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Core-Modified, *meso*-Alkylidenyl Porphyrins and Their Expanded Analogues: A New Family of Nonplanar Porphyrinoids

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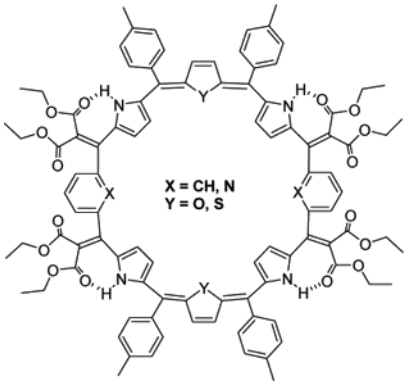

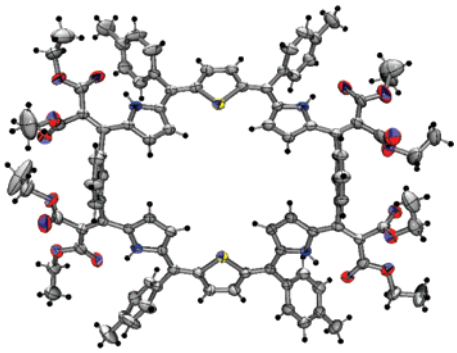

New core-modified, *meso*-alkylidenyl porphyrinoids bearing multiple exocyclic double bonds were synthesized and characterized. The synthesis was accomplished using a typical "3 + 1"-type condensation approach. Stable exocyclic tautomers bearing double bonds at the meso positions, as well the corresponding endocyclic tautomers, were isolated in the case of both thiabenziporphyrin and thiapyriporphyrin products prepared in the course of this study. On the other hand, only the exocyclic tautomer was isolated in the case of the congeneric oxapyriporphyrin and oxabenziporphyrin. Expanded analogues of the exocyclic forms of oxabenziporphyrin and thiabenziporphyrin were also isolated as minor products. A single-crystal X-ray diffraction analysis of the expanded thiabenziporphyrin (**20**) revealed that all four pyrrole rings displayed an inverted geometry, presumably reflecting the strong hydrogen-bonding extant between the pyrrole N−H proton and the carbonyl group of the malonate moiety in the solid state. On the other hand, the expanded oxabenziporphyrin (**14**) was found to possess a severely distorted geometry with only one pyrrole ring being inverted. Careful analysis of the structure revealed that the solid-state geometry of the expanded macrocycles correlates well with the internal angle defined by the 2- and 5 substituents and the centers of the furan (**14**) or thiophene (**20**) subunits.

Introduction

Many structural analogues of porphyrins such as isomeric porphyrins, aromatic or nonaromatic porphyrin analogues, and expanded porphyrins have been prepared over the last few decades and studied extensively due to their diverse applications in areas such as photomedicine,[1] supramolecular chemistry,[2] and materials science.[3] Within the cadre of this generalized effort, core-modified porphyrins, such as carbaporphyrinoids[4] and their metal complexes,[5] pyridine-containing porphyrinoids,[6] and thia-

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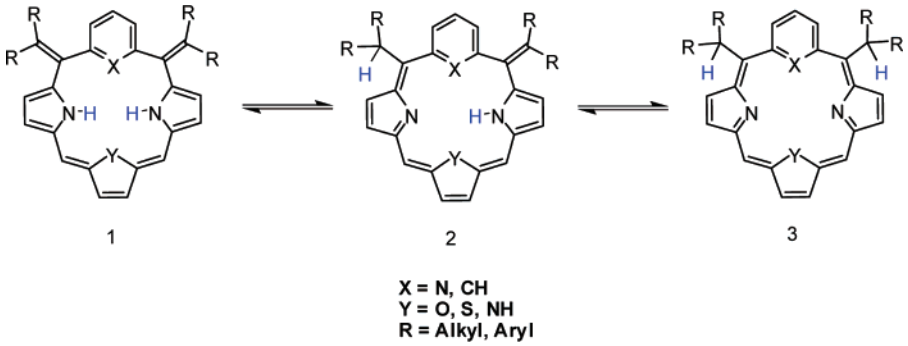
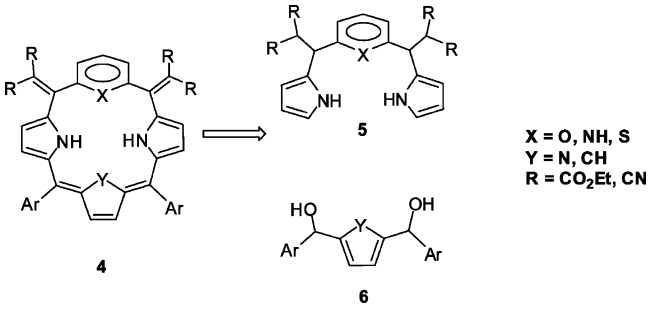
SCHEME 1. Tautomeric Equilibrium between Exocyclic Form and Endocyclic Form of *meso*-Alkylidenyl Porphyrinoids



SCHEME 2. Retrosynthetic Analysis of Target Compound 4



or oxa-porphyrinoids,[7] have stimulated particular interest due to their unique physicochemical properties. They provide a means for better understanding the electronic features of the porphyrinoid macrocycles. For instance, it was found that the benziporphyrins and pyriporphyrins[8,9] bearing a benzene or pyridine subunit as a part of the core structure did not exhibit porphyrin-like macroaromatic properties due to the disruption of the overall conjugation pathway. However, it was observed that the presence of tautomerizable functional groups can facilitate aromaticity in some cases.[10] These observations have provided a stimulus to prepare and study new kinds of porphyrinoid macrocycles, and this has resulted in many examples being described in recent years. In spite of this progress, porphyrinoids bearing multiple *meso*-alkylidenyl double bonds have attracted relatively little attention, with only a handful of examples having been reported in the literature. The first such systems, the so-called xanthoporphyrinogens, structural analogues of porphyrin bearing exocyclic double bonds at the meso positions, were reported in 1976.[11] Ni(II) complexes of a different system, 5,10,15,20-tetraisopropylporphyrin-containing exocyclic methylenes, were reported in 1998.[12] Oxidation products of *meso*-tetrakis(3,5-di-*t*-butyl-4-hydroxyphenyl)porphyrin also contain exocyclic double bonds,[13] as does tetra-*meso*-methyleneporphyrinogen.[14] Unfortunately, however, these species are relatively unstable. Most recently, cumulene-type, quinonoidal metalloporphyrins were reported by Anderson et al.,[15] with the compounds in question showing promising optoelectronic properties. These interesting properties and the rather unusual conjugation of *meso*-alkylidenyl porphyrins has led us to attempt the synthesis of novel porphyrinoids bearing stable exocyclic double bonds at multiple meso positions. We were also motivated by an appreciation that benziporphyrinoids or pyriporphyrinoids bearing exocyclic double bonds at more than one meso position would constitute useful model compounds for exploring the interplay between global aromaticity, molecular geometry, and substituent effects. With such considerations in mind, we report here the synthesis, characterization, and spectroscopic properties of new core-modified porphyrinoids bearing alkylidenyl double bonds at multiple meso positions. The presence of the exocyclic double bond at the meso position(s) serves to disturb the full conjugation of the macrocycle, leading to systems that are rather destabilized. Nonetheless, in several cases, different tautomers were found to coexist, albeit with differing levels of apparent stability.

