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Regioselective β-pyrrolic electrophilic substitution of hydrodipyrrin–dialkylboron complexes facilitates access to synthetic models for chlorophyll *f*†

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Substituents in ring A of chlorophylls can exert profound effects on spectral properties. A *de novo* route to synthetic chlorins employs a tetrahydrodipyrrin reactant containing pyrrole and pyrroline rings. Complexation of the tetrahydrodipyrrin with a dialkylboron motif caused electrophilic substitution (bromination, formylation) to proceed predominantly at the β^7- rather than α-position of the pyrrole ring, whereas an analogous dihydrodipyrrin underwent substitution equally at the 7- and 8-positions. The fully unsaturated dipyrrin–difluoroboron complex is known to undergo electrophilic substitution at the 8-position. The 7-position of the hydrodipyrrin ultimately gives rise to substituents at the chlorin 2-position (ring A), which heretofore has been little accessed. The position of substitution was confirmed by four single-crystal X-ray structures. Two isomeric formylchlorins were prepared by Pd-mediated carbonylation of the corresponding bromochlorins. Access to a 2-formylchlorin relied on bromination of the tetrahydrodipyrrin–dibutylboron complex, whereas a 3-formylchlorin was prepared by installation of the bromo group in the earliest precursor, pyrrole-2-carboxaldehyde. The two formylchlorins differ in absorption spectral properties: the Q_y absorption maximum is 654 or 664 nm for the 2- or 3-formylchlorin, respectively. The synthetic formylchlorins provide initial models for understanding the strong red absorption of native 2- or 3-formylchlorophylls (*f* and *d*).

Introduction

Native chlorophylls are distinguished by the presence of auxochromes at specific sites about the perimeter of the macrocycle. Chlorophyll *a* and *b* both bear a vinyl group at the 3-position, for example, whereas chlorophyll *d* contains a 3-formyl group (Chart 1).[1] The location of auxochromes at the 3-position causes a hyperchromic and bathochromic effect on the long-wavelength absorption band (Q_y band), which stems from a transition that is polarized along the axis that bisects rings A and C.[2] The presence of a methyl group at the 2-position was long considered a universal feature of chlorophylls. However, the recently discovered chlorophyll *f* contains a formyl group at the 2-position in addition to a 3-vinyl substituent.[3,4] The synthesis of model chlorins that contain diverse auxochromes at the 3-position has proved incisive for probing the effects of auxochromes on spectral, electronic, and photophysical features.[5–8] We sought similar access to synthetic 2-substituted chlorins for fundamental comparisons of the effects of substituents at the 2- *versus* 3-positions.

The synthetic chemistry of chlorins has been a topic of widespread interest and has advanced considerably over the years.[9–23] A *de novo* route that we have developed to gain access to chlorins is shown in Scheme 1.[24] Two halves, a Western half and an Eastern half, are joined in a convergent ring-forming process. The Western half is a 2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (or corresponding dihydrodipyrrin[25]) whereas the Eastern half is a 9-bromo-1-formyldipyrromethane. The chlorin bears a geminal dimethyl group in the pyrroline ring thereby precluding adventitious dehydrogenation leading to the porphyrin.

The synthesis of the Western half begins with a pyrrole-2-carboxaldehyde. A substituent can be incorporated at the 3-position of the chlorin by beginning with a 4-bromopyrrole-2-carboxaldehyde (*via* the intermediacy of the 8-substituted Western half).[5] Pyrrole-2-carboxaldehyde readily undergoes electrophilic bromination at the 4-position.[26] Similarly, a 13-substituted chlorin can be prepared by beginning with a

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† Electronic supplementary information (ESI) available: Summary of NMR characterization of selected formyltetrahydrodipyrrins; X-ray data table for four compounds (**1-BBu$_2$**, CCDC 974409; **1-Br^{8}BBu$_2$**, CCDC 974410; **1-Br^{8}F^{7}BBu$_2$**, CCDC 974411; **2-BBu$_2$**, CCDC 974412); display of the enantiomers of compound **1-Br^{8}F^{7}BBu$_2$**; exploratory results for decomplexation of **1-BR$_2$**; characterization data for all new compounds. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c3nj01508d

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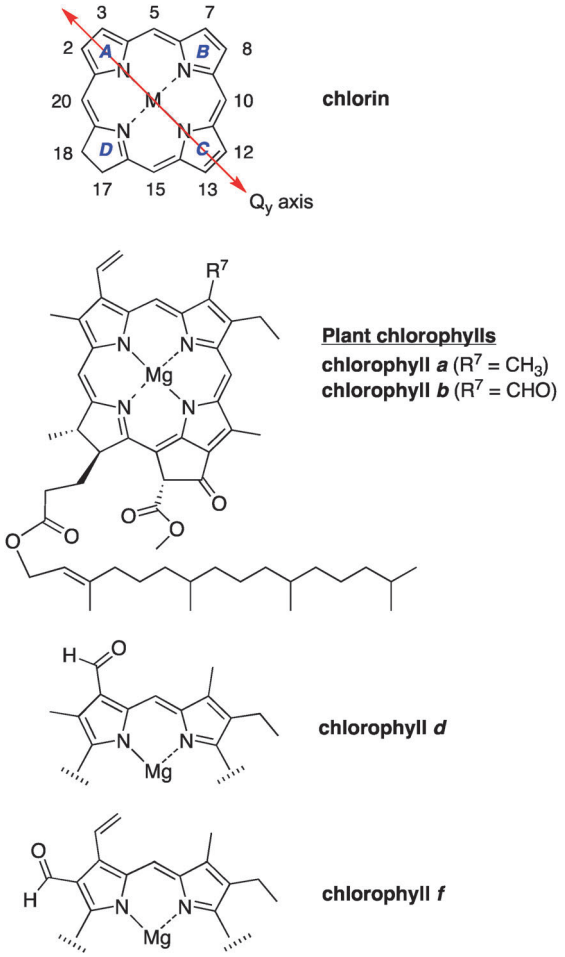
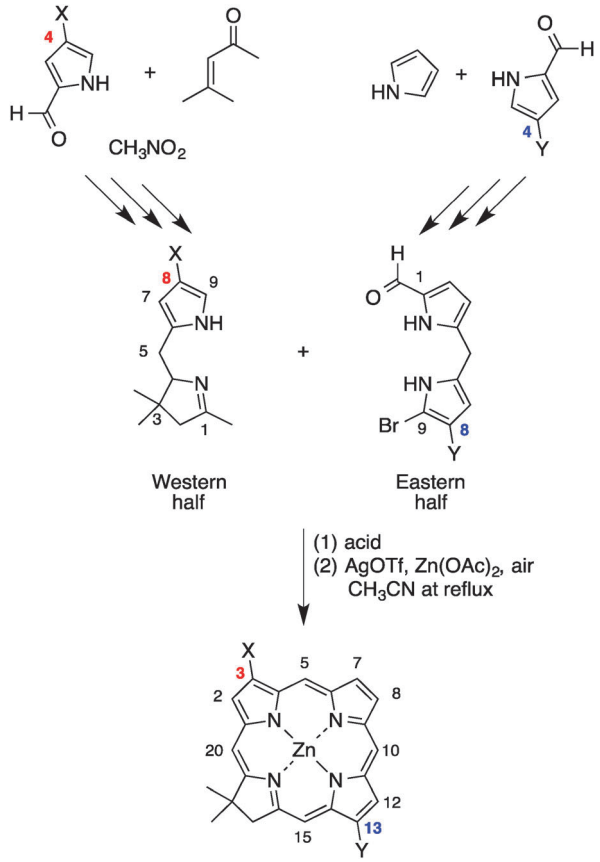


Chart 1 Chlorin nomenclature and natural chlorophylls.



Scheme 1 *De novo* route to 3,13-disubstituted chlorins.

4-bromopyrrole-2-carboxaldehyde *via* the intermediacy of the 8-substituted Eastern half.[5,27] By means of these and related approaches, all sites have been accessed (*vide infra*) to date with the sole exception of the chlorin 2-position (a 2-arylchlorin has been prepared[28] but the route employed is not compatible with the introduction of a 2-formyl group). The synthesis of a 2-bromochlorin building block could begin with the corresponding 3-substituted pyrrole-2-carboxaldehyde, but the synthesis of such pyrroles is lengthy.[29] During the course of this work, Fukuda *et al.* reported a method for the directed lithiation at the 2-position of a 3-bromo-*N*-benzensulfonylpyrrole, which also could be employed as an early point of departure to access 2-substituted pyrroles.[30,31] Regardless, the motivation here was to investigate complementary approaches for elaborating advanced precursors (*i.e.*, hydrodipyrrins) to chlorins. While this work began as an effort in pure synthesis, the subsequent discovery,[3,32] structure determination,[4] and spectroscopic investigation[33,34] of chlorophyll *f*; the growing appreciation of the rich ecological variety of photosynthesis including use of the strong-red absorbing chlorophylls *d* and *f*;[35–39] and consideration of the expanded (and possibly further expandable) spectral range of photosynthesis[40,41] together have heightened our focus on routes to chlorins that could accommodate diverse substituents in ring A.

As part of a program to improve tetrapyrrole synthetic methodology, complexation aides were found to facilitate the isolation, handling, and derivatization of acyldipyrromethanes, the precursors to tetrapyrroles. The complexation aides include a dibutyltin complex of a 1,9-diacyldipyrromethane (A)[42] and a dialkylboron complex of a 1-acyldipyrromethane (B)[43] (Chart 2). The coordination complex of each of these ligands was hydrophobic and could be easily purified by silica pad filtration and/or crystallization, whereas the uncomplexed species streaked upon chromatography and/or were poorly crystalline. Such dialkylboron complexation aides were applied to imidazolyl–dipyrromethanes (C and D),[44] whereupon the isolated complex contained a covalent pyrrolic N–B bond and a dative imidazolyl N–B bond.

Here, we sought to explore analogous complexation aides for tetrahydrodipyrrins and dihydrodipyrrins, the precursors to hydroporphyrins, wherein the bonding was expected to resemble that in the dialkylboron–imidazolyl–dipyrromethanes C and D. Tetrahydrodipyrrins typically are highly polar, streak on chromatographic media, and do not readily crystallize. Moreover, the presence of two heterocyclic rings with far different reactivity (pyrrole and pyrroline) can lead to unexpected reactions and synthetic difficulties.[45] Dihydrodipyrrins are less polar but also less stable than tetrahydrodipyrrins.[24] Initially, our goal was to facilitate purification and handling of the tetrahydrodipyrrin, but in the course of our work we realized that boron complexation alters the usual selectivity of the pyrrole upon electrophilic aromatic substitution.

