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RESEARCH ARTICLE

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SYNTHESIS, CHARACTERIZATION AND STUDY BIOLOGICAL ACTIVITY OF SOME NEW PYRIMIDINE DERIVATIVES

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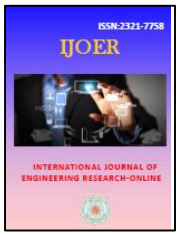

ABSTRACT
New pyrimidine derivatives were prepared by new chalcone derivatives and thiourea via a cyclization reaction. The first step includes synthesized of 4-formylphenyl acetate by the reaction of 4-hydroybezaldehyde with acetic anhydride. Chalcone compounds were prepared via the cliesen –shemidt condensation of 4-formylphenyl acetate with (4-Chloro,4-Bromo,4-N, N-dimethyl amino) acetophenone. Then cyclization of chalcone compounds with thiourea to produce pyrimidine derivatives [3a-3c]. Some of the prepared compounds were study biological activity, all the prepared compound was characterized by melting point, FT-IR, H1 NMR spectroscopy.
Keywords: Chalcone, 4-Formylphenyl acetate and pyrimidine.

I. INTRODUCTION

Chalcone with its Chalcone structure consider a useful antibacterial drug. By combining of Chalcone with antitumor agent in one compound this will lead to formation new antitumor agent with different activity 1. Chalcone are important class of five membered aromatic heterocyclic compound which have a broad spectrum of biological activity in both medicinal and pharmaceutical, such as new antimicrobial and antibacterial agent especially when it possesses sulfadiazine as a functional group in the whole structure 2. Also having anti-fungal, anti-viral, anti-inflammatory 3.

II. EXPERIMENTAL

Melting points were recorded using electro thermal melting point apparatus. FT-IR spectra were recorded using alpha broker Infrared spectrophotometer. H1 NMR were recorded on bruker spectrometer operating on (300 MHz) with DMSO-d6 as solvent.TLC was performed on aluminum plates and coated with layer of silica gel; compounds were detected by iodine vapor. This research involves synthesis new pyrimidine derivatives mixed with new chalcone and study biological activity of the prepared compounds. Chalcone are synthesized by base catalyzed Claisen-Schmidt condensation of aromatic aldehyde and ketone followed by dehydration to yield desired product4.chalcone are exhibit a wide spectrum of biological activity due to presence of a reactive α, β-unsaturated keto group. Schiff bases are important intermediates for synthesis of some bioactive compounds, which are prepared by the condensation of a primary amine with compound who contain carbonyl compound such as aldehyde or ketone5. Furthermore, they are reported to show a variety of interesting biological actions, including antibacterial, antifungal, anticonvulsant, anti-inflammatory and ant tubercular. Pyrimidine derivatives play avital role in many biological processes and in synthesis of many drugs. Many derivatives of pyrimidine have displayed diverse biological activities such as antitumor, hypnotensive, antiulcer, and anticonvulsant6.

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PREPARATION METHODS

A- *Synthesis of 4-Formylphenyl Acetate General Procedure*[7]

An equimolar mixture of 4-hydroxybenzaldehyde (0.01mole) and acetic anhydride (0.01mole) in 20 ml of ethanol was stirred for 2 hrs in the presence of 40%NaOH. The precipitate was obtained washed well with cold D.W and recrystallized from ethanol. The TLC was used to monitoring reaction progress by using (ethylacetate:n-hexan, 3:1).

FT-I. R Spectra (cm-1) A. (aromatic –C-H str. 3070), (Alkyl –C-H- str. 2968), (Alpha, beta unsaturated ester -C=O str. 1762) (-C-O str. 1117).

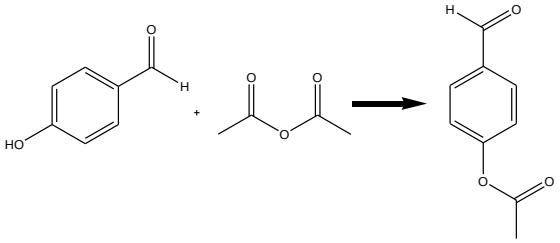


Figure 1: Synthesis of Compound 1

B- *Synthesis of chalcone derivatives general procedure*[7].

