BEHAVIOUR OF O-PHENYLENEDIAMINE AND O-AMINOTHIOPHENOL WITH AZIACTONES. A NEW SYNTHESIS OF SOME BENZIMIDAZOLE AND BENZOTHIAZOLE DERIVATIVES

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Abstract- A new route for the preparation of benzimidazoles (5) and benzothiazoles (10) is described. o-Phenylenediamine reacted with 2-aryl-4-arylidene-2-oxazolin-5-ones to give the corresponding benzimidazole derivatives (5) while o-aminothiophenol produced either benzothiazole (10) or intermediates (8) and (9) which could be cyclised to (10).

2-Aryl-4-arylidene-2-oxazolin-5-ones (1) react readily with aromatic amines to give the corresponding imidazolin-5-ones[1-3]. This reaction was found to be general and occurred by ring opening followed by recyclisation.

In continuation of our work aiming to clarify the synthetic potentialities of 2-aryl-4-arylidene-2-oxazolin-5-ones[4-7], we report here our farther results in this direction. Thus interaction of 2-aryl-4-arylidene-2-oxazolin-5-ones with aromatic amines containing two adjacent nucleophilic groups such as amino or amino and sulphohydryl groups; no imidazolin-5-one deirvatives were isolated. Instead a new route of reaction was undertaken and other new products were found. In the reaction of o-phenylenediamine with 2-phenyl-4-benzylidene-2-oxazolin-5-one (1a) either in ethanol or glacial acetic acid as a solvent and fused sodium acetate as catalyst, a product of molecular formula $C_{22}H_{17}ON_3$ (M^+, m/z 339) was formed. Three theoretically possible isomeric structures (3), (4) and (5) were considered for this product. Structures (3) and (4) were readily ruled out based

on IR and ^{1}H-NMR spectra of the product as well as its chemical behaviour. The ir spectrum showed no absorption bands at 3450-3100 cm^{-1} (for NH_2 group) or at that corresponding for C=O of imidazolone ring (1730 cm^{-1}). This readily eliminates structure (3). Also the ir spectrum is free from any band corresponding to -OH group (3500 cm^{-1}) and this fact, beside sterric hiderance opposed the formation of isomer (4). Thus the only theoretically possible structure for our derivative will be isomer (5).

The structure of (5) was established on the basis of spectral data: mass spectrometery measurements revealed the presence of an ion at m/z 105, which represents the base peak in all the derivatives isolated and accurate mass measurements indicate that the ion at m/z 105 is C_6H_5CO. ^{1}H-NMR data was found to be in agreement with structure (5) and indicate the following signals δ 12.5(s,1H, benzimidazole NH) δ 10.2(s,1H CONH) and δ, 7.95-7 (m, 15H, aromatic and CH=C) (cf. Table 1).

