JOC The Journal of Organic Chemistry

Article

pubs.acs.org/joc

Synthesis of Three Asymmetric N-Confused Tetraarylporphyrins

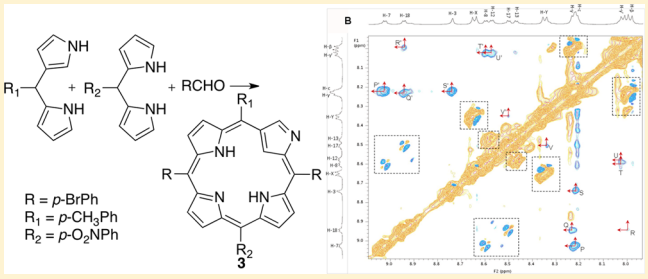
Rajendra Acharya,[†,‡] Liladhar Paudel,[†] Jojo Joseph,[†,‡] Claire E. McCarthy,[§] Venkat R. Dudipala,[†] Jody M. Modarelli,[§] and David A. Modarelli*[,†,‡]

[†]Department of Chemistry and [‡]The Center for Laser and Optical Spectroscopy, Knight Chemical Laboratory, The University of Akron, Akron, Ohio 44325-3601, United States

[§]Department of Chemistry, Hiram College, Hiram, Ohio 44234, United States

Supporting Information

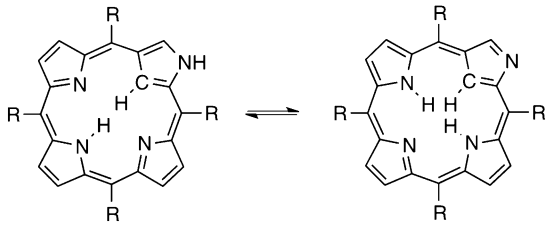
ABSTRACT: Two monosubstituted and one tetrasubstituted N-confused porphyrins (**1**–**3**) were prepared in ca. 3–5% yields using a [2 + 2] synthesis. The monosubstituted porphyrins have carbomethoxy (**1**) or nitro (**2**) substituents on one of the *meso*-phenyl groups, while the *meso*-phenyl groups of the third NCP (**3**) are substituted with nitro, bromo, and methyl groups in an AB_2C pattern. The specific regiochemistry of the aryl rings around the macrocycle in each porphyrin was definitively determined using a combination of 1D (^{1}H and ^{13}C) and 2D (gHMBC, gHSQC and ROESY) NMR spectroscopy. The absorption spectra of **1**–**3** in CH_2Cl_2 are similar to those of N-confused tetraphenylporphyrin (NCTPP) but have Soret and Q bands that are shifted to lower energies with smaller extinction coefficients in comparison to those for NCTPP.



INTRODUCTION

Naturally occurring porphyrins and their derivatives[1,2] are ubiquitous in nature, where they are utilized in the light-harvesting complexes (LHCs) and the photosynthetic reaction centers (PRCs) of purple bacteria and green plants.[3−7] The synthesis of many regular porphyrins is straightforward, and a significant body of work has therefore used synthetically derived porphyrins such as tetraphenylporphyrin (H_2TPP) and its various metallo derivatives (MTPP) in electron donor–acceptor arrays.[8−11] The high symmetry present in free-base (D_{2h}) and metallo (D_{4h}) porphyrins leads to near-degeneracies in the four interacting Gouterman molecular orbitals (MOs). The resulting absorption spectra typically have an intense Soret band but weak low-energy Q-band transitions. The lower symmetry (C_1) of BChl*a*s and chlorins lifts the degeneracies in the four interacting orbitals, resulting in significantly more intense Q bands[12,13] that are red-shifted from those of their porphyrin analogues and are better suited for absorbing solar radiation. The synthesis of chlorophylls is nontrivial,[12−14] and their incorporation into arrays and devices for energy conversion is not common. Interest in the preparation of unusual porphyrins and porphyrinoids is therefore partly driven in response to solar energy related research.

N-confused tetraphenylporphyrins (NCTPP) are analogues of regular porphyrins that differ from H_2TPP by inversion of one pyrrole ring. Two tautomeric forms of NCTPP are observed in solution,[15] one (NCTPPe) of which has an external N–H group and appears to be stabilized by highly polar solvents, while the other (NCTPPi) has two internal N–H groups and appears to be preferred in less polar solvents. The Soret ($S_0 \rightarrow S_2$) and Q-band ($S_0 \rightarrow S_1$) transitions in the absorption spectra of both tautomers are red-shifted relative to those of H_2TPP, while the Q-band transitions are more intense than those of H_2TPP and have larger extinction coefficients. The changes in these absorption properties have been attributed[16−18] to a break in the degeneracy of the four Gouterman orbitals.[19] We have explored the excited-state properties of the two tautomers in detail and found fluorescence quantum yields of 0.023 (NCTPPi) and 0.046 (NCTPPe) and excited state lifetimes of 1.47 ns (NCTPPi) and 1.84 ns (NCTPPe),[16,17,20] all of which indicate they might be useful in solar energy conversion applications.



Proper substitution on the NCP macrocycle is a prerequisite for the covalent incorporation of NCPs into electron donor–acceptor arrays.[21] We previously prepared tetraaryl NCPs (where all four *meso* substituents were identical; i.e., A_4) bearing

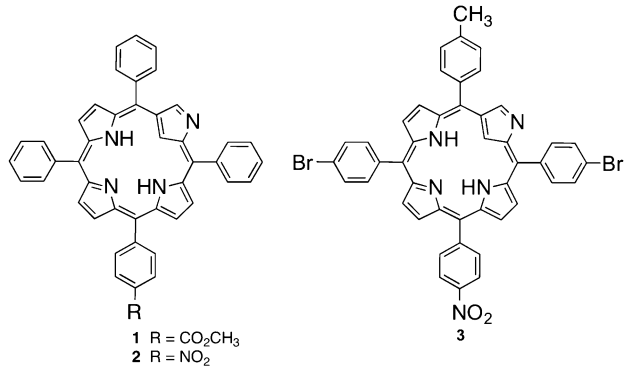
Received: April 20, 2012
Published: June 25, 2012

a variety of functional groups on the *meso*-phenyl groups in good yields[22] using Lindsey's conditions.[23] Our subsequent attempts to use a statistical approach to prepare disubstituted (i.e., A_2B_2, where A and B represent different *meso* aryl groups) NCPs using equal amounts of two different aldehydes were very much limited by the fact the regiochemistry of the final product could not be controlled, and multiple chromatographic separations were required to isolate the isomers that were characterized completely.[24]

MacDonald's pioneering report[25] of porphyrin synthesis via the [2 + 2] addition of *meso*- or *β*-substituted dipyrromethanes opened the field toward the rational, nonstatistical synthesis of asymmetrically substituted porphyrins (A_2B_2, A_3B, AB_2C, and ABCD).[26−29] The most common approach is to use 5-substituted dipyrromethanes,[30,31] and the related 1,9-diformyldipyrromethane, 1,9-dicarboxyldipyrromethane, and 1,9-carbinoldipyrromethane derivatives, as synthetic precursors for the final porphyrin.[32] Tripyrromethanes[33] and 2,5-dicarbinolpyrrole have also been extensively used in [3 + 1] synthetic approaches.[34−37] Mixtures of porphyrin isomers are often obtained in these methods as a result of scrambling of the dipyrromethane and tripyrromethane groups during the cyclization.[38] The Lindsey group has done much work to minimize scrambling, focusing in particular on reaction conditions, choice of acid catalyst, and concentration effects.[30,39]

Because the N-confused porphyrin macrocycle is itself asymmetric, the synthesis of NCPs having different *meso* substituents using the [2 + 2] methodology requires the use of a confused dipyrromethane group to prepare half of the macrocycle. N-confused dipyrromethane (2,3-dipyrromethane) is an isomer of 2,2-dipyrromethane with the *meso* carbon attached to C-3 instead of C-2 in one of the pyrrole rings. Lindsey has shown that acylation of 1-(triisopropylsilyl)pyrrole, followed by deprotection, reduction, and finally acid-catalyzed condensation with pyrrole, yields N-confused dipyrromethanes in good yields.[30]

In addition to the [2 + 2] approach to substituted NCPs, Furuta,[40] Lash,[41] and others[42] have pioneered the synthesis of asymmetric N-confused porphyrins (AABB, A_2B_2, A_3B) using the [3 + 1] condensation reaction between tripyrromethane and 2,4-dicarbinolpyrroles or 2,4-dicarbaldehydepyrroles. Condensation reactions between 1,9-dicarbinoldipyrromethane[43] and N-confused dipyrromethane or between dipyrromethane and N-confused dipyrromethane derivatives[21,44,45] have also been used to prepare substituted NCPs.



