Tetraethylammonium bromate mediated synthesis of 2-arylbenzothiazole

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A simple and convenient method is described for the synthesis of 2-arylbenzothiazoles mediated by quaternary ammonium bromate at room temperature. Short reaction time at ambient temperature, high yield of the product and simple product recovery are the chief features of the present method.

Keywords: 2-Arylbenzothiazole, tetraethylammonium bromate, o-aminothiophenols, aromatic aldehydes

2-Arylbenzothiazoles and their derivatives are important heterocycles having medicinal applications. They are the basic constituent of several antitumor, anticonvulsant, antiviral and anticancer drugs. Furthermore benzothiazoles, having the important biaryl pharmacophore have emerged as β-amyloid, anti parasitic and chemiluminescent agents, and also have gained importance as photosensitizers. Benzothiazoles can function as Ca²⁺ channel antagonists. It has also been reported that a 2-arylbenzothiazole has recently been isolated as a cytotoxic metabolite from the extract of streptomyces. In the industry, benzothiazoles have been used as antioxidants, vulcanization accelerators and as dopant in light emitting organic electroluminescent devices. Owing to the wide range of pharmacological and biological activities, the synthesis of substituted benzothiazoles is gaining importance in recent times. Various methods of synthesis are known, the oldest being the Jacobson synthesis.

Some reported synthesis include the use of Pd₂dba₂/xantphos as catalyst as also via Suzuki biaryl coupling, use of Mn(OAc)₃ in cyclization of thioformanilides, coupling of benzothiazole with arylbromides, Cu catalyzed cyclization of o-halobenzanilides and cyclization of ketamines. A one pot synthesis starting from o-haloanilides with a tendem thionation with Lawesson's reagent and intramolecular cyclization mediated by Cs₂CO₃, hypervalent iodine mediated intramolecular cyclisation of thioformanilides and several solvent free synthesis and solid phase synthesis have also been reported. In continuation of the work with tetraethylammonium bromates, herein is reported an efficient synthesis of 2-arylbenzothiazole from o-aminothiophenols and an aromatic aldehyde mediated by Et₄NBrO₃ in aqueous methanol. The tetraethylammonium bromate is prepared by a procedure reported earlier. In earlier studies, the Et₄NBrO₃ was conveniently used as an oxidizing agent for the purpose of oxidative degradation of oximes and the semicarbazones.

Results and Discussion

During the investigation, it was observed that in addition to being an oxidizing agent the Et₄NBrO₃ could be used as a versatile reagent for carrying out cyclization reaction in the synthesis of heterocyclic compounds. In the present study, the versatility of Et₄NBrO₃ in mediating cyclization reaction for the synthesis of heterocycles is extended to the synthesis of 2-arylbenothiazoles in a simple and efficient process at RT in aqueous methanol solution. The synthesis was carried out with aromatic aldehydes having a variety of substitutents in the phenyl ring and the results indicate the absence of any influence of electronic factors on the yields of the products. However, time of completion of the reactions increases considerably when electron withdrawing substituents are present in the aromatic aldehyde (Table I, entry 6,7). Several solvent systems such as water, dichloromethane, chloroform, aqueous ethanol, acetone, aqueous methanol were screened for their suitability and the best results were obtained in aqueous MeOH (Table II). Consequently all reactions were performed with tetraethylammonium bromate as the catalyst for the cyclocondensation in aqueous methanol at RT under stirring. The general procedure involves stirring an aqueous solution of Et₄NBrO₃, an aromatic aldehyde and o-aminothiophenol at RT for varying period of time as shown in Table I. The reaction was also performed using aqueous NaBrO₃ without any success. The reaction is shown in Scheme I and the results are summarized in Table I.
Experimental Section

The o-aminothiophenol and all aromatic aldehydes were purchased from Sigma-Aldrich. Liquid aldehydes were purified by distillation and o-aminothiophenol was used as received. The products 2-arylbenzothiazoles were identified by recording their m.p., IR, $^1$H and $^{13}$C NMR spectra and comparing the results with those reported in literature. Melting points were recorded in a VMP-D model melting point apparatus and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Advance Digital 300 MHz spectrometer in CDCl$_3$. TMS was used as internal standard. IR spectra were obtained on a Perkin Elmer FT-IR 1600 spectrophotometer in KBr pellets.

General procedure for the synthesis of 2-aryl-substituted benzothiazole using tetraethylammonium bromate as catalyst

A mixture of o-aminothiophenol (1 mmol) and aromatic aldehydes (1 mmol) were added to 5 mL of methanol in a RB flask and stirred. To this tetraethylammonium bromate (10 mol%) in deionized water was added in portions with stirring. The progress of the reaction was monitored by TLC in
prepared silica gel plates with ethylacetate: n-hexane (5% ethyl acetate) as the eluent. The completion of the reaction was indicated by the absence of the substrates. After completion of the reaction, the reaction mixture was poured into an aqueous solution of brine and the precipitated solid recovered. The crude product was purified by column chromatography over silica gel (Merck) 60-120 mesh and 5% ethylacetate and 95% n-hexane (v/v) as eluent. The solid product was obtained by removal of solvent at reduced pressure and characterized.

