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Oxidation of Secondary Alcohols with Phenyltrimethylammonium Tribromide in the Presence of a Catalytic Amount of Antimony(III) Bromide or Copper(II) Bromide

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Abstract: The oxidation of alcohols was carried out with phenyltrimethylammonium tribromide in the presence of a catalytic amount of SbBr₃ or CuBr₂. 1,2-Diols, such as hydrobenzoin, were converted into 1,2-diketones or α -ketols without oxidative cleavage of the glycol C-C bond at room temperature. A variety of secondary alcohols were also oxidized to the corresponding carbonyl compounds in a chemoselective manner.

Key words: oxidation, alcohol, phenyltrimethylammonium tribromide, antimony(III) bromide, copper(II) bromide

The oxidation of alcohols to the corresponding ketones plays an important role in organic synthesis. Many effective oxidation systems have been developed and new ways to achieve this transformation continue to receive wide attention in terms of economic benefit, environmental impact and safety.¹⁻⁹

Br₂ has been used as a reagent in oxidation systems such as *bis*(tributyltin)oxide-bromine and Ph₃Sb-bromine, which have been shown to be efficient reagents for the oxidation of alcohols to ketones.^{1,10,11} However, elemental bromine is associated with hazards because of its rapid vaporization. Therefore, there has been much interest in a new mild and convenient method for the chemoselective oxidation of alcohols without using bromine.

Though phenyltrimethylammonium tribromide (PTAB) is known to be a convenient reagent for brominating the α position of carbonyl compounds and for the addition of bromine to alkenes, other uses of the compound in organic synthesis have not been studied in detail.¹² As PTAB has been much easier to handle and it maintains the desired stoichiometry in comparison with bromine, the use of PTAB was more advantageous and attractive than that of Br₂ in organic synthesis. Since selective oxidation of alcohols with PTAB has not previously been reported, we decided to investigate.

Further, it has been reported in previous papers that the combinations of complex metal hydrides (LiAlH₄, NaBH₄) and antimony halides (SbBr₃, SbCl₃) were more effective for the conjugate reduction of 2-butene-1,4-diones and the reductive debromination of aromatic α -bro-

SYNLETT 2004, No. 13, pp 2369–2373 Advanced online publication: 28.09.2004 DOI: 10.1055/s-2004-832840; Art ID: U20904ST © Georg Thieme Verlag Stuttgart · New York mo ketones in comparison with those of complex metal hydrides and other metal halides, $AlCl_3$, $CuCl_2$, $FeCl_3$.^{13,14} Antimony halides are more effective for organic synthesis and are easier to handle than other metal halides, such as $AlCl_3$ and $TiCl_4$.^{14–16} There has been interest in the effect of using a catalytic amount of antimony halide in the oxidation of alcohols with PTAB. In this paper, we would like to report on the results of our studies concerning the selective oxidation of a variety of alcohols with PTAB in the presence of antimony halide or other metal halides.

The oxidation of *meso*-hydrobenzoin (1), chosen as a representative 1,2-diol for this study, with PTAB-SbBr₃ in various stoichiometric ratios was carried out.^{1,17-23} The results are summarized in Table 1. A mixture of benzaldehyde (2) and benzil (3) was obtained at 1.5 molar equivalents of PTAB over meso-hydrobenzoin (1) in the presence of a catalytic amount of SbBr₃ (run 2). Benzil (3) was mainly obtained at the molar ratio of 1, PTAB, pyridine, and SbBr₃ (1:2:2:0.2, run 3). At the ratio of 1:3:3:0.2, 1 was oxidized to give 3 without oxidative cleavage of the glycol C-C bond in nearly quantitative yield (run 4). To examine the effects of PTAB, SbBr₃ and pyridine in this oxidation system, the following experiments were carried out. In the absence of SbBr₃, 1 was recovered in over 60% yield accompanied by benzoin (4, run 7). meso-Hydrobenzoin (1) was also recovered unchanged without using PTAB (runs 8, 9). Compound 1 was oxidized to give mixtures of 2 and 3 without pyridine (run 10). Satisfactory yields and selectivity for oxidation of 1 to 3 or 4 were not observed. PTAB, SbBr₃, and pyridine were each confirmed to be essential for the oxidation of 1 to 3 quantitatively.

