International Journal of Chemical and Physical Sciences, ISSN:2319-6602
IJCPS Vol. 4 Special Issue – NCSC Jan-2015
www.ijcps.org

Mild and Efficient Synthesis of 2-Aryl Benzimidazoles in Water Using SDS

S. D. PARDESHI, S. N. THORE

Department of chemistry, VinayakraoPatilMahavidyalaya,
Vaijapur, Dist.-Aurangabad. 423701, Corresponding author: msnthore@rediffmail.com

Abstract:

A practical and convenient procedure for the synthesis of 2-Aryl Benzimidazoles has been developed by reacting o-phenylenediamine with aromatic aldehydes in presence of 10 mol% sodium dodecyl sulphate in aqueous medium at room temperature in open air atmospheric condition with and without use of sonication

Keywords: *o*-phenylenediamine, aromatic aldehydes, 2-Aryl Benzimidazoles, sodium dodecyl sulphate, sonication.

Introduction

It is found that 2- substituted benzimidazoles are important part of drug molecules or act as precursor for them. They exhibits various biological activities like antibacterial,[1] antiviral,[2] antifungal,[3] anticancer,[4] anticonvulsant,[5] immunosuppressant agents[5] and Antiulcer,[6] hence their synthesis has gain strong attention to the researchers. Conventionally, benzimidazoles are obtained from the reaction of 1,2- phenylenediamine with carboxylic acid[7] or its derivative (nitriles, imidates, or orthoesters)[8] in harsh acidic condition at relatively high temperatures which many time require tedious workup. In the recent years, the synthetic approach rather than conventional has been moved to greener synthesis. The greener way is use of safe, cheap and fast way of organic synthesis. In conventional methods inorganic acids were used as catalyst and cyclizing agents. The other side of this is the toxicity, hazards, corrosiveness and difficulty of recovery. Hence many people are trying to find the safer way for such synthesis. Various materials like I_2,[9] DDQ,[10] Air,[11] Oxone,[12] $FeCl_3 \cdot 6H_2O$,[13] $In(OTf)_3$,[14] SiO_2-$FeCl_3$,[15] $TiCl_4$[16] were used for synthesis of 2- aryl benzimidazoles. Many of these methods are suiTable for synthesis of 2-aryl benzimidazoles by reacting aryl aldehyde with *o*-phenylenediamine, because of availability of substituted aryl aldehydes.

Recently Sodium dodecyl sulphate (SDS) was used as catalyst in number of organic reaction.[18] 1, 2-disubstituted benzimidazoles were synthesis by using SDS as a catalyst. [19] and 2-aryl benzimidazoles was reported using ammonium persulphate as a reagent in presence of SDS. [19]

As a part of our continued work to develop organic reactions in aqueous media,[20] we have tried to develop synthesis of 2- aryl benzimidazole in aqueous media, here we report a simple, efficient and selective method for synthesis of 2- aryl benzimidazole through reaction of *o*-phenylenediamine with aryl aldehydes in aqueous media in presence of sodium dodecyl sulphate

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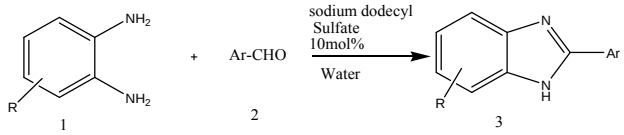

Scheme 1

Experimental

^{1}H NMR spectra were recorded on Mercury Plus Varian in DMSO at 400 MHz using TMS as an internal standard. Bandelinsonorex (35 kHz) ultrasonic bath was used for ultrasonic irradiation. IR spectra were recorded on a Perkin-Elmer FTIR using KBr discs. Mass spectra were recorded on Micromass Quattro II using electrospray Ionization technique, showing (M+1) peak as a base peak. The progress of the reactions was monitored by TLC (silica, 80:20 hexane/ ethyl acetate).

