Dodecasubstituted metallochlorins (metallodihydroporphyrins)

Kalyn M. Shea, Laurent Jaquinod, Richard G. Khoury and Kevin M. Smith*†

Department of Chemistry, University of California, Davis, CA 95616, USA

Regioselective bromination of 2-nitro-5,10,15,20-tetraphenylporphyrin, cyclopropa[b]chlorins, or *trans*-bis-(dicyanomethyl)chlorins occurs in the pyrrole subunit opposite the substituted ring; exhaustive bromination of functionalized tetraphenylchlorins provides a route to dodecasubstitued dihydroporphyrins for the first time.

The existence of nonplanar hydroporphyrins in photosynthetic chromophores is increasingly evident in X-ray structures of protein complexes.¹ A series of synthetic nonplanar porphyrin models, obtained by steric crowding of β - and *meso*-positions, has established that such conformational variations can have significant effects on the physical and chemical properties of nonplanar porphyrins.^{2,3} Results show that the excited state properties of some of these chromophores are exquisitely sensitive to structural and vibrational variations.⁴ The synthesis of such model systems often requires the relatively inaccessible 3,4-disubstituted pyrrole for condensation with aldehydes.⁵ Nonplanar \beta-brominated porphyrins, on the other hand, are easily accessed via controlled bromination of porphyrins⁶ or metalloporphyrins,7 and have since provided intermediates for a range of nonplanar β -arylporphyrin syntheses.⁸ Extension of these synthetic efforts to hydroporphyrin systems will allow facile entry into highly nonplanar dihydroporphyrins (chlorins) and thus provide a means to more effectively test the theoretical predictions⁹ of the consequences of nonplanar distortions in this biologically important class of compounds.

2-Nitro-5,10,15,20-tetraphenylporphyrins have been shown to undergo nucleophilic attack at the β - β' bond bearing the nitro group leading to a range of β -substituted porphyrins,¹⁰ and more recently, work completed in our laboratory has provided new methodology for the preparation of a wide range of highly substituted dihydroporphyrin systems by way of nucleophilic attack of 2-nitro-5,10,15,20-tetraphenylporphyrin **1** (2-nitroTPP), with 'active' methylene compounds.¹¹ It has also been shown that regiospecific functionalization of pyrrolic positions on the porphyrin periphery occurs *via* fixation of the delocalization pathway.¹²

Here we show that either a nitro group or a reduced pyrrole substituents directs the bromination to the antipodal pyrrolic ring, leading to 12,13-dibromoporphyrin products. We also demonstrate that, *via* hexabromination of metallated dihydroporphyrins, highly nonplanar dodecasubstitued dihydroporphyrins can be prepared for the first time.



Fig. 1 Regioselective reactivity in 2-nitroTPP

Treatment of 2-nitroTPP **1** (2 g scale) with 2.5 equiv. of NBS in refluxing CHCl₃ afforded 2-nitro-12,13-dibromoTPP **3** in good yield (82%). Reaction of **3** (100 mg scale) with malononitrile (10 equiv.) and K₂CO₃ in THF afforded the cyclopropyl derivative **7** in 65% yield. The ¹H NMR spectrum of **7** displayed a singlet at δ 5.08, characteristic of the reduced pyrrole protons, and two doublets at δ 8.43 and 8.71. Similar treatment of **3** at 60 °C led to a second chlorin compound, **6**, in 62% yield. This set of reactions reveals the bimodal reactivity of 2-nitroTPP: (i) nucleophilic attack at the double bond bearing the nitro group and (ii) electrophilic regiospecific attack at the antipodal double bond (Fig. 1). The molecular structure of compound **6** was further confirmed by X-ray crystallography [Fig. 2(*a*)].‡



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Fig. 2 Molecular structure of (a) 6 (below: from top; above: edge-on view) and (b) 11 (below: from top; above: edge-on view). Hydrogen atoms have been omitted for clarity.

A second route leading to dibromochlorin compounds involves initial formation of the chlorin chromophore.¹¹ In this case, the reduced pyrrole functionality induces a favored delocalization pathway, via thermodynamically more stable N(22)H-N(24)H tautomerism, allowing regiospecific bromination to take place. Treatment of 5 (200 mg scale) with 2.5 equiv. of NBS in CHCl₃ at 65 °C afforded 7 quantitatively. Dropwise addition of bromine (2.5 equiv. in CHCl₃) to 4 afforded the desired brominated product 6 in 91% yield. A characteristic 10 nm red shift of the Soret band was observed $(\lambda_{max} 408 \text{ to } 418 \text{ nm})$ as a result of this reaction. As expected, reaction of a Ni-chlorin 7 with 2.5 equiv. of bromine led to a mixture of brominated products.12

Reaction of the metal-free nitroporphyrin 1 with excess NBS (or chlorin 4, with excess bromine, 10 equiv.) afforded only dibrominated products 3 (or 6). In contrast, subjecting metallated 2-nitroTPP and metallated dihydroporphyrins to excessive bromination conditions produced the desired hexabrominated products. When Cu-nitroTPP 2 was allowed to react with 16 equiv. of NBS in refluxing 1,2-dichloroethane, hexabromo-2-nitroTPP 8 was produced in 70% yield.