The oxidation of **1** in the presence of a variety of metal halides was carried out to compare the utility of SbBr₃ with that of other metal halides. The results are shown in Table 2. First, the oxidation of **1** was examined with PTAB and bismuth halides (BiBr₃, BiCl₃) as a homology of antimony halide. The mixtures of **3** and **4** were obtained unexpectedly (runs 1, 2). Antimony halides were more selective for the oxidation of **1** to **3** than homologous bismuth halides. *meso*-Hydrobenzoin (**1**) was not oxidized to give **3** or **4** in good yields in the presence of other metal halides, NiCl₂, ZnBr₂ (runs 6, 7). On the other hand, **1** was predominantly converted into **4** in the presence of copper(II) halides (runs 3–5).^{1.24,25} Thus, the addition of a catalytic amount of SbBr₃, CuBr₂ or CuCl₂ was found to

Table 1 Oxidation of meso-Hydrobenzoin (1) with PTAB in MeOH^a

OH Ph Ph OH	PTAB/SbBr ₃ /Pyrid MeOH	$\xrightarrow{\text{ine}}$ PhCHO P	$h \downarrow Ph Ph V OI $	O ↓ Ph H				
Run	Molar ratio of			Time (h)		Yie	ld (%) ^b	
	PTAB	SbBr ₃	Pyridine		2	3	4	1
1	2.0	_	_	16	2	6	50	38
2	1.5	0.2	-	16	54	31	-	6
3	2.0	0.2	2.0	17	-	78	-	18
4	3.0	0.2	3.0	16	_	96	-	_
5	4.0	0.2	2.0	14	2	90	-	4
6	4.0	0.2	4.0	24	_	96	-	_
7	4.0	_	4.0	17	_	_	32	66
8	_	0.2	4.0	15	3	_	-	93
9	_	2.0	_	22	_	_	-	96
10	4.0	2.0	_	15	45	45	-	6
11	4.0	_	_	22	5	2	47	30

^a Compound 1: 0.5 mmol, MeOH (15 mL), r.t.

^b Isolated yield.

Table 2 Oxidation of meso-Hydrobenzoin (1) with PTAB-Metal Halides-Pyridine in MeOHa

Run	MXn	Time (h)	Time (h)			Yield (%) ^b	
			2	3	4	1 ^c	
1	BiBr ₃	70	2	8	62	23	
2	BiCl ₃	70	2	19	53	22	
3	CuBr ₂	67	_	2	78	18	
4	CuBr ₂	7 ^d	-	5	81	8	
5	CuCl ₂	70	-	2	77	18	
6	NiCl ₂	72	2	12	56	25	
7	ZnBr ₂	72	3	7	61	24	

^a Compound 1: 0.25 mmol, PTAB (1.0 mmol), pyridine (1.0 mmol) MXn (0.05 mmol), MeOH (8 mL), r.t.

^b Isolated yield.

^c Recovered yield of **1**.

^d Temp: 65 °C.

be more effective for obtaining benzil or benzoin than other metal halides in the oxidation of 1 with PTAB-pyridine.

The oxidation of a variety of 1,2-diols and α -ketols was carried out to elucidate the oxidizing power of the PTAB–SbBr₃–pyridine and PTAB–CuBr₂–pyridine systems. The results are shown in Table 3. *dl*-Hydrobenzoin (**5**), hydroanisoin (**6**), and 1,2-dicyclohexyl-1,2-ethanediol (**8**) with PTAB–SbBr₃–pyridine, were selectively oxidized to the corresponding 1,2-diketones without oxidative clea-

vage of the glycol C-C bonds (runs 1–3). The oxidation of α -ketols, benzoin (4), anisoin (10), and 11 also afforded the corresponding 1,2-diketones in high yields (runs 4–6). On the other hand, the oxidation of 5 and 8 with PTAB–CuBr₂–pyridine took place to give corresponding α -ketols 4, 11 predominantly (runs 7, 8).²⁶ To examine this selectivity for the oxidation of 1,2-diols to α -ketols with PTAB–CuBr₂–pyridine, the oxidation of α -ketols 4, 10 was carried out under the same reaction conditions. Compounds 4 and 10 were not oxidized to give the corresponding 1,2-diketones or other ketones in high yields. Benzoin

(4) and anisoin (10) were recovered in over 76% yields (runs 9, 10). The system PTAB–CuBr₂–pyridine was supposed to be applicable for the oxidation of 1,2-diol to α -ketols consequently. 1,1,2-Triphenyl-1,2-ethanediol (12) was oxidized to α -ketol 13 without rearrangement of the phenyl group by PTAB–SbBr₃–pyridine (run 11). The PTAB–SbBr₃–pyridine and PTAB–CuBr₂–pyridine systems were ascertained to be more selective for the oxidation of 1,2-diols to 1,2-diketones or α -ketols than PTAB–other metal halide systems.

