

INDIRECT ELECTROCHEMICAL SIDE-CHAIN OXIDATION OF ALKYL AROMATIC  
COMPOUNDS - SELECTIVE SYNTHESIS OF METHYL BENZOATES OR ORTHO-  
BENZOIC ACID TRIMETHYLESTERS

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DIETER DEGNER

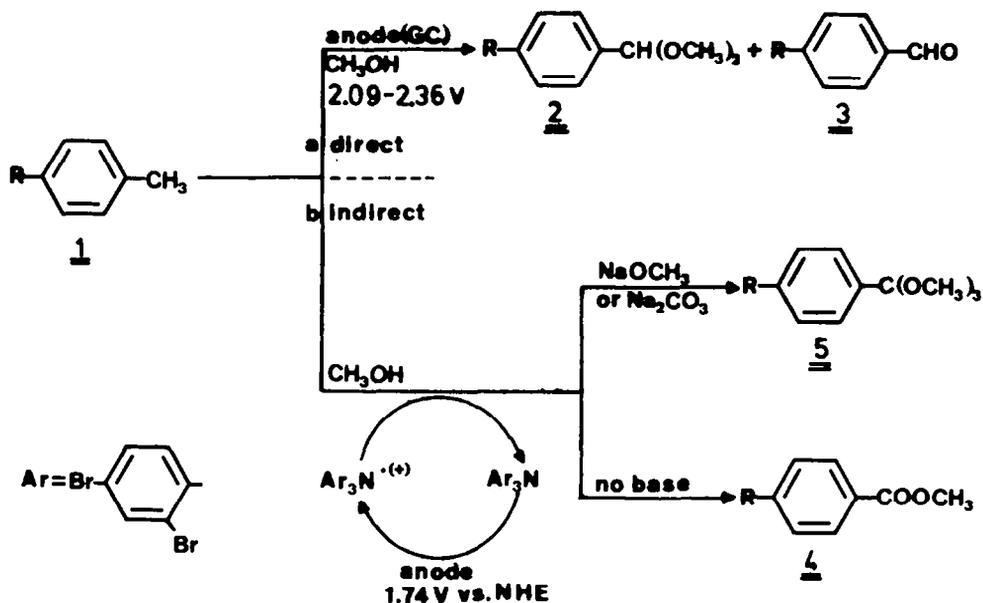
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**Abstract:** The technically important side-chain oxidation of alkyl aromatic compounds to form either methyl benzoates or orthobenzoic acid trimethylesters can be performed electrochemically at low potentials in methanol solution using an undivided cell and tris(2,4-dibromophenyl)amine as redox catalyst. Under neutral or slightly acidic conditions methyl benzoates are selectively formed while under basic conditions the orthoesters are predominating. In a similar way ortho benzoic acid trimethylesters are formed selectively starting from benzaldehyde dimethylacetals. The redox catalyst is stable under the reaction conditions so that several thousand cycles can be performed without noticeable loss.

Side-chain oxidation of alkyl aromatic compounds to the redox state of the benzoic acids or esters is of great technical importance. Aromatic acids are mostly generated by catalytic oxygenation of the respective toluene derivatives<sup>1)</sup> replacing the formerly important chromic acid oxidation<sup>2)</sup>. Direct anodic side-chain oxidation of alkyl aromatic compounds is possible in methanol solution but will only lead to the selective formation of benzaldehyde dimethylacetals<sup>3)</sup> (Scheme I, path a). Further oxidation to the benzoates is very difficult and results in very low selectivity (less than 10 %) even with a large charge excess<sup>4)</sup>.

