

## Synthesis and characterization of some new mannich base derivatives from oxadiazole compounds

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### ABSTRACT

Novel 5-alkyl 1,3,4-oxadiazole 2-thione derivatives were synthesized by converting of carboxylic acid to ester by esterification process or secondary amine to ester by treated it with ethylchloroacetate to give compound(1) this compound treated with hydrazine hydrate to give acid hydrazide(2) and with potassium hydroxide and carbon disulfide to give 1,3,4-oxadiazole derivative compound (3) this compound treated with different primary amines and with terephthaldehyde to give mannich bases <sup>[1]</sup> (Scheme 1).

**Key Words:** Oxadiazoles, Thiadiazole, Thiazole, Tetrazole, Pyrimidine, Mannich bases.

### 1. INTRODUCTION

Heterocyclic compounds are very important compounds which have been found to maintain significant biological activity are represent important moiety in creation of novel medical materials, adversity of biological activities and pharmaceutical uses have been attributed to them such as anti-inflammatory ,antifungal, antibacterial, antitumor and analgesic <sup>[2-3]</sup>.

The oxadiazole chemistry has been developed extensively and still developing. presently, there are a number of drugs used clinically ,which comprise oxadiazole, tetrazole moiety in association with various heterocyclic rings<sup>[4]</sup>. A series of substituted tetrazole has been synthesized by different methods such as from pyridine (2-azido azines) which equilibrium with fused tetrazoles <sup>[5]</sup>. Besides, mannich bases have a wide biological activates. A new 5-alkyl and 3-(2,4-dimethylphenyl) substituted 1,3,4-oxadiazole-2-thionederivatives were synthesized by the ring closure reaction of various acyl hydrazide with carbondisulfide <sup>[6]</sup>.

Accordingly, we synthesized new compounds, which possess a chemical important to achieve better antimicrobial, antibacterial activities....etc.

### 2. MATERIAL AND METHODS

All melting points were recorded using open capillary tube and uncorrected. Fourier transform Infrared spectra were recorded in KBr disc on Shimadzu 8300 spectrophotometer. <sup>1</sup>H NMR spectra were measured in DMSO solutions on a Bruker Av spectrophotometer (300 MHz) using TMS as an internal reference (chemical

shifts in  $\delta$  ppm). All synthesized compounds were elemental analysis C, H, N and S on a European Elemental analyzer. Thin layer chromatography was performed on silica gel as a stationary phase ,ethyl acetate as eluent.

