The Rapid and Efficient Synthesis of Bromohydrins from Olefins under HBr/H₂O₂ System by Visible Light Induced

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A simple and safe method has been presented for conversion of olefins into bromohydrins using hydrogen bromide and hydrogen peroxide as bromide source by visible light induced within a very short time to get high yield bromohydrins along with a little mount dibromo-product. In this paper, cyclohexene is firstly carried out as the model substrate and investigated the bromination under HBr/H₂O₂ system using 150 W incandescent light irradiated in CCl₄ within short time to get good yield of 2-bromocyclohexanol along with a little mount of 1,2-dibromocyclohexane; then, a series of alkenes are brominated to corresponding bromohydrins using the same protocol.

Key Words: Alkenes, Bromohydrin, Dibromination, Hydrogen bromide, Hydrogen peroxide

Introduction

Selective vicinal functionalization of alkenes with the functional groups such as hydroxyl or alkoxy and halogen finds applications in various useful organic transformations.[1-2] The resulting halohydrins and alkoxylhalides are important building blocks of different compounds valuable to organic, medicinal as well as industrial chemistry.[3] The most common method for preparation of halohydrins involves ring opening of epoxides[4] or cyclic sulfate[5] by hydrogen halides or metalhalides.

In general heterolytic additions of water and halogen to an alkene involves the use of molecular halogen,[6] *N*-halosuccinimides,[7-10] *N*-halosaccharin[11] or metal halides along with an oxidizing agent,[12] bromates oriodates(V) in combination with NaHSO₃[13] or periodate mediated oxyfunctionalization of organic compounds using alkali metal halides.[14] However molecular bromine in preparative chemistry is a serious cause of concern, due to its toxicity and corroding properties.[15] *N*-bromosuccinimide (NBS) has become for many years the reagent of choice for brominations. However, the atomic yield is still poor and succinimide is obtained as a concomitant product which, although not harmful, must be either disposed or recycled to NBS, and very frequently complicates crystallizations for isolation and purification of products.[16] And others have the drawbacks of toxicity and danger of handling.

Development of newer and environmentally preferred synthetic methodologies in organic chemistry has been an important area of current research. In oxybromination, hydrogen bromide or alkali metal bromide, is being used as a bromine source, hydrogen peroxide (such as H₂O₂) as an oxidant, which is thought to be possible solution to overcome these difficulties.[17-18]

Although HBr/H₂O₂ system also has been using bromohydrin of some olefins, these reactions often occur by some metal catalyzing, such as Sels and co-workers using WO₄²⁻ on layered double hydroxide to carry out the reaction within 24 h to obtain some good yield bromohydrin,[19] Levecque with group also presenting the synthesis of halohydrins and β-halo ethers from dihydropyrans, dihydrofurans and anhydro sugar in the

presence of a halide salt and hydrogen peroxide with tungstate exchanged takovite as oxidant catalyst,[20] and the NH₄VO₃ also being used to catalyze bromination of α-methylstyrene in H₂O to afford the bromohydrin with good yield after 24 h.[21]

We studied the formation of bromohydrin from olefins with a simple and safe method using HBr/H₂O₂ only by visible light induced. The conversion proceeded at room temperature or refluxing and the reaction took place within short time to afford the bromohydrin products in moderate to excellent yields with amount of dibromo-product.
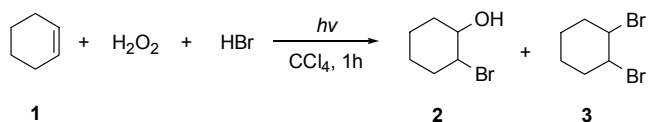
Results and Discussion

At first, we choose the cyclohexene (**1**) as the model substrate and investigate the bromination using HBr/H₂O₂ by visible light induced to yield 2-bromocyclohexanol (**2**) as the main product along with a little mount of 1,2-dibromocyclohexane (**3**) (Scheme 1).

In order to get the optimum bromohydrin reaction condition of cyclohexene, we change the reaction condition, including solvent, temperature *etc* (Table 1).

It has been ascertained previously that only trace bromohydrin **2** produced in the absence of photochemical activation. Similarly, changing in the concentration of substrate, the influence has no obvious effect.

