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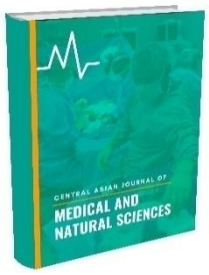

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Synthesis, Characterization and Biological Activity Evaluation of Some New Pyrimidine Derivatives by Solid Base Catalyst AL_2O_3-OBa

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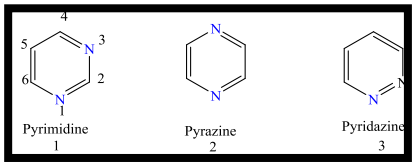
Abstract: This work involve the preparation and characterization of new derivatives of pyrimidine compounds from the reaction of chalcones with Urea via solid base catalyst (prepared through the reaction of Ba(NO3)2 with AL2O3 at (300-700) °C to obtain metal oxide as a solid base catalyst) and using physical methods. And spectroscopic (melting point, color, product ratio, IR, 1H-NMR, and 13C-NMR), the compositions were confirmed to be correct. The antibacterial activity has been tested in vitro by the disk diffusion assay method against two kinds of bacteria gram positive and gram negative. The minimum inhibitory concentration [MIC] have been determined with the reference of stander drugs, the results showed that the Pyrazoline derivatives are better than growth of both types of bacteria (gram- positive and germ–negative) compared to drug.

Key words: Chalcones, Solid base catalyst, AL2O3, Pyrimidine, Biological activity.

1. Introduction

pyrimidine They are heterocyclic compounds similar to pyridine [1], consisting of two nitrogen atoms and four carbon atoms in the ring, and are in the form of 1,3- hexacyclic heterocyclic diazines, as the location of the nitrogens [2] in the ring determines the type and name of the compound on as follows:



Recently researchers have been interested in pyrimidine compounds and their derivatives, due to their importance in the field of pharmacy [3], medicine, and industrial applications. and many previous studies have shown that it has great importance in the medical field, cytotoxic activity [4], activity Analgesics, antimicrobial activity [5,6], anti-inflammatory [7,8], antioxidant activity [9,10], antibacterial activity [11], and anticancer agents [12]. Solid base catalyst the most basic heterogeneous

catalysts It is one of the most common and used acid catalysts because it is not soluble and easy to separate and can be used more than once [13]. The effectiveness of these catalysts is evaluated on the basis of the physical properties of the surface such as the surface area, the size of the holes, and the concentration of the active groups [14]. Among the most prominent heterogeneous basic catalysts are alkaline elements, transition elements, and metal oxides [15], as well as the composition of the metallic carbon that carries effective basic groups, which are oxides of the first and second group elements [16]. They are of a basic nature and have limited solubility in polar solutions [17]. Examples of them are sodium oxide, magnesium oxide and calcium oxide, as these oxides contain oxygen ions with a negative charge [18].

2. Experimental

2.1. Material: All chemicals were used through this work purchased from Fluka, BDH Companies.

2.2. Devices used: Melting points are uncorrected and were recorded in an open capillary tube on Stuart melting point apparatus. Infrared spectra have been recorded on a Shimadzo FTIR-8100 spectrophotometer using KBr discs–and ^{1}H NMR Spectra have been measured on a MH_Z spectrometer using DMSO-d_6) as solvent. reaction monitoring and verification of the purity of the compounds was done by TLC on silica gel-percolated alumni sheets (type 60 F254 Merck, Darmstadt, Germany).

2.3. Preparation of the solid basic catalyst AL_2O_3-OBa [19]

Mixture of $Ba(NO_3)_2$ (1 mol) and Al_2O_3 (3 mol) were crushed in mortar, and then appropriate deionized water was added which can be absorbed by Al_2O_3. After grinding, the mixture was dried at 110 ℃ for one hour, and then activated at 600 ℃ for three hours.

