A new Route to the Synthesis of Pyrazines and Oxazoles

***M.N.Mohamed,** Faez.a.Al-rammahy and ***Sh.A.Beheget**

* Dep. of Chemistry /College of Science /University of Al-Qadisiya **Dep. of Chemistry /College of Education for Girls /University of Kufa, **E-mile: faez_1961@yahoo.com** ****Dep. of Chemistry /College of education/ Universityof Al-Qadisyia

Abstract

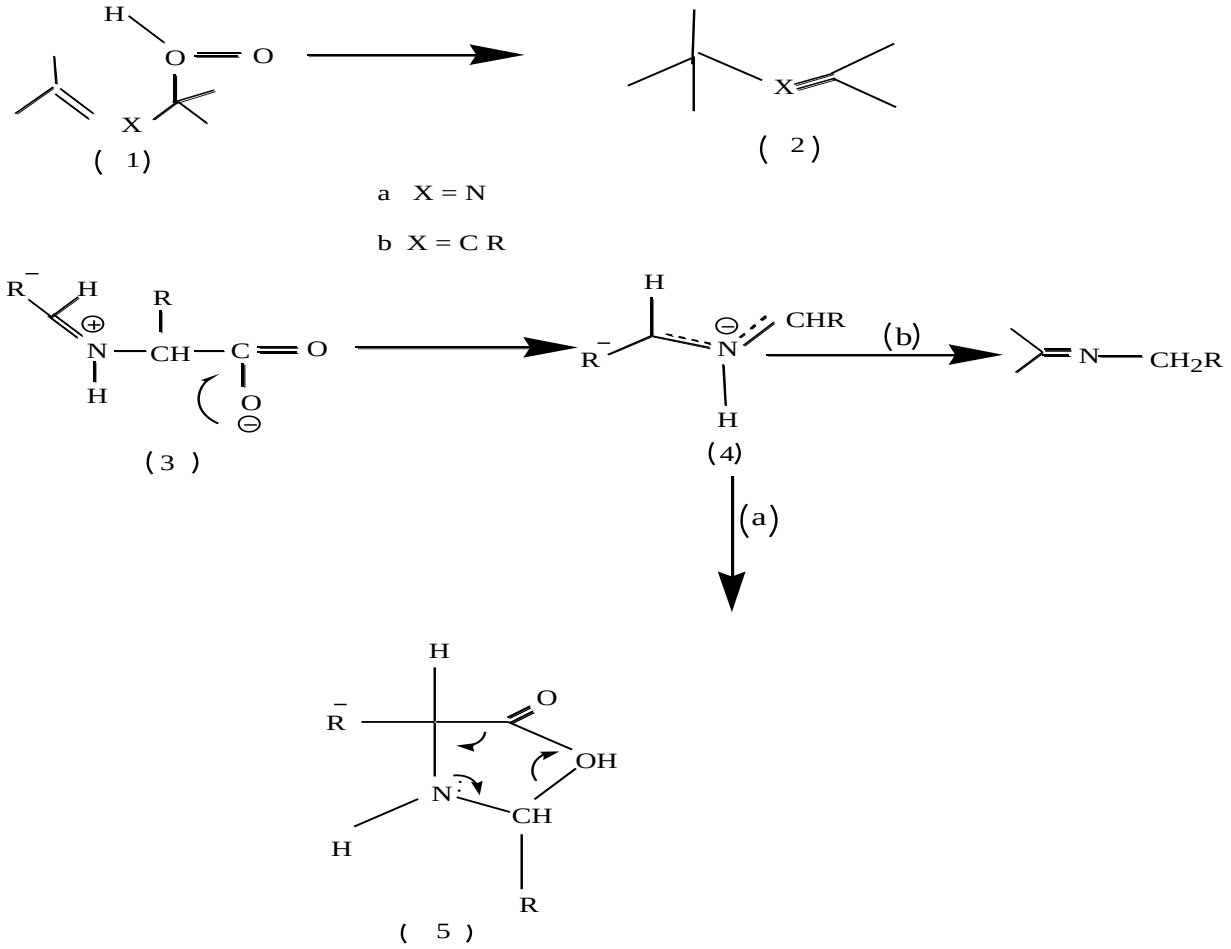
Decaboxylative transamination of the α-amino acids glycine, alanine and tyrosine in the presence of the symmetrical and a symmetrical benzoins ; [4 -N- di Methyl amino benzoin] , [4,4 – di chloro benzoin] ,[4– hydroxy benzoin] , [4 -chloro benzoin] , [3,3- di bromo benzoin] and [2- nitro benzoin]. This has led to the formation of oxazoles , tetra substituted pyrazine and the corres ponding benzils .

