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Progress Towards Synthetic Chlorins with Graded Polarity, Conjugatable Substituents, and Wavelength Tunability

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Abstract

Advances in chlorin synthetic chemistry now enable the *de novo* preparation of diverse chlorin-containing molecular architectures. Five distinct molecular designs have been explored here, including hydrophobic bioconjugatable (oxo)chlorins; a hydrophilic bioconjugatable chlorin; a *trans*-ethynyl/iodochlorin building block; a set of chlorins bearing electron-rich (methoxy, dimethylamino, methylthio) groups at the 3-position; and a set of ten 3,13-disubstituted chlorins chiefly bearing groups with extended π -moieties. Altogether 23 new chlorins (17 targets, 6 intermediates) have been prepared. The challenge associated with molecular designs that encompass the combination of “hydrophilic, bioconjugatable and wavelength-tunable” chiefly resides in the nature of the hydrophilic unit.

Keywords

auxochrome; artificial photosynthesis; chlorophyll; hydroporphyrin; hydrophilic; photomedicine

INTRODUCTION

The central role of chlorophylls in plant photosynthesis has motivated studies of vast scope concerning the interplay of molecular structure, supramolecular chemistry, optical spectra, photochemical properties, and electronic structure in this family of macrocycles. Synthetic chemistry has played a very strong supporting role in such studies by making available diverse chlorins that are not accessible via naturally occurring biosynthetic pathways. Studies in artificial photosynthesis provide both a direct biomimetic mirror for natural

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Supporting Information

Crystallographic data for **11** have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication data no. CCDC-1029006. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 2EZ, UK (email: deposit@ccdc.cam.ac.uk, fax: +44 1223-336033).

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photosynthesis and also enable fundamental studies of excited-state energy- and electron-transfer processes that are not possible with the natural systems.

Two distinct methods for gaining access to chlorin macrocycles entail semisynthesis, where naturally occurring tetrapyrroles (e.g., heme, chlorophylls, bacteriochlorophylls) provide the initial starting material [1–4], and *de novo* synthesis, where the macrocycle is created from relatively simple, acyclic starting materials [5–7]. Semisynthesis has the advantage of abundant feedstocks but the disadvantage of a full complement of β -pyrrolic substituents, which can limit synthetic maneuverability. *De novo* syntheses have the advantage of a *tabula rasa* thereby enabling – at least in principle – full synthetic control over all substituents, but the disadvantage of a considerable amount of synthetic work to construct and derivatize the chlorin macrocycle.

An offshoot of synthetic studies in chlorin chemistry has entailed the preparation of chlorins for use in photomedicine, which encompasses diagnostics, imaging and therapeutics. Our research groups have been engaged in the *de novo* synthesis of chlorins. In Raleigh, we have been working to develop methodology for the preparation of chlorins for diverse photochemical studies [8–22]. In Baltimore, we have been working to design and synthesize chlorins for use in photomedicine, particularly laser-guided surgery [23–28]. A common challenge in all such studies is the ability to (1) control overall molecular polarity, (2) dial-in the position of the long-wavelength absorption band (which determines the maximum energy for photochemical processes emanating from the excited singlet state), and (3) install one or more reactive functional groups for attachment to other moieties such as proteins, surfaces, or other molecular entities.

In this paper, we describe the synthesis of a collection of chlorins for use in diverse studies. The paper is divided into three sections. The sections encompass (I) the synthesis of lipophilic or hydrophilic chlorins that bear a single (bio)conjugatable group; (II) the synthesis of a chlorin bearing two reactive aryl functional groups attached to opposing β -pyrrole rings; and (III) the synthesis and spectral properties of diverse 3-substituted or 3,13-disubstituted chlorins. Studies of functional properties of the chlorins are beyond the scope of the present article. Taken together, this work provides an overview of the rich capabilities of chlorin synthetic chemistry, and provides milestones concerning versatility of molecular design of chromophores with red-region spectral features.

RESULTS AND DISCUSSION

The methodology for preparing chlorins is outlined in Scheme 1. Chlorin formation entails the convergent joining of an Eastern half and a Western half under acid-catalyzed condensation followed by metal-mediated oxidative cyclization [8,10]. The Eastern half is a dipyrromethane bearing an α -bromo atom and an α -carbinol or carboxaldehyde; the linear tetrapyrrole derived from the former is a tetrahydrobilene-*a* whereas the latter is a tetrahydrobiladiene-*ab*. The Western half is a tetrahydrodipyrin that contains the geminal-dimethyl-substituted pyrroline ring [29]. The resulting zinc chlorin can be modified in a number of ways, including conversion to the 17-oxochlorin [11], derivatization at the 15-position [12,14], alteration of the various pyrrolic substituents [13,15,17], de/remetalation,

and various combinations of such approaches. By use of these and other approaches, access to each peripheral position of the chlorin macrocycle is now available [22]. Complementary routes to analogous chlorins have been developed by the groups of Battersby [30,31], Jacobi [32–36] and Montforts [37–44].

I. Bioconjugatable chlorins

A. Lipophilic (bio)conjugatable chlorins—The synthesis of a lipophilic chlorin bearing a single bioconjugatable group can be achieved by incorporation of the latter in protected form as a substituent on one of the meso-aryl units. A key design issue is that the bioconjugatable motif must be able to survive the conditions for formation of the Eastern half and conversion to the chlorin. Two examples are shown here, which include a phenol and an arylcarboxylic acid as bioconjugatable groups.

The synthesis of an oxochlorin–phenol is shown in Scheme 2. The synthesis of the Eastern half begins with dipyrromethane **1** [45–47], which contains the protected phenol. Treatment of **1** with EtMgBr at room temperature for 10 min followed by Mukaiyama reagent **2** [48] at $-78\text{ }^{\circ}\text{C}$ for 20 min gave the 1-acyldipyrromethane **3** in crude form. The latter was complexed with 9-BBN-OTf in the presence of triethylamine (TEA) to afford the complex **4** in 73% yield (two steps from **1**). Such 1-acyldipyrromethane–boron complexes are more readily handled and derivatized given the masking of the α -acylpyrrole motif [48,49]. Bromination of **4** using NBS following a standard procedure [48] afforded the compound **5** in 77% yield. Compound **5** was used directly for the chlorin-forming reaction without decomplexation of the boron moiety. Thus, treatment of **5** with NaBH_4 gave the 1-bromo-dipyrromethane-monocarbinol (**5**–OH, not shown), the Eastern half. The crude Eastern half was combined with Western half **6** [10] and subjected to two-step one-flask chlorin-forming conditions [10] to afford the zinc chlorin **ZnC-1** in 36% yield. The **ZnC-1** was converted to zinc oxochlorin **ZnC-2** following a standard procedure [11]. Reaction of **ZnC-2** with BBr_3 in CH_2Cl_2 at room temperature [50] followed by treatment with $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ afforded the zinc oxochlorin–phenol **ZnC-3**.

The synthesis of a chlorin–carboxylic acid followed the same synthetic approach. The resulting chlorin–ester (**ZnC-4**) [10] was treated with KF to cleave the trimethylsilylethyl unit under relatively mild conditions, thereby affording the chlorin–carboxylic acid **ZnC-5** (Scheme 3). It warrants mention that both the oxochlorin–phenol and the chlorin–carboxylic acid are amphiphilic given the presence of the polar bioconjugatable group attached to the lipophilic chlorin. As such, both compounds if not bioconjugated are expected to assemble at an aqueous–surfactant interface (e.g., micelle, lipid bilayer membrane, liposome) thereby representing an additional application for studies with such chlorins. In this regard, Jacobi and Ehrenberg have studied the membrane depth penetration of members of a set of amphiphilic chlorins that bear alkanolic chains of a range of lengths [36].

B. Hydrophilic bioconjugatable chlorins—A general challenge in tetrapyrrole chemistry concerns appropriate molecular designs to impart high solubility in either organic or aqueous solution. The core unsaturated, unsubstituted tetrapyrrole skeleton, porphine, is hideously insoluble. The solubility increases upon ‘bulking up’ the tetrapyrrole framework

with substituents that suppress aggregation phenomena. Examples include β -alkyl (e.g., octaethylporphyrin), *meso*-aryl (e.g., *meso*-tetraphenylporphyrin), and *meso*-swallowtail (i.e., symmetrically branched alkyl) [51] substituents for solubilization in organic media. The use of *meso*-aryl units that bear *ortho*-substituents (e.g., methyl, ethyl, benzyloxy) provide increased solubility in organic media versus that of the unsubstituted phenyl unit [52]. The *ortho*-substituents project above and below the plane of the macrocycle (Figure 1). An extension of this approach of “facial encumbrance” has afforded solubilization of porphyrins and chlorins [19] in aqueous media. Thus, 2,6-disubstituted aryl groups or swallowtail substituents with terminal polar groups (e.g., phosphate, phosphonate) have been found to impart water solubility of synthetic chlorins, as shown for the chlorins **C-6** and **C-7** shown in Figure 1 [19].

Our first approach to a hydrophilic bioconjugatable chlorin focused on a molecular architecture that (1) represented a hybrid of the *meso*-aryl and swallowtail motifs, (2) incorporated a carboxylic acid for bioconjugation, and (3) could be incorporated to the chlorin macrocycle via Suzuki coupling. Precedence in considering this route include phenol alkylation with diethyl chloromethylphosphonate [53] as well as Suzuki coupling with hindered aryl units [54] (including 2,6-dialkoxyaryl halides with aryl boronic acids [55]), albeit under forcing conditions. Thus, the commercially available methyl 4-bromo-3,5-dihydroxybenzoate (**I**) was alkylated [19,56] with $\text{TrfOCH}_2\text{PO}(\text{OEt})_2$ (**II**) [57] to give methyl 4-bromo-3,5-bis(diethylphosphonomethoxy)benzoate (**7**) in 92% yield (Scheme 4). Compound **7** is a potential snap-on motif that bears the requisite facially encumbering phosphonate groups and the bioconjugatable carboxylate unit. A homologue of **7** containing a longer alkyl spacer between the alkoxyarene and the phosphonate moiety also was prepared by alkylation of **I** with diethyl 3-bromopropylphosphonate (**III**) to give **8**. Attempts to convert synthon **7** or **8** to the boronate derivative, however, were unsuccessful.

The chlorin examined for pilot studies, **C-8** [17], smoothly underwent bromination at the 15-position to give **C-9** [17] followed by Pd-mediated borylation [58] to give chlorin–boronate **C-10** (Scheme 5). On the other hand, Pd-mediated coupling of **C-10** with the 2,6-dialkoxyaryl bromide (**7** or **8**) proceeded quite poorly. The product in each case (**C11** or **C12**) was suggested by a molecular ion peak upon ESI-MS analysis, but the trace quantity thwarted isolation. Alternatively, attachment of 1,3-dimethoxy-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)benzene [59,60] (derived here from 2,6-dimethoxyphenyl boronic acid and pinacol) to the 15-position of the chlorin was investigated but found non-advantageous versus incorporation of the 2,6-dimethoxyaryl unit via the dipyrromethane in the Eastern half synthesis. The failure to incorporate the snap-on motif prompted return to an established route wherein the facially encumbering diphosphonate group is installed via the use of the Eastern half.

Chlorin **C-13** is readily prepared and contains a 2,6-dimethoxyphenyl unit at the 10-position; cleavage of the methyl ethers reveals the diphenol, which is alkylated with **II** [19]. In the present work, the resulting bis(diethylphosphonomethoxy)phenylchlorin **C-14** was further manipulated to install a bioconjugatable handle. Bromination [14,17] of **C-14** led to the 15-bromo-10-arylchlorin **C-15** in 96% yield. Suzuki coupling of **C-15** with boronic ester **IV** under standard conditions employed for porphyrins [61,62], chlorins [12] and

bacteriochlorins [63] led to the formation of chlorin **C-16** in 50% yield. Saponification followed by deprotection of the ethyl phosphonate groups led to the water-soluble bioconjugatable chlorin **C-17** as a green solid in excellent yield (Scheme 6). The ^1H NMR spectrum in CD_3OD indicated exchange of 7 protons (two NH , one CO_2H , four P-OH), as expected, but upon integration only 26 of the remaining 29 protons were identified. The characteristic chlorin absorption spectrum and accurate (negative ion) mass spectrum support a provisional assignment of the target compound. In summary, this approach offers a rational route to a chlorin bearing a facially encumbering bis(phosphonate) group and a single bioconjugatable group.

II. β -Disubstituted chlorin building block

Chlorins bearing two orthogonal functional groups enable successive derivatization. Two such functional groups at diametrically opposed positions are particularly attractive for the construction of linear multipigment arrays that function as energy-transfer cascades or hole-hopping relays. We have found that the extent of electronic communication between porphyrins of a given electronic composition depends on the site of attachment of a linker on the macrocycle [64]. The availability of chlorins with diverse substitution patterns would enable study of such electronic effects in chlorins, complementing our prior studies with porphyrins. For the construction of linear arrays, substitution at opposing β -pyrrole positions is quite attractive.

We previously prepared several β -substituted chlorins wherein each bears an ethyne group and a halogen atom in diametrically substituted (2,12-; 3,13-) positions; the chlorins include **ZnC-18** [9], **ZnC-19** [13], and **ZnC-20** [65] (Chart 1). Here we present the synthesis of an analogue of **ZnC-18** that contains a 3,5-di-*tert*-butylphenyl group (rather than a *p*-tolyl group) at the 5-position to impart increased solubility in organic solvents. While in principle either the 2,12- or 3,13-positions can be employed, given the bulk of the 3,5-di-*tert*-butylphenyl group at the 5-position, we chose the 2,12-positions for installation of the iodo and ethynyl groups. The synthesis of such *trans*- β -substituted chlorin building blocks requires the availability of β -substituted Eastern and Western halves. The synthesis also makes use of improved methods, including the intermediacy of a tetrahydrodipyrin as the Western half (versus the dihydrodipyrin employed previously).

A. Substituted Western halves—The β -arylpyrrole is conveniently prepared via a van Leusen reaction. Formylation of the resulting β -(*p*-iodophenyl)pyrrole [9] typically affords the 2-formyl-3-arylpyrrole and the 2-formyl-4-arylpyrrole (due to substitution at either the α - or α' -position), which must be separated and identified. Such distinction can be difficult by ^1H NMR spectroscopy [9]. Accurate identification of the two products (or derivatives therefrom along the later steps of the pathway) is essential because the two patterns of substitution ultimately yield chlorin building blocks with substitution at different β -positions. Subsequent nitrovinyl condensation followed by reduction gave the 2-(2-nitroethyl)pyrrole **9** (Scheme 7). Michael reaction with mesityl oxide (**V**) gave the nitrohexanone (**10**), which upon treatment with zinc/acetic acid gave the tetrahydrodipyrin-*N*-oxide (**11**) in 43% yield. The synthesis of the tetrahydrodipyrin target(s) has been described previously in concise form [66], and **9** and **V** have been used previously to form

the dihydrodipyrin Western half [9]; the presentation here supplements the prior presentation with additional data and context.

A single-crystal X-ray structure of **11** was obtained. The structure determination was not required to confirm the substitution pattern (Figure 2, Table 1), which was established previously by the X-ray structure of the 2-(2-nitroethyl)pyrrole **9** [9]. On the other hand, X-ray structure analysis of **11** adds to the very limited data available for hydrodipyrins (considerable data are available for dipyrromethanes or dipyrins, which lack the pyrroline ring). To our knowledge, structural data concerning hydrodipyrins related to chlorin syntheses are available only for three tetrahydrodipyrin–dibutylboron complexes [22], one dihydrodipyrin [67], one dibutylboron complex of a dihydrodipyrin–dibutylboron complex [22], and one nitrohexanone (a precursor for a dihydrodipyrin or tetrahydrodipyrin) [67].

Completion of the synthesis required deoxygenation of the *N*-oxide **11**. The prior route to a β -substituted *dihydrodipyrin* Western half [9] was used herein with modification to obtain the β -substituted *tetrahydrodipyrin* counterpart. Thus, deoxygenation of *N*-oxide **11** yielded the β -substituted tetrahydrodipyrin Western half **12** in 38% yield (Scheme 7). Sonogashira coupling of **12** with (trimethylsilyl)acetylene afforded the trimethylsilylethynyl substituted Western half **13** in 76% yield.