Table 1. Spectral data of the compounds synthesized

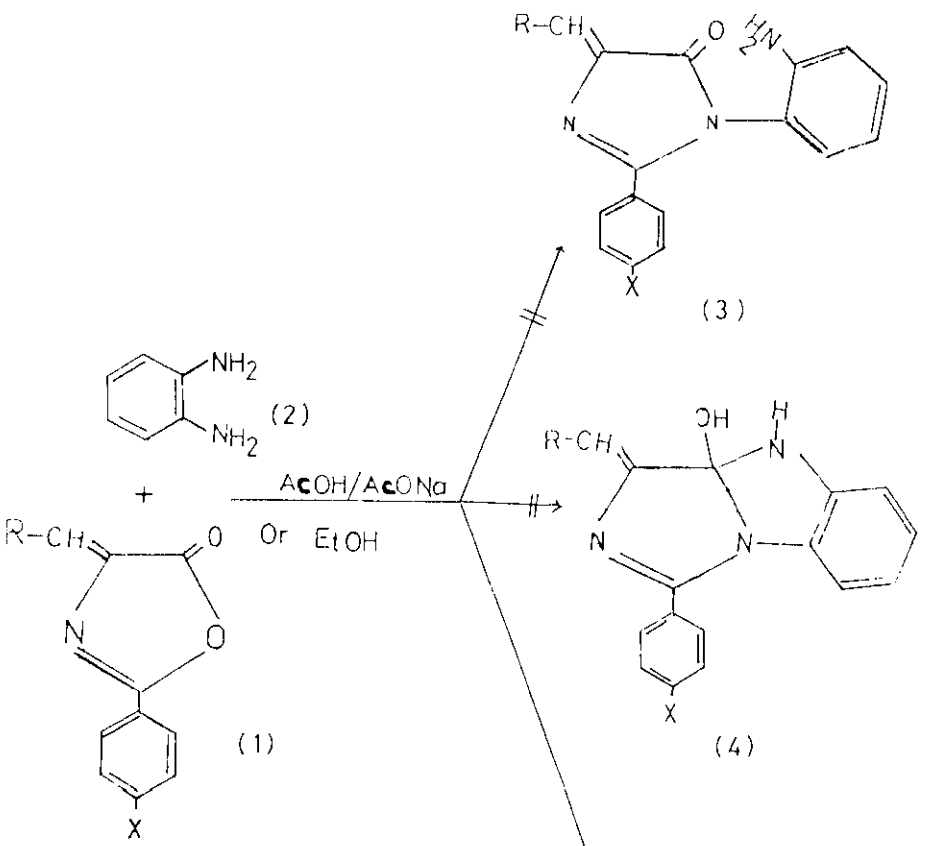
Comp.	IR, KBr, cm^{-1}	^{1}H-NMR, δ ppm
5a	3450-3100(NH and CO.NH) 1640 (amidic Co.)	12.5(s,1H,ring NH), 10.2(s, 1H CONH) 7.85-7 (m, 15H, aromatic and CH=C)
5b	3450-3150 (ring NH) and amidic NH) 1640 (amidic Co.)	12.5(s,1H, ring NH), 10.2 (s, 1H CONH) 0.8-7 (m 14H, aromatic and CH=C)
5c	3410-3100 (ring NH and amidic NH) 1640 amicid Co.	12.5(s,1H, ring NH), 10.2 (s,1H CONH) 8.0-6.8 (m,13H, aryl, thinyl and CH=C)
5d	3410-3100 (ring NH and CONH 1650 (amidic Co.) 1540, 1350 (NH_2)	
5e	3450-3100 (ring NH,CONH 1650 amidic (Co) 1540, 1350 (NO_2)	12.5(s,1H, ring NH), 10.2 (s, 1H CONH) 7.9 - 7 (m,13, aromatic and CH=C)
8a	3310, 3100 (two amidic NH) 1645, 1640(two amidic Co.)	10.2, 10.1 (s, 2H, two CONH protons) 7.95-7 (m, 1H, aromatic and CH=C)
8b	3310, 310C(two amidic NH) 1645, 1640 (two amidic Co)	3.60 (s, 1H, SH).
8c	3310, 3100 (two amidic NH) 1645, 1640 (two amidic Co) 1540, 1350 NO_2	10.2, 10.1 s, 2H two CONH protons 7.95-7 m, 15H, aromatic and CH=C
8d	3310, 3100 two amidic NH 1645, 1640 two amidic Co 1540, 1350 NO_2	10.2, 10.1 s, 2H two CONH protons 7.90-7 m, 13H, aromatic and CH=C 3.60 s, 1H, SH

Table 1 : Continued

Comp.	IR, KBr, cm^{-1}	^1H-NMR, δ ppm
8e	3310, 3100 two amidic NH 1645, 1640 to amidic Co 1540, 1350 NO_2	10.2, 10.1 s, 2H two CONH protons 7.90-7 m, 13H, aromatic and CH=C 3.60 s, 1H, SH 3.2 s, 3H OCH_3
9a	3500, 3300 (NH_2) 1690 (-CO.S-) 1640 (amidic-CO)	10.2 (s, 1h, CONH-proton) 8.0-6.9 (m, 15H, aromatic and CH=C) 4.6(br, 2H, NH_2)
9b	3500, 3300 - NH_2 1690 (-CO.S-) 1640 (amidic -CO.)	10.2 (s, 1H, CONH-proton) 8.0 - 7(m, 14H aromatic and CH=C) 4.6 (br, 2H, NH_2)
9c	3500, 3300 (NH_2) 1690(-CO.S-) 1540 amidic -CO.	10.2(s, 1H, CONH proton) 7.0-6.7 (m, 13H aroamtic, thinyl and CH=C) 4.6 (br, 2H, NH_2).
9e	3500, 3300 NH_2 1690 (-CO.S-) 1690(-CO.S-) 1640 amidic -CO.	10.2 (s, 1H, CONH proton) 7.-7 (m, 14H aromatic and CH=C) 7.-7(m, 14H aroatic and CH=C) 4.6 (br, 2H, NH_2). 3.2 (s, 3H - OCH_3)
10a	3310 (amidic NH) 1640 (amidic Co.)	10.2(s, 1H, CONH proton) 7.9 - 6.8 (m, 15H aromatic and CH=C)
10c	3310 (amidic NH) 1640 (amidic CO)	10.2 (s, 1H CONH proton) 7.- 6.7 (m, 13H aromatic, thinyl and CH=C)
10e	3310 (amidic NH)	10.2(s, 1H CONH proton) 7.9 -6.9 (m, 14H aromatic and CH=C) 3.2 (s, 3H - OCH_3).

