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Electrosynthesis of Medium- and Large-sized Rings. Part II.* Mechanism of the Anodic Cyclization of Bis(3,4-dimethoxyphenyl)alkanes and -alkenes

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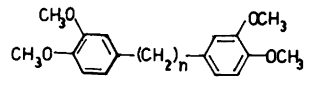
The anodic oxidation of 1,*n*-bis(3,4-dimethoxyphenyl)alkanes with n=6, 8, 10, 11 or 12 and of 1,6-bis(3,4-dimethoxyphenyl)trans-3-hexene in acetonitrile has been studied. In all cases a moderate yield of cyclic dimer was obtained. When n=11 or 12 intramolecular cyclization also occurred. HPLC-analysis at intervals during electrolysis revealed that the cyclic dimer is formed in a consecutive reaction sequence, with an open chain dimer as a stable and isolable intermediate.

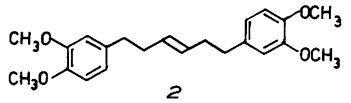
The anodic oxidation of the bis(3,4-dimethoxyphenyl)alkanes, 1-*n* (n=1, 2, 3, 4, 5, 6, 7, 8, 9, 10 and 16) in trifluoroacetic acid (TFA)–dichloromethane (DCM) solution has been described in a short communication.[1] We found that when n<6 only intramolecular cyclization occurred. When n was equal to 6 or 7 polymers and a very low yield of the cyclic dimers, *3*–6 or *3*–7, were obtained. When n was equal to 8, 9, or 10 an approximately 40 % yield of the cyclic dimers, *3*–8, *3*–9, or *3*–10, was obtained along with polymers. When n was equal to 16, both intramolecular cyclization with formation of *5*–16 and formation of the cyclic dimer, *3*–16, took place. In this communication we speculated that formation of the cyclic dimers, *3-n*, involved dimerization of an anodically generated dication diradical with a positive charge and a free electron on each aryl group. However, the results presented in this paper show that this assumption is incorrect. Furthermore, we have found that identical products are obtained in the same yield as in TFA/DCM when the electrolyses are carried out in acetonitrile. As the latter solvent is much more convenient for electrochemical studies this medium has been used throughout this work.

RESULTS AND DISCUSSION

The dependence of the products and yields on the amount of current consumed in the anodic



1-n



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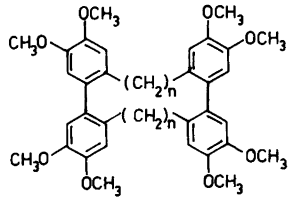

3-n

* Part I, see Ref. 1.

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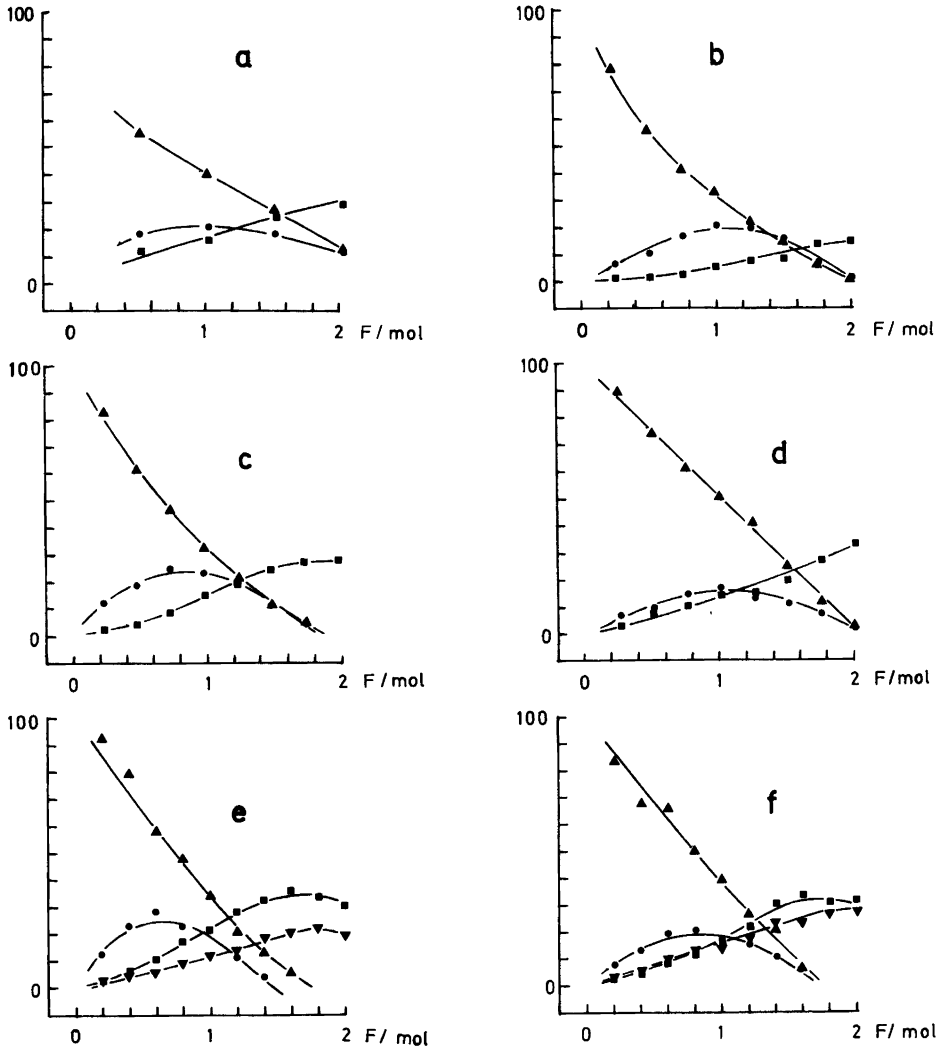
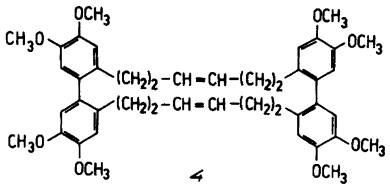


