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PLANT ASSISTED ZINC OXIDE NANOPARTICLES FOR SYNTHESIS OF BENZIMIDAZOLE DERIVATIVE

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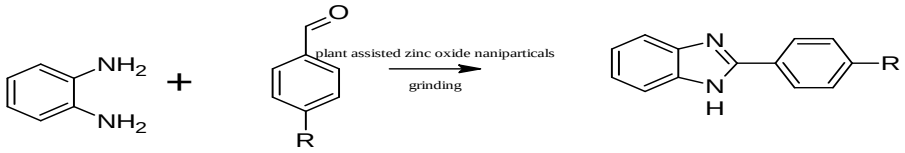
ABSTRACT
Benzimidazole is nitrogenous heterocyclic aromatic organic compound. It is used as an important pharmacophore due to its structure. It plays vital role with many of useful therapeutic diseases such as anti-vital , anticancer, antiulcer, antihypertensive, analgesic, anti-inflammatory, antifungals, and antihistaminic. Various methods are used for the synthesis of benzimidazole derivatives.in this research work we have prepared various benzimidazole derivatives with green approach having good antimicrobial activity. For this plant assisted nanoparticles are used. This gives good yield with high purity.

KEYWORDS: Benzimidazole, nanoparticles, Green route.

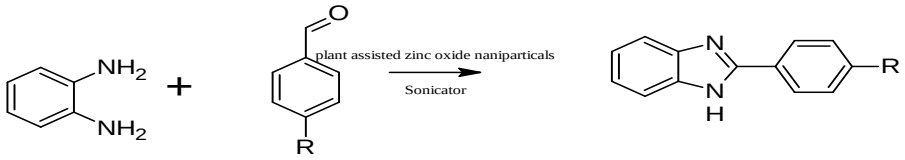
INTRODUCTIONS
From various reviews it was found that benzimidazole and its substituent compounds have very good pharmaceutical activity. This substituted benzimidazole have good activity against various microorganisms these derivatives used against various analgesic,[1] anti-inflammatory,[2] antiviral,[3] antibacterial,[4] anti-helminthic,[5] anticonvulsant,[6] anticancer,[7-8] antiulcer,[9] antihypertensive.[10-11]

Many decades there has been good approach for improving the chemical processes in industry, and colleges with respect to environmental and health related issues, which would also eventually reduce chemical waste, recycle and refuse toxic materials. Various catalyst and activation of substrate under heterogeneous condition have been developed using various acid and base catalysts.to develop important ways so that process become environmental friendly and low cost. Therefore, lot of research is done on synthesis of methods commonly reported by several groups for the synthesis of benzimidazole and Benzothiazole is the condensation reaction between o-phenylenediamine or o-thio amino phenol and an aldehyde or a ketone respectively. Catalytic activities of different Lewis acids have been investigated in the synthesis of benzimidazole and benzothiazole by different groups highlighting the advantages of their protocol over the other methods. Methods of substituted benzimidazole synthesis include the condensation of o-aryldiamines and various aromatic aldehydes ,ketones or various carboxylic acids or its derivatives in the presence of strong acids[12-14] and even sometimes catalyst used in combined form or with very high temperature without any catalyst.[15] The other method is that benzimidazole by cyclocondensation of *o*-phenylenediamine and aldehydes under oxidative conditions employing sulfamic acids,[17] Ionic liquid,[18] $In(OTf)_3$,[19] $Sc(OTf)_3$[20] activated carbon,[22] sulfonic acid functionalized silica[23] DDQ[24] NH_4OAc,[25] IL (Bromo dimethyl)[26] sulfonium bromide,[27] iodo benzene diacetate as catalysts. Unfortunately, these methods have one or more drawbacks such as very expensive reagents, highly drastic reaction conditions, very low yields, tedious work up procedures and co-occurrence of several side reactions or impurity formation. Therefore, this discovery of mild and practical routes for synthesis of 2- substituted benzimidazole continues to attract the attention of researchers.

Reaction Scheme 1



Reaction Scheme 2



EXPERIMENTAL

Paraffin bath methods used to determine Physical constant. With reference compounds. ^{1}H NMR spectra ($CDCl_3$) was recorded on Bruker Advance II 400 NMR spectrophotometer using TMS as internal standard used for the study. IR spectra were recorded on Schmidzu FTIR spectrophotometer in the frequency range 4000-450 cm^{-1} Chemicals used were of AR grade. Thin layer chromatography used to check purity of compounds.

Preparation of the Leaf Extract

Fresh leaves of Acacia nilotica were thoroughly washed with water and then distilled water to remove dirt and other contaminations, followed by distilled water and air dried at room temperature. Leaves were finely cut into small pieces. The aqueous extract of sample was prepared by boiling the freshly collected cut leaves (10 g), with 80 cm^3 of distilled water, at 60˚C for about 15-20minutes, then color of the aqueous solution changes from watery to light brown. Then the extract was cooled to room temperature and filtered using Whatman filter paper. The extract was stored in a refrigerator in order to be used for further experiments.

