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Reaction of aldimines and difluoroenoxysilane, an unexpected protocol for the synthesis of 2,2-difluoro-3-hydroxy-1-ones

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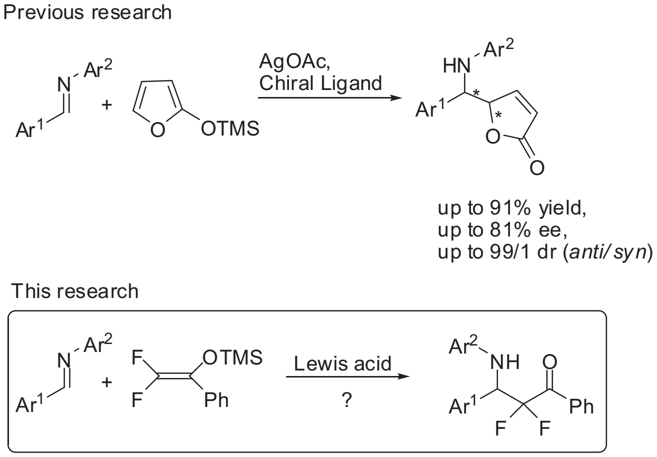
ABSTRACT

An unexpected reaction of aldimines and difluoroenoxysilane promoted with $Zn(OTf)_2$ was disclosed. The reaction gave the unexpected Mukaiyama-aldol adducts **3** in excellent yields (up to 87%) with the addition of H_2O and the corresponding Mannich-type adduct **4** was not observed in this catalytic system.

1. Introduction

Since the introduction of fluorine atoms into organic molecules causes changes in physical, chemical and pharmacological properties,[1] organofluorine chemistry provides stimulation in synthetic, biomedical, and material science.[2] Among some reported fluorine-containing units, a difluoromethylene unit, which plays a significant role in current organofluorine chemistry,[3] was revealed containing in some biologically interesting compounds, such as in phosphotyrosine (pTyr) mimetics,[4] anticancer agent gemcitabine,[5] and HIV-1 protease inhibitors.[6] Furthermore, due to the importance in chemical biology, α,α-difluoro-β-amino acids have attracted much interest in the past decades.[7] Recently, scientists have developed a variety of methods for the preparation of difluoromethylene units containing compounds. Among them, difluoroenolsilylanes, which could be readily prepared by Mg(0) promoted selective defluorination of trifluoromethyl ketones in the presence of TMSCl,[8] are considered as excellent building blocks for the synthesis of *gem*-difluorinated compounds.

Our previous research has disclosed a catalytic asymmetric vinylogous Mannich (AVM) reaction of readily available aldimines with trimethylsiloxyfuran promoted by silver salts.[9] The catalytic system gave the AVM products in high yields along with good enantioselectivities (Scheme 1). We envisioned that the use of difluoroenoxysilanes in the AVM reaction instead of trimethylsiloxyfuran might be a novel method to achieve chiral *gem*-difluorinated compounds. To the best of our knowledge, the direct catalytic asymmetric difluoromethylation of imines has not been reported. However, it was found that the reaction of aldimines **1** and difluoroenoxysilane **2** formed an unexpected Mukaiyama-aldol adducts **3** rather than the corresponding Mannich adduct **4**, which we expected to obtain. Therefore, we wish to investigate this novel route for the synthesis of 2,2-difluoro-3-hydroxy-1-ones via the reaction of aldimines and difluoroenoxysilane promoted by Lewis acids.



Scheme 1. Previously studied Lewis acid catalyzed AVM reaction and the proposal in this research.

