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Regioselective Bromination Tactics in the de Novo Synthesis of Chlorophyll *b* Analogues

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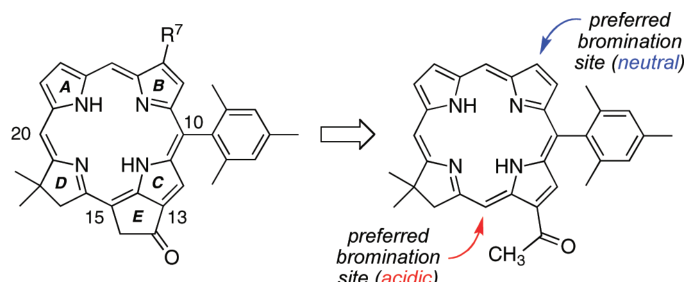

FbOP-A^{7}M^{10}: R^7 = Ac
FbOP-F^{7}M^{10}: R^7 = CHO
FbOP-E^{7}M^{10}: R^7 = TIPS-ethynyl

FbC-M^{10}A^{13}

The ability to introduce substituents at designated sites about the perimeter of the chlorin or 13^1-oxophorbine macrocycle is essential for fundamental studies related to chlorophylls. A chlorin is a dihydroporphyrin, whereas a 13^1-oxophorbine is a chlorin containing an annulated oxopentano ring spanning positions 13 and 15. 13^1-Oxophorbines bearing auxochromes at the 7-position of the macrocycle are valuable targets given their resemblance to chlorophyll *a* or *b*, which contains the 13^1-oxophorbine skeleton and bears a 7-methyl or 7-formyl group, respectively. A rational route to 7-substituted 13^1-oxophorbines was developed that relies on a new method for regioselective bromination. Under neutral conditions, a 13-acetyl-10-mesitylchlorin (**FbC-M^{10}A^{13}**) undergoes bromination (with 1 molar equiv of NBS in THF) both in ring B (7-position) and at the 15-position (42% versus 28% isolated yield), thereby thwarting installation of the isocyclic ring (ring E, spanning the 13−15 positions). Under acidic conditions (10% TFA in CH_2Cl_2), ring B is deactivated, and bromination occurs preferentially at the 15-position (87% yield). The capability for preferential 15-bromination is essential to install the isocyclic ring, after which bromination can be directed to the 7-position of ring B (neutral conditions, 86% yield). The ability to suppress bromination in ring B (under acidic media) has been exploited in syntheses of sparsely substituted analogues of chlorophyll *b*. The analogues contain a 7-substituent (acetyl, formyl, or TIPS-ethynyl), a 10-mesityl group, and the 18,18-dimethyl group as the only substituents in the 13^1-oxophorbine skeleton. The three analogues exhibit absorption spectral features that closely resemble those of free base analogues of chlorophyll *b*. Taken together, the facile access to chlorins and 13^1-oxophorbines bearing substituents at distinct sites should enable fundamental spectroscopic studies and diverse applications.

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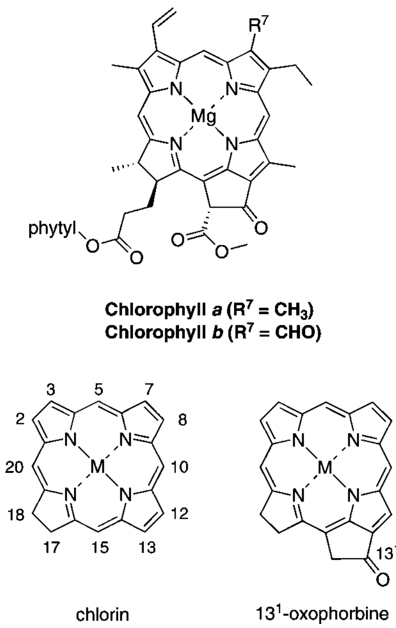
CHART 1



Introduction

A deep understanding of the effects of substituents on the spectral and photophysical properties of chlorins is essential for applications ranging from artificial photosynthesis to photomedicine. The long-wavelength absorption band ranges from 610 nm in a magnesium chlorin lacking any pyrrole substituents,[1] to 642 nm in chlorophyll *b*, to 661 nm in chlorophyll *a*.[2] Chlorophyll *a* bears methyl groups at positions 2, 7, and 12; an 8-ethyl group; a 3-vinyl group; and a keto group at position 13 (which is integral to the isocyclic ring spanning the 13−15 positions). Chlorophyll *b* differs from chlorophyll *a* only in the presence of a 7-formyl rather than a 7-methyl group (Chart 1).[3,4]

To better understand the effects of distinct substituents at specific positions, we have for some time been working to develop rational methods for preparing stable, synthetically tailorable chlorins, wherein each chlorin (dihydroporphyrin) bears a geminal dimethyl group in the reduced, pyrroline ring. The geminal dimethyl group blocks adventitious dehydrogenation and thereby affords a more stable chlorin. In this regard, we now have routes to access every peripheral site of the chlorin macrocycle, including the 2, 3, 5, 7, 8, 10, 12, 13, 15, 17, 18, and 20-positions[5−14] and also can install the isocyclic ring (13^1-oxophorbine),[15] which spans positions 13 and 15 (Chart 1). The resulting chlorins typically have relatively few substituents about the perimeter of the macrocycle. The availability of chlorins bearing substituents at designated sites has enabled a set of fundamental spectroscopic studies.[1,8,16−23] Such sparsely substituted chlorins require considerable synthetic investment for preparation yet are distinct from the chlorins obtained by derivatization of porphyrins or by semisynthetic modification of chlorophylls.[24−37]

A next challenge in chlorin chemistry entails the introduction of multiple substituents at designated sites, primarily to examine the impact on spectral properties, but also to achieve molecular designs required for specific applications. For example, the 13^1-oxophorbines that we recently prepared contained substituents

(1) Taniguchi, M.; Ptaszek, M.; McDowell, B. E.; Boyle, P. D.; Lindsey, J. S. *Tetrahedron* **2007**, *63*, 3850–3863.
(2) Strain, H. H.; Thomas, M. R.; Katz, J. J. *Biochim. Biophys. Acta* **1963**, *75*, 306–311.
(3) Smith, J. H. C.; Benitez, A. In *Modern Methods of Plant Analysis*; Paech, K., Tracey, M. V., Eds.; Springer-Verlag: Berlin, 1955; Vol. IV, pp 142−196.
(4) Scheer, H. In *Chlorophylls*; Scheer, H., Ed.; CRC Press: Boca Raton, 1991; pp 3−30.
(5) Strachan, J.-P.; O'Shea, D. F.; Balasubramanian, T.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 3160–3172.
(6) Balasubramanian, T.; Strachan, J. P.; Boyle, P. D.; Lindsey, J. S. *J. Org. Chem.* **2000**, *65*, 7919–7929.
(7) Taniguchi, M.; Ra, D.; Mo, G.; Balasubramanian, T.; Lindsey, J. S. *J. Org. Chem.* **2001**, *66*, 7342–7354.
(8) Taniguchi, M.; Kim, H.-J.; Ra, D.; Schwartz, J. K.; Kirmaier, C.; Hindin, E.; Diers, J. R.; Prathapan, S.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Org. Chem.* **2002**, *67*, 7329–7342.
(9) Taniguchi, M.; Kim, M. N.; Ra, D.; Lindsey, J. S. *J. Org. Chem.* **2005**, *70*, 275–285.
(10) Laha, J. K.; Muthiah, C.; Taniguchi, M.; McDowell, B. E.; Ptaszek, M.; Lindsey, J. S. *J. Org. Chem.* **2006**, *71*, 4092–4102.
(11) Ptaszek, M.; McDowell, B. E.; Taniguchi, M.; Kim, H.-J.; Lindsey, J. S. *Tetrahedron* **2007**, *63*, 3826–3839.
(12) Taniguchi, M.; Ptaszek, M.; McDowell, B. E.; Lindsey, J. S. *Tetrahedron* **2007**, *63*, 3840–3849.
(13) Muthiah, C.; Bhaumik, J.; Lindsey, J. S. *J. Org. Chem.* **2007**, *72*, 5839–5842.
(14) Muthiah, C.; Ptaszek, M.; Nguyen, T. M.; Flack, K. M.; Lindsey, J. S. *J. Org. Chem.* **2007**, *72*, 7736–7749.
(15) Laha, J. K.; Muthiah, C.; Taniguchi, M.; Lindsey, J. S. *J. Org. Chem.* **2006**, *71*, 7049–7052.
(16) Muthukumaran, K.; Loewe, R. S.; Kirmaier, C.; Hinden, E.; Schwartz, J. K.; Sazanovich, I. V.; Diers, J. R.; Bocian, D. F.; Holten, D.; Lindsey, J. S. *J. Phys. Chem. B* **2003**, *107*, 3431–3442.
(17) Kirmaier, C.; Hinden, E.; Schwartz, J. K.; Sazanovich, I. V.; Diers, J. R.; Muthukumaran, K.; Taniguchi, M.; Bocian, D. F.; Lindsey, J. S.; Holten, D. *J. Phys. Chem. B* **2003**, *107*, 3443–3454.
(18) Taniguchi, M.; Ra, D.; Kirmaier, C.; Hindin, E. K.; Schwartz, J. K.; Diers, J. R.; Bocian, D. F.; Lindsey, J. S.; Knox, R. S.; Holten, D. *J. Am. Chem. Soc.* **2003**, *125*, 13461–13470.
(19) Hindin, E.; Kirmaier, C.; Diers, J. R.; Tomizaki, K.-Y.; Taniguchi, M.; Lindsey, J. S.; Bocian, D. F.; Holten, D. *J. Phys. Chem. B* **2004**, *108*, 8190–8200.
(20) Kee, H. L.; Kirmaier, C.; Tang, Q.; Diers, J. R.; Muthiah, C.; Taniguchi, M.; Laha, J. K.; Ptaszek, M.; Lindsey, J. S.; Bocian, D. F.; Holten, D. *Photochem. Photobiol.* **2007**, *83*, 1110–1124.
(21) Kee, H. L.; Kirmaier, C.; Tang, Q.; Diers, J. R.; Muthiah, C.; Taniguchi, M.; Laha, J. K.; Ptaszek, M.; Lindsey, J. S.; Bocian, D. F.; Holten, D. *Photochem. Photobiol.* **2007**, *83*, 1125–1143.
(22) Muthiah, C.; Taniguchi, M.; Kim, H.-J.; Schmidt, I.; Kee, H. L.; Holten, D.; Bocian, D. F.; Lindsey, J. S. *Photochem. Photobiol.* **2007**, *83*, 1513–1528.
(23) Stromberg, J. R.; Marton, A.; Kee, H. L.; Kirmaier, C.; Diers, J. R.; Muthiah, C.; Taniguchi, M.; Lindsey, J. S.; Bocian, D. F.; Meyer, G. J.; Holten, D. *J. Phys. Chem. C* **2007**, *111*, 15464–15478.
(24) Flitsch, W. *Adv. Heterocycl. Chem.* **1988**, *43*, 73–126.
(25) Hynninen, P. H. In *Chlorophylls*; Scheer, H., Ed.; CRC Press: Boca Raton, 1991; pp 145−209.
(26) Smith, K. M. In *Chlorophylls*; Scheer, H., Ed.; CRC Press: Boca Raton, 1991; pp 115−143.
(27) Montforts, F.-P.; Gerlach, B.; Höper, F. *Chem. Rev.* **1994**, *94*, 327–347.
(28) Montforts, F.-P.; Glasenapp-Breiling, M. *Prog. Heterocycl. Chem.* **1998**, *10*, 1–24.
(29) Jaquinod, L. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 1, pp 201−237.
(30) Vicente, M. G. H. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard R., Eds.; Academic Press: San Diego, 2000; Vol. 1, pp 149−199.
(31) Pandey, R. K.; Zheng, G. In *The Porphyrin Handbook*; Kadish, K. M., Smith, K. M., Guilard, R., Eds.; Academic Press: San Diego, 2000; Vol. 6, pp 157−230.
(32) Montforts, F.-P.; Glasenapp-Breiling, M. *Fortschr. Chem. Org. Naturst.* **2002**, *84*, 1–51.
(33) Pavlov, V. Y.; Ponomarev, G. V. *Chem. Heterocycl. Cmpds.* **2004**, *40*, 393–425.
(34) Senge, M. O.; Wiehe, A.; Ryppa, C. In *Chlorophylls and Bacteriochlorophylls. Biochemistry, Biophysics, Functions and Applications*; Grimm, B., Porra, R. J., Rüdiger, W., Scheer, H., Eds.; Advances in Photosynthesis and Respiration; Springer: Dordrecht, The Netherlands, 2006; Vol. 25, pp 27−37.
(35) Fox, S.; Boyle, R. W. *Tetrahedron* **2006**, *62*, 10039–10054.
(36) Galezowski, M.; Gryko, D. T. *Curr. Org. Chem.* **2007**, *11*, 1310–1338.
(37) Silva, A. M. G.; Cavaleiro, J. A. S. In *Progress in Heterocyclic Chemistry*; Gribble, G. W., Joule, J. A., Eds.; Elsevier: Amsterdam, 2008; Vol. 19, Chapter 2, pp 44−69.

