Chapter 3 *Preparation of Non-hazardous Brominating Reagents for Substitution and Addition Reactions of various Organic Substrates*

3.1. Introduction

Halogenated aromatic compounds have been used over a century as important chemicals, intermediates in many applications and widely in synthetic organic chemistry.[1,2] Bromine is being used as a conventional brominating agent in all aromatic substitution and olefinic addition reactions.[3,4] Liquid bromine is highly corrosive and volatile liquid making it more hazardous substance by nature and thus it requires extreme care in its production, transportation, and utilization. Besides this, special equipments are required to handle liquid bromine. Besides, the maximum atom efficiency of bromine in all aromatic substitution reactions (Eq 3.1) is only 50% as the rest is transformed into much more corrosive hydrobromic acid which is essential to be reprocessed or neutralized before being discharged as a waste.

$$\mathrm{Ar{-}H} \quad + \quad \mathrm{Br_2} \longrightarrow \mathrm{ArBr} \quad + \quad \mathrm{HBr} \qquad (3.1)$$

Although, the atom efficiency of liquid bromine can reach upto near 100% in all addition reactions across −C=C− double bonds in olefins (Eq 3.2) but the need to handle the hazardous liquid bromine remains same.

$$\mathrm{R{-}CH{=}CH_2} \; + \; \mathrm{Br_2} \longrightarrow \mathrm{RCHBrCH_2Br} \qquad (3.2)$$

Several brominating reagents have been reported recently as alternative to the use of liquid bromine. Some of the worth mentioning reagents are N-bromosuccinimide[5]

(NBS)– for allylic brominations in presence of lithium acetate, tetrabutyl ammonium trifluoro acetate or triethylamine as catalyst and pyridiniumbromide perbromide[6] for the bromination of 2-naphthols, phenols, amines and styrene in acetic acid medium. However, the difficulty with these reagents are that NBS however useful for carrying out some specific bromination reactions, is a costly, its use cannot be justified in those bromination reactions where liquid bromine would suffice and its preparation[7a] even involves the use of liquid bromine. The N-bromosuccinimide is reported to be prepared by reacting succinimide with liquid bromine below 0 °C in potassium hydroxide solution. On the other hand, the brominating agent, pyridiniumbromide perbromide too requires liquid bromine and hydrobromic acid in its preparation,[7b] making it more costlier than liquid bromine.

Other brominating agents that are easy to handle, are also known but are used mainly for more selective transformations. $NaBrO_3$-H_2SO_4[8-11] is used for bromination of aromatic compounds that contain deactivating substituents such as nitrobenzene, benzoic acid, benzaldehyde, 4-nitrofluorobenzene and 4-fluorobenzoic acid etc. Oxybrominations using NaBr/KBr/HBr-H_2O_2 systems[12-22] have been believed to be a possible alternative to elemental bromine, but many attempts have been made with partial success. The hydrobromic acid is not too kind to the environment. The reported methods of direct oxybromination of aromatic systems with bromide salts involve the use of expensive transition metal based catalysts, which are costly and cumbersome to prepare. Smith *et al.*[23] used Br_2-NaY zeolite for the selective bromination of toluene at *para*– position. This method again involves the liquid bromine and costly zeolite catalyst to catalyze the reaction. Vega *et al.*[24] reported the *para*– selective bromination of toluene with Br_2-Na-Y zeolite in presence of propylene oxide as scavenger for hydrobromic acid produced as byproduct during the reaction. However, the achieved yield was 10% only. Most of the reactions have serious limitations like need of costly zeolite, some times moisture free-reaction conditions and some times the zeolites are not commercially viable for industrial applications.

Elnagar *et al.*[25] have described the bromination of some activated aromatic compounds using BrCl as brominating reagent at 0-100°C. The reagent BrCl was prepared by mixing equimolar amounts of bromine and chlorine to yield approximately 15% (w/v) in 3 M NaCl solution. However, the process of BrCl preparation still requires the corrosive liquid bromine along with another equally bad chlorine, which again relates to the conventional methods.

Zolotarsky *et al.*[26] have patented the preparation of brominating reagent by complexing bromate and bromide salt with sulfamic acid and sulfuric acid at pH less than 1. The brominating reagent was stable for 20 days.

