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The Use of Trifluoroacetaldehyde Ethyl Hemiacetal or Hydrate in a Simple and Practical Regioselective Synthesis of β-Hydroxy-β-trifluoromethyl Ketones from Enamines and Imines

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The reaction of trifluoroacetaldehyde ethyl hemiacetal or hydrate with an equimolar amount of enamines, derived from various methyl ketones, smoothly proceeded to give the corresponding β-hydroxy-β-trifluoromethyl ketones in high yields. An equimolar amount of imines derived from various methyl ketones with aliphatic, aromatic, and heteroaromatic substituents also readily reacted with trifluoroacetaldehyde ethyl hemiacetal or hydrate to afford the corresponding β-hydroxy-β-trifluoromethyl ketones in good to excellent yields. Difluoroacetaldehyde ethyl hemiacetal as well as pentafluoropropionaldehyde also participated in the reaction, affording good yields of the corresponding β-hydroxy-β-difluoromethyl or β-pentafluoropropyl ketones.

Introduction

Much attention has been addressed to the effective introduction of fluorine and the trifluoromethyl group in both academia and industry, since the replacement of hydrogen by the fluorine atom sometimes brings about a dramatic change in the physical properties and bioactivity of the compounds arising due to the special properties of the fluorine atom, such as the highest electronegativity of fluorine and high carbon−fluorine bond energy.[1] α-Trifluoromethylated alcohols are some of the most valuable compounds in organofluorine synthesis, and several types of syntheses of such compounds have been developed over the last two decades[2] because they can serve as the useful core system of liquid crystals imparted by a trifluoromethyl group.[3] Most syntheses of these compounds utilize the α-trifluoromethylated building blocks such as trifluoroacetaldehyde (CF_3CHO),[4,5,6] its derivatives,[7,8] and α-trifluoromethyl ketones[9] as the

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starting substrates. Among them, CF_3CHO is especially the most attractive compound like fluorine-free aldehydes for the construction of β-trifluoromethylated aldol units. However, it normally exists as a hydrate or hemiacetal form due to the strong electron-withdrawing properties of the trifluoromethyl group.[10] Therefore, before the use of CF_3CHO, the aldehyde must be generated by the early protocols, which rely on not only using a large amount of concentrated H_2SO_4 or P_2O_5 but also utilizing a high reaction temperature.[11] Furthermore, the boiling point (−18 °C) as well as the high hygroscopicity of CF_3CHO seems to cause handling problems at room temperature.

Although there are some reports about the efficient generation of CF_3CHO and the reaction with various nucleophiles to give functionalized α-trifluoromethylated alcohols,[12] it is highly desirable to develop a more environmentally friendly, convenient, and efficient methodology for the generation of CF_3CHO and successive carbon−carbon bond forming reactions. Herein, we report a novel reaction of CF_3CHO ethyl hemiacetal or hydrate with enamines or imines, demonstrating an expedient access to β-trifluoromethylated aldol units. The present reaction will provide a new, promising, effective, and practical synthetic method for the β-hydroxy-β-trifluoromethyl ketones because it has some significant advantages such as no need of an excess amount of strong acid for the generation of CF_3CHO, the use of only an equimolar amount of CF_3CHO ethyl hemiacetal or hydrate, a high generality of the reaction, high yields of the products, and no serious handling problems.[13,14]

Results and Discussion

Reaction with Enamines. The treatment of hemiacetal **1a** with an equimolar amount of enamine **2a**, prepared between morpholine and acetophenone, at room temperature in hexane for 1 h gave the β-hydroxy-β-trifluoromethyl ketone **3a** in 88% yield (Table 1, entry 1).

The reactions of the CF_3CHO ethyl hemiacetal **1a** or hydrate **1b** with enamines **2** under various conditions are summarized in Table 1. Other solvents, such as 1,2-dichloroethane, tetrahydrofuran (THF), toluene, and acetonitrile, were also used for the reaction (entries 2−5). Noteworthy is that the presence of a small amount of water did not have a significant influence on the yield of the product (entry 6). The use of the enamine **2b** having a piperazino group instead of the morpholino one gave a similar yield of **3a** (entry 7). Other aromatic- or heteroaromatic-substituted enamines **2c**,**d**,**e**,**g**,**h** participated nicely in the reaction to afford the corresponding β-hydroxy-β-trifluoromethyl ketone **3b**,**c**,**d**,**e**,**g** in good yields, respectively (entries 8, 9, 10, 13, and 14). Enamine **2f** with a nitro substituent on the phenyl group did not react smoothly, providing only 13% of the product **3e**, due to the low solubility of the enamine **2f** (entry 11). The yield of **3e** could be improved by carrying out the reaction in toluene (entry 12). The reaction of the hemiacetal **1a** with the mixture of aliphatic enamines, such as **2i** and 4-(3-methybut-1-en-2-yl)morpholine (29:71), gave **3h** in 25% yield, and there is no detectable amount of the product, which reacts with the 4-(3-methybut-2-en-2-yl)-morpholine, in the crude reaction mixture (entry 15).

The CF_3CHO monohydrate **1b** can also be used for the reaction. The reaction of the hydrate **1b** with the enamine **2a** under the various reaction conditions as well as with various enamines **2c**−**f**,**h**,**i** are also summarized in Table 1. Among the solvents examined at room or reflux temperature (entries 16, 18−26), using toluene at reflux gave the best yield of **3a** (entry 25). The addition of MS 3A to the reaction mixture at room temperature was not very effective, giving **3a** in 43% yield (entry 17). The reaction of **1b** with various other aromatic or heteroaromatic enamines smoothly occurred to provide the corresponding β-hydroxy-β-trifluoromethyl ketones **3** in good yields (entries 27−31). When a mixture of enamines **2i**

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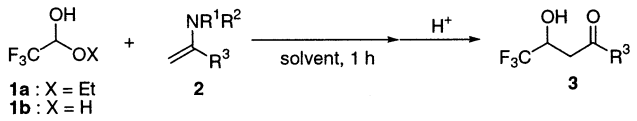
TABLE 1. Reaction of Trifluoroacetaldehyde Ethyl Hemiacetal or Hydrate with Various Enamines[a]