at the 5- and 10-positions but no substituents at the β-pyrrole positions.[15] On the other hand, a set of 7-substituted chlorins did not contain the isocyclic ring.[14]

One synthetic approach is to build into the acyclic precursors to the chlorin those groups or synthetic handles that are destined for specific sites on the chlorin macrocycle. A complementary approach is to construct the chlorin macrocycle and employ selective derivatization to introduce the desired substituents. Both approaches have been employed; the former is more versatile yet requires the more extensive synthesis. The derivatization approach has relied on bromination followed by substitution of positions 7, 8, 15, and 20, whereas position 17 has been selectively oxidized.[8,9,12,14,15,19] Access to all other positions has required introduction of a group or synthetic handle at the outset of the synthesis. The bromination of chlorins is an approach that dates primarily to the work of Woodward, who showed that the two meso positions flanking the pyrroline ring are more reactive toward electrophilic substitution than the other two meso positions.[38] The chlorins deuterated by Woodward, and brominated by a number of subsequent groups,[39−44] contained a full complement of β-substituents. Accordingly, the issue of competing bromination at β-sites in chlorins has been relatively unexamined. Our own studies have shown that the pattern of bromination of chlorins at the 7, 8, 15, and 20 positions is highly influenced by steric effects of neighboring substituents.[9,14] Our results are consistent with those of Varamo et al. where the bromination of a 10,20-diarylchlorin afforded a mixture of the 15-bromo- and 7,15-dibromochlorins.[45] The chief results concerning regioselective bromination that are pertinent to the present paper are described here.

A completely unsubstituted chlorin macrocycle is anticipated to undergo bromination preferentially at the meso-sites flanking the pyrroline ring (i.e., 15- and 20-positions), followed by the β-sites in the ring *trans* to the pyrroline ring (ring B, the 7- and 8-positions) (Figure 1). This exact study has not actually been performed owing to the lack of access, and expected instability, of the fully unsubstituted chlorin (**u-FbC**) lacking geminal dimethyl substitution (or other stabilizing motif) in the pyrroline ring. The expectation is supported on the basis of results from diverse chlorins, including the following data obtained with sparsely substituted chlorins.

(i) A chlorin (**FbC**) bearing substituents only in the pyrroline ring, namely the stabilizing 18,18-dimethyl group, undergoes regioselective bromination at the 15-position; the 20-position is hindered by the adjacent *gem*-dimethyl group.[12]

(ii) A similar chlorin wherein the 15-position is substituted with a phenyl group (**FbC-P^{15}**) undergoes bromination equally at the 7- and 8-positions.[14]

(iii) A similar chlorin also bearing a *p*-tolyl group at the 10-position (**FbC-T^{10}P^{15}**) undergoes bromination preferentially at the 7-position; the 8-position is hindered by the flanking 10-aryl group.[14]

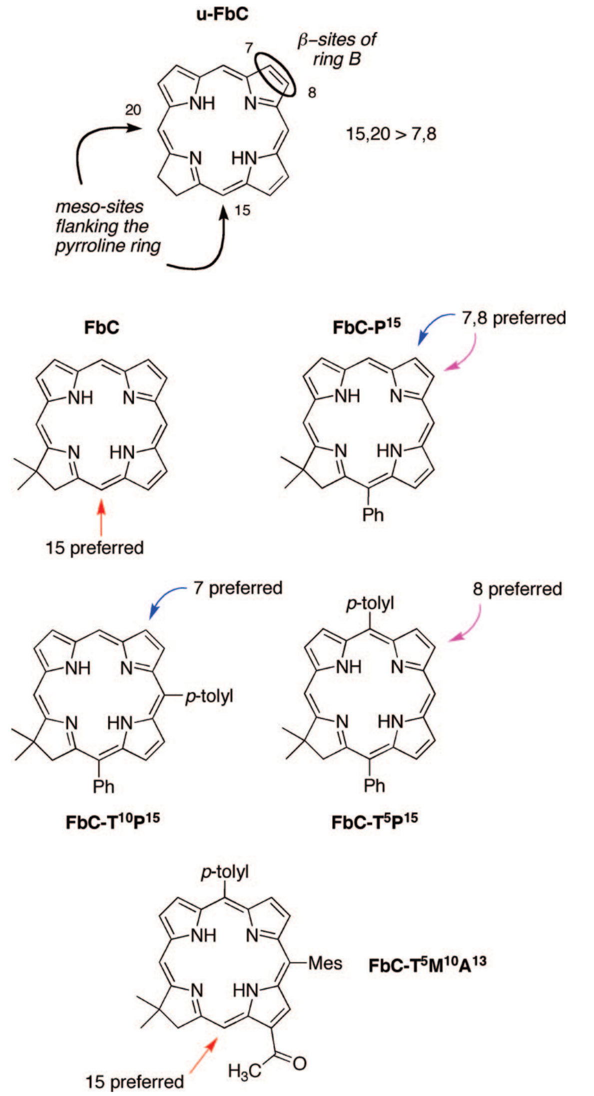


FIGURE 1. Preferred sites of bromination of free base chlorins under neutral conditions.

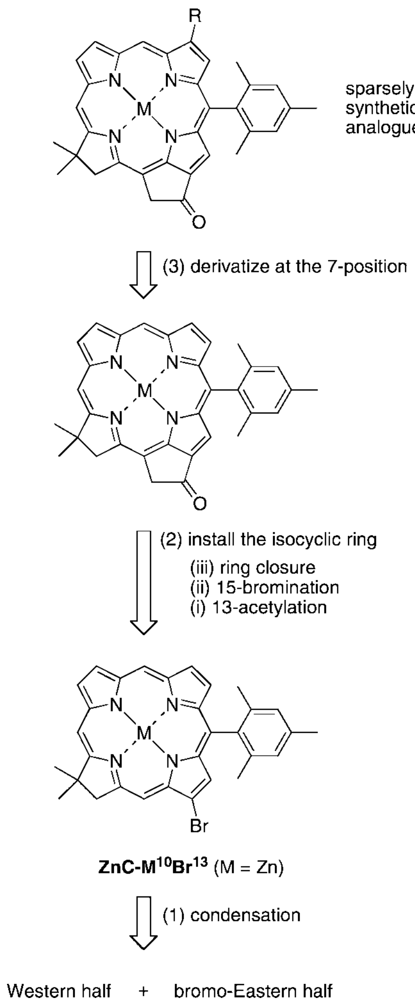
(iv) An analogous chlorin bearing a *p*-tolyl group at the 5-position (**FbC-T^{5}P^{15}**) rather than the 10-position undergoes bromination preferentially at the 8-position; the 7-position is now hindered by the flanking 5-aryl group.[14]

(v) A chlorin bearing aryl groups at the 5- and 10-positions, and a 13-acetyl group, undergoes bromination selectively at the 15-position, which constitutes a key step in the installation of the isocyclic ring.[15] The results in i−v illustrate the overlay of steric factors on fundamental electronic preferences.

In this paper, we describe the development of conditions that provide an additional level of control for the regioselective bromination of chlorin macrocycles. Such conditions are exploited in the synthesis of sparsely substituted chlorins that bear desirable patterns of substituents, including analogues of chlorophyll *b*. The motivation for preparing sparsely substituted analogues is to be able to understand the effects of individual substituents at designated sites on the spectral properties of chlorins.

(38) Woodward, R. B.; Škarić, V. *J. Am. Chem. Soc.* **1961**, *83*, 4676–4678.
(39) Bonnett, R.; Gale, I. A. D.; Stephenson, G. F. *J. Chem. Soc. C* **1966**, 1600–1604.
(40) Kenner, G. W.; McCombie, S. W.; Smith, K. M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 2517–2523.
(41) Michalski, T. J.; Appelman, E. H.; Bowman, M. K.; Hunt, J. E.; Norris, J. R.; Cotton, T. M.; Raser, L. *Tetrahedron Lett.* **1990**, *31*, 6847–6850.
(42) Kureishi, Y.; Tamiaki, H. *J. Porphyrins Phthalocyanines* **1998**, *2*, 159–169.
(43) Kelley, R. F.; Tauber, M. J.; Wasielewski, M. R. *J. Am. Chem. Soc.* **2006**, *128*, 4779–4791.
(44) Sasaki, S.-I.; Mizoguchi, T.; Tamiaki, H. *J. Org. Chem.* **2007**, *72*, 4566–4569.
(45) Varamo, M.; Loock, B.; Maillard, P.; Grierson, D. S. *Org. Lett.* **2007**, *9*, 4689–4692.