Fig. 1. Products and yields as a function of the amount of current (in Faradays per mol, F/mol) used for the anodic oxidation of compounds *1-n* (*n*=6, 8, 10, 11, 12) and *2*. Electrolyte: Acetonitrile/LiBF4. Concentration of starting compound: 67 mmol. Current density: 2 mA/cm^2. ▲ Starting compound. ● "Open dimer" (*6-n* or *7*). ■ "Cyclized dimer" (*3-n* or *4*). ▼ Cyclized product (*5-n*). (a) Oxidation of compound *2*. (b) Oxidation of compound *1*–6. (c) Oxidation of compound *1*–8. (d) Oxidation of compound *1*–10. (e) Oxidation of compound *1*–11. (f) Oxidation of compound *1*–12.

oxidation of *1-n* (*n*=6, 8, 10, 11, or 12) or *2* is shown in Figs. 1a–f. The yields in these experiments were determined by HPLC analysis. The yields of the products actually isolated in pure form were, of course, lower than the HPLC-yields (see Experimental). Changes in current density did not result in any significant changes in products or yields. However, working at lower substrate concentrations than in the experiments summarized in Fig. 1 resulted – as expected – in improved yields of the cyclic dimer. For example, reduction of the concentration of *2* from 16.7 mmolar to 8.3 mmolar resulted in a 10 % increase in the yield of *4*. The amount of charge



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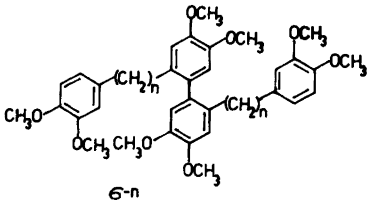
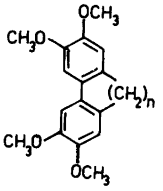
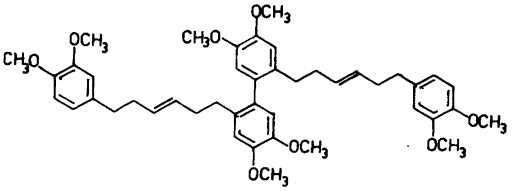


6-n



5-n



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F/mol used to oxidize the substrate was crucial.

For the compounds *1-n* the yield of the cyclic dimer *3-n* decreased rapidly if more than 2 F/mol of charge was used for the oxidation. If, for example, 3 F/mol was used to oxidize *1*–8 the yield of *3*–8 was 16.0 %, whereas the yield when 2 F/mol of charge was used was 28.8 %. As can be seen from Fig. 1 the current yield in the oxidations of compounds *1-n* is virtually 100 %, as 2 F/mol of charge suffices to achieve complete oxidation of the substrates. For compound *2* the current yield is less than 100 % (Fig. 1f), but increasing the amount of charge above 2 F/mol does not increase the yield of *4* very much. For example, oxidizing *2* with 3 F/mol leads to complete conversion of *2* with a 33.5 % yield of *4*.

