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SBA-15/TFE (SBA-15/2,2,2-trifluoroethanol) as a suitable and effective metal-free catalyst for the preparation of the tri- and tetra-substituted imidazoles via one-pot multicomponent method

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Adduct of unfunctionalized SBA-15 mesoporous and 2,2,2-trifluoroethanol (SBA-15/TFE) acts as a catalyst for the reaction between of an aldehyde, amine and ammonium acetate with benzil to provide an entry in the synthesis of high substituted imidazole derivatives as a synthetic potential and a pharmaceutical interest compound via one-pot multicomponent method. The present method carries the advantages of being performed under the neutral conditions and requires no activation or modification of the substrates. The catalyst can be reused without an obvious loss of the catalytic activity.

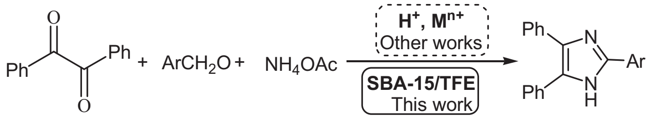
1. Introduction

In recent years, fluorinated alcohols (R_FOH) have been made a display of their unique properties to be as solvents, co-solvents and additives in the organic synthesis [1–3]. The ready availability of fluorinated alcohols has initiated a boom in their applications in the past decade [4]. The utility of fluorinated alcohols such as 2,2,2-trifluoroethanol (TFE) as a reaction medium and co-solvents was highlighted by Bégué et al. and Uneyama [4]. Based on their proposed the unique nature of fluorinated alcohols, the acid-catalyzed organic process can be done in fluorinated alcohols [4].

Recently, the multicomponent reactions over high surface area functionalized-porous material such as MCM-41/SO_3H and SBA-15/SO_3H have lately been studied [5]. In these studies, the researchers have tried to find the optimized conditions for the organic reactions to increase the selectivity or yield of the reaction. Normally unfunctionalized MCM-41 and SBA-15 have shown no acceptable reactivity in the course of acid-catalyzed multicomponent reactions [5]. This work set in motion by multicomponent reaction of benzil, aldehyde with ammonium acetate in reflux ethanol medium over unfunctionalized SBA-15. In this condition the yield of imidazole was less than 20% for 30 min. To our surprise, the yield of imidazole increased due to the change in the medium of reaction from ethanol to TFE.

The different substituted imidazoles are varied biological activities [6]. In the last decade numerous methods have been developed for the synthesis of the substituted imidazoles using various catalytic systems including molecular iodine [7], SiO_2/$NaHSO_4$ [8], $BF_3{\cdot}SiO_2$ [9], H_3PO_4 [10], H_2SO_4 [11] and AcOH [12]. Many of the reported synthetic protocols for the synthesis of imidazoles suffer from one of the disadvantages or more such as the harsh reaction condition, the poor yields, the prolongation of time in the reaction and the use of heavy metal catalysts hazards.

Recently, we developed the synthetic methods for the synthesis of the biologically interest heterocycles by multicomponent reaction [13]. The preliminary results of our done investigations have formed the subject of this paper for they expose some novel reactivity patterns of the SBA-15/TFE (Scheme 1).



Scheme 1.

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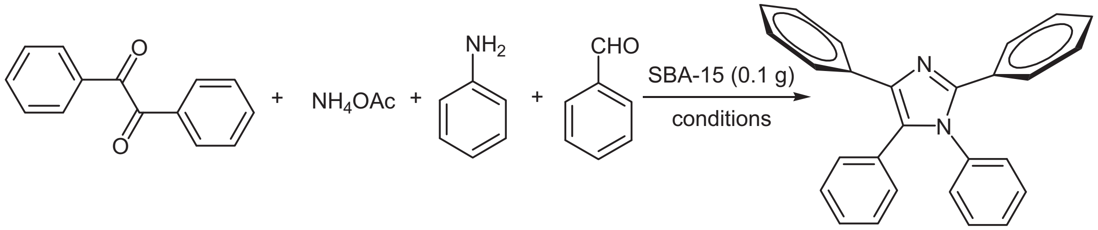


Scheme 2.

Table 1
Study of conditions by model reaction.[a]

Solvent	Temp (°C)	Time (h)	% yield
EtOH	r.t.	24	15<
EtOH	70	24	50
MeOH	95	14	53
CCl_3CH_2OH	100	10	45
TFE	120	3	83
TFE	90	3	82

[a] Reaction condition: benzil (1 mmol), aldehyde (1 mmol), amine (1 mmol), and NH_4OAc (1.3 mmol) was added SBA-15 (0.1 g) and heated to appropriate temperature in 3 mL solvent.

2. Results and discussion

Herein the condensation of benzil, ammonium acetate and benzaldehyde with aniline selected as a model (Scheme 2).

