

## The Reaction of the $\text{CCl}_3\text{O}_2^\cdot$ Radical with Indoles

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In its reaction with indoles the  $\text{CCl}_3\text{O}_2^\cdot$  radical adds predominantly to the C(2)–C(3) double bond. Only a minor fraction accounts for one-electron oxidation. The 3-adduct undergoes rapid cleavage along the peroxidic bond while several rearrangement paths are indicated for the 2-adduct. In addition, the latter was found to break down into an indolyl radical cation in the presence of protons. The C(3) carbon adduct eventually reduces oxygen to  $\text{O}_2^{\cdot-}$ . The major end products formed from indoles unsubstituted at the 3-position are indoxyl compounds while substantial amounts of open amides are found among the end products derived from 3-methylindoles.

The  $\text{CCl}_3\text{O}_2^\cdot$  radical is considered to be a moderately strong oxidant.<sup>1–4</sup> In most of the cases studied it has been found to bring about one-electron oxidation. An exception is its reaction with tryptophan<sup>5</sup> where adduct formation was clearly discerned. However, even in cases where net one-electron oxidation is established the process is believed to occur *via* adduct formation followed by an inner-sphere electron transfer.<sup>6</sup> The latter mode of reaction is not unexpected given its predominant occurrence with the  $\text{OH}^\cdot$  radical.<sup>7</sup> The results reported for tryptophan suggested to us that the reaction of  $\text{CCl}_3\text{O}_2^\cdot$  with indoles could constitute an instructive area displaying the versatility of indole chemistry in the presence of peroxidating agents. In addition, the mixed solvent used allowed for a larger variation of indole concentration than would have been possible in aqueous solution.

### Experimental

The solvent used throughout this work consisted of 48% propan-2-ol, 48% water and 4%  $\text{CCl}_4$  (v/v) which prior to irradiation was saturated with oxygen. Henceforth we will simply refer to it as the solvent. The microtron accelerator<sup>8</sup> (producing 7 MeV electrons) and the computer-based pulse-radiolysis detection system<sup>9</sup> have been described elsewhere. Detection was achieved by optical spectroscopy and conductometry.<sup>10</sup> Dosimetry was performed by means of air-saturated KSCN solution ( $10^{-2}$  mol  $\text{dm}^{-3}$ ) using  $G_E = 2.22 \times 10^{-4}$  mol  $\text{J}^{-1}$  at 500 nm.<sup>11</sup> The equivalent conductivities of HCl, NaOH, and NaCl were taken from reference 12. Conductivity measurements on the indole solutions were performed either in unbuffered neutral solutions or after addition of specified amounts of  $\text{HClO}_4$  or NaOH.

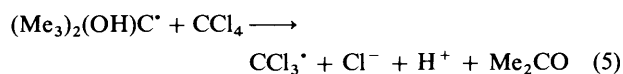
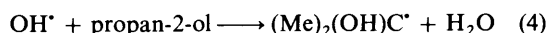
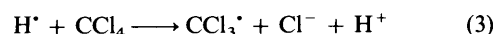
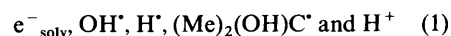
The dose per pulse was kept below 20 Gy when studying monomolecular radical rearrangements with rates around  $10^5$   $\text{s}^{-1}$ . Interception of  $\text{O}_2^{\cdot-}$  was by  $\text{C}(\text{NO}_2)_4$  and the absorbance of the resulting stable nitroform anion was measured at 350 nm.<sup>13</sup> The minor absorbance in the absence of  $\text{C}(\text{NO}_2)_4$  was corrected for. Due to the instability of tetranitromethane in the presence of base the yields of  $\text{O}_2^{\cdot-}$  in basic solutions were obtained upon rapid mixing of the basic sample with neutral  $\text{C}(\text{NO}_2)_4$  immediately before irradiation. The dose rate of gamma-irradiation (AECL  $^{60}\text{Co}$   $\gamma$ -source) was 0.49 Gy  $\text{s}^{-1}$ . Determination of  $\text{H}_2\text{O}_2$  was by means of  $\text{Cu}^{2+}$  catalysed luminol chemiluminescence after separation on an h.p.l.c. column<sup>14</sup> (Beckman RP-18 column). Uptake of  $\text{O}_2$  was measured with an oxygen electrode immersed in the reaction vessel during irradiation. The solubility of  $\text{O}_2$  in the present solvent was determined by gas chromatography (AGA argograph) to be

$1.5 \times 10^{-3}$  mol  $\text{dm}^{-3}$ . Carbon dioxide was measured gas chromatographically. The consumption of the parent indoles as well as the yield of the various end products were determined by h.p.l.c. Identification of the individual peaks was by comparison with authentic samples or by m.s. The total yield of 3-hydroxyindoles (indoxyls) was estimated from the optical absorbance around 400 nm using  $\epsilon_{\text{max}} = 275 \pm 25$   $\text{m}^2$   $\text{mol}^{-1}$ .<sup>15,16</sup> Among the products this absorbance is unique for 3-hydroxyindoles.<sup>15</sup> All yields in the tables are expressed as fractions of the initial value of  $G(\text{CCl}_3\text{O}_2^\cdot) = 6.2$ .

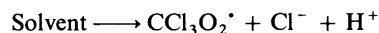
### Results and Discussion

Irradiation of the solvent gives rise to the following set of reactions.