Choudhuri *et al.*[27] have disclosed a quaternary ammonium tribromides as brominating reagent from quaternary ammonium bromides. Its preparation involves the oxidation of bromides using hydrogen peroxide in presence of molybdic acid monohydrate in acidic medium. However, the quaternary ammonium bromide yet requires elemental bromine for its preparation. Mortensen *et al.*[28] have reported the thermal benzylic bromination of a wide variety of benzylic compounds using gaseous bromine under nitrogen atmosphere at 110 °C.

In order to avoid the above difficulties facing in many of the organobromine compounds preparations, we have undertaken the present work to prepare a new and eco-friendly method for the preparation of brominating reagents by utilizing cheaply available raw material and very simple procedures. The objectives of the present study are (i) to prepare brominating reagents BR(S) and BR(A) in desired liquid or solid form that are easy to handle, stable on storage and can replace the corrosive liquid bromine in the substitution (Eq 3.1) and for addition (Eq 3.2) reactions, ii) to use the combination of bromide and bromate in a desired (2:1 or 5:1) composition as safe and eco-friendly brominating agents, iii) to utilize the readily available industrial alkaline bromine mixtures in the preparation of BR(S) and BR(A), iv) to utilize hypochlorite and chlorine as strong oxidizing agents to alter the bromide-bromate composition in industrial alkaline bromine mixture to the desired extent in the preparation of BR(S), v) to affect the bromide-bromate composition in industrial alkaline bromine mixture to the desired extent in the preparation of BR(A) or BR (S) by alkali bromide or alkali bromates addition, respectively, vi) to improve the bromine atom efficiency nearly to 100% and minimize the generation of byproduct HBr in Eq 3.1 and vii) to make the discharges safe to the environment.

3.2. Bromine recovery process and generation of alkaline bromine intermediates

Bromine is recovered world wide mainly by two popular methods called i) *Steaming out process* and ii) *Absorption or Cold process*. In the second method, bromine is liberated from its source seawater or bittern by controlled addition of chlorine at pH between 3 and 4. The bromine thus, liberated is blown out from water at room temperature by a stream of air and crude bromine is allowed to absorb in chemical absorbents such as CaO, NaOH, Na_2CO_3, etc under supersaturated conditions to a solution called alkaline bromine. Liquid bromine is again generated in purest form by reacting the alkaline bromine mixture with a mineral acid followed by distillation and cooling. The intermediate, **alkaline bromine** mixture basically contains salts of corresponding bromide and bromate approximately in the ratio 5:1 based on the bromine disproportionation (Eq 3.3) in highly basic medium.[R] On acidification of this intermediate mixture, the bromide and bromate salts react in 5:1 stochiometry and liberate bromine again as shown in Eq. 3.4.

$$3\,Br_2 + 6\,NaOH \longrightarrow 5\,NaBr + NaBrO_3 + 3\,H_2O \qquad (3.3)$$

$$5\,NaBr + NaBrO_3 + 6\,H^+ \longrightarrow 3\,Br_2 + 3\,H_2O + 6\,Na^+ \qquad (3.4)$$

The chemical composition of bromide and bromate ions in Eq 3.3 may be adjusted to the desired extent if necessary by either adding suitable oxidizing agents or bromide and/or bromate salts externally for its specific purposes/uses.

3.3. Experimental Section

3.3.1. Materials and methods. Analytical grade NaBr, $NaBrO_3$, NaOH, NaOCl (SD′s chemicals, India) and H_2SO_4 (Ranbaxy Fine Chemicals, India) were purchased, and used in these investigations. A solution of 50% (v/v) H_2SO_4 was used to adjust its composition to 4% in all experimental solutions. Alkaline bromine mixtures–lime from M/s Saurashtra Chemicals Limited, Porbander and -soda ash from M/s Agrocel Industries Limited, Dhordo, Greater Rann of Kutch, Bhuj, both situated in Gujarat, India were collected. The alkaline bromine in sodium hydroxide having 29.3% (w/v) bromine had

37.2 °Be, and pH 8.73 while that in lime having 28.1% (w/v) bromine had 37.2 °Be and pH 10.25. One ml of each of these equilibrated solutions were diluted to 100 ml and used as stock in the estimation of Br^- and BrO_3^- contents.

3.3.2. Equipment. Absorption spectra were recorded on Shimadzu UV-160 spectrophotometer with a built-in thermo stated (± 0.1 °C) cell compartment coupled to a temperature controlling unit. An Adair Dutt digital *p*H meter sensitive to 0.01 *p*H was used to measure *p*H of all experimental solutions.

