Reactions of 3-(Polyfluoroacyl)chromenones with Heterocyclic Amines: Novel Synthesis of Polyfluoroalkyl-Containing Fused Pyridines

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Dedicated to Professor Peter Langer on the occasion of his 40th birthday

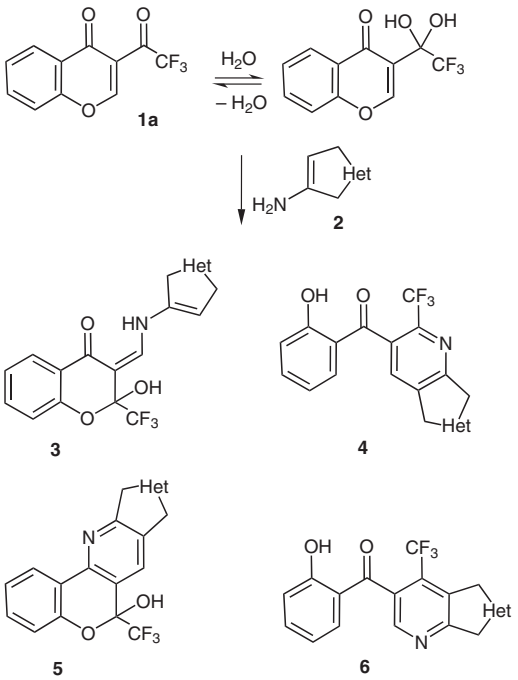
Abstract: The selectivity of the reactions of 3-(polyfluoroacyl)-4*H*-chromen-4-ones with a wide range of aminoheterocycles and arylamines has been evaluated. The method described facilitates access to polyfluoroalkyl-containing fused pyridines.

Key words: aminoheterocycles, arylamines, condensation, chroman-4-ones, polyfluoroalkyl, fused pyridines

Regiospecific annulation of the pyridine and pyrimidine core to electron-rich aminoheterocycles recently became one of the basic methods for purine (purine isosteres) assembly.[1] Application of this method gave rise to the synthesis of many purines and their isosteres, such as desazapurines[1a–c] and a numbers of different azapurines.[1d]

Elaboration of novel reagents in the class of 1,3-dielectrophiles for the synthesis of purine analogues is one of the challenges of modern heterocyclic chemistry. A special position among purine isosteres and purine analogues is occupied by fluorinated derivatives, which show a wide spectrum of biological activity and have been identified as pharmacophores of high potency. For example, some polyfluoroalkyl-substituted purines have been recognized as antiviral[2] and phosphodiesterase inhibitory agents.[3] Previously, we have reported the synthesis of many fluorinated purines and their analogues,[4] such as 7-thiopurines,[4a] a number of 1-desazapurines,[4b] 1,7-desazapurines,[4c] azapurines,[4d,e] and 7-desazapurines.[4c]

3-Formyl-4*H*-chromen-4-ones are frequently used in organic chemistry. The majority of the reactions with these compounds are nucleophilic additions at C2 with concomitant opening of the pyrone ring leading to various types of heterocyclic compounds including pyrimidines[5] and pyridines.[6] 3-(Polyfluoroacyl)-4*H*-chromen-4-ones are novel building blocks, the chemistry of which has not yet been fully elaborated. Recent advances in the chemistry of these compounds, especially 3-(trifluoroacetyl)-4*H*-chromen-4-one (**1a**), show that they easily react with water to form stable covalent hydrates and with primary aromatic and aliphatic amines to give 3-[(aryl/alkylamino)methylene]-2-hydroxy-2-(polyfluoroalkyl)chroman-4-ones.[7] Very recently we have shown that chromenones **1** are suitable for the synthesis of polyfluoroalkyl-containing pyridines,[8] either by annulation of the pyridine core[8a] by addition of **1** to enamines or by hetero-Diels–Alder protocol with enol ethers followed by ammonolysis of the thus formed adducts.[8b,c] The reaction of **1** with enamines arising from active methylene compounds starts predominantly with attack at the unsubstituted C2 (1,4-addition) and is accompanied by pyrone ring-opening to form β-dicarbonyl intermediates capable of regioselective intramolecular heterocyclizations.[8a] Alternatively, the initial attack can also occur at the 3-(trifluoroacetyl) group (1,2-addition), which does not exclude the variant of recyclization due to the intramolecular Michael reaction and subsequent ring-opening with cleavage of the O1–C2 bond.[9]



Scheme 1 General structures of the obtained products **3–6**

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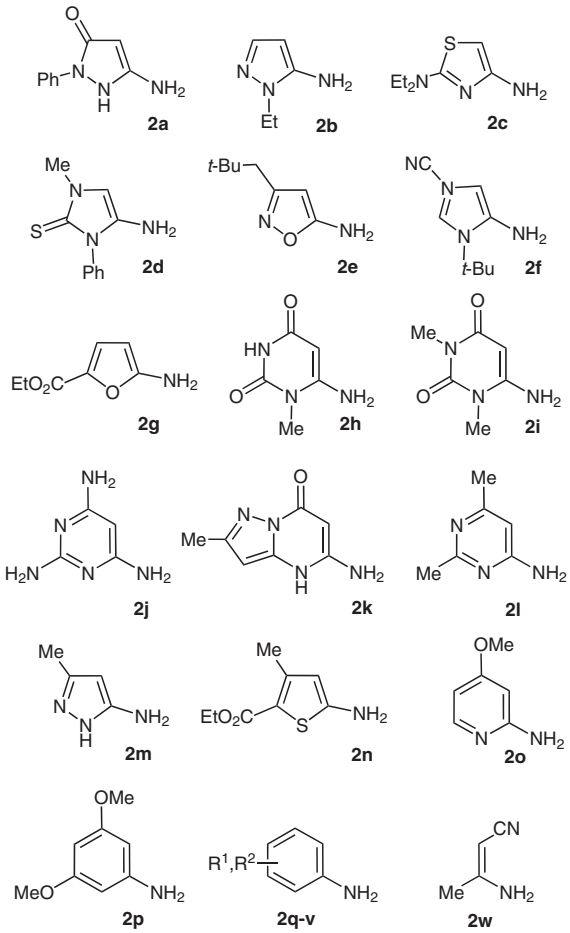
Considering these findings and the electron-withdrawing force of a 3-(trifluoroacetyl) group, we thought that the reaction of **1a** with electron-rich heterocyclic amines and arylamines could produce the corresponding fused pyridines. At the same time, we reasoned that when compounds such as **1a** were coupled with 1,3-C,N-dinucleophiles **2**, the similar electrophilic character of their reactive centers would lead to a mixture of regioisomeric products such as **3**–**6** (Scheme 1). To obviate this problem, a wide range of electron-rich aminoheterocycles and aromatic amines bearing electron-donating substituents **2a**–**v** were designed and various reaction conditions were used in order to develop a simple and convenient synthesis of novel polyfluoroalkyl-containing fused pyridines. In this current publication we report the application of chromenones **1a** for pyridine ring annulation to electron-rich aminoheterocycles **2** (Figure 1).



q: R^1 = 3-NMe_2, R^2 = H; **r:** R^1,R^2 = 3,4-OCH_2O; **s:** R^1,R^2 = 3,4-$O(CH_2)_2O$; **t:** R^1 = 2-OH, R^2 = 5-Cl, **u:** R^1 = 2-OH, R^2 = 5-NO_2; **v:** R^1 = 2-$CONH_2$, R^2 = H

Figure 1 Structures of the used enamines **2**

It was found that the ratio of the products is strongly dependent not only on the structure of aminoheterocycle **2**, but also on the solvent used. Reacted enamines, solvents, and ratios of compounds **3**–**6**, when obtained, are listed in Table 1.

Table 1 Isolated Yields of Compounds **3**–**6**

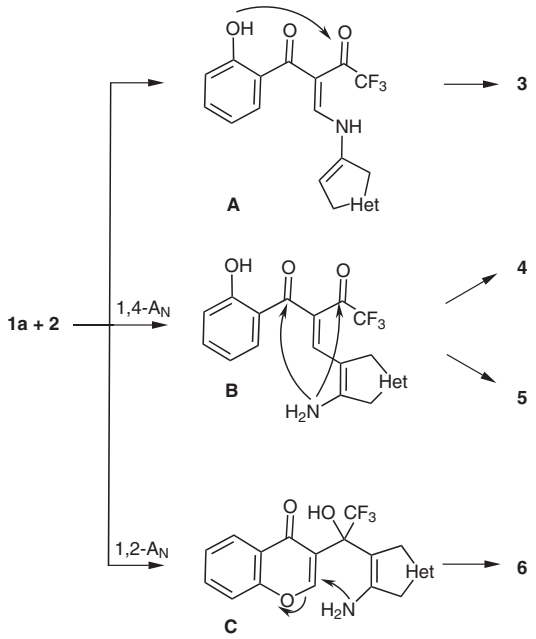
Entry	Substrate	Yield (%)			
		3 (DMF)	**4** (DMF)	**5** (DMF)	**6** (AcOH)
1	**2a**	n.d.	97	n.d.	–
		–	56 (AcOH)	–	37
2	**2b**	85	5[a]	5[a]	–
		–	60 (AcOH)	–	34
3	**2c**	–	94 (AcOH)	–	3[a]
4	**2d**	–	46 (AcOH)	–	n.d.
5	**2e**	n.d.	33	64	–
		–	72 (AcOH)	–	8
6	**2f**	22	21	52	–
7	**2g**	32[a]	25	36	–
8	**2h**	n.d.	30[a]	70	–
9	**2i**	n.d.	74	24	–
10	**2j**	30	59	n.d.	–
11	**2k**	5[a]	64	4[a]	–
12	**2l**	96	2[a]	n.d.	–
13	**2m**	99	n.d.	n.d.	–
14	**2n**	94	4[a]	n.d.	–
15	**2o**	76	n.d.	n.d.	–
16	**2p**	94	n.d.	n.d.	–
		–	48 (AcOH)	–	n.d.
17	**2q–v**	64–98	n.d.	n.d.	–
18	**2w**	n.d.	34	62	–

[a] Identified based on the ^{19}F NMR spectrum of the mixture; n.d. = not detected.

Based on the literature data,[8a] the formation of four possible classes of end-products **3**–**6** can be anticipated, however, during ^{19}F NMR analysis of the mixtures obtained from reactions of **1a** with **2** in anhydrous *N*,*N*-dimethylformamide in the temperature range 60–100 °C, only three products were observed. Heterocycles **2a**,**i**–**k** react with **1a** to give the corresponding pyridines **4** as the main products, while in the case of **2e**–**h**,**w** the formation of chromeno[4,3-*b*]pyridines **5** was preferred (a mixture of approximately equal amounts of compounds **3g**, **4g**, and **5g** was obtained with **2g**). At the same time, aminoheterocycles **2b**,**l**–**o** in *N*,*N*-dimethylformamide gave mainly chromanones **3** (Table 1). Reactions of heterocycles **2a**–**e** and 3,5-dimethoxyaniline (**2p**), performed in glacial acetic acid yielded preferably products **4** and **6**, which represent fused pyridines with a trifluoromethyl group located in the α- or γ-position. All products can be easily separated by column chromatography on silica gel. Thus, chromenone **1a** reacts with **2** giving four types of products, depending on the nature of the 1,3-C,N-dinucleo-

phile and the solvent. By correct choice of these parameters the trifluoromethyl-containing pyridines **4**–**6** could be selectively obtained in moderate to good yields. Arylamines **2p**–**v** react with **1a** almost exclusively as N-nucleophiles to give the corresponding chromanones **3p**–**v** in 64–98% isolated yields. This finding is consistent with data reported for similar compounds.[7]

Electron-rich aminoheterocycles **2a**–**o** can be considered as enamines with two nucleophilic centers and the initial nucleophilic attack can proceed either at the 2-position (1,4-addition) or at the trifluoroacetyl group (1,2-addition) of chromenone **1a**. One might expect that the selectivity between C- and N-attack on chromenone **1a** and, thus, the ratio between products depends on the difference of nucleophilicity between two centers; obtaining of compounds **3**–**6** can be rationalized by the reaction paths depicted in Scheme 2.