2. Results and discussion

We initially investigated the reaction of aldimine **1a** with difluoroenoxysilane **2** in the presence of a catalytic amount of AgOAc. Unfortunately, the reaction could not be promoted by AgOAc that has shown good catalytic activity in our previously studied AVM

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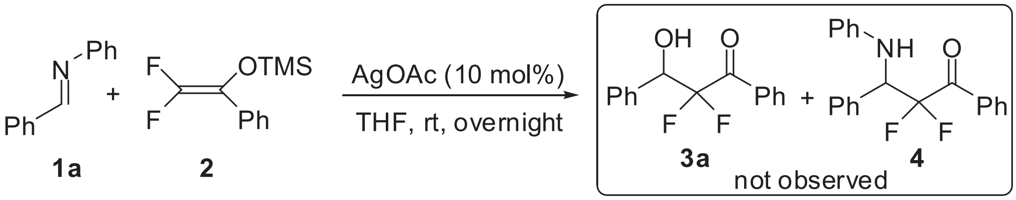
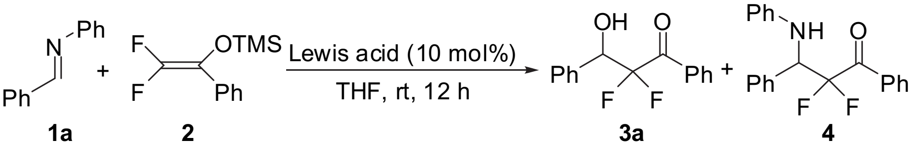


Scheme 2. Initial survey in the reaction of aldimine **1a** with difluoroenoxysilane **2**.

reaction (Scheme 2). Then another Lewis acid $Zn(OTf)_2$ was tested as a promoter. To our surprise, the reaction of aldimine **1a** and difluoroenoxysilane **2** proceeded efficiently when 10 mol % $Zn(OTf)_2$ was used as the promoter, giving an unexpected Mukaiyama-aldol adduct **3a** in 67% yield instead of Mannich adduct **4** (Table 1, entry 1).

Table 1

Reaction of aldimine **1a** (1.0 equiv) with difluoroenoxysilane **2** (1.5 equiv) in the presence of Lewis acids (10 mol %) at ambient temperature[a]



Entry	Lewis acid	Yield/(%)[b]	
		3a	**4**
1	$Zn(OTf)_2$	67	0
2	$Cu(OTf)_2$	52	13
3[c]	$(CuOTf)_2{\cdot}C_6H_6$	60	0
4	AgOTf	66	0
5	$Sc(OTf)_3$	30	29
6	$Yb(OTf)_3$	45	25

[a] The reaction was carried out with 0.20 mmol of **1a**, 0.30 mmol of **2**, and 10 mol % of Lewis acids in THF (2.0 mL) at room temperature.

[b] Isolated yield.

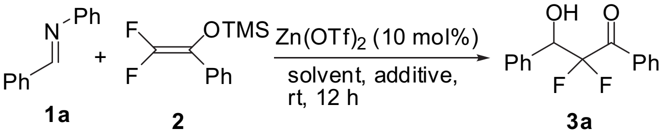
[c] $(CuOTf)_2{\cdot}C_6H_6$ (5 mol %) was used.

An extensive survey of several commonly used Lewis acids (10 mol %) was carried out in the reaction of aldimine **1a** (0.20 mmol) with difluoroenoxysilane **2** (0.30 mmol) in 2 mL tetrahydrofuran (THF) at ambient temperature. The results are summarized in Table 1. It was found that the reaction proceeded smoothly when using $(CuOTf)_2{\cdot}C_6H_6$ and AgOTf as the promoters (Table 1, entries 3 and 4), affording aldol-type adduct **3a** in up to 66% yield without forming adduct **4**. When several other Lewis acids were applied into this reaction, such as $Cu(OTf)_2$, $Sc(OTf)_3$, and $Yb(OTf)_3$, however, the reactions proceeded inefficiently (Table 1, entries 2, 5, and 6). For example, it was found that Mannich adduct **4** was formed in up to 29% yield along with aldol-type adduct **3a** in 30% yield when $Sc(OTf)_3$ was used as a Lewis acid (Table 1, entry 5), and the main product **3a** was achieved in 52% yield along with 13% of adduct **4** when $Cu(OTf)_2$ was employed as a Lewis acid (Table 1, entry 2).

