SELECTIVE ANODIC OXIDATION OF CAMPHOR

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Abstract - Camphor (1) was anodically oxidized at Pb/PbO$_2$ and Pt in 1M H$_2$SO$_4$ (50 Vol.% MeCN). 1,2-campholide (4) as the main product was obtained with material yields up to 96% and current efficiencies up to 39% at the PbO$_2$ anode. The most important side products were oxygen and 1,8,8-trimethyl-2-oxa-bicyclo[3.3.0]octan-3-one (5). A quantitative conversion of 4 to 5 is possible in strong acids. The effects of current densities and concentrations were studied in detail.

In connection with our previous investigation into the anodic oxidation of mono-cyclic 1,3-diketones,[1,2] it became interesting to study the anodic oxidation of bicyclic monoketones, which has received little attention so far. Camphor (1) was selected as an inexpensive starting material. Its oxidation has been extensively studied by chemical means.[3-10] Oxidation with nitric acid yielded the dicarboxyclic acid, camphoric acid (2).[3-5] The Baeyer-Villiger oxidation of camphor, which leads to α-campholide or 1,8,8-trimethyl-3-oxabicyclo[3.2.1]octan-2-one (3) and alternatively to 1,2-campholide or 1,8,8-trimethyl-2-oxabicyclo[3.2.1]octan-3-one (4) has been well investigated.[6-9] The oxidation of camphor with peracetic acid followed different paths depending on the acidity. In the presence of strong acid, α-campholide (3) was isolated in 30% yield . With sodium acetate buffer present, the isomer 1,2-campholide (4) was formed in 62% yield. The two bicyclic lactones are key intermediates for important organic syntheses.[11]
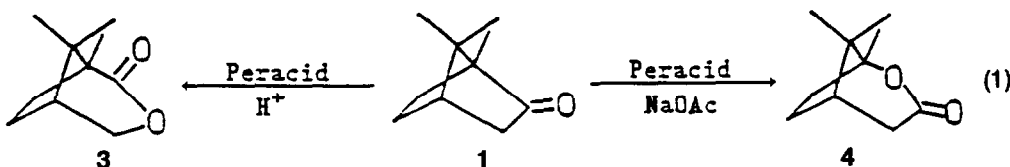

A method complementary to the Baeyer-Villiger oxidation was the thermal decomposition of ozonides.[10] All of these chemical methods are somewhat disadvantageous. Severe reaction

conditions, long reaction time, and expensive oxidants lead to relatively low yields of the desired products.

With respect to the electrochemical alternative, F. Barba et al. reported the anodic oxidation of camphor in dilute Na_2CO_3 aqueous/organic electrolytes, which gave the lactone 4 and 5.[12] However, low material yields were obtained, 15 - 20% for 4 and about 1% for 5. We are able to demonstrate that anodic oxidation of camphor in 1 M H_2SO_4 may lead to 4 with very high material yields. Our conditions were quite conventional due to practical reasons, namely aqueous acid electrolytes, conventional anodes as Pb/PbO_2 and Pt and current densities of 10 - 100 mA cm^{-2}.

Results

The main product for the anodic oxidation of camphor under our conditions is 1,2-campholide (4).

$$1 + H_2O \longrightarrow 4 + 2H^+ + 2e^- \tag{2}$$
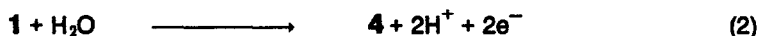
The preparative results for the anodic oxidation of camphor are compiled in Tables 1 and 2. It can be seen that 4 formed at the PbO_2 anode in 1M H_2SO_4, MeCN/H_2O (V/V = 1 : 1) with material yields MY of up to 96% and current efficiencies CE of up to 39%. Preparative runs in the quasidivided cell (cf. [13]) demonstrate according to Table 1 a weak influence of the current density (entries 1 - 3). The current efficiencies are generally low, but they are somewhat improved at higher concentrations of the starting material (entries 2 and 4). Platinum as an anode material is quite inferior to Pb/PbO_2 (entries 1 and 5).

