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## Solvent free approaches for the synthesis of Lophine derivatives

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### Abstract:

Solvent free synthesis comes with many advantages like cost reductions, waste reduction, ease of operation, sustainability, environmentally benign operations, etc. These benefits have prompted many chemists to develop new protocols for solvent free synthesis of variously interesting chemical compounds. One such class of compounds is 2,4,5-triarylimidazoles famously known as Lophines due to their applications in materials science, chemo- and bio-sensors and pharmacology. This minireview focuses on solvent free synthesis of Lophine derivatives via different protocol including use of inorganic-, organic- and bio-catalysts, solid supported catalysts, microwave mediated heating and grinding.

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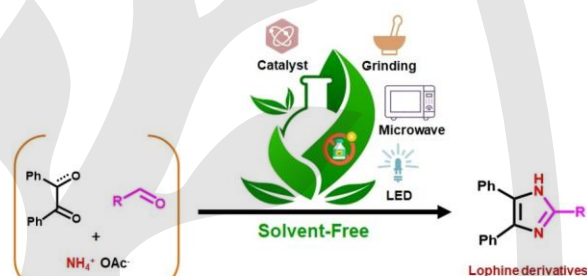
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## SIGNIFICANCE

Lophines also known as 2,4,5-triaryl imidazoles have demonstrated numerous applications as fluorescent, chemiluminascent and biologically interesting scaffold. Thousands of research articles have been published that include synthesis and applications of this fascinating class of heterocyclic compounds. Few of these reports have focused on solvent free approaches towards synthesis of Lophines including catalysis, microwave radiation, grinding and visible light mediated synthesis. This review will serve as a first hand information about these sustainable and green approaches for synthesis of Lophines.



## Keywords

Lophine, Triaryl imidazoles, Imidazoles, Solvent free, Neat, Sustainable Chemistry, Green Chemistry, Multicomponent reactions

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## ABSTRACT

Solvent free synthesis comes with many advantages like cost reductions, waste reduction, ease of operation, sustainability, environmentally benign operations, etc. These benefits have prompted many chemists to develop new protocols for solvent free synthesis of variously interesting chemical compounds. One such class of compounds is 2,4,5-triarylimidazoles famously known as Lophines due to their applications in materials science, chemo- and bio-sensors and pharmacology. This minireview focuses on solvent free synthesis of Lophine derivatives via different protocol including use of inorganic-, organic- and bio-catalysts, solid supported catalysts, microwave mediated heating and grinding.

## Introduction

Green chemistry also called sustainable or environmentally benign chemistry is the recent and continuously developing approach for designing nature friendly synthetic procedures. The well-known twelve principles of green chemistry were introduced by Dr. Paul Anastas and Dr. John Warner in 1998.<sup>1</sup> Since last three decades focus is shifting towards development of approaches that follow the principles of green chemistry.<sup>2</sup>

Organic solvents are extensively used in chemical science field including in the academic and industrial research for mass production of countless products.<sup>3</sup> This results in the increasing rate of health and safety issues as well as having environmental and economic impacts.<sup>4</sup> Eliminating or significantly reducing the use of solvents can provide cost efficiency in synthesis likewise handling skills and managing special storage conditions can be minimized as well. The syntheses carried out without the use of solvents are known as solvent-free synthesis also known as neat synthesis.<sup>5</sup> Solvent-free synthesis adheres to more than one principle of the green chemistry and adopting this in a sustainable manner is the duty of scientists to protect environment and society from destructive consequences.

2, 4, 5-triaryl-1*H*-imidazole (TAI) also called as Lophine was firstly synthesized before more than a century and have achieved remarkable relevance as a result of their extensive use in synthetic chemistry.<sup>6</sup> Lophine derivatives exhibit a wide range of characteristics and demonstrate applications in medicine, luminous materials, etc.<sup>7</sup> So many interesting studies on TAI and its derivatives have been already carried out and applications were explored, which include dye sensitized solar cell<sup>8</sup>, fluorescent probes<sup>9</sup>, photo responsive materials<sup>10</sup>, chemiluminescent molecules<sup>11</sup>, temperature probes<sup>12</sup>, colorimetric sensors<sup>13</sup>, nano wires<sup>14</sup>, etc. TAIs have potential to address the shortcomings associated with the other relevant molecules, and thus might be employed as new building blocks to generate effective functional molecules.

Lophine derivatives can be synthesized using multicomponent reaction of Benzil, Amine source and various substituted benzaldehyde.<sup>15</sup> There are several methods reported for the synthesis of Lophine derivatives using solvent-free conditions, under microwave irradiation, grinding, catalysis, etc. These methods are environment friendly as well as less toxic than the methods which generally use a solvent.

## Catalysis

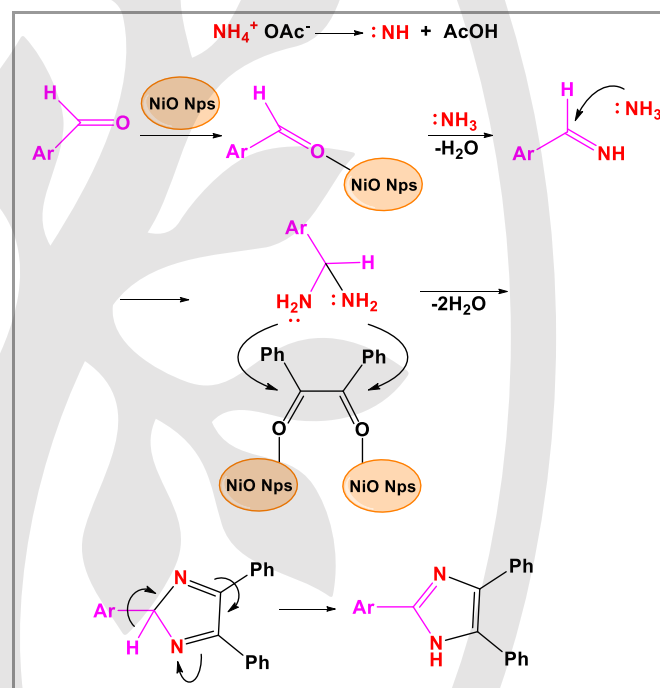
Catalysis provides the enhancement of efficiency, selectivity and sustainability of chemical reactions while it minimizes the energy and time consumption. There are various types of catalysts developed according to the requirements of the organic reactions. The versatility in the use of catalysts are classified in the Table 1.

### (A) Inorganic catalysts

Z. Jaber and M. Barekat (2010) synthesized Lophine derivatives by reaction of benzil, substituted benzaldehyde and ammonium acetate using 33 mol% of Sodium dihydrogen phosphate ( $\text{NaH}_2\text{PO}_4$ ) under solvent free conditions and got 98 to 99 % yield in 25 to 45 minutes at 120 °C (Table 1, entry 1).<sup>16</sup> Authors applied the same protocol for the synthesis 1,2,4,5-tetrasubstituted imidazoles as well and got 80-92 % yields.

M. Esmailpour and coworkers (2016) used Dendrimer-PWA<sup>n</sup> (Dendrimer- $\text{H}_3\text{PMO}_{12}\text{O}_4$  nano particles) nanocatalyst for an efficient synthesis of Lophine derivatives (Table 1, entry 2).<sup>17</sup> Authors developed two reaction conditions, one having conventional heating under solvent free system while in the other they used ultrasound and ethanol solvent. In terms of yields a better output with heating under solvent-free condition was observed. The protocol was successfully applied in the synthesis of 1,2,4,5-tetrasubstituted imidazoles as well.

B. M. Bhanage (2021) prepared NiO nano-particles using different cyclodextrins as capping agents under ultrasound conditions. The prepared nano catalyst was then used in the synthesis of various Lophine derivatives under solvent-free conditions. In the one pot reaction,<sup>18</sup> benzil (1 mmol), aryl aldehydes (1 mmol), ammonium acetate (2.5 mmol) and the nano catalyst (10 mg) were heated together at 120 °C neat to obtain the desired Lophine derivatives in good to excellent yields (Table 1, entry 3).



**Scheme 1** Mechanism of NiO nano-particle catalyzed synthesis of Lophine derivatives.

The proposed mechanism depicted NiO Nano particles (Nps) coordination increases the electrophilicity of aryl benzaldehyde and diketone. This facilitates the coupling, condensation, and insertion of two ammonia molecules to produce the diamine intermediate. Further it attacks on electrophilic diketone and rearranges to give desired Lophine derivative (Scheme 1).

In comparison of cost, simplicity and yields the use of sodium dihydrogen phosphate as an inorganic catalyst seems better than the other two inorganic catalysts discussed above. Reduction in the amount of inorganic catalyst used is indeed desirable in future.

