Radical intermediates in the peroxidation of indoles

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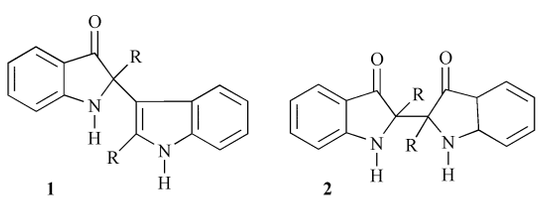
2-Substituted and 1,2-disubstituted indoles react with *m*-chloroperbenzoic acid and hydrogen peroxide in the presence of acid or calcium chloride affording 2- and 3-(3-oxoindol-2-yl)indoles; whereas 2,3-disubstituted indoles, reacting with the same oxidants, lead to the formation of products typical of pentaatomic ring opening. The reaction mechanisms are discussed in terms of electron transfer processes based on the redox potentials of the reagents, the Marcus theory and the reaction products distribution. The reactions of 1-hydroxy-2-phenylindole, which yield 2-phenylisatogen (2-phenyl-3-oxo-3*H*-indole 1-oxide), bisnitrone and 3-(3-oxoindol-2-yl)indole are also explained by an electron transfer mechanism depending on the oxidant and on the conditions of the reaction. The structures of 2- and 3-(3-oxoindol-2-yl)indoles have been elucidated by X-ray analysis.

Introduction

The peroxidation of indoles has been extensively studied since the beginning of the 1950's.[1,2] Most of the work was performed on 2-alkylindoles[3–5] whose dimers of type **1** and **2** were isolated.



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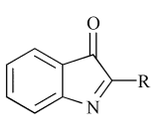

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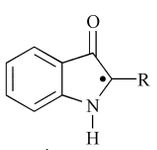

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The identification of these two compounds was the subject of discussion and controversy,[5] but in the end agreement was reached.[3] From the mechanistic point of view, compounds **1** and **2** were explained by the intermediate formation of 2-alkylindolone **3**.[3,5] The latter could truly be the intermediate in the formation of **1**; in fact **1** could derive from the nucleophilic attack of an indole molecule on indolone **3**.[6] However, the ionic mechanism proposed is highly unlikely to explain the formation of compound **2**,[5] which is more likely to arise from the dimerization of radical **4**.

Indoles are generally compounds with rather low oxidation potentials[7–9] and oxidants such as hydrogen peroxide in acids and peroxides are strong enough to promote an electron transfer process. When the peroxidation of indoles was first investigated, the concept of electron transfer processes was still not well known and many reactions involving radical intermediates were explained by ionic mechanisms. Starting from the 1960's, the development of electrochemistry in organic chemistry,[10] the introduction of the concepts of outer- and inner-sphere electron transfer and their rationalization by the Marcus theory,[11] the increasing technology concerning detection and study of radicals[12] have permitted the reinvestigation of the peroxidation of indoles from an electron transfer standpoint. An outer-sphere electron transfer between an electron donor (D) and an electron acceptor (A) occurs when the difference between the oxidation potential of the donor (E_{Dox}) and the reduction potential of the acceptor (E_{Ared}) measured *versus* the same reference electrode is less than 0.4 V.[13] An oxidant is usually also a good electrophile, just as a donor is a good nucleophile, so it is not always easy to distinguish which is the true mechanism involved in a reaction. In fact, both the mechanisms could be operating competitively at the same time. For the reasons described above, we have reinvestigated the peroxidation of differently substituted indoles with *m*-chloroperbenzoic acid and hydrogen peroxide in order to verify the involvment of a radical mechanism. In the present study, the redox potentials of the reagents, the Marcus theory, the reactions carried out in the presence and in the absence of oxygen and the reaction products distribution were all considered.

Results

The indoles studied in the present work were 2-alkylindoles (R′ = methyl, **5**; R′ = *tert*-butyl, **6**; R′ = phenyl, **7**), 1,2-dialkylindoles (R = R′ = methyl, **8**; R = ethyl, R′ = phenyl, **9**) (Scheme 1), 2,3-dialkylindoles (R = R′ = methyl, **14a**; R = R′ = phenyl **14b**; see Scheme 2) and 1-hydroxy-2-phenylindole **16**. All indoles were reacted in the presence of oxygen with *m*-chloroperbenzoic acid and hydrogen peroxide using trichloroacetic acid or calcium chloride as catalysts.

Reaction with *m*-chloroperbenzoic acid

The reactions were carried out at room temperature in dichloromethane. The 2-substituted **5**–**7** and the 1,2-disubstituted **8** and **9** indoles essentially afforded 3-(3-oxoindolin-2-yl)indoles **10** and 2,2′-biindolinyls **11**. The only exceptions were with indole **6** where compound **10** was not isolated, whereas the

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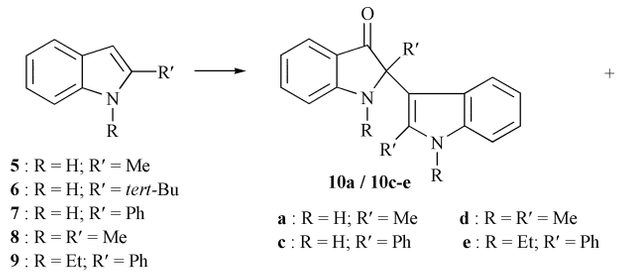
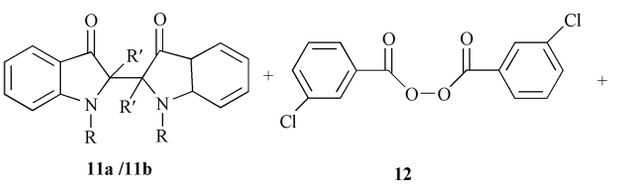


