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SYNTHESIS AND CHARACTERIZATION AND BIOLOGICAL STUDY OF SOME CYCLOHEXENONE DERIVATAVES FROM 2-ACETYL PYROL

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Abstract: The research includes the preparation of various α-β unsaturated compounds by reacting 2-acetylpyrrole with different aromatic benzaldehyde substituents (S1-S5) and by reacting the compounds (S1-S5) with ethyl acetoacetate in a basic medium of 10% NaOH. A hexagonal ring derived from cyclohexenone (S21-S26) was obtained in this compound. The ability to inhibit both Gram-positive and Gram-negative microorganisms, including Staphylococcus aureus and E. coli was then examined. The composition was confirmed by several spectroscopic methods: IR, H1-NMR and C13-NMR. And using.

Keywords: Chalcone, Cyclohexanone, biological activity.

Introduction

Chalcone Unsaturated α-β carbonyls are among the most abundant organic compounds because they possess two important functional groups: two double bonds: one between carbon and carbon (C=C) and the other between carbon and oxygen (C=O) (carbonyl). Since these two functional groups are in a coupled state, the electrons spread across the four atoms, resulting in resonance [1], as shown in the figure below:

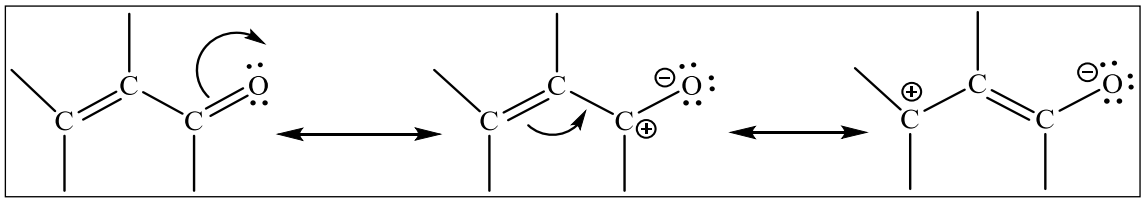


Figure (1) Resonance in alpha-beta carbonyl compounds

Chalcones have several important uses in the pharmaceutical industry [2]. and in agriculture, where they are important as antibacterial agents and are also used as antibacterial [3] antifungal [4] and anti-inflammatory [5]. Cyclohexanone and its derivatives are considered one of the most important multi-purpose compounds. They consist of the condensation of chalconate with ethyl acetate, , and are employed in the synthesis of several natural compounds as well as other crucial chemical derivatives. steroids and antibiotics [6]. Cyclohexanone derivatives possess antitumor, antibacterial, and antifungal properties and are widely used in many biological fields [7]. In addition, they can be used to manufacture natural products with a variety of biological functions [8]. Functional cyclohexanone compounds have received great attention from academic circles and are widely used in the production of a series of important chemicals, such as perfumes and some. Medicines [9]. Cyclohexenone derivatives have shown high biological activity against some diseases, and the following compounds have also shown activity against infections and bacteria [10].

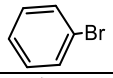
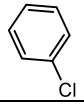
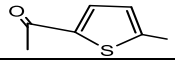
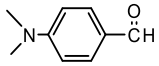
2.1.Chemicals used: Chemicals prepared by Aldrich, BDH Thomas, Fluka, and Merck were used.

2.2. Instruments used: The melting point is measured using a thermometer 9300, KBr disk with a scale of 400-4000 cm-1, FT-IR 8400S Shimadzu spectrophotometer; 1H- and 13C-NMR spectra of Bruker equipment operating at 400 MHz. Thin-layer chromatography (TLC) was analysed using 0.2 mm thick Fluka silica gel plates.

