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A Comparative Synthesis of Ring-Substituted 3-(3-Bromo-4-Oxo-4h-Chromen-2-Yl)-4h-Chromen-4-One

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Abstract:

An efficient procedure for the preparation of substituted 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one via the condensation of acetophenones with 6-sub-4-oxo-4H-chromene-3-carbaldehyde in the presence of catalytic amount of ethylenediammoniumdiacetate (EDDA)using different ionic liquids at room temperature is described. The advantages of this method are generality, high yield, short reaction times, ease of product isolation, and ecologically friendly.

A series of substituted 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-one were prepared by the reaction of 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one in the presence of copper bromide and DMSO. A comparison of conventional heating and microwave irradiation in the synthesis of 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-ones is discussed. Microwave irradiation was found to increase the yields of the desired products, shorten the reaction time. The newly synthesized compounds were characterized on the basis of elemental analysis, IR, ^{1}H NMR and mass spectra.

Keywords: Chromone, acetophenone, aldehyde, ionic liquids, copper bromide, ethylenediammoniumdiacetate (EDDA),microwave

Introduction:

Natural products having a chromonic and flavonoidic structure exhibit important biological properties such as antiviral, cardioprotective, antioxidant, hepatoprotective, antitumoral and antiflammatory activities.[1] The 3-Formylchromone derivatives have been extensively used as versatile solution phase building blocks for the synthesis of a large number of heterocyclic systems. A number of 3-formylchromone[2] were synthesized by formylating 2-hydroxy acetophenone (Vilsmeier- Hack reaction). The most suitable formylating reagent is a complex of DMF and $POCl_3$. A number of reports have appeared in the literature, describing the isolation of chromones (flavonoids) from various plants: roots stem, bark, heartwood, seeds, leaves, and flowers. These compounds exists in the free state as chromones or in the combined from as glycosides. 2-Phenyl chromones and other constitute of heartwood and bark are relatively stable “end products” which may some times functions as fugisides, insecticides, etc. 2-Aryl chromones are known to prevent the contraction of rabbit intestine and other muscles.[3]Chromones like querecetin and routine possesses vitamin ‘p’ activity and are use in the treatment of condition in which there is capillary bleeding due to an increased capillary fragility.[4]

Result and Discussion:

The strategy for the synthesis of substituted 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-one(**5a-j**) involves the preparation of substituted 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one (**4a-j**)intermediates in the presence of copper bromide and DMSO. The substituted 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one (**4a-j**) was prepared by the condensation reaction between substituted acetophenone and 6-sub-4-oxo-4H-chromene-3-carbaldehyde using different ionic liquids.

The present method for the synthesis of 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one (**4b**) has many obvious advantages over classical procedures, including being environmentally more benign, simple, the ease of product isolation, higher yield, shorter reaction time. In recent years, organic reactions in ionic liqids without using harmful organic solvents are of great importance especially in relation to today's environmental concerns. On the other hand, organic reactions using reusable ionic liquids[5] have also received much attention because of their versatile and multifaceted characteristics. In continuation of our research in using ionic liquids as a green reaction medium for the condensation of carbonyl compounds with active methylene compounds catalyzed by ethylenediammoniumdiacetate (EDDA).[6]

The reaction was found to be general and applicable to aromatic aldehydes. The substituted acetophenone bearing various substituents such as chloro, nitro, methyl, etc. could successfully react with 6-sub-4-oxo-4H-chromone-3-carbaldehyde at room temperature within two hour with high yield. The examined ionic liquids general type [amine] $[HSO_4]$ and $[Bmim]BF_4$, $[Bmim]PF_6$ compared with the classical molecular solvents were all efficient and gave excellent results, with the advantage of rate acceleration and increase of yield which is depicted in table 1.

As we expected, the reaction could hardly proceed in the absence of EDDA. In conclusion, we have demonstrated that the condensation between 6-sub-4-oxo-4H-chromone-3-carbaldehyde with active methylene compounds could be effectively performed at room temperature in the ionic liquids $[Bmim]BF_4$ or $[Bmim]PF_6$ catalyzed by EDDA.

In this communication synthesis of $[Bmim]BF_4$, $[Bmim]PF_6$ [7] and three different ionic liquids of general type [amine] $[HSO_4]$ [8] was synthesized byliteratureand has been utilized for the comparative study.

The influence of molar conc. of $[Et_3NH][HSO_4]$, temperature, time was also recorded in case of 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromon-4-one **(4b)** at 100^0C in toluene. Water soluble ionic liquid was recovered by removing water under vacuum and oven dried after every cycle, table 2.