B. Substituted Eastern half—The synthesis of the β -substituted Eastern half began in the same manner as our prior synthesis of β -substituted dipyrromethanes [9,68]. A BOC-protected dipyrromethane (**14**) was obtained from 2-formyl-3-(4-iodophenyl)pyrrole through the protection of the pyrrolic nitrogen, reduction of the aldehyde and condensation with pyrrole (not shown) [9]. Treatment of the BOC-protected dipyrromethane **14** with 3.0 equiv of EtMgBr in THF followed by 3,5-di-*tert*-butylbenzoyl chloride afforded the monoacyldipyrromethane **15** in 45% yield (Scheme 8). Removal of the BOC group under standard conditions [69] gave **16**. Sonogashira coupling [70] of **16** with (trimethylsilyl)acetylene afforded trimethylsilylethynyl–dipyrromethane **17** in 82% yield. Reaction of **17** with NBS at -78°C gave the corresponding monobromo-monoacyl dipyrromethane **18** in 72% yield. Compound **18** serves as the precursor to the Eastern half dipyrromethane-monocarbinol **18-OH**.

C. Chlorin formation—The chlorin-forming reaction was carried out using a two-step two-flask procedure of acid-catalyzed condensation followed by metal-mediated oxidative cyclization. Thus, treatment of **18** with NaBH_4 in methanol gave the corresponding dipyrromethane-monocarbinol (**18-OH**), which was used without extensive purification in the next step. The reaction of **12** and **18-OH** employed early conditions for metal-mediated oxidative cyclization (using AgIO_3 , subsequently replaced with AgOTf [10]) afforded chlorin **ZnC-21** in 8% yield (Scheme 9). The absorption spectrum was characteristic of a chlorin, with a molar absorption coefficient ($\log \epsilon = 4.86$ at 629 nm) in close accord with that of the *p*-tolylchlorin counterpart **ZnC-18** ($\log \epsilon = 4.90$ at 629 nm) [13]. ^1H NMR spectroscopy confirmed the expected structure: (i) the geminal dimethyl groups of **ZnC-21** resonate as a singlet at δ 1.97 ppm, (ii) the CH_2 in the reduced pyrrole ring gives rise to a singlet downfield at δ 4.51 ppm, (iii) the four β -pyrrole protons resonate in the region of δ

8.56–8.81 ppm, and (iv) the eight protons of the β -aryl rings resonate in the region of δ 7.82–8.14 ppm as two pairs of doublets. In summary, the β -substituted Eastern and Western halves enable the rational synthesis of a chlorin building block with synthetic handles at diametrically opposed positions at the perimeter of the macrocycle. Such a building block should be quite valuable for the construction of model systems in biomimetic or materials chemistry.

III. Wavelength-tunable chlorins

A major finding from the preparation of chlorins that bear diverse substituents is that the position of the long-wavelength absorption band can be tuned across the 600–700 nm region. The chief method for such tuning entails placement of auxochromes at the 3- and 13-positions [13]. The 3- and 13-positions are both in a pyrrole ring that lies along the Q_y axis, with the 3-position distal and 13-position proximal to the pyrroline ring. Auxochromes such as ethynyl, phenylethynyl, carboethoxy, acetyl, or formyl at the 3- and/or 13-position result in a bathochromic shift of both the B and Q_y bands, as well as an increase in the intensity of the Q_y band relative to the B band. Such substituents are regarded as electron-withdrawing groups. By contrast, few studies have concerned the effects of electron-donating groups on the chlorin spectral properties.

This lacuna prompted us to prepare three chlorins with groups that are electron-releasing by resonance (methoxy, methylthio, and dimethylamino) in the 3-position [71], which is described in the first section below. In the second section, we have prepared a collection of 3,13-disubstituted chlorins that bear aryl groups with extended conjugation. The motivation for preparing both classes of chlorins reflects the dual desires to gain a deeper understanding of chlorin electronic/photophysical properties and to understand how to design chlorins with deep-red (or near-IR) absorption and (preferably intense) fluorescent properties. Such chlorins could be used as fluorophores for *in vivo* bioimaging applications (e.g., fluorescence-guided surgery [23,24]) or as the energy donor in energy-transfer arrays for artificial photosynthesis or *in vivo* multicolor bioimaging [18,20,25,26].

A. 3-Substituted chlorins—The requisite 3-bromochlorin building block has been prepared previously using 0.20 mmol reactants (Western half **19** [13] and Eastern half **20** [13]), which afforded 45 mg of the chlorin **ZnC-22** (37%) [13]. The same synthesis carried out here at 0.57 mmol reactants gave 119 mg of the chlorin (34%) as shown in Scheme 10. Palladium coupling of **ZnC-22** with dimethylamine (10 equiv) with $\text{Pd}(\text{OAc})_2$ (40 mol%), (*tert*-Bu) $_3\text{PHBF}_4$ (40 mol%), and *tert*-BuONa (3 equiv) in refluxing toluene for 48 h [72] afforded 3-dimethylaminochlorin **ZnC-23** in 49% yield. Palladium coupling of **ZnC-22** with sodium thiomethoxide under conditions used for aryl thioether formation (20 mol% of $\text{Pd}_2(\text{dba})_3$ and Xantphos in refluxing xylene) [73] afforded 3-methylthiochlorin **ZnC-24** in 95% yield. Similarly, palladium coupling of **ZnC-22** with sodium methoxide in the presence of 20 mol% of $\text{Pd}_2(\text{dba})_3$ and Xantphos in refluxing xylene gave 3-methoxychlorin **ZnC-25** in 16% yield. Attempts to mitigate the low yield of the 3-methoxychlorin **ZnC-25**, either by methoxylation [74] of the tosyl-protected Western half **19-Ts** [13] (not shown here) or by use of modified Pd-mediated coupling conditions (as used for the *meso*-position of a porphyrin) [75] were ineffective [71].

The spectral properties of the zinc chlorins obtained in toluene are listed in Table 2 and displayed in Figure 3. The absorption spectrum in each case is typical of a chlorin, as is the fluorescence emission spectrum, with a stronger Q(0,0) band and weaker Q(0,1) band. The absorption spectral properties of the three 3-substituted chlorins (**ZnC-23**, **ZnC-24**, and **ZnC-25**) can be compared with the benchmark zinc chlorin **ZnC-26**, which lacks a 3-substituent. The spectral shift of the B band and the Q_y band is listed for each compound. While the former is more intense, the position of the latter is of greater interest given that the Q_y band position sets an upper limit on the energy of the excited singlet state, and inter alia, that of the excited triplet stated derived therefrom. The Q_y band spans the range from 603–616 nm along the series of chlorins with 3-methoxy (**ZnC-25**), benchmark (3-unsubstituted, **ZnC-26**), 3-(*N,N*-dimethylamino) (**ZnC-23**), and 3-methylthio (**ZnC-24**) substituents. The Q_y band of **ZnC-25** is thus shifted hypsochromically with respect to that of the unsubstituted chlorin **ZnC-26**. A similar effect of the methoxy group has been noted with bacteriochlorins [76]. In parallel with the progressive bathochromic shift of the Q_y band position, the relative intensity of the Q_y band also increased (i.e., I_B/I_Q decreased from 4.3 to 2.5). The 603-nm absorption band of the methoxychlorin (**ZnC-25**) is identical to that of the corresponding zinc chlorin that lacks any substituents, not even the 10-mesityl group (**ZnC-27**) [77]. We have not determined the molar absorption coefficient of the various chlorins but instead rely on the I_B/I_Q ratio to indicate the relative intensity of long-wavelength absorption, which can be reliably determined regardless of sample quantity. For perspective, however, the molar absorption coefficient for the benchmark chlorins are as follows [13]: **ZnC-26**, log ε = 4.81 (606 nm) and **ZnC-27**, log ε = 4.84 (603 nm). The molar absorption coefficients of some 50 other gem-dimethyl substituted chlorins also have been determined [8, 9,11,13,14]. In summary, the effects of the three substituents examined here, methoxy, dimethylamino, and methylthio are rather insubstantial in altering the position of the Q_y band. The extent to which the little-changed spectra stem from intrinsically weak interactions of such groups with the four individual frontier molecular orbitals of the chlorin, or stronger interactions that are muted by cancellation of opposing effects (e.g., induction versus resonance of the substituent) will require in-depth experimental and theoretical studies.

B. 3,13-Disubstituted chlorins—Phenylethynyl substituents, which effectively expand the conjugated system of tetrapyrrolic macrocycles, are known to significantly alter the electronic and optical properties of porphyrins [78], chlorins[15,16], and bacteriochlorins [28,79]. For example, 3,13-bis(phenylethynyl)chlorin **C-28** (Chart 2) exhibits a significant bathochromic shift of absorption and emission ($\lambda_{\text{abs}} = 676$ nm, $\lambda_{\text{em}} = 678$ nm), and large increase in fluorescence quantum yield ($\Phi_f = 0.37$, in toluene), compared to the analogous chlorin that lacks substituents at the 3,13-positions [18].

We aimed to determine whether a further bathochromic shift in absorption and emission for chlorins could be achieved by more elaborate substituents at the chlorin 3- and 13-positions. The synthesis makes use of the 3,13-dibromo-10-*p*-tolylchlorin (**C-29**) building block (Scheme 11), which has been prepared following a reported procedure [13,21]. Thus, condensation of the 8-bromotetrahydropyrrin (**19**) [29] and 7,8-dibromo-1-formyl-10-*p*-tolylidipyrromethane (**21**) [23] in the presence of *p*-TsOH·H₂O followed by oxidative cyclization (mediated by Zn(OAc)₂ in the presence of 2,2,6,6-tetramethylpiperidine) and

demetalation (dilute TFA in dichloromethane) afforded free base chlorin **C-29** in 12% yield. The lower yield of **C-29** (compared to that of analogous chlorins reported previously) [13,21] may be due to the poor solubility of Eastern half **21** (and presumably the resulting tetrahydrobiladiene) in the reaction solvents.

With the 3,13-dibromochlorin building block in hand, we prepared a series of 3,13-disubstituted chlorins to probe the effect of several factors on the optical properties of chlorins (Table 3). One reference compound is a chlorin with no 3,13-substituents (**C-30**) [17] or a phenylethynyl substituent at both the 3- and 13-positions (**C-31**). The factors include the length of the conjugated system of substituents (compounds **C-32** and **C-33**), presence of electron-withdrawing (**C-33** – **C-35**) or electron-donating groups (**C-36**), size of the aromatic portion of a substituent (**C-37**), and replacement of the aryl group with an alkyl group (**C-38**), TMS group, or no substituent (**C-39**, **C-40**).

The installation of ethynyl substituents was achieved via Sonogashira reaction of the corresponding acetylene derivatives with **C-29**. Two sets of copper-free conditions, which were previously reported for Sonogashira reaction of hydroporphyrin have been followed; (A) $(\text{PPh}_3)_2\text{PdCl}_2$ in DMF/TEA [28] or (B) $\text{Pd}_2(\text{dba})_3$ and $\text{P}(o\text{-tol})_3$ in toluene/TEA [13]. The requisite ethynes were obtained commercially, or for the case of methyl 4-ethynylbenzoate [80], 4-ethynyl-1-(2-phenylethynyl)benzene [81], and methyl 4-[2-(4-ethynylphenyl)ethynyl]benzoate [82], prepared as described in the literature. The yield varied from 16–91% (Table 3). In the case of **C-35**, the low yield was a consequence of the presence of a small amount of impurities visible in the aromatic region of the ^1H NMR spectrum. These impurities were most probably unreacted starting 4-formylphenylacetylene (or product of its homocoupling reaction) and/or dibenzylideneacetone (dba) remnants, the removal of which required two additional column chromatography purifications. A sample of **C-32**, purified by column chromatography, contained a trace amount of blue-fluorescent contaminant (visible upon TLC analysis and in the fluorescence emission spectrum, but not in the ^1H NMR spectrum). This contaminant co-eluted with the product. Conversion of **C-32** to the corresponding Zn(II) complex (by reaction with $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ in $\text{CHCl}_3/\text{MeOH}$) caused an increase in polarity and thereby allowed separation from the blue-fluorescent contaminant; subsequent demetalation (using dilute TFA in CH_2Cl_2) afforded a spectroscopically pure sample. The 3,13-diethynylchlorin (**C-40**) was obtained by deprotection of the corresponding 3,13-TMS-ethynyl derivative (**C-39**) using K_2CO_3 in MeOH/THF . It is noteworthy that attempts to obtain **C-40** by deprotection of the corresponding TIPS-ethynyl derivative, using TBAF in THF, led to decomposition of the chlorin.

All new chlorins were characterized by ^1H NMR spectroscopy, LD-MS or ESI-MS; selected chlorins also were characterized by ^{13}C NMR spectroscopy. The characterization data are consistent with the expected structures. In particular, the ^1H NMR spectra show two sets of resonances from the 3,13-substituents, as expected given the presence of the geminal dimethyl group at position 18 and the *p*-tolyl group at the 10-position.

Absorption and emission maxima of the chlorins in toluene are listed in Table 4, and selected spectra are displayed in Figure 4. The benchmark lacking any β -pyrrole substituents

in this case is the 10-*p*-tolylchlorin (**C-30**). Analysis of these data leads to the following conclusions: (1) The position of the Q_y band of the ethynylchlorin **C-40** is bathochromically shifted by ~30 nm versus the unsubstituted benchmark chlorin **C-30**. (2) The position of the Q_y band of the phenylethynylchlorin **C-31** is bathochromically shifted by ~10 nm versus the ethynylchlorin **C-38** or **C-40**. (3) The further expansion of the size of the π -conjugated substituent attached to the terminus of the ethyne (phenanthryl, **C-37**) or extension by addition of a second arylethynyl unit (**C-32**, **C-33**) has a rather minute bathochromic shift (~5–6 nm) on the position of the Q_y band compared to **C-31**. (4) The largest bathochromic shift occurs with the electron-withdrawing 4-formylphenylethynyl substituent (**C-35**), though even in that case the shift is 8 nm and 9 nm for absorption and emission, respectively. (5) Attachment of the electron-donating 4-(*N,N*-dimethylamino)phenylethynyl substituent (**C-36**) results in the largest relative Q_y absorption intensity ($I_B/I_Q = 1.2$; $\log \varepsilon = 4.97$ at 679 nm, to be compared with $\log \varepsilon = 4.90$ at 675 nm for a 3,13-bis(phenylethynyl)chlorin constituent of a dyad [20]). At the same time, **C-36** exhibits a significant broadening of the B band, compared to the other derivatives in the series. Overall, elaboration of the arylethynyl substituents at the 3,13-positions has a rather small effect on the position of the long-wavelength Q_y band and emission maxima.

It warrants mention that the I_B/I_Q ratio can depend on the extent to which the B_x and B_y bands are spectrally separated or overlapped, which in turn can be affected by environmental factors (e.g., solvent, temperature). Regardless, the difference between the unsubstituted reference chlorin **C-30** ($I_B/I_Q = 2.8$) and all of the 3,13-diethynylchlorin analogues (**C-31** – **C-38**, **C-40**; $I_B/I_Q = 1.8$ – 1.3) is pronounced, and reflects the shifting of oscillator strength from the B bands to the Q_y band. A more pronounced bathochromic shift than observed herein appears to require more extensive modification of the macrocyclic structure. The research reported here predated and somewhat inspired our recent studies on strongly conjugated hydroporphyrin arrays, which appears to be an efficient way to bathochromically shift the chlorin absorption [27].

OUTLOOK

The ability to create stable chlorins with features of graded polarity, conjugatable substituents, or wavelength tunability provides the foundation for pursuit of diverse applications. While each feature alone can be attained in a fairly straightforward manner, combinations of two or all three features presents challenges:

- Chlorins with hydrophobic, hydrophilic, or amphiphilic properties are readily obtained.
- Hydrophobic chlorins with one or more conjugatable substituents also are readily obtained, as demonstrated by the synthesis of two such chlorins here as well as by the recent work of others [26,83,84].
- One hydrophilic, bioconjugatable chlorin was prepared herein; the chlorin contains facially encumbering phosphonate groups and a carboxylic acid tether.
- The introduction of auxochromes, chiefly at the 3,13-positions, enables the long-wavelength Q_y band to be tuned from 603 nm to 715 nm [21,77]. Attempts to

employ a previously unexamined set of potential auxochromes (methoxy, dimethylamino, methylthio, phenanthryl, *p*-substituted phenyl, and oligomeric ethynylphenyl substituents) led to establishment of valuable data concerning structure versus spectral properties but did not enlarge the spectral window for wavelength tuning with chlorins.

