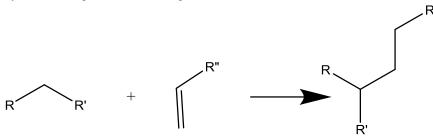
Michael Addition Reaction Under Green Chemistry

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INTRODUCTION

Since its discovery in 1889, the Michael reaction has been one of the maximum critical reactions in organic chemistry [1]. Due to the friendly experiment conditions and excellent reaction efficiency, Michael additional reactions have long been preferred in both synthetic organic and polymer chemistry [2]. The introduction of ecologically benign and clean artificial strategies has emerge as a essential subject matter in each instructional and commercial studies with inside the 21st century with inexperienced chemistry turning into a relevant situation in each. The motive of present day natural synthesis has advanced as a result. There is a need to produce Michael addition in water using a recyclable material. Since there has been no use of any dangerous organic solvent as a catalyst and since there has been no use of any harmful organic solvent [7]. The nucleophilic addition of a carbanion or every other nucleophile to an,-unsaturated carbonyl molecule containing an electron chickening out organization is called the Michael reaction or Michael addition. It's part of the bigger category of conjugate additions. This is one of the most useful ways for forming C–C bonds in a gentle manner [1-3].



In a Michael reaction, the unsaturated carbonyl serves as an electrophilic acceptor, and the enolate serves as a nucleophilic donor. Within the mechanism, an alpha-substitution for the enolate and a conjugate addition for the unsaturated carbonyl are employed. [4].

The Michael addition of acetyl acetone to methyl acrylate was catalysed by a lipase variation. Because it creates a carbon-carbon bond, the Michael addition is a crucial process in the synthesis of organic compounds [5].

The 1,5 dicarbonyl chemical is produced when the enolate of a carbonyl molecule is combined with an,-unsaturated carbonyl compound. This product is frequently referred to as a Michael Adduct [6].

Green Chemistry: Theory and Practice, co-authored by Paul Anastas and John C. Warner, was published in 1998 and was a gamechanger. The study's 12 Principles of Green Chemistry revealed a philosophy that at the time motivated academic and industrial scientists and still guides the green chemistry movement today.



Paul Anastas



John C. Warner

The creation of chemical goods and procedures that lessen or do away with the use of harmful substances is known as "green chemistry." A chemical product's whole life cycle, which includes its creation, manufacture, use, and disposal, is covered by green chemistry.

Green chemistry is a method of making and using chemicals that efficiently employs renewable raw resources, minimises waste, and does without dangerous and toxic chemicals.

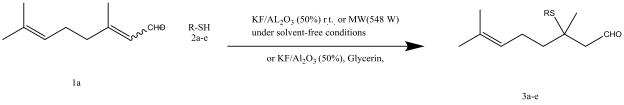
A branch of chemistry and chemical engineering known as "green chemistry," often known as "sustainable chemistry," is concerned with developing products and processes that reduce or totally eliminate the usage of harmful compounds.

Animals and vegetation are less harmed by environmental toxic substances. Smog production, ozone depletion, and global warming are all decreased. Less chemicals are used to harm ecosystems. Less garbage, especially hazardous waste dumps, is dumped in landfills.

Chemical industry procedures like distillation, product drying, electrolysis, and waste treatment all use it to heat reactants. Although there are a number of strategies to lower this, the majority of energy is still produced from fossil fuels at the time [7].

1.1 As a catalyst for the solvent-free process, KF/Al2O3 Alkenes are added thiols by Michael:-

As well as the usage of glycerin as a biodegradable solvent.



 $KF/Al_2O_3 = (4.0g)$ of $Al_2O_3 + KF.2H_2O(6.0g) + water at 65 degree C stirred 1 hour and dried at 80 degree Celsius Alkenes are given thiols 1, 4, in addition:$

1.2 Method

Thiols 2 (1.2 mmol) and KF/Al2O3 (0.079) were mixed with glycerin (1 ml) before the alkene 1 was added (1 mmol). TLC was used to monitor the reaction progress as the mixture was agitated at room temperature.

