



## Alum [KAL(SO<sub>4</sub>)<sub>2</sub>·12H<sub>2</sub>O]: An Inexpensive and Efficient Catalyst for Knoevenagel Condensation in Water

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### Abstract

*The green, mild and efficient synthesis of 2, 2-dimethyl-5- [(4-oxo-4H-chromen-3-yl)methylene]-1, 3-dioxane-4, 6-diones by Knoevenagel condensation of 4-oxo-4H-benzopyran-3-carbaldehydes with Meldrum's acid in the presence of catalytic amount of alum in water medium at room temperature. This method gives remarkable advantages such as simple work-up procedure, mild reaction conditions, short reaction times and excellent yield of products. Moreover, the catalyst used is easily available, inexpensive, non-toxic and eco-friendly.*

**Keywords:** Knoevenagel reaction, alum, water, 4-oxo-(4H)-1-benzopyran-3-carbaldehyde, Meldrum's acid

### Introduction

Knoevenagel condensation is one of the most important method for the preparation of substituted alkenes by reactions of carbonyl compounds with active methylene compound [1]. The Knoevenagel condensation reactions are classically catalyzed by base in liquid-phase systems; various catalysts are known to effect the reaction with different aldehydes and active methylene group.

Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) is an active methylene compound having rigid cyclic structure with high acidity (pK<sub>a</sub> = 4.9) and it undergoes hydrolysis very easily [2]. Recently, there are several methods reported in literature for the Knoevenagel condensation of aldehydes with Meldrum's acid [3].

Compounds having chromone moiety are synthetically versatile molecules with a reactive carbonyl group. They have considerable significance for their biological activities [4] and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles. The substrate, 4-oxo-(4H)-1-benzopyran-3-carbaldehyde has three active sites such as, α, β-unsaturated carbonyl group, a carbon-carbon double bond and a formyl group. Of these, the formyl group has the highest reactivity towards active methylene compound. The condensation reactions of 4-oxo-(4H)-1-benzopyran-3-carbaldehyde with active methylene compounds are well known [5]. It is well known that 2, 2-dimethyl-



5- [(4-oxo-4H-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones are generally synthesized by condensation of 4-oxo-4H-benzopyran-3-carbaldehyde with Meldrum's acid in presence of alumina under microwave irradiation [6].

To date, many organic transformations have been carried out in water [7] Water is unique solvent due to easy availability, cheap, non-toxic, safer to organic solvents and environmental benign.

Alum were found to be effective in the synthesis of cis-isoquinolicacids[8a], mono- and disubstituted 2,3-dihydroquinazolin-4(1H)-ones[8b], dihydropyrimidineviaBiginelli reaction[8c]and coumarins[8d]. Since the alum has exploited in the organic synthesis as a non-toxic, inexpensive, eco-friendly nature, easy handling and mild catalyst. We investigated alum as a catalyst for the Knoevenagel reaction. It was found that alum is an effective promoter for the synthesis of 2, 2-dimethyl-5- [(4-oxo-4H-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones by condensation of heteroaryl aldehydes with Meldrum's acid.

### Materials and Methods

All chemicals were purchased from Merck, Aldrich and Rankem chemical companies and used without further purification. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. The progress of the reactions was monitored by TLC (Thin Layer Chromatography). IR spectra were recorded on Perkin-Elmer FTIR spectrophotometer in KBr disc. <sup>1</sup>H NMR spectra were recorded on an 300 MHz FT-NMR spectrometer in CDCl<sub>3</sub> as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me<sub>4</sub>Si) as an internal standard.

### General Procedure

A mixture of 4-oxo-4H-benzopyran-3-carbaldehyde (1 mmol), Meldrum's acid (1 mmol), alum (2 mol%) and 10 mL water were taken in a single neck round bottom flask equipped with mechanical stirrer and stirred at room temperature for the appropriate time given in Table 2. The completion of the reaction was monitored by TLC. The solid product was filtered and recrystallized from ethyl acetate to get pure product. All the products were characterized by IR, <sup>1</sup>H NMR and mass spectra and by comparison of their physical characteristics with those of the authentic compounds.

