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Anodic Oxidation of Hexamethoxybiphenyls into either stable Cation Radical Salt or Spiro(fluorene-9,1'-cyclohexadienones)

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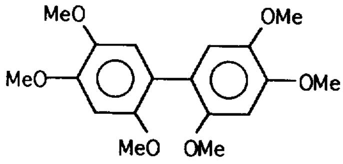
Abstract: Three symmetrically substituted hexamethoxybiphenyls were subjected to electrooxidation at a platinum anode. 2,2',4,4',5,5'-hexamethoxybiphenyl led to the stable cation radical salt expected, whereas 3,3',4,4',5,5'-hexamethoxybiphenyl and 2,2',3,3',4,4'-hexamethoxybiphenyl afforded unexpected spiro(fluorene-9,1'-cyclohexadienones).

INTRODUCTION

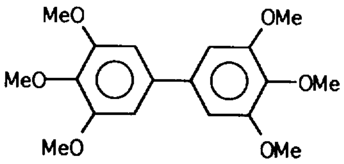
Previously we studied the behavior of methoxylated dibenzothiophenes in electrooxidation at a platinum anode[1]. Very stable cation radical salts were isolated in good yields (70 % or more). The study of the effect of the number and position of methoxy groups on dibenzothiophene showed that the presence of two substituents in the ortho position on each benzene ring was required. With two methoxy groups in the meta position and with more than two methoxy groups, coupling products were formed.

These results prompted us to extend the field of this research to methoxylated biphenyls to find out what change the removal of the sulfur atom from dibenzothiophene would bring about.

The cation radical of biphenyl itself was not observed[2], but the observation of the cation radical of biphenyls substituted by methoxy groups, such as 4,4'-dimethoxybiphenyl and 3,3',4,4'-tetramethoxybiphenyl was reported. Actually the biphenyl structure enhances the stability of cation radicals, as long as coplanarity of the two rings is possible[3]. This phenomenon and the fact that the presence of methoxy groups on an aromatic ring stabilize cation radicals[4] gave us hope of electrogenerating stable cation radical salts from hexamethoxybiphenyls **1**, **2** and **3** which had never heen studied in electrooxidation :



1



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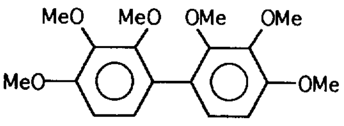

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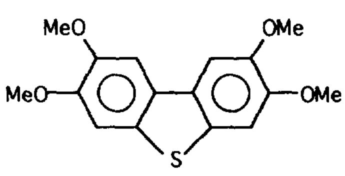
Structure **1** has been chosen first because of its similarity to 2,3,7,8-dibenzothiophene **4** whose electrogenerated cation radical was found to be quite stable[1]. The choice of other structures **2** and **3** corresponds to the shift of the methoxy substituents, in the ortho position to the biphenyl linkage in compound **1**, to the meta position in compound **2** and to the ortho' position in compound **3**, so as to test all the possibilities from basic structure **5**.

Let us note that only biphenyl **2** does not present a steric hindrance brought about by the methoxy groups. The two rings in compounds **1** and **3** have a restricted rotation ; actually, in the case of 2,2',4,4',5,5'-hexamethoxybiphenyl **1**, the twist angle about the central bond between the two phenyl rings was found equal to 81.1 degrees[5].



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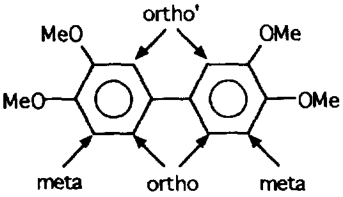

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RESULTS AND DISCUSSION

Anodic behavior of hexamethoxybiphenyls 1, 2 and 3.

Cyclic voltammetry

The cyclic voltammograms of hexamethoxybiphenyls **1**, **2** and **3** (c = 2.5 mM) were recorded at a stationary platinum microanode (area = 0.785 mm^2) in MeCN-$LiClO_4$ 0.1 M. The reference electrode was Ag / Ag^+ 0.01 M in acetonitrile and the sweep rate was 100 mVs^{-1}.

