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Ruthenium-Catalyzed Oxidation of Cyclic Acetals with *tert*-Butyl Hydroperoxide. A Facile Synthesis of Glycol Monoesters

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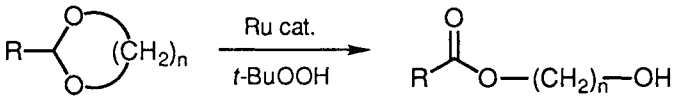
The ruthenium-catalyzed oxidation of cyclic acetals with *tert*-butyl hydroperoxide under mild conditions gives the corresponding glycol monoesters efficiently. The present oxidation reaction provides a useful method for the synthesis of glycol monoesters from 1-alkenes by combination with palladium-catalyzed acetalization of 1-alkenes.

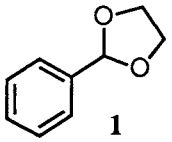
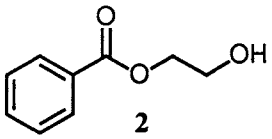
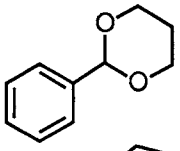
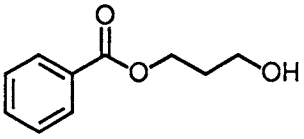
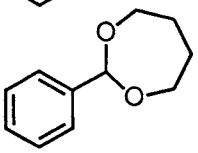
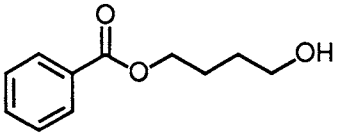
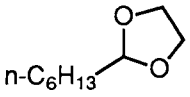
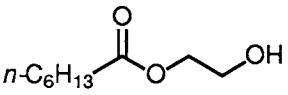
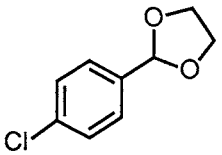
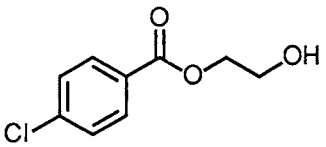
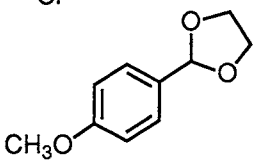
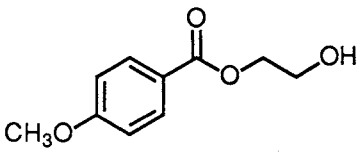
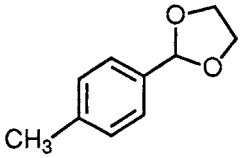
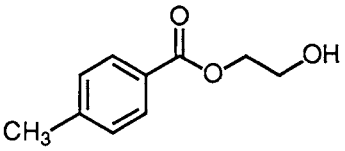
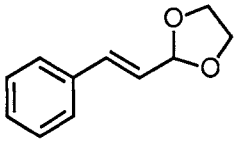
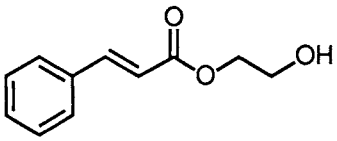
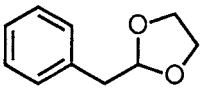
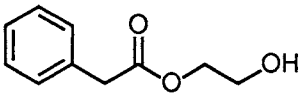
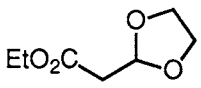
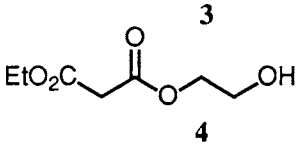
Oxidation of aldehydes to carboxylic acids is one of the fundamental transformations in organic synthesis.[1] Acetals are often used as protected aldehydes; however, direct oxidations of acetals to esters are limited to few cases because of their lower reactivities. During the course of our systematic study on cytochrome P-450 type-oxidation with metal catalysts, low valent ruthenium catalyst / *t*-BuOOH system has been found to be effective for the oxidations of various substrates such as amines,[2,3] amides,[4] nitriles,[5] and alcohols.[6] As a consequence of these studies, we have found that ruthenium-catalyzed oxidation of cyclic acetals with *t*-BuOOH proceeds under mild conditions to give the corresponding glycol monoesters efficiently (Eq. 1). The present oxidation of cyclic acetals is advantageous over the previous methods using peroxides,[7] ozone,[8] and hypochlorous acid[9] with respect to its generality and ease of handling.



