

# One Pot Three Component Diastereoselective Synthesis of Tricyclic Furoquinolones and Furocoumarins

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**Abstract.** A new synthetic strategy for the construction of dihydrofuro coumarins and quinolones has been developed by a three component reaction. Formation of 2,3-dihydrofuran ring and the trans orientation is supported by <sup>1</sup>H-NMR and confirmed single X-ray diffraction studies.

**Keywords:** One-pot multicomponent, furo-coumarin, furo-quinoline, X-ray, diastereoselective synthesis, 4-hydroxy-coumarin and carbostyryl.

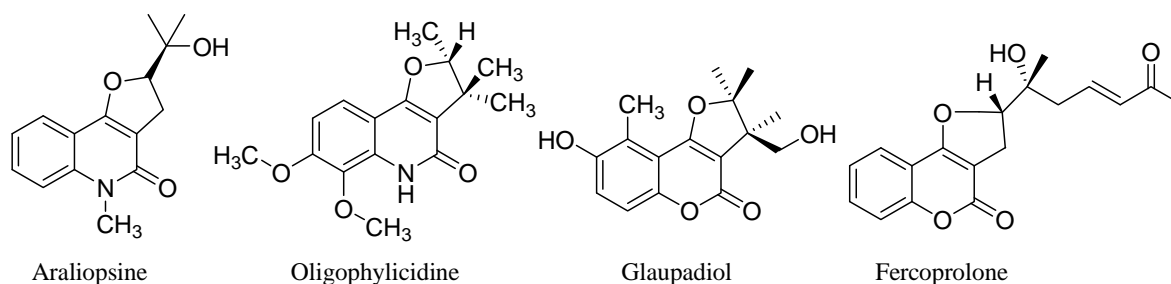
## 1. Introduction

Multicomponent reactions (MCR) have played an important role in modern organic synthesis since they provide a short route to moderately complex molecular assemblies in a stereo-selective fashion [1]. Multi component strategies have been developed for asymmetric synthesis [2], natural product synthesis [3] and diversity oriented organic synthesis [4]. Three component reactions have been employed for the synthesis of a variety of heterocycles [5]. Coumarins are a group of naturally occurring lactones, the derivatives of which have been obtained by employing the multicomponent reaction methodology. 3-Bromocoumarins [6], 3-amino coumarins [7], and tricyclic pyrimidine fused coumarins [8] have been synthesized by a three component reaction strategy from salicylaldehydes. 4-hydroxy coumarins have been used in the construction of pyran and furan fused tricyclic systems [9-11]. Ugi-4CR reactions involving coumarin 3-carboxylic acid were employed for the construction of amides with lipophilic spacers [12] and chromeno [3,4-c] pyrroles [13].

Quinoline and dihydroquinoline fused tetracyclic coumarins have been generated by a three component reaction of 4-hydroxy coumarins, aromatic amines and aldehydes [14]. Biginelli multi component reaction strategy using coumarin-3-β-ketoester, aromatic aldehydes and urea/thiourea has resulted in fluorescent 4-3' coumarinyl dihydropyrimidinones and pyrimidinthiones [15]. An interesting non-Ugi 4CR has been reported on coumarin 3-β-ketoester with chlorobenzaldehydes, phenylhydrazine and malononitrile leading to a one pot synthesis of coumarin linked dihydropyrano [2,3-c] pyrazoles [16]. Recently, Lanthanum triflate catalyzed diastereoselective synthesis of fluorescent indolyl malonamides has been reported by using a three component reaction between coumarin 3-carboxylates, indoles and aromatic amines [17].

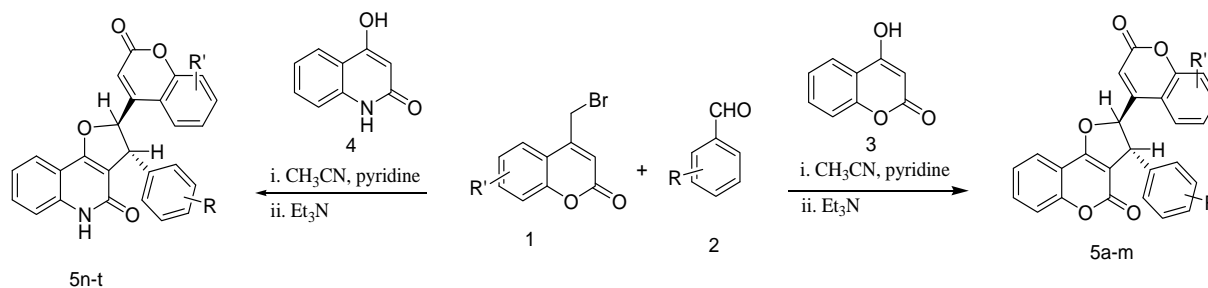
Dihydro furo [3,2-c]coumarin and corresponding quinolone skeleton has been a part of many naturally occurring compounds (Figure 1) [18-22]. It is pertinent to mention that dihydro furoquinolones have been found to exhibit broad spectrum of anti-fungal activity [23-24]. Corresponding furocoumarins with trans orientation of the groups at C-2 and C-3 positions in the furan ring exhibited anti-mitotic activity which synergistically enhanced the action of paclitaxel [25]. Naturally occurring 5-methyl furocoumarins have been found to be inhibitors of Plasmodium falciparum [26].

