Facile Aerial Oxidation of a Porphyrin. Part 18 [1]. *N*-Alkylation of the Oxidised Product Derived from *Meso*-tetrakis(3,5-di-*t*-butyl-4-hydroxyphenyl)porphyrin

Lionel R. Milgrom,* Jonathan P. Hill, and Gokhan Yahioglu

Department of Chemistry, Brunel University, Uxbridge, Middlesex, UB8 3PH, UK

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In basic solutions, the oxidised porphyrin **2** readily undergoes macrocyclic *N*-alkylation, with up to four bulky alkyl groups, including decyl and substituted benzyl moieties, being accomodated: an argument is presented to show that *N*-di-alkylation occurs on opposite nitrogen atoms, on the same side of the macrocycle.

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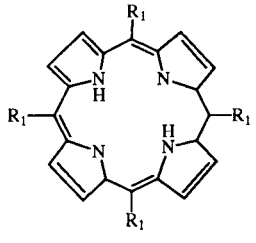
Introduction.

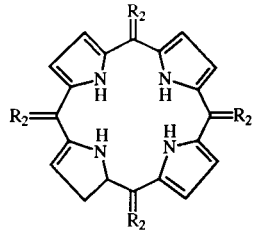
The formation of *N*-methylated β- and *meso*-substituted porphyrins is achieved using methyl iodide, which gives the N_{21}-mono- and N_{21},N_{23}-di-methylated products in reasonable yield [2]. Tri-*N*-methylated porphyrins are obtained with stronger methylating agents, such as methylfluorosulphonate [3], but these usually prove unstable, *e.g.*, decomposing upon chromatography. The N_{21},N_{22},N_{23},N_{24}-tetramethylporphyrins are inaccessible by direct methylation, and attempts to synthesise them, *via* oxidation of the corresponding *N*-tetramethylporphyrinogen (prepared by cyclisation of the *N*-methylpyrrole), have proved unsuccessful [4a]. Steric crowding by methyl groups probably leads to distortion of the macrocycle, (present in the tetra-*N*-methylated porphyrinogen) [4b] which disrupts the planarity needed for aromatic stabilisation of the porphyrin *pi*-system.

Meso-tetrakis(3,5-di-*t*-butyl-4-hydroxyphenyl)porphyrin **1** (Scheme 1) undergoes facile two-electron aerial oxidation [5a] in basic solutions to yield the oxidised porphryin **2**, which, in the solid-state, exists as the highly puckered *meso*-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxa-