الخلاصة

في هذا البحث تم نقل مجموعة الامين المصحوبة بفقدان ثنائي اوكسيد الكاربون للحوامض الامينية كلايسين ، الانين والتايروسين بوجود مركبات البنزوين المتماثلة وغير المتماثلة (٤- ثنائي مثيل امينو بنزوين , ٤،٤- ثنائي كلورو بنزوين , ٤- كلورو بنزوين,٣،٣- ثنائي برومو بنزويين , ٤- هيدروكسي بنزوين و ٢- نتروبنزوين) ادى الى تكوين مركبات البايرازين الرباعية التعويض و الاوكسازولات كذلك اكسدة مركبات البنزوين الى مركبات البنزيل .

Introduction

The previous accepted mechanism for decarboxylative Transamination of α- amino acids involving the concerted process 1a → 2a1,(1-4) analogous to that established for β, γ – unsaturated acids 1b → 2b2 was renovated by grigg(3) who proposed the intervention of 1 , 3 – dipolar species (4) via the Zwitterionic from (3) . In a later work(4) , Grigg's showed that primary and secondary α- amino acids react with aldehydes and ketones , with concomitant decarboxylation to give azomethine ylide (4) via an intermediate Oxazolidine - 5 - one(5).



In the absence of added dipolarophile the azomethine ylide undergoes 1 , 2 - prototropy from nitrogen to (1) or (3) generating imines the region chemistry of the protoropy is control led by the electron density at (1) or (3) in (4). This suggested mechanism seems to fit the result of our previous work (5-10). We looked to expand our work by decarboxylation the α- amino acids (5 . a - c) in the presence of symmetrically substituted benzyl (6.a – e) and (10).

Experimental

Unless otherwise stated the following generalization apply . I.R spectra were measured in FT.IR Shimadz 2434 spectro photometer using Nujol. 1H n.m.r spectra were measured with A-CL815a (300μ Hz) in cDCl3 with TMS as internal standard Microanalytical were analyzed at the1106 carloerba .

General Methods

(A) By Fusion

The α - amino acids was through mixed with benzoin in equivocal , the resulting mixture was then heated inan oil bath to the minimum temperature required for decarboxylation (140-80) . when the evolution of carbon dioxides had ceased , ethanol was then added and the mixture was refluxed for 15 minutes .

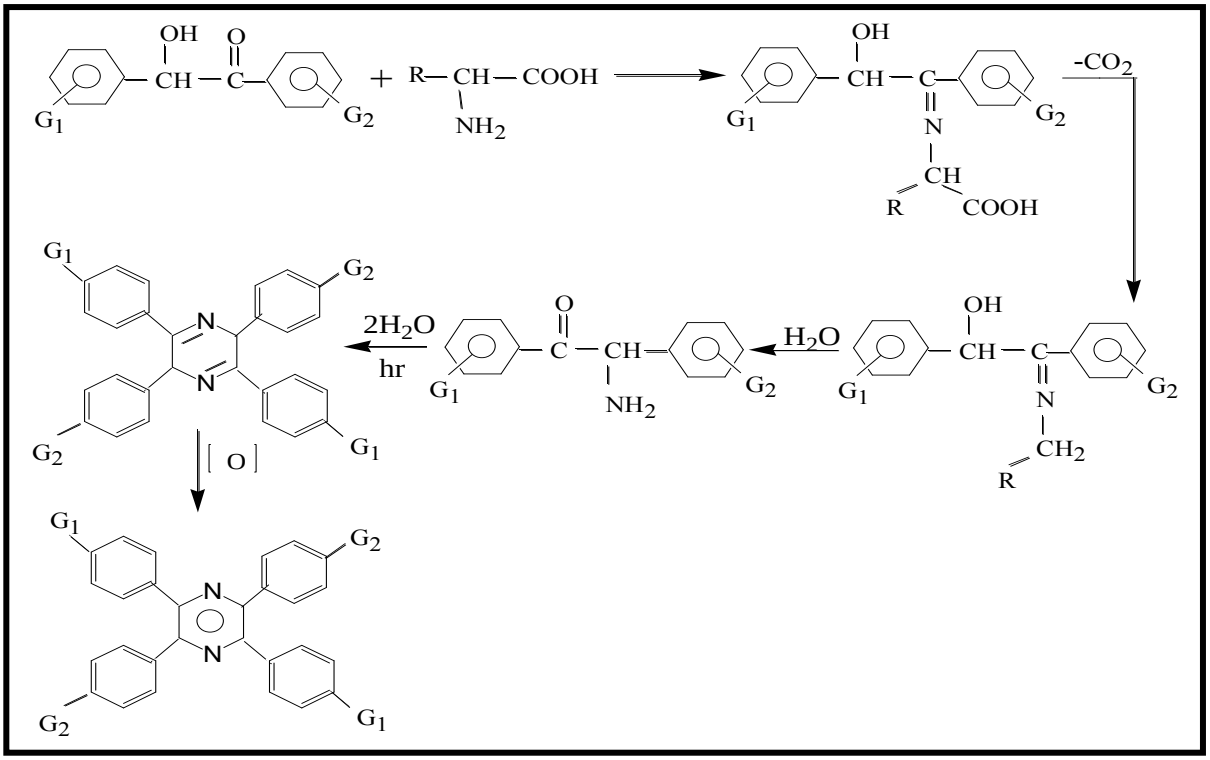
The solution was then cooled and set aside for fractional cooled and set aside for fractional crystallization ,pyrazine was obtained first, then benzil and finally the oxazoles . These products were purified by crystallization from hot ethanol .