2.3. Preparation of Chalcones derivatives[S1-S5]. [9]

(0.004 mol. 0.82 g) 2- Acetyl pyrrole was dissolved in (7 ml) 10% solution (NaOH) with stirring and in the presence of a cold water bath, (0.004 mol • 0.42 g) of the aromatic solution was added. Aldehydes dissolved in (7 ml) ethanol. Stir the prepared mixture in a water bath (20-40°C) for 3-4 hours and then cool the mixture in the refrigerator overnight [11]. It was then added to ice and neutralized with concentrated hydrochloric acid, and the precipitate was collected and recrystallised with ethanol. As in Table No. (1):

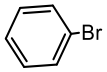
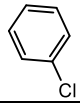
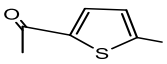
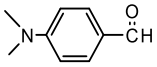
Table (1) shows the physical constants and percentage of chalcones (S1-S5)

Comp.	R	Molecular formula	m.p. °C	Yield%	Colour
S_1		$C_{13}H_9FON$	127-130	93	Light yellow
S_2		$C_{13}H_9BrON$	153-150	89	Yellow
S_3		$C_{13}H_9ClON$	150-145	88	Yellow
S_4		$C_{12}H_{11}ONS$	135-140	83	0range
S_5		$C_{15}H_{16}ON_2$	95-100	79	Light orange

2.3. Preparation of Cyclohexanone derivatives (S21-S25).[10,11]

Dissolve 0.0008 mol of chalcone derivative S1-5 in 8 ml ethanol in a beaker, and in another beaker, dissolve 0.0008 mol of methyl acetoacetate in 8 ml ethanol and 6 ml of 10% sodium hydroxide solution, then the reaction mixture is heated Gradually for six hours, then the solution prepared by heating is concentrated to half or less, then added to crushed ice and left for a whole night, then filtered to obtain a sediment and dried. If a precipitate does not form, add a drop of concentrated hydrochloric acid to neutralize the alkali, then filter. Then leave it to dry [12].

Table (2) Some physical values and percentage of compounds (S 21-S25)

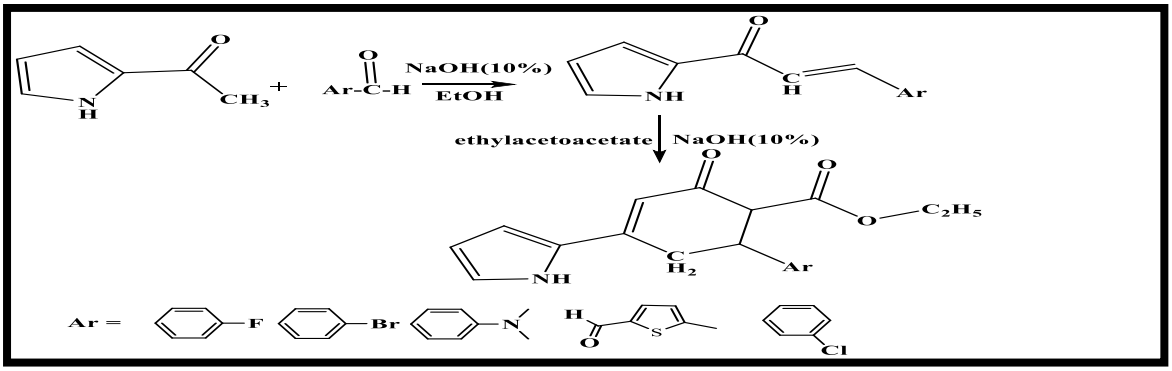
Comp.	Ar	Molecular formula	m.p. °C	Yield%	Colour
S_{21}		$C_{18}H_{16}FO_2N$	129-122	79	**YELLOW**
S_{22}		$C_{18}H_{16}BrO_2N$	140-135	77	**Light orange**
S_{23}		$C_{18}H_{16}ClO_2N$	125-120	75	**Gold**
S_{24}		$C_{16}H_{17}O_2NS$	119-114	72	**Light yellow**
S_{25}		$C_{20}H_{22}O_2N_2$	134-130	73	**Red**