Figure 1 represents the voltammogram of 2,2',4,4',5,5'-hexamethoxybiphenyl **1** which exhibits two anodic peaks located at 0.56 V and 0.77 V corresponding to both oxidation steps of this compound. On the reverse scan, the two cathodic peaks which appear, represent the reduction of species issued from the preceding oxidation. This recording indicates that compound **1** undergoes two reversible one-electron oxidation. The peak separation for the anodic and corresponding cathodic processes (E_{pa}-E_{pc}) is 60 mV and the ratio of peak currents (i_{pa} / i_{pc}) is close to 1.

On the first forward scan, the voltammogram of 3,3',4,4',5,5'-hexamethoxybiphenyl **2** exhibits two irreversible oxidation peaks at 0.81 V and 1.34 V and, on the reverse scan, a reduction peak at 0.50 V. In figure 2, only the first oxidation step is represented; right from the second sweep, always a new oxidation peak appears at 0.56 V and remains after several sweeps. As will be seen below, the macroscale electrooxidation of **2** led to a product **7** resulting from a coupling reaction of **2** followed by a cyclization into a fluorene derivative along with the conversion of a methoxy group into a carbonyl function. The voltammogram of this product **7** exhibits an oxidation peak at 0.89 V. Therefore it is likely that the peak at 0.56 V, emerging at the second sweep, is the oxidation peak of a coupling product of **2** not isolated and slowly transformed anodically into product **7**.

The preceding data are in contrast to the voltammogram of 2,2',3,3',4,4'-hexamethoxybiphenyl **3** which exhibits completely irreversible oxidation peaks at 1.05 V and 1.86 V. Only the first peak is represented in figure 3.

The examination of the values of the oxidation potentials of hexamethoxybiphenyls **1**, **2** and **3** (table 1) additionally demonstrates the importance of the position of the methoxy groups on the benzene rings. Above all let us note that compound **1**, in spite of the steric hindrance of methoxy groups in positions 2 and 2', possesses reversible oxidation peaks showing a lower reactivity of the cation radical and dication, with potentials markedly lower than those of its unhindered isomer **2** :

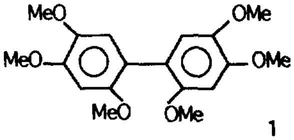
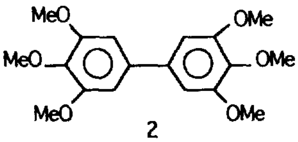
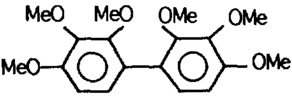
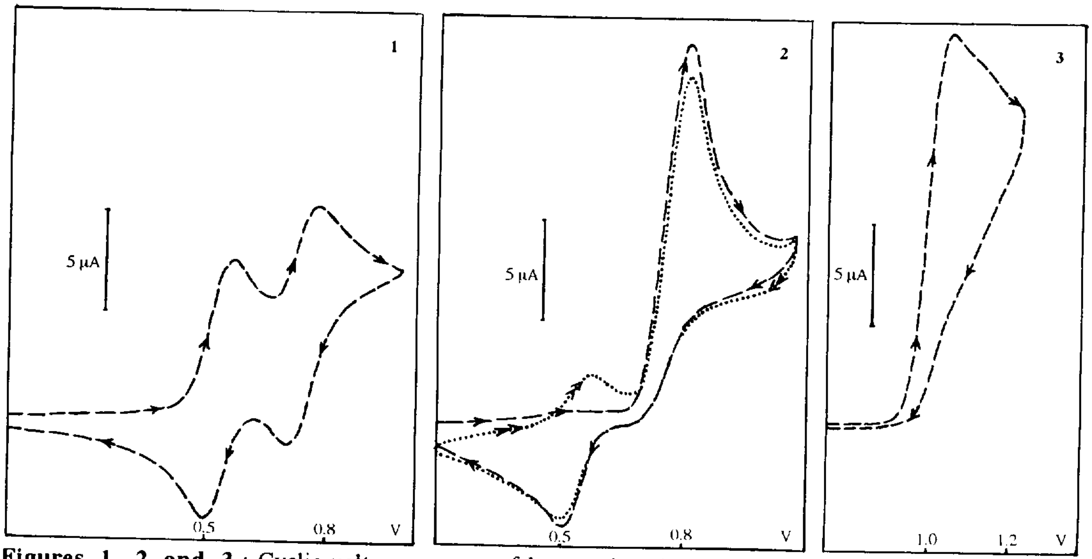
biphenyl	 1	 2	 3
Epa1 (V)	0.56 (rev.)	0.81	1.05
Epa2 (V)	0.77 (rev.)	1.34	1.36

