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Preparation, Characterization, Biological Activity Evaluation, and Liquid Crystallography Study of New Diazepine Derivatives

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Abstract

This research included the use of solid basic catalysts as a catalyst, where the crystalline surface was confirmed using scanning electron microscopy, where it was introduced into the reaction of prepared chalcones, which are intermediate compounds in the preparation of heterogeneous rings, with 2-aminoaniline to prepare heterogeneous heptad rings derived from diazepine, where the correctness of the prepared structures was confirmed using infrared spectra and proton and carbon nuclear magnetic resonance spectra. Its biological activity was also tested against two types of Gram-positive bacteria, Staphylococcus epidermidis and Gram-negative Klebsiella pneumoniae. The crystalline phases of some of the prepared compounds were studied, where some of them gave crystalline phases.

Keywords: Diazepine, Catalyst, biological activity, Liquid crystals.

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1. Introduction

Diazepine is a seven-ring compound formed by the condensation of unsaturated alpha-beta carbonyl compounds with 2-amino-aniline. This ring contains two nitrogen atoms at the 1,4 position, five carbon atoms, and a double bond linking carbon to nitrogen called azomethine [1]. It has recently gained wide medical importance as it is used as an anti-inflammatory [2], anti-fungal [3], and anti-bacterial agent [4]. It has also shown good effectiveness against cancer [5]. **Catalyst** The term catalyst was first defined by

Berzelius in 1836 as a chemical substance added in small quantities to a reacting medium to increase the rate of a chemical reaction by reducing the energy required to reach the activated complex stage in which the reactants interact through their molecular orbitals and then decompose to produce products. A catalyst does not cause thermodynamically impossible reactions but rather accelerates possible reactions. It has been found that adding small amounts of metallic materials such as transition elements to the center of some reactions increases the reaction rates compared to the absence of these materials [6]. Very small amounts of catalysts can catalyze reactions that contain chemicals thousands or even millions of times their mass [7]. **Liquid crystals** are an intermediate state between the regular irregular liquid state and the regular crystalline solid state [8]. Research on liquid crystals began in 1888 AD when the scientist Rentizera noticed that a substance called cholesterol benzoate had two melting points, that is: it melts into a cloudy liquid at a temperature of 146 degrees Celsius, but it completely melts into a liquid at a temperature of 179 ˚C, which is called the properties, or the liquid becomes solid after cooling, which indicates that the process is reversible [9].

2. Materials and Methods

2.1. Chemicals used: Chemicals prepared by Aldrich, BDH Thomas, Fluka, and Merck were used

2.2. Instruments used: The melting point was ascertained using a Shimadzu 8400S FT-IR spectrometer, a 400-4000 cm-1 sulfur bromide disk, a 9300 thermometer, and 400 MHz Bruker 1H- and 13C-NMR spectra. The catalyst surface was verified by SEM examination. Fluka silica gel plates with a thickness of 0.2 mm were used for thin-layer chromatography (TLC).

2.3. Preparation of sold base Catalyst.[10]

Take (1 mole) of nickel nitrate and (3 moles) of aluminum oxide and grind them in a mortar. During the grinding process, add a few drops of deionized water until a paste is formed and dry at a temperature of (110)°C for a full hour put it in a ceramic bowl and activate (3 hours) at a temperature of (600)°C and leave the resulting catalyst to cool in the air. The product percentage of the catalyst was 80%.

2.4. Preparation of diazepine derivatives (F11-F15):[11]

The chalcone (0.015 mol) was dissolved in dilute ethanol (10 ml), 0.225 mol (0.22 g) 2-aminoaniline dissolved in ethanol (10 ml) was added, stirred for (15) minutes, the catalyst (Al2O3-ONi 20.% by weight of chalcone) was added and stirred in a water bath at (40) °C for 4-5 hours. The solution was then filtered, the precipitate was discarded, and the filtrate was taken out, dried, and recrystallized in absolute ethanol. A TLC plate was used to confirm the completion of the reaction. As shown in Table

Table 1: Some physical properties of for Prepared compounds (F11-F15)

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
F11	4-NO2	$C_{19}H_{14}N_5O_2$	278-*218	70	Light Brown
F12	4-Cl	$C_{19}H_{14}ClN_4$	221-290*	68	Dark Yellow
F13	4-F	$C_{19}H_{14}FN_4$	208-210	73	light yellow
F14	4-Br	$C_{19}H_{14}BrN_4$	217-219	65	whit
F15	4-H	$C_{19}H_{15}N_4$	305-*225	76	Blue

*

.Compounds marked with * have liquid crystalline phases

2.5. Study of Biological activity

A liter of distilled water was used to dissolve the Mueller-Hinton agar, which was then heated, agitated, and sterilized using an autoclave set at 121 °C and 1.5 bar of pressure. After cooling to 50 °C for two hours, it was transferred to a Petri plate and allowed to freeze at room temperature [12,13]. Using the agar

diffusion technique, the synthesized compounds' efficacy against two strains of negative bacteria, Klebsiella pneumoniae, and positive Staphylococcus epidermidis was evaluated. Using the cylinder measurement method (per USP 35), holes were created in the Petri plates following the inoculation of the culture medium with the bacterial isolates [14,15].

