Accepted Manuscript

One-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones using K10 montmorillonite clay as heterogeneous catalyst

Jin Zhang, Wenhao Xue, Pei Wang, Tao Wang, Yong Liang, Zunting Zhang

PII: S0040-4020(18)30839-1

DOI: 10.1016/j.tet.2018.07.018

Reference: TET 29678

To appear in: *Tetrahedron*

Received Date: 11 May 2018

Revised Date: 28 June 2018

Accepted Date: 9 July 2018

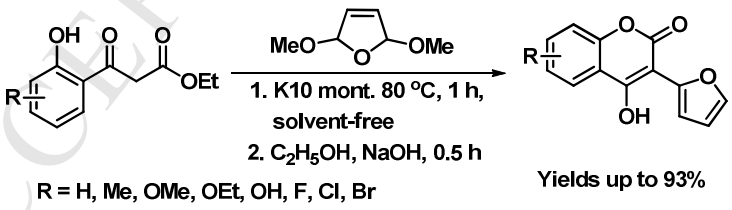
Please cite this article as: Zhang J, Xue W, Wang P, Wang T, Liang Y, Zhang Z, One-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones using K10 montmorillonite clay as heterogeneous catalyst, *Tetrahedron* (2018), doi: 10.1016/j.tet.2018.07.018.

Graphical Abstract

One-Pot Synthesis of 3-(Furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones using K10 Montmorillonite Clay as Heterogeneous Catalyst

Jin Zhang, Wenhao Xue, Pei Wang, Tao Wang, Yong Liang and Zunting Zhang*

The reaction of ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates and 2,5-dimethoxy-2,5-dihydrofuran was performed in presence of K10 Montmorillonite Clay heterogeneous catalyst under the solvent-free condition, and followed by further converted to 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones *via* refluxing in the alkaline EtOH solution.



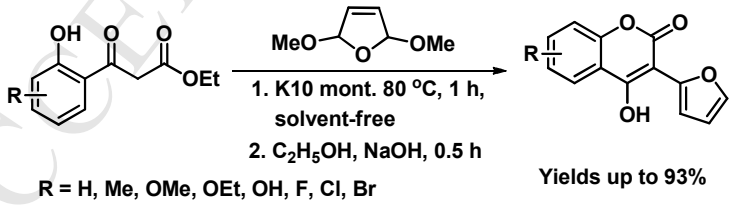
One-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones using K10 montmorillonite clay as heterogeneous catalyst

Jin Zhang, Wenhao Xue, Pei Wang, Tao Wang, Yong Liang[†] and Zunting Zhang*

Key Laboratory of the Ministry of Education for Medicinal Resources and Natural Pharmaceutical Chemistry, National Engineering Laboratory for Resource Development of Endangered Crude Drugs in Northwest of China, and School of Chemistry and Chemical Engineering, Shaanxi Normal University, Xi'an 710119, People's Republic of China. E-mail: zhangzunting@sina.com; Fax: (+86)-29-81530727; Tel: (+86)-29-85303940.

ABSTRACT: A facile and efficient one-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones was developed. The reaction of ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates and 2,5-dimethoxy-2,5-dihydrofuran were performed in presence of K10 Montmorillonite Clay heterogeneous catalyst under the solvent-free condition at 80 ^{o}C for 1 h, and followed by further converted to 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones *via* refluxing in the alkaline EtOH solution for 0.5 h. The demonstrate method not only avoided the usage of any expensive transition-metals, but also eliminated the tedious intermediate purification. Moreover, due to the wide functional group tolerance, it could be applied to various substrates and gave product in good to excellent yields.

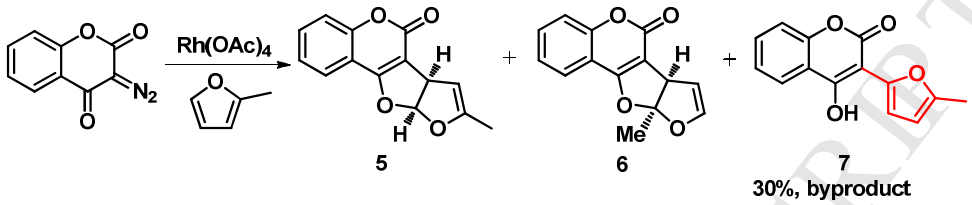
Keywords: Coumarin; K10 Montmorillonite Clay; Solvent-free; Transition-metals



1. Introduction

Coumarin was an important heterocyclic core structure, which was present in a large variety of natural plants, and constituted a member of significant organic compounds due to their wide applications. For example, various of biological and pharmaceutical properties have been reported for coumarin analogues, e.g. antimicrobial,[1] anti-inflammatory,[2] anticancer,[3] antihypertensive,[4]

anti-HIV[5] and anticoagulants.[6] It has also been utilized as corrosion inhibitors[7] and urease-inhibitors.[8] Moreover, coumarin could be also found in fluorochrome,[9] cosmetics and pigments.[10] The 3-aromatic substituted coumarin analogues exhibited various important potential biological activities as well, e.g. antileishmanial,[11] antioxidant[12] properties, MAO inhibitors[13] and inhibit cell proliferation.[14]



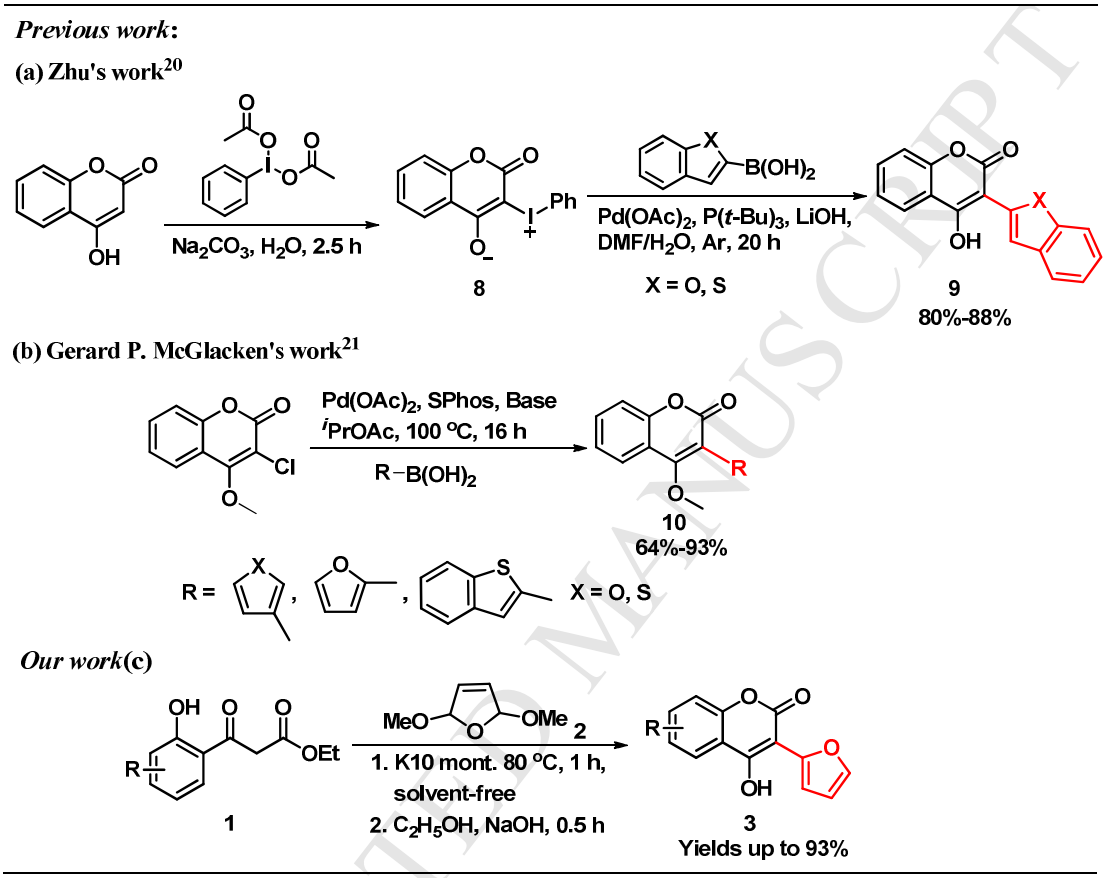
Scheme 1. Preparation of 4-hdroxy-3-(5-methylfuran-2-yl)-2*H*-chromen-2-one (**7**).

