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Synthesis and Characterization of some Oxadiazoles and Thiadiazoles derivatives

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Abstract: A number of heterocyclic compounds was synthesized from the reaction of methyl benzoate (1) with hydrazine hydrate in the presence of alcohol to give phenyl hydrazide (2). The phenyl hydrazide (2) had been treated with various aromatic aldehydes in absolute ethanol yield corresponding Schiff bases (4a – g), and these compounds were treated with acetic anhydride to give (5a – g). Phenyl hydrazide (2) was treated with Carbon disulfide in alcoholic Potassium hydroxide solution to give (3) and the reaction of (3) with hydrazine hydrate give substituted -1, 2, 4-triazole (6). Finally the reaction of (3) with various Aryl halides in the presence of alcoholic Potassium hydroxide solution gave substituted -1, 3, 4- Oxadiazole -2- Aryl thioether (7a – g). The synthesized compounds were identified by physical, chemical and spectroscopic data.

Key words: Synthesis , Characterization , Oxadiazoles ,, Thiadiazoles, derivatives

Introduction:

The five membered ring heterocyclic compounds have been studied by many researchers because of chemical and variable biological effects⁽¹⁾. 1,3,4-Oxadiazoles and thiadiazoles represent an important class of heterocyclic compounds that have many applications in the daily life⁽²⁾ as exhibit bactericidal, agricultural^(3,4), antimalarial, anti-inflammatory, insecticides compounds^(5,6), antitubercular⁽⁷⁾, hypertensive⁽⁸⁾, hypoglycemic⁽⁹⁾, analgesic, anticonvulsive⁽¹⁰⁾, insecticidal⁽¹¹⁾, antiemetic diuretic⁽¹²⁾, muscle relaxant, herbicide⁽⁵⁻⁸⁾, moreover derivatives from oxadiazole which contain thioamide group CNS. Its importance lies in removing the poisons in much of medicine used by human beings⁽¹³⁾.

Experimental:

Uncorrected melting points were determined using an electro thermal 9300 digital melting point apparatus, FT-IR spectra were recorded on 8500s shimadzu FT-IR Japan spectrophotometer on potassium bromide pellets, reaction progress were monitored by the T. L. C. technique.

Synthesis of ester (1):

The ester prepared following a reported procedure (1) the structure of the ester was confirmed by IR spectral and physical properties.

Synthesis of phenyl hydrazide (2) (10):

A mixture of methyl benzoate (1) (0.01 mole, 1.5 gm) in (50ml) ethanol absolute was added to (99%) hydrazine hydrate (0.025 mole, 2.5ml) and the reaction mixture was refluxed for (3hrs), after cooling the solid

material precipitated was filtered, washed with ethanol, dried and crystallized from ethanol gave phenyl hydrazide (yield 90%) m.p (113-115Co) lit. (114-115Co).

Synthesis of 5-Phenyl -1,3,4- oxadiazole-2-thiol (3) (5):

To a solution of phenyl hydrazide (0.01 mole, 1.5gm) and KOH (0.01mole) in ethanol (30ml) CS₂ (6ml) was added. The resulting mixture heated under reflux till the evolution of H₂S was stopped (over night). The excess solvent was removed and the residue was washed with water, dried and recrystallized from ethanol gave the product yield (85%) m.p (221-222Co), (lit.222 Co).

Synthesis of substituted benzylidene phenyl hydrazide (4a-g) (12):

A mixture of phenyl hydrazide (2) (0.01mole, 1.5gm) and appropriate subs. Aromatic aldehydes in absolute ethanol (50ml) was heated under reflux for (2hrs). The solid obtained was filtered and recrystallization with suitable solvent. The physical properties of the synthesized products are listed in table (1).

Synthesis of 2-Aryl-3-acetyl-5-phenyl-1,3,4-Oxadiazole (5a-g) (9):

A mixture of compounds (4a-g) (0.002 mole) and acetic anhydride (10 ml) was refluxed for (2hrs). 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 suitable solvent to give (5a-g). The physical properties of the synthesized are listed in table (2).

