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ARTICLE TYPE

Facile construction of novel heterocyclic compounds: Three-component, one-pot synthesis of 2-hydroxybenzoyl-1,2-dihydropyridine-3-carboxylates, ketones, pyridone-3-carboxylates and benzopyrido-1,3-oxazole-4-carboxylates†

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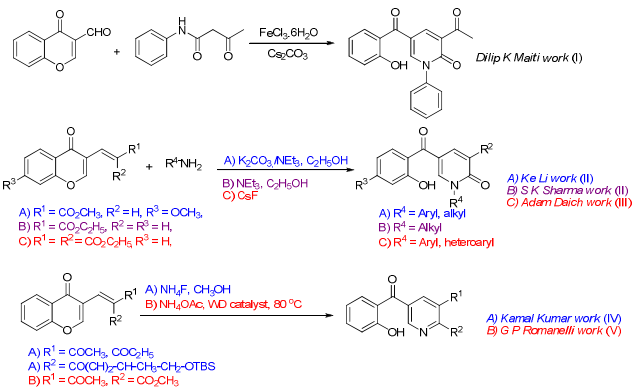
A facile method has been developed for the preparation of four novel heterocyclic compounds by the reaction of 3-formylchromones, benzylamines, 2-aminophenols with 3-oxobutanoates. 3-Oxobutanoates bearing trifluoro, trichloro substituents and trifluoro containing 1,3-diketones facilitated the reaction. The reaction is proceeding via Schiff base, Michael addition followed by selective addition of enamine to the carbonyl group adjacent to the trihalo group due to a strong electron withdrawing effect. The present three-component, one-pot protocol provided heterocyclic compounds without catalyst.

Introduction

The Chromone[1] (4*H*-chromen-4-one, 4*H*-1-benzopyran-4-one) scaffold has been found in natural products and structurally interesting due to phenolic oxygen is attached to α,β-unsaturated ketone. Consequently, chromone chemistry continues to draw considerable attention of synthetic and medicinal chemists. 4-Oxo-4*H*-chromen-3-carbaldehyde (3-formylchromone), a useful precursor for the preparation of biologically active compounds.[2] 3-Formylchromone have three functional groups namely, an electrophilic centre at C-2, a conjugated carbonyl group at C-3 and an unsaturated keto function at C-4. Various useful heterocyclic compounds were prepared by utilizing electrophilic centre (C-2) and conjugated second carbonyl group (C-3).[3] Dihydropyridines, pyrano pyridopyrimidinones, benzopyranopyridinones and tricyclic benzopyrones were prepared by the chemical transformation of 3-formylchromone with the retention of the chromone ring.[4] Further, ring opening of the pyran-4-one resulted in the formation of 2-hydroxybenzoyl derivatives.[5] The previous approaches for the synthesis of 2-hydroxybenzoylpyridones and pyridines were depicted in Scheme 1. I) Maiti *et al*[5f] reported 2-hydroxybenzoylpyridones by the reaction of 3-formylchromone with 3-oxo-*N*-phenylbutanamide in the presence of $FeCl_3$. II) Li *et al*[5g-i] and Sharma *et al*[5j] reported from chromenyl acrylates with alkyl, aryl amines in the presence of base under reflux conditions, however, III) Daich *et al*[5k] reported from the *Knoevenagel* derivative of 3-formylchromone with aniline in the presence of CsF. IV) Kumar *et al*[5d] reported 2-hydroxybenzoylpyridines from the *Knoevenagel* derivative of 3-formylchromone in the presence of ammonium salt. V) Romanelli *et al*[3d] reported similar reaction from the *Knoevenagel* derivative of 3-formylchromone using Wells-Dawson heteropolyacid as the catalyst.



Scheme 1 Previous approaches for the preparation of 2-pyridones and pyridines.

Our research focused on feasible reactions of salicylaldehydes, carbonyl compounds with 3-oxobutanoates bearing chloro, trichloro and trifluoro substituents. In this context, we studied the reactivity of salicylaldehydes with ethyl 4-chloro-3-oxobutanoate using piperidine to provide 2*H*-chromenes,[6a] interim these derivatives were successfully converted to useful heterocycles.[6b-e] We also studied the reactivity of salicyladehydes with ethyl 4,4,4-trichloro-3-oxobutanoate using piperidine to provide 2*H*-chromene-3-carboxylates.[7] Next, we studied the reaction between the carbonyl compounds and ethyl 4,4,4-trifluoro-3-oxobutanoate using piperidine to provide series of (*E*)-α,β-unsaturated esters and ketones.[8] Earlier, we reported 3-formylchromone based heterocyclic compounds such as 4*H*-chromen-1,2,3,4-tetrahydropyrimidine-5-carboxylates as potential anti-mycobacterial and anticancer agents.[9] The present manuscript describe a facile approach for the preparation of novel heterocyclic compounds by three-component, one-pot reaction

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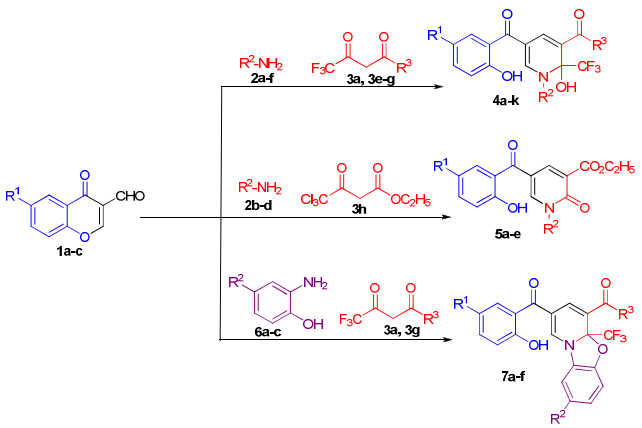
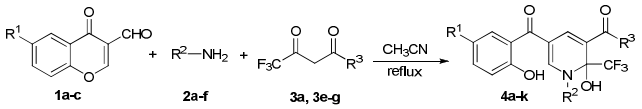
between 3-formylchromones, benzylamines, 2-aminophenols and 3-oxobutanoates bearing trifluoro, trichloro substituents and trifluoro containing 1,3-diketones (Scheme 2).



Scheme 2 Present approaches for the preparation of heterocyclic compounds.

Results and discussion

In an initial experiment, we conducted the reaction between 3-formylchromone (**1a**, 1 equiv), aniline (**2a**, 1 equiv) and ethyl 4,4,4-trifluoro-3-oxobutanoate (**3a**, 1 equiv) in dry DCM at room temperature for 24 h. This provided ethyl 2-hydroxy-5-(2-hydroxybenzoyl)-1-phenyl-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate **4a** in 10% isolated yield (Scheme 3). The compound **4a** was characterized by using IR, ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectroscopies. The result encouraged us to optimize the reaction conditions. The model reaction was investigated with various solvents such as acetonitrile, CH_3OH, C_2H_5OH, 1,4-dioxane, THF, ether, benzene, and toluene under reflux conditions. We found that acetonitrile produced the compound **4a** in 28% yield (Scheme 3, Table 1, entry 1). Experiments have been carried out by changing the mole ratio, time and temperature to improve the yield. However, the yield could not improve beyond 28% (**4a**). The reason could be the lone pair electrons on the nitrogen atom of aniline are in resonance and become less reactive.