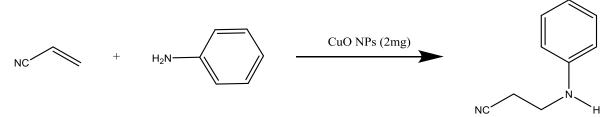
After consuming the initial ingredients, the result was extracted from the glycerin by washing the mixture with dry ether (5ml). By simply adding more thiols and alkene to the residue in the reaction tank after the solvent had been vaporised under reduced pressure, it was possible to reuse the mixture of glycerin and KF/Al2O3 up to three times while still getting the same results. [1].

<u>1.3</u> In conclusion This environmentally friendly procedure can be used to make 3,7 dimethyl-3-(phenylthio) oct-6-enal from crude lemon grass oil without the need for citral sepration (1a).Glycerin has been successfully employed as a reneawable, unpolluted, and biodegradable solvent, paving the way for new green and sustainable chemistry applications.

The techniques are straightforward, employing renewable and readily available starting materials a solvent – free or reusable catalytic system and the ability to reuse the catalytic system[1].

2.1 The aza Michael reaction is catalyzed by CuO

Devlopment of the reaction condition for aza Michael reaction.



Hethod

2.2 Latana camara flower extract preparation :

The phytochemicals were extracted from plant sources using the approach we previously described[2]. To create a 2.5 weight percent extract solution in water, the dried material was employed.

2.3 CuO Nps synthesis :

When latana camara flower extract was present, CuO Np was produced using a hydrolysis process that included copper (2) acetate as a forerunner and NaOH as the oxidising agent. Copper(2) acetate solution (10ml;0.370m), plant extract (30ml;2.0wt%), and enough water were combined in a stopper glass vessel under continuous stirring at 65 degrees Celsius. 13 ml of 1.120 m NaOH solution was added dropwise to the reaction mixture after 10 minutes of stirring to raise the PH to 12.. The reaction mixture was heated for another 2 hours at the same temperature with constant stirring the reaction mixture was then allowed to spontaneously cool to ambient temperature. The end result centrifugation at 10,000 [thin space [1/6em]rpm for 10 minutes was used to isolate it. after that ,the isolated product was purified using two cycles of water washing and sepration.

The solid bulk was ultimately dried overnight at 60 degrees Celsius in a vacuum oven. The dry byproduct was calcined at 400 °C in a muffle furnace for two hours to eliminate any hydroxyl ions or water molecules that may have stuck to the CuO product. When the extract concentration was changed, the same set of responses occurred in order

2.4 Aza Michael addition process catalyzed by CuO:

In an aza Michael addition reaction carried out at room temperature, the catalytic activity of processed CuO Nps was evaluated. For the initial experiment, we employed CuO (2 mg; 0.022 mmol) as a nanocatalyst in solvent-free conditions at room temperature with model substrates such as acrylonitrile (130 L; 2 mmol) and aniline (180 L; 2 mmol). All substrates were combined in a glass round bottom flask equipped with a reflux condenser, and the reaction was let to continue. TLC was used to track the reaction's progress. The reaction mixture was extracted with ethyl acetate and water when the reaction was completed to seprate the solid, the aqueous

layer containing the solid catalyst was centrifuged for 15 minutes at 12,000[thin space (1/6 em)] rpm Na₂SO₄, filtering and removing the solvent at decreased pressure, the solvent was removed. By passing the raw material through a silica gel column and eluting it with ethyl acetate-n-hexane, the raw material was purified. All of the product were known compounds with melting points[3].