(B) The solvent Method

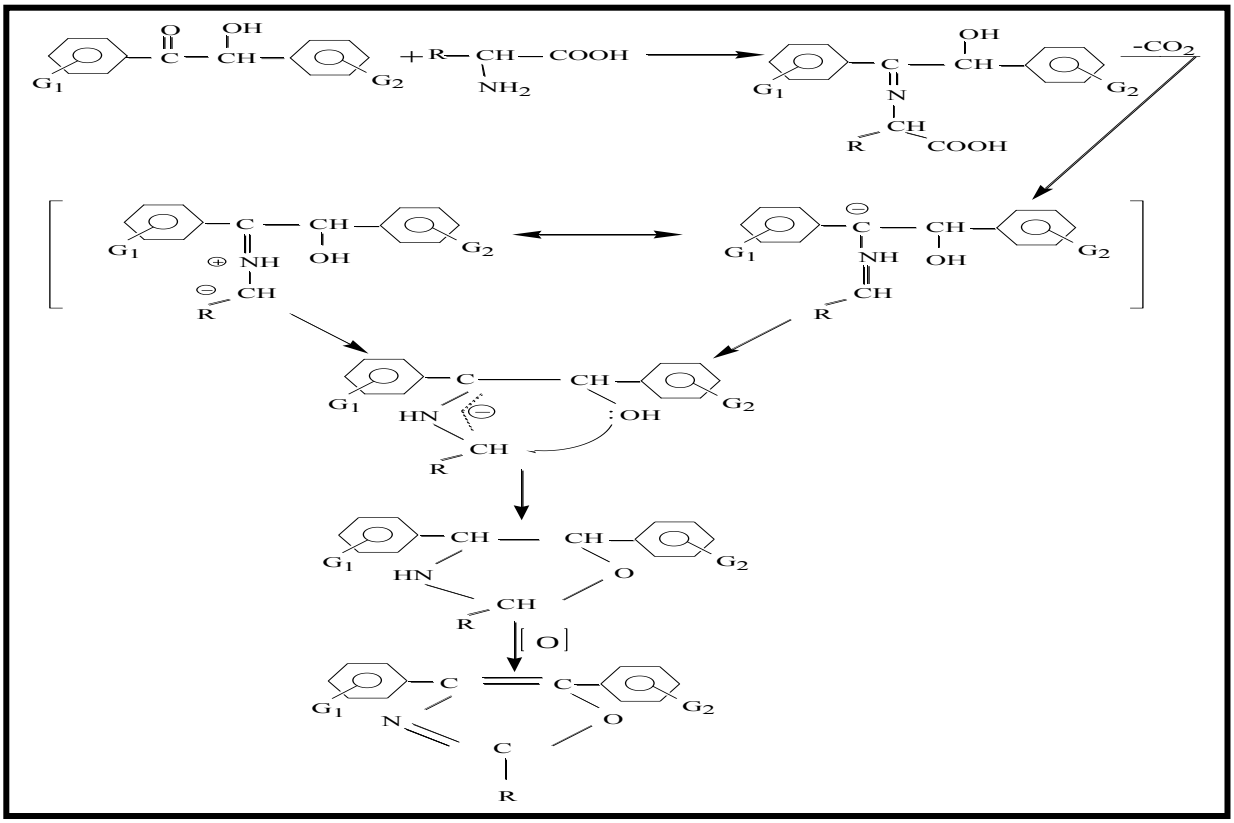
Benzoin (0.01 mole) was added to solution made of α – amino acids (0.01 mole) and sodium ethoxide (0.01 mole) in absolute ethanol (30ml) the reaction mixture was refluxed on a water bath until the evolution of carbon dioxide had ceased; the hot mixture was filtered and set aside for fractional crystallization. The procedure was continued as in (A).

