Synthesis of a New Series of Schiff Bases Using Both Traditional and the Ultrasonic Techniques

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(Received 20 / 5 / 2008 , Accepted 29 / 10 / 2008)

Abstract
A series of Schiff bases have been synthesized by the reaction of the prepared aldehyde (4-benzyloxy 3-methoxy-benzaldehyde) with substituted anilines in the presence of glacial acidic acid by both traditional and ultrasonic irradiation techniques. The synthesized products were tested for antimicrobial activity against a variety of test organisms. Structures of the synthesized products were confirmed by using chemical and spectroscopic methods such as IR, ^{1}H-NMR, ^{13}C-NMR & element analysis.

Introduction
Schiff base are class of important compounds in the pharmaceutical field [1]. They show biological activities, including antibacterial, antifungal, and anticancer [2]. Furthermore, Schiff bases are utilized as a starting material in the industrial synthesis,Schiff bases are a class of important compounds in the pharmaceutical fields and have gained prominence for their anti-tuberculostatic activity [3]. Certain Schiff bases are known to be liquid crystals [4], and are used in medicinal [7] and polymer chemistry [6]. The condensation of α-methylbenzylamine or α,α-dimethyl benzylamine with glyoxal has apparently been described previously , the product contains di-imine groups [7 ,8] . Mohan [9] has shown that the reaction of 4-amino-3-hydroxy phenyl benzoate with RC_6H_4CHO (R= H, Me, MeO, Cl, NO_2) gave 69-85% of Schiff bases. In 1998 Aleksander and his co-workers [10] synthesized Schiff bases from the condensation of salicyaldehyde and methyl amine, that can form intra-molecular hydrogen bonds.

Experimental section
1. Synthesis of 4-Benzyloxy-3-methoxy bezaldehyde The above aldehyde was prepared according literature procedure. [11]

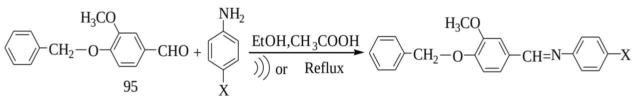
2. Synthesis of N-(4-Benzyloxy-3-methoxy-benzaldehyde) -(4-substituted-phenyl) imines by Traditional method:

The following procedure describes the synthesis of some imines by the reaction of aromatic aldehyde with some aromatic amines, in a 100ml two necked round-bottom flask, a mixture of 3-methoxy-4-benzyloxy benzaldehyde (2.42g, 0.01mol), different anilines (1a-j) (0.01mol) and absolute ethanol (10ml) were added. To this mixture, glacial acetic acid (1drop) was added. The overall reaction mixture was refluxed for (1-4.5) hours ,the reaction was monitored by TLC until the disappearance of starting materials. Reaction times, solvents used for recrystalization, percentage of yield, mp. R_f and color of the synthesized Schiff bases (2a-j) are shown in table (1)

3. Synthesis of N-(4-benzyloxy-3-methoxy-benzald-ehyde)-(4-substituted-phenyl) imines (2a-j) by ultrasonic wave:

In a 100ml of round-bottom flask, a mixture of 3-methoxy-4-benzyloxy benzaldeyde (2.42g, 0.01mol), difference amines (1a-j) (0.01mol) and absolute ethanol (10ml) were added. To this mixture, glacial acetic acid (1drop) was added. The mixture was partially submerged in the sonic bath at room temperature at 25-30°C, reaction time, solvents used for recrystalization, percentage of yield, mp., and color of the synthesized Schiff bases (2a-j) were showed in table (2).

Results and discussion
The following reaction describes the synthesis of some imines by the reaction of aromatic aldehyde (4-benzyloxy 3-methoxy-benzaldehyde) with substituted anilines and the reaction occurred by traditional method and ultrasonic wave. The reaction was monitored by TLC until disappearance of starting materials. Reaction times, solvents used for recrystalization, percentage of yield, mp., R_f and color of the synthesized Schiff bases (2a-j) have been shown in Table (1) and (2).the reaction under the ultrasonic technique has significant effects by giving high yield and very short reaction times comparing with traditional methods, which corresponds to the finding of many researchers[14, 15]. Comparison results are summarized in Table (3).



