



# Microwave Irradiation-assisted Synthesis of Schiff's Bases – A Review

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## ABSTRACT

The use of Schiff's bases in the creation of bioactive molecules is incredible. Many of these methods require a lot of energy and involve risky substances, solvents, and expensive work-ups. Large amounts of organic waste are produced by complicated processes and low yields. Researchers therefore concentrated on safe and environmentally friendly methods to construct heterocyclic analogues and medicinal compounds. To overcome the drawbacks associated with the conventional method for the synthesis of Schiff's bases the new methodology uses microwave as an energy source for the organic synthesis. Microwave assisted method for preparation of the target organic moieties often facilitates higher product yields than any other approaches. The advantages of Microwave irradiation synthesis are solvent free or lower solvent conditions are a good method for reducing the pollution, lowering the cost, and increasing the product together with simplicity in processing and handling. It focused on microwave -assisted

methods to use for synthesizing Schiff's bases compounds. The benefits and drawbacks of yields and reaction conditions had been assessed.

**KEY WORDS:** Microwave-assisted Schiff's bases; eco-friendly; Green chemistry.

## INTRODUCTION

The energy science of using microwave radiation to stimulate chemical reactions is known as microwave irradiation [1 – 10] since 1986, MAOS, or microwave-assisted organic synthesis, has been known. Many chemical reactions can be accelerated very effectively using this "unconventional" synthetic approach, which results in improved selectivity, reduced side product amounts, quicker work-up procedures, and higher yields and yields. Because numerous organic processes may be carried out with MAOS without the use of solvents, it is characterized as a "green" technique.

Microwave facilitated synthesis represents an advanced development in the synthetic organic chemistry methodology; sensational alternative technical performances have been applied in the manner for the synthesis of Schiff's bases. Microwave irradiation has thus been discovered to be a precisely suitable thermal source not merely in the kitchen but also in a research laboratory. Chemists looked at the viability of conducting organic synthesis processes in a standard microwave oven. Since the organic chemical reactions are described in the first literature article on the use of microwave irradiation. More than 6000 articles have been reported in this rapid-moving and sensational field along with Schiff's base synthesis. [11-18] Over the past two decades, there has been a notable advancement in the use of microwave irradiation to stimulate and accelerate chemical processes. Microwave chemistry is a common mainstream for both industry and academic research. The main benefits [19-30] of microwave-irradiated organic synthesis are accelerating reaction rates, better yields, higher purity, uniformly selective heating

with lower energy requirements, achieving more notable reproducibility of reactions, and aiding in the development of more practical and hygienic synthetic methods for the synthesis of various Schiff's bases. Microwave-irradiated solid-phase synthesis has received a lot of attention recently from scientists and organic chemists. Solid-supported catalysts like alumina, silica, montmorillonite clay, and zeolites have been utilized in "dry media" processes, and their catalytic activity has been studied. Techniques for microwave-assisted synthetic method can be used in the search for new drugs. Researchers have successfully carried out many solid-phase organic reactions, according to a literature review. The methodology is noteworthy and gave a respectable awareness of the area of microwave supported organic synthesis. [31-40]

