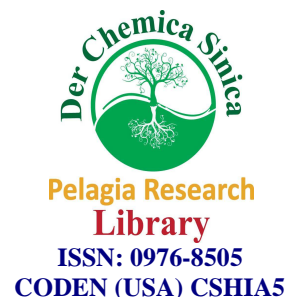




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Lignin sulphonic acid catalyzed rapid and clean synthesis of 2-aryl-1 (aryl methyl)benzimidazoles

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ABSTRACT

Lignin Sulphonic Acid was found to be an efficient polymer supported catalyst for the synthesis of 1, 2-disubstituted benzimidazoles from the reaction of *o*-phenylene diamine with several aryl aldehydes. The excellent chemo selectivity of the reaction in presence of methanol at room temperature within 30-40 min was found.

Keywords: Lignin Sulphonic Acid, Benzimidazole, Chemo selectivity.

INTRODUCTION

Substituted benzimidazoles are the important class of heterocyclic compounds having significant applications in medicinal and pharmaceuticals such as antihistamics, antihypertensives, antiparasitics, antifungals, anticancers and antiulcers [1, 2]. 2-Aryl substituted and 1,2-diaryl substituted benzimidazole has an activity against HIV [3], and influenza [4]. Some current clinical examples are antihistamine Astemizole [5]. The antiulcerative esomeprazole [6], Albendazole [7] used for the treatment of parasitic diseases. Selective neuropeptides YY1 receptor antagonists [8-11], 5-Lipoxygenase inhibitors for use as novel antiallergic agents [12], factor FXa inhibitor [13]. Benzimidazoles are present in Vit.B₁₂ related to DNA base purines. Bisbenzimidazoles are developed as DNA minor groove binding agents with antitumor activity [14]. Consequently researchers are attracted to invent new methods for the synthesis of substituted benzimidazoles. Moreover there are numerous methods reported, some of them are condensation of arylene diamine with carboxylic acid or its derivative under harsh dehydrating reaction conditions [15], condensation of arylene diamine with aromatic aldehyde [16], using Hypervalent Iodine as oxidant [17], Oxalic acid [18], H₂O₂/HCl [19], TiCl [20], PPA [21], SOCl₂/SiO₂[22], L-Proline [23], Sulphamic acid [24], Zeolite [25], Laccase [26], NH₄Cl [27], Ytterbium perfluorooctane sulphonates [28], Cu(II) Complex [29], LiBr [30], SiO₂/ZnCl₂ [31], Sodium dodecylsulfate (SDS) [32], Amberlite IR-120 [33], Chlorosulphonic acid [34], Polystyrene sulphonic acid [35], Boric acid [36], Silica bonded propyl-S-sulphonic acid [37], Silica-p-sulphonic acid [38] etc. In continuation of our early work [39-42] herein we have utilized sulphonic acid supported on naturally occurring polymer i.e. Lignin as a solid acid catalyst for the synthesis of 1, 2-disubstituted benzimidazoles.

MATERIALS AND METHODS

All chemicals were purchased from Merck, Fluka and Aldrich fine chemicals.

Melting points were observed in open capillary tubes in a circulating oil melting point apparatus. Products were characterized by comparison of their spectral and physical data with authentic samples. IR spectra were obtained using a Shimadzu FT-IR spectrophotometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instrument. ¹HNMR spectra were recorded on a Bruker Avance Dpx-250.

General procedure for the synthesis of 1, 2-disubstituted benzimidazole

A mixture of one equivalent of *o*-phenylene diamine, two equivalent of aromatic aldehyde, Lignin Sulphonic acid (LSA) 10 Wt. % and methanol (5 mL) as a solvent were stirred magnetically at room temperature for respective time (**Table IV**). After completion of reaction indicated by TLC, the solvent is removed by using Rota evaporator. The residue was dissolved in ethyl acetate, filtered and washed with water. The organic layer was separated using separating funnel, dried over anhydrous sodium sulphate, filtered and then ethyl acetate was evaporated to get crude product. This was further recrystallised from hot ethanol to get pure product which was further purified by flash column chromatography.

