Modified Preparation Method of Trifluoromethylated Propargylic Alcohols and Its Application to Chiral 2,6-Dideoxy-6,6,6-trifluorosugars

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Convenient generation of 3,3,3-trifluoropropynyl anion was realized from 2-bromo-3,3,3-trifluoropropene, and the anion's reaction with various electrophiles proceeded in excellent isolated yields. One of the products, 1-(benzyloxy)-6,6,6-trifluoro-4-hexyn-3-ol (**4b**), was further employed for the diastereoselective construction of 2,6-dideoxy-6,6,6-trifluorosugars after enzymatic optical resolution and osmium dihydroxylation of the corresponding olefins. The strongly electron-withdrawing trifluoromethyl moiety, significantly affecting the nucleophilic nature of neighboring functionalities, allows the ready differentiation of hydroxy groups by routine chemical transformation, which results in the shortening of the reaction sequence.

Unlike mono- or difluorinated compounds which are readily obtained by fluorination reactions of the corresponding alcohols or carbonyls, respectively,[1] CF_3-containing molecules are difficult to obtain,[2] especially in optically active form.[3] Although several reagents[4] and reaction sequences[5] have been developed for the introduction of this group, there remain problems to be solved, such as the handling of the materials, availability of reagents, and selectivity (stereo-, regio-, and/or chemo-). Toward an alternative means of obtaining trifluoromethylated compounds, we have been studying the preparation of chiral building units possessing a CF_3 moiety as well as readily-distinguishable plural functionalities.[6,7] As such, 2-butenolides with this group were recently synthesized for the formation of L-amicetose, L-rhodinose, D-rhamnose, and so on as their 6,6,6-trifluorinated derivatives.[7,8] Such trifluorinated analogs are interesting since their nonfluorinated counterparts are broadly found as constituent sugars in naturally occurring antibiotics[9] and the introduction of fluorine(s) might give rise to enhancement or alteration of the native biological activity.[10] For attaining higher biological activities, it is essential to construct analogs with diverse stereochemistries. Our previous route provided limited access to, for example, the 2,6-dideoxy-6,6,6-trifluoro structure. In this paper, we would like to describe a modified, convenient, and economical route for the preparation of 1-substituted 4,4,4-trifluorobut-2-yn-1-ol, which enabled us to conveniently synthesize the desired 2,6-dideoxy-6,6,6-trifluorosugars in their optically active forms.[11]

Results and Discussion

***In Situ* Preparation and Reactions of 3,3,3-Trifluoropropene.** Due to the wide applicability of propargylic alcohols, such compounds with a CF_3 group at the terminal carbon atom have been previously synthesized,[12] mainly from 3,3,3-trifluoropropyne (**1**) by its successive treatment with *n*-BuLi and appropriate carbonyl compounds (Scheme 1, path A). Although this reaction is very straightforward, there are some shortcomings such as only moderate yields of products, the very high cost of **1**, the handling of gaseous **1** (bp −48 °C), and so on. We have devised an alternative route starting from 2-bromo-3,3,3-trifluoropropene (**2**) (path C), which is less expensive (1/3−1/4)[13] and based on much easier procedure (bp 33 °C).

[⊗] Abstract published in *Advance ACS Abstracts,* September 1, 1995.

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(3) As far as we know, there have been only two fluorination examples with complete retention of optical purities as well as high chemoselectivities. (a) Peters, H. M.; Feigl, D. M.; Mosher, H. S. *J. Org. Chem.* **1968**, *33*, 4245–4250. (b) Shustov, G. V.; Denisenko, S. N.; Chervin, I. I.; Kostyanovskii, R. G. *Bull. Acad. Sci. USSR Div. Chem. Sci.* **1988**, *37*, 1422–1427.

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(5) (a) Kitazume, T.; Ishikawa, N. *J. Am. Chem. Soc.* **1985**, *109*, 5186–5191. (b) Kobayashi, Y.; Yamamoto, K.; Kumadaki, I. *Tetrahedron Lett.* **1979**, *20*, 4071–4072. (c) Iseki, K.; Nagai, T.; Kobayashi, Y. *Tetrahedron Lett.* **1993**, *34*, 2169–2170.

(6) (a) Yamazaki, T.; Iwatsubo, H.; Kitazume, T. *Tetrahedron: Asymmetry* **1994**, *5*, 1823–1830. (b) Yamazaki, T.; Haga, J.; Kitazume, T. *BioMed. Chem. Lett.* **1991**, *1*, 271–276. (c) Yamazaki, T.; Haga, J.; Kitazume, T. *Chem. Lett.* **1991**, 2175–2178.

(7) (a) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Synth. Org. Chem. Jpn.* **1994**, *52*, 734–745. (b) Yamazaki, T.; Mizutani, K.; Kitazume, T. *J. Org. Chem.* **1993**, *58*, 4346–4359. (c) Yamazaki, T.; Mizutani, K.; Kitazume, T. *Tetrahedron: Asym.* **1993**, *4*, 1059–1063. (d) Yamazaki, T.; Mizutani, K.; Takeda, M.; Kitazume, T. *J. Chem. Soc., Chem. Commun.* **1992**, 55–57.

(8) For the other 6-deoxy-6,6,6-trifluorosugars, see the following: (a) Differding, E.; Frick, W.; Lang, R. W.; Martin, P.; Schmit, C.; Veenstra, S.; Greuter, H. *Bull. Soc. Chim. Belg.* **1990**, *99*, 647–671. (b) Bansal, R. C.; Dean, B.; Hakomori, S.; Toyokuni, T. *J. Chem. Soc., Chem Commun.* **1991**, 796–798. (c) Hanzawa, Y.; Uda, J.; Kobayashi, Y.; Ishido, Y.; Taguchi, T.; Shiro, M. *Chem. Pharm. Bull.* **1991**, *39*, 2459–2461.

(9) *Bioactive Carbohydrates in Chemistry, Biochemistry, and Biology*; Kennedy, J. F., White, C. A., Eds.; Ellis Horwood: Chichester, 1983; Chapter 12.

(10) (a) Resnati, G. *Tetrahedron* **1993**, *42*, 9385–9445. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemisrty*; John Wiley & Sons: New York, 1990.

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Scheme 1

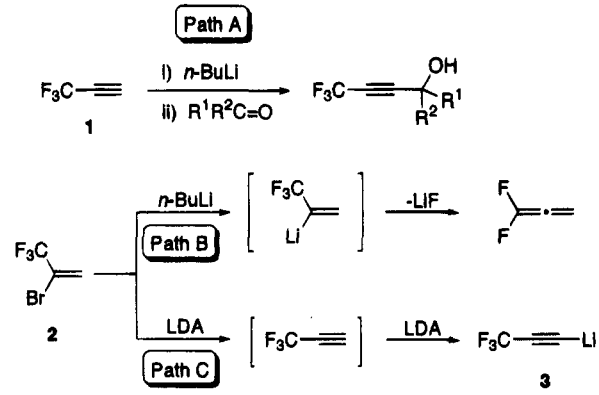
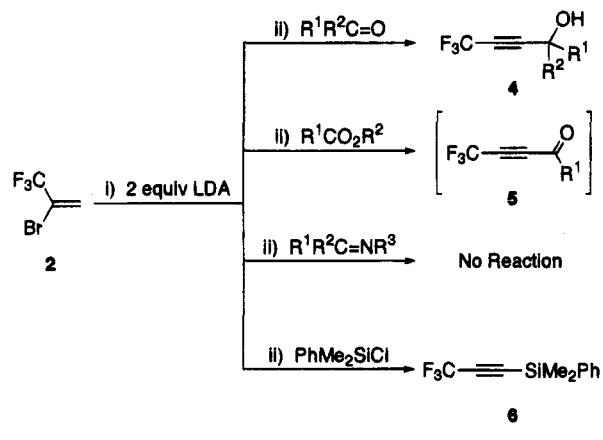


Table 1. Reaction of *in Situ* Prepared 3 with Carbonyl Compounds

entry	R^1	R^2	yield[a] (%)	product
1	$PhCH_2CH_2$	H	99	**4a**
2	$BnOCH_2CH_2$	H	92	**4b**
3	$BnOCH_2$	H	90	**4c**
4	Ph	H	99	**4d**
5	*c*-C_6H_{11}	H	93	**4e**
6	(*E*)-PhCH=CH	H	99	**4f**
7	*n*-$C_3H_7(CH_3)CH$	H	75 (50:50)	**4g**
8	$CH_3(BnO)CH$	H	94 (64:36)	**4h**
9	$Ph(CH_3)CH$	H	97 (89:11)	**4i**
10	Ph	Me	89	**4j**
11	$-(CH_2)_5-$		99	**4k**

[a] Isolated yield. The diastereomer ratio determined by capillary GC is shown in parentheses.

Scheme 2



At first, compound **2** was thought to undergo a dehydrobromination reaction upon treatment with a strong base, but consideration of the experimental result[12a] that lithium–bromine exchange followed by lithium fluoride elimination occurred upon treatment of **2** with *n*-BuLi above −90 °C (path B) led us to employ less nucleophilic LDA (path C). Thus, addition of **2** to a THF solution containing 2 equiv of LDA at −78 °C smoothly afforded the acetylide **3**, which was then readily trapped with benzaldehyde in quantitative yield. The combination of this base and solvent turned out to be important, and the use of a base such as Grignard reagent (EtMgBr) or a solvent such as diethyl ether proved fruitless.

Table 1 summarizes the reaction of **3** prepared *in situ* with various types of aldehydes (entries 1–9) and ketones (entries 10 and 11), usually furnishing products in very high isolated yields. Only 1,2-addition was observed when an α,β-unsaturated aldehyde was employed as an electrophile (entry 6). The low level of diastereoselectivity observed for entries 7 and 8 might stem from the minimal steric requirement of linear acetylide **3**, while 2-phenylpropanal, an exception, showed relatively high selectivity (9:1, the relative stereochemistry being undetermined; entry 9).[14] Compound **3** was also reacted with both cyclic and acyclic ketones at the same temperature, and the corresponding *tert*-alcohols, **4j** or **4k**, were obtained in high yields (entries 10 and 11). Addition of ester as an electrophile only furnished a complex mixture, and this observation might be explained by the formation of a reactive intermediate, α,β-unsaturated ketones **5**, which was further attacked by another acetylide molecule or diisopropylamine from LDA in various fashions (Scheme 2).[15] While reaction of **3** with imines did not proceed, possibly due to the less active imine carbon, successful reaction occurred with dimethylphenylsilyl chloride to produce the corresponding alkynylsilane **6** (74% yield).

Synthetic Utilization of Trifluoromethylated Propargylic Alcohols. In the next stage of this project, we have performed osmium-catalyzed dihydroxylations[16] of the allylic alcohols derived from the above propargylic alcohols because of the requirement of such materials for the construction of the target sugars. For obtaining basic information on this reaction with trifluoromethylated compounds, propargylic alcohols **4a–c** were employed as representative substrates.

Their transformations into the corresponding allylic alcohols **7** were carried out by Red-Al reduction (for *E* series) or with Lindlar catalyst (for *Z* series), affording single isomers in more than 90% yield in every case (Scheme 3). Previously, Kobayashi and co-workers reported[17] the stereoselective reduction of the same type of propargylic alcohols with LAH in ether at −78 °C (for *E* series), or R_2BH or *in situ* prepared "CuH" (for *Z* series), although the isolated yields were not always high. In our hands, when Red-Al reduction was conducted in an ethereal solution at higher temperature (−20 to 0 °C), a byproduct was detected by ^{19}F NMR spectroscopy, whose chemical shift (−15 ppm from external CF_3CO_2H) suggested the loss of a fluoride anion, leading to the formation of difluorovinylic materials.

The resultant allylic alcohols, (*E*)- or (*Z*)-**7**, were then subjected to the usual dihydroxylation conditions using a catalytic amount of OsO_4 with *N*-methylmorpholine *N*-oxide as a cooxidant to afford the desired triols as diastereomeric mixtures (Scheme 3, Table 2).[18] Diastereomeric ratios were determined after derivatization to

(13) 2-Bromo-3,3,3-trifluoropropene (**2**) has reported to be accessible from a much less expensive industrial material, trifluoropropene, in only two steps (bromination and dehydrobromination) with quantitative total yields.[12a] In our case, this starting material was obtained from F-Tech, Inc., Japan, and used without further purification.

(14) Our previous investigation of the diastereoselective introduction of a trifluoromethyl group by use of (trifluoromethyl)trimethylsilane ($TMSCF_3$)[4a] revealed that its reaction with aldehydes having substituent α to the carbonyl group gave similar disappointing selectivities with the exception when 2-phenylpropanal was employed. See ref 7 in the above ref 7b.

(15) It might be also probable that these nucleophiles reacted with the resultant alkynyl ketone in an "*anti*-Michael" manner. See: (a) Martin, V.; Molines, H.; Wakselman, C. *J. Org. Chem.* **1992**, *57*, 5530–5532. (b) Bumgardner, C. L.; Bunch, J. E.; Whangbo, M. H. *J. Org. Chem.* **1986**, *51*, 4082–4083.

(16) Haines, A. H. In *Comprehensive Organic Synthesis*; Trost, B. M., Ed.; Pergamon Press: New York, 1991; Vol. 7, pp 437–448. Osumium dihydroxylation of 3,3,3-trifluoropropene was reported. See: (a) Herrmann W. A.; Eder, S. J. *Chem. Ber.* **1993**, *126*, 31–37. (b) Herrmann, W.; Eder, S. J.; Scherer, W. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 1345–1347.

(17) Hanzawa, Y.; Kawagoe, K.; Takahashi, N.; Kobayashi, Y. *Tetrahedron Lett.* **1984**, *25*, 4749–4752.

(18) The same type of reaction with $KMnO_4$ only afforded a complex mixture.

