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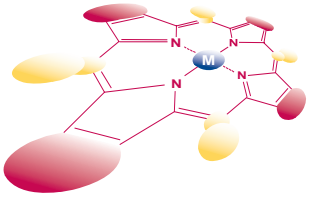

Syntheses of boronic-acid-appended metalloporphyrins as potential colorimetric sensors for sugars and carbohydrates

Chen Zhang and Kenneth S. Suslick*◊

Department of Chemistry, School of Chemical Sciences, University of Illinois at Urbana-Champaign, 600 S. Mathews Av., Urbana, Illinois 61801, USA

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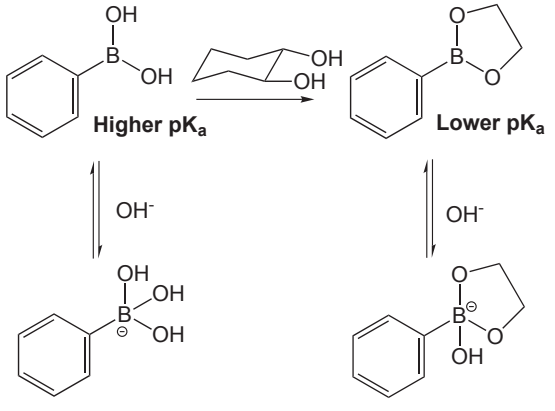
ABSTRACT: Boronic-acid-based dyes have been widely studied in the past decade as potential sensors for sugars and carbohydrates, owing to the strong interaction of boronic acid and diols. In this work, two boronic-acid-appended metalloporphyrins were synthesized by new routes and tested as potential sugar and carbohydrate sensors. Boronic acid substituents were attached either to a β-pyrrolic position ((2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II), **1**) or to the *meso*-position ((10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II), **2**) of the porphyrin core. These complexes were tested as potential carbohydrate sensors; unfortunately, no UV-vis or fluorescence spectra changes were observed with the addition of glucose or fructose. Molecular orbital calculations confirm little electronic conjugation between the porphyrin π-system and the boronic acid substituents in either pyrrolic or *meso*-positions. Copyright © 2005 Society of Porphyrins & Phthalocyanines.

KEYWORDS: boronic-acid-appended metalloporphyrins, colorimetric carbohydrate sensor.

INTRODUCTION

Molecular sensing and recognition of carbohydrates in the liquid phase is of great scientific and practical importance due to the prevalence of carbohydrates in nature and particularly to the need to monitor sugar concentrations in maintenance of patients with diabetes. Recently, boronic acid has been widely explored as carbohydrate recognition and binding moiety for sensor applications, owing its strong and reversible interaction with diols [1-3]. It has been well established that the boronic acid moiety binds to the *cis*-1,2- or 1,3-diols of carbohydrates to form a five- or six-membered cyclic esters, respectively (Scheme 1), and the resulting ester normally has a much lower pK_a than the boronic acid (Scheme 1) [2]. Therefore, in an aqueous solution whose pH is between those two pK_a values, the electron density at the boron atom will change dramatically after binding with a diol (*e.g.* carbohydrates) by changing from neutral to anionic state. A variety of carbohydrate sensors have been synthesized taking advantage of the changes in electrochemical properties [4, 5], fluorescence spectra [6, 7], CD spectra [8, 9] and UV-



Scheme 1. The binding equilibria between phenylboronic acid and a diol in an aqueous solution indicating the difference in pK_a values between a boronic acid and its ester

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*Correspondence to: Kenneth S. Suslick, email: ksuslick@uiuc.edu, fax: +1 217-333-2685

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vis spectra [10, 11].

A porphyrin-based colorimetric sensor array system has been developed in our laboratory, and it has been applied to both gas and liquid phase sensing of simple organic compounds as well as complex mixtures [12]. The great simplicity and versatility of this method have made it an ideal technology for wide-variety of real world applications. For its application in liquid samples, a colorimetric carbohydrate sensor is highly desired. Metalloporphyrins are a natural choice for this application: they are very stable, are intensly colored, show large spectral shifts with changes in electron density distribution, and are easily modified synthetically. Several boronic-acid-appended metalloporphyrins have been synthesized recently and utilized as sensors for carbohydrates using circular dichroic, fluorescence, or electrochemical changes [7, 9], but no data has been published on their possible use as simple colorimetric sensors.

