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Total syntheses of three copper (II) tetracarboranylphenylporphyrins containing 40 or 80 boron atoms and their biological properties in EMT-6 tumor-bearing mice

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Abstract—Three carboranyltetraphenylporphyrins containing 40 or 80 boron atoms were synthesized and evaluated for their biodistribution and toxicity in EMT-6 tumor-bearing mice. Copper (II) *meso*-5,10,15,20-tetrakis[3-methoxy-4-(*o*-carboranylmethoxy)phenyl]porphyrin, **6**, and copper (II) *meso*-5,10,15,20-tetrakis[3-hydroxy-4-(*o*-carboranylmethoxy)phenyl]porphyrin, **8**, are B_{40} congeners with different lipophilicities, each less than their B_{80} congener, copper (II) *meso*-5,10,15,20-tetrakis[*m*-(3,5-di-*o*-carboranylmethoxybenzyloxy)phenyl]porphyrin, **18**. Two days after the last of a series of ip injections in BALB/c mice bearing EMT-6 mammary tumors, a dose of 185 mg/kg **6** (54 mg/kg B) delivered over 3.5 times the concentration of boron to tumor (169 μg/g B) than did 118 mg/kg **8** (36 mg/kg B), which delivered 35 μg/g B, or 87 mg/kg **18** (30 mg/kg B), which delivered 46 μg/g B. The tumor-to-blood and tumor-to-brain boron concentration ratios at that time for all three porphyrins exceeded 80:1. Two days after the last injection, there resulted moderate thrombocytopenia that essentially disappeared two days later from **6** and **18**, and mild leukocytosis from **6**, **8**, and **18**, all of which were clinically inconsequential. Thus, **6** may rank among the most clinically promising carboranyl porphyrins ever made to deliver ^{10}B to tumors for boron neutron-capture therapy (BNCT) that has also been tested for its toxicity in vivo.

1. Introduction

Boron neutron-capture therapy (BNCT) is an experimental binary radiotherapy[1,2] currently used for high-grade gliomas, brain metastases, melanomas, and head and neck cancers.[3,4] BNCT is based on the nuclear reaction, $^{10}B(n,\alpha)^{7}Li$, whereby ^{10}B captures low-energy neutrons and produces high linear-energy-transfer (LET) charged particles with short range in tissues (approximately one cell diameter, 5–10 μm). Even one such particle traversing any part of the nucleus of a normal or neoplastic stem cell may disable that cell's clonogenicity. Hence, effective preferential destruction of neoplastic cells in the presence of normal cells relies heavily on the tumor selectivity of the boron-containing drug within the irradiated target volume.

Currently, two boron agents are undergoing Phase I/II BNCT clinical trials for BNCT; sodium sulfhydryl boron hydride, $Na_2B_{12}H_{11}SH$(BSH),[5,6] and 4-boronophenylalanine (BPA).[7,8] However, BSH has only moderate selectivity for tumor cells and both BSH and BPA have low retention times in tumors. At least 15–30 μg/g ^{10}B is required for effective BNCT assuming homogeneous distribution of boron in cells.[9] Improved compounds should have higher selectivity (ideally, tumor-to-blood and tumor-to-normal tissues ratios > 5) and inconsequential toxicities.[9,10] During the past 15 years various candidate BNCT agents have been synthesized and tested, including boronated nucleosides, amino acids, peptides, phospholipids, liposomes, monoclonal antibodies, porphyrins, and more recently, nanotubes.[11–14] Among those, several boron-containing porphyrins appear to be particularly attractive on account of their high boron content, tumor selectivities, and long retention times in tumors.[15–18]

Many carboranylporphyrins have been reported, with both hematoporphyrin or *meso*-tetraphenylporphyrin structure and ester, amide, ether or carbon–carbon linkages to carborane clusters.[13,17,19] Porphyrins in the TCP class have shown promising biodistribution and toxicological properties at BNCT-relevant doses; CuTCPH, in particular, has enabled ablation of some murine leg tumors in vivo.[15] Although the low toxicity and high

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selectivity of CuTCPH and its analogs in the irradiated target volume make them worthwhile candidates for BNCT, the high lipophilicity of CuTCPH necessitated large amounts of excipient for its parenteral administration into animals. In our endeavor to improve CuTCPH we sought two avenues: one was to construct a porphyrin that is somewhat more polar than CuTCPH but not water-soluble and the other was to increase the percentage of boron in the porphyrin. To increase polarity, a porphyrin bearing hydroxyl moieties directly attached to the phenyl group bearing the *o*-carborane cage was synthesized via the methoxy derivative. Syntheses of porphyrins that contain eight rather than two or four carborane cages have been described previously, but to our knowledge, their properties in vivo have not yet been reported.[20,21] Herein we report the total synthesis of copper (II) *meso*-5,10,15,20-tetrakis[3-methoxy-4-(*o*-carboranylmethoxy)phenyl]porphyrin, **6**, copper (II) *meso*-5,10,15,20-tetrakis[3-hydroxy-4-(*o*-carboranylmethoxy)phenyl]porphyrin, **8**, and copper (II) *meso*-5,10,15,20-tetrakis[*m*-(3,5-di-*o*-carboranylmethoxybenzyloxy)phenyl]porphyrin, **18**. Some biodistribution and toxicological properties of **6**, **8**, and **18** in EMT-6 tumor-bearing mice are also presented.

