

A Mild and Environmentally benign Synthesis of Benzimidazoles: Relevance to the pectin hetero Polysaccharide as a Catalyst

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Abstract

We have developed a green procedure by using benzaldehyde and *o*-phenylene diamine as the model substrate, hetero polysaccharide pectin as a catalyst and water as a solvent. The generality and scope of this protocol was determined by synthesizing various derivatives of benzimidazole in good to excellent yield through this environment friendly, time and energy saving, green method.

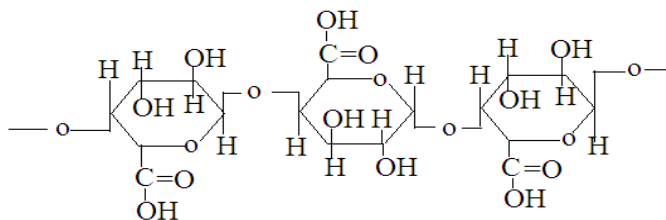
Keywords: Hetero polysaccharide, pectin, Cyclocondensation, green method, benzimidazole.

Introduction

Synthesis of benzimidazole derivatives are very important due to their great pharmacological importance. They can be used as anticonvulsant, antibacterial, antifungal, antitumor, antihelminthic, antiamebic analgesic and antiulcer¹⁻⁹. So, it is in great demand to develop the environmentally benign and easy procedure for the synthesis of benzimidazole. For this purpose the use of those easily available organic catalysts which do not produce any harmful effect is very necessary. Some of already used methods and catalysts are CAN microwave, *p*-TsOH, transition metal nitrate, lead peroxide, Cu nano particle, ring closing agent as hydrochloric acid or polyphosphosphoric acid, HFIP, NH₄Cl¹⁰⁻¹⁸. In recent days the use of biocatalytic methods are preferred over chemical methods¹⁹. In continuation to our greener method development programme, we have found hetero polysaccharide pectin as a green catalyst which is cheap and easily available. We investigated its potential for catalyzing the reaction and the results are presented in this paper²⁰. The process is remarkably simple, high yielding, highly efficient, time and energy saving. To the best of our knowledge this is the first report for the use of pectin as a catalyst to form substituted benzimidazole. Along with Benzimidazole the synthesis of various other useful compounds using different methods are increasing²¹⁻²⁴.

Material and Methods

Catalyst: Pectin is a compound belongs to carbohydrate family, it is a heteropolysaccharide also named as α -1,4-galacturonic acid. The structure of pectin can be shown as:



400 mg of pectin heteropolysaccharide mixed with 10 ml water in a 100 ml round bottom flask and stirred for 5 minute on magnetic stirrer to form a paste of pectin in water.

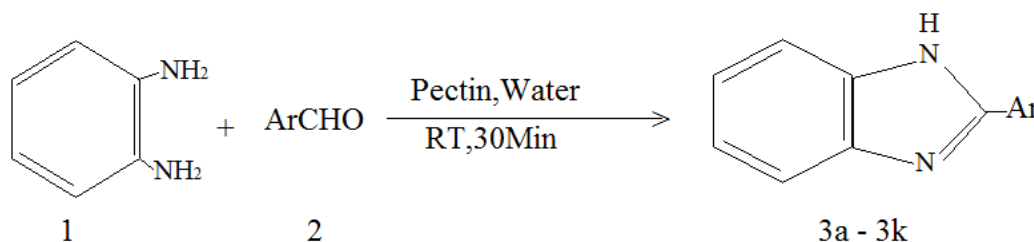
General procedure of Formation of Benzimidazole Derivatives: 10 m mole benzaldehyde, 10 m mole *o*-phenylenediamine are mixed in above paste and put the reaction mixture on magnetic stirrer once again for half an hour. The purity of products and reaction progress was checked by TLC on silica gel plates using hexane and ethyl acetate (80:20) solvent system and visualized using iodine vapours and UV detection. After completion of reaction, if the product is solid, it is collected by filtration, washed with water, dried and recrystallized with ethanol, if product is gummy it is extracted with ethyl acetate and organic phase is washed with water and dried over sodium sulphate. Finally formation of compounds was confirmed by NMR and IR analysis.

Results and Discussion

With success on the development of this green procedure we used different derivatives of benzaldehyde and *o*-phenylenediamine as the model substrate for this reaction in which benzimidazole and its derivatives are obtained in different yields (table-1).

Experiments were performed in absence of catalyst at the same conditions, a low yield is obtained which proves the importance of our catalyst. Different derivatives of Benzimidazole and their yield formed are shown in table-1, The importance of our catalyst to the others are shown in table-2.

The plausible mechanism of the reaction is proposed. Electrophilicity of carbonyl carbon of benzaldehyde is enhanced by the catalyst pectin followed by cyclisation and the dehydration (scheme.2).

