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Microwave assisted synthesis of 2-arylheteroaryl benzimidazoles using star fruit juice as catalyst cum solvent

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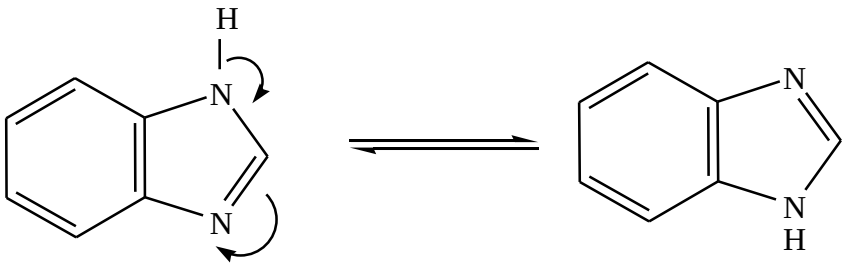
Abstract

A series of benzimidazole derivative were synthesized through one pot reaction of ortho phenylenediamine with various aromatic aldehydes in the presence of star fruit juice as catalyst without any solvent. The reaction was performed under microwave irradiation. The Synthesized benzimidazoles were m.p., elemental analysis, IR and ^{1}HNMR characterized by their spectral studies. The benzimidazoles were evaluated for their fungicidal activity against *C. albicans* and *A. Flavus* by cup-plate agar diffusion method.

Key words: Star fruit juice, microwave irradiation, aldehyde.

Introduction

Benzimidazoles consist of imidazole ring fused with benzene ring. Aza heterocyclic are a crucial group of compounds which possess wide range biological significance. Benzimidazole contains a hydrogen atom attached to nitrogen at position readily tautomerize.



Benzimidazoles have significant role as inhibitor of smooth muscle cell proliferation[1]. Benzimidazoles are privileged class of N-containing heterocyclic compounds which possess

excellent pharmaceutical activity such as antiulcers[2], protein inhibitor[3], antitumor, antifungal[4], antihypetension[5], antihistamic[6], antitubercular[7], antiasthmatic[8], anti-diabetic[9] and antiprotazoal[10].

Kauffman[11] had synthesized 2-p-bromophenyl benzimidazole with o-phenylenediamine and p-bromo. Benzoic acid in presence of polyphosporic acid at 80ºC. In 1872 benzimidazole was first synthesized by Hobreckerf[12] by reduction of 2-nitro4-methylacetanilide.

Benzimidazole derivatives were synthesized by alkylation of 2-bromophenyl benzimidazole[8]. Maleinikhaledi [13] had synthesized benzimidazole derivative with o-phenylenediamine and 3-alkyl phenyl aldehydes in presence of EtOH. Kidwai et al[14] synthesized benzimidazole derivatives using cericammoniom nitrate from o-phenylenediamine derivative in solvent free condition. Castro et al[15] synthesized benzimidazole derivative with air lacase in buffer solution (pH- 6.0) at room temperature. Various workers had employed different catalyst such as Bi $(NO_3)_3.5H_2O$, CO $(NO_3)_2.6H_2O$, Zn $(OTf)_2$, NH_4Cl/CH_3Cl, I eq TMS Cl, KSF Clay, metal halide with alumina, Yb $(OTf)_3$ palladium, copper nano particle, ZnCl/PEG for synthesis of benzimidazole. These catalyst are toxic hazardous and providing least yield. Now various ecofriendly methods[15] have been developed those minimize toxicity, reaction time and providing good yield.

Now a days synthesis of benzimidazole carried out by fruit juice medium. Khanday[16] et al reported the synthesis of benzimidazole with lemon juice as biocatalyst. Other biocatalyst such as coccus nucifera[17], citrus limetta[17], we have used star fruit juice for synthesis of benzimidazole derivative under microwave irradiation. There will be possibility that synthesis completed within shorter time with higher yield of products.

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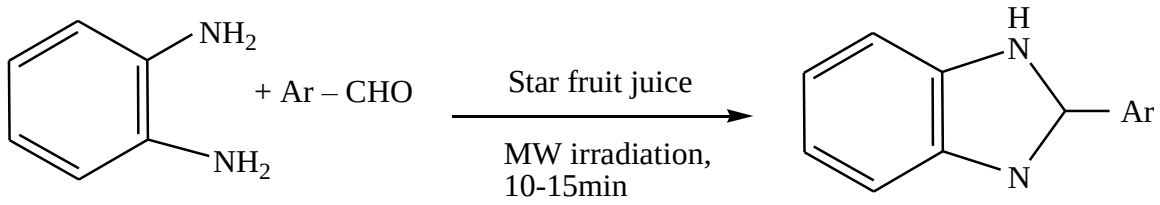
Present work

In last decades researchers reported the ecofriendly synthesis of benzamidazoles catalysed by fruit juices under microwave irradiation. Star fruit juice catalysed synthesis of some heterocyclic compounds has been reported by different researchers, but it has not been used for the synthesis of benzimidazoles. Hence we have synthesized benzimidazoles from reaction of o-phenylenediamine with substituted aromatic aldehydes in presence of star fruit juice as a catalyst cum solvent, we found substantial effect of substitutnets on yield and time of reaction.