The tricyclic dihydroquinolones have been synthesized by photochemical transformations [27], 2+3 cycloaddition [28], Silver (I) promoted oxidative addition [29] and stepwise approach [30]. The corresponding oxygen analogues have been synthesized from 4-O-alkylated coumarins [31], Rhodium (II)



**Figure 1.** Naturally occurring dihydro [3,2-c] furo quinolones and coumarins

catalysed reaction of cyclic diazodicarbonyl compounds [32], tandem reactions of 4-hydroxycoumarins [33] and other routes [34]. In view of the hitherto mentioned variety of synthetic approaches for the two isosteric tricyclic skeletons, it is quite challenging to evolve a common synthetic strategy through which the two skeletons can be generated in a single step. We have shown that 2,3-dihydro benzofurans linked to C-4 position of coumarin moiety can be generated by the room temperature intramolecular aldol reaction of ortho carbonylated 4-aryloxymethyl coumarins [35] or the corresponding imines [36]. In continuation of our earlier work, design of a three component reaction was envisaged (Scheme 1). The ambident nucleophilicity of 4-hydroxy coumarin and 4-hydroxy carbostyryl was effectively used *in-situ*, in a cascaded manner in its reaction with aromatic aldehydes and 4-bromomethyl coumarins in presence of pyridine and triethylamine.



**Scheme 1.** Synthesis of furo[3,2-c]chromen-4-one/quinolin-4(5H)-ones by one-pot reaction.

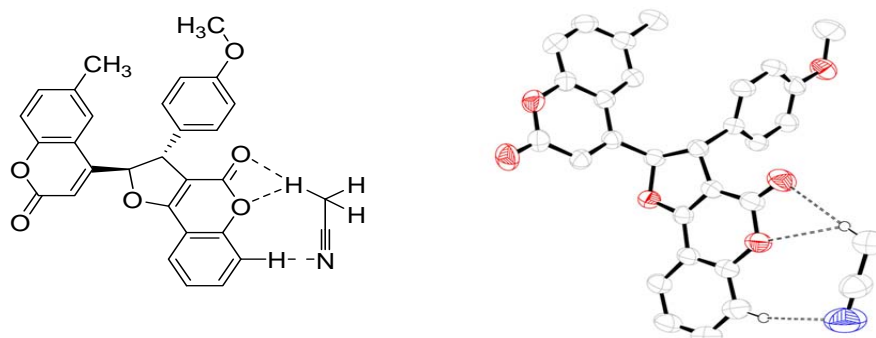
## 2. Results and Discussions

The required substituted 4-bromomethylcoumarins [37] **1** were prepared by the Pechmann cyclization of substituted phenols with 4-bromoethylacetoacetate [38] using sulfuric acid as the condensing agent.

The three component reaction between 4-bromomethyl coumarins **1** and benzaldehyde **2** (R= H) and 4-hydroxy coumarin **3** in presence of pyridine using chloroform as solvent at room temperature resulted in the formation of a white crystalline solid corresponding to the 4-coumarinomethyl pyridinium hydrobromide. Employing reflux conditions and using acetonitrile as solvent also did not bring about any change as the expected Knoevenagel condensation between 4-hydroxy coumarin **3** and benzaldehyde **2**. Hence it was thought of using another base in conjunction with pyridine allowing sufficient time for the two reactive species to be generated. The three reactants viz. 4-bromomethyl coumarin **1**, aromatic aldehyde **2** and 4-hydroxy coumarin **3** were refluxed in acetonitrile for 2 h, using three equivalents of pyridine followed by the addition of one equivalent of triethyl amine. The reaction conditions ensured the formation of pyridinium bromide and a Knoevenagel product from Benzaldehyde **2** and 4-hydroxy coumarin **3**. Excess of base in this reaction was found to be necessary for the *in-situ* generation of the ylide stabilized carbanion at the allylic position of coumarin. Refluxing was continued overnight, the usual work up and purification afforded the tricyclic furanocoumarins **5**.

In a typical case, compound **5k**, three proton singlets at 2.24 and 3.80 ppm indicated methyl and methoxy group respectively. Protons in the dihydrofuran ring appeared as doublets at 6.17 and 4.44 ppm ( $J = 4.8$  Hz) which are assigned to C2-H and C3-H respectively. Assignment of the downfield signal to the C2-H is also confirmed by its allylic relationship with C3-H of coumarin, which is reflected

in compound 5d in which the C2-H at 6.59 ppm appears as doublet of doublet ( $J = 0.8, 5.6$  Hz), the C3-H of coumarin appears at 6.35 ppm as doublet ( $J = 0.8$  Hz) and the C3-H of dihydrofuran is observed at 4.53 ppm as doublet ( $J = 5.6$  Hz). Observed  $J$  values are in conformity with reported  $^3J_{\text{H-H}}$  values for the *trans*-2,3 dihydrofurans [29]. X-ray structure for 5k (CCDC 898526) which is solvated with acetonitrile provides a proof for the proposed stereochemistry (Figure 2). Crystal determination and refinement data of compound 5k are provided in Table 1. Lactone carbonyl oxygen of coumarin shows the intermolecular association with the CH<sub>3</sub> group and C8-H is associated with nitrogen atom of acetonitrile.



