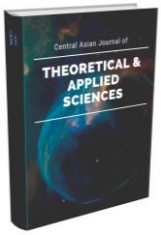

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Article

Preparation and Characterization of Tetrazole Derivatives Derived from Schiff Bases and Evaluation of Biological Activity

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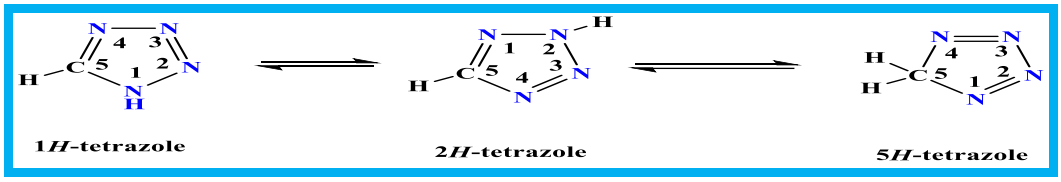
Abstract: This study included the preparation of heterogeneous pentagonal rings derived from tetrazole ring by reacting Schiff's radicals derived from 6-methyl-2-uracil and using them as nuclei in the preparation with sodium azide using tetrahydrofuran solvent. The compounds were confirmed using physical measurements such as color, melting point, and product percentage. Spectroscopic measurements, such as the infrared spectrum and nuclear magnetic resonance spectrum, were also used to determine the composition of the compound. The effectiveness of some of these compounds was also tested against two types of Gram-positive and Gram-negative bacteria using amoxicillin as an antibiotic.

Keywords: Heterocyclic, Tetrazole, Biological Activity

1. Introduction

Heterocyclic Most therapeutic substances contain nitrogen-atom-containing molecules. Tetrazole derivatives are important because they have a wide range of actions, good pharmacokinetics, minimal toxicity, and pharmacodynamics [1]. The vast range of biological activity shown by fused heterocyclic compounds, such as tetrazole, has recently garnered significant interest. This is because of their significance, their potent biological activities that have a solid place in heterocyclic chemistry, and their synthetic medicinal and pharmacological activities. Numerous dyes and pigments have heterocyclic rings and, low toxicity and pharmacokinetic and pharmacodynamic qualities. They may also be utilized as corrosion inhibitors and optical brighteners [2]. Tetrazole is a heterocyclic five-membered compound containing one carbon atom and four nitrogen atoms. The molecular formula CH2N4 has the following three isomers [3]:



These compounds are considered to be the most vital cyclic compounds. Because they contain four pairs of free electrons, equivalent to four nitrogen atoms, they are one of the compounds that excite electrons [4]. Previous studies have shown that tetrazole compounds and their derivatives are of great importance in the medical field, especially in the biological field. They exhibit antimicrobial activity [5], antifungal activity [6], and antiviral activity [7].

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2. Materials and Methods

Chemicals Used

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

Preparation of Tetrazole derivatives (30-38).[8]

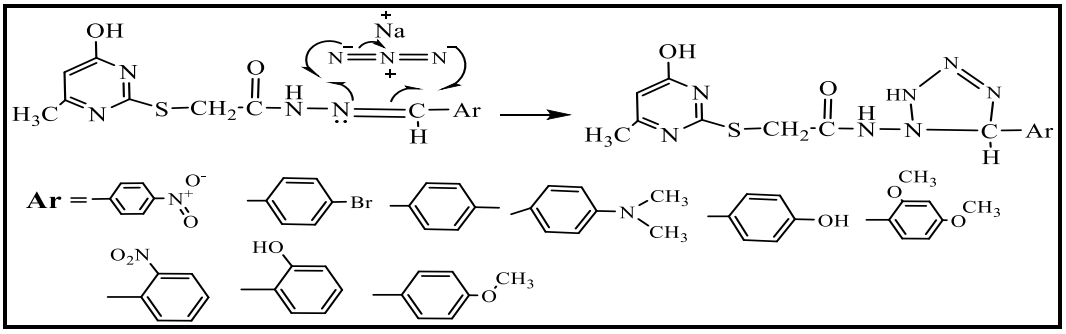
Compounds were generated by treating Schiff bases in THF as a solvent at (55-600C) with sodium azide. Biologically active chemical molecules with a wide range of functions are 2,5-dihydrotetrazoles. As [3+2] cycloadditions, the reaction mechanism was systematically studied and named 1,3-dipolar cycloadditions. It involved the combination of a 1,3-dipolar - a molecule with resonant contributions where positive and negative charges are present at the 1,3 position concerning each other - with unsaturated, polar-loving systems. The result of the addition is a five-membered ring. As shown in Table 1,

