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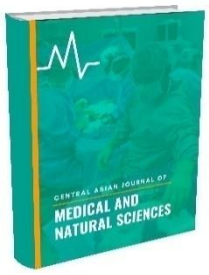

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Preparation, Characterization of New 2-Oxo Pyran Derivatives by AL_2O_3-OK Solid Base Catalyst and Biological Activity Evaluation

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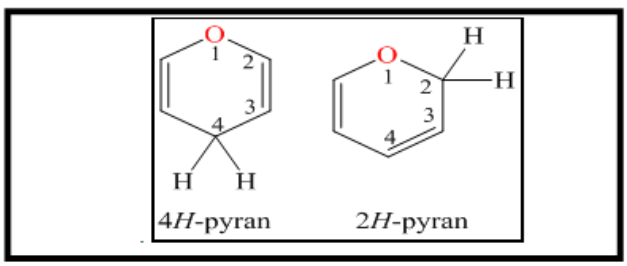
Abstract: This work included the synthesis of new derivatives of 2-Oxo pyran compounds from the reaction of chalcone with ethyl cyano acetate via a solid basic catalyst (prepared by the reaction of KNO3 with Al2O3 at (300-700) °C to obtain potassium oxide as a solid base catalyst)

Where the chalcone was prepared from the reaction of 5-bromoindanone with aromatic benzaldehyde substitutes, using physical methods and spectral analysis such as melting point, color, nuclear magnetic resonance spectroscopy 1H-NMR, 13C-NMR and FT-IR to ensure the accuracy and validity of the prepared compounds. The activity of the basophil was confirmed using scanning electron microscopy (SEM) and the biological activity was evaluated on two types of bacteria, Escherichia coli and Staphylococcus aureus.

Key words: Solid base catalyst, Pyran, Biological activity.

1. Introduction

Pyran is a heterocyclic, unsaturated (non-aromatic) hexagonal compound consisting of six main atoms, five of which are carbon atoms and an oxygen atom [1], and it contains two double bonds, with the chemical formula C_5H_6O, and its regular name (IUPAC) 2H-Pyran, 4H-Pyran Other names are 2H-Oxine, 4H-Oxine [2],. There are two pyran isomers that differ in the location of the double bonds. In 2H-pyran, the saturated carbon is in position 2, while in 4H-pyran, the saturated carbon is in position 4[3],



It plays a major role in organic biochemistry and has a wide range of interesting biological activities [4], 4H-cyanopyrans and its derivatives constitute an important class because they are present in a wide range of biologically active compounds as antioxidants[5], anticancer [6], anti-inflammatories [7], anxiolytic [8]], antiviral [9], antifungal [10], antibacterial [11]. Sold base catalyst Catalysis plays a major role in chemical, physical and biological sciences. It has become one of the most important areas in chemistry [12]. It is now accepted that 85 to 90% of industrial processes involve at least one catalytic step [13]. Recently, catalysis has been recognized as very important in environmental chemistry for a more sustainable society [14], especially heterogeneous vs. [15]. Solid base catalysts play an important role in various chemical reactions, including the Michael addition reaction [16]. Solid base catalysts typically consist of porous materials, such as zeolites, metal oxides, or supported organic bases. These materials have an inherent basis due to the presence of basic sites on their surface, such as hydroxyl groups, Lewis basic sites, or basic functional groups. The catalyst base plays a crucial role in the reaction kinetics and selectivity [17]. One of the widely used solid base catalysts for the Michael addition reaction is metal oxides, especially those of the alkali and alkaline earth metals. Metal oxides, such as magnesium oxide (MgO) or potassium carbonate (K2CO3) cemented on a solid, show high alkalinity and catalytic activity [18]. The base sites on the metal oxide surface strip protons from the Michael donor, activating them for the nucleophile to attack the Michael acceptor.

