g of bicyclo[4.2.1]nona-2,4,7-trien-9-one. The solution was refluxed for 63 h and work up as previously described. The purified carbinol had mp 82.5–84.0°: δ_{Me_4Si} (CS_2) 5.81 (m, 2 H, H_2 and H_5), 5.67 (m, 2 H, H_3 and H_4), 5.12 (d (J = 1.5 Hz), 2 H, monoene), 2.79 (dd (J = 7.5 and 1 Hz), 2 H, bh), 2.28 (s, 1 H, OH).

No signal was detected at δ 3.77 (<1%). The alkyl toluenesulfonate ester of *anti*-9-*d*-I-OH was recrystallized from 4:1 hexane–chloroform as white crystals, mp 79.2–79.8°: δ_{Me_4Si} (CS_2) 7.22 and 7.56 (q, 4 H, aromatic), 5.82 (m, 4 H, butadiene), 5.12 (2 H, monoene), 3.00 (d, 2 H, bh), and 2.39 (s, 3 H, methyl). No signal was detected at δ 4.53 (<1%).

***anti*-9-Bicyclo[4.2.1]nona-3,7-dienyl Toluenesulfonate (*anti*-IV-OTs).** The carbinol was available to us from another study. The ester, *anti*-V-OTs, was prepared as above and recrystallized from pentane as white needles, mp 113–114°: δ_{Me_4Si} (CCl_4) 7.2 and 8.0 (q, 4 H, aromatic), 5.62 (s, 2 H, olefinic), 5.26 (m, 2 H, bh), 2.53 (s, 3 H, methyl), and 2.25 (m, 4 H, methylene).

***anti*-9-Bicyclo[4.2.1]nonyl Alcohol (*anti*-VII-OH).** Hydrogenation of 167 mg of *anti*-I-OH in 1 ml of ethanol containing 20 mg of PtO_2 during ca. 16 h produced *anti*-VII-OH in quantitative yield. The carbinol was recrystallized from pentane, mp 172–174°: δ_{Me_4Si} (CCl_4) 3.97 (s, 1 H, α-H), 2.30 (m, 5 H), and 1.51 (m, 10 H).

***anti*-9-Bicyclo[4.2.1]nonyl Toluenesulfonate (*anti*-VII-OTs).** The carbinol, *anti*-VII-OH, was esterified as above. Recrystallization of *anti*-VII-OTs from 5:1 pentane–ether yielded white crystals, mp 127–128°: δ_{Me_4Si} (CS_2) 7.33 (q, 4 H, aromatic), 4.58 (s, 1 H, δ H), 2.45 (s, 3 H, methyl), 2.38 (m, 2 H, bh), and 1.45 (m, 12 H, methylenes).

Kinetic measurements were performed as previously described.[3]

Product analysis was performed on *anti*-I-OTs as previously described.[3] As is the case with *syn*-I-OTs, analysis by GLC (10% Carbowax, 100°) of the acetolysis products from *anti*-I-OTs failed to reveal any other ROAc product (<0.15%) besides *exo*-III-OAc. These conditions are sufficient to separate *syn*- and *anti*-I-OAc by 35 min.

A solution of *syn*-I-OTs (290 mg) and 2,6-lutidine (0.17 ml) in 20 ml anhydrous methanol was heated to 50° for 30 h in a sealed tube. The solution was extracted with ether, washed with sodium bicarbonate and water, and dried over magnesium sulfate. GLC analysis on 10% Carbowax 20M, 120°, revealed three products. The product mixture contained 94% *exo*-III-OMe readily identified by NMR, plus 6% of another ROMe product appropriate for *endo*-III-OMe, along with 0.5% indene.

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On the Mechanism of the Sensitized Photooxygenation of Pyrroles[1]

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Abstract: In the dye-sensitized photooxygenation of alkylpyrroles, 1,4 addition of singlet oxygen leads to the formation of unstable *endo*-peroxides whose existence was provided by low-temperature NMR. The *endo*-peroxides have been shown to undergo rapid ground-state reactions leading, inter alia, to 5-hydroxy-Δ^3-pyrrolinones by two mechanisms: internal rearrangement and reaction with water. The extent of the latter mechanism was investigated by the incorporation of [^{18}O]water with the conclusion that, except in water solvent, the former mechanism predominates. The more stable *endo*-peroxide of *N*-phenylpyrrole liberates singlet oxygen upon warming.

