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Prepare several substituted pyridines derived from Chalcone and evaluate their bioactivity

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***Abstract*---**In this research, Chalcone (M_{1-10}) was prepared by reaction of aromatic aldehydes with substituted acetophenone, through reaction of Chalcone with Malononitrile in an acidic medium, where pyridine compounds (M_{19-26}) were obtained. The bioactivity of the prepared compounds was tested against Gram-negative and Gram-positive bacteria (Klebsellia pneumonia, Pseudomnas putida, Staph aureus, Enterococcus faecalis). the lowest inhibitory concentration compared to (Ciprofloxacin) and the prepared compounds were diagnosed by physical spectrophotometric methods using spectrophotometers. I.R, ^{1}H-NMR, ^{13}C-NMR.

***Keywords*---**Chalcone, bioactivity, Malononitrile.

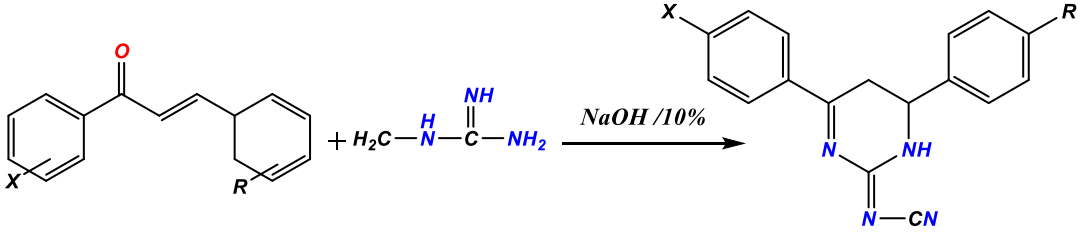
Introduction

Chalcone

Chalcone is (1,3 Diphenyl 2 Propen 1 One.) It is one of the unsaturated ketone alpha-beta carbonyl compounds and it is called [(1)] (Benzylidenacetophenones) (Phenylstrylketo). They are ketogenic compounds that include between them the carbonyl group that contains the double bond at the alpha-beta site [(2)(3)(4)] , which is mixed by the method of Aldol Condensation [(5)(6)] between (acetophenone) and (benzaldehyde) in alkaline conditions, as well as by microwave radiation [(7)], The name Chalcone was given for the first time by the scientist (8) (Kastaneck) in 1899 AD, where he conducted preliminary experiments in preparing colored natural compounds, It can be seen that the aromatic rings in Chalcone are linked to three carbon atoms, which are Aliphatic hydrocarbons. [(1)(9)] Chalcone has been used as an important medium for preparing compounds of therapeutic value, and its use has increased widely in pharmaceutical applications, cosmetics and many other industries[(10)(11)], it is also used as a drug regimen designed to discover new factors to treat diseases[(12)], They are also important media for the preparation of many different active organic compounds such as pyrazoline [(13)(14)], β-lactam

[15][16]. Also, interest has increased in the use of Chalcone for the purpose of developing many antibacterial compounds[17][18], anti-ulcer, [19] antimicrobial [20] [21], gave activity against three types of human cancer cells (HepG2) liver, (HCT116) colon, (MCF-7) breast [22], Chalcone chemistry is still a source of great interest For scientists in the 21st century, a variety of promising drugs were produced, such as antifungals [23] [24], anti-inflammatory, [25] [26], antitumor [27], anti-diabetic [28] [29], Also among the examples of compounds in which the Chalcone derivative is included is a compound (2) anti-genetic and cytotoxic [30], a compound (3) anti-inflammatory [32] [31]

The first pyrimidine derivative (23) was isolated in the year (1818) and is alloxan by the scientist (Brugnatelli) [33] by oxidation of uric acid and nitric acid. Pyrimidine has three isomers that depend on the positions of the two nitrogen atoms in the hexagonal ring [34], and they have a structure similar to the pyridine ring in that they contain a hexagonal ring and a nitrogen atom [35], If the substitution is in position 1,2, it is known as pyridazine, at position 1,3 it is known as pyrimidine, and at position 1,4 it is known as pyrazine [36] [37]. The interest in pyrimidine derivatives has also increased in the past years because they give a wide range of biological activities such as antibacterial, antifungal, antihypertensive, heart disease, bronchodilator or antitumor activity. The pyrimidine ring is also found in vitamin B, riboflavin, and folic acid, many of which are in clinical applications and have biological activities [38] [39] and we also find it in many medicines [40] [41]



Materials and working methods

FT-IR 470 infrared- specterphotometer- (IR) shimadzu and nuclear magnetic resonance spectroscopy (H-NMR) using BRUKER 400 MHz and Electro thermal point apparatus 9300 (M.B) were used.