1a-j 2a-j

All physical and spectroscopic data clearly indicated the disappearance of starting material and also confirm the formation of desired products.

From the FTIR spectra of Schiff bases (2) the disappearance of the carbonyl group and NH_2 groups, which only show one band of NH region at 3382cm^{-1} for compound (2a)(Fig.1). The ^{1}H-NMR data of Schiff bases (2a):

signal for the proton of CH=N group is observed at 8.5ppm of compound (2a) (Fig.2) it shows also a single band for one proton of NH group at 8.22ppm as a singlet peak. In the ^{13}C-NMR spectra of compounds (2a) (fig.3), there are two signals for OCH_3 & OCH_2 carbon group at 55 & 70 ppm respectively, but a signal for carbon of CH=N groups of each above compounds appears at 157 ppm.

Qualitatively, it seems that the effect of the substituents on p-positions increases the yield of products which appear that the electron releasing substituents like NH-Ph, OC_2H_5, and OCH_3, increases the electron density around the nitrogen atom which tends to increase the nucleophilicity of the nitrogen and thus increases the rate and hence the yield of the products. But the electron withdrawing groups like COOH tends to decrease electron density around nitrogen atom which didn't have any product by traditional method but we observed that the effect the ultrasonic which increase the energy of reaction and a result for that the reaction occurred by the compound (2j), see table (2).

Finally, the elemental analysis of some Schiff bases (2a, f) is shown in (Table 4), which are in good agreement with the calculated values.

Determination of bacterial sensitivity [12, 13]:

The sensitivity of four kinds of bacterial S-aureus, E-coli, Enterobacteria and Klebsiella, to the prepared Schiff bases was carried out using compound discs of KBr (1:3). The effects of these compounds on four types of microorganisms are represented in table 5. There is significant difference between the effects of the compounds used against various bacteria. The prepared Schiff bases were highly effective a gainst s-aureus and Enterobacteria but only slightly active against E-coli and Khebsiella type of bacteria.

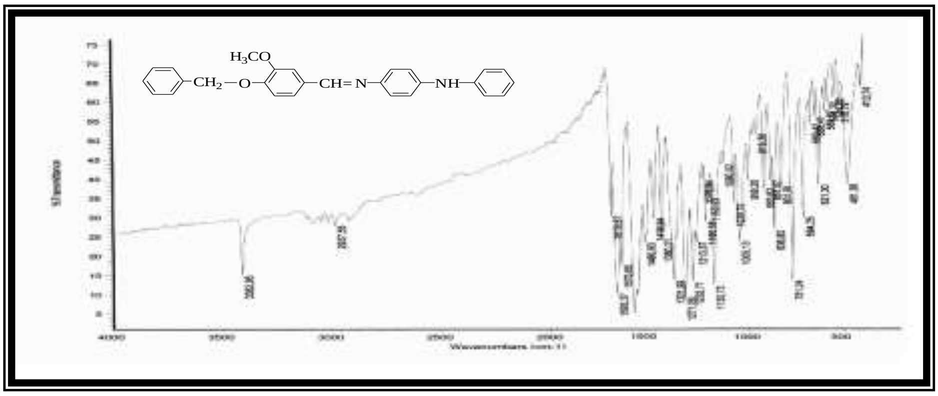


Fig (1) : FTIR spectrum of compound (2a)

