ISSN: 0974 - 7516 Volume 11 Issue 2

Organic CHEMISTRY

An Indian Journal

Full Paper

OCAIJ, 11(2), 2015 [055-058]

A simple and efficient one-pot phenyl phonic acid catalyzed synthesis of 2-aryl-benzimidazoles derivatives under mild conditions

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ABSTRACT

Various 2-aryl-benzimidazoles can be prepared by reaction of the *o*-phenylenediamine with various arylaldehydes at 80 °C catalyzed by phenyl phonic acid as an effective reagent under neutral conditions in satisfactory yields.

KEYWORDS

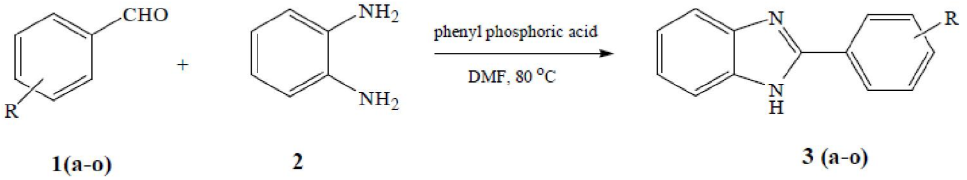
Phenyl phonic acid;
2-aryl-benzimidazoles;
Neutral conditions;
O-phenylenediamine.

INTRODUCTION

Benzimidazoles are very useful intermediates for the development of molecules of pharmaceutical and biological interest. Substituted benzimidazole derivatives have found applications in diverse therapeutic areas including antiulcer, antihypertensive, antiviral, antifungal, anticancer, and antihistaminics[1,2]. The widespread interest in benzimidazole containing structures has prompted extensive studies for their synthesis. There are two general methods for the synthesis of 2-substituted benzimidazoles. One is the coupling of *o*-phenylenediamines and carboxylic acids[3] or their derivatives (nitriles, ortho esters), which often require strong acidic conditions and sometimes combine with very high temperatures (i.e., PPA, 180 °C) [4,5-6]. The other way involves a two-step procedure that includes the oxidative cyclo dehydrogenation of aniline Schiff's bases, which are often generated in situ from the condensation of *o*-phenylenediamines and aldehydes[7-12]. However, suffer from longer reaction times, unsatisfactory yields, harsh reaction conditions and excessive use of reagents and catalysts. It is therefore important to find more convenient methods for the preparation of these compounds.

RESULT AND DISCUSSION

In continuation with the search for simple non-hazardous methods for the transformations in organic synthesis [13-21], herein we report a highly versatile



Scheme 1 : Synthesis of 2-aryl-benzimidazoles with phenyl phosphoric acid

TABLE 1 : Phenyl phosphoric acid catalyzed synthesis of benzimidazoles

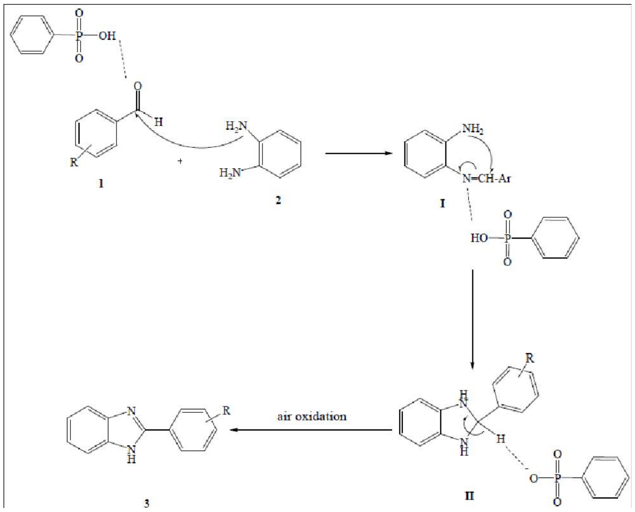
Entry	Product ^{a}	R	Time (min)	Yields (%)^b	M.p., ^{o}C
1	3a	H	40	98	286-290
2	3b	4-OMe	60	95	225-227
3	3c	4-Me	30	95	272-273
4	3d	3-Me	50	94	215-217
5	3e	2-NO_2	28	92	263-265
6	3f	4-Cl	21	93	289-291
7	3g	4-NO_2	20	96	310-312
8	3h	3,4-OMe_2	49	95	178-180
9	3i	3-Br	24	94	217-219
10	3j	3-NO_2	26	90	205-207
11	3k	4-$N(Me)_2$	39	93	250-251
12	3l	2-Cl	26	92	156-158
13	3m	4-CN	27	91	262-264
14	3n	4-F	22	96	202-203
15	3o	2-OH	31	92	235-236

a) Isolated yields. b) All the products are known, characterized by IR, NMR spectral analysis and compared with the authentic samples.

