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Conversion of a porphyrin into a 5,6-dihydroporphyrin. Synthesis and X-ray crystal structure of (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin†

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Summary — Treatment of the porphyrin-α-dione **7** with 3-chloroperoxybenzoic acid gives the ring-expanded porphyrin anhydride, 7,8a-dioxo-5,10,15,20-tetraphenyl-7*H*,8a*H*-8-oxa-8a-homoporphyrin **8**. Hydrolysis of **8** affords the porphyrin lactone, 8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **11**. Methanolysis of **8** gives (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**, the structure of which was determined by X-ray diffraction methods and refined to a residual of 0.059 for 1 841 independent observed reflections. The crystals of **12** are monoclinic, $P2_1$, a = 13.030(3), b = 12.132(4), c = 13.632(2) Å, β 113.27(2)°, Z = 2. Compound **12** has a non-aromatic macrocyclic ring and is the only example of a stable 5,6-dihydroporphyrin. Compound **12** is an isomer of 2,3-dihydroporphyrins (chlorins) **2**, 5,22-dihydroporphyrins (phlorins) **3** and 5,15-dihydroporphyrins (porphodimethenes) **4** but is restricted from tautomerizing to these well-known ring systems by the fact that the 6-position is tetrasubstituted. The distortion caused by the sp^3-hybridized C-5 and C-6 atoms in compound **12** is accommodated in the remainder of the macrocyclic ring by the formation of two nearly planar dipyrromethene-like units (one formed by rings B and C and the other by rings A and D), which are hinged about the *meso* carbon (C-15) opposite the sp^3 atoms. A mechanistic rationale for the formation of compound **12** is presented.

non-aromatic porphyrin / 5,6-dihydroporphyrin / X-ray

Résumé — Conversion d'une porphyrine en une 5,6-dihydroporphyrine. Synthèse et détermination de la structure aux rayons X de la (5*RS*,6*SR*)-5,6-dihydro-6-(méthoxycarbonyl)-8-oxo-5,10,15,20-tétraphényl-8*H*-7-oxaporphyrine. *Le traitement de la porphyrin-α-dione **7** par l'acide 3-chloroperbenzoïque conduit à la 7,8a-dioxo-5,10,15,20-tétraphényl-7*H*,8a*H*-8-oxa-8a-homoporphyrine **8**. L'hydrolyse de **8** fournit la lactone 8-oxo-5,10,15,20-tétraphényl-8*H*-7-oxaporphyrine **11**. La méthanolyse de **8** conduit à la (5RS,6SR)-5,6-dihydro-6-(méthoxycarbonyl)-8-oxo-5,10,15,20-tétraphényl-8*H*-7-oxaporphyrine **12** dont la structure a été déterminée par les méthodes de diffraction aux RX et affinée jusqu'à 0.059 pour 1 841 réflexions indépendantes observées. Les cristaux de **12** sont monocliniques,* $P2_1$, a = *13.030(3),* b = *12.132(4),* c = *13.632(2) Å,* β = *113.27(2)°,* Z = *2. Le composé **12** possède un macrocycle non aromatique et représente le seul exemple d'une 5,6-dihydroporphyrine stable. Le dérivé **12** est un isomère de 2,3-dihydroporphyrines (chlorines) **2**, 5,22-dihydroporphyrines (phlorines) **3** et 5,15-dihydroporphyrines **4**, mais ne peut réaliser de tautomérisation pour conduire à ces cycles bien connus car la position 6 est tétrasubstituée. Dans le composé **12** la distorsion provoquée par les carbones C5 et C6 hybridés en* sp^3 *est compensée par la formation de deux proches unités dipyrrométhène planes (une formée par les cycles B et C et l'autre par les cycles A et D) qui sont sur le carbone* méso *(C15) opposé aux atomes* sp^3. *Un mécanisme pour la formation de **12** est présenté.*

porphyrine non aromatique / 5,6-dihydroporphyrine / rayon-X

Introduction

The porphyrin ring system **1**, which is the framework of a very large number of compounds, is the most studied of all aromatic macrocyclic ring systems. Porphyrins have been subjected to a considerable number of structural and physicochemical techniques and yet they continue to yield new information and insights about redox processes, photochemistry and tautomerism, to select just a few of their important properties.

The reduced derivatives of porphyrins, and in particular the dihydroporphyrin and tetrahydroporphyrin systems, have also been much studied principally because of their occurrence in a number of important natural products. Of the dihydroporphyrins, the 2,3-dihydroporphyrin (chlorin) ring system **2** is best known because it constitutes the macrocyclic frame-

† In appreciation of the contributions to porphyrin chemistry and structure by Prof Raymond Weiss.