Ar = Aryl or heteroaryl

Selection of Catalyst

Star fruits belong to the family oxilidaceae and known as Averrhoa carambola. The pH of star berry juice is 3.26-3.39. The synthesis of benzimidazole with fruit juice is ecofriendly and produced fewer amounts of toxic byproducts. It is tropical fruit and native to the Philippines, Indonesia, India, Nepal, Vietanam, Bangaladesh and Srilanka. It contains oxalic acid which characteristic of acidity. Approximately 74% of its total acid content varies on fruit maturity. Due to its low pH and easily libration of proton which suitable for synthesis of benzimidazole[18].

Preparation of fruit juice

Unriped mature green star fruits were purchased from Varanasi (U.P.) India. The fruits were cut into small pieces. The hard green piece of fruit (20g) was boiled in 100ml water. It was cooled and was centrifuged using micro-centrifuge. The clear aqueous extract of fruit was used as catalyst cum solvent for the synthesis.

Acid composition of star fruits

Major amount of oxalic acid present in fruits which compositions vary with maturity. Other acid as ascorbic acid, Gallic acids and caramboxin. Some other organic acids are acetic acid, citric acid, formic acid, lactic acid. It contains approximately 60% cellulose, 27% hemicelluloses and 13% of pectin[19].

Chemical and Apparatus

All the chemicals of AR grade used without further purification. M.P. of synthesized product were observed in open capillary tube on paraffin bath and are uncorrected. Silica gel used for TLC plate. IR spectra were recorded in Perkin-Elmer spectrophotometer. NMR spectra were recorded on Bruker-FT NMR spectrometer at 500 MHz in deuterated dimethyl sulfoxide as a solvent with chemical shift in □□ppm.

General procedure for the synthesis of Benzimidazole under M.W.

The 100 ml neat and clean conical flask aryl aldehyde (1.0 m mole), Ortho phenylene diamine (1.0 m mol) and star fruit juice (10 ml). The reaction mixture was then irradiated domestic microwave at 210W for suitable time as mentioned in Table-1. The reaction progress was checked by TLC. After completion of reaction the contents of flask was poured over

crushed ice and stirred. The solid product obtained was filtered and recrystallised from ethanol to result pure benzimidazole derivatives.

Result and Discussion

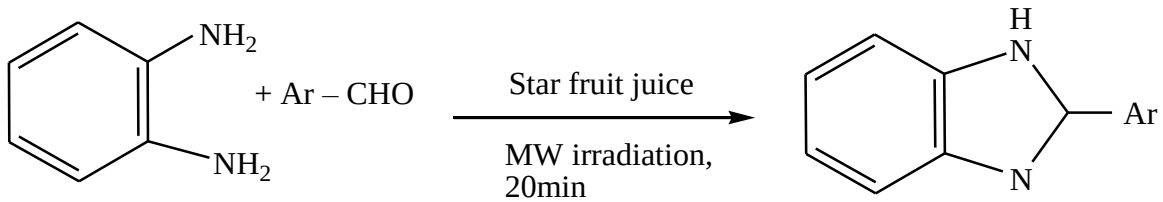
Optimisation of reaction condition

To optimize reaction conditions we select 4-chloro-benzaldehyde for reaction. Reaction was performed at R.T. with catalyst but even after 4 hours trace amount of product formed.

Table-1: Optimisation of reaction conditions (Ar = 4-ClC$_6$H$_4$)

S.No.	Catalyst (ml)	Condition	Reaction time (min)	Yield (%)
1	2.0	MW 100W	20 min	Jrace
2	4.0	MW 100W	20 min	55
3	6.0	MW 140W	20 min	61
4	8.0	MW 140W	20 min	74
5	10.0	MW 210W	20 min	95

Synthesis of Benzimidazole derivative



(Compound 1-9)

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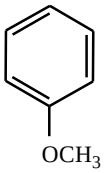
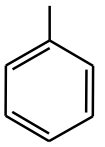
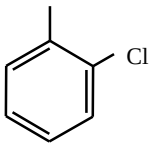
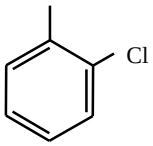
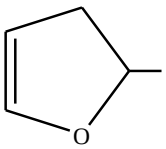
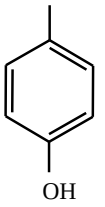
Table-2: Synthesis of Benzimidazoles catalysed by star fruit juice

S. No.	Ar	M.P.		Yield %	Molecular formula	Elemental analysis	
		Obs. ºC	Reported ºC			C	N
1		292	290-292[20]	91	$C_{15}N_2OH_{12}$	75	12.5
2		293	292-294[23]	98	$C_{13}N_2H_{10}$	80.4	14.4
3		234	231-233[21]	92	$C_{13}N_2ClH_9$	68.27	12.25
4		293	290-292[21]	95	$C_{13}N_2ClH_9$	68.27	12.25
5		296	296[23]	90	$C_{11}N_2OH_9$	71.35	15.13
6		254	253-255[20]	95	$C_{13}N_2OH_{10}$	74.28	13.33

