

Electrochemical conversion of 4-alkyloxytoluenes to cyclic and non-cyclic 4-alkyloxybenzaldehyde acetals. A new approach to liquid-crystalline 1,3-dioxanes*

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4-Ethoxytoluenes bearing substituents in the β -position such as a hydroxy group, a halogen atom, or an ester group were anodically oxidized to give the corresponding benzaldehydes or their derivatives (dimethyl acetals, hydrogen sulphite addition products). The electrochemical oxidation of 4-alkyloxytoluenes in alcoholic solutions in the presence of alkanediols led to cyclic acetals, e.g. 1,3-dioxolanes and 1,3-dioxanes. Various 2,5-disubstituted 1,3-dioxanes were thus prepared, the trans isomers exhibiting liquid-crystalline properties. The ratio of cis and trans isomers formed during the electrolysis was found to be in correspondence with the thermodynamic equilibrium.

1. Introduction

The direct anodic oxidation of toluenes has attracted considerable attention for several years. This method allows for substitution both at the side chain, i.e. the methyl group, and the nucleus [1, 2]. The former process is interesting because of the access to aromatic aldehydes or their derivatives. Thus, the anodic oxidation of 4-methoxytoluene has been used to produce 4-methoxybenzaldehyde (anisaldehyde) [3].

The motivation of our investigation arose from the application of aromatic aldehydes as starting compounds for the formation of liquid crystals. 4-Alkyloxybenzaldehydes with alkyloxy groups containing a medium number of carbon atoms were particularly taken into consideration, the parameters of the desired liquid crystals depending partially on the alkyloxy chain length. Furthermore, the anodic oxidation of 4-ethoxytoluenes bearing various substituents in the β -position has been examined in order to offer a new route to substituted alkyloxybenzaldehydes or their derivatives.

Cyclic acetals of substituted benzaldehydes have been prepared by electrooxidation of toluenes in the presence of alkanediols. The influence of the reaction conditions on the product distribution has been studied. Based on these experiments the technique has been adapted in order to prepare liquid-crystalline 1,3-dioxane derivatives.

2. Experimental details

The anodic oxidations were performed with a Statron 3206 power supply at constant current in a flow-through cell equipped with graphite plate electrodes (35 cm² each). The temperature was between 35 and

40°C. The detailed electrolysis conditions are summarized in Tables 1-3. The workup procedures were as follows:

At first the solvent was evaporated.

A The crude product was filtered and subjected to fractional distillation.

B Ether was added to the residue. After neutralization (solid Na₂CO₃) and filtration the ether was removed. The product was recrystallized from methanol or subjected to fractional distillation.

C The residue was shaken with 150 cm³ saturated NaHSO₃ solution. The precipitating adduct was separated and recrystallized from ethanol-water.

D The residue was treated with 20 cm³ dichloromethane. After filtration the solvent was removed. The product was recrystallized from ether.

E The anolyte was neutralized (solid NaHCO₃) before evaporating the solvent. Water (100 cm³) and dichloromethane (150 cm³) were added. The separated organic layer was dried (Na₂SO₄). Then the solvent was removed. The crude product was distilled. The fraction of b.p. 105-110°C (45 Pa) was digested with n-heptane, from which the product crystallized.

The structures of the products were confirmed by spectroscopic data and by elemental analyses. The i.r. spectra were recorded on a Specord 71 IR spectrometer (Carl Zeiss Jena). The ¹H-NMR spectra were determined on a AC 80 or a WP 200 spectrometer (Bruker) with TMS as the internal standard. Elemental analyses of solid compounds were determined on a Carlo Erba 1104 elemental analyser. Analytical data of some representative products are given in the Appendix.

* This paper is dedicated to Professor Dr Fritz Beck on the occasion of his 60th birthday.

Table 1. Anodic oxidation of β -substituted 4-ethoxytoluenes 5

Starting material (mmol)	Solvent (cm ³)	Supporting electrolyte KF (mmol)	Workup	Product yield (%)
5a (95)	MeOH (170)	8.6	A	6a (32)
5a (95)	MeOH (165)	2.1*	B	6a (42)
5a (95)	MeOH (170)	8.6	C†	7a (36)
5b (90)	MeOH (170)	6.9	D	6b (41)
5c (26)‡	MeOH (175)§	95§	E	7c (21)
5d (33)	MeOH (126) HOAc (14)	8.6	C	8d (46)
5e (33)	MeOH (126) HOAc (14)	8.6	C	8e (54)
5f (33)	MeOH (126) HOAc (14)	8.6	C	8f (44)

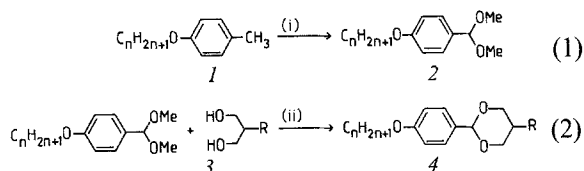
* Supporting electrolyte: p-TsOH.