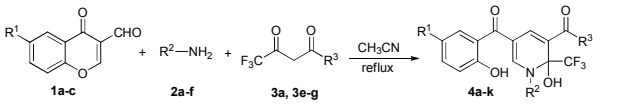


Scheme 3 Synthesis of 2-hydroxybenzoyl-1,2-dihydropyridine-3-carboxylates and ketones.

Further, we have carried out the reaction between 3-formylchromone (**1a**, 1 equiv), benzylamine (**2b**, 1.2 equiv) and ethyl 4,4,4-trifluoro-3-oxobutanoate (**3a**, 1.5 equiv) in acetonitrile under reflux conditions for 2 h. The reaction proceeded smoothly and afforded ethyl 1-benzyl-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate **4b** in 63% yield (Scheme 3, Table 1, entry 2). The compound **4b** was characterized using IR, ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectroscopies. This work represents the first example for the construction of novel heterocyclic compound, the usefulness of this reaction is shown by the formation of Schiff base, Michael addition (C-C bond formation), ring opening (C-O bond cleaved), and intramolecular cyclization (C-N bond formation) in one-pot. We also investigated the present three-component, one-pot protocol with various β-ketoesters such as ethyl 3-oxobutanoate **3b**, ethyl 3-oxo-3-phenylpropanoate **3c**, and ethyl 4-chloro-3-oxobutanoate **3d**. In all these experiments, the 3-formylchromone **1a** and benzylamine **2b** provided corresponding Schiff base, interim the Schiff base did not react with the β-ketoesters (**3b-d**) to give the corresponding products. Among the tested β-ketoesters **3a-d**, ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** only facilitated the reaction due to strong electron withdrawing nature of trifluoro group to produce the compounds.

In order to evaluate the efficiency of the methodology, we investigated the substrate scope present on 3-formylchromones **1a-c** and benzylamines **2b-d**. The electron withdrawing and donating groups were well tolerated to produce 2-hydroxybenzoylpyridine-3-carboxylates **4c-f** in good yields (Table 1, entry 3-6). To expand the scope of the present method, next, 2-(1*H*-indol-3-yl)ethanamine **2e** and ethanolamine **2f** were examined. Accordingly, the reaction of **1a** and **2e, 2f** with ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** has been carried out under optimized conditions. This provided corresponding 2-hydroxybenzoyl-pyridine-3-carboxylates **4g-h** (Table 1, entry 7-8).

Table 1 Synthesis of 2-hydroxybenzoyl-1,2-dihydropyridine-3-carboxylates and ketones

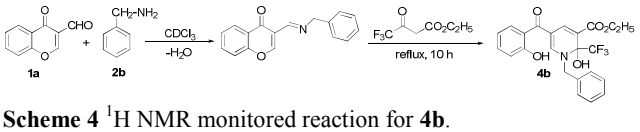


Entry	R^1	R^2	R^3	Compound	Yield[a] (%)
1	H (**1a**)	(**2a**)	OC_2H_5 (**3a**)	**4a**	28
2	H (**1a**)	(**2b**)	OC_2H_5 (**3a**)	**4b**	63
3	CH_3 (**1b**)	(**2b**)	OC_2H_5 (**3a**)	**4c**	65
4	Cl (**1c**)	(**2b**)	OC_2H_5 (**3a**)	**4d**	60
5	H (**1a**)	(**2c**)	OC_2H_5 (**3a**)	**4e**	68
6	H (**1a**)	(**2d**)	OC_2H_5 (**3a**)	**4f**	62
7	H (**1a**)	(**2e**)	OC_2H_5 (**3a**)	**4g**	66
8	H (**1a**)	(**2f**)	OC_2H_5 (**3a**)	**4h**	52
9	H (**1a**)	(**2b**)	CH_3 (**3e**)	**4i**	44
10	H (**1a**)	(**2b**)	(**3f**)	**4j**	65
11	H (**1a**)	(**2b**)	(**3g**)	**4k**	40

[a]Isolated yields

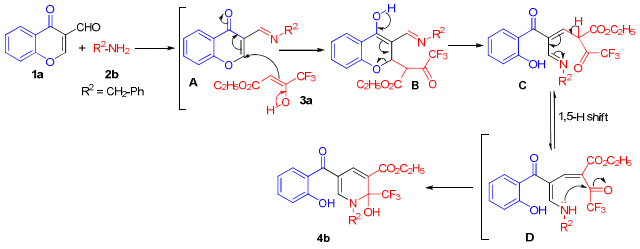
Having achieved the preparation of 2-hydroxybenzoylpyridine-3-carboxylates **4a-h**, we extended this protocol with trifluoro containing 1,3-diketones. Accordingly, 3-formylchromone **1a** and benzylamine **2b**, with 1,1,1-trifluoropentane-2,4-dione **3e**, 4,4,4-trifluoro-1-phenylbutane-1,3-dione **3f**, and 4,4,4-trifluoro-1-(furan-2-yl)butane-1,3-dione **3g** have been carried out under optimized conditions. The reactions proceeded smoothly to produce corresponding 2-hydroxybenzoyl-1,2-dihydropyridinyl-3-ones **4i-k** (Table 1, entry 9-11). Thus, synthesized compounds **4a-k** are new and well characterized by spectral data (see ESI).

In order to evaluate the mechanism, the experiment has been carried out to monitor the reaction by ^{1}H NMR (Scheme 4). Accordingly, the 3-formylchromone **1a** and benzylamine **2b** were stirred in $CDCl_3$ at room temperature for 10 min to provide Schiff base (^{1}H NMR, see ESI). Then, ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** in $CDCl_3$ was added slowly to the Schiff base. The reaction mixture was refluxed and the samples were obtained for 2 h, 4 h, and 8 h to record the ^{1}H NMR (see ESI).



Scheme 4 ^{1}H NMR monitored reaction for **4b**.

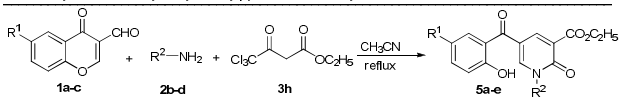
A plausible mechanism for this new reaction is depicted in Scheme 5. The 3-formylchromone **1a** reacts with benzylamine **2b** gives Schiff base **A**. Michael addition of ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** with the Schiff base **A** gives benzyliminomethylchromenyl intermediate **B** (C-C bond formation). Then, the intermediate **B** by the cleavage of C-O bond gives intermediate **C**. Finally, intramolecular cyclization occurs by selective addition to the carbonyl group adjacent to the CF_3 group of the nucleophilic enamine in intermediate **D** obtained from **C** through an 1,5-H shift to give target compound **4b**.