Introduction

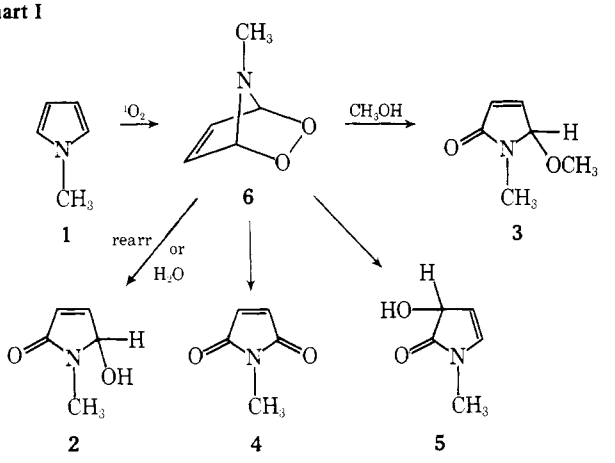
Although dye-sensitized photooxygenations of pyrroles[1] and furans[2,3] have been widely studied, there are few details describing the mechanism of their initial reaction with singlet oxygen ($^1O_2$) or the subsequent reaction of the $^1O_2$ adducts. It has been assumed that the major final products arise from nonphotochemical reactions of an *endo*-peroxide intermediate, which itself is derived from 1,4 cycloaddition of $^1O_2$ to the recipient pyrrole[4,5] or furan.[6] A direct observation of a pyrrole *endo*-peroxide has not been reported, although Foote and Kane[7] have observed the formation of furan *endo*-peroxides by NMR and have studied their photochemistry and ground-state reactions. The ground-state chemistry of *endo*-peroxides derived from furans has been examined in aprotic and alcoholic solvents[2,3,6,7] but not water. The incorporation of solvent is clearly implicated in some cases, e.g., methanolysis, but the ambiguity associated with hydrolysis[4,8] did not arise. Since the first reported photooxidations of pyrrole[4,9,10] involved aqueous solvent, and because of the importance of pyrrole compounds, e.g., hemopyrrole,[11] porphobilinogen,[12] and bilirubin,[13,14] in

(aqueous) biological systems, mechanistic questions regarding their photooxidation become important to resolve. In order to determine how the various principal products are formed, we have examined the photooxygenation reaction of pyrrole, its *N*-methyl, 2-methyl, 3-methyl, and *N*-phenyl derivatives, as well as kryptopyrrole, at low temperatures by NMR and with $H_2{}^{18}O$ in various solvent systems.

Results and Discussion

One of the most general reactions which we have observed in our studies of dye-sensitized pyrrole photooxygenation is the formation of 5-hydroxylactams[1] in methanol solvent. Such products occur whether the pyrrole α positions are free[4,8,15] or substituted by alkyl,[16] formyl,[17] carbomethoxy,[18] or acyl[19] groups. Even with phenyl substitution at one α position (and H at the other), 5-hydroxylactams are obtained.[20] However, the reaction course is typically quite different when both α positions are substituted by phenyl[21,22] or *tert*-butyl[23] groups but, interestingly, not with methyl groups.[5] The formation of hydroxylactams by photooxygenation of pyrroles in water is less surprising. Thus, De Mayo and Reid[4] reported a high yield of *N*-methyl-5-hydroxy-Δ^3-pyrrolin-2-one (**2**) from eosin-sensitized photooxidation of *N*-methylpyrrole (**1**) in water. When **1** is photooxygenated in anhydrous methanol (Rose Bengal sensitizer), a 20% yield of **2** is isolated along with 11% of the expected 5-methoxy compound (**3**) and a trace (3%) of *N*-methylmaleimide (**4**), whereas in acetone (Methylene Blue sensitizer) 16% of **2**, 4% of **4**, and an isomeric

Chart I



hydroxylactam (**5**) are isolated. In either solvent, **1** undergoes only a minor autoxidation: less than 5% loss of **1** after 24 h.

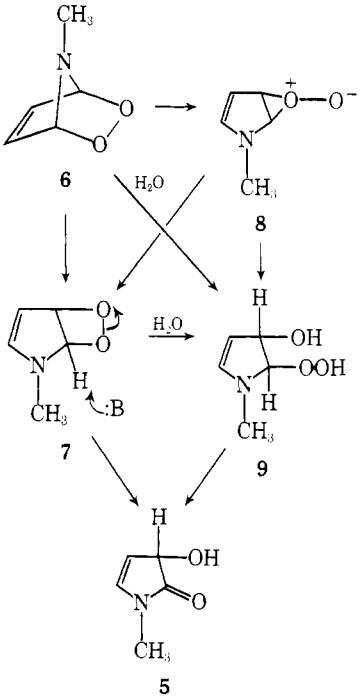
We have established that under the reaction conditions, with and without light, **2** is not converted to **3, 4,** or **5,** and **5** is not converted to **2, 3,** or **4.** Hence, we believe that products are derived from a common reactive *endo*-peroxide intermediate (**6**) which is formed by 1,4 addition of $^1O_2$ to **1.** Thus, **3** can be accommodated by methanolysis of **6** followed by rapid decomposition of the resultant hydroperoxide,[24] and **4** can be viewed as originating from **6** either by thermal or photochemical[7] O–O homolysis followed by H· loss from the alkoxy radicals[25,26] or by H· abstraction from **6** by ^{3}Sens or oxygen. However, the origins of **5** are uncertain, as is that of **2,** which may arise by internal rearrangement of **6** or hydrolysis of **6** by adventitious water.

In order to prove the intermediacy of *endo*-peroxide **6, 1** was photooxygenated at −78°C in a NMR tube using acetone-d_6 or Freon-11 as solvents and dinaphthalenethiophene sensitizer. In either solvent, the reaction of 1–2 mg of **1** in 0.3 ml of solvent was complete within 40 min, during which time we observed by NMR at −80° the complete disappearance of the pyrrole signals at δ 3.66 (s, 3 H, N–CH_3), 5.97 (m, 2 H, β-H), and 6.61 (m, 2 H, α-H) ppm and the emergence of new set of signals at δ 2.86 (s, 3 H, N–CH_3), 5.42 (s, 2 H, α-H), and 6.18 (d, 2 H, β-H) ppm, which we assign to *endo*-peroxide **6.**[27] The solutions are stable at −80° for 4 h, but on warming to −20°, **6** has a half-life of 20 min, and at 0° **6** disappears completely within 7 min. At the higher temperatures, new NMR signals for products **2, 4,** and **5** emerge as those for **6** decline.

