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The synthesis is reported of nine unsymmetrical, *meso*-substituted porphyrins. Among the compounds prepared are the following 5-(*R*)-10,15,20-tri-*p*-tolylporphyrins; R = 2,6-dinitrophenyl, 4-hydroxy-3-ethoxyphenyl, 4-hydroxy-3-methoxy-5-nitrophenyl, 5-hydroxy-2-nitrophenyl and 4-hydroxy-3-nitrophenyl. Other porphyrins reported include 5-(2-(1-butoxy)phenyl)-15-(2-nitrophenyl)-10-15-di-*p*-tolylporphyrin and the two 5-(*R*)-10-15,20-tripropylporphyrins in which R = 2-nitrophenyl and 2-hydroxyphenyl. The disubstituted porphyrins offer a rational route to the synthesis of difunctional "tailed-porphyrins".

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Introduction.

Because of their ease of preparation the tetraarylporphyrins have been widely used as models for the naturally occurring porphyrins. The utility of the tetraarylporphyrins has been limited by the fact that these porphyrins are difficult to functionalize (1-5). Recently we reported a mixed-aldehyde method (6) for the one-step synthesis of functionalized tetraarylporphyrins of the type shown in Figure I. Since our initial report Loach, Hambright, Collman and others have used the mixed aldehyde approach to synthesize a variety of carboxyl (7), pyridyl (8) and nitro(9-11) substituted tetraarylporphyrins. These compounds have been subsequently utilized for the synthesis of models for myoglobin (12), cytochrome-c (13), cytochrome oxidase (9), the photosynthetic active site (14-15) and synthetic blood (11). In the present paper we wish to report the extension of the mixed-aldehyde method to the synthesis of other mono-functional *meso*-substituted porphyrins and to the synthesis of unsymetrically substituted porphyrins which contain two different functional groups. The latter compounds allow a rational synthesis of "tailed porphyrins" (12) which contain two different tails and to the synthesis of polymer bound tailed porphyrins (11).

Results and Discussion.

The compounds synthesized in this work are listed in Table I along with the yields. All of the compounds have been characterized by ^{1}H-nmr, ir and/or C, H, and N analyses. The analytical data are given in Table II. The difunctional porphyrins I-IV were prepared by two routes. Compounds I-III were prepared by reacting from 1.0 to 1.5 moles of the appropriately substituted hydroxynitrobenzaldehyde with three moles of tolualdehyde and four moles of pyrrole in a normal mixed aldehyde procedure. Compound IV, 5-(2-hydroxyphenyl)-15-(2-nitrophenyl)-10,20-ditolylporphyrin was prepared, in modest yield, by carrying out the mixed aldehyde synthesis with three different aldehydes. The *trans*-isomer of the desired hydroxy, nitrotetraarylporphyrin was isolated chromatographically from the reaction mixture, along with appreciable amounts of monohydroxy- and mononitrotritolylporphyrins. The porphryin was converted to the *n*-butoxy derivative to simplify characterization since the parent porphyrin exists as two atropoisomers which were difficult to separate. The *n*-butoxy derivative is less polar than the parent porphyrin.

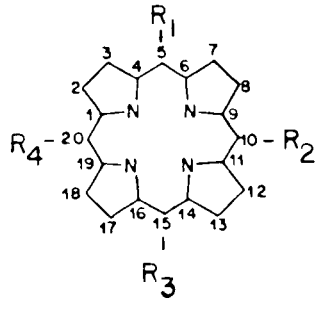

Figure 1. A diagram illustrating the numbering system of the porphyrin ring. In the mono-substituted compounds reported in this and earlier work R_1 = a pyridyl or a substituted phenyl group and R_2,R_3,R_4 = *para*-tolyl or *n*-propyl.

Compound V, 5-(2,6-dinitrophenyl)-10,15,20-tritolylporphyrin was prepared in 0.4% yield. The parent tetra-(2,6-dinitrophenyl)porphyrin could not be prepared. This result is similar to that seen in the *ortho*-hydroxy and *ortho*-carbomethoxytetraarylporphyrin series, where the mono-substituted porphyrins were prepared quite readily despite the fact that the tetraarylporphyrins could not be prepared. It appears that the interference of substituents with the cyclotetramerization reaction (16) is greatly reduced as the number of substituents is reduced.