Scheme 3

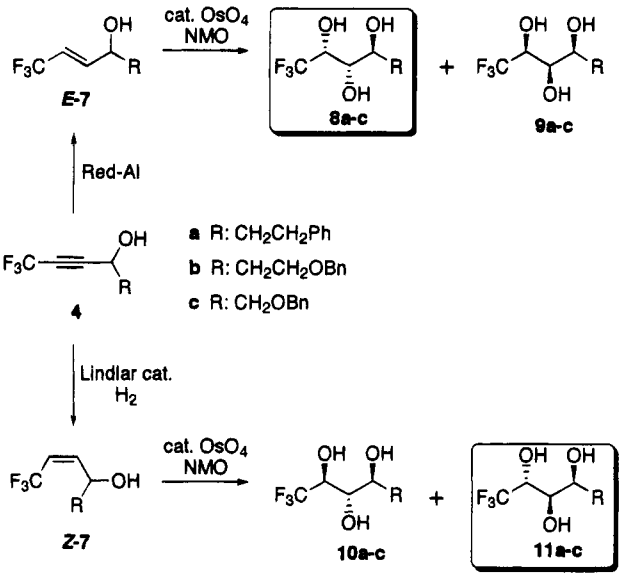
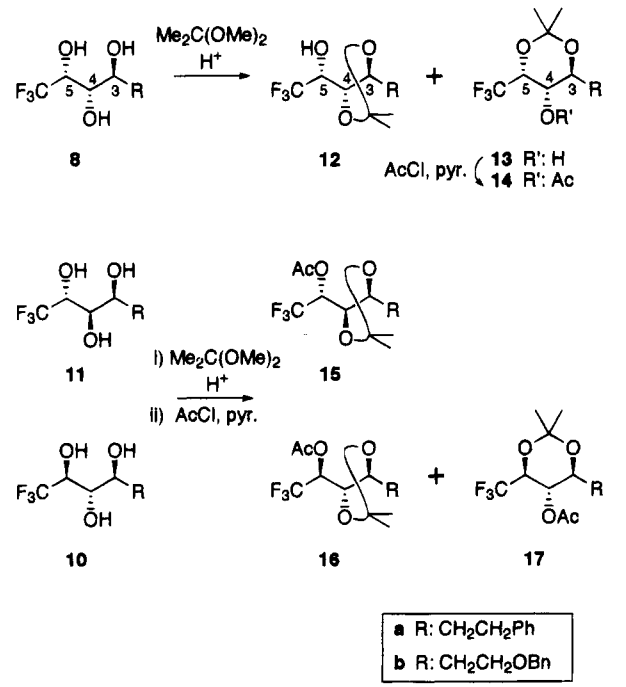


Table 2.

entry	substrate	yield (%)	selectivity[a]
1	(*E*)-**7a**	83	85:15
2	(*E*)-**7b**	86	86:14
3	(*E*)-**7c**	76	80:20
4	(*Z*)-**7a**	83	9:91
5	(*Z*)-**7b**	74 (19[b])	26:74
6	(*Z*)-**7c**	66 (34[b])	42:58

[a] Ratio of **8**:**9** or **10**:**11** determined by capillary GC analysis after acetylation. [b] Recovery of starting material.

Scheme 4



the corresponding triacetates by capillary GC analysis. The relative stereochemistry of the products, on the other hand, was deduced from the ^{1}H NMR coupling constants after transformation into the corresponding 6-membered acetonides (Scheme 4). The major triol **8b** was, after separation from **9b**, reacted with 2,2-dimethoxypropane in the presence of a catalytic amount of *p*-TsOH to furnish a mixture of 5-membered and 6-membered acetonides, **12b** (91% yield) and **13b**, respectively. Acetylation of the latter allowed us to obtain the requisite material **14b** in 3% total yield. On the other hand, because the diastereomeric triols **10b** and **11b** from (*Z*)-**7b** were inseparable by column chromatography, this mixture (**10b**:**11b** = 26:74) was employed for the same reaction, yielding **15b** from **11b** (70% yield) and a mixture of **16b** and **17b** from **10b** (26% yield, 58:42).

Table 3.

substrate	R	product	coupling constant (Hz) H_3-H_4	coupling constant (Hz) H_4-H_5
8a	CH_2CH_2Ph	**14a**	6.7	4.0
8b	CH_2CH_2OBn	**14b**	7.0	4.0
10a	CH_2CH_2Ph	**17a**	9.8	9.8
10b	CH_2CH_2OBn	**17b**	9.7	9.7

^{1}H NMR coupling constants between H_3-H_4 and H_4-H_5[19] of **14b** and **17b** as well as the similar compounds **14a** and **17a** (R: CH_2CH_2Ph) are summarized in Table 3. In the case of acetonides **17a** or **17b**, it is apparent that the protons C_3-C_5 all occupy axial positions, as supported by the typical axial–axial coupling constants of *ca.* 10 Hz. Thus, the corresponding substrates, minor diastereomers **10a** or **10b** from *Z* allylic alcohols, should have the relationship of 3,4-*anti*, 4,5-*anti* and the major isomers **11a** or **11b** should be 3,4-*syn*, 4,5-*anti*, assuming that the OsO_4 oxidation proceeds in a *cis* fashion.

On the other hand, the stereostructure of **14a** or **14b** was assumed to be 3,4-*anti*, 4,5-*syn* from the coupling constants of *ca.* 7.0 Hz[20] between H_3-H_4 as well as the following experimental results. Debenzylation of **12b** followed by the regioselective oxidation of the terminal hydroxy group furnished the cyclized 6-membered lactol via the corresponding hydroxy aldehyde, while no lactol formation was observed for **15b** after hydrolysis, followed by debenzylation and oxidation. This can be understood as the result of the different relative stereochemistry of the two substituents at the 3- and 4-positions of the acetonide 5-membered ring, suggesting that the structure of **12b** is *cis* and **15b** is *trans*.

Starting from allylic alcohols or the corresponding ethers, this osmylation reaction usually enables the isolation of triol products in an *anti* selective fashion with respect to the preexisting hydroxy (or alkoxy) and the adjacent, newly formed hydroxy moieties (between C_3 and C_4 in **8** in Scheme 4) irrespective of the olefinic structure of the substrate.[16] This *anti* selectivity has been explained experimentally[21a,b] and computationally[21c] by virtue of the different major rotational isomers at the allylic center containing a hydroxy (or alkoxy) moiety. On the other hand, to the best of our knowledge, only three research groups reported the exceptional *syn* preference,[22] where substrates possessed the common α,β-unsaturated carbonyl structure with *Z* configuration. These factors apparently control the diastereofacial selectivity because *Z*-substrates without a carbonyl group and *E*-substrates with a carbonyl (or a trifluoromethyl) showed the usual *anti* preference, though the reason is unclear.

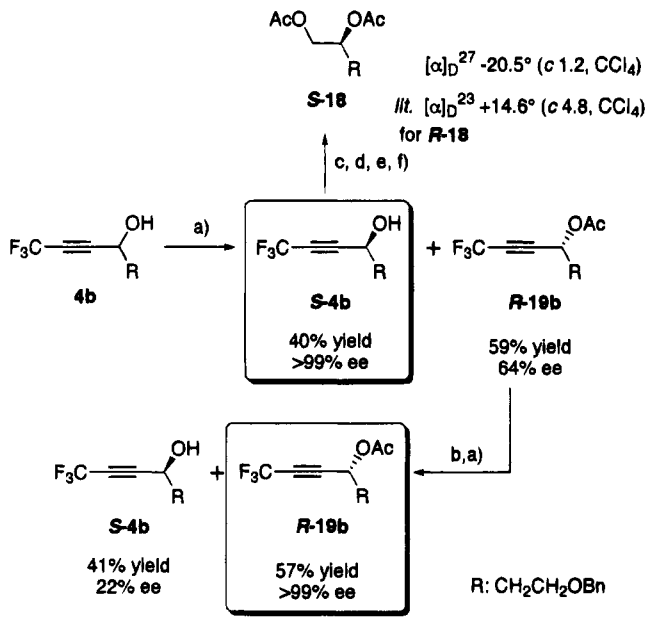
(19) The sugar numbering was employed throughout the text.

(20) Our MM2 calculation predicted the coupling constants between H_3-H_4 and H_4-H_5 as follows: 3,4-*anti*, 4,5-*anti*, 10.2 Hz, 10.2 Hz; 3,4-*anti*, 4,5-*syn*, 5.0 Hz, 3.7 Hz; 3,4-*syn*, 4,5-*anti*, 3.1 Hz, 4.1 Hz; 3,4-*syn*, 4,5-*syn*, 3.3 Hz, 3.3 Hz.

(21) (a) Cha, J. K.; Christ, W. J.; Kishi, Y. *Tetrahedron* **1984**, *40*, 2247–2255. (b) Vedejs, E.; McClure, C. K. *J. Am. Chem. Soc.* **1986**, *108*, 1094–1096. (c) Houk, K. N.; Duh, H.-Y.; Wu, Y.-D.; Moses, S. R. *J. Am. Chem. Soc.* **1986**, *108*, 2754–2755.

(22) (a) Stork, G.; Kahn, M. *Tetrahedron Lett.* **1983**, *24*, 3951–3954. (b) Brimacombe, J. S.; Hanna, R.; Kabir, A. K. M. S.; Bennett, F.; Taylor, I. D. *J. Chem. Soc., Perkin Trans. 1* **1986**, 815–821. (c) Fujioka, H.; Christ, W. J.; Cha, J. K.; Leder, J.; Kishi, Y.; Uemura, D.; Hirata, Y. *J. Am. Chem. Soc.* **1982**, *104*, 7367–7369.

Scheme 5[a]



[a] Key: (a) lipase QL, vinyl acetate (2 equiv)/*n*-hexane; (b) K_2CO_3/MeOH; (c) Red-Al; (d) O_3; (e) $LiAlH_4$; (f) AcCl, pyr.

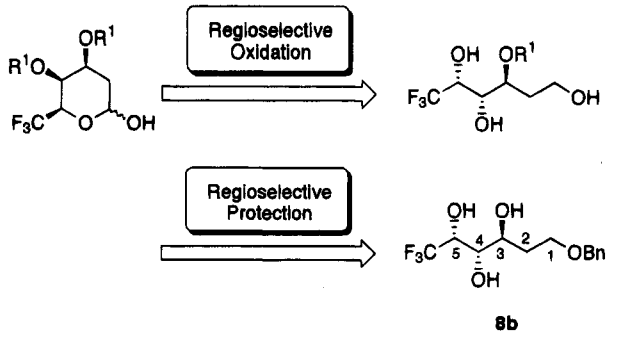
Construction of Chiral 2,6-Dideoxy-6,6,6-trifluorosugars. As was discussed above, we successfully obtained all of the diastereoisomers of triols **8b**–**11b**, important precursors for the desired 2,6-dideoxy-6,6,6-trifluorosugars. Given the purpose of these target molecules as biologically active substances, these materials were needed in their homochiral forms, which was conveniently realized by the enzymatic kinetic resolution.

After several explorations of reaction conditions, it was determined that lipase QL (*Alkaligenes sp.*, Meito Sangyo Co., Ltd., Japan) in *n*-hexane with vinyl acetate (2 equiv) preferentially acetylates *R* alcohol (E = 20, Scheme 5). Thus, this system allowed us to obtain the unreacted chiral alcohol, (***S***)-**4b**, with the *S* configuration (>99% ee, 40% yield) at 60% conversion. In this reaction, *R* acetate (***R***)-**19b** with 64% ee (59% yield) was also isolated, which was resolved by further enzymatic esterification using the same system (>99% ee, 57% yield). The absolute stereochemistry of (***S***)-**4b** was assigned as *S* by conversion of the chiral propargylic alcohol into the known diacetate (***S***)-**18**,[23] followed by comparison of their optical rotation values.

This enzymatic resolution allowed us to synthesize optically active triols for use as the intermediates in the formation of the desired 2,6-dideoxy-6,6,6-trifluorosugars. The next problems to be solved were (i) how to protect the two hydroxy groups at the 3- and 4-positions while leaving the same moiety at the 5-position intact and (ii) how to oxidize the terminal hydroxy group with high regioselectivity (Scheme 6, with triol **8b** as the representative example). On the basis of the characteristic electron-withdrawing nature of a trifluoromethyl group, the hydroxy group at the 5-position, the most proximate, would be most resistant to oxidation and least nucleophilic of the three hydroxy functions on **8b**. If this is the case, subjection of triol **8b** or its terminally deprotected diol after protection at the 3- and 4-position, for example, to an appropriate amount of reagent for protection or oxidation, respectively, would readily induce the desired regioselective reaction at the specific site.

(23) Brookes, M. H.; Golding, B. T. *J. Chem. Soc., Perkin Trans. 1* **1988**, 9.

Scheme 6



Actually, one example has already been described in Scheme 4 for the regioselective protection of hydroxy groups as acetonides. It is widely accepted that triols like **8b** favorably form 1,2-acetonides over their 1,3-counterparts, but the ratio is highly dependent on the structure.[24] This is also the case for our materials **8b**, **10b**, and **11b**, all of which afford 1,2-acetonides preferentially. **11b** was transformed to **15b** without any formation of the corresponding 1,3-acetonide, which can be explained by the fact that **15b** possesses the more stable *trans* configuration in its 5-membered ring system. Because of the unfavorable *cis* relationship in 5-membered systems, the corresponding 1,3-acetonides were obtained from both **8b** (3% of **14b**) and **10b** (42% of **17b**), and the stronger 1,3-acetonide preference of the latter might be due to the energetically preferable location of all of the substituents of **17b** at the equatorial positions. However, it is interesting to note that only 5-membered acetonide **12** was observed, without formation of the other possible 5-membered acetonide cyclized with hydroxy groups at both 4- and 5-positions, *even though the former possesses a syn relationship of the two substituents and the latter bears the more favorable anti arrangement*. The same trend was observed for the conversion of **8a** or **10a** (R: CH_2CH_2Ph), giving **12a** in 94% yield or a mixture of **16a** and **17a** (27:73) in 83% total yield, respectively.

Regioselectively protected alcohol **12b** was then debenzylated by Raney Ni to furnish the corresponding 1,5-diol *anti,syn*-**20**, which was, after further oxidation with 3 equiv of PDC, conveniently transformed into the desired 6,6,6-trifluoro-L-oliose **21** (50% yield) along with the corresponding overoxidized lactone **22** (33% yield), without any evidence of oxidation at the 5-position. The latter lactone was reduced with DIBALH in the usual manner to afford **21** in an almost quantitative yield. The final oxidation step could also be realized by Swern oxidation instead of PDC, but the formation of byproducts lacking fluorine decreased the isolated yield to 59% (Scheme 7).

The same procedures were also carried out for the conversion of the diastereomeric triol **9b** to 6,6,6-trifluorinated D-boivinose, but oxidation of *syn,syn*-**20** furnished only the corresponding hydroxy aldehyde **23**. As was discussed in the previous section for the determination of relative stereochemistry, this failure was presumably due to the unfavorable *trans* relationship of the two substituents required at the 3- and 4-positions of the 5-membered ring for the construction of lactol. This result clearly suggested that triols with the 3,4-*syn* structure, such as **9** or **11** in Scheme 3, should be protected in a more flexible, acyclic, manner.

(24) *Protective Groups in Organic Synthesis*; 2nd ed.; Greene, T. W., Wuts, P. G. M., Eds.; John Wiley & Sons: New York, 1991; pp 123–127.

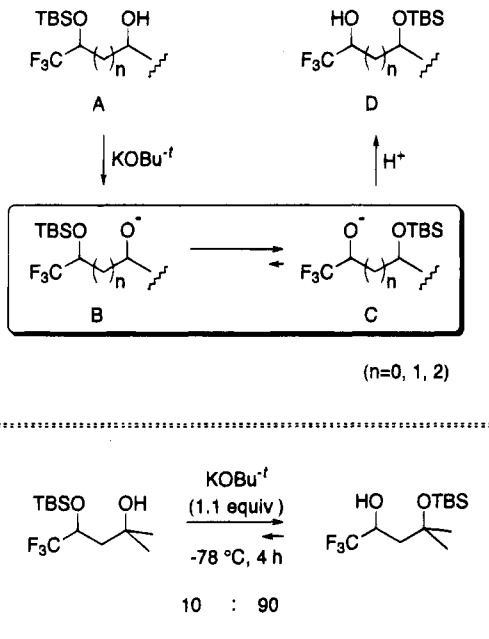
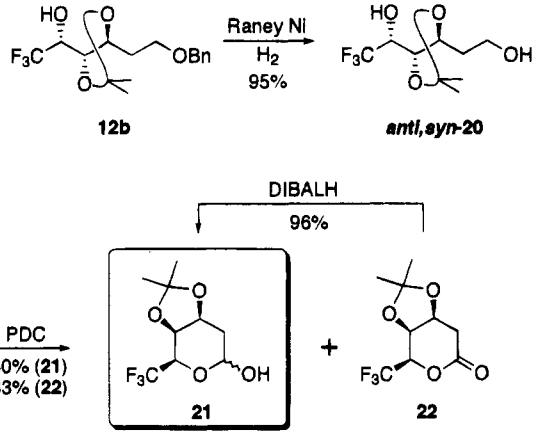


Figure 1.