Result and Discussion

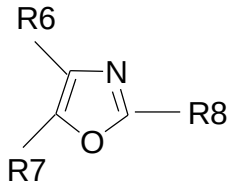
Rizzi(11) isolated low yields of oxazolidine from the aldehyde induced – decarboxylation of sarcosins under forcing conditious , Oxazolidine was also obtained , but in good yield , from decarboxylating cyclic secondary α – amino acids in the Presence of aldehydes bearing electron with drawing substituents(12) , during this work , we obtained different Oxazoles (9.a-h) from both methods (A) and (B) , using α – amino acids (5a-c) in the presence of different benzoins (6a-f) . The decarboxylation led also to the formation of two products Pyrazine derivatives (8a-f) and corresponding benzils (7a-f). The oxazoles could be formed according to scheme . the azomethine ylides are Known to undergo alarge range of 1,3- dipolar cylo adation as they were traped with arange of added dipolaephiles(13,14) . In the present investigation the azomethine ylide (14) was trapped intramol- chlary by the adjacent hydroxyl group forming the unsolvable. Oxazolicline derivative (15) which upon oxidation under the conditions used led to derivative (16) .The Oxazoles 9a was obtained from the decarboxylation of 4 - dimethyl amino benzoin with tyrosine and 96-f benzoins reaction with glycine , alanine and tyrosine. All the analysis fit with the product oxazoles table(1and2),Benzils(7a-f) obtained during this work are more probably formed throught the oxidation of the corresponding benzoins under the conditions used .



Scheme (1)

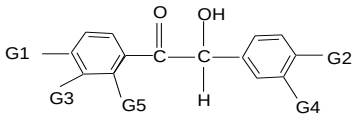


Scheme(2)

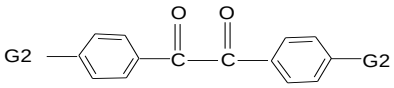


Table(1) shows the totals redeeming compounds oxazole prepared new

Compound No.	R6	R7	R8
9a	PhN(CH3)2	Ph	-CH2-Ph-OH
9b	PhCl	PhCl	-CH2-Ph-OH
9c	PhCl	Ph	H
9d	m-Br-Ph	m-Br-Ph	CH2-PhOH
9e	O-NO2Ph	Ph	CH2-PhOH
9f	O-NO2-Ph	Ph	H



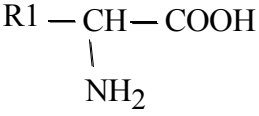
(6)

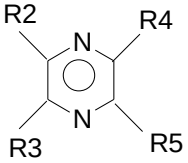


(7)

Table(2) shows the totals redeeming compounds benzoin prepared new

Compound No	G1	G2
ba	N(CH3)2	H
bb	Cl	Cl
bc	OH	H
bd	Cl	H
be	G3=Br	G4=Br
bf	G5=NO2	G2=H





Table(3) shows the totals redeeming compounds pyrazine prepared new

Comp No	R1	R2		R3	R4	R5
5a	H	8a	PN(CH3)2C6H4	C6H5	P-N(CH3)2C6H4	C6H5
5b	CH3	8b	P-Cl-C6H4	P-Cl-C6H4	P-Cl-C6H4	P-Cl-C6H4
5c	HOPhCH2	8c	P-OH-C6H4	C6H5	P-OH-C6H4	C6H5
		8d	P-Cl-C6H4	C6H5	P-Cl-C6H4	C6H5
		8e	m-Br-C6H4	m-Br-C6H5	m-Br-C6H4	m-Br-C6H4
		8f	O-NO2-C6H4	C6H5	O-NO2-C6H4	C6H5

Table(4) Some phedical and analytical data of prepared pyrazine

Comp No	M.P	Yield %	Formula	Found calc. C	H	N
8a	275CO (15,16,17)	68	C32H30N4	81.70 81.7	6.38 6.276	11.73 11.91
8a	302CO (18,19)	38	C28H16N2Cl4	63.615 63.815	2.677 2.978	4.384 4.978
9c	135CO	19	C22H16NCl	61.60 61.72	4.86 4.85	4.21 4.19

Table(5) The N.M.R. Spectral data for (8a) and (8c) prepered pyrazines

Come no	N.M.R DMSO
8a	δ3.0(4x3H(N(CH3)2) (d) (d) and7.3(s)(2x5H-2 C6H5) ;6.7,7.6(2x4H-2C6H4)
8c	δ7.3(d)(2x5H-2 C6H5);7.5(s),7.8(s) (2x4H-2C6H4) and6(s)(2x1H)(OH)

Table(6) The I.R spectral data of Pyrazines and Oxazole

Comp. No	C=Cύ benzine	C=Nύ Pyrazine	C-Brύ	N=Oύ	C=Cύ Oxazole	C-Clύ
8a	1590					
8e	1590	1580-1570	500-600			
8f	1590			1300-1370		
9c	1590				1650	
9b	1590				1650	٨٠٠-٥٠٠