entry	1	enamine	R^1, R^2	R^3	solvent	*T*	product	yield[b] (%)
1	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	hexane	rt	**3a**	88
2	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	$ClCH_2CH_2Cl$	rt	**3a**	78
3	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	THF	rt	**3a**	73
4	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	toluene	rt	**3a**	88
5	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_3CN	rt	**3a**	75
6	**1a**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	hexane-H_2O (40:1)	rt	**3a**	68
7	**1a**	**2b**	$-(CH_2)_5-$	Ph	hexane	rt	**3a**	86
8	**1a**	**2c**	$-(CH_2)_2O(CH_2)_2-$	4-MeC_6H_4	hexane	rt	**3b**	87
9	**1a**	**2d**	$-(CH_2)_2O(CH_2)_2-$	4-$MeOC_6H_4$	hexane	rt	**3c**	72
10	**1a**	**2e**	$-(CH_2)_2O(CH_2)_2-$	4-ClC_6H_4	hexane	rt	**3d**	86
11	**1a**	**2f**	$-(CH_2)_2O(CH_2)_2-$	4-$NO_2C_6H_4$	hexane	rt	**3e**	13
12	**1a**	**2f**	$-(CH_2)_2O(CH_2)_2-$	4-$NO_2C_6H_4$	toluene	rt	**3e**	52
13	**1a**	**2g**	$-(CH_2)_2O(CH_2)_2-$	2-MeC_6H_4	hexane	rt	**3f**	87
14	**1a**	**2h**	$-(CH_2)_2O(CH_2)_2-$	2-thienyl	hexane	rt	**3g**	75
15	**1a**	**2i**	$-(CH_2)_2O(CH_2)_2-$	*i*-Pr[c]	hexane	rt	**3h**	25
16	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	hexane	rt	**3a**	46
17[d]	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	hexane	rt	**3a**	43
18	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	THF	rt	**3a**	20
19	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_2Cl_2	rt	**3a**	66
20	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	toluene	rt	**3a**	77
21	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_3CH_2CN	rt	**3a**	39
22	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	hexane	reflux	**3a**	54
23	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	THF	reflux	**3a**	77
24	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_2Cl_2	reflux	**3a**	65
25	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	toluene	reflux	**3a**	84
26	**1b**	**2a**	$-(CH_2)_2O(CH_2)_2-$	Ph	CH_3CH_2CN	reflux	**3a**	56
27	**1b**	**2c**	$-(CH_2)_2O(CH_2)_2-$	4-MeC_6H_4	toluene	reflux	**3b**	80
28	**1b**	**2d**	$-(CH_2)_2O(CH_2)_2-$	4-$MeOC_6H_4$	toluene	reflux	**3c**	80
29	**1b**	**2e**	$-(CH_2)_2O(CH_2)_2-$	4-ClC_6H_4	toluene	reflux	**3d**	78
30	**1b**	**2f**	$-(CH_2)_2O(CH_2)_2-$	4-$NO_2C_6H_4$	toluene	reflux	**3e**	72
31	**1b**	**2h**	$-(CH_2)_2O(CH_2)_2-$	2-thienyl	toluene	reflux	**3g**	77
32	**1b**	**2i**	$-(CH_2)_2O(CH_2)_2-$	*i*-Pr[e]	toluene	reflux	**3h**	18

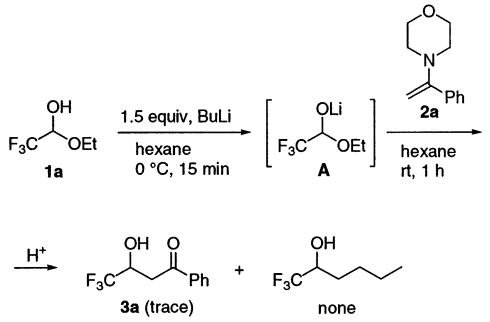
[a] All reactions were carried out as decsribed in the Experimental Section. [b] Isolated yields of analytical pure products. [c] A mixture of **2i** and 4-(3-methylbut-2-en-2-yl)morpholine (29:71) was used. [d] MS 3A (0.5 g) was added. [e] A mixture of **2i** and 4-(3-methylbut-2-en-2-yl)morpholine (30:70) was used.

and 4-(3-methylbut-2-en-2-yl)morpholine (30:70) (1 equiv) was used for the reaction of the hydrate **1b**, the corresponding *β*-hydroxy-*β*-trifluoromethyl ketone **3h** was only obtained in 18% yield and the product derived from the major enamine was not detected in the reaction mixture (entry 32).

Treating the hemiacetal **1a** with a 1.5 equimolar amount of BuLi exclusively gave the lithium alkoxide **A′**, which did not react with the enamine **2a** at all under the same conditions, and neither a trace amount of the *β*-hydroxy-*β*-trifluoromethyl ketone **3a** nor a detectable amount of 1,1,1-trifluoro-2-hexanol was obtained in this reaction with quantitative recovered acetophenone (Scheme 1).

In a previous paper,[15] the difluoroacetaldehyde ethyl hemiacetal smoothly reacted with various Grignard reagents or organolithiums affording good yields of the α-difluoromethylaled alcohols, but the CF_3CHO ethyl hemiacetal **1a** did not react at all with any organometallics. These results are attributed to the much higher stability of the intermediate trifluoromethylated lithium alkoxide **A** than the difluoromethylated one due to the potent electron-withdrawing properties of the trifluoromethyl group.

SCHEME 1



Furthermore, as shown in Scheme 2, after the CF_3CHO hemiacetal reacted with an equimolar amount of the enamine **2a** at reflux temperature for 1 h, an equimolar amount of another enamine **2e** was added to the reaction mixture and stirred at room temperature for 1 h, followed by hydrolysis with 10% HCl to give the product **3a** (81%) with a trace amount of **3d**. On the other hand, succesive reaction with another enamine **2e** at reflux temperature gave a mixture of **3a** and **3d** in 50% and 36% yields, respectively.

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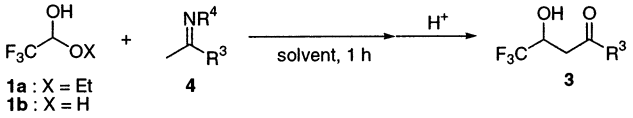
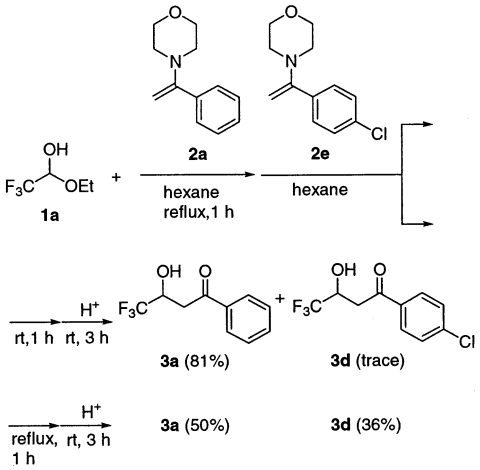
TABLE 2. Reaction of Trifluoroacetaldehyde Ethyl Hemiacetal or Hydrate with Various Imines[a]



