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Oxidation Using Quaternary Ammonium Polyhalides. III.[1) An Effective Oxidation of Alcohols and Ethers by the Use of Benzyltrimethylammonium Tribromide

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The reaction of primary alcohols or simple ethers and α,ω-diols or cyclic ethers with a stoichiometric amount of benzyltrimethylammonium tribromide (BTMA Br_3) in carbon tetrachloride in the presence of Na_2HPO_4 aq or in acetic acid in the presence of CH_3CO_2Na aq at 60—70 °C gave dimeric esters and lactones respectively in good yields. The reaction of secondary alcohols with 1 equiv of BTMA Br_3 in the presence of a buffer at 60 °C gave ketones.

The dimeric esterification of primary alcohols **1** has been presented in several reports. For example, bromine-potassium bromate in water,[2) sodium dichromate-sulfuric acid,[3) sodium hypochlorite in acetic acid,[4) calcium hypochlorite in acetonitrile-acetic acid,[5) and sodium bromite ($NaBrO_2$) in acetic acid[6) have been used for the dimeric esterification of **1**. Dimeric esters **3** can be obtained by bubbling oxygen into a solution of **1** in acetic acid in the presence of cobalt acetate bromide.[7) Reduced copper-[8) and ruthenium-[9) catalyzed transformation of **1** to **3** have also been reported. The treatment of tributylstannyl alkoxides by NBS in carbon tetrachloride affords **3**.[10) We have recently reported that **1** can be converted into **3** by the use of sodium bromate in the presence of a catalytic amount of hadrobromic acid.[11)

Methods for the oxidative esterification of simple ethers **2** have also been described in the literature (Refs. 5 and 11).

Silver carbonate on Celite[12) and the ruthenium catalyst[9) has been used for the intramolecular oxidative lactonization of α,ω-diols **4**. Compounds **4** have also been oxidized to lactones **6** by sodium bromite in aqueous acetic acid[6) and by sodium bromate in 47% hydrobromic acid.[11) Bromine in an aqueous acetate buffer at pH 5 acts as an oxidant for the cleavage of THF to afford γ-butyrolactone.[13)

There are a number of methods concerning the oxidation of secondary alcohols **7** to ketones **8**. Several methods have been shown in the literature (Refs. 4, 10, and 11).

During the course of our investigation of the utility of benzyltrimethylammonium tribromide (BTMA Br_3) as a brominating agent,[14) we have now found that BTMA Br_3 is also an effective oxidizing agent.[15) In this paper, we wish to report on the oxidation of alcohols and ethers using BTMA Br_3 in the presence of such buffer as aqueous Na_2HPO_4 or CH_3CO_2Na.

Results and Discussion

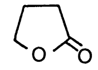
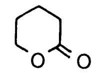
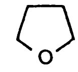
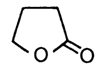
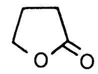
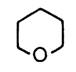
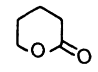
The reaction of **1** or **2** with a calculated amount of BTMA Br_3 in carbon tetrachloride-water in the presence of Na_2HPO_4 at 60 °C gave **3** in good yields. In

Table 1. Oxidation of Primary Alcohols **1** and Simple Ethers **2** with BTMA Br_3 in the Presence of aq Na_2HPO_4[a) (in CCl_4 at 60 °C)

