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Synthetic Study on Chalcone and their Dihydropyrimidinone and Dihydropyrimidinethione Derivatives

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ABSTRACT

A series of chalcones, dihydropyrimidinone and dihydropyrimidinethione derivatives were synthesized in good yields by Claisen Schmidt reaction of acetophenones with substituted aldehydes in the presence of sodium hydroxide in water-ethanol mixture followed by the condensation reaction of chalcones with urea and thiourea in ethanol respectively. The structures of the synthesized compounds were elucidated based on spectroscopic evidence.
Keywords : Chalcone, Urea, Thiourea, Dihydropyrimidinone, Dihydropyrimidinethione.

I. INTRODUCTION

Pyrimidine derivatives such as dihydropyrimidinones, dihydropyrimidinthiones are having important drug potential due to their pharmacological activities. Dihydropyrimidinones exhibit a wide range of biological activities such as antiviral [1], antitumour [2, 3], antibacterial [4, 5], and anti-inflammatory [6] properties. In addition, these compounds have emerged as potential calcium channel blockers [7], antihypertensive [8], α1a–adrenergic antagonists [9] and neuropeptide antagonists [10]. Over the past decade, dihydropyrimidin-2(1H)-thiones and their derivatives have been used as the dihydropyrimidine scaffold displays a fascinating array of pharmacological and therapeutic properties [11]. These dihydropyrimidinthiones compounds possess a wide spectrum of biological and therapeutic properties such as antibacterial [12], anti-viral [13], anti-tumor [14, 15], anti-inflammatory [16], anti-fungal [17], antihypertensive [18], anti-HIV [19], as well as α1a-antagonists [20, 21], neuropeptide Y (NPY) antagonists [22] and anticarcinogencic [23] activity. These compounds are also used as analgesic [24], blood platelet [25], aggregation inhibitory activity [26] and calcium channel blockers [27]. This observation led us to synthesize some newer dihydropyrimidinones and dihydropyrimidinethiones derivatives.

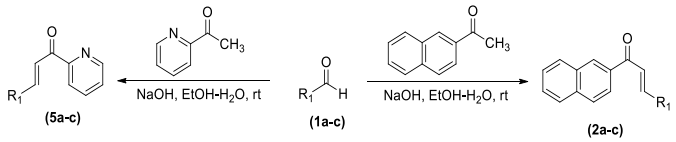
II. METHODS AND MATERIAL

All the reagents and chemicals were purchased from Merck. They were used without further purification. Melting points were taken in open capillary tubes and are uncorrected. Thin layer chromatography (TLC) is performed with E. Merck precoated silica gel plates (60F-254) with iodine as a spot developing agent. Acme, India silica gel, 60–120 mesh is used for column chromatography. IR spectra in KBr pellets were recorded on Perkin-Elmer model 683 spectrometers. ^{1}H NMR (400 MHz) spectra were recorded using tetramethyl silane (TMS) as an internal reference on Bruker spectrometer, Elemental analysis were performed on a Perkin-Elmer 2400. Mass spectra were obtained by Water-Q-TOF ultima spectrometer. Micro analytical data were obtained by elemental-Vario EL-III.

III. RESULT AND DISCUSSION

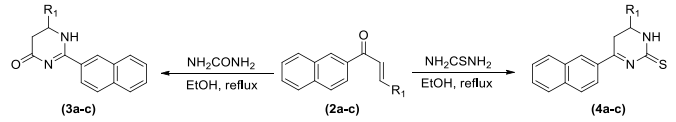
In this study, a series of novel chalcones, dihydropyrimidinone and dihydropyrimidinethione derivatives were synthesized by known chalcone route. Scheme 1 illustrates the synthetic route for the preparation of chalcones. Chalcones were prepared by the Claisen-Schimdt condensation reaction of an aryl methyl ketones in the presence of a sodium hydroxide to form an α,β-unsaturated ketone (enone) in water-ethanol mixture. The base sodium hydroxide abstracts acidic

proton from acetophenones. Acetyl group in acetophenones which is readily resonance with adjacent carbonyl groups to form enolate ion. It readily reacts with carbonyl groups of the substituted aldehydes. Later oxy anion abstracts a proton from ethanol. The β hydroxyl ketone looses a molecule of water to form chalcones. In the initial step, chalcones **(2a-c)** and **(5a-c)** were synthesized by condensing 1-(naphthalen-2-yl)ethanone (0.85 g, 5 mmol) and/or 1-(pyridin-2-yl)ethanone with substituted aromatic aldehydes in ethanolic sodium hydroxide solution at room temperature (scheme 1).



