The Synthesis of Some Substituted Tetraarylporphyrins

Robert C. Little, John A. Anton, Paul A. Loach and James A. Ibers

Department of Chemistry, Northwestern University, Evanston, Illinois 60201

Received June 17, 1974

The synthesis of six unsymmetrically substituted tetraarylporphyrins is reported. The compounds prepared are 5-(R),10,15,20-tritolylporphyrins, where R = 2-pyridyl, 3-pyridyl, 4-acetamido, and 2,3 or 4-hydroxyphenyl. Four new tetrasubstituted tetraarylporphyrins (5,10,15,20-tetra-(R)-porphyrin) are also reported, where R = 3-pyridyl, 4-acetylphenyl, 4-hydroxyphenyl and 4-butoxyphenyl. The proton nmr spectra of these porphyrins are presented.

Introduction

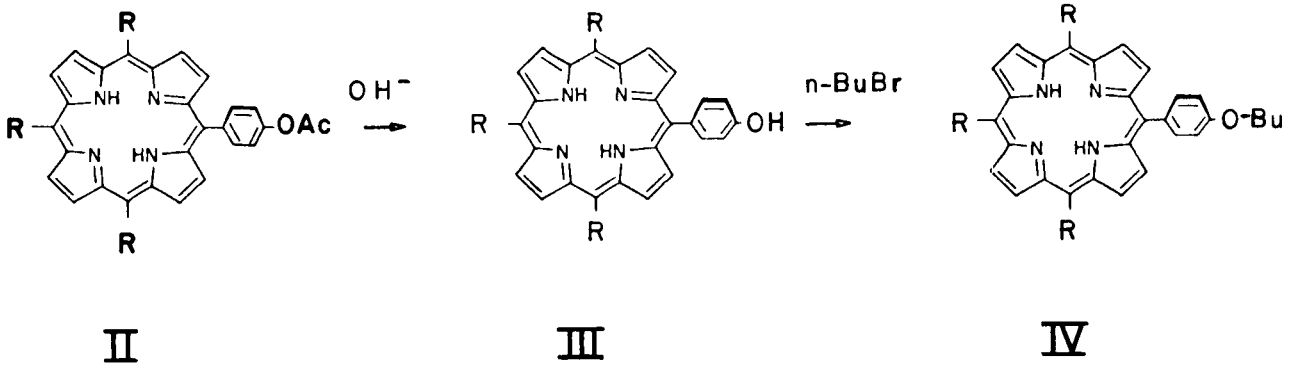
The tetraarylporphyrins have been widely used as models for the naturally occurring porphyrins because of their ease of preparation. The syntheses of numerous substituted tetraarylporphyrins have been reported, (Table I, Figure 1). These porphyrins contain a symmetric pattern of substitution since the synthesis of choice (23) involves the condensation of four moles of pyrrole with four moles of aldehyde. Because of the many isomers which are possible, the preparation of substituted tetraarylporphyrins by direct substitution of a tetraphenylporphyrin has received little attention, (14-19), and yet these compounds are of interest since they serve as starting materials for the synthesis of models for the active sites in hemoproteins.

In this paper we report the syntheses of several unsymmetrically substituted tetraarylporphyrins by a mixed-aldehyde approach. We also report the preparation of several tetrasubstituted tetraarylporphyrins whose syntheses have not previously appeared. The compounds prepared in this study are listed in Table II along with the yields obtained. Table III presents the analytical data for these compounds.

Results and Discussion

The tetraacetyl compound II was synthesized to investigate the feasibility of protecting the hydroxyl group of the aldehyde with the acetyl moiety. Compound II was readily hydrolyzed in refluxing alcoholic potassium hydroxide to the tetrahydroxy compound III. Since the product could not be easily characterized it was converted to the tetrabutyl ether, IV, by reaction with *n*-butyl bromide (Scheme I). The latter chromatographed easily and gave an nmr spectrum (Figure 2A) consistent with IV, thus confirming the identity of II and III. The overall yield of the tetrahydroxy compound by this route was 17%.

The use of the acetyl group in the synthesis of the monohydroxy compound, VII, proved to be unsatisfactory. The yield of the monoacetyl compound, VIII, (*vide infra*) was low, and the subsequent hydrolysis step was made difficult by the low solubility of VIII and the low solubility of the accompanying tetratolylporphyrin, from which VIII could not be easily separated. The direct synthesis of the monohydroxy compound, VII, (*vide infra*), proved to be a more straightforward route.



