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NEW AND EFFICIENT GREEN CATALYST ONE-POT SYNTHESIS OF BENZIMIDAZOLE AND DERIVATIVES

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ABSTRACT

A series of substituted benzimidazole were prepared through the one-pot reaction of o-phenylenediamine with various aromatic aldehydes in the presence of ferrous sulphate as catalyst both in Ethanol and water as solvent under Sonication and Grinding. The reactions proceed smoothly in excellent yield, high chemo selectivity and with an easy work-up with better yield.

KEYWORDS: Benzimidazole, Ferrous sulphate Aldehyde, Green Route.

INTRODUCTION

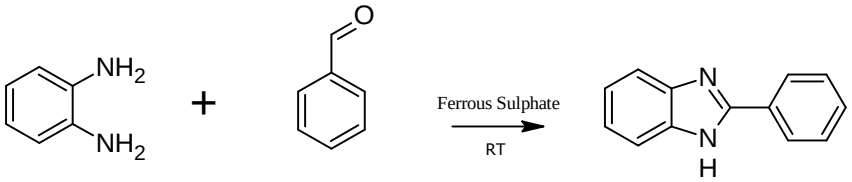
Heteroaromatic ring system is the important part of any biologically active drug molecule. These rings are essential because have similarity with respect to the biologically active compounds in animal body which include acids, hormones, neurotransmitters, which constitutes one or the other heteroaromatic ring. Many Heteroaromatic rings present, fused and pendent benzimidazole are also different feature of many pharmaceutical products. Heterocyclic compounds possessing two hetero atoms in a ring are of massive biological importance in clinical research field. Heterocyclic compounds possess a cyclic structure with two or more different kinds of atoms in the ring. These type of compounds are very widely distributed in nature very important to life, playing a vital role in the metabolism of all living cells e.g. the pyrimidine and purine bases of the genetic material DNA, the essential amino acids like alanine, valine, isoleucine's proline, hisitidine, the

vitamins and coenzymes etc. There are a large number of pharmacologically active heterocyclic compounds, many of which are in regular clinical use.[1] A wide range of synthetic and naturally occurring heterocyclic compounds find their use in medicine and also as pesticides, agrochemicals, polymers plastic, drugs and dyes are the way for considerable amount of research leading to new heterocyclic molecules having better biological activity.[2-7] They are important as antitumor,[8] antimicrobial agents[9] and LTD_4 receptor antagonist.[10] Despite their importance of these heterocyclic moieties from pharmacological, industrial and synthetic points of view, comparatively few methods for the preparation of benzimidazole and Benzothiazole have been reported. The literature assay shows that the two general methods for the synthesis of benzimidazoles and Benzothiazoles are cyclo condensation of o-phenylenediamine or o amino-thiophenol with carboxylic acids or their derivatives and oxidative cyclo-dehydrogenation of o-phenylenediamine or o-amino thiophenol with aldehydes.[11] Various oxidative reagents such as DDQ,[12] $NaHSO_3$(aq),[13] nitrobenzene,[14] MnO_2,[15] 1,4-benzoquinone,[16] benzofuroxan,[17] tetracyanoethylene,[18] $Pb(OAc)_4$[19] and Oxone[20] have been employed for the synthesis of benzimidazoles and benzothiazoles. However, a number of these methods have some drawbacks such as low yields, long reaction times, drastic reaction conditions, tedious work-up procedures, and co-occurrence of several side reactions. Promoted by the need for finding another new and efficient method for the synthesis of these heterocyclic compounds and in continuations of our previous work,[21-24] we became interested in the synthesis of 2-substituted benzimidazole and benzothiazole by the condensation of phenylenediamine and o-aminothiophenol with various aldehydes in the presence of ferrous sulphate as an oxidative catalyst.

EXPERIMENT

A mixture of o-phenylenediamine (1 mmol), arylaldehyde (1 mmol) and Ferrous sulphate (1 mmol) in appropriate solvent Ethanol 10 mL were sonicated at room temperature. The progress of the reaction was followed by TLC. After the completion of the reaction, water (20 mL) was added. The resulting precipitate was filtered, washed with hot water. These products were pure enough but further purification can be obtained by recrystallization from ethanol. catalyst can be reused for reactions.