Although a number of methods for the preparation of 3-aryl substituted coumarin analogues were known in the last decade,[15-18] only a few reports on the synthesis of 3-furan-4-hydroxycoumarins was disclosed. Palmisano and co-workers reported a [3+2] cycloaddition of 3-diazo-4-hydroxycoumarin and 2-methylfuran in the presence of $Rh_2(OAc)_4$ for the synthesis of furo[3,2-*c*]coumarin analogues **5** and **6**, along with the formation of 4-hydroxy-3-(5-methylfuran-2-yl)-2*H*-chromen-2-one **7** in 30% yields as a byproduct (Scheme 1).[19]

Later on, Zhu's group reported the synthesis of 3-arylcoumarin analogues **9** *via* Pd-catalyzed cross-coupling of aryl boronic acids with phenyliodonium zwitterion **8** in 80%-88% yields, which were obtained by the iodination of 4-hydroxycoumarin with iodobenzene diacetate (Scheme 2a).[20] Recently, it was reported that Pd-catalyzed Sukuzi coupling of 3-chloro-4-alkoxy coumarins with heteroarylboronic acids in the presence of base and SPhos gave 3-(benzo)furyl/thiophenyl substituted 4-alkoxycoumarin analogues **10** in 64%-93% yields (Scheme 2b).[21] The reported methods required both prolonged heating and expensive transition-metal catalysts, which were difficult to recycle and not environmental friendly.

Montmorillonite K10 clay has been known for its tunable Bronsted and Lewis acidities and used as an environmental friendly catalyst in synthetic organic chemistry.[22-24] The K10 clay offered several advantages compared with other catalysts, such as non-corrosive properties, non-toxic, low cost, ease of handling and mild reaction conditions.[25-27] Moreover, it could be easily separated and recycled, which made it an excellent heterogeneous green catalyst.[28-30]

Herein, we would like to report a facile and efficient K10 Montmorillonite Clay heterogeneously catalyzed two-step one-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones **3** from ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates **1** and 2,5-dimethoxy-2,5-dihydrofuran (DHDMF, **2**) (Scheme 2c).



Scheme 2. Synthesis of 3-eteroHcyclicaryl-4-hydroxy-2*H*-chromen-2-ones.

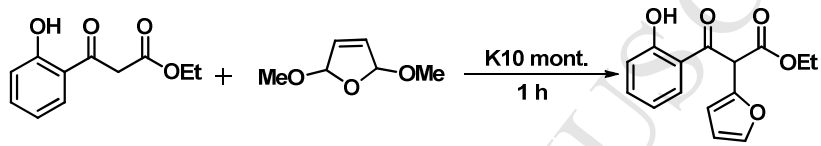
2. Results and discussion

On the basis of literature report,[31, 32] refluxing ethyl 3-(2-hydroxyphenyl)-3-oxopropanoate **1a**[33] with DHDMF in the presence of K10 montmorillonite Clay in anhydrous dichloromethane (DCM) for 2 h, ethyl 2-(furan-2-yl)-3-(2-hydroxyphenyl)-3-oxopropanoate **4a** was given in 12% yield (Table 1, Entry 1). Replacement of DCM with hexane, the reaction was heated at a higher temperature (70 ^{o}C), which led to the formation of **4a** in 25% yields (Entry 2). It was interesting to find out that the yield of **4a** was significantly improved when reaction was carried out under solvent-free condition (86%, Entry3). In order to further optimized the reaction conditions, various ratios of **1a** : DHDMF : K10 were carefully screened (Entries 4-7). The result showed that **4a** was

obtained as high as 96 % yields with 1.5 equiv. of **2** (Entry 4), while the yield was not significantly affected by the continued increased loading of **2** (Entry 5). Reducing or increasing the loading of K10 led to the lower yield of **4a** (Entries 6-7). Taking into account for the economic and environmental factors, further temperature optimization was performed with the ratio listed in Entry 4. Slight adjusting the reaction temperature did not improved the yield of **4a** as well (Entries 8-9). The K10 montmorillonite was recycled and it's reaction activity showed a gradual decrease. The yields of five recycles were 85%, 82%, 75%, 70% and 64%, respectively.

Table 1

Optimization of the synthesis of ethyl 2-(furan-2-yl)-3-(2-hydroxyphenyl)-3-oxopropanoate [a].



1a **2** **4a**

Entry	Ratio **1a** : **2** : K10[b]	T (°C)	Solvent	Yield (%)[c]
1	1 : 1 : 1	40 °C	DCM (1.5 mL)	12
2	1 : 1 : 1	70 °C	*n*-Hex (1.5 mL)	25
3	1 : 1 : 1	80 °C	–	86
4[d]	**1 : 1.5 : 1**	**80 °C**	–	**96**
5	1 : 2 : 1	80 °C	–	97
6	1 : 1.5 : 0.5	80 °C	–	63
7	1 : 1.5 : 1.5	80 °C	–	94
8	1 : 1.5 : 1	70 °C	–	79
9	1 : 1.5 : 1	90 °C	–	95

[a] All reactions were carried out on a 0.2 mmol of **1a** and the reaction mixture was heated (oil bath) for 2 h (Entries 1, 2) and 1 h (Entries 3-9).

[b] DHDMF and **1a** were calculated in molar ratio, K10 mont. and **1a** were calculated in weight ratio.

[c] Isolated yields was calculated based on **1a**.

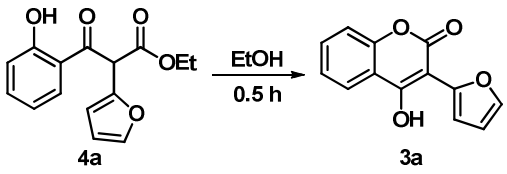
[d] The K10 montmorillonite could be recycled. The yields of five recycles were 85%, 82%, 75%, 70% and 64%, respectively.

The cyclization of **4a** was initially performed in the mixture of hydrochloric acid ethanol solution for refluxing 0.5 h, which gave corresponding cyclization product 3-furan-4-hydroxycoumarin **3a** in 22% yields (Table 2, Entry 1). It has been found out that different acids slightly affected the yield of **3a**. Product **3a** was obtained in higher yield in the presence of CF_3COOH (Entry 2), while only trace amount of **3a** was detected in the presence of

p-$CH_3C_6H_4SO_3H$ (Entry 3). Surprisingly, the addition of a base significantly increased the yield of **3a** compared with an acid (85%, Entry 4). Further investigation on the loading of base revealed that 2 equiv. of NaOH gave product **3a** in best yield (92%, Entries 4-6). In the end, the optimal conditions for the generation of **3a** was Entry 5.

Table 2

Optimization of the synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones [a].



4a 3a

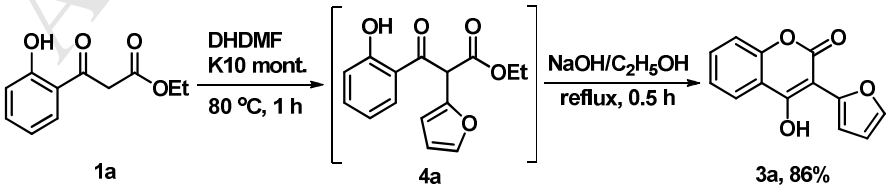
Entry	Acid/Base	**4a** : Acid/Base[b]	Yield[c]
1	HCl	1 : 1	22
2	CF_3COOH	1 : 1	35
3	*p*-$CH_3C_6H_4SO_3H$	1 : 1	trace
4	NaOH	1 : 1	85
5	**NaOH**	**1:2**	**92**
6	NaOH	1 : 3	91

[a] Compound **4a** (0.2 mmol) was refluxing in the mixture of additives and EtOH (1 mL) for 0.5 h.

[b] Molar ratio.

[c] Isolated yields was calculated based on **4a**.

To further simplify the methodology and operation, we attempted to perform the coupling and cyclization under the optimized conditions without isolation and purification of **4a** (Scheme 3). Treatment of **1a** (0.2 mmol) with DHDMF (1.5 equiv, molar ratio to **1a**) were performed in the presence of K10 Montmorillonite Clay (1 equiv, mass ratio to **1a**) at 80 °C for 1 h without addition of any solvent to provide intermediate **4a**. Without further purification, EtOH (1 mL) and NaOH (2.0 equiv, 3 M) were added to the crude reaction mixture refluxing for 0.5 h, and followed by the cyclization product **3a** was given in yield of 86%.



1a 4a 3a, 86%

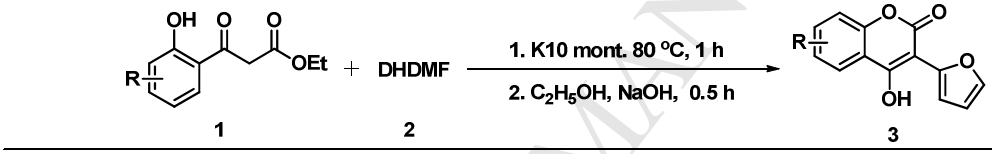
Scheme 3. One-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones (**3a**).

