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Electrosynthesis of 2-Methyl-1,4-naphthoquinone (Vitamin K_3) Directly from 2-Methyl-5,8-dihydro-1,4-naphthalenediol by a Four-electron Oxidation Procedure

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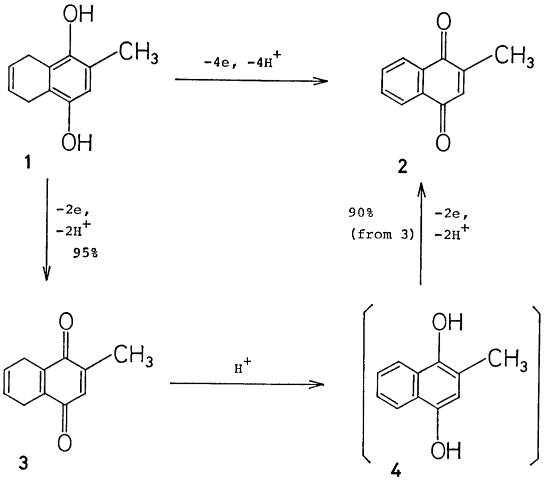
Synopsis. A straightforward synthesis of Vitamin K_3 was performed by electrolysis of 2-methyl-5,8-dihydro-1,4-naphthalenediol in a MeCN-*t*-BuOH (9/1)-$LiClO_4$-(Pt or C electrodes) system. The use of perchlorate salts or tetrafluoroborate salts as supporting electrolytes in various electrolysis systems, such as AcOH-*t*-BuOH (9/1)-$LiClO_4$-(Pt) and AcOEt-*t*-BuOH (9/1)-Bu_4NClO_4-(Pt), also provided good results, while the use of Et_4NOTs in MeOH afforded 2-methyl-5,8-dihydro-1,4-naphthoquinone, preferentially.

2-Methyl-1,4-naphthoquinone (vitamin K_3) (**2**) and its homologs constitute a class of biologically active quinones as well as precursors in the synthesis of vitamin K series.[1)] Many efforts have been made to devise a simple route to **2** based on the oxidation of 2-methyl-5,8-dihydro-1,4-naphthalenediol (**1**),[2a)] 2-methyl-1,4-naphthalenediol (**4**),[2b)] 2-methylnaphthalene,[2c)] and related compounds[2d)] with oxidizing agents *i.e.*, CrO_3, $Mn_2(SO_4)_3$, H_2O_2, $Ce(NH_4)_2(NO_3)_6$, and so on. The lack of product-selectivity in the oxidation of 2-methylnaphthalene to **2**[2a,3)] as well as the disadvantages of using stoichiometric amounts of the oxidizing agents spurred us to develop the present procedure.



Here, we wish to report a clean and straightforward electrosynthesis of **2** from 2-methyl-5,8-dihydro-1,4-naphthalenediol (**1**) without isolating the intermediate, 2-methyl-5,8-dihydro-1,4-naphthoquinone (**3**), which can also be obtained by the choice of another electrolysis system.

Electrooxidation of **1** to the desired **2** was carried out by employing a MeCN-*t*-BuOH (9/1)-$LiClO_4$-(Pt or C electrodes) system at a constant current of 1.67 mA/cm^2 in a divided cell. As shown in the Table (entries 1 and 2), passage of 9 F/mol of electricity yielded **2** in 91—94% yields. The two systems of AcOH-*t*-BuOH (9/1)-$LiClO_4$-(Pt) and AcOEt-*t*-BuOH (9/1)-Bu_4NClO_4-(Pt) also provided good results (entries 9 and 12). Interestingly, the presence of *t*-BuOH in acetic acid can suppress the formation of by-products (*cf.* entry 10),[4)] in contrast to the result obtained in MeCN-$LiClO_4$ system (entry 3).

Particularly noteworthy is the effect of the supporting electrolytes. As shown in entries 1—7, use of perchlorate salts, lithium tetrafluoroborate, and lithium trifuloroacetate, as supporting electrolytes facilitated the formation of **2**. However, use of tetraethylammonium *p*-toluenesulfonate (Et_4NOTs) in various electrolysis systems (entries 8, 11, and 14) mainly afforded **3** (70—84%) along with **2** (7—13%) after passage of 8—9 F/mol of electricity. The selective formation of **3** was achieved in a MeOH-Et_4NOTs-(Pt) system by passage of 2—4 F/mol of electricity (entries 15 and 16). Most of the starting material **1** was converted into **3** in each case when *ca.* 2 F/mol of electricity were passed. However, efficient conversion of **3** into **2** took place smoothly in the MeCN-*t*-BuOH (9/1)-$LiClO_4$-(Pt) system.

Transformation of **3** into **2** can be reasonably explained by assuming the acid-catalyzed isomerization of **3** to 2-methyl-1,4-naphthalenediol (**4**) with strong acid in the vicinity of the electrode and a subsequent two-electron oxidation of **4** at the anode.[5)] The isomerization of **3** into **4** takes place more effectively in the anode compartment, in which most of counter ions, *i.e.*, ClO_4^-, BF_4^-, and $CF_3CO_2^-$, of strong acids are concentrated by the electrolysis.[6)] In contrast, TsOH arising from Et_4NOTs, seems less effective in catalyzing this isomerization.[7)]

Experimental[8)]

Materials. 2-Methyl-5,8-dihydro-1,4-naphthalenediol (**1**) was obtained by the acid-catalyzed isomerization of Diels-Alder adduct of 2-methyl-1,4-benzoquinone and butadiene.[2a)] Authentic samples of **3** and **4** were derived from **1** according to reported procedures.[2a)] Commercially available vitamin K_3 (**2**) was used as an authentic sample. Acetic acid, methanol, *t*-butyl alcohol, and acetonitrile were distilled before use. Reagent-grade supporting electrolytes were used.