II III IV

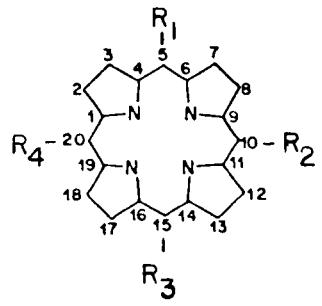


Figure 1.

A diagram illustrating the numbering system of the porphyrin ring. The nature of the aryl groups, R_1, R_2, R_3, R_4 are given in Table II.

The synthesis of the mono-substituted porphyrins V-XI was accomplished by means of a mixed-aldehyde approach. One equivalent of a substituted aldehyde and three equivalents of *para*-tolyladehyde were condensed with four equivalents of pyrrole. The resulting mono-substituted porphyrin crystallized from the reaction mixture along with tetratolylporphyrin. These two porphyrins, along with small amounts of polysubstituted tetraaryl porphyrins, were then separated by column chromatography. The separation was facilitated by the strongly basic or acidic nature of the substituents used in this study.

The yields obtained with the mixed-aldehyde method are low, but are nonetheless reasonable when one considers the fact that yields of tetra-substituted porphyrins rarely exceed 25% (1-21). Elemental analyses of those compounds which could be purified by chromatography in some instances presented unexpected difficulties. While the molar ratios C:H:N were consistent with the assigned structures, the percentages of C, H, and N were low. These analyses were improved slightly by using samples that were obtained by repeated filtering of solutions of the given porphyrin through a sintered glass frit followed by drying at 125° for 24 hours. Finally, successful analyses were obtained by converting the free-base porphyrins to their Cu(II) complexes and then analyzing the resultant metalloporphyrins after purification by chromatography.

The nmr spectra of the porphyrins prepared in this study clearly indicate the structure of the compounds. Figure 2 compares the spectra of two tetrasubstituted porphyrins, I and IV, with the spectra of two monopyridyltritolylporphyrins, IX and X. In the latter two compounds the absorptions from the protons in the pyridyl rings are seen superimposed on the absorptions from the three tolyl groups. Integration of the aromatic region (24 protons) relative to the tolyl methyl resonance (nine protons in the mono-substituted compounds) is diagnostic of the purity of the compounds.

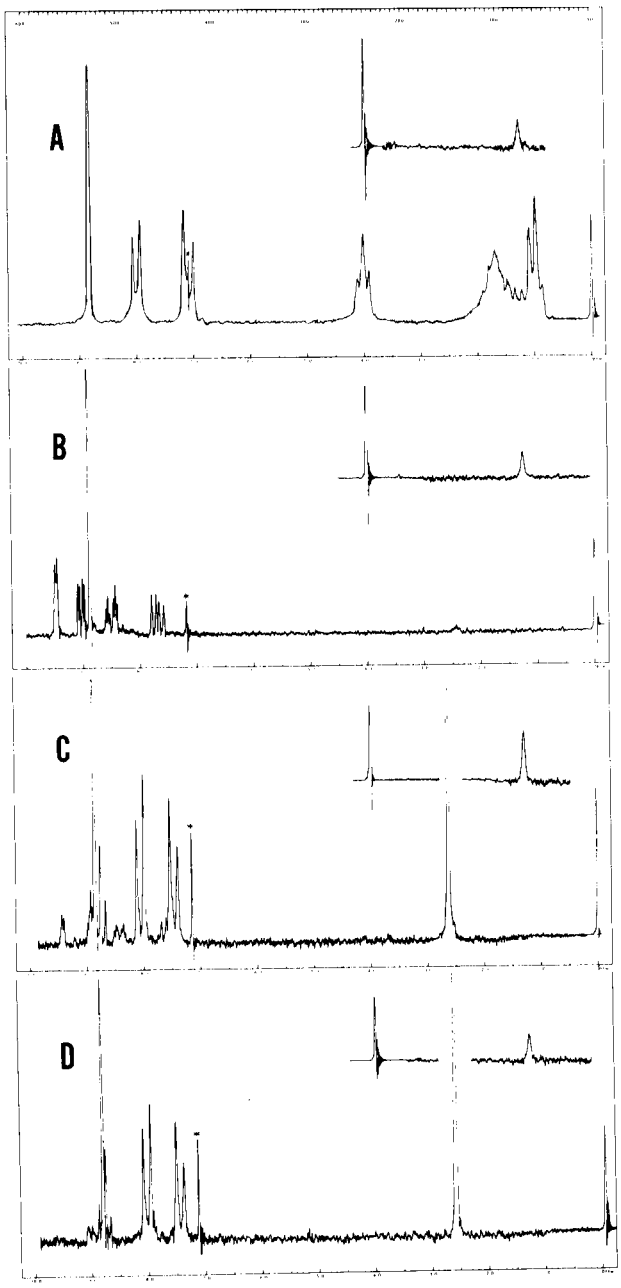


Figure 2.

