Synthesis and study of antibacterial activity of some new bis 1,3,4-oxadiazole derivatives

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Abstract

Some of succinic acid hydrazone derivatives were prepared from the reaction of succinic acid hydrazide(3) with different benzaldehydes, then cyclization of hydrazones (4a-e) in glacial acetic acid and lead dioxide resulted into the formation of new bis-1,3,4-oxadiazole derivatives (5a-e). The reactions were followed by TLC and the synthesized compounds were confirmed by their IR and U.V. spectra. The antibacterial activity of the synthesized compounds against the four bacterial species was also studied.

Keywords: Hydrazone, 1,3,4-Oxadiazole, Antibacterial Activity.

Introduction

Hydrazone and their derivatives have versatile applications in the biological fields as antimicrobial, anticonvulsant, analgesic, anti-inflammatory, antiplatelet, antitubercular, antitumoral and antibacterial activity[1-5].

Oxadiazoles have been prepared by many procedures[6-13]. The synthesis of 1,3,4-oxadiazoles is also of considerable interest due to their various biological activities, such as, nervous system depressing[14], analgesic[15,16], herbicidal[17], muscle relaxant[18] and tranquilizing activities[19].

Experimental

Uncorrected melting points were determined using Electrothermal melting point apparatus(Electrothermal Engineering LTD S-N 10853), IR spectra were recorded by Shimadzu FT-IR spectrophotometer as KBr disc. The UV measurements were obtained using Schimadzu (UV-Visible) spectrophotometer UV-1650 PC. Dimethyl succinate (1) was prepared according to a published procedure[20]. Dimethyl succinate dihydrazide (2) was prepared following literature reported procedure[21], See Fig.(1).

Preparation of 1,2- bis (1-(4-substituted benzylidene)hydrazon-3-oyl)ethane(4a-e).

A mixture of compound (3) (0.01 mole) and substituted benzaldehydes (0.01 mole) in ethanol 25 ml was refluxed for 3 hrs. The precipitate was filtered and crystallized from ethanol. Melting points, yield and (U.V.,IR) spectral data are listed in Table (1), See Fig.(2,3).

Preparation of 1,2- bis (2-(substituted phenyl)-1,3,4-oxadiazole-5-yl)ethane (5a-e).

(0.01 mole) of compound (4) was dissolved in 40 ml of glacial acetic acid with stirring for until the obtaining of a homogeneous solution. Lead dioxide (0.01 mole) was added with stirring at 25 °C for 1 hr. The product was poured on crushed ice. The crude material was filtered off and washed with cold water and recrystallized from ethanol. Physical and (U.V.,IR) spectral data are illustrated in Table (2), See Fig.(4,5).

The biological activity

The bacteria species used are listed in Table (3). All strains were obtained from College of Medicine, Tikrit University. They were grown up to the stationary phase nutrient bath at 37 °C and a sample of 0.5 ml of each bacteria was spread over a surface of a nutrient agar plate[22].

Antibacterial assay[23]

Disc of filter paper (6 mm diameter) were sterilized at 140 °C for 1 hr and impregnated with the germs, absolute ethanol was used as a solvent for compounds (4a-e) and (5a-e). The same solvent was used for antibiotics, blank paper discs of absolute ethanol was used as control. The inoculated plates were incubated at 37 °C for 24 hrs., and the inhibition zone (mm) were measured[24]. In all experiments, the mean of each triplicate was measured[25].

Results and Discussion

Hydrazone compounds (4a-e) were prepared by the condensation reaction of succinic acid hydrazide with substituted benzaldehyde.

The IR characteristic absorption bands of the hydrazone compounds (4a-e) were given appeared at (1606-1656) cm^{-1} and (1660-1677) cm^{-1} for (C=N) and (C=O) respectively. While single band at (3193-3247) cm^{-1} for (N-H).See Fig.(2,3).

The 1,3,4-oxadiazoles (5a-e) was synthesized by the reaction of equimolar amounts of hydrazone (4a-e) with lead dioxide in glacial acetic acid.