(1)

The catalytic activity of various metal complexes has been examined for the reaction of 2-phenyl-1,3-dioxolane (**1**) with *t*-BuOOH. $RuCl_3 \cdot nH_2O$ has proved to be the most effective catalyst for the formation of 2-hydroxyethyl benzoate (**2**). The other ruthenium complexes such as $RuH_2(PPh_3)_4$, $Ru_3(CO)_{12}$, $RuCl_2(bpy)_2$, and $RuCl_2(PPh_3)_3$ showed moderate catalytic activity. The effect of oxidants has been examined for the oxidation of **1** in the presence of $RuCl_3 \cdot nH_2O$ catalyst. The oxidation with *t*-BuOOH gave the best results, and the other oxidants such as H_2O_2, peracetic acid, iodosyl benzene, and *N*-methylmorpholine *N*-oxide are ineffective for the present oxidation reaction. Cumyl hydroperoxide is much less effective in comparison with *t*-BuOOH.

Table 1. Ruthenium-Catalyzed Oxidation of Cyclic Acetals with *t*-BuOOH[a)]

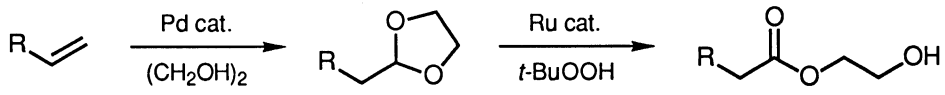
Entry	Substrate	Product[b)]	Yield/%[c)]
1	 **1**	 **2**	79
2			58
3			46
4			72
5			87
6			80
7			86
8			78
9		 **3**	62
10		 **4**	53

a) Reaction conditions are given in the text. b) The product gives satisfactory IR, NMR, and Mass spectral data. c) Isolated yield.

Typically, the oxidation of **1** was carried out as follows: To a mixture of **1** (1.20 g, 8.00 mmol), $RuCl_3 \cdot nH_2O$ (0.063 g, 0.24 mmol, 3 mol%), and dry benzene (8.0 mL) was added a 3.55 M solution of *t*-BuOOH in dry benzene (6.76 mL, 24.0 mmol) dropwise at room temperature over a period of 1 h under argon. After the addition was complete, the reaction mixture was stirred for an additional 4 h. The mixture was diluted with ether (50 mL), and the organic layer was washed successively with 10% aqueous Na_2SO_3 solution and brine, dried over Na_2SO_4, and filtered. Evaporation of the filtrate followed by column chromatography on silica gel (hexane / ethyl acetate = 1:1) gave **2** (1.05 g, 79%) as a colorless oil.

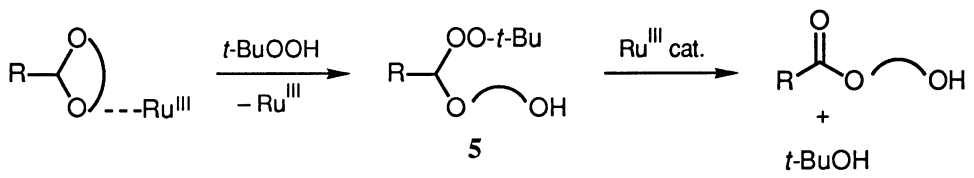
The representative results of the ruthenium-catalyzed oxidation of cyclic acetals with *t*-BuOOH are listed in Table 1. Various aliphatic and aromatic cyclic acetals can be converted into the corresponding glycol monoesters with high efficiency. The reactivity of the acetals is in the order of five > six >> seven-membered cyclic acetals (entries 1–3). It is noteworthy that the present oxidation can be performed selectively in the presence of olefinic moiety (entry 8). Ozone has been widely used for the transformation of cyclic acetals to glycol monoesters;[8] however, it can not be applied to olefinic acetals because oxidative cleavage of olefins takes place predominantly. Cyclic acetals bearing benzyl and carbonyl groups can be also oxidized to give the corresponding glycol monoesters in moderate yields (entries 9 and 10).

