Pergamon

SCIENCE DIRECT®

Tetrahedron Letters 44 (2003) 4085–4088

TETRAHEDRON LETTERS

Environmentally benign chlorination and bromination of aromatic amines, hydrocarbons and naphthols

Punita V. Vyas, Anjani K. Bhatt, Gadde Ramachandraiah and Ashutosh V. Bedekar*

Central Salt and Marine Chemicals Research Institute, G.B. Road, Bhavnagar 364002, India

Received 2 March 2003; revised 21 March 2003; accepted 28 March 2003

Abstract—A simple and efficient procedure for chlorination and bromination of aromatic amines, hydrocarbons and naphthols by the action of aqueous hydrohalic acid and hydrogen peroxide is described. This environmentally clean and safe procedure involves in situ generation of the active halogen and its uncatalyzed reaction with the substrates in this study.

Halogenated aromatic compounds are an important class of molecules in synthetic organic chemistry. They are key intermediates in the preparation of organometallic reagents[1–4] and play vital roles in transition metal mediated coupling reactions.[5–10] Numerous industrially valuable products such as pesticides, insecticides, herbicides, pharmaceutically and medicinally active molecules, fire retardants and other newer materials carry halogen functionality. Traditionally, aromatic chloro and bromo compounds are prepared by reaction with elemental halogen in the presence of a metal catalyst, and often involving harsh reaction conditions.[11] The handling of chlorine gas and liquid bromine is cumbersome due to their hazardous nature while special equipment and care are needed for the transfer of these materials in large scale. Moreover, halogenation of aromatic substrates with elemental halogens involves a substitution reaction with the formation of hydrohalic acid as a by-product, effectively reducing the atom efficiency by 50%. The generated hydrohalic acid waste must be neutralized before it can be discharged as effluent.

In order to overcome some of these problems a new and environmentally safe procedure was envisioned to involve in situ preparation of a positive halogen species by oxidation of a chloride or bromide anion using a suitable oxidant. This reactive electrophilic halogen can thus effect halogenation of organic substrates under suitable reaction conditions. This concept has been inspired by the enzymes, vanadium dependent bromoperoxidases found in marine algae which have the ability to catalyze oxidation of bromide ions by hydrogen peroxide in the biosyntheses of brominated compounds.[12–14] Some authors[15–20] have designed synthetic catalysts based on Nature's model to assist oxidation of a bromide anion with hydrogen peroxide in bromination reactions.

In our earlier studies we explored the oxidation of hydrochloric acid or hydrobromic acid by hydrogen peroxide or *tert*-butylhydroperoxide to generate positive halogen species in situ for effective halogenation of aromatics, alkenes and alkynes.[21,22] Of interest was the fact that we were able to bring about this oxidation and halogenation in the absence of any transition metal catalyst as depicted in Eq. (1).

$$\mathrm{RH} + \mathrm{HX} + \mathrm{H_2O_2} \longrightarrow \mathrm{RX} + 2\mathrm{H_2O} \qquad (1)$$

Recently other groups have reported a similar approach for the benzylic bromination,[23] and the oxidation of alcohols, aldehydes,[24] or sulphides.[25,26] In this communication we wish to report our new results on the halogenation of some inactivated aromatic hydrocarbons and naphthols.

In this account we present our modification of an earlier process[22] where we successfully examined the chlorination and bromination of aromatic amines. In this case, we used one extra equivalent of acid which is used to form the amine salt, followed by halogenation as shown in Eq. (1). A number of different aromatic

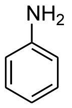
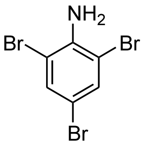
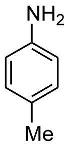
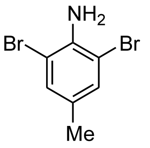
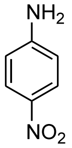
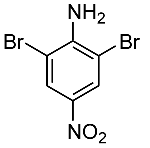
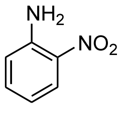
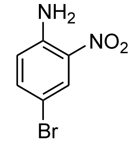
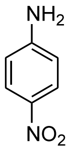
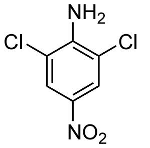
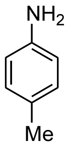
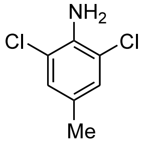
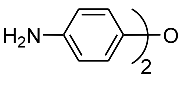
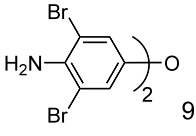
---

Keywords: halogenation; aromatic amines; aromatic hydrocarbons; naphthols.

