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Preparation and Characterization of Some 1,3-Oxazepane -7,4-Dione Derivatives and Evaluation of their Biological Activity

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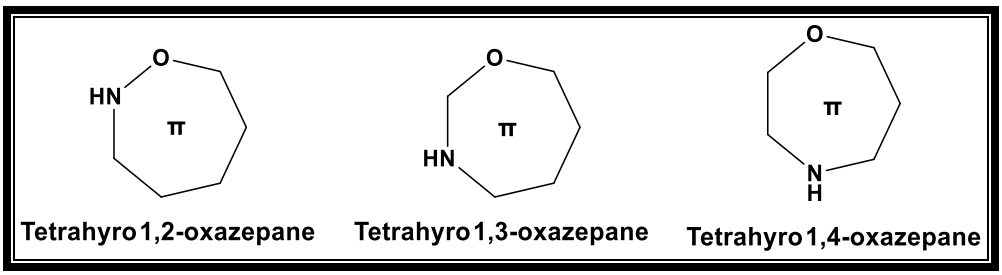
Abstract:
This study included the preparation of chaff bases using terephthaldehyde as a nucleus, reacting them with amine substitutes, and then reacting the resulting compounds with succinic anhydride in the presence of dry benzene as a solvent to obtain a heptad ring derived from oxazepane, whose biological effectiveness was tested against two types of gram-positive and gram-negative bacteria. The structures were validated using physical measurements. From the melting point, color change, and product percentage spectroscopic analyses, including proton nuclear magnetic resonance and infrared spectroscopy, were employed.

Key words: *Oxazepane, Schiff base, biological activity.*

Introduction



Oxazepane compounds have broad biological and medical importance, and therefore their chemical substitutes for nitrogen-containing heterogeneous organic compounds have a very wide range of medical uses, including heterogeneous polymers with anticancer activity [3]. Bacteria [4]. **Schiff bases** are organic substances containing an azomethine group (CH=N-), named after the scientist Schiff who created them in 1864 using a direct condensation reaction between primary amines and aldehydes or ketones [5]. The names of these bases are determined by aldehydes and ketones and contain the amines made from them. There are several names for Schiff bases, including imines, azomethines, and analytes [6]. The truth is that these compounds contain active groups, most of which are of medical importance and biological effectiveness[7], as they have proven anti-cancer activity[8,9], anti-microbial activity[10,11], anti-bacterial activity[12], antioxidant [13,14], antimalarial [15,16],

2. Materials and Methods:

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

2. Devices used: Melting points were measured with a thermoelectric melter 9300. KBr disk at 400–4000 cm-1 scale, Shimadzu FT-IR 8400S spectrophotometer; Bruker equipment running at 400 MHz for 1H-NMR and 13C-NMR spectra. Fluka silica gel plates, with a thickness of 0.2 mm, were used in thin-layer chromatography (TLC). UV light achieved visibility after fluorescent silica gel G activated the plates.

2.3. Preparation of Schiff base derivatives (H_1-H_5).[17]

20 ml of ethanol and terephthaldehyde (0.003 mol) were combined in a 100 ml round flask, and the mixture was stirred before a few drops of glacial acetic acid were added., and finally the substituted aromatic amine derivatives (0.006 mole). After six hours of heating, the mixture was cooled and filtered. The TLC method was used to verify the completion of the reaction, recrystallization with ethanol, and drying, as indicated in Table 1.

