Dodecasubstituted metallochlorins (metallodihydroporphyrins)

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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 β-brominated porphyrins, on the other hand, are easily accessed *via* controlled bromination of porphyrins[6] 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 predictions[9] 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.

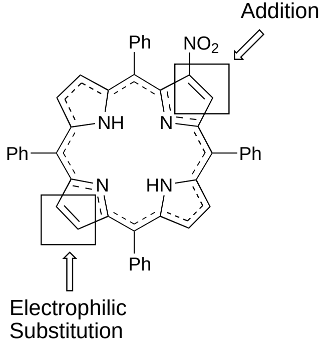
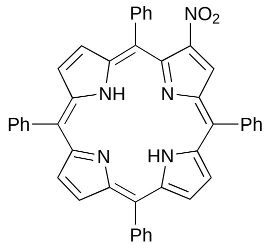


Fig. 1 Regioselective reactivity in 2-nitroTPP

Treatment of 2-nitroTPP **1** (2 g scale) with 2.5 equiv. of NBS in refluxing $CHCl_3$ afforded 2-nitro-12,13-dibromoTPP **3** in good yield (82%). Reaction of **3** (100 mg scale) with malononitrile (10 equiv.) and K_2CO_3 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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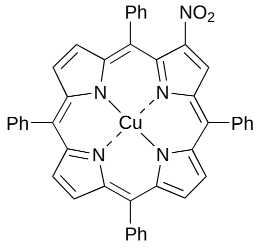

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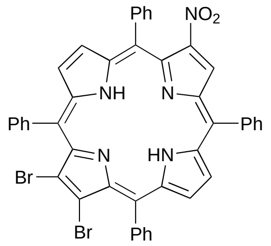

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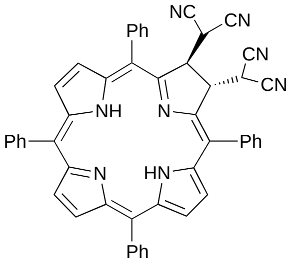

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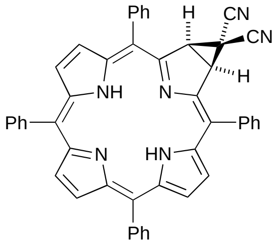

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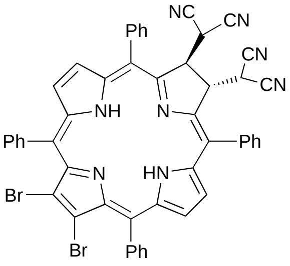

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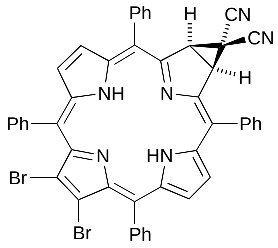

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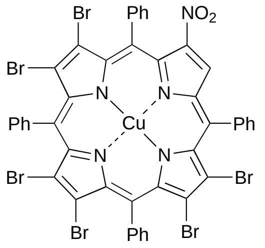

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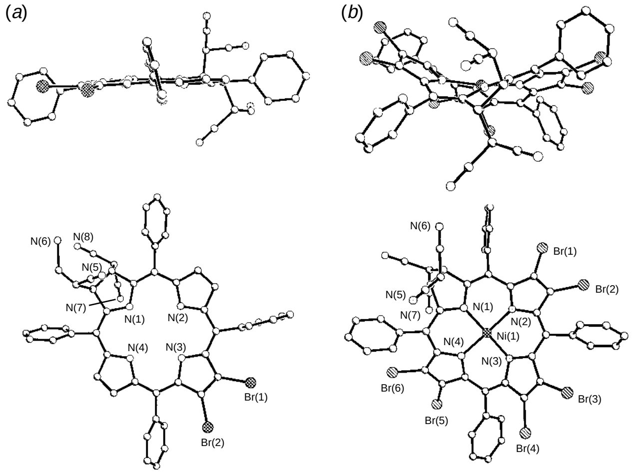
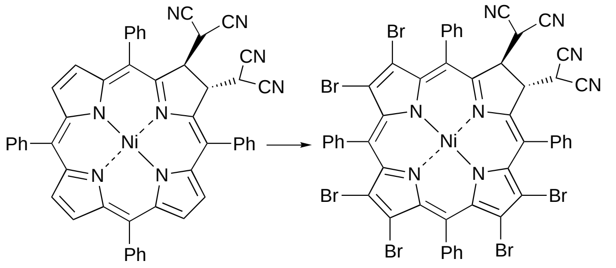


Fig. 2 Molecular structure of (*a*) **6** (below: from top; above: edge-on view) and (*b*) **11** (below: from top; above: edge-on view). Hydrogen atoms have been omitted for clarity.

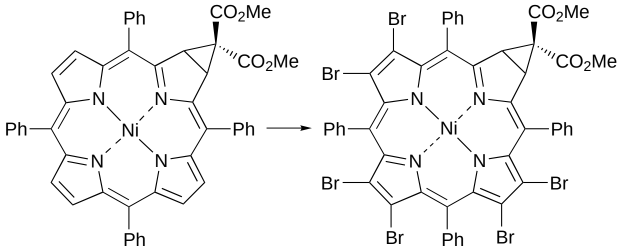
A second route leading to dibromochlorin compounds involves initial formation of the chlorin chromophore.[11] In this case, the reduced pyrrole functionality induces a favored delocalization pathway, *via* thermodynamically more stable N(22)H–N(24)H tautomerism, allowing regiospecific bromination to take place. Treatment of **5** (200 mg scale) with 2.5 equiv. of NBS in $CHCl_3$ at 65 °C afforded **7** quantitatively. Dropwise addition of bromine (2.5 equiv. in $CHCl_3$) to **4** afforded the desired brominated product **6** in 91% yield. A characteristic 10 nm red shift of the Soret band was observed (λ_{max} 408 to 418 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 hexabromochlorins, providing the first route to dodecasubstituted dihydroporphyrins. Dropwise addition of bromine (10 equiv.) in $CHCl_3$ 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*)].



9 **11**



10 **12**

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Notes and References

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‡ *Crystal data* for **6**: $C_{50}H_{30}Br_2N_8\cdot(CHCl_3\cdot0.25MeOH)$, MW = 1030.0, monoclinic, a = 33.329(5), b = 10.193(3), c = 27.787(4) Å, β = 103.28(3)°, V = 9187(3) Å^3 (by least-square refinement on diffractometer angles for 40 centered reflections), λ = 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 $0.36 \times 0.04 \times 0.02$, μ = 4.215 mm^{-1}, was collected on a Siemens P4 rotating anode diffractometer, scan type 2θ–θ, T = 130(2) K, $2\theta_{max}$ = 112°, 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**: $C_{50}H_{24}Br_6N_8Ni\cdot2(CHCl_3)$, MW = 1513.68, triclinic, a = 12.911(3), b = 13.085(3), c = 18.383(4) Å, α = 75.47(3)°, β = 71.60(3)°, γ = 65.27(3)°, V = 2651.03(1) Å^3 (by least-squares refinement on diffractometer angles for 29 centered reflections), λ = 0.71073 Å, space group $P\bar{1}$, Z = 2, D_c = 1.896 g cm^{-3}, $F(000)$ = 1468. The single, purple parallelipiped crystal with cell dimensions $0.50 \times 0.30 \times 0.20$, μ = 5.236 mm^{-1}, was collected on a Siemens R3m/V diffractometer, scan type ω, T = 130(2) K, $2\theta_{max}$ = 55°, 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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