

## Greener route for the synthesis of chromone using Amberlyst®15 via enaminones

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Dedicated to Prof. Sambasivarao Kotha on the occasion of his 65<sup>th</sup> birthday

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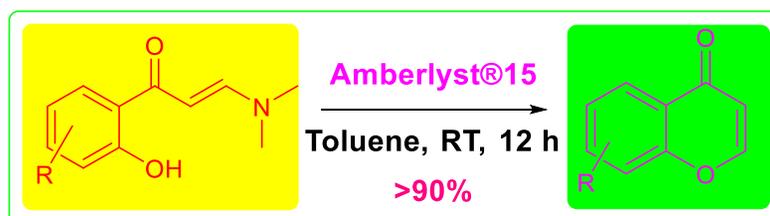
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### Abstract

An efficient and novel methodology is reported for the synthesis of various 4H-chromene-4-ones via enamino ketone followed by cyclization with Amberlyst®15 was described. The Amberlyst®15 worked well as deaminating agent as well as enhances the efficiency of cyclization reaction for the synthesis of chromones. This method offers several advantages including mild reaction conditions, high yielding, catalyst reusability, lower the reaction toxicity, operational easiness and broad substrate scope.



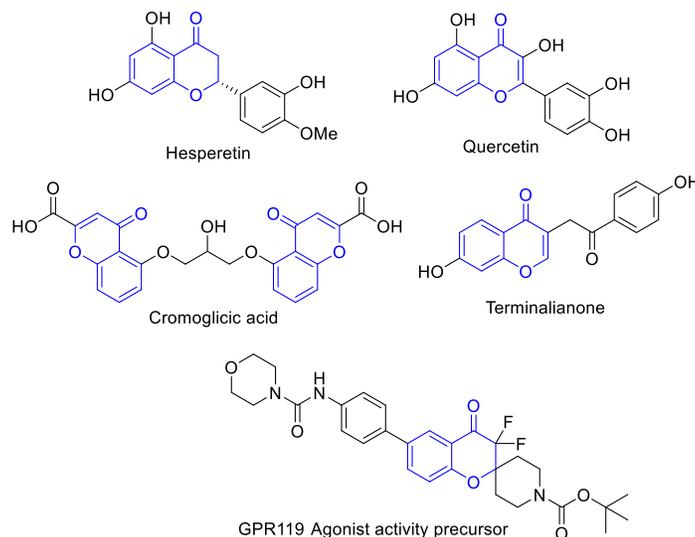
**16 examples with excellent yields**

R= Aryl, Hetero aryl, Alkyl, Halo etc.

**Keywords:** Medicinal chemistry, cyclization, chromone, enamine, Amberlyst-15

## Introduction

Chromone derivatives have a wide range of biological activities.<sup>1</sup> Chromone derivatives were shown to be tyrosine and protein kinase inhibitors,<sup>2-3</sup> anti-inflammatory,<sup>4</sup> antiviral,<sup>5</sup> antioxidant<sup>6-7</sup> and antihypertensive agents.<sup>5</sup> Compounds containing chromone moiety are also active at benzodiazepine receptors,<sup>8</sup> on lipooxygenase and cyclooxygenase.<sup>9</sup> In addition to this, they have shown to be anticancer agents<sup>10</sup> and in the treatment of cystic, as they activate the cystic fibrosis trans-membrane conductance regulator.<sup>11</sup> The vast range of biological effects associated with this chromone moiety has resulted in the chromone ring system being considered as a privilege structure.<sup>12-13</sup> A variety of biologically active compounds synthesized from chromones have been found widespread use in medicinal chemistry (**Figure 2**).<sup>14</sup>



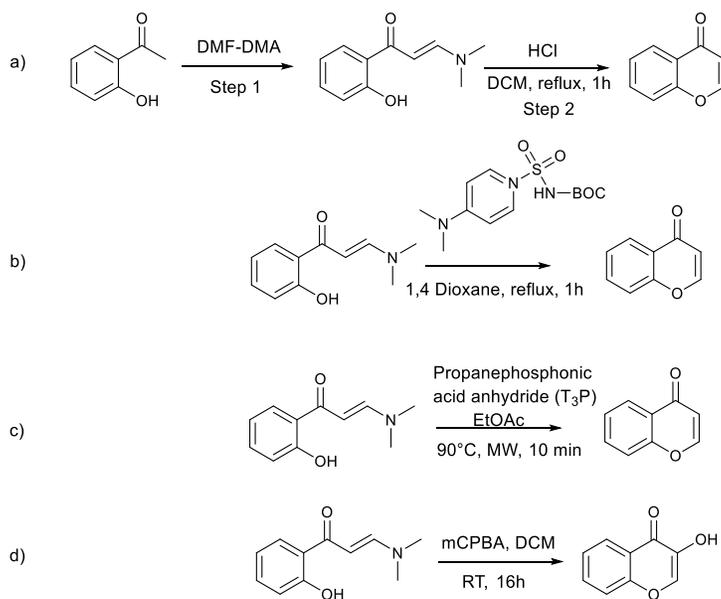
**Figure 1.** Biologically Active Compounds Derived from Chroman-4-ones