**Figure 2.** ORTEP diagram of 5k as acetonitrile solvate

**Table 1.** Crystal and experimental data of compound 5k

Crystal Data	
Chemical Formula	C <sub>28</sub> H <sub>20</sub> O <sub>6</sub> ·C <sub>2</sub> H <sub>3</sub> N
$M_r$	493.49
Crystal system, space group	Triclinic, <i>P</i> -1
Temperature (K)	296
a, b, c (Å)	7.4588 (3), 9.3676 (4), 18.8953 (8)
$\alpha, \beta, \gamma$ (°)	84.535 (3), 80.467 (3), 73.215 (3)
$V$ (Å <sup>3</sup> )	1244.96 (9)
Z	2
Radiation type	Mo K $\alpha$
$\mu$ (mm <sup>-1</sup> )	0.09
Crystal size (mm)	0.2 x 0.18 x 0.18
<b>Data collection</b>	
Diffractometer	Bruker Smart APEX CCD detector diffractometer
Absorption correction	Multi-scan
$T_{\min}, T_{\max}$	0.982, 0.984
No. of measured, independent and observed [ $I > 2\sigma(I)$ ] reflections	19318, 4628, 3118
$R_{\text{int}}$	0.034
$(\sin\theta/\lambda)_{\text{max}}$ (Å <sup>-1</sup> )	0.606
<b>Refinement</b>	
R[F <sup>2</sup> > 2 $\sigma$ (F <sup>2</sup> )], wR(F <sup>2</sup> ), S	0.051, 0.140, 1.05
No. of reflections	4628
No. of parameters	337
No. of restraints	0
H-atom treatment	H-atom parameters constrained
$\Delta_{\text{max}}, \Delta_{\text{min}}$ (e Å <sup>-3</sup> )	0.21, -0.17

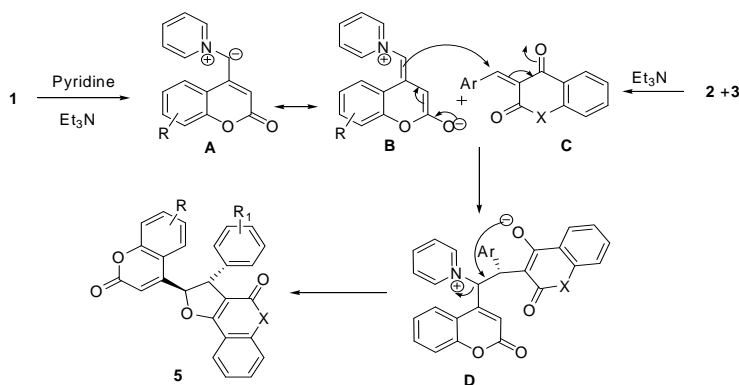
Robustness of the present methodology has been extended to other aromatic aldehydes and 4-bromomethyl coumarins to obtain various compounds 5a-5m (Table 2). Then we turned our attention to use 4-hydroxy carbostyryl 4 in this reaction. Direct application of the optimized reaction conditions resulted in the formation of isosteric compounds 5n-5t (Table 2).

**Table 2.** Physical data for compounds 5a-t.

Compd.	R'	R	Yield (%) <sup>a</sup>	m.p. <sup>b</sup> (°C)	Mass (m/z) <sup>c</sup>
5a	-H	6-OCH <sub>3</sub>	84	240-242	438
5b	4-Cl	7-CH <sub>3</sub>	87	260-262	456/458
5c	4-OCH <sub>3</sub>	7,8-CH <sub>3</sub>	83	248-250	466
5d	-H	7,8-CH <sub>3</sub>	88	272-274	436
5e	4-Cl	7,8-CH <sub>3</sub>	84	242-244	470/ 472
5f	2-Cl	6-CH <sub>3</sub>	82	237-239	456/458
5g	4-NO <sub>2</sub>	6-CH <sub>3</sub>	87	265-267	467
5h	2-Cl	7-CH <sub>3</sub>	82	238-240	456/458
5i	-H	7-CH <sub>3</sub>	89	192-194	422
5j	-H	6-CH <sub>3</sub>	85	278-280	422
5k	4-OCH <sub>3</sub>	6-CH <sub>3</sub>	86	230-232	452
5l	4-OCH <sub>3</sub>	7-CH <sub>3</sub>	88	231-233	452
5m	4-Cl	6-CH <sub>3</sub>	84	276-278	456/458
5n	2-Cl	6-CH <sub>3</sub>	87	>300	456/458
5o	4-OCH <sub>3</sub>	7-CH <sub>3</sub>	86	>300	452
5p	-H	7-CH <sub>3</sub>	89	>300	421 ( M-H)
5q	4-OCH <sub>3</sub>	6-CH <sub>3</sub>	85	290-292	451
5r	4-OCH <sub>3</sub>	6-Cl	87	261-263	471/473
5s	4-OCH <sub>3</sub>	6-OCH <sub>3</sub>	89	270-272	467
5t	4-OCH <sub>3</sub>	7,8-CH <sub>3</sub>	86	290-292	465

<sup>a</sup>Yield refers to the isolated crude compound. <sup>b</sup>Uncorrected <sup>c</sup>m/z values refer to the EI ms.

