Tetrahedron 64 (2008) 5728–5735

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A convenient one-pot synthesis of 2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one derivatives and their further transformations

Shaodi Song [a], Liping Song [a,b,*], Baifan Dai [a], Hai Yi [a], Guifang Jin [b], Shizheng Zhu [b,*], Min Shao [c]

[a] *Department of Chemistry, School of Science, Shanghai University, No. 99, Shangda Road, Shanghai 200444, China*
[b] *Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Lu, Shanghai 200032, China*
[c] *Instrumental Analysis and Research Center, Shanghai University, Shanghai 200444, China*

ARTICLE INFO

Article history:
Received 24 January 2008
Received in revised form 2 April 2008
Accepted 7 April 2008
Available online 9 April 2008

Keywords:
One-pot multi-component reaction
Fluorinated heterocycles
Trifluoromethyl-1,3-dione
Dehydration

ABSTRACT

The trifluoromethyl containing heterocycles, 2-hydroxy-4-aryl-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one derivatives **4**, were synthesized via a one-pot three-component reaction of aldehyde **1** with 1,3-cyclohexanedione **2** and 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **3** in the presence of a catalytic amount of Et_3N. The effect of bases and solvents on the reaction efficiency and yield was briefly investigated. Treatment of **4** with an excess amount of NH_4OAc in ethanol afforded 2-trifluoromethyl-1*H*-quinolin-5-one derivatives **5**. Refluxing of **4** with TsOH in $CHCl_3$ gave the corresponding dehydrated products **8**.

1. Introduction

Fluorine-containing compounds have attracted much interest because of their unique chemical, physical, and biological activities.[1–3] In particular, fluorine-containing heterocycles are now widely recognized as important organic molecules showing interesting biological activities with potential for applications in the medicinal and agricultural fields.[4,5] The reactions of fluorinated 1,3-dicarbonyl compounds as fluorine-containing building blocks have been investigated extensively,[6,7] and well established as synthetic intermediates in heterocyclic chemistry.[8] In recent years, the synthesis of fluorinated heterocyclic compounds has drawn much attention.[9]

Furthermore, the multi-component reactions (MCRs), by virtue of their convergence, productivity, facile execution, and generally high yields of products, have attracted much attention from the vantage point of combinatorial chemistry.[10] For example, the synthesis of polyhydroquinoline derivatives was the classical MCRs involving the three-component coupling of an aldehyde, ethyl acetoacetate, and ammonia in acetic acid or refluxing alcohol.[11] More recently, several alternate and more efficient methods have been developed for MCRs to polyhydroquinoline derivatives by using microwave, ionic liquid, TMSCl–NaI, metal triflates, I_2, ceric ammonium nitrate, polymer, organo-catalyst, solvent-free, and catalyst-free reactions.[12] In order to evaluate the potential applications of MCRs in the field of organofluorine chemistry and to continue our ongoing study on the synthesis of fluorine-containing heterocyclic compounds via MCRs based on the trifluoromethyl-1,3-dicarbonyl compounds, a versatile fluorine-containing building blocks, herein, we wish to report a one-pot, three-component reaction to 2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one derivatives, together with their further chemical transformations including *O*-heterocyclics to *N*-heterocyclics interconversion and dehydration reactions of α-hydro-dihydropyrane moieties to 4-*H* pyrane derivatives.

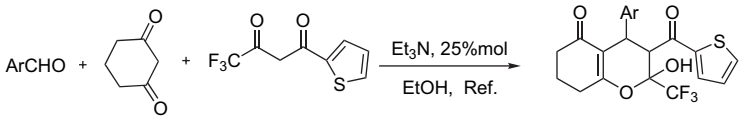
2. Results and discussion

Initially, we carried out the one-pot, three-component reaction of benzaldehyde **1a** and 1,3-cyclohexanedione **2** with 4,4,4-trifluoromethyl-1-(thien-2-yl)-butane-1,3-dione **3** in the presence of a catalytic amount of triethylamine (10%) in ethanol at room temperature, however, no reaction occurred. Subsequently, the mixture was heated to reflux, after stirring for 2 h, TLC showed that the reaction proceeded smoothly and gave the product **4a** in 60% yield (Scheme 1).

Based on the results above, the reaction conditions were optimized to improve the yield by changing bases and solvents. The effect of a variety of organic bases and the amount on the reaction efficiency and yield was firstly screened (Table 1). As shown in Table 1, when the reaction was performed in the absence of base, it only

* Corresponding authors.
E-mail addresses: lpsong@shu.edu.cn (L. Song), zhusz@mail.sioc.ac.cn (S. Zhu).

0040-4020/$ – see front matter © 2008 Elsevier Ltd. All rights reserved.
doi:10.1016/j.tet.2008.04.020



Ar = C_6H_5 a; p-$CH_3C_6H_4$ b; p-$CH_3OC_6H_4$ c; p-HOC_6H_4 d; p-$(Me)_2NC_6H_4$ e; p-ClC_6H_4 f; p-$NO_2C_6H_4$ g; m-$NO_2C_6H_4$ h; m-$PhOC_6H_4$ i; m-BrC_6H_4 j

Scheme 1.

afforded product **4a** in 10% yield (entry 1, Table 1), however, when 0.25 equiv of Et_3N was used, the yield was improved significantly (entry 3, Table 1). The reaction took much longer reaction time to give the **4a** in 40% yield when pyridine was involved as catalyst (entry 8, Table 1). Other organic bases such as DABCO, DMAP, and piperidine catalyzed the reactions giving almost the same results as the triethylamine catalyzed reaction in terms of reaction time and yields (entries 5–7, Table 1). Higher amounts of catalyst did not further improve the yield of **4a** (entry 4, Table 1).

Solvent effect was the next considered factor. As shown in Table 1, generally, the reactions gave the better yields in polar protic solvents such as MeOH or EtOH than that in polar aprotic solvents (entries 7–11, Table 1), even though the latter reactions were carried out in prolonged reaction time. Moreover, the reaction in absolute ethanol under the nitrogen atmosphere gave the same product yield as that in the commercially available ethanol, indicating that the trace of water in ethanol did not accelerate the reaction obviously (entries 12 and 13, Table 1).

With the optimal results in hand as shown in Table 1, entry 3, we investigated the scope and limitation of this one-pot, three-component reaction with a variety of aldehydes, and the appropriate **4** were generally obtained in moderate to good yields (Scheme 1). The reaction results are summarized in Table 2. On one hand, the aryldehydes bearing either electron-donating or electron-withdrawing group have not shown the obvious effort on the formation of the expected products. On the other hand, the substituents located at *para* or *meta* positions of aryldehydes have not shown the much effort on the formation of products, too (entries 8 and 9, Table 2). Prolonged reaction time from 2 h to 24 h slightly increased the yield (entries 2 and 3, Table 2). However, the steric effect of substituent was noticeable. For example, *ortho* substituted aryldehydes such as 2-methoxyl-benzaldehyde or 2-bromo-benzaldehyde gave

Table 1
The effect of a variety of bases and solvents on this one-pot reaction[a]

Entry	**1** (Ar=)	Solvent	Base (equiv)	Time/h	Yield of **4a**[b] (%)
1	C_6H_5	EtOH	—[c]	2	10
2	C_6H_5	EtOH	Et_3N (0.1)	2	60
3	C_6H_5	EtOH	Et_3N (0.25)	2	68
4	C_6H_5	EtOH	Et_3N (0.5)	2	68
5	C_6H_5	EtOH	DABCO (0.25)	8	60
6	C_6H_5	EtOH	DMAP (0.25)	2	63
7	C_6H_5	EtOH	Piperidine (0.25)	2	65
8	C_6H_5	EtOH	Pyridine (0.25)	52	40
9	C_6H_5	MeOH	Et_3N (0.25)	2	48
10	C_6H_5	DME	Et_3N (0.25)	72	11
11	C_6H_5	CH_2Cl_2	Et_3N (0.25)	72	15
12	C_6H_5	CH_3CN	Et_3N (0.25)	24	47
13	p-$NO_2C_6H_4$	EtOH	Et_3N (0.25)	2	60
14	p-$NO_2C_6H_4$	EtOH[d]	Et_3N (0.25)	2	60

[a] Reaction conditions: aryldehyde **1** (1.5 mmol), 1,3-cyclohexanedione **2** (1.5 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **3** (1.5 mmol), solvent: 15 mL, refluxing.
[b] Isolated yield.
[c] Without base.
[d] The reaction was carried out in freshly distilled absolute EtOH under nitrogen.

