

# Synthesis of unsymmetrical, Symmetrical Schiff bases by Ultrasonic Assisted Technique and Biological Evaluation of their Metal-Complex

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تحضير قواعد شفت متماثله وغير متماثله باستعمال تقنية موجات فوق الصوتيه، وتقدير التاثيرات البايولوجيه لمعقداتها

**الخلاصة :**

طريقه بسيطه وفعاله استعملت لتحضير ليكاندات قاعدة شفت، من خلال تفاعلات تكثيف الديهايدات او كيتونات الاروماتيه مع امينات اروماتيه مختلفه، وتكوين المعقدات مع الفلزات من خلال استعمال الموجات فوق الصوتيه. ومن المميزات هذه الطريقه، اقتصاديه، صديقه و مرنه للبيئه وكذلك سهله العمل و تعطى ناتج كبير فى وقت قصير.

## Abstract :

A mild and efficient method has been reported for preparation of Schiff base ligands through condensation reaction of aromatic aldehydes and keton with different aromatic amines and formation of metal complex through the use of ultrasonic assisting technique. The advantages of this friendly, economically, environmentally and mild method are such as; simple work-up, high product yields and very short reaction times.

**Keywords:** Schiff base; metal salt, aromatic (aldehydes, ketone and amine), Sonochemistry.

## Introduction

*N*-substituted imines, also known as Schiff bases represent one of the most widely used families of organic compounds and their chemistry is essential material in many organic chemistry textbooks [1]. In general, they are easily prepared by the condensation reaction of primary amines with carbonyl compounds. The first reports of this kind of reaction have been published by Hugo Schiff in the 1860s [2-4]. Metal complex play an essential role in agriculture, pharmaceutical and Industrial chemistry [5].

The field of Schiff base complexes is fast developing because of the wide variety of possible structures for the ligands, depending on the aldehyde and amine used. Many Schiff bases and their complexes have been widely studied because of their industrial and biological applications. [6-8] Some Schiff bases were tested for fungicidal activity, which is related to their chemical structure [9]. Schiff base compounds ( $RC=N-$ ) are usually formed by the condensation of a

primary amine with an active carbonyl. The cross-linking agents can also be derived from metal complexes with O, N or S ligands. For example, an intra coordination salt such as salicylates or anthranilates and aliphatic or aromatic amines can form strong five- or six-membered chelate rings which are able to produce metal containing cross-linking agents with the required properties [10-12]. The complexes of Co(II), Ni(II), and Cu(II) ions with the Schiff bases derived from the condensation of salicylaldehyde and *o*-aminophenol or 2-aminobenzoic acid were synthesized and characterized by different techniques, in particular, elemental analysis and molar conductance measurements as well as IR and electronic spectroscopy [13, 14]. The complexes of Mn(III), Co(III), Fe(III) ions with the Schiff base derived from the condensation of thiocarbohydrazide with 2-amino-4-ethyl-5-hydroxy benzaldehyde under Reflux were also synthesized and characterized by different techniques including elemental analyzer, atomic absorption spectrophotometer, IR, mass spectrometer, The purity of the Schiff base and its complexes was confirmed by the TLC and HPLC techniques [15]. The M (II) Schiff base complexes prepared from salicylaldehyde, *o*-amino benzoic acid and Cu, Ni, Fe and Zn and four metal complexes were synthesized. The chemical structure of the synthesized metal ligand complexes were confirmed IR and NMR spectral analysis and tested for their antibacterial activity against several pathogenic bacteria [16, 17]. Schiff base, crystal structure, tautomerism, quinoid effect, coordination compounds were also studied [1].

The biologically active complexes of Schiff base have been often used as chelating ligands in the coordination chemistry of transition metals as radiopharmaceuticals for cancer targeting, agrochemicals, as model systems for biological macromolecules, as catalysts and as dioxygen carriers [18].

In organic compounds the presence of  $\text{-C=N-}$  along with other functional groups form more stable complexes compared to compounds with only  $\text{-C=N-}$  coordinating moiety.

Schiff bases and their metal complexes used as metal catalysts in various biological systems, polymers, and dyes, besides some uses as anti fertility and enzymatic agent [5].

Metal complex make these compounds effective as stereo specific catalysts towards oxidation, reduction, biological activity and other transformations of organic and inorganic chemistry.

The use of Ultrasound to promote chemical reactions is called sonochemistry.

The effects of ultrasound observed during organic reactions are due to cavitations, a physical process that create, enlarges, and implodes gaseous and vaporous cavities in an irradiated liquid.

Cavitations induces very high local temperatures, and pressures inside the bubbles (cavities), leading to turbulent flow of the liquid and enhanced mass transfer.

Recently sonochemistry is discussed as a complementary technique for promoting chemical reactions. These (often called “green”) techniques can help to reduce the amount of undesired hazardous chemicals and solvents, reduce energy consumption, and increase the selectivity toward the given products [19].