- The combination of hydrophobic and wavelength tunable presents little challenge, as the chlorin is intrinsically neutral with no polar substituents, and hence is hydrophobic.
- The combination of bioconjugatable and wavelength tunable also presents little challenge, as a bioconjugatable group can be introduced at the 5- or 10-position via the Eastern half, leaving the 3- and 13-positions open for introduction of auxochromes for wavelength tuning.
- The combination of hydrophilic with wavelength tunable presents an unmet challenge, which largely stems from the absence of synthetically versatile and benign groups that impart hydrophilicity. The facially encumbering aryl-bis(phosphonate) group described herein illustrates a viable design, yet whether this approach can be extended alone to encompass wavelength tunability (or together with wavelength tunability without compromising bioconjugatability) remains unclear.

The work described herein has made use of an existing rational synthesis of the chlorin macrocycle to prepare 17 target chlorins along with 6 chlorin intermediates. The molecular architectures prepared illustrate the power of this approach yet also highlight several unmet molecular design challenges.

EXPERIMENTAL SECTION

General

¹H NMR and ¹³C NMR spectra were collected at room temperature unless noted otherwise. Absorption spectra were obtained in CH₂Cl₂ at room temperature unless noted otherwise. Hydrophobic chlorins were analyzed by fast-atom bombardment mass spectrometry (FAB-MS), laser desorption mass spectrometry (LD-MS) in the absence of a matrix [85], or matrix-assisted laser desorption mass spectrometry (MALDI-MS) with the matrix 1,4-bis-(5-phenyloxazol-2-yl)benzene (POPOP). Water-soluble chlorins were analyzed by direct infusion of water/methanol (60:40) solutions by atmospheric pressure electrospray ionization mass spectrometry (ESI-MS). In FAB-MS, LD-MS, MALDI-MS and ESI-MS analyses, positive ions were detected unless noted otherwise. Melting points are uncorrected. All commercially available materials including compounds **I–V** were used as received. All palladium-coupling reactions were carried out using standard Schlenk-line techniques. All bromination reactions were performed using freshly recrystallized NBS.

Fluorescence spectroscopy

All chlorins were excited at the peak of the B band where the absorption was set to ~0.1. Spectra were obtained in toluene at room temperature unless noted otherwise. The spectra were corrected for PMT sensitivity and instrument response.

Non-commercial compounds

Dipyrromethane **1** [45–47] was synthesized following a streamlined one-flask procedure [46] whereas dipyrromethane **14** [9] was prepared via a stepwise procedure. The following compounds were prepared via literature procedures: Mukaiyama reagent **2** [48]; Western half precursors **9** [9] and **10** [9]; Western halves **6** [10] and **19** [13]; Eastern halves **20** [13] and **21** [27]; known chlorins as precursors **ZnC-4** [10]; **C-8** [17], **C-9** [17], **C-13** [19], and **C-14** [19]; and ethynes methyl 4-ethynylbenzoate [80], 4-ethynyl-1-(2-phenylethynyl)benzene [81], and methyl 4-[2-(4-ethynylphenyl)ethynyl]benzoate [82]. Known chlorin **ZnC-22** [13] was synthesized at larger scale here. Spectroscopic data for the benchmark chlorins **ZnC-26** [13], **ZnC-27** [13], and **C-30** [17] were taken from the literature.

10-(9-Borabicyclo[3.3.1]non-9-yl)-5-(4-methoxyphenyl)-1-(4-methylbenzoyl)dipyrromethane (4)

Following a standard procedure [49], a solution of EtMgBr (10.0 mL, 10. mmol, 1.0 M in THF) was added slowly to a solution of **1** (1.26 g, 5.00 mmol) in THF (5 mL) under argon. The resulting mixture was stirred at room temperature for 10 min, and then cooled to –78 °C. A solution of *S*-2-pyridyl 4-methylbenzothioate (**2**, 1.15 g, 5.00 mmol) in THF (5 mL) was added. The solution was stirred at –78 °C for 10 min, then warmed to room temperature. The reaction mixture was quenched by addition of saturated aqueous NH₄Cl (40 mL). The mixture was extracted with ethyl acetate (30 mL). The organic layer was washed (water and brine), dried (Na₂SO₄), and filtered. The filtrate was concentrated. The crude product (a red-orange oil) thus obtained was dissolved in CH₂Cl₂ (10 mL) and treated with TEA (1.68 mL, 12.0 mmol) followed by 9-BBN-OTf (20 mL, 10.0 mmol, 0.5 M in hexane) with stirring at room temperature. After 1 h, the mixture was poured onto a pad of silica (4 × 8 cm) eluting with CH₂Cl₂. The product eluted as a fast-moving yellow band, which upon concentration afforded a yellow-orange solid 1.78 g, 73%): mp 88 °C (dec.); ¹H NMR (400 MHz, CDCl₃) δ 0.67–0.71 (m, 2H), 1.62–1.83 (m, 6H), 1.95–2.22 (m, 6H), 2.48 (s, 3H), 3.79 (s, 3H), 5.85 (s, 1H), 5.96 (s, 1H), 6.13–6.17 (m, 1H), 6.40–6.43 (m, 1H), 6.69–6.85 (m, 1H), 6.85 (d, *J* = 8.0 Hz, 2H), 7.11 (d, *J* = 8.0 Hz, 2H), 7.30–7.38 (m, 4H), 7.80–7.92 (br, 1H), 8.12 (d, *J* = 8.0 Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 22.1, 23.9, 25.2, 26.0, 26.5, 30.7, 30.9, 34.7, 44.1, 55.5, 108.0, 108.6, 114.1, 117.4, 118.3, 120.8, 128.3, 129.6, 129.8, 130.0, 132.9, 134.3, 134.9, 145.0, 152.5, 158.7, 174.4. Integration indicated one additional proton in the ¹H NMR spectrum (versus formula C₃₂H₃₅BN₂O₂), and the product was used for the next step without further purification.

10-(9-Borabicyclo[3.3.1]non-9-yl)-1-bromo-5-(4-methoxyphenyl)-9-(4-methylbenzoyl)dipyrromethane (5)

Following a general procedure [48], a solution of **4** (0.491 g, 1.00 mmol) in dry THF (10 mL) was cooled -78°C under argon. NBS (178 mg, 1.00 mmol) was added and the reaction mixture was stirred for 1 h at -78°C . Hexanes (10 mL) and water (10 mL) were added and the mixture was allowed to warm to room temperature. The organic phase was extracted with hexanes, dried (Na_2SO_4) and concentrated under reduced pressure without heating. Chromatography [silica, hexanes/ CH_2Cl_2 (1:1)] afforded a yellow orange powder (0.439 g, 77%): mp 121°C (dec.); ^1H NMR (400 MHz, CDCl_3) δ 0.64–0.72 (m, 2H), 1.64–1.88 (m, 6H), 1.94–2.24 (m, 6H), 2.48 (s, 3H), 3.80 (s, 3H), 5.85 (s, 1H), 5.72–5.77 (m, 1H), 5.90 (s, 1H), 6.05–6.08 (m, 1H), 6.40–6.43 (m, 1H), 6.86 (d, $J = 7.2$ Hz, 2H), 7.11 (d, $J = 7.2$ Hz, 2H), 7.32–7.39 (m, 4H), 7.70–7.79 (br, 1H), 8.13 (d, $J = 8.0$ Hz, 2H). Integration indicated two additional protons in the ^1H NMR spectrum (versus formula $\text{C}_{32}\text{H}_{34}\text{BrN}_2\text{O}_2$), and the product was used for the next step without further purification.

Zn(II)-17,18-Dihydro-18,18-dimethyl-10-(4-methoxyphenyl)-5-(4-methylphenyl)porphyrin (ZnC-1)

A solution of **5** (0.285 g, 0.500 mmol) in THF/methanol [12.5 mL (4:1)] was treated with NaBH_4 (0.190 g, 5.0 mmol). After 30 min (TLC indicated complete reaction), the reaction mixture was quenched with cold water and extracted with CH_2Cl_2 . The organic layer was dried (K_2CO_3) and concentrated under reduced pressure without heating to afford the dipyrromethane-monocarbinol **5-OH**. The foam-like residue was dissolved in CH_3CN (5 mL) and Western half (**6**, 0.094 g, 0.50 mmol) was added followed by TFA (39 μL , 0.50 mmol). The reaction mixture was stirred at room temperature for 30 min, diluted with CH_3CN (27 mL). Samples of AgOTf (0.385 g, 1.50 mmol), $\text{Zn}(\text{OAc})_2$ (1.38 g, 7.50 mmol), and 2,2,6,6-tetramethylpiperidine (2.53 mL, 15.0 mmol) were added. The resulting mixture was refluxed for 21 h. The reaction mixture was concentrated under reduced pressure. The residue thus obtained was chromatographed [silica, CH_2Cl_2 /ethyl acetate (2:1)] to afford a purple-green solid (0.108 g, 36%): ^1H NMR (400 MHz, CDCl_3) δ 2.02 (s, 6H), 2.66 (s, 3H), 4.04 (s, 3H), 4.49 (s, 2H), 7.19 (d, $J = 8.0$ Hz, 2H), 7.48 (d, $J = 8.0$ Hz, 2H), 7.91–8.00 (m, 4H), 8.37–8.42 (m, 2H), 8.55 (s, 1H), 8.58–8.70 (m, 5H); LD-MS obsd 598.5; FAB-MS obsd 598.1733, calcd 598.1705 (M^+ , $\text{M} = \text{C}_{36}\text{H}_{30}\text{N}_4\text{OZn}$); λ_{abs} (THF) 412, 609 nm.

Zn(II)-17,18-Dihydro-18,18-dimethyl-10-(4-methoxyphenyl)-17-oxo-5-(4-methylphenyl)porphyrin (ZnC-2)

Following a general procedure [11], a mixture of **ZnC-1** (0.060 g, 0.10 mmol) and basic alumina (activity I, 3.0 g) in toluene (4 mL) was stirred at room temperature for 7 h exposed to air. Solvent was removed under reduced pressure and the residue obtained was suspended in $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (19:1). The suspension was filtered and the filtered material was washed with a mixture of $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (19:1) until the washings were colorless. The filtrate was concentrated and the residue was dissolved in toluene (40 mL) and treated with DDQ (0.045 g, 0.20 mmol) for 5 min. The reaction was quenched with TEA and the solvent was evaporated. Chromatography [silica, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (98:2)] afforded a green-purple solid (0.036 g, 59%): ^1H NMR (400 MHz, CDCl_3) δ 1.98 (s, 6H), 2.67 (s, 3H), 4.00 (s, 3H), 7.17

(d, $J = 8.0$ Hz, 2H), 7.50 (d, $J = 8.0$ Hz, 2H), 7.93–7.99 (m, 4H), 8.55–8.63 (m, 2H), 8.75–8.83 (m, 2H), 8.86–8.92 (m, 3H), 9.44 (s, 1H); LD-MS obsd 612.4; FAB-MS obsd 612.1478, calcd 612.1498 (M^+ , $M = C_{36}H_{28}N_4O_2Zn$); λ_{abs} (THF) 420, 608 nm.

Zn(II)-17,18-Dihydro-18,18-dimethyl-10-(4-hydroxyphenyl)-17-oxo-5-(4-methylphenyl)porphyrin (ZnC-3)

Following a literature procedure [50] with slight modification, a mixture of **ZnC-2** (0.032 g, 0.050 mmol) and BBr_3 (0.20 mL, 0.20 mmol, 1M in CH_2Cl_2) in CH_2Cl_2 (5 mL) was stirred at room temperature under argon. After 15 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The organic layer was extracted with CH_2Cl_2 and dried (Na_2SO_4) and concentrated. The residue was dissolved in CH_2Cl_2 /MeOH (4:1) and treated with $Zn(OAc)_2 \cdot 2H_2O$ (0.055 g, 0.25 mmol) at room temperature for 4 h. The mixture was washed with saturated aqueous $NaHCO_3$, dried (Na_2SO_4) and concentrated. Chromatography [silica, CH_2Cl_2 /MeOH (9:1)] afforded a green-purple solid (0.026 g, 87%): 1H NMR (400 MHz, $CDCl_3$) δ 2.05 (s, 6H), 2.68 (s, 3H), 5.40–5.44 (br, 1H), 7.15 (d, $J = 8.0$ Hz, 2H), 7.51 (d, $J = 8.0$ Hz, 2H), 7.93–7.99 (m, 4H), 8.55–8.63 (m, 2H), 8.75–8.83 (m, 2H), 8.87–8.96 (m, 2H), 9.56 (s, 1H); LD-MS obsd 598.5; FAB-MS obsd 598.1371, calcd 598.1341 (M^+ , $M = C_{35}H_{26}N_4O_2Zn$); λ_{abs} (THF) 420, 608 nm.

Zn(II)-10-(4-Carboxyphenyl)-17,18-dihydro-10-mesityl-18,18-dimethyl-5-(4-methylphenyl)porphyrin (ZnC-5)

A solution of **ZnC-4** (14.3 mg, 20.0 μ mol) in dry DMF (2 mL) was treated with potassium fluoride (23.2 mg, 0.400 mmol) at 75 °C for 18 h. The reaction mixture was concentrated to dryness under reduced pressure. Chromatography [silica, CH_2Cl_2 /methanol (20:1)] followed by filtration through a 0.65 μ m filter (CH_2Cl_2 , to remove silica) afforded a greenish purple solid (6.8 mg, 55%): 1H NMR (400 MHz, $CDCl_3$) δ 2.03 (s, 6H), 2.66 (s, 3H), 4.52 (s, 2H), 7.46–7.51 (m, 2H), 7.93–7.97 (m, 2H), 8.17–8.22 (m, 2H), 8.31–8.34 (m, 1H), 8.39–8.45 (m, 3H), 8.58–8.70 (m, 6H); LD-MS obsd 612.5; FAB-MS obsd 612.1531, calcd 612.1498 (M^+ , $M = C_{36}H_{28}N_4O_2Zn$); λ_{abs} (CH_2Cl_2) 413, 608 nm.

Methyl 4-bromo-3,5-bis(diethylphosphonomethoxy)benzoate (7)

A mixture of methyl 4-bromo-3,5-dihydroxybenzoate (**I**, 741 mg, 3.00 mmol) and K_2CO_3 (1.65 g, 12.0 mmol) in CH_3CN (10 mL) was stirred at room temperature for 30 min. A sample of $TfOCH_2PO(OEt)_2$ (**II**, 2.10 g, 7.00 mmol) was added, and the mixture was refluxed for 4 h. The reaction mixture was allowed to cool to room temperature. The reaction mixture was treated with CH_2Cl_2 and water. The organic layer was separated, washed (water, brine), dried (Na_2SO_4) and concentrated. The resulting solid was chromatographed [silica, hexanes/ethyl acetate (1:1) $\rightarrow$ ethyl acetate $\rightarrow$ ethyl acetate/MeOH (98:2)] to give a white solid (1.52 g, 92%): mp 62–63 °C; 1H NMR (400 MHz, $CDCl_3$) δ 1.37 (t, $J = 7.2$ Hz, 12H), 3.92 (s, 3H), 4.24–4.33 (m, 8H), 4.38 (d, $J = 10.4$ Hz, 4H), 7.32 (s, 2H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 16.5 (d, $J = 6.1$ Hz), 52.6 (d, $J = 3.1$ Hz), 63.3 (d, $J = 6.1$ Hz), 63.5 (d, $J = 169.1$ Hz, P-C coupling), 107.3, 107.8, 130.3, 156.8, 165.7; ESI-MS obsd 547.0502, calcd 547.0492 [$(M + H)^+$, $M = C_{18}H_{29}BrO_{10}P_2$]. Anal. Calcd for $C_{18}H_{29}BrO_{10}P_2$: C, 39.50; H, 5.34. Found: C, 39.74; H, 5.46.

Methyl 4-bromo-3,5-bis[3-(diethylphosphono)propoxy]benzoate (8)

A mixture of **I** (1.23 g, 5.00 mmol), K₂CO₃ (1.38 g, 10.0 mmol) and KI (830 mg, 5.00 mmol) in CH₃CN (10 mL) was stirred at room temperature for 30 min. A sample of diethyl (3-bromopropyl)phosphonate (**III**, 2.59 g, 10.0 mmol) was added, and the mixture was refluxed for 15 h. The reaction mixture was allowed to cool to room temperature. The reaction mixture was treated with CH₂Cl₂ and water. The organic layer was separated, washed (water, brine), dried (Na₂SO₄) and concentrated. The resulting solid was chromatographed [silica, hexanes/ethyl acetate (1:1) → ethyl acetate → ethyl acetate/MeOH (97:3)] to give a viscous yellow oil (2.78 g, 92%): ¹H NMR (400 MHz, DMSO-*d*₆) δ 1.21 (t, *J* = 7.2 Hz, 12H), 1.84–2.02 (m, 8H), 3.86 (s, 3H), 3.92–4.07 (m, 8H), 4.15 (t, *J* = 5.4 Hz, 4H), 7.17 (s, 2H); ¹³C NMR (100 MHz, DMSO-*d*₆) δ 16.2 (d, *J* = 6.1 Hz), 21.0 (d, *J* = 140.3 Hz, P-C coupling), 22.2, (d, *J* = 4.6 Hz), 52.4, 60.9 (d, *J* = 6.1 Hz), 68.5 (d, *J* = 17.4 Hz), 106.1, 106.5, 130.0, 155.8, 165.5; ESI-MS obsd 603.1115, calcd 603.1118 [(M + H)⁺, M = C₂₂H₃₇BrO₁₀P₂].