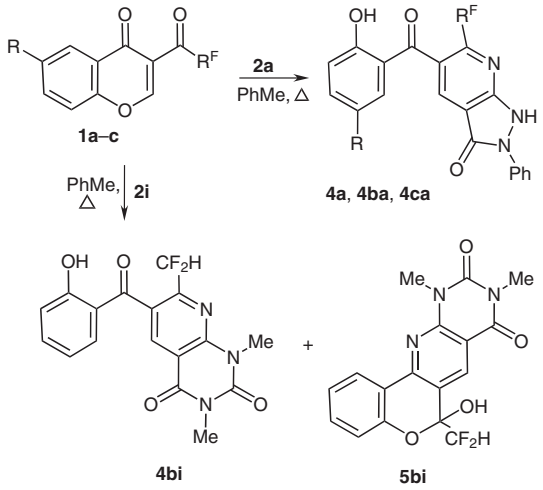


Scheme 2 Possible routes for the formation of **3**–**6**

The ambident character of enamine **2** means that nucleophilic attack of nitrogen or carbon on chromenone **1a** would lead to the production of intermediates **A** or **B**/**C**. Formation of **3** includes nucleophilic 1,4-addition of the amino group with concomitant opening of the pyrone ring and subsequent intramolecular cyclization of intermediate **A** with the participation of the phenolic hydroxy and trifluoroacetyl groups. The first step of the reaction leading to **4** and **5** in *N*,*N*-dimethylformamide consists apparently of attack at C2 of chromenone **1a** by the internal β-carbon of the enamine (in general, this atom is more nucleophilic than the primary amino group) with the pyrone ring opening (1,4-addition, intermediate **B**), and finally, the intramolecular attack at the trifluoroacetyl group or at the carbonyl of the 2-hydroxybenzoyl group by the amino group leads to pyridines **4** and **5**, respectively. In the case of **2e**–**h**, the attack of the amino group is mainly directed to the benzoyl carbonyl group, due to which the trifluoroacetyl group remains free and can participate in the formation of cyclic semiketal form **5**. The improved regioselectivity in acetic acid is probably due to the higher electrophilicity of the trifluoroacetyl carbonyl carbon atom, which is completely hydrated in *N*,*N*-dimethylformamide.

Note that for the initial attack of the trifluoroacetyl group by the internal carbon atom of enamine **2** (1,2-addition, intermediate **C**) the reaction through the ring-closure/ring-opening sequence would result in isomeric trifluoromethyl-substituted pyridines **6**. This direction was observed only in acetic acid medium where the trifluoroacetyl and 2,2,2-trifluoro-1,1-dihydroxymethyl groups are activated by protonation, while the amino group becomes less nucleophilic. In all of these reactions γ-(trifluoromethyl)pyridines **6** were formed in small quantities, while α-(trifluoromethyl)pyridines **4** dominated. It is worth mentioning that the alternative cyclization, leading to chromeno[4,3-*b*]pyridines **5** was not observed in this case.

It was also found that chromenones **1a**–**c** react with **2a** in refluxing toluene to give target products **4a**, **4ba**, and **4ca** in 73–92% yields. These compounds precipitate out of the reaction solution and analytically pure products can be isolated by simple filtration. In contrast, under the same conditions, reaction between **1b** and **2i** gave a 2:1 mixture of **4bi** and **5bi** (Scheme 3).

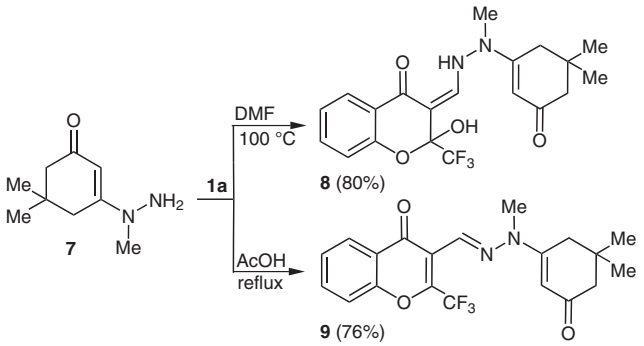


R^F = CF_3, R = H (**1a**); R^F = CF_2H, R = H (**1b**); R^F = CF_3, R = Cl (**1c**)

Scheme 3 Reaction of **1a**–**c** with **2a**,**i** in refluxing toluene

On the whole, the most important step determining the structure of a product is the addition to the first center of dinucleophile. From the enamine point of view, it clearly appears that the less aromatic heterocycles **2a**–**k** have a proclivity to form fused pyridines **4**–**6**, almost independently of the solvent. On the other hand, in aminoheterocycles **2l**–**o** and arylamines **2p**–**v** the high degree of aromatization of the ring would be responsible for their observed lack of reactivity. In terms of solvent, the trend

was that expected, namely in polar protic solvents like glacial acetic acid the nucleophilicity of the amino group is reduced and the C-attack onto **1** which leads to intermediates **B** and **C** is more favored.



Scheme 4 Reaction of chromenone **1a** with derivative **7**

Finally, the reaction of chromenone **1a** with 5,5-dimethyl-3-(1-methylhydrazino)cyclohex-2-en-1-one (**7**) in *N*,*N*-dimethylformamide at 100 °C led to chromanone **8**, while in refluxing acetic acid chromenone **9** was produced. This fact demonstrates the possibility of dehydration of 2-hydroxy-2-(trifluoromethyl)chromanone **8** under acidic conditions to give 2-(trifluoromethyl)chromenone **9**, a result which has never been achieved in *N*,*N*-dimethylformamide with chromanones **3** (Scheme 4).

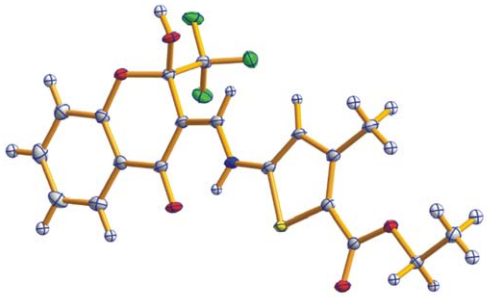


Figure 2 Molecular structure of compound **3n**

The structures of compounds **3**–**6** can be easily recognized by ^{1}H, ^{19}F, and ^{13}C NMR spectroscopy. A characteristic spectral feature of **3** is a chemical shift of the NH proton in the range of δ = 12–13 with coupling constant ^{3}J = 12–13 Hz on the olefinic proton, doublet of which was observed at δ = 7.6–8.6. In the ^{13}C NMR spectra the signal of the tetrahedral carbon atom adjacent to the polyfluoroalkyl substituent at ca. δ = 97–98 is a distinctive quartet ($^{2}J_{C,F}$ = 32–34 Hz). When R^F = CF_3, the ^{19}F NMR chemical shift of the CF_3 group was observed at δ = –84.8 to –87.0 while the ^{13}C NMR showed the CF_3 carbon as a quartet at δ = 118.7–124.8 ($^{1}J_{C,F}$ = 286–291 Hz).

Compounds **4** are aromatic heteroannulated pyridines and their spectral properties in many respects are similar to the purine isosteres we have synthesized previously.[4] Pyridines **4** were identified as α-(trifluoromethyl)-substituted isomers because their ^{13}C NMR spectra show a typical quartet (δ = 137–148, $^{2}J_{C,F}$ = 34–36 Hz) due to the *C*–CF_3; in the ^{19}F NMR spectra, the singlet of the CF_3 group appeared at δ = –62 to –64. In the ^{1}H NMR spectra, a single proton in the γ-position of the pyridine core situated at δ = 7.9–9.0, in the ^{13}C NMR spectra, the carbon in the same position appeared at δ ~ 134. In the ^{1}H NMR spectra, the chelated OH proton appeared at δ = 11–12 as a sharp singlet. In the ROESY spectrum for **4d**, the presence of the correlation between the methyl group in the 1-position, which was observed at δ = 3.78, and γ-pyridine proton (δ = 8.21) is another feature supporting the structure of type **4**.

Structures of type **5** represent systems with an annulated tricyclic core. Their ^{13}C NMR spectra resemble those of compounds **3**. The location of signals of fluorine-substituted carbon, as well as of carbon adjacent to the trifluoromethyl group and coupling constants $J_{C,F}$ are close to observed in the case of **3** due to the sp^3 hybridized carbon atom of the C–CF_3 assembly. However, the ^{1}H NMR spectra reveal the difference, the absence of the NH proton at low field. Moreover, the absence of the $[HOC_6H_4CO]^+$ and $[C_6H_4CO]^+$ fragments in mass spectra along with overall low amount of peaks confirms the tricyclic structure of their core.

A peculiarity which confirms the appearance of the structure γ-(trifluoromethyl)pyridine of **6**, is their characteristic shift of the signal for the carbon of the CF_3 group in the ^{13}C NMR spectra (δ = 129.4–131.7, $^{2}J_{C,F}$ = 35–36 Hz). At the same time, the signal of the CF_3 group is located at δ = –57 in the ^{19}F NMR spectra. This is another characteristic feature of the structure of type **6**.

Conclusive confirmation of the obtained products was obtained from X-ray single crystal analyses of **3n**, **4a**, and **5g** (Figures 2– 4).

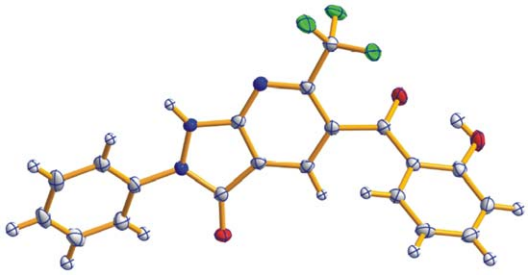


Figure 3 Molecular structure of compound **4a**

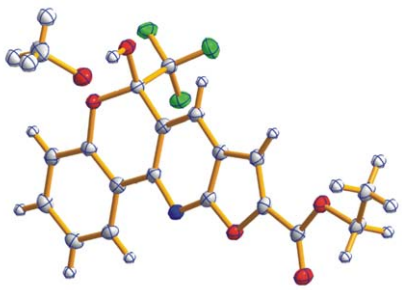


Figure 4 Molecular structure of compound **5g** as a solvate with methanol molecule

In conclusion, we have shown that it is possible to prepare a range of fluorinated heteroannulated pyridines in moderate to good yields by reaction of highly reactive 3-(polyfluoroacyl)-4*H*-chromen-4-ones with electron-rich aminoheterocycles as 1,3-C,N-dinucleophiles. Although four competitive routes were observed, the reaction pathways could be controlled with respect to prevailing fused pyridine derivatives.

