



---

**An Updated Review on Application and Biological activities of Azomethine  
Drugs in Medicinal Chemistry**

---

Amol V. Kawalkar<sup>1</sup>, Santosh M. Arade<sup>2</sup> & Santosh M. Chavan<sup>3</sup>

<sup>1</sup>Department of Chemistry, Amolakchand Mahavidyalaya Yavatmal M.S. 445001

<sup>2</sup>Department of Chemistry,

Late R. B. Arts, Commerce, and Smt S. R. Bharti Science College Arni. Dist-Yavatmal. M.S.

<sup>3</sup>Department of Chemistry,

Phulsing Naik Mahavidyalaya, Pusad Dist-Yavatmal Maharashtra-445216 India

Corresponding Author – Amol V. Kawalkar

DOI - 10.5281/zenodo.15260481

---

**Abstract:**

*In transmutation reaction Schiff bases play a role as an intermediate. Schiff bases are generally excellent chelating agents, especially when a functional group like –OH or –SH is present close to the Azomethine group so as to form a five or six membered ring with the metal ion. In antibacterial and antifungal activities heterocyclic Schiff bases play a major role. Schiff bases are synthesized by the condensation between primary amines and aldehyde or ketones by different methods. From literature survey it is observed that many researchers have done their work on Schiff bases. But only conventional method used for this work. But very few researchers were synthesized Schiff bases by green approach. Therefore, some Schiff bases were prepared with help of aromatic primary amines and highly substituted aromatic aldehydes in ethanol and in presence of lemon juice as catalyst in present work.*

**Keywords:** -Schiff base, Aldehyde, Amine, Lemon juice.

---

**Introduction:**

Hugo-Schiff reported the condensation of primary amines with carbonyl compounds in 1864.<sup>1</sup> Commonly these compounds is the Azomethine group with a general formula  $RHC=N-R_1$ , where R and R<sub>1</sub> are alkyl, aryl, cyclo alkyl or heterocyclic groups also known as anils, imines or Azomethines. Aromatic amines and aromatic aldehydes are a very important class of organic compounds from which Schiff bases derived. This short review compiles examples of the most promising antimalarial<sup>2</sup>, antibacterial<sup>3-4</sup>, antifungal<sup>5-6</sup>, and antiviral Schiff bases<sup>7-9</sup>. An overview of synthetic methodologies used for the preparation of Schiff bases is also described. These are applicable in many fields, such as biological<sup>10</sup>, inorganic<sup>11-18</sup> and analytical chemistry<sup>19-20</sup>. In the

progress of science, the chemistry of the carbon nitrogen double bond plays an important role<sup>21-23</sup>.

In the synthetic laboratories green chemistry approach and microwave assisted synthesis is now a day widely practiced. Microwave reactions gives high yields together with simplicity in processing and handling under solvent-free conditions was studied due to some factor such as low cost, pollution free reaction and shorter reaction time<sup>24-28</sup>. Acceptance and popularity among the synthetic, chemist community assures safe and reproducible experimental procedures and microwave synthesis has gained. In the present work, some Schiff's bases were synthesized by solvent free technique using microwaves.

They were purified and characterized by means of spectral data and

elemental analysis. In 1990, at the EPS, UMB's Paul Anastas and John Warner defined Green Chemistry: "The design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances". There are some environmental issues and problems which constantly facing by society such as soil and water pollution, air pollution, global climate change, ozone depletion, acid rain, the depletion of natural resources, 29 Members of the California green chemistry science advisory panel, Paul T. Anastas and John C. Warner published their important principles of green chemistry in their book in 1998, 30.

In place of treating or cleaning waste, prevent it. Incorporate all materials used in the manufacturing process in the final product. Use methods that generate substances with little or no toxicity to people or the environment. Design chemical products with least toxicity but effective. When possible Phase-out solvents and auxiliary substances. Use temperature and pressure, to reduce costs and environmental impacts. Renewable raw materials for feedstock and to reduce or eliminate waste. Use blocking agents and chemical intermediates. Use chemicals with low risk for accidents, explosions, fires and readily break down into innocuous substances in the environment Select catalysts that carry out a single reaction many times

#### **Experimental Techniques:**

1. General procedure for extraction of Lemon juice: Fresh lemon cut by using clean dry knife and then pieces were pressed manually using domestic presser to extract juice. Then juice was filtered with clean cotton cloth and then through filter paper to remove solid material and to get clear juice. Then it was used as catalyst.
2. Melting Point: The melting points were determined in a theilstube apparatus and are not corrected.