2. Experimental

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

2.2. Devices used: Melting points were recorded using a measuring device melting point type: Automatic melting point\SMP40 and were uncorrected. Thin layer chromatography (TLC) was carried out using sheet polygram silica- gel as stationary phase, the spots were enhanced using Iodine. Infrared spectra were recorded using FT-IR-600 Fourier- Transform infrared Spectrophotometer by KBr disc and with a scale of (400-4000) cm^{-1}. The nuclear magnetic resonance (^{1}H,^{13}C-NMR) spectra were measured for the compounds prepared in the laboratories of Sannati Sharif University - Iran, using MS5973 Agilent Technology, Germany Bruker 500 MHz, at 500 MHz, and using (DMSO-d^{6}) as a solvent.

2.3. Preparation of the solid basic catalyst Al_2O_3-OK[19]

The mixture of (1 mol) KNO3 with (3 mol) Al_2O_3 was then crushed in a mortar, and then appropriate deionized water was added, which can be absorbed by Al_2O_3. After grinding, the mixture was dried at 110 C for one hour and then activated at 600 C for three hours.

2.4. Preparation of 2-Oxo pyran (MH6-MH10) [20]

Mixture (0.0015 mol) of chalcone dissolved in (10 mL) of ethanol and (0.00225 mol) of Athyl cyano acetate dissolved in (10 mL) of with stirred for (30 min), then add (0.225 gm) of solid base catalyst (Al_2O_3-OK) to it is left with stirring in a water bath for three hours, then filtered and left for 24 hours until a precipitate is formed and recrystallized from ethanol. Table (1) shows some physical properties of the compounds (MH6-MH10).

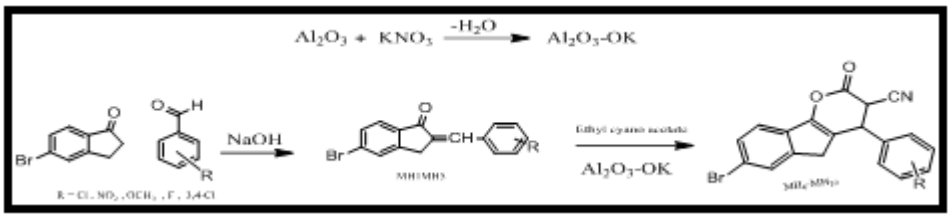
2.5. Antibacterial activity for prepared compounds (MH6, MH7, MH9, MH10)

The biological activity has been estimated using the propagation method. In contrast, the biological activity has been evaluated by the Kirby Bauer movement [21], where 0.1 ml of bacterial suspension has spread to the ager Muller Hinton dishes and left for 5 minutes to absorb the rest [22, 23]. After that, holes were prepared for each dish using a Cork Purer and a diameter of (5) mm per hole (0. 1) ml of the designed solutions of the fourth hole using (DMSO) as a control sample and incubated the

dishes for (24) hours at 37 ℃ [24, 25]. The inhibition zone diameters around each hole have been measured in millimeters, depending on the method of Prescott [26].

3. Results and Discussion

In this research, five compounds including 2-oxopyran derivatives (MH6 –MH10) were prepared by reacting chaconne derivatives with ethyl cyano acetate. Chaconne derivatives were prepared by reacting benzaldehyde substituents with 5-Bromo-Indanone in ethanol, as in Scheme (1) and featuresFT-IR, 1H-NMRand13C-NMR spectra.



Scheme (1): Route of prepared compounds (MH_6-MH_{10})

3.1. Characterization of the solid basic catalyst Al_2O_3-OK

In order to know about the homogeneity of Al2O3–OK, SEM analysis was carried out. We observed that K2O base was finely and uniformly distributed on the Al2O3 support which makes catalyst more active[27]. (Fig. 1)

