Original Article

Synthesis, Characterize and Antibacterial Evaluate of Some Novel Compounds Containing 1,3,4-thiadiazole

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Abstract

Preparation of 1,3,4-thiadiazol derivatives from the benzoic acid reaction with the thiosimicarbazide in the presence of ($POCl_3$) and (KOH) to give compound [I]. The purified product was reacted with o-hydroxy naphthaldehyde to form the azo compounds [II]**,** After that we reacted the compound [II] with different aromatic Amines to give Schiff base compounds [III]a-i.

All these compounds have been characterized based on F.T-IR, and some of them based on 1H-NMR, 13C-NMR, MP techniques, and The Biological effectiveness of part of them has been studied.

Keywords: 1,3,4-thiadiazole, Antibacterial.

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INTRODUCTION

Heterocyclic compounds can be found in a plenty of products[1], piments, and drugs. They form important structural units in synthetic pharmaceuticals and agrochemicals. Efforts have been provided to develop new successfully synthetic methods for these compounds[2].

Heterogeneous rings may contain one different atom, such as pyrrole, furan, pyridine and thiophane, or two heterogeneous atoms, such as imidazole, which contains two nitrogen atoms, as well as an oxazole ring containing nitrogen atom and oxygen, as well as carbon.

Thiadiazoles, affiliated to the classes of nitrogen–sulfur Heterogeneous rings with lots of application as structure of biologically actively molecules and as beneficial compounds in medical chemistry. The activity of the thiadiazols is proved by the drugs that used.

1,3,4-Thiadiazoles and certain of their derivatives are thoroughly studied because of their broad spectrum of medicinal activities. [3]. Compounds include thiophene and 1,3,4-thiadiazole skeletons have become interesting cyclic compounds, especially in medical chemistry [4]. The general formula of thiadiazol is $C_2H_2SN_2$ and it is found in nature in four different forms depending on the location of nitrogen and sulfur atoms.and these forms are: 1,2,3-Thiadiazole, 1.2.4-Thiadiazole,1,2,5-Thiadiazol and1,3,4- Thiadiazol.

1,3,4-Thiadiazol

1,3,4-Thiadiazol is very important In the pharmaceutical[5] and industrial field It was found to be anti-depressant, Anti-cancer and antimicrobial, Painkillers [6],and this what encouraged researchers to study it[7]. The 1,3,4-thiadiazole ring system has many substances with antibacterial, amebicide, Anti-corrosion[8][9], parasiticide and antifungal activities[10] [11]. The first to discover 1,3,4-Thiadiazole in the world was the scientist Emil Fischer in 1882 [12], the most thermally stable isomers are 1,3,4-Thiadiazole and their stability is generally controlled by electron density in atoms C2 and C5, Which is largely dependent on Compensation [13], stability of 1.3.4- Thiadiazol is particularly enhanced by alkyl and ariel Compensator in positions 2 and 5.

Azo dyes

Azo dyes constitute one of the biggest, various, and significant classes of organic compounds with a scope of uses in sci and tech [14][15]. An azo coupling is an organic reaction usually outcomes between a diazonium compound and other aromatic compound that result an azo band (-N=N-). [16][17]. More than ten thousand dyes were synthesized and used by the end of the 19th century[18].

EXPERIMENTAL

Material and methods

The starting materials were pure from sigma and BDH, and they were used for the preparation of the compounds that has been synthesized, all the chemicals, reagents and solvents were from synthetic grade and were bought commercial,Melting points were been measured by Stuart-SMP3 electronic system, SHIMADZU (FT-IR 8400S) was used to record the FT-IR spectrum was, while ^{1}H and ^{13}C-NMR spectrums were recorded by Bruker (500MHz), DMSO-d_6 was the solvent and TMS was the reference, To ensure the completion of reaction TLC technique was used, the spots were visualize by using UV Cabinet for TLC.

Synthesis compounds (I)[19]

(10 mmol, 5mL) of $POCl_3$ were added carefully and thoroughly to a mix of (10 mmol) of benzoic acid and (0.95 g, 10 mmol) from thiosemicarbazide, and refluxed for 3 hrs. After chill down the reaction mixture we add (25 mL) of distil water by dropping wisely and carefully, and then reflux it for four hrs. The mixture chilled down and then we will do neutralization by potassium hydroxide solution, and the gained deposition was liquidated, and rinsed with distil water, and dried. The compound was recrystallized with ethanol. The accomplish of the reaction and purity of acquired product were tested by TLC mobile phase (hexane: ethyl acetate) (7:3) percentage (V: V).