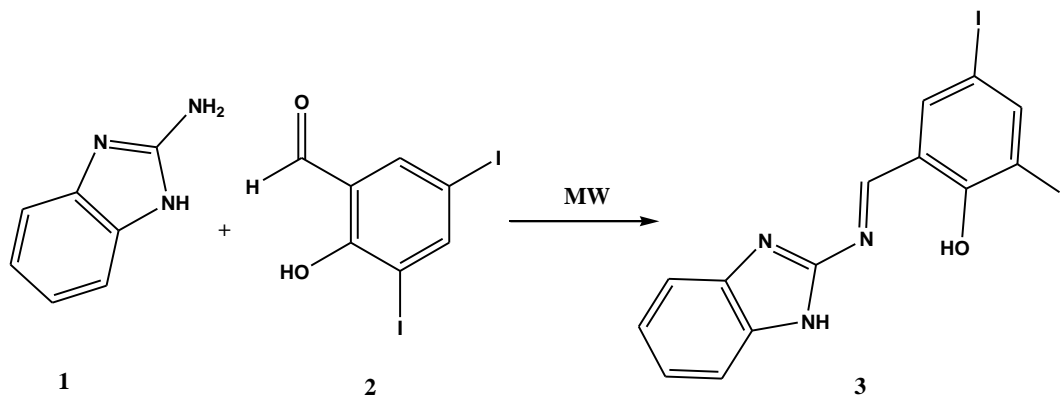
## **RESULTS AND DISCUSSION**

### **Microwave Synthesis of Schiff's Bases**

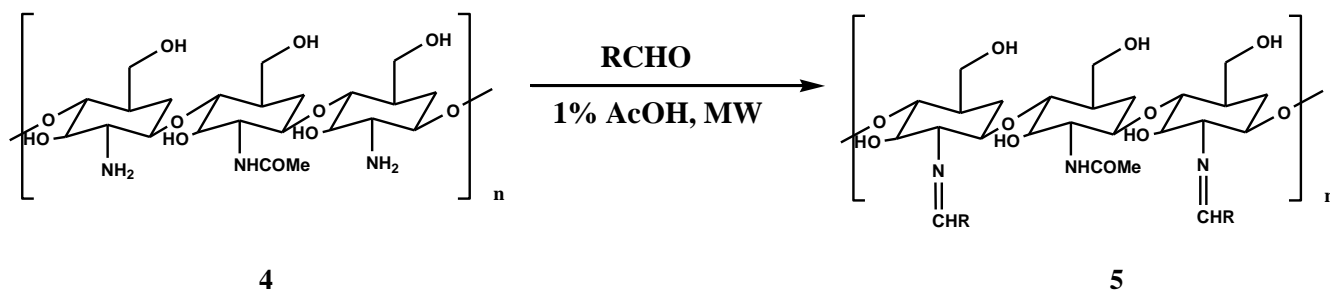
Using a microwave method, Shrivastava and coworkers [41] synthesized a novel Schiff's base (2-[(1H-benzimidazol-2-ylimino) methyl]-4,6-diiodophenol) from the condensation of 3,5-diiodosalicylaldehyde with 2-aminobenzimidazole (Scheme 1). It was shown that Schiff (2-[(1Hbenzimidazol-2-ylimino)methyl]-4,6-diiodophenol) was synthesized quickly and with higher yields using microwave aided synthesis compared to the conventional method. The reaction took 2-3 hours to complete using the conventional method, but just 8–10 minutes using the microwave method, increasing yields from 30-46 to 76–80%.

The first publication on the more environmentally friendly synthesis of three novel chitosan Schiff's bases utilizing microwave irradiation assisted condensation of chitosan and aldehydes was made by Haque and his coworkers [42] (Scheme 2). They employed an industrial microwave reactor system with a mechanical agitator, a 100 mL reaction flask connected to a reflux condenser, and an infrared temperature measurement tube. To obtain the final product, the

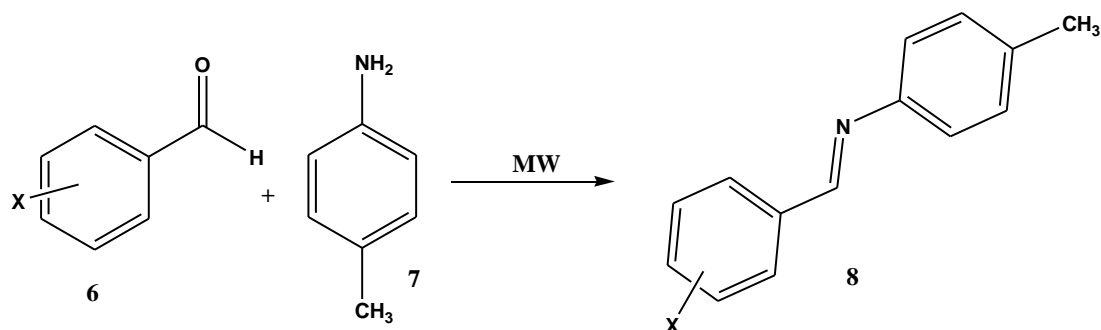
power was set at 600 W, and the sample temperature was raised to 60 °C and maintained there for 15–20 min.



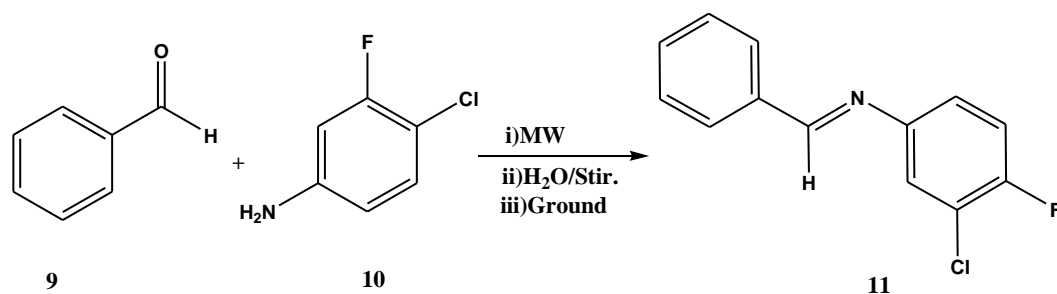
Scheme 1. Preparation of (2-[(1Hbenzimidazol-2-ylimino)methyl]-4,6-diiodophenol) derivatives.