The IR spectra of compounds **4a-j** showed peaks at 3450 cm^{-1} due the –OH function. Strong, sharp absorption bands observed at 1640-1670 cm^{-1} attributable to the carbonyl (–C=O), bands at 1564-1575 cm^{-1} suggested the presence of C=C group. In addition, bands were observed at 2880-3070 cm^{-1} corresponding to the $–CH_3$ group.

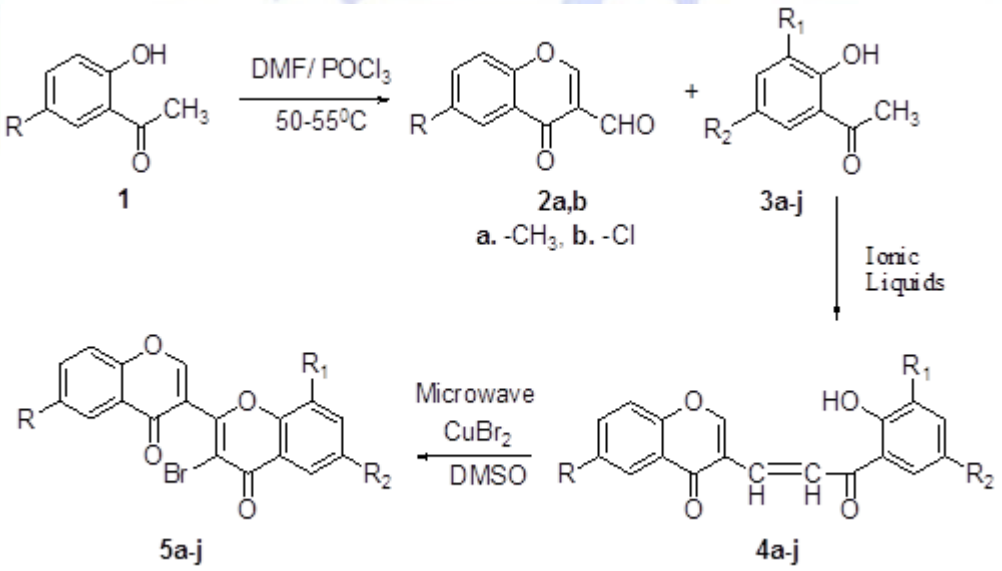
The ^1H NMR spectra of compounds **4a-j** displayed signals at δ 12.47-12.51due to the –OH. For compounds **4b, e** and **f,**the singlet at δ 2.3-2.4 integrated for the – CH_3 protons. ^1H NMR spectra of compounds **4a-j** revealed doublets at δ 7.78-8.30 indicating the presence of –CH=CH–group. An additional δ 5.3 singlet corresponding to two protons indicated the presence of an $–NH_2$ group in compound **4i**. The compounds **4a-j** gives the satisfactory elemental analysis. The physicochemical data is depicted in table 3.

Despite of the high degree of research findings over diverse area, it is intriguing to design and develop new heterocycles having novel moieties like bis-chromone within a single molecule. Literature survey shed light on the pharmacological importance of chromoneheterocycles and also upon the urgent need to develop some novel heterocycles that can act as inhibitor on various drug resistant pathogens. The title substituted 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-one (**5a-j**) have been prepared from the corresponding substituted 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one (**4a-j**)intermediates in the presence of copper bromide and DMSO.

Recently, much attention has focused on microwave assisted organic synthesis (MAOS) in the absence of a solvent. Often, thermal demanding reactions take hours in solution. However, with microwave irradiation these same reactions may be completed within a minute.

In this study subsequent ring closing affords the desired 3-(3-bromo-6-chloro-4-oxo-4H-chromen-2-yl)-6-methyl-4H-chromen-4-one (**5b**), in most instances with either warming to ambient temperature or mild heating at 75^{0}C. This ring closing required more forcing conditions to proceed effectively. In (**Scheme**) the synthesis of desired product **5b** was found to be exceedingly slow without heating above ambient temperature (7 h, ≤30%). Even heating at 75^{0}C for 7 h was found to be not optimal in providing the 3-(3-bromo-6-chloro-4-oxo-4H-chromen-2-yl)-6-methyl-4H-chromen-4-one (**5b)**.