entry	1	imine	R^4	R^3	solvent	*T*	product	yield[b] (%)
1	**1a**	**4a**	*c*-Hex	Ph	hexane	rt	**3a**	49
2[b]	**1a**	**4a**	*c*-Hex	Ph	hexane	rt	**3a**	64
3	**1a**	**4a**	*c*-Hex	Ph	hexane	reflux	**3a**	91
4	**1a**	**4a**	*c*-Hex	Ph	CH_2Cl_2	reflux	**3a**	76
5	**1a**	**4a**	*c*-Hex	Ph	THF	reflux	**3a**	83
6	**1a**	**4a**	*c*-Hex	Ph	benzene	reflux	**3a**	83
7	**1a**	**4a**	*c*-Hex	Ph	hexane−H_2O (4:1)	reflux	**3a**	70
8	**1a**	**4a**	*c*-Hex	Ph	hexane−H_2O (2:1)	reflux	**3a**	59
9	**1a**	**4a**	*c*-Hex	Ph	hexane−H_2O (1:1)	reflux	**3a**	35
10	**1a**	**4b**	*n*-Hex	Ph	hexane	reflux	**3a**	89
11	**1a**	**4c**	Ph	Ph	hexane	reflux	**3a**	51
12	**1a**	**4d**	*c*-Hex	4-MeC_6H_4	hexane	reflux	**3b**	88
13	**1a**	**4e**	*c*-Hex	4-$MeOC_6H_4$	hexane	reflux	**3c**	94
14	**1a**	**4f**	*c*-Hex	4-ClC_6H_4	hexane	reflux	**3d**	89
15	**1a**	**4g**	*c*-Hex	4-$NO_2C_6H_4$	hexane	reflux	**3e**	79
16	**1a**	**4h**	*c*-Hex	4-$EtOCOC_6H_4$	hexane	reflux	**3i**	83
17	**1a**	**4i**	*c*-Hex	2-thienyl	hexane	reflux	**3g**	78
18	**1a**	**4j**	*c*-Hex	*i*-Pr	hexane	reflux	**3h**	65
19	**1a**	**4k**	*c*-Hex	*c*-Hex	hexane	reflux	**3j**	93
20	**1a**	**41**	*c*-Hex	*t*-Bu	hexane	reflux	**3k**	61
21	**1b**	**4a**	*c*-Hex	Ph	hexane	reflux	**3a**	90
22	**1b**	**4a**	*c*-Hex	Ph	CH_2Cl_2	reflux	**3a**	92
23	**1b**	**4a**	*c*-Hex	Ph	THF	reflux	**3a**	77
24	**1b**	**4a**	*c*-Hex	Ph	toluene	reflux	**3a**	87
25	**1b**	**4a**	*c*-Hex	Ph	CH_3CH_2CN	reflux	**3a**	94
26	**1b**	**4d**	*c*-Hex	4-MeC_6H_4	hexane	reflux	**3b**	83
27	**1b**	**4e**	*c*-Hex	4-$MeOC_6H_4$	hexane	reflux	**3c**	83
28	**1b**	**4f**	*c*-Hex	4-ClC_6H_4	hexane	reflux	**3d**	75
29	**1b**	**4g**	*c*-Hex	4-$NO_2C_6H_4$	hexane	reflux	**3e**	77
30	**1b**	**4h**	*c*-Hex	4-$EtOCOC_6H_4$	hexane	reflux	**3i**	69
31	**1b**	**4i**	*c*-Hex	2-thienyl	hexane	reflux	**3g**	83
32	**1b**	**4j**	*c*-Hex	*i*-Pr	hexane	reflux	**3h**	55
33	**1b**	**4k**	*c*-Hex	*c*-Hex	hexane	reflux	**3j**	77
34	**1b**	**41**	*c*-Hex	*t*-Bu	hexane	reflux	**3k**	48

[a] All reactions were carried out as decsribed in the Experimental Section. [b] Performed for 3 h. [c] Isolated yields of analytical pure products.

SCHEME 2

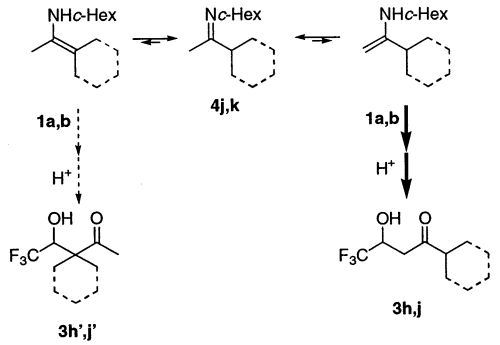


Unfortunately, ^{19}F NMR could not detect the existence of CF_3CHO in the reaction mixture, even if the use of an excess amount of CF_3CHO hemiacetal. Therefore, we cannot describe the exact reaction mechanism. As only one possibility of the reaction mechanism, a plausible reaction mechanism between **1a**,**b** and the enamines may be described as follows. Deprotonation of the hemiacetal **1a** or hydrate **1b** will proceed by the reaction of **1a**,**b** with enamines **2** to give the ammonium alkoxide, followed by elimination of the ethoxide or hydroxide leading to the in situ generation of CF_3CHO in the equilibrium. The in situ generated CF_3CHO reacts with the regenerated enamines **2** to provide the intermediates, which are hydrolyzed leading to the corresponding *β*-hydroxy-*β*-trifluoromethyl ketones **3**.

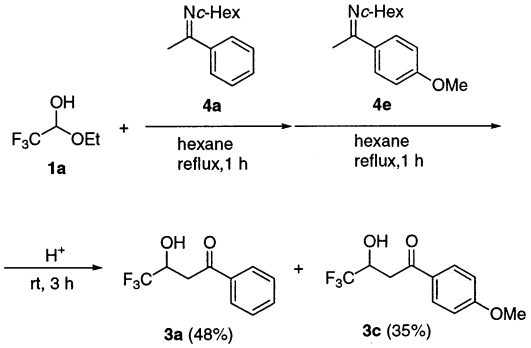
Reaction with Imines. When the hemiacetal **1a** was subjected to the reaction with an equimolar amount of the imine **4a**, derived from acetophenone and *c*-hexylamine, in hexane at room temperature, the corresponding *β*-hydroxy-*β*-trifluoromethyl ketone **3a** was produced in 49−64% yields (Table 2, entries 1 and 2).

The reactions of the CF_3CHO ethyl hemiacetal **1a** or hydrate **1b** with the imines **4** under various conditions are summarized in Table 2. An elevated temperature resulted in an extreme increase in the yield (entry 3). Out of the solvents employed, such as hexane, dichloromethane, THF, and benzene (entries 3−6), the best result was obtained for the reaction in hexane (entry 3). It should be noted that the reaction even in the presence of a significant amount of water smoothly proceeds to give **3a** in moderate to good yields (entries 7−9). The imine **4b** with the *n*-hexyl group on the nitrogen atom also can

SCHEME 3



SCHEME 4



be used, affording **3a** in 89% yield (entry 10). However, the reaction between **1a** and the imine **4c**, prepared from aniline, gave a lower yield (51%) (entry 11).

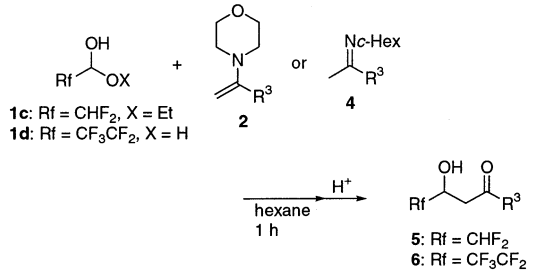
Other imines **4d**−**i** with various aromatic or heteroaromatic substituents smoothly reacted to furnish the corresponding β-hydroxy-β-trifluoromethyl ketones **3b**−**e**,**g**,**i** in good to excellent yields (entries 12−17). More significant imines, prepared from aliphatic methyl ketones, participated well in the reaction to give the β-hydroxy-β-trifluoromethyl ketones **3h**,**j**,**k** in moderate to excellent yields (entries 18−20). For the imines with an isopropyl or cyclohexyl group as a R^3, although there are two kinds of tautomeric enamines in an equilibrium, the reaction of the imines **4j**,**k** with CF_3CHO proceeded regioselectively at the sterically less hindered α-position of the kinetic enamines to furnish the corresponding β-hydroxy-β-trifluoromethyl aliphatic ketones **3h**,**j** in good yields (Scheme 3).[16] No products **3h′**,**j′** derived from the more highly substituted enamines were observed in the reaction mixture.

