Research Article

GREEN ROUTE FOR EFFICIENT SYNTHESIS OF BIOLOGICALLY ACTIVE SCHIFF BASE LIGAND DERIVED FROM 2 – HYDROXY ACETOPHENONE: STRUCTURAL, SPECTROSCOPIC, ANTI MICROBIAL AND MOLECULAR MODELING STUDIES

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Article Received on: 10/01/19 Approved for publication: 22/02/19

DOI: 10.7897/2230-8407.1003107

ABSTRACT

A Novel Schiff base as ON donor was synthesized by green methodology by condensation of 2-hydroxyacetophenone with Furfurylamine via microwave assisted reaction in fruit juice medium. Thus an efficient, green, cost-effective and eco-friendly method has been developed, using some common fruit juices as current approach of synthesizing Schiff base which has given a new direction in the field of green chemistry. This method was also compared with conventional method and grinding method for determination of production efficiency and production economic. The Schiff base was characterized based on the results obtained from CHN analysis, NMR, FTIR, LCMS and electronic spectral data. The geometry of the Schiff base was evaluated using molecular calculation with Argus lab software. The Schiff base ligand was tested for antibacterial activity against Gram positive bacteria *Staphylococcus aureus* and *Bacillus subtilis* and Gram negative bacteria *Escherichia coli* and *Pseudomonas aeruginosa*, and antifungal activity against *Fusarium oxysporum* and *Fusarium recini*, where the ligand showed good biological activity.

Keywords: Microwave methods, fruit juices, 2-hydroxyacetophenone, Schiff base, Argus lab software, antimicrobial activity.

INTRODUCTION

Green Chemistry approach is an eco-friendly approach and has tremendous applications for the synthesis of various organic compounds and key intermediates in recent past. This technique involves an alternative reaction media to replace hazardous and expensive solvents routinely used in organic synthesis¹. Solvent free reactions need shorter reaction time, simpler and more efficient workup procedures, more improved selectivity's and easier separations and purifications than conventional solvents². Recently fruit juices are known to be potential organic solvents for the synthesis of compounds of pharmaceutical importance³. The wide spread applications of different natural acid catalyst like fruit juices⁴ are due to their non-toxic, safe, inexpensive and environmental benign nature.

Schiff base is a nitrogen analogue of aldehyde or ketone in which C=O is replaced by C=N-R group, formed by the condensation of an aldehyde or ketone with a primary amine⁵. Schiff bases and their bio-active complexes have been studied extensively over the past decade. Schiff bases are useful chelators because of their ease of preparation, structural varieties, varied denticities and subtle steric and electronic control on their frame work. Many Schiff base ligands have been reported by virtue of their potential in industrial applications⁶, pharma, drug and catalysis. Schiff base ligands have shown wide variety of applications in the medicinal and biological fields such as antibacterial⁷, anti-proliferative⁸, antimalarial, antifungal⁹, anticancer¹⁰, anti-inflammatory, antiviral and antipyretic properties. Considering the numerous applications of Schiff bases in various fields of chemistry, there has been tremendous interest in developing efficient methods for

their preparation. The principles of Green chemistry apply to most of the synthetic routes with microwave irradiation. Microwave assisted reactions are cleaner, last only very few minutes, have high yield and produced minimum waste. Another method which can be more advantageous is synthesis of Schiff bases by employing fruit juice's as green catalyst for green approach.

Our present work focuses on the green synthesis of Schiff base from 2-hydroxyacetophenone, a bidentate ligand¹¹ and Furfurylamine using green catalysts like fruit juices of lemon, orange, amla¹² and a comparative study of the formed Schiff base via condensation reaction and green methods. The structure of the synthesized ligand was confirmed by elemental analysis, spectral techniques and its anti -microbial activity was studied.