Preparation of pyrimidine derivatives (M_{11-18})

In a (100 ml) circular flask, dissolve 0.01 mole) of the prepared Chalcone derivatives [M_{1-10}] in 10 ml of ethanol, then add to it a solution (0.01 mol) of cyanoguanidine dissolved in (0.01 ml) of ethanol, then add (10) ml) of 10% sodium hydroxide and the mixture rises for 6 hours with continuous stirring, the solution becomes neutral by adding drops of concentrated hydrochloric acid, then the solution is cooled and added to crushed ice, The precipitate is separated by filtration, washed with cold water, and recrystallized from ethanol. Table (3-2) shows some physical properties of pyrimidine derivatives.

Evaluate the biological activity

The effect of the prepared derivatives against four types of bacteria (antimicrobial) was studied, two of them are gram-positive and two are gram-negative.
Where the biological effectiveness of the prepared derivatives was evaluated by the nutrient diffusion method, and to study the effect of these prepared derivatives, ciprofloxacin was used, where different concentrations of the prepared derivatives were used (0.01, 0.001, 0.0001) and DMSO was used as a solvent and the diameter of the inhibition area (mm) was used as a standard The minimum concentration required to stop the growth of bacteria was considered a measure of the minimum inhibitory concentration.

Discussion

The results shown in the following table indicate some physical properties (melting point, color and product percentage) for some of the prepared compounds.

Table No.-: (1) The physical properties of the prepared compounds

Comp. No.	X	M.P. (˚C)	Yield (%)	Color	Molecular Formula
M_{11}	4-Br	188-190	70	Brown	$C_{17}H_{14}N_4Br_2$
M_{12}	4-Cl	181-182	95	White	$C_{17}H_{14}N_4BrCl$
M_{13}	4-CH3	133-136	77	White	$C_{18}H_{17}N_4Br$
M_{14}	4-OCH3	158-159	98	White	$C_{18}H_{17}N_4OBr$
M_{15}	4-Br	110-111	50	Orange	$C_{18}H_{17}N_4Br$
M_{16}	4-Cl	130-132	70	Yellow	$C_{18}H_{17}N_4Cl$
M_{17}	4-CH3	121-122	51	Yellow	$C_{19}H_{20}N_4$
M_{18}	4-OCH3	142-143	63	Brown	$C_{19}H_{20}N_4O$

The validity of the prepared structures was confirmed by spectroscopic methods, where the infrared spectrum (FT-IR) showed a band at frequency (3228-3500cm^{-1}) belonging to the stretching group (NH) and a band at frequency (3018-3267cm^{-1}) belonging to the stretching group (Ar) -H) and the band at frequency (2162-2221cm^{-1}) belonging to the stretching group (C = N) and the beam at the frequency (1581-1679cm^{-1}) belonging to the stretching group (C=N)

The compound (M16) was studied by magnetic resonance spectrometry (^{13}C-NMR) where it showed a signal at frequency (δ:40 ppm) that belongs to the carbon atoms of the used solvent (DMSO-d_6). The appearance and signal at the frequency (δ: 55 ppm) that belongs to the carbon atom of the Pyrimidine ring (C-C). and the appearance of a signal at the frequency (δ:71 ppm) that belongs to the amide carbon atom (C-N), and the appearance of a signal at frequency (δ: 114 ppm) that belongs to the carbon atom of the cyanide group ($C \equiv N$) and the

appearance of a signal at the frequency (δ: 126 ppm) that belongs to the carbon atom of the aromatic ring (C = C) and the appearance of a signal at the frequency (δ: 127 ppm) that belongs to the carbon atom of the aromatic ring (C = C). the appearance of a signal at the frequency (δ: 128 ppm)) that belongs to the aromatic ring carbon (C-C). and the appearance of a signal at the frequency (δ; 129 ppm) that belongs to the carbon atom of the aromatic ring (C-CH3). and the appearance of a signal at the frequency (δ: 131ppm) that belongs to the carbon atom of the aromatic ring (C-C). and the appearance of a signal at the frequency (δ: 138 ppm)) that belongs to the carbon atom of the aromatic ring (C-CH3). and the appearance of a signal at the frequency (δ: 162 ppm) that belongs to the carbon atom of the pyridine ring (C-C).

