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Regio- and Diastereoselective Nickel-Catalyzed Allylation of Aromatic Aldehydes with α-Halo-β,β-difluoropropene Derivatives

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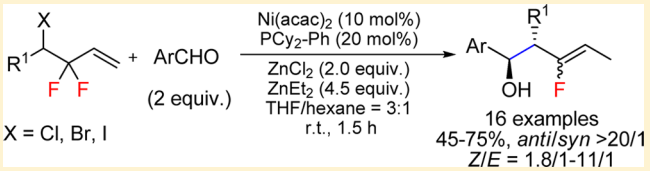
Supporting Information

ABSTRACT: A one-pot nickel-catalyzed allylation of aromatic aldehydes with α-halo-β,β-difluoropropene-containing compounds promoted by $ZnEt_2$ under mild conditions was described. The reaction displays moderate to good regio- and diastereoselectivity, tolerates a wide range of functional groups, and provides an efficient method for the synthesis of γ-fluorinated homoallylic alcohols.



INTRODUCTION

Fluoroorganic compounds have attracted increased interest as pharmaceutical agents in recent years since it has been found that fluorine modifies biological activity by altering the physicochemical properties of organic compounds.[1] Fluoroolefins, one of the most important classes of organofluorine compounds, have received great attention in material[2] and life sciences.[3] For example, the fluoroolefins have been widely utilized in mimicking the peptide bonds, because the *trans*-fluoroolefin dipeptide isostere ψ[CF═CH], compared to the natural peptide, not only has the same orientation of the dipole moment, but also can increase the lipophilicity of the target peptide.[3d,4] Given its widespread use, many efforts have been made to develop practical and efficient methods for the preparation of functionalized fluoroolefins;[4c,f,5,6] however, the stereoselective control of the olefin configuration and the use of readily available starting material are still challenging subjects. Furthermore, the methodology for the construction of versatile γ-fluorinated homoallylic alcohol structural moieties is in great demand.[7]

The allylation of carbonyl compounds is among the most efficient methodologies for the construction of C−C bond and well developed to furnish synthetically useful homoallylic alcohols motif.[8] Recently, Ni-promoted coupling of dienes with carbonyls,[9,10] first discovered by Wilke[11] and subsequent pioneering studies in catalysis by Mori[12] and Tamaru,[13] provided a new method for the synthesis of homoallylic alcohols or bishomoallylic alcohols. Mechanistic studies by Ogoshi[14] showed that the Ni-promoted reaction of dienes with aldehydes is initiated by cyclometalation of the substrates, subsequent σ-bond metathesis and reductive elimination generate 1,2-addition (homoallylation) or 1,4-addition (allylation) product (Scheme 1). In most cases, the 1,2-addition was much more favored because of the easy-accessible β-agostic interaction of the H-donor group with the vacant site on Ni in the proposed transition state.[9a−c,12i,13b,15] Cyclohexadiene is one exception among the dienes examined so far and undergoes 1,4-addition instead of 1,2-addition under the catalysis of Ni-Et_2Zn.[13b] The steric repulsion in the *syn-cis* dienes-Nickel transition state was suggested to explain the unusual 1,4-addition regioselectivity.[9a,13b]

Inspired by this body of work, we envisioned that the extremely electron-deficient 3-fluoro-1,3-dienes could be employed as the substrates of the Ni-catalyzed reductive coupling of dienes and carbonyl compounds for the efficient synthesis of fluoroolefinic alcohols.

RESULTS AND DISCUSSION

Initial experiments surveyed the Ni-catalyzed reaction of (4-fluorohexa-3,5-dienyl)benzene **2** and benzaldehyde at room temperature. Surprisingly, the unusual 1,4-addition product (γ-fluorinated homoallylic alcohol) **3a** was obtained in 30% yield (Scheme 2a). However, the further utilization of 3-fluoro-1,3-diene **2** was restricted due to its polymerization.[16] Since 3-fluoro-1,3-diene **2** was prepared from (3-bromo-4,4-difluorohex-5-enyl)benzene **1a** via reductive debromodefluorination by treatment with Mg (Scheme 2b).[17] We speculated that the vicinal bromodifluoride **1** could be used as the equivalent of 3-fluoro-1,3-dienes that can be generated in situ and coupled with aldehydes under the reductive conditions of Ni-$ZnEt_2$ (Scheme 2c).

To probe the hypothesis, the Ni-catalyzed debromodefluorination of compound **1a** was first investigated. As expected, 3-fluoro-1,3-diene **2** was produced in 83% yield with good selectivity (*Z*/*E* = 11/1) under the reductive conditions of Ni-$ZnEt_2$ using $P(O^iPr)_3$ as ligand (eq 1).

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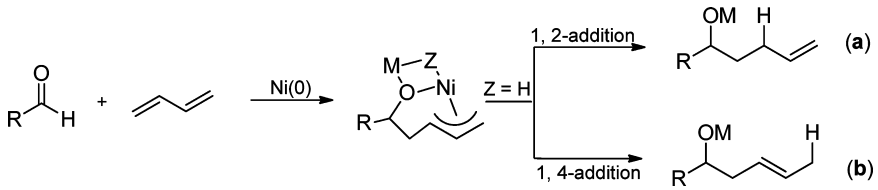
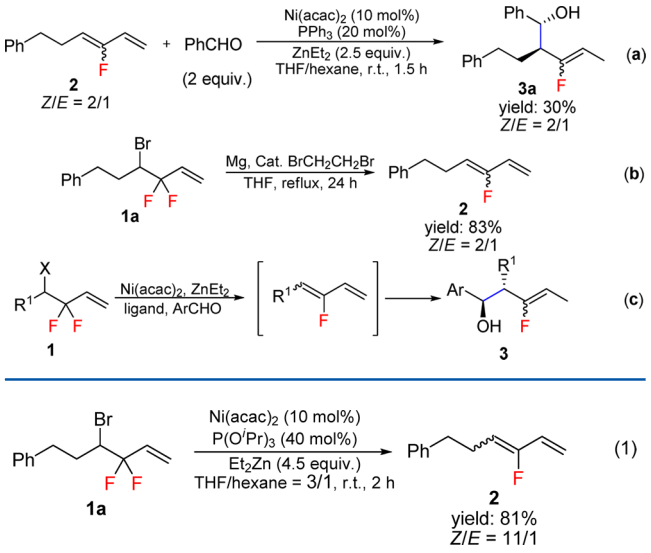
Scheme 1



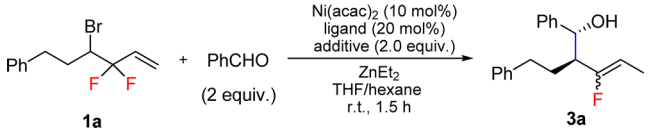
Scheme 2



Having achieved the Ni-catalyzed reductive elimination, we focused on the cascade dehalogenation−coupling reaction and chose the reaction outlined in Table 1 to screen the catalyst system. Treatment of vicinal bromodifluoride **1a** with Ni(acac)$_2$/PPh$_3$ (10 mol %) and ZnEt$_2$ (2.5 equiv) in THF gave desired coupling product **3a** in 18% yield (Table 1, entry 1). In consideration of the fact that ZnEt$_2$ serves not only as a formal hydride source as usual, but also as a reducing reagent to participate in the dehalodefluorination, the reaction would perform better with increasing amount of ZnEt$_2$. As expected, the yield of **3a** was improved to 48% when 4.5 equiv of ZnEt$_2$ were used (entries 2−4). Recently, Ikeda and co-workers[18] illustrated that ZnCl$_2$ can promote the Ni-catalyzed domino coupling of enones, alkynes and alkenes. Experimentally, the yield of product **3a** was increased to 60% in the presence of ZnCl$_2$ (2.0 equiv) (entry 5). Exploration of phosphorus ligands revealed that PCy$_2$-Ph was the best active ligand, affording product **3a** in 90% yield (entries 6−16). None of the desired product was detected in the absence of nickel catalyst (entry 17).