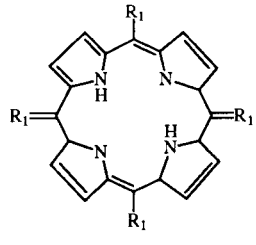
Scheme 1



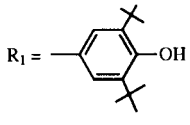
1

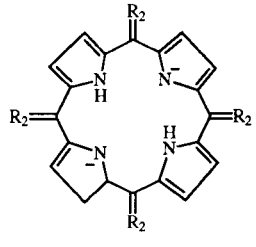


2a

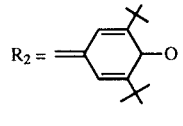


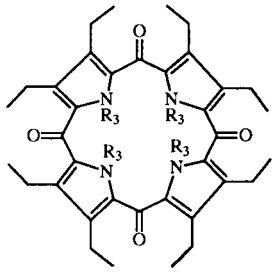
2b



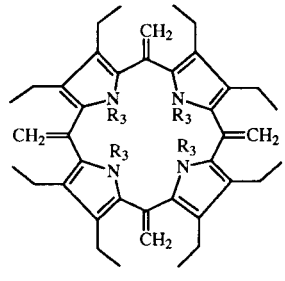


2c



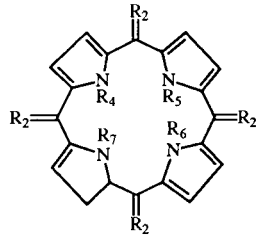


3a, $R_3 = H$
3b, $R_3 = CH_3$



4a, $R_3 = H$
4b, $R_3 = CH_3$

Scheme 2



5

	R_4	R_5	R_6	R_7
5a	$C_{10}H_{21}$	H	H	H
5b	$C_{10}H_{21}$	H	$C_{10}H_{21}$	H
5c	$C_{10}H_{21}$	$C_{10}H_{21}$	$C_{10}H_{21}$	H
5d	$C_{10}H_{21}$	$C_{10}H_{21}$	$C_{10}H_{21}$	$C_{10}H_{21}$
5e	Bz	H	Bz	H
5f	Bz	Bz	Bz	Bz
5g	NBz	H	NBz	H
5h	NBz	NBz	NBz	NBz
5i	$C_{10}H_{21}$	H	NBz	H
5j	NBz	Bz	NBz	Bz
5k	$C_{10}H_{21}$	H	ABz	H
5l	NBz	H	ABz	H
5m	ABz	H	ABz	H

Bz = benzyl; NBz = 4-nitrobenzyl; ABz = 4-aminobenzyl.

cyclohexa-2,5-dienylene)porphyrinogen **2a** [5b]. In solution, however, **2** probably exists as the tautomeric, *meso*-bis-5,15-(3,5-di-*t*-butyl-4-hydroxyphenyl)bis-10,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)porphodimethene **2b** [5c].

The oxidised porphyrin **2a** may be considered a vinylog of the octaethylxanthoporphyrinogen **3a** of Inhoffen *et. al.* [6a], and is also related to octaethyl-*meso*-tetrakismethyleneporphyrinogen **4a** of Breitmaier and Otto [6b]. Both compounds have been tetra-*N*-methylated to give, respectively, **3b** [7] and **4b** [6b], and we wished to investigate whether *N*-alkylation was possible with the oxidised compound **2**. In particular, as the macrocycle of **2a** is severely puckered, we were curious to know whether multi-*N*-alkylation could occur using alkyl halides with bulky substituents. In the event, not only has it has proved possible to *N*-alkylate with long-chain alkyl (*i.e.*, $C_{10}H_{21}$-) and benzyl halides (albeit with varying numbers of alkyl groups depending on the reactivity of the alkyl halide), we have also demonstrated stepwise mixed *N*-alkylation using more than one type of alkyl halide.

EXPERIMENTAL

The uv/visible spectra were recorded on a Cecil CF 5500 double-beam uv spectrophoto-meter using spectroscopic grade chloroform as solvent. The ^{1}H-nmr spectra were recorded on a JEOL JNM FX 200 instrument in deuterochloroform using tetramethylsilane as an internal reference. Fast Atom Bombardment Spectroscopy (FABS) mass spectra were recorded on a Vacuum Generators ZAB 2e double sector spectrometer, using 3-nitrobenzyl alcohol (3-NOBA) and chloroform as co-solvents.

The tlc were performed on Aldrich aluminium-backed silica gel 60 F254. Separation of the *N*-alkylated compounds was achieved by column chromatography on Sorbsil C60 silica gel, eluting with chloroform or dichloromethane.

Because of their solubility in all solvent systems tried, no attempt was made to crystallise the *N*-alkylated compounds. Solid materials were obtained by evaporation of solutions obtained from column chromatography. Yields have not been maximised. Other solvents, 1-bromodecane, benzyl bromide, and 4-nitrobenzyl bromide were reagent grade and used as supplied.

N-Alkylation of **2** with 1-Bromodecane in Basified *N,N*-Dimethylformamide.