RESULTS AND DISCUSSION

Initially the mixture of *o*-phenylene diamine **I** (1 mmol), *p*-chlorobenzaldehyde **II** (1 mmol), LSA (10 Wt. %) was stirred magnetically at room temperature in presence of acetonitrile. After completion of the reaction, it was found that instead of formation of 2-substituted benzimidazole there was a mixture of **III** and **IV**, (80:20) % respectively (**Scheme 1**). Surprisingly we tried the same reaction with 1:2 proportion of *o*-phenylene diamine **I** and *p*-Chlorobenzaldehyde **II** and got maximum product **III** and not the product **IV** (**Scheme 2**). The same reaction was carried out in different solvents and the results are summarized (**Table I**). It was observed that, methanol gives maximum yield with minimum reaction time; therefore further reactions were carried in presence of methanol. We also studied the effect of optimization of catalytic amount on the rate of reaction (**Table II**) and concluded that only 10 Wt. % of catalyst was sufficient for expected conversion with maximum yield, no increase in yield with increased amount of catalyst. The same reaction was carried with 1:0.9 proportions of *o*-phenylene diamine **I** and *p*-chlorobenzaldehyde. There was formation of again mixture of **III** and **IV** products (80:20 %). This excellent chemoselectivity of the catalyst lead us to convert different aromatic aldehydes **II** (2 mmol) into 1,2-disubstituted benzimidazoles by reacting *o*-phenylene diamine **I** (1 mmol) in presence of 10 Wt. % of LSA (**Table IV**). Recyclability of the catalyst was checked (**Table III**) and there was no decrease in catalytic activity of LSA for successive 3-5 runs. The plausible mechanism of the reaction (**Scheme 3**) may involve formation of *N,N'*-dibenzylidene- *o*-phenylene diamine proceeded with successive protonation and ring closure concluded with aromatization via deprotonation and 1,3 hydride transfer.

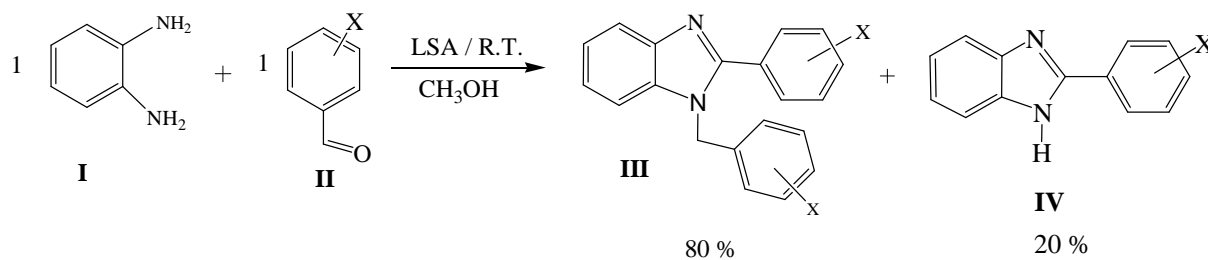
Spectral data of selected compounds

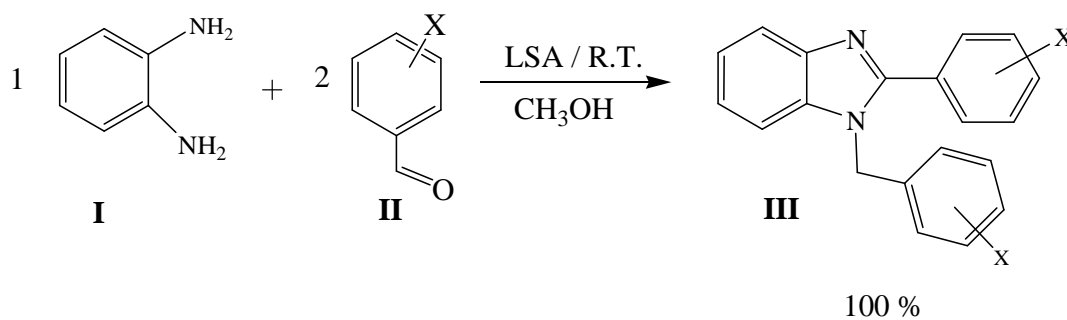
1) 2-(4-Chlorophenyl)-1-(4-Chlorophenylmethyl)benzimidazole

