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Synthesis of Functionalized Porphyrins as Oxygen Ligand Receptors

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Oxophilic synthetic receptors were designed and synthesized using a porphyrin scaffold, with the aim of constructing a preorganized complementary binding site for phenols and carbohydrates. We pursued three strategies for phenol recognition: (1) Lewis acid/Lewis base combinations serving as a hydrogen bond donor and acceptor for the OH group, (2) Lewis base/π-π stacking, targeting both the OH group and the aromatic moiety of phenols, and (3) exchange of the axial hydroxyl ligand on a trivalent and oxophilic metal center of aluminum porphyrin. For the recognition of acidic phenols, the most promising recognition motif was Lewis base/π-π stacking, which can bind to phenols with a hydrogen bond and π-π stacking interactions. [5-(8-Quinolyl)-10,15,20-triphenylporphyrinato]zinc binds to *p*-nitrophenol with a binding constant of 540 M^{-1} in $CHCl_3$ at 25 °C. For carbohydrate recognition, we designed the metalloporphyrin receptor having 8-quinolyl groups and *o*-carbomethoxymethoxyphenyl groups, where these Lewis basic parts serve as the cooperative hydrogen bonding sites for the hydroxyl groups of glucoside. The receptor binds to β-octyl glucoside with a binding constant of 7.35×10^4 M^{-1} in $CHCl_3$ at 15 °C, demonstrating importance of formation of a highly ordered hydrogen bonding network between the receptor and the guest. These binding features have significant implications for the rational design of oxophilic artificial receptors.

Introduction

A number of small biomolecules such as amino acids, oligopeptides, amines, steroids, and carbohydrates constitute an important class of compounds that behave as signaling molecules in metabolism, gene translation/transcription, and DNA replication.[1] Owing to their fundamental importance in nature, design of artificial receptors for these molecules is a challenging subject for chemists, and numerous endeavors have been carried out so far. Porphyrins have been regarded as one of the most versatile receptor scaffolds because of the following unique features:[2](1) a rigid framework to which various functional groups can be attached, (2) high susceptibility for the spectroscopic methods to probe the intermolecular interactions, (3) 7×7 Å^2 of the aromatic framework, a potentially efficient counterpart for van der Waals and charge-transfer interactions, (4) a number of metals incorporated with varying Lewis acidity, and (5) the systematic and comprehensive studies on synthesis of a range of porphyrin derivatives. Despite a variety of functional groups present in all signaling molecules involving amino groups and/or hydroxyl groups, most sophisticated porphyrin-based artificial receptors have targeted ligands having nitrogenous donor ligands.[2] The development of a highly oxophilic receptor binding phenols and carbohydrates is thus an area of active research.[2] Herein we report the design, synthesis, and characterization of porphyrin receptors in order to establish a recognition unit having an oxophilic character, particularly focusing on the efforts to prepare a preorganized complementary binding site for phenol[3] and carbohydrate derivatives.[4]

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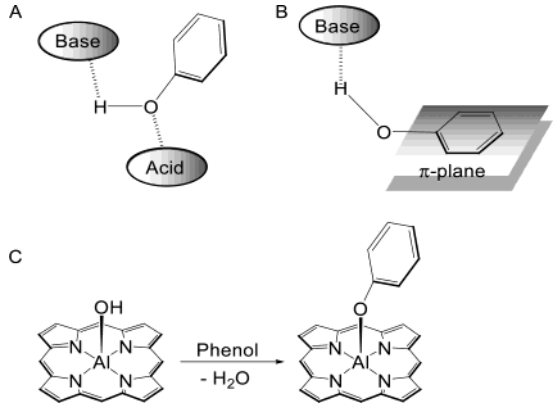


FIGURE 1. Three strategies and binding modes for phenol recognition.