Results in a plate & frame cell in a larger scale are collected in Table 2. A cation exchange membrane was employed to divide the cell compartments. These runs were accomplished at more practical levels for the current density j and the temperature T. The influence of electrolysis time, represented by β_0 (defined in Table 1) is clearly shown. It is possible to obtain nearly quantitative yields for β_0 = 400 %. This faciliates product isolation.

As shown in both tables, 1.8.8-trimethyl-2-oxabicyclo[3.3.0]octan-3-one (5), which is also known as dihydro-β-campholenolactone, was obtained as a side product. 4 can be isomerized quantitavely to 5 by a treatment with acid.[14]
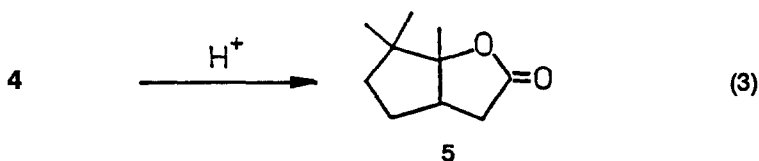

$$4 \xrightarrow{H^+} \text{5} \tag{3}$$

Table 1
Anodic oxidation of camphor in 1M H_2SO_4, $MeCN/H_2O$ (V/V = 1/1) at 13°C. Quasidivided cell, V = 250 ml. The theoretical electrochemical conversion β_0 was 200 %, corresponding to 4 F per mol camphor. MY = material yield, CE = current efficiency.

No	Anode	j mA cm^{-2}	c_0 mol dm^{-3}	β (%) (analytically)	4		5	
					MY %	CE %	MY %	CE %
1	PbO_2	10	0.1	52	62	16	3	0.8
2	PbO_2	30	0.1	46	66	15	2	0.6
3	PbO_2	75	0.1	37	60	11	3	0.6
4	PbO_2	30	0.5	83	63	26	4	1.6
5	Pt	10	0.1	25	25	11	2	0.8

Table 2
Anodic oxidation of camphor in 1 M H_2SO_4, $MeCN/H_2O$ (V/V = 1/1) at 20°C. Divided plate & frame cell, V = 600 ml. Anode : Pb/PbO_2. MY and CE cf. Table 1.

No	β_0(%)	j mA cm^{-2}	c_0 mol dm^{-3}	β (%) (analytically)	4		5	
					MY %	CE %	MY %	CE %
6	100	30	0.25	59	66	39	2	1.1
7	200	30	0.25	83	82	34	3	1.1
8	400	30	0.25	100	82	21	3	0.9
9	100	100	0.50	34	50	17	1	0.2
10	200	100	0.50	63	63	20	2	0.7
11	400	100	0.50	97	96	23	4	0.9

According to this reaction, we performed the conversion in 88% yield on treatment of **4** with concentrated sulfuric acid in glacial acetic acid.

The conversion/time-curve for run No. 9 is displayed in Fig. 1. It is confirmed, that the camphor is nearly quantitatively converted to **4** after 6-8 F/mol, that the product reaches selectivities well above about 90%, and that the side product does not appear in larger amounts.
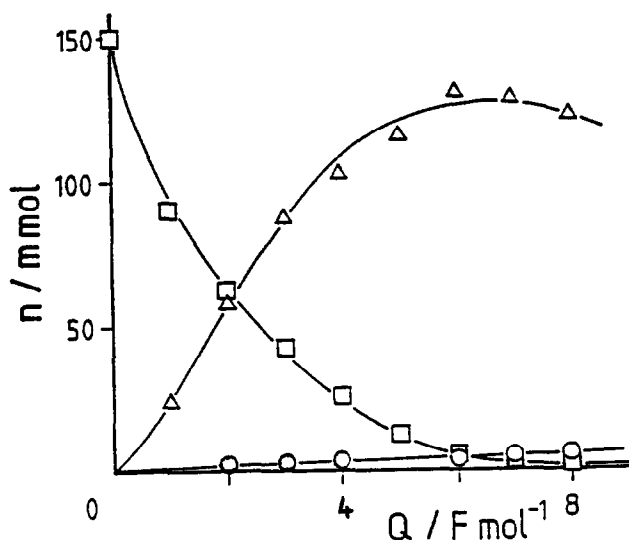

Fig. 1 Conversion/time curves for run No. 8 in Table 2

☐————————☐ camphor (1)