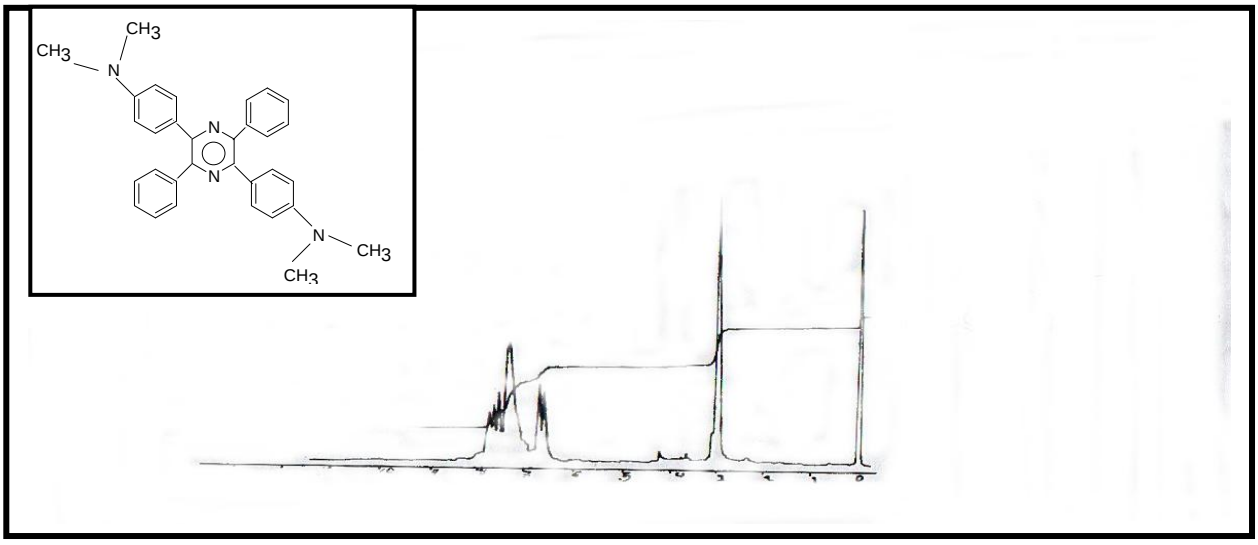


Fig (1) show the NMR spectroum of 2,5-di(4-di methyl amino phenyl)-3,6-di phenyl pyrazine

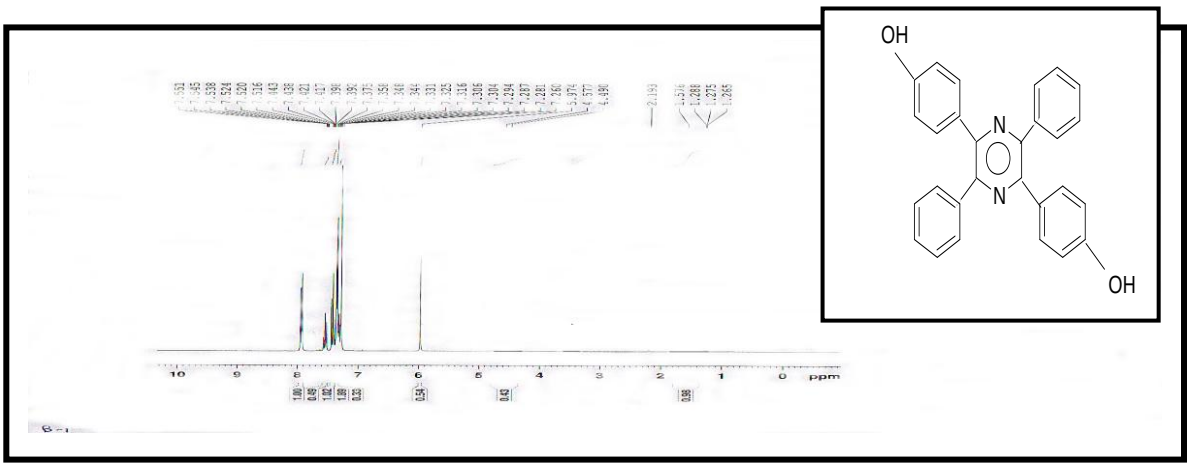


Fig (2) show the NMR spectroum of 2,5 - di (4- Hydroxy phenyl) - 3,6 - di phenyl pyrazine