3.2. Characterization of 2-Oxo pyran (MH6-MH10)

It was confirmed that the reaction occurred with the 2-oxopyran derivatives [MH6-MH10] by observing the changes that occurred in the physical characteristics of the melting point and the large change in color, when studying the infrared spectrum (FT-IR) of the 2-oxopyran derivatives [MH31 - MH35] It was observed that an absorption band appeared at the range (3059-3080) cm-1 due to the stretching of the aromatic (CH) bond, as well as the appearance of an absorption band at the range (2198-2275) cm-1 belonging to the stretching of the nitrile (CN) group, and an absorption band appeared At the range (1725-1735) cm-1, it refers to the stretching of the bond of the carbonyl group (C=O). In addition, two absorption bands appear at the range (1515-1549) cm-1 and (1450-1479) cm-1, which refer to the stretching bond (C=C) aromatics, and an absorption band appeared at the range (1331-1392) cm-1 due to the stretching of the (C-O) group, and these bands were close to what is found in the literature [28]. As shown in Figure (2,3) and Table (2).

When studying the 1H-NMR spectrum of the compound [MH7], it was observed that a multiple signal appeared in the range (7.08-8.15) ppm due to the protons of the aromatic ring, and the appearance of a binary signal in the site (3.94-4.01) ppm due to the proton of the group. (=C- CH) associated with the carbons of the double bond, and the appearance of a binary signal at the (3.51-3.56) ppm site due to the proton of the (CH-CN) group, as well as the emergence of a signal at the (3.15) ppm sites attributed to the (CH2) group proton associated with the aromatic ring. [29]. As shown in Figure (4).

When studying the 13C-NMR spectrum of the compound [MH7], it was observed that a signal appeared at the site (164.78) ppm attributed to the carbonyl group carbon (C=O), and a signal appeared at the site (116.30) ppm attributed to the carbon of the (CN) group. A signal at the site (45.59) ppm is attributed to the carbons of the (CH) group in the pyran ring adjacent to the (CN) group, as well as the emergence of signals at the site (156.06-122.9) ppm belonging to the carbons of the aromatic ring, and the appearance of a signal at the site (135.95) ppm is attributed to the carbons of the (=C-O) group of the double bond in the pyran ring, and the appearance of signals in the range

(40.31-39.64) ppm is attributed to the carbons of the solvent (DMSO-d6), [30]. As shown in Figure (5).

3.3. Evaluation of Biological activity:

Some of the synthesized compounds (MH6, MH7, MH9, MH10,) were tested against various strains of bacteria: gram positive bacteria, staphylococcus, aureus, and gram-negative bacteria, Escherichia, coli by cup plate agar diffusion method [31]. The microbial cultures were incubated at (37o C for 8 hur.) and diluted with 0.8% sterile saline. The concentration of solution for used drugs in DMSO, were kept at 100µg/mL. Amoxiline as control were used. The biological activity was measured by measuring the inhibition diameter of growth of bacteria around the disk in use [32].

Table (1): Physical properties and elemental analysis of prepared compounds (MH6-MH10)

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
MH_6	4-Cl	$C_{19}H_{11}BrClNO_2$	163-165	33	Off white
MH_7	4-NO_2	$C_{19}H_{11}BrN_2O_4$	177-180	38	Black
MH_8	4-OCH_3	$C_{20}H_{14}BrNO_3$	175-178	42	Orange
MH_9	4-F	$C_{19}H_{11}BrFNO_2$	186-190	45	Off white
MH_{10}	3,4-Cl	$C_{19}H_{10}BrCl_2NO_2$	158-160	35	Light yellow

Table (2): FT-IR data of prepared compounds (MH6-MH10)

Comp. No.	R	IR (KBr) cm^{-1}					
		ν(C-H) Arom.	ν(C-O).	ν C=O	ν (CN)	ν(C=C) Arom.	Others
MH_6	Cl	3076	1331	1735	2264	1462,1549	ν(C-Br) 620,ν(C-Cl)722
MH_7	NO_2	3068	1392	1728	2217	1460,1515	ν(C-Br) 678,ν(N-O)1340
MH_8	OCH_3	3059	1372	1730	2275	1450,1534	ν(C-Br) 628,ν(C-O)1377
MH_9	F	3072	1380	1726	2198	1479,1525	ν(C-Br)617,ν(C-F) 993
MH_{10}	3,4Cl	3080	1368	1725	2254	1467,1531	ν(C-Br) 619,ν(C-Cl)894