2-Phenyl-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.12-8.09 (m, 3H), 7.925 (d, $J = 7.8$ Hz, 1H), 7.54-7.49 (m, 4H), 7.4-7.38 (m, 1H); $^{13}$C NMR (CDCl$_3$): δ 167.98, 154.06, 134.98, 133.53, 131.89, 130.88, 128.94, 128.53, 127.48, 126.24, 125.11, 123.16, 121.54; IR (KBr): 3063, 3023, 1597, 1584 cm$^{-1}$.

2-(4-Methoxyphenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.05 (d, $J = 8.4$ Hz, 3H), 7.88 (d, $J = 7.5$, 3H), 7.49 (t, $J_1 = 7.2$ Hz, $J_2 = 7.5$ Hz, 1H), 7.36 (t, $J = 7.5$ Hz, 1H), 7.01 (d, $J = 8.4$ Hz, 2H), 3.86 (s, 3H, OCH$_3$); $^{13}$C NMR (CDCl$_3$): δ 167.8, 161.8, 158.7, 154.1, 134.7, 129, 126.3, 126.1, 124.7, 122.7, 121.4, 114.2, 55.4; IR (KBr): 3103, 3058, 1604, 1585 cm$^{-1}$.

2-(2-Chlorophenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.22-8.19 (m, 1H), 8.14 (d, $J = 6$ Hz, 1H), 7.94 (d, $J = 6$ Hz, 1H), 7.54-7.5 (m, 2H), 7.44-7.39 (m, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$): δ 164.3, 152.6, 136.2, 132.8, 132.4, 131.9, 131.3, 130.9, 127.2, 126.4, 125.6, 123.6, 121.4; IR (KBr): 3098, 3065, 1559 cm$^{-1}$.

2-(3,4-Dimethoxyphenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.05 (d, $J = 6$ Hz, 1H), 7.85 (d, $J = 6$ Hz, 1H), 7.74 (s, 1H), 7.59 (d, $J = 6.3$ Hz, 1H), 7.47 (t, $J_1 = 5.4$ Hz, $J_2 = 6$ Hz, 1H), 7.35 (t, $J_1 = 5.7$ Hz, $J_2 = 5.4$ Hz, 1H), 6.93 (d, $J = 6.3$ Hz, 1H), 4.01 (s, 3H, -OCH$_3$), 3.94 (s, 3H, -OCH$_3$); $^{13}$C NMR (CDCl$_3$): δ 167.92, 154.03, 153.53, 149.29, 134.82, 126.57, 126.21, 124.85, 122.77, 121.47, 121.12, 110.96, 109.72, 56.00; IR (KBr): 3078, 3053, 2965, 2839, 1593 cm$^{-1}$.

2-(2-Methoxyphenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.55 (d, $J = 7.9$ Hz, 1H), 8.15 (d, $J = 8.1$ Hz, 1H), 7.93 (d, $J = 8.1$ Hz, 1H), 7.53-7.45 (m, 2H), 7.41-7.36 (m, 1H), 7.18-7.01 (m, 2H), 4.074 (s, 3H); IR (KBr): 3063, 3015, 1597, 1584 cm$^{-1}$.

2-(4-Nitrophenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.32 (d, $J = 7.9$ Hz, 2H), 8.21 (d, $J = 7.9$ Hz, 1H), 8.10 (d, $J = 8.2$ Hz, 2H), 8.01 (d, $J = 8.2$ Hz, 1H), 7.44-7.53 (m, 2H); $^{13}$C NMR (CDCl$_3$): δ 161.9, 157.5, 149.4, 142.8, 133.3, 130.7, 130.2, 126.5, 126.3, 122.5, 120.3, 119.5, 111.8; IR (KBr): 3085, 3042, 1598, 1565 cm$^{-1}$.

2-(3-Nitrophenyl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.84 (s, 1H), 8.44 (d, $J = 8.0$ Hz, 1H), 8.41 (d, $J = 8.0$ Hz, 1H), 8.24 (d, $J = 8.0$ Hz, 1H), 8.16 (d, $J = 8.0$ Hz, 1H), 7.88 (t, $J = 8.0$ Hz, 1H), 7.60 (t, $J = 8.0$ Hz, 1H), 7.54 (t, $J = 8.0$ Hz, 1H); $^{13}$C NMR (CDCl$_3$): δ 161.9, 157.5, 149.4, 142.8, 133.3, 130.7, 130.2, 126.5, 126.3, 122.5, 120.3, 119.5, 111.8; IR (KBr): 3080, 3033, 1612, 1577 cm$^{-1}$.

2-(Furan-2-yl)-1,3-benzothiazole. $^1$H NMR (CDCl$_3$): δ 8.09 (d, $J = 8.4$ Hz, 1H), 7.9 (d, $J = 7.8$ Hz, 1H), 7.6 (d, $J = 1.2$ Hz, 1H), 7.54-7.48 (m, 1H), 7.43-7.32 (m, 1H), 7.31-7.16 (m, 1H), 7.15-6.55 (m, 1H); $^{13}$C NMR (CDCl$_3$): δ 157.4, 153.6, 148.6, 144.6, 134.15, 126.4, 125.1, 123.5, 121.4, 112.4, 111; IR (KBr): 3123, 3055, 1584, 1562 cm$^{-1}$.

In conclusion, a facile synthesis of 2-arylbenzothiazole has been achieved with tetraethylammonium bromate. Reaction conditions are simple and the transformation could be performed at room temperature. Simple recovery of the target molecules and high yields are the distinguishing feature of the method.

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References