Oxidation of Alcohols and Ethers Using Sodium Bromate-Hydrobromic Acid System

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Reaction of primary alcohols or simple ethers, α,ω-diols or cyclic ethers, and secondary alcohols with sodium bromate in the presence of catalytic amount of hydrobromic acid under mild conditions gave dimeric esters, lactones, and ketones in fairly good yields, respectively.

Sodium bromite ($NaBrO_2$) has recently been noted as a useful reagent in organic synthesis.[1] During the course of our investigation of the synthetic utilities of sodium bromite,[2] we have now recognized that in the presence of hydrobromic acid sodium bromate ($NaBrO_3$) is employed as a useful oxidizing and brominating agent as well as sodium bromite. In this paper, we wish to report an esterification of primary alcohols or simple ethers, lactonization of α,ω-diols or cyclic ethers, and oxidation of secondary alcohols to ketones by use of the sodium bromate-hydrobromic acid system.

Although bromate has recently been studied from the kinetic and catalytic points as oxidizing agent in connection with oscillating reactions such as Belousov-Zhabotinsky reaction,[3] organic syntheses using the above simple system are rarely found in the literature. Farkas et al. already noticed that the treatment of primary alcohols by bromine in the presence of bromate gave the dimeric esters.[4] Since bromine is easily generated from the reaction of bromate with hydrobromic acid, we now tried to obtain the esters from alcohols using the sodium bromate-hydrobromic acid system. Actually, sodium bromate is a commercially available and very stable solid and hence can handle much more easily compared with toxic liquid bromine.

Treatment of the solution of alcohols in carbon tetrachloride with aqueous sodium bromate in the presence of hydrobromic acid at 35—40 °C for 2 h gave the expected esters in excellent yields. The results are given in Table 1.

The reaction of sodium bromate with hydrobromic acid can be presented in the following equations;

$$NaBrO_3 + HBr \longrightarrow HBrO_3 + NaBr \quad (1)$$

$$HBrO_3 + HBr \longrightarrow HBrO_2 + HOBr \quad (2)$$

$$HBrO_2 + HBr \longrightarrow 2HOBr \quad (3)$$

overall:

$$NaBrO_3 + 3HBr \longrightarrow 3HOBr + NaBr \quad (4)$$

Furthermore,

$$HOBr + HBr \rightleftharpoons Br_2 + H_2O \quad (5)$$

We now believe that the major active oxidating species are hypobromous acid and/or bromine, and in either cases, the alcohol accepts Br^+ ion from these species and then transforms to dimeric ester as shown in Eq. 6.

$$2R\text{-}CH_2OH + 2Br^+ \longrightarrow R\text{-}CO_2CH_2R + 2H^+ + 2HBr \quad (6)$$

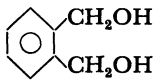
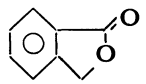
A produced hydrobromic acid may be oxidized by sodium bromate to hypobromous acid (Eq. 4) or bromine (Eqs. 4 and 5) which can be used again to

Table 1. Oxidation of Primary Alcohols and Simple Ethers by $NaBrO_3$-HBr System

Substrate	Solvent	Product	Yield[a]/%
CH_3CH_2OH	CCl_4	$CH_3CO_2CH_2CH_3$	23[b]
$CH_3(CH_2)_2OH$	CCl_4	$CH_3CH_2CO_2(CH_2)_2CH_3$	41[b]
$CH_3(CH_2)_3OH$	CCl_4	$CH_3(CH_2)_2CO_2(CH_2)_3CH_3$	89
$CH_3(CH_2)_4OH$	CCl_4	$CH_3(CH_2)_2CO_2(CH_2)_4CH_3$	93
$(CH_3)_2CH(CH_2)_2OH$	CCl_4	$(CH_3)_2CHCH_2CO_2(CH_2)_4CH(CH_3)_2$	96
$CH_3(CH_2)_5OH$	CCl_4	$CH_3(CH_2)_4CO_2(CH_2)_5CH_3$	96
$CH_3(CH_2)_7OH$	CCl_4	$CH_3(CH_2)_6CO_2(CH_2)_7CH_3$	99
$CH_3(CH_2)_{11}OH$	CCl_4	$CH_3(CH_2)_{10}CO_2(CH_2)_{11}CH_3$	78
$PhCH_2OH$	CCl_4	PhCHO	76
$[CH_3(CH_2)_3]_2O$	CH_2Cl_2	$CH_3(CH_2)_2CO_2(CH_2)_3CH_3$	54
$[CH_3(CH_2)_5]_2O$	CH_2Cl_2	$CH_3(CH_2)_4CO_2(CH_2)_5CH_3$	75

a) Isolated yield. b) The exact yield was not obtained because of the volatility of the product.

