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Mameda Naresh, Peraka Swamy, Macharla Arun Kumar, Marri Mahender Reddy, Kodumuri Srujana, Nama Narender

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Graphical Abstract

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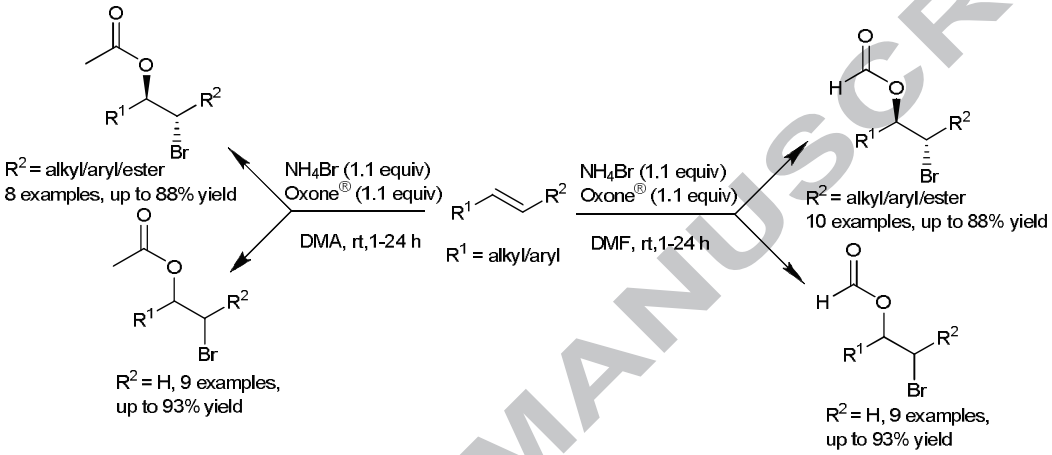

A simple and facile method for regio- and stereoselective bromoformyloxylation and bromoacetoxylation of olefins using NH_4Br and oxone®

Mameda Naresh, Peraka Swamy, Macharla Arun Kumar, Marri Mahender Reddy, Kodumuri Srujana, Nama Narender*

Inorganic and Physical Chemistry Division, CSIR-Indian Institute of Chemical Technology, Hyderabad 500 007, India

ABSTRACT

A mild and efficient protocol for the preparation of bromoformates as well as bromoacetates from olefins using NH_4Br and oxone® in nucleophile sources (DMF or DMA) without employing catalyst at room temperature is described. This method is facile, environmentally friendly and cost effective. A variety of terminal, internal, and cyclic alkenes reacted smoothly to give the corresponding bromoformate and acetate products in good to excellent yields. Moreover, 1,2-disubstituted olefins provided moderate to excellent diastereoselectivity.

Keywords: Alkenes, Cohalogenation, NH_4Br, Oxone®, Regioselectivity, Diastereoselectivity

Vicinal difunctionalization (simultaneous installation of two different functional groups into the organic structure) is a remarkable fundamental process in organic synthesis as it can be used to transform simple and readily available alkenes into value added products in regio- and stereoselective manner.[1] Among them, the co-halogenation of olefins is a valuable synthetic method to prepare the vicinal halo-functionalized synthons (halohydrins, β-haloethers and β-haloesters) regioselectively which are useful for various synthetic applications[2] and as building blocks for the preparation of epoxides.[3] Bromoformyloxylation and bromoacetoxylation of olefins are synthetically useful transformations in order to obtain bifunctionalities regioselectively.

Literature survey revealed that, in spite of its synthetic potential, bromoformyloxylation has received little attention and only a few methods using

* Corresponding author. Tel.: +91–40-27191703; Fax: +91-40-27160387/27160757.