5 : R = H; R′ = Me
6 : R = H; R′ = *tert*-Bu
7 : R = H; R′ = Ph
8 : R = R′ = Me
9 : R = Et; R′ = Ph

10a / 10c-e

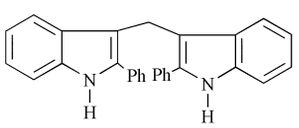
a : R = H; R′ = Me **d** : R = R′ = Me
c : R = H; R′ = Ph **e** : R = Et; R′ = Ph



11a /11b

12

a : R = H; R′ = Me
b : R = H; R′ = *tert*-Bu



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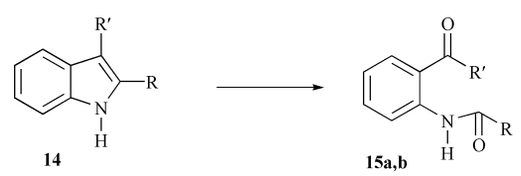
Scheme 1



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15a,b

a : R = R′ = Me
b : R = R′ = Ph

Scheme 2

dimers **11** were obtained only from indoles **5** and **6**. In the case of 2-phenylindole **7**, the bis(*m*-chlorobenzoyl) peroxide **12** was also isolated: the products obtained are shown in Scheme 1 and the yields are reported in Table 1.

The structures of compounds **10** were established by comparing their spectroscopic data with those of indolinone **10a** whose structure was determined by X-ray analysis. The IR spectra of compounds **10a** and **10c–e** show two typical absorptions at *ca.* 1700 cm^{-1} for the C=O group and at *ca.* 1600 cm^{-1} for the group represented by the sp^3 C-2, the nitrogen and the indolic benzene ring as described by Witkop[3] and others.[14] The only 2,2′-dimers isolated, compounds **11a** and **11b**, were identified by the X-ray analysis of indolinone **11a**. These compounds also show comparable IR absorptions since both kinds of dimers have the same typical groups. The ^1H NMR spectrum of compound **10e** shows two identical multiplets in the region 2.9–3.6 ppm, each multiplet corresponding to one of the hydrogens of the CH_2 group bonded to the aminic nitrogen, and two overlapping quartets in the region 3.85–3.95 ppm due to the CH_2 group of the indolic nitrogen. This particular pattern is most probably a consequence of the presence of an asymmetric center at the C-2. The detection of bis(*m*-chlorobenzoyl) peroxide **12** in the peroxidation of **7** was of great importance for the mechanistic interpretation; it was identified by its analytical and spectroscopic data. Compounds **14a** and **14b** undergo opening of the pentaatomic ring affording products **15a** and **15b**, respectively. These two compounds were identified by their analytical and spectroscopic data.

Table 1 Product distribution for the reactions of indoles with *m*-chloroperbenzoic acid and hydrogen peroxide under various conditions

Indole	Oxidant	Isolated products (yields [%])
5	$ClC_6H_4CO_3H$	**10a** (20); **11a** (61)
5	$ClC_6H_4CO_3H$ [a]	**10a** (50)
5	H_2O_2–H_3O^+	**10a** (49); **11a** (44)
5	H_2O_2–$CaCl_2$	**10a** (50)
6	$ClC_6H_4CO_3H$	**11b** (10)
6	H_2O_2–H_3O^+	**11b** (traces)
6	H_2O_2–$CaCl_2$	**11b** (traces)
7	$ClC_6H_4CO_3H$	**10c** (52); **12**
7	H_2O_2–H_3O^+	**10c** (35)
7	H_2O_2–$CaCl_2$	**10c** (15); **13** (32)
8	$ClC_6H_4CO_3H$	**10d** (30)
8	H_2O_2–H_3O^+	**10d** (81)
8	H_2O_2–$CaCl_2$	**10d** (40)
9	$ClC_6H_4CO_3H$	**10e** (45)
9	H_2O_2–H_3O^+	**10e** (40)
9	H_2O_2–$CaCl_2$	**10e** (30)
14a	$ClC_6H_4CO_3H$	**15a** (40)
14a	H_2O_2–H_3O^+	**15a** (40)
14a	H_2O_2–$CaCl_2$	**15a** (50)
14b	$ClC_6H_4CO_3H$	**15b** (95)
14b	H_2O_2–H_3O^+	**15b** (45)
14b	H_2O_2–$CaCl_2$	**15b** (20)
16	$ClC_6H_4CO_3H$	**17** (95)
16	H_2O_2–H_3O^+	**17** (40); **18** (37); **19** (10)
16	H_2O_2–$CaCl_2$	**18** (97)

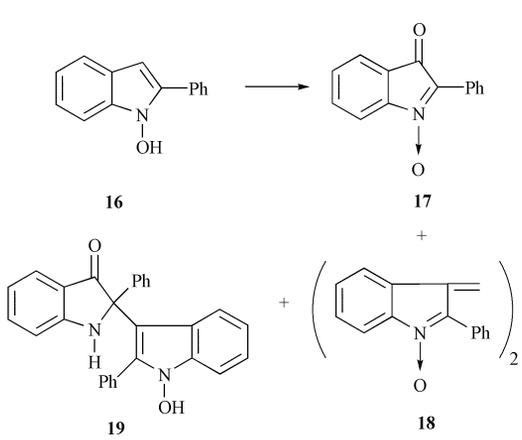
[a] In the absence of oxygen.

