# An Efficient Generation of the Aluminum Enolates of 1*H*-Perfluoroalkyl Ketones from 1-Substituted-1-perfluoroalkenyl Phosphates and Their Aldol Reaction with Aldehydes[1]

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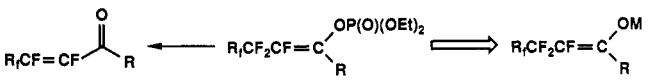
Diethyl 1-substituted-1-perfluoroalkenyl phosphates (**1**), available from perfluoroalkyl ketones and sodium diethyl phosphite, were allowed to react with a reagent derived from lithium aluminum hydride and a metal salt or bromine in tetrahydrofuran below −30 °C and successively treated with water or aldehydes to give rise to the corresponding 1*H*-perfluoroalkyl ketones (**4**) or α-fluoro-α-perfluoroalkyl-β-hydroxy ketones (**5**), respectively, in moderate to good yields. Copper(II) bromide, copper(I) bromide, and zinc chloride could be employed as the metal salt in the reaction. The phosphates also underwent reductive dephosphorylation with diisobutylaluminum hydride to generate the aluminum enolates of 1*H*-perfluoroalkyl ketones. $^{19}F$ NMR analyses indicated that their structure is not an α-metallo ketone but an oxygen-metalated species and that they are appreciably stable below 0 °C. Treatment with a wide variety of aldehydes at 0 °C yielded the corresponding aldol products **5** in good to excellent yields, whereas ketones did not react.

The aldol reaction is one of the most valuable and fundamental reactions in organic synthesis[2] and has been the subject of many investigations. In view of the high versatility of enolate intermediates, fluorine-containing enolates should serve as an extremely useful synthetic block for the preparation of a variety of specifically fluorinated molecules. In fact, the metal enolates of α-fluoro[3-5] and α,α-difluoro carbonyl compounds[6,7] have been used successfully in the synthesis of fluorinated analogues of biochemically important compounds,[8] which have received much attention due to their unique biological properties.[9] However, few or no efforts have been made to realize the generation and utilization of enolates bearing a perfluoroalkyl ($R_f$) group at the carbon center of their ambident anionic structure, except the reports of Nakai et al.[10] who succeeded in preparing the trimethylsilyl enol ethers of methyl 3,3,3-trifluoropropanoate and 3,3,3-trifluoro-1-phenyl-1-propanone.

Although the intermediates of this type are generally recognized to be susceptible to decomposition through a fluoride ion elimination, suitable choice of precursors and reagents should enable one to generate such species successfully. We recently developed a facile and high-yield method for converting perfluoroalkyl ketones into diethyl 1-substituted-1-perfluoroalkenyl phosphates (**1**),[11] which have already been utilized[11,12] as good synthetic equivalents to 1-perfluoroalkenyl ketones (**3**).[13] In our studies to

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extend the synthetic utility of these phosphates, we anticipated that they would be promising candidates for the generation of fluorinated enolates such as **2**, because of the large number of reports that enol compounds such as enol silyl ethers, enol acetates, or enol phosphates can be employed as precursors for the enolates and related species

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(4) For the lithium enolate of fluoromethyl ketone, see: Welch, J. T.; Seper, K. W. *Tetrahedron Lett.* **1984**, *25*, 5247.

(5) For the lithium enolates of fluoroacetic acid esters and amides, see: Molines, H.; Massoudi, M. H.; Cantacuzene, D.; Wakselman, C. *Synthesis* **1983**, 322. Welch, J. T.; Seper, K.; Eswarakrishnan, S.; Samartino, J. *J. Org. Chem.* **1984**, *49*, 4720. Welch, J. T.; Eswarakrishnan, S. *J. Chem. Soc., Chem. Commun.* **1985**, 186. Welch, J. T.; Eswarakrishnan, S. *J. Org. Chem.* **1985**, *50*, 5403. Welch, J. T.; Plummer, J. S. *Synth. Commun.* **1989**, *19*, 1081 and references cited therein.

(6) For the metal enolates and related compounds of difluoromethyl ketones, see: Yamana, M.; Ishihara, T.; Ando, T. *Tetrahedron Lett.* **1983**, *24*, 507. Ishihara, T.; Yamanaka, T.; Ando, T. *Chem. Lett.* **1984**, 1165. Kuroboshi, M.; Ishihara, T. *Tetrahedron Lett.* **1987**, *28*, 6481. Lang, R. W.; Schaub, B. *Ibid.* **1988**, *29*, 2943. Kuroboshi, M.; Ishihara, T. *Bull. Chem. Soc. Jpn.*, in press.

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(9) Ciba Foundation *Carbon-Fluorine Chemistry, Biochemistry, and Biological Activities*; Elsevier: Amsterdam, 1972. Filler, R. *Chemtech* **1974**, 752. Filler, R. *Biochemistry Involving Carbon-Fluorine Bonds*; American Chemical Society: Washington, DC, 1976. Drey, C. N. C. *Chemistry and Biochemistry of Amino Acids, Peptides and Proteins*; Winstein, B., Ed.; Marcel Dekker: New York, 1977. Taylor, W. G. *Synthesis* **1980**, 554. Arlt, D.; Jantelat, M.; Lantzsch, R. *Angew. Chem., Int. Ed. Engl.* **1981**, *20*, 703. Walsh, C. *Tetrahedron* **1982**, *38*, 871. Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha and Elsevier Biomedical: Tokyo and New York, 1982.

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(11) Ishihara, T.; Okada, Y.; Kuroboshi, M.; Shinozaki, T.; Ando, T. *Chem. Lett.* **1988**, 819.

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(13) For the access to certain 1*H*-perfluoroalkenyl ketones, see: Moreau, P.; Redwane, N.; Commeyras, A. *Bull. Soc. Chim. Fr.* **1984**, II-117. Burton, D. J.; Hansen, S. W. *J. Am. Chem. Soc.* **1986**, *108*, 4229.

0022-3263/90/1955-3107$02.50/0 

of parent carbonyl compounds.[14]

Based on the premise that a reagent for cleaving an enol oxygen–phosphorus bond in **1** at low temperatures would be an organometallic compound to stabilize the resultant enolate by strong coordination, we investigated the reactions of the enol phosphates **1** with various sorts of organometallic reagents, particularly the hydride reagents of oxygenophilic metals such as boron and aluminum. In this paper, we detail our results of the reactions which are effective to generate the desired enolates **2** (M = Al) of 1*H*-perfluoroalkyl ketones, together with their aldol reaction with a wide variety of aldehydes leading to α-fluoro-α-perfluoroalkyl-β-hydroxy ketones.

## Results and Discussion

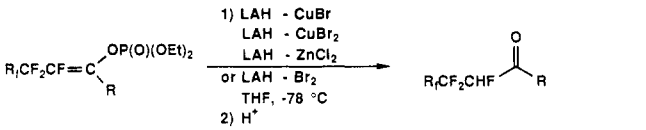
The starting enol phosphates **1** were prepared in good yields by the reaction between perfluoroalkyl ketones and sodium diethyl phosphite according to the previously reported procedure.[11]

Taking into account that the stability of enolates depends largely on the nature of their countercation,[14b] we decided to employ a variety of organometallic reagents capable of cleaving the enol oxygen–phosphorus bond. Organolithium reagents were first examined in this study, since they were reported by Borowitz et al.[14a] to cleave the enol oxygen–phosphorus bond of fluorine-free enol phosphates, giving rise to lithium enolate intermediates.

When 4-[(diethylphosphoryl)oxy]-1,1,1,2,2,3-hexafluoro-3-decene (**1c**) was allowed to react with butyllithium in tetrahydrofuran (THF) at −78 °C, a very complex mixture of products resulted. Treatment of **1c** with lithium 1-hexynide or phenylacetylide in THF at 0 °C, on the other hand, provided the corresponding (*E*)-4-(1-alkynyl)-1,1,1,2,3-pentafluoro-2-decen-4-ol in 80–86% yield. In the latter case, the lithium acetylide might attack the phosphorus atom of **1c** to generate a transient lithium enolate (**2**; $R_f$ = $CF_3$, R = Hex, M = Li), which immediately loses β-fluoride ion[15] to form 1,1,1,2,3-pentafluoro-2-decen-4-one (**3**; $R_f$ = $CF_3$, R = Hex), followed by nucleophilic addition of another lithium acetylide to this ketone leading to the final alcohol. These results allowed us to reconfirm that the lithium enolates **2** (M = Li) of 1*H*-perfluoroalkyl ketones are too labile for practical use in organic synthesis.

Apparently, the reduced stability of the enolate may be ascribed to the relatively high ionic character of the enol oxygen–lithium bond in **2**, which facilitates the β-elimination of fluoride ion. If one would employ such a reagent not only to cleave the enol oxygen–phosphorus bond but also to interact very strongly with an oxygen functionality, this unfavorable β-elimination reaction would be suppressed, and thereby the desired fluorine-containing enolates would be generated and applied to useful synthetic transformation like aldol reaction. Thus, we next examined the reactions of **1** with various hydride reagents derived from an oxygenophilic boron or aluminum metal. The observation by Jacques et al.[16] that lithium aluminum hydride (LAH) is effective for the reductive dephosphorylation of dialkyl aryl phosphates to liberate phenolic derivatives also prompted us to elaborate the reactions of interest.

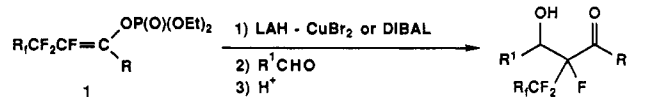
**Scheme I**




1a: $R_f$ = F, R = Hex
1c: $R_f$ = $CF_3$, R = Hex
1d: $R_f$ = $CF_3$, R = Ph
1e: $R_f$ = $CF_3$, R = *c*-Hex

4a: $R_f$ = F, R = Hex (91%)
4c: $R_f$ = $CF_3$, R = Hex (61-72%)
4d: $R_f$ = $CF_3$, R = Ph (82%)
4e: $R_f$ = $CF_3$, R = *c*-Hex (86%)

**Scheme II**

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Some preliminary experiments revealed that boron hydride reagents were insufficient to the relevant reaction: Neither borane, 9-borabicyclo[3.3.1]nonane, nor sodium borohydride reacted with the enol phosphate **1**, in spite of the reaction conditions being varied, while more powerful potassium tri-*sec*-butylborohydride merely produced a number of unidentified products.