All solvents were purified and dried by standard methods. NMR spectra were recorded on a Jeol JNM-LA 400, Varian VXR-300 or Varian Mercury-400, Bruker 600 spectrometer: ^{1}H and ^{13}C signals (300, 400 and 100 MHz, respectively) were recorded with TMS as an internal standard; ^{19}F (282.2 and 376.2 MHz) with $CFCl_3$ as internal standard. Mass spectra were obtained on a Hewlett-Packard HPGC/MS 5890/5972 instrument (EI, 70 eV) by GC inlet or on a MX-1321 instrument (EI, 70 eV) by direct inlet. Column chromatography was performed on silica gel (63–200 mesh, Merck). Silica gel Merck 60F_{254} plates were used for TLC. Satisfactory microanalysis obtained: C ± 0.33; H ± 0.25; N ± 0.25.

X-ray Crystallography of 3n, 4a, and 5g

Crystallographic measurements were performed at r.t. on a Enraf-Nonius CAD4 diffractometer operating in the ω-2θ scan mode (the scanning rate ratio ω/2θ = 1.2). The structure was solved by direct methods and refined by full-matrix least-squares technique in anisotropic approximation using SHELXS97 and SHELXL9722 program packages. Hydrogen atoms were placed at calculated position and refined as 'riding' model.[10]

Cyclization of 3-(Trifluoroacetyl)-4*H*-chromen-4-one (1a) with Aminoheterocycles 2; General Procedure

Into conical flask were placed the hydrate of **1a** (242 mg, 0.91 mmol), the corresponding dinucleophile (1 mmol), and the solvent [DMF or AcOH (10 mL)]. In the case of dinucleophile hydrochlorides, NaOAc (1 mmol) was added. The flask was equipped with a reflux condenser and was heated overnight if not reported otherwise. The solvent was removed in vacuo and the product was purified by flash chromatography (silica gel) or recrystallization. The yield refers to amount of isolated product.

(*Z*)-3-{[(1-Ethyl-1*H*-pyrazol-5-yl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3b)

Reaction conditions: DMF, 80 °C; yellow crystals; yield: 270 mg (85%); mp 153–155 °C; R_f = 0.51 (EtOAc).

^{1}H NMR (DMSO-d_6): δ = 1.37 (t, ^3J = 7.4 Hz, 3 H), 4.12 (q, ^3J = 7.4 Hz, 2 H), 6.33 (d, ^3J = 2.0 Hz, 1 H, H4′), 7.06 (d, ^3J = 7.8 Hz, 1 H), 7.15 (t, ^3J = 7.8 Hz, 1 H), 7.40 (d, ^3J = 2.0 Hz, 1 H, H3′), 7.56 (t, ^3J = 7.8 Hz, 1 H), 7.71 (d, ^3J = 12.1 Hz, 1 H, =CH), 7.86 (d, ^3J = 7.8 Hz, 1 H), 9.04 (s, 1 H, OH), 12.70 (d, ^3J = 12.1 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 14.2, 42.6, 94.1, 97.5 (q, $^2J_{C,F}$ = 33 Hz), 100.1, 109.8, 120.2 (q, $^1J_{C,F}$ = 286 Hz), 116.5, 119.6, 122.2, 125.6, 135.2, 138.1, 138.9, 149.2, 155.7, 180.4.

^{19}F NMR (DMSO-d_6): δ = –85.2.

MS: *m*/*z* (%) = 353 (51) $[M]^+$, 285 (21) $[M + 1 – CF_3]^+$, 284 (100) $[M – CF_3]^+$, 243 (27) $[M – C_5H_7N_3]^+$, 173 (39) $[C_{10}H_5O_3]^+$, 121 (41) $[HOC_6H_4CO]^+$, 111 (19) $[C_5H_9N_3]^+$, 83 (17).

1-*tert*-Butyl-5-({[2-hydroxy-4-oxo-2-(trifluoromethyl)chroman-3-ylidene]methyl}amino)-1*H*-pyrrole-3-carbonitrile (3f)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 81 mg (22%); mp 200–202 °C; R_f = 0.1 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 1.60 (s, 9 H), 7.05 (d, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.52 (t, ^3J = 7.8 Hz, 1 H), 7.55 (s, 1 H), 7.57 (d, ^3J = 7.8 Hz, 1 H), 7.67 (s, 1 H, H4), 7.82 (d, ^3J = 12.6 Hz, 1 H, = CH), 9.15 (s, 1 H, OH), 12.65 (d, ^3J = 12.6 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 29.5, 60.3, 72.3, 97.6 (q, $^2J_{C,F}$ = 33 Hz), 99.7, 103.3, 116.7, 119.6, 118.7 (q, $^1J_{C,F}$ = 289 Hz), 121.8, 125.9, 131.5, 135.5, 136.8, 138.2, 151.2, 155.9, 180.6.

^{19}F NMR (DMSO-d_6): δ = –85.4.

MS: *m*/*z* (%) = 406 (11) $[M + 1]^+$, 405 (44) $[M]^+$, 349 (11) $[M – CF_3]^+$, 281 (18) $[M – CF_3 – C_4H_9 + 1]^+$, 280 (100) $[M – CF_3 – C_4H_9]^+$, 242 (32) $[M – C_9H_{12}N_3]^+$, 173 (24) $[C_{10}H_5O_3]^+$, 121 (37) $[HOC_6H_4CO]^+$, 57 (56), 41 (19).

(*Z*)-3-{[(2,6-Diaminopyrimidin-4-yl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3j)

Reaction conditions: DMF, 100 °C, 24 h; orange crystals; yield: 105 mg (30%); mp 237–238 °C; R_f = 0.55 (EtOAc).

^{1}H NMR (DMSO-d_6): δ = 5.20 (s, 1 H, H5′), 6.35 (br s, 2 H), 6.95 (d, ^3J = 7.8 Hz, 1 H), 6.97 (t, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.55 (br s, 2 H), 7.81 (d, ^3J = 7.8 Hz, 1 H), 8.48 (d, ^3J = 12.9 Hz, 1 H, =CH), 8.60 (s, 1 H, OH), 11.80 (d, ^3J = 12.9 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 97.8 (q, $^2J_{C,F}$ = 33 Hz), 116.5, 119.3, 120.7 (q, $^1J_{C,F}$ = 288 Hz), 122.1, 125.7, 132.4, 134.4, 135.1, 136.4, 145.6, 155.7, 160.2, 164.4, 180.5.

^{19}F NMR (DMSO-d_6): δ = –85.2.

MS: *m*/*z* (%) = 367 (11) $[M]^+$, 298 (41) $[M – CF_3]^+$, 242 (49) $[M – 1 – C_4H_6N_5]^+$, 174 (27) $[C_{10}H_5O_3 + 1]^+$, 173 (100) $[C_{10}H_5O_3]^+$, 125 (89) $[C_4H_7N_5]^+$, 121 (80) $[HOC_6H_4CO]^+$, 92 (31) $[OC_6H_4]^+$.

3-{[(2,6-Dimethylpyrimidin-4-yl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3l)

Reaction conditions: DMF, 60 °C, 2 h; colorless solid; yield: 319 mg (96%); mp 195–197 °C; R_f = 0.37 (EtOAc).

^{1}H NMR (DMSO-d_6): δ = 2.38 (s, 3 H), 2.52 (s, 3 H), 7.08 (d, ^3J = 7.8 Hz, 1 H), 7.16 (s, 1 H, H5′), 7.16 (t, ^3J = 7.8 Hz, 1 H), 7.58 (t, ^3J = 7.8 Hz, 1 H), 7.85 (d, ^3J = 7.8 Hz, 1 H), 8.62 (d, ^3J = 12.0 Hz, 1 H, =CH), 9.18 (s, 1 H, OH), 12.07 (d, ^3J = 12.0 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 23.6, 25.6, 97.8 (q, $^2J_{C,F}$ = 33 Hz), 102.6, 105.1, 116.9, 119.7, 122.2, 122.7 (q, $^1J_{C,F}$ = 288 Hz), 126.0, 135.7, 142.8, 156.0, 156.8, 166.7, 168.1, 181.0.

^{19}F NMR (DMSO-d_6): δ = –84.8.

MS: *m*/*z* (%) = 365 (22) $[M]^+$, 297 (33) $[M – CF_3]^+$, 296 (100) $[M – CF_3]^+$, 176 (49), 173 (44) $[C_{10}H_5O_3]^+$, 123 (41) $[C_6H_9N_3]^+$, 121 (39) $[HOC_6H_4CO]^+$, 107 (29) $[C_6H_7N_2]^+$, 67 (18), 66 (23), 42 (24).

2-Hydroxy-3-{[(3-methyl-1*H*-pyrazol-5-yl)amino]methylene}-2-(trifluoromethyl)chroman-4-one (3m)

Reaction conditions: DMF, 60 °C; yellow solid; yield: 304 mg (99%); mp 200–203 °C; R_f = 0.57 (EtOAc).

^{1}H NMR ($CDCl_3$): δ = 2.26 (s, 3 H), 6.09 (s, 1 H, H4′), 7.07 (d, ^3J = 7.8 Hz, 1 H), 7.15 (t, ^3J = 7.8 Hz, 1 H), 7.55 (t, ^3J = 7.8 Hz, 1 H), 7.85 (d, ^3J = 7.8 Hz, 1 H), 8.07 (d, ^3J = 12.8 Hz, 1 H, =CH), 8.94 (s, 1 H, OH), 12.29 (s, 1 H, H1′), 12.36 (d, ^3J = 12.8 Hz, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 10.3, 93.1, 97.9 (q, $^2J_{C,F}$ = 33 Hz), 116.4, 116.5, 120.0, 122.2, 122.9 (q, $^1J_{C,F}$ = 288 Hz), 125.6, 134.9, 140.6, 147.1, 148.3, 155.7, 162.3, 179.6.

^{19}F NMR ($CDCl_3$): δ = –85.4.

MS: *m*/*z* (%) = 339 (64) $[M]^+$, 271 (40) $[M + 1 – CF_3]^+$, 270 (100) $[M – CF_3]^+$, 253 (30), 252 (70), 243 (26) $[M – C_4H_6N_3]^+$, 242 (22) $[M – 1 – C_4H_6N_3]^+$, 175 (24) $[C_{10}H_5O_3 + 2]^+$, 173 (87) $[C_{10}H_5O_3]^+$, 150 (74), 121 (76) $[HOC_6H_4CO]^+$, 108 (53), 97 (79) $[C_4H_7N_3]^+$, 94 (19), 65 (23), 53 (24).

Ethyl 5-({[2-Hydroxy-4-oxo-2-(trifluoromethyl)chroman-3-ylidene]methyl}amino)-3-methylthiophene-2-carboxylate (3n)
Reaction conditions: DMF, 60 °C, 2 h; colorless solid; yield: 366 mg (94%); mp 134–137 °C; R_f = 0.85 (PE–Et_2O, 1:1).