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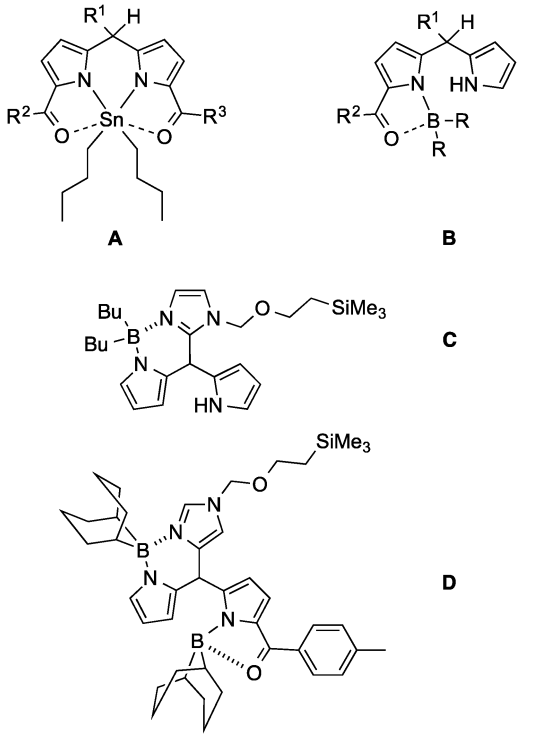


Chart 2 Complexes of pyrrolic compounds.

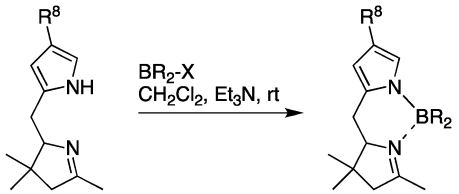
In this paper, we report the investigation of dialkylboron complexation of hydrodipyrrins. The dialkylboron unit masks both the pyrrolic and pyrrolinic nitrogen atoms of the hydrodipyrrin. The derivatization processes of interest include pyrrolic bromination and formylation for potential synthetic elaboration of the corresponding ring A of the chlorins. The dialkylboron unit directs substitution chiefly to a pyrrolic β-position rather than the α-position (as occurs in the unprotected pyrrole). One application of the dialkylboron complexation method entails the *de novo* synthesis of 2-substituted free base chlorins bearing bromo or formyl groups. An in-depth study of the spectroscopic properties of the free base chlorins and metal chelates will be described elsewhere. While our chief interests concern spectroscopic properties, we note the work of Balaban and Tamiaki, who have demonstrated that placement of carbonyl groups at distinct locations enables control over the nature of assemblies of tetrapyrrole macrocycles akin to chlorosome-like architectures.[19,46–49] Taken together, the results reported provide an initial step toward partial mimics of chlorophyll *f*, and should broaden the scope of synthetic chlorin chemistry.

Results and discussion

I. Dialkylboron complexation of hydrodipyrrins

1. Tetrahydrodipyrrin–dialkylboron complexes. Tetrahydrodipyrrin **1**[45] is a crucial building block in a rational synthesis of chlorins.[24,25,50] Reaction of **1** with dibutylboron triflate in CH_2Cl_2 containing triethylamine afforded the crude tetrahydrodipyrrin–dialkylboron complex, which upon washing with saturated aqueous $NaHCO_3$, silica-pad filtration and recrystallization (aqueous ethanol) afforded **1-BBu$_2$** in pure form (62% yield; entry 1, Table 1). The **1-BBu$_2$** complex is stable to routine handling. Crystals of **1-BBu$_2$** suitable for X-ray analysis were obtained by slow evaporation of a solution of Et_2O–MeOH.

Table 1 Synthesis of dialkylboron complexes of tetrahydrodipyrrins



1 (R^8 = H)
1-Br^8 (R^8 = Br)

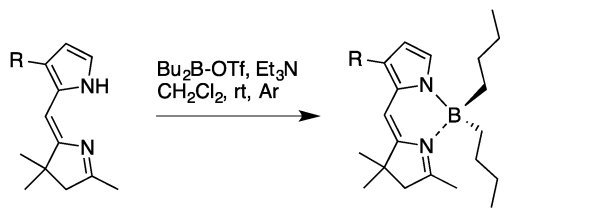
Entry	BR_2-X	Product	R	R^8	Yield (%)
1	BBu_2-OTf	**1-BBu$_2$**	Bu	H	62
2	BMe_2-Br	**1-BMe$_2$**	Me	H	67
3	BBu_2-OTf	**1-Br^{8}BBu$_2$**	Bu	Br	70

Reaction of **1** with dimethylboron bromide under nitrogen at 0 °C afforded the corresponding dimethylboron complex **1-BMe$_2$** in 67% yield (entry 2, Table 1). Compound **1-BMe$_2$** was less stable than **1-BBu$_2$**, decomposed on silica (thus purification was performed by filtration through neutral alumina), and darkened quickly when kept at room temperature. Because of instability, compound **1-BMe$_2$** was not fully characterized. Instability issues with **1-BMe$_2$** and problems with handling dimethylboron bromide (highly pyrophoric, not available commercially as a solution) makes application of **1-BMe$_2$** less attractive than **1-BBu$_2$**. The dibutylboron complex **1-Br^{8}BBu$_2$** was prepared in analogous fashion from 8-bromotetrahydrodipyrrin[5,51] **1-Br^8** in 70% yield (entry 3). A crystal of **1-Br^{8}BBu$_2$** suitable for X-ray analysis was obtained from $CHCl_3$–hexanes by slow evaporation at 4 °C.

2. Dihydrodipyrrin–boron complexes. Treatment of *p*-tolyldihydrodipyrrin **2**[52] with BBu_2OTf in the presence of Et_3N in CH_2Cl_2 afforded dihydrodipyrrin complex **2-BBu$_2$** in 87% yield (Scheme 2). A crystal of **2-BBu$_2$** suitable for X-ray analysis was obtained from Et_2O–MeOH by slow evaporation at 1 °C. The unsubstituted dibutylboron complex **3-BBu$_2$** was prepared in analogous fashion from dihydrodipyrrin **3**[53] in 27% yield.

II. Derivatization of hydrodipyrrin–dibutylboron complexes

1. Reconnaissance. Electrophilic aromatic substitution of unsubstituted pyrrole proceeds first at the pyrrole α-positions.[54]



2 (R = *p*-tolyl)
3 (R = H)

2-BBu$_2$ (R = *p*-tolyl), 87%
3-BBu$_2$ (R = H), 27%

Scheme 2 Synthesis of a dihydrodipyrrin–boron complex.

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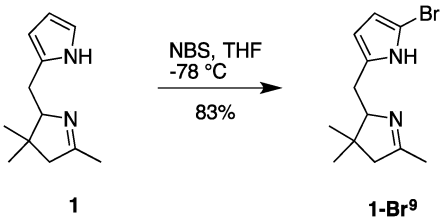


Scheme 3 Pyrrolic α-bromination.

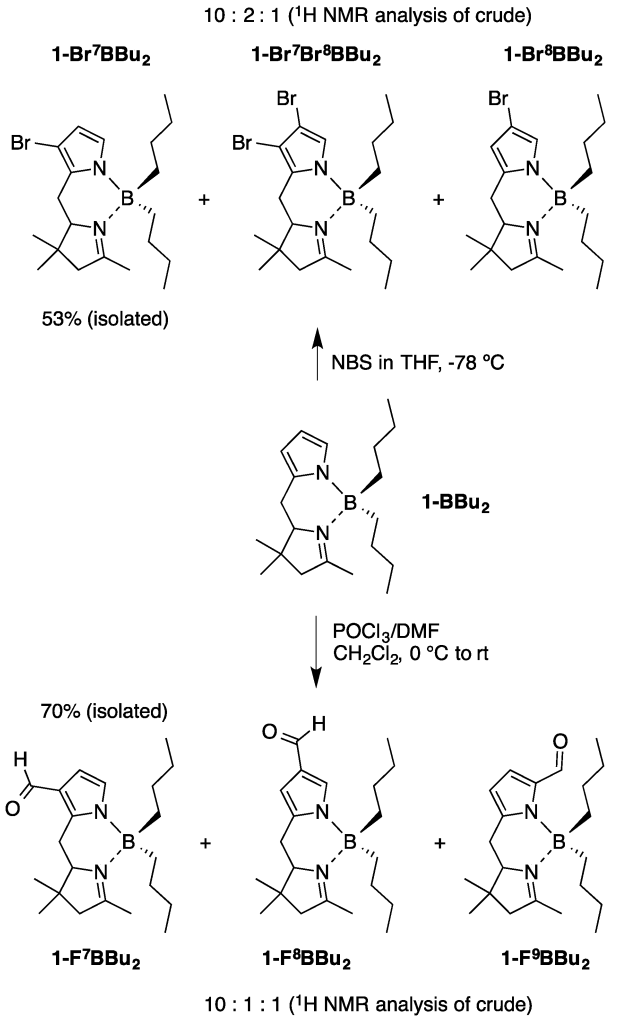
On the other hand, the regioselective bromination or acylation of pyrroles at the β-positions presents a challenge.[55] In general, electrophilic aromatic substitution at the β-positions can be directed (1) by an electron-withdrawing group at the α-position,[5] (2) by a bulky protecting group on the pyrrole nitrogen,[56,57] or in some cases (3) by rearrangement of the α-substituted pyrrole to a β-substituted pyrrole.[58–60] In accord with the expected reactivity of pyrrole, the bromination of tetrahydrodipyrrin **1** proceeded at the 9-position[53] (*i.e.*, the free α-pyrrole position) to afford **1-Br^9** (Scheme 3).

Here, we describe studies of electrophilic substitution of the hydrodipyrrin–dialkylboron complexes, of which the tetrahydrodipyrrin species are the chief focus. The motivation for developing chemistry for selective β-substitution stems from the desire to introduce diverse substituents at the corresponding positions of the pyrroles in the chlorin macrocycle, in particular those in ring A.

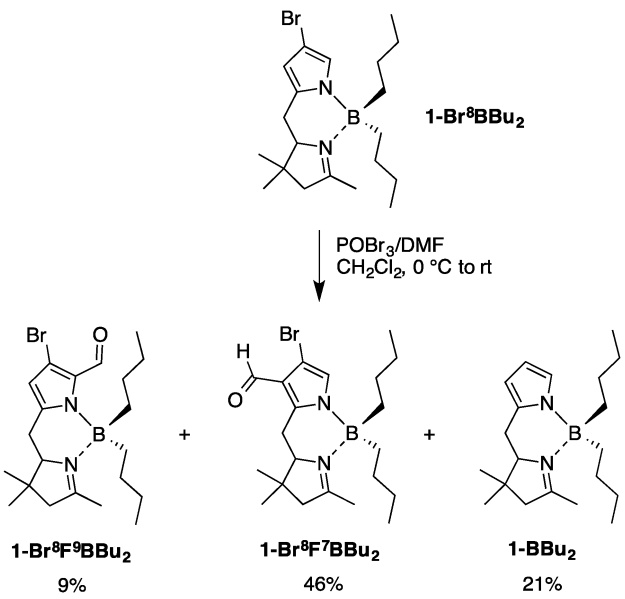
2. Bromination or formylation. Bromination of tetrahydrodipyrrin **1-BBu$_2$** with 1 molar equiv. of *N*-bromosuccinimide (NBS) at −78 °C afforded three brominated products, namely **1-Br^{7}BBu$_2$**, **1-Br^{7}Br^{8}BBu$_2$** and **1-Br^{8}BBu$_2$** in the ratio 10 : 2 : 1 on the basis of ^{1}H NMR spectroscopy of the crude reaction mixture. A small amount of unreacted starting material also was observed; regardless, no α-pyrrole-substituted products were detected. The main product, **1-Br^{7}BBu$_2$**, was isolated in 53% yield upon recrystallization three times from methanol (Scheme 4). (Note that chromatography failed to separate **1-Br^{7}BBu$_2$** and **1-Br^{7}Br^{8}BBu$_2$**.) The boron complex of bromohydrodipyrrin **1-Br^{7}BBu$_2$** is less stable than that of the parent **1-BBu$_2$**.