#### 2.1.Synthesis of 2-Acid hydrazide (2)

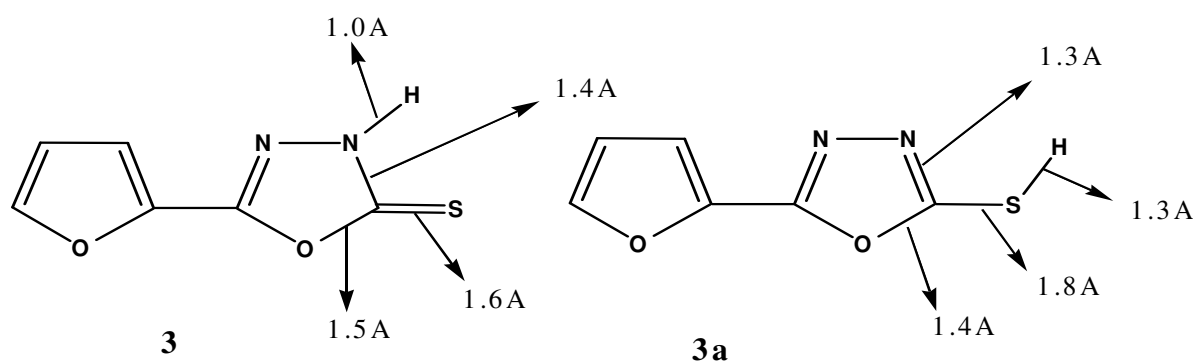
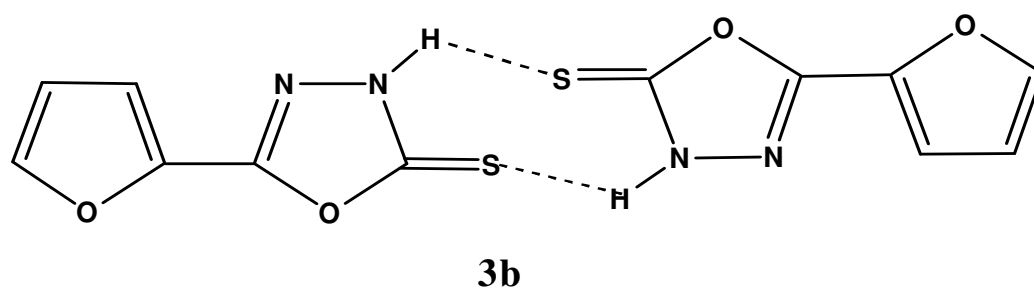
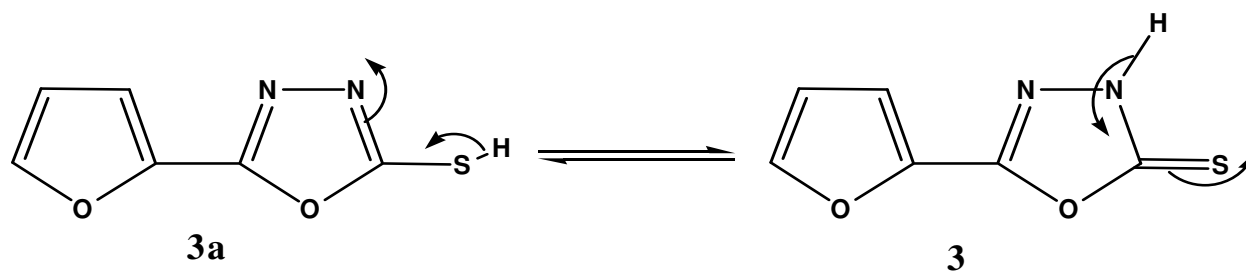
Acid hydrazide was synthesized by addition of the hydrazine monohydrate (80%) (0.01mol.) to ester compound (1) (0.01mol.) with stirring, then ethanol absolute (10ml) was added and refluxed until the precipitate formed (1.5hrs). After cooling, the precipitate was filtered and re crystallized from ethanol <sup>[7]</sup>.

#### 2.2.Synthesis of 5-(alkyl)-1,3,4-oxadiazole-2(3H)-thione(3)

A mixture of acid hydrazide (0.01mol) with (0.02mol) of potassium hydroxide in absolute ethanol (25ml) was stirred in ice bath, carbon disulphide (0.02mol) was added drop wise with vigorously stirring, and the reaction mixture was refluxed for 3hrs. After evaporation under reduced pressure, the residue was poured into acidified water .The precipitate was filtered, dried and recrystallized from ethanol <sup>[8]</sup>.

#### 2.3.Synthesis 3,3'-(1,4-phenylenebis((N-sub-phenyl)methylene))bis(5-alkyl-2-yl)-1,3,4-oxadiazole-2(3H)-thione(4a-e)

To ethanolic solution of oxadiazole compound (3) (0.02mol), terephthaldehyde (0.01mol) was added and stirred for (90min), in ice bath. Then cold solutions of different primary amines (0.02mol) were added drop wise while stirring. The resulting



**Table -1: FT-IR spectral data of compounds (4a-e).**

Comp. No.	$\nu(\text{C-H})$ aliphatic $\text{cm}^{-1}$	$\nu(\text{N-H})$ $\text{cm}^{-1}$	$\nu(\text{C=S})$ $\text{cm}^{-1}$	Other bands $\text{cm}^{-1}$
4a	2877	3371	1094	$\nu(\text{C=O})$ 1694
4b	2839	3365	1111	$\nu(-\text{NO}_2)$ 1545,1330
4c	2887	3304	1091	$\nu(\text{C=N})$ 1631
4d	2887	3358	1091	$\nu(\text{C-Cl})$ 639
4e	2895	3228	1068	$\nu(\text{C=N})$ 1633