IR (KBr, cm^{-1}): 3437, 3035 (=C-H), 2923 (-C-H) ¹HNMR (CDCl_3 , ppm): δ 5.59 (2H, s, -CH₂), 6.98- 8.18 (12H, m) Mass (m/z, %): 355 (M^{+2}) Elemental analysis: Calc. for: M.F.-C₂₀H₁₄Cl₂N₂ (M.W.=352.05); % of C=68%, H=3.99%, N=7.93% Cl=20.07 Found: C=67.78%, H 4.70 %, N=7.75%.

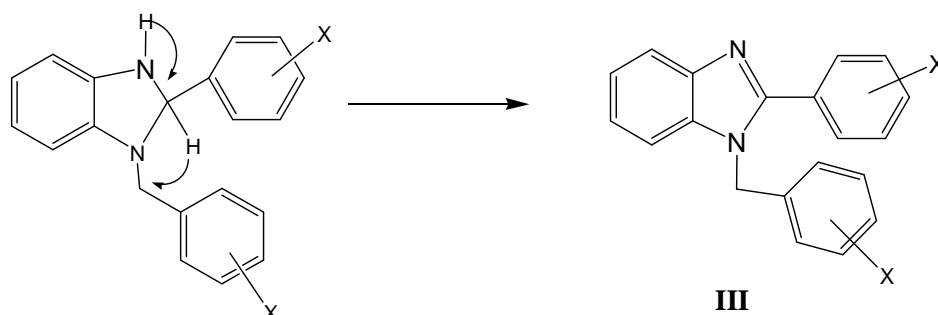
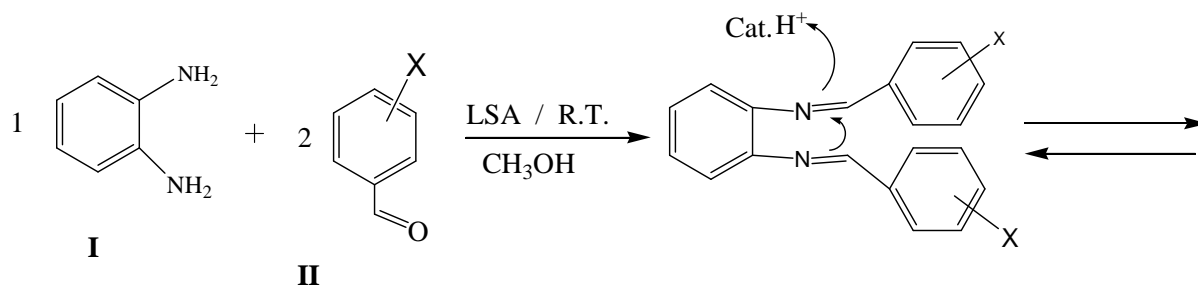
2) 2-(4-N, N-dimethylphenyl)-1-(4-N, N-dimethylephenylmethyl) benzimidazole

IR (KBr, cm^{-1}): 3414, 3076 (=C-H), 2881 (-C-H), 2800; ¹HNMR (CDCl_3 , ppm): δ 5.37 (2H, s), 2.93-3.00(12H, s), 6.66-7.8(12H, d), Mass (m/z, %): 371 (M^+); Elemental analysis: Calc. for: M.F.-C₂₄H₂₆N₄ (M. W.=370.49) C=77.80%, H= 7.07%, N= 15.12%. Found: C= 77.41%, H=7.05%, N= 15.10%





Scheme 2



Scheme 3 Plausible mechanism of the reaction

Table I: Synthesis of 2-(4-Chlorophenyl)-1-(4-Chlorophenylmethyl)benzimidazole in presence of different solvents

Sr. No.	Solvent	Reaction time in min.	Yield (%)
1	CH ₃ CN	90	85
2	CH ₂ Cl ₂	50	80
3	H ₂ O	120	80
4	C ₂ H ₅ OH	60	90
5	CH ₃ OH	30	95

