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A NOVEL SYNTHESIS OF 4,6-BIS(4-CHLOROPHENYL)-3,4-DIHYDROPYRIMIDINE-2(1*H*)-THIONE USING CHALCONE

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Abstract :
Place 5 mg of the 4-chloro benzaldehyde into a 50 ml Erlenmeyer flask. Add 5 mg of the 1-(4-chlorophenyl)ethanone and 4.0 ml of 95% ethanol to the flask containing your aldehyde. Be sure to record the exact amounts of each reagent used.Add a magnetic stir bar and stir the mixture well to dissolve any solids. It may be necessary to warm the mixture gently to dissolve the solids. If this is necessary, the solution should be cooled to room temperature before proceeding with the next step add 0.5 ml of NaOH solution. Stir the mixture until it solidifies or until the entire mixture becomes very cloudy (about four minutes). If it does not solidify, continue the reaction for at least 15 minutes. Add 10 ml of ice water to the flask. If a solid is present at this point, break up the solid mass by stirring with a spatula. Cooling and scratching may be necessary to initiate crystallization. Collect the solid by vacuum filtration and allow it to dry overnight. Weigh the dry, purified product known as (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (C), determine the percent yield, and obtain a melting point.
A mixture of [0.01M] of (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (C) with [0.01M] thiourea were refluxed in 30 ml DMF and pinch of K_2CO_3 for 6 hours. Then the reacting mixture was cooled and poured into crushed ice, then the solid product was precipitate out known as 4,6-bis(4-chlorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (D), then it was filtered, dried and recrystallized from ethanol. The reaction is monitored by TLC. All the compounds are characterized by physical and spectral data

Key Words :
4-chloro benzaldehyde, NaOH, DMF, K_2CO_3, (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one

Introduction :
Chalcones are 1,3-diphenyl-2-propene-1-one, in which two aromatic rings are linked by a three carbon with α, β- unsaturated carbonyl system as, these are abundant in edible plants and are considered to be precursors of flavonoids and isoflavonoids. The Synthon is synthesized by claisen-schmidt condensation of aromatic aldehydes with acetophenone by base catalyzed or acid catalyzed followed by dehydration to yield Chalcones.[1,2,3] These Chalcones undergo a variety of chemical reactions and are found useful in synthesis of variety of heterocyclic compounds [4,5] like Pyrimidine and Thiazole derivatives are synthesized through the reaction of Chalcones with urea and thiourea in the presence of alkaline media in refluxing ethanol; these derivatives are considered to be important for drugs and agricultural chemicals. They possess several interesting biological activities such as anticancer, anti-inflammatory, antiviral, antihypertensive, anticonvulsant, antibacterial, antitumor, antifungal activities and so on.[6] Based upon the literature we are going to synthesize the different substituted pyrimidine and thiazoles from this Chalcones so as to increases its biological values.

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Chalcone (and related compounds "chalconoids") is an aromatic ketone that forms the central core for a variety of important biological compounds, which are known collectively as chalcones. They show antibacterial, antifungal, antitumor and anti-inflammatory properties. Some chalcones demonstrated the ability to block voltage-dependent potassium channels. They are also intermediates in the biosynthesis of flavonoids, which are substances widespread in plants and with an array of biological activities. Chalcones are also intermediates in the Auwers synthesis of flavones. Methyl hydroxychalcone (MCHP, molecular formula : $C_{16}H_{14}O_2$, molar mass : 238.28 g/mol, exact mass : 238.09938, PubChem CID : 6440383), found in cinnamon, was thought to be an insulin mimetic, improving insulin response of diabetics. It has since been determined that a flavonoid is responsible for the insulin-like biological activity.

Treatment of diseases with chemical substances has been known since the fiftheenth century. Chemical agents not only provide the structure basis and energy supply of living organism but also regulate their functional activities. The interaction between potent chemical and living system contribute to the understanding of the life process and provide effective method for the treatment , prevention and diagnosis of many diseases. Fighting against diseases with drugs is the endless struggle. The field and scope of medicine is too vast[7-8].

