A Convenient Method for the Preparation of 2,4,5-triaryl Imidazoles Using Barium Chloride Dispersed on Silica Gel Nanoparticles (BaCl₂-nano SiO₂) as Heterogeneous Reusable Catalyst

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Abstract: A simple and eco-friendly procedure for the synthesis of 2,4,5-triaryl imidazoles by using Barium chloride dispersed on silica gel nanoparticles (BaCl₂-nano SiO₂) as heterogeneous reusable catalyst in high yield under thermal conditions has been described.

Keywords: 2,4,5-triaryl imidazole, BaCl₂-nano SiO₂, heterogeneous catalyst.

INTRODUCTION

Compounds containing imidazole skeletons exhibit important biological activities and play important roles in biochemical processes [1-3]. Also, large classes of imidazole derivatives are used as ionic liquids [4, 5]. Thus, these properties have instituted a diverse collection of synthetic approaches to these heterocycles. A number of routes have been developed for the synthesis of substituted imidazoles. In this content, 2,4,5-tri substituted imidazoles are generally synthesized by multi-component cyclo-condensation of 1,2diketones, α -hydroxyketones or α -ketomonoximes with aldehvdes and ammonium acetate which imparted from the assistance of sterically hindered organic bases such as DABCO [6], microwave irradiation [7-11], ionic liquids [12, 13] and Brønsted and Lewis acids in the case of liquid [14, 15], solid [16-21] or supported on solid materials such as silica and alumina [22-26]. Some of these procedures have certain limitations such as tedious process, long reaction times and harsh reaction conditions. Moreover, different and effective literatures for the preparation of highly substituted imidazoles are present, including hetero-cope rearrangement [27], four-component condensation of aryl glyoxals, primary amines, carboxylic acids and isocyanides on Wang resin [28], reaction of N-(2-oxo)-amides with ammonium trifluoroacetate [29], reaction of N-alkyl-N-(β-keto)amides with ammonium acetate [30], cyclo-addition reaction of mesoionic 1,3-oxazolium-5-olates with N-(arylmethylene)benzenesulfonamides [31] and addition of a substituted amino alcohol to a thioamide and subsequent oxidation with PDC [32]. Although these reports prepare a wide range of imidazoles but their procedures are relatively expensive for use in the laboratory and industry.

The use of heterogeneous solid supported Lewis acid catalysts instead of their unsupported salts have some advantages and they are desirable to achieve effective catalyst handling, product purification and a decrease in waste production. Some examples of them have been performed as inexpensive catalysts that can be easily separated, reused and are not contaminated by the products [33].

Herein BaCl₂-nano SiO₂ [34, 35] was employed as a useful catalyst for the synthesis and easy purification of 2,4,5-triaryl imidazole derivatives *via* one-pot three-component cyclo-condensation of benzil, ammonium acetate and aldehydes under thermal conditions in high yields (Scheme 1).

EXPERIMENTAL

All reagents were purchased from Merck and Aldrich and used without further purification. All yields refer to isolated products after purification. Products were characterized by spectroscopic data (IR, NMR spectra) and melting points with authentic samples. The NMR spectra were recorded on a Bruker Avance DEX 400 MHz instrument. The spectra were measured in DMSO-d₆ relative to TMS (0.00 ppm). IR spectra were recorded on a JASCO FT-IR 460plus spectrophotometer. All of the compounds were solid and solid state IR spectra were recorded using the KBr disk technique. Elemental analysis was performed on a Heraeus CHN-O-Rapid analyzer. Melting points were determined in open capillaries with a BUCHI 510 melting point apparatus. TLC was performed on silica gel polygram SIL G/UV 254 plates.

General Procedure

To a mixture of aldehyde (1 mmol), benzil (1 mmol) and NH₄OAc (3 mmol), BaCl₂-nano SiO₂ (0.025 g) was added

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Scheme 1.

and the mixture stirred at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction, the mixture was dissolved in hot ethanol and filtered. Solvent was evaporated and the corresponding pure product was obtained after recrystallization in ethanol. The results are summarized in Table **3**.