The IR spectra of compounds (5a-e) showed the following vibrational absorption bands (1167-1261), (1062-1176), (1008-1087) and (1610-1662) cm^{-1} which are assigned to (C-O-C, asymmetric, symmetric), (N-N) and (C=N), respectively.

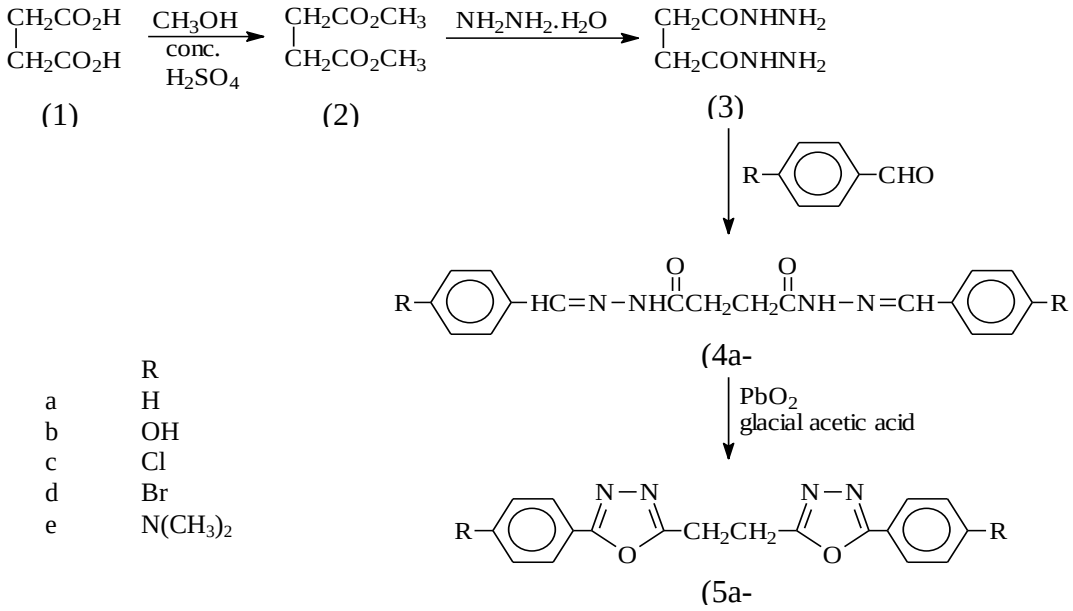
The U.V spectra gave absorption band at different wave lengths for the resulted hydrazones and 1,3,4-oxadiazoles (in % 95 EtOH), due to $n\rightarrow\pi^*$ and $\pi\rightarrow\pi^*$ transition and all these transition are listed in Table (1,2).

Antimicrobial activity of the compounds (4a-e) and (5a-e) was examined by the agar diffusion method using four different bacterial species i.e. *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi* and *Pseudomonas aeruginosa*.

The results indicated that all the assayed compounds showed activity against the tested organism up to 3.2 mg/disc.

The prepared compounds (4a-e) and (5a-e) showed higher activity towards *Staph. aureus* and *E. coli* compared with the other germs.

The hydrazones (4a-e) were more active than 1,3,4-oxadiazoles(5a-e) but the last were more selective with *E. coli* (Table 3).



	R
a	H
b	OH
c	Cl
d	Br
e	$N(CH_3)_2$

Table (1): Physical and spectral data for the compounds (4a-e)

Comp. No.	M.P. °C	Yield %	Color	UV nm λ_{max}	IR ν cm^{-1}			
					C=N	C=O	N-H	Other
4a	229-231	96	White	308	1652	1672	3193	-
4b	214-216	80	White/ Yellow	338	1606	1660	3247	3326 (OH)
4c	260-262	87	White	310	1656	1677	3201	-
4d	241-243	97	White	292	1654	1677	3201	-
4e	214-215	95	Yellow	332	1656	1676	3195	-

Table (2): Physical and spectral data for the compounds (5a-e)

