Rational Tetraarylporphyrin Syntheses: Tetraarylporphyrins from the MacDonald Route

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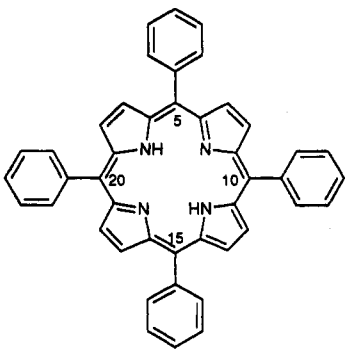
Four new synthetic routes to *meso*-tetraarylporphyrins using a MacDonald-type 2 + 2 condensation are described. Self-condensation of a 5-aryldipyrromethane (e.g., **17**) with an aryl-substituted one-carbon bridging unit affords a mixture of tetraarylporphyrins due to acid-catalyzed redistribution reactions. The second and third methods presented here show wide applicability for the preparation of 5,10,15,20-tetraaryl-substituted porphyrins (e.g., **31**, **37**, **48**, **49**) with 2-fold rotational symmetry and involve self-condensation of 5-aryl-1-aryldipyrromethanecarbinols. Finally, the fourth approach involves a 2 + 2 approach in which one of the two dipyrromethanes bears both of the bridging carbons in the porphyrin products, affording porphyrin **50** which possesses three different aryl rings, with one pair of uniquely opposite identical aryl groups. The last two 2 + 2 methods are further extended to give a tetraarylporphyrin **38** bearing four different aryl groups in a predesignated array, the structure of which is confirmed by a single-crystal X-ray study.

Over the past 50 years, much effort has been expended on development of synthetic approaches to octaalkylporphyrins and natural porphyrins related to heme and chlorophyll. Procedures have advanced systematically through monopyrrole tetramerizations, dipyrromethene self-condensations in organic acid melts,[1] MacDonald's dipyrromethane "2 + 2" methodology,[2] Woodward's landmark dipyrromethane condensation,[3] and then on to the truly general approaches through unsymmetrically substituted *b*-bilenes and *a,c*-biladienes.[4-6] However, the series of most often utilized porphyrins for physical and spectroscopic studies are the *meso*-tetraarylporphyrins, tetraphenylporphyrin (TPP, **1**) being the classical example.[7]



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TPP was first synthesized more than 50 years ago by Rothemund,[7] who allowed benzaldehyde and pyrrole in pyridine to react in a sealed bomb at 150 °C for 24 h. The yields were low, and very few substituted benzaldehydes could be used due to the severe conditions. Adler and co-workers modified the Rothemund reaction by allowing benzaldehyde and pyrrole to react for 30 minutes in refluxing propionic acid open to the air.[8] The yields were above 20%, and the milder reaction conditions allowed a wider selection of substituted benzaldehydes to be used. Lindsey[9] improved tetraarylporphyrin synthesis further by reacting benzaldehyde and pyrrole in methylene chloride under nitrogen in the presence of boron trifluoride etherate at room temperature (to give a porphyrinogen) and then oxidizing with *p*-chloranil to produce porphyrin yields of 30–40%.

Structural novelty and tailored organometallic reactivity were subsequently introduced into tetraarylporphyrin synthesis when Collman and his colleagues first reported picket-fence porphyrin[10] and when Baldwin and his collaborators began building superstructural arrays on tetraarylporphyrins.[11] Numerous "basket-handle"[12] and strapped[13] versions have subsequently been invented. On the other hand, in a comparative sense, synthetic developments in the area of unsymmetrically functionalized tetraarylporphyrins have lagged far behind. These porphyrins are usually synthesized by the condensation of pyrrole with a mixture of arylaldehydes;[14] this results in poor yields after mandatory chromatographic separation and purification.

In recent years we have embarked upon a program to bring tetraarylporphyrin synthesis up to or near the same level of sophistication employed in synthesis of porphyrins

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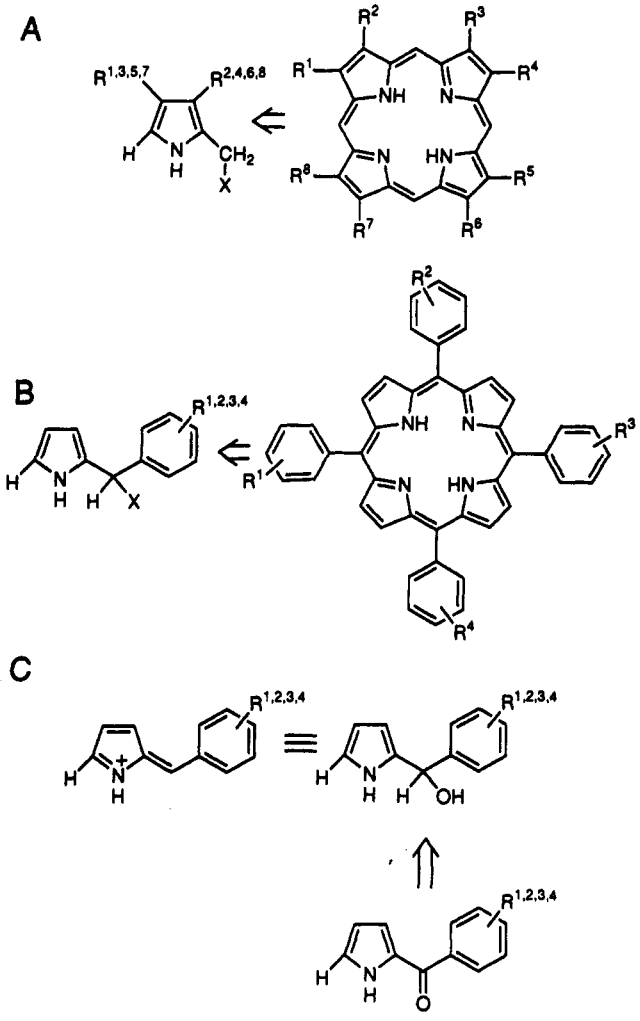
Scheme I. Simple Retrosynthetic Analysis of Porphyrin Synthesis[a]

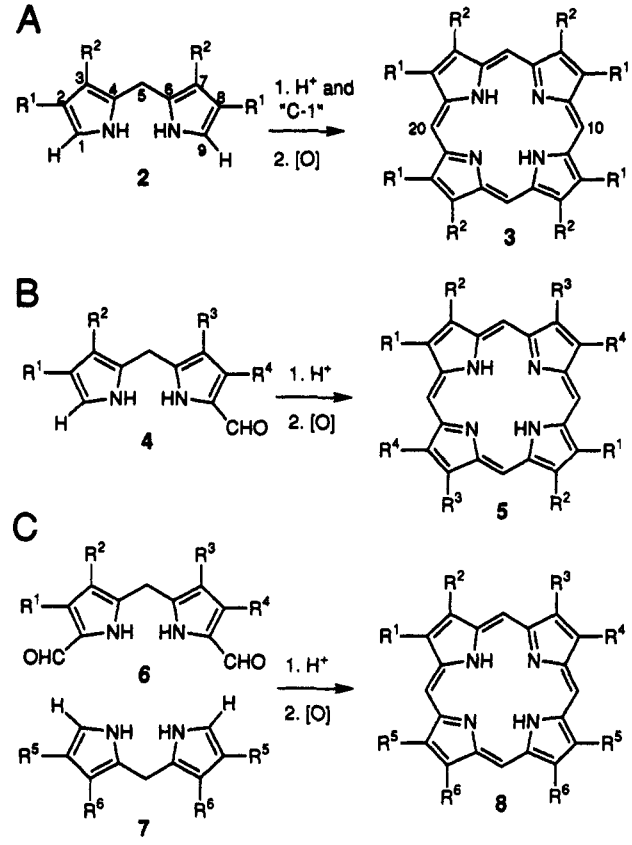


[a]A, for 2,3,7,8,12,13,17,18-octasubstituted porphyrins; B, for 5,10,15,20-tetraarylporphyrins; and C, derivation of 2-aroylpyrroles as stable building blocks.

in the heme and chlorophyll series. Scheme I shows a simple retrosynthetic analysis of porphyrin synthetic methodology, A, for 2,3,7,8,12,13,17,18-octasubstituted porphyrins and, B, for tetraarylporphyrins. In A, it can be seen that the problems relate to synthesis of monopyrroles bearing various 3- and 4-substituents (R^1, R^2; R^3, R^4; R^5, R^6; R^7, R^8), a (nucleophilic) unsubstituted 2-position, and an (electrophilic) 5-benzylic substituent with a good leaving group (e.g., Br, OAc, etc.).[5] Application of the same reasoning to tetraarylporphyrin synthesis (Scheme IB) suggests that the subunit building blocks should be the related 2-(arylmethyl)pyrroles (with four different groups R^{1-4}), bearing a good leaving group (X) on the methane carbon; a simple extension suggests (Scheme IC) that the building blocks should be the corresponding 2-aroylpyrroles.

In the present paper we employ the analysis from Scheme I to raise the art of tetraarylporphyrin synthesis to accommodate two versions of the "MacDonald-type" 2 + 2 approach. Though the MacDonald route brings with it some symmetry limitations (but see ref 3), it has served a very important role in the history of porphyrin synthesis, and we anticipate that our present work on this approach will be equally serviceable when porphyrins of the appropriate symmetry are needed. Specifically, in the

Scheme II. Three Variations of the MacDonald "2 + 2" Porphyrin Synthesis[a]



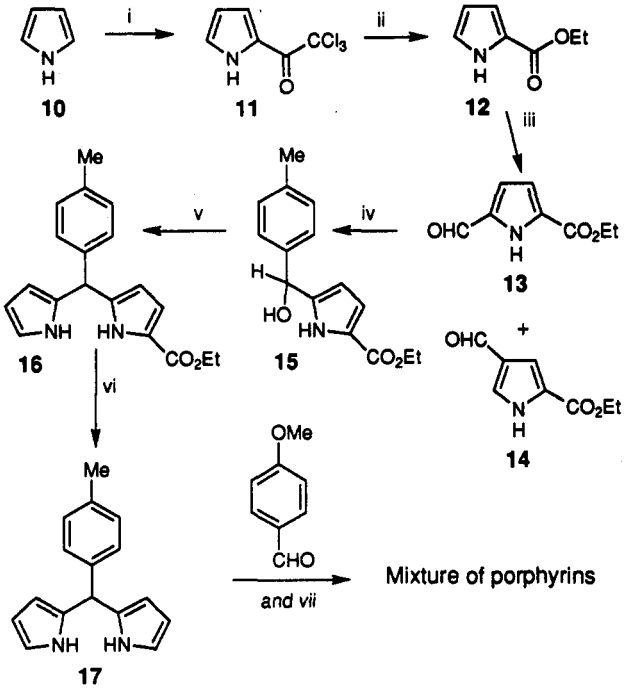
[a]A, with added external interpyrrolic (10,20) carbons; B, where the interpyrrolic carbon is attached to the dipyrromethane; and C, where both interpyrrolic carbons are attached to the same dipyrromethane.

present work we mimic the MacDonald approaches (Scheme II) in which a 1,9-diunsubstituted dipyrromethane **2** is self-condensed in the presence of a separate one-carbon meso-bridging unit (Scheme IIA) to give porphyrin **3**, where a 1-formyldipyrromethane **4** is self-condensed (Scheme IIB) to give porphyrin **5**,[2,5] and in Scheme IIC where one of the dipyrromethane halves (**6**) possesses both and the other (**7**) none of the carbons needed to form the new meso-bridges between the dipyrromethane units in the porphyrin macrocycle. All three of these general approaches are limited in their widespread applicability by symmetry considerations; future publications from our laboratories will address the issue of symmetry, but the present work does lead to the first syntheses of a *meso*-tetraarylporphyrin bearing four different aryl groups in a unique and predesignated array.