2.3. Biological activity study

Chemical solutions of heterocyclic compounds (S3 ,S23 ,S24 , S25) were prepared in the laboratory using dimethyl sulfoxide (DMSO) solvent at concentrations of (0.1, 0.01, 0.001) mg/ml as shown below[13]: Dissolve (0.1) g in (10 ml) solvent (DMSO).) to obtain a concentration of (0.01 mg/ml). To generate a fresh solution with a concentration of 0.01 mg/ml, remove 1 ml of the previous concentration (0.1 mg/ml) and add 9 ml of DMSO solvent. To get a solution with a concentration of (0.001 mg/ml), remove 1 ml of the final solution, which had a concentration of (0.01 mg/ml), and add 9 ml of solvent (DMSO). Following the addition of pollen to a test tube with diluted bacterial growth [14,15], it is inoculated into Acar Muller-Hinton (MHA) medium using a well-sterilized cotton swab, and excess pollen is removed by pressing the swab against the inner tube wall. After that, wipe the medium evenly from three directions to distribute the vaccine evenly, leave the application for (15-20) minutes to allow the culture to absorb it, and leave the medium until it dries[16].

3. Results and discussions

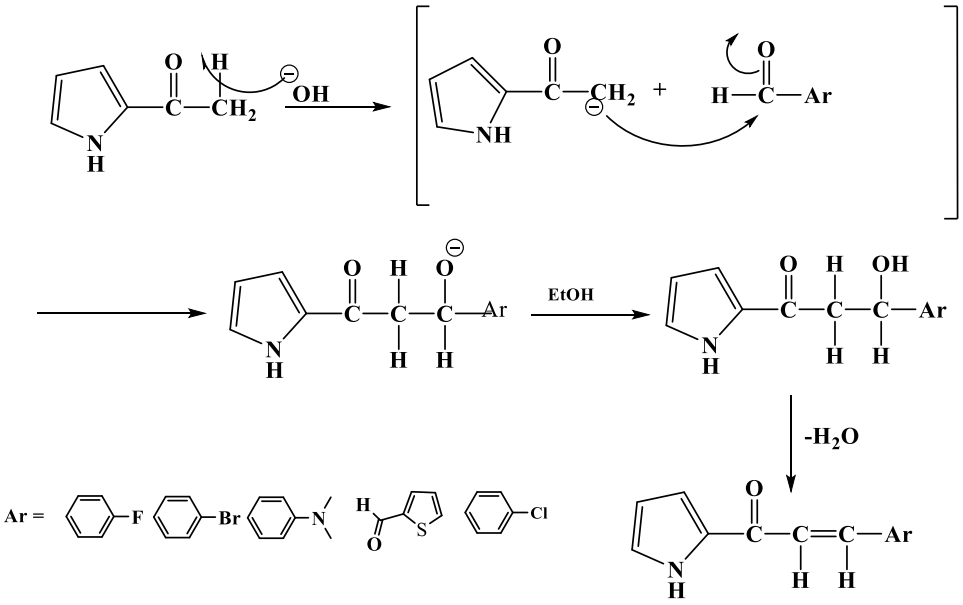
The vehicles were prepared according to the following plan



Scheme (1): Path of the Ready Compounds (S1-S25)

3.1. Characterization of Chalcone [S1-S5].

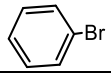
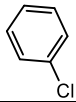
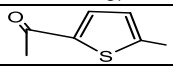
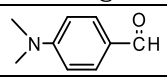
The proposed mechanism for preparing the Chalcone was as follows:



Scheme2; Mechanism of chlcone reaction

The infrared spectrum of these prepared compounds revealed a distinct band at frequency (3060-3015) cm-1, attributed to the stretching of the (Ar-H) group; additionally, a sharp band appeared at frequency (3238-3271) cm-1, attributed to the stretching of the NH group in the five-pointed ring; and finally, a clear, strong band at frequency (1585-1537) cm-1, belonging to the stretching of the Aromatic (C=C) group and another band at frequency (1655-16435) cm-1, belonging to the stretching of the carbonyl group (C=O). These compounds were identified through spectroscopic methods. As shown in Figure 2 and Table 3,

Table (3) IR spectrum values for chalcone compounds (S1–S5)

NO.	Ar	υ (Ar-H)	C=O	NH	C=C	Others
S 1		3060	1643	3247	1571	979 υ (C- F)
S 2		3026	1650	3269	1585	569 υ (C- Br)
S 3		3053	1645	3271	1575	766 υ (C-Cl)
S 4		3041	1655	3242	1569	
S 5		3015	1654	3238	1537	N-C-C υ1133