Table 1 : Potentials of the oxidation peaks of hexamethoxybiphenyls **1**, **2** and **3** (c = 2.5 x 10^{-3} M), at a stationary platinum anode, in MeCN-$LiClO_4$ 0.1M, at a sweep rate of 100 mVs^{-1}, versus Ag/Ag^+ 0.01M as a reference electrode.

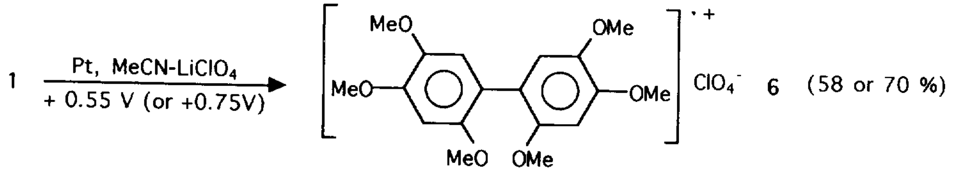


Figures 1, 2 and 3 : Cyclic voltammograms of hexamethoxybiphenyls **1**, **2** and **3** (see experimental conditions in table 1).

Macroscale electrooxidations

Anodic oxidation of 2,2',4,4',5,5'-hexamethoxybiphenyl 1

Hexamethoxybiphenyl **1**, within the time scale of voltammetry, affords stable oxidized species namely cation radical and dication. Its macroscale anodic oxidation at the potential of the first oxidation peak (0.55 V) gave, with a yield of 58 %, the stable cation radical salt of **1**, namely 2,2',4,4',5,5'-hexamethoxybiphenylium perchlorate **6**. Moreover if the anodic oxidation was carried out at the potential of the second oxidation peak (0.75 V), the yield of cation radical perchlorate **6** was better (70 %) :



The isolation of cation radical salt **6**, after oxidation at the potential of the second peak, is due to the diffusion of the soluble dication **1**$^{++}$ salt, generated at the anode, into the solution where it reacts with non electrooxidized biphenyl **1** to give insoluble cation radical **1** $^{\cdot +}$ salt :

$$1 \overset{+0.75\ V}{\rightleftarrows} 1^{++} \overset{+1}{\rightleftarrows} 2\ \ 1^{\cdot +}$$

The E.S.R. spectrum of cation radical salt **6** recorded during the electrooxidation of **1** (figure 4) exhibits a lorentzian shape with the absence of an hyperfine splitting.

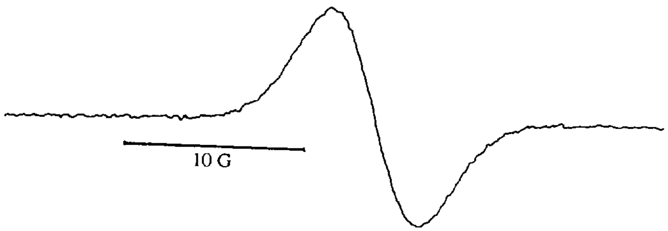
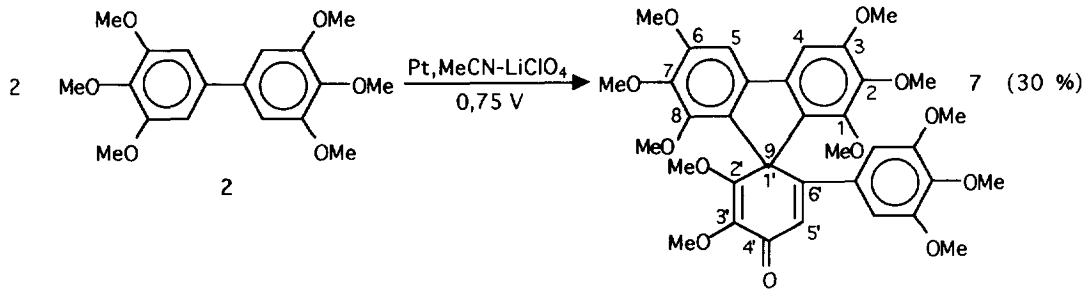


