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# Scolecite as an efficient heterogeneous catalyst for the synthesis of 2,4,5-triarylimidazoles

**Research Article**

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**Abstract:** Natural scolecite has been found as an effective catalyst for the one-pot synthesis of 2,4,5-triarylimidazole derivatives *via* a three component reaction using benzil or benzoin, aldehydes and ammonium acetate. This method provides several advantages such as being environmentally benign, reusable, possessing high yields with increased variations of the substituents in the product and preparative simplicity.

**Keywords:** *Heterogeneous catalyst • 2,4,5-Triarylimidazoles • Three-component reaction*

## 1. Introduction

The imidazole nucleus is a fertile source of biologically important molecules. They are well known as inhibitors of P38MAP kinase [1], fungicides, herbicides [2], anti-inflammatory agents [3], antithrombotic agents [4], plant growth regulators [5] and therapeutic agents [6]. In addition, they are used in photography as photosensitive compounds [7]. Some substituted triarylimidazoles are selective antagonists of the glucagons receptor [8] and inhibitors of IL-1 biosynthesis [9].

Radziszewski and Jaap proposed the first synthesis of the imidazole core in 1882, starting from 1,2-dicarbonyl compounds, aldehydes and ammonia, to obtain 2,4,5-triphenylimidazole [10]. The great biological importance of the imidazole nucleus over the years has prompted the development of new, improved methodologies. Grimmett and *et al.* proposed the synthesis of the imidazole ring using nitriles and esters [11]. A literature survey reveals several methods for the synthesis of 2,4,5-triarylimidazoles using $ZrCl_4$ [12], zeolites HY/silica gel [13], $NaHSO_3$ [14], sulphanilic acid [15], iodine [16], ceric ammonium nitrate [17], oxalic acid [18], ionic liquids [19] and also by microwave irradiation using acetic acid [20]. Each of the above methods for this reaction has its own merits, while some of the methods are plagued by the limitations of poor yield, longer reaction time, difficult work-up and effluent pollution. Moreover, there are a relatively limited number of reports on the synthesis of 2,4,5-triarylimidazoles. Consequently, there is scope for further work towards increased variations of the substituents in the product, the use of mild conditions and improvement of yields.

In recent years, the use of heterogeneous catalysts has received considerable interest in various disciplines, including organic synthesis. Synthetic organic routes using heterogeneous catalysts have an advantage over their homogeneous counterparts as the catalyst can be easily recycled. Since the last decade there has been increased improvement in the synthetic methodology

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due to the use of solid acid catalysts, such as clays and zeolites [21-23].

In view of the current activity in the area of multi-component reactions, there is merit in developing a truly catalytic method for the formation of 2,4,5-triarylimidazoles. Scolecite [24] is a natural zeolite that is available worldwide, it is inexpensive, non-toxic and reusable and has Lewis and Bronsted acidic sites that permit it to act as a bi-functional heterogeneous catalyst in an eco-friendly manner.

In continuation to our work in synthesis of organic compounds using heterogeneous catalyst [24-26], herein, we report a very simple, fast and general method for the synthesis of 2,4,5-triarylimidazoles using natural scolecite as a catalyst. Our methodology offers several advantages including mild reaction conditions, cleaner reaction, high yield of products as well as a simple experimental and isolation procedures which make it a useful and attractive process for the synthesis of these compounds.

## 2. Experimental Procedures

All chemicals were purchased from Aldrich and Rankem Chemicals Limited and used as received without purification. Scolecite is natural zeolite collected from Satara valley, Aurangabad (MS) Deccan traps of India. The uncorrected melting points of compounds were taken in an open capillary in a paraffin bath. IR spectra were recorded on a Jasco FTIR-4100 spectrophotometer. $^1$H NMR spectra were recorded on an 80 MHz FT-NMR spectrometer in $CDCl_3$ as a solvent and chemical shift values are recorded in units δ (ppm) relative to tetramethylsilane ($Me_4Si$) as an internal standard.