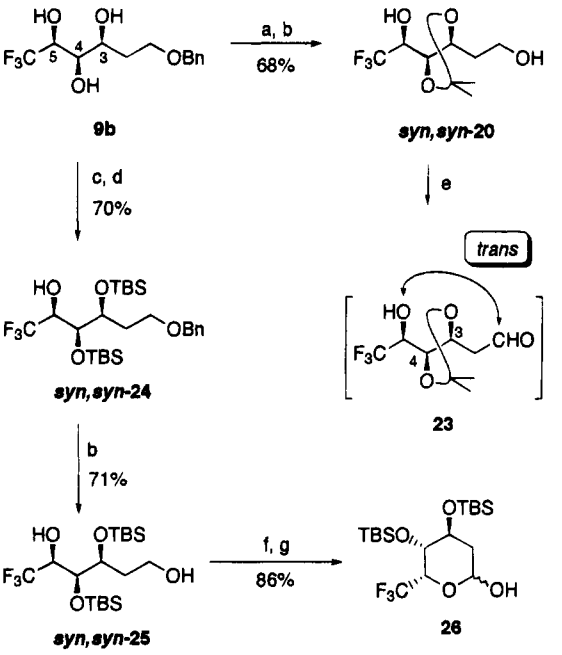
Scheme 7



A *tert*-butyldimethylsilyl (TBS) group was selected for the protection of a hydroxy group based on our previous finding.[7b] Thus, as shown in Figure 1, a TBS moiety in monoprotected CF_3-containing diol **A** could migrate in the presence of a base to the other hydroxy group under thermodynamically controlled conditions so as to produce the alkoxide **C**, which is more stable than the starting anion **B**. Of course, the strongly electron-withdrawing nature of a CF_3 group is responsible for this reaction, and the formation of a more stable anion is the driving force of this "electronically controlled" silyl migration, which is different from the conventional "sterically controlled" version.[25] We have previously reported the efficient preparation of a different type of 6-deoxy-6,6,6-trifluorosugar using this 1,2-*O*,*O*-silyl migration as a key step (n = 0 in Figure 1), and moreover, this migration was recently proved to proceed even from the secondary TBS ether to the tertiary hydroxy group, exclusively furnishing the more hindered tertiary TBS ether.[26]

This silylation step with triol **9b** was carried out under the usual TBS protection conditions (3 equiv) to furnish a regioisomeric mixture of bis-silyl ethers along with a minor amount of the corresponding monosilyl ethers (22% yield). After separation from the latter, the former was smoothly converted to the desired *syn,syn*-**24** as a single product in 70% total yield by KOBu-t (Scheme 8). The product was subjected to the PDC oxidation, followed by DIBALH[27] reduction to furnish the desired D-boivinose with three fluorines at the 6-position.

Scheme 8[a]



[a] Key: (a) $Me_2C(OMe)_2$, H^+; (b) Raney Ni (W2), H_2; (c) TBSCl, imidazole; (d) KOBu-t; (e) Swern oxidation; (f) PDC; (g) DIBALH.

For the preparation of 6,6,6-trifluoro-D-digitoxose **27** and L-olivose **28**, since the substrate triols **10b** and **11b** were not separable, the silyl protection pathway was carried out. Bis-silyl ethers, *anti,anti*- and *syn,anti*-**24**, were smoothly prepared as a separable mixture which, after separation by silica gel chromatography, led to the desired trifluorosugars in good yields (Scheme 9).

Conclusion

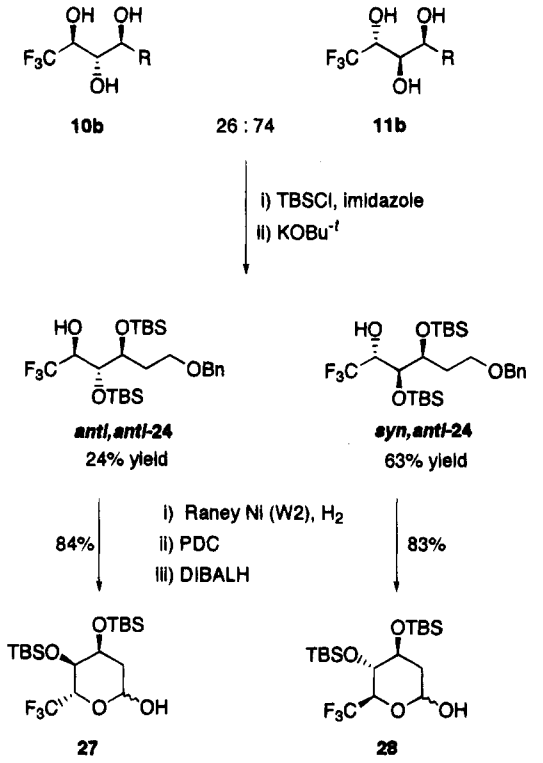
As described above, we have succeeded in developing a modified method for the easy generation of 3,3,3-trifluoropropynyl anion, starting from commercially available 3,3,3-trifluropropene in three steps with excellent total yields, and this was conveniently trapped with several types of electrophiles in good to excellent isolated yields. Considering the very high cost as well as the gaseous nature of 3,3,3-trifluoropropyne, the present method simplifies the access to molecules possessing the 3,3,3-trifluoropropynyl structure. One of the adducts, **4b**, was further transformed to the desired 2,6-dideoxy-6,6,6-trifluorosugars in a homochiral manner after enzymatic optical resolution. During formation of these target molecules, there is ready discrimination between plural hydroxy groups due to the strong inductive effect of the trifluoromethyl moiety, which renders the reaction path shorter and the total yields higher (50–70% from optically active triols).

(25) (a) Mulzer, J.; Schöllhorn, B. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 431–432. (b) Peters, U.; Bankova, W.; Welzel, P. *Tetrahedron* **1987**, *43*, 3803.

(26) Yamazaki, T.; Oniki, T.; Kitazume, T. Unpublished results. The details will be published elsewhere.

(27) Corey and co-worker have reported that the DIBALH/CH_2Cl_2 system could be employed for the deprotection of a TBS group. See: Corey, E. J.; Jones, G. B. *J. Org. Chem.* **1992**, *57*, 1028–1029. In our case, only reduced compounds were obtained probably due to the lower temperature (−78 °C), while usage of LAH might lead to the TBS migration.[7b]

Scheme 9



Experimental Section[7b]

General Procedure for Trifluoropropynylation. 4,4,4-Trifluoro-1-phenyl-2-butyn-1-ol (4d).[28] To a solution of LDA (44 mmol) in THF (40 mL) was added dropwise a precooled (−78 °C) solution of 2-bromo-3,3,3-trifluoropropene (3.5 g, 20 mmol) in THF (20 mL) at −78 °C. After the mixture was stirred for 5 min, PhCHO (2.5 mL, 24 mmol) was added and the whole was stirred for 30 min. The reaction mixture was quenched with 1 N HCl aq (100 mL) and extracted with AcOEt three times. The organic layer was dried over $MgSO_4$ and concentrated. The residue was chromatographed on silica gel to afford 3.956 g (19.8 mmol, 99%) of propargylic alcohol, **4d**: yield 98.9%; R_f 0.45 (AcOEt:Hex = 1:6); bp 71−72 °C/2 mmHg; ^{1}H NMR δ 2.7−3.2 (1 H, br), 5.517 (q, J =2.98 Hz), 7.2−7.5 (5 H, m); ^{13}C NMR δ 63.937 (q, J = 1.43 Hz), 73.447 (q, J = 42.98 Hz), 86.448 (q, J = 6.41 Hz), 124.142 (q, J = 257.35 Hz), 126.709, 129.091, 129.344, 137.870; ^{19}F NMR δ 27.84 (d, J = 2.77 Hz); IR (neat) ν 3350, 2950, 2925, 2850, 2250.

6,6,6-Trifluoro-1-phenyl-4-hexyn-3-ol (4a):[13] yield quant; bp 82−84 °C/0.8 mmHg; R_f 0.46 (AcOEt:Hex = 1:4); ^{1}H NMR δ 1.9−2.3 (2 H, m), 2.3−3.4 (1 H, br), 2.792 (2 H, t, J = 7.69 Hz), 4.420 (1 H, tq, J = 6.67, 3.42 Hz), 7.2−7.5 (5 H, m, *Ph*); ^{13}C NMR δ 30.984, 38.000 (q, J = 1.12 Hz), 60.900 (q, J = 1.47 Hz), 72.382 (q, J = 52.67 Hz), 87.655 (q, J = 6.40 Hz), 114.036 (q, J = 257.66 Hz), 126.382, 128.484, 128.654, 140.258; ^{19}F NMR δ 29.30 (d, J = 2.77 Hz); IR (neat) ν 3355, 3065, 3230, 2930, 2865, 2270.

1-(Benzyloxy)-6,6,6-trifluoro-4-hexyn-3-ol (4b): yield 92.0%; R_f 0.37 (AcOEt:Hex = 1:4); ^{1}H NMR δ 1.983 (1 H, dddd, J = 3.46, 5.57, 6.45, 14.76 Hz), 2.176 (1 H, ddt, J = 8.91, 14.77, 4.15 Hz), 3.444 (1 H, d, J = 6.84 Hz), 3.705 (1 H, ddd, J = 4.15, 5.50, 9.64 Hz), 3.864 (1 H, dt, J = 3.54, 9.28 Hz), 4.546 (2 H, s), 4.717 (1 H, dtq, J = 3.81, 6.73, 2.97 Hz), 7.2−7.4 (5 H, m); ^{13}C NMR δ 35.391, 60.914 (q, J = 1.17 Hz), 67.139, 72.035 (q, J = 52.77 Hz), 73.555, 87.502 (q, J = 6.30 Hz), 114.023 (q, J = 257.46 Hz), 127.736, 127.989, 128.534, 137.303; ^{19}F NMR δ 28.59 (d, J = 2.77 Hz); IR (neat) ν 3400, 3100, 3075, 3025, 2950, 2925, 2275; HRMS calcd for $C_{13}H_{13}F_3O_2$ m/e 258.0867, found 258.0852.

(28) Tajammal, S.; Tipping, A. E. *J. Fluorine Chem.* **1990**, *47*, 45−57.

1-(Benzyloxy)-5,5,5-trifluoro-3-pentyn-2-ol (4c):[17] yield 89.9%; R_f 0.31 (AcOEt:Hex = 1:4); ^{1}H NMR δ 2.800 (1 H, d, J = 6.09 Hz), 3.611 (1 H, dd, J = 5.94, 9.79 Hz), 3.694 (1 H, dd, J = 3.96, 9.80 Hz), 4.5−4.7 (1 H, m), 4.620 (2 H, s), 7.2−7.5 (5 H, m); ^{13}C NMR δ 61.171 (q, J = 1.42 Hz), 72.067 (q, J = 1.38 Hz), 72.356 (q, J = 53.08 Hz), 73.656, 85.447 (q, J = 6.61 Hz), 113.938 (q, J = 257.76 Hz), 127.930, 128.207, 128.646, 137.100; ^{19}F NMR δ 28.28 (s); IR (neat) ν 3425, 3100, 3075, 3050, 2915, 2875, 2275; HRMS calcd for $C_{12}H_{11}F_3O_2$ m/e 244.0710, found 244.0710.

1-Cyclohexyl-4,4,4-trifluoro-2-butyn-1-ol (4e): yield 93.3%; bp 110 °C/1.5 mmHg (bath temperature); R_f 0.34 (AcOEt:Hex = 1:6); ^{1}H NMR δ 0.9−2.0 (11 H, m), 2.4−2.7 (1 H, br), 4.1−4.3 (1 H, m); ^{13}C NMR δ 25.596, 25.621, 26.072, 27.906, 28.260, 43.360, 66.510 (q, J = 1.42 Hz), 72.814 (q, J = 52.77 Hz), 87.193 (q, J = 6.31 Hz), 114.021 (q, J = 257.05 Hz); ^{19}F NMR δ 28.57 (d, J = 2.09 Hz); IR (neat) ν 3325, 2915, 2850, 2250; HRMS calcd for $C_{10}H_{13}F_3O$ m/e 206.0918, found 206.0900.

(*E*)-6,6,6-Trifluoro-1-phenyl-1-hexen-4-yn-3-ol (4f): yield quant; R_f 0.26 (AcOEt:Hex = 1:6); bp 160 °C/0.7 mmHg (bath temperature); ^{1}H NMR δ 2.2−2.6 (1 H, br), 5.153 (1 H, ddq, J = 1.26, 5.96, 2.95 Hz), 6.257 (1 H, dd, J = 6.17, 15.84 Hz), 6.784 (1 H, dd, J = 1.34, 15.85 Hz), 7.2−7.5 (5 H, m); ^{13}C NMR δ 62.319 (q, J = 1.47 Hz), 73.222 (q, J = 52.67 Hz), 85.775 (q, J = 6.41 Hz), 114.035 (q, J = 257.56 Hz), 125.059 (q, J = 1.22 Hz), 126.940, 128.735, 128.767, 133.820, 135.268; ^{19}F NMR δ 28.20 (d, J = 2.09 Hz); IR (neat) ν 3325, 3100, 3075, 3050, 3000, 2950, 2900, 2275. Anal. Calcd for $C_{12}H_9F_3O$: C, 63.72; H, 4.01. Found: C, 63.93; H, 4.13.

1,1,1-Trifluoro-5-methyl-2-octyn-4-ol (4g): yield 74.9% (a 1:1 inseparable diastereomer mixture); bp 100 °C/5 mmHg (bath temperature); R_f 0.45 (AcOEt:Hex = 1:6); ^{1}H NMR δ 0.929 (3 H × 2, t, J = 6.78 Hz), 1.018 (3 H, d, J = 6.80 Hz), 1.024 (3 H, d, J = 6.74 Hz), 1.1−2.0 (10 H, m), 2.0−2.2 (2 H, br), 4.361 (1 H, dq, J = 0.85, 3.10 Hz), 4.387 (1 H, dq, J = 1.44, 3.05 Hz); ^{13}C NMR δ 14.131 (2 C), 14.410, 14.671, 20.017, 20.126, 33.883 (2 C), 34.455, 38.564, 66.102 (q, J = 1.42 Hz), 66.416 (q, J = 1.53 Hz), 72.723 (q, J = 52.46 Hz), 72.987 (q, J = 54.95 Hz), 86.970 (q, J = 6.50 Hz), 87.440 (q, J = 6.30 Hz), 114.049 (2 C, q, J = 257.36 Hz); ^{19}F NMR δ 28.11 (d, J = 2.77 Hz), 28.22(d, J = 2.77 Hz); IR (neat) ν 3450, 2975, 2265. Anal. Calcd for $C_9H_{13}F_3O$: C, 55.66; H, 6.75. Found: C, 55.82; H, 6.80.

