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The electrochemical oxidation of 2,5-diphenyl-3-acetylpyrrole (**I**) is described. The cyclic derivative 1,6a-dihydro-2,5,6a-triphenyl-3,4-diacetylbenzo[*g*]pyrrolo[3,2-*e*]indole (**II**) was obtained in very good yield. However, when water was present in the reaction medium, a different derivative, 4-acetyl-2-hydroxy-2,5-diphenyl-3-(4'-acetyl-2',5'-diphenyl-3'-yl)-2*H*-pyrrole (**III**), was obtained as the main product. 2,2',5,5'-Tetraphenyl-4,4'-diacetyl-3,3'-dipyrryl (**IV**), a potentially useful intermediate for the synthesis of condensed pyrroles, was synthesized by zinc reduction of **III**.

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Recent investigations on the electrochemical oxidation of some triaryl substituted pyrroles provided evidence that in the case of 4,5-diphenyl-2-(*p*-tolyl)pyrrole the intermediate radical cation chemically evolves towards the formation of a β,β' -dimer which, being electroactive at the same anodic potential, affords substantial amounts of cyclic derivative. However, by controlled potential oxidation it is possible to optimize the yield of the β,β' -dimer at

circulated charge around one third of the theoretical value [1]. In contrast in the case of 4,5-diphenyl-2-mesitylpyrrole electronic and steric effects have a strong influence on the evolution of the intermediate radical cation, which although having analogous structure, leads to the α,β' -dimers, sterically less hindered [2]. In order to perform the synthesis of dimeric compounds potentially useful as intermediates for the synthesis of pharmaceutically active derivatives we focused our attention on the electrochemical behaviour of a 2,4,5-trisubstituted pyrrole, bearing in the *beta* position an acetyl group (**I**). The results of this research are presented in this paper.

Results.

Electroanalytical Investigations of **I**.

The oxidative cyclovoltammetric path of **I** presents a bielectronic irreversible peak at 0.74 V (*vs.* Ag/Ag⁺ 0.1 M in acetonitrile). The path is not substantially altered by the addition of perchloric acid to the electrolytic medium. The addition of pyridine modifies the C.V. response, with the splitting of the first peak in two different ones, respectively at 0.57 and 0.67 V, both irreversible (Figure 1). The sum of the current values of the two new peaks corresponds to the current of the first peak of the unbuffered solution.

Controlled Potential Electrolyses (CPE) of **I**.

a) Anhydrous Conditions.

CPE of **I** at half wave potential (0.60 V) in unbuffered anhydrous acetonitrile shows a charge consumption equivalent to 2 F/M. Analyses (tlc) of the medium in the course of the electrolysis show the progressive disappearance of **I**, and the formation of a main derivative **II** ($M^+ = 518$, final yield = 65%), present in the reaction medium in its protonated form. Compound **II** was isolated by preparative column chromatography. It presents an

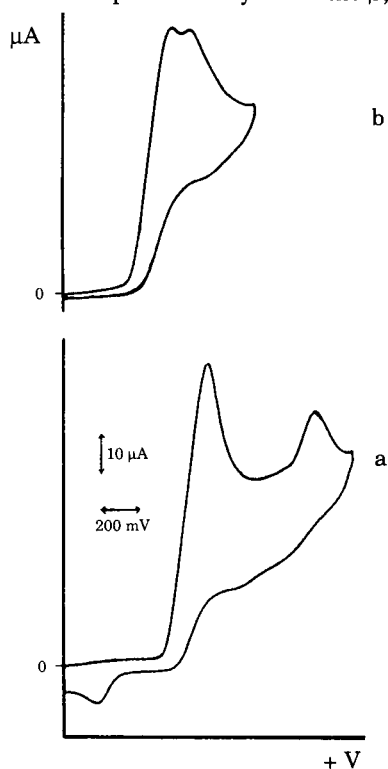


Figure 1. Cyclovoltammetric curve of **I**. SSE: acetonitrile-tetrabutylammonium perchlorate 0.1 M; $[M] = 4.69 \cdot 10^{-3}$ M; anode Pt disk (3.14 mm²); cathode Pt wire; reference electrode Ag/Ag⁺ 0.1 M in acetonitrile; scan rate 100 mV s⁻¹. a) In neutral unbuffered medium. b) In the presence of pyridine.

nmr spectrum (acetone- d_6) with a single pyrrole N-H band at δ 11.43, exchangeable with deuterium oxide, and two distinct CH_3 bands at δ 2.00 and 2.20.

b) In the Presence of Water.