Biological activity study

Two colonies of pure bacterial isolates of both Gram-positive and Gram-negative bacteria were transferred from the solid culture medium to test tubes containing (5 ml) distilled water using heat-sterilized holders. The tubes were incubated at 30°C[9-11]. (37°C) for (16-20) hours and then diluted with the physiological solution until the turbidity reached standard turbidity levels to obtain a cell count of approximately (1.5×108) cells/ml. Chemical solutions of some of the prepared compounds were prepared using dimethyl sulfoxide (DMSO) solvent at three concentrations of each substance: (0.01, 0.001, 0.001) mg/ml, and (0.1) g of each solid derivative was dissolved in (10) ml of (DMSO) to obtain a concentration of (0.01 mg/ml) then remove (1 ml) of the solution with a concentration of (0.01 mg/ml) and add (9 ml) of (DMSO) solvent to obtain a solution with a concentration of (0.001 mg/ml), then remove (1 ml) of the solution with a concentration of (0.001 mg/ml) and add (9 ml) of (DMSO) solvent to it to obtain a solution with a concentration of (0.0001 mg/ml)[12-15].

3. Results

Tetrazole derivatives were prepared according to the following scheme:



Scheme 1. Path of the Ready Compounds (30-38)

Characterization of Tetrazoe Derivatives (30-38)

FT-IR(KBr) : (3168-3487) ν (NH-OH), (1643-1685) ν (C=O), (1564-1641) ν (C=N), (1411-1510) ν(N=N), (1099-1201) ν (C-N), (3010-3091) ν(Ar C-H), (2927-2958) ν(C-H) aliph.As shown in Figures (1) and Table (2).

1H-NMR (DMSO-d_6) δ\(PPm) comp (31): (2.06) (s, CH_3), (3.01) (s, CH_2), (3.29) (s, CH) tetrazole, (3.50) (s, NH)tetrazole, (5.43) (s, =C-H) , (6.70-7.95)(m,Ar-CH) ,(8.50) (s, NH), (12.07) (s,OH) .as shown in Figure (2).

1H-NMR (DMSO-d_6) δ\(PPm) comp (33): (2.04) (s, CH_3), (3.01) (s, N-(CH_3)$_2$) , (3.43) (s, CH_2), (3.73) (s, CH)tetrazole, (5.00) (s, NH)tetrazole, (5.43) (s, =C-H) , (6.70-7.95)(m,Ar-CH) ,(8.50) (s, NH), (11.50) (s,OH) . as in Figure (3).

13C-NMR (DMSO-d_6) δ\(PPm) comp(31): (28.99) (CH_3), (35.76) (CH_2) , (100.81) (CH)tetrazole, (111.59-159.80)(,Ar C=C), (163.40,166.75) (C=N) ,(175.08)(C=O), as seen in Figure (4).

13C-NMR (DMSO-d_6) δ\(PPm) comp (33): (24.75) (CH_3), (35.84) (CH_2),(61.95) (N-($\underline{C}H_3)_2$), (100.78) (CH)tetrazole, (111.59-152.67)(,Ar C=C), (159.80,166.75) (C=N) ,(175.17)(C=O), as seen in Figure (5).

Evaluation of the Biological Activity of Prepared Compounds

The effectiveness of the prepared compounds against bacteria was tested using the agar well diffusion method (153). After inoculating the bacterial isolates in the culture medium, holes were made in the Petri dishes using the cylinder measuring method (according to USP 35)[17-20]. Using a drill: Place the compounds (40 µl) prepared at three concentrations in each well and incubate the dish at (37°C) (24 hours) before taking the results. Readings are taken after (24) hours and (48) hours to indicate the sensitivity of the derivatives used, which depends on the inhibitory diameter shown in the Petri dish surrounding the wells used, as an increase in the inhibitory diameter means an increase in the inhibitory diameter[21-25]. The inhibitory diameter of the prepared compounds was compared with the inhibitory diameter of the standard antibiotics. Standard antibiotics were used as solutions, with amoxicillin as a control sample, based on the materials and rules used in the laboratories of the Ministry of Health. WHO test [26-30]