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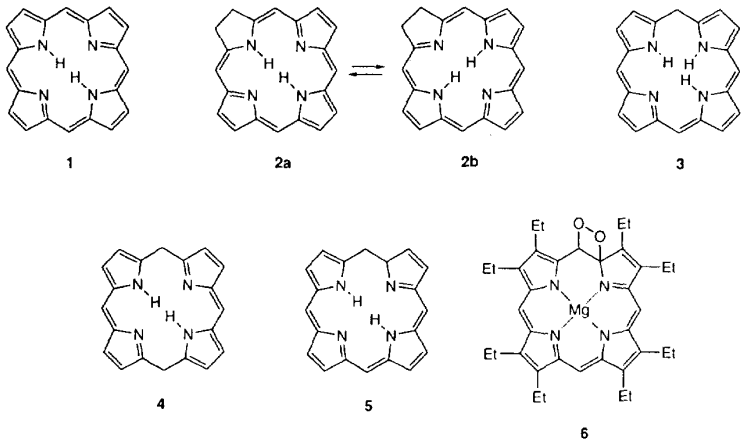
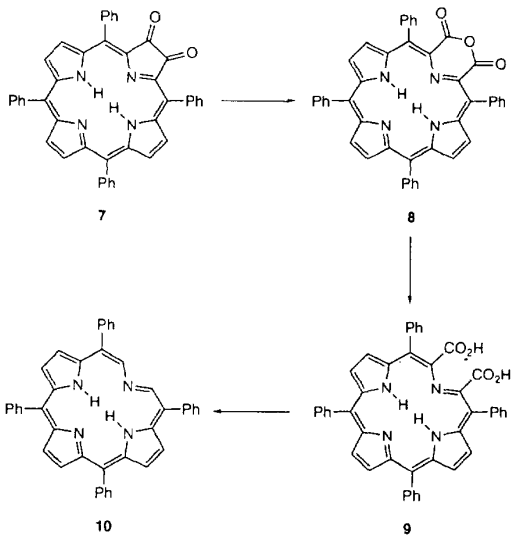


work found in chlorophylls. Free-base chlorins exist almost completely in the form of the tautomer **2b** (7,8-dihydroporphyrin) and maintain an aromatic macrocyclic ring unlike other known dihydroporphyrin systems, the 5,22-dihydroporphyrins (phlorins) **3** and the 5,15-dihydroporphyrins (porphodimethenes) **4**. Other dihydroporphyrin ring systems are possible but are apparently unstable with respect to the tautomeric systems **2**, **3**, and **4**. A metallated analogue of one of these other systems has been invoked. Fuhrhop and Mauzerall suggested that photooxidative ring opening of magnesium(II) octaethylporphyrin involves the intermediacy of the unstable peroxide **6** which has the 5,6-dihydroporphyrin ring system **5** [1].



Scheme 1

We envisaged that the seco-porphyrin **10** could be prepared by a route (scheme 1) that involved Baeyer-Villiger-type rearrangement of the α-dione **7** to the cyclic anhydride **8** followed by hydrolytic ring-opening to the seco-porphyrin-dicarboxylic acid **9** and decarboxylation to **10**. In practice, the Baeyer-Villiger-type rearrangement to give **8** went well but ring-opening of it led to novel heterocycles based on the 8*H*-7-oxaporphyrin system [2]. In the course of this work, we obtained what is to our knowledge the only example of a stable 5,6-dihydroporphyrin system and we report our studies in full here.

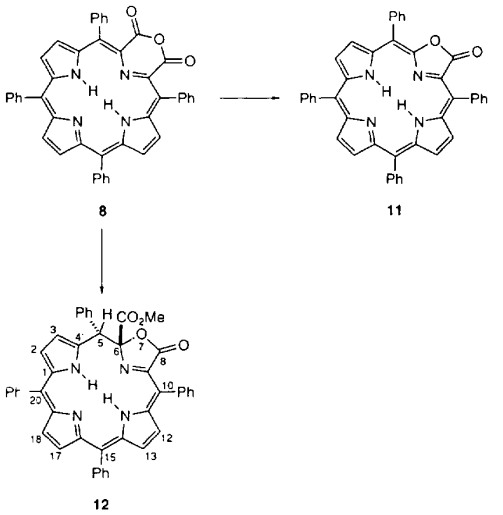
Results and discussion

The Baeyer-Villiger oxidation of porphyrin-α-dione **7** with 3-chloroperoxybenzoic acid afforded the ring expanded porphyrin anhydride, 7,8a-dioxo-5,10,15,20-tetraphenyl-7*H*,8a*H*-8-oxa-8a-homoporphyrin **8** in 39% yield. The structure of the oxidation product **8** was indicated by absorptions in the infrared spectrum at ν_{max} 1 785 and 1 742 cm^{-1} (fairly typical of anhydrides), the molecular formula, $C_{44}H_{28}N_4O_3$, which was established by high resolution mass spectrometry and by elemental analysis, and by the C_{2v} symmetry apparent in the 400 MHz ^1H NMR spectrum. The inner hydrogens on the nitrogens of the product are positioned as shown in structure **8**, which is implicit from the way we have named it. In particular the C-17 and C-18 hydrogens resonate in the ^1H NMR spectrum as a sharp singlet (δ 8.53) that is not further sharpened by irradiation of the resonance of the inner hydrogens at δ −1.58 thereby showing the absence of a ^4J coupling which would be evident if the hydrogens resided on the alternative nitrogens. At the same time the AB quartet due to the resonance of the C-2 and C-3 (and C-12 and C-13) hydrogens was broad and sharpened considerably upon irradiation of the inner hydrogens.

The free base anhydride **8** was found to be slow to hydrolyze in two phase (aqueous/organic) systems. Thus, stirring a dichloromethane solution of **8** with 10 M aqueous hydrochloric acid for 24 h caused no reaction. Similar treatment of **8** with 2 M aqueous sodium hydroxide for 24 h returned starting material in 63% yield. Rapid hydrolysis, however, occurred in a more homogeneous solution when treatment of a solution of the anhydride **8** in DMF with 10 M aqueous sodium hydroxide for 10 min resulted, on work-up, in a 95% yield of the 8-oxo-8*H*-7-oxaporphyrin **11**.

It was assumed that the 8-oxo-8*H*-7-oxaporphyrin **11** resulting from the hydrolysis of the cyclic anhydride **8**

was formed via the cyclization of an intermediate seco-porphyrin diacid or half-acid half-carboxylate, with subsequent oxidative decarboxylation. In order to trap a seco-porphyrin intermediate, the cleavage of the cyclic anhydride **8** was attempted by methanolysis.