Table 2. Lactonization of Diols and Cyclic Ethers by $NaBrO_3$-HBr System

Substrate	Reaction conditions		Solvent	Product	Yield[a]/%
	Time/h	Temp/°C			
$HO-(CH_2)_4-OH$	5	37	CCl_4		78
$HO-(CH_2)_5-OH$	9.5	40	AcOH		40[b]
$HO-(CH_2)_6-OH$	5	37	CCl_4		78
	5	35	AcOH		99
	5	35	CH_2Cl_2		67
	13.5	35	CH_2Cl_2		13

a) Isolated yield. b) δ-Valerolactone was unstable under the reaction conditions.

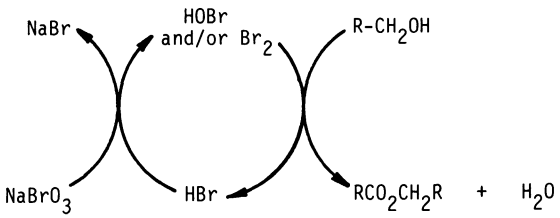


Fig. 1.

oxidize alcohols. Thus, hydrobromic acid is circulated on the reaction cycle as shown in Fig. 1. Actually, the esterification of alcohols by use of sodium bromate proceeds sufficiently in the presence of catalytic amount of hydrobromic acid. The overall reaction equation is as follows. Our experimental results also agreed stoichiometrically with the Eq. 7.

$$6RCH_2OH + 2NaBrO_3 \xrightarrow{\text{HBr (cat.)}} 3RCO_2CH_2R + 2NaBr + 6H_2O \quad (7)$$

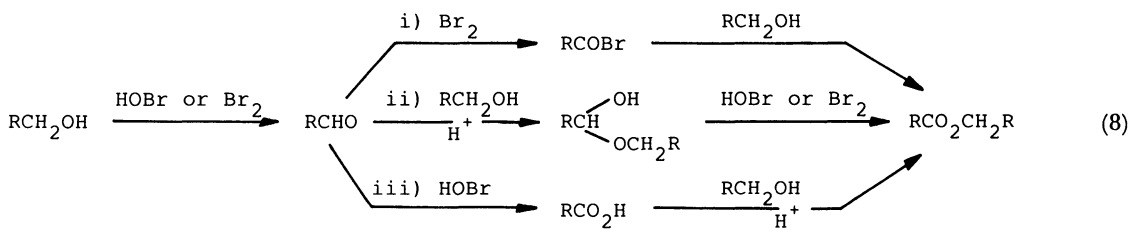
It can be realized that an aldehyde is first produced in the reaction process.[5,6] In fact, benzaldehyde was obtained from the reaction of benzyl alcohol with sodium bromate-hydrobromic acid in good yield (Table 1). The formation of esters may be explained by the three reaction pathways from aldehyde via acid bromide, hemiacetal and carboxylic acid as shown in Eq. 8. However, treatment of the mixture of alcohols (RCH_2OH) and carboxylic acids ($R'-CO_2H$) with sodium bromate-hydrobromic acid system under the adopted conditions gave only the dimeric esters (RCO_2CH_2R). We have considered that the two pathways (i and ii) via acid bromide or hemiacetal[7] may be both available. The more detailed investigation on the effects of the hypobromous acid and/or bromine as major active species is still seeking.

Oxidation of α,ω-diols under identical conditions as alcohols gave the lactones. The reaction scheme is given in Eq. 9 and results are shown in Table 2. In these cases, when product was less stable for bromine, acetic acid was chosen as solvent rather than carbon tetrachloride.

$$3HO-(CH_2)_n-OH + 2NaBrO_3 \xrightarrow{\text{HBr (cat.)}} 3\underbrace{(CH_2)_{n-1}COO} + 2NaBr + 6H_2O \quad (9)$$

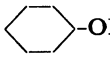
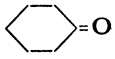
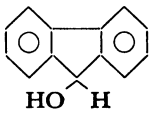
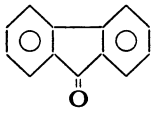
Simple ethers and cyclic ethers also reacted with sodium bromate-hydrobromic acid to afford esters and lactones, respectively. The experimental results are shown in Tables 1 and 2.

Furthermore, oxidation of secondary alcohols with sodium bromate-hydrobromic acid system afforded ketones in good yields. The reaction scheme is given in Eq. 10 and the experimental results are shown in Table 3.



