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Synthesis of 2-Amino-5-(Substituted Phenyl)-1, 3, 4-Thiadizole And Evaluation of Biological Activity

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ABSTRACT

The Thiadiazole & their derivatives have shown the number of pharmacological activity as antimicrobial, anti-inflammatory activity, antitubercular activity, ant diabetic activity, diuretics, antidepressant and cytotoxic activity. These thiadiazoles are the heterocyclic compound which contains the five member ring & nitrogen & sulphur.

Keywords: Schiff's bases, thiosemicarbazide, phosphorus oxychloride, 1,3,4-thiadizole.

INTRODUCTION

A heterocyclic compound is that which contain more than one kind of atoms if ring are only made up of the carbon atoms than that are called the homocyclic compounds but the heterocyclic ring contain more than one compounds as nitrogen, oxygen or sulfur for example, pyrole, furan, thiophene. during the recent year that has been found there are number of thiadiazole which contain the nitrogen in different position as 1,3,4-thiadaizole & 1,2,3-thiadiazole & 1,2,4- thiadiazole, and 1,2,5-thiadiazole etc. and the basic ring 1,3,4-thiadiazole are the fused heterocyclic ring compound have many biological activities as antimicrobial activity, anti inflammatory, anti fungal, antibiotic, diuretic, anti depressant etc have many example which shown these activity as acetazolamide (diuretic) sulfamethiazole (antibacterial) ceftazolene (antibiotic) atibeprone (anti-depressant) etc. In view of the standard reference work shows that more work has been carried out on the 1,3,4-thiadiazole than all other isomers combined. Members of this ring system have found their way into such diverse application as pharmaceuticals, oxidation inhibitors, cyanine dyes and metal complexing agents. The literature review showed that the thiadiazole nuclei have antimicrobial, anti-inflammatory, anticancer, anti tubercular, antifungal, analgesic, oxidative inhibitors, anti H-pylori, etc.

