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Selective oxidation of primary alkanols into the "symmetrical" esters with the H_2O_2—MBr—HCl system

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Oxidation of linear or branched primary alkanols with H_2O_2—MBr (M = Li, Na, K)—HCl system in water affords the corresponding "symmetrical" esters in almost quantitative yield.

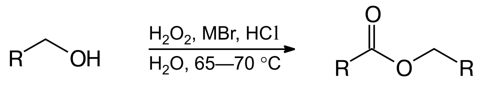
Key words: primary alkanols, esters, hydrogen peroxide, lithium bromide, sodium bromide, potassium bromide, oxidation.

Oxidation of alcohols to carbonyl compounds or carboxylic acids is one of fundamental reactions in organic chemistry.

Currently, development of novel simple and convenient methods for selective oxidation is topical. Besides, the use of available, cheap, and environmentally friendly oxidants, *e.g.*, hydrogen peroxide, are preferable. However, depending on the reaction conditions, hydrogen peroxide can oxidize primary alkanols to carboxylic acids or esters. In the presence of a system of Na_2WO_4—phase transfer catalyst (PTC is methyltrioctylammonium sulfate,[1,2] $(NBu_4)_2SO_4$ (see Ref. 3)), Co^{II} complexes,[4] and polyoxymetalate complexes,[5] the reactions proceeded non-selectively[1,2] or required significant excess (15—20 equiv.) of oxidant.[4] When Br_2 or HBr were used as redox catalysts, the reaction yielded "symmetrical" esters, the products of esterification of the resulting acid with the excess of alcohol oxidized.[6] According to the proposed mechanism, the reaction involved the formation of acyl bromide and its simultaneous alcoholysis. In the case of glycols bearing both primary and secondary hydroxyl groups, a H_2O_2—HBr system with controlled content of H_2O_2 oxidized only secondary hydroxyl group.[7] In the presence of $FeBr_3$ (see Ref. 8) or $[bmim]_4[W_{10}O_{23}]$ (bmim is 1-butyl-3-methylimidazolium),[9] secondary alkanols gave ketones, while primary alkanols were resistant to oxidation. Recently,[9] for the oxidation of alkanols to esters, we suggested to use hydrogen peroxide in the combination with two redox catalysts, namely, Ce^{III} salts and LiBr.[10]

In the present work, novel method for the synthesis of "symmetrical" esters by the oxidation of alkanols with simple oxidation system, H_2O_2—MBr—HCl, was developed. It was found that hydrogen peroxide in water at 65—70 °C in the presence of MBr (M = Li, Na, K) and hydrochloric acid effectively oxidized linear and branched primary alkanols **1a—f** to esters **2a—f** (Scheme 1).

Scheme 1



1a—f **2a—f**

M = Li, Na, K.
R = Bu^n (**a**), *n*-C_6H_{13} (**b**), *n*-C_8H_{17} (**c**), $Me_2CHCH_2CH_2$ (**d**), Et(Me)$CHCH_2$ (**e**), Bu^n(Et)CH (**f**).

The reaction proceeds only in the presence of all reagents; in the absence of any of them, no reaction occurred.

The optimal reaction conditions were determined taking heptan-1-ol (**1b**) as an example (Table 1). Heptyl heptanoate (**2b**) was prepared in quantitative yield at reagent molar ratio **1b** : H_2O_2 : LiBr : HCl = 1 : 2 : 2 : 5. Decrease in content of H_2O_2, LiBr, or HCl resulted in decrease in the yield of ester **2b** (see Table 1, entries *1—7*, *12—13*). Concentration of these components in water significantly affected the yield of the product. Thus, when the reaction was carried out at molar ratio of **1b** : H_2O_2 : LiBr : HCl = 1 : 3 : 1 : 5 in 10 mL of water per 1 mmol of **1b**, the yield of ester **2b** was 98%; at the same reactant ratio in 20 and 30 mL of water the yields of **2b** were 20 and 10% respectively; while, in 40 mL of water, the yield was 1% only (see Table 1, entries *8—11*). Similar tendency was observed in experiments *13—16*. No effect of the cation nature in MBr on oxidation was found (see Table 1, entries *17* and *18*).