Based on our observations a plausible mechanistic pathway (Figure 3) is proposed. 4-bromomethyl coumarins 1 would form a carbanion stabilized as a pyridinium ylide A and an enolate B, which explains the ease with which this reactive species can be generated. Aromatic aldehydes 2 would react with 4-hydroxy coumarin/quinoline 3/4 to form the Knoevenagel adduct C. Nucleophilic addition of B at the  $\beta$ -position of C, would generate an enolate D in a typical Michael reaction. A back side nucleophilic attack on to the carbon bearing pyridine as the leaving group leads to the formation of compounds 5 with dihydrofuran moiety which probably explains the observed trans stereochemistry. All the three steps in this pathway occur in a tandem reaction. It is interesting to note that the electrophilic carbon in compounds 1 acts as a nucleophile in the Micheal addition step and the overall three component reaction sequence a 1+3+1 approach for the construction of five membered rings.



**Figure 3.** Plausible mechanistic pathway for the formation of furo quinolones and furo coumarins 4.

## 3 Experimental

### 3.1 General Methods

Melting points were determined in open capillaries and are uncorrected. Infrared spectra were recorded on a Nicolet (FT-IR) spectrometer ( $\nu$  max in  $\text{cm}^{-1}$ ),  $^1\text{H}$  (400 MHz),  $^{13}\text{C}$  (100 MHz) were recorded on a Bruker (400 MHz) spectrometer.

### 3.2 General Procedure for Synthesis of trans-2,3-dihydro-2-(2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]chromen-4-ones/ quinolin-4(5H)-ones (5a-t)

A mixture of benzaldehyde (0.01mol, 1g), 4-hydroxy-2H-chromen-2-one/quinolin-4(5H)-ones (0.01mol, 1.26g), 4-(bromomethyl)-2H-chromen-2-one (0.01mol), and pyridine (0.03 mol, 2.37g) in acetonitrile (15 mL) was taken in 100 ml R.B flask fitted with condenser containing guard tube and reaction mixture was refluxed for 2 h. Then triethylamine (0.03mol, 3.03g) was added and resulting reaction mixture was refluxed for 12 h. Progress of the reaction was monitored by checking the TLC. After completion of the reaction, reaction mixture was cooled and obtained solid was filtered and dried. All the title compounds were further purified by crystallization in acetonitrile so as to get the pure product.

### 3.3 Physical and Spectral Data

#### 3.3a: 2,3-dihydro-2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]chromen-4-one (5a).

Colorless solid (acetonitrile), mp 240-242 oC, yield 84%; IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 1722 ( $-\text{C}=\text{O}$ ).  $^1\text{H}$ -NMR (400 MHz, DMSO): 3.38 (s, 3H,  $-\text{OCH}_3$ ), 4.60 (d, 1H,  $J = 5.6$  Hz,  $-\text{CH}-$ ), 6.43 (s, 1H, C3-H), 6.51 (d, 1H,  $J = 2.8$  Hz, Ar-H), 6.69 (d, 1H,  $J = 5.6$  Hz,  $-\text{CH}-$ ), 7.21 (dd, 1H,  $J = 2.8, 9.2$  Hz, Ar-H), 7.35-7.37 (m, 1H, Ar-H), 7.40-7.42 (m, 5H, Ar-H), 7.47-7.52 (m, 2H, Ar-H), 7.74-7.79 (m, 1H, Ar-H), 7.98 (dd, 1H,  $J = 1.2, 7.6$  Hz, Ar-H),  $m/z = 438$ .  $^{13}\text{C}$ -NMR: 52.6, 54.9, 89.1, 105.3, 107.1, 110.9, 111.5, 116.2, 116.6, 118.0, 120.2, 123.1, 124.5, 127.8, 128.1, 128.8, 133.3, 139.5, 147.8, 151.9, 154.7, 155.1, 158.1, 159.6, 164.9. MS  $m/z = 438$ . Anal. calc. for  $\text{C}_{27}\text{H}_{18}\text{O}_6$ : C, 73.97; H, 4.14. Found: C, 73.92; H, 4.16.

#### 3.3b: 3-(4-chlorophenyl)-2,3-dihydro-2-(7-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5b).

Colorless solid (acetonitrile), mp 260-262 oC, yield 87%; IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 1724 ( $-\text{C}=\text{O}$ ).  $^1\text{H}$ -NMR (400 MHz, DMSO): 2.40 (s, 3H,  $\text{CH}_3$ ), 4.63 (d, 1H,  $J = 5.6$  Hz,  $-\text{CH}-$ ), 6.37 (s, 1H, C3-H), 6.59 (dd, 1H,  $J = 0.8, 5.6$  Hz,  $-\text{CH}-$ ), 7.03 (d, 1H,  $J = 8.4$  Hz, Ar-H), 7.10 (d, 1H,  $J = 8.4$  Hz, Ar-H), 7.31 (s, 1H, Ar-H), 7.37-7.39 (m, 2H, Ar-H), 7.44-7.7.53 (m, 4H, Ar-H), 7.75-7.79 (m, 1H, Ar-H), 7.94 (dd, 1H,  $J = 1.6, 8.0$  Hz).  $^{13}\text{C}$ -NMR: 20.9, 51.7, 89.2, 105.0, 110.1, 11.6, 113.5, 116.7, 117.1, 123.1, 124.5, 124.6, 125.3, 128.8, 129.9, 132.4, 133.4, 138.5, 143.4, 151.7, 153.7, 154.8, 158.2, 159.7, 165.3. MS  $m/z = 456(\text{M})$ , 458( $\text{M}+2$ ). Anal. calc. for  $\text{C}_{27}\text{H}_{17}\text{ClO}_5$ : C, 70.98; H, 3.75. Found: C, 70.97; H, 3.73.