Scheme



Furthermore, short reaction time with heating in an oil bath at higher reaction temperature (**Table 4**) were found to result in comparatively good yield of the desired product and complete consumption of starting material. Microwave irradiation with heating to 145^{0}C for 20 min promoted the formation of the desired 3-(3-bromo-6-chloro-4-oxo-4H-chromen-2-yl)-6-methyl-4H-chromen-4-one (**5b)** in 64% yield. It is interesting to note that both microwave irradiation with heating at a lower temperature (75^{0}C for 30 min) and immersion of the reaction flask in an oil bath at 145^{0}C for 4h and 75^{0}C for 7h provided less than optimal results.

The IR spectra of compounds **5a-j** showed peaks at 2936-3045 cm^{-1} due to methyl group while the peaks at 540 cm^{-1}attributed to C-Br group. A sharp band observed at 1680-1720 cm^{-1} corresponding to the carbonyl (-C=O) function derived from flavanoid structure.

The ^{1}H NMR spectra of compounds **5 b, e,** and **f** revealed singlet at δ 1.8-2.3 ppm integrating for three protons of –CH_3 group. The signals due the –OH group and corresponding doublets for –CH=CH- of chalcone structure did not appear. Additional signals at δ 7.02-8.2 ppm in aromatic region integrating due to 7 protons indicated the formation of hybrid molecules of quinoline appended with a flavanoid moiety strongly supported the structure. The ^{1}H NMR spectra of compounds **5i** having -NH_2 group resonated at δ 5.3 ppm integrating for two protons as a singlet.

The elemental analysis and molecular ion peaks of compounds **5a-j** were consistent with the assigned structure. The physicochemical characteristics are well mentioned in table5.

The syntheses were carried out in a MW domestic oven adapted for the use of a reflux condenser, at constant power (400 W). All the reactions proceed to completion between 10 to 20 min and a longer time did not increase the yield.

Experimentals:

Melting points were determined by open capillary method and are uncorrected. All solvents were distilled prior to use. TLC was performed on silica gel G. The ^{1}H NMR spectra were recorded on a Brucker AC 400 (MHz) in DMSO-d_6 using TMS as internal reference. The IR spectra were recorded on a Perkin-Elmer 1800 spectrophotometer in the 4000–400 cm^{-1} range using KBr pellets.

3.1 General procedure

3.1.1 General procedure for synthesis of 6-chloro-3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one 4a.

A mixture of 6-chloro-4-oxo-4H-chromone-3-carbaldehyde (0.01 moles), 1-(5-choro-2-hudroxyphenyl)acetophenone (0.01 mole) was taken in toluene were [Bmim]BF_4 or [Bmim]PF_6 (2 mL) added. The reaction mixture was stirred at room temperature for appropriate time; the reaction was monitored by TLC. Upon completion of the reaction, the reaction mixture pours into crushed ice. The solid was filtered, dried and crystallized from acetic acid and alcohol. The yellow crystalline compound was obtained (yield 65%). The product was purified using column chromatography with silica-gel and *n*-hexane/EtOAc (7:3), if necessary.

IR (KBr, cm^{-1}) : 1575, 1645, 1670, 2930, 3450; ^1H NMR (DMSO-d_6) : δ 6.90-6.92 (d, 1H, *J*= 8.92Hz, Ar-Hh), 7.08-7.09 (d, 1H, *J*= 2.68Hz, Hc), 7.31-7.39 (2dd, 1H, Hi &Hb), 7.65-7.69 (d, 1H, *J*=15.4Hz, Hg), 7.78-7.80 (d, 1H, *J*= 9.2Hz, Ha), 7.88-7.88 (d, 1H, *J*= 2.52Hz, Hj), 8.21-8.25 (d, 1H, *J*= 15.44Hz, Hf), 8.46 (s, 1H, Hd), 12.47 (s, 1H, Ar-OH) ;**MS**: *m/z* 361

3.1.2 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one 4b

IR (KBr, cm^{-1}) : 695, 1675, 1890, 3500; ^1H NMR (DMSO-d_6) : δ 1.49 (s, 3H, CH_3), 6.80-6.81 (d, 1H, *J*= 1.56Hz), 7.05-7.09 (d, 1H, *J*= 3.88Hz), 7.24-7.29 (dd, 1H, Hb), 7.63-7.68 (d, 1H, *J*= 18.16Hz), 7.76-7.78 (d, 1H, *J*= 10.6Hz), 7.89-7.90 (dd, 1H), 7.99-8.02 (d, 1H, *J*= 10.6Hz), 8.47 (s, 1H, Hd), 11.30 (s, 1H, Ar-OH); **MS**: *m/z* 341

3.1.3 3-(3-(5-bromo-3-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-chloro-4H-chromen-4-one 4c