MATERIALS AND METHODS

All the chemicals and solvents used were of ARgrade (Merck, Mumbai, India) except 2-hydroxyacetophenone (E-Merck, Germany) and Furfurylamine (Sigma, USA). Melting Points of the compounds were determined in open glass capillaries and are uncorrected. Elemental analysis(C, H and N) was carried out on PERKIN ELMER, series II, 2400 CHNS/O Analyzer. Infrared spectra were recorded on Fourier transform infrared (FTIR), GX FT-IR PERKIN ELMER, in the range 4000-400cm⁻¹ by making a KBr Pellet of the compound. The electronic spectra of samples were recorded on UV Lambda, 19 PERKIN ELMER spectrophotometer. The mass spectra are obtained using API QSTARR Pulsar LC-MS quadrupole and TOF based single mass spectrometer. The antimicrobial activities of the ligand was studied by well diffusion method against *Escherichia coli* and

Pseudomonas aeruginosa (gram negative), *Staphylococcus aureus* and *Bacillus subtilis* (gram positive) bacteria and *fusarium oxysporum* and *fusarium recini* fungal species.

Synthesis of Schiff base condensation method

The Schiff base (HL²) was prepared (Figure 1) by refluxing a mixture of equimolar quantities of 2-hydroxyacetophenone (1.3615gm, 0.01M) and Furfurylamine (0.9712, 0.01M)¹³ in hot ethanol in presence of 3-4 drops of glacial acetic acid. After 6-8h of refluxing, the reaction mixture was poured in ice cooled water and pale yellow solid which separated, was filtered, washed with ethanol and ether. The product was recrystallized from hot ethanol. The elemental analysis (S:1) was carried out for the newly synthesized ligand and analytical data was tabulated in Table 1.

Synthesis of Schiff base by Grinding method

The equimolar (1:1) ratio of 2-hydroxyacetophenone and Furfurylamine was grounded¹⁴ in a motor-pestle for about 1hr until the reaction mixture solidifies little and left overnight for the completion of the reaction. The reaction progress was monitored by TLC. The product obtained is recrystallized from hot ethanol.

Synthesis of Schiff base by Microwave method

The equimolar (1:1) ratio of 2-hydroxyacetophenone and Furfurylamine was mixed in presence of 2drops of glacial acetic acid in a crucible and was then irradiated in the microwave oven

of 250W capacity. The completion of the reaction was monitored by TLC. In a span of 14-15mins the reaction was completed resulting in pale yellow solid with yield 80%-85%.

Synthesis of Schiff base in presence of Fruit juice

Preparation of catalyst: Lemon, orange and amla fruits were procured locally. lemon were pressed in fruit juicer and filtered with cotton to get liquid juice¹⁵, while orange fruits were peeled off with knife and slices were pressed in juicer and filtered through muslin cloth. The hard fleshy green material of amla fruit (5g) was boiled with water (50ml), cooled and filtered with muslin cloth to get clear juice which acts as catalyst.

Synthesis of Schiff base with lemon, orange and aq.extract of amla under solvent free condition: Equimolar amounts of 2-hydroxyacetophenone (0.1mol) with Furfurylamine (0.1mol) were taken in 100ml beaker. Variable amounts of (0.5ml, 1ml, 1.5ml, 2.0ml) of natural acid catalyst i.e., lemon juice was added to the reaction mixture and kept for stirring¹⁶ at room temperature for 2 mins and microwaved¹⁷ for 4-6 mins for completion of the reaction. Reaction progress is monitored by TLC. Melting point of the product was checked by open capillary tube. The process is repeated with orange and amla juice. The results are tabulated in Table: 5.

