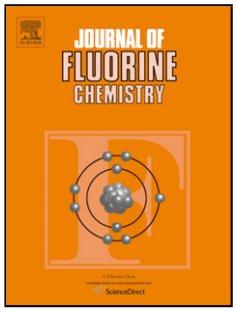

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Synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes via cyclization of (*Z*)-trifluoromethyl alkenyl triflates and salicylaldehydes

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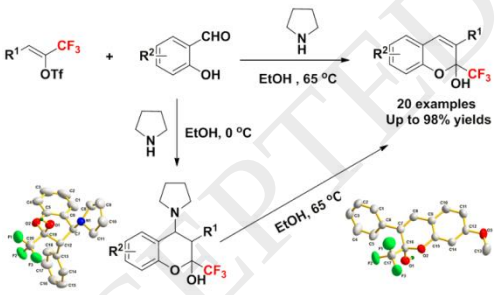
Graphical Abstract:

A new and efficient method for the synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes was developed via intermolecular cyclization of (*Z*)-trifluoromethyl alkenyl triflates and salicylaldehydes. A series of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes with *aryl* or *alkyl* groups at 3-position have been obtained in moderate to excellent yields. And a key intermediate, 3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol (**6**), was isolated and fully characterized, which suggests that the elimination of pyrrolidine from this intermediate is the last step during the formation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.



Highlights:

- A new approach to 2-trifluoromethyl-2-hydroxy-2*H*-chromenes with aryl or alkyl groups at 3-position was described.
- (*Z*)-Trifluoromethyl alkenyl triflates were applied on synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.
- Salicylaldehydes and (*Z*)-trifluoromethyl alkenyl triflates reacted smoothly in the presence of pyrrolidine.
- A key intermediate, 3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol, was isolated and fully characterized.

Abstract

A new and efficient method for the synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes was developed via intermolecular cyclization of (*Z*)-trifluoromethyl alkenyl triflates and salicylaldehydes. A series of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes with *aryl* or *alkyl* groups at 3-position have been obtained in moderate to excellent yields. And a key intermediate, 3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol (**6**), was isolated and fully characterized, which suggests that the elimination of pyrrolidine from this intermediate is the last step during the formation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.

Keywords:

2*H*-chromenes

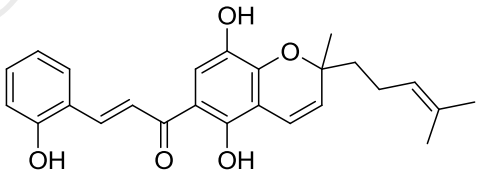
trifluoromethyl alkenyl triflates

salicylaldehydes

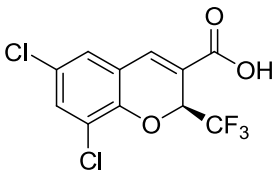
cyclization

1. Introduction

2-Substituted 2*H*-chromenes are main structural motifs of many biologically active molecules and natural products (Figure 1) [1]. They are also used as valuable intermediates in the preparation of numerous heterocyclic compounds, such as biscarbazole alkaloids murrafoline and 7-diethylamino-4-methyl coumarin [2]. As a consequence, efficient synthetic approaches to access 2-substituted 2*H*-chromenes have attracted continuous interest [3]. In addition, incorporating a trifluoromethyl group into an organic molecule has been widely accepted as a powerful tool to discover new drugs [4]. So it's not surprising that 2-trifluoromethyl-2-hydroxy-2*H*-chromenes have gained significant interest in recent years [5].



Nnatural product form leaves of flemingia grahamiana



SD-8381, a leading COX-2 inhibitor

Figure 1 Biologically active molecule and natural product containing 2-substituted 2*H*-chromenes structure

The synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes is mostly based on the Knoevenagel condensation of salicylaldehydes with trifluoromethylated 1,3-dicarbonyl species [6]. However, the use of this approach is limited to 3-carbonyl derivatives owing to the availability of respective trifluoromethylated 1,3-dicarbonyl substrates. Besides, 3-carboalkoxy substituted 2-trifluoromethyl-2-hydroxy-2*H*-chromenes can also be obtained through the reaction of salicylaldehydes with 4,4,4-trifluorobut-2-ynoate [7]. It is worth noting that using (3,3,3-trifluoroprop-1-yn-1-yl)phosphonate as a trifluoromethylated building block, the phosphoryl group has been introduced into 3-position of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes by Röschenthaler [8]. Thus, the efficient synthetic approaches to diverse 2-trifluoromethyl-2-hydroxy-2*H*-chromenes, especially 3-aryl or alkyl substituted species, are still highly desired.

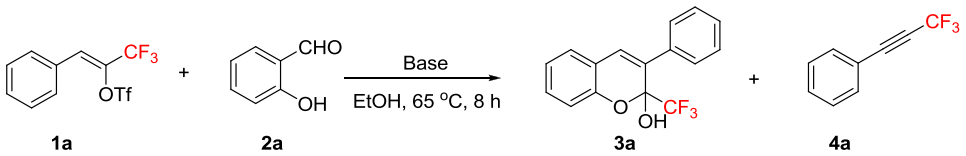
Recently, our group also focused on the synthesis of fluorine-containing compounds [9]. To this end, the useful fluorinated building blocks, (*Z*)-trifluoromethyl alkenyl triflates, were prepared and utilized successfully for the synthesis of various trifluoromethyl derivatives such as diarylethylenes, alkynes, enynes, benzofurans, allyl azides, and azirines. In this context, we herein extend the utilization of (*Z*)-trifluoromethyl alkenyl triflates to the synthesis of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.

2. Results and discussion

We began our investigation with the reaction of (*Z*)-1-phenyl-3,3,3-trifluoroprop-1-en-2-yl trifluoromethanesulfonate (**1a**) and salicylaldehyde (**2a**) in the presence of triethylamine. The desired 3-phenyl-2-(trifluoromethyl)-2*H*-chromen-2-ol (**3a**) was afforded in 30% yield (Table 1, entry 1) with 3,3,3-trifluoro-1-phenylpropyne (**4a**) as a by-product. The reaction was further tested with different bases like DBU, K_2CO_3, $KHCO_3$, pyridine, pyrrole, and pyrrolidine (Table 1, entries 2-7). It was found that the reaction using pyrrolidine gave the best result (85% yield, Table 1, entry 7), which encouraged us to screen other bases that has a similar structure to pyrrolidine (Table 1, entries 8-9). Finally, pyrrolidine proved still to be the best choice for this reaction. In addition, the amount of **1a** and pyrrolidine was screened (Table 1, entries 10-15). To our delight, when the amount of **1a** and pyrrolidine was increased to 2.0 equiv, the yield of **3a** was improved to 98% (Table 1, entry 15). To further optimize the synthesis of **3a**, several parameters such as solvent, temperature, and time were also optimized (Table 2). Switching the solvent to CH_3CN, DMF, or toluene failed to give higher yield (Table 2, entries 1-3). Then, the reaction temperature and time were altered but resulted in lower yields (Table 2, entries 4-13). Performing the reaction in air atmosphere

resulted in a slight decrease in yield (Table 2, entry 14). Through the above screening, the reaction with 2.0 equiv of **1a**, and 2.0 equiv of pyrrolidine in EtOH at 65 °C for 8 h under Ar atmosphere was found to give the highest yield of target product **3a** (Table 1, entry 15).