Synthesis of 4-Amino-5-phenyl-1, 2, 4-triazole-3-thiol (6) (1):

A mixture of substituted Oxadiazole (3) (0.005 mole, 0.9 gm) and hydrazine hydrate (99%) in ethanol absolute (20 ml), was refluxed for (6hrs). The solvent was evaporated under reduced pressure. The residue was filtered off, washed with water, dried and recrystallized from ethanol – water. m.p (199 – 200 °C) Yield (80 %).

Synthesis of thioether(5) (7a-g):

To a solution of compound (3) (0.003 mole) in Ethanol (30ml) was added KOH (0.399 mole) and substituted benzyl chloride (0.003 mole). The resulting mixture was refluxed for (2hrs). After cooling it was filtered and recrystallization with suitable solvent. The physical properties of the synthesized are listed in Table (3).

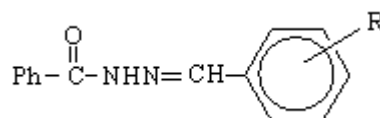


Table (1) :- The Physical and (I.R) spectroscopy properties of the compounds (4a-g).

Comp. No.	R	M.P °C	Yield %	Solvent of recrystallization	I.R/ ν cm ⁻¹		
					$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{NH} \end{array}$	C - H	NH
4a	H	209 – 210	93	5 % EtOH	1640	3030	3310
4b	P-NO ₂	228 – 230	94	5 % EtOH	1655	3080	3280
4c	m-NO ₂	196 – 198	91	5 % EtOH	1650	3080	3280
4d	P-OH	238 – 240	90	5 % EtOH	1645	3030	3300
4e	P -N,N-di methyl	185 – 187	95	acetone	1640	3080	3310
4f	2,4-di chloro	245 – 247	93	5 % AcOH	1630	3050	3800
4g	Furfural	175 – 178	85	Benzene	1645	3055	3395

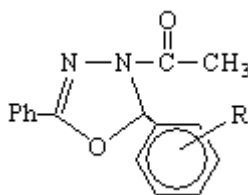


Table (2) :- The Physical and (I.R) spectroscopy properties of the compounds (5a-g).

Comp. No.	R	M.P °C	Yield %	Solvent of recrystallization	I.R/ ν cm ⁻¹		
					$\begin{array}{c} \text{O} \\ \parallel \\ \text{C}-\text{NH} \end{array}$	C - H	NH
5a	H	201 – 203	75	EtOH	1750	3040	3300
5b	P-NO ₂	152 – 155	73	50 % EtOH	1650	3060	3300
5c	m-NO ₂	101 – 103	70	50 % EtOH	1700	3060	3310
5d	P-OH	159-161	74	EtOH	1680	3040	3315
5e	P -N,N-di methyl	145 – 147	75	Benzene	1680	3080	3315
5f	2,4-di chloro	135-138	70	EtOH	1700	3060	3320
5g	Furfural	100 – 108	70	50 % EtOH	1680	3040	3300

