Direct anodic oxidation of *p*-methoxytoluene in methanol. The effect of electrolysis conditions

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The effect of anions of the supporting electrolyte (F^-, dialkylphosphate, TsO^-, and BF_4^-) and other electrolysis conditions (anode material, temperature, substrate concentration) on the selectivity of the direct anodic oxidation of *p*-methoxytoluene in methanol into 4-methoxybenzaldehyde dimethylacetal was studied. The highest selectivity was obtained in the presence of fluoride anion.

Key words: anodic oxidation, *p*-methoxytoluene, 4-methoxybenzaldehyde dimethylacetal, 4-methoxybenzaldehyde, potassium fluoride.

The direct anodic (AO) oxidation of *p*-methoxytoluene (PMT) in methanol is a convenient method for transforming it into 4-methoxybenzaldehyde dimethylacetal (**2**). Hydrolysis of the latter affords 4-methoxybenzaldehyde (**3**), a valuable fragrant compound and a multipurpose intermediate in organic synthesis[1] (Scheme 1).

Scheme 1

$$4\text{-}MeOC_6H_4Me \xrightarrow{\text{AO, MeOH}} \underset{\textbf{1}}{4\text{-}MeOC_6H_4CH_2OMe} \xrightarrow{\text{AO, MeOH}}$$

$$\longrightarrow \underset{\textbf{2}}{4\text{-}MeOC_6H_4CH(OMe)_2} \xrightarrow[-\,2\,\text{MeOH}]{H_3O^+} \underset{\textbf{3}}{4\text{-}MeOC_6H_4CH{=}O}$$

This method for synthesizing aldehyde **3** is preferred technologically as compared with indirect electrochemical oxidation of PMT in the presence of mediators, *e.g.*, manganese, cerium, and cobalt compounds.[2] However, to attain a high selectivity of the process, one should thoroughly optimize its parameters, such as the supporting electrolyte, anode material, and others, because of the oligomerization and polymerization of the aromatic substrates that necessarily accompany direct anodic oxidation. This kind of optimization[2,3] made it possible to reach, at best, a 70 % selectivity in the transformation of PMT into acetal **2**, with a degree of PMT conversion of 80 %. This result was obtained when PMT was oxidized using a graphite anode and tetrabutylammonium or sodium tetrafluoroborate as supporting electrolytes in the presence of a deprotonating additive (lutidine). A similar selectivity of PMT transformation into acetal **2** was attained using graphite anodes and sodium methoxide,[4] tetraethylammonium tosylate,[5] or dibutyl phosphate with triethylamine[6] as the supporting electrolytes. Approximately 50 % selectivity was attained when sodium perchlorate,[7] potassium fluoride, or *p*-toluenesulfonic acid[8] were used as electrolytes.

In the present work we searched for a supporting electrolyte and an anodic material which would provide a higher yield of aldehyde **3**, simple repeated regeneration of the electrolyte, and high stability of the process. For this purpose, we studied the effect of the most promising electrolytes selected from those applicable to direct anodic PMT oxidation, namely, potassium fluoride, dialkylphosphates, tetrafluoroborate, and tosylates. We also studied such anodic materials as graphite, platinum, platinized titanium, and a ruthenium—titanium oxide electrode (RTOE).

Most of the experiments were performed at a starting PMT concentration of 0.5—1.0 mol L^{-1} at 60 °C. In order to determine the effect of these parameters on the composition of the electrolysis products, a series of experiments was carried out at $[PMT]_0 = 1.5$ mol L^{-1} and at 20 and 40 °C.

The basic experimental results (obtained after hydrolysis of the electrolysis products) are presented in Tables 1 and 2. In all experiments, aldehyde **3** was the main product (Scheme 1). In addition to compound **3**, minor products such as α,4-dimethoxytoluene (**1**, an intermediate in the formation of acetal **2**), 4-methyl-4-methoxycyclohexa-2,5-dien-1-one (**4**, only in the experiments with KF), and methyl anisate (**5**) were formed. The amount of compound **4** increases when the graphite anode is replaced by a platinum or platinum—titanium anode, which provides more efficient generation of methoxyl radicals in a methanolic solution. The addition of these to the aromatic ring in PMT, oxidation and then solvolysis and hydrolysis of the resulting 1,1,4-trimethoxy-4-methylcyclohexa-2,4-diene[4] occur subsequently (Scheme 2, Table 1, experiments 1—3).

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 3, pp. 524—527, March, 1995.

