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# A convenient synthesis of benzimidazoles using sulfonated ordered nanoporous carbon as efficient solid catalyst

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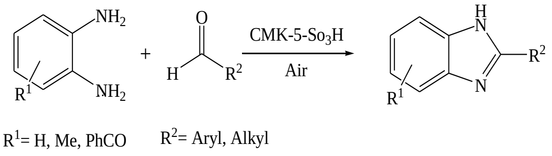
Sulfonated ordered nanoporous carbon (CMK-5-$SO_3H$) efficiently catalyzes the synthesis of 2-substituted benzimidazoles using cyclocondensation of various aldehydes and *o*-phenylenediamines. This catalyst can be recovered and reused without significant loss of activity.

**Keywords:** sulfonated ordered nanoporous carbon, heterogeneous catalyst, benzimidazole, aldehyde, 1,2-phenylenediamine.

## INTRODUCTION

High profile biological activities of benzimidazole derivatives such as anti-fungal, anti-tubercular and anti-cancer have attracted attention for their synthesis [1, 2]. They have been used as ligands, catalysts and synthetic intermediates [3]. Number of methods have been developed for the synthesis of 2-substituted benzimidazole derivatives involving the condensation of 1,2-phenylenediamines with aldehydes [4], carboxylic acids [5], orthoesters [6], nitriles [7] and amidates [8]. Recently, several improved protocols for the synthesis of benzimidazoles have been reported by modification of condensation reaction of aldehydes with *o*-phenylenediamines using various oxidants and catalysts including $H_2O_2$–CAN [9], $K_3Fe(CN)_6$ [10], $Mn(OAc)_3$ in AcOH [11], $NaHSO_3$ [12], $K_2S_2O_8$–$CuSO_4$ [13], $SiO_2$-$Mn(acac)_3$ [14], nanoCuO [15], tetrabutylammonium fluoride [16], *P*-TsOH [17], $MoO_3/CeO_2$-$ZrO_2$ [18], WOx/$ZrO_2$ [4], nanoporousaluminosilicate [19], $Yb(OPf)_3$ [20], $I_2$ [21], $FeCl_3$ [22], $In(OTf)_3$ [23], $Yb(OTf)_3$ [24], $Co(OH)_2$/CoO(II) [25], $MnZrO_2$ [26] SBA-Pr-$SO_3H$ [27], KF/$Al_2O_3$ [28] and scolecite [29] etc. Some of these methods suffer from various limitations, which include long reaction times, difficult work-up procedures and the use of corrosive and not recyclable catalysts. Therefore, development of new protocols continues to attract the attention of researchers. On the other hand, increasing awareness of the environmental costs of traditional acid-catalyzed chemical reactions has created an opportunity for solid acids as a catalyst in organic transformations due to their operational simplicity, selectivity and reusability [30]. Carbonaceous sulfonic acids have attracted considerable interest as a solid catalyst in synthetic organic chemistry [31, 32]. Recently, Wang et al. prepared a novel sulfonic functionalized ordered nanoporous carbon (CMK-5-$SO_3H$) by covalent attachment of sulfonic acid-containing aryl radical on the surface of nanoporous carbon. CMK-5-$SO_3H$ showed stable and highly efficient catalytic performance and it could be reused for several times without loss of activity [33]. However, to the best of our knowledge, there is no report available on the synthesis of benzimidazoles using CMK-5-$SO_3H$ catalysts in the literature.

Here in, we report a simple, convenient, and efficient method for the syntheses of 2-substituted benzimidazoles by cyclocondensation of various aldehydes with 1,2-phenylenediamines in the presence of CMK-5-$SO_3H$ as a reusable and eco-friendly catalyst (Scheme 1).



Scheme 1

## EXPERIMENTAL

Materials were purchased from Fluka and Merck companies. CMK-5-$SO_3H$ was prepared according to the reported procedure [33]. The amount of acid in CMK-5-$SO_3H$ was determined by thermogravimetric analysis (TGA) and ion-exchange pH analysis. The structure of products was characterized by spectral data ($^1H$ NMR, $^{13}C$ NMR) and physical properties and comparison with authentic samples.