Our methodology, which not only avoided the usage of any expensive transition-metals but also eliminated the tedious intermediate purification, was expanded to the synthesis of various

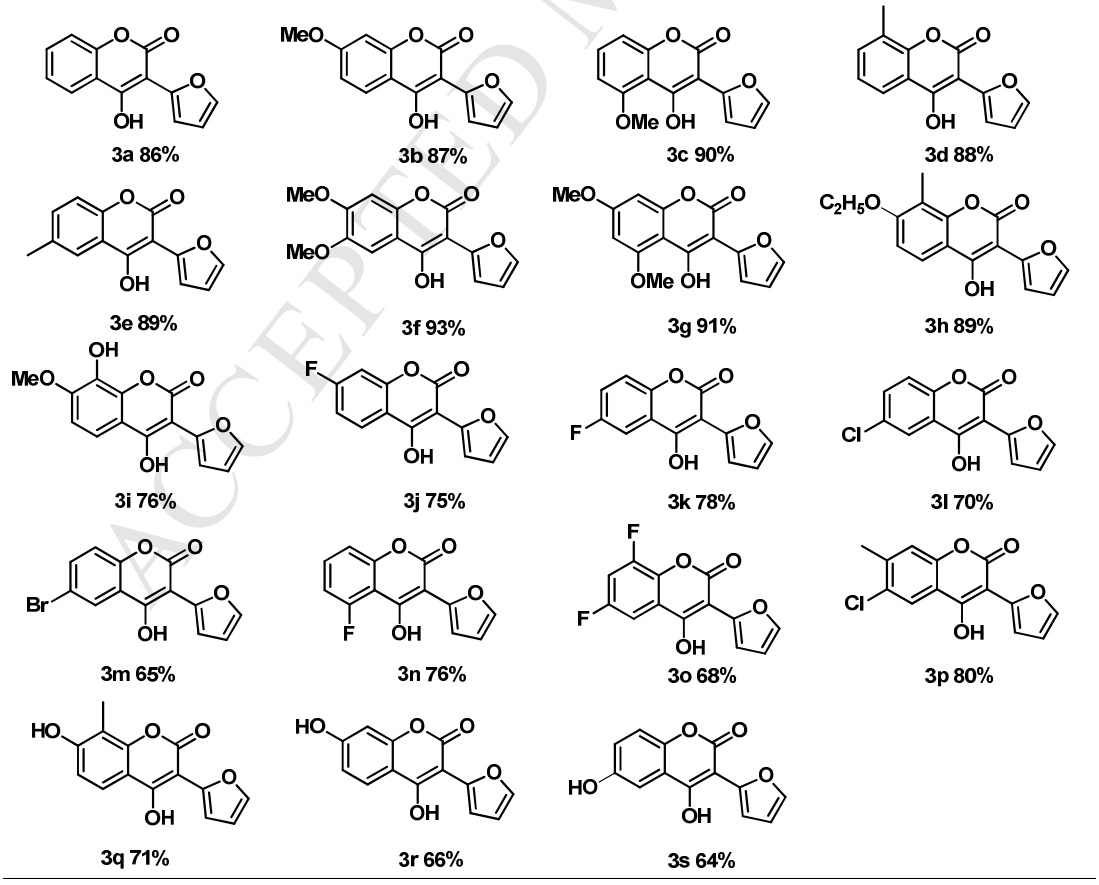
functional group substituted 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-one analogues (Table 3). Due to the tolerance of various functional groups, presence of either electron donating group (EDG) or electron with drawing group (EWG) in the substrate could afford product **3** in good to excellent yields. Generally, substrates bearing an electron donating group (EDG), such as –Me, –OMe or –OEt give the corresponding products in better yields (87–93%, **3b-3h**) comparing to the yields of those carrying an electron withdrawing group (EWG), including –F, –Br or –Cl (65–78%, **3j-3o**). The presence of halides in the final cyclization provides possibility for further modification. It is note worthy that introducing an additional hydroxyl group on the benzene ring could be also tolerated and the corresponding cyclization products were obtained in moderate yields (64–76%, **3i, 3q-3s**).

Table 3

Synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones [a].



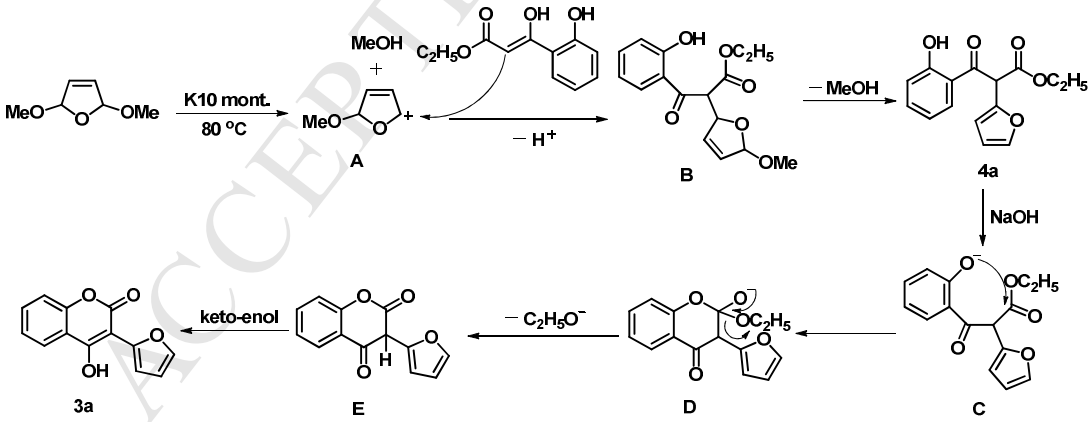
1 2 3



[a]All reactions were carried out on a 0.5 mmol of **1** in the presence of DHDMF (1.5 equiv, molar ratio to **1**) and K10 Montmorillonite Clay (1 equiv, mass ratio to **1**) at 80 °C for 1 h, followed by the addition of EtOH (2 mL) /NaOH (2 equiv., 3 M) and the mixture was refluxed for 0.5 h. Isolated yields.

To demonstrate the practicality and scalability of our methodology, the synthesis of **3a** in gram-scale was investigated. Ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates (**1a**, 1 g, 4.8 mmol), DHDMF (**2**, 7.2 mmol) and K10 (**1a**, 1 g) were stirred without any solvent to obtained **4a** at 80 °C for 1 h, then EtOH (5 mL) and NaOH (2.0 equiv, 3 M) was added. Then the mixture was refluxed for 0.5 h to produce **3a** in 65% isolated yield (0.69 g) by the column chromatography.

In 1999, Zhu's group reported the reaction between 1,3-dicarbonyl compounds and DHDMF, and found it underwent a fast process of Michael addition and *α*-alkoxyalkylation, then 2-furan-1,3-butane diones were obtained. According to this literature reported,[28, 31] a plausible mechanism for the 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones **3** was proposed and depicted in Scheme 4. Initially, treatment of DHDMF with K10 montmorillonite led to a fast and efficient formation of intermediate **A**, which reacted with **1** to give intermediate **B** along.[31] Intermediate **4a** was obtained with the release of MeOH.[31] Abstraction of phenolic hydrogen with external base led to the formation of intermediate **C**, followed by the intramolecular cyclization and leaving of alkoxide to produce intermediate **E**. Then, intermediate **E** tautomerized to the final product **3a** due to the thermodynamic stability.



Scheme 4. Proposed mechanism for the synthesis of compounds **3.**

3. Conclusion

In summary, we have successfully demonstrated a facile and efficient one-pot synthesis of 3-(furan-2-yl)-4-hydroxy-2*H*-chromen-2-ones **3** from ethyl 3-(2-hydroxyphenyl)-3-oxopropanoate

1 and DHDMF with the presence of K10 Montmorillonite Clay without requirement of any transition-metal catalyst. Since the isolation of the intermediate was not required, the operation procedure was simplified and reaction time was dramatically shortened. Notable features of our strategy include (a) K10 Montmorillonite Clay as the catalyst and could be recycled, (b) good to excellent yields, (c) excellent functional group tolerance, (d) easy to work-up.

4. Experimental section

4.1. General

K10 Montmorillonite Clay was purchased from Energy Chemical, and all reagents were obtained from commercial sources and used without further purification. Melting points were measured with a X-5 micro-melting point apparatus and are uncorrected. IR spectra were recorded with a Nicolet 170SX FT-IR spectrophotometer on KBr pellets. High-resolution mass spectrometry (HRMS) was performed using electron-spray ionization quadrupole-time of flight (ESI-Q-TOF) techniques. Thin-layer chromatography was performed on precoated silica gel 60 GF254 plates. Silica gel (200−300 mesh) was used for column chromatography. ^{1}H NMR spectra were recorded on 400 or 600 MHz spectrometers. Spectra were referenced internally to the residual proton resonance in $CDCl_3$ or DMSO-d_6. ^{13}C NMR spectra were recorded on 100 or 150 MHz spectrometers and the spectra were referenced to $CDCl_3$ or DMSO-d_6.

