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Synthesis and Characterization of 1,3,4- oxadiazole Derivatives using an Ultrasonic Technique

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Abstract

In the present study, a new of 1,3,4-oxadizole derivatives(4a1,4a2,4b1,4b2) were synthesized using an ultrasonic technique.
Benzohydrazine and its substituted (2a, 2b) were obtained from the reaction of hydrazin with benzoylchloride and its substituted (1a, 1b). Compounds (2a, 2b) react with chloroacetic acid to form compounds (3a,3b) which react with p-phenylene diamine and hydrazine in presence of DMSO as a solvent to obtain new compounds (4a1,4a2, 4b1,4b2) by ultrasonic technique. The structures of the synthesized compounds were elucidated by spectral data: infrared spectra (FT-IR) and 1HNMR and CHN analysis. The synthesis compounds (4b1, 4b2, 4a1, and 4a2) were evaluated for antibacterial (Staphylococcus1 aureus) by the serial dilution method.

Keywords: Spectroscopic study; antibacterial activity; Nitrogen, Oxygen heterocyclic compound.

الخلاصة

يتضمن البحث تخليق مركبات جديدة من 3,1, 4- اوكسادايازول ومشتقاته ($4a_1$,$4a_2$,$4b_1$,$4b_2$) بتقنية الموجات فوق الصوتية . تم الحصول على مركب بنزوهيدرازين ومشتقه (2a,2b) من تفاعل البنزويل كلورايد ومشتقه(1a,1b) مع الهيدرازين . من تفاعل (2a,2b) مع كلورو استيك اسيد تم الحصول على مركبات (3a,3b) الذي بتفاعلهم مع بارا – فينلين داي امين و مع الهيدرازين بوجود ثنائي مثيل سلفونيل كمذيب بطريقة الموجات فوق الصوتية للحصول على مركبات جديدة ($4a_1$,$4a_2$,$4b_1$,$4b_2$) . تم توضيح هياكل المركبات المحضره بواسطة البيانات الطيفي باستخدام تحليل العناصر وطيف الاشعة تحت الحمراء وتقنية الرنين المغناطيسي. تم فحص المركبات ($4b_1$,$4b_2$,$4a_1$,$4a_2$) للمضاد للبكتيريا (*Staphylococcus aureuss*) بواسطة طريقة التخفيف المسلسل.

Introduction

Heterocyclic compounds, considered as class having a great effects in treatments of diseases studies, for this reasons chemists advantage for those compounds ,they develop a wider ranges of products interests [1].

As a result of studies and facts ,those kinds of compounds become greater in quality over a period time and clearly gives proofs of producing a good results [2] health and treatments [3].

Compounds contain N and O [4] are very active compounds due to their important act in practical uses in studies of preparation of drugs and medicine [5, 6], scientific study of living things and analytical fields [7, 8]. Literature general view allowed a slight change in the structure can result changing in the activity, which advertise new derivatives [9] by using an ultra-sonic technique [10, 11] with the aim of having improved synthesis of organic compounds. To increasing, [12] realizing of the need to keep natural resources through the development of environmentally sustainable processes.

In organic chemistry, a large number examine facts about regularly using of nontraditional synthetic such as solvent-free reactions, the application of alternative activation techniques like ultrasound, the replacement of volatile

organic solvents by water, ionic liquids, and etc.

In some researches [13, 14] ultrasound technique producing good result to make a wide derivatives of oxadizole compounds, which have a biological effect against *Staphylococcus aureus, Escherichia coli and Bacillus Subtilis*.

Materials and Methodologies

Benzohydrazine (2a), and 4- nitro benzoyl chloride (2b): A direct result was obtained in room temperature (25 ° c) without using reflex or heating or other ways from reaction of (25 ml, 0.05 mol) benzoyl chloride(**1a) ,** and 4-nitro benzoyl chloride (**1b)** individually with hydrazine(0.01 mol, 5 ml).

2-(chloromethyl)-5-phenyl-1,3,4-oxadiazol(3a) & 2-(chloromethyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol(3b) [15]

From a reaction of benzoyl hydrazine (**2a**),and 4- nitro benzoyl chloride (**2b**) (1.36 g, 0.01 mol) individually, with mixture of chloroacetic acid (0.82g, 0.01 mol) and phosphorus oxychloride (5 ml, 0.01 mol) using ultra- sonic technique for (30 min) ,then mixture washed with water and alkaline medium,recrystallized from a mixture of (acetone and ethanol).

N^1,N^4-bis((5-phenyl-1,3,4-oxadiazol-2yl)methyl)bezene1,4-diamine($4a_1$):

A (0.01mol,1.95g) of 2-(chloromethyl)-5-phenyl-1,3,4-oxadiazol(3a) react with (0.005mole,0.54g) of p-phenylene diamine in presence of (25 ml) DMSO for (25 min) using an ultrasonic technique.