Results and Discussion

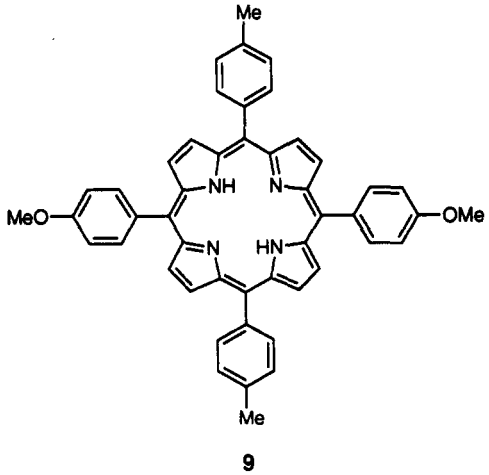
Self-Condensation of a Dipyrromethane in the Presence of External (10,20) Linking Carbons. As mentioned above, our work in this area centered on application of a version[2,5] of MacDonald's approach (Scheme IIA) in which a dipyrromethane is self-condensed with the provision of additional bridging carbons which are not attached, a priori, to the dipyrromethane. This methodology, of course, has the symmetry limitation that both dipyrromethane halves must be identical and that any substituent attached to the linking carbons will be symmetrically disposed on opposite (5,15 and 10,20) *meso*-

Scheme III. Attempted Symmetrical Tetraarylporphyrin Synthesis Using 5-Aryldipyrromethane 17 and Arylaldehyde[a]



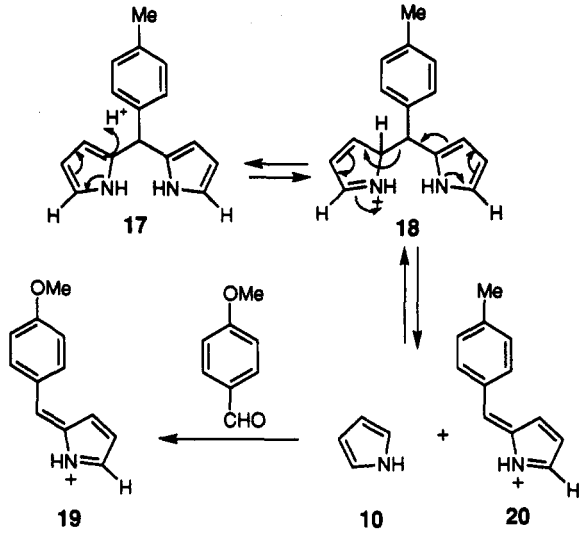
[a]Reagents: (i) $Cl_3C{\cdot}COCl$; (ii) EtOH/Na; (iii) $POCl_3$/DMF then $NaHCO_3$; (iv) MeC_6H_4MgBr; (v) pyrrole/HOAc; (vi) NaOH/$HOCH_2CH_2OH$; (vii) Δ and $CH_3CH_2CO_2H$ or $BF_3{\cdot}Et_2O$.

carbons. This arrangement of aryl groups, as found in our target porphyrin **9**, is very attractive in that it or its variants potentially allow strapping of the porphyrin across 5,15-substituents in a manner which can serve a number of purposes.



However, application of this route (Scheme III) resulted in the formation of a mixture of porphyrins in the final step. For example, pyrrole (**10**) was first acylated with trichloroacetyl chloride to form 2-(trichloroacetyl)pyrrole (**11**). Treatment with sodium ethoxide gave ethyl pyrrole-2-carboxylate (**12**) which was then formylated to yield a mixture of formylpyrrole isomers **13** and **14** in 90% overall yield. The 2,5-substituted **13** and 2,4-substituted **14** pyrroles were separated to give the desired pyrrole **13** in 65% yield. Grignard reaction with *p*-tolylmagnesium bromide produced the 5-(tolylhydroxymethyl)pyrrole **15**. Condensation with excess pyrrole (**10**) under acidic conditions produced the dipyrromethane **16**. Saponification of the ethyl ester and concomitant decarboxylation with base in ethylene glycol yielded the 1,9-diunsubstituted 5-tolyldipyrromethane **17**. Condensation of the 5-tolyldipyrromethane **17** with *p*-anisaldehyde in hot propionic acid gave a product, after workup, which was shown by TLC to consist of at least four different tetraarylporphyrins. The least polar of these was isolated and identified by ^{1}H-NMR spectroscopy and HRMS to be 5,10,15,20-tetra-*p*-tolylporphyrin. Almost certainly the mixture of porphyrins was produced in the acid-catalyzed final step of the reaction as a result of acid redistribution reactions common of many dipyrromethanes; a possible mechanism is shown in Scheme IV, which leads to the production, from **17** via **18**, of rogue intermediate **19** which can cross-condense and substitute for species **20** to produce a mixture of porphyrinic products.

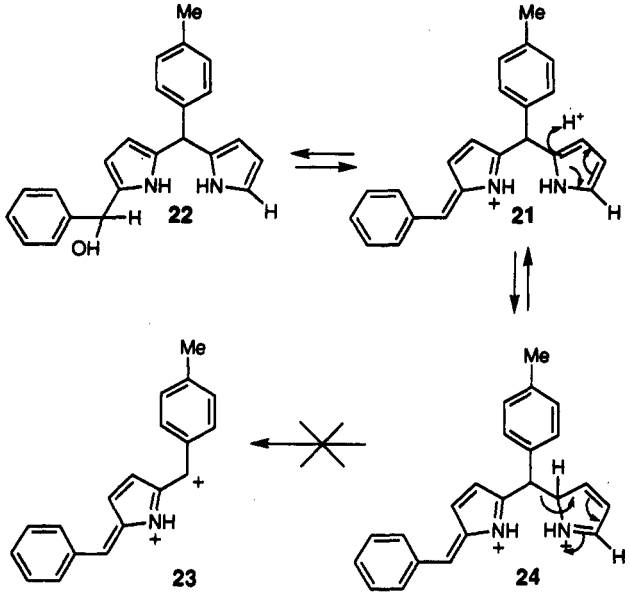
Scheme IV. Mechanistic Interpretation for Formation of Porphyrin Mixture via Production of Rogue Intermediate 19



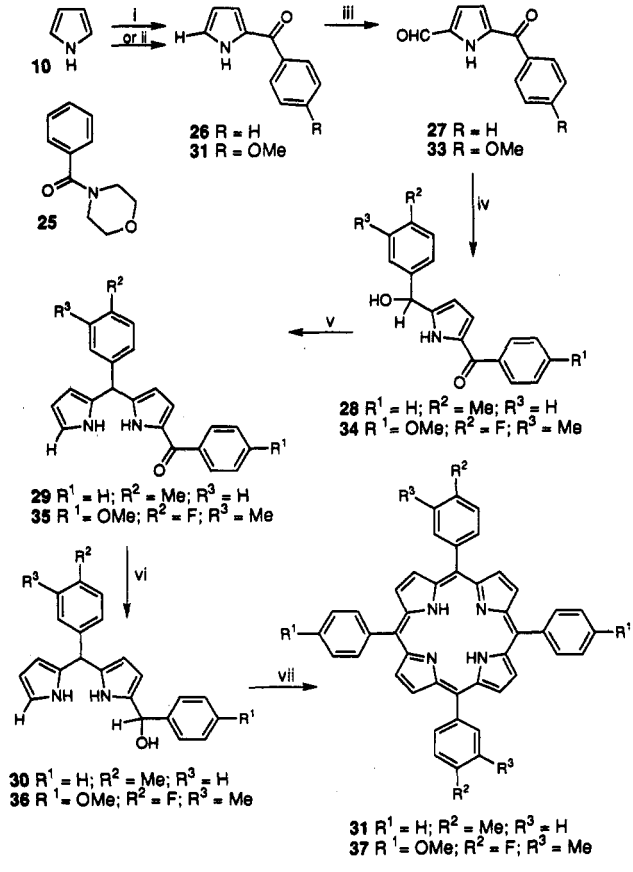
It appeared likely that all variations of the MacDonald approach shown in Scheme IIA, when applied to the tetraarylporphyrin series, would produce mixtures of porphyrins if two different aryl groups were incorporated. We surmised that linking of the bridging carbon to the dipyrromethane, as indicated generically in Scheme IIB, might produce a single, pure porphyrin. Scheme V shows our reasoning: the dipyrromethane **21** (obtained from **22** by acid catalyzed dehydration) can indeed protonate in the propionic acid (just as did **17** in Scheme IV). However, fragmentation of the type shown in Scheme IV would yield a very unstable species **23** in which two positive charges are separated by only one carbon. Thus, in contrast to the highly favored **18** → **20** step (Scheme IV), we predicted that the equally damaging analogous fragmentation **24** → **23** in Scheme V would be partially or even completely inhibited. This postulate proved to be correct, and these experiments are described below.

Self-Condensation of a Dipyrromethane Bearing Its Own Linking Carbon. This version of the MacDonald approach (Scheme IIB) is somewhat more versatile than that described above since it provides access (vide infra) to tetraarylporphyrins with four different aryl groups. However, we discuss first the simplest application of this methodology, namely the self-condensation of a (1-aryl-1-hydroxymethyl)-substituted dipyrromethane (Scheme VI).

Scheme V. Postulate To Use 1-(Arylhydroxymethyl) Substituents (as in 22) To Avoid Scrambling Apparent in Scheme IV



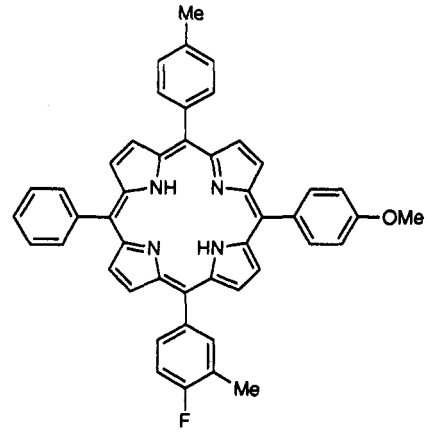
Scheme VI. Syntheses of Symmetrical Tetraarylporphyrins 31 and 37 Using Self-Condensation of Diaryldipyrromethanes 30 and 36[a]



[a]Reagents: (i) EtMgBr then RC_6H_4COCl; (ii) $POCl_3$/*N*-benzoylmorpholine (**25**) then Na_2CO_3; (iii) $POCl_3$/DMF then Na_2CO_3; (iv) $R^2,R^3C_6H_3MgBr$; (v) pyrrole/HOAc; (vi) $LiAlH_4$; (vii) $\Delta/CH_3CH_2CO_2H$.

A Vilsmeier–Haack reagent was first formed by the reaction of *N*-benzoylmorpholine (**25**) with phosphoryl chloride (Scheme VI). Pyrrole (**10**) was then added to yield the 2-aroylpyrrole **26** in 75–79% yields.[15–17] This aroylation is a much improved alternative to the previously used method[18,19] of reacting 2-pyrrolemagnesium bromide with benzoyl chloride, which afforded yields between 44 and 67%. Vilsmeier formylation of **26** gave the desired 2,5-substituted pyrrole **27** which was then treated with *p*-tolylmagnesium bromide to produce the (hydroxymethyl)pyrrole **28** which was then condensed with pyrrole (**10**) to give the dipyrromethane **29**. Reduction with lithium aluminum hydride gave the acid-sensitive alcohol **30** which was added directly to propionic acid to form the porphyrin **31** in 31% yield. A similar sequence of reactions (via **31**–**36**) gave porphyrin **37** in 24% yield.

Cross condensation of the two dipyrromethanes **30** and **36** in propionic acid gave a mixture of three porphyrins **31**, **37**, and **38**. These porphyrins were readily separated to produce the two tetraarylporphyrins with 2-fold symmetry in 6.9% (**31**) and 10.1% (**37**) yields, respectively. The third porphyrin (**38**) was obtained in 17.5% yield. In



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the proton NMR spectrum of **38**, three singlets at 2.58, 2.71, and 4.09 ppm correspond to the aryl, methyl, and methoxy protons, respectively, with each integrating for three protons. The meta protons of the *p*-methoxyphenyl ring appear as a doublet at 7.29 ppm, and the ortho protons of the ring appear at 8.12 ppm as do the ortho protons of the *p*-tolyl ring. The meta protons of the *p*-tolyl appear as a doublet at 7.56 ppm. The meta and para protons of the phenyl ring appear at 7.77 ppm whereas the ortho hydrogens fall at 8.23 ppm. The meta proton adjacent to the fluorine appears as a doublet of doublets (J = 8.8 Hz) at 7.39 ppm, and the two ortho protons appear as a multiplet at 8.01 ppm. Finally, the pyrrole-β protons appear as doublets at 8.87 ppm.

Though the proton NMR spectrum confirmed our synthesis of a tetraarylporphyrin with all four aryl rings differentially substituted, it did not, of course, confirm

(15) White, J.; McGillivray, G. *J. Org. Chem.* **1977**, *42*, 4248.
(16) White, J.; McGillivray, G. *J. Chem. Soc., Perkin Trans. 2* **1979**, 943.
(17) A similar reaction, using pyrrole *N,N*-dimethylamides or (dipyrromethane 1-*N,N*-dimethylamides), has been utilized in the synthesis of unsymmetrical dipyrro ketones or (*b*-oxobilanes): Ballantine, J. A.; Jackson, A. H.; Kenner, G. W.; McGillivray, G. *Tetrahedron*, **1966**, *22* (Suppl. 1), 241. Jackson, A. H.; Kenner, G. W.; McGillivray, G.; Smith, K. M. *J. Chem. Soc. C*, **1968**, 294.
(18) For a preliminary communication of this work, see: Wallace, D. M.; Smith, K. M. *Tetrahedron Lett.* **1990**, *31*, 7265. For a related synthesis of an unsymmetrical triarylporphyrin, see: Ema, T.; Kuroda, Y.; Ogoshi, H. *Tetrahedron Lett.* **1991**, *32*, 4529.
(19) Aurousseau, M.; Joannic, M.; Pesson, M.; Roquet, F. *Chim. Therap.* **1966**, 127.

the unique regiochemical array of the aryl rings about the porphyrin meso bridges. Further proof of the structure and its specific regiochemistry was obtained from a single-crystal X-ray structure of the zinc(II) complex of **38** (Figure 1). Though the structure is not a good one,[20] it does categorically confirm the unique substituent array in **38**. This represents the first example of a tetraarylporphyrin synthesis in which all four aryl rings are differentially substituted and in which the regiochemistry of the substituent array is definitively known.

