Explorative application of selenium catalysts in the oxidation of benzyl alcohol.

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Abstract: Oxidation mediated by hydrogen peroxide needs to be accelerate by approrpiate catalyst in order to be completed in a reasonable reaction time. As a part of our investigation in the use of organoselenium cataysts in bio-mimetic oxidative protocol we reported here some preliminary results on the oxidation of benzyl alcohol into the corresponding benzoic acid.

Keywords: alcohol; oxidation; selenium; catalysis; carboxylic acids; hydrogen peroxide; green chemistry

During the last years, some of us introduced the term “Bio-Logic-catalysis” to indicate the bioinspired use of organoselenium catalysts in some oxidation reactions (Fig. 1). These were effected using hydrogen peroxide as reactive species of oxygen, water as medium and seleninic acid as the catalyst involved in a mechanism that has been demonstrated to be very similar to that of the naturally occurring enzyme glutathione peroxidase.[1]

Following this protocol, the direct 1,2 dihydroxylation of olefins was carried out in appreciable yield and with a significant chemo and stereocontrol.[2] Similarly, the oxidation of aldehydes to the corresponding carboxylic acids or esters can be easily achieved under mild conditions, which is normally associated to a high level of atom economy.[3]

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[2] C. Santi , R. Di Lorenzo , C. Tidei , L. Bagnoli , T. Wirth. (**2012**) Stereoselective selenium catalyzed dihydroxylation and hydroxymethoxylation of alkenes, *Tetrahedron*, 68, 10530-10535.

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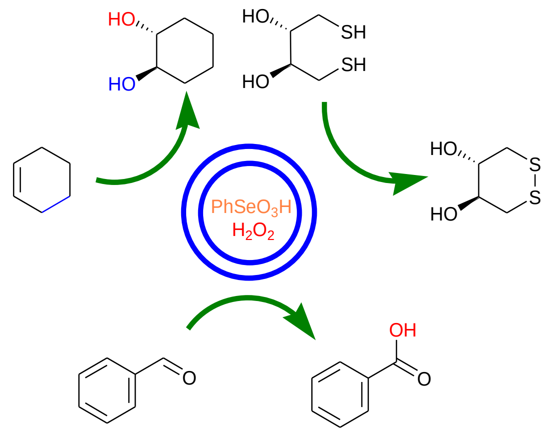

Fig.1: *“Bio-Logic” oxidations*

In these latter cases, the reaction medium, containing the water-soluble catalyst, has been efficiently recovered and reused several times, maintaining appreciable catalytic activity and contributing to enhance the greenness of the proposed protocol. Furthermore, the catalytic couple $PhSeO_3H/H_2O_2$ rapidly promote the oxidation of thiols into the corresponding disulfides. Because of the reaction mechanism, which perfectly mimics that of glutathione peroxidase, it is possible, using appropriated thiols as a probe, setup a simple and rapid test for the evaluation and the screening of the GPx-like activity of several selenium and sulfur-containing compounds. [4]

Benzoic acid is a suitable precursor for a number of fine chemicals, including phenol, caprolactam and benzoates salts and the currently industrial method to prepare benzoic acid involves high pressure and temperatures to perform the expensive and scarcely sustainable oxidation of toluene.[5] For this reason, in the last years a number of catalysts have been proposed to enable the oxidation of benzyl alcohol **1** using hydrogen peroxide as an eco-friendly oxidant to access benzoic acid **3**. [6]

Here we report the preliminary results on the investigation of the applicability of our Bio-Logic protocol to the above-mentioned reaction.

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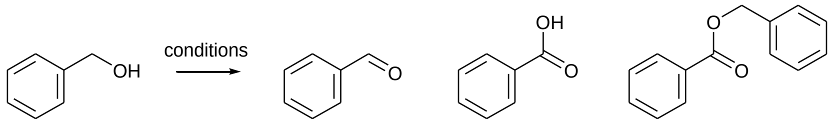
[6] (a) Li-Chen Lee, Chaoxian Xiao, Wenyu Huang, Yan Zhao. (**2015**) Palladium–gold bimetallic nanoparticle catalysts prepared by “controlled release” from metal-loaded interfacially cross-linked reverse micelles, New Journal of Chemistry, 39, 2459-2466. (b) Daniel Koonning, Tobias Olbrisch, Fanni D. Sypaseuth, C. Christoph Tzschucke, Mathias Christmann. (**2014**) Oxidation of allylic and benzylic alcohols to aldehydes and carboxylic acids, ChemComm, 50, 5014-5016. (c) Pattama Saisaha, Lea Buettner,Margarethe van der Meer,Ronald Hage, Ben L. Feringa,Wesley R. Browne, Johannes W. de Boer. (**2013**) Selective Catalytic Oxidation of Alcohols, Aldehydes, Alkanes and Alkenes Employing Manganese Catalysts and Hydrogen Peroxide, Adv. Synth. Catal, 355, 2591-2603. (d) Parasuraman Karthikeyan, Sachin Arunrao Aswar, Prashant Narayan Muskawar, Pundlik Rambhau Bhagat, S. Senthil Kumar. (**2012**) A novel CuCl2/BIL catalyst for direct oxidation of alcohol to acid at ambient temperature, Catalysis Communications, 26, 189-193.