Table 1: Physical and Analytical data of Schiff base

Ligand(molecular Formula)	C ₁₃ H ₁₃ O ₂ N		
Molecular weight	216		
Melting point	147°C		
Colour	Pale yellow		
Yield	80%		
Elemental analysis	C%	calculated	72.46
		observed	72.45
	H%	calculated	6.04
		observed	6.12
	N%	calculated	6.503
		observed	6.58

Table 2: Molecular modelling studies

Energy	Schiff base (kcal/mol)	HOMO (kcal/mol)	LUMO (kcal/mol)
Self-consistent energy	-57151.5079	-62005.2623	-62005.2623
Heat of formation	-12.0745	6.4876	6.4876

Table 3: Antibacterial activity of Schiff base

Bacteria Species	Anti-bacterial sensitivity results (Zone of inhibition in cm)	Minimum inhibitory concentration level of the ligand (Zone of inhibition in cm)				
		Conc 50µg	Conc 100µg	Conc 200µg	Conc 250µg	Streptomycin
Bacillus	0.2	0	0	0.2	0.4	1
Staphylococcus	0.3	0	0	0	0.1	1
Escherichia coli	0.2	0	0	0.1	0.2	1
Pseudomonas	0.1	0	0	0.1	0.2	1

Table 4: Antifungal activity of Schiff base

Fungal species	Anti-fungal sensitivity results	Minimum inhibitory concentration level of the ligand (zone of Inhibition in cm)				
		Conc 50 µg	Conc 100 µg	Conc 200 µg	Conc 250 µg	Mancozeb
Fusarium oxysporum	1.5	0.2	0.3	0.9	1.3	2.0
Fusarium recini	2.0	1.3	1.4	1.6	1.7	2.3

Table 5: Comparative yields of the ligand in various fruit juice media

Comparative yields	Name of the catalyst	Amount of catalyst(ml)	Percentage yield of the ligand	Time(min)
1.	Lemon juice (pH 2.0-2.8)	0.5	87.60	7
2.	Orange juice (pH 3.3-4.1)	0.5	76.11	10
3.	Aq.extract of Amla (pH 2.8-3.1)	0.5	75.9	11

Spectris of the Ligand

S 1: CHN spectra of the ligand

S 2: IR spectra of the ligand

S3: ¹H-NMR spectra of the ligand

S4: LCMS spectra of the ligand.

S5: Electronic spectra of the ligand

Fig 1: Formation of The Ligand

Fig 2: Molecular modelling structures of the Ligand, HOMO, LUMO

Fig 3: Zone Of Inhibition Against bacterial and fungal species.

Fig 4: Zone of Inhibition against bacterial and fungal strains

Fig 5: Comparative antimicrobial activity of the Ligand.

RESULTS AND DISCUSSION

Physical Properties and Elemental Analysis

The results obtained from CHN analysis (S :1) of the synthesized ligand was described in Table 1. The melting point of the ligand was found to be 147°C. The analytical data and data obtained from spectral analysis suggests its molecular formula to be C₁₃H₁₃O₂N. The proposed structure of Schiff base is given in Figure 1.

FT-IR studies

IR spectrum of the Schiff base ligand (S :2) showed a sharp band at 1614 cm⁻¹ which is assigned to ν (C=N) mode of the azomethine group and a band at 3153 cm⁻¹(s) is assigned to phenolic ν (OH). A broad band at 1267 cm⁻¹ due to ν (C-O) phenolic group¹⁸.

NMR and Mass studies

The ¹H NMR(CDCl₃) spectra of the ligand (S:3) showed broad singlet at 11.02 ppm due to phenolic hydroxyl proton-OH in the

keto moiety of the ligand and all the aromatic protons were accounted for and absorbed at δ 6.5 -7.5 ppm, CH₃ proton at δ 2.3 ppm; and CH₂ proton at δ 4.55 ppm^{11,19}. The mass spectra of the ligand (S: 4) was carried out in a polar aprotic solvent, acetonitrile as ESI-MS. The spectra showed the peak attributed at 216 m/z of (M-1) and this peak was in line with the proposed structure of the ligand.

UV – Visible studies

The electronic transition study of the ligand (S: 5) was carried out in methanol. Two distinct bands were observed at 390 nm and 280 nm. The two bands correspond to the n- π^* (-C=N) and π - π^* (phenyl ring)¹¹ transitions of the azomethine chromophore respectively.