* Corresponding author. Fax: +91-278-2567562; e-mail: avbedekar@yahoo.co.in

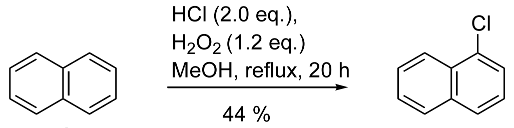
0040-4039/03/$ - see front matter
doi:10.1016/S0040-4039(03)00834-7

Table 1. Halogenation of aromatic amines

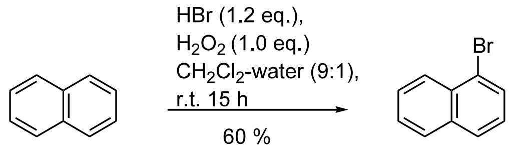
Entry	Amine	Conditions	Product	Isolated Yield
1		HBr (4.0 eq.) H_2O_2 (3.1 eq.) MeOH 0 °C to r.t., 8 h		96 %
2		HBr (3.0 eq.) H_2O_2 (2.0 eq.) MeOH 0 °C to r.t., 8 h		98 %
3		HBr (3.0 eq.) H_2O_2 (2.0 eq.) MeOH 0 °C to r.t., 10 h		95 %
4		HBr (2.0 eq.) H_2O_2 (1.0 eq.) MeOH 0 °C to r.t., 12 h		99 %
5		HCl (4.0 eq.) H_2O_2 (2.1 eq.) MeOH reflux, 15 h		87 %
6		HCl (4.0 eq.) H_2O_2 (2.1 eq.) MeOH reflux, 12 h		99 %
7		HBr (4.0 eq.) H_2O_2 (3.1 eq.) MeOH 0 °C to r.t., 12 h		90 %

amines gave satisfactory results with this reaction and the results are summarized in Table 1.

We also examined the chlorination of less activated substrates such as naphthalene with hydrochloric acid and hydrogen peroxide in methanol without any catalyst. The reaction did not occur at ambient temperature and it was necessary to maintain an elevated temperature (refluxing methanol) and careful analysis of the reaction mixture by gas chromatography indicated a moderate conversion of 44% (Eq. (2)). On the other hand the bromination of naphthalene did proceed at room temperature but with low conversion ca. 28% which showed a marginal improvement to 35% under reflux. We further studied this reaction in dichloromethane–water and observed a marked improvement. As depicted in Eq. (3), a reasonably good conversion was achieved, probably due to the better solubility of naphthalene in dichloromethane compared to methanol.

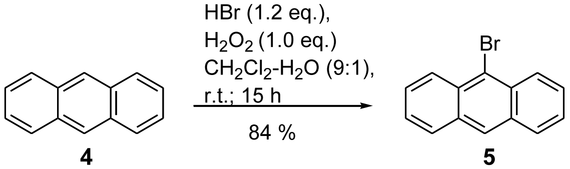


1 2 (2)

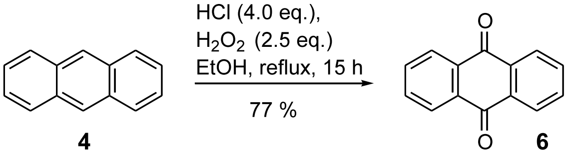


1 3 (3)

The successful halogenation of the less reactive naphthalene in the absence of any catalyst is an indication of the reasonably reactive nature of the electrophilic species. Encouraged by this observation we further investigated the halogenation of anthracene and pyrene. Bromination of anthracene resulted in the formation of 9-bromoanthracene **5** in excellent yield as the sole product (Eq. (4)). However, an attempt to extrapolate this for the chlorination of anthracene furnished 9,10-anthraquinone **6** in good yield (Eq. (5)) along with small quantities of unidentified products, including chlorinated anthracene.