A Vilsmeier formylation of tetrahydrodipyrrin **1-BBu$_2$** with $POCl_3$–DMF in CH_2Cl_2 afforded 7-formyltetrahydrodipyrrin **1-F^{7}BBu$_2$** as a major product with small amounts of regioisomers **1-F^{8}BBu$_2$** and **1-F^{9}BBu$_2$** (Scheme 4). Column chromatography afforded pure **1-F^{7}BBu$_2$** in 70% yield. The position of the formyl group in **1-F^{7}BBu$_2$** was established by ^{1}H NMR spectroscopy (see ESI†).

3. Formylation following bromination. The target **1-Br^{8}F^{7}BBu$_2$** is a potentially valuable building block for chlorin synthesis, given that the 8-position of a tetrahydrodipyrrin will become the 3-position of a chlorin. Accordingly, formylation of **1-Br^{8}BBu$_2$**, obtained by dialkylboron complexation of **1-Br^8**, was pursued. Application of the same conditions ($POCl_3$–DMF) employed for **1-BBu$_2$**, however, resulted in a mixture of products including chloro/bromo exchange. Upon replacement of $POCl_3$ with $POBr_3$,[61] several products were formed and isolated *via* chromatography for characterization and yield determination (Scheme 5). The fractions in order of elution include an unknown, isomer **1-Br^{8}F^{9}BBu$_2$**



Scheme 4 Electrophilic substitution of a dialkylboron–tetrahydrodipyrrin.



Scheme 5 Formylation of **1-Br^{8}BBu$_2$**.

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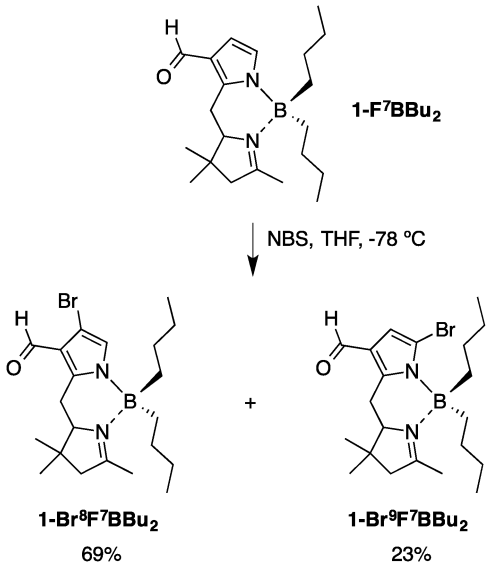
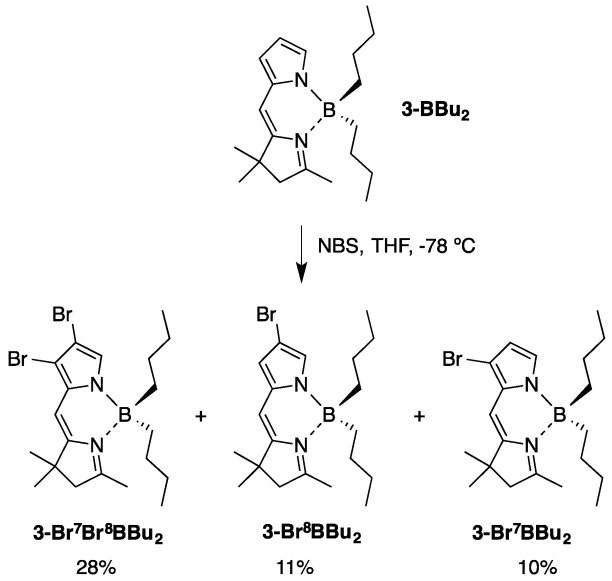


Scheme 6 Bromination of **1-F^{7}BBu$_2$**.



Scheme 7 Bromination of a dihydrodipyrrin–boron complex.

(9% yield), the desired compound **1-Br^{8}F^{7}BBu$_2$** (46% yield), and **1-BBu$_2$** (21% yield).

4. Bromination following formylation. Compound **1-Br^{8}F^{7}BBu$_2$** was also synthesized *via* another route, in which **1-F^{7}BBu$_2$** served as the starting material. Thus, treatment of **1-F^{7}BBu$_2$** with NBS at −78 °C under argon afforded **1-Br^{8}F^{7}BBu$_2$** in 69% yield along with isomer **1-Br^{9}F^{7}BBu$_2$** in 23% yield (Scheme 6). A crystal of **1-Br^{8}F^{7}BBu$_2$** suitable for X-ray analysis was obtained from CH_2Cl_2–hexanes by slow evaporation at 4 °C. In summary, the ability to gain access to the 8-bromo-7-formyl substitution pattern appears quite attractive for eventual preparation of chlorophyll *f* model compounds.

5. Bromination of dihydrodipyrrin–boron complexes. Bromination of dihydrodipyrrin **3-BBu$_2$** with 1 molar equiv. of NBS at −78 °C afforded three brominated products (Scheme 7), which upon chromatography were identified as **3-Br^{7}Br^{8}BBu$_2$** (28% yield), **3-Br^{8}BBu$_2$** (11% yield) and **3-Br^{7}BBu$_2$** (10% yield). A small amount of unreacted starting material also was observed; however, α-pyrrole-substituted products were not detected. The boron complexes of the bromodihydrodipyrrin darkened and decomposed upon standing overnight in $CDCl_3$ (NMR tubes) at room temperature, reflecting the lesser stability *versus* the corresponding bromotetrahydrodipyrrin complexes.

6. Limitations of hydrodipyrrin–boron complexes. Dialkylboron complexation of the tetrahydrodipyrrin proved very beneficial in directing electrophilic substitution to the β- rather than α-pyrrolic positions. On the other hand, a number of other transformations were unsuccessful: (1) attempts to dehydrogenate tetrahydrodipyrrin **1-BBu$_2$** using a variety of reagents (DDQ, *p*-chloranil, SeO_2, $Pb(OAc)_4$–AcOH, CuO) to give dihydrodipyrrin **3-BBu$_2$** failed (as does the reaction with **1**); (2) attempts to oxidize the 1-methyl group of tetrahydrodipyrrin **1-BBu$_2$** with SeO_2 to give the 1-formyl group failed (yet the reaction succeeds with diverse dihydrodipyrrins[62,63]); (3) the dibutylboron complex of a dihydrodipyrrin–acetal (analogue of **1** bearing a 1,1-dimethoxymethyl group), used in bacteriochlorin chemistry,[64] failed to form; (4) Pd-mediated coupling of bromotetrahydrodipyrrin–dialkylboron complexes (*e.g.*, **1-Br^{8}BBu$_2$**) such as carbonylation failed (as do such reactions in general with uncomplexed hydrodipyrrins); and (5) treatment of **1-F^{7}BBu$_2$** with *tert*-butylamine gave the aldimine but ruthenium-mediated attempts to install an alkyl group at the adjacent 8-position failed (yet the reaction works well with arenes[65]). In summary, the benefits of dialkylboron complexation, while significant, appear limited at present to regioselective electrophilic substitution of tetrahydrodipyrrins.

III. Characterization

1. NMR spectroscopy. The most pronounced changes in the ^{1}H NMR spectrum upon complexation of tetrahydrodipyrrin **1** to give **1-BBu$_2$** are as follows: (1) a downfield chemical shift of the resonance of the 1-methyl group from 2.05 ppm to 2.41 ppm; and (2) a downfield chemical shift of the resonances of H^2 (protons at the pyrroline 2-position). For dihydrodipyrrin **2-BBu$_2$** *versus* **2**, the most significant chemical shift was observed for H^5 (from 5.97 ppm to 6.30 ppm). The resonances observed for protons in selected tetrahydrodipyrrins were assigned by NOESY and are provided in the Experimental section.

Each dialkylboron complex was examined by ^{11}B NMR spectroscopy using the ^{11}B standard, $B(OH)_3$, at 19.8 ppm in DMF[66] as a standard. Each dialkylboron complex exhibited a broad singlet in the range 0.89–2.72 ppm, to be compared with that of similar compounds such as *N*-(9-borabicyclo[3.3.1]non-9-yl)pyrrole (59.9 ppm)[67] and the 9-BBN complex of 1-acyldipyrromethanes (~13 ppm).[43] The relative upfield shift of **1-BBu$_2$** is characteristic for species in which boron is coordinated with an N_{imino} nitrogen.[68]

2. X-ray characterization. X-ray structural analysis was performed of the dibutylboron complexes of three tetrahydrodipyrrins (**1-BBu$_2$**, **1-Br^{8}BBu$_2$**, and **1-Br^{8}F^{7}BBu$_2$**) and dihydrodipyrrin **2-BBu$_2$** (Fig. 1). The tetrahydrodipyrrins each contain a stereogenic center (C4) and are expected to form as racemic mixtures. In this

