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An Efficient Monosodium Glutamate (MSG) Catalyzed Multicomponent Synthesis of Isoxazolone in Water under Microwave Irradiation

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ABSTRACT

A one pot multicomponent synthesis of isoxazolone has been performed in the presence of Monosodium Glutamate (MSG) as catalyst in water under microwave irradiation. The significant features of this method are simple experimental procedure, requires short time duration, simple work up, eco-friendly and high yield.

Keywords: Aromatic aldehyde, Ethyl acetoacetate, Hydroxylamine hydrochloride, Water, MSG catalyst, Isoxazolones, Microwave irradiation

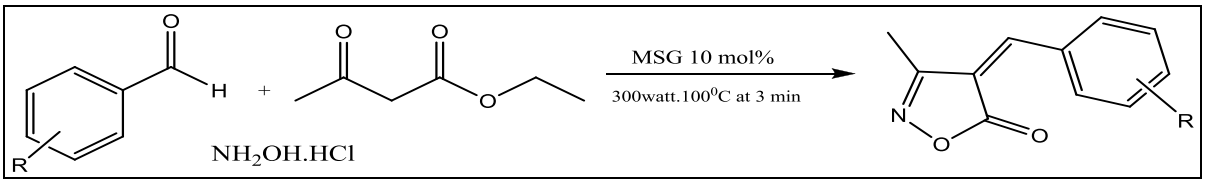
INTRODUCTION

Organic reactions in water as a solvents are ecofriendly chemical process. They are reducing use to harmful organic solvent and reaction carried out under mild conditions. Water is uniquely advantages as a solvent [1-10]. Water as reaction media in one of the major parts of green chemistry [11,12], water is most attractive solvent synthetic chemistry in view of both economic and environmental aspects. Multi Component Reaction (MCR'S) in water can be visualized as well as designed synthetic method to attain a wide range of diverse molecular frameworks [13-16]. MCR'S have been use for synthesis of several of natural products and biological active compounds because they have many advantages such as excellent functional group, compatibility, minimization of waste, versatility, atom economy, environmentally friendly and easy workup [17].

Isoxazolones are class of heterocyclic compounds featuring several of biological activities [18-36]. Isoxazolones are units of various pharmaceutical such as anti-androgen agents, merocynine dyes, some of liquid crystalline materials, pesticide, materials for electronics, analytical reagents and building blocks in organic synthetic chemistry [37-46]. Isoxazolones are also found to possess biological and pharmaceutical activities such as antitumor [47], antimicrobial [48], antioxidant [49], anti-inflammatory [35], antiviral [50], antituberculosis [22], fungicidal [25], analgesic [20] as well as antimicrobial [51].

The method for synthesis of isoxazolones are MCR'S reaction between ethyl acetoacetate, hydroxylamine hydrochloride, various aromatic aldehyde using various catalyst sodium benzoate [24], sodium sulfide [52], sodium silicate [53], 1,4-Diazabicyclo[2.2.2]octane (DABCO) [54], nano-Fe_2O_3, clinoptilolite and Phosphotungstic Acid ($H_3PW_{12}O_{40}$) [55], Different conditions and techniques such as using sodium acetate and visible light, pyridine under ultrasonic irradiation, pyridine under reflux [56-60] and catalyst-free/grinding/heating [61], sodium ascorbate [62], sodium citrate [63], sodium saccharin [64], sodium tetra borate [65], sodium azide [66], boric acid [67], as well as Potassium Phthalimide (PPI) [68].

In present work attempt has been made to synthesize of isoxazolone by multi component reaction of aromatic aldehyde with hydroxylamine hydrochloride and ethyl acetoacetate in the presence of Monosodium Glutamate (MSG) in water under Microwave irradiation.



MATERIALS AND METHODS

Aromatic aldehyde, hydroxylamine hydrochloride, ethyl acetoacetate and MSG used in this work were used without further purification melting points were taken in open capillary and are un-corrected. ^{1}H-NMR spectra were recorded on a Bucker DRX-300 instrument and IR was recorded in KBr on a Nicolet impact 410. The progress of reactions and the purity of the products were observed by TLC on silica gel.

Experimental section

A mixture of ethyl acetoacetate (1 mmol) and hydroxylamine hydrochloride (1 mmol) in 10 ml distilled water were stirred at room temperature for 10 min. Then monosodium glutamate (MSG) (10 mol%) and aromatic aldehyde (1 mmol) were microwave irradiated at power 300 watt. At 100°C at 3 min. Reaction was monitored by TLC After competition of reaction the crude product was filtered and washed with cold water and dried.

Data for selected products

4-benzylidene-3-methylisoxazol-5(4H)one: ^{1}H-NMR (300 MHz, $CDCl_3$): δ=2.30 (s, 3H), 7.43 (s, 1H), 7.487.8 (m, 3H), 8.34 (dd, J=1.3, 7.4 Hz, 2H); ^{13}C-NMR (300 MHz, $CDCl_3$): δ=11.62, 119.64, 129.02, 130.48, 132.28, 134.02, 149.97, 161.15, 167.87; IR (KBr)v: 1732, 1620, 1100, 1216, 879, 763 cm^{-1}.