Meso-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)porphyrinogen **2a** (175 mg, 1.56 x 10^{-4} mole) was refluxed (1.5 hours) with 1-bromodecane (Aldrich, 5 ml, 2.4 x 10^{-2} mole) in *N,N*-dimethylformamide (DMF, 50 ml) basified with methanolic potassium hydroxide solution (1*M*, 10 ml). After removal of the solvent by evaporation, the solid residue was subjected to column chromatography on silica gel, eluting with chloroform. Four red bands were collected which were identified, in order of elution from the column as the tetra-, tri-, di-, and mono-*N*-decyl compounds **5d-a**, respectively. Yields of **5d** and **5c** were only enough for characterisation by uv/visible spectroscopy and FABS mass spectrometry. Thus, the first band eluted from the column was evaporated to dryness to afford a small amount of *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{22},N_{23},N_{24}-tetradecylporphyrinogen **5d** as a red amorphous powder (3 mg, 1%); uv: λ max 507 nm (ε 92,300); ms: (FAB) (3-NOBA, chloroform) found m/z = 1687; $[M+3H]^+$ requires m/z = 1687. The second band to be eluted from the column was evaporated to dryness to afford a small amount of *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{22},N_{23}-tridecylporphyrinogen **5c** as a red amorphous powder (2 mg, 1%); uv: λ max 502 nm (ε 105,200); ms: (FAB) (3-NOBA, chloroform) found m/z = 1546: $[M+2H]^+$ requires m/z = 1546. The third band to be eluted from the column was evaporated to dryness to afford *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{23}-didecylporphyrinogen **5b** as a dark green amorphous powder (63 mg, 29%); uv: λ max 512 nm (ε 80,500); ms: (FAB) (3-NOBA, chloroform) found m/z = 1407, $[M+H]^+$ requires 1407; ^{1}H-nmr: (200 MHz) δ 9.86 (broad, 2H, N-*H*), 7.62 (s, 4H, pyrrole β-*H* on *N*-alkylated rings [12]), 7.28 (s, 4H, pyrrole β-*H* on non-alkylated rings), 6.85 (s, 4H, *ortho*-*H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 6.48 (s, 4H, *ortho*-*H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 3.29 (t, 4H, N-CH_2-), 1.5- 0.8 (complex, 110*H*, *t*-butyl-*H* and decyl-*H*).

Anal. Calcd. for $C_{96}H_{132}N_4O_4$ (1406.05): C, 82.00; H, 9.46; N, 3.99. Found: C, 82.12; H, 9.38; N, 3.85.

The fourth band to be eluted from the column was similarly evaporated to dryness to afford *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21}-decylporphyrinogen **5a** as a dark green amorphous powder (25 mg, 13%); uv: λ max 506 nm (ε 91,400); ms: (FAB) (3-NOBA, chloroform) found m/z =

1268, $[M+2H]^+$ requires 1268; ^{1}H-nmr (200 MHz, deuteriochloroform): δ 9.87 (broad, 2H, N-*H*), 8.55 (broad, 1H, N-*H* on pyrrole opposite *N*-alkylated pyrrole), 7.63 (s, 2H, pyrrole β-*H* on *N*-alkylated ring), 7.49, 7.36, 7.32 (singlets, 6H, pyrrole β-*H* on non-alkylated rings), 6.83, 6.67, 6.52 (singlets, 8H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexadienylene groups); 3.19 (t, 2H, N-C*H*$_2$), 2.0-0.8 (complex, 91*H*, *t*-butyl-*H* and decyl-*H*).

Anal. Calcd. for $C_{86}H_{111}N_4O_4$ (1264.78): C, 81.66; H, 8.78; N, 4.43. Found: C, 81.71; H, 8.82; N, 4.48.

N-Alkylation of **2** with Benzyl Bromide in Basified *N,N*-Dimethylformamide.