Results and Discussion

Benziporphyrin is a well-recognized nonaromatic macrocycle. Its lack of global or total macrocyclic aromaticity is ascribed to a conjugation pathway that is interupted by a fully incorporated six-membered, 1,3-linked benzene moiety.[8] To the extent such rationalizations are correct, we considered it likely that the presence of exocyclic double bonds combined with a benziporphyrin-like incoporated six-membered ring would give rise to porphyrinoid macrocycles with π-frameworks that are further destabilized and hence even more distorted from planarity. Further, if restrictions to the conformational flexibility could be imposed via the introduction of bulky substituents at the meso positions, we considered it likely that an even greater

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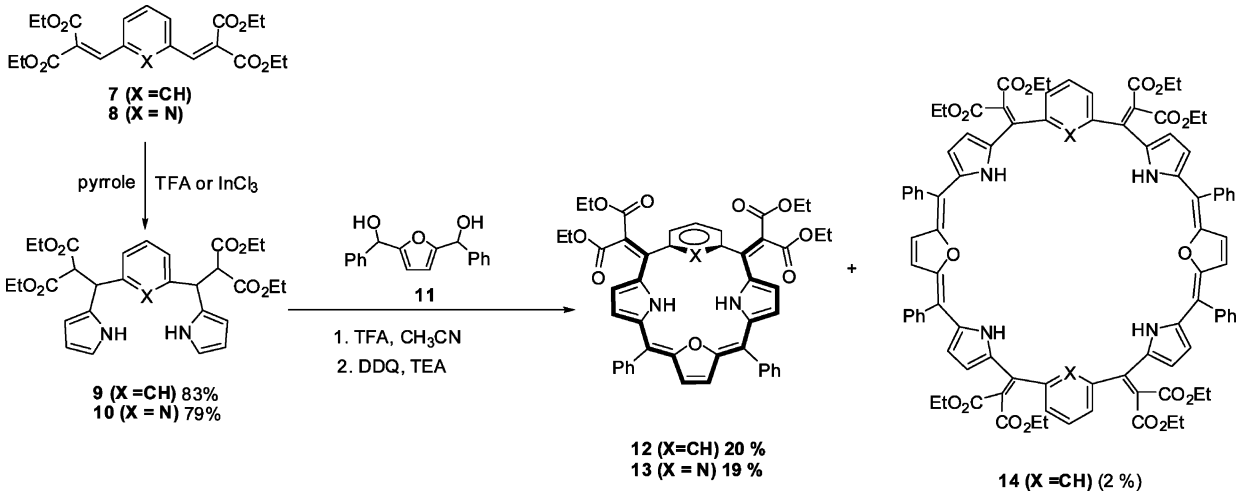
SCHEME 3. Synthetic Scheme for Oxabenziporphyrins and Oxapyriporphyrins



level of distortion could be attained. In the limit, all vestiges of global conjugation might be destroyed with the consequence that various tautomers involving endo or exocyclic double bonds would become chemically distinct in terms of isolation on the laboratory time scale. In other words, under these latter limiting conditions, the different forms illustrated by generalized structures **1**−**3** would no longer be interconvertible and could be potentially isolated as stable constitutional isomers as shown in Scheme 1. If the substituents on the *meso*-methyl/methylene/methine groups (including R in structures **1**,−**3**) are not only bulky but also electron withdrawing, it should lead to a further stabilization of the individual tautomeric forms.

With such considerations in mind, we designed a new class of porphyrin analogues, represented by the general structure **4**, that should be amenable to synthesis using the so-called modified "3 + 1" method, as shown retrosynthetically in Scheme 2.[16]

Tripyrrane analogues of generalized structure **5** are core building blocks in porphyrin analogue chemistry; likewise, the furan and thiophene diols **6** are well-known precursors in this area.[17] Further, as shown in Scheme 3, the 2,6-bisvinyl benzene derivative **7** and the 2,6-bisvinylpyridine derivative **8** could be obtained readily via a Knoevenagel condensation of diethyl malonate with 2,6-pyridinedicabaldehyde or isophthalaldehyde, respectively.[18] A subsequent acid-catalyzed addition of pyrrole served to convert **7** or **8** to the corresponding tripyrrane analogues **9** and **10**. Many different catalysts and conditions were tested in an effort to optimize the addition of pyrrole to the vinylic double bonds of **7** and **8**, and it was found that the yield of the desired product dramatically depends on the catalyst applied. For example, the best yield of **9** was obtained when $InCl_3$ was used as the catalyst. On the other hand, the highest yield of **10** was obtained when trifluoroacetic acid was employed as a catalyst. This difference was rationalized in terms of pyridine being able to coordinate to the In(III) center, with the resulting complex presumably not being activated sufficiently to undergo electrophilic substitution at the methylene α-carbon. Metal coordination could also be inhibitory as the result of steric hindrance. Such limitations would not be operative in the case of TFA-mediated catalysis, even under conditions where the pyridine nitrogen atom is protonated.

All the addition reactions proved regiospecific and afforded a single regioisomer, namely, the α,α′-dipyrryl derivatives **9** and **10**. However, proton NMR spectral analysis revealed the formation of diastereomeric mixtures; these were used directly in the ensuing condensations without further purification since the ring-forming reaction was expected to lead to the formation of achiral products. The carbinols **11** required for the condensation were synthesized by treating furan with *n*-butyllithium, followed by reaction with benzaldehyde.[19] Once all the needed building blocks were in hand, the bispyrrole-functionalized precursors **9** and **10** were condensed, respectively, with carbinol **11** as shown in Scheme 3. Specifically, the reaction pair consisting of **9** and **11** was dissolved in acetonitrile and treated with trifluoroacetic acid followed by oxidation with DDQ; this afforded the desired oxabenziporphyrin **12** in 20% yield. An expanded analogue of this macrocycle bearing four exocyclic double bonds, **14**, was also isolated in a small amount (∼2%); presumably, it was formed from the condensation of two molecules of **9** with two molecules of carbinol **11**. In contrast, a similar condensation involving **10** and **11** afforded only the oxapyriporphyrin **13** in 19% yield with no isolable quantities of putative expanded congeners being obtained.