#### 3.3c: 2,3-dihydro-3-(4-methoxyphenyl)-2-(7,8-dimethyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5c).

Colorless solid (acetonitrile), mp 248-250 oC, yield 83%; IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 1719 ( $-\text{C}=\text{O}$ ).  $^1\text{H}$ -NMR (400 MHz, DMSO): 2.29 (s, 3H,  $\text{CH}_3$ ), 2.23 (s, 3H,  $\text{CH}_3$ ), 3.76 (s, 3H,  $-\text{OCH}_3$ ), 4.48 (d, 1H,  $J = 5.6$  Hz,  $-\text{CH}-$ ), 6.32 (d, 1H,  $J = 0.8$  Hz, C3-H), 6.52 (d, 1H,  $J = 5.6$  Hz), 6.88 (d, 1H,  $J = 8.4$ ,  $-\text{CH}-$ ), 6.93-6.96 (m, 2H, Ar-H), 7.07 (d, 1H,  $J = 8\text{Hz}$ ), 7.23 (m, 2H, Ar-H), 7.46-7.52 (m, 2H, Ar-H), 7.74-7.78 (m, 1H, Ar-H), 7.95 (dd, 1H,  $J = 1.6, 8$  Hz).  $^{13}\text{C}$ -NMR: 11.2, 19.8, 52.0, 55.1, 105.5, 109.2, 111.6, 113.6, 114.2, 116.7, 121.6, 123.1, 124.3, 124.5, 125.3, 129.0, 131.5, 133.3, 141.9, 151.6, 152.5, 154.7, 158.2, 158.8, 159.7, 164.8. MS  $m/z = 466$ . Anal. calc. for  $\text{C}_{29}\text{H}_{22}\text{O}_6$ : C, 74.67; H, 4.75. Found: C, 74.64; H, 4.76.

#### 3.3d: 2,3-dihydro-2-(7,8-dimethyl-2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]chromen-4-one (5d).

Colorless solid (acetonitrile), mp 272-274 oC, yield 88%; IR (KBr,  $\nu$  in  $\text{cm}^{-1}$ ): 1705 ( $-\text{C}=\text{O}$ ).  $^1\text{H}$ -NMR (400 MHz, DMSO): 2.229 (s, 3H,  $\text{CH}_3$ ), 2.35 (s, 3H,  $\text{CH}_3$ ), 4.53 (d, 1H,  $J = 5.6$  Hz,  $-\text{CH}-$ ), 6.35 (d, 1H,  $J = 0.8$  Hz, C3-H), 6.59 (dd, 1H,  $J = 0.8, 5.6$  Hz,  $-\text{CH}-$ ), 6.85 (d, 1H,  $J = 8.4$  Hz, Ar-H), 7.05 (d, 1H,

J = 8.0 Hz, Ar-H), 7.33-7.53 (m, 7H, Ar-H), 7.74-7.79 (m, 1H, Ar-H), 7.96 (dd, 1H, J = 1.2, 7.6 Hz). MS m/z = 436. Anal. calc. for C<sub>28</sub>H<sub>20</sub>O<sub>5</sub>: C, 77.05; H, 4.62. Found: C, 77.03; H, 4.64.

**3.3e: 3-(4-chlorophenyl)-2,3-dihydro-2-(7,8-dimethyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5e).**

Colorless solid (acetonitrile), mp 242-244 °C, yield 84%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1716 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.30 (s, 3H, CH<sub>3</sub>), 2.35 (s, 3H, CH<sub>3</sub>), 4.60 (d, 1H, J = 5.6 Hz, -CH-), 6.36 (d, 1H, J = 0.8 Hz, C3-H), 6.59 (dd, 1H, J = 1.2, 6.0 Hz, -CH-), 6.87 (d, 1H, J = 8.4 Hz, Ar-H), 7.08 (d, 1H, J = 8.4 Hz, Ar-H), 7.35-7.53 (m, 6H, Ar-H), 7.75-7.79 (m, 1H, Ar-H), 7.95 (dd, 1H, J = 1.6, 8.0 Hz). MS m/z = 470. Anal. calc. for C<sub>28</sub>H<sub>19</sub>ClO<sub>5</sub>: C, 71.42; H, 4.07. Found: C, 71.44; H, 4.05.