General Procedure for the Preparation of **(3a-3l)**

Method A

o-phenylenediamine (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask, and to this Sodium dodecyl Sulphate (10 mol%) was added. The reaction mixture was stirred at RT for the appropriate time (Table 2, entries 1-12). After completion of reaction, the mixture was extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under reduced pressure; the crude material was purified by column chromatography over silica gel to afford products **3a-3l** with high purity.

Method B

o-phenylenediamine (1mmol), aromatic aldehyde (1.1mmol) and water (10mL) were mixed in 25mL single neck round bottom flask, and to this Sodium dodecyl Sulphate (10 mol%) was added. The reaction mixture was irradiated in ultrasonic bath for the appropriate time (Table 2, entries 1-12). After completion of reaction, the mixture was extracted with ethyl acetate (2×10mL). The combined organic layer was dried over anhydrous Na_2SO_4 and evaporated under

reduced pressure; the crude material was purified by column chromatography over silica gel to afford products **3a-3l** with high purity.

Result and Discussion

We have developed an ecofriendly sodium dodecyl Sulphate assisted synthesis of 2-aryl substituted benzimidazole in water. 2-(4-methoxy phenyl)benzimidazole (**3b**) was selected as a proto type compound to optimize the reaction condition(Table 1) from *o*-phenylenediamine (**1**) and anisaldehyde (**2**) (Scheme 1). We first conducted the reaction of (**1**) [1 equivalent] and (**2**) [1.1 equivalent] in water at various temperature without SDS (Table 1, entry 1-3), gives traces of **3b**. Then we carried out the reaction between 1,2-phenylene diamine (**1**)[1 equivalent] and anisaldehyde(**2**)[1.1 equivalent] in presence of sodium dodecyl sulphate (10 mol%) in water at various temperature to afford the corresponding 2-(4-methoxy phenyl)benzimidazole (**3b**) (Table 1, entry 4-5). To optimize the amount of catalyst we carried the same reaction at different mol% (Table 1, entry 5-8). To reduce the time consumption, we have moved to non-conventional way by using ultra sound (Table 1, entry 9). With optimal condition in hand, we have reacted various substituted *o*-phenylenediamine**1** and aromatic aldehyde **2** to give the corresponding substituted 2-aryl benzimidazole product **3a** to **3l** (Table 2 entries1-12).

Table 1.Optimization of condition for the reaction of anisaldehyde and *o*-phenylenediamine in presence of Sodium dodecyl sulphate.[a]

Entry	SDS Mol%	Temperature	Time(min)	Yield [%][b]
1.	--------	RT	150	Traces
2.	--------	40^0c	150	Traces
3.	-------	60^0c	150	Traces
4.	10	RT	60	85
5.	10	40^0c	60	85
6.	5	RT	60	55
7.	7.5	RT	60	85
8.	12.5	RT	60	85
9.	10	Sonication	20	89

[a]Standard condition: of *o*-phenylenediamine (1mmole) with anisaldehyde (1.1mmol) in presence of different amount of sodium dodecyl sulphate in water. [b] Isolated yield based on starting *o*-phenylenediamine.

Spectroscopic Data for Compounds

***2-phenyl-1H-benzimidazole*3a**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3046,1444,1410,1275; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 12.7 (s, 1H, NH), 7.95 (m, 2H, Ar-H), 7.25-7.35 (m, 5H, Ar-H), 7.05(2H, Ar-H) ; MS (70 eV, EI): *m/z* (%): 195(M+1). Elemental analysis Calcd.for $C_{13}H_{10}N_2$. C, 80.39; H, 5.19; N, 14.42. Found: C, 80.42; H, 5.17; N, 14.41.