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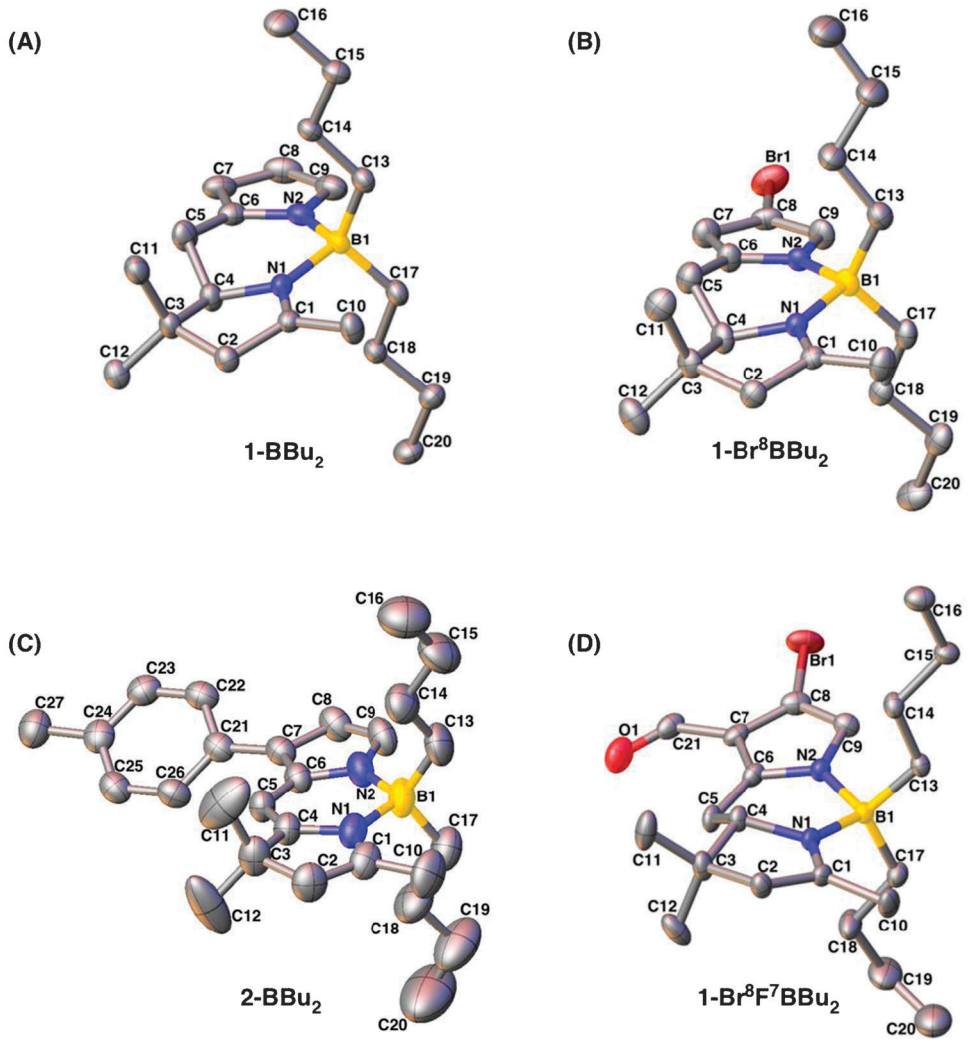

Fig. 1 ORTEP drawing of (A) tetrahydrodipyrrin **1-BBu$_2$**, (B) tetrahydrodipyrrin **1-Br^{8}BBu$_2$**, (C) dihydrodipyrrin **2-BBu$_2$**, and (D) tetrahydrodipyrrin **1-Br^{8}F^{7}BBu$_2$**. Ellipsoids are displayed at the 50% probability level and hydrogen atoms are omitted for clarity. The large spherical ellipsoids of **2-BBu$_2$** result from high thermal motion.

regard, **1-Br^{8}F^{7}BBu$_2$** crystallizes in a chiral space group $Pna2_1$, with the asymmetric unit (Z' = 2) chosen to contain one molecule of each enantiomer (see ESI†). The other materials with stereogenic centers, **1-BBu$_2$** and **1-Br^{8}BBu$_2$**, crystallize in the centrosymmetric space groups $P2_1/n$ or $P2_1/c$ respectively, containing both enantiomers in the unit cell. Electron-density peaks in the difference map of **1-Br^{8}F^{7}BBu$_2$** revealed disorder in the position of Br on both of the molecules in the asymmetric unit at the respective β-pyrrolic positions. Modeling this disorder favored (97 : 3) the bromine atom at the 8- *versus* 9-position of the tetrahydrodipyrrin system. The 9-position is the pyrrole α-position, indicating a small amount of α-bromo substituted product (**1-Br^{9}F^{7}BBu$_2$**) in the isolated sample of **1-Br^{8}F^{7}BBu$_2$**.

A key difference between the two types of compounds is the greater coplanarity of the pyrrole and pyrroline rings of dihydrodipyrrin **2-BBu$_2$** *versus* that of the tetrahydrodipyrrins due to the unsaturated *versus* saturated C4–C5 bond, respectively. Regardless, the butyl chains attached to the boron center are thrust above and below the ligand plane in each case, as expected. The B–N (pyrrolic) bond length in **1-BBu$_2$** [1.570(3) Å], **1-Br^{8}BBu$_2$**, [1.567(5) Å], **2-BBu$_2$** [1.568(4) Å] and **1-Br^{8}F^{7}BBu$_2$** [1.579(4) Å] is slightly shorter than for that of a 1-acyldipyrromethane [Chart 2B, 1.5884(14) Å].[43] The B–N (pyrrolinyl) bond length in **1-BBu$_2$** [1.631(3) Å], **1-Br^{8}BBu$_2$** [1.637(4) Å], **1-Br^{8}F^{7}BBu$_2$** [1.613(4) Å] and **2-BBu$_2$** [1.641(3) Å] is longer than that of the aforementioned B–N (pyrrolic) bond. The bromo and formyl group in **1-Br^{8}F^{7}BBu$_2$** are introduced *via* successive derivatization of **1-BBu$_2$**; thus, the single-crystal X-ray structure of **1-Br^{8}F^{7}BBu$_2$** provides proof of the regioselectivity of the electrophilic aromatic processes (bromination, formylation) in the presence of the dibutylboron unit.

IV. Decomplexation of dibutylboron–tetrahydrodipyrrins

The decomplexation of **1-BBu$_2$** was examined under several conditions, drawing on experience with conditions developed for dialkylboron complexes of 1-acyldipyrromethanes (*e.g.*, Chart 2B).[43] The exploratory studies are summarized in the ESI† (Table S4). The use of 1-pentanol at reflux[43] caused decomplexation but the liberated **1** did not precipitate from hexanes, which prompted

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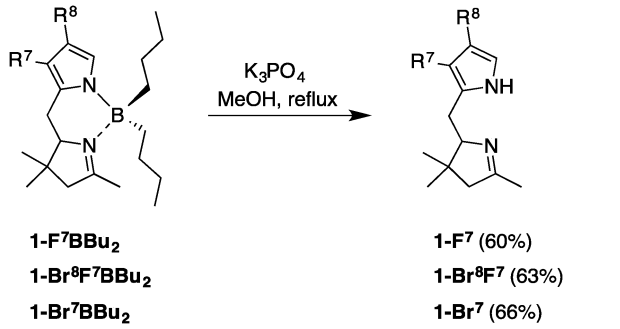
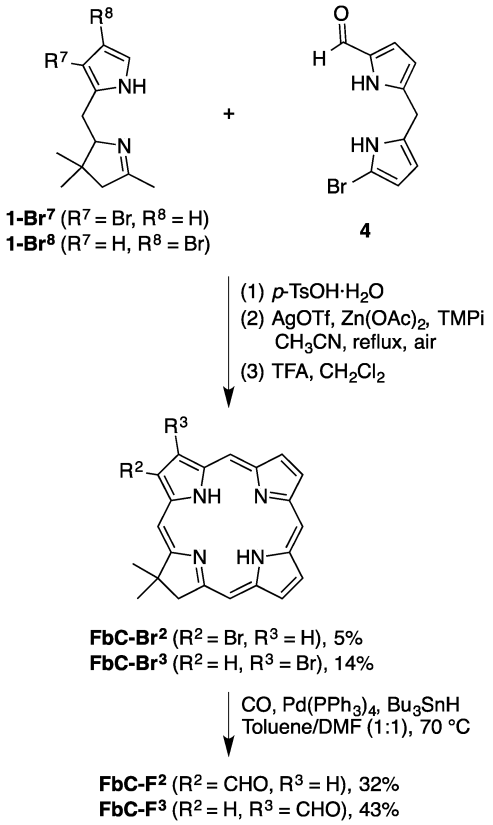


Scheme 8 Decomplexation of β-pyrrolic substituted dibutylboron–tetrahydrodipyrrins.

examination of other conditions. Refluxing solutions containing phenoxide anion, hydrazine monohydrate, or KOH were successful with **1-BBu$_2$** but upon application to the formyl compound **1-F^{7}BBu$_2$** gave only starting material. Attempts to use KOH (50 equiv.) or TBAF also did not afford **1-F^7**. The milder base K_2CO_3 in methanol led to the desired compound, but with a large amount of starting material. K_3PO_4 afforded better solubility in methanol and increased the yield to 60% yield for **1-F^7**. The same conditions with **1-Br^{8}F^{7}BBu$_2$** or **1-Br^{7}BBu$_2$** gave the free tetrahydrodipyrrin **1-Br^{8}F^7** or **1-Br^7** in 63% or 66% yield, respectively (Scheme 8).

V. Isomeric formylchlorins

1. Synthesis. Two isomeric formylchlorins were prepared in a continuation of our studies of the effects of auxochromes on the spectral properties of chlorins. Prior theoretical studies have ''walked the formyl group around the macrocycle'' but no experimental studies have yet made available the 2-formylchlorin and 3-formylchlorin (a 3-formyl-10-mesitylchlorin has been prepared previously[5]). Formylchlorins can be prepared by Pd-mediated carbonylation of the corresponding bromochlorins.[69] Access to the 2-bromochlorin was achieved by bromination of the dibutylboron-complexed Western half (**1-BBu$_2$**), whereas a 3-bromochlorin was prepared by installation of the bromo group in the earliest precursor, pyrrole-2-carboxaldehyde. Thus, the reaction of Eastern half **4**[50] and Western half **1-Br^7** or **1-Br^8** was employed to synthesize 2-bromochlorin **FbC-Br^2** or 3-bromochlorin **FbC-Br^3**, respectively, as shown in Scheme 9. Compound **1-Br^7** was obtained by bromination of **1-BBu$_2$** followed by decomplexation and chromatographic purification, whereas **1-Br^8** is a known compound[5,51] obtained from 4-bromopyrrole-2-carboxaldehyde. The chlorin-forming reaction was carried out under standard conditions of acid-catalyzed condensation (*p*-TsOH·H$_2$O in MeOH–CH_2Cl_2 under argon for 50 min) followed by zinc(II)-mediated oxidative cyclization [$Zn(OAc)_2$, 2,2,6,6-tetramethylpiperidine (TMPi), and AgOTf in CH_3CN at reflux exposed to air for 22 h]. The resulting zinc chlorins were then demetalated upon treatment with trifluoroacetic acid (TFA). This route provided access to the free base 2-bromochlorin or 3-bromochlorin in yield of 5% or 14%, respectively. The yields, while low, are typical of those for sparsely substituted chlorins.[50]



Scheme 9 Synthesis of formylchlorins.

