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Enantioselective Pd-catalyzed Allylation of Acyclic α-Fluorinated Ketones

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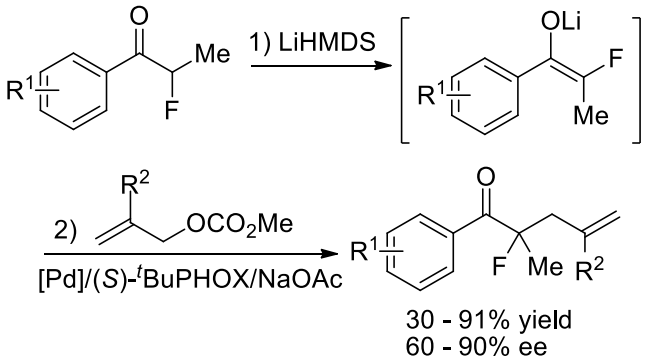


Abstract

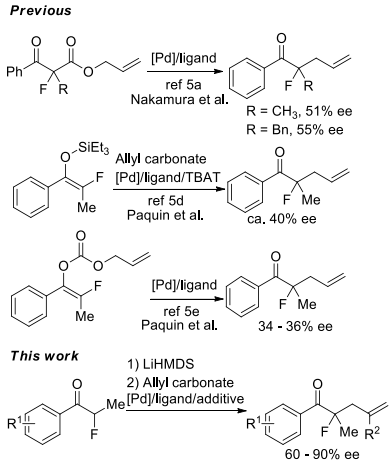
Significant synthetic challenges remain for the asymmetric synthesis of tertiary α-fluoroketones, which are potentially useful molecules for the development of drugs, agrochemicals and functional materials. Herein, we describe the development of a method for the catalytic enantioselective synthesis of tertiary α-fluoroketones via the Tsuji–Trost reaction of racemic acyclic α-fluorinated ketones. Enantioenriched acyclic α-cabonyl tertiary fluorides can be produced with the aid of a palladium/phosphinooxazoline catalyst.

The incorporation of fluorine into organic molecules has been studied extensively during the past few decades as part of the increasing demand for the development of new medicines, agrochemicals and functional materials.[1] Stereodefined tertiary alkyl fluorides possess a range of interesting properties and could potentially be applied across a number of different areas in biomedical science. For example, flurithromycin has been reported to show better bioavailability and metabolic stability properties than the corresponding nonfluorinated analogues.[1a] Although several methods have been developed for the construction of asymmetric tertiary alkyl fluorides, with a large number of these methods involving the installation of a tertiary alkyl fluoride moiety α to a carbonyl group, most of these examples have been carried out using either cyclic or doubly activated ketones.[2-6] In contrast, reports pertaining to enantioselective synthesis of simple α-carbonyl acyclic tertiary fluorides are scarce, with only one example recently appearing in the literature involving the stereoconvergent Negishi arylation of racemic α-bromo-α-fluoroketones, which was reported by Fu et al.[6]

Asymmetric allylic alkylation represents a powerful tool for the construction of asymmetric carbon centers, and has consequently attracted considerable attention from synthetic chemists.[7] In recent years, the groups of Nakamura,[5a] Tunge[5b,h] and Stoltz[5c] have all reported the development of methods for the Pd-catalyzed enantioselective decarboxylative allylation of β-ketoesters to give cyclic tertiary α-fluoroketones. Paquin et al.[5d-g] reported the Pd-catalyzed enantioselective allylation of fluorinated silyl enol ethers or with cyclic fluorinated enol carbonates. These

studies show that the highly enantioselective construction of tertiary α-fluoroketones can be efficiently realized with cyclic substrates. However, in all of the acyclic examples, the products were formed with low enantioselectivity (less than 60% ee obtained) (Scheme 1). Although there are a few successful examples for acyclic non-fluorinated subtrates,[8] the challenge still remains for the construction of asymmetric acyclic tertiary α-fluoroketones, especially those bearing two alkyl substituents. Following on from our recent study involving the development of a method capable of providing access to tertiary alkyl fluorides,[9] it was envisaged that an asymmetric allylic alkylation reaction would allow for the enantioselective formation of acyclic tertiary α-fluoroketones (Scheme 1).

SCHEME 1. Enantioselective allylation of acyclic fluorinated substrates



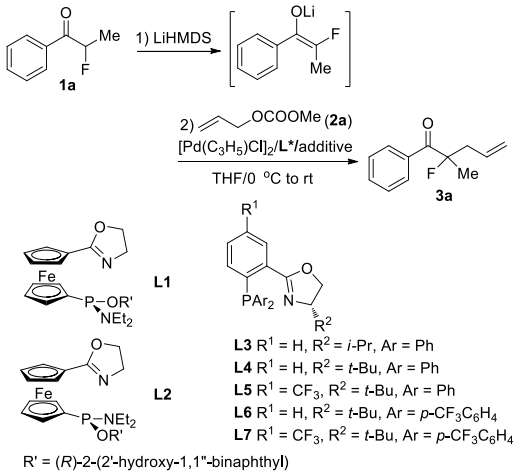
The racemic α-fluoroketone **1a** was converted to the corresponding optically active α-fluoroketone **3a** via an enolate intermediate, which was generated *in situ* by the treatment of **1a** with lithium bis(trimethylsilyl)amide (LiHMDS) in THF. Subsequent treatment of the enolate with **2a** in the presence of a $[Pd(C_3H_5)Cl]_2$ catalyst gave the desired α-fluoroketone product **3a**. This reaction was screened

against a variety of different chiral ligands in THF at temperatures in the range of 0 °C to room temperature over a period of 12 h (Table 1, entries 1–7).

Ligands **L1** and **L2**, which are known as SiocPhos,[10] gave a low ee for the desired product. A series of PHOX ligands were studied. The ee with **L3** was up to 78% (Table 1, entry 3). The best enantioselectivity (84% ee) was given by **L4** with a moderate yield (Table 1, entry 4). When CF_3 was introduced onto the rings of ligands, the ee decreased (Table 1, entries 5 to 7). The reaction was also conducted using sodium bis(trimethylsilyl)amide (NaHMDS) and potassium bis(trimethylsilyl)amide (KHMDS) as the base instead of LiHMDS to investigate the effect of different counter ions on the outcome of the reaction. It was believed that the use of different counter ions would enhance the nucleophilicity of the fluorinated ketone enolate and therefore improve the yield. In practice, although the use of different counter ions did lead to improved yields of 77 and 80% for sodium and potassium, respectively, the enantiomeric excess values of these reactions were much lower at 75 and 69% (Table 1, entries 8 and 9). We then investigated the addition of several additives to the reaction in an attempt to increase the yield without losing selectivity. Molecular sieve were also added to the reaction to remove any moisture from the solvent. Unfortunately, however, this change did not lead to an improvement in the yield (Table 1, entry 10). The addition of ammonium salts to similar reactions has been reported to improve enantioselectivity.[8a] The application of this strategy to the current reaction, however, had no discernible impact on the outcome of the reaction (Table 1, entry 11). Lewis acids have also been reported to have a significant effect on the

outcome of similar reactions.[8a] Unfortunately, however, the addition of silver bromide or lithium chloride to the current reaction led to a reduction in the yield and the selectivity (Table 1, entries 12 and 13). We also investigated the use of several weaker bases including silver carbonate, silver acetate, potassium acetate and sodium acetate (Table 1, entries 14 to 17) in an effort to improve the yield of the reaction. Although the use of these bases led to an increase in the yield of the reaction, they also led to a decrease in the enantiomeric excess values. The weak base, sodium acetate, provided the best selectivity (Table 1, entry 17). A wide variety of other conditions were also screened, including different solvents as well as the ratio of Pd to the ligand, and this information can be found in the Supporting Information.