The hydrate **1b** also reacted with various imines carrying a variety of substituents R^3, including aromatic (entries 21−30), heteroaromatic (entry 31), and alkyl groups (entries 32−34) using various reaction solvents, such as hexane, dichloromethane, THF, toluene, and propionitrile, to afford the corresponding β-hydroxy-β-trifluoromethyl ketones **3** in good to excellent yields.

As shown in Scheme 4, interestingly, the reaction was performed with an equimolar amount of imine **4a** in hexane at reflux temperature for 1 h, followed by further addition of an equimolar amount of the other imine **4e**, heating at reflux temperature for 1 h, and hydrolysis under acidic conditions, to give a mixture of the β-hydroxy-β-trifluoromethyl ketones **3a** and **3c** in 48% and 35% yields, respectively.

The formation of **3** from the imines may be explained by the mechanism, which is very similar to that of the enamines, and imines **4** probably react with **1a**,**b** via the enamines,[17] which are in tautomeric equilibrium with the imines **4**.

TABLE 3. Reaction of Difluoroacetaldehyde Ethyl Hemiacetal or Pentafluoropropionaldehyde Hydrate with Various Enamines or Imines[a]



entry	1	enamine or imine	R^1	*T*	product	yield[b] (%)
1	**1c**	**2a**	Ph	rt	**5a**	65
2	**1c**	**2c**	4-MeC_6H_4	rt	**5b**	70
3	**1c**	**2d**	4-$MeOC_6H_4$	rt	**5c**	73
4	**1c**	**2e**	4-ClC_6H_4	rt	**5d**	69
5	**1c**	**2f**	4-$NO_2C_6H_4$	rt	**5e**	32
6	**1c**	**2h**	2-thienyl	rt	**5f**	52
7	**1c**	**4a**	Ph	reflux	**5a**	67
8	**1c**	**4e**	4-$MeOC_6H_4$	reflux	**5c**	84
9	**1c**	**4f**	4-ClC_6H_4	reflux	**5d**	70
10	**1c**	**4g**	4-$NO_2C_6H_4$	reflux	**5e**	50
11	**1d**	**2a**	Ph	rt	**6a**	78
12	**1d**	**2c**	4-MeC_6H_4	rt	**6b**	83
13	**1d**	**2e**	4-ClC_6H_4	rt	**6c**	85
14	**1d**	**4a**	Ph	reflux	**6a**	70

[a] All reactions were carried out as decsribed in the Experimental Section. [b] Isolated yields of analytical pure products.

Reaction of Difluoroacetaldehyde Ethyl Hemiacetal and Pentafluoropropionaldehyde Hydrate. These methods can be successfully utilized for the synthesis of β-hydroxy-β-difluoromethyl or β-pentafluoropropyl ketones. The results of the reaction of the difluoroacetaldehyde ethyl hemiacetal **1c** as well as the pentafluoropropionaldehyde hydrate **1d** are summarized in Table 3.

The difluoroacetaldehyde ethyl hemiacetal **1c** reacted well with various aromatic enamines (entries 1−6) or imines (entries 7−10) affording the β-hydroxy-β-difluoromethyl ketones **5a**−**f** in good yields. The reaction of the pentafluoropropionaldehyde hydrate **1d** with the enamines (entries 11−13) or imines (entry 14) also smoothly proceeded to give the corresponding β-hydroxy-β-pentafluoropropyl ketones **5a**−**f** in good yields.

Conclusions

In summary, we have described a new expedient method for the simple and practical regioselective synthesis of β-hydroxy-β-trifluoromethyl ketones by the reaction of trifluoroacetaldehyde ethyl hemiacetal or

(16) For similar results, see: Arend, M.; Risch, N. *Angew. Chem., Int. Ed. Engl.* **1995**, *34*, 2639 and references sited therein.

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hydrate with enamines or imines. Diastereoselective and/or enantioselective versions of this reaction are currently investigated and will be reported in due course.

Experimental Section

General Methods. ^{1}H (400 MHz) or ^{13}C (100 MHz) NMR spectra were measured with a JEOL α-400 FT-NMR spectrometer in deuteriocholoroform ($CDCl_3$) solutions with tetramethylsilane (Me_4Si) as the internal standard. ^{19}F NMR (376 MHz) spectra were recorded on a JEOL α-400 FT-NMR in $CDCl_3$ solutions using trifluoroacetic acid as the external standard. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl. Hexane, benzene, 1,2-dichloroethane, dichloromethane (CH_2Cl_2), toluene, acetonitrile (MeCN), and propionitrile (EtCN) were distilled over calcium hydride under argon. Enamines or imines were prepared according to the previous reports.[18]

Typical Procedure for the Reaction of Trifluoroacetaldehyde Ethyl Hemiacetal with Enamines. To a solution of trifluoroacetaldehyde ethyl hemiacetal **1a** (0.144 g, 1 mmol) in hexane (4 mL) was added enamine **2a** (0.189 g, 1 mmol) at room temperature. After being stirred at room temperature for 1 h, the reaction mixture was quenched with a saturated NH_4Cl solution (50 mL) or hydrolyzed with 10% HCl (4 mL) at room temperature for 3 h, followed by extraction with diethyl ether (30 mL × 3), drying over Na_2SO_4, and concentration under vacuum. The residue was chromatographed on silica gel successive using benzene and hexanes−ethyl acetate, giving 4,4,4-trifluoro-3-hydroxy-1-phenyl-1-butanone (**3a**) (0.191 g, 88%).

Typical Procedure for the Reaction of Trifluoroacetaldehyde Ethyl Hemiacetal with Imines. Imine **4a** (0.201 g, 1 mmol) was added to a solution of trifluoroacetaldehyde ethyl hemiacetal **1a** (0.144 g, 1 mmol) in hexane (4 mL) at room temperature. The mixture was stirred at reflux temperature for 1 h. After being cooled to the room temperature, the reaction mixture was quenched with a saturated NH_4Cl (50 mL) or hydrolyzed with 10% HCl (4 mL) at room temperature for 3 h, followed by extraction with diethyl ether (30 mL × 3), drying over Na_2SO_4, and concentration under vacuum. Column chromatography of the residue on silica gel successive using benzene and hexanes−ethyl acetate gave 4,4,4-trifluoro-3-hydroxy-1-phenyl-1-butanone (**3a**) (0.198 g, 91%).

