An Efficient and Green Synthesis of 2-Arylbenzothiazoles in an Ionic Liquid, [pmIm]Br under Microwave Irradiation

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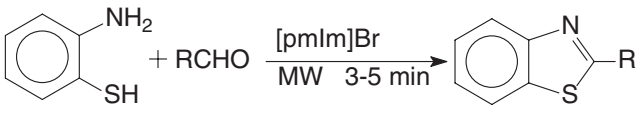
An efficient and green procedure for the synthesis of 2-arylbenzothiazoles has been developed by a simple condensation of 2-aminothiophenol and aromatic aldehyde in an inexpensive ionic liquid, 1-pentyl-3-methylimidazolium bromide ([pmIm]-Br) by microwave irradiation under solvent and catalyst-free condition. The ionic liquid is recycled for subsequent reactions.

The realization of simple and green synthetic procedures constitutes an important goal in organic synthesis. To combat the harmful effect of organic solvents frequently used in large quantities for organic transformations ionic liquids have been recently introduced as alternative green reaction media.[1,2] As a part of our drive[3] toward that direction we have recently initiated a program[4] to explore the use of benign and inexpensive ionic liquid as catalyst as well as reaction medium for the synthesis of useful molecules.

The 2-arylbenzothiazole nucleus constitutes the core unit of many therapeutic agents including antitumour drugs.[5] Thus, synthesis of this heterocyclic system is of much interest and a number of procedures have been developed.[6] However, many of these procedures are associated with one or more disadvantages such as involving toxic (nickel complex)[6d] and expensive (palladium derivative)[6g] catalysts, hazardous and carcinogenic organic solvents like nitrobenzene,[6c] acetonitrile,[6f] dioxane[6g] for reactions, multistep process and non-recovery of the catalyst. Hence, a simple, green, and efficient procedure avoiding these drawbacks will be of much use.

We report here a very simple synthesis of 2-arylbenzothiazoles by the condensation of 2-aminothiophenol and aromatic aldehydes in ionic liquid, 1-pentyl-3-methylimidazolium bromide[7] ([pmIm]Br) under microwave irradiation without requiring any other solvent and catalyst (Scheme 1).

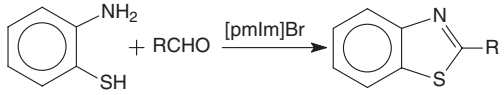
In a typical general experimental procedure, a mixture of 2-aminothiophenol (3 mmol) and an aromatic aldehyde (3 mmol) in [pmIm]Br (300 mg) was irradiated under microwave in a domestic microwave oven (10% power, 120 W) for 3–5 mins. The reaction mixture after being cooled was extracted with ether. The ether extract was evaporated to leave the crude solid. The pure product was obtained by recrystallization of the crude solid from ethanol-water. All the products are properly characterized by their mp and spectroscopic data. The residual ionic liquid was once again washed with ether, dried under vacuum (1 mm of Hg) at 80 °C for 1 h and reused for subsequent reactions without any appreciable loss of efficiency[8]

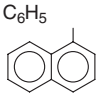
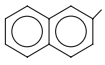
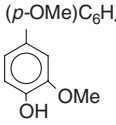
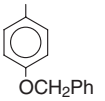
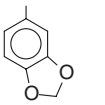


Scheme 1.

A wide variety of aromatic aldehydes underwent condensations with 2-aminothiophenol by this procedure to produce the corresponding benzothiazoles in very high yields. The results

Table 1. Synthesis of 2-arylbenzothiazoles catalyzed by [pmIm]Br



Entry	R	Microwave Heating Time/min	Yield/%[a]	Conventional Heating Time/h	Yield/%[a]
1	C_6H_5	3	99	6	90
2		5	97	6.5	83
3		4	95	7	86
4	(*p*-Cl)C_6H_4	3	98	7	88
5	(*p*-NO_2)C_6H_4	4	90	6.5	82
6	(*o*-OH)C_6H_4	3.5	92	5.5	92
7	(*m*-OH)C_6H_4	3	93	6	89
8	(*p*-OH)C_6H_4	3.5	95	6.5	92
9	(*o*-OMe)C_6H_4	3.5	94	5.5	88
10	(*m*-OMe)C_6H_4	3	95	5.5	91
11	(*p*-OMe)C_6H_4	3	98	5	94
12		4	95	5.5	87
13		5	98	5	94
14		3.5	93	6	87
15		2.5	94	6	91
16		3	92	5.5	87
17		2.5	87	5	82

[a]The yields refer to those of pure isolated products characterized by spectroscopic (IR, ^1H, ^{13}C NMR) data.

are presented in Table 1. The heterocyclic aldehydes such as furfural, 2-thiophene- and 2-pyridinecarboxaldehydes (Entries 15–17) also furnish the corresponding benzothiazoles without any difficulty. A variety of substituents like Cl, NO_2, OH, OMe, OCH_2Ph, methylenedioxy on the aromatic ring are compatible with this reaction condition.

These reactions under microwave are in general, very fast (3–5 min) and clean. For comparison, when all these reactions are carried out by conventional heating (80 °C) much longer periods (5–7 h) are required (Table 1). The activation by microwave irradiation was also reported earlier by Soufiaoui and his coworkers[6c,6e] in a similar condensation over $PhNO_2/SiO_2$ and MnO_2/SiO_2 surface. The catalytic activity of ionic liquid, [pmIm]Br has been established by the fact that when the reaction is run without ionic liquid no benzothioazole is obtained and the reaction is arrested with the formation of imine. Although mechanism of action of this ionic liquid is yet to be established by further experiments, it may be assumed that the bromide ion of [pmIm]Br is hydrogen-bonding to –SH increasing the nucleophilicity of sulfur atom. This makes the thiolate anion a stronger nucleophile towards efficient condensation with aldehydes followed by cyclization.

In conclusion, the present procedure catalyzed by a simple and inexpensive ionic liquid, [pmIm]Br provides an efficient methodology for the synthesis of 2-arylbenzothiazoles by the microwave-assisted condensation of 2-aminothiophenol and aromatic aldehydes. The significant advantages of this procedure are: a) very fast reaction (3–5 min); b) mild reaction condition compatible with a variety of sensitive groups; c) high yields (above 90%); d) cost efficiency providing recyclability of the catalyst and e) green aspects avoiding hazardous solvent, toxic catalyst and waste. Moreover, this leaves much promise for further applications of ionic liquids as catalysts.

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8 In the recycling experiment of ionic liquid carried out for the reaction in Entry 1 (Table 1) yields of products are as follows: 1_{st} Run −95%; 2_{nd} Run −92%; 3_{rd} Run −82%.

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