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Synthesis of Some New Schiff's-Bases Derived From 2-(4-methoxy phenyl)-5-(4-amino phenyl)-1,3,4-Oxadiazole

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Abstract

A new compound 2-(4-methoxyphenyl)-5-(4-aminophenyl)-1,3,4-oxadiazole [VI] was prepared by intramolecular condensation reaction followed by elimination of some simple moieties such as H_2O and HCl by using $POCl_3$ with acid hydrazide. A series of new Shiff's-bases 2-(4-methoxyphenyl)-5-[4(4-alkoxybenzoyloxy) benzylidene amino phenyl] 1,3,4-oxadiazole $[VII]_n$ was synthesized from treatment of oxadiazole derivative [VI] with an appropriate aromatic aldehyde [III]. Structure of the resulting products have been ascertained by their melting points, elemental analysis (some of them) and spectral data.

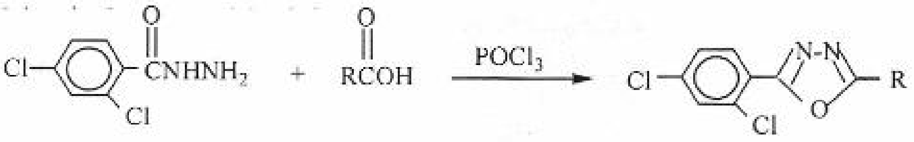
Introduction

The 1,3,4-oxadiazole derivatives are used in many diverse areas (1), for example, in the dyestuffs industry and in drug synthesis. 1,3,4-oxadiazole derivatives were known to possess various biological activities such as antiparasites (2) and antibacterial (3).

Several methods have been used to synthesize 1,3,4-oxadiazole derivatives among these: are refluxing ethanolic mixture of acid hydrazide, carbon disulfide and KOH (4), from other ring systems (5). Another pathway to synthesize 1,3,4-oxadiazole derivatives is via the reaction between acid hydrazide and orthoesters (6).

It is possible also to synthesize 1,3,4-oxadiazole ring by oxidation of aroyl anhydrazones of aldehydes with using bromine in glacial acetic acid (7).

Ramalingam (8) and Dutta (9) used $POCl_3$ in the synthesise of 2,5-disulbstituted-1,3,4-oxadiazole [1] from acid hydrazide and carboxylic acid.



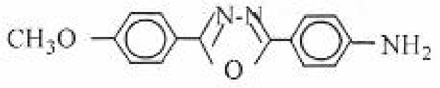
The latter method seems to be the best because of the high yield of the oxadiazole derivatives.

The aromatic amines canbe added to aromatic aldehyde to give a quite stable imines.

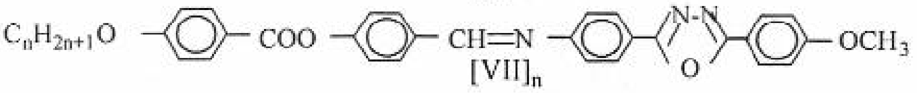
The reaction is straightforward and proceeds in high yields (10).

$$ArNH_2 \quad + \quad \overline{Ar}CHO \xrightarrow{H^+} ArN{=}CH\overline{Ar} \quad + \quad H_2O$$

This paper describes the synthesise and characterization of oxadiazole derivative [VI] and its novel Schiff's-base derivatives [VII].



[VI]



[VII]$_n$

n=1-9

Experimental

Chemicals

Most of chemicals used were supplied from Fluka and BDH Chemicals Co. and were used without further purification.

Techniques

Melting points were determined by using an (Electro thermal) melting point apparatus and were uncorrected. IR spectra were recorded on a Shimadzu 408 infrared spectrophotometer (KBr disc). The UV spectra were performed on a Shimadzu UV-visible-160 spectrophotometer. Elemental analyses were carried out by using Carlo-Erba 5500 elemental analyzer.

Synthesis

The homologous series of 2-(4-methoxyphenyl)-5-[4(4´-alkoxy benzoyloxy) benzylideneaminophenyl]-1,3,4-oxadiazole $[VII]_n$ was synthesized according to scheme (1).