We can now present a one-step electrochemical procedure by which toluene derivatives are directly converted into either methyl benzoates under neutral or slightly acidic conditions or into orthobenzoic acid trimethyl esters using slightly basic conditions. Benzaldehyde dimethylacetals, the technically available products of the direct anodic oxidation of toluene derivatives<sup>3)</sup>, are converted to the orthoesters with high selectivity, if sodium methoxide is present in small quantities. The reactions are performed in methanol solution using an undivided cell. This procedure is based on the use of catalytic amounts of tris(2,4-dibromophenyl)amine as electron transfer agent (redox catalyst) in an indirect electrolysis at potentials which are up to 900 mV more cathodic than the oxidation potentials of the substrates (Scheme I, path b). The method has already proved to be effective for the oxidation of benzylic alcohols to benzaldehydes<sup>5)</sup>. Table 1 gives a comparison of the results of direct and indirect electrochemical oxidations of substituted toluenes under neutral conditions demonstrating that the direct anodic oxidation at higher potentials stops at the aldehyde stage, while the indirect procedure at much lower potentials results in the formation of methyl



Scheme I. Pathways of direct and indirect electrochemical oxidation of toluene derivatives.

Table 1. Comparison of the results of direct and indirect electrochemical oxidations of substituted toluenes **1** in methanol under neutral conditions.

Method	Substrate <b>1</b> R =	$E_{\text{pox}}^c$ [V vs. NHE]	Turnover (%)	Yield (%) <sup>d</sup> <b>2</b> + <b>3</b>	Yield (%) <sup>d</sup> <b>4</b>
direct <sup>a</sup>	4-t-C <sub>4</sub> H <sub>9</sub>	2.09	98	66 (40)	2.5(1.5)
indirect <sup>b</sup>	"	"	98	5.1(1.8)	71 (38)
direct	4-CH <sub>3</sub>	2.10	98.5	82 (61)	1 (1.2)
indirect	"	"	95	5 (2)	76 (45)
direct	4-Br	2.23	97.2	2 (0.6)	64 (32)
indirect	"	"	86	3.8(0.2)	72 (7.2)
direct	4-Cl	2.24	98	66 (28)	1.6(1)
indirect	"	"	84	1.2(0.1)	83 (7.3)
direct	H	2.36	99	14.5(5.5)	3.3(1.9)
indirect	"	"	80	0.8(0.1)	95 (22)

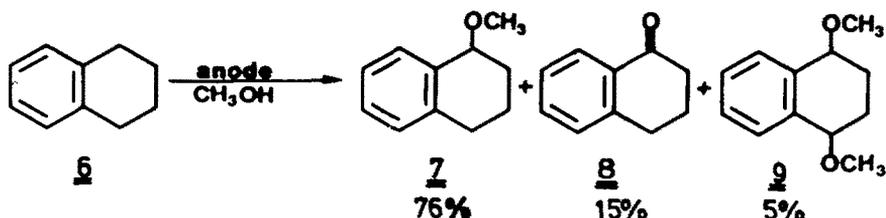
<sup>a</sup> Electrolysis at the peakpotential of the substrate in an undivided cell using  $\text{CH}_3\text{OH}/\text{LiClO}_4$  (0.2 M) as electrolyte.

<sup>b</sup> Electrolysis using tris(2,4-dibromophenyl)amine as mediator in a substrate to mediator ratio of 10:1 in an undivided cell using  $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$  (3:1)/0.15 M  $\text{NaClO}_4$  as electrolyte at 1.74 V vs. NHE.

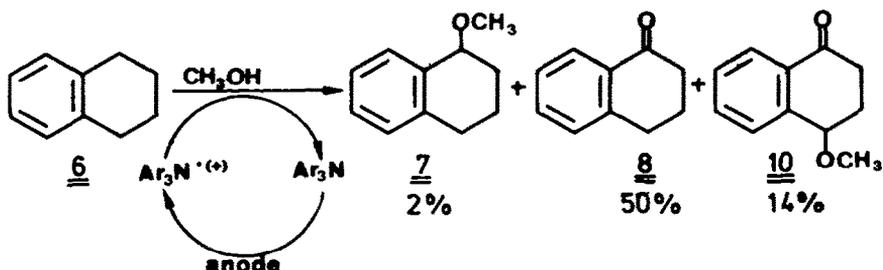
<sup>c</sup> Anodic peak potential by cyclic voltammetry measured vs.  $\text{Ag}/\text{AgCl}$ -reference electrode and converted to normal hydrogen electrode (NHE).