TABLE 1. Selected conditions for the enantioselective allylation of acyclic fluorinated ketones **1a**



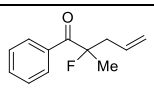
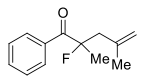
Entry[a]	L*	Additive	Yield (%)[b]	Ee (%)
1	**L1**	-	10[c]	9
2	**L2**	-	68[c]	21
3	**L3**	-	69	78
4	**L4**	-	60	84
5	**L5**	-	60	75
6	**L6**	-	74	78
7	**L7**	-	68	52
8[d]	**L4**	-	77	75
9[e]	**L4**	-	80	69
10	**L4**	4Å MS[f,g]	66	78
11	**L4**	$^{n}Bu_4NBr$[f]	50	82
12	**L4**	AgBr[f]	53	56
13	**L4**	LiCl[f]	44	67
14	**L4**	Ag_2CO_3[f]	70	71
15	**L4**	AgOAc[f]	89	12
16	**L4**	KOAc[f]	77	76
17	**L4**	NaOAc[f]	86	78

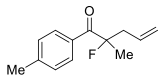
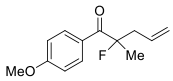
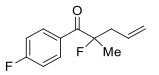
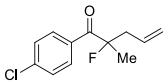
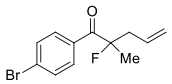
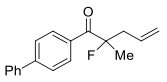
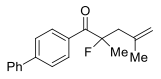
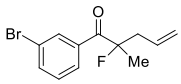
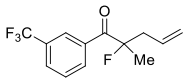
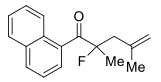
[a]Reaction conditions: 0.2 mmol **1a**, 0.22 mmol **2a**, 1.2 equivalents of LiHMDS, 1.25 mol% $[Pd(C_3H_5)Cl]_2$, 3.1 mol% **L***, 2 mL anhydrous THF, 0 °C to rt, 12 h. [b]Isolated yield. [c]Yield determined by ^{19}F NMR.

[d]NaHMDS instead of LiHMDS. [e]KHMDS instead of LiHMDS. [f]10 mol% additive was added. [g]MS = molecular sieve.

The conditions outlined in entry 17 of Table 1 were identified as the optimum conditions and used to evaluate the substrate scope of the reaction (Table 2). Substrates bearing a *para* substituent on the phenyl group of the starting ketone afforded the corresponding products (**3c–h**) in 57–91% yield with enantiomeric excess values range of 73–82% (Table 2, entries 3–8). Surprisingly, substrates bearing a *meta* substituent on the phenyl group of the ketone gave higher enantiomeric excess values (**3j**, 86% ee and **3k**, 85% ee) than those bearing a *para* substituent (Table 2, entries 10 and 11). A wide variety of functional groups, including methyl, methoxy, aryl fluoride/chloride/bromide and trifluoromethyl groups were well tolerated under the optimized reaction conditions. However, the yield and the ee value were 30 and 60% in the case with a naphthyl substituent (Table 2, entry 12). The reaction of **1a** with methyl 2-methylprop-2-enyl carbonate (**2b**) gave product **3b** in 84% yield with 88% ee (Table 2, entry 2). It is noteworthy that **3i** was synthesized with an ee value of 90%, which is, to the best of our knowledge, the best ee ever reported for an acyclic tertiary α-fluoroketones from an enantioselective allylic alkylation reaction (Table 2, entry 9).

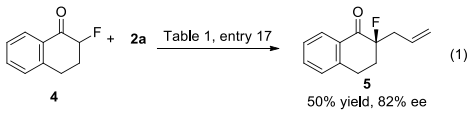
TABLE 2. Enantioselective construction of acyclic tertiary α-fluoroketones by a Pd-catalyzed allylic alkylation

Entry	Product		Yield	Ee (%)[b]
1		**3a**	86	78
2		**3b**	84	88

3		**3c**	88	73[c]
4		**3d**	74	77[c]
5		**3e**	83	77[c]
6		**3f**	88	82[c]
7		**3g**	91	84
8		**3h**	57	82
9		**3i**	44	90
10		**3j**	74	86[c]
11		**3k**	93	85[c]
12		**3l**	30	60

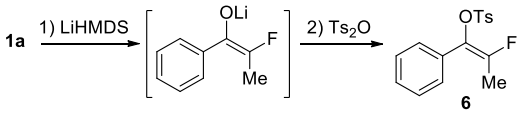
[a]Isolated yield. [b]Determined by chiral HPLC. [c]Ee was determined by chiral HPLC after Wacker oxidation.

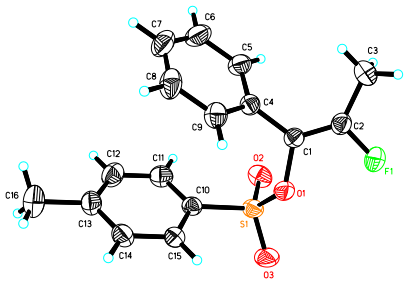
It is known that cyclic ketones always give a good level of selectivity, whereas acyclic ketones give much lower levels of enantioselectivity (Scheme 1).[5a,d,e] Nakamura attributed the low selectivity of acyclic ketones to the formation of an *E*/*Z* mixture of the palladium enolate *in situ*.[5a] Paquin also made a similar suggestion that the poor selectivity of acyclic ketones may be related to the fact that the initially formed *Z* palladium enolate rapidly equilibrates to an *E*/*Z* mixture prior to the actually allylation reaction.[5e] In this current study, the allylation of acyclic fluorinated ketones with **2a** gave an average selectivity of 80% (Table 1). Interestingly, the reaction of the cyclic fluoroketone **4** under the same conditions gave product **5** 82% ee (eq 1), which was a very similar value to that observed for the acyclic examples.[5d] This observation implied that our conditions provided a very high level



of *Z*/*E* selectivity for the generation of the acyclic enolate, as well as high selectivity for the cyclic example. To confirm the stereochemistry of this step, we observed the *Z*/*E* ratio of the *in situ* generated enolate of **1a** by ^{19}F NMR spectroscopy, and found that the use of LiHMDS as a base led to a higher *Z*/*E* ratio of the enolate isomers (> 20:1) than NaHMDS or KHMDS. The *Z*/*E* ratio can be used to explain the changes in the selectivity caused by these three strong bases (Table 1, entries 4, 8 and 9). These results therefore confirm that changes in the *Z*/*E* ratio of the *in situ* generated enolate have a significant impact on the selectivity. Finally, we used 4-methylbenzenesulfonic anhydride (Ts_2O) to trap the enolate, and the main product was isolated as a solid. The isolated product was determined to be in the *Z* configuration by single crystal X-ray analysis (Scheme 2).