SCHEME 1



Results and Discussion

I. Synthesis of Sparsely Substituted Chlorophyll *b* Analogues. A. Prelude. The anticipated retrosynthetic analysis for the sparsely substituted chlorophyll *b* analogues is shown in Scheme 1. A key reaction sequence entails synthesis of a 10-aryl-13-bromochlorin (**FbC-M^{10}Br^{13}**), which is subjected to installation of the isocyclic ring (13-acetylation, 15-bromination, and intramolecular α-arylation) followed by 7-bromination and Pd-mediated coupling to introduce substituents at the 7-position. The zinc chelates of both the 13-bromochlorin (**ZnC-M^{10}Br^{13}**) and the 13-acetylchlorin (**ZnC-M^{10}A^{13}**) are known compounds that were previously prepared in modest quantities (72 mg, 26%; 25 mg, 53%).[10] Streamlined procedures to prepare the known zinc chlorin **ZnC-M^{10}Br^{13}** (431 mg, 45% yield from acyclic precursors[46]) and the new free base chlorin **FbC-M^{10}A^{13}** (301 mg, 85% yield) are described in the Supporting Information.

Treatment of **FbC-M^{10}A^{13}** with 1 equiv of NBS in THF at room temperature for 1.5 h afforded a mixture of two bromochlorins in 42% and 28% yield. NMR analysis (^{1}H NMR, NOESY, COSY) of the isolated products showed that the major component was the 7-substituted bromochlorin **FbC-Br^{7}M^{10}A^{13}** and the minor component was the 15-substituted bromochlorin **FbC-M^{10}A^{13}Br^{15}**. Similar reaction at −78 °C afforded the 7-bromochlorin **FbC-Br^{7}M^{10}A^{13}** exclusively in 76% yield. These results were at first surprising because our prior synthesis of the oxophorbine had used the same conditions to achieve 15-bromination. However, those earlier studies had used, unwittingly, a 5,10-diarylchlorin (**FbC-T^{5}M^{10}A^{13}**, Figure 1). The aryl substituents at the 5- and 10-positions hinder the flanking 7- and 8-positions and in so doing result in substitution at the 15-position despite the steric hindrance of the 13-acetyl moiety. The failure to achieve selective 15-bromination of **FbC-M^{10}A^{13}** (Scheme 2) prompted further studies of the bromination of chlorins.

B. Bromination Studies of a Benchmark Chlorin. We have previously reported that the electrophilic bromination of chlorin **FbC** (bearing the 18,18-dimethyl substituents but no other groups) proceeds selectively at the 15-position (entry 1, Table 1).[12] To confirm our expectations about the second-, third-, and fourth-most reactive site in the chlorin macrocycle, we reexamined the bromination of **FbC** using increasing amounts of

(46) Ptaszek, M.; Bhaumik, J.; Kim, H.-J.; Taniguchi, M.; Lindsey, J. S. *Org. Process Res. Dev.* **2005**, *9*, 651–659.

SCHEME 2

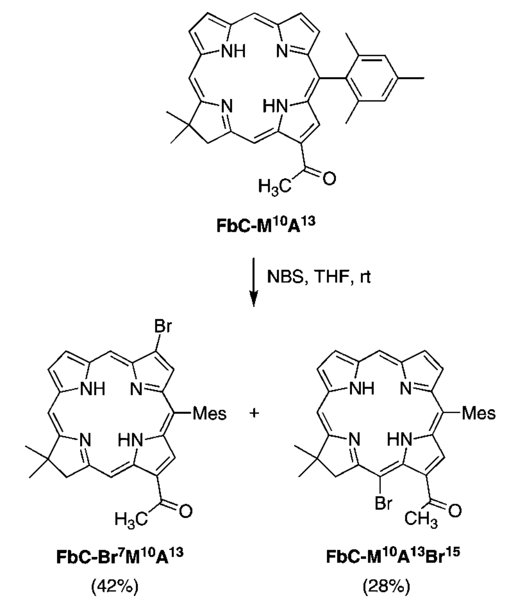
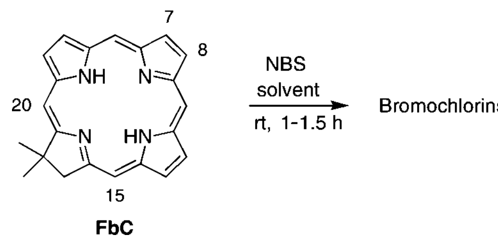


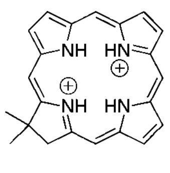
TABLE 1. Bromination of FbC[a]



entry	solvent	NBS (equiv)	position of substitution[b] (%)
1	THF	1	15 (67%)[c]
2	THF	2	15,7 and 15,8 (1:1 ratio)[d]
3	THF	3	15,7,8 (62%)[e]
4	THF	4	15,7,8 (48%)[f]
5	CH_2Cl_2/TFA (10:1)	1	15 (62%)[g]
6	CH_2Cl_2/TFA (10:1)	2	15,20 (51%)[h]

[a] All reactions were carried out at room temperature. [b] On the basis of ^{1}H NMR data. [c] Reference 12. [d] Not isolated. [e] A trace of dibromochlorin was also formed (LD-MS). [f] Inseparable mixture of tri- and tetrabromochlorins was formed (^{1}H NMR and LD-MS). [g] A trace of 15,20-dibromochlorin was also formed (LD-MS). [h] A trace of monobromochlorin was also isolated.

CHART 2



diprotonated **FbC**

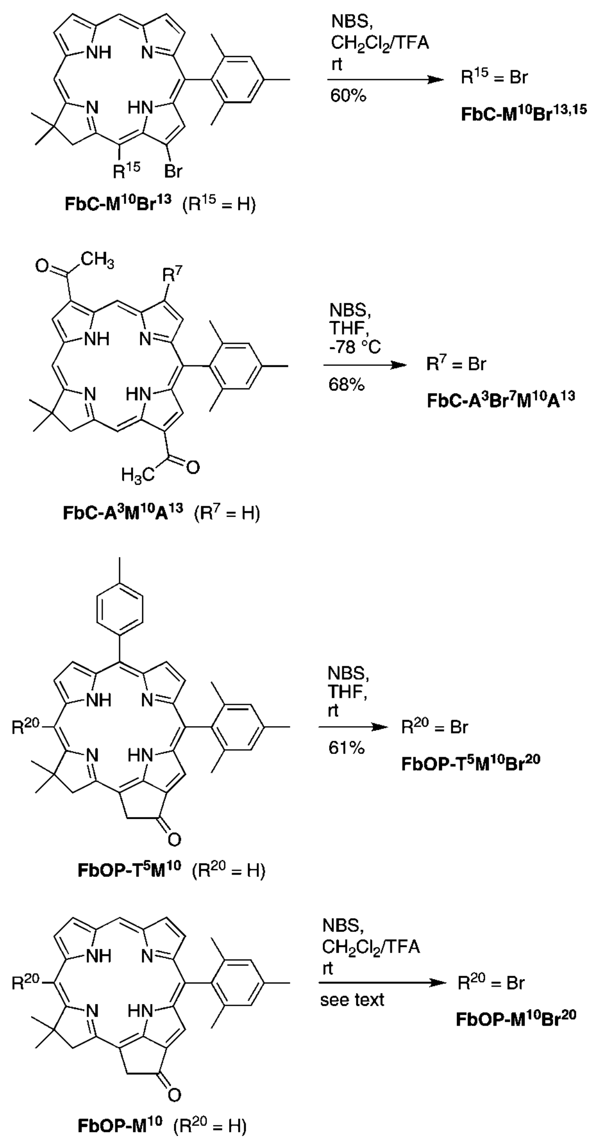
NBS (Table 1). Treatment of **FbC** with 2 equiv of NBS in THF at room temperature afforded an inseparable, nearly equimolar mixture of two dibromochlorins (entry 2), which upon NMR analysis (^{1}H NMR, COSY, NOESY) were identified as the 7,15-dibromochlorin **FbC-Br^{7,15}** and the 8,15-dibromochlorin **FbC-Br^{8,15}**. Treatment with 3 molar equiv of NBS afforded the expected 7,8,15-tribromochlorin **FbC-Br^{7,8,15}** in 61% yield (entry 3). When 4 molar equiv of NBS was employed, the only isolable product was tribromochlorin **FbC-Br^{7,8,15}**, which was accompanied by an inseparable mixture of tri- and tetrabromochlorins (entry 4). In cases where products were not isolable, the reaction mixture was examined by ^{1}H NMR spectroscopy and laser desorption mass spectrometry in the absence of a matrix (LD-MS).[47]

On the other hand, treatment of **FbC** at room temperature with 1 molar equiv of NBS under acidic conditions, achieved in the solvent CH_2Cl_2/TFA (10:1), afforded the 15-monobromochlorin **FbC-Br^{15}** (entry 5), and a trace of dibromochlorin **FbC-Br^{15,20}**. Treatment with 2 equiv of NBS gave the 15,20-dibromochlorin **FbC-Br^{15,20}** in 51% yield (entry 6), with no detectable quantity of the 7- or 8-substituted product. The motivation for this experiment was the hypothesis that an acidic medium, upon protonation of the free nitrogens (Chart 2), would preferentially deactivate ring B. This expectation was indeed borne out. Evidence in support of protonation of at least one if not both free nitrogens in the chlorin stems from absorption spectroscopy. **FbC** undergoes a hypsochromic shift of the long-wavelength $Q_y(0,0)$ band upon acidification in toluene.[1] Similar features were observed for the chlorins examined herein. Spectral data for chlorins **FbC** and **FbC-M^{10}A^{13}** in CH_2Cl_2 with and without TFA are presented in the Supporting Information.

To our knowledge, all prior reports of chlorin bromination under acidic conditions concern macrocycles bearing a full complement of β-substituents (e.g., chlorophyll *a* derivatives)[38-44] where the distinctions between neutral and acidic conditions would not be manifested. In summary, the order of reactive sites for bromination of chlorin **FbC** under neutral conditions is 15 > 7,8 > 20, whereas that under acidic conditions is 15 > 20 > 7,8. The ability to suppress the reactivity of the β-pyrrole sites of ring B merely by altering the solvent composition (neutral versus acidic) affords a versatile tactic for introducing substituents in chlorin and oxophorbine macrocycles. The resulting change in regioselectivity provides a solution to the synthesis of sparsely substituted chlorophyll *b* analogues (vide infra).

