# The *meso*-Reactivity of Porphyrins and Related Compounds. Part VII.[1] Benzoyloxylation of Phenylpyrroles and of Octaethylporphyrin [2]

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Benzoyl peroxide reacts with phenylpyrroles under mild conditions to give mixtures of which benzoyloxy-derivatives are the major components. 2,5-Diphenyl-, 1,2,5-triphenyl-, and 2,3,5-triphenyl-pyrroles give β-benzoyloxy-derivatives, and 2,3,4,5-tetraphenylpyrrole gives 2-benzoyloxy-2,3,4,5-tetraphenyl-2*H*-pyrrole. These reactions do not appear to involve substitution by benzoyloxyl radicals, although the substrate radicals (or radical cations) are possible intermediates.

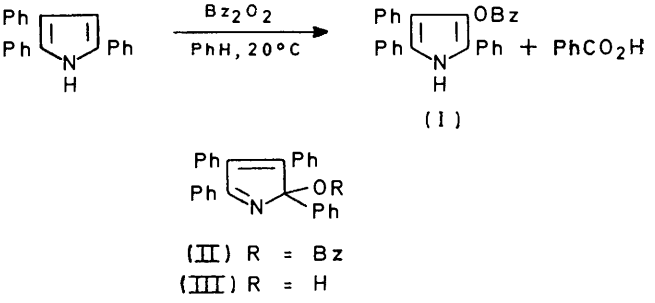
With octaethylporphyrin at 95 °C substitution at *meso*-positions (giving mono-, bis-, tris-, and tetrakis-benzoyloxy-derivatives) and at side chain ' benzylic ' positions is observed. The latter reaction is quenched by oxygen, and in iron porphyrin substrates, and is regarded as a radical-chain process.

Phenylation was not detected in any of these reactions and can be no more than a minor pathway under the conditions employed.

THE reaction of benzoyl peroxide with porphyrins provides a method of introducing an oxygen substituent into a *meso*-position,[3] a process which, for metal complexes, may have a bearing on biological phenomena such as electron transport and haem catabolism. We report here a detailed examination of the products of this reaction.

Although the reactions of pyridine and its relatives with benzoyl peroxide have been extensively studied,[4] the reactions of simple π-excessive nitrogen heteroaromatic compounds with this reagent have, until recently, received little attention. An *N*-alkylpyrrole is reported [5] to give the 2-benzoyloxy-derivative. Indole gives products of oxidative di- and tri-merisation, together with a benzoyloxy-derivative: 3-methylindole also yields a benzoyloxy-derivative, although the structures of these benzoyloxy-derivatives have not been unambiguously assigned.[6] *N*-Methylindole gives 3-benzoyloxy- and 2,3-bisbenzoyloxy-derivatives.[7] Although an early attempt to bring about the reaction of benzoyl peroxide with dipyridinecoprohaemochrome I tetramethyl ester appears to have failed,[8] reactions have occasionally been noted in the porphyrin series. Thus Krasnovski [9] observed that treatment of chlorophyll and of magnesium(II) phthalocyanin with benzoyl peroxide gave unidentified oxidation products (presumably radical cations and their transformation products): reactions have also been observed for copper(II) phthalocyanin,[10] and for metalloporphyrins.[10-12] An excess of benzoyl peroxide has been employed to bleach porphyrin samples prior to radiometric estimation.[13]

*Pyrroles.*—At the outset of this work, there appeared to be no information on the reaction of benzoyl peroxide with pyrroles. Preliminary experiments showed that both pyrrole itself and 2,5-dimethylpyrrole reacted readily, but isolation procedures were attended by the formation of tars, and it proved more convenient to make the initial study with pyrroles stabilised by phenyl substituents. Thus treatment of 2,3,5-triphenylpyrrole in benzene under nitrogen at room temperature with an equimolar amount of benzoyl peroxide gave benzoic acid (0.89 mol. equiv. isolated) and 4-benzoyloxy-2,3,5-triphenylpyrrole (0.54 mol. equiv. isolated). T.l.c. showed that two minor by-products were formed and a small amount of starting material remained. 2,3,4,5-Tetraphenylpyrrole was not detected, and, if formed, can have been present in only trace amounts. Products in which substitution occurred at nitrogen or in a phenyl substituent were not recognised, but closer examination of the by-products might reveal such compounds.

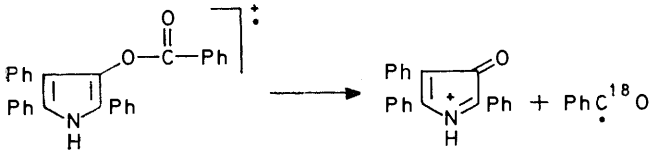



The assignment of structure (I) is based on elemental analysis and spectroscopic data. The mass spectrum showed the molecular ion (*m/e* 415) with a fragment ion (310) attributed to the loss of the benzoyl radical. The signal at δ 6.56 assigned to the β-proton in the n.m.r. spectrum of 2,3,5-triphenylpyrrole was missing in the n.m.r. spectrum of (I), which comprised merely the

[1] Part VI, R. Bonnett and A. F. McDonagh, *J.C.S. Perkin I*, 1973, 881.
[2] Preliminary communication, R. Bonnett and A. F. McDonagh, *Chem. Comm.*, 1970, 337.
[3] R. Bonnett, M. J. Dimsdale, and G. F. Stephenson, *J. Chem. Soc.* (*C*), 1969, 564.
[4] D. H. Hey, C. J. M. Stirling, and G. H. Williams, *J. Chem. Soc.*, 1955, 3962; D. H. Hey, *Adv. Free-Radical Chem.*, 1967, **2**, 41.
[5] G. Vernin, H. J. M. Dou, and J. Metzger, *Bull. Soc. chim. France*, 1972, 1173.
[6] R. B. Roy and G. A. Swan, *J. Chem. Soc.* (*C*), 1968, 80.
[7] Y. Kanaoka, M. Aiura, and S. Hariya, *J. Org. Chem.*, 1971, **36**, 458.
[8] H. Fischer and H. Libowitzky, *Z. physiol. Chem.*, 1938, **255**, 198.
[9] A. A. Krasnovski, *Doklady Akad. Nauk S.S.S.R.*, 1947, **58**, 835 (*Chem. Abs.*, 1952, **46**, 8647).
[10] C. J. Pedersen, *J. Org. Chem.*, 1957, **22**, 127.
[11] I. H. Campion-Smith, Ph.D. Thesis, London, 1973.
[12] D. Dolphin. Z. Muljiani, K. Rousseau, D. C. Borg, J. Fajer, and R. H. Felton, *Ann. New York Acad. Sci.*, 1973, **206**, 177.
[13] J. A. S. Cavaleiro, G. W. Kenner, and K. M. Smith, *J.C.S. Perkin I*, 1973, 1188.

