Aqueous Et₄NBrO₃/KBr as a versatile and environmentally benign source of bromine for the selective trans-bromination of alkenes

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An aqueous solution of tetraethyl ammonium bromate and potassium bromide is found to be an environmentally benign source of bromine at ambient temperature. This reagent is used for selective trans-dibromination of several substituted alkenes. The reaction conditions are mild and the yield of the products are high and other possible by-products such as bromohydrin formation and aromatic substitution have not been observed.

Keywords: trans-dibromination, aqueous medium, tetraethylammonium bromate, substituted alkenes

Dibromination is a key step in a variety of organic transformations. The usual product, namely the trans 1,2-dibromo compounds are precursors for several compounds of pharmaceutical and biological importance. The dibromination reaction also finds wide application in analytical chemistry. Electrophilic addition of molecular bromine to unsaturated C-C double bonds is the classical dibromination reaction. Due to adverse environmental consequences of the use of molecular bromine, there has been a continuous search for benign and cheap alternative source of bromine. Several methods have been reported for the oxidative dibromination of alkenes highlighting green approaches. Some alternative procedures that have been developed include the use of amidines for the transfer of electrophilic bromine, Mn mediated dibromination using LiBr and NBS, pyrrolidine promoted dibromination with NBS, hydrohalic acid/H₂O₂ or TBHP, a two phase procedure using NH₂VO₃ and Na₂MoO₄ in the presence of H₂O₂, HX and Cu(II) complex halides, HBr/NaNO₂ (Ref 10) and the use of pentaerythritol triol and diakyl ketones were efficiently brominated in the α-position by aqueous HBr/H₂O₂ at room temperature by the generation of bromine free radicals.

Dihalogenation has also been carried out using ionic liquids, notably the oxidative bromination of alkenes with NaBr/H₂O₂ in [bmim]trichloroacetate. The reaction was initiated and controlled by the slow addition of H₂SO₄. Finally, an efficient method of dibromination using KBr and CAN has been reported. To the best of the knowledge there has been so far no attempts at oxidative dibromination of alkenes using tetraethylammonium bromate as an oxidant in combination with KBr.

Results and Discussion

In continuation of the investigations with tetraalkylammonium bromates as oxidizing agents, it is envisioned that an aqueous solution of tetraethyl ammonium bromate and KBr could be conveniently used for the in situ generation of bromine for effecting trans-dibromination of alkenes at ambient temperature in aqueous solution. In an initial experiment, it was found that overnight stirring of a suspension of styrene in an aqueous solution of tetraethylammonium bromate and KBr gave quantitative yield of the trans-dibromo product. In order to access the generality of the reaction, the reaction was examined with a variety of alkenes, unsaturated ketones and esters. In all cases the trans-dibromo compounds were obtained in high yield (Scheme I). The results are presented in Table I. The reaction afforded exclusively the trans 1,2-dibromo compounds. Other possible side products, namely the bromohydrin and bromobenzenes arising out of electrophilic substitution of benzene ring, in phenyl substituted alkenes, were not observed. The results also indicate that in case of styrenes, electron withdrawing groups on the phenyl ring gave better yields than those with electron releasing group. Further, good yields were obtained with both the αβ-unsaturated carbonyl compounds and open chain alkenes.

A similar procedure of bromination of alkenes using a mixture of KBrO₃-KBr was reported wherein dilute mineral acid was used for the generation of the bromine electrophile. In the present study, it was observed that when tetraethylammonium bromate is used as the oxidizing agent, the use of mineral acid was not necessary for the generation of the bromine electrophile since the pH of the reaction...
medium was observed to be 3.6 in 0.05 molar aqueous solution of tetraethylammonium bromate. The conditions of the reaction have been found to be specific for dibromination and competing reactions leading to bromohydrin formation and aromatic substitution were not observed. The tetraethyl ammonium bromate could be prepared by the dropwise addition of bromic acid to a saturated aqueous solution of commercially available tetraethylammonium bromide.

