1,2,4-TRIOXANES AS MASKED, DUAL PURPOSE, FUNCTIONAL GROUPS

Charles W. Jefford, Jean-Claude Rossier, and John Boukouvalas

Department of Organic Chemistry, University of Geneva, 1211 Geneva 4, Switzerland

Abstract - 1,2,4-Trioxanes readily undergo reductive cleavage upon treatment with zinc and acetic acid to furnish the corresponding 1,2-diols and C3-derived carbonyl compounds in high yield.

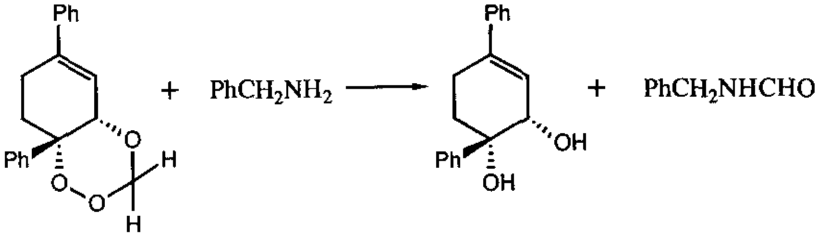
Cyclic peroxides are being increasingly employed as intermediates for creating a variety of dioxygen substituted substances such as diols, keto and epoxy alcohols by cleavage of the oxygen-oxygen bond.[1] Two related examples involving 1,2,4-trioxanes, which also contain the peroxidic link, show that they too could be of synthetic potential.[2] So far, 1,2,4-trioxanes, unlike their lower homologues, the secondary ozonides, have been relatively unknown, and therefore unexploited as chemical entities.[3] However, methods have been recently developed for preparing a wide range of monocyclic and bicyclic 1,2,4-trioxanes.[4] Consequently, they are now available for testing as synthons. Already, selective transformations to α-keto acids,[5] 1,2-diol monoesters[6] and 1,2-diols[7] have been achieved A typical case is the treatment of the *cis*-fused derivative **1** with benzylamine for several days. Aminolysis occurs to give *cis*-1,2-diol **2** and N-benzylformamide. A limiting condition for this mild process is that the C3 position be unsubstituted We now report that 1,2,4-trioxanes, regardless of the degree of C3 substitution, can be induced to cleanly liberate the 1,2-diol together with the corresponding C3 carbonyl derivative by reductive cleavage with zinc and acetic acid. In other words, the reaction can be used for unmasking either function. If the aim is to prepare diols, then trioxanes originally prepared from volatile carbonyl partners are the substrates of choice since purification will be facilitated by evaporation. The procedure is both simple and short Treatment of the trioxane, neat or in ether solution with an excess of zinc powder and glacial acetic acid followed by filtration through celite and evaporation of the solvent gives the desired diol essentially free of impurities The progress of the reduction can be conveniently monitored by tlc in order to ensure that all of the trioxane is consumed. Illustrations are provided by the trioxanes **3**, **5**, **7**, and **8** which are converted in almost quantitative yield to the corresponding 1,2-diols (**4** and **6**) in which the original configuration of the oxygen substituents remains intact. The volatile by-products acetone, acetaldehyde, and formaldehyde are easily removed (entries 1-4, Table 1).

On the other hand, the 1,2,4-trioxane entity can be regarded as a latent carbonyl group. Pertinent examples are provided by the cyclohexadione mono-acetals **9** and **10**. Treatment with a two-fold molar excess of 1,4-dimethyl-1,4-epidioxy-1,4-dihydronaphthalene (**11**) in the presence of trimethylsilyl trifluoromethanesulfonate (TMSOTf, 0.16 mol. equiv.) and 2,6-di-*t*-butylpyridine (DTBP, 0.07 mol. equiv.) in dichloromethane at -78°C affords the trioxanes **12** and

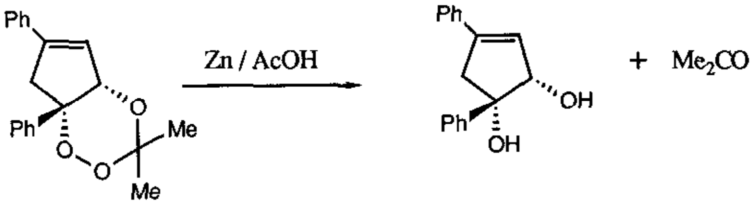
Table 1. Reduction of Some 1,2,4-Trioxanes to 1,2-Diols and Carbonyl Compounds