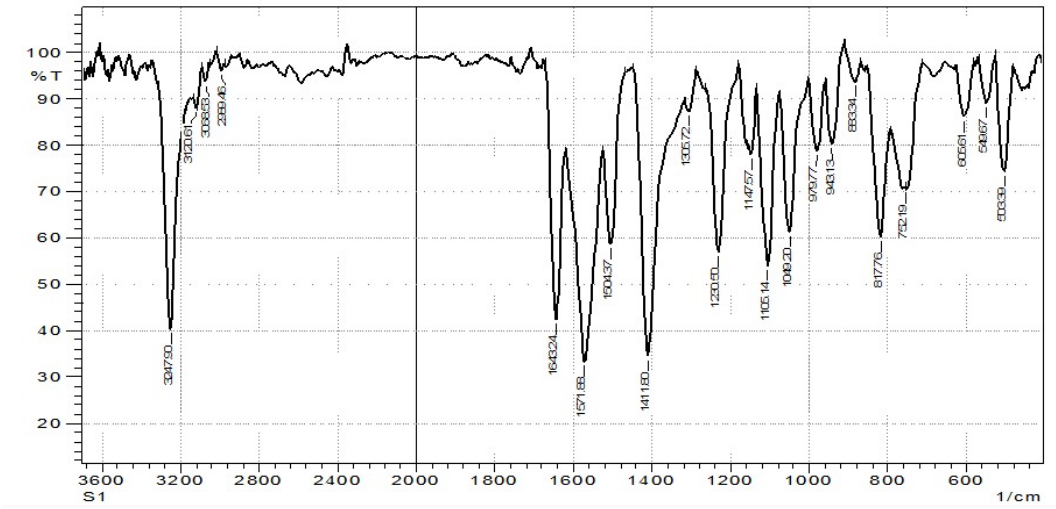


Figure (2) shows the IR values for compound S1

Upon examining the produced substance (S1)'s nuclear magnetic resonance (1HNMR) spectra, it was discovered that the protons of the asymmetric (H = CH) group had a distinct binary signal at frequencies (δ = 8.3 ppm and 7.9 ppm), and multiple signals. They range at a frequency of (δ = 6.6-8.0 ppm) belonging to the aromatic rings, and a sharp double signal at (δ = 3.4 ppm) belongs to the proton of the NH group in the five-pointed ring, and multiple overlapping signals at (δ = 7.9-7.2 ppm) belong to the aromatic ring, Figure (3).