Figure 4 :

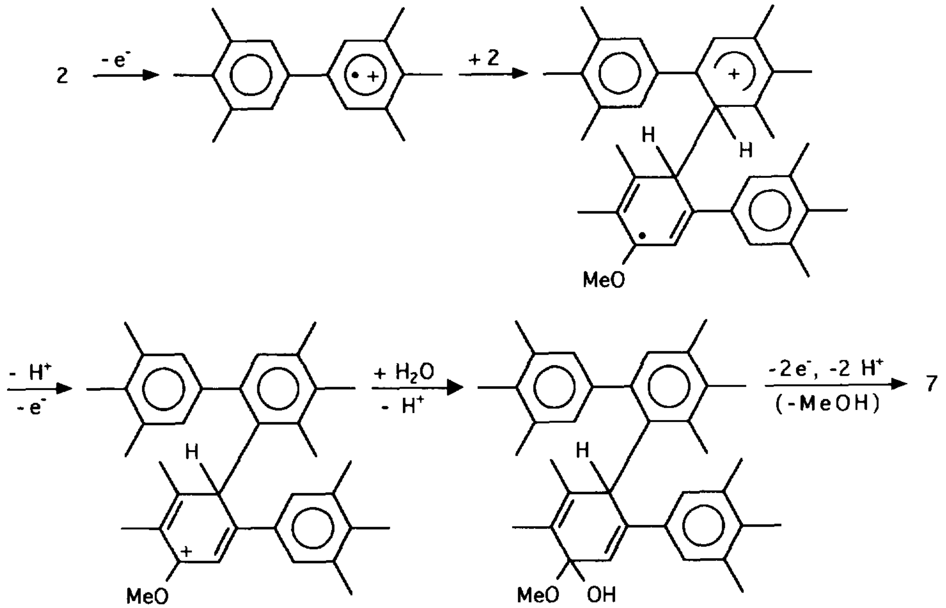
E.S.R. spectrum of cation radical perchlorate **6** formed in situ in the course of the oxidation of **1** (i = 50 μA,MeCN-LiClO$_4$ 0.1 M, Pt gauze microanode) ; g-factor = 2.0036.

Anodic oxidation of 3,3',4,4',5,5'-hexamethoxybiphenyl 2

Unlike hexamethoxybiphenyl **1**, 3,3',4,4',5,5'-hexamethoxybiphenyl **2** not showing a reversible peak in cyclic voltammetry, the obtaining of a stable cation radical salt was unlikely. Actually the macroscale electrooxidation of biphenyl **2**, in the same conditions as its isomer **1**, allows to isolate with a yield of 30 %, along with tars, a very unexpected product **7** whose structure was confirmed by an X-Ray analysis (figure 5). It is a fluorene derivative in which spirane carbon-9 is part of a conjugated cyclohexadienone :



The likely mechanism of formation of spiro[[1,2,3,6,7,8-hexamethoxyfluorene-9,1'[2',3'-dimethoxy-6'(3",4",5"-trimethoxyphenyl)]cyclohexa-2',5'-dien-4'-one]] **7** involves a prior coupling of hexamethoxybiphenyl **2** followed by the conversion of a methoxy group into a carbonyl function (after reaction with the residual water of the solvent) and by a cyclization into a fluorene derivative :



As the proposed mechanism involves the residual water of the solvent for the formation of the carbonyl function, the anodic oxidation of hexamethoxybiphenyl **2** was carried out as well, in the same conditions as above, by adding water (1 %) to acetonitrile, hoping to improve the yield. But the contrary happened ; compound **7** was not obtained ; only tars formed.

