Synthesis of Some Substituted Benzoxazole [3,4-b] imidazoles

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الملخص

تم في هذا البحث تحضير عدد من معوضات اميدازول [b-4,3] 4-اريل هكساهيدرو بنزوكسازولو (10،9) و 4-معوضات بنزوكسازولو [b-4,3] اميدازول (13،14) وذلك بمعاملة الكلايسين مع كلوريد البنزويل او بارا-نترو كلوريد البنزويل لتحضير الـ N-ارويل كلايسين (2،1) ومفاعلته مع كلوريد الثايونيل. تم مفاعلة جزء من الناتج (4،3) مع هيدروكسيد الامونيوم لتحضير N-ارويل كلايسين اميد (6،5) ثم مفاعلته مع 1-برومومسابكلوهكسانون لتحضير N-مثيلين (2-هكساهايدروبنزوكسازولو) اريل اميد (8،7) ومن ثم مفاعلته مع $POCl_3$ لإعطاء الناتج الأول (10،9). أما الجزء الثاني فيتفاعل مع الاوروثوامينو فينول لإعطاء الـ N-مثيلين (2-بنزوكسازولو) اريل امايد (12،11) ليتفاعل بدوره مع $POCl_3$ لإعطاء الناتج الثاني (14،13).

تم التأكد من صحة تراكيب جميع المركبات المحضرة من خلال المعلومات الفيزيائية والطيفية.

ABSTRACT

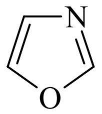
In this paper the synthesis of 4-substituted benzoxazole [3,4-b] imidazole (9,10) and 4-aryl hexahydrobenzoxazole [3,4-b] imidazole (13,14) is reported. Glycine was treated with benzoyl chloride or p-nitrobenzoyl chloride to give N-aroyl glycine (1,2), the reaction of N-aroyl glycine with thionyl chloride followed by treatment the product (3,4) with ammonium hydroxide to give N-aroyl glycine amide (5,6). Treatment of the amide with 1-bromocyclohexanone gave N-methylene-2-hexahydrobenzoxazole) aryl

amide (7,8), cyclization of this gave product (9,10), whereas the compounds (13,14) was synthesized from o-aminophenol and the acid chlorides to give N-methylene (2-benzoxazole) aryl amide (11,12) which cyclized with phosphorous oxychloride to give the products (13,14).

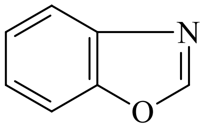
The structure of all synthesized compounds were confirmed by physical and spectral data.

INTRODUCTION

The preparation of 2-methyl benzoxazole by Ladenbyrg (1876) marks the first recognition of oxazole(1), but the name of these compounds comes from Hantzsch (1887) when gave that name to this class of compounds(2).

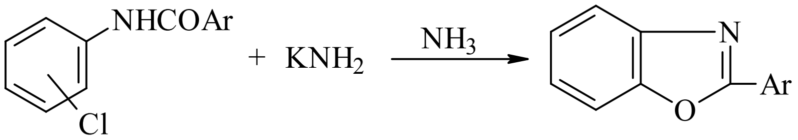


Oxazole



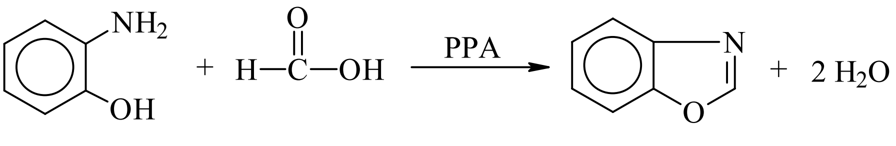
Benzoxazole

Benzoxazoles are formed by the action of potassium amide in liquid ammonia of N-aroyl derivatives of both o-and m-chloroaniline(3).

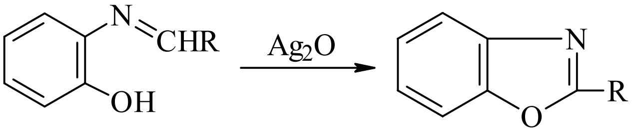


Benzoxazole may be prepared by the reaction between o-aminophenols and carboxylic acid(4) as a simple method.

There are few examples of solid-phase synthesis of benzoxazoles heterocycles using a similar strategy of cyclization of the corresponding 2-aminophenol, benzoxazole formation was initially envisioned to take place between the solid-supported aminophenol with the diversity element introduced as a carboxylic acid(5).