Comp. No.	M.P. °C	Color	UV nm λ_{max}	IR ν cm^{-1}				
				C-O-C		N-N	C=N	Other
				as.	s.			
5a	215	White	306	1167	1078	1053	1662	-
5b	246-248	Chocolate	308	1261	1108	1008	1610	3340 (OH)
5c	218-220	Milky	298	1259	1176	1087	1660	-
5d	228-229	White	318	1226	1070	1010	1654	-
5e	252	Pale Yellow	352	1172	1062	1021	1620	-

Table (3): biological activity for hydrazones (4a-e) and 1,3,4-oxadiazoles (5a-e)

Comp. No.	*Staph. aureus*	*E. coli*	*Sal. typhi*	*Ps. aeruginosa*
4a	+	+	±	-
4b	++	+	+	±
4c	+	±	±	-
4d	+	±	+	±
4e	++	+	+	+
5a	±	±	-	±
5b	+	++	+	±
5c	+	++	±	-
5d	±	+	-	-
5e	-	++	±	+
Ethanol	-	-	-	-

Note: (-) = no inhibition, (±)= 5-10mm, (+)= 10-20mm, (++) = more than 20mm.

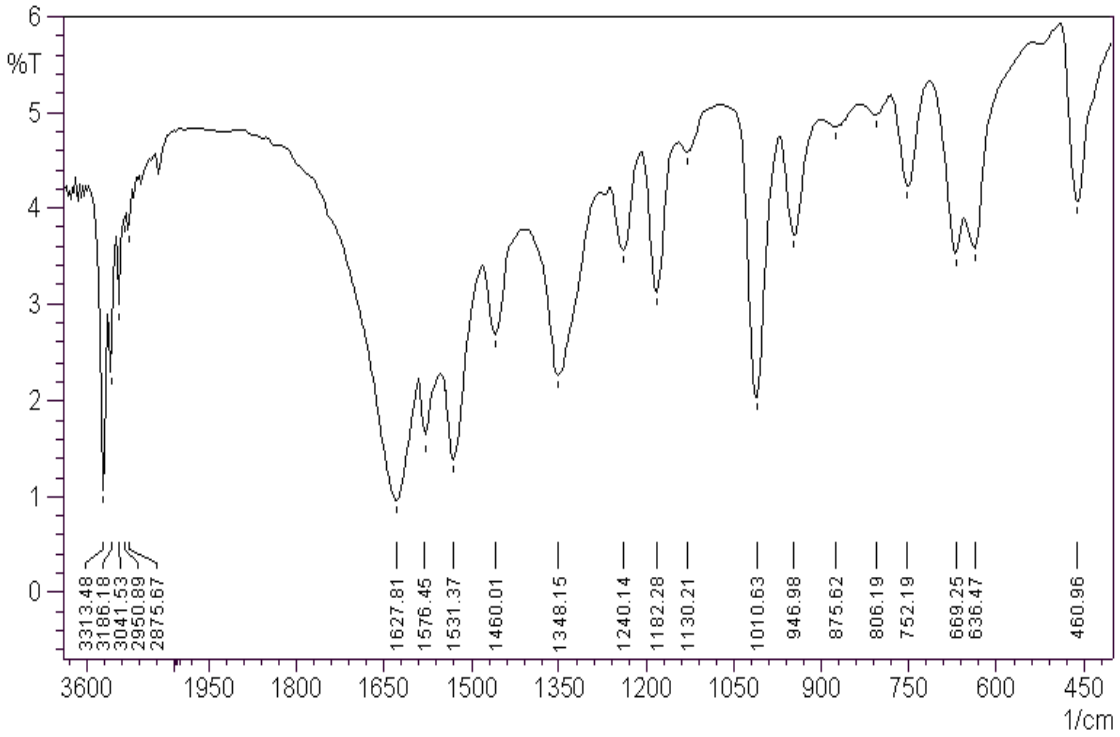


Fig.(1): IR spectrum of the compound (3)