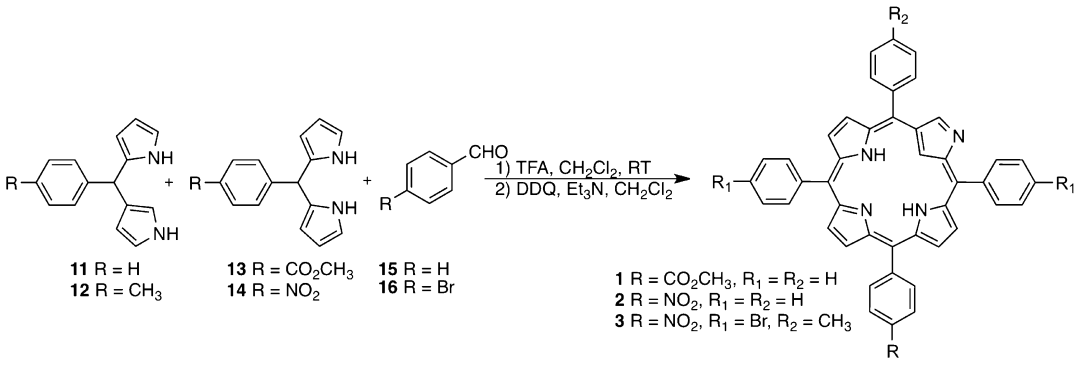
In this paper, we report the synthesis and characterization of three different asymmetric *meso*-substituted porphyrins by [2 + 2] condensation reactions of regular and N-confused dipyrromethanes using TFA as a catalyst. We were able to isolate only one N-confused porphyrin regioisomer in each synthesis, although the 5,15- and 5,10-disubstituted regular porphyrins, obtained from homocoupling of two regular dipyrromethanes in the case of the nitro- and ester-substituted reactions, were also isolated in 3 and 2% yields, respectively. The use of $BF_3{\cdot}OEt_2$ and $MeSO_3H$ as catalysts was also attempted. In our hands, $BF_3{\cdot}OEt_2$ was found to result in slow reactions and reduced NCP yields, while $MeSO_3H$ gave higher yields of NCPs but mixtures of at least three NCP regioisomers (as determined by NMR of the crude reaction mixture after separation from the regular porphyrin).

RESULTS AND DISCUSSION

Synthesis. The three N-confused porphyrins described here were prepared using a [2 + 2] approach (Scheme 1) involving 1 equiv of an inverted dipyrromethane (**11** or **12**), 1 equiv of a regular dipyrromethane (**13** or **14**), and 2 equiv of an aldehyde (**15** or **16**) (Scheme 1).

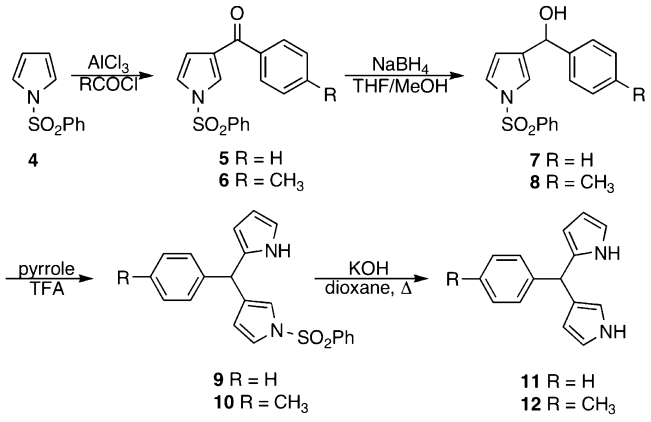
The inverted dipyrromethanes were synthesized from literature procedures in five steps from pyrrole, the syntheses of which are shown in Scheme 2. Protection of pyrrole with phenylsulfonyl chloride yielded 1-(*N*-phenylsulfonyl)pyrrole (**4**).[46] Friedel−Crafts acylation using either benzoyl chloride or 4-methylbenzoyl chloride produced 1-(*N*-phenylsulfonyl)-3-benzoylpyrrole (**5**) or 1-(*N*-phenylsulfonyl)-3-(4-methylbenzoyl)pyrrole (**6**) in 69% and 55% yields, respectively.[47] Reduction of **5** or **6** with $NaBH_4$ followed by addition of the second pyrrole group using TFA[48] resulted in formation of **9** and **10** in 67% and 65% yields, respectively. Deprotection of the sulfonyl group with KOH produced dipyrromethanes **11**

Scheme 1



dx.doi.org/10.1021/jo300810n | J. Org. Chem. 2012, 77, 6043−6050

Scheme 2



and **12** in 39% and 32% overall yields.[49] The preparation of 5-(4-carbomethoxyphenyl)dipyrromethane (**13**) and 5-(4-nitrophenyl)dipyrromethane (**14**) was accomplished using a 50-fold excess of pyrrole with the appropriate aldehyde in the presence of a catalytic amount of trifluoroacetic acid.[50]

NCPs **1**−**3** were then prepared as shown in Scheme 1 by stirring 1 equiv of the N-confused dipyrromethane (**11** or **12**), one of the appropriate regular dipyrromethanes (**13** or **14**), and 2 equiv of an aldehyde (**15** or **16**) together with a catalytic amount of trifluoroacetic acid (TFA). Oxidation with DDQ afforded the NCPs in 3−4% yields. The desired NCP was purified by sequential chromatographic separations on silica followed by alumina and then finally recrystallized from $CHCl_3$/MeOH (**1** and **2**) or $CHCl_3$ (**3**). NCPs **1**−**3** were identified using UV−vis, NMR, and high-resolution MALDI-TOF or high-resolution ESI mass spectrometry. The ^{1}H NMR spectra of NCPs are unique relative to those of regular porphyrins because of their characteristic upfield resonances resulting from the inner NH and CH protons at ca. −2.4 and −5.0 ppm, respectively. Unfortunately, the propensity for acid-catalyzed cyclizations to scramble the *meso*-phenyl groups makes identification of the regioisomer formed during synthesis difficult. With this issue in mind, we performed detailed 2D-NMR (gHMBC, gHSQC, ROESY) experiments on **1**−**3**; this work is described in the following section.

Lindsey[51] has investigated the yield and amount of scrambling in [2 + 2] cyclizations of asymmetric regular porphyrins using TFA and BF_3·OEt_2 as acid catalysts. Their work indicated that both catalysts produce reasonable yields of porphyrin with some scrambling, with the ultimate results apparently dependent on the dipyrromethane substitution. In the present work, BF_3·OEt_2 as the catalyst led to slow reaction times and small yields of the NCP. Methanesulfonic acid, which has been found[23] to produce optimal yields of NCP in the preparation of A_4-tetrasubstituted NCPs, was indeed observed to produce higher overall yields of N-confused porphyrins **1**−**3**. Unfortunately, the use of this catalyst also resulted in the formation of a mixture of additional N-confused porphyrins that were identified after separation from the regular porphyrin impurities by the presence of closely spaced TLC spots and several upfield NMR signals around the NCP peak at ca. −5.0 ppm.