The results show that the low polar solvent is better for getting bromohydrin **2** in the reaction. Chloroform as solvent, it gives a poor bromohydrin **2** product, but satisfactory results are obtained with methylene dichloride and carbon tetrachloride. When compare the reaction in CHCl₃ and in CCl₄ (runs 2 and 5), other conditions being equal, the selectivity of **2** is much lower

Scheme 1

Table 1. The bromination of cyclohexene with H_2O_2/HBr by visible light induced at different condition

Run	Solvent	Temp. (^oC)	Conversion (%)	Selectivity (%)	
				2	**3**
1[b]	CH_2Cl_2	40	90	4.1	95.9
2	CH_2Cl_2	40	100	85.4	14.1
3	$CHCl_3$	60	98	67.5	32.5
4	CCl_4	40	100	86.5	13.5
5	CCl_4	50	100	88.3	11.6
6	CCl_4	60	100	90.8	9.2
7	CCl_4	70	100	92.6	7.4
8	CCl_4	76	100	95.3	4.7
9[c]	CCl_4	76	92.6		45.2
10[d]	CCl_4	76	95.3	43.2	56.8

Condition: Cyclohexene (1 g, 12.2 mmol), 30% H_2O_2 (2.5 mL, 2.0 eq.), 40% HBr (2.7 mL, 1.5 eq.), 10 mL solvent; 150 W incandescent light irradiated, reaction 1 h. [b]Without 150 W incandescent light. [c]NBS was in place of H_2O_2/HBr, 0.02 g BPO was added, the main product was 3-bromocyclohex-1-ene (**4**) (yield 50.8%). [d]Br_2 was in place of H_2O_2/HBr, 150 W incandescent light irradiated.
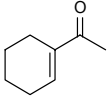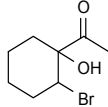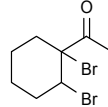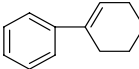
in $CHCl_3$ (only 67.5%) than in CCl_4 (90.8%); the influence of temperature is little for selectivity of bromohydrin in CCl_4 (runs 3-7), with the temperature rising, the selectivity of **2** somewhat increasing, at refluxing temperature, the selectivity of **2** gets to the highest (95.3%); for comparison purposes, bromination of cyclohexene with NBS and molecular bromine in carbon tetrachloride are carried out. Bromination with one equivalent of NBS in the presence of benzoyl peroxide, heating under reflux,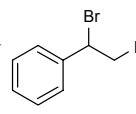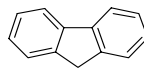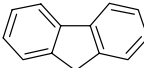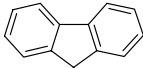 gives a 45.2 : 50.8 mixture of 1,2-dibromocyclohexane (**3**) and 3-bromocyclohex-1-ene (**4**); when with a slight excess (1.1 molar equivalents) of bromine relative to the substrate cyclohexene, the main product is dibromo-product.

On the basis of these results, it can be concluded that the H_2O_2/HBr/light bromination system is better than the NBS and Br_2 in the bromohydrin reaction; additionally, this method is simple and convenient with the easy of the work-up procedure.

Meanwhile, in order to examine this method feasibility, a series of cycloolefins are carried out the bromination with the same method (Table 2).

The results show that some alkenes are brominated with HBr/H_2O_2 by 150 W incandescent light irradiated and the yields of bromohydrins are generally moderate to good. Somewhat differences are observed in proportion of the mixture resulting as function of the electron-donating or electron-withdrawing character of the substituents in olefins. The reaction is slower and the yield of bromohydrin is little less than other olefins when the carbon double-bond connecting with phenyl, maybe for the phenyl electron withdrawing effect and the great steric hindrance effect (runs 2, 4 and 6), such as bromination of 1-phenyl cyclohexene (**6a**), only 78.6% of 2-bromo-1-phenyl-cyclohexanol (**6b**) can be obtained in this condition without 1,2-dibromo-1-phenlcyclohexane; but α-pinene in the same reaction condition gets 93.4% bromohydrin product (**7b**); in the similar condition, fluorene (**9a**) can be brominated with with HBr/H_2O_2 by 150 W incandescent light irradiated and just gets 60.2% 9-bromo-9*H*-fluorene (**9b**) as the major product for methylene connecting with two phenyl, if increasing the

Table 2. A series of olefins bromination with H_2O_2/HBr system by visible light induced

Run	Substrate (a)	Product b	Product c	Time (h)	Yield (%) b	Yield (%) c
1	**5a**	**5b**	**5c**	2	85.3	10.5
2	**6a**	**6b**	**6c**	2.5	78.6	12.9
3	**7a**	**7b**	**7c**	1.5	93.4	5.6
4	**8a**	**8b**	**8c**	2	90.3	7.2
5[b]	**9a**	**9b**	**9c**	3	60.2	
				5	61.3	6.3

Conditions: Olefin (12.2 mmol), 30% H_2O_2 (2.5 mL, 2.0 eq.), 40% HBr (2.7 mL, 1.5 eq.), 10 mL CCl_4; 150 W incandescent light irradiated. [b]Adding 1 eq. Hydrogen bromide and 1 eq. Hydrogen peroxide after reaction 3 h and continue to react 2 h.

amount of hydrogen bromide and hydrogen peroxide after reaction 3 h, the conversion of fluorine somewhat improves along with producing little dibromo-product (**9c**).