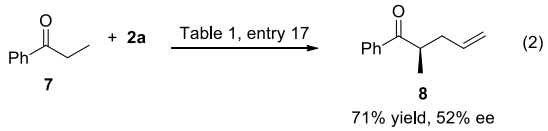
SCHEME 2. Trapping the *in situ* generated enolate with 4-methylbenzenesulfonic anhydride





The current reaction can also be applied to non-fluorinated ketones **7**, but the

selectivity was moderate (eq 2). Trost et al.[8b] reported the use of a *Z*/*E* enol carbonate to give allylic α-alkylated ketone, and found that the starting *Z*/*E* value had a significant influence on the enantioselectivity and rate of the reaction. The results of this study would therefore suggest that our current conditions would be unsuitable for non-fluorinated compounds, because the *Z*/*E* values of the *in situ* generated non-fluorinated enolates by LiHMDS would not be as high as those observed for the fluorinated compounds. This also implied that the highly electron withdrawing fluorine was having a positive influence on the selectivity of the reaction.



7 8

71% yield, 52% ee

The absolute configuration was assigned as *R* based on a comparison of the optical rotation value of an existing product **3a**.[5a]

Although the selectivity of our study was slightly lower than that encountered for the cyclic ketone substrates, the best enantiomeric excess was 90%, representing the best selectivity reported to date for the asymmetric Pd-catalyzed allylation of acyclic α-fluoroketones. Furthermore, the current reaction has several notable characteristics, including (1) the reaction directly used ketones through a formal C-H functionalization without the need for the pre-formation of the corresponding allylic enol carbonates, allylic β-ketoesters or silyl enol ethers; and (2) it can be used to introduce an allylic alkyl group, which can be used as a handle for further modification.

In summary, we have developed a method for asymmetric synthesis of acyclic

α-carbonyl tertiary alkyl fluorides. The enantioselectivity of this palladium-catalyzed allylation of acyclic α-fluoroketones reached 90% ee. The configuration of *in situ* generated enolate intermediate was determined to be *Z*, which was helpful for understanding the good selectivity observed in the reaction, and the presence of a fluorine atom in the starting material had a positive effect on the selectivity.

Experimental Section

General experiment details All reagents were comercially available and used without further purification. All reactions were carried out under nitrogen atmosphere. All solvents were purified according to standard methods prior to use. Melting points were determined by differential scanning calorimetry (DSC) measurements.NMR spectra were obtained on 400 MHz spectrometers and recorded at 25 °C. Chemical shifts for ^{1}H NMR spectra are reported in ppm downfield from TMS, chemical shifts for ^{13}C NMR spectra are recorded in ppm relative to internal chloroform (δ 77.0 ppm for ^{13}C), and chemical shifts for ^{19}F NMR are reported in ppm downfield from fluorotrichloromethane ($CFCl_3$). Coupling constants (*J*) are reported in hertz. ^{13}C NMR was broad-band decoupled from hydrogen nuclei. Infrared spectra (IR) were recorded with an infrared spectrometer; absorbance frequencies are given at maximum intensity in cm^{-1}. The mass analyzer type uesd for the HRMS is time of flight mass spectrometry (TOF-MS) or Fourier transform ion cyclotron resonance mass spectrometry (FTICR-MS). Column chromatography was performed using silica gel (mesh 300–400). Optical rotation was measured using a 2 mL cell with a 1.0 dm

path length. The following abbreviations are used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, sext = sextet.

General procedure of for the enantioselective allylic alkylation reaction. To a Schlenck tube was added α-fluorinated ketone (0.2 mmol), 1 mL freshly distilled THF under nitrogen atmosphere and cooled down to 0 ^{o}C. LiHMDS (0.24 mL, 1.0 M in THF) was added dropwise. Then the tube was kept at 0 ^{o}C for 1.5 h. $[Pd(C_3H_5)Cl]_2$ (0.0025 mmol) and (S)-*t*-Bu-PHOX (0.0062 mmol) was dissolved in 1 mL freshly distilled anhydrous THF in another Schlenck tube and stirred at room temperature for 1 h. This solution was added to the lithium enolate solution mentioned before. Allyl methyl carbonate (0.22 mmol) and NaOAc (0.02 mmol) was added successively. The reaction was allowed to warm to ambient temperature and reacted overnight. Deionized water was added to the mixture and the organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layer was washed with aqueous saturated NaCl. After drying over Na_2SO_4, the product was purified by column chromatography on silica gel (hexane/Et_2O).

2-Fluoro-2-methyl-1-phenylpent-4-en-1-one (3a). Yield 86% (33 mg). Colorless oil. All spectroscopic data were in agreement with the literature.[5a] Enantiomeric excess was determined by HPLC with a CHIRALCEL PC-3 column [λ = 214 nm; eluent: hexane/isopropanol = 95/5; flow rate: 0.70 mL/min; t_{minor} = 6.64 min, t_{major} = 7.17 min; ee% = 78%].

2-Fluoro-2,4-dimethyl-1-phenylpent-4-en-1-one (3b). Yield 84% (35 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (d, J = 8.0 Hz, 2H), 7.56 (t, J = 7.4

Hz, 1H), 7.44 (dd, J = 8.0, 7.4 Hz, 2H), 4.91 (s, 1H), 4.79 (s, 1H) 2.87 (dd, J = 24.8, 14.4 Hz, 1H), 2.60 (dd, J = 22.8, 14.4 Hz, 1H), 1.77 (s, 3H), 1.66 (d, J = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 201.7 (d, J_{CF} = 26.3 Hz), 139.9, 135.1 (d, J_{CF} = 3.9 Hz), 132.9, 129.8 (d, J_{CF} = 7.8 Hz), 128.2, 116.1, 102.2 (d, J_{CF} = 198.3 Hz), 46.2 (d, J_{CF} = 21.7 Hz), 24.3 (d, J_{CF} = 24.1 Hz), 24.0 (d, J_{CF} = 2.4 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -150.6 (sext, J = 22.6 Hz); IR (neat) v 1686, 1598, 1448, 1267 cm^{-1}; MS (EI) *m/z* 206 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{15}OF$ [M] 206.1107, found 206.1111. Enantiomeric excess was determined by HPLC with a Lux 5u Cellulose-3 Column [λ = 254 nm; eluent: hexane/isopropanol = 90/10; flow rate: 0.70 mL/min; t_{minor} = 6.11 min, t_{major} = 6.78 min; ee% = 88%; $[\alpha]_D^{25}$ -42.8 (*c* 0.90, CH_2Cl_2)].

2-Fluoro-2-methyl-1-(*p*-tolyl)pent-4-en-1-one (3c). Yield 88% (36 mg). Colorless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.5 Hz, 2H), 7.23 (d, J = 8.2 Hz, 2H), 5.85-5.73 (m, 1H), 5.15 (d, J = 4.7 Hz, 1H), 5.12 (s, 1H), 2.91-2.79 (m, 1H), 2.68-2.56 (m, 1H), 2.39 (s, 3H), 1.63 (d, J = 21.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5 (d, J_{CF} = 25.7 Hz), 144.0, 132.2 (d, J_{CF} = 3.9 Hz), 131.2 (d, J_{CF} = 4.7 Hz), 130.0 (d, J_{CF} = 7.8 Hz), 129.0, 119.7, 101.5 (d, J_{CF} = 183.0 Hz), 43.0 (d, J_{CF} = 22.6 Hz), 23.9 (d, J_{CF} = 24.2 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.4 (sext, J = 21.6 Hz); IR (neat) v 1681, 1607, 1176, 924 cm^{-1}; MS (EI) *m/z* 206 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{15}OF$ [M] 206.1107, found 206.1103. $[\alpha]_D^{26}$ -10.4 (*c* 1.30, CH_2Cl_2).