In the [2 + 2] cyclization of NCPs **1** and **2**, two regular porphyrins were also isolated from each reaction using column chromatography on alumina and identified by ^{1}H NMR. 5,10-Bis(4-carboxymethylphenyl)-15,20-diphenylporphyrin (**17**) and 5,15-bis(4-carboxymethylphenyl)-10,20-diphenylporphyrin (**18**), generated by homocoupling of the regular dipyrromethane **13**, were each isolated in ∼2% yield. 5,10-Bis(4-nitrophenyl)-15,20-diphenylporphyrin (**19**) and 5,15-bis(4-nitrophenyl)-10,20-diphenylporphyrin (**20**), similarly formed by homocoupling of **14**, were isolated in <2% yield. All four porphyrins are known compounds and were subsequently identified by ^{1}H NMR spectroscopy. The synthesis of **3** also produced a regular porphyrin (<2% yield) that has been tentatively identified by ^{1}H NMR as 5,15-bis(4-bromophenyl)-10,20-bis(4-nitrophenyl)porphyrin (**21**).

NMR Analysis. The [2 + 2] cyclization approach should predominantly produce NCPs **1**−**3**, although scrambling of the dipyrromethanes during synthesis may certainly occur. In order to determine unequivocally the structure of these N-confused porphyrins, a combination of 1D (^{1}H and ^{13}C) and 2D gradient-assisted heteronuclear multiple-bond correlation (gHMBC), gradient-assisted heteronuclear single-quantum correlation (gHSQC), and rotating frame nuclear Overhauser effect (ROESY) NMR spectroscopy was performed on each NCP. A summary of the relevant correlations follows for NCP **3**. A full interpretation of the NMR data for **3**, as well as peak assignments for **1** and **2** based on these data, is provided in the Supporting Information. Structures showing the atom numbering and the chemical shifts of each proton of NCP **3** are shown in Figure 1.

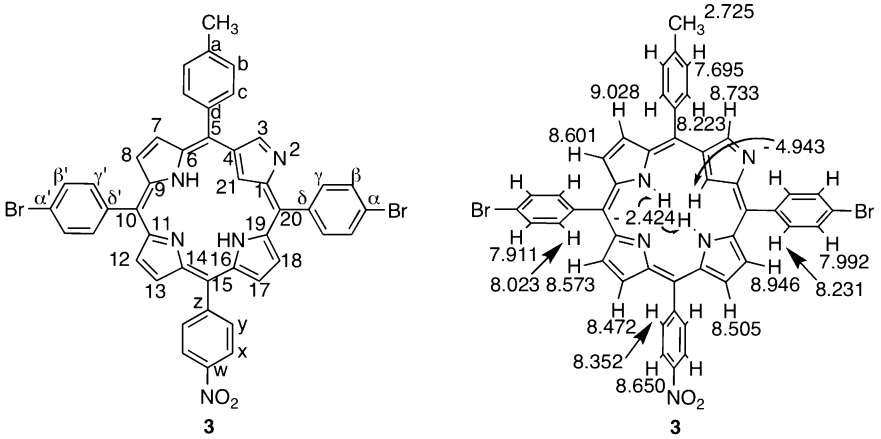


Figure 1. Atom numbers (left) and ^{1}H NMR assignments (right) for all protons of NCP **3** in $CDCl_3$.

dx.doi.org/10.1021/jo300810n | J. Org. Chem. 2012, 77, 6043−6050

The ^{1}H NMR spectra of N-confused tetraphenylporphyrins in $CDCl_3$, where NCTPPi is the predominant tautomer, are characterized by the presence of two high-field absorptions occurring at ca. −5.0 and −2.4 ppm[15] that correspond to the inner C−H and inner N−H protons, respectively. In the case of NCPs **1**−**3** these absorptions occur at δ −4.97 and −2.39 (**1**), δ −5.03 and −2.44 (**2**), and δ −4.94 and −2.42 (**3**), varying only slightly from the unsubstituted NCTPPi. The peaks corresponding to the *meso*-aryl and porphyrin resonances of **3** are clustered in the aromatic region of the ^{1}H spectrum. Similarly, the ^{13}C spectrum obtained at 500 MHz has a large number of peaks between 100 and 160 ppm. The assignments of these peaks could be unambiguously assigned only using 2D ^{1}H−^{13}C correlation experiments.

In the gHMBC spectrum, optimized to enhance three-bond ^{1}H−^{13}C cross-peaks, the singlet proton resonance (H-21, δ −4.943 ppm), which is unique to an N-confused macrocycle, shows a strong three-bond correlation to C-3 (δ 156.285 ppm). In the ROESY spectrum, the singlet proton resonance of the CH fragment at C-3 shows a pair of ROE cross-peaks to H-c on the tolyl ring, which in turn shows ROE cross-peaks to the CH proton (δ 9.028 ppm) at C-7 of the macrocycle. The proton at C-8, which shows a weak two-bond ^{1}H−^{13}C correlation to C-7 in the gHMBC spectrum, shows ROE cross-peaks to both the H-γ' proton resonance and the H-β' proton resonance on the bromophenyl group. The substitution pattern for the bromophenyl at *meso* carbon C-10 is also supported by the observation of ROE cross-peaks between both H-γ' and H-12 and H-β' and H-12. The proton resonance at H-18 exhibits a weak two-bond ^{13}C−^{1}H correlation to C-17, as well as ROE cross-peaks to both the H-γ and H-β proton resonances at the bromophenyl group at *meso* carbon C-20. Finally, the proton resonances for H-y on the nitrophenyl group show a weak ^{1}H−^{13}C two-bond correlation to C-x, and proton H-y exhibits a pair of ROE cross-peaks to the macrocyclic proton at C-17. This information is consistent only with the structure of NCP **3**, where the two bromophenyl groups are positioned at the C-10 and C-20 *meso* carbons of the NCP macrocycle and the N-confused pyrrole ring is positioned between the C-5 and C-20 *meso* carbons.

Absorption Spectra. The absorption spectra of NCPs are distinctly different from those of regular porphyrins. In the case of NCTPP, both the Soret and Q-band absorptions are significantly red-shifted relative to those of H_2TPP. These shifts, together with the increase in the extinction coefficients of the Q-band absorptions, are consistent with the break in degeneracy in the four Gouterman orbitals that is observed computationally.[16−18] In addition, the absorption spectra of the two NCP tautomers are also found to be different from one another, with NCTPPe displaying a more red-shifted Soret band and an increasing progression of band intensity with decreasing transition energy in the Q-band region. NCTPPi, on the other hand, has a Q-band structure similar to that of tetraphenylchlorin,[52] with a relatively intense low-energy $Q_y(0,0)$ at ∼724 nm.[15]

Not surprisingly, the absorption spectra of substituted NCPs **1**−**3** and NCTPPi are qualitatively similar to one another. The absorption spectra of NCPs **1**−**3** in CH_2Cl_2, together with that of NCTPPi, are shown in Figure 2 and the data summarized in Table 1. In general, the absorption bands of the substituted NCPs are all red-shifted from those of NCTPPi. For the ester-substituted **1**, the Soret band shifts 3 nm from that of NCTPPi to 440 nm, while the Q-band absorptions each shift 2−4 nm.