△————————△ 1.2-campholide (4)

◯————————◯ 1,8,8-trimethyl-2-oxa-bicyclo[3.3.0]octan-3-one (5)

Slow cyclovoltammetric curves (10 mVs^{-1}) at Pb/PbO$_2$ in the base electrolyte and in the presence of 50 mM camphor at the rotating disk electrode, 1600 min^{-1}, exhibit nearly coinciding curves. The redox peaks of PbO$_2$ are observed at about 1.6 V (SHE). At more positive potentials, the anodic branch for oxygen evolution is reached.[15] This result can be explained in terms of two competing anode processes, reaction (2) and water oxidation to oxygen. Presumably they have a common intermediate, namely OH-radicals adsorbed at the PbO$_2$. This situation seems to be common for other anodic reactions at PbO$_2$.[16] The anode potentials under the conditions of runs 1-4 and 6-11 were 2.1-2.2 V vs. SHE, well in the anodic O$_2$-branch. Volumetric measurements of the anodic O$_2$ shows, that the current efficiency complements the values in both tables to nearly 100%.

The structure of lactones **4** and **5** were determined by ^{1}H NMR and IR. The stereochemistry of **4** was clarified to be **4a**.[17] Thus in comparison to CDCl$_3$ as solvent, pyridine should induce the


4a

5a
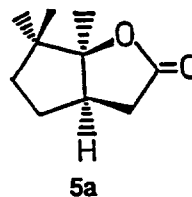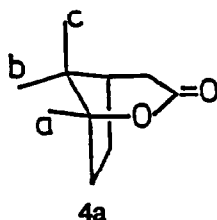
large upfield shift on a- and b-methyl signals. Our experimental data were + 0.29, + 0.13 and + 0.08 ppm for a-, b-, and c-methyl groups, respectively. The stereochemistry of **5** was assigned as **5a**.[17] Consequently a large upfield shift for the a- and b-methyl signals, and a downfield shift for c-methyl signals should be predicted for the pyridine-induced shift. Our experimental data do exhibit the a-, b-, and c-methyl signals of **5** shift + 0.17, + 0.27, and − 0.08 ppm, resepectively.

Discussion

The early work on the chemical oxidation of camphor to camphoric acid with nitric acid [3,4] promoted us to start the anodic oxidation in 0.1 - 1 M nitric acid solution in the mixed solvent. However, the results were unfavourable. In another study of the chemical oxidation of camphor to camphoric acid, FeSO$_4$ was used as catalyst.[5] This catalyst had no effect on the anode. The attempt of using Fe$_3$O$_4$ as anode also failed because of its heavy corrosion.

We have investigated previously the anodic oxidation of cyclic 1,3-diketones.[1,2] The main product was a dicarboxylic acid with one carbon less. It was obtained in good material yields and current efficiencies. The reaction intermediate was the 1,2,3-triketone. However, we did not find any trace of camphorquinone (**6**) at the anode. Its further oxidation product, camphoric acid, was not detected either.
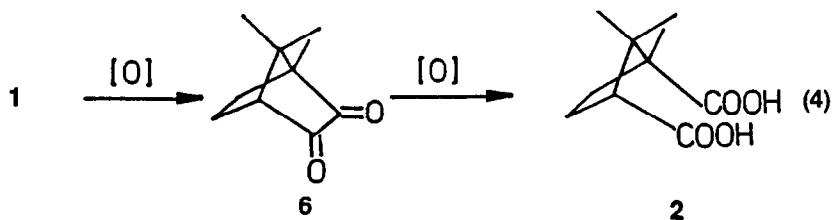
The reason may be the different degree of enolization between monoketone and 1,3-diketone. This deduction can be further supported by our previous findings for the anodic oxidation of cyclohexanone, where an oxygen insertion mechanism was concluded.[18] The same is the case in the anodic oxidation of camphor. The situation of the PbO_2-anode surface, where active OH radicals are present, is close to the conditions for the chemical Baeyer-Villiger reaction. Camphor oxidation, by this mechanism has been a subject of considerable interest [6,19-22] :