4,4,4-Trifluoro-3-hydroxy-1-phenyl-1-butanone 3a:[19] R_f 0.17 (benzene); mp 79.4−79.8 °C (hexane/ethyl acetate); IR (KBr) 1686.5 (C═O), 3390.3 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.33 (dd, J = 17.93, 3.17 Hz, 1H), 3.39 (dd, J = 17.93, 8.79 Hz, 1H), 3.47 (d, J = 2.92 Hz, 1H), 4.65−4.74 (m, 1H), 7.49−7.53 (m, 2H), 7.62−7.66 (m, 1H), 7.97−7.99 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 38.22 (s), 67.03 (q, J = 31.98 Hz), 124.69 (q, J = 280.37 Hz), 128.21 (s), 128.88 (s), 134.18 (s), 135.96 (s), 197.56 (s); ^{19}F NMR ($CDCl_3$) δ −1.80 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 218 (M^+, 11.7), 200 (4.0), 198 (12.2), 162 (3.8), 106 (7.9), 105 (100.0), 78 (4.1), 77 (38.9); HRMS (EI) found m/z 218.0553, calcd for $C_{10}H_9F_3O_2$ M, 218.0555. Anal. Calcd: C, 55.05; H, 4.16. Found: C, 54.99; H, 4.21.

4,4,4-Trifluoro-3-hydroxy-1-(4-methylphenyl)-1-butanone 3b:[20] R_f 0.19 (benzene); mp 108.4−108.8 °C (hexane/ethyl acetate); IR (KBr) 1685.0 (C═O), 3378.9 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s, 3H), 3.30 (dd, J = 16.83, 3.17 Hz, 1H), 3.36 (dd, J = 16.83, 7.57 Hz, 1H), 3.55 (d, J = 3.90 Hz, 1H), 4.62−4.72 (m, 1H), 7.30 and 7.87 (AB quartet, J = 8.05 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.73 (s), 38.00 (s), 67.08 (q, J = 31.99 Hz), 124.78 (q, J = 281.19 Hz), 128.34 (s), 129.54 (s), 133.52 (s), 145.25 (s), 197.25 (s); ^{19}F NMR ($CDCl_3$) δ −1.43 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 232 (M^+, 9.8), 214 (24.3), 195 (1.6), 145 (2.7), 134 (4.0), 120 (9.1), 119 (100.0), 91 (34.8); HRMS (EI) found m/z 232.0710, calcd for $C_{11}H_{11}F_3O_2$ M, 232.0711. Anal. Calcd: C, 56.90; H, 4.77. Found: C, 56.83; H, 4.72.

4,4,4-Trifluoro-3-hydroxy-1-(4-methoxyphenyl)-1-butanone 3c:[20,21] R_f 0.10 (benzene); mp 104.5−105.1 °C (hexane/ethyl acetate); IR (KBr) 1677.1 (C═O), 3379.3 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27 (dd, J = 17.81, 4.15 Hz, 1H), 3.32 (dd, J = 17.81, 8.05 Hz, 1H), 3.65 (d, J = 4.39 Hz, 1H), 3.90 (s, 3H), 4.62−4.71 (m, 1H), 6.97 and 7.95 (AB quartet, J = 8.79 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 37.64 (s), 55.58 (s), 67.18 (q, J = 31.98 Hz), 114.04 (s), 124.80 (q, J = 280.37 Hz), 129.05 (s), 130.61 (s), 164.34 (s), 196.13 (s); ^{19}F NMR ($CDCl_3$) δ −1.42 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 248 (M^+, 16.8), 230 (37.4), 150 (5.6), 136 (11.9), 135 (100.0), 107 (9.4), 92 (11.9), 77 (13.7); HRMS (EI) found m/z 248.0663, calcd for $C_{11}H_{11}F_3O_3$ M, 248.0660. Anal. Calcd: C, 53.23; H, 4.47. Found: C, 53.11; H, 4.44.

1-(4-Chlorophenyl)-4,4,4-trifluoro-3-hydroxy-1-butanone 3d:[20] R_f 0.25 (benzene); mp 109.3−110.0 °C (hexane/ethyl acetate); IR (KBr) 1688.3 (C═O), 3383.7 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.27 (dd, J = 17.63, 2.56 Hz, 1H), 3.37 (dd, J = 17.63, 9.27 Hz, 1H), 3.40 (d, J = 4.63 Hz, 1H), 4.65−4.74 (m, 1H), 7.49 and 7.92 (AB quartet, J = 8.79 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 38.28 (s), 66.90 (q, J = 33.08 Hz), 124.70 (q, J = 281.19 Hz), 129.24 (s), 129.60 (s), 134.29 (s), 140.76 (s), 196.18 (s); ^{19}F NMR ($CDCl_3$) δ −1.50 (d, J = 6.86 Hz, 3F); MS (EI) m/z (rel intensity) 254 (M^+ + 2, 1.3), 252 (M^+, 4.0), 236 (13.0), 235 (3.7), 234 (34.2), 232 (7.8), 142 (3.3), 141 (40.6), 140 (10.0), 139 (100.0), 123 (4.5), 113 (14.8), 112 (4.4), 111 (33.8), 76 (4.1), 75 (14.0), 74 (3.7); HRMS (EI) found m/z 254.0138, calcd for $C_{10}H_8{}^{37}ClF_3O_2$ M, 254.0135, found m/z 252.0162, calcd for $C_{10}H_8{}^{35}ClF_3O_2$ M, 252.0165. Anal. Calcd: C, 47.55; H, 3.19. Found: C, 47.54; H, 3.30.

4,4,4-Trifluoro-3-hydroxy-1-(4-nitrophenyl)-1-butanone 3e:[20,21] R_f 0.11 (benzene); mp 104.5−105.0 °C (hexane/ethyl acetate); IR (KBr) 1698.0 (C═O), 3429.7 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.15 (d, J = 4.88 Hz, 1H), 3.32 (dd, J = 17.69, 2.44 Hz, 1H), 3.47 (dd, J = 17.69, 9.51 Hz, 1H), 4.70−4.79 (m, 1H), 8.15 and 8.36 (AB quartet, J = 9.27 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 39.01 (s), 66.72 (q, J = 32.26 Hz), 124.09 (s), 124.59 (q, J = 281.19 Hz), 129.29 (s), 140.28 (s), 150.85 (s), 195.52 (s); ^{19}F NMR ($CDCl_3$) δ −1.53 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 263 (M^+, 5.1), 247 (6.7), 246 (13.3), 245 (23.8), 244 (10.6), 243 (83.9), 229 (3.3), 215 (3.8), 194 (4.8), 165 (9.6), 151 (46.7), 150 (100.0), 123 (12.8), 120 (26.8), 105 (7.1), 104 (84.3), 92 (29.1), 76 (35.0), 75 (14.9); HRMS (EI) found m/z 263.0403, calcd for $C_{10}H_8F_3NO_4$ M, 263.0405. Anal. Calcd: C, 45.64; H, 3.06; N, 5.32. Found: C, 45.68; H, 3.13; N, 5.41.