Table 1. Anodic oxidation of *p*-methoxytoluene (PMT) with the use of various supporting electrolytes and anode materials (60 °C)[a]

Experiment	Supporting electrolyte	Anode	Q/F mol^{-1}	$[PMT]_0$ / mol L^{-1}	Degree of PMT conversion (%)	Oxidation products and their yields (% of the theoretical value)[b]			
						1	**3**	**4**	**5**
1	KF	C	4.5	1.0	94	6	74	2	1
2	KF	Pt	4.5	0.5	94	7	68	3	5
3	KF	Pt/Ti	4.5	1.0	96	9	63	6	3
4	KF	RTOE	4.5	1.0	97	9	73	0.2	0.5
5	$(EtO)_2PO_2Na$	C	4.0	1.0	97	6	66	0	0.5
6	$(BuO)_2PO_2Na$	C	4.0	0.5	90	4	74	0	0
7	$(EtO)_2PO_2Na$	Pt	4.0	0.5	97	2	65	0	1
8	$(BuO)_2PO_2Na$	Pt	4.0	0.5	92	6	60	0	1
9	$(EtO)_2PO_2Na$	Pt/Ti	4.5	0.5	98	6	55	0	3
10	$(EtO)_2PO_2Na$	RTOE	4.5	0.5	98	4	67	0	0.5
11	TsOK	C	4.0	1.0	90	9	62	0	2
12	$TsONHEt_3$	C	4.4	1.0	98	4	63	0	1
13	$TsONEt_4$	C	4.9	1.0	96	3	56	0	3
14	BF_4NBu_4	C	4.0	1.0	95	6	56	0	4

[a] A solution of PMT (75—150 mmol) and supporting electrolyte (10—15 mmol) in dry methanol (130 mL); stainless steel anode; current density, 20—25 mA cm^{-2} (or 40—50 mA cm^{-2} in experiments 2, 3, and 5—8); voltage across the cell, 10—15 V (up to 30 V when an RTOE was used).

[b] According to GLC analysis data obtained after the hydrolysis of the oxidation products; for aldehyde **3**, the yield was calculated from the amount of the isolated product.

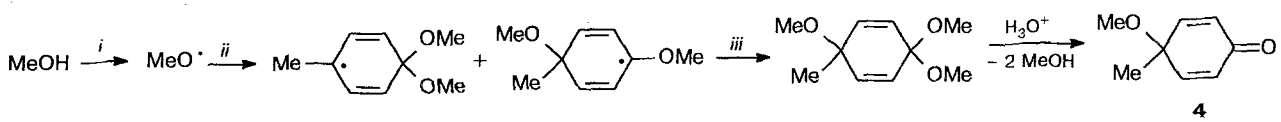
Table 2. Anodic oxidation of *p*-methoxytoluene (PMT) at various starting concentrations and electrolysis temperatures

Experiment	$[PMT]_0$ / mol L^{-1}	T / °C	Supporting electrolyte	i / mA cm^{-2}	Q / F mol^{-1}	Degree of PMT conversion (%)	Oxidation products and their yields (% of the theoretical value)[b]			
							1	**3**	**4**	**5**
1	0.5	60	KF	40	4.5	97	6	74	3	1
2	1.0	60	KF	40	4.5	94	6	74	3	1
3	1.5	60	KF	25	4.5	96	5	64	1.3	1
4	0.5	20	$(EtO)_2PO_2Na$	20	4.0	97	2	67	0	3
5	0.5	40	$(EtO)_2PO_2Na$	40	4.5	98	4	63	0	3
6	0.5	60	$(EtO)_2PO_2Na$	50	4.0	98	5	64	0	0.5
7	0.5	60	$(BuO)_2PO_2Na$	40	4.0	96	4	67	0	0
8	1.0	60	$(BuO)_2PO_2Na$	25	4.0	90	2	74	0	0
9	1.5	60	$(EtO)_2PO_2Na$	40	4.0	97	6	67	0	0.5
10	1.0	20	$(EtO)_2PO_2Na$ + $HC(OMe)_3$	20	4.0	99	2	71	0	4
11	1.5	20	$(BuO)_2PO_2H$ + NEt_3 1 : 1	20	4.0	100	—	54	2	13

[a] A graphite anode and a steel cathode; a solution of PMT (75—150 mmol) and supporting electrolyte (10—15 mmol) in dry methanol (130 mL); voltage across the cell, 10—15 V (up to 27 V in experiment 10).

[b] According to GLC analysis data obtained after the hydrolysis of the oxidation products; for aldehyde **3**, the yield was calculated from the amount of the isolated product.