$$(5)$$
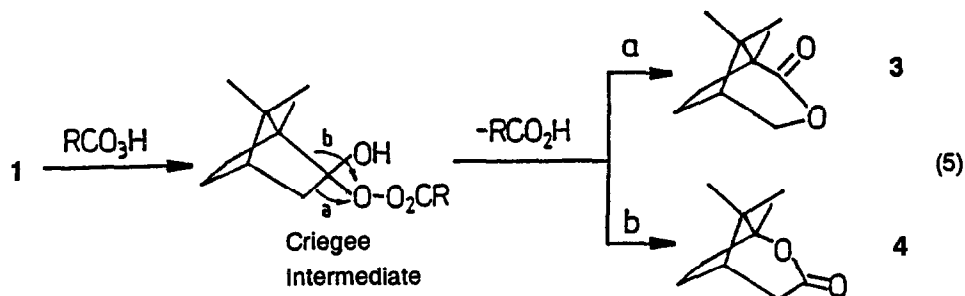
The reaction path is governed by a combination of electronic and steric effects.[8] At the PbO_2 anode, an OH-radical is added to the carbonyl :

$$(6)$$
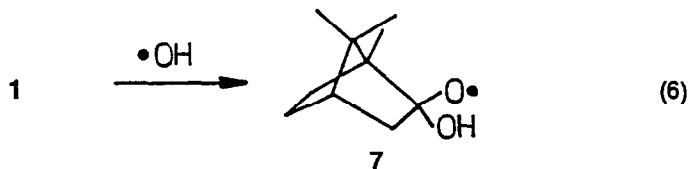
Further oxidation would lead to the formation of the lactone **4** :

$$(7)$$
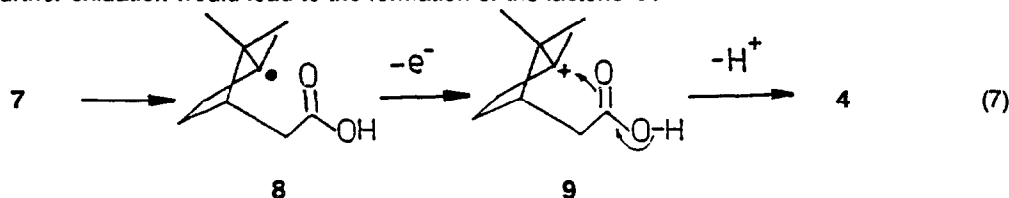
The adsorption at the anode from the endo side is indicated in eqn. (7). If one of the bridge-methyl groups would migrate to the position 1 to form **10**, the lactone **5** would be obtained :

$$(8)$$
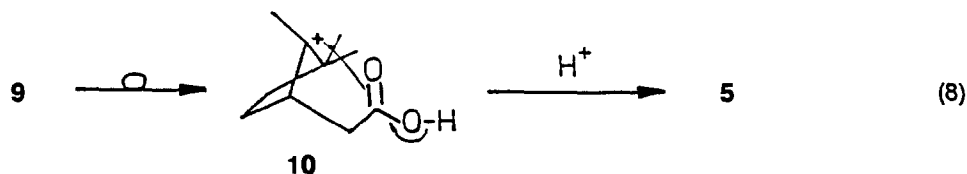
If the intermediate radical **7** would tend to cleave the C_2/C_3-bond, the α-campholide (**3**) according to reaction path (a) in eqn. (5) would be obtained. It is the main product for the chemical oxidation of camphor in the presence of strong acids. However, the α-campholide was not detected in the present case of anodic oxidation. The further oxidation of this α-campholide yields camphoric acid (**2**). The preference of 1,2-campholide (**4**) in case of anodic oxidation of camphor can be understood from steric reasons. According to eqn. (7), the endo-adsorption leads to the exo-form **4**. The same situation holds for the electroreduction of camphor-oxime to the amine, where 99% exo-form was identified.[23]

Experimental Section

Racemic camphor, 98% from Riedel-de Haen (reagent grade) was used as starting material*. Aqueous electrolytes were used. For most preparative runs 1M H_2SO_4 in $MeCN/H_2O$ (V/V - 1/1) was employed as electrolyte, only for the initial work, 0.1-1M HNO_3 in $MeCN/H_2O$ (V/V - 1/2) was used as electrolyte (MeCN reagent grade, water tridistilled, H_2SO_4 and HNO_3 analytical grade).

