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LETTER

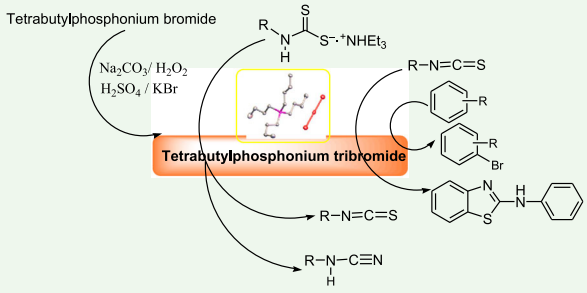
An environmentally benign synthesis of Tetrabutylphosphonium tribromide (TBPTB) – a versatile and efficient phase transfer reagent for organic transformations

Visekhonuo Kuotsu[a], Vevosa Nakro[a], Imkong Yanger[a], Tsenbeni N. Lotha[a], Ketiyala Tzudir[a], Upasana Bora Sinha[b] and Latonglila Jamir[a]

[a]Department of Environmental Science, Nagaland University, Nagaland, India; [b]Department of Chemistry, Nagaland University, Nagaland, India

ABSTRACT

Tetrabutylphosphonium tribromide (TBPTB), a mild and versatile reagent, has been synthesized following an environmentally benign protocol. The new reagent possesses inherent phase transfer properties which facilitates organic reactions in aqueous medium. Thermal stability of the reagent which enables organic reactions under microwave irradiation and recyclability of the spent reagent are special attributes of the new reagent. These properties collectively provide an opportunity for facile, practical, and eco-friendly synthesis of a wide range of pharmaceutically significant and specialty organic compounds such as bromo-organics, isothiocyanates, cyanamides and 2-aminobenzothiazoles in excellent yields on-water under microwave irradiation.



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Tetrabutylphosphonium tribromide; phase-transfer reagent; aqueous reactions; microwave reactions

Introduction

With the advent of green chemistry since the nineties, there has been a continuous effort towards environmental benignity, which, among others has led to the synthesis of numerous chemical reagents. While these efforts have resulted in tremendous advancements in addressing chemical toxicity, it has on the other hand, lead to an overload of new chemical compounds. Therefore, in order to work towards environmental protection in a holistic manner, it becomes important to identify the essential traits in a reagent and therefore plan the design in a way that these features are incorporated in the reagent. In line with this, it was envisaged that developing a reagent that could perform multiple chemical transformations would be superior to those that were reaction specific. On the other hand, with the increase in negative focus towards organic solvents in chemical synthesis, there is an effort to perform chemical reactions in aqueous medium (*1–3*). However, the most important limiting factor is the insolubility of the reagents and substrates in water. This is where the need for phase transfer reagents is realized and has been considered an important property in the development of the new reagent.

A while ago, the first phosphonium tribromide reagent, Ethyltriphenylphosphonium tribromide (ETPPTB) has been developed by our group and its reactivity has been studied (*4*). In continuation of our efforts to study this class of reagents, it has been realized that further work is required in terms of development of a range of such reagents and studies of its properties.

CONTACT Latonglila Jamir latongli.jamir@gmail.com
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And with this in mind, we have developed the first environmentally benign synthesis of the second member of the phosphonium tribromide family in the literature *vis* Tetrabutylphosphonium tribromide (TBPTB) and herein report the studies of its reactivity.

Phosphonium tribromides are derivatives of their precursor phosphonium bromides. The presence of the phosphonium moiety furnishes these reagents their phase transfer properties (*5, 6*) which in turn provide them an advantage over general hydrophobic tribromide reagents for organic transformations in water (*3*). Among the existing tribromide reagents, quaternary ammonium tribromides and pyridinium tribromides are the most widely studied because of their versatility. However, one of their biggest limitations is their insolubility in water due to which these reagents could not be generally utilized for organic reactions in aqueous medium. This very shortcoming is overcome with the phase transfer property of the new reagent. Another noteworthy character of a reagent is its thermal stability by which a reagent can perform thermal or microwave (MW) mediated reactions. The new tribromide is stable up to temperatures of about 200°C (*1*), and thus can be used for reactions at elevated temperature, making it a reagent of choice for thermal and microwave mediated reactions, which is the case in hand (*7, 8*). This is a significant attribute of the new reagent as compared to similar reagents such as ammonium based tribromides which decomposes at elevated reaction temperatures (120–150°C) (*6*). Recyclability of spent reagents is another important aspect of chemical reagents from a POV of environmental benignity (*9*) and cost effectiveness. Herein, the new reagent TBPTB could be efficiently recovered from reactions and subsequently recycled, thus adding to its greenness.