60 MHz nmr spectra of (A) 5,10,15,20-tetra-(3-pyridyl)-porphyrin, I; (B) 5,10,15,20-tetra-(4-butoxyphenyl)-porphyrin, IV; (C) 5-(3-pyridyl)-10,15,20-tritolylporphyrin, IX; and (D) 5-(2-pyridyl)-10,15,20-tritolylporphyrin, X. The solvent is deuterochloroform and the reference is TMS. The peak marked with an asterisk results from residual chloroform in the deuterochloroform. The inset shows the high field region from TMS.

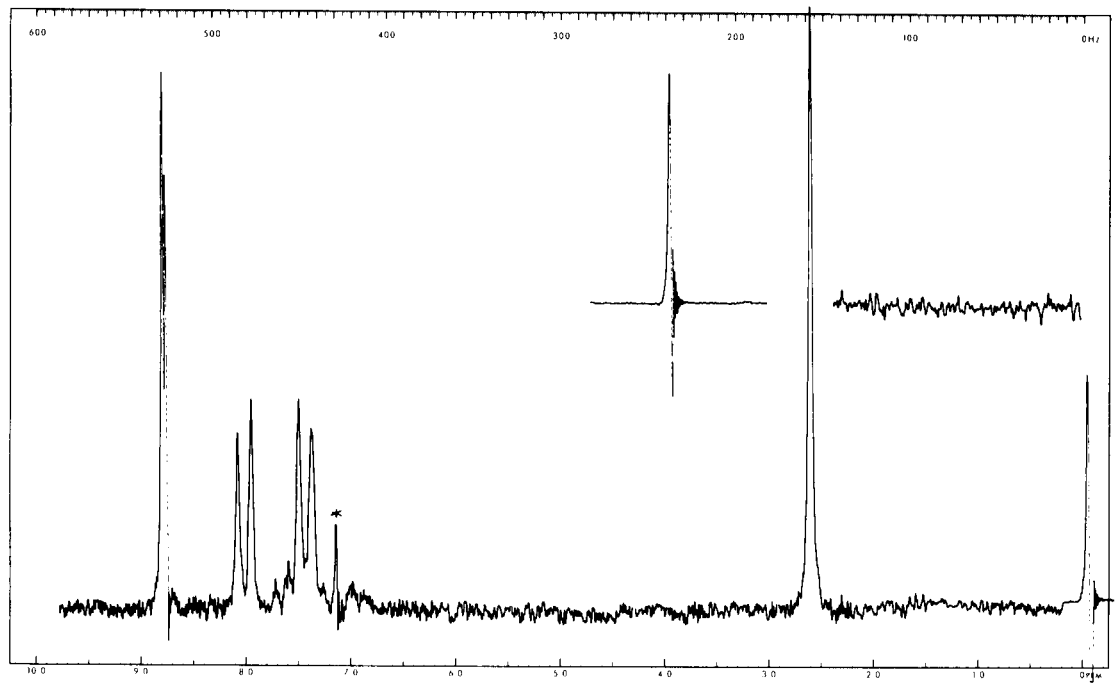


Figure 3.

60 MHz nmr spectrum of 5-(3-hydroxyphenyl)-10,15,20-tritolylporphyrin V in deuterochloroform. The reference is TMS.

Table I

References to the Synthesis of Symmetrically Substituted Tetraarylporphyrins.

Aryl Group	Substituent	Position para	meta	ortho	other
phenyl	F	(2,3)	(3)	(2-4)	2,3,4,5,6-pentafluoro (5,6)
	Cl	(2,7-10)	(2)	(2,10)	2,3,4,5,6-pentachloro (5) 2,6-dichloro (2)
	Br	(2)	---	(2)	
	D	---	---	---	2,3,4,5,6-pentadeutero (4)
	NO_2	(2,7-9)	---	(2)	
	OH	(11)	(9)	(12)	4-hydroxy-3-methoxy (9)
	$O\text{-}CH_3$	(6-10)	(9)	(2,6,10,12)	2,4,6-trimethoxy (25)
	CO_2H	(9,13)	---	---	
	CO_2CH_3	(9,13)	---	---	
	NH_2	(9)	---	---	
	CN	(9,13)	---	---	
	$CH(CH_3)_2$	(16)	---	---	
	CH_3	(2,7,8,13)	---	(2,10)	2,4,6-trimethyl (10)
	SO_3H	(17-19)	---	(9)	4-methoxy-3-sulphonato- (20)
	$CH_2\text{-}OH$	(13)	---	---	
	$N(CH_3)_2$	(13)	---	---	
pyridyl		(5,6,21,22)	(6,22)	(6,22)	
4-(*N*-methylpyridinium)		(19,23)	---	---	
1-napthyl		(6,9)	---	---	
1-anthracenyl		(9)	---	---	