^{1}H NMR ($CDCl_3$): δ = 1.29 (t, ^3J = 7.1 Hz, 3 H), 2.41 (s, 3 H), 4.23 (q, ^3J = 7.1 Hz, 2 H), 6.38 (s, 1 H, H4′), 6.86 (d, ^3J = 7.8 Hz, 1 H), 7.02 (t, ^3J = 7.8 Hz, 1 H), 7.36 (t, ^3J = 7.8 Hz, 1 H), 7.56 (d, ^4J = 12.1 Hz, 1 H, =CH), 7.81 (d, ^3J = 7.8 Hz, 1 H), 12.84 (d, ^3J = 12.1 Hz, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 14.2, 16.1, 61.0, 97.3 (q, $^2J_{C,F}$ = 34 Hz), 100.6, 116.8, 117.5, 118.2, 119.8, 122.3 (q, $^1J_{C,F}$ = 290 Hz), 122.8, 126.2, 135.5, 147.0, 147.1, 147.3, 155.9, 162.7, 181.7.

^{19}F NMR ($CDCl_3$): δ = –87.0.

MS, *m*/*z* (%) = 427 (72) $[M]^+$, 358 (100) $[M – CF_3]^+$, 330 (21), 243 (35) $[M – 1 – C_8H_{10}NO_2S]^+$, 185 (38) $[C_8H_{10}NO_2S + 1]$, 173 (51) $[C_{10}H_5O_3]^+$, 121 (58) $[HOC_6H_4CO]^+$.

2-Hydroxy-3-{[(4-methoxypyridin-2-yl)amino]methylene}-2-(trifluoromethyl)chroman-4-one (3o)
Reaction conditions: DMF, 100 °C; yellow solid; yield: 253 mg (76%); mp 159–160 °C (*i*-PrOH).

^{1}H NMR (DMSO-d_6): δ = 3.85 (s, 3 H), 6.73 (d, ^3J = 5.8 Hz, 1 H, H5′), 7.04 (d, ^3J = 7.8 Hz, 1 H), 7.07 (s, 1 H, H2′), 7.12 (t, ^3J = 7.8 Hz, 1 H), 7.52 (t, ^3J = 7.8 Hz, 1 H), 7.80 (d, ^3J = 7.8 Hz, 1 H), 8.14 (d, ^3J = 5.8 Hz, 1 H, H6′), 8.62 (d, ^3J = 12.2 Hz, 1 H, =CH), 9.11 (s, 1 H, OH), 12.21 (d, ^3J = 12.2 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 55.6, 97.8, 98.9 (q, $^2J_{C,F}$ = 33 Hz), 103.7, 107.5, 117.0, 122.3 (q, $^1J_{C,F}$ = 289 Hz), 122.4, 124.1, 125.8, 135.3, 144.5, 149.2, 155.8, 163.7, 164.4, 180.1.

^{19}F NMR (DMSO-d_6): δ = –85.1.

MS: *m*/*z* (%) = 366 (22) $[M]^+$, 298 (20) $[M + 1 – CF_3]^+$, 297 (100) $[M – CF_3]^+$, 177 (36), 173 (34) $[C_{10}H_5O_3]^+$, 124 (29), 121 (16) $[HOC_6H_4CO]^+$, 108 (25).

3-{[(3,5-Dimethoxyphenyl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3p)
Reaction conditions: DMF, 60 °C; colorless solid; yield: 338 mg (94%); mp 131–133 °C; R_f = 0.55 (CH_2Cl_2–MeOH, 20:1).

^{1}H NMR (DMSO-d_6): δ = 3.77 (s, 6 H), 6.33 (s, 1 H, H4′), 6.59 (s, 2 H, H2′, H6′), 7.06 (d, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.54 (t, ^3J = 7.8 Hz, 1 H), 7.81(d, ^3J = 7.8 Hz, 1 H), 7.95 (d, ^3J = 12.9 Hz, 1 H, =CH), 9.12 (s, 1 H, OH), 12.47 (d, ^3J = 12.9 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 55.5 (2 C), 95.9 (2 C), 97.1, 98.0 (q, $^2J_{C,F}$ = 33 Hz), 99.0, 116.5, 120.0, 122.3, 122.8 (q, $^1J_{C,F}$ = 288 Hz), 125.7, 135.1, 141.1, 147.2, 155.8, 161.5 (2 C), 180.0.

^{19}F NMR (DMSO-d_6): δ = –85.2.

MS: *m*/*z* (%) = 395 (17) $[M]^+$, 326 (41) $[M – CF_3]^+$, 242 (22) $[M – C_8H_{11}NO_2]^+$, 173 (35) $[C_{10}H_5O_3]^+$, 152 (100) $[C_8H_{10}NO_2]^+$, 124 (42) $[C_6H_9N_3 + 1]^+$, 120 (71) $[HOC_6H_4CO]^+$, 94 (12), 93 (26) $[C_6H_4CO]^+$, 53 (29).

3-({[3-(Dimethylamino)phenyl]amino}methylene)-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3q)
Reaction conditions: DMF, 80 °C, 4 h; colorless solid; yield: 219 mg (64%); mp 167–168 °C (*i*-PrOH).

^{1}H NMR (DMSO-d_6): δ = 2.93 (s, 6 H), 6.50 (d, ^3J = 8.2 Hz, 1 H, H5′), 6.63 (d, ^3J = 8.2 Hz, 1 H, H4′), 6.68 (s, 1 H, H2′), 7.05 (d, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.21 (t, ^3J = 8.2 Hz, 1 H, H5′), 7.52 (t, ^3J = 7.8 Hz, 1 H), 7.81 (d, ^3J = 7.8 Hz, 1 H), 7.97 (d, ^3J = 12.7 Hz, 1 H, =CH), 9.07 (s, 1 H, OH), 12.50 (d, ^3J = 12.7 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 40.0 (2 C), 98.0 (q, $^2J_{C,F}$ = 33 Hz), 98.4, 101.6, 104.2, 109.3, 116.5, 120.1, 122.3, 122.9 (q, $^1J_{C,F}$ = 291 Hz), 125.7, 130.4, 135.0, 140.0, 151.5, 147.4, 155.8, 179.6.

^{19}F NMR (DMSO-d_6): δ = –85.3.

MS: *m*/*z* (%) = 379 (25) $[M + 1]^+$, 378 (81) $[M]^+$, 310 (24) $[M + 1 – CF_3]^+$, 309 (100) $[M – CF_3]^+$, 243 (16) $[M – C_8H_{11}N_2]^+$, 189 (19), 173 (34) $[C_{10}H_5O_3]^+$, 136 (58) $[C_8H_{12}N_2]^+$, 135 (20) $[C_8H_{11}N_2]^+$, 121 (36) $[HOC_6H_4CO]^+$.

3-{[(1,3-Benzodioxol-5-yl)amino]methylene)-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3r)
Reaction conditions: DMF, 60 °C; colorless solid; yield: 338 mg (98%); mp 150–152 °C; R_f = 0.37 (PE–EtOAc, 2:1).

^{1}H NMR (DMSO-d_6): δ = 6.05 (s, 2 H, H2′), 6.83 (d, ^3J = 8.4 Hz, 1 H, H6′), 6.94 (d, ^3J = 8.4 Hz, 1 H, H7′), 7.04 (d, ^3J = 7.8 Hz, 1 H), 7.12 (d, ^3J = 7.8 Hz, 1 H), 7.16 (s, 1 H, H4′), 7.52 (t, ^3J = 7.8 Hz, 1 H), 7.80 (d, ^3J = 7.8 Hz, 1 H), 7.87 (d, ^3J = 12.6 Hz, 1 H, =CH), 9.01 (s, 1 H, OH), 12.54 (d, ^3J = 12.6 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 97.9 (q, $^3J_{C,F}$ = 33 Hz), 98.3, 99.7, 101.6, 108.8, 110.8, 116.4, 120.0, 122.2, 123.5 (q, $^1J_{C,F}$ = 289 Hz), 125.6, 134.0, 134.8, 144.8, 147.7, 148.4, 155.7, 173.3.

^{19}F NMR (DMSO-d_6): δ = –85.3.

MS: *m*/*z* (%) = 379 (63) $[M]^+$, 311 (26) $[M + 1 – CF_3]^+$, 310 (100) $[M – CF_3]^+$, 243 (15) $[M – C_7H_6NO_2]^+$, 190 (28) $[C_7H_5O_2 + CF_3]^+$, 173 (31) $[C_{10}H_5O_3]^+$, 155 (22), 137 (50) $[C_7H_7NO_2]^+$, 121 (53) $[HOC_6H_4CO]^+$.

3-{[(2,3-Dihydro-1,4-benzodioxin-6-yl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3s)
Reaction conditions: DMF, 100 °C, 24 h; colorless solid; yield: 351 mg (98%); mp 146 °C; R_f = 0.57 (EtOAc).

^{1}H NMR ($CDCl_3$): δ = 4.26 (d, ^3J = 8.6 Hz, 4 H), 4.45 (br s, 1 H, OH), 6.60 (d, ^3J = 8.3 Hz, 1 H, H7′), 6.63 (s, 1 H, H5′), 6.83 (d, ^3J = 8.3 Hz, 1 H, H8′), 6.89 (d, ^3J = 7.8 Hz, 1 H), 7.06 (t, ^3J = 7.8 Hz, 1 H), 7.36 (t, ^3J = 7.8 Hz, 1 H), 7.78 (d, ^3J = 12.4 Hz, 1 H, =CH), 7.89 (d, ^3J = 7.8 Hz, 1 H), 12.70 (d, ^3J = 12.4 Hz, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 64.3, 64.5, 97.7 (q, $^2J_{C,F}$ = 33 Hz), 98.1, 106.3, 110.9, 116.5, 118.2, 120.2, 122.5, 122.5 (q, $^1J_{C,F}$ = 289 Hz), 126.0, 133.0, 134.5, 141.5, 144.3, 147.6, 155.3, 180.4.

^{19}F NMR ($CDCl_3$): δ = –86.7.

MS: *m*/*z* (%) = 393 (51) $[M]^+$, 325 (21) $[M + 1 – CF_3]^+$, 324 (100) $[M – CF_3]^+$, 173 (12) $[C_{10}H_5O_3]^+$, 121 (20) $[HOC_6H_4CO]^+$, 95 (12), 69 (20).

(*Z*)-3-{[(5-Chloro-2-hydroxyphenyl)amino]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (3t)
Reaction conditions: DMF, 60 °C; pale yellow solid; yield: 294 mg (84%); mp 193 °C; R_f = 0.09 (PE–EtOAc, 2:1).

^{1}H NMR (DMSO-d_6): δ = 6.91 (d, ^3J = 8.4 Hz, 1 H, H3′), 7.02 (d, ^3J = 8.4 Hz, 1 H, H4′), 7.05 (d, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.53, (t, ^3J = 7.8 Hz, 1 H), 7.63 (s, 1 H), 7.82 (d, ^3J = 7.8 Hz, 1 H), 8.11 (d, ^3J = 13.2 Hz, 1 H, =CH), 9.02 (s, 1 H, OH), 10.69 (s, ArOH, 1 H), 12.69 (d, ^3J = 13.2 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 98.0 (q, $^2J_{C,F}$ = 32 Hz), 99.7, 114.2, 116.5, 116.8, 120.0, 122.2, 122.8 (q, $^1J_{C,F}$ = 289 Hz), 123.7, 124.5, 125.7, 128.4, 135.0, 145.4, 146.0, 155.8, 179.9.

^{19}F NMR (DMSO-d_6): δ = –85.1.

MS: *m*/*z* (%) = 385 (22) $[M]^+$, 349 (27), 347 (72), 318 (34), 316 (88) $[M – CF_3]^+$, 300 (21), 298 (46), 243 (24), 242 (25), 196 (15) $[HOC_6H_3Cl + CF_3]^+$, 173 (97) $[C_{10}H_5O_3]^+$, 154 (24), 145 (32), 143 (85) $[ClC_6H_3(NH_2)OH]^+$, 121 (100) $[HOC_6H_4CO]^+$, 80 (21).

