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Electrooxidation Products of Methylindoles: Mechanisms and Structures

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Abstract: Electrochemical oxidation of 1-methylindole, 2-methylindole and 3-methylindole on a platinum anode in acetonitrile containing $NaClO_4$ has been studied. In any case no polymeric deposit on the working electrode was obtained. The identification of the obtained soluble products is described and the mechanisms of formation are discussed. Analogously to the case of unsubstituted indole, electrooxidized **1-3** react through positions 2 and 3. The non polymerization of **1** is explained with the formation of a tetramer which is oxidized to a stable radical cation and dication without undergoing further coupling reactions. Copyright © 1996 Elsevier Science Ltd

INTRODUCTION

Polyindoles obtained from anodic coupling of indoles are electroconductive materials[1] and display a noticeable interest since they have been considered in applications such as sensors[2] and because they may be model polymers for biopolymers such as melanines.[3]

In a recent paper[4] we studied variously substituted (cyano and carboxy) indoles and isomeric biindoles (2,3; 2,2'; 3,3'). It was suggested that the coupling of indole to polymer originates from initially formed 2,2'-dimers so that the resulting structure is a regular alternance of 2,2'-3,3' couplings, as shown in Figure 1. It was clearly demonstrated that the 1 position of indole is not involved in the polymerization process, contrary to what previously assumed.[5,6]

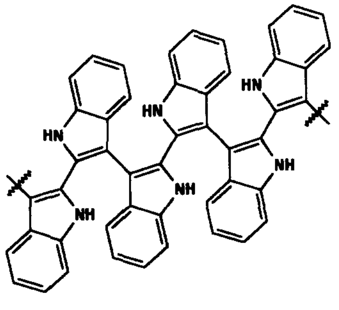


Figure 1: Chemical structure of polyindole from electrochemical oxidation of indole.

Although not reported in that paper, we also electrolyzed methyl-substituted indoles, *i.e.*, 1-methylindole **1**, 2-methylindole **2** and 3-methylindole **3**. None of them gave any polymeric deposit on the working electrode, but only soluble products that we did not identify. The same behaviour was previously observed by other authors.[5] As far as compounds **2** and **3** are concerned, the result can be obvious because one of the two polymerogenic positions is capped, while in principle 1-methylindole is able to polymerize.

This paper considers the electrochemical oxidation of **1-3** in acetonitrile + $NaClO_4$ in order to get a deeper insight into the mechanism involved and to account for the absence of polymerization in the case of **1**.

Electrochemical oxidation of 1-methylindole was previously reported in ethanol with bromide salt as supporting electrolyte,[7] but bromine insertion was involved in that case. To our knowledge no similar investigation has so far been performed in an "inert" medium such as acetonitrile with perchlorate salt as supporting electrolyte.

RESULTS AND DISCUSSION

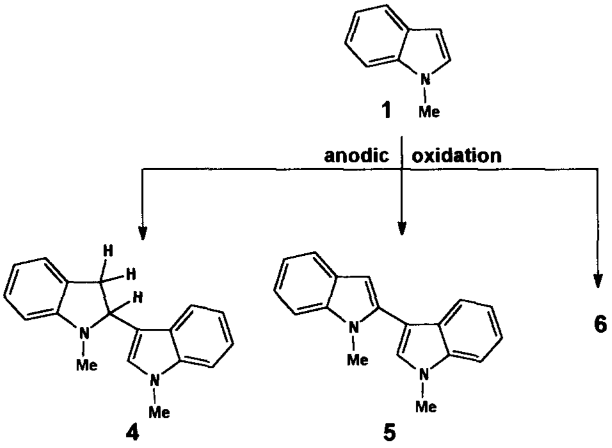
Cyclic voltammetry (CV) shows that all compounds **1-3** are oxidized irreversibly in acetonitrile (MeCN) at 0.8 V (**1**) and 0.65 V (**2** and **3**) (peak potentials at 100 mV/s vs. Ag/Ag^+), with a peak height depending on the water content. As for the generality of pyrrole-based polymers, the presence of added water (typically 1%) increases the oxidation peak height thanks to the proton scavenging action of water.[8] As an example, the peak height observed for **2** corresponds, in the absence of water, to the passage of 1 electron/molecule. In the presence of 1% water, the peak corresponds to the passage of 3, 2.5 and 1.8 electrons/molecule respectively.

Electrolyses performed at the peak potential required in any case the passage of less charge (1.3, 1.1 and 1.0 electrons/molecule respectively) than expected on the basis of the cyclic voltammetry peak heights, producing a brown, red and yellow solution respectively without any appreciable polymer deposit on the electrode. A likely explanation is that, although in the presence of water, acidity produced in the course of the electrolytic processes leads to the protonation, at least partially, of the starting products shifting their oxidation potential beyond that of polymerization. In fact, if the oxidation potential is reapplied after neutralization of the electrolytic bath with NaOH, the current restarts to flow. At the end of the electrolyses, after neutralization with NaOH, MeCN was evaporated and the residues extracted with CH_2Cl_2. In each case the crude material was chromatographed as described in the experimental section and the isolated products were characterized by means of ^{1}H NMR, ^{13}C NMR and electron impact mass spectrometry (EI-MS).

1-Methylindole **1**. Flash chromatography of the residue furnished, together with unreacted **1**, compounds **4**, **5** and a product **6** whose EI-MS spectrum shows the M^+ at *m/z* 518 corresponding to a 1-methylindole tetramer (Scheme 1A).