In all the electrolyses of the compounds *1-n* and *2* the concentration of the open dimer *16-n* or *7* goes through a maximum at 1 F/mol of charge and at 2 F/mol of charge the concentration of the open dimer is virtually zero. The sum of the concentrations of the cyclic dimer (*3-n* or *4*) and the intramolecularly cyclized product (*5-n*) increases steadily until 2 F/mol has been consumed. If more charge is passed through the electrolyte, destructive oxidation of these products occurs and the total yield starts to decrease. It is noteworthy that intramolecular cyclization only occurs when $n \leq 5$ or $n \geq 11$.

The changes in the concentrations of starting compounds and the various products observed (Fig. 1) clearly indicates that the open dimers (*6-n* and *7*) are intermediates in the formation of the cyclic dimers (*3-n* and *4*). The efficiency of the intramolecular cyclization of *6-n* or *7* to *3-n* or *4* is very high and can only be explained by assuming an ordered structure for the open chain dimer in which the two aliphatic chains are aligned parallel to each other and bound by van der Waals forces in a similar fashion as the lipophilic chains of surfactants in micelles. In such a structure the two veratryl units at the ends of the open dimer become favourably oriented for coupling. In a similar way we can explain why intramolecular coupling only occurs when $n \leq 5$ or $n \geq 11$. In the first case the two veratryl units are close enough for coupling to occur in most of the possible conformations of the molecule. In the intermediate cases ($6 \leq n \leq 10$) the hydrocarbon chain between the veratryl units is too short to give any appreciable stabilization by folding (through van der Waals interaction between the two halves of the hydrocarbon chain). This however appears to be the case when $n \geq 11$ and intramolecular coupling competes efficiently with the dimerization leading initially to the open chain dimer (*3-n*).

EXPERIMENTAL

General procedures and apparatus used for voltammetry and coulometry were conventional and have been described previously.[1] The acetonitrile was analytical grade. The NMR spectra were recorded in deuteriochloroform solution with Me_4Si as internal reference.

The diarylalkanes *1-n* (n=6, 8, or 10 and *2* were prepared in a two-step synthesis involving Friedel Crafts acylation of 2 mol of 1,2-dimethoxybenzene with the acid chlorides derived from hexanedioic, octanedioic, decanedioic, dodecanedioic and trans-3-hexenedioic acid, respectively, followed by Clemmensen reduction of the resulting diketone.

1,6-Bis(3,4-dimethoxyphenyl)hexane (1-6). M.p. 76–78 °C (lit[2] M.p. 76.5–77.5 °C). NMR δ 6.8 (6H, s), 3.93 (12H, s), 2.57 (4H, t, (J=6 Hz), 1.43 (8H, bs) p.p.m.

1,8-Bis(3,4-dimethoxyphenyl)octane (1-8). M.p. 73–75 °C (EtOH). NMR δ 6.73 (6H, s), 3.83 (12H, s), 2.55 (4H, broad t (J=6 Hz)), and 1.25 (12H, bs) p.p.m.

1,10-Bis(3,4-dimethoxyphenyl)decane (1-10). M.p. 82–84 °C (lit[3] M.p. 82–83 °C). NMR δ 6.76 (6H, s), 3.9 (12H, s), 2.55 (4H, broad t (J=6 Hz)), 1.25 (12H, bs) p.p.m.

1,12-Bis(3,4-dimethoxyphenyl)dodecane (1-12). 1,10-Bis(3,4-dimethoxybenzoyl)decane was prepared as described and subjected to catalytic hydrogenation over a Pd (5 %) on carbon catalyst in ethanol: TFA (50:1) solvent to give a virtually quantitative yield of *1*–12. M.p. 86–89 °C. NMR δ 6.7 (6H, s), 3.83 (12H, s), 2.6 (4H, broad t (J=7 Hz)), and 1.3 (20H, bs) p.p.m.

1,11-Bis(3,4-dimethoxyphenyl)undecane (1–11). 1,9-Dibromononane, 20 ml, dissolved in anhydrous ether, 50 ml, was added to magnesium turnings, 6 g, contained in anhydrous ether, 50 ml, at a rate sufficient to keep the ether boiling. After the addition, reflux was continued for 1 h. The mixture then was cooled and 3,4-dimethoxybenzaldehyde, 34 g, dissolved in ether, 200 ml, was added with stirring. After the addition the mixture was refluxed for 1 h before it was poured on crushed ice, 100 g, mixed with concentrated hydrochloric acid, 100 ml. The organic phase was separated and washed with sodium bisulfite solution (to remove excess aldehyde) and water. Evaporation of the ether yielded an oil which was directly subjected to catalytic hydrogenation (4 atm.) in ethanol solution (300 ml) with 5 % palladium on carbon (1 g) as catalyst. During the hydrogenation a crystalline precipitate formed, 18.9 g, m.p. 66–68 °C, identified as *1*–11 by their NMR δ 6.75 (6H, s), 3.87 (12H, s), 2.57 (4H, broad t (J=7 Hz)), and 1.3 (18H, bs) p.p.m; and M^+ (m/e) 428.