Scheme 2

Treatment of a dichloromethane solution of 7,8a-dioxo-5,10,15,20-tetraphenyl-7*H*,8a*H*-8-oxa-8a-homoporphyrin **8** with methanol and pyridine under reflux in an overnight reaction afforded the hydrolysis product, 8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **11**, in 29% yield, but the major product was the non-aromatic macrocycle, (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**, which was obtained in 70% yield (scheme 2). The non-aromatic nature of the macrocycle in this product **12** was evident from the chemical shifts of the three pyrrole-like β-pyrrolic AB quartets at δ 6.01–6.49 (as compared with the typical β-pyrrolic chemical shift of ca δ 8.5 in fully aromatic porphyrins and chlorins), from the downfield chemical shifts of the inner N-Hs of δ 13.45 and 14.55 (as compared with the typical upfield porphyrin N-H chemical shift of ca δ −2) in the 400 MHz ^{1}H NMR and from the absence of a Soret band in the visible spectrum. The presence of the (methoxycarbonyl)methyl group (δ 3.89 (s, 3H)) and the *meso* methine proton (δ 4.63 (s, 1H)) and the oxazolone and ester functional groups (υ_{max} (KBr) 1 796 and 1 741 cm^{-1}) were also apparent from the ^{1}H NMR and infrared spectra, respectively. That neither of the inner N-Hs were located on the oxazolone ring was indicated by the occurrence of ^4J coupling between inner N-Hs and two of the three β-pyrrolic AB quartets. The structure that was assigned **12** was the one which allowed maximum double bond conjugation to be maintained in the macrocycle and minimum steric interaction between the inner N-Hs [2]. Two structural features were uncertain, however, viz the positioning of the reduced *meso* carbon at C-5 and the location of the interior N-H protons. Structures with the additional hydrogen at any of the other *meso* positions and N-H protons located on any two of the three pyrrole rings were also consistent with the spectra of this compound **12**. That structure **12** is correct has been confirmed by X-ray crystal analysis.

Crystal data and data collection parameters are listed in table I. Positional parameters are listed in table II. An Ortep plot of molecule **12** with the atom numbering scheme used is shown in figure 1. Two side-on projections are shown in figure 2. Bond lengths and angles are listed in tables III and IV, respectively. The structure contains disordered chloroform molecules of solvation.

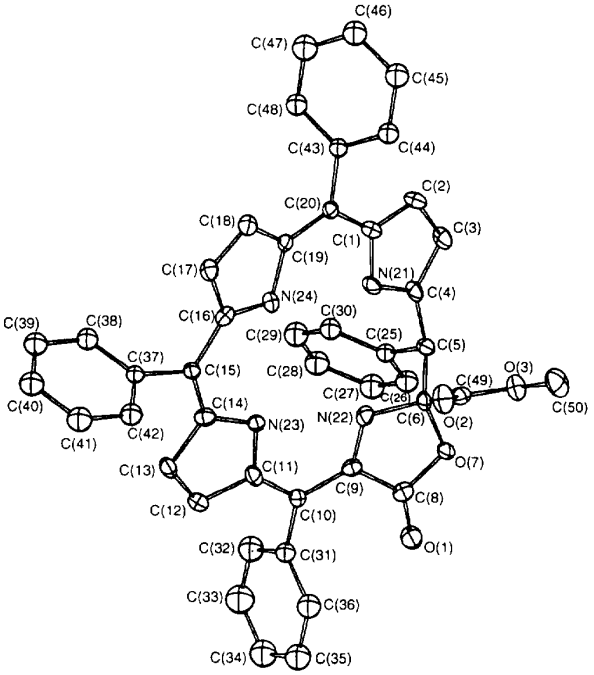


Fig 1. An Ortep plot of **12**, the hydrogen atoms are presented by spheres of arbitrary radii. The crystallographic numbering scheme is shown.

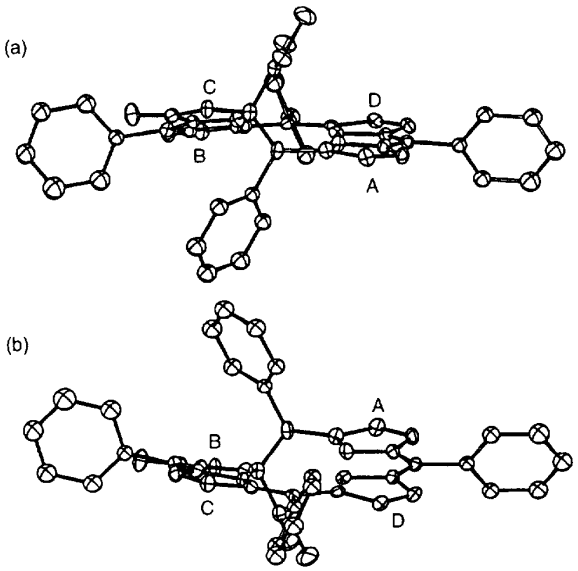


Fig 2. Ortep projections of the X-ray crystal structure of **12**.

Table I. Crystal data for **12**.

