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2,4,5-Triaryl-substituted pyrroles lead, upon chemical or electrochemical oxidation, to an intermediate β - β' -dimer, which, in the course of the reaction, undergoes further oxidation to a tetracyclic derivative. To improve the selectivity towards the uncyclized dimer the oxidation of a triarylpyrrole in which the *ortho* positions of the phenyl group in position 2 are hindered by the presence of methyl groups was attempted. The cyclization was hindered, but an α - β' -dimer was obtained as the major product. An unexpected isomeric α - β' -dimer, in which the mesityl group is shifted into the β position of the pyrrole ring which undergoes the oxidation, was obtained in minor amounts. Electroanalytical data indicate that the process goes through the formation of a monomeric radical cation, followed by a slow chemical reaction.

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Electrochemistry appears to be particularly useful for the study and for the optimization of the oligomerization processes involving pyrrole rings, as the oxidizing power of the anode can be modulated very precisely, and the overall kinetics can be easily controlled by the current density. Making use of this methodology we have recently reconsidered the dimerization of 4,5-diphenyl-2-(*p*-tolyl)pyrrole (**I**) [1]. This reaction, if performed by chemical oxidants, is not selective: the first β - β' -dimerization product, 4,4',5,5'-tetraphenyl-2,2'-di-(*p*-tolyl)-3,3'-dipyrrol (**II**), was further oxidized to a tetracyclic compound 1,6a-dihydro-8-methyl-2,3,4,5-tetraphenyl-6a-(*p*-tolyl)benzo[*g*]pyrrolo-[3,2-*e*]indole (**III**), to such an extent that **II** was found at the end of the reaction only as a minor product [2,3]. The ring closure to **III** involves the *ortho* position of the aryl group in position 2 of one of the pyrrole rings of **II**. Our electroanalytical study, followed by preparative electrolyses, allowed us to deduce that it is impossible, for the above mentioned compounds, to reach an acceptable selectivity for the production of **II**, as it has the same oxidation potential as **I**, and is progressively oxidized to **III**, as soon as it is formed in the reaction medium.

In order to obtain β - β' -dimers without further cyclizations, we have therefore tried the electrochemical oxidation of arylpyrroles bearing both the *ortho* positions of the phenyl in the α position hindered by the presence of methyl groups. 4,5-Diphenyl-2-mesitylylpyrrole (**IV**) was chosen as the substrate for this investigation and the results obtained are reported in the following account.

Results.

Electroanalytical Investigations of **IV**.

The oxidative cyclic voltammetric path of **IV** presents two monoelectronic oxidation peaks at 0.62 V and 1.14 V

(vs. Ag/Ag⁺ 0.1M in acetonitrile), respectively. The first wave is reversible at low sweep rates, whereas the second one appears to be totally irreversible (see Figure 1). The cyclic voltammetric path is not altered by the addition of perchloric acids to the electrolytic medium. The addition of pyridine modifies the C.V. response, with the disappear-

