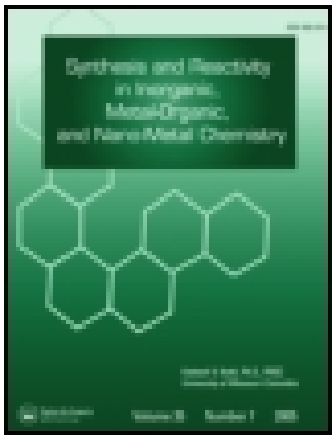

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Microwave Assisted Synthesis of 2-Substituted Benzoxazoles in the Presence of Potassium Cyanide Under Mild Conditions

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Microwave Assisted Synthesis of 2-Substituted Benzoxazoles in the Presence of Potassium Cyanide Under Mild Conditions

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ABSTRACT

Various 2-substituted benzoxazoles were prepared using microwave assisted reaction of 2-aminophenol with aromatic aldehydes in the presence of one equivalent of potassium cyanide as an equimolecular catalyst. Aldehydes having either electron-donating or withdrawing groups afforded the target products. The important features of this method were high yields, short reaction times and easy work up. The structure of synthesized products was characterized by nuclear magnetic resonance (NMR) and infrared (IR).

Keywords: Benzoxazoles; Potassium cyanide; 2-aminophenol; Microwave, Synthesis.

INTRODUCTION

Benzoxazoles and their derivatives have received considerable attention due to their biological and therapeutic activities such as anti-inflammatory,[1] antiulcer,[2] hypoglycemic,[3] antimicrobial,[4] antitumor,[5] antihistaminic[6] and anticancer[7] properties. They have also been used as fluorescent-whitening agent dyes,[8] dye lasers,[9] herbicides,[8] sensors for metals,[10] electronic devices,[11] and intermediates for organic syntheses.[12,13] The common methods used for the synthesis of benzoxazoles include the condensation of 2-aminophenol with aldehydes in the presence of oxidants such as; NaCN,[14] NiO_2,[15] DDQ,[16] Cu-nanoparticle,[17] heteropoly acids,[18] $ThClO_4$,[19] *o*-iodoxybenzoic acid (IBX)[20] and the condensation of *o*-substituted amino aromatics with carboxylic acids,[21-24] nitriles,[25] orthoesters,[26] acyl chlorides[27,28] and amides.[29] Some other methods have been reported for the synthesis of benzoxazoles, including the reaction between 1,1-dibromoethenes with 2-aminophenol,[30] the reaction of 2-hydroxy ketones with acetohydroxamic acid,[31] condensation of alcohols with 2-aminophenoles,[32,33] the reaction of 1,2-dihaloarenes with carboxamides,[34] the reaction of Ŭ-keto acides with 2-aminophenol[35] and reaction of 2-(aryloxy)-anilines.[36]

Recently, the synthesis of 2-arylbenzoxazoles from the reaction of 2-aminophenols and aromatic aldehydes in the presence of potassium cyanide at room temperature has been reported.[37] These methods suffer from one or suffer from one or more drawbacks such as; long reaction times, the usage of excess catalysts, harsh reaction conditions or low yields of the desired products. Hence, there is a scope for the development of an efficient, simple, economical and eco-friendly synthetic strategy for the preparation of 2-arylbenzoxazoles.

Preparation of organic compounds could be accelerated by microwave (MW) irradiation with higher yields and purity, lower quantities of by-products, easier work up and purification compared to other more conventional techniques.[38,39] Moreover, some reactions that do not occur by conventional thermal heating techniques or produce products in poor yields can be accomplished in high yields under microwave irradiation.[40] By keeping this point in mind, herein we report the synthesis of 2-substituted benzoxazoles by a non-conventional technique.

RESULTS AND DISCUSSION

In this research, an efficient, convenient microwave-assisted method was applied to the reaction of aromatic aldehydes and 2-aminophenol under mild conditions (Scheme 1). Fortunately, microwave irradiation as a facile and general method afforded the corresponding products within a few minutes in excellent yields.