Formula	$C_{45}H_{32}N_4O_4 \cdot CHCl_3$
Molecular weight	812.2
Crystal system	monoclinic
Space group	$P2_1$
a, Å	13.030(3)
b, Å	12.132(4)
c, Å	13.632(2)
β, °	113.27(2)
V, Å^3	2074.2
ρ, g cm^{-3}	1.362
Z	2
$F(000)$, electrons	840
Absorption coeff (cm^{-1})	2.40
Habit	needles
Dimensions (mm)	0.38 × 0.18 × 0.07
Temperature (K)	294
Diffractometer	Enraf-Nonius CAD-4F, four circle
Radiation	Mo$K\alpha$, λ 0.71069 Å
Monochromator	graphite
Scan mode	ω-1.33 θ
2θ range, degrees	2.0–45.0
Reflections measured	3167
hkl ranges	0 − 15, 0 − 14, −16 − 16
Nonequivalent reflns	2504
Merging R	0.019
Reflections used ($I > 2.5\sigma(I)$)	1841
Number of variables	375
R	0.059
R_w	0.066
shift/esd	0.05σ
Residual extrema in	±0.4 eÅ^{-3} final difference map

Table II. Positional parameters (×10^4) for (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**.

	x	y	z
N(21)	5309(6)	2511(9)	9476(7)
N(22)	3111(6)	2365(9)	7589(6)
N(23)	3703(5)	435(1)	6882(5)
N(24)	5990(5)	768(8)	8454(5)
C(1)	6402(7)	2544(10)	10133(7)
C(2)	6495(7)	3305(11)	10899(7)
C(3)	5455(7)	3734(11)	10681(7)
C(4)	4717(7)	3229(10)	9798(7)
C(5)	3466(6)	3373(10)	9254(7)
C(6)	3089(7)	3434(9)	8038(7)
O(7)	1945(4)	3786(8)	7580(5)
C(8)	1318(8)	2978(10)	6935(7)
O(1)	311(5)	3084(9)	6471(6)
C(9)	2100(7)	2084(10)	6960(7)
C(10)	1765(7)	1073(10)	6384(6)
C(11)	2554(7)	332(10)	6358(7)
C(12)	2384(8)	−665(11)	5749(7)
C(13)	3381(7)	−1138(11)	5896(7)
C(14)	4236(7)	442(10)	6617(7)
C(15)	5365(7)	−617(9)	7012(6)
C(16)	6212(7)	−9(10)	7881(7)
C(17)	7389(7)	−217(10)	8207(7)
C(18)	7903(7)	465(10)	9038(8)
C(19)	7058(6)	1066(9)	9235(7)
C(20)	7241(6)	1862(10)	10015(7)
C(25)	2801(5)	2503(8)	9573(5)
C(26)	1779(5)	2794(8)	9575(5)
C(27)	1171(5)	2036(8)	9881(5)
C(28)	1587(5)	988(8)	10183(5)
C(29)	2610(5)	697(8)	10181(5)
C(30)	3217(5)	1455(8)	9876(5)
C(31)	561(4)	785(9)	5815(5)
C(32)	83(4)	27(9)	6262(5)
C(33)	−1031(4)	−243(9)	5743(5)
C(34)	1667(4)	244(9)	4778(5)
C(35)	−1188(4)	1002(9)	4331(5)
C(36)	−74(4)	1272(9)	4850(5)
C(37)	5788(5)	−1577(8)	6563(4)
C(38)	6221(5)	−2501(8)	7179(4)
C(39)	6566(5)	−3388(8)	6751(4)
C(40)	6477(5)	−3351(8)	5708(4)
C(41)	6043(5)	−2427(8)	5092(4)
C(42)	5699(5)	−1540(8)	5520(4)
C(43)	8406(4)	2041(8)	10814(4)
C(44)	8909(4)	3050(8)	10855(4)
C(45)	9978(4)	3237(8)	11599(4)
C(46)	10545(4)	2413(8)	12304(4)
C(47)	10042(4)	1403(8)	12263(4)
C(48)	8973(4)	1217(8)	11519(4)
C(49)	3757(7)	4241(11)	7692(8)
O(2)	4291(7)	4028(9)	7182(7)
O(3)	3663(6)	−4748(9)	8011(6)
C(50)	4259(11)	6119(12)	7703(10)
Cl(1)	8774(13)	3908(15)	7879(12)
Cl(2)	6582(8)	3357(11)	7301(8)
Cl(3)	6839(10)	1815(14)	6191(10)
C(51)	2143(32)	−2192(38)	2500(30)
O(5)	8458(31)	2607(34)	7093(30)
O(6)	2635(88)	−1250(69)	2893(69)
O(7)	1827(54)	−1342(45)	2759(51)
O(8)	8871(33)	3252(43)	8244(30)
O(9)	8104(45)	3614(39)	7863(41)
O(10)	2082(12)	−2993(15)	3443(11)
O(11)	6788(18)	2499(24)	6634(19)

Table III. Bond lengths (Å) for (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**.

Atoms	*Distance*	*Atoms*	*Distance*
C(1)-N(21)	1.35(1)	C(4)-N(21)	1.35(1)
C(6)-N(22)	1.44(1)	C(9)-N(22)	1.30(1)
C(11)-N(23)	1.39(1)	C(14)-N(23)	1.39(1)
C(16)-N(24)	1.33(1)	C(19)-N(24)	1.42(1)
C(2)-C(1)	1.36(1)	C(1)-C(20)	1.43(1)
C(3)-C(2)	1.37(1)	C(4)-C(3)	1.35(1)
C(5)-C(4)	1.51(1)	C(6)-C(5)	1.53(1)
O(7)-C(6)	1.43(1)	C(8)-O(7)	1.35(1)
O(1)-C(8)	1.22(1)	C(9)-C(8)	1.48(1)
C(10)-C(9)	1.43(1)	C(31)-C(10)	1.49(1)
O(3)-C(49)	1.32(1)	O(2)-C(49)	1.19(1)
C(12)-C(11)	1.43(2)	C(10)-C(11)	1.38(1)
C(13)-C(12)	1.36(1)	C(14)-C(13)	1.43(1)
C(15)-C(14)	1.37(1)	C(16)-C(15)	1.46(1)
C(37)-C(15)	1.52(1)	C(17)-C(16)	1.44(1)
C(18)-C(17)	1.35(1)	C(19)-C(18)	1.43(1)
C(20)-C(19)	1.38(1)	C(43)-C(20)	1.49(1)
C(25)-C(5)	1.53(1)	C(49)-C(6)	1.50(2)

Table IV. Bond angles (°) for (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**.