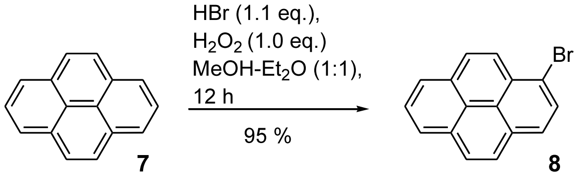


4 5 (4)



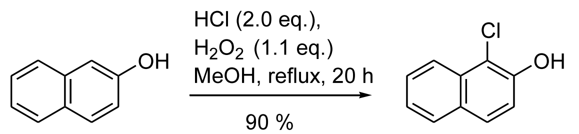
4 6 (5)

Similarly bromination of pyrene resulted in an excellent conversion to 1-bromopyrene when the reaction was conducted in a mixture of methanol and diethyl ether under ambient conditions (Eq. (6)).

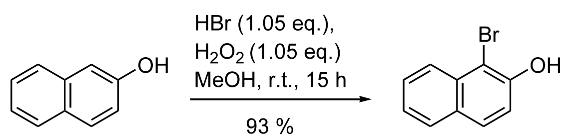


7 8 (6)

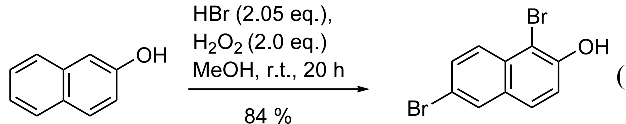
As part of our ongoing project on dehalogenation reactions we required a series of halogenated naphthols and hence we examined the present procedure for their preparation. To this end, we examined the chlorination of 2-naphthol using an excess of hydrochloric acid and hydrogen peroxide in boiling methanol. The desired 1-chloro-2-naphthol **10** was isolated in excellent yield (Eq. (7)), while the bromine analogue **11** was successfully prepared under ambient conditions (Eq. (8)). Dibromination of 2-naphthol with excess reagent resulted in the clean formation of 1,6-dibromo-2-naphthol **12** in high yield (Eq. (9)). This dibrominated product is an intermediate in the preparation of the industrially important 6-bromo-2-naphthol by a selective debromination reaction.[27]



9 **10** (7)

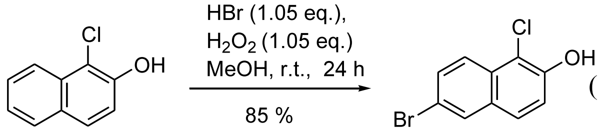


9 **11** (8)

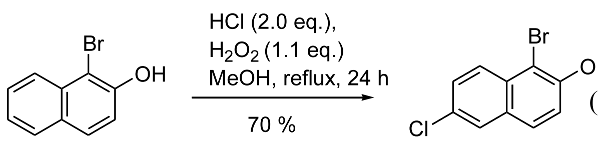


9 **12** (9)

Another derivative, 1-chloro-6-bromo-2-naphthol **13** was prepared by bromination of 1-chloro-2-naphthol (Eq. (10)) opening several possibilities to prepare heterohalogenated naphthols and phenols. Similarly, chlorination of 1-bromo-2-naphthol yielded 1-bromo-6-chloro-2-naphthol **14** in moderate yield (Eq. (11)).



10 **13** (10)



11 **14** (11)

Thus, in this communication we have presented our results towards an environmentally safe chlorination and bromination of aromatic amines, hydrocarbons and naphthols by the in situ oxidation of hydrohalic acid with hydrogen peroxide. We have prepared several important halogenated and heterohalogenated compounds in moderate to excellent yields without using any catalyst.

Experimental:

The reaction products obtained in this study were purified by column chromatography on silica gel using a suitable mixture of ethyl acetate and hexane and showed satisfactory spectral and analytical data. A representative example is described below.

Preparation of 1,6-dibromo-2-naphthol: To a stirred solution of 2-naphthol (1.44 g; 10 mmol) and hydrobromic acid (1.65 g; 3.39 mL of a 49% aq. solution; 20.5 mmol) in methyl alcohol (25 mL) was slowly added hydrogen peroxide (0.68 g; 2.27 mL of a 30% aq. solution; 20 mmol) over a period of 15 min at 10–15°C. The reaction was left at room temperature for 20 h whilst monitoring its progress by TLC. After the completion of dibromination, the solvent was removed under reduced pressure and the crude product was taken in ethyl acetate and washed with water, brine and dried over anhydrous sodium sulphate. The pure product was isolated by careful column chromatography on silica gel (100–200 mesh) using a mixture of ethyl acetate in hexane (10%) to give pure 1,6-dibromo-2-naphthol as a light brown solid (1.77 g; 84%); mp 106–107°C (lit.[28] 105–107°C); IR (KBr): ν 3485, 3444, 1617, 1586, 1381, 1210, 1183, 928, 871, 805, 645, 536, 512 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 6.20 (br s, 1H), 7.40–7.78 (dd, $J=66$ and 9 Hz, 2H), 8.15–8.36 (dd, $J=33$ and 9 Hz, 2H), 8.76 (s, 1H). Anal. calcd for $C_{10}H_6Br_2O$: C, 39.74; H, 1.99. Found: C, 40.06; H, 2.18%.