An important factor in performing reactions under microwave irradiation is choosing an appropriate solvent. Polar and ionic species interact with microwaves more efficiently. The different solvents, due to variation in polarities, have different behaviors under microwave irradiation. The ability of a specific substance (solvent or reagent) to convert electromagnetic radiation into heat is determined by the so-called loss factor (tan ŭ).[41] A reaction medium with a high tan ŭ absorbs most of the microwave energy and converts it into heat. So firstly, the solvent effect on the reaction of 2-aminophenol with benzaldehyde in the presence of KCN as a model reaction was investigated. The results are presented in Table 1.

As can be seen from Table 1, the solvents play an important role in the reaction. It was found that the best solvent for this reaction was N,N-dimethylformamide (DMF) and the reaction

in this solvent afforded the desired product in 95% yield, while the performance of acetonitrile, and ethanol as solvents led to lower yields (Table 1, entries 1-3). The reaction in dichloromethane did not produce benzoxazoles at all (Table 1, entry 4).

Also, we carried out the reaction of 1.1 mmol 2-aminophenol with 2.2 mmol benzaldehyde in the presence of various amounts of KCN under 450 Watt microwave irradiation. The corresponding results can be seen in Table 2. As shown, the desired product was obtained with high yield in a short reaction time and in the presence of 1.1 mmol KCN (Table 2, entry 4).

In continuation of this work, in order to optimize the microwave power, the reaction of 2-aminophenol with benzaldehyde in the presence of KCN was carried out under different powers of microwave irradiation. It was observed that the reaction in the presence of microwave irradiation with the power of 450 watt led to the best result, which was the obtained product with 95 % isolated yield after 3 min (Table 3, entry 3).

To ascertain the scope and limitation of the present work, the microwave-assisted reaction of 2-aminophenol with several aromatic aldehydes was carried out according to the general experimental procedure. The corresponding results are shown in Table 4. As shown, the products were prepared in high yields and short reaction times, thereby confirming the generality and scope of this efficient method for one-pot synthesis of 2-substituted benzoxazoles under microwave irradiation. The feature of this method was that, aromatic aldehydes with electron withdrawing groups (Entries 4-6) as well as electron-donating groups (Entries 2, 7 and 9) gave the excellent yields except a strong electron-withdrawing group at position 4 of benzaldehyd e that did not yield the product (Entry 15). Furthermore, heterocyclic aldehydes could also be used for the facile synthesis of several 2-heterocyclic substituted benzoxazoles (Entries 12 and 13).

Comparing the results of microwave irradiation with conventional conditions [28,30,42-44] indicates that the synthesis of benzoxazoles from the reaction of 2-aminophenol with aromatic aldehydes can be accelerated by microwave irradiation. In this study, the products were obtained in the excellent yields after a short reaction time (about min), while in the previously reported works the products were obtained in good to high yields after long reaction times (about hour). For example, in the previous report,[45] the reaction of 2-aminophenol with 4-methoxybenzaldehyde or 4-chlorobenzaldehyde catalyzed by $FeCl_3$ at 110 ^oC after 24 h afforded 2-(4-methoxyphenyl) benzoxazole and 2-(4-chlorophenyl) benzoxazole in 76% and 66% yields respectively (Table 4, entries 16 and 17). Whereas the present procedure needs only 4 min to result 2-(4-methoxyphenyl) benzoxazole in 92% yield (Table 4, entry 8) and 5.50 min to result 2-(4-chlorophenyl) benzoxazole in 93% yield (Table 4, entry 5).