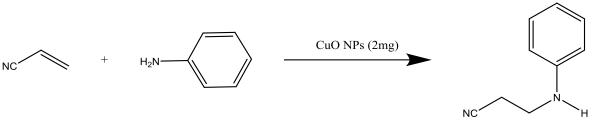
2.5 The CuO catalyst can be reused

In order to remove any organic compounds, solid catalysts were repeatedly washed in an ethylacetate and water solution, separated, and then dried at 60 degrees Celsius to ensure that they could be recycled. The dried catalyst was utilized in a new bath of reactions using aniline and acrylonitrile as substrates.

2.6 Discussion & result :

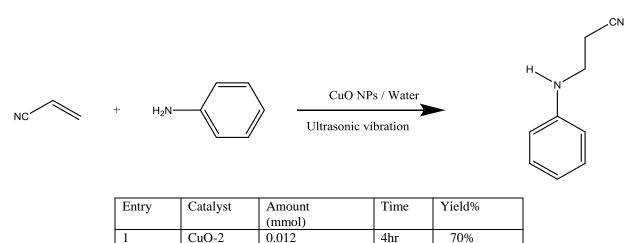
Under secure and ecologically friendly reaction circumstances, the catalytic activity of the generated CuO Nps was examined in an aza Michael addition procedure. Under solvent free conditions at room temperature, we used acrylonitrile (2mmol) & aniline (2mmol) as model substrates and CuO (2mg 0.020mmol) as nanocatalyst for the initial investigation. All other conditions remained the same, and the reaction was performed in a variety of solvent environments, including water, water and ethanol, and ethanol and acetonitrile. Water and a water ethanol mix solvent produced the best yield (70 percent), so water was chosen as the solvent system for additional research because of its environmental friendliness. At room temperature ,we performed the process in water with ultrasonic vibration.

Table 1. For the aza-michael reaction, the reaction condition was optimised



Entry	solvent	temperature	Time	yield
1	Solvent free	60° C	24hr	50
2	water	60° C	9hr	70
3	Water ethanol	60° C	9hr	70

2mmol acrylonitrile and 2mmol aniline are the reactions.the yield has been isolated. Table 2. under ultrasonic vibrations, the catalyst loading for the aza-michael reaction can be optimized.



2mmol acrylonitrile and 2mmol aniline are the reactions.the yield has been isolated.

4hr

80%

0.020

2.7 conclusion :

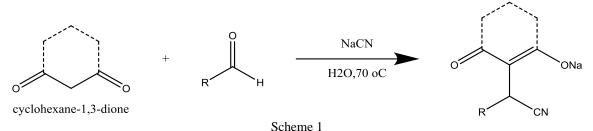
To control the size and shape of the products, a flower extract from the latana camara plant was used as a capping and shape directing agent. CuO is a substituted aza Michael compound that is non-toxic. Additionally very stable and reusable for numerous batches of reactions, CuO Nps. without substantially losing their catalytic.

3.1 Aldehyde, barbituric acid, and sodium cyanide react in a Michael addition reaction in water: Is described without the use of a satelyst on activation at 70 degree C

CuO-2

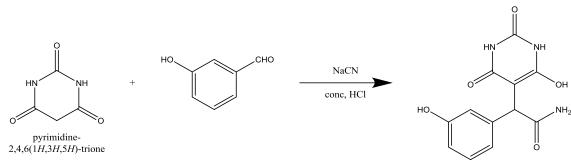
Is described without the use of a catalyst or activation at 70 degree C.

2



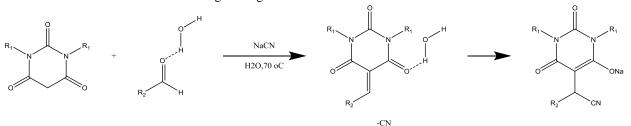
3.2 Method :

Alkyl nitriles (3) were produced as sodium salts, which could be transformed to product (4) after being treated with concentrated HCl. Barbituric acid and 3-aminopyridine are commonly used at 70 degree celsius ,hydroxybenzaldehyde was swirled for 2hours. Following that 1 parallel of sodium cyanide was added to the solution. In mixture one equivalent of conc.HCl was added after 2 hours and then mixed for another 10 minutes at room temperature.the temperature in the room the easy workup technique made it possible for the product that is desired (protonated salt and hydrolysis cyanide gp) a fantastic yield (scheme 2)