<sup>d</sup> Material yield; current yield in parentheses.

benzoates in high yields. The same behavior is also encountered in the methoxylation of tetralin (6). Direct anodic oxidation mainly yields 1-methoxy tetralin (7) together with 1-tetralone (8) and 1,4-dimethoxy tetralin (9).



Indirect oxidation using tris(2,4-dibromophenyl)amine as mediator, however, leads to the predominant formation of the higher oxidation states 1-tetralone (8) together with 4-methoxy tetralone (10).



This totally different behavior in the direct and indirect electrochemical procedure is nicely demonstrated in the diagrams which correlate the product distribution with the charge consumption (Fig. 1 and 2). While the direct anodic oxidation shows the typical behavior of a reaction in which the intermediate (benzyl methyl ether, Fig. 1) passes through a relatively high concentration level, the indirect electrolysis shows two intermediates (benzyl methyl ether and benzaldehyde dimethylacetal, Fig. 2) which are present only in relatively small but even concentrations. The concentration of the substrate drops almost linearly during most of the reaction time.

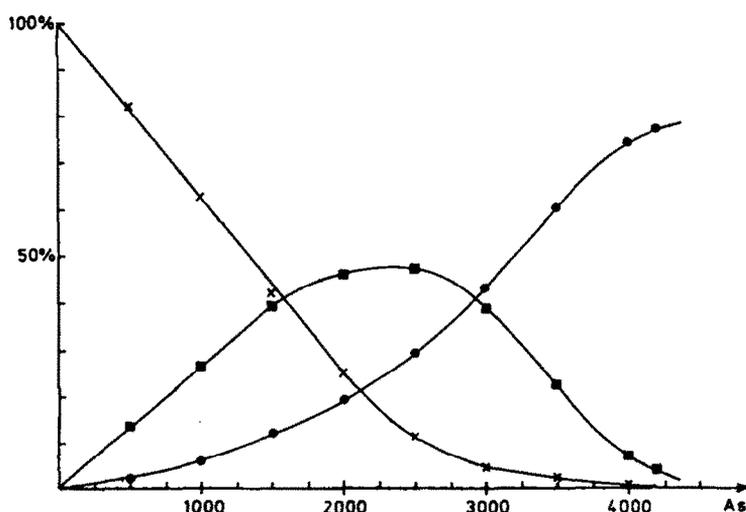


Figure 1. Product distribution during the course of the direct anodic oxidation of p-xylene vs. charge consumption.

X = p-xylene; ■ = 4-methyl-benzyl methyl ether; ● = p-tolualdehyde dimethylacetal