† The NaHSO₃ adduct was treated with H₂SO₄ (10%) to give the aldehyde.‡ Divided cell, diaphragm: Nafion 427; amount of charge: 4.2 F mol⁻¹.§ Anolyte. (Catholyte: 125 cm³ MeOH, 6.9 mmol KF).C-electrodes, current density: 17 mA cm⁻², amount of charge: 4 F mol⁻¹, undivided cell.

3. Results and discussion

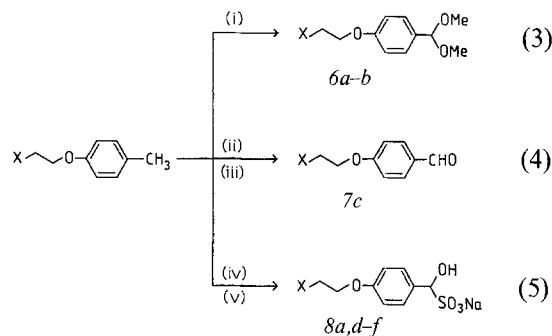
3.1. Electrochemical preparation of 4-alkoxybenzaldehydes

The anodic oxidation of 4-methoxytoluene was studied intensively both by direct [4, 5] and indirect [6–8] electrolyses. The direct electrochemical process was extended to 4-alkoxytoluenes **1** with C₄–C₁₂ alkoxy groups [9] in order to prepare the corresponding 4-alkoxybenzaldehyde dimethyl acetals **2** as starting materials for liquid-crystalline 2,5-disubstituted 1,3-dioxanes **4** described in [10]:

where R refers to alkyl, aryl, and $n = 4 \dots 12$.(i) C-anode, MeOH/KF, 4 F mol⁻¹, undivided cell
(ii) –2 MeOH, acid catalysis.

In order to widen the synthetic utility of the electrolysis (Equation 1) 4-ethoxytoluenes **5** with substituents

in the β -position were chosen as a model. After subjecting them to anodic oxidation at graphite anodes the corresponding aldehydes or derivatives were isolated:



5a X = OH

5b X = Cl

5c X = Br

5d X = OAc

5e X = OCOBu^t

5f X = OCOPh

(i) C-anode, MeOH, 4 F mol⁻¹, undivided cell(ii) C-anode, MeOH, 4.2 F mol⁻¹, divided cell(iii) H₃O⁺(iv) C-anode, MeOH-HOAc (9:1), 4 F mol⁻¹, undivided cell(v) sat. NaHSO₃

The solvents, supporting electrolytes, and isolated yields are summarized in Table 1. The electrolyses of the esters **5d–f** were carried out in the presence of acetic acid since, otherwise, only a small amount of product (~15% yield) could be isolated. 4-(2-Bromoethoxy)toluene **5c** had to be electrolyzed in a divided cell because it has been proved in a previous polarographic experiment that this compound is cathodically reducible (half-wave potential $E_{1/2} = -1.92$ V/SCE, MeOH–H₂O 4:1, 0.1 M NEt₄Br). The hydroxy compound **5a** could be converted to the corresponding side chain substituted product **6a** with medium yield although the hydroxyethoxy group was expected to markedly favour the anodic substitution at the aromatic nucleus leading to p-quinol ether ketals [11]. The influence of the hydroxyethoxy group is compensated for by the use of a graphite anode.

The advantage of the direct electrolysis becomes evident since the toluenes **5** are allowed to undergo oxidation of the methyl group, an attack of the β -substituent being prevented. The use of chemical oxidants is often connected with less mild reaction conditions, such as high oxidation potentials or opera-

Table 2. Electrooxidation of 4-methoxytoluene **9** in methanol-ethanediol. Relative product distribution in dependence on electrolyte composition, supporting electrolyte, and amount of charge

Run	4-Methoxytoluene (mmol)	Methanol (cm ³)	Ethanediol (mmol)	Supporting electrolyte (mmol)	Amount of charge (F mol ⁻¹)	Relative product distribution*		
						11	12	13
1	33	96	700	KF (8.6)	4	5	0	1
2	33	68	1100	KF (8.6)	4	8	0	1
3	80	135	60	KF (8.6)	4	0	2	3
4	80	135	60	p-TsOH (1.6)	4	3	1	1
5	80	135	60	p-TsOH (1.6)	4.4	6	1	1

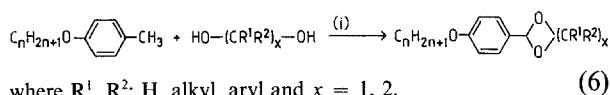
* Determined by gas chromatography after removal of the methanol.