and efficient synthesis of 2-aryl-benzimidazoles 3(a-o) from aldehyde 1(a-o), *o*-phenylenediamine 2 and catalytic amounts of phenyl phonic acid under mild reaction in high yields (Scheme 1 and TABLE 1).

To account for the facile formation of benzimidazoles, the following mechanism (Scheme 2) is proposed. The reaction between an aldehyde and a diamine leads to the formation of Schiff base (I) which is stabilized by catalyze. Intermolecular attack by the second amino group on C=N double bond facilitates the formation of hydro-benzimidazole (II) which undergoes subsequent air oxidation to give the desired benzimidazole as the ûnal product [22].

The role of the solvent was also investigated. Among the various solvents tested, DMF afforded the maximum yield of the of 2-aryl benzimidazole derivative 3a (TABLE 2). It is well known that reactions of this type are more efficient in polar solvents, which was corroborated in this study (TABLE 2). It was also observed that the inclusion of water had very little or no effect on this reaction. DMF was the best among the solvents tested. Under optimized reaction conditions, we obtained exclusively 2- substituted products (3).



Scheme 2 : Possible mechanism for the synthesis of 2-aryl-benzimidazoles

EXPERIMENTAL

Chemicals used in this work were purchased from Aldrich and Merck chemical companies and

TABLE 2 : Role of the solvent in the synthesis of 2-phenyl-benzimidazoles 3a

solvent	Time (h) ^{a}	Yield (%)
CH_2CL_2	2	50
EtOH	2	70
CH_3CN	4	80
MeOH	2	60
Dioxan	3	70
H_2O	2	60
DMF	1	98

^{a}Extension of the reaction did not improve the product yield

used without purification. IR spectra were recorded on a Shimadzu 435-U-04 FT spectrometer as KBr pellets. ^{1}H and ^{13}C NMR spectra were measured in DMSO-$CDCl_3$ with a Bruker DRX-400 Advance instrument at 400 and 100 MHz, respectively, using Me_4Si as internal standard. Mass spectra were recorded with a spectrometer Finnegan-MAT 8430 operating at an ionization potential of 70 eV. Melting points were measured on a SMPI apparatus

GENERAL PROCEDURE FOR THE SYNTHESIS OF 2-ARYL-BENZIMIDAZOLES DERIVATIVES (1A–N)

To a mixture of *o*-phenylenediamine (1 mmol), aldehyde (1 mmol) and phenylphosphonic acid (5mol %) in DMF (5ml) was stirred and heated at 80 °C for the appropriate time (TABLE 1). Completion of the reaction was indicated by Thin Layer Chromatography (TLC). After which dichloromethane (10 ml) was added to the mixture and left aside for a few minutes, the solid thus separated was recrystallized from methanol or subjected to silica gel column chromatography to get the pure product/s.

CONCLUSION

We have described an efficient and environmentally benign method for the preparation of 2-arylbenzimidazoles derivatives. This two-component reaction is efficiently catalyzed by phenyl phonic acid under mild reaction at 80 $^{oC.}$ Operational simplicity, mild reaction conditions, enhanced rates, and high isolated yields of the pure products are significant advantages of the protocol presented here.

REFERENCES

[1] A.A.Pasov, I.N.Yozhitsa, L.I.Bugaeva, V.A.Anisimova; Pharm. Chem. J., **33**, 232 **(1999)**.

[2] T.Roth, M.L.Morningstar, P.L.Boyer, S.H.Hugh-es, R.W.Buckheit; Jr.; Michejda, C. J.J.Med. Ch-em., **40**, 4199 **(1997)**.

[3] J.B.Wright; Chem. Rev., **48**, 397 **(1951)**.

[4] T.A.Fairley, R.R.Tidwell, I.Donkor, N.A.Naiman, K.A.Ohemeng, R.J.Lombardy, J.A.Bentley, M.J.C-ory; Med. Chem., **36**, 1746 **(1993)**.