Scheme 2

A knoevenagel condensation reaction involving CH-acid and aldehyde is thought to be involved in the early synthesis of activated alkene or unsaturated carbonyl 5. The intermediate 5 is then subjected to a Michael addition reaction with the cyanide to yield b-cynocarbonyls 3.(scheme 3) to better understand the mechanism, the Michael acceptor 5 was first created via moisture of barbituric acid and benzaldehyde [4]and then 5 was reacted with sodium cyanide to produce the equivalent alkyl nitrile an aldehyde was reacted with sodium cyanide in water for further clarity, but it was discovered that the reaction takes a long term to complete furthermore, at the reaction circumstances the resultant cynohydrine did not react with 1 these findings backed up the postulated mechanism although the role of water as a reaction medium and mechanism is unknown, this one-pot reaction (eg. Tendom reaction) could occur at the hang together of organic under layer and water in heterogeneous system, according to amorphous et al 3. The effectiveness of this reaction necessitates strong stirring.

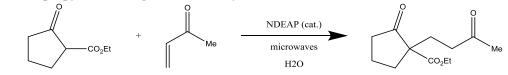


Scheme 3

In conclusion, it has been demonstrated that alkyl nitriles can be synthesized in water without the use of catalyst. A three component reaction comprising CH- acid an aromatic aldehyde, and a catalyst and a sodium cyanide resulted in high quality items yield. A variety of fragrant aldehyde were exmined[5].

This approach can be used to make wide range of chemicals. As a result, it has been established that employing water as a solvent is excellent for synthesis of alkyl nitriles are a kind of alkyl nitrile in addition, the green synthetic techniques includes the process was catalyzed by hydrogen bonding in the solvent water. In this method used green synthetic protocol. As a result, no further catalysts are needed, making the process more efficient.

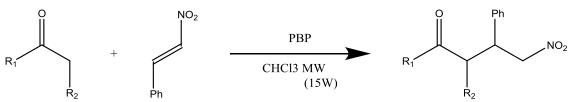
4.1 (N,N-diethylaminopropylated silica gel) NDEP catalysis Michael additions in water.



The hypersensitivity of 1,3 dicarbonyl compounds in water, employing recyclable N,N diethylamino propylated silicagel (NDEAP) as a catalyst and ethyl 2-oxocyclopentane carboxylate (31) as test substrates (scheme 4)[6]. A triphasic system was created as a result of the limited solubility of the organic building block in water, and microwave light beam and ray was used to heat interior. After 10 minutes under ideal situation adding product 33 yielded 92 percent. Other carbonyl compounds also interacted well, yielding up to four percent of the comparable Michael addition products. the relevance of microwave light beam and ray was demonstrated by the reaction of keto easter 31 with methyl acrylate, which yielded keto diester 34 in 68 percent yield after only six minutes behave the same reaction in an oil bath (without the micro radiation therapy wave) under comparable conditions. Resulted in only 44% yield[10].

Mosse and alexakis explored the consequence of microwave irradiation on an eanatioselective Michael addition using N-i-prbipyrrolidine (i-PBP,35) as a model compound organocatalyzer[7,8]. When hydroxyacetone reacts with other chemicals, the result is hydroxyacetone(36a). they were using nitro ketone (38) and 2-nitrovinylbenzene (37) to make it. able to reduce the reaction time nedded from 168 to 4 hours,

Table 8, entries 1 and 2 without changing enantioselectivity surprisingly, in the reaction with isovaleral (36b), considerably more is produced. When the reaction was carried out, a modest increase in was noticed out in the open, irradiated with microwaves (table 8, entries 4&3). In addition, the catalyst loading could be lowered from 15 to 10 percent up to 5% by mass (table 8, entry 5) Asymmetric organocatalytic conjugate additions.