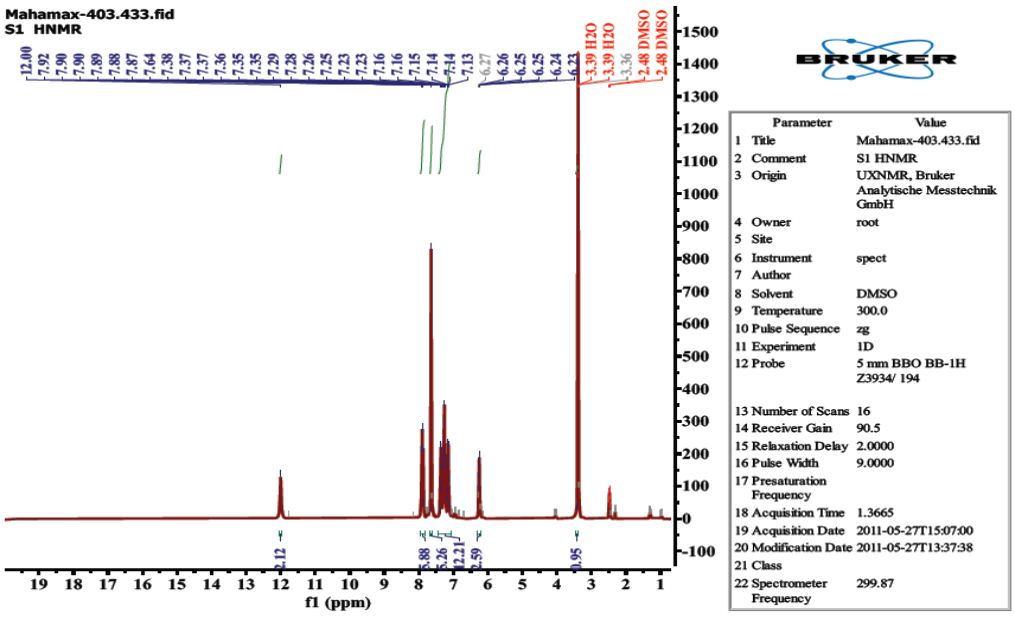


Figure 3: HNMR of compound S1

When studying the (13C-NMR) spectrum of the prepared compound (S1), it was observed that a clear signal appeared at the frequency (δ = 177.0 ppm) belonging to the carbon atom of the carbonyl, and a signal at (δ = 140 - 135 ppm) belonging to the carbon atoms (CH=CH).

Respectively, the signs (23) (δ = 135 - 110 ppm) belong to the pheny carbon atoms and the pyrrole ring, as in Figure (4).

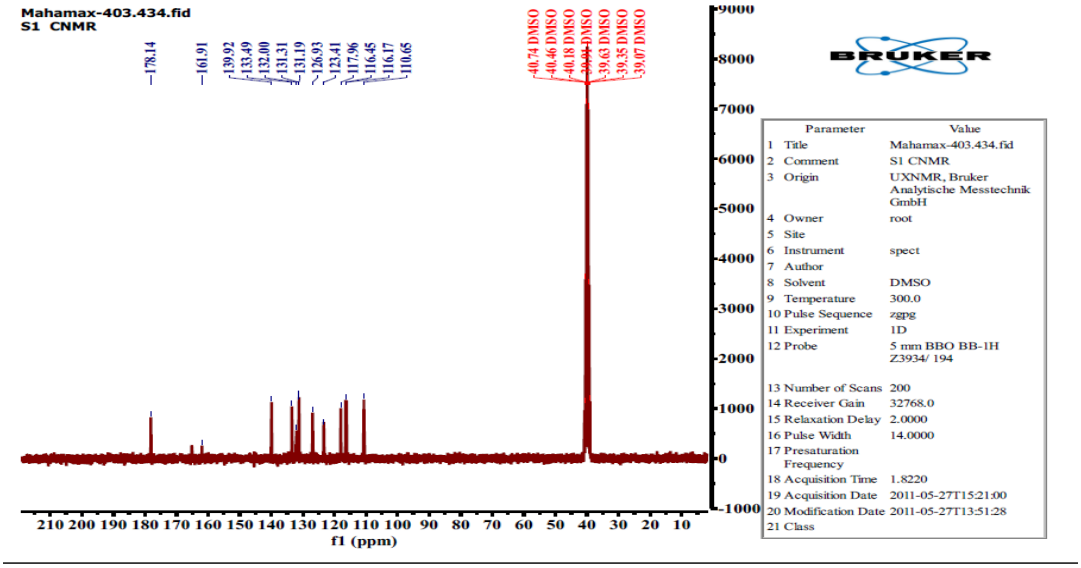
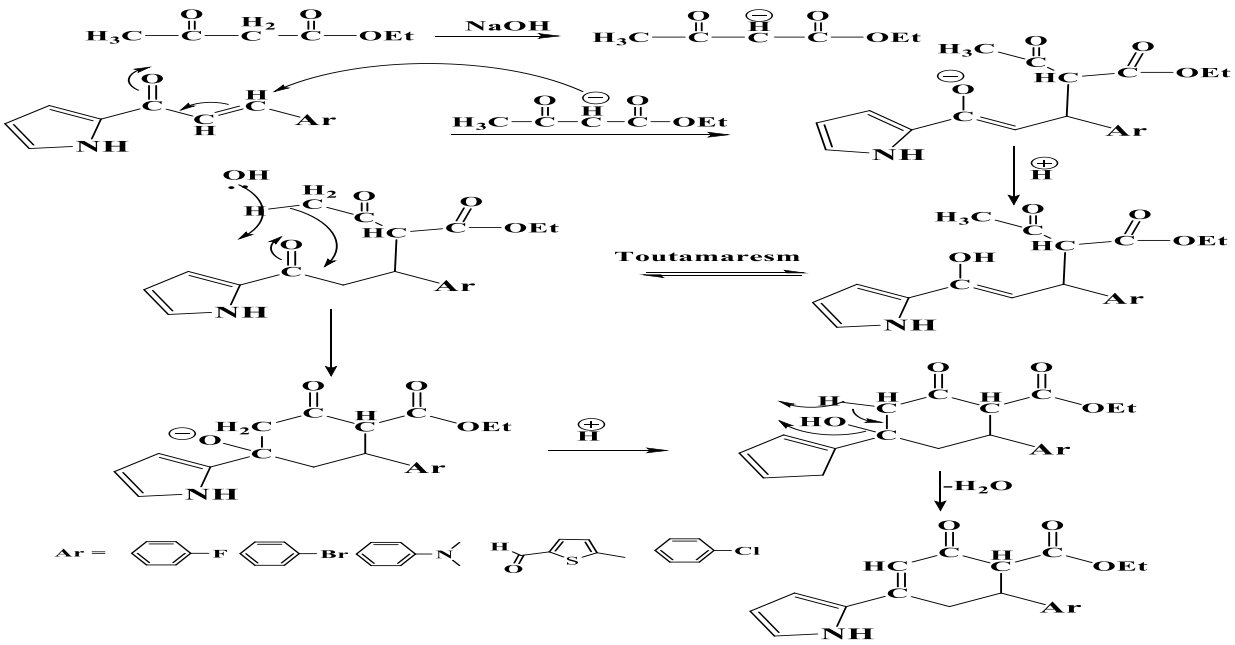


