SYNTHESIS,ANTIBACTERIAL ACTIVITY OF 2-AMINO 5-PHENYL -1,3,4- OXADIAZOLE DERIVATIVES

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Abstract

In the present investigation, five derivatives were synthesized as potential antimicrobial agents , The compounds are : 2-amino 5-phenyl - 1,3,4- oxadiazole dithi-ocarbomate, 2-amino 5-(4-amino- N,N-dimethyl phenyl)- 1,3,4- oxadiazole, 2-amino 5- (4-amino N,N. dimethyl phenyl)- 1,3,4- oxadizole dithiocarbamate, 2-amino 5-(4-nitr-ophenyl)-1,3,4-oxadiazole, 2-amino 5-(4-nirophenyl)-1,3,4-oxadiazole dithiocarbamate.

The above newly synthesized compounds were investigated for their antibacterial, antifungal activities. The results of the biological revealed that the compounds activities against S.aureuss and B.subtilis and also P.aeureoginosa and Staph. Aureus. The prepared compounds were characterized by infrared spectrum, ^{1}HNMR nuclear magnetic resonance and some physical properties.

Introduction

Heterocyclic compounds containing nitrogen,carbon, and sulfur such as derivatives of oxadiazoles[1] and triazoles [2] have been reported to have diverse pharmacological properties. Oxadiazoles are used as antifungl [3,4] antibacterial [5,6], anti-inflammatory [7] and antimicrobial [8-10] .This paper reports the synthesis of some new oxadiazole and oxadiazole dithiocarbamate derivatives. The prepared compounds are expected to reveal biological activities as bactericides.

Experimental Section

.Melting Points were determined on a Gallen Kamp MFB-600-010 melting point apparatus. IR spectra were recorded on a perkin Elmer model 127 spectrophoto meter as KBr wafers.

^{1}HNMR spectra were recorded on a make Bruker model DPX 300/300 MIIX NMR , $CDCL_3$-d was used as solvent and TMS as internal reference .All other reagents were of reagent grade and were used with out purification.

In summary we have developed the use of 2-Amino 5-phenyl 1,3,4 oxadiazoles deriva-tives as new reagent for the synthesis of oxadiazoles dithio carbamates.

Preparation of 2-Amino 5-phenyl 1,3,4 oxadiazole [11,12].

0.01 mole) of the semicarbazidhydrochloride and (0.05mol) benzaldehyde (were dissolved in an alcoholic solution of sodium acetate(0.02mole in 50 ethnol) The mixture was heated under refluxed for 1h.The residue obtained poured into ice water. The white precipitate which separated was filtered and wshed with distilled water.

To the product obtained added (0.5 ml) of bromine and dissolved in acidic solution of anhydrous sodium

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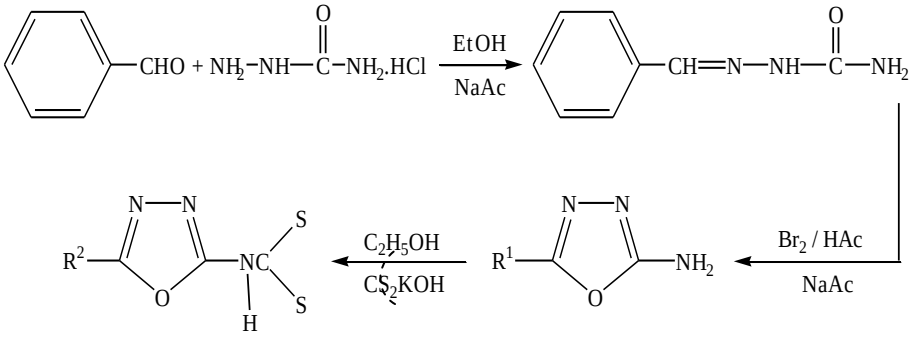
acetate(0.25mole) CH_3COONa in 50ml of glecial acetic acid with concentration (1:1) .The mixture obtained was allowed to react for 2 days. The precipitate formed oxadiazole and derivatives scheme(1). Table (1) lists the was filtered off, Washed with cold distilled water dried to gove 2-Amino 5-phenyl- 1,3,4- physical properties of the synthesized compounds(a.b.c).