Table (3): Antibacterial activity of the prepared compounds (MH6-MH10) and control antibiotic

Comp. No.	*E. Coil* Conc. mg/ml			*Staph. Aureus* Conc. mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
MH_6	19	13	8	15	10	10
MH_7	10	10	5	15	10	NIZ
MH_9	15	15	10	20	15	9
MH_{10}	18	13	5	20	16	5
Amoxicillin	18	12	10	20	20	10

Slight activity 5-10 mm, moderate activity 12-15 mm and high activity 18-20 mm; MIC: minimum inhibition concentration (μ g / mL).

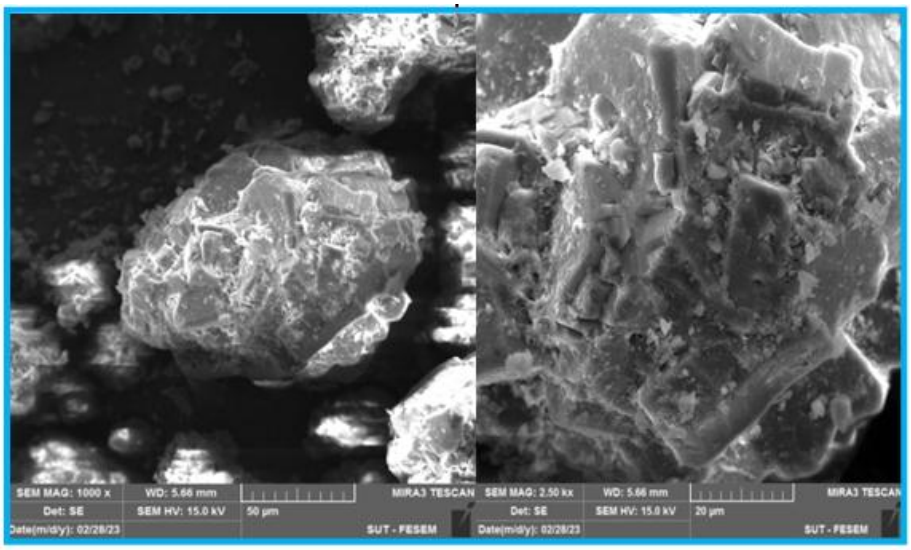


Fig. (1): Scanning electron micrograph of Al_2O_3–OK

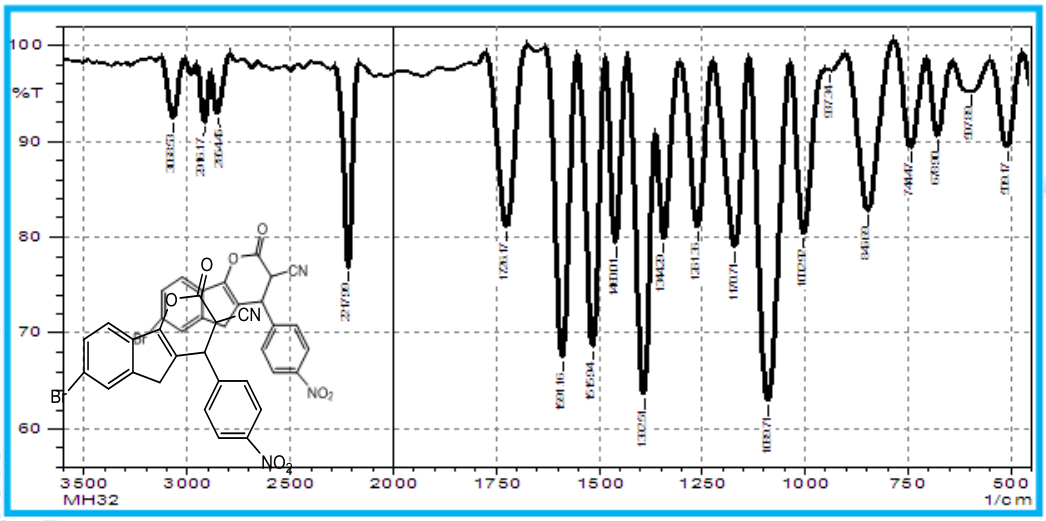


Figure (2): FT-IR spectrum of compound (MH7)