In addition, the oxidation of a variety of alcohols with PTAB–SbBr₃–pyridine or PTAB–CuBr₂–pyridine, was carried out to clarify the chemoselectivity for alcohols.^{1,27–35} The results are shown in Table 4 and Table 5. Secondary alcohols, cycloheptanol (14), 4-decanol (16), 1-phenylethanol (18), benzhydrol (20) were oxidized to the corresponding ketones 15, 17, 19, 21 in good yields at room temperature (Table 4 and Table 5, runs 1–4). On the other hand, compound 18 was converted to α -bromodimethylacetal (22) in high yield at 65 °C for 5 hours (Table 4, run 5). The oxidation of 20, at 65 °C for 5 hours,

also afforded a small amount of dimethylacetal (8%) besides ketone 21 (Table 4, run 6). The oxidation reaction of 18, 22 took place rapidly at 65 °C but ketones 19, 21 were successively converted to dimethylacetal derivatives. Room temperature turned out to be the optimum temperature for obtaining ketones in good yields. Furthermore, aliphatic primary alcohol, 1-dodecanol (23) was not affected under the same oxidation conditions (Table 4, run 7; Table 5, run 5). To clarify this chemoselectivity, the oxidation of 2-ethyl-1,3-hexanediol (24) containing both secondary and primary hydroxyl groups, was examined with PTAB-SbBr3-pyridine, PTAB-CuBr2-pyridine, respectively. Only the secondary 3-hydroxyl group of 24 was selectively oxidized to give hydroxyketone 25 in 79-93% yields (Table 4, run 8; Table 5, run 6). In contrast, mandelic acid methylester, ethyl 3-hydroxybutyrate and 1,4-dichloro-2-butanol were not oxidized to the respective ketones under the same reaction conditions. These results suggested that the steric hindrance between alkyl substituents and functional groups probably exerted a great influence on the decrease in reactivity of polyfunctional

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Table 3 Oxidation of 1,2-Diols and α-Ketols with PTAB-MXn-Pyridine in MeOH^a

Run	Substrates	S	MXn ^b	Time (h)	Product		Yield (%) ^c
1	Ph OH	5 dl	А	19	Ph O	3	91
2	HO Ph Hydroanisoin	6	Α	14	O Ph MeO $\longrightarrow - \ddot{C} - \dot{C}_{2}$	7	91
3	OH OH	8	Α	10		9	95
4	$Ph \qquad OH$	4	Α	15	$Ph \longrightarrow O$	3	98
5	Anisoin	10	Α	15	$MeO \longrightarrow O \\ -C -)_2$	7	91
6		11	Α	19		9	92
7	$Ph \qquad OH \qquad $	5 dl	В	72	$\stackrel{\text{Ph}}{\longrightarrow} \stackrel{\text{OH}}{\longleftarrow}$	4	54
8		8	В	60		11	77
9	$Ph \qquad OH$	4	В	66	Recovered	4	82
10	Anisoin	10	В	10	Recovered	10	92
11	Ph OH \rightarrow Ph HO Ph	12	Α	48	$Ph \qquad OH \qquad Ph \qquad Ph$	13	92
12	$\begin{array}{c} Ph \\ \hline \\ Ph \\ \hline \\ Ph \\ HO \\ Ph \end{array}$	12	В	48	Recovered	12	88

^a Substrate S (0.25mmol), PTAB (1.0 mmol), pyridine (1.0 mmol), MeOH (8 mL), r.t.

^b MXn: $\mathbf{A} = \text{SbBr}_3$, $\mathbf{B} = \text{CuBr}_2$.

^c Isolated yield.

Table 4 Oxidation of Alcohols with PTAB-SbBr₃-Pyridine in MeOH^a

Run	Substrates	S	Time (h)	Product	Yield	(%) ^b
1	—он	14	15	0	15	88
2	OH	16	47		17	83
3	Рһ СН ₃ —ОН	18	65	Ph CH ₃ =0	19	86
4	Ph Ph Ph	20	68 ^c	Ph Ph	21	70 ^d
5	Рһ СН ₃ —ОН	18	5 ^e	Ph OMe OMe Br	22	84 ^f
6	Ph Ph Ph	20	5 ^{c,e}	Ph Ph Ph	21	63 ^g
7	CH ₃ (CH ₂) ₁₁ OH	23	48	Recovered	23	85
8	ОН	24	6	ОН	25	93

^a Substrate *S* (0.25 mmol), PTAB (1.0 mmol), pyridine (1.0 mmol), SbBr₃ (0.05 mmol), MeOH (15 mL), r.t.