CPE of **I** at the same anodic potential as in case a), but in the presence of water (**I**/water molar ratio = 1:20) leads to a different derivative **III** showing an M^+ = 536, in a product yield up to 70%. Compound **III** presents an nmr spectrum (DMSO- d_6) with a single pyrrole N-H band at δ 12.10, exchangeable with deuterium oxide, and two distinct CH_3 bands at δ 1.65 and 1.72.

Chemical Reduction of **III**.

The reduction of **III** with Zinc in acetic acid quantitatively leads to a derivative **IV** (M^+ = 520). To **IV**, showing an nmr spectrum (acetone d_6) typical of a symmetrical compound (a single pyrrole N-H band at δ 10.90, exchangeable with deuterium oxide, and a single CH_3 band at δ 2.00), the structure of 2,2',5,5'-tetraphenyl-4,4'-diacetyl-3,3'-dipyrryl was assigned.

Electroanalytical Investigations of **II**.

The oxidative cyclovoltammetric path of **II** presents two

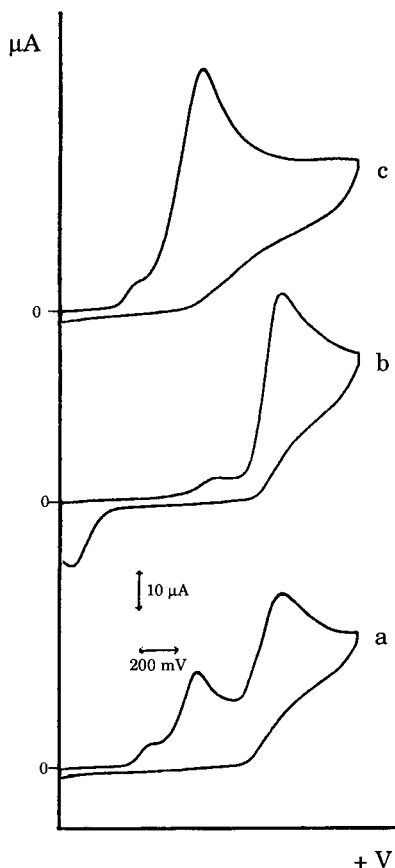


Figure 2. CV of **II**. a) In neutral medium. b) and c) In the presence of acid (perchloric acid) and pyridine respectively. $[M] = 4.06 \cdot 10^{-3} M$; other conditions as in Figure 1.

monoelectronic irreversible peaks at 0.68 and 1.2 V. By the addition of perchloric acid to the electrolytic medium, the first peak disappears, whereas the second becomes nearly bielectronic. The addition of pyridine, on the contrary, causes the disappearance of the second peak, formerly quoted, and the first one becomes bielectronic at 0.70 V (Figure 2).

Electroanalytical Investigations of **III**.

The oxidative cyclovoltammetric path of **III** presents two monoelectronic irreversible peaks at 0.77 and 1.08 V. By the addition of perchloric acid to the electrolytic medium, the first peak disappears, whereas the second becomes nearly bielectronic. The addition of pyridine modifies the C.V. response with the disappearance of the two peaks formerly quoted, and the appearance of a new irreversible bielectronic wave at 0.68 V (Figure 3).

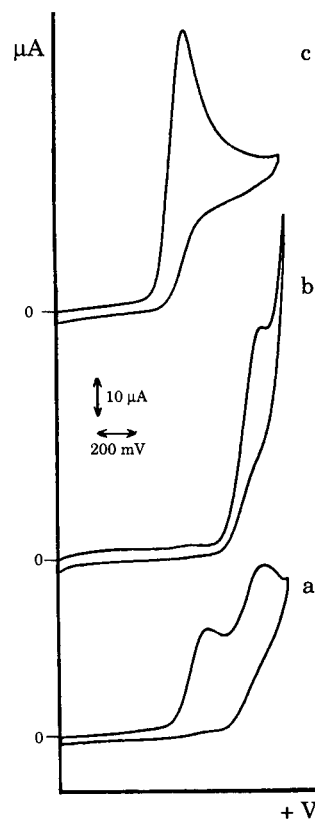


Figure 3. CV of **III**. a) In neutral medium. b) and c) In the presence of acid and pyridine respectively, $[M] = 3.84 \cdot 10^{-3} M$; other conditions as in Figure 1.

Electroanalytical Investigations of **IV**.

The oxidative cyclovoltammetric path of **IV** presents an irreversible bielectronic wave at 0.74 V. The path is not substantially altered by the addition of perchloric acid to the electrolytic medium. The addition of pyridine modifies the C.V. response, with the splitting of the peak in two different ones, respectively at 0.58 and 0.74 V, both irreversible (Figure 4).

