Anodic Oxidation of Xylenes. Electrochemical Obtention of Cyclohexa-1,4-diene Derivatives

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cis- and *trans*-3,6-dimethoxy-3,6-dimethylcyclohexa-1,4-dienes obtained by methoxylation of *p*-xylene were completely separated. The unequivocal structure of the trans isomer was assigned by X-ray diffraction, and the cis:trans ratio is satisfactorily explained by an EEC_rC_p mechanism. When the substrates were *p*- and *o*-xylene, the nuclear-addition products were obtained in a two-electron process, but when the substrate was *m*-xylene, the major nuclear-addition product was obtained in a four-electron process.

In previous publications,[1,2] we described the anodic oxidation in methanol of *o*- and *p*-xylene. Both nuclear-addition products and side-chain-substitution products were isolated. It has been proved previously that cyclohexa-1,4-dienes can be obtained in good yields from anodic oxidation of some other easily oxidizable substrates, such as methoxybenzenes.[3-7] In the anodic oxidation of alkylbenzenes in methanol, however, an analogous nuclear-addition process yielding the corresponding cyclohexa-1,4-diene products has not been detected previously.

In our previous work with *p*-xylene as substrate, the nuclear-addition products found were *cis*- and *trans*-3,6-dimethoxy-3,6-dimethylcyclohexa-1,4-dienes. These isomers were isolated together by extraction, simple distillation, and crystallization, and the ^1H NMR spectrum showed the presence of both isomers in a 3:1 ratio. The formation of these nuclear-addition products was rationalized by the classical ECEC sequence.

Since no separation of both isomers was achieved, ^1H NMR signals were not assigned; thus the ratio between isomers and the mechanistic scheme was not clarified. We now report the separation of cis and trans isomers, the X-ray data of the trans isomer, and the subsequent assignment of ^1H NMR signals. We also give a different proposal for the mechanism sequence of the reaction. Furthermore, we describe two different processes (two-electron vs four-electron oxidation products) when the substrate is *p*- or *o*-xylene and when it is *m*-xylene.

Results and Discussion

The isomer mixture was separated from a large-scale electrolysis in a cylindrical cell by extraction, fractional distillation at reduced pressure, and multiple recrystallization. NMR spectroscopy was used to determine the degree of separation achieved between both isomers.

A crystal of the isomer with preferential crystallization was used for collecting the X-ray diffraction data. The crystal was sealed in a Lindeman capillary under N_2, and it was used to determine the cell parameters on an Enraf-Nonius CAD-4 four-circle diffractometer. Lattice parameters were refined by least-squares fit of 43 reflections with $7° < \theta < 38°$.

Cell parameters: $a = 6.595$ (1) Å, $b = 7.450$ (3) Å, $c = 6.599$ (1) Å, $\alpha = 106.85$ (3)°, $\beta = 119.14$ (2)°, $\gamma = 99.45$ (2)°, $V = 252.3$ (2) Å^3, $M_r = 168.235$, $F(000) = 92$, $Z = 1$, $P\bar{1}$, $\mu = 0.704$ cm^{-1}, $D_{calcd} = 1.107$ g/cm^3, $\lambda = 0.7107$ Å.

Intensity data were collected from the same crystal on the same diffractometer with graphite-monochromated Mo K_α radiation for $2° < \theta < 30°$, ($-9 < h < 9$, $-9 < k < 9$, $0 < l < 10$), and ω-2θ scan mode. Two standard reflections were used and remeasured after every 100 reflections. No decomposition was observed. Out of the 1456 independent reflections measured, 1010 were considered as observed with $I > 2\sigma$ (I). Lorentz and polarization corrections were applied.

An attempt to resolve the structure in the $P\bar{1}$ space group by MULTAN80[8] gave no result; therefore, the $P\bar{1}$ group was adopted and the structure was resolved and refined by full-matrix least-squares methods using XRAY76[9] programs. The H atoms were located from a difference Fourier map, and geometric considerations are not refined.