Run	Substrate **1** or **2**	BTMA Br_3/ Substrate	Reaction time/h	Product **3**	Yield[b)/ %
1	CH_3CH_2OH	1.1	7	$CH_3CO_2CH_2CH_3$	11[c)
2	$CH_3(CH_2)_2OH$	1.1	5.5	$CH_3CH_2CO_2(CH_2)_2CH_3$	52[c)
3	$CH_3(CH_2)_3OH$	1.1	4.5	$CH_3(CH_2)_2CO_2(CH_2)_3CH_3$	55[c)
4	$(CH_3)_2CHCH_2OH$	1.1	12	$(CH_3)_2CHCO_2CH_2CH(CH_3)_2$	80
5	$CH_3(CH_2)_4OH$	1.1	3.5	$CH_3(CH_2)_3CO_2(CH_2)_4CH_3$	84
6	$(CH_3)_2CH(CH_2)_2OH$	1.1	5	$(CH_3)_2CHCH_2CO_2(CH_2)_2CH(CH_3)_2$	77
7	$CH_3(CH_2)_5OH$	1.1	5	$CH_3(CH_2)_4CO_2(CH_2)_5CH_3$	96
8	$(C_2H_5)_2CHCH_2OH$	1.1	24	$(C_2H_5)_2CHCO_2CH_2CH(C_2H_5)_2$	69
9	$CH_3(CH_2)_7OH$	1.1	8.5	$CH_3(CH_2)_6CO_2(CH_2)_7CH_3$	99
10	$CH_3(CH_2)_{11}OH$	1.1	4	$CH_3(CH_2)_{10}CO_2(CH_2)_{11}CH_3$	91
11	Ph-CH_2OH	1.1	5	Ph-CHO	89
12	Ph-CH_2CH_2OH	1.1	4	Ph-$CH_2CO_2CH_2CH_2$-Ph	23[d)
13	$[CH_3(CH_2)_2]_2O$	2.2	3	$CH_3(CH_2)_2CO_2(CH_2)_3CH_3$	33
14	$[CH_3(CH_2)_5]_2O$	2.2	5	$CH_3(CH_2)_4CO_2(CH_2)_5CH_3$	78
15		4.4	14	$CH_3(CH_2)_4CO_2(CH_2)_5CH_3$	90
16	(Ph-$CH_2)_2O$	2.2	10.5	Ph-CHO	63

a) About a 2 equiv of Na_2HPO_4 to BTMA Br_3 was used. b) Yield of isolated product. c) The exact yield was not calculated due to the volatility of the product, but a significant conversion was indicated by the IR and ^1H NMR analyses. d) Yield was based on ^1H NMR.

Table 2. Lactonization of α,ω-Diols **4** and Cyclic Ethers **5** with BTMA Br_3 in the Preesence of a Buffer

Run	Substrate **4** or **5**	BTMA Br_3/ Substrate	Reaction conditions			Product **6**	Yield[a)]/ %
			Temp/°C	Time/h	Buffer (Solvent)		
1	HO-$(CH_2)_4$-OH	2.1	70	5.5	Na_2HPO_4[b)] (CCl_4)		60
2	HO-$(CH_2)_5$-OH	2.1	70	2.5	CH_3CO_2Na[c)] (CH_3CO_2H)		49
3	HO-$(CH_2)_6$-OH	2.1	70	2.5	Na_2HPO_4[b)] (CCl_4)	Mixture[d)]	—
4		2.1	70	4	CH_3CO_2Na[c)] (CH_3CO_2H)	Mixture[d)]	—
5		2.1	60	4.5	Na_2HPO_4[b)] (CCl_4)		55
6		2.1	60	10	Na_2HPO_4[b)] (THF)		67[e)]
7		2.1	70	8.5	CH_3CO_2Na[c)] (CH_3CO_2H)		13

a) Yield of isolated product. b) About a 2 equiv of Na_2HPO_4 to BTMA Br_3 was used. c) About a 4 equiv of CH_3CO_2Na to BTMA Br_3 was used. d) The mixture of ε-caprolactone, a linear ester from 2 molecules of HO-$(CH_2)_6$-OH, and a polyester was confirmed by its ^{1}H NMR spectrum. e) The yield was obtained on the basis of the BTMA Br_3 used.

the absence of Na_2HPO_4, however, the reaction proceeded slowly and gave **3** in low yields. In the case of benzyl alcohol, the only oxidation product was benzaldehyde. The results are summarized in Table 1.

It is reasonable to assume that BTMA Br_3 can be dissociated by water as is shown in Eq. 1;[16)]

$$\text{BTMA Br}_3 + H_2O \rightleftharpoons \text{BTMA Br} + \text{HOBr} + \text{HBr}. \quad (1)$$

The hypobromous acid thus produced may act as the major active oxidizing species and may convert alcohols into esters as follows;

$$\underset{\mathbf{1}}{2\,\text{R-CH}_2\text{OH}} + 2\,\text{HOBr} \longrightarrow \underset{\mathbf{3}}{\text{R-CO}_2\text{CH}_2\text{R}} + 2\,H_2O + 2\,\text{HBr}. \quad (2)$$