Green Synthesis of Zinc Oxide Nanoparticles

For the preparation of zinc oxide nanoparticles, 100 cm^3 of 0.5 M zinc acetate dihydrate solution was prepared in distilled water, 5 cm^3 aqueous leaf extract of Acacia nilotica was added into the above solution after 20 minutes of stirring. In order to maintain the pH 12, 2.0 $mol \cdot dm^{-3}$ sodium hydroxide was added very slowly which resulted in a pale white aqueous solution. This was then placed in a magnetic stirrer for 2 -3 hrs. The pale white precipitate was then taken out and washed over and over again with distilled water followed by ethanol to get free of the impurities. Then a pale white powder of zinc oxide nanoparticles was obtained after drying at 60˚C in oven over night to give yield of 95%.

General procedure for the Synthesis of 2-substituted benzimidazole

o-Phenylenediamine (10 mmol) and aromatic aldehyde (10 mmol) were, add 05 mmol of zinc nanoparticles prepared from leaves of Acacia nilotica grinded in pristle and mortar for given time progress of reaction checked by TLC. As soon as the completion of the reaction, the mixture was dissolved in etylacetate, the solvent was evaporated under pressure to give the crude product, which was purified by column chromatography on silica gel eluted with petroleum hexane and ethyl acetate. Coloun chromatography is performed if require.

Zinc oxide nano particles

Observation table 1

Sr. No	Aromatic group	Time (min)	. (%)Yield	MP (0C)
1.	C6H5	10	68	292
2.	2-ClC6H4	12	78	132
3	3- ClC6H4	13	67	230
.4.	4- MeOC6H4	14	69	220
5.	2-NO2C6H4rvation	13	74	252
6.	3- NO 2C6H4	12	77	301
7.	4- NO2C6H4	16	87	308

8.	4-MeC6H5	14	65	266
9.	4-Me2NC6H4	13	67	235
10.	2-Furanyl	12	65	280
11.	4-OCH2OC6H3	14	61	246

General procedure for the Synthesis of 2-substituted benzimidazole

o-Phenylenediamine (10 mmol) and aromatic aldehyde (10 mmol) were, add 5mmol of zinc nanoparticles prepared from leaves of Acacia nilotica sonicate the reaction mixture for the appropriate time the complication of reaction was checked by TLC. After the completion of the reaction, the mixture was dissolved in etylacetate, and the catalyst was removed by filtration and the residue washed with ethyl acetate. The solvent was evaporated under pressure to give the crude product, which was purified by column chromatography on silica gel eluted with petroleum ether or the mixture of EtOAc and petroleum ether. If required perform column chromatography.

Observation table 2

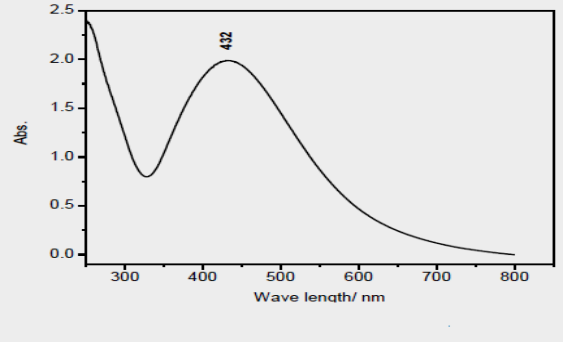
Sr. No	Aromatic group	Time (min)	. (%)Yield	MP (^{0}C)
1.	C6H5	08	78	290
2.	2-ClC6H4	05	88	133
3	3- ClC6H4	05	84	232
.4.	4- MeOC6H4	09	86	228
5.	2-NO2C6H4	05	87	254
6.	3- NO 2C6H4	05	77	304
7.	4- NO2C6H4	05	68	314
8.	4-MeC6H5	10	87	267
9.	4-Me2NC6H4	10	90	238
10.	2-Furanyl	12	68	287
11.	4-OCH2OC6H3	12	88	246