The methodology described above, however, still possesses limitations because of the use of certain reagents (e.g., $LiAlH_4$ in the transformations **29** → **30** and **35** → **36**) which are not compatible with some common aryl functional groups such as nitriles, nitro groups, and esters. In preliminary experiments, which remain unoptimized, we therefore modified our procedures as described below (Scheme VII) to remove the more obvious reduction limitations on aryl substituents.

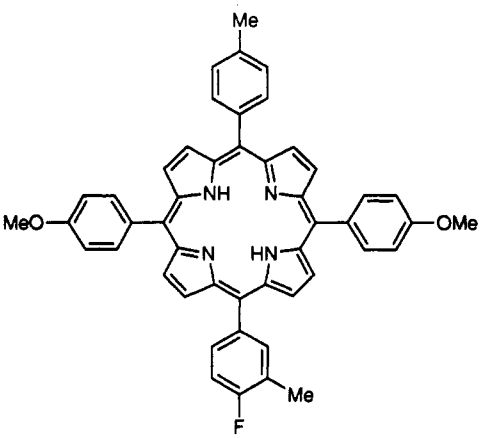
Pyrrole (**10**) was first formylated with the Vilsmeier reagent ($POCl_3$/DMF) to produce 2-formylpyrrole (**39**). The electron-withdrawing effect of the aldehyde group was countered by transformation into the corresponding cyclic dithiol **40**. Aroylation with the Vilsmeier reagent obtained from the corresponding *N*,*N*-dimethylbenzamide gave pyrroles **41** and **42**. Deprotection of the aldehyde gave the desired 2,5-disubstituted pyrroles **43** and **44**. Such 5-benzoyl-2-formylpyrroles were found to be only slightly soluble in common organic solvents, and this may be responsible for somewhat lower yields in some subsequent (unoptimized) reactions. Nucleophilic attack on the aldehyde **44** by (*o*-nitrophenyl)lithium at −100 °C produced the (arylhydroxymethyl)pyrrole **45** only, but in much lower yield than had been found with other pyrroles. The same reaction with pyrrole **43** did not proceed at all, probably due to its insolubility at low temperature. The (arylhydroxymethyl)pyrrole **45** was condensed with pyrrole **10** at 50 °C in the presence of Montmorillonite K-10 clay to give the dipyrromethane **46** in 73% yield. This yield is somewhat lower than clay-catalyzed condensations at room temperature when the (arylhydroxymethyl)pyrrole contains an ester group in place of the phenyl ketone, possibly due to the much stronger electron-withdrawing effect of the ketone stabilizing the alcohol. This may also explain why we were able to obtain the 2,5-substituted pyrrole by direct formylation in 45–50% yields when the phenyl ketone was either unsubstituted or substituted with a electron-donating group, whereas we obtained no product when the phenyl ketone was substituted with a electron-withdrawing group. Lithium aluminum hydride was needed for reduction of the carbonyl groups in electron-rich aroyl examples, but in electron-deficient cases such as **46** we were able to conveniently reduce with sodium borohydride to give the acid-sensitive alcohol **47**. This was mixed immediately with propionic acid to form the desired porphyrin as a separable mixture of *cis* and *trans* isomers (**48** and **49**) in (unoptimized yields) of 2.5% and 2.7%, respectively. Separation of these atropisomers was conveniently accomplished using preparative thick layer chromatography.

(20) Several attempts to grow suitable crystals of the free base **38** were unsuccessful. The zinc(II) complex was prepared to give crystals with slightly better diffraction than the free base. The authors have deposited atomic coordinates for the structure of Zn(II)**38**(pyridine) with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Center, 12 Union Road, Cambridge, CB2 1EZ, UK.

Condensation of a Dipyrromethane with 1- and 9-Linking Carbons with a 1,9-Unfunctionalized Dipyrromethane. This type of MacDonald approach (Scheme IIC) involves the condensation of a dipyrromethane **6** bearing both of the linking carbons with one (**7**) bearing none. Like the version discussed above, it also allows for synthesis of tetraarylporphyrins with four different aryl groups, as will be discussed later.

To test this approach, the synthesis of a porphyrin **50** with only three different aryl groups was devised first (Scheme VIII). Diaroylation of dipyrromethane **17** with benzoyl chloride gave dipyrromethane **51** in only 10% yield. An alternative method was therefore sought, involving treatment of dipyrromethane **17** with the Vilsmeier–Haack reagent formed by the reaction of aroylmorpholine **25** with phosphoryl chloride; this afforded dipyrromethane **51** in 39% yield. Reduction of **51** with lithium aluminum hydride gave the acid-sensitive alcohol **52** which was directly mixed with dipyrromethane **53**[21] in propionic acid to form the porphyrin **50**, bearing three different types of aryl ring, in 20% yield.

In order to demonstrate that this version of the MacDonald condensation can be used in syntheses of tetraarylporphyrins with *four* different aryl groups, porphyrin **38** was also synthesized using this approach (Scheme IX). Pyrrole **33** was treated with *p*-tolylmagnesium bromide to give the (hydroxymethyl)pyrrole **54** which was then condensed with pyrrole **26** to produce dipyrromethane **55**. Reduction of **55** with lithium aluminum hydride gave the acid–sensitive alcohol **56** which was directly mixed with dipyrromethane **53** in propionic acid to form a mixture of three porphyrins. The predominant, and desired, porphyrin **38** was isolated in 12% yield after an easy column chromatographic separation. Two other porphyrins (**50** and **57**) were obtained in 0.5%



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and 1% yield, respectively. The minor porphyrinic products (**50** and **57**) appear to result from terminal aryl group exchange in **55**, the mechanism of which is at present unclear. Attempts to eliminate this unwanted scrambling reaction have, so far, been unsuccessful.

Conclusions

We have accomplished, in reasonable overall yields, the synthesis of tetra-arylporphyrins **31**, **37**, **38**, **48**/**49**, and **50**

(21) Obtained as described in Scheme III, but using pyrrole **13** and 4-fluoro-3-methylphenylmagnesium bromide. See Experimental Section.

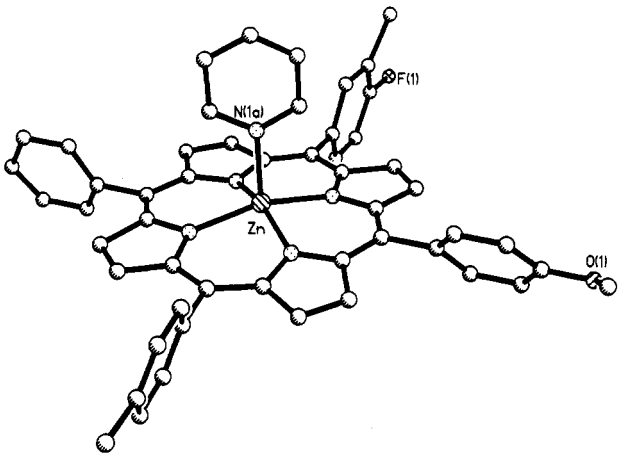

Figure 1. X-ray crystal structure[20] of the zinc(II)–pyridine complex of porphyrin 38.

by rational methods involving neither the usual "tetramerization" methodology of the Rothemund reaction nor extensive chromatographic purifications necessary when mixtures of aldehydes are condensed with pyrrole. Four versions of the MacDonald "2 + 2" approach were developed; two are successful in providing novel tetraarylporphyrins, one provides a mixture in which the desired tetraarylporphyrin is dominant, and one gives an unacceptable mixture of porphyrinic products for reasons which are fully rationalized. The methodology enables complex tetraarylporphyrins bearing a variety of *meso*-aryl groups to be synthesized, but a number of symmetry restrictions still apply to the routes reported herein *if chromatographic separations are to be avoided after porphyrin formation.* In order to overcome these drawbacks it will probably be necessary to develop tetraaryl analogues of the so-called *b*-bilene and *a,c*-biladiene[4-6] routes; our efforts in these areas will be reported in due course.

Experimental Section

Melting points were measured on a Thomas/Bristoline microscopic hot stage apparatus and were uncorrected. Silica gel 60 (70–230 and 230–400 mesh, Merck) or neutral alumina (Merck; usually Brockmann Grade III, i.e., deactivated with 6% water) were used for column chromatography. Preparative thin-layer chromatography was carried out on 20- × 20-cm glass plates coated with Merck G 254 silica gel (1-mm thick). Analytical thin-layer chromatography was performed using Merck 60 F254 silica gel (precoated sheets, 0.2-mm thick). Reactions were monitored by thin-layer chromatography and spectrophotometry and were carried out under nitrogen and in the dark. ^{1}H- and ^{13}C-NMR spectra were obtained in deuteriochloroform, and chemical shifts are expressed in ppm relative to chloroform (7.258 ppm). Elemental analyses were performed at the Midwest Microlab, Ltd., IN, and at the Microchemical Analysis Laboratory, U.C. Berkeley. Mass spectra were obtained at the Mass Spectrometry Facility, University of California, San Francisco.

2-(Trichloroacetyl)pyrrole (11). To a 2-L three-necked round-bottom flask (RBF) was added anhydrous ether (130 mL) and trichloroacetyl chloride (95 mL; 0.85 mol). The flask was flushed with N_2 before pyrrole (10) (50.03 g; 0.75 mol) dissolved in anhydrous ether (415 mL) was added via a dropping funnel over a 2-h period. The now violet ether solution began to reflux slightly during addition. Refluxing was continued for an additional 1 h before the reaction was quenched slowly with a solution of Na_2CO_3 (65 g) in water (200 mL). The layers were separated, and the red organic layer was washed four times with water and once with brine and finally dried over Na_2SO_4. The red ether solution was then treated twice with Norite (5 g) and filtered through Celite. The solvent was removed under vacuum to give the title compound (152.7 g, 96%) as an off-white solid, mp 72–74 °C (lit.[22] mp 73–75 °C). ^{1}H-NMR: ($CDCl_3$) δ 6.38 (dd, 1H), 7.17 (d, 1H), 7.39 (m, 1H), 9.58 (bs, 1H).

Ethyl Pyrrole-2-carboxylate (12). To a 3-L RBF was added absolute ethanol (1.5 L) and sodium metal (6.9 g; 0.30 mol). Once all the sodium had dissolved, 2-(trichloroacetyl)pyrrole (11) (223 g; 1.05 mol) dissolved in absolute ethanol (500 mL) was added. The mixture was then heated at reflux for 12 h. The ethanol was removed under high vacuum and the product crystallized by pouring the residue into a 2:1 ice–water/ethanol mixture (2 L). The brown solid was recrystallized from warm petroleum ether to afford the title pyrrole as off-white crystals (124.3 g, 85%), mp 38–39.5 °C (lit.[22] mp 40–42 °C). ^{1}H-NMR: ($CDCl_3$) δ 1.36 (t, 3H), 4.34 (q, 2H), 6.26 (m, 1H), 6.94 (m, 2H), 9.70 (bs, 1H).

Ethyl 5-Formylpyrrole-2-carboxylate (13). To a 250-mL RBF flushed with N_2 was added anhydrous DMF (7.0 mL; 90.4 mmol); it was then cooled to 5-10 °C. To the cooled DMF was added freshly distilled $POCl_3$ (7.8 mL; 83.7 mmol) dropwise over a couple of min. Dry 1,2-DCE (25 mL) was then added and the orange solution was cooled to 0–5 °C during the addition of ethyl pyrrole-2-carboxylate (12) (10.53 g; 75.64 mmol) in dry 1,2-DCE (25 mL). The mixture was then heated to reflux for 15 min. The reaction was cooled to room temperature, treated with a mixture of ethyl acetate (60 mL) and water (75 mL), poured into saturated $NaHCO_3$ (350 mL), and separated. The aqueous layer was washed three times with ether, and the combined organic extracts were washed twice with aqueous saturated Na_2CO_3, dried over Na_2SO_4, and evaporated under vacuum. The resulting red solid was chromatographed on a silica gel flash column, eluting with cyclohexane/ethyl acetate (70/30), to afford two compounds in a 2:1 ratio. The first to elute was the title compound which was recrystallized from hot cyclohexane as light yellow crystals (8.22 g, 65.1%), mp 72–73.5 °C (lit.[23] mp 75 °C). ^{1}H-NMR: ($CDCl_3$) δ 1.29 (t, 3H), 4.32 (q, 2H), 6.85 (m, 2H), 9.62 (s, 1H), 10.74 (bs, 1H). The second compound to elute was ethyl 4-formylpyrrole-2-carboxylate (14) which was recrystallized from hot cyclohexane as light orange crystals (3.20 g, 25.3%), mp 103–104.5 °C (lit.[23] mp 104–106 °C). ^{1}H-NMR: ($CDCl_3$) δ 1.32 (t, 3H), 4.32 (q, 2H), 7.29 (s, 1H), 7.59 (d, 1H), 9.80 (s, 1H), 10.88 (bs, 1H).