*4.2. General Procedures for Syntheses of ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates (**1a-1s**)*[33].

Under a dry argon atmosphere, lithium bis(trimethylsilyl)amide (1 M, 3 mmol) was cooled -78 ^{o}C and a mixture of 2-hydroxyacetophenone (136 mg, 1 mmol) in dry THF (2 mL) was added dropwise to the above solution in 20 min. The reaction solution was stirred at -78 ^{o}C for 1 h and in ice-bath for 2 h, and then a solution of diethyl carbonate (127.4 mg, 1.08 mmol) in dry THF (1 mL) was rapidly added to the above mixture in ice-bath for 3-4 h. Then, the mixture was stirred at room temperature. After 2-hydroxyacetophenone had disappeared completely, the reaction solution poured into a mixture of concentrated HCl (1.5 mL) and ice (20 g). The mixture was extracted with $CHCl_3$. The organic layer was dried over Na_2SO_4 and concentrated under reduced pressure. The crude products were purified using column chromatography on silica gel to give **1a** in good yields, and **1b-1s** were prepared with the same method.

*4.2.1. Ethyl 3-(2-hydroxyphenyl)-3-oxopropanoate (**1a**)*[33].

Yield: 85%, 176.8 mg; colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.85 (s, 1H), 7.67 (d, *J* = 8.0 Hz, 1H), 7.50 (m, 1H), 7.00 (d, *J* = 8.0 Hz, 1H), 6.92 (m, 1H), 4.23 (m, 2H), 4.00 (s, 2H), 1.27 (m, 3H). HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{12}O_4Na$: 231.0628; found: 231.0626.

*4.2.2. Ethyl 3-(2-hydroxy-4-methoxyphenyl)-3-oxopropanoate (**1b**).*

Yield: 95%, 226.1 mg; white solid; m.p. 28.9-29.6 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.30 (s, 1H), 7.54 (d, *J* = 8.4 Hz, 1H), 6.46-6.37 (m, 2H), 4.19 (m, 2H), 3.90 (s, 2H), 3.82 (s, 3H), 1.24 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.4, 167.2, 166.7, 165.8, 132.1, 113.2, 108.2, 101.0, 61.7, 55.7, 45.6, 14.1. IR (KBr), *v* (cm^{-1}): 3473, 2981, 1745, 1629, 1359, 1213, 1151, 958, 794, 576, 514. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{12}O_4Na$: 261.0733; found: 261.0732.

*4.2.3. Ethyl 3-(2-hydroxy-6-methoxyphenyl)-3-oxopropanoate (**1c**).*

Yield: 93%, 221.3 mg; white solid; m.p. 37.4-38.2 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.82 (s, 1H), 7.32 (m, 1H), 6.53 (d, *J* = 8.4 Hz, 1H), 6.33 (d, *J* = 8.4 Hz, 1H), 4.14 (m, 2H), 3.91 (s, 2H), 3.80 (s, 3H), 1.20 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.8, 167.9, 165.0, 160.90, 136.9, 110.9, 110.7, 101.1, 61.0, 55.5, 51.8, 14.1. IR (KBr), *v* (cm^{-1}): 3438, 2989, 1728, 1604, 1467, 1230, 1151, 1004, 786, 729, 611. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{14}O_5Na$: 261.0733; found: 261.0738.

*4.2.4. Ethyl 3-(2-hydroxy-3-methylphenyl)-3-oxopropanoate (**1d**).*

Yield: 93%, 206.5 mg; colourless oil; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.15 (s, 1H), 7.51 (d, *J* = 8.1 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 6.81 (m, 1H), 4.22 (m, 2H), 3.99 (s, 2H), 2.25 (s, 3H), 1.26 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.7, 167.2, 161.4, 137.9, 128.0, 127.9, 118.7, 118.4, 61.8, 46.1, 15.6, 14.2. IR (KBr), *v* (cm^{-1}): 2930, 1740, 1637, 1429, 1306, 1256, 1151, 1030, 750, 665, 438. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{14}O_4Na$: 245.0784; found: 245.0790.

*4.2.5. Ethyl 3-(2-hydroxy-5-methylphenyl)-3-oxopropanoate (**1e**).*

Yield: 92%, 204.2 mg; white solid; m.p. 43.4-43.8 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.68 (s, 1H), 7.43 (s, 1H), 7.31 (d, *J* = 8.4 Hz, 1H), 6.90 (d, *J* = 8.4 Hz, 1H), 4.23 (m, 2H), 3.99 (s, 2H), 2.30 (s, 3H), 1.27 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.4, 167.1, 160.8, 138.4, 130.0, 128.5, 118.8, 118.6, 61.8, 45.9, 20.6, 14.2. IR (KBr), *v* (cm^{-1}): 3417, 2987, 2025, 1741, 1643, 1488, 1386, 1153, 1035, 775, 611, 513. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{14}O_4Na$: 245.0784; found: 245.0783.

*4.2.6. Ethyl 3-(2-hydroxy-4,5-dimethoxyphenyl)-3-oxopropanoate (**1f**).*

Yield: 94%, 251.9 mg; white solid; m.p. 76.9-77.2 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.18 (s, 1H), 6.95 (s, 1H), 6.38 (s, 1H), 4.15 (m, 2H), 3.85 (m, 5H), 3.78 (s, 3H), 1.20 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 195.7, 167.1, 160.6, 157.3, 142.1, 110.9, 110.8, 100.5, 61.6, 56.4, 56.1, 45.9, 14.0. IR (KBr), *v* (cm^{-1}): 3452, 1739, 1637, 1515, 1394, 1263, 1201, 1155, 1026, 865, 765, 678, 568. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_{16}O_6Na$: 291.0839; found: 291.0840.

*4.2.7. Ethyl 3-(2-hydroxy-4,6-dimethoxyphenyl)-3-oxopropanoate (**1g**).*

Yield: 92%, 246.6 mg; white solid; m.p. 66.9-67.4 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 13.44 (s, 1H), 5.95 (s, 1H), 5.81 (s, 1H), 4.09 (m, 2H), 3.80 (s, 2H), 3.71 (s, 6H), 1.16 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.5, 168.0, 167.7, 166.7, 162.2, 105.3, 93.6, 90.6, 60.7, 55.3, 51.0, 14.0. IR (KBr), *v* (cm^{-1}): 3427, 2987, 1731, 1625, 1421, 1307, 1220, 1159, 1026, 964, 825, 686, 599. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_{16}O_6Na$: 291.0839; found: 291.0843.

*4.2.8. Ethyl 3-(4-ethoxy-2-hydroxy-3-methylphenyl)-3-oxopropanoate (**1h**).*

Yield: 90%, 239.4 mg; white solid; m.p. 62.8-63.2 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.34 (s, 1H), 7.52 (d, *J* = 8.7 Hz, 1H), 6.44 (d, *J* = 8.7 Hz, 1H), 4.21 (m, 2H), 4.12 (m, 2H), 3.93 (s, 2H), 2.09 (s, 3H), 1.45 (m, 3H), 1.26 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.6, 167.5, 163.7, 162.6, 129.7, 114.0, 113.4, 103.3, 64.3, 61.7, 45.8, 14.9, 14.2, 7.7. IR (KBr), *v* (cm^{-1}): 3431, 2985, 1728, 1633, 1504, 1415, 1284, 1209, 1122, 1028, 796, 636, 545. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{18}O_5Na$: 289.1046; found: 289.1057.

*4.2.9. Ethyl 3-(2,3-dihydroxy-4-methoxyphenyl)-3-oxopropanoate (**1i**).*

Yield: 75%, 190.5 mg; white solid; m.p. 70.3-71.2 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.95 (s, 1H), 7.19 (d, *J* = 9.0 Hz, 1H), 6.44 (d, *J* = 9.0 Hz, 1H), 5.77 (s, 1H), 4.14 (m, 2H), 3.87 (m, 5H), 1.19 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 197.2, 167.1, 152.6, 150.5, 133.4, 122.6, 114.0, 103.2, 61.6, 56.2, 45.5, 14.0. IR (KBr), *v* (cm^{-1}): 3462, 2989, 1720, 1637, 1448, 1305, 1230, 1122, 1062, 892, 786, 686, 509. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{14}O_6Na$: 277.0682; found: 277.0692.

