A Novel Method for the Conversion of Halide Anion to the Positive Halogen by Nitrobenzenesulfonyl Peroxide. Application to Oxyhalogenation of Olefin

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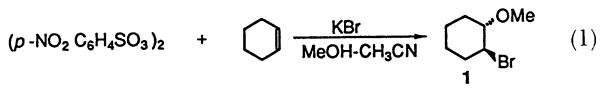
Synopsis. Bromide and chloride anions could be readily oxidized into positive halogens by treating with *p*-nitrobenzenesulfonyl peroxide. The positive halogens, thus formed, reacted with olefins to give epihalonium ions, which were trapped by oxygen nucleophiles inter- or intramolecularly to afford oxyhalogenated compounds.

Nitrobenzenesulfonyl peroxides ($(NO_2C_6H_4SO_3)_2$: NBSP) behave as good electrophiles, and have been used for various synthetic reactions.[1-3] The displacement on the O-O bond of NBSP by various nucleophiles occurs easily to introduce sulfonyloxy groups into the nucleophiles; the initially sulfonyloxylated products are expected to be used in subsequent process due to the effective leaving power of nitrobenzenesulfonyloxy groups. From these viewpoints, we have been exploring novel methods for the conversion of stable substrates into very reactive electrophilic reagents.[2,3] In the course of our studies, we found that chloride and bromide anions could be oxidized by NBSP into positive halogens, which were applied to the electrophilic halogenations of aromatic rings.[2] In this paper we wish to report on the oxyhalogenation of olefins using a combination of NBSP with hailde anions in the presence of water or alcohols.

Though NBSP attacks the π-bond of simple olefins readily, the resulting products are often complex.[1,4] Probably because a powerful inductive effect of the sulfonyloxy group destablizes the cation intermediate, a variety of reactions occur rapidly. We found, however, that when potassium bromide (1.0 mmol) is added to a solution of *p*-nitrobenzenesulfonyl peroxide (*p*-NBSP; 1.0 mmol) and cyclohexene (1.0 mmol) in 10 ml of methanol-acetonitrile (1 : 1) at 0 °C, anti-adduct (**1**) of bromine and methoxyl groups to cyclohexene was obtained in 88% yield.



(1)

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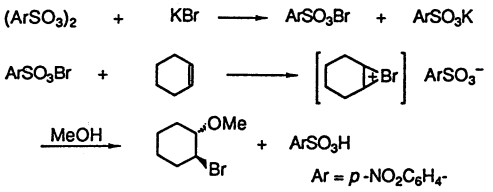
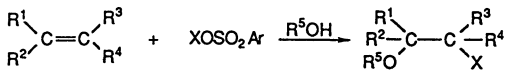
The mechanism shown in Scheme 1 is proposed. *p*-NBSP reacts with bromide anion in preference to cyclohexene to produce *p*-nitrobenzenesulfonyl hypobromite. The hypobromite reacts with cyclohexene to give epibromonium *p*-nitrobenzenesulfonate. Since the nucleophilicity of the sulfonate is weak, the attack of methanol on the epibromonium ion predominates over that of sulfonate. The stereospecific anti-addition observed in this reaction supports the formation of epibromonium salt.



Scheme 1.

The additions of bromine and other groups across double bond have been well-known, and various positive halogen sources have been studied.[5] Although bromine can be used for oxybromination, the bromide ion acts as a nucleophile which competes with methanol.[5] If it is desired to favor the introduction of methanol, it is clear that both the concentration and nucleophilicity of the competing anion should be kept as low as possible. Owing to the strong electron-withdrawing effect of sulfonyloxy group, the bromine in sulfonyl hypobromite behaves as a very reactive electrophile, while the counter anion, *p*-nitrobenzenesulfonate, is a very weak nucleophile. Thus, sulfonyl hypobromite is expected to be a very good reagent for oxybromination. Although trifluoromethanesulfonyl hypobromite is known to be prepared and act as one of the most electrophilic halogen compounds, its preparation and handling are not easy.[6] In our method, potassium bromide, which is stable and easy to handle, could be readily converted into very reactive positive halogen by *p*-NBSP.[7] Thus, various addition reactions of bromine or chlorine with nucleophile into olefins were examined; the results are given in Table 1.