2-Fluoro-1-(4-methoxyphenyl)-2-methylpent-4-en-1-one (3d). Yield 74% (33 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, J = 8.4 Hz, 2H), 6.90 (d, J = 8.8

Hz, 2H), 5.80-5.77 (m, 1H), 5.16 (d, J = 5.6 Hz, 1H), 5.13 (s, 1H), 3.87 (s, 3H), 2.90-2.78 (m, 1H), 2.67-2.56 (m, 1H), 1.64 (d, J = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.0 (d, J_{CF} = 25.5 Hz), 163.5, 132.4 (d, J_{CF} = 9.3 Hz), 131.3 (d, J_{CF} = 4.6 Hz), 127.5 (d, J_{CF} = 4.5 Hz), 119.5, 113.5 (d, J_{CF} = 1.5 Hz), 101.6 (d, J_{CF} = 184.4 Hz), 55.4, 43.1 (d, J_{CF} = 21.7 Hz), 23.8 (d, J_{CF} = 23.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -150.9 (sext, J = 21.7 Hz); IR (neat) v 1674, 1600, 1509, 1261, 1170 cm^{-1}; MS (EI) *m/z* 222 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{15}O_2F$ [M] 222.1056, found 222.1055. $[\alpha]_D^{26}$ -16.8 (*c* 0.97 CH_2Cl_2).

2-Fluoro-1-(4-fluorophenyl)-2-methylpentan-1-one (3e). Yield 83% (35 mg). Colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.10 (dd, J = 8.4, 5.6 Hz, 2H), 7.10 (dd, J = 9.2, 8.4 Hz, 2H), 5.83-5.72 (m, 1H), 5.17 (s, 1H), 5.14 (s, 1H), 2.90-2.78 (m, 1H), 2.67-2.56 (m, 1H), 1.64 (d, J = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.4 (d, J_{CF} = 25.2 Hz), 165.7 (d, J_{CF} = 248.7 Hz), 132.8(d, J_{CF} = 9.3 Hz), 132.7 (d, J_{CF} = 8.6 Hz), 130.9 (d, J_{CF} = 4.7 Hz), 119.9, 115.4 (dd, J_{CF} = 21.7, 1.6 Hz), 101.7 (d, J_{CF} = 185.1 Hz), 43.0 (d, J_{CF} = 22.5 Hz), 23.8 (d, J_{CF} = 24.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -104.8 (m, 1F), -151.4 (sext, J = 21.7 Hz, 1F); IR (neat) v 1685, 1599, 1505 1238, 1159 cm^{-1}; MS (EI) *m/z* 210 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}OF_2$ [M] 210.0856, found 210.0857. $[\alpha]_D^{27}$ -20.1 (*c* 0.83, CH_2Cl_2).

1-(4-Chlorophenyl)-2-fluoro-2-methylpent-4-en-1-one (3f). Yield 88% (40 mg). Colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.99 (d, J = 8.0 Hz, 2H), 7.42 (d, J = 8.0 Hz, 2H), 5.82-5.71 (m, 1H), 5.17 (s, 1H), 5.14 (s, 1H), 2.89-2.77 (m, 1H), 2.67-2.55 (m, 1H), 1.64 (d, J = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9 (d, J_{CF} =

26.3 Hz), 139.6, 133.1 (d, J_{CF} = 3.9 Hz), 131.4 (d, J_{CF} = 8.6 Hz), 130.9 (d, J_{CF} = 4.7 Hz), 128.6 (d, J_{CF} = 1.5 Hz), 120.0, 101.7 (d, J_{CF} = 185.2 Hz), 43.0 (d, J_{CF} = 22.4 Hz), 23.8 (d, J_{CF} = 24.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.8 (sext, J = 21.7 Hz); IR (neat) v 1687, 1588, 1092, 988 cm^{-1}; MS (EI) *m/z* 226 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}OFCl$ [M] 226.0561, found 226.0559. $[\alpha]_D^{26}$ -14.2 (*c* 1.30, CH_2Cl_2).

1-(4-Bromophenyl)-2-fluoro-2-methylpent-4-en-1-one (3g). Yield 91% (49 mg). Colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$) δ 7.91 (d, J = 8.0 Hz, 2H), 7.59 (d, J = 9.2 Hz, 2H), 5.82-5.71 (m, 1H), 5.17 (s, 1H), 5.14 (d, J = 3.2 Hz, 1H), 2.89-2.77 (m, 1H), 2.67-2.55 (m, 1H), 1.64 (d, J = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.1 (d, J_{CF} = 25.5 Hz), 133.5 (d, J_{CF} = 3.9 Hz), 131.7, 131.4 (d, J_{CF} = 8.5 Hz), 130.9 (d, J_{CF} = 4.6 Hz), 128.4, 120.0, 101.7 (d, J_{CF} = 184.4 Hz), 43.0 (d, J_{CF} = 22.5 Hz), 23.8 (d, J_{CF} = 24.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.8 (sext, J = 21.7 Hz); IR (neat) v 1687, 1583, 1073, 986 cm^{-1}; MS (EI) *m/z* 270 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}OFBr$ [M] 270.0056, found 270.0055. Enantiomeric excess was determined by HPLC with a CHIRALCEL ID3 Column [λ = 214 nm; eluent: hexane/isopropanol = 99/1; flow rate: 0.50 mL/min; t_{minor} = 5.14 min, t_{major} = 4.92 min; ee% = 84%; $[\alpha]_D^{26}$ -10.1 (*c* 0.42, CH_2Cl_2)].

1-([1,1'-Biphenyl]-4-yl)-2-fluoro-2-methylpent-4-en-1-one (3h). Yield 57% (31 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.15 (d, J = 8.4 Hz, 2H), 7.68 (d, J = 8.4 Hz, 2H), 7.64 (d, J = 7.2 Hz, 2H), 7.45 (d, J = 7.2 Hz, 2H), 7.41 (d, J = 7.2 Hz, 1H), 5.91-5.79 (m, 1H), 5.20 (d, J = 6.0 Hz, 1H), 5.17 (s, 1H), 2.98-2.86 (m, 1H), 2.74-2.63 (m, 1H), 1.69 (d, J = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.5 (d,

J_{CF} = 25.5 Hz), 145.7, 139.9, 133.5 (d, J_{CF} = 4.4 Hz), 131.2, 131.1, 130.6, 130.5, 128.9, 128.2, 127.3, 126.9, 119.8, 101.7 (d, J_{CF} = 184.5 Hz), 43.1 (d, J_{CF} = 21.9 Hz), 23.9 (d, J_{CF} = 22.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.6 (m); IR (neat) *v* 2984, 1681, 1604, 1246, 1177, 1075, 924 cm^{-1}; MS (EI) *m/z* 268 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{18}H_{17}OF$ [M] 268.1263, found 268.1261. Enantiomeric excess was determined by HPLC with a CHIRALCEL ID3 Column [λ = 214 nm; eluent: hexane/isopropanol = 98/2; flow rate: 0.70 mL/min; t_{minor} = 4.34 min, t_{major} = 4.08 min; ee% = 82%; $[\alpha]_D^{26}$ -5.5 (*c* 1.51, CH_2Cl_2)].