2.4. Preparation of pyrimidine derivatives (JA6-JA10)

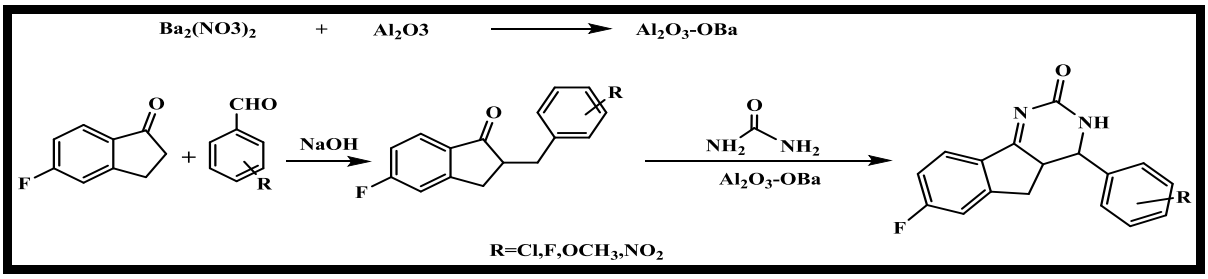
Mixture of equal moles of Chalcone and urea, dissolved in (ml10) of ethanol with stirring for 10 minutes, then the catalyst was added (25% of the weight of Chalcone), then the mixture is left in the water bath for 4hr with stirring at a temperature of 40 °C, then the solution is filtered and the filtrate is taken and left to dry. Table (1) shows some physical properties of compounds (JA6-JA10).

2.5. Evaluation of biological activity

The biological activity has been estimated by using the propagation method whereas the biological activity has been estimated by the Kirby Bauer movement [20, 21], where 0.1 ml of bacterial suspension has spread to the ager Muller Hinton dishes and left for 5 minutes to absorb the suspension [22, 23]. After that, holes were prepared for each dish using a Cork Porer and a diameter of (5) mm per hole (0.1 ml) of the prepared solutions of the fourth hole using (Amoxicillin) as a control sample and incubated the dishes for (24) hours at 37 ℃. The inhibition zone diameters around each hole has been measured in milmeter, depending on the method of Prescott [24].

3. Results and Discussion

In this paper, five pyrimidine derivatives (JA6-JA10) were prepared by reacting urea with chalcone derivatives prepared from the reaction of 5-fluoroindanone with benzaldehyde derivatives in ethanol, as in scheme (1) and characterized by FT-IR, ^{1}H-NMR, ^{13}C-NMR spectra.



Scheme (1): Route of prepared compounds (JA1-JA10)

3.1. Characterization of the solid basic catalyst Al_2O_3-OBa

And the SEM analysis of the prepared catalyst shown in Figure (1) showed that (2um) was used for the cross-sectional area and the magnification power (MAG: 20.00KX). 2.529 (nm) is among the nanocrystals[25]We observed that BaO base was finely and uniformly distributed on the Al_2O_3 support which makes catalyst more active.

3.2. Characterization of pyrimidine derivatives (JA6-JA10)

It was confirmed that the reaction of the pyrimidine derivatives (JA6-JA10) occurred by observing the changes in the physical characteristics of the melting point and the significant color change. Also, the pyrimidine derivatives (JA6-JA10) were diagnosed through infrared spectra (IR) measurements.

When studying the infrared (IR) spectrum of pyrimidine derivatives (JA6-JA10), it was observed that absorption bands appeared at the frequency (3160-3200) cm^{-1} due to the bonding of the (NH) bond, and the appearance of an absorption band at the frequency (3024-3091) cm^{-1}, it is due to the stretching of the aromatic (CH) bond, as well as the appearance of two absorption bands at the frequency (2916-2985) cm^{-1} and (2824-2898) cm^{-1} due to the stretching of the aliphatic (C-H) bond, and an absorption band appeared at the frequency (1616-1652) cm^{-1}, it is due to the stretching of the azomethine group (C=N). It was also observed that two absorption bands appear at a frequency (1585-1593) cm^{-1} and (1474-1497) cm^{-1}, which belong to the stretching of the (C=C) aromatic bond [26], as shown in Table (2) and figures (2,3).

When studying the nuclear magnetic resonance (1H-NMR) spectrum for (JA8) compounds, it was observed that a signal appeared at the site (9.02) ppm attributed to the proton of the (NH) group, as well as the appearance of a multiple signal at the site (6.72-7.62) ppm attributed to the protons of the aromatic ring. And the appearance of a signal at the (2.96) ppm position attributed to the (CH2) group proton, and the appearance of a binary signal at the (3.44) ppm position attributed to the (CH) group proton adjacent to the azomethine group, and the appearance of a signal at the (4.46) ppm position attributed to the (CH group proton)) adjacent to the benzene ring, and the appearance of a signal at the site δ=(2.52) ppm attributed to the protons of the solvent (DMSO -d^6) [27], as shown in Figures (4).