In addition to the disubstituted porphyrins prepared in this work we have prepared several new monosubstituted porphyrins VII-IX. Of particular interest among these are the 2-hydroxyphenyl and 2-nitrophenyltripropylporphyrins VII and VIII. These porphyrins represent the first examples of mixed aryl, alkyl *meso*-substituted porphyrins.

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Table I

Compound	Name	Yield (%)
I	5-(4-hydroxy-3-nitrophenyl)-10,15,20-tri-*p*-tolyporphyrin	2.1
II	5-(5-hydroxy-2-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin	4.2
III	5-(4-hydroxy-3-methoxy-5-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin	1.2
IV	5-(2-(1-butoxyphenyl)-15-(2-nitrophenyl)-10,20-tri-*p*-tolylporphyrin	0.09
V	5-(2,6-dinitrophenyl)-10,15,20-tri-*p*-tolylporphyrin	0.4
VI	5-(4-hydroxy-3-ethoxyphenyl)-10,15,20-tri-*p*-tolylporphyrin	10.8
VII	5-(2-nitrophenyl)-10,15,20-tripropylporphyrin	1.1
VIII	5-(2-hydroxyphenyl)-10,15,20-tripropylporphyrin	0.4
IX	5-(2-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin	2.1
X	5,10,15,20-tetra-(4-hydroxy-3-methoxy-5-nitrophenyl)porphyrin	11.8
XI	5,10,15,20-tetrapropylporphyrin	6.2

The yields of VII and VIII are low, as might be expected, since the parent tetrapropylporphyrin can only be synthesized in 6% yield. On the other hand we have found that the yield of a mixed porphyrin is a function of the ease of with which it can be separated from the reaction mixture, which is often 80-95% undesired material. A successful isolation depends on the co-crystallization of the mono-substituted porphyrin with the more sparingly soluble tetrasubstitued porphyrins. We have found in the case of compound VII that the amount of porphyrin isolated is increased by adding appreciable amounts of tetraphenylporphyrin to the reaction mixture. The tripropylporphyrin crystallizes out of the reaction mixture with the TPP. The two are easily separated because the TPP is relatively nonpolar.

The nmr spectra of these unsymmetrically substituted porphyrins is of interest. We have previously noted (6) a non-equivalence of the β-pyrrole protons in the ^{1}H-nmr spectrum of 5-(3-hydroxyphenyl)-10,15,20-tri-*p*-tolylporphyrin. We find an even greater magnetic non-equivalence in the nitroporphyrins prepared in this work. For example, in the 60 Mhz spectrum of 5-(2-nitro-5-hydroxyphenyl)-tri-*p*-tolylporphyrin there are three sets of β-pyrrole absorptions. The 3,7-protons appear as a doublet at 8.15 ppm, the 2,8-protons as a doublet at 8.58 ppm and the remaining 12,13,17,18-protons as a singlet at 8.77 ppm. A similar non-equivalence is evident in the nmr spectra of the phenyltripropylporphyrins VII and VIII. In the nitrotripropylporphyrin VII the β-pyrrole protons appear at 8.47, 9.22 and 9.17 ppm respectively.

It is noteworthy that in both of the tripropylporphyrins the β-pyrrole protons at the 12,13,17 and 18 positions appear at roughly the same field as the β-pyrrole protons in tetrapropylporphyrin (9.39 ppm). The spectra cleanly demonstrate the contribution of *meso*-aryl groups to the field experienced by the β-pyrrole protons

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EXPERIMENTAL

The nmr spectra were obtained on a Perkin-Elmer R24B spectrometer operating at 60 MHz. Unless otherwise specified, the solvent was deuterochloroform with TMS as an internal standard. The shifts, δ, are given in ppm from TMS and the coupling constants are in Hz. The spectra were generally taken on nearly saturated solutions. It should be noted that the shifts are often concentration dependent (17). This is especially true of the protons of the functionalized ring of mono-substituted porphyrins. The protons at the 2,3,7,8,12,13,17,18 positions of the porphyrin ring are referred to below as the β-pyrrole protons. Analyses were performed by Gallbraith Laboratories, Inc., Knoxville, Tenn. Infrared spectra were obtained in potassium bromide wafers on a Jasco, IRA-2 grating spectrometer. The abbreviation TTP is used for 5,10,15,20-tetra-(*p*-tolyl)porphyrin.

