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B-(3,3-Difluoroallyl)diisopinocampheylborane for the Enantioselective Fluoroallylboration of Aldehydes

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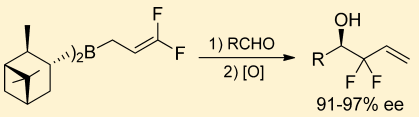
Supporting Information

ABSTRACT: The fluoroallylboration of aldehydes with *B*-(3,3-difluoroallyl)-diisopinocampheylborane, which was prepared via the hydroboration of 1,1-difluoroallene, provides chiral 2,2-*gem*-difluorinated homoallylic alcohols in good yields and 91−97% ee.



Fluorine substitution often alters the reactivity and reaction mechanism of organic molecules.[1] Medicinal chemists undertake this exercise to alter the biological properties of such molecules, with the aim of identifying more potent and bioavailable molecules.[2] Geminal difluorinated aliphatic fluoro-organic molecules are particularly attractive due to their unique pharmacological properties.[3] As part of our program involving fluoro-organic synthesis via boranes,[4] we had reported the preparation and reactions of racemic and chiral 2-benzyloxy-(3,3-difluoroallyl)boronates **1** and **2**, respectively (Figure 1), for the synthesis of 2,2-*gem*-difluorinated homoallyl alcohols and derivatives.[5]

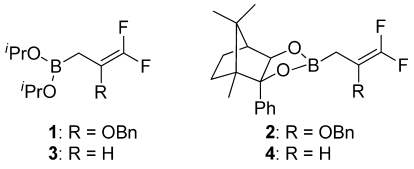
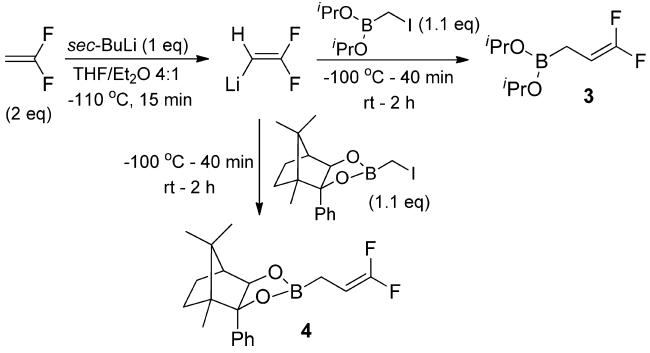


Figure 1. (3,3-Difluoroallyl)boronates.

We had also reported a low yield (≤20%) synthesis of the parent camphanediol (3,3-difluoroallyl)boronate **4**[5b] from 2,2-difluorovinyllithium[6] and the corresponding camphanediol iodomethylboronate.[7] The importance of the products 2,2-difluoro-1-aryl/alkylbut-3-en-1-ols as useful building blocks for the synthesis of bioactive molecules,[8] led us to re-examine the synthesis of racemic and chiral (3,3-difluoroallyl)boronate reagents **3** and **4**. While racemic 2,2-difluoro-1-aryl/alkylbut-3-en-1-ols have been reported via the addition of *gem*-difluoroallylmetals (Si,[9] In,[10] Li,[11] Sn,[12] Zn[13]) to aldehydes and ketones, to the best of our knowledge, chiral 2,2-*gem*-difluorohomoallyl alcohols are accessed via a lipase-mediated enzymatic resolution of racemic alcohols.[14] Reported herein are the improved synthesis of asymmetric (3,3-difluoroallyl)-boronate, the failed asymmetric allylboration with **4**, and finally, the successful preparation and reactions of difluoroallylborane-derived from α-pinene.

Diisopropyl (3,3-difluoroallyl)boronate (**3**) prepared via the homologation[15] of 2,2-difluorovinyllithium[6] with diisopropyl iodomethylboronate[16] (Scheme 1) was found to be unstable for storage. Hence, the difluoroallylboration of benzaldehyde (**5a**)

Scheme 1. Preparation of (3,3-Difluoroallyl)boronates 3 and 4



was examined with in situ generated reagents, and the optimal conditions were identified (Table 1).