*4.2.10. Ethyl 3-(4-fluoro-2-hydroxyphenyl)-3-oxopropanoate (**1j**).*

Yield: 76%, 171.8 mg; white solid; m.p. 39.2-40.1 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.12 (s, 1H), 7.66 (m, 1H), 6.60 (m, 2H), 4.18 (m, 2H), 3.93 (s, 2H), 1.23 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 197.4, 167.8 (d, ^{1}J = 256.4 Hz), 166.7, 165.3 (d, ^{3}J = 14.4 Hz), 132.9 (d, ^{3}J = 11.9 Hz), 116.2, 107.7 (d, ^{2}J = 23.1 Hz), 105.2 (d, ^{2}J = 23.9 Hz), 61.8, 45.9, 14.0. IR (KBr), *v* (cm^{-1}): 3658, 2987, 1737, 1631, 1502, 1305, 1159, 1122, 966, 802, 557. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{11}FO_4Na$: 249.0534; found: 249.0533.

*4.2.11. Ethyl 3-(5-fluoro-2-hydroxyphenyl)-3-oxopropanoate (**1k**).*

Yield: 77%, 174 mg; white solid; m.p. 41.5-42.3 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.60 (s, 1H), 7.35 (d, *J* = 8.7 Hz, 1H), 7.26 (m, 1H), 6.98 (d, *J* = 8.7 Hz, 1H), 4.24 (m, 2H), 3.97 (s, 2H), 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.8, 166.6, 159.1, 154.9 (d, ^{1}J = 238.0 Hz), 124.9 (d, ^{2}J = 23.5 Hz), 120.2 (d, ^{3}J = 7.0 Hz), 118.5 (d, ^{1}J = 6.1 Hz), 115.2 (d, ^{2}J = 23.3 Hz), 61.9, 45.9, 14.1. IR (KBr), *v* (cm^{-1}): 3670, 3205, 2927, 1728, 1490, 1238, 1166, 1035, 860, 784, 661, 513. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{11}FO_4Na$: 249.0534; found: 249.0530.

*4.2.12. Ethyl 3-(5-chloro-2-hydroxyphenyl)-3-oxopropanoate (**1l**).*

Yield: 74%, 179.1 mg; white solid; m.p. 67.1-68.6 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.74 (s, 1H), 7.62 (d, *J* = 2.2 Hz, 1H), 7.43 (dd, *J* = 8.9, 2.2 Hz, 1H), 6.96 (d, *J* = 8.9 Hz, 1H), 4.23 (m, 2H), 3.97 (s, 2H), 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.8, 166.6, 161.4, 137.1, 129.6, 124.1, 120.5, 119.7, 62.0, 45.9, 14.2. IR (KBr), *v* (cm^{-1}): 3664, 3170, 2983, 1728, 1479, 1265, 1157, 1031, 879, 744, 613, 511. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{11}ClO_4Na$: 265.0238; found: 265.0237.

*4.2.13. Ethyl 3-(5-bromo-2-hydroxyphenyl)-3-oxopropanoate (**1m**).*

Yield: 73%, 208.1 mg; white solid; m.p. 67.2-68.4 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.77 (s, 1H), 7.77 (d, *J* = 2.3 Hz, 1H), 7.57 (dd, *J* = 8.9, 2.3 Hz, 1H), 6.91 (d, *J* = 8.9 Hz, 1H), 4.24 (m, 2H), 3.97 (s, 2H), 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.7, 166.6, 139.9, 132.7, 120.9, 120.3, 110.9, 62.1, 45.9, 14.2. IR (KBr), *v* (cm^{-1}): 3645, 3305, 2939, 2017, 1728, 1475, 1265, 1157, 999, 948, 752, 617, 509. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{11}BrO_4Na$: 308.9733; found: 308.9733.

*4.2.14. Ethyl 3-(2-fluoro-6-hydroxyphenyl)-3-oxopropanoate (**1n**).*

Yield: 75%, 169.5 mg; colourless oil. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.32 (s, 1H), 7.45-7.36 (m, 1H), 6.79 (d, *J* = 8.4 Hz, 1H), 6.61 (d, *J* = 8.4 Hz, 1H), 4.22 (m, 2H), 3.98 (m, 2H), 1.26 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.3, 167.1, 164.3 (d, ^{3}J = 8.4 Hz), 163.0 (d, ^{1}J = 249.1 Hz), 137.0 (d, ^{3}J = 8.9 Hz), 114.7 (d, ^{4}J = 3.1 Hz), 109.7 (d, ^{2}J = 23.8 Hz), 106.3 (d, ^{2}J = 24.2 Hz), 61.6, 50.6, 14.2. IR (KBr), *v* (cm^{-1}): 3456, 2925, 1741, 1641, 1454, 1342, 1218, 1033, 792, 590, 528. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{11}FO_4Na$: 249.0533; found: 249.0544.

*4.2.15. Ethyl 3-(3,5-difluoro-2-hydroxyphenyl)-3-oxopropanoate (**1o**).*

Yield: 71%, 173.2 mg; yellow solid; m.p. 90.2-91.0 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.56 (s, 1H), 7.21-7.05 (m, 2H), 4.23 (m, 2H), 3.96 (s, 2H), 1.27 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.8, 166.3, 153.7 (dd, ^{3}J = 10.1 Hz, ^{1}J = 240.6 Hz), 151.7 (dd, ^{3}J = 10.1 Hz, ^{1}J

= 251.0 Hz), 148.2 (dd, ^4J = 2.7 Hz, ^2J = 25.4 Hz), 119.6 (dd, ^3J = 7.2 Hz, ^3J = 7.4 Hz), 111.9 (dd, ^2J = 21.0 Hz, ^2J = 21.0 Hz), 110.5 (dd, ^4J = 4.3 Hz, ^2J = 23.2 Hz), 62.2, 46.3, 14.1. IR (KBr), *v* (cm^{-1}): 3402, 2964, 1726, 1633, 1444, 1369, 1272, 1141, 995, 858, 798, 586. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{10}F_2O_4Na$: 267.0439; found: 267.0455.

*4.2.16. Ethyl 3-(5-chloro-2-hydroxy-4-methylphenyl)-3-oxopropanoate (**1p**).*

Yield: 73%, 186.9 mg; white solid; m.p. 96.3-97.2 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.65 (s, 1H), 7.58 (s, 1H), 6.84 (s, 1H), 4.21 (m, 2H), 3.92 (s, 2H), 2.33 (s, 3H), 1.25 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 197.2, 166.7, 161.1, 146.5, 129.9, 124.6, 120.6, 118.0 61.8, 45.7, 20.9, 14.1. IR (KBr), *v* (cm^{-1}): 3435, 2983, 1730, 1656, 1357, 1272, 1176, 1031, 939, 879, 752, 586. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{13}ClO_4Na$: 279.0394; found: 279.0408.

*4.2.17. Ethyl 3-(2,4-dihydroxy-3-methylphenyl)-3-oxopropanoate (**1q**).*

Yield: 72%, 171.4 mg; white solid; m.p. 143.0-144.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.56 (s, 1H), 7.41 (d, *J* = 8.8 Hz, 1H), 6.36 (d, *J* = 8.8 Hz, 1H), 5.98 (s, 1H), 4.22 (m, 2H), 3.93 (s, 2H), 2.11 (s, 3H), 1.27 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.5, 167.8, 163.6, 161.2, 129.6, 113.2, 111.7, 107.7, 62.0, 45.7, 14.2, 7.4. IR (KBr), *v* (cm^{-1}): 3375, 1695, 1629, 1419, 1215, 1076, 1018, 802, 678, 553. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{12}H_{14}O_5Na$: 261.0733; found: 261.0735.

*4.2.18. Ethyl 3-(2,4-dihydroxyphenyl)-3-oxopropanoate (**1r**).*

Yield: 60%, 134.4 mg; white solid; m.p. 54.0-55.0 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 12.24 (s, 1H), 7.50 (d, *J* = 8.6 Hz, 1H), 7.26 (s, 1H), 6.42-6.31 (m, 2H), 4.23 (m, 2H), 3.93 (s, 2H), 1.28 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.3, 168.4, 165.5, 164.2, 132.8, 113.3, 108.8, 103.7, 62.3, 45.5, 14.1. IR (KBr), *v* (cm^{-1}): 3317, 2985, 2025, 1631, 1510, 1330, 1168, 1137, 1018, 860, 790, 702, 619, 553. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{12}O_5Na$: 247.0577; found: 247.0589.

*4.2.19. Ethyl 3-(2,5-dihydroxyphenyl)-3-oxopropanoate (**1s**).*

Yield: 63%, 141.1 mg; white solid; m.p. 40.7-41.5 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm) 11.37 (s, 1H), 7.06 (s, 1H), 7.04 (d, *J* = 8.8 Hz, 1H), 6.84 (d, *J* = 8.8 Hz, 1H), 6.36 (s, 1H), 4.22 (m, 2H), 3.94 (s, 2H), 1.26 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 198.1, 167.9, 156.7, 148.2, 126.2, 119.6, 118.6, 114.9, 62.2, 46.0, 14.1. IR (KBr), *v* (cm^{-1}): 3429, 2931, 1633, 1380, 1269, 1153, 999, 918, 788, 698, 617, 514. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{11}H_{12}O_5Na$: 247.0577; found: 247.0591.