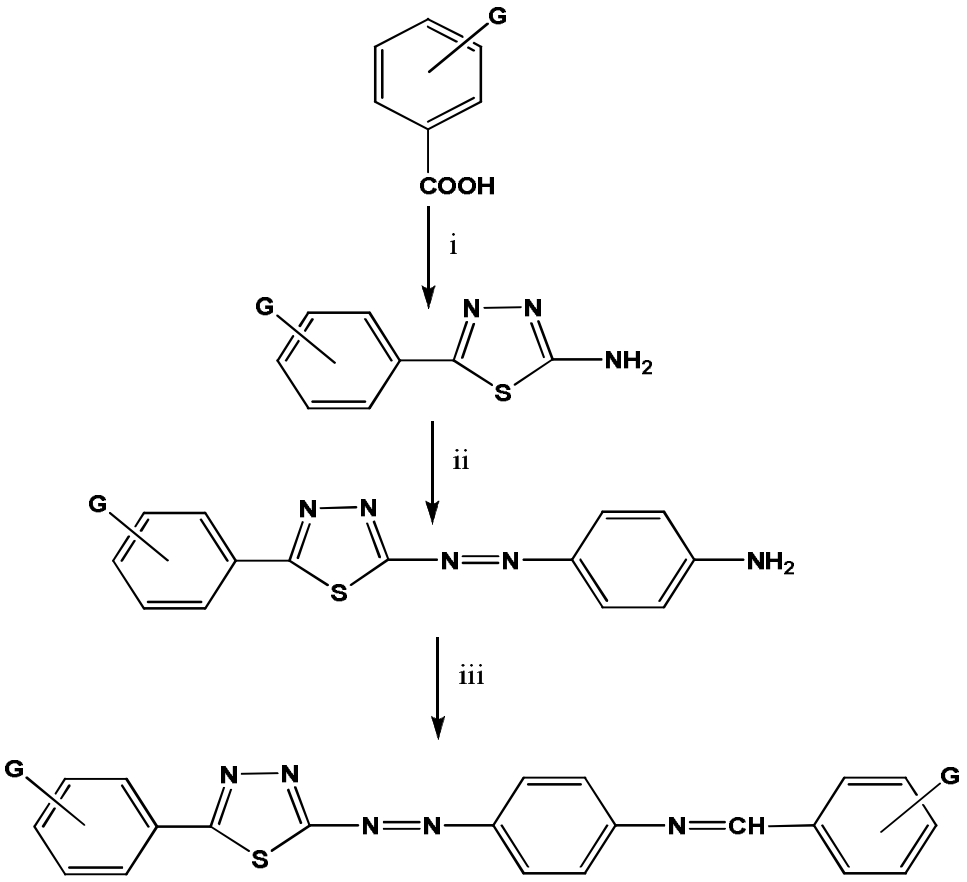
MATERIALS AND METHODS

Synthesis of 2-amino-5-(substituted phenyl)-1, 3, 4-thiadizole: A mixture of appropriate substituted benzoic acid (0.01mol) and (0.91g ,0.01 mol) of thiosemicarbazide with 5mL of phosphorus oxychloride was refluxed gently for 5 h. After cooling 50mL of water was added, the mixture was then refluxed for 7h and filtrated, neutralized with potassium hydroxide. The Precipitate was washed with water and

recrystalized from (ethanol-water) to give the titled compounds. The physical properties of the synthesized 1, 3, 4-thiadiazole derivatives are listed in table 3.

Synthesis of 4-(-5-substituted phenyl-1,3,4-thiadiazol-2-yl-diazenyl) aniline: 2-amino-5-(substituted phenyl)-1,3,4-thiadizole (0.01mol) was dissolved in slightly acidified distilled water, to it a mixture of (HCl and $NaNO_2$) (0.01 mol) was added and the reaction was occupied in ice bath, then aniline 0.01 mol was added, a bright yellow precipitate was formed and filtered and characterized using H^1-NMR spectroscopy.

Synthesis of 1-(-5-substituted phenyl-1,3,4-thiadiazol-2-yl-diazenyl)-4-(substituted benzylidene amino) benzene: 4-(-5phenyl-1,3,4-thiadiazol-2-yl-diazenyl) aniline (0.01mol) was dissolved in refluxed absolute ethanol (50 ml), benzaldehyde (0.01 mol) was slowly added to the refluxed mixture, the net mixture was refluxed for 8 h with stirring, the reflux was completed for another 2h until no more precipitate formed, after cooling to room temperature the mixture was filtered and the precipitate was dried and recrystalized from ethanol, the percentage yield was 66%, the melting point of the target molecule was measured and found to be 196^oC.



RESULTS AND DISCUSSION

Table 1. The FTIR (KBr cm^{-1}) spectral data (stretching vibrations) for the compounds (A-K).

G	Compd.	O-H	C-H aromatic	C-H aliphatic	C=N	N=N	C=C aromatic
H	A	-	3100		1625	1570	1605
p-Cl	B	-	3060		1620	1585	1557
p-Br	C	-	3070		1622	1598	1570
p-OCH_3	D	-	3020	2996-2875	1620	1622	1569
p-NO_2	E	-	3600		1619	1628	1501
p-OH	F	3290	3100		1620	1618	1587
m-Cl	G	-	3045		1630	1575	1537
m-Br	H	-	3055		1637	1580	1550
m-OCH_3	I	-	3120	2986-2905	1629	1592	1600
m-NO_2	J	-	3100		1624	1626	1581
m-OH	K	3350	3025		1620	16198	1528

Table 2. The ^{1}HNMR for the Some compounds

G	Compd.	Chemical shift ppm
p-Cl	B	(7.41– 8.02) benzen (6.65-6.92) benzylidineimin (N-CH) 8.39 (7.52-7.83) benzene
p-OCH_3	D	Methoxy 3.83 (7.05–7.68) benzen (6.65-6.92) benzylidineimin (N-CH) 8.39 (7.06-7.84) benzene
p-NO_2	E	(8.05–8.32) benzen (6.65-6.92) benzylidineimin (N-CH) 8.39 (8.9-8.33) benzene
p-OH	F	Hydroxy 5.35 benzen (6.66-7.68) benzylidineimin (6.65-6.92) (N-CH) 8.39 (6.66-7.88) benzene
m-OCH_3	I	Methoxy 3.83 (6.91–7.59) benzen (6.65-6.92) benzylidineimin (N-CH) 8.39 (7.02-7.46) benzene
m-OH	K	Hydroxy 5.35 benzen (6.66-7.68) benzylidineimin (6.65-6.92) (N-CH) 8.39 (6.66-7.88) benzene

Table 3. The physical properties of the compounds (A-K).

