

**SYNTHESIS & CHARACTERISATION OF SOME NOVEL HETEROCYCLIC COMPOUNDS FROM CHALCONES**

D. Sowjanya, D. Sowndarya, N. Mounika, K. Naga Jyothi, P. Siva Naga Lakshmi, B. Satya Sree\* and  
A. Lakshmana Rao

Department of Pharmaceutical Chemistry,

V. V. Institute of Pharmaceutical Sciences, Gudlavalleru- 521 356, A.P., India

\*Corresponding author E-mail: satyasree.bandaru@gmail.com

**Abstract:**

Various novel heterocyclic compounds were prepared by using chalcones. Chalcones are synthesized by Claisen-Schmidt condensation of aldehyde and ketone by base catalyzed or acid catalyzed followed by dehydration to yield chalcones. Chalcones were treated with urea, thiourea and hydroxylamine to give corresponding heterocyclic derivatives, the title compounds in good yields. The synthesized heterocyclic compounds were characterized by physical properties and spectral studies (IR, <sup>1</sup>H-NMR).

**Key words:**

Claisen-Schmidt condensation, oxazine, thiazine, isoxazole, aromatic aldehydes, urea, thiourea, hydroxyl amine, ethanol, sodium hydroxide.

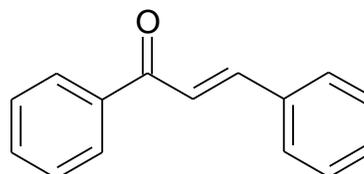
**Introduction:**

Heterocyclic chemistry has now become a separate field of chemistry with long history in present society and future prospects. The earliest compounds known to mankind were of heterocyclic origin. Life, like ours, is totally dependent on the heterocyclic compounds, it takes birth with purine/pyrimidine bases, nourishes on carbohydrates and in case of disease, is cured from medicines, many of which are heterocyclic in nature. Today, the heterocyclic chemistry delivers reagents and synthetic methods of its own traditional activity in synthesis of drugs, pesticides and detergents as well as into the related fields such as biochemistry, polymers and material sciences<sup>[1]</sup>.

These are very widely distributed in nature and are essential to life in various ways. Particularly these compounds are important because of the wide variety of physiological activities associated with this class of substances. Heterocyclic rings are present in several compounds, e.g. most of the members of vitamin B complex, antibiotics, chlorophyll, heme, other plant pigments, amino acids and proteins,

drugs, dye stuffs, enzymes, the genetic material DNA etc. Chemistry and pharmacology constantly drive the search for new methods for the construction of heterocyclic unit viz., isoxazoles and thiazoles. These isoxazoles and thiazoles were prepared from chalcones which are important products and they also possess biological and pharmacological activities<sup>[2]</sup>.

Chalcones (Fig.1) considered to be the precursor of flavonoids and isoflavonoids, are abundant in edible plants. They consist of open-chain flavonoids in which the two aromatic rings are joined by a three-carbon  $\alpha,\beta$ -unsaturated carbonyl system. Studies revealed that compounds with a chalcone based structure possess anti-microbial<sup>[3,4]</sup>, anti-inflammatory<sup>[5,6]</sup>, anti-bacterial, anti-epileptic<sup>[7]</sup> & anti-tumor activities<sup>[8]</sup>. These activities are largely attributed due to the  $\alpha,\beta$ -unsaturated ketone moiety.



**Fig. 1: Structure of chalcone**

Derived products oxazine, isoxazole & thiazine possess various activities like anti-inflammatory, anti-bacterial, anti-oxidant, anti-microbial [9] & anti-tumor activities etc. As part of ongoing studies we report the synthesis of a new class of structurally novel derivatives that incorporate two known bioactive structures thiazole and chalcone, to yield a class of compounds with interesting anti-microbial properties.

**Aim and objective:**

- Literature survey revealed that the chemistry and pharmacology of heterocyclic derivatives from chalcones have been of great interest to medicinal chemists. Because numerous chalcones have been synthesized and reported as bactericides, fungicides, herbicides, anti-inflammatory, tranquilizing agent and hypoglycemic activity.
- Literature survey reveals that heterocyclic derivatives from chalcones possess various biological activities [10] like anthelmintic, antitumor, analgesic, anticancer, anti-inflammatory, anti-bacterial and anti-fungal activity.
- Our aim is to prepare oxazine, isoxazole and thiazine derivatives from the chalcones.
- To characterize all the synthesized compounds by physical data (molecular weight, molecular formula, melting point, recrystallization and  $R_f$  value) and spectral data (IR,  $^1\text{H-NMR}$ ).