E-mail address: narendern33@yahoo.co.in; nama@iict.res.in (N. Narender)

NBS/DMF,[4] *N*-bromosuccharin/DMF,[5] dibromoamine-b/HCOOH,[6] have been reported. However, most of these methods suffer from one or more disadvantages, such as unsatisfactory product yields, prolonged reaction times, use of moisture sensitive reagents and tedious work-up procedures. Another difunctionalization reaction is the bromoacetoxylation of olefins, which also has only a few literature reports and employs tribromoisocyanuric acid (TBCA),[7] NBS-AcOH/molecular sieves,[8] NaBr/PhI(OAc)$_2$/CTAB,[9] tetrabutyl ammonium dichlorobromate/AcOH,[10] NBS-AcOH/organocatalysts,[11] TsNBr$_2$/AcOH/DMF.[12] But, most of these methods have some disadvantages. For instance, prolonged reaction times, necessity of dark, inert conditions, high catalyst loading, low yields and exothermic process. Halohydrin esters are also synthesized from haloesterfication of diols[13] and acetylation of corresponding halohydrins.[14] However, these approaches need the prior synthesis of diols or halo hydrin precursors from respective olefins. Therefore, replacement of such reagents by non-toxic, mild, selective and easy-to-handle reagents is very desirable and represents an important goal in the context of clean synthesis.

Oxone® ($2KHSO_5.KHSO_4.K_2SO_4$), a potassium triple salt containing potassium peroxymonosulfate is a white crystalline solid, easy to handle, soluble in water and yields non-polluting byproducts. Moreover, oxone® is an inexpensive and readily accessible oxidizing agent, which have been used for the oxidation of numerous functional groups.[15] In continuation of our interest on the halogenation reactions using environmentally benign, easy to handle and relatively inexpensive reagents[16] we wish to report herein a very simple, mild and efficient method for the direct synthesis of bromoformates and bromoacetates from olefins using NH_4Br as a bromine source, oxone® as an oxidant and *N*,*N*-dimethyl formamide (DMF)/*N*,*N*-dimethyl acetamide (DMA) as nucleophile sources without employing a catalyst (Scheme 1)

Earlier we reported a method for the bromohydroxylation of olefins using NH_4Br and oxone® in CH_3CN/H_2O (1:1) reaction medium.[16e] Under similar reaction conditions, the reaction was investigated with a variety of solvents using styrene as a model substrate. When DMF was used as a reaction medium, instead of bromohydrin, the bromoformyloxylation product was observed. Stimulated by these affirmative preliminary results, subsequently, we considered to develop a methodology for bromoformyloxylation of olefins.

Having optimized the reaction conditions, we subjected a variety of olefins (terminal aromatic, heteroaromatic, polyaromatic, aliphatic, 1,2-disubstituted unsymmetrical and symmetrical alkenes) to the bromoformyloxylation process to explore its scope and generality. The results are summarized in Table 2. Aromatic terminal alkenes with activated phenyl ring including 4-methylstyrene (**1b**) and 2,4-dimethylstyrene (**1c**) afforded the respective bromoformate products **2b** and **2c** in 87% and 90% yields, respectively (Table 2), whereas, 3-nitrostyrene (**1f**) provided the corresponding product in 73% yield (Table 2, entry 6). Halo substituted styrenes such as 4-chlorostyrene (**1d**) and 4-bromostyrene (**1e**) generated the corresponding bromoformate products **2d and 2e** in excellent yields due to inductive and resonance effect of halogen (Cl, Br) groups (Table 2). Heteroaromatic alkene **1g** and polyaromatic alkene **1h** also reacted smoothly and provided the respective vicinal bromoformate products **2g** and **2h** in 83% and 84% yields, respectively (Table 2). The above results indicate that, there is no significant effect of the electronic nature of aromatic ring on the bromoformyloxylation of terminal aromatic olefins.