The findings suggested that the more effective microwave irradiation might account for all differences observed between processes neglect under microwave irradiation and standard heating. The former strategy can achieve energy transfer a total [9], not produced by hea effects that have been postulated should be attributed to faulty assumptions. During the reaction, temperature reading are taken.

5.1 6-Amino-1,4 dihydro-3-methyl-1,4-phenyl pyrano[2,3-C] with the help of pyrazoles was created. General method :

Ethylacetoacetate, hydrazine hydrate, and malonitrile were all individually refluxed for one to five hours with substituted aromatic aldehydes in ethanol in the presence of cesium fluoride.

Overnight ,the reaction mixture was maintained, filtered, and recrystalized from ethanol. The end products of the different replacements are known as pyrano [2,3-C]6-amino-1,4-dihydro-3-methyl-1,4-phenyl (5a-5m) pyrazoles.

Discussion :

To create 6 amino -1,4-dihydro-3-methyl-1,4-phenyl pyrano, And the presence of cesium fluoride as the catalyst in ether as the solvent, benzaldehyde, malonitrile, hydrazine hydrate, and ethylacetoacetate were refluxed for an hour at 500 C. TLC is used to track the course of the reaction. After the reaction is finished, a solid product is obtained after being maintained overnight, the reaction mixture was filtered and recrystallized from ethanol. The result yield attained is 85 percent when 5mol % cesium fluoride was used, the highest yield of the result product was produced.

Conclusion :

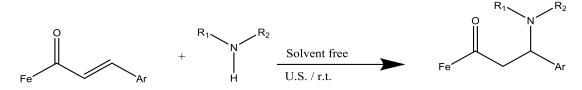
We have successfully synthesised several substituted 6-amino-1,4-dihydro-3-methyl-1,4-phenyl pyrano[2,3-C] pyrazoles by using an eco-friendly tandem knoevengal-michael reaction in ethanol catalysed by cesium fluoride. As a result, the process does not required the use of harmful organic solvents or toxic catalysts. Provides a more effective and practical alternative to current practices.

6.1 Nitro-amines and nitro-sulfides can be synthesised quickly, effectively, without the use of a catalyst, and without the use of a solvent thanks to the Michael addition

The Michael addition of amines and thiols to nitroolefins by straightforward mixing or grinding is used to create nitroamines and nitrosulfides has been improved into a simple, atom-efficient, rapid, and highly efficient green process. The addition products were quantitatively yielded in minutes at room temperature using this green technique that was free of catalysts and solvents. This method does not require the use of water quenches, solvent separations, or purification techniques like recrystallization and column chromatography.

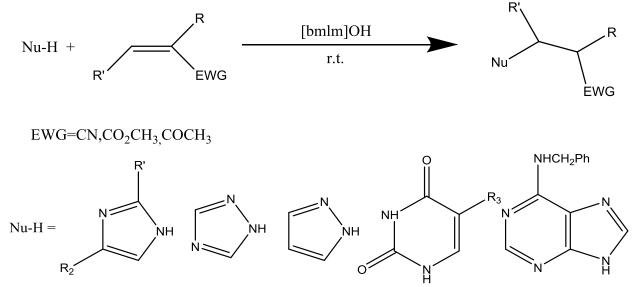
7.1 Ultrasound-irradiated Without the aid of a solvent or a catalyst, Michael addition of amines to ferrocenylenones at ambient temperature

Ferrocenylenones and aliphatic amines can be combined in a straightforward Michael reaction to give high yields of 1-ferrocenyl-3-amino carbonyl compounds when exposed to ultrasound at room temperature without the need of a solvent or catalyst. The aza-Michael reaction of additional unsaturated carbonyl compounds, such as chalcone, carboxylic ester, and others, can also be successfully carried out using this method. On the other hand, aromatic amines don't go through any conjugate addition at all, thus the procedures that are now being used either don't work or yield low yields after a long reaction time. The advantages of this technology include quick, inexpensive, and ecologically friendly processes that will support green chemistry in addition to the experiments' simplicity, generality, and selectivity.