Ethyl 5-[(4-Methylphenyl)hydroxymethyl]pyrrole-2-carboxylate (15). Ethyl 5-formylpyrrole-2-carboxylate (13) (3.98 g; 23.8 mmol) and dry THF (150 mL) were placed in a 500-mL RBF. The resulting suspension was flushed with N_2 and cooled to −23 °C (CCl_4/dry ice). A 1.0 M solution of *p*-tolylmagnesium bromide in ether (53.0 mL; 53.0 mmol) was added dropwise over a 30-min period. The mixture was stirred at this temperature for 2.5 h before being poured into an aqueous ether/ice bath. The layers were separated, and the organic layer was washed three times with water and brine, dried over Na_2SO_4, and then evaporated under vacuum to give a yellow oil. The crude product was chromatographed on a silica gel flash column eluting with cyclohexane/ethyl acetate (80/20). The appropriate eluates were combined and evaporated to give the title product (6.06 g, 98%) as a light yellow powder, mp 101–102 °C. ^{1}H-NMR: ($CDCl_3$) δ 1.32 (t, 3H), 2.35 (s, 1H), 3.12 (d, 1H), 4.26 (q, 2H), 5.85 (d, 1H), 5.93 (t, 1H), 6.82 (t, 1H), 7.17 (d, 2H), 7.27 (d, 2H), 9.66 (bs, 1H, NH). LRMS: *m/e* (%) 259 (11), 241 (9), 212 (100), 196 (16), 168 (42). HRMS: calcd for $C_{15}H_{17}NO_3$ 259.1208, found 259.1208. Anal. Calcd for $C_{15}H_{17}NO_3$: C, 69.47; H, 6.61; N, 5.40. Found: C, 69.35; H, 6.60; N, 5.39.

Ethyl 5-(4-Methylphenyl)dipyrromethane-1-carboxylate (16). To a 500-mL RBF flushed with N_2 was added glacial acetic acid (190 mL), acetic anhydride (12 mL), and pyrrole (10) (7.86 g; 117.1 mmol). To this solution was added ethyl 5-[(4-methylphenyl)hydroxymethyl]pyrrole-2-carboxylate (15) (6.06 g; 23.4 mmol) at which time the mixture was heated to 50 °C for 2.5 h. Silica gel TLC (cyclohexane/ethyl acetate (60/40)) showed none of the more polar starting material was present, and treatment of the TLC plate with Br_2 vapor developed the dipyrromethane as a bright red spot. The solvent was removed

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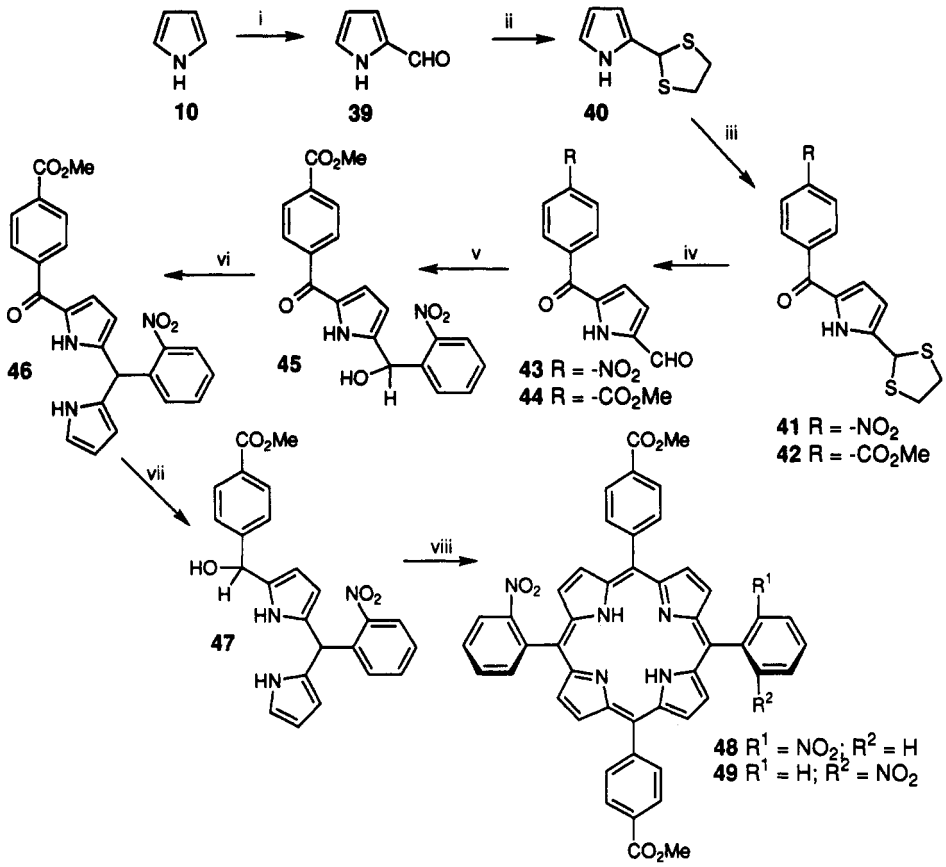
(23) Khan, M. K. A.; Morgan, K. J.; Morrey, D. P. *Tetrahedron* **1966**, *22*, 2095.

Scheme VII. Synthesis of Symmetrical Tetraarylporphyrins 48 and 49 Using Self-Condensation of Diaryldipyrromethane 47[a]



[a]Reagents: (i) $POCl_3$/DMF then Na_2CO_3; (ii) $HSCH_2CH_2SH/PhNH_3Cl$; (iii) $POCl_3/RC_6H_4CONMe_2$; (iv) NBS, acetone/H_2O; (v) $O_2NC_6H_4Li$; (vi) pyrrole/K-10 clay; (vii) $NaBH_4$; (viii) $\Delta/CH_3CH_2CO_2H$.

under high vacuum, and the resulting residue was dissolved in toluene which was then removed under high vacuum to azeotrope any remaining acetic acid. The dark oil was chromatographed on a silica gel flash column with cyclohexane/ethyl acetate (75/25). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as a brown viscous oil (6.77 g, 94%). ^{1}H-NMR: ($CDCl_3$) δ 1.32 (t, 3H), 2.34 (s, 1H), 4.23 (q, 2H), 5.44 (s, 1H), 5.94 (s, 1H), 5.98 (t, 1H), 6.16 (dd, 1H), 6.69 (d, 1H), 6.85 (t, 1H), 7.10 (dd, 4H), 8.02 (bs, 1H), 9.07 (bs, 1H). LRMS: *m/e* 308 (100), 279 (10), 261 (32), 235 (78), 171(43). HRMS: calcd for $C_{19}H_{20}N_2O_2$ 308.15247, found 308.15248.

5-(4-Tolyl)dipyrromethane (17). To a 100-mL RBF flushed with N_2 was added ethyl 5-(4-methylphenyl)dipyrromethane-2-carboxylate (**16**) (453 mg; 1.47 mmol), ethylene glycol (15 mL), and sodium hydroxide (0.8 g; 20 mmol). The suspension was then heated at 185 °C for 45 min. The brown solution was cooled to room temperature and then placed in an ice bath. The cold solution was diluted with a large amount of water and extracted six times with petroleum ether. The combined organic extracts were then washed twice with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to produce the desired dipyrromethane as a brown viscous oil (327 mg, 94%). ^{1}H-NMR: ($CDCl_3$) δ 2.44 (s, 1H), 5.44 (s, 1H), 5.99 (s, 2H), 6.24 (q, 2H), 6.68 (d, 2H), 7.19 (dd, 4H), 7.87 (bs, 2H). LRMS: *m/e* 236 (100), 219 (9), 170 (42), 154 (16), 145(72). HRMS: calcd for $C_{16}H_{16}N_2$ 236.1313, found 236.1313.

2-Formylpyrrole (39). To a three-necked 3-L RBF, equipped with a mechanical stirrer and flushed with N_2, was added anhydrous DMF (51 mL; 0.66 mol); it was then cooled to 5–10 °C. To the cooled flask was added freshly distilled $POCl_3$ (61 mL; 0.65 mol) dropwise over a 15-min period. The ice bath was removed, and the thick light orange liquid was stirred for 15 min. Dry 1,2-DCE (150 mL) was then added, and the orange solution was cooled to 0–5 °C. Pyrrole **7** (40.0g; 0.60 mol) dissolved in dry 1,2-DCE (150 mL) was added to the Vilsmeier reagent via a dropping funnel over a 1-h period. Following the addition, the yellow mixture was heated at reflux for 15 min before being cooled to room temperature. Aqueous sodium acetate (450 g in 600 mL water) was then added (slowly at first then as rapidly as possible). The mixture was again refluxed for 15 min with vigorous stirring before being cooled to room temperature. The layers were separated, and the aqueous layer was washed three times with ether. The combined ether extracts were then washed three times with saturated aqueous Na_2CO_3, dried over Na_2SO_4 and Na_2CO_3, and then evaporated under vacuum to give an oil which was crystallized from petroleum ether to produce light yellow crystals (42.33 g, 75%), mp 43–45 °C (lit.[24] mp 44–45 °C). ^{1}H-NMR: ($CDCl_3$) δ 6.34 (t, 1H), 7.01 (t, 1H), 7.18 (d, 1H), 9.50 (s, 1H), 10.89 (bs, 1H).

2-(Pyrrol-2-yl)-1,3-dithiolane (40). To a 1 L RBF was added 2-formylpyrrole **39** (25.08 g; 0.26 mol), dry methanol (340 mL), and 1,2-ethanedithiol (24.2 mL; 0.29 mol). Once all the solid had dissolved, aniline hydrochloride (660 mg; 5.09 mmol) was added, and the orange solution was stirred at room temperature for 1 h. The solvent was evaporated to produce a red oil which was dissolved in toluene, washed twice with water, three times with aqueous 0.5 N potassium hydroxide, and then with water, dried over Na_2SO_4, and evaporated under vacuum to give a red oil. The oil was chromatographed on a silica gel flash column, eluting with cyclohexane/ethyl acetate (90/10). The appropriate eluates were combined and evaporated to give the title product (36.36 g, 80.5%) as a light yellow oil which crystallized at 0 °C, mp 27–30 °C (lit.[25] oil). ^{1}H-NMR: ($CDCl_3$) δ 3.39 (m, 4H), 5.87 (S, 1H), 6.19 (m, 1H), 6.27 (s, 1H), 6.79 (d, 1H), 8.58 (bs 1H). LRMS: *m/e* 171 (92), 142 (36), 110 (100), 99 (19), 80(11). HRMS: calcd for $C_7H_9NS_2$ 171.0176, found 171.0174.

2-[5-(4-Nitrobenzoyl)pyrrol-2-yl]-1,3-dithiolane (41). To

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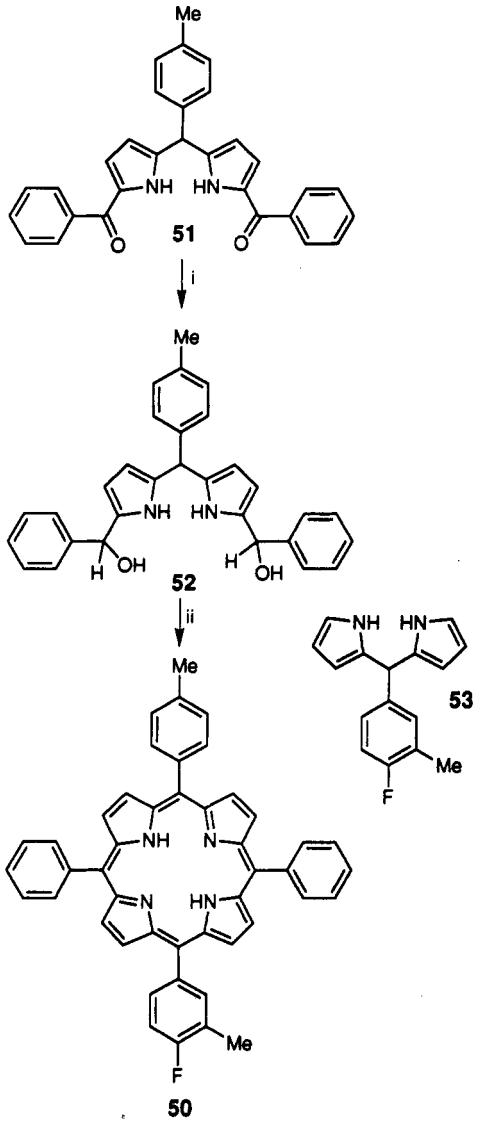
(25) Jackson, A. H.; Kenner, G. W.; Sach, G. S. *J. Chem. Soc.* **1967**, 2045.