The structures of **4**[9] and **5**[10] were inferred by comparison with authentic samples; we prepared **4** according to the procedure described in the experimental section, while **5** was prepared as reported in the literature.[10]

The structure of **6** was unambiguously determined as follows. The ^{1}H NMR spectrum of **6** exhibits 4 methyl groups (two equal intensity signals in $CDCl_3$, and a single signal in DMSO-d_6) and two equivalent protons at 6.6 ppm, which is a chemical shift typical of indolic β hydrogens. The ^{1}H-coupled ^{13}C NMR shows the presence of a sp^2 CH group at 129.4 ppm which is typical for an α indolic carbon. Inspection of the ^{1}H,^{13}C heteronuclear COSY NMR spectrum through J^1 coupling disclosed that the carbon at 129.4 ppm is bonded to the hydrogen at 6.6 ppm. Furthermore both ^{1}H and ^{13}C spectra indicate that the tetramer has a symmetric structure. On the basis of these considerations, we drew for tetramer **6** the four possible structures depicted in Figure 2. We may observe that in **6a** and **6c**, the β positions in the external indole moieties are free, unlike **6b** and **6d** in which the unsubstituted positions are the α ones.



Scheme 1A

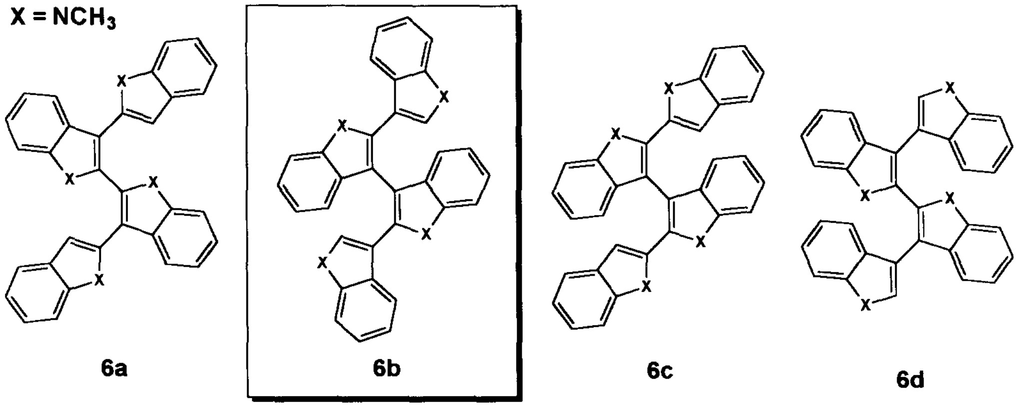


Figure 2: The four possible symmetrical structures of compound **6**.

Following the idea that **6** originates from the 2,3'-coupled dimer **5**, we performed the electrolysis of **5** under the same conditions employed for **1**. As expected, we isolated a tetrameric compound (*m/z* 518) that showed ^{1}H and ^{13}C NMR spectra identical to those of **6**. This result ruled out structures **6c** and **6d** for compound **6**, as they have no 2,3' bond between indolic units. In order to discern between structures **6a** and **6b** we synthesized compound **6a** as follows: 2,3'-biindole **5** was first lithiated with *n*-buthyllithium (*n*-BuLi) in the presence of tetramethylethylenediamine (TMEDA) and then oxidized with $CuCl_2$. The lithiation in the α position was checked by disappearance of the corresponding proton signal in the ^1H NMR spectrum (7.18 ppm in DMSO-d_6) after D_2O quenching of a lithiated sample. The $^1H,^{13}C$ heteronuclear COSY NMR spectrum of **6a** disclosed that the two hydrogens in the β position of the external indole systems (6.86 ppm) are linked to the equivalent carbons whose chemical shift is at 101.0 ppm.

Comparison of the two above mentioned COSY NMR spectra showed unambiguously that the structure of the tetramer obtained by electrochemical oxidation of **1** and **5** is **6b**. The high field resonance frequencies of the α and β indolic hydrogens in **6b** and **6a**, respectively, are due to the shielding effect of the spatially close benzene rings.

The dimerization of **5** with involvement of the 3 position to furnish **6b** can be also achieved by chemical oxidation with $CuCl_2$ in tetrahydrofuran in the presence of NaOH . A similar coupling reaction is described in the literature for indole[11] which gives 3,3'-biindole by reaction with $CuSO_4$ in pyridine.

A further confirmation of the structure of **6** comes from cyclic voltammetry experiments on **6a** and **6b**. Tetramer **6b** is oxidized in two one-electron reversible steps at E^0 = 0.13 and 0.36 V.

This behaviour is similar to that reported for the dimer 1,1'-dimethyl-3,3'-biindole **7**,[4,12] which has two external unsubstituted α indolic positions, analogously to **6b**. For both **6b** and **7** the oxidation processes are associated with the formation of stable radical cations and dications, as reported in Figure 3. In contrast,