2.3. Preparation of Oxazepane derivatives (H_6-H_{10}).[18]

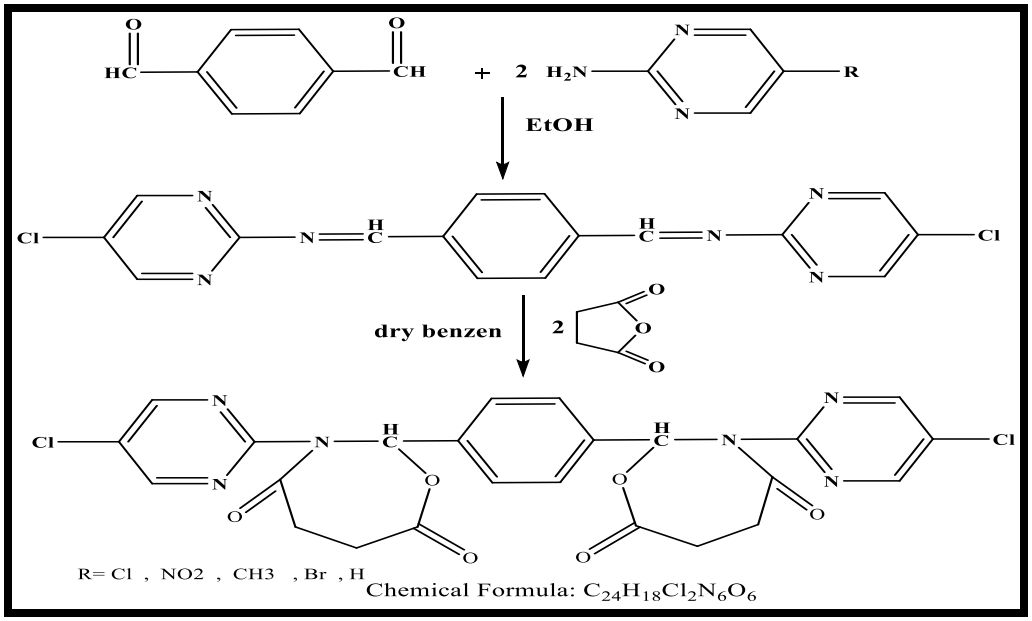
In a 100 ml round flask, dissolve 0.001 mol of the produced Schiff bases in 20 ml of dry benzene, and then add 0.002 mol of succinic anhydride drops. After eight hours of heating, the mixture is cooled, filtered, and dried. As indicated in Table 1, the crystallization is recrystallized with ethanol, and the reaction's completeness is verified using (TLC) technology.

.2.4. Biological activity study

Gram-positive Gram-negative and Staphylococcus aureus bacteria The two pathogenic bacterial species used in this study were Escherichia coli. Both the College of Pure Science Education and the Department of Life Sciences employ Molter Hinton agar as a bacterial growth medium. Chemical solutions of H6, H8, H9, and H10 were prepared using dimethyl sulfoxide (DMSO) at concentrations of (0.01, 0.001, 0.0001) mg/mL. This process determines and monitors the minimum inhibitory concentration (MIC) [19, 20]. The diffusion technique was employed to determine the susceptibility of the bacterial isolates used in the experiment, and Mueller-Hinton agar was used as the nutritional medium. Once the culture medium is ready, it is sterilized, distributed among plates, and given time to solidify. Next, make four small holes in each panel. They were then incubated at 37°C for a full day. Derivatives used. They are clarifying the sensitivity of the derivatives used. As the diameter increases, these derivatives depend on the damping diameter of the plate surrounding the hole used. When the chemical produced shows an inhibitory effect, its biological activity increases, and this can be compared to the inhibitory diameter of an antibiotic. [21, 22].

3. Results and discussions

As shown in Scheme 1, Schiff bases are prepared by reacting terephthalate with two amine derivatives in the presence of ethanol as a solvent and then reacting them with Succinic anhydride to obtain a seven-ring called Oxazepane in the presence of dioxane as a solvent.



Scheme (1): Path of the Ready Compounds (H1-H10)

3.1. Characterization of Schiff base derivatives (H1-H6)

The (C=N) bond was identified as the source of an absorption band in the region of (1629-1599) cm-1 in the FT-IR spectra. It also showed a band belonging to the aromatic (CH) bond in the range (3020-3058) cm-1, Moreover, the olefinic (CH) bond was identified as having a band in the region (3109-3197) cm-1, two bands in the range of (1553-1521) cm-1 and (1440-1485) cm-1[23], in addition to as in Table 2 and Figure 1.2

Compound H1's 1H-NMR analysis revealed two single signals at positions (7.30–79.91) ppm, which were identified as the protons of the aromatic ring., and it had a single signal at 8.77 ppm, which was identified as belonging to the proton group (N=CH). As well as a sign of solvent (d6-dmso) at (2.51) ppm. As in Figure 3