### (B) Organic catalysts

M. Yar and group (2015) used *N*-acetyl glycine (NAG) as an organic catalyst for the synthesis of Lophine derivatives without using any solvent.<sup>19</sup> Reaction of benzil with various aromatic aldehydes and ammonium acetate in presence of NAG catalyst at 150 °C in 2 h furnished the desired 2,4,5-triarylimidazoles in good to excellent yields (Table 1, entry 4). All final compounds were subjected to *in-vitro*  $\alpha$ -glucosidase inhibitory activity which revealed that compounds bearing hydroxyl group on the C2-phenyl possessed significantly higher activity compared to those which did not have a hydroxyl group.

The group of M. Khan, S. Mutahir, I. Khan (2020) investigated the catalytic performance of several organic molecules having a carboxylic acid functionality in the synthesis of Lophine derivative and found that Pyridine-2-carboxylic acid has a good catalytic potential.<sup>20</sup> Under solvent free conditions at 120 °C temperature and 50 mol% of the catalyst provided the triarylimidazoles in 2-3 hours with good to excellent yields (Table 1, entry 5).

An efficient Mandelic acid (20 mol%) catalyzed solvent free synthesis of Lophine derivatives was developed by Ghogare, Ramesh S. (2022) (Table 1, entry 6).<sup>21</sup> Interestingly the author observed diminished yields when solvent was used compared to solvent-free conditions.

Clearly the Mandelic acid catalyst is better compared to the *N*-acetyl glycine and pyridine-2-carboxylic acid catalysts as the previous is effective at 20 mol% and reaction time is shorter.

### (C) Biocatalysts

A. Maleki and R. Paydar (2015) utilized graphene oxide–chitosan bionanocomposite as a nano catalyst for synthesis of Lophine derivatives.<sup>22</sup> The reactions were carried out under solvent-free condition at 120 °C for 10 to 35 minutes and achieved 80 to 96% yields according to the substitution on benzaldehydes (Table 1, entry 7). Authors demonstrated that benzil and benzoin both could be employed in this reaction and both provided good to excellent yields however a bit longer reaction time was required in case of benzoin compared to benzil. The graphene oxide–chitosan bionanocomposite was successfully reused up to six times with little loss of yield. In the proposed mechanism the aldehyde is activated by the catalyst to allow formation of diamine intermediate. This diamine intermediate further reacts with the catalyst activated benzil to form the cyclized intermediate which upon dehydration and [1,5] hydrogen shift forms the substituted Lophine (Scheme 2).

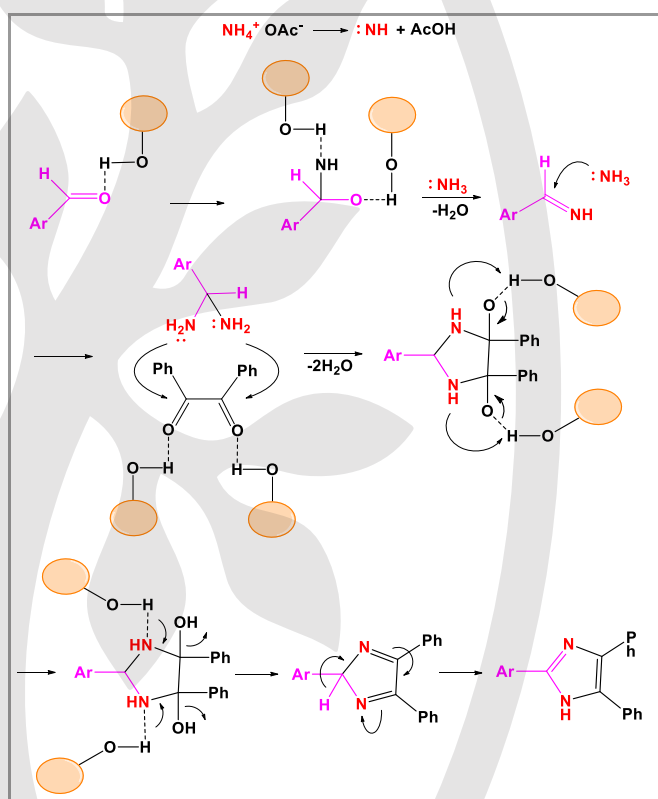
M. Bordoloi and coworkers (2017) developed a novel route of citrus fruit extract promoted efficient, inexpensive and solvent-free synthesis of Lophine derivatives.<sup>23</sup> The fresh citrus fruit Pomelo karp part was extracted with water followed by lyophilization yielded the solid WEP (Extract of Pomelo). Benzil (1 eq.), various aldehydes (1 eq.) and ammonium acetate (2 eq.) in presence of 100 mg of WEP under solvent free and ambient conditions furnished the triaryl imidazoles in excellent yields of 88-98% (Table 1, entry 8). The biocatalyst was successfully employed in the Biginelli reaction as well to demonstrate the versatility of the protocol. Authors also successfully used other citrus fruits like Lemon and star fruit extracts in the developed protocol for synthesis of triaryl imidazoles.

The reaction is at ambient conditions when Pomelo extract is used as catalyst compared to 120 °C in case of graphene oxide–chitosan bionanocomposite. The previous is cost effective for being cheaper

and requires ambient conditions and thus is a better bio-catalyst. In future, exploration of more natural citrus sources and expansion of substrate scope is desirable.

### (D) Organometallic catalysts

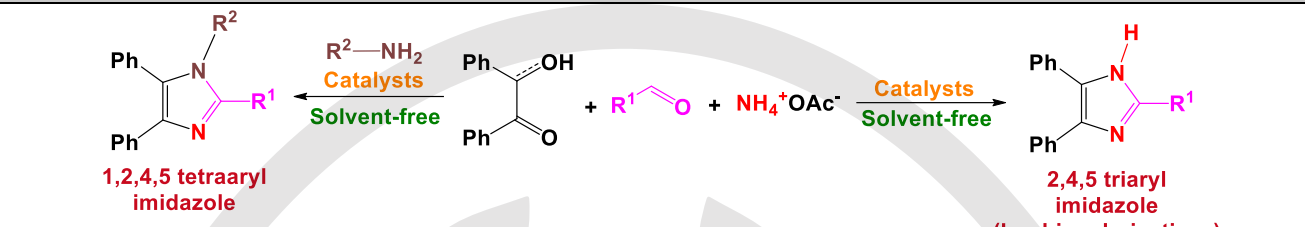
Group of K. Rangappa and S. Shashikanth (2015) prepared ZrO<sub>2</sub> supported -  $\beta$  -cyclodextrin (ZrO<sub>2</sub>- $\beta$ -CD) nano-catalyst by coprecipitation method and used in the solvent-free synthesis of various Lophine derivatives.<sup>24</sup> Benzil (1 eq.), aromatic aldehyde (1 eq.) and ammonium acetate (2 eq.) were reacted in presence of ZrO<sub>2</sub>- $\beta$ -CD heterogenous catalyst (40 mol%) at 100 °C under neat conditions for 20-35 min reaction time (Table 1, entry 9). Interestingly authors observed lower yields in reactions where solvent was used. The optimized protocol was successfully applied for the synthesis of benzimidazoles as well albeit with doubled reaction time.



Scheme 2 Mechanism of synthesis using graphene oxide–chitosan bionanocomposite as a biocatalyst

L. Z. Fekri and coworkers (2018) synthesized a magnetically separable heterogeneous catalyst, NiFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@amino glucose nanoparticles for the solvent free synthesis of Lophine derivatives (Table 1, entry 10).<sup>25</sup> Benzil or benzoin (1 eq.) reacted with substituted benzaldehyde (1 eq.) and ammonium acetate (1 eq.) in presence of 5 mol% of the heterogeneous catalyst at room temperature without solvent. The catalyst efficiency is visible in terms of short reaction time (10-18 min) and high yield (90-99%) of the desired triaryl imidazoles. The magnetically separable heterogeneous catalyst could be reused up to five times without loss of any yield. Authors also applied the optimized protocol for the synthesis of benzimidazoles and benzoxazoles.