Subsequently, we carried out the reaction of aldimine **1a** with **2** in different solvents and additives with 10 mol % of $Zn(OTf)_2$, which has been identified as the best Lewis acid in this reaction. Mannich adduct **4** was not observed yet when other solvents were used. The results are outlined in Table 2. When the reaction was carried out in dichloromethane (DCM), aldol-type adduct **3a** was obtained in 57% yield, lower than in THF (Table 2, entry 1). Solvents, such as CH_3CN and toluene are not suitable for this reaction, providing **3a** in very low yields (Table 2, entries 3 and 4). It was also observed that the reactions proceeded efficiently to give the adduct **3a** in Et_2O and 1,4-dioxane in up to 62% and 66% yields, respectively (Table 2, entries 2 and 5). Hypothetically, the water in the catalytic system may play an important role in this reaction, leading to the formation of the unexpected adduct **3**. Thus, the further studies were performed to identify the effect of H_2O in this reaction. We found that the addition of MS 4 Å (molecular sieves 4 Å, 100 mg) affected the result of the reaction of aldimine **1a** with difluoroenoxysilane **2**. When MS 4 Å was added into the reaction, only trace amount of adduct **3a** was formed (Table 2, entry 6). On the other hand, the addition of 1.0 equiv of H_2O could improve the yield of adduct **3a** up to 87% (Table 2, entry 7).

Table 2

Solvent and additive effects on the $Zn(OTf)_2$-catalyzed reaction of aldimine **1a** (1.0 equiv) with difluoroenoxysilane **2** (1.5 equiv)[a]



Entry	Solvent	Additive	Yield/(%)[b]
			3a
1	DCM	None	57
2	Et_2O	None	66
3	MeCN	None	Trace
4	Toluene	None	37
5	1,4-Dioxane	None	62
6[c]	THF	MS 4 Å	Trace
7[d]	THF	H_2O	87

[a] The reaction was carried out with 0.20 mmol of **1a**, 0.30 mmol of **2**, and 10 mol % of $Zn(OTf)_2$ in solvents (2.0 mL) at room temperature.

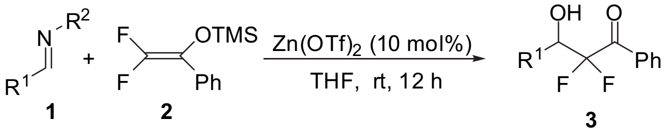
[b] Isolated yield.

[c] MS 4 Å (100 mg) was used as additive.

[d] H_2O (0.20 mmol, 1.0 equiv) was used as an additive.

With these optimized reaction conditions in hand, we next turned our attention to the reactions of a variety of aldimines **1** with difluoroenoxysilane **2**. The results are summarized in Table 3. For aldimines **1d**–**f** bearing electron-donating groups on the benzene rings, the reaction proceeded smoothly to afford corresponding aldol-type adducts **3a** and **3d** in good yields (Table 3,

Table 3
Survey of aldimine **1** (1.0 equiv) with diethyl difluoroenoxysilane **2** (1.5 equiv) in the presence of $Zn(OTf)_2$ (10 mol %) at room temperature[a]

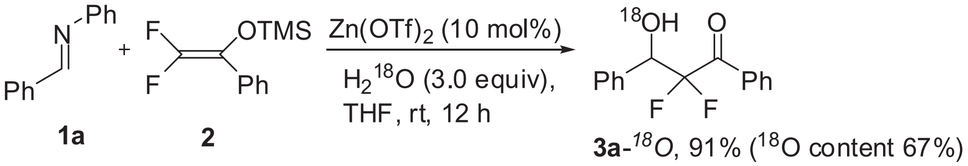


Entry	Aldimine **1** (R^1/R^2)	Yield/(%)[b] **3**
1	**1a** (C_6H_5/C_6H_5)	**3a**, 67/(87)[c]
2	**1b** ($4\text{-}ClC_6H_4/C_6H_5$)	**3b**, 67/(83)[c]
3	**1c** ($4\text{-}BrC_6H_4/4\text{-}BrC_6H_4$)	**3c**, 71/(79)[c]
4	**1d** ($4\text{-}CH_3OC_6H_4/C_6H_5$)	**3d**, 73/(79)[c]
5	**1e** ($C_6H_5/4\text{-}CH_3OC_6H_4$)	**3a**, 68/(78)[c]
6	**1f** ($C_6H_5/4\text{-}CH_3C_6H_4$)	**3a**, 70/(86)[c]
7	**1g** ($4\text{-}NO_2C_6H_4/C_6H_5$)	**3e**, 71/(80)[c]
8	**1h** ($C_6H_5/4\text{-}NO_2C_6H_4$)	**3a**, 69/(78)[c]
9	**1i** (2-Furan/C_6H_5)	**3f**, 25/(28)[c]
10	**1j** ($C_6H_5(CH_2)_2/C_6H_5$)	**3g**, 17/(16)[c]