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### *Procedure for the preparation of benzimidazole*

*o*-Phenylenediamine (1.0 mmol) and aldehyde (1.0 mmol) with 2 mol% of CMK-5-SO$_3$H (0.023 g) (mol of Ph-SO$_3$H on the CMK-5) in 10 mL 1,4-dioxane were stirred at 100$^{o}$C for an appropriate time The progress of the reaction was monitored by TLC (n-Hexane:Ethylacetat 9:1). After completion of the reaction, catalyst was recovered by simple filtration. Water was added to the mixture and product filtered off. The residue was washed with ethyl acetate and the product was obtained. If necessary the product was further purified by column chromatography on silica gel.

### *Supplementary Data*

Experimental procedure and characterization data for CMK-5-SO$_3$H is available in Supporting Information.

### *Some Product Characterization Data*

**5-Benzoyl-2- phenyl- 1*H*- benzimidazole (Table 2, entry 3): IR (KBr): 3340, 3198, 1663, 1620, 1500 cm $^{-1}$**, $^1$H NMR spectrum (DMSO-d6, 400 MHz), δ, ppm: 7.53- 7.78 (10H, m), 7.97 (s, 1H) , 8.20- 8.23 (m, 2H), δ 13.33 (br, s, 1H); $^{13}$C NMR spectrum (100MHz, CDCl$_3$), δ, ppm: 124.64, 124.67, 124.71, 124.84, 127.20, 128.50, 128.52, 128.90, 129.57, 129.93, 129.98, 130.99, 131.46, 132.56, 135.56, 196.07. CHN Calcd.C, 80.52; H, 4.73; N, 5.36. found: C, 80.50; H, 4.80; N, 5.36.

**2-(4-Nitrophenyl)-1*H*-benzimidazole (Table 2, entry 6): IR (KBr): 3350, 3100, 1612, 1280 cm$^{-1}$,** $^1$H NMR spectrum (DMSO-d6, 400 MHz), δ, ppm: 7.25–7.80 (m, 8H), 12.38 (br, 1H); $^{13}$C NMR spectrum (100MHz, CDCl$_3$), δ, ppm: 115.94, 124.52, 136.23, 140.88, 141.89, 149.20. CHN Calcd.C, 65.27; H, 3.79; N, 17.56. Found: C, 65.26; H, 3.80; N, 17.52

**4-(1H-Benzimidazole-2-yl)-phenol (Table 2, entry 9): IR (KBr): 3459, 2859, 1620, 1495 cm$^{-1}$;** $^1$H NMR spectrum (DMSO-d6, 400 MHz), δ, ppm: 7.22–8.12 (8H, m), 12.30 (br, 1H); $^{13}$C NMR spectrum (100MHz, CDCl$_3$), δ, ppm: 115.11, 120.65, 125.11, 130.20, 138.05, 141.75. CHN Calcd.C, 74.27; H, 4.79; N, 13.33. Found: C, 74.29; H, 4.80; N, 13.30.

**5-Benzoyl-2--naphthyl -1H-benzimidazole (Table 2, Entry 12): IR (KBr): 3150, 2934,1662, 1624, 1560 cm $^{-1}$,** $^1$H NMR spectrum (DMSO-d6, 400 MHz), δ, ppm: 7.57- 7.80 (9H, m), 8.07- 8.13 (m, 4H), 8.32- 8.35 (m, 1H), 8.80 (s, 1H), δ13.50 (br, s, 1H); $^{13}$C NMR spectrum (100MHz, CDCl$_3$), δ, ppm: 124.36, 124.76, 124.80, 124.84, 124.88, 126.94, 127.41, 127.53, 127.94, 128.30, 128.90, 129. 07, 129.21, 129.96, 131.55, 132.59, 133.20, 134.19, 138.56, 154.53, 156.95. CHN Calcd.C, 82.74; H, 4.59; N, 5.36. found: C, 82.80; H, 4.60; N, 4.50.