### Spectral Data Of Compound

(3a)IR (KBr, cm<sup>-1</sup>): 3062, 2996, 1732, 1670 1396, 1251. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 1.8 (6H, s, 2×CH<sub>3</sub>), 7.2-8.1 (4H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C<sub>2</sub>-H of chromone moiety). EIMS (m/z, %): = 301 [M+1].

(3c)IR (KBr, cm<sup>-1</sup>): 3055, 2990, 1710, 1650, 1390, 1280. <sup>1</sup>H NMR (300 MHz, CDCl<sub>3</sub>) δ (ppm): 2.5 (3H, s, Ar-CH<sub>3</sub>), 1.9 (6H, s, 2×CH<sub>3</sub>), 7.2-8.2 (3H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C<sub>2</sub>-H of chromone moiety). EIMS (m/z, %): = 315 [M+1].

(**3d**)IR (KBr,  $\text{cm}^{-1}$ ): 3065, 2989, 1729, 1674, 1392, 1293, 791.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.9 (6H, s,  $2\times\text{CH}_3$ ), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s,  $\text{C}_2\text{-H}$  of chromone moiety). EIMS ( $m/z$ , %): = 370 [ $\text{M}+1$ ].

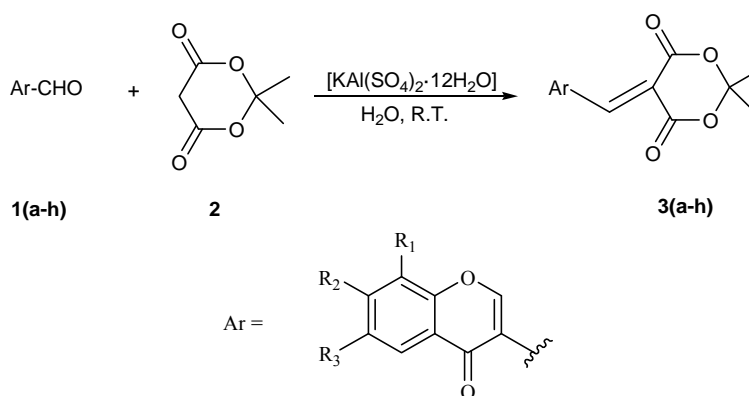
(**3g**)IR (KBr,  $\text{cm}^{-1}$ ): 3063, 2993, 1735, 1664, 1395, 1280, 805.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm): 1.8 (6H, s,  $2\times\text{CH}_3$ ), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.6 (1H, s,  $\text{C}_2\text{-H}$  of chromone moiety). EIMS ( $m/z$ , %): = 380 [ $\text{M}+1$ ].

(**3h**)IR (KBr,  $\text{cm}^{-1}$ ): 3061, 2992, 1730, 1669, 1372, 1296, 797.  $^1\text{H}$  NMR (300 MHz,  $\text{CDCl}_3$ )  $\delta$  (ppm) = 1.9 (6H, s,  $2\times\text{CH}_3$ ), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.6 (1H, s,  $\text{C}_2\text{-H}$  of chromone moiety). EIMS ( $m/z$ , %): = 319 [ $\text{M}+1$ ].

## Result and Discussion

In continuation of our research work on Knoevenagel condensation [6,9] and development of novel synthetic methodologies [10], herein, we would like to report a simple, efficient and green methodology for the synthesis of 2, 2-dimethyl-5- [(4-oxo-4H-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones. The synthetic route has been shown in Scheme 1.

In search for the best Experimental condition, the reaction of 4-oxo-(4H)-1-benzopyran-3-carbaldehyde 1a with Meldrum's acid in the presence of alum at room temperature has been considered as the standard model reaction.



**Scheme 1**

**Table 1:** Standardized the reaction condition for the synthesis of 2,2-dimethyl-5-((4-oxo-4H-chromen-3-yl)methylene)-1,3-dioxane-4,6-dione **3a**<sup>a</sup>.

