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RESEARCH ARTICLE

Microwave-Assisted, [Bmim]PF_6-Catalyzed Synthesis of Benzoxazoles Under Solvent-free Conditions

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Abstract: ***Background*:** An efficient and green strategy for the synthesis of 2-arylbenzoxazoles using [Bmim]PF6 ionic liquid as a catalyst has been investigated *via* the condensation of o-aminophenol with aldehydes. The microwave-assisted synthesis features some advantages such as good yield of products, broad substrate scope, short reaction time, and absence of metal catalyst and solvent. Furthermore, the synthesis could be conveniently expanded to a gram scale.

***Methods*:** 2-arylbenzoxazoles were obtained from o-aminophenol with aldehydes using [Bmim]PF6 ionic liquid as a catalyst under microwave irradiation at 80ºC, 120 W.

***Results*:** Twenty-three 2-arylbenzoxazole derivatives were furnished in good to excellent yields under optimized conditions. The structures of these compounds were confirmed by analysis of NMR data. In addition, the method could be conveniently expanded to gram scale.

***Conclusion*:** An efficient and straightforward protocol for the synthesis of 2-arylbenzoxazoles catalyzed by [Bmim]PF6 ionic liquid has been demonstrated. The synthesis delivers several advantages such as short reaction time, broad substrate scope, scalability, solvent-free conditions, and high efficiency. The reaction mechanism and applications of this synthesis are currently ongoing in our lab and will be reported in due course.

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1. INTRODUCTION

Benzoxazole derivatives appearing in both natural and synthetic products are one of the most important classes of heterocyclic compounds. They possess a wide range of bioactivities such as antibiotic [1, 2], anticancer agent [3], antimicrobial [4], antifungal [5], antiviral [6], antibacterial [7, 8], antiparkinson [9], anti-inflammatory [10, 11], antitumor [12], anti-convulsant [13]. Some compounds containing benzoxazole skeleton have been marketed as drugs for the treatment of various diseases such as benoxaprofen, caboxamycin, flunoxaprofen and tafamidis (Fig. **1**). Benzoxazole-based compounds are also versatile ligands for transition metal and Lewis acid catalysis [14]. The use benzoxazole derivatives as laser dyes, photoluminescents [15] and whitening agents have also been documented [16].

Not surprisingly, the synthesis of benzoxazoles has attracted intensive research interest and numerous synthetic approaches have been reported. The condensation between 2-aminophenol and aldehyde is one of the most straightforward and facile methods for the construction of benzoxazoles. Many catalysts have been developed for this condensation reaction [17]. The employment of ionic liquids as solvent and catalyst, which could improve efficiency as well as shorten reaction time for various organic transformations [18], has been well investigated for benzoxazole synthesis such as Brønsted acidic ionic liquid gel [19], phosphonium acidic ionic liquid [20], KCN/1-butyl-3-methylimidazolium hexafluorophosphate [21] and 1-pentyl-3-methylimidazolium bromide [22].

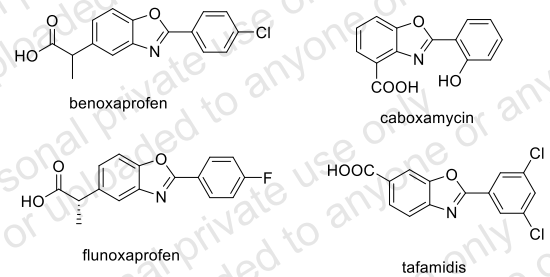

Fig. (1). Some marketed drugs containing benzoxazole skeleton.

The employment of microwave energy for conducting many chemical transformations has brought about many advantages. With microwave irradiation, many reactions can accomplish in a much shorter reaction time and result in higher yields of products than conventional heating. Herein, we reported the microwave-assisted synthesis of 2-arylbenzoxazole using [Bmim]PF_6 ionic liquid as the catalyst. The synthesis featured many advantages such as short reaction time, solvent-free conditions, low catalyst loading,

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and high efficiency. Furthermore, the reaction could be conveniently expanded to gram-scale. Although the combination of ionic liquid and microwave irradiation for organic transformation has been well reported [23, 24], the application of this combination for the synthesis of benzoxazole derivatives is very limited.

