Synthesis, Characterization and biological activity of some oxadiazoles derivatives and thiadiazoles derivatives

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Abstract

In this our research were chosen as a source number of heterocyclic compounds. Substituted hydrazide (2) was synthesized from the reaction of ester (1) with hydrazine hydrate in presence of alcohol. The ester obtained from the reactions of Para nitro benzoic acid (1) with absolute ethanol in presence concentrated sulfuric acid. The *para* nitro pheny hydrazide (2) was treated with carbon disulfide in ethanolic potassium hydroxide solution to give 5-pheny-1,3,4-oxadiazole-2-thiol (3). The reaction of compound (3) with hydrazine hydrate give 1, 2, 4 - triazole (5).The reaction of compound (3) with various aryl halid using KOH alcoholic to give *5-Phenyl-1,3,4-xadiazoleo thio ether (4a-e*).

A number of substituted -1,3,4-oxadiazole (7_{a-g}) and substituted 1,3,4-triazoles (5).

The *para* nitro phenyl hydrazide (2) which upon its reaction with various aldehydes aromatic or keto phenone in absolute Ethanol yield corresponding Schiff bases (6a-g). The compounds (6 a – g) were treated with acetic anhydride to give (7a– g).

The synthesized compounds were identified by using the melting point and infrared spectra analysis and the result are compatible with their assigned structures.

Key words:- 1,3,4-oxadiazole , 1,3,4-triazoles, biological activity

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تحضير وتشخيص وقياس الفعالية البايولوجية لبعض مركبات الاوكسازول والثايوزول

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قسم الكيمياء ، كلية العلوم ، جامعة تكريت ، تكريت ، العراق

الملخص

يتضمن البحث تحضيربارا نايترو فنيل هيدرازين (2) الذي حضر من تفاعل بارا نايترو مثيل بنزوات مع الهيدرازين المائي في الكحول وتم مفاعلة بارا نايترو فنيل هيدرازين (2) مع محلول كحولي من ال CS_2 – KOH لتعطي 5 – بارا نايترو- فنيل – 2 – مركبتو اوكسادايازول (3) ، أما عند تفاعل المركب (3) مع الهيدرازين المائي أعطى معوض – 1 ، 2 ، 4 – ترايازول (5) وأخيراً تمت مفاعلة المركب (3) مع هاليدات أريل مختلفة باستخدام هيدروكسيد البوتاسيوم الكحولي ليعطي 5 – بارا نايترو فنيل -2 – معوض الثايو أيثر – 1 ، 2 ، 4 – اوكسادايازول (4a – g) .

، وكذلك تم مفاعلة المركب (2) مع أمينات أروماتية مختلفة للحصول على قواعد شيف (6a-g) وهذه المركبات (6a – g) تمت حولقتها إلى المركبات المقابلة (7a – g) باستخدام أنهدريد حامض الخليك .

شخصت المركبات المحضر بأستخدام درجا ت الانصهار ومطيافية الاشعة تحت الحمراء وكانت النتائج مطابقة للمركبات المحضرة .

الكلمات المفتاحية:- 4,3,1-اوكسادايازول , 4,3,1 – ترايزول ، الفعالية البايولوجية

Introduction

The five member ring heterocyclic compounds have been studied by much research because of chemical and variable biological effects [1]. 1,3,4- Oxadizoles and thiadiazoles represent an important class of heterocyclic compounds that have many applications in the daily life [2] as exhibit bactericidal, agricultural[3- 4], anti malarial[5], antiflammatory, insecticidescompound[6], antitubercular[7], hypertensive, hypoglycemic[8], analgesic , anticonvulsive[9],insecticidal[10],antiemetic diuretic[11], muscle relaxant, herbicide [5-8], moreover derivative of 1,2,3- oxadiazole which contain thio amide group CNS. Its importance lies in removing the poisons in much of the medicine used human beings [10] .