Table 1 Screening of bases.[a]

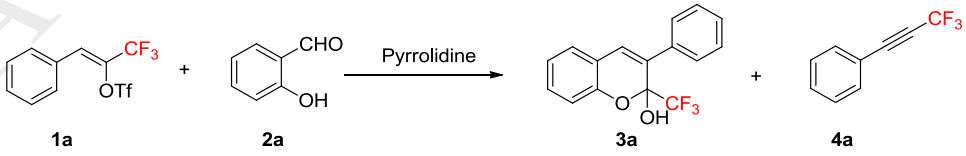


1a 2a 3a 4a

Entry	Base	Conv. 1a /%[b]	Yield 3a /%[b]
1	Et_3N (2.0 eq.)	42	30
2	DBU (2.0 eq.)	33	21
3	K_2CO_3 (2.0 eq.)	36	19
4	$KHCO_3$ (2.0 eq.)	64	29
5	Pyridine (2.0 eq.)	trace	trace
6	Pyrrole (2.0 eq.)	trace	trace
7	Pyrrolidine (2.0 eq.)	87	85
8	Piperidine (2.0 eq.)	80	76
9	Diethylamine (2.0 eq.)	75	71
10	Pyrrolidine (1.0 eq.)	43	42
11	Pyrrolidine (1.2 eq.)	70	67
12	Pyrrolidine (1.5 eq.)	77	73
13	Pyrrolidine (2.5 eq.)	67	63
14[c]	Pyrrolidine (2.0 eq.)	89	88
15[d]	Pyrrolidine (2.0 eq.)	99	98 (95)[e]

[a] Reaction conditions: A mixture of **1a** (0.6 mmol), **2a** (0.5 mmol), base (1.0 mmol) in EtOH (2 mL) was stirred at 65 °C for 8 h under Ar atmosphere. [b] The yield was determined by ^{1}H NMR with dimethyl terephthalate as an internal standard. [c] 0.75 mmol **1a** was used. [d] 1.0 mmol **1a** was used. [e] Yield of the isolated product.

Table 2 Screening of solvents, temperature and time. [a]



1a 2a 3a 4a

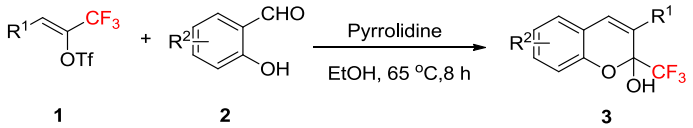
Entry	Solvent	Temp./°C	Time/h	Conv. 1a /%[b]	Yield 3a /%[b]
1	CH_3CN	65	8	70	64
2	DMF	65	8	73	68

3	toluene	65	8	70	35
4	EtOH	65	8	99	98
5	EtOH	25	8	62	14
6	EtOH	40	8	70	66
7	EtOH	50	8	88	88
8	EtOH	60	8	93	92
9	EtOH	70	8	98	95
10	EtOH	65	4	65	63
11	EtOH	65	6	73	68
12	EtOH	65	7	86	85
13	EtOH	65	9	100	95
14[c]	EtOH	65	8	99	91

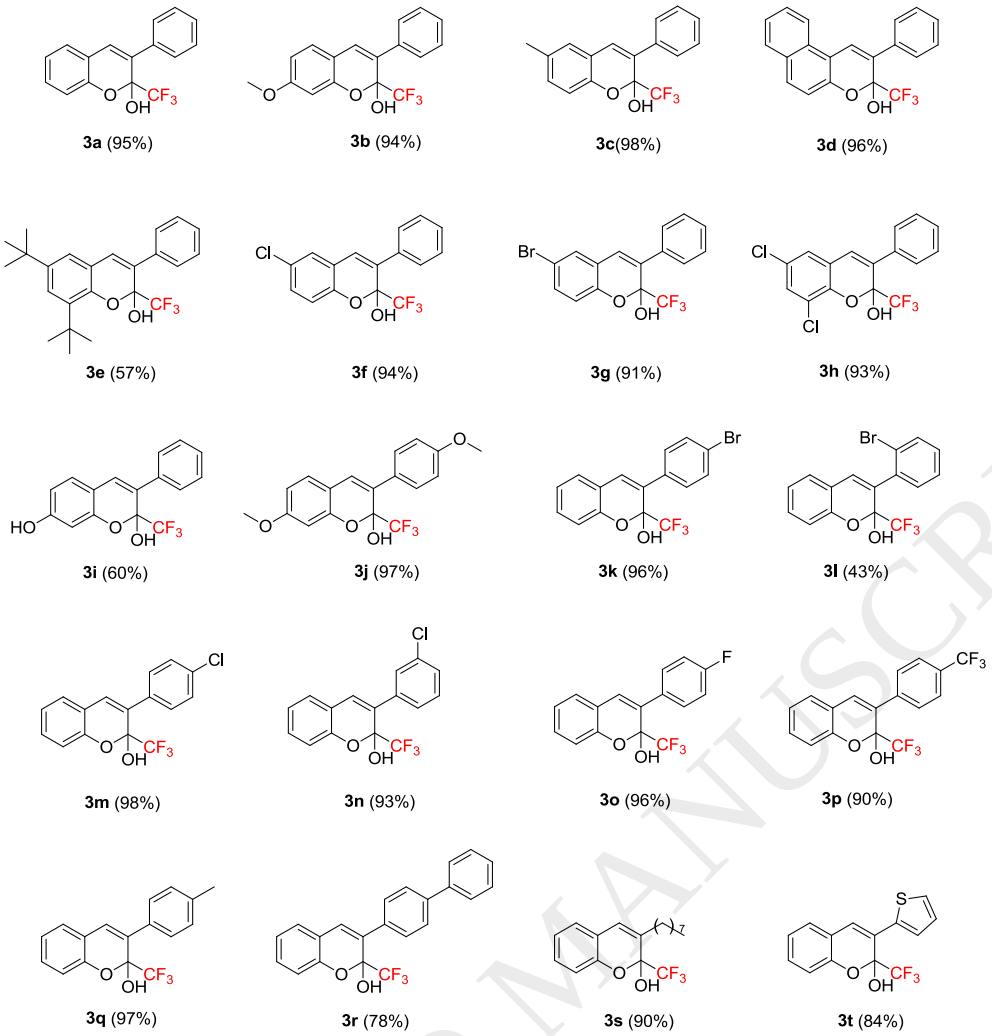
[a] Reaction conditions: A mixture of **1a** (2.0 mmol), **2a** (1.0 mmol), pyrrolidine (2.0 mmol) in solvent (3 mL) was stirred under Ar atmosphere. [b] The yield was determined by ^{1}H NMR with dimethyl terephthalate as an internal standard. [c] Reaction was performed in air.