Scheme 5 Plausible reaction mechanism for **4b**

Having succeeded the results with ethyl 4,4,4-trifluoro-3-oxobutanoate and trifluoro containing 1,3-diketones, we extended this protocol with ethyl 4,4,4-trichloro-3-oxobutanoate **3h**. Accordingly, the reaction of 3-formylchromone **1a** and benzylamine **2b** with **3h** has been carried out in acetonitrile under reflux conditions for 6 h. Interestingly, this provided ethyl 1-benzyl-5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridine-3-carboxylate **5a** (Table 2, entry 1). The pyridone **5a** was characterized using IR, ^{1}H NMR, ^{13}C NMR, and HRMS spectroscopies. This work also represents the first example for the construction of 2-hydroxybenzoylpyridone in one-pot. In order to evaluate the methodology, we have carried out the reaction with substituted 3-formylchromones **1a-c** and benzylamines **2b-d** with ethyl 4,4,4-trichloro-3-oxobutanoate **3h**. The electron withdrawing and donating groups were well tolerated and produced 2-hydroxybenzoylpyridone-3-carboxylates **5b-e** (Table 2, entry 2-5). The compounds **5a-e** are new and well characterized by spectral data (see ESI).

Table 2 Synthesis of 2-hydroxybenzoylpyridone-3-carboxylates



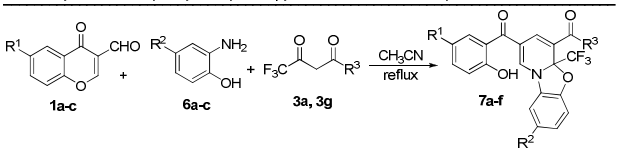
Entry	R^1	R^2	Compound	Yield[a] (%)
1	H (**1a**)	(**2b**)	**5a**	60
2	CH_3 (**1b**)	(**2b**)	**5b**	72
3	Cl (**1c**)	(**2b**)	**5c**	78
4	H (**1a**)	(**2c**)	**5d**	70
5	H (**1a**)	(**2d**)	**5e**	74

[a]Isolated yields

The above results indicated that the benzylamine and 3-formylchromone with ethyl 4,4,4-trifluoro-3-oxobutanoate, ethyl 4,4,4-trichloro-3-oxobutanoate and trifluoro containing 1,3-diketones provided the corresponding compounds with good yields. However, aniline provided the corresponding compound with low yield due to the presence of lone pair electrons on the nitrogen atom. Assuming that the aniline having hydroxy group at *ortho* position (2-aminophenol) may have the impact on reactivity and couple of experiments have been carried out as below.

The 3-formylchromone **1a** and 2-aminophenol **6a** with ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** have been carried out in acetonitrile under reflux conditions for 4 h. Interestingly, this provided ethyl 2-(2-hydroxybenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate **7a** (Table 3, entry 1). The compound **7a** was characterized using IR, ^{1}H NMR, ^{13}C NMR, ^{19}F NMR and HRMS spectroscopies. This work also represents the first example for the construction of 2-hydroxybenzoylbenzopyrido-1,3-oxazole-4-carboxylate in one-pot.

Table 3 Synthesis of 2-hydroxybenzoylbenzopyrido-1,3-oxazole-4-carboxylates



Entry	R^1	R^2	R^3	Compound	Yield[a] (%)
1	H (**1a**)	H (**6a**)	OC_2H_5 (**3a**)	**7a**	33
2	CH_3 (**1b**)	H (**6a**)	OC_2H_5 (**3a**)	**7b**	36
3	Cl (**1c**)	H (**6a**)	OC_2H_5 (**3a**)	**7c**	29
4	H (**1a**)	CH_3 (**6b**)	OC_2H_5 (**3a**)	**7d**	40
5	H (**1a**)	Cl (**6c**)	OC_2H_5 (**3a**)	**7e**	28
6	H (**1a**)	H (**6a**)	(**3g**)	**7f**	28

[a]Isolated yields

In order to evaluate the methodology, reactions have been carried out between substituted 3-formylchromones **1a-c** and 2-aminophenols **6a-c** with ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** under optimized conditions. The electron withdrawing and donating groups were well tolerated to produce 1,3-oxazole-4-carboxylates **7b-e** (Table 3, entry 2-5). Further, the 3-formylchromone **1a** and 2-aminophenol **6a** have been carried out with 4,4,4-trifluoro-1-(furan-2-yl)butane-1,3-dione **3g** to produce corresponding benzopyrido-1,3-oxazole derivative **7f** (Table 3,

entry 6). Thus, synthesized compounds **7a-f** are new and well characterized by spectral data (see ESI). Having achieved the results with 2-aminophenol, the three-component, one-pot protocol has been tested with 2-aminobenzenethiol **6d**. Accordingly, the 3-formylchromone **1a** and 2-aminobenzenethiol **6d** with ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** have been carried out under optimized conditions, however, the corresponding product did not formed. We also carried out the reaction with benzene-1,2-diamine **6e**. Accordingly, the 3-formylchromone **1a** and benzene-1,2-diamine **6e** with ethyl 4,4,4-trifluoro-3-oxobutanoate **3a** have been carried out. The formation of azepine derivative[5a] has been observed between 3-formylchromone **1a** and benzene-1,2-diamine **6e** without involvement of ethyl 4,4,4-trifluoro-3-oxobutanoate.

Conclusions

In summary, a facile and catalyst free method has been developed for the preparation of novel heterocyclic compounds such as 2-hydroxybenzoylpyridine-3-carboxylates, ketones, pyridone-3-carboxylates, and benzopyrido-1,3-oxazole-4-carboxylates by three-component, one-pot protocol for the first time. β-Ketoesters having strong electron withdrawing substitutents such as ethyl 4,4,4-trifluoro-3-oxobutanoate, ethyl 4,4,4-trichloro-3-oxobutanoate and trifluoro containing 1,3-diketones participated in Michael addition with Schiff base to produce corresponding heterocyclic compounds. Due to the importance of these heterocyclic compounds especially in pharmaceutical and medicinal chemistry, the present protocol can be extended for the synthesis of various biologically important heterocyclic compounds.

Experimental section

General

Ethyl 4,4,4-trifluoro-3-oxobutanoate, ethyl 4,4,4-trichloro-3-oxobutanoate, 1,1,1-trifluoropentane-2,4-dione, 4,4,4-trifluoro-1-phenylbutane-1,3-dione, 4,4,4-trifluoro-1-(furan-2-yl)butane-1,3-dione, and tryptamine were procured from Sigma-Aldrich. Benzyl amine, aniline, 2-aminophenol, benzene-1,2-diamine, 2-aminobenzenethiol and solvents were obtained from local suppliers. 3-Formylchromones were prepared as per the literature procedure. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Varian Gemini 200 MHz and Avance 300 MHz spectrometer in $CDCl_3$ using TMS as internal standard. IR spectra were recorded on a Nicollet 740 FT-IR spectrometer. Mass spectra were obtained on Agilent LCMS instrument. HRMS were measured on Agilent Technologies 6510, Q-TOFLC/MS ESI-Technique. Melting points were determined in open glass capillary tubes on a Metler FP 51 melting point apparatus and are uncorrected. All reactions were monitored by thin layer chromatography (TLC) on pre-coated silica gel 60 F_{254} (mesh); spots were visualized under UV light. Merck silica gel (100-200 mesh) was used for chromatography.

