1 H, d, J = 16.36 Hz), 5.28−5.33 (1 H, m), 5.79 (1 H, ddq, J = 1.47, 6.35, 15.87 Hz), 6.32 (1 H, ddq, J = 2.20, 5.86, 15.87 Hz). ^{13}C NMR ($CDCl_3$) δ 25.55, 25.88, 27.90, 28.29, 41.21, 59.13, 69.42, 75.77, 120.14 (q, J = 33.4 Hz), 122.5 (q, J = 269.8 Hz), 136.34 (q, J = 6.3 Hz), 169.19. ^{19}F NMR ($CDCl_3$) δ 97.42 (d, J = 7.63 Hz). IR (neat) ν 2980, 2933, 2857, 1762, 1685. Anal. Calcd for $C_{13}H_{19}O_3F_3$: C, 55.71; H, 6.83. Found: C, 55.39; H, 6.86.

General Procedure of [3,3]-Ireland−Claisen Rearrangement. To a 1,1,1,3,3,3-hexamethyldisilazane (0.078 mL, 0.37 mmol) in THF (2 mL) was added *n*-BuLi in hexane (1.6 M solution, 0.23 mL, 0.37 mmol) at −78 °C. The whole was stirred at that temperature for 10 min, and then to this mixture was added TMSCl (0.39 mL, 3.03 mmol), followed by the addition of 3-(trifluoromethyl)allyl ester derivatives **10** (0.31 mmol). The mixture was stirred at that temperature for 30 min and then allowed to warm to room temperature and stirred overnight. Saturated aqueous $NaHCO_3$ was poured into the mixture which was extracted with ether three times. The combined aqueous layer was acidified and extracted with ether. The organic layer was washed with brine, dried over anhydrous $MgSO_4$, and then evaporated in *vacuo*. To a stirring of lithium aluminum hydride (0.059 g, 1.55 mmol) in THF (3 mL) was added a THF solution of the resultant crude materials at 0 °C, and the whole was stirred for 2 h at room temperature. The reaction mixture was quenched with 4 N aqueous KOH, and the usual workup gave the crude materials, which were purified by silica gel column chromatography to afford the alcohol.

(2*S*,3*S*)-6-(Benzyloxy)-3-(trifluoromethyl)-2-methoxy-4(*E*)-hexen-1-ol (*anti*-11a). Yield: 68%. ^{1}H NMR ($CDCl_3$) δ 2.99 (1 H, dquint, J = 2.20, 9.52 Hz), 3.47 (3 H, s), 3.54 (1 H, dd, J = 8.79, 13.91 Hz), 3.62−3.67 (1 H, m), 3.65 (1 H, ddd, J = 2.68, 6.35, 13.18 Hz), 4.05 (2 H, dd, J = 1.47, 5.62 Hz), 4.50 (1 H, d, J = 11.96 Hz), 4.52 (1 H, d, J = 11.96 Hz), 5.73 (1 H, ddt, J = 1.46, 9.52, 15.62 Hz), 5.87 (1 H, dt, J = 5.61, 15.63 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 48.32 (q, J = 26.2 Hz), 59.27, 61.88 (q, J = 1.2 Hz), 69.86, 72.13, 78.74 (q, J = 2.0 Hz), 122.26 (q, J = 2.5 Hz), 126.20 (q, J = 280.3 Hz), 127.72, 127.93, 128.40, 135.04, 137.89. ^{19}F NMR ($CDCl_3$) δ 93.90 (d, J = 9.16 Hz). IR (neat) ν 3422, 3100, 3080, 3032, 2937, 2850. $[\alpha]^{24}_D$ = +17.1 (*c* 0.5, $CHCl_3$).