Entry	Reagent	Solvent	Time [min]	Yield [%] <sup>b</sup>
1	Alum	CH <sub>3</sub> CN	40	84
2	Alum	EtOH	30	89
3	Alum	MeOH	20	86
4	Alum	H <sub>2</sub> O	10	96

<sup>a</sup>**1a** (1 mmol) treated with Meldrum's acid (1 mmol) and alum (2 mol%) under different solvents at ambient temperature; <sup>b</sup>Isolated yields

**Table 2.** Knoevenagel condensation of 4-oxo-4H-benzopyran-3-carbaldehydes with Meldrum's acid in presence of alum in water at room temperature

Entry	Ar	Time (min)	Yield (%) <sup>a</sup>	M.p.(°C)	
				Found	Reported[6]
<b>3a</b>	R <sub>1</sub> =H, R <sub>2</sub> = H, R <sub>3</sub> =H	20	96	181-183	182
<b>3b</b>	R <sub>1</sub> =H, R <sub>2</sub> = H, R <sub>3</sub> =Cl	15	92	197-199	198
<b>3c</b>	R <sub>1</sub> =H, R <sub>2</sub> = CH <sub>3</sub> , R <sub>3</sub> =H	20	87	184-186	186
<b>3d</b>	R <sub>1</sub> =Cl, R <sub>2</sub> = H, R <sub>3</sub> =Cl	15	91	178-180	180
<b>3e</b>	R <sub>1</sub> =CH <sub>3</sub> , R <sub>2</sub> = H, R <sub>3</sub> =Cl	10	89	198-200	200
<b>3f</b>	R <sub>1</sub> =H, R <sub>2</sub> = Cl, R <sub>3</sub> =Cl	15	92	240-242	242
<b>3g</b>	R <sub>1</sub> =H, R <sub>2</sub> = H, R <sub>3</sub> =Br	15	95	202-204	205
<b>3h</b>	R <sub>1</sub> =H, R <sub>2</sub> = H, R <sub>3</sub> =F	10	96	200-202	-

<sup>a</sup>Isolated yields based upon starting aldehyde.

To study the effect of the different solvents on synthesis of 2,2-dimethyl-5-((4-oxo-4H-chromen-3-yl)methylene)-1,3-dioxane-4,6-dione **3a** and results are summarized in Table 1. We used different solvents like CH<sub>3</sub>CN, EtOH, MeOH and water at room temperature. Surprisingly, water the unique solvent gave excellent yield of the product **3a** (Table 1, entry 1). These results suggest that water is the best solvent for synthesis of 2,2-dimethyl-5-((4-oxo-4H-chromen-3-yl)methylene)-1,3-dioxane-4,6-dione. It may be due to catalyst having excellent solubility in water than organic solvent.

The best result was obtained by carrying out the reaction with 1:1 mol ratios of 4-oxo-(4H)-1-benzopyran-3-carbaldehyde **1a**: Meldrum's acid and 2 mol% of alum in water at room temperature, this condition 2,2-dimethyl-5-((4-oxo-4H-chromen-3-yl)methylene)-1,3-dioxane-4,6-dione **3a** was obtained 96% yield after 20 min (Table 2, entry 1). The same reaction was carried out in the absence of catalyst, which resulted in 47% yield after 2h reaction time

The standard model reaction proceeded smoothly and was completed within 20 min of reaction time and 96 % yield. We were encouraged by the results obtained with model reaction. In a similar fashion, we



have taken different heteroaryl aldehydes containing electron-withdrawing or electron-donating compounds with Meldrum's acid. They all gave the expected results with excellent yields in short reaction times.

We have developed a newer route for the Knoevenagel condensation of heteroaryl aldehydes with active methylene compound in presence of alum in water medium at room temperature with constant stirring (Table 2). The substrate 4-oxo-(4H)-1-benzopyran-3-carbaldehyde has three active sites:  $\alpha$ ,  $\beta$ -unsaturated carbonyl group, a carbon-carbon double bond and a formyl group. Of these, formyl has higher reactivity towards the active methylene compounds and we got exclusively single product. All the reactions were carried out at room temperature with constant stirring i.e. using mild reaction conditions. In this methodology, the products are isolated in pure form by simple filtration and as a result of which yield losses are avoided. In this methodology, condensation reactions were completed in a shorter reaction time (10-20 min) and with excellent yields (87-96%). Thus, this is an excellent method for the Knoevenagel condensation reaction.