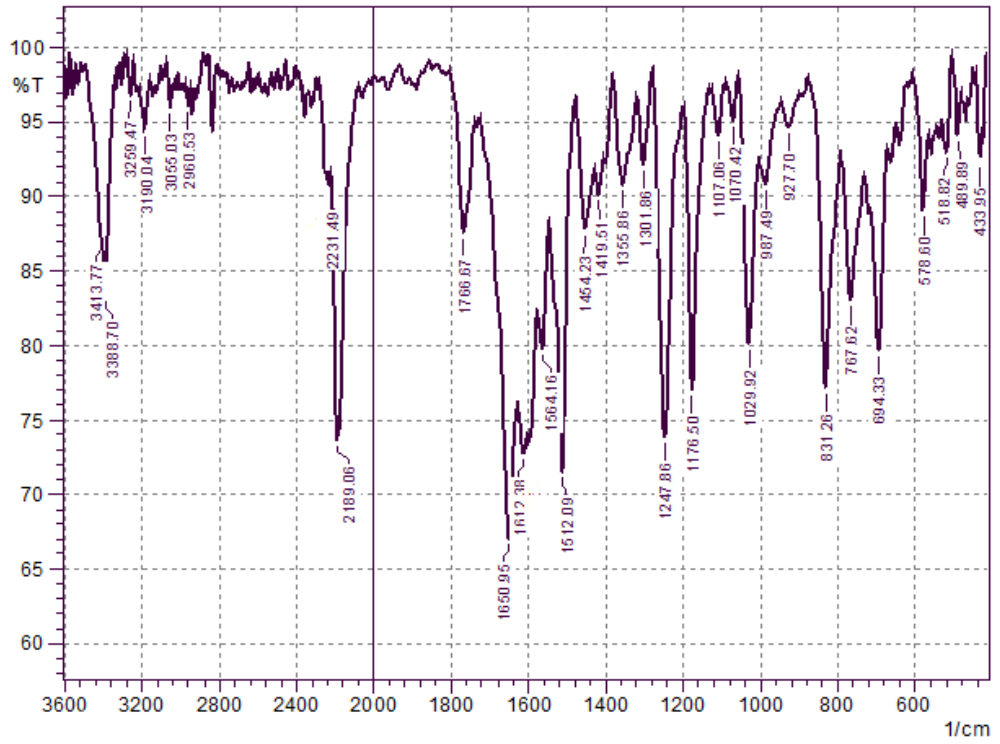


Figure No. (1) Infrared spectrum of the compound (M16)

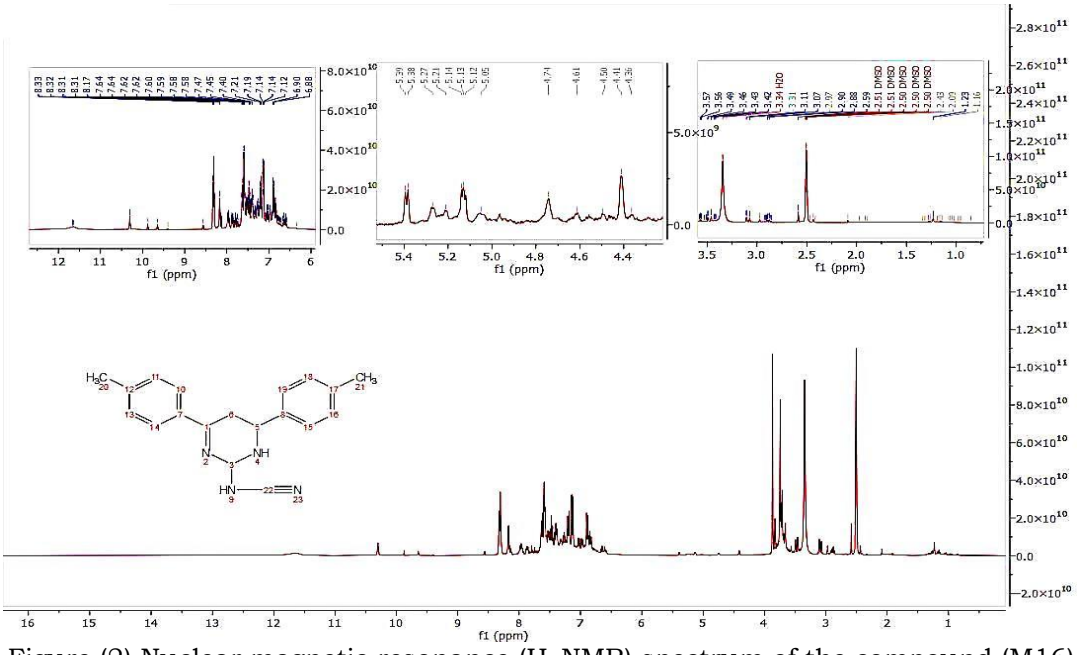


Figure (2) Nuclear magnetic resonance (H_NMR) spectrum of the compound (M16)