Product analysis was performed by HPLC (column : Nucleosil-7C18, 0.4x25cm, eluent : $MeOH/H_2O$ (V/V-1/1), MeOH analytical grade, H_2O tridistilled, flow rate 1.0ml/min., refractive index detector, temp. 30ºC). For controlling the progress of electrolysis without work up samples during the runs were prepared by diluting the electrolyte with eluent 4 : 1 (injection volume 20 μl). Samples of isolated product were prepared by dissolving in eluent.

Pb/PbO_2, Pt and Fe/Fe_3O_4 were used as anode materials. The electrode area was 2 x 5 cm² for quasi-divided cell, and 100 cm² for plate & frame cell. The anodic formation of PbO_2 proceeded in 1.0 M H_2SO_4 at 10 mA cm⁻² for 3 hours. The cleaning procedure for Pt was described in.[13] As counter electrodes served two stainless steel V2A wires (A - 2 x 0.3 cm²) for the quasi-divided cell, and a V2A plate (A - 100 cm²) for plate & frame cell.

Electrosynthesis was performed by using a 250ml cylindric glass cell with cooling jacket and planar ground cover with two small area cathodes, working as a quasi-divided cell.[13] For large, preparative electrolysis a 600 ml plate & frame cell was used at which anodic and cathodic compartments were separated by cation-exchange membranes (type SELEMION CTM of ASAHI GLASS company). The anolyte was kept moving in a loop, whereas the catholyte convection was maintained by gas-lifting in consequence of the hydrogen-evolution. Both cell compartments were cooled by cooling jackets. Thermostatization was performed by a cryostate.

1,2-Campholide (4) : In a typical run in the plate & frame cell 600 ml of a solution of 45.7 g (0.3 mol) camphor in 1 M H_2SO_4, $MeCN/H_2O$ (V/V - 1/1) was filled into the anode compartment of the cell. 750 ml 1 M H_2SO_4 served as the catholyte. The anode was a 100 cm² Pb/PbO_2 sheet, the cathode was made from stainless steel. A current of 10 A, corresponding to a current density of 100 mA cm⁻², was held constant. Temperature was controlled to be 20ºC. After an electrolysis time of 9 hours and 39 minutes, corresponding to 8 F mol⁻¹, the batch was finished. This ensures virtually complete conversion of starting material, avoiding separation of **4** and unreacted **1**.

For work up the electrolyte was saturated with Na_2SO_4 and extracted five times with each 50 ml ether. The combined ether extracts were washed with 5 wt% $NaHCO_3$ solution and then with water. The extracts were dried over anhydrous Na_2SO_4 for 24 hours. After ether stripping 35.0 g of a viscous yellow oil were obtained. The crude product was analyzed via ¹H NMR (60 MHz). $\delta(CDCl_3)$ 1.00(s), 1.07(s), 1.29(s) (9H, 3CH₃); 1.48-2.80 (m) (7H, 3 CH₂, 1 CH). δ(pyridine) 0.78(s), 0.91(s), 1.16(s) (9H, 3CH₃). IR (neat) : one strong band (lactone group) : 1744 cm⁻¹ (cf. [7] [17]). The purity of

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*All chiral compounds are racemic.

the crude product was determined by HPLC : 88% 4, 6% 5, four other unidentified products (peak areas). No camphor was found. Colourless crystals separated in the crude oil on stand at 0 °C. A melting point of about 55°C (uncorrected) was found.[6] Related to the main product material yield and current efficiency were found to be 61% and 15.3%, respectively.

1,8,8-Trimethyl-2-oxa-bicyclo[3.3.0]octan-3-one (5). A mixture of 1.30 g of the crude product 4, 1.8 ml conc. H_2SO_4 and 28 ml glacial acetic acid was stored for 17 hours at room temperature Thereafter the mixture was poured into 280 ml water, followed by ether extraction (5 x 20 ml). The combined extracts were washed with saturated Na_2CO_3 solution. Ether stripping gave 1.14g oily residue. 85% of 5 and no 4 was present (HPLC). Vacuum distillation (13 Torr) gave 0.96 g (74%) pure 5. IR and ^{1}H NMR data are consistent with those of the literature.[7,17]

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