# Superoxide ($O_2^{\cdot-}$)-Initiated Oxidation of Primary Alcohols to Carboxylic Acids

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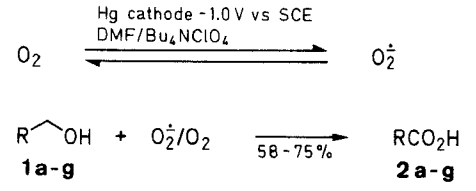
The electrogenerated superoxide-initiated oxidation of primary alcohols to carboxylic acids provides a convenient and promising alternative methodology to reported conventional methods.

The reactivity of superoxide ion, $O_2^{\cdot-}$, with organic molecules has been the subject of considerable interest for two reasons. The discovery and subsequent elaboration of the fact that superoxide ion is generated ubiquitously in aerobic organism made it biochemically important to understand the chemical reactivity of $O_2^{\cdot-}$. Furthermore, because a "new" species is in hand, this simple ion represents an opportunity to examine and broaden our understanding of elementary reactivity patterns from a purely fundamental chemical view.

Stimulants to such studies have been the development of electrochemical methods[1–6] to generate pure, stable solutions of $O_2^{\cdot-}$ and the somewhat later development of the crown-ether solubilization of potassium superoxide in organic solvents,[7–10] again to give relatively stable solution of superoxide ion.[11] Even with so many available methods for alcohol oxidation there is still a demand for a new versatile and selective oxidation procedure. As electron transfer is involved in oxidation reactions, electrogenerated superoxide-initiated oxidation of primary alcohols seems an alternative, which may avoid some disadvantages of the existing chemical methods.[12–17] This indirect electroreductive procedure[18] may provide some interesting features which prompted us to carry out this investigation. Recently, we reported the superoxide-initiated oxidation of alcohols to ketones[19] and fragmentation of some tosylhydrazones[20] using electrochemically generated superoxide ion. In continuation of our investigations on the superoxide-initiated oxidation of secondary alcohols,[19] we wish to present a simple and efficient method for conversion of primary alcohols to carboxylic acids.

Primary alcohols **1a–g** underwent reaction with the electrochemically in situ generated superoxide ion to afford products **2a–g** in good to excellent yield (Scheme **1**) (Table).




| 1, 2 | R | 1, 2 | R |
|---|---|---|---|
| **a** | $CH=CH_2$ | **e** | Ph |
| **b** | Pr | **f** | 4-$MeOC_6H_4$ |
| **c** | *i*-Pr | **g** | 2-$O_2NC_6H_4$ |
| **d** | *i*-Bu | | |

Scheme **1**

In the present investigation it is suggested that electrochemically generated superoxide ion is used sequentially as a base and as an oxidant for facile and convenient conversion of primary alcohols to corresponding carboxylic acids.

*Cyclic Voltammetry:* Cyclic voltammograms were recorded on a X-Y recorder (Servogor type 733) using platinum electrodes in dimethyl sulfoxide containing tetrabutylammonium perchlorate (TBAP) (0.1 mol) as supporting electrolyte. Typical voltammogram of superoxide ion ($O^{\cdot-}$) formation is shown in Figure 1 by dotted line; the cyclic voltammograms of oxygen reduction in presence of substrate **1e** is shown by full line. Examination of Figure 1 reveals that in the presence of substrate **1e**, there is slight decrease in reduction current and the peak potential has shifted from −1.0 V to −0.8 V. Further, the superoxide oxidation peak has disappeared in a fast follow up chemical reaction with primary alcohol resulting in the net oxidation of the latter probably via aldehyde as intermediate. It is also evident that in the potential range of voltammogram taken, no oxidation peak attributable to the oxidation of aldehyde appears.