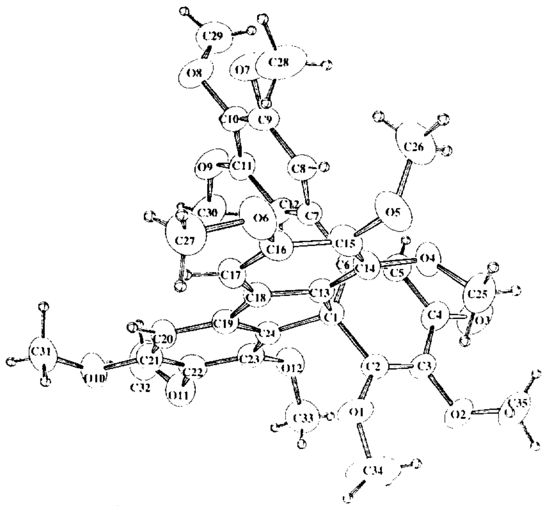


Figure 5 :

Structure of spiro compound **7** as determined by X-Ray analysis (see the experimental part for details).

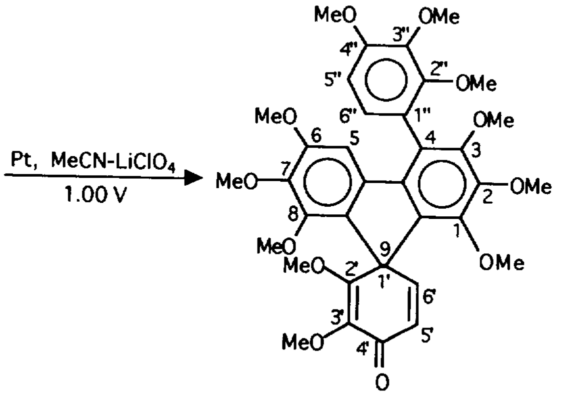
Anodic oxidation of 2,2',3,3',4,4'-hexamethoxybiphenyl 3

Surprisingly, hindered hexamethoxybiphenyl **3** led to the same kind of derivative **8** as spiro(fluorene-9,1'-cyclohexadienone) **7** obtained from unhindered hexamethoxybiphenyl **2**. Despite the failure to prepare monocrystals for an X-Ray analysis, structure **8** was identified from different spectra : IR (ν_{CO} = 1 650 cm^{-1}) M.S. [m/z = 650 ($C_{35}H_{38}O_{12}$)] and mainly 270 MHz ^{1}H-NMR. Actually, the NMR spectrum is made up of two sets of signals in the ratio of 75 to 25, owing to the presence of a 75/25 % mixture of atropisomers resulting from the hindered rotation of 4-(2",3",4"-trimethoxyphenyl) substituent of the fluorene moiety ; for one isomer 2'-OMe and 3'-OMe of the cyclohexadiene are on the same side as 2"-OMe, 3"-OMe and 4"-OMe, and for the other isomer they are on the opposite side. One can see :

- the singlet of the aromatic proton in the position 5 of the fluorene moiety (δ = 5.803 ppm for the major isomer) located in the anisotropy cone of the benzene ring in the position 4 of the same fluorene moiety.
- the AB type signals of the two vicinal ethylenic protons in 5' and 6' of the cyclohexadienone moiety (δ = 6.464-6.428-6.125-6.089 ppm for the major isomer).
- and the AB type signals of the two aromatic ortho protons in 5" and 6" of the benzene ring in position 4 on the fluorene moiety (δ = 7.026-6.994-6.854-6.822 ppm for the major isomer).
- as well as, in the case of the major isomer, ten methoxy singlets, including one with a double intensity, corresponding to eleven OMe groups.

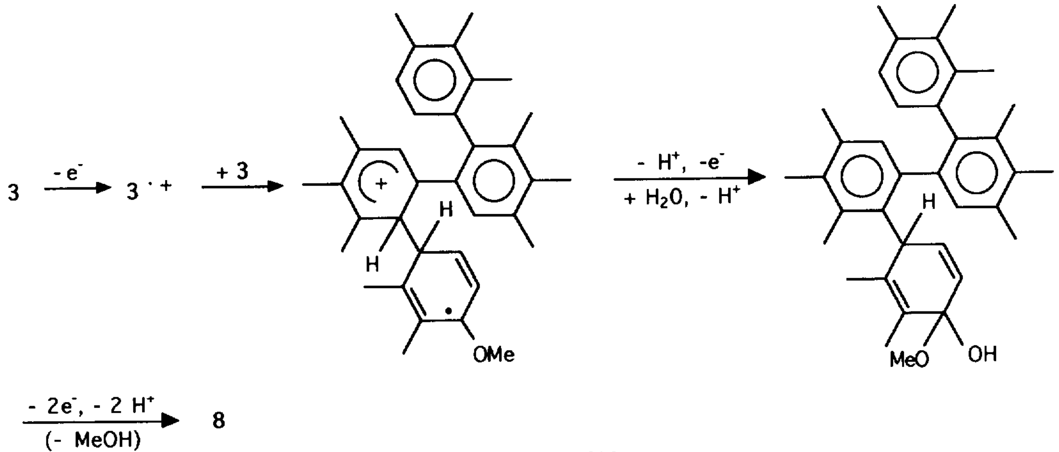
Only structure **8**, namely spiro[4-(2",3",4"-trimethoxyphenyl)-1,2,3,6,7,8-hexamethoxyfluorene-9,1'-(2,3-dimethoxycyclohexa-2',5'-dien-4'-one)], is consistent with this NMR spectrum. The yield is 62 %, when taking into account the recovered starting product :