Compounds **12**−**14** were not expected to exhibit global aromatic properties. Both the α-carbon of the diethyl malonate group and the meso carbon are sp^2-hybidized; thus, the benzene (pyridine), the pyrrole, and the two ethoxycarbonyl groups were expected to reside above or below the mean plane of the macrocycle. Further, in **12** and **13**, the benzene (or pyridine) moiety would presumably be tilted significantly so as to reduce the steric congestion that would otherwise originate from the two diethyl malonate groups and the exocyclic double bonds. The observation of the pyrrole N−H resonance at 8.09 ppm in the ^{1}H NMR spectrum, which is a typical chemical shift value for simple pyrrole N−H protons, is fully consistent with the suggested lack of extended conjugation. Moreover, the ^{13}C NMR

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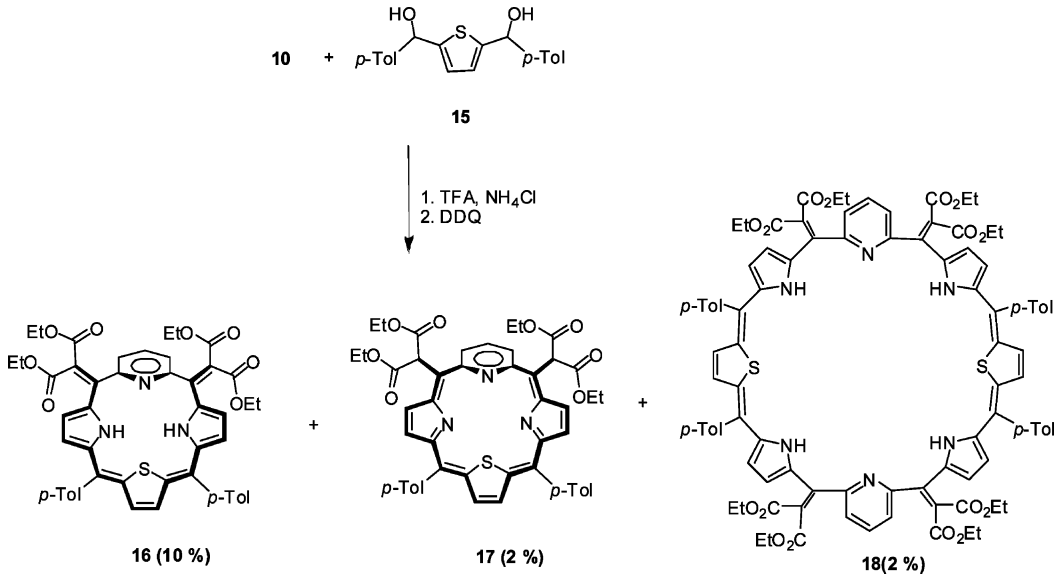
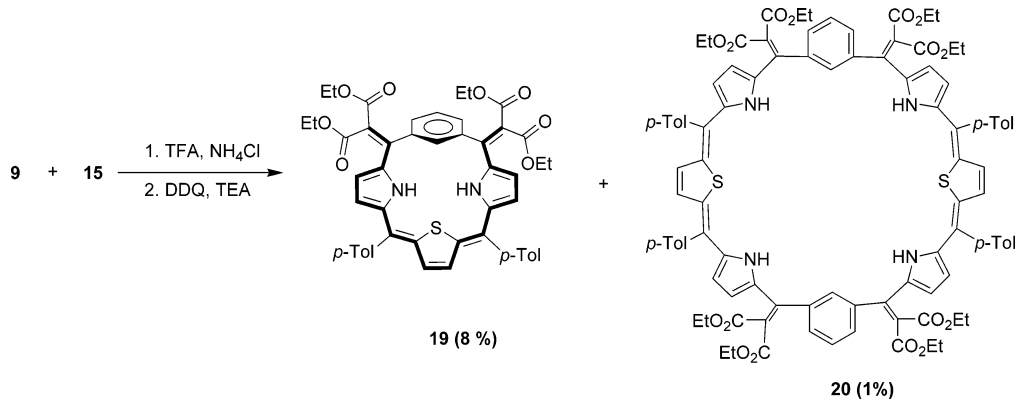
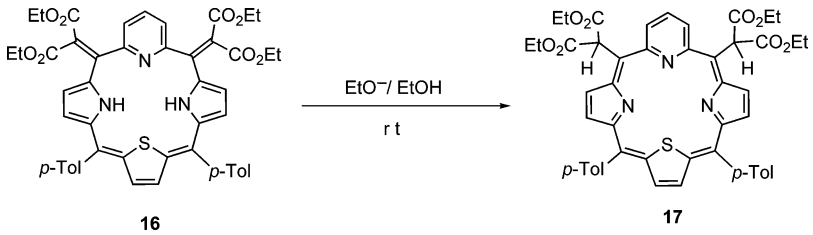
SCHEME 4. Synthetic Scheme for Thiapyriporphyrins



SCHEME 5. Synthesis of Thiabenziporphyrin 19 and a Higher Homologue, 20



SCHEME 6. Conversion of Exocyclic Thiapyriporphyrin 16 to Its Endocyclic Isomer, 17



spectrum of **12** and **13** showed features corresponding to 22 total carbon signals, a finding that is in accord with the proposed high symmetry for these macrocycles.

Similar condensations of **10** with **15** were carried out using conditions identical to those used to generate **12**. However, in this case, the reaction afforded a mixture of three different products, namely, **16**−**18** in yields of 10, 2, and 2%, respectively, as shown in Scheme 4. This is noteworthy because two stable tautomeric products, specifically **16** and **17**, were formed. These two tautomers, which were isolated by column chromatography over silica gel, proved stable in organic solvents. Thus, both tautomers could be fully characterized using regular spectroscopic methods.

Condensation of **9** with **15** also resulted in the formation of **19**, as well as a small amount of the higher homologue **20** as shown in Scheme 5. The reaction afforded only the exocyclic product **19** and none of the endocyclic analogue, at least after workup and purification. Thus, the thiapyriporphyrins **16** and **17** were the only tautomeric pair that could be isolated cleanly from the present set of condensations.

