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Short Communication

Green Synthesis of 2,4,5-trisubstituted Imidazole Derivatives using Silica Tungstic Acid as an Efficient Catalyst

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Abstract

Synthesis of 2,4,5-trisubstituted imidazole derivatives via one-pot three components reaction of benzil, aldehydes and ammonium acetate by using silica tungstic acid as an efficient catalyst. The reaction was performed under mild reaction conditions with microwave irradiation as an energy source. Compared with the classical reaction conditions, this method has an advantage of significant enhance in yields (86–95%). The advantages of this protocol include the excellent yield, operational simplicity, short reaction time and avoidance the excess use of organic solvents. The catalyst was separated and reused for several time cycles without any significant loss of activity. Products were identified using physical and IR, ^{1}H and ^{13}C NMR, MS spectroscopic technique.

Keywords: 2,4,5-trisubstituted imidazole, Silica tungstic acid, Multicomponent reaction (MCR), Microwave assisted synthesis.

Introduction

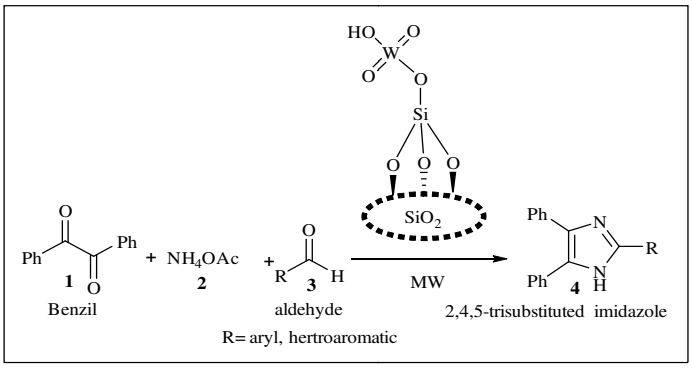
Multicomponent reaction (MCR) is type of organic reaction which give complex product from reaction of three or more starting compound in one pot. Since of operational simplicity, atom-economy, structural diversity, convergent character and complexity of the molecules in the reactions, they have attracted much attention[1,2].

Imidazole's and their derivatives, which usually have different biological activities, which performs important roles such as resourceful building blocks for the synthesis of natural products and it as therapeutic agents[3,4]. In specific 2,4,5-trisubstiuted imidazole's are biologically active and it's found in structure of a number of anti-inflammatory[5], anti-allergic[6], analgesic[7] and glucagon receptor antagonism[8]. In recently several catalysts and methods has been used for the synthesis of 2,4,5-trisubstituted imidazole. Few important catalysts are molecular iodine9, L-Proline[10], $UO_2(NO_3)_2.6H_2O$[11], $ZrOCl_2.8H_2O$[12], $Y(NO_3)_3.6H_2O$[13], $SnCl_2.2H_2O$[14], $ZrCl_4$[15]. These processes are quite costlier, involved long reaction times, unsatisfactory yield and environmental unfriendly.

Therefore, in this work, improvements have been sought continuously with simple, efficient and reusable silica tungstic acid as catalyst for synthesis of 2,4,5-trisubstituted imidazole as shown (Scheme-1).

Materials and Methods

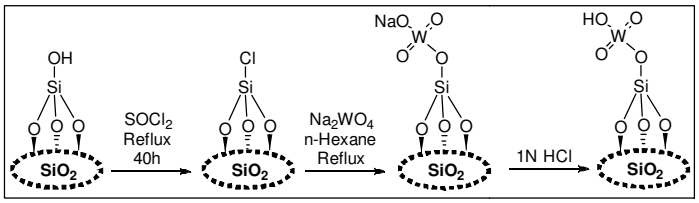
All chemical was used as it is. All melting points was determined on open capillary tube and it was uncorrected. An infrared (IR) spectrum was recorded on Bruker alpha FT-IR spectrometer. ^{1}H and ^{13}C NMR spectra was recorded on Bruker 400 MHz spectrometer using DMSO-d_6 as a solvent and TMS as internal standard. A mass spectrum was recorded on FINNIGAN-MAT 8430 mass spectrometer. Experiment in microwave irradiation was carried in Ragatech synthesizer system. Progress of reaction was monitored on TLC.