1-([1,1'-Biphenyl]-4-yl)-2-fluoro-2,4-dimethylpent-4-en-1-one (3i). Yield 44% (25 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.13 (d, *J* = 8.0 Hz, 2H), 7.68 (d, *J* = 8.0 Hz, 2H), 7.64 (d, *J* = 7.6 Hz, 2H), 7.48 (t, *J* = 7.6 Hz, 2H), 7.41 (t, *J* = 7.6 Hz, 1H), 4.94 (s, 1H), 4.83 (s, 1H), 2.91 (dd, *J* = 24.8, 14.4 Hz, 1H), 2.64 (dd, *J* = 22.4, 14.4 Hz, 1H), 1.81 (s, 3H), 1.69 (d, *J* = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 201.1 (d, J_{CF} = 26.3 Hz), 145.6, 139.9 (2C), 133.7 (2C), 130.5, 130.4, 128.9, 128.2, 127.3, 126.9, 116.2, 101.7 (d, J_{CF} = 184.5 Hz), 43.1 (d, J_{CF} = 21.9 Hz), 23.9 (d, J_{CF} = 22.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -150.5 (m); IR (neat) *v* 1686, 1642, 1508, 1409, 1242, 1264, 1228, 1175, 1060, 925 cm^{-1}; MS (EI) *m/z* 282 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{19}H_{19}OF$ [M] 282.1423, found 282.1420. Enantiomeric excess was determined by HPLC with a CHIRALCEL AD-RH Column [λ = 220 nm; eluent: acetone/water = 70/30; flow rate: 0.70 mL/min; t_{minor} = 17.06 min, t_{major} = 14.63 min; ee% = 90%; $[\alpha]_D^{26}$ -29.6 (*c* 1.23, CH_2Cl_2)].

1-(3-Bromophenyl)-2-fluoro-2,4-dimethylpent-4-en-1-one (3j). Yield 74% (42 mg).

Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.14 (s, 1H), 7.96 (d, J = 8.0 Hz, 1H), 7.69 (d, J = 7.8 Hz, 1H), 7.33 (t, J = 8.0 Hz, 1H), 5.83-5.71 (m, 1H), 5.18 (s, 1H), 5.15 (d, J = 4.8 Hz, 1H), 2.89-2.77 (m, 1H), 2.67-2.57 (m, 1H), 1.64 (d, J = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 199.9 (d, J_{CF} = 26.4 Hz), 136.6 (d, J_{CF} = 3.8 Hz), 135.9, 132.7 (d, J_{CF} = 8.5 Hz), 130.8 (d, J_{CF} = 4.7 Hz), 129.9 (d, J_{CF} = 1.5 Hz), 128.4 (d, J_{CF} = 8.5 Hz), 122.5, 120.1, 101.6 (d, J_{CF} = 185.2 Hz), 42.9 (d, J_{CF} = 21.7 Hz), 23.8 (d, J_{CF} = 24.0 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -152.1 (sext, J = 21.7 Hz); IR (neat) v 2929, 2844, 1726, 1694, 1254, 1116, 1025 cm^{-1}; MS (EI) m/z 270 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}OBrF$ [M] 270.0056, found 270.0060. $[\alpha]_D^{25}$ -15.1 (c 0.86, CH_2Cl_2).

2-Fluoro-2-methyl-1-(3-(trifluoromethyl)phenyl)pent-4-en-1-one (3k). Yield 93% (48 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (s, 1H), 8.21 (d, J = 8.0 Hz, 1H), 7.81 (d, J = 7.6 Hz, 1H), 7.59 (dd, J = 8.0, 7.6 Hz, 1H), 5.83-5.72 (m, 1H), 5.19 (s, 1H), 5.15 (d, J = 4.0 Hz, 1H), 2.91-2.79 (m, 1H), 2.69-2.58 (m, 1H), 1.67 (d, J = 22.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 200.4 (d, J_{CF} = 27.1 Hz), 135.4 (d, J_{CF} = 3.9 Hz), 133.0 (d, J_{CF} = 7.8 Hz), 131.0 (q, J_{CF} = 31.3 Hz), 130.7 (d, J_{CF} = 4.7 Hz), 129.4 (q, J_{CF} = 3.6 Hz), 128.9 (d, J_{CF} = 1.6 Hz), 126.7 (m), 123.6 (q, J_{CF} = 272.5 Hz), 120.2, 101.7 (d, J_{CF} = 192.9 Hz), 43.0 (d, J_{CF} = 21.7 Hz), 23.8 (d, J_{CF} = 23.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.9 (m, 3F), -152.3 (sext, J = 21.6 Hz, 1F); IR (neat) v 1694, 1334, 1169, 1132, 1076 cm^{-1}; MS (EI) m/z 260 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{12}OF_4$ [M] 260.0824, found 260. 0822. $[\alpha]_D^{25}$ -15.3 (c 0.76, CH_2Cl_2).

2-Fluoro-2,4-dimethyl-1-(naphthalen-1-yl)pent-4-en-1-one (3l). Yield 30% (16

mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 7.6 Hz, 1H), 7.97 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.8 Hz, 1H), 7.82 (dd, J = 7.2, 3.2 Hz, 1H), 7.56-7.47 (m, 3H), 4.94 (d, J = 34.4 Hz, 2H), 2.97 (dd, J = 25.6, 14.4 Hz, 1H), 2.67 (dd, J = 22.8, 14.4 Hz, 1H), 1.81 (s, 3H), 1.74 (d, J = 21.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 206.1 (d, J_{CF} = 22.0 Hz), 140.1, 133.8, 133.7 (d, J_{CF} = 2.2 Hz), 131.7, 130.5, 128.5, 127.5, 127.0 (d, J_{CF} = 10.2 Hz), 126.2, 125.3, 124.0, 116.5, 101.7 (d, J_{CF} = 188.8 Hz), 46.1 (d, J_{CF} = 20.4 Hz), 24.4 (d, J_{CF} = 24.1 Hz), 24.1 (d, J_{CF} = 2.9 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -150.4 (m); IR (neat) ν 1683, 1645, 1507, 1446, 1372, 1235, 1084 cm^{-1}; MS (EI) *m/z* 256 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{17}H_{17}OF$ [M] 256.1263, found 256.1260. Enantiomeric excess was determined by HPLC with a CHIRALCEL PC-3 Column [λ = 214 nm; eluent: hexane/isopropanol = 95/5; flow rate: 0.70 mL/min; t_{minor} = 9.72 min, t_{major} = 9.16 min; ee% = 60%; $[\alpha]_D^{26}$ -10.5 (*c* 0.82, CH_2Cl_2)].