The allylboration of benzaldehyde (**5a**) with **3** in THF at room temperature, monitored by ^{11}B NMR spectroscopy (chemical shift change from δ 30 to 18 ppm), furnished 2,2-difluoro-1-phenylbut-3-en-1-ol (**6a**) in only 15% yield. On the basis of Lewis acid catalyzed allylboration with allylboronates,[17] the reaction was examined in the presence of 10 mol % $Sc(OTf)_3$, which improved the yield to 43%. Raising the temperature to reflux further improved the yield to 67%. Increasing the catalyst loading to 20 mol % and the reaction time to 48 h did not improve the yield. Changing the catalyst to $In(OTf)_3$ (10 mol %) yielded 38% of the homoallylic alcohol. The influence of the solvent was then examined. Unlike the benzyloxy reagent **1**, the parent reagent **3** was only sparingly soluble in pentane. The reaction failed in refluxing dichloromethane (48 h); refluxing in toluene decomposed the reagent.

With the standardized reaction conditions, the fluoroallylboration of additional aldehydes was carried out (Table 2).

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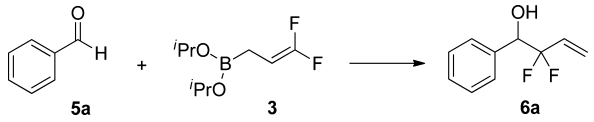
Table 1. Difluoroallylboration of Benzaldehyde (5a) with 3; Optimization of Conditions[a]



5a 3 6a

entry	L.A.[b]	solvent	temp (°C)	time (h)	yield[c] (%)
1		THF	rt	24	15
2	$Sc(OTf)_3$	THF	rt	24	43
3	$Sc(OTf)_3$	THF	reflux	24	67
4	$In(OTf)_3$	THF	reflux	24	38
5	$Sc(OTf)_3$	CH_2Cl_2	reflux	48	*d*
6	$Sc(OTf)_3$	toluene	reflux	24	*e*
7	$Sc(OTf)_3$	pentane	*f*		

[a]Reactions were carried out with 1.5 equiv of crude reagent. [b]10 mol % of the Lewis acid was used, unless otherwise stated. [c]Isolated yields of pure products. [d]No reaction observed. [e]Decomposition of reagent **3**. [f]No reaction due to the poor solubility of the reagent.

Table 2. Difluoroallylboration of Aldehydes 5 with 3[a]

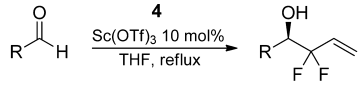
entry	RCHO (**5**)	R	**6**	time (h)	yield[b] (%)
1	**5a**	C_6H_5	**6a**	24	67
2	**5b**	*p*-MeO-C_6H_4	**6b**	48	33
3	**5c**	2-Naphthyl	**6c**	38	25
4	**5d**	$C_6H_5(CH_2)_2$	**6d**	48	62

[a]Reactions were carried out in THF at reflux with 1.5 equiv of crude reagent and 10 mol % of $Sc(OTf)_3$. [b]Isolated yields of pure products.

Surprisingly, low yields, 33% and 25%, respectively, were obtained for the allylboration of *p*-anisaldehyde (**5b**) and 2-naphthaldehyde (**5c**). Hydrocinnamaldehyde (**5d**) afforded the product in 62% isolated yield. The factors influencing the low yield are not clear at this point, although similar homoallylic alcohols have been found to undergo the elimination of fluoride under basic conditions.[18] It is noteworthy that diisopropyl (3,3-difluoroallyl)boronate (**3**) is less reactive than the 2-benzyloxy-substituted reagent **1**. This could be due to increased electron density of the vinylic ether, a fact which should favor the allyl transfer.