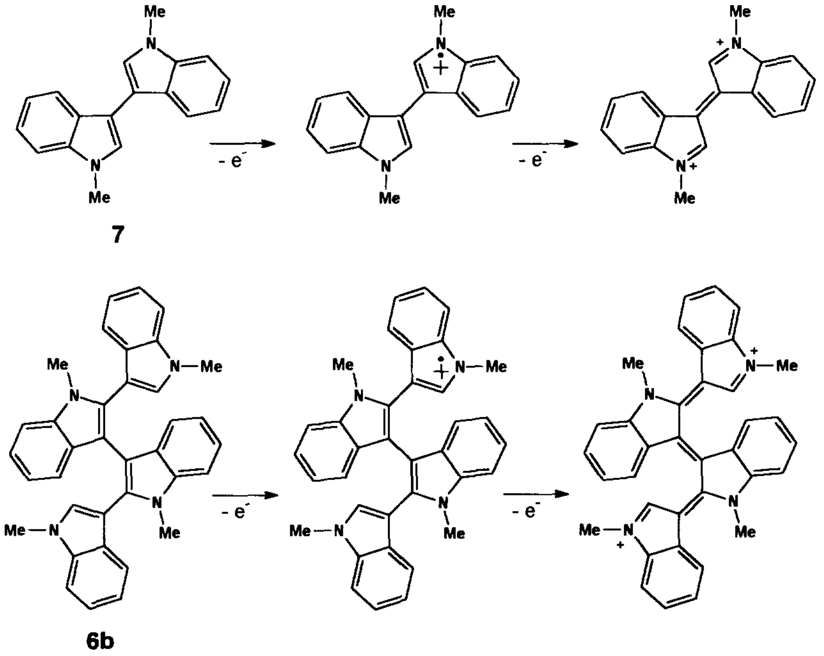
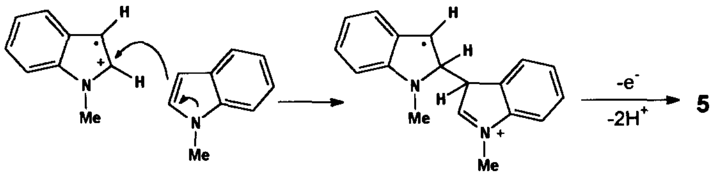


Figure 3: Oxidative pathways of compounds **7** and **6b**.

6a is oxidized in a one electron irreversible process at $E_p = 0.6$ V without production of electroactive species. This indicates that the radical cation is engaged in a degradative attack by the medium. The high reactivity of the radical cation of **6a** is due to the fact that the system has two free β indolic positions which are very reactive.[4]

As far as the formation mechanisms are concerned, the results indicate that **5** and **6b** come from oxidative processes. Since the dimer **5** is 2,3'-coupled, it is rather obvious that the initial step of coupling involves the 2 and 3 positions. This is in contrast with the 3,3' coupling expected on the basis of a radical-radical coupling mechanism, taking into account results of spin density calculations.[5] As pulse radiolysis studies have recently suggested,[13] the 2 position of 1-methylindole radical cation is an electrophilic point that attacks the electron rich site 3 in the neutral molecule producing the 2,3'-dimeric radical cation (Scheme 1B). Subsequent electrode oxidation and deprotonation give **5**.

The tetramer **6b** is likely to come from a 3,3'-radical coupling mechanism of the radical cation of the dimer **5**. Theoretical calculations, performed with the program GAUSSIAN92,[14] are in agreement with the higher spin density in the 3 indolic position of the above mentioned system (see Table). While the radical cation of 1-methylindole behaves as an electrophile, in the case of **5** the reactivity is localized at the radical centre, probably as a consequence of the greater delocalization of the positive charge in the dimer.

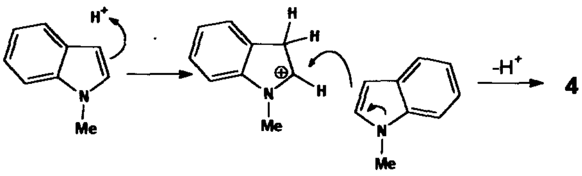


Scheme 1B

Table: Spin Densities (a.u.) in the Radical Cation of 1,1'-Dimethyl-2,3'-biindole **5** Calculated with the ROHF Method Using the 6-31G* Basis Set.

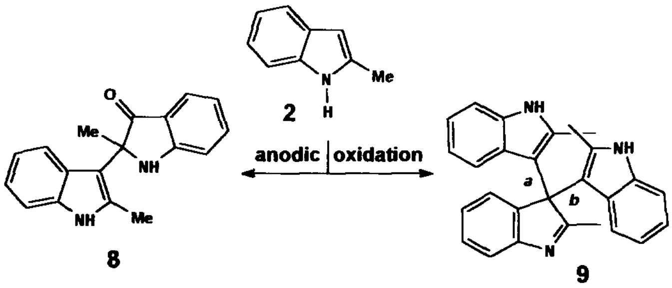
Geometry	PM3	ROHF/3-21G	Geometry	PM3	ROHF/3-21G
N(1)Me	0.000369	0.000860	N(1')Me	0.000491	0.000335
N-1	0.009506	0.024354	N-1'	0.028352	0.018522
C-2	0.128277	0.117154	C-2'	0.054094	0.034596
C-3	0.429302	0.534627	C-3'	0.066126	0.045959
C-4	0.068156	0.065612	C-4'	0.007043	0.005154
C-5	0.002693	0.001098	C-5'	0.001639	0.001603
C-6	0.075228	0.058428	C-6'	0.003633	0.002857
C-7	0.006505	0.009050	C-7'	0.002448	0.002087
C-8	0.025512	0.011238	C-8'	0.004464	0.002680
C-9	0.079748	0.056810	C-9'	0.003386	0.002704

As regards the formation of 4, it may be explained by a non oxidative dimerization (Scheme 1C). This is confirmed by the well known polymerization of indole itself which, under acid conditions, gives 3-(2-indolinyl)indole[15] through Smith's mechanism.[16] A further support to the above proposed mechanism is given by the fact that the procedure described for the synthesis of 4[9a] requires HCl treatment of 1 and that the electrolytic medium becomes increasingly acidic during coupling reactions. Moreover we found that 1-methylindole was converted to 4 by reaction with $HClO_4$ in MeCN. These conditions were chosen considering that the electrolysis was performed in the same solvent using $NaClO_4$ as supporting electrolyte.



