KAi (SO$_4$)$_2$.12H$_2$O (Alum): An Efficient Catalyst for Synthesis of Some Benzimidazoles and Benzoxazoles Derivatives under Microwave Irradiation

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Abstract
An efficient synthesis of some derivatives of benzimidazoles and benzoxazoles by the condensation of 1, 2-phenylenediamine and 2-aminophenol with orthoesters in the presence of KAl (SO$_4$)$_2$.12H$_2$O (Alum) under microwave irradiation is reported. The advantages of this method includes application of an inexpensive and readily available catalyst, short reaction times, easy workup, improved yields, and solvent-free conditions that is considered to be relatively environmentally friendly.

Keywords: Benzimidazole, Benzoxazoles, KAl (SO$_4$)$_2$.12H$_2$O (Alum), Microwave irradiation.

Introduction
In organic synthesis and reactions, attention is concentrated on green chemistry using environmentally being reagents and conditions, particularly solvent-free procedures, i.e. dry reaction [1]. Such procedures often leads to clean, eco-friendly and highly efficient procedures involving simplified work-ups. A large number of reactions have been carried out on the surface of silicagel, [2] alumina, [3] zeolites, [4] clays, [5] and polymers, [6] frequently in conjunction with microwave irradiation [7]. This leads to accelerated reaction rates and enhanced yields resulting from microwave dielectric heating.

The benzimidazoles and benzoxazoles ring are important pharmacophore in modern drug discovery [8]. Benzimidazoles and benzoxazoles derivatives exhibit significant activity against several viruses such as HIV, influenza, RNA [9]. In addition, these compounds show fungicidal, antitumor, immunosuppressant, and anticonvulsant properties. [10] Since benzimidazoles and benzoxazoles are commonly used as intermediates in synthetic routes and serve as ligands for the asymmetric catalysis [11], the preparation of benzimidazoles and benzoxazoles show its importance. Various methods for the synthesis of benzimidazoles and benzoxazoles have been reported in some papers [12].
Experimental

Melting points were measured on an Electrothermal 9200 apparatus. IR spectra were recorded on FT-IR 102MB BOMEM apparatus. 1H NMR and 13C NMR spectra were determined on a BRUKER DRX-300 AVANCE spectrometer at 300.13 and 75.47 MHz, respectively.

General Procedure for Preparation of benzimidazoles and benzoxazoles

A mixture of 1,2-phenylenediamine (1a) (0.01 mol, 1.08 g) and 2-aminophenol (1b) (0.01 mol, 1.09 g) with orthoesters (2) (2 ml) (Table 1) contained in a tall beaker, the beaker covered with a stemless funnel, and was placed in the microwave oven, then irradiated applying power and time as indicated in Table 1. The reaction mixture was allowed to cool to room temperature. Triturating of the crude product with water and recrystallization from ethanol gave the desired products.

Benzimidazole (1, C7H6N2):
Yield 90% (1.06 g); m.p. 170-3 °C [13] (170-2 °C); IR (KBr): $\tilde{\nu}$ = 3040, 2800, 1608 cm$^{-1}$; 1H-NMR (CDCl$_3$), $\delta$= 7.35-7.65(m, 4H, arom), 8.1(s, 1H, H-C2) ppm.

2-Phenylbenzimidazole (2, C13H10N2)
Yield 78% (1.51 g); m.p. 291-3 °C [14] (290-2 °C); IR (KBr): $\tilde{\nu}$ = 3022, 1620, 1578 cm$^{-1}$; 1H-NMR (CDCl$_3$), $\delta$= 7.26 (m, 2H, arom), 7.5-7.8(m, 5H, arom), 8.28 (m, 2H, arom) ppm.

2-Propylbenzimidazole (3, C10H12N2)
Yield 81% (1.29 g); m.p. 157-8 °C [15] (156-7 °C); IR (KBr): $\tilde{\nu}$ = 3030, 1612, 1576 cm$^{-1}$; 1H-NMR (CDCl$_3$), $\delta$= 0.9 (t, 3H, J=7.2 Hz, CH$_3$), 1.85 (m, 2H, CH$_2$), 3.10 (t, 2H, J=7.4 Hz, CH$_2$), 7.20 (m, 2H, arom), 7.6 (m, 2H, arom), 12.6 (s, 1H, NH) ppm.

2-Butylbenzimidazole (4, C11H14N2)
Yield 80% (1.39 g); mp 149-50 °C [15] (148 °C); IR (KBr): $\tilde{\nu}$ = 3045, 1611, 1580 cm$^{-1}$; 1H-NMR (CDCl$_3$), $\delta$= 0.7(t, 3H, J=7.3 Hz, CH$_3$), 1.25 (m, 2H, CH$_2$), 1.80 (m, 2H, CH$_2$), 2.90 (t, 2H, J=7.6 Hz, CH$_2$), 7.10 (m, 2H, arom), 7.50 (m, 2H, arom), 12.6 (s, 1H, NH) ppm.