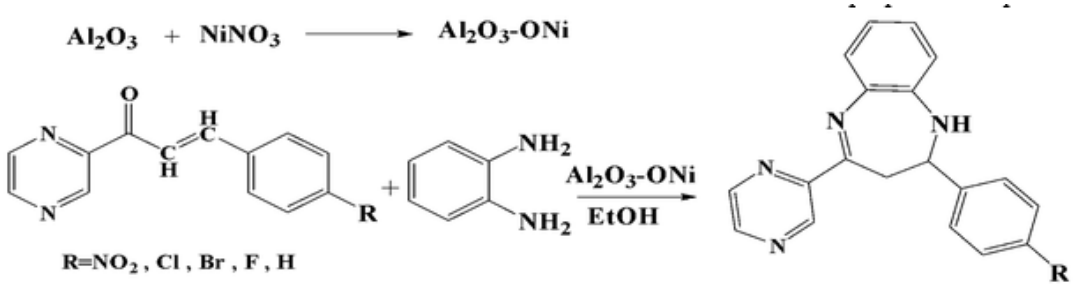
With a drill: Before obtaining the findings, place the compounds (40 µl) created at three concentrations in each well and incubate the dish at (37 °C) for 24 hours. The sensitivity of the derivatives employed is determined by taking readings after twenty-four and forty-eight hours. This is based on the inhibitory diameter that appears in the Petri dish around the wells that were utilized; an increase in the inhibitory diameter corresponds to an increase in the inhibitory diameter. Some of the common antibiotics were employed in solution form, and the inhibitory diameter of those antibiotics was compared with the bioavailability of the produced compounds [16, 17].

2.6. Study of liquid crystalline phases using a polarized light microscope:[18]

A polarizing microscope equipped with a POM electric heater was used to examine the liquid crystal phase of some of the prepared compounds (F11-F15) and equipped with a high-resolution camera with a heat-resistant lens to obtain high-resolution images. The liquid crystal phases are examined using a liquid crystal phase measuring device, where the compounds are heated to their melting point and then cooled during the process to obtain liquid crystals with clearer geometric shapes.

3. Results and discussions

Scheme 1 shows the series of prepared compounds.



Scheme (1): Path of the Ready Compounds (F11-F15)

3.1. Characterization of Catalyst.

It was found that the Ni2O base is small, uniform, and dispersed throughout the Al2O3 support, increasing the catalyst's activity. A catalyst (10 µm) was utilized, according to an SEM study of the catalyst displayed in Fig. (1). One of the catalyst particles, with a cross-sectional area and peak radius of 12.70 nm, is a nanocrystal [19].

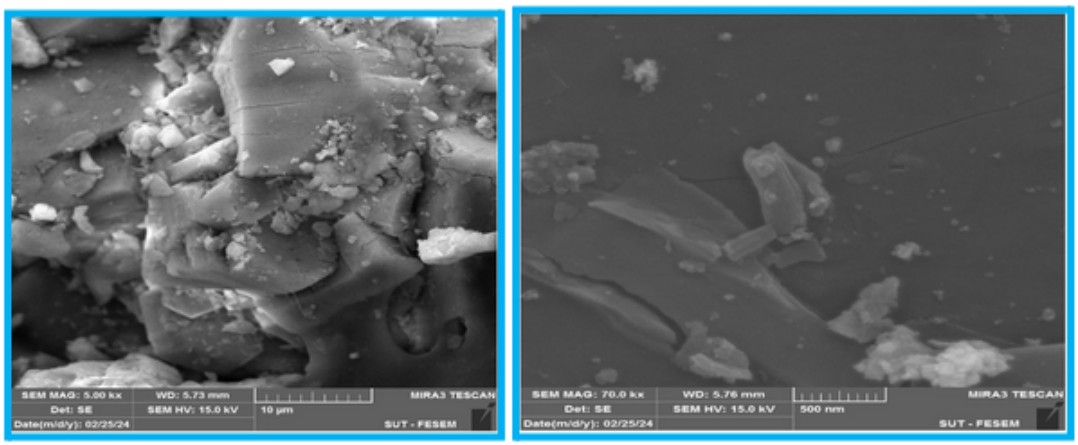


Figure (1): Shows SEM image of the catalyst.

3.2. Characterization of Diazepine derivatives (F11-F15)

When studying the infrared spectrum of (F11-F15) compounds, A band was shown to form in the (1637–1625) cm-1 area as a result of the (C=N) ring stretching, and the absorption band in the region (3267-3232) cm-1, which resulted, is often attributed to (NH) stretching, and the aromatic (C-H) stretching is responsible for the absorption band in the region (3057-3027) cm-1. The two absorption bands at water (2982–2860) cm-1are typically ascribed to the stretching of aliphatic (C–H) molecules, and two bands are attributed to the aromatic (C=C) stretching in the range (1560-1460) [20]. As in Table 2 and Figure 1.2.

Table (2): FT-IR absorption results for Prepared compounds (F11-F15)

	R	(ν(C-H .Arom	ν(C-H) Aliph.	ν(N-H)	ν(C=N)	ν(C=C) Arom.	Others
F11	4-NO2	3051	2962,2926	3236	1637 1604	1554,1460	ν(N-O) as sy1514. Sy1315
F12	4-Cl	3057	2982,2895	3238	1626 1600	1545,1487	ν (C-Cl)777
F13	4-F	3031	2943,2860	3267	1632 1618	1560,1486	ν (C-F)931
F14	4-Br	3027	2928,2871	3245	1625 1601	1563,1481	ν (C-Br) 562
F15	4-H	3034	2928,2867	3232	1631 1606	1548,1479	--

