radicals. For compound **19**, a mechanistic proposal[6] favors the presence of a dimeric intermediate via C–C bond formation at the side chain in the initial stage.

In Table I are summarized the maximum yield of each compound obtained and the reaction time, and Table II shows the spectral data of the new compounds.

Experimental Section

Apparatus. A Promax generator with a maximum output of 60 V and 2 A was used. GLC analyses were performed on a HP-5890 instrument (OV-101, 25 m × 0.22 mm column) equipped with a flame-ionization detector with N_2 as the carrier gas. Melting points were measured on a Reichert Thermovar hot-stage microscope. IR spectra were obtained on a PYE UNICAM spectrophotometer using films on NaCl crystals. ^1H NMR spectra were recorded on a Varian EM360L (60 MHz) spectrometer; data were obtained from solutions in $CDCl_3$. Chemical shifts are reported as δ values relative to tetramethylsilane as internal reference. Mass spectra were recorded on a HP-5988A GLC/MS instrument at 70 eV (EI).

General Procedure. Electrolyses were carried out in cylindrical, water-refrigerated cells without separate compartments. The temperature was controlled at 30 °C, and stirring was magnetic. A carbon-paste plate was used as the anode and a stainless-steel plate as the cathode. Reactions were carried out under constant current at an anodic current density of 57 mA cm^{-2}. The solvent was always dry methanol (70 mL), and the electrolyte was, in the electrolyses of anethole and estragole sodium methoxide (0.2 g) and in the electrolyses of safrole, isosafrole, eugenol, and isoeugenol, a mixture of sodium methoxide and sodium perchlorate (0.05 g + 0.15 g). Estragole, anethole (3.3×10^{-3} mol), safrole, isosafrole (3×10^{-3} mol), eugenol, or isoeugenol (3.1×10^{-3} mol) was then added.

At the end of each electrolysis the solution was worked up by evaporation of the solvent to dryness under reduced pressure. The brown extract was suspended in 100 mL of water and extracted with ethylic ether (3 × 30 mL). The combined organics were dried with anhydrous Na_2SO_4, and the ether was evaporated at reduced pressure.

Products were isolated by flash chromatography (Merck, SiO_2 60, 9385) using ethyl acetate–hexane (2:98 v/v) as eluent for the extracts from the electrolyses of anethole, estragole, safrole, and isosafrole, and ethyl acetate–hexane (5:95 v/v) for the extracts from eugenol and isoeugenol. Yields were calculated from gas chromatography using cyclohexanone as the internal standard.

Stereoselective Obtention of *trans*-3,6-Dimethoxy-1,3,6-trimethylcyclohexa-1,4-diene by Anodic Methoxylation of Pseudocumene

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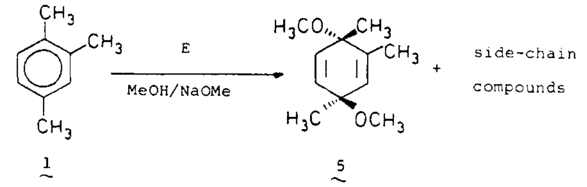
Anodic oxidation of a methanolic solution of pseudocumene (1) in a single-cell apparatus at constant current using sodium methoxide as the supporting electrolyte afforded *trans*-3,6-dimethoxy-1,3,6-trimethylcyclohexa-1,4-diene (5). This is the first time that 1,4-addition stereoselectivity has been observed in the anodic oxidation of alkylbenzenes. A rationale is provided.

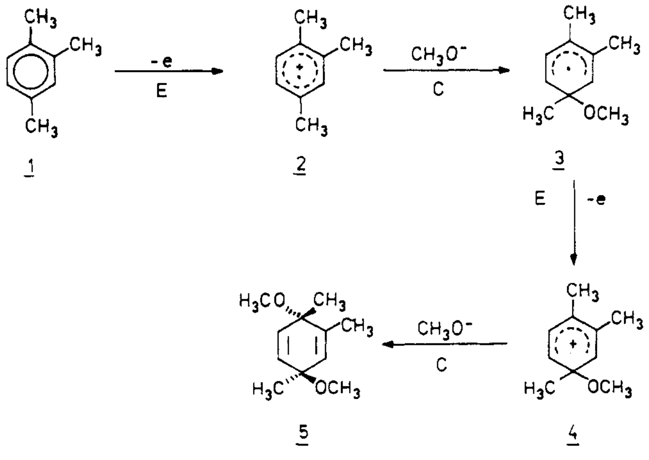
The anodic oxidation of alkylbenzenes in methanol usually gives side chain methoxylated products as well as nuclear-addition products.[1-5]