(2*S,3*S**)-7-(Benzyloxy)-3-(trifluoromethyl)-2-methoxy-4(*E*)-hepten-1-ol (*anti*-11b).** Yield: 81%. ^{1}H NMR ($CDCl_3$) δ 2.41 (2 H, tq, J = 0.98, 6.59 Hz), 2.90 (1 H, dquint, J = 2.20, 9.52 Hz), 3.47 (3 H, s), 3.53 (2 H, t, J = 6.60 Hz), 3.51−3.56 (1 H, m), 3.62 (1 H, ddd, J = 2.20, 6.10, 11.97 Hz), 4.51 (2 H, s), 5.54 (1 H, ddt, J = 1.47, 9.77, 15.63 Hz), 5.76 (1 H, dt, J = 6.84, 15.62 Hz), 7.25−7.40 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 33.00, 49.30 (q, J = 26.0 Hz) 59.26, 62.04, 69.30, 72.81, 78.87 (q, J = 2.1 Hz), 120.98 (q, J = 2.6 Hz), 126.32 (q, J = 280.1 Hz), 127.60, 127.65, 128.35, 135.74, 138.18. ^{19}F NMR ($CDCl_3$) δ 93.73 (d, J = 9.16 Hz). IR (neat) ν 3448, 3100, 3050, 3030, 2935, 2850.

(2*S*,3*R*)-6-(Benzyloxy)-3-(trifluoromethyl)-2-methoxy-4(*E*)-hexen-1-ol (*syn*-11a). Yield: 59%. ^{1}H NMR ($CDCl_3$) δ 3.19 (1 H, dquint, J = 6.84, 9.28 Hz), 3.45 (3 H, s), 3.51 (1 H, ddd, J = 2.93, 5.62, 6.84 Hz), 3.57 (1 H, dd, J = 1.71, 11.47 Hz), 4.04 (2 H, d, J = 4.89 Hz), 4.51 (2 H, s), 5.57 (1 H, ddt, J = 1.47, 9.76, 15.62 Hz), 5.90 (1 H, ddt, J = 5.38, 15.38 Hz), 7.2−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 48.29 (q, J = 25.8 Hz), 58.03, 61.07 (q, J = 1.7 Hz), 69.51, 72.21, 79.50 (q, J = 1.5 Hz), 121.96 (q, J = 2.7 Hz), 126.06 (q, J = 280.4 Hz), 127.71, 127.74, 128.41, 134.94, 137.87. ^{19}F NMR ($CDCl_3$) δ 95.12 (d, J = 9.15 Hz). IR (neat) ν 3433, 3150, 3100, 3050, 2933, 2850. $[\alpha]^{27}_D$ = +35.6 (*c* 0.2, $CHCl_3$) (98% ee).

(2*S,3*R*)-7-(Benzyloxy)-3-(trifluoromethyl)-2-methoxy-4(*E*)-hepten-1-ol (*syn*-11b).** Yield: 61%. ^{1}H NMR ($CDCl_3$) δ 2.35−2.42 (2 H, m), 3.08 (1 H, dquint, J = 7.57, 9.12 Hz), 3.43 (3 H, s), 3.45 (1 H, dd, J = 3.91, 4.88, 8.47 Hz), 3.51 (1 H, dt, J = 6.84, 9.03 Hz), 3.53 (1 H, dt, J = 6.35, 9.28 Hz), 3.56 (1 H, dd, J = 4.88, 11.96 Hz), 3.71 (1 H, dd, J = 3.76, 11.97 Hz), 4.50 (2 H, s), 5.35 (1 H, ddt, J = 1.46, 9.77, 15.39 Hz), 5.78 (1 H, dt, J = 6.83, 15.38 Hz), 7.3−7.4 (5 H, m). ^{13}C NMR ($CDCl_3$) δ 33.02, 49.26 (q, J = 25.7 Hz), 57.93, 61.11 (q, J = 1.4 Hz), 68.88, 72.89, 79.58 (q, J = 1.5 Hz), 121.70 (q, J = 2.8 Hz), 125.73 (q, J = 280.5 Hz), 127.63, 127.69, 128.34, 135.43, 138.02. ^{19}F NMR ($CDCl_3$) δ 94.69 (d, J = 9.16 Hz). IR (neat) ν 3448, 3080, 3050, 3032, 2935, 2863. Anal. Calcd for $C_{15}H_{19}O_3F_3$: C, 60.37; H, 6.65. Found: C, 60.34; H, 7.12.