Simple use of aluminum hydride reagents like LAH, lithium trimethoxyaluminum hydride, and sodium bis(2-methoxyethoxy)aluminum dihydride, afforded disappointing results. However, modified reagents of LAH with metal salts permitted the generation of the fluorinated enolates **2** from **1**. For example, treatment of the enol phosphate **1c** with a reagent prepared from two equimolar amounts of each of LAH and copper(II) bromide in THF for 4 h at −78 °C, after acidic workup, led to the formation of 1,1,1,2,2,3-hexafluoro-4-decanone (**4c**) in 72% yield (Scheme I), suggesting the intermediacy of the enolate in the reaction. The combination of LAH (2 equiv) with other metal salts such as copper(I) bromide[17] (4 equiv) and zinc chloride (2 equiv) was also found to promote the reaction under similar conditions (see the Experimental Section). To be noted, moreover, is that a reagent derived from LAH (2 equiv) and molecular bromine (2 equiv)[18] furnished the ketone **4c** in a comparable yield. This fact strongly implies that the counterionic metal of **2** is not a copper nor zinc but an aluminum species. Many attempts to delineate more accurate structures of the intermediates were unsuccessful.[19]

A fluorine-free enol phosphate, diethyl 1-*n*-propyl-1-butenyl phosphate, remained completely intact under the influence of these modified LAH reagents. Therefore, the present reductive dephosphorylation reaction is characteristic of the fluorinated enol phosphates **1**. Their high reactivity toward the reagents can be attributed in part to the presence of electron-attractive fluorine substituents, which may render the phosphorus atom of **1** more electrophilic and its enol oxygen–phosphorus bond weaker.

Expectedly, the in situ generated enolates underwent the aldol reaction with carbonyl compounds (Scheme II), though the reaction necessitated higher reaction temper-

(14) (a) Borowitz, I. J.; Casper, E. W. R.; Crouch, R. K.; Yee, K. C. *J. Org. Chem.* **1972**, *37*, 3873. (b) House, H. O. *Modern Synthetic Reactions*; W. A. Benjamin: Menlo Park, 1972; Chapters 9 and 10. (c) Kuwajima, I.; Nakamura, E. *Acc. Chem. Res.* **1985**, *18*, 181.

(15) Nakai et al. also observed an analogous defluorination in their initial attempts[10a] to generate the enolate of methyl 3,3,3-trifluoropropanoate through α-deprotonation process.

(16) Jacques, J.; Fouquey, C.; Viterbo, R. *Tetrahedron Lett.* **1971**, 4617.

(17) The LAH–copper(I) iodide combination has been used for the conjugate reduction of α,β-unsaturated carbonyl compounds. See: Ashby, E. C.; Lin, J. J. *Tetrahedron Lett.* **1975**, 4453. Ashby, E. C.; Lin, J. J. *Ibid.* **1976**, 3865. Ashby, E. C.; Lin, J. J.; Kovar, R. *J. Org. Chem.* **1976**, *41*, 1939. Tsuda, T.; Fujii, T.; Kawasaki, K.; Saegusa, T. *J. Chem. Soc., Chem. Commun.* **1980**, 1013.

(18) This stoichiometry between LAH and bromine corresponds to that producing bromoaluminum dihydride, lithium bromide, and hydrogen.

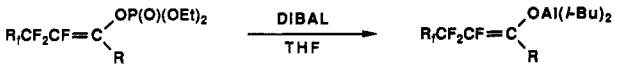
(19) $^{19}F$ NMR analyses performed at low temperatures (−30 to −78 °C) showed appearance of very broad signals, which were useless for the structural elucidations.

**Table I. Aldol Reaction of Fluorinated Enol Phosphates 1 with Aldehydes Using LAH–$CuBr_2$**

| entry | phosphate $R_f$ | phosphate R | aldehyde | yield,[a] % | t:e[b] |
|---|---|---|---|---|---|
| 1 | F | Hex (1a) | $CH_3CH_2CHO$ | **5a**, 70 | 59:41 |
| 2 | | 1a | $CH_3(CH_2)_2CHO$ | **5b**, 70 | 56:44 |
| 3 | | 1a | (*E*)-$CH_3CH$=$CHCHO$ | **5d**, 39 | 50:50 |
| 4 | $CF_3$ | Hex (1c) | $CH_3CH_2CHO$ | **5h**, 58 | 59:41 |
| 5 | | 1c | $CH_3(CH_2)_2CHO$ | **5i**, 49 | 64:36 |
| 6 | | 1c | $(CH_3)_2CHCHO$ | **5j**, 51 | 71:29 |
| 7 | | 1c | $CH_3(CH_2)_5CHO$ | **5k**, 51 | 52:48 |
| 8 | | 1c | (*E*)-$CH_3CH$=$CHCHO$ | **5l**, 66 | 57:43 |
| 9 | | 1c | $C_6H_5CHO$ | **5m**, 51 | 60:40 |
| 10 | $CF_3$ | Ph (1d) | $CH_3(CH_2)_2CHO$ | **5n**, 49 | 41:59 |
| 11 | | 1d | $(CH_3)_2CHCHO$ | **5o**, 37 | *c* |
| 12 | | 1d | (*E*)-$CH_3CH$=$CHCHO$ | **5p**, 34 | 41:59 |
| 13 | $CF_3$ | *c*-Hex (1e) | $CH_3(CH_2)_2CHO$ | **5r**, 72 | 41:59 |
| 14 | | 1e | (*E*)-$CH_3CH$=$CHCHO$ | **5s**, 38 | 44:56 |

[a] Yields refer to pure isolated products. [b] The figures t and e stand for threo and erythro isomers, respectively. The isomer ratios were determined by $^{19}F$ NMR. [c] Not determined.

**Scheme III**




1a: $R_f$ = F, R = Hex
1b: $R_f$ = F, R = Ph
1c: $R_f$ = $CF_3$, R = Hex
1d: $R_f$ = $CF_3$, R = Ph

6a: $R_f$ = F, R = Hex
6b: $R_f$ = F, R = Ph
6c: $R_f$ = $CF_3$, R = Hex
6d: $R_f$ = $CF_3$, R = Ph

atures than −78 °C. Thus, treatment of the enol phosphate **1c** with two equimolar amounts of LAH–copper(II) bromide for 2 h and with propanal for 10 h at −30 °C gave 4-fluoro-3-hydroxy-4-(1,1,2,2,2-pentafluoroethyl)-5-undecanone (**5h**) in 58% yield as a 59:41 mixture of threo and erythro isomers[20] (Table I, entry 4). Table I summarizes the results of the reactions of several enol phosphates **1**. Diastereochemical assignment of the products will be discussed later. Whereas ketones like 3-pentanone and cyclohexanone were unreactive, aldehydes yielded the corresponding β-hydroxy ketones **5**, whose ratios of threo to erythro isomers fell in a range of 0.7–2.5:1. The yields of **5** were not necessarily good enough to evaluate the stereochemistry of the present aldol reactions.

Further endeavors were made to improve some serious disadvantages encountered above. In view of the effectiveness of the LAH–bromine reagent,[22] we felt that trivalent aluminum hydrides would function as more potential reagents in the desired reaction. In fact, when the enol phosphate **1c** was exposed to diisobutylaluminum hydride (DIBAL) (5 equiv) in THF[23] for 0.5 h at room temperature, the corresponding 1*H*-perfluoroalkyl ketone **4c** was obtained in 86% yield after acidic hydrolysis. This is clearly suggestive of highly efficient generation of an aluminum enolate intermediate.

Monitoring the reactions by $^{19}F$ NMR provided direct evidence indicating the existence of the enolates (**6**) as depicted in Scheme III. Table II tabulates the $^{19}F$ NMR spectral data for some typical species **6** together with those for the corresponding starting enol phosphates **1**, and

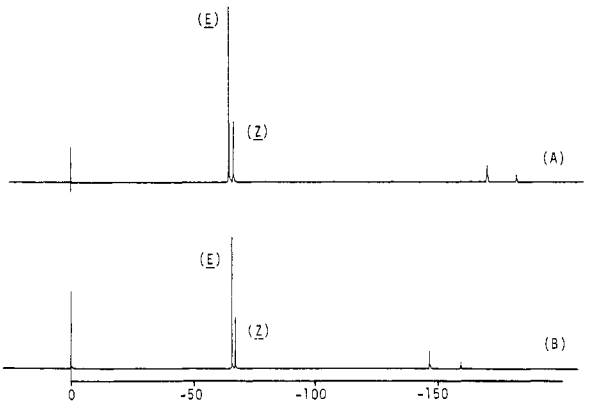
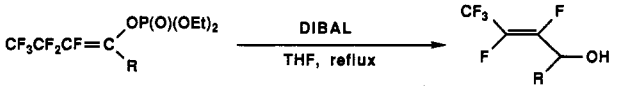



**Figure 1.** $^{19}F$ NMR spectra for the aluminum enolate **6a** of 1,1,1,2-tetrafluoro-3-nonanone (A) and for 3-[(diethylphosphoryl)oxy]-1,1,1,2-tetrafluoro-2-nonene, **1a** (B).

**Scheme IV**




1c: R = Hex
1d: R = Ph
1e: R = *c*-Hex

7c: R = Hex (73%)
7d: R = Ph (73%)
7e: R = *c*-Hex (72%)

Figure 1 exhibits the representative spectra of them. As shown in Table II, the enol phosphate **1b**, in particular, had long-range fluorine–phosphorus couplings of 2.4 and 6.1 Hz for the *E* isomer and of 2.4 and 9.8 Hz for the *Z* isomer, but the corresponding enolate **6b** did not. The spectral patterns of the enolates **6a–d** markedly resembled those of the corresponding phosphates **1a–d**, respectively. These findings are fully consistent with the structure of **6** where the diisobutylaluminum group is bound to the oxygen atom. The structure may also be supported by large vicinal fluorine–fluorine couplings (11–19 Hz) between the trifluoromethyl or difluoromethylene group and the vinylic fluorine in **6**. Of most importance is the fact that in all the cases the *E* to *Z* ratios of **6** were identical with those of the starting phosphates **1**, since this means that the transformation of **1** into the enolate takes place with complete retention of configuration. The *E* and *Z* geometry of **6** as well as **1** could be assigned based upon the stereochemical outcome (see Table III) in their aldol reactions. These aluminum enolates showed a relatively high stability below 0 °C; the half-lives for **6c** and **6d** were 20 and 0.5 h, respectively, at room temperature. However, they decomposed readily on heating to give good yields of (*E*)-allylic alcohols (**7**) (Scheme IV) arising from the 1,2-reduction of intermediately formed α,β-unsaturated ketones (**3**) with DIBAL.