Molecular modelling studies

The possible structure of the Schiff base was evaluated using molecular calculation with Argus Lab software²⁰. The structure was built using quantum mechanics, molecular orbital

calculations were performed with AM1 (Austin Method 1) approximation, for the synthesized ligand. The electron density surfaces of highest occupied molecular orbitals (HOMO) and lowest unoccupied molecular orbitals (LUMO), are also generated for the ligand (Figure 2). The Self consistent field (SCF) energy value and heat of formation H_f for the optimized structure are reported for the ligand, HOMO and LUMO (Table 2).

Antimicrobial Testing

The biological activity of Schiff base synthesized has been studied for the antibacterial and antifungal activities by well diffusion method²¹. Fresh Culture of microbes having 5×10^5 colonies was mixed with nutrient agar medium and poured into plates. Wells were made in the cooled agar plates (1cm). 10mg of the compound of was dissolved in 2mL DMSO and 100uL was loaded in the well. The activity or sensitivity was observed after 24 – 48h incubation at 37°C. MIC ranges of concentrations were tested. The zone of inhibition was recorded in centimeters^{22,23} (Figure 3 & 4). The obtained zone of inhibition (in cm) of Schiff base was compared with commercially available controls²⁴. The antimicrobial data of ligand is given in Table 3 & 4. The ligand exhibited good antimicrobial activity.

CONCLUSION

The Microwave method using fruit juices as catalyst proves to be simple, efficient and ecofriendly compared to conventional method of synthesizing the ligand by condensing 2-hydroxyacetophenone with Furfurylamine. The ligand under study was characterized by elemental analysis, IR, H^1 – NMR, mass spectra and electronic spectral studies. The in-vitro antimicrobial results showed that the ligand showed good biological activity against Gram positive, Gram negative and fungal strains.

ACKNOWLEDGEMENT

Authors are thankful to HCU, Hyderabad; CFRD and Department of Chemistry, Osmania University for providing spectral and analytical data.