The two tautomers **16** and **17** showed unique signals in their respective proton NMR spectra. For example, the pyrrole NH resonance was observed at 8.63 ppm in **16**, whereas, as expected, no pyrrole NH signal was seen in the case of **17**. Instead, a signal ascribable to the α-protons of the diethyl malonate groups was observed at 5.18 ppm as a singlet. However, when macrocycle **16** was treated with a strong base (EtOH/EtO$^-$), conversion to **17** was observed along with extensive decomposition (Scheme 6). On the other hand, treatment of **17** with a base did not produce observable quantities of **16** and, instead, resulted

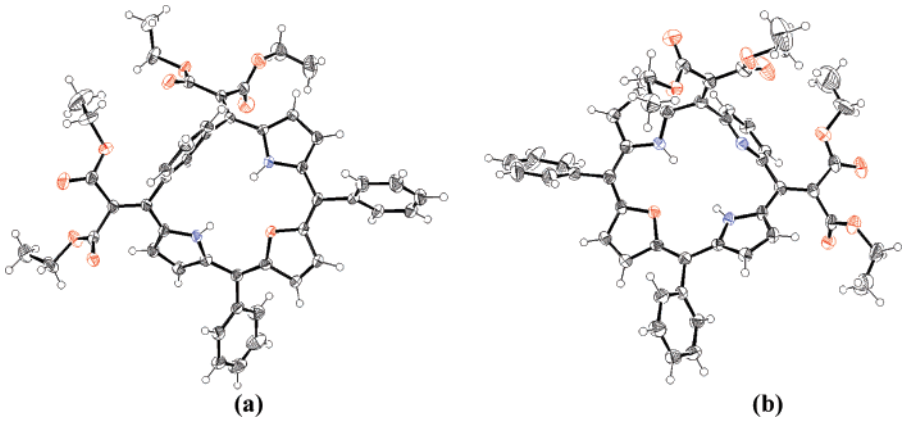


FIGURE 1. Ortep rendered structures of (a) oxabenziporphyrin **12** and (b) oxapyriporphyrin **13** highlighting their structural similarity. The top alkylidenyl double bonds exhibit a distorted geometry with the dihedral angle looking down the C=C double bond being 19.8° in panel a and 21.0° in panel b, respectively.

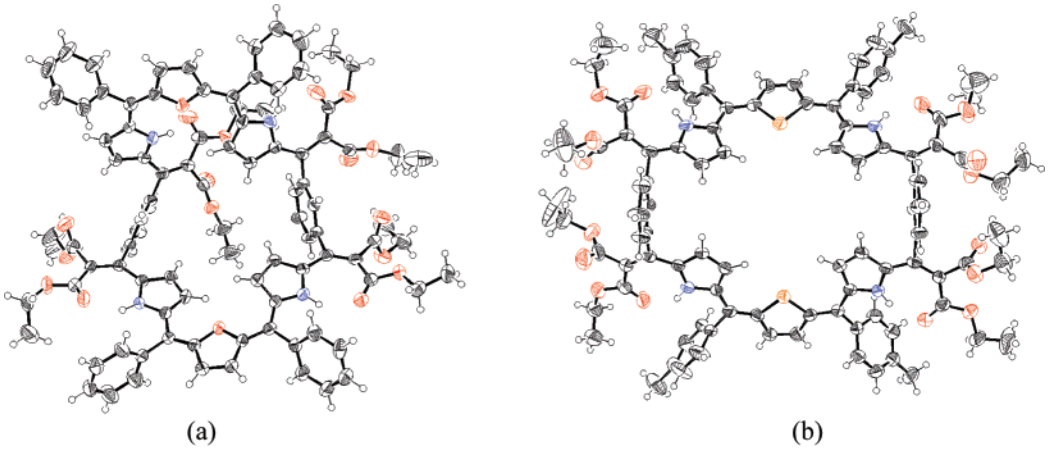


FIGURE 2. Ortep rendered single-crystal X-ray diffraction structures of (a) expanded oxabenziporphyrin **14** and (b) expanded thiabenziporphyrin **20**. Note that all four pyrrole rings in panel b adopt an inverted conformation due to the intramolecular hydrogen bonding between pyrrole N−H and carbonyl group, while in panel a, three pyrrole rings are inverted, and one pyrrole ring is involved in hydrogen-bonding interactions with a carbonyl group residing within the cavity.

only in extensive decomposition. Thus, it was possible to effect partial interconversion between these two tautomers using chemical means.

The UV−vis absorption spectrum of oxabenziporphyrin **12** recorded in CH_2Cl_2 revealed two dominant peaks at λ_{max} at 390 ($\epsilon = 3.6 \times 10^4$) and 530 nm ($\epsilon = 2.2 \times 10^4$). The oxapyriporphyrin **13** also showed two dominant absorption features at 389 ($\epsilon = 2.7 \times 10^4$) and 534 nm ($\epsilon = 1.6 \times 10^4$) in its spectrum when it was recorded under identical conditions. Similar spectral features were seen for thiapyriporphyrin **16**, a species that also displayed λ_{max} at 382 ($\epsilon = 4.0 \times 10^4$) and 555 nm ($\epsilon = 1.7 \times 10^4$) in CH_2Cl_2. On the other hand, **17**, the endocyclic tautomer of **16**, exhibited red-shifted absorption features with λ_{max} at 395 ($\epsilon = 3.9 \times 10^4$) and 560 nm ($\epsilon = 1.4 \times 10^4$), again in CH_2Cl_2.

Single-crystal X-ray diffraction structural studies of oxabenziporphyrin **12** and oxapyriporphyrin **13**[20] revealed that both porphyrins adopt severely puckered geometries. The benzene (or pyridine) moiety was found to lie almost perpendicular to the mean plane of the macrocycle (Figure 1). The lengths of the double bonds appended to the meso positions were found to be 1.381 and 1.389 Å, respectively.

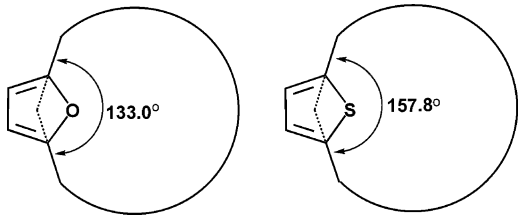
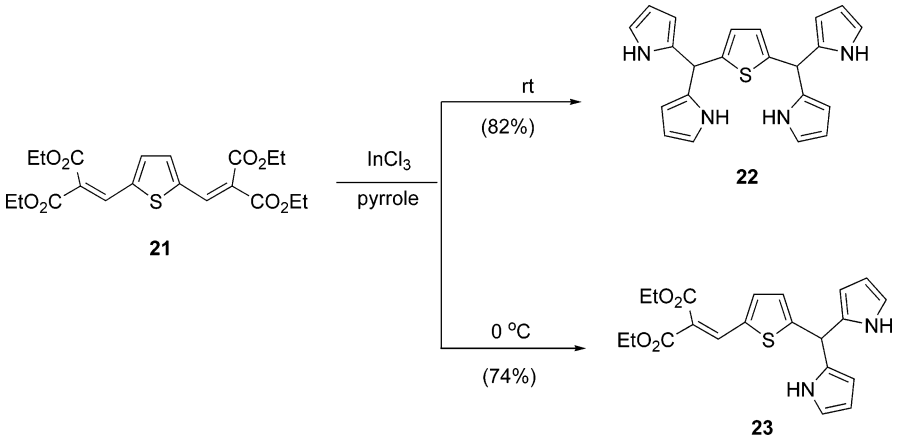