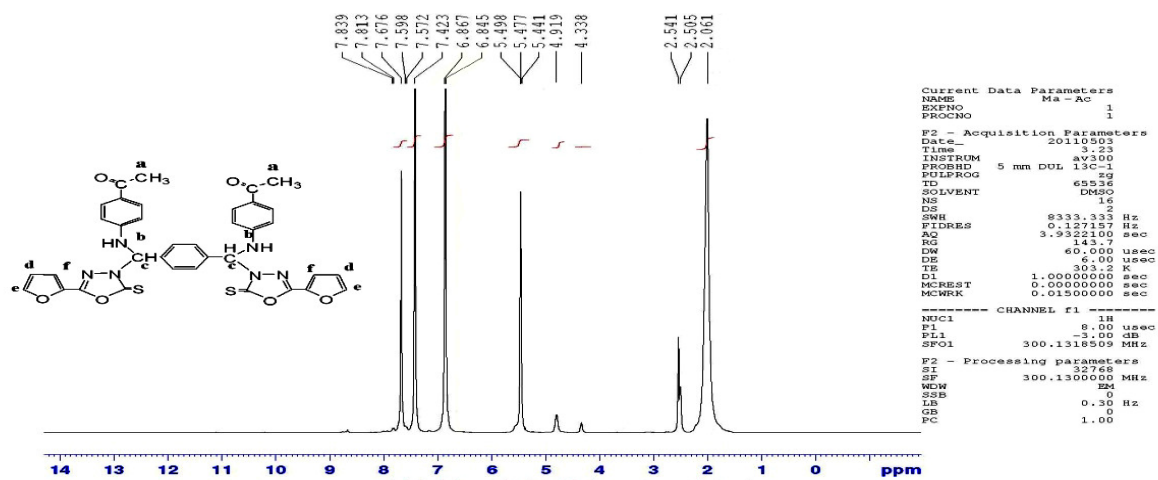


Figure 1:- <sup>1</sup>H-NMR spectrum of compound (a)