General reaction for preparation of benzimidazoles



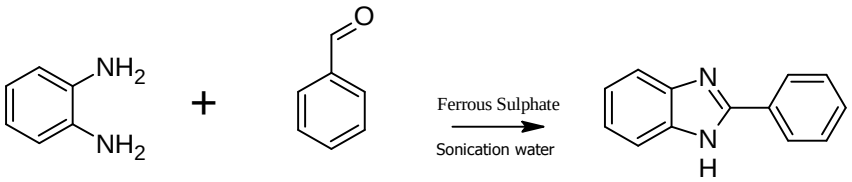
A) Water as Solvent in Sonication

A mixture of o-phenylenediamine (1 mmol), arylaldehyde (1 mmol) and Ferrous sulphate (1 mmol) in appropriate solvent (1-0 ml H_2O were stirred at room temperature in sonicator for different time. The progress of the reaction was followed by TLC. After the completion of the reaction, water 20 mL was added. The resulting precipitate was filtered, washed with hot water. These products were pure enough but further purification can be obtained by recrystallization from ethanol catalyst can be reused for reactions.

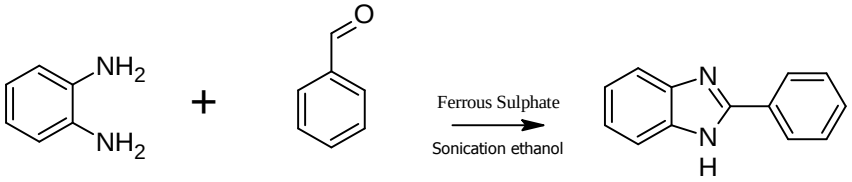
B) Ethanol as Solvent in Sonication

A mixture of o-phenylenediamine (1 mmol), arylaldehyde (1 mmol) and Ferrous sulphate (1 mmol) in appropriate solvent like Ethanol 10 mL were stirred at room temperature in sonicator for specified time. The progress of the reaction was followed by TLC. After the completion of the reaction, 20 ml of cold water was added. The resulting precipitate was filtered, washed with hot water. These products were pure enough but further purification can be obtained by recrystallization from ethanol. Catalyst can be reused for reactions.

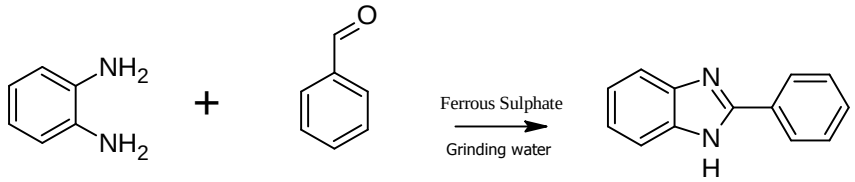
Scheme 1



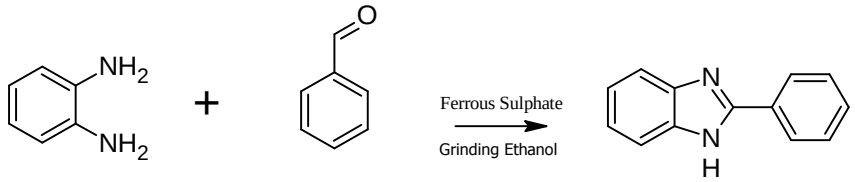
Scheme 2



Scheme 3



Scheme 4



Observation Table 1

Under Sonication at Room Temperature by using water as Solvent

Entry I	Aldehyde	Time (min)	Yields	M.P. ^{o}C
1	Benzaldehyde	45	71	288
2	Anisaldehyde	58	55	232
3	4-methyl benzaldehyde	53	73	224
4	4-chlorobezaldehyde	47	79	291
5	4-flurobenzaldehyde	32	89	248
6	3- Bromo benzaldehyde	30	90	267
7	Furan-2carbaldehyde	48	95	287
8	Cinnamaldehyde	60	70	199-202
9	3-nitrobanzaldehyde	20	91	309-311