2. MATERIALS AND METHODS

All chemicals were purchased from Sigma-Aldrich and used without further purification. NMR spectra were recorded on a Varian Inova NMR Spectrometer (^{1}H NMR running at 500 MHz and ^{13}C NMR running at 125 MHz) instrument using $CDCl_3$ as solvent and Me_4Si as internal standard, and the broad-band decoupling of carbon data was proton-decoupled 13C{1H}. Chemical shifts (δ) are reported in ppm, and spin-spin coupling constants (*J*) are given in Hz. For microwave synthesis, all reactions were performed in a CEM microwave reactor at 80 ºC, 120 W in a 10 mL capped vial.

3. EXPERIMENTAL

3.1. General Procedure for the Benzothiazole Synthesis

2-aminophenol (**1a**, 2 mmol), benzaldehyde (**2a**, 2.1 mmol, 2.0 equiv.), and $[Bmim]PF_6$ catalyst (0.2 mmol, 0.1 equiv.) were added to 10 mL microwave containing a magnetic stirring bar. The mixture was irradiated in a microwave reactor at 80°C and 120 W for 10 minutes. After the reaction was completed, the mixture was cooled to room temperature and washed with water. The residue was purified by silica gel column chromatography using petroleum ether and ethyl acetate as eluent (99:1) to provide the corresponding product **3a** as a light yellow solid (359 mg, 92% yield).

3.2. Supplementary Data

3.2.1. 2-phenylbenzo[d]oxazole (3a)

359 mg, 92% yield, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.28-8.25 (m, 2H), 7.80-7.77 (m, 1H), 7.59-7.52 (m, 4H), 7.36-7-33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.0, 150.7, 142.2, 131.4, 128.9, 127.6, 127.3, 125.0, 124.4, 120.0, 110.6. NMR data are consistent with literature report [25].

3.2.2. 2-phenylbenzo[d]oxazole (3b)

376 mg, 90%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, *J* = 8.0 Hz, 2H), 7.78–7.75 (m, 1H), 7.57–7.55 (m, 1H), 7.33–7.31 (m, 4H), 2.43 (s, 3H, CH_3); ^{13}C NMR (125 MHz, CDCl3) δ 163.3, 150.7, 142.2, 141.8, 129.6, 127.7, 124.8, 124.3, 119.8, 110.5, 21.6 (CH_3). NMR data are consistent with literature report [26].

3.2.3. 2-(4-methoxyphenyl)benzo[d]oxazole (3c)

410 mg, 91%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.19 (d, *J* = 8.5 Hz, 2H), 7.75-7.72 (m, 1H), 7.56-7.53 (m, 1H), 7.35-7.28 (m, 1H), 7.01 (d, *J* = 8.5 Hz, 2H), 3.87 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.2, 162.3, 150.6, 142.3, 129.5, 124.5, 124.3, 119.7, 119.5, 114.3, 110.4, 55.4 (OCH_3). NMR data are consistent with literature report [27].

3.2.4. 2-(4-fluorophenyl)benzo[d]oxazole (3d)

379 mg, 89%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.26-8.22 (m, 2H), 7.77-7.74 (m, 1H), 7.57-7.52 (m, 1H), 7.35-7.32 (m, 2H), 7.22-7.16 (m, 2H); 13C NMR (125 MHz, $CDCl_3$) δ 164.7 (d, *J* = 251.0 Hz, CF), 162.1, 150.6, 142.0, 129.6 (d, *J* = 8.8 Hz), 125.0, 124.6, 123.4 (d, *J* = 3.1 Hz), 119.8, 116.1 (d, *J* = 22.0 Hz), 110.4. NMR data are consistent with literature report [28].

3.2.5. 2-(4-chlorophenyl)benzo[d]oxazole (3e)

418 mg, 91%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.16 (d, *J* = 8.5 Hz, 2H), 7.77-7.74 (m, 1H), 7.57-7.52 (m, 1H), 7.48 (d, *J* = 8.5 Hz, 2H), 7.38-7.31 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 150.8, 142.0, 137.6, 129.1, 128.8, 125.8, 125.1, 124.7, 120.2, 110.6. NMR data are consistent with literature report [23].