Also, in this study, 2-aminophenol:KCN were used as 1:1 mol ratio and 2-phenyl benzoxazole as desired product was obtained in excellent yield (95 %) after short reaction time (3 min) (Table 4, entry 1). While, in the previously reported work, 2-aminophenol:KCN has been used as 1:2 mol ratio and the corresponding product has been obtained in 85 % yield after 5 hours [37] (Table 4, entry 18). This method offered several advantages including excellent yields, high purity, simple reaction conditions, high reaction rates and the easy work up procedures. These results demonstrated that the microwave irradiation is an efficient method for the one-pot synthesis of 2-substituted benzoxazoles. The structures of products were completely characterized by spectroscopic and physical data and they were found to be in a good agreement with earlier reports. [19,42,43 ,46-48]

The Proposed Reaction Mechanism

The proposed mechanism for the formation of 2-substituted benzoxazoles is presented in Scheme 2. As can be seen, the reaction likely proceeds according to the benzoin condensation, which involves formation of the benzoin (2). Intermediate (3) is formed by the reaction of 2-aminophenol with benzoin. Then, nucleophilic attack of hydroxyl group affords the corresponding product (4). To prove the correctness of this mechanism, the reaction of 2-aminophenol (1 mmol) with benzoin (1mmol) in DMF as solvent was carried out in a microwave oven at power of 450 W and the desired product was obtained. This result was confirmed that the mechanism of reaction proceedes according the benzoin condensation (Scheme 3). As mentioned before, by considering the proposed mechanism through the formation of benzoin, the 4-nitrobenzaldehyde could not be active in this reaction because of the very low nucleophilicity of cyanohydrin anion intermediate (1). This was due to the delocalization of minus charge via resonance of NO_2 group in para situation of the benzaldehyde.[49]

EXPERIMENTAL

Chemicals and Instruments

All materials were of commercial reagent grade. The aromatic aldehydes and *o*-aminophenol were purified by standard procedures and purity was determined by thin layer chromatography (TLC). IR spectra were recorded as KBr pellets on a Perkin-Elmer 781 spectrophotometer or an Impact 400 Nicolet fourier transform infrared spectrophotometer (FTIR). ^{1}H NMR and ^{13}C NMR were recorded in $CDCl_3$ solvent on a Bruker DRX-400 spectrometer with tetramethylsilane as internal reference. Melting points obtained with a

Yanagimoto micro melting point apparatus are uncorrected. The purity determination of the substrates and reaction monitoring were accomplished by TLC on silica-gel polygram SILG/UV 254 plates (from Merck Company). Microwave irradiations were carried out in microwave oven specially designed for the organic synthesis (Milestone LAVIS 1000 Basic Microwave).

Typical Procedure for the Synthesis of Benzoxazoles from Arylaldehydes

A mixture of 2-aminophenol (0.13 gr, 1.1 mmol), substituted benzaldehydes (2.2 mmol) and potassium cyanide (1.1 mmol) in 4 ml N,N-dimethylformamide was irradiated in a microwave oven at 450 W. The progress of the reaction was monitored using thin-layer chromatography (petroleum ether/ethyl acetate, 6/2). After the completion of the reaction, the mixture was cooled and extracted with ethyl acetate (3 × 10 ml) and the organic layer was concentrated under reduced pressure. Then, recrystallization of the crude product was carried out in a boiling mixture of ethanol/water (1:1) to give the pure product.

2-Phenyl-1,3-benzoxazole: Light brown solid; m.p= 98-100 °C (Lit[42]. 102-103 °C); IR (KBr)/ ɜ (cm^{-1}) 1615 (C=N), 1551, 1448 (C=C, Ar), 1242 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm):* 8.29-8.26 (2H, m, Ar), 7.80-7.78 (1H, m, Ar), 7.62-7.59 (1H, m, Ar), 7.56-7.54 (3H, m, Ar), 7.38-7.36 (2H, m, Ar).

2-(2-Hydroxyphenyl)-1,3-benzoxazole: White solid; m.p= 123-124 °C (Lit[43]. 125-126 °C); IR (KBr)/ ɜ (cm^{-1}) 3143 (OH), 1630 (C=N), 1544, 1485 (C=C, Ar), 1248 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm):* 11.50 (1H, s, OH), 8.05-8.03 (1H, dd, J= 7.6, 1.4 Hz, Ar), 7.75 (1H, m, Ar), 7.63 (1H, m, Ar), 7.47-7.40 (3H, m, Ar), 7.14-7.12 (1H, m, Ar), 7.04-7.00 (1H, m,

Ar); ^{13}C NMR ($CDCl_3$, 100 MHz)/ *δ (ppm)* 162.90, 158.70, 149.13, 140.00, 133.56, 127.10, 125.30, 125.00, 119.56, 119.25, 117.40, 110.66.