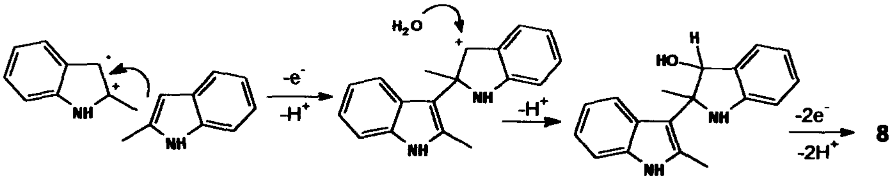
Scheme 1C

2-Methylindole 2. As far as the electrolysis of 2 is concerned together with unreacted 2, compounds 8 and 9 were isolated (Scheme 2A).



Scheme 2A

Compound 8 is known in the literature[17] and has been defined as a product of auto oxidation of 2-methylindole.[15] In our case the mechanism involved in its formation is likely to be the one reported in Scheme 2B. The radical cation of 2-methylindole behaves as an electrophile and reacts with the parent neutral

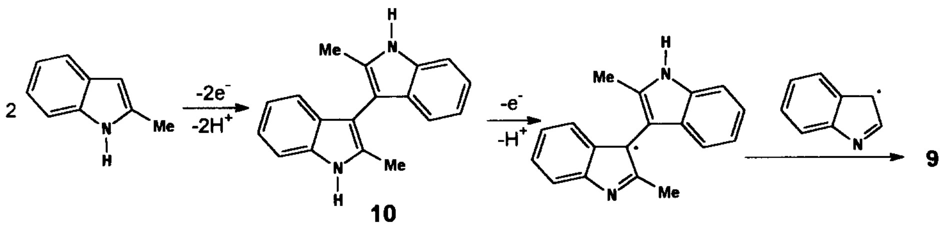


Scheme 2B

species to give a dimeric cation, after one electron oxidation and proton loss. Reaction with water and subsequent oxidation lead to compound **8**.

The structure of **9** was assigned on the basis of the following spectroscopic data. The EI-MS spectrum shows the M^+ at *m/z* 389 corresponding to three methylindole units minus four hydrogens. The ^1H NMR spectrum of **9** in DMSO-d_6 was recorded at different temperatures in the range 25-160 °C. At 25 °C there is a signal at 2.20 ppm attributable to the methyl group of the 3*H*-indole moiety, while a very broad signal in the range 1.70-2.20 ppm is attributable to the other two methyl groups. In the aromatic zone sharp signals between 7.20 and 7.60 ppm and broad ones between 6.45 and 7.15 ppm are observed. Increasing the temperature of recording, the broad signals become sharper and sharper till 130 °C. At this temperature the two methyls linked to the indole systems appear as two singlets at 1.89 and 1.97 ppm respectively and the aromatic protons are well defined. With a further increase of the temperature, the two singlets become larger and at 160 °C are merged into a very broad signal at around 1.96 ppm. Also some aromatic protons are badly defined at this temperature. This particular trend of the ^1H NMR spectrum with temperature is in agreement with the proposed structure **9**. Assuming a high rotational energy barrier around the ***a*** and ***b*** bonds indicated in Scheme 2A, the broad signal of the methyls, recorded at room temperature, comes from an envelope of many different signals belonging to all the possible stable rotational conformers. At 130 °C two sharp signals are recorded for the methyls linked to the aromatic systems; this is an evidence that, although enough energy is given for the rotational conformers to interconvert, the two methyl groups are always diastereotopic. This means that the rotation must be always concerted in order to allow conformers to interconvert through non symmetrical transition states. Raising the temperature to 160 °C, symmetrical transition states are allowed and the two methyls become enantiotopically correlated. The ^{13}C NMR spectrum registered at 50 °C agrees with the assigned structure. The methyl linked to the 3*H*-indole is at 19.00 ppm and the other two, which appear to be equivalent, are at 12.50 ppm. The spectrum shows the sp^3 quaternary carbon at 62.0 ppm, the sp^2 quaternary carbons of the benzene ring in the 3*H*-indole system at 145 and 154 ppm respectively, and the quaternary -C=N- at 185 ppm.

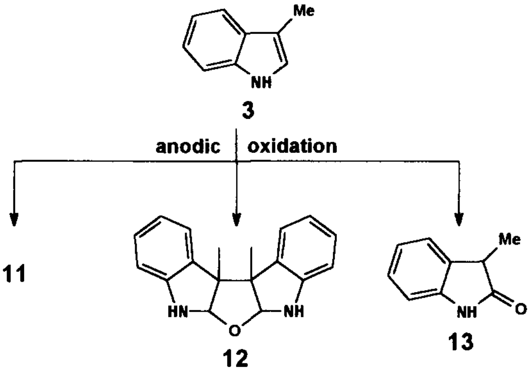
The mechanism we propose for the formation of **9** is reported in Scheme 2C. The first step is a 3-3' radical dimerization of the neutral radical originated by electrooxidation and proton loss of **2**. The 3,3'-dimer **10** is in its turn oxidized to the corresponding radical cation which, after proton loss, couples with the neutral radical of **2**, with involvement again of the 3 indolic position. The formation by coupling reaction of an sp^3 carbon at position 3 is analogous to the case of oxidative dimerization of 2,3-diphenyl substituted indoles.[18] Furthermore the high density of π electrons at the 3 position of the indole ring makes this position the most reactive.[19]



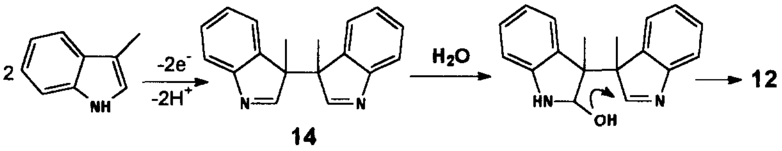
Scheme 2C

3-Methylindole **3**. In the case of electrooxidation of **3** we isolated, together with unreacted **3**, compounds **11**, **12** and **13** (Scheme 3A).