We have recently studied[1-5] the electrooxidative methoxylation of a series of alkylbenzenes and have found that nuclear-addition products are obtained from unactivated substrates which do not stabilize the cation radical (**2**) electrogenerated (Scheme I). In the substrates previously studied a mixture of the two possible cis, trans isomers was obtained.

Unexpectedly, the anodic methoxylation of pseudocumene (1,2,4-trimethylbenzene) (**1**) afforded only the trans isomer **5**. The structure was assigned by using ^1H NMR data and was supported by chemical mass spectrometry.



Scheme I



Results and Discussion

The anodic oxidation of pseudocumene (**1**) in methanol–sodium methoxide was carried out under constant current intensity. *trans*-3,6-Dimethoxy-1,3,6-trimethylcyclohexa-1,4-diene (**5**) was isolated as the major product (30%), while 4-(dimethoxymethyl)-1,2-dimethylbenzene (7%), 1-(dimethoxymethyl)-2,4-dimethylbenzene (14%), 1,2-dimethyl-4-(trimethoxymethyl)benzene (5%), and 2,4-dimethyl-1-(trimethoxymethyl)benzene (8%) were isolated as side products in a parallel process of side-chain

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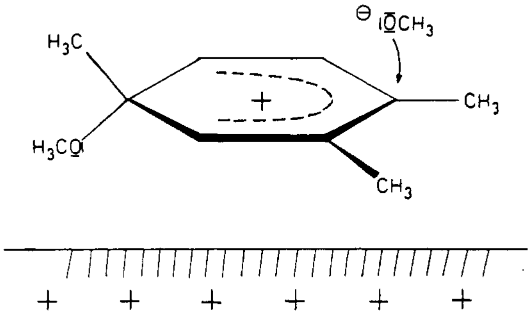

Figure 1.

substitution. Polymethoxylated products were detected in the crude reaction mixture.

Comparable results were obtained using vitreous carbon, platinum, or graphite electrodes, as expected.[6]

Comparison of the spectral data of **5** (Scheme I) with those of the *trans*-3,6-dimethoxy-3,6-dimethylcyclohexa-1,4-diene, in particular ^1H NMR data, allowed the stereochemical assignment to be made.[4]

In a recent work,[7] CI mass spectrometry was used to distinguish between stereoisomeric in cyclohexa-1,4-diene derivatives. In general, the trans isomers displayed $[M + H]^+$ and $[M + NH_4]^+$ peaks in the CH_4 and NH_3 CI spectra less intense than the cis isomers.[8-11] The CI spectrum for **5** displayed peaks of 1% and 3% of abundance for the CH_4 and NH_3 spectra, respectively. The results found for similar compounds (*cis*- and *trans*-3,6-dimethoxy-1,2,6-trimethylcyclohexa-1,4-diene),[7] supported the stereochemical assignment for compound **5**.

When anodic methoxylation is carried out in CH_3OH/NaOMe at a potential at which both discharge of CH_3O^- and oxidation of **1** may occur simultaneously, two mechanisms appear reasonable: the classical ECEC sequence[12,13] (cation-radical–methoxide-anion reaction) and a more recent proposal[14,15] involving methoxy-radical attack on the aryl radical cation, an EEC_rC_p process.