3.2. Characterization of Oxazepane derivatives (H6-H10)

It was discovered that a stretch band occurred in the region of (1689–1703) cm-1, which is associated with the ester carbonyl group when examining the FT-IR spectra of oxazepane derivatives. A band in the range (1645-1664) cm-1 belongs to the amide carbonyl bond. There are two bands in the range (2945-2982) cm-1 and (2891-2933) cm-1, which belong to the aliphatic (CH) bond, in addition to a band belonging to the aromatic (CH) stretch in the range. (3031-3071) cm-1[24], as shown in Table 2 and Figure 4.5

The 1H-NMR spectrum of compound H 6 .showed two binary signals in the range (3.04-3.66) ppm, belonging to the protons of the (CH2) group of the oxazepane ring. The signal at location (6.79) ppm is due to the proton of the (CH) group of the oxazepane ring. The signal at location (6.79) ppm is due to the proton of the (CH_3) group. Two signals are attributed to the protons of the aromatic ring at the location (7.38-7.83) ppm. As well as a sign of solvent (d6-dmso) at (2.51) ppm. As in Figure 6

The 1H-NMR spectrum of compound H8 showed two binary signals in the range (3.09-3.45) ppm, belonging to the protons of the (CH2) group of oxazepane in the ring. The signal at location (6.83) ppm is due to the proton of the (CH) group of the oxazepane ring. Two signals are attributed to the protons of the aromatic ring at the location (7.11-7.86) ppm.). As well as a sign of solvent (d6-dmso) at (2.51) ppm. As in Figure 7

3.3. Evaluation of the Biological Activity of Prepared Compounds

These bacteria were chosen for their medical importance, as they cause many diseases. In addition, they differ in their resistance to antibiotics[25,26]. The bioavailability of some of the prepared compounds was evaluated

using the etching method and measuring the antibiotic levels[27,28]. The results showed that different ratios of positive and negative compounds of the Gram stain can inhibit bacterial growth, as shown in Table 3.

Table (1): Some physical properties of for Prepared compounds (H1-H10).

Comp. No.	R	Molecular formula	m.p. °C	Yield%	Color
H1	4-Cl	$C_{16}H_{10}Cl_2N_6$	-191 189	56	White
H2	4-NO2	$C_{16}H_{10}N_{10}O_4$	156-158	67	Yellow
H3	4-CH3	$C_{18}H_{16}N_6$	-180 178	69	Orange
H4	4-Br	$C_{16}H_{10}Br_2N_6$	-202 200	75	Brown
H5	4-H	$C_{16}H_{12}N_6$	-169 167	77	White
H6	4-Cl	$C_{24}H_{18}Cl_2N_6O_6$	-136 234	75	Brown
H7	4-NO2	$C_{24}H_{18}N_8O_{10}$	221-223	87	Brown
H8	4-CH3	$C_{26}H_{24}N_6O_6$	-219 217	75	Orange
H9	4-Br	$C_{24}H_{18}Br_2N_6O_6$	-277 275	74	Yellow
H10	4-H	$C_{24}H_{20}N_6$	-243 241	82	Yellow

Table (2): FT-IR absorption results for Prepared compounds (H1-H10)