4,4,5,5-Tetramethyl-2-(2,6-dimethoxyphenyl)-1,3,2-dioxaborolane

A solution of 2,6-dimethoxyphenylboronic acid (909 mg, 4.99 mmol) in toluene (25 mL) was treated with pinacol (2.95 g, 25.0 mmol) and refluxed with continuous azeotropic removal of water with Dean-Stark trap for 15 h. The reaction mixture was allowed to cool to room temperature and washed with water (5 × 25 mL). The organic layer was separated, dried (Na₂SO₄) and concentrated. The resulting residue was dried under high vacuum to obtain a white solid (1.30 g, 98%): mp 78 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.19 (s, 12H), 3.78 (s, 6H), 6.46 (d, *J* = 8.4 Hz, 2H), 7.23 (t, *J* = 8.4 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 24.8, 55.7, 83.8, 103.3, 131.4, 163.5; GC-MS obsd 264, calcd 264 (M⁺, M = C₁₄H₂₁BO₄). Anal. Calcd for C₁₄H₂₁BO₄: C, 63.66; H, 8.01. Found: C, 63.87; H, 8.03.

17,18-Dihydro-15-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-10)

Following a procedure for Pd-mediated borylation [58], a mixture of **C-9** (36.8 mg, 0.0722 mmol) and (PPh₃)₂PdCl₂ (5.0 mg, 0.0072 mmol, 10 mol%) was dried in a Schlenk flask for 1 h. 1,2-Dichloroethane (8.5 mL), 4,4,5,5-tetramethyl-1,3,2-dioxaborolane (89 μL, 0.61 mmol) and TEA (100 μL, 0.722 mmol) were added. The reaction mixture was heated at 90 °C for 3 h. The reaction mixture was allowed to cool to room temperature. The reaction mixture was treated with CH₂Cl₂ and water. The organic layer was separated, washed (water, brine), dried (Na₂SO₄) and concentrated. The resulting solid was chromatographed [silica, hexanes → hexanes/CH₂Cl₂ (1:3)] to afford a purple solid (35.5 mg, 88%): ¹H NMR (400 MHz, CDCl₃) δ -1.67 (brs, 2H), 1.73 (s, 12H), 2.04 (s, 6H), 2.69 (s, 3H), 4.79 (s, 2H), 7.52 (d, *J* = 8.0 Hz, 2H), 8.00 (d, *J* = 8.0 Hz, 2H), 8.55 (d, *J* = 4.4 Hz, 1H), 8.78 (d, *J* = 4.4 Hz, 1H), 8.84 (s, 1H), 8.87 (d, *J* = 4.4 Hz, 1H), 8.89 (d, *J* = 4.4 Hz, 1H), 9.16 (d, *J* = 4.4 Hz, 1H), 9.34 (d, *J* = 4.4 Hz, 1H), 9.71 (s, 1H); LD-MS obsd 556.6; calcd 556.3 (M⁺, M = C₃₅H₃₇BN₄O₂).

15-[2,6-Bis(diethylphosphonomethoxy)-4-(methoxycarbonyl)phenyl]-17,18-dihydro-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-11)

Following a reported procedure for Pd-mediated Suzuki-coupling at the 15-position of chlorins [12], samples of **C-10** (20.8 mg, 0.0373 mmol), **7** (20.4 mg, 0.0373 mmol), (Pd(PPh₃)₄) (12.9 mg, 0.0112 mmol) and K₂CO₃ (41.2 mg, 0.298 mmol) were placed in a Schlenk flask. The flask was pumped-purged with argon three times. A degassed sample of DMF was added. The resulting mixture was stirred at 90 °C for 18 h. The reaction mixture was allowed to cool to room temperature. The reaction mixture was diluted with CH₂Cl₂ and filtered. The filtrate was concentrated. The resulting crude product was dissolved in CH₂Cl₂ and chromatographed [silica, hexanes/CH₂Cl₂ (1:1) → CH₂Cl₂ → CH₂Cl₂/MeOH (98:2)] to afford deborylated chlorin (**C-8**, 14.4 mg, 90%) followed by a trace amount of the title compound admixed with de-brominated **7**, which could not be purified. The presence of the product was strongly suggested by ESI-MS: obsd 897.3512, calcd 897.3388 [(M + H)⁺, M = C₄₇H₅₄N₄O₁₀P₂].

15-[2,6-Bis[3-(diethylphosphono)propoxy]-4-(methoxycarbonyl)phenyl]-17,18-dihydro-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-12)

Following a reported procedure for Pd-mediated Suzuki-coupling [12], samples of **C-10** (7.1 mg, 0.012 mmol), Pd(PPh₃)₄ (4.4 mg, 0.0038 mmol) and K₂CO₃ (14 mg, 0.10 mmol) were placed in a Schlenk flask. The flask was pumped-purged with argon three times. A solution of **8** (7.6 mg, 0.012 mmol) in toluene/DMF (1 mL, 2:1) was added. The resulting mixture was stirred at 90 °C for 18 h. The reaction mixture was allowed to cool to room temperature. The reaction mixture was diluted with CH₂Cl₂ and filtered. The filtrate was concentrated. The crude product was dissolved in CH₂Cl₂ and chromatographed [silica, hexanes/CH₂Cl₂ (1:1) → CH₂Cl₂ → CH₂Cl₂/MeOH (98:2)] to afford the deborylated chlorin (**C-8**, 4.8 mg, 87%) followed by a trace amount of the title compound admixed with de-brominated **8**, which could not be purified. The presence of the product was strongly suggested by ESI-MS: obsd 953.4008, calcd 953.4013 [(M + H)⁺, M = C₅₁H₆₂N₄O₁₀P₂].

15-Bromo-10-[2,6-bis(diethylphosphonomethoxy)phenyl]-17,18-dihydro-18,18-dimethylporphyrin (C-15)

Following a reported procedure for selective bromination of chlorin [14,17], a solution of chlorin **C-14** (30. mg, 0.040 mmol) in anhydrous THF (17 mL) was treated with NBS (7.2 mg, 0.040 mmol). The reaction mixture was stirred for 2 h at room temperature. The mixture was diluted with CH₂Cl₂ (50 mL), washed with (saturated aqueous NaHCO₃, H₂O, brine). The organic phase was dried (Na₂SO₄) and filtered. The filtrate was concentrated to obtain a blue solid. Column chromatography [silica, CH₂Cl₂/MeOH (0 → 5%)] afforded a blue solid (32 mg, 96%): ¹H NMR (400 MHz, CDCl₃) δ -2.18 (brs, 1H), -2.11 (brs, 1H), -0.20 (m, 12H), 2.08 (s, 6H), 2.5 (m, 8H), 4.15 (s, 2H), 4.18 (s, 2H), 4.70 (s, 2H), 7.07 (d, *J* = 8.4 Hz, 2H), 7.75 (t, *J* = 8.4 Hz, 1H), 8.49 (d, *J* = 4.4 Hz, 1H), 8.68 (d, *J* = 5.2 Hz, 1H), 8.81 (d, *J* = 4.4 Hz, 1H), 8.88 (s, 1H), 8.95 (d, *J* = 4.4 Hz, 1H), 9.18 (m, 2H), 9.68 (s, 1H); ESI-MS obsd 827.1966, calcd 827.1969 [(M + H)⁺, M = C₃₈H₄₅BrN₄O₈P₂]; λ_{abs} (CH₂Cl₂) 361, 402, 503, 643 nm.

15-[4-(Ethoxycarbonylmethoxy)phenyl]-10-[2,6-bis(diethylphosphonomethoxy)phenyl]-17,18-dihydro-18,18-dimethylporphyrin (C-16)

A mixture of chlorin **C-15** (25 mg, 0.030 mmol), Pd(PPh₃)₄ (5.00 mg, 0.00433 mmol), anhydrous K₂CO₃ (8.5 mg, 0.060 mmol) and **IV** (14 mg, 0.045 mmol) was dried in a Schlenk flask for 1 h. Toluene (6 mL) and DMF (3 mL) were degassed for 10 min and then added to Schlenk flask under an inert atmosphere. The mixture was heated to 90 °C for 24 h. After cooling to room temperature, the suspension was diluted with ethyl acetate and filtered over Celite. The flask and the filter cake were rinsed with ethyl acetate until the filtrate was colorless. The filtrate was washed (H₂O, brine), dried (Na₂SO₄) and filtered. The filtrate was concentrated. The resulting residue was subjected to column chromatography [silica, ethyl acetate/MeOH (0 → 5%)] to afford a green solid (14 mg, 50%): ¹H NMR (400 MHz, CD₃OD) δ -0.31 (m, 12H), 1.39 (t, *J* = 6.8 Hz, 3H), 2.01 (s, 6H), 2.31 – 2.55 (m, 8H), 4.24 (s, 2H), 4.29 (s, 2H), 4.32 (s, 2H), 4.37 (q, *J* = 6.8 Hz, 2H), 4.63 (s, 2H), 7.23 (d, *J* = 8.8 Hz, 2H), 7.31 (d, *J* = 8.4 Hz, 2H), 7.80 (d, *J* = 8.8 Hz, 2H), 7.83 (t, *J* = 8.4 Hz, 1H), 8.29 (d, *J* = 4.8 Hz, 1H), 8.49 (d, *J* = 4.4 Hz, 1H), 8.61 (d, *J* = 4.8 Hz, 1H), 8.94 (d, *J* = 4.0 Hz, 1H), 9.09 (d, *J* = 4.8 Hz, 1H), 9.10 (s, 1H), 9.34 (d, *J* = 4.4 Hz, 1H), 9.86 (s, 1H) (two protons were not observed); ESI-MS obsd 926.3416, calcd 926.3421 [(M + H)⁺, M = C₄₈H₅₆N₄O₁₁P₂]; λ_{abs} (CH₂Cl₂) 361, 409, 502, 590, 642 nm.

15-(4-(Carboxymethoxy)phenyl)-10-[2,6-bis(phosphonomethoxy)phenyl]-17,18-dihydro-18,18-dimethylporphyrin (C-17)

A solution of chlorin **C-16** (14 mg, 0.015 mmol) in THF/H₂O (5 mL, 4:1) was treated with aqueous 2M KOH (100 μL, 0.200 mmol). The mixture was stirred for 24 h at room temperature. Then, THF was removed under vacuum. The residue was partitioned between water (5 mL) and CH₂Cl₂ (5 mL). The aqueous layer was freeze-dried to obtain the potassium salt of the chlorin. The solid was dissolved in CH₂Cl₂ (5 mL) and few drops of acetic acid were added. The mixture was filtered. The filtrate was concentrated to dryness. The resulting green solid was dried under high vacuum. The solid was dissolved in CH₂Cl₂ (3 mL), whereupon TMSBr (140 μL, excess) was added. The mixture was stirred for 4 h at room temperature. The solvent and excess TMSBr were removed in vacuo, then methanol/water (5 mL, 4:1) was added. The mixture was stirred for 1 h. The solvent was removed under high vacuum, and the resulting green solid was dried under high vacuum. The residue was triturated with CH₂Cl₂ (3 × 10 mL) and dried to obtain a green solid (12 mg, quantitative): ¹H NMR (400 MHz, CD₃OD) δ 2.01 (s, 6H), 4.13 (s, 2H), 4.15 (s, 2H), 5.49 (s, 2H), 7.33 (m, 4H), 7.91 (m, 3H), 8.71 (m, 1H), 8.85 (d, *J* = 4.8 Hz, 1H), 9.25 (d, *J* = 4.4 Hz, 1H), 9.36 (d, *J* = 4.4 Hz, 1H), 9.51 (s, 1H), 9.65 (d, *J* = 4.4 Hz, 1H), 10.45 (s, 1H), the integration was deficient by 10 protons, of which 7 are exchangeable; ESI-MS obsd 785.1813, calcd 785.1783 [(M – H)[–], M = C₃₈H₃₆N₄O₁₁P₂]; λ_{abs} (H₂O) 405, 503, 583, 634 nm.

1,3,3-Trimethyl-7-(4-iodophenyl)-2,3,4,5-tetrahydrodipyrin N¹⁰-oxide (11)

A solution of **10** (0.500 g, 1.14 mmol) in acetic acid (10 mL) was treated with zinc dust (1.74 g, 26.5 mmol) all-at-once and the mixture was stirred vigorously for 1 h at room temperature. The crude reaction mixture was filtered (Celite) and concentrated. The residue

was dissolved in CH₂Cl₂, washed (10% aq Na₂CO₃), dried (Na₂SO₄) and evaporated to afford a yellow solid. Recrystallization from ethyl acetate gave a white powder (200 mg, 43% yield): mp 173–174 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.98 (s, 3H), 1.17 (s, 3H), 2.10 (s, 3H), 2.36 (d, *J* = 17.4 Hz, 1H), 2.52 (d, *J* = 17.4 Hz, 1H), 3.07 (m, 2H), 3.96 (m, 1H), 6.20 (m, 1H), 6.74 (m, 1H), 7.08 (d, *J* = 7.8 Hz, 2H), 7.67 (d, *J* = 7.8 Hz, 2H), 11.31 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 13.2, 22.7, 23.5, 26.8, 37.8, 46.8, 81.0, 90.1, 107.8, 117.0, 120.6, 125.7, 130.2, 137.0, 137.3, 145.5. Anal. Calcd. for C₁₈H₂₁N₂IO: C, 52.95; H, 5.18; N, 6.86. Found: C, 52.91; H, 5.23; N, 6.78.

1,3,3-Trimethyl-7-(4-iodophenyl)-2,3,4,5-tetrahydrodipyrin (12)

Following a procedure for the deoxygenation of *N*-oxides [10], TiCl₄ (1.0 mL, 8.8 mmol) was slowly added to a stirred solution of dry THF (20 mL) under argon at 0 °C. To the resulting yellow solution, LiAlH₄ (220 mg, 5.9 mmol) was added slowly and the black mixture was stirred at room temperature for 15 min, then TEA (7.7 mL) was added. The black mixture was then poured into a solution of **11** (500 mg, 1.22 mmol) in THF (20 mL). The mixture was stirred for 2 h at room temperature and then water (20 mL) was added. The mixture was filtered to remove inorganic materials. The filtrate was extracted (CH₂Cl₂). The organic layer was dried (Na₂SO₄) and evaporated under reduced pressure. The resulting brown oil was purified by chromatography (silica, ethyl acetate) to give a light brown oil which solidified on cooling (180 mg, 38%): mp 90–91 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.92 (s, 3H), 1.08 (s, 3H), 2.05 (s, 3H), 2.34 (m, 2H), 2.59 (m, 1H), 2.92 (m, 1H), 3.64 (d, *J* = 11.7 Hz, 1H), 6.25 (m, 1H), 6.73 (m, 1H), 7.13 (d, *J* = 6.6 Hz, 2H), 7.66 (d, *J* = 6.6 Hz, 2H), 10.30 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 21.2, 23.5, 27.0, 27.8, 42.6, 54.9, 80.5, 90.4, 108.4, 117.0, 120.3, 128.9, 130.6, 137.8, 137.9, 175.3; FAB-MS obsd 393.0841, calcd 393.0743 (M⁺, M = C₁₈H₂₁IN₂).

