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PREPARATION AND DIAGNOSIS OF SOME HETEROCYCLIC COMPOUNDS OF 2-THIOPYRIMIDINE AND STUDYING THE BIOLOGICAL EFFECTIVENESS OF SOME OF THEM

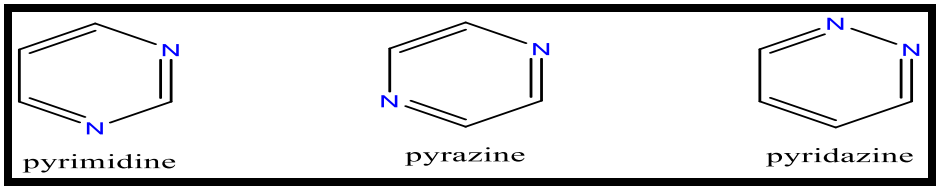
Nazhan Abdel Muhammad, Ayad Suleiman Hamad
Department of Chemistry - CollegeEducation for pure sciences – Tikrit Tikrit University – Iraq

Abstract: B This work includes the preparation of new derivatives of 2-thiopyrimidine compounds from the reaction of chalcone with thiourea through the basic environment.Chalcone was prepared by reacting equal moles of 1-methyl-2-acetylpyrrole with one of the aromatic benzaldehyde substituents using physical methods and spectroscopic analysis such as melting point, color, 1H-NMR, 13C-NMR, and FT-IR spectroscopy to ensure precision and accuracy. Validity of prepared vehicles. The biological activity was evaluated on two types of bacteria, Escherichia coli and Staphylococcus aureus.

Key words: 2-thiopyrimidine, biological activity.

Introduction:

Hexacyclic compounds in the form of 1,3-dipyrimidines consist of four carbon atoms and two nitrogen atoms, and the type of compound determines its location[1]. Two nitrogen atoms in the ring [2], depending on their location in the atoms



Some pyrimidine derivatives are used as drugs because pyrimidine rings are found in vitamin B, thymine, riboflavin, and folate [3]. It plays a major role in organic biochemistry and has a wide range of interesting biological activities [4]. Since the ring contains two nitrogen atoms, many pyrimidine compounds Pyrimidines display important biological and medicinal activities. Studies of the following compounds have shown high activity against certain types of fungi[5]

2. Experimental

2.1. Materials: All chemicals used throughout this work were purchased from Fluka, Aldrich, BDH.

2.2. Equipment used: Melting points were recorded using a measuring device melting point type: Automatic Melting Point\SMP40 and were not corrected. The reaction was traced by thin layer chromatography (TLC) using silica gel polygram plates as the stationary phase, and the spots were enhanced with iodine. The infrared spectrum was recorded using a Fourier transform infrared device with a KBr disk and a scale of (400-4000) cm-1 FT-IR-600. Nuclear magnetic resonance spectra (1H, 13C-NMR) of the prepared

compounds were measured in the laboratories of Santi Sharif University - Iran, using MS5973 Agilent Technology, Germany Bruker 500 MHz, at a frequency of 500 MHz, and using (DMSO-d) 6) as a solvent.

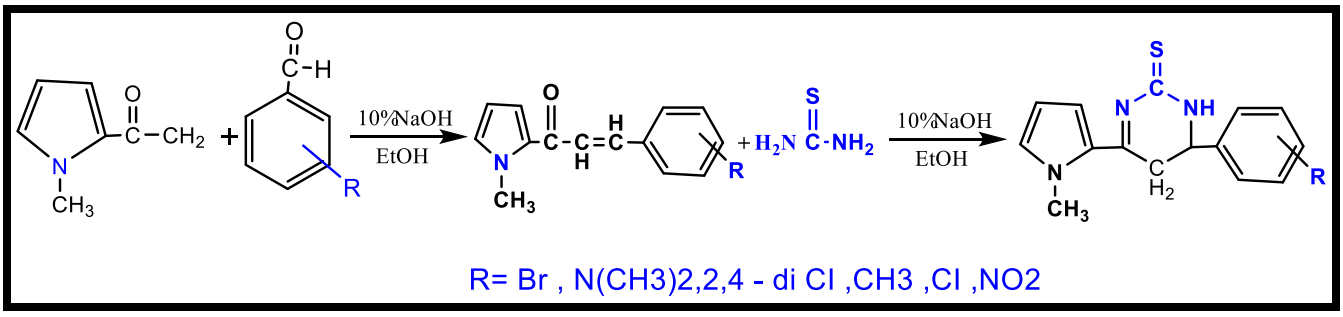
2.3. Prepared pyrimidine compounds [6] (N19Sh / N24Sh)