3.3.3. Samples preparation. To 1-4 ml of alkaline bromine stock in 25 ml standard flask, 2 ml of 50% H_2SO_4 was added and made upto the mark under cooling and allowed 10-15 min for equilibration. 1 g of NaBr in the case of BrO_3^- estimation was also added to it. The absorbance at 390 nm was measured and calculated the concentrations of bromide and bromate ions in the respective alkaline bromine mixtures using Eq 2.22 (Chapter 2)

The brominating reagent (solid and solution) was characterized by determining its bromate and bromide contents. 1 g of solid or 1 ml of liquid brominating reagent was dissolved/diluted with water to a volume of 100 ml and used as stock in the estimation of bromate and bromide. To estimate bromide, 1-4 ml of the stock was taken in a 25 ml volumetric flask and 2 ml of 9 M sulfuric acid was added and the solution was diluted up to the mark. For bromate estimation, 0.1-0.4 ml of the stock was likewise taken in a 25 ml volumetric flask and into it was added a large excess (1 g) of sodium bromide and 2 ml of 9 M sulfuric acid and the volume made up to the 25 ml mark. The liberated bromine as a result of the reaction between bromide and bromate in presence of acid was estimated spectrophotometrically[29] by measuring the absorbance at 390 nm and using the appropriate molar extinction coefficient (ε, 167 M^{-1} cm^{-1} in absence and 522 M^{-1} cm^{-1} in the presence of excess of bromide) values. The homogeneity of solid brominating reagent was confirmed by estimating bromate and bromide composition in 1 g samples drawn from different parts of the sample.

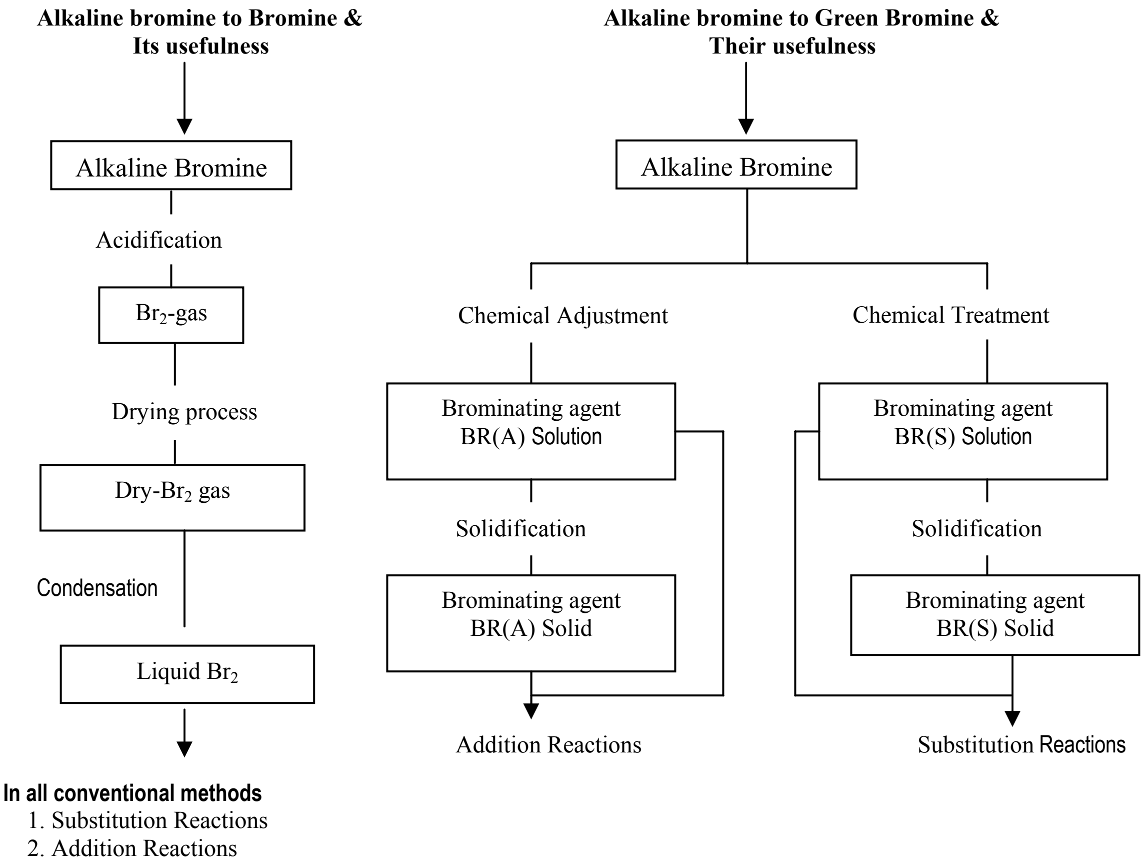
3.3.4. Spectrophotometric measurements. Absorption spectra of the equilibrated samples under investigation were recorded between 200-600 nm in a 10 mm quartz cuvette at 25