3. I.R Spectrum:- I.R.Spectra was recorded on Shimadzu FTIR (Model ISI118675A) using KBr pallets.
4. Thin Layer Chromatography: Thin layer chromatography is detected on chromatographic paper. The TLC was performed using mobile phase, petroleum ether: ethyl acetate (4:1) and detected in U.V.Chamber.

#### **Materials and Methods:**

Experimental all required chemicals were used from Merck, Fluka and Acros chemical companies. Shimadzu FT-IR 8000 spectrophotometer used for IR spectra. <sup>1</sup>H NMR and <sup>13</sup>C NMR spectra were recorded in CDCl<sub>3</sub> using a Bruker Avance DPX instrument (<sup>1</sup>H NMR 250 MHz, <sup>13</sup>C NMR 62.9 MHz). Chemical shifts were reported in ppm (N) downfield from TMS. All of the coupling constants (J) are in Hertz. Shimadzu GC-MS QP 1000 EX instrument were recorded mass spectra. Melting points were determined in open capillaries with Buchi 510 melting point apparatus and are not corrected. Thin-layer chromatography was carried out on silica gel 254 analytical sheets obtained from Fluka.

#### **Method of Synthesis of Schiff Bases Derivatives:**

General procedure for the synthesis of Schiff bases: for this synthesis we use finely powdered of Solid starting materials. A mixture of aldehyde (0.5 mole) and amino benzoic acid (0.5 mole) was grinded in a small amount of lemon juice (2ml) at room temperature for the mentioned time. After completion of the reaction as indicated by TLC. All solvent-free reactions were performed by grinding the mixture. Then pour the mixture in crushed ice stirr it for 5 min. The crystalline powder formed was collected by filtration, washed with cold water and dried in an infrared light. Then recrystallize from ethanol.

1. 4-[(4-methoxybenzylidene) amino] benzoic acid: - L1
2. 4- {[(Z) (3hydroxyphenyl)methylidene]amino} benzoic acid :- L2
3. 4 - (Methylideneamino) benzoic acid: - L3

### Synthesis Of Schiff Base:

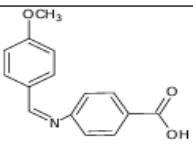
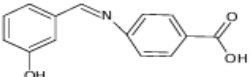
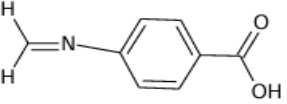
**1. 4-[(4-methoxybenzylidene) amino] benzoic acid: - L1** 4- Amino benzoic acid {0.5 mole} first taken in a mortar pestal and grind for a while then add Anisaldehyde {0.5 mole} then add lemon juice and grind for a while then add in to crush ice. Wash with cold water then filter it and dry it recrystallize from ethanol.

IR :(v max) cm-1: - (Metasusti Ph ring bend)= 700.16 cm-1 ,(Ar C-H str) = 2941.4 cm-1 (C=C str ) = 1421.5 cm-1, ( C= N str ) = 1591.2 cm -1 ,(C=O str ) = 1674.2 cm -1 (C-O str ) = 1161.1 cm-1