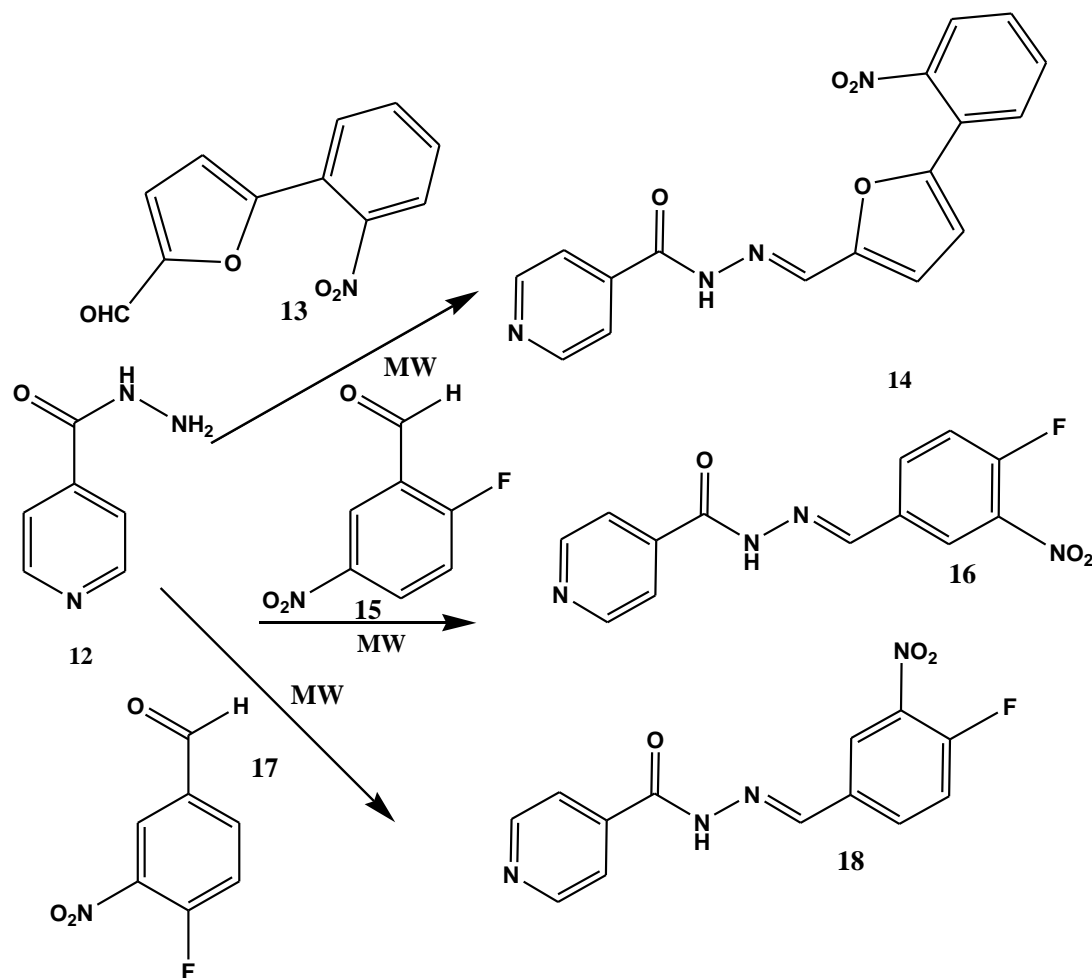
Scheme 2. Preparation of chitosan base Schiff base derivatives.



Scheme 3. Preparation of p-toluidine based Schiff base derivatives.



Scheme 4. Preparation of Schiff base derivatives.



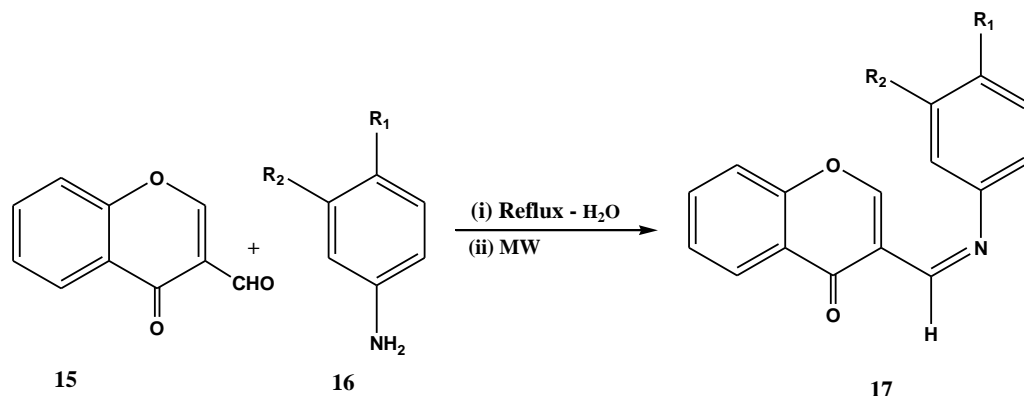
Scheme 5. Preparation of N-substituted-benzylidene)isonicotino hydrazide derivatives

Using *p*-toluidine and other aromatic aldehydes as reactants, Pooja et al. [43] reported the synthesis of several Schiff's bases using microwave irradiation method. Glucose was used as a green catalyst (Scheme 3). A microwave (180 W) was used to irradiate the reaction mixture for the appropriate amount of time. The series of reactions were conducted using an equimolar

combination of p-toluidine and several benzaldehyde derivatives having both functional groups that donate electrons and those that withdraw them. It used to take 2 to 9 minutes to finish the reactions.

The synthesis of Schiff's bases was investigated by Naqvi and his colleagues [44] using water-based, microwave, and grindstone green methods (Scheme 4). They discovered that the creation of Schiff's bases is an exothermic process, and the products obtained were very pure (90%) and yielded. Water-based reactions are the most appropriate way in these three environmentally friendly synthetic methodologies since water is convenient to handle and obtain. Water is still an affordable and non-carcinogenic medium for reactions.

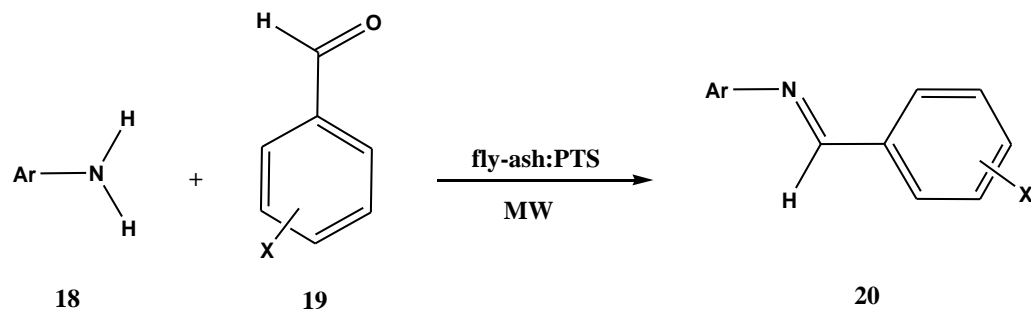
Schiff's bases of isonicotino hydrazides, such as N-(substituted-benzylidene) isonicotino hydrazides, were synthesized more effectively and environmentally friendly by Bayan et al. [45] Microwave assisted condensation of benzaldehydes in ethanol media with glacial acetic acid produced the best yields (Scheme 5). The outcomes demonstrated that microwave-assisted synthesis, which takes 6 to 8 hours, is 20 to 45 times faster than the conventional technique.