The formation of pyrrole *endo*-peroxides doubtless plays a major role in their photooxygenation, and we cite further general evidence for the formation of such *endo*-peroxides in Table I. Addition of a nucleophile, e.g., CH_3OH, to the cold (−80°) *endo*-peroxide solution led to the formation of products similar to **2** and **3.** In all instances, attempted observation of *endo*-peroxides formed in methanol was unsuccessful because of their apparent rapid decomposition to products, even at −78°. In these cases we observed only final product signals in the NMR. In addition, in some instances, slow decomposition of the *endo*-peroxides in acetone-d_6 was already begun at −80° during the NMR measurement. In one interesting example, *N*-phenylpyrrole *endo*-peroxide in acetone-d_6 or Freon-11 was observed to liberate a gas upon warming to −20°C. The liberated gas was shown to be $^1O_2$ by trapping experiments at −20°C with 2,3-dimethyl-2-butene to give 2,3-dimethyl-3-butene 1-hydroperoxide.[28] In a related case, Dufraisse et al.[29] noted that pentaphenylpyrrole *endo*-peroxide gave some pentaphenylpyrrole after warming.

Returning to the 3-hydroxylactam (**5**) of Chart I, the unresolved question of the mechanism of its formation is not easily settled. It may arise, inter alia, via a heterolytic pathway (base-catalyzed, possibly by solvent on the dioxetane),[30] by rearrangement or hydrolysis of dioxetane **7** or peroxirane **8,**[31,32] or by vinylogous attack of H_2O on C-3 of **6** and opening of the *endo*-peroxide ring, followed by decomposition of an intermediate hydroperoxide (**9**) (see Chart II). Since the occurrence of **5** (and **4**) in significant

Chart II



amounts depends specifically on the photooxygenation solvent used (acetone-d_6 or Freon-11), and the stability of the *endo*-peroxide (**6**) is also greatest in those solvents, we

Table I. NMR Data on *endo*-Peroxides Formed in the Photooxygenation of Pyrroles at −78°C in Acetone-d_6

	Starting pyrrole, δ (ppm), Me_4Si[a]						*endo*-Peroxide, δ (ppm), Me_4Si[a]						
	H_α	H_β	$H_{\alpha'}$	$H_{\beta'}$	N–CH_3	C–CH_3	N–Ph	H_α	H_β	$H_{\alpha'}$	$H_{\beta'}$	N–CH_3	C–CH_3	N–Ph
Pyrrole	6.78	6.09						Br	5.6–6.4					
N-Methylpyrrole	6.61	5.97			3.66			5.42	6.18			2.86		
	6.48[b]	5.90			3.65			5.30	6.05			2.83		
N-Phenylpyrrole	7.22	6.27					7.3–7.5	6.79	6.98					7.2–7.4
	7.22[b,c]	6.21[c]					7.43[c]	6.58	6.70					6.9–7.3
N-*tert*-Butylpyrrole	6.84	5.99				1.52		5.7[d]	6.2				1.18	
2-Methylpyrrole	6.57[e]	5.93		5.76		2.15		5.95	7.4		6.6		1.43	
3-Methylpyrrole	6.61[e]	5.86	6.50			2.1		5.5	7.1	5.0			1.85	
2-*tert*-Butylpyrrole[f]	6.57	5.89		5.78		1.27		5.98[d]	7.4 (d)		7.0 (d)		1.16	
3-*tert*-Butylpyrrole	6.65	6.06	6.56			1.23		6.34	8.16	5.96			1.29	
1,2,5-Trimethylpyrrole		5.67			3.33	2.1			6.07[d]			2.4	1.15	

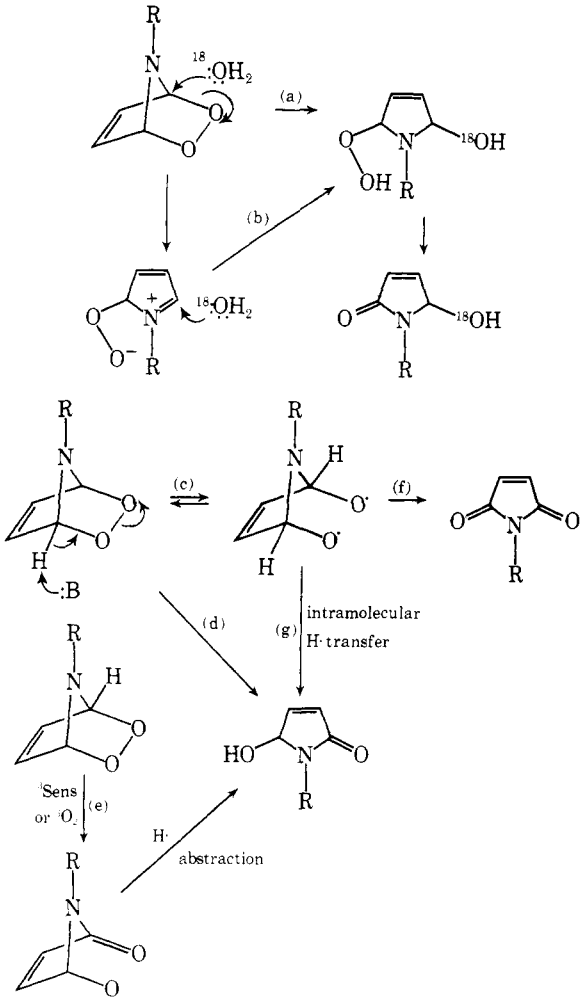
[a] Data were taken on a Varian XL-100 NMR spectrometer in which the probe temperature was adjusted to −80°C. [b] These sets of data were obtained in $CFCl_3$ solvent. [c] Ambient temperature. [d] End products were already present at this temperature during the NMR measurement. [e] These data sets were obtained on a Jeolco 4H-100 NMR spectrometer in which the probe (JES-VT-3) variable temperature was adjusted to −80°C. [f] Evidence for the formation of some hydroperoxide is shown by a weak signal at δ 13.5.