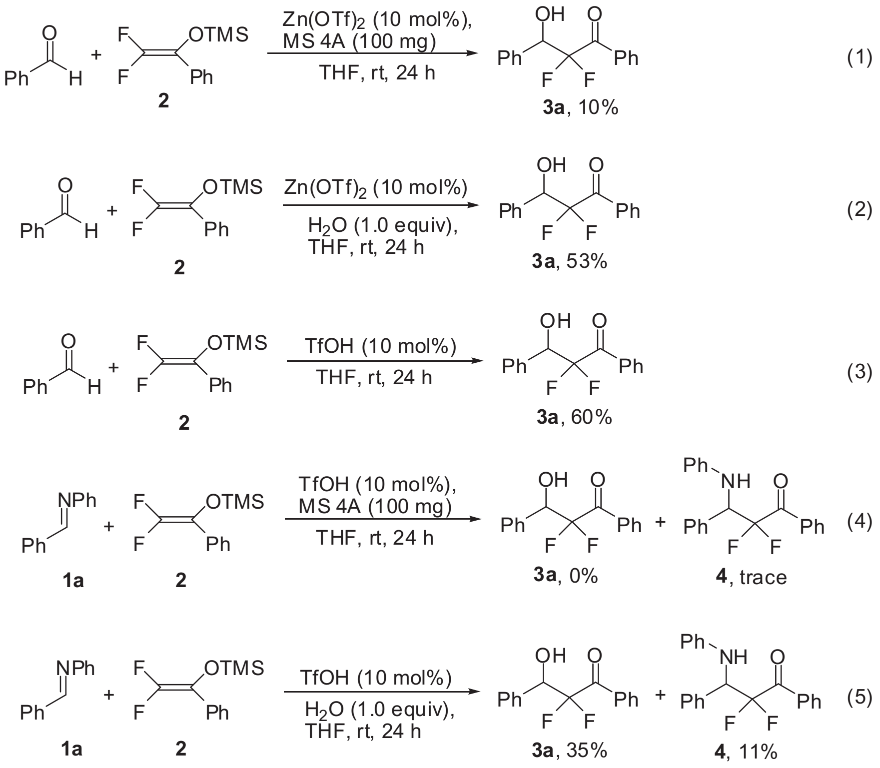
[a] The reaction was carried out with 0.20 mmol of **1**, 0.30 mmol of **2**, and 10 mol % of $Zn(OTf)_2$ in THF (2.0 mL) at room temperature.
[b] Isolated yield.
[c] H_2O (0.20 mmol, 1.0 equiv) was used as an additive.

entries 4–6). As for aldimines bearing electron-withdrawing groups on the benzene rings, the corresponding products **3a–c** and **3e** were also achieved in moderate to good yields (Table 3, entries 2, 3, 7, and 8). Unfortunately, the reaction of aldimine **1i**, which containing a furan ring with difluoroenoxysilane **2** formed the corresponding adduct **3f** in only 25% yield (Table 3, entry 9). Using aliphatic aldimine **1j** as a reactant under the optimized reaction conditions, the reaction proceeded inefficiently to form the corresponding product **3g** in low yield even 1.0 equiv of H_2O was added as an additive (Table 3, entry 10). Gratifyingly, when 1.0 equiv of H_2O was added, the reaction proceeded more efficiently, affording the desired aldol-type adducts **3a–e** in excellent yields (up to 86%) under the optimized reaction conditions irrespective of the electronic properties of substrates **1** (Table 3, entries 2–8) except aldimines **1i** and **1j** (Table 3, entries 9 and 10).