Treatment of the bromochlorin **FbC-Br^2** or **FbC-Br^3** with Bu_3SnH and a stoichiometric amount of $Pd(PPh_3)_4$ in toluene/DMF (1 : 1) at 70 °C under an atmosphere of CO gave the corresponding 2-formylchlorin **FbC-F^2** or 3-formylchlorin **FbC-F^3** in 32% or 43% yield, respectively. Each target chlorin was characterized by absorption spectroscopy, ^{1}H NMR spectroscopy, ^{13}C NMR spectroscopy and high-resolution mass spectrometry.

2. Absorption spectral properties. The absorption spectra of formylchlorins **FbC-F^2** and **FbC-F^3** in toluene are shown in Fig. 2, along with that of the benchmark chlorin[70] **FbC** that lacks any β-pyrrole substituents (Scheme 9, $R^2 = R^3 = H$). Each chlorin exhibits an intense B (Soret) band and a characteristic strong Q_y band. The spectra are normalized at the B (Soret) band for facile comparison of the relative intensity of the long-wavelength Q_y band.

The unsubstituted chlorin **FbC** exhibits B and Q_y absorption at 389 and 634 nm, respectively. The presence of a formyl group in ring A causes a pronounced bathochromic shift of both B and Q_y bands, the magnitude of which depends on the position. While the position of both B and Q_y bands determines the extent of light harvesting, the position of the Q_y band is of particular importance as this sets an upper limit on the energy of the first excited singlet state, from which photochemical processes emanate. Thus, **FbC-F^2** or **FbC-F^3** exhibits Q_y absorption maximum at 654 or 664 nm ($\Delta\lambda$ = 20 or 30 nm relative to **FbC**), respectively. A parallel bathochromic shift is exhibited by the B band, which appears at 404 or 416 nm for **FbC-F^2** or **FbC-F^3**, respectively.

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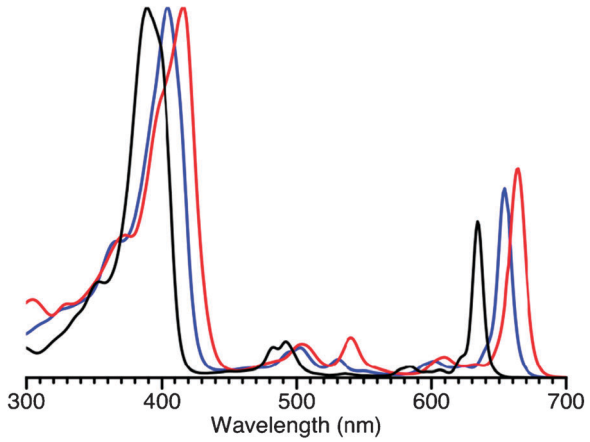

Fig. 2 Absorption spectra in toluene at room temperature (normalized at the B bands) of **FbC** (black), **FbC-F²** (blue) and **FbC-F³** (red).

Table 2 Absorption spectral properties of chlorins[a]

Chlorins	λ_B (fwhm) in (nm)	λ_{Q_y} (fwhm) in (nm)	B/Q_y ratio
FbC	389 (33)	634 (9)	2.4
FbC-F²	404 (34)	654 (11)	2
FbC-F³	416 (38)	664 (14)	1.8

[a] In toluene at room temperature.

The ratio of the intensities of the B and Q_y bands provides a measure of the relative absorption, and is particularly convenient given the difficulty of accurate determination of molar absorption coefficients with small samples. In this regard, the B/Q_y band intensity ratio decreases slightly along the series **FbC** (2.4), **FbC-F²** (2.0), and **FbC-F³** (1.8). Thus, the formyl group introduces a bathochromic and relative hyperchromic shift on the Q_y band, with the effect larger at the 3- *versus* 2-position. Such shifts are accompanied by a broadening of both the B and Q_y bands, as measured by the full-width-at-half-maximum (fwhm). The fwhm increases along the series **FbC**, **FbC-F²**, and **FbC-F³** from 33 to 38 nm for the B band and 9 to 14 nm for the Q_y band. The spectral data are listed in Table 2. The large fwhm (38 nm) of the B band of **FbC-F³** stems from a short-wavelength shoulder of significant intensity, as seen in Fig. 2.

Conclusions and outlook

Directed routes to stable hydroporphyrins rely extensively on hydrodipyrrin chemistry, a domain of chemistry where much methodology development remains to be done. In general, the synthetic methods available for manipulating hydrodipyrrins are incommensurate with the architectural challenges and scientific opportunities presented by the target macrocycles. The work described herein has established a new route to 2-substituted chlorins. The route relies on the formation of a dibutylboron complex of a tetrahydrodipyrrin, the Western half precursor to the chlorin. The introduction of dialkylboron unit directs electrophilic aromatic substitution (bromination, formylation) chiefly to the β-pyrrolic 7-position, which ultimately gives rise to the chlorin 2-position. The role of steric *versus* electronic factors that underpin the unusual substitution pattern in the tetrahydrodipyrrin–dialkylboron complex remains unknown. Regardless, in combination with literature data, a trend has emerged for electrophilic substitution of increasingly unsaturated substrates, as shown in Fig. 3. Substitution of the tetrahydrodipyrrin–dialkylboron complex proceeds chiefly at the 7-position (adjacent to the alkyl substituent); for the dihydrodipyrrin–dialkylboron complex, reaction proceeds equivalently at the 7- and 8-positions; and for the dipyrrin–difluoroboron complex (*i.e.*, a BODIPY dye), bromination (Br_2),[71] chlorination (NCS),[72] or formylation (Vilsmeier, 80 °C)[73] proceeds selectively at the 8-position. The steric effects of the 5-aryl group in these substitution processes remain unknown.

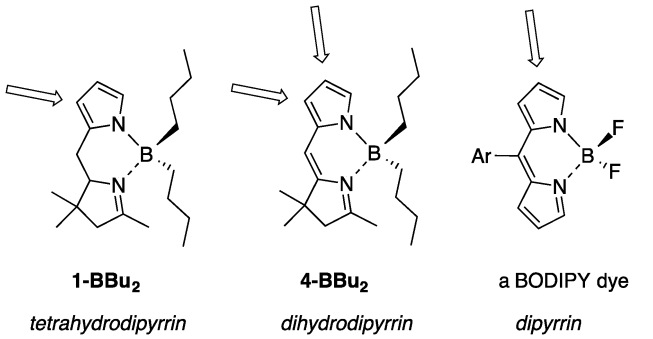

Fig. 3 Preferred site(s) of electrophilic substitution in hydrodipyrrin–boron complexes.

The availability of the 2-formyl and 3-formylchlorins lacking any other substituents enables fundamental studies to assess the origin of the spectral and photophysical properties of the more highly substituted natural chlorophylls.[40,74] The *de novo* route complements semisynthesis approaches that begin with natural chlorophylls.[75] The access to 2-substituted chlorins now completes our circumambulation of the ring, as access to the 3,[5,76] 5,[24,25,50] 7,[69,76,77] 8,[77] 10,[24,25,50] 12,[27,28] 13,[2,5,78] 15,[70,76,78,79] 17,[70,80] 18,[80] and 20[69,79] positions has already been achieved, as has installation of the isocyclic ring[2,81] (and 6-membered imide analogues[78] thereof) characteristic of the native chlorophyll structures. More generally, the availability of 2-substituted chlorins provides an initial approach toward sparsely substituted chlorophyll *f* analogues.

Experimental section

I. General procedures

^{1}H (400 MHz) and ^{13}C (100 MHz) NMR spectra were recorded in $CDCl_3$ at room temperature unless noted otherwise. ^{11}B NMR spectroscopy (160 MHz) was performed at room temperature using a boron-free NMR tube, $CDCl_3$ as solvent, and $B(OH)_3$ in DMF as external standard (referenced to 19.8 ppm).[66] Absorption spectra were collected in toluene at room temperature. Melting points are uncorrected. Silica gel (40 μm average particle size) was used for column chromatography. Compounds **1**,[45] **1-Br**[8],[5,51] **2**,[52] **3**,[53] and **4**[50] were prepared as described in the literature.

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II. Preparations

10-(Dibutylboryl)-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-BBu$_2$). A solution of **1** (380 mg, 2.00 mmol) in CH_2Cl_2 (4.0 mL) was treated with triethylamine (1.0 mL) and dibutylboron triflate (4.00 mL of 1 M solution in CH_2Cl_2, 2 mmol). The reaction mixture was stirred at room temperature. After 1 h, CH_2Cl_2 was added. TLC analysis [silica, hexanes/CH_2Cl_2 (2 : 1)] showed the presence of a yellow, highly fluorescent, non-polar product (trace amount, R_f = 0.57) in addition to the title compound (R_f = 0.50). The yellow impurity could not be removed by chromatography or crystallization, but was removed upon washing the organic phase three times with aqueous $NaHCO_3$. The organic phase was concentrated. The resulting oil was filtered through a pad of silica (CH_2Cl_2). The filtrate was concentrated. Crystallization from hot EtOH–water afforded pale yellow crystals that gave a single spot upon TLC analysis (389 mg, 62%): mp 135–136 °C; ^{11}B δ 0.98; ^{1}H NMR δ 0.42–0.55 (m, 2H), 0.62–0.66 (m, 2H), 0.79–0.82 (m, 6H), 1.11 (s, 3H), 1.14–1.19 (m, 4H) 1.21 (s, 3H), 1.20–1.22 (m, 4H), 2.38–2.39 (m, 3H), 2.60–2.65 (m, 1H), 2.77–2.81 (m, 1H) 2.82–2.85 (m, 2H), 3.82–3.86 (m, 1H), 5.90–5.91 (m, 1H), 6.09–6.10 (m, 1H), 6.66–6.67 (m, 1H); ^{13}C NMR δ 14.29, 14.38, 19.1, 23.0, 23.5, 25.2, 26.2, 26.6, 26.7, 28.1, 28.4, 38.8, 56.1, 80.0, 102.8, 106.1, 121.1, 130.1, 180.4; ESI-MS obsd 315.2970, calcd 315.2966 [(M + H)$^+$, M = $C_{20}H_{35}BN_2$].

10-(Dimethylboryl)-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-BMe$_2$). A solution of **1** (0.190 g, 1.00 mmol) in CH_2Cl_2 (4.0 mL) was treated with triethylamine (0.5 mL) and dimethylboron bromide (0.195 mL, 2.00 mmol) at 0 °C. After 5 min, the cooling bath was removed and the mixture was stirred at room temperature for 1 h. Then, the mixture was concentrated. The resulting material was filtered through neutral alumina (CH_2Cl_2) to afford an off-white solid (0.154 g, 67%). Due to instability, the characterization of the title compound was incomplete: ^{1}H NMR δ 0.00 (s, 3H), 0.20 (s, 3H), 1.03 (s, 3H), 1.21 (s, 3H), 2.39–2.40 (m, 3H), 2.58–2.63 (m, 1H), 2.73–2.78 (m, 1H), 2.82–2.85 (m, 1H), 2.87–2.91 (m, 1H), 3.96–4.00 (m, 1H), 5.90–5.91 (m, 1H), 6.12–6.13 (m, 1H), 6.70–6.71 (m, 1H); ^{13}C NMR 19.4, 23.3, 25.5, 26.3, 38.7, 56.2, 78.8, 103.5, 106.8, 129.2.

