Oxidative Esterification of Primary Alcohols by $NaBrO_3/NaHSO_3$ Reagent in Aqueous Medium

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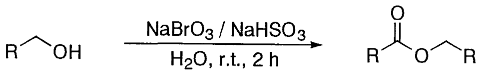
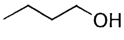
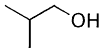
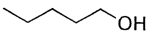
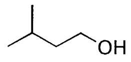
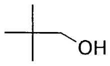
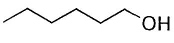
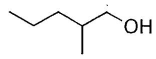
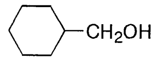
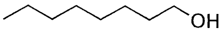
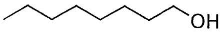
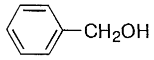
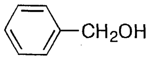
$NaBrO_3$ combined with $NaHSO_3$ was found to be an efficent reagent for the oxidative esterification of primary alcohols. Thus, a variety of esters was prepared from primary alcohols, aldehydes, and acetals in aqueous medium under mild conditions. Treatment of α,ω-diols with $NaBrO_3/NaHSO_3$ reagent afforded the corresponding lactones and/or dicarboxylic acids in fair yields.

Esters are one of the most popular and frequently used compounds in organic chemistry. In particular, they are important as components of fruity deodorants in perfumery industry. The most common methods in preparing of esters are the esterification of carboxylic acids, acid chlorides, or acid anhydrides with alcohols.[1] Ester formation from alcohols has been carried out not only by the stoichiometric oxidation using $Na_2Cr_2O_7$,[2] $Ca(OCl)_2$,[3] $NaBrO_2$,[4] and bromate in the presence of Br_2[5] and HBr,[6] but also by the catalytic oxidation with Pd[7] and Ru[8] complexes.

Recently we have reported that hypohalous acid, XOH (X=I or Br), is readily generated *in situ* from H_5IO_6 or $NaBrO_3$ in the presence of an appropriate reducing agent such as $NaHSO_3$. Thus, H_5IO_6 and $NaBrO_3$ combined with $NaHSO_3$ serve as excellent reagents introducing both X (X=I or Br) and OH functions into carbon-carbon double bonds of a wide variety of olefinic compounds under mild conditions.[9]

Table 1. Oxidative esterification of primary alcohols[a]



Run	Substrate	Ester, %	Acid, %
1		76	5
2		65	7
3		81	6
4		76	5
5		70	4
6		87	6
7		85	4
8		85	4
9		94	3
10[b]		18	63
11		 (51)	17

[a] Reactions were carried out by the same method as that described in the text.
[b] 1-Octanol (5 mmol) was allowed to react with $NaBrO_3$ / $NaHSO_3$ (15 / 15 mmol) in a 1:1 mixture of CH_3CN / H_2O (20 mL / 20 mL).

In the course of our study to extend the synthetic use of these reagents, $NaBrO_3/NaHSO_3$ reagent was found to be an efficient oxidizing agent of primary alcohols to esters in aqueous medium under mild conditions.

Typical reaction was carried out as follows: To a solution of $NaBrO_3$ (1.81 g, 12 mmol) in water (4 mL) was added 1-octanol (1.30 g, 10 mmol) followed by dropwise a solution of $NaHSO_3$ (1.25 g, 12 mmol) in water (4 mL) over a period of about 15 min, and the mixture was stirred at room temperature for 2 h. Products were extracted with ether (50 mL x 3). After purification of the extracts by column chromatography on silica gel (hexane : ethyl acetate = 10 : 1), octyl octanoate was obtained in 94 % yield along with a small amount of octanoic acid (3%).

Table 1 shows the representative results for the conversion of various primary alcohols to the corresponding esters by $NaBrO_3$/ $NaHSO_3$ reagent.

Linear alcohols such as 1-butanol and 1-hexanol were converted into the corresponding esters in high yields (76-94%) under these conditions. Yields of these esters were comparable to those by $NaBrO_2$.[4] Branched alcohols such as 2-methylpropanol and 2-methylpentanol were also oxidized to the corresponding esters in 65-85% yields. Even a sterically crowded alcohol, 2,2-dimethylpropanol, was smoothly esterified by the present oxidation system. However, benzyl alcohol was not converted to benzyl benzoate, but to benzaldehyde and benzoic acid in 51 and 17% yields, respectively.