The reaction scope in terms of salicylaldehydes and (*Z*)-trifluoromethyl alkenyl triflates was next explored under the optimized conditions (Table 3). As expected, this reaction tolerated a wide range of salicylaldehydes bearing either electron-donating or electron-withdrawing groups, affording the desired 2-trifluoromethyl-2-hydroxy-2*H*-chromenes in moderate to excellent yields (**3a**-**3j**). Reaction of salicylaldehyde derivatives containing *tert-butyl* groups at 3-position and 5-position, however, occurred in lower yields as a result of the steric effect (**3e**). In addition, reaction of salicylaldehyde derivatives containing a *hydroxyl* group at 4-position gave lower yields due to the effect of *hydroxyl* group (**3i**). Likewise, the reactions of (*Z*)-phenyl-trifluoromethyl alkenyl triflates bearing electron-withdrawing groups or electron-donating groups were also proved to be effective to afford desired products in moderate to excellent yields (**3j**-**3t**). Specially, *alkyl* and *thiophenyl* substituted (*Z*)-trifluoromethyl alkenyl triflates were investigated to proceed smoothly and gave the corresponding products in good yields (**3s** and **3t**). However, the reaction of (*Z*)-1-(2-bromophenyl)-3,3,3-trifluoroprop-1-en-2-yl trifluoromethanesulfonate gave relatively lower yield because of the steric effect (**3l**). The structure of compound **3b** was further confirmed by X-ray diffraction (Figure 2).

Table 3 Preparation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.



1 **2** **3**



Reaction conditions: A mixture of **1** (2.0 mmol), **2** (1.0 mmol), pyrrolidine (2.0 mmol) in EtOH (3 mL) was stirred at 65 °C for 8-10 h under Ar atmosphere. Yield of the isolated product.

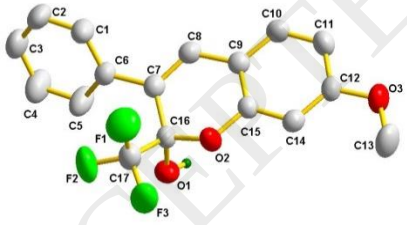
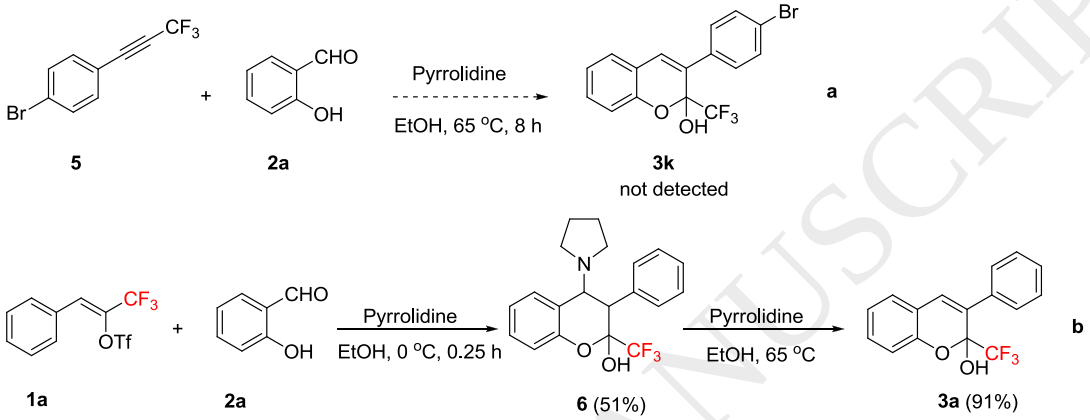


Figure 2 X-ray crystal structure of **3b**.

Some control experiments were conducted to understand the reaction mechanism (Scheme 1). At first, in consideration of the reaction of salicylaldehydes with alkynyl esters [7,8,10] and the fact that (*Z*)-trifluoromethyl alkenyl triflates are easy to form alkyne through an elimination reaction under basic conditions [9b], the reaction between 1-bromo-4-(3,3,3-trifluoroprop-1-yn-1-yl)benzene (**5**) and salicylaldehyde (**2a**) was investigated under the optimal reaction conditions. But the desired product **3k** was not detected (Scheme 1, **a**). In addition, when the reaction of **1a** and **2a** was carried out at 0 °C, the intermediate **6**,

3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol, was isolated in 51% yield, which can be transformed into the final product **3a** upon heating in the presence of pyrrolidine (Scheme 1, **b**). The structure of **6** was further confirmed by X-ray diffraction (Figure 3). To the best of our knowledge, this is the first example of the isolation and full characterization of the key intermediate **6** in the reaction of salicylaldehyde and trifluoromethylated species. And it also suggests that the elimination of pyrrolidine from intermediate **6** is the last step during the formation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.



Scheme 1 Investigations of the reaction mechanism.

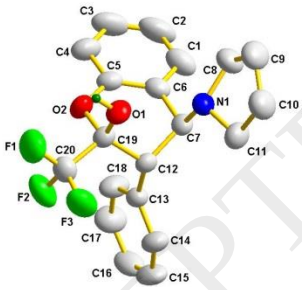
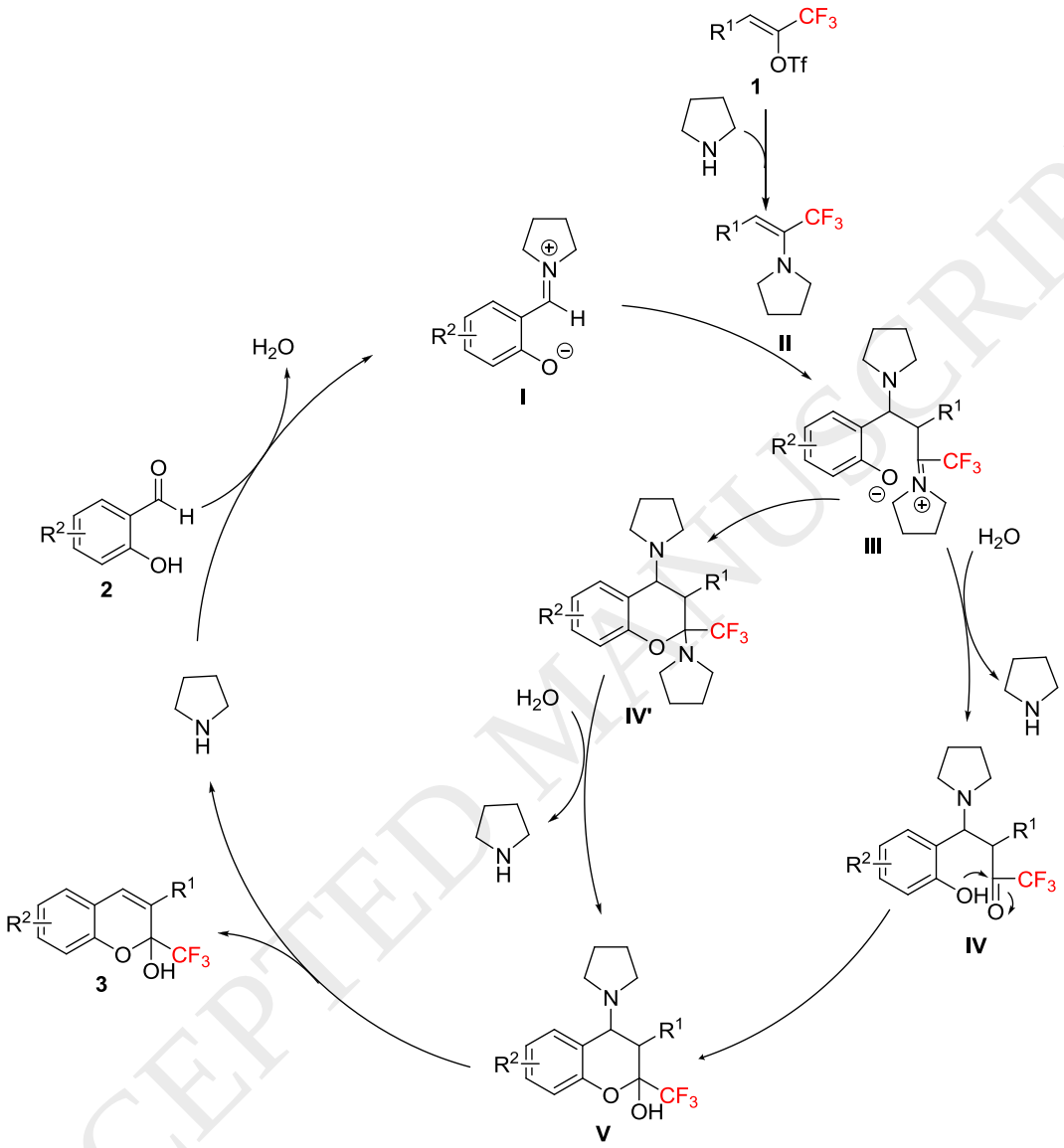