2 3



8 (62 %)

The mechanism is very similar to that proposed previously for compound **7** :



CONCLUSION

Thus, the anodic behavior of hexamethoxylated biphenyls **1**, **2** and **3** varies greatly according to the respective position of the methoxy groups. So, despite a steric hindrance, 2,2',4,4',5,5'-hexamethoxybiphenyl **1** shows two perfectly reversible anodic peaks and leads to a quite stable cation radical salt, whereas 3,3',4,4',5,5'-hexamethoxybiphenyl **2**, without steric hindrance, does not show the least anodic reversibility in cyclic voltammetry and gives, after coupling and cyclization, a very unexpected spiro(fluorenecyclohexadienone) **7**.

The anodic behavior of 2,2',3,3',4,4'-hexamethoxybiphenyl **3** was unpredictable as well. Despite a steric hindrance and the fact that electrophilic substitutions (such as halogenations[6]) take place in positions 5 and 5', **3** leads, after a 6-6 coupling and a subsequent cyclization, to the same kind of spiro compound **8** as biphenyl **2**.

We contemplate studying the anodic behavior of the other three methoxylated biphenyls, respectively substituted in positions 2,2',3,3',5,5'-, 2,2',3,3',6,6'- and 2,2',4,4',6,6'-, in order to explain globally these surprising results.

EXPERIMENTAL

General methods

The progress of reactions and purity of samples were checked by T.L.C. on silica gel plates (Merck n° 5714). The purification of starting materials and electrolysis products was carried out by column chromatography on silica gel (Merck n° 7736). Proton NMR spectra were recorded at 60 MHz, with TMS as an internal reference, in $CDCl_3$, unless otherwise stated. Acetonitrile was purchased from Carlo-Erba, dried over molecular sieves (3Å) and used without further purification. $LiClO_4$ was purchased from Fluka and kept in a desiccator.

Starting materials

2,2',4,4',5,5'-hexamethoxybiphenyl **1** was prepared quantitatively by the catalytic coupling[7] of 1-iodo-2,4,5-trimethoxybenzene[8] in the presence of boron trifluoride etherate :

m.p. = 179° C (MeOH) [lit.[8,9] : m.p. = 177-179° C].

N.M.R. ($CDCl_3$) : δ OMe 3.75 (s, 6 H), 3.85 (s, 6 H) and 3.93 (s, 6 H) ; δ Ar 6.86 (s, 2 H) and 6.89 (s, 2 H).

3,3',4,4',5,5'-hexamethoxybiphenyl **2** was prepared by Ullmann coupling (in the presence of copper bronze, at 235° C, for 4 hours, under a nitrogen atmosphere) of 1-iodo-3,4,5-trimethoxybenzene[10] obtained by iodination of diazotized 3,4,5-trimethoxyaniline[11] :

m.p. = 127° C (EtOH) [lit.[10] : m.p. = 126° C].

N.M.R. ($CDCl_3$) : δ OMe 3.91 (s, 6 H) and 3.95 (s, 12 H) ; δ Ar 6.75 (s, 4 H).

2,2',3,3',4,4'-hexamethoxybiphenyl **3** was synthesized according to reference[8]. The preparation of 1-iodo-3,4,5-trimethoxybenzene required for Ullmann coupling was improved by overnight reaction of iodine with 1,2,3-trimethoxybenzene in the presence of mercuric oxide, in methanol, at room temperature :

m.p. = 124° C (MeOH) [lit.[10] : m.p. = 123° C].