Solvent  $\xrightarrow{\text{irradiation}}$



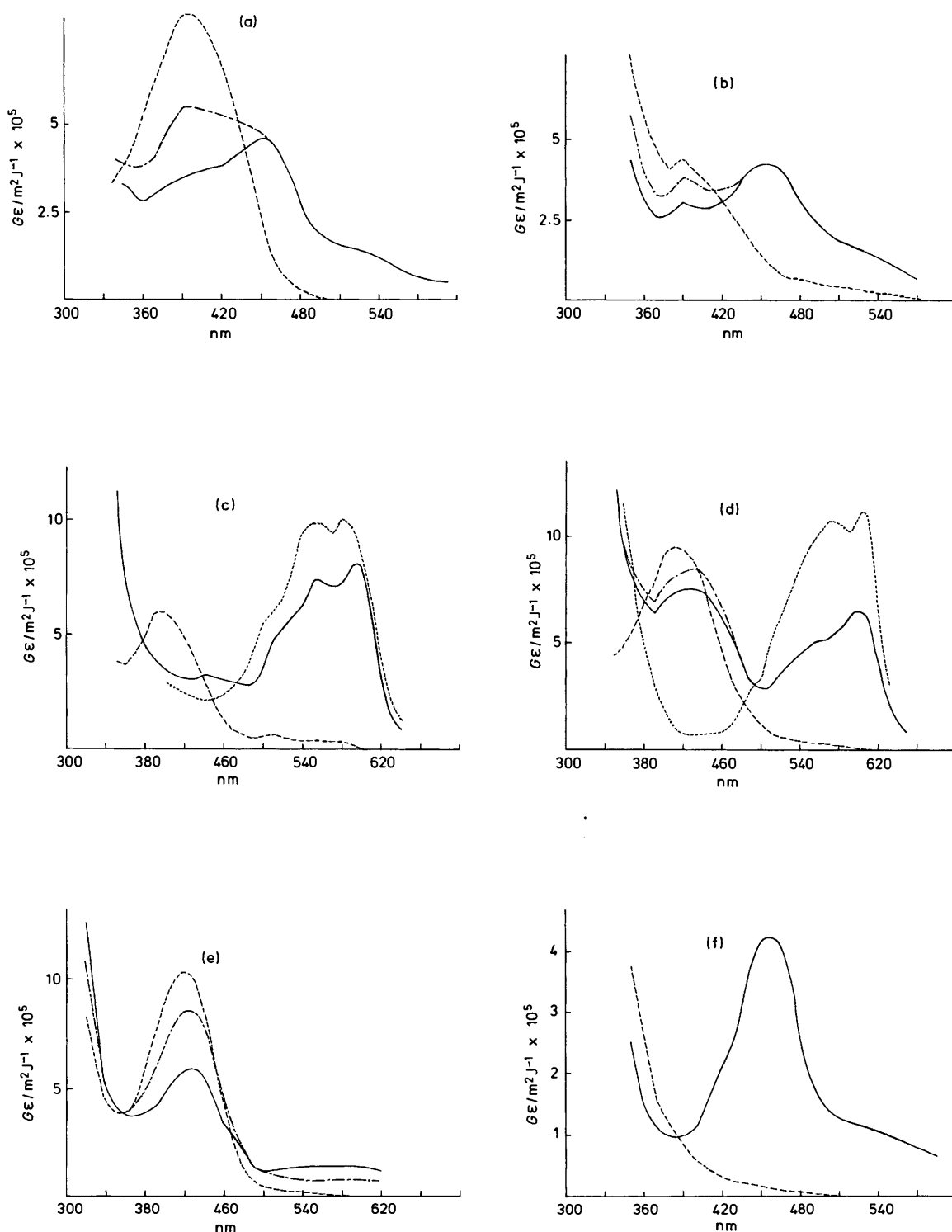
The overall reaction is:



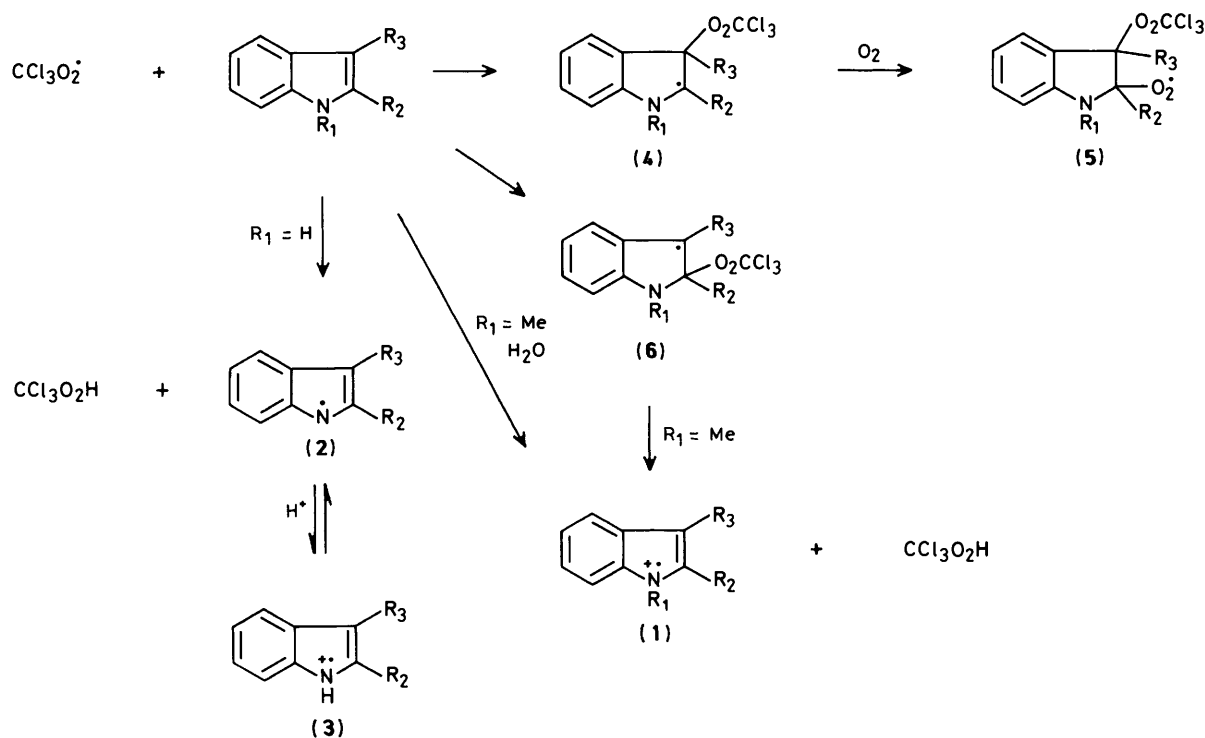
The value of  $G(\text{CCl}_3\text{O}_2^\cdot) = 6.2$  has been determined before<sup>12</sup> and other possible oxygen radical reactions with the solvent have been found to be negligible. The concentration of the added indoles was kept sufficiently high for their reaction rates with  $\text{CCl}_3\text{O}_2^\cdot$  to suppress the monomolecular rearrangement<sup>12</sup> ( $k = 3 \pm 1 \times 10^4$   $\text{s}^{-1}$ ) of the latter. Except when determining initial attack rates, the indole concentrations were chosen so as to have the initial attacks complete within 1  $\mu\text{s}$ .

