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Synthesis and reactions of *meso*-(*p*-nitrophenyl)porphyrins

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Abstract—An improved methodology is reported for the regioselective nitration of the phenyl groups of *meso*-tetraphenylporphyrin **1**, using $NaNO_2$ and TFA. The degree of nitration is easily controlled by the equivalent amount of $NaNO_2$ used and the reaction time. The nitroporphyrins are reduced to the corresponding aminoporphyrins under standard $SnCl_2$/HCl conditions. Reaction of tri-aminoporphyrin **9** with 1-formyl-*o*-carborane followed by reduction using $NaBH_4$ gave a novel tri-carboranylporphyrin bearing amine linkages between the porphyrin and the carborane groups.

1. Introduction

Porphyrin-type compounds have been actively investigated as sensitizing drugs for application in cancer diagnosis and treatment using photodynamic therapy (PDT)[1] and also using boron neutron capture therapy (BNCT).[2] PDT and BNCT are binary therapies that involve activation of a tumor-localized sensitizer with light (in PDT) or low-energy neutrons (in BNCT). The main cytotoxic species generated in PDT is believed to be singlet oxygen, which causes effective photo-oxidative damage to tumor tissue.[3] On the other hand in BNCT, the high linear energy transfer particles $^4He^{2+}$ and $^7Li^{3+}$ are produced, which cause cell damage via ionization processes.[2,4] In the last decade, two porphyrin derivatives were approved by the Food and Drug Administration for the PDT treatment of various conditions and many other promising derivatives are currently being evaluated in preclinical and clinical studies.[5] From these investigations it is known that certain porphyrin derivatives have the ability to selectively localize in tumor tissues, possibly as a result of their affinity for carrier biomolecules and/or biological membranes.[6] In particular, positively-charged porphyrins, such as *meso*-tetra(methylpyridyl)- and tetra-(trimethylaminophenyl)-porphyrins, have been shown to strongly interact with the negatively charged groups of potential biological targets, such as certain proteins,[5] DNA[7] and RNA,[8] and to be effective photosensitizers for PDT.[5,9] It has been shown that the number and distribution of positive charge about the porphyrin macrocycle plays a very important role in photodynamic efficacy.[5] Amphiphilic porphyrin derivatives bearing one, two or three water-solubilizing groups, such as $-NMe_3^+$, have demonstrated increased photodynamic efficacy compared with more hydrophilic, symmetric macrocyles.[5,10,11] On the other hand, nitro-substituted aromatic compounds have been found to be effective electron-affinity radiosensitizers.[12] Therefore, nitro- and amino-substituted amphiphilic porphyrins are useful synthetic precursors to biologically active molecules. Furthermore, nitro and amino groups can be easily functionalized,[11,13,14] and conjugated with bioactive molecules, such as monoclonal antibodies,[15] oligomeric carboranyl phosphate diesters,[16] polymer backbones,[17] and cyclodextrins.[18]

Current synthetic routes to mono-, di- and tri-nitro functionalized *meso*-tetraphenylporphyrins involve total synthesis via a crossed Rothemund approach,[17] or by electrophilic nitration of the *p*-phenyl groups of *meso*-tetraphenylporphyrin (TPP, **1**).[19,20] In the first method co-condensation of pyrrole, benzaldehyde and nitrobenzaldehyde, results in low to moderate yields of the targeted porphyrins, which can be tedious to purify from the resulting reaction mixtures. Whereas this is the methodology of choice for the synthesis of *o*- and *m*-nitrophenylporphyrins, higher yields of *p*-nitrophenylporphyrins can be obtained by direct nitration of the *p*-positions of the *meso*-phenyl groups. Using fuming nitric acid Kruper et al.[19] obtained mono-nitroporphyrin **2** in moderate yields (46–56%) by direct nitration of TPP **1** in chloroform solution. Under these conditions further nitration of **2** gave up to 28% yield of the di-nitroporphyrins and about 20% of the tri-nitroporphyrin. Macrocyclic degradation products were also observed. Higher yields were reported by Meng et al.[20] using a combination of nitric acid and acetic or sulfuric acids (namely up to 74% yield for mono-nitroporphyrin **2**), and

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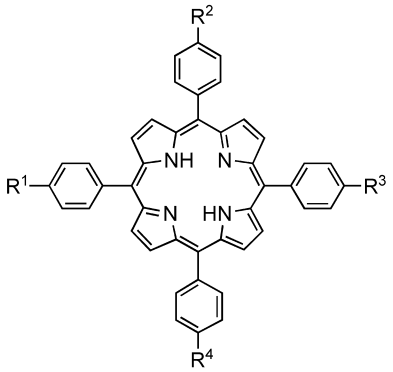
reaction times ranging from 1 h to 7 days. These somewhat milder reaction conditions produced better yields of the targeted nitroporphyrins; we rationalized that even milder conditions should lead to higher yields and regioselectivity of mono-, di- and tri-nitroporphyrins, with minimum macrocyclic degradation. These resulting nitroporphyrins can then be easily reduced to the corresponding aminoporphyrins and/or further derivatized.[19–21]