Reaction with hydrogen peroxide

All indoles (**5**–**9**, **14a** and **14b**) were reacted in acetone at room temperature in the presence of trichloroacetic acid and in methanol in the presence of $CaCl_2$ under reflux. In all the experiments, the products isolated using both H_2O_2–Cl_3CCOOH and H_2O_2–$CaCl_2$ were the same as those obtained from the reaction with *m*-chloroperbenzoic acid; the yields are reported in Table 1. Only with 2-phenylindole **7** was the diindolylmethane **13** isolated as the main product. Compound **13** was identified by its analytical and spectroscopic data and by comparison with a sample obtained from an independent synthesis (see Experimental).

Reaction of 1-hydroxy-2-phenylindole

1-Hydroxy-2-phenylindole **16** gave rise to phenylisatogen (2-phenyl-3-oxo-3*H*-indole 1-oxide) **17**[15] (Scheme 3) after



16

17

19

18

Scheme 3

oxidation with *m*-chloroperbenzoic acid in almost quantitative yield, whilst with hydrogen peroxide in the presence of $CaCl_2$ the bis-nitrone **18**[16] was isolated. In the reaction with hydrogen peroxide in the presence of trichloroacetic acid a mixture of

Table 2 Selected bond distances (Å) and angles (°) for compounds **10a** and **11a**

	10a	**11a**
O(1)–C(2)	1.230(3)	1.222(2)
N(1)–C(1)	1.477(3)	1.466(2)
N(1)–C(8)	1.372(3)	1.374(2)
N(2)–C(11)	1.395(3)	
N(2)–C(18)	1.381(3)	
C(1)–C(1)′[a]		1.559(3)
C(1)–C(2)	1.557(3)	1.548(2)
C(1)–C(12)	1.506(3)	
C(2)–C(3)	1.440(3)	1.455(2)
C(3)–C(8)	1.396(3)	1.402(2)
C(11)–C(12)	1.378(3)	
C(12)–C(13)	1.446(3)	
C(13)–C(14)	1.404(3)	
C(1)–N(1)–C(8)	110.9(2)	110.3(1)
C(11)–N(2)–C(18)	109.3(2)	
N(1)–C(1)–C(2)	101.7(2)	103.1(1)
C(1)–C(2)–C(3)	107.5(2)	106.9(1)
C(2)–C(3)–C(8)	108.0(2)	107.4(1)
N(1)–C(8)–C(3)	111.7(2)	112.2(2)
N(2)–C(11)–C(12)	108.8(2)	
C(11)–C(12)–C(13)	106.8(2)	
C(12)–C(13)–C(18)	107.4(2)	
N(2)–C(18)–C(13)	107.7(2)	

[a] A prime denotes a transformation of $1 - x, -y, -z$.

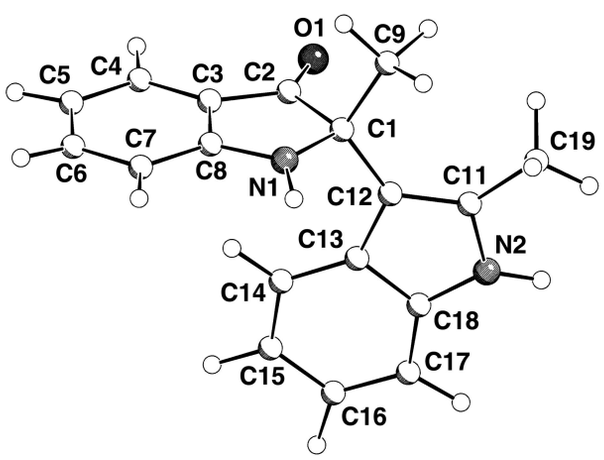


Fig. 1 A SCHAKAL perspective view of compound **10a**.

phenylisatogen **17**, bis-nitrone **18** and 3-(3-oxoindolin-2-yl)-indole **19** was obtained. Compounds **17**,[15] **18**[16] and **19**[17] were identified by comparison with authentic samples. Compound **19** was also oxidized with lead dioxide and the EPR spectrum of the new product was compared with that of the compound obtained from the reaction between 1-hydroxy-2-phenylindole and 2-phenyl-3*H*-indol-3-one.[17]

Molecular geometry of compounds 10a and 11a

Selected bond distances and angles are quoted in Table 2. A perspective view of **10a** and **11a** is given in Figs. 1 and 2, respectively.

Compound **11a** possesses a crystallographically imposed C_i symmetry, the inversion centre lying midway along the C(1)–C(1)′ bond (′ = $1 - x, -y, -z$). In both compounds bond distances and angles are in line with the hybridization expected for the atoms involved and in agreement with those of analogous compounds reported in the literature.[18] In **10a** the planar indole system [maximum deviation: 0.008(2) Å for C(14)] forms a dihedral angle of 91.5(1)° with the oxoindole system which shows significant distortion from planarity [maximum deviation: 0.060(3) Å for C(3)]. A small but significant deviation

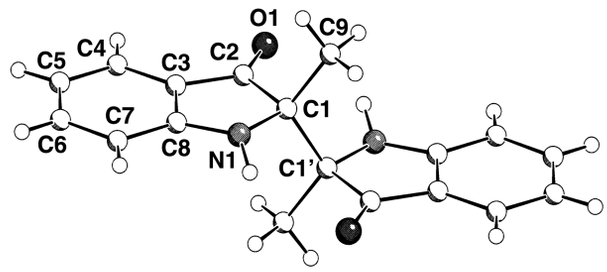


Fig. 2 A SCHAKAL perspective view of compound **11a**. A prime denotes a transformation of $1 - x, -y, -z$.

from planarity is also observed for the oxoindole systems in **11a** [maximum deviation: 0.008(2) Å for C(14)], which are strictly parallel to each other for symmetry requirements. The orientations assumed by the indole/oxoindole systems are consistent with the presence of weak attractive intramolecular C–H · · · N interactions (Table 3).