*Spectral Observations.*—Before a detailed discussion it will be worthwhile to consider the transient spectra displayed in

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**Figure 1.** (a) Transient spectra of indole in neutral solvent. *Conditions:*  $2 \times 10^{-2}$  mol  $\text{dm}^{-3}$  indole and  $\text{O}_2$  saturation; full line:  $1.5 \times 10^{-6}$  s after eop (end of pulse); dotted line:  $2 \times 10^{-5}$  s after eop; broken line:  $2 \times 10^{-3}$  s after eop. (b) Transient spectra of indole in basic solvent. *Conditions:* same as (a) but  $10^{-2}$  mol  $\text{dm}^{-3}$  NaOH added; full line:  $1.0 \times 10^{-6}$  s after eop; dotted line:  $3 \times 10^{-6}$  s after eop; broken line:  $2 \times 10^{-3}$  s after eop. (c) Transient spectra of indole in acidic solvent. *Conditions:* same as (a) but  $0.1$  mol  $\text{dm}^{-3}$   $\text{HClO}_4$  added; full line:  $3 \times 10^{-6}$  s after eop; long broken line:  $2 \times 10^{-3}$  after eop; short broken line: transient spectrum of indole in  $\text{N}_2\text{O}$  saturated acidic water containing  $\text{Br}^-$ . (d) Transient spectra of 1-methylindole in neutral solvent. *Conditions:*  $2 \times 10^{-2}$  mol  $\text{dm}^{-3}$  1-methylindole and  $\text{O}_2$  saturation; full line:  $1.5 \times 10^{-6}$  s after eop; dotted line:  $2 \times 10^{-5}$  s after eop; long broken line:  $2 \times 10^{-3}$  after eop; short broken line: transient spectra of 1-methylindole in  $\text{N}_2\text{O}$  saturated neutral water containing  $\text{N}_3^-$ . (e) Transient spectra of 1-methylindole in basic solvent. *Conditions:*  $2 \times 10^{-2}$  mol  $\text{dm}^{-3}$  1-methylindole,  $10^{-2}$  mol  $\text{dm}^{-3}$  NaOH and  $\text{O}_2$  saturation. full line:  $5 \times 10^{-7}$  s after eop (when the 580 nm absorbtion has its maximum); dotted line:  $1 \times 10^{-5}$  s after eop; broken line:  $2 \times 10^{-3}$  s after eop. (f) Transient spectra of 3-methylindole in neutral solvent. *Conditions:*  $10^{-2}$  mol  $\text{dm}^{-3}$  3-methylindole and  $\text{O}_2$  saturation; full line:  $2 \times 10^{-6}$  s after eop; broken line:  $2 \times 10^{-3}$  s after eop.



Scheme 1.

Figures 1(a)–(f). These spectra were recorded upon pulse radiolysis of the  $O_2$ -saturated solvent containing any one of the three representative indoles *i.e.* indole, 1-methylindole or 3-methylindole. The spectra obtained from 2-methylindole (similar to indole) and from 2,3-dimethylindole and tryptophan (both resembling that of 3-methyl indole) have been omitted. The following general observations can be made concerning these spectra. In the neutral solvent 1-methylindole displays a distinct absorbance peaking at around 600 nm. As it is similar to the spectrum of the 1-methylindolyl cation (1) (Scheme 1) formed in water we assign it to the latter. For the other indoles we suggest the long wavelength tail above 500 nm to pertain to the corresponding neutral indolyl radical (2) (Scheme 1).

In the presence of indoles unsubstituted at the 3-position both the intermediate and final spectra feature broad absorbances in the vicinity of 400 nm. By comparison with the spectra of authentic samples the final spectra can be shown to derive from indoxylic compounds. Now, an absorbance at 400 nm characterises a carbonyl group separated by a saturated carbon from the amino group in the five-membered ring. As such it should not be overly sensitive to the unpaired electron on the carbon. In fact,  $O_2$  addition will be shown to occur at the C(2) position resulting in a peroxy radical (5) (Scheme 1) where the unpaired electron is isolated from the ring system. As this absorbance is not observed with 3-methylindoles we ascribe the intermediate absorbance around 400 nm to an indoxylic radical formed from a 3-( $CCl_3O_2$ )-indole adduct (4). This assignment will be discussed in more detail.

The absorbance at *ca.* 460 nm is clearly seen with 3-methylindole and indole itself. In the latter case, base pronounces this absorbance by suppressing the corresponding absorbance at lower wavelengths. The 460 nm peak is apparently absent in 1-methylindole spectra. Clearly, the species absorbing in this spectral region is indicative of a rather delocalised radical. In addition, it appears unreactive towards oxygen as oxygen addition to form a peroxy radical would have blocked delocalisation.

One-electron oxidation of 4- and 5-hydroxyindoles resulted

in radical species which did not absorb at *ca.* 460 nm. This observation, coupled with a failure to detect any end product substituted on the benzene ring, would seem to rule out adducts to the six-membered ring. Therefore, we tentatively assign the 460 nm absorbance to the 2-( $CCl_3O_2$ )-indole adduct (6) which will be discussed later.

Addition of acid is seen to enhance the amount of the indolyl radical cation (3) in all indoles except 1-methylindole. In contrast, in the presence of base, the amount of the neutral indolyl radical (2) seems unaffected while the indolyl radical cation of 1-methylindole is strongly reduced. Finally, while the amount of indoxylic species absorbing around 400 nm diminishes in base (with the exception of 1-methylindole), the amount of 2-adducts (6) remains essentially the same.