*4.2.20. Ethyl 2-(furan-2-yl)-3-(2-hydroxyphenyl)-3-oxopropanoate (**4a**).*

Yield: 94%, 157.6 mg; white solid; m.p. 46.3-49.2 °C. ^1H NMR (400 MHz, $CDCl_3$) δ (ppm)

11.74 (s, 1H), 7.73 (d, *J* = 8.1 Hz, 1H), 7.48 (m, 1H), 7.42 (s, 1H), 7.00 (d, *J* = 8.1 Hz, 1H), 6.88 (m, 1H), 6.46 (d, *J* = 3.1 Hz, 1H), 6.39 (s, 1H), 5.73 (s, 1H), 4.26 (m, 2H), 1.26 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 196.9, 166.7, 163.4, 146.1, 143.1, 137.3, 130.4, 119.4, 119.0, 118.4, 111.2, 110.3, 62.4, 54.5, 14.1. IR (KBr), *v* (cm^{-1}): 3375, 2979, 1739, 1637, 1492, 1226, 1188, 1016, 881, 748, 603. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{15}H_{14}O_5Na$: 297.0733; found: 297.0732.

*4.3. General Procedures for Syntheses of 3-(Furan-2-yl)-4-hydroxy-2H-chromen-2-ones (**3a-3s**).*

The ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates were prepared according to the literature report.[34] The mixture of ethyl 3-(2-hydroxyphenyl)-3-oxopropanoates (0.5mmol), DHDMF (1.5 equiv) and K10 Montmorillonite Clay (1equiv, mass ratio) was stirred at 80 °C under solvent-free conditions for 1 h. Without further purification, EtOH (1 mL) and NaOH (2 equiv.) were added to crude reaction mixture and the resulting suspension was refluxed for 0.5 h. After cooled down to ambient temperature, K10 Montmorillonite Clay was recycled by vacuum filtration and the filtrate was adjusted to pH 6–7 with 20% HCl. Volatiles were removed under reduced pressure and the oily residue was column chromatographed (dichloromethane) to give **3** in moderate to excellent yields.

*4.3.1. 3-(Furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3a**).*

Yield: 86%, 102.3 mg; white solid; m.p. 152.1-154.6 ^{o}C. ^{1}H NMR (600 MHz, $CDCl_3$) δ (ppm) 9.56 (s, 1H), 7.98 (d, *J* = 7.7 Hz, 1H), 7.57 (m, 2H), 7.33 (m, 3H), 6.62 (dd, *J* = 3.5, 1.8 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 159.7, 158.7, 152.1, 148.6, 140.6, 132.6, 124.4, 123.8, 116.5, 115.6, 112.4, 111.3, 96.8. IR (KBr), *v* (cm^{-1}): 3053, 2986, 2854, 2191, 1541, 1398, 1194, 1159, 993, 793, 611. HRMS (ESI): *m/z* $[M + H]^+$ calculated for $C_{13}H_9O_4$: 229.0495; found: 229.0486.

*4.3.2. 3-(Furan-2-yl)-4-hydroxy-7-methoxy-2H-chromen-2-one (**3b**).*

Yield: 87%, 99.2 mg; white solid; m.p. 200.1-201.3 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.50 (s, 1H), 7.87 (d, *J* = 8.9 Hz, 1H), 7.53 (s, 1H), 7.26 (d, *J* = 3.2 Hz, 1H), 6.90 (dd, *J* = 8.9, 2.1 Hz, 1H), 6.81 (d, *J* = 1.6 Hz, 1H), 6.60 (dd, *J* = 3.2, 1.6 Hz, 1H), 3.89 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 163.6, 160.1, 159.4, 154.0, 148.9, 140.2, 124.9, 112.9, 112.3, 110.3, 108.8, 100.2, 94.6, 55.9. IR (KBr), *v* (cm^{-1}): 3356, 3088, 2183, 1717, 1609, 1433, 1366, 1205, 1124, 1018, 735, 586. HRMS (ESI): *m/z* $[M + H]^+$ calculated for $C_{14}H_{11}O_5$: 259.0601; found: 259.0595.

*4.3.3. 3-(Furan-2-yl)-4-hydroxy-5-methoxy-2H-chromen-2-one (**3c**).*

Yield: 90%, 102.6 mg; white solid; m.p. 182.1-184.0 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm)

10.28 (s, 1H), 7.55 (s, 1H), 7.44 (m, 1H), 6.98 (d, *J* = 8.0 Hz, 2H), 6.78 (m, 1H), 6.51 (s, 1H), 4.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.6, 160.1, 156.4, 153.3, 146.1, 141.9, 132.4, 112.3, 111.1, 106.0, 105.0, 97.6, 57.3. IR (KBr), *v* (cm^{-1}): 3425, 3259, 1703, 1633, 1440, 1365, 1257, 1095, 954, 794, 730, 592. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{10}O_5Na$: 281.0420; found: 281.0416.

*4.3.4. 3-(Furan-2-yl)-4-hydroxy-8-methyl-2H-chromen-2-one (**3d**).*

Yield: 88%, 106.5 mg; white solid; m.p. 153.4-155.1 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.48 (br, 1H), 7.80 (d, *J* = 7.7 Hz, 1H), 7.53 (s, 1H), 7.38 (d, *J* = 7.7 Hz, 1H), 7.31 (d, *J* = 2.3 Hz, 1H), 7.19 (m, 1H), 6.60 (s, 1H), 2.45 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.7, 159.0, 150.5, 148.8, 140.5, 133.8, 125.9, 123.8, 121.4, 115.3, 112.3, 111.2, 96.4, 15.7. IR (KBr), *v* (cm^{-1}): 3381, 2921, 1708, 1600, 1481, 1309, 1191, 1128, 1020, 908, 750, 582. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{10}O_4Na$: 265.0471; found: 265.0468.

*4.3.5. 3-(Furan-2-yl)-4-hydroxy-6-methyl-2H-chromen-2-one (**3e**).*

Yield: 89%, 107.7 mg; white solid; m.p. 167.6-170.3 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.53 (br 1H), 7.76 (s, 1H), 7.56 (s, 1H), 7.37 (d, *J* = 8.6 Hz, 1H), 7.33 (d, *J* = 3.6 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 1H), 6.62 (dd, *J* = 3.5, 1.7 Hz, 1H), 2.44 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.8, 158.8, 150.3, 148.8, 140.5, 134.1, 133.7, 123.4, 116.3, 115.2, 112.4, 111.2, 96.7, 21.1. IR (KBr), *v* (cm^{-1}): 3400, 3082, 2172, 2026, 1688, 1549, 1367, 1271, 1192, 1020, 814, 716, 590. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{10}O_4Na$: 265.0471; found: 265.0465.

*4.3.6. 3-(Furan-2-yl)-4-hydroxy-6,7-dimethoxy-2H-chromen-2-one (**3f**).*

Yield: 93%, 133.9 mg; white solid; m.p. 205.2-206.9 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.52 (s, 1H), 7.54 (d, *J* = 1.3 Hz, 1H), 7.31 (s, 1H), 7.27 (d, *J* = 3.5 Hz, 1H), 6.82 (s, 1H), 6.61 (dd, *J* = 3.4, 1.9 Hz, 1H), 3.97 (m, 6H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.2, 159.1, 153.7, 149.0, 148.2, 146.6, 140.2, 112.3, 110.3, 107.6, 103.6, 99.5, 94.9, 56.5, 56.4. IR (KBr), *v* (cm^{-1}): 3283, 2097, 1763, 1610, 1514, 1346, 1248, 1036, 818, 669, 554. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{15}H_{12}O_6Na$: 311.0526; found: 311.0518.

*4.3.7. 3-(Furan-2-yl)-4-hydroxy-5,7-dimethoxy-2H-chromen-2-one (**3g**).*

Yield: 91%, 131 mg; white solid; m.p. 168.2-169.5 ^oC. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 10.03 (s, 1H), 7.52 (s, 1H), 6.91 (d, *J* = 2.8 Hz, 1H), 6.49 (s, 1H), 6.44 (s, 1H), 6.32 (s, 1H), 3.99 (s, 3H), 3.81 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 163.4, 161.3, 160.4, 157.4, 155.1, 146.4, 141.6, 111.5, 111.0, 98.6, 95.8, 95.1, 94.3, 57.2, 56.0. IR (KBr), *v* (cm^{-1}): 3423, 3257, 2947, 1610, 1454, 1365, 1149, 1116, 960, 900, 808, 729, 496. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{15}H_{12}O_6Na$: 311.0526; found: 311.0523.