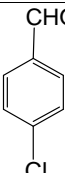
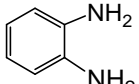
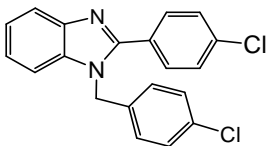
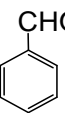
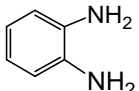
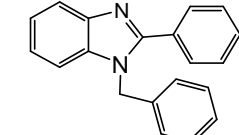
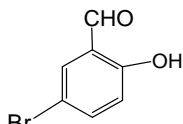
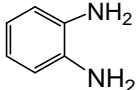
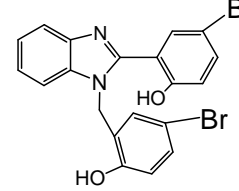
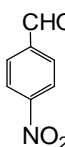
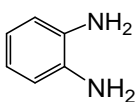
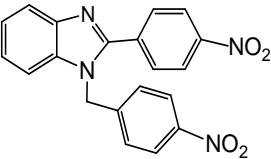
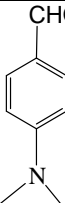
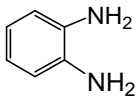
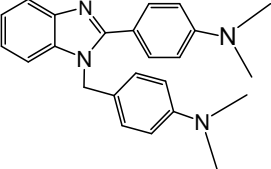
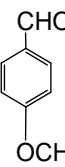
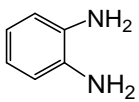
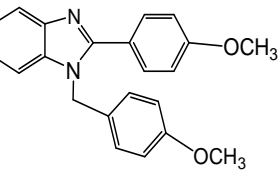
Table II: Synthesis of 2-(4-Chlorophenyl)-1-(4-Chlorophenylmethyl) benzimidazole with increasing amount of Lignin Sulphonic Acid

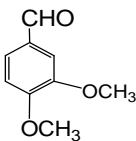
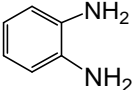
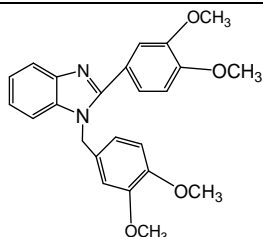
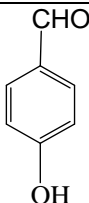
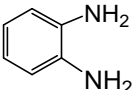
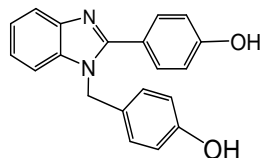
Sr. No.	Amount of catalyst used (Wt. %)	Time (Min.)	Yield ^b (%)
1	5	50	90
2	6	30	95
3	8	30	95
4	10	30	95
5	12	30	95

Table III: Recyclability of Lignin sulphonic acid for the Synthesis of 2-(4-Chlorophenyl)-1-(4-Chlorophenylmethyl) benzimidazole

No. of Runs	X	Time(min)	Yield ^b (%)
1	Cl	15	95
2	Cl	15	92
3	Cl	15	90
4	Cl	15	89
5	Cl	15	87

Table IV: Synthesis of 2-Aryl-1-(arylmethyl) benzimidazole from *o*-phenylene diamine and various aromatic aldehydes

Sr. No.	Aldehyde	Diamine	Product ^b	Time (min.)	M. P. °C (Lit.)
1				30	137 (137-139) ⁴³
2				45	130 (132-134) ⁴³
3				30	264 (264-267)
4				30	190 (192-194) ⁴³
5				35	254 (252-254) ⁴³
6				30	130 (130-131) ⁴³

7				35	280 (278-280)
8				40	225 (226-228) ¹⁶

CONCLUSION

In conclusion, we have proved that Lignin sulphonic acid was found to be more efficient, easily available, low cost, environmentally renewable solid acid catalyst for the synthesis of 1,2-diaryl substituted benzimidazoles from o-phenylene diamine and various aromatic aldehydes. The catalyst is easily separable and reusable for 3-4 cycles without any loss in its catalytic activity.