Overall:

$$\underset{\mathbf{1}}{2\,\text{R-CH}_2\text{OH}} + 2\,\text{BTMA Br}_3 \longrightarrow \underset{\mathbf{3}}{\text{RCO}_2\text{CH}_2\text{R}} + 2\,\text{BTMA Br} + 4\,\text{HBr}. \quad (3)$$

In the case of ethers:

$$\underset{\mathbf{2}}{\text{R-CH}_2\text{OCH}_2\text{R}} + 2\,\text{BTMA Br}_3 + H_2O \longrightarrow \underset{\mathbf{3}}{\text{R-CO}_2\text{CH}_2\text{R}} + 2\,\text{BTMA Br} + 4\,\text{HBr}. \quad (4)$$

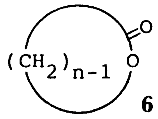
Generated hydrobromic acid can be removed by the Na_2HPO_4 which has been added previously:

$$\text{HBr} + Na_2HPO_4 \longrightarrow NaH_2PO_4 + \text{NaBr} \quad (5)$$

Thus, the equilibrium in Eq. 1 lies to the right, and the reaction (Eqs. 3 and 4) should proceed smoothly. In practice, a 2 equiv of Na_2HPO_4 to BTMA Br_3 was used.[17)] Our experimental results agreed stoichiometrically with these equations, 3 and 4.

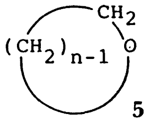
The reaction of **4** or cyclic ethers **5** with a stoichiometric amount of BTMA Br_3 in carbon tetrachloride or in acetic acid in the presence of aqueous Na_2HPO_4 or CH_3CO_2Na respectively at 60—70 °C gave **6**. The results are summarized in Table 2. The reactions can be presented in the following equations:

$$\underset{\mathbf{4}}{\text{HO-(CH}_2)_n\text{-OH}} + 2\,\text{BTMA Br}_3$$



6

$$\longrightarrow \mathbf{6} + 2\,\text{BTMA Br} + 4\,\text{HBr}. \quad (6)$$



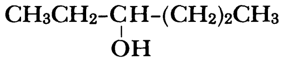
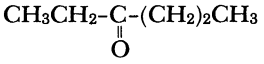
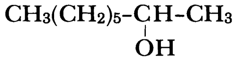
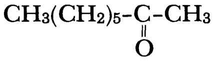
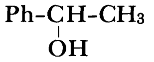
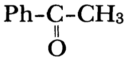
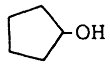
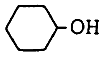
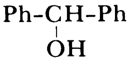
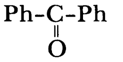
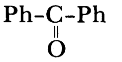
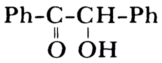
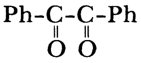
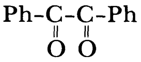
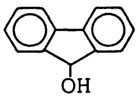
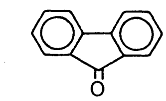
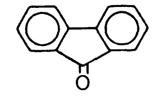
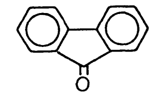
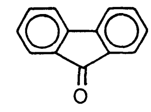
5

$$+ 2\,\text{BTMA Br}_3 + H_2O \longrightarrow \mathbf{6} + 2\,\text{BTMA Br} + 4\,\text{HBr}. \quad (7)$$

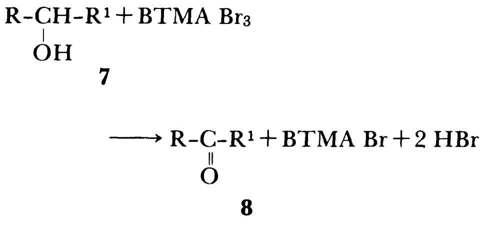
The ring cleavage of **5** should occur first in the case of the reaction of **5** with BTMA Br_3.

The oxidation of **7** with an equimolar amount of BTMA Br_3 in the presence of a buffer (CH_3CO_2Na aq in acetic acid or Na_2HPO_4 aq in carbon tetrachloride) at 60 °C afforded the corresponding **8** in good yields. The results are summarized in Table 3.