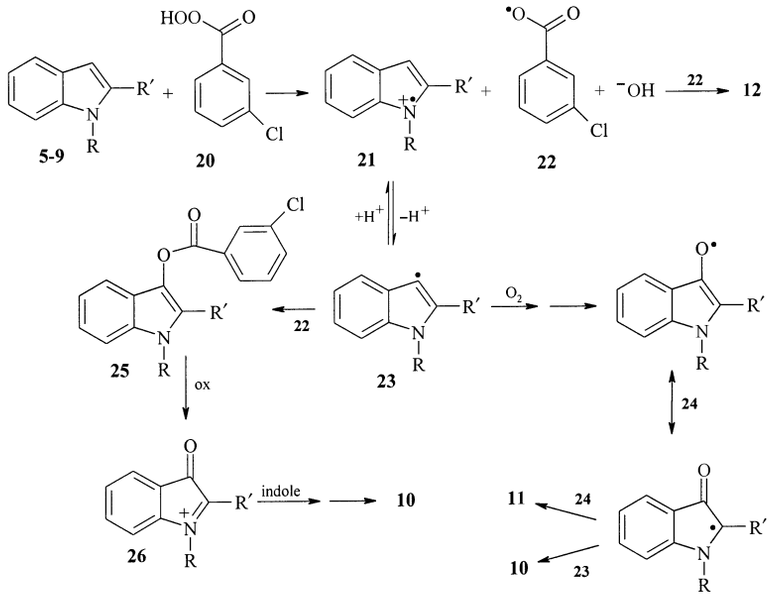
Molecular packing in both compounds is mainly determined by N–H · · · O and N–H · · · N intermolecular attractive interactions (Table 3). Other contacts are consistent with van der Waals interactions.

Discussion

As stated in the introduction, no clear indication is available in the literature on the mechanism (radical or ionic) of indole peroxidation. Only recently, an electron transfer process involving the formation of indole radical cations was admitted for the oxidation of indoles with copper chloride[19] and thallium acetate.[20] On the basis of the experimental results here described and from those obtained in a previous electrochemical study on the oxidation of indoles,[21] this mechanism could be considered the one implicated in the reaction with peracids and activated hydrogen peroxide. In fact, there is more than one piece of evidence to support this hypothesis. The studied indoles, except 1-hydroxy-2-phenylindole **16**, have oxidation potentials in the range 0.57–0.75 V *vs.* Ag/Ag^+ in CH_3CN (see Table 4), whereas *m*-chloroperbenzoic acid and H_2O_2 have reduction potentials more positive than those of all the studied indoles (Table 4).

On the basis of the Marcus theory, the electron transfer process is fully justified. In fact, the difference between the oxidation potentials of indoles **5**–**9** and the reduction potentials of *m*-chloroperbenzoic acid and hydrogen peroxide is, in all cases, less than 0.4 V, the upper limit for the feasibility of an electron transfer process. Considering that in an electron transfer process the entropy changes are neglegible, from the redox potentials of the reagents involved it could be deduced that all the reactions show a negative ΔG value and hence they are thermally favoured. Some of the reactions have been performed in the EPR cavity, but no signals were detected and this is in agreement with the low stability of the indole radical cation;[21] experiments based on the spin trapping technique failed. However, the reaction product distribution supports the radical mechanism. The isolation of bis(3-chlorobenzoyl) peroxide **12** can only be explained by admitting the coupling of two *m*-chlorobenzoyloxy radicals which arise from an electron transfer process in the first step of the reaction according to Scheme 4.

The indole radical cation **21** can give rise to a deprotonating equilibrium with the corresponding indolyl radical **23**, which readily reacts with atmospheric oxygen to give peroxy radical. This, through successive reactions affords the alkoxy radical **24** (see below). Indolyl radical **23** may couple with the benzoyloxy **22** leading to the formation of **25**. According to Scheme 4, only the 3-(3-oxoindolin-2-yl)indole can be explained by either the alkoxy radical **24** or by the benzoyloxy derivative **25**, and this latter path has been previously demonstrated.[21] On the other



Scheme 4

Table 3 Relevant hydrogen bonds in compounds **10a** and **11a**

	D–H/Å	H···A/Å	D···A/Å	D–H···A/°
Compound **10a**				
N(1)–H(1)···N(2)[a]	0.98	2.51	3.362(3)	146
N(2)–H(2)···O(1)[b]	0.99	1.96	2.925(2)	164
C(14)–H(14)···N(1)	1.07	2.89	3.347(3)	106
Compound **11a**				
N(1)–H(1)···O(1)[c]	0.91	2.69	3.297(2)	125
N(1)–H(1)···O(1)[d]	0.91	2.33	2.970(3)	127
C(9)–H(92)···O(1)	1.00	2.78	3.011(2)	94
C(9)–H(92)···N(1)[d]	1.00	2.66	2.967(3)	98

[a] $-1-x, -y, -z$. [b] $-1-x, -y, -z$. [c] $1+x, y, z$. [d] $1-x, -y, -z$.