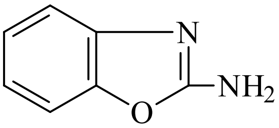
Benzoxazoles and other condensed oxazoles are obtained by oxidative ring-closure of phenolic Schiff's bases(2).



Aromatic polybenzoxazole are another class of heterocyclic polymer that exhibit excellent thermooxidative stability, high-tensile modulus and strength and superior chemical resistance. A few rigid-rod polybenzoxazole are reported to have potential for fabrication into high-modulus high-strength fiber(6).

It was known that poly (benzoxazole)$_s$ is among the most thermally stable polymers containing high-rigid heterocycles in the Backbon(7).

In other side some of benzoxazole compound have activity against the bacteria and fungi(8) and anticancer activity(9), for example zoxazolamine have effective against a wide range of enteric infections(2).



EXPERIMENTAL

All chemicals were purchased from Flucka and BDH Chemical Ltd. The melting points were measured on an Electrothermal 9300 Engineering LTD and were uncorrected. IR spectra were recorded on Infrared Spectrophotometer Model Tensor 27, Bruker Co., Germany, using KBr discs. UV spectra were recorded on Shimadzu Double-Beam Spectrophotometer UV-210 A using chloroform as a solvent.

Preparation of N-aroyl glycine (1,2)(10)

(0.02 mol, 1.5 g) of glycine in 20 ml of 1 N sodium hydroxide was cooled at 0-5 °C and the cold solution was added dropwise to a solution of (0.02 mol) of acid chloride in (30 ml) of chloroform. The reaction mixture was continued under stirring for an additional an hour. The aqueous layer was separated and acidified with 2 N hydrochloric acid. The solid product was filtered by filtration and washed with water. The physical properties and spectral data are listed in Tables (1 and 2).

Preparation of N-aroyl glycine chloride (3,4)(11)

Thionyl chloride (10 ml) was added to (0.025 mol) of compound (1,2) the mixture was refluxed for 30 min. in a water bath with stirring until the releasing of hydrochloric acid stopped. The reaction mixture was cooled and the formed solid was collected by filtration. The physical properties and spectral data are listed in Tables (1 and 2).

Preparation of N-aroyl glycine amide (5,6)(12)

Ammonium hydroxide solution (10 ml) was added to (0.01 mol) of compound (3,4) with stirring for 10 min and the formed solid was collected by filtration and recrystallized from ethanol-water. The physical properties and spectral data are listed in Tables (1 and 2).

Preparation of N-methylene(2-hexahydrobenzoxazole) aryl amide (7,8)(13)

To (0.06 mol, 10.5 g) of 1-bromocyclohexanone in (40 ml) of ethanol was added (0.06 mol) of (5,6) and the reaction mixture was refluxed for 17 hours. Then the reaction mixture was cooled and the precipitate was filtered, washed with petroleum ether and dried and crystallized from ethanol-water. The physical and spectral data are listed in Tables (1 and 2).

Preparation of 4-aryl hexahydrobenzoxazolo[3,4-b]amidazole (9,10)(9,12)

To (0.01 mol) of compound (7,8) soluble in (25 ml) of benzene (20 ml) of phosphorous oxychloride was added and the mixture was refluxed for 4 hours. The reaction mixture was treated with ice-water and extracted with methylene chloride and dried. The product was recrystallized from ether-petroleum ether. The physical properties and spectral data are listed in Tables (1and 2).

Preparation of N-methylene (2-benzoxazolo) aryl amide (11,12)(14)

(0.01 mol, 1 g) of o-aminophenol in (25 ml) methylene chloride was added to (0.01 mol) of compound (3,4) was added and the reaction mixture was refluxed for 7 hours. The product was distilled under vacuum to give the compound (11) which was recrystallized by ether-petroleum ether. The physical and spectral data are listed in Tables(1and2).