1,3,3-Trimethyl-7-[4-[2-(trimethylsilyl)ethynyl]phenyl]-2,3,4,5-tetrahydrodipyrin (13)

Samples of **12** (450 mg, 1.15 mmol), Pd₂(dba)₃ (81 mg, 0.090 mmol), Ph₃As (220 mg, 0.72 mmol), and CuI (17 mg, 0.090 mmol) were added to a 50 mL Schlenk flask. The flask was evacuated and purged with argon three times. Then deaerated anhydrous THF/TEA (12 mL, 1:1) was added followed by (trimethylsilyl)acetylene (243 μL, 1.72 mmol). The flask was sealed, immersed in an oil bath (37 °C), and the mixture was stirred overnight. Then CH₂Cl₂ (30 mL) was added and the mixture was filtered (Celite) and washed (CH₂Cl₂). The filtrate was concentrated. The resulting residue was purified by flash chromatography (silica, ethyl acetate) to afford a dark brown viscous oil (316 mg, 76%): ¹H NMR (300 MHz, CDCl₃) δ 0.25 (s, 9H), 0.92 (s, 3H), 1.07 (s, 3H), 2.05 (s, 3H), 2.34 (m, 2H), 2.61 (m, 1H), 2.95 (m, 1H), 3.65 (d, *J* = 11.7 Hz, 1H), 6.29 (m, 1H), 6.74 (m, 1H), 7.32 (d, *J* = 7.8 Hz, 2H), 7.47 (d, *J* = 7.8 Hz, 2H), 10.27 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 0.7, 21.1, 23.5, 27.1, 27.7, 42.6, 54.8, 80.5, 94.1, 106.3, 108.4, 117.0, 119.8, 120.9, 128.3, 129.3, 132.7, 138.7, 175.4; FAB-MS obsd 363.2271, calcd 363.2172 (M⁺, M = C₂₃H₃₀N₂Si).

3-(4-Iodophenyl)-9-(3,5-di-*tert*-butylbenzoyl)-10-*N*-(*tert*-butoxycarbonyl)-dipyrromethane (15)

A solution of **14** (0.90 g, 2.0 mmol) in anhydrous THF (30 mL) under argon at 0 °C was treated slowly with EtMgBr (1M in THF, 6 mL, 6.0 mmol). The mixture was stirred for 10 min at 0 °C. Then a solution of 3,5-di-*tert*-butylbenzoyl chloride (760 mg, 3.0 mmol) in anhydrous THF (5 mL) was added slowly and stirring was continued for 1.5 h at 0 °C. The reaction was quenched with saturated aqueous NH₄Cl and extracted (CH₂Cl₂). The combined organic layers were washed with water and brine, dried (Na₂SO₄), and concentrated. The product was purified by flash column chromatography [silica, hexanes/ethyl acetate (4:1)] to yield a brown viscous oil which was cooled overnight in the refrigerator. A minimum amount of hexanes was added followed by sonication, affording a white solid (598 mg, 45%): mp 178–179 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.35 (s, 18H), 1.58 (s, 9H), 4.30 (s, 2H), 5.97 (m, 1H), 6.26 (m, 1H), 6.73 (m, 1H), 7.11 (d, *J* = 6.6 Hz, 2H), 7.30 (m, 1H), 7.60 (m, 1H), 7.70 (m, 2H), 7.72 (m, 2H), 9.92 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 25.8, 28.5, 32.0, 35.6, 85.5, 93.0, 110.1, 112.3, 120.4, 122.1, 123.9, 126.3, 127.1, 128.2, 131.2, 131.3, 135.4, 138.2, 138.6, 139.2, 150.5, 151.3, 185.7. Anal. Calcd for C₃₅H₄₁N₂O₃: C, 63.25; H, 6.22; N, 4.21. Found: C, 64.03; H, 6.35; N, 4.15.

3-(4-Iodophenyl)-9-(3,5-di-*tert*-butylbenzoyl)dipyrromethane (16)

A solution of **15** (0.60 g, 0.90 mmol) in anhydrous THF (10 mL) under argon at room temperature was treated with methanolic NaOMe (146 mg, 2.70 mmol, in 1.0 mL of anhydrous methanol). After 10 min, the reaction was quenched with a mixture of hexanes and water (20 mL, 1:1) and extracted with ethyl acetate. The combined organic layers were washed with water and brine, dried (Na₂SO₄), and concentrated. The residue was recrystallized from ethanol to give a pale brown solid (430 mg, 84%): mp 202–203 °C; ¹H NMR (300 MHz, CDCl₃) δ 1.30 (s, 18H), 4.18 (s, 2H), 6.23 (m, 2H), 6.48 (m, 1H), 6.93 (m, 1H), 7.25 (d, *J* = 8.1 Hz, 2H), 7.68 (m, 1H), 7.75 (m, 4H), 10.23 (br, 1H), 11.85 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 25.6, 31.9, 35.6, 91.1, 109.0, 111.2, 118.1, 121.6, 124.0, 124.2, 124.8, 127.0, 130.9, 131.5, 137.3, 138.0, 138.2, 141.5, 151.8, 187.5. Anal. Calcd for C₃₀H₃₃N₂O: C, 63.83; H, 5.89; N, 4.96. Found: C, 63.74; H, 6.09; N, 5.00.

3-[4-(2-(Trimethylsilyl)ethynyl)phenyl]-9-(3,5-di-*tert*-butylbenzoyl)dipyrromethane (17)

Samples of **16** (1.0 g, 1.8 mmol), Pd₂(dba)₃ (125 mg, 0.140 mmol), Ph₃As (334 mg, 1.09 mmol), and CuI (26 mg, 0.14 mmol) were added to a 50 mL Schlenk flask. The flask was evacuated and purged with argon three times. Then deaerated anhydrous THF/TEA (18 mL, 1:1) was added followed by (trimethylsilyl)acetylene (376 μL, 2.66 mmol). The flask was sealed, immersed in an oil bath (37 °C), and the mixture was stirred overnight (16 – 18 h). Then CH₂Cl₂ (30 mL) was added and the mixture was filtered (Celite) and washed (CH₂Cl₂). The filtrate was concentrated. The resulting residue was purified by flash chromatography [silica, hexanes/ethyl acetate (3:1)] to afford a yellow oil which solidified on cooling (780 mg, 82%): mp 126–127 °C; ¹H NMR (300 MHz, CDCl₃) δ 0.26 (s, 9H), 1.27 (s, 18H), 4.20 (s, 2H), 6.20 (m, 2H), 6.44 (m, 1H), 6.87 (m, 1H), 7.40 (d, *J* = 8.1 Hz, 2H), 7.50 (d, *J* = 8.1 Hz, 2H), 7.64 (m, 1H), 7.72 (m, 2H), 10.14 (br, 1H), 11.73 (br, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 0.7, 25.7, 31.9, 35.5, 94.4, 106.2, 109.1, 111.1, 118.1,

120.4, 122.0, 123.9, 124.1, 124.9, 126.9, 128.5, 131.5, 132.7, 138.1, 138.2, 141.3, 151.7, 187.45. Anal. Calcd for $C_{35}H_{42}N_2OSi$: C, 78.60; H, 7.92; N, 5.24. Found: C, 78.09; H, 8.03; N, 5.13.

1-Bromo-3-[4-(2-(trimethylsilyl)ethynyl)phenyl]-9-(3,5-di-*tert*-butylbenzoyl)-dipyrromethane (18)

A solution of **17** (100 mg, 0.19 mmol) in anhydrous THF (6 mL) was cooled to $-78\text{ }^{\circ}\text{C}$ under argon. NBS (33 mg, 0.19 mmol) was added and the reaction mixture was stirred for 1 h ($-78\text{ }^{\circ}\text{C}$), then the mixture was quenched with a mixture of hexanes and water (20 mL, 1:1) and allowed to warm to $0\text{ }^{\circ}\text{C}$. The aqueous portion was extracted with anhydrous ether and the combined organic layers were dried (K_2CO_3). The solvent was evaporated under vacuum without heating. Purification by flash chromatography [silica, hexanes/ether (2:1)] afforded a pale yellow solid (83 mg, 72%): mp $163\text{--}165\text{ }^{\circ}\text{C}$ (dec.); ^1H NMR (300 MHz, $CDCl_3$) δ 0.27 (s, 9H), 1.30 (s, 18H), 4.20 (s, 2H), 6.08 (m, 1H), 6.23 (m, 1H), 6.94 (m, 1H), 7.36 (d, $J = 7.8\text{ Hz}$, 2H), 7.52 (d, $J = 7.8\text{ Hz}$, 2H), 7.66 (s, 1H), 7.74 (s, 2H), 10.75 (br, 1H), 12.14 (br, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 0.7, 24.8, 31.2, 34.9, 94.0, 97.9, 105.2, 110.0, 110.7, 120.3, 123.1, 123.7, 123.8, 125.5, 126.5, 127.9, 130.8, 132.0, 136.3, 137.3, 140.5, 151.1, 187.3; FAB-MS obsd 612.2184, calcd 612.2166 (M^+ , $M = C_{35}H_{41}BrN_2OSi$). Anal. Calcd for $C_{35}H_{41}BrN_2OSi$: C, 68.50; H, 6.73; N, 4.56. Found: C, 68.06; H, 6.64; N, 4.49.

Zn(II)-17,18-Dihydro-18,18-dimethyl-2-(4-iodophenyl)-5-(3,5-di-*tert*-butylbenzoyl)-12-[4-(2-(trimethylsilyl)ethynyl)phenyl]porphyrin (ZnC-21)

Following the two-flask procedure [10], to a solution of **18** (123 mg, 0.200 mmol) in anhydrous THF/methanol (7.5 mL, 4:1) was added excess $NaBH_4$ (100 mg, 2.60 mmol) in small portions at room temperature. The reaction was monitored by TLC [alumina, hexanes/ethyl acetate (1:1)]. Upon completion, the reaction was quenched with cold water (10 mL), and then the mixture was extracted with distilled CH_2Cl_2 ($3 \times 25\text{ mL}$). The combined organic extract was washed with brine (50 mL), dried (K_2CO_3) and concentrated in vacuo without heating to leave the resulting dipyrromethane-monocarbinol **18-OH** in $\sim 1\text{--}2\text{ mL}$ of CH_2Cl_2 . A solution of **12** (78 mg, 0.20 mmol) in a few milliliters of anhydrous CH_3CN was combined with the carbinol, then additional anhydrous CH_3CN was added to give a total of 20 mL of CH_3CN . The solution was stirred at room temperature under argon and TFA (20 μL , 0.26 mmol) was added. The reaction was monitored by TLC [alumina, hexanes/ethyl acetate (3:1)]; after 1 h **18-OH** had disappeared. The reaction mixture was quenched with 10% aqueous $NaHCO_3$ and extracted with distilled CH_2Cl_2 ($3 \times 25\text{ mL}$). The combined organic layers were washed with water and brine, then dried (Na_2SO_4). The solvent was removed in vacuo at room temperature. The residue was dissolved in 14 mL of anhydrous toluene under argon, then $AgIO_3$ (848 mg, 3.00 mmol), piperidine (300. μL , 3.00 mmol) and $Zn(OAc)_2$ (550 mg, 3.00 mmol) were added. The resulting mixture was heated at $80\text{ }^{\circ}\text{C}$ for 3 h. The reaction was monitored by TLC [silica, hexanes/ CH_2Cl_2 (1:1)], which showed a single green spot. The mixture was cooled to room temperature, then passed through a short column (silica, CH_2Cl_2). The major fraction was concentrated and again chromatographed [silica, hexanes/ CH_2Cl_2 (2:1 then 1:1)] to give a greenish blue solid (15 mg, 8%): ^1H NMR (300 MHz, $CDCl_3$) δ 0.35 (s, 9H), 1.51 (s, 18H), 1.97 (s, 6H), 4.51 (s, 2H), 7.42 (s, 1H), 7.82 (d, $J = 9.0\text{ Hz}$, 2H), 7.87 (d, $J = 7.8\text{ Hz}$, 2H), 7.96 (m, 2H), 8.03 (d, $J = 8.1\text{ Hz}$, 2H),

8.14 (d, $J = 8.1$ Hz, 2H), 8.56 (d, $J = 4.5$ Hz, 1H), 8.66 (m, 2H), 8.72 (m, 2H), 8.81 (d, $J = 4.5$ Hz, 1H), 9.61 (s, 1H); LD-MS obsd 964.60; FAB-MS obsd 964.2382, calcd 964.2370 (M^+ , $M = C_{53}H_{53}IN_4SiZn$); λ_{abs} (toluene)/nm 417 (log $\epsilon = 5.30$, fwhm = 20 nm), 629 (4.86); λ_{em} 634, 691 nm.

Zn(II)-3-Bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (ZnC-22)

Following a streamlined procedure [17], a solution of Western half **19** (153 mg, 0.569 mmol) and Eastern half **20** (210 mg, 0.569 mmol) in distilled CH_2Cl_2 was treated with a solution of *p*-TsOH- H_2O (541 mg, 2.85 mmol) in anhydrous methanol (6 mL) under argon. The resulting red reaction mixture was stirred at room temperature for 40 min. A sample of 2,2,6,6-tetramethylpiperidine (1.2 mL, 7.11 mmol) was added. The reaction mixture was concentrated. The resulting solid was dissolved in CH_3CN (56.9 mL) and subsequently treated with 2,2,6,6-tetramethylpiperidine (2.4 mL, 14 mmol), $Zn(OAc)_2$ (1.62 g, 8.81 mmol), and $AgOTf$ (446 mg, 1.74 mmol). The resulting suspension was refluxed for 14 h exposed to air. The crude mixture was filtered through a pad of silica (CH_2Cl_2). The filtrate was chromatographed [silica, hexanes/ CH_2Cl_2 (2:1 $\rightarrow$ 1:1 $\rightarrow$ 1:2)] to afford a green solid (119 mg, 34%): 1H NMR (300 MHz, $CDCl_3$) δ 1.84 (s, 6H), 2.01 (s, 6H), 2.59 (s, 3H), 4.50 (s, 2H), 7.22 (s, 2H), 8.30 (d, $J = 3.4$ Hz, 1H), 8.49 (s, 1H), 8.53 (d, $J = 3.9$ Hz, 1H), 8.60 (d, $J = 4.5$ Hz, 1H), 8.67 (s, 1H), 8.78 (s, 1H), 8.87 (d, $J = 3.9$ Hz, 1H), 9.73 (s, 1H); LD-MS obsd 599.8; ESI-MS obsd 598.0710, calcd 598.0705 (M^+ , $M = C_{31}H_{27}BrN_4Zn$); λ_{abs} 410, 614 nm; λ_{em} ($\lambda_{ex} = 410$ nm) 617, 647 nm.

Zn(II)-17,18-Dihydro-3-(*N,N*-dimethylamino)-10-mesityl-18,18-dimethylporphyrin (ZnC-23)

Following a procedure for amination of aryl bromides [72] with slight modification, a mixture of **ZnC-22** (10.0 mg, 0.017 mmol), $Pd(OAc)_2$ (1.5 mg, 0.0068 mmol, 40 mol %), (*t*-Bu) $_3$ PHBF $_4$ (1.9 mg, 0.0068 mmol, 40 mol %), and sodium *tert*-butoxide (4.9 mg, 0.051 mmol, 3 equiv) were dried in a Schlenk flask for 1 h. Degassed toluene (1.6 mL) and dimethylamine (85 μ L, 2.0 M in toluene, 0.17 mmol, 10 equiv) were added, and the mixture was purged with argon. The reaction mixture was heated to reflux for 48 h. After cooling to room temperature, the reaction mixture was treated with CH_2Cl_2 and water. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting residue was chromatographed [silica, hexanes/ CH_2Cl_2 (1:1 $\rightarrow$ 1:2)], followed by a second column (silica, CH_2Cl_2 with 1% TEA) to give a green solid (4.6 mg, 49%, 95% purity): 1H NMR (300 MHz, $CDCl_3$) δ 1.87 (s, 6H), 1.95 (s, 6H), 2.58 (s, 3H), 3.61 (s, 6H), 4.36 (s, 2H), 7.19 (s, 2H), 7.69 (s, 1H), 8.18 (s, 1H), 8.22 (d, $J = 4.1$ Hz, 1H), 8.39 (m, 3H), 8.61 (d, $J = 4.1$ Hz, 1H), 9.49 (s, 1H); MALDI-MS obsd 563.1; ESI-MS obsd 564.2097, calcd 564.2100 [$(M + H)^+$, $M = C_{33}H_{33}N_5Zn$]; λ_{abs} (toluene) 410, 612 nm; λ_{em} ($\lambda_{ex} = 410$ nm, toluene) 617, 664 nm.