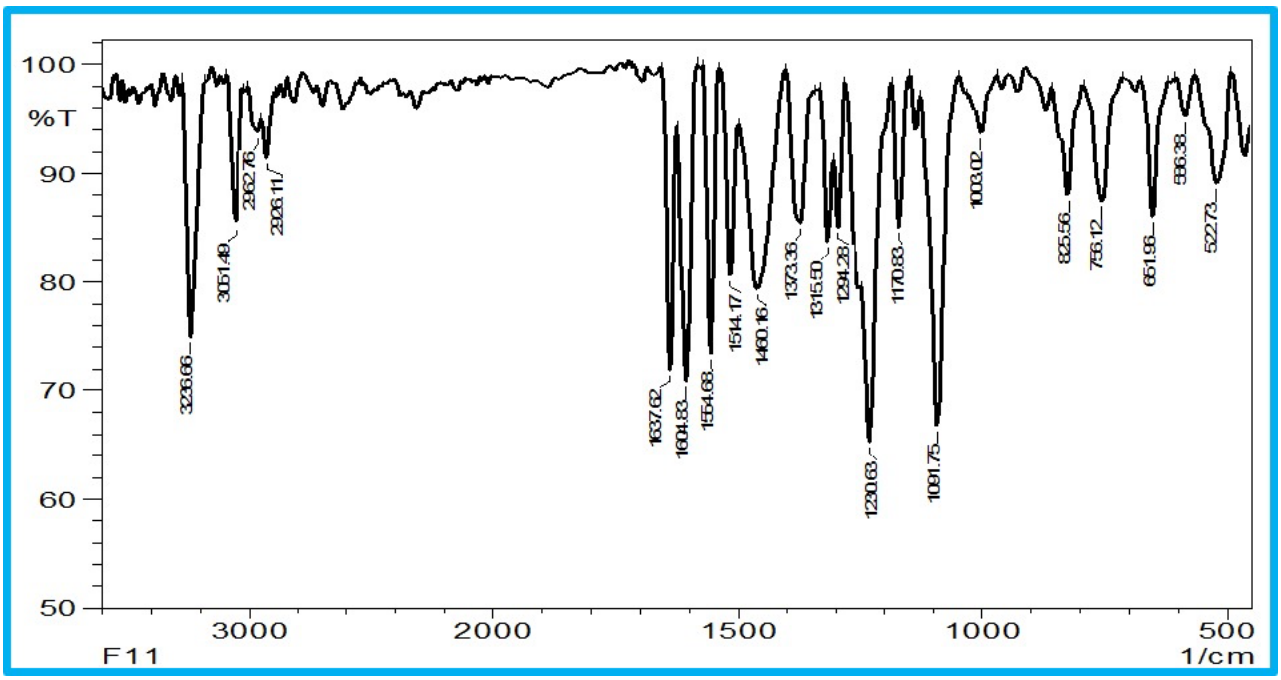


Figure (2): The compound's FT-IR spectra (F11).

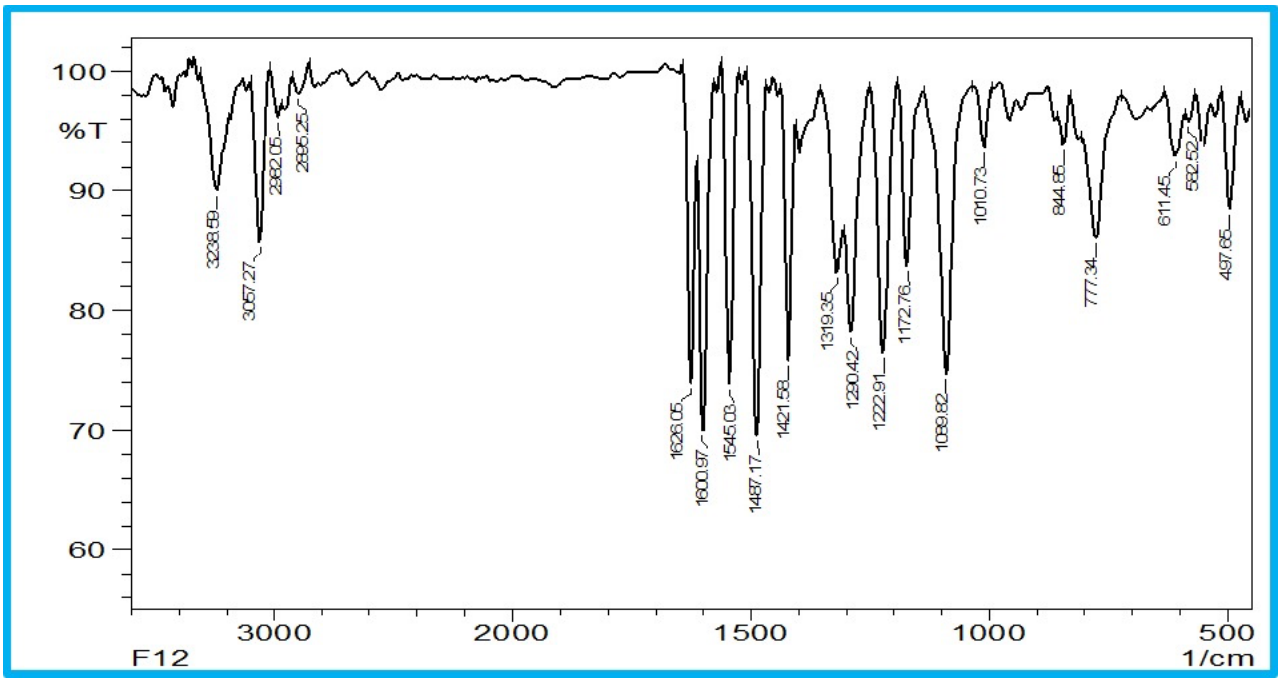


Figure (3): The compound's FT-IR spectra (F12)