At that point a molecular inversion center was checked and the atomic parameters were referred to the (000) inversion center. A new refinement on $P\bar{1}$ produced better standards on the dimensions, and consequently, the $P\bar{1}$ space group was definitively adopted.

Final $R = 0.076$ and $R_w = [\Sigma o(|F_o| - |F_c|)^2]^{1/2} = 0.069$ with $w = 1$ as an empirical weighting scheme[10] give no trends in $\langle w\Delta^2F \rangle$. Final $(\Delta/\sigma)_{max} = 0.02$ and $\Delta\rho_{max} = 0.11$ e Å^{-3}. The calculations were carried out on a VAX 11/750 computer. Scattering factors and anomalous dispersion coefficients were taken from *International Tables for X-ray Crystallography*.[11]

The positional parameters of the non-H atoms are given in Table I (supplementary material), and Table II (supplementary material) lists the bond lengths, bond angles, and torsion angles involving non-H atoms. Figure 1 shows the a molecular view.

The two symmetric bonds C2–C3 and C2′–C3′ show double-bond character consistent with the planarity of the hexane ring. The two radicals on C1 and C1′ are in trans position, and they are virtually situated on a plane per-

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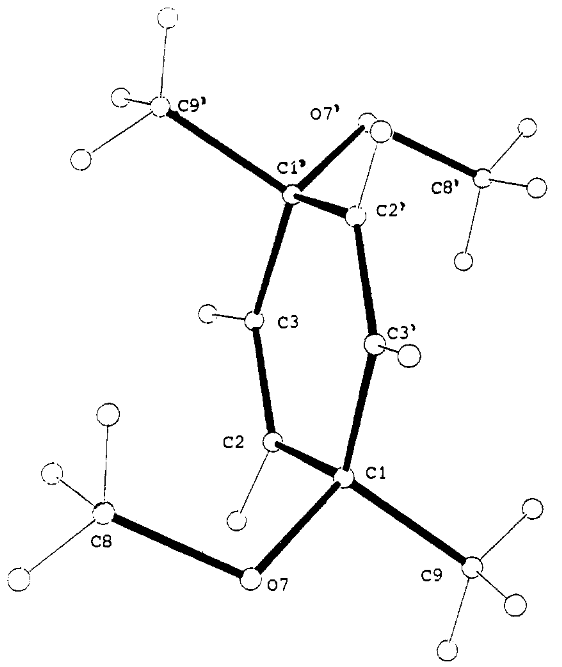

Figure 1. Perspective drawing of the trans isomer.

pendicular to the hexagonal ring. None of the intermolecular distances is less than a normal van der Waals contact.

The compound to which the trans structure was assigned gave peaks at δ 1.22 (CH_3), 2.90 (OCH_3), and 5.58 (vinyl H). The compound to which the cis structure was assigned gave peaks at δ 1.15 (CH_3), 3.03 (OCH_3), and 5.65 (vinyl H). In both cases the relative areas were 3:3:2.

A quantitative study on the isomer ratio was effected by reactions at small scale under different conditions. ^1H NMR spectroscopy and specifically the peaks of vinyl protons were used to control these experiments (there are not any other peaks in this region of the spectrum). There was no noticeable difference in the isomer ratio under the different electrolytic conditions. The cis:trans ratio in all cases was about 5:6. The difference with our earlier work is that the isomer ratio was obtained from the ^1H NMR signals of the isolated crystalline solid. As the trans isomer shows a preferential crystallization, the trans:cis ratio was higher than the real. In this work the isomer ratio was obtained at the end of the electrolyses, directly from the crude extracts.

Since the isomer ratio was almost the same, the mechanism previously described did not account for the results satisfactorily. We have reexamined the mechanistic studies on similar compounds,[3,13] and between the different possibilities we have chosen the Swenton proposal.[13] The preferred mechanism to form nuclear-addition products is named an EEC_rC_p process and involves reaction of anodically generated methoxy radical with the aromatic radical cation. In this case, the formation of the cation occurs in a chemical step (C_r), and the electrode surface does not influence the formation of a determined isomer.