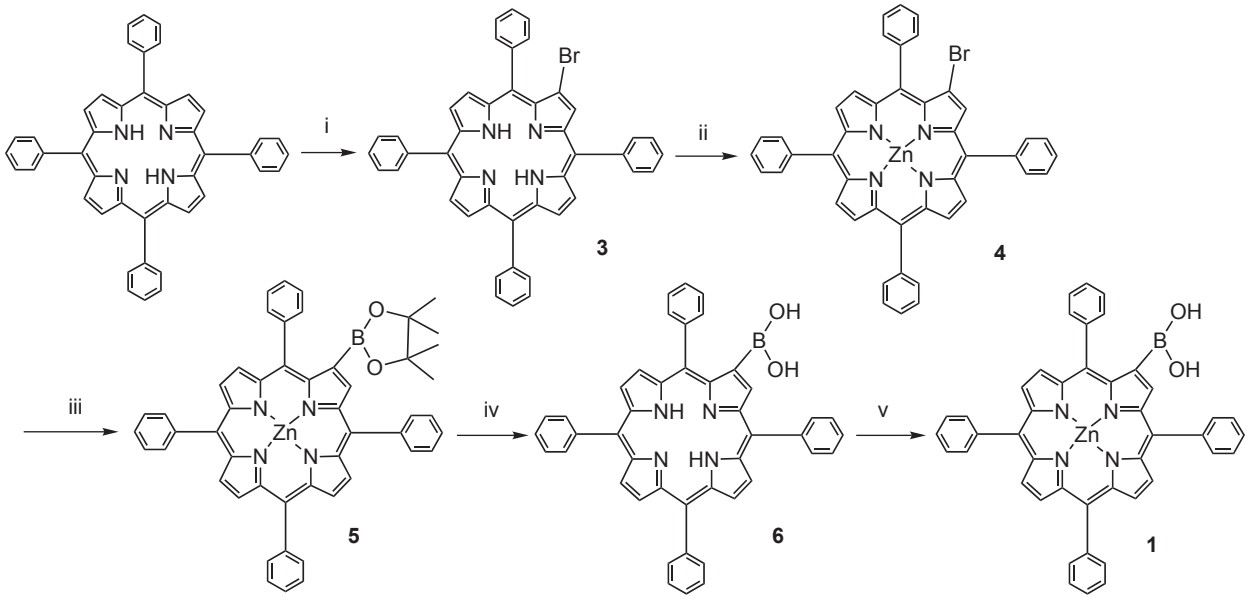
Here we present facile syntheses of two boronic-acid-appended metalloporphyrins with the substituent in either pyrrolic or *meso*-positions. Since the boronic acid moiety in those metalloporphyrins are in close proximity to the porphyrin π-system, we had hoped that the change of the electron density on the boron before and after binding to carbohydrate molecules would sufficiently perturb the electron density of the metalloporphyrin cores to produce significant spectra shifts (and therefore color changes) of the metalloporphyrins. The sensing ability of those boronic-acid-appended metalloporphyrins was tested using spectroscopic methods, and to the contrary, we find essentially no change in the porphyrin spectra in the presence of either glucose or fructose nor over the range of pH 4 to 12.

RESULTS AND DISCUSSION

Synthesis of (2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II), 1

As shown in Scheme 2, 5,10,15,20-tetraphenylporphyrin (TPP) was used as the starting material for the synthesis of (2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II), **1**, and was synthesized following the Lindsey procedure [13]. The precursor TPP was first brominated with N-bromosuccinimide (NBS) [14, 15]. Depending on the amount of NBS used, a mixture of various bromo-substituted TPP can be obtained. Mono-brominated product was the major component when 1 equiv. of NBS was used and can be easily separated using column chromatography. The free base porphyrin was then readily metalated with the addition of zinc acetate [16], which facilitates the following cross-coupling reaction by increasing the polarity of the halide-arene bond [17, 18]. Metalation also blocks the reactive N-H sites present in free-base porphyrin, which might interfere with further reactions.

The palladium(0)-catalyzed cross-coupling reaction between an aryl halide and an ester of diboronic acid [19] or dialkoxyhydroborane [20] has been widely used for the synthesis of arylboronates from haloarenes [11, 21], and it has also been applied to



Scheme 2. Synthesis of (2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II). Reaction conditions: (i) 1 equiv. NBS, 1 h reflux in $CHCl_3$; (ii) 5 equiv. $Zn(OAc)_2{\cdot}2H_2O$, MeOH/$CHCl_3$, room temperature overnight; (iii) 1,4-dioxane, 5 equiv. KOAc, 10% mol $Pd[P(t\text{-}Bu)_3]_2$, 5 equiv. bis(pinacolato)diboron, reflux overnight; (iv) THF/H_2O, 4:1, 6 equiv. $NaIO_4$, 2M HCl; (v) 5 equiv. $Zn(OAc)_2{\cdot}2H_2O$, MeOH/$CHCl_3$, room temperature overnight

metalloporphyrins for the introduction of boronic acid ester functionality [17, 22]. However, for [2-bromo-5,10,15,20-tetraphenylporphyrinato]zinc(II), the cross-coupling reaction did not work readily under the conditions as reported in the literature [22]: reflux in 1,4-dioxane with the addition of pinacolborane, TEA and transdichlorobis(triphenylphosphine)-palladium(II). Instead, we generally recovered the starting material with some reduction product H_2TPP. Changing the boronation agent and base or further drying the solvent was not successful. Recently, Fu and co-workers developed a much more reactive palladium catalyst for Stille's reaction [23, 24] and this is now commercially available. This catalyst worked well for our cross-coupling reaction. With the use of a diboronic acid ester bis(pinacolato)diboron, instead of the hydroborane pinacolborane to eliminate the possibility of forming reduction product, almost quantitative conversion was achieved. This is the first time that Fu's catalyst has been reported for the cross-coupling reaction for the synthesis of arylboronates.