Figure 3 X-ray crystal structure of intermediate **6**

On the basis of the above investigations and previous reports [11], the possible mechanism is shown in Scheme 2. Presumably, the starting material **2** was condensed with pyrrolidine to give iminium cation intermediate **I**. Meanwhile, (*Z*)-trifluoromethyl alkenyl triflates **1** was reacted with pyrrolidine to form enamine intermediate **II**. Afterwards nucleophilic addition of intermediate **II** to electrophilic carbon atom of **I** occurs, that lead to formation of compound **III**. Then **III** has two possible ways to convert to intermediate **V**. One way was that hydrolysis of iminium moiety to carbonyl group took place in the presence of water and gave intermediate **IV**, then intramolecular cyclization of intermediate **IV** furnished intermediate **V**. The

other was ring closure in **III** to give intermediate **IV'** and subsequent hydrolysis of the aminal to form intermediate **V**. Finally, intermediate **V** underwent an elimination process to generate product **3** and release another pyrrolidine. The hemiketal structure in intermediate **V** and products **3** were stabled by CF_3 group.



Scheme 2 Possible mechanism for preparation of products **3**.

3. Conclusions

In conclusion, an efficient method to afford novel 2-trifluoromethyl-2-hydroxy-2*H*-chromenes containing *aryl* or *alkyl* groups at 3-position was developed. Salicylaldehydes and (*Z*)-trifluoromethyl alkenyl triflates reacted smoothly to afford corresponding 2-trifluoromethyl-2-hydroxy-2*H*-chromenes promoted by pyrrolidine. The functional group, such as fluorine, chlorine, bromine,

alkyl, alkoxy, and trifluoromethyl, were all tolerated well, and the desired products were obtained in moderate to excellent yields. A key intermediate, 3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol (**6**), was isolated and fully characterized, which suggests that the elimination of pyrrolidine from **6** is the last step during the formation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes.

4. Experimental

4.1. General information

Unless otherwise noted, all reactions were performed under an Ar atmosphere in glassware with magnetic stirring. NaH (60% in mineral oil) was washed with dry *n*-hexane to remove mineral oil prior to use. Other reagents and solvents were purchased from commercial sources and used without further purification. Column chromatography was performed on silica gel (200–300 mesh) using petroleum ether/ethyl acetate as an eluent. All ^{1}H NMR (400 MHz), ^{13}C NMR (101 MHz) and ^{19}F NMR (377 MHz or 470 MHz) were recorded on Bruker AVANCE II-400 or Bruker AVANCE III-500 spectrometer with chemical shifts reported as ppm (in $CDCl_3$, CD_3OD or CD_3CN with TMS as an internal standard). HRMS (ESI) were recorded on a Micromass GCT spectrometer. X-ray analysis was performed on a Bruker SMART APEX CCD diffractometer.

4.2. General procedure for the preparation of (*Z*)-trifluoromethyl alkenyl triflates **1**.

(*Z*)-Trifluoromethyl alkenyl triflates **1** were prepared according to our previous works [9b]. To a suspension of NaH (480 mg, 20.0 mmol) in MTBE (10 mL) was added ethyl trifluoroacetate (2.4 mL, 20.0 mmol) at room temperature under an Ar atmosphere. After 1 min of stirring, enolizable ketone (10.0 mmol) was added, and the mixture was refluxed for 6-12 h. After the reaction was complete (monitored by TLC or GC analyses), the reaction solution was cooled to 0 °C. Tf_2O (2.86 mL, 20.0 mmol) was added slowly into the reaction mixture. After the reaction was complete (monitored by TLC or GC analyses), the reaction was quenched with ice-water. The aqueous layer was separated and extracted with EtOAc. The combined organic extracts were washed with brine, dried over $MgSO_4$, and the solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether as the eluent) to afford the products **1**.

(*Z*)-3,3,3-Trifluoro-1-(4-methoxyphenyl)prop-1-en-2-yl trifluoromethanesulfonate (**1j**)

Colorless liquid; yield 72% (2.52 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.58 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H), 7.03 (s, 1H), 6.96 (d, $^{3}J_{HH}$ = 8.7 Hz, 2H), 3.85 (s, 3H). ^{13}C NMR (101

MHz, $CDCl_3$) δ 161.8, 132.0, 130.5 (q, $^2J_{CF}$ = 38.3 Hz), 127.6 (q, $^3J_{CF}$ = 7.0 Hz), 120.9, 119.4 (q, $^1J_{CF}$ = 273.7 Hz), 118.0 (q, $^1J_{CF}$ = 322.2 Hz), 114.6, 55.4. ^{19}F NMR (470 MHz, $CDCl_3$) δ -68.6 (q, $^6J_{FF}$ = 4.7 Hz, 3F), -72.7 (q, $^6J_{FF}$ = 4.7 Hz, 3F). IR (KBr, cm^{-1}) ν = 1675, 1608, 1516, 1429, 1265, 1023, 886, 831, 681, 604. HRMS (ESI) *m/z*: calcd for $C_{11}H_7F_6O_4S$ $[M - H]^-$ 348.9969, found: 348.9967.