**2-Pentyl-1H-benzimidazole (Table 2, entry 17): IR (KBr) 3324, 2898, 1640, 3250 cm$^{-1}$ .**$^1$H NMR spectrum (DMSO-d6, 400 MHz), δ, ppm: 0.83–0.88 (m, 3H), 1.23–1.24 (m, 4H), 1.75–1.89 (m, 2H) 2.90 (t, J = 7.4 Hz, 2H), 6.41 (br, 1H), 7.18–7.36 (m, 2H), 7.50–7.50 (m, 2H), $^{13}$C NMR spectrum (100MHz, CDCl$_3$), δ, ppm: 13.91, 21.68, 27.31, 28.50, 30.66,110.55, 118.10, 120.87, 134.37, 143.35, 155.10. CHN Calcd.C, 76.56; H, 8.57; N, 14.88. found: C, 76.53; H, 8.58; N, 14.89.

## RESULTS AND DISCUSSION

TGA and ion-exchange pH analysis determined the amount of acid in CMK-5-SO$_3$H. Typically a loading of ca. 0.84 mmol/g was obtained.

In this work, we showed the effect of solvent and catalyst for the preparation of 2-phenyl-1*H*-benzimidazole. Benzaldehyde (1 mmol) was treated with *o*-phenylenediamine (1 mmol) in the presence of CMK-5-SO$_3$H (0.023 g: 2 mol%) in various solvents (Table 1). As it is clear from this Table, the highest yield of 2-phenyl-1*H*-benzimidazole was obtained in 1,4-dioxane (Table 1, entry 1).

**Table 1.** Preparation of 2-phenyl-1H-benzimidazole in different solvents

| Entry | Solvent | Time (h) | Yield(%)[a] |
|---|---|---|---|
| 1 | 1,4-Dioxane | 3 | 96 |
| 2 | Acetonitrile | 5 | 60 |
| 3 | Toluene | 5 | 40 |
| 4 | Water | 5 | 50 |
| 5 | Ethanol | 5 | 40 |
| 6 | Dichloromethane | 7 | 25 |

[a] Yields refer to isolated products.

To evaluate the quantity of the catalyst, the model reaction was performed in the presence of different mol% of CMK-5-SO$_3$H in dioxane at reflux condition (Table 2). It was observed that this reaction carried out well in the presence of 2 mol% catalyst (Table 2 entry2). Using higher amounts of catalyst did not considerable effect on the yield and reaction time (Table 2, entry3 and 4).

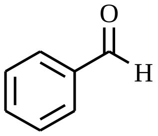
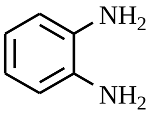
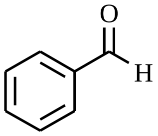
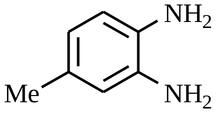
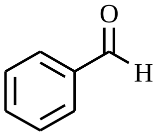
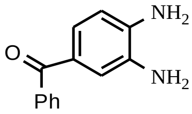
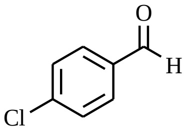
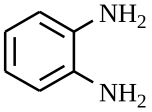
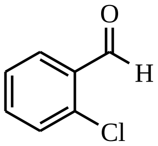
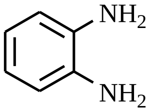
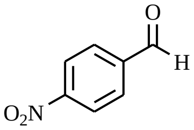
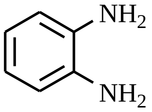
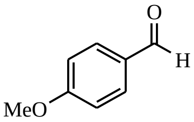
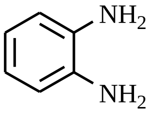
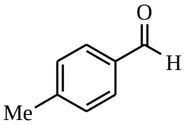
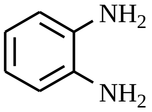
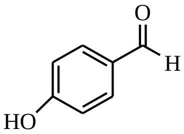
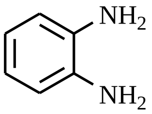
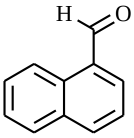
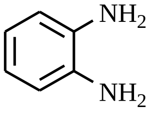
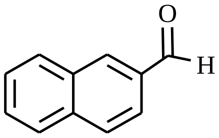
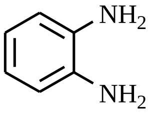
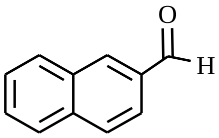
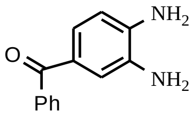
In order to evaluate the scope and generality of this process, various aromatic and aliphatic aldehydes were reacted with several *o*-phenylenediamines under the optimized reaction conditions (Table 3).