**Materials and methods:**

Materials and reagents were obtained from commercial suppliers (Merck grade) and were used without further purification. Melting points were determined by using electrical melting point apparatus and are uncorrected. The progress of the reaction was monitored by TLC using Silica Gel G (Merck). IR spectra were recorded in KBr discs on a Bruker analyzer.  $^1\text{H-NMR}$  spectra were recorded on a Bruker (400 MHz) spectrometer (chemical shifts in  $\gamma$ , ppm) in DMSO using TMS as internal standard.

**Experimental work:****Procedure for synthesis of chalcones:**

A mixture of acetophenone (1.16 ml), benzaldehyde (1.5 g), ethanol (30 ml) and 10% NaOH were taken and kept at 25°C. Stir vigorously until mixture gets thickened. Kept it overnight at room temperature. Pour it in crushed ice and acidified with HCl. Filter out the precipitated chalcone and recrystallized by using 95% ethanol.

**General procedure for synthesis of heterocyclic compound** [11, 12, 13]:

A mixture of chalcone (0.02 mol) and urea/thiourea/hydroxylamine HCl (0.02 mol) was dissolved in 10 ml of ethanolic NaOH/sodium acetate and stir continuously for 3hrs. The above mixture was poured in 200 ml of cold water with continuous stirring for 1 hr and left it for overnight. The solid is separated out and filtered. Wash with cold water and recrystallize with 95% ethanol.

**Various synthesized heterocyclic compounds from Chalcones are**

Synthesis of 2-amino-4,6-diphenyl oxazine (Ia)

Synthesis of 2-amino-4,6-diphenyl thiazine (Ib)

Synthesis of 3,5-diphenyl isoxazole (Ic)

Synthesis of 2-amino-4(4-nitro phenyl)-6-phenyl oxazine (IIa)

Synthesis of 2-amino-4(4-nitro phenyl)6-phenyl thiazine (IIb)

Synthesis of 3-(4-nitro)-3,5-di phenyl isoxazole (IIc)

**Physical Characterization of the Synthesized Compounds:**

Melting points were determined by open ended capillary tube and are uncorrected. Purity of the compounds was identified by the TLC by using silica gel-G as stationary phase.

**Spectral Data (IR &  $^1\text{H-NMR}$ ) of Compound Ib & IIb:****2-amino-4,6-diphenyl thiazine (Ib):**

IR [ $\text{Cm}^{-1}$ , KBr]: 2370 (C-S-C), 1655 (C = C), 1624 (C = N), 1610 ( $\text{NH}_2$ )

 **$^1\text{H-NMR}$  (400 MHz, DMSO- $d_6$ )  $\delta$ (ppm):**

2.1 (s,2H, $\text{NH}_2$ ), 3.5 (s,1H), 5.7 (s,1H), 6.8-7.9 (m,9H,Ar-H).

**2-amino-4-(4-nitrophenyl)-6-phenyl thiazine (IIb):**

IR [ $\text{Cm}^{-1}$ , KBr]: 2370 (C-S-C), 1655 (C = C), 1624 (C = N), 1610 ( $\text{NH}_2$ ), 1570 ( $\text{NO}_2$ ).

**Results and discussion:**

Chalcones were prepared by using Claisen-Schmidt condensation reaction. Various title compounds were synthesized using the appropriate synthetic procedure i.e. reaction of chalcones, urea/thiourea/hydroxylamine HCl in presence of sodium hydroxide. A mixture of chalcone and urea/thiourea/hydroxylamine HCl was dissolved in 10ml of ethanolic NaOH/ sodium acetate and stir continuously for 3 hrs. The above mixture was poured in 200 ml of cold water with continuous stirring for 1hr and left it for overnight. The progress of reaction was monitored by TLC. Finally the reaction mixture was poured onto the crushed ice and then recrystallized from ethanol. The melting point of the compound was found to be same as that of reported.

Melting points were determined in open capillaries and are uncorrected.

IR spectra were recorded in KBr discs on a Bruker (300 FT-IR)

Thin layer chromatography was performed on silica gel G (Merck).

<sup>1</sup>H-NMR spectra were recorded on a Bruker 400 spectrometer operating at 400.13 MHz in DMSO.