Table 2
Reaction results of the one-pot, three-component reaction of aryldehyde **1** and 1,3-cyclohexanedione **2** with 4,4,4-trifluoro-1-(thien-2-yl)-butane-1,3-dione **3**[a]

Entry	Ar=	Time/h	Product	Yield[b] (%)
1	C_6H_5	2	**4a**	68
2	p-$CH_3C_6H_4$	3	**4b**	85
3	p-$CH_3C_6H_4$	24	**4b**	88
4	p-$CH_3OC_6H_4$	8	**4c**	65
5	p-HOC_6H_4	12	**4d**	36
6	p-$(Me)_2NC_6H_4$	12	**4e**	65
7	p-ClC_6H_4	2	**4f**	60
8	p-$NO_2C_6H_4$	5	**4j**	60
9	m-$NO_2C_6H_4$	2	**4h**	66
10	m-$PhOC_6H_4$	10	**4i**	48
11	m-BrC_6H_4	12	**4j**	47

[a] Reaction conditions: aryldehyde **1** (1.5 mmol), 1,3-cyclohexanedione **2** (1.5 mmol), 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **2** (1.5 mmol), Et_3N (25% equiv), EtOH (15 mL), refluxing.
[b] Isolated yield.

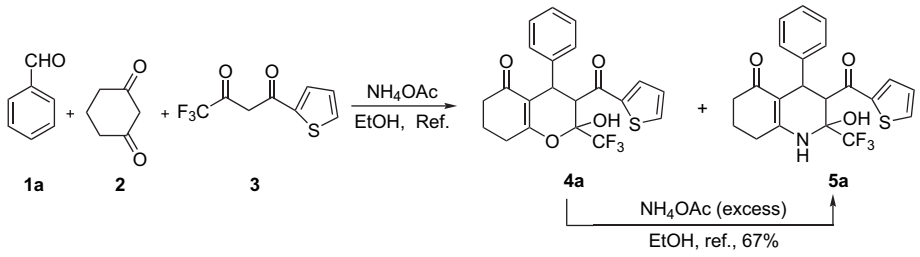
no expected product, TLC analysis showed that the starting material remained. Similarly, steric aromatic hindered aryldehydes such as 1-naphthaldehyde[13] or 3,4-dimethoxyl-benzaldehyde, gave no expected product, too. The above results have shown that the reactivity of the aryldehyde differs significantly depending on the steric effect, other than the nature of electronic effect of the substituents. Other aldehydes, either the furan-2-carbaldehyde or the aliphatic aldehydes such as acetaldehyde and cinnamic aldehyde were also invested in the reaction, unfortunately, there was no expected product obtained. It should be noted that in the case of **4d** (entry 5, Table 2), the yield was lower than that of other aryldehydes, even after modification of the reaction conditions like prolonged reaction time.

The structures of compounds **4** were fully confirmed by ^1H NMR, ^{19}F NMR, MS, IR spectroscopies and elemental analysis. For instance, the characteristic features of the ^1H NMR in $CDCl_3$ spectra of **4b** were the appearances of doublets at δ 4.02 and 3.80 ppm with J_{H-H}=11.7 Hz for 3-H and 4-H protons, respectively, indicating that a *trans* configuration of the vicinal two hydrogen atoms. The chemical shift of CF_3 group in ^{19}F NMR was a singlet peak at δ −80.66 ppm (s, 3F), which indicated that the CF_3 group was bonded to a quaternary carbon atom. In most cases, the products **4**

Table 3
One-pot reaction of **1**a with **2** and **3** in different amount of NH_4OAc[a]

Entry	NH_4OAc (equiv)	Time/h	Yields[b] (%)	
			Product **4a**	Product **5**
1	0.25	10	65	10
2	1	10	60	33
3	30	10	Trace	55

[a] Reaction conditions: **1a** (1.5 mmol), **2** (1.5 mmol), **3** (1.5 mmol), EtOH (12 mL), refluxing.
[b] Isolated yield.



Scheme 2.

had poor solubility in $CDCl_3$, therefore, most of ^1H NMR spectra of products **4** were recorded in DMSO-d_6, however, the characteristic peaks for 3-H and 4-H in DMSO-d_6 somehow revealed one broad peak in the range of δ 4.1 ppm.

More recently, ammonium acetate has been used widely as a base or a catalyst in Hantzsch reactions as well as other reactions.[14] With this aim in view, we applied ammonium acetate to the above one-pot reaction. It was hoped that the expected products **4** would be obtained in the presence of catalytic amount of NH_4OAc, whereas the polyhydroquinoline derivatives should be formed in the presence of stoichiometric amount of NH_4OAc. Thus, we examined the amount of NH_4OAc affecting the formation of products and the yields. The reaction results are listed in Table 3.

As expected, the reaction occurred smoothly under refluxing in ethanol in the presence of catalytic amount of NH_4OAc (0.25 equiv) and afforded **4a** as the major product in 65% yield, along with minor