Besides benzoic acid **3**, the oxidation of **1** can theoretically afford three different compounds (**2**-**4**): the aldehyde **2** as an intermediate oxidation product and the ester **4** as a product of the oxidation of the hemiacetal intermediate arising from the condensation between **1** and **2**.

Based on our previous experience, we already demonstrated that benzaldehyde **2** is not stable in the presence of H_2O_2 and a selenium catalyst and, even in very bland conditions, **2** rapidly is oxidized to the corresponding carboxylic acid **3**.

This explains the results reported in Table 1, entry 1 in which at room temperature in the presence of 20 mol % of the preformed phenyl selenenic acid, the conversion is very low (10%) and only benzoic acid **3** is present in the NMR spectra of the crude, beside the pattern of resonances characteristic of the starting material **1**. Increasing the temperature to 100 °C, the consumption of the starting material is complete after 2 hours and the same effect was observed when using a stoichiometric amount of $PhSeO_3H$ at lower temperature (Table 1, entries 2 and 3 respectively).

In order to improve the efficiency of the thermal activation, the use of microwaves (MW) was explored and, interestingly, a 64% of conversion was obtained after 4 cycles of irradiation for 1 minute at 400 watts. It is noteworthy that in all the cases, benzoic acid **3** was the only product of the reaction. This led us to speculate that in the oxidation the *in situ* formed benzaldehyde **2** is not only too much unstable to be isolated at the end of the reaction, but reacts with the excess of the oxidant faster than with the benzyl alcohol **1** still present in the reaction, preventing the formation of the ester **4**. In order to control the selectivity of the reaction toward the formation of **2**, several different combinations of milder reaction conditions were investigated, unfortunately without success.



1 **2** **3** **4**

Table 1: Oxidation of benzyl alcohol promoted by seleninic acid/H_2O_2[a]

entry	%cat	T°C	Reaction time	ratio by NMR 1:2:3:4 (conv%)
1	20	r.t.	24h	90:0:**10**:0 (10%)
2	20	100	2h	0:0:**100**:0 (100%)
3	100	60	2h	0:0:**100**:0 (100%)
4	20	r.t.	4 min	36:0:**64**:0 (64%)

[a] The oxidations were effected using Hydrogen Peroxide 30% v/v (20 eq) in water.

Several papers reports that Oxone ® in a boiling mixture of water/MeCN converts very efficiently the benzyl alcohol into benzoic acid,[7] even in the absence of catalyst.[8]

We verified that in the conditions reported in Table 2 entry 1, the reaction affords, after 30 minutes, the conversion of 57% of the starting material in to the acid **3**.

Nevertheless the presence of a catalytic amount of organoselenium catalyst accelerated the process affording 81% of conversion. The reaction is quantitative after two hours (Table 2 entry 4). In order to reduce the amount of Oxone that is a large atom consuming reagent and, for this reason, not compatible with the postulates of the green chemistry we perform the reaction in the conditions depicted in Table 2 entry 5 obtaining a conversion of 78% but after 9 hour of reaction.

Table 2: Oxidation of benzyl alcohol promoted by seleninic acid/Oxone[a]

entry	%cat	T°C	Reaction time	ratio by NMR 1:2:3:4 (conv%)
1	--	70	30 min	43:0:**57**:0 (57%)
2	20	70	30 min	19:0:**81**:0 (81%)
3	20	70	1h	9:0:**91**:0 (91%)
4	20	70	2h	0:0:**100**:0 (100%)
5	20	70	9h	22:0:**78**:0 (78%)[b]

[a] The oxidations were effected using OXONE ®(20 eq) in water/MeCN; cat.: ($PhSeO_3H$). [b] Using 5 eq of OXONE ®

Experimental

Benzoic Acid has been characterized according the results of the 1H and 13CNMR spectral analysis performed in a Bruker DRX-400 and herein reported *Benzoic acid* **(3).** White solid, 99% yield, m.p. 122 °C ^{1}H-NMR ($CDCl_3$) δ: 7.49 (dd, 2H, *J* = 7.6 and 6.8 Hz), 7.63 (t, 1H, *J* = 6.8 Hz), 8.13 (d, 2H, *J* = 7.6 Hz), 11.88 (brs, 1H); ^{13}C-NMR (100 MHz, CDCl3) δ: 128.5, 129.3, 130.2, 133.8, 172.5.

In conclusion, we reported that benzene selenenic acid could activate hydrogen peroxide in the oxidation of benzyl alcohol to the corresponding acid. The reaction can be conveniently effected in water conditions and is nicely accelerated by MW irradiation. Comparing the results with those obtained with Oxone® as over-stoichiometric oxidant, the couple organoselenium catalyst /hydrogen peroxide resulted to be largely preferable in terms of sustainability mainly in relation to the higher atom economy of the process.

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Acknowledgments

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