All solvents and reagents were purchased commercially and used as supplied except as follows. Commercial, reagent grade chloroform contains 0.6% ethanol. In the chromatographic separations described below the commercial chloroform was used as supplied unless specifically specified to have been ethanol free. Dry chloroform was prepared by distilling chloroform from phosphorus pentoxide.

The chromatographic separations were effected by the dry-column procedure (18) using either alumina (Fisher Scientific A-540) or aluminum oxide, basic (Baker, 1-0539), aluminum oxide, acidic (Baker, 1-0538), silica gel (Baker, 5-3405), silica gel (Woelm-04526; obtained through ICN Pharmaceuticals, Inc.). The thin layer chromatographic plates were obtained from the Eastman Kodak Company (Eastman Chromagram sheets; 13252 and 13181), or from E. Merck Laboratories, Merck 5539, Silica Gel 60 F-254.

5-(4-Hydroxy-3-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin (I).

para-Tolualdehyde (17.30 g., 0.144 mole) and 4-hydroxy-3-nitrobenzaldehyde, (0.8 g. 0.048 mole) were dissolved in 25 ml. of propionic acid and added to 12.9 g. (0.192 mole) of pyrrole in 650 ml. of refluxing propionic acid. The mixture was refluxed for one hour, cooled and then filtered. The solid material was boiled with 95% ethanol and then filtered off. The resulting black solids were dissolved in 2l. of chloroform and the filtered solution applied to a 75 x 10 cm column of silica (Baker) using chloroform as the eluant. The first, violet band to elute from the column contains TTP and the desired porphyrin.

The eluate was reduced in volume and applied to a 40 x 2.5 cm alumina column (Fisher) using chloroform as the eluant. The desired porphyrin sticks to the top of the column. When the TTP has been eluted, elution with 20:1 chloroform ethanol is started. This removes a purple green material. The alumina containing the brick-red porphyrins is

Table II

Analytical Data

Compound No.	Formula	M.W.	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
I	$C_{47}H_{35}N_5O_3$	717.8	78.64	78.56	4.92	4.88	9.76	9.66
II	$C_{47}H_{35}N_5O_3$	717.8	78.84	78.94	4.94	4.93	9.76	9.79
III	$C_{48}H_{37}N_5O_4$	747.7	77.09	77.00	4.99	5.05	9.37	9.45
IV	$C_{50}H_{41}N_5O_3$	759.9	79.03	78.95	5.44	5.50	9.22	9.28
V	$C_{47}H_{34}N_6O_4$	746.8	75.58	75.66	4.59	4.63	11.25	11.16
VI	$C_{49}H_{40}N_4O_2$	716.8	82.10	82.05	5.62	5.68	7.82	7.89
VII	$C_{35}H_{35}N_5O_2$	557.77	75.38	75.34	6.33	6.30	12.56	12.51
VIII	$C_{35}H_{36}N_4O$	528.76	79.51	79.60	6.86	6.93	10.60	10.58
IX	$C_{47}H_{35}N_5O_2$	701.8	80.43	80.34	5.03	5.10	9.98	10.01
X	$C_{48}H_{34}N_8O_{16}$	978.7	58.90	58.99	3.50	3.61	11.45	11.40
XI	$C_{32}H_{38}N_4$	478.6	80.31	80.29	8.00	7.92	11.70	11.65