1: R^1, R^2, R^3, R^4 = H
2: R^1 = NO_2: R^2, R^3, R^4 = H
3: R^1, R^3 = NO_2; R^2, R^4 = H
4: R^1, R^2 = NO_2; R^3, R^4 = H
5: R^1, R^2, R^3 = NO_2; R^4 = H
6: R^1 = NH_2: R^2, R^3, R^4 = H
7: R^1, R^3 = NH_2; R^2, R^4 = H
8: R^1, R^2 = NH_2; R^3, R^4 = H
9: R^1, R^2, R^3 = NH_2; R^4 = H

2. Results and discussion

We have developed an alternative route to nitro-substituted porphyrins via regioselective *para*-phenyl nitration of TPP **1**, using sodium nitrite in TFA.[22,23] High yields of nitrated benzene and substituted benzenes have been reported under these conditions, and both NO_2^+ and N_2O_3 were proposed as the electrophiles in these reactions.[23] By varying the amount of sodium nitrite and the reaction time, selective nitration of one or more of the phenyl groups of TPP can be achieved, leading to the ready preparation of porphyrins **2**, **3**, **4** and **5** in high yields. Reduction of the nitro groups with excess tin(II) chloride gives the corresponding aminoporphyrins (**6**, **7**, **8** and **9**).

When a concentrated solution of TPP **1** in TFA was treated with 1.8 equiv. of $NaNO_2$ for 3 min, the mono-nitroporphyrin **2** was obtained as the major product in 80–90% yield. Increasing the amount of $NaNO_2$ to 8.1 equiv. resulted in the formation of a mixture of the two isomeric di-nitrophenylporphyrins **3** and **4** as the major products, after only 1.5 min. Thin layer chromatography (TLC) of the reaction mixture showed two spots of similar rf in the ratio of about 1:2, and trace amounts of a more polar fraction, the trinitroporphyrin **5**.

Based on statistics, the fastest running band was identified as the *opp*-isomer **3**, and the main second band as the *adj*-isomer **4**. After mono-nitration, there are two phenyl rings that can be nitrated to give the *adj*-isomer whereas there is only one that can be nitrated to produce the *opp*-isomer. To obtain the tri-nitrophenylporphyrin **5** as the major product a large excess of sodium nitrite was used and the reaction time was increased to 1 h. Longer reaction times resulted in the formation of the tetra-nitro derivative, which was identified by comparison with a sample of *meso*-tetra(4-nitrophenyl)-porphyrin obtained from the condensation of 4-nitrobenzaldehyde with pyrrole.

Due to the poor solubility of the nitro-substituted porphyrins, these were converted into the corresponding aminoporphyrins by reduction with tin(II) chloride and HCl in yields of about 50%, as previously reported in the literature.[19–21] The resulting aminoporphyrins **6**, **7**, **8** and **9** were easily separated by flash column chromatography on silica gel, using a gradient elution (dichloromethane/petroleum ether). The two di-aminoporphyrin regioisomers **7** and **8** were isolated in a 1:2 ratio and showed similar electronic and NMR spectra. However, there were characteristic differences in the shifts of the β-hydrogens in their ^{1}H NMR spectra and the resonances observed in the ^{13}C NMR, which allowed us to distinguish between the two regioisomers. The β-hydrogens of **8** appear as two singlets at 8.92 and 8.81 ppm, whereas those of **7** were two doublets with a coupling constant J=4.5 Hz, characteristic of β-H/β-H proton coupling of highly symmetrical di-substituted porphyrins. The larger number of signals in the ^{13}C NMR spectrum of the *adj*-isomer **8** further confirmed its lower symmetry compared with the *opp*-isomer **7**. The structures of mono-aminoporphyrin **6** and di-aminoporphyrins **7** and **8** were further confirmed by X-ray crystallography (Figs. 1–3). Figure 1 shows one of the three crystallographically independent, centrosymmetric porphyrin molecules for **6**. For this molecule, the porphyrin N atoms are symmetry-constrained to be coplanar, and the 24-atom porphyrin ring system is nearly so, exhibiting mean and maximum deviations of 0.042 and 0.081(3) Å, respectively. This porphyrin plane forms a dihedral angle of 82.3(1)° with the unsubstituted phenyl ring, and a smaller angle, 66.37(4)° with the phenyl ring carrying the NH_2 group. Figure 2 shows one of the three crystallographically independent, centrosymmetric porphyrin molecules for **7**. For this molecule, the 24-atom porphyrin ring system is slightly less coplanar than in **6**, exhibiting mean and maximum deviations of 0.081 and 0.168(2) Å, respectively. The phenyl rings are twisted out of the porphyrin plane by about 60°, forming dihedral angles of 58.22(6)° (phenyl) and 63.23(9)° (aminophenyl) with it. The structure of porphyrin **8** is shown in Figure 3. Its 24-atom porphyrin ring system is also nearly planar, exhibiting a mean deviation of 0.055 Å and a maximum of 0.131(7) Å, as a result of the internal hydrogen bonds, with N···N distances of 2.905(7)–2.954(7) Å. The phenyl rings are twisted out of the porphyrin plane by about 60° (torsion angle magnitudes 58.2(8)–77.0(8)°).