Thus, after the successful synthesis of the new reagent TBPTB, we have developed a range of organic reactions on water which, in most cases, has proven to be further enhanced by the implementation of MW. All the processes are very simple, fast and efficient. The following findings are significant specially from the perspective that the classes of compounds presently being reported, namely bromo-organic compounds, isothiocyanates, cyanamides, benzothiazoles holds very important places in organic chemistry and in pharmaceutical sciences owing to their various significant applications. For instance, the bromo-organic compounds are popular in the manufacture of pharmaceuticals, intermediates for agrochemicals, and other specialty chemicals such as pesticides, insectides, herbicides, fire retardants (*10–12*). They also hold a special place in carbon–carbon bond formation via cross-coupling reactions such as Stille-Suzuki (*13*) and Sonogashira (*14*) or carbon-heteroatom bond formation via aromatic functionalization protocols (*15*).

Isothiocyanates possess biological activities such as anti-bacterial (*16*), anti-proliferatives (*17*), anticancer properties (*18, 19*), enzyme inhibitors for the HIV virus (*19*), reagent in Edman peptide sequencing (*20*) and other biological assays of DNA and proteins (*21, 22*). They have proven to be important precursors for synthesis of heterocycles (*23*) and agrochemicals that have antifungal and anthelmintic activities (*24*).

Cyanamides have also gained enormous attention as important precursors for synthesis of tumor inhibitors (*25, 26*), as prebiotic phosphate activating agent (*27*) and in the synthesis of pharmaceutically active heterocycles such as herbicides and minoxidil – a vasodilator used for treatment of hair loss and promotion of hair regrowth (*28, 29*). Cyanamides are also key precursors to N-alkyl or N-aryl imides and also serve as useful protecting group in the synthesis of heterocycles containing secondary and tertiary amines (*30*).

On the other hand, benzothiazoles have gained tremendous popularity in the fields of bioorganic and medicinal chemistry finding its applications in the treatment of diabetes (*31–33*), antileishmania (*34*), analgesia (*35*), tuberculosis(*36*), viral infection(*37*), bacterial infections (*38*), as DNA Gyrase B Inhibitors (*39, 40*), etc.

In line with the important applications of the above compounds, one can find a plethora of methodologies for their synthesis in the literature (*41–44*).

However, most of these methodologies involve the use of toxic metal catalysts and corrosive reagents, expensive catalysts and reagents, expensive and toxic bases, environmentally hazardous solvents, high reaction temperatures and long reaction times leading to high consumption of energy. These qualities render most of the reported methods as environmentally unacceptable. And therefore, despite the stockpile of synthetic methodologies found in the literature, development of new and improved, energy efficient, easy to execute, environmentally innocuous methodologies, for the synthesis of bromoorganic compounds, isothiocyanates, cyanamides, benzothiazoles and esters, still stand significant.

Results and discussion

Synthesis of TBPTB reagent

While it might be safely stated that the most commonly adopted method of synthesis of QATBs is *via* the peroxo-metal mediated reaction strategy (*45, 46*), the major drawback of the protocol lies in the use of heavy metal as catalyst for activation of hydrogen peroxide. A