The chemistry of Amberlyst®15 is well known in the past decade.<sup>15</sup> It is a heterogeneous macro reticular polystyrene-based ion exchange resin and contains strongly acidic sulfonic group functionality. Amberlyst®15 has many advantages viz. safe to use, easy to measure and easily separable at the end of reaction. Amberlyst-15 is now commonly used as a heterogeneous reusable acid catalyst in organic synthesis for a variety of selective transformations of simple and complex molecules.<sup>16-17</sup>

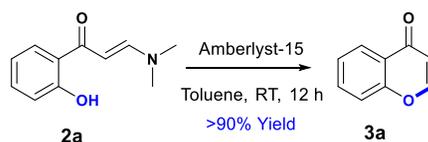
In general, synthesis of chromones has required acidic or basic conditions. One of the first methods for the synthesis of chromone was introduced by Heywang and Kostanecki which involved decarboxylation of chromone-2-carboxylic acid.<sup>18</sup> The traditional 2,3-disubstituted benzopyranone were synthesized under acidic condition with 3-aryl-1-(2-hydroxyphenyl) propane-1,3-dione derivatives undergoing intramolecular condensation. Mostly, Claisen ester condensation and Bayer-Venkatarman rearrangement are commonly used for synthesis of 1,3-dione derivatives. Most of the synthesis was reported under acidic reaction conditions whereas by using basic reaction condition for ring closure required several hours. *Gammill, R. B. et.al* was reported synthesis of chromone scaffolds and their 3-halogenated derivatives.<sup>19-20</sup> Recently, *Joussot and co-workers* reported an efficient synthesis of 3-substituted chromones via enamino ketones.<sup>21</sup> Synthesis of 3-benzylated chromones are also reported in the presence of NaI from enamino ketones and benzyl bromide.<sup>22</sup> There are limited studies on the synthesis of 2, 3-unsubstituted chromones from enamino ketones, compared to 3-substituted chromones.<sup>23</sup> For example, chromone **3a** was synthesized by cyclization via deamination of enamino ketone **2a** by using TMSCl/DMF. By using hydrochloric acid, Chromone synthesis was

reported by Pleier A.K. et al, (Scheme 1, entry a).<sup>25</sup> Chromone-3-one was synthesized from enamino ketones (2a) using several sulfamoylating reagents was reported by *Thiel Engelhart* and *Aldrich* (Scheme 1, entry b).<sup>26</sup> T3P was used for chromone synthesis under micro-wave reaction condition, reported by *C. Balakrishna et al*, (Scheme 1, entry c).<sup>27</sup> Using *mCPBA* as an oxidative reagent was used for 3-Hydroxy Chromone synthesis reported by *R. Gudipati et al.* (Scheme 1, entry d).<sup>28</sup> The reported method involves use of stringent reaction conditions like micro-wave, elevated temperature and not used environmental compatibility solvents. To overcome all these limitations, the development of new methodologies for the synthesis of chromone-4-one is still required.

**Previous work:**



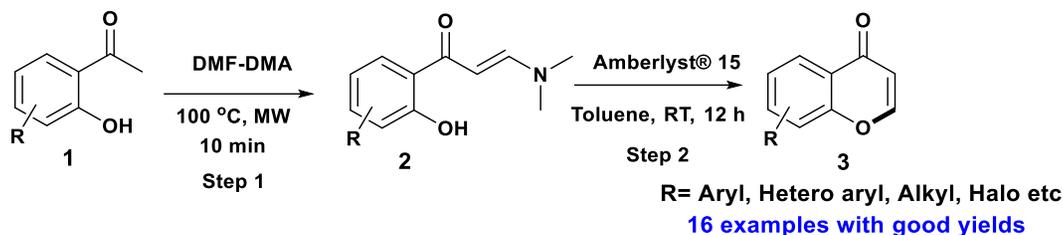
**Present Work:**



**Scheme 1** : Synthetic approach of chromone using Ameberlyst®15

## Results and Discussion

In our continued ongoing efforts to produce innovative synthetic methodologies<sup>29-34</sup> for the synthesis of Chromone-4-one analogues. We envisioned that Amberlyst-15 can be used for the cyclization of enamino ketone to prepare the chromone-4-one by taking advantage of suitable position of the hydroxyl group in the aromatic ring. Herein, we have described the synthesis of chromone-4-one derivatives by using Amberlyst®15. We have introduced first time, Amberlyst-15 as deamination reagent for the synthesis of chromone derivatives.