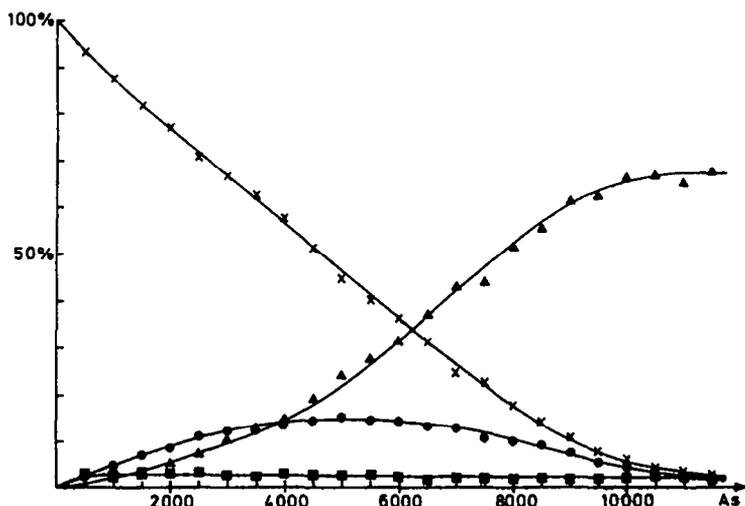
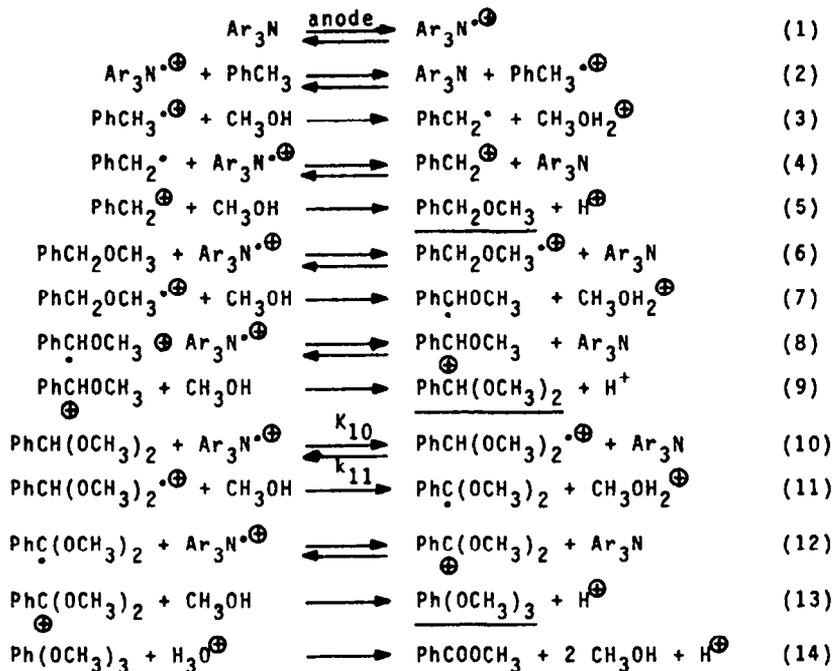


Figure 2. Product distribution during the course of the indirect anodic oxidation of p-xylene with tris(2,4-dibromophenyl)amine as mediator vs. charge consumption.

X = p-xylene; ■ = 4-methyl-benzyl methyl ether; ● = p-tolualdehyde dimethylacetal; ▲ = methyl p-toluate

The reason for this behavior can be given by the presumed reaction mechanism:



The reaction rate of the direct electrolysis is mainly dependent on the oxidation potentials of the substrate and the intermediates and only to a very small extent on the deprotonation rates of the cation radicals. As the oxidation potential of the dimethylacetal (p-tolualdehyde dimethylacetal:  $E_{\text{pox}} = 2.21 \text{ V}$ ) is about 100 mV more positive than those of either the substrate (p-xylene:  $E_{\text{pox}} = 2.10 \text{ V}$ ) or the intermediate ether (4-methyl-benzyl methyl ether:  $E_{\text{pox}} = 2.07 \text{ V}$ ) the acetal is the final product. The reaction rate of the indirect electrochemical oxidation, however, is influenced by the standard potential difference of the substrate and

the mediator as well as by the rate of the follow-up deprotonation. The overall rate for the oxidation of the dimethylacetal to the ester is given by:

$$v = k_{11}K_{10} \frac{[\text{acetal}][\text{Ar}_3\text{N}^{\oplus}]}{[\text{Ar}_3\text{N}]}$$