Equal moles (0.00081mole) of the prepared chalconate (N19Sh / N24Sh) were reacted with thiourea, where the chalconate was dissolved in (10ml) of sodium hydroxide solution dissolved in ethanol at a concentration of (10%), and it was left on the heat and stirring for (10) minutes. Then, the thiourea dissolved in (6ml) of ethanol was added to the reaction flask. The mixture rose for (5-6 hours)[6], and sediments of different colors and percentages were obtained, which were filtered, dried, and purified. The course of the reaction was traced using TLC plates, as shown in Table (1): Some physical properties of the compounds (N19Sh / N24Sh)

2.4. Antibacterial activity of the prepared compounds (N19Sh/N24Sh) The biological activity was estimated using the diffusion method. In contrast, biological activity was assessed by Kirby-Bauer action[7], where 0.1 ml of bacterial suspension was spread into old Mueller-Hinton dishes and left for 5 minutes to absorb the remainder[8][9]. After that, holes were prepared for each dish using cork purifier and (5) mm diameter for each hole (0.1) ml of solutions designed for the fourth hole using (DMSO) as a control sample, and the dishes were incubated for (24) hours at 37 o'clock [10, 11]. The diameters of the inhibition zone around each hole were measured in millimeters, based on the Prescott method [12,13].

3. Results and discussion

In this research, six compounds were prepared, including 2-thiopyrimidine derivatives (N19Sh/N24Sh) through the reaction of jacone derivatives with thiourea. 2-Thiopyrimidine derivatives were prepared by reacting equal moles of chalcones prepared in the first step with thiourea using (NaOH) as the basic medium and ethanol as the solvent, as shown in Scheme (1) and characterized by FT-IR, 1H-NMR, and 13C-NMR spectra.



Scheme (1): Prepared Vehicle Road (N19Sh / N24Sh)

3.1. Characterization of 2-thiopyrimidine (N19Sh/N24Sh)

It was confirmed that the reaction took place with 2-thiopyrimidine derivatives (N19Sh / N24Sh) by observing the changes in the physical properties of the melting point and the significant change in color. Likewise, 2-thiopyrimidine derivatives (N19Sh / N24Sh) were diagnosed by measuring the spectrophotometer Infrared (IR), 1H-NMR, and 13C-NMR.

The compounds (N19Sh / N24Sh) were identified using spectroscopic methods. The infrared spectrum showed the appearance of the stretch band of the N-H bond, which appears in the range (3325-3207) cm-1. Also, the appearance of a band belonging to the stretching of the sphincter (C=S) at the range (1056-1090) cm-1, in addition to the stretching of the sphincter (C=N), which appears at the range of 1664-1625)) cm-1. It was also observed that two absorption bands appeared at the range (1535-1591) cm-1 and (1406-1519) cm-1 are due to the stretching of the aromatic (C=C) bond, and the appearance of a band at (3071-3013) cm-

1 due to the stretching of the aromatic (C-H) bond, as well as the appearance of bands at (2823-2993) cm-1 is attributed to the stretching of the aphatic (C-H) bond. Also, the appearance of bands at (1201-1309) cm-1 is attributed to the stretching of the bond (C-N) [14]. It was found in the literature that these results were similar to those shown in the table. (2.(

