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Dodecylbenzenesulfonic acid catalyzed one pot efficient synthesis of 2-substituted benzimidazole

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ABSTRACT

Synthesis of various benzimidazole derivatives by the reaction of o-phenylene diamine with substituted benzaldehyde in presence of dodecylbenzenesulfonic acid as catalyst. The reaction is performed in ethanol-water at room temperature. Furthermore, a series of compounds were synthesized and characterized by melting point, NMR and IR tools. The method was proved to be simple, convenient, ecofriendly and product was isolated with good yield.

Keywords: DBSA, efficient synthesis, substituted benzaldehyde, benzimidazole.

INTRODUCTION

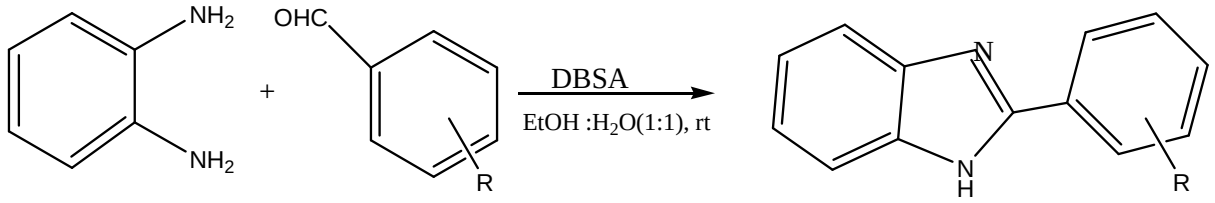
Bendzimidazole scaffold has extensive demand in pharmaceutical chemistry[1-3]. Several pharmaceutically active structures, containing benzimidazole moiety, have been found to exhibit significant activity against viruses such as HIV[4], HSV-1[5]. Furthermore, they are used as, antibacterial[6], anthelmintic[7],antifungal[8], anti-inflammatory[9], antiviral[10]

analgesic[11a] properties. In addition, these compounds are found to be ligand for transition metals in biological system. Therefore, synthesis of substituted benzimidazole has received more importance in recent years.

Several methodologies are available for synthesis of benzimidazole. One of the popular method of benzimidazole synthesis involve condensation of o-phenylene diamine with carboxylic acid derivatives. This method often employ use of strong acids like HCl, PPA[11b], boric acid as catalyst, sometimes combined with high temperature. An alternative method involve oxidative condensation of o-phenylene diamine with aldehyde using various oxidative and catalytic reagents such as MnO_2, DDQ, Oxone, $Sc(OTf)_3$, $Yb(OTf)_3$[12-13], $In(OTf)_3$[14], $CdCl_2$, ionic liquid[15], $KHSO_4$, CAN, $ZrCl_4$[16], NH_4Cl[17]. However all these methods have one or more drawbacks like prolonged reaction time, high temperature, tedious workup, low yield.

Nowadays, the organic reactions in aqueous media have attracted much attention in synthetic organic chemistry as water is the most abundant, cheapest, and eco-friendly solvent. Recently, it has been reportedthat some organic molecules can react on the surface of water. Often a very strong enhancement of reaction rates was noticed in this case, particularly when at least one component involved in this reaction have a polar group, enabling some degree of solubility.

As a continuation of our research work devoted to the development of biologically active substituted benzimidazole derivatives, we herein report an eco-friendly, facile, and efficient methodology for the synthesis of benzimidazole. This method involves a one-pot reaction of o-phenylene diamine and substituted aryl aldehydes in ethanol-water and DBSA as catalyst.



3a-g

MATERIALS AND METHODS

Experimental section

All the reagents & chemicals purchased were of analytical grade. Melting points of all synthesized compounds were determined in open capillary tubes on an electro thermal apparatus and are uncorrected. The progress of reaction was monitored by silica gel coated TLC plate as adsorbent and visualize under UV chamber. Isolation and purification of products were by flash chromatography on 100-200 mesh silica gel. ^{1}H NMR spectra were recorded in DMSO on Broker Avalce-400MHz using TMS as internal standard. Mass spectra were recorded on Micro mass Q-T micro (TOF MS ES+). Electronic spectra were recorded on Shimadzu UV-3600 using DMSO. The IR spectra were recorded on a PerkinElmer 257 spectrometer using KBr discs.