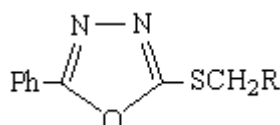
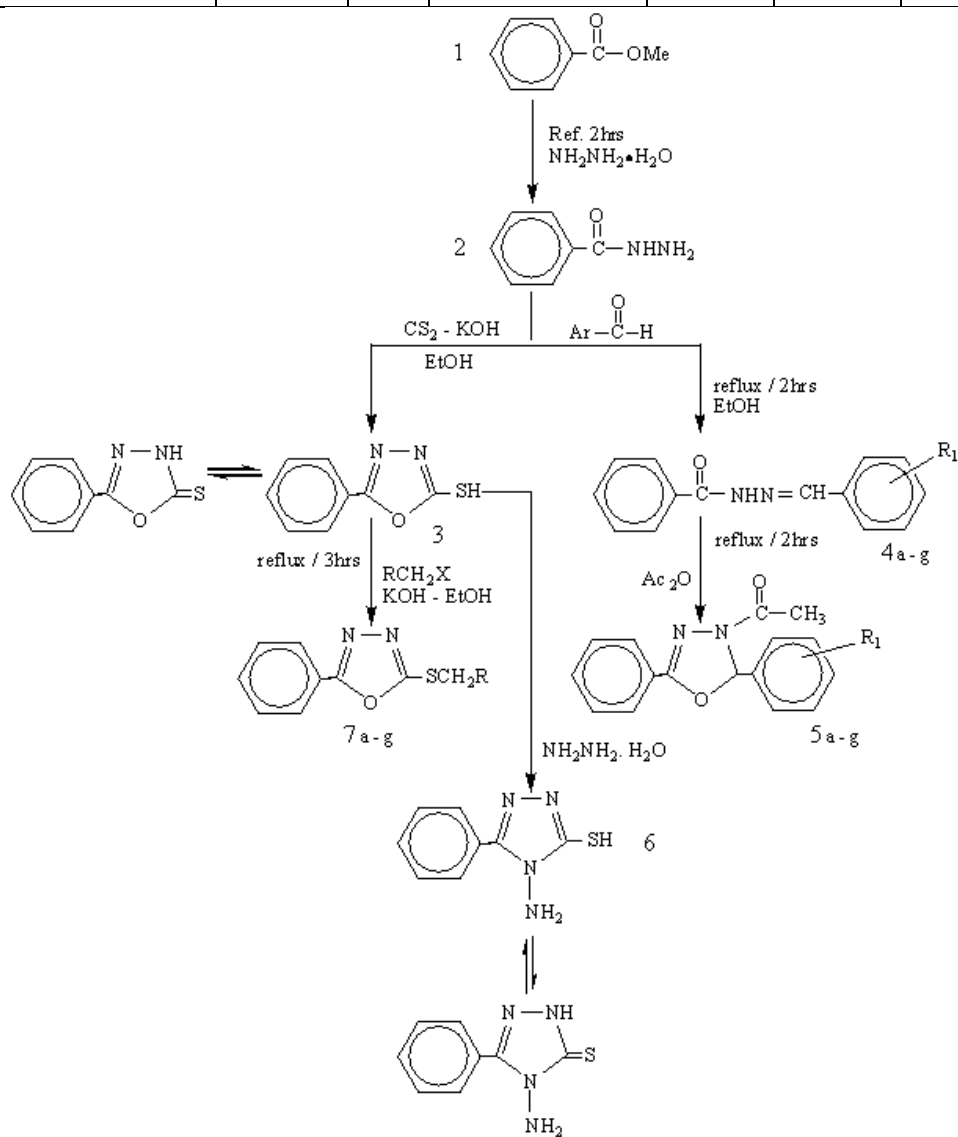


Table (3) :- The Physical and (I.R) spectroscopy properties of the compounds (7a-g).

Comp. No.	R	M.P °C	Yield %	Solvent of recrystallization	I.R/ ν cm ⁻¹			
					C = N	C – O – C	C – S	Ar-H
7a	P – Bromo phenyl	260 d	93	EtOH	1610	1120 1140	1400	3030
7b	Phenyl	210 d	80	Benzene	1620	1150 1165	1405	3100
7c	-COOH	250 d	85	acetone	1610	1130 1145	1405	3020
7d	2,4- di nitro Phenyl	141 – 143	87	50 % EtOH	1620	1150 1165	1400	3070
7e	m - nitro Phenyl	192 – 194	90	50 % EtOH	1618	1120 1145	1415	3030
7f	P-N,N-di methyl Phenyl	145 – 147	86	EtOH	1615	1150 1165	1410	3100
7g	P-nitro Phenyl	152 – 154	93	EtOH	1610	1130 1145	1400	3030



R = Phenyl, Para Bromo Phenyl, m - nitro phenyl, Para - N, N - dimethyl phenyl, P - nitrophenyl, 2,4 - dinitro phenyl, -COOH.