Table 3. Oxidation of Secondary Alcohols **7** with BTMA Br_3 in the Presence of a Buffer (at 60 °C)

Run	Substrate **7**	BTMA Br_3/ Substrate	Reaction conditions			Product **8**	Yield[a]/ %
			Temp/ °C	Time/ h	Buffer (Solvent)		
1	 $CH_3CH_2\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}(CH_2)_2CH_3$	1.1	60	2	CH_3CO_2Na[b] (CH_3CO_2H)	 $CH_3CH_2\text{-}\underset{O}{\underset{\|}{C}}\text{-}(CH_2)_2CH_3$	80
2		1.1	60	3	Na_2HPO_4[c] (CCl_4)	Mixture	—
3	 $CH_3(CH_2)_5\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}CH_3$	1.1	60	2	CH_3CO_2Na[b] (CH_3CO_2H)	 $CH_3(CH_2)_5\text{-}\underset{O}{\underset{\|}{C}}\text{-}CH_3$	98
4	 $Ph\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}CH_3$	1.1	50	2	CH_3CO_2Na[b] (CH_3CO_2H)	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}CH_3$	87
5		1.1	50	1	— (CH_3CO_2H)	Mixture[d]	—
6		1.1	60	1	CH_3CO_2Na[b] (CH_3CO_2H)	Mixture[e]	—
7		1.1	60	1	CH_3CO_2Na[b] (CH_3CO_2H)	Mixture[f]	—
8	 $Ph\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}Ph$	1.1	60	12	CH_3CO_2Na[b] (CH_3CO_2H)	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}Ph$	100
9		1.1	60	15	Na_2HPO_4[c] (CCl_4)	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}Ph$	100
10	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}Ph$	1.1	60	10.5	CH_3CO_2Na[b] (CH_3CO_2H)	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}\underset{O}{\underset{\|}{C}}\text{-}Ph$	83
11		1.1	60	11	Na_2HPO_4[c] (CCl_4)	 $Ph\text{-}\underset{O}{\underset{\|}{C}}\text{-}\underset{O}{\underset{\|}{C}}\text{-}Ph$	64
12		1.1	60	15	CH_3CO_2Na[b] (CH_3CO_2H)		23
13		2.1	60	24	Na_2HPO_4[c] (CCl_4)		100
14		1.1	60	15	Na_2HPO_4[c] (CCl_4)		73
15		1.1	60	12	Na_2HPO_4[c] ($CHCl_3$)		89

a) Yield of isolated product. b) About a 4 equiv of CH_3CO_2Na to BTMA Br_3 was used. c) About a 2 equiv of Na_2HPO_4 to BTMA Br_3 was used. d) A mixture of acetophenone, α-bromoacetophenone, and the starting material, e) a mixture of cyclopentanone, 2-bromocyclopentanone, and the starting material, and f) a mixture of cyclohexanone, 2-bromocyclohexanone, and the starting material, were confirmed by mean of their respective ^1H NMR spectra.



$$\underset{\mathbf{7}}{R\text{-}\underset{OH}{\underset{\mid}{CH}}\text{-}R^1} + \text{BTMA } Br_3 \longrightarrow \underset{\mathbf{8}}{R\text{-}\underset{O}{\underset{\|}{C}}\text{-}R^1} + \text{BTMA Br} + 2\,HBr \qquad (8)$$

We believe that, although other procedures for the esterification of primary alcohols and ethers, the lactonization of α,ω-diols and cyclic ethers, and the oxidation of secondary alcohols have been reported, our methods are more effective because of their ease, simplicity, mildness of conditions, and good product yields.

Experimental

Preparation of Ester from Alcohol. Typical Procedure (Run 9 in Table 1): To a solution of 1-octanol (1.30 g, 10 mmol) in carbon tetrachloride (10 ml) we added BTMA Br_3 (4.29 g, 11 mmol) and a solution of $Na_2HPO_4 \cdot 12\ H_2O$ (9.31 g, 26 mmol) in water (10 ml). The reaction mixture was stirred for 8.5 h at 60 °C until the initial orange color faded. The solution was then cooled to room temperature and treated with a 20% aqueous solution of $NaHSO_3$ (10 ml). The organic layer was separated and washed with water (100 ml), dried over $MgSO_4$, and evaporated in vacuo to give octyl octanoate as a colorless oil; yield: 1.27 g (99%), bp 153.5 °C/7 mmHg (lit,[18] bp 305.9 °C/760 mmHg; 1 mmHg≈133.322 Pa).