4-n-alkoxybenzoic acid $[I]_n$ and 4-n-alkoxybenzoyl chloride $[II]_n$ were prepared following the procedure described by Apfel et. al.(11).

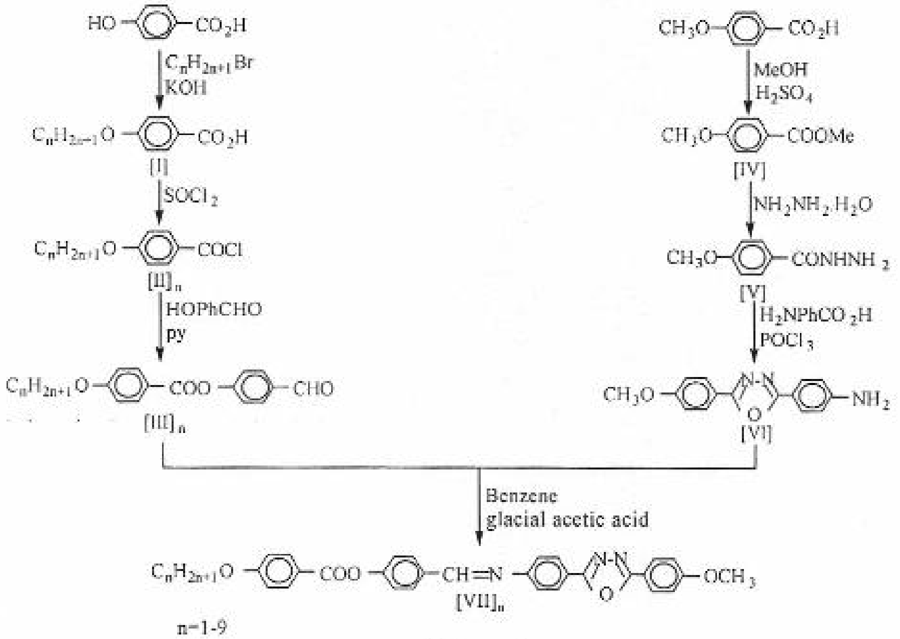
4-(4´-alkoxybenzoyloxy) benzaldehyde $[III]_n$

Alkoxybenzoyl chloride (0.01 mol) was added to a stirred solution of 4- hydroxybenzaldehyde (1.22gm, 0.01 mole) and dry pyridine (1 ml) in dry DMF (5 ml) at 5°C. Then the stirring was continued for 3hrs at room temperature. Afterwards, the reaction mixture was poured into (100 ml) of 10% HCl. The precipitate was filtered and washed with solution of 10% $NaHCO_3$. And then washed with water several times, dried and recrystallized from ethanol (12) (yield 85-92%).

The IR characteristic absorption bands of these compounds are given in Table (1).

Methyl-4-methoxybenzoate [IV]

These were prepared following the procedure described by Vogel (13) m.p. 49-51°C (lit m.p. 49-51°C).



Scheme I

4-Methoxybenzoyl hydrazine [V]

To a solution of methyl-4-methoxybenzoate (5gm, 0.03mol) in ethanol (10ml), hydrazine hydrate (12ml) was added, the mixture was refluxed for 2hrs, the precipitate was filtered, washed with ice-water and crystallized from ethanol (14)(yield 98%). m.p.: 135-137°C.

IR: 3160 cm^{-1} (ν_s, NH_2, stretch), 3300cm^{-1} (ν_{as}, NH_2, stretch), 3060 (ν_{NH}, stretch), 1645cm^{-1} (C=O of amide group, stretch).

2-(4-Methoxy phenyl)-5-(4-aminophenyl)-1,3,4-oxadiazole [VI]

A mixture of 4-methoxybenzoyl hydrazine (0.01mol), 4-amino benzoic acid (0.01mol) and phosphorus oxy chloride (5ml) was refluxed for 7hrs. The cold reaction mixture was poured into ice-water and made basic by adding sodium bicarbonate solution (6). The resulting solid was filtered, dried and purified by refluxing with ethanol (yield 89%).

m.p.: 196°C

IR: NH_2, stretch, coupled doublet at: asym. 3320cm^{-1} and sym. 3200cm^{-1}, C=N stretch, 1620, C-O-C stretch, two peaks at: asym. 1245cm^{-1} and sym. 1070 cm^{-1}.

