Reductive per-N-alkylation of cyclo[8]pyrroles


I Synthetic Experimental

II X-ray Experimental

III Electrochemical and Spectroelectrochemical and ESR

I Synthetic Experimental

2,3,6,7,10,11,14,15,18,19,22,23,26,27,30,31-Hexadecaethyl-33,34,35,36,37,38,39,40-octamethyl-[32]octaphyrin(0.0.0.0.0.0.0.0) (3a)

Under an argon atmosphere, cyclo[8]pyrrole 1b (35 mg, 33 µmol) was dissolved in 20 ml of dry THF. Sodium hydride (60% suspension in mineral oil: 100 mg, 2.5 mmol) was added and the reaction mixtrue was stirred at room temp for 30 minutes. Iodomethane (methyl iodide, 0.31 ml, 4.9 mmol) was added and the solution heated at reflux for 12 hours. After allowing the solution to cool to room temperature, 10 ml of aqueous 1 M NaOH was added, along with 20 ml of CH2Cl2. After stirring this mixture for 20 more minutes, the phases were separated, and the aqueous phase extracted further with 10 ml of CH2Cl2. The combined organic phases were dried over anhydrous sodium sulfate and the solvent removed in vacuo. The residue was flushed through a short plug of silica gel, using CH2Cl2 as the eluent. Recrystallization from CH2Cl2/MeOH gave the product 3a in the form of yellowish-white needles (22.7 mg, 64%). 1H-NMR (400 MHz, CDCl3) δ [ppm] 1.03 (t, J=7.5Hz, 48H, CH2CH3), 2.48 (m, 32H, CH2CH3), 2.65 (s, 24H, NCH3); 13C-NMR (100 MHz, CDCl3) δ [ppm] 16.19, 18.46, 30.83, 122.82, 124.37; HRMS (CI): m/z 1080.8393 (HM+), calcd for C72H104N8 1080.8384.
2,3,6,7,10,11,14,15,18,19,22,23,26,27,30,31-Hexadecamethyl-33,34,35,36,37,38,39,40-octaethyl-[32]octaphyrin(0.0.0.0.0.0.0.0) (3b)

Under an argon atmosphere, cyclo[8]pyrrole 1a (42.1 mg, 50 µmol) was dissolved in 20 ml of dry THF. Sodium hydride (60% suspension in mineral oil; 130 mg, 3.25 mmol) was added and the reaction mixture was stirred at room temperature for 30 minutes. At this juncture, ethyl iodide (320 µL, 4 mmol) was added and the solution heated under reflux for 12 hours. The work up procedure used for 3a was followed, affording 3b as a white microcrystalline compound (34 mg, 70%). 1H-NMR (300 MHz, CDCl₃) δ [ppm] 0.61 (t, J_HH = 6.9 Hz, 24H, CH₂C₃H₃), 2.02 (s, 48H, NC₃H₃), 3.22 (q, J_HH = 6.9 Hz, 16H, CH₂CH₃); 13C-NMR (75 MHz, CDCl₃) δ [ppm] 10.06, 15.80, 39.49, 119.23, 122.79; HRMS (CI): m/z 969.7211 (HM⁺), calcd for C₆₄H₈₉N₈ 969.7210.

2,3,6,7,10,11,14,15,18,19,22,23,26,27,30,31-Hexadecamethyl-33,34,35,36,37,38,39,40-octabenzyl-[32]octaphyrin(0.0.0.0.0.0.0.0) (3c). Under an argon atmosphere, cyclo[8]pyrrole 1a (49.2 mg, 58.5 µmol) was dissolved in 20 ml of dry THF. Sodium hydride (60% suspension in mineral oil; 95 mg, 2.38 mmol) was added and it was stirred at room temperature for 30 minutes. At this juncture, benzyl bromide (335 µL, 2.8 mmol) was added and the solution heated under reflux for 12 hours. After a workup analogous to that used for 3a, compound 3c was isolated as an off white, slightly amber crystalline product (66 mg, 70%). 1H-NMR (300 MHz, CDCl₃) δ [ppm] 1.68 (s, 48H, CH₃), 5.09 (s, 16H, benzyl-CH₂), 6.34-6.37 (m, 16H, phenyl-H), 6.83-6.88 (m, 16H, phenyl-H), 6.94-6.99 (m, 8H, phenyl-H); 13C-NMR (75 MHz, CDCl₃) δ [ppm] 9.82, 48.91, 121.08, 123.96, 126.50, 126.67, 127.76, 138.17. HRMS (FAB); m/z 1464.8410 (M⁺), calcd for C₁₀₄H₁₀₄N₈ 1464.8384