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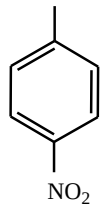
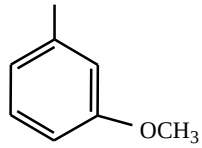
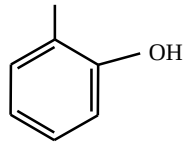
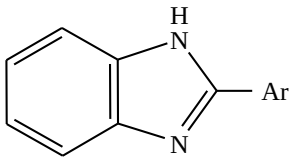
7		316	315-317[21]	98	$C_{13}N_3O_2H_9$	65.27	17.57
8		205	203-205[22]	89	$C_{14}N_2OH_{12}$	75.0	12.50
9		240	239-241[20]	90	$C_{13}N_2OH_{10}$	78.28	13.33

Table-4: Spectral study of synthesized benzimidazole derivatives



S.No.	Compounds name	I.R.	^{1}HNMR
1	2-(4-methoxy phenyl) benzimidazole	3050, 2839, 1610, 1508, 1479, 1440, 1403, 1301, 1250, 1185, 1031, 954, 825, 808, 780, 765, 740cm^{-1}	3.83 (s, 3H, –OCH_3), 7.10-7.13 (d, 2H, ArH, 7H_2); 7.15-7.19 (m, 2H ArH); 7.55-7.59 (m, 2H ArH); 8.10-8.13 (d, 2H, Ar H, 7H_2), 1270 (br, S, 1H, N–H)
2	2-(phenyl) benzimidazole	3050, 2625, 1460, 1442, 1410, 1315, 1274, 1226, 1120, 968, 766, 734, 700, 684cm^{-1}	7.20 (s, 2H, ArH), 7.47-7.50 (m, 1H, ArH), 7.53-7.57 (m, 3H, ArH), 7.66 (s, 1H, ArH), 8.18-

			8.20 (m, 2H, ArH), 12.91 (s, 1H, N–H)
3	2-(2-chloro phenyl) benzimidazole	2640, 1592, 1462, 1440, 1406, 1375, 1319, 1278, 1236, 1128, 1056, 970, 920, 874, 760, 739cm^{-1}	7.22-7.25 (m, 2H, ArH), 7.50-7.59 (m, 2H, ArH), 7.61-7.68 (m, 3H, ArH), 7.90-7.92 (m, 1H, ArH), 1271 (s, 1H, N–H)
4	2-(4-chloro phenyl) benzimidazole	2746, 1492, 1476, 1448, 1428, 1320, 1274, 1109, 1082, 960, 878, 832, 766, 730cm^{-1}	7.21 (s, 2H, ArH), 7.55 (s, 1H, ArH), 7.62-7.64 (m, 3H, ArH), 8.17-8.20 (m, 2H), 12.98 (s, 1H, N–H)
5	2-(furyal) benzimidazole	2650, 2625, 1226, 1274, 1625-55cm^{-1}, 1590, 1380, 740, 765, 830	7.20 (d, 1H)
6	2-(4-hydroxy phenyl) benzimidazole	3051, 1609, 1500, 1435, 1299, 1090, 3600-3500, 959, 811, 736, 742cm^{-1}	7.10-7.12 (d, 2H, ArH), 7.17-7.19 (m, 2H, ArH), 7.53-7.57 (m, 2H, ArH), 8.10-8.12 (d, 2H, ArH), 9.12 (s, 1H, OH), 12.9 (s, 1H, NH)
7	2-(4-nitro phenyl) benzimidazole	3100, 2625, 1409, 1314, 1225, 1350-1530, 735, 700, 680cm^{-1}	7.20-7.24 (s, 2H, ArH), 7.48-7.50 (m, 1H, ArH), 7.55-7.57 (m, 3H, ArH), 7.63 (s, 1H, ArH), 8.15-8.17 (m, 2H, ArH), 12.70 (s, 1H, NH)
8	2-(3-methoxy phenyl) benzimidazole	3050, 2836, 1500, 1435, 1248, 1300, 1029, 830, 760, 740cm^{-1}	4.01 (s, 3H, –OCH3), 9.15-7.19 (m, 2H, ArH), 7.10-7.71 (d, 2H, ArH), 7.54-7.57 (m, 2H, ArH), 8.8-8.10 (d, 2H, ArH), 12.6 (s, 1H, NH)

9	2-(2-hydroxy phenyl) benzimidazole	3050, 1608, 1500, 3600-3500, 1305, 1100, 811, 950, 730cm^{-1}	7.52-7.55 (m, 2H, ArH), 7.10-7.12 (d, 2H, ArH), 7.17-7.18 (m, 2H, ArH), 8.10 (d, 2H, ArH), 9.10 (s, 1H, OH), 12.81 (s, 1H, NH)

Conclusion

We conclude that star fruit extract is acting as an efficient green catalyst cum solvent for synthesis of 2-substituted benzimidazoles under MW irradiation. The reaction is ecofriendly resulting high yield of product in shorter time.

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