^b Isolated yield.

^c PTAB (0.75 mmol), pyridine (0.75 mmol).

^d Recovered **20**: 25%.

^e Temp: 65 °C.

^f Recovered **18**: 11%.

^g Dimethyl acetal was obtained in 8% yield. Recovered 20: 24%.

secondary alcohols such as α - and β -hydroxyesters, α -haloalcohol.³⁶ As aromatic primary alcohols behaved quite differently from aliphatic ones and were oxidized easily by many oxidation systems, the oxidation of benzyl alcohol was carried out to test the limitation of this chemoselectivity with PTAB–SbBr₃–pyridine and PTAB–CuBr₂–pyridine. Benzyl alcohol was not oxidized to benzaldehyde and benzoic acid easily.³⁷ The oxidation of a variety of mono-substituted benzylic alcohols was

 $\label{eq:Table 5} \begin{array}{ll} \mbox{Table 5} & \mbox{Oxidation of Alcohols with PTAB-CuBr}_2\mbox{-Pyridine in } \\ \mbox{MeOH}^a \end{array}$

Run	Substrates S	Time (h)	Product	Yield (%) ^b
1	14	20	15	90
2	16	34	17	88
3	18	42	19	84
4	20	42	21	80
5	23	17	23	93
6	24	60	25	79 ^c

^a Substrate *S* (0.25 mmol), PTAB (1.0 mmol), pyridine (1.0 mmol), CuBr₂ (0.05 mmol), MeOH (15 mL), r.t.

^b Isolated yield.

[°] Recovered **24**: 13%.

also examined. 2-Chloro-, 4-bromo-, 2-bromo-, 4-methyl and 2-methyl benzyl alcohols were recovered unchanged in over 50–80% yields under the same reaction conditions. These results sufficiently accounted for the mild and chemoselective oxidation of secondary alcohols by PTAB–SbBr₃–pyridine and PTAB–CuBr₂–pyridine.³⁸

In conclusion, the combination of PTAB and a catalytic amount of SbBr₃ or CuBr₂ provided an alternative and convenient chemoselective procedure for the oxidation of secondary alcohols and substituted 1,2-diols to the corresponding ketones, 1,2-diketones and α -ketols. Further application to the oxidation of alcohols with ammonium tribromides is now in progress.

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- (26) In particular, the oxidation of 1,2-diols 5, 8 to α-ketols with PTAB–CuBr₂–pyridine proceeded slowly at r.t. For example, compound 8 was converted to 11 in 42% yield for 14 h. 1,2-Dicyclohexyl-1,2-ethanediol (8) was recovered

unchanged in 49% yield. It was assumed that the coordination of CuBr₂ to 1,2-diols or α -ketols was stronger than that of SbBr₃. Consequently, it required long reaction time to oxidize 1,2-diols to ketols with PTAB–CuBr₂– pyridine at r.t.

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- (36) Mandelic acid methylester and ethyl 3-hydroxybutyrate were recovered unchanged in 92–95% yields at r.t. for 17–18 h. 1,4-Dichloro-2-butanol was also recovered unchanged in 90% yield at r.t. for 17 h.
- (37) Benzyl alcohol was recovered in 60–75% yields for 17–24 h. Benzaldehyde dimethylacetal was gradually afforded in 13– 32% yields for 48–72 h.
- (38) A typical procedure is described for the oxidation of *meso*hydrobenzoin **1**. To a solution of SbBr₃ (18 mg, 0.05 mmol) in MeOH (8 mL) were added pyridine (60 μ L) and PTAB (281 mg, 0.75 mmol) at r.t. After stirring for 5 min *meso*hydrobenzoin **1** (53 mg, 0.25 mmol) was added. The reaction mixture was treated with 0.5 M aq Na₂S₂O₃ after stirring for 16 h at r.t. and extracted with EtOAc. The organic layer was washed by 0.5 M aq Na₂S₂O₃ and successively sat. aq NaCl and dried by MgSO₄. After removal of the solvent in vacuo, the residue was purified by column chromatography on silica gel (Wakogel C-200) with CCl₄ and CHCl₃ (3:1 v/v). Benzil (**3**, 50 mg, 0.24 mmol) was obtained in 96% yield.