10-(Dibutylboryl)-2,3-dihydro-1,3,3-trimethyl-7-(4-methylphenyl)-dipyrrin (2-BBu$_2$). A solution of **2** (0.100 g, 0.359 mmol) and triethylamine (0.18 mL, 1.3 mmol) in CH_2Cl_2 (5.1 mL) was treated with dibutylboron triflate (0.72 mL, 1 M in CH_2Cl_2, 0.72 mmol) under argon at room temperature. The reaction mixture was stirred for 1 h under argon. The reaction mixture was quenched with water. The organic phase was dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/CH_2Cl_2 (1 : 1)] to afford a light yellow solid (0.13 g, 87%): mp 87–88 °C; ^{1}H NMR δ 0.70–0.89 (m, 12H), 0.96–1.04 (m, 2H), 1.17–1.22 (m, 7H), 1.27 (s, 3H), 2.35 (s, 3H), 2.42 (s, 3H), 2.74 (s, 3H), 6.32–6.34 (m, 1H), 6.83–6.84 (m, 1H), 7.20 (d, J = 8.1 Hz, 2H), 7.38 (d, J = 8.1 Hz, 2H); ^{13}C NMR δ 8.9, 14.4, 19.1, 21.3, 26.3, 28.0, 29.2, 37.6, 46.8, 54.6, 108.7, 124.0, 125.3, 128.1, 129.3, 134.5, 135.0, 147.9, 174.7; ESI-MS obsd 402.3320, calcd 402.3315 [(M + H)$^+$, M = $C_{27}H_{39}BN_2$].

10-(Dibutylboryl)-2,3-dihydro-1,3,3-trimethyldipyrrin (3-BBu$_2$). A solution of **3** (45 mg, 0.24 mmol) and triethylamine (0.10 mL, 0.72 mmol) in CH_2Cl_2 (0.5 mL) was treated with dibutylboron triflate (0.48 mL, 1 M in CH_2Cl_2, 0.48 mmol) under argon at room temperature. The reaction mixture was stirred for 1 h under argon. The reaction mixture was quenched with water. The organic phase was washed (brine), dried (Na_2SO_4), concentrated, and chromatographed [silica, hexanes/CH_2Cl_2 (1 : 1)] to afford a light yellow solid (20 mg, 27%): mp 98–100 °C; ^{1}H NMR δ 0.60–0.72 (m, 2H), 0.73–0.78 (m, 10H), 0.84–0.92 (m, 2H), 1.11–1.20 (m, 4H), 1.25 (s, 6H), 2.44 (s, 3H), 2.77 (s, 2H), 6.07 (s, 1H), 6.09–6.13 (m, 1H), 6.16–6.20 (m, 1H), 6.78–6.82 (m, 1H); ^{13}C NMR δ 14.3, 18.9, 25.9, 26.3, 27.9, 29.1, 29.8, 37.2, 54.5, 107.5, 108.5, 109.6, 125.5, 128.3, 147.4, 175.0; ESI-MS obsd 313.2720, calcd 313.2813 [(M + H)$^+$, M = $C_{20}H_{33}BN_2$].

7,8-Dibromo-10-(dibutylboryl)-2,3-dihydro-1,3,3-trimethyl-dipyrrin (3-Br^{7}Br^{8}BBu$_2$). A solution of **3-BBu$_2$** (18 mg, 0.058 mmol) in THF (1.2 mL) was chilled in a dry ice–acetone bath for 10 min under argon. Then, the solution was treated with one portion of NBS (10.3 mg, 0.058 mmol). After stirring for 1 h at −78 °C, hexanes was added, and the mixture was allowed to warm by removal of the dry ice–acetone bath. Water was added when the internal reaction temperature reached 0 °C. The organic phase was washed (water), dried (Na_2SO_4), concentrated and chromatographed [silica, CH_2Cl_2/hexanes (1 : 4)]. Four bands were observed in the following order of elution: unreacted starting material, **3-Br^{7}BBu$_2$** (2.0 mg, 10%), **3-Br^{8}BBu$_2$** (2.4 mg, 11%), and the title compound (7.6 mg, 28%). The title compound was a yellow solid with fluorescence under long-wavelength UV illumination. Each of the isolated compounds is somewhat unstable, hence the assignments are provisional on the basis of limited characterization data. Data for the title compound: ^{1}H NMR δ 0.60–0.72 (m, 2H), 0.73–0.78 (m, 10H), 0.84–0.92 (m, 2H), 1.11–1.20 (m, 4H), 1.25 (s, 6H), 2.42 (s, 3H), 2.80 (s, 2H), 6.05 (s, 1H), 6.74 (s, 1H); ESI-MS obsd 468.1055, calcd 468.1056 [(M + H)$^+$, M = $C_{20}H_{31}BBr_2N_2$].

Data for 8-bromo-10-(dibutylboryl)-2,3-dihydro-1,3,3-trimethyl-dipyrrin (**3-Br^{8}BBu$_2$**): ^{1}H NMR δ 0.60–0.72 (m, 2H), 0.73–0.78 (m, 10H), 0.84–0.92 (m, 2H), 1.11–1.20 (m, 4H), 1.25 (s, 6H), 2.44 (s, 3H), 2.80 (s, 2H), 6.10 (s, 1H), 6.12 (d, J = 2.8 Hz, 1H), 6.71 (d, J = 2.8 Hz, 1H).

Data for 7-bromo-10-(dibutylboryl)-2,3-dihydro-1,3,3-trimethyl-dipyrrin (**3-Br^{7}BBu$_2$**): ^{1}H NMR δ 0.60–0.72 (m, 2H), 0.73–0.78 (m, 10H), 0.84–0.92 (m, 2H), 1.11–1.20 (m, 4H), 1.25 (s, 6H), 2.42 (s, 3H), 2.80 (s, 2H), 6.05 (s, 1H), 6.12 (s, 1H), 6.74 (s, 1H); ESI-MS obsd 390.1959, calcd 390.1951 [(M + H)$^+$, M = $C_{20}H_{32}BBrN_2$].

7-Bromo-10-(dibutylboryl)-2,3,4,5-tetrahydro-1,3,3-trimethyl-dipyrrin (1-Br^{7}BBu$_2$). A solution of **1-BBu$_2$** (200 mg, 0.636 mmol) in THF (12.8 mL) at −78 °C under argon was treated with NBS (112 mg, 0.636 mmol). The reaction mixture was stirred for 1 h at −78 °C under argon. Hexanes was added. Water was added when the internal reaction temperature reached 0 °C. The organic phase was separated, dried (Na_2SO_4), and concentrated. Recrystallization three times from methanol afforded the title compound (100 mg, 40%). The mother liquor was collected and recrystallized three times from methanol to afford an additional 32 mg, giving a total yield of 53% (132 mg): mp 105–107 °C; ^{11}B δ 1.19; ^{1}H NMR δ 0.35–0.55 (m, 2H),

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0.58–0.85 (m, 8H), 0.89–1.27 (m, 8H), 1.03 (s, 3H), 1.24 (s, 3H), 3.38 (d, J = 1.9 Hz, 3H), 2.59–2.69 (m, 2H), 2.78–2.93 (m, 2H), 3.77–3.83 (m, 1H), 6.12 (d, J = 2.8 Hz, 1H), 6.61 (d, J = 2.8 Hz, 1H); ^{13}C NMR δ 14.33, 14.39, 19.1, 23.0, 23.3, 23.6, 26.3, 26.47, 26.62, 27.9, 28.2, 38.8, 56.1, 79.3, 90.5, 108.6, 120.7, 127.3, 181.1; ESI-MS obsd 392.2111, calcd 392.2108 [$(M + H)^+$, M = $C_{20}H_{34}BBrN_2$]. The same procedure at the 50 mg (0.16 mmol) scale with chromatography [silica, hexanes/CH_2Cl_2 (4 : 1)] afforded the title product (28 mg, 45%) containing 10% of dibromo impurity (**1-Br^{7}Br^{8}BBu$_2$**). Also, no increase in selectivity was achieved upon treatment of a 5-fold less concentrated solution of **1-BBu$_2$** (10 mM) with NBS solution (20 mM) *via* cannula (dropwise) over 1 h.

8-Bromo-10-(dibutylboryl)-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-Br^{8}BBu$_2$). A solution of **1-Br^8** (600 mg, 2.23 mmol) in anhydrous CH_2Cl_2 (15 mL) was treated with triethylamine (1.1 mL, 8.00 mmol) and dibutylboron triflate (4.5 mL, 1 M in CH_2Cl_2, 0.45 mmol). The reaction mixture was stirred at room temperature for 1 h. Water was added. The organic extract was washed (brine), dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/CH_2Cl_2 (2 : 1)] to afford white crystals (612 mg, 70%): mp 118–120 °C (dec.); ^{11}B δ 0.97; ^{1}H NMR δ 0.39–0.54 (m, 2H), 0.55–0.91 (m, 10H), 1.01 (s, 3H), 1.07–1.18 (m, 4H), 1.19–1.30 (m, 2H), 1.22 (s, 3H), 2.38 (d, J = 2.2 Hz, 3H), 2.64 (dd, J = 18 Hz, J = 1.5 Hz, 1H), 2.76–2.83 (m, 3H), 3.78–3.82 (m, 1H), 5.89 (d, J = 1.8 Hz, 1H), 6.58 (d, J = 1.8 Hz, 1H); ^{13}C NMR δ 14.0, 14.1, 18.8, 23.2, 24.7, 25.9, 26.23, 26.29, 27.6, 27.9, 38.5, 55.7, 79.1, 93.1, 105.3, 120.2, 130.3, 180.8; ESI-MS obsd 392.2097, calcd 392.2108 [$(M + H)^+$, M = $C_{20}H_{34}BBrN_2$].