**Scheme 2.** Preparation of Chromone Using Amberlyst®15

Initially, 1-(2-hydroxyphenyl) ethanone **1a** was treated with N, N-Dimethylformamide dimethyl acetal under microwave irradiation to synthesize enaminone **2a**,<sup>32</sup> was analyzed by LCMS and <sup>1</sup>H-NMR data. The peak at 8.2 ppm in <sup>1</sup>H-NMR Spectrum shows the olefinic proton which was close to the nitrogen. The conversion of enaminoketone (**2a**) to chromone (**3a**) was executed by using Amberlyst®15 at room temperature. Thus the model reaction was conducted by treating enaminone (**2a**, 1 mmol) in Toluene solvent with Amberlyst 15 (40% w/w) at ambient temperature. We are pleased to find that this reaction condition worked well for synthesis of chromone with the good yield. (**Table 1, Entry 4**).

**Table 1: Screening optimal reaction conditions:**

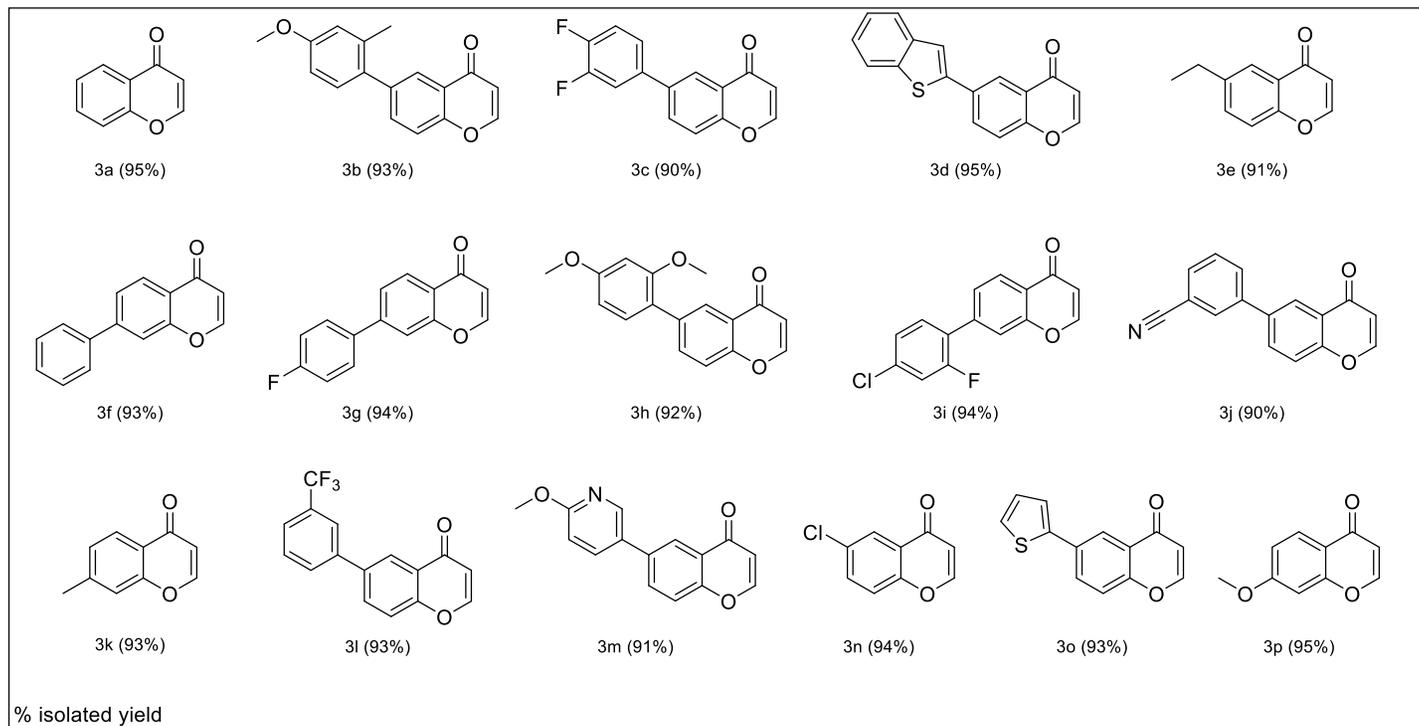
Entry	Reaction conditions <sup>a</sup>	Yield (%)
1	Toluene, RT, 12 h	00
2	Amberlyst, Toluene, RT, 2 h	46
3	Amberlyst, Toluene, RT, 6 h	61
4	Amberlyst, Toluene, RT, 12 h	<b>95</b>
5	Amberlyst, Toluene, 100°C, MW, 2 h	55
6	Amberlyst, DCM, RT, 16 h	89
7	Amberlyst, Acetone, RT, 18 h	40
8	Amberlyst, Dimethyl carbonate, RT, 24 h	46
9	Amberlyst, Acetonitrile, RT, 12 h	59
10 <sup>b</sup>	Amberlyst (25 %, w/w), Toluene, RT, 12 h	43