An equimolar mixture of 4-formylphenyl acetate (0.01mole) and aromatic aldehyde derivatives (4-chloro, 4-bromo, 4-N, N-dimethylamino benzaldehyde) (0.01mole) in 20 ml of ethanol was stirred for 2 hrs in the presence of 40%NaOH. The precipitate was obtained washed well with cold D.W and recrystallized from ethanol. The TLC was used to monitoring reaction progress by using (ethylacetate:n-hexan, 3:1).

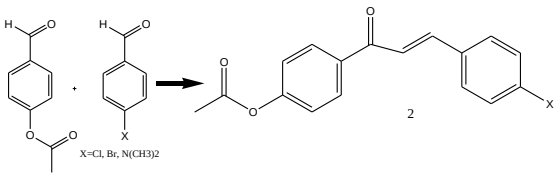


Figure 2: Synthesis of compound 2a-2c

FT-I.R Spectra (cm^{-1}) A. (pri. –N-H str. 3565), (-C=C- str. 1826), (-C=O str. 1864), (-C-H str. 3147 Aromatic), (C-Cl str. 785). B. (pri. –N-H str. 3565), (-C=C- str. 1855), (-C=O str. 1871), (-C-H str. 3165 Aromatic), (C-Cl str. 799). C. (pri. –N-H str. 3531), (-C=C- str. 1802), (-C=O str. 1741), (-C-H str. 3074 Aromatic, aliphatic 2995,2809). D. (pri. –N-H str. 3678), (-C=C- str. 1754), (-C=O str. 1786), (-C-H str. 3066 Aromatic, aliphatic 2827), (-OH str. 3223). E. (pri. –N-H str. 3422), (-C=C- str. 1651), (-C=O str. 1682), (-C-H str. 3039 Aromatic), (C-Br str. 1192).

Table 1: Chemical and physical properties for prepared compounds(2a-2c)

No.	Molecular formula	M.wt	Yield %	Color	Melting point	Rf
2a	$C_{16}H_{11}ClO_3$	286.5	81	Yellow	149-151	0.75
2b	$C_{18}H_{21}NO_3$	299	92	Orange	141-143	0.92
2c	$C_{16}H_{11}BrO_3$	378.9	75	Pale yellow	163-165	0.86

C- ***Synthesis of pyrimidines derivatives general procedure:***

A mixture of chalcone compounds [1-3] (0.01mole) with thiourea (0.01) were prepared in 25ml of absolute ethanol with stirred for 8 hrs.in the presence of 10% KOH. The reaction progress was monitored by TLC, the solvent was partially evaporated and the product was recrystallized from absolute ethanol

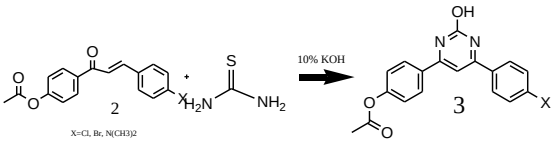


Figure 3: Synthesis of compound 3a-3c

Test of Biological Activity[13].

The test of biological activity of prepared chemical compounds which includes the following steps:

1. Prepare bacterial suspension from used bacteria (Streptococcus ssp. *Staphylococcus arueus, Granulecatella adiacens, proteus mirabilus, prophyromonas gingivalis* and *Escherichia coli*) and compared with McFarland tube 1.5× 108 cell /ml.

2. Spread bacterial suspension on (Muller Hinton Agar) homogeneously (0.1 ml) to cover the whole medium.

3. Make holes in the paten dish by the cork piercing to diameter 6 mm at concentration used.

4. Prepare dilute solutions (30, 60) mg/ml for each compound at physiological pH (7).

5. Put the prepared concentrated solutions from chemical compounds in holes to know their effectiveness for biological activity.

6. Incubate the paten dish at temperature 37°C for 24 hours.

7. Measure the diameter of inhibition zone for each disc by the ruler to determine the effectiveness of each compound and compare with the standard limits of sensitivity of the same species of bacteria against antibiotics.