The reaction mechanism for the formation of (5) is assumed to proceed by 1,4-addition of the NH_2 group to the carbonyl and C=N bonds to give the intermediate (6) which eliminates one molecule of water to form the benzimidazole derivative(5)(Scheme 1). The driving force for such formation is the stabilisation

resonance energy encountered in the benzimidazole system (5).

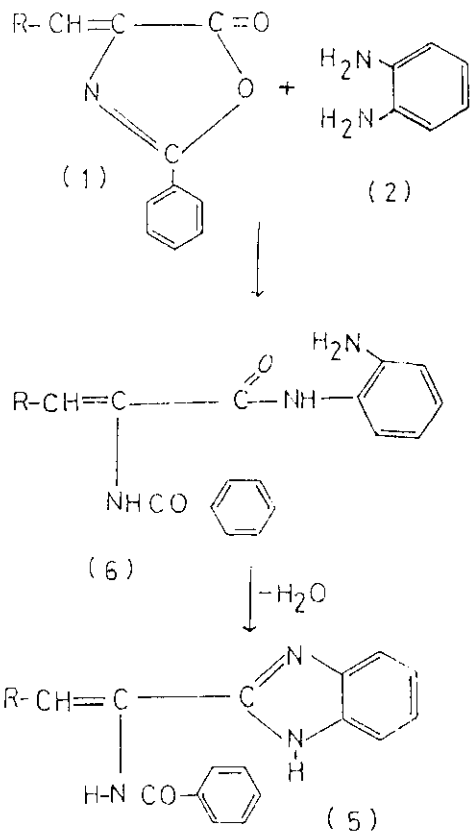


(1), (5)	R	X
a-	C_6H_5	H
b-	p-Cl-C_6H_4	H
c-		H
d-	C_6H_5	NO_2
e-	p-CH_3O-C_6H_4	NO_2

Scheme (1)

In addition to the previous factor, the sterric factor should play a contributed rule and hinder imidazolone formation (Scheme 2).

Scheme (2)



In this work we were unable to isolate the reaction intermediate (6), but similar derivatives were obtained by other workers[3].

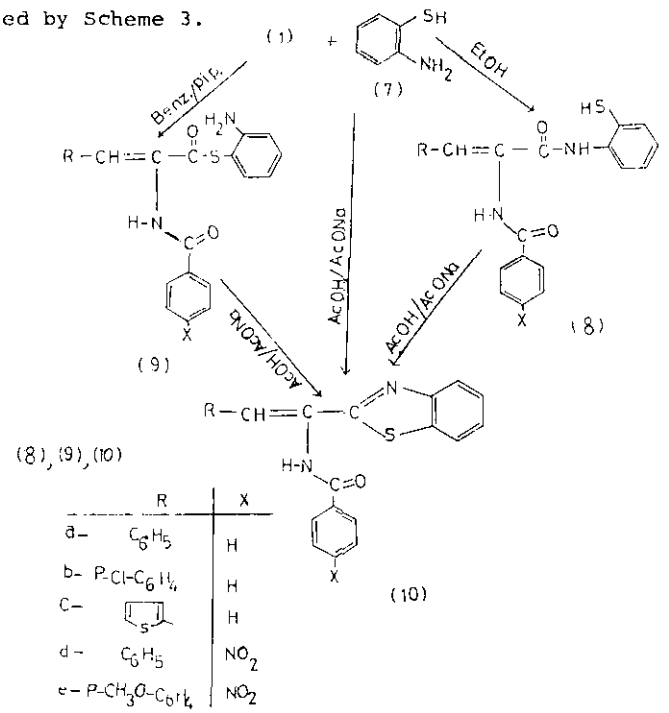
Similar to the behaviour of (1a) with (2), oxazolones (1_{b-e}) reacted with (2) to give the corresponding benzimidazole derivatives (5_{b-e}).

