Oxidative Cleavage of Vicinal Diols at the Nickel Hydroxide Electrode[1]

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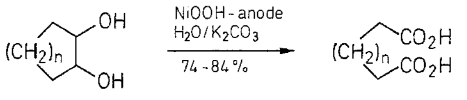
Vicinal Diols are oxidatively cleaved with good yields by electrolysis at an oxide covered nickel electrode in an aqueous alkaline electrolyte and an undivided cell. The method is applied in the synthesis of optical pure derivatives of 2,2-dimethyl-1,3-dioxolane-4-carboxylic acid.

The nickel hydroxide electrode has proved to be a mild and versatile reagent for the oxidation of primary alcohols to carboxylic acids and secondary alcohols to ketones.[2,3] The conversions usually proceed with good to excellent yields. The oxidant is nickel(III) oxide hydroxide, formed as a black coat on the anode surface, which is continuously regenerated by electric current, so that it works as an electrocatalyst bound to the electrode.[4]

We have now found, that the nickel(III) oxide hydroxide electrode is very suited for the oxidative cleavage of vicinal diols. The diols are dissolved in an aqueous electrolyte of pH 9.0 to 13 and are oxidized at a nickel-net electrode. The alkaline medium is necessary for the regeneration of the oxide layer on the electrode. Contrary to oxidations with lead tetraacetate and periodate, cleavage at the nickel hydroxide electrode leads to products in the highest possible oxidation state, namely carboxylic acids or ketones. Most of these electrochemical oxidations were carried out in a "swiss-roll" cell[5] of 1500 cm^2 electrode area at room temperature, whereby the conversions were followed by GLC. The crude product is easily purified by recrystallization or column chromatography. The results are summarized in Table 1.



1a-g **2a-d**

1	n	configuration of **1**
a	2	*cis*
b	2	*trans*
c	3	*cis*
d	3	*trans*
e	4	*cis*
f	4	*trans*
g	8	*cis*

The oxidation is insensitive to the configuration of the diols. This is in contrast to the reaction with lead tetraacetate and periodate. *trans*-1,2-Cyclohexanediol, for example, is cleaved by lead tetraacetate more than 20 times slower than the corresponding *cis*-diol.[7] The more hydrophobic diol **1g** is much less reactive than the diols **1a–f** and therefore needs quite vigorous reaction conditions. This decreasing reactivity at the nickel hydroxide electrode with increasing hydrophobicity of the substrate is already known for other compounds.[2,3,8]

Some observations led to the assumption, that the initial step in the oxidation of secondary/secondary 1,2-diols is the formation of a α-hydroxy ketone, which is subsequently cleaved and further oxidized to the dicarboxylic acid. The hydroxy ketone has been identified in the oxidation of *trans*-1,2-cyclohexanediol after low conversion when continuously extracted with ether. It could easily be converted into adipic acid under the usual reaction conditions.

Table 1. Oxidation of 1,2-Diols **1a–g** to Dicarboxylic Acids **2a–d** at the Nickel Hydroxide Electrode[a]

1	Product	Yield[b] (%)	mp[c] (°C)	
			found	reported[6]
a	**2a**	74	151–152	153
b	**2a**	75	151–152	153
c	**2b**	81	105	106
d	**2b**	79	105	106
e	**2c**	80	142	144
f	**2c**	77	142	144
g[d]	**2d**	84	127–129	128

[a] Diols (5 mmol) in 0.1 M aq. K_2CO_3 (500 mL) were electrolyzed at room temperature and at 0.3 A constant current in a "swiss-roll" cell for 2.7h.

[b] Yield of isolated product after purification. The structures of all compounds were confirmed by their IR, ^{1}H-NMR and mass spectra. Purity was checked by GLC after esterification with diazomethane (25 m quartz column, ∅ 0.15 mm, 0.3% OV 225).

[c] Melting points are not corrected.

[d] Diol (2.5 mmol) and stearic acid (0.25 mmol) as an emulsifier were electrolyzed at 50 °C for 22.5 h.