Compound **12** is known in the literature.[20] Its synthetic access is described through oxidation of **3** promoted by $CuCl_2$ in the presence of pyridine or by $FeCl_3$. We obtained **12** as a single diastereomer identical to that described in reference 20. The formation of **12** has also been claimed by pulse radiolysis of 3-methylindole.[13] The mechanism involved in its formation (Scheme 3B) is a 3,3' radical dimerization of the neutral radical of **3** to give **14**, followed by water addition.

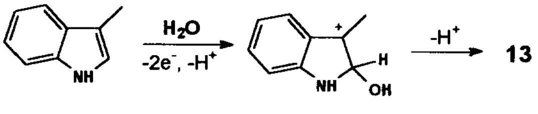


Scheme 3A



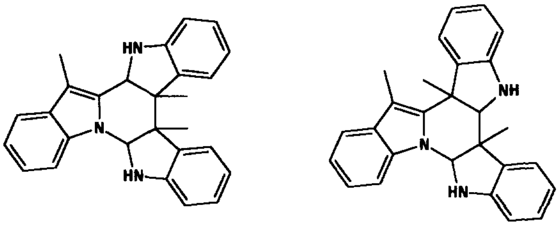
Scheme 3B

3-Methyl-2-oxiindole **13** is also a known compound that can be obtained by cyclization of propanoylphenylhydrazide[21] or by oxidation of 3-methylindole with different oxidizing agents, like peracetic acid.[22] The mechanism we propose for its formation is reported in Scheme 3C. The radical cation of **3**, which can dimerize through the β position as previously suggested, can also react with water in the α position and subsequently be further oxidized to give compound **13** after proton loss.



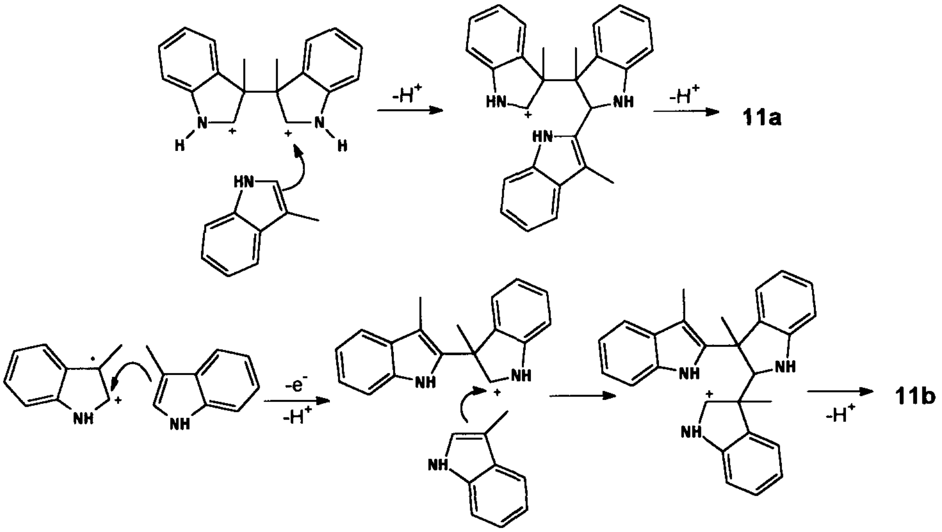
Scheme 3C

We could not unambiguously assign the structure of compound **11**. Its EI-MS spectrum shows the M^+ at *m/z* 391 corresponding to three methylindole units minus two hydrogens. The ^1H NMR spectrum in $CDCl_3$ shows the presence of three different methyl groups (one of which linked to an aromatic indole), two rather different aliphatic CH (one at 4.33 ppm as a singlet, and the other at 5.39 ppm as a doublet), and two different NH (the first at 4.21 ppm as a broad singlet, and the second at 4.65 ppm as a broad doublet). These two last signals disappear by D_2O exchange and the signal at 5.39 ppm becomes a singlet. In DMSO-d_6 the above mentioned two CH appear both as a doublet, while the signals of the two NH groups are shifted into those of the aromatic protons. Furthermore the spectrum exhibits twelve aromatic protons. The ^{13}C NMR spectrum is in agreement with the presence of three different methyls and two different sp^3 CH groups. Having these data in mind we drawn two possible structures for compound **11**, namely **11a** and **11b** in Figure 4. Both structures have three different methyls, one of which is linked to an aromatic indole ring, and two very different sp^3 CH groups. The mechanisms we can imagine for the formation of **11** are reported in Scheme 3D. For **11a**



11a **11b**

Figure 4: Suggested structures of compound **11**.



Scheme 3D

3-methylindole undergoes an electrophilic attack at the α position by the protonated **14** to give, after proton loss, a trimeric cationic system which cyclizes. For **11b** the radical cation of 3-methylindole behaves as an electrophile reacting with the parent neutral species to give a dimeric cation, after one electron oxidation and proton loss. This cation reacts with another neutral molecule to give a trimeric system which cyclizes. The indolic nitrogen usually does not behave as a nucleophile, but in both the above mentioned mechanisms the last step could be favoured by the formation of a six-member ring.