Entry	**Trioxane**	**Reaction Conditions**	**Product**	**Yield (%)**[a]
1	**3**	Zn/AcOH/20 min/16°	**4**	98
2	**5**	Zn/AcOH/20 min/16°	**6**	100
3	**7**	Zn/AcOH/Et$_2$O/90 min/-5°	**6**	94
4	**8**	Zn/AcOH/15 min/16°	**6**	99
5	**12**	Zn/AcOH/20 min/16°	**9**[b]	77
6	**13**	Zn/AcOH/90 min/-17°	**10**[b]	98
7	**12**	aq. 1M H_2SO_4/THF/16 h/20°	**14**	85

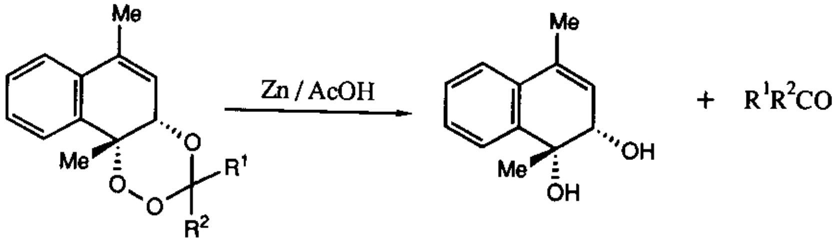
[a] Yield of chromatographically purified product, except for entries 5 and 6 where yield was estimated by ^{1}H nmr. [b] Diol **6** was also formed in commensurate yields.



1 **2**



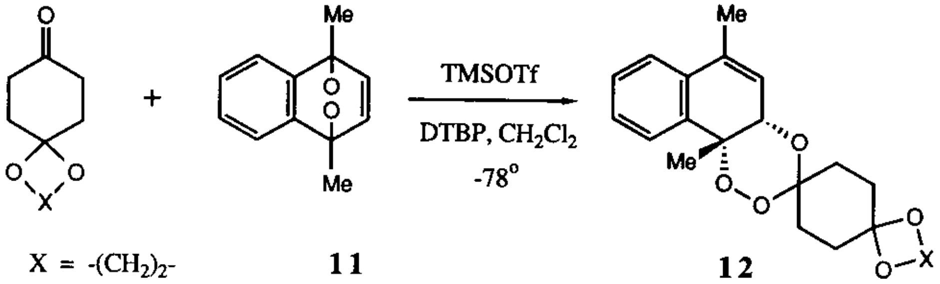
3 **4**



5 $R^1 = R^2 =$ Me **6**

7 $R^1 =$ H, $R^2 =$ Me

8 $R^1 = R^2 =$ H

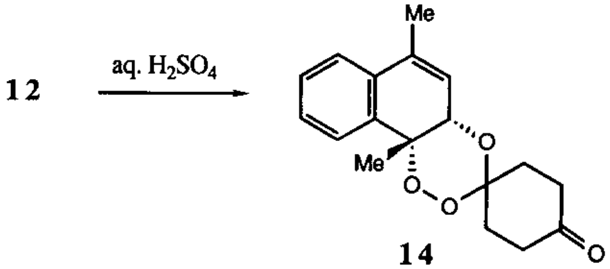


9 X = $-(CH_2)_2-$ **11** **12**

10 X = $-CH_2CMe_2CH_2-$ **13**

$$\mathbf{12} \xrightarrow{\text{Zn / AcOH}} \mathbf{6} + \mathbf{9}$$

$$\mathbf{13} \xrightarrow{\text{Zn / AcOH}} \mathbf{6} + \mathbf{10}$$



14

13[8] *in virtually quantitative yield.*[9] *Reductive scission of* ***12*** *and* ***13*** *with zinc and acetic acid regenerates the parent* ketones **9** and **10** in high yield together with the diol **6** (entries 5-6, Table 1). Selective removal of the acetal group is also realizable. The action of aqueous sulfuric acid on **12** furnishes the trioxane-ketone **14** in 85% yield after purification (entry 7, Table 1).

In conclusion, we have demonstrated that 1,2,4-trioxanes can serve two purposes; they can be used either as a source of 1,2-diols or as acid-insensitive homologues of acetals. In this latter capacity they should be particularly valuable for the selective transformation of polycarbonyl compounds.[10]

Acknowledgments. We thank the Swiss National Science Foundation (grant No 2.632-0.87) for financial support of this work.

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Received, 8th September, 1988