Aminoporphyrins **6**, **7**, **8** and **9** are readily converted into amphiphilic water-soluble molecules, for example by alkylation or by condensation with carboxylic acid-containing molecules.[13–18,24] We recently reported the condensation of porphyrin **6** with a dimeric carboranyl phosphate diester via an amide linkage, to give a negatively-charged conjugate, which is currently being evaluated in our

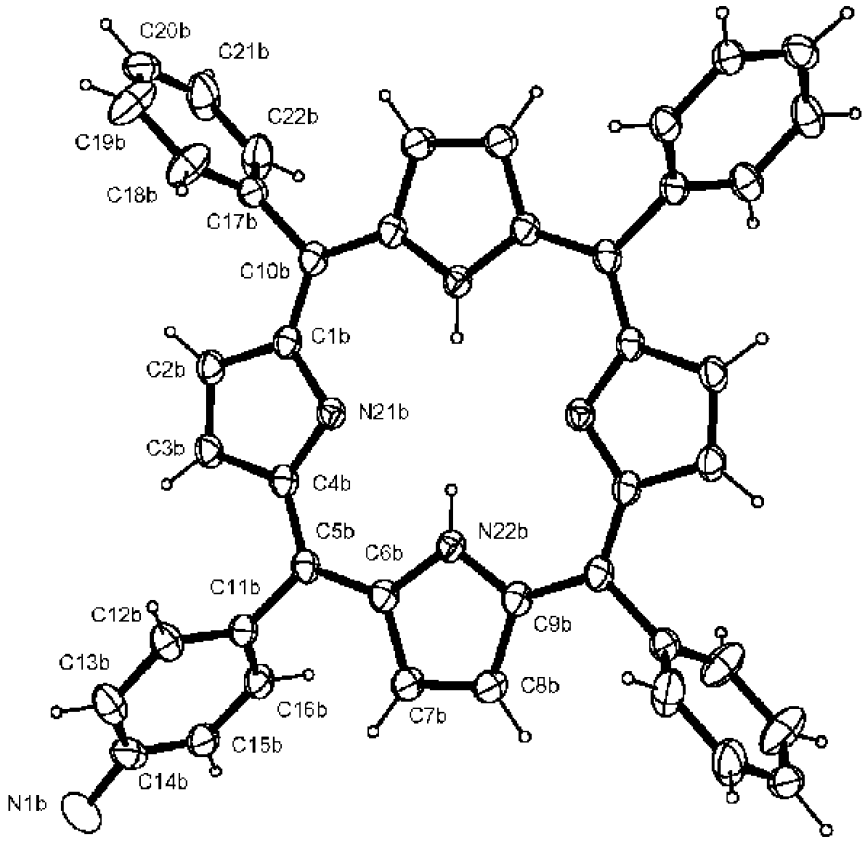


Figure 1. ORTEP diagram, showing the molecular structure of **6**. The molecule packs in the crystal such that there is 50% population of the amino group on the two diametrically opposed phenyl rings; only one form is shown.