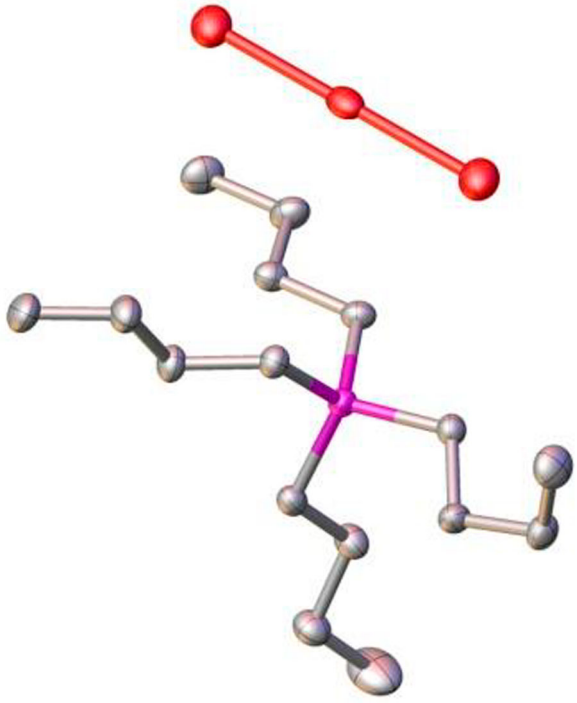


Figure 1. ORTEP view of TBPTB.

$KMnO_4$ mediated synthesis of quaternary ammonium tribromides has been reported (*47*). However, being a hazardous chemical, the use of $KMnO_4$ for the present synthesis has been ruled out. As a part of our efforts to develop benign methods for synthesis of QATBs, we have developed a peroxocarbonate mediated synthetic protocol that works as efficiently but is more innocuous in nature than the use of peroxometal catalysts (*48*). Since the desired target of the present work was to achieve environmentally benign synthetic methodologies, the metal-free synthetic pathway has been adopted wherein an excess of hydrogen peroxide, sodium carbonate as well as sodium bicarbonate rapidly react into an equilibrium mixture of carbonate ions and peroxo carbonate ions. Thus, the tetrabutylphosphonium tribromide (CCDC No. 194831) (Figure 1) formation has been achieved via a peroxocarbonate ion mediated oxidation of bromide to tribromide as shown in Scheme 1.

Bromination reaction using TBPTB and subsequent regeneration of reagent

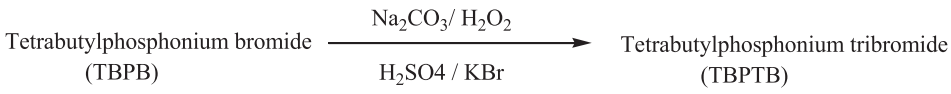
While several tribromide reagents have been utilized for bromination of organic substrates, there are no reports available of the same being carried out under an ethyl acetate / water biphasic medium. In this new and improved methodology, organic substrate (Table 1, Entry **1**) was taken in an RB flask along with 5 ml of ethyl acetate and 3 ml of water. This was followed by portion wise addition of the reagent TBPTB with vigorous stirring at rt. The product (Table 1, Entry **1a**) was obtained within 3 mins of total addition of the reagent. Herein, molecular bromine released from the reagent is proposedly made available to the substrates in organic phase due to the phase transfer properties of the new reagent. Further, the affinity of the spent reagent TBPB for water enhances the availability of molecular bromine in the solvent phase for the organic bromination to take place. The dissolution of the reaction by-product HBr in water, thus partial removal from the solvent phase also enhances the quicker bromination of the organic substrates.

The reactions were quick, convenient due to non-involvement of chilled or thermal conditions, and high yielding. Several organic substrates underwent this protocol smoothly to give their corresponding brominated products in excellent yields as shown in Table 1.

Keeping with the green chemistry's no waste principle; we have further attempted to regenerate the tribromide reagent from the spent reagent TBPB. The aqueous layer separated from the above reaction contains the spent reagent TBPB and HBr. The presence of dissolved HBr was not considered a setback as there was the requirement for low pH to tide the tribromide formation over. The spent reagent in aqueous media was collected in a beaker which was further introduced to peroxocarbonate intermediate. Addition of KBr and 1M H_2SO_4 generates the tribromide reagent in 84% yield.