Table 4 Redox potentials of the reagents

Compound	$E_{½}^{ox}$ *vs.* Ag/Ag^+ in CH_3CN	Reference
5	0.60	27
6	0.57	9
7	0.73	28
8	0.60	27
9	0.72	[a]
14a	0.48	[a]
14b	0.66	[a]
16	0.4	29
	$E_{½}^{red}$ *vs.* SCE in H_2O	
m-$ClC_6H_4CO_3H$	0.93	30
H_2O_2	1.33	31
H_2O_2–H_3O^+	1.77	31

[a] This paper.

hand, the formation of the 2,2′-dimer can only be justified by the dimerization of radical **24** and not through an intermediate such as **3** as predicted by the mechanism previously proposed.[3] Significant results in favour of this hypothesis were obtained in the reaction of 2-methylindole **5** with *m*-chloroperbenzoic acid in the presence and in the absence of oxygen; in fact in the experiment carried out in the absence of oxygen only the compound **10a** was isolated. The chemical behaviour of 2-substituted **5**–**7** and 1,2-disubstituted **8** and **9** indoles with *m*-chloroperbenzoic acid and hydrogen peroxide is that shown in Scheme 4, since the oxidants used have a similar oxidation power. The diindolylmethane **13**, isolated in the reaction of 2-phenylindole with hydrogen peroxide in the presence of calcium chloride, may be explained by the reaction between the indole and the formaldehyde derived from the oxidation of methanol, the reaction solvent. In fact, the same product is obtained in the reaction between 2-phenylindole and formaldehyde.

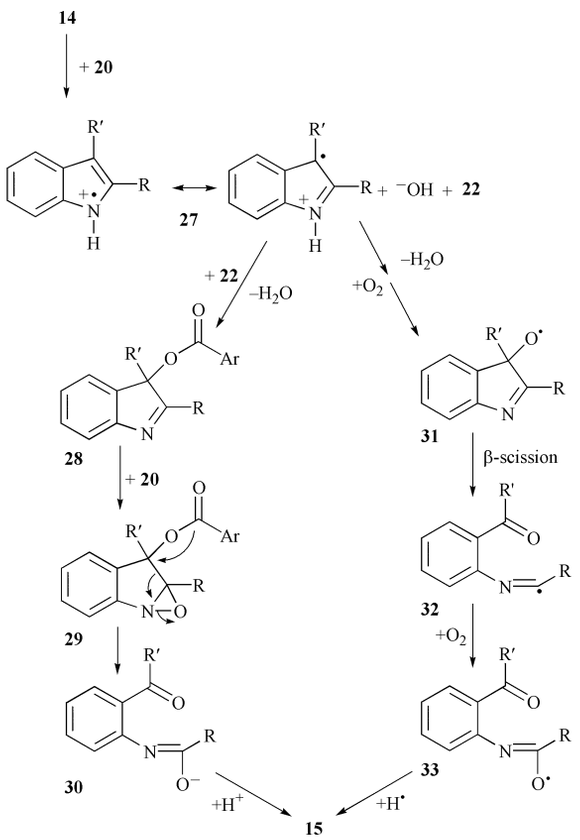
2,3-Substituted indoles **14a** and **14b** in the first step of the reaction may react similarly to other indoles on the basis of their oxidation potentials. The indole radical cation **27** formed can couple with the benzoyloxy radical **22** leading to the intermediate **28** which evolves to product **15** according to Scheme 5. Otherwise, it may interact with oxygen yielding alkoxy radical **31**, which undergoes β-scission to give radical **32**. Alkoxy **33** is subsequently formed which then leads to the final product.

Indeed, with these kinds of indoles the presence or the absence of oxygen may only modify the path taken but not the final reaction product and therefore it is difficult to establish which is the true pathway. The mechanism described in Scheme 5 could also be extended to the reactions with hydrogen peroxide. The interaction of indolyl radical with oxygen described in Schemes 4 and 5 has been well demonstrated recently;[22] the formation of alkoxy radicals arising from peroxy radicals formed in the interaction of indolyl radicals with oxygen is also a well documented reaction, previously discussed.[23]

1-Hydroxy-2-phenylindole **16** shows an oxidation potential which is *ca.* 300 mV less positive than those of other indoles. Thus, in this case, electron transfer certainly occurs in the reactions (compound **16** undergoes autoxidation in solution[24]).

Although radical **34** (Scheme 6) is an intermediate in all the studied oxidative conditions, the products formed are different in every case.

In particular, with *m*-chloroperbenzoic acid only phenylisatogen **17** was obtained, whereas with hydrogen peroxide in the presence of calcium chloride only the bis-nitrone **18** was isolated. It is our opinion that their different behaviour could likely be due either to the concentration of the radical intermediates formed or to their tendency to couple. In other words, if indolyl radical **35** reacts quickly with the aroyloxy radical **22**, the intermediate formed could give phenylisatogen **17**, through a mechanism similar to the one shown in Scheme 4 (see the transformation of **25** into **26**). In the reaction with hydrogen peroxide in the presence of calcium chloride, which was carried out in methanol under reflux, the dimerization of **35** could be favoured; in fact, only bis-nitrone **18** was isolated. In the reaction performed in trichloroacetic acid under atmospheric air, compound **19** was isolated together with phenylisatogen **17** and bis-nitrone **18**. In this case, the radical intermediate **36** could be formed by interaction of indolyl radical **35** with oxygen. This hypothesis is supported by the fact that 2,3-disubstituted-1-hydroxyindoles afford 2,3-disubstituted-3-hydroxyindole *N*-oxides by simple exposure of their solutions to air.[25] The formation of 3-(3-oxoindolin-2-yl)indole **19** could be reasonably explained by nucleophilic attack of 1-hydroxy-2-phenylindole **16** on phenylisatogen **17** under acid catalysis (Scheme 6, path b);[25] however, a mixture of these two compounds in the same reaction conditions did not lead to the formation of **19**. It is noteworthy that the interaction of **35** with **39** affords the intermediate **37**, which is further converted into **19** (Scheme 6, path a) by dehydroxylation, in agreement with the common behaviour of aromatic hydroxylamines in acidic medium in the presence of electron donors.[26]