General experimental procedure

To a mixture of o-phenylene diamine (0.100g, 0.92mmol) and various substituted aldehyde (0.100g, 0.92mmol) in ethanol-water(10 ml, 1:1)) and DBSA (10 mol%) was added in round bottom flask. The resulting mixture was stirred for 2 h at room temperature. Completion of reaction mixture was confirmed by TLC (ethyl acetate : hexane, 1:2). The reaction mixture was poured in ice cold water and the product was precipitated as yellow solid. The content was filtered and product was washed with water and then purified by recrystallization from ethanol. The product was further subjected to column chromatography to obtain pure benzimidazole.

Compound 3a: 2-phenyl-1H-benzo[*d*]imidazole

1H NMR (DMSO-d6): δ 13.02 (br s, 1H), 8.20 (d, J=7.6 Hz, 2H), 7.67-7.65 (m, 1H), 7.56-7.49 (m, 4H), 7.22-7.18 (m, 2H); **(LC-MS) m/*z*:** 195.08 [M+H]+; **IR (KBr, cm-1)**: 3420, 2920, 2627, 1623, 1410, 1276, 1119, 970, 738.

Compound 3b: 2-(p-tolyl)-1H-benzo[*d*]imidazole

1H NMR (DMSO-d6): δ12.81 (br s, 1H), 8.06 (d, J=8 Hz, 2H), 7.56 (m, 2H), 7.36 (d, J=8 Hz, 2H), 7.19 (m, 2H), 2.38 (s, 3H); **(LC-MS) m/*z*:** 209.10 [M+H]+

Compound 3c: 2-(4-methoxyphenyl)-1H-benzo[*d*]imidazole

1H NMR (DMSO-d6): δ12.55 (br s, 1H), δ8.21 (d, J=8.4 Hz, 2H), 7.70-7.68 (m, 2H), 7.38-7.36 (m, 2H), 7.21 (d, J=8.8 Hz, 2H), 3.88 (s, 3H); **(LC-MS) m/*z*:** 225.07 [M+H]+

Compound 3e: 2-(4-nitrophenyl)-1H-benzo[d]imidazole:

1H NMR (400 MHz, CDCl3, d ppm): 12.98 (s, 1H) 8.41 (d, 2H, J = 8.05 Hz), 8.02 (d, 2H, J = 8.1 Hz), 7.92–7.95 (m, 2H), 7.51–7.55 (m, 2H); **IR (KBr)**: 3447 (–NH), 3083, 2961, 1631 (C N) 1506, 1372, 972 cm_1; **MS: m/z:** 240.1; **Anal. Calcd** for $C_{13}H_9N_3O_2$: C, 65.27; H, 3.79; N, 17.56. Found: C, 65.48; H, 3.74; N, 15.58

Compound 3f: 2-(furan-2-yl)-1H-benzo[d]imidazole:

1H NMR (400 MHz, CDCl3, d ppm): 12.87 (s, 1H), 8.07 (d, 1H, J = 1.19 Hz), 7.47 (d, 2H, J = 1.50 Hz), 7.15–7.19 (m, 3H), 6.78 (m, 1H); **IR (KBr**): 3442 (-NH), 3093, 1625 (C-N) 1521, 1438, 1355, 973 cm_1; **MS: m/z:** 185.1;**Anal. Calcd** for $C11H_8N_2O$: C, 71.73; H, 4.38; N, 15.21. Found: C, 71.68; H, 4.39; N, 15.48

Compound 3g: 2-(4-Chlorophenyl)-1H-benzo[d]imidazole:
1H NMR (DMSO-d6): δ12.9(s,1H), 8.15(d,2H), 7.5-7.65(m,4H), 7.20(m,2H), **IR (KBr):** 3038, 1440, 1410, 1268, 950, 754 cm^{-1}. **MS: m/z:** 194.