IR (KBr, cm^{-1}) : 1635, 1665, 3035; ^1H NMR (DMSO-d_6) : δ 7.01-7.03 (d, 1H, *J*= 8.32Hz), 7.29-7.33 (dd, 1H, Hb), 7.58-7.59 (d, 1H, J=4.04Hz, Hc), 7.85-7.86 (d, 1H, *J*= 6.04Hz, Ha), 8.01-8.04 (d, 1H, *J*= 11.92Hz, Hg), 8.12-8.15 (d, 1H, *J*= 12.08Hz, Hf), 8.27 (s, 1H, Hd), 11.50 (s, 1H, Ar-OH); **MS**: *m/z* 440;

3.1.4 6-chloro-3-(3-(3-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one 4d

IR (KBr, cm^{-1}) : 650, 1645, 1705, 3430; ^1H NMR (DMSO-d_6) : 6.29-6.34 (dd, 2H, Hi&j), 7.13-7.15 (d, 2H, *J*= 8.64Hz, Hg), 7.26-7.27 (d, 1H *J*= 2.48Hz, Hc), 7.39-7.41 (dd, 1H, Hb), 7.75-7.76 (d, 1H, *J*= 2.08Hz, Ha), 7.84-7.86 (d, 1H, *J*= 9.24Hz, Hf), 8.24 (s, 1H, Hd), 10.09 (s, 1H, Ar-OH); **MS**: *m/z* 361

3.1.5 6-chloro-3-(3-(2-hydroxy-5-methyl-3-nitrophenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one 4e

IR (KBr, cm^{-1}) : 735, 1610, 1680, 2980, 3530; ^1H NMR (DMSO-d_6) : δ 1.52 (s, 3H, CH_3), 2.16 (s, 3H, Ar-CH_3), 6.90-6.92 (d, 1H, *J*= 8.36Hz, Hc), 7.09-7.09 (d, 1H, *J*=2.6Hz, Hg),7.31-7.34 (dd, 1H, Hb), 7.62-7.64 (d, 1H, *J*= 8.36Hz, Hi), 7.75-7.76 (d, 1H, *J*= 6.4Hz, Ha), 7.87-7.88 (d, 1H, *J*= 2.96Hz, Hf), 8.21-8.25 (d, 1H, *J*= 15.52Hz, Hj,), 8.46 (s, 1H, Hd), 12.31 (s, 1H, Ar-OH); **MS**: *m/z* 386

3.1.6 3-(3-(3-bromo-5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one 4f

IR (KBr, cm^{-1}) : 689.3, 1690, 2910, 3450; ^1H NMR (DMSO-d_6) : δ 1.42 (s, 3H, CH_3), 7.01-7.03 (d, 1H, *J*= 8.8Hz, Hc), 7.2-7.3 (dd, 1H, Hi), 7.5-7.6 (dd, 1H, Hb), 7.85-7.86 (d, 1H, *J*= 6.04Hz, Hg), 8.01-8.04 (d, 1H, *J*= 11.92Hz, Ha), 8.12-8.15 (d, 1H, *J*= 8.56Hz, Hf), 8.27 (s, 1H, Hd), 11.5 (s, 1H, Ar-OH); **MS**: *m/z* 419;

3.1.7 3-(3-(3-bromo-5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-chloro-4H-chromen-4-one 4g

IR (KBr, cm^{-1}) : 1585, 1655, 1675, 3495; ^1H NMR (DMSO-d_6) : δ 6.77-6.78 (d, 1H, *J*= 4.88Hz), 7.31-7.34 (dd, 1H, Hb), 7.41-7.42 (d, 1H, *J*= 4.08Hz, Hg), 7.72-7.75 (d,

1H, *J*= 13.9Hz, Ha), 7.78-7.79 (d, 1H, *J*= 4.08Hz, Hf), 7.87-7.88 (d, 1H, *J*= 4.66Hz, Hi), 8.18-8.19 (d, 1H, *J*= 2.64Hz, Hj), 8.42 (s, 1H, Hd), 11.83 (s, 1H, Ar-OH); **MS**:

3.1.8 3-(3-(3-bromo-2-hydroxy-5-methylphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one 4h

IR (KBr, cm^{-1}) : 695, 1590, 1680, 2988, 3490; ^1H NMR (DMSO-d_6) : δ 2.16 (s, 6H, -CH_3), 6.95-6.96 (d, 1H, *J*= 2.76Hz, Hc), 7.20-7.20 (d, 1H, *J*= 2.98Hz, Ha), 7.38-7.39 (dd, 1H, Hb), 7.73-7.77 (d, 1H, *J*= 15.52Hz, Hg), 7.85-7.87 (d, 1H, *J*= 9.2Hz, Hi), 7.9-8.03 (m, 1H, Ar-H), 8.09-8.13 (d, 1H, *J*= 15.68Hz, Hf), 8.57 (s, 1H, Hd), 11.96 (s, 1H, Ar-OH); **MS**: *m/z* 399