Scheme 2



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i. AO. *ii*. 4-$MeOC_6H_4Me$. *iii*. AO, MeOH

Ester **5**, present in the products of most of the experiments, was formed due to the oxidation of acetal **2** into methyl orthoanisate followed by its hydrolysis.[7]

$$\mathbf{2} \xrightarrow{i} \text{4-MeOC}_6\text{H}_4\text{C(OMe)}_3 \xrightarrow[-\,2\ \text{MeOH}]{ii} \underset{\mathbf{5}}{\text{4-MeOC}_6\text{H}_4\text{COOMe}}$$

i. AO, MeOH. *ii.* H_2O

Of the electrolytes studied, potassium fluoride provided the highest selectivity of PMT transformation into acetal **2**. When this electrolyte was used, the formation of compound **2** on graphite and platinum anodes and on RTOE occured with 68—74 % selectivity and involved almost complete conversion of PMT and over 90 % conversion of the intermediate ether **1** (Table 1, experiments 1, 2, and 4). This result was attained after a 4.5 F charge was passed per 1 mol PMT. The side processes giving ketone **4** and ester **5** occur more readily in the presence of KF than with other electrolytes, particularly on platinum and platinized titanium (Table 1, experiments 2 and 3). The oxidation of PMT on graphite and on RTOE occurs more selectively. The use of graphite is preferable because when RTOE is used, a 2—3 times higher voltage is required to maintain the necessary current (up 30 V; Table 1, experiments 1 and 4).

The transformation of PMT into acetal **2** in the presence of sodium diethyl- and dibutylphosphates as supporting electrolytes occurs with almost the same selectivity as with KF (Table 1, experiments 5—10). The important distinguishing feature of these electrolytes is that they prevent the side process leading to ketone **4** and considerably inhibit the formation of the other side product, ester **5**. This feature is more pronounced when a graphite or RTOE electrode is used (Table 1, experiments 5, 6, and 10).

The other electrolytes, namely, potassium, triethylammonium, and tetraethylammonium tosylates and tetrabutylammonium tetrafluoroborate, affect the selectivity of PMT transformation into acetal **2** similarly to the dialkylphosphate electrolytes. However, they suppress the formation of ester **5** less efficiently.

When the initial concentration of PMT is increased to more than 1 mol L^{-1}, the selectivity of the transformation of PMT into compound **2** in the presence of KF decreases (Table 2, experiment 3), but this does not occur with phosphate electrolytes (Table 2, experiments 6—9).

A study of the effect of temperature on the process showed that the concentration of KF required to conduct the electrolysis in methanol is attained only at 60 °C. With dialkylphosphate supporting electrolytes, varying the temperature from 20 to 60 °C has virtually no effect on the selectivity of the transformation of PMT into acetal **2**, while decreasing the temperature favors the side formation of ester **5** (Table 2, experiments 4—6). The addition of ethyl orthoformate, which traps the water formed during the neutralization of dialkylphosphonic acids with sodium carbonate, did not decrease the yield of ester **5** (Table 2, experiment 5) but sharply increased the ohmic resistance of the system and the voltage across the cell (from 10 to 27 V). This allowed us to consider that the formation of ester **5** through hydrolysis of acetal **2** into the semiacetal followed by the oxidation of the latter did not occur.

The yield of ester **5** increases considerably (from 0.5—3 % to 13 %) when PMT is anodically oxidized under the conditions used in Ref. 6 (Table 2, experiment 11), but we were unable to obtain aldehyde **3** in the yield reported in that work (80 %).

Thus, the use of KF as the supporting electrolyte and the use of a graphite anode makes it possible to perform the anodic oxidation of PMT into acetal **2** followed by its hydrolysis into the target aldehyde **3** with a selectivity not worse than that reported previously.[2,3] In addition, the following additional advantages are provided: (a), a higher overall conversion of PMT and ether **1** (90 %) is attained; (b), a deprotonating additive is not required; (c), the recovery of the electrolyte and the isolation of the target product **3** are simplified.

Experimental

GLC analyses were performed on a Varian 3700 chromatograph with a flame-ionization detector, in a stream of nitrogen, using 200 × 0.3 cm glass columns with 5 % XE-60 on Chromaton N-AW (0.125—0.160 mm), and 200 × 0.3 cm glass columns with 5 % Carbowax 20M on Inerton N-AW (0.15—0.20 mm). ^{1}H NMR spectra of solutions of the compounds in $CDCl_3$ were recorded on Joel FQ-90Q and Bruker WM-250 spectrometers using $SiMe_4$ as the internal standard. Mass spectra were recorded on a Varian MAT CH-III mass spectrometer with injection of samples through a chromatograph (electron impact, 80 eV).

para-Methoxytoluene (PMT) was used as a "pure"-grade reagent distilled *in vacuo*, b.p. 65 °C (12 Torr). Potassium fluoride, diethyl- and dibutylphosphates, and triethylamine were used as "pure"-grade reagents. Potassium and triethylammonium tosylates were obtained by treatment of *p*-toluenesulfonic acid (TsOH) with KOH and triethylamine, respectively. Tetraethylammonium tosylate was obtained from ethyl tosylate and triethylamine according to the procedure in Ref. 9. The supporting electrolytes were dried with P_2O_5 before use. Methanol was dried by distillation with magnesium methoxide.

