ISSN: 2249 –4820

Chemistry & Biology Interface, 2012, 2, 2, 122-125

Chemistry & Biology Interface

An official Journal of ISCB, Journal homepage; www.cbijournal.com

Research Paper

Microwave mediated solvent free synthesis of 2-arylbenzimidazoles from aldehydes using a solid base catalyst.

Pranab Jyoti Das*, Akashi Baruah

Department of Chemistry, Gauhati University, Guwahati 781 014, India
Received 17February 2012; Accepted 29 February 2012

Keywords: 2-arylbenzimidazole, aromatic aldehyde, *o*-phenylenediamine, solid base, microwave, solvent free.

Abstract: A solvent free synthesis of 2-arylbenzimidazoles was carried out using catalytic amount of a solid base mediated by microwave. Reaction time is short, recovery is simple and clean products obtained. The yields of the products are good.

Introduction

2-arylbenzmidazoles are biologically active compounds[1]. They also find application as chiral auxiliaries[2], chiral catalyst[3], ligands for asymmetric synthesis[4], and also as synthetic intermediates[5]. Further, the benzimidazole moiety is found in many synthetic pharmaceuticals displaying a wide spectrum of biological activity including anti ulcer, anti tumor and antiviral effects[6]. There are two general methods of synthesis of 2-aryl-benzimidazoles namely the coupling of *o*-phenylenediamine and carboxylic acid or its derivatives and the other involve the oxidative cyclodehydration of appropriate Schiff bases. Some previously reported synthesis are cyclocondensation of N-(trifluoroacetamido)-o-aryldiamines mediated by montmorillonite K-10[7],Oxone promoted condensation of 1,2-phenylenediamine with an aldehyde in wet DMF[8],one pot cyclodehydration of N-acyl-1,2-phenylenediamine using BF_3-Et_2O[9]. A four component Ugi reaction of monoBoc-o-phenylenediamine[10] and $In(OTf)_3$ catalyzed condensation reaction[11]. Some of the recent synthesis of 2-arylbenzimidazoles includes a mild and efficient solvent free method using CAN and H_2O_2[12], a synthesis catalyzed by tetrabutylammonium Fluoride (TBAF) [13], the use of an efficient catalyst in phenylboronic acid [14] besides others [15,16].

Organic synthesis using solvent free techniques, especially those mediated by microwave have attracted the attention of synthetic organic chemist because of short reaction time, formation of clean products and high turnover of the target molecule[17]. These microwave assisted reactions are

Corresponding Author*
E-mail: pjd123@sify.com

ISSN: 2249 –4820

Chemistry & Biology Interface, 2012, 2, 2, 122-125

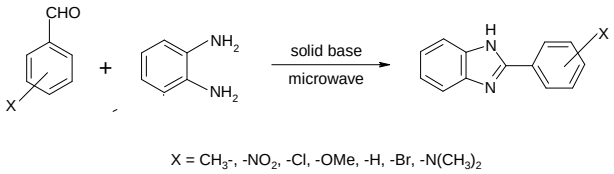
particularly attractive when carried out under solvent free conditions using a solid catalyst especially because of their low cost, reduction in pollution and simplicity in process and handling[18].

Herein, we report an efficient microwave mediated solvent free synthesis of 2-aryl-benzimidazoles from aromatic aldehydes and *o*-phenylenediamine using a solid base. Aldehydes have been a popular substrate for the synthesis of 2-arylbenzimidazoles and several methods have been reported[19]. However, some methods have used organic solvents with dubious reputation of being toxic and in others, high temperature, long reaction time and moderate yields are the notable drawbacks.

Results and Discussions

To the best of our knowledge, solid base have never been used as a catalyst for the synthesis of 2-arylbenzimidazoles and we report herein the use of a solid base for the synthesis of the target molecule mediated by microwave under solvent free condition.This method appears to be an improvement over method reported earlier. The solid base used in this synthesis was earlier prepared by Li [20] by fusing a mixture of KNO_3 and Al_2O_3 at 600^{o}C. Fusion of the mixture at that temperature , gave a solid base of composition Al_2O_3-OK which reportedly has a layered structure of basic material K_2O and Al_2O_3 resulting in the availability of super basic sites on the surface. In a typical method, the aldehyde, *o*-phenylenediamine and the solid base was thoroughly ground to a homogeneous mixture in a mortar. The mixture was then exposed to microwave at 750 W power for a short period of time (2-3 min). The solid mass obtained was extracted with the relatively benign ethanol. Reduced pressure removal of the solvent gave the crude 2-arylbenzimidazoles which was purified by column chromatography in silica gel column with 20% ethylacetate: pet. ether (40-60) as eluent. The reaction is shown in Scheme 1 and the experimental results are summarized in Table I.