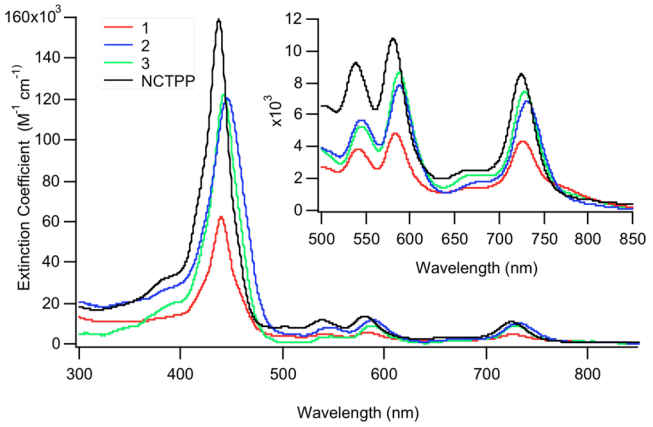


Figure 2. Absorption spectra of NCPs **1**−**3** and NCTPP in CH_2Cl_2. The inset in the upper right shows an expanded view of the Q-band region.

The changes in absorption are more pronounced for **2** and **3**. For nitro-substituted NCP **2**, the Soret band is observed to red-shift by 8 nm compared to that of NCTPPi and occurs at 445 nm. Similarly, the Q bands in this porphyrin are all red-shifted from those of NCTPPi by 6−8 nm. For tetrasubstituted **3**, the $Q_y(0,0)$ transition is red-shifted to 729 nm, and the Soret band is observed at 442 nm; the remaining Q_y band and both Q_x bands are at energies identical with those of **2**. The extinction coefficients for the Soret and Q bands of **1** are less intense than NCTPPi by a factor of ∼2−3 and are smaller than those of **2** or **3** (which are similar to one another) by ∼50%. The relative intensities of the absorption bands in each N-confused porphyrin spectrum are similar to the relative intensities in the spectrum of NCTPPi.

In summary, three asymmetric N-confused tetraarylporphyrins (**1**−**3**) have been synthesized using a modified [2 + 2] synthesis. The regiochemistry of each porphyrin was definitively determined using 1D and 2D NMR spectroscopy. The absorption spectra of **1**−**3** are found to be similar to those of NCTPPi and other previously prepared NCPs and have Soret and Q bands that are red-shifted by 2−8 nm.

EXPERIMENTAL SECTION

Synthesis of 1-(Phenylsulfonyl)-3-benzoylpyrrole (5).[48] The title compound was purified on a column of neutral silica using hexane/dichloromethane (4/6) to yield the pure compound as a viscous liquid, which turned into a white solid after a few days (3.11 g, 69%, mp 76−78 °C, lit. mp 69−72 °C[54] and 59−60 °C[53]). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 6.82 (m, 1H); 7.23 (m, 1H); 7.46−7.67 (m, 7H); 7.81 (d, 2H, J = 8.7 Hz); 7.90 (d, 2H, J = 8.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 114.3, 121.7, 126.2, 127.3, 128.1, 128.6, 129.1, 129.9, 132.5, 134.8, 138.2, 138.6, 190.0.

Synthesis of 1-(Phenylsulfonyl)-3-(4-methylbenzoyl)pyrrole (6).[55,54] The title compound was purified on a column of neutral silica using hexane/dichloromethane (4/6) to yield the pure compound as a viscous liquid, which slowly turned into a pale white solid (3.12 g, 65.8%, mp 95−97 °C). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 2.44 (s, 3H); 6.81 (t, 1H); 7.22 (t, 1H); 7.29 (d, 2H, J = 7.8 Hz); 7.50−7.57 (m, 2H); 7.66 (m, 2H); 7.74 (d, 2H, J = 8.1 Hz); 7.91 (d, 2H, J= 7.5 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 21.6, 114.2, 121.5, 125.8, 127.1, 128.2, 129.2, 129.7, 134.6, 135.8, 138.1, 143.1, 189.5.

Synthesis of (1-Phenylsulfonylpyrro-3-yl)phenylmethanol (7).[49] To a solution of **5** (2.03 g, 6.52 mmol) in 100 mL of a 3/7 mixture of methanol and THF was slowly added sodium borohydride (1.06 g, 28 mmol). After 15 min, the solvent was evaporated under vacuum, and the residue was washed with water and extracted with

dx.doi.org/10.1021/jo300810n | J. Org. Chem. 2012, 77, 6043−6050

Table 1. Experimental Absorption Data in CH_2Cl_2 for N-Confused Tetraphenylporphyrin (NCTPPi) and N-Confused Tetraarylporphyrins 1−3

		Q band (nm) (ε (10^3 M^{-1} cm^{-1}))			
compd	Soret (nm) (ε (10^4 M^{-1} cm^{-1}))				
NCTPPi	437 (15.9)	539 (7.8)	580 (10.8)	665 (2.7)	724 (10.4)
1i	440 (5.74)	541 (3.31)	583 (4.36)	664 (1.14)	726 (4.21)
2i	445 (11.9)	545 (5.70)	588 (7.88)	671 (1.71)	731 (6.86)
3i	442 (12.0)	545 (5.28)	588 (8.70)	671 (2.25)	729 (7.43)

CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed to give the product as a white solid (1.88 g, 92%, mp 80−81 °C). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 2.33 (m, 1H); 5.69 (d, 1H, J = 2.7 Hz); 6.22 (t, 1H); 7.06 (s, 1H); 7.12 (m, 1H); 7.29−7.34 (m, 5H); 7.48−7.63 (m, 3H); 7.84 (d,d, 2H, J = 7.8 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 70.8, 113.0, 118.1, 121.7, 126.6, 127.0, 128.0, 128.7, 129.6, 132.8, 134.1, 139.0, 143.1. HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{17}H_{15}NO_3SNa$ 336.0670, found 336.0667.

Synthesis of (1-Phenylsulfonylpyrro-3-yl)(3-methylphenyl)-methanol (8). To a solution of **6** (2.01 g, 6.17 mmol) in 100 mL of a 3/7 mixture of methanol and THF was slowly added sodium borohydride (1.02 g, 27 mmol). After 15 min, the solvent was evaporated under vacuum, and the residue was washed with water and extracted with CH_2Cl_2 (2 × 25 mL). The combined organic layers were dried over Na_2SO_4, and the solvent was removed to give the product as a white solid (1.91 g, 95%, mp 94−96 °C). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 2.10 (m, 1H); 2.34 (s, 3H); 5.66 (d, 1H, J = 3.9 Hz); 6.22 (t, 1H); 7.05 (s, 1H); 7.10−7.23 (m, 5H); 7.48−7.63 (m, 3H); 7.84 (d, 2H, J = 8.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 21.3, 70.6, 113.0, 118.1, 121.6, 126.6, 127.0, 129.4, 129.6, 133.0, 134.0, 137.8, 139.1, 140.2. HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{18}H_{17}NO_3SNa$ 350.0826, found 350.0815.

Synthesis of 1-(Phenylsulfonyl)-5-phenyl N-Confused Dipyrromethane (9). To a solution of pyrrole (5 mL) in 100 mL of CH_2Cl_2 was added **7** (1.50 g, 4.78 mmol). TFA (0.50 mL, 2.86 mmol) was then added and the solution stirred at room temperature for 1 h. The reaction was quenched with 50 mL of a 5% Na_2CO_3 solution. The organic layer was separated, dried over Na_2SO_4, and evaporated. The crude product was obtained as a viscous liquid, which was then purified by passing through a silica gel column with an eluent of CH_2Cl_2/EtOAc (90/10) to isolate the product as a light brown gummy solid (1.15 g, 66%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.27 (s, 1H); 5.85 (s, 1H); 6.15 (t, 1H); 6.20 (m, 1H); 6.67 (m, 1H); 6.89 (s, 1H); 7.14−7.18 (m, 3H); 7.25−7.33 (m, 3H); 7.50−7.55 (m, 2H); 7.63 (m, 1H); 7.80 (br, overlapped, 1H); 7.84 (d, 2H, J = 9 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 43.3, 107.3, 108.4, 115.0, 117.3, 119.1, 121.6, 126.9, 127.1, 128.6, 128.8, 129.6, 131.8, 133.2, 134.0, 139.2, 142.6. HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{21}H_{18}N_2O_2SNa$ 385.0986, found 385.0970.