Together with these nuclear-addition products, the expected side-chain-methoxylated products, previously reported,[1] as well as some other products with a higher degree of side-chain substitution, α,α,α'-trimethoxy-*p*-xylene (1%), $\alpha,\alpha,\alpha',\alpha'$-tetramethoxy-*p*-xylene (0.4%), and α,α,α-trimethoxy-*p*-xylene (1.5%), were observed. The acidic hydrolysis of these products leads to the corresponding aldehydes and the methyl ester.

Two- vs Four-Electron Products of Xylenes

When the substrates were *p*- and *o*-xylene, the products of nuclear addition were the corresponding 3,6-dimethoxycyclohexa-1,4-dienes,[1,2] in a two-electron process. But when the substrate was *m*-xylene, the major product was 3,6,6-trimethoxy-1,3-dimethylcyclohexa-1,4-diene (24%) (**1**) in a different process, four electrons in this case. This nuclear-trimethoxylated product was isolated by chromatography on a carbon–Celite column[14] (ether as solvent). Spectroscopic data [^1H NMR, MS (EI), and IR] were clearly consistent with the proposed structure.

The nuclear-dimethoxylated products (two-electron process) *cis*- and *trans*-3,6-dimethoxy-1,3-dimethylcyclohexa-1,4-diene (**2** and **3**) are also formed, but the yields were low (5%). The formation of these last products can be explained by the same sequence previously described for *p*-xylene, but these products are not very stable and would decompose to 2,4-dimethylanisole. There is another path to account for the formation of this product, which consists of a nuclear methoxylation of the substrate. The methoxylation on the C4 is in agreement with the fact that the highest positive charge density is found at C4 in the *m*-xylene cation radical.[12] In the 2,4-dimethylanisole, the aromatic nucleus is activated by the methoxy group and rapidly leads to the nuclear-trimethoxylated product **1**, through a new methoxylation process.

These cyclohexa-1,4-diene derivatives **1**–**3** have not been detected previously. Furthermore, the formation of three side-chain-methoxylated products, α-methoxy-*m*-xylene (11%), α,α-dimethoxy-*m*-xylene (3%), and trimethyl 3-methylorthobenzoate (1%), was observed. These products were identified by gas chromatography–mass spectrometry. The identity of α,α-dimethoxy-*m*-xylene and trimethyl 3-methylorthobenzoate was confirmed through acidic hydrolysis, which gave 3-methylbenzaldehyde and methyl 3-methylbenzoate, respectively.

Experimental Section

Melting points were measured with a Reichert Thermovar micro melting point apparatus and are uncorrected. IR spectra were recorded with a Pye Unicam SP3-200 spectrophotometer. Nuclear magnetic resonance spectra were recorded on a Varian EM-360L (60 MHz) spectrophotometer, in deuteriochloroform and carbon tetrachloride; peak positions are reported in parts per million from tetramethylsilane as an internal standard. Mass spectra were obtained from a Hewlett-Packard 5988A spectrometer. GC analyses were performed on a Hewlett-Packard 5890 gas chromatograph with a FID detector. An Arrosu generator with a maximum output of 100 V and 25 A was used in the electrolyses at large scale, and a Promax generator with a maximum output of 60 V and 2 A, in the electrolyses at small scale. A Perkin-Elmer 240 microanalyzer was used.

Electrolysis Procedures. The small-scale electrolyses were carried out in 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 platinum plate as the cathode. Electrolyses were carried out under constant current intensity at an anodic current density of 63 mA/cm^2, the electron consumption being 9 F mol^{-1}. The solvent-supporting electrolyte system was formed by adding metallic sodium (0.2 g) to dry methanol (70 mL). The corresponding xylene (10^{-2} mol) was then added.