*4.3.8. 7-Ethoxy-3-(furan-2-yl)-4-hydroxy-8-methyl-2H-chromen-2-one (**3h**).*

Yield: 89%, 127.3 mg; white solid; m.p. 171.0-172.5 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.46 (s, 1H), 7.79 (d, *J* = 8.9 Hz, 1H), 7.52 (d, *J* = 1.8 Hz, 1H), 7.27 (d, *J* = 3.7 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 1H), 6.60 (dd, *J* = 3.7, 1.8 Hz, 1H), 4.14 (m, 2H), 2.32 (s, 3H), 1.47 (m, 3H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 160.7, 160.3, 159.6, 151.5, 149.2, 140.1, 121.9, 113.8, 112.3, 110.2, 108.8, 108.1, 94.3, 64.5, 15.0, 8.4. IR (KBr), *v* (cm^{-1}): 3355, 2929, 1703, 1610, 1402, 1276, 1122, 1016, 769, 729, 644, 484. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{16}H_{14}O_5Na$: 309.0733; found: 309.0727.

*4.3.9. 3-(Furan-2-yl)-4,8-dihydroxy-7-methoxy-2H-chromen-2-one (**3i**).*

Yield: 76%, 104.1 mg; white solid; m.p. 161.7-163.3 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.54 (s, 1H), 7.53 (m, 2H), 7.28 (d, *J* = 3.1 Hz, 1H), 6.92 (d, *J* = 8.8 Hz, 1H), 6.61 (dd, *J* = 3.1, 1.1 Hz, 1H), 5.74 (s, 1H), 4.01 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm) 161.4, 160.3, 151.2, 146.0, 142.1, 141.6, 133.2, 113.8, 111.0, 110.9, 110.1, 108.4, 94.8, 56.3. IR (KBr), *v* (cm^{-1}): 3390, 2921, 1676, 1591, 1487, 1330, 1089, 1004, 734, 592. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{10}O_6Na$: 297.0369; found: 297.0364.

*4.3.10. 7-Fluoro-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3j**).*

Yield: 75%, 92.3 mg; white solid; m.p. 143.2-144.3 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.55 (s, 1H), 7.96 (m, 1H), 7.54 (s, 1H), 7.28 (d, *J* = 8.8 Hz, 1H), 7.06 (d, *J* = 8.8 Hz, 1H), 7.02 (s, 1H), 6.60 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 165.1 (d, ^{1}J = 252.9 Hz), 159.4, 158.3, 153.2 (d, ^{3}J = 12.9 Hz), 148.4, 140.6, 125.7 (d, ^{3}J = 10.3 Hz), 112.6 (d, ^{2}J = 22.9 Hz), 112.4, 112.1 (d, ^{4}J = 2.5 Hz), 112.2, 104.5 (d, ^{2}J = 25.5 Hz), 95.9. IR (KBr), *v* (cm^{-1}): 3377, 3080, 1712, 1554, 1492, 1315, 1188, 1083, 962, 740, 611. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_7FO_4Na$: 269.0221; found: 269.0218.

*4.3.11. 6-Fluoro-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3k**).*

Yield: 78%, 95.9 mg; white solid; m.p. 173.5-174.4 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.56 (s, 1H), 7.65 (dd, *J* = 8.4, 2.8 Hz, 1H), 7.58 (d, *J* = 1.3 Hz, 1H), 7.36 (d, *J* = 3.6 Hz, 1H), 7.31 (m, 2H), 6.63 (dd, *J* = 3.4, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.3, 159.0 (d, ^{1}J = 252.9 Hz), 157.6, 148.3, 148.2, 140.9, 120.1 (d, ^{2}J = 24.6 Hz), 118.2 (d, ^{3}J = 8.3 Hz), 116.6 (d, ^{3}J = 9.2 Hz), 112.5, 112.0, 109.4 (d, ^{2}J = 25.4 Hz), 97.4. IR (KBr), *v* (cm^{-1}): 3377, 3080, 2183, 1713, 1555, 1493, 1367, 1315, 1188, 1148, 988, 741, 611. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_7FO_4Na$: 269.0221; found: 269.0215.

*4.3.12. 6-Chloro-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3l**).*

Yield: 70%, 91.7 mg; white solid; m.p. 203.8-204.9 ^{o}C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.55 (s, 1H), 7.96 (d, *J* = 2.0 Hz, 1H), 7.58 (s, 1H), 7.51 (dd, *J* = 8.8, 2.0 Hz, 1H), 7.36 (d, *J* = 3.4

Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 6.64 (dd, *J* = 3.6, 2.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.1, 157.3, 141.0, 132.5, 130.0, 123.3, 118.0, 116.8, 112.5, 112.0. IR (KBr), *v* (cm^{-1}): 3367, 3076, 1722, 1542, 1315, 1120, 1020, 935, 815, 725, 607. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_7ClO_4Na$: 284.9925; found: 284.9920.

*4.3.13. 6-Bromo-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3m**).*

Yield: 65%, 99.5 mg; white solid; m.p. 169.1-171.2 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.54 (s, 1H), 8.11 (d, *J* = 2.4 Hz, 1H), 7.65 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.58 (d, *J* = 1.3 Hz, 1H), 7.36 (d, *J* = 3.6 Hz, 1H), 7.23 (d, *J* = 8.8 Hz, 1H), 6.63 (dd, *J* = 3.6, 1.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 159.0, 157.2, 150.9, 148.3, 141.0, 135.3, 126.3, 118.3, 117.2, 112.8, 112.5, 112.0, 97.5. IR (KBr), *v* (cm^{-1}): 3371, 1718, 1608, 1363, 1313, 1107, 1018, 931, 813, 725, 597. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_7BrO_4Na$: 328.9420; found: 328.9413.

*4.3.14. 5-Fluoro-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3n**).*

Yield: 76%, 93.5 mg; white solid; m.p. 181.7-183.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.75 (s, 1H), 7.56 (s, 1H), 7.50 (m, 1H), 7.34 (d, *J* = 3.6 Hz, 1H), 7.16 (d, *J* = 8.4 Hz, 1H), 7.02 (m, 1H), 6.63 (dd, *J* = 3.5, 1.7 Hz, 1H). ^{13}C NMR (151 MHz, $CDCl_3$) δ (ppm) 159.4 (d, ^1J = 253.7 Hz), 158.7 (d, ^2J = 25.6 Hz), 158.52, 153.0 (d, ^4J = 4.2 Hz), 148.2, 140.8, 132.5 (d, ^3J = 10.7 Hz), 112.8 (d, ^4J = 4.2 Hz), 112.4, 112.0 (d, ^2J = 21.6 Hz), 111.9, 105.8 (d, ^3J = 11.8 Hz), 97.2. IR (KBr), *v* (cm^{-1}): 3352, 3149, 2921, 1942, 1722, 1612, 1481, 1315, 1051, 734, 636, 584. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_7FO_4Na$: 269.0220; found: 269.0217.

*4.3.15. 6,8-Difluoro-3-(furan-2-yl)-4-hydroxy-2H-chromen-2-one (**3o**).*

Yield: 68%, 89.8 mg; white solid; m.p. 166.2-167.6 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.58 (s, 1H), 7.58 (s, 1H), 7.44 (d, *J* = 7.8 Hz, 1H), 7.36 (d, *J* = 2.7 Hz, 1H), 7.12 (m, 1H), 6.63 (s, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ (ppm) 158.0 (dd, ^3J = 9.9 Hz, ^1J = 246.8 Hz), 157.9, 156.9, 149.4 (dd, ^3J = 12.3 Hz, ^1J = 253.2 Hz), 147.8, 141.2, 137.1 (dd, ^4J = 2.9 Hz, ^2J = 22.8 Hz), 117.7 (dd, ^3J = 10.1 Hz, ^3J = 10.3 Hz), 112.6, 112.5, 107.7 (dd, ^2J = 20.7 Hz, ^2J = 20.6 Hz), 104.8 (dd, ^4J = 2.1 Hz, ^2J = 25.0 Hz), 98.12. IR (KBr), *v* (cm^{-1}): 3421, 3342, 1662, 1550, 1375, 1307, 1164, 993, 914, 763, 742, 634, 509. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_6F_2O_4Na$: 287.0126; found: 287.0124.