## Conclusions

We developed a simple, safe, efficient and green methodology for the synthesis of 2, 2-dimethyl-5- [(4-oxo-4H-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones from the condensation of substituted 4-oxo-4H-benzopyran-3-carbaldehyde with Meldrum's acid in presence of alum in water at room temperature. The notable merits offered by this methodology are mild reaction conditions, simple work-up procedure, cleaner reactions, short reaction times without phase transfer catalyst (PTC) and excellent yield of products. Moreover, the catalyst used is easily available, inexpensive, non-toxic, eco-friendly and water was chosen as a unique solvent, which makes the reaction convenient, more economic and environmentally benign.

## References

- [1] (a) R S Mahalle, P D Netankar, S P Bonde, R A Mane, *Green Chem Lett Rev*, 2008, 1, 103; (b) M Saha, S Roy, S Chaudhuri, S Bhar, *Green Chem Lett Rev*, 2008, 1, 113.
- [2] H McNab, *Chem Soc Rev*, 1978, 7, 345.
- [3] (a) S Aimin, W Xiaobing, S L Kit, *Tetrahedron Lett*, 2003, 4, 1755; (b) U V Desai, D M Pore, R B Mane, S B Solabannavao, P P Wadgaonkar, *Synth Commun*, 2004, 34, 25.
- [4] W H Gerwick, A Lopez, G D Van Duyne, J Clardy, W Ortiz, A Buez, *Tetrahedron Lett*, 1979, 270, 1986.
- [5] (a) J Prousek, *Czech Chem Commun*, 1993, 58, 3014; (b) G V S Rama Sarma, V M Reddy *Ind J Hetero Chem*, 1993, 3, 111.
- [6] S S Shindalkar, B R Madje, M S Shingare *Ind J Chem Sec B*, 2006, 45, 2571.



- [7] (a) Y Ren, C Cai, *CatalLett* 2007, 118, 134; (b) K Gong, Z W He, Y Xu, D Fang, Z L Liu, *Monatsh Fur Chem*, 2008, 139, 913.
- [8] (a) J Azizian, A AMohammadi, A R Karimi, M R Mohammadizadeh, *J Org Chem*, 2005, 70, 350; (b) M Dabiri, P S Salehi, M G Otokesh, A AKozehgary, *Tetrahedron Lett*, 2005, 46, 6123; (c) J Azizian, A AMohammadi, A R Karimi, M R Mohammadizadeh, *Applied Catalysis*, 2006, 300, 85; (d) M Dabiri, M Baghbanzadeh, S Kiani, Y Baghbanzadeh, *Monatsh Fur Chem*, 2007, 138, 997.
- [9] (a) S SShindalkar, B R Madje, M S Shingare, *J Korean ChemSoc*, 2005, 49, 377; (b) B R Madje, S SShindalkar, M N Ware, M S Shingare, *Arkivoc*, 2005, 14, 82.
- [10] (a) K F Shelke, S B Sapkal, M S Shingare, *Chine ChemLett*, 2009, 20, 283; (b) K F Shelke, S B Sapkal, S SSonar, B R Madje, B BShingate, M S Shingare, *Bull Korean ChemSoc*, 2009, 30, 1057; (c) ) K F Shelke, S B Sapkal, N V Shitole, B BShingate, M S Shingare, *Org Commun*, 2009, 2, 72; (d) K F Shelke, S B Sapkal, N V Shitole, B BShingate, M S Shingare, *Bull Korean ChemSoc*, 2009, 30, 2883; (e) K F Shelke, S B Sapkal, G K Kakade, B BShingate, M S Shingare, *Green ChemLettRevi*, 2010, 3, 27.