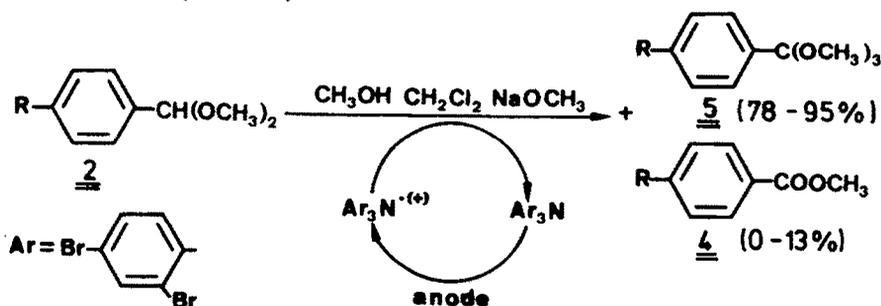
with

$$\lg K_{10} = 1/58 [E_{\text{Ar}_3\text{N}/\text{Ar}_3\text{N}^{\oplus}}^{\ominus} - E_{\text{acetal}/\text{acetal}^{\oplus}}^{\ominus}] (\text{mV})$$

Because of the capto-dative stabilization of the resulting radical the deprotonation rate of the acetal cation radical should be much higher than that of the toluene cation radical. Therefore the higher oxidation potential of the acetal can be overcompensated and the reaction goes beyond the redox state of the acetal. The fact that 4-methoxytoluene does not react in an acceptable way can also be explained on this basis. The methoxy substituent in the aromatic nucleus lowers the deprotonation rate of the primarily formed toluene cation radical in such a way that side reactions can compete. Not all of the aspects of this reaction can, however, be explained by a pure homogeneous electron transfer. For example a difference of 900 mV between the standard potentials of the substrate and the mediator is about 300 mV larger than the value which can be overcompensated by a fast follow-up chemical reaction<sup>6</sup>). Therefore a complex formation between mediator and substrate before the electron transfer very likely takes place. This is in accordance with the analysis of this type of reactions by Ebersson<sup>7</sup>) who is calling it a "bonded" electron transfer mechanism.

If the indirect electrochemical oxidation of alkyl aromatics by the use of tris(2,4-dibromophenyl)amine as mediator is performed under basic conditions adding sodium carbonate or small amounts of sodium methoxylate, the orthoester formation becomes dominant: for example p-xylene is transformed to ortho-4-methylbenzoic acid trimethylester in 55 % yield together with 24 % of 4-methylbenzoic acid methyl ester, if 1 to 5 mol percent NaOMe are used as a base. Dichloromethane should not be used as a cosolvent as it will cathodically form HCl thus consuming the base. 4-t-butyltoluene yields ortho-4-t-butylbenzoic acid trimethyl ester in 50 % yield together with 4-t-butylbenzoic acid methyl ester (17 %) if sodium carbonate is present in the electrolyte.

Orthobenzoic acid trimethyl esters are also formed in high selectivity, if one starts from the benzaldehyde dimethylacetals in the presence of methoxylate (Scheme II). In this case even para-alkoxy substituted acetals give high yields of the ortho esters (Table 2).



Scheme II. Pathway of the indirect electrochemical oxidation of benzaldehyde dimethylacetals

Table 2. Formation of orthobenzoic acid trimethyl esters (**5**) from benzaldehyde dimethylacetals (**2**) by indirect electrochemical oxidation in methanol with tris(2,4-dibromophenyl)amine as mediator.

Substrate <b>2</b> R =	Turnover <sup>a</sup> (%)	Yield <b>5</b> <sup>b</sup> (%)	Yield <b>4</b> <sup>b</sup> (%)
4- <u>t</u> -C <sub>4</sub> H <sub>9</sub>	100	90.4 (14)	6.5 (1)
4-CH <sub>3</sub>	90	87 (10)	---
4-Br	92	95.1 (9.6)	3.8 (0.4)
4-Cl	89.7	84.2 (5.8)	12.9(0.9)
H	96.4	85.6 (10.6)	12.2(1.5)
4-CH <sub>3</sub> O	100	78.3 (12.6)	13.2(2.1)
4- <u>t</u> -C <sub>4</sub> H <sub>9</sub> O	96	93.2 (13.3)	2.1 (0.3)

<sup>a</sup> Electrolysis using tris(2,4-dibromophenyl)amine as mediator in a substrate to mediator ratio of 10:1 in an undivided cell using CH<sub>3</sub>OH/CH<sub>2</sub>Cl<sub>2</sub> (3:1)/0.2 M LiClO<sub>4</sub> and 50 mol % NaOMe as electrolyte at 1.74 V vs. NHE.

