BIGYAN **3**, 13 (2023)

Synthesis of α-Haloketones from Olefins- A mini review

Kalyan Senapati [1]

[1] Department of Chemistry, Mahatma Gandhi College, Lalpur, Purulia-723130, India

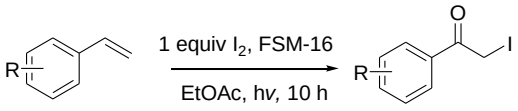
Abstract

α-haloketones play important role for the synthesis of N-, S-, O-heterocyclic compounds. α-haloketones can be synthesized form different building blocks. One of them is converting α-haloketones form olefins. In this review different types of synthetic methods have been discussed which were reported in last two decades.

Keywords: Haloketo, olefin.

In last couple of decades, several synthetic methodologies have been developed for the synthesis of α-haloketones by α-halogination of aryl ketones, oxyhalogenation of hydrocarbons, oxidative halogenation of secondary alcohols, oxidation of functionalised hydrocarbons, Hydration of 1-Haloalkynes, etc. α-haloketones are valuable intermediates for the synthesis of heterocyclic compounds.[1-2] The presence of two adjacent different types of electrophilic center composes the intermediate, flexible to manufacture industrially and pharmaceutically valuable compounds. Out of all above mentioned methods oxyhalogenation of hydrocarbons is very significant way to prepare α-haloketones from olefins.

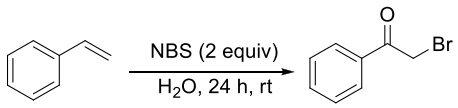
In 2007, Itoh et al. reported the synthesis of α-iodoketones derivatives from Styrene derivatives, Scheme 1.[3] In this methodology they have used FSM-16 (a mesoporous silica), 1 equiv I_2 and molecular oxygen under fluorescence lamp in ethyl acetate at room temperature. The experimental data showed that the reaction condition is equally applicable for electron-rich as well as electron-deficient olefins with 38-77% yield.



R= H, Me, ^{t}Bu, Ph, Cl, NO_2

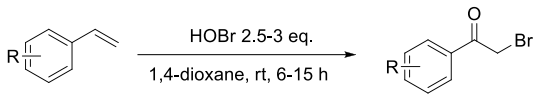
Scheme 1. Synthesis of α-iodoketones derivatives using molecular oxygen and I_2

In 2009, Iskra et al. showed the synthesis of α-bromoketone from styrene using 2 equiv of NBS in aqueous medium, Scheme 2.[4] The reaction was allowed to stir for 24 hours at room temperature. Here the major side product was bomohydrine.



Scheme 2. Synthesis of α-bromoketone from styrene using NBS-H_2O

In the same year Ranu et al. reported facile one-pot synthesis of α-bromoketones from olefins using NaBr, NaOBr and H_2SO_4 at room temperature, Scheme 3.[5] It was observed that with respect to other organic solvent like acetonitrile, DCM, DMSO and THF, 1,4-dioxane gives better result for this methodology. A series of olefins undergo this conversion under the same condition to give 40-87% yield.



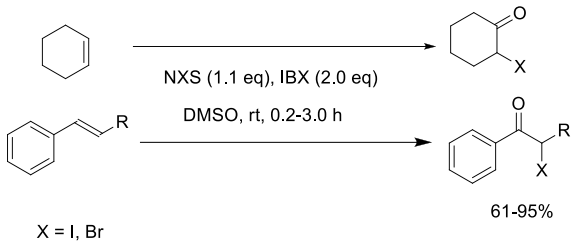
Scheme 3. Synthesis of α-bromoketone from styrene using NaBr, NaOBr and H_2SO_4

Almost at the same time Moorthy et al. documented protocol for conversion of olefins to α-bromo/ α-iodoketones using IBX and NBS/NIS respectively, Scheme 4.[6] The reactions were carried out with 1.1 equiv NBS or NIS under mild reaction condition i.e. at room temperature in DMSO to get 61-95% yield. Later in the year 2014 Mal et al. demonstrated the same reaction methodology under solvent free condition

E-mail: kalyanbubun@yahoo.com

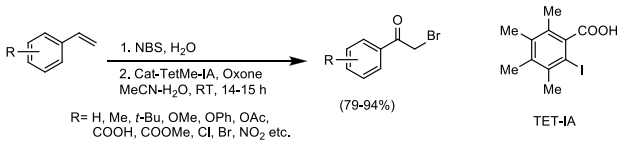
December, 2023

in ball milling.[7] Ball milling condition is equally effective to give very excellent isolated yield.