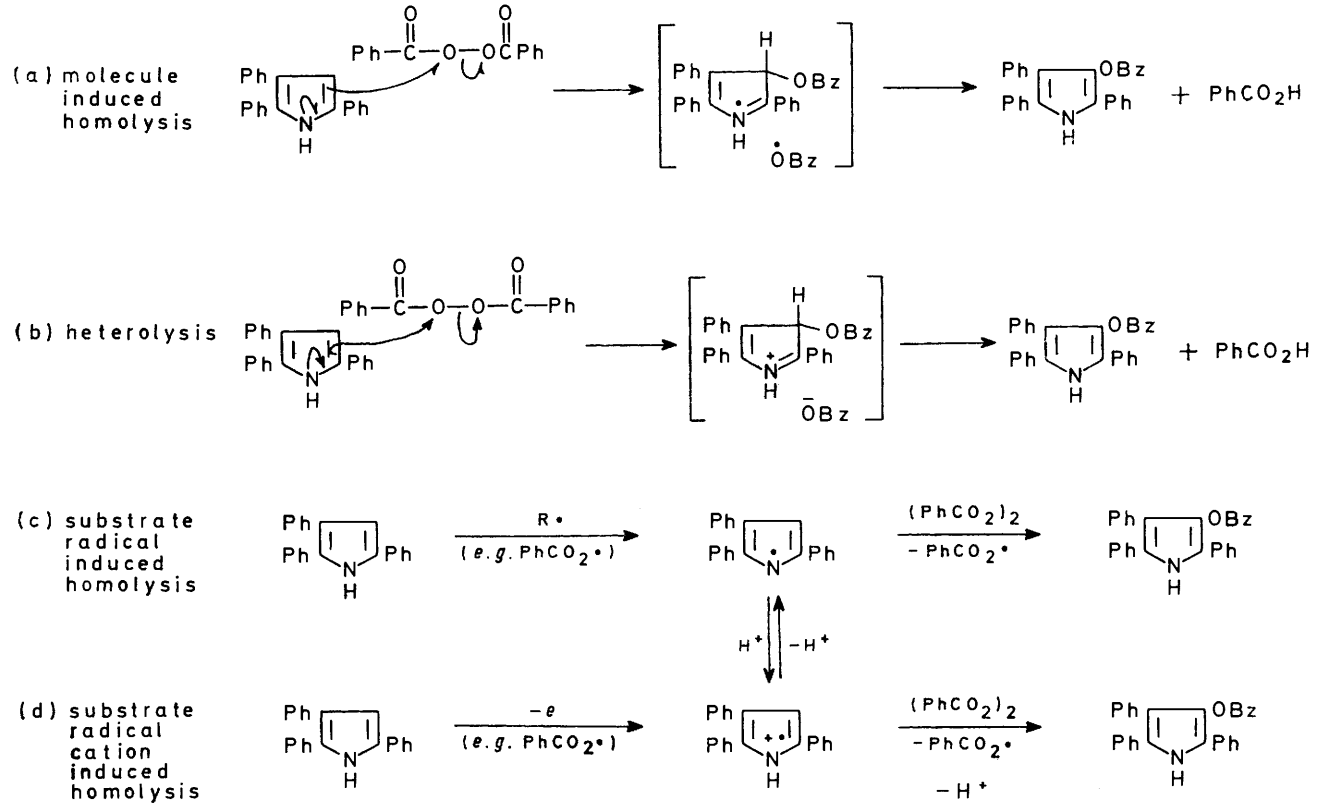
complex multiplets at lower field (δ 7.2—8.2) attributed to the phenyl protons. The i.r. spectrum possessed a weak band at 3 420 $cm^{-1}$ (NH stretching) and a carbonyl stretching vibration at 1 722 $cm^{-1}$.

The reactions of some other polyphenylpyrroles were also examined: the isolated products, which were the




major but not the sole ones, were in each case benzoyloxy-derivatives. Thus 2,5-diphenylpyrrole gave 3-benzoyloxy-2,5-diphenylpyrrole (31%), accompanied by several other products, some of which are believed to arise by oxidative dimerisation. 1,2,5-Triphenylpyrrole gave the 3-benzoyloxy-derivative in 78% yield. The major product from 2,3,4,5-tetraphenylpyrrole is formulated as 2-benzoyloxy-2,3,4,5-tetraphenyl-2*H*-pyrrole (II), on the basis of elemental analysis, spectroscopic evidence, and its conversion, on careful hydrolysis, into the known [14] hydroxy-derivative (III).

That reaction occurred under such mild conditions (benzene; 20 °C) suggested that the attacking species was not a free benzoyloxyl radical generated by thermolysis. This was confirmed by employing [*carbonyl*-$^{18}$O]-benzoyl peroxide as reagent with 2,3,5-triphenylpyrrole. Mass spectrometry of the resulting 4-benzoyloxy-derivative (Table 3) showed no evidence for scrambling of the label during the reaction. Hence the reaction involves attack on molecular benzoyl peroxide. At least four possible pathways remain (see Scheme): a molecule–molecule reaction could involve homolytic (a) and/or heterolytic (b) fission of the oxygen–oxygen bond, and the initial formation of a pyrrolyl radical (c) or cation radical (d), which then induces the homolysis of benzoyl peroxide, also needs to be considered. Although one normally thinks of benzoyl peroxide as a radical reagent undergoing homolysis, a tendency to follow a heterolytic pathway in the present case is not unreasonable in view of the well known nucleophilicity of the pyrrole system. The situation is in some ways analogous to that obtaining in the reaction of amines with benzoyl peroxide.[15]




SCHEME

However, both molecule and radical (cation) induced homolytic pathways are reasonable alternatives, and, indeed, are not mutually exclusive: in one case we have been able to detect the substrate radical which slowly disappears during the course of the reaction. Treatment of 2,3,4,5-tetraphenylpyrrole with benzoyl peroxide in benzene generated a cherry-red solution, the electronic and e.s.r. spectra of which accord with those reported

[14] R. E. Lutz and D. W. Boykin, *J. Org. Chem.*, 1967, **32**, 1179.
[15] D. B. Denney and D. Z. Denney, *J. Amer. Chem. Soc.*, 1960, **82**, 1389.

for the 2,3,4,5-tetraphenylpyrrolyl radical.[16] Attempts to observe an e.s.r. signal in the analogous reaction with 2,3,5-triphenylpyrrole proved unsuccessful, but this may merely reflect the shorter lifetime expected for the radical derived from this pyrrole, which would make it an unsuitable candidate for detection in a static system.