Subsequently, 1,2-disubstituted unsymmetrical and symmetrical olefins were submitted to the vicinal bromoformyloxylation and obtained the corresponding products **2i-2q** in good to excellent yields with moderate to excellent diastereoselectivity (Table 2). In all cases complete regio- and predominant *trans*-diastereoselective addition was observed. Unsymmetrical and symmetrical *trans*-alkenes (**1i-1m**) yielded the corresponding *erythro* bromoformate products **2i-2m** in 72-90% yields (Table 2). Whilst, symmetrical *cis*-alkene i.e. *cis*-stilbene (**1n**) proceeded to give the diastereomeric mixture of bromoformates **2n** in 93% (dr 3.65:1) yield (Table 2), unsymmetrical cyclic olefins, such as indene (**1o**) and 1,2-dihydronaphthalene (**1p**) reacted smoothly and furnished the vicinal bromoformate products **2o** and **2p** in 89% (dr 9.99:1) and 85% (dr 44.45:1) yields, respectively (Table 2). Similarly, symmetrical cyclic olefin **1q** produced the respective vicinal bromoformate product **2q** in 70% (dr 5.99:1) yield (Table 2). In case of aliphatic linear olefins regioselectivity was not observed, for example 1-octene (**1r**) and *trans*-2-octene (**1s**) gave the corresponding Markovnikov's products (**2r** and **2s**) as well as *anti*-Markovnikov's products (**2r^1** and **2s^1**) (Table 2, entries 18 and 19).

Encouraged by these results, we also successfully carried out the bromoacetoxylation of various olefins by using DMA as a nucleophilic solvent under similar reaction conditions and obtained the corresponding products in moderate to

excellent yields (Table 3). Olefins having either moderately activated (**1b-1c**) or inactivated arenes (**1d-1f**) reacted smoothly and rendered the respective vicinal bromoacetate products **3b**-**3f** in 52-80% yields (Tables 3). Heteroaromatic olefin (**1g**) and 2-vinylnaphthalene (**1h**) also furnished the corresponding bromoacetate products **3g** and **3h** in 62% and 82% yields, respectively (Tables 3). Unsymmetrical *trans*-alkenes **1i-1k** selectively formed the corresponding *erythro* isomers **3i-3k** (Table 3). In case of symmetrical olefins, such as *trans*- and *cis*-stilbenes **1l-1m**, gave a diastereomeric mixture of bromoacetates **3l** and **3m** in 82% (dr 2.8:1) and 88% (dr 1.51:1) yields, respectively (Table 3). Similarly, cyclic olefins including indene (**1n**) and cyclohexene (**1o**), afforded the respective vicinal bromoacetate products **3n** and **3o** in 63% (dr 11.6:1) and 58% (dr 10:1) yields, respectively (Table 3). Moreover, the aliphatic terminal and internal alkenes such as 1-octene (**1p**) and *trans*-2-octene (**1q**) produced the corresponding vicinal bromoacetate products in 71% (as a mixture of regioisomers **3p** and **3p**[1]) and 94% (as a mixture of regioisomers **3q** and **3q**[1]) yields, respectively, (Table 3, entries 16 and 17). 1,4-Naphthoquinone (**1v**) furnished the 2-bromo-1,4-naphthoquinone (**2v**) instead of the expected bromoformate/bromoacetate products in 40% yield (Scheme 2). Bromoformyloxylation/bromoacetoxylation of electron deficient double bond in coumarin failed to react (Table 2, entry 20 and Table 3, entry 18). In case of benzofuran, a complex mixture of products was obtained which contained virtually no bromoformate/bromoacetate products (Table 2, entry 21 and Table 3, entry 19).

In the case of aromatic olefins, the incoming nucleophile attacks exclusively at the benzylic position of cyclic intermediate.[17] The regioselectivity of aromatic olefins can be explained by considering the fact that the α-position (benzylic) is more positive than the β-position due to the presence of the aromatic ring. As seen from Tables 2 and 3, it is evident that, the bromoformyloxylation and acetoxylation of 1,2-disubstituted alkenes provided the corresponding bromoformate and acetate products with predominant *anti*-stereoselectivity. The stereochemistry of the vicinal bromoformate and acetate products was established based on ^{1}H NMR spectroscopy by comparing chemical shift (δ) and coupling constant (J) values of protons attached to the carbons bearing –OCHO/–$OCOCH_3$ and -Br groups with previously reported data (*see* Supporting Information).

A probable mechanistic pathway to explain the regio- and stereoselectivity of the bromoformyloxylation and bromoacetoxylation of olefins is depicted in Scheme 3. It is assumed that oxidation of bromide ion (Br^-) by oxone® could generate the hypobromite ion (HO^-Br^+) *in situ*, which further reacts (electrophilic addition) with olefin **I** to give a three-membered cyclic bromonium ion intermediate **II**. The cyclic intermediate **II** undergoes ring opening by the oxygen of DMF or DMA via S_N2 pathway to produce an iminium ion **III** intermediate, which upon hydrolysis gave the vicinal bromoformate/acetate product **IV**.

