J. Org. Chem. **1985**, *50*, 539-541

1570, 970, 760, 700 cm^{-1}; ^{1}H NMR (CDCl$_3$, 60 MHz) δ 2.36 (s, 3 H, CH$_3$), 6.80–7.60 (m, 11 H), 7.75–8.00 (m, 2 H).

2,6-Dimethyl-8-phenyl-5,7-octadien-4-one (2e) (*E,Z* mixture): IR (neat) 1680, 1580, 1500, 960, 750, 690 cm^{-1}; ^{1}H NMR (CCl$_4$, 60 MHz) δ 0.92 (d, *J* = 6 Hz, 6 H, CH$_3$), 1.87–2.50 (m, 6 H, =C(CH$_3$)—, —CH(Me)$_2$, —CH$_2$—), 5.90, 6.08 (s, 1 H, =CH— (*Z* and *E*)), 6.40–8.50 (m, 7 H, Ph, —CH=CH—). Anal. Calcd for $C_{16}H_{20}O$: C, 84.16; H, 8.82. Found: C, 84.03; H, 8.84.

6-Methyl-2-(4-formylphenyl)-2-hepten-4-one (2f) (*E,Z* mixture): IR (neat) 1700, 1600, 1250, 1170, 700 cm^{-1}; ^{1}H NMR (CCl$_4$, 60 MHz) δ 0.86 (d, *J* = 6 Hz, 6 H, CH$_3$), 1.70–2.50 (m, 3 H, -CH(Me)$_2$, -CH$_2$-), 2.38 (s, 3 H, =C(CH$_3$)—), 6.10 (s, 1 H, =CH—), 7.05–7.55 (m, 4 H, Ph), 9.45 (s, 1 H, CHO); ^{13}C NMR (CDCl$_3$, 22.5 MHz) 18.20; 22.65, 25.19, 53.91, 126.35, 127.11, 129.60, 129.82, 136.43, 151.49, 191.37, 201.01. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.23; H, 7.88. Found: C, 78.25; H, 8.02.

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Electroorganic Synthesis. 4. Facile Synthesis of Aromatic Aldehydes by Direct Anodic Oxidation of Para-Substituted Toluenes[1]

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Highly selective oxidation of ring-substituted toluenes to aromatic aldehydes may be one of the most important reactions in organic synthesis and industrial chemistry because of much usefulness of the latter compounds as key intermediates for production of a variety of fine or speciality chemicals such as pharmaceutical drugs, dyestuffs, pesticides, and perfume compositions.

Although numerous methods using a variety of oxidizing agents such as chromyl chloride,[2] ceric ammonium nitrate,[3] benzeneseleninic anhydride,[4] or peroxydisulfate/copper ion[5] have been reported for transformation of ring-substituted toluenes to aromatic aldehydes, their synthetic utility has been considerably limited owing to low yield, poor selectivity, serious pollution of environment, and troublesome procedure.

In this study, we present highly selective and versatile direct electrooxidation of para-substituted toluenes 1 followed by acid-catalyzed hydrolysis of the resulting product mixture to give the corresponding aromatic aldehydes 2 in good to excellent yields.

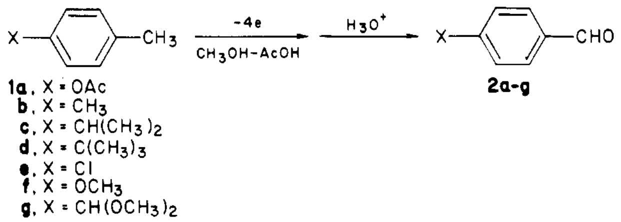


Table I. Anodic Oxidation of *p*-Acetoxytoluene (1a)[a]