When studying the hydrogen NMR spectrum of compound F12, At (2.31, 2.33) ppm, a twofold signal was seen, which was ascribed to the proton (CH2) of the resultant ring, a triple signal in the range (2.98-3.03) ppm, usually for the proton (CH), a signal attributed to the proton (NH) at position (5.83) ppm. Usually for the proton of the resulting ring, and a multiple signal in the range (6.64-8.64) ppm indicates the protons of the aromatic ring. The signal of the solvent DMSO at position (2.49) ppm. As in Figure 4

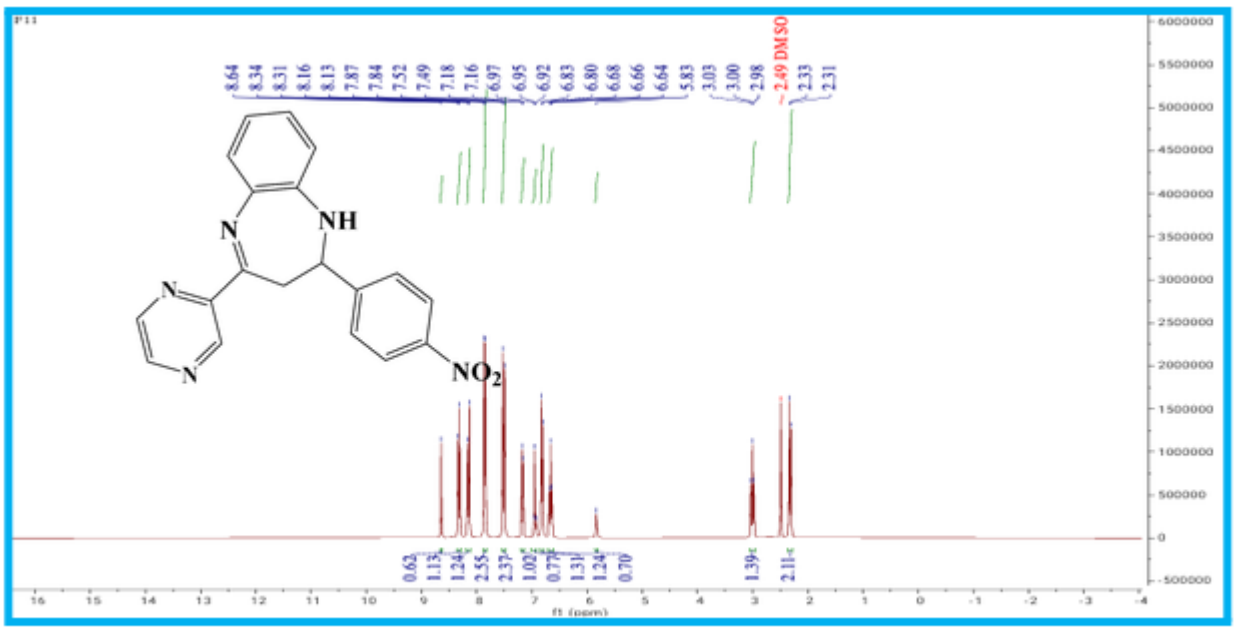


Figure (4): 1-H NMR spectra of the substance (F11).

When studying the NMR spectrum of F14, a double signal at position (2.12, 2.14) ppm was observed attributed to the (CH2) proton of the resulting ring, a triple signal in the range (3.56-3.60) ppm for the (CH) proton, The (NH) proton is the source of the signal at location (5.82) ppm, and the proton of the resulting ring in the range (6.61-8.67) ppm is usually associated with the protons of the aromatic ring. The signal for the solvent DMSO is at position (2.51) ppm. As shown in Figure 5