Synthesis of 1-(Phenylsulfonyl)-5-(4-methylphenyl) N-Confused Dipyrromethane (10). To a solution of pyrrole (5 mL) in 100 mL of CH_2Cl_2 was added **8** (1.51 g, 4.6 mmol). TFA (0.5 mL, 2.86 mmol) was then added and the solution stirred at room temperature for 1 h. The reaction was quenched with 50 mL of a 5% Na_2CO_3 solution. The organic layer was separated, dried over Na_2SO_4, and evaporated. The crude product was obtained as a viscous liquid, which was then purified by passing through a silica gel column with an eluent of CH_2Cl_2/EtOAc (90/10) to isolate the product as a light brown gummy solid (1.11 g, 65%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 2.35 (s, 3H); 5.22 (m, 1H); 5.82 (s, 1H); 6.14−6.28 (m, 2H); 6.67 (s, 1H); 6.88 (s, 1H); 7.04−7.14 (m, 5H), 7.50−7.68 (m, 3H), 7.80 (br, 1H, overlapped); 7.83 (d, 2H, J = 8.4 Hz). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 21.2, 42.9, 107.1, 108.4, 115.0, 117.2, 119.1, 121.6, 126.9, 128.0, 129.4, 129.5, 132.0, 133.4, 134.0, 136.6, 139.2, 139.5. HRMS-ESI (m/z): [M + Na]$^+$ calcd for $C_{22}H_{20}N_2O_2SNa$ 399.1140, found 399.1131.

Synthesis of 5-Phenyl N-Confused Dipyrromethane (11).[30] Compound **9** (1.09 g, 3 mmol) was refluxed in 50 mL of dioxane and 25 mL of KOH (5 M) overnight. The dioxane layer was separated and the aqueous layer extracted with 25 mL of ethyl acetate. The dioxane layer was mixed with 50 mL of ethyl acetate, and the ethyl acetate layers were combined and then washed twice with water to remove dioxane. The ethyl acetate was dried over Na_2SO_4 and evaporated to yield a light yellow solid (0.63 g, 94%, mp 90−91 °C). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.40 (s, 1H); 5.93 (d,d, 1H, J = 3.9 Hz); 6.14−6.19 (m, 2H), 6.47 (m, 1H); 6.68 (m, 1H); 6.76 (m, 1H); 7.22−7.36 (m, 5H); 7.95−8.03 (br, 2H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): δ 43.5, 106.7, 108.3, 108.9, 116.6, 116.7, 118.4, 125.9, 126.5, 128.5, 128.6, 135.2, 144.7. HRMS-ESI (m/z): [M − H, ion polarity negative] calcd for $C_{15}H_{14}N_2$ 221.1078, found 221.1064.

Synthesis of 5-(4-Methylphenyl) N-Confused Dipyrromethane (12). Compound **10** (1.12 g, 2.97 mmol) was refluxed in 50 mL of dioxane and 25 mL of KOH (5 M) overnight. The dioxane layer was separated and the aqueous layer extracted with 25 mL of ethyl acetate. The dioxane layer was mixed with 50 mL of ethyl acetate, and the ethyl acetate layers were combined and then washed twice with water to remove dioxane. The ethyl acetate was dried over Na_2SO_4 and evaporated to yield **12** as an off-white gummy solid (0.64 g, 93%). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 2.34 (s, 3H); 5.35 (s, 1H); 5.91 (m, 1H); 6.12−6.18 (m, 2H); 6.49 (d, 1H, J = 1.5 Hz); 6.67 (d, 1H, J = 3.3 Hz); 6.76 (m, 1H); 7.13 (m, 4H); 7.93−8.04 (br, 2H). ^{13}C NMR (300 MHz, $CDCl_3$, ppm): 21.2, 43.1, 106.6, 108.3, 108.9, 116.4, 116.6, 118.3, 126.2, 128.5, 129.2, 135.4, 136.0, 141.7. HRMS-ESI (m/z): [M − H, ion polarity negative] calcd for $C_{16}H_{16}N_2$ 235.1235, found 235.1220.

General Procedure for the Preparation of 5-Aryl Dipyrromethanes (13 and 14).[51] To a solution of the appropriate aldehyde (20 mmol) in 70 mL of pyrrole was added TFA (0.05 mL, 0.67 mmol). After the mixture was stirred for 1.5 h at room temperature, NaOH powder (~1 g, 25 mmol) was added and the mixture was stirred for 30 min to quench the reaction. The reaction mixture was filtered, and the filtrate was collected. Excess pyrrole was recovered by distillation. The remaining dark residue was washed with hexane and purified by column chromatography on silica gel using hexane, dichloromethane, and ethyl acetate.

*Synthesis of 5-(4-Carbomethoxyphenyl)dipyrromethane (**13**).*[51] The title compound was obtained as an off-white solid (2.18 g, 39%, mp 159−161 °C, lit. mp 162−163 °C[51]). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 3.91 (s, 3H, $-CH_3$); 5.52 (s, 1H, *meso*-H); 5.90 (m, 2H, pyrrole); 6.17 (m, 2H, pyrrole); 6.71 (m, 2H, pyrrole); 7.28 (d, 2H, J = 8.4 Hz, Ar H); 7.98 (m, 4H, Ar H and NH overlapped).

*Synthesis of 5-(4-Nitrophenyl)dipyrromethane (**14**).*[51] The title compound was obtained as a light yellow solid (1.86 g, 36%, mp 161−162 °C, lit. mp 159−160 °C[58]). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 5.59 (s, 1H, *meso*-H); 5.88 (t, 2H, pyrrole); 6.18 (m, 2H, pyrrole); 6.75 (m, 2H, pyrrole); 7.37 (d, 2H, J = 8.4 Hz, Ar H); 8.00 (br, 2H, NH); 8.17 (d, 2H, J = 8.7 Hz, Ar H).

General Method for the Synthesis of *meso*-Substituted Asymmetric N-Confused Tetraphenylporphyrins (1−3). To a 500 mL round-bottom three-neck flask, the appropriate N-confused dipyrromethane (1 mmol), the appropriate regular dipyrromethane (1 mmol), and the aldehyde (2 mmol) were dissolved in a 300 mL mixture of dichloromethane and chloroform (9/1). TFA (2 mmol) was then added slowly and the reaction mixture was stirred for 3 h. DDQ (3 mmol) was added all at once and the reaction mixture stirred for 20 min more, before triethylamine (1.5 mL) was added to quench the reaction. The crude mixture was concentrated under vacuum,

dx.doi.org/10.1021/jo300810n | J. Org. Chem. 2012, 77, 6043−6050

before 5 g of alumina (neutral) was added and the solvent was evaporated. Column chromatography on alumina was performed using a gradient of CH_2Cl_2/hexane (80/20) to CH_2Cl_2/EtOAc (90/10), which first eluted the regular porphyrin, and then a dark band that contained the NCP. The NCP was further purified on subsequent columns (silica followed by alumina) as described below. ^{13}C NMR peaks are reported to three significant figures where necessary.