G	Compd.	M.P.(^{o}C)	% Yield	IUPAC Name
H	A	133	71	N-benzylidene-4-((5-phenyl-1,3.4-thiadiazol-2-yl)diazenyl)aniline
p-Cl	B	157	64	N-(4-chlorobenzylidene-4-((5-(4-hlorophenyl-1,3.4-thiadiazol-2-yl)diazenyl) aniline
p-Br	C	162	66	N-(4-bromo benzylidene)-4-((5-(4-bromophenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline
p-OCH_3	D	168	60	N-(4-methoxybenzylidene)-4-((5-(4-methoxyphenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline
p-NO_2	E	157	65	N-(4-nitrobenzylidene)-4-((5-(4-nitrophenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline

p-OH	F	178	72	4-(5-((4-hydroxybenzylidene)amino) phenyl)diazenyl)1,3,4-thiadiazol-2yl)phenol
m-Cl	G	154	56	N-(3-chlorobenzylidene-4-((5-(3-hlorophenyl-1,3.4-thiadiazol-2-yl)diazenyl) aniline
m-Br	H	162	63	N-(4-bromo benzylidene)-4-((5-(4-bromophenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline
m-OCH_3	I	160	68	N-(3-methoxybenzylidene)-4-((5-(3-methoxyphenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline
m-NO_2	J	145	60	N-(4-nitrobenzylidene)-4-((5-(4-nitrophenyl)-1,3,4 thiadiazol-2-yl)diazenyl) aniline
m-OH	K	185	74	4-(5-((3-hydroxybenzylidene)amino) phenyl)diazenyl)1,3,4-thiadiazol-2yl)phenol

APPLICATIONS

Biological Activity: Compounds prepared have been studied on the growth of three types of bacteria (**Escherichia.coli, Pseudomonas. areuginosa, Staphylococcus. aureus**) its importance in the medical field because they cause many diseases and has a wide resistance to antibiotics.

Modifiable agar diffusion method is the method used in the study of biological activity of the compounds prepared , where the cenberis prepared zorai and sterility and then distributed in the dishes and left solidifies and placed in incubator for 24 h until they are sure not contaminated and distributed to the dishes and placed in the incubator for one hour.

Drove dishes from the incubator and then drilled at a rate of five hole in one dish and then took concentrations equal to five compounds and placed in the center of the drill zorai first changes the concentrations in the second so on for the third. Then put the dishes in the incubator for 24 h and the temperature37^{o}C and the next day read the results of inhibition zones were measured to indicate the sensitivity of the compounds prepared and used in the stud , it was noted that to the most of the compounds that have been selected have the ability to the inhibit to the bacteria used in the study , when you increase the concentration of the increase diameter of inhibition zone free of bacterial growth .

This study has shown that, the biological activity of all these compounds at what can be the biggest user of the highest concentration of these compounds.

Table 4 The diameter of inhibition zone(millimeter) some compounds

G	Comp	Conc Mg/ml	*Psedo monas. reuginosaa*	*Escherichia .coli*	*Staphylococcus .aureus*
H	**A**	**15** **10** **5**	**12** **10.5** **8**	**10** **8** **6**	**5** **3** **-**
***p*-Br**	**C**	**15** **10** **5**	**4** **-** **-**	**9** **8.5** **4**	**-** **-** **-**
***p*-OH**	**F**	**15** **10** **5**	**10** **9.5** **8**	**11** **10** **8**	**12** **10** **9.5**
m-Br	H	**-** **-** **-**	**-** **-** **-**	**5** **4.5** **4**	**4** **-** **-**
***m*-OCH_3**	**I**	**15** **10** **5**	**-** **-** **-**	**5** **4.5** **4**	**4** **-** **-**
***m*-NO_2**	**J**	**15** **10** **5**	**7** **5** **4**	**8** **7** **6.5**	**-** **-** **-**
***m*-OH**	**K**	**15** **10** **5**	**8** **7** **6**	**9** **6** **5**	**6** **-** **-**

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