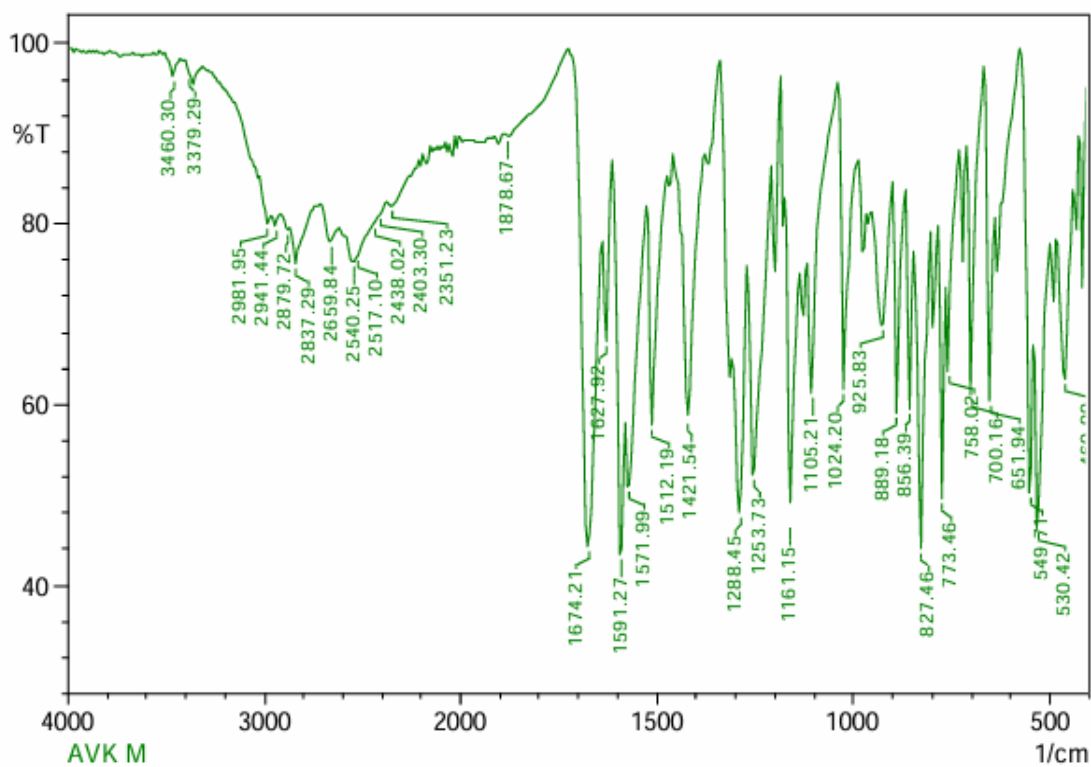
**2. 4- {[(Z) (3hydroxyphenyl)methylidene]amino} benzoic acid :- L2** IR:(v max) cm-1: - Ar (C-H str)= 2883.3 cm -1,Ar ( C=O Str) = 1681.9 cm-1 (C-O str ) = 1278.8cm-1, (O-H Str) = 3371.5 cm-1, (C=N Str) = 1566.2 cm-1 (C=C str) = 1516.2 cm-1

**3. 4 - (Methylideneamino) benzoic acid: - L3** IR :(v max) cm-1: - Ar (C-H str)= 2970.3 cm -1, Ar ( C=O Str) = 1683.8 cm-1 (C-O str ) = 1282.6 cm-1, (C=N Str) = 1571.9 cm-1