<sup>a</sup> Reaction conditions: Compound **2** (1 mmol), Amberlyst (40% w/w according to **2a**),

<sup>b</sup> 25 % w/w according to **2a**

To optimize the reaction conditions, we have screened several reaction conditions (**Table 1**). Initially, we have performed the reaction without Amberlyst-15 at room temperature and observed no product formation (**entry 1**) then we have introduced the Amberlyst-15 and monitored the reaction and showed 46% conversion of desired chromone product, further we have continued the reaction at room temperature for 12 h and observed 95% conversion of desired chromone product (**entry 2 to 4**). In order to reduce the reaction time, we have performed the reaction under micro-wave irradiation at 100°C however, not observed much promising conversion of chromone (**entry 5**).

**Table 2.** Synthesis of Substituted Chromones with Amberlyst®15



**Standard condition** : Enaminone (1 mmol), Amberlyst (40%, w/w), Toluene, RT, 12 h.

To validate further we have changed the solvents like acetone, dimethyl carbonate, acetonitrile and DCM. However, these solvents not shown the good conversion compared to toluene and in DCM conversion was observed 89% (**entry 6 to 9**). In addition, we have performed controlled experiment by a decrease in the amount to 25% w/w of Amberlyst-15, resulted 43% conversion of chromone (**entry 10**). These experiments showed that the optimized reaction conditions were 40 wt% Amberlyst-15 in toluene at room temperature for 12 h to obtain an 95% yield of **3a** (entry 4, Table 1). The work-up procedure also simplified by filtering the Amberlyst-15 and evaporated the reaction mixture under reduced pressure to get pure chromone product. We did not used any toxic solvents or reagents.

We have examined the recyclability of Amberlyst-15 ion-exchange resin up to five cycles. In the first and second cycle, we have observed the 95% yield of chromone (**3a**) consistently. From third to five cycles yields are 88%, 84% and 75% respectively. We have activated the recycled catalyst Amberlyst-15 using aqueous HCl followed by water and methanol. When we have used recovered catalyst as such without activation, the reaction was unsuccessful.

Thus, a series of enaminones **2a-p** were taken for the reaction to prove this method applicability. Excellent yield of the intended chromone derivatives **3a-p** (**table 2**) was obtained in each case under the optimum reaction conditions. This methodology was tolerant of various halides (Cl, Br, and F) and aryl halides. Both electron rich and deficient aromatic rings showed reactivity similar under this optimal conditions. In Table 2, synthesized Chromones **3a**<sup>27</sup>, **3e**<sup>35</sup>, **3k**<sup>36</sup>, **3n**<sup>27</sup>, **3o**<sup>37</sup> and **3p**<sup>38</sup> are reported in the literature, **3b**, **3c**, **3d**, **3f**, **3g**, **3h**, **3i**, **3j**, **3i** and **3m** are unknown compounds. A one-pot chromone synthesis was also tried, *o*-hydroxy acetophenone (**1a**) and DMF-DMA in toluene with amberlyst®15 at RT for 12 hours, chromone **3a** was not formed, instead we have observed the formation of compound **2a** which was confirmed by LCMS data.

## Conclusions

In summary, we have developed an efficient and novel methodology, simply reproducible of substituted chromone derivatives by using an excellent Heterogeneous catalyst as amberlyst®15. This method offers an effective alternative to the mild acidic conditions that are required generally for this conversion. The reaction

conditions are easy and sufficiently mild to tolerate various functionalities which will function the potential for further functionalization of the chromone products. We anticipate that this method is going to be find widespread application in preparation of chromone derivatives. This methodology can also be used to synthesize chromones on a gram scale.

