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Note

N-octylquinolinium tribromide: A task specific quinoline based ionic liquid as a new brominating agent

M P Kaushik* & Vivek Polshettiwar

Process Technology Development Division, Defence R & D Establishment, Jhansi Road, Gwalior 474 002 (MP), India

E-mail: mpkaushik@rediffmail.com

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The *N*-octylquinolinium tribromide has been synthesized and explored as a new efficient brominating agent. It has high active bromine content per molecule and shows a remarkable reactivity towards various substrates. No organic solvent has been used during any stage of the reaction. The *N*-octylquinolinium tribromide is stable for months and acts as a safe source of bromine for complete bromination of phenols, aromatic amines, alkenes and alkynes.

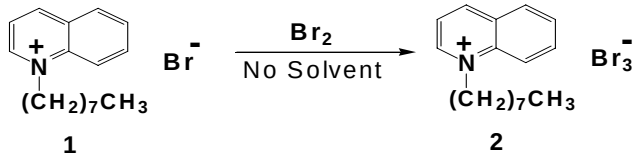
Keywords: Ionic liquid, *N*-octylquinolinium tribromide, bromination, phenols, aromatic amines, alkenes and alkynes.

IPC Code: Int. Cl.[8] C07D

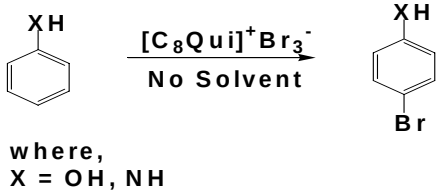
Bromination of organic compounds has received significant interest in recent years[1,2] owing to increasing commercial importance of bromoorganics in the synthesis of large number of natural products as well as in the manufacture of pharmaceuticals, intermediates for agrochemicals and other specialty chemicals. It is worthy to note that protection and deprotection of double bonds via brominatio *N*-debromination strategy is finding increasing applications in organic synthesis[3]. Various methods are known in the literature for bromination of organic to compounds[4–10]. Prominent among them are the use of elemental bromine[11,12] under harsh reaction conditions and *N*-bromosuccinimide (NBS)[13] or the combination of aqueous TBHP or hydrogen peroxide with a hydrohalic acid[14]. To achieve higher efficiency and selectivity, the conventional reagent bromine has been employed with a variety of new techniques; however, handling of bromine is cumbersome due to its hazardous nature. Although the latter method is considered the most effective from the environmental point of view, as the by-product is water, it often requires an excess of hydohalic acid along with the use of chlorinated solvents, essentially to achieve the complete solubilization of the substrates. In this respect it has already been demonstrated that the use of ionic liquids[15,16] may be advantageous for the bromination of organic compounds, as the use of the ionic liquids avoid the formation of solvent containing by-products. Recently, room temperature ionic liquids have received increased attention as novel and promising solvents in synthetic organic chemistry essentially because their chemical and physical properties can be adjusted by proper selection of cation/anion. In the last few years, ionic liquid research had provided another approach for achieving task-specific ionic liquids in which the functional group is covalently tethered to cation or anion of the ionic liquid, especially to the N atom of the quinoline ring. It is expected that this ionic liquid may further enhance the application and scope of ionic liquid chemistry[17].

We report herein *N*-octylquinolinium tribromide, a quinoline based room temperature ionic liquid, as an effective brominating agent (**Scheme I**).

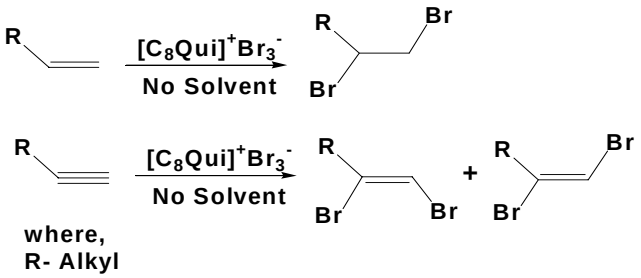
The combination of *N*-octylquinolinium cation with tribromide anion led to room temperature ionic liquid **2** (*N*-octylquinolinium tribromide) as a bromine analogue. Adding elemental bromine dropwise under stirring to octylquinolinium bromide **1** formed the red liquid of **2,** which displayed density of 2.12 g/cm^{-3}. The UV-vis spectrum showed a characteristic absorption at λ = 236 and 279 nm. The ESI-MS-MS spectrum showed a molecular ion peak at *m/z* 242 and a base peak at *m/z* 130. Purification of reagent **2** was done by removing excess bromine under vacuum and purity of reagent was checked by high performance liquid chromatography (HPLC). The ionic nature of **2** thus effectively eliminates any noxious residual bromine vapour pressure. The reagent **2** was then tested as a brominating agent for a bromination of phenol, aromatic amines **(Scheme II)**, alkenes and alkynes **(Scheme III)**. To prove the versatility of reagent, a variety of substrates were treated with the reagent to reflect a variety of structural types. Phenols, aromatic amines, alkenes and alkynes react smoothly with *N*-octylquinolinium tribromide at room temperature to produce corresponding bromo derivative in good to excellent yields.