When studying the nuclear magnetic resonance spectrum (13C-NMR) of the compound (JA8), it was observed that a signal appeared at the site (161.2) ppm attributed to the carbon of the group (C = N), as well as the appearance of a signal at the site (158.84) ppm attributed to the carbon of the group (C = O), as well as the appearance of a multiple signal at the position (115.08-155.24)ppm attributed to the carbons of the aromatic ring, the emergence of a signal at the position (29.18)ppm attributed to the carbon of the (CH2) group, and the emergence of a binary signal at the position (32.20)ppm due to the carbon of the aromatic ring (CH) adjacent to the azomethin group, and the appearance of a signal in the position (55.86) ppm attributed to the carbon of the (CH) group adjacent to the benzene ring, and the emergence of signals at the range (39.99) ppm attributed to the carbons of the solvent (DMSO-d6),. [28], as shown in Figures (5).

3.3. Evaluation of Biological activity:

Some of the synthesized compounds (JA6, JA7, JA9) were tested against various strains of bacteria: gram-positive bacteria Staphylococcus aureus, and gram-negative bacteria Escherichia coli by cup plate agar diffusion method [29]. The microbial cultures were incubated at (37 ℃ for 8 hours) and diluted with 0.8% sterile saline [30]. The solution concentration for used drugs in DMSO was kept at 100µg/mL. Amoxicillin as a negative control was used. The biological activity was measured by measuring the inhibition diameter of the growth of bacteria around the disk in use [31]. as shown in Table (3).

Table (1) Physical properties of the prepared compounds (JA6-JA10)

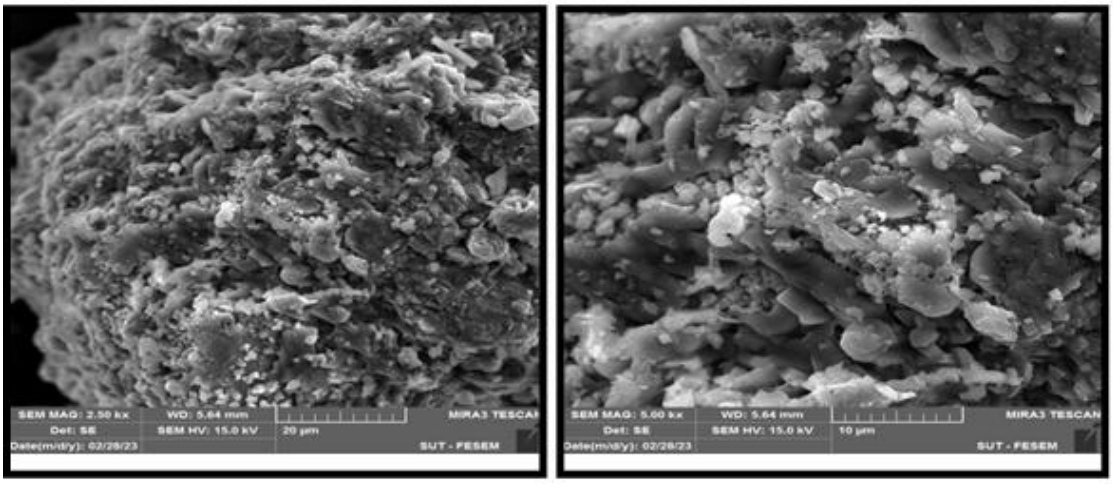
Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
JA6	2,3-Cl	$C_{17}H_{11}FCl_2N_2O$	180-182	46	Light yellow
JA7	4-Cl	$C_{17}H_{12}FClN_2O$	120-122	34	Blue
JA8	4-F	$C_{17}H_{12}F_2N_2O$	110-112	32	Dark yellow
JA9	4-OCH_3	$C_{18}H_{15}FN_2O_2$	140-142	35	Dark
JA10	4-NO_2	$C_{17}H_{12}FClN_3O_3$	144-146	41	Light brown

Table (2): FT-IR data of prepared compounds (JA6-JA10) cm^{-1}

Comp. No.	R	νNH	νC-H Arom.	νC-H Aliph.	νC=O	νC=N	ν C=C Arom.	Others
JA6	2,4 Cl	3189	2056	2923, 2846	1674	1643	1596, 1489	ν(C-Cl) 744
JA7	4-Cl	3196	3073	2980, 2856	1679	1646	1593, 1487	ν(C-Cl) 817
JA8	4-F	3195	3060	2941, 2878	1687	1644	1580, 1497	ν(C-F)1033
JA9	4-OCH_3	3184	3064	2927, 2868	1667	1647	1589, 1493	ν(C-O-C) 1363
JA10	4-NO_2	3186	3057	2943, 2876	1681	1652	1597, 1486	ν(NO_2)1342,1251

Table (3): Inhibitory effectiveness of some prepared compounds (JA6, JA7, JA10) and control treatments (antibiotics) on the growth of a number of positive and negative bacteria