(2*S*,3*S*)-3-(Trifluoromethyl)-2-methoxy-4(*E*)-decen-1-ol (*anti*-11c). Yield: 75%. ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 6.85 Hz), 1.2−1.3 (4 H, m), 1.38 (2 H, quint, J = 7.32 Hz), 1.8−1.9 (1 H, m), 2.07 (2 H, dq, J = 1.46, 7.08 Hz), 2.86 (1 H, dquint, J = 2.44, 9.52 Hz), 3.48 (3 H, s), 3.52−3.58 (1 H, m), 3.60−3.63 (1 H, m), 3.65 (1 H, dd, J = 6.34, 9.52 Hz), 5.41 (1 H, ddt, J = 1.47, 9.52, 15.38 Hz), 5.71 (1 H, dt, J = 6.38, 15.38 Hz). ^{13}C NMR ($CDCl_3$) δ 13.97, 22.39, 28.54, 31.22, 32.53, 48.73 (q, J = 1.5 Hz), 79.15 (q, J = 2.1 Hz), 118.68 (q, J = 2.5 Hz), 126.40 (q, J = 280.1 Hz), 139.69. ^{19}F NMR ($CDCl_3$) δ 93.67 (d, J = 9.16 Hz). IR (neat) ν 3424, 2950, 2931, 2850, 2800. $[\alpha]^{26}_D$ = +16.1 (*c* 0.3, $CHCl_3$). Anal. Calcd for $C_{12}H_{21}O_2F_3$: C, 56.68; H, 8.32. Found: C, 56.54; H, 8.55.

(2*S*,3*R*)-3-(Trifluoromethyl)-2-methoxy-4(*E*)-decen-1-ol (*syn*-11c). Yield: 67%. ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 6.83 Hz), 1.22−1.34 (4 H, m), 1.38 (2 H, quint, J = 7.08 Hz), 1.9−2.0 (1 H, m), 2.06 (2 H, dq, J = 1.47, 6.84 Hz), 3.08

(1 H, dquint, J = 7.32, 9.52 Hz), 3.45 (3 H, s), 3.47 (1 H, ddd, J = 2.93, 5.61, 7.08 Hz), 3.76 (1 H, dd, J = 2.93, 11.97 Hz), 5.21 (1 H, ddt, J = 1.47, 9.77, 15.38 Hz), 5.75 (1 H, dt, J = 6.84, 15.38 Hz). ^{13}C NMR ($CDCl_3$) δ 13.98, 22.39, 28.42, 31.20, 32.49, 48.62 (q, J = 25.7 Hz), 58.04, 61.25 (q, J = 1.6 Hz), 79.68 (q, J = 1.5 Hz), 119.18 (q, J = 2.7 Hz), 126.31 (q, J = 280.3 Hz), 139.55. ^{19}F NMR ($CDCl_3$) δ 94.84 (d, J = 9.16 Hz). IR (neat) ν 3450, 2970, 2933, 2880, 2850. $[\alpha]^{25}_D = +36.6$ (*0*.3, $CHCl_3$) (100% ee). Anal. Calcd for $C_{12}H_{21}O_2F_3$: C, 56.68; H, 8.32. Found: C, 56.58; H, 8.37.

(2*S,3*S**)-5-Cyclohexyl-3-(trifluoromethyl)-2-methoxy-4(*E*)-penten-1-ol (*anti*-11d).** Yield: 80%. ^{1}H NMR ($CDCl_3$) δ 1.0−1.3 (5 H, m), 1.5−1.8 (6 H, m), 1.9−2.1 (1 H, m), 2.83 (1 H, dquint, J = 2.44, 9.77 Hz), 3.48 (3 H, s), 3.5−3.7 (3 H, m), 5.37 (1 H, ddd, J = 1.23, 9.53, 15.39 Hz), 5.66 (1 H, dd, J = 6.83, 15.62 Hz). ^{13}C NMR ($CDCl_3$) δ 25.81, 26.01, 32.49, 32.57, 40.70, 48.80 (q, J = 25.9 Hz), 59.39, 62.40 (q, J = 1.5 Hz), 79.20 (q, J = 1.9 Hz), 116.36 (q, J = 2.6 Hz), 126.39 (q, J = 280.1 Hz), 145.21. ^{19}F NMR ($CDCl_3$) δ 93.66 (d, J = 9.16 Hz). IR (neat) ν 3405, 2927, 2854. Anal. Calcd for $C_{13}H_{21}O_2F_3$: C, 58.63; H, 7.95. Found: C, 58.88; H, 7.84.