We were able to significantly improve upon our previous results,[5b] enhancing the yield of (1*R*,3*S*)-1,2,2-trimethylcyclopent-1,3-diyl (4*R*)-2-(3,3-difluoroprop-2-enyl)-4-phenyl-1,3,2-dioxaborolane (**4**) from ≤20% to 80%, simply by decreasing the reaction temperature. Unlike the achiral reagent, **4** is stable to silica gel chromatography and the yield represents isolated yield of the pure reagent and further reactions were carried out using pure reagent. The fluoroallylboration of aldehydes with **4** was also facilitated by the presence of a Lewis acid, higher reaction temperature, and longer reaction times (Scheme 2). Allylborations were carried out with 1.25 equiv of reagent **4** in the presence of 10 mol % of $Sc(OTf)_3$ at reflux in THF and

Scheme 2. Asymmetric Difluoroallylboration of Aldehydes 5 with 4



5a R = C_6H_5 60 h (*R*)-**6a** 38%, 20% ee
5b R = *p*-MeO-C_6H_4 110 h (*R*)-**6b** 25%, 20% ee

were monitored by the ^{11}B NMR spectroscopy (chemical shift change from δ 33 to 22 ppm).

As in the case of the racemic fluoroallylboration (Table 1), no reaction took place in dichloromethane and decomposition was observed in toluene. Allylboration of benzaldehyde (**5a**) afforded the chiral homoallyl alcohol (*R*)-**6a** in 38% yield and surprisingly low 20% ee, as was determined by ^1H and ^{19}F NMR analysis of the corresponding α-methoxy α,α,α-trifluoromethylphenyl acetates (Mosher esters).[19] The configuration of the alcohol was assigned on the basis of the sign of the optical rotation of the alcohol, as reported in the literature.[14]

The use of $In(OTf)_3$ (20 mol %) decreased the ee to 12%, but with similarly poor yield (37%). Low enantioselectivity (20%) was also observed for *p*-anisaldehyde (**5b**), where the reaction required 4.5 days (^{11}B NMR).

The disappointing results from chiral (3,3-difluoroallyl)-boronates and the established success of pinane-mediated allyl-, crotyl-, and alkoxyallylborations[20] prompted the preparation of *B*-(3,3-difluoroallyl)diisopinocampheylborane and fluoroallylboration of aldehydes. Hydroboration of substituted allenes have been utilized for the preparation of novel achiral and chiral allylboranes.[21] Accordingly, we examined the hydroboration of 1,1-difluoroallene with racemic and chiral diisopinocampheylborane (Ipc_2BH) (Scheme 3).

The successful, reagent-dependent, and regioselective hydroboration of a variety of fluoroolefins have been described by us earlier.[22] Hydroboration of fluoroalkynes have also been reported in the literature.[23] However, there has been no report on the hydroboration of fluoroallenes. Accordingly, freshly prepared 1,1-difluoroallene,[24] was added to a suspension of (−)-Ipc_2BH in diethyl ether at −78 °C and was warmed to 0 °C over 3 h, whereafter the reaction medium became homogeneous. The ^{11}B NMR spectrum revealed two peaks at δ 79 and 49 ppm in a 7:3 ratio, presumably corresponding to the difluoroallylborane **7** and (2,2-difluoro-1-methylvinyl)-borane (on the basis of ^{11}B NMR of vinylboranes) (Scheme 3).

Benzaldehyde (**5a**) was added to the above mixture at −78 °C, and the reaction, which was monitored by ^{11}B NMR spectroscopy, was complete within 4 h. The NMR spectrum revealed a broad peak at δ 50 ppm, along with a shoulder peak, presumably due to the unreacted vinylborane. Alkaline oxidative workup with hydrogen peroxide over 12 h at rt, provided the expected 2,2-difluoro-1-phenylbut-3-en-1-ol (**6a**) in 43% yield, based on the allylborane present in the medium. Since allylboration has been shown to be a fast reaction even at low temperatures,[25] the yield of **6a** is most likely limited by the formation of the allylborane from hydroboration. ^1H and ^{19}F NMR analysis of the Mosher ester derivative of **6a** revealed an enantiomeric excess of 94%, and a configurational assignment of *R*.[14] It is observed that the stereochemistry of the product of the reaction with difluoroallylborane **7** is the same as that of the nonfluorinated analogue.[25]