2-allyl-2-fluoro-3,4-dihydronaphthalen-1(2H)-one (5). Yield 50% (21 mg). Colorless oil. All spectroscopic data were in agreement with the literature.[5a] Enantiomeric excess was determined by HPLC with a CHIRALCEL IC column [λ = 214 nm; eluent: hexane/isopropanol = 90/10; flow rate: 0.50 mL/min; t_{minor} =12.21 min, t_{major} = 13.13 min; ee% = 82%].

2-methyl-1-phenylpent-4-en-1-one (8). Yield 50% (21 mg). Colorless oil. All spectroscopic data were in agreement with the literature.[8b] Enantiomeric excess was determined by HPLC with a CHIRALCEL PC-3 column [λ = 214 nm; eluent:

hexane/isopropanol = 90/10; flow rate: 0.50 mL/min; t_{minor} = 6.99 min, t_{major} = 7.45 min; ee% = 52%].

General procedure of for the Wacker oxidation. Product of the enantioselective allylic alkylation (0.2 mmol) was added to a mixture of $PdCl_2$ (0.02 mmol) and $Cu(OAc)_2$ (0.04 mmol) in DMA:H_2O (7:1) (4 mL). The resulting mixture was stirred for 48 h at room temperature under O_2 atmosphere. After that time the reaction mixture was diluted with Et_2O, washed with brine, dried with anhydrous Na_2SO_4. After removal of the solvent, the residue was submitted to column chromatography on silica gel (EtOAc:Hexane, 1:4) giving the corresponding diketone.

2-Fluoro-2-methyl-1-(*p*-tolyl)pentane-1,4-dione (9c, Table 1, entry 3). Yield 71% (32 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94 (d, J = 7.4 Hz, 2H), 7.24 (d, J = 7.4 Hz, 2H), 3.48 (dd, J = 32.5, 17.3 Hz, 1H), 3.03 (dd, J = 17.3, 12.2 Hz, 1H), 2.39 (s, 3H), 2.14 (s, 3H), 1.65 (d, J = 21.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.4, 200.8 (d, J_{CF} = 24.9 Hz), 143.7, 132.2 (d, J_{CF} = 3.9 Hz), 129.9 (d, J_{CF} = 7.8 Hz), 129.0, 99.1 (d, J_{CF} = 188.4 Hz), 52.6 (d, J_{CF} = 22.6 Hz), 30.2, 24.9 (d, J_{CF} = 24.1 Hz), 21.6; ^{19}F NMR (376 MHz, $CDCl_3$) δ -151.4 (m); IR (neat) ν 1718, 1682, 1601, 1364, 1176 cm^{-1}; MS (EI) *m/z* 222 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{15}O_2F$ [M] 222.1056, found 222.1052. Enantiomeric excess was determined by HPLC with a CHIRALCEL AD-H Column [λ = 214 nm; eluent: hexane/isopropanol = 95/5; flow rate: 0.70 mL/min; t_{minor} = 7.23 min, t_{major} = 8.08 min; ee% = 73%; $[\alpha]_D^{27}$ 27.7 (*c* 1.02, CH_2Cl_2)].

2-Fluoro-1-(4-methoxyphenyl)-2-methylpentane-1,4-dione (9d, Table 1, entry 4).

Yield 64% (30 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, J = 8.8 Hz, 2H), 6.93 (d, J = 9.2 Hz, 2H), 3.86 (s, 3H), 3.48 (dd, J = 32.2, 17.4 Hz, 1H), 3.02 (dd, J = 17.2, 12.0 Hz, 1H), 2.15 (s, 3H), 1.66 (d, J = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.5, 199.0 (d, J_{CF} = 24.0 Hz), 163.3, 132.3 (d, J_{CF} = 8.5 Hz), 127.4 (d, J_{CF} = 4.0 Hz), 113.5 (d, J_{CF} = 1.5 Hz), 99.3 (d, J_{CF} = 186.5 Hz), 55.4, 52.4 (d, J_{CF} = 22.5 Hz), 30.3, 24.9 (d, J_{CF} = 23.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -150.7 (m); IR (neat) v 2976, 1723, 1676, 1600, 1572, 1509 cm^{-1}; MS (EI) m/z 238 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{15}O_3F$ [M] 238.1005, found 238.1008. Enantiomeric excess was determined by HPLC with a CHIRALCEL IC Column [λ = 214 nm; eluent: hexane/isopropanol = 80/20; flow rate: 0.70 mL/min; t_{minor} = 25.28 min, t_{major} = 20.98 min; ee% = 77%; $[\alpha]_D^{26}$ 46.5 (c 1.08, CH_2Cl_2)].

2-Fluoro-1-(4-fluorophenyl)-2-methylpentane-1,4-dione (9e, Table 1, entry 5). Yield 72% (34 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (dd, J = 7.8, 5.4 Hz, 2H), 7.13 (dd, J = 8.8, 7.8 Hz, 2H), 3.53 (dd, J = 34.4, 17.6 Hz, 1H), 3.09 (dd, J = 17.6, 10.8 Hz, 1H), 2.16 (s, 3H), 1.65 (d, J = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 199.9 (d, J_{CF} = 24.8 Hz), 165.5 (d, J_{CF} = 253.3 Hz), 132.7(d, J_{CF} = 8.6 Hz), 132.5 (d, J_{CF} = 9.3 Hz), 115.3(dd, J_{CF} = 21.7, 1.5 Hz), 99.0 (d, J_{CF} = 187.5 Hz), 52.9 (J_{CF} = 22.5 Hz), 30.0, 24.8(d, J_{CF} = 23.3 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.5 (m, 1F), -151.6 (m, 1F); IR (neat) v 1721, 1682, 1599, 1505, 1233, 1159 cm^{-1}; MS (EI) m/z 226 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}O_2F_2$ [M] 226.0805, found 226.0800. Enantiomeric excess was determined by HPLC with a CHIRALCEL PC-3 Column [λ = 214 nm; eluent: hexane/isopropanol = 90/10; flow rate: 0.70

mL/min; t_{minor} = 19.63 min, t_{major} = 17.09 min; ee% = 77%; $[\alpha]_D^{26}$ 42.0 (*c* 0.98, CH_2Cl_2)].

1-(4-Chlorophenyl)-2-fluoro-2-methylpentane-1,4-dione (9f, Table 1, entry 6). Yield 67% (32 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 8.4 Hz, 2H), 7.43 (d, *J* = 8.4 Hz, 2H), 3.53 (dd, *J* = 34.6, 17.8 Hz, 1H), 3.10 (dd, *J* = 17.8, 11.0 Hz, 1H), 2.15 (s, 3H), 1.64 (d, *J* = 21.6 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.3, 200.5(d, J_{CF} = 24.8 Hz), 139.2, 133.3 (d, J_{CF} = 4.7 Hz), 131.3 (d, J_{CF} = 8.5 Hz), 128.5 (d, J_{CF} = 1.5 Hz), 99.0 (d, J_{CF} = 187.5 Hz), 53.0 (d, J_{CF} = 22.5 Hz), 30.0, 24.8(d, J_{CF} = 24.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -152.0 (m); IR (neat) *v* 1721, 1686, 1617, 1588, 1488, 1444, 1400, 1366, 1090 cm^{-1}; MS (EI) *m/z* 242 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}O_2FCl$ [M] 242.0510, found 242. 0507. Enantiomeric excess was determined by HPLC with a CHIRALCEL PC-3 Column [λ = 214 nm; eluent: hexane/isopropanol = 90/10; flow rate: 0.70 mL/min; t_{minor} = 18.13 min, t_{major} = 14.28 min; ee% = 84%; $[\alpha]_D^{26}$ 29.2 (*c* 1.15, CH_2Cl_2)].