N^1,N4-bis((5-(4-nitrophenyl)-1,3,4-oxadiazol-2yl) methyl) bezene1,4-diamine($4b_1$):

A (0.01mol, 2.39g) of 2-(chloromethyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol(3b) react with (0.005mole,0.54g) of p-phenylene diamine in presence of (25 ml) DMSO for (25 min) using an ultrasonic technique.

1,2-bis((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)hydrazine($4a_2$):

A (0.01mol,1.95g) of 2-(chloromethyl)-5-phenyl-1,3,4-oxadiazol(3a) react with (0.005mole,0.2g) of hydrazine in presence of (25 ml) DMSO for (25 min) using an ultrasonic technique.

1,2-bis((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl)hydrazine($4b_2$):

A (0.01mol, 2.18g) of 2-(chloromethyl)-5-(4-nitrophenyl)-1,3,4-oxadiazol(3b) react with (0.005mole,0.2g)of hydrazine in presence of (25ml) DMSO for (25 min) using an ultrasonic technique .

Results and Discussion

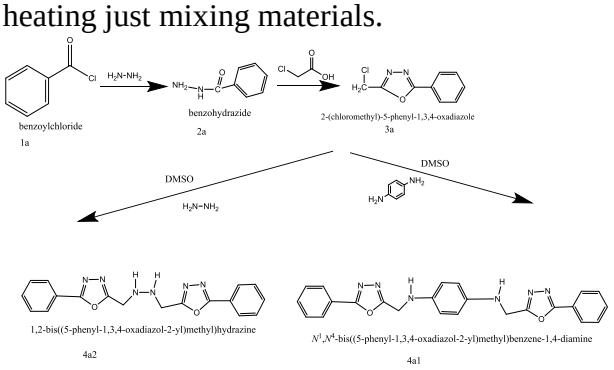
All prepared compounds were identified by some techniques like elemental analysis, infrared [16] and ^{1}HNMR[17].

All melting points reported are uncorrected and were determined in open glass capillary tubes using an electro-thermal 9300 digital melting point apparatus. The micro analyses were within ±0.4 % of theoretical values and were measured using an elemental analyzer CHNS Model Fison EA1108. The infrared spectra were recorded as potassium bromide discs using a Perkin-Elmer spectrophotometer GX.

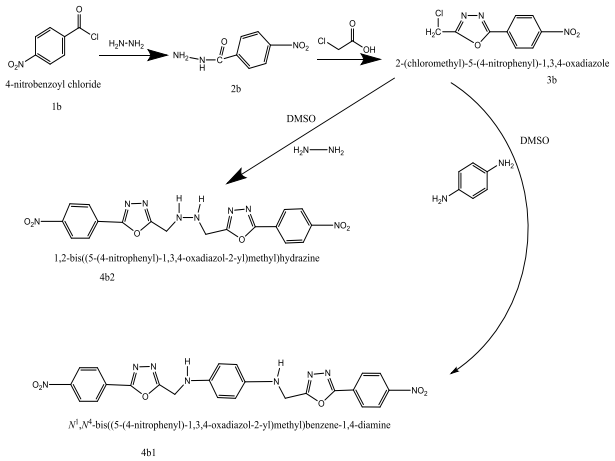
The 1H nuclear magnetic resonance spectra were recorded using the JEOL JNM-ECP 400, using TMS as internal standard with chemical shifts (δ) expressed in ppm.

Table 1 explains M.P. yield and R_f of the prepared compounds Table 2 illustrates CHNS data, and Table 3 shows the biological activity against Staphylococcus aureus bacteria. Scheme 1 and Scheme 2 illustrate preparation of compounds.

Compounds (2a, 2b) were prepared from reaction of compounds (1a, 1b). They were very fast reaction with 100% yield without refluxing or using ultrasonic technique or heating just mixing materials.



Scheme 1: Preparation of compounds (2a, 3a, 4a1, 4a2)



Scheme 2: Preparation of compounds (2b,3b,$4b_1$,$4b_2$).

Compound (2a) show bands at (3202cm^{-1}, 3503cm^{-1}) for -NH_2, -NH. while compound (2b) show bands at 3004 cm^{-1},3073cm^{-1}) for -NH_2 ,-NH . Compounds (3a, 3b) had no bands for (-NH_2,-NH). Compound (3a) had bands at(1602cm^{-1} for CN ,1291$cm^{-1}$for COC,707$cm^{-1}$for substituted benzene ring ,665cm^{-1} for CCl),while compound(3b)had bands at(1618cm^{-1} for CN ,1287$cm^{-1}$for COC ,720$cm^{-1}$for subsited benzene ring ,648$cm^{-1}$for CCl) .In compounds ($4b_1$, $4b_2$) show a stretching band for(N-O in NO_2 group) at (1309.60,1384.42) cm^{-1}.