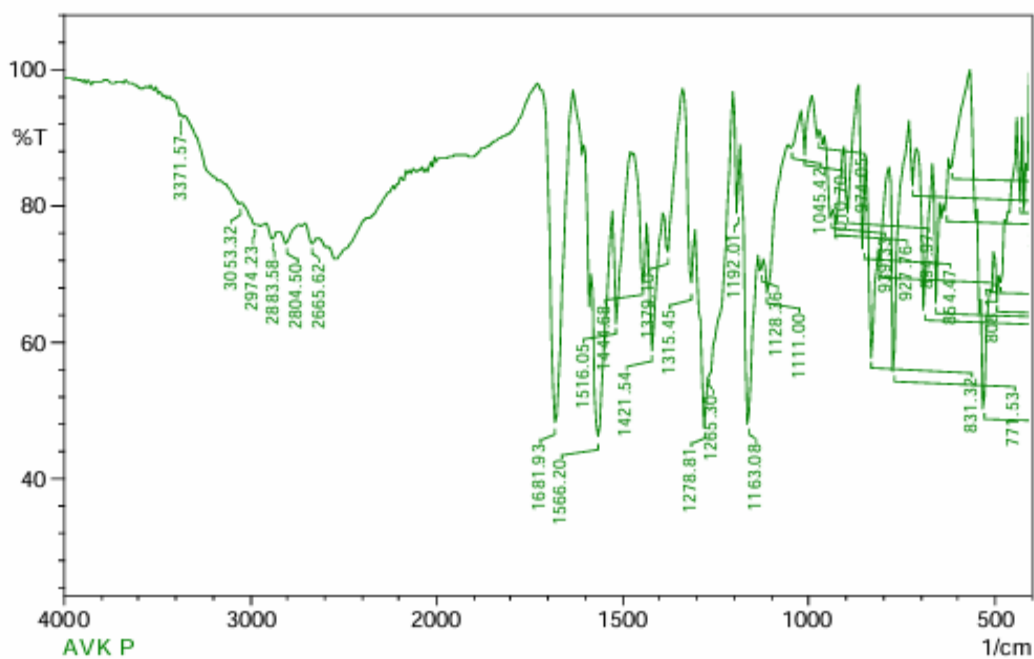
Chart 1:- New Synthesized Schiff Base

Sr no	Compound	Colour	Reaction Time	% yield	Melting Point
1	 4-[(Z)-(4-methoxyphenyl)methylidene]amino]benzoic acid	Cremish	3 hours 45 minutes	85.93%	203 °c
2	 4-[(Z)-(3-hydroxyphenyl)methylidene]amino]benzoic acid	Reddish yellow	3 hour's	98.43%	198 °c
3	 4-(methylideneamino)benzoic acid	Cremish	2 hour's 35 minutes	95.08%	171 °c

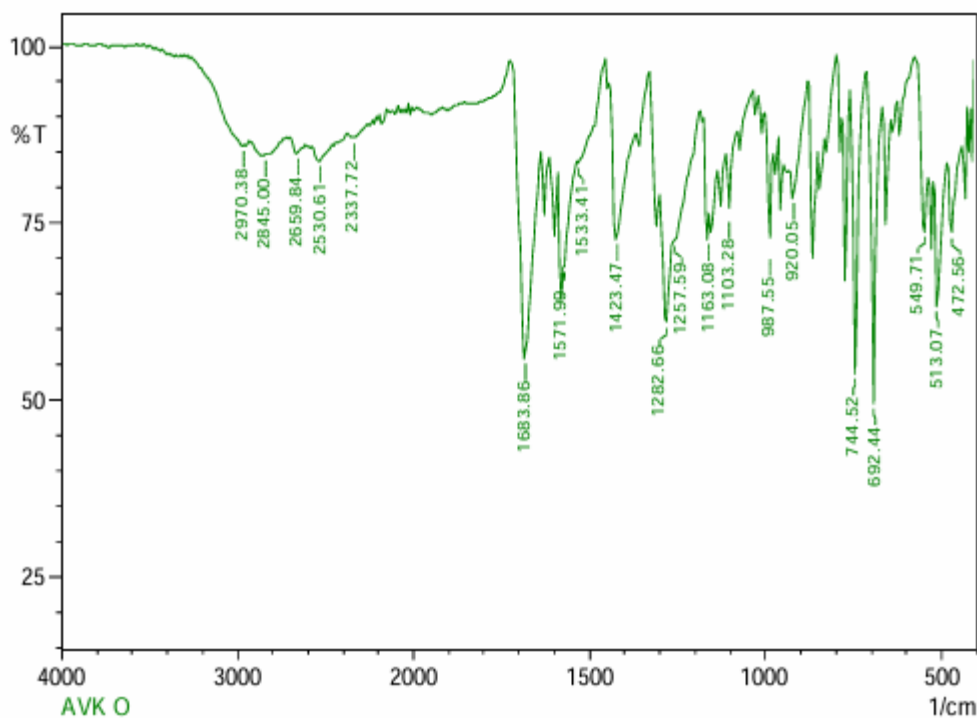
### 5. Results and Discussion:



1. 4-[(4-methoxybenzylidene)amino] benzoic acid :- L1



2. 4- { [(Z)(3hydroxyphenyl)methylidene]amino}benzoic acid :- L2



3. 4 - (Methylideneamino) benzoic acid:- L3

The newly synthesized Schiff base is stable at room temperature. The Schiff bases are soluble in common organic solvents, such as ethanol, methanol, and chloroform but partially soluble in synthesized compounds were characterized by elemental analysis, spectra data. The biological properties of the compounds are in progress. hexane. The Schiff base compounds were relatively well soluble in DMF and DMSO.