1,6-Bis(3,4-dimethoxyphenyl)trans-3-hexene (2). M.p. 80–82 °C. NMR: 6.73 (6H, m) 5.50 (2H, m), 3.87 (12H, s) and 2.50 (8H, m).

Electrolyses. General. The substrate to be oxidized, 1 mmol, was dissolved in acetonitrile, 60 ml, containing lithium tetrafluoroborate, 0.5 g, and subjected to constant current (100 mA) electrolysis in an open one-compartment cell, fitted with a platinum cylinder anode (50 cm^2) and a nickel coil cathode. The reaction mixture was stirred magnetically and its temperature was kept at 10 °C by external cooling. When the desired amount of charge had been passed through the cell, the reaction mixture was worked up and analyzed by HPLC. For two compounds, *1*–11 and *1*–12, a different procedure was followed. At intervals, samples, 0.5 ml, of the reaction mixture were taken out, diluted with 5 ml of the HPLC solvent, washed with bicarbonate solution and water and injected on the HPLC-column. A straight phase column with cyclohexane–chloroform mixture as eluent and UV-detector was used. When all of the starting material had been consumed (which normally required 2F/mol) only the cyclic dimer (*3-n*) and the cyclized compound (*5-n*) were obtained and the separation and purification of the products were without complications. In the electrolysis experiments aimed at the isolation of the "open" dimers *6-n* and *7* only 0.7 F/mol of charge was passed through the cell. Column chromatography of the product gave starting material (*1-n* or *2*), the cyclized compound (*5-n*) and an inseparable mixture of the "open" dimer (*6-n* or *7*) and the cyclic dimer (*3-n* or 4). Crystallization of the latter mixture from pentane–diethyl ether gave the cyclic dimer as pure crystals whereas the "open" dimer was concentrated in the mother liquor. Repeated crystallizations of the mother liquor followed by column chromatography on silica gel (dichloromethane–diethyl ether eluent) eventually gave the open dimer as a pure compound. The pure compounds obtained in this way were used as internal standards in the HPLC analysis of the various electrolysis mixtures (see Fig. 1).

Electrolysis of 2. 1,1'-Bis(6-(3,4-dimethoxyphenyl)-hex-3-enyl)-3,3',4,4'-tetramethoxybi phenyl (7). M.p. 92–94°C, NMR δ 6.73 (10H, m), 5.4 (4H, bs), 3.93 (6H, s), 3.83 (18H, s), and 2.3 (16H, bs) p.p.m. M^+ 710-3819 (*m/e*). M^+ calculated for $C_{44}H_{54}O_8$: 710.3818.

[1,2],[3,4],[11,12],[13,14]-Tetra(4,5-dimethoxybenzo)cycloeicosa-trans,trans-7,17-diene (4). M.p. 190–192 °C. NMR: 6.73 (4H, s), 6.57 (4H, s), 5.2 (4H, bs), 3.87 (12H, s), 3.75 (12H, s) and 2.2 (16H, s) p.p.m. M^+ 708.3723 (*m/e*). M^+ calculated for $C_{44}H_{52}O_8$: 708.3662.

Electrolysis of 1-6. 1,1'-Bis(6-(3,4-dimethoxyphenyl)hexyl)-3,3',4,4'-tetramethoxybiphenyl (6-6). Oil. NMR δ 6.73 (10H, m), 3.93 (6H, s), 3.83 (18H, s), 2.4 (8H, bs) and 1.3 (16H, bs) p.p.m. M^+ 714.4193 (*m/e*). Calculated M^+ for $C_{44}H_{58}O_8$: 714.4132.

[1,2],[3,4],[11,12],[13,14]-Tetra(4,5-dimeth-

oxybenzo)cycloeicosane (3-6). M.p. 185–189 °C. NMR δ 6.75 (4H, s), 6.6 (4H, s), 3.93 (12H, s), 3.81 (12H, s), 2.3 (8H, bs), and 1.1 (16H, bs) p.p.m. M^+ 712.4026 (*m/e*). Calculated for $C_{44}H_{56}O_8$: 712.3875.

Electrolysis of 1-*8. 1,1'-Bis(8-(3,4-dimethoxyphenyl)octyl)-3,3',4,4'-tetramethoxybiphenyl (6-8).* Oil. NMR δ 6.75 (10H, m), 3.93 (6H, s), 3.87 (18H, s), 2.4 (8H, bs) and 1.23 (24H, bs) p.p.m. M^+ 770–4791 (*m/e*). Calculated M^+ for $C_{48}H_{66}O_8$: 770.4758.