Additionally the vicinal diols **1h–l** have been cleaved to carboxylic acids and ketones **2e–k** (Table 2).

$$\mathbf{1h\text{-}l} \xrightarrow[44-72\%]{\text{NiOOH-anode/ aq. OH}^-} \mathbf{2e\text{-}k}$$

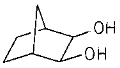
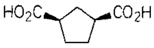
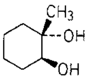
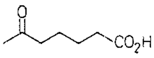
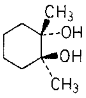
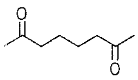
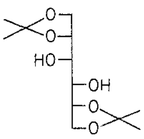
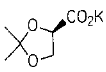
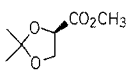
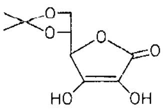
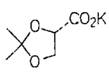
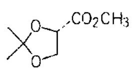
Substrates	Products	
 **1h**	 **2e**	
 **1i**	 **2f**	
 **1j**	 **2g**	
 **1k**	 **2h**	 **2i**
 **1l**	 **2j**	 **2k**

Table 2. Oxidation of 1,2-Diols **1h–l** at the Nickel Hydroxide Electrode[a]

Substrate	Product[b]	Electrolyte[c]/ Current (A)	Time/ Temperature	Yield[d] (%)	Physical constants[e]	
					found	reported
1h	**2e**	A/0.3	24 h/20°C	72	mp 119–120°C	121°C[6]
1i	**2f**	B/0.3	3.3 h/20°C	70	mp 33°C	33–34°C[9]
1j	**2g**	B/0.3	31.7 h/50°C	44[f]	mp 42–43°C	44°C[6]
1k	2 × **2h**	C/0.15	21 h[g]/30°C	70	$[\alpha]_D^{20}$ +23.5° (c = 2.0, H_2O)	+23.7°[10] (c = 2.0, H_2O)
1k	2 × **2i**[h]	C/0.15	21 h[g]/30°C	56	$[\alpha]_D^{20}$ +8.40° (c = 1.60, acetone)	+8.10°[11] (c = 1.5, acetone)
1l	**2j**	C/0.15	18 h[g]/20°C	52	$[\alpha]_D^{20}$ −23.4° (c = 2.0, H_2O)	+23.7°[10] (c = 2.0, H_2O) [(R)-isomer]
1l	**2k**[h]	C/0.15	18 h[g]/20°C	54	$[\alpha]_D^{20}$ −8.44° (c = 1.51, acetone)	−8.55°[12] (c = 1.52, acetone)

[a] Diols (5 mmol; 2.5 mmol in the case of **1k**) were electrolyzed either in a „swiss-roll" cell (compounds **1h–j**) or in a simple beaker-type cell (**1k,l**).

[b] The structures of all products were confirmed by their IR, ^{1}H-NMR and mass spectra. Purity was checked using GLC after esterification of the carboxylic acids with diazomethane (25 m quartz column, Ø 0.15 mm, 0.3% OV 225).

[c] A: 0.07 M aq. $NaHCO_3$ and 0.03 M aq. K_2CO_3;
B: 0.1 M aq. K_2CO_3;
C: 0.1 N aq. KOH.

[d] Isolated yield after purification.

[e] Melting points are not corrected. Optical rotations were measured on a Perkin Elmer 241 polarimeter.

[f] This yield refers to a conversion of 71%.

[g] Electrolysis time is not optimized.

[h] The methyl esters are formed if the crude electrolysis mixture is treated with methyl iodide. The given yields refer to both steps. See experimental section for details.

The secondary/tertiary diol **1i** reacts at a similar rate as the unsubstituted diol **1b** leading to 6-oxoheptanoic acid in good yield. In the tertiary/tertiary diol **1j**, however, the reactivity is dramatically reduced. A medium yield of the diketone **2g** together with unreacted diol is obtained even at high temperature and after 31.7 hours electrolysis time. This is possibly due to a different oxidation mechanism for this diol.