°C. Double distilled water was used in all the cases as the reference unless otherwise mentioned.

3.4. Results and discussion

The methods of preparation of bromine by conventional route and brominating reagents BR(S) and BR(A) obtained by the present routes utilizing alkaline bromine and their uses are compared in the following **Scheme 3.1.**

Scheme 1. Preparation of Bromine & Brominating Agents from Alkaline bromine and their Utilities



3.4.1. Preparation of brominating reagent BR(A). When 10 ml of the original alkaline (soda ash)-bromine mixture containing approximately 29.3% w/v bromide was evaporated on a hot water bath and dried gave 4.726 g of solid. The residue was dissolved in 100 ml deionised water and estimated the bromide and bromate composition by spectrophotometric method. The bromide to bromate ratio was found to be 4.3:1.

With solid sodium bromide. Trial 1. A 30 ml of the above original alkaline bromine mixture containing 4.3:1 bromide to bromate ratio was taken in a 100 ml round bottom flask, to it 1.286 g of sodium bromide solution (dissolved in 5 ml water) was added and stirred for 10 min on magnetic stirrer. The resultant solution was evaporated on a hot water bath and dried under vacuum at 70°C for three hours to give 15.476 g BR(A). The bromide to bromate ratio was found to be 5.4:1 by spectrophotometric method.

Trial 2. One liter of alkaline bromine mixture containing 4.3:1 bromide to bromate ratio was taken in a 5.0-liter reaction flask, to it 52.14 g of sodium bromide solution (dissolved in 250 ml water) was added and stirred for 10 min with overhead stirrer. The resultant solution was evaporated on hot water bath and dried under vacuum at 70°C for three hours to obtain 525 g and the bromide to bromate ratio was found to be 5.2: 1 by spectrophotometric estimations.

Trial 3. To the 30.0 liters of alkaline bromine mixture containing 4.3:1 bromide to bromate ratio was taken in 250 liters in an opened reaction vessel and 1.286 kg of sodium bromide in 5 liters water was added, stirred for 15-20 min for homogeneity. The solution was evaporated to dryness by passing steam under stirring over a period of four hours. The solid was taken out and air dried over night at 70°C to give 15 kg of desired product BR(A) containing 54.85% (w/w) bromine as available for addition reactions.

3.4.2. Preparation of brominating reagent BR(S). With solid sodium bromate. To 23.6 ml of alkaline bromine mixture containing 4.3:1 bromide to bromate ratio was taken in a 100 ml round bottom flask, 3.04 g of sodium bromate dissolved in 15 ml of water was added and the mixture was stirred for 10 min. The resultant solution was evaporated on a hot water bath and dried at 70 °C for three hours to give 14.12 g of BR(S). The bromide to bromate ratio was determined to be 2.05:1 by spectrophotometry.

With sodium hypochlorite solution. To 12.0 ml of alkaline bromine mixture containing 4.78:1 bromide to bromate ratio was taken in a 100 ml round bottom flask, 23.0 ml of sodium hypochlorite (4% w/v) was added and stirred for 10 min. The resulting mixture was allowed 30 min for the conversion of desired quantity of bromide to bromate to give the desired brominating reagent BR(S) in solution form. The bromide to bromate ratio was estimated to be 2.0:1 by spectrophotometry.

With chlorine gas. Trial 1. To alkaline bromine mixture (1.0 liter) having bromide to bromate ratio 4.3:1 was taken in three necked round bottom flask, 2.0 liters of deionized water having 13.05 moles (522 g) of NaOH was mixed at 25 °C under stirring. Chlorine gas was then purged through this mixture at a rate of 300 ml per minute while maintaining the temperature at 25 °C and the purging was continued till the brown color vapors were formed. The purging of chlorine gas was stopped and the reaction mixture was transferred to another vessel where it was diluted with 4.0 liters of alkaline bromine mixture and 0.5 liter of deionized water keeping the entire mass under stirring and continued for another 10 minutes. The solid brominating reagent so formed having bromide to bromate ratio 2:1, was separated by evaporation. The solid (3.33 kg) was air dried at 70 °C. The active bromine content in the isolated solid was found to be 45.3%.