3.2.6. 2-(4-bromophenyl)benzo[d]oxazole (3f)

491 mg, 90%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, *J* = 8.5 Hz, 2H), 7.747-7.74 (m, 1H), 7.63 (d, *J* = 8.5 Hz, 2H), 7.56-7.53 (m, 1H), 7.37-7.33 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.1, 150.8, 142.0, 132.1, 128.8, 126.2, 126.2, 125.3, 124.8, 120.1, 110.5. NMR data are consistent with literature report [29].

3.2.7. 2-(4-(tert-butyl)phenyl)benzo[d]oxazole (3g)

462 mg, 92%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.22 (d, J = 8.5 Hz, 2H), 7.769-7.76 (m, 1H), 7.59-7.54 (m, 3H), 7.37-7.34 (m, 2H), 1.38 (s, 9H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.3, 155.1, 150.6, 142.2, 127.3, 125.8, 124.8, 124.5, 124.3, 119.7, 110.5, 35.0 ($C(CH_3)_3$), 31.1 (CH_3). NMR data are consistent with literature report [19].

3.2.8. 2-(4-(trifluoromethyl)phenyl)benzo[d]oxazole (3h)

463 mg, 88%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.38 (d, *J* = 8.0 Hz, 2H), 7.83-7.78 (m, 3H), 7.63-7.61 (m, 1H), 7.42-7.39 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 161.2, 150.7, 141.8, 133.1, 132.6 ((q, *J* = 32.8 Hz), 130.3, 127.8, 126.0, 125.9 (q, *J* = 4.0 Hz), 125.8, 125.7, 125.5, 124.8 (q, *J* = 273 Hz, CF_3), 120.5, 110.7. NMR data are consistent with literature report [25].

3.2.9. 2-(m-tolyl)benzo[d]oxazole (3i)

389 mg, 93%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 8.09 (s, 1H), 8.05 (d, *J* = 7.5 Hz, 1H), 7.79-7.76 (m, 1H), 7.58-7.56 (m, 1H), 7.42-7.33 (m, 4H), 2.45 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) *δ* 163.2, 150.6, 142.1, 138.7, 132.2, 128.6, 128.0, 127.0, 124.9, 124.6, 124.4, 119.8, 110.6, 21.2 (CH_3). NMR data are consistent with literature report [29].

3.2.10. 2-(3-methoxyphenyl)benzo[d]oxazole (3j)

205 mg, 91%, light yellow solid, ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.85 (d, *J* = 8.0 Hz, 2H), 7.78-7.76 (m, 1H), 7.59-

7.56 (m, 1H), 7.44-7.39 (m, 1H), 7.37-7.33 (m, 2H), 7.08 (dd, J = 2.0, 8.0 Hz, 1H), 3.90 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.8, 159.9, 150.8, 142.1, 130.0, 128.3, 125.2, 124.5, 120.2, 120.0, 118.1, 111.8, 110.6, 55.4 (OCH_3). NMR data are consistent with literature report [30].

3.2.11. 2-(3-fluorophenyl)benzo[d]oxazole (3k)

379 mg, 89%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.04 (d, J = 8.0 Hz, 1H), 7.93 (d, J = 8.5 Hz, 1H), 7.79-7.76 (m, 1H), 7.59-7.56 (m, 1H), 7.51-7.45 (m, 1H), 7.39-7.36 (m, 2H), 7.25-7.19 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.9 (d, J = 245.0 Hz, CF), 161.7 (d, J = 3.0 Hz), 150.7, 141.8, 130.5 (d, J = 8.0 Hz), 129.1 (d, J = 8.5 Hz), 125.5, 124.7, 123.2 (d, J = 3.0 Hz), 120.2, 118.3 (d, J = 21.2 Hz), 114.5 (d, J = 24.0 Hz), 110.6. NMR data are consistent with literature report [31].