The fluorine-containing enolates **6** thus generated were found to react with aldehydes very efficiently (Scheme II), though either of two slightly different procedures, methods A and B, should be employed depending on the structures of **1**, as described in the Experimental Section. A wide variety of aldehydes, including aliphatic, aromatic, and α,β-unsaturated aldehydes, could participate well in the reaction to afford the corresponding α-fluoro-α-perfluoroalkyl-β-hydroxy ketones (**5**) in good to excellent yields. Sterically hindered aldehydes such as 2,2-dimethylpropanal and ketones failed to react even in the presence of a Lewis acid.[24] The results of these reactions are listed in Table III. A key to allow the reaction to

(20) The relative stereochemical nomenclature proposed by Noyori et al.[21] is pertinent throughout this work.
(21) Noyori, R.; Ishida, I.; Sakata, J. *J. Am. Chem. Soc.* **1983**, *105*, 1598.
(22) The reaction between **1c** and propanal using the LAH–bromine reagent afforded 69% yield of the aldol product **5h**.
(23) Screening the reaction solvents revealed that THF gave the best results. The reaction conducted in hexane was extremely reluctant, the starting phosphate being recovered almost quantitatively. The use of diethyl ether or 1,2-dimethoxyethane provided complex mixtures containing the starting phosphate and/or allylic alcohol **7**.
(24) The addition of boron trifluoride diethyl etherate or titanium(IV) chloride only caused the decomposition of the enolate.

**Table II. $^{19}F$ NMR Data for Some Enol Phosphates and Aluminum Enolates**

| phosphate | $\delta^a$ | enolate | $\delta^b$ |
|---|---|---|---|
| **1a**: (*E*) | −65.9 (d, *J* = 11.0, 3 F), −147.1 (m, 1 F) | **6a**: (*E*) | −64.4 (d, *J* = 13.4, 3 F), −171.0 (q, *J* = 13.4, 1 F) |
| (*Z*) | −67.3 (d, *J* = 9.8, 3 F), −160.2 (m, 1 F) | (*Z*) | −66.3 (d, *J* = 12.2, 3 F), −183.0 (m, 1 F) |
| **1b**: (*E*) | −65.6 (dd, *J* = 11.6, 2.4, 3 F), −143.5 (dq, *J* = 11.6, 6.1, 1 F) | **6b**: (*E*) | −64.5 (d, *J* = 14.7, 3 F), −167.5 (q, *J* = 14.7, 1 F) |
| (*Z*) | −67.0 (dd, *J* = 9.8, 2.4, 3 F), −156.6 (dq, *J* = 9.8, 9.8, 1 F) | (*Z*) | −66.4 (d, *J* = 11.0, 3 F), −180.0 (q, *J* = 11.0, 1 F) |
| **1c**: (*E*) | −84.8 (dt, *J* = 6.7, 3.3, 3 F), −118.9 (d, *J* = 11.0, 2 F), −159.2 (m, 1 F) | **6c**: (*E*) | −83.4 (dt, *J* = 7.7, 3.7, 3 F), −114.4 (d, *J* = 13.4, 2 F), −179.4 (m, 1 F) |
| (*Z*) | −84.9 (dt, *J* = 6.5, 3.1, 3 F), −117.6 (d, *J* = 12.2, 2 F), −145.3 (m, 1 F) | (*Z*) | −83.8 (dt, *J* = 7.7, 3.7, 3 F), −112.4 (dq, *J* = 14.6, 3.7, 2 F), −167.2 (m, 1 F) |
| **1d**: (*E*) | −84.3 (dt, *J* = 7.9, 3.9, 3 F), −118.4 (d, *J* = 10.8, 2 F), −155.7 (m, 1 F) | **6d**: (*E*) | −86.1 (dt, *J* = 7.3, 3.7, 3 F), −117.4 (dq, *J* = 13.4, 3.7, 2 F), −179.8 (m, 1 F) |
| (*Z*) | −84.0 (dt, *J* = 7.9, 3.9, 3 F), −116.1 (d, *J* = 14.8, 2 F), −141.9 (m, 1 F) | (*Z*) | −85.6 (dt, *J* = 9.8, 3.7, 3 F), −114.1 (dq, *J* = 18.9, 3.7, 2 F), −166.6 (m, 1 F) |

[a] Expressed in ppm downfield from internal $CFCl_3$; *J* values are given in hertz. [b] Denoted in ppm downfield from external $CFCl_3$; *J* values are given in hertz.

**Table III. Aldol Reaction of Fluorinated Enol Phosphates 1 with Aldehydes by Use of DIBAL**

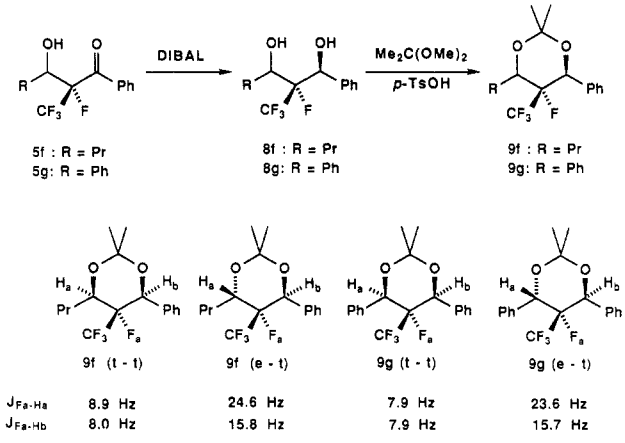
| | phosphate | | | | | |
|---|---|---|---|---|---|---|
| entry | $R_f$ | R | *E*:*Z*[b] | aldehyde | yield,[a] % | t:e[c] |
| 1 | F | Hex (**1a**) | 73:27 | $CH_3CH_2CHO$ | **5a**, 77 | 67:33 |
| 2 | | **1a** | 73:27 | $CH_3(CH_2)_2CHO$ | **5b**, 83 | 62:38 |
| 3 | | **1a** | 73:27 | $CH_3(CH_2)_5CHO$ | **5c**, 81 | 59:41 |
| 4 | | **1a** | 73:27 | (*E*)-$CH_3CH$=$CHCHO$ | **5d**, 76 | 65:35 |
| 5 | | **1a** | 73:27 | $C_6H_5CHO$ | **5e**, 84 | 61:39 |
| 6 | F | Ph (**1b**) | 15:85 | $CH_3(CH_2)_2CHO$ | **5f**, 68[d] | 46:54 |
| 7 | | **1b** | 12:88 | $C_6H_5CHO$ | **5g**, 78 | 39:61 |
| 8 | $CF_3$ | Hex (**1c**) | 65:35 | $CH_3CH_2CHO$ | **5h**, 76 | 71:29 |
| 9 | | **1c** | 72:28 | $CH_3(CH_2)_2CHO$ | **5i**, 71 | 68:32 |
| 10 | | **1c** | 65:35 | $(CH_3)_2CHCHO$ | **5j**, 59[e] | 63:37 |
| 11 | | **1c** | 70:30 | $CH_3(CH_2)_5CHO$ | **5k**, 82 | 72:28 |
| 12 | | **1c** | 70:30 | (*E*)-$CH_3CH$=$CHCHO$ | **5l**, 73 | 68:32 |
| 13 | | **1c** | 70:30 | $C_6H_5CHO$ | **5m**, 70 | 51:49 |
| 14 | $CF_3$ | Ph (**1d**) | 22:78 | $CH_3(CH_2)_2CHO$ | **5n**, 81 | 38:62 |
| 15 | | **1d** | 21:79 | $(CH_3)_2CHCHO$ | **5o**, 56[e] | 22:78 |
| 16 | | **1d** | 21:79 | (*E*)-$CH_3CH$=$CHCHO$ | **5p**, 66 | 37:63 |
| 17 | | **1d** | 22:78 | $C_6H_5CHO$ | **5q**, 71 | 23:77 |
| 18 | $CF_3$ | *c*-Hex (**1e**) | 35:65 | $CH_3(CH_2)_2CHO$ | **5r**, 80 | 45:55 |
| 19 | | **1e** | 35:65 | (*E*)-$CH_3CH$=$CHCHO$ | **5s**, 86 | 39:61 |
| 20 | | **1e** | 35:65 | $C_6H_5CHO$ | **5t**, 88 | 42:58 |

[a] Yields are of pure isolated products. [b] Measured by $^{19}F$ NMR. [c] See footnote *b* in Table I. [d] Conducted at −30 °C for 15 min by using 5 equiv of aldehyde. [e] Five equivalents of aldehyde was employed.

proceed cleanly is that the specified reaction periods and temperatures must be observed; longer reaction times or higher reaction temperatures substantially decreased the yield of **5** due to the retro-aldol reaction of **5** or the decomposition of **2**.

The stereochemistry of the aldol products was confirmed by the following procedure. Each diastereoisomer of **5**, easily separable by silica gel chromatography, was converted to the corresponding diastereomerically pure acetonides **9** through highly stereoselective reduction with DIBAL[25] followed by acid-catalyzed acetonization with 2,2-dimethoxypropane (Scheme V). Examination of the $^{19}F$ and $^1H$ NMR spectra of **9** made it possible to determine the threo and erythro configurations[20] of **9** or **5**, on the basis of the relative magnitudes of the vicinal couplings between fluorine ($F_a$) and hydrogen ($H_a$) in **9**. The isomer having a smaller coupling constant (7.9 or 8.9 Hz) was assigned to the threo configuration with a syn relationship between $F_a$ and $H_a$ and the other isomer possessing a larger coupling constant (23.6 or 24.6 Hz) to the erythro configuration. The same procedure was adopted in the determination of the stereochemistry of 2-fluoro 1,3-diol systems.[26]

**Scheme V**




As is evident from the data of Table III, the ratios of threo to erythro isomer of **5** are close to the *E* to *Z* ratios of the starting enol phosphates **1**, or the aluminum enolates

(25) The β-hydroxy ketones **5** were reduced stereoselectively with DIBAL or LAH at −78 °C, irrespective of the stereochemistry on the β-carbon, to give 1,2-threo 1,3-diols predominantly. Full details on this subject will be disclosed elsewhere. Partly presented at the 1989 International Chemical Congress of Pacific Basin Societies; Honolulu, Hawaii, December 1989; Abstr. No. 8D-325.

(26) Kitazume, T.; Kobayashi, T.; Yamamoto, T.; Yamazaki, T. *J. Org. Chem.* **1987**, *52*, 3218. Yamazaki, T.; Yamamoto, T.; Kitazume, T. *Ibid.* **1989**, *54*, 83.

6. This fact strongly suggests that the aldol reaction of 6 with aldehydes occurs preferentially via a chairlike six-membered cyclic transition state,[2,27] which is well documented to pertain to the aldol reactions of Lewis acidic metal enolates.[28] In such a process, an *E* enolate leads to threo aldol products and a *Z* enolate to erythro aldol products. This stereochemical correlation may safely be applied to the present aldol reactions.[29] Consequently, the enolates 6 which give the threo isomers of 5 can be established as *E* and the enolates which afford the erythro isomers as *Z*. It follows, furthermore, that the enol phosphates 1 generating the *E* enolates 6 possess an *E* configuration whereas the enol phosphates producing the *Z* enolates have a *Z* configuration. The discussions mentioned above are entirely compatible with all the findings obtained in this study.