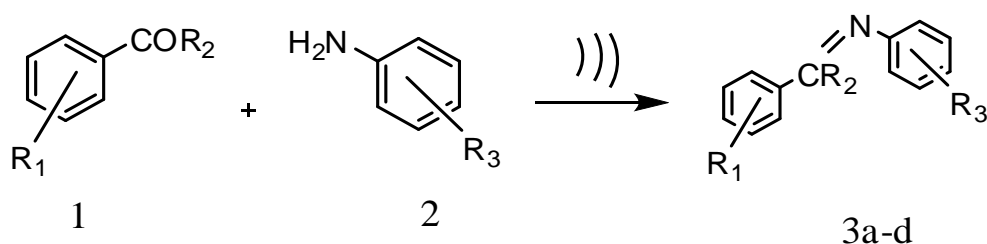
## Experimental

Infrared spectra were recorded at room temperature from  $4000\text{ cm}^{-1}$  to  $400\text{ cm}^{-1}$  with KBr pellets at a resolution of  $4\text{ cm}^{-1}$ , using Themo Mattson IR.300 Spectrometer. Most of the obtained vibration bands of the IR spectrum were identified and compared with those available in literature. The  $^1\text{H}$  (300MHz) NMR spectra was measured using TMS as internal reference. Melting points were determined in open capillaries using electro thermal 9100 digital melting point apparatus. All reagents were used without further purification. The Ultrasonic-assisted

condensation of aryl aldehyde and aryl amines and the metal-complex were carried out in electronics ultrasonic cleaner JP-060S. Chemical shifts are quoted in parts per million and the abbreviation used s= singlet. The percentage compositions of the elements (CHNS) for the Schiff bases were determined using an Elemental analyzer CHNS Model Fison EA 1108. All reactions were monitored by TLC (aluminium foil-backed, 0.25mm silica gel 60 F254; Merck).

### 1- General Procedure for the preparation of unsymmetrical Schiff base (3a-c)

In Ultrasound assisted synthesis the Schiff base was prepared by the condensation of respective Aldehyde **1** and amine **2** in 1:1 molar ratio using an Erlenmeyer flask through a conventional Ultrasound bath by taking few mL solvent (ethanol) respectively. The reaction was completed in a short period of time (Table 1). The solution when cooled gave colored crystals, which washed with Ethanol and dried over anhydrous CaCl<sub>2</sub>.



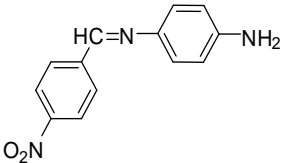
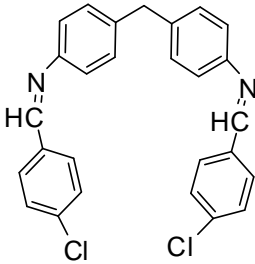
### 2- General Procedure for the preparation of symmetrical Schiff base (3d)

In Ultrasound bath the compound was prepared by condensation of (3:1) molar ratio ketone **1** with amine 4,4'-diaminodiphenylmethane **2** (after dissolving in ethanol) were mixed together at ambient temperature in an Erlenmeyer flask. The mixture was subjected to Ultrasonic waves for 1h at 60 °C, filtered; the crude products were re-crystallized with ethanol to obtain **3**.

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**Table 1**  
**Unsymmetrical and symmetrical Schiff base Synthesized (3a-d)**

No	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	Product	%Yield	Time	M.P, °C
a	-OH(2)	-H	-COOH(3)		90	1mint(r.t)	194-195
b	-OH(2)	-H	-N=N-Ar(4)		92	2mint(r.t)	158-159

c	-NO <sub>2</sub> (4)	-H	-NH <sub>2</sub> (4)		88	2mint(r.t)	165-166
d	-Cl(4)	-CH <sub>3</sub>	-CH <sub>2</sub> -C <sub>6</sub> H <sub>4</sub> -NH <sub>2</sub>		70	1h, (60)°C	142

**Table 2**  
Characterized absorption band for the synthesized compounds (3a-d)

No.	$\nu(\text{N-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$ phenolic	$\nu(\text{C=O})$	$\nu(\text{N=N})$	$\nu(\text{NH}_2)$	$\nu(\text{NO})$
a	3413	1620	1284	1677			
b	3414	1614	1281		1560		
c	3482	1627				3386	1339, 1507
d	3414	1617					

**Table 3**  
Physical data for the synthesized compound (3a-d)

Comp.	Color	Found (Calcd.)%		
		C	H	N
a	Yellow	70.03/69.70	4.20/4.60	6.22/5.81
b	Yellow	76.42/75.73	4.88/5.02	13.88/13.94
c	deep red	64.88/64.72	5.22/4.60	16.89/17.42
d	Deep brown	74.15/73.14	4.45/4.55	5.88/6.32

**Table 4**  
**<sup>1</sup>H NMR spectral data (δ,ppm) for the synthesized compounds**

Comp.	aromatic protons	CH=N	OH	NH <sub>2</sub>	CH <sub>2</sub>
a	5.32-6.51	3.32	8.86,8.95		
b	5.15-6.30	3.34	8.93		
c	4.93-6.63	3.31		8.85	
d	5.51-6.07	3.27			2.06

### 3- General procedure for the preparation of the Schiff base complex

A mixture of the Schiff base 1mmol dissolved in ethanol and the Metal salt 1mmole in Ethanol, were mixed together, the pH of the solution were adjusted to (7-8) and put in the Ultrasonic bath at 40 °C, after completion of the reaction (Table 5) the colored complex was collected by filtration then washed several times with hot ethanol until the washing becomes colorless. The Product was dried and the structure of the complex was confirmed by IR, and <sup>1</sup>H, NMR.