suggest that **7** (or **8**), if it is a precursor to **5**, is very likely *not* formed by direct 1,2 addition of $^1O_2$ to **1** but rather by rearrangement of **6**.[31] Furthermore, we can conclude that **7** (or **8**) must be present in low concentrations in acetone-d_6 or Freon-11 from the low-temperature NMR study of the photooxygenation of **1** which showed the presence of only one reactive intermediate, *endo*-peroxide **6**. The particular decomposition of **7** → **5** is an atypical behavior of dioxetanes, which tend to undergo O–O as well as C–C cleavage of the dioxetane ring to give dicarbonyl products.[33,34] In pyrrole photooxygenations, we have seldom isolated products of the C–C cleavage type and as yet only from 3,4-diethyl-2,5-dimethylpyrrole in methanol,[5] *N*-*tert*-butylpyrrole in acetone,[35] and *N*-phenylpyrrole in methanol.[28] Apparent solvolysis products of dioxetanes are also rare[34] and may in fact arise not from a dioxetane at all but rather from a peroxirane,[31,32] e.g., **8**. However, the formation of peroxiranes by rearrangement of *endo*-peroxides is unknown, and evidence to date suggests that they are formed by direct attack of $^1O_2$ on the C–C double bond and can rearrange to more stable dioxetanes and/or undergo solvolytic ring opening in acid or base.[31,32]

In previous pyrrole photooxygenations, 3-hydroxy- or 3-alkoxylactams were seldom seen and only when C-3 also had a 3-alkyl group. The isolation of **5** from **1** is the first example of the formation of a 3-hydroxylactam without also a 3-alkyl group. Kryptopyrrole,[36] hemopyrrole,[11] and 3,4-diethyl-2-methylpyrrole[11] all gave some (11–18% isolated yields) 3-hydroxy product from photooxygenation in methanol *but no 3-methoxy product*. A 4% yield of 3-hydroxy product was isolated from photooxygenation of 3-*tert*-butylpyrrole in acetone, but neither 3-hydroxy nor methoxy products were found in methanol.[35] The only instance in which a 3-alkoxylactam has been isolated is from photooxygenation of 3-methylpyrrole in methanol, but even here more (6%) 3-hydroxylactam was isolated than (3%) 3-methoxylactam.[37] These results and those of *N*-methylpyrrole are not entirely in keeping with the expectation of 3-methoxylactams from methanolysis of **8** (or even **6** or **7**).[31] Rather the repeated isolations of 3-hydroxylactams in the cases cited are more consistent with an intramolecular reorganization of **7** or **8**. Unfortunately, we have no direct evidence on the formation of either **7** or **8**.

The mechanism of formation of 5-hydroxylactams from *endo*-peroxides was explored by the use of $H_2{}^{18}O$ during photooxygenation of various pyrroles. In these photooxygenation experiments, the incorporation of ^{18}O in the 5-hydroxylactam products[38] is taken as prima facie evidence for direct (nucleophilic) involvement of $H_2{}^{18}O$ in an *endo*-peroxide decomposition mode. Exactly how ^{18}O is incorporated cannot be determined from the data, although we have ruled out ^{18}O exchange by $H_2{}^{18}O$ on the ^{16}O-5-hydroxylactam. Thus, for example, whether an *endo*-peroxide or an open zwitterion is attacked by $H_2{}^{18}O$ is unclear (Chart III). However, on the basis of our low-temperature NMR data, we can rule out high concentrations of the zwitterionic form which we would expect to see (and do not) in addition to **6**.[39] Reaction of $H_2{}^{18}O$ with the *endo*-peroxide can be viewed as a nucleophilic opening by attack on an α carbon (a) to give a hydroperoxide, which is a reasonable direct precursor to the 5-hydroxylactam.[2,5,7] Either mechanism (a or b) explains the incorporation of ^{18}O in the product. From the data of Table II, however, it appears that other routes for formation of 5-hydroxylactams must obtain in which H_2O is not involved.[40] One rationale to accommodate the nonincorporation of ^{18}O involves a base-catalyzed heterolytic pathway (d),[2,3] possibly by solvent. Another rationale involves structural reorganization of the *endo*-peroxide, which is isomeric with the product. The precise details of