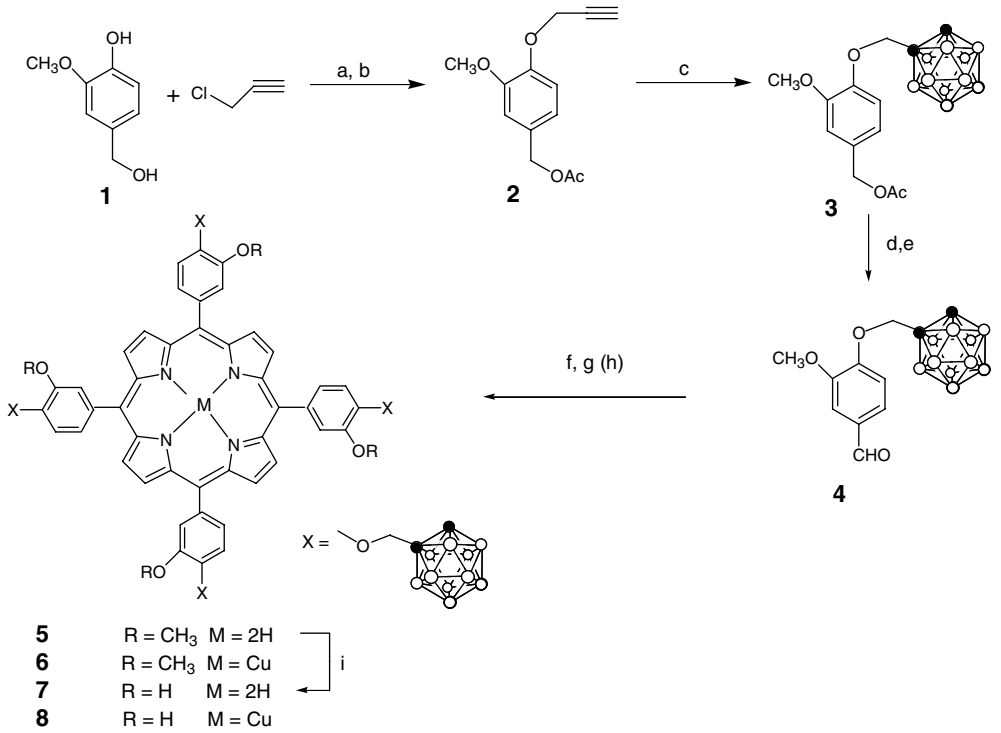
2. Results

2.1. Porphyrin syntheses

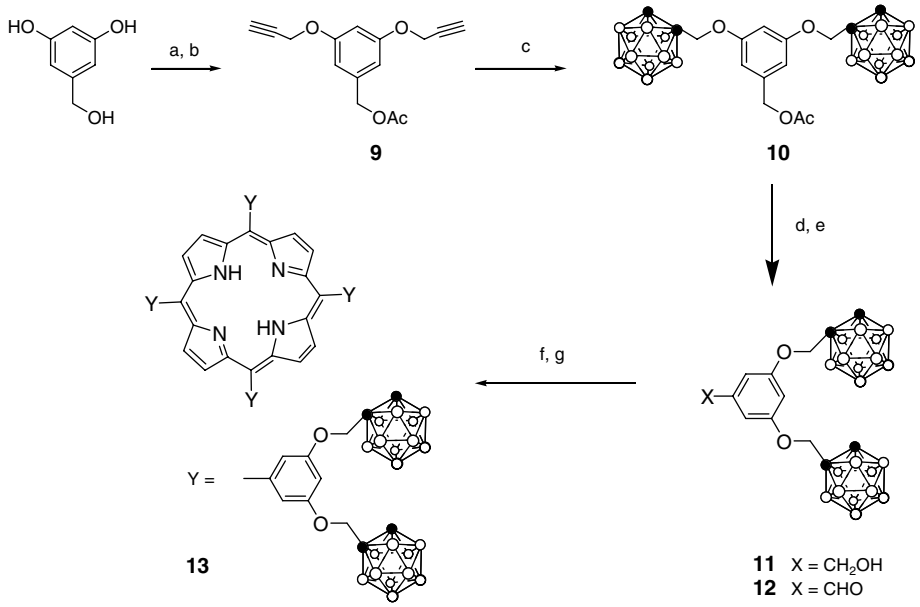
Because a free hydroxyl group will react with decaborane and because of potential solubility difficulties of the intermediates, the methoxyporphyrin **5** was targeted as the direct precursor to hydroxyporphyrin **7**. The synthetic route used to synthesize porphyrin, **5**, shown in Scheme 1, is similar to that used to synthesize CuTCPH,[22] but required 4-hydroxy-3-methoxybenzyl alcohol, **1** as the starting material instead of 3-hydroxybenzyl alcohol used for CuTCPH. All the reactions were straightforward except the alcohol oxidation to form aldehyde **4**. The reaction was often sluggish and required a stronger oxidizing agent than pyridinium chlorochromate (PCC), such as di-chlorodicyanobenzoquinone (DDQ).[23] The methoxy groups were O-demethylated to form hydroxyporphyrin **7** using BBr_3.[24] Both copper porphyrins **6** and **8** were then evaluated in tumor-bearing mice.

Scheme 2 outlines the original plan for producing octacarboranylporphyrin **13**. Although the route to the aldehyde **12** was fairly straightforward, the cyclization with pyrrole gave a complex mixture yielding only very small amounts of porphyrin **13**.

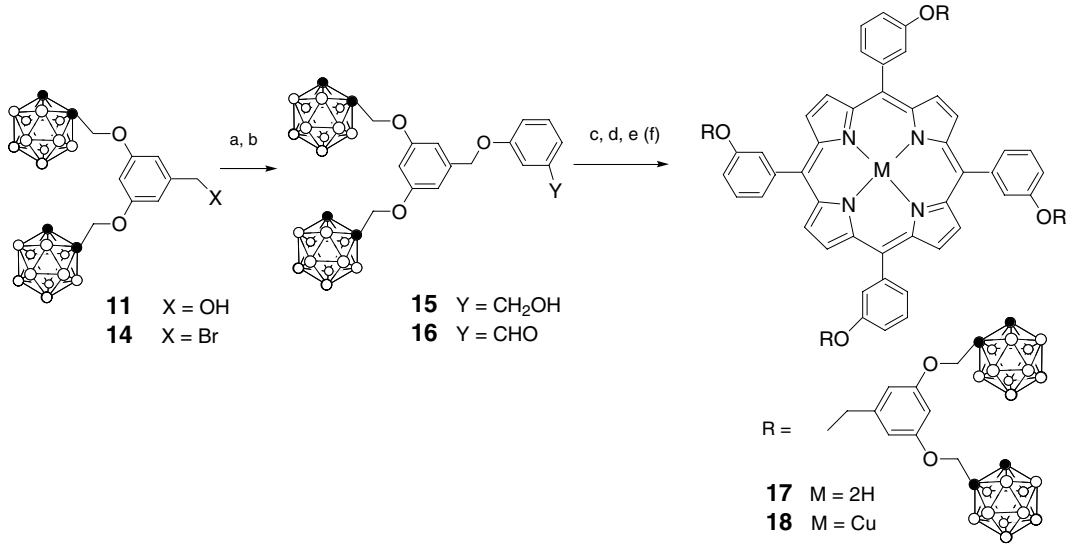
Since more sterically hindered porphyrins have been synthesized using the Lindsey cyclization method, the low yield of **13** is probably due to electronic effects. An alternative method for forming an octacarboranylporphyrin is outlined in Scheme 3. In this route, the dicarboranylphenyl group is further removed from the porphyrin macrocycle by a benzylether linkage. The dicarboranylbenzyl alcohol **11**, used in Scheme 2, was brominated in 92% yield (shown in Scheme 3) using CBr_4 with triphenylphosphine[25] and then coupled to 3-hydroxybenzyl alcohol in the presence of base to form **15** in 96% yield. After PCC oxidation, the resulting aldehyde **16** was treated with pyrrole under Lindsey condi-



Scheme 1. (a) K_2CO_3, KI, acetone, reflux 2d (94%); (b) AcCl, pyridine, 5 h (85%); (c) decaborane/CH_3CN/toluene 3 h prior to addition of **2**, after **2** added, 80–90 °C 3d (80%); (d) HCl/MeOH reflux 3 h, 98%; (e) PCC, CH_2Cl_2, 2 h (94%); (f) pyrrole, TFA, CH_2Cl_2; (g) DDQ, reflux 1 h (31%); (h) $Cu(OAc)_2$, MeOH, CH_2Cl_2 (98%). (i) BBr_3, CH_2Cl_2, 25 °C, 30 min.



Scheme 2. (a) Propargyl chloride, K_2CO_3, KI, acetone, reflux for 24 h (97%); (b) Ac_2O, H_2SO_4, 95 °C for 3 h (96%); (c) decaborane, CH_3CN, in toluene, 25 °C for 3 h; followed by **10**, 90 °C for 48 h (81%); (d) HCl, MeOH, reflux for 2 h (93%); (e) PCC, CH_2Cl_2, 2 h; (b, f) pyrrole, BF_3 ·etherate, CH_2Cl_2, 25 °C for 2 h; (g) DDQ, reflux, 1 h.