#### Conclusion:

We have developed a simple, efficient and more eco-friendly method for synthesis of substituted Schiff bases by using greener technique. The main advantages of this procedure are simple and convenient, and time consuming. In addition to this, compared to traditional method, this new method is cleaner, safer and more eco-friendly involving mild reaction conditions such as reaction time, use of hazardous solvents can be reduced by maintaining good yield of product. The yields were excellent and reactions were fast.

#### References:

1. S. Patil, S. D. Jadhav and U. P. Patil, "Natural acid catalyzed synthesis of Schiff base under solvent-free condition: as a green approach," Scholar research library, Archives of applied science research, vol. 4, no. 1, (2013), pp. 1074-1078.
2. A. Faizul, S. Satendra, L. K. Sukhbir and P. Om, "Ketimine from benzophenone and aniline, o-, m- and p-nitroanilines using toluene as solvent," J. Zhejiang Univ. Sci., vol. B, no. 8, (2007), pp. 446-21.
3. P. G. More, R. B. Bhalvankar and S. C. Pattar, "Schiff bases derived ... antibacterial and antifungal activity," J. Indian Chem. Soc., vol. 78, (2001), pp. 474-475.
4. A. H. El-Masry, H. H. Fahmy and S. H. A. Abdelwahed, "Synthesis and antimicrobial activity of some new benzimidazole derivatives," Molecules, vol. 5, no. 12, (2000), pp. 1429-1438.
5. M. A. Baseer, V. D. Jadhav and R. M. Phule, Y. V. Archana, Y. B. Vibhute, "Synthesis and antimicrobial activity of

