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Oxidative Cleavage of 4,6-O-Benzylidene Ring with t-Butyl Hydroperoxide and Copper(II) Chloride. Preparation of Methyl 4-O- and 6-O-Benzoylhexopyranoside Derivatives

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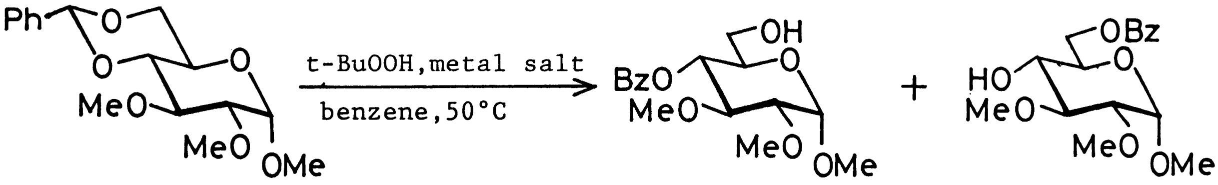
Copper(II) chloride and palladium(II) acetate were found to be highly effective catalysts for oxidative cleavage of O-benzylidene ring with t-butyl hydroperoxide. Using the former catalyst 4,6-O-benzylidenehexopyranoside derivatives were converted into the corresponding 4- and 6-benzoates in high yields. This reaction was also applicable for conversion of benzyl group into benzoyl one.

Direct conversion of one protecting group into the other, for instance, benzylidene[1)] into bromobenzoate or diol monobenzyl ether, is one of the effective methodologies in order to avoid tedious steps of deprotection and subsequent derivation. Hosokawa et al.[2)] showed that palladium(II) salt-catalyzed oxidative cleavage of cyclic acetal with t-butyl hydroperoxide (t-BuOOH) is useful for the preparation of diol monoesters. In this paper the reaction was applied at the first time to carbohydrates and it was found that copper(II) chloride was the most effective among the several metal salts tested. Many 4,6-O-benzylidene-hexopyranoside derivatives were oxidized with t-BuOOH and copper(II) chloride to give the corresponding 4- and 6-benzoates in high yields.

First of all, the reactions of methyl 4,6-O-benzylidene-2,3-di-O-methyl-α-D-glucopyranoside (1) with t-BuOOH in the absence and presence of several metal salts were examined. Even though treatment of 1 with t-BuOOH gave 4- (2) and 6-

benzoate (3), the addition of metal salts increased their yields remarkably. As shown in Table 1 the effectiveness of the salts tested decreased in the following order: Pd(OAc)$_2$, CuCl$_2$ FeCl$_3$, PdCl$_2$ NiCl$_2$. In all cases 4-benzoate (2) was formed predominantly with ratios of 1.1—1.6 to 1.



1 2 3

Table 1. Effect of metal salts on the oxidation of 1 with t-BuOOH

Metal salt	Total yield/%	2/3
none	19	1.4
Pd(OAc)$_2$	90	1.4
CuCl$_2$	87	1.1
FeCl$_2$	70	1.2
PdCl$_2$	68	1.4
NiCl$_2$	31	1.6

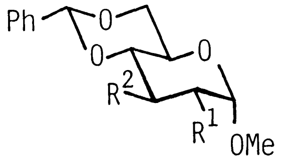
A typical reaction procedure: A solution of 1 (1 mmol) and anhydrous t-BuOOH (70% solution: 6 mmol) in dry benzene (4 ml) was stirred in the presence of a metal salt (0.1 mmol) for 15 h at 50 °C under argon. The reaction mixture was poured into water (50 ml) and extracted with chloroform (40 ml x 4). The extract was washed with saturated aqueous $Na_2S_2O_3$ and NaCl, dried with anhydrous $MgSO_4$ and evaporated to give a mixture of 4- (2) and 6-benzoate (3), which were separated by preparative TLC on silica gel.

The reaction was then applied, using CuCl$_2$ as a catalyst, to other 4,6-*O*-benzylidenehexopyranosides (4—22) with different configurations of α-D-gluco, β-D-gluco, α-D-allo, α-D-altro, α-D-manno, and α-D-galacto, having various functional groups including methyl, benzyl, acetyl, benzoyl, methanesulfonyl, p-toluenesulfonyl, azido, and anhydro groups. In each case a mixture of the corresponding

4- and 6-benzoate was obtained in high yield as shown in Table 2. However, in the case of 4 ($R^1=R^2=PhCH_2O$) oxidation of benzyl ether was also observed as described below.