2-(Benzyloxy)-6,6,6-trifluoro-4-hexyn-3-ol (4h): yield 93.9% (a 64:36 inseparable diastereomer mixture); R_f 0.31 (AcOEt:Hex = 1:4); bp 160 °C/0.8 mmHg (bath temperature); IR (neat) ν 3450, 2950, 2900, 2875, 2250. Anal. Calcd for $C_{13}H_{13}F_3O_2$: C, 60.46; H, 5.07. Found: C, 60.37; H, 5.05. **Major isomer**: ^{1}H NMR δ 1.299 (3 H, d, J = 6.22 Hz), 2.6−2.9 (1 H, br), 3.699 (1 H, dq, J = 5.82, 5.82 Hz), 4.2−4.4 (1 H, m), 4.542 (1 H, d, J = 11.64 Hz), 4.709 (1 H, d, J = 11.54 Hz), 7.2−7.5 (5 H, m); ^{13}C NMR δ 15.704, 65.583 (q, J = 1.47 Hz), 71.715, 72.551 (q, J = 52.67 Hz), 76.519, 86.111 (q, J = 6.10 Hz), 113.981 (q, J = 257.66 Hz), 128.035, 128.161, 128.622, 137.468; ^{19}F NMR δ 27.86 (d, J = 3.44 Hz). **Minor isomer**: ^{1}H NMR δ 1.288 (3 H, d, J = 6.29 Hz), 2.6−2.9 (1 H, br), 3.634 (1 H, dq, J = 3.86, 6.37 Hz), 4.3−4.5 (1 H, m), 4.503 (1 H, d, J = 11.72 Hz), 4.688 (1 H, d, J = 11.91 Hz), 7.2−7.5 (5 H, m); ^{13}C NMR δ 14.867, 64.942 (q, J = 1.52 Hz), 71.226, 72.992, 85.607 (q, J = 6.20 Hz), 127.904, 128.098, 128.622, 137.571 (*C*F$_3$ and CF$_3$*C*H were not observed); ^{19}F NMR δ 27.94 (d, J = 4.85 Hz).

6,6,6-Trifluoro-2-phenyl-4-hexyn-3-ol (4i): yield 96.5% (an 89:11 inseparable diastereomer mixture, physical properties were described only for the major isomer); bp 130 °C/4 mmHg (bath temperature); R_f 0.32 (AcOEt:Hex = 1:8); ^{1}H NMR δ 1.414 (3 H, d, J = 7.16 Hz), 2.0−2.3 (1 H, br), 3.097 (1 H, dq, J = 5.66, 7.15 Hz), 4.4−4.6 (1 H, m), 7.2−7.5 (5 H, m); ^{13}C NMR δ 15.759, 45.062 (q, J = 0.82 Hz), 66.580 (q, J = 1.42 Hz), 73.457 (q, J = 52.57 Hz), 86.682 (q, J = 6.40 Hz), 123.989 (q, J = 257.66 Hz), 127.667, 128.361, 128.640, 140.163; ^{19}F NMR δ 28.28 (s); IR (neat) ν 3375, 3075, 3050, 3025, 2975, 2925, 2900, 2875, 2275. Anal. Calcd for $C_{12}H_{11}F_3O$: C, 63.16; H, 4.86. Found: C, 63.46; H, 5.00.

5,5,5-Trifluoro-2-phenyl-3-pentyn-2-ol (4j).[12a] Yield 89.2%; R_f 0.49 (AcOEt:Hex = 1:6); bp 85 °C/2 mmHg (bath temperature); ^{1}H NMR δ 1.818 (3 H, s), 2.3−2.8 (1 H, br), 7.2−

7.5 (5 H, m); ^{13}C NMR δ 32.191, 69.740 (q J = 1.38 Hz), 72.027 (q, J = 53.08 Hz), 89.975 (q, J = 6.30 Hz), 114.240 (q, J = 257.86 Hz), 124.614, 128.531, 128.731, 143.044; ^{19}F NMR δ 28.36 (s); IR (neat) ν 3350, 3075, 3025, 3000, 2925, 2275.

1-(3,3,3-Trifluoroprop-1-yl)cyclohexan-1-ol (4k):[17] yield quant; mp 53.0–53.5 °C; R_f 0.41 (AcOEt:Hex = 1:6); ^{1}H NMR δ 1.2–2.1 (10 H, m), 2.1–2.4 (1 H, br); ^{13}C NMR δ 22.755, 24.768, 38.877, 68.373 (q, J = 1.37 Hz), 89.823 (q, J = 60.4 Hz), 90.616 (q, J = 6.30 Hz), 114.213 (q, J = 257.15 Hz); ^{19}F NMR δ 28.95 (s); IR (KBr) ν 3260, 2950, 2870, 2280.

3,3,3-Trifluoro-1-(phenyldimethylsilyl)propyne (6). To a solution of LDA (4.4 mmol) in THF (4 mL) was added dropwise a precooled (−78 °C) solution of 2-bromo-3,3,3-trifluoropropene (0.35 g, 2.0 mmol) in THF (2 mL) at −78 °C. After the mixture was stirred for 5 min, phenyldimethylsilyl chloride (0.4 g, 2.4 mmol) was added to this solution and the whole was stirred for 30 min. The reaction mixture was quenched with saturated NH_4Cl aq and extracted with AcOEt three times. The organic layer was dried over $MgSO_4$ and concentrated to afford the title compound (1.47 mmol, 74%, determined by ^{19}F NMR with $PhCF_3$ as internal standard). An analytical sample was obtained by short path distillation of the crude product: bp 90 °C/25 mmHg (bath temperature); R_f 0.49 (Hex); ^{1}H NMR δ 0.5–0.6 (6 H, m), 7.3–7.7 (5 H, m); ^{13}C NMR δ −1.978, 91.154 (q, J = 50.84 Hz), 92.353 (q, J = 5.99 Hz), 113.122 (q, J = 257.86 Hz), 128.237, 130.257, 133.021, 133.674; ^{19}F NMR δ 27.851 (s); IR (neat) ν 3075, 3050, 3025, 2975, 2200.

General Procedure for Hydrogenolysis of Alkynes to (*E*)-Alkenes. To a stirring solution of Red-Al (2.5 mmol) in toluene (3 mL) at −78 °C was added an appropriate propargylic alcohol **4** (2.12 mmol). After the reaction mixture was stirred for 3 h at that temperature, it was quenched with 1 N HCl (10 mL) and the usual workup gave the crude olefin. After purification by silica gel column chromatography, the pure allylic alcohol was obtained.

(*E*)-6,6,6-Trifluoro-1-phenyl-4-hexen-3-ol ((*E*)-7a):[17] yield 96.9%; R_f 0.42 (AcOEt: Hex = 1:4); ^{1}H NMR δ 1.703 (1 H, d, J = 4.89 Hz), 1.8–2.0 (2 H, m), 2.736 (1 H, ddd J = 7.33, 8.55, 13.92 Hz), 2.791 (1 H, ddd, J = 6.11, 8.79, 13.92 Hz), 4.2–4.3 (1 H, m), 5.907 (1 H, ddq, J = 1.71, 15.75, 6.48 Hz), 6.419 (1 H, ddq, J = 4.35, 15.79, 2.17 Hz), 7.2–7.4 (5 H, m); ^{13}C NMR δ 31.353, 37.884, 69.539, 117.944 (q, J = 34.17 Hz), 123.140 (q, J = 269.65 Hz), 126.159, 128.391, 128.551, 140.961, 141.138 (q, J = 6.10 Hz); ^{19}F NMR δ 15.00 (d, J = 6.21 Hz); IR (neat) ν 3355, 3065, 3030, 2930, 2865; HRMS calcd for $C_{12}H_{13}F_3O$ m/e 230.0918, found 230.0902.

(3*S*)-(*E*)-1-(Benzyloxy)-6,6,6-trifluoro-4-hexen-3-ol ((*E*)-7b): yield 91.8%; R_f 0.38 (AcOEt:Hex = 1:4); $[\alpha]^{18}_D$ +8.33° (c 1.55, $CHCl_3$), 99.6% ee; ^{1}H NMR δ 1.7–2.1 (2 H, m), 3.414 (1 H, d, J = 3.81 Hz), 3.654 (1 H, dt, J = 9.34, 4.27 Hz), 3.734 (1 H, dt, J = 9.38, 4.04 Hz), 4.4–4.6 (1 H, m), 4.521 (2 H, s), 5.950 (1 H, ddq, J = 2.01, 15.62, 6.57 Hz), 6.376 (1 H, ddq, J = 4.01, 15.60, 2.01 Hz), 7.2–7.4 (5 H, m); ^{13}C NMR δ 35.385 (q, J = 1.32 Hz), 68.330, 69.788, 73.535, 117.907 (q, J = 33.65 Hz), 123.375 (q, J = 268.84 Hz), 127.779, 128.011, 128.581, 137.445, 141.789 (q, J = 6.30 Hz); ^{19}F NMR δ 15.01 (d, J = 5.53 Hz); IR (neat) ν 3450, 3075, 3050, 2950, 2875; HRMS calcd for $C_{13}H_{15}F_3O_2$ m/e 260.1023, found 260.1012.

(*E*)-1-(Benzyloxy)-5,5,5-trifluoro-3-penten-2-ol ((*E*)-7c):[17] yield 91.7%; R_f 0.34 (AcOEt:Hex = 1:4); ^{1}H NMR δ 2.652 (1 H, d, J = 4.05 Hz), 3.371 (1 H, dd, J = 7.51, 9.52 Hz), 3.601 (1 H, dd, J = 3.48, 9.52 Hz), 4.4–4.6 (1 H, m), 4.572 (2 H, s), 6.014 (1 H, ddq, J = 1.93, 15.67, 6.45 Hz), 6.351 (1 H, ddq, J = 3.98, 15.67, 1.99 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ 69.149, 72.884 (q, J = 1.53 Hz), 73.535, 119.472 (q, J = 34.07 Hz), 123.105 (q, J = 268.95 Hz), 127.884, 128.096, 128.600, 137.350, 138.053 (q, J = 6.40 Hz); ^{19}F NMR δ 14.74 (d, J = 4.80 Hz); IR (neat) ν 3450, 3075, 3050, 2900, 2875; HRMS calcd for $C_{12}H_{13}F_3O_2$ m/e 246.0867, found 246.0863.

General Procedure for Hydrogenolysis of Alkynes to (*Z*)-Alkenes. A solution of propargylic alcohol **4** (2.0 mmol) and a catalytic amount of Lindlar catalyst in hexane (20 mL) was stirred under H_2. After removal of the catalyst by filtration, concentration under reduced pressure and chromatography of the residue on silica gel gave allylic alcohol.

(*Z*)-6,6,6-Trifluoro-1-phenyl-4-hexen-3-ol ((*Z*)-7a):[17] yield 94.3%; R_f 0.32 (AcOEt:Hex = 1:4); ^{1}H NMR δ 1.7–2.0 (2 H, m), 2.0–2.4 (1 H, d, J = 4.89 Hz), 2.660 (1 H, ddd J = 6.76, 9.50, 13.74 Hz), 2.797 (1 H, ddd, J = 5.80, 10.17, 13.74 Hz), 4.6–4.8 (1 H, m), 5.639 (1 H, ddq, J = 1.11, 11.86, 8.65 Hz), 6.013 (1 H, dd, J = 9.16, 11.86 Hz), 7.1–7.5 (5 H, m); ^{13}C NMR δ 31.317, 38.228, 67.243 (q, J = 1.42 Hz), 118.383 (q, J = 34.16 Hz), 122.768 (q, J = 271.79 Hz), 126.068, 128.363, 128.478, 141.174, 144.232 (q, J = 5.18 Hz); ^{19}F NMR δ 21.21 (d, J = 8.24 Hz); IR (neat) ν 3375, 3065, 3030, 2930; HRMS calcd for $C_{12}H_{13}F_3O$ m/e 230.0918, found 230.0925.

(3*S*)-(*Z*)-1-(Benzyloxy)-6,6,6-trifluoro-4-hexen-3-ol ((*Z*)-7b): yield 96.4%; R_f 0.23 (AcOEt:Hex = 1:4); $[\alpha]^{16}_D$ +5.40° (c 1.00, $CHCl_3$), 98.5% ee; ^{1}H NMR δ 1.6–2.1 (2 H, m), 3.316 (1 H, d, J = 3.25 Hz), 3.661 (1 H, ddd, J = 4.06, 4.90, 8.91 Hz), 3.739 (1 H, ddd, J = 2.56, 4.88, 9.38 Hz), 4.485 (1 H, d, J = 11.90 Hz), 4.558 (1 H, d, J = 11.72 Hz), 4.7–5.0 (1 H, m), 5.589 (1 H, ddq, J = 1.23, 11.94, 8.76 Hz), 6.033 (1 H, dd, J = 8.81, 11.94 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ 36.184, 67.536 (q, J = 1.42 Hz), 68.294, 73.416, 117.727 (q, J = 34.47 Hz), 122.879 (q, J = 272.00 Hz), 127.752, 127.908, 128.537, 137.627, 144.485 (q, J = 5.19 Hz); ^{19}F NMR δ 20.928 (d, J = 8.24 Hz); IR (neat) ν 3425, 3075, 3050, 2950, 2875, 675; HRMS calcd for $C_{13}H_{15}F_3O_2$ m/e 260.1023, found 260.1041.

(*Z*)-1-(Benzyloxy)-5,5,5-trifluoro-3-penten-2-ol ((*Z*)-7c):[17] yield 92.0%; R_f 0.19 (AcOEt:Hex = 1:4); ^{1}H NMR δ 2.0–2.8 (1 H, br), 3.426 (1 H, dd, J = 7.26, 9.64 Hz), 3.577 (1 H, dd, J = 3.45, 9.69 Hz), 4.544 (1 H, d, J = 11.78 Hz), 4.613 (1 H, d, J = 11.75 Hz), 4.8–5.0 (1 H, m), 5.693 (1 H, ddq, J = 1.30, 12.06, 8.61 Hz), 6.029 (1 H, dd, J = 8.57, 12.01 Hz), 7.3–7.4 (5 H, m); ^{13}C NMR δ 66.917, 72.971 (q, J = 1.47 Hz), 73.428, 119.753 (q, J = 34.68 Hz), 122.685 (q, J = 271.39 Hz), 127.801, 128.001, 128.547, 137.464, 140.730 (q, J = 4.78 Hz); ^{19}F NMR δ 20.42 (d, J = 7.56 Hz); IR (neat) ν 3450, 3075, 3025, 2975, 2875; HRMS calcd for $C_{12}H_{13}F_3O_2$ m/e 246.0867, found 246.0862.