*Octaethylporphyrin.* When octaethylporphyrin (*ca.* 5 mmol $l^{-1}$) is treated with benzoyl peroxide in 1,2,4-trichlorobenzene at *ca.* 95°, 5-benzoyloxyoctaethylporphyrin (IV) (28%) [3] is formed, accompanied by smaller amounts of more polar compounds. At higher concentrations (*ca.* 15 mmol $l^{-1}$) six fractions [other than starting material and (IV)] can be separated and identified.

TABLE 1

Electronic spectra of benzoyloxy-derivatives of octaethylporphyrin in chloroform [$\lambda_{max.}$/nm(ε)]

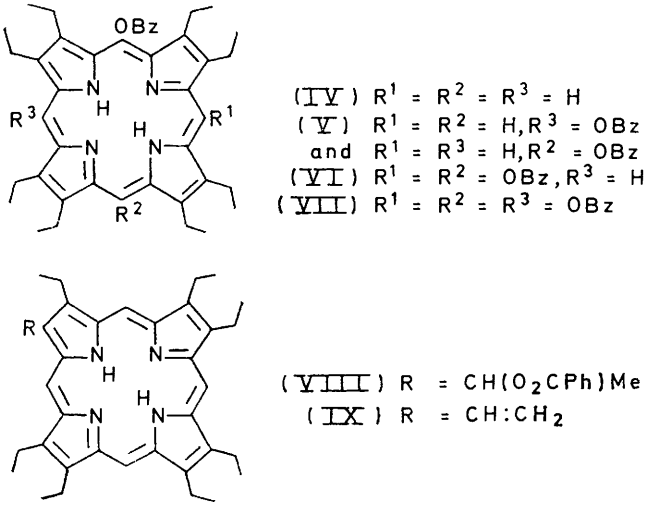
| Octaethylporphyrin derivative | Soret | IV | III | II | I | $\varepsilon_{III}/\varepsilon_{IV}$ |
|---|---|---|---|---|---|---|
| Parent [a] * | 401 (167 000) | 499 (13 300) | 534 (10 300) | 566 (6 600) | 618 (4 900) | 0.77 |
| *meso*-Benzoyloxy (IV) † | 402 (174 000) | 501 (16 100) | 533 (6 540) | 571 (6 200) | 623 (1 900) | 0.41 |
| *meso*-Bisbenzoyloxy (V) | 409 (185 000) | 506 (16 600) | 536 (3 800) | 580 (5 700) | 631 (580) | 0.23 |
| *meso*-Trisbenzoyloxy (VI) | 415 (167 000) | 511 (14 600) | 544 (3 100) | 588 (4 600) | 648 (610) | 0.21 |
| *meso*-Tetrakisbenzoyloxy (VII) | 422 (186 000) | 518 (14 800) | 556 (4 900) | 597 (4 600) | 655 (1 300) | 0.33 |
| $2^1$-Benzoyloxy (VIII) | 402 (165 000) | 500 (12 500) | 536 (10 000) | 568 (6 400) | 623 (3 500) | 0.80 |
| *meso*-Benzoyloxy-(1-benzoyloxyethyl)-heptaethylporphyrin | 406 (161 000) | 503 (12 800) | 537 (5 800) | 572 (5 500) | 627 (1 300) | 0.45 |
| Bis-(1-benzoyloxyethyl)-hexaethylporphyrin | 403 (179 000) | 502 (12 400) | 536 (9 500) | 568 (6 000) | 624 (2 700) | 0.77 |

[a] Also Ia 594 (1 200).

* R. Bonnett and G. F. Stephenson, *J. Org. Chem.*, 1965, **30**, 2791. † Ref. 3.

The products fall into two series. The first series, the expected one, consists of the bis-, tris-, and tetrakis-*meso*-benzoyloxy-derivatives [(V), (VI), and (VII)] of octaethylporphyrin. [The disubstituted derivative (V) is thought to be a mixture of two isomers, as shown, but these were not separated.] The mass spectra of these compounds showed strong molecular ions with important fragment ions representing losses of benzoyl radicals. The i.r. spectra possessed bands at 1 738—1 748 $cm^{-1}$ as expected for the carbonyl stretching mode of an aryl ester [*cf.* (IV), $\nu_{max.}$ 1 740 $cm^{-1}$]. The electronic spectra (Table 1) showed gradually increasing bathochromic shifts with increasing substitution: the spectra possessed phyllo-character (relative lowering of $\varepsilon_{III}$) [17] although only the di- and tri-substituted compounds gave spectra which were clearly of the phyllo-type. This recalls the behaviour of the *meso*-chlorooctaethylporphyrins, where the *meso*-tetrachloro-derivative does not show a phyllo-type spectrum, although such a spectrum is shown by the monochloro- (marginally) and dichloro-compounds.[17]

The n.m.r. spectrum of compound (VI) unexpectedly showed two signals in the *meso*-region. The total integration corresponded to one proton, and the signals were unaffected by treatment with $D_2O$. We interpret this as evidence for an isomerism caused by restricted rotation of a *meso*-benzoyloxy-group flanked by ethyl substituents on neighbouring β-positions, a situation which may be represented diagrammatically as in (i) and (ii), the thickened line representing the approximately planar porphyrin system. *X*-Ray analysis of compound (IV) reveals [18] that the benzoyloxy-group protrudes out of the average plane of the macrocycle as shown, and that, around the point of substitution the macrocycle is deformed in the same direction as the substituent protrudes. For 5,10,15-trisbenzoyloxyoctaethylporphyrin it is suggested that the two signals represent two species in which the 5- and 15-substituents protrude on the same face (i) or on opposite faces (ii) of the macrocycle. The situation is presumably more complex than this because in principle the same restriction applies to the 10-substituent: it is thought that either the arrangement with the three substituents protruding on the same face is an unfavourable one, or the geometry of the 10-substituent has an insignificant effect on the chemical shift of the 20-proton. For the 5,15-bisbenzoyloxyoctaethylporphyrin, two isomers corresponding to (i) and (ii) would also be anticipated, and two more might also be expected for the 5,10-disubstituted compound. Accordingly *two* pairs of signals (total 2 H) were observed in the *meso*-region of the n.m.r. spectrum of the *meso*-di-