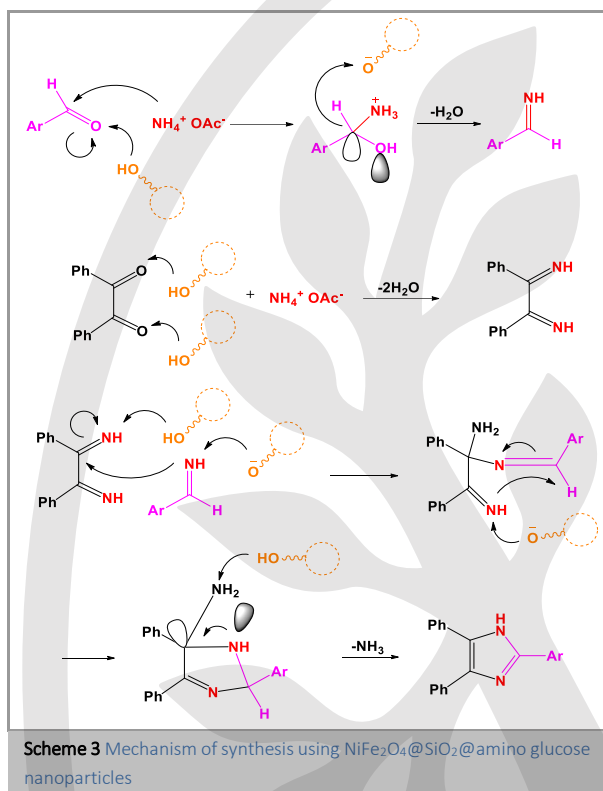
Table 1 Solvent-free synthesis of Lophine derivatives using various catalysts.



| Entry  | Catalysts <sup>a</sup>  | Quantity (mol%) or (mg) or (equiv.) | Reaction Conditions                     |                          | Examples   | Yield (%)   | Reference |
|--|---|-------------------------------------|---|--------------------------|--|---|-----------|
|  |   |                                     | Temperature (°C)/ Room temperature (RT) | Time (Min.)              |  |   |           |
| <b>[A] Inorganic catalysts</b>                     |   |                                     |   |                          |  |   |           |
| 1  | Sodium dihydrogen phosphate (NaH <sub>2</sub> PO <sub>4</sub> )   | 33 mol%                             | 120                                     | 25-45                    | 3, 11*   | 98-99, 80-92*   | 16        |
| 2  | Dendrimer-PWA <sup>1</sup> nanocatalyst   | 35 mol%                             | 90                                      | 10-100                   | 15, 30*  | 78-96, 82-96*   | 17        |
| 3  | NiO nano-particles  | 10 mg                               | 120                                     | 60                       | 8  | 81-98   | 18        |
| <b>[B] Organic catalysts</b>                       |   |                                     |   |                          |  |   |           |
| 4  | N-acetyl glycine (NAG)  | 1 equiv.                            | 150                                     | 120                      | 8  | 62-85   | 19        |
| 5  | Pyridine-2-carboxylic acid  | 50 mol%                             | 120                                     | 120-180                  | 13   | 74-96   | 20        |
| 6  | Mandelic acid   | 20 mol%                             | 120                                     | 30                       | 10   | 80-91   | 21        |
| <b>[C] Biocatalysts</b>                            |   |                                     |   |                          |  |   |           |
| 7  | Graphene oxide–chitosan bio nanocomposite   | 12 mol%                             | 120                                     | 8-35, 18-40 <sup>#</sup> | 15   | 80-96   | 22        |
| 8  | Extract of Pomelo   | 50 mol%                             | RT                                      | 240-360                  | 6  | 88-98   | 23        |
| <b>[D] Organometallic catalysts</b>                |   |                                     |   |                          |  |   |           |
| 9  | ZrO <sub>2</sub> supported - β -cyclodextrin (ZrO <sub>2</sub> -β-CD) nano-catalyst                                     | 40 mol%                             | 100                                     | 20-35                    | 14   | 80-98   | 24        |
| 10   | NiFe <sub>2</sub> O <sub>4</sub> @SiO <sub>2</sub> @amino glucose nanoparticles   | 5 mol%                              | RT                                      | 10-18                    | 13   | 90-99   | 25        |
| 11   | MIL-101 (Chromium(III) benzene-1,4-dicarboxylate)   | 5 mol%                              | 120                                     | 7-25                     | 14   | 85-95   | 26        |
| <b>[E] Lewis acid catalysts</b>                    |   |                                     |   |                          |  |   |           |
| 12   | (Ce(SO <sub>4</sub> ) <sub>2</sub> ·4H <sub>2</sub> O)  | 3 mol%                              | 120                                     | 10-20                    | 14, 14*  | 78-97, 85-93*   | 27        |
| <b>[F] Solid support catalysts</b>                 |   |                                     |   |                          |  |   |           |
| <b>(a) Solid supported Brønsted acid catalysts</b> |   |                                     |   |                          |  |   |           |
| 13   | Silica bonded S-sulfonic acid (SBSSA)   | 0.068 mol%                          | 130                                     | 30                       | 23   | 84-95   | 28        |
| 14   | MCM-41-SO <sub>3</sub> H  | 40 mg                               | 100                                     | 9-15                     | 9  | 70-95   | 29        |
| 15   | MCM-41-nPr-NHSO <sub>3</sub> H  | 100 mg                              | 130                                     | 20-150                   | 13   | 53-98   | 32        |
| 16   | (Carboxy-3-oxopropylamino)-3-propylsilylcellulose (COPAPSC)   | 200 mg                              | 110                                     | 240-360                  | 11, 12*  | 75-88, 75-87*   | 33        |
| 17   | Silica-bonded Propyl-N-sulfamic acid nanocatalyst (NHSO <sub>3</sub> H-KIT-5)   | 50 mg                               | 120                                     | 10-25                    | 12   | 83-92   | 36        |
| <b>(b) Solid supported Lewis acid catalysts</b>    |   |                                     |   |                          |  |   |           |
| 18   | Silica supported tin oxide (SiO <sub>2</sub> :SnO <sub>2</sub> )  | 50 mol%                             | 80                                      | 15-30                    | 8, 8*  | 90-94, 92-94*   | 30        |
| 19   | Ferric(III) nitrate supported on kieselguhr (Fe(NO <sub>3</sub> ) <sub>3</sub> -Kie)                                    | 1.6 mol%                            | 120                                     | 60-90                    | 10   | 80-91   | 31        |
| 20   | KSF supported 10-molybdo-2-vanadophosphoric acid (H <sub>5</sub> PMO <sub>10</sub> V <sub>2</sub> O <sub>40</sub> /KSF) | 100 mg                              | 110                                     | 25-50                    | 13   | 83-96   | 34        |
| 21   | NiFe <sub>2</sub> O <sub>4</sub> @SiO <sub>2</sub> -H <sub>3</sub> PMO <sub>12</sub> O <sub>40</sub>                    | 20 mg                               | 120                                     | 10-30                    | 9, 9 <sup>#</sup> , 10 <sup>#</sup> , 10 <sup>*#</sup> | 75-96, 86-94 <sup>#</sup> , 78-90*, 75-90 <sup>*#</sup> | 35        |
| 22   | Zeolite ZSM-11  | 50 mg                               | 110                                     | 30-40                    | 10   | 78-90   | 37        |
| 23   | Nanoclinoptilolite with titanium dioxide (NCP@SiO <sub>3</sub> PrNHPRSiO <sub>3</sub> TiO <sub>2</sub> )                | 7 mg                                | 60                                      | 4-14                     | 11   | 93-98   | 38        |

|     |   |         |     |       |    |                           |    |
|-----|---|---------|-----|-------|----|---------------------------|----|
| 24  | Silica supported lanthanum trifluoroacetate and trichloroacetate                                | 40 mg   | 70  | 40    | 12 | 90-96                     | 39 |
| [G] | <b>Ionic liquid catalysts</b>   |         |     |       |    |                           |    |
| 25  | (4-sulfobutyl) tris(4-sulfophenyl) phosphonium hydrogen sulfate (4-SB)T(4-SPh)PHSO <sub>4</sub> | 15 mol% | 120 | 10-15 | 20 | 89-98, 87-96 <sup>#</sup> | 40 |

<sup>a</sup> All the reactions are carried out under solvent-free conditions; <sup>\*</sup>Examples and yields of 1,2,4,5-tetrasubstituted imidazoles; <sup>#</sup>Examples and yields for the synthesis using Benzoin.



The proposed mechanism involves activation of aldehyde by the catalyst followed by attack of ammonia from the ammonium acetate to form the corresponding imine. Similarly, benzoin via activation forms bisimine intermediate. Catalyst activated imine attacks the bisimine carbon followed by subsequent cyclization and loss of ammonia forms the desired triaryl imidazole (Scheme 3).