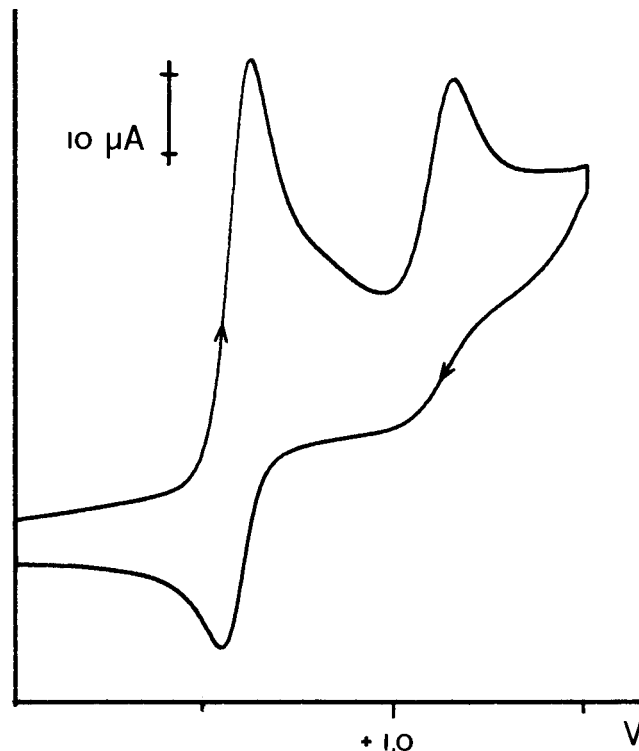


Figure 1. Cyclic voltammogram curve of **IV**. SEE: acetonitrile-tetra-butylammonium perchlorate 0.1 M. **IV**, 2.28×10^{-3} M; anode Pt disk (3.14 mm²); cathode Pt wire; reference electrode Ag/Ag⁺ 0.1 M in acetonitrile; scan rate 100 mV s⁻¹.

ance of the two waves formerly quoted and the appearance of a new irreversible bielectronic wave at 0.54 V. The addition of water qualitatively gives the same response, but with a less pronounced effect, and no shifting of the peak potential towards less positive values was observed.

Controlled Potential Electrolyses (CPE) of IV.

CPE of IV at half wave potential (0.57 V) shows a charge consumption equivalent to 1.2 F/M. Analyses (tlc) of the medium in the course of the electrolysis show the progressive disappearance of IV, and the formation of two main isomeric products V ($M^+ = 672$) (present in the reaction medium in its protonated form) and VI which were isolated by preparative column chromatography. As far as V is considered, it behaves like a base, and its nmr spectrum (DMSO- d_6) has only one pyrrole N-H band at δ 11.12, exchangeable with deuterium oxide. On the basis of these data the structure of 2-mesitylyl-4,5-diphenyl-2-(2'-mesitylyl-4',5'-diphenylpyrrole-3'-yl)-2H-pyrrole is assigned. To VI the structure of 4,4',5,5'-tetraphenyl-2,3'-dimesitylyl-3,2'-dipyrrol is assigned, on the basis of the nmr spectrum (DMSO- d_6) which presents two distinct pyrrole N-H bands at δ 11.06 and 11.45, exchangeable with deuterium oxide.

The concentration of protonated V is continuously increasing with the disappearance of IV since the beginning of the electrolysis. On the contrary the concentration of VI increases progressively in the first stages of the electrolyses, but, after that approximately 0.8 F/M were passed the concentration of VI was observed to decrease quickly, with the contemporary appearance of some products most probably arising from its further oxidation.

Preparative Electrolyses on IV.

Different products are obtained if the electrolysis is stopped after the passage respectively of 0.8 or 1.2 F/M. Figures are quoted in the Experimental. In the first case, besides the unreacted starting material IV, the already mentioned isomeric products V and VI, were found in the effluent. In the second case only V is found, together with the already mentioned products which probably arise from further oxidation of VI.

Electroanalytical Determinations on V and VI.

The cyclovoltammetric path of V presents two irreversible oxidation peaks at 0.58 and 0.68 V, superimposed in a single wave (Figure 2); a single monoelectronic reversible wave appears at 0.70 V by addition of acids, whereas by addition of pyridine to V a single irreversible bielectronic wave appears at 0.58 V.

A different situation is observed for the CV path of VI; two reversible oxidation waves, respectively at 0.50 and 0.70 V are observed (Figure 3). The addition of perchloric acid does not alter the CV path, whereas by addition of pyridine the two waves become bielectronic, their reversibility disappears and the peak potentials shift towards

slightly lower values (0.44 and 0.66 V respectively).

