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A SIMPLE AND CONVINIENT ONE POT SYNTHESIS OF 2-ARYL BENZIMIDAZOLE DERIVATIVES USING ZIRCONIUM OXYCHLORIDE AS A CATALYST

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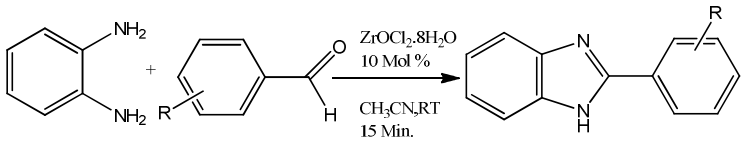
Abstract
A one pot synthesis of 2-aryl benzimidazole has been described on reaction with o-phenylenediamine and various aromatic aldehydes using zirconium oxychloride as a catalyst. This protocol offers the significant advantages in terms of simplicity, low catalyst loading, very good yields, the use of available catalysts, simple workup procedure, short reaction time, no need of purification and non toxic in nature.



Scheme: 1 Synthesis of 2-aryl benzimidazoles using zirconium oxychloride as a catalyst

Keywords: Aromatic aldehydes, catalysis, Benzimidazoles, zirconium oxychloride octahydrate, o-phenylenediamine.

Introduction

Benzimidazoles constitutes an important group of heterocyclic compounds and they exhibit wide range of biological activities such as antifungal, [i] antiviral, [ii, iii] antibacterial [iv], anticancer, [v]anti-inflammatory [vi]. Their potential biological activity encouraged us to prepare new heterocyclic derivatives as these heterocycles can be conveniently synthesized under laboratory conditions.

Different synthetic methodologies are reported in literature for the synthesis of benzimidazoles. Generally, condensation of o-phenylenedimine with carboxylic acids and their derivatives is most common and widely practiced. Also substituted benzimidazoles can be synthesized from o-phenylenedimine and orthoester such as orthoformate, orthoacetate and orthovalarate using $ZrOCl_2.8H_2O$ at room temperature and under microwave irradiation. [vii] Simple and efficient method for convenient synthesis of 2-aryl benzimidazoles on reaction with phenylene diamine and various aromatic aldehydes using Cobalt (II) chloride hexahydrate as a catalyst is reported. [viii]

Condensation of o-phenylene diamine with the carbonyl compounds in the presence of strong acids such as polyphophoric acid or mineral acids [ix], and other reagents such as $KI/I_2/K_2CO_3$ [x], $Yb(OTF)_3$[xi] , N-halosuccinaamide (X=Cl, Br,I)[xii],PEG-100 [xiii], $(NH_4)H_2PW_{12}O_{40}$ [xiv] and palladium as well as Microwave irradiation and solid phase reaction [xv] are reported in literature.

The present study describe synthesis of 2- substituted benzimidazoles on reaction of 2-phenylenediamine with aldehydes in acetonitrile in the presence of zirconium oxychloride octahydrate as a catalyst at room temperature within a short time (15 min).

Result and Discussion

The synthesis of 2-aryl benzimidazoles is carried out by condensation of aromatic diamine in acetonitrile in presence of zirconium oxychloride as catalyst.

The reaction of o-phenylene diamine with 4-chlorobenzaldehyde has been chosen as a model reaction to find out a suitable catalyst in acetonitrile, for the synthesis of 2-arylbenzimidazole derivatives. We carried out reaction with several catalysts like NH_4Cl, NH_4Br, NH_4F, $(NH_4)_2SO_4$, $(NH_4)_2CO_3$, $CoCl_2.6H_20$, $ZnCl_2$ and were examined to obtained better yields, but it is our finding that all these catalysts took long time duration as compared to $ZrOCl_2.8H_2O$ as catalyst with better yield within short time (15 min).