Elemental analysis: $C_{15}H_{13}N_3O_2$; Found: C%=67.89, H%=5.44, N%=15.49.

Calcd.: C%=67.41, H%=4.86, N%=15.73.

UV (DMSO): λ_{max} 305.4nm.

2-(4-methoxyphenyl)-5-[4(4-alkoxybenzoyloxy)benzylideneamino phenyl]-1,3,4-oxadiazole [VII]$_n$

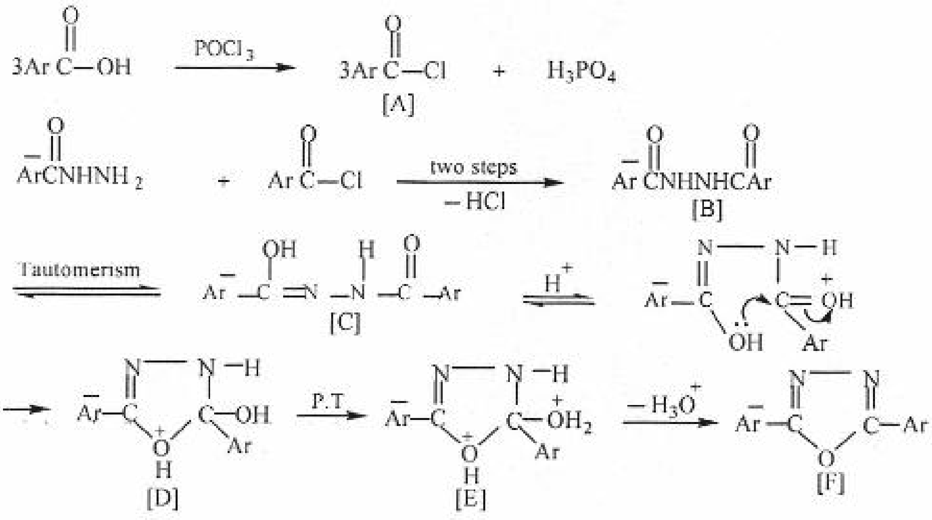
A mixture of compound [VI] (0.01 mol), 4-(4-n-alkoxy benzoyloxy) benzaldehyde (0.01 mol), dry benzene (15ml), and glacial acetic acid (5 drops) was refluxed for 8hrs . The solvent was evaporated and the risidue purified by refluxing with ethanol. The physical properties for the synthesized compounds are given in table (2), the elemental analysis of some of them is listed in table (3). The IR characteristic absorption bands of these compounds are given in table (4).

UV (DMSO) of compound [VII]$_4$: λ = 270nm,283.6nm and 290.4nm.

Results and Discussion

Methyl-4-methoxybenzoate [IV] was obtained by esterification of the carboxylic acid moiety of 4-methoxy benzoic acid, using absolute methanol in presence of H_2SO_4. This structure was identified by its melting point (49-51)°C. Condensation of [IV] with 98% hydrazine hydrate yielded the 4-methoxybenzoylhydrazine [V], which is characterized by its higher melting point (135-137°C) and by its IR-spectrum. The IR spectrum of this compound showed stretching bands at 3300, 3160, 3060 cm^{-1}, which are assigned to the asymmetric and symmetric stretching bands of NH_2 and NH groups, respectively. The IR spectrum also showed a shift in the carbonyl stretching band from 1730 cm^{-1} in ester to 1645 cm^{-1} (amid) in the acid hydrazide.

The 2,5-disubstituted-1,3,4-oxadiazole [VI] was synthesized according to the method described by Dutta (9), by a route in which the acid hydrazide was condensed with the appropriate aromatic acid in the presence of phosphorus oxychloride. The suggested mechanism of this reaction may be outlined as follows (scheme 2):



$\overline{Ar} = CH_3OPh$, $Ar = PhNH_2$

Scheme 2

The reaction is initiated by converting the acid to the acid chloride [A] by the action of phosphorus oxychloride. The diacid hydrazides [B] is formed as a result of the nucleophilic attack by the more nucleophilic amino group of the hydrazide on acid chloride, which tautomerizes to the enolic form [C].