Finally, the boronic acid was deprotected with $NaIO_4$ in an acidic solution [25]. THF was used as solvent due to its high solubility for these porphyrins and its miscibility with water. As expected, the Zn ion was removed in this process; after purification and neutralization, the free base boronic-acid-appended TPP was successfully re-metalated with zinc acetate, as before [16].

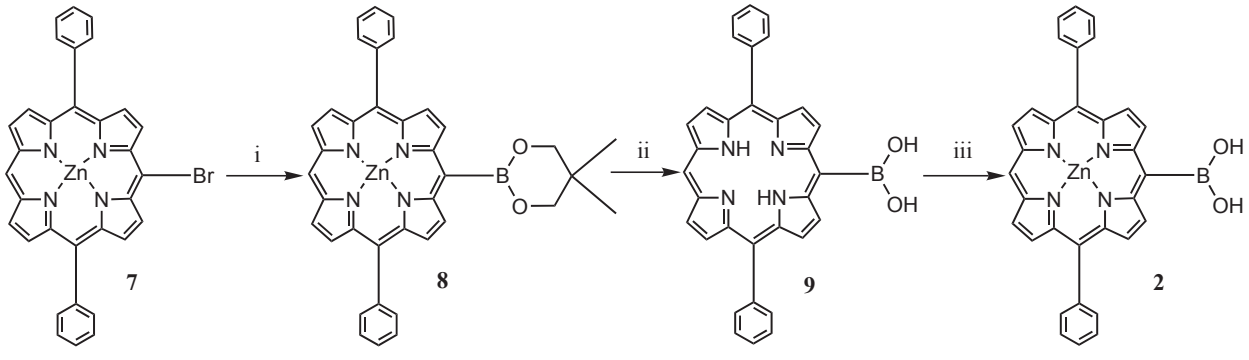
Synthesis of (10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II), 2

As shown in Scheme 3, (10-bromo-5,15-diphenylporphyrinato)zinc(II) serves as a good starting material for the synthesis of the boronic-acid-appended diphenylporphyrin (DPP), since it can be readily made in three synthetic steps from pyrrole and benzaldehyde [17, 22, 26]. A cross-coupling reaction with bis(pinacolato)diboron, similar to the synthesis of **5** (step iii in Scheme 1), generated the desired boronated porphyrin [17]. The deprotection of the boronic acid, however, proved to be non-trivial, since the pinacol protection group on the boronic acid DPP was much harder to remove than that on the boronic acid TPP. After the failure of a series of literature methods [9, 25, 27-29], a less sterically hindered and less stable protecting group was adopted by changing the boronation reagent to bis(neopentylglycolato)diboron. The protecting group was then readily removed under mild conditions [9], and the desired product **2** was obtained.

UV-vis spectra of boronic-acid-appended porphyrins

To determine the ability of the boronic-acid-appended porphyrins to act as sensors for carbohydrates, UV-vis spectra of the porphyrins were taken at different pHs and different carbohydrate concentrations. Fructose and glucose were used here as representatives for carbohydrate sensing experiments, since the former forms the most stable complex with phenylboronic acid and other monoboronic acids [1, 3], and the latter is one of the biologically most important carbohydrates (*e.g.* in the monitoring of diabetics) and has a reasonably strong affinity for boronic acids [1, 3].

Shown in Fig. 1 is the pH titration result of (10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II), **2,** from pH 2 to 10 in the absence of added carbohydrates. If the boron is conjugated to the metalloporphyrin core and the pK_a of the boronic acid is within this pH range, then the change of electron density on boron before and after protonation should affect the electron density of the metalloporphyrin core and a shift or change of the UV-vis spectrum would be expected. No distinctive differences, however, were observed in those UV-vis spectra. This metalloporphyrin was also tested in solutions with different concentrations of glucose and fructose, as shown in Fig. 2. Again, the UV-vis spectrum was found to be independent of the carbohydrate concentration within the limits of the instrument sensitivity. Similar-



Scheme 3. Synthesis of (5-dihydroxylboryl-10,20-diphenylporphyrinato)zinc(II). Reaction conditions: (i) 1,2-dichloroethane, 3 equiv. KOAc, 10% mol Pd[P(*t*-Bu)$_3$]$_2$, 5 equiv. bis(neopentylglycolato)diboron, reflux overnight; (ii) THF/H_2O, pH 10.5, N-methyldiethanolamine, room temperature 10 h; (iii) 5 equiv. $Zn(OAc)_2{\cdot}2H_2O$, MeOH/$CHCl_3$, room temperature overnight

ly, no change in UV-vis spectrum was observed for the TPP counterpart (2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II), **1** (Fig. 5), with varying pH values or carbohydrate concentrations. Free base porphyrin 10-dihydroxylboryl-5,15-diphenylporphyrin, **9,** were also tested using similar procedures and here too no changes were obtained (Figs 3 and 4). Fluorescence spectra were also taken for those porphyrins at various carbohydrate concentrations, and still no distinguishable spectra changes were observed (Fig. 6). All of the experiments were done in THF/H_2O solvent system. Good solubility for both porphyrins and carbohydrates were achieved and no interferences of spectra were observed from the solvents.