Selected Data

2-(4-tert-butylphenyl)-4,5-diphenyl-1H-imidazole

m.p: 290-292 °C; ¹H NMR (400 MHz, DMSO-d₆): 1.34 (s, 9H), 7.23 (t, J = 7.2 Hz, 1H), 7.32 (t, J = 7.6 Hz, 2H), 7.38 (t, J = 7.2 Hz, 1H), 7.45 (t, J = 7.2 Hz, 2H), 7.51 (m, 4H), 7.57 (d, J = 7.6 Hz, 2H), 8.03 (d, J = 8.4 Hz, 2H), 12.63 (s, 1H, NH); ¹³C NMR (100 MHz, DMSO-d₆): $\delta = 31.5$, 34.9, 125.5, 125.9, 126.9, 127.6, 128.2, 128.3, 128.4, 128.6, 128.9, 129.1, 131.6, 131.7, 135.7, 137.4, 146.0, 146.1, 151.3 ppm; IR (KBr): 3417, 3058, 2963, 2903, 1603, 1586, 1504, 1492, 1450, 1434, 1407, 1392, 1362, 1321, 1268, 1201, 1181, 1156, 1134, 1105, 1071, 1025, 967, 946, 839, 774, 765, 720, 696 cm⁻¹; Found: C, 85.25; H, 6.93; N, 7.99 C₂₅H₂₄N₂; requires: C, 85.19; H, 6.86; N, 7.95%].

2-(3-bromophenyl)-4,5-diphenyl-1H-imidazole

m.p: 308-310 °C; ¹H NMR (400 MHz, DMSO-d₆): 7.25 (t, J = 6.8 Hz, 1H), 7.32 (t, J = 6.8 Hz, 2H), 7.40 (t, J = 6.8 Hz, 1H), 7.44-7.59 (m, 8H), 8.10 (d, J = 7.6 Hz, 1H), 8.32 (s, 1H), 12.84 (s, 1H, NH); ¹³C NMR (100 MHz, DMSO-d₆): $\delta = 122.6$, 124.5, 127.2, 127.6, 128.0, 128.4, 128.7, 128.9, 129.2, 131.3, 131.4, 132.9, 135.4, 137.9, 144.2, 144.3 ppm; IR (KBr): 3423, 3063, 2963, 2923, 2852, 1602, 1583, 1502, 1478, 1456, 1412, 1379, 1321, 1204, 1132, 1071, 1026, 996, 969, 915, 890, 841, 766, 759, 723, 698 cm⁻¹; Found: C, 67.27; H, 4.11; N, 7.55 C₂₁H₁₅BrN₂; requires: C, 67.21; H, 4.03; N, 7.47%].

RESULTS AND DISCUSSIONS

The processes for the preparation of 2,4,5-triaryl imidazoles are usually carried out in the presence of Lewis and Brønsted acidic catalysts [7-26] and thermal condition. It was observed that in a control reaction where no catalyst was used, no product was formed and the conversion of benzil was found to be 0% after 5 h. This shows that the catalyst is



In order to estimate the catalytic efficiency of BaCl₂-nano SiO₂ and to determine the most appropriate reaction conditions, at first a model study was carried out in the synthesis of 2,4,5-triphenyl-1*H*-imidazole using the reaction of benzil, benzaldehyde and ammonium acetate in different systems of reaction conditions (Table 2).

Among the various tested amounts of the catalyst and temperature, the condensation of benzil, benzaldehyde and ammonium acetate was best catalyzed by 0.025 g of catalyst (Table 2). In order to improve the yields, we performed reaction using different quantities of reagents. The best results were obtained with 1:1:3 molar ratios of benzil, aryl aldehyde and ammonium acetate, respectively. The results are summarized in Table 2.

Using these optimized reaction conditions, the scope and efficiency of these procedures were explored for the synthesis of corresponding 2,4,5-triaryl imidazole derivatives.

Generally, the cyclo-condensation reaction between benzil, arylaldehydes and ammonium acetate proceeded well and afforded the desired products (Table **3**, Entries 1-23) in good to excellent yields. As shown in Table **3**, the reaction was successfully compatible with a variety of aryl aldehydes having electron-donating and electron-withdrawing substituents.

In all the cases, aromatic aldehydes containing electronwithdrawing groups (such as nitro-) gave shorter time than



Scheme 2. preparation of 2,4,5-triphenyl-1*H*-imidazole using BaCl₂-nano SiO₂ as catalyst.

Table 1. Catalyst Screening

Entry	Catalyst	Time (min)	Yield (%) ^a
1	-	300	-
2	MgCl ₂ (0.02 mmol)	140	35
3	MgO (0.02 mmol)	300	25
4	$SiO_2-MgCl_2 (0.02 \text{ g} = 0.02 \text{ mmol } MgCl_2)$	150	35
5	ZnO (0.02 mmol)	210	25
6	CaCl ₂ (0.02 mmol)	170	15
	SiO_2 -CaCl ₂ (0.025 g = 0.02 mmol CaCl ₂)	210	20
7	BaCl ₂ (0.02 mmol)	110	40
8	SiO_2 -BaCl ₂ (0.05 g = 0.02 mmol BaCl ₂)	120	42
9	$BaCl_2$ -nano $SiO_2 (0.05 g = 0.02 mmol BaCl_2)$	100	47

^aIsolated yield; Reaction condition: benzaldehyde (1 mmol), benzyl (1 mmol), and ammonium acetate (3 mmol); solvent-free, 100 °C.