(2*S,3*R**)-5-Cyclohexyl-3-(trifluoromethyl)-2-methoxy-4(*E*)-penten-1-ol (*syn*-11d).** Yield: 64%. ^{1}H NMR ($CDCl_3$) δ 1.0−1.4 (5 H, m), 1.6−1.8 (5 H, m), 1.9−2.1 (2 H, m), 3.04 (1 H, dquint, J = 7.33, 9.28 Hz), 3.44 (3 H, s), 3.46 (1 H, ddd, J = 2.93, 5.62, 7.08 Hz), 3.52−3.58 (1 H, m), 3.70−3.78 (1 H, m), 5.17 (1 H, ddd, J = 0.97, 9.52, 15.38 Hz), 5.70 (1 H, dd, J = 6.83, 15.62 Hz). ^{13}C NMR ($CDCl_3$) δ 25.79, 25.99, 32.34, 32.48, 40.61, 48.66 (q, J = 25.5 Hz), 58.05, 61.24 (q, J = 1.6 Hz), 79.70 (q, J = 1.6 Hz), 116.87 (q, J = 2.7 Hz), 126.32 (q, J = 280.2 Hz), 144.94. ^{19}F NMR ($CDCl_3$) δ 94.82 (d, J = 9.16 Hz). IR (neat) ν 3418, 2927, 2853. Anal. Calcd for $C_{13}H_{21}O_2F_3$: C, 58.63; H, 7.95. Found: C, 58.41; H, 7.95.

Procedure for Determination of Stereochemistry. To a solution of *anti*-**9c** (0.856 g, 3.19 mmol) in CH_2Cl_2 (30 mL) was added ethyl vinyl ether (0.407 mL, 4.25 mmol) and a catalytic amount of pyridinium *p*-toluenesulfonate at 0 °C, and the reaction mixture was allowed to warm to room temperature and stirred for 2 h. Then, saturated $NaHCO_3$ was poured into the reaction mixture, and the whole was extracted with CH_2Cl_2. The organic layer was washed, dried over anhydrous $MgSO_4$, and evaporated in *vacuo*. The resultant crude materials were added into a solution of $LiAlH_4$ (0.065 g, 1.70 mmol) in THF (30 mL) at 0 °C and stirred for 1 h, and then the reaction mixture was quenched with 4 N KOH. After usual workup, a solution of the crude materials and NaH (0.227 g, 5.67 mmol) in THF (30 mL) was stirred at 0 °C for 30 min, followed by the addition of methyl iodide (0.353 mL, 5.67 mmol). After stirring for 3 h at room temperature, the reaction was quenched with aqueous $NaHCO_3$, and the mixture was extracted with ether three times. The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, and then concentrated in *vacuo* to afford the crude methyl ether which was treated with a catalytic amount of TsOH in methanol (20 mL), affording the alcohol **12**. This compound was dissolved in MeOH (10 mL) and treated with ozone at −78 °C until the alcohol **12** was consumed. Dimethyl sulfide (0.425 mL) was added into the reaction mixture, which was stirred at that temperature, and then allowed to warm to room temperature and concentrated in *vacuo* to give the crude oil. The crude materials were immediately reduced with $LiAlH_4$ (0.132 g, 3.48 mmol) in THF (20 mL) at 0 °C, and the usual workup afforded the corresponding diol, which was treated with dimethoxypropane (0.199 mL, 1.62 mmol)/acetone (5 mL)/pyridinium *p*-toluenesulfonate (cat.). The reaction mixture was stirred at room temperature for 3 h and then quenched with saturated $NaHCO_3$, and the whole was concentrated in *vacuo*, extracted with ether, dried over anhydrous $MgSO_4$, filtered, and evaporated to furnish the crude acetonide. Purification by silica gel column chromatography gave acetonide as a yellow oil (0.033 g, 0.146 mmol).

(4*S*,5*S*)-5-(Trifluoromethyl)-4-(methoxymethyl)-2,2-dimethyl-1,3-dioxacyclohexane (13). Yield: 5%. ^{1}H NMR ($CDCl_3$) δ 1.41 (3 H, s), 1.44 (3 H, s), 2.71 (1 H, m), 3.41 (3 H, s), 3.52 (1 H, dd, J = 4.88, 10.98 Hz), 3.59 (1 H, m), 3.90 (1 H, dd, J = 7.08, 12.21 Hz), 3.96 (1 H, dd, J = 5.86, 11.96 Hz), 4.08 (1 H, ddd, J = 1.96, 4.89, 9.83 Hz). ^{13}C NMR ($CDCl_3$) δ 20.48, 27.10, 40.05 (q, J = 24.6 Hz), 53.41, 56.96 (q, J = 3.8 Hz), 59.51, 66.82 (q, J = 1.9 Hz), 73.24 (q, J = 1.4 Hz), 99.49, 125.97 (q, J = 280.1 Hz). ^{19}F NMR ($CDCl_3$) δ 93.52 (d, J = 8.94 Hz). IR (neat) ν 2990, 2935, 2920, 2850.