poured off the top of the column and washed repeatedly with a 1:1 mixture of chloroform and glacial acetic acid. The resulting emerald green solution is flashed to dryness and the solids neutralized with ammonium hydroxide. The solids are filtered off and washed repeatedly with water, 95% ethanol and then dried. The porphyrin dissolved in chloroform and chromatographed on a 16 x 2.5 cm column of deactivated alumina (Fisher), (20 ml. of water per 250 ml. of alumina). The porphyrin elutes as a broad smear. The column has a light brown tint with a brown band at the top. The yield was 0.73 g. (2.12%). The compound has an R*f* of 0.75 on silica tlc plates (Kodak) with toluene as the eluant; R*f* 0.78, alumina (Kodak), chloroform; nmr: δ 2.68 (s, 9H, CH_3), 7.49 (d, 6H, J = 8.0, tolyl-3,5-protons), 7.6-9.0 (m, 3H, phenyl), 8.06 (d, 6H, J = 8.0, tolyl-2,6-protons), 8.86 (m, 8H, β-pyrrole); ir (potassium bromide): ν asym NO_2 1539, ν sym NO_2 1353 cm^{-1}.

5-(5-Hydroxy-2-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin (II).

The porphyrin was prepared as described for compound I except for the substitution of 5-hydroxy-2-nitrophenylbenzaldehyde. After boiling the porphyrinic materials with ethanol the volume of the solution was reduced and the slurry stored in a freezer overnight. The collected porphyrins were divided into two equal portions and each portion chromatographed on a 60 x 5 cm column of silica (Baker) using chloroform as the eluant. The second band eluted from the column contains II. The slow moving, brown band was collected, taken to dryness and the solids dissolved in dichloromethane. The porphyrin was twiced chromatographed on 50 x 2.5 cm columns of silica (ICN) using dichloromethane as the eluant to remove a slower moving green material. The total yield was 1.44 g. (4.18%). The compound has an R*f* of 0.4 on silica tlc plates (Kodak) with chloroform as the eluant; nmr: δ -0.27 (broad s, 3H, N-H, OH), 2.39 (s, 6H, 10,20-tolyl-CH_3), 2.44 (s, 3H, 15-tolyl-CH_3), 7.02-8.0 (m, 3H, phenyl), 7.24 (d, 6H, tolyl-3,5-protons), 7.85 (d, 6H, tolyl-2,6-protons), 8.15 (d, 2H, J = 5.0, β-pyrrole-3,7-protons), 8.58 (d, 2H, J = 5.0, β-pyrrole-2,8-protons), 8.77 (d, 4H, β-pyrrole-12,31,17,18-protons).

Compound II was converted to the *n*-butyl ether by stirring 0.15 g. of the porphyrin in 25 ml. of DMF with 2 g. of 1-bromobutane and 2 g. of anhydrous potassium carbonate for 24 hours. The porphyrin was precipitated by pouring the reaction mixture in 100 ml. of 1:1 methanol/water. The collected porphyrins were chromatographed on alumina using chloroform as the eluant; nmr: δ -2.71 (s, 2H, N-H), 0.76 (t, 3H), 1.35 (m, 4H), 2.59 (s, 9H, tolyl-CH_3), 3.80 (t, 2H), 7.48 (d, 6H, J = 8.0, tolyl-3,5-protons), 7.6-8.5 (m, 3H, phenyl), 8.20 (d, 6H, J = 8.0, tolyl-2,6-protons), 8.71 (d, 2H, J = 5.5, β-pyrrole-3,7-protons), 8.92 (s, 4H, β-pyrrole-12,13,17,18-protons), 8.94 (d, 2H, J = 5.5, β-pyrrole-2,8-protons).

5(4-Hydroxy-3-methoxy-5-nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin (III).

The porphyrin was prepared as described for compound I, with the substitution of 5-nitrovanillin (9.47 g.). The propionic acid reaction mixture was allowed to sit at room temperature for 4 days. The solution was poured off the gum coating the flask and the solution was taken to dryness under vacuum and neutralized with ethanolic ammonium hydroxide. The dried material was dissolved in a minimal amount of chloroform. The solution was applied to a 75 x 10 cm silica column (Baker) using chloroform as the eluant. The first band off the column is TTP. The second band contains the red-brown porphyrin. It is followed by bands containing polysubstituted porphyrins.