Table 1. Some Physical Properties of For Prepared Compounds (30-38)

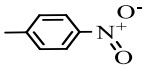
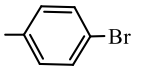
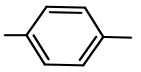
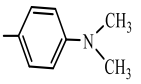
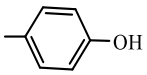
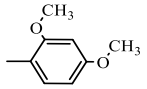
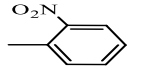
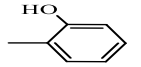
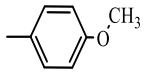
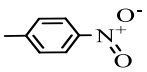
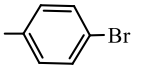
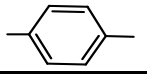
Comp. No.	Ar	Yield%	m.p.^{0}C	Color
30		**75**	**223-225**	**White**
31		**60**	**238-240**	**Off white**
32		**55**	**250-254**	**Yellow**
33		**69**	**260-261**	**brown**
34		**72**	**258-261**	**white**
35		**59**	**280-283**	**orange**
36		**66**	**270-273**	**red**
37		**52**	**266-268**	**Yellow**
38		**70**	**261-263**	**Yellow**

Table (2). FT-IR Absorption Results for Prepared Compounds (30-38)

Com No.	Ar	FT-IR(KBr), spectral data ✾cm^{-1}							
		C=N Thiour.	C-H Aro.	C-H Ali.	N=N	C-N	C=O	O –H	Others
30		1641	3080	2958	1450	1099	1672	3427	(NO_2)1512,1338 (N-H)3380
31		1600	3035	2958	1411	1130	1666	3417	C-Br 632 C-O1180
32		1564	3030	2927	1456	1135	1649	3407	N-H3355 C-O1269

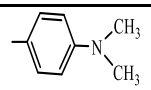
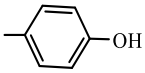
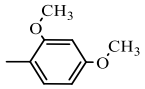
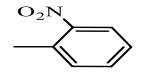
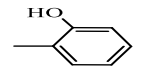
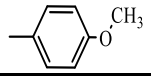
33		1602	3016	2952	1485	1130	1660	3450	C=C1573 N-N1058
34		1581	3012	2931	1442	1168	1678	3425	C=C1600 C-O1060
35		1608	3010	2937	1506	1112	1670	3433	N-N1029 C-O1207
36		1591	3032	2929	1438	1201	1643	3384	(NO_2)1525,1353 (N-H)3460
37		1610	3060	2947	1438	1149	1665	3168	N-N1064 N-H3390
38		1631	3091	2956	1510	1172	1685	3487	N-H3386 C-O1251

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		
	0.001	0.01	0.1	0.001	0.01	0.1
Mh6	10	12	15	5	5	10
Mh7	12	12	17	-	5	10
Mh8	-	5	5	10	15	17
Mh9	5	10	12	11	15	20
Mh10	3	8	12	8	14	19
Amoxicillin	15	20	23	14	19	25