2, 5, 6-Trimethylbenzimidazole (5, C10H12N2)
Yield 89% (1.42 g); m.p. 235-6 °C [16] (233-4 °C); IR (KBr): $\tilde{\nu}$ = 3085, 1620, 1573 cm$^{-1}$; 1H-NMR (CDCl$_3$), $\delta$= 2.10 (s, 6H, 2 CH$_3$), 2.40 (s, 3H, CH$_3$), 7.10-7.3 (s, 2H, arom) ppm.
2-Ethyl-5, 6-dimethylbenzimidazole (6, C_{11}H_{14}N_{2})
Yield 83% (1.45 g); m.p. 222-4 °C [17] (223-4 °C); IR (KBr): \( \bar{\nu} = 3085, 1622, 1575 \text{ cm}^{-1} \); \(^1\)H-NMR (CDCl\(_3\)), \( \delta = 1.30 \text{ (t, 3H, J=7.2 Hz, CH}_3\)), 2.25 \text{ (s, 6H, CH}_3\)), 2.85 \text{ (q, 2H, J=7.2 Hz, CH}_2\)), 7.25 \text{ (s, 2H, arom) ppm.}

2-Phenylbenzoxazole (7, C_{13}H_{9}NO)
Yield 70% (1.36 g); m.p. 101-3 °C [18] (102-4 °C); IR (KBr): \( \bar{\nu} = 1620, 1578 \text{ cm}^{-1} \); \(^1\)H-NMR (CDCl\(_3\)), \( \delta = 7.26 \text{ (m, 2H, arom), 7.5-7.8(m, 5H, arom), 8.28 (m, 2H, arom) ppm.}

5-Nitrobenzoxazole (8, C_{7}H_{4}N_{2}O_{3})
Yield 78% (1.28 g); m.p. 151-2 °C [19] (152-3 °C); IR (KBr): \( \bar{\nu} = 1606, 1510, 1506, 1345 \text{ cm}^{-1} \); \(^1\)H-NMR (CDCl\(_3\)), \( \delta = 7.90-8.43 \text{ (m, 3H, arom), 8.53 (s, 1H, H-C2) ppm.}

2-Methyl-5-nitrobenzoxazole (9, C_{8}H_{6}N_{2}O_{3})
Yield 79% (1.40 g); m.p. 154-5 °C [20] (153-4 °C); IR (KBr): \( \bar{\nu} = 1611, 1573, 1570, 1351 \text{ cm}^{-1} \); \(^1\)H-NMR (CDCl\(_3\)); \( \delta = 2.80 \text{ (s, 3H, CH}_3\)), 7.80-8.30 \text{ (m, 3H, arom) ppm.}

Results and Discussion
We have recently described an efficient and rapid synthesis of a variety of heterocyclic compounds under microwave irradiation in an unmodified commercial microwave oven [21]. We have also reported the ability of KAl (SO4)2.12H2O (Alum) as an effective catalyst in the synthesis of cis-isoquinolonic acid, [22a] di-hydropyrimidinones, [22b] and trisubstituted imidazoles. [22c] In the course of our research on application of KAl (SO4)2.12H2O in organic reactions, we have found that alum was an effective promoter in the preparation of benzimidazoles and benzoxazoles derivatives.

We have also discovered that the condensation of 1,2-phenylenediamine (1a) and 2-aminophenol (1b) with orthoesters (2) results in rapid formation of the corresponding benzimidazoles (1-5) and benzoxazoles (6-9) when the reaction were conducted in open vessels in a microwave oven (scheme 1).
All reactions were performed in a tall beaker covered with a stemless funnel and it was found that if the irradiation sequence were interrupted with a cooling period in between, there would be little vaporization and high degrees of conversion can be reached (Table 1). Furthermore, to find the best reaction conditions, the reaction mixtures were irradiated for variable times. The optimized results are summarized in Table 1.

The remarkable advantages of this procedure are the simple work up of the reaction mixtures which provide products of high purity, and the simplicity of the operations.

**Table 1:** Synthesis of some derivatives of benzimidazoles and benzoxazoles. (a: Irradiation condition were 385 (p/w). b: Yield of pure isolated product based on 1,2-phenylenediamine and 2-aminophenol).

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**Conclusion**

Summary, we have developed a simple, convenient, and effective method for the synthesis of benzimidazoles and benzoxazoles employing KAl (SO4)2.12H2O under mild conditions. The catalyst can be prepared easily with readily available inexpensive regents that are heterogeneous, reusable, and non-hazardous.
Acknowledgements

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References