In summary, we have successfully achieved the generation and aldol reaction of the aluminum enolate intermediates (6) of 1*H*-perfluoroalkyl ketones by using the unique dephosphorylation of the fluorinated enol phosphates 1. The present reactions will constitute an efficient and practical means for the synthesis of $\alpha$-fluoro-$\alpha$-perfluoroalkyl-$\beta$-hydroxy ketones (5), which are very difficult to prepare by other methods.

## Experimental Section

**General Methods and Materials.** All reactions were performed under an atmosphere of dry argon. Unless otherwise noted, materials were obtained from commercial sources and used without further purification. The use of a syringe or cannula is recommended for transferring a THF solution of LAH and a hexane solution of DIBAL. Diethyl 1-substituted-1-perfluoroalkenyl phosphates 1 were prepared according to the method reported recently by us.[11] Diethyl ether and THF were distilled from LAH immediately prior to use. Aldehydes and ketones used were distilled (or vacuum distilled) from calcium hydride and stored under argon. Column chromatography was carried out on silica gel C-200 (Wako, Tokyo), 100–200 mesh, with the indicated solvents. Infrared (IR) spectra were recorded on either a Shimadzu IR-400 or a JASCO IR-810 spectrometer. $^1$H NMR spectra were acquired with a Varian EM-390 (90 MHz), a Varian XL-200 (200 MHz), or a JEOL JNM-PMX60SI (60 MHz) spectrometer in deuteriochloroform ($CDCl_3$) with tetramethylsilane as an internal reference. A JEOL FX90Q (84.25 MHz) spectrometer was used to measure $^{19}$F NMR spectra in $CDCl_3$ with trichlorofluoromethane as an internal standard. Proton and fluorine chemical shifts downfield from the reference are expressed positive in parts per million (ppm). Mass spectra (MS) were taken at 20 eV by using a Shimadzu GCMS-QP1000 instrument.

**Reductive Dephosphorylation of 1 with LAH-Based Reagents Leading to 1*H*-Perfluoroalkyl Ketones (4). Typical Procedure for 1c.** A THF solution (1 M) of LAH (2.0 mL, 2.0 mmol) was gradually added to a suspension of $CuBr_2$ (0.447 g, 2.0 mmol) in THF (5 mL) below −30 °C, and the mixture was stirred for 2 h at the same temperature. To the resulting mixture was added dropwise 1c (0.400 g, 1.0 mmol) at −78 °C. After the mixture was stirred for 4 h at this temperature, the reaction was quenched with a mixture of saturated $NH_4Cl$ solution (5 mL) and aqueous HCl (6 M, 10 mL). The resultant mixture was extracted with diethyl ether (20 mL × 4), and the combined extracts were washed with water, dried ($Na_2SO_4$), filtered, and concentrated. Silica gel column chromatography (hexane-AcOEt) of the residue gave 1,1,1,2,2,3-hexafluoro-4-decanone (4c) (0.190 g, 72%): IR (neat) 2930, 1741, 1222, 1203, 1159 cm$^{-1}$; $^1$H NMR $\delta$ 4.96 (ddd, $J$ = 46.4, 17.1, 6.1 Hz, 1 H), 2.61 (dt, $J$ = 3.0, 6.4 Hz, 2 H), 2.0–1.1 (m, 8 H), 0.89 (t, $J$ = 5.4 Hz, 3 H); $^{19}$F NMR $\delta$ −82.82 (d, $J$ = 11.0 Hz, 3 F), −122.12 (ddd, $J$ = 286.9, 9.8, 6.1 Hz, 1 F), −128.34 (ddd, $J$ = 286.9, 17.1, 13.4 Hz, 1 F), −206.16 (dq, $J$ = 46.4, 11.0 Hz, 1 F); MS $m/z$ (relative intensity) 264 (M$^+$, 0.3), 113 (80), 85 (100).

When CuBr (0.574 g, 4 mmol), $ZnCl_2$·TMEDA (0.505 g, 2 mmol), or bromine (0.320 g, 2 mmol) was used in place of $CuBr_2$, 4c was obtained in a 72%, 65%, or 61% yield, respectively.

**1,1,1,2-Tetrafluoro-3-nonanone (4a):** 91%; IR (neat) 2930, 1741, 1265, 1201, 1141 cm$^{-1}$; $^1$H NMR $\delta$ 4.87 (dq, $J$ = 46.4, 7.3 Hz, 1 H), 2.65 (dt, $J$ = 6.4, 3.0 Hz, 2 H), 2.0–1.0 (m, 8 H), 0.84 (t, $J$ = 5.4 Hz, 3 H); $^{19}$F NMR $\delta$ −75.82 (dd, $J$ = 12.2, 7.3 Hz, 3 F), −205.09 (dq, $J$ = 46.4, 12.2 Hz, 1 F); MS $m/z$ (relative intensity) 214 (M$^+$, 0.1), 113 (100), 84 (37), 72 (83).

**2,3,3,4,4,4-Hexafluoro-1-phenyl-1-butanone (4d):** 82%; IR (neat) 3064, 2928, 1706, 1271, 1205, 1157, 686 cm$^{-1}$; $^1$H NMR $\delta$ 8.1–7.1 (m, 5 H), 5.75 (ddd, $J$ = 46.4, 17.1, 4.9 Hz, 1 H); $^{19}$F NMR $\delta$ −82.85 (d, $J$ = 11.0 Hz, 3 F), −120.82 (ddd, $J$ = 286.9, 11.0, 4.9 Hz, 1 F), −127.46 (ddd, $J$ = 286.9, 17.1, 14.7 Hz, 1 F), −202.85 (dq, $J$ = 46.4, 11.0 Hz, 1 F); MS $m/z$ (relative intensity) 256 (M$^+$, 0.4), 105 (100).

**1-Cyclohexyl-2,3,3,4,4,4-hexafluoro-1-butanone (4e):** 86%; IR (neat) 2934, 1734, 1220, 1201, 1159 cm$^{-1}$; $^1$H NMR $\delta$ 5.04 (ddd, $J$ = 47.6, 18.3, 7.3 Hz, 1 H), 3.1–2.6 (m, 1 H), 2.2–0.7 (m, 10 H); $^{19}$F NMR $\delta$ −82.76 (d, $J$ = 11.0 Hz, 3 F), −121.26 (ddd, $J$ = 286.9, 9.8, 7.3 Hz, 1 F), −127.67 (ddd, $J$ = 286.9, 18.3, 12.2 Hz, 1 F), −206.93 (dddq, $J$ = 47.6, 12.2, 9.8, 11.0 Hz, 1 F); MS $m/z$ (relative intensity) 262 (M$^+$, 0.4), 111 (90), 83 (100).

**Typical Procedure for the Aldol Reaction of 1 with Aldehydes Using LAH–$CuBr_2$ Reagent.** Into a suspension of $CuBr_2$ (0.447 g, 2.0 mmol) in THF (5 mL) was introduced via a syringe a THF solution (1 M) of LAH (2.0 mL, 2.0 mmol) at −30 °C, and the mixture was stirred for 30 min. After addition of 1a (0.350 g, 1.0 mmol), followed by stirring for additional 3 h at −30 °C, propanal (0.174 g, 3.0 mmol) was added dropwise to the mixture at the same temperature. After 10 h of stirring at −30 °C, the reaction mixture was hydrolyzed with a cold saturated $NH_4Cl$ solution (15 mL) containing aqueous HCl (6 M, 5 mL). The resulting mixture was extracted with diethyl ether (30 mL × 3), and the ethereal extracts were washed with water, dried ($Na_2SO_4$), filtered, and concentrated under vacuum. The ratio of threo to erythro isomer listed in Table I was determined by $^{19}$F NMR of the crude product, which thereafter was chromatographed (hexane–AcOEt) on a column of silica gel to give 4-fluoro-3-hydroxy-4-(trifluoromethyl)-5-undecanone (5a) (0.190 g, 70%): IR (Nujol) 3426, 1734, 1279, 1200, 1112 cm$^{-1}$; $^1$H NMR $\delta$ 4.5–3.5 (m, 1 H), 2.9–2.3 (m, 2 H), 2.3–0.6 (m, 17 H); $^{19}$F NMR $\delta$ −74.06 (d, $J$ = 6.1 Hz, 3 F), −189.79 (m, 1 F) for the erythro isomer, −73.64 (d, $J$ = 6.1 Hz, 3 F), −189.67 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 272 (M$^+$, 0.1), 223 (0.1), 207 (0.2), 113 (100), 85 (32). Anal. Calcd for $C_{12}H_{20}F_4O_2$: C, 52.93; H, 7.40; F, 27.91. Found: C, 53.14; H, 7.61; F, 28.07.

**Typical Procedure for the Aldol Reaction of 1 with Aldehydes by Use of DIBAL. Method A for 1a and 1c.** A hexane solution (1 M) of DIBAL (5.0 mL, 5.0 mmol) was slowly added to a solution of 1a (0.350 g, 1.0 mmol) in THF (5 mL) at 0 °C under an argon atmosphere. The mixture was stirred for 30 min at room temperature. To this mixture, which had been cooled to 0 °C, was added propanal (0.174 g, 3.0 mmol) by use of a syringe. After 30 min of stirring at 0 °C, the reaction mixture was poured into a mixture of ice and aqueous HCl (6 M, 5 mL), followed by extraction with diethyl ether (30 mL × 3). The extracts were washed with water, dried ($Na_2SO_4$), filtered, and concentrated in vacuo to leave an oily residue, which was subjected to $^{19}$F NMR analysis to measure the ratio of threo to erythro isomer (Table II). Column chromatography (hexane–AcOEt) on silica gel gave pure 5a (0.209 g, 77%).

**5-Fluoro-4-hydroxy-5-(trifluoromethyl)-6-dodecanone (5b):** IR (Nujol) 3434, 1732, 1294, 1198, 1165, 1110 cm$^{-1}$; $^1$H NMR $\delta$ 4.5–3.7 (m, 1 H), 2.9–2.4 (m, 2 H), 2.4–1.1 (m, 13 H), 1.1–0.6 (m, 6 H); $^{19}$F NMR $\delta$ − 73.94 (d, $J$ = 6.1 Hz, 3 F), −190.01 (m, 1 F) for the erythro isomer, −73.58 (d, $J$ = 6.1 Hz, 3 F), −189.74 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 286 (M$^+$, 0.1), 213 (0.1), 113 (100), 85 (23), 73 (21). Anal. Calcd for $C_{13}H_{22}F_4O_2$: C, 54.54; H, 7.75; F, 26.54. Found: C, 54.70; H, 7.81; F, 26.39.