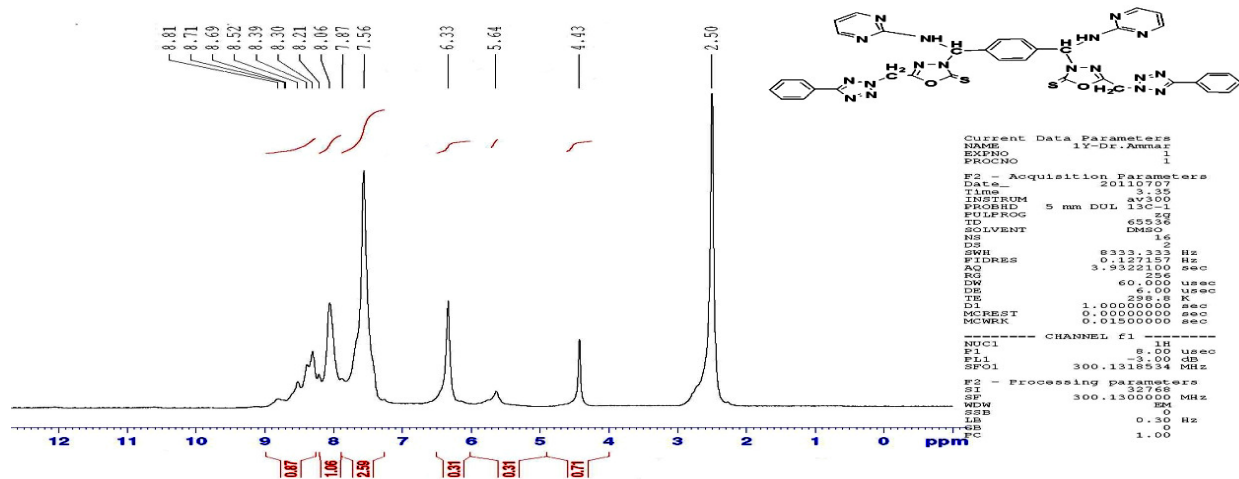
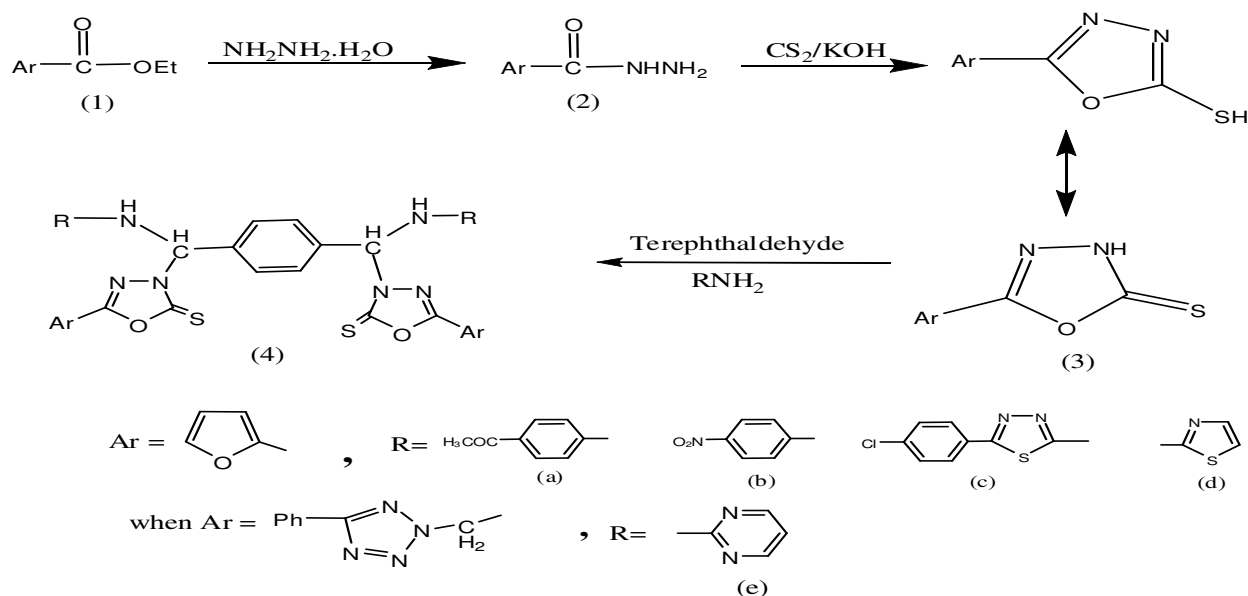


Figure 2:- <sup>1</sup>H-NMR spectrum of compound (e)



Scheme 1

mixture was refluxed for 6-7hrs in water bath and the obtained residue after the evaporation of the solvent under reduced pressure was recrystallized from ethanol <sup>[9]</sup>. m.p=(107-110)<sup>o</sup>C for compound(1) yield (66%), m.p=(110-112)<sup>o</sup>C for compound(2), yield (70%). m.p=(133-135)<sup>o</sup>C for compound(3) yield (77%) m.p=(191-193)<sup>o</sup>C for compound (4) yield (69%) m.p=(199-200)<sup>o</sup>C for compound(e) yield (62%).

### 3. RESULTS AND DISCUSSION

Compound (3) was synthesized from the reaction of compound (2) with carbon disulfide and potassium hydroxide in absolute ethanol. This compound was characterized by its melting point and F.T.IR spectrum. The F.T.IR spectrum of compound (3) indicated the disappearance of carbonyl group band at (1685)cm<sup>-1</sup> and appearance of bands at (1610) cm<sup>-1</sup> due to  $\nu$  (C=N) of oxadiazole ring and at (1290)cm<sup>-1</sup> due to  $\nu$  (C-O-C) (cyclic) group in oxadiazole, all these good evidences for the structure assigned to this compound. Besides a strong band at (1078) cm<sup>-1</sup> which due to  $\nu$  (C=S) thione group. Compound (3) may be found as two tautomeric forms thione (3) and thiol (3a) structure.