1-(3-Bromophenyl)-2-fluoro-2-methylpentane-1,4-dione (9j, Table 1, entry 10). Yield 76% (44 mg). Colorless oil. ^{1}H NMR(400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.95 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 8.0 Hz, 1H), 7.33 (t, *J* = 8.0 Hz, 1H), 3.54 (dd, *J* = 35.0, 18.0 Hz, 1H), 3.10(dd, *J* = 18.0, 10.4 Hz, 1H), 2.16 (s, 3H), 1.64 (d, *J* = 20.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 203.2, 200.2 (d, J_{CF} = 25.6 Hz), 136.8, 135.6, 132.6 (d, J_{CF} = 8.6 Hz), 129.8, 128.3 (d, J_{CF} = 8.6 Hz), 122.4, 98.8 (d, J_{CF} = 185.2 Hz), 53.1 (d, J_{CF} = 22.5 Hz), 29.9, 24.7 (d, J_{CF} = 23.2 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -152.4 (m); IR (neat) *v* 1728, 1688, 1562, 1366, 1176, 1100 cm^{-1}; MS (EI) *m/z* 286 $[M]^+$;

HRMS (EI-TOF-MS) calcd for $C_{12}H_{12}O_2FBr$ [M] 286.0005, found 286.0006. Enantiomeric excess was determined by HPLC with a CHIRALCEL AD-H Column [λ = 214 nm; eluent: hexane/isopropanol = 95/5; flow rate: 0.70 mL/min; t_{minor} = 6.68 min, t_{major} = 7.48 min; ee% = 86%; $[\alpha]_D^{26}$ 39.1 (*c* 1.03, CH_2Cl_2)].

2-Fluoro-2-methyl-1-(3-(trifluoromethyl)phenyl)pentane-1,4-dione (9k, Table 1, entry 11). Yield 61% (34 mg). Colorless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.27 (s, 1H), 8.22 (d, *J* = 8.0 Hz, 1H), 7.81 (d, *J* = 8.0 Hz, 1H), 7.60 (t, *J* = 8.0 Hz, 1H), 3.55 (dd, *J* = 35.2, 18.0 Hz, 1H), 3.13 (dd, *J* = 17.8, 10.6 Hz, 1H), 2.17 (s, 3H), 1.66 (d, *J* = 21.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) 203.3, 200.7 (d, J_{CF} = 25.5 Hz), 135.7 (d, J_{CF} = 4.7 Hz), 133.0 (d, J_{CF} = 8.6 Hz), 130.7 (q, J_{CF} = 32.0 Hz),129.1 (q, J_{CF} = 3.6 Hz), 128.8 (d, J_{CF} = 1.5 Hz), 126.6 (m), 98.9 (d, J_{CF} = 187.4 Hz), 53.3 (d, J_{CF} = 22.5 Hz), 29.8, 24.7 (d, J_{CF} = 24.1 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -62.8 (s, 3F), -152.6 (m, 1F); IR (neat) *v* 1722, 1692, 1612, 1335, 1290, 1230, 1169, 1182, 1075 cm^{-1}; MS (EI) *m/z* 276 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{13}H_{12}O_2F_4$ [M] 276.0773, found 276. 0769. Enantiomeric excess was determined by HPLC with a CHIRALCEL ID3 Column [λ = 214 nm; eluent: hexane/isopropanol = 95/5; flow rate: 0.70 mL/min; t_{minor} = 5.59 min, t_{major} = 4.84 min; ee% = 86%; $[\alpha]_D^{26}$ 43.4 (*c* 0.62, CH_2Cl_2)].

The trapping of the enolate ion. To a Schlenck tube was added α-fluoropropiophenone **1a** (0.2 mmol), 1 mL freshly distilled THF under nitrogen atmosphere. The reaction mixture was cooled down to 0 ^{o}C. LiHMDS (0.24 mL, 1.0 M in THF) was added dropwise. After 1.5 h, 4-methylbenzenesulfonic anhydride (0.3 mmol, 1.5 eq) and freshly distlled THF (1 mL) were added. The reaction was allowed

to warm to ambient temperature overnight. Deionized water was added to the mixture and the organic layer was separated. The aqueous layer was extracted with ether, and the combined organic layer was washed with saturated NaCl (aq). After drying over Na_2SO_4, the product was purified by column chromatography on silica gel (hexane/Et_2O).

(*Z*)-2-Fluoro-1-phenylprop-1-en-1-yl 4-methylbenzenesulfonate (6). Yield 55% (34 mg). White solid, m.p. 88.25 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63(d, J = 8.0 Hz, 2H), 7.26 (s, 5H), 7.17 (d, J = 8.0 Hz, 2H), 2.38 (s, 3H), 2.04 (d, J = 18.5 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.3, 150.7, 144.7, 133.7, 131.2 (d, J_{CF} = 2.3 Hz), 130.5, 130.4, 129.3, 128.8, 128.7, 128.2, 128.1, 21.6, 15.1 (d, J_{CF} = 25.8 Hz); ^{19}F NMR (376 MHz, $CDCl_3$) δ -105.7 (q, J = 17.7 Hz); IR (KBr) v 1368, 1230, 1188, 1180, 1084, 1064 790, cm^{-1}; MS (EI) *m/z* 306 $[M]^+$; HRMS (EI-TOF-MS) calcd for $C_{16}H_{15}O_3SF$ [M] 306.0726, found 306.0729.

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Supporting Information Available: Experimental detail and copies of ^{1}H NMR, ^{13}C NMR and ^{19}F NMR spectroscopies for all new compounds and Chiral HPLC analysis This material is available free of charge via Internet at http://pubs.acs.org/.

References and Footnotes

(1) (a) Purser, S.; Moore, P. R.; Swallow, S.; Gouverneur, V. *Chem. Soc. Rev.* **2008**, *37*, 320-330. (b) O'Hagan, D. *J. Fluorine Chem.* **2010**, *131*, 1071-1081. (c) Zhang, C.-P.; Chen, Q.-Y.; Guo, Y.; Xiao, J.-C.; Gu, Y.-C. *Chem. Soc. Rev.*, **2012**, *41*, 4536-4559. (d) Zhang, C.-P.; Chen, Q.-Y.; Guo, Y.; Xiao, J.-C. *Tetrahedron* **2013**, *69*, 10955-10989. (e) Zhang, C.-P.; Chen, Q.-Y.; Guo, Y.; Xiao, J.-C.; Gu, Y.-C. *Coord. Chem. Rev.* **2014**, *261*, 28-72. (f) Uneyama, K. Organofluorine Chemistry; Blackwell: Oxford, U.K., 2006.