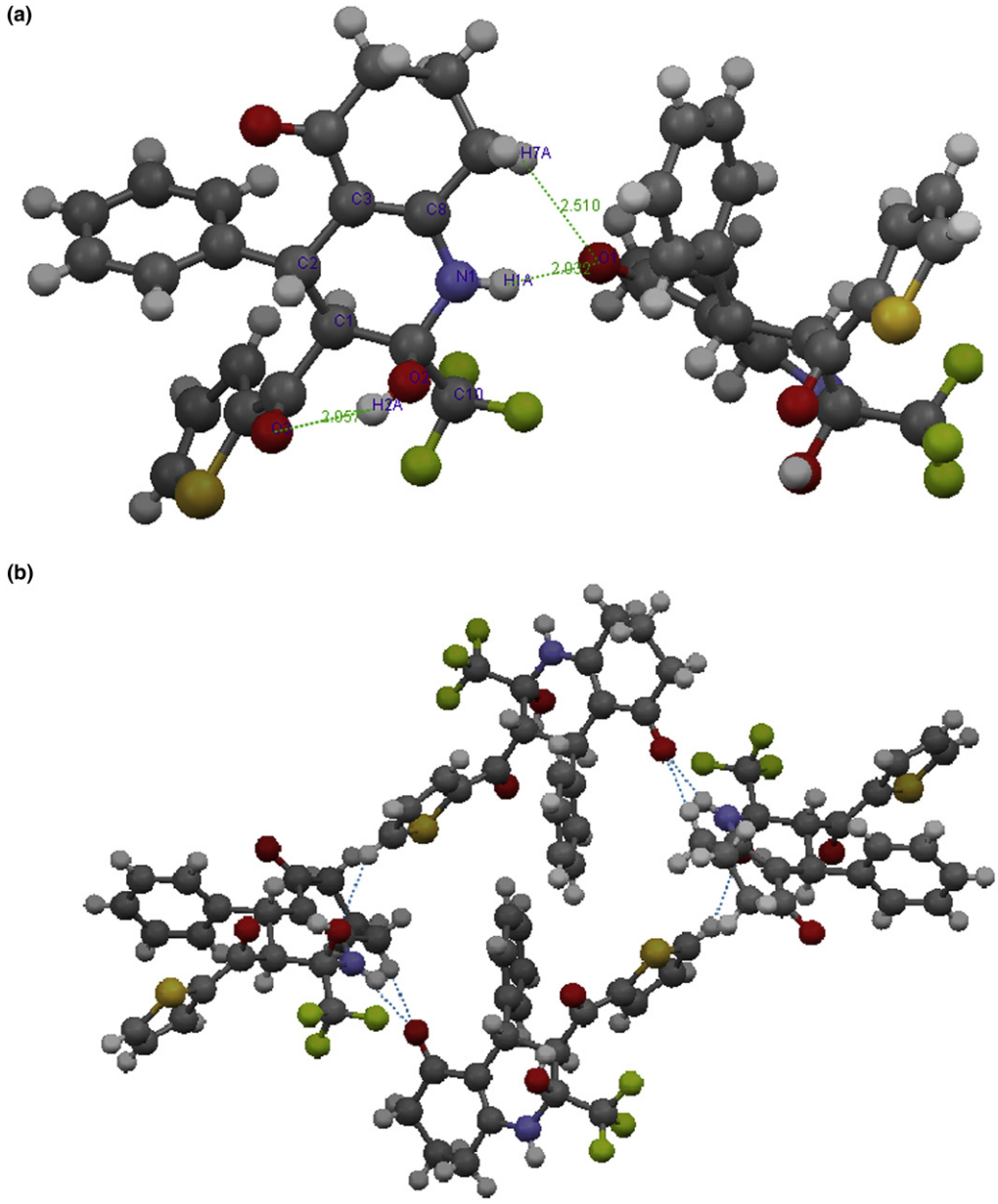


Figure 1. Crystal structure (a) and packing map (b) of **5a**.

Hantzsch product **5a** in 10% yield (Scheme 2). The low yield of **5a** was caused by the insufficiency of NH_3 source in reaction medium (entry 1, Table 3). Thus, NH_4OAc was increased to stoichiometric amount, it was noticed that, although the higher amount of NH_4OAc led to the improvement in the yield of Hantzsch product **5a** from 10% to 33%, the major product was still **4a** (entry 2, Table 3). This result was in agreement with the previous reported work,[15] in which initial formation of the Hantzsch product appeared low due to large quantities of the intermediate pyran derivative formed instead. Furthermore, the pyran derivatives could be converted by either in situ or a stepwise reaction[16] to the corresponding Hantzsch pyridine derivatives. Inspired by the above works, the one-pot reaction was carried out in the presence of 30 equiv of NH_4OAc, as expected, the reaction gave the product **5a** in 55% yield exclusively, without the formation of **4a**. This result suggested that the O-atom ring to N-atom ring interconversion could be achieved by treatment of **4** with an excess of NH_4OAc. To verify the suggestion, we carried out the ring to ring interconversion reaction by treatment of **4a** with an excess of NH_4OAc in refluxing ethanol (Scheme 2).

As expected, **5a** was obtained in 67% yield, whose structure was further confirmed by XRD analysis. It was unambiguous to observe the *trans* relationship between the vicinal six-membered ring protons in compound **5a**. The molecular structure and packing map of **5a** are shown in Figure 1. Several selected bond lengths and selected bond angles are listed in Table 4. The crystal date and refinement details are listed in Table 5. The structure solution revealed that the proton attached to oxygen O2 of hydroxyl group formed a intramolecular H-bond with the oxygen O3 of carbonyl group (D(O3···H2A)=2.057 Å; ∠(O2–H2A···O3)=143.70°). In addition, in the crystal, each of the two molecules were related by two intermolecular H-bonds involving the protons attached nitrogen N1 and carbon C7 with the oxygen O1 of carbonyl group, respectively, (D(O1···H1A)=2.032 Å; ∠(N1–H1A···O1)=154.36°; D(O1···H7A)=2.510 Å; ∠(O1···H7A–C7)=139.21°).

We also examined the one-pot, three-component reaction with other 1,3-dicarbonyl compounds such as fluorinated substrates (**6a**, **6b**) or non-fluorinated substrates (**6c**, **6d**), and similar results were found with these compounds (Scheme 3). The reaction results are summarized in Table 6. However, with 1,3-diketones yields were somewhat lower than the corresponding β-oxo ester (entries 1–4, Table 6). It is very typical for cyclic CF_3-compounds containing hemi-ketal, himi-aminal or even himi-amidal fragment because of the strong electron-withdrawing properties of CF_3 group.[15] However, it should be noted that in our cases of non-fluorinated substrates (**6c**, **6d**), the similar hemi-ketal fragments were also formed instead of the formation of 4-*H* pyran moiety (entries 3 and 4, Table 6).

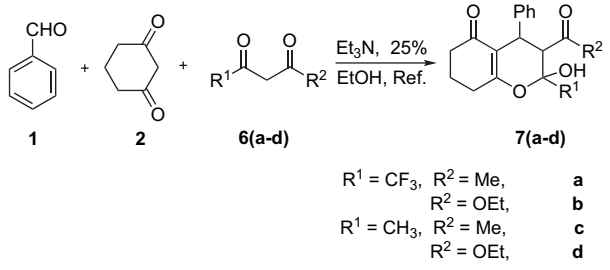
Finally, we studied the dehydration of compounds **4** and **7c**. In contrast to the previous works,[7b,c] in which the α-hydro-dihydropyrane moieties resisted to eliminate water to form the corresponding dehydrated products, compounds **4** and non-fluorinated analogue **7c** were smoothly eliminated water to form the corresponding 4-*H* pyrane derivatives in the presence of an excess of TsOH in boiling $CHCl_3$ in good yields (Scheme 4, Table 7). The structure of compound **8b** was further confirmed by XRD analysis.

Table 4
Selected bond lengths (Å) and bond angles (°) of compounds **5a** and **8b**

5a		**8b**	
Bond lengths			
C(1)–C(2)	1.554(3)	C(1)–C(2)	1.316(3)
C(2)–C(3)	1.514(3)	C(2)–C(3)	1.518(3)
C(1)–C(9)	1.543(4)	C(3)–C(4)	1.511(3)
C(3)–C(8)	1.362(4)	C(4)–C(5)	1.334(3)
C(8)–N(1)	1.361(3)	C(5)–O(1)	1.373(3)
C(9)–O(2)	1.408(3)	C(1)–O(1)	1.387(3)
C(9)–N(1)	1.429(4)	C(1)–C(6)	1.498(3)
C(9)–C(10)	1.536(4)		
Bond angles			
C(9)–C(1)–C(2)	109.6(2)	C(2)–C(1)–O(1)	124.8(2)
C(3)–C(2)–C(1)	108.95(19)	C(1)–C(2)–C(3)	121.0(2)
C(8)–C(3)–C(2)	120.6(2)	C(4)–C(3)–C(2)	109.54(19)
N(1)–C(8)–C(3)	122.3(2)	C(5)–C(4)–C(3)	122.7(2)
C(8)–N(1)–C(9)	122.5(2)	C(5)–O(1)–C(1)	117.09(18)
N(1)–C(9)–C(1)	108.9(2)	C(4)–C(5)–O(1)	122.5(2)