Scheme 3. (a) CBr_4, Ph_3P, THF, 25 °C, 30 min (92%); (b) m-hydroxybenzyl alcohol, K_2CO_3, KI, acetone, reflux for 24 h (96%); (c) PCC, CH_2Cl_2, 25 °C, 3 h; (99%); (d) pyrrole, BF_3 ·ether, CH_2Cl_2, 25 °C for 1 h; (e) DDQ, reflux, 1 h (22%); (f) $Cu(OAc)_2 \cdot H_2O$, MeOH/CH_2Cl_2, 25 °C for 20 min (92%).

tions[26] to form porphyrin **17** in 22% yield and copper was inserted to form **18** in 92% yield. As with porphyrin **13**, porphyrins **17** and **18** also bear eight carborane groups but were isolated in good yield. The percentage of boron by weight of **17** and **18** are 36% and 35%, respectively.

In order to determine relative polarities of the porphyrins, they were analyzed by reverse-phase HPLC using an acetonitrile/methanol gradient. Based on retention times, the order of decreasing polarities (increasing retention times) was: **8** (13.4 min), CuTCPH (37.3 min), **6** (40.1 min), and **18** (>120 min).

2.2. Biodistribution study

For in vivo studies, the porphyrins were first solubilized in a 9% Cremophor EL/18% propylene glycol/saline emulsion.[27,28]

The biodistribution data from mice given either porphyrin **6**, **8**, **18**, or the reference porphyrin CuTCPH, are shown in Table 1. Because the doses of boron delivered as **6**, **8**, and **18** were not identical (Table 1), the tumor boron concentrations were arithmetically normalized to the dose of boron delivered as CuTCPH, 58 μg/g in Figure 1. As with other lipophilic tetraphenylporphy-

Table 1. Median boron concentrations (and range) in various tissues of mice given porphyrins **6**, **8**, **18**, or CuTCPH by serial ip injections at 2 or 4 days after the last injection

Porphyrin	Time after last injection (days)	No. of mice	Porphyrin dose (B dose) (mg/kg)	EMT-6 tumor (μg/g B)	Blood (μg/g B)	Brain (μg/g B)	Liver (μg/g B)
6	2	5	185 (54)	169 (137–200)	0.4 (0.2–2.8)	0.1 (0.1–0.3)	537 (443–839)
8	2	5	118 (36)	35.3 (28.8–42.2)	0.3 (0.2–0.5)	0.3 (0.1–0.6)	475 (445–559)
18	2	5	87 (30)	46.4 (30.4–53.1)	0.5 (0.2–0.7)	0.2 (0.1–0.2)	353 (284–429)
CuTCPH[16]	2	7	190 (58)	59.5 (49.8–89.0)	0.0 (0–0)	0.1 (0–0.4)	550 (492–707)
6	4	5	185 (54)	142 (133–257)	0.1 (0.1–0.2)	0.0 (0–0.2)	414 (388–515)
8	4	5	118 (36)	22.2 (20.4–36.8)	0.2 (0–0.3)	0.0 (0–0.1)	448 (366–516)
18	4	5	87 (30)	26.4 (21.6–40.5)	0.2 (0.1–0.2)	0.3 (0.2–0.4)	230 (189–370)
CuTCPH[16]	4	7	190 (58)	68.3 (43.6–111)	0.3 (0.2–0.4)	0.7 (0.3–1.0)	492 (439–801)

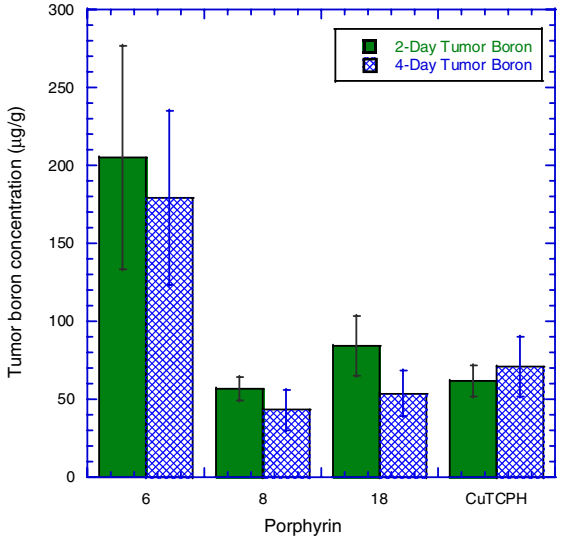


Figure 1. Tumor boron concentrations from porphyrins **6**, **8**, **18**, and CuTCPH (from Table 1) arithmetically normalized to a mean boron dose of 58 mg/g at either 2 or 4 days after the last injection.

rins, the boron in blood and in brain was negligible by 2 days after the last injection of any of the four porphyrins yielding very high tumor-to-blood and tumor-to-brain boron ratios. Although the differences in boron from blood and brain between the porphyrins were negligible, the differences in normalized liver boron concentrations were significant. Porphyrin **8** delivered the highest normalized concentration to liver by ~40% (vs the lowest from CuTCPH) at 2 days and by ~50% (vs the lowest from **6**) at 4 days. Figure 1 shows that the normalized boron concentrations in the EMT-6 carcinoma from **6** are more than three times greater than those from **8**. The resulting % injected dose per gram tumor tissue of ~19% from **6** is the highest ever observed in the EMT-6 carcinoma in our laboratory. In general water-soluble porphyrins appear to show lower liver and higher kidney uptake than their lipophilic counterparts, most likely due to greater excretion through the kidneys. It is hypothesized that the more polar a porphyrin, the less affinity for the liver, however, the more polar **8** appears to effect 47% higher average boron concentrations in liver than **6** when porphyrin doses were normalized. In any event, the microlocalization properties of porphyrin **8** are likely to be somewhat different from those of porphyrin **6**.

Unlike porphyrins **6**, **8**, and CuTCPH, **18** was administered to tumor-bearing mice by a series of three ip injections over 8 h rather than six ip injections over 32 h, totaling a lower dose of 30 mg/kg boron. No visible abnormalities were noted either physically or behaviorally in mice during and after administration of any of the porphyrins. At necropsy, all tissues appeared normal. Table 2 shows the weight changes and hematologic parameters in BALB/c mice given porphyrins **6**, **8**, **18**, or solvent only. Two days after the last injection, weight losses in mice from **6** were slightly greater than those from the other porphyrins but two days later, those weight losses were no different from solvent-only controls. The significant transient weight loss from porphyrin **6** is likely due to the higher dose of **6** relative to **8**

Table 2. Weight changes and hematologic parameters in mice given porphyrins **6**, **8**, **18** or solvent only at 2 or 4 days after the last injection

Porphyrin	Porphyrin dose (mg/kg)	Time after last injection (days)	No. of mice	% weight change	Platelets (10^3/mm^3)	Leukocytes (10^3/mm^3)
Solvent only	—	2	4	−1.3 (−4.5–1.1)	640 (568–730)	4.86 (2.52–5.62)
6	185	2	5	−4.7 (−9.3–0.9)***	181 (105–248)*	10.81 (9.41–13.21)**
8	118	2	5	−0.1 (−2.0–1.4)	617 (441–781)	7.56 (6.82–10.50)**
18	87	2	5	0.2 (−4.9–2.5)	193 (51–432)*	11.24 (9.56–15.08)**
Solvent only	—	4	4	−0.7 (−2.2–2.1)	527 (500–618)	4.26 (3.63–6.87)
6	185	4	5	5.2 (1.5–7.4)	429 (346–481)**	9.03 (8.29–10.66)**
8	118	4	5	2.4 (0.9–3.9)	633 (561–824)	7.26 (5.50–9.20)
18	87	4	5	0 (−4.7–1.5)	917 (670–1128)**	6.09 (4.04–6.41)

Values are reported as median (range).
The Wilcoxon two-sample test with the corresponding solvent-only group shows the following differences:
* $P < 0.01$.
** $P < 0.02$.
*** $P < 0.05$.