Preparation of Ester from Simple Ether. Typical Procedure (Run 14 in Table 1): To a solution of dihexyl ether (0.94 g, 5 mmol) in carbon tetrachloride (10 ml) we added BTMA Br_3 (4.29 g, 11 mmol) and a solution of $Na_2HPO_4 \cdot 12H_2O$ (8.60 g, 24 mmol) in water (10 ml). The reaction mixture was then stirred for 5 h at 60 °C until the initial orange color faded. The solution was cooled to room temperature and was worked up as has been described above for the preparation of octyl octanoate to give hexyl hexanoate as a colorless oil; yield: 0.78 g (78%), bp 238—240 °C/760 mmHg (lit,[19] bp 245.6 °C/760 mmHg).

Praparation of Lactone from α,ω-Diol. Typical Procedure (Run 1 in Table 2): To a solution of 1,4-butanediol (0.90 g, 10 mmol) in carbon tetrachloride (10 ml) we added BTMA Br_3 (8.19 g, 21 mmol) and a solution of $Na_2HPO_4 \cdot 12\ H_2O$ (16.41 g, 46 mmol) in water (20 ml). The reaction mixture was stirred for 5.5 h at 70 °C until the initial orange color faded, and then cooled to room temperature. To the mixture we added 20% $NaHSO_3$ aq (10 ml) and then a saturated Na_2CO_3 solution was added until the solution had been made alkaline enough. The reaction mixture was extracted with CH_2Cl_2 (10 ml×4), and ether (50 ml) was added to the CH_2Cl_2 solution in order to precipitate BTMA Br, which was insoluble in ether. The mixture was then filtered, and the filtrate was dried over $MgSO_4$ and evaporated in vacuo to give γ-butyrolactone as a colorless oil; yield: 0.52 g (60%), bp 205 °C/760 mmHg (lit,[20] bp 50—55 °C/3 mmHg).

Preparation of Lactone from Cyclic Ether. Typical Procedure (Run 5 in Table 2): To a solution of THF (0.72 g, 10 mmol) in carbon tetrachloride (10 ml) we added BTMA Br_3 (8.19 g, 21 mmol) and a solution of $Na_2HPO_4 \cdot 12\ H_2O$ (15.04 g, 42 mmol) in water (20 ml). The reaction mixture was stirred for 4.5 h at 60 °C until the initial orange color faded and was then worked up as has been described above to give γ-butyrolactone as a colorless oil; yield: 0.47 g (55%), bp 199 °C/760 mmHg (lit, [20] bp 50—55 °C/3 mmHg).

Preparation of Ketone from Secondary Alcohol. Typical Procedure (Run 3 in Table 3): To a solution of 2-octanol (1.31 g, 10 mmol) in acetic acid (2 ml) we added BTMA Br_3 (3.90 g, 10 mmol) and a solution of $CH_3CO_2Na \cdot 3\ H_2O$ (5.72 g, 42 mmol) in water (20 ml). The reaction mixture was stirred for 2 h at 60 °C until the initial orange color had faded and then cooled to room temperature. To the mixture we added 20% $NaHSO_3$ aq (10 ml); a saturated Na_2CO_3 solution was then added until the solution had been made alkaline enough. The organic layer was separated and washed with water (100 ml), dried over $MgSO_4$, and evaporated in vacuo to give 2-octanone as a colorless oil; yield: 1.25 g (98%), bp 175 °C/760 mmHg (lit,[21] 172 °C/760 mmHg).

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16) Actually, BTMA Br_3 was slightly dissolved in water, and the aqueous solution, which had been stirred for 5 min at 60 °C, dyed a potassium iodide starch paper a deep blue; the pH of the solution was obtained as 3.1.

17) For example, in the case of the reaction of butyl alcohol with BTMA Br_3 (1 equiv) and aqueous Na_2HPO_4 (2 equiv) in CCl_4, the pH values of the solution were obtained as follows; 8.1 (at initial time), 7.0 (at 2.5 h after), and 3.12 (at 24 h after).

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