4,4,4-Trifluoro-3-hydroxy-1-(2-methylphenyl)-1-butanone 3f: R_f 0.20 (benzene); mp 81.1−81.6 °C (hexane/ethyl acetate); IR (KBr) 1685.2 (C═O), 3408.5 (OH) cm^{-1};^{1}H NMR ($CDCl_3$) δ 2.54 (s, 3H), 3.26 (dd, J = 17.69, 3.05 Hz, 1H), 3.33 (dd, J = 17.69, 8.91 Hz, 1H), 3.55 (d, J = 4.64 Hz, 1H), 4.62−4.71 (m, 1H), 7.28−7.33 (m, 2H), 7.42−7.46 (m, 1H), 7.70−7.72 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 21.63 (s), 40.49 (s), 67.26 (q, J = 31.97 Hz), 124.77 (q, J = 280.64 Hz), 125.97 (s), 129.09 (s), 132.39 (s), 132.48 (s), 136.17 (s), 139.18 (s), 200.77 (s); ^{19}F NMR ($CDCl_3$) δ −1.42 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 232 (M^+, 34.9), 214 (22.5), 194 (16.6), 167 (13.6), 145 (100.0), 127 (17.6), 117 (11.6), 91 (61.1); HRMS (EI) found m/z 232.0710, calcd for $C_{11}H_{11}F_3O_2$ M, 232.0711. Anal. Calcd: C, 56.90; H, 4.77. Found: C, 56.94; H, 4.77.

4,4,4-Trifluoro-3-hydroxy-1-(2-thienyl)-1-butanone 3g:[22] R_f 0.18 (benzene); mp 71.3−71.7 °C (hexane/ethyl acetate);

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IR (KBr) 1663.7 (C═O), 3385.6 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.26 (dd, J = 17.20, 2.93 Hz, 1H), 3.33 (dd, J = 17.20, 9.03 Hz, 1H), 3.50 (d, J = 4.88 Hz, 1H), 4.61−4.72 (m, 1H), 7.18 (dd, J = 5.13, 3.67 Hz, 1H), 7.74 (dd, J = 5.13, 1.23 Hz, 1H), 7.78 (dd, J = 3.67, 1.23 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.73 (s), 66.93 (q, J = 31.98 Hz), 124.64 (q, J = 280.64 Hz), 128.45 (s), 133.21 (s), 135.20 (s), 143.01 (s), 190.01 (s); ^{19}F NMR ($CDCl_3$) δ −1.51 (d, J = 6.86 Hz, 3F); MS (EI) m/z (rel intensity) 224 (M^+, 9.9), 207 (4.3), 206 (44.4), 205 (7.3), 204 (8.0), 159 (3.2), 150 (3.2), 126 (5.1), 112 (8.2), 111 (100.0), 83 (6.0); HRMS (EI) found m/z 224.0121, calcd for $C_8H_7F_3O_2S$ M, 224.0119. Anal. Calcd: C, 42.86; H, 3.15. Found: C, 43.00; H, 3.22.

6,6,6-Trifluoro-5-hydroxy-2-methyl-3-hexanone 3h:[23] R_f 0.12 (benzene); mp 33.5−34.2 °C (hexane/ethyl acetate); IR (KBr) 1709.6 (C═O), 3397.0 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.15 (d, J = 6.83 Hz, 6H), 2.65 (septet, J = 6.83 Hz, 1H), 2.79 (dd, J = 17.93, 2.92 Hz, 1H), 2.87 (dd, J = 17.93, 9.03 Hz, 1H), 3.41 (d, J = 4.39 Hz, 1H), 4.44−4.55 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 17.77 (s), 39.52 (s), 41.62 (s), 66.75 (q, J = 31.98 Hz), 124.70 (q, J = 280.64 Hz), 212.63 (s); ^{19}F NMR ($CDCl_3$) δ −1.69 (d, J = 6.86 Hz, 3F); MS (EI) m/z (rel intensity) 184 (M^+, 1.9), 166 (4.4), 164 (3.7), 141 (100.0), 138 (22.7), 123 (42.9), 113 (16.9), 95 (8.5), 71 (37.0), 69 (6.3); HRMS (EI) found m/z 184.0716, calcd for $C_7H_{11}F_3O_2$ M, 184.0711. Anal. Calcd: C, 45.65; H, 6.02. Found: C, 45.47; H, 5.80.

1-(4-Ethoxycarbonylphenyl)-4,4,4-trifluoro-3-hydroxy-1-butanone 3i: R_f 0.08 (benzene); mp 124.2−124.7 °C (hexane/ethyl acetate); IR (KBr) 1688.3 (C═O), 1717.0 (C═O), 3412.3 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.43 (t, J = 7.32 Hz, 3H), 3.33 (dd, J = 17.68, 2.44 Hz, 1H), 3.33 (d, J = 4.88 Hz, 1H), 3.43 (dd, J = 17.68, 9.52 Hz, 1H), 4.42 (q, J = 7.32 Hz, 2H), 4.68−4.77 (m, 1H), 8.03 and 8.17 (AB quartet, J = 8.78 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 14.23 (s), 38.74 (s), 61.65 (s), 66.81 (q, J = 32.53 Hz), 124.73 (q, J = 280.64 Hz), 128.07 (s), 129.99 (s), 135.10 (s), 139.00 (s), 165.52 (s), 196.79 (s); ^{19}F NMR ($CDCl_3$) δ −1.81 (d, J = 6.86 Hz, 3F); MS (EI) m/z (rel intensity) 290 (M^+, 3.4), 270 (6.3), 245 (27.1), 227 (18.1), 218 (9.3), 217 (11.0), 178 (22.7), 177 (100.0), 149 (56.9), 147 (13.9), 121 (15.9), 104 (19.4), 103 (10.1), 77 (7.9), 76 (20.8), 65 (15.5). Anal. Calcd for C, 53.80; H, 4.51. Found: C, 53.84; H, 4.49.

1-Cyclohexyl-4,4,4-trifluoro-3-hydroxy-1-butanone 3j: R_f 0.16 (benzene); mp 40.9−41.6 °C (hexane/ethyl acetate); IR (KBr) 1707.3 (C═O), 3400.5 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.14−1.94 (m, 10H), 2.39 (tt, J = 11.45, 3.42 Hz, 1H), 2.78 (dd, J = 17.81, 3.42 Hz, 1H), 2.85 (dd, J = 17.81, 8.79 Hz, 1H), 3.44 (d, J = 4.39 Hz, 1H), 4.43−4.52 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 25.38 (s), 25.61 (s), 28.05 (s), 39.62 (s), 51.33 (s), 66.86 (q, J = 31.98 Hz), 124.60 (q, J = 281.19 Hz), 212.00 (s); ^{19}F NMR ($CDCl_3$) δ −1.96 (d, J = 6.87 Hz, 3F); MS (EI) m/z (rel intensity) 224 (M^+, 3.7), 206 (0.5), 169 (15.2), 141 (12.1), 123 (3.4), 113 (5.0), 111 (22.7), 95 (2.2), 83 (100.0), 68 (11.6), 67 (12.2). Anal. Calcd: C, 53.57; H, 6.74. Found: C, 53.54; H, 6.64.