With the optimized conditions in hand (Table 1, entry 15), the substrate scope (aromatic aldehydes and α-halo-β,β-difluorides) of this transformation was then examined. As shown in Table 2, 3-bromo-, 3-iodo-, and 3-chloro-4,4-difluoro-5-enyl-benzenes (**1a**, **1a**′, **1a**″) reacted with benzaldehyde smoothly to afford product **3a** in moderate yields. Benzaldehydes bearing electron-donating groups were competent coupling partners to give the desired products in moderate to good yields (**3b**−**3h**). Benzaldehydes carrying Br and Cl substituents exhibited high chemoselectivity for the coupling process to give products **3i** and **3j**, respectively, and no products arising from the Negish-type coupling were observed. However, the reaction of 4-(trifluoromethyl)benzaldehyde and

Table 1. Optimization of the Ni-Catalyzed Allylation of Benzaldehyde with (3-Bromo-4,4-difluorohex-5-enyl)benzene 1a[a]



entry	ligand	$ZnEt_2$ (equiv)	additive	yield **3a** (%)[b]
1	PPh_3	2.5		18
2	PPh_3	3.5		40
3	PPh_3	4.5		48
4	PPh_3	5.5		45
5	PPh_3	4.5	$ZnCl_2$	60
6	$P(OMe)_3$	4.5	$ZnCl_2$	31
7	$P(OEt)_3$	4.5	$ZnCl_2$	48
8	$P(O^iPr)_3$	4.5	$ZnCl_2$	73
9[c]	P(*o*-Tol)$_3$	4.5	$ZnCl_2$	20
10[c]	P(*m*-Tol)$_3$	4.5	$ZnCl_2$	49
11[c]	P(*p*-Tol)$_3$	4.5	$ZnCl_2$	35
12	PPh_2-Me	4.5	$ZnCl_2$	20
13	PPh_2-OEt	4.5	$ZnCl_2$	70
14[d]	PPh_2-Cy	4.5	$ZnCl_2$	56
15[d]	**PCy_2-Ph**	**4.5**	**$ZnCl_2$**	**90**
16[d]	PCy_3	4.5	$ZnCl_2$	60
17[d,e]	PCy_2-Ph	4.5	$ZnCl_2$	0[f]

[a]Reactions were carried out on a 0.2 mmol scale. acac = acetylacetone. [b]Yield determined by ^{19}F NMR using fluorobenzene as an internal standard. [c]Tol = tolyl. [d]Cy = cyclohexyl. [e]Without Ni(acac)$_2$. [f]**1a** was recovered completely.

methyl 4-formylbenzoate with (3-bromo-4,4-difluorohex-5-enyl)benzene **1a** under the optimized conditions gave only trace amount of the desired products. Instead, the direct ethylation of aldehydes took place. This is apparently owing to the high reactivity of electron-deficient aldehydes, which resulted in the first direct ethylation of aldehydes with ZnEt$_2$ and retardation of the debromodefluorination of (3-bromo-4,4-difluorohex-5-enyl)benzene **1a**. We anticipated that the desired product should be formed if (4-fluorohexa-3,5-dienyl)benzene **2** was formed first in situ from **1a** and then aldehydes were added to the reaction mixture. To our delight, treatment of (3-bromo-4,4-difluorohex-5-enyl)benzene **1a** with ZnEt$_2$ and followed by addition of the aldehydes gave the desired products **3k** and **3l** in 57 and 54% yields, respectively. Furthermore, the Ni-catalyzed allylation of 2-naphthaldehyde and furan-2-carbaldehyde performed well to give compounds **3m** and **3n** in good yields. Finally, our attention was turned to the compatibility of α-bromo-β,β-difluorides **1**. It was found that the allylation of benzaldehyde with octyl- and benzyl-substituted α-bromo-β,β-difluorides (**1b**, **1c**) gave compounds **3o** and **3p**, respectively, in moderate yields. It should be noted that the 1,2-*anti*-γ-fluorinated homoallylic alcohols were obtained exclusively in most cases.

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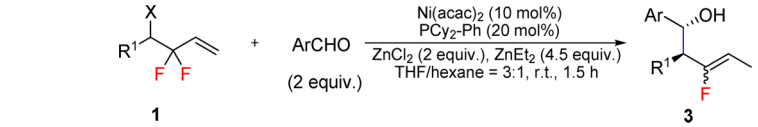
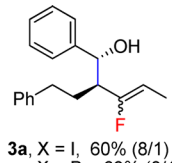
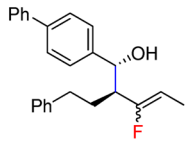
Table 2. Ni-Catalyzed Allylation of Aromatic Aldehydes with α-Halo-β,β-difluorides[a]

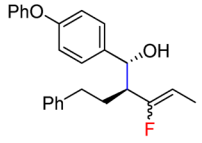




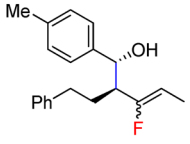
3a, X = I, 60% (8/1)
X = Br, 63% (8/1)
X = Cl, 58% (7/1)



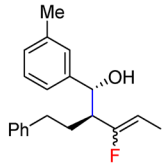
3b, X = Br, 61% (9/1)



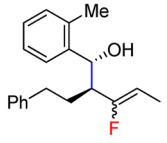
3c, X = Br, 67% (8/1)



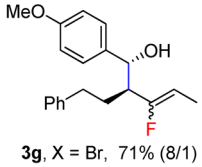
3d, X = Br, 75% (8/1)



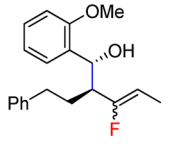
3e, X = Br, 64% (8/1)



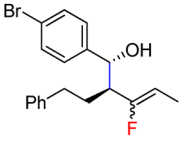
3f, X = Br, 55% (5/1)



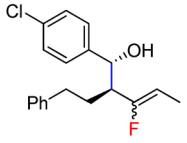
3g, X = Br, 71% (8/1)



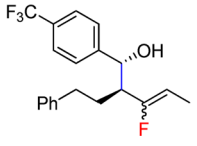
3h, X = Br, 55% (10/1)



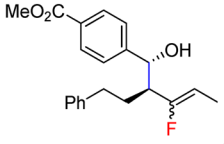
3i, X = Br, 61% (6/1)



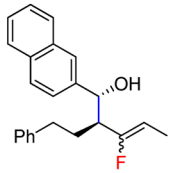
3j, X = Br, 72% (7/1)



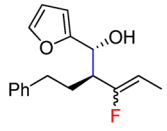
3k, X = Br, 57% (1.8/1)[b]



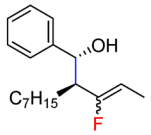
3l, X = Br,54% (3.5/1)[b]



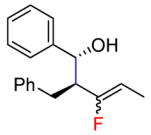
3m, X = Br, 66% (11/1)



3n, X = Br,70% (8/1)



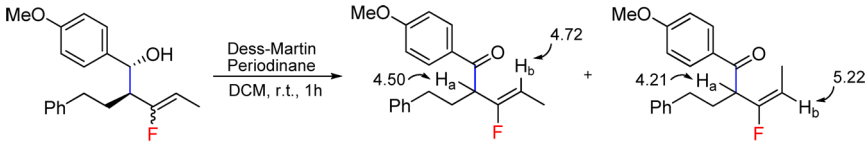
3o, X = Br, 56% (8/1)



3p, X = Br, 45% (5/1)

[a]Unless stated otherwise, the reaction was performed using **1** (0.2 mmol), R_2CHO (2 equiv), $ZnEt_2$ (4.5 equiv), $Ni(acac)_2$ (10 mol %), PCy_2-Ph (20 mol %) and $ZnCl_2$ (2 equiv) in THF (1.5 mL) at room temperature for 1.5 h under Argon. The ratios of *Z*/*E* in parentheses were determined by ^{19}F NMR spectra of crude mixtures. [b]The reaction was performed according to the General Procedure B. See the Experimental Section for details.

Scheme 3. Determination of the Configuration of the Double Bond in 3g



The relative configuration of the major isomer (*anti*, *Z*) of homoallylic alcohol **3a** was determined by single crystal X-ray diffraction analysis (see the Supporting Information).[19] The configuration of the double bond in **3g** was confirmed by the formation of *Z*-ketone **4a** and *E*-ketone **4b** (Scheme 3). The stereochemical assignments of other γ-fluorinated homoallylic alcohols were based on comparison spectra data with **3g**.

To learn whether the *Z*/*E* ratio of diene in situ generated by the Ni-catalyzed elimination matched the *Z*/*E* ratio of product **3** and the diene was isomerized during the reaction, diene **2** (*Z*/*E* = 11/1, prepared by Ni-catalyzed reductive elimination) was subjected to the optimized coupling conditions with benzaldehyde and 4-trifluoromethylbenzaldehyde respectively. Interestingly, the *Z*/*E* ratio of product **3a** was the same as that of diene **2** (Scheme 4a). However, in case of 4-trifluoromethylbenzaldehyde, the *Z*/*E* ratio of product **3k** was decreased to 3/1 (Scheme 4b). These results indicated that the coordination ability of the aldehyde to the Lewis acid $ZnCl_2$ played an