General Procedure for the Synthesis of (2*S*,3*S*)-2-(Trifluoromethyl)-3-methoxybutane-1,4-diol (14). Method A. To a suspension of Ag_2O (excess, *ca*. 1.0 g) in ether (5 mL) was added an ether solution of [2,3]-Wittig-rearranged product (*anti*-**9a**, and *anti*-**9c**, 1.09 mmol) and methyl iodide (excess, 2.0 mL), and then the reaction mixture was stirred at 40 °C overnight. The solution was cooled, filtered, and concentrated in *vacuo* to give crude materials, which were treated with a large excess amount of $LiAlH_4$ (*ca*. 2 mmol) in THF at 0 °C. The reaction mixture was stirred at room temperature for 2 h and then quenched with 4 N KOH, and the usual workup gave the crude [3,3]-Ireland−Claisen rearrangement product which was purified by silica gel column chromatography to afford the alcohol. The obtained material was treated with ozone in methanol at −78 °C until the methyl ether was consumed. Then, dimethyl sulfide (1.62 mL) was added into the reaction mixture, which was stirred for 30 min at room temperature and then evaporated. The resultant was treated with $LiAlH_4$ (excess) in THF, and the usual workup afforded the diol. **Method B.** [2,3]-Wittig rearrangement product, *anti*-**9b** (0.33 g, 1.00 mmol) was converted into the methyl ether (0.246 g, 0.710 mmol, 71% yield) by the same method as described in method A. The obtained methyl ether was treated with ozone in methanol at −78 °C, and the usual workup gave the aldehyde. A solution of the aldehyde and $LiAlH_4$ (ca. 0.076 g, 2 mmol) in THF was stirred for 2 h at room temperature, and the usual workup gave the title compound (0.059 g, 0.314 mmol, 44% yield). ^{1}H NMR ($CDCl_3$) δ 2.3−2.4 (1 H, m), 2.54 (1 H, dtq, J = 3.42, 6.83, 10.01 Hz), 2.9−3.2 (1 H, m), 3.50 (3 H, s), 3.69 (1 H, dd, J = 4.03, 11.48 Hz), 3.72 (1 H, q, J = 3.91 Hz), 3.87−3.94 (1 H, m), 3.99 (1 H, dd, J = 6.83, 11.72 Hz). ^{13}C NMR ($CDCl_3$) δ 47.27 (q, J = 24.0 Hz), 56.71 (q, J = 3.3 Hz), 58.50, 61.51, 77.82 (q, J = 2.3 Hz), 126.48 (q, J = 280.5 Hz). ^{19}F NMR ($CDCl_3$) δ 94.26 (d, J = 10.68 Hz). IR (neat) ν 3385, 2941, 2930, 2900. $[\alpha]^{20}_D = -6.4$ (*c* 0.6, $CHCl_3$). Anal. Calcd for $C_6H_{11}O_3F_3$: C, 38.30; H, 5.89. Found: C, 38.62; H, 6.08. Racemic rearranged products (*anti*-**9d** and *anti*-**9e**) were converted into (2*S**,3*S**)-2-(Trifluoromethyl)-3-methoxybutane-1,4-diol according to method A.