**3.3f: 3-(2-chlorophenyl)-2,3-dihydro-2-(7,8-dimethyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5f).**

Colorless solid (acetonitrile), mp 236-238 °C, yield 82%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1729 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.07 (s, 3H, CH<sub>3</sub>), 2.297 (s, 3H, CH<sub>3</sub>), 4.76 (d, 1H, J = 5.6 Hz, -CH-), 6.37 (d, 1H, J = 1.2 Hz, C3-H), 6.47 (d, 1H, J = 2.8 Hz, Ar-H), 6.52 (m, 1H, Ar-H), 6.68 (dd, 1H, J = 1.2, 5.6 Hz, -CH-), 7.15 (s, 1H, Ar-H), 7.37 (d, 1H, J = 8.4, Ar-H), 7.47-7.55 (m, 3H, Ar-H), 7.74-7.80 (m, 2H, Ar-H), 7.96 (dd, 1H, J = 1.6, 8.0 Hz). MS m/z = 470. Anal. calc. for C<sub>28</sub>H<sub>19</sub>ClO<sub>5</sub>: C, 71.42; H, 4.07. Found: C, 71.38; H, 3.72.

**3.3g: 2,3-dihydro-2-(6-methyl-2-oxo-2H-chromen-4-yl)-3-(4-nitrophenyl)furo[3,2-c]chromen-4-one (5g).**

Colorless solid (acetonitrile), mp 265-267 °C, yield 87%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1727 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.130 (s, 3H, CH<sub>3</sub>), 5.29 (d, 1H, J = 4.0 Hz, -CH-), 6.57 (s, 1H, C3-H), 6.77 (d, 1H, J = 4.0 Hz, -CH-), 6.98 (s, 1H, Ar-H), 7.37 (d, 1H, J = 8.4 Hz, Ar-H), 7.45-7.79 (m, 7H, Ar-H), 7.91 (d, 1H, J = 7.2 Hz, Ar-H), 8.03 (d, 1H, J = 8.4 Hz). MS m/z = 451(M-16). Anal. calc. for C<sub>27</sub>H<sub>17</sub>NO<sub>7</sub>: C, 69.38; H, 3.67; N, 3.00. Found: C, 69.36; H, 3.68; N, 3.02.

**3.3h: 3-(2-chlorophenyl)-2,3-dihydro-2-(7-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5h).**

Colorless solid (acetonitrile), mp 238-240 °C, yield 82%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1735(-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.45 (s, 3H, CH<sub>3</sub>), 5.07 (d, 1H, J = 5.4 Hz, -CH-), 6.21 (d, 1H, J = 5.4 Hz, -CH-), 6.44 (s, 1H, C3-H), 6.91-7.70 (m, 10H, Ar-H), 7.86 (d, 1H, J = 7.2 Hz). m/z: 456. Anal. calc. for C<sub>27</sub>H<sub>17</sub>ClO<sub>5</sub>: C, 70.98; H, 3.75. Found: C, 70.96; H, 3.77.

**3.3i: 2,3-dihydro-2-(7-methyl-2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]chromen-4-one (5i).**

Colorless solid (acetonitrile), mp 192-194 °C, yield 89%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1719 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.32 (s, 3H, CH<sub>3</sub>), 4.32 (d, 1H, J = 4.0 Hz, -CH-), 6.11 (d, 1H, J = 4.0 Hz, -CH-), 6.21 (s, 1H, C3-H), 6.83-6.88 (m, 2H, Ar-H), 7.07 (s, 1H, Ar-H), 7.20-7.31 (m, 7H, Ar-H), 7.53-7.56 (m, 1H, Ar-H), 7.76 (d, 1H, J = 4.5 Hz). MS m/z 422. Anal. calc. for C<sub>27</sub>H<sub>18</sub>O<sub>5</sub>: C, 76.77; H, 4.29. Found: C, 76.74; H, 4.25.

**3.3j: 2,3-dihydro-2-(6-methyl-2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]chromen-4-one (5j)**

Colorless solid (acetonitrile), mp 278-280 °C, yield 85%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1734 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.20 (s, 3H, CH<sub>3</sub>), 4.47 (d, 1H, J = 4.8 Hz, -CH-), 6.22 (d, 1H, J = 4.5 Hz, -CH-), 6.46 (s, 1H, C3-H), 6.82 (s, 1H, Ar-H), 7.26-7.44 (m, 9H, Ar-H), 7.67 (t, 1H, J = 7.5 Hz, Ar-H), 7.90 (d, 1H, J = 7.5 Hz). MS m/z 422. Anal. calc. for C<sub>27</sub>H<sub>18</sub>O<sub>5</sub>: C, 76.77; H, 4.29. Found: C, 76.76; H, 4.30.

**3.3k: 2,3-dihydro-3-(4-methoxyphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5k).**

Colorless solid (acetonitrile), mp 230-232 °C, yield 86%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1722 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.24 (s, 3H, CH<sub>3</sub>), 3.83 (s, 3H, -OCH<sub>3</sub>), 4.44 (d, 1H, J = 4.8 Hz, -CH-), 6.17 (d, 1H, J = 4.5 Hz, -CH-), 6.44 (s, 1H, C3-H), 6.87 (s, 1H, Ar-H), 6.96 (d, 2H, J = 8.4 Hz, Ar-H), 7.26-7.44 (m, 6H, Ar-H), 7.64-7.69 (m, 1H, Ar-H), 7.89 (d, 1H, J = 7.8 Hz, Ar-H). MS m/z 451 (M-1). Anal. calc. for C<sub>28</sub>H<sub>20</sub>O<sub>6</sub>: C, 74.33; H, 4.46. Found: C, 74.32; H, 4.48.