In the presence of acid, the cyclization takes place by intramolecular nucleophilic substitution to form intermediate [D], which would undergo rapid proton transfer to afford [E]. Finally, loss of proton takes place to give the oxadiazole product [F].

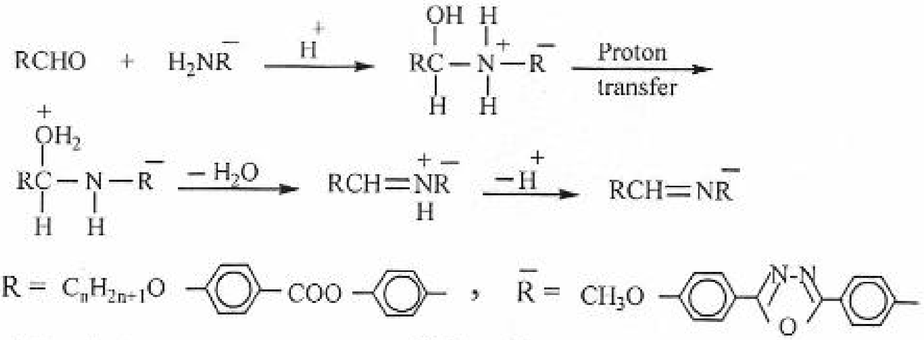
The structure of oxadiazole derivative [VI] was confirmed by elemental analysis and spectroscopy (IR and UV).

The IR-absorptions spectrum of this compound showed disappearance of absorption bands due to C=O stretching (amid) of hydrazide [V] together with the appearance of a stretching band at 1620 cm^{-1} which is assigned to C=N stretching (15) of oxadiazole moiety. It also showed two peaks at 3200cm^{-1}, 3320cm^{-1}, which are assigned to the symmetric and asymmetric stretching bands of NH_2 group and at 1070 cm^{-1}, 1245cm^{-1} due to symmetrical and asymmetrical C-O-C stretching vibration (16).

UV spectrum of oxadiazole [VI] in DMSO [C(M)=$1x10^{-3}$] gives the λ_{max} at 305.4nm (Abs=1.71).

The Schiff's-bases of series $[VII]_n$ were prepared by refluxing equimolar quantities of compound [VI] and 4(4-alkoxybenzoyloxy) benzaldehyde in dry benzene.

The mechanism of this reaction may be outlined as follows (Scheme 3)(17) :



Schem 3

The synthesized compounds were characterized by elemental analysis (Which are consistent with their proposed structures) and spectroscopy data.

The characteristic IR-absorption spectra showed the disappearance of two absorption bands of NH_2 group of compound [VI] together with the appearance of a stretching band at (1638-1645) cm^{-1} assignable to C=N stretching, it also shows a stretching band around 1720cm^{-1} assigned to carbonyl of the ester group. Table (4) shows the characteristic absorption bands of prepared compounds.

UV spectrum of compound $[VII]_4$ was obtained in DMSO $[C(M)=1x10^{-3}]$ give the three absorption bands at λ=270nm (Abs=1.42), 283.6nm (Abs=1.46) and 290.4nm (Abs=1.36).

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Table (1) Characteristic IR absorption band of series $[III]_n$

Comp. No.	ν_{C-H} aliphatic	$\nu_{-C=O}$ ester	$\nu_{-C=O}$ aldehyde	δO-C=O of ester group two peak	δC-H out of plane p-substituted
$[III]_1$	2850-2930	1716	1692	1125-1185	825
$[III]_2$	2865-2945	1722	1692	1120-1185	830
$[III]_3$	2820-2915	1725	1695	1115-1182	830
$[III]_4$	2850-2950	1720	1690	1120-1180	825
$[III]_5$	2810-2900	1720	1692	1110-1175	835
$[III]_6$	2865-2950	1722	1690	1115-1180	828
$[III]_7$	2850-2945	1720	1692	1120-1175	822
$[III]_8$	2820-2945	1722	1698	1115-1182	822
$[III]_9$	2810-2930	1722	1692	1120-1182	828