Table 2. Optimization of the Reaction Conditions in the Synthesis of 2,4,5-triphenyl-1*H*-imidazole Under Solvent-Free Condition

Entry	Catalyst	T (°C)	Time (min)	Yield (%) ^a
1	0.05	r.t.	300	-
2	0.05	80	250	30
3	0.05	100	100	47
4	0.05	130	12	83
5	0.1	130	10	82
6	0.075	130	12	86
7	0.025	130	15	89
8	0.01	130	30	86
9	0.005	130	70	75

^aIsolated Yield.

Table 3. Synthesis of 2,4,5-triaryl Imidazoles Using BaCl₂-nano SiO₂ as Catalyst

Entry	Aldehyde	Amine source	Time (min)	Yield (%) ^a
1	Benzaldehyde	NH4OAc	15	89
2	3-Hydroxybenzaldehyde	NH ₄ OAc	120	80
3	4-Hydroxybenzaldehyde	NH4OAc	160	67
4	4-Methoxybenzaldehyde	NH4OAc	120	62
5	4-Methylbenzaldehyde	NH ₄ OAc	70	68
6	4-tert-Butylbenzaldehyde	NH ₄ OAc	25	83
7	2-Methylbenzaldehyde	NH ₄ OAc	85	79
8	2,4-Dimethylbenzaldehyde	NH ₄ OAc	100	70
9	2-Methoxybenzaldehyde	NH4OAc	200	78
10	2,3-Dimethoxybenzaldehyde	NH4OAc	200	70
11	3,4-Dimethoxybenzaldehyde	NH ₄ OAc	120	86
12	4-Fluorobenzaldehyde	NH4OAc	15	80
13	4-Bromobenzaldehyde	NH4OAc	10	71
14	3-Bromobenzaldehyde	NH ₄ OAc	10	79
15	2-Bromobenzaldehyde	NH ₄ OAc	30	81

(Table 3). Contd....

Entry	Aldehyde	Amine source	Time (min)	Yield (%) ^a
16	2-Chlorobenzaldehyde	NH ₄ OAc	60	89
17	4-Chlorobenzaldehyde	NH ₄ OAc	10	64
18	2,4-Dichlorobenzaldehyde	NH ₄ OAc	100	85
19	2-Nitrobenzaldehyde	NH ₄ OAc	30	80
20	3-Nitrobenzaldehyde	NH ₄ OAc	10	75
21	Furfural	NH ₄ OAc	120	59
22	Cyclohexanecarbaldehyde	NH ₄ OAc	220	80
23	Butyraldehyde	NH ₄ OAc	200	53

^aIsolated yields. All known products have been reported previously in the literature and were characterized by comparison of IR and NMR spectra with authentic samples [6-26].

that with electron-donating groups (such as methoxy-). Though *meta-* and *para-* substituted aromatic aldehydes gave good results, *ortho-*substituted aromatic aldehydes (such as 2-nitrobenzadehyde) gave lower yields and longer reaction time because of the steric effects. As a result, the reaction of aliphatic was successfully done to have the product in moderate yield (Table **3**; Entries 22-23).

The work-up procedure is very clear-cut, that is, the products were isolated and purified by simple filtration and crystallization from ethanol. Our protocol avoids the use of dry media during the reaction process, making it superior to the previous methods.

The reusability of the catalyst was tested in the synthesis of 2,4,5-triphenyl-1*H*-imidazole, as shown in Fig. (1). The catalyst was recovered after each run, washed 3 times with CH_2Cl_2 , dried prior to use and tested for its activity in the subsequent run and fresh catalyst was not added. The catalyst was tested for 5 runs. It was seen that the catalyst displayed very good reusability.



Fig. (1). Reusability of BaCl₂-nano SiO₂.

CONCLUSION

In conclusion, a reliable, rapid, and environmentally benign method for synthesizing 2,4,5-triaryl imidazoles has been developed. Compared to previous reported methodologies, the present protocol features simple operations, shorter reaction time, environmental friendliness and good yields. Another advantage of this protocol is the use of BaCl₂-nano SiO₂. This catalyst is one of the useful examples of heterogeneous catalysts which has been performed as an inexpensive catalyst that can be easily separated, reused and is not contaminated by the products and can be prepared from cheap materials. The present methodology offers several advantages such as excellent yields, simple procedure and shorter reaction times.

CONFLICT OF INTEREST

Declared none.

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