



4-Dodecylbenzenesulfonic Acid (DBSA): an Inexpensive and Efficient Catalyst for Knoevenagel Condensation in Water

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ABSTRACT

An efficient method has been developed for the Knoevenagel condensation of 4-oxo-4H-benzopyran-3-carbaldehydes with Meldrum's acid using 4-Dodecylbenzenesulfonic acid (DBSA) as a catalyst in water medium at room temperature. The good yields, short reaction time, easy work-up, simplicity in operation and using an easily available and inexpensive catalyst are important features of this method.

Keywords: Knoevenagel reaction, DBSA, 4-Oxo-(4H)-1-benzopyran-3-carbaldehyde, Meldrum's acid

I. INTRODUCTION

Knoevenagel condensation is one of the most important methods for the preparation of substituted alkenes by reactions of carbonyl compounds with active methylene compounds [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 groups.

Meldrum's acid (2,2-dimethyl-1,3-dioxane-4,6-dione) is an active methylene compound having a rigid cyclic structure with high acidity ($pK_a = 4.9$) 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 compounds. 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-dione is 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 a unique solvent due to its easy availability, cheap, non-toxic, safer than organic solvents and environmentally benign.

Dodecylbenzenesulfonic acid (DBSA) an anionic surfactant can act as a combined Brønsted acid-surfactant-catalyst (BASC). It performs the dual role of both an acid catalyst to activate the substrate molecules and a surfactant to increase the concentration of organic reactants by forming micellar aggregates in water [8]. It is used in various chemical syntheses such as synthesis of xanthenes [9], bis(indol-3-yl)alkane derivatives [10], carbon-carbon bond-forming reactions [11], reaction of homoallyl alcohols and aldehydes in water [12], synthesis of tetrahydrobenzopyrans [13], dehydration reactions in water [14] and N-alkylation of aldoximes [15].

II. EXPERIMENTAL

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 CDCl₃ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane (Me₄Si) as an internal standard.

Selected Spectral data

(3a) IR (KBr, cm⁻¹): 3061, 2996, 1730, 1670 1396, 1251. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 1.8 (6H, s, 2×CH₃), 7.2-8.1 (4H, m, aromatic), 8.7 (1H, s, olefinic), 9.6 (1H, s, C₂-H of chromone moiety). EIMS (m/z, %): = 301 [M+1].

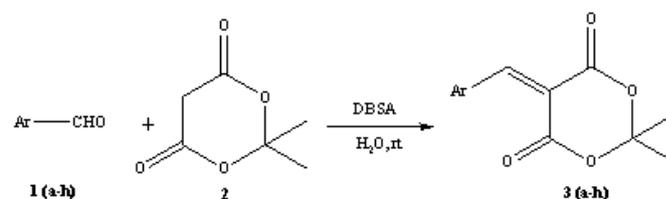
(3d) IR (KBr, cm⁻¹): 3065, 2989, 1729, 1674, 1392, 1293, 791. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 1.9 (6H, s, 2×CH₃), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C₂-H of chromone moiety). EIMS (m/z, %): = 370 [M+1].

(3f) IR (KBr, cm⁻¹): 3084, 3018, 1714, 1662, 1392, 1280, 798. ¹H NMR (300 MHz, CDCl₃) δ (ppm): 1.8 (6H, s, 2×CH₃), 7.2-8.3 (2H, s, aromatic), 8.6 (1H, s, olefinic), 9.5 (1H, s, C₂-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, CDCl₃) δ (ppm): 1.8 (6H, s, 2×CH₃), 7.2-8.2 (3H, m, aromatic), 8.6 (1H, s, olefinic), 9.6 (1H, s, C₂-H of chromone moiety). EIMS (m/z, %): = 380 [M+1].

General Procedure for Preparation of 3(a-h):

A mixture of 4-oxo-4H-benzopyran-3-carbaldehyde (1 mmol), Meldrum's acid (1 mmol), 4-Dodecylbenzenesulfonic acid (10 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.