Solvents such as THF, pentane, and CH_2Cl_2 decreased the yield of the reaction. Although there was no change in the enantioselectivity, lowering the allylboration temperature to −100 °C improved the yield to 72%. The use of catalytic $Sc(OTf)_3$ did not improve the yield or enantioselectivity. Accordingly, further difluoroallylboration of a series of aldehydes with **7** was carried out at this temperature (Table 3). *p*-Anisaldehyde (**5b**) provided (*R*)-**6b** in 71% yield and 93% ee. Similarly, high ee (94%) was obtained for 2-naphthaldehyde (**5c**) as well. While α,β-unsaturated aldehyde, cinnamaldehyde

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Scheme 3. Preparation and Reaction of *B*-(3,3-Difluoroallyl)diisopinocampheylborane (7)

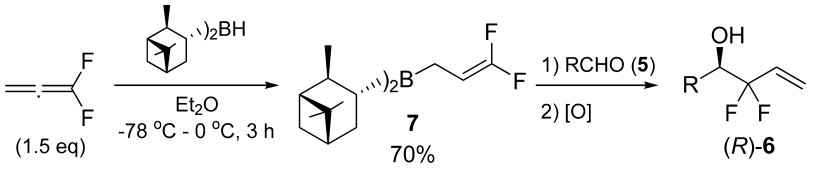

Table 3. Asymmetric Difluoroallylboration of Aldehydes 5 with 7[a] in Et_2O

entry	5	R	temp (°C)	(*R*)-6[b]	yield[c] (%)	ee[d] (%)
1	**5a**	C_6H_5	−78	**6a**	43	94
2	**5a**	C_6H_5	−100	**6a**	72	94
3	**5b**	*p*-MeO-C_6H_4	−100	**6b**	71	93
3	**5c**	2-Naphthyl	−100	**6c**	70	94
5	**5d**	$C_6H_5(CH_2)_2$	−100	**6d**	76	97
6	**5e**	*E*-C_6H_5CH=CH	−100	**6e**	70	91
7	**5f**	2-Furyl	−100	**6f**	69	92

[a]Reactions were carried out with 1 equiv of crude reagent over 4 h. [b]Determined by comparison of the optical rotation with those of known compounds.[14] [c]Yields of pure products based on the number of equivalents of reagent in the mixture. [d]Determined by ^1H and ^{19}F NMR analysis of Mosher esters.

(**5e**) afforded the product in 91% ee, hydrocinnamaldehyde (**5d**) afforded the highest ee, 97%, for the homoallylic alcohol in 76% yield. A heteroaromatic aldehyde, 2-furaldehyde (**5f**), provided the product in 69% yield and 92% ee. It is gratifying to note that pinane-derived reagent **7** provides very high ee for the allylboration, even with the presence of the fluorine atoms. In comparison, the camphor-derived allylboronate reagent **4** provides poor ee.

In conclusion, higher yields were achieved for the synthesis of racemic and chiral (3,3-difluoroallyl)boronates, although the allylboration results in poor yields and ee of the homoallyl alcohols. The hydroboration of 1,1-difluoroallene with diisopinocampheylborane provides a 7:3 mixture of the corresponding (3,3-difluoroallyl)- and (2,2-difluoro-1-methylvinyl) borane. Difluoroallylboration of representative aldehydes with *B*-(3,3-difluoroallyl)diisopinocampheylborane provides 2,2-*gem*-difluorinated homoallyl alcohols in good yields and high ee.

EXPERIMENTAL SECTION

General Information. Unless otherwise noted, all manipulations were carried out under inert atmosphere in flame-dried glassware. Tetrahydrofuran (THF) was freshly distilled before use from sodium benzophenone ketyl. All other chemicals and solvents were purchased commercially and used without further purification, unless otherwise noted.