In conclusion, we have reported a selective, highly efficient and convenient protocol for the regio- and stereoselective bromoformyloxylation as well as bromoacetoxylation of olefins using NH_4Br/oxone® in DMF/ DMA (nucleophile sources) without employing catalyst. This method is applicable to different kinds of olefins, such as terminal aromatic, 1,2-disubstituted unsymmetrical and symmetrical olefins. The noteworthy feature of the present method is the use of NH_4Br/oxone® system as a mild, non-toxic, economically acceptable and inexpensive reagent system coupled with simple operation and formation of cleaner products with high yields.

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Supplementary data

General procedure, spectroscopic data, and copies of ^1H and ^{13}C NMR spectra.

References and notes

1. (a) Singh, S.; Singh, B. *Ind. Eng. Chem. Res.* **2007**, *46*, 983; (b) Taber, D. F.; Liang, J. I. *J. Org. Chem.* **2007**, *72*, 431; (c) Minakata, S.; Yoneda, Y.; Oderaotoshi, Y.; Komatsu, M. *Org. Lett.* **2006**, *8*, 967; (d) Yeung, Y. Y.; Gao, X.; Corey, E. J. *J. Am. Chem. Soc.* **2006**, *128*, 9644; (e) Urankar, D.; Rutar, I.; Modec, B.; Dolenc, D. *Eur. J. Org. Chem.* **2005**, *11*, 2349; (f) Muñiz, K. *New J. Chem.* **2005**, *29*, 1371; (g) Phukan, P.; Chakraborty, P.; Kataki, D. J. *J. Org. Chem.* **2006**, *71*, 7533.

2. (a) Rodriguez, J. M.; Dulcère, J. P. *Synthesis* **1993**, 1177; (b) Da Silva, F. M.; Jones, J. J.; De Mattos. M. C. S. *Curr. Org. Synth.* **2005**, *2*, 393; (c) Roocker, A.; Radzitzky, P. *Bull. Soc. Chim. Belg.* **1970**, *79*, 531; (d) Micev, I.; Christova, N.; Panajotova, B.; Jovtscheff, A. *Chem. Ber.* **1973**, *106*, 606; (e) Kim, J. N.; Kim, H. R.; Ryu, E. K. *Synth. Commun.* **1992**, *22*, 2521.

3. Kolb, H. C.; Sharpless, K. B. *Tetrahedron* **1992**, *48*, 10515.

4. Dalton, D. R.; Smith, R. C. J.; Jones, D. G. *Tetrahedron* **1970**, *26*, 575.

5. De Souza, A. V. A.; Mendonça, G. F.; Bernini, R. B.; De Mattos, M. C. S. *J. Braz. Chem. Soc.* **2007**, *18*, 1575.

6. (a) Niizato, H.; Ueno, Y.; Takemura, S. *Chem. Pharm. Bull.* **1972**, *20*, 2707; (b) Ueno, Y.; Yamasaki, A.; Terauchi, H.; Takemura, S. *Chem. Pharm. Bull.* **1974**, *22*, 1646.

7. Almeida, L. S.; Esteves, P. M.; Marcio, C. S.; De Mattos, M. C. C. *Synlett* **2006**, *10*, 1515.

8. Chen, F.; Jiang, X.; Cheng, E. J.; Yeung, Y. Y. *Tetrahedron Lett.* **2010**, *51*, 3433.

9. Pandit, P.; Gayen, K. S.; Khamarui, S.; Chatterjee, N.; Maiti, D. K. *Chem. Commun.* **2011**, *47*, 6933.

10. Negoro, T.; Ikeda, Y. *Bull. Chem. Soc. Jpn.* **1986**, *59*, 3519.

11. Ahmad, S. M.; Braddock, D. C.; Cansell, G.; Hermitage, A. S.; Redmonda, M. J.; Whitea, J. P. A. *Tetrahedron Lett.* **2007**, *48*, 5948.