Scheme I



X = CH_3-, -NO_2, -Cl, -OMe, -H, -Br, -$N(CH_3)_2$

Experimental

All chemicals were purchased from Merck (India) and used without further purification. Melting points of the products were recorded in open capillaries and are uncorrected. Melting points were compared with those found in literature. IR spectra were recorded in KBr pallets in Perkin Elmer FT-IR 1600. Elemental analysis of the products were recorded in Perkin Elmer CHN analyzer 2400 and ^{1}H-NMR spectra were recorded in Varian 400MHz FT-NMR using TMS as the internal standard. The solid base catalyst was prepared as reported by Li [20]. Microwave reactor used was procured from Catalyst (India) Pvt. Ltd, Pune, India

General procedure

Aromatic aldehyde (1 mmol) was mixed with *o*-phenylenediamine (2 mmol ,0.138 mL) and 500 mg of the solid base and ground in a pestal grinder to a free flowing homogeneous powder. This mixture was exposed to microwave radiation at 750 W power for 2-4 min. The products were recovered by extraction with 10 mL of ethanol and the crude products obtained by reduced pressure distillation of the solvent in a rotavapor. The crude products were purified by column chromatography in silica

ISSN: 2249 –4820

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gel column and 20% ethyl acetate: pet. ether (40-60) as the eluent.

Table 1: Microwave mediated solvent free synthesis of 2-arylbenzimidazole using a solid base

Entry	X	Mp (^oC)		Time	Yield (%)
		obs	lit		
1	4-CH_3-	261-263	270[18]	2	80
2	2-Cl-	oil	234[18]	3	75
3	4-Cl-	290	294[11]	2.5	80
4	-H	290	292[11]	2	85
5	-OMe	232	235-36[21]	3	80
6	-Br	oil	--	2	78
7	-NO_2	309	316[22]	2	75
8	-$N(CH_3)_2$	oil	--	4	80
9	3-NO_2-	oil	--	4	70
10	2-NO_2-	oil	--	2.5	72

Spectroscopic data of 2-arylbenzimidazoles

Product : 2-(4-methylphenyl)benzimidazole: IR(KBr): cm^{-1} 3310(N-H), 1615(>C=N-) ^1H NMR (400 MHz, $DMSOd_6$) δ 8.1(broad), s,NH) 7.8-7.9 (m, aromatic 4H) , 7.5-7.8 (m, aromatic, 5H) 2.38 (s,3H)

Product 2:2-(2-chlorophenyl)benzimidazole: IR(KBr) : cm^{-1} 3304(N-H), 1609(>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ 8.3 (broad), s,NH) 7.8-7.9 (m, aromatic 4H) , 7.1-7.3 (m,5H).

Product 3: 2-(4-chlorophenyl)benzimidazole: IR(KBr) : cm^{-1} 3320(N-H),1611 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.3(broad), s,NH) 7.5-7.8(m, aromatic 4H) , 7.3-7.4(m, aromatic, 5H).

Product 4 : 2-phenylbenzimidazole: IR(KBr) : cm^{-1} 3436(N-H), 1595 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.2(broad, s,NH) 8.04(m, aromatic 5H) , 7.58 (m,aromatic 5H).

Product 5: 2-(4-methoxy)phenylbenzimidazole: IR(KBr):cm^{-1}3436(N-H),1595 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.2(broad, s,NH) 8.04(m, aromatic 5H) ,7.58 (m ,aromatic 4H).

Product 6: 2-(4-bromo)phenylbenzmidazole: IR(KBr):cm^{-1}3283(N-H),2962 and 2944 (CH), 1609 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.1(broad, s,NH) 7.7-7.9(m, aromatic 5H) , 7.3-7.5 (m ,aromatic 4H).

Product 7: 2-(4-nitro)phenylbenzimidazole: IR(KBr):cm^{-1}3310(N-H), 1620 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.1(broad, s,NH) 7.7-7.9(m, aromatic 4H) , 7.0-7.2 (m ,aromatic 5H).

Product 8: 2-(4-N,N-dimethylamino)phenyl benzimidazole: IR(KBr):cm^{-1}3310(N-H), 1610 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.2(broad, s,NH) 7.7-7.9(m, aromatic 5H) , 7.3-7.5 (m ,aromatic 4H), 3.1 (s,6H).

Product 9: 2-(3-nitro)phenylbenzimidazole: IR(KBr):cm^{-1}3278(N-H), 2962 and 2918 (C-H), 1620 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.1(broad, s,NH) 7.9(m, aromatic 4H) , 7.5-7.7 (m ,aromatic 5H).