Various animals experiments have been designed to study the study the effect of drug on living organism and isolated tissue. These gave an insight into where and how a drug act. By knowledge of mode of action of adrug, it's effect on various body system and probable adverse effects are important[9-11].

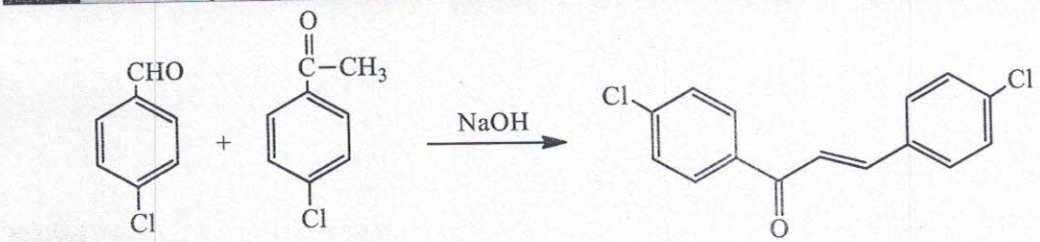
Experimental Section:

Melting points were determined in open capillary tube with anhydrous substance and were uncorrected. IR spectra of the newly synthesized compound were recorded with potassium bromide pellets technique, ^{1}H NMR spectra were recorded with the help of AVANCE 300 MHz Spectrometer in DMSO using TMS as internal standard. Mass spectra of the compound were recorded on a FT VG-7070H. Mass Spectrometer using EI technique at 70 eV is used. All the reactions of the newly synthesized were monitored by Thin layer chromatography.

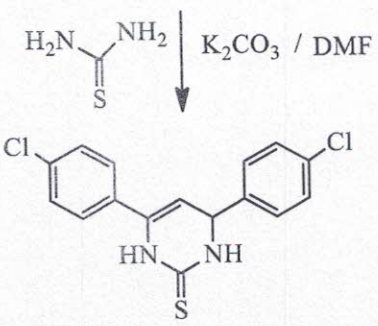
Material and Methods :

Synthesis of 4,6-bis(4-chlorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione:

4-chloro benzaldehyde (5 mg), 1-(4-chlorophenyl)ethanone (5 mg) and 4.0 ml of 95% ethanol to the Erlenmeyer flask containing aldehyde. Add a magnetic stir bar and stir the mixture well to dissolve any solids. It may be necessary to warm the mixture gently to dissolve the solids. If this is necessary, the solution should be cooled to room temperature before proceeding with the next step adds 0.5 ml of NaOH solution. Stir the mixture until it solidifies or until the entire mixture becomes very cloudy. If it does not solidify, continue the reaction for at least 15 minutes. Add 10 ml of ice water to the flask. If a solid is present at this point, break up the solid mass by stirring with a spatula. Cooling and scratching may be necessary to initiate crystallization. Collect the solid by vacuum filtration and allow it to dry overnight. Weigh the dry, purified product known as (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (C), determine the percent yield, and obtain a melting point. A mixture of [0.01M] of (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (C) with [0.01M] thiourea were refluxed in 30 ml DMF and pinch of K_2CO_3 for 6 hours. Then the reacting mixture was cooled and poured into crushed ice, then the solid product was precipitate, filtered, dried and recrystallized from ethanol known as 4,6-bis(4-chlorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (D).



4-chlorobenzaldehyde (A) + 1-(4-chlorophenyl) ethanone (B) → (*E*)-1,3-bis(4-chlorophenyl)prop-2-en-1-one (C)



4,6-bis(4-chlorophenyl)-3,4-dihydropyrimidine-2(1*H*)-thione (D)

Results and Discussion :

From the obtained results, it is evident that most of the compounds possess very good activity against bacterial strains like *Streptococci, Pseudomonas aeruginisa*, *Staphylococcus aureus* and *Escherichia coli* and some compounds possess very good activity against fungi like *Candida albicans* and *Aspergillus flavus* and remaining compounds showed moderate activity against all bacteria and fungi tested.

Conclusion:

In conclusion we have developed a simple methodology for the preparation of substituted pyrimidinethione derivatives. The advantage of this method are extremely mild reaction conditions, short reaction time, high yield, simple experimental technique and compliance with green chemistry protocols.

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