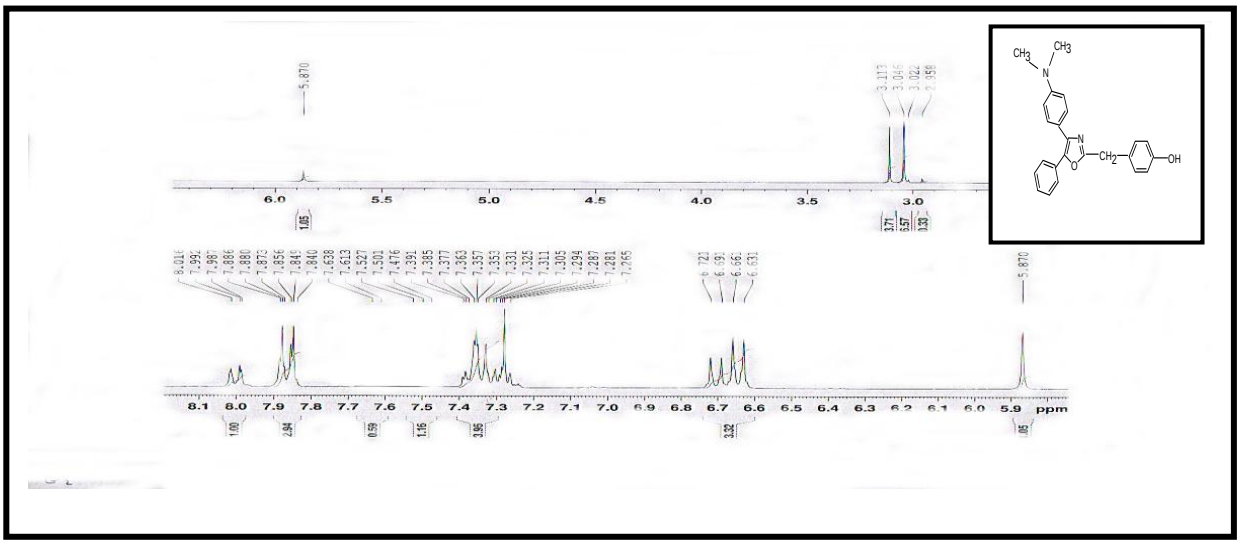


Fig (3) show the NMR spectroum of 2-p(hydroxy benzyl) 4-(p-di methyl amine phenyl) 5 phenyl Oxazol

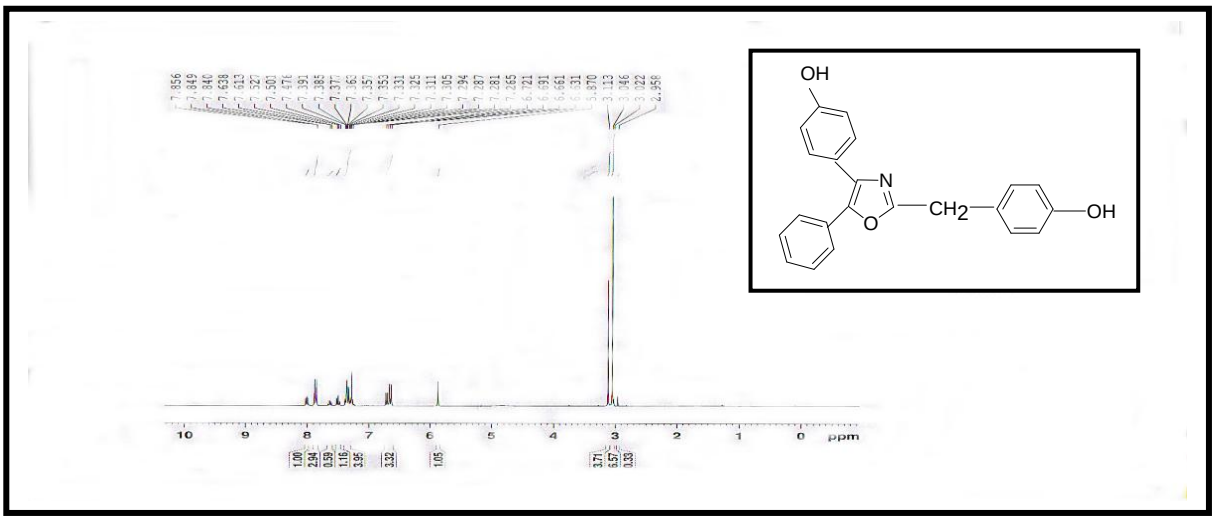


Fig (4) show the NMR spectroum of 2-(p-hydroxy benzyl) 4-(p-hydroxy phenyl) 5 phenyl Oxazol