Chart III



the latter, *e.g.*, the timing and possible intermediates and whether H-abstraction by ^{3}Sens or $^3O_2$ or by base occurs (d, e, and f), cannot be determined from these data. It is important to note, however, that whereas 5-hydroxylactams are formed during photooxygenation of pyrroles whenever they have at least one free (H-substituted) α position,[4,8,11,15,16,28,36,37,41] when both α positions are methyl-substituted,[5,42] only 5-methoxylactams (and not hydroxylactams) are formed. The role of the pyrrole α hydrogen therefore is extremely important in a mechanism of decomposition of the *endo*-peroxides. This information suggests that α-H abstraction, either intramolecularly or by other agents (d, e, or f), is responsible for a nonhydrolytic pathway to 5-hydroxylactams. Routes c and f also offer a mechanism for maleimide formation by loss of both pyrrole α groups, either H[8,35,36] or alkyl,[5,11,36,41] from the diradical.[26]

From an examination of the data of Table II, it is interesting to note the expected higher levels of ^{18}O when $H_2{}^{18}O$ is the solvent, but also the unexpected differences in levels of incorporation in different pyrroles. Whereas the high levels of ^{18}O incorporation in the photooxygenation of pyrrole and *N*-methylpyrrole indicate that rate of *endo*-peroxide hydrolysis is faster than the rate of rearrangement, with 2-methyl- and 3-methylpyrrole both rates are nearly equal. The reason for change is not clear and may be due to differences in ($H_2{}^{18}O$) solvation of the *endo*-peroxides or decreased electrophilic character of the pyrrole α carbons in 2-methyl and 3-methylpyrrole *endo*-peroxides.

When the solvent is predominantly anhydrous acetone or methanol, with an added 10–40-fold molar excess of H_2O, incorporation of ^{18}O is considerably less than in water solvent. We interpret this as being due to lowering of the effective rate of hydrolysis (Chart III, a or b) by the reduced concentration of the aqueous component. However, the reason for large discrepancy in incorporation between acetone and methanol solvent is unclear, except perhaps that water is more tightly bound in the methanol solvent matrix than in acetone, benzene, tetrahydrofuran, or dichloromethane (see Table II) and as such is less available for reaction with *endo*-peroxides. Alternatively, since the stability of the *endo*-peroxides is greater in acetone than in methanol (low-temperature NMR data), the longer-lived *endo*-peroxide may thus be given a greater opportunity for finding a water molecule.[43] What is clear from the data of Table II, however, is that in nonaqueous solvents the major route for formation of 5-hydroxylactones is by rearrangement of *endo*-peroxides and not by hydrolysis. Also, as judged from the ^{18}O content of the 3-hydroxylactam from kryptopyrrole or *N*-methylpyrrole, the formation of even these products need not involve water in a major way.

Table II. ^{18}O Incorporation in 5-Hydroxylactams from Photooxygenation of Pyrroles[a]

Compound	Percent incorporation of ^{18}O in 5-hydroxylactams (molar ratio H_2O:pyrrole)		
	^{18}O-Water[b]	$H_2{}^{18}O$-Acetone[c]	$H_2{}^{18}O$-Methanol[c]
Pyrrole	100	10 (10:1–5:1)	1 (10:1–5:1)
N-Methylpyrrole[d]	90	12[e] (10:1–1:1)	0 (10:1–1:1)
2-Methylpyrrole	40	13 (5:1)	0 (10:1)
3-Methylpyrrole	60	12 (5:1)	0 (10:1)
N-Phenylpyrrole	Insol	10 (7:1)	0 (15:1 –10:1)
Kryptopyrrole[f]	Insol	3[g] (7:1)	

[a] The data are derived from a careful mass spectrometric determination of the relative intensities of the [M] and [M + 2] peaks representing ^{16}O and ^{18}O, respectively. Correction is made for the natural isotopic abundance contribution of [M] to [M + 2] and for the enrichment (20–95%) of ^{18}O in the H_2O used. Each datum is an average of several independent experiments and is accurate to *ca.* ±5%. [b] Rose Bengal sensitizer. [c] Methylene Blue sensitizer. [d] In tetrahydrofuran, dichloromethane, and benzene, the incorporation was 12% (5:1), 18% (5:1), and 6% (2.5:1), respectively. The sensitizers used were Rose Bengal, dinaphthalenethiophene, and dinaphthalenethiophene, respectively. In dichloromethane, the ^{18}O incorporation in the 3-hydroxy isomer was 17% (5:1). [e] The ^{18}O incorporation in the 3-hydroxy isomer was 8%. [f] In benzene the incorporation of ^{18}O was 0% (4:1). [g] The ^{18}O incorporation in the 3-hydroxy isomer was 0% (7:1).

Conclusions

In this work we have observed (by NMR) pyrrole *endo*-peroxides formed during dye-sensitized photooxygenation of various pyrroles. Evidence (NMR and $H_2{}^{18}O$ studies) has been brought forth to show that the *endo*-peroxides are precursors to the isolated photoproducts. They may undergo rearrangement to dioxetanes or peroxiranes to account for 3-hydroxy-Δ^4-pyrrolin-2-one products. Methanolysis or hydrolysis of the *endo*-peroxides accounts for the formation of 5-methoxy- or 5-hydroxy-Δ^3-pyrrolin-2-ones. The latter substances are usually formed mainly by *endo*-peroxide rearrangement, and not hydrolysis, in nonaqueous (wet) solvents.