(27) Zimmerman, H. E.; Traxler, M. D. *J. Am. Chem. Soc.* **1957**, *79*, 1920. For a recent theoretical investigation, see: Li, Y.; Paddon-Row, M. N.; Houk, K. N. *Ibid.* **1988**, *110*, 3684.

(28) For example, see: Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23. Masamune, S.; Choy, W. *Ibid.* **1982**, *15*, 47.

(29) The aldol reaction of the boron enolates of *N,N*-dialkyl-2,3,3,3-tetrafluoropropanamides has also been found[30] to follow the same stereochemical relationship.

(30) Kuroboshi, M.; Ishihara, T. *Bull. Chem. Soc. Jpn.*, in press.

**8-Fluoro-9-hydroxy-8-(trifluoromethyl)-7-pentadecanone (5c).** Erythro isomer: IR (neat) 3436, 1736, 1288, 1198, 1161, 1150 $cm^{-1}$; $^1H$ NMR $\delta$ 4.6–3.7 (m, 1 H), 2.8–2.2 (m, 2 H), 2.2–1.9 (d, $J$ = 9.0 Hz, 1 H), 1.9–0.7 (m, 24 H); $^{19}F$ NMR $\delta$ –73.97 (d, $J$ = 6.1 Hz, 3 F), –189.71 (m, 1 F); MS $m/z$ (relative intensity) 328 ($M^+$, 0.1), 243 (0.1), 213 (1), 131 (19), 113 (100), 85 (19). Threo isomer: IR (neat) 3430, 1733, 1290, 1201, 1185, 1150 $cm^{-1}$; $^1H$ NMR $\delta$ 4.6–3.7 (m, 1 H), 2.9–2.5 (m, 2 H), 2.1–1.9 (d, $J$ = 8.0 Hz, 1 H), 1.9–0.7 (m, 24 H); $^{19}F$ NMR $\delta$ –73.57 (d, $J$ = 6.1 Hz, 3 F), –189.72 (d, $J$ = 22.0 Hz, 1 F). Anal. Calcd for $C_{16}H_{28}F_4O_2$: C, 58.52; H, 8.59; F, 23.14. Found: C, 58.40; H, 8.53; F, 23.02.

**(*E*)-5-Fluoro-4-hydroxy-5-(trifluoromethyl)-2-dodecen-6-one (5d).** Erythro isomer: IR (neat) 3446, 1736, 1672, 1288, 1202, 1148 $cm^{-1}$; $^1H$ NMR $\delta$ 5.86 (dq, $J$ = 15.5, 6.5 Hz, 1 H), 5.46 (dd, $J$ = 15.5, 6.0 Hz, 1 H), 4.58 (ddd, $J$ = 20.5, 7.0, 6.0 Hz, 1 H), 2.9–2.5 (m, 2 H), 2.07 (d, $J$ = 7.0 Hz, 1 H), 1.72 (d, $J$ = 6.5 Hz, 3 H), 1.6–0.7 (m, 11 H); $^{19}F$ NMR $\delta$ –74.23 (d, $J$ = 7.3 Hz, 3 F), –191.34 (ddq, $J$ = 17.7, 3.7, 7.3 Hz, 1 F); MS $m/z$ (relative intensity) 284 ($M^+$, 0.1), 264 (0.1), 249 (5), 207 (1), 154 (13), 124 (47), 113 (43), 85 (17), 71 (100). Threo isomer: IR (neat) 3440, 1734, 1672, 1287, 1206, 1147 $cm^{-1}$; $^1H$ NMR $\delta$ 5.73 (dq, $J$ = 15.5, 6.5 Hz, 1 H), 5.35 (dd, $J$ = 15.5, 6.0 Hz, 1 H), 4.53 (ddd, $J$ = 20.5, 7.0, 6.0 Hz, 1 H), 2.8–2.3 (m, 2 H), 1.97 (d, $J$ = 7.0 Hz, 1 H), 1.66 (d, $J$ = 6.5 Hz, 3 H), 1.6–0.6 (m, 11 H); $^{19}F$ NMR $\delta$ –73.58 (d, $J$ = 6.1 Hz, 3 F), –190.07 (dq, $J$ = 23.2, 6.1 Hz, 1 F). Anal. Calcd for $C_{13}H_{20}F_4O_2$: C, 54.92; H, 7.09; F, 26.73. Found: C, 55.07; H, 7.21; F, 26.66.

**2-Fluoro-1-hydroxy-1-phenyl-2-(trifluoromethyl)-3-nonanone (5e).** Erythro isomer: IR (Nujol) 3380, 1735, 1283, 1194, 1140 $cm^{-1}$; $^1H$ NMR $\delta$ 7.5–7.3 (m, 5 H), 5.29 (d, $J$ = 22.0 Hz, 1 H), 2.8–2.2 (m, 2 H), 1.9–1.4 (m, 2 H), 1.4–0.8 (m, 10 H); $^{19}F$ NMR $\delta$ –74.05 (d, $J$ = 7.3 Hz, 3 F), –189.37 (dq, $J$ = 22.0, 7.3 Hz, 1 F); MS $m/z$ (relative intensity) 320 ($M^+$, tr), 300 (1), 229 (4), 190 (24), 113 (57), 108 (100), 85 (23), 77 (10). Threo isomer: IR (Nujol) 3434, 1733, 1286, 1203, 1131 $cm^{-1}$; $^1H$ NMR $\delta$ 7.5–7.3 (m, 5 H), 5.34 (d, $J$ = 25.6 Hz, 1 H), 2.8–2.3 (m, 2 H), 1.9–1.4 (m, 2 H), 1.4–0.8 (m, 10 H); $^{19}F$ NMR $\delta$ –73.23 (d, $J$ = 6.1 Hz, 3 F), –194.14 (dq, $J$ = 25.6, 6.1 Hz, 1 F). Anal. Calcd for $C_{16}H_{20}F_4O_2$: C, 59.99; H, 6.29; F, 23.72. Found: C, 60.21; H, 6.43; , 23.79.

**4-Fluoro-3-hydroxy-4-(1,1,2,2,2-pentafluoroethyl)-5-undecanone (5h)**: IR (neat) 3430, 1735, 1219, 1203, 1175 $cm^{-1}$; $^1H$ NMR $\delta$ 4.3–4.0 (m, 1 H), 2.8–2.6 (m, 2 H), 2.4–2.1 (m, 1 H), 1.7–1.5 (m, 4 H), 1.4–1.2 (m, 6 H), 1.1–1.0 (m, 3 H), 0.89 (m, 3 H); $^{19}F$ NMR $\delta$ –80.70 (d, $J$ = 12.2 Hz, 3 F), –118.48 (d, $J$ = 289.3 Hz, 1 F), –122.39 (dd, $J$ = 289.3, 6.1 Hz, 1 F), –185.29 (m, 1 F) for the erythro isomer, –80.60 (d, $J$ = 12.2 Hz, 3 F), –118.02 (d, $J$ = 289.3 Hz, 1 F), –122.17 (dd, $J$ = 289.3, 6.1 Hz, 1 F), –183.22 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 322 ($M^+$, 0.1), 273 (1), 194 (4), 174 (6), 113 (100). Anal. Calcd for $C_{13}H_{20}F_6O_2$: C, 48.45; H, 6.25; F, 35.37. Found: C, 48.26; H, 6.15; F, 35.18.

**5-Fluoro-4-hydroxy-5-(1,1,2,2,2-pentafluoroethyl)-6-dodecanone (5i)**: IR (neat) 3430, 1734, 1219, 1201, 1174 $cm^{-1}$; $^1H$ NMR $\delta$ 4.4–4.1 (m, 1 H), 2.8–2.6 (m, 2 H), 2.4–2.1 (m, 1 H), 1.8–1.5 (m, 4 H), 1.5–1.2 (m, 8 H), 1.0–0.9 (m, 6 H); $^{19}F$ NMR $\delta$ –80.68 (d, $J$ = 12.2 Hz, 3 F), –118.40 (d, $J$ = 289.3 Hz, 1 F), –122.28 (dd, $J$ = 289.3, 7.3 Hz, 1 F), –185.23 (m, 1 F) for the erythro isomer, –80.58 (d, $J$ = 12.2 Hz, 3 F), –117.90 (d, $J$ = 290.5 Hz, 1 F), –122.11 (dd, $J$ = 290.5, 6.1 Hz, 1 F), –183.22 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 336 ($M^+$, 0.1), 273 (1), 194 (3), 173 (4), 131 (11), 113 (100), 85 (76), 73 (30). Anal. Calcd for $C_{14}H_{22}F_6O_2$: C, 50.00; H, 6.59; F, 33.89. Found: C, 50.27; H, 6.71; F, 33.73.

**4-Fluoro-3-hydroxy-2-methyl-4-(1,1,2,2,2-pentafluoroethyl)-5-undecanone (5j)**: IR (neat) 3420, 1734, 1217, 1202, 1160 $cm^{-1}$; $^1H$ NMR $\delta$ 4.25 (d, $J$ = 28.5 Hz, 1 H) for the threo isomer, 4.15 (d, $J$ = 21.0 Hz, 1 H) for the erythro isomer, 2.8–2.6 (m, 2 H), 2.2–1.7 (m, 2 H), 1.7–1.5 (m, 2 H), 1.4–1.2 (m, 6 H), 1.1–0.8 (m, 9 H); $^{19}F$ NMR $\delta$ –80.50 (d, $J$ = 11.0 Hz, 3 F), –119.08 (dd, $J$ = 289.3, 3.7 Hz, 1 F), –122.70 (dd, $J$ = 289.3, 7.3 Hz, 1 F), –189.82 (m, 1 F) for the threo isomer, –80.22 (d, $J$ = 12.2 Hz, 3 F), –117.89 (d, $J$ = 289.3 Hz, 1 F), –121.55 (dd, $J$ = 289.3, 4.9 Hz, 1 F), –185.98 (m, 1 F) for the erythro isomer; MS $m/z$ (relative intensity) 336 ($M^+$, 0.1), 273 (1), 246 (1), 113 (100), 85 (23), 73 (17). Anal. Calcd for $C_{14}H_{22}F_6O_2$: C, 50.00; H, 6.59; F, 33.89. Found: C, 50.19; H, 6.62; F, 34.10.

