

# Green Techniques to Synthesize Schiff Bases

## Advance Research in Organic and Inorganic Chemistry (AROIC)

Atul R Bendale\*, Manali Borse, Laxmikant Borse, Vasim Pathan, Anil Jadhav  
Sandip Institute of Pharmaceutical Sciences, Nashik, 422213 (M.S) India

Volume 3 Issue 2, 2022

### Article Information

Received date : June 10, 2022

Published date: June 20, 2022

### \*Corresponding author

Atul R Bendale, Associate professor,  
Department of Pharmaceutical  
Chemistry, Sandip Institute of  
Pharmaceutical Sciences, Nashik,  
422213 (M.S) India. Mob No: +91  
8000701337

Orcid id: 0000-0002-3219-0377

### Keywords

Schiff Bases; Imines; Green Synthesis;  
Sonochemistry; Mechanochemistry;  
Microwave Assisted Synthesis

Distributed under Creative Commons  
CC-BY 4.0

### Abstract

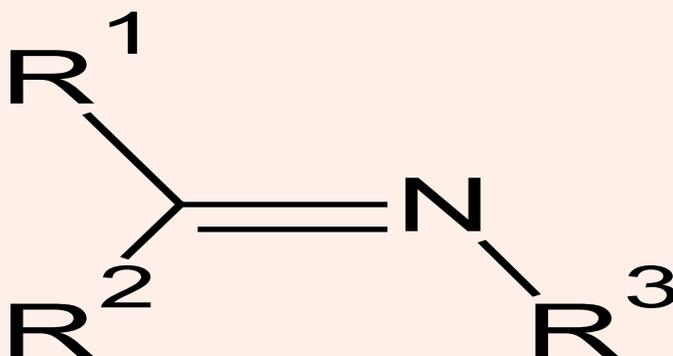
From ancient times, the chemistry of Schiff base-containing molecules has been a fascinating subject of study. They've been found to be a flexible pharmacophore for the creation and development of a wide range of bioactive lead compounds. Schiff bases are compounds containing the imine functional group. Different Schiff base containing byproducts have recently been synthesized and studied for activities such as antioxidant, antibacterial, antituberculosis, anti-inflammatory, antidepressant and anxiolytic activity, antihypertensive, anticonvulsants, anticancer, and antifungal activity. Different green chemistry techniques like-solid state, sonochemical, microwave assisted synthesis for synthesis of Schiff bases are discussed in this review.

### Introduction

Schiff bases are aldehyde or ketone-like compounds with an azomethine or imine group in place of the carbonyl group [1]. It can also be defined as a compound having a functional group that comprises a carbon-nitrogen double bond, with the nitrogen atom linked to an aryl or alkyl group, rather than a hydrogen atom [2]. Schiff bases are named after Hugo Schiff, a German chemist, in 1864 and won a Noble prize for the same. Schiff bases is a form of organic compound that has a widespread of uses in an array of domains, including analytical, and inorganic chemistry [3]. Due to a myriad of activities such as Antimalarial, Antibacterial, Antifungal, Antiviral, Antidyslipidemic activity, Antihelminthic activity, Antitubercular activity, Antioxidant activity, Antidiabetic activity and so on, Schiff bases have extended prominence in the pharmaceutical as well as medicinal fields [4]. There are other uses of Schiff bases other than the above-mentioned pharmacological uses. They can be used as intermediate in reactions, catalysts, dyes, etc... [5].

### General structure of Schiff bases

Schiff bases are basically the nitrogen analogue of aldehyde or ketone. The modification that persists in the structure is replacement of the carbonyl group with the imine group (-N=CH-). SBs are the byproduct of the acid catalyzed condensation of 1° amines and carbonyl compounds [5-7].