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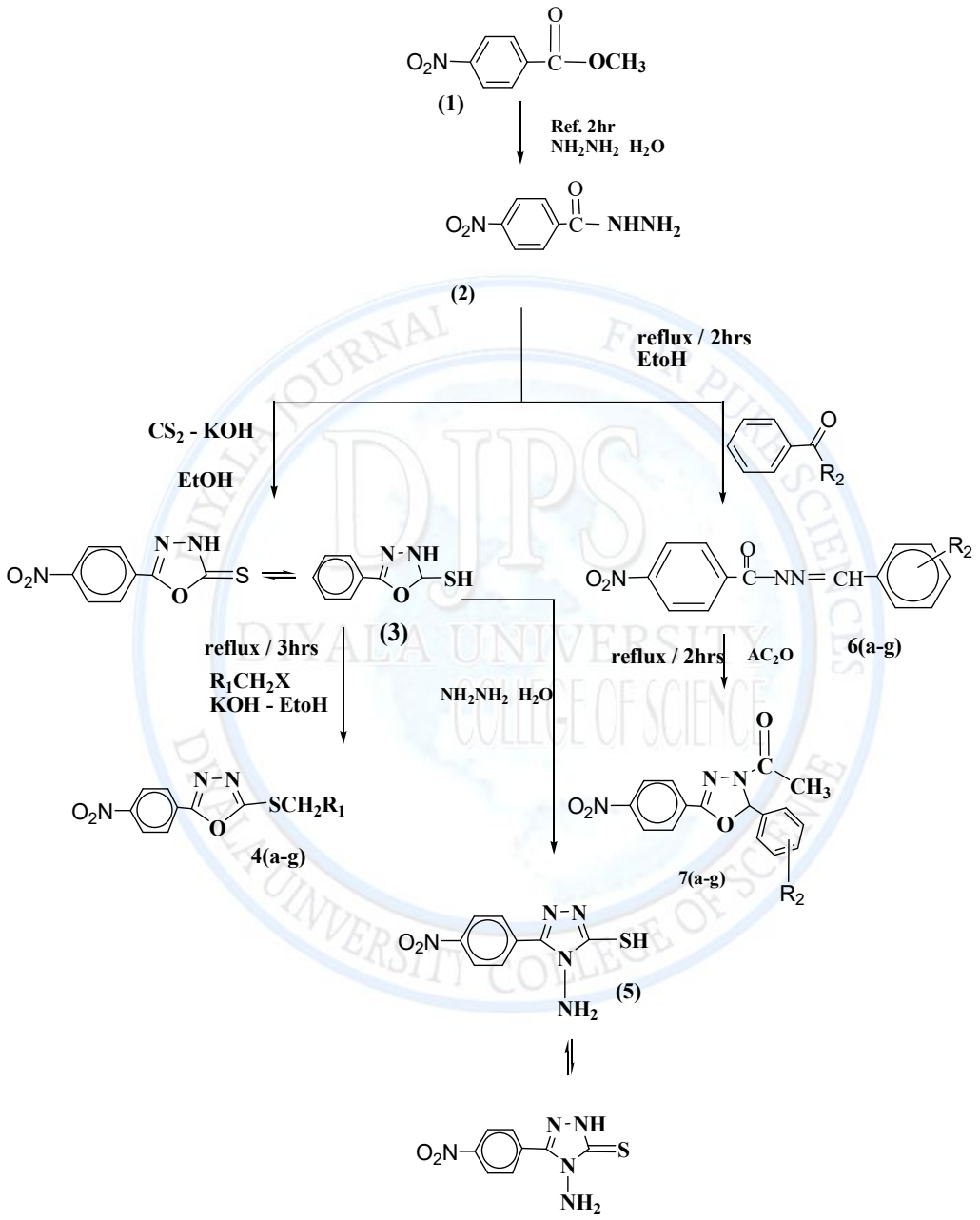


R_2 = H; m - NO_2 ; *P* - OH; *P* - N, N - Dimethyl 2,4 - dichloro;
R_1 = benzyl ; *P*ara Bromo benzyl ; Propylchloride ; Ethylchloride ; m - nitro phenyl ; *P* - nitroPhenyl ; 2,4 - dinitrophenyl ; *P*ara - N,N_ dimethyl phenyl ethyl.

Scheme (1)

Experimental

Melting point were determined using an electro thermal 9300 digital melting point apparatus and are un corrected FT-IR spectra were recorded on 85005 shimadzu FTIR Japan spectrophotometer on potassium bromide pellets.

The ester prepared following a reported procedure [1] the structure of these compounds was confirmed by IR spectral data.

Syntheses of para nitro phenyl hydrazide (2) [10]

To mixture of para nitro phenyl benzene (0.01 mole, 1.5 gm) in ethanol (50ml) and was added to (99%) hydrazide hydrate (0.025 mole, 2.5ml) and the reaction mixture was refluxed for 3 hrs. after cooling the solid material precipitated was filtered off washed with ethanol dried and re crystallized from ethanol to give para nitro phenyl hydrazide (yield 90%) melting point (230- 233ºC) .