Atoms	*Angle*	*Atoms*	*Angle*
C(4)-N(21)-C(1)	110.8(8)	C(9)-N(22)-C(6)	109.3(7)
C(14)-N(23)-C(11)	110.1(7)	C(19)-N(24)-C(16)	104.1(7)
C(20)-C(1)-N(21)	124.1(8)	C(2)-C(1)-N(21)	106.2(8)
C(2)-C(1)-C(20)	129.6(8)	C(3)-C(2)-C(1)	108.1(8)

C(4)-C(3)-C(2)	108.4(8)	C(3)-C(4)-N(21)	106.5(7)
C(5)-C(4)-N(21)	124.1(7)	C(5)-C(4)-C(3)	129.4(7)
C(6)-C(5)-C(4)	111.0(7)	C(25)-C(5)-C(4)	113.7(7)
O(7)-C(6)-N(22)	106.0(6)	O(7)-C(6)-C(5)	108.5(6)
C(49)-C(6)-N(22)	110.0(7)	C(49)-C(6)-C(5)	113.1(7)
C(49)-C(6)-O(7)	107.5(7)	C(8)-O(7)-C(6)	108.9(6)
O(1)-C(8)-O(7)	120.7(8)	C(9)-C(8)-O(7)	106.4(7)
C(9)-C(8)-O(1)	132.9(9)	C(8)-C(9)-N(22)	109.4(8)
C(10)-C(9)-N(22)	126.6(7)	C(10)-C(9)-C(8)	124.0(7)
C(9)-C(10)-C(11)	120.4(7)	C(5)-C(6)-N(22)	111.4(7)
C(12)-C(11)-N(23)	105.2(8)	C(10)-C(11)-N(23)	126.4(8)
C(10)-C(11)-C(12)	128.3(8)	C(13)-C(12)-C(11)	110.5(8)
C(14)-C(13)-C(12)	106.9(8)	C(13)-C(14)-N(23)	107.2(7)
C(15)-C(14)-N(23)	125.7(8)	C(15)-C(14)-C(13)	127.0(9)
C(16)-C(15)-C(14)	126.3(8)	C(37)-C(15)-C(14)	117.7(7)
C(37)-C(15)-C(16)	115.9(7)	C(15)-C(16)-N(24)	124.4(7)
C(17)-C(16)-N(24)	113.4(8)	C(17)-C(16)-C(15)	122.2(8)
C(18)-C(17)-C(16)	105.5(8)	C(19)-C(18)-C(17)	107.8(7)
C(18)-C(19)-N(24)	109.1(7)	C(20)-C(19)-N(24)	124.9(7)
C(20)-C(19)-C(18)	125.9(7)	C(1)-C(20)-C(19)	125.6(7)
C(43)-C(20)-C(19)	118.6(7)	C(43)-C(20)-C(1)	115.8(7)
C(25)-C(5)-C(6)	111.3(6)	C(31)-C(10)-C(11)	118.5(7)
C(31)-C(10)-C(9)	121.2(7)	C(26)-C(25)-C(5)	118.6(4)
C(30)-C(25)-C(5)	121.4(4)	C(32)-C(31)-C(10)	119.5(4)
C(36)-C(31)-C(10)	120.5(4)	C(38)-C(37)-C(15)	120.3(4)
C(42)-C(37)-C(15)	119.6(4)	C(44)-C(43)-C(20)	119.2(4)
C(48)-C(43)-C(20)	120.8(4)	O(3)-C(49)-C(6)	111.1(8)
O(2)-C(49)-C(6)	125.9(9)	O(2)-C(49)-O(3)	123.0(9)
C(50)-O(3)-C(49)	116.4(8)		

It is apparent from these projections that the reduced (sp^3) *meso* atom was correctly assigned as C-5, adjacent to the C-6 sp^3 α-pyrrolic atom bearing the methoxycarbonyl substituent. Bond lengths to C-5 and C-6 are typical of single bond distances. The X-ray structural data also confirm the location of the interior N–H protons on nitrogens (21 and 23).

It is also evident from the projection in figure 2 that the incorporation of the two adjacent sp^3 atoms at C-5 and C-6 in **12** results in a *trans*-diaxal conformation of the phenyl and methoxycarbonyl substituents of the macrocyclic ring. As chirality has been introduced into the molecule in the reaction, the product is necessarily racemic.

The reduction of the C-5–C-6 double bond disrupts the planarity of the porphyrin and produces a skew conformation. The distortion caused by these sp^3 atoms is accommodated in the remainder of the ring by the formation of two nearly planar dipyrromethene-like units (one formed by rings B and C and the other by rings A and D), which are hinged about the *meso* carbon (C-15) opposite the sp^3 atoms. This adoption of two hinged planar dipyrromethene units is apparent from calculations of the least-squares planes for the three pairs of conjugated adjoining pyrrole (or oxazolone) rings (table V). Rings B and C and rings A and D are shown to be each relatively planar, with the average deviation of the constituent atoms from the least-squares plane formed by rings B and C being 0.064 Å and from the least-squares plane formed by rings A and D, 0.045 Å. In contrast, the average deviation of the constituent atoms from the least-squares plane formed by rings C and D (across the hinging C-15 *meso* carbon) is significantly greater, being 0.093 Å.