10-(Dibutylboryl)-7-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-F^{7}BBu$_2$). A solution of **1-BBu$_2$** (568 mg, 1.81 mmol) and DMF (1.00 mL, 13.0 mmol) in CH_2Cl_2 (13.9 mL) was treated with $POCl_3$ (0.185 mL, 1.99 mmol) at 0 °C under argon. After stirring for 3 h at 0 °C, the reaction mixture was treated with 2 M aqueous NaOH (10 mL) at 0 °C. The reaction mixture was vigorously stirred for 20 min at 0 °C. The organic phase was washed (water, brine), dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/ethyl acetate (1 : 1)]. Three products were isolated in the following order: **1-F^{9}BBu$_2$** (yellow solid, 9 mg, 1%), **1-F^{8}BBu$_2$** (yellow solid, 9 mg, 1%), and the title compound **1-F^{7}BBu$_2$** (yellow solid, 435 mg, 70% yield). (Note that thorough removal of DMF prior to chromatography is crucial for the separation.) Data for **1-F^{7}BBu$_2$**: TLC R_f = 0.40 [silica, hexanes/ethyl acetate (1 : 1)]; mp 114–116 °C; ^{11}B δ 0.89; ^{1}H NMR δ 0.44–0.55 (m, 2H), 0.58–0.83 (m, 10H), 0.87–0.99 (m, 2H), 1.08 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.26 (m, 2H), 1.27 (s, 3H), 2.41 (d, J = 5.0 Hz, 3H), 2.69–2.87 (m, 3H), 3.57–3.63 (m, 1H), 3.81–3.86 (m, 1H), 6.53 (d, J = 2.7 Hz, 1H), 6.61 (d, J = 2.7 Hz, 1H), 9.77 (s, 1H); ^{13}C NMR δ 13.46, 13.50, 18.3, 22.2, 22.8, 23.2, 25.46, 25.52, 25.6, 27.1, 27.4, 38.1, 55.3, 77.2, 109.7, 120.0, 121.9, 137.9, 181.2, 184.8; ESI-MS obsd 343.2945, calcd 343.2952 [$(M + H)^+$, M = $C_{21}H_{35}BN_2O$].

Data for 10-(dibutylboryl)-8-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (**1-F^{8}BBu$_2$**): TLC R_f = 0.50 [silica, hexanes/ethyl acetate (1 : 1)]; mp 104.5–106.5 °C; ^{11}B δ 1.09; ^{1}H NMR δ 0.44–0.55 (m, 2H), 0.58–0.83 (m, 10H), 0.87–0.99 (m, 2H), 1.08 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.26 (m, 2H), 1.25 (s, 3H), 2.41 (d, J = 5.0 Hz, 3H), 2.70–2.74 (m, 1H), 2.79–2.87 (m, 3H), 3.79–3.81 (m, 1H), 6.36–6.38 (m, 1H), 7.29 (s, 1H), 9.68 (s, 1H); ^{13}C NMR δ 14.4, 19.2, 23.5, 25.1, 26.1, 26.43, 26.52, 27.8, 28.1, 39.0, 56.1, 79.5, 102.9, 126.6, 132.7, 133.6, 181.8, 185.7; ESI-MS obsd 343.2924, calcd 343.2919 [$(M + H)^+$, M = $C_{21}H_{35}BN_2O$].

Data for 10-(dibutylboryl)-9-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (**1-F^{9}BBu$_2$**): TLC R_f = 0.65 [silica, hexanes/ethyl acetate (1 : 1)]; mp 94–95 °C; ^{11}B δ 2.44; ^{1}H NMR δ 0.44–0.55 (m, 2H), 0.58–0.83 (m, 10H), 0.87–0.99 (m, 2H), 1.08 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.26 (m, 2H), 1.26 (s, 3H), 2.46 (d, J = 5.0 Hz, 3H), 2.70–2.91 (m, 3H), 2.95 (dd, J = 3.6 Hz, J = 15.4 Hz, 1H), 3.93–3.97 (m, 1H), 6.02 (d, J = 3.9 Hz, 1H), 7.14 (d, J = 3.9 Hz, 1H), 9.81 (s, 1H); ^{13}C NMR δ 14.3, 19.5, 23.7, 26.23, 26.34, 26.43, 27.2, 28.54, 28.64, 29.9, 38.0, 56.4, 78.2, 107.9, 120.9, 136.4, 140.3, 180.9, 181.6; ESI-MS obsd 343.2925, calcd 343.2919 [$(M + H)^+$, M = $C_{21}H_{35}BN_2O$].

8-Bromo-10-(dibutylboryl)-7-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-Br^{8}F^{7}BBu$_2$). The route here entailed formylation following bromination. A solution of **1-Br^{8}BBu$_2$** (100 mg, 0.255 mmol) and DMF (0.078 mL) in CH_2Cl_2 (2.5 mL) was treated with $POBr_3$ (80.2 mg, 0.280 mmol) at 0 °C under argon. After stirring for 2.5 h at 0 °C, a 2 M aqueous solution of NaOH (10 mL) was added at 0 °C. The reaction mixture was vigorously stirred for 20 min at 0 °C. The organic phase was washed (water, brine), dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/ethyl acetate (2 : 1)] to give the title compound as a dark red solid. Data for **1-Br^{8}F^{7}BBu$_2$**: mp 90–92 °C; ^{11}B δ 0.98; ^{1}H NMR δ 0.41–0.46 (m, 2H), 0.57–0.84 (m, 10H), 0.87–0.99 (m, 2H), 1.07 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.24 (m, 2H), 1.26 (s, 3H), 2.41 (d, J = 1.8 Hz, 3H), 2.66–2.88 (m, 3H), 3.68–3.84 (m, 2H), 6.57 (s, 1H), 9.76 (s, 1H); ^{13}C NMR δ 14.31, 14.32, 19.2, 22.9, 23.6, 24.1, 26.28, 26.31, 26.36, 27.9, 28.1, 39.0, 56.0, 77.6, 99.5, 117.0, 122.0, 138.5, 182.5, 186.6; ESI-MS obsd 421.2032, calcd 421.2024 [$(M + H)^+$, M = $C_{21}H_{34}BBrN_2O$].

Data for 8-bromo-10-(dibutylboryl)-9-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (**1-Br^{8}F^{9}BBu$_2$**): ^{11}B δ 1.45; ^{1}H NMR δ 0.41–0.46 (m, 2H), 0.57–0.84 (m, 10H), 0.87–0.99 (m, 2H), 1.07 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.24 (m, 2H), 1.26 (s, 3H), 2.41 (d, J = 2.0 Hz, 3H), 2.56–2.86 (m, 3H), 3.74–3.82 (m, 2H), 7.33 (s, 1H), 9.73 (s, 1H); ^{13}C NMR δ 14.19, 14.23, 19.1, 22.3, 23.6, 24.5, 26.03, 26.07, 26.2, 27.6, 27.8, 38.9, 56.0, 78.7, 122.7, 129.7 130.8, 182.4, 185.3; ESI-MS obsd 421.2020, calcd 421.2024 [$(M + H)^+$, M = $C_{21}H_{34}BBrN_2O$].

The title compound was also synthesized by bromination following formylation. A solution of **1-F^{7}BBu$_2$** (200 mg, 0.583 mmol) in THF (11.6 mL) was chilled in an acetone–dry ice bath for 10 min under argon. Then the solution was treated with one portion of NBS (104 mg, 0.583 mmol). After stirring for 1 h at −78 °C, hexanes was added. Water was added when the internal reaction temperature reached 0 °C. The organic phase was washed (water), dried (Na_2SO_4), concentrated and chromatographed [silica, hexanes/ethyl acetate (2 : 1)] to give the title compound as a dark red solid (168 mg, 69%) as well as isomer **1-Br^{9}F^{7}BBu$_2$** (56 mg, 23%). Data for **1-Br^{8}F^{7}BBu$_2$** are the same

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as above. Data for 9-bromo-10-(dibutylboryl)-7-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (**1-Br^{9}F^{7}BBu$_2$**): mp 159–161 °C; ^{11}B δ 2.72; ^{1}H NMR (300 MHz) δ 0.41–0.46 (m, 2H), 0.57–0.83 (m, 10H), 0.87–0.99 (m, 2H), 1.08 (s, 3H), 1.10–1.18 (m, 2H), 1.19–1.26 (m, 2H), 1.27 (s, 3H), 2.41 (d, J = 1.8 Hz, 3H), 2.65–2.89 (m, 3H), 3.69 (dd, J = 16.2 and 3.6 Hz, 1H), 3.88–4.00 (m, 1H), 6.59 (s, 1H), 9.70 (s, 1H); ^{13}C NMR δ 14.2, 14.3, 19.3, 23.3, 23.5, 23.7, 25.2, 26.0, 26.2, 27.4, 28.0, 28.5, 37.9, 56.3, 77.5, 104.1, 114.7, 121.3, 139.8, 181.7, 184.9; ESI-MS obsd 421.2038, calcd 421.2024 [(M + H)$^+$, M = $C_{21}H_{34}BBrN_2O$].

7-Formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-F^7). A sample of **1-F^{7}BBu$_2$** (343 mg, 1.00 mmol) in CH_3OH (40 mL) was treated with K_3PO_4 (10.6 g, 50.0 mmol) and refluxed for 20 h. Upon cooling to room temperature, the mixture was washed with water and brine. The organic layer was dried ($NaSO_4$) and concentrated. The crude product was chromatographed (silica, ethyl acetate) to afford a light yellow oil (130 mg, 60%) and recovered starting material (21 mg, 6%). Data for the title compound: ^{1}H NMR (300 MHz) δ 0.98 (s, 3H), 1.16 (s, 3H), 2.05 (d, J = 1.6 Hz, 3H), 2.34 (AB, ^2J = 16.8 Hz, 1H), 2.42 (AB, ^2J = 16.8 Hz, 1H), 2.61 (ABX, ^2J = 15.6 Hz, ^3J = 12.0 Hz, 1H), 3.41 (ABX, ^2J = 15.6 Hz, ^3J = 2.8 Hz, 1H), 3.63–3.69 (m, 1H), 6.54–6.57 (m, 1H), 6.66–6.69 (m, 1H), 9.90 (s, 1H), 10.73–10.89 (br s, 1H); ^{13}C NMR δ 20.7, 23.1, 26.0, 27.2, 42.3, 54.5, 79.4, 109.0, 118.2, 121.6, 141.2, 175.6, 186.0; ESI-MS obsd 219.1500, calcd 219.1492 [(M + H)$^+$, M = $C_{13}H_{18}N_2O$].

8-Bromo-7-formyl-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-Br^{8}F^7). A sample of **1-Br^{8}F^{7}BBu$_2$** (120 mg, 0.286 mmol) in CH_3OH (11 mL) was treated with K_3PO_4 (3.00 g, 14.3 mmol) and refluxed for 20 h. Upon cooling to room temperature, the mixture was washed with water and brine. The organic layer was dried ($NaSO_4$) and concentrated. The crude product was chromatographed (silica, ethyl acetate) to afford a yellow oil (54 mg, 63%) and recovered starting material (7 mg, 6%). Data for the title compound: ^{1}H NMR (300 MHz) δ 0.96 (s, 3H), 1.18 (s, 3H), 2.03 (d, J = 1.6 Hz, 3H), 2.35 (AB, ^2J = 12.6 Hz, 1H), 2.40 (AB, ^2J = 12.6 Hz, 1H), 2.54 (ABX, ^2J = 11.8 Hz, ^3J = 9.0 Hz, 1H), 3.54 (ABX, ^2J = 11.8, ^3J = 2.6 Hz, 1H), 3.65–3.68 (m, 1H), 6.59 (s, 1H), 9.89 (s, 1H), 11.28–11.50 (br s, 1H); ^{13}C NMR δ 20.4, 23.0, 26.3, 26.9, 42.2, 54.4, 79.0, 99.4, 117.4, 122.0, 140.4, 175.8, 187.2; ESI-MS obsd 297.0600, calcd 297.0597 [(M + H)$^+$, M = $C_{13}H_{17}BrN_2O$].