(*Z*)-3,3,3-Trifluoro-1-(4-fluorophenyl)prop-1-en-2-yl trifluoromethanesulfonate (**1o**)

Colorless liquid; yield 78% (2.64 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 – 7.58 (m, 2H), 7.20 – 7.12 (m, 2H), 7.10 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0 (d, $^1J_{CF}$ = 253.7 Hz), 132.1 (d, $^3J_{CF}$ = 8.8 Hz), 126.9 (q, $^3J_{CF}$ = 3.6 Hz), 124.7 (d, $^4J_{CF}$ = 3.5 Hz), 123.1 (q, $^2J_{CF}$ = 14.4 Hz), 119.1 (q, $^1J_{CF}$ = 273.7 Hz), 118.2 (q, $^1J_{CF}$ = 322.2 Hz), 116.5 (d, $^2J_{CF}$ = 24.2 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -68.1 – -70.3 (m, 3F), -71.5 – -77.6 (m, 3F), -107.1 – -107.4 (m, 1F). IR (KBr, cm^{-1}) ν = 1682, 1605, 1514, 1432, 1241, 1027, 887, 834, 682, 605. HRMS (ESI) *m/z*: calcd for $C_{10}H_4F_7O_3S$ $[M - H]^-$ 336.9769, found: 336.9767.

(*Z*)-3,3,3-Trifluoro-1-[4-(trifluoromethyl)phenyl]prop-1-en-2-yl trifluoromethanesulfonate (**1p**)

Colorless liquid; yield 74% (2.87 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (m, 4H), 7.18 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 134.0 (q, $^2J_{CF}$ = 38.9 Hz), 132.7 (q, $^2J_{CF}$ = 33.2 Hz), 132.1, 130.0, 126.6 (q, $^3J_{CF}$ = 3.5 Hz), 126.1 (q, $^2J_{CF}$ = 18.9 Hz), 123.5 (q, $^1J_{CF}$ = 272.7 Hz), 118.9 (q, $^1J_{CF}$ = 274.7 Hz), 118.2, (q, $^1J_{CF}$ = 322.2 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -63.3 – -63.5 (m, 3F), -69.6 (q, $^6J_{FF}$ = 4.7 Hz, 3F), -72.8 (q, $^6J_{FF}$ = 4.7 Hz, 3F). IR (KBr, cm^{-1}) ν = 1434, 1326, 1284, 1070, 1029, 886, 834, 682, 603. HRMS (ESI) *m/z*: calcd for $C_{11}H_4F_9O_3S$ $[M - H]^-$ 386.9737, found: 386.9733.

(*Z*)-1,1,1-Trifluoroundec-2-en-2-yl trifluoromethanesulfonate (**1s**)

Colorless liquid; yield 74% (2.63 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.34 (t, $^3J_{HH}$ = 7.7 Hz, 1H), 2.39 – 2.28 (m, 2H), 1.57 – 1.45 (m, 2H), 1.38 – 1.22 (m, 10H), 0.93 – 0.84 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.9 (q, $^2J_{CF}$ = 39.1 Hz), 131.3 (q, $^3J_{CF}$ = 3.1 Hz), 118.9 (q, $^1J_{CF}$ = 273.7 Hz), 118.1 (q, $^1J_{CF}$ = 322.2 Hz), 31.7, 29.1, 29.0, 27.7, 26.0, 22.6, 14.0. ^{19}F NMR (470 MHz, $CDCl_3$) δ -70.1 (s, 3F), -73.2 (q, $^6J_{FF}$ = 4.7 Hz, 3F). IR (KBr, cm^{-1}) ν = 2931, 2860, 1695, 1427, 1330, 1221, 1137, 1010, 882, 753, 608. HRMS (ESI) *m/z*: calcd for $C_{12}H_{17}F_6O_3S$ $[M - H]^-$ 355.0803, found: 355.0800.

(*Z*)-3,3,3-Trifluoro-1-(thiophen-2-yl)prop-1-en-2-yl trifluoromethanesulfonate (**1t**)

Colorless liquid; yield 70% (2.28 g); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (d, $^3J_{HH}$ = 5.0 Hz, 1H), 7.56 (d, $^3J_{HH}$ = 3.6 Hz, 1H), 7.24 (s, 1H), 7.18 – 7.14 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.7, 131.8, 130.3, 129.7 (q, $^2J_{CF}$ = 39.0 Hz), 128.1, 121.5 (q,

$^{3}J_{CF}$ = 3.9 Hz), 119.5 (q, $^{1}J_{CF}$ = 273.7 Hz), 118.4 (q, $^{1}J_{CF}$ = 322.2 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -67.7 (q, $^{6}J_{FF}$ = 4.7 Hz, 3F), -71.9 (q, $^{6}J_{FF}$ = 4.7 Hz, 3F). IR (KBr, cm^{-1}) ν = 1671, 1432, 1134, 1019, 885, 805, 658, 609. HRMS (ESI) *m/z*: calcd for $C_8H_3F_6O_3S_2$ $[M - H]^-$ 324.9428, found: 324.9426.

4.3. General procedure for the preparation of 2-trifluoromethyl-2-hydroxy-2*H*-chromenes **3**.

To a solution of (*Z*)-trifluoromethyl alkenyl triflates **1** (2.0 mmol) in EtOH (3 mL) was added salicylaldehydes (1.0 mmol) at room temperature under an Ar atmosphere. Then pyrrolidine (2.0 mmol) was added, and the mixture was stirred at 65 °C for 8-10 h. After the reaction was complete (monitored by TLC), solvent was removed under reduced pressure. The crude product was purified by column chromatography on silica gel (petroleum ether/EtOAc =30:1 as the eluent) to afford the product **3**.

3-Phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3a**)

Light yellow liquid; yield 95% (277 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (d, $^{3}J_{HH}$ = 2.5 Hz, 2H), 7.34 – 7.33 (m, 3H), 7.27 – 7.22 (m, 1H), 7.15 (dd, $^{3}J_{HH}$ = 7.8, 1.4 Hz, 1H), 7.00 (dd, $^{3}J_{HH}$ = 7.2, 4.0 Hz, 2H), 6.76 (s, 1H), 3.47 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 136.7, 130.3, 129.2, 129.1, 128.3, 128.1, 127.4, 122.7, 122.2 (q, $^{1}J_{CF}$ = 290.9 Hz), 119.1, 115.9, 96.4 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.4. IR (KBr, cm^{-1}) ν = 3486, 1491, 1458, 1235, 1194, 1116, 1055, 937, 764, 700. HRMS (ESI) *m/z*: calcd for $C_{16}H_{10}F_3O_2$ $[M - H]^-$ 291.0633, found: 291.0641.

7-Methoxy-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3b**)

Light yellow solid; mp. 142 – 143 °C (crystallized in CH_2Cl_2/petroleum ether); yield 94% (303 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.51 (dd, $^{3}J_{HH}$ = 6.4, 2.8 Hz, 2H), 7.36 – 7.28 (m, 3H), 7.08 – 6.99 (m, 1H), 6.76 (s, 1H), 6.60 – 6.53 (m, 2H), 3.80 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.4, 150.6, 136.9, 129.0, 128.7, 128.2, 128.0, 126.3, 122.2 (q, $^{1}J_{CF}$ = 289.9 Hz), 112.6, 109.1, 101.4, 96.6 (q, $^{2}J_{CF}$ = 33.3 Hz), 55.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.3. IR (KBr, cm^{-1}) ν = 3423, 1505, 1446, 1203, 1163, 1118, 1003, 943, 767, 700. HRMS (ESI) *m/z*: calcd for $C_{17}H_{12}F_3O_3$ $[M - H]^-$ 321.0739, found: 321.0747.