General procedure for the preparation of ethyl 2-hydroxy-5-(2-hydroxybenzoyl)-1-phenyl-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4a)

Ethyl 4,4,4-trifluoro-3-oxobutanoate (**3a**, 1.5 mmol) was added to a stirred solution of 3-formylchromone (**1a**, 1 mmol) and aniline (**2a**, 1.2 mmol) in CH_3CN (2 mL). The contents were stirred under reflux conditions for 2 h. After completion of the reaction (TLC), the residue was purified by column chromatography by using silica gel (100:200, ethyl acetate/hexane 2:98) afforded ethyl 2-hydroxy-5-(2-hydroxybenzoyl)-1-phenyl-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate **4a** as yellow solid in 28% yield; mp 128-130 °C; FT-IR (KBr): 3062, 1965, 1670, 1631, 1586, 1523, 1484, 1377, 1340, 1263, 1236, 1182, 1121, 1091, 957, 765, 700 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.46 (s, 1H, OH), 8.58 (s, 1H, OH), 8.22 (d, 1H, J = 1.5 Hz, hetero aromatic), 7.66 (d, 1H, J = 1.5 Hz, hetero aromatic), 7.50 (dd, 1H, J = 7.9, 1.6 Hz, aromatic), 7.47-7.44 (m, 1H, aromatic), 7.44-7.43 (m, 1H, aromatic), 7.42 (d, 2H, J = 2.1 Hz, aromatic), 7.42-7.41 (m, 1H, aromatic), 7.41-7.39 (m, 1H, aromatic), 7.02 (dd, 1H, J = 0.9, 8.3 Hz, aromatic), 6.91 (m, 1H, aromatic), 4.35 (q, 2H, J = 7.2 Hz, OCH_2), 1.39 (t, 3H, J = 7.2 Hz, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.1, 168.5, 161.8, 151.1, 140.0, 137.3, 135.2, 130.6, 128.9, 128.7, 123.1 (d, J = 295.1 Hz), 119.4, 118.7, 118.3, 109.7, 104.9, 86.0 (q, J = 33.6 Hz), 62.1, 14.1 ppm; MS (ESI): (*m/z*) 434 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{19}F_3NO_5$ $[M+H]^+$ 434.1209, Found: 434.1209.

General procedure for the preparation of 2-hydroxybenzoyl-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylates (4b-h) and ketones (4i-k)

Ethyl 4,4,4-trifluoro-3-oxobutanoate (**3a**, 1.5 mmol) was added to a stirred solution of 3-formylchromone (**1a**, 1 mmol) and benzylamine (**2b**, 1.2 mmol) in CH_3CN (2 mL). The contents were stirred under reflux conditions for 2 h. After completion of the reaction (TLC), the residue was purified by column chromatography by using silica gel (100:200, ethyl acetate/hexane 2:98) afforded ethyl 1-benzyl-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate **4b**. Similarly, compounds **4c-h** was prepared from corresponding 3-formylchromones **1a-c**, and benzylamines **2b-d**. However, compounds **4i-k** were prepared from 3-formylchromone **1a**, benzylamine **2b** and trifluoro containing 1,3-diketones such as 1,1,1-trifluoropentane-2,4-dione **3e**, 4,4,4-trifluoro-1-phenylbutane-1,3-dione **3f**, and 4,4,4-trifluoro-1-(furan-2-yl)butane-1,3-dione **3g** under optimized conditions.

Ethyl 1-benzyl-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4b). Yellow solid; mp 111-113 °C; FT-IR (KBr): 3326, 3032, 2983, 1672, 1637, 1587, 1528, 1480, 1348, 1233, 1182, 971, 758, 701, 540, 454 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.4 (s, 1H, OH), 8.53 (s, 1H, OH), 8.14 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.49 (d, J = 1.4 Hz, 1H, hetero aromatic), 7.41-7.30 (m, 4H, aromatic), 7.26 (m, 2H, aromatic), 7.21 (dd, J = 7.8, 1.5, Hz, 1H, aromatic), 6.97 (dd, J = 8.4, 0.9, Hz, 1H,aromatic), 6.76 (m, 1H, aromatic), 5.10 (d, J = 15.2 Hz, 1H, CH), 4.62 (d, J = 15.2 Hz, 1H, CH), 4.33 (q, J = 7.2 Hz, 2H, OCH_2), 1.37 (t, J = 7.2 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.5, 168.6, 161.6, 150.8, 137.7, 136.0, 134.9, 130.4, 129.1, 128.3, 128.1, 123.3 (d, J = 295.1 Hz), 119.3, 118.4, 118.2, 108.5, 103.8, 84.92 (q, J = 33.6 Hz), 62.0, 52.1, 14.1 ppm; MS (ESI): (*m/z*) 448 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{21}F_3NO_5$ $[M+H]^+$ 448.1366, Found: 448.1355.

Ethyl 1-benzyl-2-hydroxy-5-(2-hydroxy-5-methylbenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4c). Yellow solid; mp 115-117 °C; FT-IR (KBr): 3219, 2919, 1667, 1627, 1542, 1470, 1373, 1280, 1261, 1160, 1091, 968, 824, 720, 701, 536 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.13 (s, 1H, OH) 8.51 (s, 1H, OH), 8.14 (s, 1H, hetero aromatic), 7.49 (s, 1H, hetero aromatic), 7.41-7.31 (m, 3H, aromatic), 7.31-7.26 (m, 2H, aromatic), 7.19 (d, J = 7.0 Hz, 1H, aromatic), 6.95 (s, 1H, aromatic), 6.87 (d, J = 8.4 Hz, 1H, aromatic), 5.03 (d, J = 15.2 Hz, 1H, CH), 4.65 (d, J = 15.2 Hz, 1H, CH), 4.33 (q, J = 7.1 Hz, 2H, OCH_2), 2.17 (s, 3H, CH_3), 1.37 (t, J = 7.1 Hz, 3H, CH_3) ppm;

^{13}C NMR (75 MHz, $CDCl_3$): δ 192.5, 168.6, 159.3, 150.6, 137.8, 135.9, 135.7, 130.2, 129.1, 128.4, 128.2, 127.6, 123.2 (d, J = 295.1 Hz),119.1, 117.9, 108.6, 103.9, 84.8 (q, J = 34.5 Hz), 61.9, 52.1, 20.5, 14.1 ppm; MS (ESI): (*m/z*) 462 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{24}H_{23}F_3NO_5$ $[M+H]^+$ 462.1528, Found: 462.1495.

Ethyl 1-benzyl-5-(5-chloro-2-hydroxybenzoyl)-2-hydroxy-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4d). Yellow solid; mp 128-130 °C; FT-IR (KBr): 3201, 2970, 1667, 1623, 1586, 1543, 1470, 1373, 1329, 1275, 1260, 1185, 1169, 1095, 969, 831, 695, 577 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.23 (s, 1H, OH) 8.53 (s, 1H, OH), 8.12 (d, J = 1.4 Hz, 1H, hetero aromatic), 7.48 (s, 1H, hetero aromatic), 7.43-7.26 (m, 6H, aromatic), 7.16 (d, J = 2.6 Hz, 1H, aromatic), 6.92 (d, J = 8.8 Hz, 1H, aromatic), 5.03 (d, J = 15.1 Hz, 1H, CH), 4.68 (d, J = 15.1 Hz, 1H, CH), 4.33 (q, J = 7.1 Hz, 2H, OCH_2), 1.38 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.1, 168.5, 159.9, 150.7, 137.3, 135.4, 134.5, 129.3, 128.6, 128.3, 123.2, 123.1 (d, J = 295.1 Hz), 119.7, 108.2, 104.3, 84.8 (q, J = 34.5 Hz), 62.1, 52.3, 14.0 ppm; MS (ESI): (*m/z*) 482 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{20}ClF_3NO_5$ $[M+H]^+$ 482.0982, Found: 482.0971.