*4.3.16. 6-Chloro-3-(furan-2-yl)-4-hydroxy-7-methyl-2H-chromen-2-one (**3p**).*

Yield: 80%, 110.4 mg; white solid; m.p. 227.8-229.1 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm) 9.52 (s, 1H), 7.94 (s, 1H), 7.57 (s, 1H), 7.33 (d, *J* = 3.5 Hz, 1H), 7.22 (s, 1H), 6.62 (dd, *J* = 3.1, 1.6 Hz, 1H), 2.48 (s, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm) 159.7, 159.6, 150.4, 145.6, 142.4, 140.8, 128.9, 123.2, 118.6, 115.6, 111.6, 111.1, 97.1, 19.9. IR (KBr), *v* (cm^{-1}): 3382, 2923, 1718, 1616, 1523, 1301, 1141, 1020, 931, 813, 727, 603. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for

$C_{14}H_9ClO_4Na$: 299.0081; found: 299.0080.

*4.3.17. 3-(Furan-2-yl)-4,7-dihydroxy-8-methyl-2H-chromen-2-one (**3q**).*

Yield: 71%, 91.6 mg; white solid; m.p. 127.8-130.0 ^oC. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.48 (s, 1H), 7.69 (d, *J* = 8.8 Hz, 1H), 7.68 (d, *J* = 1.8Hz, 1H), 6.86 (d, *J* = 8.7 Hz, 1H), 6.70 (d, *J* = 3.3 Hz, 1H), 6.55 (dd, *J* = 3.3, 1.9 Hz, 1H), 2.16 (s, 3H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) 162.6, 160.7, 159.4, 152.0, 146.7, 141.6, 121.9, 111.7, 110.9, 110.2, 108.4, 93.4, 8.1. IR (KBr), *v* (cm^{-1}): 3444, 2923, 2850, 1676, 1465, 1276, 1089, 1006, 927, 765, 732, 559. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{14}H_{10}O_5Na$: 281.0420; found: 281.0419.

*4.3.18. 3-(Furan-2-yl)-4,7-dihydroxy-2H-chromen-2-one (**3r**).*

Yield: 66%, 80.5 mg; white solid; m.p. 145.8-147.1 ^oC. ^1H NMR (400 MHz, DMSO-d_6) δ (ppm) 10.7 (br, 1H), 7.8 (d, *J* = 8.8 Hz, 1H), 7.7 (s, 1H), 6.8 (d, *J* = 8.7 Hz, 1H), 6.70 (s, 2H), 6.56 (s, 1H). ^{13}C NMR (101 MHz, DMSO-d_6) δ (ppm) 161.9, 161.7, 160.5, 154.0, 146.2, 141.9, 125.4, 113.0, 111.0, 110.6, 108.0, 101.8, 93.9. IR (KBr), *v* (cm^{-1}): 3440, 3365, 2921, 2027, 1612, 1460, 1232, 1022, 842, 727, 586. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_8O_5Na$: 267.0264; found: 267.0264.

*4.3.19. 3-(Furan-2-yl)-4,6-dihydroxy-2H-chromen-2-one (**3s**).*

Yield: 64%, 78.1 mg; white solid; m.p. 198.2-199.4 ^oC. ^1H NMR (400 MHz, DMSO-d_6) 11.50 (br, 1H), 9.80 (s, 1H), 7.75 (d, *J* = 1.8 Hz, 1H), 7.32 (d, *J* = 2.8 Hz, 1H), 7.26 (d, *J* = 8.9 Hz, 1H), 7.08 (dd, *J* = 8.9, 2.9 Hz, 1H), 6.81 (d, *J* = 3.2 Hz, 1H), 6.60 (dd, *J* = 3.3, 1.8 Hz, 1H). ^{13}C NMR (151 MHz, DMSO-d_6) δ (ppm) 160.2, 160.1, 153.7, 145.9, 145.3, 142.3, 120.8, 117.2, 116.6, 111.4, 111.1, 107.8, 97.0. IR (KBr), *v* (cm^{-1}): 3392, 3288, 2025, 1668, 1550, 1313, 1191, 1020, 918, 829, 740, 621. HRMS (ESI): *m/z* $[M + Na]^+$ calculated for $C_{13}H_8O_5Na$: 267.0264; found: 267.0261.

Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (No: 21672132, 21502110) and the Fundamental Funds Research for the Central Universities (No: GK201503034).

Author Information

Corresponding Author

*Tel.: (+86)-29-85303940. Fax: (+86)-29-81530727. E-mail: zhangzunting@sina.com.

Present address

[†]Department of Molecular Medicine, Beckman Research Institute of City of Hope, Duarte,

California 91010, United States.

Appendix A. Supplementary data

General experimental procedures of **1**, spectroscopic data, ^{1}H NMR, ^{13}C NMR and HRMS. Spectra of all compounds (PDF)

References

1.Abida MI, Alsalman AJ. *Trop. J. Pharm. Res*. 2016, 15: 393-404.
2. Selim YA, Ouf NH. *Org. Med. Chem. Lett.* 2012, 2: 1-4.
3. Gourdeau H, Leblond L, Hamelin B. *Mol. Cancer. Ther*. 2004, 3: 1375-1383.
4. Venugopala KN, Rashmi, V, Odhav B. *Biomed. Res. Int.* 2013, 2013: 963248-963262.
5. Kirkiacharian S, Thuy DT, Sicsic S. *Il Farmaco*. 2002, 57: 703-708.
6. Marvig C L. Verhoef TI. De BA. *Thromb. Res.* 2015, 136: 69-75.
7. Al-Amiery AA, Al-Majedy YK, Kadhum AAH. *Molecules.* 2015, 20: 366-383.
8. Khan KM, Iqbal S, Lodhi MA. *Bioorgan. Med. Chem*. 2004, 12: 1963-1968.
9. Tang L, Li F, Liu M, Nandhakumar R. *B. Korean. Chem. Soc*. 2011, 32: 3400-3404.
10. Piltan MJ, Ghomi JS. *Bull. Chem. Soc. Ethiop.* 2016, 30: 289-296.
11. Zaheer Z, Khan FAK, Sangshetti JN. *Chinese. Chem. Lett*. 2016, 27: 287-294.
12. Rodriguez SA, Nazareno MA, Baumgartner MT. *Bioorgan. Med. Chem*. 2011, 19: 6233-6238.
13. Serra S, Ferino G, Matos MJ, Vazquez-Rodriguez S. *Bioorgan. Med. Chem. Lett*. 2012, 22: 258-261.
14. Stanchev S, Momekov G, Jensen F. *Eur. J. Med. Chem*. 2008, 43: 694-706.
15. Kalinin AV, Silva AJMD, Lopes CC. *Tetrahedron. Lett.* 1998, 39: 4995-4998.
16. Serra S, Chicca A, Delogu G. *Bioorgan. Med. Chem. Lett*. 2012, 22: 5791-5794.
17. Xi GL, Liu ZQ. *J. Agr. Food. Chem.* 2014, 62: 5636-5642.
18. Tang L, Pang Y, Yan Q. *J. Org. Chem*. 2011, 76: 2744-2752.
19. Cenini S, Cravotto G, Giovenzana GB. *J. Mol. Catal. A-Chem.* 2000, 164: 165-171.
20. Zhu Q, Wu J, Fathi R. *Org. Lett.* 2002, 4: 3333-3336.
21. Prendergast AM, McGlacken GP. *Eur. J. Org. Chem.* 2017, 2017: 4827-4835.
22. Bahulayan D, Das SK, Iqbal J. *J. Org. Chem.* 2003, 68: 5735-5738.
23. Jeganathan M, Dhakshinamoorthy A, Pitchumani K. *ACS. Sustain. Chem. Eng*. 2014, 2: 781-787.
24. Kannan V, Sreekumar K. *Mod. Res. Catal*. 2013, 2: 42-46.
25. Kumar BS, Dhakshinamoorthy A, Pitchumani K. *Catal. Sci. Technol*. 2014, 4: 2378-2396.
26. Marques IJ, Vaz PD, Fernandes AC. *Micropor. Mesopor. Mat*. 2014, 183: 192-200.
27. Fang Z, Liu B, Luo J. *Biomass. Bioenerg.* 2014, 60: 171-177.
28. Han J, Wang T, Feng S. *Green. Chem.* 2016, 18: 4092-4097.
29. Jeganathan M, Pitchumani K. *RSC. Adv*. 2014, 4: 38491-38497.
30. Jeganathan M, Dhakshinamoorthy A, Pitchumani K. *Tetrahedron. Lett.* 2014, 55: 1616-1620.
31.Soriente RAA, Rosa MD, Palombi L. *Green. Chem*. 1999, 1: 157-162.
32. Malanga C, Mannucci S. *Tetrahedron. Lett*. 2001, 42: 2023-2025.
33. Cushman M, Nagarathnam D, Burg DL. *J. Med. Chem.* 1991, 34: 798-806.
34. Cushman M, Nagarathnam D, Burg DL. *J. Med. Chem.* 1991, 34: 798-806.