III- RESULTS AND DISCUSSION

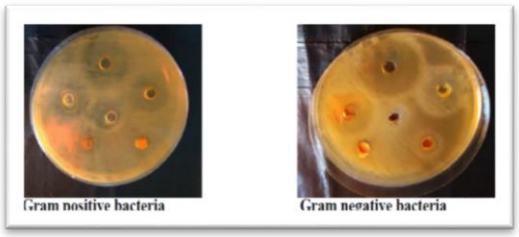
The compound 4-formylphenyl acetate which is the starting material of this research was first synthesized from the reaction of 4-hydroxybenzaldehyde with acetic anhydride by SN2 mechanism and the reaction progression was monitored via TLC. FT-IR showed the formation of the product according to the disappear of phenolic group at para position 3200-3500 cm^{-1}. Chalcone were synthesized by by cliesen–shemidt condensation which are characterized by FT-IR where the aliphatic (-C-H) at 2875-2998 cm-1 and also aldehyde (-C-H) at 2683-2875 cm-1 were disappear and new absorption bands due to stretching vibration of (-C=C-) at 1640-1680 cm-1 and conjugation (-C=O) bellow 1700 cm-1 were appeared. Compounds[2a-2c] are cyclized with thiourea in a separated reaction to obtain pyrimidine derivatives [3a-3c]. FT-IR spectrum good evidence to formation these compounds by inspection the changing in the absorption bands the major difference is disappearing of (-C=O) of the [2a-2c] compounds and appearing (-N=CH-) of the pyrimidine ring at 1516-1590 cm-1. The FT-IR is used to detect formation of this compound by showing the stretching vibration band of imine group (-N=CH) at 1519-1625 cm-1 also the stretching vibration of amine group (-NH2) are disappeared. Some extra characteristic bands were mentioned in experimental part. H1 NMR and mass spectra were recorded for the prepared compound. The biological activity of the synthesized compounds was screened against two types of bacteria, and the results were better than many available antibiotics.

Biological activity

The prepared compounds [3a-3c] were examined for antibacterial activity against Streptococcus ssp. (Gram-positive) and prophyromonas gingival is(Gram-negative) by well diffusion method in Mueller-Hinton agar medium. After 24 hours' zone of inhibition around each disc. The test results presented in Table (2) showed that [3a] exhibited slight active against S. spp. it was highly active against Prophy. Gingivals.

Table 2: Antibacterial activity of some synthesized compounds.

Comp.	Diameter of inhibition zone (mm)	
	Streptococcus spp. **(Gram positive bacteria)**	***Prophyromonasgingivalis*** **(Gram negative bacteria)**
3a	**8**	**14**
3b	**30**	**34**
3c	**25**	**29**



HNMR spectrum of the synthesized compounds

DMSO-d6) as a solvent: [(6H), (N-(CH3)2), 2.895], [(1H), (CH of Imine group), 8.669], [(13H), (Ar-H), 6.809-8.297], [(1H), (-SH), 11.763].

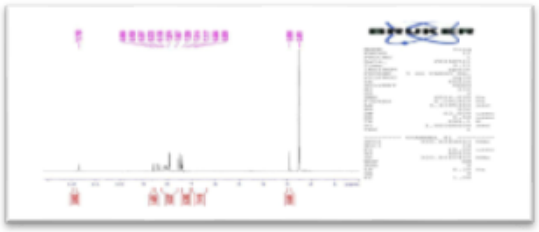


Figure 4: 1HNMR Spectra for selected compound 3a
Figure 5: 1HNMR Spectra for selected compound 3b

(DMSO-d6) as a solvent: [(6H), (N-(CH3)2), 3.425],[(1H), (CH of Imine group), 8.674], [(12H), (Ar-H), 6.697-8.299], [(1H), (-SH), 12.014]

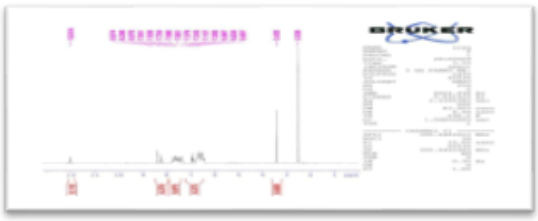


Figure 5: 1HNMR spectrum of the compound [3b]
Figure 6: 1HNMR spectrum of the compound [3c]

Compound Figure [6] (DMSO-d6) as a solvent: [(1H), (-CH of Imine group), 8.584], [(13H), (Ar-H), 6.467-8.436], [(2H), (-NH2), 6.319].

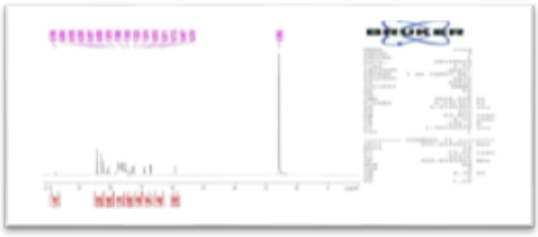


Figure 6: 1HNMR spectrum of the compound [3c]

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