Scheme I



Scheme II



Scheme III

Rajagopal has reported[15], ionic liquid assisted bromination of aromatic substrates by making use of NBS as a brominating agent and ionic liquid as a solvent, whereas in the present method, we have developed a new brominating agent by reacting elemental bromine with *N*-octylquinolinium bromide. This reagent itself behaves both as a solvent as well as a brominating agent. The advantage of this method over the exiting method is that it is simple, efficient, easy work-up and more cost-effective. Moreover this method is essentially versatile because it is applicable in almost all the substrates susceptible to bromination (e.g. phenols, aromatic amines, alkenes and alkynes) contrary to the reported[15] method, which is applicable only to aromatic substrates. This method is also advantageous in terms of reactivity, product yield and applicable to wide range of substrates over pyridinium based brominating agent[16].

The reaction was carried out by stirring a mixture of phenols/aromatic amines (0.01 mole) and *N*-octylquinolinium tribromide $[C_8Qui]^+Br_3^-$ (0.01 mole) at room temperature without using organic solvent. Although the reactions were slightly exothermic, no special precautions were taken for cooling. Using above standard reaction conditions, the bromination of series of phenol and aromatic amines were examined. The reagent reacts smoothly with phenols and aromatic amines to produce the corresponding bromo derivatives in good to excellent yields under solvent free conditions.

Phenol was cleanly mono brominated in the solvent-free condition at room temperature affording exclusively *p*-bromo phenol. The simplicity and selectivity of this phenol bromination compare favourably with current methods, which use solvents and tend to lead to mixtures of isomer and polybromination. Likewise, aromatic amines were monobrominated in the presence of $[C_8Qui]^+Br_3^-$ in excellent yield exclusively in *para* position. All the bromo derivatives isolated are known compounds reported in the literature. Their identities were confirmed by IR, ^{1}HNMR and mass spectral analysis. The purity of product was confirmed by TLC and GC analysis. Ether extraction allowed the separation of the product from reagent. The results are summarized in **Table I**.

The ionic liquid *N*-octyl quinolinium bromide was recycled from the reaction mixture and the reagent was regenerated by its treatment with bromine. The effectiveness of this recycling and regenerating process was tested and found effective up to 6 cycles. Conversion and selectivity of the reagent have been found to be as follows: 1 (95/100), 2(95/100), 3(95/100), 4(95/100), 5(96/100), 6(95/100) respectively. The versatility of the methodology also lies in the fact that apart from aromatic electrophillic bromination of phenols and amines, this reagent also brominated several other functionalities such as ethylenic and acetylinic functions efficiently (**Scheme III**). For example, cyclodecene, cyclooctene, 1-hexadecenecyclooctene, 4-vinyl pyridine (Entry 1-4, **Table II**) containing ethylenic functionality were all brominated to corresponding *trans*-dibromo compounds. Substrates (Entry 5-11, **Table II**) containing acetylinic functionality could also be efficiently brominated with this reagent in excellent yields. Since all the substrate have the terminal acetylinic functionality, gave a mixture of *cis* and *trans* product in approximately 20:80 ratio as obtained from GC mass analysis.

The reaction was carried out by stirring a mixture of alkenes/alkynes (0.01 mole) with $[C_8Qui]^+Br_3^-$ (0.02 mole) at room temperature without any solvent to produce exclusively dibromo derivatives of alkenes and alkynes. In order to assess the versatility of