N.M.R. ($CDCl_3$) : δ OMe 3.73 (s, 6 H), 3.91 (s, 6 H) and 3.93 (s, 6 H) ; δ Ar 6.66-6.93 (m, 4 H).

Anodic oxidations

Macroscale electrooxidations were carried out at room temperature, without bubbling inert gas, in a three-compartment H-shaped cell. The compartments were separated by two glass frits (inside diameter : 2 cm) ; an intermediate compartment (useful volume : 5 mL) minimizes mixing of catholyte (30 mL) and anolyte (65 mL). The anode was a square platinum foil (4 cm x 4 cm), cathode a graphite rod (diameter : 1 cm) and reference electrode Ag/Ag^+ 0.01 M in acetonitrile. A volume of 100 mL of MeCN-$LiClO_4$ 0.1 M was divided among the three compartments and salt bridge. 1 or 2 mmol of biphenyl **1**, **2** or **3** was added into the anodic compartment which was closed with a silicone stopper.

Anodic oxidation of 2,2',4,4',5,5'-hexamethoxybiphenyl 1

668 mg (2 mmol) of hexamethoxybiphenyl **1** were electrooxidized at the potential of 0.70 V. A deep blue precipitate formed. After 24 h., at the end of the electrolysis, the electricity consumption was about 1 Faraday per mole. The precipitate was filtrated off, washed three times with 2 mL of acetonitrile and dried in the open air. The yield of cation radical salt, 2,2',4,4',5,5'-hexamethoxybiphenylium perchlorate **6** was 70 % (603 mg) :

m.p. = 248° C (decomp.) ; IR (KBr) ν ClO_4^- 1090 cm^{-1} ; Anal. calcd. % for $C_{18}H_{22}O_{10}Cl$: C 49.83, H 5.11, O 36.88, Cl 8.17, found : C 49.80, H 5.20, O 36.26, Cl 7.88 ; E.S.R. spectrum : see theoretical part.

If the electrolysis was carried out, in the same conditions at the potential of 0.55 V, the yield of cation radical perchlorate **6** was lower (58 %) and the filtrate was more colored owing to the formation of a red by-product (m.p. 196° C) which was identified as a 1,1'-bi(dimethoxycyclohexadienylidenone) according to IR (νCO 1640 cm^{-1}) and M.S. [m/z 304 ($C_{16}H_{16}O_6$)].

Anodic oxidation of 3,3',4,4',5,5'-hexamethoxybiphenyl 2

334 mg (1 mmol) of hexamethoxybiphenyl **2** were electrooxidized at the potential of 0.75 V for 22 h. At the end of the electrolysis, the electricity consumption was about 3 Faradays per mole. The anolyte was diluted with 200 mL of dichloromethane, washed several times with 50 mL of water and dried over Na_2SO_4. After usual work-up, the remainder was purified by column chromatography on silica gel, with dichloromethane 98-methanol 02 as an eluent. This leads to the isolation of 98 mg (yield : 30 %) of spiro [[1,2,3,6,7,8-hexamethoxyfluorene-9,1',[2',3'-dimethoxy-6'-(3",4",5"-trimethoxyphenyl)]cyclohexa-2',5'-dien-4'-one]] **7** :

m.p. = 179° C (EtOH) ; IR (KBr) νCO 1640 and 1660 cm^{-1} ; 270 MHz-^1H N.M.R. ($CDCl_3$) δ OMe 3.488 (s, 6 H), 3.702 (s, 3 H), 3.745 (s, 3 H), 3.805 (s, 6 H), 3.873 (s, 3 H), 3.883 (s, 6 H), 3.929 (s, 6 H) ; δ Ar 5.865 (s, 2 H) and 6.811 (s, 2 H) ; δ = CH 6.542 (s, 1 H) ; Anal. calcd for $C_{35}H_{38}O_{12}$: C 64.60, H 5.89, O 29.51, found : C 64.43, H 5.62, O 29.38 ; M.S. m/z 650 ($C_{35}H_{38}O_{12}$).