As the results described above indicated that the addition of H_2O could improve the yields of the corresponding adducts **3**, another control experiment was carried out by adding 3.0 equiv of $H_2{}^{18}O$ into the reaction system instead of H_2O under the optimized reaction conditions (Scheme 3). We observed that in the presence of 3.0 equiv of $H_2{}^{18}O$, the reaction proceeded efficiently, giving the adduct **3a**–^{18}O in 91% yield along with 67% of ^{18}O content as determined by EIMS. This result indicates that H_2O is involved into the formation of the corresponding aldol adduct **3a**. Some other control experiments were also carried out in order to reveal the role of H_2O in the catalytic cycle and rationalize the reaction results. When benzaldehyde was used as a substrate instead of aldimine **1a** under the optimized reaction conditions (MS 4 Å 100 mg was added into the reaction system), the aldol adduct **3a** was achieved in very low yield even after a prolonged reaction time [Scheme 4, Eq. 1].



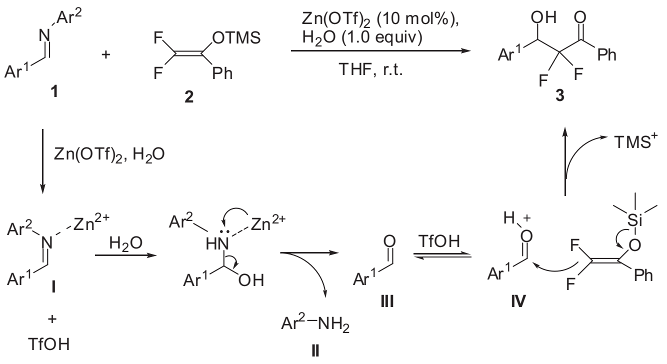
Scheme 3. Isotope labeling experiment of $Zn(OTf)_2$ promoted reaction of aldimine **1a** with difluoroenoxysilane **2**.



Scheme 4. Control experiments of reactions of benzaldehyde or aldimine **1a** with difluoroenoxysilane **2**.

This result suggests that aldehydes cannot produce the corresponding aldol adducts efficiently when $Zn(OTf)_2$ was used as the catalyst. However, the reaction of benzaldehyde with difluoroenoxysilane **2** could be promoted by 10 mol % $Zn(OTf)_2$ when 1.0 equiv of H_2O was added into this reaction system, and the corresponding product **3a** was achieved in 53% yield [Scheme 4, Eq. 2]. It should be noted that when we utilized trifluoromethanesulfonic acid CF_3SO_3H (TfOH) (10 mol %) as a promoter instead of zinc salt into the reaction of benzaldehyde with difluoroenoxysilane **2** [Scheme 4, Eq. 3], this reaction proceeded efficiently, giving the aldol-adduct **3a** in 60% yield. We also found that, in the reaction of benzaldehyde with difluoroenoxysilane **2**, treatment of aldimine **1a** with difluoroenoxysilane **2** in the presence of 10 mol % TfOH and MS 4 Å (100 mg) could not afford aldol-adduct **3a** or Mannich adduct **4** (in trace) [Scheme 4, Eq. 4]. We assumed that H_2O may participate in the decomposition of aldimines in the presence of TfOH. Therefore, we attempted to add 1.0 equiv of H_2O into the reaction of aldimine **1a** with difluoroenoxysilane **2** in the presence of 10 mol % TfOH to examine the reaction outcome. Fortunately, it was found that not only the aldol-type product **3a** was formed in 35% yield, but the Mannich adduct **4** was also obtained in 11% yield, suggesting again that H_2O and HOTf play key roles in the formation of aldol-adduct **3a** [Scheme 4, Eq. 5].

On the basis of the control experiments, a plausible mechanism is shown in Scheme 5. Since the addition of H_2O played a key role in this reaction, we believed that $Zn(OTf)_2$ activated aldimine **1** and generated TfOH spontaneously at the first step. After being treated with H_2O, the decomposition of activated aldimine **I** generated aldehyde **III** with the elimination of amine **II**. The protonation of aldehyde **III** with TfOH afforded an activated carbonyl compound **IV**, which then reacted with difluoroenoxysilane **2** in a Mukaiyama-aldol type reaction to give the corresponding aldol-adduct **3**. Generally, nitrogen containing organic bases are considered as efficient additives to improve a lot of catalytic processes involving silylenol ethers,[11] we believed that the in situ generated amine **II** acted as an efficient additive to activate the Lewis acid and promote the elimination of silyl group to enhance the reaction rates and the yields of the corresponding aldol-adducts **3** in this catalytic cycle. A more detailed mechanistic investigation is undergoing.