(2)

2: $R^1=R^3=-(CH_2)_4-$ $R^2=R^4=R^5=H$ X = Br
3: $R^1=R^3=-(CH_2)_4-$ $R^2=R^4=H$ $R^5=Ac$ X = Br
4a: $R^1=C_4H_9$ $R^2=R^3=R^4=H$ $R^5=Me$ X = Br
4b: $R^3=C_4H_9$ $R^1=R^2=R^4=H$ $R^5=Me$ X = Br
5: $R^1=Ph$ $R^2=R^3=R^4=H$ $R^5=Me$ X = Br
6: $R^1=R^3=-(CH_2)_4-$ $R^2=R^4=H$ $R^5=Me$ X = Cl
7a: $R^1=C_4H_9$ $R^2=R^3=R^4=H$ $R^5=Me$ X = Cl
7b: $R^3=C_4H_9$ $R^1=R^2=R^4=H$ $R^5=Me$ X = Cl
8: $R^1=Ph$ $R^2=R^3=R^4=H$ $R^5=Me$ X = Cl

Water and acetic acid were examined as nucleophiles in the reactions of cyclohexene with hypobromite. Water reacted with the epibromonium ion to give cyclohexane bromohydrin (**2**), whereas acetic acid

Table 1. Oxyhalogenation of Olefin

Run	Olefin	Nucleopile	Method[a]	Salt	Products	Yield/%[b]
1	Cyclohexene	MeOH	A	KBr	**1**	88
2	Cyclohexene	H_2O	A	KBr	**2**	51
3	Cyclohexene	AcOH	A	KBr	**3**	0[c]
4	1-Hexene	MeOH	A	KBr	**4**	89[d]
5	Styrene	MeOH	B	KBr	**5**	91
6	Styrene	MeOH	B	KBr[e]	**5**	93
7	Styrene	MeOH	B	Et_3NHBr	**5**	86
8	Cyclohexene	MeOH	A	Et_3NHCl	**6**	50
9	1-Hexene	MeOH	A	Et_3NHCl	**7**	80[d]
10	Styrene	MeOH	B	Et_3NHCl	**8**	86

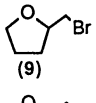
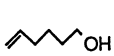
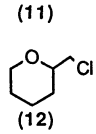
a) See Experimental part. b) Yields were determined by GC based on *p*-NBSP. c) 1,2-Dibromocyclohexane (44%) and *N*-(2-bromohexyl)acetamide (15%) were obtained. d) Ratios of **4a** : **4b**=75 : 25, and **7a** : **7b**=54 : 46. e) 18-Crown-6 (0.025 mmol) was added.

did not; in the latter case the epibromonium ion reacted with excess bromide anion to afford dibromo compounds (Table 1, runs 2 and 3). The addition of bromine and methoxy groups could be introduced into 1-hexene to give **4a** and **4b** by similar procedure (Table 1, run 4). *p*-NBSP reacted rapidly with styrene before the addition of potassium bromide. Therefore, the potassium bromide (0.5 mmol) was allowed to react with *p*-NBSP (0.5 mmol) in advance in 5 ml of acetonitrile for 1 h; the reaction mixture was then added to a solution of styrene (1.0 mmol) in methanol (5 ml) (Table 1, run 5). The reaction time of bromide anion with *p*-NBSP could be reduced to 15 min when 0.025 mmol of 18-crown-6 was added to a reaction system of potassium bromide with *p*-NBSP or triethylamine hydrobromide was used as a bromide anion source (Table 1, runs 6 and 7). Though chlorinations could be achieved to afford **6**, **7**, and **8**, respectively, by a similar procedure, in this case triethylamine hydrochloride was better than potassium chloride as a chloride anion source (Table 1, runs 8—10).

Intramolecular ring closure by electrophilic activation of an unsaturated alcohol is a useful synthetic methodology for the synthesis of complex natural products. Reagents composing of reactive electrophiles and weak nucleophiles are expected to have a particular advantage of being applicable for cyclofunctionalization. We thus examined cyclizations of 4-penten-1-ol and 5-hexen-1-ol using our method for the preparation of positive halogens; the results are summarized in Table 2. 2-(Bromomethyl)tetrahydrofuran (**9**) and 2-(bromomethyl)tetrahydropyran (**10**) were obtained selectively in good yields (Table 2, runs 1 and 2). The cyclizations by positive chlorine were not so effective compared with bromine (Table 2, runs 3 and 4).