run	solvent (volume ratio)	supporting electrolyte	convn, %	yield,[b] % 2a	3a
1	AcOH	Et$_4$NOTs	0	0	0
2	MeOH	Et$_4$NOTs	98	25	12
3	AcOH-MeOH (1:9)	Et$_4$NOTs	90	39	25
4	AcOH-MeOH (1:9)	NaBF$_4$	96	72	1
5	AcOH-MeOH (2:8)	NaBF$_4$	96	59	12
6	AcOH-MeOH (3:7)	NaBF$_4$	96	51	3
7	AcOH-MeOH (1:1)	NaBF$_4$	95	42	6
8	AcOH-MeOH (1:9)	LiClO$_4$	92	70	0
9	AcOH-MeOH (1:9)	NH$_4$BF$_4$	96	68	1
10	AcOH-MeOH (1:9)	NaClO$_4$	87	55	1
11	AcOH-MeOH (1:9)	NEt$_3$	27	2	16
12	AcOH-MeOH (1:9)	NH$_4$OAc	6	1	3

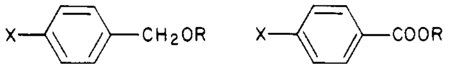
[a] Reaction was carried out in an undivided cell equipped with carbon rods as an anode and a cathode until 8.0 F/mol of electricity was passed through the reaction system. [b] Isolated.

Table II. Anodic Oxidation of Para-Substituted Toluenes 1

1	X	supporting electrolyte	amount of current (F/mol)	isolated yield, % 2	3[a]	4[b]
1a	OAc	NaBF$_4$	8.0	72	1	0
1a	OAc	LiClO$_4$	8.0	70	0	0
1b	CH$_3$	NaBF$_4$	5.6	86	0	0
1b	CH$_3$	Et$_4$NOTs	5.6	82	0	0
1c	CH(CH$_3$)$_2$	NaBF$_4$	6.0	74	0	8
1c	CH(CH$_3$)$_2$	Et$_4$NOTs	6.0	87	0	4
1d	C(CH$_3$)$_3$	NaBF$_4$	7.0	80	0	6
1d	C(CH$_3$)$_3$	Et$_4$NOTs	7.0	89	0	2
1e	Cl	NaBF$_4$	8.0	78	5	0
1e	Cl	Et$_4$NOTs	8.0	46	19	0
1f	OCH$_3$	Et$_4$NOTs	4.0	78	0	2
1f	OCH$_3$	KF	6.0	3	0	80
1g	CH(OCH$_3$)$_2$	NaBF$_4$	8.0	81[c]	3[d]	10[e]
1g	CH(OCH$_3$)$_2$	LiClO$_4$	8.0	74[c]	4[d]	10[e]

[a] Para-substituted benzyl methyl ethers. [b] Methyl para-substituted benzoates. [c] Terephthalaldehyde. [d] 4-Formylbenzyl methyl ether. [e] Methyl 4-formylbenzoate.

Hitherto reported methods for direct anodic oxidation[6,7] of para-substituted toluenes 1 followed by hydrolysis have generally resulted in nonselective formation of three types of products, namely, the corresponding benzaldehydes **2**, benzylic ethers (or benzylic alcohols) **3**, and benzoates (or benzoic acids) **4**.



3 **4**

The yield of the desired aldehydes 2 was substantially influenced by the character of the solvent or the supporting electrolyte employed in the electrochemical oxidation of 1. For example, *p*-acetoxybenzaldehyde (**2a**) was isolated in 70–72% yield as an almost sole product under the optimum conditions where the reaction was carried out in a mixed solvent of methanol and acetic acid (volume ratio 9:1) containing sodium tetrafluoroborate or lithium perchlorate as a supporting electrolyte in an undivided cell equipped with carbon rods as an anode and a cathode, as shown in Table I.

Similar anodic oxidation of some other para-substituted toluenes (**1b–g**) in the same mixed solvent containing an

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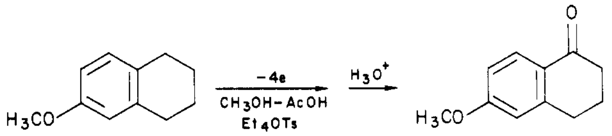
appropriate supporting electrolyte followed by hydrolysis of the resulting product mixture gave the corresponding aromatic aldehydes (**2b–g**) as the main products in good to excellent yields accompanying only a small amount of the corresponding benzyl methyl ethers **3b–g** (R = CH_3) and/or methyl benzoates **4b–g** (R = CH_3), as shown in Table II.