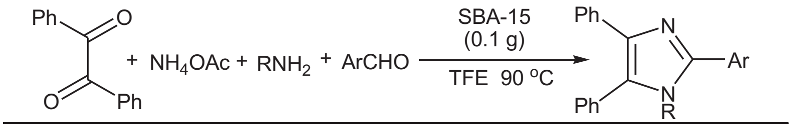
As the model reaction set over the unfunctionalized SBA-15 [14] the given yield for imidazole was less than 25% for 30 min at 90 °C in a medium of ethanol, but by changing the medium in the reaction from ethanol to TFE, then the yield of imidazole became more than 45% obtained in the same temperature and with the same amount of SBA-15 during 30 min, while in the absence of SBA-15 the yield was about 25%.

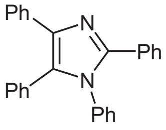
The given result shows an unusual behavior for TFE in the presence of silica-mesoporous SBA-15 nanomaterial (Fig. 1). A further increase in the amount of SBA-15 (0.1 g) and reaction temperature of reaction showed not significant effect on the yield of product or time of reaction.

Owing to the fact that both the nature of the alcohols and its amount may play an important role in this process, different types and amount of alcohols screened for this reaction.

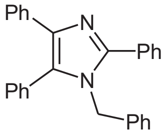
First the model reaction examined in ethanol, methanol, 2,2,2-trichloroethanol and 2,2,2-trifluoroethanol medium over the SBA-15. The reaction in which 2,2,2-trifluoroethanol used as a medium in the presence of the SBA-15, gave condensation products were obtained in 82% yield at 90 °C, for 3 h (Table 1).

Table 2
Synthesis of 1,2,4,5-tetrasubstituted imidazoles in the presence of SBA-15/TFE.[a]

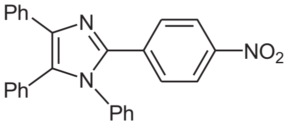




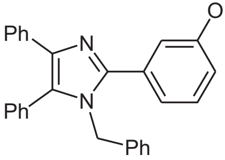
(**1a**, 82%)



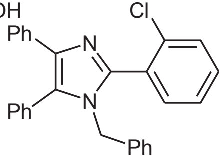
(**1b**, 90%)



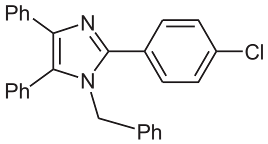
(**1c**, 80%)



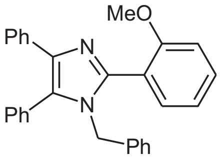
(**1d**, 82%)



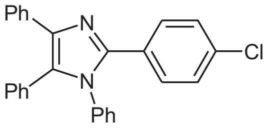
(**1e**, 92%)



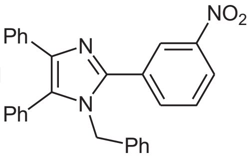
(**1f**, 90%)



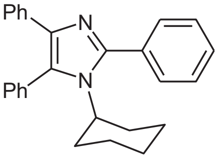
(**1g**, 82%)



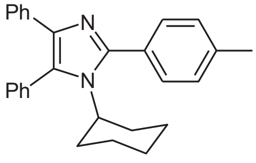
(**1h**, 92%)



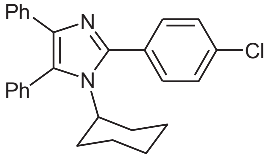
(**1i**, 80%)



(**1j**, 83%)



(**1k**, 86%)



(**1l**, 89%)

[a] Reaction condition: benzil (1 mmol), aldehyde (1 mmol), amine (1 mmol), and NH_4OAc (2.5 mmol) was added SBA-15 (0.1 g) and heated at 90 °C in 3 mL TFE.

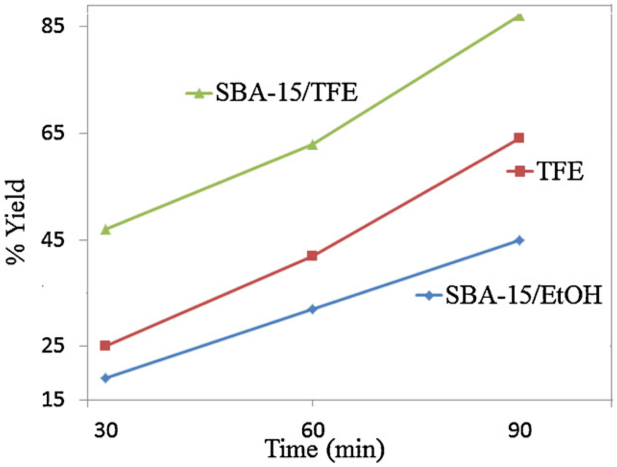


Fig. 1. Model reaction over the SBA-15/EtOH, TFE and SBA-15/TFE: influence of trifluoroethanol as a catalytic additive.