- some new Schiff bases," *Orient. J. Chem.*, Vol.16,(2000), pp. 553-556.
6. S. N. Pandeya, D. Sriram, G. Nath and E. De Clercq, "Synthesis and antimicrobial activity of Schiff and Mannich bases of isatin and its derivatives with pyrimidine," *Farmaco*, vol.54,(1999), pp. 624-628.
  7. W. M. Singh and B. C. Dash, "Synthesis and characterization of novel schiff bases containing pyrimidine unit Pesticides," vol.22, (1988),pp 33-37.
  8. E. M. Hodnett and W. J. Dunn, "Synthesis of Novel Azo Schiff Base Bis[5,(4 methoxyphenylazo)-2-hydroxy-3-methoxy benzaldehyde]-1,2-Phenylenediamine," *J. Med. Chem.*, Vol.13,(1970), pp.768.
  9. S. B. Desai, P. B. Desai and K. R. Desai, "synthesis of some schiff bases, thiazolidones, and azetidinones derived from 2,6-diaminobenzo[1,2-d:4,5-d']bisthiazole and their anticancer activities," *Heterocycl. Commun.*,vol. 7 ,no. 83,(2001), pp. 83-90.
  10. S. Samadhiya and A. Halve, "synthetic utility of schiff bases as potential herbicidal agents,"*Orient. J. Chem.*, vol.17, no.1,(2001), pp119-123.
  11. W. P. Narocka, B. Sztuba, A. Drys, J. Wietrzyk. J. Ietrzyk, J. Kosendiak and A. Opolski, "Synthesis and antiproliferative activity in vitro of new 2-aminobenzimidazole derivatives. Part 3. Reactions of 2-arylideneaminobenzimidazole with selected 1, 3-diketones," *Pol. J. Chem.*,vol. 80 ,(2006),pp.279-287.
  12. J. P. Kaplan and B. M. Rizon, " -1-(substituted benzylidene)benzohydrazides'(PDF) synthesis and antimicrobial activities of some (E)-N ,"*J. Med. Chem.*,vol.23,(1980) , pp.702.
  13. M. Verma, S. N. Pandeya, K. N. Singh and J. P. Stables, "Anticonvulsant activity of schiff bases of isatin derivatives," *Acta Pharm.*,vol. 54,(2004), pp.49-56 .
  14. B. Rada and T. L. Leto, "Oxidative innate immune defenses by nox/duox family NADPH oxidases,"*Contrib. Microbiol.*,vol.15 ,(2008), pp. 164-187.
  15. A. Almasirad, R. Hosseini, H. Jalalizadeh, Z. Rahimi-Moghaddam, N. Abeian, M. Janafrooz, M. Abbaspour, V. Ziaee, A. Dalvandi and A. Shafiee, "Synthesis and analgesic activity of 2-phenoxybenzoic acid and N-phenylanthranilic acid hydrazides." *Biol. Pharm. Bull.*,vol. 29,no. 6,(2006), pp. 1180-5.
  16. C. J. Clarke and J. W. Eaton, "Hydrophobic ion chelators as antimalarial drugs" *Clin. Res.*vol. 38,(1990), 300A.
  17. A. Tsafack, M. Loyevski, P. Ponks and Z. I. Cabantchik, "An efficient synthesis and spectroscopic characterization of Schiff bases containing the 9,10-anthracenedione moiety," *J. Lab. Clin. Med.*,vol. 127, (1996),pp.575.
  18. J. C. Pessoa, J. Cavaco, J. Covreia, D. Costa, R. T. Henriques and R. D. Gillard, "Preparation and characterisation of new oxovanadium(IV) schiff base complexes derived from salicylaldehyde and simple dipeptides," *Inorg. Chim. Acta.*,vol.305,(2000), pp.7-13.
  19. Z. M. Zaki, S. S. Haggag, and A. A. Soayed, *Spectrosc. Lett.*,vol. 31,(1998),pp.757.
  20. N. W. Alcock, D. F. Cook, E. D. McKenzie and J. M. Worthington, "Metal(III) compounds of potentially septadentate [N4O3] ligands. Part II. Crystal and Molecular structures of [M(C27H24Cl3N4O3)·3H2O," *Inorg. Chem. Acta.* ,vol.38,(1980), pp.107.
  21. M. K. Adwankar and M. P. Chitnis, "In vivo anti-cancer activity of RC-18: a plant isolate from *Rubia cordifolia*, Linn. against a spectrum of experimental tumour models," *Chemotherapy*,vol. 28, (1982),pp.291-3.
  22. S.Thamarai Selvi, V. Nadaraj, S.Mohan, R.Sasi, and M.Hema , "Solvent free microwave synthesis and evaluation of

- antimicrobial activity of pyrimido [4, 5-b]-and pyrazolo [3, 4-b] quinolines Bioorg.” Med. Chem., vol. 14, no.11,(2006), pp. 3896-3903.
23. V. Nadaraj, S Thamarai Selvi , and T Daniel Thangadurai , Microwave synthesis of pyrimido[5,4-C] quinolines by modified biginelli reaction and evaluation of their antimicrobial activity,” J. Pharm. Res., vol.4,(2011), pp. 1541-1544.
24. D. Adam, Out of the kitchen, Nature, vol.421 , (2003),pp. 571-2.
25. A. Loupy, L.Perreux , M.Liagre K.Burle and M.Moneuse , "Microwaves in Organic synthesis," Pure Appl. Chem. vol.73, (2001),pp. 161.
26. P.T. Anastas and J.C. Warner, Green Chemistry: Theory and Practice, Oxford University Press: NewYork, Vol.30, (1980).
27. V.Nadaraj ,S. Thamarai Selvi ,S. Mohan , and T.Daniel Thangadurai ,`Microwave assisted synthesis and pharmacological studies of novel 5-deazaalloxazine derivatives, “ Med. Chem. Res.,vol.21,(2012), pp.2911-2919.
28. V. Nadaraj and S. Thamarai Selvi , `synthesis of schiff base under solvent-free condition: as a green approach,” Res. J. Chem. Environment,vol.17,(2013), pp.46-48.
29. Hamelin J. Bazureau J.P. and Texier F., `Microwaves in organic synthesis, ”Wiley Vch, Weinheim,vol. 253, (2002).
30. F.D.Popp, J.Org.Chem., vol.26,(1961), pp.1566.