Product 10: 2-(2-nitro)phenylbenzimidazole: IR(KBr):cm^{-1}3340(N-H), 1610 (>C=N-), ^1H NMR (400 MHz, $DMSOd_6$) δ8.1(broad, s,NH), 7.5-7.7 (m ,aromatic 4H).7.2-7.3 (aromatic, 5 H)

Conclusion

The study describes a successful approach for the synthesis of the 2-arylbenzimidazoles under solvent free condition using a solid base. It was also observed that the reaction failed in the absence of the solid base. The reaction required short reaction time and the recovery of the products was easy and convenient. The yields of the products have also been found satisfactory.

Acknowledgement

The authors are grateful to CIF, IIT, Guwahati, for instrumental facilities A. Baruah is thankful to Council of Scientific

ISSN: 2249 –4820

Chemistry & Biology Interface, 2012, 2, 2, 122-125

and Industrial Research, India, for grant of Senior Research Fellowship.

References

[1] M R Grimmet, Comprehensive Heterocyclic Chemistry, Edited by A R Katrizky, C W Rees & E F V Seriven,(Pergamon: Oxford), **1996**,3,77
[2] M.C.W Ueno, K.Imaizumi,T.Sugita,I.Takata, M. Takeshita, Int J Immunopharmac, **1995**,17, 597
[3] M. E. Jung, A .Huang, Org Lett, **2000**, 2, 2659
[4] T .Marimoto, K .Tachibana, K. Achiwa, Synlett, **1997**, 783
[5] R.C. F Jones, J. R. Nichols, Tetrahedron Lett, **1990**, 31, 1774
[6] K.H.Michel, L.D.Boeck, M.M.Hoehn, N.D.Jones, M.O.Chaney, Antibiot,**1984**,37,441
[7] V.J.Grenda, R.E.Jones, G. Gal, M.J. Siettzinger, J.Org. Chem, **1965**,30,259.
[8] P.L.Beaulier, B. Hache, E.Von Moos, Synthesis, **2003**,1683.,
[9] V.K.Tandon, M.Kumar, Tetrahedron Letters, **2004**,45,4185.
[10] P.Tempest, V.Ma, S.Thomas, H.Zheng, M.Kelly, C. Hulme, Tetrahedron Lett **2001**,42,4959.
[11] R.Trivedi, S.K.De, R.A.Gibbs, J.Mol.Cat.A. Chem, **2006**,245,8.
[12] K. Bahrami, M. M. Khodaei, F. Naali, J. Org. Chem., **2008**, *73*, 6835-6837.
[13] Ratnadeep S. Joshi, Priyanka G. Mandhane, Sanjay K. Dabhade and Charansingh H. Gill, Journal of the Chinese Chemical Society, **2010**, 57, 1227.
[14] Santosh V. Goswami, Prashant B. Thorat, Vijay N. Kadam and Sudhakar R. Bhusare J. Chem. Bio. Phy. Sci. **2011**, 1, Sec.A, 164
[15] R.Wang, X.Lu,; X.Yu,; L.Shi,; Y. Sun,.; J.Mol.Cat.A. Chem,**2007**,266,198.
[16] K.Niknam, A.Fatehi-Raviz, J.Iran.Chem Soc, **2007**,4,438.
[17] a) L .Perreux , A, Laupy, Tetrahedron, **2001**,57, 9199 b) P.Libstrom, J .Tierney, B Athery , J Westman, Tetrahedron, **2001**, 57, 9225 c) D.M. P. Mingos, D. R. Baghirst, in Microwave Enhanced Chemistry ,edited by H M Kingstone, S J Haswell (*Am. Chem.. Soc. Washington D. C).* **1997**, p4
[18] a) A.McKillop , D. W. Young, Synthesis, **1979**, 401, b) R.S. Varma , Green Chem, **1999**,1, 43; c) K .Tanaka, F .Toda , Chem Rev, **2000**,100, 1025
[19] a) M. Ishihara , H.Togo, Synlett, **2006**, 227 ; b) P .Gogoi D. Konwar, Tetrahedron Lett, **2006**, 47, 79; c) S .Sayama , Synlett, **2006**, 1479; d) J. M. Mitchell, N. S. Finney, Tetrahedron Lett, **2000**, 41, 8431 e) H .Fujioka, K .Murai, O .Kubo, Y .Ohba, A. Hiramatsu , Y. Kita, Tetrahedron Lett, **2005**,46, 2197; f) H .Fujioka, K .Murai, O. Kubo, Y .Ohba, A .Hiramatsu , Y .Kita, Tetrahedron Lett, **2007**,63, 638
[20] T.S.Jin, J.S. Zhang, A.Q.Wang, T.S. Li, , *Chemistry-An Indian journal*, **2004**,1, 353
[21] A. Ben-Alloum, K.Bougrin, M.Soufiaoui, Tetrahedron Lett. **2003**, 44,5935.
[22] D.V.Ramanna, E. Kantharaj, J.Chem. Soc, Perkins Trans. 2, **1995**,1497.