<sup>b</sup> Material yield; current yield in parentheses.

The current yields can drastically be improved, if the educt instead of dichloromethane is used as a cosolvent. In this case formation of HCl is avoided and therefore the amount of methoxylate can be diminished to about 1 to 5 mol %. Results are given in Table 3.

Table 3. Formation of orthobenzoic acid trimethyl esters (**5**) from benzaldehyde dimethylacetals (**2**) by indirect electrochemical oxidation in methanol with tris(2,4-dibromophenyl)amine as mediator and the acetal as cosolvent.

Substrate <b>2</b> R = (g; mol)	Turnover <sup>a</sup> (%)	MY <b>5</b> <sup>b</sup> % (g; mol)	CY <b>5</b> <sup>c</sup> %	MY <b>4</b> <sup>b</sup> % (g; mol)	CY <b>4</b> <sup>c</sup> %	Cycles <sup>d</sup>
4-CH <sub>3</sub> (894; 5.38)	74	31 (240;1.23)	16	13.5 (81;0.54)	10.5	2500
4-CH <sub>3</sub> O (869; 4.77)	92	53 (492;2.32)	32	18.4 (135;0.81)	17	2240
4- <u>t</u> -C <sub>4</sub> H <sub>9</sub> O (894; 4.0)	85	55 (474;1.87)	55	6 (44;0.21)	9	1100

<sup>a</sup> Electrolysis using tris(2,4-dibromophenyl)amine as mediator in a substrate to mediator ratio of about 350:1 in an undivided cell using 1780 g CH<sub>3</sub>OH, 9 g KSO<sub>3</sub>C<sub>6</sub>H<sub>5</sub>, and 9 g NaOCH<sub>3</sub> as electrolyte at a constant current density of 2 A/dm<sup>2</sup>.

<sup>b</sup> Material yield based on consumed **2**.

<sup>c</sup> Current yield.

<sup>d</sup> Number of regenerative cycles based on charge consumption.

The mediator is very stable under these conditions. Even after about 2500 cycles it can be recovered almost totally.

A technical application of the indirect electrochemical method seems to be very promising as it is very simple using an undivided cell, methanol as solvent, and a mediator, which is stable over several thousand cycles.

## EXPERIMENTAL

M.p.s. were determined with a Reichert hot-stage microscope and are uncorrected. I.r. spectra were obtained using a Pye Unicam SP 1100 unit. NMR spectra were measured with Varian EM 360, EM 390, and Bruker WH 90 instruments (solutions in deuteriochloroform, tetramethylsilane as internal standard). Mass spectra were obtained at 70 eV using an AEI MS 50 spectrometer with a data system. G.l.c./MS coupling analyses were performed at 70 eV using a Varian MAT 111 or a Finnigan MAT 1020 B instrument.

Materials

Toluene derivatives were either commercially available or obtained from BASF AG (4-methoxy toluene, 4-*t*-butoxy toluene). Benzaldehyde dimethylacetals were prepared from the corresponding aldehydes by standard procedures(8). Tris(2,4-dibromophenyl)amine was synthesized by direct bromination of triphenylamine(9). The purity was determined by g.l.c. on a OV 101 (1 % on Chromosorb W) column and by cyclic voltammetry. Dichloromethane was purified by distillation while methanol (Merck, p.a.) was used as obtained.  $\text{LiClO}_4$  and  $\text{NaClO}_4$  (Fluka, Buchs) were applied without further purification.

