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Facile and green syntheses of substituted-5-arylidene-2,4-thiazolidinediones using L-tyrosine as an Eco-Friendly catalyst in aqueous medium

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ABSTRACT

*L-tyrosine has been utilized as an efficient catalyst for the Knoevenagel condensation of arylaldehydes **1(a-k)** with 2,4-thiazolidinedione**(2)** containing cyclic active methylene group in aqueous medium at room temperature to afford substituted -5-arylidene-2,4-thiazolidinediones **3(a-k)***

Key words: arylaldehydes, Knoevenagel condensation, 2,4-thiazolidinedione, L-tyrosine, water.

INTRODUCTION

Carbon–carbon bond formation reaction is the most important reaction in organic synthesis[1-3]**.** The Knoevenagel condensation is one such reaction which facilitates C-C bond formation and has been widely used in synthesis of fine chemicals[4], hetero Diels-Alder reactions[5] and in synthesis of carbocyclic[6] as well as heterocyclic compounds [7] of biological significance. These reactions are usually catalyzed by bases[8-10] such as primary and secondary amines and their corresponding ammonium salts, potassium fluoride in organic solvents. Lewis acids [11-12],alumina[13],Al_2O_3-$AlPO_4$[14], zeolite[15] and ionic liquids [16-20] have also been added to the existing list of substances that assisted Knoevenagel condensation in organic synthesis. The use of water[21-24] as solvent, the most environmentally benign of all solvents, offers a very useful green methodology from both the economical and synthetic points of view. It not only reduces the problem of disposal of organic solvents, but also at times enhances the progress of many organic reactions.

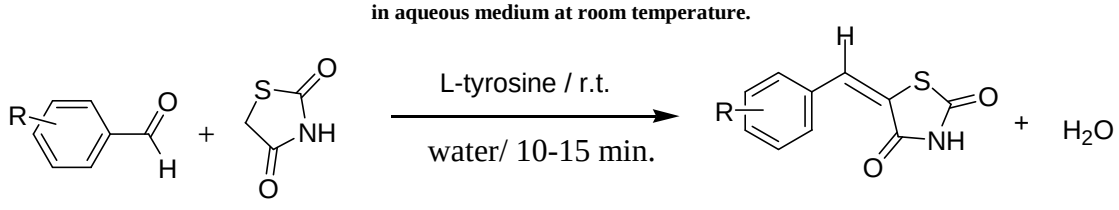
2,4-Thiazolidinedione and its derivatives have been found to be esteemed variety of pharmacological activities [25–27]. 5-Arylidene derivatives of 4-thiazolidinones have been found to be good fungistatic agents than parental the 4-thiazolidinones[28]**.**It was reported that 5-arylidene-2,4-thiazolidinediones can act as potentially challenging aldose reductase inhibitors [29] and 15-hydroxyprostaglandin dehydrogenase inhibitors[30].There is great interest in 5-benzylidenethiazolidine-2,4-dione derivatives will influence on inhibitors of MurD ligase[31].

Thus, the synthesis of 5-arylidene-2,4-thiazolidinediones is recently of very much importance. There are several methods reported in the literature for the synthesis of 5-arylidene-2,4-thiazolidinediones such as sodium acetate in acetic acid under reflux conditions [32], sodium acetate in acetic acid under microwave irradiation [33], piperidine in ethanol under reflux conditions[29, 34–36], piperidinium acetate in toluene under reflux conditions [30, 37],piperidinium acetate in ethanol under microwave irradiation[31], piperidinium acetate in DMF under microwave irradiation[38], glycine and sodium carbonate in H_2O under reflux conditions[39], grinding with ammonium acetate in the absence of solvents [40],$KAl(SO_4)_2 \cdot 12H_2O$ in H_2 O at 90°C [41], baker's yeast[42], KF-Al_2O_3 under microwave irradiation[43], glycine under microwave irradiation[44]and polyethylene glycol-300 at 100–120°C [45]. Recently, ionic liquids ([bnmim] C_l,C_3 [min] 2 ·2[Br−]) catalyzed synthesis of 5-arylidene-2,4thiazolidinediones have also been reported[46, 47]. Each of these methods have their own advantages but also be

affected from disadvantages such as long reaction times, low to moderate yields, tedious work-up procedures, requirement of special apparatus, use of organic solvents, requirement of excess of catalysts, and difficulty in recovery and reusability of the catalysts.

To the best of our knowledge, L-tyrosine has not been used as a catalyst for the synthesis of 5-arylidene-2,4-thiazolidinediones and attracted our attention to investigate the application of L-tyrosine as a catalyst. The aqueous medium reaction has many advantages: reduced pollution, low costs, and simplicity in process and handling. Here in, we reported a simple and efficient synthesis of 5-arylidene-2,4-thiazolidinediones by the Knoevenagel condensation of aromatic aldehydes with 2,4-thiazolidinedione containing cyclic active methylene group in the presence of L-tyrosine in aqueous medium **(Scheme 1)**.