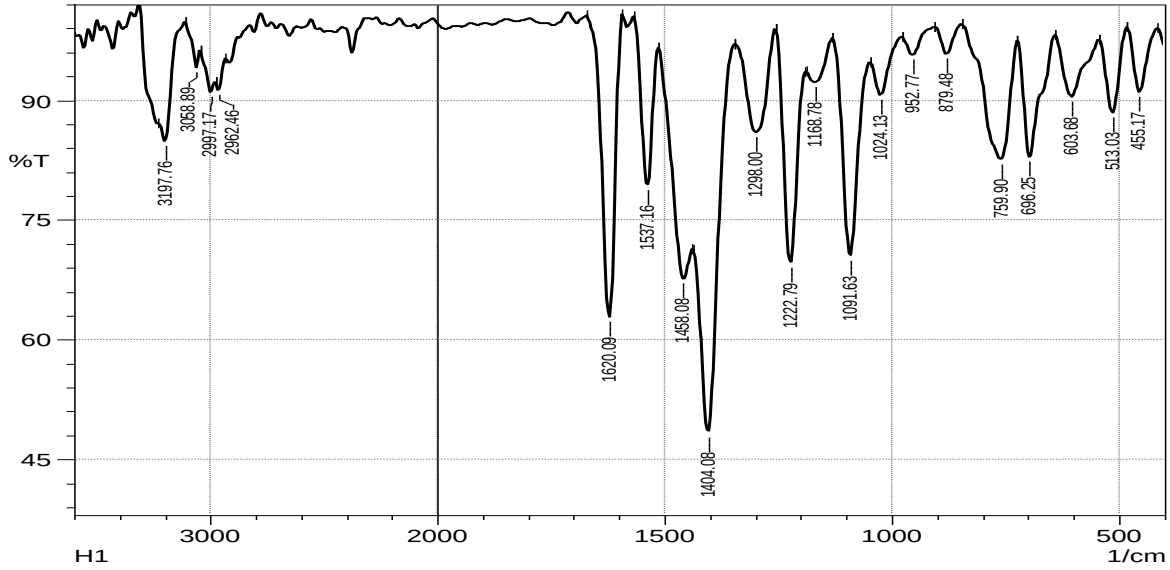
Comp. No.	R	**ν(C-H) Arom.**	**ν(C-H) Olph.**	**ν(C=N)**	**ν(C=C) Arom.**	**Others**
H1	4-Cl	3041	3167	1599	1549, 1478	ν (C-Cl) 739
H2	4-NO2	3025	3154	1616	1553, 1485	ν (N-O) 1385
H3	4-CH3	3058	3197	1620	1537, 1458	--

H4	4-Br	3020	3109	1606	1544, 1460	ν (C-Br) 513
H5	4-H	3030	3136	1629	1521, 1440	--
Comp. No.	R	**ν(C-H) Arom.**	**ν(C-H) Aliph.**	**ν(C=O) Lactone Lactam**	**ν(C=C) Arom.**	**Others**
H6	4-Cl	3061	2976,2933	1701,1645	1558, 1462	ν (C-Cl) 759
H7	4-NO2	3031	2945,2891	1691,1651	1531, 1478	ν (N-O) 1335
H8	4-CH3	3065	2951,2912	1694,1649	1542, 1467	--
H9	4-Br	3071	2967,2931	1703,1664	1551, 1463	ν (C-Cl) 570
H10	4-H	3066	2982,2908	1689,1654	1521, 1460	--

Table (3): Biological efficacy of produced substances and control methods (measured in millimeters of inhibition).

Comp. No.	E. Coil Conc. mg/ml			Staph. Aureus Conc. mg/ml		
	0.01	0.001	0.0001	0.01	0.001	0.0001
H6	17	15	10	20	15	10
H8	16	14	10	10	10	5
H9	21	15	10	15	10	5
H10	23	14	10	10	5	- -

Amoxi cillin	2 2	1 7	1 6	2 0	1 9	1 5



H3

Figure (1): The compound's FT-IR spectra (H3).