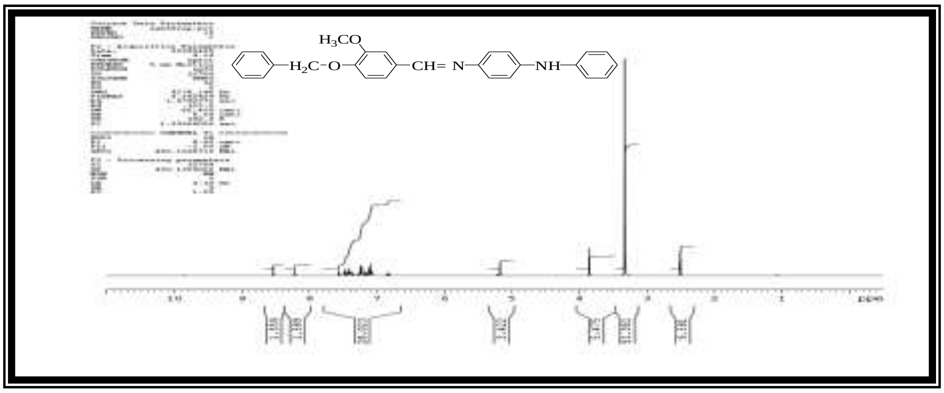


Fig (2): ^{1}H-NMR spectrum of compound (2a)

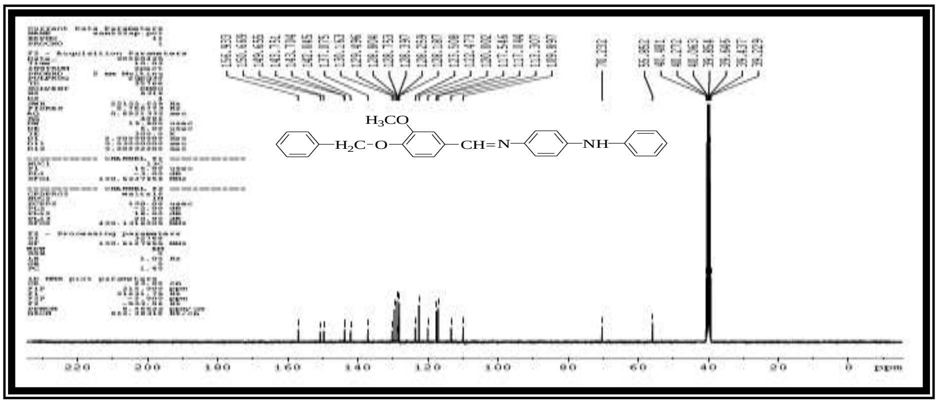
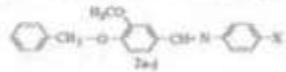


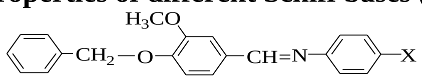
Fig (3): ^{13}C-NMR spectrum of Compound (2a)

Table (1): The physical properties of different Schiff bases (2a-j) & R_f (Solvent) by traditional method

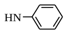
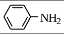


compound	*X**	*Nomenclature of Schiff bases*	*M.F. of Schiff bases*	*Reaction time(hr)*	*Solvent used for Recrystalization*	*Yield %*	*Color &shape*	*MP. (°C)*	*R_f(Solvent)*	
2a		(4-benzyloxy-3-methyl-benzylidene)-N[1]-phenyl-Benzene-1,4-diamine	$C_{27}H_{24}N_2O_2$	2.5	ethanol	70	green pow.	128-130	0.82	(Me)2O/EtAc 4 / 2
2b	OCH_2CH_3	(4-benzyloxy-3-methyl-benzylidene)-(4-ethoxy- phenyl)-amine	$C_{23}H_{23}NO_3$	2.5	ethanol - dioxan	74.5	yellow-white pow.	155-157	0.82	Hexane/EtAc 5 / 1
2c	OCH_3	(4-benzyloxy-3-methyl-benzylidene)-(4-methoxy-phenyl)-amine	$C_{22}H_{21}NO_3$	2.0	ethanol	77	yellow-white crystals	147-148	0.85	Hexane/EtAc 5 / 1
2d		N[1],N[4]-bis-(4-benzyloxy-3-methyl-benzylidene)-biphenyl-4,4'-diamine	$C_{42}H_{36}N_2O_4$	1.0	dioxan	62	deep – yellow pow.	245-247	0.74	(Me)2O/EtAc 4 / 2
2e	NH_2	N[1],N[4]-bis-(4-benzyloxy-3-methyl-benzylidene)-phenyl-1,4-diamine	$C_{36}H_{32}N_2O_4$	1.5	dioxan	61.5	deep – yellow pow.	195-197	0.60	(Me)2O/EtAc 4 / 1
2f	H	(4-benzyloxy-3-methyl-benzylidene)-(phenyl)-amine	$C_{21}H_{19}NO_2$	3.5	ethanol	63	lemon pow.	114-115	0.65	(Me)2O/EtAc 4 / 2
2g	OH	(4-benzyloxy-3-methyl-benzylidene)-(4-hydroxy-phenyl)-amine	$C_{21}H_{19}NO_3$	5.0	ethanol - hexane	51	brown crystals	135-137	0.65	(Me)2O/EtAc 4 / 2
2h	Cl	(4-benzyloxy-3-methyl-benzylidene)-(4-chloro-phenyl)-amine	$C_{21}H_{18}NO_2Cl$	3.0	ethanol	48	yellow-brown crystals	82-84	0.55	EtOH/(Me)2O 5 / 1
2i	I	(4-benzyloxy-3-methyl-benzylidene)-(4-iodo-phenyl)-amine	$C_{21}H_{18}NO_2I$	4.5	ethanol	45	yellow-white pow.	97-99	0.81	EtOH/(Me)2O 5 / 1
2j	COOH	(4-benzyloxy-3-methyl-benzylidene)-(4-carboxy-phenyl)-amine	$C_{22}H_{19}NO_4$	-	-	-	-	-	-	-