(*Z*)-2-Hydroxy-3-{[(2-hydroxy-5-nitrophenyl)amino]methylene}-2-(trifluoromethyl)chroman-4-one (3u)

Reaction conditions: DMF, 60 °C; yellow solid; yield: 295 mg (82%); mp 221–223 °C (*i*-PrOH–H_2O).

^{1}H NMR (DMSO-d_6): δ = 7.06 (d, ^3J = 7.2 Hz, 1 H), 7.11 (d, ^3J = 8.4 Hz, 1 H, H3′), 7.13 (t, ^3J = 7.2 Hz, 1 H), 7.54 (t, ^3J = 7.2 Hz, 1 H), 7.84 (d, ^3J = 7.2 Hz, 1 H), 7.95 (d, ^3J = 8.4 Hz, 1 H, H4′), 8.22 (d, ^3J = 12.6 Hz, 1 H, =CH), 8.33 (s, 1 H, H6′), 9.12 (s, 1 H, OH), 12.10 (s, 1 H, ArOH), 12.68 (d, ^3J = 12.6 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 98.2 (q, $^2J_{C,F}$ = 33 Hz), 100.4, 110.7, 115.2, 116.6, 120.0, 121.2, 122.3, 124.8 (q, $^1J_{C,F}$ = 289 Hz), 125.8, 127.8, 135.3, 140.2, 146.1, 152.9, 155.9, 180.4.

^{19}F NMR (DMSO-d_6): δ = –85.0.

MS: *m*/*z* (%) = 396 (9) $[M]^+$, 358 (47), 327 (54) $[M – CF_3]^+$, 243 (24) $[M – C_6H_5N_2O_3]^+$, 242 (23) $[M – C_6H_5N_2O_3 – 1]^+$, 173 (100) $[C_{10}H_5O_3]^+$, 154 (39) $[C_6H_6N_2O_3]^+$, 121 (86) $[HOC_6H_4CO]^+$, 80.0 (19).

2-({[2-Hydroxy-4-oxo-2-(trifluoromethyl)chroman-3-ylidene]methyl}amino)benzamide (3v)

Reaction conditions: DMF, 60 °C; colorless solid; yield: 279 mg (82%); mp 204–205 °C (MeOH–H_2O).

^{1}H NMR (DMSO-d_6): δ = 7.05 (d, ^3J = 7.8 Hz, 1 H), 7.13 (t, ^3J = 7.8 Hz, 1 H), 7.22 (t, ^3J = 7.8 Hz, 1 H), 7.52 (t, ^3J = 7.8 Hz, 2 H), 7.58 (t, ^3J = 7.8 Hz, 1 H), 7.63 (s, 1 H), 7.75 (d, ^3J = 7.8 Hz, 1 H), 7.82 (d, ^3J = 7.8 Hz, 1 H), 7.90 (d, ^3J = 13.2 Hz, 1 H, =CH), 8.17 (s, 1 H), 9.09 (s, 1 H, OH), 13.50 (d, ^3J = 13.2 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 98.1 (q, $^2J_{C,F}$ = 33 Hz), 100.2, 114.3, 116.0, 116.5, 122.2, 122.6, 122.9 (q, $^1J_{C,F}$ = 288 Hz), 123.7, 125.8, 129.1, 132.6, 135.0, 139.5, 145.3, 155.8, 169.8, 179.1.

^{19}F NMR (DMSO-d_6): δ = –85.0.

MS: *m*/*z* (%) = 378 (19) $[M]^+$, 309 (57) $[M – CF_3]^+$, 243 (15) $[M – C_7H_7N_2O]^+$, 242 (26), 173 (100) $[C_{10}H_5O_3]^+$, 172 (88) $[C_{10}H_4O_3]^+$, 136 (98) $[C_7H_8N_2O]^+$, 121 (92) $[HOC_6H_4CO]^+$, 120 (43) $[C_7H_6NO]^+$, 119 (77) $[C_7H_5NO]^+$, 92 (46), 65 (27).

2-Phenyl-5-salicyloyl-6-(trifluoromethyl)-1,2-dihydro-3*H*-pyrazolo[3,4-*b*]pyridin-3-one (4a)

Reaction conditions: DMF, 100 °C, 24 h; colorless solid; yield: 352 mg (97%); mp 188 °C; R_f = 0.35 (PE–EtOAc, 1:1).

^{1}H NMR ($CDCl_3$): δ = 6.86 (t, ^3J = 7.8 Hz, 1 H), 7.13 (d, ^3J = 7.8 Hz, 2 H), 7.28 (t, ^3J = 7.8 Hz, 1 H), 7.45 (t, ^3J = 7.8 Hz, 2 H), 7.58 (t, ^3J = 7.8 Hz, 1 H), 7.80 (d, ^3J = 7.8 Hz, 2 H), 8.23 (s, 1 H, H4), 9.09 (br s, 1 H), 11.67 (s, 1 H).

^{1}H NMR (DMSO-d_6): δ = 6.97 (td, *J* = 7.8, 1.1 Hz, 1 H), 7.00 (d, *J* = 8.4 Hz, 1 H), 7.34 (tt, *J* = 7.4, 1.0 Hz, 1 H), 7.53–7.61 (m, 4 H), 7.89–7.93 (m, 2 H), 8.46 (s, 1 H, H4), 10.88 (s, 1 H, OH), 11.7–13.5 (br s, 1 H, NH).

^{13}C NMR ($CDCl_3$): δ = 113.1, 118.8, 119.2, 119.4, 120.4, 123.4 (q, $^1J_{C,F}$ = 279 Hz), 127.7, 129.6, 132.9, 135.3, 135.8, 138.0, 146.7, 148.2 (q, $^2J_{C,F}$ = 35 Hz), 155.6, 157.2, 163.4, 197.6.

^{19}F NMR ($CDCl_3$): δ = –63.6.

MS: *m*/*z* (%) = 400 (17) $[M + 1]^+$, 399 (70) $[M]^+$, 331 (22) $[M + 1 – CF_3]^+$, 330 (100) $[M – CF_3]^+$, 279 (25), 122 (29), 121 (94) $[HOC_6H_4CO]^+$, 93 (22) $[HOC_6H_4]^+$, 77 (44), 65 (24).

1-Ethyl-5-salicyloyl-6-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridine (4b)

Reaction conditions: AcOH, reflux; colorless solid; yield: 187 mg (60%); mp 137–139 °C; R_f = 0.23 (PE–Et_2O, 2:1).

^{1}H NMR ($CDCl_3$): δ = 1.62 (t, ^3J = 7.0 Hz, 3 H), 4.70 (q, ^3J = 7.0 Hz, 2 H), 6.83 (t, ^3J = 7.8 Hz, 1 H), 7.10 (d, ^3J = 7.8 Hz, 1 H), 7.19 (d, ^3J = 7.8 Hz, 1 H), 7.55 (t, ^3J = 7.8 Hz, 1 H), 8.16 (s, 1 H, H3), 8.19 (s, 1 H, H4), 11.83 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 14.9, 42.8, 115.3, 118.6, 119.1, 119.7, 121.0 (q, $^1J_{C,F}$ = 275 Hz), 125.4, 131.3, 132.6, 133.3, 137.5, 143.5 (q, $^2J_{C,F}$ = 36 Hz), 148.1, 163.3, 199.4.

^{19}F NMR ($CDCl_3$): δ = –61.5.

MS: *m*/*z* (%): 335 (38) $[M]^+$, 267 (20) $[M + 1 – CF_3]^+$, 266 (85) $[M – CF_3]^+$, 242 (14) $[M – HOC_6H_4]^+$, 121 (78) $[HOC_6H_4CO]^+$, 120 (100) $[OC_6H_4CO]^+$, 93 (26) $[HOC_6H_4]^+$, 92 (21) $[OC_6H_4]$, 65 (31).

2-(Diethylamino)-6-salicyloyl-5-(trifluoromethyl)thiazolo[4,5-*b*]pyridine (4c)

Reaction conditions: AcOH, reflux; colorless solid; yield: 338 mg (94%); mp 150–151 °C; R_f = 0.42 (EtOAc).

^{1}H NMR ($CDCl_3$): δ = 1.35 (t, ^3J = 7.1 Hz, 6 H), 3.69 (br s, 4 H), 6.83 (t, ^3J = 8.0 Hz, 1 H), 7.07 (d, ^3J = 8.0 Hz, 1 H), 7.21 (d, ^3J = 8.0 Hz, 1 H), 7.53 (t, ^3J = 8.0 Hz, 1 H), 7.86 (s, 1 H, H7), 11.81 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 12.7 (2 C), 46.1 (2 C), 116.1, 118.4, 119.2, 119.9, 121.4 (q, $^1J_{C,F}$ = 277 Hz), 128.4, 131.1, 133.2, 137.4, 141.9 (q, $^2J_{C,F}$ = 35 Hz), 162.8, 165.0, 170.6, 199.4.

^{19}F NMR ($CDCl_3$): δ = –63.7.

MS: *m*/*z* (%) = 395 (54) $[M]^+$, 366 (24) $[M – Et]^+$, 352 (16) $[M + 1 – Et – Me]^+$, 327 (20) $[M + 1 – CF_3]^+$ (21), 326.0 (80) $[M – CF_3]^+$, 298 (19) $[M + 1 – CF_3 – Et]^+$, 246 (24), 232 (25), 205 (15), 146 (100) $[M – 2\,Et – CF_3 – HOC_6H_4CO]^+$, 121 (29) $[HOC_6H_4CO]^+$, 120 (23) $[OC_6H_4CO]^+$, 118 (49), 97 (19), 93 (17) $[HOC_6H_4]^+$, 92 (80) $[OC_6H_4]^+$.

1-Methyl-3-phenyl-6-salicyloyl-5-(trifluoromethyl)-1,3-dihydro-2*H*-imidazo[4,5-*b*]pyridine-2-thione (4d)

Reaction conditions: AcOH, reflux; colorless solid; yield: 180 mg (46%); mp 170–173 °C (EtOH).

^{1}H NMR (DMSO-d_6): δ = 3.78 (s, 3 H, Me), 6.95 (t, ^3J = 7.5 Hz, 1 H), 7.02 (d, ^3J = 8.0 Hz, 1 H), 7.50–7.67 (m, 7 H), 8.21 (s, 1 H, H7), 11.03 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 30.9, 115.6, 117.8, 119.4, 121.1, 122.1 (q, $^1J_{C,F}$ = 272 Hz), 128.2, 128.4, 129.2, 130.9, 132.5, 134.0, 135.0 (q, $^2J_{C,F}$ = 34 Hz), 137.1, 144.9, 160.1, 173.8, 195.7.

3-Neopentyl-5-salicyloyl-6-(trifluoromethyl)isoxazolo[5,4-*b*]pyridine (4e)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 115 mg (33%); mp 141–142 °C; R_f = 0.81 (CH_2Cl_2).