The obtained results allow suggestion of the reaction mechanism, which involved metathesis, oxidation of HBr formed with H_2O_2 to molecular bromine, and subsequent reaction of Br_2 with alkanol (Scheme 2). Formation of molecular bromine was confirmed by the characteristic color of the reaction mixture.

Most likely that the reaction of alkanols with Br_2 proceeded *via* formation of hemi-acetal and its subsequent

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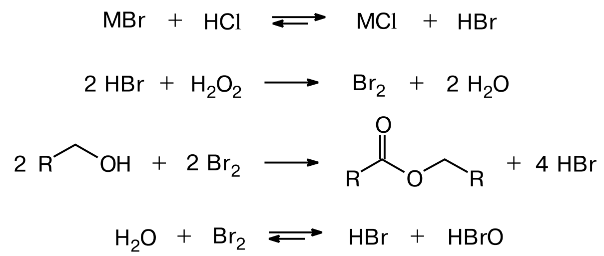
Table 1. Oxidation of heptan-1-ol (**1b**) with the H_2O_2—MBr—HCl system[a]

Entry	Molar ratio **1b** : H_2O_2 : MBr : HCl	MBr	Conversion of **1b** (%)	Yield (%) of compound **2b**
1	1 : 2 : 2 : 5	LiBr	100	>99
2	1 : 1 : 2 : 5	LiBr	88	87
3	1 : 2 : 1 : 5	LiBr	70	69
4	1 : 3 : 2 : 2	LiBr	66	65
5	1 : 3 : 2 : 3	LiBr	95	94
6	1 : 3 : 2 : 4	LiBr	98	96
7	1 : 3 : 2 : 5	LiBr	100	>99
8	1 : 3 : 1 : 5	LiBr	98	98
9[c]	1 : 3 : 1 : 5	LiBr	20	20
10[d]	1 : 3 : 1 : 5	LiBr	4	4
11[e]	1 : 3 : 1 : 5	LiBr	1	1
12	1 : 5 : 1 : 5	LiBr	86	85
13	1 : 5 : 2 : 5	LiBr	100	>99
14[c]	1 : 5 : 2 : 5	LiBr	80	80
15[d]	1 : 5 : 2 : 5	LiBr	10	10
16[e]	1 : 5 : 2 : 5	LiBr	4	4
17	1 : 3 : 2 : 5	NaBr	100	>99
18	1 : 3 : 2 : 5	KBr	100	>99

[a] **1b** (1 mmol); solvent, H_2O (10 mL); reaction temperature, 65—70 °C; reaction time, 3 h.
[b] Based on the starting **1b**.
[c] Solvent, H_2O (20 mL).
[d] Solvent, H_2O (30 mL).
[e] Solvent, H_2O (40 mL).

Scheme 2



oxidation to ester, *i.e.*, similar to oxidation of alkanols with a cerium ammonium nitrate—lithium bromide system.[11] The above-mentioned mechanism[6] involving formation of acyl bromide as the intermediate is impossible due to its susceptibility to rapid hydrolysis to carboxylic acid in aqueous media. At low concentration of the alkanol in a water solution, most of bromide is consumed in the competitive reaction with water to give hydrobromic and unstable hypobromous acids.

Similarly to heptan-1-ol (**1b**), pentan-1-ol (**1a**), nonan-1-ol (**1c**), 4-methylpentan-1-ol (**1d**), 3-methylpentan-1-ol (**1e**), and 2-ethylhexan-1-ol (**1f**) oxidized in the optimal conditions to the corresponding esters (Table 2).

In summary, we developed simple, facile, and effective procedure for the synthesis of esters by the oxidation of linear and branched primary alkanols with the redox system H_2O_2—MBr (M = Li, Na, K)—HCl in water. No expensive reagents are required, the results of the experiments are well reproducible. The method is useful for the practical applications.