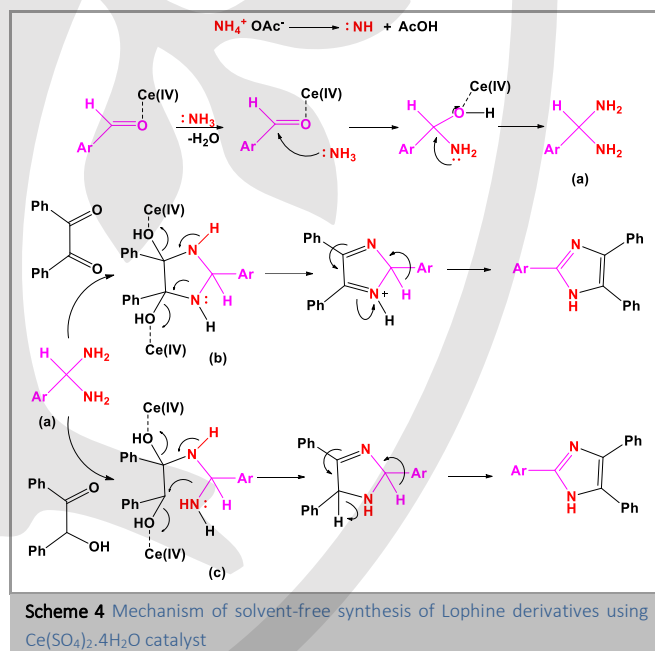
Team of Z. Tehrani and F. Manteghi (2021) used chromium-containing metal-organic framework (MOF), MIL-101 (Chromium(III) benzene-1,4-dicarboxylate) for the synthesis of Lophine derivatives under solvent-free conditions.<sup>26</sup> Benzil or benzoin (1 mmol), substituted benzaldehyde (1 mmol) and ammonium acetate (2.5 mmol) in presence of 5 mg of MIL-101 under neat conditions at 120 °C temperature produced the triaryl imidazoles in excellent yields (Table 1, entry 11). It is noteworthy that benzil required less time (7-20 min) compared to benzoin (14-25 min) while yields were slightly better with the previous compared to the latter in all cases. The reusability was demonstrated by reusing the catalyst for up to six times with 95% yield in the first run compared to 80% in the sixth.

Among all three organometallic catalysts the NiFe<sub>2</sub>O<sub>4</sub>@SiO<sub>2</sub>@amino glucose nanoparticles outperform the other two as only 5 mol% of this catalyst under ambient reaction conditions give excellent yields. More organometallic catalysts

should be tested in future to find out new cost effective organometallic catalyst systems.

#### (E) Lewis acid catalysts

Y. Li and his team (2016) used the Lewis acid catalyst (Ce(SO<sub>4</sub>)<sub>2</sub>·4H<sub>2</sub>O) for the efficient synthesis of Lophine derivatives under solvent-free condition.<sup>27</sup> Benzil or benzoin (1 eq.) reacted with substituted benzaldehyde (1 eq.) and ammonium acetate (3 eq.) in presence of 3 mol% of the Ce(SO<sub>4</sub>)<sub>2</sub>·4H<sub>2</sub>O catalyst at 120 °C without solvent to furnish the 2,4,5-triaryl imidazoles in excellent yields within 10-25 min (Table 1, entry 12). The synthesis of 1,2,4,5-tetrasubstituted imidazoles (14 examples, 85-93% yields) was carried out as well using the optimized conditions. The Lewis acid (Ce<sup>IV</sup>) enhanced the formation of diamine intermediate (a) and activated the Benzil or Benzoin molecule by increasing the electrophilicity of the carbonyl group of the aryl aldehyde and diketone respectively. Intermediate (a) condenses with activated Benzil or Benzoin molecule and form intermediate (b) or (c). Intermediate (b) gets rearranged to form the desired Lophine derivatives via a [1,5] hydrogen shift; while intermediate (c) oxidized in presence of air and form the desired Lophine derivatives (Scheme 4). The high efficiency of this Lewis acid suggests that there is lot of scope for testing other Lewis acid catalysts to further improve the cost efficiency and simplicity of this reaction.



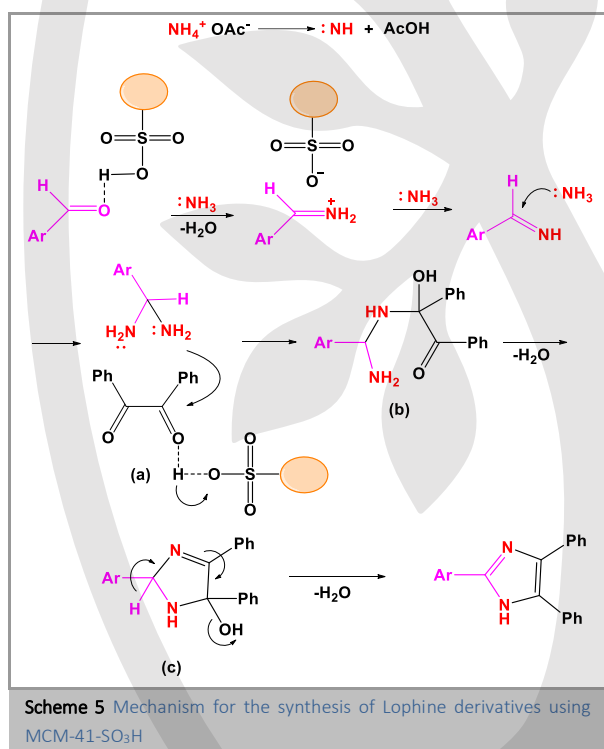
#### (F) Solid support catalysts

Solid supported catalysts are well known due to the ease of recovery after completion of reactions and thus adding value in terms of recoverability and reusability. According to its catalytic activity, it can be further classified in two parts which are as follows.

### Solid supported Brønsted acid catalysts

N. Khodabakhsh and his group (2010) prepared silica bonded S-sulfonic acid (SBSSA) as a solid support catalyst for the synthesis of various Lophine derivatives and achieved 84-95% yield at 130 °C temperature and solvent free conditions (Table 1, entry 13).<sup>28</sup>

G. Mahadavinia and coworkers (2012) prepared MCM-41-SO<sub>3</sub>H (Mobil Composition of Matter No. 41 – SO<sub>3</sub>H); which was used as a solid supported nano catalyst in the synthesis of Lophine derivatives (Table 1, entry 14).<sup>29</sup> Solvent free reaction of benzil, aldehyde and ammonium acetate in presence of MCM-41-SO<sub>3</sub>H at 100 °C temperature in few minutes gives good to excellent yields of triarylimidazoles. The sulphonic acid part of reported nanocatalyst activates the carbonyl group of substituted aromatic aldehydes and Benzil. Attack of ammonia on imine intermediate gives diamine intermediate (a); which attacks benzil followed by cyclocondensation forms imidazol-5-ol intermediate (c). Finally, elimination of water molecule results in desired Lophine derivatives (Scheme 5). The recyclability and reusability of the solid supported nano catalyst was proved by reusing the catalyst for up to four reactions with yields of 92, 92, 85 and 83% respectively.



A. Choghamarani and group (2015) synthesized MCM-41-nPr-NHSO<sub>3</sub>H and used as an efficient heterogeneous catalyst for the one-pot synthesis of Lophine derivatives under solvent free conditions (Table 1, entry 17).<sup>32</sup> Benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (2.5 mmol) under the influence of MCM-41-nPr-NHSO<sub>3</sub>H (0.1 g) was heated neat in oil bath at 130 °C temperature to obtain the desired Lophine derivatives in average to excellent yields. The catalyst could be recycled by simple filtration after completion of the reaction and reused for up to five times without any appreciable loss of yield.

M. Salimi and coworkers (2015) prepared (Carboxy-3-oxopropylamino)-3-propylsilylcellulose (COPAPSC) as a biodegradable solid supported organic catalyst for the solvent-free synthesis of Lophine derivatives (Table 1, entry 18).<sup>33</sup> The consecutive surface functionalization of cellulose involved reaction of cellulose with 3-aminopropyltriethoxysilane followed by the condensation of the surface –NH<sub>2</sub> groups with succinic anhydride. This allowed synthesis of –COOH group functionalized cellulose (COPAPSC). 0.2 g of this catalyst (equal to 0.05 mmol H<sup>+</sup>) was enough to drive the reaction to completion within 4-6 hrs at 110 °C temperature. Reusability of the solid supported catalyst was also demonstrated for up to five cycles with little loss of yield. The optimized protocol was successfully applied towards the synthesis of 1,2,4,5-tetrasubstituted imidazoles as well.

M. Heravi and coworkers (2016) developed silica-bonded Propyl-N-sulfamic acid nanocatalyst (NHSO<sub>3</sub>H-KIT-5) and performed catalytic synthesis of various Lophine derivatives.<sup>36</sup> In this one pot reaction of benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (2 mmol) were reacted together with 0.05 g of the nano catalyst NHSO<sub>3</sub>H-KIT-5 at 120 °C temperature under neat conditions to furnish the desired Lophine derivatives (Table 1, entry 21). The catalyst could be easily recycled and reused for up to 5 cycles without significant loss of catalytic activity.

