



CADMIUM CHLORIDE AN EFFECTIVE CATALYST FOR KNOEVENAGEL REACTION IN WATER

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ABSTRACT :

Efficient synthesis of 2, 2-dimethyl-5- [(4-oxo-4H-chromen-3-yl) methylene]-1, 3-dioxane-4, 6-diones by Knoevenagel condensation of aldehydes with Meldrum's acid in the presence of catalytic amount of cadmium chloride in water medium at room temperature. Simple work-up procedure, mild reaction conditions, short reaction times and good yield of products are the advantages of this method. Moreover, the catalyst used is easily available, inexpensive, non-toxic and eco-friendly.

KEYWORDS : *Knoevenagel reaction, Cadmium chloride, Aldehyde, Meldrum's acid.*

1. INTRODUCTION

Knoevenagel condensation is one of the most important reaction 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 ($pK_a = 4.9$) and it undergoes hydrolysis very easily [2].

Compounds having chromone moiety are synthetically versatile molecules with a reactive carbonyl group. They have considerable significance for their biological activities [3] and for their reactivity towards nucleophiles, which allow the synthesis of a wide variety of heterocycles.

Water is unique solvent due to easy availability, cheap, non-toxic, safer to organic solvents and environmental benign[4]. Cadmium chloride ($CdCl_2$) has exploited in the organic synthesis as a non-toxic, inexpensive, eco-friendly nature, easy handling and Lewis acid mild catalyst [5].

2. EXPERIMENTAL SECTION

2.1. Reagents and analysis:

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. 1H NMR spectra were recorded on an 300 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me_4Si) as an internal standard.

2.2. Spectral data of compounds

(3a) IR (KBr, cm^{-1}): 3062, 2996, 1732, 1670 1396, 1251. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 1.8 (6H, s, $2\times\text{CH}_3$), 7.2-8.1 (4H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, $\text{C}_2\text{-H}$ of chromone moiety). EIMS (m/z , %): = 301 [M+1].

(3d) IR (KBr, cm^{-1}): 3065, 2989, 1729, 1674, 1392, 1293, 791. ^1H NMR (300 MHz, CDCl_3) δ (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 [M+1].

(3f) IR (KBr, cm^{-1}): 3084, 3018, 1714, 1662, 1392, 1280, 798. ^1H NMR (300 MHz, CDCl_3) δ (ppm): 1.8 (6H, s, $2\times\text{CH}_3$), 7.2-8.3 (2H, s, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, $\text{C}_2\text{-H}$ of chromone moiety). EIMS (m/z , %): = 370 [M+1].

(3g) IR (KBr, cm^{-1}): 3063, 2993, 1735, 1664, 1395, 1280, 805. ^1H NMR (300 MHz, CDCl_3) δ (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 [M+1].

2.3. Synthesis of 2, 2-dimethyl-5-[(4-oxo-4H-chromen-3-yl) methylene]-1,3-dioxane-4, 6-dione 3(a-h):

A mixture of aromatic aldehyde (1 mmol), Meldrum's acid (1 mmol), CdCl_2 (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, ^1H NMR and mass spectra and by comparison of their physical characteristics with those of the authentic compounds