The band containing the porphyrin was taken to dryness and dissolved in 800 ml. of hot benzene. The porphyrin was twice chromatographed on 75 x 6 cm columns of silica gel (Baker) using benzene. The first band off the column contains TTP. The desired porphyrin moves slowly down the column leaving a broad, red-brown tail. The first and major portion of the band was collected. The tail is contaminated with a reddish, purple impurity. The yield was 0.411 g. (1.2%) R*f* 0.8, silica gel (Kodak), chloroform; ir (potassium bromide): ν asym NO_2 1538, ν sym NO_2 1351 cm^{-1}; nmr: δ 3.52 (s, 9H, tolyl-methyl), 3.98 (s, 3H, CH_3-O-), 7.46 (d, 6H, tolyl-3,5-protons), 7.5-8.8 (m, 3H, phenyl), 8.06 (d, 6H, tolyl-2,6-protons), 8.85 (s, 8H, β-pyrrole).

5-(2-(1-Butoxy)-phenyl)-15-(2-nitrophenyl)-10,15-di-*p*-tolylporphyrin (IV).

Tolualdehyde, (54.06 g., 0.45 mole), *o*-nitrobenzaldehyde (17.00 g., 0.11 mole), and salicylaldehyde (13.74 g., 0.11 mole) were dissolved in 2l. of refluxing propionic acid. Pyrrole (40.25 g., 0.60 mole) was added and the mixture refluxed for one hour. The mixture was cooled on ice, and the purple crystalline porphyrins filtered off, washed with methanol and dried. The resulting 20.5 g. of mixed porphyrins were dissolved in 2.5 l. of hot chloroform and then chromatographed on a 65 x 5 cm column of alumina (Fisher) using chloroform as the eluant. The first and major band off the column is a mixture of TTP and mononitrotritolylporphyrin IX (1.6 g.). Elution with chloroform containing 1% by volume ethanol was commenced and this removed a purple-brown band containing *o*-hydroxytritolylporphyrin and the desired *o*-hydroxy-*o*-nitroditolylporphyrin.

The eluant was taken to dryness and the solids redissolved in chloroform. The porphyrins were chromatographed on a 90 x 4 cm column of silica (Baker) using chloroform as the eluant. The major, slow-moving band of *o*-hydroxytritolylporphyrin is followed by a 10 cm wide dark band containing IV. The latter band was collected, taken to dryness and redissolved in dichloromethane. The porphyrins were chromatographed on a 60 x 2.5 cm silica column (ICN) using 1:1 dichloromethane/-

benzene as the eluant. The porphyrin is preceded by a small amount of brown material. The major band, containing the desired porphyrin was collected, taken to dryness, and converted to the *n*-butyl ether, using butyl bromide, dimethylformamide and anhydrous potassium carbonate. The porphyrin was chromatographed on silica (ICN) using benzene as the eluant and then rechromatographed on basic alumina using 9:1 benzene/ether as the eluant. The yield was 0.105 g. (0.09%); R*f* 0.8, silica gel (Kodak), toluene; R*f* 1.0, alumina (Kodak), toluene; nmr: δ -2.63 (s, 2H, N-H), 0.27 (t, 3H), 0.9 (m, 4H), 2.56 (s, 6H, tolyl-methyl), 3.78 (t, 2H, -O-CH_2), 7.06 (d, 1H), 7.20 (d, 1H), 7.5-8.5 (m, 6H, phenyls), 7.43 (d, 4H, J = 8.0, tolyl-3,5-protons), 8.02 (d, 4H, J = 8.0, tolyl-2,6-protons), 8.51 (d, 2H, J = 5.5, β-pyrrole-13,17-protons), 8.78 (s, 4H, β-pyrrole-2,3,7,8-protons), 8.79 (d, 2H, J = 5.5, β-pyrrole-12,18-protons); ir (potassium bromide): ν asym NO_2 1530, ν sym NO_2 1350 cm^{-1}

5-(2,6-dinitrophenyl)-10,15,20-tri-*p*-tolylporphyrin (V).