(57% higher) and **18** (113% higher), respectively. Relative to controls, blood platelet counts were decreased (thrombocytopenia) 2 days after the last injection of **6** and **18** and although they had not fully recovered after two more days, platelet counts from **6** were closer to those of the controls by that time. The thrombocytopenia from **18** had been completely reversed by then; platelet counts were higher than control values—a common overshooting during compensatory hyperplasia following transient depletion of platelets.

3. Discussion

The failure of the BNCT clinical trials in the 1950s and 1960s was attributed to the lack of selectivity of the boron carriers and the poor quality of the thermal neutron irradiation.[2] The quality of the reactor components has since been greatly improved by the use of a more penetrating epithermal beam and sophisticated moderators and filters, thus providing a neutron beam of greater purity. Although the boron carriers BPA and BSH are a considerable improvement over those used in earlier clinical trials, the next breakthrough in BNCT will come from further improvement in the boron carrier. This is because the maximum allowable dose to tumor is determined by normal tissue tolerance dose thresholds, which are, in turn, determined by the biodistribution properties of the boron carrier.

The requirements that minimum average boron concentration be >30 μg/g B in tumor tissue and that tumor:normal tissue boron concentration ratios >5:1 with acceptable toxicity have been met by only a small fraction of the boron agents synthesized to date. Agents that are able to deliver tumor boron levels greater than 100 μg/g B are even fewer but, allowing for intra-tumoral administration techniques into intracranial gliomas, such agents include monoclonal antibodies conjugated with boronated dendrimers[29] and water-soluble porphyrins.[30] Porphyrin **6**, described herein, as well as other lipophilic porphyrins[27] and BPA[31] have also delivered boron concentrations >100 μg/g B to various tumors but serial ip injections or iv infusions were used rather than intra-tumoral injection. However, of the latter, only BPA could deliver such high concentrations to intracranial gliomas as it appears to be difficult for compounds greater than 500 Da such as porphyrins to accumulate in malignancies within brain tissues even with their blood–brain barriers disrupted.

Nevertheless, among the various categories of boron carriers, porphyrins remain as one of the more promising due primarily to their long retention time, high affinity for a variety of types of tumors, and substantial clearance from the blood. Within the porphyrin category, a number of porphyrins have been synthesized with variable polarities, although most porphyrins synthesized for BNCT are water-soluble.[13,18,19] On one end are lipophilic porphyrins such as CuTCPH[15] and CuTCPBr[27] and on the other end are highly polar, water-soluble porphyrins such as VCDP[32] and DCPK,[33,34] which use anionic *nido*-carboranes instead of neutral *closo*-carboranes as the boron moiety. In comparing the lipophilicity of CuTCPH with the porphyrins in this report, porphyrin **6** appears to be as lipophilic, while porphyrin **18** is more lipophilic and the hydroxyporphyrin **8** is much less lipophilic. Although the lipophilic porphyrins have the disadvantage of requiring excipients for in vivo administration and generally higher liver boron concentrations, the advantages are that the tumor boron concentrations often reach 100 ppm levels from 200 mg/kg doses, the kidney boron is lower, and the blood boron decreases to levels less than 1 ppm, which are 10-fold lower than those from the water-soluble porphyrins. Furthermore, serious thrombocytopenia and high mortality have been reported after some water-soluble porphyrins have been administered at doses relevant to BNCT.[16]

The octacarboranylporphyrin **18** is considered more lipophilic than CuTCPH judging by its longer HPLC retention time. It appears that no advantage was gained by the addition of four more carborane moieties in terms of boron delivery or toxicity per mass of porphyrin. In fact, mild thrombocytopenia was observed at a dose less than 100 mg/kg, whereas neither CuTCPH nor CuTCPBr had levels of platelets different from solvent-only controls at double this dose.[27] Porphyrin **6** shows tremendous ability in delivering large concentrations of boron to the EMT-6 carcinoma. Although the weight loss and decrease in platelets were significantly different from solvent-only controls at 2 days after administration, their robust rebound after two more days indicates it was a mild and reversible toxicity. Porphyrin **8** delivered the lowest boron concentration to tumor but the differences between **8**, **18**, and CuTCPH were not as large as those between **6** and the remaining three porphyrins (Fig. 1). Because of the greater polarity of the hydroxyporphyrin **8**, its microlocalization in tumor tissue may be considerably different from that of CuTCPH. If distributed more homogeneously, it could prove more efficacious in BNCT even at a lower average concentration of boron in tumor. Since neither mouse body weights nor the platelets were affected at 118 mg/kg, dose escalation may be possible, which would enable higher tumor boron concentrations without serious thrombocytopenia.

4. Conclusions

Three new carboranylporphyrins have been synthesized as potential ^{10}B carriers for BNCT. Of the three, porphyrins **6** and **8** are the most promising as possibly superior to CuTCPH given their robust tumor boron delivery, their equally low toxicity, and their similarly thorough blood clearances.

5. Experimental

5.1. Animals

All in vivo experiments were approved by the Brookhaven National Laboratory Institutional Animal Care and Use Committee. Food and water were provided ad libi-

tum. Subcutaneous (sc) EMT-6 tumors were initiated on the dorsal thorax of 18–22 g BALB/c mice (Taconic Farms, Germantown, NY) using single-cell suspensions of 2.5×10^5 cells in 0.05–0.10 mL culture medium. EMT-6 tumor cells were grown in vivo and in vitro in succession.[35] Single-cell monolayers were prepared from mouse-grown tumors by trypsinization, expanded in alpha MEM with 10% FBS (Gibco BRL Products, Grand Island, NY) for several passages. Aliquots of the cells in 10% DMSO were frozen in liquid nitrogen for storage and were thawed and regrown in tissue culture medium prior to implantation. Porphyrin injections were initiated 11 days after tumor cell implantation.

5.2. Porphyrin administration

Tumor-bearing mice were given porphyrins **6** and **8** in six ip injections at 3/day (within 8 h) over a period of 2 days using a volume of 0.01 mL/g body weight per injection. Those given porphyrin **18** were given three ip injections within 8 h. Mice given any of the three porphyrins were euthanized 2 or 4 days after the last injection.

5.3. Euthanasia and necropsy

Under deep Halothane inhalation anesthesia leading to euthanasia, right ventricular blood (0.2–0.5 mL total) was put into a Microtainer™ (Becton–Dickinson, Rutherford, NJ) tube containing EDTA for hematological analyses, which was subsequently used for boron analyses. Tumor, brain, muscle, and liver were sampled at necropsy for boron analyses.

