

# Green Oxidations of Aldehydes to Carboxylic Acids and Esters

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**Abstract:** Oxidation reactions are fundamental and useful chemical transformations, especially for industries. However the use of heavy metals or stoichiometric organic agents as common oxidants are nowadays rejected, preferring greener and cheaper procedures. Here we propose a simple and sustainable method to oxidize aldehydes at room temperature using hydrogen peroxide in water or in *on water* conditions and diphenyl diselenide as not expensive and commercially available catalyst. Using an hydroalcoholic medium the oxidation affords the corresponding esters.

## Introduction

The transformation of aldehydes to carboxylic acids is an important reaction in organic synthesis. Even if a large number of methods is available to effect this oxidation, most of them require stoichiometric amounts of toxic or expensive oxidants such as potassium permanganate, chromium VI reagents, chlorite and peroxides often in association with organic solvents (benzene, formic acid, methylene chloride).[1]

The modern paradigm of the "Green Chemistry" and the growing awareness of the environment require the developing of new procedures to effect old reactions in a more eco-friendly manner, increasing the efficiency of the process, reducing the production of wastes, avoiding the use of toxic or potentially dangerous reagents, solvents and additives.

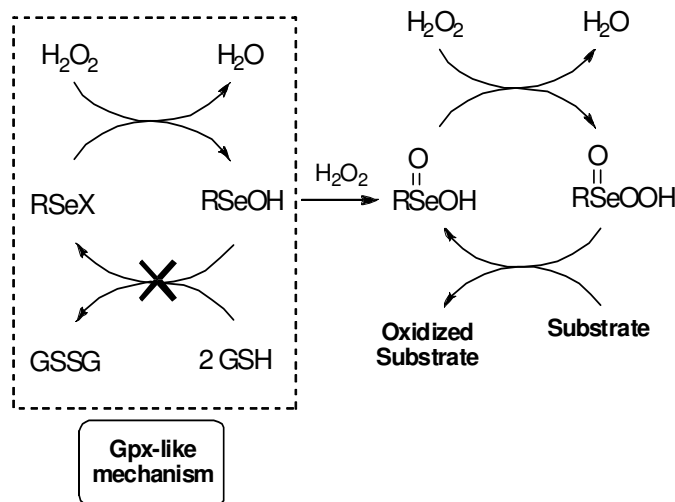
Concerning the oxidation reactions, this should be achieved by the employment of environmentally friendly oxidants, such as molecular oxygen or hydrogen peroxide, in combination with efficient and highly recyclable catalysts in order to effect the reaction in mild conditions increasing the overall yield of the process in benign reaction medium and reducing the formation of side products and wastes.

In continuation to our efforts on exploring the use of organoselenium reagents in organic synthesis and more recently as catalysts in hydrogen peroxide mediated oxidation reactions, we report here a new simple protocol to effect the conversion of aldehydes to the corresponding acid or esters using a slight excess of hydrogen peroxide and 5% of selenium containing catalyst at room temperature, atmospheric pressure and in *on water* conditions.

Very recently we demonstrated that diphenyl diselenide and selenocystine can be conveniently employed as pre-catalysts on the *anti*-dihydroxylation of olefins, using hydrogen peroxide as stoichiometric oxidant and water as reaction medium. These reactions involve an olefin epoxidation promoted by a perselenenic acid followed by the addition of water.[2] The catalytic cycle was optimized taking inspiration from the catalytic cycle of the glutathione peroxidase (GPx). The selenium atom in the proposed catalyst, contrary to that present in the enzyme, is not stabilized

toward the overoxidation and in the absence of a thiol, it is possible to obtain the corresponding selenenic and perselenenic acids that were supposed to be the actual catalysts in the oxidation of more stable substrates such as the olefins.[3] We named this kind of catalysis "Bio-Logic" catalysis.(Scheme 1)

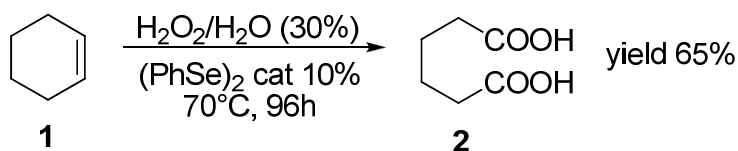
**Scheme1:** Bio-Logic oxidations



## Results and discussion

Continuing to explore the dihydroxylation reaction of olefins, diphenyl diselenide has been used to catalyze the synthesis of adipic acid by the oxidation of cyclohexene through a one pot, six step mechanism similar to that reported by Noyori which involves four consecutive oxidations of the initially formed diols. [4] After 96 hours at 70 °C using 10 mol% of diselenide and 40 equivalents of 30% aqueous hydrogen peroxide, colorless crystalline adipic acid was obtained in 65% yield.