6,6,6-Trifluoro-5-hydroxy-2,2-dimethyl-3-hexanone 3k: R_f 0.17 (benzene); mp 44.4−44.8 °C (hexane/ethyl acetate); IR (KBr) 1708.9 (C═O), 3518.7 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 1.18 (s, 9H), 2.80 (dd, J = 17.81, 2.69 Hz, 1H), 2.91 (dd, J = 17.81, 9.03 Hz, 1H), 3.42 (d, J = 4.39 Hz, 1H), 4.42−4.53 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 26.01 (s), 36.34 (s), 44.52 (s), 66.92 (q, J = 31.98 Hz), 124.80 (q, J = 280.64 Hz), 214.23 (s); ^{19}F NMR ($CDCl_3$) δ −1.59 (d, J = 6.86 Hz, 3F); MS (EI) m/z (rel intensity) 198 (M^+, 0.8), 141 (9.3), 87 (12.2), 85 (73.3), 84 (10.4), 83 (100.0), 82 (39.6), 71 (4.5). Anal. Calcd: C, 48.48; H, 6.61. Found: C, 48.33; H, 6.42.

4,4-Difluoro-3-hydroxy-1-phenyl-1-butanone 5a:[15] R_f 0.08 (benzene); IR (KBr) 1684.1 (C═O), 3508.2 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.29 (dd, J = 17.93, 7.81 Hz, 1H), 3.34 (dd, J = 17.93, 4.15 Hz, 1H), 3.43 (br s, 1H), 4.41−4.50 (m, 1H), 5.91 (dt, J = 55.87, 3.42 Hz, 1H), 7.48−7.52 (m, 2H), 7.60−7.65 (m, 1H), 7.96−7.99 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 37.77 (s), 67.74 (t, J = 24.81 Hz), 115.50 (t, J = 243.15 Hz), 128.16 (s), 128.77 (s), 133.92 (s), 136.24 (s), 198.79 (s); ^{19}F NMR ($CDCl_3$) δ −50.93 (ddd, J = 287.92, 55.87, 9.73 Hz, 1F), −53.75 (ddd, J = 287.92, 55.87, 14.12 Hz, 1F); MS (EI) m/z (rel intensity) 200 (M^+; 14.2), 180 (80.8), 136 (11.9), 149 (47.1), 120 (33.5), 105 (100.0), 91 (17.2), 77 (89.8); HRMS (EI) found m/z 200.0620, calcd for $C_{10}H_{10}F_2O_2$ M, 200.0649.

4,4-Difluoro-3-hydroxy-1-(4-methylphenyl)-1-butanone 5b: R_f 0.06 (benzene); mp 42.5−43.5 °C (hexane/ethyl acetate); IR (KBr) 1680.2 (C═O), 3501.2 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.43 (s, 3H), 3.25 (dd, J = 18.05, 8.29 Hz, 1H), 3.31 (dd, J = 17.81, 4.15 Hz, 1H), 3.50 (d, J = 4.88 Hz, 1H), 4.38−4.49 (m, 1H), 5.89 (dt, J = 55.86, 3.41 Hz, 1H), 7.29 and 7.87 (AB quartet, J = 8.30 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.71 (s), 37.46 (s), 67.88 (t, J = 24.81 Hz), 115.50 (t, J = 243.98 Hz), 128.29 (s), 129.49 (s), 133.75 (s), 145.02 (s), 198.58 (s); ^{19}F NMR ($CDCl_3$) δ −50.87 (ddd, J = 287.73, 55.86, 9.92 Hz, 1F), −53.67 (ddd, J = 287.73, 55.86, 14.31 Hz, 1F); MS (EI) m/z (rel intensity) 214 (M^+, 1.1), 196 (2.2), 145 (0.9), 134 (1.9), 120 (10.2), 119 (100.0), 91 (40.6), 77 (2.7), 65 (15.2). Anal. Calcd: C, 61.68; H, 5.65. Found: C, 61.72; H, 5.47.

4,4-Difluoro-3-hydroxy-1-(4-methoxyphenyl)-1-butanone 5c: R_f 0.04 (benzene); mp 43.0−44.0 °C (hexane/ethyl acetate); IR (KBr) 1680.2 (C═O), 3503.2 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.22 (dd, J = 17.56, 4.15 Hz, 1H), 3.28 (dd, J = 17.56, 7.81 Hz, 1H), 3.68 (d, J = 3.91 Hz, 1H), 3.88 (s, 3H), 4.37−4.48 (m, 1H), 5.89 (dt, J = 55.87, 3.41 Hz, 1H), 6.95 and 7.93 (AB quartet, J = 8.79 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 37.15 (s), 55.49 (s), 67.87 (t, J = 24.81 Hz), 113.91 (s), 115.54 (t, J = 243.15 Hz), 129.26 (s), 130.51 (s), 164.13 (s), 197.35 (s); ^{19}F NMR ($CDCl_3$) δ −50.84 (ddd, J = 287.23, 55.87, 9.92 Hz, 1F), −53.56 (ddd, J = 287.23, 55.87, 14.12 Hz, 1F); MS (EI) m/z (rel intensity) 230 (M^+; 6.9), 213 (1.3), 212 (5.4), 150 (3.1), 136 (9.6), 135 (100.0), 107 (10.0), 92 (12.5), 77 (18.2). Anal. Calcd for C, 57.39; H, 5.25. Found: C, 57.60; H, 5.25.

1-(4-Chlorophenyl)-4,4-difluoro-3-hydroxy-1-butanone 5d: R_f 0.09 (benzene); mp 91.5−92.5 °C (hexane/ethyl acetate); IR (KBr) 1693.7 (C═O), 3426.0 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.25 (dd, J = 18.05, 5.13 Hz, 1H), 3.29 (dd, J = 18.05, 6.59 Hz, 1H), 3.45 (d, J = 4.88 Hz, 1H), 4.40−4.51 (m, 1H), 5.90 (dt, J = 55.74, 3.41 Hz, 1H), 7.46 and 7.90 (AB quartet, J = 8.78 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 37.74 (s), 67.60 (t, J = 24.81 Hz), 115.38 (t, J = 243.98 Hz), 129.13 (s), 129.56 (s), 134.49 (s), 140.50 (s), 197.46 (s); ^{19}F NMR ($CDCl_3$) δ −50.83 (ddd, J = 287.92, 55.74, 9.92 Hz, 1F), −53.71 (ddd, J = 287.92, 55.74, 14.31 Hz, 1F); MS (EI) m/z (rel intensity) 234 (1.9), 141 (34.7), 139 (100.0), 113 (7.4), 111 (24.3). Anal. Calcd: C, 51.19; H, 3.87. Found: C, 51.31; H, 3.98.