Ethyl 2-hydroxy-5-(2-hydroxybenzoyl)-1-(4-methoxybenzyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4e). Wine red viscous liquid; FT-IR (KBr): 3446, 2986, 1667, 1620, 1585, 1373, 1335, 1284, 1175, 1094, 971, 761 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.41 (s, 1H, OH) 8.54 (s, 1H,OH), 8.12 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.48 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.42-7.38 (m, 1H, aromatic), 7.23-7.18 (m, 3H, aromatic), 6.97 (dd, J = 8.2, 0.9 Hz, 1H, aromatic), 6.91-6.85 (m, 2H), 6.80-6.73 (m, 1H), 5.00 (d, J = 14.9 Hz, 1H, CH), 4.56 (d, J = 14.9 Hz, 1H, CH), 4.33 (q, J = 7.1 Hz, 2H, OCH_2), 3.80 (s, 3H), 1.37 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.4, 168.6, 161.5, 159.6, 150.7, 137.8, 134.8, 130.4, 129.9, 127.6, 123.2 (d, J = 295.1 Hz), 119.4, 118.4, 118.1, 114.5, 108.3, 103.6, 84.9 (q, J = 33.6 Hz), 61.9, 55.2, 51.6, 14.0 ppm; MS (ESI): (*m/z*) 478 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{24}H_{23}F_3NO_6$ $[M+H]^+$ 478.1477, Found: 478.1472.

Ethyl 1-(4-fluorobenzyl)-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4f). Yellow solid; mp 96-98 °C; FT-IR (KBr): 3071, 2989, 1667, 1629, 1582, 1566, 1532, 1375, 1343, 1267, 1232, 1216, 1152, 1101, 974, 824, 758, 659 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.38 (s, 1H, OH) 8.56 (s, 1H, OH), 8.13-8.10 (m, 1H, hetero aromatic), 7.47 (s, 1H, aromatic), 7.44-7.40 (m, 1H, aromatic), 7.28-7.21 (m, 4H, aromatic), 7.05 (t, J = 8.6 Hz, 2H, aromatic), 6.99 (d, J = 8.3 Hz, 1H, aromatic), 6.82-6.77 (m, 1H, aromatic), 5.08 (d, J = 15.2 Hz, 1H, CH), 4.57 (d, J = 15.2 Hz, 1H, CH), 4.33 (q, J = 7.1 Hz, 2H, OCH_2), 1.37 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.6, 168.6, 161.6, 150.5, 137.7, 135.0, 131.9, 130.4, 130.1, 130.0 119.3, 118.5, 118.3, 116.1, 116.0, 108.7, 103.9, 84.9 (d, J = 33.6 Hz), 62.0, 51.5, 14.1 ppm; MS (ESI): (*m/z*) 466 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{20}F_4NO_5$ $[M+H]^+$ 466.1272, Found: 466.1261.

Ethyl 1-(2-(1*H*-indol-3-yl)ethyl)-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4g). Yellow solid; mp 167-169 °C; FT-IR (KBr): 3383, 3012, 2928, 1662, 1626, 1565, 1531, 1485, 1377, 1340, 1239, 1188, 1159, 1096, 1028, 972, 761, 735, 656 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.22 (s, 1H, OH) 8.51 (s, 1H, OH), 8.07 (d, J = 1.5 Hz, 1H, hetero aromatic), 8.02 (s, 1H, NH), 7.50 (d, J = 7.8 Hz, 1H, aromatic), 7.37-7.30 (m, 1H, aromatic), 7.28 (d, J = 8.1 Hz, 1H, aromatic), 7.12 (t, J = 7.0 Hz, 1H, aromatic), 7.05 (dd, J = 10.9, 4.0 Hz, 1H, aromatic), 7.00-6.94 (m, 3H, aromatic), 6.88 (d, J = 2.2 Hz, 1H, aromatic), 6.69-6.61 (m, 1H, aromatic), 4.34 (q, J = 7.1 Hz, 3H, OCH_2), 3.62-3.50 (m, 1H, CH), 3.29-3.17 (m, 1H, CH), 3.15-3.02 (m, 1H, CH), 1.38 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.2, 168.7, 161.0, 151.8, 137.9, 136.2, 134.5, 130.1, 126.6, 123.1 (d, J = 295.1 Hz), 122.9, 122.4, 119.7, 119.3, 118.4, 118.1, 117.9, 111.4, 111.0, 107.6, 103.1, 85.11 (q, J = 33.6 Hz), 61.8, 50.9, 28.2, 14.1 ppm; MS (ESI): (*m/z*) 523 $[M+Na]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{26}H_{24}F_3N_2O_5$ $[M+H]^+$ 501.1631, Found: 501.1621.

Ethyl 2-hydroxy-5-(2-hydroxybenzoyl)-1-(2-hydroxyethyl)-2-(trifluoromethyl)-1,2-dihydropyridine-3-carboxylate (4h). Pale yellow solid; mp 123-120 °C; FT-IR (KBr): 3464, 3160, 2987, 1664, 1620, 1587, 1543, 1427, 1369, 1338, 1265, 1243, 1163, 1089, 1044, 979, 952, 769 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.45 (s, 1H, OH) 8.61 (s, 1H, OH), 8.14 (d, J = 1.3 Hz, 1H, hetero aromatic), 7.74 (s, 1H, hetero aromatic), 7.45 (t, J = 7.1 Hz, 2H, aromatic), 7.02 (d, J = 8.1 Hz, 1H, aromatic), 6.90 (t, J = 7.40 Hz, 1H, aromatic), 4.32 (q, J = 7.1 Hz, 2H, OCH_2), 4.13 (dt, J = 14.5, 3.7 Hz, 1H, CH), 3.84 (s, 2H, CH_2), 3.62-3.48 (m, 1H, CH), 2.03 (d, J = 3.4 Hz, 1H, OH), 1.36 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.8, 168.6, 161.5, 152.2, 135.0, 130.7, 128.0, 123.1 (d, J = 295.1 Hz), 119.5, 118.6, 118.1, 108.0, 103.1, 84.77 (q, J = 33.6 Hz), 62.7, 61.9, 52.1, 14.0 ppm; MS (ESI): (*m/z*) 402 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{18}H_{19}F_3NO_6$ $[M+H]^+$ 402.1159, Found: 402.1176.