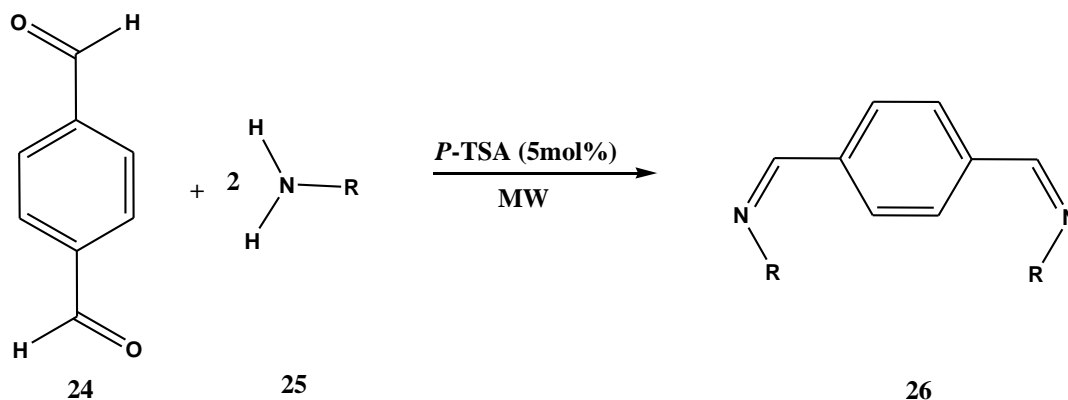
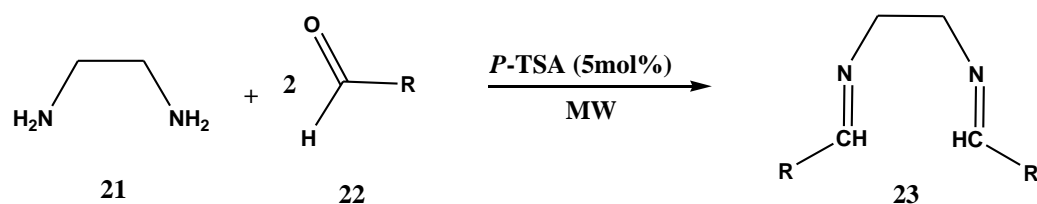
Scheme 6. Preparation of chromonel based Schiff base derivatives

Using 3-formyl chromonel and aromatic amines in a water medium, Mhaske and his coworkers [46] reported the synthesis of different Schiff's bases using standard heating and microwave aided (Scheme 6) techniques. We draw the conclusion from the results that the

reaction can be completed using a microwave in 2-3 minutes with an 81-84% yield, whereas the conventional technique requires 3–4 hours and yields 65-70%.



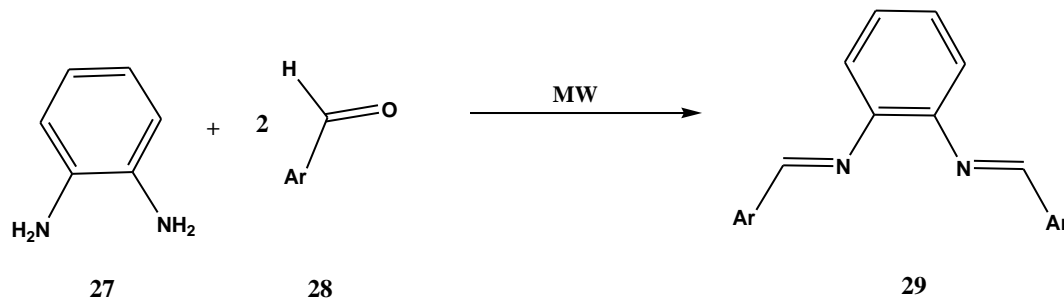
Scheme 7. Preparation of Schiff base derivatives.



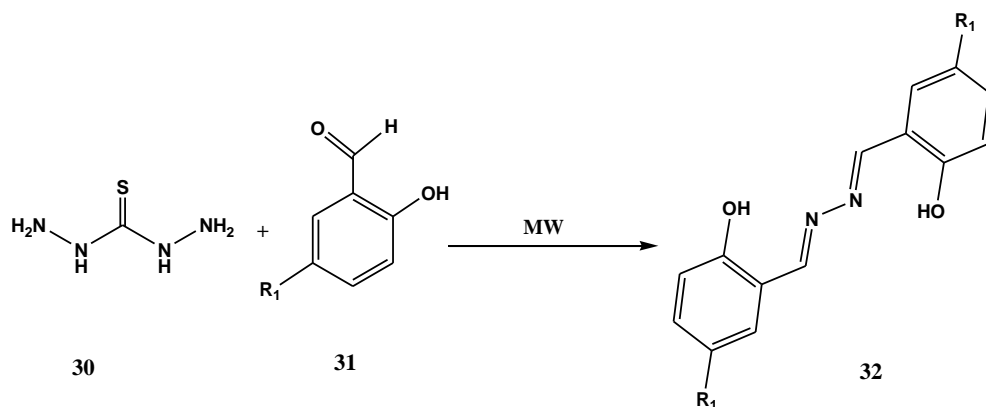
Scheme 8. Preparation of Schiff base derivatives

Through condensation of 4-chloroaniline and substituted benzaldehydes employing microwave irradiation in the presence of fly-ash PTS catalyst under a solvent-free green approach, Suresh, and his coworkers [47] produced some E-imines (Scheme 7). With this approach, the reaction produced higher imine yields without releasing any waste into the environment. By changing the catalyst quantity from 0.1 g to 1 g, they looked at the catalytic

impact of fly ash: PTS on the synthesis of benzylidene-4-chloroaniline. The percentage of product yield rose from 85 to 92% under microwave conditions as the catalyst quantity was raised from 0.1 g to 1 g. (650W and 6-12 min.).