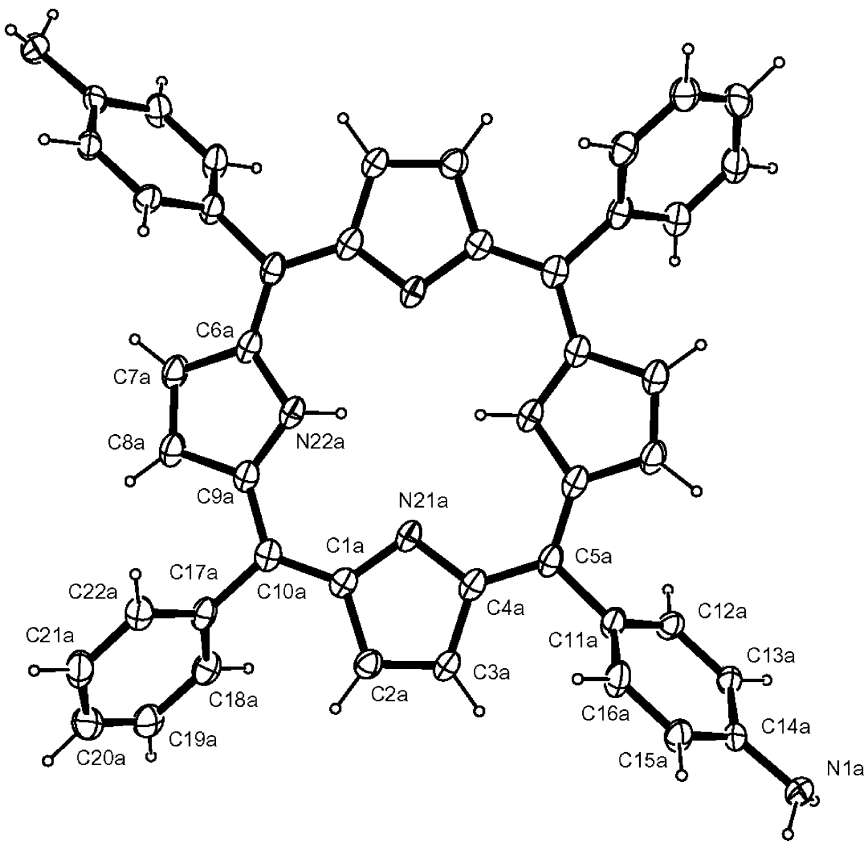


Figure 2. ORTEP diagram showing the molecular structure of **7**.

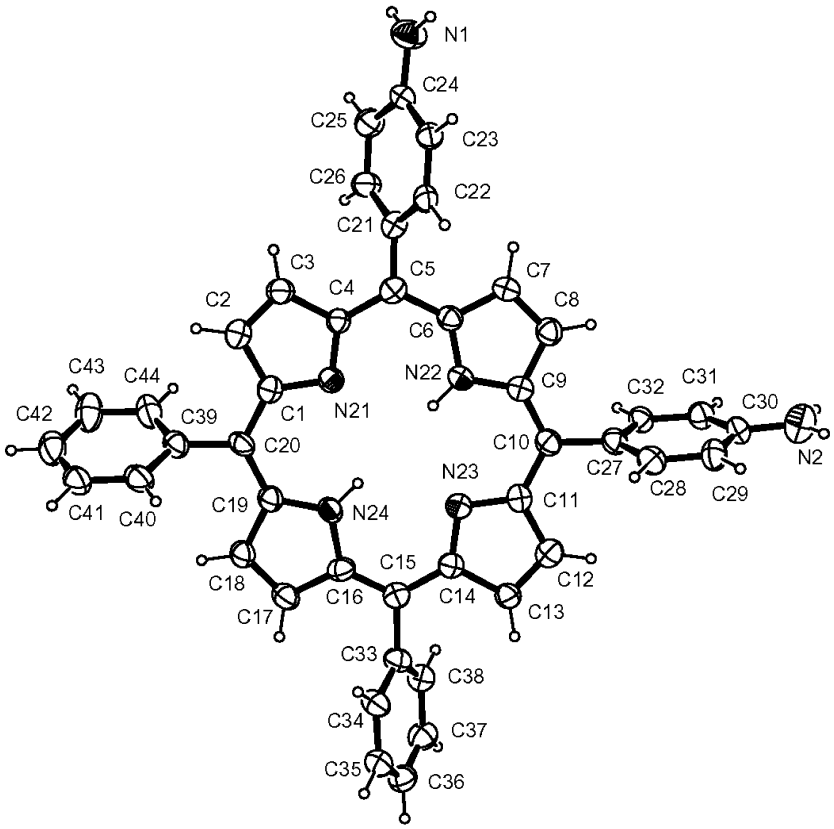


Figure 3. ORTEP diagram showing the molecular structure of **8**.

laboratories as a boron delivery agent for BNCT.[16] Alkylation of aminoporphyrins **7** and **8** with methyl iodide in the presence of a bulky base produced two positively charged porphyrins, DADP-o and DADP-a, with potential application in PDT.[11] Reductive amination[25] of 1-formyl-*o*-carborane using tri-aminoporphyrin **9**, leads to a tri-carboranylporphyrin with potential application in BNCT (Scheme 1).

Reaction of porphyrin **9** with 1-formyl-*o*-carborane **10**[26] produced the imineporphyrin **11**, which upon reduction with sodium borohydride afforded porphyrin **12** in 47% overall yield. In order to increase the solubility of this porphyrin in water, the *closo*-carboranyl cages were degraded to the corresponding *nido*-cages using a mixture of pyridine and piperidine (3:1) as reported previously,[27,28] to afford the negatively-charged water-soluble porphyrin **13**. The biological evaluation of porphyrin **13** is currently underway in our laboratories.