2-(3-Hydroxy-phenyl)-1,3-benzoxazole: White solid; m.p=172-174 °C; IR (KBr)/ ɜ (cm^{-1}) 3428 (OH), 1600 (C=N), 1550, 1452 (C=C, Ar), 1241 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm):* 8.91 (1H, s, OH), 7.75-7.73 (3H, m, Ar), 7.70 (1H, m, Ar), 7.42-7.41 (3H, m, Ar), 7.00 (1H, m, Ar).

2-(2-Chlorophenyl)-1,3-benzoxazole: Light yellow solid; m.p= 63-65 °C (Lit[19]. 61-64 °C); IR (KBr)/ ɜ (cm^{-1}) 1606 (C=N), 1537, 1452 (C=C, Ar), 1244 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm):* 8.18-8.15 (1H, dd, J= 7.20, 1.6 Hz, Ar), 7.88-7.86 (1H, m, Ar), 7.65-7.63 (1H, m, Ar), 7.60-7.58 (1H, m, Ar), 7.49-7.38 (4H, m, Ar).

2-(4-Chlorophenyl)-1,3-benzoxazole: Light brown solid; m.p= 149-151 °C (Lit[42]. 153-154 °C); IR (KBr)/ ɜ (cm^{-1}) 1614 (C=N), 1482, 1550 (C=C, Ar), 1243 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm)*: 8.20-8.19 (2H, m, Ar), 7.79-7.77 (1H, m, Ar), 7.61-7.58 (1H, m, Ar), 7.53-7.51 (2H, m, Ar), 7.39-7.37 (2H, m, Ar).

2-(2,4-Dichlorophenyl)-1,3-benzoxazole: Light brown solid; m.p= 120-123 °C (Lit[46]. 118-119 °C); IR (KBr)/ ɜ (cm^{-1}) 1662 (C=N), 1588, 1466 (C=C, Ar), 1241 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm)*: 8.14-8.12 (1H, d, J= 8.40 Hz, Ar), 7.86-7.84 (1H, m, Ar), 7.64-7.60 (2H, m, Ar), 7.43-7.40 (3H, m, Ar); ^{13}C NMR ($CDCl_3$, 100 MHz)/ *δ (ppm):* 160.07, 150.51, 141.58, 137.54, 134.24, 132.51, 131.30, 127.43, 125.81, 124.82, 124.71, 120.56, 110.77.

2-(3-Methoxyphenyl)-1,3-benzoxazole: Light yellow solid; m.p= 72-74 °C (Lit[47]. 71.3-73.8 °C); IR (KBr)/ ɜ (cm^{-1}) 1642 (C=N), 1541, 1453 (C=C, Ar), 1278 (C-O-C); ^{1}H NMR ($CDCl_3$, 400

MHz)/ *δ(ppm)*: 8.11 (1H, m, Ar), 7.47 (1H, m, Ar), 7.44-7.42 (2H, m, Ar), 7.26 (1H, m, Ar), 7.18-7.14 (1H, m, Ar), 7.09-7.07 (1H, m, Ar), 6.95-6.91 (1H, m, Ar), 3.89 (3H, s, Me).