The MCM-41-SO<sub>3</sub>H solid supported Brønsted acid catalyst requires short reaction time of 9-15 min only and at 100 °C temperature furnished good to excellent yields. Thus, it trumps the other solid supported Brønsted acid catalysts as per our understanding. In future scope, recyclability and reusability of other solid supported Brønsted acid catalyst should be tested and reaction temperature could be lowered to further improve monetary benefits.

### Solid supported Lewis acid catalysts

A. Borhade and his team (2012) developed silica supported tin oxide (SiO<sub>2</sub>:SnO<sub>2</sub>) as a nanocatalyst and successfully used for the synthesis of Lophine derivatives.<sup>30</sup> Under the optimized conditions benzil (1 mmol), aromatic aldehyde (1.2 mmol) and ammonium acetate (1 mmol) was stirred at 80 °C for stipulated time in presence of 50 mol% of the catalyst to produce the triaryl imidazoles in good to excellent yields (Table 1, entry 15). Authors also applied the developed protocol for the synthesis of 1,2,4,5-tetrasubstituted imidazoles.

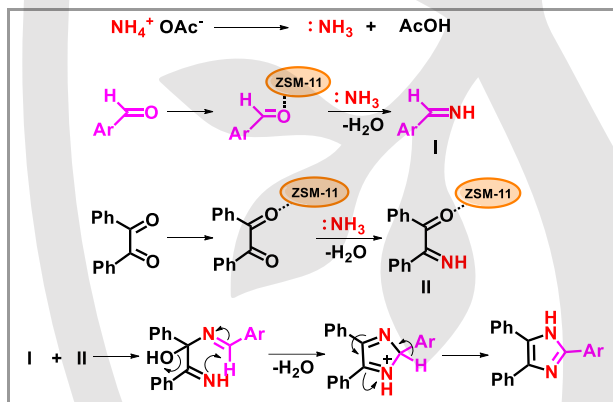
Solvent-free procedure for the synthesis of Lophine derivatives using a catalytic amount of ferric(III) nitrate supported on kieselguhr (Fe(NO<sub>3</sub>)<sub>3</sub>-Kie) as a Lewis acid catalyst was developed by X. Xu and Y. Li (2014).<sup>31</sup> Benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (2 mmol) were reacted in presence of the Fe(NO<sub>3</sub>)<sub>3</sub>-Kie (1.6 mol%) at 120 °C neat until completion. The desired 2,4,5-triarylimidazoles were obtained in good to excellent yields (Table 1, entry 16). Authors observed longer reaction times and diminished yields when a solvent was used instead of neat conditions.

S. Shankarwar and L. Chavan (2015) synthesized variety of Lophine derivatives under thermal solvent-free conditions in the presence of a KSF (Montmorillonite KSF clay) supported 10-molybdo-2-vanadophosphoric acid catalyst.<sup>34</sup> Reaction of Benzil (1 mmol), aromatic aldehyde (1 mmol) and ammonium acetate (2 mmol) in presence of the 20% H<sub>5</sub>PMO<sub>10</sub>V<sub>2</sub>O<sub>40</sub>/KSF (0.1 g) under solvent free conditions at 110 °C temperature furnished excellent yields of the 2,4,5-triarylimidazoles (Table 1, entry 19). The catalyst could be

recycled and reused for up to three reactions with little loss of yield.

B. Maleki and group (2015) developed  $\text{NiFe}_2\text{O}_4@\text{SiO}_2\text{-H}_3\text{PMo}_{12}\text{O}_{40}$  as a magnetically recoverable nano catalyst which was further used in the synthesis of Lophine derivatives under solvent-free conditions (Table 1, entry 20).<sup>35</sup> Here both benzil and benzoin were employed as reactant and yields from both were compared under the optimized reaction conditions of 120 °C temperature and 10-30 min reaction time. After completion of the reaction catalyst was removed using external magnetic field while addition of 1 mL of ethanol followed by pouring the reaction mixture in to crushed ice afforded the crude which was further purified by recrystallization. The protocol was also applied in the synthesis of 1,2,4,5-tetrasubstituted imidazoles.

S. Gaikwad and his group (2021) developed ZSM-11 (Zeolite Socony Mobil 11) catalyst for the efficient synthesis of Lophine derivatives under solvent-free condition (Table 1, entry 22).<sup>37</sup> Suspension of benzaldehyde (1 mmol), benzil (1 mmol) and ammonium acetate (3 mmol) were heated in oil bath at 110 °C in presence of 0.05 g of the heterogenous catalyst ZSM-11 until reaction completion. Efficient recyclability and reusability were also demonstrated for up to five reaction cycles. The proposed mechanism involves activation of the aldehyde as well as benzil by catalyst coordination with carbonyl oxygen. Attack of in situ generated ammonia on aldehyde and benzil could generate the imines I and II. Nucleophilic attack of the intermediate I on the II followed by cyclization could form the desired Lophines (Scheme 6).



**Scheme 6** Mechanism of the synthesis of Lophine derivatives using Zeolite ZSM-11 as a solid supported catalyst

K. Rabiei and group (2023) synthesized functionalized nanoclinoptilolite with titanium dioxide ( $\text{NCP}@\text{SiO}_3\text{PrNHPRSIO}_3\text{TiO}_2$ ), which was used as nano catalyst for the solvent-free synthesis of Lophine derivatives and achieved more than 90% yields (Table 1, entry 23).<sup>38</sup> It is noteworthy that full conversion is observed within few minutes under solvent-free conditions.

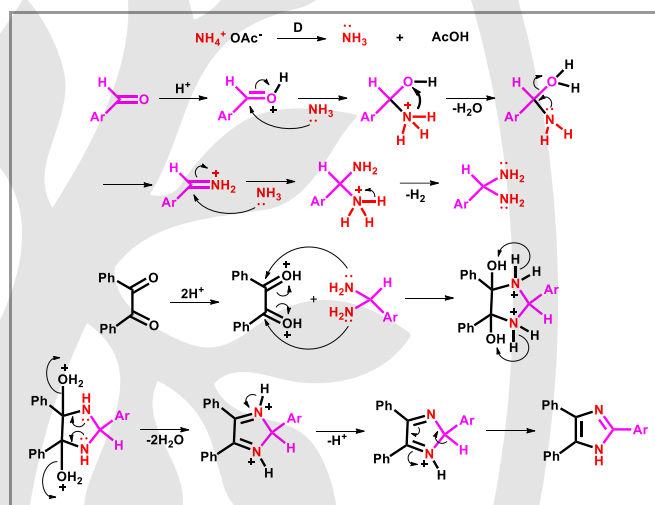
M. K. Lande and group (2023) prepared silica supported lanthanum trifluoroacetate and trichloroacetate green Lewis acid catalysts and utilized them in the solvent-free synthesis of various Lophine derivatives (Table 1, entry 24).<sup>39</sup> Both Lanthanum trifluoroacetate and trichloroacetate catalysts were successfully employed separately in the reaction of benzil (1 mmol), substituted benzaldehyde (1 mmol) and ammonium acetate (3 mmol) under neat conditions at 70 °C temperature in reaction times of 14-16 min

and 17-20 min respectively. Authors also demonstrated the reusability of the catalysts for up to five times with little loss of yields.

Considering cost and amount of catalyst the Ferric(III) nitrate supported on kieselguhr ( $\text{Fe}(\text{NO}_3)_3\text{-Kie}$ ) Lewis acid catalyst is better compared to other catalysts of the same category as only 1.6 mol% of this catalyst gives the desired Lophines in good to excellent yields. Lowering of reaction temperature and increased substrate scope is desirable in future scope.

### (G) Ionic liquid catalyst

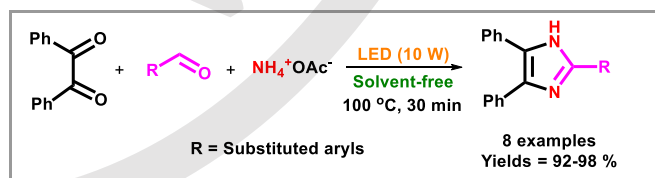
R. Bavantula (2013) used Brønsted acidic ionic liquid, (4-sulfobutyl) tris(4-sulfophenyl) phosphonium hydrogen sulfate (4-SB)T(4-SPh)PHSO<sub>4</sub> as catalyst for the solvent free synthesis of the series of Lophine derivatives (Table 1, entry 25).<sup>40</sup> In the optimized reaction conditions, the benzil or benzoin (1 mmol), aryl aldehydes (1 mmol), ammonium acetate (3 mmol) and the catalyst (15 mol%) were heated together at 120 °C neat to obtain the desired 2,4,5-trisubstituted imidazoles. The reaction times were slightly lower and yields were slightly higher for benzil compared to benzoin.