Meso-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)porphyrinogen **2a** (200 mg, 1.78 x 10^{-4} mole) was refluxed (3 hours) with benzyl bromide (Aldrich, 3 ml, 2.5 x 10^{-2} mole) in *N,N*-dimethylformamide (DMF, 50 ml) basified with methanolic potassium hydroxide solution (1*M*, 10 ml). After removal of the solvent by evaporation, the solid residue was subjected to column chromatography on silica gel, eluting with chloroform. Two main bands were collected and their components identified as the tetra-*N*-benzylporphyrinogen **5f** and the di-*N*-benzylporphyrinogen **5e**. Two other minor bands were discarded. The first major component to be eluted from the column was evaporated to dryness and afforded a small amount of *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{22},N_{23},N_{24}-tetrabenzylporphyrinogen **5f** as a red amorphous powder (8 mg, 3%); uv: λ max 502 nm (ε 103,600); ms: (FAB) (3-NOBA, chloroform) found m/z = 1486; M^+ requires m/z = 1486; ^{1}H-nmr (200 MHz, deuterochloroform): δ 7.27 (s, 8H, pyrrole β-*H* on *N*-alkylated rings), 7.18-7.12 (complex, 20H, phenyl-*H* from benzyl groups), 6.67 (singlets, 8H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 4.65 (broad singlet, 8H, benzylic-C*H*$_2$-), 1.26 (complex, 72*H*, *t*-butyl-*H*).

Anal. Calcd. for $C_{104}H_{116}N_4O_4$ (1486.00): C, 84.05; H, 7.87; N, 3.77. Found: C, 84.21; H, 7.74; N, 3.6.

The second major component (and the third band) to be eluted from the column was evaporated to dryness and afforded *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{23},-dibenzylporphyrinogen **5e** as a dark blue-green amorphous powder (74 mg, 32%); uv: λ max 510 nm (ε 93,000); ms: (FAB) (3-NOBA, chloroform) found m/z = 1306; $[M+H]^+$ requires m/z = 1306; ^{1}H-nmr (200 MHz, deuterochloroform): δ 9.89 (broad singlet, 2H, N-*H*) ,7.28 (s, 4H, pyrrole β-*H* on *N*-alkylated rings), 7.22-7.12 (complex, 14H, pyrrole β-*H* from non-alkylated pyrrole rings and phenyl-*H* from benzyl groups), 6.67 (singlets, 8H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 4.64 (broad singlet, 4H, benzylic-C*H*$_2$-), 1.26 (singlets, 72*H*, *t*-butyl-*H*).

Anal. Calcd. for $C_{90}H_{104}N_4O_4$ (1305.77): C, 82.78; H, 8.03; N, 4.29. Found: C, 82.72; H, 8.00; N, 4.33.

N-Alkylation of **2** with 4-Nitrobenzyl Bromide in Basified *N,N*-Dimethylformamide.

Meso-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)porphyrinogen **2a** (250 mg, 2.2 x 10^{-4} mole) was refluxed (3 hours) with 4-nitrobenzyl bromide (Aldrich, 950 mg, 4.4 x 10^{-3} mole) in *N,N*-dimethylformamide (DMF, 50 ml) basified with methanolic potassium hydroxide solution (1*M*, 10 ml). After removal of the solvent by evaporation, the solid residue was subjected to column chromatography on silica gel, eluting with chloroform. Two main bands were collected and their components identified as the tetra-*N*-4-nitrobenzylporphyrinogen **5h** and the di-*N*-4-nitrobenzylporphyrinogen **5g**. Two other minor bands were discarded. The first major component to be eluted from the column was evaporated to dryness and afforded a *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{22},N_{23},N_{24}-tetra-4-nitrobenzylporphyrinogen **5h** as a dark red amorphous powder (65 mg, 17%); uv: λ max 505 nm (ε 95,400); ms: (FAB) (3-NOBA, chloroform) found m/z = 1666; M^+ requires m/z = 1666; ^{1}H-nmr (200 MHz, deuterochloroform): δ 8.08, 7.97, 6.83, 6.72 (pair of doublets, 16H, 4-nitrobenzyl-*H*, AB spin system, J_{AB} = 8.4 Hz), 7.17 (s, 8H, pyrrole β-*H*), 6.69 (singlets, 8H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 4.59 (broad singlet, 8H, 4-nitrobenzylic-C*H*$_2$-), 1.24 (several singlets, 72*H*, *t*-butyl-*H*).

Anal. Calcd. for $C_{104}H_{112}N_8O_{12}$ (1666.01): C, 74.97; H, 6.78; N, 6.73. Found: C, 74.85; H, 6.82; N, 6.69.