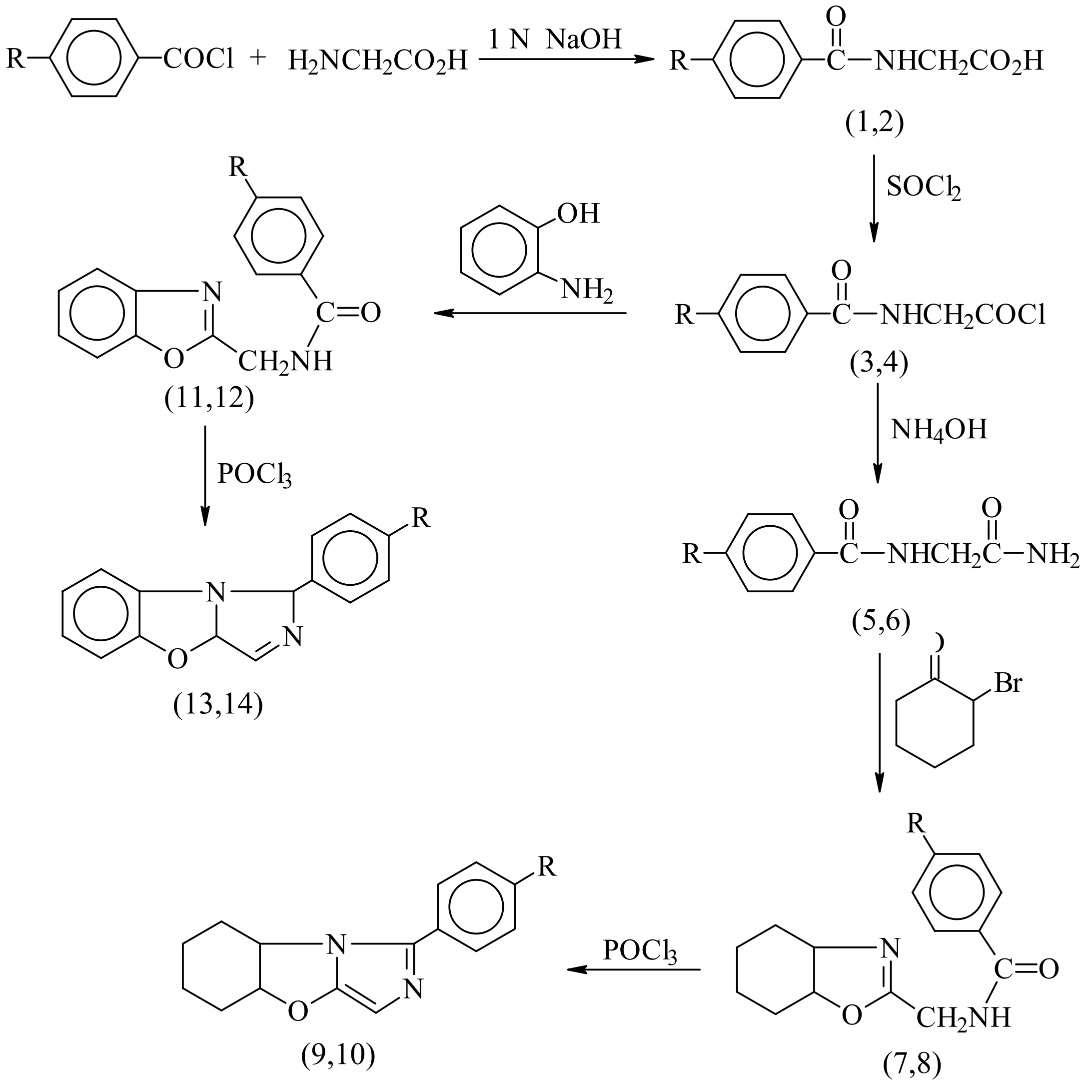
Preparation of 4-substituted benzoxazole [3,4-b] imidazole (13,14)(10,14)

To (0.01 mol) of (11,12) soluble in (25 ml) benzene was added (20 ml) of phosphorous oxychlirde and refluxed for 4 hours. The reaction mixture was treated with ice-water and extracted with methylene chloride and dried. The product was recrystallized from ether-petroleum ether. The physical and spectral data are listed in Tables (1 and 2).