Equipment for Preparative Electrolyses

Preparative electrolyses were performed using a stabilized current source, model NTN 700M-200 (FUG, Rosenheim), modified as potentiostat together with a digital coulometer based on a voltage to frequency converter(10).

Electrochemical Cells

Cell A: Undivided beaker type cell (120 ml) with cooling mantle equipped with a glassy carbon cylinder anode (Sigradur K, Sigri Elektrographit, Meitingen, inner  $\varnothing$  26 mm, height 50 mm), Pt-wire cathode, and Ag/AgCl-reference electrode. Temperature 30°C.

Cell B: Undivided capillary gap cell (ca. 2 l) equipped with 9 or 11 bipolar graphite disc electrodes. Flow of electrolyte maintained by pumping it at a rate of 200 l/h. Temperature 22 - 36°C.

General Procedure for the Indirect Electrolysis of Toluene Derivatives 1 in Methanol Under Neutral Conditions

Using cell A 1 mmol (720 mg) of the mediator tris(2,4-dibromophenyl)amine are dissolved in 100 ml  $\text{CH}_3\text{OH}/\text{CH}_2\text{Cl}_2$  (3:1)/0.15 M  $\text{NaClO}_4$ . The electrolyte was dried over molecular sieve. After application of 1.56 V vs. Ag/AgCl-reference electrode and a short pre-electrolysis of 30 s a current of 10 to 40 mA is obtained. By adding 10 mmol of the toluene derivative 1 the current increases to 150 to 200 mA. When a turnover of 80 to 95 % is obtained (g.l.c. control) the electrolysis is terminated. For work-up half of the solvent is evaporated. After addition of 20 ml water the residue is perforated with pentane, the pentane phase dried over magnesium sulfate and the solvent evaporated. The products are separated and purified by bulb-to-bulb distillation. The products are identified by comparison of their physical and spectral data with literature values.

General Procedure for the Indirect Electrolysis of Benzaldehyde Dimethylacetals (2) in Methanol/Dichloromethane/ Sodium Methoxide

Using cell A 1 mmol (720 mg) of the mediator tris(2,4-dibromophenyl)amine are dissolved in 100 ml methanol/dichloromethane (3:1)/ 0.2 M  $\text{LiClO}_4$  containing 5 mmol of sodium methoxide. The electrolyte is dried over molecular sieve. After application of 1.56 V vs. Ag/AgCl-reference electrode and a short pre-electrolysis of 30 s 10 mmol of the benzaldehyde dimethylacetal (2) are added. Hereby the current increases to about 150 to 200 mA. When a turnover of 90 to 100 % is obtained (g.l.c. control) the electrolysis is terminated. Work-up is performed as described above with the only difference that instead of 20 ml water 20 ml sodium carbonate solution (5 % in water) are added.

General Procedure for the Indirect Electrolysis of Benzaldehyde Dimethylacetals (2) in Methanol/Sodium Methoxide Using 2 as a Cosolvent

Using cell B 12 to 13 mmol (8.9 - 9.2 g) of the mediator tris(2,4-dibromophenyl)amine are dissolved in 1780 g methanol and 4 to 5 mol (870 - 900 g) of substrate 2. Between 8.9 and 9.2 g of  $\text{KSO}_3\text{C}_6\text{H}_5$  and sodium methoxide are added. Electrolysis is performed at a constant current density of 2 or 3.3 A/dm<sup>2</sup>. For work-up methanol is evaporated. The remaining salt is separated by filtration. The products are isolated by distillation of the residue at 5 or 4 mbar.