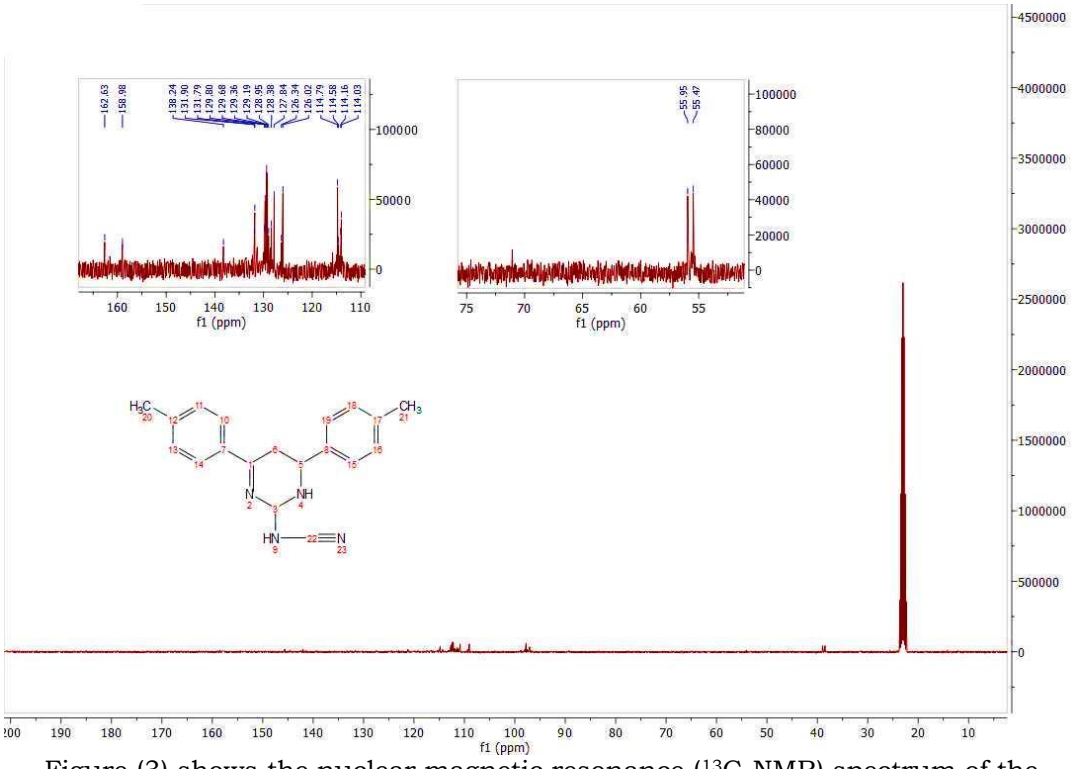
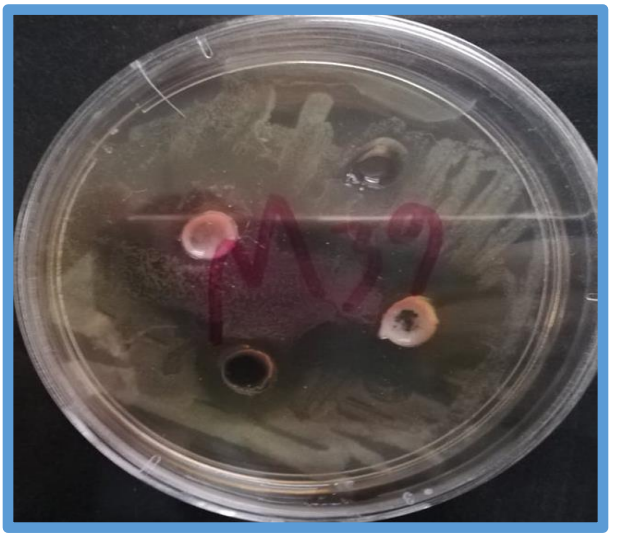


Figure (3) shows the nuclear magnetic resonance (^{13}C-NMR) spectrum of the compound M

Com No	Conc. mg/m	*S.A*	*E.F*	*P.P*	*K.P*	*D.A*
1	0.01	20	15	32	11	21
	0.001	24	25	24	10	20
	0.0001	21	20	21	24	25
2	0.01	23	14	23	23	12
	0.001	21	15	15	25	11
	0.0001	23	21	22	14	10
3	0.01	25	11	21	15	14
	0.001	21	13	23	10	16
	0.0001	23	10	20	15	23



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