

SYNLETT Spotlight 239

KX/H₂O₂ – An Efficient and Non-Polluting Halogenating Reagent in Organic Synthesis

Compiled by Navath Suryakiran



This feature focuses on a reagent chosen by a postgraduate, highlighting the uses and preparation of the reagent in current research

Navath Suryakiran was born in 1980 in D. Dharmaram, Andhra Pradesh, India. He obtained his M.Sc. in Organic Chemistry from Babasaheb Ambedkar Marathwada University, Aurangabad in 2002, and subsequently passed the National Eligibility Test (CSIR-UGC-NET) for registering in a Ph.D. programme. He is currently working towards his Ph.D. under the supervision of Dr. Y. Venkateswarlu at the Indian Institute of Chemical Technology (IICT), India. His research interests focus on the synthesis of bioactive natural products and the development of new synthetic methodologies.

Organic Chemistry Division-I, Indian Institute of Chemical Technology (IICT), Hyderabad 500007, India
E-mail: suryakiran.navath@gmail.com

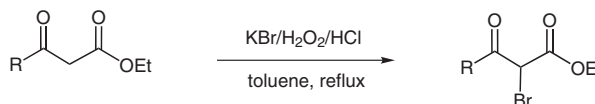
Introduction

Halogenated organic compounds have long been known as useful synthetic intermediates, which are not only man-made, but also synthesized by a large number of different organisms.¹ Halogenated organic compounds are important components in a variety of biologically active molecules and pharmaceutical agents.² They form an important class of intermediates as they can be converted efficiently into other functionalities by simple chemical transformations. For example aryl, vinyl and benzylic halides serve as important precursors to organolithium³ and Grignard⁴

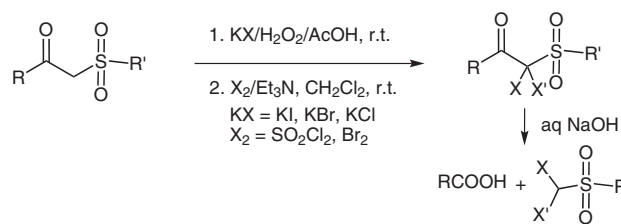
reagents in C–C bond formation. Aryl halides have been employed as substrates for nucleophilic aromatic substitutions⁵ and for benzyne generation.⁶ Additionally, both aryl^{7,8} and vinyl⁹ halides have found widespread utility as substrates for a variety of cross-coupling reactions. As a result of the diverse potential applications of organic halides, the development of new regioselective, chemoselective and functional-group tolerant approaches using non-polluting reagents for the synthesis of these molecules remains an important challenge. In this context, KX/H₂O₂ serves as an efficient and non-polluting halogenation reagent in organic synthesis.

Abstracts

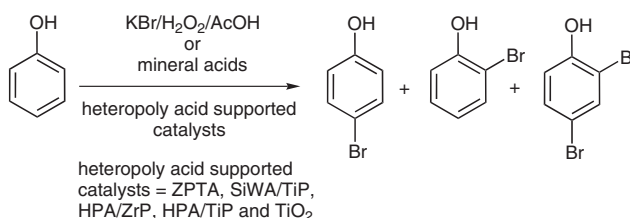
(A) Kiriara et al. reported chemoselective mono-bromination of active methylene and methine compounds using potassium bromide, hydrochloric acid and hydrogen peroxide.¹⁰



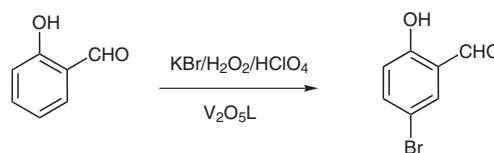
(B) α -Halo β -keto sulfones were synthesized by reaction of β -keto sulfones with potassium halide in the presence of hydrogen peroxide and acetic acid in aqueous medium.¹¹ Further, the α -halo β -keto sulfones on treatment with SO₂Cl₂/Br₂ afforded α,α -symmetrical and asymmetrical dihalo β -keto sulfones,¹² which on further treatment with aqueous alkali underwent base-induced cleavage to afford α,α -symmetrical and asymmetrical dihalomethyl sulfones, respectively. This method is very simple, highly economical and eco-friendly for the synthesis of a wide variety of α -halo and α,α -dihalo β -keto sulfones.



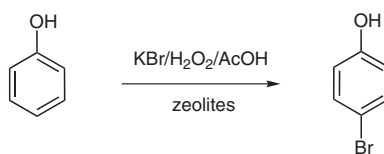
(C) Parida and co-workers reported an oxidative bromination of phenols using metal-supported heteropoly acid such as zirconia,¹³ titanium phosphate (TiP),¹⁴ zirconium phosphate (ZrP),¹⁵ titania pillared zirconium phosphate (ZrP)¹⁶ and titanium phosphate (TiP)¹⁷. In these reactions KBr acts as brominating agent and hydrogen peroxide as an oxidant in the presence of acetic acid or mineral acids at room temperature. The reaction proceeds through the formation of a bromonium ion, which attacks the phenol ring to form different brominated products.