Compound ($4a_1$) show bands at (1257.06 cm^{-1} stretching CN, 3428.77 cm^{-1} stretching NH, 1558.35 cm^{-1} bending NH).

Compound ($4a_2$) show bands at (1558.46 cm^{-1} stretching CN, 3433.04 cm^{-1} stretching NH, 1558.46 cm^{-1} bending NH).

Compound ($4b_1$) show bands at (1170.60cm^{-1} stretching CN, 2846.91cm^{-1} stretching NH, 1568.88cm^{-1} cm^{-1} bending NH).

Compound ($4b_2$) show bands at (1202.01cm^{-1} stretching CN, 3428.88 cm^{-1} stretching NH, undetected bending NH).

N^1,N^4-bis((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)benzene-1,4-diamine($4a_1$):

4.1(1H,s) of CH in 1,3,4-oxadiazol ring which connected to phenyl ring, 3.1(1H,s) of CH in 1,3,4-oxadiazol ring connected to -CH_2NH.

3.1-3.4 (4H,t) position of 2CH_2 between –CH in oxadiazole ring & -NH 7.36-7.38(4H,d), (6H,t) for two phenyl group connected to oxadiazole ring.

6.38 (4H,d) for C_6H_4 connected to two – NH group.

8.06(1H,t)for two –NH between phenyl ring and –CH_2.

N^1,N^4-bis((5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl)methyl)benzene-1,4-diamine($4b_1$):

4.1(1H,s) of CH in 1,3,4-oxadiazol ring which connected to phenyl ring, 3.1(1H,s) of CH in 1,3,4-oxadiazol ring connected to -CH_2NH.

3.1-3.4 (4H,t) position of 2CH_2 between –CH in oxadiazole ring & -NH 7.62-8.19(8H,d) for two nitro phenyl group.

6.38 (4H, d) for C_6H_4 connected to two – NH group. 8.06(1H, t)for two –NH between phenyl ring and –CH_2.

1,2-bis((5-phenyl- 1,3,4-oxadiazol-2-yl)methyl)hydrazine($4a_2$):

4.1(1H,s) of CH in 1,3,4-oxadiazol ring which connected to phenyl ring, 3.1(1H,s) of CH in 1,3,4-oxadiazol ring connected to -CH_2NH.

2.7-2.9 (4H,t) position of 2CH_2 between –CH in oxadiazole ring & -NH.

7.36-7.38 (4H,d) & (6H,t) for 2C_6H_5 connected to two ring of oxadiazol.

2(1H,q) for two -NH in hydrazine.

1,2-bis((5-(4-nitrophenyl)- 1,3,4-oxadiazol-2-yl)methyl)hydrazine($4b_2$):

4.1(1H, s) of CH in 1,3,4-oxadiazol ring which connected to phenyl ring, 3.1(1H, s) of CH in 1,3,4-oxadiazol ring connected to -CH_2NH.

2.7-2.9 (4H, t) position of 2CH_2 between –CH in oxadiazole ring & -NH.

7.62-8.19(8H, d) for two nitro phenyl group.

2(1H,q) for two -NH in hydrazine.

The antibacterial activity was determined applying the agar cup-plate method. Results were obtained in duplicate, and results with differences higher than 5 % were discarded and the measurements repeated.

Table 1: R_f, M.p, and percentage yield of compounds.

Comp.no	R_f	M.p(^oC)	Yield%
$4a_1$	0.968	48-50	49.53
$4a_2$	0.855	95	67.24
$4b_1$	0.790	70	37.11
$4b_2$	0.887	78-80	64.22

Table 2: CHNS data of the prepared compounds

Comp.no	CH analysis (C,H,N,O) %
$4a_1$	C= 67.3 ,H= 5.6 ,N= 19.6 ,O= 7.5
$4a_2$	C= 55.6 ,H= 4.25 ,N= 21.6 ,O= 18.53
$4b_1$	C= 61.36 ,H= 5.68 ,N= 23.86 ,O= 9.09
$4b_2$	C= 48.87 ,H= 4.07 ,N= 25.34 , O= 21.72

Table 3: Biological activity

Compds.no.	Anti-bacterial activity against (*Staphylococcus aureus*)
$4a_1$	++
$4b_1$	+
$4a_2$	-
$4b_2$	++

Conclusion

In this research a new technique was used which considered as a green chemical reaction by using ultra sound technique. Using an ultra-sonic technique reduced reaction time which usually used in reflex technique in similar reactions. In another hand the biological effect of produced compounds gives wide variety in medical industry, which can be improved in future studies.

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