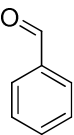
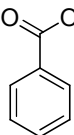
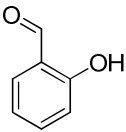
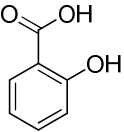
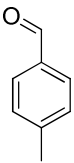
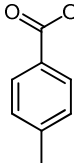
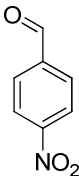
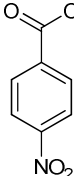
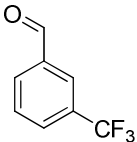
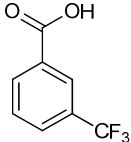
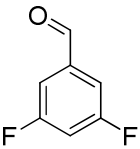
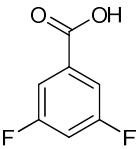
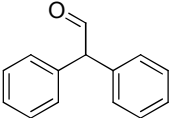
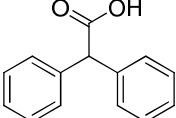
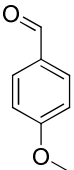
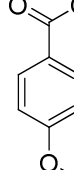
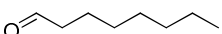
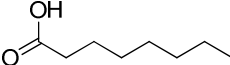
**Scheme 2:** Oxidation of cyclohexene



This result prompted us to investigate the possibility to use this catalytic cycle to effect the oxidation of aldehydes to the corresponding carboxylic acids.

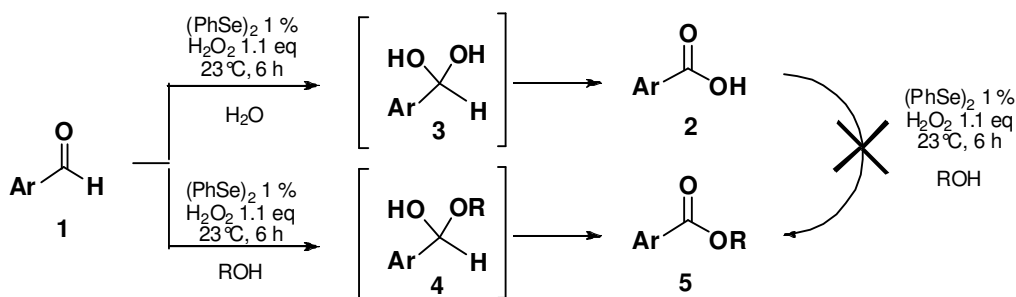
Benzaldehyde **1a** has been converted in six hours into the corresponding benzoic acid **2a** in 92% yield, using 1 equivalent of hydrogen peroxide (10%) and 2% of diphenyl diselenide. We repeated the reaction using similar conditions but without diphenyl diselenide obtaining the not significant formation of **2a** (28%), confirming the role of the catalyst. The method was extended to variously substituted aromatic **1a-j** and aliphatic **1k** aldehydes and the results are summarized in Table 1. The results are generally good and only in the case of the p-nitro benzaldehyde **1d** a poor conversion has been observed.

**Table 1.** Oxidation of aldehydes **1a-k** to carboxylic acids **2a-k**.

Entry	Substrates 1	Products 2	Yield %
a			92
b			73
c			85
d			30
e			99
f			78
g			80
i			80
j			100

The oxidation reasonably proceeds through the oxidation of the initially formed hydrated aldehyde **3** as depicted in Scheme 3. On the basis of this mechanism it is possible to envision that in the presence of an alcohol, the oxidation could occur on the corresponding hemiacetal **4** affording the formation of the ester **5**.

**Scheme3:** Proposed mechanism



The optimized condition for this latter reaction required acidic conditions and heating at  $50^\circ\text{C}$ . The best result has been obtained using methanol (Table 2 entry a) and in the case of more bulky alcohols the yield of ester decreased. In all the cases, it was not possible to recover the starting aldehydes but the corresponding benzoic acid (Table 2). In order to confirm the proposed mechanism, we excluded the possibility that the ester was the result of a direct esterification of the benzoic acid.

**Table 2.** Oxidation of benzaldehyde to esters.

Entry	Alcohol	Ester <b>5</b>	Yield %
a	$\text{CH}_3\text{OH}$		100
b			70
c			60
d			51

In conclusion, this bioinspired oxidative approach has shown to be versatile and represents a convenient alternative to the classical procedures for the green conversion of aldehydes to carboxylic acids or esters with good yields.

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#### References:

- [1] Johnson, E. V.; Backvall, J. E. "Oxidation of Carbonyl Compounds" in *Modern Oxidation Methods* Second Edition Backvall, J-E. Ed.Wiley VCH, **2010** and references cited therein.
- [2] (a) Santi, C.; Tiecco, M.; Testaferri, L.; Tomassini, C.; Santoro, S.; Bizzoca, G. *Phosphorus Sulfur* **2008**, *183*, 956-960. (b) Santoro, S.; Santi, C.; Sabatini, M.; Testaferri, L.; Tiecco, M. *Adv. Synth. Catal.* **2008**, *350*, 2881-2884.(c) Santi, C.; Di Lorenzo, R.; Tidei, C.; Bagnoli, L.; Wirth, T. *Tetrahedron*, **2012**, <http://dx.doi.org/10.1016/j.tet.2012.08.08>
- [3] Bhabak, K. P.; Mugesh, G. *Chem. Eur. J.* **2008**, *14*, 8640-8651.
- [4] Sato, K.; Aoki, M.; Noyori, R. *Science* **1998**, *281*, 1646-1647.