3.1.9 3-(3-(5-amino-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-chloro-4H-chromen-4-one 4i

IR (KBr, cm^{-1}) : 725, 1610, 1710, 3550; ^1H NMR (DMSO-d_6) : δ 5.3 (s, 2H, Ar-NH_2), 7.39-7.39 (d, 1H, *J*= 2.32Hz, Hc), 7.50-7.53 (dd, 1H, Hb), 7.67-7.69 (d, 1H, *J*= 8.88Hz, Hg), 7.78-7.81 (dd, 1H, Hi), 7.92-7.94 (d, 1H, *J*= 9.04Hz, Hf), 8.09-8.09 (d, 1H, *J*= 2.4Hz, Hj,), 8.63 (s, 1H, Hd), 9.6 (s, 1H, Ar-OH); **MS**: *m/z* 341

3.1.10 3-(3-(2-hydroxy-5-methylphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one 4j

IR (KBr, cm^{-1}) : 1600, 1645, 2900, 3000, 3400; ^1H NMR (DMSO-d_6) : δ 2.38 (s, 6H, -CH_3), 6.96-6.98 (d, 1H, *J*= 8.48Hz, Hh), 7.14-7.15 (d, 1H, *J*= 2.68Hz, Hc), 7.35-7.44 (2dd, 1H, Hi & Hb), 7.71-7.75 (d, 2H, *J*= 15.56Hz, Ha), 7.91-7.94 (d, 1H, *J*= 9.2Hz, Hg), 8.27-8.30 (d, 1H, *J*= 15.48Hz, Hf), 8.39 (s, 1H, Hd), 12.51 (s, 1H, Ar-OH) ; **MS**: *m/z* 320

3.2.1 General procedure for synthesis of 3-(2-bromo-7-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5a.

A mixture of 6-chloro-3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-4H-chromen-4-one, cupper bromide in DMSO was taken in a conical flask covered with filter funnel. The reaction mixture was irradiated in microwave oven (domestic) at 145^{0}C for 10-12 min. The reaction periods were standardized by irradiating the reaction mixtures in 1-6 cycles, each of 2min interval and 1min rest. The progress of reaction was monitor by TLC (in each 2 min interval). After cooling to room temp., the solvent was evaporated and the residue was extracted in ethyl acetate (10mL x 3) and dried over Na_2SO_4. The organic layer was evaporated on rotary evaporator solid mass obtained.

IR (KBr, cm^{-1}) : 1670, 2930-3070, 750 cm^{-1}; ^1H-NMR(DMSO-d_6) : δ7.02-7.04 (dd, 1H, J=9.36 Hz, Hd), 7.11-7.12 (dd, 1H, Hi), 7.26-7.27 (d, 1H, J=2.48 Hz, Hc), 7.75-7.76 (d, 1H, J=2.08 Hz, Hj), 7.84-7.86 (d, 1H, J=9.24 Hz, Ha), 8.0 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 16.89, 96.23, 116.71, 119.00, 123.78, 125.30, 128.93, 132.98, 138.82, 141.21, 141.44, 145.12, 147.04, 158.0, 169.82, 174.03; **MS (**m/z**):** 436 M^+

3.2.2 3-(2-bromo-7-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-methyl-4H-chromen-4-one 5b

IR (KBr, cm^{-1}) : 3150, 2978, 1680, 1510, 775cm^{-1}; ^1H-NMR(DMSO-d_6) : δ 1.22 (s, 3H, -CH_3), 6.88-6.89 (d, 1H, J=3.8Hz, Hc), 7.15-7.17 (d, 1H, J=7.76Hz, Ha), 7.33-

7.37 (dd, 1H, Hb), 7.89-7.91 (d, 1H, J=7.32Hz), 8.00 (s, 1H, Hh), 8.45 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 18.2, 102.1, 105.8, 106.7, 118.2, 122.3, 126.3, 127.8, 128.2, 131.2, 133.3, 142.3, 145.2, 158.3, 165.2, 168.5, 174.5; **MS (m/z):** 416 M^+