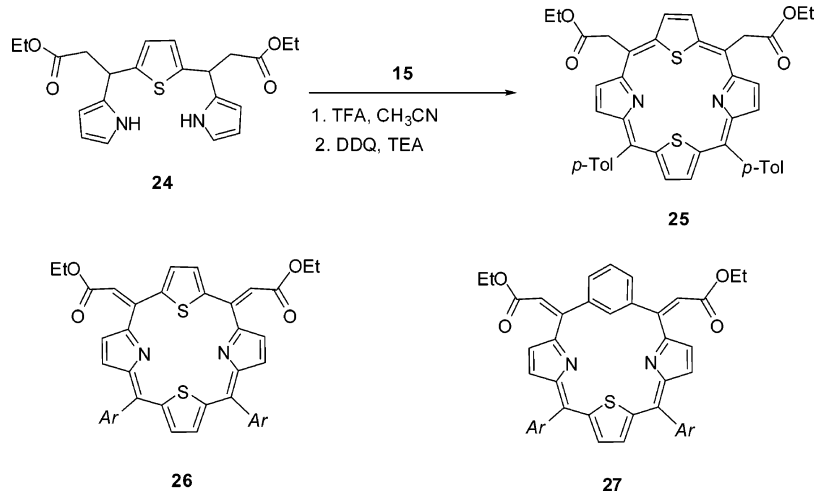
FIGURE 3. Effective angle between 2 and 5 substituents in the furan and thiophene subunits of **14** and **20**, as calculated from the corresponding solid-state structures.

The puckered geometry of **12** and **13** appears to have its origin in the steric congestion arising from the two diethyl malonyl groups and the benzene or pyridine rings, as well as the electronic effect of the malonate carbonyl groups. Presumably, as a consequence of these effects, both molecules adopt a conformationally locked structure that precludes any appreciable conjugation between the respective six π-electron subunits (benzene or pyridine) with the rest of the π-electron periphery.

SCHEME 7. Reaction of 2,5-Bisvinylthiophene Derivative with Pyrrole



SCHEME 8. "3 + 1" Condensation Product of 24 with 15



Expanded macrocycles **14** and **20** were also subject to single-crystal X-ray diffraction analysis.[19,20] Figure 2 shows the resulting structures with the hydrogen atoms omitted for clarity. As can be seen from an inspection of this figure, the expanded oxabenziporphyrin **14** adopts a severely disordered conformation. Three pyrrole rings (N1, N2, and N4) are inverted and are involved in hydrogen-bonding interactions with the carbonyl functions of the malonate groups. One pyrrole ring (N3) is not inverted, and instead, one of the malonate groups resides close to the cavity. On the other hand, the crystal structure of **20** reveals a molecule with near perfect C_{2v} symmetry where all four pyrrole rings are inverted and forming hydrogen bonds with the malonate carbonyls. Support for the proposed intramolecular hydrogen-bonding interactions came from the proton NMR spectra, with significant downfield shifts for the pyrrolic N−H resonances being observed; these signals were seen at 11.61 ppm in **20** and 11.10 ppm in **18**.

Careful analysis of the solid-state structure reveals that the bond angle (cf. Figure 3 for a schematic definition) about the 2,5-substituted furan in **14** is 133.0°, while the corresponding angle in the thiophene subunit of **20** is 157.8°. These values provide support for the notion that thiophene is better able to accommodate the formation of a larger macrocycle without being subject to undue angle strain.

With the synthesis of the benzene and pyridine-containing *meso*-alkylidenyl porphyrins **12**, **13**, **16**, and **19** accomplished, efforts were made to prepare congeneric systems containing a five-membered ring. Toward this end, 2,5-bisvinylthiophene **21** was reacted with pyrrole in the presence of $InCl_3$ in the hopes of obtaining open chain precursors analogous to **9** and **10**. However, in contrast to what was seen in the case of reactions involving the benzene and pyridine derivatives **7** and **8**, the reaction resulted in the formation of retro-Knoevenagel products, such as **22**. Lowering the reaction temperature to 0 °C afforded the thiophene-functionalized dipyrromethane **23** (Scheme 7).

Given this lack of success, precursor **24**, bearing a single ethoxycarbonyl group on each methylene bridge, was prepared; it was synthesized by condensing the corresponidng carbinol with pyrrole as shown in Scheme 8. Condensing **24** with diol **15** in the usual manner then provided porphyrin **25** bearing a single ethyl acetate group on the meso positions.

The introduction of a single ethoxycarbonyl substituent on each of the *meso*-methylene groups was expected to reduce the steric congestion about these positions, leading to the prediction that in the case of **25**, the analogous alkylidenyl porphyrin **26** would not be formed. Indeed, no evidence of the latter species was observed, with the aromatic porphyrin **25** being the sole product isolated when precursors **15** and **24** were subject to condensation according to the conditions of Scheme 5. This result stands in contrast to what was seen in the case of the

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phenyl- and pyridine-containing systems described earlier in this paper and provides support for the notion that an appropriate combination of factors is needed to obtain the nonaromatic alkylidenyl products. On the basis of the present study, two such leading factors are (i) the presence of a subunit, such as a 1,3-linked benzene ring, that disrupts the conjugation pathway and (ii) a highly hindered exocyclic *meso*-methylene substituent.

Unfortunately, a full distinction between these two effects is not currently possible. In particular, the exact effect of the size of the exocyclic *meso*-methylene substituent is difficult to quantify at present. This is because attempted syntheses of the *meso*-ethylaceto-substituted version of **9**, the key intermediate required for a synthesis of an alkylidenyl porphyrin analogous to **26** (e.g., **27**), proved to be unsuccessful. Attempts to prepare such a product via the reaction of 1,3-bis(2-ethoxycarbonyl-vinyl)-benzene with pyrrole in the presence of various acids (BF_3, TFA, In(III), K-10 clay, Pd(II), trifluoromethane sulfonic acid, etc.) resulted only in extensive decomposition of the pyrrole with, in particular, no *meso*-(*mono*-ethoxycarbonyl) analogues of **9** being obtained.

Conclusion

We have demonstrated that *meso*-alkylidenyl porphyrins, bearing multiple exocyclic double bonds at the meso positions, can be synthesized using a simple "3 + 1" condensation. Introduction of bulky electron-withdrawing groups at the meso positions in combination with conjugation-disrupting core modifications permits the isolation and characterization of what would otherwise be expected to be rather unstable tautomeric forms. The resulting structures are all nonaromatic and are characterized by puckered geometries. The distortion is most apparent near the bridging six-membered ring (benzene or pyridine in the present case), while the other parts of the porphyrinoids exhibit features consistent with a partially conjugated electronic structure. In one particular case, it was found that both an exocyclic tautomer **16** and the corresponding endocyclic tautomer **17** could be isolated from the same reaction sequence and independently characterized. The former could be transformed to the latter by treatment with a strong base, albeit not with complete conversion.