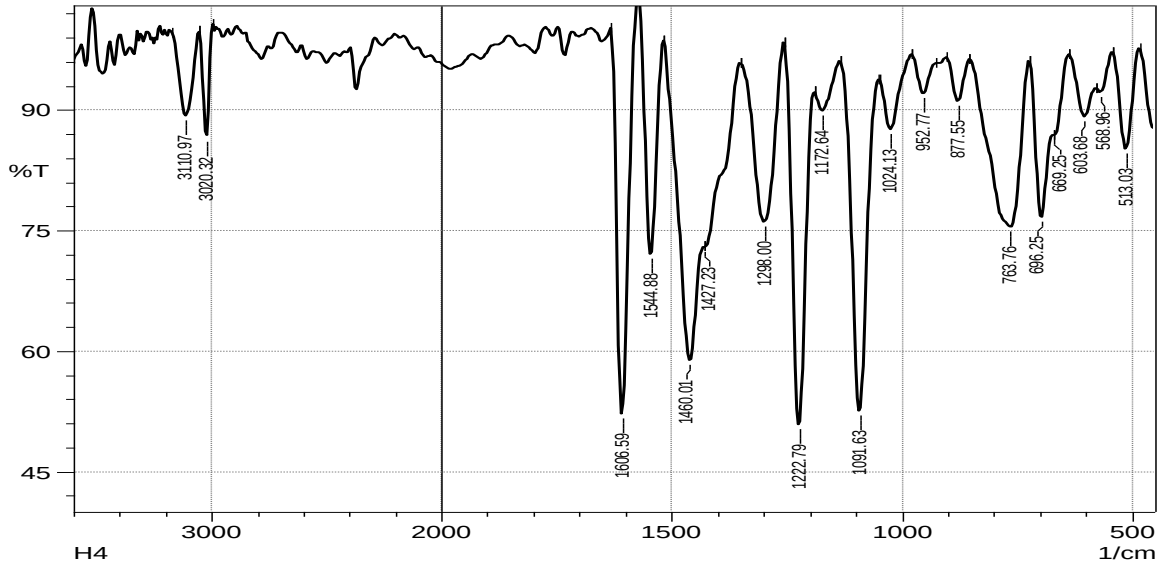


Figure (2): The compound's FT-IR spectra (H4).

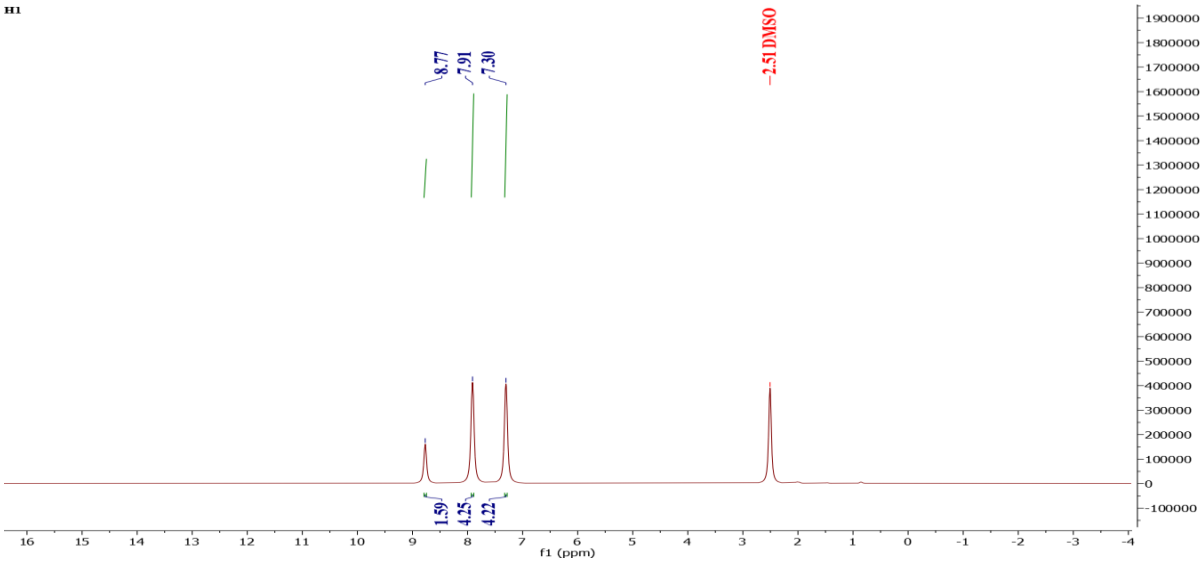


Figure (3): 1-H NMR spectra of the substance (H1).