8-Bromo-2,3,4,5-tetrahydro-1,3,3-trimethyldipyrrin (1-Br^7). A sample of **1-Br^{7}BBu$_2$** (250 mg, 0.633 mmol) in CH_3OH (25.0 mL) was treated with K_3PO_4 (6.67 g, 31.3 mmol) and refluxed for 14 h. Upon cooling to room temperature, the mixture was washed with water and brine. The organic layer was dried ($NaSO_4$) and concentrated. The crude product was chromatographed (silica, ethyl acetate) to afford a red oil (112 mg, 66%): ^{1}H NMR (300 MHz) δ 0.96 (s, 3H), 1.14 (s, 3H), 2.04 (d, J = 1.8 Hz, 3H), 2.331 (AB, ^2J = 16.8 Hz, 1H), 2.335 (AB, ^2J = 16.8 Hz, 1H), 2.41 (ABX, ^2J = 16.0 Hz, ^3J = 11.4 Hz, 1H), 2.84 (ABX, ^2J = 16.0 Hz, ^3J = 4.0 Hz, 1H), 3.56–3.62 (m, 1H), 6.10 (t, J = 3.0 Hz, 1H), 6.60 (t, J = 3.0 Hz, 1H), 10.00–10.26 (br s, 1H); ^{13}C NMR (75 MHz) δ 20.4, 22.8, 26.0, 27.0, 42.0, 54.3, 79.5, 93.8, 109.9, 116.5, 129.0, 175.1; ESI-MS obsd 269.0652, calcd 269.0648 [(M + H)$^+$, M = $C_{12}H_{17}BrN_2$].

2-Bromo-17,18-dihydro-18,18-dimethylporphyrin (FbC-Br^2). Following a general procedure,[24] a solution of **1-Br^7** (300 mg, 1.12 mmol) and **4** (282 mg, 1.12 mmol) in anhydrous CH_2Cl_2 (26.4 mL) was treated with a solution of p-TsOH·H_2O (1.05 g, 5.54 mmol) in anhydrous methanol (5.28 mL) under argon. The reaction mixture immediately turned red. The mixture was stirred for 50 min under argon, then treated with 2,2,6,6-tetramethylpiperidine (2.03 mL, 11.9 mmol) and concentrated to dryness. The resulting brown solid was suspended in acetonitrile (110 mL) followed by the successive addition of 2,2,6,6-tetramethylpiperidine (5.28 mL, 30.8 mmol), $Zn(OAc)_2$ (3.04 g, 16.6 mmol) and AgOTf (854 mg, 3.32 mmol). The resulting suspension was refluxed for 22 h exposed to air. The crude mixture was filtered through a silica pad with CH_2Cl_2. The filtrate was concentrated and dissolved in anhydrous CH_2Cl_2 (66 mL). TFA (880 μL) was added dropwise to the resulting mixture. After 5 min, saturated aqueous $NaHCO_3$ was added slowly. The organic layer was extracted, dried ($NaSO_4$) and concentrated. The crude product was chromatographed [silica, CH_2Cl_2/hexanes (1 : 2)] to afford a green solid (23 mg, 5%): ^{1}H NMR δ −2.48 (br s, 2H), 2.10 (s, 6H), 4.63 (s, 2H), 8.94 (d, J = 4.4 Hz, 1H), 9.06–9.07 (m, 3H), 9.10 (s, 1H), 9.25 (d, J = 4.4 Hz, 1H), 9.29 (s, 1H), 9.80 (s, 1H), 9.85 (s, 1H); ^{13}C NMR δ 31.6, 47.0, 52.2, 92.8, 97.3, 105.0, 106.52, 106.62, 124.4, 128.1, 128.6, 132.8, 133.2; ESI-MS obsd 419.0874, calcd 419.0866 [(M + H)$^+$, M = $C_{22}H_{19}BrN_4$]; λ_{abs} 391, 641 nm.

3-Bromo-17,18-dihydro-18,18-dimethylporphyrin (FbC-Br^3). Following a general procedure,[24] a solution of **1-Br^8** (534 mg, 1.98 mmol) and **4** (498 mg, 1.98 mmol) in anhydrous CH_2Cl_2 (52 mL) was treated with a solution of p-TsOH·H_2O (1.88 g, 9.90 mmol) in anhydrous methanol (13 mL) under argon. The reaction mixture immediately turned red. The mixture was stirred for 50 min under argon, then treated with 2,2,6,6-tetramethylpiperidine (2.5 mL, 15 mmol) and concentrated to dryness. The resulting brown solid was suspended in acetonitrile (200 mL) followed by the successive addition of 2,2,6,6-tetramethylpiperidine (6.6 mL, 40 mmol), $Zn(OAc)_2$ (5.45 g, 29.4 mmol) and AgOTf (1.53 g, 5.94 mmol). The resulting suspension was refluxed for 22 h exposed to air. The crude mixture was filtered through a silica pad with CH_2Cl_2. The filtrate was concentrated and dissolved in anhydrous CH_2Cl_2 (100 mL). TFA (1.5 mL) was added dropwise to the resulting mixture. After 5 min, saturated aqueous $NaHCO_3$ was added slowly. The organic layer was extracted, dried ($NaSO_4$) and concentrated. The crude product was chromatographed [silica, CH_2Cl_2/hexanes (1 : 2)] to afford a green solid (116 mg, 14%): ^{1}H NMR δ −2.49 (s, 2H), 2.03 (s, 6H), 4.60 (s, 2H), 8.84 (s, 1H), 8.90 (d, J = 4.0 Hz, 1H), 9.00 (s, 1H), 9.01–9.03 (m, 2H), 9.08 (d, J = 4.0 Hz, 1H), 9.19 (d, J = 4.8 Hz, 1H), 9.78 (s, 1H), 9.92 (s, 1H); ^{13}C NMR δ 31.4, 46.7, 52.0, 94.2, 97.0, 105.0, 106.6, 124.2, 128.6, 132.7, 133.2; ESI-MS obsd 419.0875, calcd 419.0866 [(M + H)$^+$, M = $C_{22}H_{19}BrN_4$]; λ_{abs} 391, 640 nm.

2-Formyl-17,18-dihydro-18,18-dimethylporphyrin (FbC-F^2). Following a procedure for reductive carbonylation,[69] a mixture of **FbC-Br^2** (30.0 mg, 0.0715 mmol) and $Pd(PPh_3)_4$ (82.6 mg, 0.0715 mmol) was dried under vacuum for 1 h. The reaction

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flask was filled with CO gas and anhydrous toluene/DMF [3.6 mL, (1 : 1)]. CO gas was bubbled through the stirred reaction mixture for 2 h at 70 °C. The reaction mixture then was treated with Bu_3SnH (20.0 μL, 0.0715 mmol) and stirred for 10 min. The reaction mixture was then cooled to room temperature, concentrated and subjected to column chromatography [silica, CH_2Cl_2/hexanes (1 : 1)] to afford a green solid (8.5 mg, 32%): ^{1}H NMR δ −1.58 (br s, 2H), 2.05 (s, 6H), 4.54 (s, 2H), 8.32 (d, J = 5.0 Hz, 1H), 8.85–8.87 (m, 2H), 8.97 (d, J = 4.0 Hz, 1H), 9.08 (d, J = 4.0 Hz, 1H), 9.53 (s, 1H), 9.54 (s, 1H), 9.69 (s, 1H), 9.76 (s, 1H), 11.25 (s, 1H); ^{13}C NMR δ 31.6, 46.4, 52.7, 94.5, 97.1, 105.6, 110.6, 126.2, 129.9, 131.4, 132.6, 134.7, 137.6, 141.9, 151.5, 155.1, 167.0, 176.6, 188.6; ESI-MS obsd 369.1706, calcd 369.1710 [$(M + H)^+$, M = $C_{23}H_{20}N_4O$]; λ_{abs} 404, 654 nm.

3-Formyl-17,18-dihydro-18,18-dimethylporphyrin (FbC-F^3). Following a procedure for reductive carbonylation,[69] a mixture of **FbC-Br^3** (0.100 g, 0.238 mmol) and $Pd(PPh_3)_4$ (0.275 g, 0.238 mmol) was dried under vacuum for 1 h. The reaction flask was filled with CO gas and anhydrous toluene/DMF [12.0 mL, (1 : 1)]. CO gas was bubbled through the stirred reaction mixture for 2 h at 70 °C. The reaction mixture then was treated with Bu_3SnH (63.7 μL, 0.238 mmol) and stirred for 10 min. The reaction mixture was then cooled to room temperature, concentrated and subjected to column chromatography [silica, CH_2Cl_2/hexanes (1 : 1)] to afford a brown solid (38.0 mg, 43%): ^{1}H NMR δ −2.16 (br s, 2H), 2.04 (s, 6H), 4.60 (s, 2H), 8.91 (d, J = 4.0 Hz, 1H), 8.93–8.95 (m, 2H), 9.00 (s, 1H), 9.08 (d, J = 4.0 Hz, 1H), 9.15 (d, J = 4 Hz, 1H), 9.35 (s, 1H), 9.65 (s, 1H), 10.52 (s, 1H), 11.4 (s, 1H); ^{13}C NMR δ 31.6, 46.2, 52.7, 96.9, 98.0, 105.1, 106.9, 126.0, 126.2, 129.3, 133.3, 135.3, 136.4, 137.6, 140.7, 153.2, 155.0, 165.3, 173.7, 188.9; ESI-MS obsd 369.1718, calcd 369.1710 [$(M + H)^+$, M = $C_{23}H_{20}N_4O$]; λ_{abs} 416, 664 nm.

III. X-ray structural determinations

All X-ray measurements were made on a Bruker-Nonius X8 Apex2 CCD system. The frame integration was performed using SAINT+ or SAINT.[82] The structures **1-BBu$_2$** and **2-BBu$_2$** were solved using direct methods from SIR92[83] and refined using the NRCVAX[84] crystallographic suite. The structures of **1-Br^{8}BBu$_2$** and **1-Br^{8}F^{7}BBu$_2$** were solved by direct methods using the SHELX2013[85] package. The calculated structure factors included corrections for polarization, and an absorption correction using SADABS.[86] The structure was refined using the SHELXL program from the SHELX2013[85] package, and graphic plots were produced using the OLEX2[87] crystallographic package. Additional positions for disordered atoms were found in subsequent difference maps during multiple rounds of refinement. The hydrogen-atom positions were placed at idealized positions and were allowed to ride on the parent atom with isotropic displacement parameters of 1.2 or 1.5 times the parent.

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