Calculations of the least-squares planes for each of the pyrrole rings and the oxazolone ring (table VI)

Table V. Deviation of the constituent atoms from the least-squares plane formed by two adjoining five-membered rings and the bridging *meso* carbon in (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**.

Rings B and C		*Rings C and D*		*Rings A and D*	
Atom	*Deviation* (Å)	*Atom*	*Deviation* (Å)	*Atom*	*Deviation* (Å)
N(22)	−0.090	N(23)	0.183	N(21)	0.061
N(23)	−0.029	N(24)	−0.085	N(24)	−0.067
C(6)	−0.031	C(11)	0.088	C(1)	0.003
O(7)	0.110	C(12)	−0.124	C(2)	−0.053
C(8)	0.090	C(13)	−0.151	C(3)	−0.006
C(9)	−0.035	C(14)	0.048	C(4)	0.052
C(10)	−0.099	C(15)	0.053	C(16)	−0.054
C(11)	−0.070	C(16)	0.026	C(17)	0.050
C(12)	0.000	C(17)	0.103	C(18)	0.079
C(13)	0.084	C(18)	0.010	C(19)	−0.357
C(14)	0.071	C(19)	−0.151	C(20)	−0.030
Average	0.064	Average	0.093	Average	0.045

Table VI. Deviation of the constituent atoms from the least-squares plane formed by two five-membered rings in (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12**.

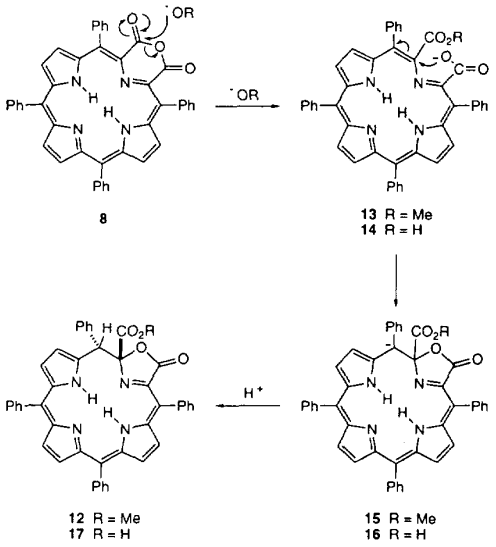
Ring A		*Ring B*	
Atom	*Deviation* (Å)	*Atom*	*Deviation* (Å)
N(21)	0.000	N(22)	0.008
C(1)	0.004	C(6)	−0.010
C(2)	−0.006	O(7)	0.010
C(3)	0.006	C(8)	−0.006
C(4)	−0.004	C(9)	−0.002
Average	0.004	Average	0.007
Ring C		*Ring D*	
Atom	*Deviation* (Å)	*Atom*	*Deviation* (Å)
N(23)	−0.002	N(24)	0.018
C(11)	0.002	C(16)	−0.011
C(12)	0.000	C(17)	−0.001
C(13)	−0.001	C(18)	0.012
C(14)	0.002	C(19)	−0.018
Average	0.001	Average	0.012

reveal that ring D is somewhat less planar than the other pyrrole rings. This is presumably also a reflection of the hinging of the two dipyrromethene-like units brought about by the two sp^3 atoms on the opposite side of the macrocycle from ring D. This distortion of ring D is also evident in the ^{1}H NMR spectrum in which the two β-pyrrolic proton resonances for ring D (δ 6.07 and 6.49) exhibit a much larger chemical shift difference than the resonances for the β-pyrrolic protons on the other rings.

Pyrrolic rings A and C are shown to be very planar by the data in table VI. This planarity, coupled with the similar, aromatic bond lengths observed for all of the bonds in ring A, suggests that ring A has the character of an aromatic pyrrole ring as might be expected from the Lewis structure of the ring. This is further supported by the observation that one of

the pyrrolic rings has a typically pyrrole-like ^3J coupling constant (3.9 Hz) between the β-pyrrolic protons, which are therefore assigned as the protons on ring A (C-2 and C-3) [3]. The other protonated pyrrole ring β-pyrrolic protons (C-12 and C-13) have a substantially higher, more cyclopentene-like coupling constant of 5.6 Hz, while the coupling constant for the β-pyrrolic protons for the non-protonated pyrrolenine ring (C-17 and C-18) is 4.5 Hz.

This compound **12** represents the first isolated example of a 6-(methoxycarbonyl)-5,6-dihydroporphyrin derivative. Intermediates with this general structure have been implicated in chemical porphyrin ring opening reactions [4, 5] and, more significantly, have been proposed as intermediates in the degradation of haem to bile pigments [6]. The structure of compound **12** is therefore particularly of note.



Scheme 3

A mechanistic rationale for the formation of compounds **11** and **12** is presented in scheme 3. The non-aromatic methoxycarbonyl-oxazolone **12** clearly results from the cyclization of the seco-porphyrin half-acid half-carboxylate **13**. The *trans*-diaxal conformation of the phenyl and methoxycarbonyl substituents in compound **12** reduces steric interactions between substituents. That this conformation is clearly favored suggests that the cyclization **13** to **12** is probably not concerted as the requirements of such a process would require initial formation of the very hindered diequatorial conformer. The isolation of product **12** indicates the relative ease with which the porphyrin 18-annulene-like aromatic pathway may be disrupted, perhaps to relieve overriding steric buttressing between the coplanar *meso*-phenyl groups and the two carboxyl substituents in the presumed seco-porphyrin intermediate. The restoration of aromaticity, however, is presumably the driving force for the formation of the 8-oxo-8*H*-7-oxaporphyrin **11** when oxidative decarboxylation of an analogous carboxy-oxazolone (either **16** or **17**) is not impeded, as is the case in species **15** and **12**, by the esterification of the carboxyl group. Rapid conversion of methoxycarbonyl-oxazolone **12** to the 8-oxo-8*H*-7-oxaporphyrin **11** in 44% yield was also effected by treatment of **12** with boiling quinoline/water (98:2), most likely via successive ester hydrolysis, decarboxylation and aerial oxidation. This observation provides good support for the premise that a common mechanistic pathway operates.