C. Bromination of More Elaborate Chlorins. To further develop our understanding of regioselective bromination, we also examined the bromination of several more highly substituted chlorins or 13^1-oxophorbines (Scheme 3). Thus, a chlorin bearing both a 13-bromo group and a 10-mesityl group (**FbC-M^{10}Br^{13}**) was employed in a lengthy study of bromination. The chief results are that neutral bromination conditions (NBS in THF, $CHCl_3$, or CH_2Cl_2) afford predominantly the 7,13-dibromochlorin **FbC-M^{10}Br^{7,13}**, whereas acidic bromination affords the 13,15-dibromochlorin **FbC-M^{10}Br^{13,15}** in 60% yield with only traces of chlorins containing two or more bromo atoms (see the Supporting Information for a table of data). Treatment of the 3,13-diacetylchlorin **FbC-A^{3}M^{10}A^{13}** with NBS under neutral conditions at −78 °C gave the 7-bromo product **FbC-A^{3}Br^{7}M^{10}A^{13}** in 68% yield, an expected regiochemical outcome given the similar result upon low temperature bromination of **FbC-M^{10}A^{13}** (vide supra).

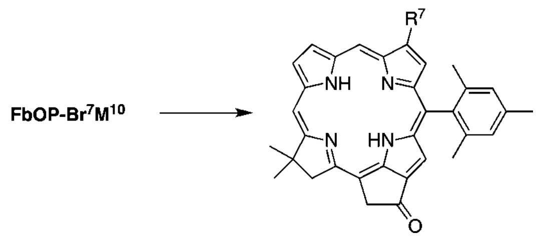
SCHEME 3

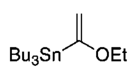


Treatment of the 5,10-diaryl-substituted oxophorbine **FbOP-T^{5}M^{10}** with 1 equiv of NBS in THF at room temperature for 1.5 h afforded the 20-bromooxophorbine **FbOP-T^{5}M^{10}Br^{20}** in 61% yield. Thus, for a 5,10-disubstituted oxophorbine, the order of reactivity is 20 > 7, 8 even under neutral conditions. On the other hand, the absence of the steric effect of the 5-aryl unit affords less clean results. Thus, **FbOP-M^{10}** under the standard acidic bromination conditions [1 equiv of NBS in CH_2Cl_2/TFA (10:1) at room temperature for 1.5 h] afforded a mixture of products including the expected **FbOP-M^{10}Br^{20}** as the main product (accompanied by a small amount of an inseparable, unidentified monobromochlorin), a significant quantity of starting material (separable in 40% yield), and a small amount of

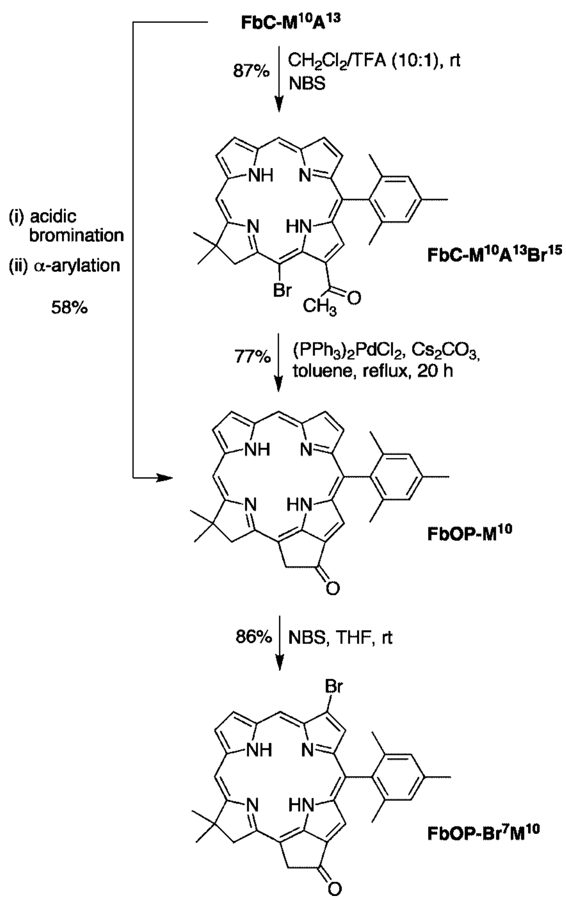
(47) Baillargeon, V. P.; Stille, J. K. *J. Am. Chem. Soc.* **1986**, *108*, 452–461.

TABLE 2. Derivatization of 7-Bromooxophorbine FbOP-Br^{7}M^{10}



entry	reactant	conditions	R^7	product	yield
1		(1) $(PPh_3)_2PdCl_2$, THF, reflux (2) aq HCl	acetyl	**FbOP-A^{7}M^{10}**	76%
2	CO	$Pd(PPh_3)_4$, Bu_3SnH, 70 °C	formyl	**FbOP-F^{7}M^{10}**	78%
3	TIPS-ethyne	$Pd_2(dba)_3$, P(o-tol)$_3$, toluene/Et_3N (5:1), 60 °C	TIPS-ethynyl	**FbOP-E^{7}M^{10}**	67%

SCHEME 4



an unidentified dibromooxophorbine (separable). While the acidic bromination of **FbOP-M^{10}** did not give particularly clean results, the neutral bromination (vide infra) was quite clean.

D. Bromination Tactics in a Route to Chlorophyll *b* Analogues. Bromination of 13-acetylchlorin **FbC-M^{10}A^{13}** under acidic conditions [NBS in CH_2Cl_2/TFA (10:1) at room temperature for 1.5 h] gave the 15-bromochlorin **FbC-M^{10}A^{13}Br^{15}** in 87% yield (Scheme 4). The 7-bromochlorin was not observed in this reaction, and only a trace of the 15,20-dibromochlorin was identified (^{1}H NMR, LD-MS). Subsequent ring closure via α-arylation[15] under Pd-mediated conditions gave the desired 13^1-oxophorbine **FbOP-M^{10}** in 77% yield. In a streamlined reaction sequence, acidic bromination of **FbC-M^{10}A^{13}** afforded the crude 15-bromochlorin (10 mM), which upon treatment under the standard conditions for α-arylation [$(PPh_3)_2PdCl_2$ (20 mol%) and Cs_2CO_3 (50 mM) in toluene at reflux] afforded the 13^1-oxophorbine **FbOP-M^{10}** in 58% overall yield. This method provides facile access to the 13^1-oxophorbine lacking a 5-substituent. Bromination of **FbOP-M^{10}** under neutral conditions with 1 molar equiv of NBS in THF at room temperature for 2 h gave the 7-bromo-13^1-oxophorbine **FbOP-Br^{7}M^{10}** in 86% yield. As expected, the 20-position is hindered owing to the presence of the *gem*-dimethyl group, the 15-position is blocked, and the 8-position is sterically hindered by the 10-substituent, leaving the 7-position as the most accessible site.

The structure of **FbOP-Br^{7}M^{10}** was confirmed by NOESY (see the Supporting Information). The position of the adjacent β-proton (H^8) shifted from 8.42 to 8.41 ppm in going from **FbOP-M^{10}** to **FbOP-Br^{7}M^{10}**, whereas the adjacent meso proton (H^5) shifted from 9.35 to 9.57 ppm. In general, the introduction of a β-bromo atom causes hardly any effect on the adjacent β-H, whereas the neighboring meso-H undergoes a chemical shift of 0.2 ppm, making the identification of β-bromochlorins (3, 7, 13 position, etc.) relatively straightforward. Prior 7-substituted chlorins prepared in the same manner have been analyzed by X-ray crystallography.[14]

E. Derivatization of 7-Bromo-13^1-oxophorbines. The 7-bromo-13^1-oxophorbine **FbOP-Br^{7}M^{10}** was derivatized with potential auxochromes such as acetyl and formyl groups (Table 2). The formyl group was introduced to mimic chlorophyll *b*. The coupling of **FbOP-Br^{7}M^{10}** (20 mM) and tributyl(1-ethoxyvinyl)tin (80 mM) in the presence of 20 mol % of $(PPh_3)_2PdCl_2$ in THF for 20 h followed by hydrolysis with 10% aqueous HCl gave 7-acetylchlorin **FbOP-A^{7}M^{10}** in 76% yield (entry 1). The synthesis of formylchlorins[13] has been achieved by Pd-mediated carbonylation. Similar treatment of **FbOP-Br^{7}M^{10}** (10 mM) with sodium formate (25 mM) in the presence of $(PPh_3)_2PdCl_2$ (20 mol %) and PPh_3 (20 mol %) in DMF at 108 °C under an atmosphere of CO[48] afforded the 7-formyloxophorbine **FbOP-F^{7}M^{10}** in 34% yield. Upon use of Bu_3SnH

(48) Srinivasan, N.; Haney, C. A.; Lindsey, J. S.; Zhang, W.; Chait, B. T. *J. Porphyrins Phthalocyanines* **1999**, *3*, 283–291.

TABLE 3. Absorption Spectral Properties of 13-Substituted Chlorins and 7-Substituted 13^1-Oxophorbines[a]

compd	λB [fwhm] (nm)	ΔB (cm^{-1})[b]	λQ$_y$(0,0) [fwhm] (nm)	ΔQ$_y$(0,0) (cm^{-1})[b]	$I_B/I_{Qy(0,0)}$[c]	$\Sigma_B/\Sigma_{Qy(0,0)}$[d]
FbC-M^{10}[e]	400 [34]		638 [9]		2.5	7.9
FbC-M^{10}Br^{13}	398 [36]	130	645 [10]	−170	2.1	7.0
FbC-M^{10}A^{13}	415 [36]	−900	659 [12]	−500	1.9	5.5
FbOP-M^{10}	413 [58]	−790	656 [11]	−430	1.7	6.3
FbOP-Br^{7}M^{10}	425 [40]	−680	656 [12]	0	2.3	7.1
FbOP-E^{7}M^{10}	434 [32]	−1200	660 [11]	−90	2.6	7.7
FbOP-A^{7}M^{10}	440 [21]	−1500	654 [11]	50	4.1	10
FbOP-F^{7}M^{10}	442 [20]	−1600	653 [11]	70	4.5	14
Pheo a[f]	408.5 [54]		667.5 [18]		2.0	4.4
Pheo b[f]	432.5 [18]	−1350	656.5 [18]	250	4.6	7.8

[a] In toluene at room temperature unless noted otherwise. [b] The shift of the band relative to that of the parent chlorin (**FbC-M^{10}**) or parent oxophorbine (**FbOP-M^{10}**). [c] Ratio of the intensities of the B and Q$_y$(0,0) bands. [d] Ratio of the integrated intensities of the B band (360−450 nm for **FbC-M^{10}**, **FbC-M^{10}Br^{13}**, and **Pheo *a***; 360−480 nm for all other compounds) and Q$_y$(0,0) band (615−665 nm for **FbC-M^{10}** and **FbC-M^{10}Br^{13}**; 625−700 nm for **Pheo *a*** and **Pheo *b***; 630−690 nm for all other compounds). [e] Absorption data from ref 1 (in toluene). [f] Absorption data for pheophytin *a* and pheophytin *b* in diethyl ether.[49]

and a stoichiometric amount of Pd(PPh$_3$)$_4$, the yield of 7-formylation was increased to 78% (entry 2). Reaction with (triisopropylsilyl)acetylene gave the 7-ethynyl-substituted oxophorbine **FbOP-E^{7}M^{10}** in 67% yield (entry 3).