Experimental Section

General. All mass spectra were obtained from an AEI MS-9, a Varian-MAT 311, or Jeolco JMS-07 mass spectrometer at 70 and

Table III. Amount of Pyrrole Compound per Volume of Water (% ^{18}O) per Volume of Solvent in the Photooxygenations[a]

Compound	Solvent		
	^{18}O-Water[b]	$H_2{}^{18}O$–Acetone[c]	$H_2{}^{18}O$–Methanol[c]
Pyrrole	1.2 mg/50 μl (20%)	2 mg/2.5 μl (20%)/1.25 ml	4.5 mg/5 μl (20%)/2.5
		2 mg/5 μl (20%)/1.25 ml	1.2 mg/5 μl (20%)/5 ml
N-Methylpyrrole[d]	1 mg/50 μl (20%)	4 mg/10 μl (40%)/2.5 ml	4 mg/10 μl (40%)/2.5 ml
		4 mg/5 μl (20%)/2.5 ml	4 mg/5 μl (40%)/2.5 ml
		4 mg/1.25 μl (20%)/2.5 ml	4 mg/2.5 μl (20%)/2.5 ml
			4 mg/1.25 μl (40%)/2.5 ml
2-Methylpyrrole	1.2 mg/50 μl (20%)	4 mg/5 μl (95%)/2.5 ml	4 mg/10 μl (20%)/2.5 ml
		4 mg/5 μl (20%)/2.5 ml	
3-Methylpyrrole	4 mg/50 μl (20%)	4 mg/5 μl (95%)/2.5 ml	4 mg/20 μl (20%)/5 ml
		8 mg/5 μl (20%)/2.5 ml	8 mg/10 μl (20%)/2.5 ml
N-Phenylpyrrole	Insol	5.1 mg/5 μl (20%)/1.25 ml	5 mg/10 μl (40%)/2.5 ml
		10.4 mg/10 μl (20%)/5 ml	11.1 mg/40 μl (20%)/5 ml
Kryptopyrrole[e]	Insol	4 mg/5 μl (40%)/2.5 ml	
		4 mg/2.5 μl (95%)/2.5 ml	

[a] Usually 0.1 mg of sensitizer was added. [b] Reaction in a 4 mm × 50 mm test tube. [c] Reaction in a 15 mm × 120 mm centrifuge tube. [d] In tetrahydrofuran. 8 mg/10 μl (20%)/5 ml; in dichloromethane. 4 mg/5 μl (95%)/2.5 ml; and benzene, 4 mg/1.25 μl (95%)/2.5 ml. [e] In benzene, 103.4 mg/50 μl (30%)/100 ml.

20 eV ionizing voltage. All ordinary NMR spectra were run on a Varian EM-360, T-60, or XL-100 instrument using $CDCl_3$ solvent and Me_4Si internal standard unless otherwise noted. Low-temperature NMR data were obtained on a Varian XL-100 or Jeol 4H-100 instrument in acetone-d_6 (Merck), Freon-11 (Matheson), or methanol-*O*-d[44] at −80°. Ir spectra were determined on a Perkin-Elmer 457 or Beckman IR-8 instrument. All melting points are uncorrected and were obtained on a Thomas Hoover capillary apparatus. Column chromatography was carried out using silica gel [M. Woelm, Eschwege, 70–325 mesh ASTM], and in all thin-layer chromatography, silica gel F [M. Woelm, Eschwege] was used. The singlet oxygen sensitizers used were Rose Bengal (Matheson), Methylene Blue (Matheson), and dinaphthalenethiophene (K&K). A Sylvania 500 Q/CL 500-W tungsten–halogen lamp was used throughout. Oxygen was dried by passing over anhydrous $CaCl_2$.

Solvents. Analytical reagent grade solvents were repurified and dried. Methanol (Baker Analyzed) was first dried using Mg activated by I_2 followed by distillation into 3A molecular sieves (Linde, Union Carbide), then redistilled into 3A molecular sieves. Acetone (Baker Analyzed) was distilled from $KMnO_4$ and then from P_2O_5 into 4A molecular sieves. It was then redistilled into 4A molecular sieves and used shortly after purification. Dichloromethane (Fisher) was stirred overnight with Act I Woelm neutral alumina and then passed through a column of Act I neutral alumina. Benzene (Fisher) was dried first by azeotropic distillation and redistilled into 4A molecular sieves. Tetrahydrofuran (Matheson) was distilled from $LiAlH_4$ into 4A molecular sieves and redistilled into molecular sieves. Water (^{16}O) used was triply distilled and deionized. Water (^{18}O) was obtained from Monsanto and used without further purification. The chromatography solvents, ethyl acetate (Fisher), acetone (Fisher), methanol (Baker), and ether (Fisher), were reagent grade.

Photooxygenations with $H_2{}^{18}O$. Pyrrole samples greater than 50 mg were photooxygenated in a water-cooled photolysis apparatus[3,7] using a continuous recycled flow of oxygen. Pyrrole samples less than 50 mg and in organic solvents were irradiated in a small centrifuge tube (15 mm × 120 mm), and the solutions were swept with dry oxygen for 30 s prior to irradiation (30–60 min). Aqueous solutions in a 4 mm × 50 mm tube were swept periodically during the photooxygenation period (60 min). Photooxygenation controls were run in each instance using $H_2{}^{16}O$, and the reactions were worked up in identical ways. After photooxygenation, the solvents were removed at room temperature on a rotatory evaporator, and the products were separated by preparative thin-layer chromatography (0.5–1.0 mm) using ethyl acetate or ethyl acetate–acetone. The products were identified by comparison with authentic samples corun on the same plate. ^{18}O analyses were made by mass spectrometry. The amounts of pyrrole and volumes of $H_2{}^{18}O$ (% abundance) and solvent are given in Table III.