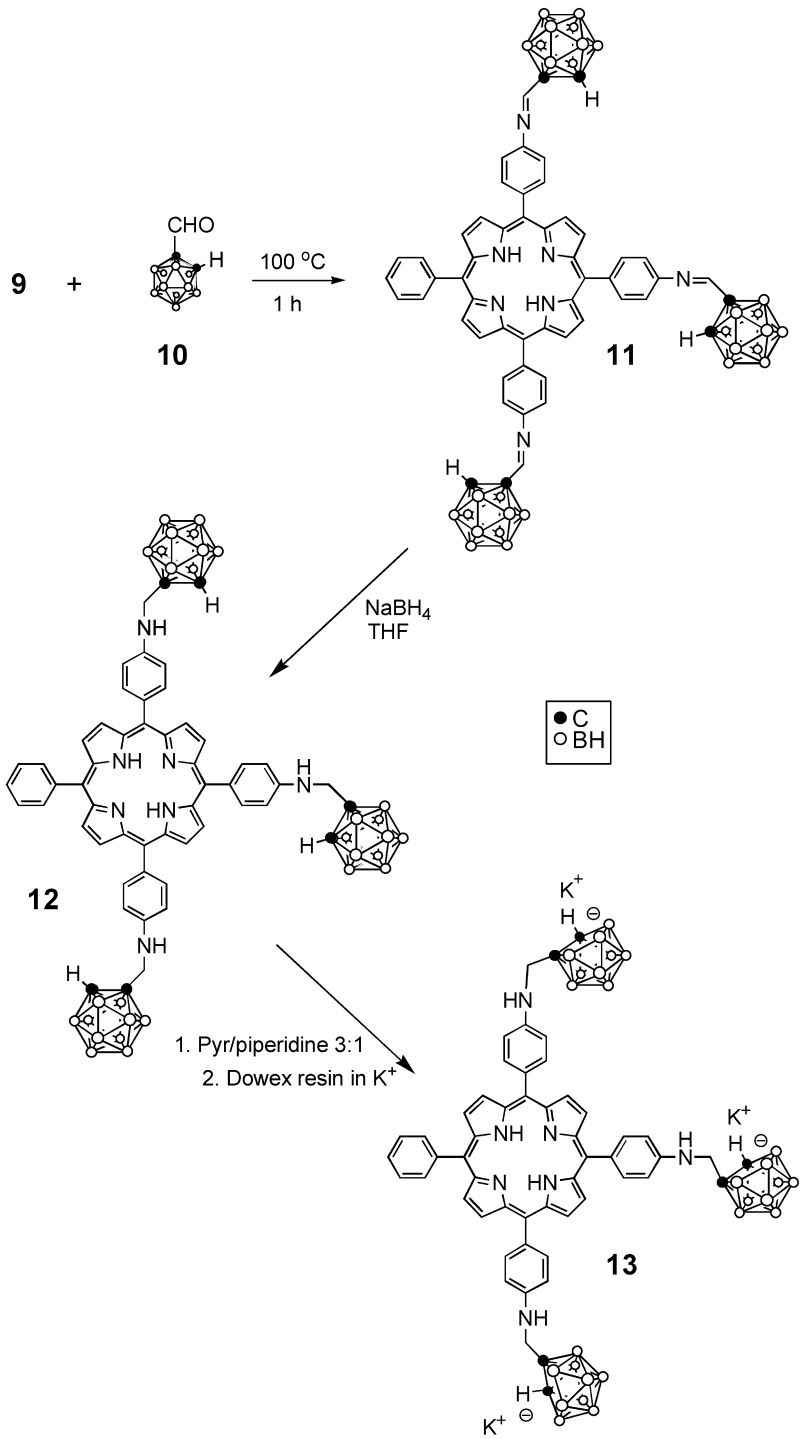
3. Conclusions

We have developed a mild method for electrophilic nitration of the phenyl groups of TPP, by using sodium nitrite in the presence of TFA. This approach is highly regiospecific allowing only nitration at the *para* position of the phenyl groups in TPP and provides selective control in the number of phenyl groups nitrated by varying the amount of sodium nitrite and the duration of the reaction. The nitroporphyrins are easily reduced to their corresponding aminoporphyrins, which are valuable intermediates in the synthesis of water-soluble, amphiphilic porphyrins for application as sensitizers in the PDT and/or the BNCT of cancers. As an example of their versatility, a tri-aminoporphyrin was condensed with 1-formyl-*o*-carborane to produce a tri-carboranyl-imineporphyrin, which was reduced to the corresponding amine and converted into a water-soluble tri-carboranylporphyrin, bearing amine linkages between the porphyrin and the carborane groups.