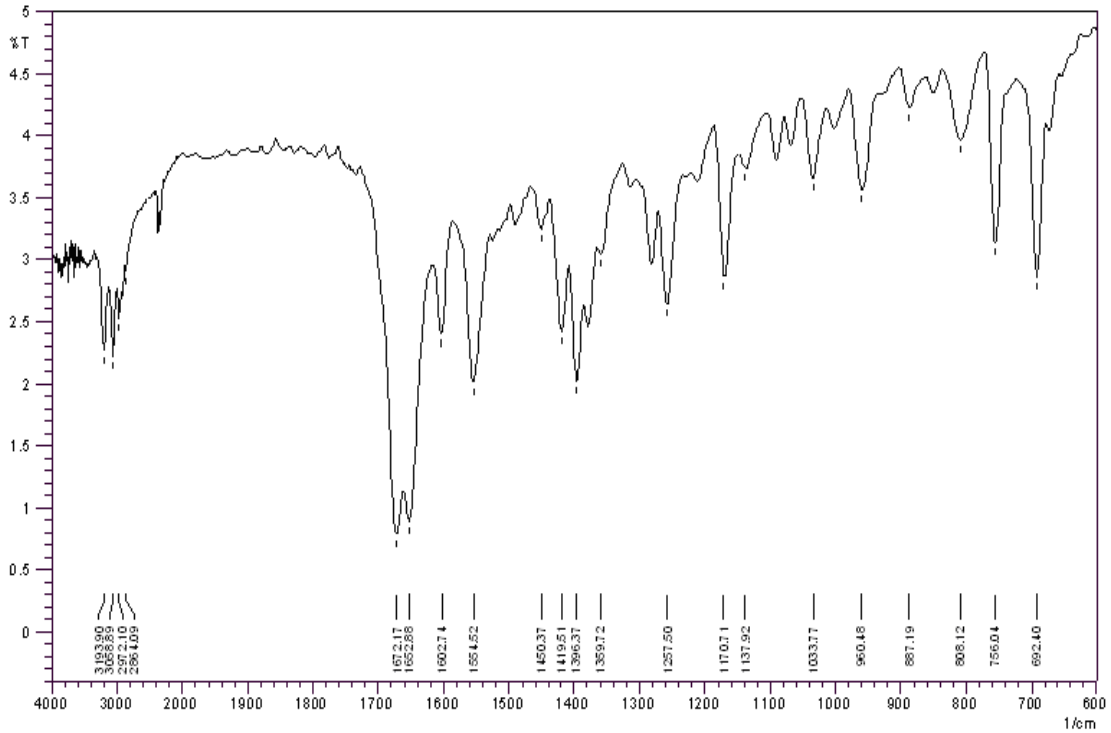


Fig.(2): IR spectrum of the compound (4a)