II X-ray Experimental

3a

X-ray Experimental for C₇₂H₁₀₄N₈ - ½ (CH₂Cl₂): Crystals grew as pale yellow needles by slow evaporation from methylene chloride and methanol. The data crystal was cut from a cluster of crystals and had approximate dimensions; 0.60 x 0.18 x 0.12 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073 Å). A total of 418 frames of data were collected using ω-scans.
with a scan range of 0.8° and a counting time of 121 seconds per frame. The data were collected at 153 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table S1. Data reduction were performed using DENZO-SMN. The structure was solved by direct methods using SIR97 and refined by full-matrix least-squares on F^2 with anisotropic displacement parameters for the non-H atoms using SHELXL-97. The hydrogen atoms were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms).

A methyl carbon of an ethyl group was disordered about two orientations. The site occupancy factors for the affected atoms, C56 and C56a, were refined while refining a common isotropic displacement parameter for the two atoms. The site occupancy factor for C56 was assigned the variable x while that for C56a was set to (1-x). In this way, the site occupancy factor for C56 refined to 60(2)%. In addition to this disorder, a molecule of solvent was found to be disordered about a crystallographic inversion center at ½, ½, 0.

The solvent molecule appeared to be methylene chloride. The Cl⁻–Cl intramolecular contact was restrained to be 2.7Å, while the C-Cl bond length was restrained to be approximately equal. The site occupancy for the atoms were fixed at ½.

The function, Σw(|Fo|^2 - |Fc|^2)^2, was minimized, where w = 1/[(σ(Fo)^2 + (0.02*P)^2] and P = (|Fo|^2 + 2|Fc|^2)/3. R_w(F^2) refined to 0.193, with R(F) equal to 0.109 and a goodness of fit, S, = 1.50. Definitions used for calculating R(F), R_w(F^2) and the goodness of fit, S, are given below. The data were corrected for secondary extinction effects. The correction takes the form: Fcorr = kFc/[1 + (3.0(3)x10^-6)* Fc^2 λ^3/(sin2θ)]^{0.25} where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992). All figures were generated using SHELXTL/PC.
References


4) $R_w(F^2) = \left\{ \sum w(|F_0|^2 - |F_c|^2)^2/\sum w(|F_0|)^4 \right\}^{1/2}$ where $w$ is the weight given each reflection.

$R(F) = \sum (|F_0| - |F_c|)/\sum |F_0|$ for reflections with $F_0 > 4(\sigma(F_0))$.

$S = [\sum w(|F_0|^2 - |F_c|^2)^2/(n - p)]^{1/2}$, where $n$ is the number of reflections and $p$ is the number of refined parameters.


Table S1. Crystal data and structure refinement for 3a.