## Experimental Section

**General.** Dry solvents were purchased from chemical suppliers. Analytical thin-layer chromatography (TLC) was performed on commercially available Merck TLC Silica gel 60 F<sub>254</sub>. Silica gel column chromatography was performed on silica gel 60 (spherical 100-200  $\mu\text{m}$ ). IR spectrawere recorded on Perkin-Elmer FT/IR-4000 using ATR.<sup>1</sup>H NMR spectra were recorded on Varian-400 (400 MHz) spectrometer. Chemical shifts of <sup>1</sup>H NMR spectra were reported relative to tetramethylsilane (<sup>13</sup>C NMR spectra were recorded on Varian-400 (100 MHz) spectrometer. Chemical shifts of <sup>13</sup>C NMR spectra were reported to relative to CDCl<sub>3</sub> (77.16) and DMSO-d<sub>6</sub> (39.5). Splitting patterns were reported as s, singlet ; d, doublet ; t, triplet ; q, quartet ; m, multiplet ; br, broad.

**General procedure for the synthesis of chromen-4-one derivatives.** To a stirred solution of compound Enaminone **2** (1 mmol) was dissolved in toluene (4 ml), was added amberlyst-15 (40% w/w) and the reaction mixture was stirred at RT for 12 h. The progress of the reaction was monitored by TLC (30% Ethyl acetate & Pet ether). After completion of the reaction, the reaction mixture was filtered through celite pad and washed with toluene. The filtrate was evaporated under reduced pressure to obtained crude compound **3**, which was further triturated with n-pentane to get pure compound **3** as off white solid.

**4H-Chromen-4-one (3a).** The title compound was prepared following general procedure compound **3a** was off white solid in 95% yield. Mp 51-54°C. FTIR (KBr): 3479, 3078, 2926, 1647, 1465, 1406, 1348, 1246, 1192, 1128, 1045, 1008 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.23 (dd, *J* 8 Hz, 1.6 Hz, 1 H), 7.85 (d, *J* 6 Hz, 1 H), 7.70-7.65 (m, 1 H), 7.47-7.39 (m, 2 H), 6.34 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 177.6, 156.5, 155.3, 133.8, 125.8, 125.2, 124.9, 118.2, 113.0. MS (EI): *m/z* 147(M+1,100). HRMS : (ESI) : Calcd for C<sub>9</sub>H<sub>7</sub>O<sub>2</sub> [M+H]<sup>+</sup> : 147.1450; Found: 147.1368.

**7-(4-Methoxy-2-methylphenyl)-4H-chromen-4-one (3b).** The titled compound was prepared following general procedure compound **3b** was isolated as off white solid in 93% yield. Mp 118-121°C. FTIR (KBr) : 3406, 3055, 2833, 2223, 1622, 1504, 1421, 1330, 1251, 1141, 1037 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>) :  $\delta$  8.14 (d, *J* 1.6 Hz, 1 H), 7.88 (d, *J* 6 Hz, 1 H), 7.63(dt, *J* 8.4 Hz, 1.2 Hz, 1 H), 7.49 (d, *J* 8.4 Hz, 1 H), 7.18(d, *J* 8.4 Hz, 1 H), 6.83-6.80 (m, 1H), 6.37 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>):  $\delta$  = 177.7, 159.1, 155.3, 155.2, 139.0, 136.7, 135.2, 132.6, 131.0, 125.9, 124.5, 117.8, 115.9, 113.0, 111.3, 55.3, 20.7. MS (EI) : *m/z* 267(M+1,100). HRMS : (ESI) : Calcd for C<sub>17</sub>H<sub>14</sub>O<sub>3</sub> [M+H]<sup>+</sup> : 267.2960; Found: 267.3283.

**6-(3,4-Difluorophenyl)-4H-chromen-4-one (3c).** The titled compound was prepared following general procedure compound **3c** was isolated as off-white solid in 90% yield. Mp 161-163°C. FTIR (KBr): 3278, 3095, 3024, 2943, 2860, 1649, 1562, 1485, 1404, 1286, 1205, 1130, 1035 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>):  $\delta$  8.36 (d, *J* 2 Hz, 1 H), 7.89 (d, *J* 6 Hz, 1 H), 7.84 (dd, *J* 8.8 Hz, 2.4 Hz, 1 H), 7.56 (d, *J* 8.8 Hz, 1 H), 7.54-7.43 (m, 1 H), 7.39-7.38 (m, 1 H), 7.38-7.27 (m, 1 H), 6.38 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>):  $\delta$  = 177.4, 156.1, 155.4, 136.3, 132.3, 125.1, 123.7, 123.2, 119.0, 117.9, 117.8, 116.2, 116.1, 113.1. MS (EI): *m/z* 259(M+1,100). HRMS: (ESI): Calcd for C<sub>15</sub>H<sub>8</sub>F<sub>2</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 259.2238; Found: 259.2113.