1-(1-Benzyl-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridin-3-yl)ethanone (4i). Yellow solid; mp 103-105 °C; FT-IR (KBr): 3052, 2928, 1626, 1583, 1537, 1396, 1263, 1215, 1188, 1156, 1078, 970, 754, 704, 594 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ = 11.32 (s, 1H, OH), 9.40 (s, 1H, OH), 8.08 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.52 (d, J = 1.2 Hz, 1H, hetero aromatic), 7.42-7.30 (m, 4H, aromatic), 7.27-7.24 (m, 2H, aromatic), 7.19 (dd, J = 7.8, 1.5 Hz, 1H, aromatic), 6.98 (dd, J = 8.4, 1.1 Hz, 1H, aromatic), 6.76 (m, 1H, aromatic), 5.09 (d, J = 15.1 Hz, 1H, CH), 4.63 (d, J = 15.2 Hz, 1H, CH), 2.53 (s, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 202.3, 192.3, 161.6, 151.5, 139.6, 135.7, 135.0, 130.2, 129.1, 128.4, 128.3, 123.2 (d, J = 296.1 Hz), 119.3, 118.5, 118.3, 111.6, 108.7, 85.9 (q, J = 33.6 Hz), 52.0, 26.3 ppm; MS (ESI): (*m/z*) 418 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{19}F_3NO_4$ $[M+H]^+$ 418.1266, Found: 418.1264.

(5-Benzoyl-1-benzyl-6-hydroxy-6-(trifluoromethyl)-1, 6-dihydropyridin-3-yl)(2-hydroxyphenyl) methanone (4j). Yellow solid; mp 118-120 °C; FT-IR (KBr): 3421, 3061, 2924, 1644, 1618, 1581, 1483, 1444, 1339, 1280, 1244, 1196, 1175, 1149, 1096, 985, 760, 695, 536 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.28 (s, 1H, OH) 9.43 (s, 1H, OH), 7.77 (d, J = 0.9 Hz, 1H, aromatic), 7.75 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.70 (d, J = 1.5 Hz, 1H, hetero aromatic), 7.63-7.59 (m, 1H, aromatic), 7.58 (d, J = 1.6 Hz, 1H, aromatic), 7.50 (t, J = 7.7 Hz, 2H, aromatic), 7.41-7.33 (m, 4H, aromatic), 7.31 (m, 2H, aromatic), 7.21 (dd, J = 1.7, 8.0 1H, Hz, aromatic), 6.94 (dd, J = 0.9, 8.4 Hz, 1H, aromatic), 6.73 (m, 1H, aromatic), 5.15 (d, J = 15.1 Hz, 1H, CH), 4.70 (d, J = 15.1 Hz, 1H, CH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 200.4, 192.4, 161.5, 150.7, 141.2, 137.1, 135.7, 135.0, 133.2, 130.3, 129.5, 129.2, 128.6, 128.5, 128.4, 123.1 (d, J = 294.2 Hz), 119.1, 118.3, 118.2, 111.3, 108.1, 86.3 (q, J = 33.6 Hz), 52.1 ppm; MS (ESI): (*m/z*) 480 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{27}H_{21}F_3NO_4$ $[M+H]^+$ 480.1393, Found: 480.1402.

(1-Benzyl-2-hydroxy-5-(2-hydroxybenzoyl)-2-(trifluoromethyl)-1,2-dihydropyridin-3-yl)(furan-2-yl) methanone (4k). Wine red viscous liquid; FT-IR (KBr): 3031, 2927, 1628, 1584, 1536, 1460, 1389, 1338, 1283, 1246, 1176, 1131, 976, 760, 700, 664, 539 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.36 (brs, 1H, OH), 9.36 (s, 1H, OH), 8.26 (d, J = 1.5 Hz, 1H,

hetero aromatic), 7.68 (brs, 1H, aromatic), 7.59 (s, 1H, aromatic), 7.32-7.41 (m, 5H, aromatic), 7.23-7.31 (m, 3H, aromatic), 6.93 (d, J = 8.2 Hz, 1H, aromatic), 6.76 (t, J = 7.9 Hz, 1H, aromatic), 6.60 (m, 1H, aromatic), 5.12 (d, J = 15.1 Hz, 1H, CH), 4.68 (d, J = 15.1 Hz, 1H, CH) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 192.5, 184.2, 161.6, 151.4, 150.6, 147.6, 139.8, 135.7, 135.0, 130.4, 129.1, 128.4, 128.3, 123.0 (d, J = 294.2 Hz), 120.8, 119.2, 118.3, 118.2, 112.5, 110.3, 108.4, 86.0 (q, J = 33.6 Hz), 52.1 ppm; MS (ESI): (*m/z*) 470 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{25}H_{19}F_3NO_5$ $[M+H]^+$ 470.1209, Found: 470.1197.

General procedure for the preparation of 2-hydroxybenzoyl-1,2-dihydropyridone-3-carboxylates (5a-e)

Ethyl 4,4,4-trichloro-3-oxobutanoate (**3h**, 1.5 mmol) was added to a stirred solution of 3-formylchromone (**1a**, 1 mmol) and benzylamine (**2b**, 1.2 mmol) in CH_3CN (2 mL). The contents were stirred under reflux conditions for 6 h. After completion of the reaction (TLC), the residue was purified by column chromatography by using silica gel (100:200, ethyl acetate/hexane 24:76) afforded ethyl 1-benzyl-5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridine-3-carboxylate **5a**. Similarly, compounds **5b-e** prepared from corresponding 3-formylchromones **1a-c** and benzylamines **2b-d** with **3h**.

Ethyl 1-benzyl-5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (5a). Colour less solid; mp 104-106 °C; FT-IR (KBr): 3050, 2977, 1729, 1650, 1622, 1537, 1481, 1425, 1340, 1271, 1237, 1175, 1146, 1115, 1018, 949, 885, 754, 699 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.36 (s, 1H, OH), 8.51 (d, J = 2.6 Hz, 1H, hetero aromatic), 8.13 (d, J = 2.6 Hz, 1H, hetero aromatic), 7.51 (t, J = 7.4 Hz, 1H, aromatic), 7.44-7.28 (m, 6H, aromatic), 7.06 (d, J = 8.3 Hz, 1H, aromatic), 6.85 (t, J = 7.5 Hz, 1H, aromatic), 5.24 (s, 2H, CH_2), 4.39 (q, J = 7.1 Hz, 2H, OCH_2), 1.38 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.2, 164.0, 162.4, 158.6, 146.1, 143.5, 136.4, 134.7, 131.3, 129.2, 128.7, 128.7, 120.3, 118.9, 118.7, 118.3, 115.7, 61.6, 53.1, 14.2 ppm; MS (ESI): (*m/z*) 400 $[M+Na]^+$; HRMS (ESI) calcd. for $C_{22}H_{19}NO_5Na$ $[M + Na]^+$ 400.1155, Found: 400.1148.