2-(4-Methoxyphenyl)-1,3-benzoxazole: Light yellow solid; m.p= 100-101 °C (Lit[42]. 103-105 °C); IR (KBr)/ ɜ (cm^{-1}) 1613 (C=N), 1501, 1452 (C=C, Ar), 1249 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ(ppm)*: 8.22-8.20 (2H, d, J= 8.40 Hz, Ar), 7.75-7.74 (1H, m, Ar), 7.58-7.56 (1H, m, Ar), 7.35-7.32 (2H, m, Ar), 7.05-7.03 (2H, d, J= 8 Hz, Ar), 3.90 (3H, s, Me); ^{13}C NMR ($CDCl_3$, 100 MHz)/ *δ(ppm):* 163.18, 162.32, 150.68, 142.30, 129.39, 124.60, 124.42, 119.70, 119.62, 114.36, 110.39, 55.45.

2-(3-Methylphenyl)-1,3-benzoxazole: Light yellow solid; m.p= 80-81 °C (Lit[47]. 79-80 °C); IR (KBr)/ ɜ (cm^{-1}) 1598 (C=N), 1550, 1451 (C=C, Ar), 1244 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm)*: 8.08 (1H, s, Ar), 8.07-8.05 (1H, d, J= 7.60 Hz, Ar), 7.79-7.77 (1H, m, Ar), 7.60-7.58 (1H, m, Ar), 7.45-7.41 (1H, t, J= 7.80 Hz, Ar), 7.37-7.35 (3H, m, Ar), 2.47 (3H, s, Me).

2-(4-Methylphenyl)-1,3-benzoxazole: Light brown solid; m.p= 114-115 °C (Lit[42]. 115-116 °C); IR (KBr)/ ɜ (cm^{-1}) 1619 (C=N), 1500, 1451 (C=C, Ar), 1241 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ(ppm)*: 8.16-8.14 (2H, d, J= 8 Hz, Ar), 7.78-7.75 (1 H, m, Ar), 7.59-7.54 (1H, m, Ar), 7.36-7.34 (4H, m, Ar), 2.45 (3H, s, Me).

2-(4-Isopropyl-phenyl)-1,3-benzoxazole: Light brown solid; m.p= 80-82 °C (Lit[48]. 76-78 °C); IR (KBr)/ ɜ (cm^{-1}) 1613 (C=N), 1553, 1451 (C=C, Ar), 1240 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ(ppm)*: 8.20-8.18 (2H, d, J= 8 Hz, Ar), 7.78ï 7.76 (1H, m, Ar), 7.60ï 7.58 (1H, m, Ar), 7.41ï 7.39 (2H, d, J= 8 Hz, Ar), 7.36-7.34 (2H, m, Ar), 3.00-2.99 (1H, m, CH), 1.32-1.30 (6H, d, J= 6.80 Hz, Me).

2-(2-Thiophen-2-yl)-1,3-benzoxazole: Brown solid; m.p= 82-84 °C (Lit[42]. 82-83 °C); IR (KBr)/ ɜ (cm^{-1}) 1659 (C=N), 1576, 1481 (C=C, Ar), 1310 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ(ppm)*: 7.93-7.92 (1H, d, J= 4 Hz, Ar), 7.76-7.74 (1H, m, Ar), 7.58-7.54 (2H, m, Ar), 7.36-7.34 (2H, m, Ar), 7.22-7.19 (1H, t, J= 4.1 Hz, Ar).

2-(2-Furan-2-yl)-1,3-benzoxazole: Red brown solid; m.p= 80-82 °C (Lit[42]. 85-86 °C); IR (KBr)/ ɜ (cm^{-1}) 1640 (C=N), 1553, 1451 (C=C, Ar), 1246 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm)*: 7.77-7.76 (1H, m, Ar), 7.68 (1H, s, Ar), 7.57-7.56 (1H, m, Ar), 7.38-7.36 (2H, m, Ar), 7.29 (1H, m, Ar), 6.63 (1H, m, Ar).

2-(4-N,N-Dimethylaminophenyl)-1,3-benzoxazole: Light Brown solid; m.p=185-187 °C; IR (KBr)/ ɜ (cm^{-1}) 1613 (C=N), 1510, 1447 (C=C, Ar), 1239 (C-O-C); ^{1}H NMR ($CDCl_3$, 400 MHz)/ *δ (ppm)*: 8.13-8.11 (2H, d, J= 8 Hz, Ar), 7.71-7.69 (1H, d, J= 7.20 Hz, Ar), 7.54-7.52 (1H, d, J= 7.20 Hz, Ar),7.31-7.27 (2H, m, Ar), 6.79-6.77 (2H, d, J= 8 Hz, Ar), 3.08 (6H, s, Me).