Synthesis of 5,10,20-Triphenyl-15-(4-carbomethoxyphenyl) N-Confused Porphyrin (1). Column chromatography on silica column using a gradient of CH_2Cl_2 (100%) to CH_2Cl_2/EtOAc (80/20) separated the dark impurities from the NCP. After careful chromatography on an alumina (neutral) column using CH_2Cl_2/EtOAc (80/20), the pure product was isolated as a purple solid (21 mg, 3.7%). ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 8.99 (d, 1H, J = 5.0 Hz, pyrrole); 8.94 (d, 1H, J = 4.5 Hz, pyrrole); 8.77 (s, 1H, pyrrole); 8.62 (d, 1H, J = 5.0 Hz, pyrrole); 8.58 (d, 1H, J = 4.5 Hz, pyrrole), 8.53 (m, 2H, pyrrole); 8.45 (d, 2H, J = 8.0 Hz, Ar H); 8.37 (d, 2H, J = 7.5 Hz, Ar H); 8.34 (d, 2H, J = 7.5 Hz, Ar H); 8.27 (d, 2H, J = 8.0 Hz, Ar H); 8.16 (m, 2H, Ar H); 7.87−7.75 (m, 9H, Ar H); 4.12 (s, 3H, -OCH_3); −2.40 (br, 2H, NH); −4.97 (s, 1H, −CH). ^{13}C NMR (500 MHz, $CDCl_3$, ppm): δ 52.4, 99.5, 117.5, 125.0, 129.7, 128.49, 128.45, 128.36, 125.6, 126.5, 126.6, 127.0, 127.6,127.7, 127.9, 128.2, 134.395, 134.402, 134.57, 134.58, 134.67, 134.97, 136.90, 136.93, 137.2, 137.4, 139.7, 140.5, 146.7, 149.8, 155.7, 156.2, 167.3. MALDI-HRMS (m/z): calcd for $C_{46}H_{32}N_4O_2$ 672.2525, found 672.2495.

Synthesis of 5,10,20-Triphenyl-15-(4-nitrophenyl) N-Confused Porphyrin (2). Chromatography on silica column using a gradient of CH_2Cl_2 (100%) to CH_2Cl_2/EtOAc (80/20) separated the dark impurities from the NCP. After careful chromatography on an alumina (neutral) column using CH_2Cl_2/EtOAc (80/20), the pure product was isolated as a dark green solid (25 mg, 3.2%). ^1H NMR (500 MHz, $CDCl_3$, ppm): δ 9.06 (d, 1H, J = 5.0 Hz, pyrrole); 8.90 (d, 1H, J = 4.5 Hz, pyrrole); 8.77 (s, 1H, pyrrole); 8.71 (d, 2H, J = 8.5 Hz, Ar H); 8.65−8.67 (m, 4H); 8.57 (d, 1H, J = 5.0 Hz, pyrrole); 8.55 (d, 2H, J = 8.5 Hz, Ar H); 8.47 (d, 1H, J = 4.5 Hz, pyrrole); 8.32−8.37 (m, 4H, Ar H); 8.17 (m, 2H, Ar H) 7.90−7.78 (m, 7H, Ar H); −2.44 (br, 2H, NH); −5.03 (s, 1H, −CH). ^{13}C NMR (500 MHz, $CDCl_3$, ppm): δ 99.5, 111.4, 115.1, 122.2, 124.5, 125.5, 126.5, 126.6, 127.1, 127.5, 127.8, 128.2, 128.7, 129.2, 134.0, 134.6, 135.1, 135.2, 135.9, 136.9, 137.16, 137.19, 139.0, 140.0, 145.7, 147.4, 147.6, 148.3, 156.2, 156.3, 156.6. MALDI-HRMS (m/z): calcd for $C_{44}H_{29}N_5O_2$ 659.2321, found 659.2291.

Synthesis of 5-(4-Tolyl)-10,20-bis(4-bromophenyl)-15-(4-nitrophenyl) N-Confused Porphyrin (3). Column chromatography on silica column using CH_2Cl_2/hexane (80/20) to CH_2Cl_2/EtOAc (90/10) separated the dark impurities from NCP. A second column chromatography using alumina (neutral) with CH_2Cl_2/EtOAc (90/10) removed all the impurities and gave the pure product as a green solid (28 mg, 3.4%). ^1H NMR (750 MHz, $CDCl_3$, ppm): δ 9.03 (d, 1H, J = 4.5 Hz, pyrrole); 8.95 (d, 1H, J = 4.5 Hz, pyrrole); 8.73 (s, 1H, pyrrole); 8.65 (d, 2H, J = 8.2 Hz, Ar H); 8.60 (d, 1H, J = 4.5 Hz, pyrrole); 8.57 (d, 1H, J = 4.5 Hz, pyrrole); 8.51 (d, 1H, J = 4.5 Hz, pyrrole); 8.47 (d, 1H, J = 4.5 Hz, pyrrole); 8.35 (d, 2H, J = 8.2 Hz, Ar H); 8.23 (m, 4H, Ar H); 8.02 (d, 2H, J = 7.5 Hz, Ar H); 7.99 (d, 2H, J = 8.2 Hz, Ar H); 7.91 (d, 2H, J = 8.2 Hz, Ar H); 7.69 (d, 2H, J = 7.5 Hz, Ar H); 2.73 (s, 3H, $-CH_3$); −2.42 (br, 2H, NH); −4.94 (s, 1H, −CH). ^{13}C NMR (750 MHz, $CDCl_3$, ppm): δ 21.5, 100.0, 115.5, 116.8, 122.2, 122.7, 123.8, 124.8, 126.1, 126.7, 127.0, 128.4, 128.7, 128.9, 130.3, 130.8, 134.3, 134.9, 135.1, 135.3. 135.9, 136.5, 136.7, 137.1, 137.6, 138.1, 138.5, 138.8, 138.9, 140.2, 140.5, 147.8, 148.5, 149.4, 155.6, 156.3, 156.7. MALDI-HRMS (m/z): calcd for $C_{45}H_{29}Br_2N_5O_2$ 829.0687, found 829.0652.

NMR/UV−Vis Characterization of 5,10-Bis(4-carboxymethylphenyl)-15,20-diphenylporphyrin (17).[55] ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.88 (overlapped d and s, 4H), 7.80 (overlapped s and d, 4H); 8.45 (d, 4H, J = 8.1 Hz); 8.31 (d, 4H, J = 8.4 Hz); 8.22 (d, 4H, J = 7.5 Hz); 7.78 (m, 6H); 4.12 (s, 6H); −2.76 (s, 2H). UV−vis (CH_2Cl_2): λ_{max} 418, 514, 550, 590, 645 nm.

NMR/UV−Vis Characterization of 5,15-Bis(4-carboxymethylphenyl)-10,20-diphenylporphyrin (18).[56] ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.87 (d, 4H, J = 4.8 Hz); 8.80 (d, 4H, J = 4.8 Hz); 8.45 (d, 4H, J = 8.1 Hz); 8.31 (d, 4H, J = 8.1 Hz); 8.22 (d, 4H, J = 7.2 Hz); 7.77 (m, 6H); 4.12 (s, 6H); −2.76 (s, 2H). UV−vis (CH_2Cl_2): λ_{max} 418, 514, 550, 590, 645 nm.

NMR/UV−Vis Characterization of 5,10-Bis(4-nitrophenyl)-15,20-diphenylporphyrin (19).[57] ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.92 (d, 2H, J = 4.5 Hz); 8.88 (s, 2H); 8.79 (s, 2H); 8.76 (d, 2H, J = 4.5 Hz); 8.65 (d, 4H. J = 8.4 Hz); 8.22 (d, 4H, J = 7.2 Hz); 7.79 (m, 6H); −2.76 (s, 2H). UV−vis (CH_2Cl_2): λ_{max} 420, 516, 553, 590, 646 nm.