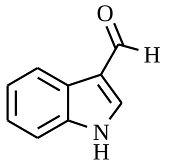
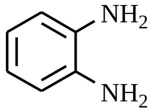
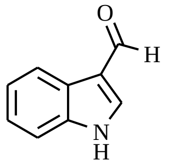
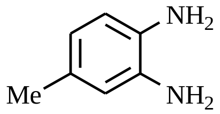
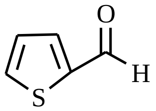
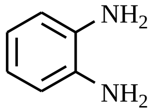
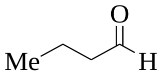
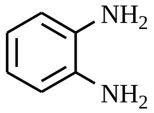
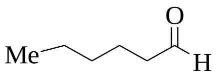
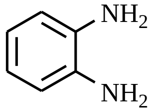
**Table 2.** Screening of catalyst amount on model reaction

| Entry | Catalyst amount (mol %) | Time (h) | Yield(%)[a] |
|---|---|---|---|
| 1 | 1 | 6 | 92 |
| 2 | 2 | 3 | 96 |
| 3 | 3 | 3 | 90 |
| 4 | 5 | 4 | 92 |

[a] Yields refer to isolated products.

**Table 3.** Synthesis of 2-substituted benzimidazoles using a CMK-5-SO3H catalyst [a]

| Entry | Aldehyde | Diamine | Time (h) | Yield$^b$ | m.p./Lit. |
|---|---|---|---|---|---|
| 1 |  |  | 3 | 96 | 290-293 [4] |
| 2 |  |  | 2.5 | 98 | 240–242 [19] |
| 3 |  |  | 7 | 95 | 216-219 [-] |
| 4 |  |  | 2 | 93 | 290-292 [4] |
| 5 |  |  | 2 | 92 | 231-235 [4] |
| 6 |  |  | 2 | 95 | 300-302 [4] |
| 7 |  |  | 5 | 95 | 223-225 [4] |
| 8 |  |  | 4 | 93 | 270-272 [4] |
| 9 |  |  | 3.5 | 96 | 218-220 [4] |
| 10 |  |  | 3 | 90 | 267-269 [16] |
| 11 |  |  | 3 | 91 | 212-215 [19] |
| 12 |  |  | 7 | 92 | 239-240 [-] |

| | | | | | |
|---|---|---|---|---|---|
| 13 |  |  | 7 | 95 | 202-204 [13] |
| 14 |  |  | 5 | 97 | 210-213 [34] |
| 15 |  |  | 6 | 90 | 230-233 [21] |
| 16 |  |  | 5 | 72 | 160–162 [19] |
| 17 |  |  | 5 | 80 | 164–165 [23] |

[a] Yields refer to isolated products.

Reactions of benzaldehyde (1 mmol) with various 1,2-diamines (1 mmol) in the presence of CMK-5-$SO_3H$ (2 mol%) in 1,4-dioxane at reflux condition, afforded 2-phenyl-1*H*-benzimidazoles in excellent yields (Table 3, entries 1-3). Similarly benzaldehydes with possessing both electron-donating and electron-withdrawing groups reacted with *o*-phenylenediamine under optimal reaction conditions, to give excellent yield of the desired imidazoles (Table 3, entries 4-9).

In the optimal reaction conditions 1-naphtaldehyde and 2-naphtaldehyde as sterically hindered aldehydes reacted with 1,2-phenylenediamines to afford excellent yield of the corresponding benzimidazoles (Table 3, entries 10 - 12).