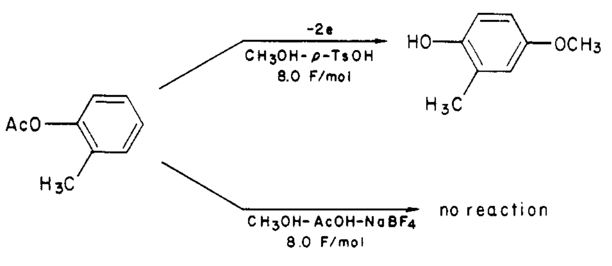
Thus, highly selective and efficient transformation of readily available toluenes **1** to useful aldehydes **2** by the present direct method may be apparently superior to indirect electrochemical oxidation using a poisonous metal's salt such as ceric ammonium nitrate,[8] cupric acetate,[9] sodium dichromate,[10] or manganese sulfate[11] from the viewpoint of nonpollution of environment and simplicity of procedure.

Furthermore, electrooxidation of 6-methoxytetraline (**5**) under similar conditions easily afforded 6-methoxytetralone (**6**), an important intermediate of some pharmaceutical drugs, in a 75% yield.



5 **6**

It may be interesting that anodic oxidation of ortho- and meta-substituted toluenes under similar conditions resulted in almost quantitative recovery of the starting substrate, or formation of the corresponding aromatic aldehydes in fairly poor yields as one minor component of the complex product mixture. Thus, 4-methoxy-2-methylphenol (**8**) was formed in 42% yield from anodic oxidation of acetoxytoluene (**7**) in methanol containing *p*-toluenesulfonic acid as a supporting electrolyte, while the reaction of **7** under the same conditions as employed for the oxidation of the para isomer **1a** led to almost quantitative recovery of **7**. Although details of this remarkable difference are not always clear, noteworthy differences between the oxidation potential of a para isomer of substituted toluenes and that of the corresponding ortho or meta isomer would provide one of the most plausible explanations.[12,13]



At any rate, the present direct electrooxidation of para-substituted toluenes **1** may possess high potentiality for synthesis of aromatic aldehydes **2** as both a laboratory method and an industrial technique in view of good yield, high selectivity, and simplicity of procedure.

Experimental Section

General Procedure for Anodic Oxidation of Para-Substituted Toluenes 1 and 6-Methoxytetraline (5) Followed by Hydrolysis. Into a 100-mL undivided electrolysis cell equipped with a thermometer and carbon rod electrodes was placed 80 mL of a mixed solvent of 9:1 v/v methanol–acetic acid containing 0.05 mol/L of an appropriate supporting electrolyte and 0.02 mol of a para-substituted toluene (**1**) or 6-methoxytetraline (**5**). Stirred with a magnetic bar and cooled with a water bath, the solution was electrochemically oxidized at the constant current of 200 mA (current density: 1.6 A/dm^2). After the amount of electricity described in Table II was passed through the reaction system, the reaction mixture was poured into 100 mL of an aqueous sodium chloride solution and extracted with three 50-mL portions of ether. The combined ethereal solution was evaporated to remove the solvent and then poured into 100 mL of 10% aqueous sulfuric acid. The mixture was stirred for 3 h at room temperature, and extracted with three 50-mL portions of ether. The combined solution was washed with 10% aqueous sodium bicarbonate solution and dried over anhydrous magnesium sulfate. After filtration of the drying agent and evaporation of the solvent, the residual oil was subjected to distillation to give the corresponding aromatic aldehyde **2** as a main product in a good yield. All of the products were isolated by further fractional distillation or by preparative gas chromatography and were identified by comparison of their gas chromatographic and spectroscopic behaviors with those of authentic samples,[14–27] except *p*-acetoxybenzyl methyl ether (**3a**) which was identified by spectroscopic and elemental analyses.