General Procedure for Osmium Oxidation of Allylic Alcohol. To a solution of *N*-methylmorpholine *N*-oxide hydrate (2.7 g, ca. 20 mmol) in 66% acetone−H_2O (12 mL) was added a 2.5 wt % solution of OsO_4 in *t*-BuOH (0.48 mL, 0.3 mol %) under N_2 at 0 °C, followed by the addition of an allylic alcohol (12.87 mmol). After the reaction was quenched after 2 days at ambient temperature by addition of Na_2SO_3 aq (10 mL) and the residue was removed through a pad of Celite, the filtrate was extracted with AcOEt, dried over by $MgSO_4$, and evaporated. Purification by silica gel column chromatography gave two separable stereoisomers of triols.

(2*S,3*R**,4*R**)-1,1,1-Trifluoro-6-phenylhexane-2,3,4-triol (8a) and (2*R**,3*S**,4*R**)-1,1,1-trifluoro-6-phenylhexane-2,3,4-triol (9a):** yield 82.7% (a 91:9 separable diastereomer mixture). **Major isomer (8a):** R_f 0.48 (AcOEt:Hex = 1:2); mp 98.5–99.0 °C; ^{1}H NMR (acetone-d_6) δ 1.6–1.9 (1 H, m), 2.0–2.3 (1 H, m), 2.701 (1 H, ddd, J = 6.60, 10.10, 13.53 Hz), 2.915 (1 H, ddd, J = 4.88, 10.17, 13.62 Hz), 3.5–3.8 (2 H, m), 4.0–4.3 (2 H, m), 4.385 (1 H, dq, J = 8.15, 8.15 Hz), 4.717 (1 H, d, J = 4.40 Hz), 7.0–7.4 (5 H, m); ^{13}C NMR (acetone-d_6) δ 32.147, 36.288, 68.704 (q, J = 29.08 Hz), 70.515, 71.840 (q, J = 1.58 Hz), 126.243, 126.557 (q, J = 282.88 Hz), 128.912, 129.082, 143.296; ^{19}F NMR (acetone-d_6) δ 1.33 (d, J = 7.62 Hz); IR (KBr) ν 3400, 3050, 2950, 2925, 2850; HRMS calcd for $C_{12}H_{15}F_3O_3$ m/e 260.0972, found 260.0983. **Minor isomer (9a):** R_f 0.31 (AcOEt:Hex = 1:2); mp 97.5–98.5 °C; ^{1}H NMR δ 1.6–2.1 (2 H, m), 2.2–2.4 (1 H, br), 2.6–2.7 (1 H, br), 2.711 (1 H, ddd, J = 7.03, 8.77, 13.79 Hz), 2.880 (1 H, ddd, J = 5.85, 9.32, 13.56 Hz), 3.537 (1 H, d, J = 7.32 Hz), 3.7–3.9 (2 H, m), 4.230 (1 H, dq, J = 7.22, 7.22 Hz), 7.2–7.4 (5 H, m); ^{13}C NMR δ 31.815, 34.571, 68.451 (q, J = 29.99 Hz), 70.427, 72.164, 123.560 (q, J = 280.33 Hz), 126.236, 128.414, 128.636, 141.160; ^{19}F NMR δ 1.35 (d, J = 7.56 Hz); IR (KBr) ν 3455, 3375, 3330, 3035, 3010, 2965, 2930, 2860. Anal. Calcd for $C_{12}H_{15}F_3O_3$: C, 54.55; H, 5.72. Found: C, 54.49; H, 5.80.

(2*R,3*R**,4*R**)-1,1,1-Trifluoro-6-phenylhexane-2,3,4-triol (10a) and (2*S**,3*S**,4*R**)-1,1,1-trifluoro-6-phenylhexane-2,3,4-triol (11a):** yield 75.1% (an 85:15 inseparable diastereomer mixture); R_f 0.40 (AcOEt:Hex = 1:2); IR (KBr) ν 3350, 3050, 2950, 2925, 2850; HRMS calcd for $C_{12}H_{15}F_3O_3$ m/e 264.0972, found 264.0955. **Major isomer (11a):** ^{1}H NMR

(with a few drop of DMSO-d_6) δ 1.7–2.1 (2 H, m), 2.5–3.0 (2 H, m), 3.5–3.9 (3 H, m), 3.9–4.2 (2 H, m), 5.4–5.6 (1 H, m), 7.1–7.4 (5 H, m); ^{13}C NMR (with a few drop of DMSO-d_6) δ 31.869, 34.920, 69.739 (q, J =1.37 Hz), 70.649 (q, J = 1.43 Hz), 71.516 (q, J = 28.57 Hz), 125.174 (q, J = 283.08 Hz), 125.659, 128.207, 128.282, 141.762; ^{19}F NMR (with a few drop of DMSO-d_6) δ 3.73 (d, J = 7.56 Hz). **Minor isomer (10a):** ^{1}H NMR δ 1.864 (1 H, ddt, J = 5.86, 14.05, 9.17 Hz), 2.056 (1 H, dddd, J = 2.68, 6.87, 9.48, 14.19 Hz), 2.1–2.5 (3 H, br), 2.712 (1 H, ddd, J = 6.91, 9.09, 13.79 Hz), 2.884 (1 H, ddd, J = 5.90, 9.06, 13.62 Hz), 3.6–4.2 (3 H, m), 7.2–7.4 (5 H, m); ^{13}C NMR δ 31.631, 33.770, 72.114, 72.325 (q, J = 31.62 Hz), 72.639, 124.790 (q, J = 283.08 Hz), 126.143, 128.420, 128.587, 141.435; ^{19}F NMR δ 3.44 (d, J = 5.48 Hz).

(2*R*,3*S*,4*S*)-6-(Benzyloxy)-1,1,1-trifluorohexane-2,3,4-triol (8b) and (2*S*,3*R*,4*S*)-6-(benzyloxy)-1,1,1-trifluorohexane-2,3,4-triol (9b): yield 86.4% (an 87:13 separable diastereomer mixture). **Major isomer (8b):** R_f 0.39 (AcOEt:Hex = 1:1); mp 99.0–99.5 °C; $[\alpha]^{16}_D$ −9.03° (*c* 1.01, $CHCl_3$), 99.6% ee; ^{1}H NMR (with a few drop of DMSO-d_6) δ 1.7–1.9 (1 H, m), 2.106 (1 H, dddd, J = 2.48, 4.27, 6.60, 14.75 Hz), 3.6–3.8 (4 H, m), 3.8–4.1 (3 H, m), 4.303 (1 H, dq, J = 1.06, 7.78 Hz), 4.523 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR (with a few drop of DMSO-d_6) δ 32.626, 67.800 (q, J = 29.59 Hz), 68.660, 70.619, 70.183 (q, J = 1.83 Hz), 73.317, 125.333 (q, J = 282.96 Hz), 127.714, 127.795, 128.456, 137.743; ^{19}F NMR (with a few drop of DMSO-d_6) δ 2.41 (d, J = 7.56 Hz); IR (KBr) ν 3355, 2960, 2880, 2865. Anal. Calcd for $C_{13}H_{17}F_3O_4$: C, 53.06; H, 5.82. Found: C, 52.77; H, 6.03. **Minor isomer (9b):** R_f 0.30 (AcOEt:Hex = 1:1); mp 79.5–80.0 °C; $[\alpha]^{16}_D$ −21.20° (*c* 0.77, MeOH), 99.6% ee; ^{1}H NMR δ 1.6–2.1 (2 H, m), 3.5–4.3 (8 H, m), 4.512 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR δ 32.498, 68.007, 69.780 (q, J = 1.68 Hz), 70.3672 (q, J = 30.20 Hz), 72.342 (q, J = 1.27 Hz), 73.381, 124.358 (q, J = 282.67 Hz), 127.766, 127.950, 128.498, 137.324; ^{19}F NMR δ 1.94 (d, J = 5.48 Hz); IR (KBr) ν 3410, 3355, 2955, 2930, 2900, 2875; HRMS calcd for $C_{13}H_{17}F_3O_4$ *m/e* 294.1078, found 294.1091.

(2*S*,3*S*,4*S*)-6-(Benzyloxy)-1,1,1-trifluorohexane-2,3,4-triol (10b) and (2*R*,3*R*,4*S*)-6-(benzyloxy)-1,1,1-trifluorohexane-2,3,4-triol (11b): yield 71.2% (a 74:26 inseparable diastereomer mixture, 16.7% of starting material was recovered); R_f 0.30 (AcOEt:Hex = 1:1); IR (KBr) ν 3290, 2925, 2875. Anal. Calcd for $C_{13}H_{17}F_3O_4$: C, 53.06; H, 5.82. Found: C, 52.89; H, 5.93. **Major isomer (11b):** ^{1}H NMR δ 1.716 (1 H, ddt, J = 4.44, 15.19, 6.20 Hz), 2.179 (1 H, ddt, J = 5.24, 15.01, 9.21 Hz), 2.931 (1 H, d, J = 9.70 Hz), 3.8–4.4 (7 H, m), 4.537 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR δ 32.696, 69.091, 70.292 (q, J = 1.53 Hz), 72.097 (q, J = 1.43 Hz), 73.057 (q, J = 29.59 Hz), 73.646, 124.688 (q, J = 283.08 Hz), 127.817, 128.128, 128.638, 137.166; ^{19}F NMR δ 2.94 (d, J = 6.89 Hz). **Minor isomer (10b):** ^{1}H NMR δ 1.8–2.2 (2 H, m), 2.7–2.9 (1 H, br), 3.6–4.1 (7 H, m), 4.4657 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR δ 31.905 (2C), 68.411, 71.118 (q, J = 1.27 Hz), 72.550 (q, J = 28.87 Hz), 73.670, 124.746 (q, J = 282.88 Hz), 127.863, 128.138, 128.625, 137.051; ^{19}F NMR δ 3.28 (d, J = 6.21 Hz).

(2*S,3*R**,4*R**)-5-(Benzyloxy)-1,1,1-trifluoropentane-2,3,4-triol (8c) and (2*R**,3*S**,4*R**)-5-(benzyloxy)-1,1,1-trifluoropentane-2,3,4-triol (9c):** yield 76.4% (an 80:20 separable diastereomer mixture). **Major isomer (8c):** R_f 0.36 (AcOEt:Hex = 1:1); mp 105.5–106.0 °C; ^{1}H NMR (with a few drop of DMSO-d_6) δ 3.7–4.0 (7 H, m), 4.310 (1 H, dq, J = 0.82, 7.81 Hz), 4.576 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR (with a few drop of DMSO-d_6) δ 67.867 (q, J = 29.69 Hz), 69.002 (q, J = 1.67 Hz), 69.404, 71.547, 73.470, 125.328 (q, J = 283.39 Hz), 127.760, 127.801, 128.401, 137.876; ^{19}F NMR (with a few drop of DMSO-d_6) δ 2.58 (d, J = 7.62 Hz); IR (KBr) ν 3395, 2930, 2870; HRMS calcd for $C_{12}H_{15}F_3O_4$ *m/e* 280.0921, found 280.0941. **Minor isomer (9c):** R_f 0.26 (AcOEt:Hex = 1:1); mp 129.5–130.5 °C; ^{1}H NMR (acetone-d_6) δ 3.608 (1 H, dd, J = 5.50, 9.75 Hz), 3.703 (1 H, dd, J = 4.38, 10.20 Hz), 3.9–4.0 (2 H, m), 4.1–4.3 (3 H, m), 4.555 (2 H, s), 4.872 (1 H, d, J = 7.33 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR (acetone-d_6) δ 69.414 (q, J = 1.58 Hz), 70.442 (q, J = 29.39 Hz), 72.111 (q, J = 1.17 Hz), 72.393, 74.061, 126.374 (q, J = 275.15 Hz), 128.529, 128.644, 129.327, 139.704; ^{19}F NMR (acetone d_6) δ 1.39 (d, J = 7.62 Hz); IR (KBr) ν 3425, 3360, 2940, 2905. Anal. Calcd for $C_{12}H_{15}F_3O_4$: C, 51.43; H, 5.39. Found: C, 51.51; H, 5.21.

(2*R,3*R**,4*R**)-5-(Benzyloxy)-1,1,1-trifluoropentane-2,3,4-triol (10c) and (2*S**,3*S**,4*R**)-5-(benzyloxy)-1,1,1-trifluoropentane-2,3,4-triol (11c):** yield 66.1% (34.8% of starting (*Z*)-**8c** was recovered, a 58:42 inseparable diastereomer mixture); R_f 0.30 (AcOEt:Hex = 1:1); IR (neat) ν 3425, 2930; HRMS calcd for $C_{12}H_{15}F_3O_4$ *m/e* 280.0921, found 280.0927. **Major isomer (11c):** ^{1}H NMR δ 2.0–4.3 (8 H, m), 4.539 (2 H, s), 7.2–7.5 (5 H, m); ^{13}C NMR δ 69.040, 69.513 (q, J = 1.22 Hz), 71.567 (q, J = 29.89 Hz), 72.311, 73.786, 124.657 (q, J = 273.08 Hz), 127.944, 128.176, 128.606, 136.996; ^{19}F NMR δ 3.07 (d, J = 6.89 Hz). **Minor isomer (10c):** ^{1}H NMR δ 2.0–4.3 (8 H, m), 4.552 (2 H, s), 7.2–7.5 (5 H, m); ^{13}C NMR δ 70.421, 70.649 (q, J = 2.13 Hz), 70.825, 71.543 (q, J = 29.84 Hz), 73.758, 127.981, 128.232, 128.640, 136.927, CF_3 was not observed; ^{19}F NMR δ 3.40 (d, J = 6.21 Hz).

Determination of the Relative Configuration. General Procedure for Acetonide Formation of a Triol. A solution of triol (2.27 mmol), dimethoxypropane (3 mmol), and a catalytic amount of *p*-TsOH in THF (4 mL) was stirred for 12 h at room temperature. To this solution was added $NaHCO_3$ aq and the resulting solution extracted with AcOEt. The usual workup and purification by silica gel column chromatography gave the desired acetonide.

(2*R*,3*R*,4*S*)-6-(Benzyloxy)-1,1,1-trifluoro-3,4-*O*-isopropylidenehexane-2,3,4-triol (12b). The acetonide formation procedure described above gave the title compound **12b** (yield 91.0%) and 2,4-acetonide **13b**. The structure of the latter was identified after acetylation by the usual esterification procedure (**14b**, yield 3.3% from triol): R_f 0.51 (AcOEt:Hex = 1:4); $[\alpha]^{18}_D$ +4.09° (*c* 1.57, $CHCl_3$), 99.6% ee; ^{1}H NMR δ 1.396 (3 H, q, J = 0.73 Hz), 1.522 (3 H, q, J = 0.61 Hz), 2.000 (1 H, dddd, J = 4.11, 5.27, 7.63, 14.13 Hz), 2.040 (1 H, ddt, J = 8.95, 14.13, 5.41 Hz), 2.838 (1 H, d, J = 10.13 Hz), 3.606 (1 H, dt, J = 5.25, 9.22 Hz), 3.672 (1 H, ddd, J = 4.06, 5.34, 9.37 Hz), 4.00–4.15 (1 H, m), 4.353 (1 H, dd, J = 1.04, 7.14 Hz), 4.483 (1 H, dt, J = 5.37, 7.39 Hz), 4.509 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR δ 24.719, 26.671, 30.385, 67.178, 67.988 (q, J = 30.15 Hz), 73.300, 73.324 (q, J = 1.57 Hz), 74.993, 108.637, 124.479 (q, J = 283.48 Hz), 127.712, 127.731, 128.436, 138.060; ^{19}F NMR δ 1.36 (d, J = 7.56 Hz); IR (neat) ν 3525, 3025, 3000, 2950, 2875; HRMS calcd for $C_{16}H_{21}F_3O_4$ *m/e* 334.1391, found 334.1396.