The second major component (and the third band) to be eluted from the column was evaporated to dryness and afforded *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{23},-di-4-nitrobenzylporphyrinogen **5g** as a dark green-black amorphous powder (140 mg, 46%); uv: λ max 503 nm (ε 110,100); ms: (FAB) (3-NOBA, chloroform) found m/z = 1398; $[M+2H]^+$ requires m/z = 1398; ^{1}H-nmr (200 MHz, deuterochloroform): δ 9.90 (broad singlet, 2H, N-*H*), 8.08, 7.97, 6.83, 6.72 (pair of doublets, 8H, 4-nitrobenzyl-*H*, AB spin system, J_{AB} = 8.4 Hz), 7.58 (s, 4H, pyrrole β-*H* on *N*-alkylated rings), 7.19 (s, 4H, pyrrole β-*H* from non-alkylated pyrrole rings), 6.69 (s, 8H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups); 4.64 (broad singlet, 4H, 4-nitrobenzylic-C*H*$_2$-), 1.3 (complex singlets, 72*H*, *t*-butyl-*H*).

Anal. Calcd. for $C_{90}H_{102}N_6O_8$ (1395.77): C, 77.44; H, 7.37; N, 6.02. Found: C, 77.51; H, 7.31; N, 5.96.

N-Alkylation of **5a** with 4-Nitrobenzyl Bromide in Basified *N,N*-Dimethylformamide.

Meso-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21}-decylporphyrinogen **5a** (15 mg, 1.19 x 10^{-5} mole) was refluxed (2 hours) with 4-nitrobenzyl bromide (Aldrich, 50 mg, 2.33 x 10^{-4} mole) in *N,N*-dimethylformamide (DMF, 20 ml) basified with methanolic potassium hydroxide solution (1*M*, 1 ml). After removal of the solvent by evaporation, the solid residue was subjected to column chromatography on silica gel, eluting with dichloromethane. The mauve solution was evaporated to dryness to afford *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21}-decyl-N_{23}-4-nitrobenzylporphyrinogen **5i** as a dark blue-purple amorphous powder (8 mg, 48%); uv: λ max 507 nm (ε 95,300); ms: (FAB) (3-NOBA, chloroform) found m/z = 1403; $[M+2H]^+$ requires m/z = 1403; ^{1}H-nmr (200 MHz, deuterochloroform): δ 8.03, 7.98 (d, 2H, half of AB spin-system from 4-nitrobenzyl-*H*, J_{AB} = 8.4 Hz), 7.63, 7.55, 7.30, 7.02 (singlets, 8H, pyrrole β-*H*), 6.85 (complex, 6H, other half of AB spin-system and *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 6.56, 6.53 (singlets, 4H, *ortho-H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 4.51 (broad singlet, 2H, 4-nitrobenzylic-C*H*$_2$-), 3.4 (t, 2H, N-C*H*$_2$- of decyl group), 1.37-1.21 (complex, 91*H*, *t*-butyl-*H* and decyl-*H*).

Anal. Calcd. for $C_{93}H_{117}N_5O_6$ (1400.91): C, 79.73; H, 8.42; N, 5.00. Found: C, 79.57; H, 8.51; N, 4.88.

N-Alkylation of **5g** with Benzyl Bromide in Basified *N,N*-Dimethylformamide.