RESULTS AND DISCUSSION

In this paper the synthesis of 4-substituted benzoxazole [3,4-b] imidazole (13,14) and 4-aryl hexahydrobenzoxazole [3,4-b] imidazole (9,10) from glycine and benzoyl chloride is reported (Scheme 1). Glycine was treated with benzoyl or 4-nitrobenzoyl chloride to give N-aroyl glycine (1,2), IR spectra of compound (1) show absorption peak ν cm^{-1} at 1745 and 1600 (2C=O), 3341 (O-H), 1181 (C-O). Compounds (1 and 2) were converted to its acid chloride by their reaction with thionyl chloride. The IR spectra of compound (3) shows absorption peaks at 1770, 1690 cm^{-1} (2C=O) and 3445 (N-H). The acid chlorides (3 and 4) were treated with ammonium hydroxide solution to give the corresponding amides (5,6), there amides show absorption peak at ν cm^{-1} 3410 (N-H) and 1645 (C=O). Compounds (5 and 6) were treated with 1-bromocyclohexanone in ethanol to give N-methylene (2-hexahydro-benzoxazole) aryl amide (7 and 8). The IR spectra for compound (7) shows absorption peaks νcm^{-1} at 3422 (N-H), 1636 (C=N), 1653 (C=O) and 1031 (C-O). The cyclization of compounds (7 and 8) with phosphorous oxychloride (dehydrations agent) gave 4-aryl hexahydrobenzoxazole [3,4-b] amidazole (9,10).

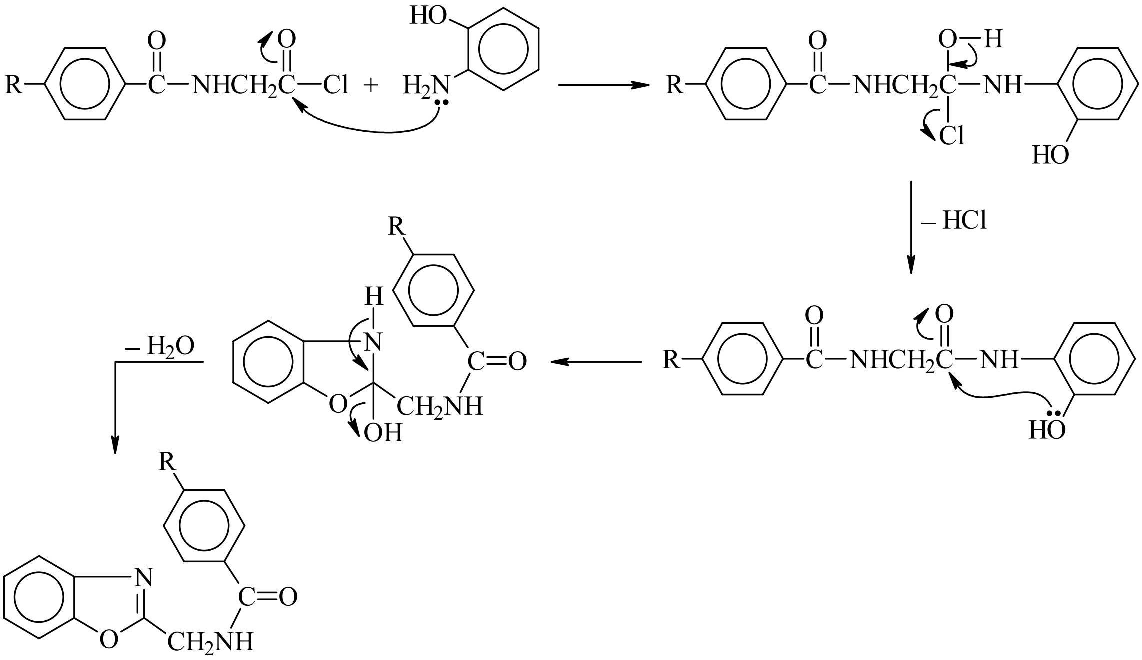
Whereas the reaction of acid chlorides (3 and 4) with o-aminophenol in methylene chloride gave N-methylene (2-benzoxazolo) aryl amide (11,12), the IR spectra of compound (11) shows absorption peaks ν cm^{-1} at 3359 (N-H) and 1649 (C=O).