**3.3l: 2,3-dihydro-3-(4-methoxyphenyl)-2-(7-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5l).**

Colorless solid (acetonitrile), mp 231-233 °C, yield 88%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1716 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.45 (s, 3H, CH<sub>3</sub>), 3.83 (s, 3H, -OCH<sub>3</sub>), 4.43 (d, 1H, J = 4.5 Hz, -CH-), 6.17 (d, 1H, J = 4.5 Hz, -CH-), 6.36 (s, 1H, C3-H), 6.94 (d, 2H, J = 8.7 Hz, Ar-H), 7.01 (s, 2H, Ar-H), 7.22-

7.44 (m, 5H, Ar-H), 7.63-7.69 (m, 1H, Ar-H), 7.87 (d, 1H, J = 7.5 Hz). MS m/z 452. Anal. calc. for C<sub>28</sub>H<sub>20</sub>O<sub>6</sub>: C, 74.33; H, 4.46. Found: C, 74.37; H, 4.44.

**3.3m: 3-(4-chlorophenyl)-2,3-dihydro-2-(6-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]chromen-4-one (5m).**

Colorless solid (acetonitrile), mp 276-278 °C, yield 84%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1715 (-C=O). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.24 (s, 3H, CH<sub>3</sub>), 4.46 (d, 1H, J = 4.8 Hz, -CH-), 6.17 (dd, 1H, J = 0.9, 4.8 Hz, -CH-), 6.44 (s, 1H, C3-H), 6.78 (s, 1H, Ar-H), 7.26-7.45 (m, 8H, Ar-H), 7.65-7.71 (m, 1H, Ar-H), 7.89 (d, 1H, J = 8.1 Hz). MS m/z 456. Anal. calc. for C<sub>27</sub>H<sub>17</sub>ClO<sub>5</sub>: C, 70.98; H, 3.75. Found: C, 70.92; H, 3.76.

**3.3n: 3-(2-chlorophenyl)-2,3-dihydro-2-(6-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]quinolin-4(5H)-one (5n).**

Colorless solid (acetonitrile), mp >300 °C, yield 87%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1704 (-C=O), 3368 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.15 (s, 3H, CH<sub>3</sub>), 4.94 (d, 1H, J = 5.6 Hz, -CH-), 6.37 (d, 1H, J = 1.2 Hz, C3-H), 6.49 (dd, 1H, J = 1.2, 5.6 Hz, Ar-H), 6.84 (s, 1H, Ar-H), 7.28-7.64 (m, 9H, Ar-H), 7.89 (d, 1H, J = 6.8 Hz), 11.54 (s, 1H, -NH). MS m/z = 455. Anal. calc. for C<sub>27</sub>H<sub>18</sub>ClNO<sub>4</sub>: C, 71.13; H, 3.98; N, 3.07. Found: C, 71.13; H, 3.97; N, 3.04.

**3.3o: 2,3-dihydro-3-(4-methoxyphenyl)-2-(7-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]quinolin-4(5H)-one (5o).**

Colorless solid (acetonitrile), mp >300 °C, yield 86%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1736 (-C=O), 3431 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.41 (s, 3H, CH<sub>3</sub>), 3.76 (s, 3H, -OCH<sub>3</sub>), 4.40 (d, 1H, J = 4.0 Hz, -CH-), 6.18 (d, 1H, J = 0.8 Hz, C3-H), 6.38 (d, 1H, J = 4.0 Hz), 6.94 (d, 2H, J = 8.8 Hz, Ar-H), 7.11 (s, 2H, Ar-H), 7.20 (d, 2H, J = 8.4 Hz), 7.27-7.40 (m, 3H, Ar-H), 7.58-7.62 (m, 1H, Ar-H), 7.86 (d, 1H, J = 7.2 Hz), 11.51 (s, 1H, -NH). MS m/z = 455. Anal. calc. for C<sub>28</sub>H<sub>21</sub>NO<sub>5</sub>: C, 74.49; H, 4.69; N, 3.10. Found: C, 74.48; H, 4.67; N, 3.12.

**3.3p: 2,3-dihydro-2-(7-methyl-2-oxo-2H-chromen-4-yl)-3-phenylfuro[3,2-c]quinolin-4(5H)-one (5p).**

Colorless solid (acetonitrile), mp >300 °C, yield 89%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1736 (-C=O), 3399 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.41 (s, 3H, CH<sub>3</sub>), 4.46 (d, 1H, J = 4.0 Hz, -CH-), 6.20 (s, 1H, C3-H), 6.45 (d, 1H, J = 4.0 Hz, -CH-), 7.09 (s, 1H, Ar-H), 7.29-7.41 (m, 9H, Ar-H), 7.61 (t, 1H, J = 8.0 Hz, Ar-H), 7.88 (d, 1H, J = 8.0 Hz), 11.53 (s, 1H, NH). MS m/z 421. Anal. calc. for C<sub>27</sub>H<sub>19</sub>NO<sub>4</sub>: C, 76.95; H, 4.54; N, 3.32. Found: C, 76.96; H, 4.50; N, 3.33.