Table 5
The crystal data of **5a** and **8b**

Compounds	**5a**	**8b**
CCDC	681206	681207
Empirial formula	$C_{21}H_{18}F_3NO_3S$	$C_{22}H_{17}F_3O_3S$
fw	421.42	418.42
Temp (K)	273(2)	298(2)
Wavelength (Å)	0.71073	0.71073
Cryst syst	Monoclinic	Monoclinic
Space group	*P*2(1)/*n*	*P*2(1)/*c*
Unit cell dimens		
a (Å)	8.4560(8)	10.123(3)
b (Å)	18.8442(18)	16.980(4)
c (Å)	12.0666(12)	12.138(3)
α (deg)	90	90
β (deg)	95.4540(10)	102.915(4)
γ (deg)	90	90
Volume ($Å^3$)	1914.1(3)	2033.6(9)
Z	4	4
Calcd density (Mg/m^3)	1.462	1.367
Absorp coeff (mm^{-1})	0.221	0.206
F(000)	872	864
Cryst size (mm)	0.30×0.20×0.20	0.30×0.20×0.15
θ range for data collection (deg)	2.01–25.05	2.06–25.05
Limiting indices	$-10\le h\le 10$, $-22\le k\le 10$, $-14\le l\le 14$	$-10\le h\le 12$, $-20\le k\le 17$, $-9\le l\le 14$
Reflections collected/unique	9738/3390 [*R*(int)=0.0140]	10,462/3586 [*R*(int)=0.0319]
Goodness-of-fit on F^2	1.056	0.996
Final *R* indices [$I>2\sigma$ (I)]	R_1=0.0569, wR_2=0.1662	R_1=0.0442, wR_2=0.0869
R indices (all data)	R_1=0.0644, wR_2=0.1740	R_1=0.0738, wR_2=0.1006
Largest diff peak and hole (e $Å^{-3}$)	0.668 and −0.7043	0.319 and −0.239

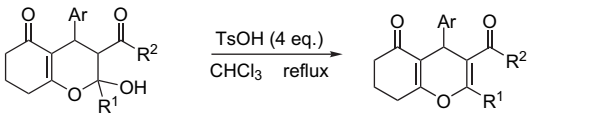


Scheme 3.

Table 6
The one-pot reaction of **1** with **2** and 1,3-dicarbonyl compounds **6**[a]

Entry	R^1	R^2	Time/h	Products	Yield[b] (%)
1	CF_3	Me	5	**7a**	53
2	CF_3	OEt	3	**7b**	86
3	CH_3	Me	3	**7c**	62
4	CH_3	OEt	3	**7d**	79

[a] Reaction conditions: **1** (1.5 mmol), **2** (1.5 mmol), **6** (1.5 mmol), Et_3N (0.25 equiv), EtOH (12 mL), refluxing.
[b] Isolated yield.



4a, 4b, 7c **8(a-c)**

$R^1 = CF_3$, R^2 = Thien-2-yl, Ar = C_6H_5, **a**
$R^1 = CF_3$, R^2 = Thien-2-yl, Ar = *p*-MeC_6H_4, **b**
$R^1 = CH_3$, $R^2 = CH_3$, Ar = C_6H_5, **c**

Scheme 4.

Table 7
Dehydration of α-hydrodihydropyrane derivatives[a]

Entry	Ar	R^1	R^2	Time/h	Product	Yield/%[b]
1	C_6H_5	CF_3	Thien-2-yl	12	**8a**	67
2	*p*-$CH_3C_6H_4$	CF_3	Thien-2-yl	12	**8b**	83
3	C_6H_5	CH_3	CH_3	4	**8c**	73

[a] Reaction conditions: **4a**,**4b**,**7c** (0.5 mmol), *p*-TsOH (2.0 mmol, 4 equiv), solvent: $CHCl_3$ (15 mL), refluxing.
[b] Isolated yields.

The crystal structure is shown in Figure 2. The selected bond lengths and selected bond angles are listed in Table 4.

3. Conclusions

In conclusion, we have developed a one-pot reaction for the synthesis of 2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one derivatives **4** from easily available starting materials. Under the same reaction conditions, non-fluorinated substrates afforded the similar himi-ketal moieties. Besides the organic base catalysts, NH_4OAc catalyzed reaction also gave the same reaction results. However, in the presence of an excess of NH_4OAc, the one-pot reaction directly afforded 2-(trifluoromethyl)-1,2,3,4,7,8-hexahydroquinolin-5(6*H*)-one derivative **5**, which could also be obtained from **4** by O-atom ring to N-atom ring interconversion reaction. Meanwhile, the further chemical transformation including dehydration of α-hydrodihydropyrane derivatives **4** and **7c** with *p*-TsOH in refluxing $CHCl_3$ proceeded smoothly and gave the corresponding fluorinated and non-fluorinated products **8**, respectively.

4. Experimental section

4.1. General

Melting points were measured with digital melting point apparatus (WRS-1B, Shanghai precision & scientific instrument Co., Ltd.) and were uncorrected .^{1}H and ^{19}F NMR spectra were recorded in DMSO-d_6 (unless mentioned in text) on Bruker AM-300 or AM-500 instruments with Me_4Si and $CFCl_3$ (with upfield negative) as the internal and external standards, respectively. IR spectra were obtained with a Nicolet AV-360 spectrophotometer. Lower resolution mass spectrum were determined with Finnigan GC–MS 4021 using the electron impact ionization technique (70 eV). High resolution mass spectra (HRMS) were run on Ionspec 4.7 Tesla FTMS using MALDI/DHB. Elemental analyses were performed in this Institute.

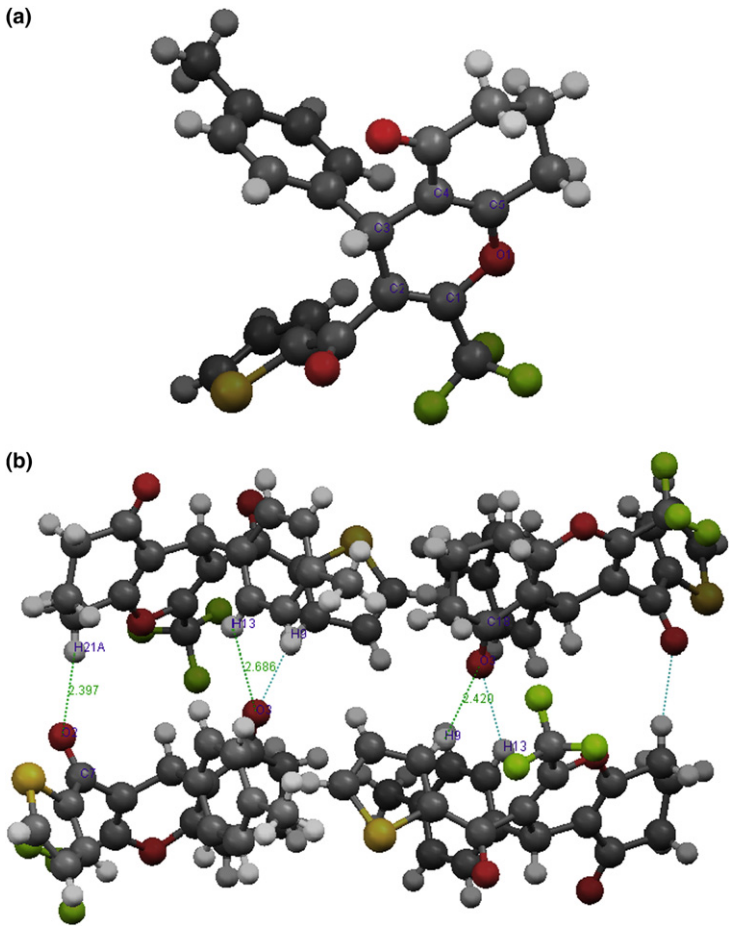


Figure 2. Crystal structure (a) and packing map (b) of **8b**.