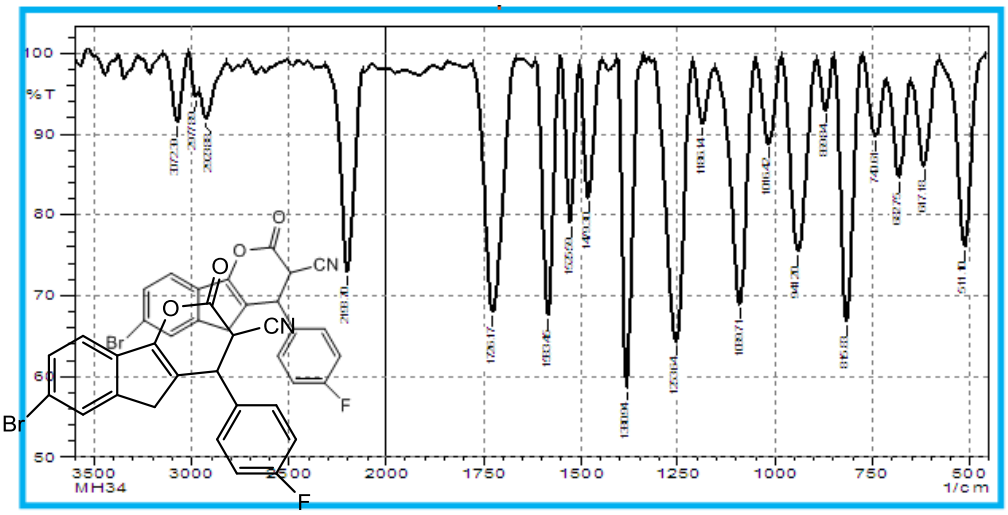


Figure (3): FT-IR spectrum of compound (MH9)