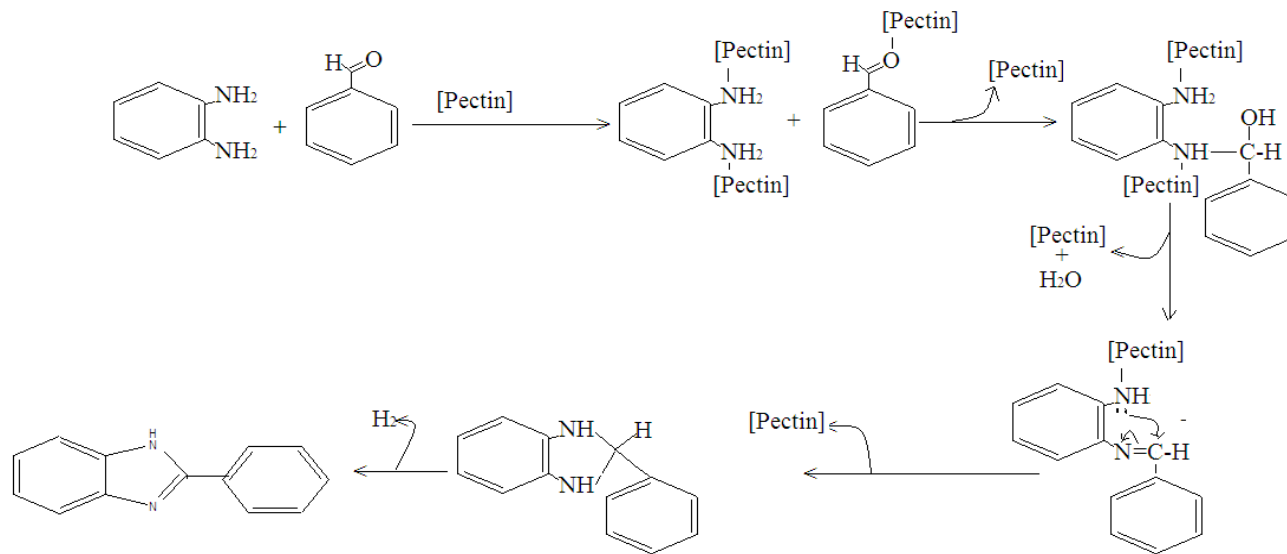


Scheme-1

Formation of benzimidazole by o-phenylenediamine and benzaldehyde using benzaldehyde using Pectin as Catalyst

Table-1
 Synthesis of Benzimidazole derivatives in water using Pectin as a catalyst

Entry	Ar	Time(Min)	Product	Yield	Phase
1.	-C ₆ H ₅	15	3a	84	Gummy
2	3-(NO ₂)-C ₆ H ₄	12	3b	87	Solid
3	4-(NO ₂)-C ₆ H ₄	18	3c	88	Solid
4	3-(OCH ₃)-C ₆ H ₄	20	3d	85	Solid
5	4-(OCH ₃)-C ₆ H ₄	15	3e	86	Solid
6	4-(Cl)-C ₆ H ₄	25	3f	90	Solid
7	4-(OH)-C ₆ H ₄	22	3g	91	Solid
8	3-(OH)-C ₆ H ₄	30	3h	86	Solid
9	4-(F)-C ₆ H ₄	20	3i	90	Solid
10	3-(Br)-C ₆ H ₄	15	3j	88	Gummy
11	4-(CH ₃)-C ₆ H ₄	20	3k	87	Gummy



Scheme-2

Plausible Mechanism for Synthesis of benzimidazole using pectin as a catalyst:

Table-2
Investigation of Time, Yield and Temperature of Synthesis of Benzimidazole Derivatives using some other Catalyst and solvents in literature

Entry	Catalyst	Time	Solvent	Temperature (°C)	Yield (%)	Literature
1	CAN	2h	PEG	50	90	[10]
2	p-TsOH	10min	DMF	80	82	[12]
3	Trans. Metal Nitrate	20-30min	Methanol	RT	60-88	[13]
4	Ring closing	30-120 Agent min	-	100(Reflux)	50-73	[16]
5	NH ₄ Cl	2h	Ethanol	80-90	78	[18]
6	Pectin	30 min	Water	RT	90	Our Work

IR and NMR Analysis of some Compounds: Entry 2 - 2-(3-nitrophenyl)-benzimidazole (3b), IR : 3376cm⁻¹, 2881 cm⁻¹, 1616 cm⁻¹, 1492 cm⁻¹. ¹H NMR (CDCl₃, 500MHz): δ ppm 10.15 (s, H, -NH), 7.1-8.7 (m, 8H, -Ar),

Entry 3- 2-(4-nitrophenyl)-benzimidazole (3c): IR : 3398 cm⁻¹, 2847 cm⁻¹, 1604 cm⁻¹, 1344 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz): δ ppm 10.20 (s, H, -NH), 7.317-8.52 (m, 8H, -Ar),.

Entry 6- 2-(4-chlorophenyl)-benzimidazole (3d): IR 3370 cm⁻¹, 3051 cm⁻¹, 1599 cm⁻¹, 1426 cm⁻¹, 1293 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz): δ ppm 9.8 (s, H, -NH) 6.80-8.10 (m, 8H, -Ar) .

Entry 7- 2-(4-hydroxyphenyl)-benzimidazole (3e): IR 3317 cm⁻¹, 3007 cm⁻¹, 1605 cm⁻¹, 1449 cm⁻¹, 1271 cm⁻¹. ¹H NMR (CDCl₃, 500 MHz): δ ppm 10.20 (s, H, NH-) 6.5-8.5 (m, 8H, -Ar).

Conclusion

We have developed an easy, highly efficient, time and energy saving, high yielding and greener approach for the synthesis of benzimidazole by cyclo condensation of different derivatives of benzaldehyde and o-phenylene diamine in water using pectin heteropolysaccharide as a catalyst. The key advantages of this procedure are cost effectiveness of catalyst, easy work-up and purification of product by non chromatographic methods and excellent yield.

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