preparation of 2-Amino 5-phenyl- 1,3,4- oxadiazole dithiocarbamte

(0.005mole) of 2-amino 5-phenyl- 1,3,4- oxadiazole was dissolved in 10ml of ethanol .(30ml)of alcoholic solution of potassium hydroxide (0.03mole KOH in 50ml ethanol)was added . To this mixture (1.5)ml of carbon disulfide was added gradually and were stirred on an ice bath for 2h. The obtained residue was filtered off, washed with distilled water and dried to give 2-amino 5-phenyl- 1,3,4- oxadiazole dithiocarbamate scheme(1). Table(1) lists the physical properties of the synthesized compounds (d.e.f).

Results and discussion:

Scheme(I)summarizes all the performed reactions in this work . Structure and physical properties of the synthesized compounds are given in Table (1). The IR, H^1NMR spectral data are given in Tables (2) and (3). The inhibition zones are given in Table(4).



(d),R^2 = ph . **(a),R^1 = ph .**
(e),4-($N(CH_3)_2$) C_6H_4 . **(b),4-($N(CH_3)_2$) C_6H_4 .**
(f),4-(NO_2) C_6H_4 . **(c),4-(NO_2) C_6H_4 .**

Scheme (1): preparation of prepared compounds.

The X-ray determination for compound 2-amino-5-phenyl- 1,3,4- oxadiazole shows, a perspective view of the molecule, which has the phenyl ring inclined to the plane of the oxadaizole ring at an angle of 12.6 the geometry of the oxadiazole ring is similar to that previously observed in other 2-amino-1,3,4-oxadiazoles [13].

The structures of the prepared compounds have been characterized by IR and NMR analysis. The structures of 2-amino-5-phenyl- 1,3,4- oxadiazole and derivatives (a, b, c) were confirmed by their melting points Table (1), IR, and ^{1}HNMR spectroscopy.

IR spectra showed two bands at (3370 – 3418) cm^{-1} (vNH) and (1515 – 1525) cm-1 bending C = N and NH. Furthermor their spectra showed a band at (1160 – 1165) cm-1 due to C – O – C (Dadly A.J. et al 1986) , table (2).

Compounds 2-amino-5-phenyl- 1,3,4-oxadiazole dithiocarbamate showed absorption bands at (3170 – 3150) cm^{-1} (vN – H) and (1150 – 1170)

cm^{-1} due to (C – O – C). thio amide band due to (vC…..N) minor (vC…..S) major band in the region (960 – 965) cm^{-1} and showed stretching band at (1625 – 1640) cm^{-1} which corresponded to (vC = S)[14].

Biological Effect

Agar diffusion method [15],were used for the determination of antibacterial activity of the prepared compounds .0.1 ml of an overnight broth bacterial culture was spread on anutrient agar.Sterilized discs(6mm in diameter).Evalution of the above-mentioned compounds for their antimicrobil activities showed that these compound exhibited both antibacterial and antifungal actives.The results are presented in table (4).

The tested compounds showed activity against Staphylococcus aureus , Bacillus subtilis and Pseudomonas aeruginosa . However, compounds a ,b showed aweak activity against Pseudomonas aeruginosa .It should be mentioned that the antimicrobial results were obtin- -ed concentration of 500µg/ml for all tested compounds .

Table (1): physical properties of the synthesized compounds

Compound	Color	m.p	yield %
a $C_8H_7N_3O$	White	240.245	86
b $C_{10}H_{12}N_4O$	White	256-258	70
c $C_8H_6N_4O_3$	Yellow	250-252	63
d $C_9H_7N_3OS_2$	yellow	230-225	80
e $C_{11}H_{11}N_4OS_2$	yellow	260-258	58
f $C_9H_5N_4O_3S_2$	Red	275-270	60

Table (2): Selected I.R of oxadiazole and oxadizoldithiocarbamate .