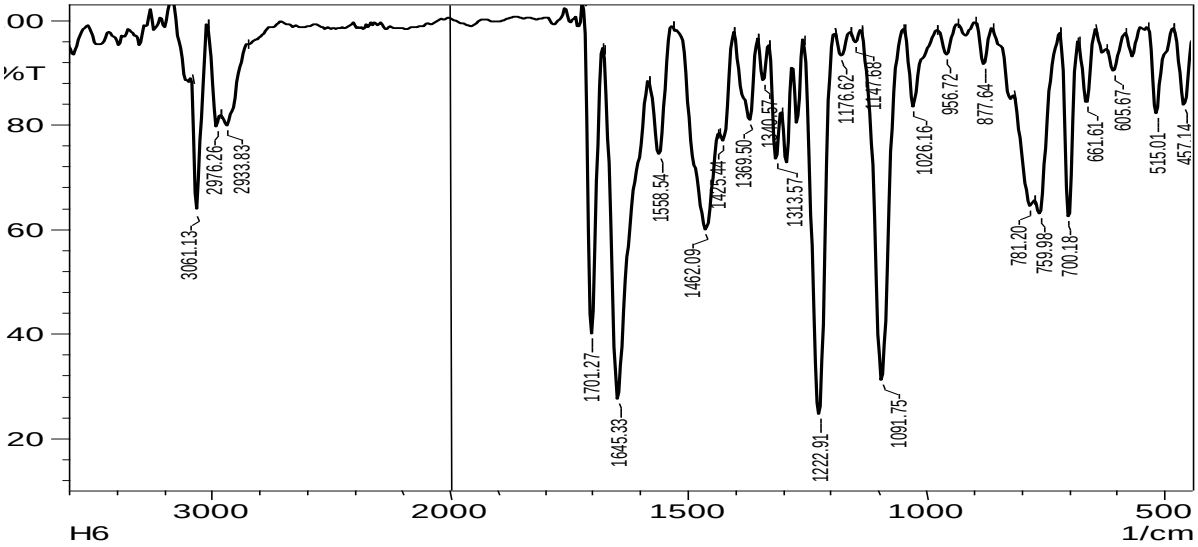


Figure (4): The compound's FT-IR spectra (H6).

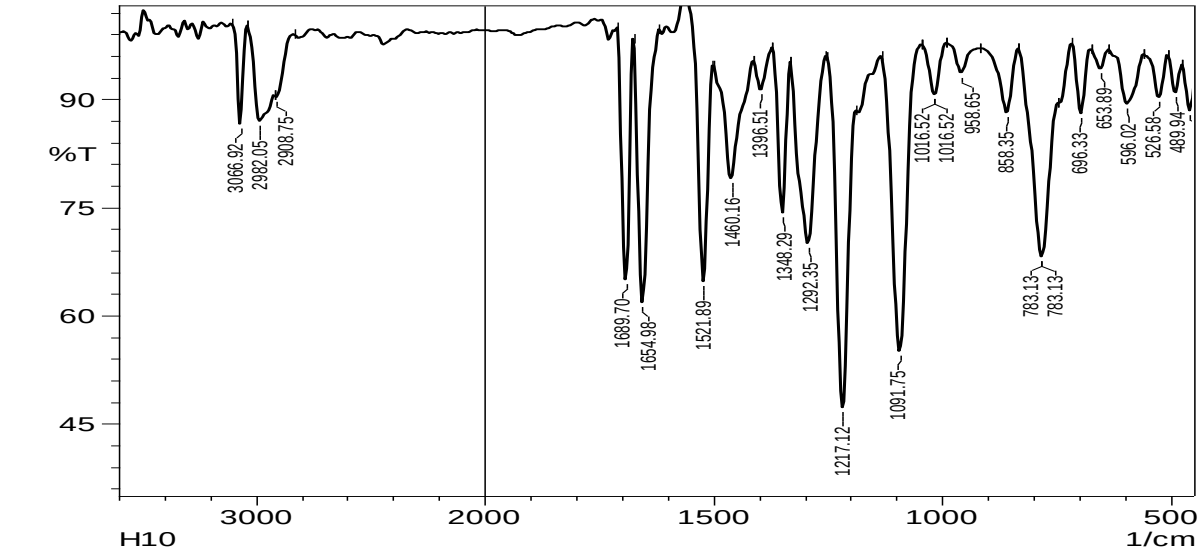


Figure (5): The compound's FT-IR spectra (H10).