Table II

Compound	Aryl Groups	Name	Yield (%) (Based on pyrrole)
	R_1, R_2, R_3, R_4 =		
I	3-pyridyl	5,10,15,20-tetra-(3-pyridyl)porphyrin	17.4
II	4-acetylphenyl	5,10,15,20-tetra-(4-acetylphenyl)porphyrin	17.5
III	4-hydroxyphenyl	5,10,15,20-tetra-(4-hydroxyphenyl)porphyrin	17.5
IV	4-butoxyphenyl	5,10,15,20-tetra-(4-butoxyphenyl)porphyrin	16.6
	R_2, R_3, R_4 = tolyl R_1 =		
V	3-hydroxyphenyl	5-(3-hydroxyphenyl)-10,15,20-tritolylporphyrin	1.8
VI	2-hydroxyphenyl	5-(2-hydroxyphenyl)-10,15,20-tritolylporphyrin	4.0
VII	4-hydroxyphenyl	5-(4-hydroxyphenyl)-10,15,20-tritolylporphyrin	6.7
VIII	4-acetylphenyl	5-(4-acetylphenyl)-10,15,20-tritolylporphyrin	~2
IX	3-pyridyl	5-(3-pyridyl)-10,15,20-tritolylporphyrin	4.1
X	2-pyridyl	5-(2-pyridyl)-10,15,20-tritolylporphyrin	4.7
XI	4-acetamidophenyl	5-(4-acetamidophenyl)-10,15,20-tritolylporphyrin	2.0

Table III

Analytical Data

Compound	Formula (free base)	M.W. (free base)	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
I	$C_{40}H_{26}N_8$	618.7	70.63 (a)	70.31	3.56	3.53	16.47	16.48
IV	$C_{60}H_{62}N_4O_4$	903.2	79.79	79.10	6.92	7.01		
V	$C_{47}H_{36}N_4O_1$	672.8	76.87 (a)	76.31	4.67	4.66	7.63	7.56
VI	$C_{47}H_{36}N_4O_1$	672.8	76.87 (a)	76.29	4.67	4.60	7.63	7.69
VII	$C_{47}H_{36}N_4O_1$	672.8	76.87 (a)	76.24	4.67	4.66	7.63	7.64
IX	$C_{46}H_{35}N_5$	657.8	76.81 (a)	76.04	4.62	4.57	9.74	9.85
X	$C_{46}H_{35}N_5$	657.8	76.81 (a)	76.80	4.62	4.62	9.74	9.96
XI	$C_{49}H_{39}N_5O_1$	713.9	82.44	81.73	5.51	5.43	9.81	9.46

(a) These compounds were analyzed as the Cu(II) metalloporphyrins --- see text.

Figure 3 shows the nmr spectrum of 5-(3-hydroxyphenyl)-10,15,20-tritolylporphyrin, VII. The pyrrole β-hydrogen nuclei are magnetically non-equivalent, whereas the protons of the more remote tolyl groups are still equivalent. In these phenolic porphyrins, as well as in various carboxylic acid derivatives, the pyrrole N-H protons apparently undergo fast exchange in deuterochloroform solution, since their resonances are not visible in the nmr spectra. The nmr assignments are given in the experimental section and are consistent with those previously reported for various tetraarylporphyrins (7-9,11,15,25,26).

The synthesis of various functionalized porphyrins from the compounds prepared in this study will be reported later.

Acknowledgments

The authors would like to thank Dr. Rainer Schlodder for stimulating discussions. We are also indebted to Prof. F. R. Longo for his helpful comments. We gratefully acknowledge support of this work by the National Institutes of Health (HL 13157 and GM 11741) and by the National Science Foundation (GB 27439-X2 and GB 42860). P. A. L. acknowledges a Research Career Development Award from the U.S. Public Health Service (5K04 GM-70133).