Meso-tetrakis-5,10,15,20-(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{23}-di-4-nitrobenzylporphyrinogen **5g** (80 mg, 5.7 x 10^{-5} mole) was refluxed (4 hours) with benzyl bromide (Aldrich, 1 ml, 8 x 10^{-3} mole) and methanolic potassium hydroxide (0.4*M*, 5 ml) in chloroform (50 ml). After removal of the solvent by evaporation, the solid residue was subjected to column chromatography on silica gel, eluting with chloroform. One band was eluted which on evaporation to dryness, afforded *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21},N_{23}-dibenzyl-N_{22},N_{24}-di-4-nitrobenzylporphyrinogen **5j** as a dark red amorphous powder (75 mg, 83%); uv: λ max 504 nm (ε 99,500); ms: (FAB) (3NOBA, chloroform) found m/z = 1576; M^+ requires m/z = 1576; ^{1}H-nmr (200 MHz, deuterochloroform): δ 8.09, 8.05, 6.84, 6.80 (pair of doublets, 8H, 4-nitrobenzyl-*H*, AB spin system, J_{AB} = 8.4 Hz); 7.27-7.12 (complex, 12H, pyrrole β-*H* and phenyl-*H*), 6.77, 6.66 (two singlets, 8H, *ortho*-*H* on 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene groups), 4.64 (broad singlet, 4H, benzylic-CH_2-), 4.52 (broad s, 4H, 4-nitrobenzylic-CH_2-), 1.26, 1.23 (two singlets, 72*H*, *t*-butyl-*H*).

Anal. Calcd. for $C_{104}H_{114}N_6O_8$ (1576.01): C, 79.25; H, 7.29; N, 5.33. Found: C, 79.41; H, 7.20; N, 5.24.

Reduction of Compound **5i** with Stannous Chloride and Hydrochloric Acid.

Meso-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21}-decyl-N_{23}-4-nitrobenzylporphyrinogen **5i** (8 mg, 5.7 x 10^{-6} mole) was taken into a small amount of chloroform (2 ml). Concentrated hydrochloric acid (10 ml) was added, and the mixture degassed with nitrogen. A nitrogen-degassed solution of stannous chloride (90 mg, 4.7 x 10^{-4} mole) in concentrated hydrochloric acid (10 ml) was added dropwise to the mixture containing **5i** and the whole brought to 70° and kept at this temperature for 30 minutes. The uv/visible spectroscopy of this mixture showed a characteristic porphyrin dication spectrum. The mixture was cooled, neutralised with sodium bicarbonate solution (3*M*) and the chloroform layer washed with water (50 ml) three times. The green colour of the porphyrin dication was replaced with the mauve-pink colour of the oxidised porphyrin. The chloroform layer was dried (anhydrous sodium sulphate), filtered, chromatographed on silica gel, eluting with chloroform. The single mauve-pink band was collected and evaporated to dryness to afford *meso*-5,10,15,20-tetrakis(3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene)-N_{21}-4-aminobenzyl-N_{23}-decylporphyrinogen as a dark mauve amorphous solid (5 mg, 64%); uv: λ max 506 nm (ε 98,200); ms: (FAB) (3-NOBA, chloroform) found m/z = 1373; $[M+2H]^+$ requires m/z = 1373; ^{1}H-nmr (200 MHz, deuterochloroform): δ 9.88 (broad singlet, 2H, N-*H*), 7.64 (s, 2H, pyrrole β-*H* on decylated pyrrole), 7.59 (s, 2H, pyrrole β-*H* on pyrrole alkylated with 4-aminobenzyl group), 7.28, 6.98 (two singlets, 4H, non-alkylated pyrrole β-*H*), 6.89 (overlapping singlets, 4H, *ortho*-H of 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene substituent), 6.57, 6.53, 6.38, 6.34 (pair of doublets, 4H, 4-aminobenzyl-*H*, AB spin system, J_{AB} = 8.3 Hz), 6.51, 6.46 (pair of singlets, 4H, *ortho*-H of 3,5-di-*t*-butyl-4-oxacyclohexa-2,5-dienylene substituent), 4.64 (broad singlet, 2H, benzylic-*H*); 3.20 (t, 2H, N-CH_2-), 2.0-0.8 (complex, 91H, *t*-butyl-*H* and decyl-*H*).

Anal. Calcd for $C_{93}H_{119}N_5O_4$ (1370.07): C, 81.46; H, 8.75; N, 5.11. Found: C, 81.22; H, 8.91; N, 5.04.

Results and Discussion.

Initial attempts to *N*-alkylate **2** with 1-bromoheptane or 1-bromodecane in refluxing DMF did not give any alkylated products. Refluxing the oxidised porphyrin **2** in neat (*i.e.*, a large excess) 1-bromoheptane also failed to produce *N*-alkylates but, interestingly, regenerated the parent porphyrin **1**, presumably by oxidising the alkyl halide. We are currently studying the mechanism of this reaction.