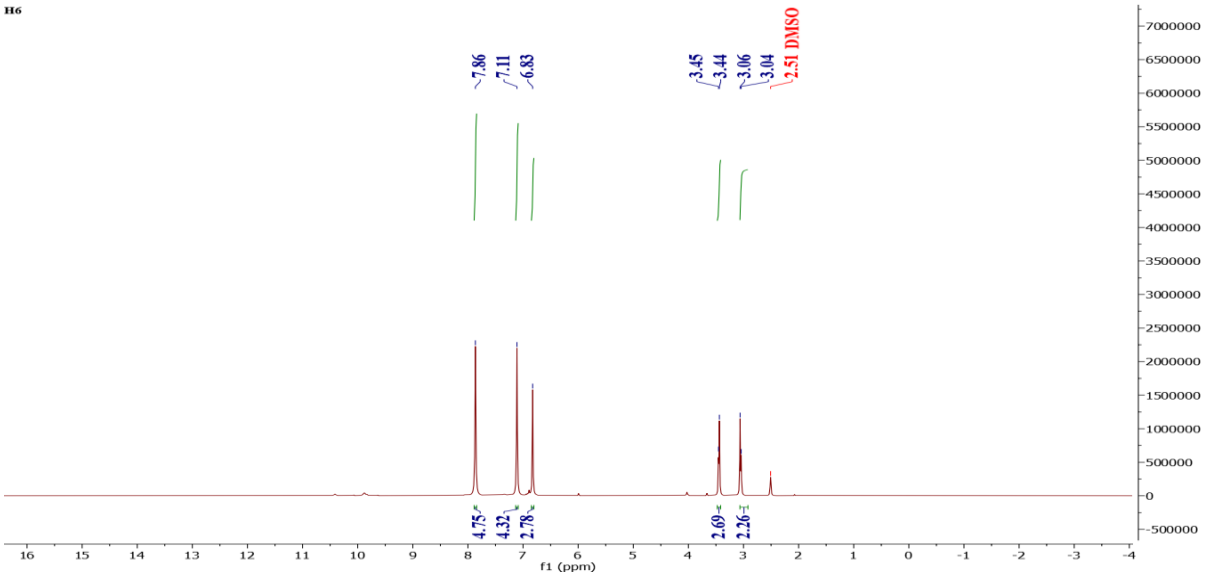


Figure (6): 1-H NMR spectra of the substance (H6).

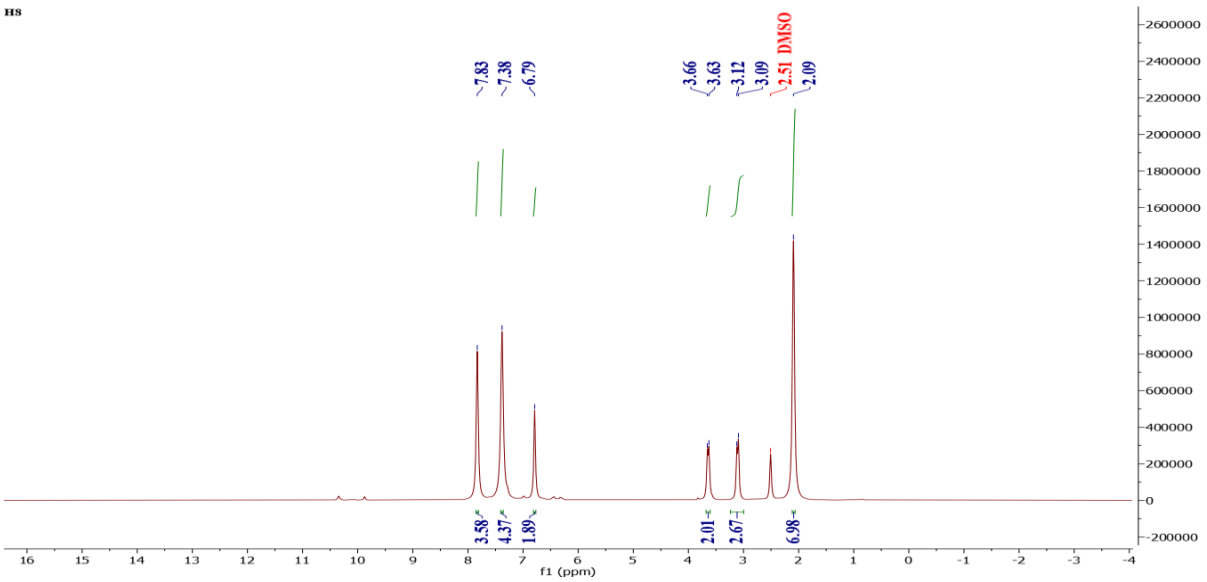


Figure (7): 1-H NMR spectra of the substance (H8).

Conclusions

Every time Schiff bases react with succinic anhydride, oxazepane-derived heptacyclic rings are the end product. Proton NMR spectroscopy, infrared spectroscopy, and spectroscopic equipment were used to verify the validity of the produced structures. Also, the compounds showed good efficacy against two different kinds of bacteria, both Gram-positive and Gram-negative.

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