Scheme 5

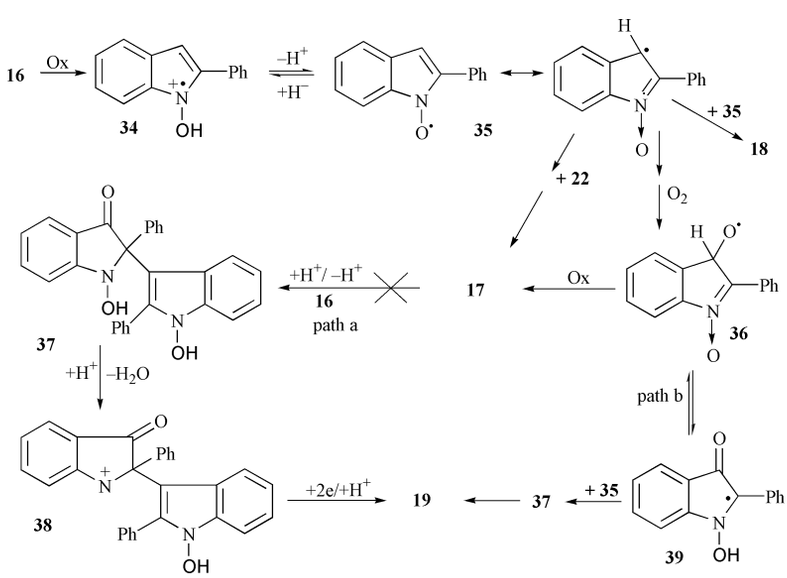
Experimental

Melting points are uncorrected and were measured with an Electrothermal apparatus. IR spectra were recorded in the solid state on a Nicolet Fourier Transform Infrared 20-SX Spectrophotometer equipped with a Spectra Tech. ^{1}H NMR spectra were recorded at room temperature in $CDCl_3$ solution on a Varian Gemini 200 spectrometer (TMS was taken as reference peak). Mass spectra were performed on a Carlo Erba QMD 1000 mass spectrometer. EPR spectra were run on a Varian E4 instrument.

2-*tert*-Butylindole **6**,[9] *N*-ethyl-2-phenylindole **9**[32] and *N*-hydroxy-2-phenylindole **16**[33] were synthesised according to the literature. Indoles **1**–**5**, **7**, **8**, **14a** and **14b**, *m*-chloroperbenzoic acid, hydrogen peroxide, calcium chloride, trichloroacetic acid were Aldrich products. All solvents were Carlo Erba or Aldrich RP-ACS grade.

Reaction of indoles with *m*-chloroperbenzoic acid. General procedure

A solution of *m*-chloroperbenzoic acid (1.2 mmol) in dichloromethane was added dropwise at room temperature to a stirred solution of indole (1 mmol) in the same solvent. The mixture was stirred for 1 h, then poured into 5% NH_4Cl and extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and evaporated to dryness; the residue was chromatographed on a silica gel column (eluant cyclohexane–ethyl acetate 8 : 2).



Scheme 6

Reaction of 2-methylindole 5 with *m*-chloroperbenzoic acid in the absence of oxygen

A sample of indole **5** in 5 mL of CH_2Cl_2 and *m*-chloroperbenzoic acid in 5 mL of solvent were separately introduced into the two legs of an inverted Y flask, saturated with argon and then mixed at room temperature. The reaction mixture was chromatographed on a small preparative silica gel column (cyclohexane–ethyl acetate 8 : 2), the main product was isolated and its mass spectrum was compared with that of the 3-(3-oxoindolin-2-yl)indole **10a**.

Reaction of indoles with hydrogen peroxide and trichloroacetic acid. General procedure

A solution of hydrogen peroxide (1 mmol) and tricloroacetic acid (1.2 mmol) in acetone was added dropwise to a stirred solution of indole (1 mmol) in acetone. The mixture was stirred for 2 h, poured into 5% NH_4Cl and extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and evaporated to dryness; the residue was chromatographed on a silica gel column (eluant cyclohexane–ethyl acetate 8 : 2).

Reaction of indoles with hydrogen peroxide and calcium chloride. General procedure

Indole (1 mmol) was dissolved in methanol (5 mL) and calcium chloride (10 mmol) was added. The stirred solution was heated at *ca.* 70 °C under reflux. At this temperature hydrogen peroxide (2 mmol) was added dropwise and the mixture was stirred, under reflux, for 4 h. The reaction mixture was then poured into 5% NH_4Cl and extracted with CH_2Cl_2. The organic layer was dried with Na_2SO_4 and evaporated to dryness; the residue was chromatographed on a silica gel column (eluant cyclohexane–ethyl acetate 8 : 2).

Synthesis of bis(2-phenylindol-3-yl)methane 13

Formaldehyde vapour from thermal decomposition of paraformaldehyde (800 mg) was bubbled through a solution of 2-phenylindole **7** (2 mmol) and toluene-*p*-sulfonic acid (traces) in ethanol (50 mL) cooled at *ca.* 7–8 °C. The mixture was stirred and after 2 h evaporated to dryness. The residue was chromatographed on a silca gel column (eluant cyclohexane–ethyl acetate 8 : 2).