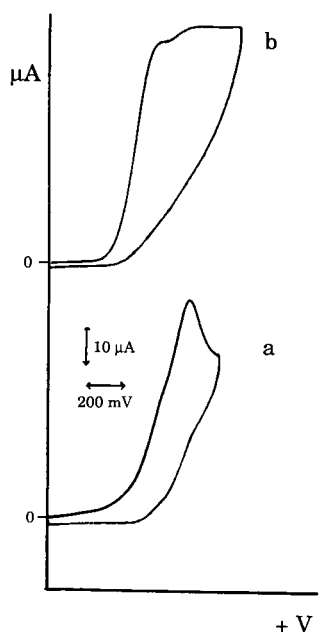


Figure 4. CV of **IV**. a) In neutral unbuffered medium. b) In the presence of pyridine; $[M] = 4.06 \cdot 10^{-3} M$; other conditions as in Figure 1.

Controlled Potential Electrolyses of **IV**.

a) Anhydrous Conditions.

CPE of **IV** as half wave potential (0.60 V) in unbuffered anhydrous acetonitrile shows a charge consumption equivalent to 2 F/M. Analyses (tlc) of the medium in the course of the electrolysis show the progressive disappearance of **IV**, and the quantitative formation of the already quoted **II**.

b) In the Presence of Water.

CPE of **IV** at the same anodic potential as in case a), but in the presence of water (IV/water molar ratio 1:20) leads to the quantitative formation of **III**.

Discussion of Results.

On the basis of the cyclovoltammetric behaviour of **I**, it is possible to deduce that also for this pyrrole, as in the case of the preceding ones, the first electrochemical oxidation leads to a monomeric radical cation $I^{\cdot+}$, which should have quite a fast evolution, since the cyclovoltammetric wave is totally irreversible, at a scan speed up to 500 mV sec^{-1} . On the basis of the products isolated from the reaction, the radical cation $I^{\cdot+}$ should evolve towards the formation of a dimeric intermediate, which at the same potential is further oxidized, leading, depending on the composition of the reaction medium, to **II** or **III**.

As already presented in the previous chapter, the chemical reduction of **III** quantitatively leads to the stable 3,3'-pyrrol dimer **IV**. Recalling that by oxidation of **IV** at the same potential as **I**, in anhydrous medium **II** is obtained, whereas in the presence of water **III** is obtained, it is

possible to deduce that **IV** is the intermediate of the oxidation of **I** to **II** or **III**. This result, together with the nmr and mass spectral data, allow us to assign to **II** the structure of 1,6a-dihydro-2,5,6a-triphenyl-3,4-diacetylbenzo[*g*]pyrrolo[3,2-*e*]indole.

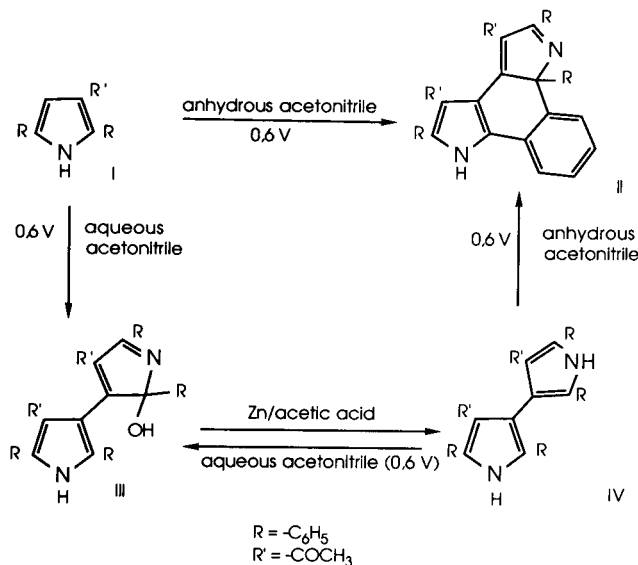
In fact, it was already observed in the case of triaryl substituted pyrroles [1] that intramolecular cyclization reactions can take place, by electrophilic aromatic substitution of pyrrole cations on aromatics linked to the position 2 of the pyrrole ring. The same reaction can reasonably supposed in the case of the formation of **II** from IV^{++} .

Of course, if water is present in the reaction medium, the electrophilicity of the pyrrole cation is blocked by the formation of an oxydrilated derivative **III**, to which, also on the basis of the nmr and mass spectral data, the structure of 4-acetyl-2-hydroxy-2,5-diphenyl-3-(4'-acetyl-2',5'-diphenyl-3'-yl)-2*H*-pyrrole can be assigned.

Conclusions.