^{1}H NMR ($CDCl_3$): δ = 1.06 (s, 9 H), 2.91 (s, 2 H), 6.85 (t, ^3J = 8.2 Hz, 1 H), 7.05 (d, ^3J = 8.2 Hz, 1 H), 7.12 (d, ^3J = 7.8 Hz, 1 H), 7.58 (t, ^3J = 7.8 Hz, 1 H), 8.12 (s, 1 H, H4), 11.64 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 29.7, 32.0, 39.4, 112.5, 116.2, 118.9, 119.4, 120.7 (q, $^1J_{C,F}$ = 275 Hz), 128.9, 132.8, 133.2, 138.0, 145.4 (q, $^2J_{C,F}$ = 34 Hz), 157.7, 163.4, 168.0, 197.8.

^{19}F NMR ($CDCl_3$): δ = –63.0.

MS: *m*/*z* (%) = 379 (24) $[M + 1]^+$, 378 (89) $[M]^+$, 363 (53) $[M – CH_3]^+$, 322 (43) $[M – C_4H_9 + 1]^+$, 310 (30) $[M – CF_3 + 1]^+$, 309 (100) $[M – CF_3]^+$, 253 (27) $[M – CF_3 – C_4H_9]^+$, 239 (32) $[M – CF_3 – C_5H_{11} + 1]^+$, 121 (61) $[HOC_6H_4CO]^+$, 120 (34) $[OC_6H_4CO]^+$, 65 (15), 57 (98) $[C_4H_9]^+$, 55 (20), 43 (38), 41 (43).

1-*tert*-Butyl-5-salicyloyl-6-(trifluoromethyl)-1*H*-pyrrolo[2,3-*b*]pyridine-3-carbonitrile (4f)

Reaction conditions: DMF, 100 °C, 32 h; colorless solid; yield: 75 mg (21%); mp 207 °C; R_f = 0.68 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 1.81 (9 H), 6.94 (t, ^3J = 7.8 Hz, 1 H), 6.98 (d, ^3J = 7.8 Hz, 1 H), 7.51 (d, ^3J = 7.8 Hz, 1 H), 7.57 (t, ^3J = 7.8 Hz, 1 H), 8.43 (s, 1 H, H2), 9.05 (s, 1 H, H4), 10.90 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 28.3, 59.5, 83.0, 114.4, 117.6, 119.4, 121.6 (q, $^1J_{C,F}$ = 273 Hz), 121.7, 122.0, 128.2, 129.0, 132.5, 136.6 (q, $^2J_{C,F}$ = 34 Hz), 136.7, 144.9, 160.2, 196.0.

^{19}F NMR (DMSO-d_6): δ = –61.3.

MS: *m*/*z* (%) = 387 (30) $[M]^+$, 318 (29) $[M – CF_3]^+$, 262 (100) $[M + 1 – CF_3 – C_4H_9]^+$, 121 (21) $[HOC_6H_4CO]^+$, 69 (16), 57 (39).

Ethyl 5-Salicyloyl-6-(trifluoromethyl)furo[2,3-*b*]pyridine-2-carboxylate (4g)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 86 mg (25%); mp 149–150 °C; R_f = 0.57 (toluene–Et_2O, 5:1).

^{1}H NMR ($CDCl_3$): δ = 1.46 (t, ^3J = 7.1 Hz, 3 H), 4.50 (q, ^3J = 7.1 Hz, 2 H), 6.84 (t, ^3J = 7.8 Hz, 1 H), 7.10 (d, ^3J = 7.8 Hz, 2 H), 7.57 (t, ^3J = 7.8 Hz, 1 H), 7.62 (s, 1 H, H3), 8.16 (s, 1 H, H4), 11.69 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 14.1, 62.5, 111.7, 118.8, 119.4, 119.4, 121.0 (q, $^1J_{C,F}$ = 275 Hz), 121.4, 129.8, 132.7, 133.1, 138.0, 142.3 (q, $^2J_{C,F}$ = 35 Hz), 149.3, 158.2, 160.3, 163.4, 198.4.

^{19}F NMR ($CDCl_3$): δ = –62.7.

MS: *m*/*z* (%) = 379 (22) $[M]^+$, 311 (19) $[M + 1 – CF_3]^+$, 310 (100) $[M – CF_3]^+$, 282 (31) $[M + 1 – CF_3 – Et]^+$, 121 (91) $[HOC_6H_4CO]^+$, 120 (17) $[OC_6H_4CO]^+$, 93 (23) $[HOC_6H_4]^+$, 65 (32).

1,3-Dimethyl-6-salicyloyl-7-(trifluoromethyl)pyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4i)

Reaction conditions: DMF, 80 °C, 30 h; colorless solid; yield: 276 mg (74%); mp 254–256 °C (AcOH).

^{1}H NMR ($CDCl_3$): δ = 3.53 (s, 3 H), 3.80 (s, 3 H), 6.85 (t, ^3J = 7.4 Hz, 1 H), 7.10 (d, ^3J = 7.4 Hz, 1 H), 7.11 (d, ^3J = 7.4 Hz, 1 H), 7.58 (t, ^3J = 7.4 Hz, 1 H), 8.55 (s, 1 H, H5), 11.62 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 28.9, 30.0, 111.8, 118.9, 119.1, 119.5, 120.3 (q, $^1J_{C,F}$ = 276 Hz), 127.4, 132.7, 138.4, 139.2, 148.3 (q, $^2J_{C,F}$ = 35 Hz), 150.8, 150.8, 159.7, 163.4, 197.1.

^{19}F NMR ($CDCl_3$): δ = –64.2.

MS: *m*/*z* (%) = 379 (28) $[M]^+$, 311 (30) $[M + 1 – CF_3]^+$, 310 (100) $[M – CF_3]^+$, 121 (51) $[HOC_6H_4CO]^+$, 120 (43), 93 (14) $[HOC_6H_4]^+$, 65 (14).

6-Salicyloyl-7-(trifluoromethyl)pyrido[2,3-*d*]pyrimidine-2,4-diamine (4j)

Reaction conditions: DMF, 100 °C, 24 h; colorless solid; yield: 187 mg (59%); mp 278 °C; R_f = 0.64 (EtOAc).

^{1}H NMR (DMSO-d_6): δ = 6.84 (br s, 2 H), 6.95 (t, ^3J = 7.7 Hz, 1 H), 6.98 (d, ^3J = 7.7 Hz, 1 H), 7.53–7.58 (m, 2 H), 7.92 (br s, 2 H), 8.59 (s, 1 H, H5), 10.92 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 105.7, 117.8, 119.7, 121.1 (q, $^1J_{C,F}$ = 278 Hz), 121.9, 125.8, 132.6, 134.8, 136.7, 147.6 (q, $^2J_{C,F}$ = 34 Hz), 160.7, 162.6, 163.1, 164.6, 195.8.

^{19}F NMR (DMSO-d_6): δ = –63.4.

MS: *m*/*z* (%) = 350 (17) $[M + 1]^+$, 349 (89) $[M]^+$, 280 (50) $[M – CF_3]^+$, 256 (14) $[M – HOC_6H_4]^+$, 230 (12), 229 (100), 121 (39) $[HOC_6H_4CO]^+$, 120 (30) $[OC_6H_4CO]^+$, 93 (15) $[HOC_6H_4]^+$, 65 (20).

2-Methyl-7-salicyloyl-6-(trifluoromethyl)pyrazolo[1,5-*a*]pyrido[2,3-*d*]pyrimidin-9(4*H*)-one (4k)

Reaction conditions: DMF, 80 °C, 24 h; yield: 227 mg (64%); mp >300 °C (MeOH).

^{1}H NMR (DMSO-d_6): δ = 2.33 (s, 3 H), 6.04 (s, 1 H, H3), 6.99 (m, 2 H), 7.57 (m, 2 H), 8.64 (s, 1 H, H8), 10.79 (s, 1 H, OH), 13.42 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 14.3, 89.9, 109.5, 117.8, 119.7, 120.9 (q, $^1J_{C,F}$ = 286 Hz), 122.3, 128.1, 132.2, 136.7, 139.7, 142.3, 146.7 (q, $^2J_{C,F}$ = 35 Hz), 149.4, 154.2, 155.8, 159.8, 194.2.

^{19}F NMR (DMSO-d_6): δ = –63.2.

MS: *m*/*z* (%) = 389 (12) $[M + 1]^+$, 388 (54) $[M]^+$, 320 (23) $[M + 1 – CF_3]^+$, 319 (100) $[M – CF_3]^+$, 268 (20) $[M – 1 – HOC_6H_4CO]^+$, 121 (74) $[HOC_6H_4CO]^+$, 93 (17) $[HOC_6H_4]^+$, 65 (18).

5,7-Dimethoxy-3-salicyloyl-2-(trifluoromethyl)quinoline (4p)

Reaction conditions: AcOH, reflux, 84 h; colorless solid; yield: 167 mg (48%); mp 141–143 °C; R_f = 0.67 (Et_2O).

^{1}H NMR ($CDCl_3$): δ = 3.94 (s, 3 H), 3.97 (s, 3 H), 6.88 (s, 1 H, H4′), 6.95 (m, ^3J = 7.8 Hz, 2 H), 7.21 (s, 1 H), 7.55 (m, ^3J = 7.8 Hz, 2 H), 8.46 (s, 1 H, H4), 10.78 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 56.5, 56.8, 100.2, 101.6, 115.9, 118.0, 119.8, 121.7 (q, $^1J_{C,F}$ = 275 Hz), 123.1, 128.9, 132.1, 132.4, 136.7, 144.0 (q, $^2J_{C,F}$ = 34 Hz), 148.0, 156.0, 160.0, 163.9, 195.7.

^{19}F NMR ($CDCl_3$): δ = –61.6.

MS: *m*/*z* (%) = 378 (12) $[M + 1]^+$, 377 (58) $[M]^+$, 308 (35) $[M – CF_3]^+$, 257 (15) $[M + 1 – HOC_6H_4CO]^+$, 256 (100) $[M – HOC_6H_4CO]^+$, 121 (53) $[HOC_6H_4CO]^+$, 93 (15) $[HOC_6H_4]^+$, 65 (14).

2-Methyl-5-salicyloyl-6-(trifluoromethyl)pyridine-3-carbonitrile (4w)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 95 mg (34%); mp 139 °C; R_f = 0.77 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 2.80 (s, 3 H), 6.94 (d, ^3J = 7.8 Hz, 1 H), 6.97 (t, ^3J = 7.8 Hz, 1 H), 7.56 (t, ^3J = 7.8 Hz, 1 H), 7.65 (d, ^3J = 7.8 Hz, 1 H), 8.65 (s, 1 H, H4), 10.71 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 22.5, 111.8, 115.5, 117.7, 119.6, 120.7 (q, $^1J_{C,F}$ = 275 Hz), 121.5, 131.5, 134.1, 137.0, 141.2, 143.6 (q, $^2J_{C,F}$ = 34 Hz), 159.7, 161.6, 192.0.

^{19}F NMR (DMSO-d_6): δ = –63.7.

MS: *m*/*z* (%) = 306 (25) $[M]^+$, 237 (100) $[M – CF_3]^+$, 121 (99) $[HOC_6H_4CO]^+$, 93 (22) $[HOC_6H_4]^+$, 65 (27).