4.2. General procedure for the preparation of 4-aryl-2-hydroxy-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one (4a–4j)

To a mixture of aryldehyde **1** (1.5 mmol), 1,3-cyclohexanaedione **2** (168 mg, 1.5 mmol), and 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **3** (333 mg, 1.5 mmol) in 12 mL EtOH was added 0.3 mmol of Et_3N as catalyst under stirring at room temperature. The mixture was refluxed and continuously stirred for specified hour (monitored by TLC). After cooling, the resulting solid was filtered, washed with 10–15 mL of cold EtOH and air-dried to afford the crude product. The pure product was obtained by recrystallization from ethanol.

*4.2.1. 2-Hydroxy-4-phenyl-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4a**)*

White solid; mp 222–223 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.91–1.94 (m, 2H), 2.15–2.19 (m, 2H), 2.60–2.63 (m, 2H), 4.06 (s, 1H), 4.13 (s, 1H), 6.93–7.25 (m, 6H), 7.45–7.48 (m, 1H), 7.83–7.88 (m, 1H), 8.74–8.77 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.66 (s, 3F); IR (KBr) ν_{max}: 3431, 3100, 2789, 1702, 1659, 1609, 1520, 1496, 1457, 1418, 1360, 1077, 729 cm^{-1}; MS (70 eV, EI) *m*/*z* (%): 422 (M^+, 3.13), 311 [$(M-C_5H_3OS)^+$, 15.00], 222 ($C_8H_5F_3O_2S^+$, 25.06), 199 ($C_{13}H_{11}O_2^+$, 100), 69 (CF_3^+, 31.34); Anal. Calcd for $C_{21}H_{17}F_3O_4S$: C, 59.71; H, 4.06. Found: C, 59.57; H, 3.93.

*4.2.2. 2-Hydroxy-3-(thien-2-oyl)-4-p-tolyl-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4b**)*

White solid; mp 216–218 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 2.02–2.10 (m, 2H), 2.16 (s, 3H), 2.28–2.38 (m, 2H), 2.58–2.66(m, 2H), 3.80 (d, *J*=11.7 Hz, 1H), 4.03 (d, *J*=11.7 Hz, 1H), 6.33 (br s, 1H), 6.87–7.01 (m, 6H), 7.64 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −83.43 (s, CF_3); IR (KBr) ν_{max}: 3305, 3090, 3032, 2968, 2878, 1662, 1606, 1519, 1458, 1419, 1377, 1073, 816, 752 cm^{-1}; MS (70 eV, EI) *m*/*z* (%): 436 (M^+, 1.65), 325 [$(M-C_5H_3OS)^+$, 10.48], 222 ($C_8H_5F_3O_2S^+$, 9.43), 199 ($C_{13}H_{11}O_2^+$, 100), 69 (CF_3^+, 13.12); Anal. Calcd for $C_{22}H_{19}F_3O_4S$: C, 60.54; H, 4.39. Found: C, 60.38; H, 4.24.

*4.2.3. 2-Hydroxy-4-(4-methoxyphenyl)-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4c**)*

White solid; mp 226–227 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.91–1.95 (m, 2H), 2.17–2.21 (m, 2H), 2.48–2.59 (m, 2H), 3.32 (s, 1H), 3.58 (s, 3H), 4.08–4.11 (m, 2H), 6.61–6.65 (m, 2H), 6.96–7.02 (m, 3H), 7.50–7.58 (m, 1H), 7.86–7.88 (m, 1H), 8.65–8.75 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.65 (s, 3F); IR (KBr) ν_{max}: 3431, 3090, 2967, 2835, 1660, 1605, 1513, 1459, 1418, 1375, 1255, 1072, 834 cm^{-1}; MS (ESI) *m*/*z*: [$(M+H)^+$, 453.3], [$(M+Na)^+$, 475.2], [$(M+K)^+$, 491.2]; Anal. Calcd for $C_{22}H_{19}F_3O_5S$: C, 58.40; H, 4.23. Found: C, 58.39; H, 4.03.

*4.2.4. 2-Hydroxy-4-(4-hydroxyphenyl)-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4d**)*

White solid; mp 203–204 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.88–1.92 (m, 2H), 2.15–2.18 (m, 2H), 2.34–2.70 (m, 2H), 3.98–4.07 (m, 2H), 6.43–6.46 (m, 2H), 6.86–7.03 (m, 3H), 7.49–7.56 (m, 1H), 7.87–7.89 (m, 1H), 8.65–8.70 (m, 1H), 8.95–9.01 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.73 (s, 3F); IR (KBr) ν_{max}: 3510, 3430, 3096, 2981, 2768, 1664, 1655, 1605, 1517, 1448, 1419, 1185, 1072, 805, 745 cm^{-1}; MS (ESI) m/z: [$(M+H)^+$, 439.3], [$(M+2H)^+$, 440.2], [$(M+Na)^+$, 461.0], [$(M+K)^+$, 477.0], [$(M+K+H_2O)^+$, 493.0]; HRMS for $C_{21}H_{17}F_3O_5S^{+1}$ Calcd: 438.0749; Found: 438.0762.

*4.2.5. 4-(4-(Dimethylamino)phenyl)-2-hydroxy-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4e**)*

Light yellow solid; mp 205–207 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.90–1.92 (m, 2H), 2.14–2.18 (m, 2H), 2.44–2.53 (m, 2H), 2.73–2.81 (s, 6H), 4.01–4.09 (m, 2H), 6.42–6.45 (m, 2H), 6.88–6.90 (m, 3H), 7.51–7.53 (m, 1H), 7.85–7.88 (m, 1H), 8.62–8.66 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.64 (s, 3F); IR (KBr) ν_{max}: 3432, 3090, 2961, 2792, 1662, 1609, 1520, 1452, 1418, 1377, 1358, 1071, 820, 745 cm^{-1}; MS (ESI) *m*/*z*: [$(M+H)^+$, 466.2], [$(M+2H)^+$, 467.3]; HRMS for $C_{23}H_{23}NO_4F_3S^{+1}$ Calcd: 466.1300; Found: 466.1294.

*4.2.6. 4-(4-Chlorophenyl)-2-hydroxy-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4f**)*

White solid; mp 224–225 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.83–2.05 (m, 2H), 2.15–2.25 (m. 2H), 2.37–2.61 (m, 2H), 4.10–4.14 (m, 2H), 7.03–7.24 (m, 5H), 7.50–7.60 (m, 1H), 7.89–7.92 (m, 1H), 8.78–8.82 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.58 (s, 3F); IR (KBr) ν_{max}: 3444, 1657, 1607, 1519, 1493, 1417, 1374, 1073, 810, 727 cm^{-1}; MS (ESI) *m*/*z*: [$(M+H)^+$, 459.0/457.0]; Anal. Calcd for $C_{21}H_{16}ClF_3O_4S$: C, 55.21; H, 3.53. Found: C, 54.88; H, 3.58.