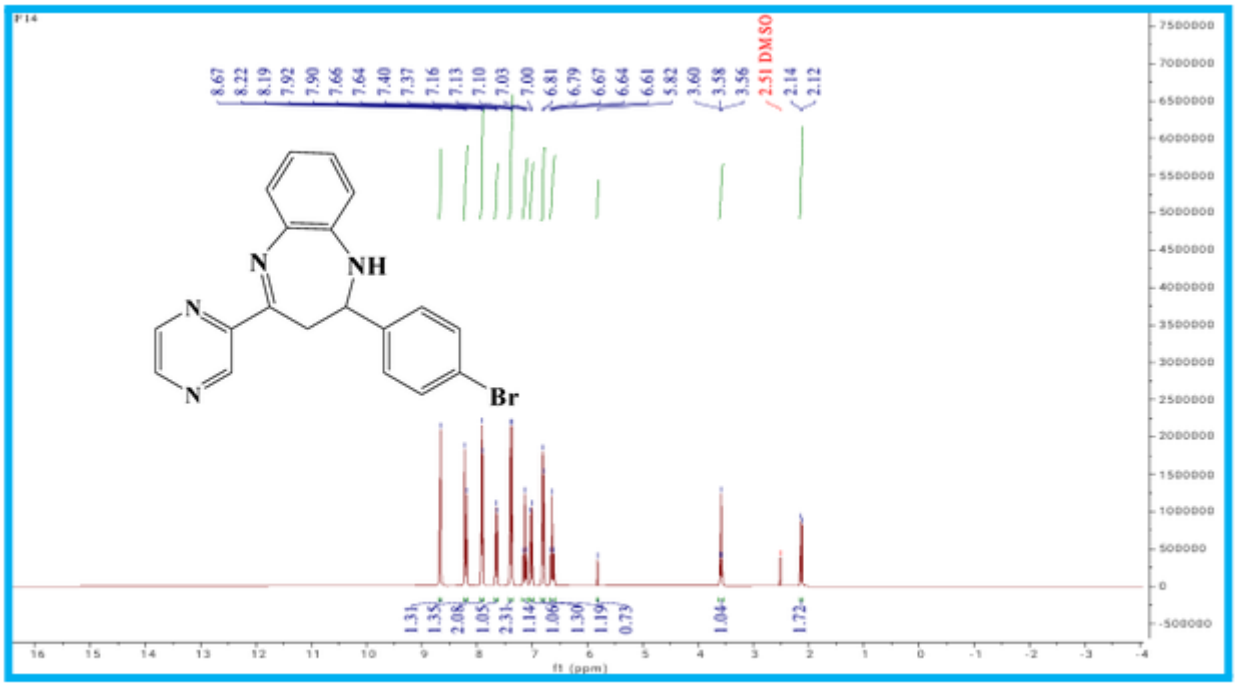


Figure (5): 1-H NMR spectra of the substance (F14).

When examining the C13 NMR spectra of compound F14, the signal at (26.17) ppm was detected, which was identified as the carbon of the resulting ring (CH2), the signal at (42.26) ppm was usually attributed to the carbon of the resulting ring (CH), the signals in the range (119.79-152.75) ppm usually refer to the carbon atoms of the aromatic ring, and the signal at position (167.25) ppm was attributed to azomethine (C=N). The solvent signals are DMSO at position (39.37-40.62) ppm. As shown in Figure 6

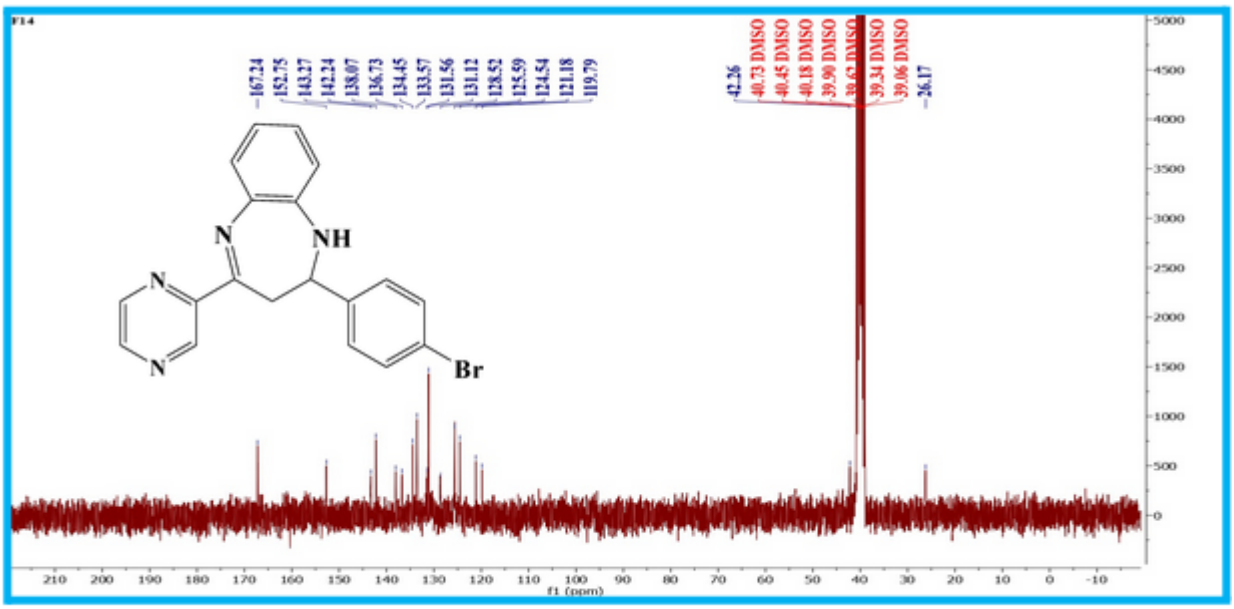
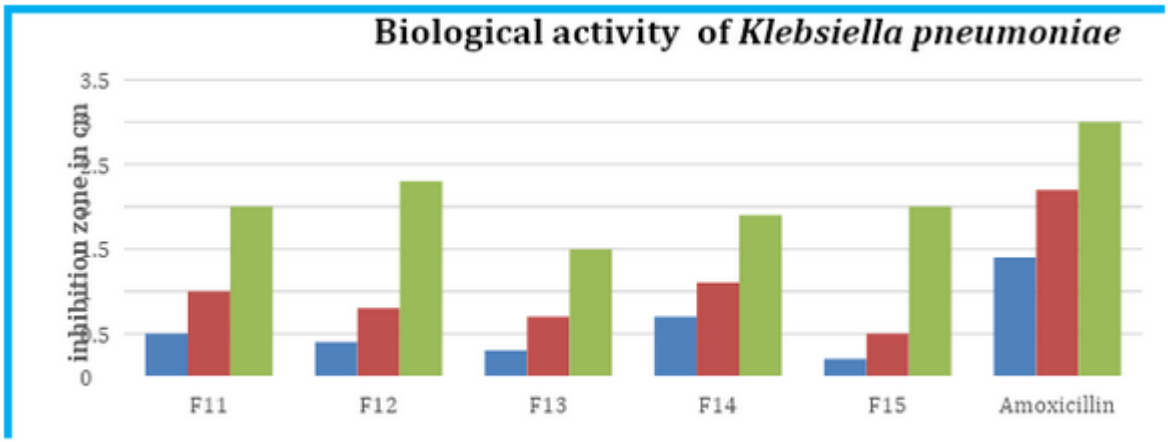


Figure (6): ^{13}C- NMR spectra of the substance (F14).