Table 2

Under Sonication at Room Temperature by using alcohol as Solvent

Entry I	Aldehyde	Time (min)	Yields	M.P. ^{o}C
1	Benzaldehyde	35	60	287
2	Anisaldehyde	40	58	234
3	4-methyl benzaldehyde	39	70	223
4	4-chlorobezaldehyde	30	88	291
5	4-flurobenzaldehyde	25	90	244
6	3- Bromo benzaldehyde	22	92	265
7	Furan-2carbaldehyde	25	95	285
8	Cinnamaldehyde	42	89	199-201
9	3-nitrobanzaldehyde	27	91	309-310

Observation Table 3

Grinding at Room Temperature by using water as Solvent

Entry I	Aldehyde	Time (min)	Yields	M.P. ^{o}C
1	Benzaldehyde	55	61	288
2	Anisaldehyde	68	57	232
3	4-methyl benzaldehyde	63	63	224
4	4-chlorobezaldehyde	57	69	291
5	4-flurobenzaldehyde	42	85	248
6	3-Bromobenzaldehyde	40	93	267
7	Furan-2carbaldehyde	48	95	287
8	Cinnamaldehyde	70	68	199-202
9	3-nitrobanzaldehyde	40	95	309-311

Table 4

Grinding at Room Temperature by using alcohol as Solvent

Entry I	Aldehyde	Time (min)	Yields	M.P. ^{o}C
1	Benzaldehyde	40	64	287
2	Anisaldehyde	45	60	234
3	4-methyl benzaldehyde	38	74	223
4	4-chlorobezaldehyde	33	87	291
5	4-flurobenzaldehyde	28	92	244
6	3- Bromo benzaldehyde	25	92	265
7	Furan-2carbaldehyde	27	96	285
8	Cinnamaldehyde	45	89	199-201
9	3-nitrobanzaldehyde	30	92	309-310

Spectral Data

Phenyl-1H-benzimidazole: pale-yellow solid. mp: 293–296 ºC; IR (KBr) 3042, 1440, 1403, 1271, 971 cm^{-1}. MS: *m*/*z* = 193(M+). 1H NMR (300 Hz, DMSO): δ 7.22 (m, 2H), 7.48 (m, 5H), 7.58 (s, IH), 8.04 (d,2H, J = 1.6 Hz).

CONCLUSION

Ferrous sulphate is a cheap and easily available oxidizing agent has been synthesized according to our previously published method, but its application as an oxidant in the synthesis of 2-arylbenzimidazoles and 2-arylbenzothiazoles has not been studied. In order to study the effect of solvent on the rate and yield of reaction, we performed a set of preliminary experiments on the reaction of o-phenylenediamine. The observed results showed that ethanol is the best organic solvent for the reaction under sonication as well as in grinding. This study shows that ferrous sulphate is an efficient oxidant in the synthesis of 2 arylbenzimidazoles. 2-Arylbenzimidazoles are obtained by the condensation reaction of 1,2 phenylenediamine with different aromatic aldehydes in ethanol at room temperature (Scheme 1-4). A variety of

aromatic aldehydes bearing electron-donating and electron-withdrawing substituents are successfully used to prepare the corresponding benzimidazole derivatives in excellent yields. Electron-withdrawing groups on benzaldehyde accelerate the reaction rate in comparison to electron-donating groups which decrease the rate. Substitution at ortho position of aldehydes decreases the rate which their reactions were completed in longer times. On the other hand, electron-withdrawing group on o phenylenediamine ring extended the reaction times to 50-80 min. In order to explore an eco-friendly synthesis.

In summary, ferrous sulphate has been employed as a novel, mild and efficient catalyst and oxidant for the convenient preparation of benzimidazole in good to excellent yields from the treatment of o-phenylenediamine with various aldehydes, respectively. This method has several advantages like short reaction time, easy and quick work-up and excellent chemo selectivity. Also, by using ferrous sulphate as catalyst, the mentioned reactions do not need toxic solvents and do not give environmentally harmful by-products.

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