2-Methyl-2-(2-methyl-1*H*-indol-3-yl)-1,2-dihydro-3*H*-indol-3-one (10a). Mp = 195–197 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.92 (s, 3H), 2.42 (s, 3H), 5.02 (br s, 1H), 6.86–6.92 (m, 2H), 6.98–7.12 (m, 2H), 7.22–7.28 (m, 1H), 7.38–7.40 (m, 1H), 7.48–7.6 (m, 1H), 7.68–7.75 (m, 1H), 7.88 (br s, 1H) ppm; FT-IR: ν/cm^{-1} = 3200, 1650 and 1600; MS (EI$^+$): *m*/*z* = 276 (55%), 261 (100); 247 (50), 233 (70), 157 (45).

2-Phenyl-2-(2-phenyl-1*H*-indol-3-yl)-1,2-dihydro-3*H*-indol-3-one (10c). Mp = 227–229 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 6.68–6.75 (m, 2H), 6.89–7.03 (m, 2H), 7.14–7.24 (m, 6H), 7.25–7.35 (m, 4H), 7.39–7.56 (m, 4H), 8.08 (br s, 1H) ppm; FT-IR: ν/cm^{-1} = 1670 and 1610; MS (EI$^+$): *m*/*z* = 400 (20%), 371 (95), 323 (25), 295 (60), 193 (100).

2-(1,2-Dimethyl-1*H*-indol-3-yl)-1,2-dimethyl-1,2-dihydro-3*H*-indol-3-one (10d). Mp = 155–157 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.90 (s, 3H), 2.28 (s, 3H), 2.86 (s, 3H), 3.64 (s, 3H), 6.71–6.80 (m, 2H), 6.93–7.01 (m, 1H), 7.08–7.16 (m, 1H), 7.42–7.58 (m, 3H), 7.66–7.7 (m, 1H) ppm; FT-IR: ν/cm^{-1} = 1670 and 1595; MS (EI$^+$): *m*/*z* = 304 (10%), 289 (5); 269 (40); 97 (40%); 69 (100).

1-Ethyl-2-(1-ethyl-2-phenyl-1*H*-indol-3-yl)-2-phenyl-1,2-dihydro-3*H*-indol-3-one (10e). Mp = 129–131 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 0.55 (t, 3H, *J* = 7.2 Hz), 1.15 (t, 3H, *J* = 6.9 Hz), 2.95–3.12 (m, ½ CH_2), 3.35–3.55 (m, ½ CH_2), 3.88 (q, 2H, *J* = 6.9 Hz), 3.89 (q, 2H, *J* = 6.9 Hz), 6.45–6.60 (m, 2H), 6.82–7.00 (m, 4H), 7.10–7.55 (m, 12H) ppm; FT-IR: ν/cm^{-1} = 2976, 1700 and 1615; MS (EI$^+$): *m*/*z* = 456 (45%), 427 (70); 351 (57), 221 (30%); 149 (77), 105 (60), 84 (100).

2-Methyl-2-(2-methyl-3-oxo-2,3-dihydro-1*H*-indol-2-yl)-1,2-dihydro-3*H*-indol-3-one (11a). Mp = 168–172 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.14 (s, 6H), 6.06 (br s, 2H), 6.8 (t, 2H, *J* = 7.5 Hz), 6.94 (d, 2H, *J* = 8.2 Hz), 7.49 (t, 2H, *J* = 7.3 Hz), 7.61 (d, 2H, *J* = 7.7 Hz) ppm; FT-IR: ν/cm^{-1} = 3300, 1650 and 1600; MS (EI$^+$): *m*/*z* = 146 (60%), 117 (95); 77 (80).

2-*tert*-Butyl-2-(2-*tert*-butyl-3-oxo-2,3-dihydro-1*H*-indol-2-yl)-1,2-dihydro-3*H*-indol-3-one (11b). Mp = 88–90 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 1.06 (s, 18H), 5.00 (br s, 2H), 6.82 (m, 4H), 7.44 (dd, 2H, *J* = 7.1 Hz and *J* = 1.3 Hz), 7.55 (dd, 2H, *J* = 7.7 Hz and *J* = 1.3 Hz) ppm; FT-IR: ν/cm^{-1} = 3370 and 1650; MS (EI$^+$): *m*/*z* = 187 (93%), 120 (89); 57 (71).

3-Chlorobenzoyl 3-chlorobenzeneperoxycarboxylate (12). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.25–7.32 (m, 3H), 7.33–7.48 (m, 2H), 7.48–7.64 (m, 3H) ppm; FT-IR: ν/cm^{-1} = 2924, 1736; MS (EI$^+$): *m*/*z* = 312 (5%), 311 (35), 310 (100), 165 (40), 77 (60).

2-Phenyl-3-[(2-phenyl-1*H*-indol-3-yl)methyl]-1*H*-indole (13). ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 4.57 (s, 2H), 6.82–6.9 (m, 2H), 7.05–7.12 (m, 2H), 7.20–7.45 (m, 10H), 7.56–7.6 (m, 4H), 8.02 (br s, 1H) ppm; FT-IR: ν/cm^{-1} = 3051 and 1604; MS (EI$^+$): *m*/*z* = 398 (100%), 321 (30); 204 (55), 193 (30).