In its porphodimethene tautomeric form **2b**, the oxidised porphyrin has two phenolic and two 4-oxacyclohexa-2,5-dienylene *meso*-substituents. We reasoned that addition of base to solutions of **2b** should convert the phenolic groups into phenoxides that then delocalise their negative charge onto two of the macrocyclic nitrogen atoms and the other *meso*-substituents to give **2c**. Support for this view comes from an observed red shift in the main visible absorption band (mirrored by solution colour changes from mauve to deep blue) on addition of base to **2b** [5c]. This increased delocalisation of the phenoxy negative charge should lead to an equivalence of the *meso*-substituents, which is demonstrated by nmr spectrsocopy [5c]. The addition of base to solutions of **2** should, therefore, increase the nucleophilicity of the central nitrogens, so improving the likelihood of *N*-alkylation.

Thus, solutions of oxidised porphyrin **2**, 1-bromodecane, and methanolic potassium hydroxide, in refluxing *N,N*-dimethylformamide, after 1.5 hours gave two major products. These were identified as the N_{21}-decyl **5a** and N_{21},N_{23}-di-decyl **5b** compounds, respectively (Scheme 2). Reaction was slow and incomplete; much starting material was recovered from the reaction after 90 minutes. We have not at this stage attempted to maximise reaction conditions, but we found that longer reaction times led to greater yields of **5b**. Two minor products were also isolated, but only in amounts suitable for analysis by mass spectrometry. On the basis of these two analytical, we have tentatively identified these compounds as the N_{21},N_{22},N_{23}-tridecyl **5c** and N_{21},N_{22},N_{23},N_{24}-tetradecyl **5d** compounds, respectvely.

Repeating this reaction, using benzyl or nitrobenzyl bromide in place of 1-bromodecane, again produced two major products, this time the N_{21},N_{23}-dibenzyl **5e** (or di-4-nitrobenzyl **5g**) and, in smaller quantities, the N_{21},N_{22},N_{23},N_{24}-tetrabenzyl **5f** (or tetra-4-nitrobenzyl **5h**). Minor products in both cases were not identified. Clearly, multi-*N*-alkylation of **2** is more favoured with aryl-alkyl halides, such as benzyl bromide, than straight-chain alkyl halides, *e.g.*, decyl bromide.

The separation of products at different stages of alkylation suggested that mixed *N*-alkylates might also be obtainable, by further alkylation of *N*-mono- and di-alkylated compounds. Thus, the N_{21}-monodecyl compound **5a** was further alkylated with nitrobenzyl bromide in basified (methanolic potassium hydroxide) refluxing *N,N*-dimethylformamide, to give the N_{21}-decyl-N_{23}-4-nitrobenzyl compound **5i**. Similarly, the N_{21},N_{23}-di-4-nitrobenzyl compound compound **5g**, was alkylated further with benzyl bromide, to give the *N*-tetra-alkylated compound **5j** in good yield. This preparation demonstrates that the more sterically-hindered *N*-tetra-alkylated compounds can be obtained in good yields. Other mixed *N*-alkylated compounds can be obtained by reduction of *N*-4-nitrobenzyl moieties to *N*-4-aminobenzyl groups with stannous chloride in hydrochloric acid. Thus, the N_{21}-monodecyl-N_{23}-mono-4-aminobenzyl compound **5k** was prepared and characterised. Similarly, reduction of **5g** gave the N_{21}-4-aminobenzyl-N_{23}-4-nitrobenzyl- and the N_{21},N_{23}-di-4-aminobenzyl compounds, **5l** and **5m**, but these last

two were only identified by their molecular ions in FABS mass spectrometry.