NMR/UV−vis Characterization of 5,15-Bis(4-nitrophenyl)-10,20-diphenylporphyrin (20).[58] ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.92 (d, 4H, J = 4.2 Hz); 8.77 (d, 4H, J = 4.5 Hz); 8.68 (d, 4H, J = 7.5 Hz); 8.41 (d, 4H, J = 7.5 Hz); 8.22 (d, 4H, J = 7.5 Hz); 7.79 (m, 6H); −2.76 (s, 2H). UV−vis (CH_2Cl_2): λ_{max} 420, 516, 552, 590, 646 nm.

NMR/UV−Vis Characterization of 5,15-Bis(4-bromophenyl)-10,20-bis(4-nitrophenyl)porphyrin (21). ^1H NMR (300 MHz, $CDCl_3$, ppm): δ 8.90 (d, 4H, J = 5.0 Hz); 8.78 (d, 4H, J = 4.8 Hz); 8.66 (d, 4H, J = 8.4 Hz); 8.39 (d, 4H, J = 8.4 Hz); 8.08 (d, 4H, J = 8.4 Hz); 7.94 (d, 4H, J = 8.1 Hz); −2.82 (s, 2H). UV−vis (CH_2Cl_2): λ_{max} 421, 516, 552, 590, 646 nm.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Text, figures, and tables giving characterization data (^1H and ^{13}C NMR, high-resolution ESI, and TOF-MS data) of N-confused porphyrins **1**−**3** and intermediates **5**−**12**, synthetic procedures for the preparation of **1**−**3** and **5**−**12**, and detailed 1D and 2D NMR analysis of **1**−**3**. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

*E-mail: dmodarelli@uakron.edu.

Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

D.A.M. gratefully acknowledges the support of the National Science Foundation (CHE-0216371), the Ohio Board of Regents, and The University of Akron. J.M.M. acknowledges the support of the National Science Foundation (MRI-1039259). We also acknowledge the National Science Foundation (DMR-0073346 and DMR-0324964) for support of part of this research, the Kresge Foundation, and donors to the Kresge Challenge program at the University of Akron for funds used to purchase the 750 MHz NMR instrument, the Ohio Board of Regents, and the National Science Foundation (CHE-0341701 and DMR-0414599) for funds used to purchase the 500 MHz NMR instrument used in this work.

■ REFERENCES

(1) See: *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000.

(2) Gouterman, M. J. In *The Porphyrins*; Dolphin, D., Ed.; Academic Press: New York, 1978; Vol. *III*, pp 1−165.

(3) Kühlbrandt, W.; Wang, D. N.; Fujiyoshi, Y. *Nature* **1994**, *367*, 614−621.

(4) McDermott, G.; Prince, S. M.; Freer, A. A.; Hawthornthwaite-Lawless, A. M.; Papiz, M. Z.; Cogdell, R. J.; Isaacs, N. W. *Nature* **1995**, *374*, 517−521.

(5) Karrasch, S.; Bullough, P. A.; Ghosh, R. *EMBO J.* **1995**, *14*, 631−638.

(6) For reviews of the events occurring in the photosynthetic reaction center and light-harvesting complex, see: (a) Arnett, D. C.;