II. Spectroscopic Studies. The chlorins and oxophorbines were characterized by ^{1}H NMR spectroscopy, LD-MS, high-resolution mass spectrometry (FAB-MS or ESI-MS), absorption spectroscopy, and, where permitted by solubility and sample size, ^{13}C NMR spectroscopy. The spectral properties of the free base 13-acetylchlorin and 13^1-oxophorbines are listed in Table 3, accompanied by those of the benchmark free base chlorin (**FbC-M^{10}**)[1] lacking any 13-substituent, and free base derivatives (i.e., pheophytins, abbreviated **Pheo *a*** and **Pheo *b***)[49] of chlorophyll *a* and chlorophyll *b*. The corresponding absorption spectra of the synthetic chlorins are displayed in Figure 2.

The spectral properties of the 13-acetylchlorin (**FbC-M^{10}A^{13}**) or the 13^1-oxophorbine (**FbOP-M^{10}**) are similar to those observed previously for analogous compounds that contain an additional 3-substituent or 5-aryl substituent, respectively.[10,15,20,21] Both compounds contain a 13-keto group, which functions as an auxochrome to cause the following effects versus the benchmark free base chlorin **FbC-M^{10}**: (i) a 13−15 nm bathochromic shift of the B band, (ii) a 18−21 nm bathochromic shift of the Q$_y$(0,0) band, and (iii) a hyperchromic effect on the Q$_y$(0,0) band.[10,15] The hyperchromic effect is assessed by the ratio of the intensities of the B versus Q$_y$(0,0) bands, $I_B/I_{Qy}(0,0)$ (which is a long-established metric in chlorin chemistry[2]), or by the ratio of the integrated absorbances ($\Sigma_B/\Sigma_{Qy(0,0)}$). The latter is a more accurate measure when the full-width at half-maximum (fwhm) of either band changes substantially upon substitution, as is the case here: the fwhm of the entire B band for **FbC-M^{10}A^{13}** is 36 nm, while that of **FbOP-M^{10}** is 58 nm. By such measures the Q-band gains relative strength of 1.2−1.5-fold, as shown in Table 3. The only noticeable differences in the spectra of the two compounds occur in the visible region, where the Q$_x$(0,0) band of **FbOP-M^{10}** shows further bathochromic shifts with stronger intensity compared to that of **FbC-M^{10}A^{13}** (see spectra in the Supporting Information).

Whereas the presence of the oxophorbine ring in **FbOP-M^{10}** versus the chlorin benchmark **FbC-M^{10}** causes bathochromic shifts of both the B and Q$_y$ bands and a hyperchromic effect on the Q$_y$(0,0) band, the introduction of auxochromes at the

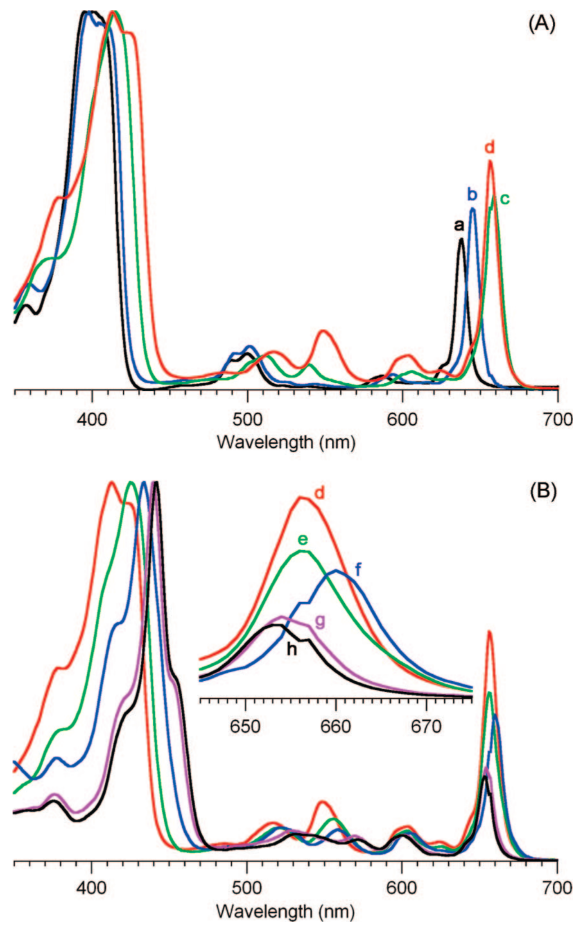


FIGURE 2. Absorption spectra in toluene at room temperature of 13-substituted chlorins and 13^1-oxophorbines (normalized at the B bands). The label and the color in the graph are as follows. (A): **FbC-M^{10}** (a, black), **FbC-M^{10}Br^{13}** (b, blue), **FbC-M^{10}A^{13}** (c, lime), **FbOP-M^{10}** (d, red). (B): **FbOP-M^{10}** (d, red), **FbOP-Br^{7}M^{10}** (e, lime), **FbOP-E^{7}M^{10}** (f, blue), **FbOP-A^{7}M^{10}** (g, purple), **FbOP-F^{7}M^{10}** (h, black).

7-position of oxophorbines affords a quite different outcome (Figure 2B). The presence of a 7-acetyl or 7-formyl group in a 13^1-oxophorbine causes a significant bathochromic shift of the B band (27 nm for **FbOP-A^{7}M^{10}**, 29 nm for **FbOP-F^{7}M^{10}**) versus that of **FbOP-M^{10}**. On the other hand, the position of the Q$_y$(0,0) band is essentially unchanged (2−3 nm hypsochromic shift) yet the relative intensity is profoundly decreased

(49) Zass, E.; Isenring, H. P.; Etter, R.; Eschenmoser, A. *Helv. Chim. Acta* **1980**, *63*, 1048–1067.

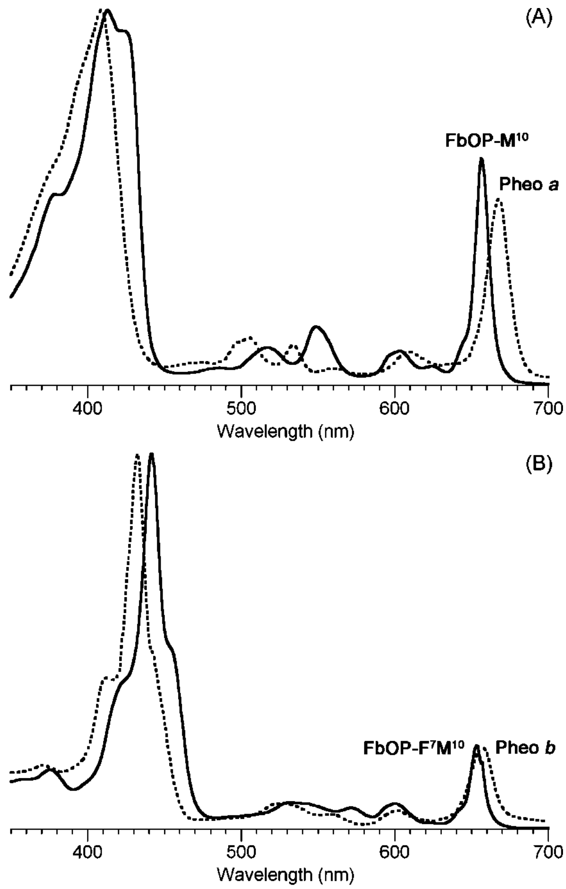


FIGURE 3. Absorption spectra at room temperature of natural versus synthetic 13^1-oxophorbines (normalized at the B bands). (A) Absorption spectra of pheophytin *a* (dashed) and **FbOP-M^{10}** (solid). (B): Absorption spectra of pheophytin *b* (dashed) and **FbOP-F^{7}M^{10}** (solid). The pheophytins are in diethyl ether, whereas the synthetic analogues are in toluene.

(2.5−2.7-fold) as illustrated by the change in the $I_B/I_{Qy(0,0)}$ ratio from 1.7 to 4.1 (**FbOP-A^{7}M^{10}**) or 4.5 (**FbOP-F^{7}M^{10}**). The altered $I_B/I_{Qy(0,0)}$ ratio stems in part from the sharpening (nearly one-third decrease in fwhm) of the B band upon introduction of the 7-acetyl or 7-formyl group. Thus, the general trend with auxochromes at the 7-position of 13^1-oxophorbines is to bathochromically shift and sharpen the B band, leaving the $Q_y(0,0)$ band relatively unchanged in position but significantly decreased in relative intensity.

A key outcome of our work with sparsely substituted chlorins is the realization that the placement of essential groups at designated sites about the perimeter of the chlorin macrocycle can afford suitable analogues of chlorophylls. Figure 3 compares the absorption spectra[49] of pheophytins *a* and *b* with oxophorbines **FbOP-M^{10}** and **FbOP-F^{7}M^{10}**. Pheophytin *a* incorporates a 7-methyl substituent, whereas pheophytin *b* is equipped with a 7-formyl group. In each case, the spectral features are relatively well matched, both in terms of position and relative intensity of absorption, despite the absence of the 3-vinyl group characteristic of the naturally occurring oxophorbines.

Conclusions

New regioselective bromination tactics have opened a rational route to 13^1-oxophorbines bearing 7-conjugative groups. The route entails preparation of a 13-acetylchlorin, which undergoes regioselective bromination (acidic conditions) at the 15-position. The resulting 13^1-oxophorbine, obtained upon Pd-mediated α-arylation to form the isocyclic ring, undergoes regioselective bromination (neutral conditions) at the 7-position. Although most prior brominations of chlorins employed acidic conditions,[39−44] the use of chlorins bearing a full complement of β-substituents hid this otherwise new aspect of the chemistry of chlorins. Subsequent derivatization affords analogues of chlorophyll *b*. The analogues are sparsely substituted given that the only substituents other than that at the 7-position are (i) the geminal dimethyl group in the pyrroline ring and (ii) the mesityl group at the 10-position.

The presence of the keto group at the 13-position in **FbOP-M^{10}** causes a bathochromic shift and a relative increase in the intensity of the $Q_y(0,0)$ band. On the other hand, the introduction of an acetyl or formyl group at the 7-position in **FbOP-M^{10}** causes a bathochromic shift and sharpening of the B band, leaves the position of the $Q_y(0,0)$ band essentially unchanged, and affords a significant relative decrease in $Q_y(0,0)$ intensity. The ability to install the isocyclic ring and selectively brominate the chlorin macrocycle should facilitate a range of fundamental studies. The ability to achieve spectral features similar to those of free base chlorophylls in structurally simpler molecular architectures bodes well for applications ranging from artificial photosynthesis to photomedicine.