The 13C-NMR spectrum of carbon showed the appearance of a signal at the site ppm (186.87) attributed to the carbon of the group (C=S), and the appearance of a signal at the site ppm (160.75) attributed to the carbon of the group (C=N). A signal appeared at the site ppm (54.74) attributed to the carbon of the (C-H) group of the pyrimidine, as well as the appearance of a signal at the site ppm (47.99) attributed to the carbon of the (C-H) group attached to the amine group, in addition to the appearance of signals at the site ppm (127.60-137.75) attributed to Carbons of the aromatic ring, and a signal at the ppm site (32.53) is attributed to the carbon of the (3CH) group of the five-point ring linked to the benzene ring, and the appearance of signals in the ppm range (39.10-40.77)[15] is attributed to the carbons of the solvent (DMSO-d6), and as shown in Figure(1)

When studying the 1H-NMR spectrum of the compound (N29Sh), it was observed that multiple signals appeared in the range (7.19-7.86) ppm attributed to the protons of the aromatic ring, and the appearance of a single signal at the location (2.83) ppm attributed to the proton of the (N-H) group. A triple signal in the range (3.32-3.35) ppm is attributed to the protonation of the aliphatic (C-H) group, as well as the appearance of a double signal in the sites (3.43, 3.44) ppm attributed to the protonation of the (CH2) group, [16] as well as the appearance of a signal in the site (3.91) ppm attributed to the protons of the (CH3) group, and the appearance of a signal at location (2.47) ppm attributed to the protons of the solvent (DMSO-d6), as shown in Figure.(2)

3.2. Evaluation of biological activity:

Some of the prepared compounds (N19Sh, N20Sh, N21Sh, N22Sh, N23Sh, N24Sh) were tested against different strains of bacteria: Gram-positive bacteria, Staphylococci, Staphylococcus aureus, and Gram-negative bacteria, Escherichia coli, by cup agar plate diffusion method [17,18]. Microbial cultures were incubated at 37°C for 8 h and diluted with 0.8% sterile saline. The concentration of the drug solution used in DMSO was kept at 100 **µ**g/ml. Amoxicillin was used as a control[19]. Biological activity was measured by measuring the diameter of bacterial growth inhibition around the disc used**.**

Table (1): Physical properties and elemental analyiss of the prepared compounds (N19Sh / N24Sh)

.Comp .No	R	Molecular Formula	.m.p C°	%Yield	Color
N19Sh	**Br-4**	**$C_{15}H_{14}N_3SBr$**	**175-177**	**63**	Yellow
N20Sh	**di $N(CH_3)_2$-4**	**$C_{12}H_{20}N_4S$**	**160-162**	**59**	Light Yellow
N21Sh	**diCl-2,4**	**$C_{15}H_{13}N_3SCl_2$**	**158-160**	**54**	Golden
N22Sh	**CH_3-4**	**$C_{16}H_{17}N_3S$**	**155-157**	**48**	Light Yellow
N23Sh	**Cl-4**	**$C_{15}H_{14}N_3SCl$**	**165-167**	**48**	Light Yellow
N24Sh	**NO_2 -4**	**$C_{15}H_{14}N_4SO_2$**	**162-160**	**61**	Dark Yellow

Table (2): FT-IR data for the prepared compounds (N19Sh/N24Sh)

Comp. No.	R	IR (KBr) cm^{-1}						
		νNH	**ν C-H Arom.**	**ν C-H Aliph.**	**νC=N**	**ν(C=C) Arom.**	**νC-N**	Others
N19Sh	**4-Br**	**3207**	**3032**	**2923 2850**	**1647**	**1562 1481**	**1201**	ν (C-Br) 688
N20Sh	**4-N(CH_3)$_2$**	**3325**	**3013**	**2933 2815**	**1664**	**1535 1443**	**1282**	ν (C-N) 1282
N21Sh	**2,4- di Cl**	**3276**	**3029**	**2927 2858**	**1645**	**1546 1461**	**1305**	ν (C-CI)740
N22Sh	**4-CH3**	**3298**	**3071**	**2925 2812**	**1649**	**1591 1419**	**1205**	…
N23Sh	**4-Cl**	**3225**	**3032**	**2923 2860**	**1625**	**1571 1406**	**1309**	ν (C-CI)811
N24Sh	4-NO_2	3320	3062	2945 2825	1641	1581 1415	1218	ν (N-O)1330