Acknowledgement

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REFERENCES

- [1] (a) H. Zarriumayeh, D. M. Zimmerman, B. E. Cantrell, D. A. Schober, R. B. Bruns, S. L. Gackenheimer, P. L. Ornstein, P. A. Hipskind, T. C. Brittan, D. R. Gchlert, *Bioorg. Med. Chem. Lett.* **1999**, 9, 647; (b) N. Terzioglu, R. M. V. Rijin, R. A. Bakker, I. J. Desch, R. Lecurs, *Bioorg. Med. Chem. Lett.*, **2004**, 14, 5251.
- [2] (a) P. N. Preston, *Chem., Rev.* **1974**, 279; (b) P. W. Erhardt, *J. Med. Chem.*, **1987**, 3, 231;
- (c) R. Cedillo-Rivera, O. Munoz, M. Entzeroth, J. C. V. Weel, W. Wienen, N. H. Hael., *J. Med. Chem.* **1993**, 36, 4040; (e) J. Mann, A. Baron, Y. Opoku-Boahen, E. Johansson, G. Parkinson, L. R. Kelland, S. Neidle, *J. Med. Chem.*, **2001**, 44, 138; (f) X. Song, B. S. Vig, P. L. Lorenzi, J. C. Darach, L. B. Townsend, G. L. Amiadon, *Med. J.; chem.* **2005**, 48, 1274.
- [3] A. R. Porcari, R. V. Devivar, L. S. Kucera, J. C. Drach, L. B. Townsend, *J. Med. Chem.* **1998**, 4, 252.
- [4] I. Tamm, *J. Science*, **1957**, 126, 1235.
- [5] H. A. Muhaimeed, *J. Int. Med. Res.* **1997**, 25, 175.
- [6] L. J. Scott, C. J. Dunn, G. Mallarkey, M. Sharpe, *Drugs.* **2002**, 62, 1503.
- [7] P. J. Venkatesan, *Antimicrob Chem. Other*, **1998**, 41, 145.
- [8] H. Zarrinmayeh, A. M. Nunes, P. L. Ornstein, D. A. Zimmerman, S. L. Gackenheimer, R. F. Bruns, P. P. Hipskind, T. C. Britton, B. E. Cantrell, D. R. Gchlert, *J. Med. Chem.*, **1998**, 41, 2709
- [9] G. L. Gravatt, B. C. Baguley, W. R. Wilson, W. A. Denny, *J. Med. Chem.*, **1994**, 37, 4338
- [10] B. Jayashankara, K. M. L. Rai., *ARKIVOC*, **2008**, 11, 75.
- [11] K. C. Ravindra, H. M. Vagdevi, V. P. Vaidya., *ARKIVOC*, **2008**, 11, 1.
- [12] H. Nakano, T. Inoue, N. Kawasaki, H. Miyataka, H. Matsumoto, T. Taguchi, N. Inagaki, H. Nagai, T. Satoh *Bioorg. Med. Chem.*, **2000**, 8, 373.
- [13] Z. S. Zhao, D. O. Amaiz, B. Griedel, S. Sakata, J. L. Dallas, M. Whitlow, L. Trinh, J. Post, A. Liang, M. M. Morrissey, K. J. Shaw, *Bioorg. Med. Chem. Lett.*, **2000**, 10, 963.
- [14] J. Mann, A. Baron, Y. OpokuBoahen, E. Johansson, G. Parkinson, L. R. Kelland, S. Neidle, *Chem.*, **2001**, 44, 138.
- [15] (a) J. Lu, H. G. Ge, Y. J. Bai., *Chin. J. Org. Chem.* **2002**, 22, 782. (b) L. M. Dudd, V. E. Venardou, P. Garcia, A. Licence, J. Blake, C. Wilson, M. Poliakoff., *Green Chem.* **2003**, 5, 187
- [16] (a) R. R. Nagawade, D. B. Shinde, *Chin Chem Lett.* **17**, **2006**, 453. (b) F. M. Moghaddam, G. R. Bardajee, H. Ismaili, S. M. D. Taimoory, *Synth. Commun.* **2006**, 36, 2543.