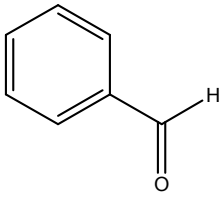
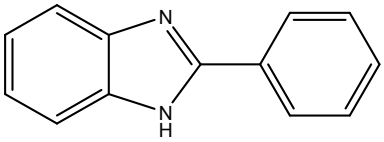
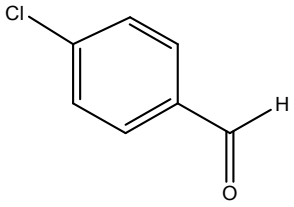
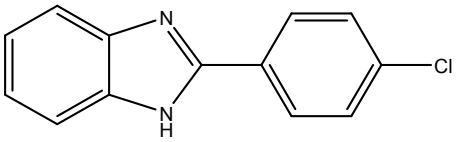
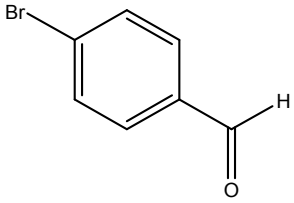
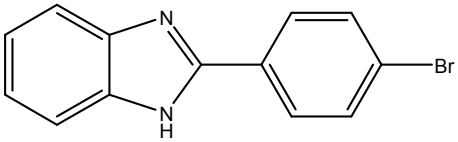
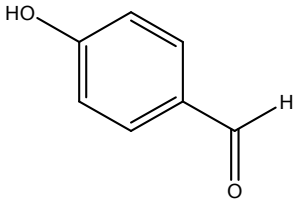
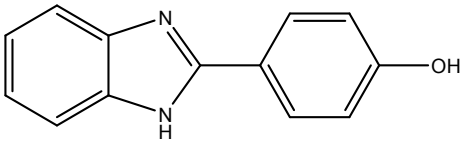
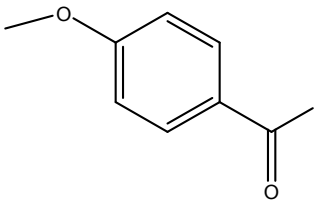
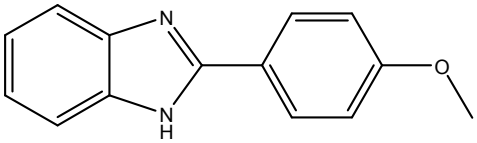
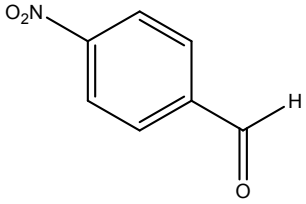
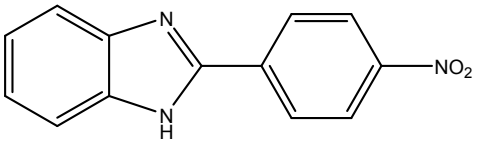
Table. I-: Optimization of reaction condition for the synthesis of 2-phenyl benzimidazole derivative by the condensation of o-phenylenedimine with benzaldehyde using different catalysts at room temperature in CH_3CN.

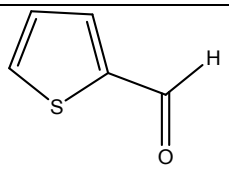
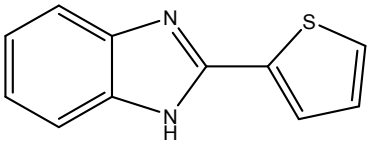
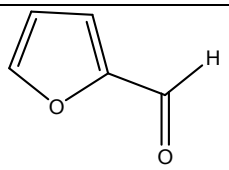
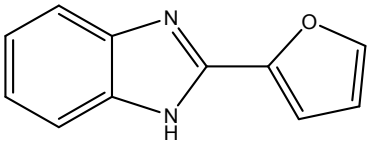
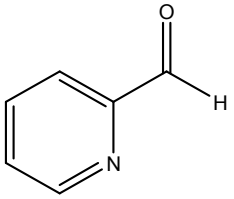
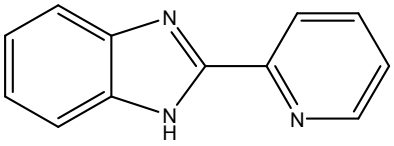
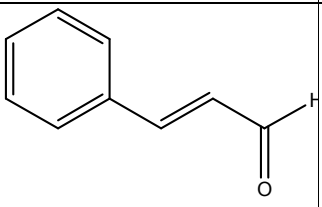
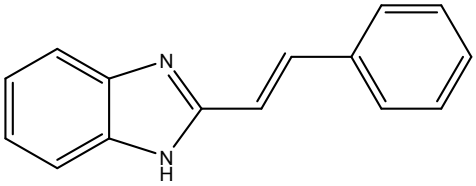
Sr.No.	Catalyst	Time(hrs & min)	Yield %
1	**$ZrOCl_2.8H_2O$**	**15 min**	**95**
2	NH_4F	5hrs	72
3	NH_4Cl	4hrs	92
4	NH_4Br	4hrs	86
5	$(NH_4)_2SO_4$	12hrs	78
6	$(NH_4)_2CO_3$		82
7	$CoCl_2.6H_20$	6hrs	88

This catalyst is cheaper, soluble in water and recyclable. This recycled catalyst was reused thrice for the same reaction.