(2*R,3*S**,4*S**)-3-Acetoxy-6-(benzyloxy)-1,1,1-trifluoro-2,4-*O*-isopropylidenehexane-2,4-diol (14b):** R_f 0.43 (AcOEt:Hex = 1:5); ^{1}H NMR δ 1.363 (3 H, s), 1.453 (3 H, s), 1.804 (1 H, ddt, J = 9.58, 14.39, 4.81 Hz), 1.996 (1 H, ddt, J = 3.47, 14.37, 7.21 Hz), 2.082 (3 H, s), 3.548 (2 H, dd, J = 4.81, 7.19 Hz), 3.936 (1 H, ddd, J = 3.47, 6.90, 9.48 Hz), 4.298 (1 H, dq, J = 4.03, 7.02 Hz), 4.450 (1 H, d, J = 11.31 Hz), 4.513 (1 H, d, J = 11.84 Hz), 5.239 (1 H, dd, J = 3.99, 6.88 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ 20.872, 23.268, 24.421, 32.822, 65.583, 68.749 (q, J = 31.72 Hz), 68.700, 70.805, 73.104, 102.461, 123.233 (q, J = 280.13 Hz), 127.674, 127.731, 128.415, 138.254, 169.857; ^{19}F NMR δ 5.43 (d, J = 6.89 Hz); IR (neat) ν 3065, 3030, 2995, 2940, 2865, 1749. Anal. Calcd for $C_{18}H_{23}F_3O_5$: C, 57.44; H, 6.16. Found: C, 57.59; H, 6.25.

(2*R,3*R**,4*S**)-1,1,1-Trifluoro-6-phenyl-3,4-*O*-isopropylidenehexane-2,3,4-triol (12a).** Acetonide formation procedure of a triol (**8a**) described above gave a mixture of separable 3,4-acetonide **12a** (94.3%) and its two regioisomers (**13a** and 4-hydroxy-2,3-acetonide as a 1:1 inseparable mixture, 5.7%). After separation by silica gel column chromatography, the structure of the latter mixture were identified after acetylation by usual esterification procedure to afford an inseparable mixture of **14a** and 4-acetyl-2,3-acetonide: R_f 0.46 (AcOEt:Hex = 1:5); ^{1}H NMR δ 1.399 (3 H, s), 1.566 (3 H, s), 1.806 (1 H, dddd, J = 2.81, 7.46, 9.40, 13.52 Hz), 2.111 (1 H, dddd, J = 4.89, 8.94, 10.11, 13.58 Hz), 2.684 (1 H, ddd, J = 7.57, 8.85, 13.73 Hz), 2.909 (1 H, d, J = 10.01 Hz), 2.929 (1 H, ddd, J = 4.70, 9.34, 13.77 Hz), 3.852 (1 H, ddq, J = 0.85, 9.87, 7.30 Hz), 4.277 (1 H, dt, J = 2.81, 7.08 Hz), 4.296 (1 H, dd, J = 1.10, 7.08 Hz), 7.1–7.4 (5 H, m); ^{13}C NMR δ 24.279, 26.823, 31.825, 32.749, 67.867 (q, J = 30.20 Hz), 73.011 (q, J = 1.57 Hz), 76.028, 108.993, 123.705 (q, J = 289.2 Hz), 126.177, 128.506, 128.536, 141.008; ^{19}F NMR δ 1.23 (d, J = 6.77 Hz); IR (neat) ν 3550, 3100, 3050, 3025, 2975, 2875. **Minor product ((2*R**,3*S**,4*S**)-3-acetoxy-6-phenyl-1,1,1-trifluoro-2,4-*O*-**

isopropylidenehexane-2,4-diol (14a) and (2*R,3*R**,4*S**)-4-acetoxy-6-phenyl-1,1,1-trifluoro-2,3-*O*-isopropylidenehexane-2,3-diol, a 51:49 inseparable mixture):** R_f 0.53 (AcOEt:Hex = 1:6); ^{1}H NMR δ 1.409 (6 H, s), 1.427 (3 H, s), 1.461 (3 H, s), 1.8–2.0 (4 H, m), 2.053 (3 H, s), 2.061 (3 H, s), 2.595 (1 H, dt, J = 13.75, 8.24 Hz), 2.635 (1 H, ddd, J = 6.39, 9.52, 13.92 Hz), 2.712 (1 H, ddd, J = 5.86, 9.65, 13.84 Hz), 2.815 (1 H, ddd, J = 4.94, 9.09, 13.97 Hz), 3.649 (1 H, ddd, J = 3.18, 6.60, 9.94 Hz), 4.17–4.34 (3 H, m), 5.158 (1 H, ddd, J = 3.42, 5.86, 9.03 Hz), 5.209 (1 H, dd, J = 4.03, 6.72 Hz), 7.1–7.4 (10 H, m); ^{13}C NMR δ 20.827, 20.852, 23.389, 24.431, 26.127, 27.458, 31.230, 31.380, 32.393, 34.172, 68.742 (q, J = 32.03 Hz), 70.761, 70.880, 72.520, 76.460 (q, J = 32.43 Hz), 77.781 (q, J = 1.57 Hz), 102.541, 112.859, 126.048, 126.143, 128.345, 128.426, 128.492, 140.844, 141.046, 169.798, 170.492, CF_3 was not observed; ^{19}F NMR δ 2.58 (d, J = 6.15 Hz), 5.76 (d, J = 6.89 Hz); IR (neat) ν 3550, 3065, 2995, 2940, 2865, 1752.

(2*R,3*R**,4*S**)-2-Acetoxy-6-(benzyloxy)-1,1,1-trifluoro-3,4-*O*-isopropylidenehexane-3,4-diol (15b).** Acetonide formation procedure of a diastereomer mixture of triols (**10b**:**11b** = 26:74) described above gave a mixture of three isomers. Their structures were identified after acetylation by the usual procedure to afford **15b** (yield 70%) and a mixture of two regioisomers (yield 26%, **16b** and **17b** as a 58:42 inseparable mixture): R_f 0.44 (AcOEt:Hex = 1:4); ^{1}H NMR δ 1.377 (3 H, q, J = 0.61 Hz), 1.411 (3 H, q, J = 0.73 Hz), 1.836 (1 H, ddt, J = 8.89, 14.18, 5.25 Hz), 1.982 (1 H, dddd, J = 2.93, 6.37, 8.20, 14.218 Hz), 2.111 (3 H, s), 3.593 (1 H, ddd, J = 5.49, 8.30, 9.40 Hz), 3.642 (1 H, ddd, J = 4.95, 6.41, 9.34 Hz), 4.042 (1 H, dd, J = 6.34, 7.33 Hz), 4.188 (1 H, ddd, J = 2.93, 7.35, 8.76 Hz), 4.498 (1 H, d, J = 12.21 Hz), 4.524 (1 H, d, J = 11.97 Hz), 5.490 (1 H, dq, J = 6.35, 6.96 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ 20.670, 26.950, 27.642, 34.581, 67.057, 69.805 (q, J = 31.11 Hz), 73.385, 75.510, 77.154 (q, J = 1.58 Hz), 110.542, 123.256 (q, J = 281.04 Hz), 127.951, 128.727, 138.663, 169.094; ^{19}F NMR δ 4.96 (d, J = 6.89 Hz); IR (neat) ν 2990, 2935, 2865, 1769; HRMS calcd for $C_{18}H_{23}F_3O_5$ m/e 376.1496, found 376.1470.

(2*S,3*S**,4*S**)-2-Acetoxy-6-(benzyloxy)-1,1,1-trifluoro-3,4-*O*-isopropylidenehexane-3,4-diol (16b) and (2*S**,3*S**,-4*S**)-3-Acetoxy-6-(benzyloxy)-1,1,1-trifluoro-2,4-*O*-isopropylidenehexane-2,4-diol (17b):** R_f 0.37 (AcOEt:Hex = 1:4); ^{13}C NMR δ 19.368, 20.838, 21.028, 25.937, 28.082, 29.006, 29.152, 32.425, 65.255, 65.504, 67.125, 67.692, 70.470 (q, J = 30.51 Hz), 73.410, 73.513, 74.138 (q, J = 32.27 Hz), 100.085, 109.642, 123.712 (q, J = 280.94 Hz), 128.007, 128.038, 128.753, 128.791, 138.572, 138.701, 168.991, 169.691; IR (neat) ν 3015, 2970, 1780. **17b:** ^{1}H NMR δ 1.439 (3 H, s), 1.500 (3 H, s), 1.6–2.0 (2 H, m), 2.050 (3 H, s), 3.5–3.6 (2 H, m), 4.005 (1 H, dt, J = 2.44, 9.71 Hz), 4.161 (1 H, dq, J = 9.70, 5.70), 4.454 (1 H, d, J = 12.09 Hz), 4.529 (1 H, d, J = 12.45 Hz), 4.908 (1 H, t, J = 9.71 Hz), 7.2–7.4 (5 H, m); ^{19}F NMR δ 2.39 (d, J = 5.48 Hz). **16b:** ^{1}H NMR δ 1.366 (3 H, s), 1.449 (3 H, s), 1.6–2.0 (2 H, m), 2.112 (3 H, s), 3.5–3.6 (2 H, m), 4.287 (1 H, dd, J = 5.19, 9.34 Hz), 4.4–4.5 (1 H, m), 4.498 (1 H, d, J = 12.00 Hz), 4.528 (1 H, d, J = 12.18 Hz), 5.253 (1 H, dq, J = 9.31, 6.51 Hz), 7.2–7.4 (5 H, m); ^{19}F NMR δ 6.52 (d, J = 6.15 Hz).

(2*S,3*S**,4*S**)-2-Acetoxy-6-phenyl-1,1,1-trifluoro-3,4-*O*-isopropylidenehexane-3,4-diol (16a) and (2*S**,3*S**,4*S**)-3-Acetoxy-6-phenyl-1,1,1-trifluoro-2,4-*O*-isopropylidenehexane-2,4-diol (17a).** Acetonide formation of a triol **10a** followed by the usual acetylation afforded a mixture of **16a** and **17a** in 83.8% total yield (27:73): R_f 0.41 (AcOEt:Hex = 1:6); IR (neat) ν 3065, 2995, 2930, 2865, 1752; HRMS calcd for $C_{17}H_{21}F_3O_4$ m/e 346.1391, found 346.1410. **17a:** ^{1}H NMR δ 1.457 (3 H, s), 1.501 (3 H, s), 1.60–1.95 (2 H, m), 2.030 (3 H, s), 2.605 (1 H, dt, J = 13.75, 8.73 Hz), 2.827 (1 H, ddd, J = 5.25, 8.82, 13.92 Hz), 3.712 (1 H, ddd, J = 3.42, 8.18, 9.52 Hz), 4.110 (1 H, dq, J = 9.69, 5.81 Hz), 4.946 (1 H, t, J = 9.77 Hz), 7.1–7.4 (5 H, m); ^{13}C NMR δ 18.996, 28.883, 29.480, 30.501, 33.178, 64.679 (q, J = 1.33 Hz), 69.400, 70.792 (q, J = 30.71 Hz), 99.749, 123.340 (q, J = 277.07 Hz), 125.981, 128.403, 128.547, 141.342, 169.252; ^{19}F NMR δ 2.44 (d, J = 6.21 Hz). **16a:** ^{1}H NMR δ 1.361 (3 H, s), 1.493 (3 H, s), 1.60–1.95 (2 H, m), 2.051 (3 H, s), 2.674 (1 H, dt, J = 13.91, 8.18 Hz), 2.886 (1 H, ddd, J = 5.13, 8.80, 13.92 Hz), 4.141 (1 H, ddd, J = 3.17, 5.13, 10.50 Hz), 4.245 (1 H, dd, J = 5.25, 9.40 Hz), 5.284 (1 H, dq, J = 9.34, 6.47 Hz), 7.1–7.4 (5 H, m); ^{13}C NMR δ 20.630, 25.589, 27.813, 32.306, 35.857, 66.984 (q, J = 29.95 Hz), 73.612, 76.107, 109.313, 126.161, 128.403, 128.505, 140.860, 168.561, CF_3 was not observed; ^{19}F NMR δ 6.55 (d, J = 6.21 Hz).

Enzymatic Transesterification. To a 0.5 M solution of a racemic propargylic alcohol **4b** (20.084 g, 77.772 mmol) in *n*-hexane were added vinyl acetate (13.3 mL, 160 mmol) and Lipase QL (7.8 g, 234,000 Unit; Meito Sangyo Co., Ltd., Japan), and the whole was stirred at 40 °C for 12 h. After removal of the residue by filtration and concentration of this solution, separation by silica gel column chromatography afforded an optically active alcohol (7.943 g, 30.757 mmol, 39.5%) and an ester (13.825 g, 46.041 mmol, 59.2%). The enantiomeric excess was determined by capillary GC after derivatization into the corresponding MTPA esters. **(3*S*)-1-(Benzyloxy)-6,6,6-trifluoro-4-hexyn-3-ol ((*S*)-4b).** Physical properties of this compound were the same as the ones described for the racemic compound except for the optical rotation: $[\alpha]^{17}_D$ −36.13° (*c* 1.24, $CHCl_3$), 99.6% ee (determined after derivatization into the corresponding MTPA ester). **(4*R*)-4-Acetoxy-6-(benzyloxy)-1,1,1-trifluoro-2-hexyne ((*R*)-19b):** R_f 0.43 (AcOEt:Hex = 1:4); $[\alpha]^{17}_D$ +37.31° (*c* 1.33, $CHCl_3$), 64.4% ee; ^{1}H NMR δ 2.062 (3 H, s), 2.0–2.3 (2 H, m), 3.538 (1 H, dt, J = 9.83, 5.70 Hz), 3.596 (1 H, dt, J = 9.86, 5.89 Hz), 4.462 (1 H, d, J = 11.94 Hz), 4.529 (1 H, d, J = 11.94 Hz), 5.632 (1 H, tq, J = 7.02, 2.88 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ 20.638, 34.083, 60.043 (q, J = 1.32 Hz), 64.851, 72.295 (q, J = 52.87 Hz), 73.167, 84.401 (q, J = 6.31 Hz), 113.812 (q, J = 257.86 Hz), 127.738, 127.807, 128.462, 137.826, 169.398; ^{19}F NMR δ 28.38 (d, J = 2.77 Hz); IR (neat) ν 3090, 3065, 3035, 2935, 2865, 2800, 2275, 1750; HRMS calcd for $C_{15}H_{15}F_3O_3$ m/e 300.0972, found 300.0959.