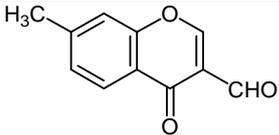
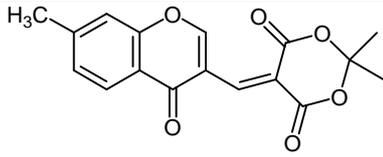
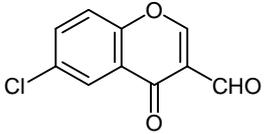
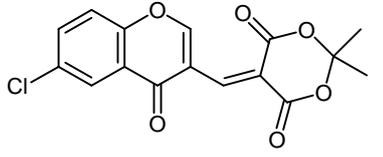
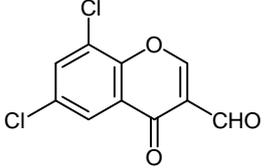
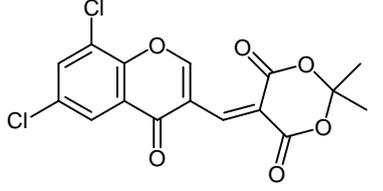
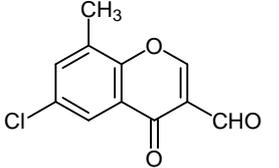
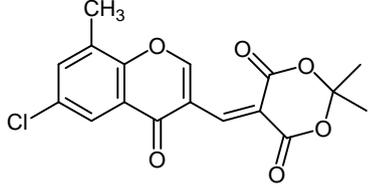
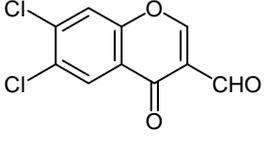
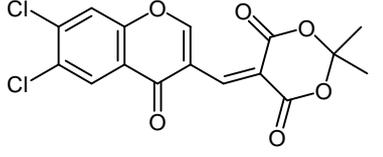
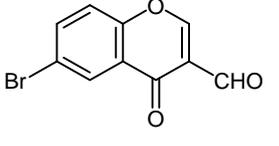
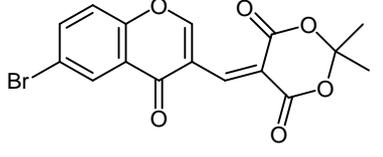
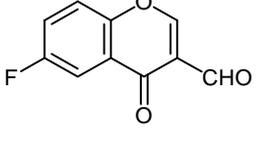
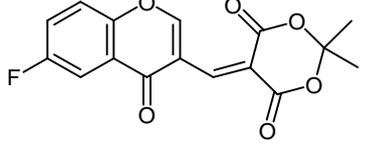
Scheme 1

Table 1. Synthesis of 3a

Entry	Catalyst (mol %)	Time (min)	Yield (%)
1	No catalyst	60	22
2	2.5	30	82
3	5	10	97
4	7.5	10	97

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

Entry	Ar-CHO	Product	Time (min)	Yield (%) ^a	M.p.(°C)	
					Found	Reported[6]
3a			10	97	179-181	182

3b			20	85	184-186	186
3c			15	91	198-200	198
3d			15	90	178-180	180
3e			10	87	199-201	200
3f			15	93	241-242	242
3g			15	95	202-204	205
3h			10	94	198-200	-

^aIsolated yields based upon starting aldehyde.

III. RESULTS AND DISCUSSION

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 DBSA at room temperature has been considered as the standard model reaction.

The effect of the catalyst loading on the reaction indicated that less than 10 mol% of DBSA led to less yield and required more reaction time. Excellent yield was obtained with 10 mol% of the catalyst. No further increase in the yield was observed on increasing the amount of catalyst under the same condition Table 1.

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 10 mol% of DBSA 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 97% yield after 10 min (Table 2, entry 1).

The standard model reaction proceeded smoothly and was completed within 10 min of reaction time and 97 % 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 DBSA in water medium at room temperature with constant stirring Table 2. The substrate 4-oxo-(4H)-1-benzopyran-3-carbaldehyde has three active sites: α , β -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 (10-20min) and with excellent yields (85-97%). Thus, this is an excellent method for the Knoevenagel condensation reaction.

IV. CONCLUSION

We developed an 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 DBSA in water at room temperature. The catalyst is inexpensive and easily commercially available. Water is used as a reaction medium which is eco-friendly, inexpensive and abundantly available. There are few advantages of this procedure such as good yields, short reaction time, simplicity in operation, use of green solvents and mild reaction conditions.

V. REFERENCES

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