Ortho phenylenediamine was treated with different aromatic aldehydes in presence of $ZrOCl_2.8H_2O$ under similar experimental conditions which gives better yields in short time duration are shown in following table.

Table.II zirconium oxychloride octahydrate as a catalysed synthesis of 2-aryl benzimidazole derivatives-:

Entry	Aldehydes	Time (min)	Product	Yield (%)
a		15		90
b		12		95
c		12		92
d		13		90
e		12		91
f		12		95

g		15		80
h		15		82
i		12		79
j		15		80

Conclusion

The significant features of this method are; the time required for the completion of the cyclocondensation is markedly reduced and the yields of the products are near to stoichiometric, clean reactions, as well as avoidance of column chromatographic purifications. We believe this novel method is a useful contribution to the existing methodologies. These merits of this method make this synthetic route rapid, economical, efficient and eco-friendly.

Experimental

Chemicals used were of synthetic grade and made by S.D. fine or spectrochem and used without further purification.1H-NMR spectra were recorded on a Bucker DRX-300 instrument and Mass spectra was recorded on a Jeol SX-102 (FAB) instrument. Melting points were taken open capillaries and are uncorrected.IR was recorded in KBr on a Nicolet impact 410.

General experimental procedure-:

To a mixture of 4-chlorobenzaldehyde (1.40g,10mmol) and o-phenylenediamine (1.08g,10mmol) in acetonitrile (5ml) in a round bottom flask zirconium oxychloride octahydrate (0.32g,10mol%) was added. The resulting reaction mixture was stirred at room temperature for 15 minutes. Progress of reaction was monitored by TLC. After completion of reaction solvent was evaporated. To the obtained crude compound water was added, the solid obtained was filtered which was recrystallized from ethanol to give pure benzimidazole derivatives. All the products were fully characterised by spectroscopic techniques mention as above.

Data

2-(4-Chloro phenyl) benzimidazole (b)-: Mp 297^0 C, (lit.[viii]), IR (KBr) :600, 724, 1692,2332,2800,3094cm^{-1} 1H NMR (400MHz, $CDCl^3$): 7.31-8.28(m,8H), 12.83 (s,1H, NH), MS m/z:227(M+1), 13C NMR (75MHz, DMSO-*d*6): δ:111.3, 118.7,122.2, 128.2, 129.1, 129.2, 134.3, 143.5, 150.1.

2-(4-Hydroxyphenyl) benzimidazole (e)-: Mp 168^0 C, (lit.[viii]), IR (KBr) :1610 (C=N), 3362 (NH),3572 (OH) cm-1 1H NMR (400MHz, DMSO-d6): 6.92(d, J=8.4Hz,2H), 7.10-7.14 (m,2H),7.48 (d, J=6.8 Hz,1H), 7.57 (d, J=7.4 Hz,1H), 7.97 (d, J=8.6 Hz,2H), 9.92 (bs,1H),12.61(bs,1H).13 C NMR (300 MHz, DMSO-d6): 114.4, 115.0, 120.2, 121.2, 128.1, 138.4, 145.4, 158.6.

2-(4-Nitroyphenyl) benzimidazole (f)-: Mp 301_C (lit.[viii]), IR (KBr): 1345, 1552 (NO2), 1618 (C¼N), 3445 (NH) cm_1. 1H NMR (400 MHz, DMSO-d6): 7.16–7.20 (m, 2 H), 7.52–7.55 (m, 1 H), 7.63–7.65 (m, 1 H), 8.30 (d, J¼8.0 Hz, 2 H), 8.35(d, J¼8.8 Hz, 2 H), 13.22 (bs, 1 H). 13C NMR (100 MHz, DMSO-d6):120.2, 123.2, 124.5, 127.6, 129.8, 136.3, 147.8, 149.3.

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