Scheme 9. Preparation of Schiff base derivatives.



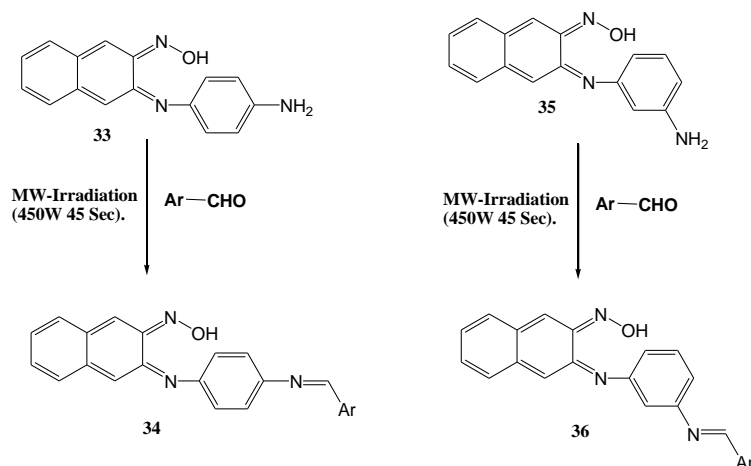
Scheme 10. Preparation of thiocarbohydrazone based Schiff base derivatives.

By using *p*-toluenesulphonic acid to catalyze the microwave-assisted condensation of dialdehydes and monoamines (or diamines and mono aldehydes) in the presence of P-TSA catalyst, Das and his coworkers [48] (Scheme 8) successfully synthesized several symmetrical bis-imines. As a result, it was determined that 5 mol% of *p*-TSA (600 Watts) was the best value. In each of the schemes, different MW powers and reaction temperatures were also examined Yields-(99%).

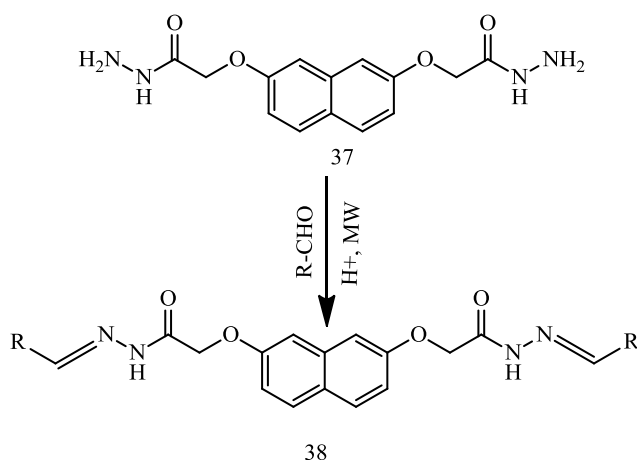
By effectively condensing phenylenediamine with a variety of aromatic aldehydes using the microwave irradiation approach, Mohmad et al. [49] created some of Schiff's bases (Scheme 9). The Schiff's bases were made by condensing phenylenediamine in a ratio of 1:2 with an aromatic



aldehyde, followed by exposure to microwave radiation at 350 watts for a period of 2–3 minutes at 60°C. The microwave approach produced excellent yields of synthesized chemicals (87-97%).



Scheme 11. Preparation of naphthalene based Schiff base derivatives

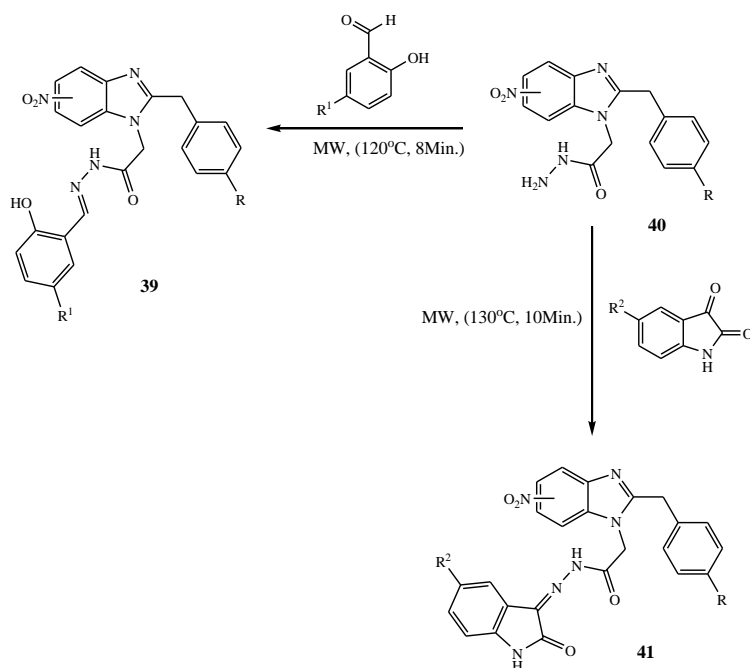


Scheme 12. Preparation of naphthalene substituted Schiff base derivatives

Using microwave irradiation, Kassim and his coworkers [50] reported two diazine Schiff's base ligands from thiocarbohydrazide and salicylaldehyde. The thione (C=S) link is broken by the high energy of microwave irradiation, allowing the amine to reassociate with another amine terminal (Scheme 10). Contrary to the microwave irradiation approach, which can finish the synthesis in 5 minutes (single-step method) using only ethanol as the solvent, the two-step