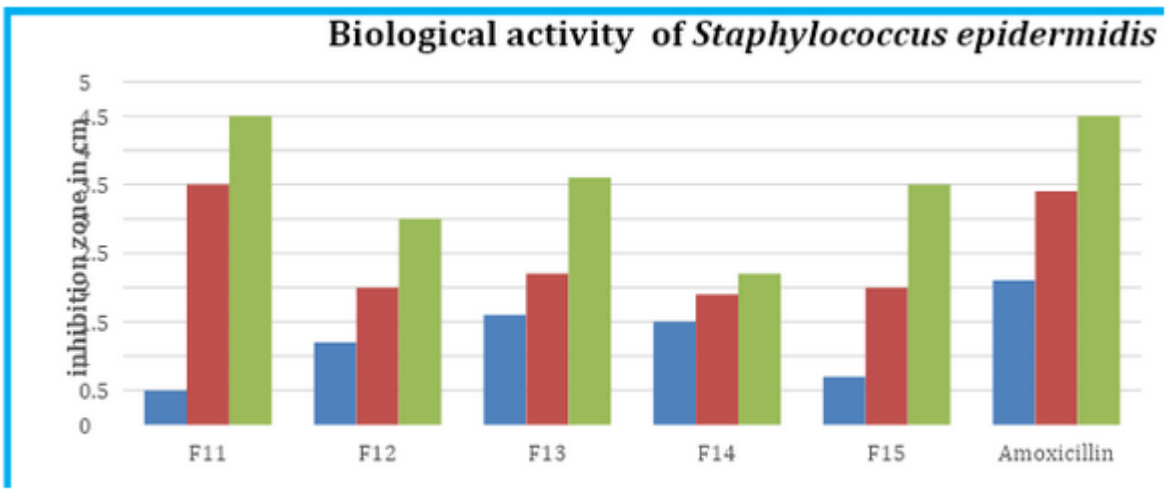
3.3. Evaluation of the Biological Activity of Prepared Compounds

These bacteria were chosen because they are important to medicine since they cause various illnesses and exhibit distinct antibiotic resistance. Methods such as drilling and measuring were used to assess the bioavailability of some of the produced compounds. The outcomes demonstrated that the produced compounds had variable degrees of ability to suppress the development of both Gram-positive and Gram-

negative bacteria[21, 22]. Based on the tests conducted by the World Health Organization and the Ministry of Health laboratories, these antibiotics are broadly categorized, particularly for these two categories of bacteria but also for many other types. Their great selectivity when examining the bacterial sensitivity to the produced compounds accounts for the amount of inhibition. Some of the compounds produced in this study were tested against two kinds of bacteria, namely Staphylococcus epidermidis (Gram-positive bacteria) and Klebsiella pneumoniae (Gram-negative bacteria), because these antibiotics treat many illnesses and disorders. The diffusion technique was used to conduct the test on Petri dishes. Using Mueller-Hinton medium, the diameter of the inhibitory zone (cm) was evaluated for several compounds synthesized at dosages (0.1, 0.01, and 0.001 mg/ml). The outcomes were contrasted with those obtained using traditional antibiotics [23, 24]. Some compounds have a more pronounced impact on type I bacteria than on type I bacteria, while some compounds have a more pronounced effect on type I bacteria than on type I bacteria, based on the effects of some of these produced compounds on bacteria. The result of microorganisms.regarding type I bacteria. It has strong effects on type II bacteria and strong effects on other types of bacteria. A different kind [25, 26]. As in Scheme 2.3and Figure 7.8



Scheme (2): Inhibitory activity of (F11-F15) for K. pneumoniae



Scheme (3): Inhibitory activity of (F11-F15) for Staph. epidermidis

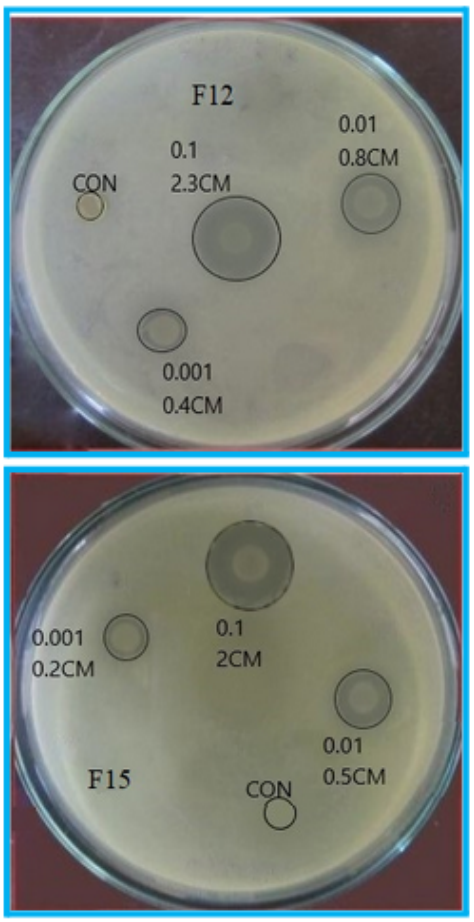


Figure 7: Biological effectiveness of the compound F12,F15 against becteral K.pneumoniae