The results obtained provide evidence that also in the case of 2,5-diphenyl-3-acetylpyrrole, as already seen for other triaryl-substituted pyrroles, it is impossible to stop the oxidative process at the stage of the dimer, since the one at the same anodic potential is further oxidized. If the reaction is performed in anhydrous medium the intramolecular cyclization is unavoidable, but in the presence of a moderate excess of water, the reaction can be oriented towards the formation of an oxygenated uncyclized dimer, from which the desired 3,3'-pyrrol dimer is easily obtained (see Scheme).

Scheme



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 a Perkin Elmer 299 spectrophotometers as Nujol mulls. 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-01SG-2 double focusing Mass Spectrometer at 75 eV (100 A). The analyses of the products of the electrolyses were performed with a Perkin Elmer Series 10 HPLC apparatus, with a UV-Vis LC 95 detector. The tlc determinations were performed on Merck DC-Alufolien Kieselgel 60 F254. Preparative chromatography was performed in columns of Fluka silicagel 60 F 254.

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.

2,5-Diphenyl-3-acetylpyrrole.

2,5-Diphenyl-3-acetylpyrrole was prepared by reaction of 2,5-diphenyl-3-pyrrolylmagnesium bromide with acetyl chloride in anhydrous ether according to a formerly described procedure [3].

Preparative Oxidation of I.

a) Anhydrous Medium.

Compound I (0.26 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 +0.60 V (*vs.* Ag-Ag⁺ 0.1M). The current intensity during the potentiostatic electrolysis drops from the initial value of 75 mA to the final value of 2 mA. The total amount of charge passed was 189 Coulombs, corresponding to 2F mole⁻¹. The anolyte was poured into water (200 ml) and neutralized with sodium hydrogen carbonate. The resulting mixture was extracted with diethyl ether (2 x 100 ml). The ethereal phase was dried and evaporated under reduced pressure. The residue was eluted on a silicagel (100 g) column. By elution with cyclohexane-ethyl acetate 80/20 II was isolated and crystallized from ethanol as yellow crystals mp 240-241° (0.17 g, product yield 65%); ir: 3230 cm⁻¹ broad (pyrrole NH), 1640, 1680 cm⁻¹ (2 x C=O); ^1H nmr (acetone-d₆): δ 2.00 (3H, s, CH₃), 2.20 (3H, s, CH₃), 7.20-7.70 (19 H, m, aromatic H), 11.43 (1H, b, pyrrole NH, exchangeable with deuterium oxide); ms: 518

(M⁺).

Anal. Calcd. for C₃₆H₂₆N₂O₂: C, 83.37; H, 5.05; N, 5.40. Found: C, 83.40; H, 5.02; N, 5.45.

b) In the Presence of Water.

Compound I (0.26 g, 0.001 mole) was dissolved in 30 ml of acetonitrile with tetrabutylammonium perchlorate 0.1 M, and added with 0.36 g of water (0.02 mole) and was electrolyzed at the anodic potential of +0.60 V (*vs.* Ag-Ag⁺ 0.1M). The electrolysis ended after the passage of 186 Coulombs. Following the procedure already described at point a), but eluting the residue of the ethereal extracts with cyclohexane-ethyl acetate 50/50, III was isolated and crystallized from acetone as yellow crystals, mp 210-211° (0.19 g, 70% product yield); ir: 3240 cm⁻¹ (pyrrole NH), 1640, 1660 cm⁻¹ (2 x C=O); ^1H nmr (DMSO-d₆): δ 1.65 (3H, s, CH₃), 1.72 (3H, s, CH₃), 7.00-7.75 (20H, m, aromatic H), 12.1 (H, b, pyrrole NH exchangeable with deuterium oxide); ms: 536 (M⁺).

Anal. Calcd. for C₃₆H₂₈N₂O₃: C, 80.57; H, 5.26; N, 5.22. Found: C, 80.69; H, 5.32; N, 5.08.

Reduction of III with Zn.

Compound III (0.52 g, 0.001 mole) was dissolved in 50 ml of acetic acid and, under continuous stirring, Zn powder was added until the solution becomes pale yellow. The suspension was filtered, poured into water, brought to alkalinity with ammonium hydroxide, and extracted with ethyl ether. The ethereal extract, after drying, was evaporated under reduced pressure. The residue was crystallized from ethanol (pale yellow crystals, mp 150-151°); ir: 3300 cm⁻¹ (pyrrole NH), 1635 cm⁻¹ (C=O); ^1H nmr (DMSO d₆): δ 2.00 (3H, s, CH₃), 7.03-7.85 (10H, m, aromatic H), 10.87 (1H, b, pyrrole NH exchangeable with deuterium oxide); ms: 520 (M⁺).

Anal. Calcd. for C₃₆H₂₈N₂O₂: C, 83.05; H, 5.42; N, 5.38. Found: C, 83.18; H, 5.48; N, 5.30.

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REFERENCES AND NOTES

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