The large-scale electrolyses were carried out in a cylindrical cell with a carbon-paste anode and a stainless steel cathode, without separate compartments. The solvent-supporting elec-

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Table III. X-ray Diffraction: Experimental Data and Structure Refinement Procedures

Crystal Data	
formula	$C_{10}H_{16}O_2$
crystal habit	prismatic
crystal size (mm)	0.2 × 0.3 × 0.4
symmetry	triclinic, $P\bar{1}$
unit cell determination	least-squares fit from 56 reflections ($\theta < 38°$)
unit cell dimensions	6.595 (1) Å, 7.450 (3) Å, 6.599 (1) Å, 106.85 (3)°, 119.14 (2)°, 99.45 (2)°
packing: V (Å^3), Z	252.3 (2), 1
D_{calcd} (g cm^{-3}), M_r, $F(000)$	1.107, 168.235, 92
μ(Mo Kα) (cm^{-1})	0.704
Experimental Data	
technique	four-circle diffractometer, Enraf-Nonius CAD-4; bisecting geometry; graphite-oriented monochromator, Mo Kα ω–2θ scans; detector apertures 1 × 1, up θ_{max} 30°; 1.5 min/reflection
number of reflections	
measured	1550
independent	1456
observed	1010 [$I > 2\sigma(I)$ criterion] $-9 < h < 9$, $-9 < k < 9$, $0 < l < 10$, $(\sin\theta/\lambda)_{max} = 0.60$
value of R_{int}	0.010
Solution and Refinement	
solution	direct methods
refinement	least squares on F_{obsd} with 1 block
parameters	
no. of variables	108
degrees of freedom	902
ratio of freedom	9.4
H atoms	difference synthesis and geometric considerations; nonrefined
final shift/error	0.02
final F peaks	0.11 e Å^{-3}
final R and R_w	0.076, 0.069
computer and programs	VAX 11/750, MULTAN80,[8] XRAY76[9]
scattering factors	*International Tables for X-ray Crystallography*[11]

trolyte system was formed by adding metallic sodium (2 g) to dry methanol (3 L); *p*-xylene (1.88 mol) was then added. The solution was passed through the cell cavity during the electrolyses at a flow rate of 2.5 L min^{-1}. The temperature was maintained at 35 °C by external cooling. The anodic current density was 43 mA/cm^2. When 14.3 F mol^{-1} had been consumed, the electrolysis was interrupted.

Extraction and Characterization of the Products. At the end of each electrolysis, the solution was worked up by evaporation of the solvent to dryness under reduced pressure, addition of water, and multiple extraction with ether. The combined extracts were dried (anhydrous Na_2SO_4), and then the ether was evaporated at reduced pressure.

The large-scale electrolysis (*p*-xylene as substrate) was distilled through a Vigreux column of 24 cm with a Büchi 165 vacuum controller, the isomer mixture having distilled at 27 °C (1.5 mmHg). This mixture (24%) was crystallized from *n*-hexane at −20 °C to afford large colorless crystals, their melting point being 64 °C; when this mixture was in the liquid state, it vaporized rapidly. Multiple recrystallizations of this mixture were carried out in *n*-hexane at 5 °C, and the degree of separation achieved was determined by ^{1}H NMR spectroscopy. The isomers were completely separated and the melting points in both cases were 65 °C, slightly higher than the melting point of the mixture. IR (KBr) (trans isomer): 3040, 2960, 2840, 1450, 1410, 1370, 1150, 1100, 1070, 940, 875, 680 cm^{-1}. IR (cis isomer): the intensity of the bands is lower than in the trans isomer, and all the bands are coincident, except the 1130-cm^{-1} band instead the 1150-cm^{-1} band; furthermore, in this isomer there is a band at 655 cm^{-1}. ^{1}H NMR ($CDCl_3$, 60 MHz) (trans isomer): δ 1.22 (s, 3 H), 2.90 (s, 3 H), 5.58 (s, 4 H). ^{1}H NMR (cis isomer): δ 1.15 (s, 3 H), 3.03 (s, 3 H), 5.65 (s, 4 H). Mass spectrum (EI, 70 eV): no differences between both isomers are observed.