**Experimental Section**

All chemicals were bought from Aldrich (India) and used as received. HBrO₃ was prepared by the action of H₂SO₄ on Ba(BrO₃)₂ and the resultant bromic acid was concentrated by reduced pressure distillation. Ethylcinnamate, methylcinnamate and chalcone were prepared by established procedures⁴. Column chromatography was carried out using silica gel (60-120 mesh) and TLC was performed on prepared silica gel plates using appropriate solvent system. ¹H and ¹³C NMR spectra were recorded in 300 MHz Bruker instrument. Chemical shifts (δ) are reported in ppm relative to TMS as the internal standard in CDC₃. Melting points were determined in a VMP-D model melting point apparatus and are uncorrected. Mass spectra were recorded in GC-MS spectrometer and IR spectra were recorded in a Shimadzu FTIR spectrometer.

**Preparation of Ba(BrO₃)₂.H₂O:** A solution of 33.4 g KBrO₃ in 100 mL water was prepared; a hot solution of 24.4 g BaCl₂.2H₂O in 50 mL of water was added. The mixture was cooled and the supernatant liquid was decanted. The residue was washed several times with 50 mL portion of cold water and then suction filtered to recover the solid product. The yield was found to be almost quantitative. The product was purified by recrystallization from boiling water. The white crystal of Ba(BrO₃)₂.H₂O obtained had melting point 260°C (dec).

**Preparation of HBrO₃:** Finely powdered Ba(BrO₃)₂ (10 g) was added to a cold solution of 5 mL of concentrated H₂SO₄ in 50 mL of water. The reaction flask was placed in an ice salt bath during addition. After addition, the flask was left for several hours in the bath with frequent shaking. The flask contents were then diluted by addition of 60 mL of water. 10% Ba(OH)₂ solution was added dropwise to remove the excess H₂SO₄. Precipitation of BaSO₄ occurred. The mixture was then allowed to settle and the clear HBrO₃ solution was decanted. The BaSO₄ was filtered off and the filtrate combined with the decanted solution. The HBrO₃ was concentrated to 50% volume by vacuum evaporation at 50°C. Colorless solution of HBrO₃ was then obtained.

**Preparation of Et₄NBrO₃:** To a saturated solution of Et₄NBr in water, HBrO₃ was added drop-wise with constant stirring at RT till a yellow precipitate was obtained. The solid was filtered, dried and kept in a desiccator for subsequent use. The melting point of tetraethylammonium bromate was found to be 79°. 81°C and the structure confirmed by ¹H NMR and CHN analysis.
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*a* (i) KBr (2.2 mmol), alkene (1 mmol), Et₄NBrO₃ (1 mmol), water (5 mL). (ii) Isolated yield.

*b* Comparision with Lit. m.p. and ¹H coupling constants gave evidence of the E isomer.
General procedure for dibromination in aqueous medium

To a solution of KBr (2.2 mmol) in water (5 mL), the alkene (1 mmol) was added under constant stirring at RT followed by the addition of an aqueous solution of Et₄NBrO₃ (1 mmol). The suspension was stirred for 0.5 hr at RT. Completion of the reaction was indicated by discharge of orange color of the solution. In case of solid product, the solid mass separated out from the solution and could be recovered by simple filtration. For liquid products, the reaction mixture was extracted with DCM (3×10 mL). The combined organic layer was dried over anhydrous Na₂SO₄ and the solvent evaporated to get the liquid product which was almost pure. Further purification was carried out by column chromatography using a short column and petroleum ether (boiling range 40-60) as eluent. Complete conversion was observed.

**E-1,2-Dibromo-1-phenyl ethane (Product 1, Table I):** Colourless solid; m.p. 74-76°C; ¹H NMR (300 MHz, CDCl₃, Me₂Si): δ 4.007-4.127(m, 2H), 5.13-5.19(m, 1H), 7.386-7.418(m, 5H); ¹³C NMR (75 MHz, CDCl₃): δ 34.99, 50.82, 127.61, 128.82, 129.16, 138.55; GC-MS: m/z (%) 266(1.5), 264(2), 257(25), 255(25), 185(20), 183(22), 171(25), 163(15), 151(15), 137(13), 129(12), 111(9), 213(11), 195(11), 130(11), 123(11), 109(10). Complete conversion was observed.

