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A FACILE METHOD FOR THE OXIDATIVE REMOVAL OF BENZYL ETHERS: THE OXIDATION OF BENZYL ETHERS TO BENZOATES BY RUTHENIUM TETRAOXIDE

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Abstract. A series of benzyl ethers has been prepared and their oxidation to benzoate esters by ruthenium tetraoxide has been studied. Yields for the oxidation step range from 54 to 96%.

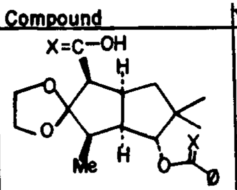
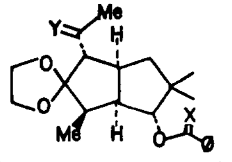
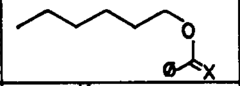
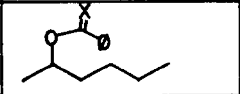
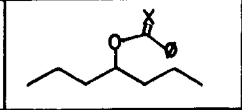
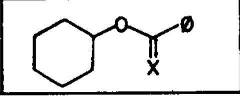
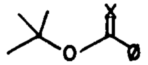
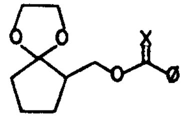
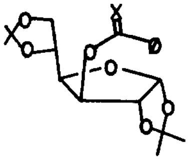
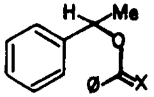
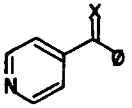
We recently required a simple and efficient method for conversion of a primary alcohol to a carboxylic acid. To this end, alcohol 1 was treated with ruthenium tetraoxide and sodium metaperiodate. Although this expected oxidation readily occurred, it was also clear that the benzyl ether had been oxidized to the benzoate ester 2 in the process. (See Table I) This observation prompted us to further investigate the possibility of using ruthenium tetraoxide as an oxidative method of removing benzyl ether protecting groups via oxidation to benzoate esters.

The benzyl ether group is most commonly removed by reductive methods.[1] Less commonly used are oxidative methods.[1] Recently, Sharpless and co-workers discovered and reported reaction conditions that drastically improve ruthenium tetraoxide oxidations.[2] In fact, they also reported a single example of a benzylic ether oxidation-benzyl methyl ether → methyl benzoate (89%)-conversion using their new reaction conditions. In order to test the scope, efficiency, and limitations of this benzyl ether → benzoate conversion, we prepared a series of benzyl ethers (see Table I). In general, the ethers were prepared by the method of Provelenghiou and co-workers.[3] The benzyl ethers prepared in this manner (see Table I for yield) were subjected to the ruthenium tetraoxide oxidation reaction (0.005 moles ether/4.2 eq $NaIO_4$/175 mL 2:2:3 CCl_4:CH_3CN:H_2O/.02 eq $RuO_2 \cdot XH_2O$/r.t.). In some cases, we observed that agitation of the thick slurry using the Sharpless[2] conditions was difficult and the yield was sometimes affected. In all cases this problem was solved by using approximately 3x the dilution.

Examination of Table I shows that this procedure works well (54-96% yield) with benzyl ethers of primary, secondary, and tertiary alcohols (entries 3-7). In addition, ethylene ketals, acetonides, benzoates, and aromatic rings are also stable under these conditions (entries 1,2,8-10). We have also noted (entry 11) that 4-benzylpyridine can be oxidized to the 4-benzoyl derivative in this way.

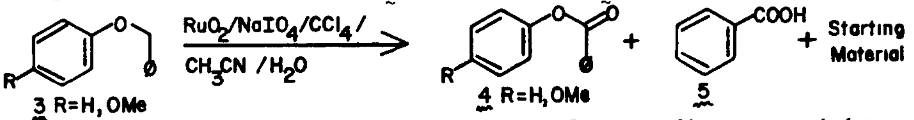
One obvious limitation of this method is that benzyl ethers in molecules having other readily oxidizable groups (e.g., olefins, acetylenes, alcohols, etc.) cannot be oxidized in this manner. A somewhat less obvious limitation is that benzyl ethers of phenols are not

Table I

Entry	Compound	Yield (X=H,H)	Yield(X=O)
1		1 —	2 96%
2		—	69%
3		70%	82%
4		60%	85%
5		73%	89%
6		75%	84%
7		77%	54%
8		47%	76%
9		99%	86%
10		72%	92%
11		—	67%

readily oxidized by this method. Phenyl- and p-methoxyphenyl benzyl ethers (3) (see Scheme I) react to give a mixture of benzoate (4), benzoic acid (5), and starting material. The reaction stops after a period of time and the addition of more sodium metaperiodate and/or ruthenium dioxide hydrate has no effect. A possible explanation is that the phenyl benzoates formed are much more easily hydrolyzed[4] than the aliphatic cases, giving benzoic acid that stops reaction by complexation[2] with the ruthenium oxidant. We are currently examining the use of buffers that would hold the pH of the oxidation medium at a higher level.

Scheme I



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References

1. a."Protective Groups in Organic Synthesis", by T.W. Greene, p. 29, John Wiley and Sons, 1981, New York, b. Hanessian, S., Liak, T.J. and Vanasse, B., Synthesis 1981, 396.

2. Carlsen, P.H.J.; Katsuki, T.; Martin, V.S. and Sharpless, K.B. J. Org. Chem. 1981, 46, 3936.

3. Czernecki, S., Georgoulis, C. and Provelenghiou, C. Tetrahedron Letters 1976, 3535.

4. A dilute aqueous solution of $NaIO_4$ has a pH near 4.0 (cf. Jackson, E.L. Organic Reactions 1944, 2, 341.

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