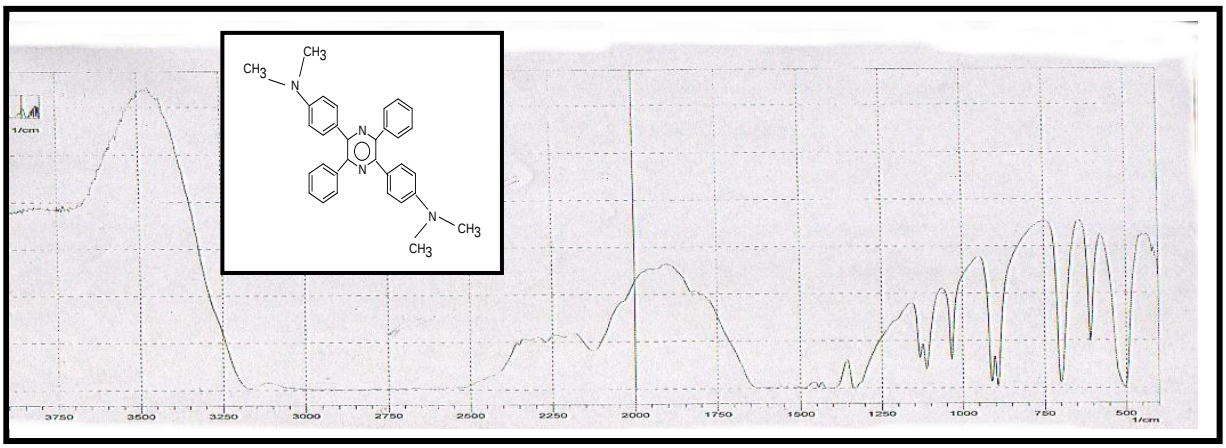


Fig (5) show the I.R spectroum of 2,5 - di (4 -di Hydroxy phenyl)- 3,6- di phenyl pyrazine

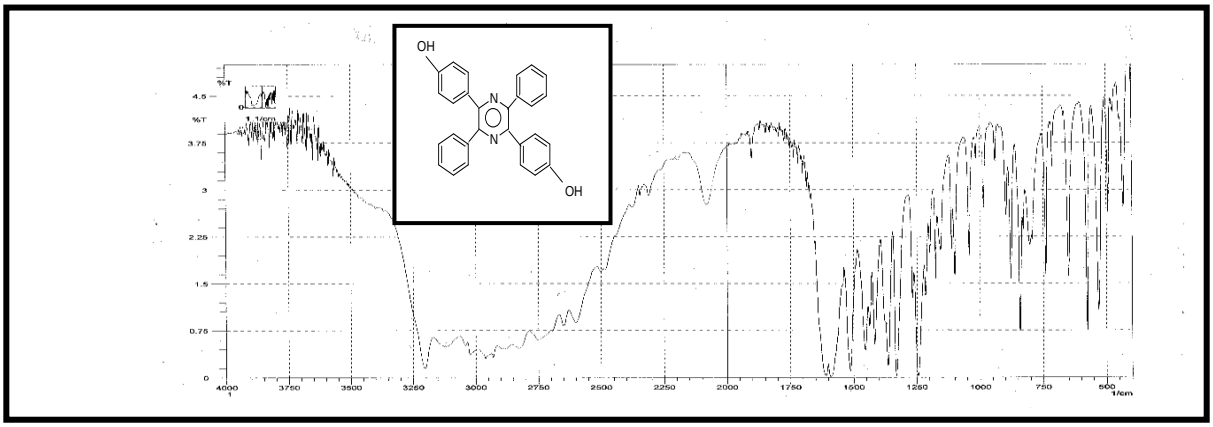


Fig (6)

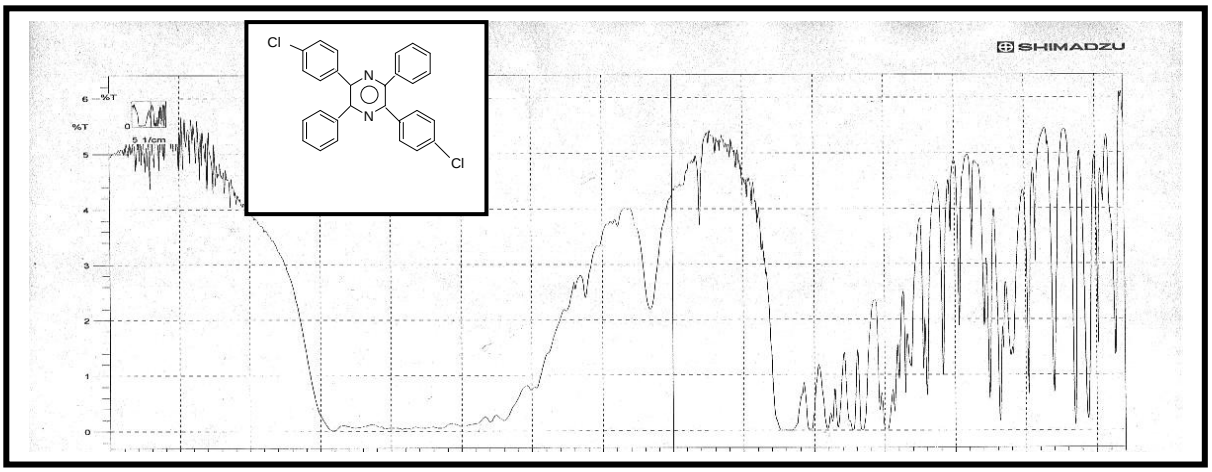


Fig (7) show the I.R 2,5 - di (4 -di Chloro phenyl)- 3,6- di phenyl pyrazine spectroum