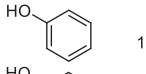
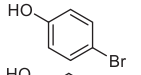
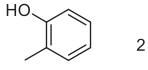
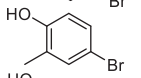
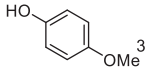
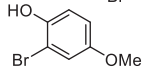
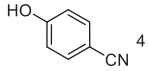
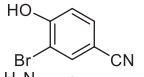
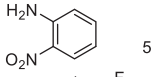
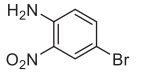
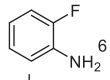
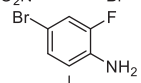
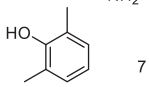
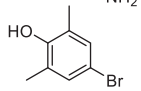
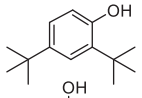
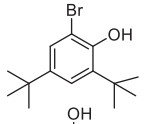
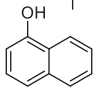
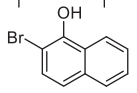
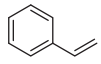
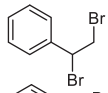
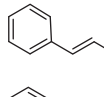
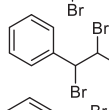
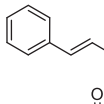
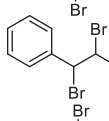
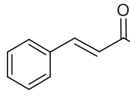
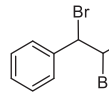
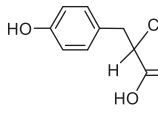
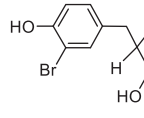
Synthesis of isothiocyanates using TBPTB

While literature reveals few reports of isothiocyanate preparation using tribromides (*48*), all such reports involves the use of stoichiometric amounts of the concerned tribromide which is rendered unacceptable from environmental as well as economic perspectives. As a green alternative to existing protocols, the isothiocyanate have been prepared from dithiocarbamate salts using catalytic amount of TBPTB, using



Scheme 1. Peroxocarbonate ion mediated synthesis of TBPTB.

Table 1. Synthesis of bromoorganic compounds using TBPTB[a].

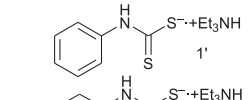
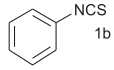
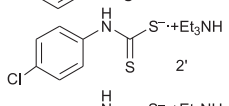
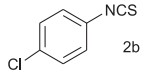
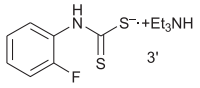
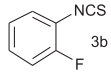
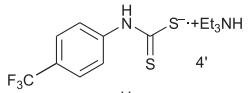
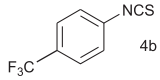
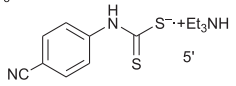
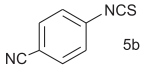
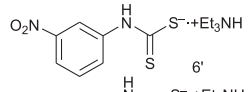
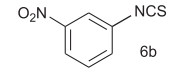
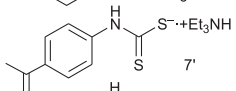
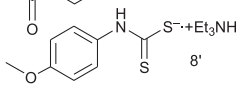
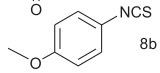
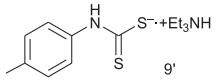
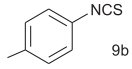
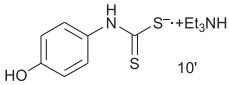
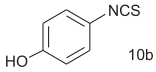
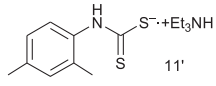
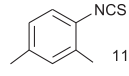
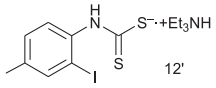
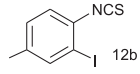
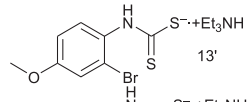
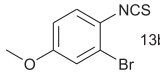
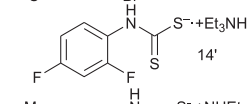
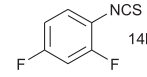
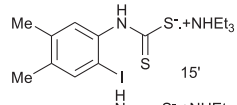
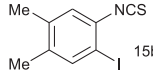
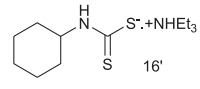
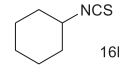
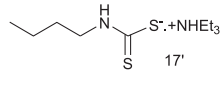
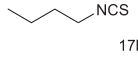
Substrate	Reaction Time	Product[b]	Yield[c] %
 1	20	 1a	92
 2	15	 2a	90
 3	20	 3a	84
 4	35	 4a	88
 5	32	 5a	90
 6	30	 6a	81
 7	40	 7a	86
 8	43	 8a	80
 9	20	 9a	79
 10	22	 10a	81
 11	30	 11a	77
 12	45	 12a	89
 13	35	 13a	81
 14	30	 14a	78

[a] Reactions were monitored by TLC; [b] Confirmed by IR, ^{1}H NMR and ^{13}C NMR; [c]Isolated yield.