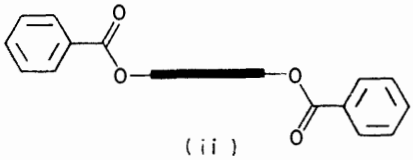

[16] S. M. Blinder, M. L. Paller, N. W. Lord, L. C. Aamodt, and N. S. Ivanchukov, *J. Chem. Phys.*, 1962, **36**, 540.

[17] R. Bonnett, I. A. D. Gale, and G. F. Stephenson, *Canad. J. Chem.*, 1966, **44**, 2503.

[18] M. B. Hursthouse and S. Neidle, *J.C.S. Chem. Comm.*, 1972, 449.

benzoyloxy fraction. Such isomerism finds analogy in the restricted rotation of the *meso*-aryl group observed with 5,10,15,20-tetrakis-(*o*-hydroxyphenyl)porphyrin.[19]

(i)

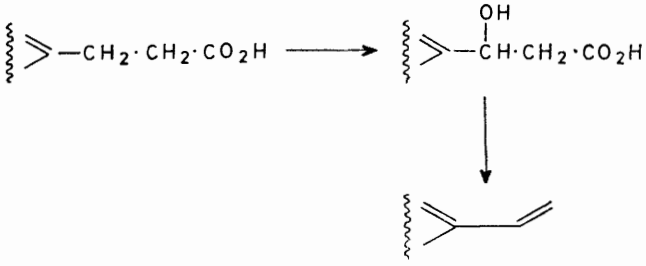


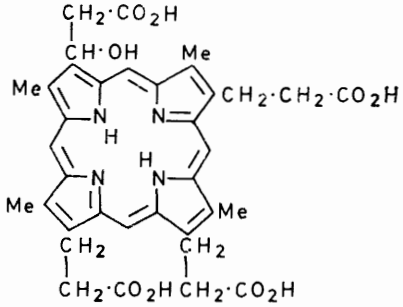
(ii)

The second series of products from the reaction of octaethylporphyrin with benzoyl peroxide proved to be substances in which a benzoyloxy-group had been introduced into the side chain at the ' benzylic ' position. The simplest compound of this series, 2-(1-benzoyloxyethyl)heptaethylporphyrin (VIII) was less mobile than its isomer (IV) on t.l.c. and was isolated in 12% yield. The visible spectrum (Table 1), which showed a small bathochromic shift with respect to the parent, was clearly of the etio-type. The i.r. spectrum had $\nu_{max.}$ 1 718 $cm^{-1}$, consistent with a carbonyl stretch for an alkyl ester. The presence of a side chain benzoyloxy-group was confirmed by the n.m.r. spectrum, which showed four *meso*-protons, and a doublet ($J$ 7 Hz) at $\delta$ 2.51 assigned to the function $CH(OR)\cdot CH_3$. In sharp contrast with compounds of the *meso*-substituted series, the side-chain ester (VIII) gave a very weak molecular ion (654), the base peak (532) arising from the loss of benzoic acid, the molecular ion (122) of which was also pronounced. Pyrolysis of (VIII) at *ca.* 250 °C gave benzoic acid (88%) and heptaethylvinylporphyrin (IX) (65%).

Two other fractions belonging to this series were isolated. One is regarded as bis-(1-benzoyloxyethyl)-hexaethylporphyrin (isomers) since it had a visible spectrum of the etio-type, $\nu_{max.}$ 1 722 $cm^{-1}$, and a mass spectrum which, while it showed no molecular ion, had an important fragment at 530 ($M$ — $2PhCO_2H$). The other fraction is regarded as *meso*-benzoyloxy-(1-benzoyloxyethyl)heptaethylporphyrin (isomers). It had a visible spectrum possessing phyllo-character (*cf.* $\varepsilon_{III}/\varepsilon_{IV}$, Table 1) and showed i.r. bands at both 1 720 and 1 738 $cm^{-1}$ consistent with this formulation; the mass spectrum showed no molecular ion, but an appreciable fragment at 652 ($M$ — $PhCO_2H$).

The introduction of an oxygen function at the ' benzylic ' positions of an alkylporphyrin is reasonable on chemical grounds, although there are few previous examples of it. It is of particular interest because of the structural relationship to the intermediate step postulated in the biochemical conversion of a propionic acid side chain into a vinyl group in the biosynthesis of protoporphyrin.[20] Indeed hydroxylated porphyrins of this structural pattern [*e.g.* (X)] have been isolated from patients with defective porphyrin metabolism.[21] However, the biosynthetic hydroxylation is believed to occur at the porphyrinogen, and not the porphyrin, oxidation level.





(X) (or positional isomer)

The known rate of decomposition of benzoyl peroxide into radicals (benzoyl peroxide is reported [22] to have a half-life of 30 min at 100 °C) makes it likely that at 95 °C both free-radical and induced homolysis pathways are operating. Conditions for the reaction were varied, and products estimated spectroscopically (Table 2). The results show that the reaction is complete within 15 min at 95 °C, and that after 1 h products of ester pyrolysis can be detected in small quantity. Increasing the molar proportion of benzoyl peroxide from *ca.* 1 to *ca.* 2 increases the yields of the polysubstituted products as expected. When the reaction is carried out in an atmosphere of oxygen, side-chain substitution virtually ceases. It is thought that the side-chain substitution which occurs in an inert atmosphere is of the radical-chain type, and that oxygen serves to interrupt the chain: attempts to quench the side-chain reaction with hydroquinone have been unsuccessful.[11] The effect of a central metal ion on the reaction is best examined by analysing the mixture of metallated products,[11] but since the iron complexes are difficult to separate by t.l.c. the products

[19] L. K. Gottwald and E. F. Ullman, *Tetrahedron Letters*, 1969, 3071.