The ^1H, ^{19}F, ^{13}C, and ^{11}B nuclear magnetic resonance (NMR) spectra were plotted on 300 MHz spectrometer with Nalorac-quad probes using $CDCl_3$ as a solvent at room temperature. The NMR chemical shifts (δ) are reported in ppm. Abbreviations for ^1H and ^{19}F NMR: s = singlet, d = doublet, m = multiplet, b = broad, t = triplet, q = quartet. High-resolution mass spectra were obtained by electro spray impact ionization in combination with a single quadrupole mass analyzer. The reactions were monitored by TLC using silica gel F_{254} precoated plates. Flash chromatography was performed using flash grade silica gel (particle size: 40−63 μm, 230 × 400 mesh). Optical rotations were measured on an automatic polarimeter at the Na D line (λ = 589 nm) using a 1 dm cell.

Preparation of diisopropyl iodomethylboronate,[16] (1*R*,2*R*,3*R*,4*S*)-4-iodomethyl-1,10,10-trimethyl-2-phenyl-3,5-dioxa-4-boratricyclo-[5.2.1.$0^{0,0}$]decane,[7] 1,1-difluoropropa-1,2-diene,[24] (-)-diisopinocampheylborane[26] were achieved as reported.

*1. General Procedure for the One-Pot Synthesis of Diisopropyl (3,3-Difluoroallyl)Boronate (**3**) and Procedure for the Difluoroallylboration of Aldehydes for the Preparation of **6a−d**.* To a solution of 1,1-difluoroethene (1.14 mL, 10.64 mmol) in THF (10 mL) and diethyl ether (2.5 mL) at −110 °C was added dropwise *s*-BuLi (3.80 mL, 1.4 M in cyclohexane, 5.32 mmol). The reaction mixture was stirred at the same temperature for 15 min and then diisopropyl iodomethylboronate (1.58 g, 5.85 mmol) was slowly added at −100 °C. After 40 min at this temperature, the mixture was stirred at rt for 2 h and filtered through a short bed of Celite. The solvents were removed under vacuum and the crude difluoroallylboronate **3** was then dissolved in THF (3.5 mL), aldehyde (3.52 mmol), and $Sc(OTf)_3$ (0.17 g, 0.35 mmol) were added, and the reaction mixture was refluxed for 24 h (^{11}B NMR shift from δ 29.5 to 18 ppm). The reaction was quenched with satd aq NH_4Cl solution (5 mL), and the product was extracted with diethyl ether, washed with brine, dried (anhyd $MgSO_4$), filtered, and concentrated. The residue was purified by flash silica gel chromatography (hexane/ethyl acetate = 8:1) to yield homoallyl alcohols **6a−d**. The spectral data were consistent with those reported in the literature.[8c,12,14,27]

*2. General Procedure for the Synthesis of (1R,3S)-1,2,2-Trimethylcyclopent-1,3-diyl (4R)-2-(3,3-difluoroprop-2-enyl)-4-phenyl-1,3,2-dioxaborolane (**4**).* To a solution of 1,1-difluoroethene (0.85 mL, 7.96 mmol) in THF (7.5 mL) and diethyl ether (1.9 mL) at −110 °C was added dropwise *s*-BuLi (2.85 mL, 1.4 M in cyclohexane, 3.98 mmol). The reaction mixture was stirred at the same temperature for 15 min, and then (1*R*,2*R*,3*R*,4*S*)-4-iodomethyl-1,10,10-trimethyl-2-phenyl-3,5-dioxa-4-boratricyclo[5.2.1.$0^{0,0}$]decane[7] (1.74 g, 4.38 mmol) was slowly added at −100 °C. After 40 min at this temperature, the mixture was stirred at rt for 2 h and filtered through a short bed of Celite. The solvents were removed and the residue was purified by flash silica gel chromatography (hexane/ethyl acetate = 8:1) to yield difluoroallylboronate **4** as a light yellow oil (1.06 g, 80%). R_f: 0.55 (hexane/ethyl acetate = 8:1). ^1H NMR (300 MHz, $CDCl_3$): δ 7.44−7.29 (m, 5H), 4.75 (s, 1H), 4.19 (dtd, J = 25.5, 7.8, and 2.4 Hz, 1H), 2.16 (d, J = 5.1 Hz, 1H), 1.89−1.81 (m, 1H), 1.51 (d, J = 7.8 Hz, 1H), 1.22 (s, 3H), 1.20−1.15 (m, 2H), 1.10−1.00 (m, 1H), 0.97 (s, 3H), 0.94 (s, 3H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −91.73 (d, J = 50.5 Hz, 1F), −94.62 (dd, J = 50.5 and 25.4 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 155.9 (t, J = 282.5), 141.4, 127.4, 127.2, 126.5, 95.9, 88.7, 73.3 (t, J = 23.3 Hz), 51.9, 50.1, 48.7, 29.4, 24.6, 23.4, 20.5, 9.2. ^{11}B NMR (96 MHz, $CDCl_3$): δ 33.2. MS EI: m/z = 332 [M^+]. HRMS (ESI): calcd for $C_{19}H_{23}BF_2O_2$ 332.1759, found 332.1765.