Scheme 5. A plausible reaction mechanism of the reaction of aldimine **1** with difluoroenoxysilane **2**.

In summary, we have presented a new catalytic reaction system applicable to the reactions of aldimines and difluoroenoxysilane using Lewis acid $Zn(OTf)_2$ as a catalyst. On the basis of this synthetic route, we can achieve unexpected Mukaiyama-aldol adducts **3** in excellent yields. Adducts **4** could be formed simultaneously in low yields when other Lewis acids, such as $Cu(OTf)_2$, $Sc(OTf)_3$, and $Yb(OTf)_3$, were applied into this reaction instead of $Zn(OTf)_2$. On the basis of the control experiments and ^{18}O-labeling experiment, we found that adducts **3** cannot be achieved efficiently when $Zn(OTf)_2$ used as a promoter in the reaction of benzaldehyde with difluoroenoxysilane. The reaction proceeds through an oxygen transfer from H_2O, which contains in the reaction system. As compared with these reactions to synthesize 2,2-difluoro-3-hydroxy-1-ones utilizing 0.50 equiv of $TiCl_4$ or 1.0 equiv of $BF_3 \cdot Et_2O$ as a promoter,[12,13] herein, we reported an unprecedented route, which could approach to these *gem*-difluorinated compounds under the promotion of catalytic amount of $Zn(OTf)_2$ and mild reaction conditions to give the products in higher yields.

3. Experimental section

3.1. General remarks

^1H, ^{13}C, and ^{19}F NMR spectra were recorded on a Bruker AM-400 spectrometer for solution in $CDCl_3$ with tetramethylsilane (TMS) as an internal standard; *J*-values are in hertz. Mass spectra were recorded by EI methods, and HRMS was measured on a Finnigan MA^+ mass spectrometer. THF and toluene were distilled from sodium (Na) under argon (Ar) atmosphere. CH_3CN and 1,2-dichloromethane were distilled from CaH_2 under argon (Ar) atmosphere. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with Huanghai GF_{254} silica gel coated plates. Flash column chromatography was carried out using 300–400 mesh silica gel at increased pressure.

3.2. General procedure for the preparation of difluoroenoxysilane 2[10]

A mixture of chlorotrimethylsilane (TMSCl) (6.0 mmol), Mg (6.0 mmol), and THF (10 mL) was cooled down to 0 °C under argon atmosphere. Then trifluoroacetophenone (1.5 mmol) was added dropwise and the resulting mixture was stirred for additional 1.0 h. After the solvent was removed under vacuum, hexane (15 mL) was added to the residue. The resulting salt was filtered and the filtrate was then concentrated to give the crude product of difluoroenoxysilane **2** under reduced pressure. This crude product **2** was used for the Mukaiyama-aldol type reaction without further purification.

3.3. General procedure for the reaction of aldimine 1 with difluoroenoxysilane 2 in the presence of 1 equiv of H_2O and catalytic amount of $Zn(OTf)_2$

The solution of aldimine **1a** (0.20 mmol), $Zn(OTf)_2$ (0.02 mmol) and THF (2.0 mL) was allowed to stir for 5.0 min at ambient temperature. A freshly prepared difluoroenoxysilane **2** (0.30 mmol) was added dropwise by syringe and followed by addition of 1.0 equiv of H_2O. The reaction mixture was allowed to stir for 12 h at ambient temperature. The reaction was quenched by addition of a saturated aqueous solution of NH_4Cl (5.0 mL). After stirring for 15 min at room temperature, the mixture was extracted by DCM and washed with brine. The organic layer was dried over anhydrous Na_2SO_4. Then the solvent was removed under reduced pressure and the residue was purified by flash column chromatography (SiO_2) to give the corresponding product **3a**.