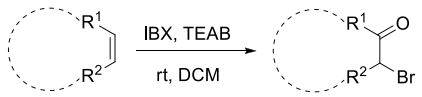
Scheme 4. Synthesis of α-haloketones from olefins using NBS/NIS and IBX

In 2017 Moorthy et al. reported one pot two step synthesis of α-bromoketones from olefins Scheme 5.[8] In the first step olefin converted to bromohydrine in presence of NBS-H_2O and in the second step bromohydrine was oxidised to α-bromoketones by Catalist TetMe-IA in presence of co-oxidant oxone in acetonitrile-watermedium at room temperature in the same pot.

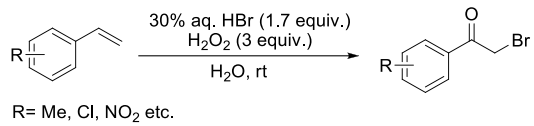


Scheme 5. one pot synthesis of α-bromoketones by NBS, Cat-TetMe-IA and oxone.

Akamanchi et al. reported direct conversion of olefins into α-bromoketone susing IBX and TEAB in DCM at room temperature, Scheme 6.[9] In this reaction 1.1 equiv of both IBX and TEAB were used to get 45-92% isolated yield.



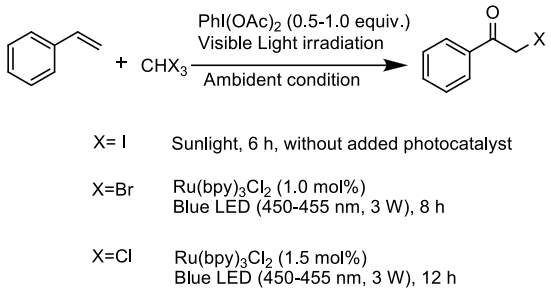
Scheme 6. Synthesis of α-bromoketones from olefins using IBX and TEAB



Scheme 7. Synthesis of α-bromoketones derivatives using HBr-H_2O_2

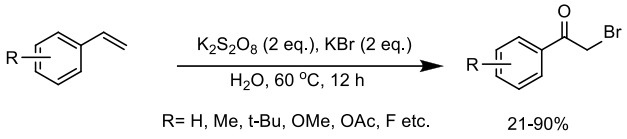
In 2010, Adimurthy et al. disclosed the synthesis of α-bromoketones from olefins using HBr-H_2O_2 under mild aqueous condition, Scheme 7.[10] In this methodology 1.7 equiv of HBr and 3 equiv of H_2O_2 were used to get 20-94% GC yield. In all the cases the side product is bromohydrine.

In 2019, Wang et al. reported a practical synthesis of α-bromo/iodo/chloroketones from olefins under visible-light irradiation conditions, Scheme 8.[11] The reaction was carried out in presence of hypervalent iodine $PhI(OAc)_2$, trihalomethane in water at room temperature. For the synthesis of α-iodoketones derivatives the reaction was carried out without addition of phtotocatalyst where as for the synthesis of α-bromoketones and α-chloroketones the reaction was carried out using $Ru(bpy)_3Cl_2$ as a photocatalyst.