Figure 4: ^{13}C-NMR of compound S1

3.2. Characterization of Cyclohexanone derivatives [S21-S25].

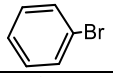
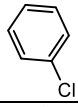
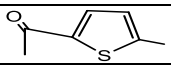
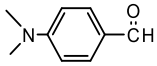
The proposed mechanism for preparing the Cyclohexanone was as follows:



Scheme (3): Mechanism of preparation of Cyclohexanone derivatives [S21-S25]

These banned compounds were identified using spectroscopic methods, as the IR of the compounds (S21-S25) showed a band at the frequency (1658-1680) returning to the stretching of the bond (C=O) in the hexagonal ring of the compound, and another band at the frequency (3060-3098) cm-1 returning The aromatic (Ar-H) bond is stretched, and a band at the frequency (1582-1593) cm-1 is due to the bond stretching (C=C) of the hexagonal ring, and another band at the frequency (3157-3221) cm-1 is due to the NH bond stretching of the pyrrole ring[18]. As shown in table 4 and Figure (5).

Table (4): Infrared absorption results (cm-1) for [S21-S25] compounds

NO.	Ar	υ (Ar-H)	C=O	NH	C=C	Others
S 21		3060	1658	3157	1593	1120 υ (C- F)
S 22		2068	1680	3201	1585	746 υ (C- Br)
S 23		3098	1679	3221	1587	766 υ (C-Cl)
S24		3083	1678	3197	1585	
S 25		3091	1671	3204	1590	N-C-C υ1103

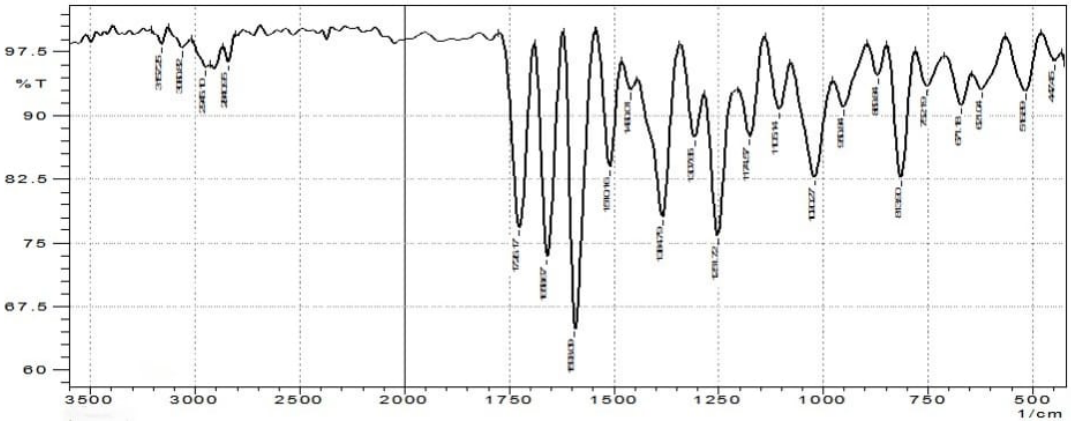


Figure (5): The infrared spectrum of the compound [S21]