5.4. Boron analyses

Direct current plasma-atomic emission spectroscopy (DCP-AES) (ARL/Fisons Model SS-7) was used to assay boron (detection limit: 0.1 μg B/mL). Samples from individual mice (50–130 mg) were digested at 60 °C with sulfuric acid/nitric acid (1:1). Triton X-100 and water were added to give final concentrations of ~50 mg tissue/mL, 15% total acid v/v, and 5% Triton X-100 v/v. Tissue samples were analyzed from individual mice. Boron concentrations of injection solutions were determined by prompt γ-ray spectroscopy,[36] which was carried out at the Massachusetts Institute of Technology Reactor Prompt-Gamma Neutron Activation Facility.

5.5. Blood analyses

Hematologic assays were carried out at BNL using a VetScan HMT Hematology Analyzer (Abaxis, Sunnyvale, CA). Mice were weighed daily and necropsies were carried out promptly after euthanasia.

5.6. Chemicals and procedures

Melting points were measured on a Mel-Temp II apparatus and are uncorrected. Silica gel (200–400 mesh) was used for chromatography. Analytical thin-layer chromatography (TLC) was performed using Baker-flex F254 silica gel (precoated sheets, 2.5×7.5 cm, J. T. Baker Inc., Phillipsburg, NJ). Reactions were monitored by TLC and by optical absorption spectroscopy (CARY 50 CONC UV–vis spectrophotometer, Varian Inc., Palo Alto, CA). ^{1}H NMR spectra were obtained on a Bruker 400 MHz/50 mm Ultrashield™ spectrometer (Rheinstetter, Germany) with tetramethylsilane (TMS) as the reference and all ^{13}C NMR are proton-decoupled. Fast-atom bombardment mass spectra (FAB MS) were obtained at the Mass Spectrometry Facility, State University of New York at Stony Brook, NY. All reagents were purchased from Aldrich Chemical Co. (Milwaukee, WI) unless otherwise stated and used without further purification. Decaborane was purchased from Strem Chemicals (Newburyport, MA).

Standard work-up of a reaction product consisted of dilution of the reaction mixture or evaporated residue with dichloromethane (DCM), washing of the organic layer with water three times, drying over anhydrous Na_2SO_4, $MgSO_4$, or K_2CO_3, and rotary evaporation of solvents.

HPLC column: Phenomenex Prodigy 5μ, ODS3, 100A, 150×4.6 mm, 5 μm particle size.

HPLC system: Hewlett Packard HP 1050; software: LC ChemStation revision A.06.04.

Detector: diode array detector; wavelength: 463 nm; 4 nm bandwidth (reference: 599 nm, 2 nm bandwidth). Solvent flow rate: 1 mL/min. Solvent system: acetonitrile/methanol gradient 50:50–0:100 in 15–35 min to 50:50 in 40 min.

5.7. Preparation of Cremophor EL/propylene glycol emulsion

To prepare a solution of ~2.9 mg/mL porphyrin in 9% Cremophor EL (CRM) and 18% propylene glycol (PRG), the porphyrin was dissolved in tetrahydrofuran (THF) (1.5% of the total volume) and then heated at 40 °C for 15 min.[28] CRM (9% of total volume) was then added and the mixture was heated to 60 °C for 2 h removing most if not all the THF. After cooling to room temperature, PRG (18% of total volume) was added, followed by slow dropwise addition of saline (71.5% of total volume) with rapid stirring. The solution was degassed by stirring under vacuum (~30 mmHg) for 30–60 min and then filtered (Millipore, 8 μm).

5.8. 3-Methoxy-4-propargyloxybenzyl alcohol

Finely powdered K_2CO_3 (10.4 g, 0.075 mol), KI (9.1 g, 0.060 mol), and acetone (150 mL) were stirred at room temperature as 3-methoxy-4-hydroxybenzyl alcohol, **1** (7.71 g, 0.050 mol) and propargyl chloride (4.10 g, 0.055 mol) were added. The mixture was stirred at reflux for approximately 2 days. The reaction was monitored by TLC, which showed no starting material at this time. The solution was first filtered and then worked up using standard method. The organic layer was purified using a 2-cm silica pad eluting with DCM. The solvents were

removed leaving a colorless liquid (9 g, 94% yield). ^{1}H NMR ($CDCl_3$) δ ppm: 2.49 (t, 1H, C≡CH); 2.57 (s, 1H, OH); 3.81 (s, 3H, OCH_3); 4.55 (d, 2H, $CH_2C{\equiv}C$); 6.83 (m, 1H, ArH); 6.89 (m, 1H, ArH); 6.94 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 55.8 ($ArOCH_2$); 56.8 (CH_3); 64.8 ($ArCH_2$); 75.8 (C≡CH); 78.5 (C≡CH); 110.2 (ArC); 114.3 (ArC); 119.0 (ArC); 135.2 (ArC); 146.0 (ArC); 149.7 (ArC). $C_{11}H_{12}O_3$ requires 192.20 MS (FAB) *m/e* 192.1 (M^+).

5.9. 3-Methoxy-4-propargyloxybenzyl acetate (2)

Acetyl chloride (5.0 g, 0.064 mol) and pyridine[37] (20 mL) were cooled in an ice-water bath while stirring as a solution of 3-methoxy-4-propargyloxybenzylalcohol (9.5 g, 0.050 mol) in pyridine (20 mL) was added dropwise. After the mixture was stirred for 5 h, the reaction mixture was poured into conc. HCl/ice and worked up extracting with DCM. The resulting oily residue was crystallized using hot 95% ethanol, to yield a yellowish solid (9.2 g, 79%). Mp 69–71 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 2.09 (s, 3H, CH_3); 2.50 (t, 1H, C≡CH); 3.89 (s, 3H, CH_3); 4.76 (d, 2H, $CH_2C{\equiv}C$); 5.05 (s, 2H, $ArCH_2$); 6.92 (s, 1H, ArH); 6.93 (m, 1H, ArH); 7.01 (d, 1H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 21.2 (CH_3); 56.1 ($ArOCH_2$); 56.9 (OCH_3); 66.6 ($ArCH_2$); 76.0 (C≡C); 78.6 (C≡C); 112.4 (ArC); 114.3 (ArC); 121.1 (ArC); 130.0 (ArC); 147.0 (ArC); 149.8 (ArC); 171.0 (CO). $C_{13}H_{14}O_4$ requires 234.25 MS (FAB) *m/e* 234.6 (M^+).