In conclusion, we have presented a simple and safe method to obtain good yield of bromhydrin as well as little dibromo-product using H_2O_2/HBr system by visible light induced within a short time at mild condition. Cyclohexene is brominated to get 2-bromocyclohexanol (**2**) as the main product as well as little 1,2-dibromocyclohexane (**3**) using H_2O_2/HBr system by visible light induced after 1 h in CCl_4, and some other olefins also give corresponding bromohydrin from moderate to good yield with the same method. Mild reaction conditions, simple experimental procedures, rapid conversion, clear reaction profiles and good yields are the noteworthy advantages of the present protocol.

Experimental

All compounds were purchased from commercial source and used without further treatment. GC analysis was performed with a flame ionization detector using a 0.2 mm × 30 m capillary column (OV-17). GC-MS spectra were obtained at ionization

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energy of 70 eV. The selectivity of products was estimated from the peak areas based on the internal standard technique by the use of GC. ^{1}H NMR spectra were measured with a Bruker-400 MHz nuclear magnetic resonance spectrometer using TMS as internal reference.

General procedure for brominiation of olefins with H$_2$O$_2$/ HBr by visible light induced. A definite amount of olefin and H$_2$O$_2$ were in solvent 40%, and aqueous HBr was added to the reactants by drops, using 150 W incandescent light irradiated. The mixture was stirred at the temperatures for the reported; The progress of the reaction was monitored by thin-layer chromatography (TLC). After the reaction finishing, the reaction organic layer was separated and washed with water. The organic layer was evaporated on a rotary evaporator and the oily residue was got. Then the sample was taken to GC-MS analysis. And the residue was purified by column chromatography.

2-Bromocyclohexanol (2): m/z 178/180 (M$^+$, 5), 99 (M$^+$-Br, 40), 65 (M$^+$-H- HBr-CH$_2$, 5), 51 (M$^+$-H-HBr-C$_2$H$_4$, 15); ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.88 (q, 1H, CH(1)), 3.63 (q, 1H, CH(2)), 2.43～2.33 (m, 2H(6)), 2.02～1.88 (m, 2H(3)), 1.69～1.59 (m, 2H(4)), 1.49～1.39 (m, 2H(5)).

1,2-Dibromocyclohexane (3): m/z 240/242/244 (M$^+$, 5), 161/ 163 (M$^+$-Br, 20), 81 (M$^+$- Br-HBr, 100), 67 (C$_5$H$_7$$^+$, 10); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.05 (m, 2H, CH-Br), 2.09～1.90 (m, 4H), 1.82～1.64 (m, 4H).

3-Bromocyclohex-1-ene (4): m/z 159/161 (M$^+$-H, 15), 79 (M$^+$- H-HBr, 100), 65 (M$^+$-H-HBr-CH$_2$, 5), 51 (M$^+$-H-HBr-C$_2$H$_4$, 15); ^{1}H NMR (400 MHz, CDCl$_3$) δ 5.73 (q, 2H, CH＝CH), 4.82～4.89 (m, H, CH-Br), 2.23～2.15 (q, 2H(4)), 1.98～1.95 (q, 2H(6)), 1.70～1.55 (m, 2H(5)).

1-(2-Bromo-1-hydroxycyclohexyl)ethanone (5b): m/z 220/ 222 (M$^+$, 2), 202/204 (M$^+$-H$_2$O, 4), 141 (M$^+$-Br, 50), 175 (M$^+$- COCH$_3$, 2), 160 (M$^+$-H$_2$O-COCH$_3$, 15), 123 (M$^+$-HBr-H$_2$O, 17), 111 (M$^+$-Br-H$_2$O-CH$_3$, 2), 81 (M$^+$- H$_2$O-COCH$_3$-Br, 100), 69 (C$_5$H$_9$$^+$, 15), 53 (C$_4H_7$$^+$, 17); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.32 (t, H, CH-Br), 2.33～2.15 (q, 2H(4)), 2.21 (s, 3H, CH$_3$), 2.18～ 1.95 (t, 2H), 1.70～1.55 (m, 4H).

1-(1,2-Dibromocyclohexyl)ethanone (5c): m/z 282/284/286 (M$^+$, 5), 203 (M$^+$-Br, 100), 188/190 (M$^+$-Br-CH$_3$, 20), 124 (M$^+$-2Br, 5), 109 (M$^+$-2Br-CH$_3$, 20), 81 (M$^+$- M$^+$-2Br-COCH$_3$, 7); ^{1}H NMR (400 MHz, CDCl$_3$) δ 4.52 (t, H, CH-Br), 2.75 (t, 2H), 2.69～ 2.61 (q, 2H), 2.32 (s, 3H), 2.30～2.22 (m, 2H), 1.73～1.65 (m, 2H).