4. Experimental

4.1. General

Silica gel 60 (70–230 and 230–400 mesh, Merck) or neutral alumina (Merck; usually Brockmann Grade III) were used for column chromatography. Analytical thin layer chromatography (TLC) was performed using Merck 60 F254 silica gel (pre-coated sheets, 0.2 mm thick). Reactions were monitored by TLC and spectrophotometry. ^{1}H NMR spectra were obtained in deuterochloroform or acetone-d_6 solution, using a Brucker 250 or 400 MHz spectrometer; chemical shifts are expressed in ppm relative to chloroform (7.26 ppm) and/or TMS (0 ppm). Unless otherwise stated, electronic absorption spectra were measured in dichloromethane solution using a Hewlett–Packard 8450A spectrophotometer. Mass spectra were obtained at the Mass Spectrometry Facility at Louisiana State University, or at the University of California, San Francisco. Sodium nitrite, sodium borohydride, tin(II) chloride and trifluoroacetic acid (TFA) were purchased from Sigma-Aldrich and used without further purification. Anhydrous sodium sulfate,



Scheme 1. Syntheses of tri-carboranylporphyrins **11**–**13**.

sodium bicarbonate and all solvents were purchased from Fisher Scientific. Dried solvents were obtained according to literature procedures.[29]

4.1.1. 5,10,15-Tris(4-nitrophenyl)-20-phenylporphyrin (5). To a solution of **1** (160 mg, 0.261 mmol) in TFA (10 mL) was added sodium nitrite (660 mg, 9.57 mmol). After 55 min stirring at room temperature, the reaction was quenched with water (100 mL) and the mixture extracted with dichloromethane (6×25 mL). The organic layers were washed once with saturated aqueous $NaHCO_3$ and once with water before being dried over anhydrous Na_2SO_4. Recrystalization from dichloromethane gave 120 mg (62%) of porphyrin **5**. MS (MALDI) *m*/*z* 749.8 (M^+); ^1H NMR ($CDCl_3$) δ ppm: −2.80 (br, 2H), 7.80 (m, 3H), 8.20 (m, 2H), 8.40 (d, *J*=7.50 Hz, 6H), 8.65 (d, *J*=7.50 Hz, 6H), 8.80 (m, 6H), 8.93 (d, *J*=5.0 Hz, 2H). UV–Vis ($CHCl_3$) λ_{max}: 420 nm (ε 368,500), 514 (28,400), 549 (14,100), 589 (9800) and 645 (5600). Anal. Calcd for $C_{44}H_{27}N_7O_6 \cdot 1.5H_2O$: C, 68.03; H, 3.89; N, 12.66. Found: C, 67.82; H, 3.71; N, 12.75.

4.1.2. 5-(4-Aminophenyl)-10,15,20-triphenylporphyrin

(6). To a solution of **1** (100 mg, 0.163 mmol) in TFA (10 mL) was added sodium nitrite (20 mg, 0.29 mmol). After 3 min stirring at room temperature, the reaction mixture was poured into water (100 mL) and extracted with dichloromethane (6×25 mL). The organic layer was washed with saturated aqueous $NaHCO_3$ and water as described above and then the solvent was removed under vacuum. The residue was purified on a plug of silica gel, eluting with dichloromethane. After evaporation of the solvent, the residue was dissolved in concentrated hydrochloric acid (10 mL) and, while stirring, tin(II) chloride (220 mg, 0.975 mmol) was carefully added. The final mixture was heated to 65 °C for 1 h under argon before being poured into cold water (100 mL). The aqueous solution was neutralized with ammonium hydroxide until pH 8. The aqueous solution was extracted with dichloromethane until colorless. The organic layer was then concentrated under vacuum and the residue was purified on a plug of alumina using dichloromethane for elution. The final residue was recrystallized from methanol, yielding 55.3 mg (54%) of porphyrin **6**. The spectroscopic data obtained for the title compound are in agreement with those in the literature;[19] MS (MALDI) *m/z* 629.8 (M^+); ^{1}H NMR ($CDCl_3$) δ ppm: −2.75 (br, 2H), 4.02 (s, 2H), 7.07 (d, *J*=9.0 Hz, 2H), 7.75 (m, 9H), 7.98 (d, *J*=9.0 Hz, 2H), 8.20 (m, 6H), 8.84 (s, 6H), 8.96 (s, 2H). UV–Vis ($CHCl_3$) λ_{max}: 417.5 nm (ε 315,800), 514 (28,900), 551 (20,600), 589 (15,600) and 645.5 (12,800). Anal. Calcd for $C_{44}H_{31}N_5{\cdot}0.5H_20$: C, 82.79; H, 4.98; N, 10.98. Found: C, 82.55; H, 5.11; N, 10.95.