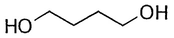
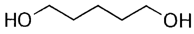
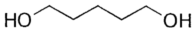
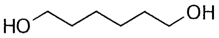
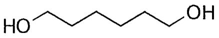
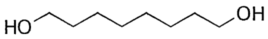
When alcohols were allowed to react in a mixed solvent of acetonitrile and water, carboxylic acids were obtained as main products rather than esters. For example, 1-octanol was oxidized with $NaBrO_3/NaHSO_3$ (3 equiv.) in a 1 : 1 mixed solvent of CH_3CN and H_2O to form octanoic acid in 63% yield.

Despite the fact that benzyl alcohol was not converted into benzyl benzoate by the present method, the cross-esterification was achieved with relatively high selectivity when a 1:1 mixture of benzaldehyde and 1-butanol was treated with $NaBrO_3/NaHSO_3$ reagent. Thus, the reaction of an equimolar mixture of benzaldehyde and 1-butanol with 1.2 equiv of $NaBrO_3/NaHSO_3$ led to butyl benzoate (50%) along with butyl butanoate (32%), benzaldehyde (11%) and benzoic acid (14%). In contrast, the same procedure for butanal and benzyl alcohol led to butanoic acid (43

$$PhCHO + C_4H_9OH \xrightarrow{NaBrO_3\ /\ NaHSO_3} \underset{50\%}{PhCOOC_4H_9} + \underset{32\%}{C_3H_7COOC_4H_9} + \underset{14\%}{PhCOOH} \quad (1)$$

$$C_3H_7CHO + PhCH_2OH \xrightarrow{NaBrO_3\ /\ NaHSO_3} \underset{43\%}{C_3H_7COOH} + \underset{15\%}{PhCHO} + \underset{18\%}{PhCOOH} \quad (2)$$

Table 2. Oxidation of several α,ω–diols[a]

Run	Substrate	Product, %	
1		γ–Butyrolactone	62
2[b d]		δ–Valerolactone	35
3		Glutalic acid	68
4[c d]		ε–Caprolactone	6
5		Adipic acid	71
6		Suberic acid	91

[a]Diol (5 mmol) was allowed to react with $NaBrO_3$ (15 mmol in 10 mL of H_2O) / $NaHSO_3$ (15 mmol in 10 mL of H_2O) in CH_3CN (10 mL) at refluxing temperature for 2 h. [b]At room temperature. [c]Reaction time was 4 h. [d]CH_3CN (20 mL) was used as solvent.

%), benzaldehyde (15%), and benzoic acid (18%), but no ester was formed.

In order to obtain the information of the reaction path in the present reaction, a mixture of octanoic acid and 1-butanol was allowed to react with $NaBrO_3/NaHSO_3$ reagent. The reaction produced butyl butanoate (63%) and butyric acid (8%), but not butyl octanoate. This fact excludes the possibility of esterification of the alcohol by the acid derived from alcohols in the present ester formation.[10] However, the oxidation of 1-butanol in the presence of octanal resulted in butyl octanoate (70%), as a main product, with a small amounts of butyl butanoate (17%) and octanoic acid (13 %). In addition, the treatment of octanal dimethylacetal with $NaBrO_3/NaHSO_3$ produced methyl octanoate in 54% yield.

On the basis of these results, the following route is suggested for the present esterification of alcohols. The reaction is probably initiated by the dehydrogenation of alcohols to aldehydes which rapidly react with alcohols existing in the reaction system to form hemiacetals and/or acetals. The resulting acetals are immediately oxidized to esters by $NaBrO_3/NaHSO_3$. Hence no ester formation by the oxidation of benzyl alcohol by this system is believed to be due to the difficulty of the formation of acetal from the resulting benzaldehyde and benzyl alcohol.

Treatment of α,ω-diol such as 1,4-butanediol by $NaBrO_3/NaHSO_3$ resulted in γ-butyrolactone in 62% as shown in Table 2. However, 1,5-pentanediol and 1,6-hexanediol under these conditions formed glutalic acid (68%) and adipic acid (71%) rather than lactone.[11] In the oxidation of 1,3-butanediol, the secondary alcoholic function was oxidized with high selectivity to form 4-hydroxy-2-butanone in 90% yield.

References and Notes

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10 M. Hudlicky, in "Oxidation of Organic Chemistry,"ACS Monograph 186, Washington DC. (1990), p 134.
11 Treatment of ε-caprolactone with $NaBrO_3/NaHSO_3$ under these conditions afforded a complex mixture of oxidized products.