(2*R*)-2-(Trifluoromethyl)-1-[(4-methylphenyl)sufenyl]-nonene (17). Method A. To a solution of $LiAlH_4$ (0.166 g, 4.37 mmol) in THF (5 mL) was added *anti*-**9c** (0.195 g, 0.729 mmol) at 0 °C and stirred for 1 h at room temperature. The reaction mixture was quenched with 4 N KOH, and the organic layer was dried over anhydrous $MgSO_4$ and concentrated in *vacuo*. Purification of the resultant crude materials by silica gel column chromatography gave the corresponding diol (0.134 g, 0.561 mmol), which was treated with Raney Ni (excess)/H_2 in ethanol (10 mL) under 10 atm. The reaction mixture was stirred overnight and then filtered, the filtrate was evaporated, and the residue was purified by silica gel column chromatography to furnish the saturated diol (0.136 g, 0.561 mmol). To a suspension of $Pb(OAc)_4$ (0.760 mmol, 0.337 g) in CH_2Cl_2 (20 mL) was added slowly the obtained compound at 0 °C under nitrogen atmosphere. The reaction mixture was stirred for several hours, filtered through Florisil, and washed with ethyl acetate. The filtrate was concentrated to give the crude materials, which were treated immediately with $LiAlH_4$ (0.064 g, 1.68 mmol) in THF (5 mL), and the usual workup gave the alcohol ((*S*)-**16**, $[\alpha]^{21}_D = +3.1$ (*c* 0.6, $CHCl_3$).). To a solution of this compound and CBr_4 (0.942 g, 2.84 mmol) in CH_2Cl_2 (15 mL) was added PPh_3 (0.742 g, 2.83 mmol) at 0 °C, and the reaction mixture was allowed to warm to room temperature and stirred for 2 h. Then a large amount of hexane was added into the reaction mixture which was filtered, and concentrated in *vacuo*. The resultant oil was passed through silica gel, and the obtained crude materials were treated with *p*-toluenethiol (0.248 g, 2.0 mmol) and sodium hydride (0.080 g, 2.0 mmol) at 0 °C. The reaction mixture was stirred at room temperature for 2 h and then poured into 3 N HCl, extracted with ether, washed with brine, dried over anhydrous $MgSO_4$, and evapo-

rated. The residue was purified by silica gel column chromatography to give **17** (0.022 g, 0.069 mmol, 9% yield). **Method B.** The sulfoxide **18** (0.110 g, 0.418 mmol) was treated with $LiAlH_4$ (0.022 g, 0.585 mmol) in THF (3 mL) at 0 °C, and the mixture was stirred at room temperature for 1 h. The reaction was quenched with 4 N aqueous KOH and the usual workup gave the alcohol (0.095 g, 0.360 mmol). To a solution of oxalyl chloride (0.138 mL, 1.61 mmol) in CH_2Cl_2 (10 mL) at −78 °C was added dimethyl sulfoxide (0.17 mL) in CH_2Cl_2 (3 mL). After the mixture was stirred for 10 min, a CH_2Cl_2 solution of the alcohol obtained above was introduced and the resulting mixture stirred for 30 min. To this was added triethylamine (0.646 mL). The mixture was further stirred at −78 °C for 2 h and quenched with 20 mL of saturated aqueous NH_4Cl. This mixture was extracted with CH_2Cl_2. The combined organic extracts were dried over anhydrous $MgSO_4$, filtered, and concentrated in *vacuo*. Purification of the resultant crude materials was carried out by silica gel column chromatography to afford the corresponding aldehyde. To a suspension of *n*-pentyltriphenylphosphonium iodide (0.46 g, 1 mmol) in THF (5 mL) was added dropwise *n*-BuLi/hexane (0.625 mL, 1 mmol) at 0 °C, and thw whole was stirred for 30 min at that temperature. To this was added a THF solution of the above aldehyde. After stirring for 1 h at 0 °C, the reaction was diluted with a large amount of hexane (ca. 20 mL), and the mixture was filtered and concentrated in *vacuo*. The resulting oil was purified by silica gel column chromatography to afford the desired materials as a ca. 81:19 mixture of *E* and *Z* forms. To a suspension of 10% Pd/C (0.00524 g) in ethanol (5 mmol) was dissolved the obtained sulfide, and the reaction mixture was stirred under 10 atm hydrogen pressure for 24 h. The mixture was filtered and concentrated in *vacuo* to give crude materials, which were purified by silica gel column chromatography to obtain the desired compound (0.073 g, 0.232 mmol, 59% yield). ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 6.85 Hz), 1.20−1.40 (10 H, m), 1.65−1.70 (2 H, m), 2.15−2.25 (1 H, m), 2.33 (3 H, s), 2.78 (1 H, dd, J = 8.79, 13.67 Hz), 3.22 (1 H, dd, J = 4.03, 13.55 Hz), 7.10−7.30 (4 H, m). ^{13}C NMR ($CDCl_3$) δ 14.06, 20.99, 22.61, 26.57, 27.19 (q, J = 2.1 Hz), 28.98, 29.50, 31.75, 33.15 (q, J = 2.9 Hz), 42.67 (q, J = 24.9 Hz), 127.73 (q, J = 281.1 Hz), 129.89, 130.76, 131.42, 136.99. ^{19}F NMR ($CDCl_3$) δ 91.80 (d, J = 9.15 Hz). IR (neat) ν 3150, 3000, 2960, 2926, 2857. $[\alpha]^{23}_D$ = −71.6 (*c* 0.7, $CHCl_3$) (>98% ee).