(3*R*)-1-(Benzyloxy)-6,6,6-trifluoro-4-hexyn-3-ol (*R*-4b). To a solution of the above optically active ester (6.813 g, 22.688 mmol) in MeOH (22 mL) was added K_2CO_3 (0.5 equiv) at 0 °C, and the whole was stirred for 30 min at that temperature. After concentration under reduced pressure, the usual workup and purification gave the corresponding alcohol (5.619 g, 21.757 mmol, 95.9%). Physical properties of this compound were described before.

Determination of Absolute Configuration. (2*S*)-1,2-Diacetoxy-4-(benzyloxy)butane ((*S*)-18).[19] A solution of (*S*)-**4b** (0.542 g, 2.083 mmol) in MeOH (10 mL) was treated with O_3 at −78 °C for 30 min, and $NaBH_4$ (2 mmol) was added to this solution. The whole was poured into 1 N HCl (20 mL) and extracted with AcOEt (20 mL × 3), dried with $MgSO_4$, and evaporated. The reaction mixture and starting material (0.185 g, 0.711 mmol, 34.1%) were separated by column chromatography on silica gel, and the reaction mixture was treated with $LiAlH_4$ (1 mmol) in THF (2 mL) at −78 °C. The usual workup gave the crude diol, which, without further purification, was acetylated under the usual esterification procedure to afford the title compound (0.206 g, 0.887 mmol, 42.6% from allylic alcohol): R_f 0.57 (AcOEt:Hex = 1:1); $[\alpha]^{27}_D$ −20.50° (*c* 1.15, CCl_4), 99.6% ee; ^{1}H NMR δ 1.906 (2 H, q, J = 6.27 Hz), 2.021 (3 H, s), 2.055 (3 H, s), 3.492 (1 H, dt, J = 9.52, 6.47 Hz), 3.531 (1 H, dt, J = 9.52, 5.86 Hz), 4.081 (1 H, dd, J = 6.35, 11.97 Hz), 4.284 (1 H, dd, J = 3.42, 11.96 Hz), 4.466 (1 H, d, J = 11.72 Hz), 4.498 (1 H, d, J = 11.96 Hz), 5.249 (1 H, dq, J = 3.42, 6.43 Hz); ^{13}C NMR δ 20.789, 21.036, 31.026, 65.150, 65.949, 69.341, 73.118, 127.659, 127.726, 128.399, 138.074, 170.455, 170.748; IR (neat) ν 3030, 2935, 2865, 1730.

Preparation of 6,6,6-Trifluoro-L-oliose. A solution of a alcohol **12b** (0.996 g, 2.98 mmol) and Raney Ni (ca. 0.5 g, 3 equiv) in EtOH (30 mL) was stirred for 12 h at room temperature under H_2. After filtration to remove the catalyst, the solution was concentrated to afford the corresponding diol **20**. To a suspension of PDC (10 mmol) in CH_2Cl_2 (12 mL) was added this crude diol at 0 °C under N_2, and the whole was stirred for 2 d at room temperature. After removal of the solid materials by filtration through a pad of Celite and concentration under reduced pressure, separation by silica gel column chromatography gave a mixture of a lactone **22** (0.223 g, 0.93 mmol, 31.1%) and a lactol **21** (0.343 g, 1.42 mmol, 47.7%).

(3*S*,4*R*,5*R*)-6,6,6-Trifluoro-3,4-*O*-isopropylidenehexane-1,3,4,5-tetrol (*anti,syn*-20): R_f 0.20 (AcOEt:Hex = 1:1); $[\alpha]^{18}_D$ +18.21° (*c* 1.20, $CHCl_3$), 99.6% ee; ^1H NMR δ 1.418 (3 H, s), 1.550 (3 H, s), 1.849 (1 H, dddd, *J* = 3.63, 5.30, 7.19, 14.07 Hz), 2.048 (1 H, dddd, *J* = 4.63, 5.81, 9.84, 14.09 Hz), 1.6–2.2 (1 H, br), 2.7–3.3 (1 H, br), 3.822 (1 H, ddd, *J* = 4.62, 7.14, 10.76 Hz), 3.895 (1 H, dt, *J* = 10.89, 5.37 Hz), 3.9–4.1 (1 H, m), 4.391 (1 H, dd, *J* = 1.22, 7.22 Hz), 4.522 (1 H, ddd, *J* = 3.54, 7.08, 9.68 Hz); ^{13}C NMR δ 24.246, 26.695, 32.273, 60.536, 67.950 (q, *J* = 30.10 Hz), 73.160 (q, *J* = 1.83 Hz), 75.597, 109.142, 124.431 (q, *J* = 283.79 Hz); ^{19}F NMR δ 1.31 (d, *J* = 6.89 Hz); IR (neat) ν 3420, 3000, 2940. **(3*S*,4*S*,5*R*)-6,6,6-Trifluoro-3,4-dihydroxy-3,4-*O*-isopropylidenehexan-5-olide (22):** R_f 0.55 (AcOEt:Hex = 1:1); mp 90.0–91.0 °C; $[\alpha]^{16}_D$ −15.28° (*c* 0.98, $CHCl_3$), 99.6% ee; ^1H NMR (with a few drops of DMSO-d_6) δ 1.352 (3 H, s), 1.420 (3 H, s), 2.794 (1 H, dd, *J* = 2.39, 16.10 Hz), 2.919 (1 H, dd, *J* = 3.19, 16.05 Hz), 4.719 (1 H, dd, *J* = 1.83, 7.61 Hz), 4.813 (1 H, dt, *J* = 7.72, 2.77 Hz), 4.924 (1 H, dq, *J* = 1.85, 6.55 Hz); ^{13}C NMR (with a few drops of DMSO-d_6) δ 24.107, 25.771, 34.684, 70.122 (q, *J* = 1.42 Hz), 71.692, 73.040 (q, *J* = 32.23 Hz), 110.170, 122.056 (q, *J* = 280.33 Hz), 167.455; ^{19}F NMR (with a few drops of DMSO-d_6) δ 5.99 (d, *J* = 6.21 Hz); IR (KBr) ν 3000, 2950, 1765; HRMS calcd for $C_9H_{11}F_3O_4$ *m/e* (M + H) 241.0687, found 241.0701. **6,6,6-Trifluoro-3,4-*O*-isopropylidene-L-oliose (21):** 90:10 anomer mixture: R_f 0.43 (AcOEt:Hex = 1:1); mp 96.5–97.0 °C; $[\alpha]^{16}_D$ −67.82° (*c* 1.39, $CHCl_3$), 99.6% ee. **Major isomer**: ^1H NMR δ 1.359 (3 H, s), 1.496 (3 H, s), 1.705 (1 H, ddd, *J* = 3.35, 6.88, 15.33 Hz), 2.380 (1 H, ddd, *J* = 4.33, 5.32, 15.32 Hz), 3.3–3.7 (1 H, br), 4.229 (1 H, dq, *J* = 2.05, 6.74 Hz), 4.380 (1 H, dd, *J* = 2.05, 7.30 Hz), 4.578 (1 H, dt, *J* = 7.40, 3.76 Hz), 5.482 (1 H, dd, *J* = 5.68, 6.71 Hz); ^{13}C NMR δ 25.116, 26.236, 30.675, 68.148 (q, *J* = 31.31 Hz), 70.241, 70.566 (q, *J* = 1.47 Hz), 90.856, 110.285, 123.437 (q, *J* = 280.33 Hz); ^{19}F NMR δ 5.57 (d, *J* = 6.89 Hz); IR (KBr) ν 3475, 2995, 2970, 2930. Anal. Calcd for $C_9H_{13}F_3O_4$: C, 44.63; H, 5.41. Found: C, 44.73; H, 5.56. This lactol **21** was also obtained in 96% yield by treatment of the lactone **22** with DIBALH (1.1 equiv) at −78 °C for 1 h, followed by usual workup and purification.

Preparation of 6,6,6-Trifluoro-D-boivinose. (3*R,4*R**,5*R**)-6,6,6-Trifluoro-3,4,5-trihydroxy-3,4-*O*-isopropylidenehexanal (23).** A 0.259 g sample of **9b** (0.88 mmol) was subjected to the above acetonide formation, followed by debenzylation, to give the crude diol, *syn,syn*-**20**. To a solution of DMSO (0.2 mL, 3 mmol) in CH_2Cl_2 (5 mL) containing oxaryl chloride (0.15 mL, 1.5 mmol) were added at −78 °C this crude diol and Et_3N (0.6 mL, 4 mmol), and the whole was stirred at that temperature for 1 h. The usual workup and purification by silica gel column chromatography gave hydroxy aldehyde **23** (0.034 g, 0.14 mmol, 19.2%). **(3*R**,4*R**,5*R**)-6,6,6-Trifluoro-3,4-*O*-isopropylidenehexane-1,3,4,5-tetrol (*syn,syn*-20):** R_f 0.26 (AcOEt:Hex = 1:1); ^1H NMR δ 1.455 (3 H, q, *J* = 0.65 Hz), 1.468 (3 H, q, *J* = 0.65 Hz), 1.884 (2 H, dt, *J* = 5.37, 6.11 Hz), 1.9–2.3 (1 H, br), 2.7–3.4 (1 H, br), 3.819 (1 H, dt, *J* = 11.12, 5.50 Hz), 3.855 (1 H, dt, *J* = 11.11, 5.56 Hz), 3.907 (1 H, dq, *J* = 1.10, 7.33 Hz), 3.950 (1 H, dd, *J* = 1.10, 8.50 Hz), 4.164 (1 H, dt, *J* = 8.55, 6.07 Hz); ^{13}C NMR δ 26.568, 27.391, 34.431, 60.041, 67.567 (q, *J* = 31.01 Hz), 76.285, 77.060 (q, *J* = 1.99 Hz), 110.524, 124.219 (q, *J* = 283.28 Hz); ^{19}F NMR δ 1.33 (d, *J* = 6.89 Hz); IR (neat) ν 3420, 2990, 2940. **23:** R_f 0.52 (AcOEt:Hex = 1:1); mp 87.5–89.0 °C; ^1H NMR δ 1.456 (3 H, q, *J* = 0.61 Hz), 1.468 (3 H, q, *J* = 0.61 Hz), 2.740 (1 H, ddd, *J* = 1.10, 5.25, 17.46 Hz), 2.919 (1 H, ddd, *J* = 1.80, 6.98, 17.49 Hz), 3.012 (1 H, d, *J* = 10.38 Hz), 3.949 (1 H, dd, *J* = 1.28, 8.24 Hz), 4.0–4.1 (1 H, m), 4.486 (1 H, ddd, *J* = 5.25, 7.04, 8.25 Hz), 9.805 (1 H, dd, *J* = 1.10, 1.71 Hz); ^{13}C NMR δ 26.513, 27.201, 46.492, 67.635 (q, *J* = 31.11 Hz), 72.188, 77.135 (q, *J* = 1.68 Hz), 110.964, 124.136 (q, *J* = 282.87 Hz), 198.916; ^{19}F NMR δ 1.48 (d, *J* = 6.89 Hz); IR (KBr) ν 3475, 2995, 2930, 1725.

(2*S*,3*S*,4*S*)-6-(Benzyloxy)-3,4-bis((*tert*-butyldimethylsilyl)oxy)-1,1,1-trifluorohexan-2-ol (*syn,syn*-24). To a solution of triol **9b** (0.631 g, 2.14 mmol) in DMF (1 mL) were added at 0 °C TBSCl (3 equiv) and imidazole (3 equiv), and the mixture was stirred for 12 h at room temperature. The resultant crude materials containing bis-silyl ethers and monosilyl ethers were, without purification, treated with *t*-BuOK at −78 °C in THF for 2 h to yield *syn,syn*-**24** (0.784 g, 1.50 mmol, 70.1%) along with a 21.5% recovery of monosilyl ethers: R_f 0.42 (AcOEt:Hex = 1:12); $[\alpha]^{17}_D$ −28.31° (*c* 1.08, $CHCl_3$), 99.6% ee; ^1H NMR δ 0.055 (3 H, s), 0.057 (3 H, s), 0.113 (3 H, s), 0.140 (3 H, s), 0.880 (9 H, s), 0.913 (9 H, s), 1.597 (1 H, ddt, *J* = 10.16, 14.23, 4.08 Hz), 2.053 (1 H, dddd, *J* = 1.87, 6.66, 9.59, 14.21 Hz), 3.251 (1 H, d, *J* = 10.25 Hz), 3.521 (1 H, dt, *J* = 4.51, 9.46 Hz), 3.551 (1 H, ddd, *J* = 3.70, 6.51, 9.11 Hz), 3.938 (1 H, d, *J* = 4.88 Hz), 3.967 (1 H, ddd, *J* = 1.56, 4.73, 10.11 Hz), 4.205 (1 H, dq, *J* = 9.83, 7.90 Hz), 4.465 (1 H, d, *J* = 11.97 Hz), 4.497 (1 H, d, *J* = 11.96 Hz), 7.2–7.4 (5 H, m); ^{13}C NMR δ −5.419, −5.142, −4.437, −4.236, 17.780, 17.918, 25.621, 25.666, 30.892, 66.116 (q, *J* = 29.69 Hz), 66.300, 69.133, 69.580 (q, *J* = 1.68 Hz), 72.598, 125.164 (q, *J* = 283.28 Hz), 127.295, 127.322, 128.189, 138.616; ^{19}F NMR δ 0.69 (d, *J* = 7.56 Hz); IR (neat) ν 3515, 3065, 3030, 2955, 2930, 2885, 2855.