2-Bromo-1-phenylcyclohexanol (6b): m/z 254/256 (M$^+$, 15), 175 (M$^+$-Br, 75), 133 (M$^+$-Br, C$_9$H$_9$O$^+$, 100), 105 (C$_7$H$_5$O$^+$, 90), 91 (C$_7$H$_7$$^+$, 20), 77 (C$_6H_5$$^+$, 30), 55 (C$_5H_5$$^+$,45); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.68～7.42 (m, 5H, PhH), 4.45～4.40 (t, 1H, CH-Br), 2.69～2.61 (q, 2H), 2.32 (s, 3H), 2.30～2.12 (m, 4H), 1.73～1.55 (m, 4H).

3-Bromo-2,6,6-trimethylbicyclo[3.1.1]heptan-2-ol (7b): m/z 232/234 (M$^+$, 5); 212 (M$^+$-H$_2$O, 5); 166 (M$^+$-Br, C$_9$H$_9$O$^+$, 100); 135(C$_7$H$_5$O$^+$, 90), 91(C$_7$H$_7$$^+$, 20), 77 (C$_6H_5$$^+$, 30), 55 (C$_5H_5$$^+$, 45). ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.45 (t, 1H(3)), 2.05～1.86 (t, 2H(4)), 1.45～1.41 (m, 1H(5)), 1.49～1.29 (t, 2H, -CH$_2$-), 1.31 (s, 3H, -CH$_3$), 1.11 (s, 6H, -CH$_3$).

2,3-Dibromo-2,6,6-trimethylbicyclo[3.1.1]heptane (7c): m/z 294/296/298 (M$^+$, 3), 215 (M$^+$-Br, 5), 159 (M$^+$-Br-C$_4$H$_8$, 10), 135 (M$^+$-2Br, 80), 107 (M$^+$-2Br-C$_2$H$_4$, 15), 91 (C$_7$H$_9$$^+$, 100), 77

(C$_6$H$_5$$^+$, 20), 69 (C$_5H_9$$^+$, 15), 53 (C$_4H_5$$^+$, 13); ^{1}H NMR (400 MHz, CDCl$_3$) δ 3.82 (t, 1H(1)), 2.12～2.03 (t, 2H(4)), 1.92 (s, 3H, -CH$_3$), 1.82 (t, 1H(1)), 1.49～1.29 (t, 2H, -CH$_2$), 1.42～1.35 (m, 1H(5)), 1.14 (s, 6H, -CH$_3$).

2-Bromo-1-phenylethanol (8b): m/z 200/202 (M$^+$, 5), 120 (M$^+$-HBr, 20), 107 (M$^+$-HBr-CH, 100), 91 (C$_7$H$_7$$^+$, 40); 77 (C$_6H_5$$^+$, 75); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45 (m, 5H, PhH), 5.02 (t, 1H, -CH-), 3.95～3.65 (m, 2H, -CH$_2$Br).

1-(1,2-Dibromoethyl)benzene (8c): m/z 262/262/262 (M$^+$, 20), 183 (M$^+$-Br, 80), 104 (M$^+$-2Br, 100), 77 (C$_6$H$_5$$^+$, 25); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.65～7.61 (m, 1H, PhH), 7.46～7.32 (m, 4H, PhH), 5.35～5.31 (t, 1H, -CHBr-), 4.22～3.97 (m, 2H, -CH$_2$Br).

9-Bromo-9*H*-fluorene (9b): m/z 244/246 (M$^+$, 30), 165 (M$^+$-Br, 100), 82 (C$_6$H$_{10}$+); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.58～ 7.53 (m, 2H, PhH), 7.42～7.32 (m, 6H, PhH), 5.95～5.31 (s, 1H, -CHBr).

9,9-Dibromo-9*H*-fluorene (9c): m/z 322 /324/326 (M$^+$, 50), 243/245 (M$^+$-Br, 100), 163 (M$^+$-2Br, 80), 137 (M$^+$-2Br-C$_2$H$_2$, 5), 122 (M$^+$-2Br-C$_3$H$_5$, 40), 87 (C$_7$H$_4$$^+$, 10), 82 (M$^+$-2Br-C$_6H_9$, 60), 63 (C$_5H_3$$^+$, 15); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.90 (d, 2H), 7.75 (m, 2H), 7.56 (t, 2H), 7.18 (d, 2H).

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