In the case of the expanded macrocycles, the thiophene-containing system **20** was characterized by a high degree of symmetry and thiophene subunits that were tilted well off the mean macrocycle plane. In this structure, all four pyrrole rings are inverted, and the pyrrolic N−H protons form hydrogen bonds with the carbonyl groups on the exocyclic malonate substituents. In contrast, the furan-derived macrocycle **14** is characterized by a rather distorted and irregular structure. The differences in structure between **20** and **14** are seen to correlate with the bite angle between the 2 and 5 substituents of the thiophene and furan subunits. Thus, to the extent that conclusions may be drawn from this kind of solid-state information, it appears as if the incorporation of thiophene, rather than furan, within these kinds of systems favors the formation of larger macrocycles since less angle strain is imposed during the course of the ring-forming process.

The synthetic approach presented here may allow for systematic studies of the interplay between global, macrocycle-based aromaticity and distortion in heterocyclic aromatic systems. A further potential benefit of the synthetic approach described here is that it should be amenable to future modification through (e.g., further expansion of ring size, self-assembly of monomeric units, and metal complexation). Work along these lines is currently in progress.

Experimental Section

Pyrrole was distilled at atmospheric pressure from CaH_2. Compounds **7**−**11**, **15**, and **21** were synthesized using slight modifications of published procedures.[18,19]

6,21-Bis(diethoxycarbonylmethylidene)-11,16-diphenyl-24-oxabenziporphyrin (12), Expanded Macrocycle (14).[21−26] Compounds **9** (0.11 g, 0.2 mmol) and **11** (0.062 g, 0.22 mmol) were dissolved in CH_3CN (20 mL) with stirring. TFA (0.040 mL, 0.52 mmol) was then added. The whole mixture was stirred for 24 h at 25 °C. At this juncture, DDQ (0.14 g, 0.62 mmol) and TEA (0.10 mL, 0.72 mmol) were added. The mixture was stirred for 1 h and extracted with CH_2Cl_2 after adding brine (40 mL). The organic layer was collected and dried (Na_2SO_4) before the solvent was removed in vacuo. The mixture was chromatographed over silica gel, eluting with CH_2Cl_2/EtOAc (19:1) to afford a crude mixture of **12** and **14**. Final purification of **12** and **14** was accomplished by repeated column chromatography over silica gel adopting EtOAc/hexanes 1:2 as the eluent. Compound **12** was eluted first followed by **14**. For **12**: Yield: 0.032 g (20%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 (br s, 2H), 7.49−7.20 (m, 14H), 6.71−6.68 (m, 2H), 6.18 (s, 2H), 5.77−5.75 (m, 2H), 4.29 (q, J = 7.13 Hz, 4H), 4.06 (q, J = 7.11 Hz, 4H), 1.29 (t, J = 7.13 Hz, 6H), 1.13 (t, J = 7.11 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 164.1, 154.6, 143.4, 138.4, 135.2, 132.2, 131.5, 128.7, 128.6, 128.3, 127.9, 126.5, 124.9, 120.3, 115.5, 115.2, 108.1, 51.6, 50.9, 13.9, 13.9; MALDI-TOF MS Calcd for $C_{48}H_{42}N_2O_9$ exact mass 790.29, found 790.34. For **14**: Yield: 0.0062 g (2%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.29 (br s, 1H), 11.58 (br s, 3H), 7.41−7.16 (m, 32H), 6.30 (s, 4H), 6.17−6.15 (m, 4H), 4.03−3.78 (m, 16H), 1.21−0.76 (m, 24H); ^{13}C NMR (100

(21) Crystal data for **14** : $C_{97}H_{86}N_4O_{18}$, triclinic, space group $P\bar{1}$, a = 16.3452(3) Å, b = 17.9863(3) Å, c = 18.0871(4) Å, α = 66.749(1)°, β = 85.227(1)°, γ = 63.118(1)°, V = 4330.46 Å^3, T = 153(2) K, Z = 2, GOF on F^2 = 0.995, R1 ($I > 2\sigma(I)$) = 0.0676, wR2 = 0.1406. Crystal data for **20**: $C_{112}H_{120}N_4O_{16}S_2$, triclinic, space group $P\bar{1}$, a = 13.3598(3) Å, b = 18.5652(4) Å, c = 23.1445(6) Å, α = 71.668(1)°, β = 84.352(1)°, γ = 77.554(1)°, 5318.2(2) Å^3, T = 153(2) K, Z = 2, GOF on F^2 = 1.202, R1 ($I > 2\sigma(I)$) = 0.1714, wR2 = 0.1831. Crystals grew as dark, almost black prisms by slow evaporation from hexanes. The data crystal was a prism that had approximate dimensions of 0.22 mm × 0.20 mm × 0.07 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with Mo Kα radiation (λ = 0.71073Å). A total of 313 frames of data was collected using ω-scans with a scan range of 1.3° and a counting time of 204 s per frame. The data were collected at 153 K using an Oxford Cryostream low temperature device. Data reduction was performed using DENZO-SMN.[22] The structure was solved by direct methods using SIR97[23] and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97.[24] The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2 × Ueq of the attached atom (1.5 × Ueq for methyl hydrogen atoms). A molecule of what appears to be *n*-hexane was found to be disordered near the center of the macrocycle. In addition, sandwiched between adjacent molecules of the macrocycle that were related by 1 − x, 1 − y, and −z, there were additional disordered solvent molecules. All solvate molecules were severely disordered. Therefore, the contribution to the scattering by the solvate was removed by use of the utility, SQUEEZE, in PLATON98.[25] PLATON98 was used as incorporated in WinGX.[26]

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MHz, $CDCl_3$) δ 166.27, 156.36, 131.19, 128.71, 127.96, 126.50, 108.70, 61.10, 60.84, 13.95; MALDI-TOF MS Calcd for $C_{96}H_{84}N_4O_{18}$ exact mass 1580.58, found 1581.62.

6,21-Bis(diethoxycarbonylmethylidene)-11,16-diphenyl-24-oxapyriporphyrin (13). Compounds **10** (0.10 g, 0.19 mmol) and **11** (0.059 g, 0.21 mmol), TFA (0.050 mL, 0.65 mmol), DDQ (0.13 g, 0.57 mmol), and TEA (0.10 mL, 0.72 mmol) were used to prepare this product using a procedure identical to that used to prepare **12**. The mixture was chromatographed over silica gel, eluting with CH_2Cl_2/EtOAc (19:1) during the first purification and then with EtOAc/hexanes (1:2) during subsequent purifications. Yield: 0.028 g (19%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.09 (brs, 2H), 7.76 (t, J = 7.76 Hz, 1H), 7.40 (d, J = 7.76 Hz, 2H), 7.38−7.26 (m, 10H), 6.74−6.17 (m, 2H), 6.17 (s, 2H), 5.80−5.78 (m, 2H), 4.29 (q, J = 7.13 Hz, 4H), 4.07 (q, J = 7.10 Hz, 4H), 1.28 (t, J = 7.13 Hz, 6H), 1.15 (t, J = 7.10 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 163.4, 156.1, 154.4, 142.1, 138.3, 136.46, 135.5, 131.5, 128.3, 127.9, 126.3, 123.6, 121.2, 115.7, 115.6, 108.1, 61.7, 61.0, 14.0, 13.9; MALDI-TOF MS Calcd for $C_{47}H_{41}N_3O_9$ exact mass 791.28, found 791.34.