R₁ = H, m - NO₂, P - NO₂, P - OH, P - N, N - Dimethyl, 2,4 - dichloro, FurFural.

Scheme (1)

Results and Discussion:

Phenyl hydrazide was prepared from the reaction of methyl benzoate and hydrazine hydrate(2) as shown in (scheme 1). The structure of the compound (2) have been identified by it's melting point (113 – 115oC) lit. (113 – 114 oC). IR Spectra showed two bands at (3290 and 3210 cm-1) of a symmetric and symmetric (N – H) stretching and (1660 cm-1) to (C=O) amide stretching vibrations.

The 5 – phenyl – 1, 3, 4 – oxadiazole – 2 – thiol (3) have been prepared by the cyclization reaction of the phenyl hydrazide (2) with carbon disulfide in the presence of Potassium hydroxide in absolute ethanol. The IR spectra of this compound showed strong band at (1608 cm-1) assigned to (C=N) stretching and strong band in the range (1298 – 1070 cm-1) assigned for (C–O –C) cyclic grouping and bands at (1180 cm-1) and (3413 – 3234 cm-1) due to (C = S) and (NH) stretching vibration respectively.

Reaction of phenyl hydrazide with different aromatic aldehydes afforded the addition dehydration hydrazone products (4a – g). The formation of these condensation products was confirmed by physical properties and spectral analysis. The IR characterization data are showed strong band in the region (1615 - 1635 cm-1) due to stretching vibration (C = N). The synthesized compounds (5a – g) have been characterized by their physical and spectra data. IR spectra showed absorption band (1650 - 1750 cm-1) due to (C = O) amide stretching vibration and appearance of a band at (1280 cm-1) for (C – O – C) cyclic grouping in oxadiazole ring, as showed in Table (2).

The resulting substituted – 1, 3, 4 – oxadiazole (3) was treated with hydrazine hydrate to give 5 – phenyl – 4 – amino 1, 2, 4 – triazole (6). The IR spectral data was showed absorption at (3320 cm1, 3355 cm-1) due to (NH), a band at (1640 cm-1) due to (C = N) and (1180 cm-1) due to (C = S) of thion form.

Finally oxadiazole derivatives (7a – g) was synthesis by their reaction with substituted benzyl

chloride (or bromide) in the presence of ethanolic potassium hydroxide, the compounds (7a – g) shows the appearance of (C – H) absorption band at (2920 – 2939 cm-1) which was utilized to confirm the formation of benzyl thioderivatives. The spectrum showed the disappearance of the band at (2580 cm-1) assigned to (S – H) stretching and a bands at (1070 cm-1) due to (C – S) stretching also the spectrum showed a typical absorptions of oxadiazole ring endo cyclic (C – O – C) at (1280 cm-1) and absorption band of (C = N) near (1617 cm-1) see Table (3).

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تحضير وتشخيص بعض مشتقات الأوكسادايازول والثايداايازول

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الخلاصة

يتضمن البحث تحضير فنييل هيدرازيد (2) من تفاعل مثيل بنزوات (1) مع الهيدرازين المائي في الكحول ، وتم مفاعلة المركب (2) مع أمينات أروماتية مختلفة للحصول على قواعد شيف (4a – g) ومن ثم تمت حولقتها إلى المركبات المقابلة (5a–g) باستخدام حامض الخليك اللامائي . وتم مفاعلة الفنييل هيدرازيد (2) مع محلول كحولي من (CS₂ – KOH) لتعطي 5 – فنييل – 2 – مركبتو اوكسادايازول (3) ، أما عند تفاعل المركب (3) مع الهيدرازين المائي أعطى معوض – 1 ، 2 ، 4 – ترايازول (6) وأخيراً تم مفاعلة المركب (3) مع هاليدات بنزيل مختلفة باستخدام هيدروكسيد البوتاسيوم الكحولي ليعطي 2 – معوض الثايو أيتز – 1، 3، 4- اوكسادايازول (7a – g). شخّصت المركبات المحضرة باستخدام درجات الانصهار وطيف الأشعة تحت الحمراء.