This method is also suitable for the preparation of benzimidazoles from a heteroaromatic aldehyde such as 2-thiophenecarbaldehyde and indole-3-carbaldehyde (Table 3, entries 13-15). Aliphatic aldehydes such as buthanal and hexanal reacted with *o*-phenylenediamine and produced the corresponding benzimidazoles (Table 3, entries 16-17).

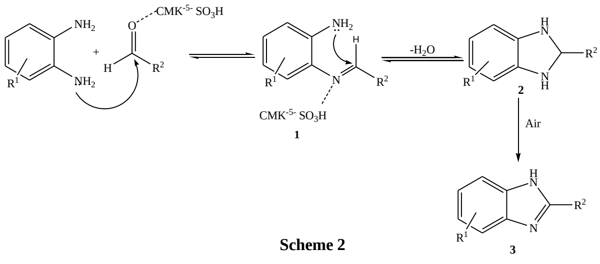
The recyclability of the catalyst was also studied (Table 4**)**. At the end of the reaction of benzaldehyde with *o*-phenylenediamine, the catalyst was filtered off, washed with dichloromethane, dried, and reused as such for subsequent experiments under same reaction conditions. The results in table 4 clearly established the recyclability and reusability of the catalyst without significant loss of activity.

**Table 4.** Results of recyclability of the catalyst

| Entry | Cycle | Time | Yield (%) |
|---|---|---|---|
| 1 | 1 | 3 | 96 |
| 2 | 2 | 3 | 95 |
| 3 | 3 | 3.5 | 90 |
| 4 | 4 | 3.5 | 89 |

To confirm the role of air as an oxidant in these reactions, the optimal reaction was carried out under $N_2$ atmosphere. It is noteworthy that only a trace of 2-phenyl-1*H*-benzimidazole was obtained in the absence of air. Hence, the role of air as an oxidant is important in these transformations.

Mechanistically, it is believed that, the electrophilic character of the carbonyl group is enhanced by CMK-5-$SO_3H$ which facilitate the generation of imine. The resulting imine further reacts with another amine group of 1,2-phenylenediamine resulting in the formation of dihydroimidazole which subsequently undergoes oxidative dehydrogenation in air under the reaction conditions to give the 2-substituted benzimidazole as shown in Scheme 2**.**



**Scheme 2**

## CONCLUSIONS

In summary, we have developed an efficient approach and simple work up for the preparation of 2-substituted benzimidazoles by condensation of acid sensitive, sterically hindered, and substituted aromatic and aliphatic aldehydes with various 1,2-phenylenediamines in the presence of CMK-5-$SO_3H$ as a highly active, stable, reusable and eco-Friendly catalyst.