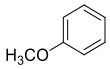
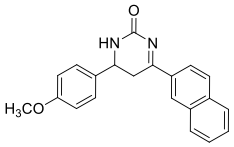
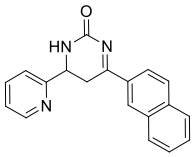
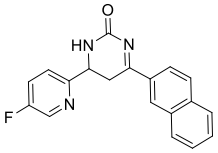
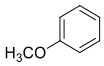
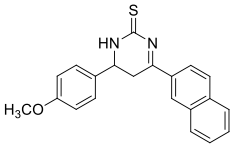
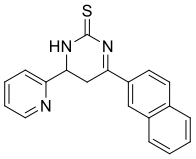
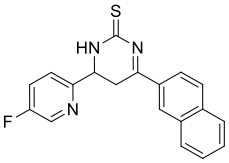
Scheme 1 Reaction protocol for newly synthesized chalcones **(2a-c)** and **(5a-c)**

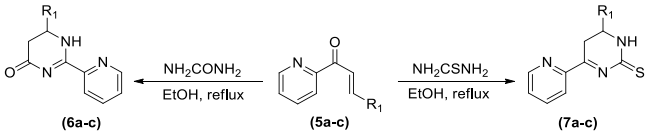
The synthetic route (scheme 2 and scheme 3) describes the synthesis of novel dihydropyrimidinone and dihydropyrimidinethione derivatives. From the chalcone derivatives, the various heterocyclic derivatives like novel dihydropyrimidinone (table 1) and dihydropyrimidinethione derivatives (table 2) were synthesized via cyclocondensation with urea and thiourea respectively. The purity of the newly synthesized compounds was checked via TLC using various mobile bases and were identified by spectral data (^{1}H NMR, IR spectroscopy, Mass Spectroscopy).



Scheme 2 Reaction protocol for newly synthesized naphthalenyldihydropyrimidinone **(3a–c)** and naphthalenyldihydropyrimidinethione derivatives **(4a-c)**

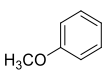
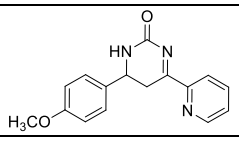
Table 1 Chemical structure of newly synthesized naphthalenyldihydropyrimidinone **(3a–c)** and naphthalenyldihydropyrimidinethione derivatives **(4a-c)**

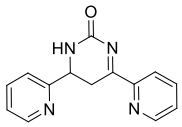
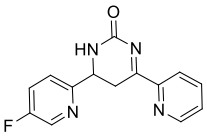
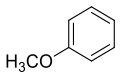
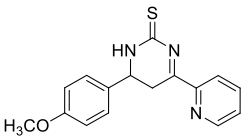
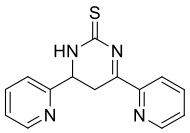
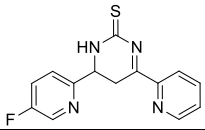
Compound No.	R_1	Product
3a		
3b		
3c		
4a		
4b		
4c		



Scheme 2 Reaction protocol for newly synthesized pyridinyldihydropyrimidinone **(6a–c)** and pyridinyldihydropyrimidinethione derivatives **(7a-c)**

Table 2 Chemical structure of newly synthesized pyridinyldihydropyrimidinone **(6a–c)** and pyridinyldihydropyrimidinethione derivatives **(7a-c)**

Compound No.	R_1	Product
6a		

6b		
6c		
7a		
7b		
7c		

IV. CONCLUSION

In conclusion we describe the Claisen-Schmidt reaction of chalcones with substituted aldehydes in the presence of sodium hydroxide in water-ethanol mixture and six membered dihydropyrimidinone and dihydropyrimidinethione moieties attached to naphthalene and pyridine moieties. The structures of all products were confirmed by the elemental analysis and spectroscopic studies.

V. ACKNOWLEDGMENT

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