Zn(II)-17,18-Dihydro-10-mesityl-18,18-dimethyl-3-methylthioporphyrin (ZnC-24)

Following a procedure for aryl thioether formation [73], a mixture of **ZnC-22** (45.1 mg, 0.0750 mmol), $Pd_2(dba)_3$ (13.7 mg, 0.0150 mmol, 20 mol %), Xantphos (8.7 mg, 0.015 mmol, 20 mol %), and sodium thiomethoxide (15.8 mg, 0.225 mmol, 3 equiv relative to **ZnC-22**) was dried in a Schlenk flask for 1 h. Degassed xylene (1.5 mL) was added, and the

mixture was purged with argon. The reaction mixture was heated to reflux for 24 h. After cooling to room temperature, the reaction mixture was treated with CH₂Cl₂ and water. The organic layer was separated, dried (Na₂SO₄), and concentrated. The resulting residue was chromatographed (silica, CH₂Cl₂) to give a green solid (40.5 mg, 95%): ¹H NMR (300 MHz, CDCl₃) δ 1.86 (s, 6H), 2.02 (s, 6H), 2.59 (s, 3H), 2.64 (s, 3H), 4.47 (s, 2H), 7.21 (bs, 2H), 8.06 (s, 1H), 8.32 (d, *J* = 4.2 Hz, 1H), 8.36 (s, 1H), 8.51 (dd, *J* = 13.5 & 4.2 Hz, 2H), 8.58 (s, 1H), 8.72 (d, *J* = 4.2 Hz, 1H), 9.25 (s, 1H); MALDI-MS obsd 566.5; ESI-MS obsd 566.1472, calcd 566.1477 (M⁺, M = C₃₂H₃₀N₄SZn); λ_{abs} (toluene) 410, 616 nm; λ_{em} (λ_{ex} = 410 nm, toluene) 621, 666 nm.

Zn(II)-17,18-Dihydro-10-mesityl-3-methoxy-18,18-dimethylporphyrin (ZnC-25)

Modifying the procedure used to synthesize **ZnC-24** [73], a mixture of **ZnC-22** (10.0 mg, 0.017 mmol), Pd₂(dba)₃ (3.1 mg, 0.0034 mmol, 20 mol %), Xantphos (2.1 mg, 0.0041 mmol, 20 mol %), and sodium methoxide (2.7 mg, 0.051 mmol) was dried in a Schlenk flask for 1 h. Degassed xylene (1.6 mL) was added, and the mixture was purged with argon. The reaction mixture was heated to reflux for 24 h. After cooling to room temperature, the reaction mixture was treated with CH₂Cl₂ and water. The organic layer was separated, dried (Na₂SO₄), and concentrated. The resulting residue was chromatographed [silica, hexanes/CH₂Cl₂ (1:1→1:2)] to give a green solid (1.5 mg, 16%): ¹H NMR (300 MHz, CDCl₃) δ 1.85 (s, 6H), 1.98 (s, 6H), 2.58 (s, 3H), 4.41 (s, 2H), 4.53 (s, 3H), 7.19 (s, 2H), 7.74 (s, 1H), 8.26 (d, *J* = 3.9 Hz, 1H), 8.29 (s, 1H), 8.44 (d, *J* = 3.9 Hz, 1H), 8.46 (d, *J* = 3.9 Hz, 1H), 8.50 (s, 1H), 8.66 (d, *J* = 3.9 Hz, 1H), 9.51 (s, 1H); MALDI-MS obsd 551.0; ESI-MS obsd 550.1707, calcd 550.1706 (M⁺, M = C₃₃H₃₀N₄OZn); λ_{abs} (toluene) 404, 603 nm; λ_{em} (λ_{ex} = 410 nm, toluene) 606, 656 nm.

3,13-Dibromo-17,18-dihydro-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-29)

Following a reported procedure [13,21], a mixture of Eastern half **21** (0.284 g, 0.674 mmol) and Western half **19** (0.202 g, 0.750 mmol) in CH₂Cl₂ (20 mL) was treated with a solution of *p*-TsOH·H₂O (0.640 g, 3.37 mmol) in MeOH (5 mL). The resulting mixture was stirred at room temperature for 30 min. A sample of 2,2,4,4-tetramethylpiperidine (3.21 mL, 18.9 mmol) was added, and the resulting mixture was concentrated. The resulting brown solid was suspended in acetonitrile (67 mL), and samples of Zn(OAc)₂ (1.86 g, 10.1 mmol), 2,2,4,4-tetramethylpiperidine (3.25 mL, 19.1 mmol), and AgOTf (0.520 g, 2.00 mmol) were added. The resulting mixture was refluxed for 18 h. The mixture was concentrated and filtered through silica using hexanes/CH₂Cl₂ as an eluent. Fractions containing chlorin were collected, concentrated, dissolved in CH₂Cl₂ (20 mL), and treated with TFA (0.400 mL, 5.23 mmol). The resulting mixture was stirred for 4 h and quenched by the addition of saturated aqueous NaHCO₃. The organic layer was separated, washed (water and brine), dried (Na₂SO₄), and concentrated. Column chromatography (silica, hexanes/CH₂Cl₂) afforded a green solid (47 mg, 12%): ¹H NMR (400 MHz, CDCl₃) δ -2.02 (bs, 1H), -1.64 (bs, 1H), 2.04 (s, 6H), 2.69 (s, 3H), 4.64 (s, 2H), 7.54 (d, *J* = 7.8 Hz, 2H), 7.99 (d, *J* = 7.8 Hz, 2H), 8.60 (d, *J* = 4.4 Hz, 1H), 8.76 (s, 1H), 8.83 (s, 1H), 8.94 (d, *J* = 4.4 Hz, 1H), 8.95 (s, 1H), 9.11 (s, 1H), 9.87 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 31.1, 46.5, 52.0, 94.4, 95.3, 105.8, 113.4, 118.5, 122.1, 124.4, 127.9, 129.3, 132.3, 132.7, 132.9, 134.1, 134.6, 137.2, 137.8, 138.0, 140.1, 151.0, 153.2, 163.3, 175.7; ESI-MS obsd 587.0450, calcd

587.0440 [(M + H)⁺, M = C₂₉H₂₄N₄Br₂]. (The same reaction on a 2.5 mmol scale provided 11% yield.)

General procedures for Sonogashira reaction with chlorin C-29

Procedure A—Samples of **C-29**, the appropriate ethyne derivative, and Pd(PPh₃)₂Cl₂ were placed in a Schlenk flask, whereupon solvent (DMF/TEA, 1:1) was added. The reaction mixture was degassed by freeze-pump-thaw (three cycles), after which the reaction flask was filled with nitrogen and placed in preheated oil bath. The reaction mixture was stirred at 80–85 °C with monitoring of the reaction by absorption spectroscopy and TLC [silica, hexanes/CH₂Cl₂ (2:1)]. Upon consumption of all starting material, the reaction mixture was allowed to cool to room temperature, diluted with ethyl acetate, washed (water, brine), dried (Na₂SO₄), and concentrated. Subsequent purification is described for each instantiation below.

Procedure B—Samples of **C-29**, the appropriate ethyne derivative, and tri-*o*-tolylphosphine were placed in a Schlenk flask, whereupon solvent (toluene/TEA, 5:1) was added. The reaction mixture was degassed by freeze-pump-thaw (two cycles), and then a sample of Pd₂(dba)₃ was added. The reaction mixture was degassed again by freeze-thaw-pump (three cycles), after which the reaction flask was filled with nitrogen and placed in a pre-heated oil bath. (When TMS-acetylene was used, the addition of TMS-acetylene was done after the final freeze-pump-thaw cycle given the low boiling point of this ethyne.) The reaction mixture was stirred at 60 °C with monitoring of the reaction progress by absorption spectroscopy and TLC. A significant amount of the starting material was typically present after ~4–5 h, whereupon another batch of Pd₂(dba)₃ and tri-*o*-tolylphosphine was added under nitrogen. Upon consumption of all starting material, the reaction mixture was allowed to cool to room temperature and concentrated. Subsequent purification is described for each instantiation below.

17,18-Dihydro-18,18-dimethyl-10-(4-methylphenyl)-3,13-bis(2-phenylethynyl)porphyrin (C-31)

Following *Procedure A*, a mixture of **C-29** (24.0 mg, 40.8 μmol), phenylacetylene (20 μL, 200 μmol), and Pd(PPh₃)₂Cl₂ (5.6 mg, 8.0 μmol) in DMF/TEA (4 mL) was allowed to react overnight. Final workup entailed column chromatography [silica, hexanes/CH₂Cl₂ 2 (2:1)] to afford a purple-brown solid (23.4 mg, 91%): ¹H NMR (400 MHz, CDCl₃) δ –1.85 (bs, 1H), –1.43 (bs, 1H), 2.06 (s, 6H), 2.69 (s, 3H), 4.66 (s, 2H), 7.45–7.59 (m, 8H), 7.86–7.88 (m, 2H), 7.97–7.99 (m, 2H), 8.02 (d, *J* = 7.9 Hz, 2H), 8.64 (d, *J* = 4.3 Hz, 1H), 8.80 (s, 1H), 8.92 (s, 1H), 8.96 (d, *J* = 4.3 Hz, 1H), 9.02 (s, 1H), 9.29 (s, 1H), 10.03 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 21.6, 31.2, 46.5, 52.2, 84.3, 84.6, 94.8, 95.5, 96.8, 98.0, 105.4, 117.8, 122.4, 122.7, 123.5, 123.6, 125.0, 127.9, 128.7, 128.8, 129.1, 130.3, 132.0, 132.2, 132.9, 133.1, 134.1, 134.8, 135.4, 137.7, 138.3, 140.15, 140.22, 151.8, 153.7, 163.8, 176.0; LD-MS obsd 631.6, calcd 631.3 [(M + H)⁺, M = C₄₅H₃₄N₄].

17,18-Dihydro-18,18-dimethyl-10-(4-methylphenyl)-3,13-bis[2-(4-(2-phenylethynyl)phenyl)ethynyl]porphyrin (C-32)

Following *Procedure A*, a mixture of **C-29** (24.0 mg, 40.8 μmol), 4-ethynyl-1-(2-phenylethynyl)benzene (41 mg, 0.20 mmol), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5.6 mg, 8.0 μmol) in DMF/TEA (4 mL) was allowed to react overnight. Final workup entailed column chromatography [silica, hexanes/ CH_2Cl_2 (2:1)] to afford a purple-brown solid (27.2 mg, 80%). The resulting product contained a trace amount of blue-fluorescent material (most probably a trace amount of 4-ethynyl-1-(2-phenylethynyl)benzene or homocoupled byproduct thereof). For fluorescence studies a sample of product (~20 mg) was dissolved in $\text{CHCl}_3/\text{MeOH}$ (6 mL, 5:1) and treated with $\text{Zn}(\text{OAc})_2 \cdot 2\text{H}_2\text{O}$ (0.180 g, 0.820 mmol). The resulting mixture was stirred for 4 h, diluted with CH_2Cl_2 , washed (aqueous NaHCO_3 and brine) dried (Na_2SO_3), and concentrated. The resulting solid was purified by column chromatography [silica, hexanes/ CH_2Cl_2 (1:1)] to afford a green solid. The resulting solid was dissolved in CH_2Cl_2 (20 mL) and treated with TFA (0.4 mL). The resulting mixture was stirred for 4 h, diluted with CH_2Cl_2 , treated with aqueous NaHCO_3 and subsequently stirred for 5 min. The organic layer was separated, washed (water and brine), dried (Na_2SO_4), and concentrated. Column chromatography [silica, hexanes/ CH_2Cl_2 (2:1)] afforded spectroscopically pure product (10.5 mg): ^1H NMR (400 MHz, CDCl_3) δ -1.84 (bs, 1H), -1.40 (bs, 1H), 2.07 (s, 6H), 2.70 (s, 3H), 4.67 (s, 2H), 7.38–7.42 (m, 6H), 7.56 (d, J = 7.8 Hz, 2H), 7.59–7.62 (m, 4H), 7.66 (d, J = 8.4 Hz, 2H), 7.69 (d, J = 8.4 Hz, 2H), 7.83 (d, J = 8.4 Hz, 2H), 7.93 (d, J = 8.4 Hz, 2H), 8.04 (d, J = 7.8 Hz, 2H), 8.64 (d, J = 4.3 Hz, 1H), 8.80 (s, 1H), 8.94 (s, 1H), 8.98 (d, J = 4.3 Hz, 1H), 9.01 (s, 1H), 9.27 (s, 1H), 9.99 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 31.2, 46.6, 52.2, 86.2, 86.5, 89.3, 91.7, 91.8, 94.9, 95.6, 96.6, 97.7, 105.4, 117.5, 122.4, 122.6, 123.2, 123.4, 123.6, 123.9, 125.1, 127.9, 128.6, 128.7, 130.4, 131.8, 131.9, 132.0, 132.1, 133.0, 133.2, 134.2, 134.9, 135.4, 137.7, 138.2, 140.17, 140.20, 151.9, 153.8, 163.8, 176.0; ESI-MS obsd 831.3441, calcd 831.3482 [(M + H)⁺, M = $\text{C}_{61}\text{H}_{42}\text{N}_4$].

17,18-Dihydro-3,13-bis[2-(4-(2-(4-methoxycarbonylphenyl)ethynyl)phenyl)ethynyl]-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-33)

Following *Procedure A*, a mixture of **C-29** (24.0 mg, 40.8 μmol), methyl 4-[2-(4-ethynylphenyl)ethynyl]benzoate (52 mg, 0.20 mmol), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5.6 mg, 8.0 μmol) in DMF/TEA (4 mL) was allowed to react overnight. Final workup entailed column chromatography (silica, CH_2Cl_2) to afford a purple-brown solid (16.1 mg, 42%): ^1H NMR (400 MHz, CDCl_3) δ -1.84 (bs, 1H), -1.40 (bs, 1H), 2.07 (s, 6H), 2.70 (s, 3H), 3.96 (s, 6H), 4.67 (s, 2H), 7.66 (d, J = 7.8 Hz, 2H), 7.63–7.68 (three overlapped doublets, 6H), 7.71 (d, J = 8.3 Hz, 2H), 7.84 (d, J = 8.2 Hz, 2H), 7.95 (d, J = 8.2 Hz, 2H), 8.03 (d, J = 7.8 Hz, 2H), 8.05 (d, J = 8.3 Hz, 2H), 8.07 (d, J = 8.3 Hz, 2H), 8.64 (d, J = 4.4 Hz, 1H), 8.81 (s, 1H), 8.94 (s, 1H), 8.98 (d, J = 4.4 Hz, 1H), 9.02 (s, 1H), 9.27 (s, 1H), 9.99 (s, 1H); LD-MS obsd 947.5, calcd 947.4 [(M + H)⁺, M = $\text{C}_{65}\text{H}_{46}\text{N}_4\text{O}_4$].

17,18-Dihydro-3,13-bis[2-(4-methoxycarbonylphenyl)ethynyl]-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-34)

Following *Procedure A*, a mixture of **C-29** (45.5 mg, 77.3 μmol), 4-methoxycarbonylphenylacetylene (37.1 mg, 232 μmol), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (10.7 mg, 15.2 μmol) in DMF/TEA (4.9 mL) was allowed to react overnight. Final workup entailed column chromatography [silica, hexanes/ CH_2Cl_2 (1:1)] to afford a purple-brown solid (25.1 mg, 43%): ^1H NMR (400 MHz, CDCl_3) δ -1.83 (bs, 1H), -1.40 (bs, 1H), 2.07 (s, 6H), 2.70 (s, 3H), 3.99 (s, 6H), 4.67 (s, 2H), 7.56 (d, J = 7.8 Hz, 2H), 7.90 (d, J = 8.3 Hz, 2H), 8.00 (d, J = 8.3 Hz, 2H), 8.03 (d, J = 7.8 Hz, 2H), 8.17 (d, J = 8.3 Hz, 2H), 8.20 (d, J = 8.3 Hz, 2H), 8.64 (d, J = 4.3 Hz, 1H), 8.81 (s, 1H), 8.95 (s, 1H), 8.98 (d, J = 4.3 Hz, 1H), 9.03 (s, 1H), 9.26 (s, 1H), 9.98 (s, 1H); ESI-MS obsd 747.2963, calcd 747.2965 [(M + H)⁺, M = $\text{C}_{49}\text{H}_{38}\text{N}_4\text{O}_4$].