4.1.3. 5,15-Bis(4-aminophenyl)-10,20-diphenylporphyrin (7) and 5,10-bis(4-aminophenyl)-15,20-diphenylporphyrin (8). To a solution of TPP (200 mg, 0.326 mmol) in TFA (10 mL) was added sodium nitrite (183 mg, 2.65 mmol). After 90 seconds stirring at room temperature, the reaction was poured into water (100 mL) and extracted with dichloromethane (6×25 mL). The residue obtained was purified as described above and then reduced using 0.8 g (3.55 mmol) of tin(II) chloride and 50 mL of HCl. The two regioisomers were eluted with dichloromethane (the 5,10-isomer eluted first) and were recrystallized from methanol, yielding 52 mg (43%) of the 5,10-isomer and 13 mg (21%) of the 5,15-isomer. The spectroscopic data obtained for the title compounds are in agreement with those in the literature.[20] For the *opp*-isomer **7**: MS (MALDI) *m/z* 644.38 (M^+), MS (ESI) 645.77 (M^++1); ^{1}H NMR^{1}H NMR ($CDCl_3$) δ ppm: −2.74 (br, 2H), 4.04 (s, 4H), 7.06 (d, *J*=9.0 Hz, 4H), 7.74 (m, 6H), 7.99 (d, *J*=9.0 Hz, 4H), 8.21 (m, 4H), 8.81 (d, *J*=4.5 Hz, 4H), 8.92 (d, *J*=4.5 Hz, 4H). ^{13}C NMR ($CDCl_3$) δ ppm: 113.7, 122.5, 126.8, 127.8, 134.7, 135.8, 142.5, 146.1. UV–Vis ($CHCl_3$) λ_{max}: 420 nm (ε 278,000), 517 (13,500), 555 (9570), 591 (4300) and 649 (4600). Anal. Calcd for $C_{44}H_{32}N_6{\cdot}1.5H_2O$: C, 78.66; H, 5.25; N, 12.52. Found: C, 78.25; H, 5.00; N, 12.22. For the *adj*-isomer **8**: MS (MALDI) *m/z* 644.38 (M^+); ^{1}H NMR ($CDCl_3$) δ ppm: −2.74 (br, 2H), 4.03 (s, 4H), 7.06 (d, *J*=8.0 Hz, 4H), 7.76 (m, 6H), 7.99 (d, *J*=8.0 Hz, 4H), 8.21 (m, 4H), 8.81 (s, 4H), 8.92 (s, 4H). ^{13}C NMR ($CDCl_3$) δ ppm: 113.7, 120.5, 126.8, 127.8, 132.7, 134.7, 135.9, 142.5, 146.1. UV–Vis ($CHCl_3$) λ_{max}: 420 nm (ε 181,100), 517 (14,700), 554 (11,400), 590 (6000) and 647 (5200). Anal. Calcd for $C_{44}H_{32}N_6{\cdot}0.5H_2O$: C, 80.89; H, 5.02; N, 12.87. Found: C, 80.73; H, 5.14; N, 12.76.

4.1.4. 5,10,15-Tris(4-aminophenyl)-20-phenylporphyrin (9). *meso*-Tris(4-nitrophenyl)phenylporphyrin **5** (100 mg, 0.163 mmol) was dissolved in hydrochloric acid (40 mL) and, while stirring, tin(II) chloride (540 mg, 2.39 mmol) was carefully added. The final mixture was heated to 65 °C for 1 h under argon before being poured into cold water (100 mL). The aqueous solution was neutralized with ammonium hydroxide until pH 8. The aqueous solution was extracted with dichloromethane until colorless. The organic layer was then concentrated under vacuum and the residue purified on a plug of alumina using dichloromethane for elution. The final residue obtained was recrystallized from petroleum ether, yielding 47 mg (54%) of the title compound. MS (MALDI) *m/z* 658.5 (M^+); ^{1}H NMR ($CDCl_3$) δ ppm: −2.72 (br, 2H), 4.05 (s, 6H), 7.08 (d, *J*=7.82 Hz, 6H), 7.76 (m, 3H), 7.99 (d, *J*=7.82 Hz, 6H), 8.22 (m, 2H), 8.81 (d, *J*=4.69 Hz, 2H), 8.92 (m, 6H). UV–Vis ($CHCl_3$) λ_{max}: 423 nm (ε 256,000), 518 (10,400), 558 (9500), 593 (3600) and 652 (4480). Anal. Calcd for $C_{44}H_{33}N_7{\cdot}H_2O$: C, 78.07; H, 5.70; N, 14.49. Found: C, 78.12; H, 5.20; N, 14.26.