Table 2. Oxidation of 4,6-O-benzylidenehexopyranoside derivatives with t-BuOOH and $CuCl_2$

	Substrate		Yield	Ratio of		Substrate		Yield	Ratio of
	R^1	R^2	%	4-/6-benzoate		R^1	R^2	%	4-/6-benzoate
5	OAc	OAc	81	1 : 2	14	OTs	OTs	97	2.5 : 1
6	OBz	OBz	96	1 : 2.4	15	OMe	OMe	98	1.1 : 1
7	OMs	OMs	99	1.5 : 1	16	OBz	OBz	99	1 : 2
8	OTs	OTs	98	3 : 1	17	OTs	OTs	97	2 : 1
9	OBz	OTs	88	2.5 : 1	18	OMe	OMe	99	1 : 1.3
10	OTs	OBz	93	1 : 2	19	OBz	OBz	96	1 : 1.2
11	-	-	82	1.1 : 1	20	OTs	OTs	90	1.1 : 1
12	OMe	OMe	82	1.1 : 1	21	OAc	N_3	87	1.1 : 1
13	OBz	OBz	99	1 : 1.1	22	-	-	99	1.2 : 1



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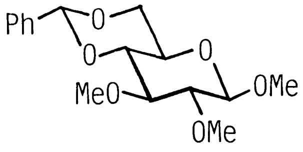

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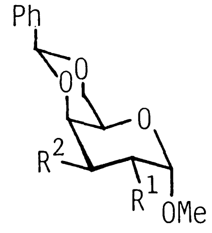

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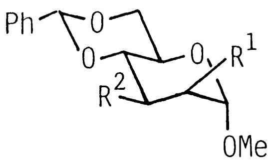

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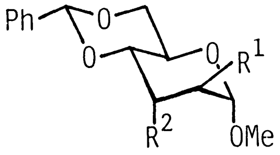

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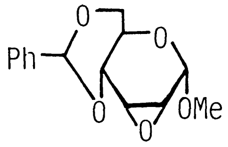

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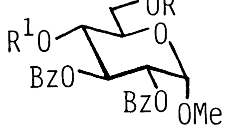
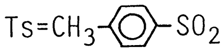


23 R^1=Bz, R^2=H
24 R^1=H, R^2=Bz

Bz=COPh
Ms=CH_3SO_2



The regioselectivity of the reaction seems to be affected by equatorially oriented substituents on O-3, that is, the acyl substituents favored the predominant formation of 6-benzoate as shown in the cases of hexopyranosides with α-D-gluco (5—10), α-D-galacto (13, 14), and α-D-manno (16, 17) configurations. On the other hand, the axially oriented substituents did not give any significant regioselectivity as shown in the cases of 19 and 20. Furthermore, it is noteworthy that the β-glucoside 11, which is generally more susceptible to oxidative conditions3) than the corresponding α-anomer, gave the expected mixture of two benzoates.

Finally, it may be worth while mentioning the fate of O-benzyl group under this oxidative condition. The reaction of 4 gave 2,3,4- (23) and 2,3,6-tri-O-benzoate (24) in 48% yield with a ratio of 1:1.3. Although conversions of O-benzyl group into O-benzoyl one with chromium and other oxidizing agents have been reported,4) the same practical conversion with the oxidizing system described herein has never been reported to our knowledge. Because it was confirmed with some another benzyl derivatives5) that O-benzyl group was converted to O-benzoyl one accompanying O-debenzoylation, this oxidative conversion may afford an alternative method for modification of benzyl group. In conclusion, this t-BuOOH oxidation of benzylidene as well as benzyl groups may provide a new useful method in the chemistry of protection and deprotection.

References

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2) T. Hosokawa, Y. Yamada, and S. Murahashi, J. Chem. Soc., Chem. Commun., 1983, 1245.
3) P. Deslongchamps, C. Moreau, D. Frehel, and R. Chaevert, Can. J. Chem., 53, 1204 (1975).
4) B. S. Bal, K. S. Kochhar, and H. W. Pinnick, J. Org. Chem., 46, 1492 (1981) and references cited therein.
5) In a preliminary experiment the oxidation of methyl 4,6-di-O-acetyl-2,3-di-O-benzyl-α-D-glucopyranoside under the same condition as described in the text gave a mixture of the corresponding 2,3-dibenzoate, 2-benzoate and 3-benzoate in 85% yield with a ratio of 2:1.5:1.

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