**8-Fluoro-9-hydroxy-8-(1,1,2,2,2-pentafluoroethyl)-7-pentadecane (5k)**: IR (neat) 3446, 1735, 1220, 1201, 1172 $cm^{-1}$; $^1H$ NMR $\delta$ 4.4–4.1 (m, 1 H), 2.8–2.6 (m, 2 H), 2.4–1.5 (m, 5 H), 1.4–1.2 (m, 14 H), 1.0–0.8 (m, 6 H); $^{19}F$ NMR $\delta$ –80.68 (d, $J$ = 11.0 Hz, 3 F), –118.36 (d, $J$ = 290.5 Hz, 1 F), –122.29 (dd, $J$ = 290.5, 7.3 Hz, 1 F), –185.15 (m, 1 F) for the erythro isomer, –80.60 (d, $J$ = 12.2 Hz, 3 F), –117.89 (d, $J$ = 289.3 Hz, 1 F), –122.08 (dd, $J$ = 289.3 Hz, 1 F), –183.26 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 378 ($M^+$, 0.1), 274 (0.1), 194 (0.2), 174 (2), 131 (20), 113 (100), 85 (45). Anal. Calcd for $C_{17}H_{28}F_6O_2$: C, 53.96; H, 7.46; F, 30.12. Found: C, 54.17; H, 7.60; F, 30.02.

**(*E*)-5-Fluoro-4-hydroxy-5-(1,1,2,2,2-pentafluoroethyl)-2-dodecen-6-one (5l)**: IR (neat) 3446, 1735, 1675, 1219, 1202, 1176 $cm^{-1}$; $^1H$ NMR $\delta$ 6.0–5.8 (m, 1 H), 5.7–5.5 (m, 1 H), 4.8–4.6 (m, 1 H), 2.8–2.6 (m, 2 H) 2.4–1.8 (m, 1 H), 1.76 (t, $J$ = 6.5 Hz, 3 H), 1.7–1.5 (m, 2 H), 1.4–1.2 (m, 6 H), 1.0–0.8 (m, 3 H); $^{19}F$ NMR $\delta$ –80.68 (d, $J$ = 12.2 Hz, 3 F), –118.73 (dd, $J$ = 288.5, 3.7 Hz, 1 F), –122.39 (d, $J$ = 288.5 Hz, 1 F), –187.18 (m, 1 F) for the erythro isomer, –80.61 (d, $J$ = 12.2 Hz, 3 F), –117.96 (d, $J$ = 290.5 Hz, 1 F), –122.45 (dd, $J$ = 6.7, 290.5 Hz, 1 F), –184.45 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 334 ($M^+$, 0.1), 300 (0.1), 204 (7), 131 (6), 113 (35). Anal. Calcd for $C_{14}H_{20}F_6O_2$: C, 50.30; H, 6.03; F, 34.10. Found: C, 50.38; H, 5.96; F, 34.23.

**2-Fluoro-1-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-1-phenyl-3-nonanone (5m)**: IR (Nujol) 3434, 1734, 1218, 1204, 1105 $cm^{-1}$; $^1H$ NMR $\delta$ 7.5–7.3 (m, 5 H), 5.34 (d, $J$ = 17.0 Hz, 1 H) for the erythro isomer, 5.41 (d, $J$ = 25.7 Hz, 1 H) for the threo isomer, 2.7–1.6 (m, 3 H), 1.5–0.7 (m, 11 H); $^{19}F$ NMR $\delta$ –80.71 (d, $J$ = 12.2 Hz, 3 F), –118.30 (d, $J$ = 288.1 Hz, 1 F), –122.41 (dd, $J$ = 288.1, 8.5 Hz, 1 F), –197.97 (m, 1 F) for the erythro isomer, –80.28 (d, $J$ = 11.0 Hz, 3 F), –117.71 (d, $J$ = 288.1 Hz, 1 F), –121.49 (dd, $J$ = 288.1, 4.9 Hz, 1 F), –183.06 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 370 ($M^+$, 0.1), 308 (1), 307 (1), 256 (19), 236 (20), 187 (9), 106 (100), 77 (62), 72 (33). Anal. Calcd for $C_{17}H_{20}F_6O_2$: C, 55.14; H, 5.44; F, 30.78. Found: C, 55.25; H, 5.48; F, 30.57.

**Typical Procedure for the Aldol Reaction of 1 with Aldehydes Using DIBAL. Method B for 1b, 1d, and 1e.** To a stirred solution of **1b** (0.342 g, 1.0 mmol) in THF (5 mL) was gradually added a hexane solution (1 M) of DIBAL (5.0 mL, 5.0 mmol) at 0 °C. After 5 min at this temperature, butanal (0.216 g, 3.0 mmol) was added to the mixture and stirring was continued for additional 15 min at 0 °C. The reaction mixture was then poured into a mixture of ice and aqueous HCl (6 M, 5 mL), followed by extraction with diethyl ether (30 mL × 3), washing with water, drying ($Na_2SO_4$), filtration, and concentration. The isomer ratio listed in Table II was determined by $^{19}F$ NMR of the crude product. Column chromatography (hexane-AcOEt) on silica gel afforded pure 2-fluoro-3-hydroxy-1-phenyl-2-(trifluoromethyl)-1-hexanone (**5f**) (0.189 g, 68%). Erythro isomer: IR (neat) 3426, 1690, 1275, 1192, 1160 $cm^{-1}$; $^1H$ NMR $\delta$ 8.1–7.7 (m, 2 H), 7.6–7.1 (m, 3 H), 4.7–3.9 (m, 1 H), 2.8–2.4 (d, $J$ = 9.2 Hz, 1 H), 1.9–1.1 (m, 4 H), 1.1–0.7 (m, 3 H); $^{19}F$ NMR $\delta$ –73.18 (d, $J$ = 7.3 Hz, 3 F), –181.81 (dq, $J$ = 19.5, 7.3 Hz, 1 F); MS, $m/z$ (relative intensity) no molecular ion, 235 (1), 105 (100). Threo isomer: IR (Nujol) 3340, 1697, 1262, 1211, 1159 $cm^{-1}$; $^1H$ NMR $\delta$ 8.07–7.73 (m, 2 H), 7.6–7.1 (m, 3 H), 4.8–3.9 (m, 1 H), 2.3–2.0 (d, $J$ = 8.5 Hz, 1 H), 1.8–1.2 (m, 4 H), 1.2–0.7 (m, 3 H); $^{19}F$ NMR $\delta$ –72.54 (d, $J$ = 6.1 Hz, 3 F), –186.01 (dq, $J$ = 23.1, 6.1 Hz, 1 F); MS $m/z$ (relative intensity) 278 ($M^+$, 0.1), 235 (1), 105 (100). Anal. Calcd for $C_{13}H_{14}F_4O_2$: C, 56.12; H, 5.07; F, 27.31. Found: C, 56.34; H, 4.96; F, 27.45.

**2-Fluoro-3-hydroxy-1,3-diphenyl-2-(trifluoromethyl)-1-propanone (5g).** Erythro isomer: IR (neat) 3474, 1689, 1265, 1203, 1142 $cm^{-1}$; $^1H$ NMR $\delta$ 8.0–7.0 (m, 5 H), 5.42 (dd, $J$ = 22.0, 6.0 Hz, 1 H), 3.05 (d, $J$ = 6.0 Hz, 1 H); $^{19}F$ NMR $\delta$ –73.28 (d, $J$ = 7.3 Hz, 3 F), –182.63 (dq, $J$ = 22.0, 7.3 Hz, 1 F); MS $m/z$ (relative intensity) 312 ($M^+$, 0.1), 292 (20), 206 (13), 186 (14), 107 (100), 105 (100), 77 (13). Threo isomer: IR (Nujol) 3520, 1672, 1269, 1209, 1133 $cm^{-1}$; $^1H$ NMR $\delta$ 8.0–7.0 (m, 10 H), 5.53 (dd, $J$ = 24.4, 6.0 Hz, 1 H), 2.80 (d, $J$ = 6.0 Hz, 1 H); $^{19}F$ NMR $\delta$ –72.36 (d, $J$ = 4.9 Hz, 3 F), –188.13 (dq, $J$ = 24.4, 4.9 Hz, 1 F). Anal. Calcd for $C_{16}H_{12}F_4O_2$: C, 61.54; H, 3.87; F, 24.34. Found: C, 61.63; H, 3.90; F, 24.28.

**2-Fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-1-phenyl-1-hexanone (5n)**: IR (neat) 3446, 1686, 1262, 1220, 1195, 1087 $cm^{-1}$; $^1H$ NMR $\delta$ 8.1–7.4 (m, 5 H), 4.39 (dd, $J$ = 15.5, 9.0 Hz,

1 H) for the erythro isomer, 4.51 (dd, $J$ = 22.0, 10.5 Hz, 1 H) for the threo isomer, 2.8–2.0 (m, 1 H), 1.8–1.3 (m, 4 H), 1.0–0.8 (m, 3 H); $^{19}$F NMR $\delta$ −80.13 (d, $J$ = 12.2 Hz, 3 F), −116.67 (dd, $J$ = 288.1, 2.4 Hz, 1 F), −121.27 (dd, $J$ = 288.1, 6.1 Hz, 1 F), −181.65 (m, 1 F) for the erythro isomer, −79.99 (d, $J$ = 12.2 Hz, 3 F), −116.08 (d, $J$ = 286.9 Hz, 1 F), −120.50 (dd, $J$ = 286.9, 4.9 Hz, 1 F), −174.43 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 328 ($M^+$, 0.1), 313 (1), 257 (6), 236 (4), 157 (4), 107 (100). Anal. Calcd for $C_{14}H_{14}F_6O_2$: C, 51.23; H, 4.30; F, 34.73. Found: C, 51.52; H, 4.47; F, 34.61.

**2-Fluoro-3-hydroxy-4-methyl-2-(1,1,2,2,2-pentafluoroethyl)-1-phenyl-1-pentanone (5o)**: IR (neat) 3466, 1685, 1259, 1221, 1199, 1085 cm$^{-1}$; $^1$H NMR $\delta$ 3.1–7.4 (m, 5 H), 4.50 (dd, $J$ = 27.5, 2.2 Hz, 1 H) for the threo isomer, 4.21 (dd, $J$ = 18.2, 4.3 Hz, 1 H) for the erythro isomer, 2.58 (br s, 1 H), 2.2–2.0 (m, 1 H) for the erythro isomer, 2.0–1.8 (m, 1 H) for the threo isomer, 1.1–0.9 (m, 3 H); $^{19}$F NMR $\delta$ −79.93 (d, $J$ = 12.2 Hz, 3 F), −116.99 (d, $J$ = 290.5 Hz, 1 F), −121.44 (dd, $J$ = 290.5, 7.3 Hz, 1 F), −177.63 (m, 1 F) for the erythro isomer, −79.69 (d, $J$ = 11.0 Hz, 3 F), −115.91 (d, $J$ = 286.9 Hz, 1 F), −120.12 (dd, $J$ = 286.9, 3.7 Hz, 1 F), −186.46 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 328 ($M^+$, tr), 285 (1), 265 (1), 236 (10), 105 (100), 72 (15). Anal. Calcd for $C_{14}H_{14}F_6O_2$: C, 51.23; H, 4.30; F, 34.73. Found: C, 51.41; H, 4.36; F, 34.70.