The naturally occurring scolecite zeolite was collected from the Ellora valley, village Satara, Aurangabad, Maharashtra, Deccan traps of India. It was subsequently washed with distilled water and acetone for several times, dried and crushed into fine powder which was further washed with distilled water 3–4 times and dried at 110°C in an oven. The resulting sample was heated at 500°C in high temperature muffle furnace (SONAR) for 1 h at rate 3°C per minute. The sample was naturally cooled and used in organic synthesis. We have shown its application earlier in the synthesis of 3,4-dihydropyrimidin-2(1H)-ones [21]. The surface area, pore volume, pore diameter of catalyst was determined by the nitrogen adsorption on Quantachrome Autosorb Instrument and acidity of the sample measured by Temperature Programmed Desorption (TPD) of ammonia on Quantachrome TPR.

### 2.1 General procedure for synthesis of 2,4,5-triarylimiazole derivatives

A mixture of benzil or benzoin (5 mmol), aromatic aldehyde (5 mmol), ammonium acetate (10 mmol) and scolecite (2 wt% with respect to initial concentration of reactant) was refluxed in ethanol (15 mL) for the time as mentioned in Table 1. The reaction was monitored by TLC. After completion of reaction, the reaction mixture was poured into crushed ice and the solid product, which separated, was filtered and recrystallized from ethanol to obtain pure compounds.

### 2.2 Spectroscopic data

2,4,5-Triphenyl-1H-imidazole (**4a**). IR (KBr, $cm^{-1}$): 3450 (N-H), 3050 (C-H), 1600 (C=C), 1580 (C=N). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm) : 7.15-8.00 (m, 15H, Ph), 9.20 (br s, NH).
EIMS (m/z, %): 297 (M+1).

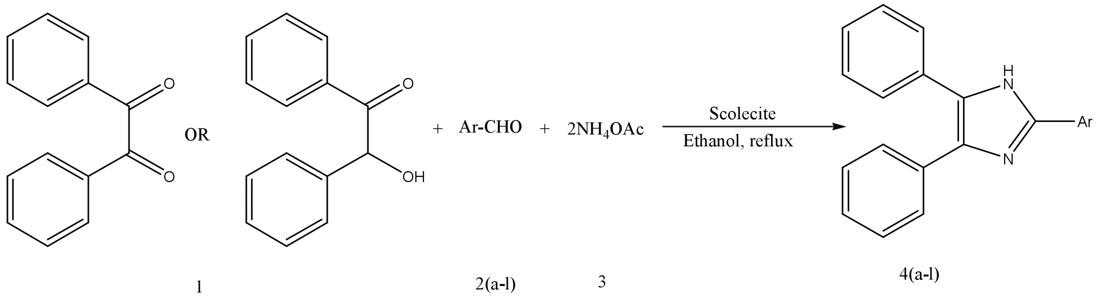
2-(4-Chlorophenyl)-4,5-diphenyl-1H-imidazole (**4c**). IR (KBr, $cm^{-1}$): 3450 (N-H), 1600 (C=C), 1580 (C=N). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 7.10-7.60 (m, 10H, Ph), 7.35 (d, 2H, J = 10 Hz, Ar), 7.85 (d, 2H, J = 10 Hz, Ar).
EIMS (m/z, %): 331 (M+1).

2-(4-Methylphenyl)-4,5-diphenyl-1H-imidazole (**4d**). IR (KBr, $cm^{-1}$): 3450 (N-H), 1600 (C=C), 1585 (C=N). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 2.30 (s, $CH_3$), 7.10-7.60 (m, 10H, Ph), 7.70 (d, 2H, J = 10 Hz, Ar), 7.30 (d, 2H, J = 10 Hz, Ar).
EIMS (m/z, %):311 (M+1).

2-(4-Methoxyphenyl)-4,5-diphenyl-1H-imidazole (**4e**). IR (KBr, $cm^{-1}$): 3450 (N-H), 1610 (C=C), 1575 (C=N), 1385 (C-O). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 3.90 (s, $OCH_3$), 7.05 (d, 2H, J = 8.8 Hz, Ar), 7.30-7.80 (m, 10H, Ph), 7.90 (d, 2H, J = 8.8 Hz, Ar).
EIMS (m/z, %): 327 (M+1).