Recently we have found a novel method for preparation of cyclic acetals by the palladium(II)-catalyzed reaction of terminal olefins with diols.[10,11] Therefore, the combination of the acetalization and the present oxidation provides a convenient method for synthesis of ethylene glycol monoesters from 1-alkenes (Scheme 1). Indeed, glycol esters **3** and **4** can be readily prepared from styrene and ethyl acrylate by the palladium(II)-catalyzed acetalization and the subsequent oxidations.



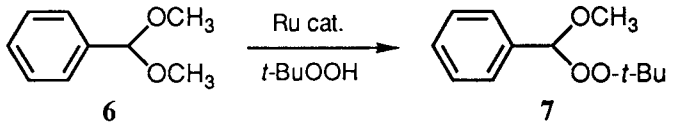
Scheme 1.

The present oxidation can be rationalized by assuming the mechanism as shown in Scheme 2. Coordination of the acetal oxygen to ruthenium(III) followed by nucleophilic attack of *t*-BuOOH on the acetal carbon atom would give intermediate **5**. Further, ruthenium(III)-promoted reaction of peroxide **5** would give glycol monoester and *t*-BuOH. The intermediacy of **5** is supported by the fact that acyclic acetal **6** was



Scheme 2.

selectively converted into the corresponding *tert*-butyldioxy compound **7** under the same reaction conditions (Eq. 2). Similar conversion of acyclic acetals to the corresponding *tert*-butyldioxy compounds and the subsequent transformation into esters have been performed by using *tert*-butyl trimethylsilyl peroxide in the presence of a catalytic amount of trityl perchlorate.[12]



6 7 (2)

In order to determine this mechanism, the relative reaction rates of the oxidation of four 2-phenyl-1,3-dioxolanes (X-$C_6H_4CH(OCH_2)_2$, X = *p*-CH_3, H, *p*-Cl, and *m*-Cl) with *t*-BuOOH in benzene were determined by GLC analysis of the product ethylene glycol monoesters. The rate data correlate well (γ = 0.955) with Hammett linear free energy relationship with use of σ values (Fig. 1). The small and positive ρ value (+0.46) supports the polar nucleophilic addition of *t*-BuOOH to the acetal.

Work is in progress to apply our method to other systems.

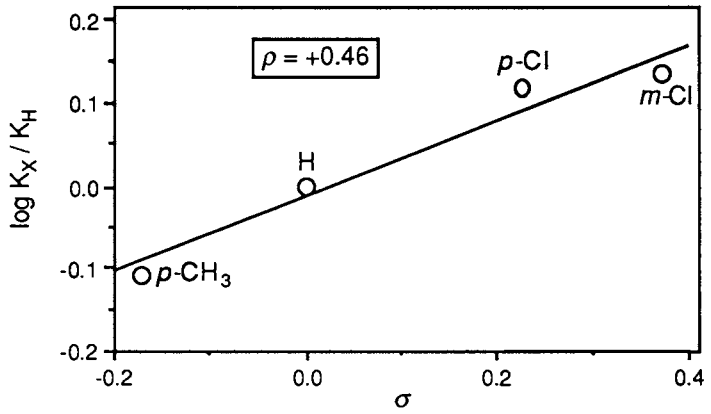


Fig. 1. Hammett plots for the $RuCl_3 \cdot nH_2O$-catalyzed oxidation of 2-phenyl-1,3-dioxolanes with *t*-BuOOH in benzene.

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