3.2.3 3-(2,7-dibromo-5-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5c

IR (KBr, cm^{-1}) : 3080, 1702, 1603, 1645,680, 565cm^{-1}; ^{1}H-NMR(DMSO-d_6) : 7.04-7.05 (d, 1H, J=3.92Hz, Hc), 7.30-7.34 (dd, 1H, Hb), 7.57-7.59 (d, 1H, J=7.6Hz, Hi), 7.64-7.66 (d, 1H, J=9.17Hz, Hj), 7.84-7.87 (d, 1H, J=14.52Hz, Ha), 8.00 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 103.4, 107.2, 118.1, 125.3, 128.2, 128.6, 129.3, 132.2, 133.4, 137.8, 138.9, 143.3, 147.8, 153.5, 167.2, 172.8; **MS (m/z):** 515 M^+

3.2.4 3-(2-bromo-5-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5d

IR (KBr, cm^{-1}) : 2991, 1690, 1590, 680cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ 6.85-6.86 (d, 1H, J=4.92Hz, Hj), 7.05-7.06 (d, 1H, J=2.68Hz, Hc), 7.26-7.35 (m, 2H, He), 7.61-7.65 (d, 1H, J=15.4Hz, Hi), 7.75-7.78 (d, 1H, J=13.2Hz, Ha), 7.84 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: δ 101.4, 107.5, 124.2, 125.5, 128.7, 132.5, 135.3, 136.2, 136.7, 137.5, 143.2, 149.8, 152.4, 170.1, 175.3; **MS (m/z):** 436.03 M^+

3.2.5 3-(2-bromo-1,4-dihydro-7-methyl-5-nitro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5e

IR (KBr, cm^{-1}) : 3101, 2990, 1962, 680cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ 1.88 (s, 3H, -CH_3), 7.12-7.14 (d, 1H, J=7.12Hz, Ha), 7.30-7.30 (d, 1H, J=3.48Hz, Hc), 7.56-7.59 (dd, 1H, Hb), 7.89-7.90 (d, 1H, J=5.4Hz, Hj), 8.00-8.02 (d, 1H, J=8.2Hz, Hi), 8.11 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 20.3, 100.8, 103.8, 122.5, 123.3, 125.5, 128.1, 130.9, 135.2, 138.3, 141.5, 148.2, 149.3, 169.5, 179.3; **MS (m/z):** 460.7 M^+

3.2.6 3-(2,5-dibromo-7-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-methyl-4H-chromen-4-one 5f

IR (KBr, cm^{-1}) : 2983, 1696, 1342, 668cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ 1.59 (s, 3H,-CH_3), 6.84-6.85 (d, 1H, J=6.88Hz, Ha), 7.07-7.10 (dd, 1H, Hb), 7.37-7.38 (d, 1H, J-3.76Hz, Hj), 7.43-7.44 (d, 1H, J=3.04Hz, Hc), 7.62-7.65 (d, 1H, J=14.72, Hh), 7.80 (s, 1H); ^{13}C-NMR(DMSO-d_6) δ: δ 14.5, 90.7, 102.3, 106.8, 122.3, 127.0, 129.3, 127.3, 131.1, 133.1, 142.5, 144.3, 147.2, 152.2, 155.2, 172.5; **MS (m/z):** 494.14 M^+

3.2.7 3-(2,5-dibromo-7-chloro-1,4-dihydro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5g

IR (KBr, cm^{-1}) : 2900, 1610, 1530, 1340, 725, 675cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ 6.74-6.76 (d. 1H, J=7.32Hz, Hi), 7.23-7.29 (dd, 1H, Hb), 7.39-7.39 (d, 1H, J=2.48Hz), 7.69-7.72 (d, 1H, J=14.00Hz, Ha), 7.77-7.79 (d, 1H, J= 7.68Hz, Hj), 7.85 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 102.1, 107.7, 117.2, 124.2, 128.7, 129.2, 131.3, 132.4, 133.5, 136.4, 138.5, 143.2, 147.6, 153.3, 170.2, 175.1; **MS (m/z):** 515.14 M^+

3.2.8 3-(2,5-dibromo-1,4-dihydro-7-methyl-1-oxonaphthalen-3-yl)-6-methyl-4H-chromen-4-one 5h

IR (KBr, cm^{-1}) : 3120, 2999, 769cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ1.67 (s, 6H, -CH_3), 6.77-6.79 (d, 1H, J=8.52Hz, Hj), 7.03-7.04 (d, 1H,J=3.24Hz, Hi), 7.22-7.25 (dd, 1H, Hb), 7.53-7.57 (d, 1H, J=15.52Hz, Ha), 7.64-7.67 (d, 1H, J=11.88Hz), 7.79-7.81 (m, 1H), 8.89 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 22.2. 99.7, 103.8, 114.9, 124.3, 126.4, 128.9, 130.1, 131.1, 132.2, 135.3, 140.5, 143.6, 147.5, 152.3, 170.3, 174.1; **MS (**m/z**):** 474.29 M^+