**Table 5**  
**Physical data for the synthesized complex compound in 40 °C**

Schiff base	Schiff metal complex	M.P. °C	Color	Time (mint)	% Yield
a	Ni(II) complex	>300	Gray-creamy	4	95
b	Ni(II) complex	156-157	Brownish- orange	2	94
c	Cr(III) complex	>296	Brown black	8	96

d	Cr(III) complex	> 300	Greenish brown	8	98
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**Table 6**  
**IR spectral bands position/cm<sup>-1</sup> and electronic spectral data (in DMF) cm<sup>-1</sup> of the Schiff base metal-complexes**

Schiff base	Complex	-OH	-OH str.	C=N bend	$\nu(\text{C}=\text{O})$	M-N str.	M-O	UV-visible( $\lambda_{\text{max}}$ )
a	Ni(II)complex	3304	1394	1534	1618	752	499	415
b	Ni(II)complex	3303	1488	1562		750	499	400
c	Cr(III)complex	3385	1340	1508		854	491	429
d	Cr(III)complex	3402	1318	1508		691	502	400

### Antibacterial activity of the metal-Schiff base

(Table 7) exhibits the zone of bacterial growth inhibition of the metal-Schiff base of Ni (II), and Cr (III) against the tested bacteria.

**Table 7**  
**The effect of metal- Schiff base on the bacterial growth**

Metal-complex	Bacteria		
	<i>E. Coli</i>	<i>Pseudomonas/Aeruginosa</i>	<i>Staphylococcus aureus</i>
a	++	++	+++
b	+++	++	++
c	++	+	+
d	+	+	+

High active = +++ (inhibition zone = 10-14 mm); moderately active = ++

(Inhibition zone = 6-9 mm); slightly active = + (inhibition zone = 3-5 mm)

## Results and Discussion

The IR of each compound confirms the formation of imine bond ( $\text{-C=N-}$ ) and absence of the original aldehydic bond ( $\text{-C=O}$ ). A band at  $1614\text{-}1627\text{ cm}^{-1}$  is assigned to the stretching vibration of the imine group  $\nu(\text{C=N})$ . compounds (a and b) displayed a band at  $1281\text{-}1284\text{ cm}^{-1}$  which is assigned to  $\nu(\text{C-O})$  stretching vibration of the phenolic  $\text{-OH}$ , respectively.

Proton NMR showed sharp singlet at  $3.27\text{-}3.34\text{ ppm}$  which further confirmed the formation of  $\text{-CH=N-}$  bonds in the Schiff bases.

The  $\nu(\text{OH})$  band at  $3402\text{-}3305\text{ cm}^{-1}$  was observed in all the complex compounds. Further conclusive evidence of the coordination of these Schiff-bases with the metal ions was shown by the appearance of new bands due to  $\nu(\text{M-N})$  and  $\nu(\text{M-O})$  in the metal complexes.

The infrared spectral data of the Schiff base and its complex with metal ion are in agreement with the expected range. The band in the range of  $3302\text{-}3405\text{ cm}^{-1}$  is attributed to the existence of water molecules. A band at  $1508\text{-}1562\text{ cm}^{-1}$  is due to  $\text{-C=N}$  vibration. The shifting of this group to lower frequency compared with the free Schiff base ( $1614\text{-}1627$ )  $\text{cm}^{-1}$  suggesting a coordination through nitrogen atom of azomethine group, meanwhile the band at  $1618\text{ cm}^{-1}$  is assigned to  $\text{-C=O}$  stretching frequency in the complex (a) which appeared at  $1677\text{ cm}^{-1}$  in the spectrum of the free Schiff base. The shifting of this band to lower region indicates the involvement of oxygen atom of hydroxyl group of  $\text{-COOH}$  group in bonding with metal ions.

The infrared spectrum of the complex under investigation displays a band at  $499\text{-}502\text{ cm}^{-1}$  which is due to the presence of a coordinate  $\text{-OH}$  group of salicylaldehyde to M ion in complex. The band at  $3303, 3304, 3385, 3402\text{ cm}^{-1}$  are due to the presence of OH group in the complex (from it's the chemical structure).

New bands which are not present in the spectrum of free Schiff base appeared at  $752, 750, 854, 691\text{ cm}^{-1}$  are attributed to  $\text{-M-N}$  vibrations. The appearance of  $\text{-M-N}$  and  $\text{-M-O}$  vibrations supports the involvement of nitrogen and oxygen atoms in complexation with metal ions under investigation [20].

And from the gravimetric determination of Ni in the Schiff base metal complex (a, and b) by using Dimethylglyoxim, it was found that they contain  $22.7, 22.8\%$  of Ni [21].

## Acknowledgements

We are very much grateful to the Almighty God, the King of Kings and the Lord of Lords for enabling us to complete this work.

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