**E-1,2-Dibromo-1-(4-chloro) phenyl ethane (Product 2, Table I):** m.p. 42-44°C; ¹H NMR (300 MHz, CDCl₃, Me₂Si): δ 7.331-7.465(m, 4H), 5.089-5.142(m, 1H), 3.941-4.1(m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 137.08, 134.90, 129.05, 128.99, 49.48, 34.63.

**E-1,2-Dibromocyclohexane (Product 4, Table I):** Viscous liquid; ¹H NMR (300 MHz, CDCl₃, Me₂Si): δ 4.45(s, 2H), 2.392-2.472(m, 2H), 1.719-1.897(m, 4H), 1.47-1.511(m, 2H); ¹³C NMR (75 MHz, CDCl₃): δ 55.05, 31.79, 22.23; GC-MS: m/z (%) 244(1), 243(1.5), 241(2.5), 239(1.5), 163(3), 162(60), 160(100), 81(70), 78(72).

**E-2,3-Dibromo-3-phenyl ethyl propanoate (Product 5, Table I):** m.p. 66-67°C; ¹H NMR (300 MHz, CDCl₃): δ 7.361-7.431(m, 5H), 5.351(d, J=11.7Hz, 1H), 4.837(d, J=12Hz, 1H), 4.33-4.406(q, 2H), 1.388(t, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 167.82, 137.6, 129.36, 128.88, 128.03, 62.65, 50.68, 47.00, 13.89; GC-MS: m/z (%) 338(0.5), 336(1), 334(0.5), 293(1), 291(2), 289(1), 281(2), 265(2), 263(2.5), 261(2), 257(25), 255(25), 185(20), 183(22), 131(80), 103(100), 91(22), 77(55).

**E-2,3-Dibromo-3-phenylmethylpropanoate (Product 6, Table I):** Colourless solid; m.p. 114-116°C; ¹H NMR (300 MHz, CDCl₃, Me₂Si): δ 7.379-7.42(m, 5H), 5.35(d, J=11.7Hz, 1H), 4.85(d, J=11.7Hz, 1H), 3.908(s, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 168.36, 137.47, 129.4, 128.9, 128.02, 53.47, 50.59, 46.63.

**E-1,2-Dibromo-1,3-diphenyl-1-oxo-propane (Product 8, Table I):** Colourless solid; m.p. 156-158°C; ¹H NMR(300 MHz, CDCl₃, Me₂Si): δ 3.84-4.211(m, 1H), 3.825(t, 1H), 3.628(t, 1H), 2.122-2.188(m, 1H), 1.766-2.108(m, 1H), 1.315-1.749(m, 4H), 0.931(t, 3H); ¹³C NMR (75 MHz, CDCl₃): δ 53.05, 36.31, 35.66, 28.82, 21.90, 13.86; GC-MS: m/z (%) 165(15), 163(15), 83(100).

**E-1,2-Dibromohexane (Product 9, Table I):** Liquid; ¹H NMR (300 MHz, CDCl₃, Me₂Si): δ 4.13-4.218(m, 1H), 3.829-3.878(q, 1H), 3.633(t, 1H), 2.083-2.182(m, 1H), 1.719-1.964(m, 1H), 1.308-1.621(m, 8H), 0.896(t, 3H); ¹³C NMR (300 MHz, CDCl₃): δ 53.15, 36.35, 35.99, 31.56, 28.46, 26.69, 22.53, 14.04; GC-MS: m/z (%) 193(10), 191(11%), 111(90), 57(100).

**Conclusion**

In conclusion, an aqueous mixture of Et₄NBrO₃ and KBr has been successfully used as an excellent substitute for molecular bromine which can be used conveniently for the trans-dibromination of C-C double bonds of alkene with diverse substituents to give selectively the 1,2-dibromo products. The reaction was found to be complete in a short time and the yield of the trans-bromo product is high. In the absence of possible by products the reaction is considered clean and work up simple.

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**References**