Synthesis of para* nitro *5-Phenyl-1,3,4-oxadiazole-2-thiol (3)

Amixture of para nitro pheny hydrazide (0.01 mole, 1.5gm), KoH (0.01mole) in ethanol (30ml) and CS_2 (6ml) was heated under reflux till the evaluation of H_2S case cover night). The excess solvent was with water, dried and recrystallized from ethanol to give yield 85%) melting point (265-267 ºC)

***syntheses of* Para nitro-*5-Phenyl-1,3,4-oxadiazole thio ether (4a-e*).**

To a solution of compound *para* nitro *5-Phenyl-1,3,4-oxadiazole-2-thiol (3)* (0.003 mole) in EtoH (30ml) was added K0H 0.399m and substituted benzyl chloride (0.003 mole). The mixture reaction was refluxed for 2hrs. After cooling was filled recrystallization with suitable. The physical properties of the synthesized are given in Table (3)

Synthesis of 4-Amino-3- phenyl -5-thiol-1, 2, 4-triazole (5)

A mixture of substituted Oxadiazole (0.9 gm) (0.005 mole) and hydrazine hydrate (2ml) in ethanol (20 ml), was refluxed for (6 h), then the solvent was evaporated under reduced pressure. The formed precipitate was filtered off; washed with water; dried and recrystallized from ethanol – water**:** melting point = 289- 292˚C .

Preparation of Schiff base (6a-g)

Synthesis of (substituted benzylidine phenyl hydrazide) [12].

A mixture of para nitro phenyl hydrazide (1.5gm, 0.01mole) with various benzaldehydes (0.01 mole) in absolute ethanol (50ml) was heat under reflux for 2 hrs. The solid obtained after subsequent concentration and cooling was filtered. The physical properties of the synthesized are given in table (1).

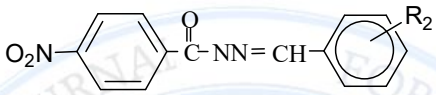
Synthesis of 2-Aryl-3-acetyl- Para nitro -5- phenyl-1, 3,4-Oxadiazole (7a-g)

A mixture of compounds (6a-g) (0.002 mole) and acetic an hydride (10 ml) was reflux for 2 hrs. After cooling the reaction mixture was poured into crushed ice and stirred vigorously until the oil become solid which was then filtered off and recrystallized from acetone which to give (7a-g) in (80 – 85 %) yield.

Results and Discussion

para nitro Phenyl hydrazide was prepared by reaction of Para nitro Ethyl benzoate with hydrazine hydrate (2).scheme (I). the structure of the prepared compounds (6_{a-e}) have been identified by their IR. spectra showed two bonds at (3290 and 3210) cm^{-1} of a symmetric and symmetric N-H stretching and (1661cm^{-1} due to the amide). The 5-phenyl oxadiazole derivatives (3) have been prepared by the cyclization reaction of the para nitro phenyl hydrazide (2) with CS_2 - KOH in Ethanol(2). The infrared spectra of compound (7a-g), Table (2) showed characterized compounds strong band at (1069cm^{-1} - 1620) due to C = N

stretching and (1292-1069) cm^{-1} assigned for (C -O- C) cyclic and bands at (1350-1380 cm^{-1}) and (3145-3240) cm^{-1} due to C = S and NH stretching 3145-3240cm^{-1} vibration respectively. The IR. Spectrum (table 3) show that appearance of reaction of para nitro phenyl hydrazine with carbonyl compounds product Schiff bases hydrazones showed strong band in the region (1605-1630)cm^{-1} as due to C = N stretching vibration.



6(a-g)

Table (1) :- The Physical and (I.R) spectroscopy properties to compound (6a-g).