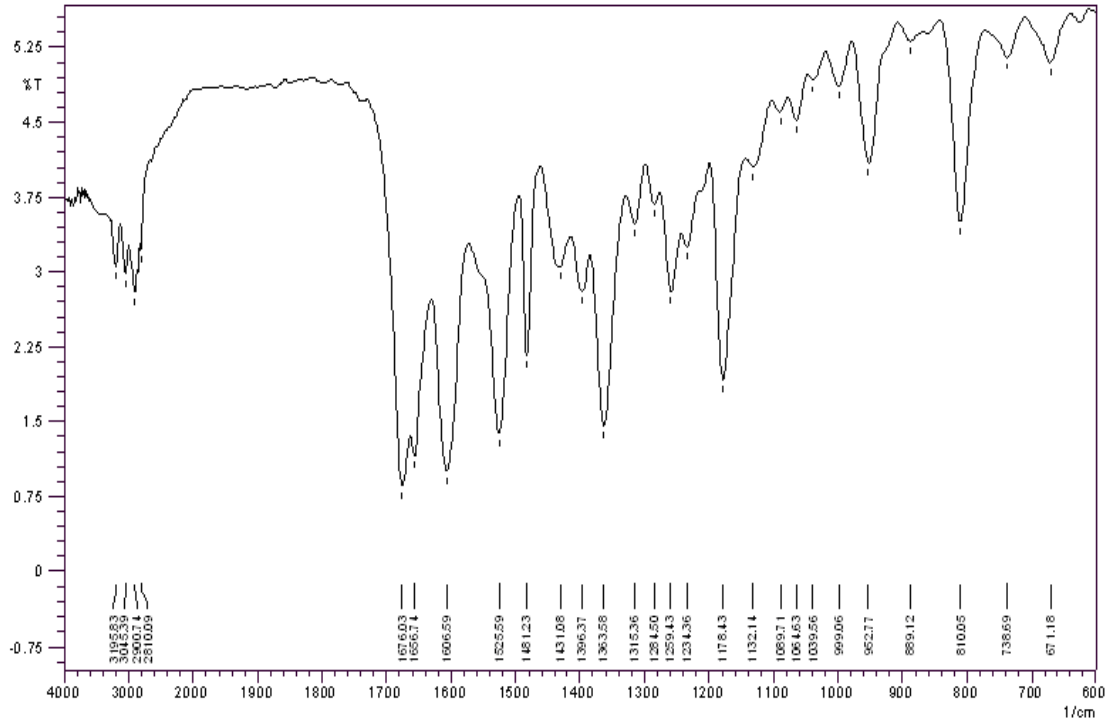


Fig.(3): IR spectrum of the compound (4e)

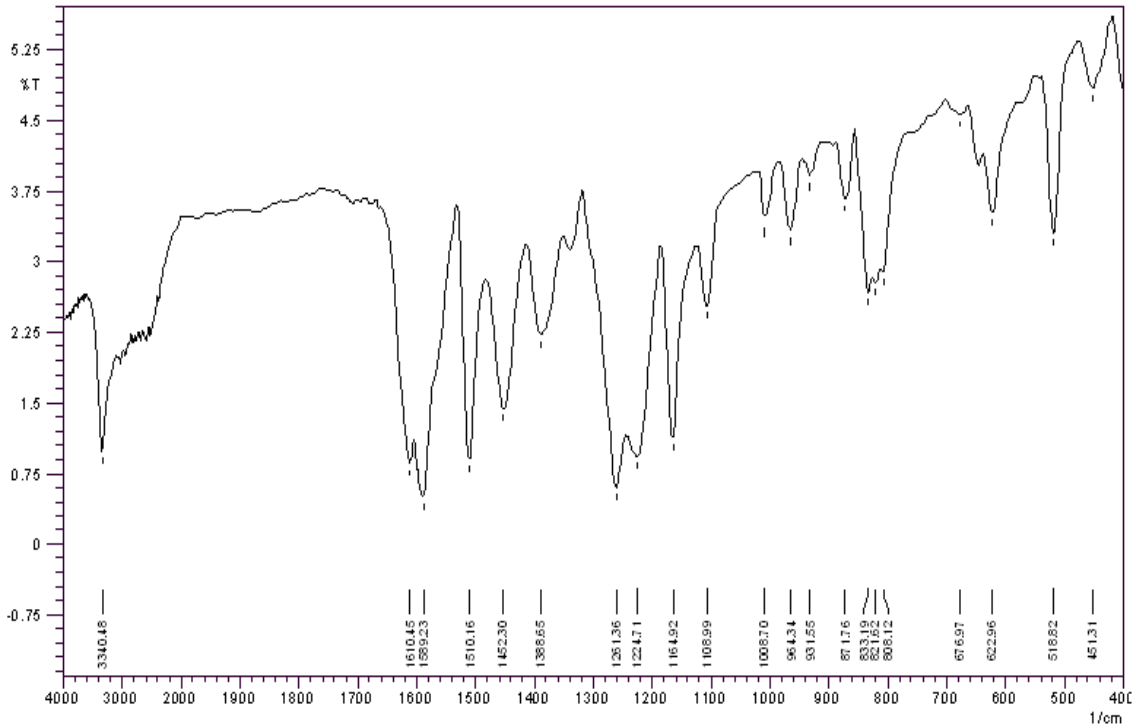


Fig.(4): IR spectrum of the compound (5b)