5.10. 3-Methoxy-4-*o*-carboranylmethoxybenzyl acetate (3)

Decaborane (2.07 g, 0.017 mol) was dissolved in toluene (100 mL) under an argon atmosphere at room temperature as acetonitrile (2.1 mL, 0.040 mol) was added and the mixture was allowed to stir for 3 h. Acetate (**2**) (3.82 g, 0.0163 mol) was added and the mixture was heated at 80–90 °C for 3 days, after which TLC showed no presence of starting material. The excess decaborane was decomposed by the slow addition of methanol (20 mL) while cooling in an ice-water bath. After the solvents were removed by rotary evaporation, the resulting residue was dissolved in DCM and worked up washing first with saturated bicarbonate solution followed by water. The resulting solid was recrystallized in DCM/hexanes (1:1) yielding a white microcrystalline solid (3.48 g, 60% yield). Mp 84–85 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 10H, BH); 2.00 (s, 3H, CH_3); 3.76 (s, 3H, OCH_3); 4.29 (s, 1H, CH); 4.54 (s, 2H, $OCH_2CCHB_{10}H_{10}$); 4.95 (s, 2H, $ArCH_2$); 6.74 (m, 2H, ArH); 7.17 (s, 1H, ArH). ^{13}C NMR (decoupled, $CDCl_3$) δ ppm: 21.1 (OCH_3); 56.0 ($ArOCH_2$); 58.0 (OCH_3); 66.4 ($ArCH_2$); 71.6 ($-CCHB_{10}H_{10}$); 72.1 ($-CCHB_{10}H_{10}$); 112.8 (ArC); 116.8 (ArC); 121.2 (ArC); 132.0 (ArC); 146.8 (ArC); 150.4 (ArC); 171.0 (CO). $C_{13}H_{24}B_{10}O_4$ requires 352.44 MS (FAB) *m/e* 352.8 (M^+).

5.11. 3-Methoxy-4-*o*-carboranylmethoxybenzyl alcohol

To a solution of acetate (**3**) (4.0 g, 11 mmol) in methanol (50 mL) concentrated HCl (2 mL) was added and the mixture was allowed to stir at reflux for 3 h. After removal of solvents, the residue was worked up leaving a yellow oil, which was purified using a silica pad with DCM as eluent, and yielded a clear oil, which crystallized upon standing (3.5 g, 99% yield). ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 10H, BH); 3.39 (s, 3H, OCH_3); 3.85 (s, 2H, CH_2-carborane); 4.33 (s, 1H, CH); 4.39 (s, 2H, $ArCH_2OH$); 6.85 (m, 2H, ArH); 6.92 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 55.9 ($ArOCH_3$); 58.0 (OCH_3); 58.3 ($ArCH_2$); 71.7 ($-CCHB_{10}H_{10}$); 74.4 ($-CCHB_{10}H_{10}$); 112.0 (ArC); 117.0 (ArC); 120.3 (ArC); 134.5 (ArC); 146.4 (ArC); 150.5 (ArC).

5.12. 3-Methoxy-4-*o*-carboranylmethoxybenzaldehyde (4)

Pyridinium chlorochromate (PCC) (2.4 g, 11 mmol) was stirred in DCM (25 mL) in an ice bath. A solution of 3-methoxy-4-*o*-carboranylmethoxy benzyl alcohol (1.71 g, 5.5 mmol) in DCM (25 mL) was added dropwise to the cooled PCC solution. The resulting mixture was stirred for two hours, at which time TLC showed no starting material. The black heterogeneous solution was filtered/purified through a 2-cm silica pad, and gave an off-white solid, which was recrystallized in 95% ethanol to yield pale yellow solid (1.4 g, 85% yield). Mp: 146–147 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 10H, BH); 3.92 (s, 3H, OCH_3); 4.28 (s, 1H, $CH_2CCHB_{10}H_{10}$); 4.51 (s, 2H, $CH_2CCHB_{10}H_{10}$); 6.92 (s, 1H, ArH); 7.44 (m, 2H, ArH); 9.88 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$) δ ppm: 56.2 ($ArOCH_2$); 58.1 (OCH_3); 70.6 ($-CCHB_{10}H_{10}$); 71.4 ($-CCHB_{10}H_{10}$); 110.3 (ArC); 114.4 (ArC); 126.0 (ArC); 132.3 (ArC); 150.6 (ArC); 190.9 (CO). $C_{11}H_{20}O_3B_{10}$ requires 308.4 MS (FAB) *m/e* 309.7 $(M+1)^+$.

Alternative method: Equimolar amounts of 3-methoxy-4-*o*-carboranylmethoxy benzyl alcohol and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ)[23] were stirred in dioxane for 1 h. The solvent was then removed by rotary evaporation. DCM was then added to selectively extract the product. The insoluble $DDQH_2$ side-product was removed by filtration. Rotary evaporation of the resulting filtrate yielded the final product.

5.13. *meso*-5,10,15,20-Tetrakis[3-methoxy-4-*o*-carboranylmethoxyphenyl] porphyrin (5)

A solution of benzaldehyde (**4**) (50 mg, 0.162 mmol) and freshly distilled pyrrole (11.3 μL, 0.162 mmol) in anhydrous DCM (40 mL) was purged with argon for 20 min. Trifluoroacetic acid (TFA) (5.4 μL, 0.045 mmol) was added and the mixture was allowed to stir under argon overnight. DDQ (34 mg, 0.149 mmol) was then added, which immediately turned the solution very dark, and the solution was stirred at reflux for 1 h. The product was then purified by flash chromatography using silica and 50% hexane/DCM yielding a purple solid (15 mg, 31% yield). ^{1}H NMR ($CDCl_3$) δ ppm: −2.77 (s, 2H, NH); 1.5–3.0 (br m, 40H, BH); 3.94 (s, 12H, OCH_3); 4.50 (s, 4H, $CHB_{10}H_{10}$); 4.74 (s, 8H, $CH_2CCHB_{10}H_{10}$); 7.21 (d, 4H, ArH); 7.72 (d, 4H, ArH); 7.77 (s, 4H, ArH); 8.85 (s, 8H, pyrrole-H). $C_{60}H_{86}N_4O_8B_{40}$ requires 1423.8, MS (FAB) *m/e* 1424.7 $(M+H)^+$. UV–vis (DCM) λ_{max} (nm): 423, 517, 554,

593, and 648. $C_{60}H_{86}N_4O_8B_{40}$ requires 1423.8, MS (FAB) *m/e* 1424.7 $(M+H)^+$.

5.14. Copper *meso*-5,10,15,20-tetrakis[3-methoxy-4-*o*-carboranylmethoxyphenyl] porphyrin (6)

A solution of $Cu(OAc)_2{\cdot}H_2O$ (20 mg, 100 mmol) in methanol (5 mL) was added to a solution of porphyrin (**5**) (130 mg, 91 mmol) in DCM (10 mL) and the mixture was stirred for 20 min, after which time TLC showed completion of reaction. After the solvents were removed, the resulting residue was worked up leaving a red solid, which was then dissolved in DCM and purified using a silica pad eluting with hexane/DCM (1:1). The solvents were removed leaving red porphyrin **6** (132 mg, 98% yield). $C_{60}H_{84}N_4O_8B_{40}Cu$ requires 1485.29, MS (FAB) *m/e* 1486.3 $(M+H)^+$. UV–vis (DCM) λ_{max} (nm): 418, 542.