Table (2) The physical properties of the Schiff's -base derivatives $[VII]_n$

Comp.No.	m.p.(°C)	Yields (%)	Formula	Color
$[VII]_1$	254	82	$C_{30}H_{23}N_3O_5$	Yellow
$[VII]_2$	184	70	$C_{31}H_{25}N_3O_5$	Pale yellow
$[VII]_3$	252	88	$C_{32}H_{27}N_3O_5$	Yellow
$[VII]_4$	246	85	$C_{33}H_{29}N_3O_5$	Yellow
$[VII]_5$	242	90	$C_{34}H_{31}N_3O_5$	Yellow
$[VII]_6$	248	85	$C_{35}H_{33}N_3O_5$	Yellow
$[VII]_7$	234	80	$C_{36}H_{35}N_3O_5$	Orange
$[VII]_8$	250	82	$C_{37}H_{37}N_3O_5$	Yellow
$[VII]_9$	228	84	$C_{38}H_{39}N_3O_5$	Brown

Table (3) Elemental analysis of the Schiff-base derivatives [VII]

Comp. No.	Theoretical			Experimental		
	C%	H%	N%	C%	H%	N%
$[VII]_3$	72.04	5.06	7.87	72.90	5.46	7.64
$[VII]_6$	73.04	5.73	7.30	73.85	5.96	7.18
$[VII]_7$	73.34	5.94	71.3	73.52	6.68	7.55
$[VII]_9$	73.90	6.32	6.80	73.22	5.98	6.96

Table (4) Characteristic IR absorption band of series $[VII]_n$

Comp. No.	ν_{C-H} aliphatic	$\nu_{-C=O}$ ester	$\nu_{-C=N}$ imine	$\nu_{-C=N}$ of oxadiazole ring	ν_{-C-O-C} $\nu_{sym.}$, $\nu_{asym.}$
$[VII]_1$	2775-2895	1722	1645	1612	1070, 1240
$[VII]_2$	2790-2900	1720	1645	1612	1065, 1240
$[VII]_3$	2750-2880	1720	1642	1610	1065, 1240
$[VII]_4$	2770-2900	1722	1645	1610	1056, 1240
$[VII]_5$	2745-2870	1720	1642	1610	1056, 1236
$[VII]_6$	2775-2890	1720	1640	1610	1046, 1232
$[VII]_7$	2750-2930	1722	1638	1615	1040, 1228
$[VII]_8$	2745-2895	1720	1638	1615	1040, 1228
$[VII]_9$	2740-2890	1720	1640	1610	1040, 1225

تحضير بعض من قواعد شف الجديدة والمشتقة من المركب الاساسي 2-(4-ميثوكسي فنيل)-5-(4-امينو فنيل)-4,3,1-اوكسادايازول.

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الخلاصة

تم تحضير المركب الاساسي الجديد 2-(4-ميثوكسي فنيل)-5-(4-امينو فنيل)-4,3,1 اوكسادايازول [VI] من تفاعل التكثيف الضمني الجزيئة، ثم حذف جزيئات بسيطة كجزيئة الماء و HCl؛ وذلك من خلال استخدام $POCl_3$ مع هيدرازيد الحامض. حضرت سلسلة جديدة من قواعد شف $[VII]_n$: 2-(4-ميثوكسي فنيل)-5-[4-(4-الكوكسي بينزوايلوكسي) بنزيليدين امين فنيل]—4,3,1اوكسادايازول؛ وذلك من خلال معاملة المركب السابق الذكر (مشتق الاوكسادايازول) [VI] مع الالديهايد الاروماتي المناسب [III] . اثبت صحة التراكيب للمركبات الناتجة من خلال درجات الانصهار وبوساطة التحليل الدقيق للعناصر (للبعض منها) وبوساطة القياسات الطيفية.