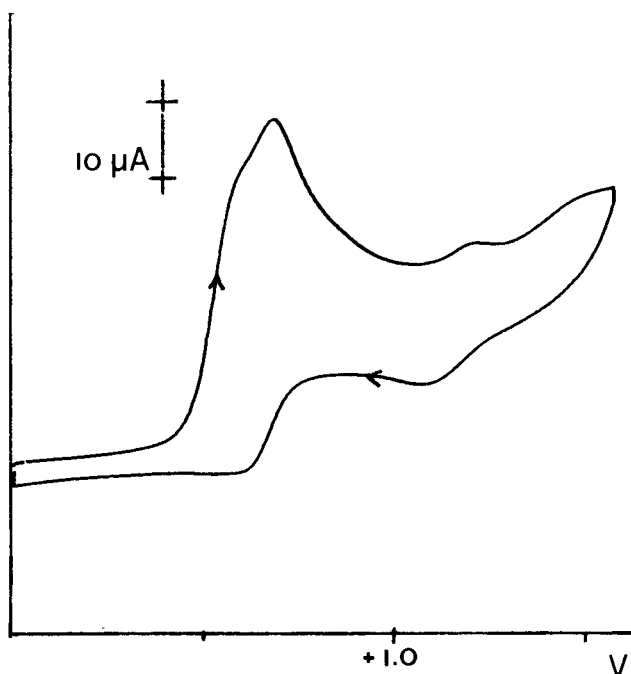


Figure 2. Cyclic voltammetric curve of V. SEE: acetonitrile-tetra-butylammonium perchlorate 0.1 M, V, 3.98×10^{-3} M; anode Pt disk (3.14 mm²); cathode Pt wire; reference electrode Ag/Ag⁺ 0.1 M in acetonitrile; scan rate 100 mV s⁻¹.

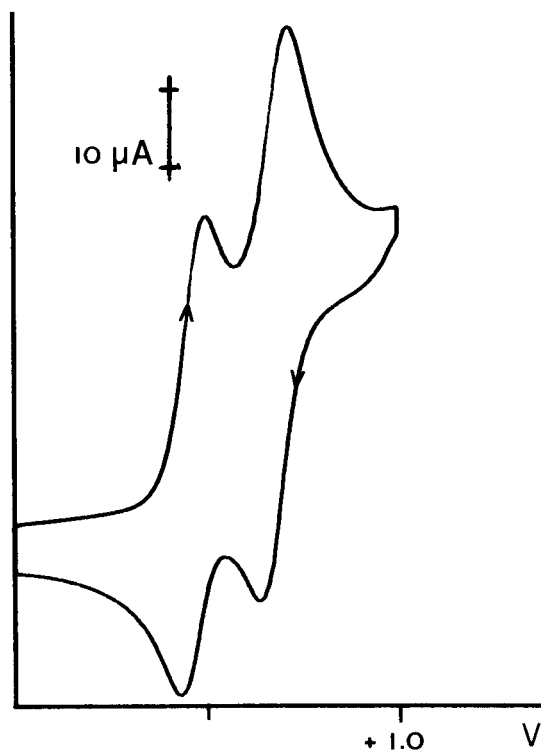
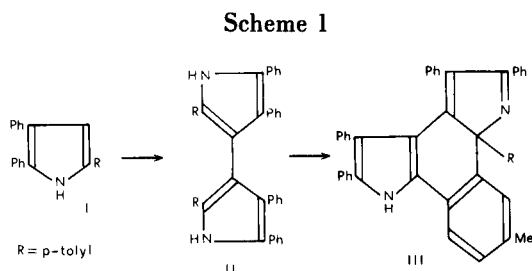
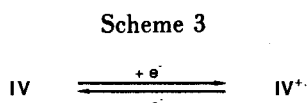
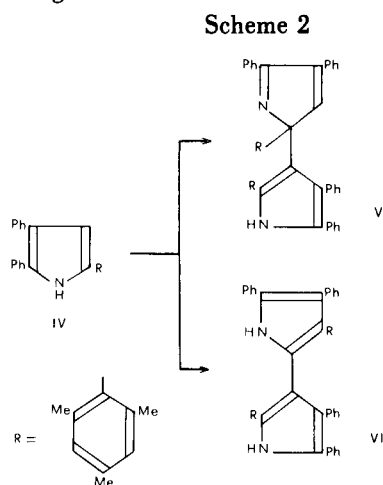


Figure 3. Cyclic voltammetric curve of VI. SEE: acetonitrile-tetra-butylammonium perchlorate 0.1 M, VI, 2.19×10^{-3} M; anode Pt disk (3.14 mm²); cathode Pt wire; reference electrode Ag/Ag⁺ 0.1 M in acetonitrile; scan rate 100 mV s⁻¹.