Moser, C. C.; Dutton, P. L.; Scherer, N. F. *J. Phys. Chem. B* **1999**, *103*, 2014−2032. (b) Pullerits, T.; Sundström, V. *Acc. Chem. Res.* **1996**, *29*, 381−389.
(7) van Amerongen, H.; van Grondell, R. *J. Phys. Chem. B* **2001**, *105*, 604−617.
(8) Collman, J. P.; Boulatov, R.; Sunderland, C. J.; Fu, L. *Chem. Rev.* **2004**, *104*, 561−588.
(9) Wasielewski, M. R. *Chem. Rev.* **1992**, *92*, 435−461.
(10) Gust, D.; Moore, T. A.; Moore, A. L. *Acc. Chem. Res.* **2001**, *34*, 40−48.
(11) Holten, D.; Bocian, D. F.; Lindsey, J. S. *Acc. Chem. Res.* **2002**, *35*, 57−69.
(12) (a) Strachan, J.-P.; O'Shea, D. F.; Balasubramanian, T.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 3160−3172. (b) Pandey, R. K.; Zheng, G. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, CA, 2000; Vol. *6*, pp 157−230. (c) Montforts, F.-P.; Gerlach, B.; Höper, F. *Chem. Rev.* **1994**, *94*, 327−347. (d) Smith, K. M. In *Chlorophylls*; Scheer, H., Ed.; CRC Press: Boca Raton, FL, 1991; pp 115−143. (e) Taniguchi, M.; Ra, D. Y.; Mo, G.; Balasubramanian, T.; Lindsey, J. S. *J. Org. Chem.* **2001**, *66*, 7342−7354.
(13) (a) Hindin, E.; Kirmaier, C.; Diers, J. R.; Tomizaki, K. Y.; Taniguchi, M.; Lindsey, J. S.; Bocian, D. F.; Holten, D. *J. Phys. Chem. B* **2004**, *108*, 8190−8200. (b) Taniguchi, M.; Kim, H. J.; Ra, D. Y.; Schwartz, J. K.; Kirmaier, C.; Hindin, E.; Diers, J. R.; Prathapan, S.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Org. Chem.* **2002**, *67*, 7329−7342. (c) Wiederrecht, G.P .; Svec, W. A.; Niemczyk, M. P.; Wasielewski, M. R. *J. Phys. Chem.* **1995**, *99*, 8918−8926. (d) Wiederrecht, G. P.; Niemczyk, M. P.; Svec, W. A.; Wasielewski, M. R. *J. Am. Chem. Soc.* **1996**, *118*, 81−88.
(14) Krayer, M.; Ptaszek, M.; Kim, H.-J.; Meneely, K. R.; Fan, D.; Secor, K.; Lindsey, J. S. *J. Org. Chem.* **2010**, *75*, 1016−1039.
(15) (a) Furuta, H.; Ishizuka, T.; Osuka, A.; Dejima, H.; Nakagawa, H.; Ishikawa, Y. *J. Am. Chem. Soc.* **2001**, *123*, 6207−6208. (b) Furuta, H.; Asano, T.; Ogawa, T. *J. Am. Chem. Soc.* **1994**, *116*, 767−768.
(16) Alemán, E. A.; Rajesh, C. S.; Ziegler, C. S.; Modarelli, D. A. *J. Phys. Chem.* **2006**, *110*, 8605−8612.
(17) Belair, J. P.; Ziegler, C. S.; Rajesh, C. S.; Modarelli, D. A. *J. Phys. Chem. A* **2002**, *106*, 6445−6451.
(18) Vyas, S.; Hadad, C.; Modarelli, D. A. *J. Phys. Chem. A* **2008**, *112*, 6533−6549.
(19) (a) Gouterman, M. *J. Mol. Spectrosc.* **1961**, *6*, 138. (b) Seybold, P. G.; Gouterman, M. *J. Mol. Spectrosc.* **1969**, *31*, 1−13.
(20) Lee, J. S.; Lim, J. M.; Toganoh, M.; Furuta, H.; Kim, D. *Chem. Commun.* **2010**, *46*, 285−287.
(21) Toganoh, M.; Miyachi, H.; Akimaru, H.; Ito, F.; Nagamura, T.; Furuta, H. *Org. Biomol. Chem.* **2009**, *7*, 3027−3030.
(22) Shaw, J. L.; Wolff, S. A.; Alemán, E. A.; Ziegler, C. J.; Modarelli, D. A. *J. Org. Chem.* **2004**, *69*, 7423−7427.
(23) Geier, G. R., III; Haynes, D. M.; Lindsey, J. S. *Org. Lett.* **1999**, *1*, 1455−1458.
(24) Wolff, S. A.; Alemán, E. A.; Banerjee, D.; Rinaldi, P. L.; Modarelli, D. A. *J. Org. Chem.* **2004**, *69*, 4571−4576.
(25) Arsenault, G. P.; Bullock, E.; McDonald, S. F. *J. Am. Chem. Soc.* **1960**, *82*, 4384.
(26) Lindsey, J. S. *Acc. Chem. Res.* **2010**, *43*, 300−311 and references therein.
(27) Bothner-By, A. A.; Lindsey, J. S. *Tetrahedron* **1995**, *51*, 11645−11672.
(28) Wallace, D. M.; Leung, S. H.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1993**, *58*, 7245−7257.
(29) Young, R.; Chang, C. K. *J. Am. Chem. Soc.* **1985**, *107*, 898−909.
(30) Litter, B. J.; Miller, M. A.; Hung, C. H.; Wagner, R. W.; O' Shea, d. F.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 1391−1396.
(31) Narayanan, S. J.; Sridevi, B.; Srinivasan, A.; Chandrashekar, T. K.; Roy, R. *Tetrahedron Lett.* **1998**, *39*, 7389−7392. Laha, J. K.; Dhanalaksmi, S.; Taniguchi, M.; Ambroise, A.; Lindsey, J. S. *Org. Process Res. Dev.* **2003**, *7*, 799−812. Gryko, D. T.; Taiov, M. *Tetrahedron Lett.* **2003**, *44*, 3317−3321. Naik, R.; Joshi, P.; Kaiwar, S. P.; Deshpande, R. K. *Tetrahedron* **2003**, *59*, 2207−2213.
(32) Yu, L.; Lindsey, J. S. *J. Org. Chem.* **2001**, *66*, 7402−7419. Lee, C.-H.; Lindsey, J. S. *Tetrahedron* **1994**, *50*, 11427−11440. Rao, P. D.; Litter, B. J.; Geir, G. R.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 1084−1092. Rao, P. D.; Dhanalekshmi, S.; Litter, B. J.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 7323−7344. Badger, G. M.; Jones, R. A.; Laslett, R. L. *Aust. J. Chem.* **1964**, *17*, 1157−1163. Pandey, R. K.; Forsyth, T. P.; Gerzevske, K. R.; Lin, J. J.; Smith, K. M. *Tetrahedron Lett.* **1992**, *33*, 5315−5318. Clarke, O. J.; Boyle, R. W. *Tetrahedron Lett.* **1998**, *39*, 7167−7168.
(33) Sessler, J. L.; Johnson, M. R.; Lynch, V. *J. Org. Chem.* **1987**, *52*, 4394−4397.
(34) Ka, J.-W.; Lee, C.-H. *Tetrahedron Lett.* **2000**, *41*, 4609−4613. Young, A. M.; VonRuden, A. L.; Lash, T. D. *Org. Biomol. Chem.* **2011**, *9*, 6293. Lee, C.-H.; Park, J. Y.; Kim, H.-J. *Bull. Korean. Soc.* **2000**, *21*, 97−100. Smith, K. M.; Craig, G. W. *J. Org. Chem.* **1983**, *48*, 4302−4306.
(35) Nguyen, L. T.; Senge, M. O.; Smith, K. M. *J. Org. Chem.* **1996**, *61*, 998−1003. Baptista De Almeida, J. A. P.; Kenner, G. W.; Rimmer, J.; Smith, K. M. *Tetrahedron* **1976**, *32*, 1793−1799.
(36) Lin, Y.; Lash, T. D. *Tetrahedron Lett.* **1995**, *36*, 9441−9444. Chandrasekar, P.; Lash, T. D. *Tetrahedron Lett.* **1996**, *37*, 4873−4876.
(37) Sessler, J. L.; Genge, J. W.; Urbach, A.; Sanson, P. *Synlett* **1995**, 187−188.
(38) Geier, R. G., III; Litter, B. J.; Lindsey, J. S. *J. Chem. Soc., Perkin Trans. 2* **2001**, 701−711.
(39) Littler, B. J.; Ciringh, Y.; Lindsey, J. S. *J. Org. Chem.* **1999**, *64*, 2864−2872. Zaidi, S. H. H.; Fico, R. M., Jr.; Lindsey, J. S. *Org. Process Res. Dev.* **2006**, *10*, 118−134.
(40) Toganoh, M.; Furuta, H. *Chem. Commun.* **2012**, *48*, 937−954. Furuta, H.; Morimoto, T.; Osuka, A. *Org. Lett.* **2003**, *5*, 1427−1430. Morimoto, T.; Taniguchi, S.; Osuka, A.; Furuta, H. *Eur. J. Org. Chem.* **2005**, 3887−3890. Toganoh, M.; Harada, N.; Morimoto, T.; Furuta, H. *Chem. Eur. J.* **2007**, *13*, 2257−2265.
(41) Lash, T. D.; Von Ruden, A. L. *J. Org. Chem.* **2008**, *73*, 9417−9425. Lash, T. D.; Richter, D. T.; Shiner, C. M. *J. Org. Chem.* **1999**, *64*, 7973−7982.
(42) Heo, P.-Y.; Shin, K.; Lee, C.-H. *Tetrahedron Lett.* **1996**, *37*, 197−200.
(43) Liu, B. Y.; Brückner, C.; Dolphin, D. *Chem. Commun.* **1996**, 2141−2142.
(44) Chen, Q.; Wang, T.; Zhang, Y.; Wang, Q.; Ma, J. *Synth. Commun.* **2002**, *32*, 1051−1058.
(45) Maeda, H.; Osuka, A.; Furuta, H. *Tetrahedron* **2004**, *60*, 2427−2432.
(46) Zelikin, A.; Shastri, V. R.; Langer, R. *J. Org. Chem.* **1999**, *64*, 3379−3380.
(47) Kakushima, M.; Hamel, P.; Frenette, R.; Rokach, J. *J. Org. Chem.* **1983**, *48*, 3214−3219.
(48) Galezowski, M.; Jazwinski, J.; Lewtak, J. P.; Gryko, D. T. *J. Org. Chem.* **2009**, *74*, 5610−5613.
(49) Cadamuro, S.; Degani, L.; Dughera, S.; Fochi, R.; Gatti, A.; Piscopo, L. *J. Chem. Soc., Perkin Trans. 2* **1993**, 273−283.
(50) Laha, J. K.; Dhanalekshmi, S.; Taniguchi, M.; Ambroise, A.; Lindsey, J. S. *Org. Process Res. Dev.* **2003**, *7*, 799−812.
(51) Geier, G. R., III; Lindsey, J. S. *Tetrahedron* **2004**, *60*, 11435−11444.
(52) Dorough, G. D.; Huennekens, F. M. *J. Am. Chem. Soc.* **1952**, *74*, 3974−3976.
(53) Anderson, H. J.; Loada, C. E.; Xu, R. X.; Le, N.; Gogan, N. J.; McDonald, R.; Edwards, L. G. *Can. J. Chem.* **1985**, *63*, 896−902.
(54) Xu, R. X.; Anderson, H. J.; Gogan, N. J.; Loader, C. E.; McDonald, R. *Tetrahedron* **1980**, *22*, 4899−4900.
(55) Notaras, E. G. A.; Fazekas, M.; Doyle, J. J.; Blau, W. J.; Senge, M. O. *Chem. Commun.* **2007**, 2166−2168.
(56) Bakar, M. B.; M. Olegemoller, M.; Senge, M. O. *Tetrahedron* **2009**, *65*, 7064−7078.

(57) Kruper, W. J., Jr.; Chamberlin, T. A.; Kochanny, M. *J. Org. Chem.* **1989**, *54*, 2753−2756.
(58) Temelli, B.; Unateroglu, C. *Tetrahedron* **2009**, *65*, 2043−2050.