Research Article

Green Synthesis and Characterization of Dihydropyrimidinone Derivatives using Fruit Juice.

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ABSTRACT

A simple and precise green synthesis method that has been used to synthesis of dihydropyrimidinone (DHPMs) derivatives. The reaction involves three-component one-pot condensation of an aromatic aldehyde, β-ketoester and urea in lemon juice. A large number of Dihydropyrimidinone (DHPM) derivatives were synthesized using urea, ethyl acetoacetate with electron rich as well as electron deficient aromatic aldehydes. The different type of aldehyde used like benzaldehyde, 4-Chlorobenzaldehyde, 4-methoxybenzaldehyde, anisaldehyde, cinnamaldehyde, and salicyaldehyde etc. The fruit juice like orange, amla, lime juice without processing is used as catalyst. The recrystallized products obtained were identified using physical and spectroscopic techniques UV-Visible, IR, 1HNMR etc. The yield of these reactions were found comparatively good and in the range of (80–95%). The advantage of this method is to initiate green chemistry approach in new researchers. The excellent yield, short time, operational simplicity, and the avoidance of the use of organic solvents and friendly preparation etc are the importance of the present work.

KEYWORDS

Dihydropyrimidinones (DHPMS) Biginelli reaction, Coupling reaction,
1. INTRODUCTION
The (DHPMs) have attracted great attention recently in synthetic organic chemistry due to their applications in the field of drug research and pharmacological and therapeutic properties such as antibacterial [3, 4], anti-inflammatory [4], antiviral [5], antitumor [6], antimalarial agents [7], hypnotics, anticonvulsants, antithyroid, antihistaminic agents, antibiotics [2] and in addition, 4-aryldihydropyrimidines have emerged antihypertensive activity as well as behaving as calcium channel blockers 8,9, α-antagonists and neuropeptide antagonists [10]. Synthesis of dihydropyrimidinone and their thio analogue is increasing tremendously in current years and also synthesized earlier a series of dihydropyrimidinone/thione by three component condensation of urea/thiourea [2]. The simplest and the most straightforward procedure, originally reported by Biginelli in 1893 involve three-component one-pot condensation of an aldehyde, β-ketoester and urea or thiourea [11] in lemon juice HCl [12]. Very recently a safe, eco-friendly, economical, efficient and green method has also been developed by our group for synthesizing DHPM via Biginelli reaction at room temperature in common fruit juice (amla, orange and lime juice) medium [6]. However Biginelli reaction using electron rich aromatic aldehydes in lime juice medium has not been reported in literature so far. So hereby we are reporting a green procedure for DHPM synthesis via Biginelli reaction with electron rich as well as with electron deficient aromatic aldehydes in lime juice medium at room temperature. Bhatewara et al. have reported a microwave assisted green synthesis of DHPM and their antimicrobial properties [7]. Green synthesis and antimicrobial properties of DHPM has also been reported in literature by other researchers [8, 9]. However antimicrobial properties of DHPMs which have been synthesized in lime juice medium, is not reported in literature yet. [6, 10, 11].

Scheme 1. Synthesis of Dihydropyrimidinone Derivatives with different aromatic aldehydes in lime juice medium.

Aldehyde: 3 (I) benzaldehyde, 3 (II) 4-Chlorobenzaldehyde, 3 (III) 4-methoxybenzaldehyde, 3 (IV) anisaldehyde, 3 (V) cinnamaldehyde, and 3 (VI) salicyaldehyde etc.

2. MATERIALS AND METHODS
2.1. Synthesis of (Compound 4-I) Ethyl 6-methyl-2-oxo-4-phenyl-1, 2, 3, 4tetrahydropyrimidine-5-carboxylate
The equimolar quantities of ethyl acetoacetate (0.02 mole, 2.6 gm), urea (0.02 mole, 1.2 gm) and benzaldehyde (0.02 mole, 2.4 ml) were stirred together in 4 ml of lime juice extracted directly from the naturally lime (Citrus aurantifolia) and it was used for the reaction without any chemical treatment at room temperature continuously for 12 h. Upon completion of reaction after
12 h, the solid product was precipitated out of the reaction medium. Upon filtration of the reaction mixture, the crude solid product was collected and crude product was recrystallized from hot ethanol to get the pure compound as pale yellow solid. The compound is characterized by spectral method as, the series of the other derivatives compounds were synthesized by using different aromatic aldehyde with same procedure.