The exact quantities of the substrates and isolated yields are reported in Tables 1 to 3. Products 2<sup>13</sup>, 3<sup>11,12</sup>, 4<sup>11,12</sup>, and 5<sup>14,15</sup> with the exception of 4 (R = *tert*-butyl and *tert*-butoxy) and 5 (R = bromine, *tert*-butyl, and *tert*-butoxy)

are well known compounds. Their physical and spectroscopic data compared well with literature values. They were also identified by comparison of their g.l.c. retention times with those of authentic samples on two different columns (SE 30, OV 101).

Methyl 4-tert-butylbenzoate (4, R = tert-butyl): MS (80 eV): m/e = 192 (20 %), 177 (100), 161 (9), 149 (15), 145 (5), 118 (7), 117 (7), 115 (7), 105 (11), 91 (13), 77 (9), 65 (4), 41 (20). -  $C_{12}H_{16}O_2$  (192.26) calc. C 74.97, H 8.39; found C 74.85, H 8.43%.

Methyl 4-tert-butoxybenzoate (4, R = tert-butoxy): MS (80 eV): m/e = 208 (1.5 %), 193 (5), 177 (1), 152 (70), 121 (100), 93 (6), 65 (6), 57 (20), 41 (14), 39 (8).  $C_{12}H_{16}O_3$  (208.26) calc. C 69.21, H 7.74; found C 69.18, H 7.78%.

Trimethyl 4-tert-butylorthobenzoate (5, R = tert-butyl):  $^1H$  NMR ( $CCl_4$ , 60 MHz):  $\delta$  = 1.3 (s, 9H), 3.06 (s, 9H), 7.25 (s, 4H) ppm. - MS (80 eV): m/e = 223 (1 %), 207 (100), 177 (10), 149 (8), 105 (10), 96 (6), 91 (4), 82 (6), 59 (7), 57 (7), 41 (6).

Trimethyl 4-tert-butoxyorthobenzoate (5, R = tert-butoxy):  $^1H$  NMR ( $CCl_4$ , 60 MHz):  $\delta$  = 1.3 (s, 9H), 3.04 (s, 9H), 6.7 - 7.45 (AA'BB', 4H) ppm. - MS (80 eV): m/e = 254 (0.7 %), 239 (2.5), 223 (5), 198 (5), 167 (100), 121 (13), 105 (4), 59 (4).

Trimethyl 4-bromoorthobenzoate (5, R = Br):  $^1H$  NMR ( $CCl_4$ , 60 MHz):  $\delta$  = 3.04 (s, 9H), 7.38 (s, 4H). - MS (80 eV): m/e = 231/229 (98/100 %), 216/214 (3/3), 185/183 (40/44), 157/155 (14/15), 150 (6), 105 (14), 91 (27), 76 (19), 75 (18), 59 (37).

Compounds **7**<sup>16</sup> and **8**<sup>11</sup> were identified by comparison of their  $^1H$  NMR spectra with reported ones.

4-Methoxy-1-tetralone (10):  $^1H$  NMR ( $CDCl_3$ , 90 MHz):  $\delta$  = 2.1 - 2.5 (m, 2H), 2.6 - 3.2 (m, 2H), 3.42 (s, 3H), 4.4 - 4.53 (t, 1H), 7.3 - 7.7 (m, 3H), 7.98 - 8.12 (m, 1H) ppm. -  $^{13}C$  NMR ( $CDCl_3$ ):  $\delta$  = 27.9 ( $CH_2$ ), 34.34 ( $CH_2$ ), 56.51 ( $OCH_3$ ), 76.22 (CH), 127.33, 128.30, 128.63, 131.80, 133.51, 142.74 (arom. C), 197.70 (C=O) ppm. - MS (70 eV): m/e = 176 (81 %), 175 (8), 161 (45), 148 (88), 147 (30), 146 (25), 145 (66), 144 (26), 133 (100), 117 (73), 115 (81), 105 (15), 91 (58), 77 (34), 65 (12), 51 (25), 39 (17). -  $C_{11}H_{12}O_2$  requires  $M^+$ , 176.0838; found  $M^+$ , 176.0837.

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