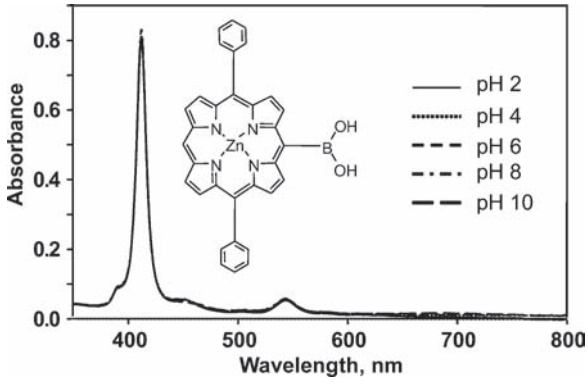


Fig. 1. UV-vis spectra for (10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II) **2** (2×10^{-5} mol/L) in a series of solutions (THF/buffer 1:4) buffered to different pHs. The spectra are essentially independent of pH over the range of pH 2 to 10

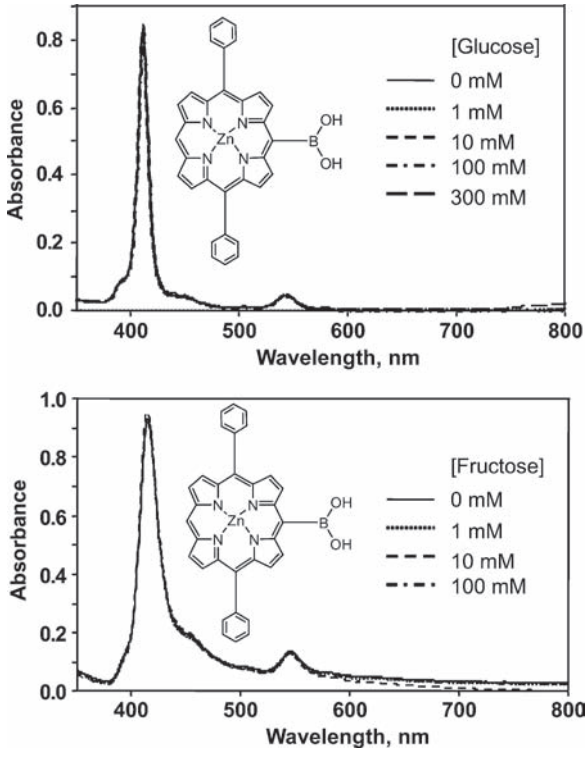


Fig. 2. UV-vis spectra for (10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II) **2** (2×10^{-5} mol/L) in a series of glucose and fructose solutions (THF/buffer 1:4) buffered to pH 7.0. Adding glucose or fructose does not affect the spectra up to 300 and 100 mM, respectively

Quantum mechanics calculations

We turned to semi-empirical quantum mechanics

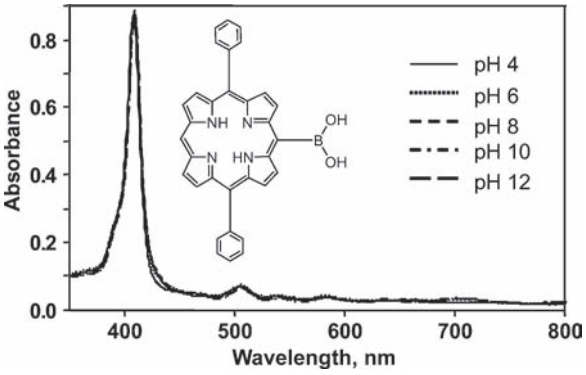


Fig. 3. UV-vis spectra for 10-dihydroxylboryl-5,15-diphenylporphyrin **9** (2×10^{-5} mol/L) in a series of buffered solutions (THF/buffer 1:4). The spectra are essentially independent of pH over the range of pH 4 to 10

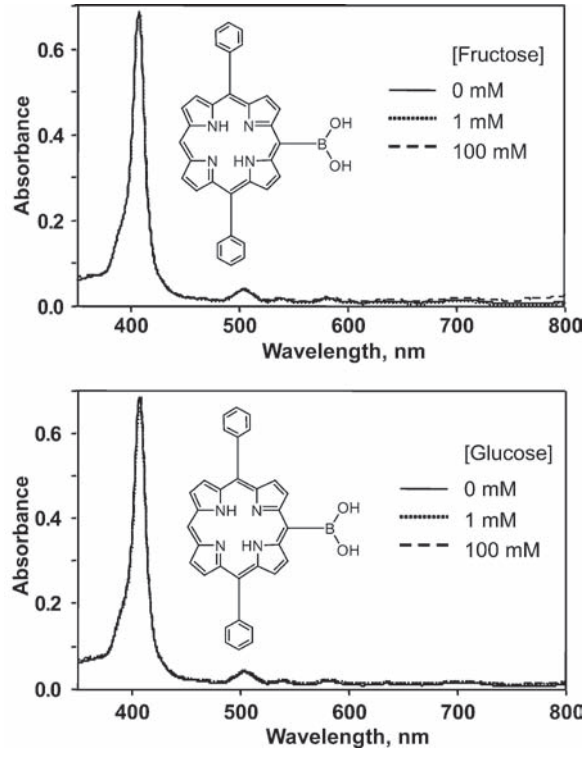


Fig. 4. UV-vis spectra for 10-dihydroxylboryl-5,15-diphenylporphyrin **9** (2×10^{-5} mol/L) in a series of glucose and fructose solutions (THF/buffer 1:4) buffered at pH 7.0. Adding glucose or fructose does not affect the spectra up to 100 mM