Tolualdehyde (10.5 g., 87.4 mmoles), and 2,6-dinitrobenzaldehyde (8.0 g., 40.8 mmoles) were dissolved in 450 ml. of refluxing glacial acetic acid. Pyrrole (8.36 g., 124.6 mmoles) dissolved in 25 ml. of acetic acid was added and the mixture refluxed for forty-five minutes and then cooled on ice. The porphyrins (1.58 g.) were filtered and washed with 95% ethanol. The porphyrins were dissolved in 650 ml. of chloroform and chromatographed on a 50 x 2.5 cm column of silica gel (Baker) using chloroform as the eluant. The porphyrinic material was collected as one fraction, reduced in volume and taken to dryness and then redissolved in dry, ethanol free chloroform. The solution was applied to a 75 x 4 cm column of acidic aluminum oxide (Baker, Brockman activity I). The first material off the column is TTP. The dinitroporphyrin remains at the top of the column as a very slow moving brown-green band. After elution of the TTP, elution with 10:1 chloroform/ethanol was begun. The desired dinitroporphyrin slowly separates from a tight, green band. The eluted porphyrin was taken to dryness, dissolved in benzene, and then chromatographed on a 45 x 2.5 cm silica column (ICN) using 3:1 benzene/hexane as the eluant. After elution of a small amount of residual TTP, elution with pure benzene is commenced. The desired porphyrin elutes as a brown-red band with a reddish tail. Chromatography of this material on alumina (Baker) in benzene gave 889 mg of pure V (0.38%). The compound has an R*f* of 0.5 on silica tlc plates (E. Merck); R*f* 0.7, silica gel (Kodak) in toluene; nmr δ -2.70 (s, 2H, N-H), 2.65 (s, 9H, methyl), 7.50 (d, 6H, J = 8.0, tolyl-3,5-protons), 7.65-8.2 (m, 3H, phenyl), 8.06 (d, 6H, J = 8.0, tolyl-2,6-protons), 8.46 (d, 2H, J = 5.0, β-3,7-protons), 8.82 (s, 4H, β-pyrrole-12,13,17,18-protons), 8.85 (d, 2H, J = 5.0, β-pyrrole-2,8-protons); ir (potassium bromide): ν asym NO_2 1545, ν sym NO_2 1354 cm^{-1}.

5-(3-Hydroxy-3-ethoxyphenyl)-10,15,20-tri-*p*-tolylporphyrin (VI).

Tolualdehyde (18.0 g., 0.15 mole) and 4-hydroxy-3-ethoxybenzaldehyde (8.3 g., 0.05 mole) were dissolved in 500 ml. of hot propionic acid. Pyrrole (13.4 g., (0.20 mole) dissolved in 50 ml. of porpionic acid was added and the reaction mixture refluxed for 45 minutes. The propionic acid was distilled off under vacuum at 100° and the resulting goo was neutralized with a solution of concentrated ammonium hydroxide dissolved in ethanol. The mixture was taken to dryness and the solids extracted repeatedly with 150 ml. portions of absolute ether until the extracts were nearly colorless (2 l. of ether). The combined ether extracts were taken to dryness, dissolved in a minimal amount of chloroform and chromatographed on a 75 x 6 cm silica column (Baker) using chloroform as the eluant. The first band off the column contains the desired porphyrin and TTP. The reddish-violet band is followed by a dark brown material. The entire column is black. The porphyrin band was reduced in volume and applied to a 75 x 5 cm column of acidic alumina (Baker) using chloroform as the eluant. The first band contains TTP; the second a greenish-yellow impurity. The desired porphyrin moves down the column as a broad, brownish smear. Elution with 10:1 chloroform/ethanol elutes the porphyrin. The tail of the porphyrin band and the broad band remaining on the column contains polysubstituted porphyrins.

The fraction containing the porphyrin is taken to dryness and then dissolved in benzene. The porphyrin was chromatographed three times on 75 x 5 cm silica columns (Baker) using 10:1 benzene/cyclohexane as the eluant. Elution was speeded-up by applying air-pressure to the top of the column. The reddish-violet porphyrin is the first material off the column. It is followed by a dark brown band containing disubstituted porphyrins. The porphyrin was thrice recrystallized from chloroform by adding a sixfold excess of methanol. The yield was 3.96 g. (10.8%); R*f* 0.65 silica gel (Kodak), toluene; nmr δ 1.47 (t, 3H), 2.65 (s, 9H, tolyl-methyl), 4.20 (q, 2H), 7.38-8.2 (m, 3H, phenyl), 7.47 (d, 6H, J = 8.0, tolyl-3,5-protons), 8.08 (d, 6H, J = 8.0, tolyl-2,6-protons), 8.83 (s, 8H, β-pyrrole).