3.2.12. 2-(3-chlorophenyl)benzo[d]oxazole (3l)

418 mg, 91%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.24 (s, 1H), 8.13 (d, J = 7.5 Hz, 1H), 7.78-7.75 (m, 1H), 7.58-7.55 (m, 1H), 7.49-7.40 (m, 2H), 7.39-7.34 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.0, 150.8, 142.0, 137.6, 129.3, 128.8, 125.7, 125.4, 124.7, 120.2, 110.6. NMR data are consistent with literature report [32].

3.2.13. 2-(3-bromophenyl)benzo[d]oxazole (3m)

497 mg, 91%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.40 (s, 1H), 8.16 (d, J = 7.5 Hz, 1H), 7.79-7.76 (m, 1H), 7.64 (d, J = 8.0 Hz, 1H), 7.58-7.55 (m, 1H), 7.40-7.34 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.4, 150.6, 141.9, 134.4, 130.4, 129.0, 126.0, 125.6, 124.6, 123.0, 120.1, 110.6. NMR data are consistent with literature report [33].

3.2.14. 2-(o-tolyl)benzo[d]oxazole (3n)

380 mg, 83%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.21-8.19 (m, 1H), 7.86-7.81 (m, 1H), 7.62-7.57 (m, 1H), 7.45-7.34 (m, 5H), 2.84 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) d 163.2, 150.2, 142.2, 138.7, 131.7, 130.8, 129.8, 126.0, 124.8, 124.3, 120.2, 110.4, 22.2 (CH_3). NMR data are consistent with literature report [29].

3.2.15. 2-(pyridin-2-yl)benzo[d]oxazole (3o)

332 mg, 86%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.84-8.82 (m, 1H), 8.35–8.38 (m, 1H), 7.93-7.83 (m, 2H), 7.68-7.65 (m, 1H), 7.47-7.37 (m, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 161.2, 150.7, 150.1, 145.7, 141.6, 136.8, 125.9, 125.3, 124.7, 123.3, 120.5, 111.0. NMR data are consistent with literature report [31].

3.2.16. 2-(furan-2-yl)benzo[d]oxazole (3p)

326 mg, 88%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$): δ 7.79-7.73 (m, 1H), 7.66 (dd, J = 2.0, 1.0 Hz, 1H), 7.57-7.54 (m, 1H), 7.37-7.32 (m, 2H), 7.27 (dd, J = 3.5, 1.0 Hz, 1H), 6.61 (dd, J = 3.5, 2.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 155.2, 150.1, 145.8, 142.7, 141.6, 125.3, 124.7, 120.1, 114.1, 112.2, 110.5. NMR data are consistent with literature report [34].

3.2.17. 2-(thiophen-2-yl)benzo[d]oxazole (3q)

358 mg, 89%, yellow solid, ^1H NMR (500 MHz, $CDCl_3$): δ 7.92 (dd, J = 4.0, 1.0 Hz, 1H), 7.76-7.70 (m, 1H), 7.57-7.52 (m, 2H), 7.36-7.30 (m, 2H), 7.18 (dd, J = 5.0, 4.0 Hz, 1H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 159.0, 150.4, 142.1, 130.3, 129.9, 129.7, 128.2, 125.0, 124.6, 119.7, 110.4. NMR data are consistent with literature report [34].

3.2.18. 5-methyl-2-phenylbenzo[d]oxazole (3r)

389 mg, 93%, light yellow solid, ^1H NMR (500 MHz, $CDCl_3$): δ 8.25-8.22 (m, 2H), 7.64-7.59 (m, 4H), 7.45 (d, J = 8.0 Hz, 1H), 7.17-7.14 (m, 1H), 2.49 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$): δ 163.2, 149.0, 142.4, 134.3, 131.3, 128.7, 127.4, 126.2, 119.8, 109.9, 21.5 (CH_3). NMR data are consistent with literature report [35].

3.2.19. 6- Methyl -2-phenylbenzo[d]oxazole (3s)

380 mg, 91%, light yellow solid, ^1H NMR (500MHz, $CDCl_3$) δ 8.25-8.22 (m, 2H), 7.64 (d, J = 8.0 Hz, 1H), 7.52-7.50 (m, 3H), 7.37 (s, 1H), 7.15 (d, J = 8.0 Hz, 1H), 2.50 (s, 3H, CH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 162.5, 151.2, 139.9, 135.4, 131.2, 128.7, 127.3, 125.8, 119.3, 110.8, 21.7 (CH_3). NMR data are consistent with literature report [36].