Conclusions

This work has resulted in the isolation of the only example of a stable 5,6-dihydroporphyrin. Compound **12** is an isomer of 2,3-dihydroporphyrins (chlorins) **2**, 5,22-dihydroporphyrins (phlorins) **3** and 5,15-dihydroporphyrins (porphodimethenes) **4** but is restricted from tautomerizing to these well-known ring systems by the fact that the 6-position is tetrasubstituted. The fact that the molecule is prepared to forego the aromatic stability of the conjugated porphyrin system is an indication that the energy penalty is not substantial, particularly as the system can compensate through increasing pyrrole-like and dipyrromethene-like aromaticity in the smaller constituent rings. It is thus evident that the formation of 5,6-dihydroporphyrin systems is energetically allowed in the reactions of porphyrins and that such compounds could be involved as intermediates in reactions that lead to more stable tautomeric species, the phlorins and the chlorins, and in reactions involving oxidative cleavage of the porphyrin ring.

Experimental section

General experimental details have been reported previously [7]. Melting points were recorded on a Kofler hot-stage microscope and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer 221 spectrometer. Visible spectra were recorded on a Hitachi 150-20 spectrophotometer. ^{1}H NMR spectra were recorded at 300 K on a Bruker WM400 (400 MHz) spectrometer with tetramethylsilane as the internal standard. Mass spectra were recorded on an AEI MS 902 spectrometer at 70 eV. Elemental analyses were performed by the Australian Mineral Development Laboratory, Melbourne, Australia.

Flash chromatography was performed on Merck Type 9385 silica gel. Preparative thin layer chromatography (TLC) plates were prepared with Merck silica gel 60 $PF_{254+366}$. All reagents were purchased from commercial sources and used as received unless otherwise noted. All solvents were redistilled prior to use. *N*,*N*-Dimethylformamide was dried over calcium hydride and distilled under reduced pressure.

*7,8a-Dioxo-5,10,15,20-tetraphenyl-7*H,*8a*H-*8-oxa-8a-homoporphyrin* **8**

To a solution of 7,8-dioxo-5,10,15,20-tetraphenyl-7*H*,8*H*-porphyrin **7** (22 mg, 0.034 mmol) in dichloromethane (50 mL) was added a solution with 3-chloroperoxybenzoic acid (85%, 12 mg, 0.069 mmol) in dichloromethane (8 mL) and the mixture was stirred for 3 h. The mixture was washed with sodium hydroxide solution (3 M, 2 × 40 mL), water (80 mL), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The crude product was chromatographed on a preparative TLC plate, developed in

dichloromethane/light petroleum (3:1) to yield a more polar, brown band of unreacted dioxoporphyrin **7** (9 mg, 41%) and a front-running green-brown band of **8** (9 mg, 39%). Mp > 350 °C.

IR (KBr): 1 785 (C=O), 1 742 (C=O) cm^{-1}.

UV-vis ($CHCl_3$): 429 (log ε 5.29), 445sh (5.09), 546 (4.01), 583 (3.86), 612 (3.79), 667 (3.44) nm.

^1H NMR ($CDCl_3$, 400 MHz): δ −1.58 (br s, 2H, NH), 7.65–7.79 (m, 12H, *m*- and *p*-Ph), 7.99–8.04 (m, 4H, *o*-Ph), 8.07–8.12 (m, 4H, *o*-Ph), 8.43 and 8.70 (br ABq, J_{AB} = 4.8 Hz, 4H, 2-, 3-, 12- and 13-H), 8.53 (s, 2H, 17- and 18-H).

MS (EI, 70 eV): *m/z* 724 (11%), 723 (21), 722 (19), 721 ($M^{+63}Cu$, 35), 693 ($M^{+63}Cu$-CO, 13), 677 ($M^{+63}Cu$-CO_2, 15), 662 (18), 661 (52), 660 (M^+, 100), 649 ($M^{+63}Cu$-C_2O_3, 13), 633 (15), 632 (M-CO, 26), 616 (M-CO_2, 18), 588 (M-C_2O_3, 32), 587 (30).

Anal calc for $C_{44}H_{28}N_4O_3$: C, 80.0; H, 4.3; N, 8.5. Found: C, 80.0; H, 4.3; N, 8.8.

Hydrolysis of 7,8a-dioxo-5,10,15,20-tetraphenyl-7H,8aH-8-oxa-8a-homoporphyrin **8**. *8-Oxo-5,10,15,20-tetraphenyl-8H-7-oxaporphyrin* **11**

To a solution of 7,8a-dioxo-5,10,15,20-tetraphenyl-7*H*,8a*H*-8-oxa-8a-homoporphyrin **8** (30 mg, 0.045 mmol) in *N*,*N*-dimethylformamide (10 mL) was added a sodium hydroxide solution (10 M, 1 mL) and the mixture was stirred for 10 min. The mixture was then diluted with dichloromethane (20 mL), washed with water (6 × 50 mL), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue was chromatographed on a column-grade silica column (1 cm diameter, 30 g) eluted with chloroform and the major red band was collected and evaporated to yield **11** (27 mg, 95%). Mp > 350 °C.

IR (KBr): 1 760 cm^{-1}.

UV-vis ($CHCl_3$): 423 (log ε 5.43), 525 (4.07), 562 (4.09), 592 (3.87), 643 (3.49) nm.