C-electrodes, current density: 17 mA cm⁻², undivided cell.

tion in strong acidic or basic media, causing low selectivity.

3.2. Electrochemical access to cyclic acetals of 4-alkyloxybenzaldehydes

During the electrolyses of substituted toluenes in alcoholic solutions the alcohols act both as a solvent and as a reactant. An addition of alkanediols to the electrolytes should result in modified acetals. For entropic reasons cyclic acetals were expected:



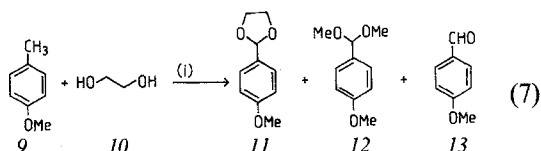
where R^1, R^2 : H, alkyl, aryl and $x = 1, 2$.

(i) $-2 H_2$; C-anode.

Recently, the formation of a 1,3-dioxolane derivative during the electrolysis of 2-benzyloxytoluene in a methanol-ethanediol mixture was mentioned [12]. However, the yield of cyclic acetal was small. Therefore, we intended to establish a more selective and effective method of preparing cyclic acetals.

3.2.1. 1,3-Dioxolanes. Because of the low electrical conductivity of ethanediol a solvent is required which provides sufficient conductivity of the electrolyte. An experiment with acetonitrile as solvent failed due to the formation of electrode films. Thus, methanol was used despite being expected to act as a competitive reactant during the electrolysis.

The electrolyses were performed with a simple electrolyte system consisting of 4-methoxytoluene **9**, methanol, and ethanediol, a supporting electrolyte was added. 2-(4-Methoxyphenyl)-1,3-dioxolane **11** was formed according to Equation 7, main by-products being 4-methoxybenzaldehyde dimethyl acetal **12** and 4-methoxybenzaldehyde **13**. The resulting product distributions determined by gas chromatography are listed in Table 2.



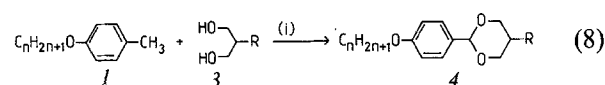
(i) C-anode, MeOH, undivided cell.

The results of runs 1 and 2 are characterized by a high yield of the desired cyclic acetal. Nevertheless, the workup procedure is complicated by the considerable content of excess ethanediol precluding a distillative workup. Neither is an aqueous workup procedure advisable. Therefore, the content of ethanediol was decreased (run 3) until it was in the range of the 4-methoxytoluene concentration to avoid excess ethanediol. Consequently, the formation of products **12** and **13** became predominant. Thus, the supporting electrolyte was changed from potassium fluoride to p-toluenesulphonic acid (run 4, 5) resulting in an inversion of the product distribution in favour of the 1,3-dioxolane. The slight increase of the charge to $4.4 F mol^{-1}$ was accompanied by a further improvement of the product distribution.

After workup (run 5, workup procedure *B*) 2-(4-methoxyphenyl)-1,3-dioxolane **11** was isolated in a 59% yield related to ethanediol **10** (48% yield related to 4-methoxytoluene **9**, conversion of **9**: 91%).

A comparison of runs 3 and 4 indicates that formation of the aldehyde **13** and its dimethyl acetal **12** should precede the formation of the 1,3-dioxolane **11**, suggesting that the cyclic acetal originates from an acid catalyzed acetalization of **13** and a transacetalization of **12** either during the electrolysis or during the removal of the solvent. Excess ethanediol, however, affords a high yield of cyclic acetal even under non-acidic conditions (run 1, 2). Thus, the experiments do not show whether the formation of the cyclic acetal is caused by a nucleophilic attack of the ethanediol to an intermediate oxidation product of the toluene **9** or an acetalization or transacetalization of the aldehyde **13** or its dimethyl acetal **12**, respectively.