**Scheme 7** Mechanism of Brønsted acidic ionic liquid (4-SB)T(4-SPh)PHSO<sub>4</sub> catalyzed synthesis of Lophine derivatives using solvent-free approach

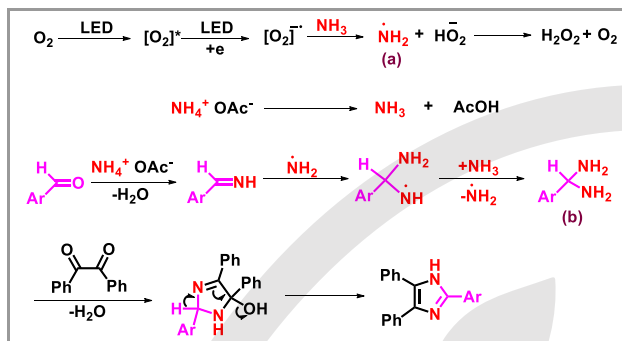
Authors proposed the mechanism for the role of given Brønsted acidic ionic liquid catalyst in which protonation of aldehyde was protonated allowed ammonia attack to form the diamine intermediate (Scheme 7). This diamine intermediate attacked the activated benzil followed by dehydration and rearrangement gives 2,4,5-trisubstituted imidazoles. More ionic liquid catalysts should be tested in future to further get insight in to the benefits of this catalytic system.

### Visible light mediated synthesis



**Scheme 8** LED mediated synthesis of Lophine derivatives under neat conditions





Scheme 9 Mechanism of LED mediated synthesis of Lophine derivatives

S. Banerjee (2020) reported a visible light and heat promoted synthetic method for series of Lophine derivatives without any catalyst and solvent.<sup>41</sup> The reaction was carried out under white LED (10 W) at 100 °C for 30 min and about 92%-98% yields were achieved (Scheme 8). Control experiments revealed that in the absence of light or heat no desired product was formed while in presence of radical quencher TEMPO or under argon atmosphere diminished yield was observed. This observation indicated light mediated formation of super oxide from oxygen and amine radical from ammonia (Scheme 9). The amine centered radical could attack the imine to form diamine species b followed by cyclocondensation with benzil to give the Lophine derivatives. Here there is lot of scope for testing different sensitizers as photocatalysts and lowering of reaction temperature.

### Microwave assisted synthesis

Table 2 Microwave assisted synthesis of Lophine derivatives in neat

| Entry | Reaction conditions   |           |            | Example | Yields        | Ref. |
|-------|---|-----------|------------|---------|---------------|------|
|       | Catalyst (mg)   | Watts (W) | Time (min) |         |               |      |
| 1     | -   | 150       | 3-5        | 14      | 80-99         | 42   |
| 2     | Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> -Imid-PMA <sup>a</sup> | 100       | 50-180     | 14, 19* | 80-97, 81-97* | 43   |
| 3     | Fe <sub>3</sub> O <sub>4</sub> @SiO <sub>2</sub> -HM-SO <sub>3</sub> H  |           | 7-8        | 14      | 76-93         | 44   |
| 4     | Pumice@SO <sub>3</sub> H  | 280       | 11-15      | 11      | 80-92         | 45   |

<sup>a</sup> All the reactions are carried out under solvent-free conditions; \*Examples and yields of 1,2,4,5-tetra-substituted imidazoles.

J. Zhou and team (2010) used catalyst-free, solvent-free and heat promoted microwave assisted synthesis of variety of Lophine derivatives and achieved good yields in short reaction time (Table 2, entry 1).<sup>42</sup> Benzil (1 mmol), aryl aldehydes (1 mmol), ammonium acetate (3 mmol) were charged in a vial and sealed with septum containing cap. The reaction mixture was irradiated at 150 W at 120 °C temperature for 3-5 minutes.

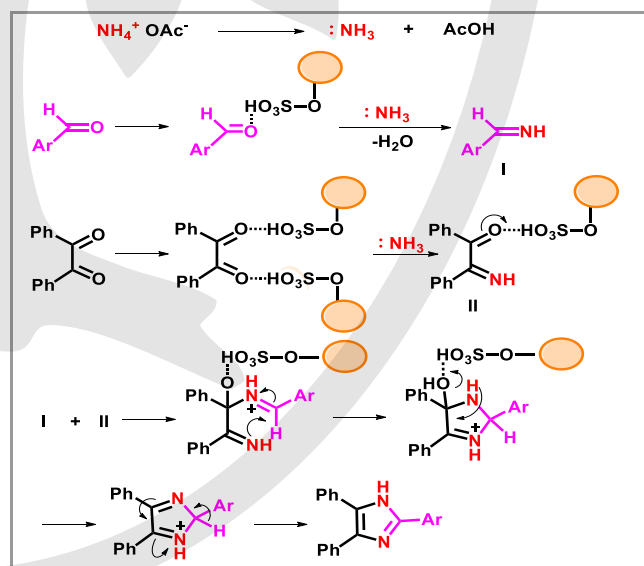
The group of M. Esmailpour (2015) prepared Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-Imid-PMA<sup>a</sup> as magnetic nano catalyst and used it in the synthesis of various Lophine derivatives under microwave heating (Table 2, entry 2).<sup>43</sup> Benzil (1 mmol), aryl aldehyde (1 mmol) and ammonium acetate (3 mmol) were heated neat under microwave irradiation in presence of

the nano catalyst at 110 °C temperature to afford the desired Lophine derivatives. Authors compared microwave and conventional heating conditions to found that the later required around 8 to 10 times longer reaction time in general. The catalyst could also be recycled and reused for up to six cycles without loss of significant yield.

H. Naeimi and D. Aghaseydkarimi (2015) developed an ionic liquid coated nano magnetite catalyst and used it as a reusable nano catalyst in the solvent free synthesis of Lophine derivatives under microwave irradiation.<sup>44</sup> Under the optimized conditions benzil (1 mmol), aryl aldehyde (1 mmol) and ammonium acetate (3 mmol) were heated neat under microwave irradiation in presence of 30 mg of the nano catalyst Fe<sub>3</sub>O<sub>4</sub>@SiO<sub>2</sub>-HM-SO<sub>3</sub>H (Table 2, entry 3). In just 7-8 minutes reaction time the desired substituted Lophines were obtained in good to excellent yields. The catalyst recyclability and reusability were found to be excellent as after six run the yield only dropped to 85 from 93%.

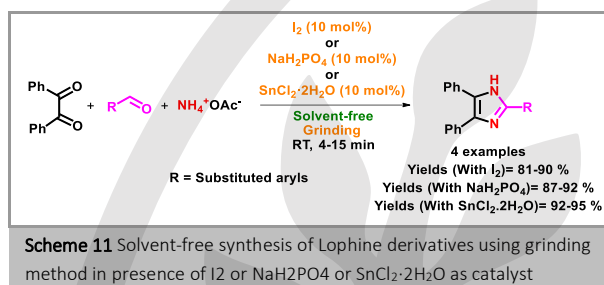
Shirole and coworkers (2021) studied the catalytic performance of pumice@SO<sub>3</sub>H for the synthesis of 2,4,5-triaryl imidazoles under solvent-free microwave irradiation.<sup>45</sup> Benzil (1 mmol), aryl aldehyde (1 mmol) and ammonium acetate (3 mmol) were heated neat under microwave irradiation in presence of the pumice@SO<sub>3</sub>H catalyst (100 mg) to afford the 2,4,5-triaryl imidazoles in excellent yields (Table 2, entry 3). The catalyst was found to be reusable successfully for up to four cycles without loss of significant yield. The optimized protocol was also applied in the synthesis of acridine-1,8-diones to demonstrate versatility of the catalyst. The mechanism starts with the pumice@SO<sub>3</sub>H catalyzed activation of benzaldehydes and the Benzil molecules by which imine intermediates of both molecules is produced (**I** and **II**), cyclocondensation followed by rearrangement gives desired Lophine derivatives (Scheme 10).

Clearly in comparison the first method (Table 2, entry 1) which is catalyst-free under microwave irradiation is the best as it produced the desired Lophines in excellent yields in a dramatically short reaction time of 3-5 min. All conventionally heated reactions discussed earlier could be tested under Microwave irradiation for comparison and thus holds lot of value for future scope.