3.2.9 3-(7-amino-2-bromo-1,4-dihydro-1-oxonaphthalen-3-yl)-6-chloro-4H-chromen-4-one 5i

IR (KBr, cm^{-1}) : 3370, 3010, 1390, 670cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ 5.30 (s, 2H, Ar-NH_2), 7.39-7.39 (d, 1H, J=3.64Hz), 7.50-7.53 (dd, 1H, Hb), 7.67-7.69 (d, 1H, J=8.88Hz, Ha), 7.78-7.79 (1H, d, J=2.36Hz, Hc), 7.81-7.81 (d, 1H, J=2.44Hz, Hj), 7.92-7.94 (d, 1H, J=8.96Hz, Hi), 8.02 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: δ 167.1, 103.3, 108.4, 117.3, 118.5, 122.5, 125.3, 127.8, 129.2, 132.4, 136.3, 142.7, 148.3, 148.8, 157.1, 171.2; **MS (**m/z**):** 417.08 M^+

3.2.10 3-(2-bromo-1,4-dihydro-7-methyl-1-oxonaphthalen-3-yl)-6-methyl-4H-chromen-4-one 5j

IR (KBr, cm^{-1}) : 3110, 1690,1629, 788cm^{-1}; ^{1}H-NMR(DMSO-d_6) : δ1.72 (s, 6H, -CH_3), 7,28-7.30 (d, 1H, J=8.96Hz, Ha), 7.47-7.48 (d, 1H, J=5.24Hz,), 7.66-7.69 (dd, 1H, Hb), 7.73-7,76 (dd, 1H, Hi), 8.03-8.07 (d, 2H, J=17.4, Hh), 8.25 (s, 1H, Hd); ^{13}C-NMR(DMSO-d_6) δ: 24.3, 98.23, 105.6, 117.6, 123.9, 129.0, 131.0, 130.1, 134.4, 135.6, 133.1, 142.7, 147.2, 154.3, 168.00, 173.01; **MS (**m/z**):** 395.08 M^+

Conclusion:

In summary, a synthesis of chromone based substituted 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-one compounds (**5a-j**) using at 140°C microwave oven (domestic) DMSO, without any special activation was well examined.

From the experimental evidences of influence of molar conc. of [Et_3NH][HSO_4], temperature, time was also recorded in case of (**4b**) at 100°C in toluene. The recycling efficiency of ionic liquid was found to be decreased after each cycle.

With this facile method, we achieved maximum yield. This method works with a wide variety of primary as well as secondary amines and aldehydes. The mild reaction conditions, cheap and easily available raw material required for ionic liquids and simplicity of the reaction procedure and dual nature of recyclable ionic liquids will certainly attract attention among organic chemists.

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Table.1- Selectivity proper solvent for synthesis of 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromon-4-one **(4b)**.

S. No	Ionic liquid	Solvent	Presence of EDDA (0.1mmole)		Absence of EDDA	
			Time (h)	Yield (%)	Time (h)	Yield (%)
1	[Bmim]PF_6	DMF	3	72	6	25
		Toluene	3	75	6	28
		THF	3	70	6	19
2	[Bmim]BF_4	DMF	3	70	6	22
		Toluene	3	73	6	28
		THF	3	69	6	21
3	Triethylamine sulfate $[Et_3NH][HSO_4]$	DMF	3	65	6	23
		Toluene	3	67	6	25
		THF	3	66	6	20
4	n-Tripropyl amine sulfate [n-$Pr_3NH][HSO_4$]	DMF	3	66	7	22
		Toluene	3	66	7	24
		THF	3	64	7	20
5	IsoPropylamine sulfate [iso-$PrNH_2][HSO_4$]	DMF	3	62	7	22
		Toluene	3	63	7	20
		THF	3	60	7	20
6	Classical way	Ethanol/Piperidine	The reaction mixture was kept for 35-40^{0}C for 3 h. (Yield 30%)			

Table2: Effect of reuse of $[Et_3NH][HSO_4]$ ionic liquid on the formation of 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromon-4-one **(4b)** at 100^{0}C in toluene.

Entry	Recycling	Time (h)	Isolated Yield %
1	0	3	75
2	1	3	73
3	2	3	71
4	3	3	70
5	4	3	69
6	5	3	67
7	6	3	66
8	7	3	64
9	8	3	63
10	9	3	62

Table 3: Physical characterization data of substituted 3-(3-(5-chloro-2-hydroxyphenyl)-3-oxoprop-1-enyl)-6-methyl-4H-chromen-4-one(**4a-j**).