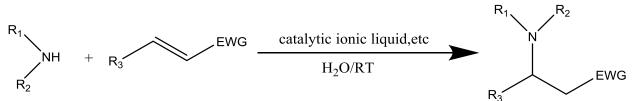
8.1For the Michael addition of N- heterocycles to unsaturated molecules, a quick and highly efficient procedure has been developed using basic ionic liquid [bmIm] OH as the catalyst and environmentally friendly solvent.

One basic ionic liquid, 1-methyl-3-butylimidazolium hydroxide, or [bmIm] OH, was used as a catalyst and reaction medium to provide a fast and ecologically acceptable approach for the Michael addition of N-heterocycles to unsaturated molecules at room temperature. The reactions took place at room temperature and produced successful results quickly (0.5-3 h). Numerous N-heterocycles, including five-membered N-heterocycles, pyrimidines, and purines can be used with this technique. The recovered ionic liquid might potentially be used for numerous cycles at the same degree of activity.



9.1 In water, ethylenic compounds and amines undergo an aza-Michael reaction that is catalysed by a green ionic liquid and quaternary ammonium salt.

The first extremely efficient conjugate addition of aliphatic amines to unsaturated molecules that is environmentally benign is revealed. This addition is catalysed by simple quaternary ammonium salts and ionic liquids in the environmentally favourable solvent, water.

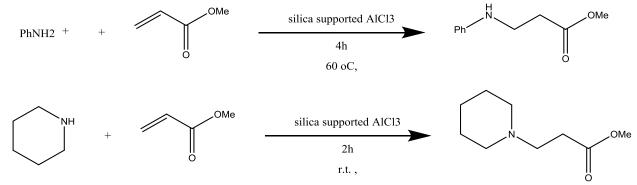


10.1 Hydrogen-bonding-mediated, quick, and asymmetric Adding Michael to a ball mill

In a planetary ball mill without the use of any solvents, chiral squaramide derivatives were produced to serve as hydrogen bonding catalysts for the Michael addition reactions of 1,3-dicarbonyl compounds to nitroolefins. With moderate catalyst loading, excellent yields, high enantioselectivities, and shorter reaction durations were attained.

11.1 Michael addition of aromatic amines

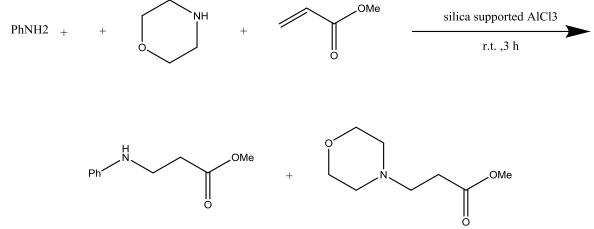
Using silica-supported aluminium chloride as a catalyst, Using Michael excellent to quantita- tive yields were achieved when aromatic amines were added at 60 °C and aliphatic amines were added at room temperature.



Scheme 1 combines methyl acrylate with Michael additions of aromatic and aliphatic amines.

11.2 Method

Aniline reacts at room temperature with methyl acrylate and 0.2 g of supported aluminium chloride without the use of a solvent on silica. Within 4 hours, there was partial conversion, resulting in Michael adduct. Utilizing After 4 hours at 60 °C with 0.1 g of silica-supported aluminium chloride, the reaction was finished but was not after 4 hours at the lower temperature. There were some polymeric compounds produced as a byproduct when 0.3 g of catalyst was utilised. At room temperature and without We used piperidine, methyl acrylate, and 0.2 g of catalyst in place of any solvent in the following step. With quantitative yields of the Michael adduct, the reaction was finished after two hours. Scheme 1.