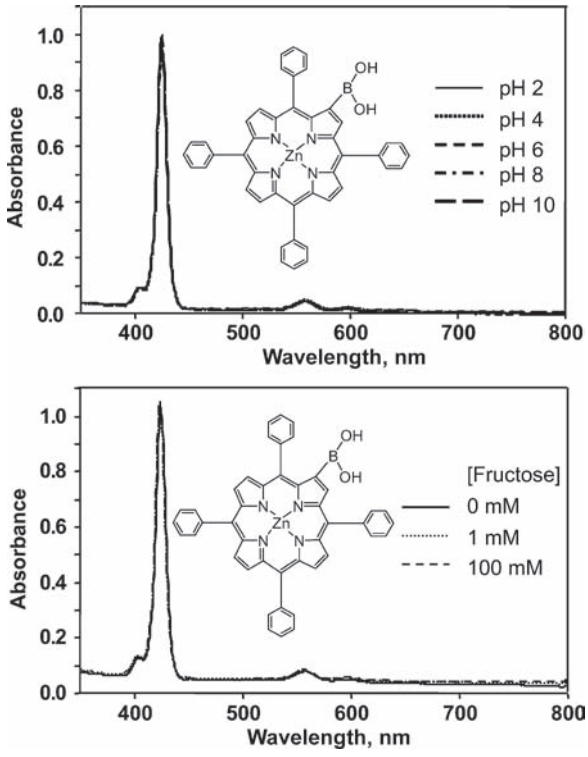


Fig. 5. UV-vis spectra for (2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II) **1** (2×10^{-5} mol/L) in a series of solutions (THF/buffer 1:4) buffered to different pHs and a series of fructose solutions (THF/buffer 1:4) buffered at pH 7.0. Neither changes in pH nor changes in fructose concentration affect the spectra

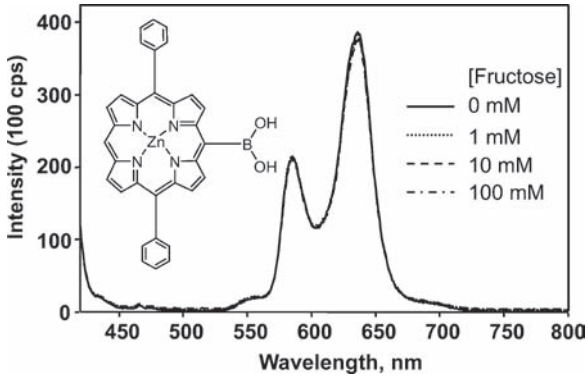


Fig. 6. Fluorescence spectra for (10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II) **2** (2.5×10^{-6} mol/L) in a series of fructose solutions (THF/buffer 1:4) buffered at pH 7.0. Adding fructose does not affect the spectra up to 100 mM

calculations (MOPAC) to provide a rationalization for the lack of response of these porphyrins to the presence of carbohydrates. MOPAC calculations were performed on those molecules to optimize the predicted geometry and determine the molecular orbitals (Fig. 7). The calculated lowest energy geometry indicated that the boronic acid moiety was not on the same plane with the metalloporphyrin cores (neither TPP **1** nor DPP **2**), but rather almost perpendicular to the plane. Therefore, the boronic acid is not well conjugated to the porphyrin π-electron system. Moreover, the calculated HOMO and LUMO of the two boronic-acid-appended metalloporphyrins did not involve the p-orbital on the boron atom (sp^2 hybridization), which means the change of electron density of the boron atom will not have a substantial effect on the metalloporphyrin core. Those calculations support the experimental results, and roughly explain the lack to spectra changes of those two boronic-acid-appended metalloporphyrins upon binding with carbohydrates.

EXPERIMENTAL

Materials and instrumentation

CH_2Cl_2 and $CHCl_3$ were purified in our laboratory using common alumina solvent purification columns. Pyrrole and benzaldehyde (Aldrich) were dried with molecular sieves and distilled under Ar gas protection and kept at -20 °C before use. Pyridine was distilled before use and stored under Ar. Triethylamine was distilled from BaO and stored with molecular sieve under Ar. 1,2-dichloroethane was distilled from CaH_2 under Ar and stored with molecular sieve under Ar. 1,4-dioxane was distilled from Na/benzophenone under Ar and stored with molecular sieve under Ar. Bis(pinacolato)diboron, bis(neopentylglycolato)diboron and N-methyldiethanlamine were obtained from Aldrich and used as received. Pd[P(*t*-Bu)$_3$]$_2$ (Fu's catalyst) was obtained from Strem and was stored under Ar at -20 °C after opening. Sodium periodate was purchased from Acros Organics and was used as received. All other reagents and solvents were used as purchased. Column chromatography was performed on Silica Gel (32-63 micron, 230-400 mesh) from Merck.