General Procedure for the Difluoroallylboration of Aldehydes Using Reagent 4. To a solution of chiral (3,3-difluoroallyl)-boronate **4** (1.25 mmol) in THF (1 mL) were added aldehyde **5** (1.00 mmol) and $Sc(OTf)_3$ (0.10 mmol), and the reaction mixture was refluxed for the desired time (shown in Table 3) (^{11}B NMR shift from δ 33.2 to 22.4 ppm). The reaction was quenched with satd aq NH_4Cl solution (1.5 mL), and the product was extracted with diethyl ether, washed with brine, dried (anhyd. $MgSO_4$), filtered, and concentrated. The residue was purified by flash silica gel chromatography to yield homoallyl alcohol **6**.

*3. General Procedure for the One Pot Synthesis of B-(3,3-Difluoroallyl)Diisopinocampheylborane (**7**) and Representative Procedure for the Difluoroallylboration of Aldehydes for the Preparation of (R)-2,2-Difluoro-1-phenylbut-3-en-1-ol [(R)-**6a**].* To

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a suspension of (−)-Ipc_2BH[26] (1.25 g, 4.38 mmol) in Et_2O (10 mL) at −78 °C was added 1,1-difluoropropa-1,2-diene[24] (0.50 g, 6.57 mmol). After the mixture was stirred for 3 h at 0 °C, the solid dissolved completely, indicating the completion of hydroboration (^{11}B NMR δ 79 and 49 ppm, ratio 7:3). The reaction mixture was cooled to −100 °C, and benzaldehyde (**5a**) (0.46 g, 4.38 mmol) was added dropwise. The mixture was stirred at this temperature for 4 h (^{11}B NMR: δ 79 ppm to 50 ppm), oxidized with 3 M NaOH (3.2 mL) and 30% H_2O_2 (3.2 mL), and stirred at rt for 12 h. The product was extracted with diethyl ether, washed with brine, dried (anhyd. $MgSO_4$), filtered, and concentrated. The residue was purified by flash silica gel chromatography (hexane/ethyl acetate = 8:1) to yield homoallyl alcohol (*R*)-**6a** as a colorless viscous liquid (0.36 g, 45%, calculated to 72% on the basis of 7:3 mixture of the reagents). R_f = 0.21 (hexane/ethyl acetate = 8:1). $[\alpha]^{23}_D$ = −16.96 (*c* 1.25, $CHCl_3$), 94% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester (lit.[14] $[\alpha]^{23}_D$ = −14.7 (*c* 1.13, $CHCl_3$), 79% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42−7.35 (m, 5H), 5.86 (ddd, *J* = 23.1, 17.4, and 11.1 Hz, 1H), 5.59 (d, *J* = 17.4 Hz, 1H), 5.46 (d, *J* = 11.1 Hz, 1H), 4.88 (t, *J* = 9.6 Hz, 1H), 2.81 (bs, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.32 (dt, *J* = 246.4 and 10.4 Hz, 1F), −110.99 (dt, *J* = 246.4 and 10.4 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.9, 129.2 (t, *J* = 25.5 Hz), 128.6, 128.1, 127.5, 121.5 (t, *J* = 8.7 Hz), 119.5 (t, *J* = 243.1 Hz), 75.7 (td, *J* = 29.6 and 5.8 Hz). MS EI: *m*/*z* = 184 [M^+]. HRMS (ESI): calcd for $C_{10}H_{10}F_2O$ 184.0700, found 184.0711.