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## REFERENCES

1. M. B. Maradolla, S. K. Allam, A. Mandha and G. V. P. Chandramouli, *Arkivoc (*xv*)*, 42 (2008).
2. R. Vinodkumar, S. D. Vaidya, B. V. S. Kumar, U. N. Bhise, S. B. Bhirud and U. C. Mashelkar, *Arkivoc (xiv)*, 37 (2008).
3. (a) T. Isobe, K. Fukuda, Y. Araki and T. Ishikawa, *Chem Commun*., 243 (2001). (b) M. Jung and *E.* Huang, *Org. Lett*., **2**, 2659 (2000). (c) I. Y. Oren, I. Yalcin, E. A. Sener and N. Ucarturk, *Eur J. Med. Chem*., **39**, 291 (2004).
4. R. V. Shingalapur and K. M. Hosamani, *Catal. Lett*., **137**, 63 (2010).
5. Y. H. So and J. P. Heeschen, *J. Org. Chem*. **62,** 3552 (1997).
6. G. P. Sagitullina, A. K. Garkushenko, E. G. Atavin and R. S. Sagitullin, *Mendeleev Commun.*, **19,** 155 (2009).
7. D. W. Hein, R. J. Alheim and J. Leavitt, *J Am Chem Soc.* **79**, 427 (1957).
8. M. Terashima and M. Ishii, *Synthesis*, 484 (1982).
9. K. Bahrami, M. M. Khodaei and F. Naali, *J. Org. Chem.,* **73,** 6835 (2008).
10. I. Hutchinson, M. F. G. Stevens and A. D. Westwel, *Tetrahedron Lett.*, **41**, 425 **(**2000).
11. X. J. Mu, J. P. Zou, R. S. Zeng and J C. Wu, *Tetrahedron Lett*., **46**, 4345 (2005).
12. X. Han, H. Ma and Y. Wang, *Russ J Org Chem*., **44**, 863**(**2008).
13. A. Kumar, R. A. Maurya and D. Saxena, *Mol. Divers.,* **14**, 331**(**2010).
14. R. K. Sodhi and S. Paul, *Catal. Lett*., **141**, 608 (2011).
15. P. Saha, T. Ramana, N. Purkait, M. A. Ali, R. Paul and T. Punniyamurthy, *J .Org. Che*m., **74**, 8719 **(**2009).
16. R. S. Joshi, P. G. Mandhane, S. K. Dabhade and C. H. Gill, *J. Chinese Chem.* Soc., **57**, 1227 (2010).
17. H. Xiangming, M. Huiqiang and W. Yulu *Arkivoc* (*xiii*), 150 (2007).
18. S. B. Rathod, M. K. Lande and B. R. Arbad, *Bull. Korean Chem. Soc*., **31**, 2835 (2010).
19. M. A. Chari, D. Shobha, E. R. Kenawy, S. S. Al-Deyab, B. V. Reddy and A.Vinu, *Tetrahedron, Lett*. **51,** 5195 (2010).
20. G. Shen and C. Cai, *J. Fluorine. Chem.*, **128**, 232 (2007).
21. G. Pranjal and K. Dilip, *Tetrahedron Lett.*, **47**, 79 (2006).
22. C. Ke, T. U. Yong Qiang and Z. Fu Min, *Sci. China. Che*m., **53**, 130 (2010).
23. R. Trivedi, S. K. De and R. A. Gibbs, *J. Mol. Catal. A: Chem*., **245**, 8 (2006).
24. M. Curini, F. Epifano, F. Montanari, O. Rosati and S. Taccone, *Synlett*, 1832 (2004).
25. M. A. Chari, D. Shobha and T Sasaki, *Tetrahedron Lett.,* **52**, 5575 (2011).
26. M. Rekha, A. Hamza, B. R. Venugopal and N. Nagaraju, *Chin. J. Catal.*, 439 (2012).
27. G. Mohammadi Ziarani, A. Badiei, M. Shakiba Nahad and S. Ghadim Alizadeh, *J. N. S.,* **2** 213 (2012).
28. S. Bahadori Khalili and A. R. Sardarian, *Monatsh. Chem*., **143**, 841, (2012).
29. L. S. Gadekar, B. R. Arbad and M. K. Lande, *Chinese Chem. Lett.*, **21**, 1053 (2010).
30. B. Karimia and D. Zareyee, *Tetrahedron let.*, **46**, 4661 (2005).
31. M. Okamura, A. Takagaki, M. Toda, J. N. Kondo, K. Domen, T. Tatsumi, M. Hara and S. Hayashi, *Chem. Mater*., **18**, 3039 (2006).
32. D. Zareyee, M. S. Ghandali and M. A. Khalilzadeh, *Catal. Lett*., 1521 (2011).
33. X. Wang, R. Liu, M. M. Waje, Z. Chen, Y. Yan, K. N. Bozhilov and p. Feng, *Chem. Mater.*, **19**, 2395 (2007).
34. J. S. Biradar and B. Sharanbasappa, *Synth Commun.* **41**, 885 (2011).

# Удобна синтеза на бензимидазоли със сулфониран подреден нанопорьозен въглерод като ефикасен твърд катализатор

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(Резюме)

Сулфониран подреден нанопорьозен въглерод (CMK-5-$SO_3H$) ефикасно катализира синтезата на 2-заместени бензимидазоли чрез циклокондензация на различни алдехиди и *o*-фенилендиамини. Катализаторът може да се отдели и употреби повторно без значителна загуба на активност.