8-Neopentyl-6-(trifluoromethyl)-6*H*-chromeno[4,3-*b*]isoxazolo[4,5-*e*]pyridin-6-ol (5e)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 220 mg (64%); mp 137 °C; R_f = 0.68 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 0.99 (s, 9 H), 2.99 (s, 2 H), 7.16 (d, ^3J = 7.8 Hz, 1 H), 7.23 (t, ^3J = 7.8 Hz, 1 H), 7.52 (t, ^3J = 7.8 Hz, 1 H), 8.28 (d, ^3J = 7.8 Hz, 1 H), 8.63 (s, 1 H, H7), 9.65 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 29.0 (3 C), 31.9, 37.4, 96.7 (q, $^1J_{C,F}$ = 33 Hz), 113.8, 116.8, 118.7, 119.7, 122.4 (q, $^1J_{C,F}$ = 289 Hz), 123.2, 125.1, 133.6, 134.0, 148.7, 153.1, 158.2, 169.4.

^{19}F NMR (DMSO-d_6): δ = –84.3.

MS: *m*/*z* (%) = 379 (24) $[M + 1]^+$, 378 (89) $[M]^+$, 363 (53) $[M – Me]^+$, 322 (43) $[M + 1 – C_4H_9]^+$, 310 (30) $[M + 1 – CF_3]^+$, 309 (100) $[M – CF_3]^+$, 253 (27) $[M – CF_3 – C_4H_9]^+$, 239 (32) $[M + 1 – CF_3 – C_5H_{11}]^+$, 121 (61) $[HOC_6H_4CO]^+$, 120 (34) $[OC_6H_4CO]^+$, 57 (98) $[C_4H_9]^+$, 55 (20), 43 (38) $[C_3H_7]^+$, 41 (43).

10-*tert*-Butyl-6-hydroxy-6-(trifluoromethyl)-6,10-dihydrochromeno[4,3-*b*]pyrrolo[3,2-*e*]pyridine-8-carbonitrile (5f)

Reaction conditions: DMF, 100 °C; pale yellow solid; yield: 183 mg (52%); mp 173–175 °C; R_f = 0.19 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 1.84 (s, 9 H), 7.13 (d, ^3J = 7.8 Hz, 1 H), 7.23 (t, ^3J = 7.8 Hz, 1 H), 7.44 (t, ^3J = 7.8 Hz, 1 H), 8.16 (s, 1 H, H9), 8.27 (d, ^3J = 7.8 Hz, 1 H), 8.67 (s, 1 H, H7), 9.41 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 28.6 (3 C), 59.0, 82.6, 96.6 (q, $^1J_{C,F}$ = 32 Hz), 114.9, 116.6, 117.5, 119.9, 120.2, 122.5 (q, $^1J_{C,F}$ = 262 Hz), 123.0, 123.9, 126.6, 131.8, 138.5, 142.2, 147.2, 152.1.

^{19}F NMR (DMSO-d_6): δ = –83.9.

MS: *m*/*z* (%) = 388 (11) $[M + 1]^+$, 387 (46) $[M]^+$, 318 (55) $[M - CF_3]^+$, 263 (22) $[M + 1 - CF_3 - C_4H_9]^+$, 262 (100) $[M - CF_3 - C_4H_9]^+$, 57 (32) $[C_4H_9]^+$, 41 (22).

Ethyl 6-Hydroxy-6-(trifluoromethyl)-6*H*-chromeno[4,3-*b*]furo[3,2-*e*]pyridine-9-carboxylate (5g)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 124 mg (36%); mp 133–135 °C; R_f = 0.46 (toluene–Et_2O, 5:1).

^{1}H NMR ($CDCl_3$): δ = 1.44 (t, ^3J = 7.1 Hz, 3 H), 4.46 (q, ^3J = 7.1 Hz, 2 H), 7.07 (d, ^3J = 7.8 Hz, 1 H), 7.20 (t, ^3J = 7.8 Hz, 1 H), 7.41 (t, ^3J = 7.8 Hz, 1 H), 7.54 (s, 1 H, H8), 8.35 (s, 1 H, H7), 8.38 (d, ^3J = 7.8 Hz, 1 H), 10.43 (s, OH).

^{13}C NMR ($CDCl_3$): δ = 14.2, 62.1, 96.4 (q, $^2J_{C,F}$ = 33 Hz), 112.8, 116.6, 118.8, 119.5, 122.3 (q, $^1J_{C,F}$ = 279 Hz), 123.5, 123.5, 125.4, 131.8, 132.6, 146.3, 147.0, 152.2, 158.9, 162.9.

^{19}F NMR ($CDCl_3$): δ = –85.3.

MS: *m*/*z* (%) = 379 (24) $[M]^+$, 311 (20) $[M + 1 - CF_3]^+$, 310 (100) $[M - CF_3]^+$, 282 (33) $[M + 1 - CF_3 - C_2H_5]^+$, 149 (18), 121 (21) $[HOC_6H_4CO]^+$, 69 (26).

6-Hydroxy-11-methyl-6-(trifluoromethyl)-6*H*-chromeno[3′,4′:5,6]pyrido[2,3-*d*]pyrimidine-8,10(9*H*,11*H*)-dione (5h)

Reaction conditions: DMF, 80 °C; colorless solid; yield: 233 mg (70%); mp 200–201 °C (MeOH).

^{1}H NMR (DMSO-d_6): δ = 3.61 (s, 3 H), 7.16 (d, ^3J = 7.8 Hz, 1 H), 7.24 (t, ^3J = 7.8 Hz, 1 H), 7.54 (t, ^3J = 7.8 Hz, 1 H), 8.31 (d, ^3J = 7.8 Hz, 1 H), 8.34 (s, 1 H, H7), 9.59 (s, 1 H, OH), 11.85 (s, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 27.9, 95.9 (q, $^2J_{C,F}$ = 33 Hz), 110.7, 116.4, 116.8, 118.2, 123.1, 124.1 (q, $^1J_{C,F}$ = 285 Hz), 125.4, 133.9, 135.8, 150.7, 150.7, 153.2, 160.6, 192.7.

^{19}F NMR (DMSO-d_6): δ = –84.6.

MS: *m*/*z* (%) = 365 (22) $[M]^+$, 297 (34) $[M + 1 - CF_3]^+$, 296 (100) $[M - CF_3]^+$, 197 (16), 196 (15), 152 (23).

6-Hydroxy-9,11-dimethyl-6-(trifluoromethyl)-6*H*-chromeno[3′,4′:5,6]pyrido[2,3-*d*]pyrimidine-8,10(9*H*,11*H*)-dione (5i)

Reaction conditions: DMF, 80 °C, 30 h; yellow solid; yield: 98 mg (24%); mp 183 °C (AcOH).

^{1}H NMR ((DMSO-d_6): δ = 3.31 (s, 3 H), 3.69 (s, 3 H), 7.17 (d, ^3J = 7.8 Hz, 1 H), 7.25 (t, ^3J = 7.8 Hz, 1 H), 7.55 (t, ^3J = 7.8 Hz, 1 H), 8.31 (d, ^3J = 7.8 Hz, 1 H), 8.39 (s, 1 H, H7), 9.66 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 27.8, 29.0, 95.8 (q, $^2J_{C,F}$ = 33 Hz), 109.7, 117.0, 118.1, 116.5, 122.1 (q, $^1J_{C,F}$ = 289 Hz), 122.8, 125.1, 133.6, 136.0, 150.6, 151.6, 153.0, 160.0, 205.8.

^{19}F NMR (DMSO-d_6): δ = –84.4.

MS: *m*/*z* (%) = 379 (15) $[M]^+$, 311 (50) $[M + 1 - CF_3]^+$, 310 (100) $[M - CF_3]^+$, 152 (10).

5-Hydroxy-2-methyl-5-(trifluoromethyl)-5*H*-chromeno[4,3-*b*]pyridine-3-carbonitrile (5w)

Reaction conditions: DMF, 100 °C; colorless solid; yield: 173 mg (62%); mp 146–147 °C; R_f = 0.64 (CH_2Cl_2).

^{1}H NMR (DMSO-d_6): δ = 2.78, (s, 3 H), 7.14 (d, ^3J = 7.8 Hz, 1 H), 7.22 (t, ^3J = 7.8 Hz, 1 H), 7.52 (t, ^3J = 7.8 Hz, 1 H), 8.25 (d, ^3J = 7.8 Hz, 1 H), 8.38 (s, 1 H, H4), 9.62 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 23.2, 95.7 (q, $^2J_{C,F}$ = 33 Hz), 107.7, 116.5, 116.8, 118.1, 119.8, 122.2 (q, $^1J_{C,F}$ = 289 Hz), 123.1, 125.0, 133.8, 139.8, 149.2, 152.9, 163.4.

^{19}F NMR (DMSO-d_6): δ = –84.2.

MS: *m*/*z* (%) = 306 (15) $[M]^+$, 238 (17) $[M + 1 - CF_3]^+$, 237 (100) $[M - CF_3]^+$.

2-Phenyl-5-salicyloyl-4-(trifluoromethyl)-1,2-dihydro-3*H*-pyrazolo[3,4-*b*]pyridin-3-one (6a)

Reaction conditions: AcOH, 100 °C, 36 h; yield: 134 mg (37%); mp 188 °C; R_f = 0.24 (PE–EtOAc, 1:1).

^{1}H NMR (DMSO-d_6): δ = 6.96 (t, ^3J = 8.2 Hz, 2 H), 7.33 (t, ^3J = 7.2 Hz, 1 H), 7.54 (m, 3 H), 7.64 (d, ^3J = 7.8 Hz, 1 H), 7.89 (d, ^3J = 8.2 Hz, 2 H), 8.73 (s, 1 H, H6), 10.89 (s, 1 H, OH).

^{13}C NMR (DMSO-d_6): δ = 104.5, 117.5, 119.3, 120.3, 121.5 (q, $^1J_{C,F}$ = 275 Hz), 121.8, 125.8, 126.9, 128.8, 131.7 (q, $^2J_{C,F}$ = 36 Hz), 131.8, 136.4, 136.5, 151.8, 155.1, 155.7, 159.9, 194.8.

^{19}F NMR (DMSO-d_6): δ = –57.0.

MS: *m*/*z* (%) = 400 (19) $[M + 1]^+$, 399 (71) $[M]^+$, 331 (20) $[M + 1 - CF_3]^+$, 330 (96) $[M - CF_3]^+$, 279 (20) $[M + 1 - HOC_6H_4CO]^+$, 121 (100) $[HOC_6H_4CO]^+$, 93 (23) $[HOC_6H_4]^+$, 77 (69) $[C_6H_5]^+$, 65 (36).

1-Ethyl-5-salicyloyl-4-(trifluoromethyl)-1*H*-pyrazolo[3,4-*b*]pyridine (6b)

Reaction conditions: AcOH, 100 °C; yield: 104 mg (34%); mp 163–164 °C; R_f = 0.38 (PE–Et_2O, 2:1).

^{1}H NMR ($CDCl_3$): δ = 1.60 (t, ^3J = 7.4 Hz, 3 H), 4.69 (q, ^3J = 7.4 Hz, 2 H), 6.84 (t, ^3J = 7.8 Hz, 1 H), 7.11 (d, ^3J = 7.8 Hz, 1 H), 7.17 (d, ^3J = 7.8 Hz, 1 H), 7.56 (t, ^3J = 7.8 Hz, 1 H), 8.27 (q, *J* = 1.6 Hz, 1 H, H3), 8.59 (s, 1 H, H6), 11.81 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 14.9, 42.8, 110.6 (q, $J_{C,F}$ = 2.4 Hz), 118.6, 119.3, 120.1, 122.5 (q, $^1J_{C,F}$ = 274 Hz), 125.0 (q, $J_{C,F}$ = 2.5 Hz), 129.4 (q, $^2J_{C,F}$ = 35 Hz), 131.7 (q, $J_{C,F}$ = 2.4 Hz), 137.7, 147.4, 150.3, 163.2, 199.2.