$NaHCO_3$, on water, under MW irradiation. When phenyl dithiocarbamate salt (Table 2, Entry **1'**) was reacted with a catalytic amount of TBPTB (.02 mg /.05 mmol) and $NaHCO_3$ (0.336 g / 4 mmol) on water and irradiated under microwave at p7, total conversion to the corresponding isothiocyanate (Table 2, Entry **1b**) was observed within 47 s. The completion of reaction using catalytic amount of the reagent can be explained by referring to reaction mechanism (Scheme 2) as given below (*49*).

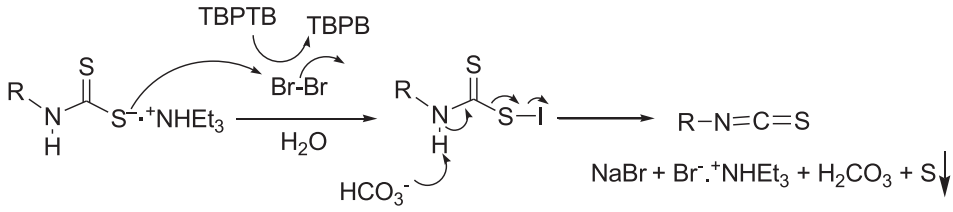
It is proposed herein that since the reaction is carried out in water, the resultant salt ($Br^{-}.^{+}NHEt_3$) and acid (NaBr) remains dissolved in water and therefore the bromide ion is repeatedly made available for pushing more reactants forward to form the product. Bases play inevitable roles of initiating the intermediate forward to formation of the products whereas the use of environmentally unacceptable bases has been another area of concern in the preparation of isothiocyanates. This concern has been solved by the use of

Table 2. Synthesis of isothiocyanate using TBPTB[a].

Substrate	Product[b]	Yield[c] %
 1'	 1b	93
 2'	 2b	90
 3'	 3b	82
 4'	 4b	80
 5'	 5b	82
 6'	 6b	78
 7'	 7b	80
 8'	 8b	91
 9'	 9b	90
 10'	 10b	92
 11'	 11b	90
 12'	 12b	87
 13'	 13b	84
 14'	 14b	80
 15'	 15b	92
 16'	 16b	90
 17'	 17b	85

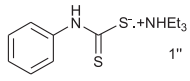
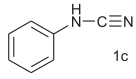
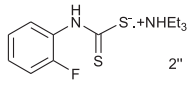
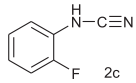
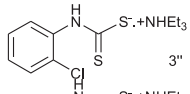
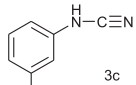
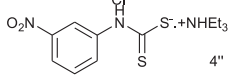
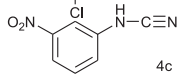
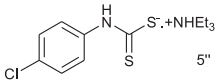
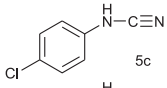
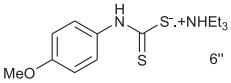
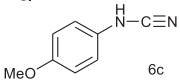
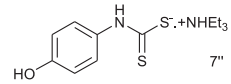
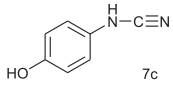
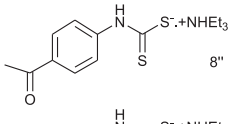
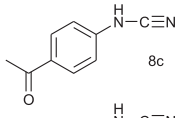
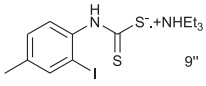
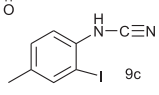
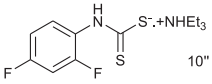
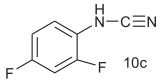
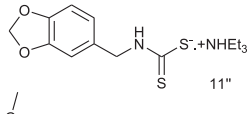
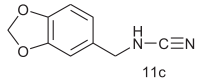
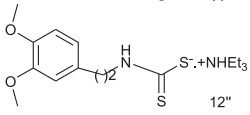
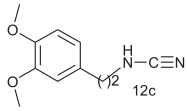
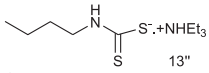
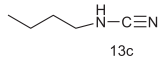
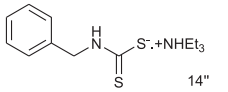
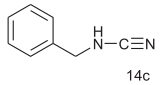
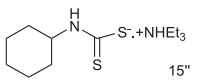
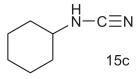
[a] Reactions were monitored by TLC; [b] Confirmed by IR, ^{1}H NMR and ^{13}C NMR; [c]Isolated yield.