[5] R.Wang, X.Lu, X.Yu, L.Shi, Y. Sun; J.Mol. Catal. A. Chem., **266**, 198 **(2007)**.

[6] P.L.Beaulieu, B.Hache, E.Von Moos; Synthesis, **11**, 1683 **(2003)**.

[7] M.Chakrabarty, S.Karmakar, A.Mukherji, S.Arima, Y.Harigay; Heterocycles, **68**, 967 **(2006)**.

[8] M.Curini, F.Epifano, F.Montanari, O.Rosati, S.Taccone; Synlett, 1832 **(2004)**.

[9] K.R.Hornberger, G.M.Adjabeng, H.D.Dickson, R.G.Davis-Ward; A mild, one-pot synthesis of disubstituted benzimidazoles from 2-nitroanilines, Tetrahedron Lett, **47**, 5359-5361 **(2006)**.

[10] V.Mirkhani, M.Moghadam, S.Tangestaninejad, H.Kargar; Rapid and efficient synthesis of 2-imidazolines and bis-imidazolines under ultrasonic irradiation, Tetrahedron Lett., **47**, 2129-2132 **(2006)**.

[11] B.Das, H.Holla, Y.Srinivas; Efficient (bromodimethyl) sulfonium bromide mediated synthesis of benzimidazoles, Tetrahedron Lett., **48**, 61-64 **(2007)**.

[12] U.Srinivas, Ch.Srinivas, P.Narender, V.J.Rao, S.Palaniappan, Catal Commun, **8**, 107 **(2007)**.

[13] C.D.Wilfred, R.J.K.Taylor, Synlett, 1628 **(2004)**.

[14] D.Azarifar, H.Ghasemnejad-Bosra, M.A.Zolfigol, M.Tajbaksh; Microwave-assisted synthesis of N-arylglycines : improvement of sydnone synthesis, Heterocycles, **68**, 175-181 **(2006)**.

[15] M.Forouzani, H.Ghasemnejad-Bosra, S.Habibzadeh; The synthesis of 14-aryl-14H-dibenzo [a,j] xanthenes under solvent-free conditions. Science China Chemistry, **6**, 957-960 **(2011)**.

[16] H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh, F.Ramzaniyan-Lehmali; An efficient one-pot synthesis of highly substituted furans catalyzed by N-bromosuccinimide, J. Serb. Chem. Soc., **75**, 299-305 **(2010)**.

[17] H.Ghasemnejad-Bosra, M.Haghdadi, I.Gholampour-Azizi; N-Bromosuccinimide (NBS) as promoter for acylation of sydnones in the presence of acetic anhydride under neutral conditions, Heterocycles, **75**, 391-395 **(2008a)**.

[18] H.Ghasemnejad-Bosra, M.Haghdadi, O.Khanmohamadi, M.Gholipour, G.Asghari; Bis-bromine-1,4-diazabicyclo[2.2.2]octane (Br2-DABCO) as an efficient promoter for one-pot conversion of N-arylglycines to N-arylsydnones in the presence of NaNO2/Ac2O under neutral conditions, J. Chin. Chem. Soc., **55**, 464-467 **(2008)**.

[19] H.Ghasemnejad-Bosra, M.Faraje, S.Habibzadeh; Efficient one-Pot 1,3-dibromo-5,5-dimethylhydantoin (DBH)-catalyzed synthesis of highly substi-

tuted furans. Helv. Chim. Acta., **92**, 575-578 **(2009)**.

[20] H.Ghasemnejad-Bosra, M.Forouzani; A simple and efficient one-pot bis-bromine-1,4-diazabicyclo [2.2.2] octane(Br2-ABCO) catalyzed synthesis of 14-aryl-14H-dibenzo[a,j]xanthenes under solvent free conditions Heterocycl, Commun, **17(1-2)**, 83-85 **(2011)**.

[21] S.Habibzadeh, H.Ghasemnejad, M.Faraji; Efficient one-Pot 1, 3-dibromo-5, 5-dimethylhydantoin (DBH)-catalyzed synthesis of highly substituted furans, Helv, Chim. Acta., **94**, 429-578 **(2011)**.

[22] S.Lin, L.Yang; A simple and efficient procedure for the synthesis of benzimidazoles using air as the oxidant, Tetrahedron Lett., **46**, 4315-4319 **(2005)**.