^{18}O Analyses. All determinations of ^{18}O incorporation were made using the mass spectrometric relative intensities of the [M] and [M + 2] peaks as referred to the ^{16}O and ^{18}O compounds, respectively. The ionizing voltages used were 70 and 20 eV. Corrections were made for the abundance of ^{18}O in the water used. Typical values were 20, 30, 40, and 95% enriched $H_2{}^{18}O$. Corrections were also made for the natural isotopic contribution of [M] to [M + 2], and likewise, for any fragmentation of the type [M] → [M − 2] which would become important when [M + 2] increases. Controls were run using the corresponding ^{16}O compounds obtained by the use of $H_2{}^{16}O$ in parallel experiments. In order to rule out the remote possibility of ^{18}O–^{16}O exchange (presumably $H_2{}^{18}O$–$H_2{}^{16}O$ or ^{18}OH–^{16}OH) on the walls of the mass spectrometers inlet system and source, *N*-methyl-5-hydroxy-Δ^3-pyrrolin-2-one was allowed to react with CH_2N_2–BF_3·Et_2O to give the corresponding 5-methoxy compound which had an identical [M + 2]/[M] ($^{18}O/^{16}O$) ratio as its precursor as determined by mass spectrometry. The ^{18}O incorporation results are given in Table II.

Low-Temperature NMR Studies. Low-temperature photooxygenations were carried out as follows. In a NMR tube were placed 1–2 mg of the pyrrole, *ca.* 0.3 ml of solvent (acetone-d_6, Freon-11, or methanol-*O*-d) and approximately 0.1 mg of Methylene Blue, dinaphthalenethiophene, or Rose Bengal sensitizer. The tube was placed in a half-silvered dewar. A slow stream of small oxygen bubbles was passed through the solution by means of a finely drawn glass capillary, and the system was irradiated using a tungsten–halogen lamp. (Reaction does not proceed in the absence of the oxygen supply.)

The disappearance (30 min) of the starting pyrrole was followed by NMR by periodically quickly transferring the NMR "reaction" tube to the precooled probe. When the starting pyrrole had disappeared, in acetone-d_6 or Freon-11, essentially one new substance, the *endo*-peroxide, was present. Its stability was studied by allowing the probe to warm and examining its disappearance and the emergence of new products by NMR.

Photosensitized Oxygenation of *N*-Methylpyrrole (1) in Methanol. *N*-Methylpyrrole (500 mg, 6.17 mmol) and Rose Bengal (15 mg) in 500 ml of methanol were irradiated with a 500-W quartz-iodine lamp (Sylvania Q/CL) at 80 V in a water-cooled immersion apparatus through which O_2 was recirculated.[3,7] The O_2 uptake was measured at regular intervals and ceased abruptly after 10 min of irradiation and 140 ml (STP 6.25 mmol). The solvent was removed on a rotatory evaporator below 45°, and the dark residue was roughly separated by column chromatography on silica gel (10 in. × 1 in.) using successively 400 ml of ethyl acetate, 300 ml of acetone, and 200 ml of methanol. The ethyl acetate and acetone fractions were evaporated and submitted to preparative thin-layer chromatography to give two major and one minor products separated by ethyl acetate:

***N*-Methyl-5-methoxy-Δ^3-pyrrolin-2-one (3),** 86 mg, 11% yield, NMR δ 2.90 (3 H, s, NCH_3), 3.10 (3 H, s, OCH_3), 5.30 (1 H, s, O–CH–), 6.23 (1 H, d, J = 6 Hz, =CHC=O), 6.83 (1 H, d, J = 6 Hz, CH=CC=O) ppm; mass spectrum *m/e* (rel intensity) 127 [M^+] (35%), 112 [M − CH_3] (9%), 96 [M − OCH_3] (100%); ir ($CHCl_3$) 3420 cm^{-1} br (OH), 1690 cm^{-1} (C=O), (KBr) 1695 cm^{-1}. *Anal.* Calcd for $C_6H_9NO_2$: mol wt, 127.0633. Found: mol wt, 127.0634.

***N*-Methyl-5-hydroxy-Δ^3-pyrrolin-2-one (2),**[4] 137 mg, 20% yield, mp 77.5–78° (sublimed, 0.25 Torr, 60°) [lit.[4] mp 84–85°, cryst]: NMR δ 2.91 (3 H, s, CH_3), 5.29 (1 H, s, HC-O), 6.05 (1 H, d, J = 6 Hz, CHC=O), 6.93 (1 H, d, J = 6 Hz, CH=C—C=O) ppm; mass spectrum *m/e* (rel intensity) 113 [M] (59%), 96 [M − OH] (51%), 85 (52%), 84 (53%), 69 (30%), 55 (100%); ir ($CHCl_3$) 3350 cm^{-1} br (OH), 1690 cm^{-1} (C=O), (KBr) 1670, 1590 cm^{-1}. *Anal.* Calcd for $C_5H_7NO_2$: mol wt, 113.0477. Found: mol wt, 113.0478.