EXPERIMENTAL

The nmr spectra were obtained on a Perkin-Elmer R24B or Varian T60 spectrometer operating at 60 MHz. Unless otherwise specified, the solvent was deuterochloroform with TMS as internal standard. The shifts, δ, are given in ppm and the coupling constants are in Hz. The spectra were taken on saturated solutions. It should be noted that the shifts are concentration dependent (27). This is especially true of the protons of the functionalized ring of the mono-substituted prophyrins. 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 Micro-Tec Laboratories, Skokie, Illinois and by the Analytical Services Laboratory, Northwestern University. When the resultant analyses of the free-base porphyrins were unsatisfactory (see text) these porphyrins were converted to their Cu(II) derivatives by standard methods (28) and then analyzed.

The chromatographic separations described below were effected by the dry-column procedure (29) using either alumina (Fisher Scientific, A-540) or silica gel (Woelm-04526; obtained through ICN Pharmaceuticals, Inc.). The chloroform used as eluant was USP grade, unless otherwise specified.

The general synthetic porcedure was that developed by Adler, *et al.* (30) in which equimolar amounts of the appropriate aldehyde(s) and pyrrole are allowed to react in boiling propionic acid solvent. Cooling of the reaction mixture, followed by filtration on a large Buchner funnel normally produced purple crystals of the crude prophyrins. Specific synthetic and chromatographic details are given below. The analytical results are presented in Table III.

Compound I. 5,10,15,20-Tetra-(3-pyridyl)porphyrin. MW 618.7.

3-Pyridylcarboxaldehyde (16.0 g., 0.149 mole) and 10.1 g. (0.150 mole) of pyrrole (Eastman Kodak, practical) were added to a mixture of 520 ml. of propionic acid and 7.5 ml. of acetic acid that was near boiling temperature. The reaction mixture was refluxed for one hour and then taken to dryness under vacuum by means of a rotary evaporator. The resulting black tar was washed briefly with water, and then with dilute ammonium hydroxide. The slightly wet material was triturated with a minimum amount of methanol on a steam bath until the purple crystals of the porphyrin were free from tar. The slurry was then stored overnight in a freezer at -5°. The purple solid was filtered off and washed with a minimal amount of methanol and then dried.

The material was dissolved in a minimal amount of chloroform and chromatographed on a 60 x 5 cm column of alumina using chloroform as the eluant. The first band is a yellow impurity. The dark maroon band which follows contains the porphyrin. The top of the column is green. The yield was 4.04 g. (17.4%). The material may be further purified by chromatography on a 50 x 2 cm column of silica gel using reagent grade chloroform as the eluant. The porphyrin band moves very slowly and separates from a brown impurity which sticks to the top of the column; nmr: δ = 9.47 (dd, 4H, [$^4J_{2,6}$ = 2.2, $^5J_{2,5}$ = 0.8]); 9.03 (dd, 4H, [$^4J_{4,5}$ = 4.6, $^4J_{4,6}$ = 1.7]); 8.90 (s, 8H, β-pyrrole); 8.50 (dt, 4H, [$^3J_{6,5}$ = 7.5, $^4J_{6,2}$ = 2.2, $^4J_{6,4}$ = 1.7]); 7.70 (qd, 4H, [$^3J_{5,6}$ = 7.5, $^4J_{5,4}$ = 4.6, $^5J_{5,2}$ = 0.8]); -2.76 (s, 2H, pyrrole N-H).

Compound II. 5,10,15,20-Tetra(4-acetylphenyl)porphyrin. MW 846.8.

para-Acetylbenzaldehyde (24.4 g., 0.148 mole) (31) was added to 240 ml. of refluxing propionic acid and followed by the addition of 10.1 g. (0.150 mole) of pyrrole. The reaction mixture was refluxed for one hour and then cooled overnight at -5. The crude porphyrin (purple needles, or a brown-black amorphous powder) was filtered off and repeatedly washed with cold ethanol. If the product is non-crystalline it should be stirred overnight with absolute ethanol and then filtered. The porphyrin, which is soluble in chloroform, could not be chromatographed on either alumina or silica gel because of the rapid hydrolysis of the acetyl groups. The yield was 5.56 g. (17.5%); nmr: δ = 8.78 (s, 3H, β-pyrrole); 8.09 (d, 8H, J = 8.4, tolyl-2,6-protons); 7.35 (d, 8H, J = 8.4, tolyl-3,5-protons); 2.37 (s, 12H, methyl).

Compound III. 5,10,15,20-Tetra(4-hydroxyphenyl)porphyrin. MW 678.8.