#### Summary and conclusion:

In the present work chalcones were used to prepare various heterocyclic compounds by cyclization with urea/thiourea/hydroxylamine HCl in presence of ethanolic sodium hydroxide/ sodium acetate gives good yields.

A facile method under mild conditions has been developed for the synthesis of the title compounds.

All the compounds synthesized were characterized by physically (*R<sub>f</sub>* values, melting point, molecular weight, molecular formula) and few compounds were characterized by spectral data (IR, <sup>1</sup>H-NMR,).

Among the synthesized compounds 2-amino-4,6-diphenyl oxazine (**Ia**) and 2-amino-4,6-diphenyl thiazine (**Ib**) gives high % yield.

#### References:

1. P. N. Balaji, M. Sai Sreevani, P. Harini, P. Johnsi Rani, K. Prathusha and Chandu. Antimicrobial activity of some novel synthesized heterocyclic compounds from substituted chalcones. *Journal of Chemical and Pharmaceutical Research*, 2010; 2(4): 754-775.
2. V. D. Joshi, M. D. Kshirsagar and S. Sarita. Synthesis and pharmacological study of some novel pyrimidines. *Journal of the Chinese Chemical Society*, 2008; 55: 394-40.
3. M. Ali, M. Azad and H. L. Siddiquia. Synthesis and antimicrobial studies of some quinolinylpyrimidine derivatives. *Journal of Chemical and Pharmaceutical Research*, 2013; 5(7): 46-55.
4. N. M. Goudgaon et al., synthesized 3-{6-[3-(substituted phenyl)-1-phenyl-1*H*-pyrazole-4-yl]-2-thioxo-1,2,5,6-tetrahydropyrimidine-4-yl}-2*H*-chromane-2-one as anti-microbial agent. *Molecules* 2014; 19: 19648-19664.
5. T. Karabasanagouda, A. V. Adhikari and M. Girisha. Synthesis of some new pyrazolines and isoxazoles carrying 4-methylthiophenyl moiety as anti-inflammatory and analgesic. *Indian Journal of Chemistry*, 2009; 48B: 430-437.
6. I. Sudeer Babu and S. Selvakumar and N. Chidambaranathan. Pharmacological evaluation of some potent 2-substituted benzimidazolyl chalcones for analgesic, anti-inflammatory activities. *International Journal of Phytopharmacology*, 2012; 3(2): 163-172.
7. B. Maruthirao, S. Ramesh, B. Dipankar, H. Rahman. Synthesis of 4-pyrazoline derivatives as anti-epileptics. *Scholars Journal of Applied Medical Sciences*, 2013; 1(1): 20-27.
8. P. M. Ranjit, S. A. Rahaman and K. P. Kumar. Synthesis, screening and in-vitro anticancer activity piperazine nucleus containing novel chalcones. *International Journal of PharmTech Research*, 2013; 5: 284-293.
9. D. Sunil, H. U. Sadhana, Savitha and M. Rama. Synthesis, characterization and QSAR studies of some new 1,3-oxazines as potent antimicrobial agents. *Research Journal of Pharmaceutical Sciences*, 2013; 2(2): 15-19.
10. D. Jayaseelan, M. Ganapathi, S. Guhanathan. Synthesis of 4,6-Diphenyl

- oxazines and its characterization. International Journal innovative research in sciences and engineering, 2014; 2(1): 18-24.
11. V. D. Joshi, M. D. Kshirsagar, S. Sarita. Synthesis and Pharmacological study of some novel isoxazoles. Journal of Chemical and Pharmaceutical Research, 2012; 4(6): 3234-3238.
  12. R. Gosh and D. Abhijit. Synthesis and biological activities of chalcones and their heterocyclic derivatives. World Journal of Pharmacy and Pharmaceutical Sciences, 2014; 3(3): 578-595.
  13. S. Anjani, P. Rajanikant and P. Kirti. Synthesis and evaluation of some novel S-triazine based chalcones and their derivatives. Der Pharma Chemica, 2011; 3(6): 317-324.