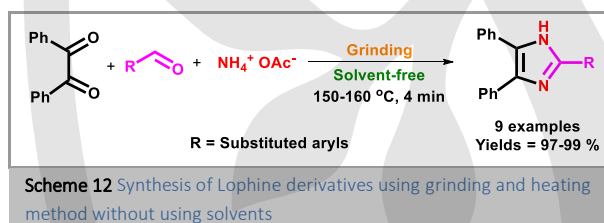
Scheme 10 Mechanism of the microwave assisted synthesis in presence of pumice@SO<sub>3</sub>H catalyst

## Synthesis by grinding

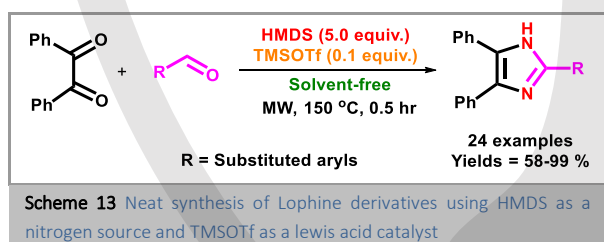
S. Patil and coworkers (2015) synthesized Lophine derivatives under solvent-free conditions by grinding reaction components together in the presence of  $I_2$  or  $NaH_2PO_4$  or  $SnCl_2 \cdot 2H_2O$  as catalyst (Scheme 11).<sup>46</sup> The catalytic activity was observed in the order of  $SnCl_2 \cdot 2H_2O$ ,  $NaH_2PO_4$  and  $I_2$  accordingly with the Lewis acid character of individual catalyst.



A. K. Nanda (2016) and coworkers reported a solvent free synthesis of various Lophine derivatives using mechanical grinding and heating method (Scheme 12).<sup>47</sup> Due to the high polarizability of carbonyl bonds, the extremely weak dipole of carbonyls can generate polarization in bulk, which ultimately increases the electrophilicity of carbonyls and makes the synthesis of Lophine derivatives easy due to self-catalysis. Benzil (1 mmol), aryl aldehyde (1 mmol) and ammonium acetate (10 mmol) were taken in an agate mortar and thoroughly ground. The reaction mixture was then transferred to a test tube and heated to 150-160 °C for 4-5 minutes.



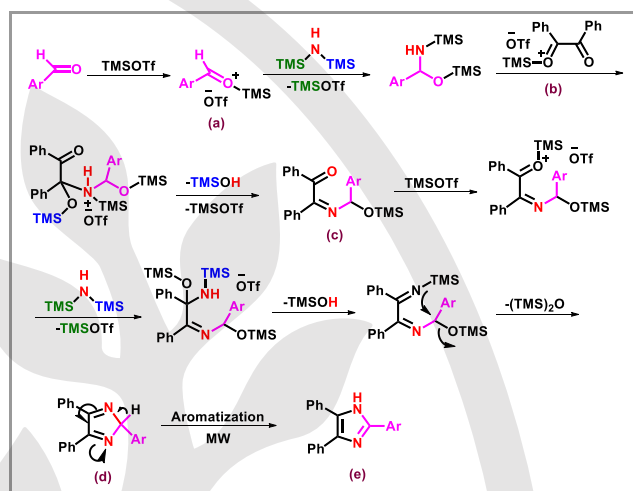
## Miscellaneous



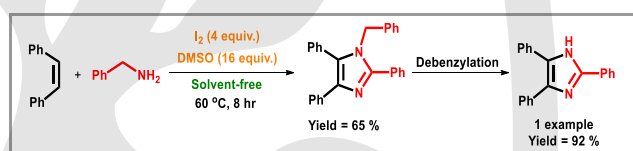
Cheng-Chung Wang (2021) reported a solvent free microwave synthesis for various Lophine derivatives for which Hexamethyldisilazane (HMDS) was used as a nitrogen source and trifluoromethanesulfonate (TMSOTf) as a Lewis acid catalyst (Scheme 13).<sup>48</sup> They used both electron rich and electron deficient groups attached with the aldehydes and got average to excellent yields.

In the mechanism, first TMSOTf activates the carbonyl oxygen of aldehyde (a) as well as one of the diketone molecule (b) reaction

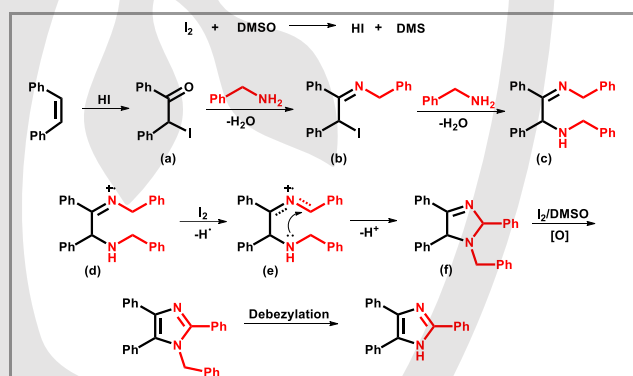
between intermediate a and b forms imine (c) which is further activated by the TMSOTf to allow attack of the HMDS nitrogen. Elimination of TMSOH and intramolecular cyclisation gives the five-membered ring intermediate (d) followed by [1,5] H-shift furnishes the desired 2,4,5-triarylimidazoles (Scheme 14).



**Scheme 14** Mechanism of synthesis using HMDS as a nitrogen source and TMSOTf as a Lewis acid catalyst



**Scheme 15** Synthesis of Lophine from *cis*-stilbene as a starting material



**Scheme 16** Mechanism of the synthesis of Lophine using *cis*-stilbene as a precursor

Recently, a unique approach was reported for the synthesis of Lophine by the group of R. Dandela (2023).<sup>49</sup> They used *cis*-stilbene instead of diketone as a starting material and the reaction was carried out with 2 mole equiv. of benzyl amine in presence of  $I_2$ -DMSO catalyst at 60 °C for 8 hours followed by debenylation to produce Lophine (Scheme 15). *cis*-stilbene first converted to 2-iodo-1,2-diphenylethan-1-one (a) in the presence of iodine-DMSO which facilitate Kornblum oxidation. Resulting intermediate undertakes condensation reaction with first benzyl amine to give the iodinated imine intermediate (b). Afterward, intermediate (b) is coupled with another molecule of benzyl amine and gives intermediate (c). Then intermediate (c) loses one electron and gets

oxidized to nitrogen centered radical cation intermediate (**d**). Intra molecular cyclization gives intermediate (**f**) and subsequent oxidation forms tetrasubstituted dihydro imidazole. Debenzylation was carried out using the standard conditions of Pd/C and hydrogen gas to form the Lophine (Scheme 16).

## Conclusions and Outlooks

In conclusion, we have demonstrated solvent free synthesis of Lophine derivatives via different protocols which included inorganic-, organic-, bio-, solid supported-, Lewis acid- and ionic liquid-catalysts, microwave mediated synthesis, grinding method as well as visible light mediated synthesis. Due to the neat reaction conditions all of these protocols inherently possess cost effectiveness and have minimum impact on environment, biodiversity and human health. The ease of operation is demonstrated by almost all examples, while recyclability and reusability are demonstrated particularly by the solid supported catalyst systems. In future, new catalyst systems that work under neat conditions should be tested and recyclability as well as reusability should be explored further to improve the benefits of the neat Lophine synthesis. We hope that this review will be of great interest to the chemistry community and will further promote research and development in the fascinating field of solvent free synthesis.

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## Conflict of Interest

The authors declare no conflict of interest.