Table (3): Antibacterial activity of the prepared compounds (N19Sh/N24Sh) and the control antibiotic

COMP NO	*E.COLI mg/ml*			Staphylococcus aureus *mg/ml*		
	0.01	0.001	0.0001	0.01	0.001	0.0001
N19Sh	18	12	7	16	11	9
Sh20N	11	11	6	14	12	NIZ
Sh21N	14	14	9	19	16	8
Sh22N	17	12	6	19	18	7
Sh23N	17	13	8	16	13	6
Sh24N	20	17	9	18	14	7
Amoxicillin	18	11	9	19	19	9

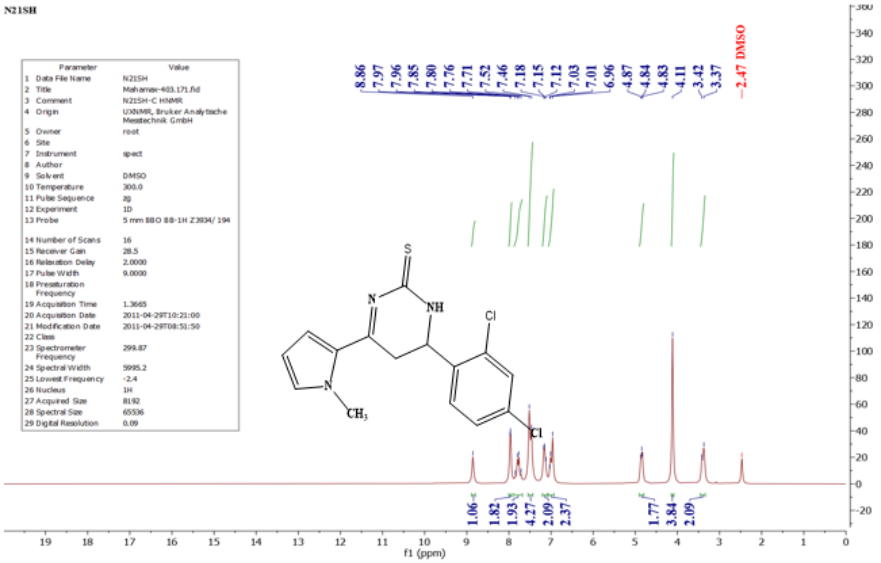


Figure (1): H-NMR spectrum of the compound (N21Sh)