Table I — Bromination of phenols and aromatic amines by $[C_8Qui]^+Br_3^-$

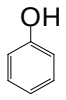
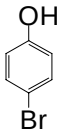
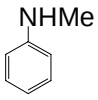
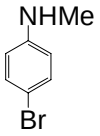
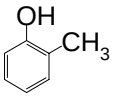
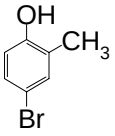
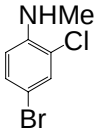
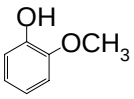
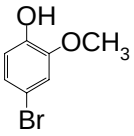
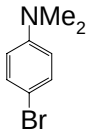
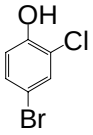
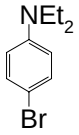
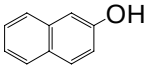
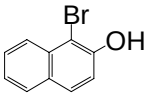
Entry yield	Substrate	Product	Reaction time (hr)	Product (%)	Entry yield	Substrate	Product	Reaction time (hr)	Product (%)
1			4	95	6			4	90
2			4	96	7			4	89
3			4	91	8			4	92
4			4	92	9			4	93
5			4	92	10			4	91

Table II — Bromination of alkenes and alkynes by $[C_8Qui]^+Br_3^-$

Entry	Substrate	Product	Reaction time (hr)	Ratio of isomers (*cis/trans)*	Product yield (%)
1	Cyclodecene	Dibromo cyclodecane	4		96
2	Cyclooctene	Dibromo cyclooctane	4		95
3	1-Hexadecene-cyclooctene	Dibromo cyclooctane	4		95
4	4-Vinyl pyridine	4-(1,2-Dibromo ethyl) pyridine	4		89
5	1-Nonyne	1,2-Dibromo nonene	4	17:83	91
6	1-Octadecyne	1,2-Dibromo octadecene	4	18:82	90
7	1-Hexadecyne	1,2-Dibromo hexadecene	4	20:80	94
8	1-Tetradecyne	1,2-Dibromo tetradecene	4	18:82	93
9	1-Undecyne	1,2-Dibromo undecene	4	17:83	94
10	1-Pentadecyne	1,2-Dibromo pentadecene	4	20:80	90
11	1-Tyidecyne	1,2-Dibromo tridecene	4	18:82	92

All compounds gave satisfactory IR, NMR and MS data and were compared with authentic samples. All acetylinic substrates (**5-11**) gave a mixture of *cis* and *trans* product in the ratio mentioned in the table as obtained from GC mass analysis.

reaction, $[C_8Qui]^+Br_3^-$ mediated bromination was carried out with series of alkenes and alkynes. In all cases a corresponding dibromides were obtained in high yield. **Table II** summarizes the results.

In conclusion, an efficient reagent in the form of ionic liquid as a brominating agent has been developed. This reagent behaves both as a solvent as well as the brominating agent. The advantage of this method over the exiting method is that it is simple, efficient, easy work-up and cost-effective. Moreover this method is essentially versatile because it is applicable in almost all the substrates susceptible to bromination (e.g. phenols, aromatic amines, alkenes and alkynes).

Experimental Section

Synthesis of reagent *N*-octylquinolinium tribromide. Bromine (11.57 g, 0.072 mole) was added over 30 min to *N*-octylquinolinium bromide (19.26 g, 0.06 mole) under stirring and cooling in water bath gave a deep red liquid. After stirring for 2 hr the liquid was left *in vacuo* for 3 to 4 hr to remove excess of bromine to yield pure *N*-octylquinolinium tribromide, Yield: 26 gm (90%), m.p.: 0°C, d= 2.12, UV: λ_{max} 236, 270 nm; IR (KBr): 3462, 3069, 2925, 2853, 1594, 1526, 1379, 809, 771, 608 cm^{-1}; ESI-MS-MS: *m/z* 242 (M^+), 130 (Base peak)

Bromination of phenols and aromatic amines

To phenol/aromatic amines (0.025 mole) was added dropwise *N*-octylquinolinium tribromide (0.025 mole) over 10 min. The resulting viscous reaction mixture was stirred for the time period given in **Table I**. The reaction was monitored by TLC (silica plates, 10% acetone in chloroform) and GC. After completion of reaction, bromo derivative was extracted with ether yielded a pure product. The residue yellowish ionic liquid *N*-octylquinolinium bromide was recovered, dried, identified as a pure ionic liquid and again reacted with bromine to regenerate the reagent.

Bromination of alkenes and alkynes

To alkenes/alkynes (0.025 mole) was added dropwise *N*-octylquinolinium tribromide (0.05 mole) over 10 min. The resulting viscous reaction mixture was stirred for the time period given in **Table II**. The reaction was monitored by TLC (silica plates, 10% acetone in chloroform) and GC. After completion of reaction, dibromo derivative was extracted with ether yielded a pure product. The residue yellowish ionic liquid *N*-octylquinolinium bromide was recovered, dried, identified as a pure ionic liquid and again reacted with bromine to regenerate the reagent.

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