6-Methyl-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3c**)

Colorless liquid; yield 98% (300 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.49 (m, 2H), 7.36 – 7.32 (m, 3H), 7.08 – 7.03 (m, 1H), 6.96 (s, 1H), 6.91 (d, $^{3}J_{HH}$ = 8.2 Hz, 1H), 6.75 (s, 1H), 3.88 (br s, 1H), 2.31 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.2, 136.8, 132.1, 130.9, 129.2, 129.0, 128.2, 128.0, 127.7, 122.2 (q, $^{1}J_{CF}$ = 290.9 Hz), 118.8, 115.6, 96.4 (q, $^{2}J_{CF}$ = 33.3 Hz), 20.6. ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.2. IR

(KBr, cm^{-1}) ν = 3531, 1607, 1493, 1237, 1190, 1129, 1055, 901, 817, 700. HRMS (ESI) *m/z*: calcd for $C_{17}H_{12}F_3O_2$ $[M - H]^-$ 305.0789, found: 305.0798.

2-Phenyl-3-trifluoromethyl-3*H*-benzo[f]chromen-3-ol (**3d**)

Light yellow liquid; yield 96% (328 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 7.71 – 7.65 (m, 2H), 7.56 – 7.55 (m, 2H), 7.43 – 7.41 (m, 2H), 7.35 – 7.33 (m, 4H), 7.17 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 3.95 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.5, 137.0, 130.9, 130.0, 129.6, 129.3, 128.9, 128. 5, 128.2, 128.1, 127.4, 124.8, 124.7, 122.3 (q, $^1J_{CF}$ = 289.9 Hz), 121.2, 117.1, 111.9, 96.3 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -80.5. IR (KBr, cm^{-1}) ν = 3464, 1641, 1534, 1293, 1242, 1185, 1051, 955, 750, 703. HRMS (ESI) *m/z*: calcd for $C_{20}H_{12}F_3O_2$ $[M - H]^-$ 341.0789, found: 341.0796.

6,8-Di-*tert*-butyl-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3e**)

Colorless liquid; yield 57% (231 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 (d, $^3J_{HH}$ = 3.1 Hz, 2H), 7.34 – 7.33 (m, 2H, 2H), 7.07 (d, $^3J_{HH}$ = 2.2 Hz, 1H), 6.80 (d, $^3J_{HH}$ = 2.6 Hz, 1H), 3.84 (br s, 1H), 1.47 (s, 9H), 1.32 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 145.8, 144.8, 136.8, 136.7, 130.2, 129.0, 128.4, 128.1, 128.0, 125.3, 122.5, 122.3 (q, $^1J_{CF}$ = 289.9 Hz), 118.8, 96.2 (q, $^2J_{CF}$ = 33.3 Hz), 34.8, 34.5, 31.5,29.8. ^{19}F NMR (377 MHz, $CDCl_3$) δ -80.0. IR (KBr, cm^{-1}) ν = 3483, 1433, 1365, 1238, 1188, 1057, 1030, 981, 772, 703. HRMS (ESI) *m/z*: calcd for $C_{24}H_{26}F_3O_2$ $[M - H]^-$ 403.1885, found: 403.1898.

6-Chloro-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3f**)

Colorless liquid; yield 94% (307 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 2H), 7.39 – 7.30 (m, 3H), 7.22 – 7.16 (m, 1H), 7.13 (d, $^3J_{HH}$ = 2.5 Hz, 1H), 6.93 (d, $^3J_{HH}$ = 8.0 Hz, 1H), 6.69 (s, 1H), 3.93 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 147.8, 136.1, 130.5, 130.0, 129.0, 128.6, 128.2, 128.0, 127.6, 126.8, 122.0 (q, $^1J_{CF}$ = 289.9 Hz), 120.4, 117.2, 96.3 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.2. IR (KBr, cm^{-1}) ν = 3502, 1485, 1445, 1232, 1190, 1105, 1055, 905, 811, 701. HRMS (ESI) *m/z*: calcd for $C_{16}H_9ClF_3O_2$ $[M - H]^-$ 325.0243, found: 325.0255.

6-Bromo-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3g**)

Colorless liquid; yield 91% (337 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.53 – 7.46 (m, 2H), 7.36 – 7.32 (m, 4H), 7.27 (d, $^3J_{HH}$ = 2.4 Hz, 1H), 6.87 (d, $^3J_{HH}$ = 8.6 Hz, 1H), 6.68 (s, 1H), 3.67 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 148.3, 136.1, 132.9, 130.4, 129.8, 129.0, 128.6, 128.2, 127.9, 122.0 (q, $^1J_{CF}$ = 290.9 Hz), 120.9, 117.6, 114.8, 96.5 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.2. IR (KBr, cm^{-1}) ν

= 3507, 1644, 1483, 1233, 1191, 1100, 1054, 905, 809, 701. HRMS (ESI) *m/z*: calcd for $C_{16}H_9BrF_3O_2$ $[M - H]^-$ 368.9738, found: 368.9751.

6,8-Dichloro-3-phenyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3h**)

Colorless liquid; yield 93% (335 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.52 – 7.50 (m, 2H), 7.41 – 7.33 (m, 3H), 7.31 (d, $^3J_{HH}$ = 2.3 Hz, 1H), 7.07 (d, $^3J_{HH}$ = 2.3 Hz, 1H), 6.70 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 135.7, 131.3, 130.0, 128.9, 128.8, 128.2, 127.5, 127.4, 125.3, 121.8 (q, $^1J_{CF}$ = 290.9 Hz), 121.8, 121.4, 96.0 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.4. IR (KBr, cm^{-1}) ν = 3548, 1600, 1459, 1248, 1219, 1095, 1018, 901, 854, 705. HRMS (ESI) *m/z*: calcd for $C_{16}H_8Cl_2F_3O_2$ $[M - H]^-$ 358.9853, found: 358.9866.

3-Phenyl-2-trifluoromethyl-2*H*-chromene-2,7-diol (**3i**)

Colorless liquid; yield 60% (185 mg); ^{1}H NMR (400 MHz, CD_3OD) δ 7.42 (dd, $^3J_{HH}$ = 7.6, 1.7 Hz, 2H), 7.24 – 7.16 (m, 3H), 6.95 (d, $^3J_{HH}$ = 8.1 Hz, 1H), 6.62 (s, 1H), 6.37 – 6.34 (m, 2H), 4.76 (s, 2H). ^{13}C NMR (101 MHz, CD_3OD) δ 159.3, 151.1, 137.8, 128.7, 128.0, 127.9, 127.4, 127.1, 126.7, 122.5 (q, $^1J_{CF}$ = 289.9 Hz), 111.8, 109.3, 102.1, 96.6 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, CD_3OD) δ -82.0. IR (KBr, cm^{-1}) ν = 3318, 1622, 1508, 1211, 1159, 1127, 1094, 905, 838, 764. HRMS (ESI) *m/z*: calcd for $C_{16}H_{10}F_3O_3$ $[M - H]^-$ 307.0582, found: 307.0592.