The other products of the reaction were chromatographed on a silica gel column (Merck 60), 0.040–0.063 mm, using *n*-hexane/ethyl acetate (98:2) as eluent. The following side-chain products, previously obtained,[1] were identified: [α-methoxy-*p*-xylene (22%), α,α-dimethoxy-*p*-xylene (33%), and α,α'-dimethoxy-*p*-xylene (4%)], and besides, α,α,α'-trimethoxy-*p*-xylene (1%), $\alpha,\alpha,\alpha',\alpha'$-tetramethoxy-*p*-xylene (0.4%), and trimethyl 4-methylorthobenzoate (1.5%). α,α,α'-Trimethoxy-*p*-xylene: mass spectrum (EI, 70 eV), m/z (relative intensity) 196 M$^+$ (3), 166 (11), 165 (100), 134 (13), 119 (9), 105 (10), 91 (23), 77 (10), 75 (8), 65 (7). $\alpha,\alpha,\alpha',\alpha'$-Tetramethoxy-*p*-xylene: mass spectrum, m/z (relative intensity) 226 M$^+$ (5), 196 (12), 195 (100), 177 (9), 149 (24), 121 (44), 105 (10), 91 (7), 77 (8), 75 (11). Trimethyl 4-methylorthobenzoate: mass spectrum, m/z (relative intensity) 196 M$^+$ (2), 166 (11), 165 (100), 150 (3), 119 (33), 105 (9), 91 (20), 65 (8), 59 (4). By acid electrolysis of the acetals and the ortho ester, the corresponding aldehydes and ester were obtained quantitatively, which were identified through gas chromatography and mass spectrometry, by using pattern samples.

In the small-scale electrolyses with *m*-xylene as substrate, addition of water in the extraction process was changed for addition of a buffer solution, KH_2PO_4/Na_2HPO_4 (0.025 M). The electrolysis extracts were analyzed by a gas chromatography–mass spectrometry system, using a HP-1 column (12 m), and showed the presence of α-methoxy-*m*-xylene, α,α-dimethoxy-*m*-xylene, and trimethyl 3-methylorthobenzoate as the side-chain-methoxylated products. Nuclear-addition products were also detected (single peak for a mixture of isomers). The following mass spectral peaks (EI, 70 eV) were observed. α-Methoxy-*m*-xylene: mass spectrum, m/z (relative intensity) 136 M$^+$ (90), 135 (51), 121 (94), 106 (26), 105 (100), 104 (39), 103 (16), 91 (44), 77 (26), 65 (10). α,α-Dimethoxy-*m*-xylene: mass spectrum, m/z (relative intensity) 166 M$^+$ (6), 136 (10), 135 (100), 119 (13), 105 (5), 91 (22), 75 (8), 65 (5), 40 (9). Trimethyl 3-methylorthobenzoate: mass spectrum, m/z (relative intensity) 196 M$^+$ (8), 166 (12), 165 (100), 150 (18), 149 (30), 135 (10), 122 (10), 105 (5), 91 (13), 77 (12). The peak corresponding to the nuclear-addition products and **2** and **3** showed the following mass spectral data: m/z (relative intensity) 168 M$^+$ (2), 153 (79), 138 (34), 137 (81), 123 (21), 122 (100), 121 (31), 107 (47), 105 (20), 93 (20), 91 (52), 79 (24), 77 (56). The isolation of the nuclear-addition product **1** gave a colorless oil, the ^{1}H NMR ($CDCl_3$, 60 MHz) of which showed the following signals: δ 6.1 (dd, 1 H, J = 10 Hz, J = 3 Hz), 5.8 (d, 1 H, J = 10 Hz), 5.7 (m, 1 H), 3.2 (s, 3 H), 3.1 (s, 3 H), 3.0 (s, 3 H), 1.8 (d, 3 H, J = 0.4 Hz), 1.3 (s, 3 H). Mass spectrum (EI, 70 eV): m/z (relative intensity) 198 M$^+$ (4), 183 (25), 167 (100), 152 (65), 151 (53), 136 (29), 121 (25), 91 (29), 79 (10), 65 (11). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.61; H, 9.17.

X-ray Diffraction. See Table III for experimental data and structure refinement procedures.

Supplementary Material Available: Coordinates and thermal parameters of the non-H atoms for the trans isomer (Table I) and bond lengths, bond angles, and torsion angles involving non-H atoms for the trans isomer (Table II) (1 page). Ordering information is given on any current masthead page.