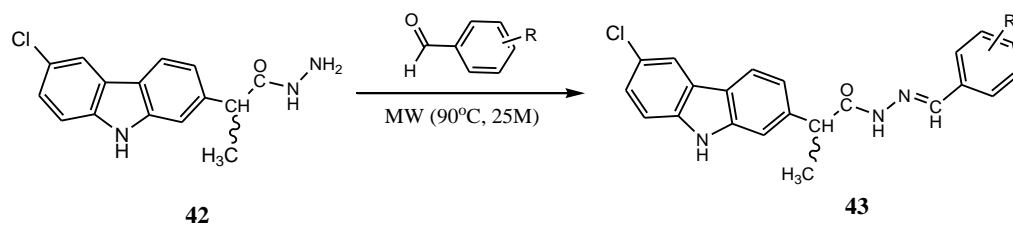
method used to obtain the final product requires up to a total of 27 hours of reaction time. This is despite the high yield.

In a novel (*E*)-3-(4-or 3-Aminophenylimino) quinoxaline 2(3H)-one oxime Schiff base derivative, Chandravadivelu Gopi et al. [51] assess the anti-leptospiral activity against *Leptospira icterohaemorrhagiae*. By performing microwave-assisted condensation processes of (*E*)-3-(4-or 3-aminophenyl imino) quinoxaline-2(3H)-one with aromatic aldehydes, the mentioned compounds were created (Scheme 11). (Compared to the conventional approach, moderate yields (55-81%) in a short period of time).

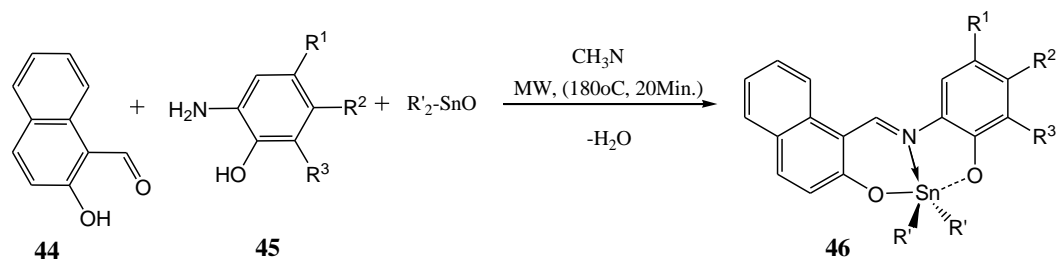


Scheme 13. Preparation of benzimidazoles substituted Schiff base derivatives.

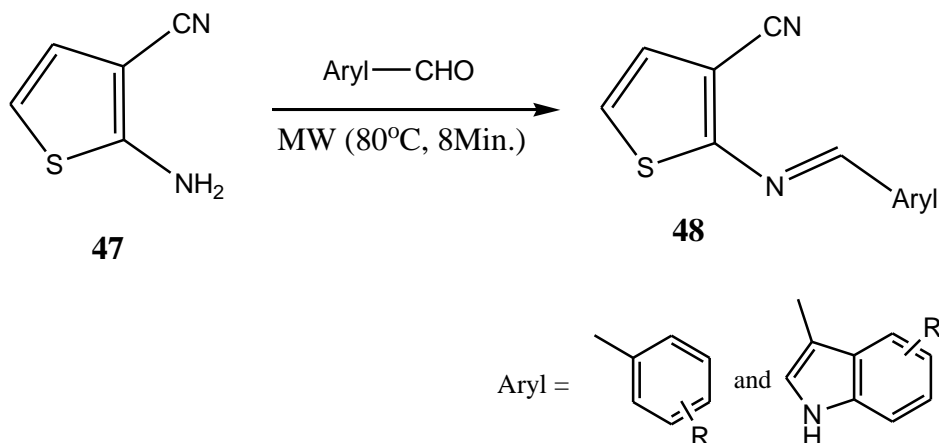
Venkatesan [52] et. al. synthesized a series of Schiff base of 2,2'-(naphthalene-2,7-diylbis(oxy))bis(*N*'-substituted acetohydrazide) derivatives by with the acid catalyst (Scheme 12). The advantages of the method employed contain simple reaction set-up, high product yield (82-90% compared to conventional methods), short reaction times, and use of a small amounts of solvent or no solvents.



Scheme 14. Preparation of carbazole substituted Schiff base derivatives



Scheme 15. Preparation of naphthalene substituted Schiff base derivatives



Scheme 16. Preparation of thiophene substituted Schiff base derivatives

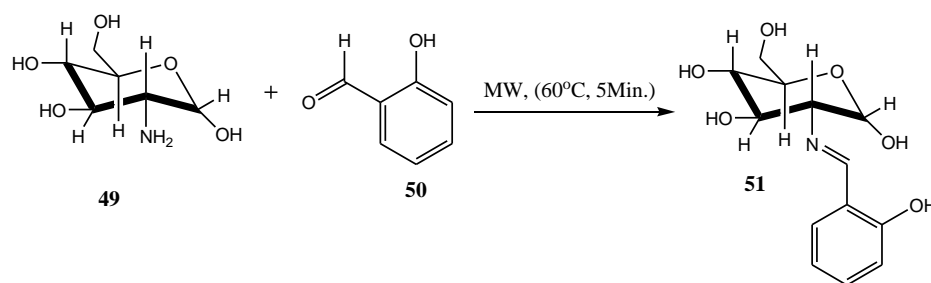
Fatih Yilmaz [53] and co-workers synthesized some 5(6)-nitro benzimidazoles and their salicyl and isatin Schiff bases, which are important pharmacophores in drug design, by using microwave irradiation (Scheme 13). The microwave method gave good yields (Microwave 71-93% Conventional method 51-78%) to compare with the conventional technique.