Table: 1 Synthesis of benzimidazole (3a-3g) using DBSA

Entry	Aryl-aldehyde	Time(min)	Yield(%)	mp(^{0}C) found	Lit.(reported)
3a	Ph	65	84	292–293	292
3b	4-Tol	80	78	286-289	285-290
3c	4-MeOC$_6$H$_4$	65	80	227–228	226
3d	1-Naphthyl	70	82	264–265	266
3e	4-O$_2$NC$_6$H$_4$	60	88	314–316	316
3f	2-Furyl	60	89	295-297	296
3g	4-ClC$_6$H$_4$	65	86	291–293	290-292

Table: 2 Optimization conditions for Solvent

Entry	Solvent	Time(min)	Yield (%)
1	water	120	50
2	methanol	80	70
3	ethanol	60	75
4	THF	90	60
5	DMF	120	45
6	Toulene	180	Trace
7	Ethanol: water	60	88

RESULTS AND DISCUSSION

In present work, an efficient method was tried for synthesis of benzimidazole from o-phenylene diamine and various substituted benzaldehyde in presence of dodecylbenzenesulfonic acid as homogeneous catalyst. The reaction was performed in ethanol: water (1:1) at room temperature for 60-80 minutes. Several aldehydes having electron donating and electron withdrawing groups underwent the conversion to form series of aryl benzimidazole. It was observed that aldehydes having electron withdrawing groups afford good yield with shorter reaction time compared to aldehyde having electron donating groups. The physical charecterstic of DBSA is acidic soluble, in ethanol as well as water and used as source of H^+ ion to catalyse this reaction. Product were isolated in high yields (80-90%) and purified by using 60-120 mesh silica gel for column chromatography with ethyl acetate in hexane. Products were confirmed by comparing with authentic sample (IR, NMR, MS). NH signal clearly appeared in the region d̃11.5 to 13. Attempts were made to study and optimize the reaction condition in order to show that reaction performed in water with low yield while using ethanol: water (1:1) found to be satisfactory results. DBSA was found to be suitable catlalyst for the reaction in 1:1 ethanol: water medium, the efforts were made to optimize the catalyst loaded for condensation reaction. The present optimization studies revealed that the yield increased with catalyst load upto 20 mol %.

CONCLUSION

We have developed a simple, efficient and green method for synthesis of substituted benzimidazole derivatives by using efficient catalyst DBSA and ethanol: water as solvent. The method offers several advantages like simple reaction conditions, short reaction time, high yields of products and simple experimental operation, which leads to a useful and attractive process for synthesis of benzimidazole derivatives.

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REFERENCES

[1] S Bhattacharya & P Chaudhuri , *curr. med chem*, **2008**,15, 1762.
[2] L Townsend, G Ravankar, *Chem. Rev.*,**1970**,70,389-438.

[3] P Kattimani, R Kamble, G Meti, *RSC Adv*. **2015**,1-23.
[4]A procari, Devivar,L Kucera,J Drach,*J.Med.Chem*.**1998**,2623,1252-1262
[5] M Migawa, J Girardet, J Walker,J Drach. *J.Med.Chem* **1998**,2623,1242-1251.
[6] M Rehman, M Imran, M Arif, M Farooq, *Journal of Chemistry*, 1[5] (**2013**) 56–66.
[7] S Murugesan, S Sathiyamoorthy, *J Pharm. Res*, **2011**, 4, 2679–2681.
[8] V Kamlesh, V Patel, S Arun, *Eur. J. Chem*, **2009**, 6, 281–288.
[9] B Reddy, *Eur. J. Chem*, **2010**, 7, 222–226.
[10] S Periyasamy,R Dhani, P Christophe, *Int. J.Pharmaceut. Sci. Res*.**2010**, 1, 105-109.
[11]a) E Jesudason, S Sridhar, E Padma, *Eur. J. Med. Chem*, **2009**, 44, 2307–2312.
b) E Alcalde, I Dinares, L Garcia and T Roca, *Synthesis*, **1992**, 4, 395-398.
[12] K Nagata, T Itoh, H Ishikawa, A Ohsawa, *Heterocycles*, **2003**,61, 93.
[13] M Curini, F Epifano, F Montanari, O Rosati, S Taccone, *Synlett*, **2004**, 1832
[14] R Trivedi, S De and R Gibbs, "A Convenient *J. Molecular Catalysis A*: *Chemical*, **2006**,245, 1-2, 8-11.
[15] M Qin, Y Fu, X Wang, Y Zhang,W Ma, *J Iranian Chem.Soc*.**2014**, 11,06, 1553-1559.
[16] Z Zhang, L Yin, Y Wang, *Cat. Communication*, **2007**, 8,7, 1126-1131.
[17] D Kathirvelan, P Yuvraj, K Bablu, S Arasampattu , S Reddy, *Ind. J. Chem*.**2013**,52B, 1152-1156.