innocuous $NaHCO_3$ (*49*) but need for further improvisation has been realized specially in the context of utilization of organic solvent. This concern is taken care of by the phase transfer properties of TBPTB which assists in proper availability of the reactants to each other in water, which in turn fulfills the avoidance of organic

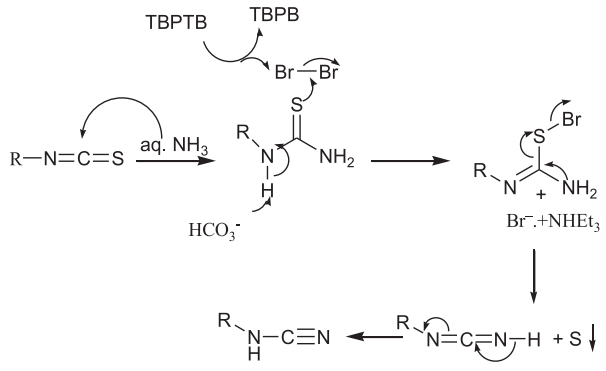


Scheme 2. Mechanism of formation of isothiocyanate from dithiocarbamate salt.

Table 3. Preparation of cyanamides using TBPTB[a].

Substrate	Product[b]	Yield[c]%
 1''	 1c	72
 2''	 2c	70
 3''	 3c	70
 4''	 4c	71
 5''	 5c	77
 6''	 6c	70
 7''	 7c	68
 8''	 8c	65
 9''	 9c	78
 10''	 10c	78
 11''	 11c	67
 12''	 12c	66
 13''	 13c	60
 14''	 14c	64
 15''	 15c	62

[a]Reactions were monitored by TLC; [b]Confirmed by IR,[1] HNMR and [13]CNMR; isolated yield[c]



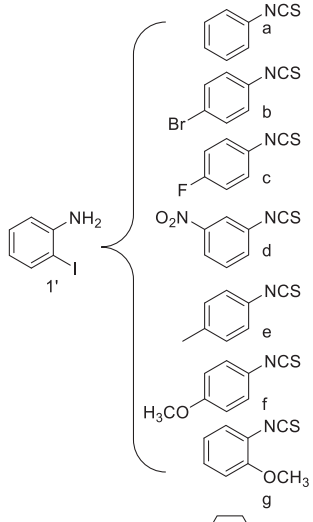
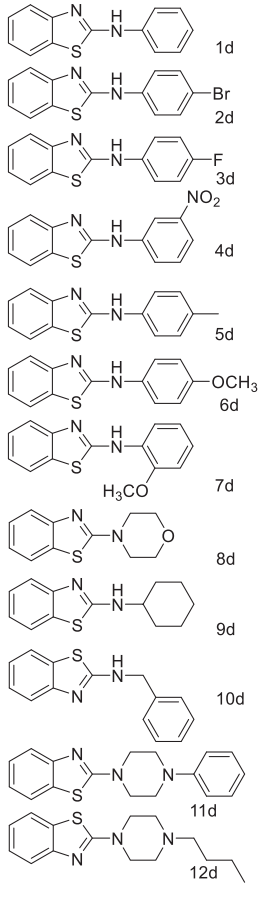
Scheme 3. Mechanism of formation of cyanamide from dithiocarbamate salt.

solvents. The versatility of the present methodology is recognized in the range of organic substrates that has undergone the reaction efficiently to form the corresponding isothiocyanates in excellent yields (Table 2).

Synthesis of cyanamides

Development of newer methodologies for cyanamide synthesis has been a common quest of ours in the recent past and after having successfully synthesized isothiocyanates using TBPTB under MW in water, we were interested in testing the same protocol for the preparation of cyanamides from dithiocarbamate salts. Therefore, in line with our earlier report (*50*, *51*), we have attempted a one pot strategy for cyanamide synthesis starting from dithiocarbamate salt in water, with catalytic amount of TBPTB under MW irradiation. In this modified procedure, in-situ generated Phenyl isothiocyanate (.270 mg/ 2 mmol) from the above reaction was treated to 25% aqueous NH_3 (2.5 mL) to obtain the phenyl thiourea. The in-situ generated phenyl thiourea was further treated to $NaHCO_3$ (0.336 g, 4 mmol) and a catalytic amount of TBPTB (.02 mg/.05 mmol) in water (× ml) and irradiated with

Table 4. Preparation of benzothiazoles using TBPTB[a].