A.T. Bordei [54] et al., developed a new series of Schiff bases synthesized by the treatment of (2RS)-2-(6-chloro-9H-carbazol-2-yl) propane hydrazide (carprofen hydrazide) with few benzaldehyde derivatives under microwave irradiation (Scheme 14). The microwave synthesis

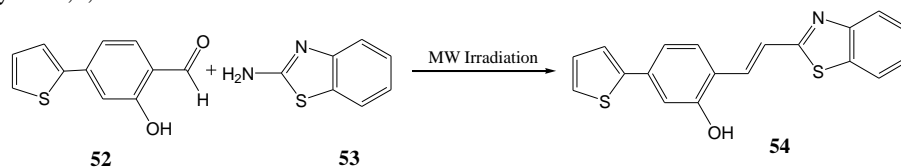
was carried out at various temperatures (40°C, 70°C, and 90°C) and for various amounts of time (15 minutes, 20 minutes, and 25 minutes), with the NMR spectroscopy used to monitor the outcome of the reaction. Thus they have established that a heating temperature of 90° C for 25 minutes produces the optimum output (6-87.5%).

With high yields and minimal economic/environmental impact, A.M. Conton-diaz [55] (Scheme 15) and colleagues created four organotin compounds containing Schiff bases. These compounds were created through a multicomponent microwave-assisted synthesis between 2-hydroxy-1-naphthaldehyde, 2-aminophenol derivatives, and the corresponding di-organotin oxide ( $R_2SnO$ ,  $R=nBu$  or  $Ph$ ). As shown in, the microwave-assisted multicomponent condensation reaction of 2-hydroxy-1-naphthaldehyde and an aminophenol derivative in the presence of diorganic tin oxide produced four penta coordinated tin compounds in high yields of between 75 and 95 percent in a relatively short amount of time (20 to 30 minutes) (Scheme 15). Generally, microwave-assisted multicomponent synthesis has been shown to be an inexpensive, straightforward, quick, and reproducible synthetic approach (1: 95%; 2: 75%; 3: 75%, 4: 91%) with low environmental values.

Seventeen Schiff bases carrying 2-aminothiophene derivatives were created and made utilizing molecular simplification by I. S. Luna [56] et al. The resultant compounds were tested for their dermatophyte-specific in vitro antifungal activity (Scheme 16). Microwave aided synthesis produced compounds with good yields (35-85%) using a green process. In 60% of the procedures (11 of 18 reactions), the microwave method-conducted reactions were more effective (producing better yields) than the conventional methods. Shorter reaction times (10 min), energy savings, and the use of an inorganic base (sodium bicarbonate) as opposed to the conventional organic base are just a few of the benefits of the microwave assisted syntheses of Schiff bases carrying derivatives of 2-aminothiophene that were demonstrated.



Scheme 17. Preparation of (3R,4R,6R) -3- (((E)-2-hydroxybenzylidene) amino)-6-(hydroxymethyl) tetrahydro-2Hpyran-2,4,5-triol derivatives.

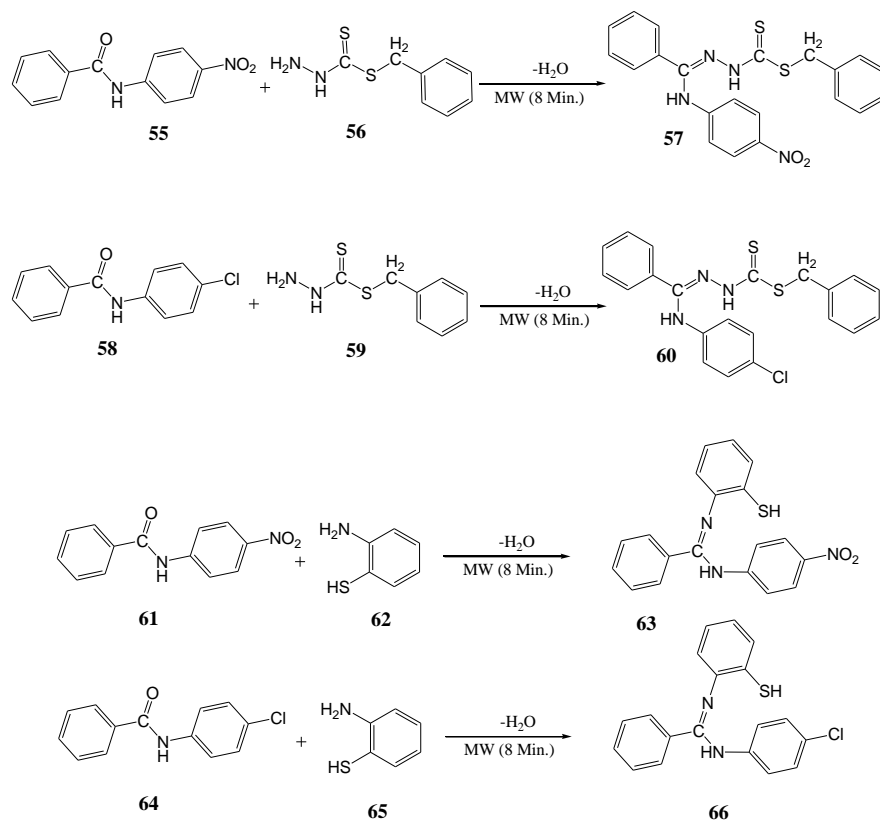


Scheme 18. Preparation of benzo thiazole substituted Schiff base derivatives.