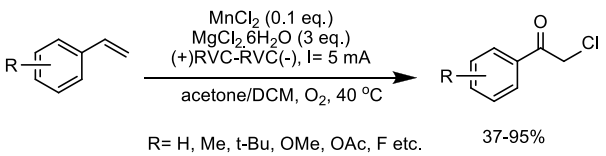
Scheme 8. Synthesis of α-bromo/iodo/chloroketones derivatives using $PhI(Oac)_2$

In 2013, Guo et al. showed the synthesis of α-bromoketones through $K_2S_2O_8$-mediated tandem hydroxybromination and oxidation of olefins, Scheme 9.[12] The reaction was carried out with 2 equiv. of KBr and 2.5 equiv. of $K_2S_2O_8$ in water at 60 ^oC for 12 h.



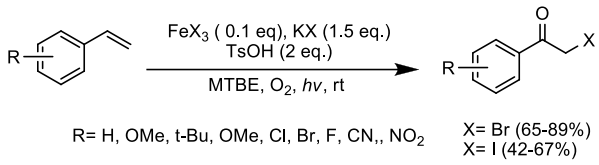
Scheme 9. Synthesis of α-bromoketones derivatives using $K_2S_2O_8$

In 2019 Chen et al. reported a facile electrochemical Mn-catalyzed synthesis of α-chloroketones derivatives from styrenes via oxygen reduction in acetone/DCM medium at 40 ^oC, Scheme 10.[13] The advantage of this reaction is that the method is eco friendly with very high yield.



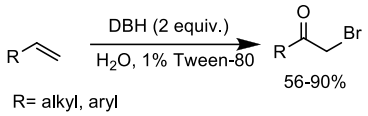
Scheme 10. Synthesis of α-chloroketones derivatives using Mn-catalyst

In 2020, Zhu et al. reported Iron-catalysed α-haloketone synthesis using KBr and KCl, Scheme 11.[14] A wide range of electron-rich and electron-deficient styrene derivatives undergo α-haloketones formation reaction by molecular oxygen in presence of 12W blue LEDs in Methyl tert-Butyl Ether to give upto 89% yield.



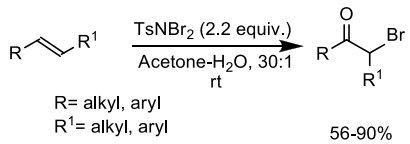
Scheme 11. Synthesis of α-bromo/iodoketones derivatives using KBr/KI

In 2016 Zhang et al. documented 1,3-Dibromo-5,5-dimethylhydantoin (DBH) mediated one-pot syntheses of α-bromoketones from olefins in water, Scheme 12.[15] The reaction was performed in presence of 1% tween-80 in water to avoid the solubility problem of the organic compound at 60 ^{o}C to get good yield. DBH plays a dual role in this reaction, that is as an oxidant and a halogenating agent. This protocol is not effective for the sterically hindered olefins.



Scheme 12. Synthesis of α-bromoketones using DBH

In 2014, Phukanet et al. reported the synthesis of α-bromoketones from olefins using N,N-dibromo-p-toluenesulfonamide ($TsNBr_2$),Scheme 13.[16] This method is equable applicable to the electron-rich and electron-poor styrene system. The reaction was performed with 2.2 equiv. of $TsNBr_2$ in aqueous-acetone medium at room temperature to get 80-87% yield. Here the thing that needs to be noted is that $TsNBr_2$ is not an easily accessible chemical.



Scheme 13. Synthesis of α-bromoketones using $TsNBr_2$

In this review several methodologies were discussed for the synthesis of α-haloketones that is α-bromoketones, α-iodoketones and α-chloroketones from olefins. Overall, this review analyzed several methodologies to access aromatic α-haloketones where the source of halogen are N-halosuccinimides, metallic halides, hydrohalic acid, salt of halides etc. Apart from them molecular halogen also has been used for such conversion. Although many of the methodologies gave promising results but this review is made with the expectation that the results collectively may give a way to a more effective methodology for the said conversion.