***p*-Acetoxybenzaldehyde (2a)**: bp 115–116 °C (5 mm) [lit.[14] 119–120 °C (6 mm)].

***p*-Acetoxybenzyl methyl ether (3a)**: bp 113–115 °C (5 mm); IR (neat) 1745, 1210, 1190, 1080 cm^{-1}; NMR ($CDCl_3$) δ 2.24 (s, 3 H), 3.28 (s, 3 H), 4.30 (s, 2 H), 6.85 (d, J = 8.0 Hz, 2 H), 7.12 (d, J = 8.0 Hz, 2 H). Anal. ($C_{10}H_{12}O_3$) C, H.

***p*-Tolualdehyde (2b)**: bp 61–62 °C (5 mm) [lit.[15] bp 203–205 °C.

Cuminaldehyde (2c): bp 87–88 °C (5 mm) [lit.[16] bp 103–104 °C (10 mm)].

Methyl cuminate (4c): bp 98–100 °C (5 mm) [lit.[17] bp 126 °C (14 mm)]. ***p*-*tert*-Butylbenzaldehyde (2d)**: bp 97–98 °C (5 mm) [lit.[18] bp 130 °C (25 mm)]. **Methyl *p*-*tert*-butylbenzoate (4d)**: bp 110–112 °C (5 mm) [lit.[19] bp 247 °C]. ***p*-Chlorobenzaldehyde (2e)**: bp 72–73 °C (5 mm) [lit.[20] bp 108–111 °C (25 mm)]. ***p*-Chlorobenzyl methyl ether (3e)**: bp 69–70 °C (5 mm) [lit.[21] bp 49–54 °C (1.7–1.8 mm)]. ***p*-Anisaldehyde (2f)**: bp 111–114 °C (5 mm) [lit.[22] bp 245–248 °C]. **Methyl *p*-anisate (4f)**: bp 126–129 °C (5 mm) [lit.[23] mp 49–49.5 °C]. **Terephthalaldehyde (2g)**: mp 115–116 °C [lit.[24] mp 116 °C]. ***p*-Formylbenzyl methyl ether (3g)**: bp 98–100 °C (5 mm) [lit.[25] bp 125 °C (16 mm)]. **Methyl *p*-formylbenzoate (4g)**: mp 62–63 °C [lit.[26] mp 63 °C]. **6-Methoxy-1-tetralone (5)**: mp 81–82 °C [lit.[27] mp 81 °C].

Anodic Oxidation of *o*-Acetoxytoluene (7). With the same type of electrolysis cell as described for anodic oxidation of para-substituted toluenes, a solution of 0.02 mol of *o*-acetoxytoluene (**7**) and 0.50 g of *p*-toluenesulfonic acid dissolved in 80 mL of methanol was electrolyzed at the constant current of 200

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mA (current density: 1.6 A/dm^2). After 8.0 F/mol of electricity was passed, the reaction mixture was poured into 100 mL of a saturated sodium chloride solution and extracted with three 50-mL portions of ether. The combined ethereal solution was dried over anhydrous magnesium sulfate, filtered, and concentrated to give an oily material, which was then fractionally distilled to form almost pure 2-methyl-4-methoxyphenol (8) in 42% yield; mp 71–72 °C [lit.[28] mp 71–72 °C].

Registry No. **1a**, 140-39-6; **1b**, 106-42-3; **1c**, 99-87-6; **1d**, 98-51-1; **1e**, 106-43-4; **1f**, 104-93-8; **1g**, 3395-83-3; **2a**, 878-00-2; **2b**, 104-87-0; **2c**, 122-03-2; **2d**, 939-97-9; **2e**, 104-88-1; **2f**, 123-11-5; **2g**, 623-27-8; **3a**, 38177-36-5; **3e**, 1195-44-4; **3g**, 93943-06-7; **4c**, 20185-55-1; **4d**, 26537-19-9; **4f**, 121-98-2; **4g**, 1571-08-0; **5**, 1730-48-9; **6**, 1078-19-9; **7**, 533-18-6; **8**, 5307-05-1.