All ^{1}H spectra were recorded on a VARIAN UNITY 400 FT-NMR (400 MHz). The low-resolution mass spectra were obtained on an Applied Biosystems Voyager-DE STR (MALDI), and high-resolution mass spectra, Micromass Q-Tof Ultima (HR-ESI). UV-vis spectra were recorded on a Hitachi U-3300 spectrophotometer, and fluorescence spectra were taken on a Jobin Yvon FluoroMax-3 spectrofluorometer.

Synthesis

General procedure for the Zn metallation of free base porphyrins. The free base porphyrin was dissolved in $CHCl_3$ to make a ~10 mM solution in a round-bottom flask. A 2 M solution of $Zn(OAc)_2 \cdot 2H_2O$ was made in methanol, and 5 equivalents of the zinc

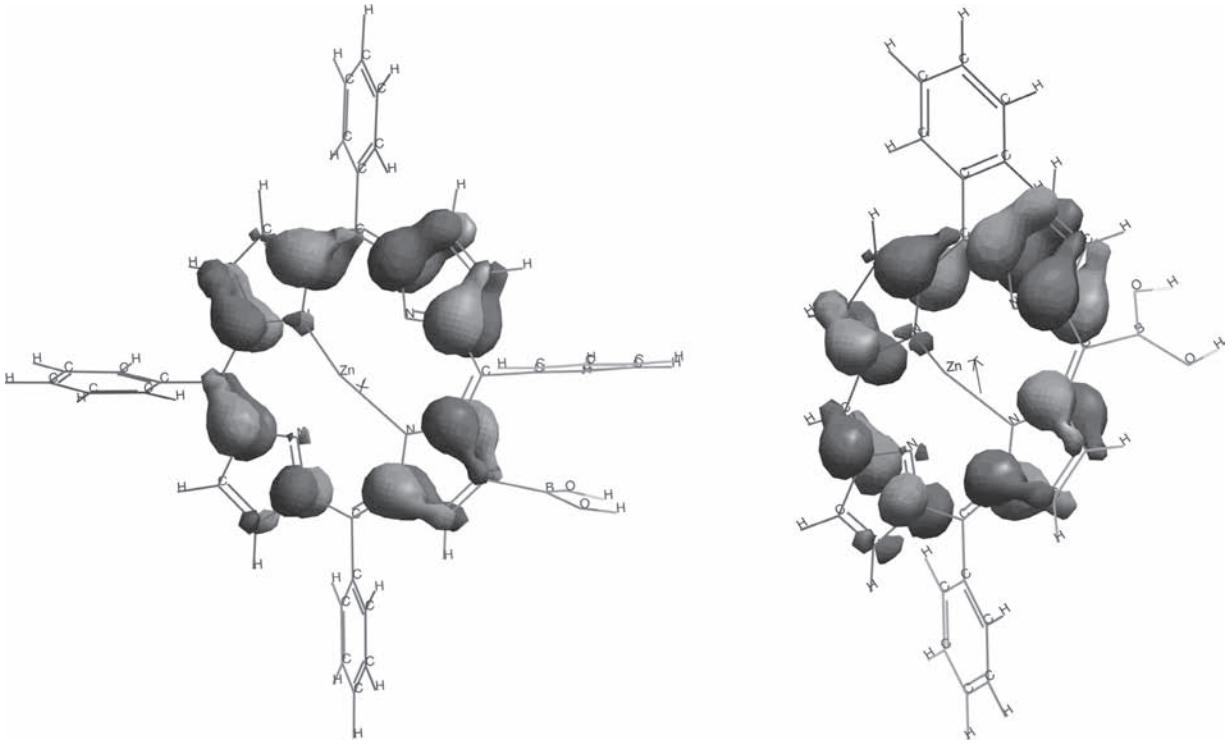


Fig. 7. MOPAC calculation of the minimum energy geometry and HOMO of **1** (left) and **2** (right)

salt solution was added dropwise into the reaction mixture. The flask was covered with aluminum foil to avoid ambient light and was stirred overnight at room temperature. The organic layer was then washed thoroughly with water, separated and evaporated *in vacuo* to make the metalloporphyrin, generally in quantitative yield.

2-bromo-5,10,15,20-tetraphenylporphyrin, 3. 5,10,15,20-tetraphenylporphyrin (TPP, 216 mg, 0.35 mmol) was dissolved in $CHCl_3$ (60 ml) with N-bromosuccinimide (NBS, 41.3 mg 0.35 mmol). The solution was refluxed while stirring for 1 h. After neutralized with several drops of pyridine, a dark-red solid was obtained by removing the solvent *in vacuo* and it was chromatographed on a column packed with silica gel using hexane/CH_2Cl_2 1:1 as eluent. The eluate obtained was evaporated to dryness to yield 0.12 g (49%) of **3** as a red solid. The starting material TPP was recovered from the column and was put through the same procedure. ^{1}H NMR ($CDCl_3$): δ, ppm -2.67 (br s, 2H), 7.74-7.83 (m, 12H), 8.26-8.32 (m, 8H), 8.76-8.98 (m, 7H). LR-MS (MALDI-TOF): *m/z* 692.2 calcd. for $C_{44}H_{29}BrN_4$, found 692.3.