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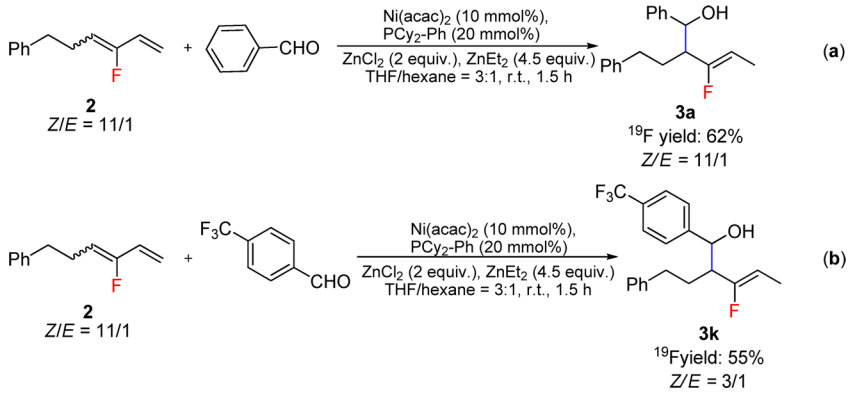
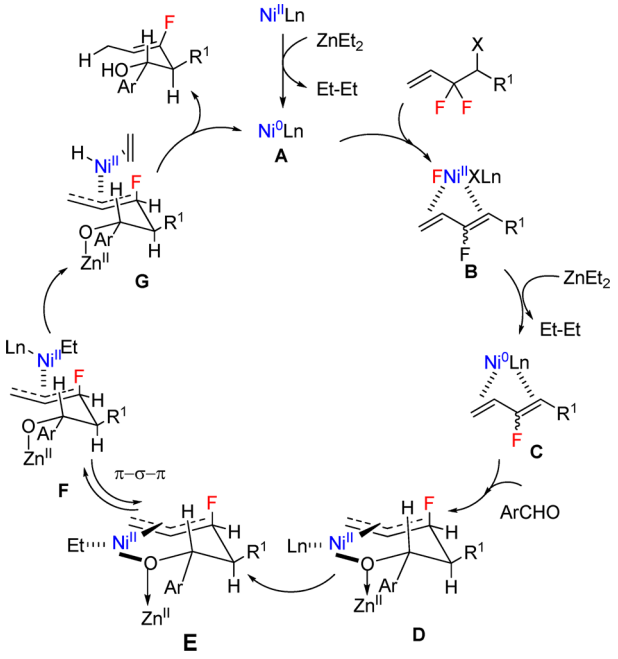
Scheme 4



important role in determining the *Z*/*E* ratio of the product. For the relative electron-rich benzaldehyde with good affinity to Zn(II), the coupling reaction underwent faster than the diene isomerization, and the *Z*/*E* ratio remained unchanged in product. While, on the other hand, the electron-deficient 4-trifluoromethylbenzaldehyde could not be activated by Zn(II) efficiently, and thus the coupling proceeded slowly and the diene isomerization occurred.

In view of the similar reaction conditions, a possible mechanistic scenario, which is similar to the mechanisms suggested by Tamaru[9a,13b] and Mori,[12i] is proposed to understand the unusual 1,4-addition regiochemical course of this coupling process. As depicted in Scheme 5, the ethyl

Scheme 5. Proposed Mechanism



transfer from $ZnEt_2$ to $Ni(acac)_2$, accompanied with reductive elimination from bis(ethyl)nickel intermediate, led to a zerovalent nickel complex **A**. Oxidative addition of *α*-halo-*β*,*β*-difluoropropene-containing compound with the zerovalent nickel complex and *β*-fluorine elimination of the nickel(II)-alkyl intermediate generated the 3-fluoro-1,3-diene **B** and a two-valent nickel complex. The latter was reduced to a zerovalent complex again and coordinated to the formed 3-fluoro-1,3-diene **B**. Subsequently, oxidative cyclization of the zerovalent nickel complex across 3-fluoro-1,3-diene **B** and aldehyde generated the intermediate **D**, in which R^1 and Ar groups properly occupied the *anti* vicinal pseudoequatorial positions. After that, *σ*-bond metathesis with $ZnEt_2$ would then deliver *π*-allyl intermediate **E** that may engage in *π*−*σ*−*π* isomerization prior to *β*-H elimination and reductive elimination. Then, *β*-H elimination of the intermediate **F** led to the intermediate G. Finally, reductive elimination of the intermediate **G** provided the product **3** and completed the catalytic cycle. It is conceivable that with a 3-fluoro substituted *π*-allyl, the *π*−*σ*−*π* isomerization could proceed more smoothly, leading to a less hindered intermediate **F**. The release of the nonbonding repulsion in η^1-*π*-allyl nickel complex could narrow down the energy gap between η^1- and η^3-*π*-allyl nickel complexes, which may facilitate their interconversion.

CONCLUSION

In conclusion, we have demonstrated an efficient one-pot allylation of aromatic aldehydes with *α*-halo-*β*,*β*-difluoropropene-containing compounds promoted by $Ni(acac)_2/PCy_2$-Ph/$ZnCl_2/ZnEt_2$ system. This protocol provided a useful method for the synthesis of *γ*-fluorinated homoallylic alcohols. The reaction shows moderate to good regio- and stereoselectivity and tolerates a wide range of functional groups.

EXPERIMENTAL SECTION

General Experimental Methods. ^1H NMR (TMS as the internal standard) and ^{19}F NMR spectra ($CFCl_3$ as the external standard and low field is positive) were recorded on a 300 or 400 MHz spectrometer. ^{13}C NMR were recorded on a 400 MHz spectrometer. Chemical shifts (*δ*) are reported in ppm, and coupling constants (*J*) are in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, br = broad. Reagents were either purchased from commercial sources and used without further purification, unless specified otherwise, or prepared as described in the literature. Dry THF was distilled from sodium and benzophenone immediately before use. 4,4-Difluoro-1-phenylhex-5-en-3-ol was prepared according to the published procedure.[20]

General Procedure for the Preparation of *α*-Hydroxy-*β*,*β*-difluoroethylene-Containing Compounds.[20] A vigorously stirred suspension of indium powder (1.38 g, 12 mmol), aldehyde (10 mmol), tetrahydrofuran (5 mL) and water (20 mL) was cooled to 0 °C in an ice bath, and 3-bromo-3,3-difluoropropene (1.88 g, 12 mmol) was slowly added via a dropping funnel. After the addition was completed, the reaction mixture was allowed to warm to room temperature, and stirring was continued overnight. To work up, 10% aqueous hydrochloric acid (15 mL) was added to the reaction mixture, excess

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indium was removed by suction filtration, and the residues were washed with ether (30 mL). The organic layer was separated, and the aqueous layer was extracted with ether (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give the desired compound.

3,3-Difluoroundec-1-en-4-ol (1b-OH). Prepared from octanal using general procedure to afford **1b-OH** as a colorless oil (1.57 g, 76%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 6.04−5.91 (m, 1H), 5.73−5.67 (m, 1H), 5.54−5.51 (m, 1H), 3.79−3.71 (m, 1H), 2.15 (br, 1H), 1.63−1.55 (m, 2H), 1.47−1.28 (m, 10H), 0.88 (t, J = 6.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −108.2 (AB, J_{AB} = 248.2 Hz, $^3J_{HF}$ = 10.4 Hz, 1F), −111.8 (AB, J_{AB} = 248.2 Hz, $^3J_{HF}$ = 10.2 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 129.9 (t, J = 26.2 Hz), 121.0 (t, J = 9.5 Hz), 120.4 (t, J = 241.3 Hz), 73.6 (dd, J = 29.9 Hz, J = 28.4 Hz), 31.8, 30.1 (dd, J = 2.9 Hz, J = 1.5 Hz), 29.4, 29.1, 15.5, 22.6, 14.0; IR (thin film) υ_{max} 3602, 3415, 2927, 2858, 1466, 1421, 1075, 989, 949, 723 cm^{-1}; MS (ESI) m/z 229 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{11}H_{20}F_2NaO$ $[M + Na]^+$ 229.1374, found 229.1374.

3,3-Difluoro-1-phenylpent-4-en-2-ol (1c-OH). Prepared from 2-phenylacetaldehyde using general procedure to afford **1c-OH** as a colorless oil (1.59 g, 80%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.33−7.23 (m, 5H), 6.11−5.97 (m, 1H), 5.80−5.74 (m, 1H), 5.59−5.56 (m, 1H), 3.99 (ddd, J = 19.6 Hz, J = 10.0 Hz, J = 2.4 Hz), 3.01−2.97 (m, 1H), 2.71−2.65 (m, 1H), 1.96 (br, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −106.8 (AB, J_{AB} = 249.0 Hz, $^3J_{HF}$ = 9.3 Hz, 1F), −112.1 (AB, J_{AB} = 249.0 Hz, $^3J_{HF}$ = 10.4 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 137.3, 129.8 (t, J = 25.5 Hz), 129.4, 128.7, 126.9, 121.4 (t, J = 9.4 Hz), 119.9 (t, J = 241.3 Hz), 74.6 (t, J = 29.9 Hz), 36.6 (t, J = 2.9 Hz); IR (thin film) υ_{max} 3442, 3087, 3064, 3004, 2930, 1604, 1496, 1420, 1219, 1165, 1065, 740, 699 cm^{-1}; MS (EI) m/z (%) 198 (M^+), 121, 107, 103, 91 (100), 77, 65, 51, 41; HRMS (EI-TOF) Calculated for $C_{11}H_{12}F_2O$ 198.0856, found 198.0856.