Scheme VIII. Synthesis of Tetraarylporphyrin 50 Using Condensation of Triaryldipyrromethane 52 with Aryldipyrromethane 53[a]



[a]Reagents: (i) $LiAlH_4$; (ii) **53**, $\Delta/CH_3CH_2CO_2H$.

a 1-L RBF flushed with N_2 was added *N,N*-dimethyl-4-nitrobenzamide (12.9 g; 66.4 mmol) and freshly distilled $POCl_3$ (13.5 mL; 144.8 mmol). The suspension was warmed at 35 °C until all the solid had dissolved before being cooled to room temperature and stirred for 7.5 h. 2-(Pyrrol-2-yl)-1,3-dithiolane (**40**) (5.52 g; 32.2 mmol) dissolved in dry 1,2-DCE (170 mL) was added swiftly to the Vilsmeier reagent before being allowed to stir at room temperature for 15 h. Aqueous saturated Na_2CO_3 (338 mL) was then added to the dark yellow solution, and the mixture was stirred at room temperature for 15 min and then at reflux for 45 min. The mixture was cooled before the organic layer was separated, washed with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to give a red oil. The oil was chromatographed on a silica gel flash column, eluting with CH_2Cl_2 (100%). The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light green solid (6.89 g, 67%), mp 181.5–183 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.41 (m, 4H), 5.73 (s, 1H), 6.34 (d, 1H), 6.74 (t, 1H), 7.99 (d, 2H), 8.32 (d, 2H), 9.89 (bs, 1H). LRMS: *m/e* 320 (61), 292 (100), 260 (47), 244 (33), 142 (65). HRMS: calcd for $C_{14}H_{12}N_2O_3S_2$ 320.0289, found 320.0284. Anal. Calcd for $C_{14}H_{12}N_2O_3S_2$: C, 52.49; H, 3.78; N, 8.74. Found: C, 52.49; H, 3.71; N, 8.60.

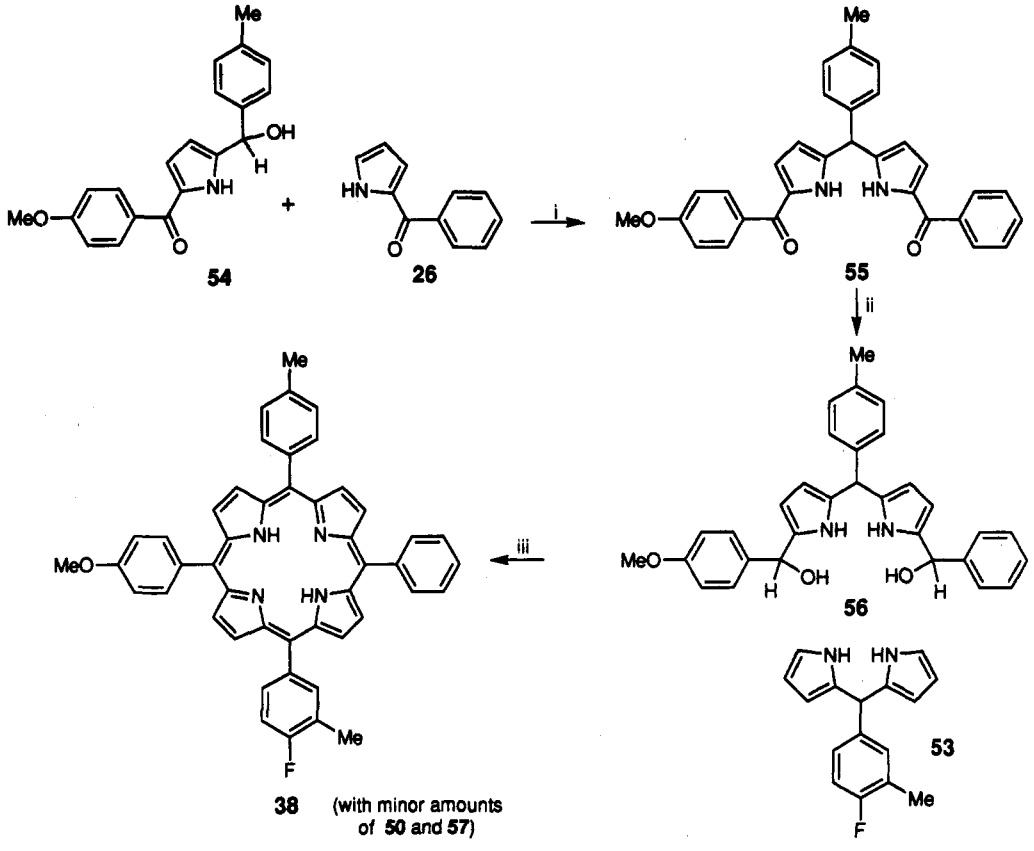
2-[5-[4-(Methoxycarbonyl)benzoyl]pyrrol-2-yl]-1,3-dithiolane (42). To a 1-L RBF flushed with N_2 was added *N,N*-dimethyl-4-(methoxycarbonyl)benzamide (18.05 g; 87.1 mmol) and freshly distilled $POCl_3$ (18.0 mL; 193.1 mmol). The suspension was warmed at 35 °C until all the solid had dissolved before being cooled to room temperature and stirred for 7 h. 2-(Pyrrol-2-yl)-1,3-dithiolane (**40**) (7.23 g; 42.2 mmol) dissolved in dry 1,2-DCE (223 mL) was added rapidly to the above Vilsmeier reagent before being allowed to stir at room temperature for 13.5 h. Saturated Na_2CO_3 (450 mL) was then added to the dark yellow solution, and the mixture was stirred at room temperature for 15 min and then at reflux for 45 min. The mixture was cooled before the organic layer was separated, washed with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to give a red oil. The oil was chromatographed on a silica gel flash column, eluting with CH_2Cl_2/cyclohexane (90/10). The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light tan solid (10.37 g, 74%), mp 155.5–157 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.38 (m, 4H), 3.94 (s, 3H), 5.74 (S, 1H), 6.31 (t, 1H), 6.74 (t, 1H), 7.90 (d, 2H), 8.12 (d, 2H), 10.08 (bs, 1H). LRMS: *m/e* 333 (100), 303 (33), 272 (100), 163 (60), 142 (80). HRMS: calcd for $C_{16}H_{15}NO_3S_2$ 333.0493, found 333.0516. Anal. Calcd for $C_{16}H_{15}NO_3S_2$: C, 57.64; H, 4.53; N, 4.20. Found: C, 57.44; H, 4.50; N, 4.12.

2-Formyl-5-(4-nitrobenzoyl)pyrrole (43). To a solution of *N*-bromosuccimide (27.48 g; 154.4 mmol) in 10% aqueous acetone (441 mL) cooled to 0 °C was added 2-[5-(4-nitrobenzoyl)pyrrol-2-yl]-1,3-dithiolane (**41**) (6.18 g; 19.3 mmol) mostly dissolved in acetone (required heating). The solution quickly turned red (bromine) but soon faded to a yellow-orange color. The solution was stirred at 0 °C for 2 h. The reaction mixture was diluted with CH_2Cl_2, and then a saturated solution of sodium bisulfite (75 mL) was added and stirred for 15 min. The organic layer was separated and washed again with $NaHSO_3$ and water, dried over Na_2SO_4, and then evaporated under vacuum to give an orange solid. The solid was chromatographed on a silica gel flash column, eluting with CH_2Cl_2 (100%). The appropriate fractions were combined and the solvent was removed to give the title pyrrole as a light green solid [2.94 g, 62% (93% based on consumed starting material)], mp 230–232 °C. ^{1}H-NMR: ($CDCl_3$) δ 6.14 (t, 1H), 6.29 (q, 1H), 7.36 (d, 2H), 7.66 (d, 2H), 9.15 (s, 1H), 12.34 (bs, 1H). LRMS: *m/e* 244 (100), 227 (17), 197 (23), 122 (84), 66 (18). HRMS calcd for $C_{12}H_8N_2O_4$ 244.0484, found 244.0473.

2-Formyl-5-[4-(methoxycarbonyl)benzoyl]pyrrole (44). This compound was prepared as described above from 2-[5-[4-(methoxycarbonyl)benzoyl]pyrrol-2-yl]-1,3-dithiolane (**42**) (9.31 g; 27.9 mmol), N-bromosuccimide (40.0 g; 168.5 mmol), and 10% aqueous acetone (560 mL) at 0 °C. The solution was stirred at 0 °C for 2.5 h and worked up as described above to give an orange solid. The solid was chromatographed on a silica gel flash column, eluting with CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light green solid [4.07 g, 57% (92% based on consumed starting material)], mp 199.5–201.5 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.59 (s, 3H), 6.46 (q, 1H), 6.62 (t, 1H), 7.56 (d, 2H), 7.78 (d, 2H), 9.47 (s, 1H), 12.19 (bs 1H). LRMS: *m/e* 257 (100), 242 (24), 226 (29), 198 (46), 122 (45). HRMS: calcd for $C_{14}H_{11}NO_4$ 257.0688, found 257.0666.

2-[4-(Methoxycarbonyl)benzoyl]-5-[(2-nitrophenyl)hydroxymethyl]pyrrole (45). To a 250-mL RBF flushed with N_2 was added 1-bromo-2-nitrobenzene (1.66 g; 8.16 mmol) and dry THF (35 mL); it was then cooled to −105 °C (ether/liquid N_2). A solution of 1.8 M phenyllithium in 70/30 cyclohexane/ether (4.6 mL; 8.28 mmol) was added dropwise over a 10-min period. The black-red organolithium reagent mixture was stirred at this temperature for 2 h. 2-Formyl-5-[4-(methoxycarbonyl)benzoyl]-pyrrole (**44**) (1.04 g; 4.06 mmol) was added as a slurry in dry THF (15 mL) over a 15-min period. The dark solution was then allowed to stir at −100 °C for 2 h before being poured into an aqueous ether/ice bath. The layers were separated, and the aqueous layer was washed three times with ether. The combined ether extracts were then washed with brine, dried over Na_2SO_4, and evaporated under vacuum to give a red oil. The oil was chromatographed on a silica gel flash column, eluting with cyclohexane/ethyl acetate (70/30). The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light yellow foamlike solid (824 mg, 54%), mp 111–113 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.94 (s, 3H), 4.45 (d, 1H), 6.01 (t, 1H), 6.63 (d, 1H), 6.76 (bs 1H), 7.49 (dt, 1H), 7.65 (dt, 1H), 7.79 (dd, 1H), 7.85 (d, 2H), 8.00 (dd, 1H), 8.12 (d, 2H), 10.60 (bs, 1H). LRMS: *m/e* 380 (1), 346 (58),

Scheme IX. Synthesis of Completely Unsymmetrical Tetraarylporphyrin 38 Using Condensation of Triaryldipyrromethane 56 with Aryldipyrromethane 53[a]



[a]Reagents: (i) K-10 clay; (ii) $LiAlH_4$; (iii) **53**, $\Delta/CH_3CH_2CO_2H$.

330 (83), 185 (39), 163 (100). HRMS: calcd for $C_{20}H_{16}N_2O_6$ 380.1008, found 380.0993. Anal. Calcd for $C_{20}H_{16}N_2O_6 \cdot 0.5H_2O$: C, 61.70; H, 4.40; N, 7.19. Found: C, 61.31; H, 4.16; N, 6.78.

1-[[4-(Methoxycarbonyl)phenyl]carbonyl]-5-(2-nitrophenyl)dipyrromethane (46). To a 100-mL RBF was added 2-[4-(methoxycarbonyl)benzoyl]-5-[(2-nitrophenyl)hydroxymethyl]-pyrrole (**45**) (358.6 mg; 0.94 mmol), pyrrole **10** (341 mg; 5.08 mmol), chloroform (35 mL), and Montmorillonite K-10 clay (1.4 g). The greenish suspension was heated at 50 °C overnight. The reaction mixture was filtered to remove the clay, and the filtrate was evaporated to give a light yellow oil. The oil was chromatographed on a silica gel flash column, eluting with cyclohexane/ethyl acetate (75/25). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as a light yellow glasslike solid (297 mg, 73%), mp 117–120 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.94 (s, 3H), 5.92 (s, 1H), 6.00 (t, 1H), 6.14 (dd, 1H), 6.34 (s, 1H), 6.71 (dd, 1H), 6.76 (t, 1H), 7.30 (dd, 1H), 7.42 (dt, 1H), 7.51 (dt, 1H), 7.84 (d, 2H), 7.91 (dd, 1H), 8.11 (d, 2H), 8.44 (bs, 1H), 9.88 (bs, 1H). LRMS: *m/e* 429 (32), 412 (66), 395 (79), 219 (78), 163 (100). HRMS: calcd for $C_{24}H_{19}N_3O_5$ 429.1325, found 429.1317. Anal. Calcd for $C_{24}H_{19}N_3O_5$: C, 67.13; H, 4.46; N, 9.78. Found: C, 66.99; H, 4.51; N, 9.51.