Electrolysis Procedure. A conventional H-type cell divided with fritted glass was used, which was fitted with two platinum or carbon electrodes (1.5×2 cm^2). Regurated DC power was supplied by Kowa Electronics model PGS-1550 potentio-galvanostat. The conditions and results are summarized in Table 1. A typical electrolysis procedure is as follows.

*Electrooxidation of 2-Methyl-5,8-dihydro-1,4-naphthalenediol (1) in MeCN-*t*-BuOH(9/1)-$LiClO_4$-(Pt electrodes) System (Entry 1 in Table 1).* A solution of **1** (30 mg, 0.17 mmol) and $LiClO_4$ (600 mg) in MeCN (13.5 ml) and *t*-BuOH (1.5 ml) was charged into the anode compartment fitted

TABLE 1. ELECTROOXIDATION OF 2-METHYL-5,8-DIHYDRO-1,4-NAPHTHALENEDIOL[a]

Entry	Electrolysis system Solvent-Electrolyte-(Electrodes)[b]	Electricity F/mol	Products yields/%[c]	
			Compd **3**	Compd **2**
1	MeCN-*t*-BuOH[d]-$LiClO_4$-(Pt)	9		94
2	MeCN-*t*-BuOH[d]-$LiClO_4$-(C)	9		91
3	MeCN-$LiClO_4$-(Pt)	6		90
4	MeCN-*t*-BuOH[d]-Et_4NClO_4-(Pt)	9	Tracc	88
5	MeCN-*t*-BuOH[d]-Bu_4NClO_4-(Pt)	8.5		81
6	MeCN-*t*-BuOH[d]-$LiBF_4$-(Pt)	7.5		93
7	MeCN-*t*-BuOH[d]-$LiOCOCF_3$-(Pt)	9		66
8	MeCN-*t*-BuOH[d]-Et_4NOTs-(Pt)	9	74	7
9	AcOH-*t*-BuOH[d]-$LiClO_4$-(Pt)	9	7	92
10	AcOH-$LiClO_4$-(Pt)	6		57[e]
11	AcOH-*t*-BuOH[d]-Et_4NOTs-(Pt)	9	70	13
12	AcOEt-*t*-BuOH[d]-Bu_4NClO_4-(Pt)	9		92
13	MeOH-$LiClO_4$-(Pt)	9	18	68
14	MeOH-Et_4NOTs-(Pt)	8[f]	84	11
15	MeOH-Et_4NOTs-(Pt)	4[f]	95	
16	MeOH-Et_4NOTs-(Pt)	2.25[f]	89[g]	

a) Carried out at a constant current density (1.67 mA/cm^2) at 16—22 °C. b) Pt: platium foil electrodes (1.5 × 2 cm^2); C: carbon plate electrodes (1.5 × 2 cm^2). c) Isolated yields. d) Containing 10% (v/v) of *t*-BuOH. e) Tarry materials were obtained. f) Current density: 10 mA/cm^2. g) Monomethyl ether of **1** (11%) was recovered.

with Pt electrode (1.5 × 2 cm^2) and a thermometer. A solution of $LiClO_4$ (400 mg) in MeCN (9 ml) and *t*-BuOH (1 ml) was charged into the cathode compartment fitted with Pt electrode (1.5 × 2 cm^2). Nine F/mol of electricity was passed at a constant current of 1.67 mA/cm^2 at 16—18 °C for 8.6 h.[9] The anode solution was concentrated *in vacuo* and the residue was taken up in CH_2Cl_2. The extracts were washed with brine, dried (Na_2SO_4), concentrated *in vacuo*, and chromatographed on silica gel with hexane/ether (5/1) to give **2** (28.9 mg, 94%): mp 102—103.5 °C (lit,[2a] 105—106 °C).

Electrooxidation of 2-Methyl-5,8-dihydro-1,4-naphthalenediol (1) in MeOH-Et_4NOTs-(Pt) System (Entry 16). In a similar manner, a solution of **1** (67 mg, 0.38 mmol) and Et_4NOTs (600 mg) in MeOH (15 ml) [catholyte: MeOH (10 ml)-Et_4NOTs (400 mg)] was electrolyzed at 10 mA/cm^2 at 20—22 °C for 1.35 h (4 F/mol of electricity passed). Usual workup of the anolyte gave **3** (63 mg, 95%): mp 83—85 °C (lit, mp 91—92 °C[2a] 82—84 °C,[10] 86 °C[11]).

Electrooxidation of 2-Methyl-5,8-dihydro-1,4-naphthoquinone (3) in MeCN-$LiClO_4$-(Pt) System. A solution of **3** (30 mg, 0.17 mmol) and $LiClO_4$ (600 mg) in MeCN [catholyte: MeCN (10 ml)-$LiClO_4$ (400 mg)] was electrolyzed at 1.67 mA/cm^2 at 16—17 °C. After passage of 3.5 F/mol of electricity (3.2 h), usual workup of the anolyte gave **2** (26.5 mg, 90%) and **3** (1 mg, 4%).

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6) The pH value of the electrolysis solution was more acidic than pH 1, after the electrolysis.

7) Exposure of **3** in MeOH (2 ml)-TsOH (40 mg) at 24 °C for 7 h resulted in the recovery of **2** (≈90%) along with monomethyl ether of **1** (≈2%) and **3** (≈5%).

8) All melting points are uncorrected.

9) The anode potential of 0.40—0.45 V *vs.* Ag/Ag$^+$ at the initial stage of the electrolysis shifted up to 2—2.1 V vs. Ag/Ag$^+$ after passing 2 F/mol of electricity.

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