REFERENCES

- Vahabi,V. and Hatamjafari,F., Microwave assisted convenient one –pot synthesis of coumarin derivatives via Pechmann condensation catalyzed by FeF₃ under solvent free conditions and antimicrobial activities of the products.Molecules,2014,19,13093-13103.
- Patil,S.,Jadhav,S.D. and Patil,U.P., Natural acid catalyzed synthesis of Schiff base under solvent–free condition: As a green approach. Archives of Applied science Research,2012,4,1074-1078.
- Patil,S., Jadhav, S.D., and Mane,S.Y., Pineapple juice as a natural catalyst:an excellent catalyst for Biginelli reaction. International Journal of Organic Chemistry,2011,1,125-131.
- Rammohan Pal*,Fruit juice: a natural ,green and biocatalyst system in organic synthesis, open journal of organic chemistry,2013,1(4):47-56.
- Enamul Hassains, chaluvarajuKC, Niranjana MS, Zaranappa, Santosh C, International research Journal of Pharmacy., 2013,4(11).
- Mohsin Abbas khan, Samar Akhtar,Khadija Shahid., Synthesis, characterization and In-vitro biological assay of Triphenyltin derivatives of phenylhydrazones ;International journal of pharmaceutical sciences and research.,28(1),Sep-Oct 2014:147-151.
- Mabrouk MS, Soad G.A., Safaa.SH., Synthesis, characterisations, biological and molecular docking studies of some amino acid Schiff bases with their cobalt(II) complexes, Advances in Biological Chemistry,2017,(7),182-194.
- Ashu.C.,Anshul. S., Schiff bases: An emerging potent class of Pharmaceuticals, International Journal of Current Research in Medical Sciences.,2017,3(5),60-74.
- Suman.M.,Bharti.J.,Amar.S.M.,Archana.S., Review study on metal complexes synthesized from therapeutically important Schiff bases., The Pharmaceutical and Chemical Journal,2016,3(4),119-214.
- Mohammad Nasiruddin*, Didarulalam Chowdhury, Md. Moniruzzman Rony., Complexes of Schiff bases derived from 2-hydroxy aldehyde and propane-1,2-diamine:synthesis,characterization and antibacterial screening, American Journal of Chemistry and Applications,2014,1(2),12-18.
- A.M.Hamil, K.M. Khalifa, A .AL-Houni and M.M.El-ajaily, ynthesis, Spectroscopic investigation and antimicrobial activity of Schiff base complexes of cobalt(II) and copper(II)ions, Rasayan Journal of Chemistry,Vol.2, No.2,2009,261-266.
- Suman, Anjani, Suprita, Sheetal, Sheetal, Susheel Gulati and Rajvir singh., Green and environmentally bening organic synthesis by using fruit juice as biocatalyst: a review, International research journal of pure and applied chemistry 16(1):1-15, 2018.
- Adesh Kumar, Shanu Das and Rajesh Dhakarey.,Studies on Mn(II),Co(),Ni() and Cu() Complexes of Schiff bases derived from furfurylamine with benzaldehyde and phenyl glyoxal, Asian journal of chemistry,Vol.20,No.7,2008,5019-5026.
- Harshita Sachdeva, Rekha Saroj, Saritakhaturia and Diksha Dwivedi., Operationally simple green synthesis of some Schiff bases using grinding chemistry technique and evaluation of antimicrobial activities, Green processing and synthesis,2012,1,469-477.
- Azadeh Alikhani, Naserforouhifar, Hoda Pashdar.,Lemon juice as a natural catalyst for synthesis of Schiff base: green chemistry apporaoch, International journal of advanced engineering research and science ,vol.5,issue-2,feb-2018.
- Garima Yadhav¹,JyotiV.Mani²,Green synthesis of Schiff bases by using natural acid catalysts, International journal of scientific research ,2013, ISSN (online)2319-7064.
- Suman, Sheetal, Suprita, Susheel Gulati, Rajvir Singh., Go green with green catalysis: A focus and review on advancement of biocatalysts, International journal of scientific research 2016:79.57.
- A.P.Mishra and Monika Soni.,Synthesis,Structural,and biological studies of some Schiff bases and their maetalcomplexes,Metal based drugs,vol,2008,article id 875410.
- Manoj Kumar Agarwala, Manish Kaushik, Amitsinghale.,Synthesis of Schiff's base ligands by condensation of 2-hydroxyacetophenone and chiral diamines, Indian streams research journal,vol.2, issue 8,sept 2012
- Arguslab 4.0 Marky Thomson, Planaria software IC, Seattle, WA.
- B.K.Park, P.M. Kitteringham, O.NEILL., Metabolism of fluorine containing drugs, Annual review of pharmacology and toxicology, 2001,41:443.
- MohamedK. Awad, MahmudF. Abdel-Aal, FatenM. Atlam, HendA.Hekal., Molecular docking molecular modeling vibrational and biological studies of some new heterocyclic aminophosphonates, Spectrochimica Acta part A:Molecular and Biomolecular spectroscopy 2016, 206, 78-88.
- V.Thamilarasan,N.Sengottunvelan,N.Stalin,P.Srinivasan,G. Chakkaravarthi.,Synthesis,interactions, molecular structure, biological properties and molecular docking studies on Mn,

Co, Zn complexes containing acetylacetone and pyridine ligands with DNA duplex, Journal of photochemistry and photobiology B: Biology, 2016,160:110-120.

24. Y.T.Liu,J.Sheng,D.W.Yin,H.Xin,X.M.Yang,Q.Y.Qiao,Z.J.Yang.,Ferroenyl chaconne-based Schiff bases and their metal complexes, highly efficient, solvent-free synthesis, characterization, biological research, Journal of Organometallic chemistry, 2018,856, 27-33.

Cite this article as:

M. Sravanthi *et al.* Green route for efficient synthesis of biologically active Schiff base ligand derived from 2 – hydroxy acetophenone: Structural, spectroscopic, anti microbial and molecular modeling studies. Int. Res. J. Pharm. 2019;10(3):215-220 <http://dx.doi.org/10.7897/2230-8407.1003107>

Source of support: Nil, Conflict of interest: None Declared

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