*3.3.1. 2,2-Difluoro-3-hydroxy-1,3-diphenylpropan-1-one (**3a**).* A pale yellow solid. This is a known compound.[8,11] ^1H NMR (400 MHz, $CDCl_3$, TMS): δ 3.13 (br, 1H, OH), 5.37 (dd, 1H, J=18.4, 5.6 Hz, CH), 7.37–7.39 (m, 3H, ArH), 7.40–7.50 (m, 4H, ArH), 7.60–7.64 (m, 1H, ArH), 8.04 (d, J=8.4, 0.8 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −104.8 (dd, 1F, J=290, 6.0 Hz), −116.3 (dd, 1F, J=290, 18.0 Hz).

*3.3.2. 3-(4-Chlorophenyl)-2,2-difluoro-3-hydroxy-1-phenylpropan-1-one (**3b**).* A pale yellow solid. This is a known compound.[8,11] ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.10 (d, 1H, J=4.8 Hz, OH), 5.37 (dt, 1H, J=18.8, 4.8 Hz, CH), 7.36–7.38 (m, 2H, ArH), 7.43–7.51 (m, 4H, ArH), 7.63–7.67 (m, 1H, ArH), 8.06 (dd, 2H, J=8.0, 1.2 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −104.3 (dd, 1F, J=297, 5.0 Hz), −116.7 (dd, 1F, J=297, 19.0 Hz).

*3.3.3. 3-(4-Bromophenyl)-2,2-difluoro-3-hydroxy-1-phenylpropan-1-one (**3c**).* A pale yellow solid. This is a known compound.[8,11] ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.27 (br, 1H, OH), 5.33 (dd, 1H, J=18.8, 4.8 Hz, CH), 7.36 (d, 2H, J=8.0 Hz, ArH), 7.45–7.53 (m, 4H, ArH), 7.61–7.66 (m, 1H, ArH), 8.05 (dd, 2H, J=8.0, 1.2 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −104.3 (dd, 1F, J=295, 5.0 Hz), −116.6 (dd, 1F, J=295, 20.0 Hz).

*3.3.4. 2,2-Difluoro-3-hydroxy-3-(4-methoxyphenyl)-1-phenylpropan-1-one (**3d**).* A pale yellow oil. This is a known compound.[11,12] ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.21 (br, 1H, OH), 3.79 (s, 3H, OCH$_3$), 5.29 (dd, 1H, J=18.4, 6.0 Hz, CH), 6.89 (dt, 2H, J=8.8, 2.8 Hz, ArH), 7.39 (d, 2H, J=8.4 Hz, ArH), 7.43–7.47 (m, 2H, ArH), 7.58–7.63 (m, 1H, ArH), 8.03 (dd, 2H, J=8.4, 1.2 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −105.2 (dd, 1F, J=287, 7.0 Hz), −116.5 (dd, 1F, J=287, 19.0 Hz).

*3.3.5. 2,2-Difluoro-3-hydroxy-3-(4-nitrophenyl)-1-phenylpropan-1-one (**3e**).* A yellow solid. This is a known compound.[8,11] ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.49 (br, 1H, OH), 5.52 (dd, 1H, J=19.2, 4.0 Hz, CH), 7.48–7.53 (m, 2H, ArH), 7.65–7.72 (m, 3H, ArH), 8.07 (dd, 2H, J=8.8, 1.2 Hz, ArH), 8.25 (dt, 2H, J=8.8, 2.0 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −103.4 (dd, 1F, J=300, 5.0 Hz), −116.6 (dd, 1F, J=300, 19.0 Hz).