***N*-Methylmaleimide (4),**[4] 20 mg, 3% yield: NMR δ 3.0 (3 H, s, CH_3), 6.67 (2 H, s, =CH) ppm; mass spectrum[45] *m/e* (rel intensity) 111 [M] (100%), 83 (23%), 82 (24%), 54 (87%).

The same reaction with Methylene Blue sensitizer (15 mg) gave a 20% yield of **2** and a 10% yield of **3.** With Ⓟ-Rose Bengal[46] (23 mg) in dichloromethane, we isolated a 17% yield of **2** and with Methylene Blue a 10% yield of **2.** In water[4] with Rose Bengal, we isolated a 46% yield of **2.**

Under the conditions of the reaction in methanol, **3** does not convert to **2** and is recovered unchanged, and **2** does not convert to **3.** The rate of autoxidation of **1** is slow as evidenced by the observation that attempted autoxidation (O_2 bubbling, no light) gave only starting pyrrole back after 8 h and more than 95% after 24 h.

Photosensitized Oxygenation of *N*-Methylpyrrole (1) in Acetone. To a large test tube (25 mm × 200 mm) were added 81 mg (1.0 mmol) of *N*-methylpyrrole, 50 ml of dry acetone, and 4 mg of Methylene Blue. The test tube was cooled to −78° in a half-silvered dewar containing dry ice–acetone and irradiated for 90 min with a quartz–iodine lamp (Sylvania Q/CL) at 80 V while a slow stream of O_2 bubbles was swept through the solution. After warming to room temperature, the acetone was evaporated on a rotatory evaporator below 45°. Product separation was accomplished by preparative thin-layer chromatography on silica gel using ether to yield 16% of **2**, 4% of **4**, and a new substance.

***N*-Methyl-3-hydroxy-Δ^4-pyrrolin-2-one (5),** 12 mg, 2.6% yield, NMR δ 2.97 (3 H, s, CH_3), 6.17 (1 H, s, HC-O), 6.33 (1 H, d, J = 7 Hz, C=CHC), 6.92 (1 H, d, J = 7 Hz, NCH=C) ppm; mass spectrum *m/e* (rel intensity) 113 [M] (100%), 96 [M − OH] (69%), 84 (14%), 71 (13%), 67 (28%), 57 (23%), 55 (47%); ir ($CHCl_3$) 3300 cm^{-1} br (OH), 1690 cm^{-1} (C=O), (KBr) 1708, 1600 cm^{-1}. *Anal.* Calcd for $C_5H_7NO_2$: mol wt, 133.0477. Found: mol wt, 113.0412.

***N*-Methyl-5-methoxy-Δ^3-pyrrolin-2-one (3) from *N*-Methyl-5-hydroxy-Δ^3-pyrrolin-2-one (2).** Approximately 10 mg (0.09 mmol) of *N*-methyl-5-hydroxy-Δ^3-pyrrolin-2-one (from photooxygenation of *N*-methylpyrrole in benzene (40% isotopically pure $H_2{}^{18}O$) and 5 ml of ether were added to a 50-ml Erlenmeyer flask. Diazomethane, prepared from Diazald (Aldrich), aqueous KOH, and ether, was codistilled with ether into the pyrrole solution. Addition of a few drops of $BF_3{\cdot}Et_2O$ to the yellow solution caused rapid decoloration. Additional ethereal diazomethane was added until the yellow color persisted, and the solution was concentrated by evaporation on a steam bath. Preparative thin-layer chromatography on silica gel (ether) yielded the 5-methoxylactam, 5 mg, 44%, which had exactly the same ^{18}O incorporation (6%) as its precursor alcohol by mass spectrometry.

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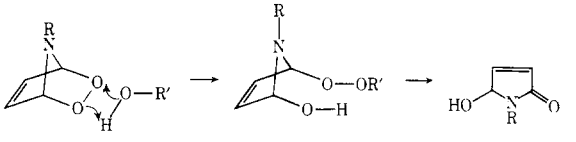
(38) The ^{18}O incorporation was determined by measurement of the increased ratio of [M + 2]/[M] in the ^{18}O experiment *vs.* the same ratio in samples prepared by photooxygenation in normal water. In order to exclude the possible, but unlikely loss of label by exchange reaction in the mass spectrometer inlet system and source before electron impact ionization, labeled **2** was converted to labeled **3** by diazomethane–$BF_3{\cdot}Et_2O$. Both **2** and **3** (derived from **2**) showed the same ^{18}O incorporation. Also, the ^{16}OH-hydroxylactam has been shown not to undergo exchange with $H_2{}^{18}O$ under the photooxygenation conditions.
(39) A structure close to the zwitterion is the corresponding hydroperoxide isolated from photooxygenation of 2,5-di-*tert*-butylpyrrole, ref 23. Whether a zwitterion can also be prepared from *N*-methyl-2,5-di-*tert*-butylpyrrole has not been explored.
(40) One alternative which involves solvent without oxygen incorporation is attack by hydroxylic solvent on both oxygens of the *endo*-peroxide to give an intermediate hydroxy hydroperoxide (R′ = H) or hydroxy alkylperoxide (*e.g.*, R = CH_3). In this mechanism, ^{18}O would not be incorporated. However, hydroxy alkylperoxides (R′ = CH_3) have not been observed in the pyrrole series (too unstable?) and only methoxyhydroperoxy intermediates have been isolated with furans.



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