5.15. *meso*-5,10,15,20-Tetrakis[3-hydroxy-4-*o*-carboranylmethoxyphenyl] porphyrin (7)

Porphyrin **5** (44 mg, 0.031 mmol) was stirred in dry DCM (15 mL) under argon at room temperature while BBr_3 (1.0 mmol of a 1 M solution in DCM) was added and the solution was allowed to stir for 30 min.[24] At this time an ice-cold saturated aqueous sodium bicarbonate or dilute ammonium hydroxide solution (~10 mL) was added to hydrolyze the porphyrin borate and to destroy excess BBr_3. The product was worked up and the resulting green solution was purified with a silica pad eluting with acetone/methanol (5:1 v/v) solvent mixture. A reddish brown solid was obtained in 91% yield (38 mg). ^{1}H NMR ($CDCl_3$) δ ppm: −2.88 (s, 2H, NH); 1.5–3.0 (br m, 40H, BH); 4.04 (s, 4H, $CHB_{10}H_{10}$); 4.71 (s, 8H, $CH_2CCHB_{10}H_{10}$); 5.64 (s, 4H, ArOH); 7.10 (s, 4H, ArH); 7.63 (s, 4H, ArH); 7.77 (s, 4H, ArH); 8.82 (s, 8H, pyrrole-H). UV–vis (acetone) λ_{max} (nm): 420, 513, 549, 591, 648. $C_{56}H_{78}N_4O_8B_{40}$ requires 1367.7, MS (FAB) *m/e* 1368.0 (M^+).

5.16. Copper *meso*-5,10,15,20-tetrakis[3-hydroxy-4-*o*-carboranylmethoxyphenyl] porphyrin (8)

Porphyrin **7** (50 mg, 36 mmol) and $Cu(OAc)_2{\cdot}H_2O$ (8 mg, 40 mmol) were dissolved in methanol (10 mL) and stirred for 20 min during which time the color turned red. After the solvent was removed, the resulting residue was worked up, leaving a red compound, which was purified using a silica pad eluting with a solvent mixture of hexane/DCM/acetone (3:1:1, v/v/v). The porphyrin (36 mg) was isolated in 70% yield. UV–vis (acetone) λ_{max} (nm): 417, 534. $C_{56}H_{78}N_4O_8B_{40}Cu$ requires 1429.2, MS (FAB) *m/e* 1428.0 $(M-1)^+$.

5.17. 3,5-Dipropargyloxybenzyl acetate (9)

Finely powdered K_2CO_3 (14 g, 0.10 mol) and KI (17 g, 0.10 mol) were stirred in acetone (200 mL) under a nitrogen atmosphere. 3,5-Dihydroxybenzyl alcohol (4.2 g, 0.030 mol) and propargyl chloride (5.3 g, 0.070 mol) were added and mixture was allowed to stir at reflux overnight. After the solution was filtered and evaporated down to dryness, the residue was worked up leaving a pale yellow oil, which solidified upon standing to give 5.7 g in 88% yield. Mp 79–80 °C; ^{1}H NMR ($CDCl_3$) δ ppm: 2.52 (t, 2H, C≡CH); 2.15 (br s, 1H, hydroxyl); 4.65 (d, 4H, $ArOCH_2$); 4.60 (s, 2H, ArH_2); 6.52 (s, 1H, ArH); 6.60 (s, 2H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 56.1 ($ArOCH_2$); 65.1 ($ArCH_2$); 75.9 (C≡C); 78.6 (C≡C); 101.6 (ArC); 106.4 (ArC); 143.8 (ArC); 159.0 (ArC). $C_{13}H_{12}O_3$ requires 216.4, MS (FAB) *m/e* 217.5 $(M+H)^+$.

The above 3,5-dipropargyloxybenzyl alcohol (5.7 g, 0.026 mol) was stirred in acetic anhydride (5.4 g, 0.053 mol) as concentrated sulfuric acid (two drops) was added and the solution was stirred for 3 h at 90 °C. After cooling to room temperature, the solution was poured into ice water, neutralized with a saturated sodium carbonate solution and the product was worked up, leaving a yellow oil, which was purified by recrystallization in ethanol to give a pale yellow compound (5.2 g in 76% yield). Mp 65–66 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 2.11 (s, 3H, CH_3); 2.54 (t, 2H, C≡CH); 4.67 (d, 4H, $ArOCH_2$); 5.05 (s, 2H, $ArCH_2$); 6.58 (s, 1H, ArH); 6.61 (s, 2H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 21.3 (CH_3); 56.0 ($ArOCH_2$); 66.2 ($ArCH_2$); 76.2 (C≡C); 78.6 (C≡C); 102.3 (ArC); 108.0 (ArC); 138.8 (ArC); 159.0 (ArC); 171.1 (CO). $C_{15}H_{14}O_4$ requires 258.3, MS (FAB) *m/e* 259.5 $(M+H)^+$.

5.18. 3,5-Di-*o*-carboranylmethoxybenzyl acetate (10)

Decaborane (2.70 g, 0.022 mol) was dissolved in dry toluene (80 mL) and stirred at room temperature under a nitrogen atmosphere. Acetonitrile (12 mL, 0.22 mol) was added and the solution was allowed to stir for 3 h. A solution comprised of compound **9** (2.84 g, 0.011 mol) in toluene (80 mL) was added to the decaborane solution. The rest of the procedure was similar to that for compound **3**. The resulting yellow oil solidified upon standing yielding 4.40 g in 81% yield. Mp 122–123 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 2.12 (s, 3H, CH_3); 4.06 (s, 2H, $CCHB_{10}H_{10}$); 4.39 (s, 4H, $ArOCH_2$); 5.01 (s, 2H, $ArCH_2$); 6.32 (s, 1H, ArH); 6.52 (s, 2H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 21.4 (CH_3); 58.3 ($ArOCH_2$); 65.8 ($ArCH_2$); 69.6 (–*C*CHB$_{10}$H$_{10}$); 71.5 (–*C*CHB$_{10}$H$_{10}$); 102.3 (ArC); 108.5 (ArC); 139.8 (ArC); 158.6 (ArC); 171.0 (CO). $C_{15}H_{34}O_4B_{20}$ requires 494.6, MS (FAB) *m/e* 496.0 $(M+H)^+$.

5.19. 3,5-Di-*o*-carboranylmethoxybenzyl alcohol (11)

The hydrolysis conditions using methanol and HCl were carried out in a procedure similar to that used to hydrolyze compound **3**. A white solid was obtained (3.4 g) in 93% yield. Mp 267–269 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 2.54 (br s, 1H, OH); 4.04 (s, 2H, $CCHB_{10}H_{10}$); 4.40 (s, 4H, $ArOCH_2$); 4.65 (s, 2H, $ArCH_2$); 6.28 (s, 1H, ArH); 6.54 (s, 2H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 58.0 ($ArOCH_2$); 64.7 ($ArCH_2$); 69.4 (–*C*CHB$_{10}$H$_{10}$); 71.3 (–*C*CHB$_{10}$H$_{10}$); 101.5 (ArC); 106.6 (ArC); 144.7 (ArC); 158.5 (ArC). $C_{13}H_{32}O_3B_{20}$ requires 452.6, MS (FAB) *m/e* 453.0 (M^+).

5.20. 3,5-Di-*o*-carboranylmethoxybenzaldehyde (12)

The oxidation of alcohol **11** was carried out in a procedure similar to that used to synthesize **5**. Aldehyde **12** was obtained in 70% yield (0.70 g). ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 4.0 (s, 2H, carborane CH); 4.5 (s, 4H, OCH_2); 6.7 (s, 1H, *p*-ArH); 7.0 (s, 2H, *o*-ArH); 9.9 (s, 1H, CHO).