SCHEME-1:Knoevenael condensation of arylaldehydes with 2,4-thiazolidinedione in presence of L-tyrosine as an Eco-Friendly catalyst in aqueous medium at room temperature.



1(a-j) **(2)** **3(a-j)**

(a)R= C_6H_5,
(b)R = CH_3-C_6H_4,
(c)R = OCH_3-C_6H_4,
(d)P-(Me_2N)-C_6H_4 ,
(e)P-(OH)-C_6H_4,
(f)P-(NO_2)-C_6H_4 ,
(g)P-(Cl)-C_6H_4 ,
(h) P-(F)-C_6H_4 ,
(i) m-(NO_2)-C_6H_4,
(j) m-(OCH_3)-C_6H_4,
(k) o-(OH)-C_6H_4,

MATERIALS AND METHODS

Melting points were measured in open capillary tubes and are uncorrected. TLC was done on plates coated with silica gel-G and spotting was done using iodine or UV lamp. IR-spectra were recorded using FT-IR in KBr phase. ^{1}H-NMR spectra were recorded at 400 MHz, respectively. Compounds are known, and products were identified by spectral and melting-point comparison with the authentic samples.

General Procedure for the preparation of 3(a-k) from 1 (a-k) and 2,4-thiazolidinedione(2).
A mixture of **1** (10 mmol), 2,4-thiazolidinedione **2** (10 mmol) and L-tyrosine (2 mmol) was stirred in aqueous medium at room temperature for a specified period of time **(Table 1).** After completion of reaction (as shown by TLC checking), the mixture was poured into ice-cold water (50 mL).The separated solid was filtered, washed with water(100 mL) and dried to obtain crude **3(a-k).** The latter were then recrystallised from ethanol to afford pure **3(a-k).** Compounds are known, and products were identified by spectral and melting-point comparison with the authentic samples.

Table-1. Synthesis of substituted-5-arylidene-2,4-thiazolidinediones with Knoevenagel condensation in aqueous medium at room temperature

S.NO	R	Condition	Time (min)	Yield (%)	mp (°C)	Lit.mp. (°C)
a	C_6H_5	r.t.	10	93	240-241	240-242 [41]
b	4-CH_3-C_6H_4	r.t.	14	91	224-226	225-226 [47]
c	4-OCH_3-C_6H_4	r.t.	13	91	235-237	235-238 [48]
d	p-(Me_2N)-C_6H_4	r.t.	15	92	281-282	282-283 [49,41]
e	p-(OH)-C_6H_4	r.t.	14	92	283-284	282-285 [48,41]
f	p-(NO_2)-C_6H_4	r.t.	10	94	182-183	183-184 [49,41]
g	p-(Cl)-C_6H_4	r.t.	12	94	279-280	278-280 [49,41]
h	p-(F)-C_6H_4	r.t.	11	93	218-220	220-221 [43]
i	m-(NO_2)-C_6H_4	r.t.	10	93	186-188	185–190 [43]
j	m-(OCH_3)-C_6H_4	r.t.	13	92	189-190	187–190 [29]
k	o-(OH)-C_6H_4	r.t.	14	92	278-279	278-280 [48,41]

RESULTS AND DISCUSSION

Treatment of aromatic aldehydes **1(a-k)** with 2,4-thiazolidinedione(2) containing cyclic active methylene group in the presence L-tyrosine in aqueous medium at room temperature for 10-15min. resulted in the formation of 5-arylidene-2,4- thiazolidinediones **3(a-k)** in **91–94%** yields **(table-1) (scheme-1).** This method is very facile and convenient for the preparation of large amount of Knoevenagel products with high yields in less time. L-tyrosine acts as a base to induce the reaction.