- [17] L. H. Du, Y. J. Wang, *Synthesis*. **2007**, 5, 675.
- [18] N. D. Kokare, J. N. Sangshetti, D. B. Shinde, *Synthesis* **2007**, 18, 2829.
- [19] K. Bahrami, M. M. Khodaei, I. Kavianinia, *Synthesis*. **2007**, 4, 547.
- [20] R. R. Nagawade, D. B. Shinde., *Indian Journal of Chem.* **2007**, 46b, 349.
- [21] J. Lu, B. Yang, Y. Yai, *Synth. Comm.* **2000**, 32, 3703.
- [22] A. B. Alloum, K. Bougrin; Soufiaoui, M., *Tetrahedron Lett.* **2003**, 44, 5935.
- [23] R. Varala, A. Nasreen, R. Enugala, S. R. Adapa. *Tetrahedron. Lett.* 2007, 48, 69.
- [24] Z. H. Zhang, T. S. Li, J. J. Li, *Monatsh Chem* **2007**, 138, 89.
- [25] M. H. Majid, T. Mahmood, N. A. Amir, M. Bagher, *MonatshChem.* **2006**, 137, 175.
- [26] R. G. Jacob, L. G. Dutra, C. S. Radatz, S. R. Mendes, G. Perin, E. J. Lenardao. *Tetrahedron Letters*, **2009**, 50, 1495-1497.
- [27] H. Leutbecher, M. Constantin, S. Mika, J. Conrad, U. Beifuss, *Tetrahedron Letters*. **2011**, 52, 604-607.
- [28] B. Maleki, H. Salehabadi, *European Journal of Chemistry*, **2010**, 4, 377-380.
- [29] M. Shen, C. CAI., *Journal of Fluorine Chemistry*. **2007**, 128, 232-235.
- [30] H. Sarghi, M. Hosseini-Sarvari, F. Moeini., *Can. J. Chem.*, **2008**, 86, 1044-1051.
- [31] D. V. Dekhane, S. S. Pawar, S. V. Gupta, M. S. Shingare, S. N. Thore, *Chinese Chemical Letters*. **2010**, 21, 519-523.
- [32] K. Bahrami, M. M. Khodaei, A. Nejati, *Green Chem.*, **2010**, 12, 1237-1241
- [33] S. H. Nile, et al., *Arabian Journal of Chemistry* **2013**.
- [34] N. V. Shitole, N. V. et al., *Arabian Journal of Chemistry* **2012**.
- [35] P. P. Patil, M. B. Deshmukh, A. G. Mulik, D. R. Chandam, D. R. Patil, S. D. Jagdale, P. V. Anbhule, D. K. Salunkhe, S. A. Sankpal, *Scholars Research Library*, **2011**, 3, 599.
- [36] P. H. Mohammad Reza, A. Marjan, *Journal of Chemistry Volume* **2013**, Article ID 496413, 5.
- [37] S. M. Ghaem Ahemadi-Ana, B. Moitaba, N. Khodabakhsh, *Chinese J. of Chemistry*, 30, **2012**, 3, 517-521.
- [38] G. M. Ziarani, A. Badii, M. Hassanzadeh *Volume: 2: Issue-1: 2011*, ISSN 0976-455.
- [39] A. D. Sagar, S. M. Reddy, J. S. Pulle, M. V. Yadav, *J. Chem. Pharm. Res.*, **2011**, 3(6), 649-654.
- [40] A. D. Sagar, S. M. Reddy, M. V. Yadav and J. S. Pulle, *Int. J. Chem. Sci.*, **2011**, 9(4), 1979
- [41] A. D. Sagar, J. S. Pulle, S. M. Reddy and M. V. Yadav, *Int. J. Chem. Sci.*, **2012**, 10(1), 36.
- [42] A. D. Sagar, S. N. Chamle, M. V. Yadav, *Int. J. Chem. Sci.: 11(4)*, **2013**, 1849-1857.
- [43] S. B. Sapkal, K. F. Shelke, S. S. Sonar, B. B. Shingate, M. S. Shingare, *Cat. Soc. of India*, **2009**, 2, 78.