Experimental Section

A. Bromination Studies. Practical Aspects Concerning the Bromination of Chlorins. The bromination of chlorins described herein for synthetic applications generally occurs with high regioselectivity. Still, the main product often is accompanied by a small amount of other isomers, overbrominated chlorins, and unreacted chlorin. The amount of the undesired side products varies for different chlorins, and the identity of chlorins formed as byproducts typically has not been fully determined due to the small amount of isolated material. In most cases, the reaction mixture was separable by column chromatography. The composition of the reaction mixture depends on the amount of brominating agent used. The ratio of dibromochlorins and unreacted starting chlorins can slightly vary for a given starting material from reaction to reaction, due to the small inaccuracy in measurement of the amount of brominating agent. In some instances, a 0.10 M stock solution of NBS in an appropriate solvent was used where specified for bromination to facilitate more accurate measurements. The addition of solid NBS typically was performed all-at-once whereas the stock solution of NBS was added over 10–30 sec for reactions on the scale of 0.01–0.06 mmol (or longer for larger reactions). The bromination studies were performed using free base chlorins rather than zinc complexes because (1) free base chlorins form narrow, well-resolved bands on silica gel whereas zinc complexes tend to streak upon chromatography and (ii) prior results[12] concerning the bromination of Zn(II) chlorins afforded side products which may include dimers of chlorins.

Dibromination of FbC under Neutral Conditions: 1:1 Mixture of FbC-Br^{7,15} and FbC-Br^{8,15}. A solution of **FbC**[12] (24.0 mg, 0.0705 mmol) in THF (35 mL) was treated with NBS (25.1 mg, 0.140 mmol). The resulting reaction mixture was stirred at room temperature for 1.5 h. The reaction mixture was diluted with CH_2Cl_2 (∼50 mL) and quenched by the addition of saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. Column chromatography of the resulting solid [silica, hexanes/CH_2Cl_2 (4:1) then hexanes/CH_2Cl_2 (1:1)] provided the dibromochlorin (first fraction, purple) and a trace of monobromochlorin (second fraction, green). The dibromochlorin was rechromatographed [silica, hexanes/CH_2Cl_2 (1:1)] to afford a purple solid

(23.1 mg, 66%): ^{1}H NMR δ −2.97 (brs, 1H), −2.77 (brs, 1H), 2.03 (s, 6H), 4.61 (s, 2H), 8.81 (s + d, 2H), 8.88 (dd, J = 2.0, 4.4 Hz, 1H), 8.95 (d, J = 4.4 Hz, 0.5H), 9.05−9.08 (m, 1H), 9.12 (d, J = 4.4 Hz, 0.5H), 9.16 (s, 1H), 9.38 (d, J = 4.4 Hz, 1H), 9.75 (s, 1H); LD-MS obsd 497.8, calcd 498.2131 ($C_{22}H_{18}Br_2N_4$); λ_{abs} (toluene) 403, 638 nm.

Tribromination of FbC under Neutral Conditions: 7,8,15-Tribromo-17,18-dihydro-18,18-dimethylporphyrin (FbC-Br^{7,8,15}). A solution of **FbC** (50.6 mg, 0.148 mmol) in THF (74 mL) was treated with NBS (79.3 mg, 0.445 mmol). The resulting reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (∼50 mL) and quenched by the addition of saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. Column chromatography of the resulting solid [silica, hexanes then hexanes/CH_2Cl_2 (4:1)] provided a tribromochlorin (first fraction, blue) and a dibromochlorin (second fraction, greenish blue). The tribromochlorin was rechromatographed [silica, hexanes/CH_2Cl_2 (4:1)] to afford a purple solid (53.2 mg, 62%): ^{1}H NMR δ −3.05 (brs, 1H), −2.88 (brs, 1H), 2.05 (s, 6H), 4.62 (s, 2H), 8.82 (s, 1H), 8.88 (dd, J = 2.0, 4.4 Hz, 1H), 9.04 (dd, J = 2.0, 4.4 Hz, 1H), 9.13−9.15 (m, 2H), 9.63 (s, 1H), 9.65 (s, 1H); LD-MS obsd 575.9; FAB-MS obsd 574.9063, calcd 574.9083 [(M + H)$^+$, M = $C_{22}H_{17}Br_3N_4$]; λ_{abs} (toluene) 406, 637 nm.

Attempted Tetrabromination of FbC under Neutral Conditions. A solution of **FbC** (46.2 mg, 0.136 mmol) in THF (68 mL) was treated with NBS (96.8 mg, 0.544 mmol). The resulting reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (∼50 mL) and quenched by the addition of saturated aqueous $NaHCO_3$. The organic extract was washed with water and brine, dried (Na_2SO_4), and concentrated. Column chromatography of the resulting solid [silica, hexanes then hexanes/CH_2Cl_2 (4:1)] provided a mixture of tribromo and tetrabromochlorins (first fraction, purple) and a tribromochlorin (second fraction, blue). The latter was rechromatographed [silica, hexanes/CH_2Cl_2 (2:1)] to afford the tribromochlorin **FbC-Br^{7,8,15}** as a purple solid (37.5 mg, 48%). The characterization data (^{1}H NMR, LD-MS, FAB-MS, UV−vis) were consistent with those for the product obtained as described in the tribromination procedure.

Monobromination of FbC under Acidic Conditions: 15-Bromo-17,18-dihydro-18,18-dimethylporphyrin (FbC-Br^{15}). A solution of **FbC** (18.4 mg, 0.0542 mmol) in CH_2Cl_2/TFA [27 mL, (10:1), 2 mM chlorin concentration] was treated with NBS (0.542 mL, 0.100 M in CH_2Cl_2) by syringe over a 30 s period. The resulting reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (∼50 mL) and quenched by the addition of saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extract was washed with water and brine, dried (Na_2SO_4), and concentrated. Column chromatography of the resulting solid [silica, hexanes/CH_2Cl_2 (2:3)] afforded a dibromochlorin (first fraction, purple) and the title compound (second fraction, greenish blue). The latter was rechromatographed [silica, hexanes/CH_2Cl_2 (1:1)] to afford a brown solid (12.1 mg, 62%). The ^{1}H NMR, ^{13}C NMR, LD-MS, FAB-MS, and absorption spectra were consistent with the reported data for **FbC-Br^{15}**.[12]

Dibromination of FbC Under Acidic Conditions: 15,20-Dibromo-17,18-dihydro-18,18-dimethylporphyrin (FbC-Br^{15,20}). A solution of **FbC** (23.8 mg, 0.0699 mmol) in CH_2Cl_2/TFA [35 mL (10:1)] was treated with NBS (25.0 mg, 0.140 mmol). The resulting reaction mixture was stirred at room temperature for 1 h. The reaction mixture was diluted with CH_2Cl_2 (∼50 mL) and quenched by the addition of saturated aqueous $NaHCO_3$. The organic layer was separated, and the aqueous phase was extracted with CH_2Cl_2. The combined organic extract was washed with water and brine, dried (Na_2SO_4), and concentrated. Column chromatography of the resulting solid [silica, hexanes/CH_2Cl_2 (4:1) then hexanes/CH_2Cl_2 (1:1)] gave the title dibromochlorin (first fraction, purple) and a monobromochlorin (second fraction, greenish blue). The dibromochlorin was rechromatographed [silica, hexanes/CH_2Cl_2 (2:1)] to afford a purple solid (17.8 mg, 51%): ^{1}H NMR δ −2.73 (brs, 1H), −2.63 (brs, 1H), 2.26 (s, 6H), 4.75 (s, 2H), 8.83 (d, J = 4.4 Hz, 1H), 8.87 (d, J = 4.4 Hz, 1H), 9.04 (d, J = 4.4 Hz, 1H), 9.10 (d, J = 4.4 Hz, 1H), 9.25 (d, J = 4.4 Hz, 1H), 9.41 (d, J = 4.4 Hz, 1H), 9.55 (s, 1H), 9.63 (s, 1H); ^{13}C NMR δ 29.7, 49.1, 60.5, 96.6, 96.7, 107.7, 108.8, 126.5, 126.6, 128.7, 133.0, 133.5, 135.2, 136.2, 138.3, 140.0, 152.0, 153.0, 162.2, 171.9 (one carbon resonance was not apparent); LD-MS obsd 496.5; FAB-MS obsd 496.1002, calcd 496.9898 [(M + H)$^+$, M = $C_{22}H_{18}Br_2N_4$]; λ_{abs} (toluene) 402, 648 nm.

Monobromination of 13-Acetylchlorin FbC-M^{10}A^{13}. A solution of **FbC-M^{10}A^{13}** (44.7 mg, 0.0893 mmol) in THF (45 mL) was treated with NBS (15.9 mg, 0.0893 mmol) at room temperature for 1.5 h. CH_2Cl_2 was added. The mixture was washed with saturated aqueous $NaHCO_3$ solution. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting solid was chromatographed [silica, hexanes/CH_2Cl_2 (3:7)] to give two fractions, each of which contained a chlorin. The first fraction was confirmed to be **FbC-Br^{7}M^{10}A^{13}** (21.7 mg, 42% of total yield), and the second fraction was confirmed to be **FbC-M^{10}A^{13}Br^{15}** (14.8 mg, 28% of total yield). Data for 13-acetyl-7-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (**FbC-Br^{7}M^{10}A^{13}**): ^{1}H NMR δ −1.41 (brs, 1H), −1.16 (brs, 1H), 1.86 (s, 6H), 2.02 (s, 6H), 2.63 (s, 3H), 3.06 (s, 3H), 4.58 (s, 2H), 7.25 (s, 2H), 8.37 (s, 1H), 8.74 (s, 1H), 8.85 (d, J = 4.4 Hz, 1H), 8.90 (s, 1H), 9.14 (d, J = 4.4 Hz, 1H), 9.75 (s, 1H), 10.07 (s, 1H); LD-MS obsd 577.3; FAB-MS obsd 578.1692, calcd 578.1681 ($C_{33}H_{31}BrN_4O$); λ_{abs} (toluene) 418, 656 nm. Data for 13-acetyl-15-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (**FbC-M^{10}A^{13}Br^{15}**): ^{1}H NMR δ −1.47 (brs, 2H), 1.84 (s, 6H), 2.04 (s, 6H), 2.61 (s, 3H), 3.07 (s, 3H), 4.57 (s, 2H), 7.24 (s, 2H), 8.39 (d, J = 4.4 Hz, 1H), 8.48 (s, 1H), 8.72−8.74 (brs, 2H), 8.85 (d, J = 4.4 Hz, 1H), 9.10 (d, J = 4.4 Hz, 1H), 9.54 (s, 1H); ^{13}C NMR δ 21.4, 21.6, 31.4, 34.8, 46.6, 55.3, 95.2, 95.3, 106.2, 123.7, 125.3, 126.0, 128.0, 129.4, 130.8, 132.9, 133.3, 133.9, 137.0, 137.3, 137.6, 138.1, 139.0, 142.1, 152.3, 154.7, 162.7, 178.0, 202.4; LD-MS obsd 578.5; FAB-MS obsd 578.1692, calcd 578.1681 ($C_{33}H_{31}BrN_4O$); λ_{abs} (toluene) 406, 649 nm.