***2-(4-methoxy phenyl)-1H-benzimidazole*3b**

IR (KBr) $\upsilon_{max}(cm^{-1})$:3442, 1475, 1441, 1275,1240 ; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 3.8(s, 3H, OCH3), 7.09-7.11(d, 2H, *J* 9.2Hz,, ArH), 7.16-7.18(m, 2H, ArH), 7.53-7.56(m, 2H, ArH), 8.08-8.11(d, 2H, *J* 8.8Hz, ArH) ; MS (70 eV, EI): *m/z* (%): 225 (M+1) .Elemental analysis Calcd.for $C_{14}H_{12}N_2O$. C, 74.98; H, 5.39; N, 12.49. Found: C, 75.03; H, 5.36; N, 12.45.

***2-(4-chlorophenyl)-1H-benzimidazole*3c**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3041,1450,1402,1280 ; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 12.5 (s, 1H NH), 8.20 (d, 2H, Ar H), 7.6 (d, 2H, Ar H), 7.3 (m, 2H, Ar H), 7.1 m (m, 2H, Ar H) ; MS (70 eV, EI): *m/z* (%): 229(M+1). Elemental analysis Calcd.for $C_{13}H_9N_2Cl$. C, 68.28; H, 3.97; N, 12.25. Found: C, 68.20; H, 4.01; N, 12.28.

***5-Chloro-2-(4-methoxyphenyl)-1H-benzimidazole*3d**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3356, 3178, 1635, 869; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 7.97 (d, *J* 9.2 Hz, 2H), 7.86 (s, 1H), 7.67 (d, *J* 8.1 Hz, 1H), 7.35 (d, *J* 8.1 Hz, 1H), 6.92 (d, *J* 9.2 Hz, 2H), 3.75 (s, 3H) ; MS (70 eV, EI): *m/z* (%): 276 (M+1). Elemental analysis Calcd.for $C_{14}H_{11}ClN_2O$. C, 65.00; H, 4.29; N, 10.83. Found: C, 65.05; H, 4.25; N, 10.80.

***5-Chloro-2-(4-nitrophenyl)-1H-benzimidazole*3e**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3374, 3108, 1604, 1515, 1348, 857; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 8.52 (d, *J* 9.4 Hz, 2H), 7.96 (d, *J* 9.4 Hz, 2H), 7.85 (s, 1H), 7.71 (d, *J* 8.2 Hz, 1H),7.32 (d, *J* 8.2 Hz, 1H); MS (70 eV, EI): *m/z* (%): 274 (M+1).Elemental analysis Calcd.for $C_{13}H_8ClN_3O_2$. C, 57.05; H, 2.95; N, 15.35. Found: C, 56.98; H, 3.01; N, 15.30.

***5-Chloro-2-(4-N,N-dimethylaminophenyl)-1H-benzimidazole*3f**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3456, 3047, 2917, 1607, 820; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 7.94 (d, *J* 8.9 Hz, 2H), 7.85 (s, 1H), 7.66 (d, *J* 8.3 Hz, 1H), 7.37 (d, *J* 8.3 Hz, 1H), 6.82 (d, *J* 8.9 Hz, 2H), 3.35 (s, 6H); MS (70 eV, EI): *m/z* (%): 272 (M+1).Elemental analysis Calcd.for $C_{15}H_{14}ClN_3$. C, 66.30; H, 5.19; N, 15.46. Found: C, 66.38; H, 5.12; N, 15.40.

***2-(3-nitrophenyl)-1H- benzimidazole*3g**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3063,1523,1444,1357; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 12.9 (s, 1H, NH), 8.90 (s, 1H, Ar H), 8.50 (d, 1H, Ar H), 8.10 (d, 1H, Ar H), 7.70 (t, 1H, Ar H), 7.50 (m, 2H, ArH), 7.2 (m, 2H, ArH); MS (70 eV, EI): *m/z* (%): 240(M+1). Elemental analysis Calcd.for $C_{13}H_9N_3O_2$. C, 65.27; H, 3.79; N, 17.56. Found: C, 65.32; H, 3.70; N, 17.62.