## References

- [1] Anastas, P.; Eghbali, N. *Chem. Soc. Rev.* **2010**, *39*.
- [2] (a) Anastas, P. T.; Kirchoff, M. M. *Acc. Chem. Res.* **2002**, *35*, (b) Anastas, P. T.; Beach, E. S. *Green Chem. Lett. Rev.* **2007**, *1*, (c) Kreuder, A. D.; House-Knight, T.; Whitford, J.; Ponnusamy, E.; Miller, P.; Jesse, N.; Rodenborn, R.; Sayag, S.; Gebel, M.; Aped, I.; Sharfstein, I.; Manaster, E.; Ergaz, I.; Harris, A.; Grice, L. N. *ACS Sustainable Chem. Eng.* **2017**, *5*, (d) Federsel, H.-J. *Synthesis* **2022**, *54*.
- [3] Clarke, C. J.; Tu, W.-C.; Levers, O.; Bröhl, A.; Hallett, J. P. *Chem. Rev.* **2018**, *118*.
- [4] (a) Capello, C.; Fischer, U.; Hungerbühler, K. *Green Chem.* **2007**, *9*, (b) Joshi, D. R.; Adhikari, N. J. *Pharm. Res. Int.* **2019**, *1*.
- [5] (a) Martins, M. A. P.; Frizzo, C. P.; Moreira, D. N.; Buriol, L.; Machado, P. *Chem. Rev.* **2009**, *109*, (b) Singh, M. S.; Chowdhury, S. *RSC Adv.* **2012**, *2*, (c) Obst, M.; König, B. *Eur. J. Org. Chem.* **2018**, *2018*, (d) Sarkar, A.; Santra, S.; Kundu, S. K.; Hajra, A.; Zyryanov, G. V.; Chupakhin, O. N.; Charushin, V. N.; Majee, A. *Green Chem.* **2016**, *18*.
- [6] Desai, S. R.; Bhoraniya, R. B.; Koladiya, M.; Bhopekar, V. V.; Patel, C. R.; Mori, T.; Modha, S. G. *J. Photochem. Photobiol., A* **2024**, *455*.
- [7] (a) Kimura, M.; Tsunenaga, M.; Takami, S.; Ohbayashi, Y. *Bull. Chem. Soc. Jpn* **2005**, *78*, (b) Dietz, M. S.; Wehrheim, S. S.; Harwardt, M.-L. I. E.; Niemann, H. H.; Heilemann, M. *Nano Lett.* **2019**, *19*, (c) Wang, Y.; Qiu, D.; Li, M.; Liu, Y.; Chen, H.; Li, H. *Spectrochim. Acta A Mol. Biomol. Spectrosc.* **2017**, *185*, (d) Wang, Y.; Liu, S.; Chen, H.; Liu, Y.; Li, H. *Dyes Pigm.* **2017**, *142*.
- [8] Gangadhar, P. S.; Jagadeesh, A.; Rajesh, M. N.; George, A. S.; Prasanthkumar, S.; Soman, S.; Giribabu, L. *Mater. Adv.* **2022**, *3*.
- [9] Zhou, Z.; Ding, Y.; Si, S.; Wu, W.; Deng, C.; Wu, H.; Xiang, J. J. *Hazard. Mater.* **2021**, *417*.
- [10] Akamatsu, M. J. *Jpn. Soc. Colour Mater.* **2020**, *93*.
- [11] (a) Zhang, Z.; Lai, J.; Wu, K.; Huang, X.; Guo, S.; Zhang, L.; Liu, J. *Talanta* **2018**, *180*, (b) Yamaguchi, S.; Kishikawa, N.; Ohyama, K.; Ohba, Y.; Kohno, M.; Masuda, T.; Takadate, A.; Nakashima, K.; Kuroda, N. *Anal. Chim. Acta* **2010**, *665*, (c) Pavlova, E.; Kaloyanova, S.; Deligeorgiev, T.; Lesev, N. *Eur. Biophys.* **2015**, *44*.
- [12] (a) Singh, A. K.; Zhu, Y.; Han, M.; Huang, H. *Smart Mater. Struct.* **2016**, *25*, (b) Yoo, W. J.; Seo, J. K.; Jang, K. W.; Heo, J. Y.; Moon, J. S.; Park, J.-Y.; Park, B. G.; Lee, B. *Opt. Rev.* **2011**, *18*.
- [13] Bhattacharyya, P.; Medda, A.; Samanta, A.; Guchhait, N.; Das, A. R. *ChemInform* **2012**, *43*.
- [14] Zhao, Y. S.; Xiao, D.; Yang, W.; Peng, A.; Yao, J. *Chem. Mater.* **2006**, *18*, 2302.
- [15] Saxer, S.; Marestin, C.; Mercier, R.; Dupuy, J. *Polym. Chem.* **2018**, *9*.
- [16] Karimi-Jaberi, Z.; Barekat, M. *Chin. Chem. Lett.* **2010**, *21*, 1183.
- [17] Esmaeilpour, M.; Javidi, J.; Dehghani, F.; Zahmatkesh, S. *Res. Chem. Intermed.* **2017**, *43*, 163.
- [18] Gajengi, A. L.; Chaurasia, S.; Monflier, E.; Ponchel, A.; Temel, J.; Bhanage, B. M. *Catal. Commun.* **2021**, *161*.
- [19] Yar, M.; Bajda, M.; Shahzad, S.; Ullah, N.; Gilani, M. A.; Ashraf, M.; Rauf, A.; Shaukat, A. *Bioorg. Chem.* **2015**, *58*, 65.
- [20] Pervaiz, S.; Mutahir, S.; Ullah, I.; Ashraf, M.; Liu, X.; Tariq, S.; Zhou, B. J.; Khan, M. A. *Chem. Biodiversity* **2020**, *17*.
- [21] Ghogare, R. S. *Org. Commun.* **2022**, *15*, 44.
- [22] Maleki, A.; Paydar, R. *RSC Adv.* **2015**, *5*, 33177.
- [23] Tamuli, K. J.; Dutta, D.; Nath, S.; Bordoloi, M. *ChemistrySelect* **2017**, *2*, 7787.
- [24] Girish, Y. R.; Kumar, K. S. S.; Thimmaiah, K. N.; Rangappa, K. S.; Shashikanth, S. *RSC Adv.* **2015**, *5*, 75533.
- [25] Fekri, L. Z.; Nikpassand, M.; Shariati, S.; Aghazadeh, B.; Zarkeshvari, R.; pour, N. N. *J. Organomet. Chem.* **2018**, *871*, 60.
- [26] Manteghi, F.; Zakeri, F.; Guy, O. J.; Tehrani, Z. *Nanomaterials* **2021**, *11*.
- [27] Wang, D.; Li, Z.; Huang, X.; Li, Y. *ChemistrySelect* **2016**, *1*, 664.
- [28] Mirzaee, M. R.; Saberi, S. *Chin. J. Chem.* **2010**, *28*, 663.
- [29] Mahdavinia, G. H.; Amani, A. M.; Sepehrian, H. *Chin. J. Chem.* **2012**, *30*, 703.
- [30] Ghorbani-Choghamarani, A.; Ghorbani, F.; Yousofvand, Z.; Azadi, G. *J. Porous Mater.* **2015**, *22*, 665.
- [31] Salimi, M.; Nasser, M. A.; Chapesshloo, T. D.; Zakerinasab, B. *RSC Adv.* **2015**, *5*, 33974.
- [32] Mirsafaei, R.; Heravi, M. M.; Ahmadi, S.; Hosseinnejad, T. *Chem. Pap.* **2016**, *70*, 418.
- [33] Borhade, A. V.; Tope, D. R.; Gite, S. G. *Arab. J. Chem.* **2017**, *10*, S559.
- [34] Xu, X.; Li, Y. *Res. Chem. Intermed.* **2015**, *41*, 4169.
- [35] Chavan, L. D.; Shankarwar, S. G. *Cuihua Xuebao/ Chin. J. Catal.* **2015**, *36*, 1054.
- [36] Maleki, B.; Eshghi, H.; Khojastehnezhad, A.; Tayebee, R.; Ashrafi, S. S.; Kahoo, G. E.; Moeinpour, F. *RSC Adv.* **2015**, *5*, 64850.
- [37] Dipake, S. S.; Lande, M. K.; Rajbhoj, A. S.; Gaikwad, S. T. *Res. Chem. Intermed.* **2021**, *47*, 2245.
- [38] Rabiiei, K.; Pouramiri, B.; Neshati, M.; Imanvand, A. J. *Organomet. Chem.* **2023**, *1001*.
- [39] Gholap, D. P.; Huse, R.; Dipake, S.; Lande, M. K. *RSC Adv.* **2023**, *13*, 2090.
- [40] Banothu, J.; Gali, R.; Velpula, R.; Bavantula, R. *Arab. J. Chem.* **2017**, *10*, S2754.
- [41] Patel, G.; Patel, A. R.; Banerjee, S. *New J. Chem.* **2020**, *44*, 13295.
- [42] Zhou, J. F.; Gong, G. X.; Sun, X. J.; Zhu, Y. L. *Synth. Commun.* **2010**, *40*, 1134.
- [43] Esmaeilpour, M.; Javidi, J.; Zandi, M. *New J. Chem.* **2015**, *39*, 3388.
- [44] Naemi, H.; Aghaseyedkarimi, D. *New J. Chem.* **2015**, *39*, 9415.
- [45] Tambe, A.; Gadhave, A.; Pathare, A.; Shirole, G. *Sustain. Chem. Pharm.* **2021**, *22*.
- [46] Patil, S.; Patil, J.; Dharap, S. *World J. Pharm. Res.* **2015**, *4*, 2476.
- [47] Pradhan, K.; Tiwary, B. K.; Hossain, M.; Chakraborty, R.; Nanda, A. K. *RSC Adv.* **2016**, *6*, 10743.
- [48] Asressu, K. H.; Chan, C. K.; Wang, C. C. *RSC Adv.* **2021**, *11*, 28061.
- [49] Bhukta, S.; Chatterjee, R.; Dandela, R. *Synthesis* **2022**, *55*, 846.

## Biosketches

|   |   |
|---|---|
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