Substate	Product[b]	Yield[c]
		87 84 78 73 88 80 77 74 80 83 69 70

[a] Reactions were monitored by TLC; [b] Confirmed by IR, ^{1}H NMR and ^{13}C NMR; [c]Isolated yield.

MW at p7 to obtain phenylcyanamide (Table 3, Entries **1c**). Tribromides are carriers of a molecule of bromine which is made available in the medium to carry the reaction forward via the mechanism as shown below (Scheme 3).

In this case as well, the smooth utilization of water as the solvent for a reaction involving organic substrates has been made possible due to the phase transfer property of the reagent. On the other hand, the utilization of water as the solvent enabled the employment of $NaHCO_3$ for the transformation thus making the present protocol highly environmentally acceptable.

It might be interesting to note that, when the reaction was carried out with base only, in the absence of TBPTB, at least 20% conversion to the product was observed in 3 mins of irradiation which remained unchanged even on irradiation for another 10 mins. Conversely, utilization of a catalytic amount of the TBPTB reagent enhances the reaction to completion within a minute.

The present methodology has been tested and found efficient for the preparation of a wide range of cyanamide possessing various substitutions and functionalities. (Table 3)

Synthesis of 2-aminobenzothiazoles

Keeping with the important applications of benzothiazoles in the fields of bioorganic and medicinal chemistry, tremendous effort has been put into the development of green methods for its synthesis (*44*). In line with this, we have studied the efficacy of the newly synthesized reagent TBPTB in the oxidative conversion of in-situ generated thioamide to 2-amino benzothiazoles. The present methodology starts with the reaction of aryl/alkyl isothiocyanate and aryl/alkyl amine to afford the corresponding thiourea which on treatment with innocuous base, $NaHCO_3$ and initiated by TBPTB, performed on-water, under MW irradiation, affords the corresponding N-arylated benzothiazole in high yields within seconds. The present methodology has been found to be efficient for the preparation of various substituted N- arylated and aliphatic 2-amino benzothiazoles as noted in Table 4.

Conclusion

Environmentally acceptable first synthesis of TBPTB reagent and study of its reactivity is reported. The new reagent has been found to be an efficient brominating agent its inherent phase transfer properties has been instrumental in the transformation of dithiocarbamate salts to corresponding isothiocyanates and in the conversion of thiourea to cyanamides and 2-amino benzothiazoles on water. Its easy method of preparation, mildness and efficacy in organic reactions shows that the reagent could be a practical alternative to other existing toxic reagents for the mentioned conversions.

Experimental

Procedure for preparation of TBPTB

Measured amount of $NaHCO_3$ (0.1 g, 0.2 mmol) was added to 50% H_2O_2 (9 ml, 79.74 mmol) in a beaker and mixed gently till the mixture was completely dissolved and the solution attained clarity. Then, TBPB (5.089 g, 15 mmol) and KBr (4.165 g, 35 mmol) were dissolved in 100 ml of H_2O and added in small portions to the above mixture. This was followed by portion-wise addition of 1M H_2SO_4 (40 ml). Fine yellow microcrystals of TBPTB could be observed within 1–2 min of complete addition of the acid. Complete precipitation of the reagent was obtained within 2.5 h which were filtered under suction using filter paper and dried in a vacuum desiccator using calcium chloride. Thereafter, recrystallization of the product was performed in Ethyl acetate/Hexane (99:1%). The yield was found to be 94%.

Procedure for bromination of organic substrates using TBPTB

In a typical reaction, the phenol (Table 1, Entry **1**) (282 mg, 3 mmol) was taken in water / ethyl acetate (5:10 mL) biphasic solvent medium. To this, crushed and powdered TBPTB (1.47 g, 3 mmol), was added portion-wise with constant stirring at room temperature. The progress of the reaction was monitored by TLC. After completion of the reaction as adjudged by TLC, the aqueous layer having the spent reagent was separated and kept aside for further regeneration of the reagent. The organic layer was washed with dil.$NaHCO_3$ solution (5 ml × 2 times) to remove the *in-situ* generated HBr. The crude product thus obtained was concentrated and then subjected to column chromatography over a pad of silica gel to get 92% of the product.