**(*E*)-2-Fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-1-phenyl-4-hexen-1-one (5p)**: IR (neat) 3382, 1686, 1599, 1264, 1221, 1200, 1091 cm$^{-1}$; $^1$H NMR $\delta$ 8.0–7.7 (m, 2 H), 7.6–7.2 (m, 3 H), 6.2–5.4 (m, 2 H), 5.4–4.5 (m, 1 H), 2.8–2.1 (m, 1 H), 1.8–1.5 (m, 3 H); $^{19}$F NMR $\delta$ −80.14 (d, $J$ = 11.0 Hz, 3 F), −117.06 (d, $J$ = 288.1 Hz, 1 F), −121.27 (dd, $J$ = 288.1, 7.3 Hz, 1 F), −181.11 (m, 1 F) for the erythro isomer, −80.07 (d, $J$ = 12.2 Hz, 3 F), −116.10 (d, $J$ = 288.1 Hz, 1 F), −121.01 (dd, $J$ = 288.1, 4.9 Hz, 1 F), −180.74 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 326 ($M^+$, tr), 306 (3), 291 (20), 255 (4), 236 (20), 105 (100), 71 (82). Anal. Calcd for $C_{14}H_{12}F_6O_2$: C, 51.54; H, 3.71; F, 34.94. Found: C, 51.75; H, 3.63; F, 35.16.

**2-Fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-1,3-diphenyl-1-propanone (5q)**: IR (neat) 3446, 1692, 1261, 1220, 1202, 1099 cm$^{-1}$; $^1$H NMR $\delta$ 7.8–7.2 (m, 10 H), 5.55 (dd, $J$ = 6.0, 25.0 Hz, 1 H) for the threo isomer, 5.43 (dd, $J$ = 7.0, 18.5 Hz, 1 H) for the erythro isomer, 3.32 (d, $J$ = 7.0 Hz, 1 H) for the erythro isomer, 2.73 (d, $J$ = 6.0 Hz, 1 H) for the threo isomer; $^{19}$F NMR $\delta$ −80.15 (d, $J$ = 12.2 Hz, 3 F), −116.77 (d, $J$ = 285.6 Hz, 1 F), −121.33 (dd, $J$ = 285.6, 8.6 Hz, 1 F), −178.66 (m, 1 F) for the erythro isomer, −79.78 (d, $J$ = 11.0 Hz, 3 F), −115.84 (d, $J$ = 285.6 Hz, 1 F), −120.13 (d, $J$ = 285.6 Hz, 1 F), −186.64 (m, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 362 ($M^+$, tr), 343 (6), 342 (3), 256 (20), 236 (10), 187 (5), 108 (100), 105 (100). Anal. Calcd for $C_{17}H_{12}F_6O_2$: C, 56.36; H, 3.34; F, 31.47. Found: C, 56.59; H, 3.46; F, 31.66.

**1-Cyclohexyl-2-fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-1-hexanone (5r)**: IR (neat) 3454, 1725, 1220, 1200, 1072 cm$^{-1}$; $^1$H NMR $\delta$ 4.6–3.7 (m, 1 H), 3.2–2.6 (m, 1 H), 2.6–0.7 (m, 18 H); $^{19}$F NMR $\delta$ −80.60 (d, $J$ = 12.2 Hz, 3 F), −117.27 (dd, $J$ = 290.5, 2.4 Hz, 1 F), −121.18 (dd, $J$ = 290.5, 6.1 Hz, 1 F), −186.04 (m, 1 F) for the threo isomer, −80.41 (d, $J$ = 13.4 Hz, 3 F), −116.24 (dd, $J$ = 291.8, 2.4 Hz, 1 F), −120.45 (dd, $J$ = 291.8, 3.7 Hz, 1 F), −184.96 (m, 1 F) for the erythro isomer; MS $m/z$ (relative intensity) 334 ($M^+$, 0.1), 262 (3), 111 (49), 83 (100), 73 (10). Anal. Calcd for $C_{14}H_{20}F_6O_2$: C, 50.30; H, 6.03; F, 34.10. Found: C, 50.44; H, 6.08; F, 33.96.

**(*E*)-1-Cyclohexyl-2-fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-4-hexen-1-one (5s)**: IR (neat) 3412, 1726, 1672, 1219, 1201, 1091 cm$^{-1}$; $^1$H NMR $\delta$ 6.3–5.1 (m, 2 H), 5.0–4.3 (m, 1 H), 3.2–2.6 (m, 1 H), 2.6–0.9 (m, 14 H); $^{19}$F NMR $\delta$ −80.57 (d, $J$ = 11.0 Hz, 3 F), −117.47 (dd, $J$ = 290.5, 3.7 Hz, 1 F), −121.29 (dd, $J$ = 290.5, 6.1 Hz, 1 F), −187.39 (m, 1 F) for the threo isomer, −80.41 (d, $J$ = 12.2 Hz, 3 F), −116.42 (d, $J$ = 293.0 Hz, 1 F), −120.74 (dd, $J$ = 293.0, 4.9 Hz, 1 F), −186.69 (m, 1 F) for the erythro isomer; MS $m/z$ (relative intensity) 332 ($M^+$, 0.1), 262 (1), 204 (4), 111 (33), 84 (100), 71 (48). Anal. Calcd for $C_{14}H_{18}F_6O_2$: C, 50.61; H, 5.46; F, 34.30. Found: C, 50.42; H, 5.15; F, 34.11.

**1-Cyclohexyl-2-fluoro-3-hydroxy-2-(1,1,2,2,2-pentafluoroethyl)-3-phenyl-1-propanone (5t)**: IR (Nujol) 3470, 1721, 1228, 1205, 1091 cm$^{-1}$; $^1$H NMR $\delta$ 7.4–7.3 (m, 5 H), 5.31 (d, $J$ = 17.0 Hz, 1 H) for the erythro isomer, 5.39 (d, $J$ = 25.5 Hz, 1 H) for the threo isomer, 3.9–2.9 (m, 1 H), 2.7–2.6 (m, 1 H) for the erythro isomer, 2.4–2.2 (m, 1 H) for the threo isomer, 1.9–0.5 (m, 10 H); $^{19}$F NMR $\delta$ −80.65 (d, $J$ = 12.2 Hz, 3 F), −117.12 (dd, $J$ = 290.5, 3.7 Hz, 1 F), −121.18 (dd, $J$ = 290.5, 7.3 Hz, 1 F), −183.82 (m, 1 F) for the erythro isomer, −80.07 (d, $J$ = 12.2 Hz, 3 F), −115.65 (d, $J$ = 290.5 Hz, 1 F), −119.65 (d, $J$ = 290.5 Hz, 1 F), −193.76 (dq, $J$ = 25.5, 12.2 Hz, 1 F) for the threo isomer; MS $m/z$ (relative intensity) 368 ($M^+$, 0.1), 348 (0.1), 262 (1), 240 (5), 111 (39), 107 (70), 83 (100). Anal. Calcd for $C_{17}H_{18}F_6O_2$: C, 55.44; H, 4.93; F, 30.95. Found: C, 55.67; H, 5.06; F, 31.02.

**Generation and Detection of Diisobutylaluminum Enolates (6).** To a solution of 1 (1.0 mmol) in THF (5 mL) was added dropwise a hexane solution (1 M) of DIBAL (5.0 mL, 5.0 mmol) at 0 °C. After the mixture was stirred for 30 min at room temperature for **1a** and **1c** or for 5 min at 0 °C for **1b** and **1d**, an aliquot of the mixture was immediately subjected to $^{19}$F NMR, whose data and spectra are shown in Table II and in Figure 1, respectively.

**Typical Procedure for High-Temperature Reaction of 1 with DIBAL Giving Allylic Alcohols (7).** A hexane solution (1 M) of DIBAL (5.0 mL, 5.0 mmol) was added dropwise to a solution of **1c** (0.400 g, 1.0 mmol) in THF (5 mL) at 0 °C. This mixture was heated to gentle reflux. After 3 h, the reaction was quenched with a mixture of ice and aqueous HCl (6 M, 5 mL), and the resulting mixture was extracted with diethyl ether (30 mL × 3). The extracts were dried ($Na_2SO_4$), filtered, and concentrated in vacuo to give a residual oil, which was column chromatographed (hexane–AcOEt) on silica gel to provide (*E*)-1,1,1,2,3-pentafluoro-2-decen-4-ol (**7c**) (0.180 g, 73%): IR (neat) 3348, 1724, 1378, 1216, 1150 cm$^{-1}$; $^1$H NMR $\delta$ 4.52 (ddt, $J$ = 24.6, 4.9, 6.2 Hz, 1 H), 2.59 (br s, 1 H), 2.0–1.1 (m, 8 H), 0.87 (t, $J$ = 5.4 Hz, 3 H); $^{19}$F NMR $\delta$ −68.65 (dd, $J$ = 21.7, 10.8 Hz, 3 F), −157.65 (ddq, $J$ = 133.9, 24.6, 21.7 Hz, 1 F), −173.15 (ddq, $J$ = 133.9, 4.9, 10.8 Hz, 1 F); MS $m/z$ (relative intensity) 229 ($M^+$ − OH, tr), 161 (11), 143 (7), 85 (100).

**(*E*)-2,3,4,4,4-Pentafluoro-1-phenyl-2-buten-1-ol (7d)**: 73%; IR (neat) 3380, 1736, 1244, 1208, 1156 cm$^{-1}$; $^1$H NMR $\delta$ 7.30 (s, 5 H), 5.65 (dd, $J$ = 23.6, 4.9 Hz, 1 H), 2.99 (br s, 1 H); $^{19}$F NMR $\delta$ −68.60 (dd, $J$ = 21.7, 10.8 Hz, 3 F), −155.53 (ddq, $J$ = 133.9, 23.6, 21.7 Hz, 1 F), −172.25 (ddq, $J$ = 133.9, 4.9, 10.8 Hz, 1 F); MS $m/z$ (relative intensity) 238 ($M^+$, 100), 220 (40), 217 (68), 169 (9).

**(*E*)-1-Cyclohexyl-2,3,4,4,4-pentafluoro-2-buten-1-ol (7e)**: 72%; IR (neat) 3326, 1730, 1242, 1207, 1154 cm$^{-1}$; $^1$H NMR $\delta$ 4.22 (br d, $J$ = 24.4 Hz, 1 H), 2.3–0.6 (m, 12 H); $^{19}$F NMR $\delta$ −68.41 (dd, $J$ = 22.0, 11.0 Hz, 3 F), −155.78 (ddq, $J$ = 133.1, 24.4, 22.0 Hz, 1 F), −172.81 (ddq, $J$ = 133.1, 3.7, 11.0 Hz, 1 F); MS $m/z$ (relative intensity) no molecular ion, 83 (100).