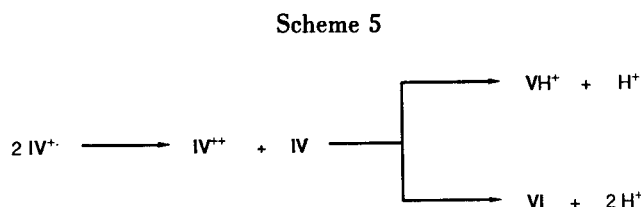
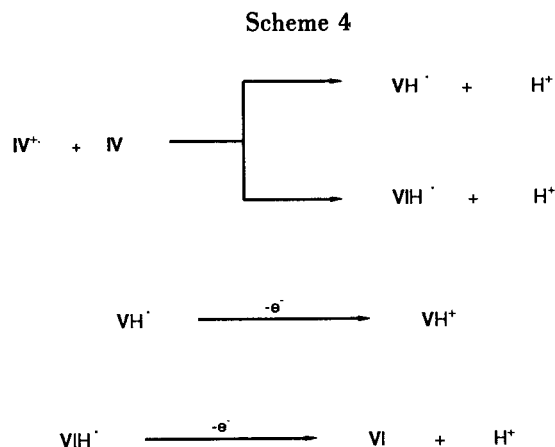
Discussion of Results.

On the basis of the results presented above, one can deduce that the first step of the reaction leading to **V** and **VI** (Scheme 2) is the reversible oxidation of **IV** to the corresponding radical cation.



The variation of the peak current function with the rate of voltage scan, and the ratio of cathodic to anodic peak currents as a function of rate of voltage scan recorded for **IV** are consistent with an EC mechanism, indicative of a slow chemical reaction following the formation of the radical cation. The experimental evidence gained up to now does not allow us to make reasonable hypotheses on the nature of this slow chemical reaction. Surely a radical radical coupling leading to dimeric products can be excluded by the absence of symmetrical $\alpha\text{-}\alpha'$ - or $\beta\text{-}\beta'$ -derivatives.

Two possible evolutions of the radical cation of **IV** appear possible: a) the reaction with a neutral **IV** molecule, and formation of a dimeric radical cation which could evolve according to Scheme 4; b) a disproportionation reaction of two radical cations of **IV**, leading to a dication and a neutral **IV** molecule, then reaction of the two species according to Scheme 5.



The unexpected $\alpha\text{-}\beta$ -migration of the mesityl group leading to **VI**, in both cases should involve one of the cationic intermediates formed in the course of the reaction. In our opinion the path b) is unlikely to occur, as the hypothetical dication of **IV** should not receive any stabilization from the three aryl groups, which all lay out of the plane of the pyrrole ring. Furthermore no monomeric oxygenated derivatives were found, as described by other authors [4-6] when a dicationic intermediate was hypothesized for tetra and pentaaryl substituted pyrroles, nor traces of dimeric products deriving from a β -substitution on the dication of **IV** were detected among the reaction products.

The cyclovoltammometric behaviour of **V** and **VI** provides evidence that both the products can be oxidized at potential values very near to that of **IV**. The behaviour of these two compounds is significantly different with respect to the acidity of the medium; the path of **VI** is not modified at all by the addition of perchloric acid, whereas a shifting of the first wave of **V** towards more positive values by addition of the same reactant is observed. These data easily explain the progressive accumulation of **V**, protected by the increase of its oxidation potential due to the protonation, and the disappearance of **VI**, which, being without basic centres, remains unprotected and is progressively oxidized at the same potential as **IV**.

Conclusions.