[20] S. Sano, *J. Biol. Chem.*, 1966, **241**, 5276; A. R. Battersby, 23rd IUPAC Congress, Boston, 1971, issued as Special Supplement vol. V, 1971, p. 1 to *Pure Appl. Chem.*, Butterworths, London.

[21] G. H. Elder and J. R. Chapman, *Biochim. Biophys. Acta*, 1970, **208**, 535.

[22] W. A. Pryor, ' Free Radicals,' McGraw-Hill, New York, 1966, p. 91.

have been demetallated before separation.* The results for octaethylhaemin and dipyridineoctaethylhaemochrome are rather similar: in contrast to earlier reports,[8,12] both substances react extensively (though less extensively than octaethylporphyrin itself), and *meso*-substitution now preponderates, *i.e.* under these conditions side-chain substitution is a minor pathway even under nitrogen. Presumably interruption of the occurrence of the side-chain benzoyloxylation accords with this view, as do preliminary experiments[11] with [$^{18}$O]benzoyl peroxide, which indicate partial scrambling of the label.

No products of phenylation were detected in either system. For the pyrrole, some of the possible phenylation products were to hand for comparison. This was not the case for the porphyrin, but an inspection of the mass balances in Table 2 (often >80%) indicates that phenylation can be no more than a minor process in the reactions studied here.

TABLE 2

Benzoyloxylation of octaethylporphyrin and its iron complexes (0.016 mol $l^{-1}$) in 1,2,4-trichlorobenzene at *ca.* 95 °C

| Conditions | | | | Products (% yield) * | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Substrate | Mol. proportion of $Bz_2O_2$ | Atmosphere | Time (min) | A | (IV) | (V) | (VI) | (VII) | (VIII) | B | C |
| Octaethylporphyrin | 1.1 | $N_2$ | 60 | 28 [a] | 27 | 7 | *b* | *b* | 20 | 7 | 3 |
| | 1.0 | $N_2$ | 15 | 33 | 34 | 8 | *b* | *b* | 11 | 4 | 2 |
| | 1.1 | $O_2$ | 15 | 31 [c] | 37 | 10 | *b* | *b* | 1 | N.d.† | N.d. |
| | 2.2 | $N_2$ | 15 | 4 | 18 | 15 | 8 | 2 | 14 | 17 | 8 |
| | 2.2 | $O_2$ | 15 | 8 | 30 | 22 | 10 | 3 | 1 | 2 | N.d. |
| Octaethylhaemin | 2.2 | $N_2$ | 19 | 15 (12) [d] | 27 (34) | 15 (20) | 8 (10) | 4 (11) | 6 (4) | 6 (10) | 1 (2) |
| Dipyridineoctaethylhaemochrome | 2.3 (2.9) | $N_2$ | 15 | 22 (15) | 35 (31) | 19 (24) | 8 (14) | 5 (11) | 0.8 (1.5) | *b* (3) | N.d. (N.d.) |

*A, octaethylporphyrin recovered; B, *meso*-benzoyloxy-(1-benzoyloxyethyl)heptaethylporphyrin; C, bis-(1-benzoyloxyethyl)-hexaethylporphyrin. † N.d. = not detected.

[a] Contains *ca.* 8% heptaethylvinylporphyrin. [b] Not collected; but small amount only. [c] No heptaethylvinylporphyrin detected. [d] Parentheses refer to the repetition of the two metalloporphyrin experiments by Dr. I. H. Campion-Smith, whom we thank.

radical-chain process by the co-ordinated one-electron redox system is involved here: such a process would be analogous to the inhibition of styrene polymerisation by iron(III) chloride.[23] Thus the iron porphyrin system appears to be susceptible to attack by radicals (or by incipient radical species) at the *meso*-positions: this may have a bearing on the chemistry of haem catabolism.

A comment is needed on the recent report by Castro and his colleagues[24] on this reaction. The reaction was studied in somewhat more dilute solution (7 mmol $l^{-1}$) and with a lower molar proportion (0.5) of benzoyl peroxide. As expected polysubstitution was not important. It is surprising, however, that (under argon) the product (VIII) of side-chain substitution was not detected. It seems likely that (VIII) was indeed formed, but was converted into heptaethylvinylporphyrin (which is difficult to separate from octaethylporphyrin) under the rather strenuous reaction conditions (120 °C; 2 h; *cf.* first item in Table 2, which refers to 95 °C; 1 h).

With the pyrroles and porphyrins studied here nuclear benzoyloxylation is the major reaction: with octaethylporphyrin some side-chain substitution occurs, but the reaction is quenched by oxygen, or by co-ordination to iron, and is regarded as a minor radical-chain pathway. For the room temperature reaction with the pyrrole, the nuclear benzoyloxylation does not involve attack by benzoyloxyl radicals, but is considered to involve one or more of the pathways shown in the Scheme. Analogous mechanisms to those shown can be envisaged for the porphyrin reaction, but at 95 °C it seems likely that *meso*-attack by benzoyloxyl radicals also occurs. The

* This process is itself not without dangers, such as hydrolysis and elimination, but as the Table shows it is reasonably reproducible.

## EXPERIMENTAL

Preparative t.l.c. was carried out on Merck silica gel HF 254, the plates (400 × 300 × 1.5 mm) being washed with methanol and reactivated (110 °C; 4 h) before use. By-products are sometimes designated by $R_S$ values [t.l.c.: (distance moved)/(distance moved by starting material)]. Commercial benzoyl peroxide was shaken with chloroform. The chloroform layer was separated from water, dried ($MgSO_4$), and diluted with methanol. The resulting crystalline benzoyl peroxide was dried over calcium chloride. Petroleum refers to that fraction of light petroleum with b.p. 60—80°. Solvent ratios refer to volumes.

Spectroscopic data were obtained and are reported as indicated previously.[1,25] Unless otherwise noted, electronic spectra (λ in nm) refer to solutions in chloroform, n.m.r. spectra to solutions in [$^2$H]chloroform, and i.r. spectra (ν in $cm^{-1}$) to KBr discs. Some electronic spectra of benzoyloxylated porphyrins are collected in Table 1.