The crude material II (5.56 g.) was refluxed for several hours in 95% ethanol containing 4 g. of potassium hydroxide. The resulting dark green solution was filtered, acidified with acetic acid, and then taken to dryness yielding an amorphous purple solid which was very soluble in ethanol and alkaline aqueous solution. The solid was taken up in chloroform, filtered, and evaporated to dryness. The yield was 4.4 g. (essentially quantitative). The material could not be chromatographed effectively, although it could be slowly eluted from an alumina column with 2% acetic acid in chloroform. The compound was not soluble enough in deuterochloroform to obtain an nmr spectrum.

Compound IV. 5,10,15,20-Tetra(4-butoxyphenyl)porphyrin. MW 903.2.

Compound III (0.200 g.) was stirred in 15 ml. of dimethylformamide with 0.120 g. of crushed sodium hydroxide. *n*-Butyl bromide (0.5 g.) was added over a period of an hour from a dropping funnel. After thirty hours, 10 ml. of ethanol was added to the green solution, followed by 80 ml. of water. The purple product was filtered off and washed with absolute ethanol and then dried. It was chromatographed on alumina with chloroform. The porphyrin moves with the solvent front and separates easily from any unreacted starting material and from two slowly-moving green and brown bands near the top of the column. The yield was 0.253 g. (95.0%, based on tetrahydroxyporphyrin); nmr: δ = 8.70 (s, 8H, β-pyrrole); 7.96 (d, 8H, J = 8.1, tolyl-2,6-protons); 7.05 (d, 8H, J = 8.1, tolyl-3,5-protons); 4.06, (t, 8H, J = 6.0, -O-CH_2-); 1.73 (m, 16H, -CH_2-CH_2-); 1.04 (t, 12H, J = 6.0, methyl).

Compound V. 5-(3-Hydroxyphenyl)-10,15,20-tritolylporphyrin. MW 672.8.

meta-Hydroxybenzaldehyde (4.6 g., 0.038 mole) and 13.5 g. (0.112 mole) of *para*-tolylaldehyde were thoroughly mixed with 500 ml. of hot propionic acid. Pyrrole (10.1 g., 0.150 mole) was added and the reaction mixture refluxed for one hour. After cooling, the reaction mixture was filtered and the purple crystals washed with ethanol.

The porphyrins were dissolved in 750 ml. of chloroform and chromatographed on a 60 x 5 cm column of alumina using chloroform as the eluant. The first band off the column was the tetratolylporphyrin by-product. It was followed closely by a tight green band of chlorin impurity. A third band, which moved very slowly and which had spread out over the top 30 cm. of the column, contained the mono-hydroxyporphyrin. This band was eluted with 1:10 ethanol-chloroform and then taken to dryness under vacuum on a rotary evaporator. This material was redissolved in reagent grade chloroform and chromatographed on a 40 x 2 cm column of silica gel using chloroform as the eluant. The elution pattern was similar to that of the alumina column except that a dark brown band sticks at the top of the column and a second band separates slowly from the tail of the main porphyrin band. The yield was 0.46 g. of V (1.8%); nmr: 8.81, 8.77 (two s, 3H, β-pyrrole); 8.02 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.73 (m); 7.59 (m); 7.37 (d, 6H, J = 8.0, tolyl-3,5-protons); 6.8 (m); 6.7 (m); 2.58 (s, 9H, methyl).

Compound VI. 5-(2-Hydroxyphenyl)-10,15,20-tritolylporphyrin. MW 672.8.

The porphyrin was prepared as described above for compound V, except for the substitution of salicylaldehyde. The crude prophyrins, 3.1 g., were chromatographed as described above, except that the mono-hydroxyporphyrin, VI, was eluted with straight chloroform. The material was rechromatographed on silica gel to give 1.00 g. (4.0%) of pure VI; nmr: δ = 8.90 (s, 8H, β-pyrrole);

8.80 (m), 8.07 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.9 (m); 7.7 (m); 7.46 (d, 6H, J = 8.0, tolyl-3,5-protons); 7.24 (m); 2.65 (s, 9H, methyl).

Compound VII. 5-(4-Hydroxyphenyl)-10,15,20-tritolylporphyrin. MW 276.8.

The porphyrin was prepared as described for compound V, except for the substitution of *para*-hydroxybenzaldehyde. The crude porphyrins, 4.1 g., were chromatographed in chloroform on a 60 x 5 cm column of silica gel. The second band was collected to yield 1.85 g. of VII. The material was rechromatographed on a 40 x 2 cm column of silica gel to give 1.7 g. of pure VII (6.7%); nmr: 8.83 (s, 8H, β-pyrrole); 8.05 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.94 (m); 7.49 (d, 6H, J = 8.0, tolyl-3,5-protons); 7.15 (m), 7.00 (m); 2.68 (s, 9H, methyl).

