



Cellulose sulphuric acid as an efficient catalyst for the synthesis of 5-arylidene-2,4-thiazolidinedione under microwave irradiation

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ABSTRACT

An efficient and solvent-free conditions for the synthesis of 5-arylidene-2,4-thiazolidinediones by the Knoevenagel condensation of aromatic aldehydes with 2,4-thiazolidinedione in the presence of cellulose sulphuric acid (CSA) as a catalyst carried out under the influence of microwave irradiation. The major advantages of this method are short reaction time, high yields and green aspects by avoiding toxic catalyst and hazardous solvent. Moreover, the CSA was successfully reused for four cycles without significant loss of activity. © 2015 Trade Science Inc. - INDIA

KEYWORDS

Knoevenagel condensation;
Cellulose sulphuric acid;
2,4-Thiazolidinedione;
Aromatic aldehyde;
Microwave irradiation.

INTRODUCTION

The Knoevenagel condensation is a basic reaction for carbon-carbon bond formation, which is of paramount importance in organic synthesis^[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.

Thiazolidinedione represents a class of chemical products with interesting pharmacological and a biological activity includes antibacterial^[2], antifungal^[3] and antidiabetic^[4]. Moreover, 2,4-thiazolidinedione derivatives has remarkable antiproliferative effect on vascular smooth muscle^[5]. In additionally, thiazolidinedione based molecules have been popular as small molecule inhibitors such as aldose reductase^[6]. Thus, the synthesis of thiazolidinedione derivatives is currently of much importance. There are several methods reported in the literature for the synthesis of 5-arylidene-2,4-

thiazolidinediones such as piperidine in EtOH^[7a], NaOAc in DMF-AcOH^[7b], thylenediammonium diacetate in MeOH^[7c], morpholine in AcOH^[7d], polyethylene glycol (PEG)^[7e]. However, in above some reported methods suffer from one or more drawbacks like prolonged reaction times, use of environmentally unfavorable solvents and frequently low yields. Therefore, the development of mild, efficient and versatile method is still strongly desirable.

Organic synthesis in the absence of solvent is a powerful tool for the generation of structurally diverse molecules due to their special selectivity, the ease of set-up and work-up^[8]. Moreover, solvent-free reactions sometimes are faster, taking just a contact with each other. This aspect, coupled with the lower overall costs of running a reaction without solvent and no specially needed equipment.

The science of green chemistry is developed to meet the increasing demand of environmentally benign chemical processes. The application of microwaves, as an

TABLE 1 : Synthesis of 5-arylidene-2,4-thiazolidinediones catalyzed by CSA under microwave irradiation

Compound ^a	Aldehyde	Time(min)	Yield (%) ^b	Mp (°C)
3a	H	2	95	240
3b	3-NO ₂	3	93	180
3c	3-Cl	3	92	270
3d	2,4-(Cl) ₂	4	90	215
3e	4-OH	3	92	281
3f	2-OH	4	88	276
3g	4-MeO	4	88	235
3h	4-CF ₃	3	87	234
3i	3-MeO,4-OH	3	86	194
3j	4-NMe ₂	4	87	281
3k	3,4-(OH) ₂	4	85	267

^aAll compounds are known compounds, which were characterized by IR, and ¹H NMR spectral data and melting points compared with literature procedure^[7a]. ^bIsolated yields based upon starting aldehyde.

TABLE 2 : Comparisons of results of other reported procedures with the present method^a

Entry	Reagent	Reaction condition	Time	Yield (%)	References
1	Piperidine	EtOH/reflux	4 h	51-90	[7a]
2	PEG- 300	reflux	3 h	75-80	[7e]
3	CSA	MW	2-4 min	85-95	[Present]

^aSynthesis of 5-arylidene-2,4-thiazolidinediones

TABLE 3 : Recycling of CSA for the synthesis of 5-benzylidene-2,4-thiazolidinedione^a [TABLE 1, compound 3a]

Entry	1	2	3	4	5
Cycle ^b	Fresh	First reuse	Second reuse	Third reuse	Fourth reuse
Yield (%) ^c	95	93	91	90	90

^aReaction condition: 1a (1 mmol), 2 (1 mmol) and CSA (1 mol%) under microwave irradiation; ^bReaction time 2 min; ^cIsolated yield.

¹H NMR (CDCl₃/DMSO-d₆): 2.85 (6H, s, CH₃), 7.26 (4H, m, aromatic protons). MS m/z (%): 249 (M+1).

RESULTS AND DISCUSSION

In continuation of our research work on Knoevenagel condensation^[13] and development of novel synthetic methodologies^[14], herein, we would like to report a simple, efficient and rapid method for the synthesis of 5-arylidene-2,4-thiazolidinediones.

In order to find optimum reaction conditions, the reaction of benzaldehyde 1a with 2,4-thiazolidinedione 2 was selected as model to investigate the effect of different amount of catalyst on the yield. The best results was obtained by carrying out the reaction with 1:1 mole ratios of benzaldehyde:

2,4-thiazolidinediones and 1 mol% of CSA under solvent-free conditions using microwave irradiation and under this conditions 3a was obtained 95% yield after 2 min (TABLE 1, compound 3a). 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 2,4-thiazolidinedione. They all gave the expected results with high yields in short reaction times.

We have developed a newer route for the condensation of various aldehydes with 2,4-thiazolidinedione in the presence of CSA under solvent-free conditions using microwave irradiation. In this methodology, condensation reactions were completed in a shorter time (2- 4 min) and with excellent yields (85-95%). The reactions were compatible with various substituents such as, nitro, me-

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thyl, chloro, hydroxyl, methoxy etc. No any significant substituents effect was observed in regarding the reaction time and yield of product (TABLE 1). Thus, this is an excellent method for the Knoevenagel condensation reaction.

Further investigation of the ability to recycle the catalyst is important for potential large-scale. Therefore, the recovery and reusability of CSA was examined. The catalyst can be separated and reused after extracting the desired product. The reusability of the catalyst was investigated in the model reaction. The results illustrated in (TABLE 3) showed that the catalyst could be used at least four times without significant loss of activity.

In order to show the merits of present method in comparisons with other reported methods for the similar reactions, we have tabulated some of the results in TABLE 2. As it is evidence from the results, present method found to be effective for the synthesis of 5-arylidine-2,4-thiazolidinediones.

CONCLUSIONS

In conclusion, we have reported a new and effective methodology for the synthesis of 5-arylidine-2,4-thiazolidinedione derivatives *via* the condensation of substituted aldehydes with 2,4-thiazolidinedione in presence of CSA under solvent-free conditions using microwave irradiation. The notable merits offered by this methodology are cleaner reactions, short reaction times, simple work-up procedure and high yield. Moreover, the CSA was successfully reused for four cycles without significant loss of activity which makes the reaction convenient and environmentally benign.

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