Also, the yield of the reaction was not sensitive to the amount of TFE.

These results encouraged us to investigate the generality of this new SBA-15/TFE adducted protocol system for various aldehydes and amines under the optimized conditions. The results are given in Table 2.

This reaction was further explored for the synthesis of 2,4,5-trisubstituted imidazoles by the condensation of aldehyde, benzil with ammonium acetate under the similar conditions and at the desired products produced in high yields (Table 3).

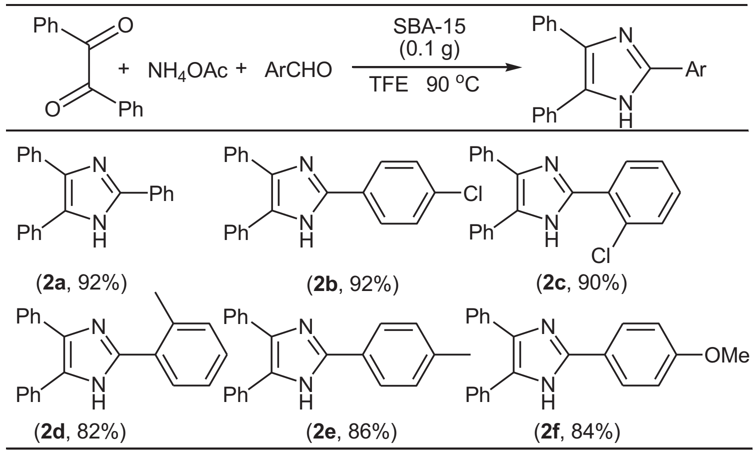
We have not yet established a mechanism process for the synthesis of imidazoles over the SBA-15/TFE adduct in an experimental manner, though a possible explanation [15–17] is proposed in Scheme 3.

3. Conclusion

In summary, the reaction of aldehyde, amine and ammonium acetate with benzil in the presence of unfunctionalized SBA-15 and TFE provides a simple one-pot entry into the synthesis of high substituted imidazole derivatives as synthetic potential and a pharmaceutical interest compounds. The present method carries the advantages of being performed under the neutral conditions and requires no activation or modification of the substrates.

In optimized condition the recycling performance of SBA-15 in the model reaction investigated showing the catalyst could be reused five times at least without a significant decrease in the catalytic activity. Further studies and effort to extend the scope of this method for other useful reactions are underway.

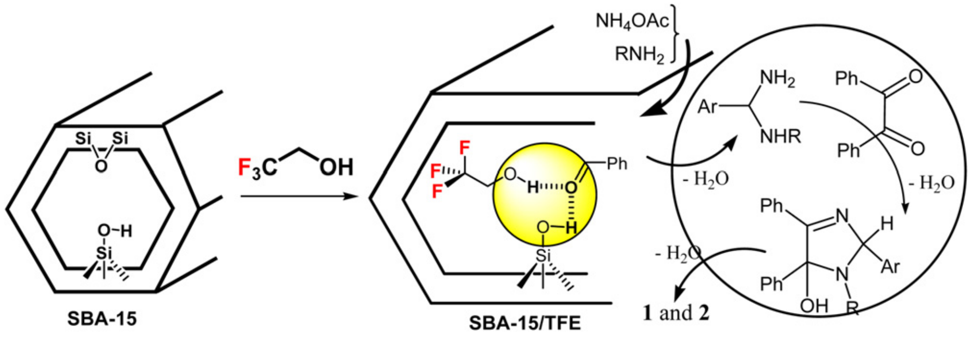
Table 3
Synthesis of 2,4,5-trisubstituted imidazoles over SBA-15/TFE.[a]



(**2a**, 92%) (**2b**, 92%) (**2c**, 90%)

(**2d**, 82%) (**2e**, 86%) (**2f**, 84%)

[a] Reaction condition: benzil (1 mmol), aldehyde (1 mmol), and NH_4OAc (3 mmol) was added SBA-15 (0.1 g) and heated at 90 °C in 3 mL TFE.



Scheme 3.

4. Experimental

4.1. Chemicals and apparatus

All reagents were obtained from Merck (Germany) and Fluka (Switzerland) and were used without further purification. Melting points were measured on an Electrothermal 9100 apparatus. Progress of reactions was monitored by Thin Layer Chromatography (TLC). ^{1}H and ^{13}C NMR spectra were measured ($CDCl_3$) with a Bruker DRX-300 AVANCE spectrometer at 300 and 75 MHz, respectively. IR spectra were recorded on a Shimadzu IR-460 spectrometer, absorbencies are reported in cm^{-1}.