5-(2-Nitrophenyl)-10,15,20-tripropylporphyrin (VII).

n-Butanal (14.42 g., 0.20 mole) and *o*-nitrobenzaldehyde (7.56 g., 0.05 mole) were dissolved in 1750 ml. of refluxing propionic acid. Pyrrole (13.42 g., 0.20 mole) dissolved in 50 ml. of propionic acid was added and the mixture refluxed for one hour. The reaction mixture was flashed to dryness and remaining solids neutralized with ammonium hydroxide-ethanol. The solids were treated with hot absolute ethanol and the volume reduced. The slurry was cooled and the black solids filtered off. The solids were dissolved in 1 l. of chloroform and the solution filtered. The porphyrins were applied to a 75 x 5 cm silica column (Baker) using chloroform as the eluant. The porphyrinic materials were collected as one fraction and volume of the solution reduced by flash evaporation. The collected porphyrins were applied to a 30 x 2.5 cm column of basic aluminum oxide (Baker, Brockmann activity I). Dichloromethane was used as the eluant. The first band off the column is tetrapropylporphyrin. The desired nitrotripropyl porphyrin is eluted from the column with 1% ether in dichloromethane. The tail of the porphyrin band should be discarded. The material was rechromatographed once more in the same fashion and then taken to dryness. The porphyrin was dissolved in toluene and chromatographed on a 18 x 2.5 cm column of silica (ICN) using toluene as the eluant. The nitroporphyrin was the first and major band off the column. A bluish, purple smear trailed behind it. The porphyrin was twice recrystallized from toluene by the addition of hot heptane yielding 0.246 g. (1.1%). R*f* 0.75, silica gel (Kodak), toluene; R*f* 0.95, alumina (Kodak), toluene; nmr: δ -2.73 (s, 2H, N-H), 1.18 (t, 9H, CH_3), 2.28 (q, 6H, CH_2), 4.61 (dt, 6H, O-CH_2), 7.3-8.3 (m, 4H, phenyl), 8.47 (d, 2H, J = 5.0, β-pyrrole-3,7-protons), 9.17 (s, 4H, β-pyrrole-12,13,17,18-protons), 9.22 (d, 2H, J = 5.0, β-pyrrole-2,8-protons; ir (potassium bromide): ν asym NO_2 1531, ν sym NO_2 1350 cm^{-1}.

5-(2-Hydroxyphenyl)-10,15,20-tripropylporphyrin (VIII).

The porphyrin was prepared as was described from compound VII except for the substitution of *o*-hydroxybenzaldehyde. After neutralization with ammonium hydroxide the solids were dissolved in a minimal amount of chloroform and a two fold excess of 95% ethanol added. The volume was reduced on a rotary evaporator and more ethanol added. More and more ethanol were added as the volume was repeatedly reduced until the solvent was essentially chloroform free. The concentrated solution was cooled in ice and then filtered. The collected solids were saved. TTP (1.5 g.) dissolved in a minimum amount of chloroform was added to the brown filtrate. Excess ethanol was added and volume reduced as described above. The porphyrins were filtered off and combined with those obtained in the first step. The porphyrins were dissolved in 250 ml. of chloroform and applied to a 75 x 4 cm silica column and eluted with chloroform. The first and major band contained TPrP and TTP. A second, slower moving purple band contained VIII. The porphyrin was collected, dissolved in dichloromethane and chromatographed on a 60 x 2.5 cm silica column (ICN) using dichloromethane as the eluant. The second band on the column was collected and loaded on a 10 x 2.5 cm alumina column (Fisher). Elution with dichloromethane removes a green material. Elution with chloroform brought the porphyrin off. It was closely followed by a bluish-purple material. The porphyrin was rechromatographed on silica with dichloromethane to give 0.11 g. of pure VIII (0.42%); R*f* 0.35, silica gel (Kodak), toluene; R*f* 0.9, silica gel (Kodak), chloroform; nmr: δ 1.27 (t, 9H, CH_3), 2.47 (q, 6H), 4.79 (m, 6H,-O-CH_2), 7.1-8.2 (m, 4H, phenyl), 8.79 (d, 2H, J = 5.5,

β-pyrrole-3,7-protons), 9.33 (d, 2H, J = 5.5, β-pyrrole-2,8-protons), 9.41 (s, 4H, β-pyrrole-12,13,17,18-protons).

