

Bromamine-T/RuCl₃ as an efficient system for the oxidation of tertiary amines to *N*-oxides

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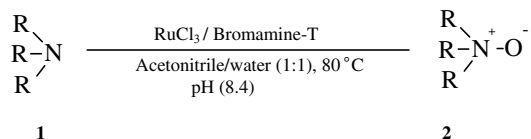
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Abstract—A variety of tertiary amines were efficiently and selectively oxidized to the corresponding *N*-oxides by bromamine-T using ruthenium trichloride as catalyst in alkaline (pH 8.4) acetonitrile/water (1:1) at 80 °C.

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N-Halo-*N*-metallosulfonamides, due to their ability to act as sources of halonium cations, hypohalite species, and *N*-anions, which act both as bases and nucleophiles, have proved to be valuable intermediates for a variety of functional group transformations.¹ Bromamine-T and other related reagents act as strong oxidants both in alkaline and acidic media and have been widely used for the oxidation of alcohols,² aldehydes,³ primary amines,⁴ thiols,⁵ and esters.⁶ *N*-Oxides are synthetically important building blocks and are extensively used as oxidants.⁷ A variety of stoichiometric⁸ as well as catalytic methods are reported in the literature for the oxidation of tertiary nitrogen compounds to *N*-oxides.⁹ In continuation of our studies on oxidation,^{9i,j,10} we report herein a new and simple method for the oxidation of a variety of tertiary nitrogen compounds **1** to *N*-oxides **2** in near quantitative yields using bromamine-T as oxidant and ruthenium trichloride as the catalyst (Scheme 1).



Scheme 1.

Keywords: Bromamine-T; Ruthenium trichloride; Tertiary nitrogen compounds; *N*-Oxides; Oxidation.

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

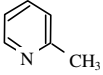
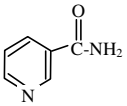

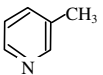
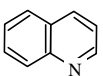
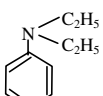
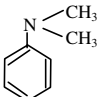
Oxidation of a variety of tertiary nitrogen compounds was achieved by using a catalytic amount of ruthenium trichloride in acetonitrile/water (1:1) at 80 °C with bromamine-T, the substrate/bromamine-T ratio being (1:1.2) under alkaline pH (8.4) to yield *N*-oxides in excellent yields.¹¹ These results are summarized in Table 1. In general substituted anilines were found to be more reactive compared to pyridines and among substituted pyridines those substituted with electron donating groups were found to be more reactive and required shorter reaction times for their oxidation.

The reaction was found to be highly dependent upon the pH of the system. To evaluate the effect of pH, oxidation of 4-picoline was carried out under similar conditions at different pH's. At neutral pH, the oxidation of 4-picoline was found to be very slow and the reaction required 8 h, while at pH 8.4 the reaction was complete within 4.5 h. It was also observed that at higher pH's (9–11) the rate of the reaction became very slow and was not complete even after 12 h. This type of pH dependent behavior for bromamine-B has been reported in the literature.¹² The oxidation of 4-picoline was found to be very slow at room temperature (20 °C) requiring 10 h for completion.

The effect of various solvents was also studied using 4-picoline as substrate. Among the solvents examined [acetonitrile, 1,2-dichloromethane, ethanol, and an acetonitrile/water (1:1) mixture], the mixture of acetonitrile/water (1:1) was found to be the best solvent system, perhaps due to the high dielectric constant of water.

The oxidation of 4-picoline was found to be very slow using chloramine-T in place of bromamine-T under

Table 1. Oxidation of tertiary nitrogen compounds to *N*-oxides^a

Entry	Substrate	Time (h)	Yield (%) ^b
1		3.0	75
2		2.5	85
3		3.0	80
4		6.0	50
5		4.5	65
6		10	65
7		12	50
8		2.5	92
9		2.5	90
10	(C ₂ H ₅) ₃ N	5	92

^a Reaction conditions: substrate/bromamine-T (1:1.2), RuCl₃·xH₂O (0.5 mol%), acetonitrile/water (1:1), pH 8.4 at 80 °C.

^b Isolated yields.

similar reaction conditions. The enhanced reactivity of bromamine-T is probably due to the weak bonding between nitrogen and bromine.

Although mechanism of this reaction is not clear at this stage, the reaction probably involves the RuCl₃ catalyzed formation of HOBr from bromamine-T in aqueous alkaline medium,¹³ which effects the oxidation of tertiary amine to *N*-oxide.

In summary, we have developed a simple ruthenium catalyzed oxidation of tertiary nitrogen compounds to *N*-oxides using bromamine-T as oxidant under mild reaction conditions.

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- Typical experimental procedure: To a stirred solution of 4-picoline (0.93 g, 10 mmol), bromamine-T (12 mmol, 3.2 g) in alkaline (pH 8.4) acetonitrile/water (1:1) mixture (15 mL), RuCl₃·xH₂O (1 mg, 0.5 mol%) was added and the mixture was heated at 80 °C for 2.5 h. The reaction progress was monitored by TLC (SiO₂) gel. After completion of the reaction, the solvent was evaporated under reduced pressure and the residue was dissolved in dichloromethane. The dichloromethane layer was washed twice with water and dried over sodium sulfate. The solvent was evaporated under reduced pressure and the residue thus

obtained was purified by passing through a short silica gel column using dichloromethane as eluent. Evaporation of the solvent yielded 4-picoline *N*-oxide (0.92 g, 85%). Other nitrogen compounds were oxidized using this procedure and their reaction times and yields are given in Table 1. The products were identified by comparing their physical

and spectral data with those of authentic samples reported in the literature.

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