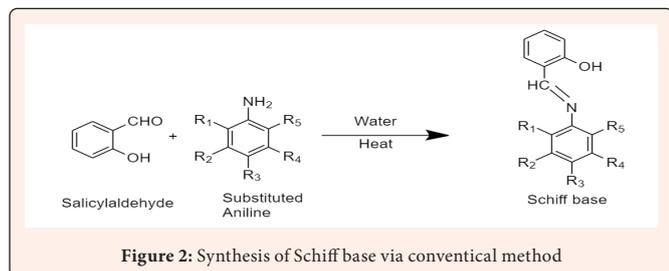
R1, R2, R3 = alkyl or aryl group

Figure 1: Basic structure of Schiff base

### Synthesis of Schiff bases

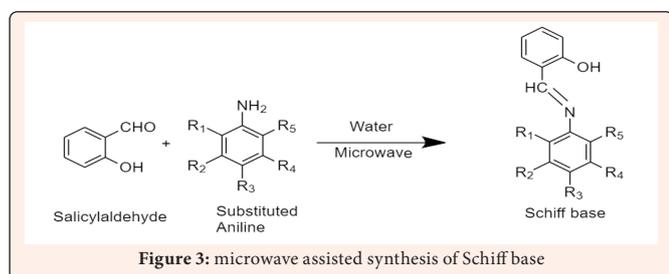
#### Conventional methods of synthesis of Schiff base

The majority of SBs are made via condensation of 2-hydroxybenzaldehyde with aromatic and aliphatic amines. Calvin and Bailes discovered a number of imines by combining salicylaldehyde with substituted phenylamines and other aromatic amines in a condensation process [8-11].



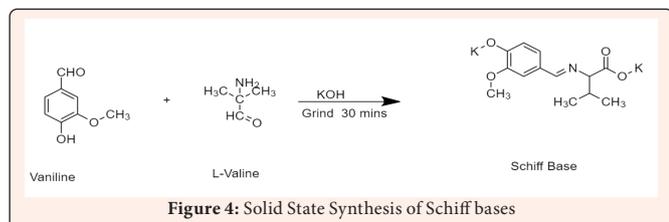
#### Microwave assisted method

Rousell and Majetich's independent studies first led to the microwave irradiation method. Because it eliminates the need of aromatic solvents and the Dean-Stark equipment for azeotropic water removal, microwave irradiation is environmentally less harmful than other approaches [5,12]. Another advantage of this method is that the reactions are more efficient in a shorter amount of time [13,14].



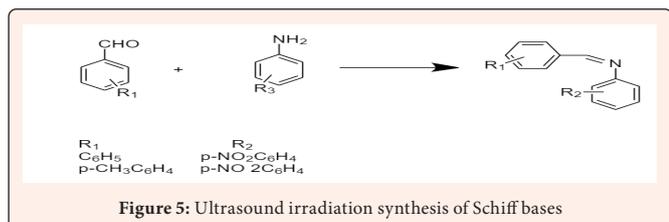
#### Solid State Synthesis

Grinding a mixture of more than two distinct substances provides the mechanical energy required to cause molecules to react. Heating, particle size reduction with accompanying increase in surface area and formation of new surfaces, local melting, and even phase transitions to alternate polymorphs are all possible impacts of the kinetic energy delivered during grinding on a crystalline solid [13,15,16].



#### Ultrasound Irradiation

Ultrasonic irradiation can be used to substitute the heating method in some cases. The KQ-218 ultrasonic cleaner (20 kHz/50 W) is used for ultrasonic irradiation [13,1]. The general process for the synthesis is - take the solvent of choice at 50°C, the reactants in the molar ratio substitute benzaldehydes/substitute anilines (1:1) are resolved. The mixture is then introduced to the ultrasound. The chemical is irradiated for 10-20 minutes and the reaction is monitored using TLC, after which the solvent is evaporated [15,17].



#### Water suspension method

This method is carried out without the use of any acid catalyst or any other type of organic solvents. The reaction occurs in a water suspension medium [18]. The condensation of Isatin and 5-fluoroisatin in water with the diamines leads to the synthesis of the corresponding SBs. The condensation occurs at room temperature for about 30 hours. The product is separated by simple filtration, is washed with water and dried [8,19].

#### Synthesis using natural catalyst

Grapes, sweet lime, and unripe mango fruits were purchased locally, then pressed through a fruit mixer and filtered with cotton to get liquid juice. While luscious lime fruits were peeled with a knife and fruit slices were squeezed into a fruit juicer to get a semisolid mass, the semisolid mass was then filtered with cotton to obtain liquid juice for use as a catalyst [12].

#### Conclusion

Schiff base is considered as one of the most versatile compounds. They're used as reactants in an array of synthetic organic processes, as significant frameworks in organometallic chemistry, as the backbones of valuable catalysts, and as pharmacological praesidium for a range of diseases and pathological conditions. The synthesis of SBs mainly takes place with aldehyde or ketone as the reactant with amines. There are various ways of synthesizing the compound including the water suspension method, microwave assisted synthesis, ultrasound irradiation and solid-state synthesis; these are more efficient and ecofriendly than conventional method. The methods discussed above can be applied for synthesis of novel Schiff bases via green chemistry approach.