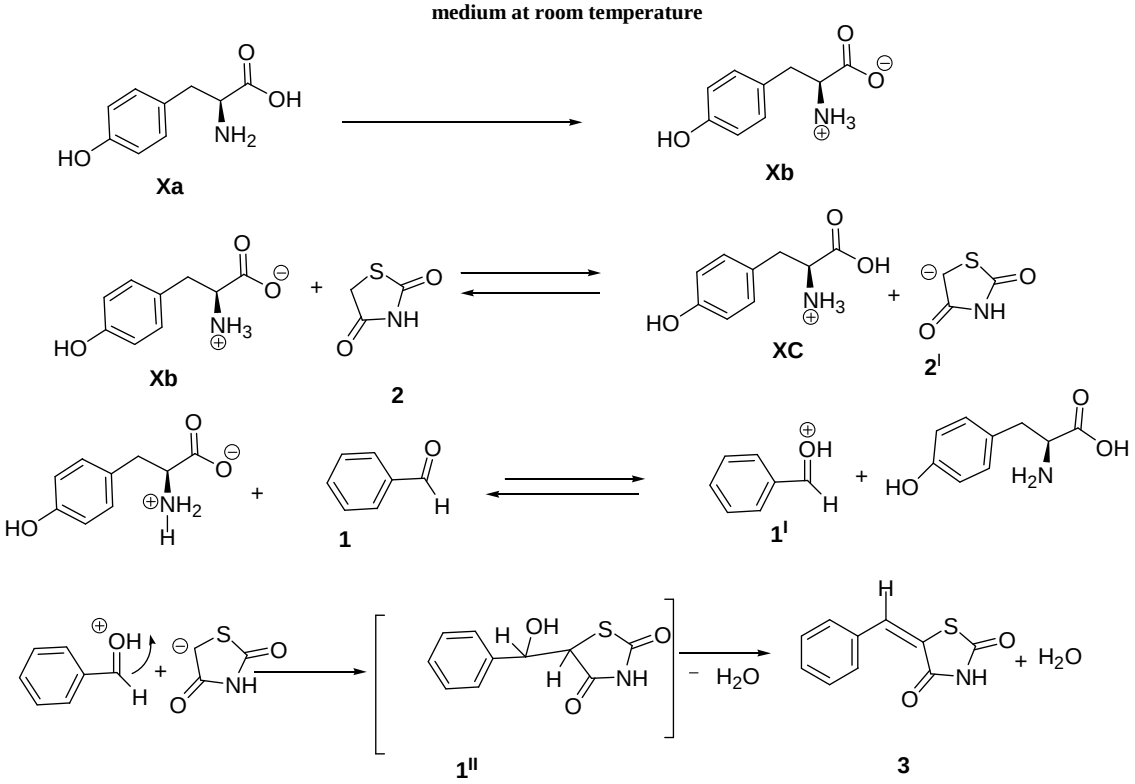
In the absence of L-tyrosine, the reaction does not proceed the reactants in aqueous medium at room temperature for 24 h. The use of L-tyrosine as a catalyst helps to avoid the use of environmentally unfavourable organic solvents as reaction medium. In all cases, the reaction proceeded smoothly with catalytic amount of L-tyrosine to give products of good purity.

The above reactions of arylaldehydes **1(a-k)** with 2,4-thiazolidinedione **(2)** containing cyclic active methylene group was attempted in the presence of various bases like NaOH, KOH were too strong bases to result in more by-products. Low yield was obtained and long reaction time is needed using K_2CO_3, ammonium acetate, piperidine and triethylamine as catalyst for condensation of arylaldehydes **1(a-k)** with 2,4-thiazolidinedione **(2)** containing cyclic active methylene group in aqueous medium at room temperature.

From **Table-1**, it was shown that the condensation of arylaldehydes with electron withdrawing group such as $–NO_2$ and -Cl at para position with 2,4-thiazolidinedione **(2)** containing cyclic active methylene group can be carried out in relatively shorter time and higher yield than with electron donating group such as –OH and N, N-dimethyl arylaldehydes in aqueous medium at room temperature.
A plausible mechanism for the formation of **3** from **1** and **2** in the presence of L-tyrosine as catalyst is shown in the **Scheme-2.**

In the mechanism shown in **Scheme-2**, L-tyrosine, in its zwitterionic form **(Xb),** abstracts a proton from 2,4-thiazolidinedione **(2)** containing cyclic activemethylene group forming the carbanion of 2,4-thiazolidinedione **(2^{I})**. Which then attacks the protonated arylaldehydes **(1^{I})** forming the corresponding intermediate **(1^{II})** that loses water to form the end product **3.**

Scheme-2: plausible mechanism for the formation of 3 from 1 and 2 in the presence of L-tyrosine as an Eco- Friendly catalyst in aqueous medium at room temperature



CONCLUSION

In summary, L-tyrosine as an efficient catalyst for the preparation of 5-arylidene-2,4-thiazolidinediones by Knoevenagel reaction in aqueous medium at room temperature. This method is applicable to a wide range of arylaldehydes **1(a-k)** and 2,4-thiazolidinedione **(2)** containing cyclic active methylene group to afford substituted-5-arylidene-2,4-thiazolidinediones in aqueous medium at room temperature.

The attractive features of this procedure are the mild reaction conditions, high conversions, operational simplicity and inexpensive and ready availability of the catalyst, all of which make it a useful and attractive strategy for the preparation of substituted-5-arylidene-2,4-thiazolidinediones in aqueous medium at room temperature.

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