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ONE-STEP CONVERSION OF PROTECTED LACTOLS INTO LACTONES

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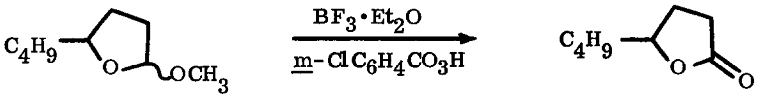
The regeneration of a lactone from a protected lactol (e.g. cyclic methyl acetal) requires hydrolysis to the cyclic hemiacetal followed by oxidation. We describe below the direct one-step conversion of protected lactols to lactones. The new method obviates the necessity of carrying out a two-step procedure and provides a new alternative for the unleashing of a masked or protected lactone which we required in connection with a complex synthesis.

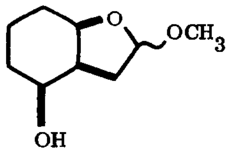
The method as indicated in equation 1 involves treatment of the protected lactol[1] with 1.1 equiv of m-chloroperbenzoic acid in methylene chloride containing a catalytic amount of boron trifluoride etherate. Yields for the conversion of protected γ-lactols to γ-lactones are generally high.[2] The simplicity of the method is illustrated below for the conversion of the cyclic methyl acetal 1 into γ-octanoic lactone (2).



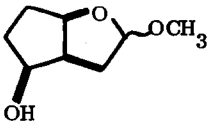
(1)

1 2

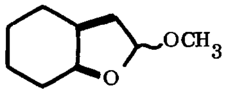
A solution of protected γ-lactol 1 (156 mg, 1.0 mmol) in 3.6 ml of dry methylene chloride containing a catalytic amount of boron trifluoride etherate was treated at room temperature with m-chloroperbenzoic acid (223 mg, 1.1 mmol). After 3 hr the reaction mixture was diluted with 30 ml of ether and washed successively with 10% aq sodium thiosulfate, saturated sodium bicarbonate, and brine. The crude product obtained after drying ($MgSO_4$) was chromatographed on 20 g of silica gel using hexane-ether (1:1) giving 133 mg (94%) of pure lactone 2 as a colorless oil. Application of this method to protected δ-lactols gave disappointingly low yields of δ-lactones.

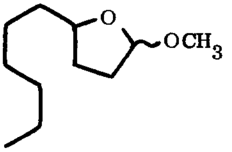


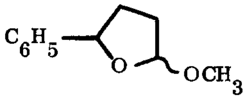
3(83%)



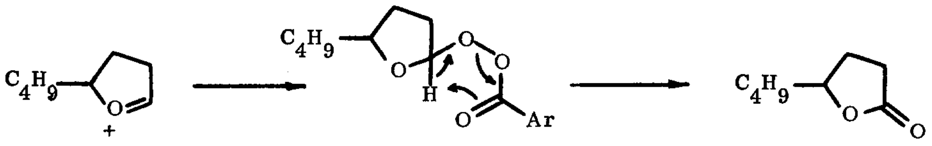
4(86%)


5(96%)


6(92%)

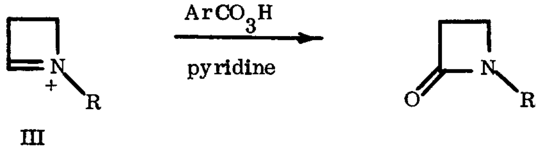

7(82%)

We believe that the above reaction proceeds via oxonium I which reacts with peracid giving rise to intermediate II. Rapid fragmentation of II as indicated by the arrows leads to the observed lactone in the absence of base.[3]



I II 2

Wasserman[4] has recently observed and reported a similar reaction in which the iminium salt III generated from azetidine-2-carboxylic acid reacted with m-chloroperbenzoic acid in the presence of pyridine to form β-lactams.



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References and Notes

1. The protected lactols were prepared in >90% yield from the corresponding lactones via reduction with diisobutylaluminum hydride in toluene at -78° followed by treatment (0°) with methanol in the presence of a catalytic amount of boron trifluoride etherate.
2. The yields for the conversion of cyclic methyl acetals into their respective γ-butyrolactones are given in the parentheses under the structures 3-7.
3. The oxidation of noncyclic acetals to esters in moderate yield employing peracetic acid-sulfuric acid at 40-60°C has been reported [D. L. Heywood and B. Phillips, J. Org. Chem., 25, 1699 (1960)].
4. H. H. Wasserman and A. W. Tremper, Tetrahedron Letters, 1449 (1977).