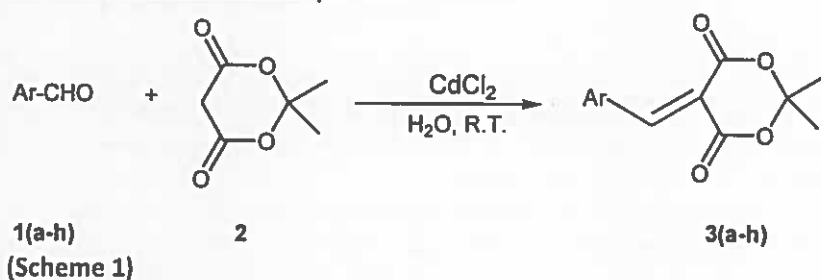


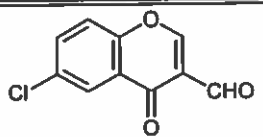
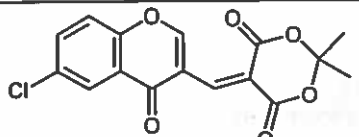
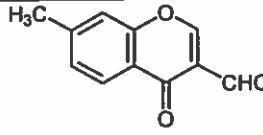
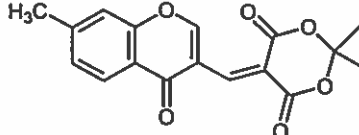
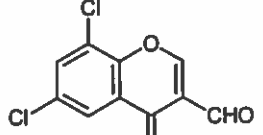
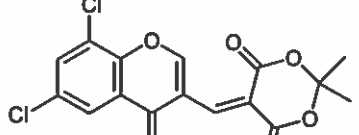
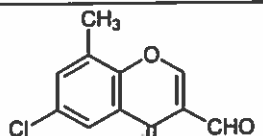
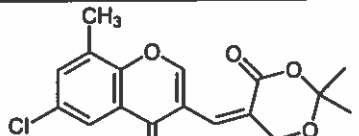
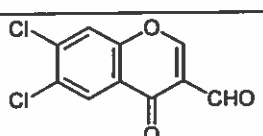
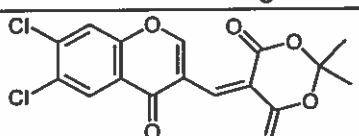
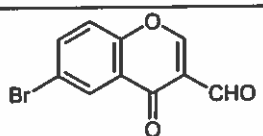
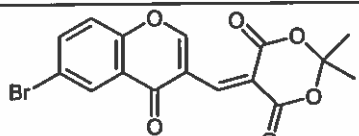
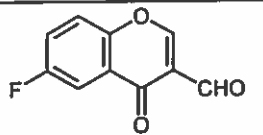
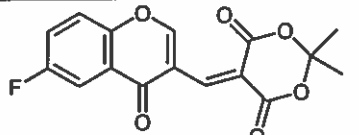
Table 1. Standardized the reaction condition for the synthesis of 2,2-dimethyl-5-[(4-oxo-4H-chromen-3-yl)methylene]-1,3-dioxane-4,6-dione 3a^a.

Entry	Reagent	Solvent	Time [min]	Yield [%] ^b
1	CdCl_2	EtOH	30	89
2	CdCl_2	MeOH	20	86
3	CdCl_2	H_2O	10	93

^a1a (1 mmol) treated with Meldrum's acid (1 mmol) and CdCl_2 (2 mol%) under different solvents at ambient temperature; ^bIsolated yields

Table 2. Knoevenagel condensation of 4-oxo-4H-benzopyran-3-carbaldehydes with Meldrum's acid in presence of CdCl_2 in water at room temperature

Entry	Ar	Product	Time (min)	Yield (%) ^a	M.p.(°C) Found Reported[6]	
3a			25	93	181-183	182

3b			15	92	197-199	198
3c			20	87	184-186	186
3d			15	91	178-180	180
3e			10	89	198-200	200
3f			15	92	240-242	242
3g			15	95	202-204	205
3h			10	96	200-202	-

^aIsolated yields based upon starting aldehyde.

3. RESULTS AND DISCUSSION

In continuation our development of novel synthetic methodologies [7], 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 cadmium chloride at room temperature has been considered as the standard model reaction.

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 EtOH, MeOH and water at room temperature. Surprisingly, water the unique solvent gave excellent yield of the product 3a (Table 1, entry 3). 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. 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 CdCl_2 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 93% yield after 25 min (Table 2, entry 1). The same reaction was carried out in the absence of catalyst, which resulted in 44% yield after 1h reaction time

The standard model reaction proceeded smoothly and was completed within 25 min of reaction time and 93 % 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 good 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 CdCl_2 in water medium at room temperature with constant stirring (Table 2). 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.

4. CONCLUSION

We have developed a novel 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 cadmium chloride in water at room temperature. The major 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.

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