17,18-Dihydro-3,13-bis[2-(4-formylphenyl)ethynyl]-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-35)

Following *Procedure B*, a mixture of **C-29** (22.3 mg, 39.8 μmol), 4-formylphenylacetylene (12.7 mg, 99.5 μmol), $\text{Pd}_2(\text{dba})_3$ (7.1 mg, 7.7 μmol), and $\text{P}(o\text{-tol})_3$ (15.4 mg, 50.6 μmol) in toluene/TEA (3.9 mL) was allowed to react overnight. TLC analysis showed complete consumption of starting material, and formation of one major product accompanied by a smaller amount of byproducts. Final workup entailed column chromatography (silica, CH_2Cl_2) to provide a semi-pure product, for which ^1H NMR spectroscopy showed a small amount of impurities in the aromatic region (probably dba remnants, and/or a product of homocoupling of 4-formylacetylene). Further purification by column chromatography [silica, hexanes/ CH_2Cl_2 (1:2), twice] afforded a pure product as a purple-brown solid, but with a significant loss in yield (4.4 mg, 16%; no effort has been made to optimize the reaction conditions to improve the yield): ^1H NMR (400 MHz, CDCl_3) δ -1.79 (bs, 1H), -1.36 (bs, 1H), 2.08 (s, 6H), 2.70 (s, 3H), 4.68 (s, 2H), 7.56 (d, J = 7.7 Hz, 2H), 7.98–8.12 (m, 10H), 8.64 (d, J = 4.3 Hz, 1H), 8.82 (s, 1H), 8.97 (s, 1H), 8.98 (d, overlapped with a singlet, 1H), 9.06 (s, 1H), 9.27 (s, 1H), 9.99 (s, 1H), 10.11 (s, 1H), 10.17 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 31.2, 46.6, 52.2, 88.2, 88.8, 95.2, 95.6, 96.0, 97.0, 105.3, 116.9, 121.8, 122.9, 125.4, 125.7, 127.9, 128.4, 129.2, 129.6, 129.8, 129.98, 129.99, 130.00, 130.91, 132.4, 132.6, 133.3, 134.1, 134.9, 135.5, 135.7, 136.0, 137.9, 138.0, 140.2, 148.0, 152.1, 153.9, 163.9, 176.2, 191.6 (only one signal from the formyl carbon is visible; due to the low quantity of sample, the ^{13}C NMR spectrum shows a low signal-to-noise ratio, in which case identification of several low-intensity signals in aromatic region was ambiguous); LD-MS obsd 686.4, calcd 686.3 (M^+ , M = $\text{C}_{47}\text{H}_{34}\text{N}_4\text{O}_2$).

17,18-Dihydro-18,18-dimethyl-10-(4-methylphenyl)-3,13-bis[2-(4-(*N,N*-dimethylamino)phenyl)ethynyl]porphyrin (C-36)

Following *Procedure B*, a mixture of **C-29** (20.0 mg, 34.0 μmol), 4-(*N,N*-dimethylamino)phenylacetylene (14.8 mg, 102 μmol), $\text{Pd}_2(\text{dba})_3$ (6.2 mg, 6.7 μmol), and $\text{P}(o\text{-tol})_3$ (13.4 mg, 44.1 μmol) in toluene/TEA (6.8 mL) was allowed to react overnight. Final workup entailed column chromatography (silica, CH_2Cl_2) to provide a semi-pure product, which was washed with MeOH (with sonication, twice) to afford a purple solid

(15.0 mg, 61%): ^1H NMR (400 MHz, CDCl_3) δ -1.87 (bs, 1H), -1.44 (bs, 1H), 2.05 (s, 6H), 2.86 (s, 3H), 3.08 (s, 6H), 3.11 (s, 6H), 4.64 (s, 2H), 6.81 (d, J = 8.9 Hz, 2H), 6.85 (d, J = 8.8 Hz, 2H), 7.53 (d, J = 7.8 Hz, 2H), 7.74 (d, J = 8.8 Hz, 2H), 7.85 (d, J = 8.9 Hz, 2H), 8.02 (d, J = 7.8 Hz, 2H), 8.62 (d, J = 4.3 Hz, 1H), 8.76 (s, 1H), 8.85 (s, 1H), 8.93 (s, 1H), 8.96 (d, J = 4.3 Hz, 1H), 9.28 (s, 1H), 10.02 (s, 1H); ESI-MS obsd 717.3692, calcd 717.3700 $[(\text{M} + \text{H})^+]$, $\text{M} = \text{C}_{49}\text{H}_{44}\text{N}_6$.

17,18-Dihydro-18,18-dimethyl-10-(4-methylphenyl)-3,13-bis[2-(phenanthren-9-yl)ethynyl]porphyrin (C-37)

Following *Procedure A*, a mixture of **C-29** (19.7 mg, 33.5 μmol), 9-ethynylphenanthrene (16.2 mg, 80.2 μmol), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (4.7 mg, 6.7 μmol) in DMF/TEA (2.3 mL) was allowed to react overnight. Final workup entailed column chromatography [silica, hexanes/ CH_2Cl_2 (3:2)] to afford a violet-brown solid (7.4 mg, 27%): ^1H NMR (400 MHz, CDCl_3) δ -1.77 (bs, 1H), -1.35 (bs, 1H), 2.10 (s, 6H), 2.72 (s, 3H), 4.71 (s, 2H), 7.60 (d, J = 7.8 Hz, 2H), 7.66–7.79 (m, 4H), 7.81–7.94 (m, 4H), 7.99–8.02 (m, 1H), 8.04–8.06 (m, 1H), 8.09 (d, J = 7.8 Hz, 2H), 8.41 (s, 1H), 8.52 (s, 1H), 8.68 (d, J = 4.3 Hz, 1H), 8.74–8.75 (m, 2H), 8.77–8.79 (m, 1H), 8.81–8.83 (m, 1H), 8.85 (s, 1H), 8.96–8.98 (m, 1H), 9.02 (d, J = 4.3 Hz, 1H), 9.05 (s, 1H), 9.05–9.07 (m, 1H), 9.14 (s, 1H), 9.45 (s, 1H), 10.16 (s, 1H); ^{13}C NMR (100 MHz, CDCl_3) δ 21.7, 31.3, 45.6, 52.2, 88.8, 89.1, 95.0, 95.2, 95.7, 96.4, 105.5, 117.9, 119.9, 120.0, 122.5, 122.8, 122.9, 123.1, 123.2, 125.2, 127.2, 127.3, 127.4, 127.48, 127.54, 127.8, 127.9, 128.9, 129.0, 130.3, 130.4, 130.5, 130.6, 130.7, 131.4, 131.5, 132.4, 132.8, 133.0, 133.2, 134.2, 135.0, 135.5, 137.7, 138.3, 140.3, 140.4, 151.9, 153.8, 163.9, 176.1; LD-MS obsd 830.6, calcd 830.3 (M^+ , $\text{M} = \text{C}_{61}\text{H}_{42}\text{N}_4$).

17,18-Dihydro-18,18-dimethyl-3,13-bis(3-*N,N*-dimethylamino-1-propyn-1-yl)-10-(4-methylphenyl)porphyrin (C-38)

Following *Procedure A*, a mixture of **C-29** (24.0 mg, 40.8 μmol), *N,N*-dimethylpropargylamine (21 μL , 0.20 mmol), and $\text{Pd}(\text{PPh}_3)_2\text{Cl}_2$ (5.6 mg, 8.0 μmol) in DMF/TEA (4 mL) was allowed to react overnight. Final workup entailed column chromatography [silica, $\text{CH}_2\text{Cl}_2/\text{MeOH}$ (25:1)] to afford a violet-brown solid (21.4 mg, 88%): ^1H NMR (400 MHz, CDCl_3) δ -1.99 (bs, 1H), -1.58 (bs, 2H), 2.04 (s, 6H), 2.64 (s, 6H), 2.68 (s, 3H), 2.70 (s, 6H), 3.89 (s, 2H), 3.97 (s, 2H), 4.62 (s, 2H), 7.53 (d, J = 7.8 Hz, 2H), 8.00 (d, J = 8.00 Hz, 2H), 8.60 (d, J = 4.3 Hz, 1H), 8.77 (s, 1H), 8.83 (s, 1H), 8.94 (d, overlapped with singlet, 1H), 8.94 (s, 1H), 9.21 (s, 1H), 9.95 (s, 1H); LD-MS obsd 593.0; ESI-MS obsd 593.3406, calcd 593.3387 $[(\text{M} + \text{H})^+]$, $\text{M} = \text{C}_{39}\text{H}_{40}\text{N}_6$. Note that the most prominent peak in the LD-MS spectrum is m/z = 637, which corresponds to $[\text{M} + \text{N}(\text{CH}_3)_2]^+$.

17,18-Dihydro-18,18-dimethyl-10-(4-methylphenyl)-3,13-bis[2-(trimethylsilyl)ethynyl]porphyrin (C-39)

Following *Procedure B*, a mixture of **C-29** (45.5 mg, 77.3 μmol), trimethylsilylacetylene (17 μL , 0.12 mmol), $\text{Pd}_2(\text{dba})_3$ (14.2 mg, 15.5 μmol), and $\text{P}(o\text{-tol})_3$ (28.3 mg, 93.0 μmol) in toluene/TEA (30.7 mL) was reacted for 5 h. Another batch of trimethylsilylacetylene (17 μL , 0.12 mmol), $\text{Pd}_2(\text{dba})_3$ (14.2 mg, 15.5 μmol), and $\text{P}(o\text{-tol})_3$ (28.3 mg, 93.0 μmol) was

added, whereupon the reaction mixture was allowed to react overnight. Final workup entailed column chromatography [silica, hexanes/CH₂Cl₂ (4:1)] to provide a purple solid (21.2 mg, 44%): ¹H NMR (400 MHz, CDCl₃) δ -1.93 (bs, 1H), -1.50 (bs, 1H), 0.54 (s, 9H), 0.61 (s, 9H), 2.06 (s, 6H), 2.70 (s, 3H), 4.67 (s, 2H), 7.55 (d, *J* = 7.9 Hz, 2H), 8.02 (d, *J* = 7.9 Hz, 2H), 8.64 (d, *J* = 4.3 Hz, 1H), 8.78 (s, 1H), 8.91 (s, 1H), 8.98 (d, *J* = 4.3 Hz, 1H), 8.99 (s, 1H), 9.23 (s, 1H), 9.95 (s, 1H); ¹³C NMR (100 MHz, CDCl₃) δ 0.40, 0.43, 21.6, 31.2, 46.5, 52.2, 94.9, 95.6, 99.4, 99.9, 102.4, 103.9, 105.4, 108.9, 117.6, 122.5, 122.6, 125.8, 127.8, 131.0, 131.9, 132.9, 133.2, 134.1, 134.5, 135.6, 137.7, 138.2, 139.9, 140.4, 151.8, 153.7, 163.8, 176.0; ESI-MS obsd 623.3027, calcd 623.3021 [(M + H)⁺, M = C₃₉H₄₂N₄Si₂].

3,13-Diethynyl-17,18-dihydro-18,18-dimethyl-10-(4-methylphenyl)porphyrin (C-40)

A solution of **C-29** (11 mg, 18 μmol) in THF/MeOH (2 mL, 1:1) was treated with K₂CO₃ (7.5 mg, 54 μmol). The resulting mixture was stirred at room temperature for 2 h. The reaction mixture was diluted with CH₂Cl₂, washed (water, brine), dried (Na₂SO₄), and concentrated. Column chromatography [silica, hexanes/CH₂Cl₂ (3:2)] provided a brownish-violet solid (6.8 mg, 79%): ¹H NMR (400 MHz, CDCl₃) δ -1.97 (bs, 1H), -1.54 (bs, 1H), 2.04 (s, 6H), 2.68 (s, 3H), 3.88 (s, 1H), 4.03 (s, 1H), 4.63 (s, 2H), 7.53 (d, *J* = 7.7 Hz, 2H), 7.99 (d, *J* = 7.7 Hz, 2H), 8.62 (d, *J* = 4.3 Hz, 1H), 8.79 (s, 1H), 8.91 (s, 1H), 8.94 (d, *J* = 4.3 Hz, 1H), 9.02 (s, 1H), 9.23 (s, 1H), 9.96 (s, 1H); LD-MS obsd 487.8, calcd 478.2 (M⁺, M = C₃₃H₂₆N₄).

X-ray structure determination for 1,3,3-trimethyl-7-(4-iodophenyl)-2,3,4,5-tetrahydrodipyrin N¹⁰-oxide (11)

The sample, mounted on the end of a glass fiber using 5-min epoxy, was transferred to the diffractometer. All X-ray measurements were made on an Enraf-Nonius CAD4 diffractometer at room temperature. The unit cell dimensions were determined by a symmetry-constrained fit of 25 well centered reflections and their Friedel pairs with theta 31° < 2(θ) < 36°. A unique quadrant of data was collected using θ/2θ scan mode. Three standard reflections were measured every 4800 seconds of X-ray exposure time. Scaling the data was accomplished using a 5-point smoothed curved routine fit to the intensity check reflections. The intensity data was corrected for Lorentz and polarization effects. An empirical absorption correction was applied using psi scan data. The data were reduced using routines from the NRCVAX set of programs [86]. The structure was solved using SIR92 [87]. All non-hydrogen atoms were refined anisotropically. Hydrogen atom positions were introduced at calculated positions, and were allowed to ride on the parent carbon or nitrogen atom. The hydrogen atom displacement parameters were also allowed to ride according to the following expression: U(H) = U_{eq}({C|N}) + 0.01. The calculated structure factors were fit to the data using full matrix least-squares based on F. The calculated structure factors included corrections for anomalous dispersion from the usual tabulation [88]. A secondary extinction correction was included in the final cycles of refinement.

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References

1. Hynninen, PH. Chlorophylls. Scheer, H., editor. CRC Press; Boca Raton, FL: 1991. p. 145-209.
2. Vicente, MGH. The Porphyrin Handbook. Kadish, KM.; Smith, KM.; Guillard, R., editors. Vol. 1. Academic Press; San Diego, CA: 2000. p. 149-199.
3. Pavlov VY, Ponomarev GV. Chem Heterocyc Cmpds. 2004; 40:393–425.
4. Balaban TS, Tamiaki H, Holzwarth AR. Top Curr Chem. 2005; 258:1–38.
5. Montforts F-P, Gerlach B, Höper F. Chem Rev. 1994; 94:327–347.
6. Galewski M, Gryko DT. Curr Org Chem. 2007; 11:1310–1338.
7. de Oliveira KT, Momo PB, de Assis FF, Ferreira MAB, Brocksom TJ. Curr Org Syn. 2014; 11:42–58.
8. Strachan J-P, O'Shea DF, Balasubramanian T, Lindsey JS. J Org Chem. 2000; 65:3160–3172. *Additions and Corrections*: Strachan J-P, O'Shea DF, Balasubramanian T and Lindsey JS. *J. Org. Chem.* 2001; **66**: 642. [PubMed: 10814212]
9. Balasubramanian T, Strachan J-P, Boyle PD, Lindsey JS. J Org Chem. 2000; 65:7919–7929. [PubMed: 11073599]
10. Taniguchi M, Ra D, Mo G, Balasubramanian T, Lindsey JS. J Org Chem. 2001; 66:7342–7354. [PubMed: 11681947]
11. Taniguchi M, Kim H-J, Ra D, Schwartz JK, Kirmaier C, Hindin E, Diers JR, Prathapan S, Bocian DF, Holten D, Lindsey JS. J Org Chem. 2002; 67:7329–7342. [PubMed: 12375962]
12. Taniguchi M, Kim MN, Ra D, Lindsey JS. J Org Chem. 2005; 70:275–285. [PubMed: 15624933]
13. Laha JK, Muthiah C, Taniguchi M, McDowell BE, Ptaszek M, Lindsey JS. J Org Chem. 2006; 71:4092–4102. *Additions and Corrections*: Laha JK, Muthiah C, Taniguchi M, McDowell BE, Ptaszek M and Lindsey JS. *J. Org. Chem.* 2009; **74**: 5122. [PubMed: 16709048]
14. Taniguchi M, Ptaszek M, McDowell BE, Lindsey JS. Tetrahedron. 2007; 63:3840–3849. [PubMed: 17479170]
15. Kee HL, Kirmaier C, Tang Q, Diers JR, Muthiah C, Taniguchi M, Laha JK, Ptaszek M, Lindsey JS, Bocian DF, Holten D. Photochem Photobiol. 2007; 83:1110–1124. [PubMed: 17880506]
16. Kee HL, Kirmaier C, Tang Q, Diers JR, Muthiah C, Taniguchi M, Laha JK, Ptaszek M, Lindsey JS, Bocian DF, Holten D. Photochem Photobiol. 2007; 83:1125–1143. [PubMed: 17880507]
17. Muthiah C, Ptaszek M, Nguyen TM, Flack KM, Lindsey JS. J Org Chem. 2007; 72:7736–7749. [PubMed: 17803319]
18. Muthiah C, Kee HL, Diers JR, Fan D, Ptaszek M, Bocian DF, Holten D, Lindsey JS. Photochem Photobiol. 2008; 84:786–801. [PubMed: 18208458]
19. Borbas KE, Chandrasher V, Muthiah C, Kee HL, Holten D, Lindsey JS. J Org Chem. 2008; 73:3145–3158. [PubMed: 18341349]
20. Kee HL, Nothdurft R, Muthiah C, Diers JR, Fan D, Ptaszek M, Bocian DF, Lindsey JS, Culver JP, Holten D. Photochem Photobiol. 2008; 84:1061–1072. [PubMed: 18673324]
21. Ptaszek M, Lahaye D, Krayner M, Muthiah C, Lindsey JS. J Org Chem. 2010; 75:1659–1673. [PubMed: 20121051]