*4.2.7. 2-Hydroxy-4-(4-nitrophenyl)-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4g**)*

White solid; mp 230–231 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.96–1.98 (m, 2H), 2.18–2.25 (m, 2H), 2.46–2.57 (m, 2H), 4.25–4.27 (m, 2H), 7.02 (s, 1H), 7.43 (d, *J*=8.6 Hz, 2H), 7.64–7.66 (m, 1H), 7.90–7.94 (m, 1H), 7.95 (d, *J*=8.6 Hz, 2H), 8.98–9.00 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.92 (s, 3F); IR (KBr) ν_{max}: 3430, 3078, 2792, 1655, 1606, 1520, 1458, 1416, 1074, 806, 760 cm^{-1}; MS (ESI) *m*/*z*: [$(M+H)^+$, 468.0], [$(M+2H)^+$, 469.0], [$(M+H+H_2O)^+$, 486.7]; Anal. Calcd for $C_{21}H_{16}F_3NO_6S$: C, 53.96; H, 3.45; N, 3.00. Found: C, 53.91; H, 3.71; N, 2.70.

*4.2.8. 2-Hydroxy-4-(3-nitrophenyl)-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4h**)*

Light yellow solid; mp 236–237 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.97–1.98 (m, 2H), 2.22–2.28 (m, 2H), 2.44–2.66 (m, 2H), 4.28 (br s, 2H), 7.00 (s, 1H), 7.36–7.39 (m, 1H), 7.57–7.68 (m, 2H), 7.85–8.00 (m, 3H), 8.90–8.95 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.54 (s, 3F); IR (KBr) ν_{max}: 3298, 3097, 2970, 2895, 2785, 2584, 2005, 1944, 1885, 1840, 1763, 1660, 1609, 1500, 1481, 1457, 1417, 1077, 750, 690, 711 cm^{-1}; MS (70 eV, EI) *m*/*z* (%): 467 (M^+, 5.83), 356 [$(M-C_5H_3OS)^+$, 17.24], 245 [$(M-C_8H_5F_3O_2S)^+$, 32.15], 228 ($C_{13}H_{10}NO_3^+$,100), 222 ($C_8H_5F_3O_2S^+$, 95.90), 199 ($C_{13}H_{11}O_2^+$, 45.17), 153 ($C_7H_5O_2S^+$, 94.29), 111 ($C_5H_3OS^+$,78.45), 69 (CF_3^+,96.79); Anal. Calcd for $C_{21}H_{16}F_3NO_6S$: C, 53.96; H, 3.45; N, 3.00. Found: C, 53.89; H, 3.58; N, 2.88.

*4.2.9. 2-Hydroxy-4-(3-phenoxyphenyl)-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4i**)*

Light yellow solid; mp 196–197 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.90–1.98 (m, 2H), 2.21–2.24 (m, 2H), 2.51 (s, 2H), 4.11 (br s, 2H), 6.59–6.63 (m, 3H), 6.67 (s, 1H), 6.75–6.79 (m, 1H), 7.04–7.15 (m, 3H), 7.29 (m, 2H), 7.58 (m, 1H), 7.98 (m, 1H), 8.81 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −81.13 (s, 3F); IR (KBr) ν_{max}: 3310, 3040, 2782, 2581, 1660, 1600, 1518, 1480, 1445, 1416, 1357, 1200, 1070, 750, 727, 708 cm^{-1}; MS (ESI) *m*/*z*: [$(M+H)^+$, 515.2], [$(M+2H)^+$, 516.3]; Anal. Calcd for $C_{27}H_{21}F_3O_5S$: C, 63.03; H, 4.11. Found: C, 62.51; H, 4.36.

*4.2.10. 4-(3-Bromophenyl)-2-hydroxy-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**4j**)*

Light yellow solid; mp 236–237 °C; ^{1}H NMR (DMSO-d_6, 300 MHz): δ 1.95–1.98 (m, 2H), 2.20–2.23 (m, 2H), 2.50–2.56 (m, 2H), 4.13 (br s, 2H), 7.03–7.04 (m, 2H), 7.12–7.18 (m, 2H), 7.27–7.30 (m, 1H), 7.61–7.64 (m, 1H), 7.90–7.92 (m, 1H), 8.80–8.85 (m, 1H); ^{19}F NMR (DMSO-d_6, 282 MHz): δ −80.57 (s, 3F); IR (KBr) ν_{max}: 3436, 3079, 2964, 2891, 1658, 1608, 1518, 1476, 1457, 1416, 1362, 1189, 806, 726 cm^{-1}; MS (70 eV, EI) *m*/*z* (%): 500 (M^+, 1.58), 391/389

[(M−C_5H_3OS)$^+$, 4.63/5.10], 222 ($C_8H_5F_3O_2S^+$, 16.77), 199 ($C_{13}H_{11}O_2^+$, 100), 69 (CF_3^+, 18.50); Anal. Calcd for $C_{21}H_{16}BrF_3O_4S$: C, 50.31; H, 3.22. Found: C, 50.01; H, 3.35.

4.3. Preparation of 2-hydroxy-4-phenyl-3-(thien-2-oyl)-2-(trifluoromethyl)-1,2,3,4,7,8-hexahydroquinolin-5(6*H*)-one 5

Method A: To a mixture of benzaldehyde **1a** (159 mg, 1.5 mmol), 1,3-cyclohexanedione **2** (168 mg, 1.5 mmol), and 4,4,4-trifluoro-1-(thien-2-yl)butane-1,3-dione **3** (333 mg, 1.5 mmol) in 10 mL EtOH was added 30 equiv of NH_4OAc under stirring at room temperature. The mixture was refluxed and continually stirred for specified hour (monitored by TLC). After cooling, the mixture was poured into 20 mL water, and extracted with CH_2Cl_2 three times (3×15 mL). The combined organic layer was dried with Na_2SO_4 overnight. The solvent was removed by rotavapor and the residue was purified by column chromatography on silica gel using petroleum/ethyl acetate=2:1(v/v) as eluent to afford pure product **5**.

Method B: Preparation of **5** from **4**. The procedure is same as the above except the 2-hydroxy-4-phenyl-3-(thien-2-oyl)-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2*H*-chromen-5(6*H*)-one **4a** (422 mg,1 mmol) and 30 equiv of NH_4OAc were engaged as starting materials.

*4.3.1. 2-Hydroxy-4-phenyl-3-(thien-2-oyl)-2-(trifluoromethyl)-1,2,3,4,7,8-hexahydroquinolin-5(6H)-one (**5a**)*

Yellow solid; 231–232 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.18–2.22 (m, 2H), 2.28–2.41 (m, 2H), 2.52–2.55 (m, 2H), 3.83 (d, J=11.5 Hz, 1H), 4.19 (d, J=11.5 Hz, 1H), 5.10 (s, 1H), 6.04 (s, 1H), 6.84–6.86 (m, 1H), 6.98–7.00 (m, 2H), 7.06–7.11 (m, 4H), 7.60–7.62 (m, 1H); ^{19}F NMR ($CDCl_3$, 470 MHz): δ −82.24 (s, 3F); IR (KBr) ν_{max}: 3269, 3109, 3044, 2958, 2928, 2890, 1634, 1599, 1533, 1455, 1411, 1034, 1192, 734, 705 cm^{-1}; MS (ESI) m/z: [(M+H)$^+$, 422], [(M+2H)$^+$, 423]; Anal. Calcd for $C_{21}H_{18}F_3NO_3S$: C, 59.85; H, 4.31; N, 3.32. Found: C, 60.12; H, 4.42; N, 3.20.

4.4. General procedure for preparation of 7a–7d

The procedure is same as the preparation of **4** except that after cooling, the solvent was removed by rotavapor, and the residue was purified by column chromatography on silica gel using petroleum/ethyl acetate=1.5:1(v/v) as eluent to afford the pure products **7**.