***2-pyridin-3yl-1H-benzimidazole*3h**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3068,1449,1402,1280; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 13.05 (s, 1H, NH), 9.35(d, 1H, ArH), 8.75(m, 1H, ArH), 8.60(m, 1H, ArH), 7.70(m, 3H, ArH) 7.40 (m, 2H, ArH); MS (70 eV, EI): *m/z* (%): 196(M+1). Elemental analysis Calcd.for $C_{12}H_9N_3$. C, 73.83; H, 4.65; N, 21.52. Found: C, 73.90; H, 4.60; N, 21.50.

***2-(2,3-Dimethoxyphenyl)-1H-benzimidazole*3i**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3010, 2835, 1603, 1583; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 12.19 (s, 1H, NH), 7.84 (dd, 1H, *J* 7.3 & 1.1 Hz, ArH), 7.64 (m, 3H, ArH), 7.20 (m, 3H, ArH), 3.90 (s, 3H, OCH3), 3.85 (s, 3H, OCH3); MS (70 eV, EI): *m/z* (%): 255 (M+1).Elemental analysis Calcd.for $C_{15}H_{14}N_2O_2$. C, 70.85; H, 5.55; N, 11.02. Found: C, 70.89; H, 5.49; N, 11.07.

***2-(3-Fluorophenyl)-1H-benzimidazole*3j**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3053, 2685, 1616, 1582; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 13.00 (s, 1H, NH), 8.02 (d, 1H, *J* 7.7 Hz, ArH), 7.96 (m, 1H, ArH), 7.69 (m, 1H, ArH), 7.59 (m, 2H, ArH), 7.34 (m, 1H, ArH), 7.23 (m, 2H, ArH); MS (70 eV, EI): *m/z* (%): 213 (M+1).Elemental analysis Calcd.for $C_{13}H_9FN_2$. C, 73.57; H, 4.27; N, 13.20. Found: C, 73.51; H, 4.32; N, 13.28.

***2-(3-chloro phenyl)-1H-benzimidazole*3k**

IR (KBr) $\upsilon_{max}(cm^{-1})$:3447, 1621, 1275, 1240; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 8.41(t, 1H, *J* 1.2 & 2.0Hz, ArH), 8.20-8.29(dd, 1H, *J* 1.2 & 7.6Hz, ArH), 7.80-7.84(m, 2H, ArH), 7.69-7.77(m, 2H, ArH), 7.50-7.54(m, 2H, ArH); MS (70 eV, EI): *m/z* (%): 229 (M+1).Elemental analysis Calcd.for $C_{13}H_9ClN_2$. C, 68.28; H, 3.97; N, 12.25. Found: C, 68.35; H, 3.92; N, 12.20.

***2-(4-nitrophenyl)-1H- benzimidazole*3l**

IR (KBr) $\upsilon_{max}(cm^{-1})$: 3444, 1624, 1275,1245; H^1 NMR(400MHz, DMSO-d_6, ppm):δ 8.37-8.39(d, 2H, *J* 8.4Hz, ArH), 8.14-8.17(d, 2H, *J* 8.8Hz, ArH), 7.70-7.72(d,1H, *J* 7.6 Hz, ArH), 7.65-7.67(d, 1H, *J* 8.4Hz, ArH) 7.32-7.35(m, 1H, ArH), 7.25-7.29(m, 1H, ArH); MS (70 eV, EI): *m/z* (%): 240(M+1).Elemental analysis Calcd.for $C_{13}H_9N_3O_2$. C, 65.27; H, 3.79; N, 17.56. Found: C, 65.20; H, 3.87; N, 17.50.

Conclusions

Sodium dodecyl Sulphate provides an efficient methodology for the synthesis of 2-aryl substituted benzimidazole from various aromatic aldehydes with 1,2-phenylene diamine. The advantages offered by this method are the use of a sTable and inexpensive catalyst, a simple procedure, mild conditions and good yield of products, without need of any oxidizing agents.

Acknowledgment

The authors are grateful to the Head, Department of Chemistry, VinayakraoPatilMahavidyalaya, Vaijapur for providing the laboratory facility and Director, SAIF, Chandigarh for providing spectral analysis of synthesized compounds.