There is much evidence proved for preference of compound (3) because it is more stable than (3a). Compound (3) may be found as dimer (3b), this dimer has hydrogen bonding between the(C=S) of the first molecule and (-NH) of the second molecule. There are many theoretical calculations which proved that the compound (3) is more stable than (3a) by using the chem. Office program 2006, as the measuring of bond lengths and bonds angles between atoms.

The length of the bond between (-N-C=S) is (1.4 <sup>o</sup>A) in compound (3) but in (3a) (-N=C-SH) is (1.3<sup>o</sup>A), (-O-C=S) is (1.5<sup>o</sup>A) in (21) but (O-C-SH) is (1.4<sup>o</sup>A) these values lead to decrease the stress in oxadiazole ring in compound (3) is less than stress in compound (3a).the distance between (N-H) is (1.0<sup>o</sup>A) but the distance between(-S-H) is (1.3<sup>o</sup>A) ,these values indicated that the more preferred form is (3). Characterization of (1,4-phenylenebis((N-sub-phenyl) methylene) )bis(5-(furan-2-yl)-1,3,4-oxadiazole-2(3H)-thione(4a-e).

These compounds were prepared from the reaction of two moles of primary amine, oxadiazole derivatives (3), and one mole of terephthaldehyde in ethanol absolute as a solvent. Compounds (4a-e) are a Mannich bases because the reactants are aldehyde derivatives, secondary and primary amines. The structures of the prepared compounds (4a-e) are characterized by C.H.N. analysis and FT.IR, <sup>1</sup>HNMR, spectroscopy, the melting point is recorded and the purity of

these compounds are checked by T.L.C. technique and gas chromatography.

The FT.IR spectra of compounds (4a-e), showed the following bands: at (3371-3304) cm<sup>-1</sup> due to  $\nu$  (NH), at (2887-3837) cm<sup>-1</sup> for  $\nu$  (CH) aliphatic, and at (1091-1111) cm<sup>-1</sup> for  $\nu$  (C=S) thione group. All the spectral data for these compounds are listed in (Table 1). <sup>1</sup>HNMR spectrum of compound (a) shows singlet signal at  $\delta$ (2.0) ppm for (-CH<sub>3</sub>)(a) (NH) proton is appeared as a singlet at (4.338)ppm(b). Another singlet signal appeared at  $\delta$ (4.919) ppm of a proton of (-CH) (proton c). A triplet signals appeared at  $\delta$  (5.4) ppm for (a proton d)in furan ring, a doublet signal appeared at(6.8) ppm for (proton e) in the same ring. Multiplate signal appeared at  $\delta$ (7.4-7.8) ppm of aromatic ring protons but another doublet signal appeared at  $\delta$  (5.4) protons (d,e)ppm due to protons in furan ring. <sup>1</sup>H-NMR spectrum of compound (e), shows the following characteristic chemical shifts (DMSO-d<sub>6</sub>, ppm). The aromatic protons appeared at:  $\delta$  (7.5-8.8)ppm,(-CH)proton at  $\delta$  (6.33)ppm fused with oxadiazole ring, besides the band at  $\delta$  (5.64) ppm was appeared due to (-NH), a two protons of (-CH<sub>2</sub>) group gave a signal at  $\delta$  (4.43)ppm <sup>[10]</sup>.

### 4. CONCLUSION

The mannich bases have been synthesized for the discovering of new structure escorts. These compounds were synthesized form condensation oxadiazole derivatives with trephthaldehyde and primary amine derivatives. These compounds were synthesized because have a wide spectrum in medicinal chemistry.

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