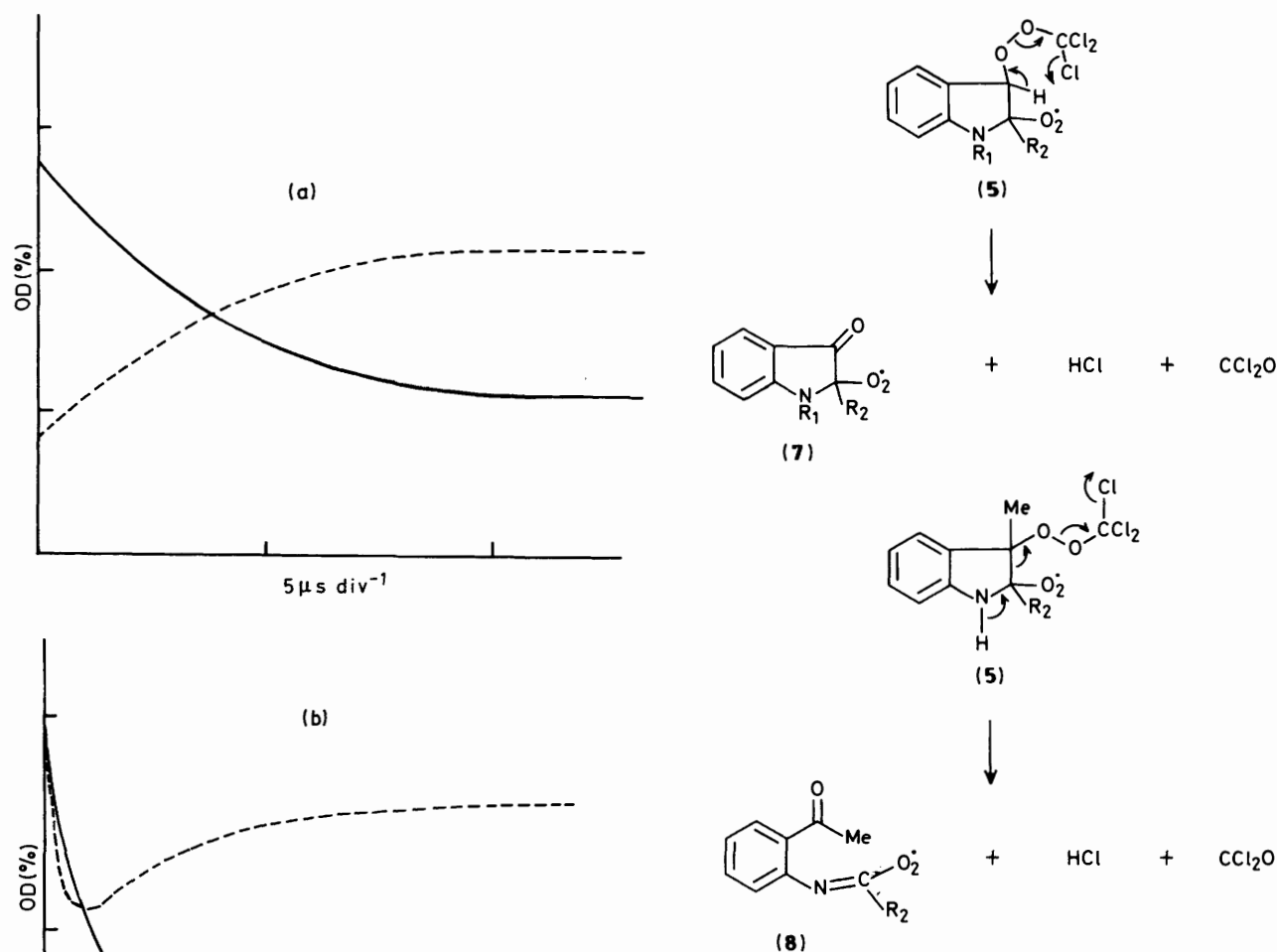
*One-electron Oxidation vs. Adduct Formation.*—The initial attack. The addition of  $CCl_3O_2^\bullet$  to the indoles appears to proceed along the three parallel channels depicted in Scheme 1. When the indole concentration is varied over a small range the exponential build up of the transient absorbance is proportional to the indole concentration. From this concentration dependence the second-order rate constants for attack of the  $CCl_3O_2^\bullet$  radical on the indoles were evaluated (Table 1). While this variation is small the rates are found to reflect the trend in the measured redox potentials<sup>17</sup> in the indole series. However, as the spectra in Figures 1(a)–(f) have revealed, one-electron oxidation accounts for only a minor fraction of the overall reaction. A similar finding with tryptophan as the substrate has been reported in a previous publication.<sup>5</sup>

*Evidence for the indolyl radical.* With 1-methylindole as the parent the partial production of the indolyl radical cation (1) on reaction with  $CCl_3O_2^\bullet$  has been confirmed by the following observations. Addition of ascorbate or  $ClO_2^-$  results in a first-order decay of the 600 nm absorbance, the decay being proportional to addend concentration. This behaviour is characteristic of a strong oxidant which the indolyl radical cation is certainly expected to be.<sup>17</sup> Furthermore, when base is present, the above absorbance decays proportionally to  $[OH^-]$ .

**Table 1.** Pulse radiolytically obtained rate constants.

Indole	$k_{(\text{CCl}_2\text{O}_2 + \text{ind})}^a/\text{mol}^{-1} \text{dm}^3 \text{s}^{-1}$	$k_{(460 \text{ nm})}^b/\text{s}^{-1}$	$k_{(400 \text{ nm})}^c/\text{s}^{-1}$	$k_{(\text{cond})}^d/\text{s}^{-1}$
Indole	$(1.0 \pm 0.2) \times 10^8$	$1.6 \times 10^5$	$(4.0 \pm 0.3) \times 10^5$	$(4.2 \pm 0.3) \times 10^5$
<i>N</i> -Methylindole	$(1.1 \pm 0.2) \times 10^8$	—	$(5.0 \pm 0.5) \times 10^5$	$(4.5 \pm 0.7) \times 10^5$
2-Methylindole	$(6 \pm 1) \times 10^8$	$3.5 \times 10^5$	$(2.3 \pm 0.3) \times 10^5$	—
3-Methylindole	$(9 \pm 1) \times 10^8$	$2.4 \times 10^5$	—	$(4 \pm 1) \times 10^5$
2,3-Dimethylindole	$(1.2 \pm 0.1) \times 10^9$	$4.8 \times 10^5$	—	$(3.5 \pm 0.5) \times 10^5$
Tryptophan	$(8.5 \pm 1.5) \times 10^7$	$10^5$	—	—

<sup>a</sup> Initial attack rate. <sup>b</sup> First-order decay at 460 nm in basic solutions. <sup>c</sup> Rate of the build up at 400 nm in neutral solutions. <sup>d</sup> Rate of the increase of conductivity in neutral solutions. <sup>e</sup> Reference 5.

**Scheme 2.**

**Figure 2.** (a) Kinetic traces obtained from pulse radiolysis of 3-methylindole. Conditions:  $10^{-2} \text{ mol dm}^{-3}$  3-methylindole;  $8 \times 10^{-4} \text{ mol dm}^{-3} \text{H}^+$  and  $\text{O}_2$  saturation; broken line: decay at 460 nm; full line: build up at 580 nm; left hand scale  $0.01 \text{ OD unit div}^{-1}$ . (b) Same as (a) but  $10^{-2} \text{ mol dm}^{-3} \text{H}^+$ ; left hand scale  $0.03 \text{ OD units div}^{-1}$ .

The same reaction occurs in alkaline water, where the indolyl radical cation (1) from 1-methylindole (generated quantitatively by  $\text{N}_3^{\cdot-}$  or  $\text{Br}_2^{\cdot-}$ ) was observed to form a pseudo-base with

$\text{OH}^-$ . As for the rate of formation of the 600 nm absorbance in the neutral solvent, at concentrations greater than  $5 \times 10^{-3} \text{ mol dm}^{-3}$ , its build up occurred in two steps. The first part was proportional to the concentration of 1-methylindole whereas the additional increase was independent of concentration ( $k \approx 10^6 \text{ s}^{-1}$ ). This second phase presumably reflects a radical adduct as the precursor. It has already been pointed out that the red tail in the spectra of the other indoles can be assigned to the neutral indolyl radicals (2). This assignment is supported by the observation that upon addition of acid to  $< 10^{-4} \text{ mol dm}^{-3}$  with respect to  $\text{H}^+$ , the spectrum corresponding to cation (3) appears. Due to the small size of the indolyl radical absorbances it was not possible to establish whether their appearance contained a delay phase or not. Finally, assuming equal extinction coefficients in water and the mixed solvent for the

**Table 2.** Various yields estimated from the transient spectra observed after pulse irradiation of oxygenated 48% propan-2-ol, 48% water and 4% CCl<sub>4</sub> solutions containing various indoles.