S. No.	R	R_1	R_2	Yield (%)	m.p. (^{0}C)	Mol. formula	(Calcd) (%) Found		
							C	H	O
4a	Cl	H	Cl	65	166	$C_{18}H_{10}Cl_2O_4$	59.75 (59.86)	2.45 (2.79)	17.69 (17.72)
4b	CH_3	H	Cl	75	219	$C_{19}H_{13}ClO_4$	66.86 (66.97)	3.70 (3.85)	18.64 (18.78)
4c	Cl	Cl	Br	66	225	$C_{18}H_9BrCl_2O_4$	49.10 (49.13)	2.01 (2.06)	14.45 (14.54)
4d	Cl	Cl	H	69	230	$C_{18}H_{10}Cl_2O_4$	59.80 (59.86)	2.73 (2.79)	17.65 (17.72)
4e	Cl	NO_2	CH_3	63	238	$C_{19}H_{12}ClNO_6$	59.10 (59.16)	3.10 (3.14)	24.80 (24.89)
4f	CH_3	Br	Cl	65	240	$C_{19}H_{12}BrClO_4$	54.32 (54.38)	2.84 (2.88)	15,19 (15.25)
4g	Cl	Br	Cl	55	198	$C_{18}H_9BrCl_2O_4$	49.06 (49.13)	2.00 (2.06)	14.45 (14.54)
4h	CH_3	Br	CH_3	58	260	$C_{20}H_{15}BrO_4$	60.01 (60.17)	3.62 (3.79)	16.00 (16.03)
4i	Cl	H	NH_2	60	177	$C_{18}H_{12}ClNO_4$	63.17 (63.26)	3.45 (3.54)	18.69 (18.73)
4j	CH_3	H	CH_3	61	181	$C_{20}H_{16}O_4$	74.56 (74.99)	5.00 (5.03)	19.76 (19.98)

Table 4: Synthesis of 3-(3-bromo-6-chloro-4-oxo-4H-chromen-2-yl)-6-methyl-4H-chromen-4-one **(5b).**

Entry	Temp	Time	Heating Method	Yield (%)
1	75	7 h	Oil bath	30
2	145	4 h	Oil bath	45
3	75	30 min	Microwave reactor	50
4	145	20 min	Microwave reactor	64

Table 5: Physical characterization data of Substituted 3-(3-bromo-4-oxo-4H-chromen-2-yl)-4H-chromen-4-one(**5a-j**).

S. No	R	R_1	R_2	MW Time (min)	Yield (%)	m.p.	Mol. formula	(Calcd) (%) Found		
								C	H	O
5a	Cl	H	Cl	10	76	120	$C_{19}H_9BrCl_2O_3$	52.30 (52.33)	2.03 (2.08)	11.00 (11.01)
5b	CH_3	H	Cl	10	64	125	$C_{20}H_{12}BrClO_3$	57.60 (57.79)	2.89 (2.91)	11.52 (11.55)
5c	Cl	Cl	Br	12	72	123	$C_{19}H_8Br_2Cl_2O_3$	44.28 (44.31)	1.60 (1.57)	9.28 (9.32)
5d	Cl	Cl	H	12	65	112	$C_{19}H_9BrCl_2O_3$	52.35 (52.33)	2.10 (2.08)	11.02 (11.01)
5e	Cl	NO_2	CH_3	10	67	120	$C_{20}H_{11}BrClNO_5$	52.16 (52.15)	2.39 (2.41)	3.02 (3.04)
5f	CH_3	Br	Cl	12	64	120	$C_{20}H_{11}Br_2ClO_3$	48.60 (48.57)	2.26 (2.24)	9.70 (9.71)

5g	Cl	Br	Cl	10	75	240	$C_{19}H_8Br_2Cl_2O_3$	44.27 (44.31)	1.53 (1.57)	9.24 (9.32)
5h	CH_3	Br	CH_3	10	62	230	$C_{21}H_{14}Br_2O_3$	52.16 (53.20)	2.92 (2.98)	9.89 (10.12)
5i	Cl	H	NH_2	12	62	130	$C_{19}H_{11}BrClNO_3$	54.67 (54.77)	2.56 (2.66)	11.2 (11.52)
5j	CH_3	H	CH_3	12	64	255	$C_{21}H_{15}BrO_3$	63.83 (63.81)	3.85 (3.83)	12.06 (12.14)

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