2-(4-Nitrophenyl)-4,5-diphenyl-1H-imidazole (**4g**). IR (KBr, $cm^{-1}$): 3400 (N-H), 1580 (C=N), 1515 ($NO_2$), 1335 ($NO_2$). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 7.15-7.70 (m, 10H, Ph), 7.90-8.25 (AB, 4H, J .9 Hz, Ar).
EIMS (m/z, %): 342 (M+1).

2-(4-Dimethylaminophenyl)-4,5-diphenyl-1H-imidazole (**4h**). IR (KBr, $cm^{-1}$): 3050 (C-H), 2850 (C-H), 1615 (C=C), 1600 (C=N), 1360 (C-N). $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 2.90 (s, $2CH_3$), 6.60 (d, 2H, J = 8.9 Hz, Ar), 7.10-7.60 (m, 10H, Ph), 7.70 (d, 2H, J = 8.9 Hz, Ar).
EIMS (m/z, %): 340 (M+1).



**Scheme 1.** Synthesis of 2,4,5-triarylimidazole derivatives using benzil or benzoin **(1)**, aldehydes **(2)**, ammonium acetate **(3)** and scolecite as a catalyst in ethanol.

2-(2-Furyl)-4,5-diphenyl-1H-imidazole (**4k**). IR (KBr, cm$^{-1}$): 639, 719, 874, 1169, 1210, 1660, 2470, 2993, 3316 cm$^{-1}$. $^1$H NMR ($CDCl_3$, 80 MHz, δ, ppm): 7.21 (m, 1H, NH), 7.46–7.58 (m, 4H, Ar), 7.60–7.70 (m, 3H, Ar), 7.96–8.02 (m, 6H, Ar).
EIMS (m/z, %): 287 (M+1).

## 3. Results and Discussion

The cumulative desorption surface area of catalyst from adsorption-desorption isotherm of nitrogen, pore volume at $p/p_0 = 0.993$ and pore diameter was determined by the BJH method and it was found to be $S_{BJH} = 26.39$ m$^2$ gm$^{-1}$, $P_v = 0.0344$ cm$^3$ gm$^{-1}$ and $P_d = 11.08$ Å respectively. The Temperature Programmed Desorption method (TPD) was used to determine the acidic properties of solid catalyst. This provides information about the total concentration and strength of acidic sites (Bronsted and Lewis). It was found that the total ammonia desorbed is 0.376 mmol/gm of the catalyst.

Initially, we studied the catalytic efficiency of scolecite catalyst for synthesis of 2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole **(4c)** using 1: 1: 2 ratio of benzil, ammonium acetate and 4-chlorobenzaldehyde in different solvents and various wt% of scolecite catalyst with respect to the initial concentration of reactant (Scheme 1). Compound 4c was isolated with 95% yield using optimized reaction condition (Table 1), in ethanol and 2 wt% scolecite catalyst. Using the optimized reaction conditions, a range of 2,4,5-triarylimidazole derivatives were synthesized and results are summarized in Table 2.

It is interesting to note that the nature of substituent on the aromatic ring does not affect on the yield of product. The reactions of aromatic aldehydes carrying electron-donating or electron-withdrawing groups were also successfully carried out with this method. The use of water as a solvent in this reaction gave only moderate yield of product (57%). So we studied the effect of different solvents in the synthesis of 2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole **(4c)** and the results are summarized in Table 1. Among those examined, ethanol was found to be the most efficient with respect to shorter reaction time and maximum yield of product.

To determine the role of the catalyst, the same reaction was carried out in the absence of catalyst, which resulted in less product formation (37%), after 90 min. These results indicate that the catalyst exhibits a high catalytic activity in this transformation. The reusability of the catalyst is important for the large scale operation and an industrial point of view. Therefore, the recovery and reusability of catalyst was examined. The catalyst was separated and reused after washing it with n-hexane and drying at 80°C in the synthesis of 2-(4-chlorophenyl)-4,5-diphenyl-1*H*-imidazole **(4c)** and it was found that the catalyst shows good results with three successive reaction giving 95, 93, 92% yield of product.