Yousef Hijji [57] and co-workers reported efficient ecofriendly microwave synthesis under the mild condition of a water-soluble sugar derivative (3R, 4R, 6R) -3- (((E)-2-hydroxybenzylidene) amino)-6-(hydroxymethyl) tetrahydro-2Hpyran-2,4,5-triol water-soluble GASB-1 within 5 min at 60 °C under microwave heating conditions (Scheme 17). The intended ligand is synthesized without by-products in a 5-minute process. Furthermore, compared to traditional methods, microwave-assisted approaches have a 90% yield in 5 minutes and require only easy handling.

E. Ermis and K. Durmus [58] successfully synthesized three novel thiophene-benzothiazole derivative azomethine compounds [(2-((Benzo[d]thiazol-2-ylimino)methyl)-4-(thiophen-2-yl)phenol (3a), 2-(((6-Methylbenzo[d]thiazol-2-yl)imino)methyl)-4-(thiophen-2-yl)phenol (3b) and 2-(((6-Methoxybenzo[d]thiazol-2-yl)imino)methyl)-4-(thiophen-2-yl)phenol (3c)] with excellent yields by using conventional heating and microwave assisted synthesis methods (Scheme 18). These findings show that as compared to the traditional method, the reactions of microwave-assisted synthesis were performed more quickly and with a greater yield. It was found that using the microwave irradiation method, reactions that took the conventional method

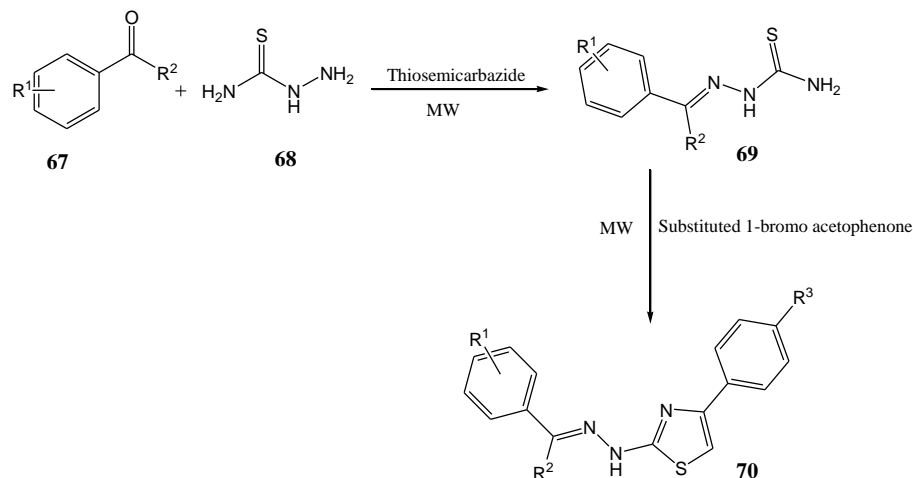
24–36 hours to complete took only 5 hours, and the yields increased from 60.8–83.5% to 74.8–88.8%.



Scheme 19. Preparation of substituted Schiff base derivatives.

Ran Vir Singh [59] et al. reported the Microwave-assisted synthesis of Trigonal bipyramidal and octahedral complexes of tin (IV) have been synthesized by the reaction of dimethyl tin (IV) dichloride with 4-nitrobenzanilide-S-benzyl dithiocarbamate (L<sub>1</sub>H), 4-chlorobenzanilide-S-benzyl dithiocarbamate (L<sub>2</sub>H), 4-nitrobenzanilidebenzothiazoline (L<sub>3</sub>H) and 4-chlorobenzanilidebenzothiazoline (L<sub>4</sub>H) (Scheme 19). Dimethyltin (IV) dichloride was subjected to reactions with its corresponding sodium salts of the ligands (L<sub>1</sub>H, L<sub>2</sub>H, L<sub>3</sub>H, and L<sub>4</sub>H). The reaction time has been dramatically shortened with improved yield in the microwave approach (4–8 Minutes) compared to the conventional method (14–17 Hours), however the cause is not

purely thermal. The significant microwave effect and the substantial reaction rate enhancement are likely to blame for the difference that was observed.



Scheme 20. Preparation of thiazole substituted Schiff base derivatives.

Yu Zhang [60] and associates have created several 2-thiazolylylhydrazone compounds and examined their biological effects as antioxidants and tyrosinase inhibitors (Scheme 20). The reaction mixture was placed in a round-bottomed flask and exposed to 800 W of microwave radiation for 5–10 minutes in a microwave reactor. This provided a yield of up to 97.99%.

## Conclusion

Microwave is an easy way to achieve green/sustainable chemistry, and it is highly advised to employ this method with organic preparations. The identity is impressive and offers useful context for the field of microwave assisted organic synthesis. Microwave-assisted organic synthesis is becoming more and more common throughout the world because of its advantages. All the reactions that have been reported show clear advantages when exposed to microwave radiation, indicating the capacity of this novel, environmentally safe, and user-friendly method to make it easier to build Schiff bases. One of the most fascinating present synthetic methodologies will be affected by the review's discussion of recent developments in this field.

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