References

1. Bangalore, P.K.; Vagolu, S.K.; Bollikanda, R.K.; Veeragoni, D.K.; Choudante, P.C.; Misra, S.; Sriram, D.; Sridhar, B.; Kantevari, S. Usnic acid enaminone-coupled 1,2,3-triazoles as antibacterial and antitubercular agents. J. Nat. Prod. 2020, 83, 26–35.
2. Yang, Y.W.; Yang, W.B. Divergent synthesis of N-heterocycles by Pd-catalyzed controllable cyclization of vinylethylene carbonates. Chem. Commun. 2018, 54, 12182–12185
3. Nakayama, H.; Itoh, A. Facile synthesis of phenacyl iodides from styrenes under visible light irradiation with fluorescent lamps. Tetrahedron Lett.2007, 48, 1131–1133.
4. Podgorsek, A.; Stavber, S.; Zupan, M.; Iskra, J. Environmentally benign electrophilic and radical bromination 'on water': H_2O_2-HBr system versus N-bromosuccinimide. Tetrahedron 2009, 65, 4429–4439.
5. Patil, R. D.; Joshi, G.; Adimurthy, S.; Ranu, B.C. Facile one-pot synthesis of α-bromoketones from olefins using bromide/bromated couple as a nonhazardous brominating agent. Tetrahedron Lett. 2009, 50, 2529–2532.
6. Moorthy, J. N.; Senapati, K.; Singhal, N. An expedient protocol for conversion of olefins to α-bromo/iodoketones using IBX and NBS/NIS. Tetrahedron Lett. 2009, 50, 2493–2496.
7. Achar, T. K.; Maiti, S.; Mal, P. IBX works efficiently under solvent free conditions in ball milling. Rsc Adv. 2014, 4, 12834–12839.
8. Chandra, A.; Parida, K.N.; Moorthy, J. N. One-pot synthesis of α-bromo- and α-azidoketones from olefins by catalytic oxidation with in situ-generated modified IBX as the key reaction. Tetrahedron 2017, 73, 5827–5832.
9. Deshmukh, S. S.; Chaudhari, K. H.; Akamanchi, K. G. Direct Conversion of Olefins into α-Bromo Ketones Using O-Iodoxybenzoic Acid and Tetraethylammonium Bromide Synlett 2011, 1, 81–83.x
10. Patil, R. D.; Joshi, G.; Adimurthy, S. HBr-H_2O_2: A facile protocol for regioselective synthesis of bromohydrins and α-bromoketones and oxidation of benzylic/secondary alcohols to carbonyl compounds under mild aqueous conditions. Ind. Eng. Chem. Res. 2010, 49, 8100–8105.
11. Wang, Z.H.; Wang, L.; Wang, Z.M.; Li, P.H.; Zhang, Y.C. A practical synthesis of α-bromo/iodo/chloroketones from olefins under visible-light irradiation conditions. Chin. Chem. Lett. 2021, 32, 429–432.
12. Jiang, Q.; Sheng, W. B.; Guo, C. C. Synthesis of phenacyl bromides via $K_2S_2O_8$-mediated tandem hydroxybromination and oxidation of styrenes in water. Green Chem. 2013, 15, 2175–2179.
13. Tian, S.Y.; Jia, X.F.; Wang, L.; Li, B.Y.; Liu, S.Y.; Ma, L.; Gao, W.; Wei, Y.Q.; Chen, J.B. The Mn-catalyzed paired electrochemical facile oxychlorination of styrenes via the oxygen reduction reaction. Chem. Commun. 2019, 55, 12104–12107.
14. Luo, Z. B.; Meng, Y. E.; Gong, X. C.; Wu, J.; Zhang, Y. L.; Ye, L. W.; Zhu, C. Y. Facile Synthesis of α-haloketones by aerobic

oxidation of olefins using KX as nonhazardous halogen source. Chin. J. Chem. 2020, 38, 173–177.
15. Xu, S. H.; Wu, P.; Zhang, W. 1,3-Dibromo-5,5-dimethylhydantoin (DBH) mediated one-pot syntheses of α-bromo/amino ketones from alkenes in water. Org. Biomol. Chem. 2016, 14, 11389–11395.
16. Rajbongshi, K. K.; Hazarika, D.; Phukan, P. Metal-free protocol for the synthesis of α-bromo ketones from olefins using TsNBr2. Tetrahedron Lett. 2015, 56, 356–358.