3.2.20. 5- Methoxy -2-phenylbenzo[d]oxazole (3t)

(405 mg, 90%), light yellow solid ^1H NMR (500 MHz, $CDCl_3$) δ 8.24-8.21 (m, 2H), 7.45 (d, J = 9.0 Hz, 1H), 7.54-7.51 (m, 3H), 7.26 (d, J = 2.0 Hz, 1H), 6.96 (dd, J = 2.0, 9.0 Hz, 1H), 3.87 (s, 3H, OCH_3); ^{13}C NMR (125 MHz, $CDCl_3$) δ 163.6, 157.4, 145.3, 142.8, 131.3, 128.8, 127.5, 127.3, 113.8, 110.6, 102.8, 55.9 (OCH_3). NMR data are consistent with literature report [37].

3.2.21. 5-Fluoro-2-phenylbenzo[d]oxazole (3u)

(379 mg, 89%), light yellow solid, ^1H NMR (500 MHz, $CDCl_3$) δ 8.24-8.21 (m, 2H), 7.53-7.43 (m, 5H), 7.10-7.03 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.8, 160.1 (d, J = 239.0 Hz, CF), 147.1, 143.0, 131.6, 128.8, 127.6, 126.7, 112.6 (d, J = 26.0 Hz), 110.9 (d, J = 10.0 Hz), 106.4 (d, J = 25.5 Hz). NMR data are consistent with literature report [36].

3.2.22. 5-Chloro-2-phenylbenzo[d]oxazole (3v)

(413 mg, 90%), light yellow solid ^1H NMR (500 MHz, $CDCl_3$) δ 8.24-8.22 (m, 2H), 7.74 (s, 1H), 7.54-7.48 (m, 4H), 7.33-7.30 (m, 1H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.2, 149.3, 143.4, 131.8, 130.0, 128.9, 127.7, 126.6, 125.2, 120.0, 111.3. NMR data are consistent with literature report [37].

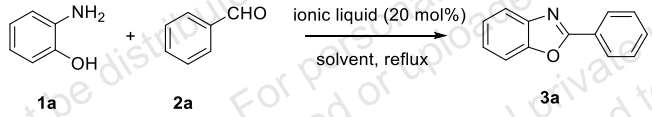
3.2.23. 5-Bromo-2-phenylbenzo[d]oxazole (3x)

(497 mg, 91%), light yellow solid ^1H NMR (500 MHz, CDCl3) δ 8.25-8.22 (m, 2H), 7.91 (s, 1H), 7.59-7.53 (m, 3H), 7.46 (s, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 164.1, 149.7, 143.6, 131.8, 128.9, 128.0, 127.8, 126.6, 122.8, 117.2, 111.7. NMR data are consistent with literature report [37].

4. RESULTS AND DISCUSSION

The reaction between 2-aminophenol (**1a**, 2 mmol) and benzaldehyde (**2a**, 2.1 mmol, 1.05 equiv.) in a selected solvent at reflux was chosen as model transformation to identify the optimum reaction conditions by screening a variety of different ionic liquids as catalysts (20 mol%), solvents, and reaction times. The results were summarized in Table **1**. Firstly, the condensation reaction was performed in water for 3 h. The use of [Bmim]BF_4 as the catalyst led to the desired product **3a** in 46% yield (entry 1). Reaction yields were slightly improved when [Bmim]HSO_4 and [Bmim]OTf catalysts were employed (entries 2 and 6). Further improvement was obtained under [Bmim]Br and [Bmim]OAc catalysts resulting in products in 62 and 64% yields, respectively (entries 3 and 4). Gratifyingly, when [Bmim]PF_6 was added into the reaction mixture, the desired product was afforded in 86% yield (entry 5). [Bmim]PF_6 then was chosen for further investigation. In the next attempts, changing the solvent into MeCN or reducing the reaction to 1 h lowered the reaction yields to 75 and 79%, respectively.