Initial preparation of Ni^{II}-chlorins 9 and 10,¹¹ followed by excessive bromination, afforded the desired hexabromo-

Br

Ph

Br

R

Br

Β́r

Br

Br

NC

Βı

Br

Ph

11

Ph

Ph

12

CN

CN

Ph

B

CO₂Me

B

″CO₂Me

CN

10

NC

Ph

Ρh

Ph

9

CN

CN

CO₂Me

CO₂Me

CN

chlorins, providing the first route to dodecasubstituted dihydroporphyrins. Dropwise addition of bromine (10 equiv.) in CHCl₃ to 9 and 10 (100 mg scale) produced 11 and 12 in 88 and 84% yields, respectively. Hexabromination of 11 resulted in a 26 nm red shift of the Soret band (λ_{max} 414 to 440 nm) and a 56 nm shift for the Q band (λ_{max} 604 to 660 nm). The ¹H NMR spectrum of 11 displayed two doublets at δ 3.52 and 4.83, characteristic of the trans chlorin functionality, and no peaks in the aromatic β proton region. The molecular structure of compound 11 was further confirmed by X-ray crystallography (Fig. 2).[‡] The macrocycle exhibits a ruffled-type conformation with a mean deviation of 0.536 Å for the 24 core atoms from their least-squares plane, and is significantly more nonplanar than dibromochlorin 6 [Fig. 2(a)].

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Notes and References

† E-mail: kmsmith@ucdavis.edu

Crystal data for **6**: $C_{50}H_{30}Br_2N_8$ (CHCl₃·0.25MeOH), MW = 1030.0, monoclinic, a = 33.329(5), b = 10.193(3), c = 27.787(4) Å, $\beta = 103.28(3)^{\circ}$, V = 9187(3) Å³ (by least-square refinement on diffractometer angles for 40 centered reflections), $\lambda = 1.54178$ Å, space group C2/c, Z = 8, D_c = 1.489 g cm⁻³, F(000) = 4148. The single, purple parallelipiped crystal with cell dimensions $0.36 \times 0.04 \times 0.02$, $\mu = 4.215$ mm-1, was collected on a Siemens P4 rotating anode diffractometer, scan type $2\theta - \theta$, T = 130(2) K, $2\theta_{max} = 112^{\circ}$, 10227 data, 6074 unique $[R(int) = 0.079], 4030 > 2\sigma(I)$. The number of parameters was 529. Final R factors were wR (all data) = 0.2206 and R (obs. data) = 0.085; the maximum residual electron density was 0.883 e Å-3.

For 11: $C_{50}H_{24}Br_6N_8Ni \cdot 2(CHCl_3)$, MW = 1513.68, triclinic, a = 12.911(3), b = 13.085(3), c = 18.383(4) Å, $\alpha = 75.47(3)^{\circ}$, $\beta = 71.60(3)^\circ$, $\gamma = 65.27(3)^\circ$, V = 2651.03(1) Å³ (by least-squares refinement on diffractometer angles for 29 centered reflections), $\lambda = 0.71073$ Å, space group $P\overline{1}$, Z = 2, $D_c = 1.896$ g cm⁻³, F(000) = 1468. The single, purple parallelipiped crystal with cell dimensions $0.50 \times 0.30 \times 0.20$, $\mu = 5.236$ mm⁻¹, was collected on a Siemens R3m/V diffractometer, scan type ω , T = 130(2) K, $2\theta_{\text{max}} = 55^{\circ}$, 12887 data, 12269 unique [R(int) = 0.039], 9104 > $2\sigma(I)$. The number of parameters was 658. Final R factors were wR (all data) = 0.1939 and R (obs. data) = 0.067; the maximum residual electron density was 1.358 e Å⁻³. Both structures 6 and 11 were solved by direct methods and refined (based on F^2 using all independent data) by full-matrix least-squares methods (Siemens SHELXTL ver. 5.03). Hydrogen atom positions were located by their idealized geometry and refined using a riding model. An absorption correction was applied using XABS2 (ref. 13). CCDC 182/769.

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