The results so far presented show a remarkable behaviour difference between the 4,5-diphenyl-2-*p*-tolylpyr-

role (**I**) and the corresponding mesityl derivative **IV**. Compound **I** is oxidized at less positive potentials, and the electroanalytical data were consistent with an ECE mechanism, indicative of a fast chemical reaction after the first oxidation step, whereas for **IV** the chemical follow-up reaction appears to be slow. This difference could be explained taking into consideration the steric situations of the two compounds; in the case of **I** the *p*-tolyl group is likely to be coplanar with the pyrrole ring, whereas in the case of **IV** the presence of the methyl groups in the *ortho* positions hinder the coplanarity. The mesomeric effects which can take place between the two rings in the case of coplanarity stabilize the intermediate radical cation, and consequently lower the values of the oxidation potentials. As far as the different reversibility of the oxidation waves of **I** and **IV** is considered, most probably it is due to the fact that a fast radical-radical coupling is easy for the radical cation of **I**, but difficult for the radical cation of **IV**, which is strongly hindered by the presence of the *ortho* methyl groups.

This hypothesis was confirmed taking under consideration the behaviour of 4,5-diphenyl-2-*o*-tolylpyrrole; two reversible oxidation waves, at the same potential values as **IV**, were observed. Structurally analogous derivatives were found as the result of controlled potential electrolyses at an anodic potential corresponding to the first wave.

As a conclusion of this part of the research we could deduce that although the first oxidative step, leading to the radical cation, was the same for both the arylpyrroles **I** and **IV**, electronic and steric effects have a strong influence on the chemical evolution of the first intermediates. The desired β - β' -dimers cannot be selectively obtained from neither of the two starting compounds **I** and **IV**; in the case of **I**, the dimer, once obtained, is unavoidably oxidized to a cyclization derivative, whereas in the case of **IV** the radical-radical coupling does not take place at all, and the unexpected α , β' -dimers are obtained.

EXPERIMENTAL

Melting points were determined on a Buchi-Tottoli capillary apparatus and are uncorrected. The ir spectra were recorded on a Perkin Elmer Infracord 137 and Perkin Elmer 299 spectrophotometers as Nujol mulls, and the uv spectra on a Hitachi Perkin-Elmer 200 for ethanolic solutions. The ¹H nmr spectra were recorded on a Varian FT-80 A spectrometer, using tetramethylsilane as the internal standard. The mass spectra were measured with a Jeol-O1SG-2 double focusing Mass Spectrometer at 75 eV (100 μ A). The analyses of the products of the electrolyses were performed with a Perkin-Elmer Series 10 HPLC apparatus with a UV-Vis LC95 detector. The tlc determinations were performed on Merck DC-Alufolien Kieselgel 60 F254.

Cyclic voltammetric experiments were performed with an Amel apparatus, formed by a 552 potentiostat equipped with a 731 digital coulometer, a 566 function generator and a 863 xy recorder. A Nicolet 3091 oscilloscope was used in fast cyclovoltammetric determinations. Preparative controlled potential electrolyses were carried out in H shaped cells with a G4 glass frit diaphragm. Platinum sheet (surface 4 cm²)

as anode and platinum wire as cathode were used. Reagent grade acetonitrile was redistilled and stored over 4A molecular sieves.

1,2-Diphenyl-4-mesityl-1,4-butanedione.

A mixture of 21.2 g (0.1 mole) of benzoin, 16.2 g of 2,4,6-trimethylacetophenone, 2.4 g of potassium cyanide in ethanol (60 ml) and water (8 ml) was heated under reflux for 1.5 hours. After standing overnight, the crystals were filtered and washed with water. Crystals were obtained from acetic acid mp 110°; ir: 1675, 1700 cm⁻¹ (2 x CO).

Anal. Calcd. for C₂₅H₂₈O₂: C, 84.27; H, 6.74. Found: C, 84.35; H, 6.80.

4,5-Diphenyl-2-mesitylpyrrole (**IV**).

