One-pot Synthesis of 2-Aminobenzothiazoles Using a New Reagent of [Bmim]Br_3 in [Bmim]BF_4

Zhang-Gao Le[a*], Jian-Ping Xu[a], Huo-Yu Rao[a], Min Ying[b]

[a] Department of Applied Chemistry, East China Institute of Technology, Fuzhou, Province of JiangXi 344000, P. R. China
E-mail: zhgle@ecit.edu.cn
[b] Zhejiang Wanli University, Ningbo, 315100, P. R. China

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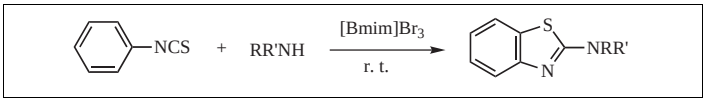

The one-pot direct synthesis of 2-aminobenzothiazoles from phenyl isothiocyanate and amines using a new reagent of 1-butyl-3-methylimidazolium tribromide ([Bmim]Br_3) in ionic liquid 1-butyl-3-methyl-imidazolium tetraflouoroborate ([Bmim]BF_4) is described.

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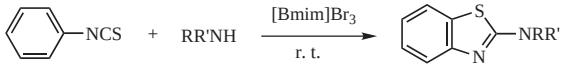
The synthesis and reaction of 2-aminobenzo-thiazoles have been a topic of research interest for over a century because these possess a variety of important biological activities and have been developed for the treatment of diatebes [1], muscle relaxants [2], analgesia [3], tuberculosis [4], epilepsy [5], inflammation [6] and viral infection [7]. 2-Aminobenzothiazoles are usually obtained by cyclization of arylthiourea with bromine in chloroform [8] or acetic acid [9]. Although this reaction usually proceeds efficiently at room temperature, some of these methods suffer from the disadvantages that bromine is a highly toxic, corrosive, and volatile reagent, reaction times are long and some material are expensive *etc*. An improved method for the synthesis of 2-aminobenzothiazoles was reported by Jordan and coworkers [10], who employed benzyltrimethyl-ammonium tribromide ($PhCH_2NMe_3Br_3$) as an alternative electrophilic bromine source. However, in this method the yields in some case were relatively low and reaction times were long. Therefore the development of a simple, efficient, environmentally more benign synthesis of 2-aminobenzothiazoles is still urgent.

In recently years room temperature ionic liquids (RTIL) have attracted increasing interest as green reagents for synthetic organic chemistry [11]. To date, some of the more important reactions have been carried out and investigated [12]. Our recent interest has been in the development of new synthetic methods using ionic liquids as reaction reagents [13]. Herein, we describe an efficient method for synthesis 2-aminobenzothiazoles *via* an one-pot, two step reaction of phenyl isothiocyanate, amine and 1-butyl-3-methylimidazolium tribromide ([Bmim]Br_3) in ionic liquid [Bmim]BF_4.

Scheme 1



First, we examined the reaction of phenyl isothiocyanate with methyl amine and [Bmim]Br_3 in the ionic liquid 1-butyl-3-methylimidazolium tetraflouoroborate ([Bmim] BF_4) (Scheme 1). The reaction occurred at room temperature and was complete within 10 h and the yield was 60% (Table 1, Entry 1). In similar fashion, the reaction of phenyl isothiocyanate, and [Bmim]Br_3 with a variety of primary amines was investigated, we found that the reaction is general and applicable to different primary amines, such as propylamine, isopropylamine, 2-hydroxy-ethylamine and methyl 4-aminobutyrate. The yields were high, and the results are summarized in Table 1 (Entries 2-5). In order to explore the generality of the method developed for the synthesis of 2-aminobenzothiazoles, we conducted the experiments of phenyl isothiocyanate and [Bmim]Br_3 with pyrrolidine and piperidine, which were also effective and gave the corresponding 2-aminobenzo-thiazole products in good yields (Table 1, Entries 6-7). The related ionic liquid 1-butyl-3-methylimidazolium tetraflouoro-borate [Bmim]PF_6 is also effective (Table 1, Entries 2, 6).

All the products gave satisfactory mp, IR, and ^{1}H NMR data, which were consistent with the literature data.

The present method has many obvious advantages compared to those reported in the literature, including high yield, and the shorter reaction time. For example, the synthesis of 2-(propylamino)benzothiazole and 2-(*N*-piperidino)benzothiazole by the recently reported method [10] required overnight, and the yields were only 73% and 69%, respectively. But using the present method, the same reaction was complete within 10 h and gave good yields of 80% and 75%, respectively. The literature

Table 1

Direct Synthesis of 2-Alkylaminobenzothiazoles from phenyl isothiocyanate and amine with $[Bmim]Br_3$ in $[Bmim]BF_4$ [a]

Entry	RR'NH	Yield(%)	Mp(°C)	Lit.mp(°C)
1	$MeNH_2$	60	141-142	140-141[10]
2	$PrNH_2$	80 (78) [b]	79-80	79-80[10]
3	*i*-$PrNH_2$	78	93-94	93-94.5[14]
4	$HOCH_2CH_2NH_2$	81	105-106	104-105.5[10]
5	$MeOCO(CH_2)_3NH_2$	60	111	110-111[10]
6	pyrrolidine	78 (77) [b]	99-100	98-100[15]
7	Piperidine	75	93	92.5-93.5[10]

[a] Isolated yield based on phenyl isothiocyanate; [b] In ionic liquid $[Bmim][PF_6]$.

method [15] reports 2-pyrrolidinobenzotriazole was only 7%, however, using the present method, the yield was 78%.

In conclusion, we have demonstrated the synthesis of 2-aminobenzothiazoles from phenyl isothiocyanate and amines using a new reagent of 1-butyl-3-methylimidazolium tribromide ($[Bmim]Br_3$) in the ionic liquid 1-butyl-3-methylimidazolium tetraflouoroborate ($[Bmim]BF_4$). This method will be highly useful because of its ease, simplicity, high yields, short reaction time and environmentally benign nature.

EXPERIMENTAL

Melting points were determined on a digital melting point apparatus and were not corrected. Infrared spectra were recorded on a VECTOR22 (Bruker). Nuclear magnetic resonance spectra were recorded on AVANCE DMX 400 (Bruker) spectrometer. The ionic liquids $[Bmim]Br_3$ was synthesized by reaction of an equimolar amount of [Bmim]Br and Br_2 for 3 h at room temperature. The ionic liquids $[Bmim]BF_4$ and $[Bmim]PF_6$ were synthesized according to reported procedures [16]. The other materials were commercially available and were used without further purification.

General Procedure for Synthesis of 2-Aminobenzothiazoles.

Amine (1.2 mmol) and phenyl isothiocyanate (1 mmol) were added to $[Bmim]BF_4$ (1 mL). The resultant mixture was stirred for 5 min at room temperature, treated with $[Bmim]Br_3$ and stirred 10 h. The crude product was extracted with Et_2O, and purified or directly purified by recrystallization with ethanol or separated by preparative thin-layer chromatography on silica gel using a mixture of chloroform and petroleum ether as developer to give the corresponding pure product.

Acnowlegement.

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