On the same bases the behaviour of o-aminothiophenol (7) towards (1) was also investigated. This reaction was found to be dependent on solvent. Using ethanol as the reaction medium, the product isolated (8) possesses nearly the same elemental analytical figures as that (9) obtained by using benzene as solvnet and piperidine as basic catalyst.

The two products were different in mp., mixed mp. and ir spectra although having the same molecular formula $C_{22}H_{18}O_2N_2S$. The ir spectrum of compound (8) revealed two absorption bands at 1645 and 1640 cm^{-1} indicating the presence of two amidic C=O groups. On the other hand, compound (9) proves the presence of free amino group as shown in ir spectrum at 3500 and 3300 cm^{-1}. This was verified by the ^{1}H-nmr spectrum for this derivative which showed signals for two amino group protons at δ4.6 ppm, which disappeared after deuterium oxide exchange. In the meantime we have studied the reaction of (1) and (7) using glacial acetic acid as a solvent and in presence of fused sodium acetate, whereby a product with molecular formula $C_{22}H_{16}ON_2S$ was obtained. We have assigned the benzothiazole structure (10) for this product on the following findings: The mass spectrum showed the presence of an ion at m/z 105 which represents the base peak and accurate mass measurement proved C_6H_5CO as the structure of this ion.

On the other hand, we were able to convert both compounds (8a) and (9a) to the benzothiazole derivative (10a). This was achieved by refluxing these derivatives for 2 h in glacial acetic acid and in the presence of fused sodium acetate.

The formation of the benzothiazole derivative (10) can be explained by the route in which the attack on the oxazolone ring is done either by the amino group or preferably by the sulphohydryl group[3,4] according to the reaction medium. This can be represented by Scheme 3.



Scheme (3)

Derivatives (5), (8), (9) and (10) which contained NO_2 group as a substituent in the arylidene moity give the ion at m/z 150 which represents the base peak. Accurate mass measurements indicate that the ion at m/z 150 is $P\text{-}NO_2C_6H_4CO^+$

EXPERIMENTAL

All melting points are uncorrected. Ir were obtained (KBr) on Pye-Unicam SP-1100 spectrophotometer. ^{1}H-nmr spectra were recorded on XL 100 nmr spectrophotometer using TMS as the internal standard and chemical shifts are experessed as ppm. Mass spectra were obtained on Pont Model 21-104 mass spectrometer. Analytical data were obtained from the analytical unit at Cairo University. Compounds, (1_{a-e}) were prepared following literature producedres[4-8].

Reaction of 2-Oxazolin-5-ones(1) with o-Phenylenediamine in Acetic Acid. Preparation of 2-Substituted Benzimidazoles (5_{a-e}):

A mixture of oxazolin-5-ones (1_{a-e}, 0.01 mol) and o-phenylenediamine(0101 mole) either in ethanol (50 ml) or in glacial acetic acid (30 ml) containing freshly fused sodium acetate (0.5 g) was heated under reflux for 3 h then cooled and poured into water. The solid product, so formed, was collected by filtration and crystallised from the proper solvent to give benzimidazoles (5_{a-e}) (cf. Table 2).

Table 2 : Benzimidazole Derivatives (5)

Comp.	Mp.	Solvent	Yield %	Formula M^+ (m/z)	Analysis (Calculated-Found) C%	H%	N%	S%
5a	250	E	72	$C_{22}H_{17}N_3O$	77.88	5.01	12.39	
				339	77.52	5.31	12.72	
5b	282	Ac	78	$C_{22}H_{16}Cl\ N_3O$	70.61	4.28	11.24	
				373	70.61	4.33	11.35	
5c	265	E	66	$C_{20}H_{15}N_3OS$	69.57	4.35	12.17	9.28
				345	69.40	4.43	12.32	9.54
5d	289	Ac	75	$C_{22}H_{16}N_4O_3$	68.75	4.17	14.58	
				384	68.81	4.25	14.39	
5e	296	E	70	$C_{23}H_{18}N_4O_4$	66.67	4.35	13.53	
					66.48	4.47	13.76	

E = Ethanol, Ac = Acetic acid.