5,15-Bis[4-(methoxycarbonyl)phenyl]-10,20-bis(2-nitrophenyl)porphyrin (48 and 49). To a solution of 1-[4-(methoxycarbonyl)benzoyl]-5-(2-nitrophenyl)dipyrromethane (**46**) (125.9 mg; 0.29 mmol) in dry methanol (10 mL) was added $NaBH_4$ (166 mg; 4.40 mmol). The light orange solution was stirred at 0 °C under N_2 for 30 min. The reaction was diluted with CH_2Cl_2, washed twice with water, dried over Na_2SO_4, and evaporated under vacuum to give the unstable 1-[[4-(methoxycarbonyl)-phenyl]hydroxymethyl]-5-(2-nitrophenyl)dipyrromethane (**47**) as a brown oil. This crude material was added to a 100-mL RBF along with propionic acid (30 mL). The brownish red solution was heated at 80 °C for 30 min and then set aside at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2 and washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a dark oil. The oil was dissolved in toluene, and this was evaporated to facilitate the removal of residual acid. To oxidize any chlorin impurities, the residue was dissolved in absolute ethanol (10 mL) to which was added DDQ (20 mg) in dry benzene (2 mL). This solution was refluxed for 45 min, cooled to room temperature, and filtered through a bed of alumina (Brockmann Grade III) with CH_2Cl_2 as solvent. The crude product was chromatographed on a silica gel flash column, eluting with CH_2Cl_2/cyclohexane (70/30). The appropriate eluates were combined and evaporated to give a mixture of *cis* (**48**) and *trans* (**49**) atropisomers. The mixture was separated on preparative TLC using CH_2Cl_2/cyclohexane (70/30). Complete separation required five cycles of developing and drying and eventually produced two porphyrins. Most mobile porphyrin **49**: (3.0 mg, 2.5%), mp >300 °C. UV–vis λ_{max}: 420 nm (ϵ 260 300), 516 (15 200), 550 (7200), 590 (5500), and 646 (3500). ^{1}H-NMR: ($CDCl_3$) δ −2.70 (s, 2H), 4.11 (s, 6H), 7.98 (m, 4H), 8.24 (m, 2H), 8.29 (d, 4H), 8.43 (d, 4H), 8.46 (dd, 2H), 8.66 (d, 4H), 8.78 (d, 4H, β-H). LRMS: *m/e* 821 (56) (MH^+), 820 (100), 774 (7), 729 (7), 598 (5). HRMS: calcd for $C_{48}H_{32}N_6O_8$ 820.2281, found 820.2304. Least mobile porphyrin **48** (3.3 mg, 2.7%), mp >300 °C. UV–vis λ_{max}: 420 nm (ϵ 210 400), 482 (4800), 514 (11 600), 550 (5600), 592 (3850), and 646 (2100). ^{1}H-NMR: ($CDCl_3$) δ −2.69 (s, 2H), 4.11 (s, 6H), 7.98 (m, 4H), 8.23 (t, 2H), 8.43 (m, 10H), 8.66 (d, 4H), 8.78 (d, 4H). LRMS: *m/e* 821 (59) (MH^+), 820 (100), 788 (9), 774 (10), 589 (7). HRMS: calcd for $C_{48}H_{32}N_6O_8$ 820.2281, found 820.2296.

Porphyrin Mixture from 17 and *p*-Anisaldehyde. 5-(4-Tolyl)dipyrromethane **17** (183 mg; 0.59 mmol), *p*-anisaldehyde (82.0 mg; 0.60 mmol), and propionic acid (80 mL) were mixed together and then heated at reflux for 30 min before being allowed to stir at room temperature overnight. The purple/brown solution was diluted with methylene chloride and washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a dark oil. The oil was dissolved in toluene, and this was evaporated to facilitate the removal of all the acid. The crude product was chromatographed on a silica gel flash column, eluting with methylene chloride/cyclohexane (40/60). The appropriate

eluates were combined and evaporated to give a product which was shown by TLC to consist of at least four different porphyrins. The least polar of these products was isolated and identified by ^{1}H-NMR spectroscopy and high-resolution mass spectra to be tetra(4-tolyl)porphyrin (calcd for $C_{48}H_{38}N_4$ 670.3096, found 670.3093).

2-Benzoylpyrrole (26). Method A. To a 250-mL RBF flushed with N_2 containing a 3.0 M solution of ethylmagnesium bromide in ether (37 mL; 0.111 mol) was added pyrrole **10** (7.22 g; 0.108 mol) in dry ether (44 mL) dropwise so as to cause slight reflux. The solution was refluxed for an additional 30 min. The mixture was cooled to room temperature before being added through a dropping funnel over a 1.5-h period to a solution of benzoyl chloride (15 mL; 0.129 mol) in dry ether (44 mL) under N_2. The orange-red suspension was stirred at room temperature for 23 h and then poured into saturated aqueous ammonium chloride. The precipitate was dissolved in CH_2Cl_2 and added to the aqueous solution. The layers were separated, and the organic layer was washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a red oil. The oil was chromatographed on a silica gel flash column, eluting with CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give a orange solid which was recrystallized from cyclohexane to give the title pyrrole as light tan crystals (8.29 g, 44%).

Method B. *N*-Benzoylmorpholine (2.38 g; 12.46 mmol) and freshly distilled $POCl_3$ (2.5 mL; 26.8 mmol) were mixed under N_2. The suspension was heated at 35 °C until all the solid had dissolved before being cooled to room temperature and stirred for 5.5 h. Pyrrole **10** (552.7 mg; 8.24 mmol) dissolved in dry 1,2-DCE (46 mL) was added quickly to the Vilsmeier reagent before being stirred at room temperature for 20 h. Aqueous saturated Na_2CO_3 (63 mL) was then added to the dark yellow solution, and the mixture was stirred at room temperature for 15 min and then at reflux for 45 min. The mixture was cooled before the organic layer was separated, washed with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to give a dark oil. The oil was chromatographed on a silica gel flash column, eluting with ethyl acetate/cyclohexane (30/70). The appropriate fractions were combined, and the solvent was removed to give the desired pyrrole as a white solid (1.05 g, 74%), mp 76.5–77.5 °C (lit.[26] mp 77–78 °C). ^{1}H-NMR: ($CDCl_3$) δ 6.37 (t, 1H), 6.96 (d, 1H), 7.25 (s, 1H), 7.50 (t, 2H), 7.60 (t, 1H), 7.95 (d, 2H), 10.95 (bs, 1H). LRMS: *m/e* 171 (92), 143 (27), 94 (100), 77 (40), 51 (37). HRMS: calcd for $C_{11}H_9NO$ 171.0684, found 171.0656.

2-(4-Methoxybenzoyl)pyrrole (32). Method A. Using method A described above, 3.0 M ethylmagnesium bromide in ether (30 mL; 90.0 mmol), pyrrole **10** (5.93 g; 88.4 mmol), and *p*-anisoyl chloride (18.1 g; 0.106 mol) in dry ether (36 mL) under N_2 gave a white solid which was recrystallized from hot cyclohexane to give the title pyrrole as white crystals (11.94 g, 67%).

Method B. Using method B, as above, *N*-(4-methoxyphenyl)-morpholine (2.50 g; 11.28 mmol), freshly distilled $POCl_3$ (2.3 mL; 24.7 mmol), and pyrrole **10** (502 mg; 7.49 mmol) in dry 1,2-DCE (42 mL) gave the title pyrrole as a white solid (1.173 g, 78%), mp 110.5–112.5 °C (lit.[26] 110–111 °C). ^{1}H-NMR: ($CDCl_3$) δ 3.88 (s, 3H), 6.33 (q, 1H), 6.90 (d, 1H), 6.98 (d, 2H), 7.13 (d, 1H), 7.95 (d, 2H), 10.18 (bs 1H). LRMS: *m/e* 201 (100), 186 (18), 170 (35), 135 (46), 108 (19), 94 (34). HRMS: calcd for $C_{12}H_{11}NO_2$ 201.0790, found 201.0784.

2-Benzoyl-5-formylpyrrole (27). To a 50-mL RBF flushed with N_2 was added anhydrous DMF (2.7 mL; 34.9 mmol), and it was then cooled to 5–10 °C. To the cooled flask was added freshly distilled $POCl_3$ (3.0 mL; 32.2 mmol) dropwise over a couple of minutes. Dry 1,2-DCE (5 mL) was then added, and the orange solution was cooled to 0–5 °C and stirred for 10 min. 2-Benzoylpyrrole (**26**) (2.68 g; 15.7 mmol) was dissolved in dry 1,2-DCE (48 mL) and cooled to 0 °C under N_2. Following the addition of the above Vilsmeier reagent, the greenish mixture was heated at 80 °C for 105 min before being cooled to room temperature. Saturated aqueous sodium acetate (40 mL) was then added, followed by saturated aqueous $NaHCO_3$ (80 mL); the mixture was stirred overnight. The layers were separated, and the organic layer was washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a red-brown solid. The solid was chromatographed on a silica gel flash column, eluting with CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give a red solid which was recrystallized from hot cyclohexane to give the title pyrrole as light tan needles (1.33 g, 43%), mp 117.5–118.5 °C (lit.[27] mp 118–119 °C). ^{1}H-NMR: ($CDCl_3$) δ 6.90 (q, 1H), 7.00 (q, 1H), 7.49 (t, 2H), 7.60 (t, 1H), 7.92 (d, 2H), 10.73 (bs 1H). LRMS: *m/e* 199 (100), 170 (48), 167 (16), 122 (36), 105 (29. HRMS: calcd for $C_{12}H_9NO_2$ 199.0633, found 199.0633.

2-Formyl-5-(4-methoxybenzoyl)pyrrole (33). To a 50-mL RBF flushed with N_2 was added anhydrous DMF (8.6 mL; 0.11 mol) which was then cooled to 5-10 °C. Freshly distilled $POCl_3$ (9.5 mL; 0.102 mol) was added dropwise over a couple of min. Dry 1,2-DCE (15 mL) was then added, and the orange solution was cooled to 0–5 °C and stirred for 10 min. 2-(4-Methoxybenzoyl)pyrrole (**32**) (10.11g; 50.2 mmol) was dissolved in dry 1,2-DCE (180 mL) and cooled to 0 °C under N_2. Following the addition of the above Vilsmeier reagent, the dark yellow mixture was heated at 90 °C for 110 min before being cooled to room temperature. Saturated aqueous sodium acetate (150 mL) was then added followed by saturated aqueous $NaHCO_3$ (450 mL), and the mixture was stirred for 1.5 h. The layers were separated, and the organic layer was washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a red-brown solid. The solid was chromatographed on a silica gel flash column with CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give a red solid which was recrystallized from hot cyclohexane to give the title pyrrole as pink crystals (5.06 g, 44%), mp 164–166 °C. ^{1}H-NMR: ($CDCl_3$) δ 3.89 (s, 3H), 6.88 (q, 1H), 6.99 (d, 3H), 7.95 (d, 2H), 9.74 (s, 1H), 10.42 (bs, 1H). LRMS: *m/e* 229 (100), 200(39), 167 (16), 135 (76), 92 (18). HRMS: calcd for $C_{13}H_{11}NO_3$ 229.0739, found 229.0741. Anal. Calcd for $C_{13}H_{11}NO_3$: C, 68.10; H, 4.84; N, 6.11. Found: C, 68.24; H, 4.86; N, 6.12.

2-Benzoyl-5-[(4-tolyl)hydroxymethyl]pyrrole (28). 2-Benzoyl-5-formylpyrrole (**27**) (1.33 g; 6.68 mmol) and dry ether (38 mL) were placed in a 250-mL RBF. The resulting suspension was flushed with N_2 and cooled to −23 °C (CCl_4/dry ice). A 1.0 M solution of *p*-tolylmagnesium bromide in ether (15 mL; 15.0 mmol) was added dropwise over a 9 min period. The mixture was stirred at this temperature for 2 h before being poured into an aqueous ether/ice mixture. The layers were separated, and the organic layer was washed three times with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to give a brown oil. The crude product was chromatographed on a silica gel flash column, eluting with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated to give the title pyrrole (1.46 g, 75%) as a tan solid, mp 134.5–136.5 °C. ^{1}H-NMR: ($CDCl_3$) δ 2.36 (s, 3H), 5.14 (d, 1H), 5.99 (d, 1H), 6.04 (q, 1H), 6.85 (q, 1H), 7.16 (d, 2H), 7.35 (d, 2H), 7.48 (t, 2H), 7.57 (t, 1H), 7.82 (d, 2H), 11.27 (bs 1H). LRMS: *m/e* 291 (44), 273 (58), 230 (17), 168 (100), 105 (89). HRMS: calcd for $C_{19}H_{17}NO_2$ 291.1259, found 291.1269. Anal. Calcd for $C_{19}H_{17}NO_2$: C, 78.32; H, 5.89; N, 4.81. Found: C, 78.51; H, 5.84; N, 4.86.

2-[(4-Fluoro-3-methylphenyl)hydroxymethyl]-5-(4-methoxybenzoyl)pyrrole (34). 2-Formyl-5-(4-methoxybenzoyl)-pyrrole (**33**) (710 mg; 3.1 mmol) and dry ether (20 mL) were placed in a 100-mL RBF. The resulting suspension was flushed with N_2 and cooled to −23 °C (CCl_4/dry ice). A 1.0 M solution of (4-fluoro-3-methylphenyl)magnesium bromide in THF (7 mL; 7.0 mmol) was added dropwise over an 8-min period. The mixture was stirred at this temperature for 2 h before being poured into an aqueous ether/ice bath. The layers were separated, the organic layer was washed three times with water and then with brine, dried over Na_2SO_4, and evaporated under vacuum to give a red solid. The crude product was chromatographed on a silica gel flash column, eluted with cyclohexane/ethyl acetate (70/30). The appropriate eluates were combined and evaporated to give the title product (839 mg, 80%) as a pink powder, mp 115.8–116.8

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°C. ^{1}H-NMR: ($CDCl_3$) δ 2.21 (s, 3H), 3.85 (s, 3H), 5.30 (d, 1H), 5.94 (d, 1H), 5.97 (t, 1H), 6.83 (t, 1H), 6.95 ($d_{(with\ partially\ hidden\ t)}$, 3H), 7.18 (m, 1H), 7.25 (d, 1H), 7.83 (d, 2H), 11.34 (bs, 1H). LRMS: *m/e* 339 (42), 321 (45), 214 (16), 202 (21), 135 (100). HRMS: calcd for $C_{20}H_{18}FNO_3$ 339.1271, found 339.1270. Anal. Calcd for $C_{20}H_{18}FNO_3$: C, 70.77; H, 5.35; F, 5.60; N, 4.13. Found: C, 71.38; H, 5.27; F, 5.90; N, 4.06.