In Table 3, we have compared our result with results obtained by some other reported procedures for the synthesis of 2-(4-nitrophenyl)-4,5-diphenyl-1*H*-imidazole **(4g)**. The data presented in this table shows the promising features of this method in terms of reaction rate and the yield of product.

**Table 1.** Optimization of reaction conditions and wt% of scolecite catalyst for the synthesis of 2-(4-chlorophenyl)-4,5-diphenyl-1H-imidazole.

| Solvent | Wt% of catalyst | Reaction time (min) | Yield (%)$^a$ |
|---|---|---|---|
| Water | 3 | 30 | 57 |
| Acetonitrile | 3 | 30 | 79 |
| Acetonirile-water (1:1) | 3 | 30 | 69 |
| Ethanol | 3 | 30 | 95 |
| Ethanol-water (1:1) | 3 | 30 | 75 |
| Ethanol | 2 | 30 | 95 |
| Ethanol | 1 | 30 | 78 |

$^a$*All yields refer to isolated products*

**Table 2.** Synthesis of 2,4,5-triaryl-1H-imidazole derivatives in EtOH using benzil or benzoin, ammonium acetate, aromatic aldehydes, and 2 wt% scolecite catalyst.

| Entry | Ar | Time (min) | | Yield (%)[a] | | M.P. (°C) | |
|---|---|---|---|---|---|---|---|
| | | Benzil | Benzoin | Benzil | Benzoin | Found | Literature |
| 4a | $C_6H_5$ | 35 | 60 | 96 | 94 | 274-276 | 276-277 [13] |
| 4b | $2\text{-}ClC_6H_4$ | 45 | 70 | 93 | 93 | 195-196 | 195-196 [14] |
| 4c | $4\text{-}ClC_6H_4$ | 30 | 55 | 95 | 95 | 259-260 | 260-262 [14] |
| 4d | $4\text{-}MeC_6H_4$ | 45 | 75 | 92 | 89 | 230-232 | 231-232 [13] |
| 4e | $4\text{-}OMeC_6H_4$ | 50 | 65 | 87 | 87 | 227-228 | 228-230 [13] |
| 4f | $3,4\text{-}(OMe)_2C_6H_3$ | 50 | 75 | 89 | 79 | 220-221 | 220-221 [13] |
| 4g | $4\text{-}NO_2C_6H_4$ | 45 | 70 | 94 | 87 | 233-234 | 232-233 [14] |
| 4h | $4\text{-}N(Me)_2C_6H_4$ | 30 | 65 | 95 | 89 | 258-259 | 257-258 [13] |
| 4i | $4\text{-}OHC_6H_4$ | 40 | 70 | 92 | 85 | 268-269 | 268-270 [14] |
| 4k | $4\text{-}FC_6H_4$ | 35 | 60 | 91 | 92 | 190-191 | 190 [12] |
| 4l | 2-Furyl | 45 | 65 | 94 | 89 | 199-200 | 199-201 [14] |
| 4m | 2-thienyl | 45 | 70 | 90 | 83 | 259-260 | 260-261 [15] |

[a] *All yields refer to isolated products*

**Table 3.** Comparisons of some other reported procedures with the present method for the synthesis of 2-(4-nitrophenyl-4,5-diphenyl-1H-imidazole (entry **4g**, Table 2).

| Entry | Literature | Catalyst | Solvent | Reaction condition | Time | Yield (%)[c] |
|---|---|---|---|---|---|---|
| 1[a] | Present | Scolecite | EtOH | reflux | 45 min | 94 |
| 2[b] | [12] | $ZrCl_4$ | $CH_3CN$ | r.t., stirring | 7 h | 89 |
| 3[b] | [13] | Zeolite/silica gel | - | MW | 6 min | 94/96 |
| 4[b] | [14] | $NaHSO_4$ | $EtOH:H_2O$ | 80°C | 40 min | 90 |
| 5[b] | [15] | Sulphanilic acid | $EtOH:H_2O$ | 80°C | 70 min | 87 |

[a] *reaction carried out in benzil:4-nitrobenzaldehyde:ammonium acetate (1:1:2) in ethanol.*
[b] *reactions carried out in benzil:4-nitrobenzaldehyde:ammonium acetate (1:1:2.5) under different reaction conditions.*
[c] *All yields refer to isolated products.*

# 4. Conclusions

In summary, the use of inexpensive natural scolecite in a catalytic quantity is a general practical alternative to existing procedures for multicomponent synthesis of 2,4,5-triarylimidazole derivatives. The procedure offers several advantages including increased variations of substituents in the product with high yields, operational simplicity, minimum environmental effects and above all, the ease in purification of products simply by recrystallization.