General Procedure for the Preparation of α-Bromo-β,β-difluoropropene-Containing Compounds. A dry 250 mL flask, equipped with a mechanical stirrer and a septum, was charged with 4,4-difluoro-1-phenylhex-5-en-3-ol (2.12 g, 10 mmol), PPh_3 (5.25 g, 20 mmol), CBr_4 (6.63 g, 20 mmol) and toluene (100 mL); the resulting mixture was stirred at 110 °C for 3 h. The reaction was quenched with water (50 mL). The organic layer was separated and the aqueous layer was extracted with hexane (2 × 50 mL). The combined organic extracts were washed with brine (50 mL) and then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give the desired compound.

(3-Bromo-4,4-difluorohex-5-en-1-yl)benzene (1a). Prepared from 4,4-difluoro-1-phenylhex-5-en-3-ol using general procedure to afford **1a** as a colorless oil (2.34 g, 85%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.32−7.20 (m, 5H), 6.09−6.00 (m, 1H), 5.71 (dt, J = 17.2 Hz, J = 2.4 Hz, 1H), 5.56−5.53 (m, 1H), 4.00−3.88 (m, 1H), 3.30−3.00 (m, 1H), 2.76−2.69 (m, 1H), 2.35−2.27 (m, 1H), 2.11−2.01 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −99.2 (AB, J_{AB} = 243.9 Hz, $^3J_{HF}$ = 9.3 Hz, 1F), −103.0 (AB, J_{AB} = 243.9 Hz, $^3J_{HF}$ = 11.3 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 140.0, 129.9 (t, J = 25.6 Hz), 128.7, 128.6, 126.5, 121.9 (t, J = 9.0 Hz), 118.7 (t, J = 242.8 Hz), 53.3 (t, J = 30.6 Hz), 33.4, 33.1; IR (thin film) υ_{max} 3063, 3028, 2927, 2861, 1603, 1496, 1454, 1419, 985, 754, 749, 700 cm^{-1}; MS (EI) m/z (%) 276, 274 (M^+), 195, 91 (100), 77, 65, 51; HRMS (EI-TOF) Calculated for $C_{12}H_{13}BrF_2$ 274.0169, found 274.0169.

4-Bromo-3,3-difluoroundec-1-ene (1b). Prepared from 3,3-difluoroundec-1-en-4-ol (**1b-OH**) using general procedure to afford **1b** as a colorless oil (2.18 g, 81%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 6.11−6.00 (m, 1H), 5.73 (dt, J = 17.2 Hz, J = 2.0 Hz, 1H), 5.56−5.54 (m, 1H), 4.03−3.95 (m, 1H), 2.02−1.94 (m, 1H), 1.78−1.63 (m, 2H), 1.42−1.29 (m, 9H), 0.89 (t, J = 6.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −99.2 (AB, J_{AB} = 242.8 Hz, $^3J_{HF}$ = 9.3 Hz, 1F), −103.3 (AB, J_{AB} = 242.8 Hz, $^3J_{HF}$ = 11.6 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 130.1 (t, J = 26.2 Hz), 121.0 (t, J = 9.5 Hz), 118.7 (t, J = 242.1 Hz), 54.3 (t, J = 30.6 Hz), 31.8 (t, J = 2.9 Hz), 29.0, 28.7, 27.3, 22.6, 14.0; IR (thin film) υ_{max} 2957, 2928, 2858, 1466, 1419, 1307, 999, 952 cm^{-1}. Anal. Calculated for $C_{11}H_{19}BrF_2$: C 49.08, H 7.11. Found: C 48.79, H 6.96.

(2-Bromo-3,3-difluoropent-4-en-1-yl)benzene (1c). Prepared from 3,3-difluoro-1-phenylpent-4-en-2-ol **1c-OH** using general procedure to afford **1c** as a colorless oil (2.01 g, 77%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.34−7.21 (m, 5H), 6.18−6.06 (m, 1H), 5.79 (dt, J = 17.6 Hz, J = 2.0 Hz, 1H), 5.60 (d, J = 11.2 Hz, 1H), 4.22−4.13 (m, 1H), 3.49 (dd, J = 14.8 Hz, J = 2.8 Hz, 1H), 2.94 (dd, J = 14.8 Hz, J = 11.2 Hz, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −99.1 (AB, J_{AB} = 242.8 Hz, $^3J_{HF}$ = 8.2 Hz, 1F), −104.6 (AB, J_{AB} = 242.8 Hz, $^3J_{HF}$ = 12.4 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 137.0, 130.1 (t, J = 23.1 Hz), 129.3, 128.6, 127.2, 122.1 (t, J = 9.4 Hz), 118.7 (t, J = 243.4 Hz), 54.8 (t, J = 29.9 Hz), 38.2 (t, J = 2.2 Hz); IR (thin film) υ_{max} 3088, 3065, 3031, 3005, 2960, 2922, 2849, 1604, 1496, 1455, 1419, 1303, 1200, 748, 697 cm^{-1}; MS (EI) m/z (%) 262, 260 (M^+), 184, 182, 91 (100), 77, 65, 51, 41; HRMS (EI-TOF) Calculated for $C_{11}H_{11}BrF_2$ 260.0012, found 260.0012.

(4,4-Difluoro-3-iodohex-5-en-1-yl)benzene (1a′). A dry 250 mL flask, equipped with a mechanical stirrer and a septum, was charged with 4,4-difluoro-1-phenylhex-5-en-3-ol (2.12 g, 10 mmol), PPh_3 (10.49 g, 40 mmol), imidazole (1.84 g, 27 mmol), iodine (6.85 g, 27 mmol) in toluene (100 mL), and the resulting mixture was stirred at 110 °C for 3 h. The reaction was quenched with water (50 mL). The aqueous layer was extracted with hexane (2 × 50 mL). The combined organic extracts were washed with brine (50 mL), dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give (4,4-difluoro-3-iodohex-5-en-1-yl)benzene **1a′** as a colorless oil (2.25 g, 70%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.31−7.20 (m, 5H), 6.07−5.94 (m, 1H), 5.68 (dt, J = 17.2 Hz, J = 2.4 Hz, 1H), 5.51−5.49 (m, 1H), 4.03−3.94 (m, 1H), 3.01−2.94 (m, 1H), 2.70−2.62 (m, 1H), 2.18−2.00 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −95.5 to −97.4 (m, 2F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 139.9, 130.4 (t, J = 26.2 Hz), 128.7, 128.6, 126.5, 121.9 (t, J = 8.7 Hz), 118.8 (t, J = 242.1 Hz), 35.6, 34.7 (t, J = 2.9 Hz), 33.3 (t, J = 28.4 Hz); IR (thin film) υ_{max} 3085, 3062, 3027, 3002, 2940, 2858, 1603, 1496, 1454, 1418, 784, 749, 699 cm^{-1}; MS (EI) m/z (%) 322 (M^+), 195, 91 (100), 77, 65, 51; HRMS (EI-TOF) Calculated for $C_{12}H_{13}F_2I$ 322.0030, found 322.0030.

(3-Chloro-4,4-difluorohex-5-en-1-yl)benzene (1a″). To a solution of 4,4-difluoro-1-phenylhex-5-en-3-ol (636 mg, 3 mmol) in CH_2Cl_2 (40 mL) was added DMAP (1.10 g, 9 mmol), followed by p-toluenesulfonyl chloride (1.71 g, 9 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 16 h. The solvent was concentrated in vacuo, and the residues were purified by column chromatography to give 4,4-difluoro-1-phenylhex-5-en-3-yl 4-methylbenzenesulfonate **1a″-Ts** as a white solid (1.01 g, 92%): mp 69−71 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.80−7.13 (m, 9H), 5.86−5.73 (m, 1H), 5.62−5.58 (m, 1H), 5.47−5.45 (m, 1H), 4.84−4.76 (m, 1H), 2.81−2.63 (m, 2H), 2.43 (s, 3H), 2.08−1.90 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −104.1 (AB, J_{AB} = 253.2 Hz, $^3J_{HF}$ = 9.3 Hz, 1F), −109.0 (AB, J_{AB} = 253.2 Hz, $^3J_{HF}$ = 12.3 Hz, $^3J_{HF}$ = 8.2 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 145.1, 140.4, 134.1, 129.8, 129.1, 128.8, 128.6, 128.5, 127.9, 126.3, 122.3 (t, J = 9.5 Hz), 118.1 (t, J = 244.3 Hz), 80.7 (dd, J = 32.5 Hz, J = 30.7 Hz), 31.1, 21.7; IR (thin film) υ_{max} 3087, 3063, 3029, 3003, 2964, 2933, 2866, 1598, 1469, 1372, 1190, 814, 748, 701, 668 cm^{-1}; MS (EI) m/z (%) 366 (M^+), 194, 117 (100), 91, 77, 65, 51, 41; HRMS (EI-TOF) Calculated for $C_{19}H_{20}F_2O_3S$ 366.1101, found 366.1101.