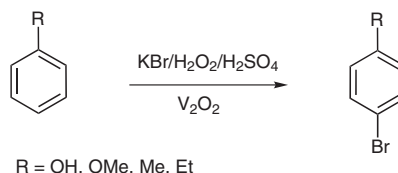
(D) Vanadate-dependent haloperoxidase complexes as selective bromination agents of phenols have been reported. Starting from salicylaldehyde in the presence of $\text{KBr}/\text{H}_2\text{O}_2$, the anionic complex catalyses the oxidative bromination in water to afford 5-bromosalicylaldehyde in 40% yield and 87% selectivity.¹⁸



(E) An efficient, simple, mild and regioselective liquid-phase bromination of phenols using potassium bromide and hydrogen peroxide over zeolites CrZSM-5(30) has been reported. The reaction proceeds via electrophilic substitution of phenols with an electrophilic bromonium ion generated in situ from KBr in the presence of hydrogen peroxide as an oxidant.¹⁹



(F) Vanadium-catalyzed oxidative bromination using dilute mineral acids and hydrogen peroxide has been reported. In this system, kinetic studies show that HBr can be replaced with a combination of an alkali bromide salt (NaBr/KBr) and a dilute mineral acid (e.g., HCl , H_2SO_4 , HNO_3 , H_3PO_4). The salt/acid/peroxide system may be used for in situ or ex situ oxidative bromination of various aromatic compounds. The application of the above concept towards the recycling of industrial acid waste is discussed.²⁰



(G) A simple, efficient, regioselective and environmentally safe liquid-phase regioselective bromination of aromatic compounds over HZSM-5 catalyst has been reported. The electrophilic bromine was generated from KBr using HZSM-5 zeolites as a catalyst and H_2O_2 as an oxidant.²¹



References

- Gribble, G. W. *Acc. Chem. Res.* **1998**, *31*, 141.
- Butler, A.; Walker, J. V. *Chem. Rev.* **1993**, *93*, 1937.
- (a) Suryakiran, N.; Srikanth Reddy, T.; Ashalatha, K.; Lakshman, M.; Venkateswarlu, Y. *Tetrahedron Lett.* **2006**, *47*, 3853. (b) Sotomayor, N.; Lete, E. *Curr. Org. Chem.* **2003**, *7*, 275.
- Handbook of Grignard Reagents*; Silverman, G. S.; Rakita, P. E., Eds.; Dekker: New York, **1996**.
- Crampton, M. R. In *Organic Reaction Mechanisms*; Knipe, A. C.; Watts, W. E., Eds.; Wiley: New York, **2003**, 237.
- Levin, R. H. In *Reactive Intermediates*, Vol. 1; Jones, M.; Moss, R. A., Eds.; Wiley: New York, **1985**, 1.
- (a) *Metal-Catalyzed Cross-Coupling Reactions*; Dietrich, F.; Stang, P. J., Eds.; Wiley-VCH: New York, **1998**. (b) Ley, S. V.; Thomas, A. W. *Angew. Chem. Int. Ed.* **2003**, *42*, 5400. (c) Beletskaya, I. P.; Cheprakov, A. V. *Coord. Chem. Rev.* **2004**, *248*, 2337.
- (a) Hassan, J.; Sévignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359. (b) Hartwig, J. F. In *Handbook of Organopalladium Chemistry for Organic Synthesis*; Negishi, E.-I., Ed.; Wiley Interscience: New York, **2002**, 1097.
- (a) Rossi, R.; Carpita, A.; Bellina, F. *Org. Prep. Proced. Int.* **1995**, *27*, 127. (b) Kotha, S.; Lahiri, K.; Kashinath, D. *Tetrahedron* **2002**, *58*, 9633.
- Kirihara, M.; Ogawa, S.; Noguchi, T.; Okubo, K.; Monma, Y.; Shimizu, I.; Shimozaki, R.; Hatano, A.; Hirai, Y. *Synlett* **2006**, 2287.
- Suryakiran, N.; Srinivasulu, M.; Venkateswarlu, Y. *J. Sulf. Chem.* **2007**, *28*, 345.
- Suryakiran, N.; Prabhakar, P.; Srikanth Reddy, T.; Chinni Mahesh, K.; Rajesh, K.; Venkateswarlu, Y. *Tetrahedron Lett.* **2007**, *48*, 877.
- Mallik, S.; Parida, K. M. *Catal. Commun.* **2007**, *8*, 889.
- Mallik, S.; Parida, K. M.; Dash, S. S. *J. Mol. Cat. A: Chem.* **2007**, *261*, 172.
- Das, D. P.; Parida, K. M. *J. Mol. Cat. A: Chem.* **2006**, *253*, 70.
- Das, D. P.; Parida, K. M. *Appl. Catal., A* **2006**, *305*, 32.
- Das, D. P.; Parida, K. M. *Catal. Commun.* **2006**, *7*, 68.
- Maurya, M. R.; Agarwal, S.; Bader, C.; Rehder, D. *Eur. J. Inorg. Chem.* **2005**, *147*, 157.
- Narender, N.; Krishna Mohan, K. V. V.; Vinod Reddy, R.; Srinivasu, P.; Kulkarni, S. J.; Raghavan, K. V. *J. Mol. Catal. A: Chem.* **2003**, *192*, 73.
- Rothenberg, G.; Clark, J. H. *Org. Proc. Res. Dev.* **2000**, *4*, 270.
- Narender, N.; Srinivasu, P.; Kulkarni, S. J.; Raghavan, K. V. *Synth. Commun.* **2000**, *30*, 3669.