**Table.** Electrogenerated Superoxide-Initiated Oxidation of Alcohols **1** with Oxygen

| Substrate[23] | Current (mA) | | Reaction Time (h) | Product | Yield[a] (%) | mp (°C)[b, c] or bp (°C)/Torr | |
|---|---|---|---|---|---|---|---|
| | Initial | Final | | | | found | reported |
| **1a** | 85 | 10 | 10 | **2a** | 65 | 139[d] | 139[d] |
| **1b** | 112 | 15 | 15 | **2b** | 60 | 161[d] | 162[d] |
| **1c** | 75 | 12 | 12 | **2c** | 58 | 153[d] | 153–154[d] |
| **1d** | 100 | 15 | 15 | **2d** | 62 | 174[d] | 175–177[d] |
| **1e** | 85 | 25 | 15 | **2e** | 60[e] | 121 | 122–123 |
| **1f** | 110 | 15 | 15 | **2f** | 60 | 183 | 182–185 |
| **1g** | 95 | 12 | 12 | **2g** | 75 | 145 | 146–148 |

[a] Yield of isolated product. All products are known compounds and were characterized by their spectral data.
[b] Uncorrected.
[c] Measured with a Büchi melting point apparatus (capillary method).
[d] Boiling points refer to atmospheric pressure.
[e] Benzaldehyde was isolated in 10% yield.

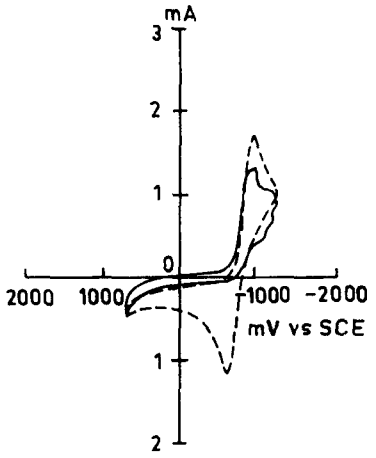
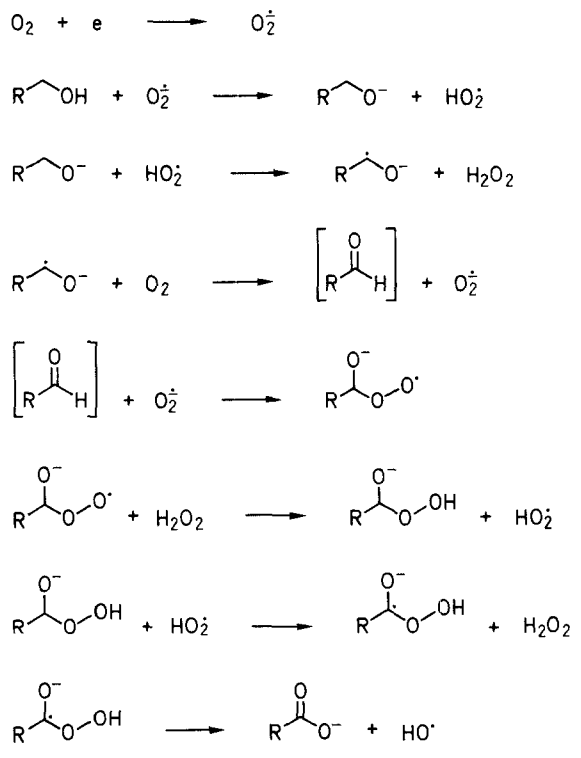



**Figure 1:** Cyclic Voltammogram for Oxygen Reduction (---) and in the presence of Benzylalcohol (**1e**) (–). Solvent: DMSO + 0.1 M TBAP; T = 20 °C, Scan Rate = 200 mV $s^{-1}$ at Pt



Scheme **2**

The net oxidation reaction seems to be a complex multi-step process. Based on earlier studies[19–22] and known behaviour of superoxide ion in aprotic media, the product formation and cyclic voltammetric studies, the initial step of the reaction may be assumed to be the deprotonation of the hydroxyl group by $O_2^{\cdot-}$, dismutation, loss of proton from alcoholic carbon followed by nucleophilic addition[21] of superoxide to carbonyl group leading to the formation of carboxylic acid (Scheme **2**).