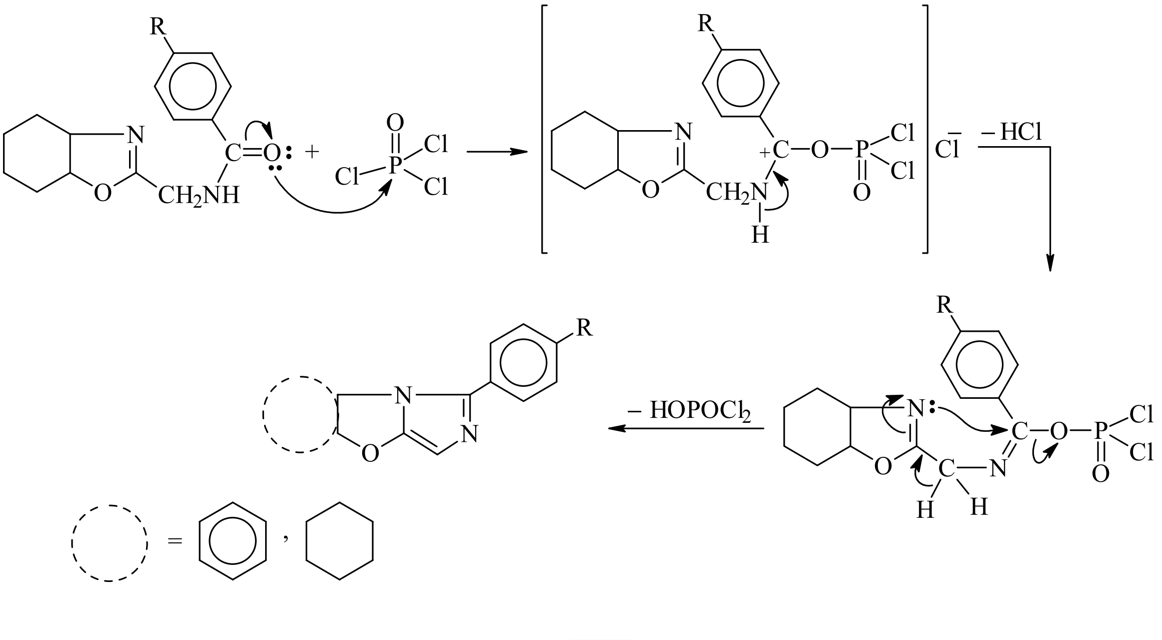
R = H , NO_2

Scheme (1)

The reaction proceed through the well-known tetrahedral mechanism, which can be shown in the following Scheme:



Compounds (11,12) were treated with phosphorous oxychloride to give 4-substituted benzoxazole [3,4-b] imidazole (13,14). The suggested mechanism for the preparation of compounds (9,10) and (13,14) is illustrated in the following Scheme:



The UV spectra for the synthesized compounds shows maximum absorption range λ_{max} 280-392 nm due to n-π^* transition. The physical and spectral data for the synthesized compounds are shown in Tables (1 and 2).

Table (1): Physical properties of compounds

Color	m.p. (°C)	Yield (%)	Molecular formula	Comp. No.
White	186-188	92	$C_9H_9NO_3$	1
White-yellow	212-214	94	$C_9H_8N_2O_5$	2
Brown	325 d	90	$C_9H_8NO_2Cl$	3
White-yellow	163-165	91	$C_9H_7N_2O_4Cl$	4
Brown	273-275	95	$C_9H_{10}N_2O_2$	5
Yellow	332-334	95	$C_9H_9N_3O_4$	6
Brown	211-213	68	$C_{15}H_{17}N_2O_2$	7
Black	100-102	71	$C_{15}H_{16}N_3O_4$	8
Brown	98-100	60	$C_{15}H_{16}N_2O$	9
Brown	82-84	61	$C_{15}H_{15}N_3O_3$	10
Brown	102-104	67	$C_{15}H_{12}N_2O_2$	11
Red	b.p. 123-125	61	$C_{15}H_{11}N_3O_4$	12
Brown	90-92	74	$C_{15}H_{11}N_2O$	13
Colorless	oily	70	$C_{15}H_{10}N_3O$	14

Table (2): I.R and U.V spectral data

λ	I.R ν cm^{-1} (KBr)						
	C=N	N-H	C-O	C=O (amide)	C=O	O-H	
282	-	3172	1181	1630	1745	3341	1
336	-	3116	1127	1639	1694	3414	2
296	-	3445	-	1670	1770	-	3
312	-	3421	-	1652	1730	-	4
280-264	-	3405	-	1623	-	-	5
280	-	3410	-	1645	-	-	6
314-300	1636	3422	1031	1653	-	-	7
286	1625	3405	1021	1647	-	-	8
304	1601	-	1025	-	-	-	9
302	1620	-	1040	-	-	-	10
336-321	1600	3359	1108	1649	-	-	11
282	1658	3417	1021	1690	-	-	12
302	1601	-	1026	-	-	-	13
390-338	1601	-	1025	-	-	-	14

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