A dry 25 mL flask, equipped with a mechanical stirrer and a septum, was charged with the sulfonate **1a″-Ts** (547 mg, 1.5 mmol), LiCl (252 mg, 6 mmol) and DMF (10 mL); the resulting mixture was stirred at 130 °C for 24 h. The reaction was quenched with water (10 mL), and the organic layer was separated. The aqueous layer was extracted with

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hexane (2 × 20 mL). The combined organic extracts were washed with brine (10 mL), then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give (3-chloro-4,4-difluorohex-5-en-1-yl)benzene **1a″** as a colorless oil (235 mg, 71%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.32−7.19 (m, 5H), 6.05−5.92 (m, 1H), 5.71 (dt, J = 17.2 Hz, J = 2.0 Hz, 1H), 5.56−5.53 (m, 1H), 3.93−3.85 (m, 1H), 3.01−2.94 (m, 1H), 2.76−2.68 (m, 1H), 2.29−2.21 (m, 1H), 2.02−1.93 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −101.5 (AB, J_{AB} = 245.9 Hz, $^3J_{HF}$ = 9.3 Hz, 1F), −106.7 (AB, J_{AB} = 245.9 Hz, $^3J_{HF}$ = 11.3 Hz, 1F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 140.1, 129.5 (t, J = 26.2 Hz), 128.7, 128.6, 126.4, 121.9 (t, J = 9.5 Hz), 118.9 (t, J = 242.8 Hz), 61.2 (t, J = 31.4 Hz), 32.9 (t, J = 2.2 Hz), 32.0; IR (thin film) υ_{max} 3087, 3064, 3028, 3004, 2960, 2930, 2864, 1603, 1496, 1455, 1420, 800, 750, 700 cm^{-1}; MS (EI) m/z (%) 230 (M^+), 195, 107, 91 (100), 77, 65, 51, 41; HRMS (EI-TOF) Calculated for $C_{12}H_{13}ClF_2$ 230.0674, found 230.0674.

General Procedure A for the Nickel-Catalyzed Coupling of Aldehydes with α-Halo-β,β-difluoropropene-Containing Compounds. To a solution of Ni(acac)$_2$ (5.1 mg, 10 mol %), PCy_2-Ph (11.0 mg, 20 mol %) and $ZnCl_2$ (54.4 mg, 0.4 mmol) in THF (2 mL) was added PhCHO (42.5 mg, 0.4 mmol) and (3-bromo-4,4-difluorohex-5-en-1-yl)benzene **1a** (55.0 mg, 0.2 mol) in THF (1 mL) at room temperature under argon by syringe. Then $ZnEt_2$ (0.9 mL of 1.0 M hexane solution, 0.9 mmol) was added dropwise to the resulting mixture. The reaction mixture was stirred at room temperature for an additional 1.5 h. The reaction was quenched with 2 mL of 1 M HCl. The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 2 mL). The combined organic extracts were washed with brine (5 mL) and then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give 3-fluoro-2-phenethyl-1-phenylpent-3-en-1-ol **3a**.

***anti*-3-Fluoro-2-phenethyl-1-phenylpent-3-en-1-ol (3a).** Prepared from **1a** and benzaldehyde using general procedure A to afford **3a** as a white solid (35.8 mg, 63%): mp 89−91 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.34−7.00 (m, 10 H), 4.79 (dq, J = 38.0 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.60 (d, J = 8.8 Hz, 1H), 2.67−2.61 (m, 1H), 2.45−2.32 (m, 2H), 1.94 (br, 1H), 1.76−1.66 (m, 1H), 1.69 (dd, J = 6.8 Hz, J = 2.0 Hz, 3H), 1.39−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.2 (dd, J = 32.9 Hz, J = 23.7 Hz, 0.05 F), −122.9 (dd, J = 38.0 Hz, J = 28.8 Hz, 0.95 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.9 (d, J = 253.7 Hz), 141.9, 141.6, 128.5, 128.4, 128.3, 128.1, 126.9, 125.8, 104.6 (d, J = 15.3 Hz), 74.7, 50.9 (d, J = 24.8 Hz), 33.3, 29.1, 8.9 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3565, 3445, 3062, 3027, 2924, 2865, 1708, 1602, 1453, 1301, 1188, 1028, 978, 754, 699 cm^{-1}; MS (ESI) m/z 307 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{19}H_{21}FNaO$ $[M + Na]^+$ 307.1474, found 307.1468.

***anti*-1-(Biphenyl-4-yl)-3-fluoro-2-phenethylpent-3-en-1-ol (3b).** Prepared from **1a** and [1,1′-biphenyl]-4-carbaldehyde using general procedure A to afford **3b** as a white solid (43.9 mg, 61%): mp 96−98 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.58−6.90 (m, 14H), 4.75 (dq, J = 38.2 Hz, J = 14.0 Hz, J = 6.8 Hz, 1H), 4.64 (d, J = 8.8 Hz, 1H), 2.70−2.63 (m, 1H), 2.49−2.36 (m, 2H), 2.05 (br, 1H), 1.79−1.72 (m, 1H), 1.70 (dd, J = 6.4 Hz, J = 2.0 Hz, 3H), 1.43−1.37 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.9 (dd, J = 32.4 Hz, J = 23.7 Hz, 0.10 F), −122.7 (dd, J = 36.9 Hz, J = 28.7 Hz, 0.90 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.9 (d, J = 254.2 Hz), 141.6, 141.0, 140.9, 140.8, 128.8, 128.4, 128.3, 127.5, 127.4, 127.2, 127.1, 125.9, 104.7 (d, J = 15.5 Hz), 74.5, 50.9 (d, J = 24.1 Hz), 33.3, 29.1, 9.0 (d, J = 6.9 Hz); IR (thin film) υ_{max} 3565, 3434, 3061, 3027, 2925, 2864, 1708, 1589, 1506, 1488, 1453, 1287, 1029, 871, 748, 696 m^{-1}; MS (ESI) m/z 383 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{25}H_{25}FNaO$ $[M + Na]^+$ 383.1787, found 383.

***anti*-3-Fluoro-2-phenethyl-1-(4-phenoxyphenyl)pent-3-en-1-ol (3c).** Prepared from **1a** and 4-phenoxybenzaldehyde using general procedure A to afford **3c** as a white solid (50.4 mg, 67%): mp 72−74 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.35−6.95 (m, 14 Hz), 4.76 (dq, J = 38.0 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.59 (d, J = 8.8 Hz, 1H), 2.70−2.63 (m, 1H), 2.44−2.30 (m, 2H), 1.95 (br, 1H), 1.77−1.67 (m, 1H), 1.70 (dd, J = 6.8 Hz, J = 2.0 Hz, 3H), 1.41−1.32 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.9 (dd, J = 32.2 Hz, J = 23.69 Hz, 0.06 F), −122.9 (dd, J = 38.1 Hz, J = 28.8 Hz, 0.94 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.8 (d, J = 253.8 Hz), 157.2, 157.1, 141.6, 136.7, 129.8, 128.4, 128.3, 128.2, 125.9, 123.4, 118.9, 118.8, 104.8 (d, J = 15.3 Hz), 74.2, 51.0 (d, J = 24.1 Hz), 33.2, 29.1, 8.9 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3564, 3445, 3061, 3026, 2925, 2865, 1707, 1589, 1505, 1488, 1454, 1243, 1024, 872, 749, 694 cm^{-1}; MS (ESI) m/z 399 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{25}H_{25}FNaO_2$ $[M + Na]^+$ 399.1736, found 399.1731.

***anti*-3-Fluoro-2-phenethyl-1-*p*-tolylpent-3-en-1-ol (3d).** Prepared from **1a** and 4-methylbenzaldehyde using general procedure A to afford **3d** as a white solid (44.8 mg, 75%): mp 90−92 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.25−7.00 (m, 9H), 4.75 (dq, J = 38.2 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.57 (d, J = 9.2 Hz, 1H), 2.68−2.61 (m, 1H), 2.45−2.36 (m, 2H), 2.33 (s, 3H), 2.01 (br, 1H), 1.74−1.64 (m, 1H), 1.69 (dd, J = 7.0 Hz, J = 2.0 Hz, 3H), 1.39−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.1 (dd, J = 32.0 Hz, J = 21.4 Hz, 0.05 F), −122.8 (dd, J = 38.2 Hz, J = 29.0 Hz, 0.95 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 158.1 (d, J = 254.5 Hz), 141.7, 138.9, 137.7, 129.2, 128.4, 128.2, 126.9, 125.8, 104.5 (d, J = 16.1 Hz), 74.5, 50.9 (d, J = 24.1 Hz), 33.3, 29.1, 21.2, 89 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3366, 3059, 3024, 2999, 2924, 2861, 1713, 1600, 1515, 1495, 1452, 1308, 823, 756, 697 cm^{-1}; MS (ESI) m/z 321 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{23}FNaO$ $[M + Na]^+$ 321.1631, found 321.1625.