Of more general synthetic interest is the oxidation of the inexpensive chiral substrates **1k** and **1l**. In the cleavage of 1,2:5,6-di-*O*-isopropylidene-D-mannitol (**1k**) and 5,6-*O*-isopropylidene-L-ascorbic acid (**1l**) the optical pure enantiomers of 2,2-dimethyl-1,3-dioxolane-4-carboxylic acid are obtained. They have been isolated as their potassium salts **2h** and **2j**. If the crude electrolysis product is treated with methyl iodide the corresponding methyl esters **2i** and **2k** are formed.[13] Both acids and esters are useful building blocks for the synthesis of chiral compounds.[14,15]

For the details of the electrolysis cells and activation of the electrode see Ref. 2.

Heptanedioic Acid (2b); Typical Procedure:

trans-1,2-Cycloheptanediol (**1d**; 0.65 g, 5 mmol) in 0.1 M aq. K_2CO_3 (500 mL) is electrolyzed at room temperature for 2.7 h in a "swiss-roll" cell at a constant current of 0.3 A. The electrolyte is concentrated under reduced pressure to about 50 mL, acidified with 12 N HCl (9 mL), saturated with NaCl and extracted with Et_2O (4 × 40 mL). The combined organic phase is dried ($MgSO_4$), the solvent is removed, and the crude product recrystallized from water giving **2b**; yield: 0.63 g (79%).

^{1}H-NMR (CD_3OD/TMS): δ = 1.32–1.43 (m, 2H, 2 × H-4); 1.57–1.67 (m, 4H, 2 × H-3, 2 × H-5); 2.27–2.32 (m, 4H, 2 × H-2, 2 × H-6).

Potassium (4*R*)-2,2-Dimethyl-1,3-dioxolane-4-carboxylate (2h) and Methyl (4*R*)-2,2-Dimethyl-1,3-dioxolane-4-carboxylate (2i); Typical Procedure:

1,2:5,6-Di-O-isopropylidene-D-mannitol (**1k**; 0.66 g, 2.5 mmol) is electrolyzed in 0.1 N aq. KOH (400 mL) in a simple beakertype cell with 150 cm^2 anode surface at 30°C and a current of 0.15 A for 21 h. After evaporation of water under reduced pressure to about 50 mL, the electrolyte is carefully neutralized to pH 6.5 by dropwise addition of 2 M H_2SO_4 (ca. 20 mL) with stirring. Water is then evaporated completely, and the remaining solid is dried first by azeotropic distillation with anhydrous EtOH (2 × 40 mL) and then *in vacuo* (< 1 Torr). Triturative extraction of the dry residue with anhydrous EtOH (4 × 50 mL) and evaporation of the solvent yield the potassium salt **2h**, which crystallizes within several hours when covered by an anhydrous Et_2O layer; yield: 0.64 g (70%).

^{1}H-NMR (D_2O/TMS): δ = 1.42, 1.48 (2s, 3H each, 2 × CH_3); 3.95 (dd, 1H, J = 6.8 Hz, 8.3 Hz, H-5); 4.32 (dd, 1H, J = 7.5 Hz, 8.3 Hz, H-5); 4.54 (dd, 1H, J = 6.8 Hz, 7.5 Hz, H-4).

Alternatively, the dry residue in MeCN (40 mL) is treated with CH_3I (7.1 g, 50 mmol) in the presence of *N,N,N′,N′*-tetramethylethylenediamine (62.5 mg, 0.5 mmol) at 50°C for 5 h with stirring. After evaporation of the solvent, the reaction mixture is extracted with Et_2O (4 × 40 mL). Evaporation of the combined organic phase yields the crude product, which is purified by column chromatography on silica gel using CH_2Cl_2/EtOAc (10:1) as eluent to give **2i**; yield: 0.45 g (56%).

^{1}H-NMR ($CDCl_3$/TMS): δ = 1.41, 1.50 (2s, 3H each, 2 × CH_3); 3.78 (s, 3H, OCH_3); 4.11 (dd, 1H, J = 5.3 Hz, 8.7 Hz, H-5); 4.25 (dd, 1H, J = 7.2 Hz, 8.7 Hz, H-5); 4.60 (dd, 1H, J = 5.3 Hz, 7.2 Hz, H-4).

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(1) Electroorganic Synthesis, 36; for 35, see: Michaelis, R., Müller, U., Schäfer, H.J. *Angew. Chem.* **1987**, *99*, 1049; *Angew. Chem. Int. Ed. Engl.* **1987**, *26*, 1026.
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