This compound has the formula(C8H7N3S) and it's M.W is 177.23 with a pale brown color and 196.5° C and yield Percentage about 85%. FTIR by (Cm^{-1}) 3269 and 3189 (NH_2), 3089(C-H, aromatic), 1628(C=N), 1585 and 1480 (C=C, aromatic).), ^{1}H-NMR (DMSO- d6, 500MHz) 7.49- 8.11 (m, 8H, Ar),7.22 (s, 2H.NH_2). ^{13}C-NMR (DMSO- d6, 125MHz) 133.35-141.82 (Ar-rings), 165.91 (C-N), 180.58 and 174.35 (1,3,4-thiadiazole,, C=N)

Synthesis of compounds (II) [11]

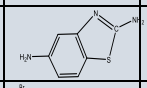
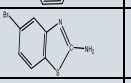
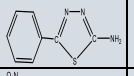
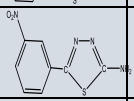
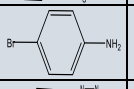
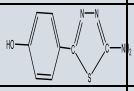
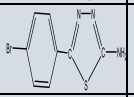
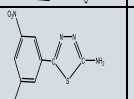
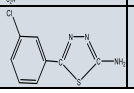
Dissolve (1.78 mmol) from compounds (I) in (8 mL) of 85% H_3PO_4 by heating with stirring, we added The nitrate and 4mL of concentrated HNO_3 to the solution with fast stirring and keeping the temperature under 5 °C in 10 mints. Then we made a mixture of 2-hydroxynaphthaldehyde (1.79 mmol, 0.18 g in 2.5 mL of ethanol) were added by dropping with stirring. The solution was spilled into (80 mL) of iced-water. The obtained deposition was filtered, and rinsed with chill water multiple times, and dried. The accomplish of the reaction and purity of acquired product were tested by (TLC) technique mobile phase (hexane: ethyl acetate) (7:3) percentage (V: V).

This compound has the formula ($C_{19}H_{12}N_3S$) and its M.W is 314.38 with a dark orang color and 81.5° C M.P. and yield Percentage about 85%.FT-IR spectrum of this compound showed the disappearance of the N-H frequency near (3070 and 3023 cm-1) of (NH2) and the appearance of a broad beam near (3441 cm-1) belong to the O-H and a peak near (1641 cm_-1) belong to C=O and N=N frequency near (1465 cm_-1), ^{1}H-NMR (DMSO- d6, 500MHz) 7.3- 8.95 (m 10 H, A r), 9.10 (s 1H, OH), ^{13}C-NMR (DMSO- d6, 125MHz) 109.49-149.80 (Ar-rings), 165.89 (C - OH), 181.60 and 159.44 (1,3,4-thiadiazole C=N).

Synthesis of Schiff base derivatives (III_{a-i}) [20]

We solved (10 mmol,0.2 g) of the aldehyde in (Ethanol 5 ml) and added 5-7 drops of glacial acetic acid, put (0.2g) of the Amen in a round flask and then poured the mixture of aldehyde into the glass round flask and reflects in a water bath for 4 hours.

Table (1) physical properties of the prepared compounds

Comp No.	G	Molecular formula	M.wt	Color	M. P (° C)	Yield %
III_a		$C26H_{16}ON_7S_2$	506.58	Dark Yellow	167-171	81
III_b		$C_{26}H_{15}BrN_6OS_2$	571.47	Yellow	165-168	80
III_c		C27H17N7OS$_2$	519.6	Orange	144-147	85
III_d		C27H16ClN7OS$_2$	554.05	Dark Yellow	108-112	83
III_e		C25H16BrN5OS	514.4	Dark Red	110-112.5	89
III_f		C27H16N7OS$_2$	615.51	Brown	179-182	82
III_g		C27H16N7OS$_2$Br	598.5	Dark Yellow	158-161	85
III_h		$C_{27}H_{16}ON_7S_2Br$	609.6	Dark Brown	117-120	83
III_i		$C_{27}H_{16}O_3N_8S_2$	564.6	Brown	80-82	82

FTIR (III_a) infrared spectrum showed an absorption pack at (3051 cm-1) belong to the C-H aromatic band stretch, while the frequency of the C=N appears at (1620 cm-1) and two absorption packs belong to the C=C aromatic beam at (1558, 1465 cm-1) and absorption packs at (3417cm-1) belong to O-H. ^{1}H-NMR (DMSO- d6, 500MHz) 6.08- 8.48 (m, 14H, Ar), 8.68 (s, H, OH), 931(s1H, C=N), ^{13}C-NMR (DMSO- d6, 125MHz) 119.53-140.80 (Aromatic), 155.89 (C - OH), 174.60 and 166.36 (1,3,4-thiadiazole C=N).