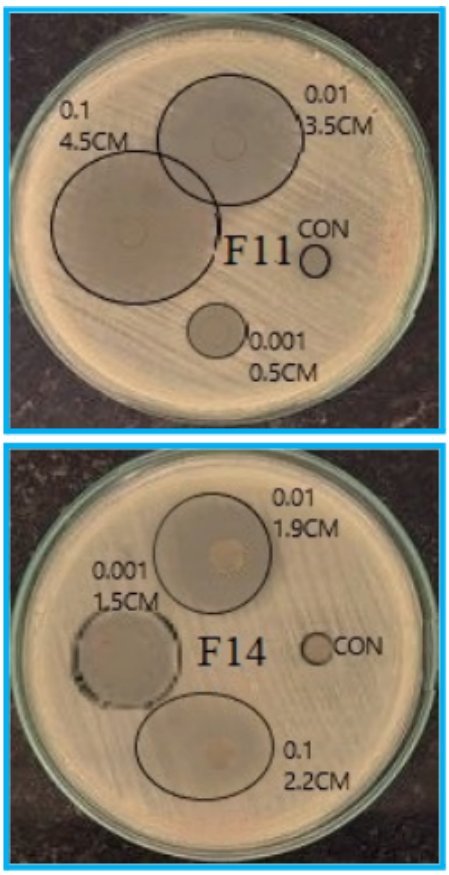


Figure8: Biological effectiveness of the compound F11,F14 against becteral Staph. epidermidis

3.4. Identification and discussion of liquid crystal .

Tables (3) illustrate how the degrees of thermal transition of the liquid and isotropic crystalline phases of the majority of the prepared compounds were determined, their nature examined, and liquid crystal forms identified with a polarized light microscope and heater [27]

Table (3): liquid crystal phase transitions in a device Mic.SC for some prepared compounds

Apparatus	.NO	Crystal	Smectic A	Nematic	$T_{SA}\Delta$	$T_{N}\Delta$
Microscope	F11	218	260	278	42	60
	F12	221	277	290	56	69
	F13	210	------	------	-----	-----
	F15	225	280	305	50	75

As for the compound [F11], it showed three transitions, the first transition is due to the melting point, the second transition is due to the transition from the crystalline phase to the Semactic crystal phase (S) and the last transition is the transition from the Semactic phase (S) to the nematic phase (N). As shown in Figure (9, 10):

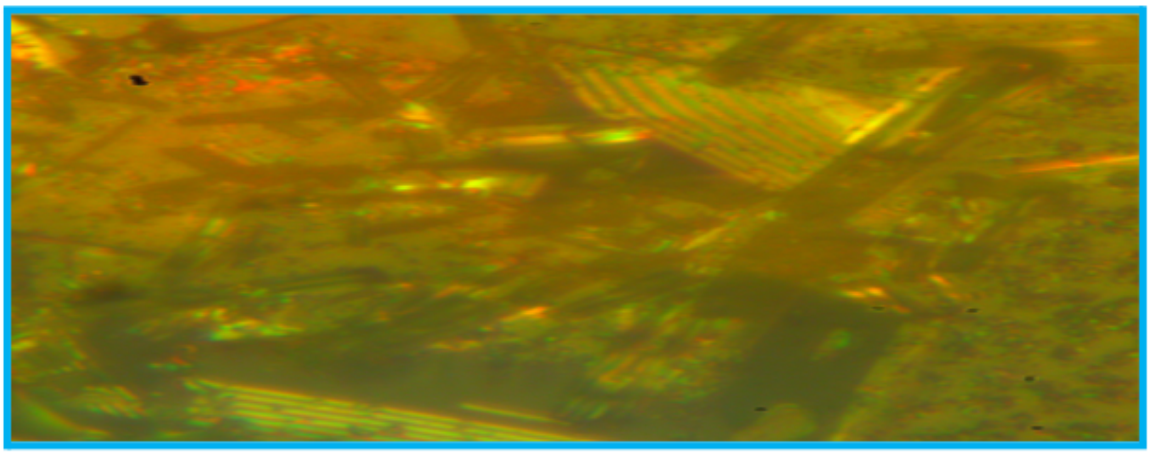


Figure (9) histological structure of the Semcatic of the compound[F11]

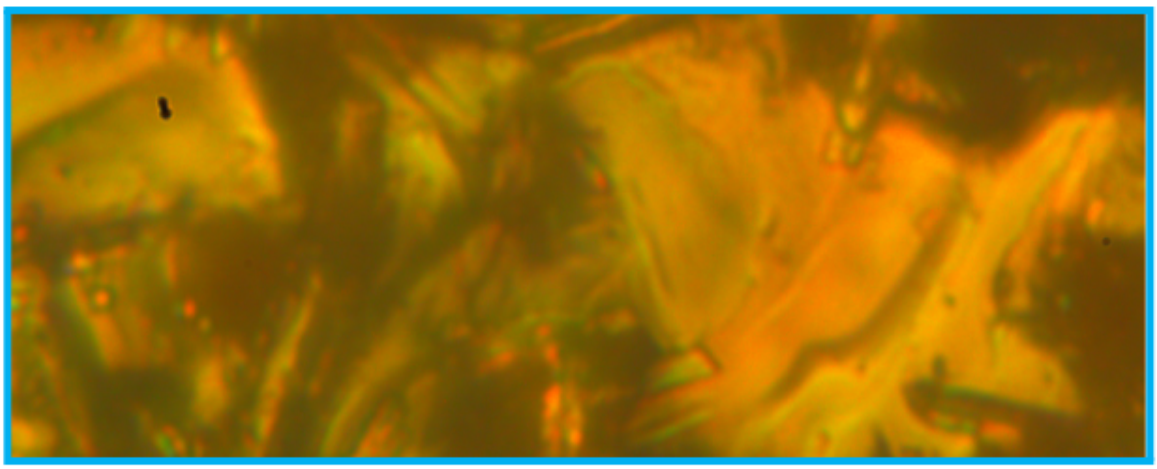


Figure (10) histological structure of Nematic compound[F11]