Scheme-1
Synthesis of 2,4,5-trisubstituted imidazole using silica tungstic acid

General Procedure: Preparation of silica tungstic acid (STA): Silica tungstic acid (STA) was synthesized by literature method[16] with slight modification. To a dried Silica gel 60-120mesh (5 g) in 150 mL RBF (Round bottomed flask) enclosed with condenser & calcium guard tube, $SOCl_2$ (thionyl chloride) (20 mL) was drop wise added and mixture was refluxed for 40 h. The resulting grayish-white silica chloride powder was

filtered and dried under vacuum. To a mixture of silica chloride (2 gm) and sodium tungstate (3.5 gm) in n-hexane (12 mL) was added. The mixture was refluxing under stirring condition at 69°C for 5 h. After completion of reaction, a reaction mixture was filtered than washed with deionized water and dried. Than resulting mixture stirred in to 0.1N HCl (35 mL) for two hours. Finally, a mixture was filtered and was with deionized water and dried under vacuum to afford silica tungstic acid (STA) (Scheme-2). Synthesized silica tungstic acid (STA) was confirmed by FTIR (Figure-1) comparison with literature[16].



Scheme-2
Preparation of silica chloride and silica tungstic acid

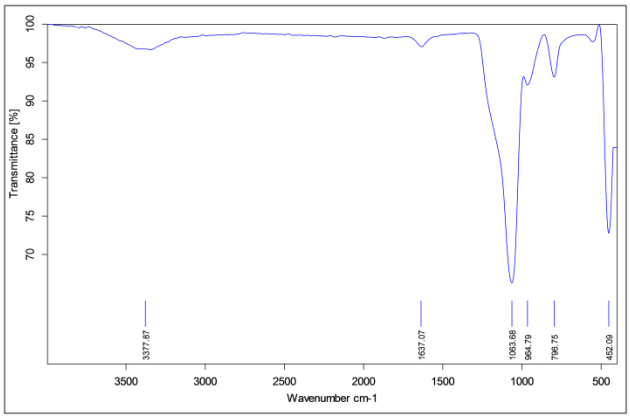


Figure-1
FT-IR Spectra of silica tungstic acid (STA)

Preparation of 2,4,5-trisubstituted imidazole derivatives using silica tungstic acid (STA): A mixture of aldehyde (1 mmol), benzyl (1mmol), ammonium acetate (2 mmol) and silica tungstic acid (STA) (20 wt%) were placed in 50 mL in RBF and place in microwave for required time. Reaction was monitored by using TLC. After completion of reaction, mixture was diluted with chloroform (12 mL) and reaction mass was stirred. The slurry was filtered to remove the catalyst and washed with chorofrom (4×5mL). Combined filtrate was evaporating on rotary-evaporator to obtain a solid residue. The solid residue was stirred in water than filtered and recrystallized from ethanol to give pure product. The product was characterized by IR, ^{1}H and ^{13}C –NMR spectroscopic data.

Results and Discussion

A efficient synthesis of 2,4,5-trisubustituted imidazole by using reusable silica tungstic acid as an catalyst. In the order to evaluate feasibility of silica tungstic acid for synthesis of 2,4,5-trisubustituted imidazole, the prototype reaction (Scheme-1) with mole ratio of 1:1:2 of benzaldehyde, benzil and ammonium acetate correspondingly, to achieved 2,4,5-triphenyl-1H-imidazole (4a) was shown under different conditions both in the presence and in absence of silica tungstic acid and result are given in Figure-2. In the absence of silica tungstic acid trace amount of product was obtained. Where as in the presence of silica tungstic acid (5 wt%) under the same condition's yield significantly increased. These result further studies were shown and it was establish that (20 wt%) of silica tungstic acid was ideal for reaction and offered a product of 95% yield in just 15 min. Extent of yield reached to maximum at 20wt% and no any additional growth show any benefits (Figure-2).