*Benzoyloxylation of Pyrroles.*—*2,5-Diphenylpyrrole.* Benzoyl peroxide (1.5 g, 0.9 mol.) in benzene (50 ml) was added to a stirred solution of 2,5-diphenylpyrrole (1.5 g) in benzene (100 ml) under nitrogen at room temperature. After 2 h the solution was shaken in turn with aqueous sodium hydroxide (30%; 12 ml) and water (3 × 50 ml); and dried ($MgSO_4$). Removal of the solvent gave a brown gum which was separated by preparative t.l.c. (30% acetone–petroleum). Several bands, some of which appeared to be unstable on the adsorbent, were detected. However no

[23] C. H. Bamford, A. D. Jenkins, and R. Johnston, *Proc. Roy. Soc.*, 1957, *A*, **239**, 214.

[24] C. E. Castro, C. Robertson, and H. Davis, *Bio-org. Chem.*, 1974, **3**, 343.

[25] R. Bonnett and R. Holleyhead, *J.C.S. Perkin I*, 1974, 962.

2,3,5-triphenylpyrrole was detected in the reaction product on mixed t.l.c. The fractions isolated were as follows: $R_S$ 1.3, a trace of material which was not further examined; $R_S$ = 1.0, 2,5-diphenylpyrrole (150 mg); $R_S$ = 0.7, 3-*benzoyloxy*-2,5-*diphenylpyrrole* (0.65 g, 31%), from benzene–petroleum as off-white crystals, m.p. 140—140.5° (Found: C, 81.45; H, 5.05; N, 4.25. $C_{23}H_{17}NO_2$ requires C, 81.4; H, 5.05; N, 4.15%), λ(EtOH) 232 (25 400) and 321 (28 800), ν 3 390, 1 720, 1 265, 1 085, 760, 750, 710, and 695, δ 6.65 (d, *J* 3 Hz, β-H), and 8.0—8.4 and 7.1—7.6 (m, Ph), *m/e* (130 °C) 339 (*M*, 100%), 234 (*M* − PhCO, 60), and 219 (*M* − $PhCO_2$ + H, 35).

2,3,5-*Triphenylpyrrole*. Benzoyl peroxide (0.638 g, 1 mol. equiv.) in benzene (25 ml) was added to a stirred solution of 2,3,5-triphenylpyrrole (0.772 g) in benzene (75 ml) under nitrogen at room temperature. After 2.5 h the solution was extracted with 2N-sodium hydroxide (3 × 25 ml) and with water (3 × 50 ml). Benzoic acid (mixed m.p. 122—123°) was recovered (0.285 g, 89%) from the alkaline extract. The benzene solution was dried and evaporated, and the residue was crystallised from benzene–petroleum to give a crude sample (m.p. 169—172°) of 4-*benzoyloxy*-2,3,5-*triphenylpyrrole* (0.59 g, 54%). T.l.c. revealed two minor impurities (neither of which was 2,3,4,5-tetraphenylpyrrole), which were removed by recrystallisation from benzene–petroleum to give crystals, m.p. 179—181° (Found: C, 83.4; H, 5.05; N, 3.5. $C_{29}H_{21}NO_2$ requires C, 83.85; H, 5.1; N, 3.35%), ν 3 420, 1 722, 1 270, 1 115, 758, 710, and 690, δ 7.9—8.2 and 7.2—7.77 (m, Ph), *m/e* (139 °C) 415 (*M*, 30%), 310 (*M* − PhCO, 8), 295 (*M* − $PhCO_2$ + H, 100), 122 ($PhCO_2H$, 97), and 105 (PhCO, 100).

A similar experiment was carried out with $(PhC^{18}O{\cdot}O)_2$ (12% enrichment). Mass spectroscopic data for the two samples are compared in Table 3.

TABLE 3

Mass spectroscopic data [relative abundances (%), 139 °C] for 4-benzoyloxy-2,3,5-triphenylpyrrole

| | | Prepared from $(PhCO{\cdot}O)_2$ | Prepared from $(PhC^{18}O{\cdot}O)_2$ |
|---|---|---|---|
| | 417 | 6.3 | 18.2 |
| | 416 | 34.5 | 33.2 |
| *M* | 415 | 100 * | 100 |
| | 312 | 2.15 | 15 |
| | 311 | 49 | 34 |
| *M* − PhCO | 310 | 100 * | 100 |
| | 124 | 1.7 | 14.3 |
| | 123 | 8.9 | 12.3 |
| $PhCO_2H$ | 122 | 100 * | 100 |

* For each set of ions (*m*, *m* + 1, *m* + 2) relative abundance is based on *m* = 100. Data are averages of two runs.

1,2,5-*Triphenylpyrrole*. Benzoyl peroxide (1.0 g, 1.2 mol. equiv.) in benzene (50 ml) was added to 1,2,5-triphenylpyrrole (1.0 g) in benzene (300 ml). The solution was kept at room temperature under nitrogen for 24 h, and the product was worked up as described immediately above to give crystals (1.1 g, 78%) of 3-*benzoyloxy*-1,2,5-*triphenylpyrrole*, m.p. 242—245° (Found: C, 83.8; H, 5.25; N, 2.95. $C_{29}H_{21}NO_2$ requires C, 83.85; H, 5.1; N, 3.35%), λ (EtOH) 228 (26 000) and 290 (15 600), ν (Nujol) 1 725, 1 595, 1 255, 1 055, 750, and 690, δ 8.0—8.4 (2 H, m), 7.1—7.7 (18 H, m), and 6.4 (1 H, s), *m/e* 415 (*M*, 100%), 310 (43), 294 (42), and 217 (28).