CONCLUSIONS

Analogous to the case of unsubstituted indole,[4] electrooxidized **1-3** react through positions 2 and 3 solely.

The non polymerization of **1** can now be explained. Instead of undergoing a radical-radical coupling, the corresponding radical cation behaves as an electrophile and reacts with a neutral counterpart to give the 2,3'-dimer, which does not polymerize, as previously observed.[4] The dimer **5** is oxidized to the corresponding radical cation which dimerizes to the tetramer **6b**. As shown by cyclic voltammetry, the radical cation of **6b** is stable enough to prevent further coupling reactions to give higher oligomers.

On the contrary, in the case of indole, the corresponding radical cation can undergo proton dissociation of the NH group and dimerizes through a radical-radical coupling mechanism to give the 2,2'-dimer, from which the polymer originates, together with the 3,3'-dimer.[4]

The radical-radical coupling mechanism of the corresponding neutral radicals is instead operating in the case of **2** and **3** and involves the 3 indolic position.

EXPERIMENTAL SECTION

The calculations were carried out with the program GAUSSIAN92.[14] *Ab-initio* spin densities values were obtained using the ROHF method with the 6-31G* basis set on both ROHF/3-21G and PM3 optimized geometries.

Electrochemical experiments were performed at 25°C under nitrogen in three electrode cells in acetonitrile + 0.1 M $NaClO_4$. The counter electrode was platinum. Reference electrode was silver/0.1 M silver perchlorate in acetonitrile (0.34 V versus SCE). A two-compartment cell was used in preparative electrolyses. The working electrode for cyclic voltammetry was a platinum minidisk electrode (0.003 cm^2) while a platinum sheet (15 cm^2) was used in preparative electrolyses. The voltammetric apparatus (AMEL, Italy) included a 551 potentiostat modulated by a 568 programmable function generator coupled to a 731 digital integrator.

All reactions of air- and water-sensitive materials were performed in flame-dried glassware under nitrogen atmosphere. Air- and water-sensitive solutions were transferred with double ended needles. The solvents used in the reactions were dried by conventional methods and freshly distilled under nitrogen. Acetonitrile was distilled twice over P_2O_5 and once over CaH_2. Compounds **5**,[10] **8**,[17] **12**[20] and **13**[21] were prepared according to literature prescriptions. All other chemicals were reagent grade and used as received.

All melting points are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Bruker AC 300 (300 MHz for ^1H, 75.47 MHz for ^{13}C) spectrometer; chemical shift values are given in ppm and are referred to tetramethylsilane. *J* values are given in Hz. Electron-impact mass spectra (EI-MS) were taken on a VG 7070 EQ-HF spectrometer. IR spectra were carried out on a Perkin-Elmer 1725X FTIR.

General procedure for the electrochemical oxidation of **1**, **2** *and* **3**. A solution of methylindole (650 mg, 4.96 mmol) in MeCN (25 cm^3) + 0.1 M $NaClO_4$ + 1% H_2O was exhaustively electrolyzed at 0.8 V, in the case of **1**, and 0.65 V, in the case of **2** and **3**, with the passage of 1.3, 1.15 and 1 F/mol respectively. After neutralization with NaOH, the resulting solution was evaporated to dryness. The residue was taken up with water and exhaustively extracted with dichloromethane. The combined organic phases were dried over Na_2SO_4 and the solvent was distilled off. The crude was product flash chromatographed on silica gel. The obtained compounds are reported below. The remaining part, consisting of extra-oxidized products as revealed by IR analysis, was in every case unmovable from the top of the column in the conditions used for the flash chromatography.

Electrochemical oxidation of 1-methylindole **1**. Electrolysis of **1** afforded a residue (580 mg) which was flash chromatographed with petroleum ether-ethyl acetate (9:1) to give, in elution order, **1** (105 mg), 1-methyl-3-(1-methyl-2-indolinyl)indole **4** (91 mg), 1,1'-dimethyl-2,3'-biindole **5** (110 mg) and 1,1',1'',1'''-tetramethyl-3,2':3',3'':2'',3'''-quaterindole **6b** (133 mg).

4: mp 134-136 °C (lit.,[9a] 133-135 °C); δ_H ($CDCl_3$) 2.65 (3H, s, indolinic Me), 3.15-3.35 (2H, m, CH_2), 3.80 (3H, s, indolic Me), 4.60 (1H, dd, *J* 8.8, *J* 11.2, *CH*CH_2), 6.52-7.70 (9H, m, aromatic protons); δ_C ($CDCl_3$) 32.7 (Me), 34.1 (Me), 37.8 (CH_2), 64.7 (*CH*CH_2), 107-128 (aromatic CH); *m/z* 262 (M+, 87%), 144 (100), 131 (33).

5: mp 140 °C (lit.,[10] 133-135 °C); δ_H ($CDCl_3$) 3.75 (3H, s, Me), 3.90 (3H, s, Me), 6.60 (1H, s, 3-H), 7.10-7.42 (7H, m, 2'-, 5-,5'-, 6-, 6'-, 7-and 7'-H), 7.63 (1H, d, *J* 7.7, 4- or 4'-H), 7.69 (1H, d, *J* 7.9, 4- or 4'-H); δ_C (DMSO-d_6) 30.9 (Me), 32.7 (Me), 100.0 (C-3), 105.5 (C-3'), 109.5 (C-7 or -7'), 110.5 (C-7 or -7'), 119.0-122.0 (C-4, -4', -5, -5', -6 and -6'), 126.8 (C-8 or -8'), 128.0 (C-8 or -8'), 129.2 (C-2'), 135.0 (C-2), 136.8 (C-9 or -9'), 137.5 (C-9 or -9'); *m/z* 260 (M+, 100%), 245 (15), 131 (80), 130 (70).