A mixture of 3.4 g of 1,2-diphenyl-4-mesityl-1,4-butanedione, 6 g of ammonium acetate and 20 ml of acetic acid was refluxed for 3 hours. The solution was poured into crushed ice, and the product **IV** was filtered and crystallized from ethanol, mp 194°; ir: 3380 cm⁻¹ (pyrrole N-H); ms: 337 (M⁺); uv: λ max nm log ϵ 309 (4.03) 256 (3.91).

Anal. Calcd. for C₂₅H₂₃N: C, 89.02; H, 6.82; N, 4.15. Found: C, 89.19; H, 6.90; N, 4.21.

Preparative Oxidation of **IV**.

Compound **IV** (0.34 g, 0.001 mole) was dissolved in 30 ml of acetonitrile with tetrabutylammonium perchlorate 0.1 M, and was electrolyzed at the anodic potential of +0.55 V. The electrolysis was stopped after the passage of 77 coulombs. Then the anolyte was poured into water (200 ml), and neutralized with sodium hydrogen carbonate. The resulting solution was extracted with diethyl ether (2 x 100 ml). The ethereal solution, once dried with anhydrous sodium sulphate, was evaporated under reduced pressure to a dry powder. The residue was eluted on a silicagel (100 g) column. Fractions of 60 ml were collected. By elution with cyclohexane-ethyl acetate 95/5 unreacted pyrrole (80 mg, fractions 7-11), then **VI** (50 mg, fractions 15-19) were collected. By elution with cyclohexane-ethyl acetate 90/10 **V** (180 mg) was obtained.

2-Mesityl-4,5-diphenyl-2(2'-mesityl-4',5'-diphenylpyrrol-3'-yl)-2H-pyrrole (**V**).

Pale yellow crystals were obtained from light petroleum ether, mp 139-140°; ir: 3400 cm⁻¹ broad (pyrrole N-H); uv: λ max nm log 304 (4.49) 260 (4.44); ¹H nmr (DMSO-d₆): δ 1.98-2.40 (18 H, m, 6 x CH₃) 6.91-7.60 (24 H, m, aromatic H) 11.12 (1H, broad, NH, exchangeable with deuterium oxide); ms: 672 (M⁺).

Anal. Calcd. for C₅₀H₄₄N₂: C, 89.29; H, 6.55; N, 4.16. Found: C, 89.55; H, 6.75; N, 4.28.

4,4',5,5'-Tetraphenyl-2,3'-dimesityl-3,2'-dipyrrole (**VI**).

Pale yellow crystals were obtained from ethanol, mp 172-173°; ir: 3420 cm⁻¹ (pyrrole N-H); uv: λ max nm log ϵ 325 (4.26), 260 (4.09); ¹H nmr (DMSO-d₆): δ 1.93-2.43 (18 H s, 6 x CH₃), 6.66-7.66 (24 H, m, aromatic H), 11.06 (1H, broad, exchangeable with deuterium oxide), 11.46 (1 H, broad, N-H, exchangeable with deuterium oxide); ms: 672 (M⁺).

Anal. Calcd. for C₅₀H₄₄N₂: C, 89.29; H, 6.55; N, 4.16. Found: C, 89.51; H, 6.70; N, 4.19.

REFERENCES AND NOTES

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- [1] G. Filardo, S. Gambino, G. Silvestri, S. Caronna, S. Petruso and V. Sprio, *Gazz. Chim. Ital.*, **117**, 751 (1987).
- [2] V. Sprio, S. Petruso and L. Lamartina, *J. Heterocyclic Chem.*, **11**, 307 (1974).
- [3] V. Sprio, S. Petruso, L. Ceraulo and L. Lamartina, *J. Heterocyclic Chem.*, **14**, 797 (1977).
- [4] P. Libert and C. Caultet, *Bull. Soc. Chim. France*, 1947 (1971).
- [5] P. Libert, C. Caultet and J. Huguet, *Bull. Soc. Chim. France*, 3639 (1972).
- [6] P. Libert, C. Caultet and G. Barbey, *Bull. Soc. Chim. France*, 536 (1972).