2,3,4,5-*Tetraphenylpyrrole*. Benzoyl peroxide (1.5 g, 1.15 mol. equiv.) in benzene (50 ml) was added to a solution of 2,3,4,5-tetraphenylpyrrole (2.0 g) in benzene (200 ml; room temperature; nitrogen flush). The solution became cherry-red (λ 525i and 564) and showed a broad e.s.r. signal (width 8 G) in which hyperfine structure was not resolved (access of oxygen during manipulation). The e.s.r. signal reached a maximum after about 35 min. After 2 h the solution was colourless; it was worked up as before to give crystals (1.4 g, 53%) of 2-*benzoyloxy*-2,3,4,5-*tetraphenyl*-2H-*pyrrole*, m.p. 251—252° (Found: C, 85.3; H, 5.15. $C_{35}H_{25}NO_2$ requires C, 85.5; H, 5.15%), ν 3 200, 1 700, 1 670, 1 630, 1 320, 1 290, 760, 710, and 690, δ 7.9—8.1 (2 H, m) and 7.0—7.5 (23 H, m). Hydrolysis of the benzoate with methanolic sodium hydroxide gave 72% of 2-hydroxy-2,3,4,5-tetraphenyl-2*H*-pyrrole, white crystals, m.p. 168—170° (lit.,[26] 171—173°; lit.,[14] 183—185°; lit.,[27] 204—205°) (from chloroform–petroleum), identical (mixed t.l.c., mixed m.p. 168—170°) with an authentic sample (m.p. 171—173°) prepared by the action of lead tetra-acetate on 2,3,4,5-tetraphenylpyrrole.[14]

*Benzoyloxylation of Octaethylporphyrin. Preparative Experiments*.—(a) *Under nitrogen*. Benzoyl peroxide (49.8 mg, 1.1 mol. equiv.*) in 1,2,4-trichlorobenzene (3 ml) was added during *ca*. 3 min to octaethylporphyrin (100 mg) in 1,2,4-trichlorobenzene (10 ml; continuous nitrogen flush; 95—97 °C). The solution was kept at this temperature for 1 h, and the solvent was then removed under reduced pressure (<95 °C). The product was chromatographed on neutral alumina (activity III): octaethylporphyrin was eluted with benzene–petroleum (1 : 1), 2-(1-benzoyloxyethyl)heptaethylporphyrin with benzene–petroleum (7 : 3) and 5-benzoyloxyoctaethylporphyrin with benzene. Intermediate fractions, and more polar material eluted with benzene–chloroform, were found (t.l.c. in 10% acetone–petroleum) to be mixtures, which were separated by preparative t.l.c. (20% acetone–petroleum). Appropriate fractions were combined, and the following compounds, in order of decreasing mobility, were obtained: octaethylporphyrin [33 mg, after recrystallisation from chloroform–methanol; probably contains some heptaethylvinylporphyrin (see Table 2)]; 2-(1-*benzoyloxyethyl*)-3,7,8,12,13,17,18-*heptaethylporphyrin* (15 mg, 12%), red-brown rosettes (from chloroform–methanol), slowly decomp. >250° (Found: C, 79.1; H, 7.55; N, 8.65. $C_{43}H_{50}N_4O_2$ requires C, 78.85; H, 7.7; N, 8.55%), ν 1 718, δ 10.57 (s, 20-H), 10.11 (s, 5-H), 10.04 (s, 10- + 15-H), 8.2—8.4 (m, *o*-H of Ph), 7.5—7.6 (m, *m*- and *p*-H of Ph), 3.96—4.26 (m, $CH_2$), 2.51 [d, *J* 7 Hz, $CH(OR){\cdot}CH_3$], 1.80—2.06 (m, $CH_2{\cdot}CH_3$), and −3.7br (s, NH), *m/e* (305 °C) 654 (*M*, 0.7%), 532 (*M* − $PhCO_2H$, 100), and 122 ($PhCO_2H$, 100); 5-*benzoyloxyoctaethylporphyrin* (31 mg, 25%), dark purple prisms, m.p. 282° (from chloroform–methanol), identical (mixed m.p., i.r., and n.m.r.) with an authentic sample;[3] bis-(1-benzoyloxyethyl)-hexaethylporphyrin (1 mg, 0.7%), amorphous red solid, m.p. 123—126°, ν 1 722, *m/e* (150 °C) 652 (*M* − $PhCO_2H$, trace), 530 (*M* − 2$PhCO_2H$, 20), 122 (88), 105 (93), and 57 (100); *meso*-benzoyloxy-(1-benzoyloxyethyl)heptaethylporphyrin (0.7 mg, 0.5%), brown needles, m.p. 152—200° (from chloroform–methanol), ν 1 720 and 1 738, *m/e* (290 °C)

* Some of the data reported for minor components are based on accumulated products obtained by repeating the experiment as described, or with 2.1 mol. equiv. of benzoyl peroxide.

[26] R. Kuhn and H. Kainer, *Annalen*, 1952, **578**, 227.

[27] C. Dufraisse, G. Rio, A. Ranjou, and O. Pouchot, *Compt. rend.*, 1965, **261**, 3133.

652 ($M$ − $PhCO_2H$, 5%), 547 ($M$ − $PhCO_2H$ − PhCO, 14), and 122 (100); *meso*-bisbenzoyloxyoctaethylporphyrin (2.2 mg, 1.5%), dark red prisms, m.p. 211—250° (from chloroform–methanol) (see below for further characterisation). The disubstituted compounds are presumably mixtures of positional isomers: attempts to separate these by t.l.c. were unsuccessful.