Indole	Conc./mol dm <sup>-3</sup>	H <sup>+</sup> /OH <sup>-</sup> /mol dm <sup>-3</sup>	Indolyl radical/ radical cation (%)	Total indoxyl (%)	G <sub>ε<sub>460 nm</sub></sub> /10 <sup>-5</sup> m <sup>2</sup> J <sup>-1</sup>	O <sub>2</sub> <sup>-•</sup> (%)
Indole	10 <sup>-2</sup>	10 <sup>-1</sup> H <sup>+</sup>	69 ± 8	44 ± 4	—	—
Indole	10 <sup>-2</sup>	neutral	15 ± 4	51 ± 6	4.6	<5
Indole	10 <sup>-2</sup>	10 <sup>-2</sup> OH <sup>-</sup>	17 ± 4	<28	4.4	42
N-Methyl	10 <sup>-2</sup>	10 <sup>-1</sup> H <sup>+</sup>	51 ± 5	33 ± 5	—	—
N-Methyl	10 <sup>-2</sup>	neutral	51 ± 5	39 ± 5	none	<5
N-Methyl	4 × 10 <sup>-2</sup>	10 <sup>-3</sup> OH <sup>-</sup>	51 ± 5	60 ± 6	none	22
N-Methyl	10 <sup>-2</sup>	10 <sup>-2</sup> OH <sup>-</sup>	—	64 ± 8	none	—
2-Methyl	7 × 10 <sup>-3</sup>	10 <sup>-1</sup> H <sup>+</sup>	58 ± 5	30 ± 4	—	—
2-Methyl	7 × 10 <sup>-3</sup>	neutral	26 ± 4	48 ± 5	3.9	12
2-Methyl	7 × 10 <sup>-3</sup>	10 <sup>-2</sup> OH <sup>-</sup>	27 ± 4	<19	3.8	64
3-Methyl	5 × 10 <sup>-3</sup>	10 <sup>-1</sup> H <sup>+</sup>	77 ± 8	—	—	—
3-Methyl	10 <sup>-2</sup>	neutral	17 ± 2	—	5.2	11
3-Methyl	7 × 10 <sup>-3</sup>	10 <sup>-2</sup> OH <sup>-</sup>	17 ± 2	—	5.3	38
2,3-Dimethyl	3 × 10 <sup>-3</sup>	10 <sup>-1</sup> H <sup>+</sup>	89 ± 6	—	—	—
2,3-Dimethyl	4 × 10 <sup>-3</sup>	neutral	32 ± 4	—	4.2	20
2,3-Dimethyl	4 × 10 <sup>-3</sup>	10 <sup>-2</sup> OH <sup>-</sup>	28 ± 4	—	4.3	20
Tryptophan	10 <sup>-2</sup>	10 <sup>-2</sup> OH <sup>-</sup>	24 ± 4	—	5.9	51

indolyl radical (2) or its cation (3) their percentage with respect to the initial yield of CCl<sub>3</sub>O<sub>2</sub><sup>•</sup> was estimated. These values are compiled in Table 2.

*The 3-adduct.* With indoles bearing a hydrogen atom in the 3-position the absorbance build up around 400 nm is a first-order process unrelated to the dynamic events at longer wavelengths [*cf.* the temporal change in Figures 1(a) and (d)]. The rate constants extracted from this build-up are presented in Table 1. This spectral event is consistent with the 3-adduct (4) (transparent around 400 nm) transforming into an indoxyl radical (7) according to Scheme 2. As detailed earlier, species (7) should absorb around 400 nm by way of the indoxyl chromophore. The simultaneous expulsion of HCl and phosgene will be confirmed later in the discussion on conductivity experiments. The amount of the final indoxyl products is estimated by assuming an average extinction coefficient of 275 ± 25 m<sup>2</sup> mol<sup>-1</sup> (see Table 2).

In the case of 3-methylindoles no build up of indoxyl absorbances can be observed. By way of analogy, however, we assume that the 3-CCl<sub>3</sub>O<sub>2</sub>-indole adduct (4) is formed. The latter presumably decomposes by fission of the C(2)–C(3) bond (Scheme 2). The ring-opened radical (8) is a feasible precursor to the open amides (7) detected in substantial quantities in irradiated samples of 3-methyl- and 2,3-dimethyl-indole (see Table 5).

*The 2-adduct.* The assignment of the 460 nm absorbance to the 2-CCl<sub>3</sub>O<sub>2</sub>-indole adduct (6) rests on circumstantial evidence. Consistent with this assignment is the steric hindrance of a methyl group to the approach of CCl<sub>3</sub>O<sub>2</sub><sup>•</sup> (reflected by the trend in the observed G<sub>ε</sub> values at 460 nm; see Table 2). In the presence of protons the yield of the indolyl radical cation (3) is dramatically enhanced. At the same time the breakdown of the 460 nm species is accelerated in the same way as the rate of production of the indolyl radical cation. In Figures 2(a) and (b) the change with time in the absorbances at 600 and 460 nm, respectively, is presented at two different acidities. This is evidence that the 2-adduct of 3-methylindole (6) is the precursor of the indolyl radical cation (3) in acidic solutions. Figure 3 shows the maximum yields of the cation and the 2-adduct as a function of proton concentration. We note that the 2-adduct is an intermediate in a consecutive reaction sequence where its formation rate is constant while its breakdown is accelerated by protons [see Figures 2(a) and (b)]. Therefore, its total yield is obtained after kinetic correction of its maximum measured yield. All indoles studied (except 1-methylindole) display the

above behaviour. Thus, the estimated yield of the indolyl radical cation in acidic solutions (presented in Table 2) is a measure of the sum of indolyl radical (2) and 2-adduct (6) initially formed.

In neutral or basic solutions the 460 nm absorbance decays in a first-order manner giving rise to species which also absorb, albeit more weakly, at ca. 460 nm. This indicates that at least some of the breakdown products from the 2-adduct still retain the benzylic character of the 2-adduct. The first-order rate constants measured at 460 nm are presented in Table 1. For 1-methylindole, protons increase the rate of formation but not the yield of indolyl cations (1). This finding suggests the existence of an intermediate which we assume to be the 2-adduct. If so, a methyl group in the 1-position would seem to bar every mode of decomposition except an inner-sphere electron transfer. On the other hand, the 2-adducts of indoles possessing H in the 1-position are proposed to break down the species (9) and (10) (Scheme 3).