Comp. No.	Escherichia coli			Staphylococcus aureus		
	0.0001	0.001	0.01	0.0001	0.001	0.1
JA6	15	15	20	0	12	12
JA7	14	17	20	0	12	12
JA10	10	15	17	12	0	0
Amoxicillin	10	16	24	10	20	20



(b) Scanning electron micrograph at 2*0* μ m (c) Scanning electron micrograph at 10 μ m

Fig. (1): Scanning electron micrograph of Al2O3–OBa

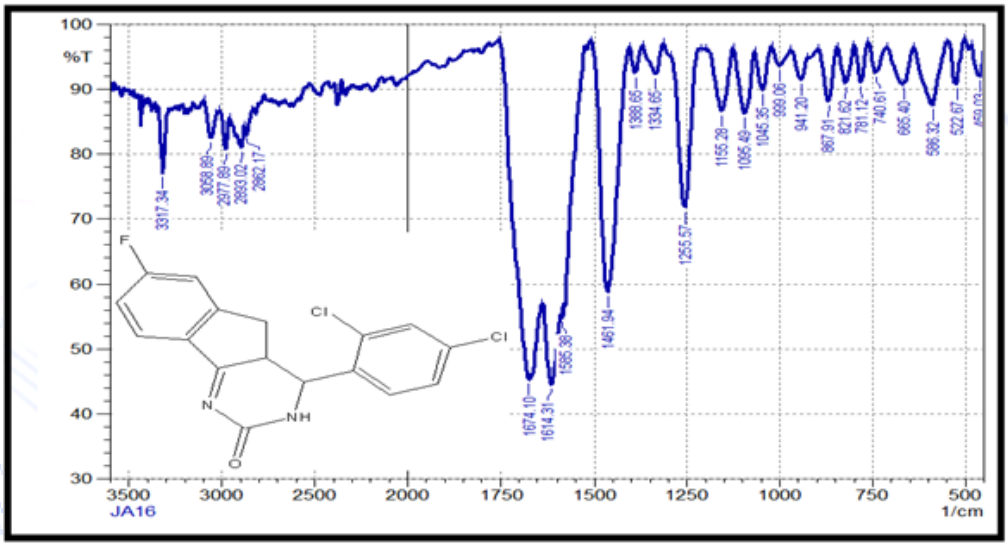


Figure (2): The infrared spectrum of the compound (JA7)

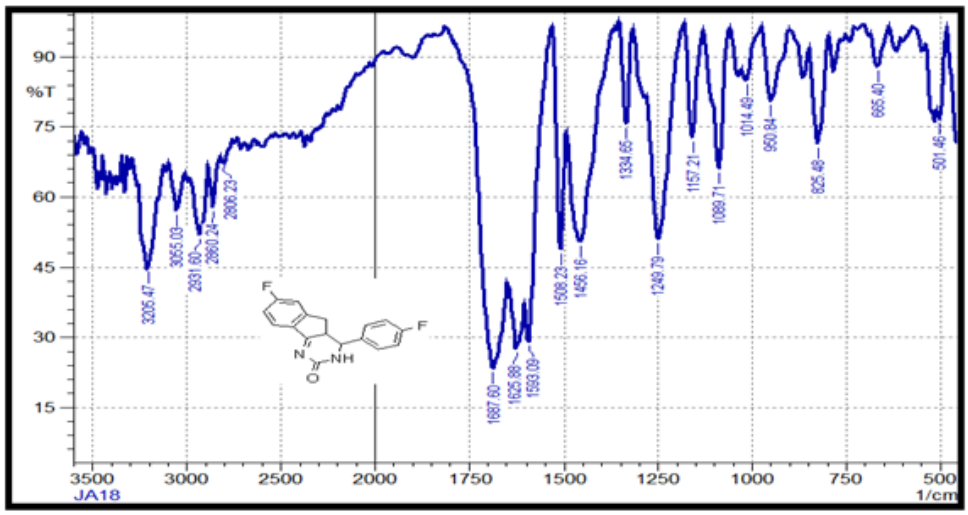


Figure (3): The infrared spectrum of the compound (JA8)