(b) *Under oxygen.* The experiment described above was repeated except that (i) 2.2 mol. equiv. of benzoyl peroxide were used, (ii) the nitrogen flush was replaced by an oxygen flush, (iii) the reaction time was 12 min, and (iv) after rapid removal of solvent under reduced pressure the products were separated by preparative t.l.c. (25% acetone–petroleum). This gave (in order of decreasing mobility): octaethylporphyrin (7.4 mg, 7%); 2-(1-benzoyloxyethyl)heptaethylporphyrin (1.5 mg, 1%); 5-benzoyloxyoctaethylporphyrin (35 mg, 29%); *meso*-benzoyloxy-(1-benzoyloxyethyl)-heptaethylporphyrin (3.9 mg, 3%); meso-*bisbenzoyloxyoctaethylporphyrin* (42 mg, 29%), dark red platelets, m.p. 246—248° (from chloroform–methanol) (Found: C, 77.3; H, 6.3; N, 7.7%; $M^+$, 774.415. $C_{50}H_{54}N_4O_4$ requires C, 77.5; H, 7.0; N, 7.25%; $M$, 774.4145), ν 1 748, δ 10.14 (s), 10.11 (s), 9.89 (s), and 9.86 (s) (total 2 H, *meso*-H), 8.53—8.81 (m, *o*-H of Ph), 7.61—7.83 (m, *m*- and *p*-H of Ph), 3.42—5.84 (m, $CH_2$), and 1.54—2.00 (m, Me), *m/e* (290 °C) 774 ($M$, 16%), 669 ($M$ − PhCO, 42), 563 ($M$ − 2PhCO + H, 6), and 105 (100); 5,10,15-*trisbenzoyloxy*-2,3,7,8,12,13,17,18-*octaethylporphyrin* (23 mg, 14%), attempted recrystallisation of which from chloroform–methanol gave an amorphous red-brown solid (12 mg), m.p. 292—295° (Found: $M^+$, 894.437. $C_{57}H_{58}N_4O_6$ requires $M$, 894.436), ν 1 742, δ 9.78 and 9.86 (s, *meso*-H), 8.46—8.70 (m, *o*-H of Ph), 7.46—7.78 (m, *m*- and *p*-H of Ph), 3.44—4.06 (m, $CH_2$), and 1.44—1.90 (m, Me), *m/e* (294 °C) 894 ($M$, 23%), 789 ($M$ − PhCO, 45), 669 (40), 654 (26), 565 (55), and 550 (100); and 5,10,15,20-*tetrakisbenzoyloxy*-2,3,7,8,12,13,17,18-*octaethylporphyrin* (14 mg, 7%), which crystallised from chloroform–petroleum as rectangular prisms (5 mg), m.p. >320° (Found: $M^+$, 1 014.461. $C_{64}H_{62}N_4O_8$ requires $M$, 1 014.457), ν 1 738, δ (noisy spectrum) 8.54—8.74 (m, *o*-H of Ph), 7.64—7.86 (m, *m*-*p*-H of Ph), 3.46—3.88 (m, $CH_2$), and 1.16—2.00 (m, Me), *m/e* (302 °C) 1 014 ($M$, 17%), 908 (24), 894 (18), 789 (33), 743 (24), 685 (32), 670 (28), 669 (29), 654 (20), 565 (60), 550 (100), and 549 (85).

*Reaction of Benzoyl Peroxide with Octaethylporphyrin. Spectroscopic Estimation of Products.*—Benzoyl peroxide (5 or 10 mg) in 1,2,4-trichlorobenzene (0.1 ml) was added to a solution of octaethylporphyrin (10 mg) in trichlorobenzene (1 ml; nitrogen or oxygen flush; 95 °C) as described above. (The benzoyl peroxide solution was rinsed in with a further 0.1 ml of solvent.) At the appropriate time the solvent was removed (reduced pressure; <95 °C) and the residue was fractionated by t.l.c. (200 × 200 × 1 mm; developing with 15% acetone–petroleum; extracting with chloroform). Product yields were estimated spectrophotometrically. The identity of the products was confirmed by mixed t.l.c. In two experiments the recovered octaethylporphyrin fraction was rechromatographed (t.l.c.; benzene–petroleum, 1 : 1) and the proportion of vinylheptaethylporphyrin present was estimated. The results are presented in Table 2.

Octaethylhaemin and dipyridineoctaethylhaemochrome were treated with benzoyl peroxide in the same way. Trichlorobenzene was removed and the residue was dissolved in pyridine (3 drops) and acetic acid (10 ml). A saturated solution of iron(II) sulphate in concentrated hydrochloric acid (2 ml) was added under nitrogen. After 5 min the solution was diluted with water and extracted with chloroform (3 × 10 ml). The extract was washed in turn with water (2 × 10 ml) and saturated aqueous sodium hydrogen carbonate (10 ml), filtered, and evaporated under reduced pressure. (A separate experiment showed that this procedure did not appreciably alter the composition of a mixture produced by the reaction of octaethylporphyrin with 2 mol. equiv. of benzoyl peroxide.) The residue was subjected to t.l.c. and yield estimation was performed as before (Table 2).

*Pyrolysis of Benzoyloxy-derivatives of Octaethylporphyrin.*—(a) *Small-scale experiments.* A small sample between microscope slide and coverslip was pyrolysed in air by placing the slide on the preheated block (temperature in parentheses) of a Kofler hot-stage apparatus. The sample was left for *ca.* 1 min, and the product was examined by t.l.c. 5-Benzoyloxyoctaethylporphyrin (284—287 °C) was essentially unchanged (trace of octaethylporphyrin). 2-(1-Benzoyloxyethyl)heptaethylporphyrin (250 °C) was converted into 2-vinylheptaethylporphyrin. *meso*-Benzoyloxy-(1-benzoyloxyethyl)heptaethylporphyrin (280—290 °C) was converted into a new porphyrin (presumably *meso*-benzoyloxyheptaethylvinylporphyrin) having the same $R_F$ value as 5-benzoyloxyoctaethylporphyrin. Bis-(1-benzoyloxyethyl)-hexaethylporphyrin (280—290 °C) gave mainly a compound having the same $R_F$ value as octaethylporphyrin.

(b) *Preparation of* 3,7,8,12,13,17,18-*heptaethyl*-2-*vinylporphyrin.* 2-(1-Benzoyloxyethyl)heptaethylporphyrin (9.1 mg) was heated in a sublimation tube at 250—260 °C (Woods metal) and 0.1 mmHg for 3 min. The white sublimate was resublimed at 100 °C and 0.1 mmHg to give benzoic acid (1.5 mg, 88%) identified by mixed m.p. (123—124°; sealed capillary) and i.r. spectrum. Chromatography of the residue on alumina gave *heptaethyl*-2-*vinylporphyrin*, eluted with benzene–petroleum (1 : 1) and crystallised from chloroform–methanol to give purple prisms (4.8 mg, 65%), m.p. 288—290° (Found: $M^+$, 532.357. $C_{36}H_{44}N_4$ requires $M$, 532.357), λ 403 (130 000), 503 (11 600), 539 (10 600), 570 (6 300), 626 (3 600), and 663 (930, impurity?), δ 10.22, 10.09, and 10.04 (s, 1 : 1 : 2, *meso*-H), 6.0—6.4 (m, $=CH_2$), 3.86—4.30 (m, $CH_2$), and 1.89 and 1.90 (overlapping t, $CH_3$), δ ($CF_3{\cdot}CO_2D$)[11] 10.90 (2 H, s, *meso*-H), 10.70 (2 H, s, *meso*-H), 7.63 (m, =CH−), 5.60—6.16 (m, $=CH_2$), 3.45—4.06 (m, $CH_2$), and 1.35 (t, Me), *m/e* (290 °C) 532 ($M$, 100%), 517 (15), 502 (6), 487 (6), and 266 ($M^{2+}$, 3).

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