*4.4.1. 3-Acetyl-2-hydroxy-4-phenyl-2-(trifluoromethyl)-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**7a**)*

White solid; mp 203–204 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.72 (s, 3H), 1.97–2.08 (m, 2H), 2.22–2.38 (m, 2H), 2.51–2.66 (m, 2H), 3.28 (d, J=11.5 Hz, 1H), 3.83 (d, J=11.5 Hz, 1H), 5.73 (s, 1H), 7.12 (d, J=7.0 Hz, 2H), 7.24 (t, J=7.0 Hz, 1H), 7.31 (t, J=2.0 Hz, 2H); ^{19}F NMR ($CDCl_3$, 470 MHz): δ −83.52 (s, 3F); IR (KBr) ν_{max}: 3447, 3051, 2950, 2920, 2870, 1726, 1680, 1495, 1456, 1423, 1360, 1191, 714 cm^{-1}; MS (70 eV, EI) m/z (%): 354 (M$^+$, 3.09), 311 [(M−CH_3CO)$^+$, 95.65], 199 ($C_{13}H_{11}O_2^+$, 198.25), 69 (CF_3^+, 32.16), 43 (CH_3CO^+, 100); Anal. Calcd for $C_{18}H_{17}F_3O_4$: C, 61.02; H, 4.84. Found: C, 61.02; H, 4.93.

*4.4.2. Ethyl 2-hydroxy-5-oxo-4-phenyl-2-(trifluoromethyl)-3,4,5,6,7,8-hexahydro-2H-chromene-3-carboxylate (**7b**)*

White solid; mp 220–221 °C; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 1.00 (t, J=7.2 Hz, 3H), 1.99–2.09 (m. 2H), 2.23–2.39 (m, 2H), 2.53–2.66 (m, 2H), 2.98 (d, J=11.7 Hz, 1H), 3.94 (d, J=11.7 Hz, 1H), 4.04 (q, J=7.2 Hz, 2H), 5.57 (s, 1H), 7.08–7.26 (m, 5H); ^{19}F NMR ($CDCl_3$, 282 MHz): δ −84.19 (s, 3F); IR (KBr) ν_{max}: 3465, 3050, 2985, 2774, 2585, 1741, 1610, 1373, 1354, 1238, 1193, 1162, 1018, 704, 619 cm^{-1}; MS (70 eV, EI) m/z (%): 384 (M$^+$, 3.46), 311 [(M−CO_2Et)$^+$, 47.32], 241 [(M−1−CF_3−CO_2Et)$^+$, 100], 199 [(M−1−$CF_3COCH_2CO_2Et$)$^+$, 33.20], 69 (CF_3^+, 66.20); Anal. Calcd for $C_{19}H_{19}O_5F_3$: C, 59.38; H, 4.95. Found: C, 59.29; H, 4.78.

*4.4.3. 3-Acetyl-2-hydroxy-2-methyl-4-phenyl-3,4,7,8-tetrahydro-2H-chromen-5(6H)-one (**7c**)*

White solid; mp 178–180 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.50 (s, 3H), 1.80 (s, 3H), 1.88 (t, J=5.5 Hz, 2H), 2.24–2.34 (m, 2H), 2.44–2.51 (m, 2H), 3.14 (d, J=8.0 Hz, 1H), 3.91 (d, J=8.0 Hz, 1H), 7.11–7.25 (m, 5H); IR (KBr) ν_{max}: 3202, 3029, 2963, 2925, 2880, 1719, 1631, 1585, 1492, 1453, 1421, 1380, 1071, 727, 702 cm^{-1}; MS (70 eV, EI) m/z (%): 300 (M$^+$, 1.52), 257 [(M−CH_3CO)$^+$, 18.58], 215 [(M−CH_3−C_4H_6O)$^+$, 46.61], 199 ($C_{13}H_{11}O_2^+$, 79.54), 43 (CH_3CO^+, 100), 116 ($C_5H_8O_3^+$, 10.39); Anal. Calcd for $C_{18}H_{20}O_4$: C, 71.98; H, 6.71. Found: C, 71.95; H, 6.76.

*4.4.4. Ethyl 2-hydroxy-2-methyl-5-oxo-4-phenyl-3,4,5,6,7,8-hexahydro-2H-chromene-3-carboxylate (**7d**)*

White solid; mp 142–144 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.07 (t, J=7.0 Hz, 3H), 1.52 (s, 3H), 1.99 (s, 2H), 2.59–2.63 (m, 4H), 2.97 (d, J=9.5 Hz, 1H), 4.05 (q, J=7.0 Hz, 2H), 4.09 (d, J=9.5 Hz, 1H), 7.12–7.18 (m, 3H), 7.21–7.27 (m, 2H); IR (KBr) ν_{max}: 3318, 3031, 2941, 2998, 2871, 1735, 1642, 1612, 1491, 1453, 1422, 1373, 1071, 728, 699 cm^{-1}; MS (70 eV, EI) m/z (%): 330 (M$^+$, 5.50), 287 [(M−EtO+2H)$^+$, 18.10], 241 [(M−EtOCO−OH)$^+$, 100], 199 ($C_{13}H_{11}O_2^+$, 76.64), 129 ($C_6H_9O_3^+$, 16.66), 43 (CH_3CO^+, 94.78); Anal. Calcd for $C_{19}H_{22}O_5$: C, 69.07; H, 6.71. Found: C, 69.10; H, 6.79.

4.5. General procedure for dehydration reaction

The solution of 0.5 mmol of **4** or **7** and 4 equiv of *p*-TsOH in 15 mL of $CHCl_3$ was refluxed for several hours until complete of reaction (monitored by TLC). The solvent was removed by rotavapor and the residue was purified by column chromatography using petroleum/ethyl acetate=2:1(v/v) as eluent to afford pure product **8**.

*4.5.1. 4-Phenyl-3-(thien-2-oyl)-2-(trifluoromethyl)-7,8-dihydro-4H-chromen-5(6H)-one (**8a**)*

Light red solid; mp 134–136 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.02–2.17 (m, 2H), 2.39–2.45 (m, 2H), 2.65–2.78 (m, 2H), 4.74 (s, 1H), 6.91 (dd, J_1=4.8 Hz, J_2=5.0 Hz, 1H), 7.10 (d, J=3.5 Hz, 1H), 7.12–7.17 (m, 3H), 7.19–7.23 (m, 2H), 7.61 (dd, J_1=4.8 Hz, J_2=5.0 Hz, 1H); ^{19}F NMR ($CDCl_3$, 470 MHz): δ −66.98 (s, 3F); IR (KBr) ν_{max}: 3438, 3088, 2961, 2921, 2867, 1699, 1640, 1518, 1489, 1454, 1376, 1152, 725, 743, 700 cm^{-1}; MS (70 eV, EI) m/z (%): 404 (M$^+$, 69.73), 335 [(M−CF_3)$^+$, 17.99], 111 ($C_5H_3OS^+$, 100); Anal. Calcd for $C_{21}H_{15}F_3O_3S$: C, 62.37; H, 3.74. Found: C, 62.39; H, 3.86.

*4.5.2. 3-(Thien-2-oyl)-4-p-tolyl-2-(trifluoromethyl)-7,8-dihydro-4H-chromen-5(6H)-one (**8b**)*

White solid; mp 145–147 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 2.00–2.15 (m, 2H), 2.24 (s, 3H), 2.34–2.44 (m, 2H), 2.63–2.78 (m, 2H), 4.69 (s, 1H), 6.94 (dd, J_1=4.8 Hz, J_2=5.0 Hz, 1H), 7.00–7.06 (m, 4H), 7.17 (d, J=3.5 Hz, 1H), 7.63 (dd, J_1=4.8 Hz, J_2=5.0 Hz, 1H); ^{19}F NMR ($CDCl_3$, 470 MHz): δ −66.99 (s, 3F); IR (KBr) ν_{max}: 3439, 3090, 2964, 2923, 2867, 1697, 1641, 1515, 1453, 1412, 1372, 1152, 818 cm^{-1}; MS (70 eV, EI) m/z (%): 418 (M$^+$, 60.18), 403 [(M−CH_3)$^+$, 47.37], 307 [(M−C_5H_3OS)$^+$, 22.71], 111 ($C_5H_3OS^+$, 100); Anal. Calcd for $C_{22}H_{17}F_3O_3S$: C; 63.15; H, 4.10. Found: C, 62.92; H, 4.09.