**6-(Benzo[b]thiophen-2-yl)-4H-chromen-4-one (3d).** The titled compound was prepared following general procedure compound **3a** was isolated as off white solid in 95% yield. Mp 121-125°C. FTIR (KBr): 3074, 1647,

1527, 1510, 1433, 1309, 1236, 1134, 1028, 839, 748 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.43 (d, *J* 2 Hz, 1 H), 7.93-7.89 (m, 4 H), 7.60 (d, *J* 8.8 Hz, 1 H), 7.50 (s, 1 H), 7.43-7.41 (m, 2 H), 6.40 (d, *J* 6 Hz, 1 H). <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 177.5, 155.9, 155.3, 140.7, 137.4, 136.1, 134.1, 133.4, 125.3, 125.1, 124.7, 124.6, 123.0, 122.5, 118.7, 113.1. MS (EI): *m/z* 279(M+1,100). HRMS: (ESI): Calcd for C<sub>17</sub>H<sub>10</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 279.3250; Found: 279.2479.

**6-Ethyl-4H-chromen-4-one (3e).** The titled compound was prepared following general procedure compound 3e was isolated as pale yellow solid in 91% yield. Mp 85-88°C. FTIR (KBr): 2980, 2916, 2858, 1653, 1541, 1490, 1425, 1319, 1257, 1199, 1128, 1029 cm<sup>-1</sup>. <sup>1</sup>H NMR (500 MHz, CDCl<sub>3</sub>): δ 8.02 (d, *J* 1.5 Hz, 1 H), 7.84 (d, *J* 6 Hz, 1 H), 7.52 (dd, *J* 8.5 Hz, 2 Hz, 1 H), 7.39 (d, *J* 8.5 Hz, 1 H), 6.33 (d, *J* 6 Hz, 1 H), 2.76 (m, 2 H), 1.28 (t, *J* 15 Hz, 3 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 176.8, 154.1, 140.5, 132.9, 123.6, 122.9, 117.0, 111.7, 28.7, 27.3, 14.4. MS (EI): *m/z* 175(M+1,100). HRMS: (ESI): Calcd for C<sub>11</sub>H<sub>10</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 175.1990; Found: 175.1980.

**7-Phenyl-4H-chromen-4-one (3f).** The titled compound was prepared following general procedure compound 3f was isolated as pale yellow solid in 93% yield. Mp 147-150°C. FTIR (KBr): 3332, 3151, 3078, 2920, 2848, 1641, 1544, 1494, 1460, 1421, 1352, 1313, 1242, 1145, 1010 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.27 (d, *J* 8.8 Hz, 1 H), 7.88 (d, *J* 6 Hz, 1 H), 7.67-7.04 (m, 4 H), 7.52-7.42 (m, 3H), 6.37 (d, *J* 7.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 177.5, 156.9, 155.4, 147.0, 139.1, 129.1, 128.7, 127.4, 126.3, 124.4, 123.6, 116.2, 113.1. MS (EI): *m/z* 223(M+1,100). HRMS: (ESI): Calcd for C<sub>15</sub>H<sub>10</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 223.2430; Found: 223.2121

**7-(4-Fluorophenyl)-4H-chromen-4-one (3g).** The titled compound was prepared following general procedure compound 3g was isolated as off white solid in 94% yield. Mp 111-114°C. FTIR (KBr): 3421, 3055, 2964, 2918, 2850, 1649, 1606, 1462, 1386, 1346, 1261, 1178, 1097, 1020 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.41 (d, *J* 2 Hz, 1 H), 7.90-7.87 (m, 2 H), 7.56 (d, *J* 8.8 Hz, 1 H), 7.44-7.40 (m, 2 H), 7.34 (dt, *J* 10 Hz, 1.6 Hz, 1 H), 7.11-7.06 (m, 1H), 6.39 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 176.4, 163.4, 161.0, 155.1, 154.3, 140.4, 136.1, 131.4, 129.4, 124.0, 122.8, 121.8, 117.9, 113.6, 112.9, 112.0. MS (EI): *m/z* 241(M+1,100). HRMS: (ESI): Calcd for C<sub>15</sub>H<sub>9</sub>FO<sub>2</sub> [M+H]<sup>+</sup>: 241.2334; Found: 241.2789.