Ethyl 5-(2-hydroxybenzoyl)-1-(4-methoxybenzyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (5b). Yellow solid; mp 142-144 °C; FT-IR (KBr): 3050, 2923, 1732, 1654, 1580, 1451, 1378, 1344, 1302, 1226, 1207, 1140, 1020, 960, 835, 737, 701, 674 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.15 (s, 1H), 8.51 (d, J = 2.7 Hz, 1H, hetero aromatic), 8.12 (d, J = 2.7 Hz, 1H, hetero aromatic), 7.42-7.36 (m, 5H, aromatic), 7.31 (dd, J = 8.4, 2.0 Hz, 1H, aromatic), 7.12 (d, J = 1.3 Hz, 1H, aromatic), 6.96 (d, J = 8.5 Hz, 1H, aromatic), 5.23 (s, 2H, CH_2), 4.39 (q, J = 7.1 Hz, 2H, OCH_2), 2.21 (s, 3H, CH_3), 1.39 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.1, 163.9, 160.3, 158.6, 146.0, 143.5, 137.3, 134.8, 131.0, 129.2, 128.7, 128.7, 120.1, 120.4, 118.4, 118.1, 115.7, 61.4, 52.9, 20.3, 14.1 ppm; MS (ESI): (*m/z*) 414 $[M+Na]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{22}O_5N$ $[M + H]^+$ 392.1492, Found: 392.1481.

Ethyl 5-(2-hydroxybenzoyl)-1-(4-methoxybenzyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (5c). Colour less solid; mp 130-132 °C; FT-IR (KBr): 3444, 3013, 1728, 1623, 1603, 1537, 1426, 1404, 1340, 1270, 1204, 1175, 1122, 1019, 949, 825, 741, 703, 641 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ 11.20 (s, 1H), 8.50 (d, J = 2.7 Hz, 1H, hetero aromatic), 8.13 (d, J = 2.7 Hz, 1H, hetero aromatic), 7.45 (dd, J = 8.9, 2.6 Hz, 1H, aromatic), 7.43-7.36 (m, 5H, aromatic), 7.35 (d, J = 2.5 Hz, 1H, aromatic), 7.03 (d, J = 8.9 Hz, 1H, aromatic), 5.23 (s, 2H, CH_2), 4.40 (q, J = 7.1 Hz, 2H, OCH_2), 1.39 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.1, 163.7, 160.7, 158.2, 146.1, 143.1, 136.1, 134.4, 130.2, 129.3, 128.9, 128.8, 123.7, 120.7, 120.3, 119.1, 115.1, 61.6, 53.3, 14.1 ppm; MS (ESI): (*m/z*) 412 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{19}O_5N$ Cl $[M + H]^+$ 412.0946, Found: 412.0932.

Ethyl 5-(2-hydroxybenzoyl)-1-(4-methoxybenzyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (5d). Colour less solid; mp 100-102 °C; FT-IR (KBr): 3050, 2853, 1726, 1650, 1624, 1536, 1515, 1426, 1341, 1270, 1218, 1179, 1144, 1035, 803, 752, 656 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.37 (s, 1H, OH), 8.49 (d, J = 2.4 Hz, 1H, hetero aromatic), 8.12 (d, J = 2.4 Hz, 1H, hetero aromatic), 7.51 (t, J = 7.4 Hz, 1H, aromatic), 7.37 (d, J = 7.4 Hz, 1H, aromatic), 7.33 (d, J = 8.3 Hz, 2H, aromatic), 7.06 (d, J = 8.3 Hz, 1H, aromatic), 6.91 (d, J = 8.5 Hz, 2H, aromatic), 6.86 (t, J = 7.4 Hz, 1H, aromatic), 5.17 (s, 2H, CH_2), 4.39 (q, J = 7.1 Hz, 2H, OCH_2), 3.81 (s, 3H), 1.39 (t, J = 7.1 Hz, 3H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.2, 164.0, 162.4, 159.9, 158.7, 145.9, 143.4, 136.3, 131.3, 130.4, 126.6, 120.1, 118.9, 118.7, 118.4, 115.6, 114.5, 61.5, 55.2, 52.7, 14.2 ppm; MS (ESI): (*m/z*) 430 $[M+Na]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{22}NO_6$ $[M + H]^+$ 408.1247, Found: 408.1261.

Ethyl 1-(4-fluorobenzyl)-5-(2-hydroxybenzoyl)-2-oxo-1,2-dihydropyridine-3-carboxylate (5e). Colour less solid; mp 120-122 °C; FT-IR (KBr): 3052, 2982, 1722, 1625, 1603, 1538, 1511, 1401, 1342, 1272, 1222, 1142, 1092, 802, 758, 657, 593, 439 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.35 (s, 1H, OH), 8.51 (d, J = 2.7 Hz, 1H, hetero aromatic), 8.15 (d, J = 2.7 Hz, 1H, hetero aromatic), 7.56-7.50 (m, 1H, aromatic), 7.42-7.39 (m, 3H, aromatic), 7.11-7.05 (m, 3H, aromatic), 6.91-6.86 (m, 1H, aromatic), 5.21 (s, 2H, CH_2), 4.39 (q, J = 7.1 Hz, 2H, OCH_2), 1.41-1.35 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 194.2, 163.8, 163.8, 163.7, 162.4, 161.8, 158.5, 145.9, 143.5, 136.4, 131.3, 130.6, 130.6, 120.3, 118.9, 118.8, 118.3, 116.2, 116.0, 115.9, 61.5, 52.7, 14.1 ppm; MS (ESI): (*m/z*) 418 $[M+Na]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{19}FNO_5$ $[M + H]^+$ 396.1247, Found: 396.1263.

General procedure for the preparation of 2-hydroxy-benzoyl-trifluoromethyl-benzopyrido-1,3-oxazole-4-carboxylates (7a-f)

Ethyl 4,4,4-trifluoro-3-oxobutanoate (**3a**, 1.5 mmol) was added to a stirred solution of 3-formylchromone (**1a**, 1 mmol) and 2-aminophenol (**6a**, 1.2 mmol) in CH_3CN (2 mL). The contents were stirred under reflux conditions for 4 h. After completion of the reaction (TLC), the residue was purified by column chromatography by using silica gel (100:200, ethyl acetate/hexane 8:92) afforded ethyl 2-(2-hydroxybenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate **7a**. Similarly, compounds **7b-f** were prepared from corresponding 3-formylchromones **1a-c** and 2-aminophenols **6a-c** with **3a** and **3g**.

Ethyl 2-(2-hydroxybenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate (7a). Yellow solid; mp 160-162 °C; FT-IR (KBr): 3066, 2963, 1699, 1622, 1590, 1528, 1488, 1314, 1287, 1213, 1179, 1161, 1069, 966, 764, 737, 707 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$): δ 11.49 (s, 1H, OH) 8.25 (s, 1H, hetero aromatic), 7.98 (s, 1H, hetero aromatic), 7.49-7.59 (m, 2H, aromatic), 7.14-7.24 (m, 3H, aromatic), 7.08 (d, 2H, J = 8.3 Hz, aromatic), 7.02-6.94 (m, 1H, aromatic), 4.30 (m, 2H, OCH_2), 1.38 (t, 3H, J = 7.0 Hz, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.2, 162.5,162.1, 148.2, 138.2, 135.7, 135.6, 131.0, 129.7, 127.1, 122.9, 121.2 (d, J = 296.9 Hz), 119.5, 118.9, 118.5, 112.2, 111.4, 110.5, 106.2, 84.3 (q, J = 35.4 Hz), 61.2, 14.2 ppm; MS (ESI): (*m/z*) 454 $[M+Na]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{17}F_3NO_5$ $[M+H]^+$ 432.1053, Found: 432.1044.