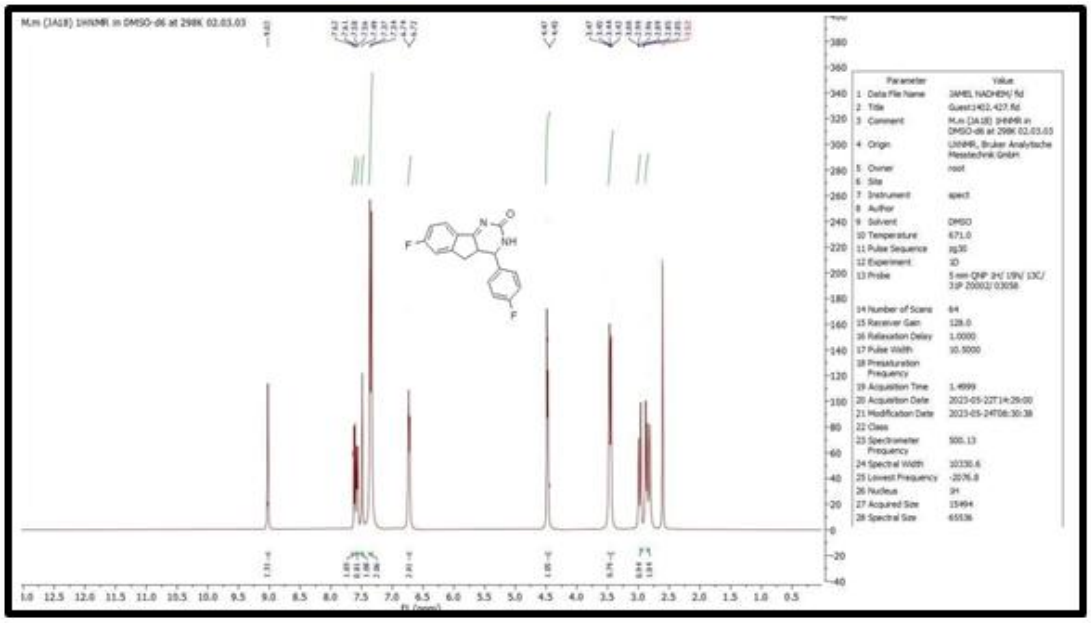


Figure (4): The ^{1}H-NMR spectrum of the compound (JA8)

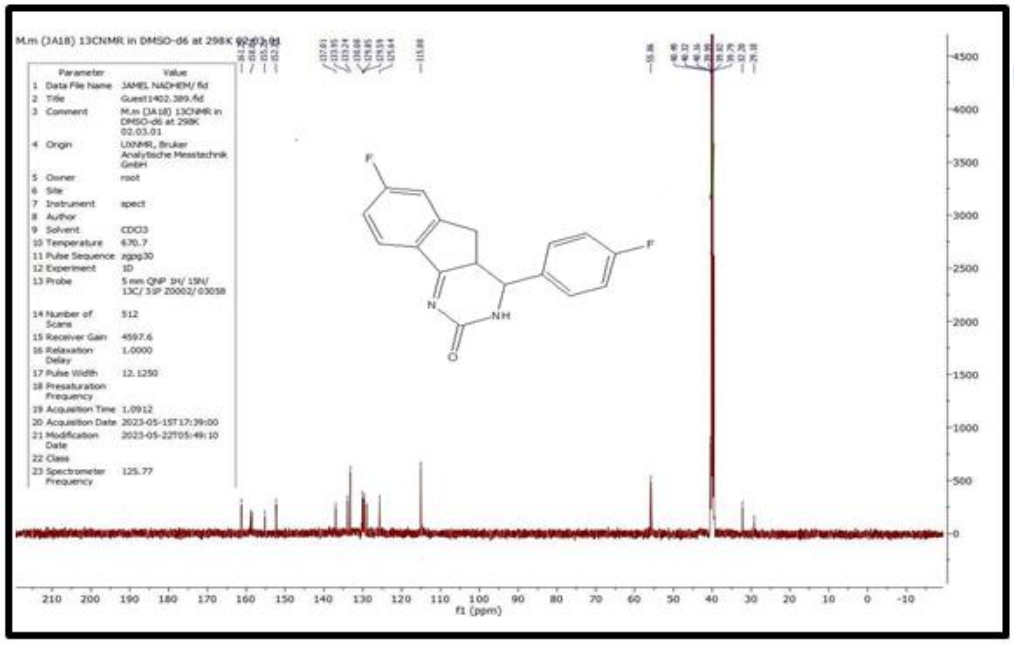


Figure (5): The ^{13}C-NMR spectrum of the compound (JA8)

4. Conclusions: The accuracy and validity of the prepared compounds were confirmed through spectral and physical measurements, where the infrared spectrum proved the presence of active aggregates accurately, and this confirmation increased the nuclear magnetic resonance spectrum of the proton and carbon spectrum, which accurately agreed on the validity of the structures of the prepared compounds. These compounds are stable at laboratory temperature and do not degrade or change color. The prepared compounds showed high and good inhibitory activity against Gram-positive and Gram-negative bacteria, and the results were compared with control samples, which are antibiotics.

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