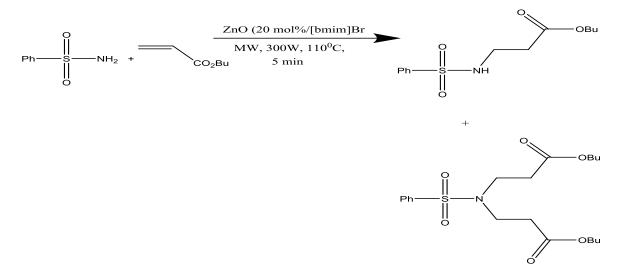


Scheme-2: Reaction of aniline and morpholine with methyl acrylate.

The reaction was carried out at room temperature using methyl acrylate (1 mmol), aniline (1 mmol), and morpholine (1 mmol) with silica-supported aluminium chloride. After three hours, a silica-supported aluminium chloride catalyst was created as the primary byproduct. (Scheme 2).

11.3 Conclusion

One of the most efficient catalysts for the solvent-free Michael addition of various Michael acceptors to amines, notably aromatic amines is silica-supported aluminium chloride. The catalyst can be easily removed from the product after the reaction with this method because an organic solvent is not needed to carry out the reaction. The catalyst is simple to handle and has multiple uses. **12.1 Michael addition of sulfonamides**



Scheme-1: Micheal addition of benzenesulfonamide to n-butyl acrylate

12.2 Method

Sulfonamides are added to, -unsaturated esters via Michael addition in the presence of catalytic amounts of zinc oxide in [bmim]Br under MWI (Scheme 1). In this process, N,N-dialkyl sulfonamides produced in extremely low yields together with the N-alkylated compounds.

12.3 Results & Disconnection

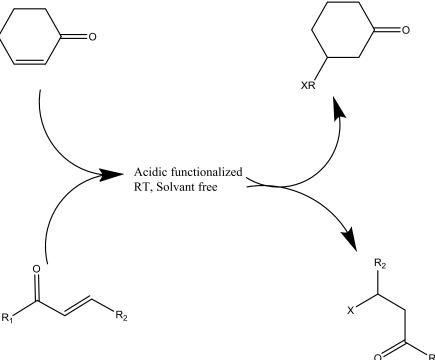
As a model reaction to produce chemicals, the Michael addition of benzenesulfonamide to n-butyl acrylate was investigated (Scheme 1). First, under MWI (300 W, maximum 110 °C), the effectiveness of numerous ionic liquids, including [bmim]Br, [bmim]Cl, [bmim]BF4, and [bmim]PF6, was examined.

12.4 Conclusion

For ionic-liquid-accelerated Michael addition of sulfonamides with,-unsaturated esters under MWI, we have developed a highly effective catalyst. The promising points for the presented methodology are high conversion, ease of handling and low cost of the

catalyst, cleaner reaction profile, and short reaction times, which makes it a useful and attractive process for the rapid synthesis of N-alkyl sulfonamides as biological intresting compounds.

13.1 Hetero-Michael addition



Scheme-1: Nitrogen, sulphur, and oxygen nucleophiles undergo a hetero-Michael reaction with,-unsaturated enones. **13.2 Method**

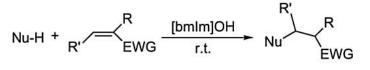
The,-unsaturated substrate (0.5 mmol) was added the catalyst ([Hmim]OTs 30 mol%, 38.1 mg) and nucleophile (0.6 mmol) were completely mixed, and the mixture was then stirred for the allotted reaction period. After the reaction was finished, the mixture was extracted with ethyl acetate (5 mL), the organic layer was washed with salt water, dried (Na2SO4), evaporated, and purified using column chromatography to produce the pure product. The melting point, IR, 1H NMR, 13C NMR, and HRMS measurements were used to describe the products.