Neutral Bromination at Low Temperature of a 13-Acetylchlorin: 13-Acetyl-7-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (FbC-Br^{7}M^{10}A^{13}). A solution of **FbC-M^{10}A^{13}** (17.0 mg, 0.0339 mmol) in THF (16 mL) was treated with NBS (340 μL, 0.100 M THF solution) at −78 °C for 1.5 h. CH_2Cl_2 was added. The mixture was washed with saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes/CH_2Cl_2 (3:7)] to give a purple solid (13.5 mg, 76%); ^{13}C NMR (75 MHz) δ 21.4, 21.6, 30.0, 31.0, 46.9, 51.9, 95.2, 98.0, 103.7, 121.4, 123.1, 125.7, 128.1, 129.3, 130.0, 13.2, 130.7, 132.3, 136.7, 137.0, 137.7, 138.3, 139.1, 143.2, 149.6, 150.1, 165.3, 178.6, 197.2; LD-MS obsd 578.4; FAB-MS obsd 578.1692, calcd 578.1681 ($C_{33}H_{31}BrN_4O$); λ_{abs} (toluene) 418, 656 nm. This sample gave a somewhat poor quality ^{1}H NMR spectrum and hence was converted to the zinc chelate for further characterization.

Zn(II)-13-Acetyl-7-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (ZnC-Br^{7}M^{10}A^{13}). A solution of **FbC-Br^{7}M^{10}A^{13}** (13.4 mg, 0.0231 mmol) in $CHCl_3$ (4.0 mL) was treated with a solution of $Zn(OAc)_2 \cdot 2H_2O$ (76.1 mg, 0.346 mmol) in methanol (1.0 mL). The reaction mixture was stirred at room temperature for 16 h. CH_2Cl_2 was added. The reaction mixture was washed with saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting residue was chromatographed (silica, CH_2Cl_2) to afford a green solid (11.4 mg, 77%): ^{1}H NMR (THF-d_8) δ 1.87 (s, 6H), 2.01 (s, 6H), 2.59 (s, 3H), 2.83 (s, 3H), 4.50 (s, 2H), 7.26 (s, 2H), 8.18 (s, 1H), 8.52 (s, 1H), 8.67 (d, J = 4.4 Hz, 1H), 8.87 (s, 1H), 9.00 (d, J = 4.4 Hz, 1H), 9.45 (s, 1H), 9.78 (s, 1H); ^{13}C NMR (THF-d_8) δ 21.6, 21.7, 29.6, 31.1, 46.4, 51.2, 95.1, 98.8, 105.4, 117.3, 124.6, 128.7, 129.3, 130.0, 134.6, 135.1, 136.5, 138.4, 139.5, 139.6, 142.5, 145.4, 145.5, 149.4, 151.1, 157.1, 160.4, 173.8, 196.1; LD-MS obsd 642.4; ESI-MS obsd 640.0801, calcd 640.0810 ($C_{33}H_{29}BrN_4OZn$); λ_{abs} (toluene) 423, 631 nm.

Neutral Bromination at Low Temperature of a 3,13-Diacetylchlorin: 3,13-Diacetyl-7-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (FbC-A^{3}Br^{7}M^{10}A^{13}). A solution of **FbC-A^{3}M^{10}A^{13}** (8.50 mg, 0.0156 mmol) in THF was treated with NBS (156 μL, 0.100 M solution in THF, 0.0156 mmol) at −78 °C for 1.5 h. CH_2Cl_2 was added. The mixture was washed with saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting solid was dissolved in CH_2Cl_2 and chromatographed (silica, hexanes then CH_2Cl_2) to give a purple solid (6.6 mg, 68%): ^{1}H NMR δ −1.36 (brs, 2H), 1.84 (s, 6H), 2.02 (s, 6H), 2.62 (s, 3H), 3.05 (s, 3H), 3.27 (s, 3H), 4.60 (s, 2H), 7.25 (s, 2H), 8.35 (s, 1H), 8.82 (s, 1H), 8.92 (s, 1H), 9.31 (s, 1H), 10.08 (s, 1H), 10.85 (s, 1H); LD-MS obsd 620.5; FAB-MS obsd 620.1785, calcd 620.1787 ($C_{35}H_{33}BrN_4O_2$); λ_{abs} (toluene) 428, 678 nm.

Acidic Bromination of a 13-Bromochlorin: 13,15-Dibromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (FbC-M^{10}Br^{13,15}). A sample of **FbC-M^{10}Br^{13}** (20 mg, 0.037 mmol) was treated with a CH_2Cl_2/TFA mixture [18.7 mL, (9:1)]. Protonation of the chlorin was observed by UV−vis spectroscopy, as seen by the disappearance of the Q_y(0,0) band at 643 nm and formation of a new band at 619 nm. Then 1.4 mL (0.037 mmol) of a fresh NBS solution (26.3 mM in CH_2Cl_2) was added dropwise to the green solution. The reaction mixture was stirred at room temperature. The progress of the bromination reaction was followed by TLC analysis (by taking a small aliquot of the reaction mixture and quenching it with triethylamine). After 40 min, acetone was added (3 mL) and the reaction was quenched with triethylamine (2.8 mL) at 0 °C, whereupon the reaction mixture turned from green to purple pink. The organic layer was washed with saturated aqueous $NaHCO_3$ and water, dried (Na_2SO_4), and filtered. The filtrate was concentrated. The dark purple residue obtained was dissolved in a hexanes/CH_2Cl_2 solution (4:1) and chromatographed [silica, hexanes/CH_2Cl_2 (4:1)] slowly. Some tribromochlorin species eluted first followed by the title compound and closely thereafter by the starting material. The title compound was concentrated to afford a dark purple solid (13.6 mg, 60%): ^{1}H NMR (300 MHz) δ −1.66 (br, 2H), 1.81 (s, 6H), 2.01 (s, 6H), 2.60 (s, 3H), 4.62 (s, 3H), 7.23 (s, 2H), 8.38 (d, J = 3.9 Hz, 1H), 8.68 (s, 1H), 8.73 (d, J = 4.5 Hz, 1H), 8.76 (s, 1H), 8.84 (d, J = 4.8 Hz, 1H), 9.07 (d, J = 4.8 Hz, 1H), 9.56 (s, 1H); ESI-MS obsd 615.0755, calcd 615.0753 [(M + H)$^+$, M = $C_{31}H_{29}N_4Br_2$]; λ_{abs} (CH_2Cl_2) 415, 508, 534, 598, 650 nm.

Neutral Bromination of a 5,10-Diaryl-13^1-oxophorbine: 20-Bromo-10-mesityl-18,18-dimethyl-13^1-oxo-5-*p*-tolylphorbine (FbOP-T^{5}M^{10}Br^{20}). A solution of **FbOP-T^{5}M^{10}** (15.4 mg, 0.0261 mmol) in THF (13.0 mL) was treated with NBS (261 μL, 0.100 M THF solution) at room temperature for 1.5 h. CH_2Cl_2 was added. The mixture was washed with saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes then hexanes/CH_2Cl_2 (1:4)], which provided a trace of an unidentified chlorin (first fraction, greenish blue) and a second fraction (green). The latter was rechromatographed [silica, hexanes/CH_2Cl_2 (1:4)] to afford a green solid (10.2 mg, 61%): ^{1}H NMR (300 MHz) δ −1.54 (s, 1H), 1.22 (s, 1H), 1.88 (s, 6H), 2.27 (s, 6H), 2.56 (s, 3H), 2.66 (s, 3H), 4.38 (s, 2H), 5.14 (s, 2H), 7.21 (s, 2H), 7.48 (d, J = 8.2 Hz, 2H), 7.91 (d, J = 8.2 Hz, 2H), 8.20 (d, J = 4.4 Hz, 1H), 8.25 (d, J = 4.4 Hz, 1H), 8.60 (s, 1H), 8.63 (dd, J = 2.0, 4.4 Hz, 1H), 9.25 (dd, J = 2.0, 4.4 Hz, 1H); ^{13}C NMR (75 MHz) δ 21.4, 21.5, 21.7, 29.2, 49.1, 51.3, 52.2, 95.9, 100.0, 105.7, 117.1, 122.2, 126.2, 127.2, 127.7, 128.1, 131.3, 131.8, 133.5, 133.8, 134.3, 135.4, 137.7, 138.3, 138.8, 139.3, 140.7, 142.7, 148.9, 153.8, 154.7, 157.3, 173.5, 195.6; LD-MS obsd 666.3; FAB-MS obsd 666.1998, calcd 666.1994 ($C_{40}H_{35}BrN_4O$); λ_{abs} (toluene) 423, 670 nm.

Acidic Bromination of a 10-Aryl-13^1-oxophorbine. A solution of **FbOP-M^{10}** (12.0 mg, 0.0241 mmol) in CH_2Cl_2/TFA [9.9 mL (10:1)] was treated with NBS (0.241 mL, 0.0241 mmol, 0.100 M solution in CH_2Cl_2). The resulting deep-green mixture was stirred at room temperature for 1 h. Saturated aqueous $NaHCO_3$ was added, and vigorous stirring for 5 min afforded a purple reaction mixture. The organic layer was separated, dried (Na_2SO_4), and concentrated. Column chromatography (silica, CH_2Cl_2) afforded a trace of unidentified chlorin (first fraction, green), unidentified dibromochlorin (second fraction, green), **FbOP-M^{10}Br^{20}** (third fraction, green-purple), and unreacted starting material (fourth fraction, purple). Concentration of the third fraction gave a green solid (7.0 mg, 50%) consisting of **FbOP-M^{10}Br^{20}** contaminated with ∼15% of unidentified chlorin: ^{1}H NMR δ −1.64 (brs, 1H), 1.25 (brs, 1H), 1.88 (s, 6H), 2.26 (s, 6H), 2.58 (s, 2H), 4.39 (s, 2H), 5.16 (s, 2H), 7.21−7.22 (m, 2H), 8.41 (d, J = 4.4 Hz, 1H), 8.64 (s, 1H), 8.72 (d, J = 4.4 Hz, 1H), 9.09−9.11 (m, 1H), 9.34−9.36 (m, 1H), 9.52 (s, 1H); LD-MS obsd 576.4; ESI-MS obsd 576.1519, calcd 576.1525 ($C_{33}H_{29}BrN_4O$); λ_{abs} (toluene) 418, 437 (sh), 666 nm.