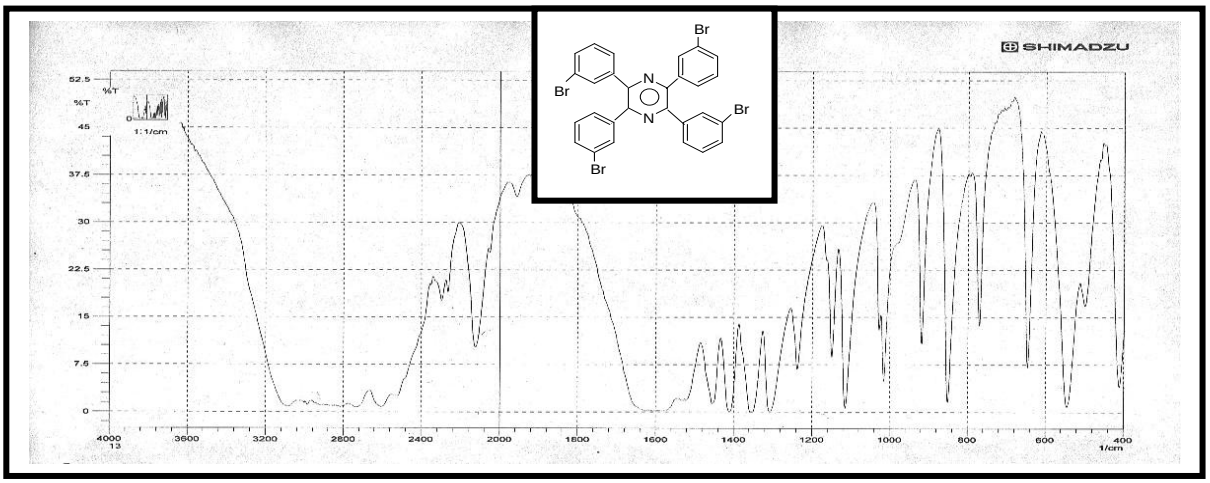


Fig (8) show the I.R spectroum 2,3,5,6 -tetra (3 -Bromo phenyl)pyrazine

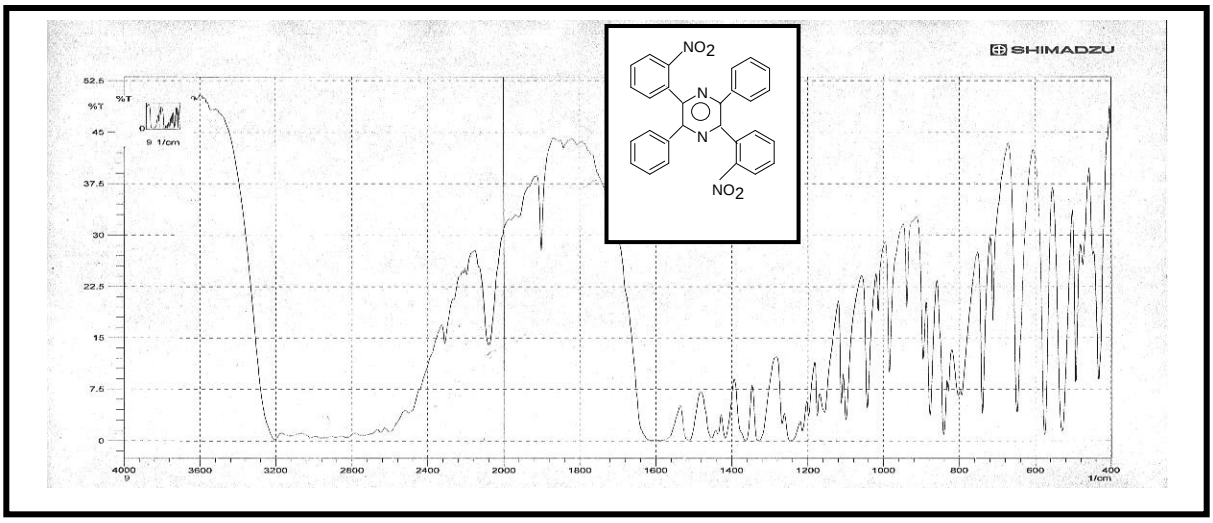


Fig (9) show the I.R spectroum 2,5 - di (2 -di nitro phenyl)- 3,6- di phenyl pyrazine

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