1-Benzoyl-5-(4-tolyl)dipyrromethane (29). To a 100-mL RBF flushed with N_2 was added glacial acetic acid (12 mL), acetic anhydride (2 mL), and pyrrole **10** (502 mg; 7.48 mmol). To this solution was added 2-benzoyl-5-[(4-tolyl)hydroxymethyl]pyrrole (**28**) (419 mg; 1.44 mmol) at which time the mixture was heated to 50 °C for 3.5 h. Silica gel TLC (cyclohexane/ethyl acetate (70/30)) showed none of the more polar starting material was present, and treatment of the TLC plate with Br_2 vapor developed the dipyrromethane as a bright red spot. The solvent was removed using an evaporator under high vacuum, and the residue was dissolved in toluene which was then removed under high vacuum to azeotrope any remaining acetic acid. The dark oil was chromatographed on a silica gel flash column with cyclohexane/ethyl acetate (70/30). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as a cream foamlike solid (438 mg, 90%), mp 54.5–57.5 °C. ^{1}H-NMR: ($CDCl_3$) δ 2.32 (s, 1H), 5.57 (s, 1H), 6.01 (s, 1H), 6.14 (m, 2H), 6.63 (t, 1H), 6.82 (q, 1H), 7.08 (s, 4H), 7.46 (t, 2H), 7.56 (t, 1H), 7.78 (d, 2H), 8.52 (bs, 1H), 10.41 (bs 1H). LRMS: *m/e* 340 (86), 274 (9) 249 (28), 235(94), 170 (26), 105 (100). HRMS: calcd for $C_{23}H_{20}N_2O$ 340.1575, found 340.1614. Anal. Calcd for $C_{23}H_{20}N_2O$: C, 81.14; H, 5.93; N, 8.23. Found: C, 80.99; H, 5.93; N, 7.92.

5-(4-Fluoro-3-methylphenyl)-1-(4-methoxybenzoyl)dipyrromethane (35). To a 100-mL RBF flushed with N_2 was added glacial acetic acid (14 mL), acetic anhydride (3 mL), and pyrrole (**10**) (595 mg; 8.87 mmol). To this solution was added 2-[(4-fluoro-3-methylphenyl)hydroxymethyl]-5-(4-methoxybenzoyl)-pyrrole (**34**) (563.7 mg; 1.66 mmol) after which the mixture was heated to 50 °C for 3.5 h. Silica gel TLC (cyclohexane/ethyl acetate (70/30)) showed none of the (more polar) starting material remained, and treatment of the TLC plate with Br_2 vapor developed the dipyrromethane as a bright red spot. The solvent was removed using an evaporator under high vacuum, and the residue was dissolved in toluene which was then removed under high vacuum to azeotrope any remaining acetic acid. The dark oil was chromatographed on a silica gel flash column with cyclohexane/ethyl acetate (70/30). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as a light tan foamlike solid (491 mg, 76%), mp 58–61 °C. ^{1}H-NMR: ($CDCl_3$) δ 2.09 (s, 3H), 3.89 (s, 3H), 5.57 (s, 1H), 5.99 (s, 1H), 6.14 (m, 2H), 6.65 (d, 1H), 6.77 (t, 1H), 6.82 (q, 1H), 6.87 (m, 1H), 6.97 (d, 3H), 7.82 (d, 2H), 8.97 (bs, 1H), 11.08 (bs, 1H). LRMS: *m/e* 388 (100), 322 (10), 279 (30), 253 (79), 188 (18), 135 (56). HRMS: calcd for $C_{24}H_{21}FN_2O_2$ 388.1587, found 388.1609. Anal. Calcd for $C_{24}H_{21}FN_2O_2$: C, 74.20; H, 5.45; F, 4.89; N, 7.22. Found: C, 74.07; H, 5.48; F, 5.09; N, 7.01.

5,15-Di(4-tolyl)-10,20-diphenylporphyrin (31). To a suspension of $LiAlH_4$ (196 mg; 5.16 mmol) in dry THF (10 mL) was added 1-benzoyl-5-(4-tolyl)dipyrromethane (**29**) (351 mg; 1.03 mmol) in dry THF (20 mL). The dark yellow solution was stirred at room temperature under N_2 for 2 h. A water/CH_2Cl_2 mixture was carefully added, and then the layers were separated. The organic layer was washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give unstable 5-(4-tolyl)-1-(phenylhydroxymethyl)dipyrromethane (**30**) as a dark yellow oil. This crude material was added to a 250-mL RBF along with propionic acid (120 mL). The purple solution was refluxed for 45 min and then set aside at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2, washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a purple solid. The crude product was chromatographed on a silica gel flash column, eluting with CH_2Cl_2. The appropriate eluates were combined and evaporated to give the desired porphyrin (75 mg, 31%) as a purple solid. To oxidize any chlorin impurities, the porphyrin was dissolved in absolute ethanol (10 mL) to which was added DDQ (20 mg) in dry benzene (2 mL). This solution was refluxed for 45 min, cooled to room temperature, and filtered through a bed of alumina (Brockmann Grade III) eluted with CH_2Cl_2. The solvent was reduced to a couple of mL and placed in the freezer to give chlorin-free porphyrin, mp > 325 °C. UV-vis λ_{max}: 418 nm (ε 332 000), 446 (69 300), 516 (13 000), 550 (7700), 590 (5500), and 664 (9200). ^{1}H-NMR: ($CDCl_3$) δ −2.73 (s, 2H), 2.72 (s, 6H), 7.57 (d, 4H), 7.78 (s, 6H), 8.13 (d, 4H), 8.25 (d, 4H), 8.89 (2 × $d_{(AB)}$, 8H). LRMS: *m/e* 643 (100) (MH^+), 642 (15) (M^+), 289 (8). HRMS: calcd for $C_{46}H_{34}N_4$ 642.2783, found 642.2762.

5,15-Bis(4-fluoro-3-methylphenyl)-10,20-bis(4-methoxyphenyl)porphyrin (37). To a suspension of $LiAlH_4$ (162 mg; 4.26 mmol) in dry THF (10 mL) was added 5-(4-fluoro-3-methylphenyl)-1-(4-methoxybenzoyl)dipyrromethane (**35**) (331.5 mg; 0.85 mmol) in dry THF (20 mL). The solution was stirred at room temperature under N_2 for 2 h. A water/CH_2Cl_2 mixture was carefully added, and then the layers were separated. The organic layer was washed three times with water, dried over Na_2SO_4, and then evaporated under vacuum to give unstable 5-(4-fluoro-3-methylphenyl)-1-[(4-methoxyphenyl)hydroxymethyl]-dipyrromethane (**36**) as a red oil. This crude material was added to a 250-mL RBF along with propionic acid (120 mL). The purple solution was refluxed for 45 min and then set aside at room temperature overnight. The reaction mixture was diluted with CH_2Cl_2 and washed three times with water, dried over Na_2SO_4, and evaporated under vacuum to give a purple solid. The crude product was chromatographed on a silica gel flash column, eluting with CH_2Cl_2. The appropriate eluates were combined and evaporated to give the title porphyrin (76.8 mg, 24%) as a purple solid. To oxidize any chlorin impurities, the porphyrin was dissolved in absolute ethanol (10 mL) to which was added DDQ (20 mg) in dry benzene (2 mL). This solution was refluxed for 45 min, cooled to room temperature, and filtered through a bed of alumina (Brockmann Grade III) eluted with CH_2Cl_2. The solvent was reduced to 2 mL and placed in the freezer to give the title chlorin-free porphyrin, mp > 325 °C. UV-vis λ_{max}: 420 nm (ε 331 500), 452 (83 800), 516 (12 400), 552 (7800), 592 (5000), and 678 (12 800). ^{1}H-NMR: ($CDCl_3$) δ −2.76 (s, 2H), 2.59 (s, 6H), 4.09 (s, 6H), 7.29 (d, 4H), 7.40 (t, 2H), 8.01 (m, 2H), 8.04 (d, 2H), 8.13 (d, 4H), 8.88 (2 × $d_{(AB)}$, 8H). LRMS: *m/e* 739 (100) (MH^+), 738 (85) (M^+), 327 (9), 207 (18). HRMS: calcd for $C_{48}H_{36}F_2N_4O_2$ 738.2806, found 738.2830. Anal. Calcd for $C_{48}H_{36}F_2N_4O_2$: C, 78.02; H, 4.91; F, 5.15; N, 7.59. Found: C, 78.15; H, 5.02; F, 5.05; N, 7.15.

5-(4-Fluoro-3-methylphenyl)-10-(4-methoxyphenyl)-15-(4-tolyl)-20-phenylporphyrin (38). (A) From Dipyrromethanes **29** and **35**. 1-Benzoyl-5-(4-tolyl)dipyrromethane (**29**) (207.4 mg; 0.61 mmol) and 5-(4-fluoro-3-methylphenyl)-1-(4-methoxybenzoyl)dipyrromethane (**35**) (270.1 mg; 0.70 mmol) were both reduced separately to their corresponding alcohols **30** and **36** by the previously mentioned procedures. These two compounds were dissolved together in CH_2Cl_2 (10 mL) and stirred vigorously while propionic acid (130 mL) was added. The purple solution was refluxed for 30 min and then allowed to sit at room temperature overnight. After the usual workup, including treatment with DDQ (20 mg) in dry benzene (2 mL), the appropriate eluates from the chromatography were combined and evaporated to give three major compounds. The first to elute was 5,15-ditolyl-10,20-diphenylporphyrin (**28**) (13.5 mg, 6.9% based on **29**). The third to elute was 5,15-bis(4-fluoro-3-methylphenyl)-10,20-bis(4-methoxyphenyl)porphyrin (**37**) (26.0 mg, 10% based on **35**). The second compound to elute was the title porphyrin (73.5 mg, 17.5%), mp > 300 °C. UV-vis λ_{max}: 418 nm (ε 340 700), 450 (77 100), 516 (15 200), 552 (9100), 592 (6700), and 672 (11 800). ^{1}H-NMR: ($CDCl_3$) δ −2.76 (s, 2H), 2.57 (s, 3H), 2.72 (s, 3H), 4.05 (s, 3H), 7.25 (d, 2H), 7.39 (t, 1H), 7.56 (d, 2H), 7.77 (s, 3H), 8.02 (m, 1H), 8.04 (d, 2H), 8.12 (m, 4H), 8.23 (d, 2H), 8.87 (d, 8H). LRMS: *m/e* 691 (51) (MH^+), 690 (100) (M^+), 345 (13). HRMS: calcd for $C_{47}H_{35}FN_4O$ 690.2795, found 690.2808. Anal. Calcd for $C_{47}H_{35}FN_4O \cdot 3H_2O$: C, 75.79; H, 5.55; N, 7.52. Found: C, 76.13; H, 5.59; N, 7.30.

(B) From Dipyrromethanes **53** and **55**. 1-*p*-Anisoyl-9-benzoyl-5-*p*-tolyldipyrromethane (**55**) (274 mg, 0.577 mmol) in dry THF (15 mL) was added to a suspension of $LiAlH_4$ (148 mg, 3.90 mmol) in dry THF (10 mL). The reaction mixture was stirred under argon at room temperature for 2 h. Water was carefully added with stirring until the evolution of hydrogen ceased. The mixture was then diluted with CH_2Cl_2, and the solid aluminum oxide was

filtered off. The organic layer from the filtrate was washed three times with water and dried over anhydrous Na_2SO_4. This solution (containing the unstable dipyrromethane **56**) was directly mixed with 5-(4-fluoro-3-methylphenyl)dipyrromethane (**53**) (150 mg, 0.590 mmol), and the solvent was then evaporated to give a dark orange oil. This oil was dissolved in propionic acid (100 mL) and heated at reflux for 45 min under argon in the dark. It was then allowed to stand at room temperature overnight (open to the air). The reaction mixture was diluted with CH_2Cl_2 and washed three times with water. The organic layer was dried over anhydrous Na_2SO_4, and the solvent was evapoarated to give a dark oil which was dissolved in toluene and then evaporated to facilitate the removal of all the residual propionic acid. The crude product was chromatographed on a silica gel flash column, eluting with cyclohexane/CH_2Cl_2 (1:1). The second compound to elute was the title porphyrin. To remove chlorin impurities, the porphyrin was dissolved in absolute ethanol (10 mL), and DDQ (20 mg) in benzene (2 mL) was added. This solution was heated at reflux for 45 min before being allowed to cool to room temperature and filtered through a pad of neutral alumina (Brockmann Grade III). The solvent was evaporated, and the residue was recrystallized from methylene chloride/methanol to give the title porphyrin as a purple solid (48 mg, 12%), mp > 300 °C, identical in all respects with the material obtained in method A. See Figure 1 for the X-ray structure of the zinc(II) complex of **38**. [The zinc complex was prepared by treatment of **38** in dichloromethane with zinc(II) acetate in methanol, followed by workup, and crystallization by diffusion of a pyridine/methanol mixture into a concentrated dichloromethane solution of Zn(II)**38**.] Other porphyrins isolated from the chromatographic separation were **50** (0.5%; identical with the material reported elsewhere in this paper) and **57** (1%); the latter porphyrin was not fully characterized but was identified using its characteristic proton NMR peaks at 4.10 (s, 6H, 2 × C_6H_4OMe), 2.71 (s, 3H, C_6H_4Me), and 2.57 ppm (s, 3H, C_6H_3FMe).