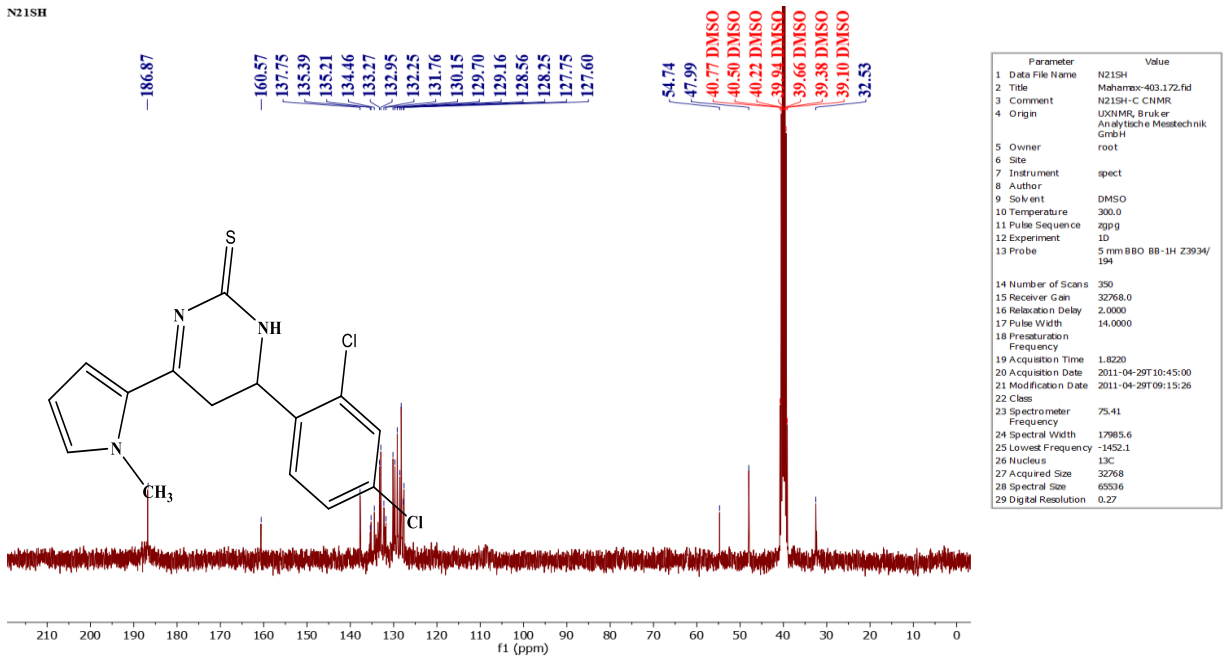


Figure (2): 13 C-NMR spectrum of the compound (N21Sh)