CONCLUSIONS

In summary, we have used microwave irradiation as a facile and efficient method for preparing of 2-substituted benzoxazole derivatives. This method involved one pot synthesis of 2-substituted benzoxazoles by the reaction of 2-aminophenol with benzaldehydes, which was assisted by potassium cyanide under microwave irradiation. The reaction was performed to afford the desired products in good to excellent yields and short reaction times.

SUPPLEMENTARY MATERIAL

Supplemental data for the article is available at the publisherôs website.

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Table 1 Optimizition of solvent effect on the reaction[a]

Entry	Solvent	Time (min)	Yield (%)
1	Ethanol	12	43
2	N,N-Dimethylformamide	3	95
3	Acetonitrile	15	25
4	Dichloromethane	15	-

[a]Reaction of benzaldehyde with *o*-aminophenol in the presence of different solvents.

Table 2 Optimization of the amounts of KCN[a]

Entry	Amount of KCN (mmol)	Time (min)	Yield (%)
1	0.5	10	45
2	0.8	10	78
3	1	5	91
4	1.1	3	95
5	1.4	3	95
6	1.8	3	95

[a]Reaction conditions: 2-aminophenol 1.1 mmol (0.13 gr), benzaldehyde 2.2 mmol, DMF as solvent (5 ml), under 450 Watt microwave irradiation.

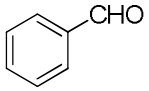
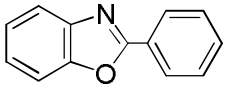
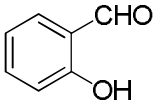
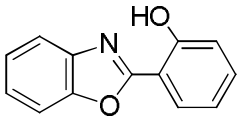
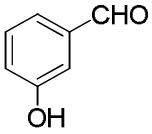
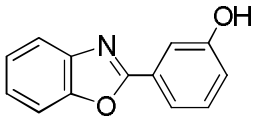
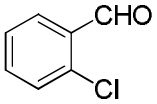
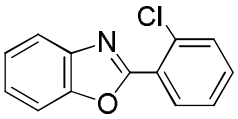
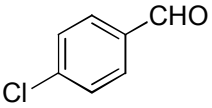
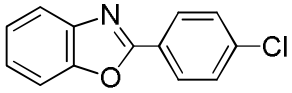
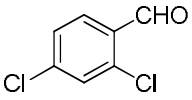
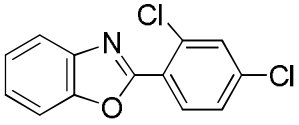
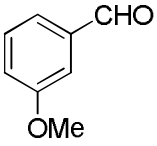
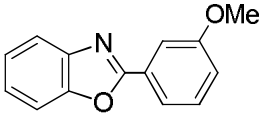
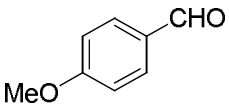
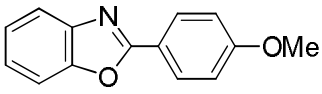
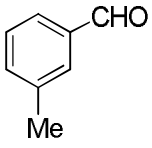
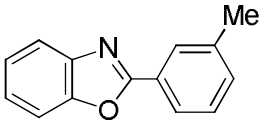
Table 3 Optimization of the microwave power[a]