1,9-Dibenzoyl-5-*p*-tolyldipyrromethane (51). *N*-Benzoylmorpholine (1.22 g, 6.38 mmoles) and freshly distilled $POCl_3$ (1.1 mL, 11.8 mmol) were mixed under argon. The suspension was heated at 40 °C until all the solid had dissolved; it was then stirred at room temperature for 5.5 h. Dipyrromethane **17** (607 mg, 2.57 mmoles) dissolved in dry CH_2Cl_2 (15 mL) was added slowly to the Vilsmeier reagent. The resulting reaction mixture was stirred at room temperature under argon for 17 h before being cooled in an ice bath and slow addition of sodium acetate (1.5 g) in water (15 mL). The ice bath was removed, and solid sodium carbonate was then added directly to the mixture until the pH was about 8. The mixture was stirred at room temperature for 8 h and then diluted with water and CH_2Cl_2. The organic layer was washed with water and brine and dried over anhydrous Na_2SO_4, and the solvent was evaporated to give a dark brown oil. The oil was chromatograhphed on a silica gel flash column eluting with ethyl acetate/cyclohexane (25/75). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as brown flakes (449 mg, 39%), mp 93-95 °C. ^{1}H-NMR: ($CDCl_3$): δ 2.38 (s, 3H), 5.60 (s, 1H), 6.03 (t, 2H), 6.67 (t, 2H), 7.21 (d, 2H), 7.31 (d, 2H), 7.42 (t, 4H), 7.52 (t, 2H), 7.81 (t, 4H), 10.57 (bs, 2H). Anal. Calcd for $C_{30}H_{24}N_2O_2$: C, 81.06; H, 5.44; N, 6.30. Found: C, 80.40; H,5.53; N, 6.12.

5-(4-Fluoro-3-methylphenyl)-10,20-diphenyl-15-*p*-tolylporphyrin (50). 1,9-Dibenzoyl-5-*p*-tolyldipyrromethane (**51**) (243 mg, 0.547 mmol) in dry THF (15 mL) was added to a suspension of $LiAlH_4$ (138 mg, 3.64 mmol) in dry THF (10 mL). The mixture was stirred under argon at room temperature for 2 h. Water was carefully added with stirring until the evolution of hydrogen ceased. The mixture was then diluted with CH_2Cl_2, and the solid aluminum hydroxide was filtered off. The organic layer from the filtrate was washed three times with water and dried over anhydrous Na_2SO_4. This solution (containing the sensitive dipyrromethane **52**) was directly mixed with 5-(4-fluoro-3-methylphenyl)dipyrromethane (**53**) (150 mg, 0.590 mmol), and the solvent was then evaporated to give a dark orange oil. This oil was dissolved in propionic acid (100 mL) and heated at reflux for 45 min under argon in the dark. It was then allowed to stand at room temperature overnight (open to the air). The reaction mixture was diluted with CH_2Cl_2 and washed three times with water. The organic layer was dried over anhydrous Na_2SO_4, the solvent was evapoarated to give a dark oil which was dissolved in toluene, and this was evaporated to facilitate the removal of all the acid. The crude product was chromatographed on a silica gel flash column with CH_2Cl_2 as eluent to yield the title porphyrin. To remove chlorin impurities, the porphyrin was dissolved in absolute ethanol (10 mL), and DDQ (20 mg) in benzene (2 mL) was added. This solution was heated at reflux for 45 min. It was then allowed to cool to room temperature and filtered through a pad of neutral alumina (Brockmann Grade III). The solvent was evaporated, and the residue was recrystallized from CH_2Cl_2/methanol to give the title porphyrin as a purple solid (73mg, 20%), mp > 300 °C. UV-vis λ_{max}: 416 nm (ϵ 248 000), 514 (17 400), 548 (9500), 590 (7400), 666 (3500). ^{1}H-NMR: ($CDCl_3$) δ -2.76 (s, 2H), 2.58 (s, 3H), 2.72 (s, 3H), 7.40 (t, 1H), 7.58 (d, 2H), 7.78 (d, 6H), 8.02 (m, 2H), 8.10 (d, 2H), 8.23 (d, 4H), 8.85 (m, 8H). HRMS: $C_{46}H_{33}FN_4$ requires 660.2689, found 660.2719. Anal. Calcd for $C_{46}H_{33}FN_4$: C, 83.61; H, 5.03; N, 8.48; F, 2.88. Found: C, 83.20; H,5.40; N, 8.19; F, 2.98.

5-(4-Fluoro-3-methylphenyl)dipyrromethane (53). (A) Ethyl 5-[(4-Fluoro-3-methylphenyl)hydroxymethyl]pyrrole-2-carboxylate. Ethyl 5-formylpyrole-2-carboxylate (**13**) (3.06 g, 18.3 mmol) was suspended in dry THF (120 mL) under argon and was cooled to -23 °C (CCl_4/dry ice). A 1.0 M solution of (4-fluoro-3-methylphenyl)magnesium bromide in THF (40 mL, 40 mmol) was added dropwise over a period of 10 min. The reaction mixture was stirred under argon at -23 °C for 3 h and was then poured into an aqueous ether/ice bath. The organic layer was washed twice with water and brine and then dried over anhydrous Na_2SO_4. The solvent was evaporated to give a crude oil which was chromatographed on a silica gel flash column eluting with 2.5% methanol/CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give the desired pyrrole as a light yellow solid (2.70 g, 53%), mp 103-104°C. ^{1}H-NMR: ($CDCl_3$) δ 1.34 (t, 3H), 2.26 (s, 3H), 2.25 (bs, 1H), 4.28 (q, 2H), 5.82 (d, 1H), 5.94 (t, 1H), 6.81 (t, 1H), 6.99 (t, 1H), 7.23 (m, 2H), 9.25 (bs, 1H). Anal. Calcd for $C_{15}H_{16F}N_2O_3$: C, 64.97; H, 5.82; N, 5.05. Found: C, 65.23; H, 5.90; N, 4.99.

(B) Ethyl 5-(4-Fluoro-3-methylphenyl)dipyrromethane-1-carboxylate. Ethyl 5-[(4-fluoro-3-methylphenyl)hydroxymethyl]-pyrrole-2-carboxylate (4.20 g, 15.1 mmol) and pyrrole **10** (5.30 g, 79.0 mmol) were dissolved in dry CH_2Cl_2 (120 mL). To this solution was added Montmorillonite K10 clay (20.6 g). The resulting green suspension was stirred at room temperature under argon in the dark (reaction flask was covered with aluminum foil) for 2 h. It was then filtered to remove the clay, and the filtrate was evaporated to give a crude orange oil which was chromatographed on a silica gel flash column eluting with 2% methanol/CH_2Cl_2. The appropriate fractions were combined, and the solvent was removed to give the desired dipyrromethane as a light brown oil (4.03 g, 82%). ^{1}H-NMR: ($CDCl_3$) δ 1.33 (t, 3H), 2.23 (s, 3H), 4.26 (q, 2H), 5.42 (s, 1H), 5.93 (s, 1H), 5.94 (t, 1H), 6.17 (dd, 1H), 6.72 (dd, 1H), 6.83 (t, 1H), 6.97 (m, 3H), 7.88 (bs, 1H), 8.76 (bs, 1H). HRMS: $C_{19}H_{19}FN_2O_2$ requires 326.1430 found 326.1423.

(C) 5-(4-Fluoro-3-methylphenyl)dipyrromethane (**53**). Ethyl 5-(4-fluoro-3-methylphenyl)dipyrromethane-1-carboxylate (132 mg, 0.404 mmol) and sodium hydroxide (270 mg, 6.75 mmol) were mixed in ethylene glycol (5 mL). This suspension was heated at 185 °C for 50 min under argon. After being cooled to room temperature, the reaction mixture was diluted with a large amount of water. The resulting solution was exhaustively extracted with petroleum ether. The combined organic layers were then washed twice with water and brine and dried over anhydrous Na_2SO_4, and the solvent was evaporated to give the title dipyrromethane as a brown oil (99 mg, 96%). ^{1}H-NMR: ($CDCl_3$) δ 2.24 (s, 3H), 5.42 (s, 1H), 5.91 (s, 2H), 6.17 (q, 2H), 6.71 (d, 2H), 6.97 (m, 3H), 7.91 (bs, 2H). HRMS: $C_{16}H_{15}FN_2$ calcd 254.1219, found 254.1208.

2-*p*-Anisoyl-5-[(4-tolyl)hydroxymethyl]pyrrole (54). 2-*p*-Anisoyl-5-formylpyrrole (**33**) (1.00 g, 4.36 mmol) was suspended in dry THF (30 mL) under argon and cooled to -23 °C (CCl_4/dry ice). A 1.0 M solution of *p*-tolylmagnesium bromide in ether (9.6 mL, 9.6 mmo) was added dropwise over a period of 5 min. The reaction mixture was stirred under argon at -23 °C for 2.5 h before being poured into an aqueous ether/ice bath. The organic layer was washed with water and then twice with brine and dried over anhydrous Na_2SO_4. The solvent was evaporated to give a

crude solid which was chromatographed on a silica gel flash column eluting with ethyl acetate/cyclohexane (30/70). The appropriate fractions were combined, and the solvent was removed to give the title pyrrole as a light tan solid (1.00 g, 71%), mp 145–146 °C. ^{1}H-NMR: ($CDCl_3$) δ 2.37 (s, 3H), 3.87 (s, 3H), 4.05 (bs, 1H), 5.95 (s, 1H), 6.00 (t, 1H), 6.80 (t, 1H), 6.94 (d, 2H), 7.18 (d, 2H), 7.30 (d, 2H), 7.83 (d, 2H), 10.65 (bs, 1H). Anal. Calcd for $C_{20}H_{19}NO_3$: C, 74.75; H, 5.96; N, 4.36. Found: C, 74.90; H, 5.96; N, 4.42.

1-*p*-Anisoyl-9-benzoyl-5-*p*-tolyldipyrromethane (55). 2-*p*-Anisoyl-5-[(4-tolyl)hydroxymethyl]pyrrole (**54**) (706 mg, 2.20 mmol) and 2-benzoylpyrrole (**26**) (407 mg, 2.38 mmoles) were dissolved in dry CH_2Cl_2 (70 mL). To this solution was added Montmorillonite K10 clay (2.0 g). The resulting suspension was stirred under argon at room temperature for 3 h before being filtered to remove the clay and the filtrate evaporated to give a crude orange solid. The solid was chromatographed on a silica gel flash column eluting with ethyl acetate/cyclohexane (30/70). The appropriate fractions were combined, and the solvent was removed to give the title dipyrromethane as an orange solid (469 mg, 45%), mp 111–114 °C. ^{1}H-NMR: ($CDCl_3$) δ 2.37 (s, 3H), 3.86 (s, 3H), 5.60 (s, 1H), 6.03 (s, 2H), 6.64 (m, 2H), 6.93 (d, 2H), 7.21 (d, 2H), 7.31 (d, 2H), 7.42 (t, 2H), 7.52 (t, 1H), 7.81 (t, 2H), 10.61 (bs, 2H). Anal. Calcd for $C_{31}H_{26}N_2O_3$: C, 78.46; H, 5.52; N, 5.90. Found: C, 78.33; H, 5.60; N, 5.94.

Crystal Structure Analysis of **38** Derivative. Zn(II)**38**(pyridine) was prepared from **38** by first preparing the Zn(II) complex using zinc(II) acetate in methanol, followed by diffusion of 10% pyridine in methanol into a concentrated solution of Zn(II)**38** in dichloromethane. Blue parallelepipeds of Zn(II)**38**(pyridine) were obtained by diffusion of methanol (containing 10% pyridine) into a dichloromethane solution of the zinc(II) porphyrin. Crystal data at 130 K (Mo Kα radiation, λ = 0.710 73 Å, $2\Theta_{max}$ = 48°), monoclinic space group $P2_1/n$, a = 18.976(15) Å, b = 9.784(9) Å, c = 24.08(2) Å, β = 111.62(6)°, V = 4156(6) Å^3, R = 0.119, Rw = 0.12 for 2530 reflections with $I > 2\sigma(I)$ and 253 parameters. The structure suffers from poor crystal quality and disordering of the different aryl groups over all four meso positions.

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