Table (2): The physical properties of different Schiff bases (2a-j) by ultrasonic waves



2a-j

compound	*X**	*M.F. of Schiff bases*	*Reaction time(min)*	*Solvent used for Recrystalization*	*Yield %*	*Color & shape*	*MP. (°C)*
2a		**$C_{27}H_{24}N_2O_2$**	**3.0**	**ethanol**	**77**	**green pow.**	**128-130**
2b	OCH_2CH_3	**$C_{23}H_{23}NO_3$**	**7.0**	**ethanol - dioxan**	**80.5**	**yellow- white pow.**	**155-157**
2c	OCH_3	**$C_{22}H_{21}NO_3$**	**6.0**	**dioxan**	**80**	**yellow- white crystals**	**147-148**
2d		**$C_{42}H_{36}N_2O_4$**	**0.3**	**dioxan**	**69**	**deep- yellow pow.**	**245-247**
2e	NH_2	**$C_{36}H_{32}N_2O_4$**	**1.0**	**dioxan**	**71**	**deep- yellow pow.**	**195-197**
2f	H	**$C_{21}H_{19}NO_2$**	**3.0**	**ethanol**	**71.5**	**lemon pow.**	**114-115**
2g	OH	**$C_{21}H_{19}NO_3$**	**6.0**	**ethanol -hexane**	**60.5**	**brown crystals**	**135-137**
2h	Cl	**$C_{21}H_{18}NO_2Cl$**	**9.0**	**ethanol**	**55**	**yellow- brown crystals**	**82-84**
2i	I	**$C_{21}H_{18}NO_2I$**	**2.0**	**ethanol**	**54**	**yellow- white Pow.**	**97-99**
2j	COOH	**$C_{22}H_{19}NO_4$**	**25**	**ethanol**	**45.5**	**yellow pow.**	**218-220**

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Acknowledgments

I would like to Special thanks are due to **Mr. Deler** in Bochum University (Germany) for his kind help and recording ^{1}H-NMR, ^{13}C-NMR & CHN analysis.

الملخص

تم تحضير سلسلة جديدة من قواعد شف من تفاعل الالديهايد ٤– بنزايلوكسي-٣- ميثوكسي بنزالديهايد مع ألانيلين المعوض بوجود الحامض الخليك الثلجي بواسطة الطريقة التقليدية و الطريقة فوق الصوتية، وتم اختبارالمركبات الناتجة والمحضرة ضد أربعة أنواع مختلفة من البكتريا. وتم تثبيت تركيب المركبات المحضرة بواسطة الطريقة الكيمياوية والطرق الطيفية مثل" FTIR ، ^{1}H-NMR، ^{13}C-NMR " وتحليل العناصر.