3.2.2. 1,3-Dioxanes. Taking as a pattern the electrochemical preparation of 2-(4-methoxyphenyl)-1,3-dioxolane, 1,3-dioxanes substituted in the 2- and 5-position have been prepared:



(i) C-anode, MeOH/p-TsOH, $4.4 F mol^{-1}$, undivided cell.

4	n	R
a	6	C ₃ H ₇
b	6	C ₄ H ₉
c	6	C ₆ H ₁₃
d	6	C ₈ H ₁₇
e	6	C ₉ H ₁₉
f	6	p-C ₆ H ₄ -C ₆ H ₁₃
g	8	p-C ₆ H ₄ -C ₆ H ₁₃
h	10	p-C ₆ H ₄ -C ₆ H ₁₃

Numerous 1,3-dioxanes **4** exhibit liquid-crystalline properties, provided that they possess transconfiguration. Therefore, an electrochemical approach has been developed as an alternative to the route starting from 4-alkyloxybenzaldehydes and propane-1,3-diols [10].

An excess of the propane-1,3-diols **3** during the reaction had to be avoided because they are accessible only by multi-step syntheses in general. Hence, the ratio of 4-alkyloxytoluenes **1** and propane-1,3-diols **3** was changed over only a small range. The isolated yields of several liquid-crystalline 1,3-dioxanes **4** (related to propane-1,3-diols **3**) are summarized in Table 3.

The 5-butyl-2-(4-hexyloxyphenyl)-1,3-dioxane (run 7) consisted of 27% cis isomer **4b.1** and 73% trans isomer **4b.2** (Equation 9) determined by HPLC and ¹H-NMR spectroscopy. According to Sorkin [13] the thermodynamic equilibrium is characterized by a cis/trans ratio of 25%:75%, which is in agreement with the above mentioned ratio. The trans isomer was isolated by repeated recrystallization from methanol. To improve the yield of liquid-crystalline material the cis isomer accumulated in the mother liquors can be partially transformed by acid-catalyzed equilibration with an intermediate ring opening [14].

Table 3. Starting materials and isolated yields (related to propane-1,3-diols 3) of liquid-crystalline 2,5-disubstituted 1,3-dioxanes 4 by electrooxidation

Run	4-Alkyloxytoluene 1		Propane-1,3-diol 3		Product, yield
	<i>n</i>	(mmol)	R	(mmol)	(trans isomer) (%)
6	6	60	C ₃ H ₇	60	4a (46) (79)*
7	6	70	C ₄ H ₉	52	4b (42)
8	6	60	C ₆ H ₁₃	45	4c (40)
9	6	36	C ₈ H ₁₇	27	4d (40)
10	6	36	C ₉ H ₁₉	40	4e (46)
11	6	36	p-C ₆ H ₄ -C ₆ H ₁₃	27	4f (51)
12	8	36	p-C ₆ H ₄ -C ₆ H ₁₃	27	4g (37)
13†	10	36	p-C ₆ H ₄ -C ₆ H ₁₃	27	4h (42)

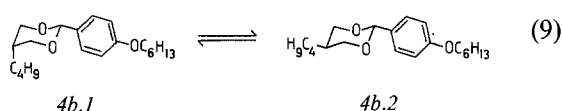
* Related to starting material 3 converted.

† Solvent used: ethanol.

C-electrodes, current density: 17 mA cm⁻², solvent: MeOH (135 cm³), supporting electrolyte: p-TsOH (1.6 mmol), amount of charge: 4.4 F mol⁻¹, undivided cell, workup: B.

Table 4. Dependence of the yield of 1,3-dioxanes 4a, 4e, and 4f on the starting material ratio

Product	R	Molar ratio of starting compounds		Isolated yield of 4 related to	
		1 (<i>n</i> = 6): 3	1 (<i>n</i> = 6): 3	1 (<i>n</i> = 6) (%)	3 (%)
4a	C ₃ H ₇	4:3		38	50
		3:3		46 (59) ^a	46 (79) ^a
4e	C ₉ H ₁₉	4:3		38	50
		4:4.4		51	46
4f	p-C ₆ H ₄ -C ₆ H ₁₃	6:3		26	51
		4:3		39	51

^a Related to converted starting material 1 and 3, respectively.

The yields of the 1,3-dioxanes 4a, 4e, and 4f with respect to 4-hexyloxytoluene 1 (*n* = 6) and to the corresponding propane-1,3-diols 3 dependent on the molar ratio 1 (*n* = 6): 3 are listed in Table 4. Surprisingly, the yield related to the propane-1,3-diols 3 is almost independent of the starting material ratio within the range observed, whereas the yield related to 1 (*n* = 6) increases with lower molar ratio 1 (*n* = 6): 3 as expected.