Compound VIII. 5-(4-Acetylphenyl)-10,15,20-tritolylporphyrin. MW 714.8.

The porphyrin was prepared as described for V, except for the substitution of *para*-acetylbenzaldehyde (30). The crude porphyrins, 4.2 g., could not be separated chromatographically. A nmr spectrum of the mixture clearly showed a small peak at 2.43 ppm due to the acetyl methyl group. The mixture was hydrolyzed by refluxing for 24 hours with potassium hydroxide in ethanol-chloroform and then acidifying with acetic acid. Chromatography of this material on alumina, with chloroform, eluted the tetratolylporphyrin. The mono-hydroxyporphyrin, VII was then eluted from the column with ethanol-chloroform, 1:3. This material was rechromatographed on silica gel using reagent grade chloroform as the eluant. The nmr spectrum of the product was identical with that of an authentic sample of VII, prepared as described above. The yield of VII, by this route, was less than 1%. A nmr spectrum of the hydrolized reaction mixture showed that hydrolysis was incomplete.

Compound IX. 5-(3-Pyridyl)-10,15,20-tritolylporphyrin. MW 657.8.

meta-Pyridinecarboxyldehyde (4.01 g., 0.038 mole) and 13.5 g. (0.122 mole) of *para*-tolylaldehyde were thoroughly mixed with 500 ml. of hot propionic acid. Pyrrole (10.1 g.) was then added and the mixture refluxed for one hour. After cooling the reaction mixture was filtered and the purple crystals washed with methanol. The yield was 2.87 g. of mixed porphyrins.

The crude porphyrins were dissolved in 600 ml. of chloroform and chromatographed on alumina in a manner similar to that described for compound VIII. The material was rechromatographed on silica gel with reagent grade chloroform. A brown impurity separates out at the tail of the *mono*-pyridylporphyrin band. The yield was 1.05 g. of IX (4.1%); nmr: δ = 9.34 (d, 1H, J = 2.1, pyridyl-2-proton.); 8.83 (s); 8.76 (s, 8H, β-pyrrole); 8.66 (s); 8.58 (s); 8.26 (dd, 1H); 7.92 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.28 (d, 6H, J = 8.0, tolyl-3,5-protons; 7.25 (m); 2.62 (s, 9H, methyl); -2.62 (s, 2H, pyrrole N-H).

Compound X. 5-(2-Pyridyl)-10,15,20-tritolylporphyrin. MW 657.8.

Compound X was prepared by a procedure similar to that described for IX, with the substitution of *ortho*-pyridinecarboxaldehyde. The yield of mixed porphyrins was 4.2 g. The yield of X was 1.21 g. (4.7%); nmr: δ = 9.10 (d, 1H); 8.8 (m); 8.78 (s, 8H, β-pyrrole); 7.98 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.42 (d, 6H, J = 8.0, tolyl-3,5-protons); 2.62 (s, 1H, pyrrole N-H). In contrast to IX, X did not readily react with alkyl bromides in refluxing dimethylformamide. It could be quaternized with methyltoluene sulphonate in boiling DMF.

Compound XI. 5-(4-Acetamidophenyl)-10,15,20-tritolylporphyrin. MW 713.9.

para-Acetamidobenzaldehyde (4.90 g., 0.03 mole) and 10.8 g. (0.09 mole) of *para*-tolualdehyde were heated to reflux in 500 ml. of propionic acid. Pyrrole (8.06 g., 0.12 mole) was then added and reflux was continued for ½ hour. The reaction mixture was allowed to cool and put in a refrigerator overnight. The reaction mixture was filtered and the purple solid obtained washed with methanol to remove traces of a tarry residue. Crude mixed porphyrins (1.2 g.) were obtained. This material was chromatographed on 120 g. of silica gel with reagent grade chloroform. The first band to be eluted contained the tetratolylporphyrin. the second band contained XI. The yield was 0.43 g. (2.0%). The material was rechromatographed on preparative silica gel plates with reagent grade chloroform; nmr: 8.82, 8.80 (two s, 8H, β-pyrrole); 8.02 (d, 6H, J = 8.0, tolyl-2,6-protons); 7.30-7.80 (m, 2,3,5,6-*para*-acetamidophenyl); 7.48 (d, 6H, J = 8.0, tolyl-3,5-protons); 2.67 (s, 9H, tolyl-methyl); 2.22 (s, 3H, methyl); -2.72 (s, 2H, pyrrole N-H).