Experimental

GC analysis was performed on a Chrom-5 chromatograph with the flame-ionization detector and 3×3000 mm analytical glass columns with 5% SE-30 and 5% FFAP on Chromaton N-AW-HMDS (0.16—0.20 mm). The product yields were determined by an internal standard method with the empirical correlation coefficients. The IR spectra (Nujol) were recorded on a Perkin—Elmer 577 spectrophotometer. The ^1H and ^{13}C NMR spectra were recorded on a Bruker AC-200 instrument in $CDCl_3$. The GC-MS analysis was performed on a Finnigan MAT ITD-700 spectrometer (EI, 70 eV, the source of ion—ionic trap system temperature was 220 °C) connected with Carlo Erba 4200 chromatograph with a 0.2×2500 mm Ultra-1 column (Hewlett—Packard), the stationary phase (polymethylsiloxane) thickness 0.33 μm, helium was used as a carrier gas. The reaction products were isolated by column chromatography (silica gel L, 40—100 μm, elution with heptane—ethyl acetate). Pentan-1-ol (**1a**), heptan-1-ol (**1b**), nonan-1-ol (**1c**), 4-methylpentan-1-ol (**1d**), 3-methylpentan-1-ol (**1e**), and 2-ethylhexan-1-ol (**1f**)

Table 2. Oxidation of alcohols **1a—f** with the H_2O_2—LiBr—HCl system[a]

Alkanol **1a—f**	Conversion of **1a—f** (%)	Product **2a—f**	Yield[b] (%)
$C_5H_{11}OH$ (**1a**)	99	$C_4H_9COOC_5H_{11}$ (**2a**)	98
$C_7H_{15}OH$ (**1b**)	100	$C_6H_{13}COOC_7H_{15}$ (**2b**)	>99
$C_9H_{19}OH$ (**1c**)	100	$C_8H_{17}COOC_9H_{19}$ (**2c**)	>99
$Me_2CH(CH_2)_3OH$ (**1d**)	98	$Me_2CHCH_2CH_2COO(CH_2)_3CHMe_2$ (**2d**)	98
$EtCH(Me)CH_2CH_2OH$ (**1e**)	98	$EtCH(Me)CH_2COOCH_2CH_2CH(Me)Et$ (**2e**)	97
$Bu^nCH(Et)CH_2OH$ (**1f**)	99	$Bu^nCH(Et)COOCH_2CH(Et)Bu^n$ (**2f**)	98

[a] **1a—f** (1 mmol); molar ratio, **1** : H_2O_2 : LiBr : HCl = 1 : 3 : 2 : 5; solvent, H_2O (10 mL); reaction temperature, 65—70 °C; reaction time, 3—3.5 h.
[b] Based on the starting **1a—f**.

(Acros) were distilled prior to use. Hydrogen peroxide (35% aq. solution, pure, Acros) and HCl (35% aq. solution, pure) were used as purchased.

Oxidation of primary alkanols with the H_2O_2—MBr—HCl system (general procedure). To a vigorously stirred solution of alkanol **1** (1 mmol), MBr, and 35% aqueous HCl in water (5 mL), a solution of 35% aqueous H_2O_2 in water (5 mL) was added by portions of 0.8—1.0 mL within ~3 h at 65—70 °C (reagent ratios are given in Tables 1 and 2). After the addition of the first portion of H_2O_2, the reaction mixture became pale yellow, the color disappeared after 20—30 min. The reaction mixture was cooled, extracted with diethyl ether (3×15 mL), the organic layer was washed with water, dried with $MgSO_4$, and the solvent was removed *in vacuo*. The yields of esters **2a**—**f** and conversion of alkanols **1a**—**f** were determined by HPLC with internal standard. The products were isolated by column chromatography on silica gel.

The structure of the synthesized compounds **2a**—**f** was evaluated from ^{1}H and ^{13}C NMR and IR spectroscopic data, GC-MS data and by comparison with authentic samples.[12]

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