4. Conclusion

A new synthetic approach to a variety of 4-alkyloxybenzaldehydes or their derivatives has been developed. This approach is characterized by a simple procedure starting from readily accessible substituted toluenes. Thus, certain β -substituted 4-ethoxytoluenes can be converted to the corresponding benzaldehydes without changing the β -substituent, suggesting that direct electrolysis conditions can preserve substituents such as a hydroxy group, a halogen atom, or an ester group, which may be attacked under less mild conditions.

The electrooxidation of substituted toluenes in the presence of ethanediol or propane-1,3-diols affords cyclic acetals of benzaldehydes. The method is applicable to the synthesis of numerous liquid-crystalline

1,3-dioxanes. An improvement of the trans/cis ratio of these compounds in comparison with the thermodynamic equilibrium, however, was not observed. Nevertheless, it has been proved that the isolated yields are satisfactory, especially if unreacted starting materials are either recovered or recycled to the electrolysis cell.

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Appendix

Analytical data of representative compounds

Product	(i.r.) (cm^{-1})	$^1\text{H-NMR}$ (TMS/ CDCl_3) δ (p.p.m.)
4f (clearing point 143°C)	(nujol) 1615, 1515, 1250, 1150, 1020	7.44 (d, 2H, $J = 9$ Hz) 7.14 (s, 4H) 6.89 (d, 2H, $J = 9$ Hz) 5.52 (s, 1H) 4.33 (dd, 2H, $^2J_{\text{ca}} = 12$ Hz, $^3J_{\text{ca}} = 5$ Hz) 4.00 (dd, 2H, $^2J_{\text{ca}} = 11$ Hz, $^3J_{\text{aa}} = 10$ Hz) 3.95 (t, 2H, $J = 7$ Hz) 3.32 (m, 1H) 2.58 (t, 2H, $J = 8$ Hz) 1.80 – 1.39 (m, 16H) 0.85 (m, 6H)
6a (b.p. 127–128°C/20 Pa)	(neat) 3410, 1620, 1520, 1250, 1050	7.34 (d, 2H, $J = 9$ Hz) 6.87 (d, 2H, $J = 9$ Hz) 5.32 (s, 1H) 4.20–3.80 (m, 4H) 3.29 (s, 6H) 2.29 (t, 1H, $J = 5$ Hz)
6b (m.p. 44–46°C)	(nujol) 1615, 1515, 1250, 1100, 1040, 815	7.37 (d, 2H, $J = 9$ Hz) 6.89 (d, 2H, $J = 9$ Hz) 5.34 (s, 1H) 4.22 (t, 2H, $J = 5$ Hz) 3.79 (t, 2H, $J = 5$ Hz) 3.30 (s, 6H)
7a (m.p. 33–34°C)*	(KBr) 3380, 1665, 1600, 1500, 1250, 1050	9.83 (s, 1H) 7.79 (d, 2H, $J = 9$ Hz) 6.98 (d, 2H, $J = 9$ Hz) 4.20–4.00 (m, 4H) 2.62 (s, 1H)
7c (m.p. 47–48.5°C)†	(KBr) 1685, 1605, 1515, 1260, 1070, 835	9.89 (s, 1H) 7.84 (d, 2H, $J = 9$ Hz) 7.01 (d, 2H, $J = 9$ Hz) 4.37 (t, 2H, $J = 6$ Hz) 3.66 (t, 2H, $J = 6$ Hz)
8e	(KBr) 3235, 1620, 1520, 1460, 1380, 1355, 1200, 1030	9.85 (s, 1H) 7.88 (d, 2H, $J = 9$ Hz) 7.11 (d, 2H, $J = 9$ Hz) 5.03 (s, 1H) 4.38 (m, 4H) 1.19 (s, 9H)
11 (b.p. 86–89°C/0.6–0.7 kPa)	(neat) 1620, 1520, 1250, 1080, 830	7.39 (d, 2H, $J = 9$ Hz) 6.89 (d, 2H, $J = 9$ Hz) 5.73 (s, 1H) 4.04 (m, 4H) 3.78 (s, 3H)

* Lit [15]: m.p. 34°C.

† Lit [15]: m.p. 52°C.

Satisfactory elemental analyses obtained: C \pm 0.5%, H \pm 0.3%, Br \pm 0.1%, Cl \pm 0.4%.