^1H NMR ($CDCl_3$, 400 MHz): δ −2.05 (br s, 1H, NH), −1.68 (br s, 1H, NH), 7.67–7.81 (m, 12H, *m*- and *p*-Ph), 7.95–7.99 (m, 2H, *o*-Ph), 8.07–8.16 (m, 6H, *o*-Ph), 8.53 and 8.60 (ABq, J_{AB} = 4.5 Hz, 2H, 17- and 18-H), 8.57 and 8.70 (dABq, J = 5.0 and 2.0 Hz, 2H, β-pyrrolic H), 8.76 and 8.80 (dABq, J = 5.0 and 2.0 Hz, 2H, β-pyrrolic H).

MS (EI, 70 eV): *m/z* 634 (12%), 633 (38), 632 (M^+, 100), 576 (14), 499 (13), 302 (13).

Anal calc for $C_{43}H_{28}N_4O_2$: C, 81.6; H, 4.5; N, 8.9. Found: C, 81.8; H, 4.3; N, 9.1.

(5RS,6SR)-5,6-Dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8H-7-oxaporphyrin **12**

A solution of 7,8a-dioxo-5,10,15,20-tetraphenyl-7*H*,8a*H*-8-oxa-8a-homoporphyrin **8** (71 mg, 0.11 mmol) in a mixture of methanol (25 mL), dichloromethane (25 mL) and pyridine (2 mL) was heated under reflux for 18 h. The mixture was then allowed to cool and the solvent was removed by rotary evaporation and then under high vacuum. The residue was chromatographed on preparative TLC plates, developed in dichloromethane/light petroleum (3:1). Two bands were collected, a front-running red band of **11** (20 mg, 29%) (identical in all respects with authentic material prepared as described above) and a more polar green band of **12** (52 mg, 70%). Mp 230–231 °C.

IR (KBr): 1 796 (oxazolone C=O), 1 741 (ester C=O) cm^{-1}.

UV-vis ($CHCl_3$): 422 (log ε 4.64), 437 (4.68), 499 (3.69), 744 (4.01) nm.

^1H NMR ($CDCl_3$, 400 MHz): δ 3.89 (s, 3H, OMe), 4.63 (s, 1H, 5-H), 6.01 and 6.14 (br ABq, J_{AB} = 3.9 Hz, 2H, 2- and 3-H), 6.07 and 6.49 (ABq, J_{AB} = 4.5 Hz, 2H, 17- and 18-H), 6.09 and 6.22 (dABq, J = 5.6 and 1.5 Hz, 2H, 12- and 13-H), 7.18–7.46 (m, 17H, Ph), 7.50 (br d, J = 7.5 Hz, 1H, *o*-Ph), 7.63 (m, spacing J = 7.8 and 2 Hz, 2H, *o*-Ph), 13.45 (br s, 1H, NH), 14.55 (br s, 1H, NH).

MS (EI, 70 eV): *m/z* 692 (M^+, 5%), 664 (M-CO, 11), 650 (14), 649 (27), 648 (M-CO_2, 42), 634 (18), 633 (58), 632 (M-HCO_2Me, 100).

Anal calc for $C_{45}H_{32}N_4O_4$: C, 78.0; H, 4.7; N, 8.1. Found: C, 78.1; H, 4.3; N, 8.4.

Hydrolysis of (5RS,6SR)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8H-7-oxaporphyrin **12**

A solution of (5*RS*,6*SR*)-5,6-dihydro-6-(methoxycarbonyl)-8-oxo-5,10,15,20-tetraphenyl-8*H*-7-oxaporphyrin **12** (40 mg, 0.058 mmol) in a mixture of quinoline and water (98:2, 5 mL) was heated at reflux for 5 min. On cooling, the mixture was diluted with dichloromethane and washed with hydrochloric acid (3 M, 4 × 50 mL) and water (2 × 40 mL), dried over anhydrous sodium sulfate, filtered and evaporated to dryness. The residue was chromatographed on a preparative TLC plate developed in dichloromethane/light petroleum (3:1) and the major red band was collected to afford **11** (16 mg, 44%). This product was identical in all respects to authentic material prepared as described above.

X-ray crystallography

Crystals suitable for study by X-ray diffraction were obtained by vapor diffusion of hexane into chloroform solutions of the compound at 4 °C and were mounted on glass fibers with cyanoacrylate ester glue.

Lattice parameters were determined by a least-squares fit to the setting angles of 25 independent reflections. Crystal data and data collection parameters are listed in table I. Data were collected on a Enraf-Nonius CAD-4F four-circle diffractometer, employing graphite monochromated Mo$K\alpha$ radiation.

The structure was solved by direct methods. The phenyl rings were refined as rigid groups (C-C, 1.395 Å) with isotropic thermal parameters, all other non-hydrogen atoms were refined isotropically and hydrogen atoms were included at calculated site (C-H, 0.97 Å). Full-matrix least-squares refinement converged with all shifts less than 0.05 σ.

Positional parameters are listed in table II. Programs used were SUSCAD [8] for data reduction, SHELX 76 [9] for refinement and Ortep [10] for plotting. All scattering factors and anomalous dispersion terms were taken from the *International Tables for X-ray Crystallography* [11].

Listings of observed and calculated structure factors, non-hydrogen atom thermal parameters, hydrogen atom coordinates and thermal parameters, torsion angles and details of least-squares planes calculations have been deposited with the British Library, Document Supply Centre at Boston Spa, Wetherby, West Yorkshire, LS23 7BQ, UK, as supplementary publication N° = SUP 90427 and are available on request from the Document Supply Centre.

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