6b: mp > 240 °C (Found: C, 83.5; H, 5.9; N, 10.9. Calc. for $C_{36}H_{30}N_4$: C, 83.35; H, 5.8; N, 10.8%); δ_H (DMSO-d_6, T = 60 °C) 3.50 (12H, s, Me), 6.61 (2H, s, 2,2'''-H), 6.75-7.45 (16H, m, aromatic protons); δ_C (DMSO-d_6, T = 55 °C) 30.8 (2 x Me), 32.2 (2 x Me), 105.1 (C-3,3''' or -3',3''), 107.4 (C-3,3''' or -3',3''), 109.5 (C-7,7''' or -7',7''), 109.6 (C-7,7''' or -7',7''), 118.5-121.0 (C-4,4''', -4',4'', -5,5''', -5',5'', -6,6''' and -6',6''), 126.9 (C-8,8''' or -8',8''), 128.8 (C-8,8''' or -8',8''), 129.4 (C-2,2'''), 132.6 (C-2',2''), 136.1 (C-9,9''' or -9',9''), 137.1 (C-9,9''' or -9',9''); *m/z* 518 (M+, 100%), 259 (10), 84 (60).

Electrochemical oxidation of 2-methylindole **2**. Electrolysis of **2** furnished a residue (593 mg) which was flash chromatographed with petroleum ether-ethyl acetate (6:4) to give, in elution order, **2** (150 mg), **8** (173 mg) and **9** (121 mg).

8: mp 210 °C (decomp.) [lit.,[22] 212 °C (decomp.)]; ν_{max}(KBr pellet)/cm^{-1} 1680 (C=O); δ_H ($CDCl_3$) 1.93 (3H, s, Me), 2.48 (3H, s, Me), 5.02 (1H, br s, NH), 6.82-7.24 (5H, m, aromatic protons), 7.41 (1H, d, *J* 7.9, aromatic proton), 7.52 (1H, td, *J* 7.7 and 1.3, aromatic proton), 7.71 (1H, d, *J* 7.8, aromatic proton), 7.82 (1H, br s, NH); *m/z* 276 (M+, 85), 261 (97), 247 (75), 233 (100), 157 (90), 156 (70), 130 (60).

9: mp 201-203 °C (Found: C, 83.1; H, 5.8; N, 10.6. Calc. for $C_{27}H_{23}N_3$: C, 83.25; H, 6.0; N, 10.8%); δ_H (DMSO-d_6, T = 100 °C) 1.87 (3H, s, Me), 1.97 (3H, s, Me), 2.20 (3H, s, Me), 6.55-6.70 (3H, m, aromatic protons), 6.78 (1H, d, *J* 8.0, aromatic proton), 6.85-6.95 (3H, m, aromatic protons), 7.03 (1H, t, *J* 7.6, aromatic proton), 7.20-7.38 (4H, m, aromatic protons), 7.52 (1H, d, *J* 7.7, aromatic proton); δ_C (DMSO-d_6, T = 50 °C) 13.0 (2 x Me), 18.0 (Me), 62.0 (sp^3 C) 110-138 (aromatic carbons), 146.2 (indolenine C-8), 154.6 (indolenine C-9), 185.6 (C=N); *m/z* 389 (M+, 100%), 374 (50), 333 (27), 259 (12), 195 (15), 130 (12).

Electrochemical oxidation of 3-methylindole **3**. Electrolysis of **3** furnished a residue (586 mg) which was flash chromatographed with petroleum ether-ethyl acetate (8:2) to give, in elution order, **3** (105 mg), **11** (87 mg), **12** (118 mg) and **13** (115 mg).

11: mp > 240 °C (Found: C, 82.6; H, 6.4; N, 10.8. Calc. for $C_{27}H_{25}N_3$: C, 82.8; H, 6.45; N, 10.7%); δ_H ($CDCl_3$) 1.55 (3H, s, Me), 1.56 (3H, s, Me), 2.11 (3H, s, Me), 4.21 (1H, br s, NH), 4.33 (1H, s, CH), 4.65 (1H, br d, *J* 3.1, NH), 5.39 (1H, d, *J* 3.1, CH), 6.24 (1H, dd, *J* 1.2 and 7.9, aromatic proton), 6.39 (1H, dd, *J* 1.3 and 8.0, aromatic proton), 6.68-6.80 (2H, m, aromatic protons), 6.86-7.12 (4H, m, aromatic protons), 7.21 (1H, d, *J* 8.1, aromatic proton), 7.34-7.42 (3H, m, aromatic protons); δ_C (DMSO-d_6) 8.0 (Me), 20.5 (Me), 20.6 (Me), 36.6 (*C*Me), 37.7 (*C*Me), 54.3 (N*CH*C), 69.1 (N*CH*N), 104.0 (indole *C*Me), 110.1, 113.3, 114.4, 116.9, 117.8, 117.9, 118.9 and 120.2 (aromatic CH), 125.3 and 125.8 (aromatic C), 127.0 (double intensity), 127.2 and 127.4 (aromatic CH), 129.4, 134.0, 135.8, 141.1 and 143.3 (aromatic C); *m/z* 391 (M+, 100%), 376 (65), 260 (18), 245 (30), 158 (35).