*The yield of O<sub>2</sub><sup>-•</sup> and adduct balance.* Addition of tetranitromethane (TNM) to basic indole solutions followed by pulse irradiation results in the appearance of a strong absorption at 350 nm which characterises the formation of the nitroform anion after one-electron reduction of TNM. Recalling well known precedents<sup>18</sup> we assume that the reducing agent is O<sub>2</sub><sup>-•</sup>, formed in the base-catalysed breakdown of a peroxy radical. The last entry in Table 2 shows that the yield of superoxide varies with the indole. Most significantly, there is a good inverse correlation between the O<sub>2</sub><sup>-•</sup> yield in base and the corresponding yield of the indolyl radical cation (3) in acidic solution (Figure 4). Allowing for some uncertainty in the estimated yields the correlation is essentially quantitative. The conclusion from Figure 4 is that while the indolyl radical cation (3) in acid is a measure of the quantity of 2-adduct formed, the 3-adduct is the precursor of O<sub>2</sub><sup>-•</sup>. The expulsion of O<sub>2</sub><sup>-•</sup> is proposed to occur from a peroxy radical of the 3-adduct (7) or (8) (Scheme 4). The 3-adduct is an α-amino radical which is known to reduce O<sub>2</sub> to O<sub>2</sub><sup>-•</sup> through the intermediacy of a peroxy radical.<sup>18</sup> In contrast, the apparent inertness of the 2-adduct towards O<sub>2</sub> is reasonable for a delocalised benzylic radical.

The reduction of the indoxyl absorbance in basic solutions of indole [see Figure 1(b)] is probably connected with the expulsion of O<sub>2</sub><sup>-•</sup> as proposed in Scheme 4. This process presupposes a hydrogen atom in the 1-position; formation of a C=N double bond (11) would be expected to destroy the characteristic indoxyl absorbance. Although we lack spectral

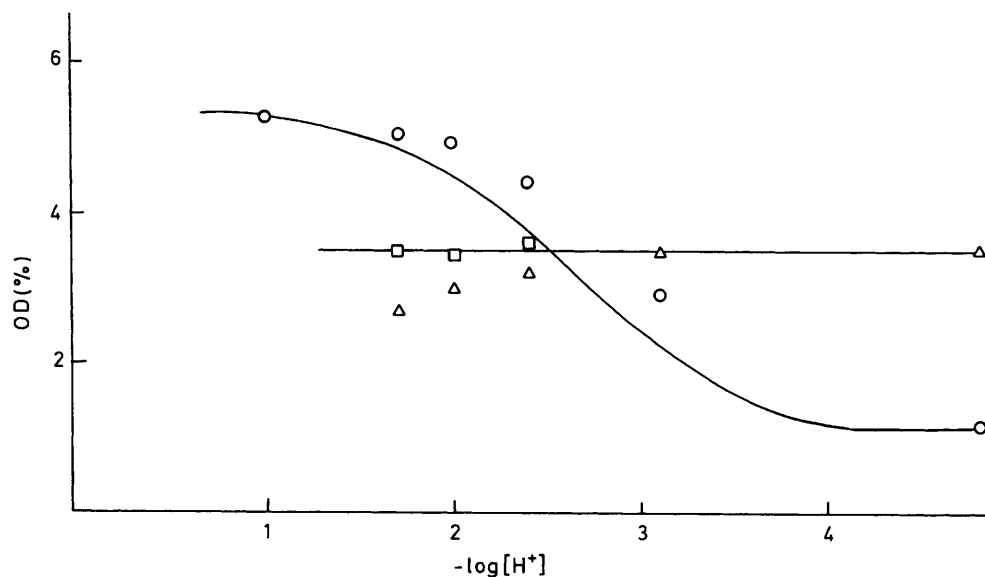
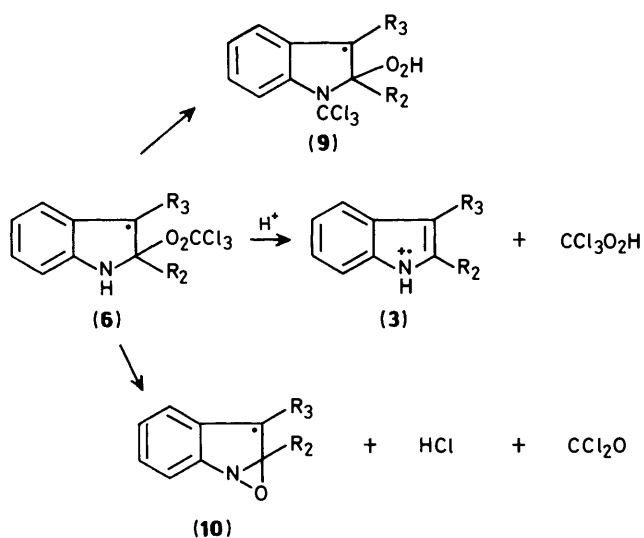


Figure 3. Variation of maximum optical densities *versus*  $[H^+]$  in pulse irradiated 3-methylindole. Conditions:  $10^{-2}$  mol  $dm^{-3}$  3-methylindole,  $O_2$  saturation, dose per pulse 70 Gy. ○ = 580 nm; △ = 460 nm; and □ = 460 nm, initial yield corrected for decay.



Scheme 3.

evidence for the 3-methylindoles, we propose that the expulsion of  $O_2^{\cdot-}$  from the ring-opened peroxy radical (7) (Scheme 4) is equally likely to occur. The presence of the methyl group in 1-methylindole should stabilize the 3-adduct against  $O_2^{\cdot-}$  expulsion. This is supported by Figure 1(e) where the 400 nm absorbance is seen to persist in base. In addition the  $O_2^{\cdot-}$  yield from 1-methylindole is seen to deviate strongly from the correlation line in Figure 4. We believe that with 1-methylindole,  $O_2^{\cdot-}$  is formed from oxidation of the pseudo-base of (1) by  $O_2$ . Finally, it should be mentioned that the  $O_2^{\cdot-}$  yields, as measured in  $\gamma$ -irradiated neutral solutions containing the indoles and TNM, were found to be close to the values obtained in basic solutions by pulse radiolysis. Thus  $O_2^{\cdot-}$  expulsion also occurs in neutral solutions although more slowly than in base.