(2*R*)-2-(Trifluoromethyl)nonan-1-ol ((*R*)-16). A solution of *syn*-**11c** (0.250 g, 0.947 mmol) and Raney Ni (excess) in ethanol (15 mL) was stirred at room temperature under 10 atm hydrogen for 2 days. The reaction mixture was filtered, and the filtrate was concentrated in *vacuo* to afford crude materials which were purified by silica gel column chromatography to give the saturated molecules (0.145 g, 0.545 mmol). To this compound in CH_2Cl_2 (3 mL) was added a BBr_3 solution in CH_2Cl_2 (1.0 M solution, 2.0 mL, 2.0 mmol) at −20 °C, and the whole was stirred at that temperature for several hours. Then the reaction mixture was poured into 1 N HCl, and extracted with CH_2Cl_2, dried over anhydrous $MgSO_4$, and evaporated to afford the diol. To a suspension of $Pb(OAc)_4$ (0.443 g) in CH_2Cl_2 (50 mL) was added the diol in CH_2Cl_2 (15 mL) over 30 min at 0 °C in nitrogen atmosphere. The reaction mixture was stirred at that temperature for several hours and then passed through florisil. The resulting solution was concentrated in *vacuo* to afford the crude materials which were purified by silica gel column chromatography to give the desired alcohol (0.090 g, 0.424 mmol). Yield: 33%. ^{1}H NMR ($CDCl_3$) δ 0.88 (3 H, t, J = 7.08 Hz), 1.2−1.7 (12 H, m), 2.0−2.1 (1 H, m), 2.15−2.25 (1 H, m), 3.50−70 (2 H, m). ^{13}C NMR ($CDCl_3$) δ 14.52, 23.09, 25.12 (q, J = 2.3 Hz), 27.31, 29.51, 30.00, 32.23, 45.89 (q, J = 23.8 Hz), 60.33 (q, J = 3.1 Hz), 128.46 (q, J = 280.6 Hz). ^{19}F NMR ($CDCl_3$) δ 92.62 (d, J = 9.15 Hz). IR (neat) ν 3346, 2950, 2926, 2900. $[\alpha]^{24}_D$ = −1.0 (*c* 0.7, $CHCl_3$).

(2*R*,3*S*)-2-(Trifluoromethyl)-3-methoxybutan-1,4-diol (20). *syn*-**11a** and *syn*-**11c** were converted into the title compound by the similar method described in the preparation of (2*S*,3*S*)-2-(trifluoromethyl)-3-methoxybutane-1,4-diol. ^{1}H NMR ($CDCl_3$) δ 2.40−2.56 (1 H, m), 2.62−2.72 (1 H, m), 2.76−2.88 (1 H, m) 3.46 (3 H, s) 3.66 (1 H, dt, J = 3.79, 5.62 Hz) 3.74−3.80 (1 H, m) 3.78−3.96 (2 H, m). ^{13}C NMR ($CDCl_3$) δ 46.74 (q, J = 23.5 Hz) 56.99 (q, J = 3.2 Hz) 57.82, 60.48 (q, J = 1.6 Hz) 78.08 (q, J = 1.8 Hz) 126.49 (q, J = 281.0 Hz). ^{19}F NMR ($CDCl_3$) δ 96.27 (d, J = 10.69 Hz). IR (neat) ν 3384, 2942, 2930, 2838. $[\alpha]^{24}_D$ = +9.7 (*c* 0.6, $CHCl_3$).

Supporting Information Available: Copies of ^{1}H NMR spectra of compounds (37 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO961246I