As for the compound [F12], it showed three transitions, the first transition is due to the melting point, the second transition is due to the transition from the crystalline phase to the Sematic crystal phase (S), and the last transition is the transition from the Sematic phase (S) to the nematic phase (N). As shown in the Figure (11,12):

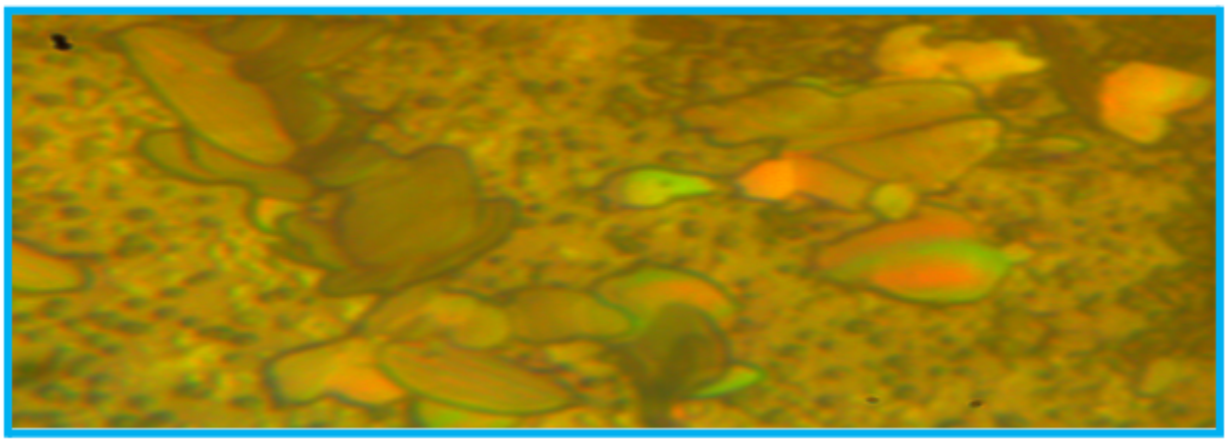


Figure (11) histological structure Sematic SA for compound [F12]

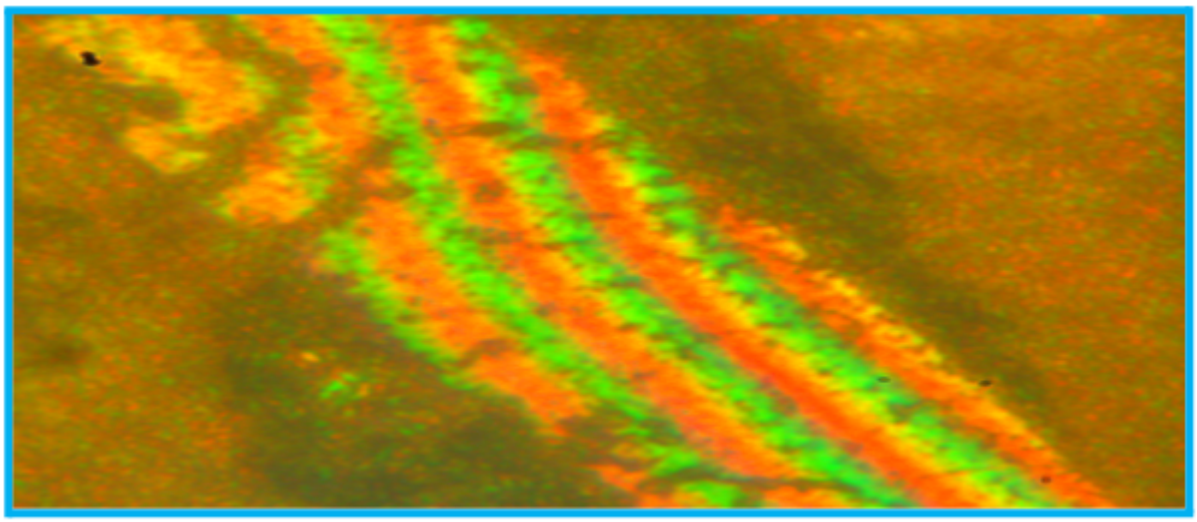


Figure (12) histological structure Nimatic N of the compound[F12]

4. Conclusions

The use of catalysts as an auxiliary factor in the preparation of heterogeneous compounds is safer than other methods and less economical because they are widely available and pure, as proven in the infrared spectrum and the nuclear magnetic resonance spectrum. When testing their bacterial sensitivity against types of bacteria, they gave a good effectiveness, especially compound F 11 against positive bacteria, as it gave an effectiveness equal to the used antibiotic. When studying the liquid phases, some compounds gave crystalline phases with semantic and nematic thermal transition, while compound F 13 did not show any crystalline phases.

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