Silica tungstic acid was easily recovered from the reaction mixture by adding chloroform. Stirred reaction mixture followed by filtration for silica tungstic acid reusability experiments. The recovered silica tungstic acid was dried in oven at 75ºC for 2h. The recovered silica tungstic acid was reused five times under same reaction condition for synthesis of product 4a, as a prototype reaction, without any major loss of activity (Figure-3).

The general efficiency of this protocol was then studied for the synthesis of a variety of 2,4,5-trisubstituted imidazole derivatives (Table-1). As it can be seen in Table-1 various aldehyde reacted efficiently with benzil and ammonium acetate to give the anticipated 2,4,5- trisubstituted imidazole in good yields. Experiment was carried out in a series of aromatic aldehyde bearing either electron-withdrawing or electron-donating groups on the ring.

A mechanism for the catalytic activity of silica tungstic acid in synthesis of imidazole is displayed in Scheme-3.

After the protonation of carbonyl group of the aldehyde and the nucleophilic attack of nitrogen atom of ammonia, obtained from ammonium acetate to it, intermediate (I) is formed. In the presence of silica tungstic acid, intermediate (I) condenses with benzil to form intermediate (II) which in turn forms trisubstituted imidazole's by dehydration.

Table-1
Silica tungstic acid catalyzed solvent-free synthesis of 2,4,5-trisubstituted imidazoles[a]

Entry	R-CHO	Product	Time (min)	Yield(%)[b]
1	Ph	4a	15	95
2	4-OCH_3-C_6H_4	4b	17	92
3	2-OH- C_6H_4	4c	19	87
4	2-Furyl	4d	20	81
5	2-Thiophene	4e	18	85

[a]Reaction condition: Benzil (1mmol), aldehyde (1mmol), NH_4OAc (2mmol), STA(20wt%), [b]Isolated yields.

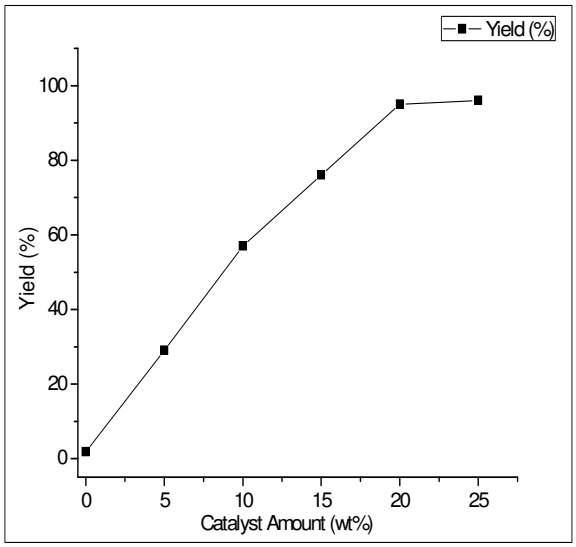


Figure-2
The effect of amount of Silica tungstic acid the preparation of 2,4,5-trisubstituted imidazole