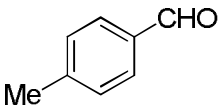
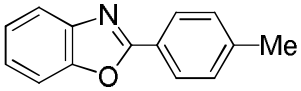
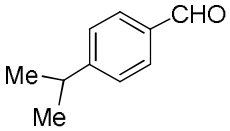
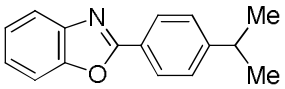
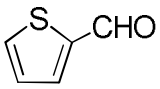
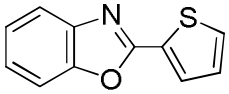
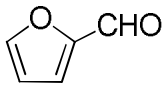
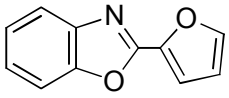
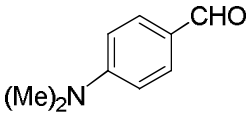
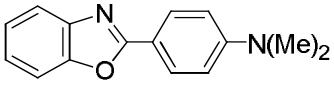
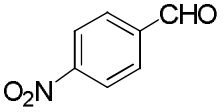
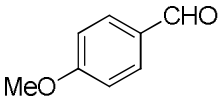
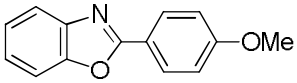
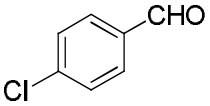
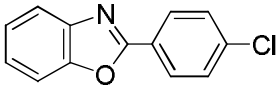
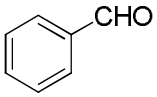
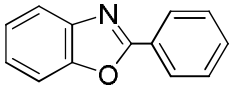
Entry	Power (Watt)	Time (min)	Yield (%)
1	150	15	53
2	300	8	71
3	450	3	95
4	600	3	94
5	750	3	81[b]

[a]Reaction conditions: 2-aminophenol 1.1 mmol (0.13 gr),benzaldehyde 2.2 mmol, 1.1 mmol KCN, DMF as solvent 5 ml, under different powers of microwave irradiation.
[b]Some side reactions were obtained under this condition.

Table 4

The reaction of 2-aminophenol with several aromatic aldehydes under microwave irradiation

Entry	Aldehyde	Product[a]	Time (min)	Yield[b] (%)	Mp(°C) Found	Mp(°C) Reported
1			3	95	98-100	102-103
2			1.5	96	123-124	125-126
3			1.6	96	172-174	-
4			6	92	63-65	61-64
5			5.5	93	149-151	153-154
6			5	86	120-123	118-119
7			3.75	89	72-74	71.3-73.8
8			4	92	100-101	103-105
9			4.3	94	80-81	79-80

10			5	91	114-115	115-116
11			3.8	94	80-82	76-78
12			6	91	82-84	82-83
13			5.6	90	80-82	85-86
14			4	92	185-187	-
15		-	15	-	-	-
16			24h[c]	76	-	-
17			24h[d]	66	-	-
18			300[e]	85	-	-

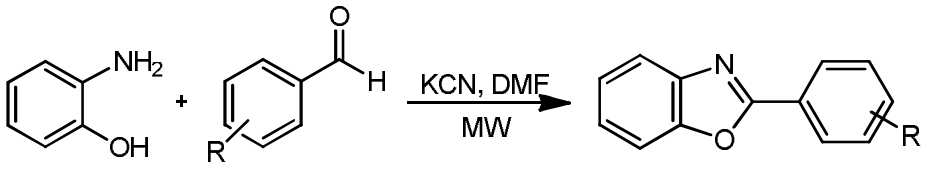
[a]All compounds are known and their physical and spectroscopic data were in good agreement with those of authentic samples.