(8)

Table 3. Oxidation of Secondary Alcohols by $NaBrO_3$-HBr System

Substrate	Reaction conditions		Solvent	Product	Yield[a]/%
	Time/h	Temp/°C			
$CH_3CH_2CH(OH)-(CH_2)_2CH_3$	3	40	AcOH	$CH_3CH_2CO(CH_2)_2CH_3$	72
$CH_3(CH_2)_5-CH(OH)-CH_3$	3	40	AcOH	$CH_3(CH_2)_5COCH_3$	98
$PhCH(OH)-CH_3$	3	40	AcOH	$PhCOCH_3$	98
	3	40	AcOH		93
	3	40	AcOH		96
$PhCH(OH)-Ph$	1.5	40	CCl_4	$PhCOPh$	99
	2	40	CCl_4		99

a) Isolated yield.

$$3R\text{-}CH(OH)\text{-}R' + NaBrO_3 \xrightarrow{HBr\ (cat.)} 3R\text{-}CO\text{-}R' + NaBr + 3H_2O \quad (10)$$

In summary, although other procedures exist recently for esterification of primary alcohols[8,9] and ethers,[9] lactonization of α,ω-diols,[1a] and oxidation of secondary alcohols,[1c,9] our methods are more effective and inexpensive to use and applicable to synthesis of dimeric esters from primary alcohols or simple ethers, lactones from α,ω-diols or cyclic ethers, and ketones from secondary alcohols.

Experimental

Preparation of Ester from Alcohol. General Procedure: To a solution of 1-butanol (0.74 g, 10 mmol) in carbon tetrachloride (10 ml) was added a solution of sodium bromate (0.76 g, 5 mmol) in water (10 ml) and then 47% hydrobromic acid (0.15 ml, ca. 1.3 mmol) at room temperature. The reaction mixture was stirred for 2 h at 35—37 °C. The reddish reaction mixture was treated with saturated aqueous sodium carbonate solution (10 ml) and then with 20% aqueous sodium sulfite (10 ml) remove excess bromine. The carbon tetrachloride solution was separated and washed with water (3×10 ml), dried with magnesium sulfate, and evaporated in vacuo to give butyl butanoate as colorless oil; yield: 0.64 g (98%), bp 163—164 °C (lit,[10] bp 165 °C).

Preparation of Ester from Simple Ether. General Procedure: To a solution of dihexyl ether (1.86 g, 10 mmol) in dichloromethane (10 ml) was added a solution of sodium bromate (1.51 g, 10 mmol) in water (10 ml) and then 47% hydrobromic acid (0.3 ml, ca. 2.6 mmol) at room temperature. The reaction mixture was stirred for 20 h at 35—40 °C and treated with saturated aqueous sodium carbonate solution (10 ml) and then with 20% aqueous sodium sulfite (10 ml) to remove excess bromine. The dichloromethane solution was separated and aqueous layer was extracted with dichloromethane (3×10 ml). The combined organic layer was dried with magnesium sulfate, and evaporated in vacuo to give hexyl hexanoate as colorless oil; yield: 1.5 g (75%), bp 244 °C (lit,[11] bp 245.6 °C/761.17 torr).

Preparation of Lactone from α,ω-Diol. General Procedure: To a solution of *o*-xylene-α,α'-diol (0.69 g, 5 mmol) in acetic acid (2 ml) was added a solution of sodium bromate (0.76 g, 5 mmol) in water (10 ml) and then 47% hydrobromic acid (0.15 ml, ca. 1.3 mmol). The reaction mixture was stirred for 5 h at 35—40 °C and then was worked up as described for the preparation of hexyl hexanoate to give phthalide as colorless crystals; yield: 0.66 g (99%), mp 59—62 °C (lit,[12] mp 65 °C).

Preparation of Lactone from Cyclic Ether. General Procedure: To a solution of tetrahydrofuran (0.72 g, 10 mmol) in dichloromethane (10 ml) was added a solution of sodium bromate (1.51 g, 10 mmol) and then 47% hydrobromic acid (1.51 ml, ca. 1.3 mmol) at room temperature. The reaction mixture was stirred for 5 h at 35—40 °C and was worked up as described for the preparation of hexyl hexanoate to give γ-butyrolactone as colorless oil; yield: 0.58 g (67%), bp 197 °C (lit,[10] bp 204 °C).

Preparation of Ketone. General Procedure: To a solution of 2-octanol (1.3 g, 10 ml) in acetic acid (2 ml) was added a solution of sodium bromate (0.76 g, 5 mmol) in water (10 ml) and then 47% hydrobromic acid (0.12 ml, ca. 1.0 mmol) at room temperature. The reaction mixture was stirred for 3 h at 40 °C and was worked up as described for the preparation of butyl butanoate to give 2-octanone as colorless oil; yield: 1.25 g (98%), bp 170—172 °C (lit,[10] bp 172—173 °C).

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