Compound	ν N-H cm^{-1}	ν C = N cm^{-1}	ν C = S cm^{-1}	N C-O -C cm^{-1}	Thioamide cm^{-1}
a $C_8H_7N_3O$	**3370 (1510) II**	**1540**	**___**	**1165 (5)**	**___**
b $C_{10}H_2N_4O$	**3450 (1520) II**	**1558**	**___**	**1165**	**___**
c $C_8H_6N_4O_3$	**3365 (1525) II**	**1555**	**___**	**1160**	**___**
d $C_9H_7N_3OS_2$	**3150 (1520) II**	**1560**	**1225**	**1170**	**(1345) I (960) II**
e $C_{11}H_{11}N_4OS_2$	**3160 (1515) II**	**1565**	**1230**	**1150**	**(1350) I (970) II**
f $C_9H_5N_4O_3S_2$	**3170 (1518) II**	**1560**	**1240**	**1160**	**(1340) I (965) II**

Table (3): ^{1}HNMR spectral data for oxadiazole and oxdiazoledithiocarbamate

compounds	HNMR parameters (ppm) S-H
a	3.95(s,-NH2), 6.86-6.90 (m,SH,Ar-H)
b	δ, 1.30(s,6H), 7.32(s,2H), 7.65(d,J= 8.3H7,2H) 7.8(d,J= 8.4HZ,2H)
c	δ7.57(s,2H), 8.00(d,J= 8.6 HZ2H),8.30(d,J= 8.8HZ,2H)
d	11.8(b,1H,-NH),6.95-7.20(m,5H,Ar-H)
e	δ, 1.2(s,6H), 11.8(b,1H-NH),7.15(m 2H,Ar-H), 7.8(m2H,Ar-H)
f	11.3(b,H-NH),7.1(m .2H,Ar-H) 7.85 (M,2H,Ar-H)

Table (4):Antibacterial and antifungal activities of the tested synthesized compounds

Comp. 500 µg /ml	E.coli	PS. Aeruginosa	B. subtilis	Staph. Aureus
a	+	-	+ +	+
b	+	-	+	+ +
c	+ +	±	+ +	+
d	+	+	+	±
e	+ + +	+ +	+	±
f	+ +	+	+	±

- = No inhibition , ± =5-9 mm ,+ = 10-12 mm
+ + = 12-15 mm, + + + = more than 15 mm

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تحضير والفعالية البايولوجية لمشتقات 2 –أمينو فنيل–4,3,1 –أوكسادايازول

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الخلاصة:

في هذا البحث تم تحضير خمسة مشتقات لمركب 2 –أمينو فنيل–4,3,1 –أوكسادايازول ذات فعالية كمضادات بكتيرية. المركبات المحضرة هي 2 –أمينو فنيل–4,3,1 –أوكسادايازول ثنائي ثايوكربمات , 2 – أمينو5 –(4 –أمينو–N,N –ثنائي مثيل فنيل)–4,3,1 –أوكسادايازول , 2 –أمينو5 –(4 –أمينو–N,N – ثنائي مثيل فنيل)–4,3,1 –أوكسادايازول ثنائي ثايوكربمات ,2 –أمينو5 –(4 –نايترو فنيل)–4,3,1 – أوكسادايازول ,2 –أمينو5 –(4 – نايترو فنيل)–4,3,1 –أوكسادايازول ثنائي ثايوكربمات . تم دراسة هذه المركبات كمضادات للبكتريا والفطريات وكانت النتائج الفعالية البايولوجية للمركبات واضحة كمضادات للانواع المدروسة كما تم تشخيص المركبات المحضرة بوساطة أطياف الاشعة تحت الحمراء وأطياف الرنين النووي المغناطيسي وبعض الخواص الفيزيائية لها.