(*R*)-2,2-Difluoro-1-(4-methoxyphenyl)but-3-en-1-ol [(*R*)-6b]. A colorless viscous liquid, 0.50 g, 44% (calculated to 71% on the basis of 7:3 mixture of the reagents). R_f 0.09 (hexane/ethyl acetate = 8:1). $[\alpha]^{23}_D$ = −19.75 (c 1.55, $CHCl_3$), 93% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester (lit.[14] $[\alpha]^{23}_D$ = −20.2 (*c* 1.01, $CHCl_3$), 94% ee). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33 (d, *J* = 8.7 Hz, 2H), 6.91−6.86 (m, 2H), 5.86 (ddd, *J* = 23.4, 17.4, and 11.1 Hz, 1H), 5.59 (dtd, *J* = 17.4, 2.4, and 0.9 Hz, 1H), 5.46 (d, *J* = 11.1 Hz, 1H), 4.84 (td, *J* = 9.6 and 3.0 Hz, 1H), 3.81 (s, 3H), 2.63 (d, *J* = 3.6 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.59 (dt, *J* = 245.9 and 10.4 Hz, 1F), −111.17 (dt, *J* = 245.9 and 10.4 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 159.7, 129.4 (t, *J* = 25.5 Hz), 128.8, 128.1, 121.3, 119.5 (t, *J* = 242.8 Hz), 113.4, 75.4 (td, *J* = 29.6 and 7.3 Hz), 55.1. MS EI: *m*/*z* = 214 [M^+]. HRMS (ESI): calcd for $C_{11}H_{12}F_2O_2$ 214.0805, found 214.0811.

(*R*)-2,2-Difluoro-1-(naphthalen-2-yl)but-3-en-1-ol [(*R*)-6c]. A light yellow oil, 0.53 g, 48% (calculated to 70% on the basis of 7:3 mixture of the reagents). R_f 0.33 (hexane/ethyl acetate = 8:2). $[\alpha]^{23}_D$ = −15.56 (*c* 1.08, $CHCl_3$), 94% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.89−7.83 (m, 4H), 7.55−7.49 (m, 3H), 5.88 (ddd, *J* = 23.4, 17.4, and 11.1 Hz, 1H), 5.61 (dt, *J* = 17.1 and 2.0 Hz, 1H), 5.46 (d, *J* = 10.8 Hz, 1H), 5.09 (t, *J* = 9.3 Hz, 1H), 2.62 (bs, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.03 (dt, *J* = 246.7 and 10.4 Hz, 1F), −110.46 (dt, *J* = 246.7 and 10.4 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 133.3, 132.8, 129.2 (t, *J* = 25.5 Hz), 128.1, 127.8, 127.6, 127.0, 126.3, 126.2, 124.9, 121.6, 119.6 (t, *J* = 243.4 Hz), 75.9 (td, *J* = 29.7 and 6.7 Hz). MS EI: *m*/*z* = 234 [M^+]. HRMS (ESI): calcd for $C_{14}H_{12}F_2O$ 234.0856, found 234.0859.