4.1.5. 5,10,15-Tris(4-carboranyliminophenyl)-20-phenylporphyrin (11). *meso*-Tris-(4-aminophenyl)phenylporphyrin **9** (50 mg, 0.076 mmol) and 1-formyl-*o*-carborane (180 mg, 1.05 mmol) were dissolved in THF (15 mL) at room temperature under argon. The mixture was heated at 100 °C for 1 h until all the porphyrin was consumed (TLC), and then poured into water and extracted with dichloromethane. The dichloromethane extract was dried over $NaSO_4$ anhydrous and then concentrated under vacuum. The residue was purified on alumina column using dichloromethane for elution. The final residue obtained was recrystallized from hexane, yielding 40 mg (48%) of the title product. HRMS (MALDI-QTOF) for $C_{53}H_{63}N_7B_{30}$+H: calculated *m/z* 1123.8230, found 1123.8210; ^{1}H NMR ($CDCl_3$) δ ppm: −2.80 (br, 2H), 1.6–3.0 (br, 30H), 4.70 (s, 3H), 7.49 (d, *J*=9.3 Hz, 6H), 7.77(m, 3H), 8.18 (m, 5H), 8.22 (d, *J*=9.3 Hz, 6H), 8.85(m, 8H). UV–Vis ($CHCl_3$) λ_{max}: 421 (364,000), 516 (17,700), 552 (10,800), 590 (6330) and 646 (5460).

4.1.6. 5,10,15-Tris[(4-carboranylaminomethyl)phenyl]-20-phenylporphyrin (12). To a solution of porphyrin **11** (40 mg, 0.036 mmol) in THF (10 mL) was added excess sodium borohydride (22 mg, 0.582 mmol) and the final mixture was stirred at room temperature for 1 h, under argon. Water was slowly added and the final mixture extracted with dichloromethane (4×20 mL). The dichloromethane extracts was dried over $NaSO_4$ anhydrous and evaporated to dryness. The residue was recrystallized from dichloromethane and methanol to give 39 mg (98%) of the title product. HRMS (MALDI-QTOF) for $C_{53}H_{69}N_7B_{30}$+H: calculated *m/z* 1129.8700, found 1129.8687; ^{1}H NMR ($CDCl_3$) δ ppm: −2.77 (br, 2H), 1.0–3.0 (br, 30H), 3.96 (s, 3H), 4.12 (d, *J*=7.4 Hz, 6H), 4.37 (t, 3H), 6.95 (d, *J*=8 Hz, 6H), 7.74 (m, 3H), 8.01(d, *J*=8 Hz, 6H), 8.19 (m, 2H), 8.82 (m, 8H). UV–Vis ($CHCl_3$) λ_{max}: 424 (ε 334,000), 519 (16,000), 558 (13,500), 592 (6140) and 651 (7040).

4.1.7. 5,10,15-Tris[(4-*nido*-carboranylaminomethyl)phenyl]-20-phenylporphyrin (13). Porphyrin **12** (20 mg,

0.018 mmol) was dissolved in pyridine/piperidine 3:1 (3 mL) and allowed to stir at room temperature for 36 h under argon. After removing the pyridine and piperidine under vacuum the residue was dissolved in 40% aqueous acetone and passed slowly through a Dowex 50WX2–100 resin in the potassium form. The porphyrin fraction was collected, dried under vacuum, redissolved in 70% aqueous acetone and again passed through the ion-exchange resin. After removal of the solvent under vacuum the title *nido*-carboranylporphyrin **13** was obtained in quantitative yield. HRMS (MALDI-QTOF) for $C_{53}H_{69}N_7B_{27}$; calculated *m/z* 365.2787; Found 365.2806. ^{1}H NMR (acetone-d_6) δ ppm: −2.40 (br, 5H), 1.6–3.0 (br, 27H), 3.50 (m, 6H), 5.10 (br, 3H), 7.07 (m, 6H), 7.79 (m, 3H), 7.96 (m, 6H), 8.22 (m, 3H), 8.76 (m, 2H), 8.99 (m, 6H). UV–Vis (ethanol) λ_{max}: 427 (ε 165,000), 520 (10,000), 567 (13,400) and 658 (6600).

4.2. Molecular structures

The crystal structures of solvates of **6**, **7** and **8** were determined, using data collected at T=100 K to =25.7° with Mo K radiation on a Nonius KappaCCD diffractometer. Compounds **6** and **7** were crystallized as the 2/3 dichloromethane solvates, and are essentially isostructural, both having three independent porphyrin molecules, all lying on inversion centers. Thus, for monoamino compound **6**, all three molecules have the NH_2 group disordered into two half-populated sites related by inversion. In **7**, two of the three independent molecules have ordered NH_2 groups, while third has its NH_2 groups disordered onto the alternate phenyl groups approximately 60% of the time. For **6**, R=0.091 for 7049 observed data of 9510 unique data. For **7**, R=0.065 for 6570 observed data of 9971 unique data. For **8**, the disordered solvent region was modeled as $0.6CH_2Cl_2$, $0.4H_2O$. R=0.106 for 3598 observed data of 5698 unique data. The X-ray crystallographic data for **6**, **7** and **8** can be found in supplementary publications CCDC-229546, CCDC-223888 and CCDC-220719 respectively, available from the Cambridge Crystallographic Data Centre.

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