6,21-Bis(diethoxycarbonylmethylidene)-11,16-di(*p*-tolyl)-24-thiapyriporphyrin (16), 6,21-Bis(diethylmalonyl)-11,16-di(*p*-tolyl)-24-thiapyriporphyrin (17), and Expanded Macrocycle (18). Compound **10** (0.32 g, 0.59 mmol) and diol **15** (0.23 g, 0.70 mmol) were dissolved in CH_3CN (60 mL) with stirring. NH_4Cl (0.31 g, 0.59 mmol) and TFA (0.16 mL, 2.05 mmol) were then added. The whole mixture was stirred for 4.5 h at 25 °C before DDQ (0.46 g, 2.05 mmol) and TEA (0.24 mL, 2.34 mmol) were added successively. The resulting mixture was stirred for 1 h and extracted with CH_2Cl_2 after adding brine (50 mL). The organic layer was collected and dried (Na_2SO_4) before the solvent was removed in vacuo. The resulting solid contained all three compounds. Column chromatography over silica gel while eluting with CH_2Cl_2/EtOAc (19:1) afforded **17** as a fast moving fraction. The other fractions were not separated clearly, and thus, further column chromatographic purifications were performed. The mixture of **16** and **18** can be separated by repeated column chromatography over silica gel using EtOAc/hexanes 1:2 as the eluent. Compound **16** was eluted first followed by **18**. For **16**: Yield: 0.047 g (10%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.63 (br s, 2H), 7.86 (t, J = 7.76 Hz, 1H), 7.42 (d, J = 7.76 Hz, 2H), 7.24−7.16 (m, 8H), 6.75−6.72 (m, 2H), 6.61 (s, 2H), 6.07−6.05 (m, 2H), 4.41−4.28 (m, 4H), 4.09 (q, J = 7.10 Hz, 4H), 2.39 (s, 6H), 1.31 (t, J = 7.13 Hz, 6H), 1.16 (t, J = 7.10 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.4, 162.8, 155.8, 140.6, 138.2, 136.7, 136.6, 136.5, 135.2, 132.7, 130.6, 130.5, 129.0, 124.0, 122.5, 121.4, 116.7, 114.8, 61.8, 61.0, 21.3, 14.0, 13.9; MALDI-TOF MS Calcd for $C_{49}H_{45}N_3O_9S$ exact mass 835.29, found 834.83. For **17**: Yield: 0.008 g (2%); ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C) δ 7.73 (t, J = 7.76 Hz, 1H), 7.30−7.21 (m, 8H), 7.19 (d, J = 7.76 Hz, 2H), 6.81−6.77 (m, 4H), 6.79 (s, 2H), 4.39−4.22 (m, 4H), 4.13 (q, J = 6.82 Hz, 4H), 2.42 (s, 6H), 1.29 (t, J = 7.14 Hz, 6H), 1.12 (t, J = 7.12 Hz, 6H); ^{1}H NMR (400 MHz, $CDCl_3$, 0 °C) δ 7.80 (t, J = 7.75 Hz, 1H), 7.33−7.28 (m, 8H), 7.25 (d, J = 7.75 Hz, 2H), 6.85−6.82 (m, 4H), 6.84 (s, 2H), 5.18 (s, 2H), 4.40−4.35 (m, 2H), 4.29−4.24 (m, 2H), 4.16−4.08 (m, 4H), 2.44 (s, 6H), 1.39 (t, J = 7.12 Hz, 6H), 1.15 (t, J = 7.11 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.5, 166.3, 163.6, 158.4, 155.0, 153.3, 147.0, 146.6, 139.6, 135.2, 135.0, 134.1, 130.9, 129.7, 128.6, 128.0, 123.4, 62.0, 61.5, 21.4, 13.9, 13.8; MALDI-TOF MS Calcd for $C_{49}H_{45}N_3O_9S$ exact mass 835.29, found 834.91. For **18**: Yield: 0.016 g (2%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.10 (br s, 4H), 7.69 (t, J = 7.70 Hz, 2H), 7.35 (d, J = 7.70 Hz, 4H), 7.26−7.20 (m, 16H), 7.10−6.83 (m, 4H), 6.52 (s, 4H), 6.02 (m, 4H), 4.12−4.06 (m, 16H), 2.40 (s, 12H), 1.15 (t, J = 7.07 Hz, 12H), 1.09 (t, J = 6.97 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.0, 156.7, 142.7, 141.9, 138.6, 137.7, 135.5, 133.0, 130.9, 130.6, 129.8, 129.3, 129.1, 128.8, 123.7, 122.9, 116.0, 114.2, 61.4, 60.9, 29.7, 21.3, 14.0, 13.9; MALDI-TOF MS Calcd for $C_{98}H_{90}N_6O_{16}S_2$ exact mass 1670.59, found 1672.26.

6,21-Bis(diethoxycarbonylmethylidene)-11,16-di(*p*-tolyl)-24-thiabenziporphyrin (19) and Expanded Macrocycle (20). Compounds **9** (0.33 g, 0.60 mmol) and **15** (0.21 g, 0.66 mmol), NH_4Cl (0.29 g, 0.54 mmol), TFA (0.15 mL, 1.88 mmol), DDQ (0.47 g, 2.09 mmol), and TEA (0.33 mL, 2.39 mmol) were used to prepare these products using a procedure identical to that used for the synthesis of **16**. The crude product mixture was chromatographed over silica gel, eluting first with CH_2Cl_2/EtOAc (9:1) during the first purification and then with EtOAc/hexanes (1:3) during a follow-up chromatographic purification step; this allowed isolation of two different products (**19** and **20**). For **19**: Yield: 0.038 g (8%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.56 (br s, 2H), 7.56 (t, J = 7.62 Hz, 1H), 7.44 (s, 1H), 7.40 (d, J = 7.62 Hz, 2H), 7.22−7.15 (m, 8H), 6.75−6.73 (m, 2H), 6.57 (s, 2H), 6.02−6.00 (m, 2H), 4.45−4.28 (m, 4H), 4.11−4.03 (m, 4H), 2.38 (s, 6H), 1.35 (t, J = 7.12 Hz, 6H), 1.14 (t, J = 7.09 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.6, 163.6, 141.5, 138.2, 137.3, 136.7, 136.4, 135.3, 132.6, 131.3, 130.6, 129.0, 128.9, 128.8, 128.1, 122.5, 120.1, 116.8, 114.6, 61.8, 60.9, 21.3, 13.9; MALDI-TOF MS Calcd for $C_{50}H_{46}N_2O_9S$ exact mass 834.30, found 834.57. For **20**: Yield: 0.013 g (1%); ^{1}H NMR (400 MHz, CD_2Cl_2) δ 11.61 (br s, 4H), 7.34−7.22 (m, 24H), 7.18−7.14 (m, 4H), 6.54 (s, 4H), 6.02 (m, 4H), 4.04−3.87 (m, 16H), 2.42 (s, 12H), 1.19−1.04 (m, 24H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.3, 144.1, 138.1, 137.7, 130.6, 129.3, 128.8, 126.4, 123.9, 123.0, 116.3, 61.3, 60.9, 53.4, 31.9, 30.2, 29.7, 29.4, 22.7, 21.3, 14.2, 14.1, 14.0, 13.9, 1.0; MALDI-TOF MS Calcd for $C_{100}H_{92}N_4O_{16}S_2$ exact mass 1668.59, found 1670.61.