REFERENCES

(1) J. B. Kim, J. J. Leonard and F. R. Longo, *J. Am. Chem. Soc.*, **94**, 3986 (1972).

(2) E. B. Fleischer, R. Foust, D. Jeter and R. Near, *Inorg. Nucl. Chem. Letters*, **9**, 1219 (1973).

(3) J. Fajer, D. C. Borg, A. Forman, D. Dolphin and R. H. Felton, *J. Am. Chem. Soc.*, **92**, 3451 (1970).

(4) F. R. Longo, M. G. Finarelli and J. B. Kim, *J. Heterocyclic Chem.*, **6**, 927 (1969).

(5) M. A. Torrens, D. K. Straub and L. M. Epstein, *J. Am. Chem. Soc.*, **94**, 4160 (1972).

(6) K. Ueno and A. E. Martell, *J. Phys. Chem.*, **60**, 934 (1956).

(7) D. W. Thomas and A. E. Martell, *J. Am. Chem. Soc.*, **78**, 1335 (1956); **78**, 1338 (1956).

(8) A. Treibs and N. Haberle, *Ann. Chem.*, **718**, 183 (1968).

(9) G. M. Badger, R. A. Jones and R. L. Laslett, *Aust. J. Chem.*, **17**, 1028 (1964).

(10) M. Meot-Ner and A. D. Adler, *J. Am. Chem. Soc.*, **94**, 4763 (1972).

(11) L. K. Gottwald and E. F. Ullman, *Tetrahedron Letters*, 3071 (1969).

(12) N. Datta-Gupta and T. Bardos, *J. Heterocyclic Chem.*, **3**, 495 (1966).

(13) R. F. Pasternack, P. R. Huber, P. Boyd, G. Engasser, L. Francesconi, E. Gibbs, P. Fasella, G. C. Venturo and L. deC. Hinds, *J. Am. Chem. Soc.*, **94**, 4511 (1972).

(14) A. R. Menotti, Doctoral Dissertation, The Ohio State University, Columbus, Ohio, 1941.

(15) S. S. Eaton, G. R. Eaton and R. H. Holm, *J. Organometal. Chem.*, **39**, 179 (1972).

(16) E. B. Fleischer, J. M. Palmer, T. S. Srivastava and A. Chatterjee, *J. Am. Chem. Soc.*, **93**, 3162 (1971).

(17) T. S. Srivastava and M. Tsutsui, *J. Org. Chem.*, **38**, 2103 (1973).

(18) R. F. Pasternack, L. Francesconi, D. Rolf and E. Spiro, *Inorg. Chem.*, **12**, 2606 (1973).

(19) W. M. Bourma, Thesis, University of Iowa (1972); *Diss. Abstr. Int. B.* **33** (4), 1438 (1972).

(20) E. B. Fleischer, *Inorg. Chem.*, **1**, 493 (1962).

(21) B. P. Neri and G. S. Wilson, *Anal. Chem.*, **45**, 442 (1973).

(22) P. Hambright and E. B. Fleischer, *Inorg. Chem.*, 9, 1757 (1970).
(23) G. H. Barnett, M. F. Hudson and K. M. Smith, *Tetrahedron Letters*, 2887 (1973), and references therein.
(24) L. Vaska, A. R. Amundsen, R. Brady, B. R. Flynn and N. Hisada, *Finn. Chem. Letters*, 66 (1974).
(25) F. A. Walker and G. L. Avery, *Tetrahedron Letters*, 4949 (1971).
(26) R. J. Abraham, A. H. Jackson, G. W. Kenner and D. Warburton, *J. Chem. Soc.*, 853 (1963).
(27) W. S. Caughey, J. O. Alben, W. Y. Fujimoto and J. L. York, *J. Org. Chem.*, 31, 2631 (1966).
(28) G. D. Dorough, J. R. Miller, and F. M. Huennekens, *J. Am. Chem. Soc.*, 73, 4315 (1951).
(29) B. Loev and M. M. Goodman, *Chem. Ind. (London)*, 2026 (1967).
(30) A. D. Adler, F. Longo, J. Finarelli, J. Goldmacher, J. Assour, and L. Korsakoff, *J. Org. Chem.*, 32, 476 (1967).
(31) A. Williams and R. A. Naylor, *J. Chem. Soc.* (B) 1967 (1971).