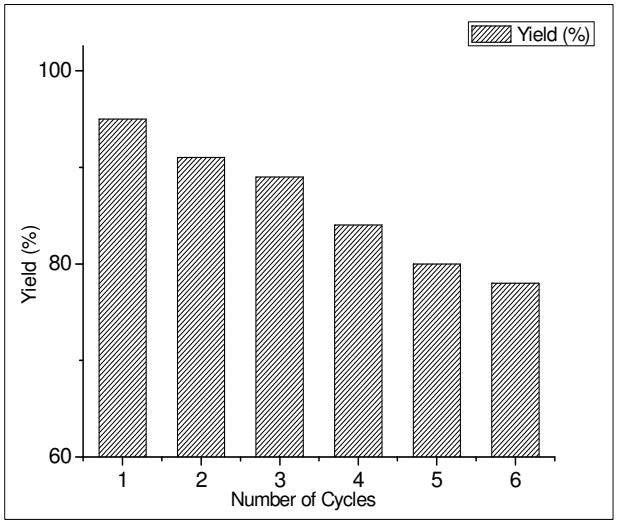
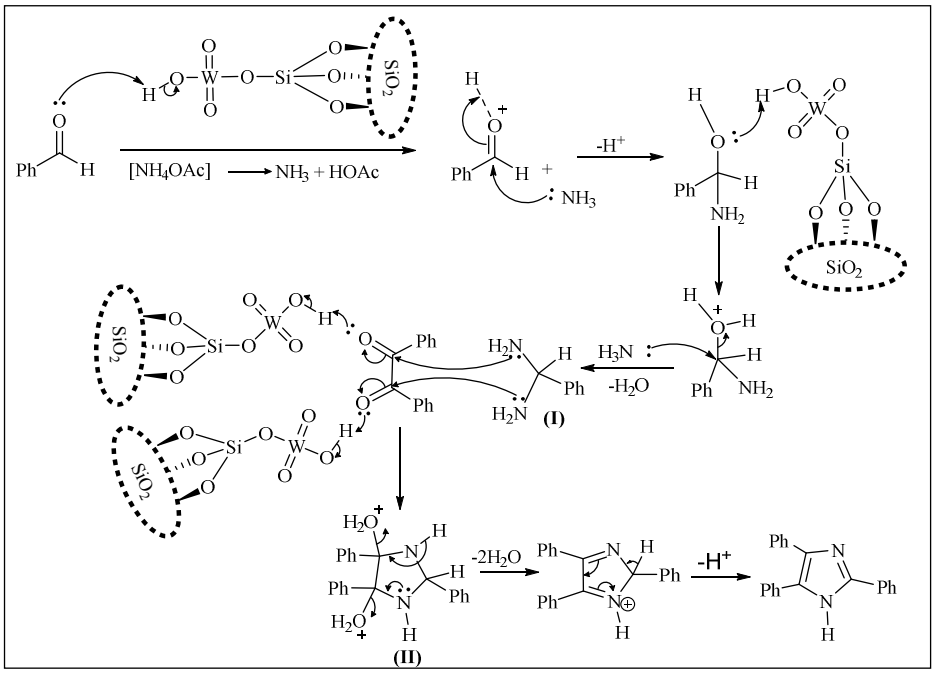


Figure-3
Recyclability of Silica tungstic acid in the synthesis of 2,4,5-trisubstituted imidazole



Scheme-3
Probable mechanism for the formation of 2,4,5-trisubstituted imidazole using Silica tungstic acid catalyst

Spectroscopic Data: 2,4,5-triphenyl-1*H*-imidazole (4a) : M.P.: 270-272 °C., IR (cm^{-1}): 3037, 1586, 1488, 1202, 1127, 764, 695; ^{1}H-NMR (400 MHz, DMSO-d_6): δ 7.23 to 7.59(m, 13H), 8.11 (d, 2H), 12.7(s, 1H); ^{13}C NMR (100 MHz, DMSO-d_6): δ 125.18, 126.48, 127.06, 127.74, 128.16, 128.21, 128.44, 128.65, 130.34, 131.08, 135.17, 137.11, 145.50; MS: m/z 296.13(M).

Conclusion

In present work, we have synthesized Silica tungstic acid and it has been employed for the synthesis of 2,4,5-trisubstituted imidazole's using a microwave reactor under solvent free condition. The attractive features of this protocol are its greenness with respect to mild reaction conditions, solvent free, short reaction time, recyclability of catalyst and high yield.

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