***anti*-3-Fluoro-2-phenethyl-1-*m*-tolylpent-3-en-1-ol (3e).** Prepared from **1a** and 3-methylbenzaldehyde using general procedure A to afford **3e** as a white solid (38.2 mg, 64%): mp 47−49 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.24−6.99 (m, 9H), 4.75 (dq, J = 38.0 Hz, J = 13.8 Hz, J = 7.2 Hz, 1H), 4.56 (d, J = 9.2 Hz, 1H), 2.68−2.61 (m, 1H), 2.45−2.34 (m, 2H), 2.32 (s, 3H), 1.90 (br, 1H), 1.75−1.66 (m, 1H), 1.69 (dd, J = 6.8 Hz, J = 2.0 Hz, 3H), 1.39−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.4 (dd, J = 32.0 Hz, J = 22.8 Hz, 0.05 F), −123.2 (dd, J = 38.1 Hz, J = 28.8 Hz, 0.95 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 158.0 (d, J = 254.5 Hz), 141.8, 141.6, 138.2, 128.8, 128.4, 128.3, 128.2, 127.6, 125.8, 124.2, 104.6 (d, J = 15.3 Hz), 74.7, 50.8 (d, J = 24.0 Hz), 33.2, 29.0, 21.4, 8.9 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3566, 3447, 3060, 3026, 2924, 2865, 1707, 1605, 1495, 1453, 1380, 1296, 1030, 978, 787, 749, 699 cm^{-1}; MS (ESI) m/z 321 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{23}FNaO$ $[M + Na]^+$ 321.1631, found 321.1625.

***anti*-3-Fluoro-2-phenethyl-1-*o*-tolylpent-3-en-1-ol (3f).** Prepared from **1a** and 2-methylbenzaldehyde using general procedure A to afford **3f** as a colorless oil (32.8 mg, 55%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.27−6.99 (m, 9H), 4.93 (d, J = 9.2 Hz, 1H), 4.73 (dq, J = 37.8 Hz, J = 13.8 Hz, J = 6.8 Hz, 1H), 2.70−2.63 (m, 1H), 2.51−2.36 (m, 2H), 2.31 (s, 3H), 1.85 (br, 1H), 1.83−1.73 (m, 1H), 1.70 (dd, J = 6.8 Hz, J = 2.4 Hz, 3H), 1.39−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.8 (dd, J = 30.7 Hz, J = 23.7 Hz, 0.04 F), −122.9 (dd, J = 37.5 Hz, J = 28.8 Hz, 0.96 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.9 (d, J = 255.0 Hz), 141.5, 140.0, 135.7, 130.5, 128.4, 128.3, 127.6, 126.4, 126.3, 125.9, 104.7 (d, J = 16.1 Hz), 70.4, 50.6 (d, J = 24.1 Hz), 33.3, 28.6, 19.5, 8.9 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3564, 3454, 3062, 3026, 2925, 2865, 1707, 1603, 1495, 1454, 1380, 1300, 979, 799, 756, 699 cm^{-1}; MS (ESI) m/z 321 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{23}FNaO$ $[M + Na]^+$ 321.1631, found 321.1625.

***anti*-3-Fluoro-1-(4-methoxyphenyl)-2-phenethylpent-3-en-1-ol (3g).** Prepared from **1a** and 4-methoxybenzaldehyde using general procedure A to afford **3g** as a white solid (44.6 mg, 71%): mp 66−68 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.24−6.83 (m, 9H), 4.75 (dq, J = 38.0 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.55 (d, J = 9.2 Hz, 1H), 3.79 (s, 3H), 2.68−2.60 (m, 1H), 2.42−2.29 (m, 2H), 1.99 (br, 1H), 1.72−1.63 (m, 1H), 1.69 (dd, J = 6.8 Hz, J = 1.2 Hz, 3H), 1.37−1.28 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.1 (dd, J = 31.9 Hz, J = 22.6 Hz, 0.06 F), −122.8 (dd, J = 38.2 Hz, J = 28.8 Hz, 0.94 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 159.4, 158.1 (d, J = 254.4 Hz), 141.7, 134.1, 128.3, 128.2, 128.1,

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125.8, 113.9, 104.5 (d, J = 15.3 Hz), 74.2, 55.3, 51.0 (d, J = 24.8 Hz), 33.3, 29.1, 8.9 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3461, 3061, 3026, 2928, 2865, 2836, 1708, 1611, 1585, 1515, 1454, 1249, 835, 750, 700 cm^{-1}; MS (ESI) m/z 337 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{23}FNaO_2$ $[M + Na]^+$ 337.1580, found 337.1574.

***anti*-3-Fluoro-1-(2-methoxyphenyl)-2-phenethylpent-3-en-1-ol (3h).** Prepared from **1a** and 2-methoxybenzaldehyde using general procedure A to afford **3h** as a colorless oil (34.6 mg, 55%): ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.26−6.83 (m, 9H), 4.86 (d, J = 8.8 Hz, 1H), 4.64 (dq, J = 38.0 Hz, J = 13.6 Hz, J = 7.2 Hz, 1H), 3.73 (s, 3H), 2.70−2.50 (m, 2H), 2.45−2.34 (m, 1H), 2.28 (br, 1H), 1.84−1.75 (m, 1H), 1.66 (dd, J = 6.8 Hz, J = 2.0 Hz, 1H), 1.45−1.37 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.3 (dd, J = 33.6 Hz, J = 22.6 Hz, 0.10 F), −121.9 (dd, J = 37.7 Hz, J = 29.9 Hz, 0.90 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 158.6 (d, J = 255.0 Hz), 156.9, 141.9, 130.1, 128.7, 128.4, 128.3, 128.2, 125.7, 120.8, 110.7, 103.7 (d, J = 16.3 Hz), 71.7, 55.2, 49.3 (d, J = 23.3 Hz), 33.3, 29.5, 8.9 (d, J = 6.8 Hz); IR (thin film) υ_{max} 3565, 3459, 3061, 3026, 2936, 2864, 2837, 1707, 1601, 1588, 1493, 1455, 1241, 1029, 797, 754, 699 cm^{-1}; MS (ESI) m/z 337 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{23}FNaO_2$ $[M + Na]^+$ 337.1580, found 337.1574.

***anti*-1-(4-Bromophenyl)-3-fluoro-2-phenethylpent-3-en-1-ol (3i).** Prepared from **1a** and 4-bromobenzaldehyde using general procedure A to afford **3i** as a white solid (44.3 mg, 61%): mp 80−82 °C; ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.46−7.00 (m, 9H), 4.72 (dq, J = 37.8 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.56 (d, J = 8.8 Hz, 1H), 2.69−2.62 (m, 1H), 2.43−2.26 (m, 2H), 1.95 (br, 1H), 1.77−1.71 (m, 1H), 1.68 (dd, J = 7.0 Hz, J = 2.0 Hz, 3H), 1.39−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.9 (dd, J = 32.4 Hz, J = 22.6 Hz, 0.10 F), −122.6 (dd, J = 38.1 Hz, J = 28.8 Hz, 0.90 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.5 (d, J = 254.4 Hz), 141.4, 140.9, 131.6, 128.6, 128.3, 125.9, 121.8, 105.0 (d, J = 15.3 Hz), 74.1, 50.9 (d, J = 24.1 Hz), 33.2, 28.9, 8.9 (d, J = 7.3 Hz); IR (thin film) υ_{max} 3564, 3444, 3061, 3026, 2925, 2864, 1706, 1602, 1488, 1453, 1406, 832, 749, 719, 699 cm^{-1}; MS (ESI) m/z 385 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{19}H_{20}BrFNaO$ $[M + Na]^+$ 385.0579, found 385.0574.

***anti*-1-(4-Chlorophenyl)-3-fluoro-2-phenethylpent-3-en-1-ol (3j).** Prepared from **1a** and 4-chlorobenzaldehyde using general procedure A to afford **3j** as a white solid (40.2 mg, 57%): mp 78−80 °C; ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.31−6.99 (m, 9H), 4.72 (dq, J = 37.8 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.58 (d, J = 8.8 Hz, 1H), 2.69−2.62 (m, 1H), 2.43−2.26 (m, 2H), 2.00 (br, 1H), 1.76−1.71 (m, 1H), 1.68 (dd, J = 6.8 Hz, J = 2.0 Hz, 3H), 1.38−1.30 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.8 (dd, J = 30.3 Hz, J = 22.8 Hz, 0.10 F), −122.5 (dd, J = 36.0 Hz, J = 28.8 Hz, 0.90 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.5 (d, J = 255.2 Hz), 141.4, 140.4, 133.7, 128.6, 128.4, 128.3, 125.9, 105.0 (d, J = 14.6 Hz), 74.0, 50.9 (d, J = 24.1 Hz), 33.2, 29.0, 8.9 (d, J = 7.3 Hz); IR (thin film) υ_{max} 3565, 3455, 3062, 3026, 2925, 2865, 1706, 1601, 1493, 1454, 1387, 1089, 834, 750, 699 cm^{-1}; MS (ESI) m/z 341 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{19}H_{20}ClFNaO$ $[M + Na]^+$ 341.1084, found 341.1079.

