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Short communication

Ammonium acetate catalyzed improved method for the regioselective conversion of olefins into halohydrins and haloethers at room temperature☆

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Abstract

An efficient and rapid method has been developed for the synthesis of vicinal bromo-/iodohydrins and β-bromo-/β-iodoethers from alkenes and *N*-bromo-/*N*-iodosuccinimides employing ammonium acetate (NH_4OAc) in water or alcohols. The reaction takes place at room temperature within short reaction times and with excellent regioselectivity.

Keywords: Alkene; Bromohydrin; Iodohydrin; β-Bromoethers; β-Iodoethers; NH_4OAc

Selective vicinal functionalization of alkenes with the functional groups such as hydroxy or alkoxy and halogen finds applications in various useful organic transformations [1]. The resulting halohydrins and alkoxyhalides are important building blocks of different compounds valuable to organic, medicinal as well as industrial chemistry [2]. The most common method for the preparation of halohydrins involves ring opening of epoxides [3] or cyclic sulfate [4] by hydrogen halides or metalhalides. These procedures generally associated with the formation of by-products such as vicinal dihalides and diols [3c,d]. In general heterolytic additions of water and halogen to an alkene involves the use of molecular halogen, *N*-halosuccinimides [5], $TsNBr_2$ [6], *N*-halosaccharin [7] or metal halides along with an oxidizing agent [8]. However, in terms of handling and availability, *N*-halosuccinimide is a superior brominating agent. A major advantage of the use of NBS or NIS is that the by-product, succinimide can be easily recovered and converted to NBS or NIS. *N*-Halosuccinimides were previously used [5] alone or in the presence of an activator to prepare halohydrins. However, it is still desirable to discover improved method (in terms of the reaction times and yields) to utilize these reagents efficiently for halohydroxylation and haloalkoxylation of olefins under mild reaction conditions.

Development of newer and environmentally preferred synthetic methodologies in organic chemistry has been an important area of current research. In continuation to our endeavors towards the development of efficient and ecofriendly synthetic methodologies for halogenations [3f,9], we observed that olefins are rapidly converted into bromo-/iodohydrins and β-bromo-/β-iodoethers using *N*-bromo-/*N*-iodosuccinimede and catalytic amount of ammonium acetate (NH_4OAc) (Scheme 1).

We studied the formation of bromo- or iodohydrins from olefins using NBS or NIS and catalytic amount of NH_4OAc in water–acetone (1:4) (Table 1). The conversion proceeded at room temperature and the reaction took place within short time to afford the products in moderate to excellent yields. Styrene derivatives (entries a–f) are rapidly reacted with NBS or NIS to form bromo-/iodohydrins within 5–10 min, while *O*-allyl phenol derivatives (entries h–k) required somewhat longer times (25–45 min) to furnish the products with moderate yields. 4-Methyl styrene (entries e and f) produced the corresponding halohydrins significantly without halogenations of the alkyl side-chain. Reaction of cyclic alkenes (entries l–s) with NBS or NIS provided *trans*-products **2l–2s** with excellent yields. Aliphatic olefins including 4-pentenoicacid (entries g, u and v) were also converted smoothly to halohydrins under the similar conditions.

We determined the scope of this procedure, in preparing a series of alkoxybromides and alkoxyiodides from styrene using NH_4OAc, NBS or NIS and different alcohols (Table 2). These

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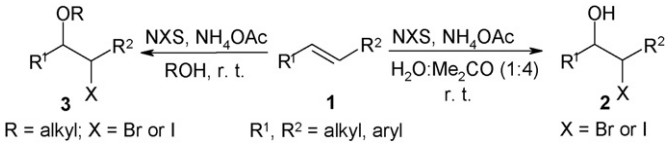


Scheme 1.

reactions also proceeded at room temperature to form the products with high yields. The structures of the products were settled from their spectral (^{1}H NMR and MS) data.