13.3 Results & Discussion

We used the current catalytic system to add hetero-Michael addition to a variety of,-unsaturated ketones with nitrogen, sulphur, and oxygen nucleophiles in order to test the practicality and applicability of this technology. First, [Hmim]OTs were used to study the hetero-Michael addition of,-unsaturated ketones with nitrogen nucleophiles. All different types of linear enones can easily react with cyclohexenone to produce yields above 80% when using ethyl carbamate as the nitrogen nucleophile. To compare the catalytic activity of conventional acids and [Hmim]OTs with similar pKa under analogical determination, various control experiments were also conducted method to our delight, [Hmim]OTs exhibited the best activity **13.4 Conclusion**

Utilizing the synthesis molecules as solutions Three kinds of hetero-Michael addition involving nitrogen, sulphur, and oxygen nucleophiles with,-unsaturated substrates have been successfully carried out in either CDCl3 or D2 O achieved. Chemical shifts were reported in parts per million (ppm, d) and referenced to CHCl3 (d 7.27) or D2 O(d 4.88). Gas chromatographic analyses were performed using an Agilent 6850 system (FID). Silica gel (200–300 microns) was used for all chromatographic separations. Anhydrousorganicsolvents were dried andstoredundernitrogen. Every other chemical employed in synthesis processes was of reagent-grade quality or above. Unless otherwise stated, A rotary evaporator was used to vacuously concentrate solutions, and a silica gel column was used to purify the leftover material. Using plates covered in silica gel, TLC was used to monitor each reaction. Iodine fuming in a jar and UV absorption (254 nm) were used for detection.

14.1 Michael addition of N-heterocycles



EWG=CN, CO2CH3, COCH3

Scheme-1: Michael addition of N-heterocycles to α,β -carbonyl compound promoted by [bmIm]OH.

14.2 Method

N-heterocycles (1 mmol), unsaturated carbonyl compounds (1.5 mmol), and 1 mL [bmIm]OH were added to a 10 mL conical flask,

and the mixture was then stirred at room temperature for some time. Ethyl acetate was used to remove the ionic liquid phase's reaction combination (10.0 mL 3). Under reduced pressure, the organic layer was dried and evaporated over anhydrous sodium sulphate. To obtain the appropriate Michael adduct, the residue was purified by flash column chroma- tography (silica gel, petroleum ether/ethyl acetate 1/2, v/v). The ionic liquid that was still in the conical flask was further cleaned with ether, removed any water that had been trapped in dampness, and dried under vacuum for two hours at 90 °C before being utilised again in following processes. Approximately 50% of fresh ionic liquid was needed after five runs to maintain continuous activity introduced.

14.3 Results & Discussion

The ionic liquid [bmIm] OH was synthesized according to the procedure reported in the literature. Reactions were typically carried out by addition of methylacrylate (1.5mmol) to the ionic liquid (1mL) containing 4-nitroimidazole (1.0mol).Generally, after 1-2h , the reaction solution turned pellucid, indicating there activity came to an end. Ethyl acetate was used to extract the adduct, and flash chromatography was used to purify it. The use of IR, 1H NMR, 13C NMR, and ESI-MS to confirm this compound's structure. The ionic liquid was cleaned with ethylether, vacuum-dried for two hours at 90°C to remove any water that had become trapped in moisture, and then reused for subsequent reactions. There covered ionic liquid could be used for four runs with 91%,96%,90% and 92% yields. After five runs about 50% fresh ionic liquid was added to maintain consistent activity due to the loss of ionic liquid.

14.4 Conclusion

Without the need for an organic solvent or a traditional catalyst, we have created a process using the basic ionic liquid [bmIm] OH to give an effective and practical technique for Michael addition of N-heterocycles to carbonyl compounds.. There actions have been carried out at room temperature to afford the desired products in good yields in short reaction times. This strategy is quite general and it works with a broad range of N-heterocycles, including five membered N-heterocycles, pyrimidines and purines. The obtained N-heterocycle derivatives may be potentially pharmacological alternatives. The complete study of the biological activity of the new derivatives will be reported in course.

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