7-Methoxy-3-(4-methoxyphenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3j**)

Light yellow liquid; yield 97% (342 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 7.09 – 7.06 (m, 1H), 6.88 (d, $^3J_{HH}$ = 8.6 Hz, 2H), 6.72 (s, 1H), 6.58 – 6.57 (m, 2H), 3.81 (s, 3H) 3.79 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 161.3, 159.4, 150.6, 130.2, 129.2, 128.0, 125.8, 122.2 (q, $^1J_{CF}$ = 290.9 Hz), 113.5, 112.7, 109.1, 101.3, 96.6 (q, $^2J_{CF}$ = 33.3 Hz), 55.5, 55.3. ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.4. IR (KBr, cm^{-1}) ν = 3372, 1620, 1511, 1244, 1178, 1112, 1015, 837, 741, 700. HRMS (ESI) *m/z*: calcd for $C_{18}H_{14}F_3O_4$ $[M - H]^-$ 351.0844, found: 351.0854.

3-(4-Bromophenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3k**)

Colorless liquid; yield 96% (355 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.40 (d, $^3J_{HH}$ = 8.0 Hz, 2H), 7.29 – 7.25 (m, 1H), 7.18 (dd, $^3J_{HH}$ = 7.4, 1.1 Hz, 1H), 7.04 – 6.98 (m, 2H), 6.77 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 135.7, 131.2, 130.6, 130.6, 129.4, 128.0, 127.5, 122.8, 122.6, 122.1 (q, $^1J_{CF}$ = 290.9 Hz), 118.8, 115.8, 96.2 (q, $^2J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.3. IR (KBr, cm^{-1}) ν = 3478, 1488, 1457, 1235, 1192, 1105, 1011, 926, 826, 755. HRMS (ESI) *m/z*: calcd for $C_{16}H_9BrF_3O_2$ $[M - H]^-$ 368.9738, found: 368.9754.

3-(2-Bromophenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3l**)

Colorless liquid; yield 43% (159 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 – 7.65 (m, 1H), 7.47 (d, $^{3}J_{HH}$ = 7.5 Hz, 1H), 7.35 – 7.28 (m, 2H), 7.25 – 7.17 (m, 2H), 7.10 – 7.01 (m, 2H), 6.77 (s, 1H), 4.21 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.6, 137.0, 132.8, 132.3, 132.2, 130.8, 129.9, 127.6, 127.1, 127.0, 124.1, 122.8, 122.0 (q, $^{1}J_{CF}$ = 289.9 Hz), 118.7, 116.3, 96.0 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -80.8. IR (KBr, cm^{-1}) ν = 3503, 1489, 1458, 1233, 1190, 1066, 1024, 931, 756, 726. HRMS (ESI) *m/z*: calcd for $C_{16}H_9BrF_3O_2$ $[M - H]^-$ 368.9738, found: 368.9752.

3-(4-Chlorophenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3m**)

Colorless liquid; yield 98% (320 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H), 7.31 (d, $^{3}J_{HH}$ = 8.0 Hz, 2H), 7.30 – 7.23 (m, 1H), 7.19 (d, $^{3}J_{HH}$ = 7.4 Hz, 1H), 7.05 – 7.01 (m, 2H), 6.79 (s, 1H), 3.99 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 135.1, 134.4, 130.5, 130.3, 129.4, 128.3, 127.9, 127.5, 122.8, 122.0 (q, $^{1}J_{CF}$ = 290.9 Hz), 118.8, 115.8, 96.2 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.4. IR (KBr, cm^{-1}) ν = 3505, 1500, 1458, 1225, 1192, 1136, 1060, 830, 772, 741. HRMS (ESI) *m/z*: calcd for $C_{16}H_9ClF_3O_2$ $[M - H]^-$ 325.0243, found: 325.0255.

3-(3-Chlorophenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3n**)

Colorless liquid; yield 93% (303 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 (s, 1H), 7.42 (d, $^{3}J_{HH}$ = 7.5 Hz, 1H), 7.32 (d, $^{3}J_{HH}$ = 8.1 Hz, 1H), 7.30 – 7.23 (m, 2H), 7.19 – 7.15 (m, 1H), 7.04 – 7.00 (m, 2H), 6.79 (s, 1H), 4.22 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 138.4, 133.9, 130.7, 129.8, 129.3, 129.1, 128.4, 127.7, 127.6, 127.3, 122.8, 122.1 (q, $^{1}J_{CF}$ = 290.9 Hz), 118.7, 115.9, 96.4 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.4. IR (KBr, cm^{-1}) ν = 3501, 1594, 1477, 1234, 1191, 1117, 1058, 893, 787, 755. HRMS (ESI) *m/z*: calcd for $C_{16}H_9ClF_3O_2$ $[M - H]^-$ 325.0243, found: 325.0254.

3-(4-Fluorophenyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3o**)

White solid; mp. 93 – 94 °C (petroleum ether/EtOAc); yield 96% (298 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.47 (m, 2H), 7.29 – 7.27 (m, 1H), 7.20 (dd, $^{3}J_{HH}$ = 7.7, 1.3 Hz, 1H), 7.09 – 7.00 (m, 4H), 6.79 (s, 1H), 3.63 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 162.8 (d, $^{1}J_{CF}$ = 248.5 Hz), 149.2, 132.6 (d, $^{4}J_{CF}$ = 3.0 Hz), 130.8 (d, $^{3}J_{CF}$ = 8.2 Hz), 130.5, 129.3, 127.9, 127.4, 122.8, 122.1 (q, $^{1}J_{CF}$ = 289.9 Hz), 118.9, 115.8, 115.0 (d, $^{2}J_{CF}$ = 21.6 Hz), 96.2 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -81.0 (s, 3F), -113.6 (s, 1F). IR (KBr, cm^{-1}) ν = 3508, 1501, 1460, 1236, 1188, 1128, 1056, 928, 835, 758. HRMS (ESI) *m/z*: calcd for $C_{16}H_9F_4O_2$ $[M - H]^-$ 309.0539, found: 309.0541.

2-(Trifluoromethyl)-3-[4-(trifluoromethyl)phenyl]-2*H*-chromen-2-ol (**3p**)

White solid; mp. 67 – 68 °C (petroleum ether/EtOAc); yield 90% (324 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.67 (d, $^{3}J_{HH}$ = 8.2 Hz, 2H), 7.62 (d, $^{3}J_{HH}$ = 8.2 Hz, 2H), 7.34 – 7.30 (m, 1H), 7.23 (d, $^{3}J_{HH}$ = 8.0 Hz, 1H), 7.08 – 7.04 (m, 2H), 6.85 (s, 1H), 3.73 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 140.3, 130.9, 130.3, 129.4, 127.6, 125.0 (q, $^{3}J_{CF}$ = 3.7 Hz), 124.1 (q, $^{1}J_{CF}$ = 273.7 Hz), 122.8, 122.0 (q, $^{1}J_{CF}$ = 289.9 Hz), 118.6, 115.9, 96.2 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -62.7 (s, 3F), -81.2 (s, 3F). IR (KBr, cm^{-1}) ν = 3572, 1492, 1460, 1236, 1198, 1128, 1055, 843, 757, 703. HRMS (ESI) *m/z*: calcd for $C_{17}H_9F_6O_2$ $[M - H]^-$ 359.0507, found: 359.0508.