NH_4OAc is commercially available in the form of delequesc crystals with acetous odor. It is also easy to prepare from acetic acid and ammonia [10]. NH_4OAc is a convenient replacement for ammonia in many reactions which would otherwise required pressure, for example enamination of 1,3-dicarbonyl compounds [11]. It is found to be an ultimate nitrogen source and as well as catalyst in many applications in organic synthesis, such as synthesis of pyrolidines [12a], *N*,*N*-bidentate lignads [12b] and imidazoles [12c,d], selective deprotection of aromatic acetates [12e] and α-bromination of ketones [12f]. Regarding mechanism of the reaction it may be mentioned here that the reaction of NBS with NH_4OAc is known [12f] to produce HOAc and HBr which can polarize the >N–Br bond of NBS and facilitate the bromination reaction of olefins. In the absence of NH_4OAc the reaction of *O*-allyl phenol with NBS required 6 h to produce 55% of the corresponding bromohydrin in water and acetone (1:4) at room temperature, while with NBS/NH_4OAc the reaction took only 25 min to form the products with an yield of 91%. Styrene produced **2a** with better yields in shorter reaction time in the presence of NH_4OAc along with NBS instead of NBS alone.

In summary, we have developed a regioselective method for the hydroxyhalogenation and alkoxyhalogenation of olefins

Table 1
Synthesis of bromo-/iodohydrins using NH_4OAc and NBS/NIS[a]

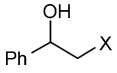
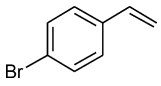
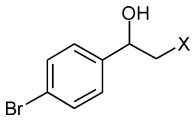
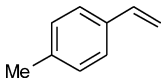
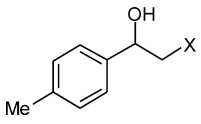
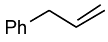
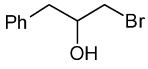
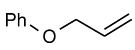
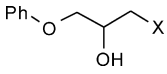
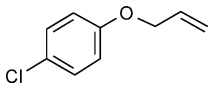
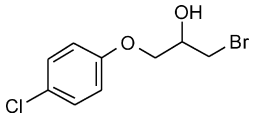
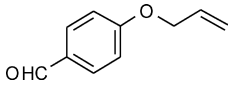
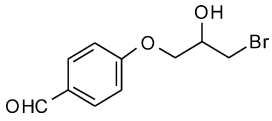
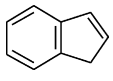
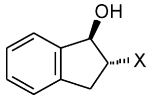
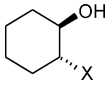
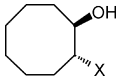
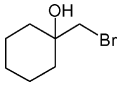
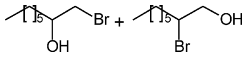
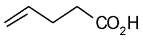
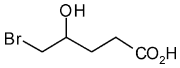
Entry	Alkene (**1**)	Time (min)	Product (**2**)	Isolated yield (%)	Reference
					
a		5	X = Br	92	[5i]
b		5	X = I	92	[5i]
					
c		10	X = Br	93	[5i]
d		10	X = I	95	–
					
e		10	X = Br	94	[5i]
f		10	X = I	94	[5j]
g		10		92	[5j]
					
h		25	X = Br	91	[5i]
I		25	X = I	91	[5i]
j		30		90	[5j]
k		45		87	[5j]
					

Table 1 (*Continued*)

Entry	Alkene (**1**)	Time (min)	Product (**2**)	Isolated yield (%)	Reference
l		10	X = Br	93	[5i]
m		10	X = I	95	[5j]
					
n		15	X = Br	91	[5j]
o		15	X = I	90	[5j]
					
p		15	X = Br	92	[5i]
q		15	X = I	92	[5i]
					
r		20	X = Br	85	[5j]
s		20	X = I	87	[5j]
t		15		89	[5i]
u		20		70&17	[5j]
v		20		80	–

[a] Structures of the products were settled from their spectral (^{1}H NMR and MS) data.

using *N*-halosuccinimides in the presence of NH_4OAc. The mild reaction conditions, simple experimental procedures, rapid conversion, clear reaction profiles, excellent yields and high regioselectivity are the noteworthy advantages of the present protocol.