22. Liu M, Ptaszek M, Mass O, Minkler DJ, Sommer RD, Bhaumik J, Lindsey JS. *New J Chem.* 2014; 38:1717–1730.
23. Alexander VM, Sano K, Yu Z, Nakajima T, Choyke PL, Ptaszek M, Kobayashi H. *Bioconjugate Chem.* 2012; 23:1671–1679.
24. Harada T, Sano K, Sato K, Watanabe R, Yu Z, Hanaoka H, Nakajima T, Choyke PL, Ptaszek M, Kobayashi H. *Bioconjugate Chem.* 2014; 25:362–369.
25. Ptaszek M, Kee HL, Muthiah C, Nothdurft R, Akers W, Achilefu C, Culver JP, Holten D. *Proc SPIE.* 2010; 7576:1–9. 75760E.
26. Yu Z, Ptaszek M. *J Org Chem.* 2013; 78:10678–10691. [PubMed: 24079536]
27. Yu Z, Pancholi C, Bhagavathy GV, Kang HS, Nguyen JK, Ptaszek M. *J Org Chem.* 2014; 79:7910–7925. [PubMed: 25061710]
28. Yu Z, Ptaszek M. *Org Lett.* 2012; 14:3708–3711. [PubMed: 22783931]
29. Ptaszek M, Bhaumik J, Kim H-J, Taniguchi M, Lindsey JS. *Org Process Res Dev.* 2005; 9:651–659. [PubMed: 19132135]
30. Battersby AR, Dutton CJ, Fookes CJR, Turner SPD. *J Chem Soc Perkin Trans 1.* 1988:1557–1567.
31. Battersby AR, Dutton CJ, Fookes CJR. *J Chem Soc Perkin Trans I.* 1988:1569–1576.
32. Jacobi PA, Briellmann HL, Hauck SI. *J Org Chem.* 1996; 61:5013–5023.
33. Jacobi PA, Lanz S, Ghosh I, Leung SH, Löwer F, Pippin D. *Org Lett.* 2001; 3:831–834. [PubMed: 11263893]
34. O'Neal WG, Roberts WP, Ghosh I, Wang H, Jacobi PA. *J Org Chem.* 2006; 71:3472–3480. [PubMed: 16626128]
35. O'Neal WG, Jacobi PA. *J Am Chem Soc.* 2008; 130:1102–1108. [PubMed: 18166060]
36. Ben Dror S, Bronshtein I, Garini Y, O'Neal WG, Jacobi PA, Ehrenberg B. *Photochem Photobiol Sci.* 2009; 8:354–361. [PubMed: 19255676]
37. Montforts F-P. *Angew Chem Int Ed Engl.* 1981; 20:778–779.
38. Montforts F-P, Schwartz UM. *Angew Chem Int Ed Engl.* 1985; 24:775–776.
39. Schmidt W, Montforts FP. *Synlett.* 1997:903–904.
40. Abel Y, Montforts F-P. *Tetrahedron Lett.* 1997; 38:1745–1748.
41. Montforts F-P, Kutzki O. *Angew Chem Int Ed.* 2000; 39:599–601.
42. Könekamp T, Ruiz A, Duwenhorst J, Schmidt W, Borrmann T, Stohrer W-D, Montforts F-P. *Chem Eur J.* 2007; 13:6595–6604. [PubMed: 17516607]
43. Könekamp T, Borrmann T, Montforts F-P. *J Porphyrins Phthalocyanines.* 2009; 13:166–170.
44. Thanh NTV, Könekamp T, Hanke D, Löwer F, Borrmann T, Montforts F-P. *J Porphyrins Phthalocyanines.* 2012; 16:626–632.
45. Littler BJ, Miller MA, Hung C-H, Wagner RW, O'Shea DF, Boyle PD, Lindsey JS. *J Org Chem.* 1999; 64:1391–1396.
46. Laha JK, Dhanalekshmi S, Taniguchi M, Ambroise A, Lindsey JS. *Org Process Res Dev.* 2003; 7:799–812.
47. Khoury RG, Jaquinod L, Aoyagi K, Olmstead MM, Fisher AJ, Smith KM. *Angew Chem Int Ed Engl.* 1997; 36:2497–2500.
48. Zaidi SHH, Muthukumaran K, Tamaru S-I, Lindsey JS. *J Org Chem.* 2004; 69:8356–8365. [PubMed: 15549807]
49. Muthukumaran K, Ptaszek M, Noll B, Scheidt WR, Lindsey JS. *J Org Chem.* 2004; 69:5354–5364. [PubMed: 15287782]
50. Iovine PM, Kellett MA, Redmore NP, Therien MJ. *J Am Chem Soc.* 2000; 122:8717–8727.
51. Tham Yongkit P, Speckbacher M, Diers JR, Kee HL, Kirmaier C, Holten D, Bocian DF, Lindsey JS. *J Org Chem.* 2004; 69:3700–3710. [PubMed: 15152999]
52. Wagner RW, Lindsey JS, Turowska-Tyrk I, Scheidt WR. *Tetrahedron.* 1994; 50:11097–11112.
53. Fürstner A, Stelzer F, Rumbo A, Krause H. *Chem Eur J.* 2002; 8:1856–1871. [PubMed: 12007096]
54. Johnson MG, Foglesong RJ. *Tetrahedron Lett.* 1997; 38:7001–7002.

55. Sivanandan K, Aathimanikandan SV, Arges CG, Bardeen CJ, Thayumanavan S. *J Am Chem Soc.* 2005; 127:2020–2021. [PubMed: 15713060]
56. Jurecka P, Vojtisek P, Novotny K, Rohovec J, Lukes I. *J Chem Soc Perkin Trans 2.* 2002;1370–1377.
57. Phillion DP, Andrew SS. *Tetrahedron Lett.* 1986; 27:1477–1480.
58. Chng LL, Chang CJ, Nocera DG. *J Org Chem.* 2003; 68:4075–4078. [PubMed: 12737594]
59. Sinclair DJ, Sherburn MS. *J Org Chem.* 2005; 70:3730–3733. [PubMed: 15845017]
60. Weimar M, Dürner G, Bats JW, Göbel MW. *J Org Chem.* 2010; 75:2718–2721. [PubMed: 20302330]
61. Zhou X, Zhou Z-Y, Mak TCW, Chan KS. *J Chem Soc Perkin Trans 1.* 1994;2519–2520.
62. Yu L, Lindsey JS. *Tetrahedron.* 2001; 57:9285–9298.
63. Fan D, Taniguchi M, Lindsey JS. *J Org Chem.* 2007; 72:5350–5357. [PubMed: 17567079]
64. Holten D, Bocian DF, Lindsey JS. *Acc Chem Res.* 2002; 35:57–69. [PubMed: 11790089]
65. Mass O, Ptaszek M, Taniguchi M, Diers JR, Kee HL, Bocian DF, Holten D, Lindsey JS. *J Org Chem.* 2009; 74:5276–5289. [PubMed: 19518104]
66. Lindsey JS, Taniguchi M, Ra D, Mo G, Balasubramanian T. *US.* 2005; 6552:946.
67. Krayner M, Balasubramanian T, Ruzié C, Ptaszek M, Cramer DL, Taniguchi M, Lindsey JS. *J Porphyrins Phthalocyanines.* 2009; 13:1098–1110.
68. Balasubramanian T, Lindsey JS. *Tetrahedron.* 1999; 55:6771–6784.
69. Hasan I, Marinelli ER, Lin L-CC, Fowler FW, Levy AB. *J Org Chem.* 1981; 46:157–164.
70. Sonogashira K, Tohda T, Hagihara N. *Tetrahedron Lett.* 1975; 16:4467–4470.
71. Gauger, KA. MS Thesis. North Carolina State University; 2010.
72. Thanh NC, Ikai M, Kajioka T, Fujikawa H, Taga Y, Zhang Y, Ogawa S, Shimada H, Miyahara Y, Kuroda S, Oda M. *Tetrahedron.* 2006; 62:11227–11239.
73. Mispelaere-Canivet C, Spindler J-F, Perrio S, Beslin P. *Tetrahedron.* 2005; 61:5253–5259.
74. Aalten HL, van Koten G, Grove DM, Kuilman T, Piekstra OG, Hulshof LA, Sheldon RA. *Tetrahedron.* 1989; 45:5565–5578.
75. Gao G-Y, Colvin AJ, Chen Y, Zhang XP. *Org Lett.* 2003; 5:3261–3264. [PubMed: 12943402]
76. Kim H-J, Lindsey JS. *J Org Chem.* 2005; 70:5475–5486. [PubMed: 15989329]
77. Taniguchi M, Ptaszek M, McDowell BE, Boyle PD, Lindsey JS. *Tetrahedron.* 2007; 63:3850–3863. [PubMed: 17479169]
78. LeCours SM, DiMaggio SG, Therien MJ. *J Am Chem Soc.* 1996; 118:11854–11864.
79. Yang E, Kirmaier C, Krayner M, Taniguchi M, Kim H-J, Diers JR, Bocian DF, Lindsey JS, Holten D. *J Phys Chem B.* 2011; 115:10801–10816. [PubMed: 21875047]
80. Li Q, Rukavishnikov AV, Petukhov PA, Zaikova TO, Jin C, Keana JFW. *J Org Chem.* 2003; 68:4862–4869. [PubMed: 12790592]
81. Dirk SM, Tour JM. *Tetrahedron.* 2003; 59:287–293.
82. Khairul WM, Albesa-Jové D, Yufit DS, Al-Haddad MR, Collings JC, Hartl F, Howard JAK, Marder TB, Low PJ. *Inorg Chim Acta.* 2008; 361:1646–1658.
83. Laakso J, Rosser GA, Szűjjártó C, Beeby A, Borbas KE. *Inorg Chem.* 2012; 51:10366–10374. [PubMed: 22978627]
84. Pershagen E, Borbas KE. *Coord Chem Rev.* 2014;273–274. 30–46.
85. Srinivasan N, Haney CA, Lindsey JS, Zhang W, Chait BT. *J Porphyrins Phthalocyanines.* 1999; 3:283–291.
86. Gabe EJ, Le Page Y, Charland J-P, Lee FL, White PS. *J Appl Cryst.* 1989; 22:384–387.
87. Altomare A, Cascarano G, Giacovazzo C, Guagliardi A, Burla MC, Polidori G, Camalli G. *J Appl Cryst.* 1994; 27:435.
88. *International Tables for X-ray Crystallography.* Vol. IV. Kynoch Press: Birmingham England; 1974.

Generic designs with porphyrins:

R = -Me, -Et, -OCH₂Ph

Specific chlorin architectures:

Figure 1.

Facial encumbrance to achieve increased solubility of porphyrins in organic media (top) [51,52]. Extension of the approach for solubilization of chlorins in aqueous media (bottom) [19].

Figure 2.
ORTEP drawing of **11**, a Western half precursor. The ellipsoids are drawn at the 50% probability.

Figure 3.

(A) Absorption spectra normalized at the B band in toluene at room temperature of (a) 3-unsubstituted chlorin, **ZnC-26**, (b) 3-methoxychlorin, **ZnC-25**, (c) 3-methylthiochlorin, **ZnC-24**, and (d) 3-(*N,N*-dimethylamino)chlorin, **ZnC-23**. (B) Corresponding fluorescence spectra upon excitation at the peak of the B band.

Figure 4.

(A) Absorption spectra normalized at the B band in toluene at room temperature of (a) benchmark **C-30**, (b) **C-40**, (c) **C-31**, and (d) **C-32**. (B) Corresponding fluorescence spectra upon excitation at the peak of the B band.

Scheme 1.
 Synthetic methods employed herein.

Scheme 2.
Synthesis of an oxochlorin-phenol.

ZnC-4: $R = \text{CO}_2\text{CH}_2\text{CH}_2\text{TMS}$

ZnC-5: $R = \text{CO}_2\text{H}$

Scheme 3.
Synthesis of a chlorin–carboxylic acid.

Scheme 4.

Synthesis of candidate snap-on units for water solubilization and bioconjugatability.

Scheme 5.
Attempted snap-on of tri-substituted aryl motif for solubilization and conjugation.

Scheme 6.
Hydrophilic bioconjugatable chlorin-carboxylic acid.

Scheme 7.
Synthesis of β -substituted Western halves.

Scheme 8.
Synthesis of a β -substituted Eastern half.

Scheme 9. Synthesis of a *trans*-disubstituted chlorin building block.

Scheme 10.

Synthesis of 3-substituted chlorins (top) and benchmark chlorins (bottom).

Scheme 11.

Synthesis of a 3,13-dibromochlorin building block (top) and a chlorin benchmark (bottom).

Chart 1.
Prior *trans*-disubstituted chlorin building blocks.

Chart 2.
A prior 3,13-bis(phenylethynyl)chlorin.

Table 1**Summary of Crystal Data for **11****

Crystal data	
Formula	C ₁₈ H ₂₁ IN ₂ O
Formula Weight (g/mol)	408.28
Crystal Dimensions (mm)	0.58 × 0.24 × 0.06
Crystal Color and Habit	colorless plate
Crystal System	monoclinic
Space Group	P 2 ₁ /n
Temperature, K	148
<i>a</i> (Å)	13.9428 (9)
<i>b</i> (Å)	8.2765 (5)
<i>c</i> (Å)	15.1619 (11)
α (°)	90.0
β (°)	93.346 (8)
γ (°)	90.0
<i>V</i> (Å ³)	1746.66 (20)
<i>Z</i>	4
<i>D_x</i> (Mg m ⁻³)	1.553
λ, Å, (MoKα)	0.71073
μ (cm ⁻¹)	1.84
Data collection	
No. of reflections measured	3046
No. of unique reflections	3046
No. of reflections with <i>I</i> > σ(<i>I</i>)	2671
θ _{max} (°)	25.00
Index range	−16 h 16
Refinement	
No. of reflections in least-squares	2670
No. of parameters in least-squares	199
R ₁ ^a	0.033
wR ₂ ^b	0.043
R ₁ (all data) ^a	0.033
wR ₂ (all data) ^b	0.043
GOF ^c	1.54
Maximum shift/error	0.000
ρ _{max} (e Å ⁻³)	1.17
ρ _{min} (e Å ⁻³)	−1.54

$$^a R_1 = \Sigma(|F_O| - |F_C|) / \Sigma F_O$$

$$^b wR_2 = [\Sigma w(F_O - F_C)^2 / \Sigma w F_O^2]^{1/2}$$

$$^c GOF = [\Sigma w(F_O - F_C)^2 / (\text{No. of reflections} - \text{No. of parameters})]^{1/2}$$

Table 2Absorption and fluorescence spectral properties.^a

Compound	λ_B (nm)	ν_B (cm ⁻¹) ^b	λ_{QS} (nm)	ν_{QS} (cm ⁻¹) ^b	I_B/I_Q	λ_{em} (nm)
ZnC-26	405	0	606	0	4.2	609
ZnC-25	404	-61	603	-82	4.3	606
ZnC-24	410	301	616	268	3.0	621
ZnC-23	410	301	612	162	2.5	617

^a In toluene at room temperature.^b Spectral shift versus that of **ZnC-26**.

Table 3

Synthesis of 3,13-disubstituted chlorins.

Entry	R	Conditions ^a	Yield
C-31		A	91%
C-32		A	80% ^b
C-33		A	42%
C-34		A	43%
C-35		B	16%
C-36		B	61%
C-37		A	27%
C-38		A	88%
C-39		B	44%
C-40		c	79%

^a A: (PPh₃)₂PdCl₂, DMF/TEA (2:1), 80 °C. B: Pd₂(dba)₃, PPh₃, toluene/TEA (5:1), 60 °C.^b The synthetic product contained a trace amount of blue-fluorescent contaminant, which was removed for fluorescence studies (see text for details).^c C-40 was synthesized by deprotection of the TMS groups of C-39 using K₂CO₃.

Table 4Absorption and emission maxima for 3,13-disubstituted chlorins.^a

Compound	λ_B (nm)	λ_{Qy}	I_B/I_Q	λ_{em} (nm)
C-30 ^b	405	635	2.8	639
C-31	427	674	1.6	678
C-32	433	679	1.4	684
C-33	434	680	1.5	685
C-34	431	679	1.4	685
C-35	435	682	1.4	687
C-36	428	679	1.3	684
C-37	431	679	1.6	684
C-38	422	665	1.8	668
C-40	422	666	1.5	669

^a All data in toluene at room temperature.^b Absorption data are in ref [17] and in Figure 4.