5-(2-Nitrophenyl)-10,15,20-tri-*p*-tolylporphyrin (IX).

Tolualdehyde (12.0 g., 0.10 mole) and *o*-nitrobenzaldehyde (7.56 g., 0.05 mole) were dissolved in 500 ml. of refluxing glacial acetic acid. Pyrrole (10.1 g., 0.15 mole) was added, the mixture refluxed for forty-five minutes and then cooled to room temperature in ice. The porphyrins were filtered off (2.0 g.), washed with methanol and then dissolved in 650 ml. of refluxing chloroform. The solution was applied to a 45 x 5 cm column of basic alumina (Baker, Brockman activity I). Elution with chloroform removed the TTP leaving the nitrotritolylporphyrin as a slow moving broad band. The first 50% of the band is nearly pure mononitrotritolylporphyrin IX. The remainder of the band is a mixture of mono and polynitrotolylporphyrins. The nitroporphyrins were collected and dissolved in 100 ml. of hot benzene and the solution diluted with 100 ml. of cyclohexane. The porphyrins were chromatographed on a 60 x 5 cm silica column (ICN) using 1:1 benzene/cyclohexane as the eluant. The second band contained the desired mononitrotritolylporphyrin. The tail of the band was contaminated with a bright red zinc mononitrotritolylporphyrin. It was demetallated by treatment with trifluoroacetic acid in chloroform. The overall yield was 0.54 g. (2.1%); R*f* 0.85, silica gel (Kodak), toluene.

5,10,15,20-Tetra-(4-hydroxy-3-methoxy-5-nitrophenyl)porphyrin (X).

Pyrrole (2.75 g., 0.041 mole) was added to 150 ml. of refluxing propionic acid in which 8.00 g. (0.041 mole) of 5-nitrovanillin had been dissolved. The mixture was refluxed for one hour, cooled, filtered and the collected solids boiled with excess propionic acid. The porphyrins were filtered from the cooled solution was washed repeatedly with 95% ethanol. The porphyrin was dissolved in 1.5 g. of hot chloroform containing 0.75 ml. of acetic acid. The material was chromatographed on a 50 x 4.5 cm silica column (Baker) using chloroform as the eluant. The eluant was collected and the volumne reduced while progressively more and more absolute ethanol was added. The porphyrin was collected by filtration. The porphyrin is so sparingly soluble an nmr spectrum could not be obtained; ir (potassium bromide): ν asym NO_2 1532, 1545, ν sym NO_2 1325 cm^{-1}, broad. The porphyrin does not move on silica gel or alumina tlc plates in chloroform.

5,10,15,20-Tetra-(*n*-propyl)porphyrin (XI).

Butanal (6.40 g., 0.089 mole) was added to pyrrole (5.36 g. 0.080 mole) dissolved in 1680 ml. of refluxing propionic acid and the mixture refluxed for 50 minutes. The mixture was flashed to dryness, and dissolved in a minimum amount of chloroform. Ethanol containing a little ammonium hydroxide was added, and the volume of the solution was reduced on a rotary evaporator. More 95% ethanol was added and the volume reduced again until the solution was essentially chloroform free. The ethanol solution was concentrated, cooled in ice and the porphyrin filtered off. The process was twice repeated and then the porphyrins were chromatographed on a silica column in dry chloroform. The first 10% of the band is discarded. The porphyrin was collected and recrystallized once from absolute ethanol yielding 0.600 g. (6.25%); R*f* 0.85, silica gel (Kodak), toluene; R*f* 0.95, alumina (Kodak); nmr: δ -2.71 (s, 2H, N-H), 1.31 (t, 12H, CH_3), 2.49 (q, 8H, $-CH_2$), 4.85 (t, 8H, $O-CH_2$), 9.39 (s, 8H, β-pyrrole).

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