(2) For reviews, see: (a) Liang, T.; Neumann, C. N.; Ritter, T. *Angew. Chem., Int. Ed.* **2013**, *52*, 8214-8264. (b) Valero, G.; Companyó, X.; Rios, R. *Chem. Eur. J.* **2011**, *17*, 2018−2037. (c) Cahard, D.; Xu, X., Couve-Bonnaire, S.; Pannecoucke X. *Chem. Soc. Rev.* **2010**, *39*, 558-568. (d) Lectard, S.; Hamashima, Y.; Sodeoka, M. *Adv. Synth. Catal.* **2010**, *352*, 2708-2732. (e) Smith, A. M. R.; Hii, K. K. (M.) *Chem. Rev.* **2011**, *111*, 1637-1656. (f) Shibatomi, K. *Synthesis* **2010**, 2679-2702. (g) Ma, J.-A.; Cahard, D. *Chem. Rev.* **2008**, *108*, PR1-PR43 and **2004**, *104*, 6119-6146.

(3) Selected recent examples of asymmetric electrophilic fluorination to construct a tertiary fluoride: (a) Yang, X.; Phipps, R. J.; Toste, F. D. *J. Am. Chem. Soc.* **2014**, *136*, 5225-5228 and references cited therein. (b) Li, J.; Cai, Y.; Chen, W.; Liu, X.; Lin, L.; Feng, X. *J. Org. Chem.* **2012**, *77*, 9148-9155. (c) Deng, Q.-H.; Wadepohl, H.; Gade, L. H. *Chem. Eur. J.* **2011**, *17*, 14922-14928. (d) Wang, L.; Meng, W.; Zhu, C.-L.; Zheng, Y.; Nie, J.; Ma, J.-A. *Angew. Chem., Int. Ed.* **2011**, *50*, 9442-9446. (e) Kang, S. H.; Kim, D. Y. *Adv. Synth. Catal.* **2010**, *352*, 2783-2786. (f) Reddy, D. S.; Shibata, N.; Nagai, J.; Nakamura, S.; Toru, T.; Kanemasa, S. *Angew. Chem., Int. Ed.* **2008**, *47*,

164-168. (g) Ishimaru, T.; Shibata, N.; Horikawa, T.; Yasuda, N.; Nakamura, S.; Toru, T.; Shiro, M. *Angew. Chem., Int. Ed.* **2008**, *47*, 4157-4161.

(4) Selected recent examples of building block methods to construct a chiral tertiary fluoride: (a) Wu, L.; Falivene, L.; Drinkel, E.; Grant, S.; Linden, A.; Cavallo, L.; Dorta, R. *Angew. Chem., Int. Ed.* **2012**, *51*, 2870-2873. (b) Shibatomi, K.; Futatsugi, K.; Kobayashi, F.; Iwasa, S.; Yamamoto, H. *J. Am. Chem. Soc.* **2010**, *132*, 5625-5627.

(5) Preparation of tertiary alkyl fluorides by Pd-catalyzed allylic alkylation: (a) Nakamura, M.; Hajra, A.; Endo, K.; Nakamura, E. *Angew. Chem., Int. Ed.* **2005**, *44*, 7248-7251. (b) Burger, E. C.; Barron, B. R.; Tunge, J. A. *Synlett* **2006**, 2824-2826. (c) Mohr, J. T.; Behenna, D. C.; Harned, A. M.; Stoltz, B. M. *Angew. Chem., Int. Ed.* **2005**, *44*, 6924-6927. (d) Bélanger, É.; Cantin, K.; Messe, O.; Tremblay, M.; Paquin, J.-F. *J. Am. Chem. Soc.* **2007**, *129*, 1034-1035. (e) Bélanger, É.; Houzé, C.; Guimond, N.; Cantin, K.; Paquin, J.-F. *Chem. Commun.* **2008**, 3251-3253. (f) Bélanger, É.; Pouliot, M.-F.; Paquin, J.-F. *Org. Lett.* **2009**, *11*, 2201-2204. (g) Bélanger, É.; Pouliot, M.-F.; Courtemanche, M.-A.; Paquin, J.-F. *J. Org. Chem.* **2012**, *77*, 317-331. (h) Chattopadhyay, K.; Jana, R.; Day, V. W.; Douglas, J. T.; Tunge, J. A. *Org. Lett.* **2010**, *12*, 3042-3045.

(6) During the preparation of our manuscript, a stereoconvergent Negishi arylation of racemic α-bromo-α-fluoroketones was reported, where an aryl group was enantioselectively introduced to form the tertiary fluoride product. See: Liang, Y.; Fu, G. C. *J. Am. Chem. Soc.* **2014**, *136*, 5520-5524.

(7) Some reviews of asymmetic Pd-catalyzed allylation: (a) Ding, C.-H.; Hou, X.-L. *Top. Organomet. Chem.* **2011**, *36*, 247-286. (b) Lu, Z.; Ma, S. *Angew. Chem., Int. Ed.* **2008**, *47*, 258-297. (c) Mohrand, J. T.; Stoltz, B. M. *Chem. Asian J.* **2007**, *2*, 1476-1491; (d) Trost, B. M.; Van Vranken, D. L. *Chem. Rev.* **1996**, *96*, 395-422.

(8) Asymmetric allylic alkylation of nonfluorinated acyclic carbonyl compounds: (a) Yan, X.-X.; Liang, C.-G.; Zhang, Y.; Hong, W.; Cao, B.-X.; Dai, L.-X.; Hou, X.-L. *Angew. Chem., Int. Ed.* **2005**, *44*, 6544-6546. (b) Trost, B. M.; Xu, J. *J. Am. Chem. Soc.* **2005**, *127*, 17180-17181. (c) Trost, B. M.; Xu, J.; Reichle, M. *J. Am. Chem. Soc.* **2007**, *129*, 282-283. (d) Trost, B. M.; Xu, J.; Schmidt, T. *J. Am. Chem. Soc.* **2008**, *130*, 11852-11853. (e) Evans, P. A.; Clizbe, E. A.; Lawler, M. J.; Oliver, S. *Chem. Sci.* **2012**, *3*, 1835-1838.

(9) (a) Guo, Y.; Tao, G.- H.; Blumenfeld, A.; Shreeve, J. M. *Organometallics* **2010**, 29, 1818-1823. (b) Guo, Y.; Twamley, B.; Shreeve, J. M. *Org. Biomol. Chem.* **2009**, *7*, 1716-1722. (c) Guo, C.; Wang, R.-W.; Guo, Y.; Qing, F.-L. *J. Fluorine Chem.* **2012**, *133*, 86-89. (d) Wang, W.; Chen, Q.-Y.; Guo, Y. *Synlett* **2011**, 2705-2708. (e) Hu, H.; Huang, Y.; Guo, Y. *J. Fluorine Chem.* **2012**, *133*, 108-114. (f) Huan, F.; Hu, H.; Huang, Y.; Chen, Q.-Y.; Guo, Y. *Chin. J. Chem.* **2012**, *30*, 798-802. (g) Wang, Q.; Chen, Q.-Y.; Yang, X.; Guo, Y. *Synthesis* **2012**, 3815-3821.

(10) You, S.-L.; Zhu, X.-Z.; Luo, Y.-M.; Hou, X.-L.; Dai, L.-X. *J. Am. Chem. Soc.* **2001**, *123*, 7471-7472.