Melting point: 210 °C
IR: 3200, 3125, 1720, 1700, 1490 cm⁻¹;
¹H-NMR (500 MHz,): δ 1.19 (t, 3H), 2.2 (s, 3H), 4.1 (q, 2H), 5.23 (d, 1H), 7.20 (m, 5H)

(Compound 4-II)
Ethyl 4-(4-chlorophenyl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate.
Melting point: 210 °C
IR: 3200, 3100, 2990, 1720, 1700, 1650, 1460 cm⁻¹
¹H-NMR (500 MHz,): δ 1.10 (t, 3H), 2.20 (s, 3H), 4.0 (q, 2H), 5.2 (d, 1H), 7.31 (m, 5H),

(Compound 4-III)
Ethyl 4-(4-methoxyphenyl)-6-methyl-2-oxo-1, 2, 3, 4-tetrahydropyrimidine-5-carboxylate
Melting point: 199 °C
IR: 3210, 3100, 3000, 2840, 1700, 1660, 1512, cm⁻¹
¹H-NMR (500 MHz,): δ 1.18 (t, 3H), 2.20(s, 3H), 3.60 (s, 3H), 4.1 (q, 2H), 5.3 (d, 1H), 6.9 (d, 2H),

(Compound 4-IV)
Ethyl 6-methyl-2-amino-4-phenyl-1, 2, 3, 4tetrahydropyrimidine-5-carboxylate
Melting point: 210 °C
IR: 3450, 3400, 3125, 1720, 1700, 1490 cm⁻¹;
¹H-NMR (500 MHz,): δ 1.19 (t, 3H), 2.2 (s, 3H), 4.1 (q, 2H), 5.23 (d, 1H), 7.20 (m, 5H)

3. RESULTS AND DISCUSSION
An equimolar mixture of urea and ethyl acetoacetate was employed to react individually with benzaldehyde, 4-methoxy benzaldehyde and 4-chloro benzaldehyde for synthesizing our desired dihydropyrimidinone (DHPM) compound 1, 2 and 3 respectively. Compound 1 is containing phenyl ring, 2 is containing electron rich 4-methoxy phenyl ring and compound 3 contains electron deficient 4-chloro phenyl ring. So compound-2 is the most electron rich DHPM among these three compounds, followed by compound-1 whereas compound-3 is an electron deficient DHPM. All the reactions were carried out at room temperature in lime juice medium. The natural acid present in the lime juice acted as the solvent cum catalyst for our Biginelli reaction. It was interesting to note that at room temperature the Biginelli reaction needs 12 h to complete in lime juice medium when electron rich 4-methoxy benzaldehyde was used whereas the same reaction (in the same medium) was completed in just 1 h when either benzaldehyde or 4-chloro benzaldehyde was used as reactant. So this is consistent with our previous findings [6] that biginelli reaction with electron rich aromatic aldehyde needs longer time for completion compared to that with electron deficient aromatic aldehyde in fruit juice medium at room
temperature. So three desired DHPM 1, 2 and 3 were synthesized successfully via Biginelli reaction in lime juice medium at room temperature.

4. CONCLUSION
Herein we have reported an eco-friendly, efficient and green methodology for the synthesis of a series of DHPM derivatives containing both electron rich as well as electron deficient aromatic ring, at room temperature in lime juice medium. It was observed that biginelli reaction with electron rich aromatic aldehyde requires longer time for completion than with electron deficient aromatic aldehyde at room temperature in lime juice medium. The yields of these reactions were found in the range of (80–95%). The advantages of this green chemistry approach the excellent yield, short time, operational simplicity, and the avoidance of the use of organic solvents and friendly preparation.

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6. REFERENCES
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