For pseudocumene (**1**) the ECEC sequence explains formation of **5** (Scheme I). The regiochemistry of the nucleophilic attack (**2** → **3**) is in accord with theoretical studies.[16] Oxidation of **3** gives a cation (**4**) that is again attacked by CH_3O^- to yield the product **5**. In Figure 1, the cation **4** is adsorbed with a face parallel to the anode surface via the same type of bond as in a π-donor–acceptor complex. This type of bonding and orientation is well documented from adsorption studies on aromatic hydrocarbons.[17,18] The electronegative OCH_3 group is oriented toward the positively charged electrode surface. In this way, the electrode surface blocks attack of the nucleophile and the trans isomer **5** is obtained. In the EEC_rC_p sequence, on the other hand, the formation of the cation **4** occurs in a chemical step (C_r) and the electrode surface cannot influence the isomer distribution.

Experimental Section

Nuclear magnetic resonance spectra were recorded at 60 MHz, the chemical shifts (δ values) are given in parts per million relative to TMS as an internal standard in $CDCl_3$ solutions, and coupling constants are reported in hertz. IR spectra are reported in cm^{-1}. Mass spectra were obtained at 70 eV (EI) and 230 eV for CI (CH_4 and NH_3 as reagent gases). GC analysis utilized a fused silica capillary column (25 m × 0.2 nm) and a flame ionization detector.

Electrolysis Procedure. Electrolysis of a solution of pseudocumene (**1**) (10 mmol) in a solvent/supporting electrolyte system prepared by adding metallic sodium (0.2 g) to dry methanol (70 mL) was carried out in a single-compartment cell using a carbon-paste plate anode and a stainless-steel plate cathode. The temperature was maintained at 10–15 °C using a cryostat, and the solution was magnetically stirred. The anodic current density was 50 mA/cm^2, and the electron consumption was 13 F/mol. The reaction was monitored by GC and judged to be completed after 3 h.

When the electrolysis was interrupted the reaction mixture was evaporated to dryness under reduced pressure, 100 mL of a buffer solution KH_2PO_4/Na_2HPO_4 (0.025 M, pH≈7) was then added, and the suspension was extracted with ether. The extracts were dried (anhydrous Na_2SO_4) and then evaporated to dryness under reduced pressure, and the products were separated by flash chromatography using *n*-hexane–ethyl acetate (97:3) as eluent. Compound **5** was isolated in 30% yield.

Both GC and GC/MS analysis of the reaction mixture assured that material was not lost during the workup.

When an amorphous graphite plate anode was used, maintaining the temperature at 10–15 °C, an anodic current density of 50 mA/Cm^2, and an electron consumption of 13 F/mol, the yield of **5** was 10%; when the temperature was maintained at 30 °C, with a carbon-paste plate anode, a current density of 50 mA/cm^2, and 13 F/mol of electron consumption, the compound **5** was obtained in a 21% yield; with an anodic current density of 50 mA/cm^2, 21 F/mol of electron consumption, maintaining the temperature at 10–15 °C, and using a carbon-paste plate anode, the yield of **5** was 25%; using an anodic current density of 75 mA/cm^2, an electron consumption of 26 F/mol, a carbon-paste plate anode, and maintaining the temperature at 10–15 °C, a 28% yield of **5** was obtained.

The spectral data for ***trans*-3,6-dimethoxy-1,3,6-trimethylcyclohexa-1,4-diene** (**5**): ^1H NMR δ 1.3 (3 H, s), 1.35 (3 H, s), 1.78 (3 H, d, J = 1.5 Hz), 2.93 (3 H, s), 3.0 (3 H, s), 5.47 (1 H, m), 5.66 (2 H, AB); IR (film) 3020, 2820, 1440, 1125, 1100, 1080, 1060, 875 and 680; MS (EI) *m/e* (rel intensity) 167 ($M^+ - 15$, 100), 151 (61), 136 (66), 121 (18), 119 (14), 105 (30), 91 (31), 77 (27); MS (CH_4-CI) *m/e* (rel intensity) 183 ($M^+ + 1$, 1), 167 (4), 151 (100), 121 (3), 119 (4); MS (NH_3-CI) *m/e* (rel intensity) 200 $M^+ + 18$, 3), 168 (21), 167 (3), 152 (11), 151 (100), 136 (12).

A satisfactory combustion analysis (±0.4% C and H) was obtained.

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