Reaction of 2-Oxazolin-5-ones (1_{a-e}) with o-Aminothiophenol (7)

Preparation of (8_{a-e}):

a) In ethanol : o-Aminothiophenol (7,0.01 mol) was mixed with oxazolin-5-one (1_{a-e}, 0.01 mol) in the presence of 30 ml of ethanol. The reaction mixture was refluxed for 3 h followed by dilution with cold water. The precipitated solid was collected, dried and crystallised from the proper solvent (cf.Table 3).

Table 3: Analytical data for compounds 8 and 9 .

Comp.	Mp.*	Yield %	Formula (M^+ (m/z)	Analysis			
				C%	H%	N%	S%
8a	128	68	$C_{22}H_{18}N_2O_2S$	70.58	4.81	7.49	8.56
			374	70.80	4.78	7.64	8.75
8b	180	78	$C_{22}H_{17}Cl\ N_2O_2S$	64.63	4.16	6.85	7.83
			408	64.62	4.43	6.75	8.02
8c	153	58	$C_{20}H_{16}N_2O_2S_3$	63.16	4.21	7.37	16.84
			380	63.32	4.41	7.49	16.99
8d	198	64	$C_{22}H_{17}N_3O_4S$	53.01	4.6	10.02	7.64
			419	53.23	4.15	10.13	7.76
8e	205	60	$C_{23}H_{19}N_3O_5S$	61.47	4.23	9.35	7.13
			449	61.54	4.52	9.21	7.43
9a	145	55	$C_{22}H_{18}N_2O_2S$	70.59	4.81	7.49	8.56
			374	70.68	4.68	7.54	8.87
9b	176	60	$C_{22}H_{17}Cl\ N_2O_2S$	64.63	4.16	6.85	7.83
			408	64.45	4.30	6.74	7.97
9c	159	50	$C_{20}H_{16}N_2O_2S_2$	63.16	4.21	7.37	16.84
			380	63.28	4.53	7.19	16.68
9d	210	53	$C_{22}H_{17}N_3O_4S$	63.01	4.06	10.02	7.64
			419	63.11	4.20	10.22	7.76
9e	183	55	$C_{23}H_{19}N_3O_5S$	61.47	4.23	9.35	7.13
			449	61.55	4.43	9.49	7.23

* Crystallised from Toluene

b) In benzene, preparation of (9_{a-e}) : A mixture of (1_{a-e}; 0.01 mol) o-aminothiophenol (7; 0.01 mol) , piperidine (3 drops) and dry benzene (30 ml) was left for 10 h at room temperature, followed by addition of light petroleum whereby white solid was precipitated. The product was collected by filtration and crystallized from the proper solvent to give derivatives (9_{a-e}) (cf.Table 3).

c) In acetic acid, prpeation of (10_{a-c}) : A mixture of (1; 0.01 mol) and o-aminothiophenol (7; 0.01 mol) in glacial acetic acid (30 ml) containing freshly fused sodium acetate (0.5 g) was heated under reflux for 1 h and then cooled and poured into water. The solid product was collected and crystallised from the proper solvent to give the benzothiazole derivatives (10_{a-e})(cf.Table 4).

Table 4: Benzothiazole Derivatives (10).

Comp.	MP.	Solvent	Yield %	Formula M^+ m/z	Analysis			
					C%	H%	N%	S%
10a	190	E	56	$C_{22}H_{16}N_2OS$	74.16	4.49	7.87	8.99
				256	74.56	4.32	7.64	8.70
10b	240	Ac	72	$C_{22}H_{15}ClN_2OS$	67.61	3.84	7.17	8.19
				390	67.76	3.97	7.23	8.21
10c	217	E	55	$C_{20}H_{14}N_2OS_2$	66.30	3.87	7.73	17.68
				263	6615	3.76	7.76	17.54
10d	280	Ac	75	$C_{22}H_{15}N_3O_3S$	65.84	3.74	10.47	7.98
				401	65.65	3.95	10.60	7.79
10e	296	Ad	75	$C_{23}H_{17}N_3O_4S$	64.04	3.94	8.74	7.42
				431	64.19	3.87	9.58	7.31

E = Ethanol, Ac = Acetic acid.

Conversion of (8a) and (9a) to (10a): A solution of either (8a) or (9a) (1g) in glacial acetic acid (30 ml) containing freshly fused sodium acetate (0.5g) was heated under reflux for 1 h then cooled and poured into water. The solid product, was collected, and crystallised from ethanol to give(10a) which was identical with product prepared under c.

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Received, 24th January, 1986