Table 2. Sodium dodecyl sulfate catalyzed synthesis of 2-arylbenzimidazole in water. [a]

Entry	R	Ar	Product	Method A		Method B		Melting Point (^{0}C)	
				Time (min)	Yield [%][b]	Time (min)	Yield [%][b]	observed	Reported
1.	H	Ph	3a	60	78	15	90	287-288	292 [17a]
2.	H	4-MeOC_6H_5	3b	60	85	20	89	228-230	226 [17a]
3.	H	4-Cl C_6H_5	3c	120	80	35	85	288-291	294 [17a]
4.	5-Cl	4-MeO C_6H_5	3d	115	82	35	85	276-279	278-279 [17h]
5.	5-Cl	4-NO_2 C_6H_5	3e	130	78	40	86	258-259	260-261 [17h]
6.	5-Cl	4-Me_2N C_6H_5	3f	120	77	45	88	311-313	310-312 [17g]
7.	H	3-NO_2 C_6H_5	3g	120	82	40	90	200-202	204-206 [17b]
8.	H	3-Pyrydyl	3h	60	80	15	92	243-246	245-248 [17f]
9.	H	2,4MeO C_6H_5	3i	145	82	65	90	175-177	178-179 [17c]
10.	H	3-F C_6H_5	3j	120	80	25	91	219-221	220-222 [17c]
11.	H	3-Cl C_6H_5	3k	125	85	40	92	230-231	234 [17a]
12.	H	4-NO_2 C_6H_5	3l	110	83	40	86	308-310	316 [17a]

[a] Standard condition: 1,2-phenylene diamine (1 mmol), ArCHO (1.1mmol), 10mol% catalyst(sodium dodecyl sulfate) , water ,. [b]Isolated yield based on starting 1,2-phenylene diamine.

References:

[1]. Yildiz, I. O.; Yalcin, I; Akisener, E.; N Ueartark, N. Eur.J.Med.Chem.2004, 39, 291.

[2]. Song, X.; Vig, B. S.; Lorenzi, P. L.; Drach, J. C.; Townsend, L. B.; Amidon, G. L. J.Med.Chem.2005, 48, 1274.

[3]. Yamoto, M. J.Pharm.Soc.Jpn.1992, 112, 81.

[4]. Kumar, D.; Jacob, M. R.; Rcynold, M. B.; Karvin, S. M. Bioorg.Med.Chem.2002, 10, 3997.

[5]. Benazzouz, A.; Boraud, T.; Dubedat, P.; Boireau, A.; Stutzmann, J. M.; Gross, C. Eur. J. Pharmacol.1995, 284, 299.

[6]. Güngör, T.; Fouquet, A.; Teulon, J. M.; Provost, D.; Cazes, M.; Cloarec, A. J. Med. Chem.1992, 35, 4455.

[7]. (a) Tidwell, R. R.; Geratz, J. D.; Dann, O.; Volz, G.; Zeh, D.; Loewe, H. J. Med. Chem.1978, 21, 613. (b) Failey, T. A.; Tidwell, R. R.; Donkor, I.; Naiman, N. A.; Ohemeng, K. A.; Lombardy, R. J.; Bentley, J. A.; Cory, M. J. Med. Chem., 1993, 36, 1746

[8]. Czarny, A.; Wilson, W. D.; Boykin, D. W. J. Heter. Chem.1996, 33, 1393.

[9]. Gogoi, P.; Konwar, D. Tetrahedron Lett., 2006, 47, 7

[10]. Lee, K. J.; Janda, K. D. Can. J. Chem., 2001, 79, 155

[11]. Lin, S.; Yang, L. Tetrahedron Lett.,2005, 46, 4315.

[12]. Beaulieu, P. L.; Hache, B.; Von Moos, E. Synthesis2003, 1683.

[13]. Singh, M. P.; Sasmal, S.; Lu, W.; Chatterjee, M. N. Synthesis2000, 1380.