4-(4-methoxybenzylidene)-3-methylisoxazol-5(4H)-one: ^{1}H-NMR (300 MHz, $CDCl_3$): δ=2.29 (s, 3H), 3.92 (s, 3H), 7.33 (s, 1H), 7.01 (d, J=8.7 Hz, 2H), 8.43 (d, J=8.7 Hz, 2H); ^{13}C-NMR (300 MHz, $CDCl_3$): δ=11.62, 55.71, 114.64, 116.32, 125.83, 136.97, 149.34, 161.28, 164.61, 167, 77; IR (KBr)v:1730, 1590, 1267, 1018, 875, 775 cm^{-1}.

4-(4-hydroxybenzylidene)-3-methylisoxazol-5(4H)-one: ^{1}H-NMR (300 MHz, $CDCl_3$): δ=2.31 (s, 3H), 6.96 (d, J=9.3 Hz, 2H), 7.81 (s, 1H), 8.49 (d, J=9.3 Hz, 2H) 11.05 (s, 1H); IR (KBr)v: 1731, 1595, 1557, 1516, 1311, 1235 cm^{-1}.

4-(4-methylbenzylidene)-3-methylisoxazol-5(4H)-one: ^{1}H-NMR (300 MHz, $CDCl_3$): δ=2.28 (s, 3H), 2.44 (s, 3H), 7.31 (d, J=7.8 Hz, 2H), 7.41 (s, 1H), 8.28 (d, J=7.8 Hz, 2H); ^{13}C-NMR (300 MHz, $CDCl_3$): δ=11.66, 22.08, 118.41, 129.87, 134.13, 145.72, 149.95, 161.23, 168.22; IR (KBr)v: 1731, 1593, 1113, 874, 776 cm^{-1}.

RESULTS AND DISCUSSION

To compare the effectiveness of Monosodium Glutamate (MSG) with other catalyst in synthesis of isoxazolone, result of the reaction of benzaldehyde, ethyl acetoacetate and hydroxylamine hydrochloride have table. With respect to results, compared to the previously reported method, MSG is relatively better in reaction times and yields (Table 1).

Table 1: Comparison of the results of the reaction of ethyl acetoacetate with hydroxylamine hydrochloride and Benzaldehyde, using MSG with those obtained by reported catalysts

Catalyst/conditions	Catalyst amount (mol %)	Time (min)	Yield (%)
Pyridine/EtOH/Reflux	100	180	71
Catalyst free/Grinding	0	48	61
Na_2S/EtOH/Retention time	5	90	88
Pyridine/H_2O/Ultrasound	100	60	82
Sodium silicate/H_2O/Retention time	5	90	91
Sodium benzoate/H_2O/Retention time	10	90	87
MSG	10	3	93

Reaction condition: 1 Ethyl acetoacetate (1 mmol); hydroxylamine hydrochloride (0.07, 1 mmol); 10 ml distilled water MSG (10 mol %); aromatic aldehyde (1 mmol) MW 300 Watt. At 100°C

The reaction is carried out in two steps; first ethyl acetoacetate reacts with hydroxylamine hydrochloride. In second step Knoevenagel reaction between aromatic aldehyde and ethyl 3-(hydroxyimino)butanoate obtain isoxazolone. MSG is the sodium salt of the non-essential amino acid glutamic acid, one of the most abundant amino acids found in nature. Isoxazolones have been synthesized using MSG as a safe catalyst, non-toxic, less expensive. We choose MSG as a catalyst as it is ecofriendly and its dual character shows multiple catalytic roles as an acid and base. MSG is enantio-selective and it shows Zwitterion which is the predominant species in aqueous solution (Table 2).

Table 2: preparation of different Isoxazolones catalyzed by monosodium glutamate in microwave irradiation conditions

S. No.	R	Time (min)	Yield (%)	Melting point (0°C)
1	C_6H_5	3	93	140-143
2	4-$CH_3OC_6H_4$	3	92	174-175
3	4-HOC_6H_4	2	91	214-215
4	3-HOC_6H_4	4	93	201-203
5	3-CH_3O-4-HOC_6H_3	3	96	211-214
6	4-FC_6H_4	2	93	142-145
7	4-$CH_3C_6H_4$	4	90	135-136

Reaction condition: Ethyl acetoacetate (1 mmol); hydroxylamine hydrochloride (0.07, 1 mmol); 10 ml distilled water MSG (10 mol %); aromatic aldehyde (1 mmol) MW 300 watt. At 100°C

CONCLUSION

We report a simple, eco-friendly, MCR reaction for the synthesis of green an efficient synthesis of isoxazolone using MSG as a catalyst. This protocol offers several advantages such as atom efficiency, short time, simple work-up and simple reaction condition. Use of water as ecofriendly solvent make to this new protocol attractive for the synthesis of these heterocycles.

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