***N*-(2-Acetylphenyl)acetamide (15a).** Mp = 70–75 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 2.02 (s, 3H), 2.67 (s, 3H), 7.12 (t, 1H, *J* = 7.1 Hz), 7.55 (t, 3H, *J* = 7.1 Hz), 7.88 (d, 1H, *J* = 8.4 Hz), 8.72 (d, 1 H, *J* = 8.4 Hz), 11.69 (br s, 1H) ppm; FT-IR: ν/cm^{-1} = 3225, 1674, and 1640; MS (EI$^+$): *m*/*z* = 177 (55%), 134 (100); 120 (95), 92 (70).

***N*-(2-Benzoylphenyl)benzamide (15b).** Mp = 78–82 °C; ^{1}H NMR (200 MHz, $CDCl_3$, 25 °C): δ = 7.08–7.18 (m, 2H), 7.50–7.71 (m, 12H), 8.07–8.12 (m, 3H), 8.89 (d, 1 H, *J* = 7.7 Hz), 11.9 (br s, 1H) ppm; FT-IR: ν/cm^{-1} = 3330, 1677, and 1634; MS (EI$^+$): *m*/*z* = 400 (20%), 371 (95), 323 (25), 295 (60), 193 (100).

Experimental data for the X-ray diffraction studies on crystalline compounds 10a and 11a [34]

Data were collected on a Siemens AED single-crystal diffractometer with graphite-monochromatized Cu-Kα radiation using $\theta/2\theta$ scan mode. Unit cell parameters were determined by automatic centering of 24 strong reflections ($25.0 < \theta < 39.5°$ and $21.5 < \theta < 35.0°$ for **10a** and **11a**, respectively) and refined by the least-squares method. The details of the X-ray data collection, structure solution and refinement are given in the supplementary material.[34] Three reflections were measured every 100 reflections collected as intensity and the orientation controlled. For both compounds no significant intensity decay was observed. Lorentz polarization but not absorption correction was applied. The crystal quality was tested by ψ scans showing that crystal absorption effects could be neglected. The structures were solved by direct methods using the SHELXS[35] computer program and refined with the SHELX93[36] computer program. Refinements were done by full matrix least-squares first isotropically and then anisotropically for all non-H atoms. The function minimized was $\Sigma w(\Delta F^2)^2$. Anomalous scattering corrections were included in all structure factor calculations.[37b] Scattering factors for neutral atoms were taken from ref. 37(*a*) for non-hydrogen atoms and from ref. 38 for H. The hydrogen atoms were located from difference Fourier maps and intro-

duced in the refinements as fixed atom contributors ($U_{iso} = 0.08$ Å^2). For both compounds the weighting scheme $w = 1/[\sigma^2(F_{o^2}) + (aP)^2]$ (with $P = (|F_o|^2 + 2|F_c|^2)/3$ was applied in the last stage of refinement, with a resulting in the value of 0.0108 and 0.0687 for **10a** and **11a**, respectively. All calculations were carried out on a Fujitsu Personal Computer equipped with an Intel Pentium II processor.

Crystal structure of 2-methyl-2-(2-methyl-1*H*-indol-3-yl)-1,2-dihydro-3*H*-indol-3-one 10a. $C_{18}H_{16}N_2O$, $M = 276.3$, triclinic, space group $P\bar{1}$, $a = 10.568(3)$, $b = 7.100(20)$, $c = 9.755(3)$ Å, $\alpha = 93.28(2)$, $\beta = 106.67(4)$, $\gamma = 95.05(3)°$, $V = 695.9(4)$ Å^3, $Z = 2$, $D_{calcd} = 1.319$ g cm^{-3}, $F(000) = 292$, λ(Cu-Kα) = 1.54178 Å, μ(Cu-Kα) = 6.18 cm^{-1}, crystal dimensions 0.07 × 0.12 × 0.29 mm. For 1549 unique observed reflections [$I > 2\sigma(I)$] the final R is 0.036 ($wR2 = 0.068$ for the 2410 unique reflections having $I > 0$ used in the refinement).

Crystal structure of 2-methyl-2-(2-methyl-3-oxo-2,3-dihydro-1*H*-indol-2-yl)-1,2-dihydro-3*H*-indol-3-one 11a. $C_{18}H_{16}N_2O_2$, $M = 293.3$, monoclinic, space group $P2_1/n$, $a = 6.155(3)$, $b = 20.219(5)$, $c = 6.556(2)$ Å, $\beta = 116.08(2)°$, $V = 723.8(5)$ Å^3, $Z = 2$, $D_{calcd} = 1.325$ g cm^{-3}, $F(000) = 308$, λ(Cu-Kα) = 1.54178 Å, μ(Cu-Kα) = 6.67 cm^{-1}, crystal dimensions 0.34 × 0.40 × 0.56 mm. For 1255 unique observed reflections [$I > 2\sigma(I)$] the final R is 0.042 ($wR2 = 0.137$ for the 1386 unique reflections having $I > 0$ used in the refinement).

Electrochemical measurements

A three-electrode multipolarograph AMEL 472 coupled with a digital x/y recorder AMEL 863 was employed for the voltammetric measurements, carried out at a pulsed (polarographic measurements) or static (cyclic voltammetries) glassy-carbon electrode in anhydrous MeCN containing tetraethylammonium perchlorate (TEAP) 0.1 mol L^{-1} as supporting electrolyte. Ag/$AgClO_4$ 0.1mol L^{-1}–MeCN/sintered glass disk/TEAP 0.1 mol L^{-1}–MeCN/sintered glass disk was used as reference,[39] and a platinum wire as counter electrode. These measurements were carried out starting from 1×10^{-3} mol L^{-1} solutions.

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