12: mp 202 °C (lit.,[20] 202-204 °C), δ_H ($CDCl_3$) 1.32 (6H, s, Me), 4.90 (2H, br s, NH), 5.00 (2H, s, NH-*CH*-O), 6.55 (2H, dd, *J* 0.6 and 7.6, 4,4'- or 7,7'-H), 6.82 (2H, td, *J* 0.6 and 7.6, 5,5'- or 6,6'-H), 7.11 (2H, td, *J* 1.1 and 7.6, 5,5'- or 6,6'-H), 7.28 (2H, td, *J* 1.1 and 7.6, 4,4'- or 7,7'-H); δ_C ($CDCl_3$) 13.1 (Me), 43.5 (*CH*Me), 95.6 (O*CH*NH), 115.0, 119.5, 126.4 and 127.9 (aromatic CH), 128.7 and 141.5 (aromatic C); *m/z* 278 (M+, 30%), 263 (80), 260 (92), 245 (100), 232 (60), 158 (70), 130 (50).

13: mp 120 °C (lit.,[21] 121-123 °C); ν_{max}(KBr pellet)/cm^{-1} 1706 (C=O); δ_H ($CDCl_3$) 1.49 (3H, d, *J* 7.7, Me), 3.46 (1H, q, *J* 7.7, *CH*Me), 6.88 (1H, d, *J* 7.7, 4- or 7-H), 7.02 (1H, t, *J* 7.5, 5- or 6-H), 7.18-7.24 (2H, m, 4- or 7-H and 5- or 6-H), 7.90 (1H, br s, NH); δ_C ($CDCl_3$) 15.25 (Me), 40.89 (*CH*Me), 109.48, 122.39, 123.89 and 127.86 (aromatic CH), 131.21 and 140.92 (aromatic C), 180.67 (CO); *m/z* 147 (M+, 100%), 132 (35), 119 (75), 118 (50), 91 (30).

Electrochemical oxidation of 1,1'-dimethyl-2,3'-biindole **5**. A solution of **5** (500 mg, 1.92 mmol) in MeCN (25 cm^3) + 0.1 M $NaClO_4$ + 1% H_2O was exhaustively electrolyzed at 0.5 V (in cyclic voltammetry the oxidation peak potential is at 0.33 V). The current ceased to flow after the passage of 1.8 F/mol. After neutralization with NaOH, the resulting solution was evaporated to dryness. The residue was taken up with water and exhaustively extracted with dichloromethane. The combined organic phases were dried over Na_2SO_4 and evaporated to dryness. The crude product (450 mg) was flash chromatographed on silica gel with petroleum ether-ethyl acetate (9:1) to furnish **5** (154 mg) and the tetramer **6b** (135 mg, 27%).

1-Methyl-3-(1-methylindolin-2-yl)indole **4**. Dry HCl gas was bubbled into a solution of **1** (1.00 g, 7.63 mmol) in benzene (30 cm^3) at room temperature for 2 h, then the solvent was evaporated. The residue was treated with aqueous 10% NaOH and extracted with diethylether. The combined organic phases were dried and evaporated to give a crude product which was purified by flash chromatography on silica gel with petroleum ether-diethylether (95:5) to give the title compound as a white solid (200 mg, 20%), mp 134-136 °C (lit.,[9a] 133-135 °C).

1,1',1",1'"-Tetramethyl-2,3':2',2":3",2'"-quaterindole **6a**. *n*-BuLi (1.6 M in hexane; 0.86 cm^3, 1.38 mmol) was added dropwise to a solution of **5** (300 mg, 1.15 mmol) and TMEDA (0.4 cm^3) in benzene (10 cm^3). The reaction mixture was stirred overnight and diluted with THF (5 cm^3). $CuCl_2$ (77 mg, 0.57 mmol) was added in one batch and the reaction mixture was refluxed for 2 h, then treated with some drops of methanol, filtered and evaporated. The residue was purified by filtration on silica gel [petroleum ether-ethyl acetate (85:15)] followed by a reverse phase flash chromatography on silica gel RP-18 with MeCN-H_2O (9:1) to give **6a** as a pale yellow solid (82 mg, 27%), mp > 240 °C (Found: C, 83.2; H, 5.6; N, 10.9. Calc. for $C_{36}H_{30}N_4$: C, 83.35; H, 5.8; N, 10.8%); δ_H (DMSO-d$_6$, T = 50 °C) 2.90 (6H, br s, Me), 3.72 (6H, s, Me), 5.86 (2H, s, 3,3'"-H), 6.92-7.67 (16H, m, aromatic protons); δ_C (DMSO-d$_6$, T = 55 °C) 29.8 (2 x Me), 30.7 (2 x Me), 101.0 (C-3,3'"), 109.0 (C-3',3"), 109.2 (C-7,7'" or -7',7"), 110.8 (C-7,7'" or -7',7"), 118.5-122.5 (C-4,4'", -4',4", -5,5'", -5',5", -6,6'" and -6',6"), 126.7 (C-8,8'" or -8',8"), 127.4 (C-8,8'" or -8',8"), 129.7 (C-2,2'" or -2',2"), 133.7 (C-2,2'" or -2',2"), 137.0 (C-9,9'" or -9',9"), 137.3 (C-9,9'" or -9',9"); *m/z* 518 (M+, 100%), 400 (12), 259 (16), 91 (47).

1,1',1",1'"-Tetramethyl-3,2':3',3":2",3'"-quaterindole **6b**. A mixture of **5** (100 mg, 384 mmol), NaOH (15 mg, 384 mmol) and $CuCl_2$ (52 mg, 384 mmol) in THF (5 cm^3) was refluxed for 8 h. After filtration, the solvent was evaporated to dryness. Flash chromatography of the residue on silica gel with petroleum ether-ethyl acetate (85:15) yielded **6b** (15 mg, 15%), mp > 240 °C.

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