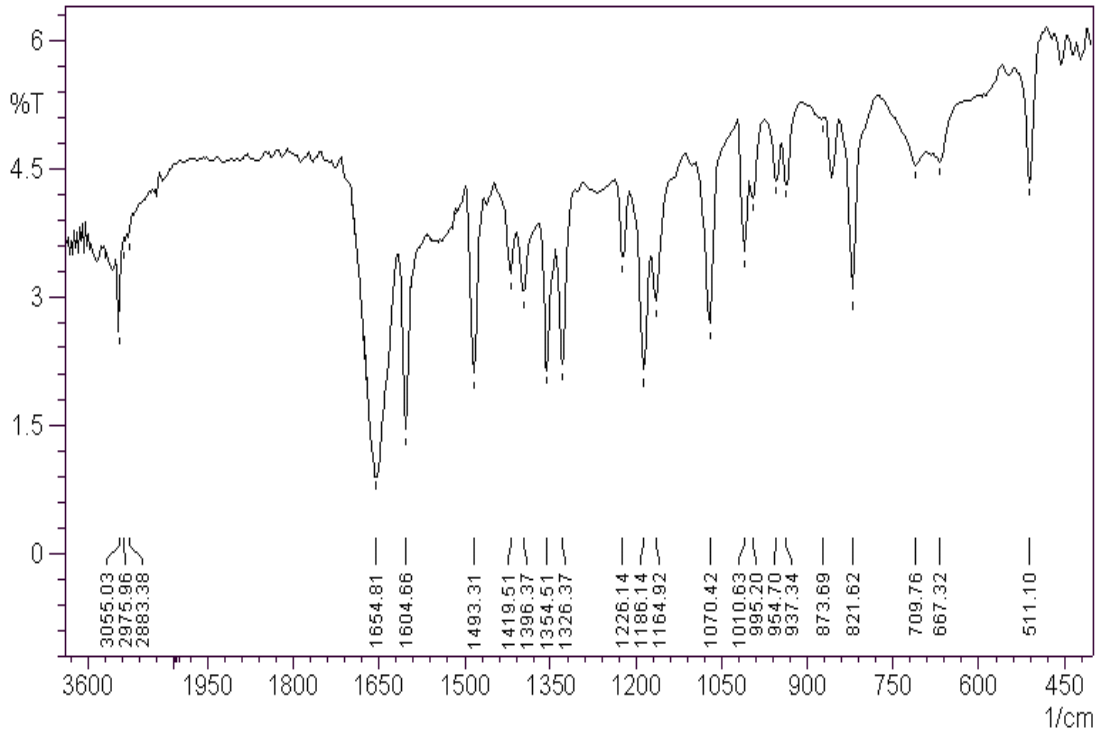


Fig.(5): IR spectrum of the compound (5d)

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تحضير ودراسة الفعالية البايولوجية لبعض المشتقات الجديدة من بس ١،٣،٤-اوكسادايازول

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(تاريخ الاستلام: / /٢٠٠٧ ، تاريخ القبول: / / ٢٠٠٧

الملخص

تم تحضير بعض مشتقات هيدرازون حامض السكسنيك من تفاعل هيدرازيد حامض السكسنيك(٣) مع بنزلديهايدات مختلفة، ثم حولقة الهيدرازونات المتكونة(4a-e) بواسطة حامض الخليك الثلجي و ثنائي اوكسيد الرصاص الى مشتقات جديدة من ١،٣،٤-اوكسادايازول الثنائية (5a-e)، تم متابعة سير التفاعلات بكرموتوغرافيا الطبقة الرقيقة وقد شخصت المركبات المحضرة باستخدام أطياف الأشعة تحت الحمراء وفوق البنفسجية، كما تمت دراسة الفعالية البايولوجية للمركبات المحضرة ضد أربعة أنواع من البكتريا.

الكلمات المفتاحية: الهيدرازون، ١،٣،٤-اوكسادايازول، الفعالية المضادة للبكتريا.