3-(*p*-Tolyl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3q**)

Light yellow liquid; yield 97% (297 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (d, $^{3}J_{HH}$ = 8.1 Hz, 2H), 7.32 – 7.25 (m, 1H), 7.23 – 7.17 (m, 3H), 7.08 – 7.02 (m, 2H), 6.74 (s, 1H), 2.34 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 138.2, 133.8, 130.2, 129.2, 128.9, 128.8, 128.6, 127.3, 122.6, 122.2 (q, $^{1}J_{CF}$ = 289.9 Hz), 119.2, 115.8, 96.3 (q, $^{2}J_{CF}$ = 33.3 Hz), 21.2. ^{19}F NMR (470 MHz, $CDCl_3$) δ -80.8. IR (KBr, cm^{-1}) ν = 3505, 1490, 1458, 1234, 1194, 1116, 1054, 932, 821, 753. HRMS (ESI) *m/z*: calcd for $C_{17}H_{12}F_3O_2$ $[M - H]^-$ 305.0789, found: 305.0797.

3-[(1,1'-Biphenyl)-4-yl]-2-trifluoromethyl-2*H*-chromen-2-ol (**3r**)

Colorless liquid; yield 78% (287 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.54 (m, 6H), 7.44 – 7.40 (m, 2H), 7.33 (t, $^{3}J_{HH}$ = 7.3 Hz, 1H), 7.28 – 7.21 (m, 1H), 7.18 – 7.13 (m, 1H), 7.02 – 6.98 (m, 2H), 6.82 (s, 1H), 4.03 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.4, 141.0, 140.5, 135.6, 130.4, 129.5, 129.1, 128.9, 128.8, 127.6, 127.5, 127.1, 126.8, 122.7, 122.2 (q, $^{1}J_{CF}$ = 289.9 Hz), 119.1, 115.8, 96.3 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (377 MHz, $CDCl_3$) δ -81.1. IR (KBr, cm^{-1}) ν = 3529, 1488, 1458, 1192, 1115, 1052, 1005, 933, 837, 765, 726. HRMS (ESI) *m/z*: calcd for $C_{22}H_{14}F_3O_2$ $[M - H]^-$ 367.0946, found: 367.0957.

3-Octyl-2-trifluoromethyl-2*H*-chromen-2-ol (**3s**)

Light yellow liquid; yield 90% (296 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.20 – 7.14 (m, 1H), 7.09 (d, $^{3}J_{HH}$ = 7.3 Hz, 1H), 6.99 – 6.93 (m, 2H), 6.56 (s, 1H), 3.17 (br s, 1H), 2.47 – 2.21 (m, 2H), 1.63 – 1.58 (m, 2H), 1.36 – 1.20 (m, 10H), 0.89 (t, $^{3}J_{HH}$ = 6.4 Hz, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 149.3, 129.8, 129.4, 126.6, 124.9, 122.4, 122.4 (q, $^{1}J_{CF}$ = 290.9 Hz), 119.4, 115.5, 96.5 (q, $^{2}J_{CF}$ = 33.3 Hz), 31.9, 30.1, 29.5, 29.4, 29.3, 28.1, 22.7, 14.1. ^{19}F NMR (377 MHz, $CDCl_3$) δ -82.7. IR (KBr, cm^{-1}) ν = 3417, 2929, 2858, 1491, 1459, 1233, 1183, 1046, 753. HRMS (ESI) *m/z*: calcd for $C_{18}H_{22}F_3O_2$ $[M - H]^-$ 327.1572, found: 327.1582.

3-(Thiophen-2-yl)-2-trifluoromethyl-2*H*-chromen-2-ol (**3t**)

Light yellow liquid; yield 84% (250 mg); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, $^{3}J_{HH}$ = 3.5 Hz, 1H), 7.26 (d, $^{3}J_{HH}$ = 5.1 Hz, 1H), 7.23 – 7.19 (m, 1H), 7.14 (d, $^{3}J_{HH}$ = 6.6 Hz, 1H), 7.04 – 6.93 (m, 4H), 3.99 (br s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 150.3, 138.0, 130.5, 128.0, 127.7, 127.4, 127.3, 126.1, 122.7, 122.4 (q, $^{1}J_{CF}$ = 292.9 Hz), 122.0, 119.1, 115.2, 96.6 (q, $^{2}J_{CF}$ = 33.3 Hz). ^{19}F NMR (470 MHz, $CDCl_3$) δ -83.2. IR (KBr, cm^{-1}) ν = 3492, 1488, 1457, 1282, 1191, 1158, 1082, 965, 761, 718. HRMS (ESI) *m/z*: calcd for $C_{14}H_8F_3O_2S$ $[M - H]^-$ 297.0197, found: 297.0200.

4.4. Preparation of 3-phenyl-4-(pyrrolidin-1-yl)-2-(trifluoromethyl)chroman-2-ol (**6**)

To a solution of (*Z*)-trifluoromethyl alkenyl triflates **1a** (2.0 mmol) in EtOH (3 mL) was added salicylaldehyde **2a** (1.0 mmol) at 0 °C under an Ar atmosphere. Then pyrrolidine (2.0 mmol) was added, and the mixture was stirred at 0 °C for 1 h to precipitate a white solid. After the reaction was complete (monitored by TLC), the white solid was filtered, washed with cool EtOH, and crystallized in toluene to afford aimed product.

White solid; mp. 127 – 128 °C (toluene); yield 51% (182 mg) ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.94 (s, 1H), 7.38 (t, $^{3}J_{HH}$ = 7.7 Hz, 1H), 7.20 – 7.12 (m, 5H), 7.06 – 6.87 (m, 3H), 3.89 (s, 1H), 3.57 (s, 1H), 3.01 (br s, 2H), 2.55 (s, 2H), 1.86 – 1.77 (m, 4H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 151.6, 135.6, 132.5, 130.8, 128.9, 128.4, 127.8, 121.8 (q, $^{1}J_{CF}$ = 286.8 Hz), 121.5, 118.4, 118.1, 97.3 (q, $^{2}J_{CF}$ = 32.0 Hz), 65.5, 52.0, 43.7, 23.2. ^{19}F NMR (470 MHz, CD_3CN) δ -82.1. IR (KBr, cm^{-1}) ν = 2982, 2832, 1586, 1456, 1297, 1219, 1197, 1128, 1097, 1016, 990, 764, 704. HRMS (ESI) *m/z*: calcd for $C_{20}H_{21}F_3NO_2$ $[M + H]^+$ 364.1524, found: 364.1522.

4.5. The X-Ray Crystal Structure Determination.

The crystals of **3b** and **6** were obtained by slow evaporation of the solution (**3b** in CH_2Cl_2 and **6** in toluene) at room temperature. The data were obtained on a CCD diffractometer with graphite-monochromated. Mo Kα radiation (λ = 0.71073 Å). Empirical absorption corrections were performed using the SADABS program [12]. Structures were solved by direct methods and were refined by full-matrix least-squares based on all data using F2 in Shelx97 [13,14]. All of the non-hydrogen atoms were refined anisotropically. All of the hydrogen atoms were generated and refined in ideal positions. CCDC-1832869/1832870 contains the supplementary crystallographic data, which can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/structures/.

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