[b]Yields refer to pure isolated products

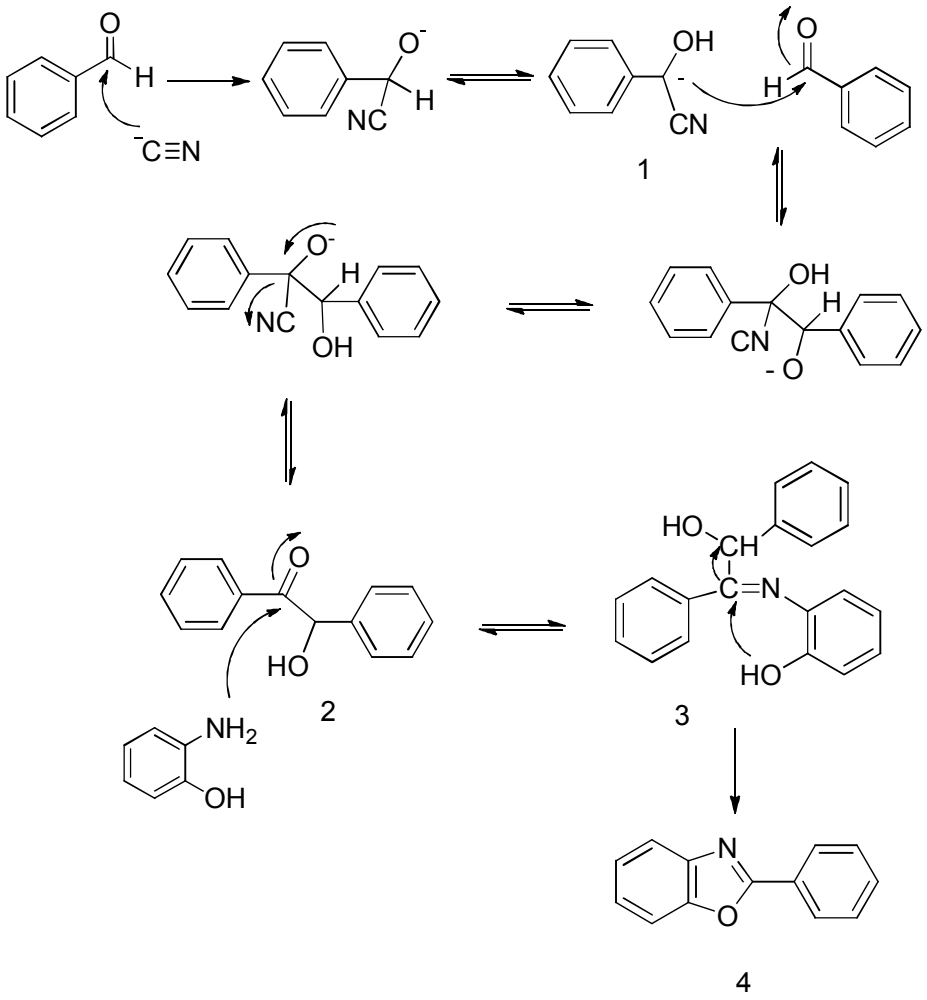
[c]Reaction conditions: 2-aminophenol 1 mmol, 4-methoxybenzaldehyde 1.1 mmol, $FeCl_3$ (0.05 mmol), toluene (1 ml), 110 ^oC, under 1 atm O_2 atmosphere.

[d]Reaction conditions: 2-aminophenol 1 mmol, 4-chlorobenzaldehyde 1.1 mmol, $FeCl_3$ (0.05 mmol), toluene (1 ml), 110 ^oC, under 1 atm O_2 atmosphere.

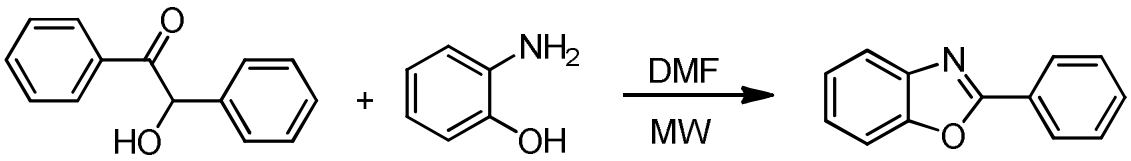
[e] Reaction conditions: 2-aminophenol 1.1 mmol, benzaldehyde 2.2 mmol, KCN (2 mmol), DMF as solvent (5 ml).



Scheme 1. Synthesis of 2-substituted benzoxazoles in the presence of KCN



Scheme 2. Proposed mechanism for the synthesis of benzoxazoles.



Scheme 3. Reaction of benzoin with 2-aminophenol under microwave irradiation.