B. Synthesis. 13-Acetyl-15-bromo-17,18-dihydro-10-mesityl-18,18-dimethylporphyrin (FbC-M^{10}A^{13}Br^{15}). A sample of **FbC-M^{10}A^{13}** (77.0 mg, 0.154 mmol) was dissolved in CH_2Cl_2 (70 mL) and treated with TFA (7 mL) to give a 2 mM chlorin concentration. The chlorin solution was treated with NBS (27.4 mg, 0.154 mmol) at room temperature for 1.5 h. CH_2Cl_2 was added. The mixture was treated with saturated aqueous $NaHCO_3$ and stirred for 5 min. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes/CH_2Cl_2 (3:7)] to give a trace of unidentified chlorin and the title compound (purple solid, 78 mg, 87%). The data (^{1}H NMR, ^{13}C NMR, LD-MS, ESI-MS, and λ_{abs}) were essentially identical to those reported above.

10-Mesityl-18,18-dimethyl-13^1-oxophorbine (FbOP-M^{10}). Following a reported procedure,[15] a mixture of **FbC-M^{10}A^{13}Br^{15}** (77.0 mg, 0.133 mmol), Cs_2CO_3 (217 mg, 0.665 mmol), and $(PPh_3)_2PdCl_2$ (18.6 mg, 0.0266 mmol) was refluxed in toluene (13.5 mL) for 20 h in a Schlenk flask. The reaction mixture was concentrated. The resulting crude solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes/CH_2Cl_2 (1:4) then CH_2Cl_2] to afford **FbC-M^{10}A^{13}** (first fraction, ∼17%; debromination apparently occurred upon Pd-coupling) and the title compound (second fraction, greenish blue solid, 51.2 mg, 77%): ^{1}H NMR δ −1.41 (s, 1H), 1.13 (s, 1H), 1.91 (s, 6H), 2.00 (s, 6H), 2.60 (s, 3H), 4.26 (s, 2H), 5.13 (s, 2H), 7.24 (s, 2H), 8.42 (d, J = 4.4 Hz, 1H), 8.58 (s, 1H), 8.59 (s, 1H), 8.66 (d, J = 4.4 Hz, 1H), 8.80 (dd, J = 2.0, 4.4 Hz, 1H), 9.00 (dd, J = 2.0, 4.4 Hz, 1H), 9.35 (s, 1H); ^{13}C NMR δ 21.3, 21.6, 31.0, 47.7, 48.5, 48.7, 94.8, 104.2, 106.3, 115.9, 126.0, 126.6, 128.1, 130.5, 132.6, 132.9, 133.0, 135.6, 138.0, 138.2, 138.8, 139.5, 143.6, 149.7, 153.0, 154.6, 157.2, 177.5, 195.9; LD-MS obsd 498.4; ESI-MS obsd 499.2492, calcd 499.2493 [(M + H)$^+$, M = $C_{33}H_{30}N_4O$]; λ_{abs} (toluene) 413, 656 nm.

Streamlined Procedure for Installing the Isocyclic Ring: 10-Mesityl-18,18-dimethyl-13^1-oxophorbine (FbOP-M^{10}). A solution of **FbC-M^{10}A^{13}** (218 mg, 0.435 mmol) in CH_2Cl_2 (200 mL) was treated with TFA (20 mL) followed by NBS (77.5 mg, 0.435 mmol) at room temperature. After 1.5 h, CH_2Cl_2 was added. The mixture was washed with saturated aqueous $NaHCO_3$. The organic layer was separated, dried (Na_2SO_4), and concentrated. The crude solid was used in the next step. Following a reported procedure,[15] a mixture of the crude solid, Cs_2CO_3 (709 mg, 2.17 mmol), and $(PPh_3)_2PdCl_2$ (61.0 mg, 0.0870 mmol) was refluxed in toluene (43 mL) for 20 h in a Schlenk flask. The reaction mixture was concentrated. The resulting crude solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, CH_2Cl_2/hexanes (1:1) then CH_2Cl_2] to afford the starting material **FbC-M^{10}A^{13}** (first fraction, 32%; from unreaction upon bromination and/or debromination upon Pd coupling) and the title compound (second fraction, greenish blue solid, 126 mg, 58%) with characterization data (^1H NMR, ^{13}C NMR, LD-MS, FAB-MS, λ_{abs}) consistent with those reported above.

7-Bromo-10-mesityl-18,18-dimethyl-13^1-oxophorbine (FbOP-Br^{7}M^{10}). A solution of **FbOP-M^{10}** (122 mg, 0.244 mmol) in THF (120 mL) was treated with NBS (43.5 mg, 0.244 mmol) at room temperature for 2 h. CH_2Cl_2 and saturated aqueous $NaHCO_3$ were added. The organic layer was separated, dried (Na_2SO_4), and concentrated. The resulting crude solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes then hexanes/CH_2Cl_2 (3:7)] to afford a purple solid (122 mg, 86%): ^1H NMR δ −1.49 (s, 1H), 0.83 (s, 1H), 1.87 (s, 6H), 2.03 (s, 6H), 2.57 (s, 3H), 4.28 (s, 2H), 5.11 (s, 2H), 7.22 (s, 2H), 8.41 (s, 1H), 8.56 (s, 1H), 8.63 (s, 1H), 8.85 (dd, J = 2.0, 4.4 Hz, 1H), 9.10 (dd, J = 2.0, 4.4 Hz, 1H), 9.57 (s, 1H); ^{13}C NMR δ 21.3, 21.6, 31.0, 47.8, 48.5, 48.7, 95.4, 101.6, 106.7, 116.7, 121.6, 125.9, 127.0, 128.2, 131.1, 132.5, 133.2, 135.1, 138.2, 138.5, 138.8, 139.3, 144.0, 149.8, 150.4, 150.5, 158.0, 178.0, 195.6; LD-MS obsd 577.1; ESI-MS obsd 577.1588, calcd 577.1597 [(M + H)$^+$ M = $C_{33}H_{29}BrN_4O$]; λ_{abs} (toluene) 425, 656 nm.

7-Acetyl-10-mesityl-18,18-dimethyl-13^1-oxophorbine (FbOP-A^{7}M^{10}). Following a procedure for Stille coupling with chlorins,[10] a mixture of **FbOP-Br^{7}M^{10}** (12.0 mg, 0.0207 mmol), tributyl(1-ethoxyvinyl)tin (28.0 μL, 0.0828 mmol), and $(PPh_3)_2PdCl_2$ (3.0 mg, 0.0041 mmol) was refluxed in THF (1.0 mL) for 18 h in a Schlenk flask. The reaction mixture was treated with 10% aqueous HCl (1.0 mL) at room temperature for 1 h. CH_2Cl_2 was added, and the organic layer was separated. The organic layer was washed (saturated aqueous $NaHCO_3$, water, and brine), dried (Na_2SO_4), and concentrated. The resulting solid was dissolved in a minimum amount of CH_2Cl_2 and chromatographed (silica, hexanes then CH_2Cl_2) to afford a purple solid (8.5 mg, 76%): ^1H NMR δ −1.45 (s, 1H), 1.17 (s, 1H), 1.90 (s, 6H), 2.01 (s, 6H), 2.60 (s, 3H), 2.97 (s, 3H), 4.24 (s, 2H), 5.07 (s, 2H), 7.25 (s, 2H), 8.53 (s, 2H), 8.77 (d, J = 4.4 Hz, 1H), 8.83 (s, 1H), 9.10 (d, J = 4.4 Hz, 1H), 10.50 (s, 1H); LD-MS obsd 540.2; ESI-MS obsd 541.2589, calcd 541.252598 [(M + H)$^+$, M = $C_{35}H_{32}N_4O_2$]; λ_{abs} (toluene) 439, 654 nm.

7-Formyl-10-mesityl-18,18-dimethyl-13^1-oxophorbine (FbOP-F^{7}M^{10}). Following a procedure for formylation with CO,[47] a mixture of **FbOP-Br^{7}M^{10}** (10.0 mg, 0.0173 mmol) and $Pd(PPh_3)_4$ (20.0 mg, 0.0173 mmol) was dried in a Schlenk flask for 30 min. DMF/toluene [1.0 mL (1:1)] was added, and CO was bubbled slowly through the reaction mixture at 70 °C. After 3 h, the reaction mixture was allowed to cool to room temperature, treated with Bu_3SnH, and stirred for 15 min. The reaction mixture was filtered through a short Celite column. The filtrate was concentrated. The resulting solid was chromatographed (silica, CH_2Cl_2) to afford a purple solid (7.1 mg, 78%): ^1H NMR δ −1.13 (brs, 1H), 1.24 (brs, 1H), 1.88 (s, 6H), 2.01 (s, 6H), 2.59 (s, 3H), 4.24 (s, 2H), 5.07 (s, 2H), 7.24 (s, 2H), 8.55 (s, 1H), 8.58 (s, 1H), 8.78 (dd, J = 2.0, 4.4 Hz, 1H), 8.93 (s, 1H), 9.10 (dd, J = 2.0, 4.4 Hz, 1H), 10.33 (s, 1H), 10.90 (s, 1H); LD-MS obsd 526.9; ESI-MS obsd 527.2435, calcd 527.2441 [(M + H)$^+$, M = $C_{34}H_{30}N_4O_2$]; λ_{abs} (toluene) 442, 652 nm.

10-Mesityl-18,18-dimethyl-13^1-oxo-7-[2-(triisopropylsilyl)ethynyl]phorbine (FbOP-E^{7}M^{10}). Samples of **FbOP-Br^{7}M^{10}** (10.7 mg, 0.0185 mmol) and (triisopropylsilyl)acetylene (12.5 μL, 0.0555 mmol) were coupled using $Pd_2(dba)_3$ (3.4 mg, 0.0037 mmol) and $P(o\text{-tol})_3$ (7.5 mg, 0.024 mmol) in toluene/triethylamine (5:1, 12 mL) at 60 °C under argon. After 24 h, the reaction mixture was concentrated under reduced pressure. The resulting residue was dissolved in a minimum amount of CH_2Cl_2 and chromatographed [silica, hexanes/CH_2Cl_2 (1:4)] to afford a greenish blue solid (8.4 mg, 67%): ^1H NMR δ −1.33 (brs, 1H), 1.14 (brs, 1H), 1.30−1.36 (m, 21H), 1.87 (s, 6H), 2.02 (s, 6H), 2.57 (s, 3H), 4.26 (s, 2H), 5.10 (s, 2H), 7.21 (s, 2H), 8.45 (s, 1H), 8.53 (s, 1H), 8.58 (s, 1H), 8.81 (d, J = 4.4 Hz, 1H), 9.00 (d, J = 4.4 Hz, 1H), 9.68 (s, 1H); LD-MS obsd 679.0; ESI-MS obsd 679.3823, calcd 679.3826 [(M + H)$^+$, M = $C_{44}H_{50}N_4OSi$]; λ_{abs} (toluene) 434, 660 nm.

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Supporting Information Available: Table of bromination results; synthesis of **ZnC-M^{10}Br^{13}** and **FbC-M^{10}A^{13}**; additional spectral data; characterization data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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