Halide anions, which are stable and easy to handle, could be readily converted into very reactive, versatile sulfonyl hypohalite. Since cations which have stable counter anions, such as trifluoromethanesulfonate, often show high and unique reactivities,[8] the method for the formation of positive halogen described herein is expected to be very attractive and potentially useful in organic synthesis.

Table 2. Cyclization of Unsaturated Alcohol

Olefin	Salt	Product	Yield/%[a]
	Et_3NHBr	 (9)	90
	Et_3NHBr	 (10)	62
	Et_3NHCl	 (11)	24
	Et_3NHCl	 (12)	0

a) Yields were determined by GC based on *p*-NBSP.

Experimental

^1H NMR spectra were taken with a JEOL JNM PMX60SI (60 MHz) spectrometer. ^{13}C NMR spectra were taken with a JEOL JNM Fx90Q FT NMR spectrometer. Gas chromatograph was performed by a Hitachi 263-30 gas chromatograph with a SE-30 (10%) 1 m stainless-steel column. Gel-permeation chromatography was performed by means of a JAI Model LC-08 liquid chromatograph equipped with two JAIGEL-1H columns (20 ϕ×600 mm) and using chloroform as an eluent. Mass spectra were obtained with JEOL JMS DX-300 spectrometer by an electron-impact (EI) ionization technique at 70 eV.

Materials. *p*-Nitrobenzenesulfonyl peroxide was synthesized from *p*-nitrobenzenesulfonyl chloride and hydrogen peroxide according to a method described in the literature; mp 120—122 °C (decomp) (lit, 128 °C (decomp)).[9]

General Procedure for Methoxyhalogenation of Olefins. Method (A): Cyclohexene (1.0 mmol) and *p*-NBSP (0.5 mmol) was dissolved in 10 ml of methanol-acetonitrilie (1 : 1). Solid potassium bromide (1.0 mmol) was added in small portions over 10 min with stirring. The reaction mixture was further stirred for 1 h at 0 °C; the acetonitrile and methanol were then evaporated. From the residue, organic compounds were extracted with dichloromethane (20 ml), and the organic layer was washed twice with water (20 ml). The separated organic layer was dried over anhydrous magnesium sulfate, and the solvent evaporated to give a yellow oil. Column chromatography on a Wakogel C-60

afforded *trans*-1-bromo-2-methoxycyclohexane (**1**) (elution with hexane–ethyl acetate 5:1), which was identified by a comparison of the spectral data with those described in a literature.[10] Similarly, *trans*-1-chloro-2-methoxycyclohexane (**6**)[11] and *trans*-2-bromocyclohexanol (**2**)[12] were obtained and identified by their spectral data. The regioisomers of 1-bromo-2-methoxy- (**4a**) and 2-bromo-1-methoxyhexane (**4b**),[13] and 1-chloro-2-methoxy- (**7a**) and 2-chloro-1-methoxyhexane (**7b**)[10] were also identified as mixtures by their spectral data.

Method (B): Potassium bromide (1.5 mmol) was added to a solution of *p*-NBSP (0.5 mmol) in acetonitrile (5 ml), and the suspension was stirred at 0 °C for 1 h. The supernatant solution was pipetted and then added to a solution of styrene (1.0 mmol) in 5 ml of methanol. The mixture was stirred for 10 min at 0 °C, and then treated with a similar procedure to that described in method (A). 2-Bromo-1-phenyl-1-methoxyethane (**5**) was obtained and the NMR spectrum agreed with the reported one.[14] Similarly, 2-chloro-1-phenyl-1-methoxyethane (**8**) was obtained by the use of triethylamine hydrochloride as a halogen source.[15]

Cyclohalogenations of hydroxyolefins were performed using a similar procedure to method (A) used for methoxyhalogenations. 2-(Bromomethyl)tetrahydrofuran (**9**),[16] 2-(bromomethyl)tetrahydropyran (**10**),[16] and 2-(chloromethyl)tetrahydrofuran (**11**)[17] were obtained and identified by their spectral data.

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