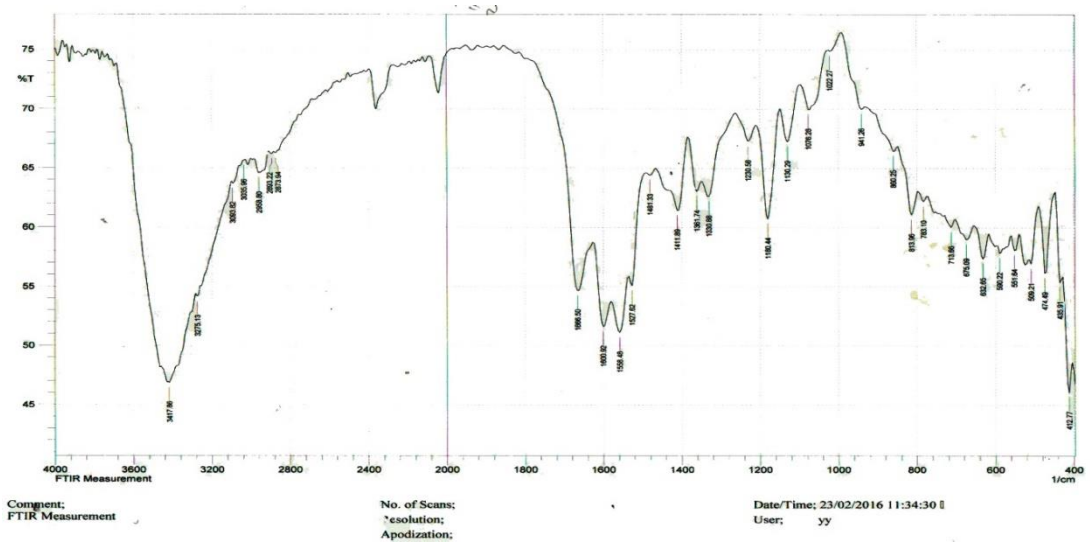


Figure 1. The compound's FT-IR spectra (31).

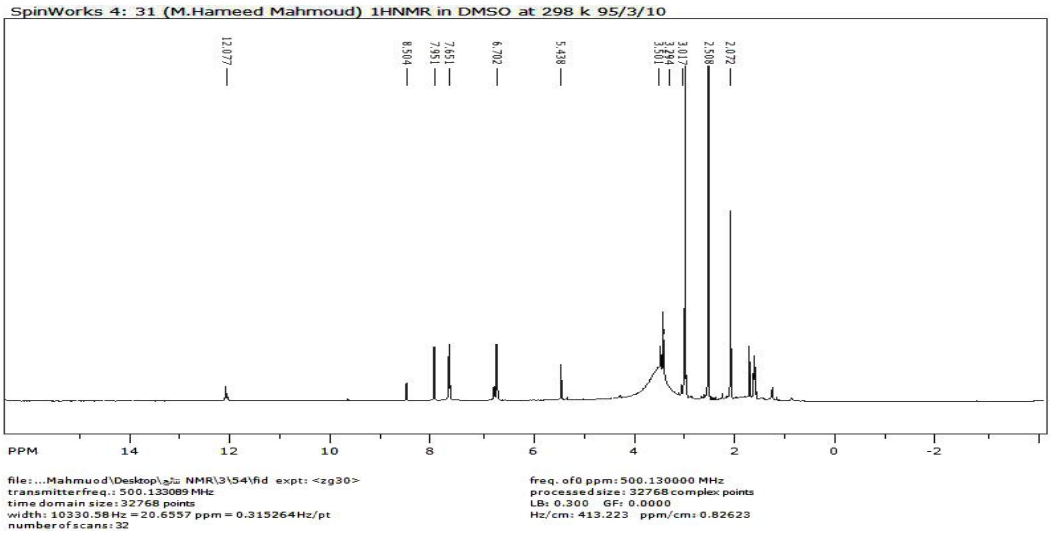


Figure 2. 1-H NMR Spectra of the Substance (31)

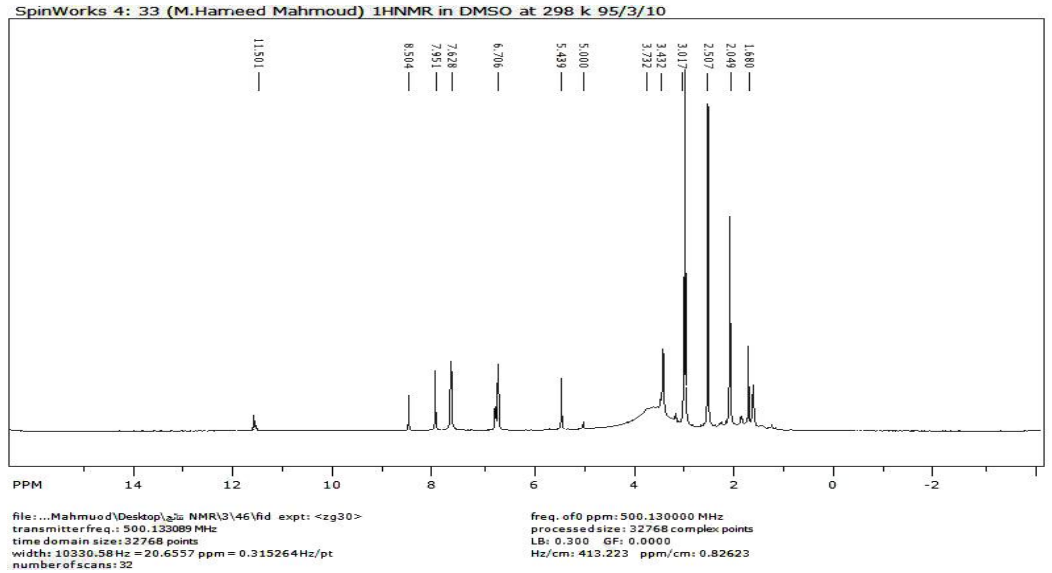


Figure 3. 1-H NMR Spectra of the Substance (33)