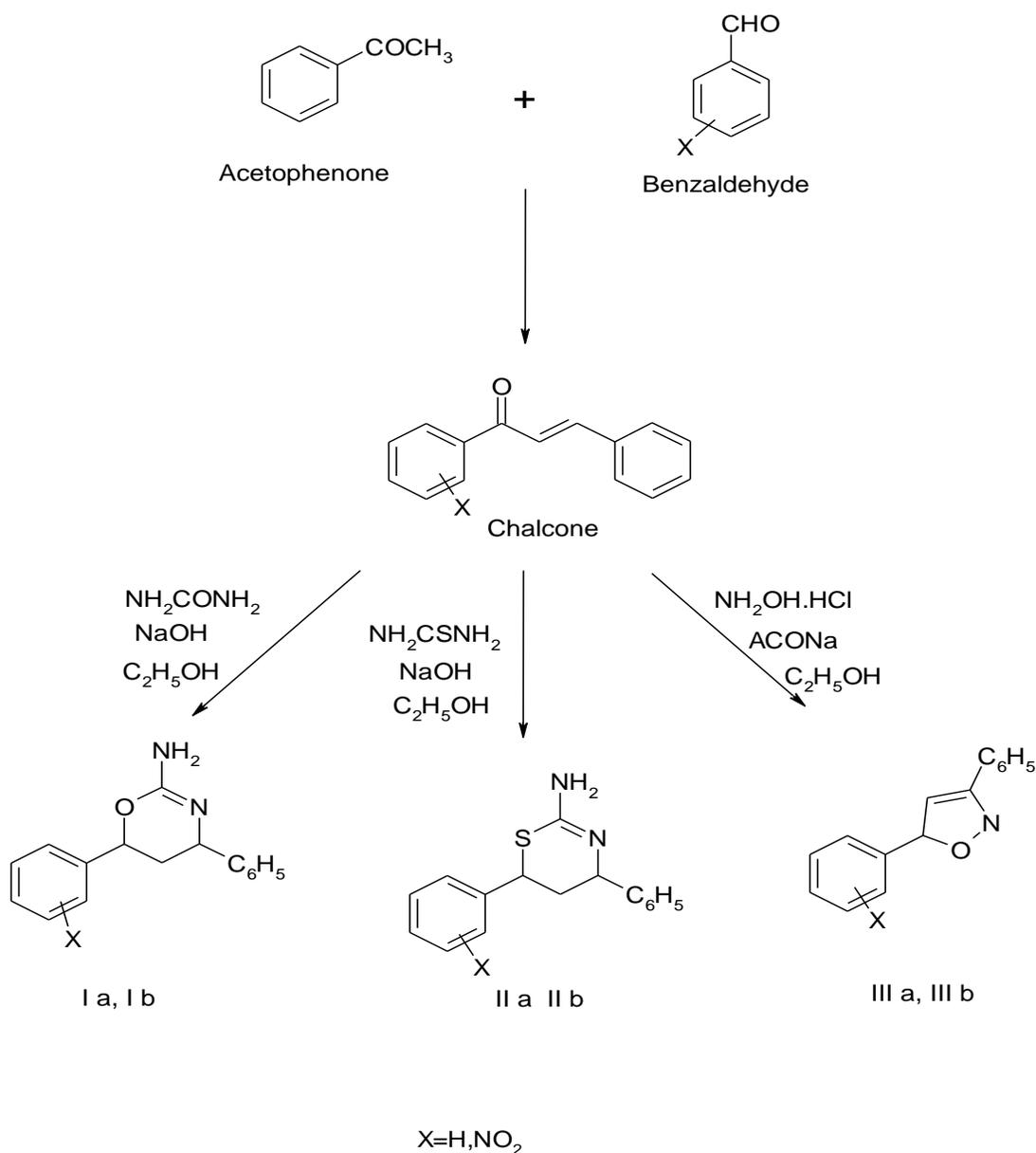


Fig. 2: Schematic representation

**Table 1: Physical data of the synthesized compounds**

<b>Compound</b>	<b>Molecular formula</b>	<b>Molecular weight (gm)</b>	<b>Melting point (°C)</b>	<b>% yield</b>	<b>R<sub>f</sub> value</b>
Ia	C <sub>16</sub> H <sub>15</sub> N <sub>2</sub> O	251	93	76.2	0.51
Ib	C <sub>16</sub> H <sub>15</sub> N <sub>2</sub> S	267	98	72.2	0.66
Ic	C <sub>15</sub> H <sub>13</sub> ON	223	78	28.2	0.7
IIa	C <sub>16</sub> H <sub>13</sub> O <sub>3</sub> N <sub>3</sub>	295	60	51.2	0.27
IIb	C <sub>16</sub> H <sub>15</sub> N <sub>3</sub> SO <sub>2</sub>	313	160	41.9	0.34
IIc	C <sub>15</sub> H <sub>13</sub> N <sub>2</sub> O <sub>3</sub>	269	130	21.02	0.41