Products characterization data

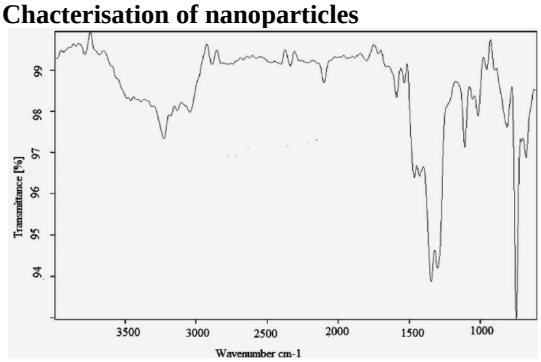
1) Benzimidazole 1H-NMR δ: 12.3 (1H, d), 8.13 (1H, d), 7.40-7.11 (4H, m). IR (KBr) cm-1: 2625, 1603, 1583, 1498, 1453, 1692, 1346, 1161. 2-Methyl-1H-benzimidazole 1H-NMR (DMSO) δ: 12.3 (1H, s), 7.35-7.10 (4H, m), 2.4 (3H, s). IR (KBr) cm-1: 2725, 1610, 1519, 1465, 1357, 1310, 1155.
2) 2-Chloromethyl-1H-benzimidazole 1H-NMR (DMSO) δ: 12.5 (1H, s), 7.80-7.30 (4H, m), 4.25 (2H, s). IR (KBr) cm-1: 2725, 1460, 1375, 1309, 1043.
3) 2-Phenyl-1H-benzimidazole 1HNMR (DMSO-d6) δ: 12.9 (1H, s), 8.20-7.21 (4H, m), 7.6 (5H, m). IR (KBr) cm-1: 2725, 1675, 1577, 1461, 1375, 1296, 1163, 725.
4) 2-(2-Chlorophenyl)-1H-benzimidazole 1H-NMR (DMSO-d6) δ: 13.35 (1H, s), 7.92-7.60 (4H, m), 7.59-7.20 (4H, m). IR (KBr) cm-1: 2705, 1580, 1564, 1508, 1456, 1582, 1120, 1167, 760, 712.

UV IR Chacterisation of nanoparticles

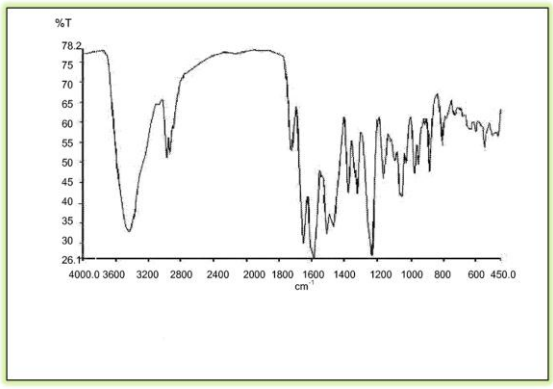
UV Chacterisation of nanoparticles



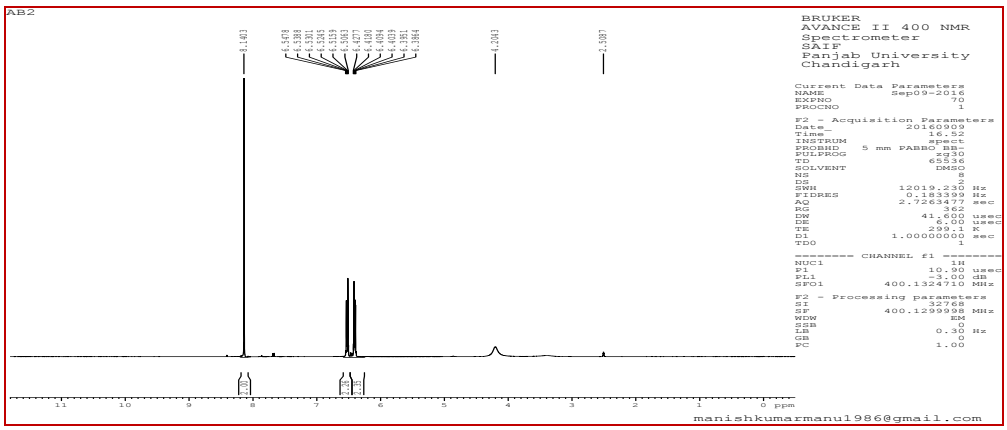
IR Chacterisation of nanoparticles



IR **Spectra of** 2-(4-chlorophenyl)-1*H*-benzimidazole



Nmr Spectra of 2-(4-chlorophenyl)-1*H*-benzimidazole



CONCLUSION

Benzimidazole aryl and heteroaryl substituted derivatives were synthesized by pristle and mortar also by sonicator methods (Figs. 1 and 2). The synthesized compounds are presented in Table 1and 2. The structures of the synthesized compounds were confirmed by 1H-NMR, IR, and physical data. The broad singlet peak between 11.0 to 12.5 ppm in 1H-NMR spectra and –C=N- peak between 1670-800 cm^{-1} in IR spectra confirm the structures. The reaction time for the synthesis of benzimidazole derivatives by conventional method was 180-250 minutes and obtained yield was 50-60 %. In comparison with the pristle and mortar assisted method using plant assisted zinc oxide nanoparticles as catalyst reaction time was 10-20 minutes and obtained yield was 73-91%. While for sonicator assisted method using assisted zinc oxide nanoparticles as catalyst reaction time was 5-10 minutes and obtained yield was 70-98%. As the reaction temperature is very important for reactant to overcome the activation energy barrier and perform the reaction, sonicator reactions has made it easy to do so. Between these two methods, the synthesis of benzimidazoles using aromatic aldehyde. The workup of the reaction mixture was easy and the used catalyst was filtered and the solvent was evaporated. The catalyst could be recycled easily without significant loss of activity.

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