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Electrochemical Oxidative Dehydrodimerization of Naphthylamines. An Efficient Synthesis of 8,8′-Dianilino-5,5′-binaphthalene-1,1′-disulfonate

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Fluorescent probes have been widely applied in the investigation of the structure and behavior of proteins. One probe that has found extensive use is 8-anilino-1-naphthalenesulfonate (1).[1] A related probe, 8,8′-dianilino-5,5′-binaphthalene-1,1′-disulfonate (2), is potentially more useful than 1 because it binds more tightly to proteins[2] and has a larger fluorescence quantum yield.[3] However, the current syntheses of 2,[3-5] by dehydrodimerization of 1 using sodium nitrite, are small-scale, low yield reactions involving tedious purifications.[6]

A number of methods for the synthesis of biaryls have been reported.[7] Many of these, such as the Gomberg reaction[8] and the Ullman reaction,[9] have the disadvantage that the aryl group must have a substituent that is lost during the coupling process. Biaryls can also be prepared by oxidative dehydrodimerization with various metal salts.[7] For example, thallium trifluoroacetate has recently been shown to be an excellent reagent for such transformations of electron-rich aromatic substrates.[7] In addition, electrochemical oxidation of electron-rich aromatic substrates often results in the formation of biaryls.[10] However, the potential of this method has not been extensively developed.

Chart I

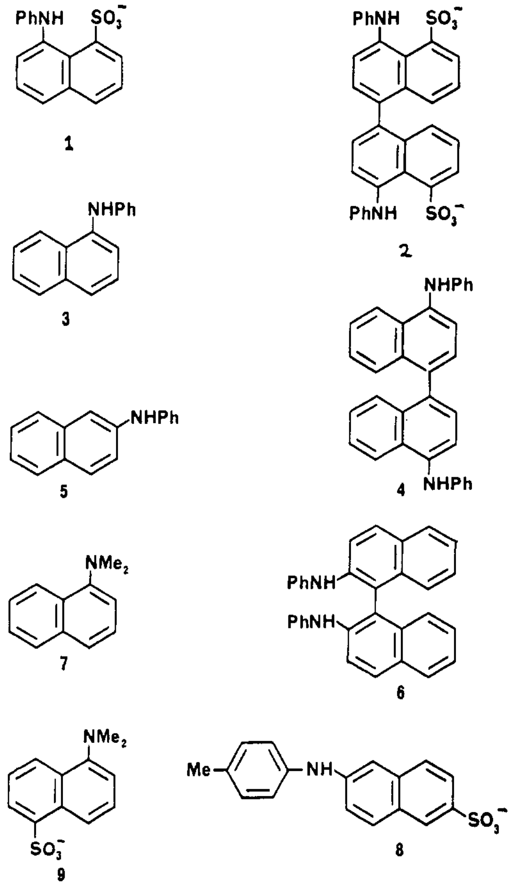

Table I. Yields and Conversions for Various Oxidants Used for the Conversion of 1 to 2

oxidant	yield of 2,[a] %	convn of 1,[b] %
$K_2Cr_2O_7$	1	81
CrO_3	4	46
CoF_3	11	73
$Pb(OAc)_4$	14	69
$NaNO_2$	18	98
$KMnO_4$	20	20
$Tl(C_2F_3O_2)_2$	31	88
anode	50 (30)[c]	92

[a] Yields are calculated on the basis of reacted 1. [b] Amount of 1 that has reacted. [c] Isolated yield.

We report here a convenient synthesis of 2 by electrochemical oxidation of 1, a comparison of the electrochemical reaction with reactions employing some selected chemical oxidants, and a brief investigation of the scope of the electrochemical reaction with some other naphthylamines.

A solution of 1 in aqueous sodium perchlorate was electrolyzed by using a carbon cloth anode and a copper cathode. Analysis by HPLC showed the formation of a single product. After most of the starting material had reacted, the product was isolated in 30% yield by column

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