**Conductivity Measurements.**—Conductivity changes mainly attest to the yield and dynamics of HCl production in the present solvent. With knowledge of the relevant specific conductivities and using comparative dosimetry it was possible to

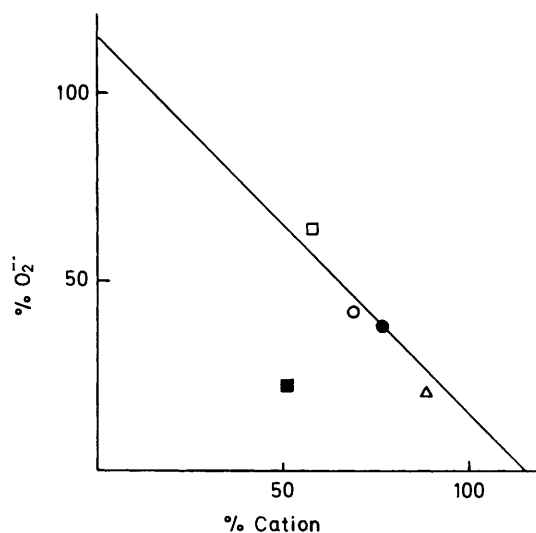
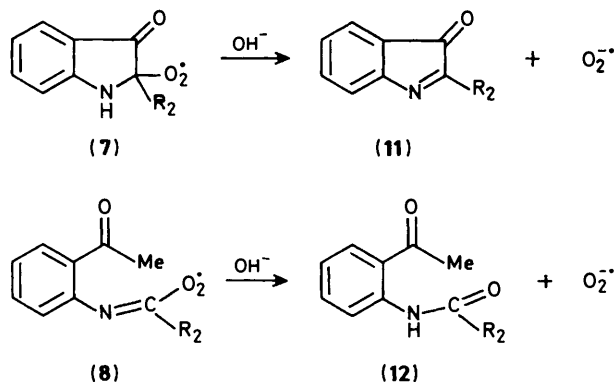


Figure 4. Correlation between the yields of  $O_2^{\cdot-}$  in base and indolyl radical cation in acid. The drawn line has a slope of  $-1$  *i.e.* complete correlation. ○ = indole; □ = 2-methylindole; ● = 3-methylindole; △ = 2,3-dimethylindole; and ■ = 1-methylindole.

determine the amount of HCl produced in the presence of indoles. Recalling that the net reaction forming  $CCl_3O_2^{\cdot}$  generates 100% protons the excess (*i.e.* the tabulated figures in Table 3 minus 100%) derives from the reaction of  $CCl_3O_2^{\cdot}$  with the indoles. The first-order rate constant for the excess conductivity changes are presented in the last entry of Table 1. Comparison with the preceding entry shows that for indole and 1-methylindole the breakdown of the 3-adduct is concomitant with HCl expulsion thus supporting the previously proposed Scheme 2. For 3-methylindoles, such a comparison cannot be made. However, it appears that the conductivity rates differ from the corresponding breakdown rates of the 2-adducts measured optically at 460 nm. It is instructive to consider the excess HCl yields in Table 3. In the neutral solvent these yields are always clearly in default of the total radical yield, *i.e.* 100%. In the case of indole and 2,3-dimethylindole the HCl yields are close to the

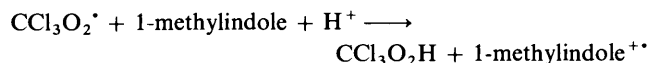


Scheme 4.

**Table 3.** The pulse-radiolytically determined conductivity of  $\text{O}_2$ -saturated solutions containing 48% propan-2-ol, 4%  $\text{CCl}_4$ , and 48% water. The HCl yields are expressed relative to the HCl yield obtained in the absence of indoles.

Solute	Conc/mol dm <sup>-3</sup>	HCl (%)	Added acid/base
2,3-Dimethylindole	$3 \times 10^{-3}$	$180 \pm 10$	$10^{-3}$ NaOH
2,3-Dimethylindole	$1 \times 10^{-3}$	$190 \pm 20$	$10^{-2}$ NaOH
2,3-Dimethylindole	$1 \times 10^{-2}$	$190 \pm 20$	$10^{-2}$ NaOH
N-Methylindole	$4 \times 10^{-3}$	$220 \pm 20$	$3 \times 10^{-3}$ NaOH
2,3-Dimethylindole	$3 \times 10^{-3}$	$130 \pm 10$	neutral
3-Methylindole	$6 \times 10^{-3}$	$160 \pm 10$	neutral
Indole	$1 \times 10^{-2}$	$147 \pm 9$	neutral
Indole	$1 \times 10^{-2}$	$127 \pm 9$	$10^{-3}$ HClO <sub>4</sub>
N-Methylindole	$1 \times 10^{-2}$	$130 \pm 10$	neutral
N-Methylindole	$1 \times 10^{-2}$	$130 \pm 10$	$10^{-3}$ HClO <sub>4</sub>

yields of the corresponding 3-adducts (4) as derived from Figure 4. The match also holds for 1-methylindole if allowance is made for the consumption of a proton in the reaction:



It seems, therefore, that the 2-adducts of these compounds do not expel HCl to any appreciable extent. In contrast, the HCl yield from 3-methylindole is significantly higher than that from the estimated 3-adduct (4). The breakdown mode of the 2-adduct appears to be sensitive to the substituent. Scrutiny of Table 3 reveals that in basic solutions the yield of HCl from  $\text{CCl}_3\text{O}_2^{\cdot}$  is essentially quantitative. Therefore, irrespective of the initial event, base probably further hydrolyses chlorinated intermediates.

In contrast to base, acid further reduces the HCl yield in comparison to neutral solutions. This is in keeping with the increased yield of indolyl radical cations implying consumption of protons. 1-Methylindole is an exception as its yield of indolyl radical cation was shown to be invariant with acid.

**The Yield of End Products.**—Table 4 shows the yields of small molecular end products. As stated in the footnote of the table the total yield of  $\text{CO}_2$  (measured subsequent to base addition to and reacidification of the samples) is equal to the initial yield of  $\text{CCl}_3\text{O}_2^{\cdot}$  radicals. The figures in the table refer to the prompt  $\text{CO}_2$  yield. In a previous publication<sup>12</sup> the origin of the additional yield of  $\text{CO}_2$  released by base was found to be phosgene. Here the interpretation is complicated by the possible interaction between indole and phosgene.

In neutral solutions the oxygen uptake is seen to be

**Table 4.** Formation of hydrogen peroxide and  $\text{CO}_2$  and oxygen consumption obtained from  $\gamma$ -radiolysis of an  $\text{O}_2$  saturated solvent containing  $10^{-2}$  mol dm<sup>-3</sup> of various indoles.