5.21. 3,5-Di-*o*-carboranylmethoxylbenzyl bromide (14)

Carboranylbenzyl alcohol **11** (0.45 g, 1.0 mmol) and CBr_4 (0.40 g, 1.2 mmol) were dissolved in dry THF (2 mL) under an argon atmosphere. Triphenylphosphine (0.31 g, 1.2 mmol) was added and the resulting mixture was allowed to stir for 20 min.[24] The mixture was then poured into water, worked up, and purified using a silica pad and DCM/hexane (1:1) as eluent. After solvent evaporation, a white solid (0.48 g) was obtained in 92% yield. Mp 230–232 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 4.02 (s, 2H, C*CH*$B_{10}H_{10}$); 4.37 (s, 2H, CH_2Br); 4.39 (s, 4H, $ArOCH_2$); 6.26 (s, 1H, ArH); 6.55 (s, 2H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 32.4 (CH_2Br); 58.0 ($ArOCH_2$); 69.5 (–C*C*$HB_{10}H_{10}$); 71.1 (–*C*$CHB_{10}H_{10}$); 102.3 (ArC); 109.2 (ArC); 141.2 (ArC); 158.4 (ArC). $C_{13}H_{31}O_2B_{20}Br$ requires 515.5, MS (FAB) *m*/*e* 516.9 $(M+H)^+$.

5.22. *3*-(3,5-Di-*o*-carboranylmethoxybenzyloxy)benzyl alcohol (15)

K_2CO_3 (1.0 g, 7.2 mmol), KI (1.0 g, 6.0 mmol), compound **14** (0.41 g, 0.80 mmol), and 3-hydroxybenzylalcohol (0.10 g, 0.81 mmol) were stirred in acetone (20 mL) and allowed to stir at reflux for 1 day under an argon atmosphere. After cooling, the solvent was removed and the residue was worked up. The residue was purified on a silica pad eluting with DCM/hexane (1:1) and a white solid was obtained (0.59 g) in 79% yield. Mp 259–261 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 1.70 (s, 1H, OH); 4.04 (s, 2H, C*CH*$B_{10}H_{10}$); 4.40 (s, 4H, CH_2C*C*$HB_{10}H_{10}$); 4.67 (s, 2H, ArCH_2OH); 5.00 (s, 2H, $ArCH_2OAr$); 6.31 (s, 1H, Ar); 6.60 (s, 2H, ArH); 6.87 (m, 1H, ArH); 7.00 (m, 2H, ArH); 7.26 (m, 1H, ArH). ^{13}C NMR ($CDCl_3$) δ ppm: 58.2 (CH_2C*C*$HB_{10}H_{10}$); 65.5 ($ArCH_2OH$); 69.6 (–C*C*$HB_{10}H_{10}$); 71.4 (–*C*$CHB_{10}H_{10}$); 102.0 (ArC); 107.4 (ArC); 113.6 (ArC); 114.3 (ArC); 120.2 (ArC); 130.2 (ArC); 141.2 (ArC); 143.1 (ArC); 158.7 (ArC); 158.8 (ArC). $C_{20}H_{38}O_4B_{20}$ requires 558.7, MS (FAB) *m*/*e* 559.0 (M^+).

5.23. *3*-(3,5-Di-*o*-carboranylmethoxybenzyloxy)benzaldehyde (16)

Pyridinum chlorochromate (PCC) (0.172 g, 0.80 mmol) in DCM (10 mL) was cooled in an ice water bath. To this a solution of **15** (0.223 g. 0.40 mmol) in DCM (10 mL) was added dropwise and the mixture was allowed to stir for 2 h. The major product was purified using a silica pad. After the removal of solvents, a white solid was obtained, 0.220 g, 99% yield. Mp 263–265 °C. ^{1}H NMR ($CDCl_3$) δ ppm: 1.5–3.0 (br m, 20H, BH); 4.04 (s, 2H, C*CH*$B_{10}H_{10}$); 4.42 (s, 4H, $ArOCH_2$); 5.00 (s, 2H, $ArCH_2O$); 6.33 (s, 1H, ArH); 6.61 (s, 2H, ArH); 7.23 (s, 1H, ArH); 7.44 (m, 1H, ArH); 7.50 (m, 2H, ArH); 9.98 (s, 1H, CHO). ^{13}C NMR ($CDCl_3$) δ ppm: 58.0 (CH_2C*C*$HB_{10}H_{10}$); 69.5 (–C*C*$HB_{10}H_{10}$); 69.7 ($ArCH_2$-OAr); 71.2 (–*C*$CHB_{10}H_{10}$); 102.0 (ArC); 107.4 (ArC); 112.8 (ArC); 122.4 (ArC); 124.8 (ArC); 130.6 (ArC); 138.1 (ArC); 138.4 (ArC); 140.3 (ArC); 158.6 (ArC); 192.1 (CHO). $C_{20}H_{36}O_4B_{20}$ requires 556.7, MS (FAB) *m*/*e* 558.0 $(M+H)^+$.

5.24. *meso*-5,10,15,20-Tetrakis[*m*-(3,5-di-*o*-carboranylmethoxybenzyloxy)phenyl] porphyrin (17)

Compound **16** (337 mg, 0.60 mmol), anhydrous DCM (100 mL), and freshly distilled pyrrole (420 μL, 0.60 mmol) were sequentially transferred to a dry 300 mL round-bottomed flask. The solution was purged with nitrogen for 15–20 min. $BF_3{\cdot}Et_2O$ (76 μL, 0.060 mmol) was then added and the solution was allowed to stir overnight. DDQ (150 mg, 0.60 mmol) was added and the solution was stirred at reflux for one hour. The major product was then purified using a silica pad followed by column chromatography using DCM/petroleum ether (1:1) as eluent, yielding a dark purple solid (78 mg) in 22% yield. ^{1}H NMR ($CDCl_3$) δ ppm: −2.84 (s, 2H, NH); 1.5–3.0 (br m, 80H, BH); 3.97 (s, 8H, C*CH*$B_{10}H_{10}$); 4.35 (s, 16H, $ArOCH_2$); 5.19 (s, 8H, $ArCH_2$); 6.31 (s, 4H, ArH); 6.65 (s, 8H, ArH); 7.40 (s, 4H, ArH); 7.70 (m, 4H, ArH); 7.79 (m, 4H, ArH); 7.86 (m, 4H, ArH); 8.84 (s, 8H, pyrrole-H). UV–vis (DCM) λ_{max} (nm): 420, 516, 550, 589, and 645. $C_{96}H_{150}N_4O_{12}B_{80}$ requires 2417.1, MS (FAB) *m*/*e* 2418.2 $(M+H)^+$.

5.25. Copper *meso*-5,10,15,20-tetrakis[*m*-(3,5-di-*o*-carboranylmethoxybenzyloxy)phenyl] porphyrin (18)

A solution of $Cu(OAc)_2{\cdot}H_2O$ (6 mg, 0.030 mmol) in methanol (5 mL) was added to a solution of porphyrin **17** (60 mg, 0.025 mmol) in DCM (20 mL) and allowed to stir for 20 min. After work-up, the resulting residue was purified by a silica column using DCM/petroleum ether (1:1, v/v) as eluent, to yield a red porphyrin (57 mg, 92% yield). UV–vis (DCM) λ_{max} (nm): 416, 539. $C_{96}H_{148}N_4O_{12}B_{80}Cu$ requires 2478.6, MS (FAB) *m*/*e* 2479.9 $(M+H)^+$.

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