(*R*)-4,4-Difluoro-1-phenylhex-5-en-3-ol [(*R*)-6d]. A colorless liquid, 0.64 g, yield 53% (calculated to 76% on the basis of 7:3 mixture of the reagents). R_f 0.20 (hexane/ethyl acetate = 8:1). $[\alpha]^{23}_D$ = +33.82 (c 0.76, $CHCl_3$), 97% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.33−7.28 (m, 2H), 7.23−7.18 (m, 3H), 6.05−5.88 (m, 1H), 5.71 (d, *J* = 17.4 Hz, 1H), 5.54 (d, *J* = 11.1 Hz, 1H), 3.82−3.73 (m, 1H), 2.93 (ddd, *J* = 14.1, 9.3, and 4.8 Hz, 1H), 2.76−2.66 (m, 1H), 1.99 (d, *J* = 5.1 Hz, 1H), 1.96−1.87 (m, 1H), 1.84−1.71 (m, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −110.26 (dt, *J* = 248.7 and 10.1 Hz, 1F), −113.71 (dt, *J* = 248.7 and 10.4 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.0, 129.5 (t, *J* = 25.8 Hz), 128.4, 126.0, 121.3 (t, *J* = 8.8 Hz), 120.2 (t, *J* = 241.5 Hz), 72.5 (t, *J* = 29.0 Hz), 31.6, 31.4. MS EI: *m*/*z* = 212 [M^+]. HRMS (ESI): calcd for $C_{12}H_{14}F_2O$ 212.1013, found 212.1015.

(*R*,*E*)-4,4-Difluoro-1-phenylhexa-1,5-dien-3-ol [(*R*)-6e]. A colorless oil, 0.39 g, yield 48% (calculated to 70% on the basis of 7:3 mixture of the reagents). R_f 0.15 (hexane/ethyl acetate = 9:1). $[\alpha]^{23}_D$ = +7.22 (*c* 1.15, $CHCl_3$), 91% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.43−7.28 (m, 5H), 6.78 (d, *J* = 15.6 Hz, 1H), 6.20 (dd, *J* = 15.6 and 5.7 Hz, 1H), 6.01 (ddd, *J* = 23.1, 17.4, and 11.1 Hz, 1H), 5.75 (dtd, *J* = 17.4 Hz, 2.1 and 0.9 Hz, 1H), 5.57 (d, *J* = 11.1 Hz, 1H), 4.57−4.46 (m, 1H), 2.23 (d, *J* = 5.1 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −109.99 (dt, *J* = 247.8 and 10.1 Hz, 1F), −112.10 (dt, *J* = 247.8 and 10.1 Hz, 1F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 135.8, 134.5, 129.5 (t, *J* = 25.4 Hz), 128.5, 128.2, 126.6, 123.0, 121.6 (t, *J* = 9.0 Hz), 119.3 (t, *J* = 242.5 Hz), 74.4 (td, *J* = 29.8 and 4.8 Hz). MS EI: *m*/*z* = 210 [M^+]. HRMS (ESI): calcd for $C_{12}H_{12}F_2O$ 210.0856, found 210.0859.

(*R*)-2,2-Difluoro-1-(furan-2-yl)but-3-en-1-ol [(*R*)-6f]. A light yellow oil, 0.25 g, yield 42% (calculated to 69% on the basis of 7:3 mixture of the reagents). R_f 0.80 (hexane/ethyl acetate = 8:1). $[\alpha]^{23}_D$ = −1.88 (*c* 1.17, $CHCl_3$), 92% ee, determined by ^{1}H and ^{19}F NMR analysis of Mosher ester. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.50 (d, *J* = 1.8 Hz, 1H), 6.51−6.50 (m, 1H), 6.47−6.45 (m, 1H), 6.13−5.96 (m, 1H), 5.78 (dt, *J* = 17.7 and 2.4 Hz, 1H), 5.60 (d, *J* = 11.1 Hz, 1H), 4.97 (td, *J* = 9.3 and 6.6 Hz, 1H), 2.86 (d, *J* = 6.6 Hz, 1H). ^{19}F NMR (282 MHz, $CDCl_3$): δ −108.90 (t, *J* = 10.8 Hz, 2F). ^{13}C NMR (75 MHz, $CDCl_3$): δ 149.4, 143.0, 129.5 (t, *J* = 25.2 Hz), 121.8 (t, *J* = 8.5 Hz), 118.7 (t, *J* = 240.0 Hz), 110.6, 109.6, 70.4 (t, *J* = 31.6 Hz). MS EI: *m*/*z* = 174 [M^+]. HRMS (ESI): calcd for $C_8H_8F_2O_2$ 174.0492, found 174.0488.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

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

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Notes

The authors declare no competing financial interest.

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