**6-(2,4-Dimethoxyphenyl)-4H-chromen-4-one (3h).** The titled compound was prepared following general procedure compound 3h was isolated as brown solid in 92% yield. Mp 119-122°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.29 (d, *J* 2 Hz, 1 H), 7.87-7.85 (m, 1 H), 7.47 (d, *J* 8.8 Hz, 1 H), 7.30 (d, *J* 8.4 Hz, 1 H), 6.59 (d, *J* 2.4 Hz, 1 H), 6.57 (s, 1 H), 6.35 (d, *J* 6 Hz, 1 H), 3.86 (s, 3 H), 3.81 (s, 3 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 176.7, 159.8, 156.4, 154.3, 154.1, 134.8, 134.4, 130.4, 124.7, 123.6, 120.6, 116.5, 111.9, 103.8, 97.9, 54.5, 54.4. MS (EI): *m/z* 283(M+1,100). HRMS: (ESI): Calcd for C<sub>17</sub>H<sub>14</sub>O<sub>4</sub> [M+H]<sup>+</sup>: 283.2950; Found: 283.3358.

**7-(4-Chloro-2-fluorophenyl)-4H-chromen-4-one (3i).** The titled compound was prepared following general procedure compound 3i was isolated as off white solid in 94% yield. Mp 131-134°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ = 8.23 (d, *J* 8.4 Hz, 1 H), 7.892 (d, *J* 6 Hz, 1 H), 7.63 (s, 1 H), 7.56(d, *J* 8 Hz, 1 H), 7.44 (t, *J* =16.8 Hz, 1 H), 7.24 (d, *J* 1.6 Hz, 1 H), 7.28 (s, 1 H), 6.38 (d, *J* 6 Hz, 1 H) ppm. MS (EI): *m/z* 275(M+1,100).

**3-(4-Oxo-4H-chromen-7-yl)benzotrile (3j).** The titled compound was prepared following general procedure compound 3j was isolated as off white solid in 90% yield. Mp 118-120°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.41 (d, *J* 2.4 Hz, 1 H), 7.93-7.87 (m, 1 H), 7.69 (d, *J* 7.6 Hz, 1 H), 7.61-7.57 (m, 2 H), 6.41 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 177.3, 156.4, 155.5, 140.5, 136.0, 132.3, 131.5, 131.3, 130.7, 129.9, 125.2, 124.1, 119.3, 118.5, 113.3, 113.2. MS (EI): *m/z* 248(M+1,100). HRMS: (ESI): Calcd for C<sub>16</sub>H<sub>9</sub>NO<sub>2</sub> [M+H]<sup>+</sup>: 248.2530; Found: 248.2057.

**7-Methyl-4H-chromen-4-one (3k).** The titled compound was prepared following general procedure compound 3k was isolated as off white solid in 93% yield. Mp 87-90°C. FTIR (KBr): 3431, 3070, 2922, 2862, 1639, 1446, 1396, 1348, 1303, 1259, 1215, 1145, 1095, 1029 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.10 (d, *J* 8.4 Hz, 1 H), 7.81 (d, *J* 6 Hz, 1 H), 7.26-7.21 (m, 2 H), 6.31 (d, *J* 6 Hz, 1 H), 2.48 (s, 3 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ =

176.5, 155.6, 154.0, 144.1, 125.7, 124.5, 121.6, 116.8, 111.9, 20.8. MS (EI):  $m/z$  161(M+1,100). HRMS: (ESI): Calcd for C<sub>10</sub>H<sub>8</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 161.1720; Found: 161.1520.

**6-(3-(Trifluoromethyl) phenyl)-4H-chromen-4-one (3l).** The titled compound was prepared following general procedure compound 3l was isolated as off white solid in 93% yield. Mp 92-95°C. FTIR (KBr): 3496, 3064, 2927, 1761, 1643, 1481, 1375, 1294, 1103, 1012 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.44 (d, *J* 2 Hz, 1 H), 7.94–7.83 (m, 4 H), 7.64–7.57 (m, 3 H), 6.41 (d, *J* 5.2 Hz, 1 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 176.4, 155.2, 154.4, 139.0, 135.9, 131.5, 129.4, 128.5, 124.1, 123.5, 123.5, 123.0, 122.9, 122.9, 118.0, 112.1. MS (EI):  $m/z$  291(M+1,100). HRMS: (ESI): Calcd for C<sub>16</sub>H<sub>9</sub>F<sub>3</sub>O<sub>2</sub> [M+H]<sup>+</sup>: 291.2412; Found: 291.2344.

