

## Direct Oxidation of Acetals and Aldehydes to Esters

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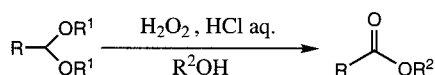
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Received 13 July 1997

**Abstract:** One step conversion of acetals and aldehydes to esters was achieved with hydrogen peroxide (35wt% solution in water) and hydrochloric acid in alcohol. This procedure was proved to be simple and effective.

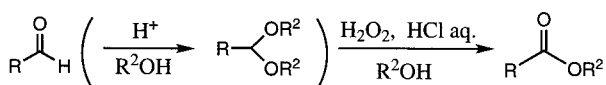
A lot of oxidative methods of aldehyde to carboxylic acid are well-known, and some of those processes are industrialized<sup>1</sup>. Oxidation of aldehydes to esters are also known, but only a few methods of direct oxidation of acetal function to esters have been reported. Peracetic acid<sup>2</sup>, peroxymonosulfuric acid<sup>3</sup>, ozone<sup>4</sup>, N-bromosuccinimide<sup>5</sup> and chromium trioxide<sup>6</sup> have been used as the oxidizing agent. None of the reports on direct oxidation of acetals to esters using hydrogen peroxide, however, has been published. Herein, we report a simple and effective procedure to oxidize acetals or aldehydes to esters with hydrogen peroxide (35wt% solution in water) and hydrochloric acid (12N HCl aq.) in alcohol. Classical oxidation of aldehydes to carboxylic acids using hydrogen peroxide was known<sup>7</sup>. Oxidation of cyclohexanone to 1-hydroxy-1'-hydroperoxydicyclohexyl peroxide by aqueous hydrogen peroxide with hydrochloric acid as a catalyst<sup>8</sup> is already reported.



Our results of the oxidation of acyclic and cyclic acetals are summarized in Table 1. In the cases of acyclic acetals (entry 1,2), both aliphatic and aromatic acetals gave the corresponding esters in excellent yields. However,  $\alpha,\beta$ -unsaturated acetal (entry 3) resulted in low yield due to the competitive addition reaction of hydrogen chloride to olefin. In the cases of cyclic acetals (entry 4-6), esters with alcohols originated from solvents were mainly obtained via transesterification. When primary alcohols were used as a solvent (entry 4,5), yields were excellent. But, in the case of secondary alcohol (entry 6), the yield decreased because the 2-hydroxyethyl ester was formed along with the transesterification product. Although oxidation of acetal with peracetic acid<sup>2</sup> or ozone<sup>4</sup> gave only the ester with alcohol originated from acetal, our procedure afforded esters with alcohols originated from solvents.

When sulfuric acid was used instead of hydrochloric acid, the reaction became much slower. This fact suggests that hydrochloric acid plays not only as acid but also other important role in the oxidation reaction. A plausible explanation of this process is the *in situ* formation of hypochlorous acid which promotes oxidation. Oxidation of aldehydes to esters by sodium hypochlorite<sup>9</sup> in the presence of acetic acid is also reported.

We also applied this procedure to oxidation of aldehydes since aldehydes were thought to be oxidized to esters via acetals under our acidic condition. The results are shown in Table 2.



Entry	$\text{R}-\begin{matrix} \text{OR}^1 \\ \diagup \\ \text{C} \\ \diagdown \\ \text{OR}^1 \end{matrix}$	$\text{R}^2\text{OH}$	$\text{R}-\text{C}(=\text{O})-\text{OR}^2$	Yield
1		MeOH		96% <sup>a</sup>
2		MeOH		95% <sup>a</sup>
3		MeOH		14% <sup>b</sup>
4		MeOH		98% <sup>a</sup>
5		EtOH		99% <sup>a</sup>
6		<sup>i</sup> PrOH		64% <sup>a</sup>

a: Isolated yield. b: <sup>1</sup>H NMR yield

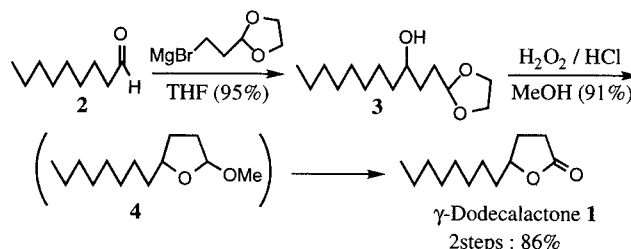
Direct oxidation of aliphatic and aromatic aldehydes to esters proceeded in high yield. In all cases it was not necessary to add large excess of hydrogen peroxide.

Entry	$\text{R}-\text{C}(=\text{O})-\text{H}$	$\text{R}^2\text{OH}$	$\text{R}-\text{C}(=\text{O})-\text{OR}^2$	Yield <sup>a</sup>
1		MeOH		90%
2		MeOH		82%

a: Isolated yield

Versatility of this process for practical use is shown in the following synthesis of  $\gamma$ -dodecalactone<sup>10</sup> **1**, which is a flavor and a pheromone component (Scheme 1).

Reaction of nonanal **2** with the acetal-containing Grignard reagent<sup>11</sup> gave hydroxy acetal in 95% yield. This hydroxy acetal **3** was oxidized via protected lactol<sup>12,4</sup> with hydrogen peroxide and hydrochloric acid in methanol to give  $\gamma$ -lactone in 91% yield. Overall yield (86%) is very good.



### Scheme 1

In conclusion, we achieved the one step oxidation of acetals and aldehydes with hydrogen peroxide (35wt% solution in water) and hydrochloric acid (12N HCl aq.), both of which are cheap reagents. In addition to that, the operation of the reaction was simple and efficient. We think that this procedure must be suitable for industrialization.

### Typical Experimental Procedure

12N HCl aq. (0.25ml, 3.0mmol) was added to a solution of decylaldehyde dimethylacetal (406mg, 2.0mmol) in methanol (4ml) at 5°C under argon. Next H<sub>2</sub>O<sub>2</sub> (34% solution in water, 300mg, 3.0mmol) was added to the solution. During this addition, the internal temperature was kept below 20 °C. The mixture was stirred for 30min with ice-cooling. It was then warmed to 40 °C and stirred for 3h. The reaction mixture was diluted with water and extracted with ethyl acetate. The organic layer was washed with aqueous sodium sulfite, dried over magnesium sulfate and concentrated in vacuo. The residue was purified by silicagel chromatography [SiO<sub>2</sub> 10g, Hexane:AcOEt=4:1] to give methyl decanoate (360mg, 96%).

<sup>1</sup>H NMR (CDCl<sub>3</sub>,90MHz): δ = 0.86 (bt, 3H), 1.24-1.61 (m, 14H), 2.29 (t, *J* = 7.1, 2H), 3.64 (s, 3H).—IR (KBr disc): ν (cm<sup>-1</sup>) = 2925, 2856, 1743, 1436, 1169.

### γ-Dodecalactone

<sup>1</sup>H NMR (CDCl<sub>3</sub>,90MHz): δ = 0.86 (bt, 3H), 1.10-1.94 (m, 16H), 2.19-2.59 (m, 2H), 4.34-4.61 (m, 1H).—IR (KBr disc): ν (cm<sup>-1</sup>) = 2929, 2854, 1778, 1180.

### References and Notes

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