Ethyl 2-(2-hydroxy-5-methylbenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate (7b). Yellow solid; mp 125-127 °C; FT-IR (KBr): 3090, 2925, 1722, 1626, 1584, 1527, 1488, 1398, 1315, 1261, 1196, 1180, 1065, 971, 758 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 11.25 (s, 1H, OH), 8.24 (d, J = 1.0 Hz, 1H, hetero aromatic), 7.98 (d, J = 1.2 Hz, 1H, hetero aromatic), 7.34 (dd, J = 8.4, 2.1 Hz, 1H, aromatic), 7.31 (d, J = 1.5 Hz, 1H, aromatic), 7.23-7.15 (m, 3H, aromatic), 7.09-7.05 (m, 1H, aromatic), 6.99 (d, J = 8.4 Hz, 1H,aromatic), 4.44-4.30 (m, 2H, OCH_2), 2.35 (s, 3H, CH_3), 1.38 (t, J = 7.0 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.1, 162.5, 159.9, 148.2, 138.0, 136.7, 135.7, 130.6, 129.7, 128.0, 127.0, 122.9, 121.2 (d, J = 296.1 Hz), 119.2, 118.2, 112.3, 111.3, 110.5, 106.1, 94.3 (q, J = 35.4 Hz), 61.2, 20.6, 14.2 ppm; MS (ESI): (*m/z*) 466 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{23}H_{19}F_3NO_5$ $[M+H]^+$ 446.1215, Found: 446.1188.

Ethyl 2-(5-chloro-2-hydroxybenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate (7c). Yellow solid; mp 150-152 °C; FT-IR (KBr): 3088, 2983, 1720, 1692, 1625, 1584, 1528, 1494, 1466, 1319, 1280, 1258, 1235, 1208, 1069, 966, 753 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$): δ 11.34 (s, 1H, OH), 8.23 (d, J = 1.1 Hz, 1H, hetero aromatic), 7.99 (d, J = 1.1 Hz, 1H, hetero aromatic), 7.51-7.45 (m, 2H, aromatic), 7.25-7.21 (m, 2H, aromatic), 7.20-7.17 (m, 1H, aromatic), 7.11-7.07 (m, 1H, aromatic), 7.04 (d, J = 8.8 Hz, 1H, aromatic), 4.44-4.31 (m, 2H, OCH_2), 1.39 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 191.9, 162.3, 130.5, 148.3, 138.4, 135.5, 135.2, 129.8, 129.5, 127.4, 123.6, 123.0, 121.1 (d, J = 296.1 Hz), 120.2, 120.1, 111.9, 11.4, 110.7, 106.6, 94.3 (q, J = 35.4 Hz), 61.3, 14.2 ppm; MS (ESI): (*m/z*) 466 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{16}ClF_3NO_5$ $[M+H]^+$ 466.0669, Found: 466.0632.

Ethyl 2-(2-hydroxybenzoyl)-8-methyl-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate (7d). Yellow solid; mp 182-184 °C; FT-IR (KBr): 3082, 2922, 1702, 1621, 1587, 1526, 1401, 1349, 1267, 1213, 1189, 1060, 965, 816, 759, 663 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 11.51 (s, 1H, OH) 8.25 (s, 1H, hetero aromatic), 7.96 (s, 1H, hetero aromatic), 7.49-7.59 (m, 2H, aromatic), 6.95-7.10 (m, 5H, aromatic), 4.27-4.45 (m, 2H, OCH_2), 2.34 (s, 3H,CH_3), 1.38 (t, 3H, J = 7.2 Hz, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.2, 162.5, 162.1, 146.3, 138.2, 135.7, 135.5, 133.1, 131.0, 129.6, 127.5, 120.5 (d, J = 297.1 Hz), 119.5, 118.9, 118.5, 112.1, 111.1, 110.9, 106.2, 95.1 (d, J = 35.7 Hz), 61.2, 21.1, 14.2 ppm; MS (ESI): (*m/z*) 446 $[M+H]^+$; HRMS-ESI (*m/z*) calcd. for $C_{23}H_{19}F_3NO_5$ $[M+H]^+$ 446.1209, Found: 446.1223.

Ethyl 8-chloro-2-(2-hydroxybenzoyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazole-4-carboxylate (7e). Yellow solid; mp 170-172 °C; FT-IR (KBr): 3086, 2923, 1701, 1624, 1592, 1530, 1485, 1396, 1295, 1237, 1208, 1162, 1069, 983, 821, 758, 693 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 11.45 (s, 1H, OH), 8.24 (d, J = 1.0 Hz, 1H, hetero aromatic), 7.87 (d, J = 0.8 Hz, 1H, hetero aromatic), 7.59-7.49 (m, 2H, aromatic), 7.15 (dd, J = 6.1, 1.9 Hz, 2H, aromatic), 7.11-7.05 (m, 2H, aromatic), 7.02-6.95 (m, 1H, aromatic), 4.46-4.28 (m, 2H, OCH_2), 1.38 (t, J = 7.1 Hz, 3H, CH_3) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.1, 162.2, 162.2, 146.9, 137.9, 136.0, 135.5, 131.0, 130.9, 128.2, 126.7, 121.0 (d, J = 296.1 Hz), 119.3, 119.0, 118.6, 112.9, 112.0, 111.1, 106.9, 95.9 (d, J = 35.4 Hz), 61.4, 14.2 ppm; MS (ESI): (*m/z*) 466 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{22}H_{16}ClF_3NO_5$ $[M+H]^+$ 466.0663, Found: 466.0388.

[4-(2-Furylcarbonyl)-4a-(trifluoromethyl)-4a*H*-benzo[*d*]pyrido[2,1-*b*][1,3]oxazol-2-yl](2-hydroxyphenyl)methanone (7f). Yellow solid; mp 154-156 °C; FT-IR (KBr): 3063, 1628, 1588, 1510, 1463, 1278, 1246, 1189, 1155, 1086, 977, 754, 711 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 11.51 (s, 1H), 8.33 (brs, 1H hetero aromatic), 8.05 (brs, 1H, hetero aromatic), 7.69 (d, J = 0.8 Hz, 1H), 7.67-7.60 (m, 1H), 7.60-7.52 (m, 1H), 7.28 (s, 1H), 7.25-7.18 (m, 3H), 7.09 (dd, J = 10.7, 5.6 Hz, 2H), 7.02 (t, J = 7.2 Hz, 1H), 6.60 (dd, J = 3.5, 1.7 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$): δ 193.2, 176.8, 162.1, 152.5, 148.7, 146.7, 137.9, 135.8, 135.3, 131.0, 129.5, 127.2, 122.9, 120.4 (d, J = 296.5 Hz), 119.6, 119.5, 118.9, 118.5, 112.5, 112.2, 111.5, 110.6, 94.6 (d, J = 35.7 Hz) ppm; MS (ESI): (*m/z*) 454 $[M+H]^+$; HRMS (ESI) (*m/z*) calcd. for $C_{24}H_{15}F_3NO_5$ $[M+H]^+$ 454.0902, Found: 454.0866.

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