**6-(6-Methoxyppyridin-3-yl)-4H-chromen-4-one (3m).** The titled compound was prepared following general procedure compound 3m was isolated as pale yellow solid in 91% yield. Mp 135-138°C. FTIR (KBr): 3317, 3138, 3068, 2922, 1722, 1635, 1543, 1475, 1327, 1255, 1199, 1136, 1095, 1058, 1014 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.44 (d, *J* 2.4 Hz, 1 H), 8.35 (d, *J* 2.4 Hz, 1 H), 7.89–7.83 (m, 3 H), 7.56 (d, *J* 8.4 Hz, 1 H), 6.86 (d, *J* 8.4 Hz, 1 H), 6.39 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 176.5, 162.9, 154.8, 154.3, 144.1, 136.4, 134.2, 131.0, 127.3, 124.1, 122.2, 118.0, 112.0, 110.0, 52.6. MS (EI):  $m/z$  254(M+1,100). HRMS: (ESI): Calcd for C<sub>15</sub>H<sub>11</sub>NO<sub>3</sub> [M+H]<sup>+</sup>: 254.2570; Found: 254.2617.

**6-Chloro-4H-chromen-4-one (3n).** The titled compound was prepared following general procedure compound 3n was isolated as off white solid in 94% yield. Mp 133-136°C. FTIR (KBr): 3479, 3078, 2926, 1647, 1465, 1406, 1348, 1246, 1192, 1128, 1045, 1008 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.18 (d, *J* 2.4 Hz, 1 H), 7.86 (d, *J* 6 Hz, 1 H), 7.63-7.60 (dd, *J* 8.8 Hz, *J* 2 Hz, 1 H), 7.43 (d, *J* 8.8 Hz, 1 H), 6.36 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 176.3, 155.4, 154.8, 134.0, 131.3, 125.8, 125.3, 119.9, 112.9. MS (EI):  $m/z$  181(M+1,100).

**6-(Thiophen-3-yl)-4H-chromen-4-one (3o).** The titled compound was prepared following general procedure compound 3o was isolated as off white solid in 93% yield. Mp 101-104 °C. FTIR (KBr): 3093, 2966, 2920, 2852, 1647, 1602, 1525, 1477, 1438, 1390, 1352, 1305, 1261, 1222, 1184, 1136, 1093, 1016 cm<sup>-1</sup>. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.41 (d, *J* 1.6 Hz, 1 H), 7.93–7.90 (dd, *J* 8.8 Hz, *J*=2 Hz, 1 H), 7.87 (d, *J* 6 Hz, 1 H), 7.56 (s, 1 H), 7.51-7.42 (m, 3 H), 6.37 (d, *J* 6 Hz, 1 H) ppm. <sup>13</sup>C NMR (125 MHz, CDCl<sub>3</sub>): δ = 177.6, 155.6, 155.3, 140.4, 133.2, 132.0, 126.8, 126.2, 125.0, 122.7, 121.3, 118.7, 112.9. MS (EI):  $m/z$  229(M+1,100). HRMS: (ESI): Calcd for C<sub>13</sub>H<sub>8</sub>O<sub>2</sub>S [M+H]<sup>+</sup>: 229.2650; Found: 229.1784.

**7-Methoxy-4H-chromen-4-one (3p).** The titled compound was prepared following general procedure compound 3p was isolated as off white solid in 95% yield. Mp 56-57°C. <sup>1</sup>H NMR (400 MHz, CDCl<sub>3</sub>): δ 8.13 (d, *J* 8.8 Hz, 1 H), 7.78 (d, *J* 6 Hz, 1 H), 6.99–6.96 (dd, *J* 8.8 Hz, *J*=2 Hz, 1 H), 6.84 (d, *J* 2 Hz, 1 H), 6.29 (d, *J* 6 Hz, 1 H), 3.90 (s, 3 H) ppm. <sup>13</sup>C NMR (100 MHz, CDCl<sub>3</sub>): δ = 177.0, 164.1, 158.2, 154.8, 127.2, 118.8, 114.5, 112.9, 100.4, 55.8. MS (EI):  $m/z$  177(M+1,100). HRMS: (ESI): Calcd for C<sub>10</sub>H<sub>8</sub>O<sub>3</sub> [M+H]<sup>+</sup>: 177.1710; Found: 177.2031.

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## Supplementary Material

Supplementary data associated with this paper can be found in the online version

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