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<th>Value</th>
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<td>Formula weight</td>
<td>1124.09</td>
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<td>Temperature</td>
<td>153(2) K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71070 Å</td>
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<tr>
<td>Crystal system</td>
<td>Monoclinic</td>
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<td>Space group</td>
<td>P21/n</td>
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<td>Unit cell dimensions</td>
<td>a = 16.7530(5) Å, α = 90.000(2)°</td>
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<tr>
<td></td>
<td>b = 24.4090(6) Å, β = 112.488(2)°</td>
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<tr>
<td></td>
<td>c = 18.3380(9) Å, γ = 90.0000(11)°</td>
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<td>Volume</td>
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<td>Z</td>
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<td>Density (calculated)</td>
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<td>F(000)</td>
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<td>Crystal size</td>
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<td>Theta range for data collection</td>
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<td>Independent reflections</td>
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<td>Absorption correction</td>
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<td>Goodness-of-fit on F²</td>
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<td>Final R indices [I&gt;2σ(I)]</td>
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<td>R indices (all data)</td>
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<tr>
<td>Extinction coefficient</td>
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</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.564 and -0.498 e.Å³</td>
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Figure S1. View of 3a showing the atom labeling scheme. Displacement ellipsoids are scaled to the 50% probability level. The hydrogen atoms have been removed for clarity.
X-ray Experimental for C₆₄H₈₈N₈O₄: Crystals grew as beautiful, colorless prisms by vapor diffusion of dichloromethane into a methanol solution of the macrocycle. The data crystal was a multifaceted prism that had approximate dimensions; 0.33x0.30x0.20 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoKα radiation (λ = 0.71073Å). A total of 352 frames of data were collected using ω-scans with a scan range of 1° and a counting time of 87 seconds per frame. The data were collected at 153 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table S2. Data reduction were performed using DENZ0-SMN.¹ The structure was solved by direct methods using SIR92² and refined by full-matrix least-squares on F² with anisotropic displacement parameters for the non-H atoms using SHELXL-97.³ The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The macrocycle lies around a crystallographic two-fold rotation axis at 0, y, ¼. The asymmetric unit consists of ½ of the full molecule. The function, \( \Sigma w(|F_o|^2 - |F_c|^2)^2 \), was minimized, where \( w = 1/[(\sigma(F_o))^2 + (0.0534*P)^2 + (3.0956*P)] \) and P = \(|F_o|^2 + 2|F_c|^2)/3.\ R_w(F^2) refined to 0.146, with R(F) equal to 0.0560 and a goodness of fit, S, = 1.04. Definitions used for calculating R(F), R_w(F²) and the goodness of fit, S, are given below.⁴ The data were corrected for secondary extinction effects. The correction takes the form: \( F_{corr} = kF_c/[1 + (3.5(6)x10^{-6})* F_c^2 \lambda^3/(\sin2\theta)]^{0.25} \) where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).⁵ All figures were generated using SHELXTL/PC.⁶
References


4) \[ R_w(F^2) = \{ \sum w(|F_o|^2 - |F_c|^2)^2 / \sum w(|F_o|^4) \}^{1/2} \] where \( w \) is the weight given each reflection.
\[ R(F) = \sum (|F_o| - |F_c|) / \sum |F_o| \] for reflections with \( F_o > 4(\sigma(F_o)) \).
\[ S = [\sum w(|F_o|^2 - |F_c|^2)^2 / (n - p)]^{1/2} \], where \( n \) is the number of reflections and \( p \) is the number of refined parameters.


Table S2. Crystal data and structure refinement for 3b.

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<td>Temperature</td>
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<td>Wavelength</td>
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<td>Crystal system</td>
<td>Orthorhombic</td>
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<tr>
<td>Space group</td>
<td>Pbcn</td>
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<td>Unit cell dimensions</td>
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<tr>
<td>α</td>
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<td>b</td>
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</tr>
<tr>
<td>β</td>
<td>90°</td>
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<tr>
<td>c</td>
<td>17.2872(2) Å</td>
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<td>γ</td>
<td>90°</td>
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<td>Density (calculated)</td>
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<td>Absorption coefficient</td>
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<td>F(000)</td>
<td>2112</td>
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<td>Crystal size</td>
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<td>Theta range for data collection</td>
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<td>Index ranges</td>
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<td>Reflections collected</td>
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<td>7067 [R(int) = 0.0368]</td>
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<td>Absorption correction</td>
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<td>Refinement method</td>
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<td>Final R indices [I&gt;2σ(I)]</td>
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<td>R indices (all data)</td>
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<td>Largest diff. peak and hole</td>
<td>0.315 and -0.272 e.Å⁻³</td>
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Figure S2. Side view of 3b. Displacement ellipsoids are scaled to the 50% probability level.