**Conflicts of Interest:** The authors declare no conflict of interest

#### References

- Wenling Q, Long S, Panunzio M, Biondi S (2013) Schiff bases: A short survey on an evergreen chemistry tool. *Molecules* 18(10): 12264-12289.
- DN Dhar, CL Taploo (1982) Schiff bases and their applications. *J Sci Ind Res* 41(8): 501-506.
- Kajal A, Bala S, Kamboj S, Sharma N, Saini V (2013) Schiff Bases: A Versatile Pharmacophore. *Journal of Catalysts* 2013: 1-14.
- Przybylski P, Huczynski A, Pyta K, Brzezinski B, Bartl F (2009) Biological properties of schiff bases and azo derivatives of phenols. *Curr Org Chem* 13(2): 124-148.
- Patil S, Jadhav SD, Patil UP (2012) Natural acid catalysed synthesis of Schiff base under solvent free condition: as a green approach. *Arch Appl Sci Res* 4(2): 1074-1078.
- Da Silva CM, Da Silva DL, Modolo LV, Alves RB, De Resende MA, et al. (2011) Schiff bases: A short review of their antimicrobial activities. *Journal of Advanced Research* 2(1): 1-8.
- Khan T, Zehra S, Alvi A, Fatima U, Lawrence AI (2021) Medicinal Utility of Some Schiff Bases and their Complexes with First Transition Series Metals: A Review. *Orient J Chem* 37(5): 1051-1061.
- M Yildiz, A Kiraz, B Dülger (2007) Synthesis and antimicrobial activity of new crown ethers of Schiff base type. *J Serb Chem Soc* 72(3): 215-224.
- Karthikeyan MS, Prasad DJ, Poojary B, Subrahmanya BK, Holla BS, et al. Synthesis and biological activity of Schiff and Mannich bases bearing 2,4-dichloro-5-fluorophenyl moiety. *Bio org Med Chem* 14(22): 7482-7489.
- Kumar A, Verma S, Mishra AK, Kumar S (2017) Synthesis of some new Schiff bases of Pharmaceutical Interest. *Ann Adv Chem* 1: 053-056.
- Wadher SJ, Puranik MP, Karande NA, Yeole PG (2009) Synthesis and Biological Evaluation of Schiff base of Dapsone and their derivative as Antimicrobial agents. *Int J Pharm Tech Res* 1: 22-33.
- Yadav G, Mani JV (2013) Green Synthesis of Schiff Bases by Using Natural Acid Catalysts. *International Journal of Science and Research* 4(2).



13. Al Zoubi W, Al-Hamdani AAS, Kaseem M (2016) Synthesis and antioxidant activities of Schiff bases and their complexes: a review. *Appl Organometal Chem* 30: 810-817.
14. Rajavel R, Vadiv MS, Anitha C (2008) Synthesis, physical characterization and biological activity of some Schiff base complexes. *Journal of Chemistry* 5(3): 620-626.
15. Bendale AR, Bhatt R, Nagar A, Jadhav AG, Vidyasagar G (2011) Schiff base synthesis by unconventional route: An innovative green approach. *Der Pharma Chemica* 3(2): 34-38.
16. Atul RB, Jigar S, Sushil PN, Anil GJ (2021) Solid Phase Synthesis of Imines via Mechanochemistry and Screening for their Antifungal Activity. *International Journal of Current Research and Review* 13(22): 7-11.
17. Nagar AA, Patel PR, Dhobi A, Bendale AR, Chugh NN (2011) An innovative approach the sono chemical solvent-free synthesis of Schiff base. *Asian Journal of Current Chemistry* 1(2): 2-3.
18. Jarrahpour AA, Khalili D (2006) Synthesis of Some New bis-Schiff Bases of Isatin and 5-Fluoroisatin in a Water Suspension Medium. *Molecules* 11(1): 59-63.
19. Shi L, Ge HM, Tan SH, Li HQ, Song YC, et al. (2007) Synthesis and antimicrobial activities of Schiff bases derived from 5-chloro-salicylaldehyde. *Eur J Med Chem* 42(4): 558-564.