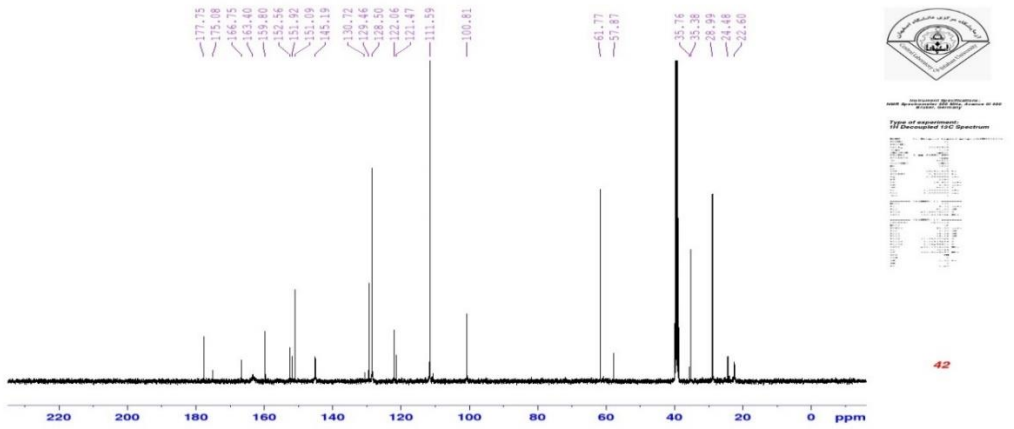


Figure 4. 13C NMR Spectra of the Substance (31)

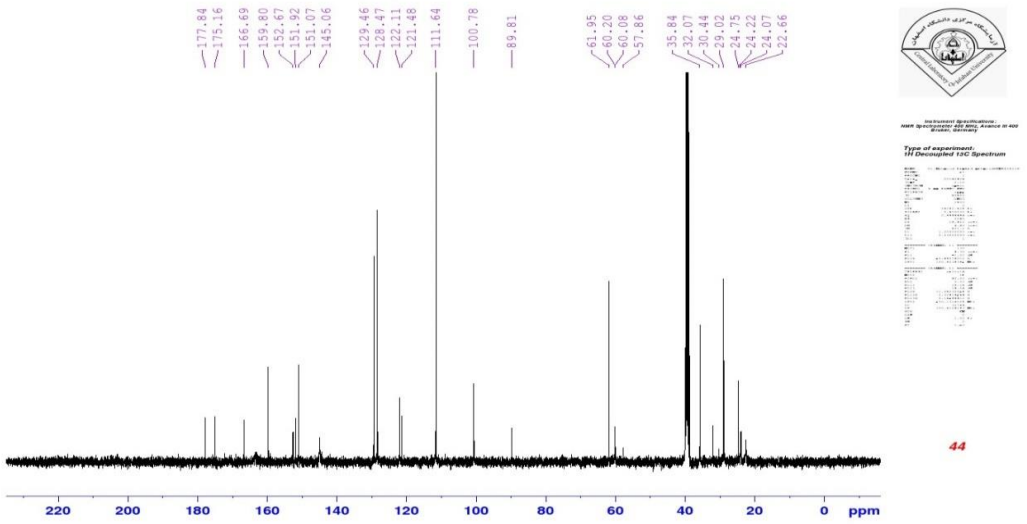


Figure 5. 13C NMR Spectra of the Substance (33)

4. Conclusion

The reactions of (C=N) with sodium azide always give five-membered rings called tetrazoles. The measurements used, including infrared spectra and nuclear magnetic resonance spectra, have proven the validity of these structures. The compounds measuring biological activity also gave good activity against the bacteria used.

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