4.2. General procedure

To a mixture of benzil (1 mmol), aldehyde (1 mmol), amine (1 mmol), and ammonium acetate (1.3 mmol) was added SBA-15 (0.1 g) and heated (schlenk flask) at 90 °C in 3 mL TFE. When the reaction was complete as judged by TLC, ethanol (8 mL) was added and the reaction mixture was filtered and the remaining solid was washed with warm ethanol (3 × 5 mL) in order to separate the SBA-15. The products were recrystallized from ethanol. For the synthesis of the tri-substituted imidazoles, reagents were only benzil (1 mmol), aldehyde (1 mmol) and ammonium acetate (3 mmol) in same condition. All the products were previously reported by other method and were characterized by comparing physical data with those. Spectroscopic data for selected examples are shown below.

1,2,4,5-Tetraphenyl-1H-imidazole (**1a**) IR (KBr ν_{max}/cm^{-1}): 1443, 1479, 1496, 1601. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 7.05 (2 H, d, *J* 7.8 Hz), 7.15 (2 H, d, *J* 6.9 Hz), 7.18–7.27 (12 CH, m), 7.44 (2 H, t, *J* 7.5 Hz), 7.62 (2 H, t, *J* 7.5 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 126.60, 127.41, 127.95, 128.09, 128.16, 128.24, 128.34, 128.43, 128.96, 129.06, 130.52, 130.65, 130.85, 131.12, 134.43, 137.11, 138.27, 146.93.

1-Benzyl-2,4,5-tetraphenyl-1H-imidazole (**1b**) IR (KBr ν_{max}/cm^{-1}): 1389, 1479, 1492, 1601. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 5.12 (2 H, s), 6.80 (2 H, s), 20–7.39 (12 CH, m), 7.57–7.65 (6 CH, m). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 48.27, 126.01, 126.34, 126.76, 127.33, 128.06, 128.23, 128.59, 128.78, 128.87, 129.06, 129.88, 131.08, 137.56, 138.46, 148.41.

2-(4-Nitrophenyl)-1,4,5-triphenyl-1H-imidazole (**1c**) IR (KBr ν_{max}/cm^{-1}): 1460, 1492, 1520, 1608. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 7.07–7.15 (4 CH, m), 7.26–7.35 (8 CH m), 7.60 (3 H, t, *J* 7.2 Hz), 8.09 (2 H, d, *J* 8.1 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 123.43, 127.03, 127.30, 128.25, 128.29, 128.38, 128.48, 129.05, 129.55, 129.91, 131.00, 132.46, 133.84, 136.50, 136.61, 144.30, 147.03.

1-Benzyl-2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole (**1f**) IR (KBr ν_{max}/cm^{-1}): 1416, 1448, 1499, 1600. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 6.81 (2 H, d, *J* 3.6 Hz), 7.14–7.27 (9 CH, m), 7.36 (4 H, t, *J* 8.1 Hz), 7.59–7.62 (4 CH, m). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 48.29, 125.87, 126.54, 126.80, 127.02, 128.16, 128.73, 128.79, 128.84, 128.89, 129.07, 130.24, 130.45, 130.75, 130.02, 134.28, 134.99, 137.31, 138.28, 146.86.

2-(4-Chlorophenyl)-1,4,5-triphenyl-1H-imidazole (**1h**) IR (KBr ν_{max}/cm^{-1}): 1446, 1479, 1496, 1597. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 7.04–7.15 (4 CH, m), 7.21–7.30 (11 CH, m), 7.38 (2 H, d, *J* 7.8 Hz), 7.41 (2 H, d, *J* 7.5 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 126.73, 127.36, 128.09, 128.21, 128.38, 128.51, 129.00, 129.25, 130.09, 130.42, 131.09, 131.17, 134.25, 134.32, 136.90, 138.44, 145.75

2,4,5-Triphenyl-1H-imidazole (**2a**) IR (KBr ν_{max}/cm^{-1}): 1441, 1461, 1488, 1587, 1601, 3037. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 7.19–7.46 (9 CH, m), 7.55 (4 H, t, *J* 6.6 Hz), 7.90 (2 H, d, *J* 8.1 Hz). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 125.31, 127.50, 127.83, 128.60, 128.90, 129.02, 129.91.

*2-(4-Chlorophenyl)-4,5-diphenyl-1*H*-imidazole* (**2b**) IR (KBr ν_{max}/cm^{-1}): 1434, 1503, 1602, 3028. ^{1}H NMR (300.1 MHz, $CDCl_3$): δ = 7.27–7.39 (8 CH, m), 7.51–7.53 (4 CH, m), 7.80–7.82 (m, of Ar). ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 126.57, 127.63, 127.82, 128.09, 128.62, 129.07, 134.74, 144.88.

Acknowledgments

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