**Reduction of 5f and 5g to 1,3-Diols 8f and 8g.** To a solution of the erythro isomer of **5f** (0.278 g, 1.0 mmol), which had been separated by chromatography, in THF (5 mL) was added dropwise a hexane solution (1 M) of DIBAL (3.0 mL, 3.0 mmol) at −78 °C. After being stirred for 3 h at −78 °C, the reaction mixture was hydrolyzed with aqueous HCl (6 M, 5 mL) containing ice. The resultant mixture was extracted with diethyl ether (20 mL × 3), and the extracts were washed with water, dried ($Na_2SO_4$), filtered, and concentrated under vacuum. The crude product was chromatographed on a column of silica gel to furnish the 1,2-threo-2,3-erythro isomer of 2-fluoro-1-phenyl-2-(trifluoromethyl)-1,3-hexanediol (**8f**) (0.258 g, 92%) with 99% isomeric purity: IR (Nujol) 3328, 2930, 1252, 1188, 1148, 1102, 1058 cm$^{-1}$; $^1$H NMR $\delta$ 7.30 (s, 5 H), 5.4–4.9 (m, 1 H), 4.4–3.6 (m, 2 H), 3.4–3.0 (m, 1 H), 1.9–0.7 (m, 7 H); $^{19}$F NMR $\delta$ −71.68 (d, $J$ = 7.3 Hz, 3 F), −180.12 (ddq, $J$ = 12.2, 12.2, 7.3 Hz, 1 F); MS $m/z$ (relative intensity) 280 ($M^+$, 2), 262 (1), 219 (1), 190 (10), 108 (100), 105 (10), 79 (9). The 1,2-threo-2,3-threo isomer of **8f** was obtained in the same manner: 85% yield (99% isomerically pure); IR (Nujol) 3438, 2922, 1261, 1198, 1183, 1047 cm$^{-1}$; $^1$H NMR $\delta$ 7.5–7.1 (m, 5 H), 5.4–4.9 (m, 1 H), 4.2–3.6 (m, 1 H), 2.7–2.3 (m, 1 H), 2.0–0.7 (m, 8 H); $^{19}$F NMR $\delta$ −69.59 (d, $J$ = 6.9 Hz, 3 F), −178.80 (ddq, $J$ = 6.9, 13.8, 6.9 Hz, 1 F). Anal. Calcd for $C_{13}H_{16}F_4O_2$: C, 55.71; H, 5.75; F, 27.12. Found: C, 55.82; H, 5.76; F, 27.01.

**2-Fluoro-1,3-diphenyl-2-(trifluoromethyl)-1,3-propanediol (8g).** 1,2-Threo-2,3-erythro isomer: 80% yield (99% isomerically pure); IR (Nujol) 3202, 2920, 1235, 1190, 1115, 1051 cm$^{-1}$; $^1$H NMR $\delta$ 7.5–7.0 (m, 10 H), 5.4–4.7 (m, 2 H), 4.4–3.9 (m, 2 H); $^{19}$F NMR $\delta$ −71.47 (d, $J$ = 8.6 Hz, 3 F), −176.43 (ddq, $J$ = 14.7, 7.3, 8.6 Hz,

1 F); MS $m/z$ (relative intensity) 314 ($M^+$, 0.1), 276 (1), 190 (16), 107 (100), 105 (29), 79 (49). 1,2-Threo-2,3-threo isomer: 87% yield (99% isomerically pure); IR (Nujol) 3480, 2924, 1229, 1179, 1122, 1047 $cm^{-1}$; $^1H$ NMR $\delta$ 7.5–7.1 (m, 10 H), 4.97 (d, $J$ = 13.4 Hz, 2 H), 2.9–2.6 (m, 2 H); $^{19}F$ NMR $\delta$ –68.85 (d, $J$ = 7.3 Hz, 3 F), –182.95 (ddq, $J$ = 13.4, 13.4, 7.3 Hz, 1 F). Anal. Calcd for $C_{16}H_{14}F_4O_2$: C, 61.15; H, 4.49; F, 24.18. Found: C, 61.23; H, 4.60; F, 24.09.

**Conversion of 8f and 8g into Acetonides 9f and 9g.** A mixture of 1,2-threo-2,3-erythro isomer of **8f** (0.280 g, 1.0 mmol), 2,2-dimethoxypropane (1.04 g, 10.0 mmol), and *p*-toluenesulfonic acid monohydrate (0.021 g, 0.11 mmol) in THF (5 mL) was refluxed for 24 h with stirring. After cooling to room temperature, the reaction mixture was poured into a saturated $NaHCO_3$ solution (10 mL), followed by extraction with diethyl ether (20 mL × 3), drying ($Na_2SO_4$), filtration, and concentration. The residue was purified by silica gel column chromatography (hexane–AcOEt) to give the 4,5-threo-5,6-erythro isomer of 5-fluoro-2,2-dimethyl-4-phenyl-6-propyl-5-(trifluoromethyl)-1,3-dioxane (**9f**) (0.316 g): IR (neat) 3066, 2960, 1263, 1200, 1182, 1115, 1083 $cm^{-1}$; $^1H$ NMR $\delta$ 7.6–7.4 (m, 5 H), 5.03 (dq, $J$ = 15.8, 1.5 Hz, 1 H), 4.09 (ddd, $J$ = 24.6, 8.8, 2.9 Hz, 1 H), 1.9–1.4 (m, 10 H), 1.1–1.0 (m, 3 H); $^{19}F$ NMR $\delta$ –75.55 (d, $J$ = 7.9 Hz, 3 F), –181.41 (ddq, $J$ = 24.6, 15.8, 7.9 Hz, 1 F); MS $m/z$ (relative intensity) 320 ($M^+$, 0.1), 305 (1), 263 (12), 262 (3), 108 (46), 106 (13), 60 (100). The 4,5-threo-5,6-threo isomer of **9f** was prepared similarly: IR (neat) 3066, 2960, 1263, 1193, 1151, 1089 $cm^{-1}$; $^1H$ NMR $\delta$ 7.6–7.3 (m, 5 H), 5.09 (dq, $J$ = 8.0, 1.8 Hz, 1 H), 4.11 (dddq, $J$ = 10.0, 5.6, 2.3, 2.2 Hz, 1 H), 2.0–1.2 (m, 10 H), 1.1–0.9 (m, 3 H); $^{19}F$ NMR $\delta$ –67.67 (d, $J$ = 8.9 Hz, 3 F), –182.24 (ddq, $J$ = 10.0, 8.0, 8.9 Hz, 1 F).

**5-Fluoro-2,2-dimethyl-4,6-diphenyl-5-(trifluoromethyl)-1,3-dioxane (9g).** 4,5-Threo-5,6-erythro isomer: IR (Nujol) 2920, 2852, 1266, 1198, 1171, 1087 $cm^{-1}$; $^1H$ NMR $\delta$ 7.6–7.5 (m, 4 H), 7.5–7.3 (m, 6 H), 5.30 (dq, $J$ = 15.7, 1.8 Hz, 1 H), 5.26 (d, $J$ = 23.6 Hz, 1 H), 1.60 (s, 3 H), 1.55 (s, 3 H); $^{19}F$ NMR $\delta$ –74.41 (d, $J$ = 7.9 Hz, 3 F), –172.98 (ddq, $J$ = 23.6, 15.7, 7.9 Hz, 1 F); MS $m/z$ (relative intensity) 354 ($M^+$, 0.1), 339 (0.1), 297 (2), 249 (2), 191 (100). 4,5-Threo-5,6-threo isomer: IR (Nujol) 2920, 2852, 1253, 1186, 1177, 1074 $cm^{-1}$; $^1H$ NMR $\delta$ 7.6–7.5 (m, 4 H), 7.5–7.3 (m, 6 H), 5.35 (dq, $J$ = 7.9, 1.8 Hz, 2 H), 1.50 (s, 3 H), 1.46 (s, 3 H); $^{19}F$ NMR $\delta$ –66.96 (d, $J$ = 7.9 Hz, 3 F), –179.10 (ddq, $J$ = 7.9, 7.9, 7.9 Hz, 1 F).

# Palladium-Catalyzed Coupling Reactions of (α-Ethoxyvinyl)trimethylstannane with Vinyl and Aryl Triflates†,‡

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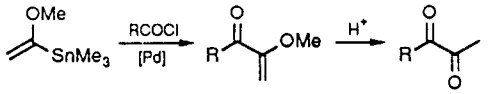
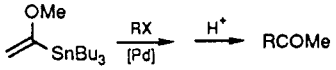
The palladium-catalyzed cross-coupling reaction of vinyl triflates and halides with (α-ethoxyvinyl)trimethylstannane gives high yields of 2-ethoxy 1,3-dienes, which can be hydrolyzed to the corresponding α,β-unsaturated ketones. Aryl triflates undergo an analogous coupling reaction, providing a facile method for replacing the hydroxyl group of a phenol by an acyl group. The use of (α-ethoxyvinyl)trimethylstannane in palladium-catalyzed carbonylative coupling gives rise to vinyl and aryl α-ethoxyvinyl ketones and indirectly to the corresponding α-diketones (which result from their hydrolysis) and glyoxylates (which result from their ozonolysis).

The palladium-catalyzed reaction of organostannanes with organic electrophiles can provide high yields of coupled products under mild reaction conditions.[1] A variety of functional groups can be brought into the coupling reaction as substituents on either or both of the coupling partners. When an (α-alkoxyvinyl)tin reagent is used in the coupling reaction, the product is an α-substituted vinyl ether; its hydrolysis yields the corresponding ketone. Thus the tin reagent serves as an acyl anion equivalent.[2] Such coupling reactions have been carried out primarily with acid chlorides[3a] (which yield α-diketones) and with arylbromides[3b] (eqs 1 and 2).




(1)




(2)

Vinyl and aryl triflates[4] can serve as electrophilic partners with a variety of tin reagents in palladium-catalyzed reactions, provided that an excess (≥3 equiv/equiv of substrate) of chloride, bromide, or iodide ion (usually introduced as the lithium salt) is present.[1] Apparently coordination of the halide ion permits the organopalladium species to undergo the transmetalation reaction with the organotin reagent. In this paper the direct[5] and carbonylative[6] coupling of (α-ethoxyvinyl)trimethylstannane with vinyl and aryl triflates is reported.

**Direct Coupling.** The palladium-catalyzed direct coupling reaction of (α-ethoxyvinyl)trimethylstannane with vinyl triflates gives high yields of 2-ethoxy 1,3-dienes. The latter can be hydrolyzed to the corresponding α,β-unsaturated ketones (Table I). For comparison, the tin reagent couples with vinyl bromide (entry 5) to produce 2-eth-

† This paper is dedicated to the memory of our friend and mentor, the late Professor J. K. Stille.

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