Table 1. Reaction with different ionic liquids.



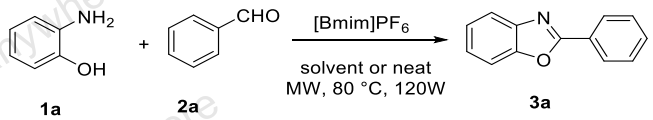
Entry	Catalyst	Solvent	Time (h)	Yield (%)[a]
1	[Bmim]BF_4	H_2O	3	46
2	[Bmim]HSO_4	H_2O	3	54
3	[Bmim]Br	H_2O	3	62
4	[Bmim]OAc	H_2O	3	64
5	[Bmim]PF_6	H_2O	3	86
6	[Bmim]OTf	H_2O	3	56
7	[Bmim]PF_6	MeCN	3	75
8	[Bmim]PF_6	H_2O	1	79

Note: [a]Isolated yield.

To design a more environmentally benign approach, the reaction then was performed under microwave irradiation at 80°C, 120 W, and the results were shown in Table **2**. Excitingly, 92 % yield of **3a** was obtained, although reaction time was reduced to 10 minutes (entry 1). Surprisingly, reaction efficiency was not affected under solvent-free conditions (entry 2). Trying to reduce catalyst loading to 10 mol% was also successful (entry 3). Unfortunately, a further attempt to lower catalyst loading to 5 mol% failed and the reaction yield decreased to 84 % (entry 4). Finally, in view of the high yield, the best reaction conditions were selected as follows: [Bmim]PF_6 catalyst (10 mol%), absence of solvent, and 10 minutes of microwave irradiation (80°C, 120 W).

Next, the synthetic potential of this reaction was evaluated with various benzaldehydes under optimal conditions and the results were outlined in Fig **(2)**. The electronic effect of substituents on benzaldehydes on reaction yield is not obvious. The synthesis worked well for benzaldehydes bearing electron-donating groups (Me, OMe, and tert-butyl) and electron-withdrawing groups (F, Cl, Br and CF_3) leading to corresponding products **3a-3n** in good to excellent yields. The reaction of 2-methylbenzaldehyde gave slightly lower yields than 3-methylbenzaldehyde and 4-methylbenzaldehyde probably due to steric hinder (**3n**). Noticeably, heteroaromatic aldehydes also proceeded smoothly under standard conditions and resulted in **3o-3q** in good isolated yield. This transformation could be performed on a large scale and compound **3a** were achieved in 90% isolated yield in 10 mmol scale.

Table 2. Reaction with microwave irradiation.



Entry	Solvent	Time (min)	Yield (%)
1	H_2O	10	92
2	None	10	92
3	None	10	92[a]
4	None	10	84[b]

Note: [a]The reaction was performed using 10 mol% of catalyst. [b]The reaction was performed using 5 mol% of catalyst.

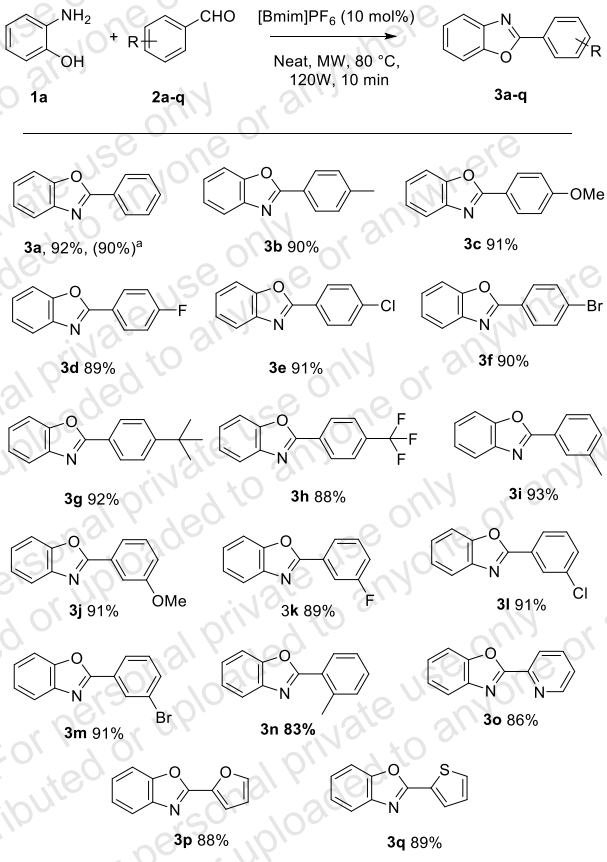


Fig. (2). Scope of aldehyde. **Note:** [a]The reaction was performed in 10 mmol scale.