[2-bromo-5,10,15,20-tetraphenylporphyrinato]-zinc(II), 4. Following the general procedure, product **3** (134.6 mg, 0.195 mmol) was metalated to make the metalloporphyrin **4** in quantitative yield. ^{1}H NMR ($CDCl_3$): δ, ppm 7.67-7.81 (m, 12H), 8.15-8.26 (m, 8H), 8.78-8.98 (m, 7H). LR-MS (MALDI-TOF): *m/z* 754.1 calcd. for $ZnC_{44}H_{29}BrN_4$, found 754.0.

[2-(4',4',5',5'-tetramethyl[1',3',2']dioxaborolan-2'-yl)-5,10,15,20-tetraphenylporphyrinato]-zinc(II), 5. Product **4** (79.2 mg, 0.1 mmol), Pd[P(*t*-Bu)$_3$]$_2$ (5.3 mg, 0.01 mmol, 10% mol), potassium acetate (51.3 mg, 0.52 mmol, 5 equiv.) and bis(pinacolato)diboron (132.8 mg, 0.52 mmol, 5 equiv.) were dissolved in 42 ml dry 1,4-dioxane in a 100 ml 3-neck round-bottom flask. The reaction mixture was degassed using a stream of Ar gas for 20 min and was refluxed under Ar protection for overnight. The reaction solution was then cooled down to room temperature and washed thoroughly with water. The organic solvent was reduced *in vacuo* and the dark-red solid obtained was subject to column chromatography (silica gel, hexane/CH_2Cl_2 1:1). The pure product **5**, after evaporation of the solvent under vacuum, was obtained in quantitative yield. ^{1}H NMR ($CDCl_3$): δ, ppm 1.24 (s, 12H), 7.68-7.79 (m, 12H), 8.20-8.27 (m, 8H), 8.74 (d, 1H), 8.87 (d, 1H), 8.91-8.94 (m, 4H), 9.28 (s, 1H). HR-MS (ESI): *m/z* 803.2545 calcd. for $ZnC_{50}H_{40}BN_4O_2$ (+H), found 803.2567.

2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrin, 6. 5 (51 mg, 0.063 mmol) and $NaIO_4$ (81.4 mg, 0.19 mmol, 6 equiv.) were dissolved in 7.5 ml 4:1 mixture of THF/H_2O in a 25 ml round-bottom flask. 2 M HCl 0.25 ml was added dropwise into the flask while stirring. The reaction mixture was allowed to stir at room temperature overnight. The mixture was then washed thoroughly with water and a pH 10.5 carbonate buffer, and the organic layer was separated, dried with anhydrous Na_2SO_4

and concentrated *in vacuo*. The resulting red solid was subject to column chromatography (silica gel, hexane/EtOAc 1:1) to yield 31 mg (74%) of product **6** as a dark red solid. ^{1}H NMR ($CDCl_3$): δ, ppm -2.71 (br s, 2H), 7.70-7.85 (m, 12H), 8.17-8.31 (m, 8H), 8.75-8.88 (m, 6H), 9.15 (s, 1H). HR-MS (ESI): *m/z* 659.2638 calcd. for $C_{44}H_{32}BN_4O_2$ (+H), found 659.2618.

(2-dihydroxylboryl-5,10,15,20-tetraphenylporphyrinato)zinc(II), 1. Following the general procedure, free base porphyrin **6** (12 mg, 0.018 mmol) was quantitatively converted to **1** as a red-purple solid. ^{1}H NMR ($CDCl_3$): δ, ppm 7.70-7.85 (m, 12H), 8.17-8.31 (m, 8H), 8.75-8.88 (m, 6H), 9.22 (s, 1H). LR-MS (MALDI): *m/z* 720.2 calcd. for $ZnC_{44}H_{29}BN_4O_2$, found 720.1. UV-vis (THF:buffer = 1:4): λ_{max}, nm (log ε) 424 (4.71), 558 (3.60), 597 (3.41).

[10-(5',5'-dimethyl[1',3',2']dioxaborinan-2'-yl)-5,15-diphenylporphyrinato]zinc(II), 8. Similar to the synthesis of **5**, starting material **7** (122 mg, 0.20 mmol) was dissolved in 20 ml dichloroethane, with bis(neopentylglycolato)diboron (220 mg, 1.0 mmol, 5 equiv.), KOAc (58.9 mg, 0.6 mmol, 5 equiv.) and $Pd[P(t\text{-}Bu)_3]_2$ (10.2 mg, 0.020 mmol, 10% mol) in a 100 ml 3-neck round-bottom flask. The reaction mixture was degassed with a stream of Ar gas for 20 min and was allowed to stir overnight at reflux under Ar protection. The reaction solution was worked up and the solid residue purified with column chromatography (silica gel, hexane/CH_2Cl_2 1:1). After evaporating off the solvent *in vacuo*, desired product **8** (82 mg, 63%) was obtained as a red-purple solid. ^{1}H NMR ($CDCl_3$): δ, ppm 1.45 (s, 6H), 4.26 (s, 4H), 7.75-7.85 (m, 6H), 8.26 (dd, J = 1.8, 7.4 Hz, 4H), 9.10 (dd, J = 4.8, 8.8 Hz, 4H), 9.39 (d, J = 4.8 Hz, 2H), 9.62 (d, J = 4.8 Hz, 2H), 10.26 (s, 1H). LR-MS (MALDI): *m/z* 636.2 calcd. for $ZnC_{37}H_{29}BN_4O_2$, found 636.2.