2,5-Bis[bis(pyrrol-2-yl)methyl]thiophene (22). Indium(III) chloride (0.13 g, 0.56 mmol) was added to a solution of 2,5-bis(2,2-diethoxycarbonylvinyl)thiophene **21** (0.18 g, 0.43 mmol) and pyrrole (1.2 mL, 17.07 mmol). The mixture was stirred for 2 h at room temperature. At this point, the mixture was combined with brine (10 mL) and extracted with CH_2Cl_2. The organic layer was collected and dried (Na_2SO_4) before the solvent was removed in vacuo. The resulting solid was purified by column chromatography over silica gel ($CHCl_3$/EtOAc/hexanes = 8:1:1) to obtain product **22**. Yield: 0.13 g (82%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.99 (br s, 4H), 6.72 (s, 2H), 6.70−6.68 (m, 4H), 6.16−6.13 (m, 4H), 6.03 (m, 4H), 5.65 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 143.7, 130.8, 124.0, 116.5, 116.4, 107.3, 107.2, 106.0, 105.9, 38.2; EI MS Calcd for $C_{22}H_{20}N_4S$ exact mass 372.14, found 372.14.

2-(2,2-Diethoxycarbonylvinyl)-5-[bis(pyrrole-2-yl)methyl] (23). 2,5-Bis(2,2-diethoxycarbonylvinyl)thiophene **21** (0.09 g, 0.22 mmol), pyrrole (0.6 mL, 8.53 mmol), and indium(III) chloride (0.06 g, 0.28 mmol) were treated in the same way as in the synthesis of **22** except the reaction temperature employed was 0 °C. Yield: 0.05 g (74%); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.06 (br s, 2H), 7.23 (s, 1H), 7.20 (d, J = 3.73 Hz, 1H), 6.82 (d, J = 3.73 Hz, 1H), 6.68−6.66 (m, 2H), 6.16−6.13 (m, 2H), 6.02 (m, 2H), 5.67 (s, 1H), 4.33−4.22 (m, 4H), 1.32−1.27 (m, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.7, 164.7, 153.7, 135.5, 135.4, 135.2, 131.3, 126.7,122.0, 118.2, 109.0, 107.8, 62.3, 62.0, 39.9, 14.6, 14.3; EI MS Calcd for $C_{21}H_{22}N_2O_4S$ exact mass 398.13, found 398.00.

2,5-Bis[(α-ethoxycarbonylmethyl-α-(pyrrole-2-yl))methyl]-thiophene (24). 3-[5-(2-Ethoxycarbonyl-1-hydroxyethyl)-thiophen-2-yl]-3-hydroxypropionic acid ethyl ester (0.9 g, 2.85 mmol) was dissolved in neat pyrrole (5 mL, 72 mmol), and then BF_3•OEt_2 (1.24 mL, 9.8 mmol) was added. The mixture was stirred for 5 h at room temperature. The reaction was quenched by the addition of aqueous NaOH (0.1 N) and extracted with CH_2Cl_2. The organic layer was collected and washed with water and dried (Na_2SO_4). The solvent was removed in vacuo, and the resulting solid was purified by column chromatography over silica gel (eluent: CH_2Cl_2/EtOAc = 19:1). Yield 0.72 g (71%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.32 (br s, 2H), 6.66−6.64 (m, 4H), 6.11−6.08 (m, 2H), 5.97 (s, 2H) 4.70 (t, J = 7.31 Hz, 2H), 4.09 (q, J = 7.14 Hz, 4H), 3.07−2.89 (m, 4H), 1.19 (t, J = 7.14, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 144.8, 132.8, 124.2, 124.2, 117.3, 108.1, 105.4, 60.8, 41.7, 41.7, 36.1; EI MS Calcd for $C_{22}H_{26}N_2O_4S$ exact mass 414.16, found 414.00.

5,20-Bis(ethoxycarbonylmethyl)-10,15-di(*p*-tolyl)-21,23-dithiaporphyrin (25). Compounds **24** (0.21 g, 0.51 mmol) and **9** (0.17 g, 0.51 mmol) were dissolved in CH_3CN (51 mL), and TFA (0.069 mL, 0.93 mmol) was added. The mixture was stirred for 30 min at room temperature. At this point, DDQ (0.34 g, 0.15 mmol) was added, and the reaction mixture was stirred an additional 1 h. The reaction was quenched by adding saturated aqueous $NaHCO_3$ (70 mL) and extracted with CH_2Cl_2. The organic layer was collected and dried (Na_2SO_4) before the solvent was removed in vacuo. The resulting solid was purified by preparative TLC (eluent: EtOAc/hexanes = 1:2). Yield 0.067 g (19%); ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.27 (s, 2H), 9.62 (s, 2H) 9.26−9.25 (d, J = 4.6 Hz, 2H), 8.75−8.73 (d, J = 4.6 Hz, 2H), 8.09−8.07 (d, J = 7.83 Hz, 4H), 7.61−7.59 (d, J = 7.83 Hz, 4H), 5.97 (s, 4H), 4.19−4.14 (q, J = 7.10, 4H), 2.70 (s, 6H), 1.13−1.09 (t, J = 7.07, 6H) ^{13}C NMR (100 MHz, CDCl3) δ 171.5, 157.1, 156.4, 148.1, 147.6, 138.1, 137.9, 135.6, 135.4, 134.34, 134.1, 133.2, 132.0, 128.2, 125.5, 124.2, 61.5, 40.8, 34.2, 30.3, 29.7, 21.5, 14.1; MALDI-TOF MS Calcd for $C_{42}H_{38}N_2O_4S_2$ exact mass 698.21, found 697.26.

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Supporting Information Available: Synthetic details of all compounds, spectroscopic data, and single-crystal X-ray data. This material is available free of charge via the Internet at http://pubs.acs.org.

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