***anti*-3-Fluoro-1-(naphthalen-2-yl)-2-phenethylpent-3-en-1-ol (3m).** Prepared from **1a** and 2-naphthaldehyde using general procedure A to afford **3m** as a white solid (44.1 mg, 66%): mp 63−65 °C; ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.82−6.95 (m, 12H), 4.84−4.69 (m, 2H), 2.68−2.61 (m, 1H), 2.56−2.34 (m, 2H), 2.06 (br, 1H), 1.80−1.71 (m, 1H), 1.70 (dd, J = 6.8 Hz, J = 2.0 Hz, 3H), 1.41−1.33 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.0 (dd, J = 32.6 Hz, J = 21.7 Hz, 0.07 F), −122.9 (dd, J = 37.8 Hz, J = 28.8 Hz, 0.93 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.9 (d, J = 255.2 Hz), 141.5, 139.3, 133.3, 133.2, 128.4, 128.3, 128.1, 127.7, 126.4, 126.2, 126.1, 125.9, 124.5, 104.8 (d, J = 16.1 Hz), 74.9, 50.8 (d, J = 24.8 Hz), 33.3, 29.2, 9.0 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3565, 3445, 3058, 3026, 2924, 2864, 1707, 1602, 1568, 1496, 1453, 1360, 978, 859, 819, 746, 699 cm^{-1}; MS (ESI) m/z 357 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{23}H_{23}FNaO$ $[M + Na]^+$ 357.1631, found 357.1625.

***anti*-3-Fluoro-1-(furan-2-yl)-2-phenethylpent-3-en-1-ol (3n).** Prepared from **1a** and furan-2-carbaldehyde using general procedure A to afford **3n** as a yellow oil (38.4 mg, 70%): ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.38−6.23 (m, 8H), 4.77 (dq, J = 38.0 Hz, J = 13.6 Hz, J = 6.8 Hz, 1H), 4.66 (d, J = 9.6 Hz, 1H), 2.71−2.57 (m, 2H), 2.48−2.41 (m, 1H), 1.92 (br, 1H), 1.80−1.72 (m, 1H), 1.68 (dd, J = 7.0 Hz, J = 2.0 Hz, 3H), 1.44−1.36 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −118.8 (dd, J = 32.0 Hz, J = 23.7 Hz, 0.08 F), −124.3 (dd, J = 37.5 Hz, J = 27.9 Hz, 0.92 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.5 (d, J = 253.8 Hz), 154.2, 142.3, 141.6, 128.4, 128.3, 125.9, 110.2, 108.0, 104.8 (d, J = 15.3 Hz), 68.1, 48.6 (d, J = 24.8 Hz), 33.2, 29.3, 8.9 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3467, 3084, 3061, 3026, 2924, 2864, 1708, 1603, 1496, 1453, 740, 700 cm^{-1}; MS (ESI) m/z 297 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{17}H_{19}FNaO_2$ $[M + Na]^+$ 297.1267, found 297.1261.

***anti*-2-(1-Fluoroprop-1-enyl)-1-phenylnonan-1-ol (3o).** Prepared from **1b** and benzaldehyde using general procedure A to afford **3o** as a white solid (31.2 mg, 56%): mp 42−45 °C; ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.36−7.24 (m, 5H), 4.71 (dq, J = 37.6 Hz, J = 13.6 Hz, J = 7.2 Hz, 1H), 4.56 (d, J = 8.8 Hz, 1H), 2.40−2.27 (m, 1H), 2.08 (br, 1H), 1.65 (dd, J = 6.6 Hz, J = 2.0 Hz, 3H), 1.43−0.90 (m, 12H), 0.84 (t, J = 6.8 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.9 (dd, J = 32.4 Hz, J = 23.7 Hz, 0.11 F), −122.7 (dd, J = 37.5 Hz, J = 28.7 Hz, 0.89 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 158.3 (d, J = 255.2 Hz), 142.3, 128.4, 127.9, 126.9, 126.8, 104.0 (d, J = 15.3 Hz), 74.8, 51.6 (d, J = 24.1 Hz), 31.8, 29.2, 29.1, 27.6, 27.2, 22.6, 14.0, 8.8 (d, J = 6.6 Hz); IR (thin film) υ_{max} 3445, 3026, 2926, 2857, 1708, 1607, 1455, 1305, 1043, 789, 761, 700 cm^{-1}; MS (ESI) m/z 301 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{18}H_{27}FNaO$ $[M + Na]^+$ 301.1944, found 301.1938.

***anti*-2-Benzyl-3-fluoro-1-phenylpent-3-en-1-ol (3p).** Prepared from **1c** and benzaldehyde using general procedure A to afford **3p** as a colorless oil (24.3 mg, 45%): ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.40−6.98 (m, 10H), 4.70 (d, J = 8.4 Hz, 1H), 4.44 (dq, J = 38.2 Hz, J = 14.0 Hz, J = 7.2 Hz, 1H), 2.72−2.42 (m, 3H), 2.04 (br, 1H), 1.51 (dd, J = 6.8 Hz, J = 2.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.8 (dd, J = 31.3 Hz, J = 23.7 Hz, 0.14 F), −121.7 (dd, J = 37.5 Hz, J = 27.9 Hz, 0.86 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.1 (d, J = 253.0 Hz), 142.1, 139.5, 128.9, 128.6, 128.2, 126.9, 126.1, 105.0 (d, J = 16.0 Hz), 74.5, 54.1 (d, J = 24.0 Hz), 34.5, 8.8 (d, J = 7.3 Hz); IR (thin film) υ_{max} 3565, 3445, 3085, 3062, 3028, 2923, 2865, 1708, 1603, 1494, 1454, 1386, 763, 700 cm^{-1}; MS (ESI) m/z 293 $[M + Na]^+$; HRMS (ESI-FT) Calculated for $C_{18}H_{19}FNaO$ $[M + Na]^+$ 293.1318, found 293.1312.

Gerneral Procedure B for the Nickel-Catalyzed Coupling of Electron-Deficient Aldehydes with α-Halo-β, β-difluoropropene-Containing Compounds. To a solution of $Ni(acac)_2$ (5.1 mg, 10 mol %), PCy_2-Ph (11.0 mg, 20 mol %) in THF (2 mL) was added (3-bromo-4,4-difluorohex-5-en-1-yl)benzene **1a** (55.0 mg, 0.2 mol) in THF (1 mL) and $ZnEt_2$ (0.6 mL of 1.0 M hexane solution, 0.6 mmol). The resulting mixture was stirred for an additional 1 h. Then 4-(trifluoromethyl)benzaldehyde (69.6 mg, 0.4 mmol) and $ZnEt_2$ (0.9 mL of 1.0 M hexane solution, 0.9 mmol) were added dropwise to the resulting mixture. The reaction mixture was stirred at room temperature for an additional 1.5 h. The reaction was quenched with 2 mL of 1 M HCl. The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 2 mL). The combined organic extracts were washed with brine (5 mL) and then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give 3-fluoro-2-phenethyl-1-(4-(trifluoromethyl)phenyl)pent-3-en-1-ol **3k**.

***anti*-3-Fluoro-2-phenethyl-1-(4-(trifluoromethyl)phenyl)-pent-3-en-1-ol (3k).** Prepared from **1a** and 4-(trifluoromethyl)-benzaldehyde using general procedure B to afford **3k** as a white solid (40.2 mg, 57%): mp 57−59 °C; ^1H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.58−6.98 (m, 9H), 5.45−4.64 (m, 2H), 2.82−2.29 (m, 3H), 2.20 (br, 1H), 1.91−1.71 (m, 1H), 1.68 (dd, J = 6.8 Hz, J = 2.4 Hz, 1.9H), 1.39 (dd, J = 7.0 Hz, J = 2.4 Hz, 1.1H), 1.49−1.31 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −62.0 (s, 8.4F), −117.3 (dd, J = 31.6 Hz, J = 23.7 Hz, 0.36 F), −122.0 (dd, J = 37.5 Hz, J = 27.6 Hz,

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0.64 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.5 (d, J = 245.7 Hz), 157.3 (d, J = 254.5 Hz), 146.1, 145.9, 141.3, 141.2, 130.2 (q, J = 32.8 Hz, J = 29.9 Hz), 128.4, 128.3, 127.3, 127.1, 126.1, 126.0, 125.4 (t, J = 3.0 Hz), 124.2 (t, J = 269.7 Hz), 105.6 (d, J = 23.4 Hz), 105.3 (d, J = 15.3 Hz), 74.7, 74.2, 50.8 (d, J = 24.1 Hz), 45.6 (d, J = 24.8 Hz), 33.2, 33.1, 29.0, 28.9, 10.2 (d, J = 9.5 Hz), 8.9 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3444, 3063, 3028, 2928, 2867, 1705, 1620, 1603, 1496, 1454, 1420, 1327, 1125, 845, 748, 700 cm^{-1}; MS (ESI) m/z 375 [M + Na]$^+$; HRMS (ESI-FT) Calculated for $C_{20}H_{20}F_4NaO$ [M + Na]$^+$ 375.1348, found 375.1343.