(10-dihydroxylboryl-5,15-diphenylporphyrinato)zinc(II), 2. Following literature method with slight modification, compound **8** (82 mg 0.13 mmol) was dissolved in a mixture of THF (130 ml) and aqueous carbonate buffer (37 ml, pH 10.5, 50 mM). Treated with N-methyldiethanlamine (0.459 ml, 3.86 mmol, 30 equiv.), the reaction mixture was stirred overnight at room temperature. 200 ml of dichloromethane was added, and the organic layer was separated, washed with saturated boric acid, saturated $NaHCO_3$ and water, dried with anhydrous Na_2SO_4 and concentrated *in vacuo*. The solid residue was subject to column chromatography (silica gel, hexane/EtOAc 2:1) to yield **9** (45 mg, 61%) as a red purple solid. A small amount of **9** was further purified with column chromatography for characterization purposes. ^{1}H NMR ($CDCl_3$): δ, ppm -3.21 (br s, 2H), 7.75-7.85 (m, 6H), 8.23 (dd, J = 3.2, 7.6 Hz, 4H), 9.04 (dd, J = 4.8, 9.6 Hz, 4H), 9.36 (d, J = 4.8 Hz, 2H), 9.45 (d, J = 4.8 Hz, 4H), 10.27 (s, 1H). LR-MS (MALDI): *m/z* 506.2 calcd. for $C_{32}H_{23}BN_4O_2$, found 506.9. HR-MS (ESI): *m/z* 507.1992 calcd. for $C_{32}H_{24}BN_4O_2$ (+H), found 507.1985. UV-vis (THF:buffer = 1:4): λ_{max}, nm (log ε) 407 (4.63), 504 (3.36), 538 (2.88), 580 (2.88), 633 (2.30). Following the general procedure, free base porphyrin **9** was metallated to yield **2** in quantitative yield,. ^{1}H NMR ($CDCl_3$): δ, ppm 7.7-7.84 (m, 6H), 8.27 (dd, J = 1.8, 7.4 Hz, 4H), 9.15 (d, J = 4.4 Hz, 4H), 9.45 (d, J = 4.4 Hz, 4H), 10.34 (s, 1H). LR-MS (MALDI): *m/z* 568.1 calcd. for $ZnC_{32}H_{21}BN_4O_2$, found 568.4. UV-vis (THF:buffer = 1:4): λ_{max}, nm (log ε) 412 (4.60), 544 (3.38), 576 (2.78).

General procedures for measuring UV-vis spectra and fluorescence spectra of porphyrins at different pH values and carbohydrate concentrations

Porphyrin solutions of various concentrations were prepared in THF. A 50 mM phosphate buffer solution at pH 7.0 was prepared by dissolving $NaH_2PO_4{\cdot}H_2O$ and Na_2HPO_4 in purified water (NANOpure Ultrapure Water System, Barnstead International). 50 mM buffer solutions at pH 2, 4, 6, 8, 10 and 12 were made in a similar way. Fructose and glucose were dissolved in the pH 7.0 buffer to make 1 M solutions.

For pH titrations, 200 μl of a porphyrin/THF solution was mixed with 800 μl of buffer solutions at difference pH values to make 1 ml solutions with a final porphyrin concentration of ~2×10^{-5} mol/L. For measurement at different carbohydrate concentrations, varying amounts of the carbohydrate were added. The UV-vis spectra of those solutions were then measured on the spectrophotometer, using a mixture of 200 μl THF and 800 μl of pH 7.0 aqueous buffer as the blank.

For fluorescence measurements, 2.5×10^{-6} mol/L solutions of the porphyrins were prepared by adding 50 μl of a 1×10^{-4} mol/L porphyrin solution to 950 μl buffer solutions having various carbohydrate concentrations. The fluorescence spectra were taken using a mixture of 50 μl THF and 950 μl of pH 7.0 buffer as the blank.

Semiemperical quantum mechanics calculation

Semiempirical quantum mechanics calculations were done using the MOPAC package (AM1) of Cerius^2 program (Accelrys, San Diego). The lowest energy geometries of the porphyrins were calculated for the boronic acid moiety with the porphyrin backbone locked in a planar geometry. The HOMO and LUMO were calculated based on the lowest energy geometry.

CONCLUSION

Two new boronic-acid-appended metalloporphyrins and their free base porphyrins were synthesized with the boronic acid moiety directly connected to the porphyrin cores in either pyrrolic or *meso*-positions. The structures were well characterized using optical spectra, NMR and MS. No changes in UV-vis or fluorescent spectra were observed in the presence of glucose or fructose up to concentrations of 300 mM over the pH range of 2 to 10. Semiempirical quantum mechanics calculations predict a geometry in which the boronic acid moiety is almost perpendicular to the porphyrin plane and not well conjugated to the porphyrin π-electron system.

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