3,4-*O*-Bis(*tert*-butyldimethylsilyl)-6,6,6-trifluoro-D-boivinose (26). Debenzylation and PDC oxidation procedures described above gave a mixture of lactone and lactol, which was treated with DIBALH in CH_2Cl_2 at −78 °C for 1 h, and the usual workup gave the crude lactol. The title compound **26** was obtained by purification with silica gel column chromatography. **(3*S*,4*S*,5*S*)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)-6,6,6-trifluorohexane-1,5-diol (*syn,syn*-25):** R_f 0.40 (AcOEt:Hex = 1:4); $[\alpha]^{18}_D$ −36.23° (*c* 0.97, $CHCl_3$), 99.6% ee; ^1H NMR δ 0.081 (3 H, s), 0.110 (3 H, s), 0.118 (3 H, s), 0.156 (3 H, s), 0.885 (9 H, s), 0.917 (9 H, s), 1.651 (1 H, ddt, *J* = 9.27, 14.32, 4.76 Hz), 1.894 (1 H, dddd, *J* = 2.13, 5.77, 9.05, 14.31 Hz), 2.6–3.6 (2 H, br, O*H*), 3.653 (1 H, ddd *J* = 4.76, 9.15, 10.50 Hz), 3.767 (1 H, ddd, *J* = 4.83, 5.80, 10.56 Hz), 3.915 (1 H, ddd, *J* = 2.20, 4.64, 9.77 Hz), 3.938 (1 H, d, *J* = 4.63 Hz), 4.196 (1 H, q, *J* = 7.81 Hz); ^{13}C NMR δ −5.478, −5.092, −4.437, −4.117, 17.736, 17.885, 25.593, 25.647, 33.416, 59.484, 66.117 (q, *J* = 29.96 Hz), 69.555 (q, *J* = 1.68 Hz), 69.778, 125.091 (q, *J* = 283.18 Hz); ^{19}F NMR δ 0.70 (d, *J* = 8.24 Hz); IR (neat) ν 3515, 2955, 2930, 2890, 2860. **26:** yield 61% (a 75:25 anomer mixture); R_f 0.47 (AcOEt:Hex = 1:6); $[\alpha]^{19}_D$ +21.74° (*c* 1.92, $CHCl_3$), 99.6% ee; IR (neat) ν 3495, 2955, 2930, 2900, 2860. Anal. Calcd for $C_{18}H_{37}F_3O_4Si_2$: C, 50.20; H, 8.66. Found: C, 50.18; H, 8.94. **Major isomer**: ^1H NMR δ 0.072 (3 H, s), 0.086 (3 H, s), 0.145 (3 H, s), 0.159 (3 H, s), 0.894 (9 H, s), 0.929 (9 H, s), 1.726 (1 H, ddt, *J* = 3.42, 14.16, 1.10 Hz), 2.288 (1 H, ddd, *J* = 2.50, 3.60, 14.22 Hz), 3.775 (1 H, d, *J* = 3.91 Hz), 3.991 (1 H, q, *J* = 2.93 Hz), 4.491 (1 H, dq, *J* = 0.98, 6.96 Hz), 5.16–5.32 (2 H, m); ^{13}C NMR δ −5.243, −5.183, −4.869, −4.666, 17.750, 17.790, 25.585, 30.545, 65.558 (q, *J* = 30.91 Hz), 66.555 (q, *J* = 1.73 Hz), 69.905, 92.999, 124.060 (q, *J* = 280.03 Hz); ^{19}F NMR δ 5.452 (d, *J* = 6.21 Hz). **Minor isomer**: ^1H NMR δ 0.072 (6 H, s), 0.080 (3 H, s), 0.093 (3 H, s), 0.894 (9 H, s), 0.899 (9 H, s), 1.778 (1 H, dddd, *J* = 0.95, 2.32, 3.33, 13.31 Hz), 1.947 (1 H, ddd, *J* = 2.45, 9.77, 13.18 Hz), 3.607 (1 H, d, *J* = 3.66 Hz), 3.922 (1 H, q, *J* = 3.09 Hz), 4.225 (1 H, dq, *J* = 0.98, 6.92 Hz), 5.136 (1 H, dd, *J* = 2.20, 9.76 Hz), 5.16–5.32 (1 H, m); ^{13}C NMR δ −4.928, −4.908, −4.725, 25.622, 35.163, 69.733, 72.483, 93.202, some peaks were not observed; ^{19}F NMR δ 5.56 (d, *J* = 6.04 Hz).

Preparation of 6,6,6-Trifluoro-D-digitoxose and 6,6,6-Trifluoro-L-olivose. (2*S*,3*R*,4*S*)-6-(Benzyloxy)-3,4-bis((*tert*-butyldimethylsilyl)oxy)-1,1,1-trifluorohexan-2-ol (*anti,anti*-24) and (2*R*,3*S*,4*S*)-6-(Benzyloxy)-3,4-bis((*tert*-butyldimethylsilyl)oxy)-1,1,1-trifluorohexan-2-ol (*syn,anti*-24). Silylation procedure using 3 equiv of both TBSCl and imidazole for a mixture of diastereomeric 10b and 11b (4.169 g, 14.166 mmol, a 26:74 diastereomer mixture) gave a complex mixture, which, without further purification, was thermodynamically isomerized with KOBu-*t* to afford a separable mixture of isomeric bis-silyl ethers *anti,anti*-24 and *syn,anti*-24 (4.673 g, 8.939 mmol, 63.1% and 1.768 g, 3.381 mmol, 23.9%, respectively). *syn,anti*-24: R_f 0.53 (AcOEt:Hex = 1:10); $[\alpha]^{18}_D$ −19.61° (*c* 0.99, $CHCl_3$), 98.5% ee; ^1H NMR δ 0.059 (3 H, s), 0.070 (3 H, s), 0.091 (3 H, s), 0.161 (3 H, s), 0.857 (9 H, s), 0.895 (9 H, s), 1.760 (1 H, ddt, *J* = 10.19, 14.28, 4.03 Hz), 2.276 (1 H, dddd, *J* = 2.20, 6.72, 9.77, 14.16 Hz), 3.565 (1 H, ddd, *J* = 4.39, 9.28, 9.88 Hz), 3.595 (1 H, ddd, *J* = 3.69, 6.52, 9.44 Hz), 3.932 (1 H, dd, *J* = 4.03, 8.67 Hz), 4.039 (1 H, ddq, *J* = 2.20, 8.79, 6.51 Hz), 4.111 (1 H, ddd, *J* = 1.95, 3.66, 10.26

Hz), 4.491 (2 H, s), 5.066 (1 H, d, J = 1.46 Hz), 7.2–7.5 (5 H, m); ^{13}C NMR δ −5.397, −5.270, −4.447, −4.287, 17.776 (2 C), 25.589, 25.614, 30.019, 65.787, 69.044 (q, J = 1.58 Hz), 72.615 (q, J = 28.16 Hz), 72.697, 72.900, 124.858 (q, J = 281.96 Hz), 127.409, 127.448, 128.236, 138.306; ^{19}F NMR δ 2.16 (d, J = 4.80 Hz); IR (neat) ν 3415, 3030, 2955, 2930, 2890, 2860. *anti,anti*-24: R_f 0.36 (AcOEt:Hex = 1:10); $[\alpha]^{19}_D$ +1.25° (*c* 0.93, $CHCl_3$), 98.5% ee; ^{1}H NMR δ 0.054 (3 H, s), 0.083 (3 H, s), 0.102 (3 H, s), 0.135 (3 H, s), 0.887 (9 H, s), 0.909 (9 H, s), 1.835 (1 H, ddt, J = 7.39, 14.80, 5.01 Hz), 2.051 (1 H, ddt, J = 5.24, 14.87, 7.17 Hz), 3.561 (2 H, dd, J = 5.02, 7.06 Hz), 3.7–3.9(1 H, br), 3.947 (1 H, d, J = 7.10 Hz), 3.95–4.06 (1 H, m), 4.157 (1 H, dd, J = 5.22, 7.42 Hz), 4.508 (2 H, s), 7.2–7.4 (5 H, m); ^{13}C NMR δ −5.737, −5.067, −4.248, −3.779, 17.987, 18.059, 25.809, 25.870, 34.473, 66.830, 73.046, 73.074 (q, J = 28.77 Hz), 74.042 (q, J = 1.17 Hz), 74.123, 124.899 (q, J = 281.66 Hz), 127.697, 128.379, 137.853; ^{19}F NMR δ 3.61 (d, J = 6.21 Hz); IR (neat) ν 3410, 3065, 3030, 2955, 2930, 2880, 2860, 2740; HRMS calcd for $C_{25}H_{45}F_3O_4Si_2$ m/e (M + H) 522.2884, found 523.2883.

3,4-Bis-*O*-(*tert*-butyldimethylsilyl)-6,6,6-trifluoro-D-digitoxose (27). Debenzylation and PDC oxidation procedures described above gave a mixture of lactone and lactol, which was treated with DIBALH in CH_2Cl_2 at −78 °C for 1 h. The title compound was obtained after usual workup and purification with silica gel column chromatography: yield 83.5% (a 79:21 anomer mixture). **(3*S*,4*R*,5*S*)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)-6,6,6-trifluorohexane-1,5-diol (*anti,anti*-25):** R_f 0.28 (AcOEt:Hex = 1:3); $[\alpha]^{17}_D$ +4.27° (*c* 0.42, $CHCl_3$), 98.5% ee; ^{1}H NMR δ 0.080 (3 H, s), 0.104 (3 H, s), 0.129 (3 H, s), 0.140 (3 H, s), 0.885 (9 H, s), 0.909 (9 H, s), 1.868 (2 H, q, J = 5.92 Hz), 2.0–4.0 (2 H, br), 3.686 (1 H, dt, J = 10.61, 6.02 Hz), 3.794 (1 H, dt, J = 10.54, 5.27 Hz), 3.9–4.1 (1 H, m), 3.981 (1 H, d, J = 4.40 Hz), 4.173 (1 H, t, J = 6.04 Hz); ^{13}C NMR δ −5.718, −5.071, −4.253, −3.721, 18.060, 18.092, 25.805, 25.914, 35.945, 59.100, 72.622 (q, J = 28.57 Hz), 72.809 (q, J = 1.37 Hz), 74.683 (q, J = 1.12 Hz), 124.784 (q, J = 282.27 Hz); ^{19}F NMR δ 3.69 (d, J = 6.89 Hz); IR (neat) ν 3360, 2960, 2930, 2860. **27:** R_f 0.36 (AcOEt:Hex = 1:6); $[\alpha]^{19}_D$ +59.12° (*c* 1.10, $CHCl_3$), 98.5% ee; IR (neat) ν 3420, 2950, 2935, 2875, 2860. Anal. Calcd for $C_{18}H_{37}F_3O_4Si_2$: C, 50.20; H, 8.66. Found: C, 50.07; H, 8.54. **Major isomer**: ^{1}H NMR δ 0.0–0.2 (12 H, m), 0.898 (9 H, s), 0.927 (9 H, s), 1.913 (1 H, ddd, J = 2.42, 3.75, 14.24 Hz), 2.00–2.15 (1 H, m), 3.777 (1 H, dd, J = 2.39, 9.09 Hz), 4.1–4.2 (1 H, m), 4.382 (1 H, dq, J = 9.14, 6.90 Hz), 5.15–5.50 (2 H, m); ^{13}C NMR δ −5.549 (q, J = 1.63 Hz), −4.635, −4.523, −3.306, 17.853, 17.938, 25.686, 25.979, 36.368, 66.905 (q, J = 29.28 Hz), 69.088, 71.381, 92.369, 124.460 (q, J = 280.23 Hz); ^{19}F NMR δ 6.07 (d, J = 6.89 Hz). **Minor isomer**: ^{1}H NMR δ 0.0–0.2 (12 H, m), 0.876 (9 H, s), 0.898 (9 H, s), 1.674 (1 H, ddd, J = 2.11, 9.34, 13.65 Hz), 2.00–2.15 (1 H, m), 3.7–3.8 (1 H, m), 4.067 (1 H, dt, J = 4.40, 2.20 Hz), 4.221 (1 H, dq, J = 8.98, 6.96 Hz), 5.15–5.50 (2 H, m); ^{13}C NMR δ −5.674 (q, J = 1.13 Hz), −4.728, −4.248, −3.589, 17.819, 18.043, 25.775, 25.866, 37.851, 69.357, 69.749, 71.642 (q, J = 29.09 Hz), 92.724, 124.024 (q, J = 280.44 Hz); ^{19}F NMR δ 5.57 (d, J = 6.89 Hz).

(3*S*,4*S*,5*R*)-3,4-Bis((*tert*-butyldimethylsilyl)oxy)-6,6,6-trifluorohexane-1,5-diol (*syn,anti*-25): R_f 0.41 (AcOEt:Hex = 1:4); $[\alpha]^{18}_D$ −23.35° (*c* 1.29, $CHCl_3$), 98.5% ee; ^{1}H NMR δ 0.085 (3 H, s), 0.117 (3 H, s), 0.148 (3 H, s), 0.188 (3 H, s), 0.876 (9 H, s), 0.904 (9 H, s), 1.6–1.8 (1 H, br), 1.787 (1 H, ddt, J = 9.30, 13.97, 4.65 Hz), 2.149 (1 H, dddd, J = 3.53, 5.99, 9.54, 14.11 Hz), 3.685 (1 H, dt, J = 4.38, 10.22 Hz), 3.829 (1 H, ddd, J = 4.39, 6.05, 10.59 Hz), 3.945 (1 H, dd, J = 3.84, 8.80 Hz), 4.0–4.2 (2 H, m), 4.9–5.1 (1 H, br); ^{13}C NMR δ −5.454 (q, J = 1.43 Hz), −5.158, −4.487, −4.101, 17.763, 17.798, 25.575, 25.613, 33.252, 58.863, 69.297 (q, J = 1.42 Hz), 72.447 (q, J = 28.68 Hz), 73.456, 124.791 (q, J = 282.37 Hz); ^{19}F NMR δ 2.28 (d, J = 5.53 Hz); IR (neat) ν 3420, 2955, 2930, 2890, 2860. **3,4-Bis-*O*-(*tert*-butyldimethylsilyl)-6,6,6-trifluoro-L-olivose (28):** yield 83.1% (an 87:13 anomer mixture); R_f 0.40 (AcOEt:Hex = 1:6); $[\alpha]^{18}_D$ −19.01° (*c* 1.28, $CHCl_3$), 98.5% ee; IR (neat) ν 3420, 2955, 2940, 2900, 2860. Anal. Calcd for $C_{18}H_{37}F_3O_4Si_2$: C, 50.20; H, 8.66. Found: C, 49.89; H, 8.64. **Major isomer**: ^{1}H NMR δ 0.094 (3 H, s), 0.098 (3 H, s), 0.104 (6 H, s), 0.874 (9 H, s), 0.893 (9 H, s), 1.838 (1 H, ddd, J = 4.32, 7.74, 13.69 Hz), 2.001 (1 H, ddd, J = 3.66, 4.65, 13.70 Hz), 2.4–3.2 (1 H, br), 3.719 (1 H, dd, J = 5.29, 7.32 Hz), 3.966 (1 H, ddd, J = 3.66, 5.23, 7.70 Hz), 4.112 (1 H, dq, J = 7.42, 7.42 Hz), 5.395 (1 H, t, J = 4.49 Hz); ^{13}C NMR δ −4.584 (q, J = 1.68 Hz), −3.970, −3.222, −2.892, 18.360, 18.599, 26.307, 26.436, 36.628, 70.787, 71.355, 73.079 (q, J = 29.29 Hz), 91.913, 124.807 (q, J = 280.74 Hz); ^{19}F NMR δ 5.42 (d, J = 6.89 Hz). **Minor isomer**: ^{1}H NMR δ 0.063 (3 H, s), 0.067 (3 H, s), 0.125 (3 H, s), 0.132 (3 H, s), 0.860 (9 H, s), 0.910 (9 H, s), 1.7–1.9 (1 H, m), 2.228 (1 H, dt, J = 13.84, 3.19 Hz), 2.4–3.2 (1 H, br), 3.7–4.2 (2 H, m), 5.0–5.5 (2 H, m); ^{13}C NMR δ −4.483 (q, J = 1.83 Hz), −4.263, −3.472, −3.337, 18.318, 18.568, 26.213, 26.362, 35.477, 93.430; ^{19}F NMR δ 6.06 (d, J = 8.3 Hz).

Supporting Information Available: Copies of ^{1}H and ^{13}C NMR spectra of compounds (32 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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