We also briefly investigated the scope of 2-aminophenol substrates by the reaction with benzaldehyde under optimal conditions and the results were shown in Fig. (**3**). In general,

most of reactions proceeded smoothly to give the expected 2-phenyl benzoxazoles in good to excellent yields regardless of the electronic character of substituents on the aromatic moieties of 2-aminophenols such as bromine, chlorine, fluorine, methyl, methoxy groups. The synthesis also showed good turnover number (TON = mmol of product/ mmol of catalyst [38]) with TON values in range of 83-93.

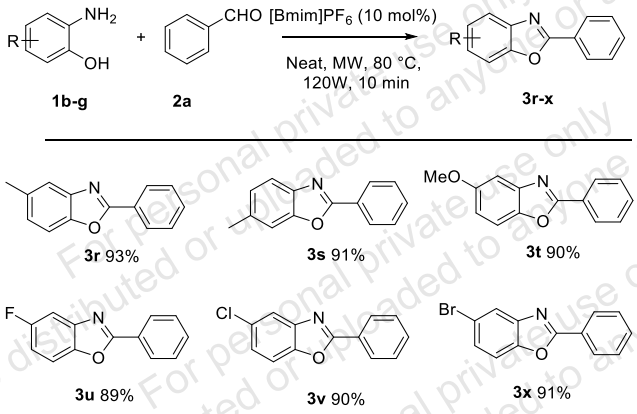


Fig. (3). Scope of 2-aminophenols.

To show the efficiency and capability of this strategy in the synthesis of different benzoxazole derivatives, Table **3** compares some of the obtained results from my work in comparison to other reports. The use of Brønsted acidic ionic liquid gel gave a higher yield but higher heating over a longer time was needed [17]. Other methods delivered lower yields or required much longer reaction times as well as the presence of a solvent [18, 39, 40].

Table 3. Comparison of this method with other methods in the literature for the synthesis of 2-phenyl-1,3-benzoxazole.

Methods	Solvent	Time	Yield (%)
Brønsted acidic ionic liquid gel, 130°C [17]	None	5 h	98
Phosphonium acidic ionic liquid, 100°C [18]	None	30 min	91
Molecular sieve, 180-190°C [39]	Xylene	48 h	87
[SMNP@GLP][Cl] nanoparticles, K_2CO_3, 80°C [40]	DMF	18 h	93
This work	None	10 min	92

CONCLUSION

In summary, an efficient and practical strategy to prepare 2-substituted benzoxazoles *via* the condensation between benzaldehydes and 2-aminophenols has been successfully developed by the outstanding catalytic performance of [Bmim]PF_6. Besides, the use of microwave energy and solvent-free conditions make the synthesis adapt to green chemistry. Other merits of the synthesis include short reaction time, broad substrate scope, scalability, and high efficiency. Reaction mechanism, further substrate scope, and application of this methodology are being pursued in our lab and will be reported in the due course.

LIST OF ABBREVIATIONS

Ac = Acetyl

Bmim = 1Butyl-3-methylimidazolium

DMF = N,N-Dimethylformamide

Me = Methyl

MW = Microwave

NMR = Nuclear Magnetic Resonance

Tf = Triflate

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

HUMAN AND ANIMAL RIGHTS

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

AVAILABILITY OF DATA AND MATERIALS

Not applicable.

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CONFLICT OF INTEREST

The author declares no conflict of interest, financial or otherwise.

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SUPPLEMENTARY MATERIALS

Supplementary Material is available on the publisher's website along with the published article.

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