[14]. Trivedi, R.; De, S. K.; Gibbs, R. A. J. Mol. Cat. A: Chem.2005, 245, 8.

[15]. Fazlinia, A.; Mosslemin, M. H.; Sadoughi, H. J. Kor. Chem. Soc.2010, 54, 5.

[16]. Nagawade, R. R.; Shinde, D. Ind. J Chem.2007, 46B, 349.

[17]. (a) Ben-Alloum, A.; Bougrin, K.; Soufiaoui, M. Tetrahedron Lett.2003, 44, 5935. (b) DeLuca, M. R.; Kerwin, S. M. Tetrahedron1997, 53, 457. (c) López, S. E.; Restrepo, J.; Pérez, B.; Ortiz, S.; Salazar, J. Bull. Korean Chem. Soc.2009, 30, 7. (d) Niralwad, K. S.; Shingate, B. B.; Shingare, M. S. Bull. Korean Chem. Soc.2010, 31, 4981. (e) Azarifar, D.; Maleki, B.; Setayeshnazar, M. Phosphorus, Sulfur Silicon Relat. Elem.2009, 184, 2097. (f) Myung, H. J.; Jung, M. P.; Ihl-Young, C. L.; Miya, A. J. Heter. Chem.2003, 40, 37. (g) Eshghi, H.; Rahimizadeh, M.; Shiri, A.; Sedaghat, P. Bull. Korean Chem. Soc.2012, 33, 2515.

[18]. (a) Sharma, G.; Kumar, R.; Chakraborti, A. K. Tetrahedron Lett., 2008, 49, 4269.(b) Manabe, K.; Mori, Y.; Kobayashi, S. Tetrahedron, 1999, 55, 11203.(c) McKay, C. S.; Kennedy, D. C.; Pezacki, J. P. Tetrahedron Lett., 2009, 50, 1893.(d) Mori, Y.; Kakumoto, K.; Manabe, K.; Kobayashi, S. Tetrahedron Lett., 2000, 41, 3107.(e) Wang,

W.; Wang, S. X.; Qin, Y.; Li, J. T. Synth. Commun., 2005, 35, 1263.(f) Gogoi, P.; Hazarika, P.; Konwar, D. J. Org. Chem., 2005, 70, 1934.(g) Orsini, F.; Sello, G.; Fumagalli, T. Synlett, 2006, 1717.(h) Deb, M. L.; Bhuyan, P. J. Tetrahedron Lett., 2006, 47, 1441.

[19]. (a) Bahrami, K.; Khodaei, M.; Nejati, A. Green Chem. 2010, 12, 1237.(b) Ghosh, P.; Mandal, A. Catal. Commun.,2011, 12, 744.

[20]. (a) Pawar, S. S.; Shingare, M. S.; Thore, S. N. Lett. Org. Chem. 2007, 4, 486.(b)Pawar, S. S.; Dekhane, D. V.; Shingare, M. S.; Thore, S. N. Tetrahedron Lett. 2008, 49, 4252. (c) Pawar, S. S.; Uppalla, L. S.; Shingare, M. S.; Thore, S. N. Tetrahedron Lett2008, 49, 5858. (d) Pawar, S. S.; Dekhane, D. V.; Shingare, M. S.; Thore, S. N. Chinese Chemical Lett. 2008, 19, 1055. (e) Pawar, S. S.; Dekhane, D. V.; Shingare, M. S.; Thore, S. N. J. Heterocyclic Chem. 2008,45, 1. (f)Pawar, S. S.; Dekhane, D. V.; Shingare, M. S.; Thore, S. N. Australian J.Chem., 2008, 61, 905. (h) Pawar, S. S.; Shingare, M. S.; Thore, S. N. Chinese Chemical Lett. 2009, 20, 32. (i) Pardeshi, S. D.; Sonar, J. P.; Pawar, S. S.; Dekhane, D.; Gupta, S.; Zine, A. M.; Thore, S. N. J. Chil. Chem. Soc.,2014, 59, 1, 2335.