*4.5.3. 3-Acetyl-2-methyl-4-phenyl-7,8-dihydro-4H-chromen-5(6H)-one (**8c**)*

Yellow solid; mp 134–136 °C; ^{1}H NMR ($CDCl_3$, 500 MHz): δ 1.84–1.93 (m, 1H), 1.96–2.04 (m, 1H), 2.12 (s, 3H), 2.27–2.41 (m, 5H), 2.45–2.58 (m, 2H), 4.80 (s, 1H), 7.14–7.18 (m, 1H), 7.23–7.30 (m, 4H); IR (KBr) ν_{max}: 3442, 3051, 3029, 2972, 2943, 1683, 1662, 1586, 1492, 1455, 1424, 714, 699 cm^{-1}; MS (70 eV, EI) m/z (%): 282 (M$^+$, 93.03),

267 [$(M-CH_3)^+$, 8.19], 239 [$(M-CH_3CO)^+$, 18.32], 205 [$(M-C_6H_5)^+$, 100], 43 (CH_3CO^+, 84.85); Anal. Calcd for $C_{18}H_{18}O_3$: C, 76.57; H, 6.43. Found: C, 76.67; H, 6.46.

4.6. X-ray crystal structure data of compounds 5a and 8b

The data were collected at 273(2) K for **5a** and 298(2) K for **8b**, respectively, on a Bruck SMART APEX2 CCD single crystal diffractometer using graphite monochromatized Mo Kα radiation (λ=0.71073 Å). The structures were solved by direct methods and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically, hydrogen atoms were included but not refined. The final cycle of full matrix least-squares refinement was based on F^2. All calculations were performed using SHELEX-97 and SHELXL-97 programs.

CCDC 681206, 681207 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

Acknowledgements

The authors thank the National Natural Science Foundation of China (NNSFC) (No.20772080), the Foundation of Education Commission of Shanghai Municipality (No. J50102) and the Innovation Fund of Shanghai University for financial support.

References and notes

1. (a) Hiyama, T. *Organofluorine Compounds*; Springer: Berlin, 2000; (b) Hudlicky, M. *Chemistry of Organic Fluorine Compounds*, 2nd ed.; Ellis Harwood: Chichester, UK, 1976.
2. (a) *Fluorine in Bioorganic Chemistry*; Welch, J. T., Eswarakrishnan, S., Eds.; Wiley: New York, NY, 1991; (b) Prabhakaran, J.; Underwood, M. D.; Parsey, R. V.; Arango, V.; Majo, V. J.; Simpson, N. R.; Heertum, R. V.; Mann, J. J.; Kumar, J. S. D. *Bioorg. Med. Chem.* **2007**, *15*, 1802–1807.
3. (a) Filler, R.; Kobayashi, Y. *Biomedicinal Aspects of Fluorine Chemistry*; Kodansha & Elsevier Biomedical: Tokyo, 1982; (b) Filler, R.; Kobayashi, Y.; Yagupolskii, L. M. *Organofluorine Compounds in Medical Chemistry and Biomedical Application*; Elsevier: Amsterdam, 1993.
4. Filler, R.; Banks, R. E. *Organofluorine Chemicals and Their Industrial Applications*; Ellis Horwood: Chichester, UK, 1979.
5. (a) Welch, J. T. *Tetrahedron* **1987**, *43*, 3123–3197; (b) Frezza, M.; Balestrino, D.; Soulère, L.; Reverchon, S.; Queneau, Y.; Forestier, C.; Doutheau, A. *Eur. J. Org. Chem.* **2006**, 4731–4736; (c) Leroux, F.; Lefebvre, O.; Schlosser, M. *Eur. J. Org. Chem.* **2006**, 3147–3151; (d) Buscemi, S.; Pace, A.; Piccionello, A.; Macaluso, G.; Vivona, N. *J. Org. Chem.* **2005**, *70*, 3288–3291 and references cited therein.
6. (a) Wang, Y. L.; Zhu, S. Z. *Org. Lett.* **2003**, *5*, 745–748; (b) Marull, M.; Schlosser, M. *Eur. J. Org. Chem.* **2003**, 1576–1588; (c) Bégué, J.-P.; Bonnet-Delpon, D.; Dogbeavou, R.; Oure'vitch, M. *J. Chem. Soc., Perkin Trans. 1* **1993**, 2787–2791; (d) Volochnyuk, D. M.; Pushechnikov, A. O.; Krotko, D. G.; Sibgatulin, D. A.; Kovalyova, S. A.; Tolmachev, A. A. *Synthesis* **2003**, 1531–1540; (e) Song, L. P.; Zhu, S. Z. *J. Fluorine Chem.* **2001**, *111*, 201–205.
7. (a) Li, X. F.; Song, L. P.; Xing, C. H.; Zhao, J. W.; Zhu, S. Z. *Tetrahedron* **2006**, *62*, 2255–2263; (b) Li, D. M.; Song, L. P.; Li, X. F.; Xing, C. H.; Peng, W. M.; Zhu, S. Z. *Eur. J. Org. Chem.* **2007**, 3520–3525; (c) Li, D. M.; Song, L. P.; Song, S. D.; Zhu, S. Z. *J. Fluorine Chem.* **2007**, *128*, 952–957.
8. Atkinson, R. S.; Barker, E.; Edwards, P. J.; Thomson, G. A. *J. Chem. Soc., Perkin Trans. 1* **1995**, 1533–1543.
9. (a) Katsuyama, I.; Ogawa, S.; Yamaguchi, Y.; Funabiki, K.; Matsui, M.; Muramatsu; Shibata, H. K. *Synthesis* **1997**, 1321–1324; (b) Amii, H.; Kobayashi, T.; Terasawa, H.; Uneyama, K. *Org. Lett.* **2001**, *3*, 3103–3105.
10. (a) Domling, A.; Ugi, I. *Angew. Chem., Int. Ed.* **2000**, *39*, 3168–3210; (b) Suresh Babu, A. R.; Raghunathan, R. *Tetrahedron Lett.* **2006**, *47*, 9221–9225 and references cited therein.
11. Love, B.; Snader, K. M. *J. Org. Chem.* **1965**, *30*, 1914–1916.
12. (a) Kumar, A.; Maurya, R. A. *Tetrahedron* **2007**, *63*, 1946–1952; (b) Kumar, S.; Kapoor, K. K.; Hundal, M. S. *Tetrahedron* **2008**, *64*, 536–542 and references cited therein.
13. Mosse, S.; Alexakis, A. *Org. Lett.* **2006**, *8*, 3577–3580.
14. (a) Kantevari, S.; Chary, M. V.; Vuppalapati, S. V. N. *Tetrahedron* **2007**, *63*, 13024–13031; (b) Sun, C.; Ji, S. J.; Liu, Y. *Tetrahedron Lett.* **2007**, *48*, 8987–8989.
15. Moseley, J. D. *Tetrahedron Lett.* **2005**, *46*, 3179–3183.
16. Nenajdenko, V. G.; Druzhinin, S. V.; Balenkova, E. S. *J. Fluorine Chem.* **2006**, *127*, 865–873.