4,4-Difluoro-3-hydroxy-1-(4-nitrophenyl)-1-butanone 5e: R_f 0.04 (benzene); mp 88.0−89.0 °C (hexane/ethyl acetate); IR (KBr) 1691.8 (C═O), 3445.3 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.12 (d, J = 4.87 Hz, 1H), 3.33 (dd, J = 18.05, 4.39 Hz, 1H), 3.39 (dd, J = 18.05, 7.81 Hz, 1H), 4.45−4.56 (m, 1H), 5.92 (dt, J = 55.62, 3.41 Hz, 1H), 8.15 and 8.35 (AB quartet, J = 9.27 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 38.48 (s), 67.50 (t, J = 24.81 Hz), 115.22 (t, J = 243.98 Hz), 124.04 (s), 129.26 (s), 140.51 (s), 150.75 (s), 196.95 (s); ^{19}F NMR ($CDCl_3$) δ −50.76 (ddd, J = 288.78, 55.62, 9.54 Hz, 1F), −53.75 (ddd, J = 288.78, 55.62, 14.12 Hz, 1F); MS (EI) m/z (rel intensity) 227 ($M^+ - H_2O$; 19.7), 176 (17.5), 151 (12.3), 150 (100.0), 149 (6.9), 134 (7.8), 133 (14.4), 120 (16.5), 105 (33.6), 104 (36.9), 103 (6.4), 102 (5.1), 92 (19.1), 83 (11.3), 77 (24.4), 76 (29.6), 75 (16.7), 74 (12.1). Anal. Calcd: C, 48.99; H, 3.70; N, 5.71. Found: C, 49.00; H, 3.76; 5.66.

4,4,4-Difluoro-3-hydroxy-1-(2-thienyl)-1-butanone 5f: R_f 0.05 (benzene); IR (neat) 1650.9 (C═O), 3442.2 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.23 (dd, J = 17.57, 5.86 Hz, 1H), 3.27 (dd, J = 17.81, 6.11 Hz, 1H), 3.49 (d, J = 4.88 Hz, 1H), 4.38−4.49 (m, 1H), 5.88 (dt, J = 55.87, 3.42 Hz, 1H), 7.17 (dd, J = 4.88, 3.90 Hz, 1H), 7.72 (dd, J = 4.88, 0.98 Hz, 1H), 7.78 (dd, J = 3.90, 0.98 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 38.23 (s), 67.81 (t, J = 25.64 Hz), 115.36 (t, J = 243.15 Hz), 128.40 (s), 133.06 (s),

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134.94 (s), 143.28 (s), 191.36 (s); ^{19}F NMR ($CDCl_3$) δ −50.80 (ddd, J = 288.63, 55.87, 9.54 Hz, 1F), −53.65 (ddd, J = 287.63, 55.87, 13.74 Hz, 1F); MS (EI) *m*/*z* (rel intensity) 206 (M^+, 2.7), 188 (10.1), 186 (4.5), 155 (4.2), 126 (8.1), 111 (100.0), 110 (15.3), 83 (10.4); HRMS (EI) found *m*/*z* 206.0246, calcd for $C_8H_8F_2O_2S$ M, 206.0213.

Pentafluoro-3-hydroxy-4,4,5,5,5−1-phenyl-1-pentanone 6a: R_f 0.23 (benzene); mp 98.0−99.0 °C (hexane/ethyl acetate); IR (KBr) 1684.1 (C═O), 3350.8 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.35−3.46 (m, 2H), 3.57 (d, J = 4.39 Hz, 1H), 4.74−4.88 (m, 1H), 7.49−7.53 (m, 2H), 7.62−7.66 (m, 1H), 7.97−7.99 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 37.49 (s), 66.26 (dd, J = 29.25, 22.92 Hz), 113.68 (ddq, J = 260.69, 253.13 and 36.01 Hz), 119.00 (qt, J = 286.00, 35.59 Hz), 128.25 (s), 128.89 (s), 134.23 (s), 136.00 (s), 198.06 (s); ^{19}F NMR ($CDCl_3$) δ −3.84 (s, 3F), −44.36 (dd, J = 276.57, 5.72 Hz, 1F), −52.96 (dd, J = 276.57, 18.70 Hz, 1F); MS (EI) *m*/*z* (rel intensity) 268 (M^+, 1.3), 248 (7.6), 149 (3.8), 106 (30.4), 105 (100.0), 78 (18.4) 77 (10.0). Anal. Calcd: C, 49.26; H, 3.38. Found: C, 49.25; H, 3.35.

4,4,5,5,5-Pentafluoro-3-hydroxy-1-(4-methylphenyl)-1-pentanone 6b: R_f 0.25 (benzene); mp 91.5−92.5 °C (hexane/ethyl acetate); IR (KBr) 1662.8 (C═O), 3481.9 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.44 (s), 3.32−3.42 (m, 2H), 3.65 (d, J = 3.42 Hz, 1H), 4.72−4.88 (m, 1H), 7.30 and 7.87 (AB quartet, J = 7.81 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 21.65 (s), 37.31 (s), 66.25 (dd, J = 29.01, 22.68 Hz), 113.75 (ddq, J = 260.20, 253.14, 36.20 Hz), 119.04 (qt, J = 286.49, 35.58 Hz), 128.38 (s), 129.54 (s), 133.58 (s), 145.33 (s), 197.70 (s); ^{19}F NMR ($CDCl_3$) δ −3.88 (s, 3F), −44.41 (dd, J = 276.76, 5.34 Hz, 1F), −53.03 (dd, J = 276.76, 18.69 Hz, 1F); MS (EI) *m*/*z* (rel intensity) 282 (M^+, 1.7), 120 (10.5), 119 (100.0), 91 (33.8), 83 (4.6), 77 (2.2), 65 (11.8). Anal. Calcd for C, 51.07; H, 3.93. Found: C, 51.13; H, 3.78.

4,4,5,5,5-Pentafluoro-1-(4-chlorophenyl)-3-hydroxy-1-pentanone 6c: R_f 0.30 (benzene); mp 93.0−94.0 °C (hexane/ethyl acetate); IR (KBr) 1686.0 (C═O), 3410.6 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 3.29−3.43 (m, 2H), 3.48 (d, J = 4.88 Hz, 1H), 4.74−4.87 (m, 1H), 7.48 and 7.92 (AB quartet, J = 8.78 Hz, 4H); ^{13}C NMR ($CDCl_3$) δ 37.55 (s), 66.01 (dd, J = 29.25, 22.91 Hz), 113.50 (ddq, J = 260.33, 253.26 and 36.22 Hz), 118.91 (qt, J = 285.84, 35.35 Hz), 129.17 (s), 129.57 (s), 134.27 (s), 140.77 (s), 196.65 (s); ^{19}F NMR ($CDCl_3$) δ −3.84 (s, 3F), −44.31 (dd, J = 276.57, 4.96 Hz, 1F), −52.90 (dd, J = 276.57, 18.70 Hz, 1F); MS (EI) *m*/*z* (rel intensity) 302 (M^+, 0.7), 141 (63.7), 140 (16.8), 139 (100.0), 113 (17.9), 111 (53.9), 76 (9.2), 75 (29.1), 69 (6.0). Anal. Calcd for C, 43.66; H, 2.66. Found: C, 43.55; H, 2.38.

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Supporting Information Available: ^{1}H and ^{13}C NMR spectra for **5a**,**f**. This material is available free of charge via the Internet at http://pubs.acs.org.

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