Previous work on the crystal structure of **2a** [5b] shows that the puckering of the macrocycle leads to the pyrrole moieties being alternately tilted up and down about their *alpha*-carbons, so that opposing pyrroles tilt in the same direction. Deprotonation of **2b** by base, followed by delocalisation of phenolic negative charges onto two opposing macroyclic nitrogens (*e.g.*, N_{22} and N_{24}) leads to **2c**, which by analogy with the structure **2a**, puts the two negative charges on opposing pyrrole moieties both tilting in the same direction. Consequently, during dialkylation of **2**, the two alkyl groups should attach themselves to the *same* side of the macrocycle on the nitrogens of *opposing* pyrrole moieties.

The uv/visible spectra of the alkylated products **5** are similar to that of the unalkylated oxidised porphyrin **2**, *i.e.*, a broad relatively intense (but much less so than the parent porphyrin's B band) absorption at *circa* 500-510 nm. This suggests that their macrocycles are structurally the same, *i.e.*, alkylation occurs without altering the conformation of the pyrrole rings in **2**. Some support for this view comes from the reaction to reduce the 4-nitrobenzyl moiety in dialkylated **5i**.

The uv/visible spectra taken after the reaction was completed, but prior to neutralisation and work up, were similar to the dication of the unoxidised porphyrin **1** [8]. This indicates that not only had the 4-nitro-group been reduced to a 4-amino-group, but that the oxidised porphyrin macrocycle had been reduced to the di-*N*-alkylated porphyrin dication. Now, it is known that *cis*-N_{21},N_{23}-dialkylporphyrins dications give uv/visible spectra very similar to the dications of non-*N*-alkylated porphyrins [9], while *trans*-N_{21},N_{23}-dialkylporphyrin dication uv/visible spectra are more complex. We conclude, therefore, that the uv/visible spectrum obtained after reduction of **5i**, prior to neutralisation and work-up, must be for a *cis*-N_{21},N_{23}-dialkylated porphyrin dication. This could only have happened if di-*N*-alkylation of **2** had occurred on the *same* side of the macrocycle. We are currently performing NOE nmr experiments to verify this point.

Interestingly, upon neutralisation and work-up, the N_{21}-aminobenzyl-N_{23}-decylporphyrin spontaneously oxidises to the corresponding oxidised compound, **5k**. It is known that *meso*-substituted porphyrin dications have much more highly puckered macrocycles than the neutral porphyrin [10]. Presumably, the macrocyclic conformational changes that usually occur on neutralisation of a porphyrin dication, cannot now take place because of the large steric repulsion between the two bulky *N*-substituents (only the *trans*-N_{21},N_{22}-dimethyl derivative of *meso*-tetrakisphenylporphyrin has been isolated as a free base [11]). Thus, formation of the neutral porphyrin is precluded in favour of spontaneous oxidation to **5k** [4].

Finally, it is worth noting that *N*-mono and *N*-di-alkylates theoretically can exist as two tautomers, corresponding to the vinylogous xanthoporphyrinogen and porphodimethene forms, **2a** and **2b**, respectively. Inspection of these structures indicates that in their vinylogous xanthoporphyrinogen form, *N*-mono- and *N*-di-alkylates of **2** would have two protons residing on pyrrolic nitrogens: in their porphodimethene form, the protons reside as phenolic protons on two 3,5-di-*t*-butyl-4-hydroxyphenol *meso*-substituents. The ^{1}H-nmr indicates that the protons in question appear at low field (*circa* 9.9 ppm), indicating their status as pyrrolic and not phenolic protons (which appear at *circa* 5.5 ppm) [5c]. This suggests that *N*-mono- and *N*-di-alkylates of **2** exist predominantly in the vinylogous xanthoporphyrinogen tautomeric form.

Conclusions.

We have synthesised some *N*-multialkylated compounds based on the oxidised porphyrin **2**. The separation of *N*-mono- and *N*-di-alkylated products from the reaction mixtures allowed further reaction with different alkyl halides, so that unsymmetrically *N*-di- and *N*-tetra-alkylated compounds were obtainable in good yield. We are currently investigating these and other *N*-multi-alkylated derivatives of **2** as novel potentially non-linear optically-active and/or liquid crystalline materials.

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