The structure of compound **7** was determined by X-Ray analysis ; crystal data :

Formula : $C_{35}H_{38}O_{12}$, Mol. Wt : 650.69, Cryst. Syst : Monoclinic, Space Group : $P2_{1/c}$, a = 18.806(5), b = 11.201(2), c = 17.045(9), β = 115.50(3), V = 3241(2), Z = 4, $\rho_{calc} g.cm^{-3}$ = 1,334, F(000) = 1376, μ(MoKα) cm^{-1} = 0.94, T(°K) = 294.

Crystal size (mm) : 0.35*0.45*0.45, Radiation : Mo Kα, Max 2Θ(°) : 50°, Scan : ω/2θ = 1, t_{max} (for one measure), s = 60, Variance of standards : 0.5 %, Range of HKL : 0.13 ; 0.20 ; -22.22, Reflections measured : 6204, Reflections observed (I>σ(I)) : 3042 (3σ), R_{int}(from merging equiv refl) : 0.010, R(isotropic) = 0.094, R(anisotropic) = 0.081, Fourier Difference : 0.45-0.19, N(obs)/N(var) : 3042/539, Final R = 0.043, Rw = 0.042, $w = 1/\sigma(F_O)^2 = [\sigma^2(I) + (0.04F_O{}^2)^2]^{-1/2}$, Sw = 1.32, Max residual e.Å^{-3}, Δ/σ : 0.20, 0.54.

Atomic scattering factors from International Tables for X-ray Crystallography (1974). The calculations were performed on a Hewlett Packard 9000-710 for structure determination (Sheldrick, 1985) and on a Digital Micro VAX 3100 computer with the MOLEN package (Enraf-Nonius, 1990) for refinement and ORTEP calculations[12].

Anodic oxidation of 2,2',3,3',4,4'-hexamethoxybiphenyl 3

334 mg (1 mmol) of hexamethoxybiphenyl **3** were electrooxidized at the potential of 1.00 V for 24 h. At the end of the electrolysis, the electricity consumption was about 2.5 Faradays per mole. The anolyte was diluted with

250 mL of dichloromethane, washed several times with 50 mL of water and dried over Na_2SO_4. After usual work-up, the remainder was purified by column chromatography on silica gel, with dichloromethane 98-methanol 02 as an eluent. Along with 136 mg of starting material **3** was isolated 120 mg [yield 37 % or 62 % (when taking into account recovered compound **3**)] of spiro[1,2,3,6,7,8-hexamethoxy-4-(2",3",4"-trimethoxyphenyl)fluorene-9,1'-(2',3'-dimethoxy)cyclohexa-2',5'-dien-4'-one] **8** :

m.p. = 191-193°C (MeOH) (some crystals melt up to 214°C) ; IR (KBr) νCO 1650 cm^{-1} ; 270 MHz-^1H NMR ($CDCl_3$) : 75/25 % mixture of atropisomers (2'-OMe and 3'-OMe on the same side as 2"-OMe, 3"-OMe and 4"-OMe or on the opposite side) :

- major isomer : δ OMe 3.945 (s, 3 H), 3.939 (s, 3 H), 3.922 (s, 3 H), 3.863 (s, 3 H), 3.853 (s, 3 H), 3.831 (s, 3 H), 3.774 (s, 6 H), 3.768 (s, 3 H), 3.666 (s, 3 H), 3.459 (s, 3 H) ; δ 5-H 5.803 (s, 1 H) ; δ -HC=CH- 6.464-6.428-6.125-6.089 (AB system, 2 H) ; δ Ar (5"-H and 6"-H) 7.026-6.994-6.854-6.822 (AB system, 2 H).
- minor isomer : δ OMe 3.956, 3.842, 3.750, 3.597 (only four singlets are visible) ; δ 5-H 5.792 (s) ; δ -HC=CH- 6.486-6.450-6.200-6.164 (AB system) ; δ Ar (5"-H and 6"-H) 6.990-6.958-6.858-6.826 (AB system) ;

Anal. calcd for $C_{35}H_{38}O_{12}$: C 64.60, H 5.89, O 29.51, found : C 65.16, H 5.96, O 29.07 ;
M.S. m/z 650 ($C_{35}H_{38}O_{12}$).

Acknowledgements
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