1. Experimental section

1.1. Experimental procedure for the preparation of bromo-/iodohydrins

To a suspension of olefin (1 mmol) and NH_4OAc (10 mol%) in acetone (4 ml), NBS/NIS (1.10 mmol) and water (1 ml) were added and the mixture was stirred at room temperature. After completion of the reaction as indicated by TLC the mixture was concentrated in vaco and extracted with EtOAc-H_2O (1:1) (3× 5 ml). The organic portion was concentrated and the residue was subjected to column chromatography (silica gel, hexane-EtOAc) to obtain pure bromo-/iodohydrins.

The spectral (^{1}H NMR and MS) data of some representative products are given below.

*1.1.1. Compound **2d***

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.48 (2H, d, J = 8.0 Hz), 7.42 (2H, d, J = 8.0 Hz), 4.83 (1H, dd, J = 8.3, 3.0 Hz), 3.57 (1H, dd, J = 11.8, 3.0 Hz), 3.44 (1H, dd, J = 11.8, 8.3 Hz), 2.71 (1H, brs); EIMS: *m*/*z* 324, 326 ($M^{+\bullet}$).

*1.1.2. Compound **2o***

^{1}H NMR (200 MHz, $CDCl_3$): δ 4.45 (1H, m), 4.04 (1H, m), 2.40 (1H, m), 2.21–1.75 (5H, m), 1.59 (1H, m); EIMS: *m*/*z* 212 ($M^{+\bullet}$).

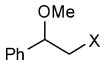
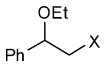
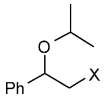
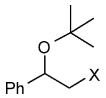
*1.1.3. Compound **2v***

^{1}H NMR (200 MHz, $CDCl_3$): δ 9.02 (1H, brs), 4.75 (1H, m), 3.67–3.46 (2H, m), 2.77 (1H, brs), 2.71–2.39 (3H, m), 2.15 (1H, m); EIMS: *m*/*z* 196, 198 ($M^{+\bullet}$).

1.2. Experimental procedure for the preparation of β-bromo-/β-iodoethers

To a suspension of styrene (1 mmol) and NH_4OAc (10 mol%) in an alcohol (3 ml), NBS (1.10 mmol) was added and the mixture was stirred at room temperature for appropriate time (Table 2). After completion of the reaction (as TLC indicated) the mixture was concentrated and extracted with EtOAc-H_2O (1:1) (3× 5 ml). The organic portion was concentrated and the residue was chromatographed over silica gel using hexane-EtOAc as an eluent to get pure β-bromo-/β-iodoethers.

Table 2
Synthesis of β-bromo-/β-iodo ethers using styrene, NH_4OAc and NBS/NIS[a]

Entry	Alcohol	Time (min)	Product (**3**)	Isolated yield (%)	Reference
	MeOH				
a		5	X = Br	96	[6]
b		5	X = I	98	[5e]
	EtOH				
c		5	X = Br	97	–
d		5	X = I	97	[5e]
	^{iso}PrOH				
e		15	X = Br	93	–
f		15	X = I	96	[5e]
	^{t}BuOH				
g		20	X = Br	90	[6]
h		20	X = I	92	[5e]

[a] Structures of the products were settled from their spectral (^{1}H NMR and MS) data.

The spectral (^{1}H NMR and MS) data of some representative products are given below.

*1.2.1. Compound **3c***

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.50–7.13 (5H, m), 4.42 (1H, dd, *J* = 7.8, 4.6 Hz), 3.53–3.29 (4H, m), 1.21 (3H, t, *J* = 7.0 Hz); EIMS: *m/z* 228, 230 ($M^{+\bullet}$).

*1.2.2. Compound **3e***

^{1}H NMR (200 MHz, $CDCl_3$): δ 7.48–7.17 (5H, m), 4.52 (1H, dd, *J* = 8.5, 4.6 Hz), 3.61–3.28 (3H, m), 1.22 (3H, d, *J* = 6.2 Hz), 1.08 (3H, d, *J* = 6.2 Hz); EIMS: *m/z* 242, 244 ($M^{+\bullet}$).

Acknowledgements

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