Acknowledgements

We wish to thank Dr. Pushpito Ghosh for his help and encouragement and the CSIR, New Delhi for financial assistance under the Quick Hire Scheme to A.V.B.

References

1. Normant, H. *Adv. Org. Chem.* **1960**, *2*, 1.
2. Wakefield, B. J. *The Chemistry of Organolithium Compounds*; Pergamon Press: Oxford, 1976.
3. Davis, S. G. *Organotransition Metal Chemistry*: *Applications to Organic Synthesis*; Pergamon Press: Oxford, 1982.
4. Cannon, K. C.; Krow, G. R. *Handbook of Grignard Reagents*; Dekker: New York, 1996.
5. Still, J. K. *Pure Appl. Chem.* **1985**, *57*, 1771.
6. Miyaura, N.; Suzuki, A. *Chem. Rev.* **1995**, *95*, 2457.
7. Beletskaya, I. P.; Cheprakov, A. V. *Chem. Rev.* **2000**, *100*, 3009.
8. Cabri, W.; Candiani, I. *Acc. Chem. Res.* **1995**, *28*, 2.
9. Meijere, A.; Meyer, F. E. *Angew. Chem.*, *Int. Ed. Engl.* **1994**, *33*, 2379.
10. Sonogashira, K. *Comprehensive Organic Synthesis*; Pergamon Press: New York, 1991; Vol. 3, p. 521.
11. De la Mare, P. B. *Electrophilic Halogenation*; Cambridge University Press: Cambridge, 1976; Chapter 5.

12. Wever, R.; Kreenn, M. B. E. *Vanadium in Biological Systems*; Kluwer Academic Publishers: Dordrecht, 1990; p. 81.
13. Butler, A.; Carrano, C. J. *Coord. Chem. Rev.* **1991**, *109*, 61.
14. Butler, A.; Walker, J. V. *Chem. Rev.* **1993**, *93*, 1937.
15. Conte, V.; Di Furia, F.; Moro, S. *Tetrahedron Lett.* **1994**, *35*, 7429.
16. Andersson, M.; Conte, V.; Di Furia, F.; Moro, S. *Tetrahedron Lett.* **1995**, *36*, 2675.
17. Bhattacharjee, M.; Ganguli, S.; Mukherjee, J. *J. Chem. Res. (S)* **1995**, 80.
18. Bhattacharjee, M.; Mukherjee, J. *J. Chem. Res. (S)* **1995**, 238.
19. Sels, B. F.; De Vos, D. E.; Jacobs, P. A. *J. Am. Chem. Soc.* **2001**, *123*, 8350.
20. Chaudhuri, M. K.; Khan, A. T.; Patel, B. K.; Dey, D.; Kharmawophlang, W.; Lakshmiprabha, T. R.; Mandal, G. C. *Tetrahedron Lett.* **1998**, *39*, 8163.
21. Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Bedekar, A. V. *Tetrahedron Lett.* **1998**, *39*, 6349.
22. Barhate, N. B.; Gajare, A. S.; Wakharkar, R. D.; Bedekar, A. V. *Tetrahedron* **1999**, *55*, 11127.
23. Mestres, R.; Palenzuela, J. *Green Chem.* **2002**, *4*, 314.
24. Espenson, J. H.; Zhu, Z.; Zauche, T. H. *J. Org. Chem.* **1999**, *64*, 1191.
25. Bravo, A.; Dordi, B.; Fontana, F.; Minisci, F. *J. Org. Chem.* **2001**, *66*, 3232.
26. Mondal, E.; Bose, G.; Sahu, P. R.; Khan, A. T. *Chem. Lett.* **2001**, 1158.
27. Sabahi, M. PCT Int. Appl. WO 9,811,041; *Chem. Abstr.* **1998**, *128*, 230147.
28. Aldrich Chemical Company Catalogue 2003–2004.