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## References

[1] J.C. Lee, et al., Nature 372, 739 (1994)

[2] T. Maier, R. Schmierer, K. Bauer, H. Bieringer, B. Sachse, US Patent, 4820335 (1989)

[3] a) J.G. Lombardino, E.H. Wiseman, J. Med. Chem. 17, 1182 (1974); b) J.G. Lombardino, Ger. Offen. 2, 155, 558 (1972)

[4] A.P. Phillips, H.L. White, S. Rosen, Eur. Pat. Appl. EP 58, 890 (1982)

[5] R. Schmierer, H. Mildenberger, H. Buerstell, German Patent 361464 (1987)

[6] J. Heeres, L.J.J. Backx, J.H. Mostmans, J. Vancustem, J. Med. Chem. 22, 1003 (1979)

[7] I. Satoru, Imidazoles derivative for chemiluminescence microanalysis, Japan Kokkai Tokyo Koho JP, 01, 117, 867, May 10 (1989)

[8] L.L. Chang, K.L. Sidler, M.A. Cascieri, Biorg. Med. Chem. Lett. 11, 2549 (2001)

[9] T.H. Gallagher, S.M. Fier-Thompson, R.S. Garigipati, Biorg. Med. Chem. Lett. 5, 1171 (1995)

[10] a) B. Radziszewski, Chem. Ber. 15, 1493 (1882); b) F. Japp, H. Robinson, Chem. Ber. 15, 1268 (1882)

[11] M. Grimmett, A. Katritzky, C. Rees, E. Scriven, Pergamon: NewYork 3, 77 (1996)

[12] G. Sharma, Y. Jyothi, P. Lakshmi, Synth. Commun. 36, 2991 (2006)

[13] S. Balalaie, A. Arabanian, M. Hashtroudi, Mont. Fur. Chemie 131, 945 (2000)

[14] J. Sangshetti, N. Kokare, A. Kotharkar, D. Shinde, Mont. Fur. Chemie 139, 125 (2008)

[15] A. Mohammed, N. Lokare, J. Sangshetti, D. Shinde, J. Korean. Chem. Soc. 51, 418 (2007)

[16] M. Kidwai, P. Mothsra, V. Bansal, R. Goyal, Mont. Fur. Chemie 137, 1189 (2006)

[17] J.N. Sangshetti, N.D. Kakare, S.A. Kotharkar, D.B. Shinde, J. Chem. Sci. 120(5), 463 (2008)

[18] N.D. Kokare, J.N. Sangshetti, D.B. Shinde, Synthesis 2829 (2007)

[19] S. Siddiqui, U. Narkhede, S. Palimkar, T. Daniel, R. Lahoti, K. Srinivasan, Tetrahedron 61, 3539 (2005)

[20] J.F. Zhou, Y.Z. Song, Y.L. Zhu, S.J. Tu, Synth. Commun. 35, 1369 (2005)

[21] J.M. Thomas, Angew Chem. 33, 913 (1994)

[22] M.M. Heravi, M. Tajbakhsh, A.N. Ahmadi, B. Mohajerani, Monatshefte fur Chemie 137, 175 (2006)

[23] A. Hegedus, Z. Hell, A. Potor, Synth. Commun. 36, 3625 (2006)

[24] S.V. Shinde, et al., Cat. Lett. 125, 57 (2008)

[25] L.S. Gadekar, S.S. Katkar, K.N. Vidhate, B.R. Arbad, M.K. Lande, Bull. Cat. Soc. Ind. 7, 79 (2008)

[26] S. Katkar, L. Gadekar, M. Lande, Rasayan J. Chem. 1(4), 865 (2008)