Methyl 4-(*anti*-3-Fluoro-1-hydroxy-2-phenethylpent-3-enyl)benzoate (3l). Prepared from **1a** and methyl 4-formylbenzoate using general procedure B to afford **3l** as a colorless oil (37.0 mg, 54%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 8.00−6.98 (m, 9H), 5.45−4.64 (m, 2H), 3.91 (s, 3H), 2.84−2.74 (m, 1H), 2.43−2.26 (m, 2H), 2.19 (br, 1H), 1.91−1.72 (m, 1H), 1.68 (dd, J = 6.8 Hz, J = 2.0 Hz, 2.4H), 1.40 (dd, J = 7.2 Hz, J = 2.0 Hz, 0.6H), 1.49−1.30 (m, 1H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −117.7 (dd, J = 31.0 Hz, J = 23.7 Hz, 0.22 F), −122.4 (dd, J = 37.1 Hz, J = 28.8 Hz, 0.78 F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 157.7 (d, J = 244.2 Hz), 157.4 (d, J = 254.5 Hz), 147.3, 147.1, 147.1, 141.3, 141.2, 129.8, 129.7, 129.6, 128.4, 128.3, 126.9, 126.8, 126.0, 125.9, 105.5 (d, J = 23.3 Hz), 105.1 (d, J = 15.3 Hz), 74.8, 74.3, 52.1, 50.9 (d, J = 24.0 Hz), 45.6 (d, J = 24.7 Hz), 33.2, 33.1, 29.1, 29.0, 10.3 (d, J = 10.2 Hz), 8.9 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3488, 3026, 2951, 2925, 2864, 1723, 1611, 1496, 1454, 1436, 1281, 801, 749, 700 cm^{-1}; MS (ESI) m/z 365 [M + Na]$^+$; HRMS (ESI-FT) Calculated for $C_{21}H_{23}FNaO_3$ [M + Na]$^+$ 365.1529, found 365.1523.

(4-Fluorohexa-3,5-dienyl)benzene (2). To a solution of Ni(acac)$_2$ (5.1 mg, 10 mol %), P(O^{i}Pr) (16.6 mg, 40 mol %) in THF (2 mL) was added (3-bromo-4,4-difluorohex-5-en-1-yl)benzene **1a** (55.0 mg, 0.2 mol) in THF (1 mL) at room temperature under argon by syringe. Then $ZnEt_2$ (0.9 mL of 1.0 M hexane solution, 0.9 mmol) was added dropwise to the resulting mixture. The reaction mixture was stirred at room temperature for an additional 2 h. The reaction was quenched with 2 mL of 1 M HCl. The organic layer was separated, and the aqueous layer was extracted with Et_2O (2 × 2 mL). The combined organic extracts were washed with brine (5 mL) and then dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give (4-fluorohexa-3,5-dienyl)benzene **2** as a colorless oil (21.1 mg, 81%): ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.28−7.20 (m, 5H), 6.14−5.97 (m, 1H), 5.44 (d, J = 17.1 Hz, 1H), 5.09 (d, J = 11.1 Hz, 1H), 4.80 (dt, J = 36.6 Hz, J = 6.6 Hz, 1H), 2.69 (d, J = 6.9 Hz, 2H), 2.49 (d, J = 6.9 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −120.1 (dd, J = 27.4 Hz, J = 20.6 Hz, 0.08F), −125.5 (dd, J = 36.1 Hz, J = 26.8 Hz, 0.92F); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 156.7 (d, J = 247.9 Hz), 141.5, 129.0 (d, J = 26.2 Hz), 128.5, 128.4, 126.0, 113.6 (d, J = 4.3 Hz), 110.0 (d, J = 16.0 Hz), 35.4 (d, J = 1.4 Hz), 25.8 (d, J = 4.4 Hz); IR (thin film) υ_{max} 3085, 3062, 2926, 2858, 1675, 1604, 1495, 1453, 1316, 981, 913, 746, 698 cm^{-1}; MS (EI) m/z (%) 176 (M$^+$), 104, 91 (100), 85, 77, 65, 51, 41; HRMS (EI-TOF) Calculated for $C_{12}H_{13}F$ 176.1001, found 176.1001.

(*Z*/*E*)-3-Fluoro-1-(4-methoxyphenyl)-2-phenethylpent-3-en-1-one (4a and 4b). Dess−Martin periodinane (63.6 mg, 1.5 mmol) was added to a solution of **3g** (31.4 mg, 0.1 mmol) in dry CH_2Cl_2 (3 mL) at room temperature under nitrogen and stirred for 1 h. Then the reaction mixture was diluted with ether and poured slowly into a $Na_2S_2O_3$:$NaHCO_3$ (1:1) solution and stirred for 5 min. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (2 × 2 mL). The combined organic extracts were washed with saturated $NaHCO_3$ (5 mL), brine (5 mL) and dried over anhydrous sodium sulfate, filtered and concentrated in vacuo. The residues were purified by column chromatography to give **4a** and **4b** (88.9 mg, 95%).

(*Z*)-3-Fluoro-1-(4-methoxyphenyl)-2-phenethylpent-3-en-1-one (4a). White solid; 83.0 mg, 89% yield: mp 58−60 °C; ^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.89−7.86 (m, 2H), 7.28−7.14 (m, 5H), 6.91−6.87 (m, 2H), 4.72 (dq, J = 37.4 Hz, J = 13.8 Hz, J = 7.2 Hz, 1H), 4.50 (dt, J = 20.0 Hz, J = 7.2 Hz, 1H), 3.83 (s, 3H), 2.67 (t, J = 7.6 Hz, 2H), 2.32−2.08 (m, 2H), 1.57 (dd, J = 6.8 Hz, J = 2.4 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −111.3 (dd, J = 37.5 Hz, J = 20.6 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 195.9, 163.7, 157.5 (d, J = 255.9 Hz), 141.3, 130.9, 129.4, 128.6, 128.5, 126.1, 113.9, 103.1, 55.5, 48.9 (d, J = 25.5 Hz), 44.3, 31.2, 9.0 (d, J = 6.5 Hz); IR (thin film) υ_{max} 3061, 3026, 2933, 2864, 1702, 1678, 1600, 1574, 1496, 1455, 1313, 1261, 1172, 841, 751, 700 cm^{-1}; MS (EI) m/z (%) 312 (M$^+$), 193, 135 (100), 107, 77, 65, 47; HRMS (EI-TOF) Calculated for $C_{20}H_{21}FO_2$ 312.1526, found 312.1526.

(*E*)-3-Fluoro-1-(4-methoxyphenyl)-2-phenethylpent-3-en-1-one (4b). White solid; 5.6 mg, 6% yield: mp 84−86 °C.^{1}H NMR (400 MHz, $CDCl_3$, 293 K, TMS) δ ppm 7.85−6.88 (m, 9H), 5.22 (dq, J = 21.2, J = 14.3 Hz, J = 7.6 Hz, 1H), 4.21 (dq, J = 30.0 Hz, J = 8.4 Hz, J = 6.0 Hz, 1H), 3.86 (s, 3H), 2.80−2.64 (m, 2H), 2.39−2.30 (m, 1H), 2.23−2.14 (m, 1H), 1.56 (dd, J = 7.4 Hz, J = 2.8 Hz, 3H); ^{19}F NMR (282 MHz, $CDCl_3$) δ ppm −110.1 (dd, J = 29.9 Hz, J = 21.2 Hz); ^{13}C NMR (100.7 MHz, $CDCl_3$, 293 K, TMS) δ ppm 195.4, 163.8, 157.1 (d, J = 248.7 Hz), 141.3, 130.5, 129.3, 128.6, 128.5, 126.1, 113.8, 103.2 (d, J = 24.0 Hz), 55.5, 45.9 (d, J = 27.0), 33.2, 29.9, 10.4 (d, J = 9.5 Hz); IR (thin film) υ_{max} 3026, 2926, 2850, 1680, 1600, 1510, 1496, 1455, 1419, 1314, 1260, 1171, 1030, 840, 746, 700 cm^{-1}; MS (EI) m/z (%) 312 (M$^+$), 208, 135 (100), 107, 77, 65, 51; HRMS (EI-TOF) Calculated for $C_{20}H_{21}FO_2$ 312.1526, found 312.1526.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Copies of ^{1}H NMR and ^{13}C NMR spectra of all the new compounds, and crystallographic data for compound **3a** (CIF). 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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