*3.3.6. 2,2-Difluoro-3-(furan-2-yl)-3-hydroxy-1-phenylpropan-1-one (**3f**).* A pale yellow oil; IR (acetone): ν 3480, 2925, 1698, 1598, 1450, 1283, 1183, 1125, 1081, 795, 745 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.35 (d, 1H, J=7.6 Hz, OH), 5.41 (dt, 1H, J=16.0, 7.8 Hz, CH), 6.36 (dd, 1H, J=3.2, 2.4 Hz, ArH), 6.49 (d, 1H, J=3.2 Hz, ArH), 7.41–7.48 (m, 3H, ArH), 7.59–7.63 (m, 1H, ArH), 8.04 (dd, 2H, J=6.0, 1.6 Hz, ArH ArH); ^{13}C NMR (75 MHz, CDCl$_3$, TMS): δ 68.0 (dd, J_{C-F}=21.5, 18.4 Hz), 110.1, 110.6, 115.5 (t, J_{C-F}=192.7 Hz), 118.0, 128.6, 130.0 (t, J_{C-F}=1.9 Hz), 132.2, 134.6, 143.2, 148.3, 189.9 (t, J_{C-F}=21.3 Hz); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −106.3 (dd, 1F, J=288, 7.0 Hz), −116.8 (dd, 1F, J=288, 16.0 Hz). MS (EI) *m*/*e* 252 [M$^+$] (2.2), 232 (62.8), 216 (1.7), 156 (35.0), 127 (6.6), 105 (93.3), 97 (100), 77 (66.1), 51 (21.1), 41 (11.9); HRMS (EI) calcd. For $C_{13}H_{10}O_3F_2$ (M+H$^+$): 252.0602, found: 252.0598.

*3.3.7. 2,2-Difluoro-3-hydroxy-1,5-diphenylpentan-1-one (**3g**).* A pale yellow oil; IR (acetone) ν 3483, 2929, 1698, 1598, 1509, 1450, 1432, 1277, 1170, 1163, 1139, 1055, 798, 750 cm^{-1}; ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 1.94–2.11 (m, 2H, CH$_2$), 2.70–2.77 (m, 1H, CH), 2.82 (d, 1H, J=5.6 Hz, OH), 2.94–2.99 (m, 1H, CH), 4.20–4.27 (m, 1H, CH), 7.16–7.27 (m, 5H, ArH), 7.44 (t, 2H, J=7.6 Hz, ArH), 7.57–7.61 (m, 1H, ArH), 8.07 (d, 2H, J=7.6 Hz, ArH); ^{13}C NMR (75 MHz, CDCl$_3$, TMS): δ 30.2, 30.3, 31.3, 70.4 (dd, J_{C-F}=20.8, 18.4 Hz), 116.5 (t, J_{C-F}=191.2 Hz), 126.0, 128.4, 128.6, 130.2 (t, J_{C-F}=2.6 Hz), 132.1, 134.6, 141.0, 190.5 (t, J_{C-F}=22.3 Hz); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −107.4 (dd, 1F, J=295, 6.0 Hz), −116.8 (dd, 1F, J=295, 16.0 Hz). MS (EI) *m*/*e* 290 [M$^+$] (4.0), 272 (1.0), 252 (6.6), 156 (4.7), 133 (3.5), 105 (100), 91 (20.1), 77 (28.1), 63 (1.0), 51 (1.7); HRMS (EI) calcd. For $C_{17}H_{16}O_2$ F_2 (M+H$^+$): 290.1123, found: 290.1118.

*3.3.8. 2,2-Difluoro-1,3-diphenyl-3-(phenylamino)propan-1-one (**4**).* A yellow solid. This is a known compound.[12] ^{1}H NMR (400 MHz, CDCl$_3$, TMS): δ 3.49 (br, 1H, OH), 5.52 (dd, 1H, J=19.2, 4.0 Hz, CH), 7.48–7.53 (m, 2H, ArH), 7.65–7.72 (m, 3H, ArH), 8.07 (dd, 2H, J=8.8, 1.2 Hz, ArH), 8.25 (dt, 2H, J=8.8, 2.0 Hz, ArH); ^{19}F NMR (376 MHz, CDCl$_3$, TMS): δ −103.4 (dd, 1F, J=300, 5.0 Hz), −116.6 (dd, 1F, J=300, 19.0 Hz).

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Supplementary data

Spectroscopic data of the compounds shown in Tables 1–3, Schemes 2–4 and the detailed descriptions of experimental procedures. Supplementary data associated with this article can be found in online version at doi:10.1016/j.tet.2010.07.034.

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