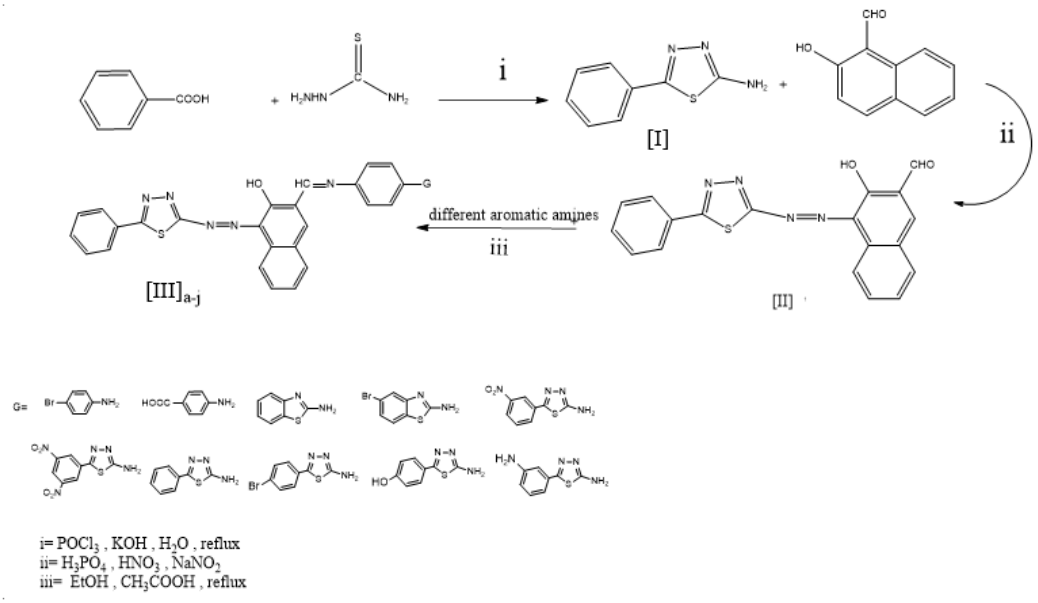
Table (2): Demonstrates gentle infrared absorption packages

FT-IR for compounds (III_{a-i})

Comp. No.	Characteristic stretching bands of FT-IR (cm^{-1}, KBr disc)			
	O-H	Ar.C-H	C=N	Ar.C=C
III_a	3417	3051	1620	1558
III_b	3464	1620	1579	1479
III_c	3410	3078	1635	1597
III_d	3564	3070	1627	1527
III_e	3417	3024	1620	1558
III_f	3448	3009	1620	1543
III_g	3410	3055	1620	1496
III_h	3417	3124	1674	1597
III_i	3410	3024	1635	1597

RESULTS AND DISCUSSION

The steps of the reaction for the different compounds for the title were in the equation below, the compound of 2-Amino-5- phenyl-1,3,4-thiadiazole (I) was produced, from the reaction of benzoic acid with thiosemicarbazide in existence of $POCl_3$; the FT-IR of this compound was showing two bands of the of NH_2 stretching with in (3397-3180) cm^{-1} and the stretching for C=N in (1620-1639) cm^{-1}. 3-hydroxy-4-((5-pheny-1,3,4-thiadiazol-2-yl)diazinyl)-2-naphthaldehyde was prepared by the reaction of 1,3,4-thiadiazole derivative (I) with H_3PO_4, HNO_3, $NaNO_2$ and m-naphthol by using ethanol as a solvent, this compound has shown dispersing of stretch of N-H of NH_2 of 1,3,4-Thiadiazole and has shown a broad band belong to the stretching of O-H (3441cm^{-1}), and apeac near (1641 cm_-1) belong to C=O, and stretching of N=N in rang (1465cm^{-1}).Preparation and characterization of Schiff base derivatives (III_{a-i})[20] by adding (10 mmol,0.2 g) of the 2-hedroxynaphthaldehyde in the solvent (Ethanol 5 ml) and added 5-7 drops of glacial acetic acid, put(0.2g)of the Amen in a round flask and then poured the mixture of aldehyde into the glass round flask and reflects in a water bath for 4 hour.



Scheme (1) reactions process for the prepared compounds

Table (3) Antibacterial activity of synthesized compounds measured with mm

Microorganism / Tested materials	*E. coli*			*S. aureus*		
	100%	*50%*	*25%*	*100%*	*50%*	*25%*
III_b	12	R	R	13	11	R
III_d	14	11	R	17	15	15
III_e	12	11	R	13	12	11
III_g	10	10	R	12	11	11
III_h	15	13	R	16	15	13

Antibacterial activity

The treatment of infection illnesses is a big confrontation,

because of multiple factors, comprise bacterial resist to antibiotics. the produced chemicals were screened averse Ge^{-ve} and Ge^{+ve} bacteria insulate. The results showing in table 3 showed the examine of the antibacterial activity of several properad compounds in three concentrations (100, 50, 25) mg/mL, and showed mild to good activity. we tested The antibacterial activity of the properad compounds against one type of Gram positive bacteria isolates (*S. aureus)* and against one type of Gram negative bacteria isolates (*E.coli*). According to table 3 all peers showed a good activity against (*S. aureus)* and the major active compounds were, III_d, III_h. While all peers showed medium activity and, in some concentrations, didn't show activity because of position and kind of substituted group. All analogs especially, IIId, III_h showed a good activity and in low concentrations didn't show any activity against *E. coli* because of position and type of substituted group.

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