**3.3q: 2,3-dihydro-3-(4-methoxyphenyl)-2-(6-methyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]quinolin-4(5H)-one (5q).**

Colorless solid (acetonitrile), mp 290-292 °C, yield 85%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1730 (-C=O), 3363 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 2.20 (s, 3H, CH<sub>3</sub>), 3.77 (s, 3H, -OCH<sub>3</sub>), 4.41 (d, 1H, J = 4.0 Hz, -CH-), 6.26 (s, 1H, C3-H), 6.37 (d, 1H, J = 4.0 Hz, -CH-), 6.95-6.98 (m, 3H, Ar-H), 7.20-7.63 (m, 7H, Ar-H), 7.89 (d, 1H, J = 8.0 Hz), 11.51 (s, 1H, NH). MS m/z 451. Anal. calc. for C<sub>28</sub>H<sub>21</sub>NO<sub>5</sub>: C, 74.49; H, 4.69; N, 3.10. Found: C, 74.47; H, 4.68; N, 3.11.

**3.3r: 2-(6-chloro-2-oxo-2H-chromen-4-yl)-2,3-dihydro-3-(4-methoxyphenyl)furo[3,2-c]quinolin-4(5H)-one (5r).**

Colorless solid (acetonitrile), mp 260-262 °C, yield 87%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1737 (-C=O), 3472 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 3.76 (s, 3H, -OCH<sub>3</sub>), 4.47 (d, 1H, J = 4.0 Hz, -CH-), 6.34 (s, 1H, C3-H), 6.43 (d, 1H, J = 4.0 Hz, -CH-), 6.96 (d, 2H, J = 8.0 Hz, Ar-H), 7.17-7.72 (m, 8H, Ar-H), 7.88 (d, 1H, J = 8.0 Hz), 11.52 (s, 1H, NH). MS m/z 471. Anal. calc. for C<sub>27</sub>H<sub>18</sub>ClNO<sub>5</sub>: C, 68.72; H, 3.84; Cl, 7.51; N, 2.97. Found: C, 68.70; H, 3.86; Cl, 7.53; N, 2.96.

**3.3s: 2,3-dihydro-2-(6-methoxy-2-oxo-2H-chromen-4-yl)-3-(4-methoxyphenyl)furo[3,2-c]quinolin-4(5H)-one (5s).**

Colorless solid (acetonitrile), mp 270-272 °C, yield 89%; IR (KBr,  $\nu$  in cm<sup>-1</sup>): 1729 (-C=O), 3363 (-OH). <sup>1</sup>H-NMR (400 MHz, DMSO): 3.49 (s, 3H, -OCH<sub>3</sub>), 3.75 (s, 3H, -OCH<sub>3</sub>), 4.45 (d, 1H, J = 4.0 Hz, -CH-), 6.27 (s, 1H, C3-H), 6.46 (d, 1H, J = 4.0 Hz, -CH-), 6.63 (d, 1H, J = 4.0 Hz, Ar-H), 6.94 (d, 2H, J = 12 Hz), 7.22-7.63 (m, 7H, Ar-H), 7.88 (d, 1H, J = 8.0 Hz), 11.51 (s, 1H, NH). MS m/z 467. Anal. calc. for C<sub>28</sub>H<sub>21</sub>NO<sub>6</sub>: C, 71.94; H, 4.53; N, 3.00. Found: C, 71.92; H, 4.55; N, 3.01.

**3.3t: 2,3-dihydro-3-(4-methoxyphenyl)-2-(7,8-dimethyl-2-oxo-2H-chromen-4-yl)furo[3,2-c]quinolin-4(5H)-one (5t).**

Colorless solid (acetonitrile), mp 290-292 °C, yield 86%; IR (KBr,  $\nu$  S in  $\text{cm}^{-1}$ ): 1733 ( $\text{-C=O}$ ), 3392 ( $\text{-OH}$ ).  $^1\text{H-NMR}$  (400 MHz, DMSO): 2.29 (s, 3H, CH<sub>3</sub>), 2.36 (s, 3H, CH<sub>3</sub>), 3.76 (s, 3H,  $\text{-OCH}_3$ ), 4.37 (d, 1H,  $J = 4.0$  Hz,  $\text{-CH-}$ ), 6.18 (s, 1H, C3-H), 6.37 (d, 1H,  $J = 4.0$  Hz,  $\text{-CH-}$ ), 6.95 (t, 3H,  $J = 8.0$  Hz), 7.09-7.62 (m, 6H, Ar-H), 7.87 (d, 1H,  $J = 8.0$  Hz), 11.52 (s, 1H, NH). MS  $m/z$  465. Anal. calc. for C<sub>29</sub>H<sub>23</sub>N<sub>5</sub>O: C, 74.83; H, 4.98; N, 3.01. Found: C, 74.82; H, 4.96; N, 3.00.

## 4. Conclusion

We have shown a tandem Knoevenagel and Michael addition reactions sequence leading to the generation of isosteric tricyclic furo coumarins and azacoumarins. The reported compounds bear a close resemblance with the naturally occurring bio-active compounds. The ability of coumarins to form solvates with acetonitrile has also been recorded for the first time during this investigation.

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