3c

X-ray Experimental for C_{104}H_{104}N_{8} – CH_{2}Cl_{2} – \( \frac{1}{2} \) (C_{6}H_{14}): Crystals grew as small, faintly pink needles by vapor diffusion of n-hexane into a methylene chloride solution of the macrocycle. The data crystal was a long lathe that had approximate dimensions; 0.21x0.11x0.11 mm. The data were collected on a Nonius Kappa CCD diffractometer using a graphite monochromator with MoK\( \alpha \) radiation (\( \lambda = 0.71073\AA \)). A total of 305 frames of data were collected using \( \omega \)-scans with a scan range of 0.9° and a counting time of 461 seconds per frame. The data were collected at 153 K using an Oxford Cryostream low temperature device. Details of crystal data, data collection and structure refinement are listed in Table S3. Data reduction were performed using DENZO-SMN.\(^1\) The structure was solved by direct
methods using SIR92² and refined by full-matrix least-squares on F² with anisotropic displacement parameters for the non-H atoms using SHELXL-97.³ The hydrogen atoms on carbon were calculated in ideal positions with isotropic displacement parameters set to 1.2xUeq of the attached atom (1.5xUeq for methyl hydrogen atoms). The function, \( \Sigma w(|F_o|^2 - |F_c|^2)^2 \), was minimized, where \( w = 1/[(\sigma(F_o))^2 + (0.02*P)^2] \) and \( P = (|F_o|^2 + 2|F_c|^2)/3 \). \( R_w(F^2) \) refined to 0.153, with R(F) equal to 0.144 and a goodness of fit, S, = 1.82. Definitions used for calculating R(F),\( R_w(F^2) \) and the goodness of fit, S, are given below.⁴ The data were corrected for secondary extinction effects. The correction takes the form: \( F_{corr} = kF_c/[1 + (3.9(5)x10^{-7})* F_c^2 \lambda^3/(\sin^2 \theta)]^{0.25} \) where k is the overall scale factor. Neutral atom scattering factors and values used to calculate the linear absorption coefficient are from the International Tables for X-ray Crystallography (1992).⁵ All figures were generated using SHELXLTPC⁶

References


4) \[ R_w(F^2) = \left\{ \Sigma w(|F_o|^2 - |F_c|^2)^2/\Sigma w(|F_o|^4) \right\}^{1/2} \] where w is the weight given each reflection.
\[ R(F) = \Sigma(|F_o| - |F_c|)/|\Sigma F_o| \] for reflections with \( F_o > 4(\sigma(F_o)) \).
\[ S = [\Sigma w(|F_o|^2 - |F_c|^2)^2/(n - p)]^{1/2}, \] where n is the number of reflections and p is the number of refined parameters.


Table S3. Crystal data and structure refinement for 3c.

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<td>Reflections collected</td>
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<td>Independent reflections</td>
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<td>Largest diff. peak and hole</td>
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Figure S3. View of 3c showing the atom labeling scheme for the nitrogen atoms and the methyl and benzyl atoms. Displacement ellipsoids are scaled to the 30% probability level. The hydrogen atoms have been removed for clarity.

Figure S4. View of 3c showing the atom labeling scheme. The phenyl rings and the hydrogen atoms have been removed for clarity. Displacement ellipsoids are scaled to the 30% probability level.
III Electrochemistry, Spectroelectrochemistry and ESR Experimental.

Absolute dichloromethane (CH$_2$Cl$_2$) and pyridine were purchased from Aldrich Co. Tetra-$n$-butylammonium perchlorate (TBAP) was purchased from Sigma Chemical or Fluka Chemika Co., recrystallized from ethyl alcohol and dried under vacuum at 40 °C for at least one week prior to use.

Cyclic voltammetry was carried out using an EG&G Princeton Applied Research (PAR) 173 potentiostat/galvanostat. A homemade three-electrode cell was used for cyclic voltammetric measurements and consisted of a platinum button or glassy carbon working electrode, a platinum counter electrode and a homemade saturated calomel reference electrode (SCE). The SCE was separated from the bulk of the solution by a fritted glass bridge of low porosity which contained the solvent/supporting electrolyte mixture. Thin-layer UV-visible spectroelectrochemical experiments were performed with a home-built thin-layer cell which had a light transparent platinum net working electrode. Potentials were applied and monitored with an EG&G PAR Model 173 potentiostat. Time-resolved UV-visible spectra were recorded with a Hewlett-Packard Model 8453 diode array spectrophotometer. ESR spectra were recorded on an IBM ESR 300 spectrometer.
Figure S5. ESR spectra of 3a (a) after 15 min. bulk controlled potential two-electron oxidation at 0.70 V (b) after 45 min. bulk controlled potential oxidation at 0.70 V and (c) after the second one-electron oxidation at 1.10 V in CH$_2$Cl$_2$, 0.2 M TBAP at 293 K.

(a) $g = 2.004$  $\Delta H = 3.9$ (G)

(b) $g = 2.003$  $\Delta H = 5.0$ (G)

(c) $g = 2.007$  $\Delta H = 7.8$ (G)