12. Saikia, I.; Krishna, K. R.; Phukan, P. *Tetrahedron Lett.* **2012**, *53*, 758.

13. Oromí-Farrús, M.; Eras, J.; Villorbina, G.; Illorbina, M.; Torres, M.; Llops-Mestre, V.; Welton, T.; Canela, R. *Anal. Sci.* **2008**, *24*, 1341.

14. Anand, N.; Kapoor, M.; Koul, S.; Taneja, S. C.; Sharma, R. L.; Qazi, G. N. *Tetrahedron: Asymmetry*, **2004**, *15*, 3131.

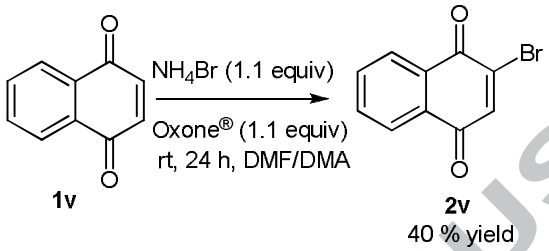
15. Hussain, H.; Green, I. R.; Ahmed, I. *Chem. Rev.* **2013**, *113*, 3329.

16. (a) Mohan, K. V. V. K.; Narender, N. *Synthesis* **2012**, *44*, 15; (b) Kumar, M. A.; Rohitha, C. N.; Reddy, M. M.; Swamy, P.; Narender, N. *Tetrahedron Lett.* **2012**, *53*, 191; (c) Reddy, M. M.; Kumar, M. A.; Swamy, P.; Narender, N. *Tetrahedron Lett.* **2011**, *52*, 6554; (d) Swamy, P.; Kumar, M. A.; Reddy, M. M.; Narender, N. *Chem. Lett.* **2012**, *41*, 432; (e) Kumar, M. A.; Rohitha, C. N.; Narender, N. *Tetrahedron Lett.* **2012**, *53*, 1401; (f) Kumar, M. A.; Naresh, M.; Rohitha, C. N.; Narender, N.; *Synth. Commun.* **2013**, *43*, 3121; (g) Naresh, M.; Kumar, M. A.;

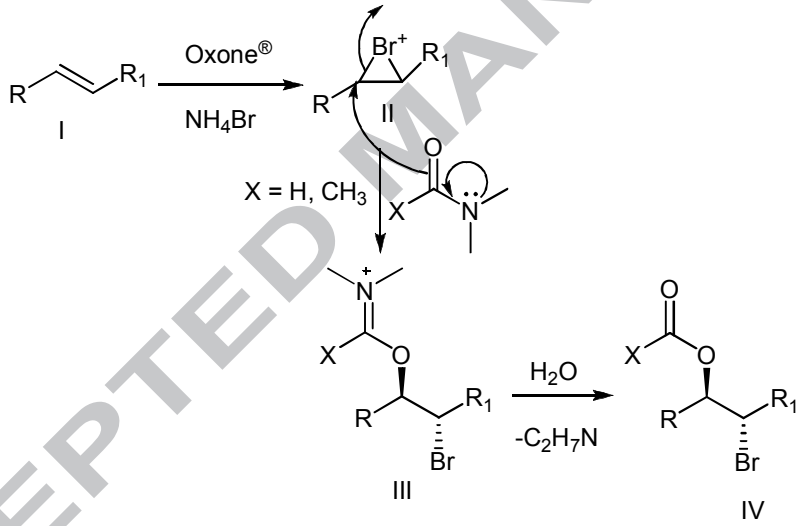
Reddy, M. M.; Swamy, P.; Nanubolu, J. B.; Narender, N. *Synthesis* **2013**, *45*, 1497.

17. (a) Desai, A.; Ren, H.; Mukherjee, M.; Wulff, W. D. *Org. Process Res & Dev*, **2011**, *15*, 1108; (b) Ren, H.; Wulff, W. D. *Org. Lett.* **2010**, *12*, 4908.

Scheme 1. Synthesis of vicinal bromoformates and acetates



Scheme 2.



Scheme 3. Plausible reaction mechanism