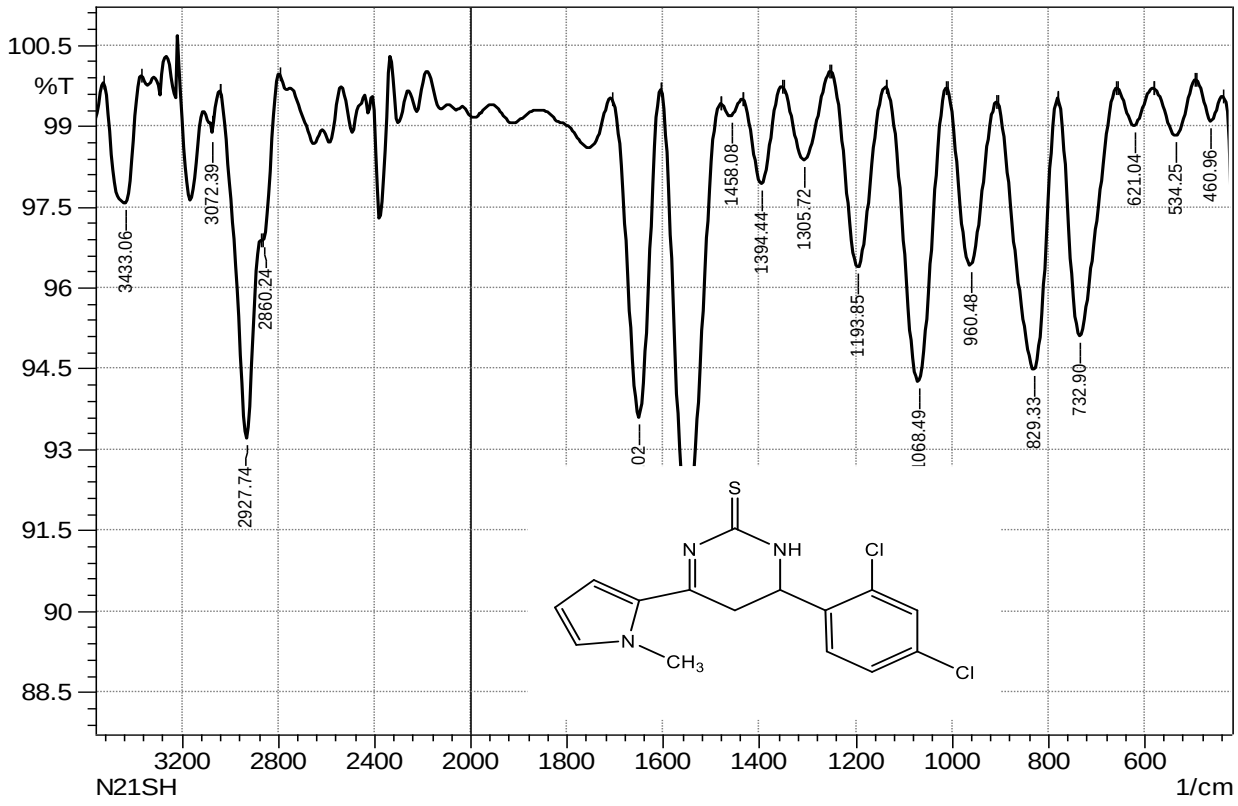


Figure (3): IR spectrum of the compound (N21Sh)

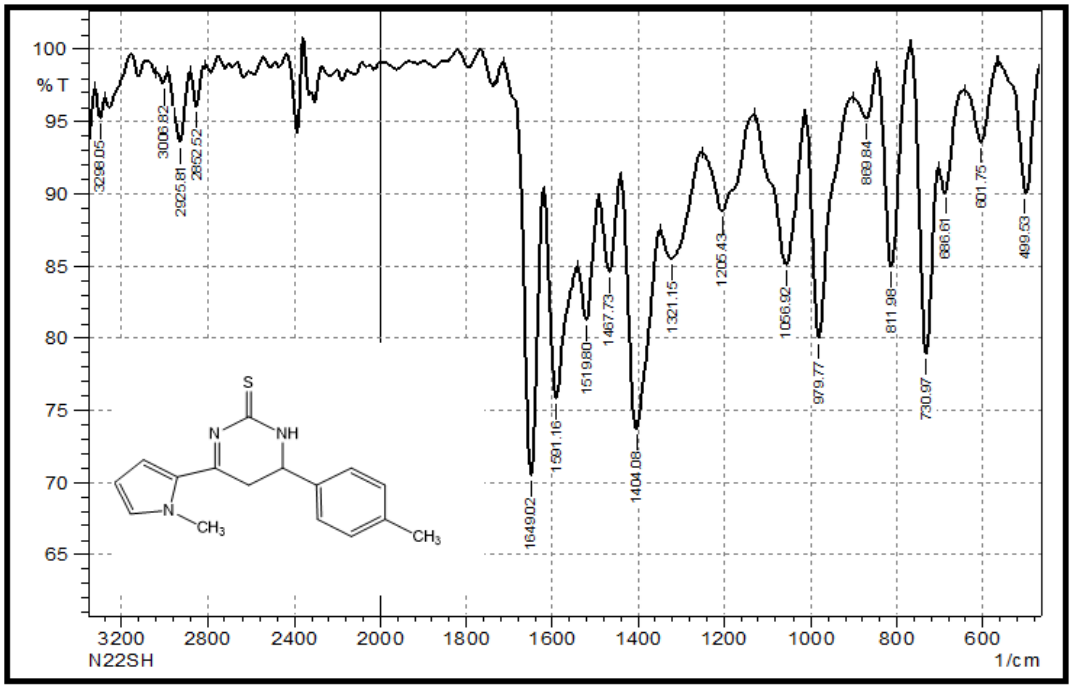


Figure (4): IR spectrum of the compound (N22Sh

4. Conclusions: The accuracy and validity of the prepared compounds were confirmed through spectroscopic and physical measurements, where infrared spectra accurately confirmed the presence of active aggregates, and this confirmation was increased by 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 decompose 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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