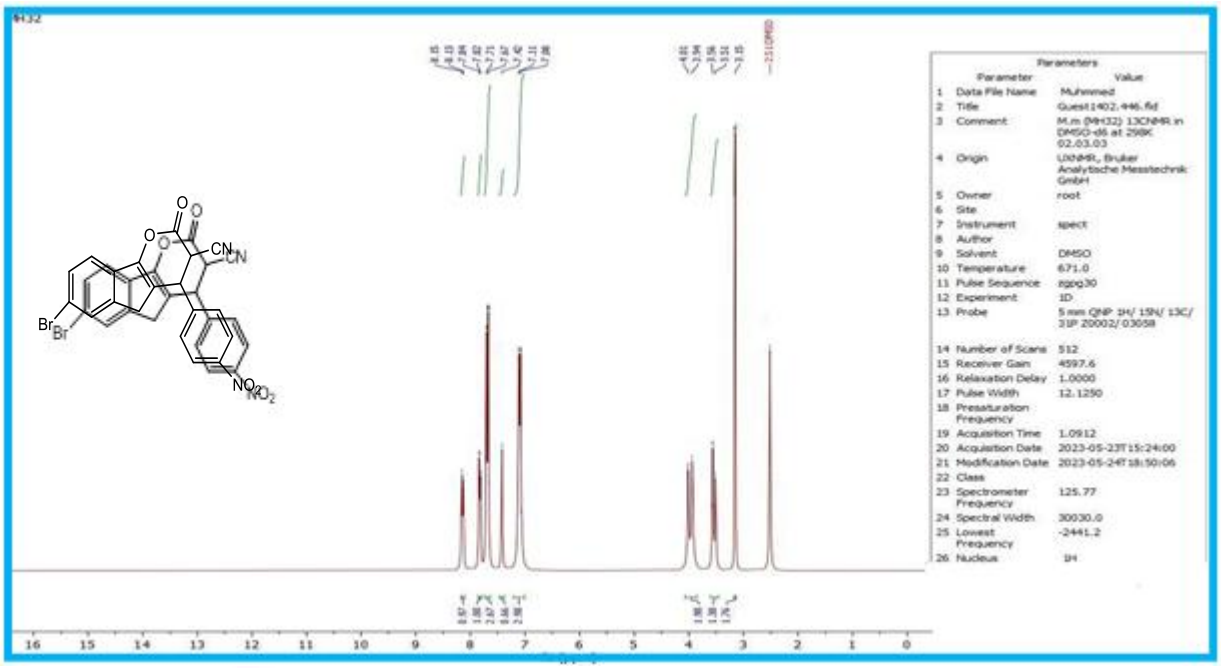


Figure (4): ^{1}H-NMR spectrum of compound (MH7)

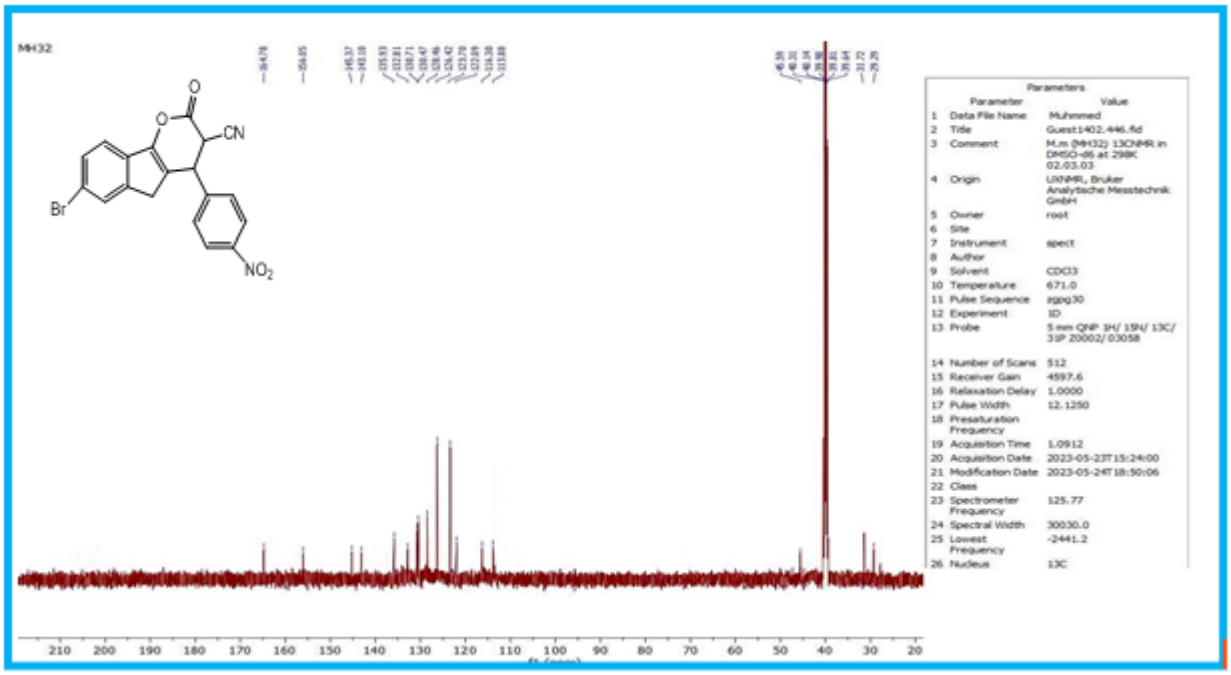


Figure (5): ^{13}C-NMR spectrum of compound (MH7)

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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