In summary, the advantages of superoxide-initiated oxidation are simple reaction conditions, low cost, easy scale-up, almost no waste problems and for these reasons the process is a good alternative to the known procedures.

**Oxidation of 4-Methoxybenzyl Alcohol (1f) to 4-Methoxybenzoic Acid (2f); Typical Procedure:**

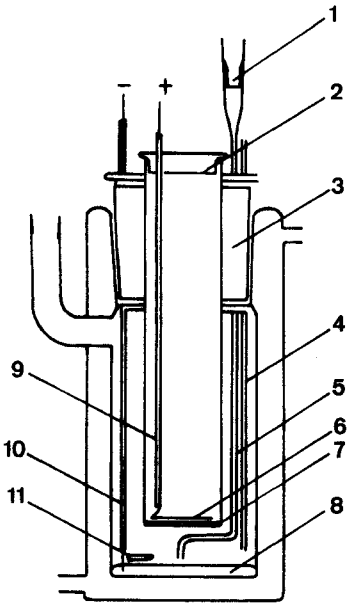
*Apparatus:* Wenking Potentioscan POS 73 (Bank-Elektronik, West Germany) is used for constant potential electrolysis. The electrochemical cell consists of a double walled cylindrical glass cell (volume 150 mL) in which the anodic and cathodic chambers are separated by a medium porosity glass frit. The mercury pool and platinum foil (horizontal) served as cathode and anode respectively. The Teflon cover at the head of the electrolytic cell contains holes for connecting mercury pool and for passing nitrogen or oxygen gas. Agitation of the catholyte is achieved using small magnetic bar and through bubbling of oxygen (Figure 2).

*Cathode:* Mercury pool, 23.76 $cm^2$.

*Anode:* Platinum foil, 3.78 $cm^2$.

*Electrolyte:* Solution of $Bu_4N^+Br^-$ (3.22 g, 0.1 mol) in anhydrous (molecular sieves 3 Å) "extrapure" DMF (100 mL).

*Oxidation and Work-up:* The cathodic chamber containing electrolyte (50 mL) is purged with $N_2$ for 5 min. The electrolyte solution is first pre-electrolysed at – 1.9 V vs SCE until the background current falls to ~ 1 mA. Cyclohexene (2 mL) is added to the anodic chamber to absorb the liberated bromine (cyclohexene is not needed when $Bu_4NClO_4$ is used as supporting electrolyte). Catholyte is saturated with oxygen for 30 min. 4-Methoxybenzyl alcohol (**1f**; 0.5 g, 3.62 mmol) is added to the cathodic chamber. Oxygen is bubbled through the solution during the period of electrolysis carried out at a constant potential of – 1.0 V vs SCE. The current decreases from an initial 110 mA to 15 mA. The catholyte is then poured into cold $H_2O$ (100 mL) and treated with sat. $Na_2CO_3$ solution (25 mL). The mixture is extracted with $Et_2O$ (3 × 30 mL) to remove the unreacted alcohol **1f**, usually present in negligible amount. Aqueous layer is




1. Reference electrode
2. Teflon cover of anode compartment
3. Teflon stopper
4. Inlet for $N_2/O_2$ gas
5. Salt-bridge to the reference electrode
6. Pt foil anode
7. $G_3$ glass frit
8. Hg pool cathode
9. Electrical connection for anode
10. Electrical connection for cathode
11. Magnet bar

**Figure 2.** Diagram of Divided Electrolytic Cell

acidified with dil HCl and extracted with $Et_2O$ ($3 \times 30$ mL). The extract is dried ($Na_2SO_4$), and evaporated; yield: 0.330 g (60%) (Table).

For the isolation of **2a–d**, the electrolysis is repeated 4 times and the product obtained after removing the organic solvent is distilled using a Kugelrohr apparatus to yield pure compound, which is characterized by physical and spectral data.

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