The compound (S23) was diagnosed with a nuclear magnetic resonance spectrometer (1HNMR), where it showed a signal at the frequency (δ 3.3 ppm) attributed to the protons of the (H, CH) group of the hexanone ring, and the appearance of another signal at the frequency (δ 2.5 ppm) attributed to the protons. (3H,CH3) group, and the appearance of another signal in (δ 3.1 ppm) attributed to the protons of the (2H,CH-CH) group of the six-ring ring, and the appearance of a multiple signal in the range (δ 7.9-6.1 ppm) attributed to the protons of the aromatic ring Figure (6),

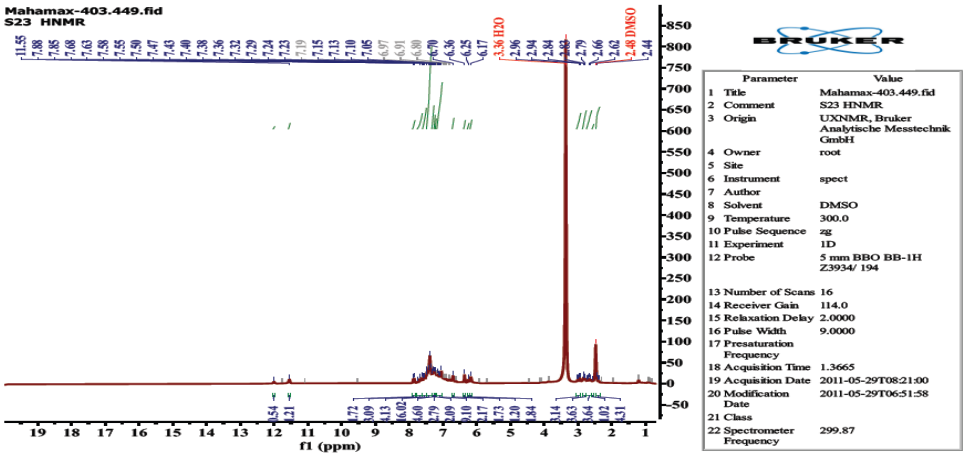


Figure (6): The HNMR spectrum of the compound [S23]

3.3. Evaluation of the Biological Activity of Prepared Compounds

Studies on the biological activity of compounds prepared at certain concentrations showed that these compounds have antagonistic activity against the bacterial species studied compared to the antibiotic (norfloxacin), which is a broad-classified antibiotic, especially in these two bacterial species[19]. in addition to many other species, and it has a huge inhibitory diameter. This allows good selectivity when studying the susceptibility of bacteria to the prepared compounds, because this antibiotic (norfloxacin) is used to treat many infections and diseases, such as urinary tract infections, especially those caused by Escherichia coli. and Staphylococcus aureus infections[20,21].

Comp. No.	E. Coil Conc. mg/ml			Staph. Aureus Conc. mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
S3	14	11	7	10	5	0
S23	13	10	8	15	13	11
S24	12	9	6	13	10	5
S25	11	7	00	10	10	5
Norfloxa	18	17	11	20	19	18

4. Conclusions

Alpha-beta unsaturated molecules are produced when the ketone and aldehyde combine. In a basic environment, these products react to form hexagonal rings that are derived from cyclohexenone. Physical measures including melting point, color, and nuclear magnetic resonance spectroscopy, together with infrared and nuclear magnetic resonance spectroscopy, were used to verify the authenticity of the produced compounds. Its efficacy was good, comparable to the antibiotic employed, when evaluated for bacterial sensitivity against two types of bacteria: positive and negative for the Gram stain.

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