[1,2],[3,4],[13,14],[15,16]-Tetra(4,5-dimethoxybenzo)cyclotetracosane (3-8). M.p. 159–161 °C. NMR δ 6.76 (4H, s), 6.6 (4H, s), 3.9 (12H, s), 3.8 (12H, s), 2.3 (8H, bs), and 1.2 (24H, bs) p.p.m. M^+ 768.4636 (*m/e*). Calculated M^+ for $C_{48}H_{64}O_8$: 768.4601.

Electrolysis of 1-*10. 1,1'-Bis(10-(3,4-dimethoxyphenyl)decyl)-3,3',4,4'-tetramethoxybiphenyl (6-10).* Oil. NMR δ 6.75 (10H, m), 3.9 (6H, s), 3.87 (18H, s), 2.4 (8H, bs), and 1.2 (32H, bs) p.p.m. M^+ 826.5374 (*m/e*). Calculated M^+ for $C_{52}H_{74}O_8$: 826.5384.

[1,2],[3,4],[15,16],[17,18]-Tetra(4,5-dimethoxybenzo)cyclooctacosane (3-10). M.p. 137–140 °C. NMR δ 6.83 (4H, s), 6.63 (4H, s), 3.93 (12H, s), 3.83 (12H, s), 2.4 (8H, bs), and 1.17 (32H, bs) p.p.m. M^+ 824.5191 (*m/e*). Calculated M^+ for $C_{52}H_{72}O_8$: 824.5227.

Electrolysis of 1-*11. 1,1'-Bis[11-(3,4-dimethoxyphenyl)-undecyl]-3,3',4,4'-teteramethoxybiphenyl (6–11).* Oil. NMR δ 6.8 (10H, m), 3.93 (6H, s), 3.87 (6H, s), 3.85 (6H, s), 2.4 (8H, bs), and 1.2 (36H, bs) p.p.m. M^+ 854.5717 (*m/e*). Calculated M^+ for $C_{54}H_{78}O_8$: 854.5697.

[1,2],[3,4],[16,17],[18,19]-Tetra(4,5-dimethoxybenzo)cyclotricontane (3-11). M.p. 133–136 °C. NMR δ 6.8 (4H, s), 6.6 (4H, s), 3.93 (12H, s), 3.83 (12H, s),2.43 (8H, bs), and 1.17 (36H, bs) p.p.m. M^+ 852.5518 (*m/e*). Calculated M^+ for $C_{54}H_{76}O_8$: 852.5540.

[1,2],[3,4]-Di-(4,5-dimethoxybenzo)cyclopentadecane (5-11). M.p. 98–102 °C. NMR δ 6.85 (2H, s), 6.6 (2H, s), 3.93 (6H, s), 3.83 (6H, s), 2.43 (4H, bs), and 1.23 (18H, bs) p.p.m. M^+ 426.2770 (*m/e*). Calculated M^+ for $C_{27}H_{38}O_8$: 426.2770.

Electrolysis of 1-*12. 1,1'-Bis(12-(3,4-dimethoxyphenyl)dodecyl)-3,3',4,4'-tetramethoxybiphenyl (6-12).* Oil. NMR δ 6.8 (10H, m), 3.9 (6H, s), 3.87 (18H, s), 2.4 (8H, bs), and 1.2 (40H, bs) p.p.m. M^+ 882.5929 (*m/e*). Calculated M^+ for $C_{56}H_{82}O_8$: 882.6010.

[1,2],[3,4],[18,19],[20,21]-Tetra(4,5-dimethoxybenzo)coclodotracontane (3-12). M.p. 93–97 °C. NMR δ 6.83 (4H, s), 6.63 (4H, s), 3.97 (12H, s), 3.85 (12H, s), 2.36 (8H, bs), and 1.2 (40H, bs) p.p.m. M^+ 880.5887 (*m/e*). Calculated M^+ for $C_{56}H_{80}O_8$: 880.5853.

[1,2],[3,4]-Di(4,5-dimethoxybenzo)cyclohexadecane (5-12). M.p. 99–102 °C. NMR δ 6.87 (2H, s), 6.63 (2H, s), 3.93 (6H, s), 3.83 (6H, s), 2.43 (4H, bs), and 1.23 (20H, bs) p.p.m. M^+ 440.2927 (*m/e*). Calculated M^+ for $C_{28}H_{40}O_4$: 440.2927.

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