^{19}F NMR ($CDCl_3$): δ = –57.5.

MS: *m*/*z* (%) = 335 (36) $[M]^+$, 267 (21) $[M + 1 - CF_3]^+$, 266 (100) $[M - CF_3]^+$, 242 (12) $[M - HOC_6H_4]^+$, 121 (66) $[HOC_6H_4CO]^+$, 120 (95) $[OC_6H_4CO]^+$, 93 (18) $[HOC_6H_4]^+$, 92 (16) $[OC_6H_4]^+$, 65 (19).

3-Neopentyl-5-salicyloyl-4-(trifluoromethyl)isoxazolo[5,4-*b*]pyridine (6e)

Reaction conditions: AcOH, 100 °C; yield: 28 mg (8%); mp 144–145 °C; R_f = 0.53 (PE–Et_2O, 2:1).

^{1}H NMR ($CDCl_3$): δ = 1.14 (s, 9 H), 3.01 (s, 2 H), 6.86 (t, ^3J = 7.8 Hz, 1 H), 7.05 (d, ^3J = 7.3 Hz, 1 H), 7.11 (d, ^3J = 7.8 Hz, 1 H), 7.56 (t, ^3J = 7.8 Hz, 1 H), 8.65 (s, 1 H, H6), 11.61 (s, 1 H, OH).

^{13}C NMR ($CDCl_3$): δ = 29.7, 32.1, 39.0 (q, $J_{C,F}$ = 3.2 Hz), 110.3 (q, $J_{C,F}$ = 2.4 Hz), 118.8, 119.6, 119.8, 121.6 (q, $^1J_{C,F}$ = 273 Hz), 128.3 (q, $J_{C,F}$ = 2.4 Hz), 131.5 (q, $^2J_{C,F}$ = 36 Hz), 132.7, 138.1, 149.6, 156.5, 163.1, 170.0, 198.0.

^{19}F NMR ($CDCl_3$): δ = –54.2.

MS: *m*/*z* (%) = 378 (35) $[M]^+$, 363 (21) $[M - CH_3]^+$, 322 (14) $[M + 1 - C_4H_9]^+$, 310 (31) $[M + 1 - CF_3]^+$, 309 (100) $[M - CF_3]^+$, 252 (13) $[M - CF_3 - C_4H_9]^+$, 239 (66) $[M + 1 - CF_3 - C_5H_{11}]^+$, 121(23) $[HOC_6H_4CO]^+$, 57 (22) $[C_4H_9]^+$.

6-(Difluoromethyl)-2-phenyl-5-salicyloyl-1,2-dihydropyrazolo[3,4-*b*]pyridin-3-one (4ba)
Reaction conditions: toluene, reflux, 20 h; yield: 260 mg (80%); mp 179–180 °C.

IR (KBr): 1656, 1625, 1599, 1578 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 6.98 (td, J = 7.8, 1.0 Hz, 1 H), 7.01 (d, ^3J = 8.3 Hz, 1 H), 7.28 (t, $^2J_{H,F}$ = 53.7 Hz, 1 H), 7.32 (tt, ^3J = 7.4, 1.0 Hz, 1 H), 7.49–7.57 (m, 4 H), 7.89–7.92 (m, 2 H), 8.26 (s, 1 H, H4), 10.67 (s, 1 H, OH), 11.6–13.6 (br s, 1 H, NH).

^{19}F NMR (DMSO-d_6): δ = –116.1 (d, $^2J_{F,H}$ = 53.7 Hz, 2 F, CF_2H).

MS: *m*/*z* (%) = 261 (58) $[M + 1 – HOC_6H_4CO]^+$, 232 (22), 212 (17), 155 (17), 77 (69) $[C_6H_5]^+$, 64 (40), 51 (32), 28 (28).

5-(5-Chloro-2-hydroxybenzoyl)-2-phenyl-6-(trifluoromethyl)-1,2-dihydropyrazolo[3,4-*b*]pyridin-3-one (4ca)
Reaction conditions: toluene, reflux, 12 h; yield: 310 mg (73%); mp 260–261 °C.

IR (KBr): 1649, 1621, 1594, 1578 cm^{-1}.

^1H NMR (DMSO-d_6): δ = 7.00 (d, ^3J = 8.8 Hz, 1 H), 7.35 (t, ^3J = 7.4 Hz, 1 H), 7.56 (t, ^3J = 7.5 Hz, 2 H), 7.59 (dd, J = 8.8, 2.7 Hz, 1 H), 7.66 (d, J = 2.7 Hz, 1 H), 7.91 (d, ^3J = 7.7 Hz, 2 H), 8.49 (s, 1 H, H4), 10.85 (s, 1 H, OH), 11.5–13.5 (br s, 1 H, NH).

^{19}F NMR (DMSO-d_6): δ = –62.5.

MS: *m*/*z* (%) = 279 (64) $[M + 1 – HO(Cl)C_6H_3CO]^+$, 250 (30), 230 (19), 77 (68) $[C_6H_5]^+$, 64 (22), 51 (23), 28 (35).

7-(Difluoromethyl)-1,3-dimethyl-6-salicyloylpyrido[2,3-*d*]pyrimidine-2,4(1*H*,3*H*)-dione (4bi) and 6-(Difluoromethyl)-6-hydroxy-9,11-dimethyl-6*H*-chromeno[3′,4′:5,6]pyrido[2,3-*d*]pyrimidine-8,10(9*H*,11*H*)-dione (5bi)
Reaction conditions: toluene, reflux, 22 h; yield: 300 mg (92%); mp 185–186 °C.

^1H NMR (DMSO-d_6): δ = (**4bi**, 65%) 3.30 (s, 3 H), 3.63 (s, 3 H), 6.97–7.02 (m, 2 H), 7.23 (t, $^2J_{H,F}$ = 53.6 Hz, 1 H), 7.47–7.58 (m, 2 H), 8.40 (s, 1 H, H5), 10.64 (s, 1 H, OH).

^{19}F NMR (DMSO-d_6): δ = (**4bi**, 65%) –116.6 (d, $^2J_{F,H}$ = 53.6 Hz, 2 F, CF_2H).

^1H NMR (DMSO-d_6): δ = (**5bi**, 35%)3.33 (s, 3 H), 3.70 (s, 3 H), 6.36 (t, $^2J_{H,F}$ = 54.5 Hz, 1 H), 7.12 (d, ^3J = 8.2 Hz, 1 H), 7.21 (t, ^3J = 7.6 Hz, 1 H), 7.52 (m, 1 H), 8.31 (dd, J = 7.8, 1.6 Hz, 1 H), 8.42 (s, 1 H, H7), 8.83 (s, 1 H, OH).

^{19}F NMR (DMSO-d_6): δ = (**5bi**, 35%) –133.5 (dd, $^2J_{F,F}$ = 281.4, $^2J_{F,H}$ = 54.5 Hz, 1 F, C*F*FH), –131.5 (dd, $^2J_{F,F}$ = 281.4, $^2J_{F,H}$ = 54.5 Hz, 1 F, CF*F*H).

3-{[2-(5,5-Dimethyl-3-oxocyclohex-1-enyl)-2-methylhydrazinyl]methylene}-2-hydroxy-2-(trifluoromethyl)chroman-4-one (8)
Reaction conditions: DMF, 100 °C, 64 h; colorless solid; yield: 286 mg (80%); mp 155–157 °C; R_f = 0.3 (EtOAc).

^1H NMR (DMSO-d_6): δ = 1.14, 1.15 (2 s, 6 H), 2.16 (s, 2 H), 2.64 (s, 2 H), 3.32 (s, 3 H), 5.21 (s, 1 H), 7.19 (d, ^3J = 7.8 Hz, 1 H), 7.26 (t, ^3J = 7.8 Hz, 1 H), 7.55 (d, ^3J = 9.8 Hz, 1 H), 7.66 (t, ^3J = 7.8 Hz, 1 H), 7.91 (d, ^3J = 9.8 Hz, 1 H), 9.19 (s, 1 H, OH), 11.78 (d, ^3J = 9.8 Hz, 1 H, NH).

^{13}C NMR (DMSO-d_6): δ = 28.0, 28.2, 32.4, 49.5, 96.9, 97.5 (q, $^2J_{C,F}$ = 34 Hz), 98.0, 99.1, 116.5, 119.5, 120.1 (q, $^1J_{C,F}$ = 290 Hz), 122.3, 124.4, 125.6, 134.9, 152.9, 155.5, 163.6, 176.6, 195.7.

^{19}F NMR (DMSO-d_6): δ = –84.7.

MS: *m*/*z* (%) = 410 (21) $[M]^+$, 342 (26) $[M + 1 – CF_3]^+$, 341 (100) $[M – CF_3]^+$, 326 (34) $[M – CF_3 – CH_3]^+$, 272 (15) $[M – COC_6H_4O]^+$, 243 (24) $[M – C_9H_{16}N_2O]^+$, 173 (18) $[C_{10}H_5O_3]^+$, 168 (15) $[M – C_{10}H_4F_3O_2]^+$, 121 (68) $[HOC_6H_4CO]^+$, 96.0 (27).

3-{[2-(5,5-Dimethyl-3-oxocyclohex-1-enyl)-2-methylhydrazono]methyl}-2-(trifluoromethyl)-4*H*-chromen-4-one (9)
Reaction conditions: AcOH, 100 °C; colorless solid; yield: 271 mg (76%); mp 172–175 °C; R_f = 0.35 (PE–EtOAc, 1:1).

^1H NMR (DMSO-d_6): δ = 0.94 (s, 6 H), 2.09 (s, 2 H, H6′), 2.62 (s, 2 H, H4′), 3.28 (s, 3 H), 5.50 (s, 1 H, H2′), 7.56 (t, ^3J = 7.4 Hz, 1 H), 7.71 (d, ^3J = 7.4 Hz, 1 H), 7.75 (s, 1 H), 7.90 (t, ^3J = 7.4 Hz, 1 H), 8.07 (d, ^3J = 7.4 Hz, 1 H).

^{13}C NMR (DMSO-d_6): δ = 27.9, 31.7, 31.9, 38.9, 49.6, 101.6, 118.3, 119.0 (q, $^1J_{C,F}$ = 274 Hz), 119.5, 122.0, 125.0, 126.5, 127.8, 135.5, 146.9 (q, $^2J_{C,F}$ = 37 Hz), 154.3, 160.9, 175.9, 196.2.

^{19}F NMR (DMSO-d_6): δ = –64.4.

MS: *m*/*z* (%) = 392 (14) $[M]^+$, 324 (30) $[M + 1 – CF_3]^+$, 323 (100) $[M – CF_3]^+$, 308 (17) $[M – CF_3 – CH_3]^+$, 307 (21) $[M – 1 – CF_3 – CH_3]^+$, 272 (15) $[M – OC_6H_4CO]^+$, 179 (13) $[M – C_{10}H_4F_3O_2]^+$, 96 (17), 55 (22).

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(10) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 721116 for **3n**, CCDC 721117 for **4a**, and CCDC 721118 for **5g** can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 (1223)336033; e-mail: deposit@ccdc.cam.ac.uk].