Trial 2. To 3.0 liter of alkaline bromine mixture having bromide to bromate ratio 4.3:1 taken in a three necked 10 liters round bottom flask, 26.10 moles (1.044 kg) of NaOH in 3.5 liters of deionized water was added under stirring at 27-30 °C. Chlorine gas was purged through this reaction mixture at a rate of 300 cc per minute while maintaining the temperature at 27-30 °C. The purging of chlorine gas was stopped when brown color vapors were started producing in the flask. The reaction mixture was taken out from the reactor and diluted with 7.0 liters of alkaline bromine mixture and 0.5 liter of deionized water to give the desired brominating reagent BR(S). The solid brominating reagent so formed having bromide to bromate ratio 2:1 was solidified by steam evaporation and air dried at 70^0C to give 6.70 kg of BR(S). The active bromine content in it was found to be 50.3%.

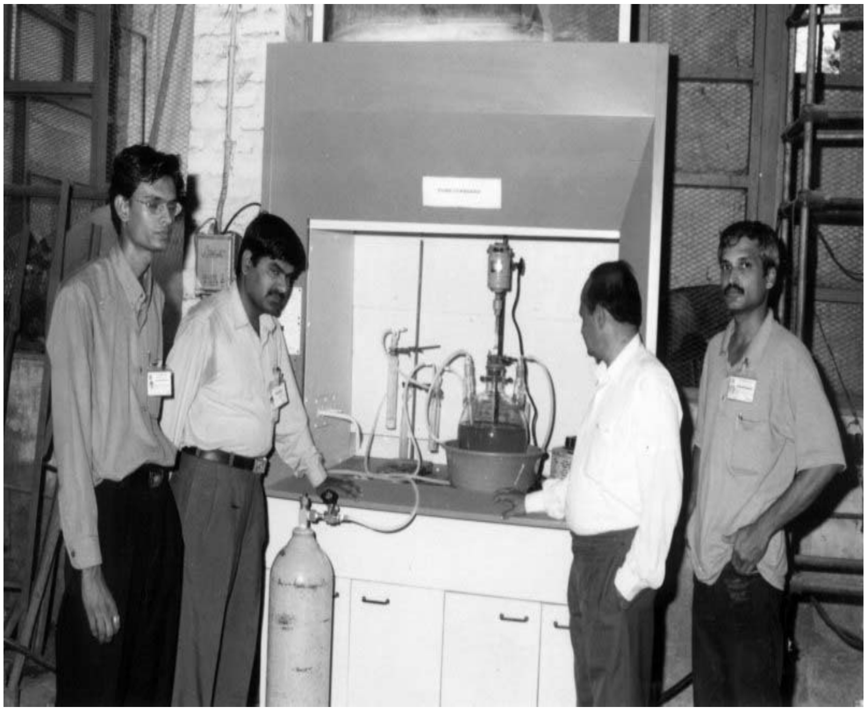
Trial 3. To 20.0 liters of alkaline bromine mixture having bromide to bromate ratio 4.3:1 was taken in a 50 liter glass reactor, 52.2 mole (2.088 kg) of NaOH in 7 liters of deionized water was added at 27-30 °C temperature under stirring. This reaction mixture was purged with chlorine gas at a rate of 600 cc per minute while maintaining the temperature between 27 and 30 °C The purging of chlorine gas was stopped when brown color vapors of bromine were started forming in the flask to obtain the desired BR(S).

Optionally the reaction mixture was steam evaporated in an SS container to give solid BR(S) which was air dried at 70 °C over night to yield 13.3 kg. The analysis data showed that it contained bromide and bromate in 2.1:1 ratio while the available bromine for all substitution reactions was 40.05% (w/w).

3.5. Some important unit operations involved in the preparation of BR(S).

Some of the unit operations during the preparation of BR(S) and BR(A) are shown below.

3.5.1. Chlorination step



3.5.2. Steam evaporation step

3.5.3. Solid brominating reagent BR(S) ready for air drying

3.6. References

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