Indole	Oxygen consump. (%)	$\text{CO}_2^a$ (%)	$\text{H}_2\text{O}_2$ (%)	Rem
Indole	77	53	24	neutral
Indole	108	—	—	$10^{-2}$ OH <sup>-</sup>
Indole	59	51	5	$10^{-2}$ H <sup>+</sup>
N-Methylindole	65	60	15	neutral
N-Methylindole	87	—	—	$10^{-2}$ OH <sup>-</sup>
N-Methylindole	62	69	5	$10^{-2}$ H <sup>+</sup>
3-Methylindole	93	84	27	neutral
3-Methylindole	117	—	—	$10^{-2}$ OH <sup>-</sup>
3-Methylindole	59	53	7	$10^{-2}$ H <sup>+</sup>
Tryptophan	93	—	29	neutral

<sup>a</sup> The value after adding base and reacidification is between 100 and 110 for all the indoles.

significantly less than 100%. For indole and 3-methylindole the oxygen uptake is lowered in acidic solutions in which the 2-adduct has been shown to transform into the indolyl radical cation (3). The invariance with acid of the oxygen uptake of 1-methylindole reflects the constancy of the cation yield. These facts find a ready explanation if one assumes that  $\text{CCl}_3\text{O}_2\text{H}$ , the expected co-product of the indolyl radical, reforms oxygen in some unspecified process. The latter behaviour of  $\text{CCl}_3\text{O}_2\text{H}$  was recently demonstrated in the presence of hydroquinone.<sup>12</sup> The production of  $\text{H}_2\text{O}_2$  could occur *via* direct expulsion of  $\text{H}_2\text{O}_2$  from a radical adduct, *e.g.* the 2-adduct. However, it may also to some extent be a result of the dismutation of  $\text{O}_2^{\cdot-}$ . Both the formation of  $\text{H}_2\text{O}_2$  and the breaking of the O—O bond of an adduct should result in oxygen consumption. Thus by subtracting the  $\text{H}_2\text{O}_2$  yield from the  $\text{O}_2$  consumption it is found that 30–50% of the adducts (including  $\text{CCl}_3\text{O}_2\text{H}$ ) do not cleave along the O—O bond. This estimate represents a lower limit based on the assumption of quantitative oxidation of the  $\text{O}_2^{\cdot-}$  initially formed to  $\text{O}_2$  by some radical intermediate(s) in the system. Compound (9) in Scheme 3 is one of the few conceivable breakdown products to include the joint findings of an intact O—O bond and low HCl production. From conductivity and  $\text{O}_2$  consumption it seems that the formation of an oxazirane radical (10) is the major breakdown route of the 2-adduct of 3-methylindole. For indole and possibly 2,3-dimethylindole the route leading to intermediate (9) seems to be favoured. The overall conclusion is that far from consuming extra oxygen the reaction of  $\text{CCl}_3\text{O}_2^{\cdot}$  with indoles restores some of it.

**The Yield of Indole-derived End Products.**—Table 5 presents the end product yields measured in irradiated indole samples. None of the major h.p.l.c. peaks could be ascribed to any product hydroxylated on the benzene ring. Also, m.s. showed none of the products to be chlorinated.

Regarding the general composition of end products it is observed that indoles with a hydrogen in the 3-position yield substantial amounts of indoxyl compounds while the main products derived from 3-methylindoles are ring-opened amides (12). The finding that the  $\gamma$ -radiolytic yield of indoxyl compounds greatly exceeds the corresponding yields in pulse-irradiated samples is significant. From the mechanistic point of view this implies that at least one of the proposed intermediates (9) or (10) is transformed into indoxyl products once radical recombination is suppressed. Table 5 shows that consumption of the indoles is essentially quantitative with the exception of 3-methyl and 2,3-dimethylindole. With 3-methylindole considerable amounts of dimers are formed. Hence the assessment of product balance is unreliable. On the

**Table 5.** End product yields measured after  $\gamma$ - or pulsed radiolysis of indoles dissolved in 48% propan-2-ol, 4%  $\text{CCl}_4$  and 48% water.<sup>a</sup>

3-H Indoles	Conc/mol dm <sup>-3</sup>	Indole consumption (%)	Total indoxyl (%)	Irradiation source
Indole	10 <sup>-3</sup>	100 ± 10	94 ± 10	$\gamma$ /air
Indole	2 × 10 <sup>-3</sup>	100	51	<i>b</i>
Indole	2 × 10 <sup>-2</sup>	80	43 ± 5	e-beam/O <sub>2</sub>
<i>N</i> -Methyl	2 × 10 <sup>-3</sup>	90	79 ± 8	$\gamma$ /air
<i>N</i> -Methyl	2 × 10 <sup>-2</sup>	—	31 ± 2	e-beam/O <sub>2</sub>
2-Methyl	1 × 10 <sup>-3</sup>	—	94 ± 9	$\gamma$ /air

3-Methyl in- doles	Conc/mol dm <sup>-3</sup>	Indole consumption	2-3 Opened amide	2-Oxyindole	3-OH Indolenine	3-OOH Indolenine	Irradiation
3-Methyl	2 × 10 <sup>-3</sup>	240 ± 10	80 ± 6	27 ± 2	—	—	$\gamma$ /air
3-Methyl	2 × 10 <sup>-3</sup>	100 ± 10	29 ± 3	11 ± 2	—	—	<i>b</i>
2,3-Dimethyl	2 × 10 <sup>-3</sup>	330 ± 40	118 ± 8	0	110 ± 10	80 ± 10	$\gamma$ /air
2,3-Dimethyl	2 × 10 <sup>-3</sup>	120 ± 10	76 ± 6	0	40 ± 10	—	<i>b</i>
2,3-Dimethyl	5 × 10 <sup>-3</sup>	180 ± 10	63 ± 6	0	62 ± 6	17 + 5	e-beam/O <sub>2</sub>

<sup>a</sup> Solutions were saturated with air or O<sub>2</sub>. <sup>b</sup>  $\gamma$ -Irradiated air samples contained 1–5 × 10<sup>-4</sup> mol dm<sup>-3</sup> ascorbate.

other hand, the high consumption of irradiated 2,3-dimethylindole is fairly balanced by the sum of oxygenated products. Thus for the latter compound a chain reaction is indicated on the gamma radiolytic time scale. Ascorbate, a well known reductant of peroxy radicals is seen to quench the chain reaction. It thus appears that the chain propagates *via* indole-based peroxy radicals which abstract hydrogen atoms from the parent 2,3-dimethylindole with further peroxy radical formation as the result.

The finding that a chain reaction is only observed with 2,3-dimethylindole is understandable given the fact that its redox potential is the lowest of the indoles investigated.<sup>17</sup> Apart from being directly formed from the 3-adduct of 2,3-dimethylindole, amide (12) is also produced through a chain reaction. 3-Hydroperoxyindolenine also arises from this chain reaction, probably originating from the 2-adduct. However, lacking irrefutable experimental evidence the proposed relationships between adduct chemistry and end product distribution should be viewed with caution.

### Conclusion

The present work provides detailed evidence for the adduct-forming ability of the trichloromethyl peroxy radical. A novel feature was shown to be the rapid monomolecular breakdown of its 2- and 3-adducts with the indoles. This occurs in part through rupture of the O–O bond initially present in  $\text{CCl}_3\text{O}_2^{\cdot}$ . In addition the demonstrated proton-catalysed inner-sphere electron transfer to yield indolyl radicals reveals that  $\text{CCl}_3\text{O}_2^{\cdot}$  has much in common with the OH<sup>•</sup> radical.

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