Comp. No. (6a-g)	R	M.P ˚C	Ylied %	Solvent of recryst.	O ‖ C– NH v.str.	NH v. str.	C – H Arom.
a	*Ph-*	209 – 210	93	50 % EtoH	1640	3310	3030
b	*p-NO_2 Phenyl*	228 – 230	94	5 0% EtoH	1655	3280	3080
c	*m-NO_2 Phenyl*	196 – 198	91	50 % EtoH	1650	3280	3080
d	*Para hydroxy Phenyl*	238 – 240	90	50 % EtoH	1645	3300	3030
e	*Para –N,N-di methyl Phenyl*	185 – 187	95	acetone	1640	3310	3080
f	*2,4-di chloro Phenyl*	245 – 247	93	50 % ACoH	1630	380	3050

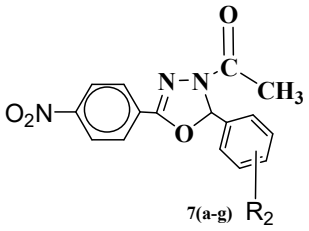
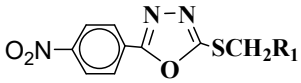


Table (2) :- The Physical and (I.R) spectroscopy properties of compound (7a-g).

Comp. No. 7a-g)	R_1	M.P °C	Yield	Solvent of recrys.	O ‖ C— NH	NH S2	C – H Arom.
a	*Phenyl*	201 – 203	75	EtoH	1750	3310	3030
b	*Para nitro Phenyl*	152 – 155	73	50 % EtoH	1740	3280	3080
c	*meta nitro Phenyl*	101 – 103	70	50 % EtoH	1755	3280	3080
d	*Para hydroxy Phenyl*	152-155d	74	EtoH	1745	3300	3030
e	*Para –N,N-di methyl Phenyl*	145 – 147	75	Benzene	1745	3310	3080
f	*2,4-di chloro Phenyl*	132-134d	70	EtoH	1735	380	3050



4(a-g)

Table (3) :- The Physical and (I.R) spectroscopy properties of compound (4a-g).

Comp. No. (4a-g)	R	M.P ˚C	Yield %	Solvent of recryst.	I.R		
					C = N	C – O – C	C – H Arom
a	*Para – Bromo benzyl*	260 d	93	EtoH	1590	1160 1030	3070
b	*benzyl*	210 d	80	Benzene	1600	1160 1030	3065
c	*2,4- di nitro Phenyl*	141 – 143	87	50 % EtoH	1620	1160 1030	3050
d	*m - nitro Phenyl*	192 – 194	90	50 % EtoH	1625	1160 1030	3050
e	*Para –N,N-di methyl Phenyl*	145 – 147	86	EtoH	1595	1160 1030	3055
f	*Para nitro Phenyl*	152 – 154	93	EtoH	1600	1160 1030	3070

As it was mentioned in the introduction part, most of the compounds of the selected lines in our research program play a great role in biological, medical and pharmaceutical fields. On these bases , in a subpart of our investigation we attempted to show that the prepared compounds are possessing anti-bacterial activity or not ,by testing against six common types of bacteria *Staphylococcus aureus, Bacillus subtillus ,Pseudonas aeruginosa ,Protans*

vulgarisginosa and Enterbacter sp., using the cup plate agar diffusion method [14] . The prepared KBr plates of compounds (3, 4a ,4b ,6a and 7b) were placed on the surface of the culture media and inculpated for 24h at 37C^{o} . During this study, it was found that the prepared compounds have anti-bacterial activity and the results were mentioned in (+) and (-) assignment.

Table (4): The Diameter of Inhibition zone (mm)of Some Synthesized Compounds Against Some *Gram^{+ve} and Gram^{-ve} Bacteria* .

Comp. No.	*Con.(mg/ml)*	*Staphylococcus aureus*	*Bacillus subtillus*	*Escherichia coli*	*Pseudonas aeruginosa*	*Protans vulgarisginosa*	*Enterbacter sp.*
3	0.01	-	-	-	-	-	-
	0.1	6	5	3	2	3	5
	1.0	7	7	5	5	7	9
	10	13	14	11	9	12	14
4a	0.01	-	-	-	-	-	-
	0.1	-	-	-	-	-	-
	1.0	-	-	-	-	-	-
	10	-	-	-	-	-	-
4b	0.01	-	-	-	-	-	-
	0.1	5	5	4	2	4	5
	1.0	7	6	7	6	6	7
	10	11	12	12	10	11	13
6a	0.01	-	-	-	-	-	-
	0.1	7	6	5	6	5	6
	1.0	8	7	8	7	7	8
	10	13	12	12	13	12	13
7b	0.01	-	-	-	-	-	-
	0.1	-	-	-	-	-	-
	1.0	-	-	-	-	-	-
	10	-	-	-	-	-	-
Chloramphenicol (30/µgm)disk	control	23	25	16	17	21	20

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