General procedure for the anodic oxidation of PMT. Electrolysis was carried out in the galvanostatic mode in a thermostatted undivided cell (200 mL in volume), equipped with a reflux condenser, a stainless steel cathode, and a graphite (a cylinder 15 mm in diameter) or a platinum anode (a 50 × 20 mm plate). The distance between the electrodes was 3—5 mm. The reagents were vigorously stirred under the conditions indicated in Tables 1 and 2. After the electrolysis, MeOH was distilled off from the reaction mixture, and the residue was diluted with petroleum ether (b.p. 40—70 °C; 50 mL). The supporting electrolyte that partially precipitated was filtered off and washed with petroleum ether (50 mL). The combined filtrates were stirred for 30 min with 10 % sulfuric acid (30 mL). The organic layer was separated, washed with 5 % $NaHCO_3$, dried with K_2CO_3, and analyzed by GLC using an internal standard (dodecane) and reference samples (the results are presented in Tables 1 and 2). The solvent was evaporated, and the residue was distilled *in vacuo* to give aldehyde **3**. The distillation fractions preceding aldehyde **3** contained PMT, 4-methoxybenzyl methyl ether (**1**), and 4-methyl-4-methoxycyclohexa-2,5-dien-1-one (**4**), and the higher-boiling fraction contained methyl 4-methoxybenzoate (**5**). Pure compounds **1**, **4**, and **5** were isolated from these fractions by column chromatography on silica gel using hexane—ether as the eluent.

4-Methoxybenzyl methyl ether[4] **(1),** b.p. 91—93 °C (8 Torr), n_D^{20} 1.5170. ^{1}H NMR, δ: 3.70 (s, 3 H), 4.13 (s, 3 H), 4.72 (s, 2 H); 7.41 (m, 4 H).

4-Methoxybenzaldehyde[10a] **(3),** b.p. 130—133 °C (10 Torr), n_D^{20} 1.5760. ^{1}H NMR, δ: 3.90 (s, 3 H), 7.05 (s, 2 H), 7.85 (s, 2 H), 9.87 (s, 1 H). 2,4-DNPH[10a], m.p. 254 °C (xylene). Found (%): C, 53.19; H, 3.95; N, 17.42. $C_{14}H_{12}N_4O_4$. Calculated (%): C, 53.16; H, 3.79; N, 17.73.

4-Methyl-4-methoxycyclohexa-2,5-dien-1-one[4] **(4),** m.p. 65—66 °C (hexane). ^{1}H NMR, δ: 1.50 (s, 3 H), 3.26 (s, 3 H), 6.60 (m, 4 H). MS, m/z ($I_{\rm rel}$ (%)): 138 (37) $M^{+\cdot}$, 123 (100) $[M-CH_3]^{+\cdot}$, 110 (36), 107 (40), 99 (38), 95 (41), 79 (55), 77 (58).

Methyl 4-methoxybenzoate[10b] **(5),** m.p. 47—48 °C. ^{1}H NMR, δ: 3.75 (s, 3 H), 3.88 (s, 3 H), 6.98 (s, 2 H), 8.08 (s, 2 H). IR, ν/cm^{-1}: 1720 (C=O).

Anodic oxidation of PMT with recovery of the supporting electrolyte (KF, Table 1, experiment 1). The experiment was carried out according to the general procedure under the conditions indicated in Table 1 using PMT (18.3 g), KF (0.7 g), and MeOH (130 mL). Standard work-up of the electrolysis product gave slightly yellow finely-crystalline potassium fluoride (0.49 g, 70 %) and aldehyde **3** (15.1 g, 74 %).

This work was financially supported by the Ministry of Science, High School and Technical Policy of the Russian Federation within the scope of the State scientific-technical program "Ecologically harmless processes of chemistry and chemical technology" (project No. 1.140 "Low-tonnage chemical products") and by the International Science Foundation (Grant Ch-2-1246-0923).

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Received October 31, 1994