Procedure for regeneration of the spent reagent

The aqueous layer from the above reaction contains roughly 3 mmoles of the spent reagent TBPB. Therefore, in a separate beaker, an amount of $NaHCO_3$ (0.02 g, 0.04 mmol) was dissolved in 50% H_2O_2 (1.8 ml, 16 mmol) till the solution attained clarity. To this, the aqueous layer was added followed by an aqueous solution of KBr (0.83 g, 7 mmol). Further, 1M H_2SO_4 (8 ml) was added slowly to which fine yellow microcrystals of TBPTB precipitated out. The collection and recrystallization of the

product was carried out as mentioned above in section 4.1. The yield was found to be 84%.

Procedure for preparation of isothiocyanates

Phenyl dithiocarbamate salt (Table 2, Entry **1'**) (540 mg, 2 mmol) was taken in water (10 ml) to which sodium bicarbonate (0.336 g, 4 mmol) and a catalytic amount of TBPTB (.02 mg/.05 mmol) were added. The mixture was irradiated under microwave at p7 and the reaction was monitored by TLC. Total conversion to the corresponding isothiocyanate (Table 2, Entry **1b**) was observed within 47 s with precipitation of elemental sulfur. Thereafter, ethyl acetate (5 ml × 3times) was added to the reaction mixture to extract the product. The organic layer was dried over anh. Na_2SO_4 and 5 mL of ethanol was added to completely precipitate the elemental sulfur. The precipitated sulfur was filtered off, organic portion concentrated under reduced pressure and purified over a short column of silica gel (100% pentane) to give the corresponding product (Table 2, Entry **1c)** (93%).

Procedure for preparation of cyanamides from isothiocyanates

Phenyl dithiocarbamate salt (Table 3, Entry **1"**) (540 mg, 2 mmol) was taken in water (10 ml) to which sodium bicarbonate (0.336 g, 4 mmol) and a catalytic amount of TBPTB (.02 mg/.05 mmol) were added. The mixture was irradiated under microwave at p7 and the reaction was monitored by TLC. Total conversion to the corresponding isothiocyanate was observed within 47 s with precipitation of elemental sulfur. The crude reaction mixture containing in-situ enerated phenyl isothiocyanate (.270 mg/ 2 mmol) was stirred with 25% aqueous NH_3 (2.5 mL) to afford 1-phenylthiourea. The excess of NH_3 was removed in a rotary evaporator, after stirring the reaction for 10 min at room temperature, as the presence of NH_3 hampers the formation of cyanamide. To the crude reaction mixture, $NaHCO_3$ (0.336 g, 4 mmol) and a catalytic amount of TBPTB (.02 mg/.05 mmol) were added and the combination was irradiated with MW at p7. After irradiation for 50 secs, complete formation of phenylcyanamide (Table 3, Entry **1c**) could be observed with precipitation of elemental sulfur. Solvent extraction and product purification were carried out as given in section 4.4.

Procedure for preparation of 2-aminobenzothiazoles

A mixture of 2-iodoaniline (Table 4, Entry **1"'**) (1 mmole, 219 mg) and phenyl isothiocyanate (Table 4, entry **a**) (1 mmol, 135 mg) was stirred in water (6 mL). Within 20 min, the reactants completely converted to thiourea as judged from TLC. To this, sodium bicarbonate (0.336 g, 4 mmol) and TBPTB (0.49 mg / 1 mmol) were added and the reaction was irradiated by MW at P7. Complete formation of the product (Table 4, Entry **1d**) was observed within mins after which the reaction mixture was cooled to room temperature and extracted with ethyl acetate (2 × 10 mL). The combined organic layer was then dried over anhydrous Na_2SO_4 and the solvent was removed under reduced pressure. The crude product was purified over a column of silica gel eluting with EtOAc–petroleum ether (2: 8) to give the pure product (Table 4, Entry **1d**) in 87% yield.

Disclosure statement

No potential conflict of interest was reported by the author(s).

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