Results and Discussion

Design and Synthesis of Phenol Receptors. We pursued three strategies for phenol recognition, as schematically illustrated in Figure 1. Part A illustrates Lewis acid/Lewis base combinations that enable the receptor to recognize the oxygen and the hydrogen of phenol cooperatively. We needed to fix acidic and basic groups at a close distance with no direct interaction between them. Part B represents Lewis base/π-π stacking that binds both the phenolic hydrogen atom and the benzene ring of phenol cooperatively. Porphyrin has a large aromatic moiety and high polarizability, thus providing an ideal framework for effective π-π stacking interactions.[5,6] Part C illustrates exchange of the axial hydroxyl ligand on a trivalent and oxophilic metal center, where the hydroxyl group is released as water. Recently Sanders et al. reported several supramolecular assemblies of heterometallic oligoporphyrins using dihydroxy-tin(IV) porphyrin along this line.[7] We studied instead the oxygen ligand exchange on the monohydroxy-aluminum porphyrin with a five-coordinate geometry,[8] where binding constant analysis of one ligand exchange may be expected to be more concise and straightforward.

We designed and prepared nine porphyrin receptors as shown in Figure 2. As to Lewis acid/Lewis base combinations, porphyrin **Zn·1** was designed to have four methyl ester groups placed near the metal with an insufficient distance for intramolecular coordination to the metal. Our previous binding studies with several amines indicated that carbomethoxymethoxy groups (CH_3OCOCH_2O-) attached at the ortho position of the phenyl groups do not coordinate to the metal center and serve as hydrogen bonding acceptor sites for the coordinated amino groups (Zn···NH_2···O=C).[9] Porphyrin **Zn·2** was also prepared as a Lewis acid−Lewis base type of receptor. Molecular modeling showed that the intramolecular coordination of the pyridyl group to the zinc caused a significant conformational strain, and the pyridyl group is expected to be a hydrogen acceptor without quenching the Lewis acidity of zinc. Porphyrins **FB·1**, **FB·2**, **FB·3**, **Zn·3**, and **Ni·3** having carbomethoxymethoxy groups, an *o*-pyridylmethoxyphenyl group, or an 8-quinolyl group on the meso position were designed on the basis of Lewis base/π-π stacking strategy. For the axial OH ligand exchange strategy, we prepared **Al·TPP** and **Al·1**, where the effect of the methyl ester groups on complexation is of particular interest. **FB·TPP** and **Zn·TPP** were used as reference receptors.

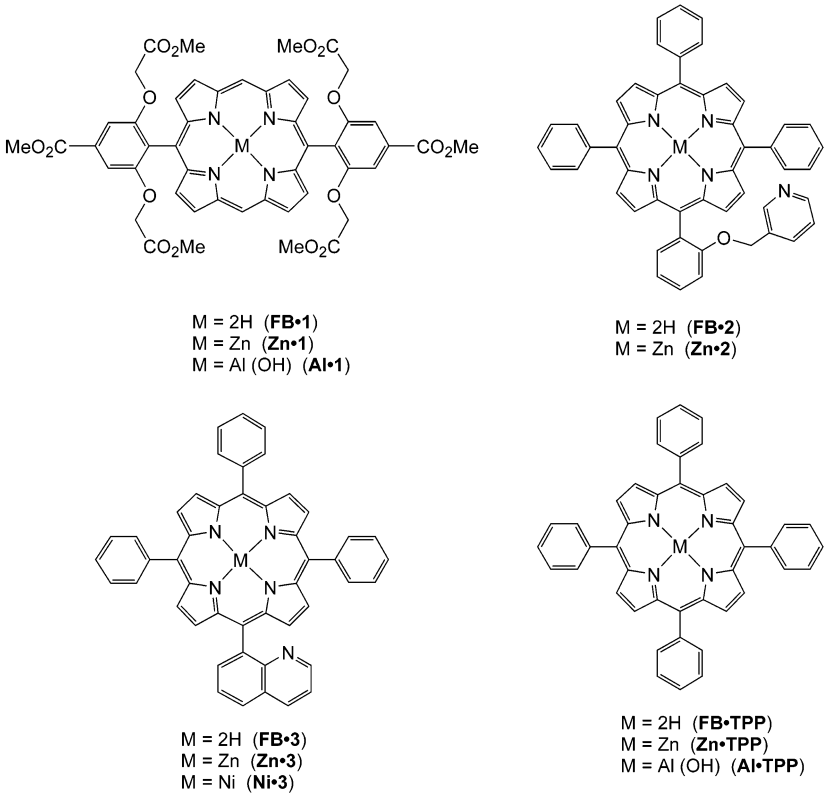
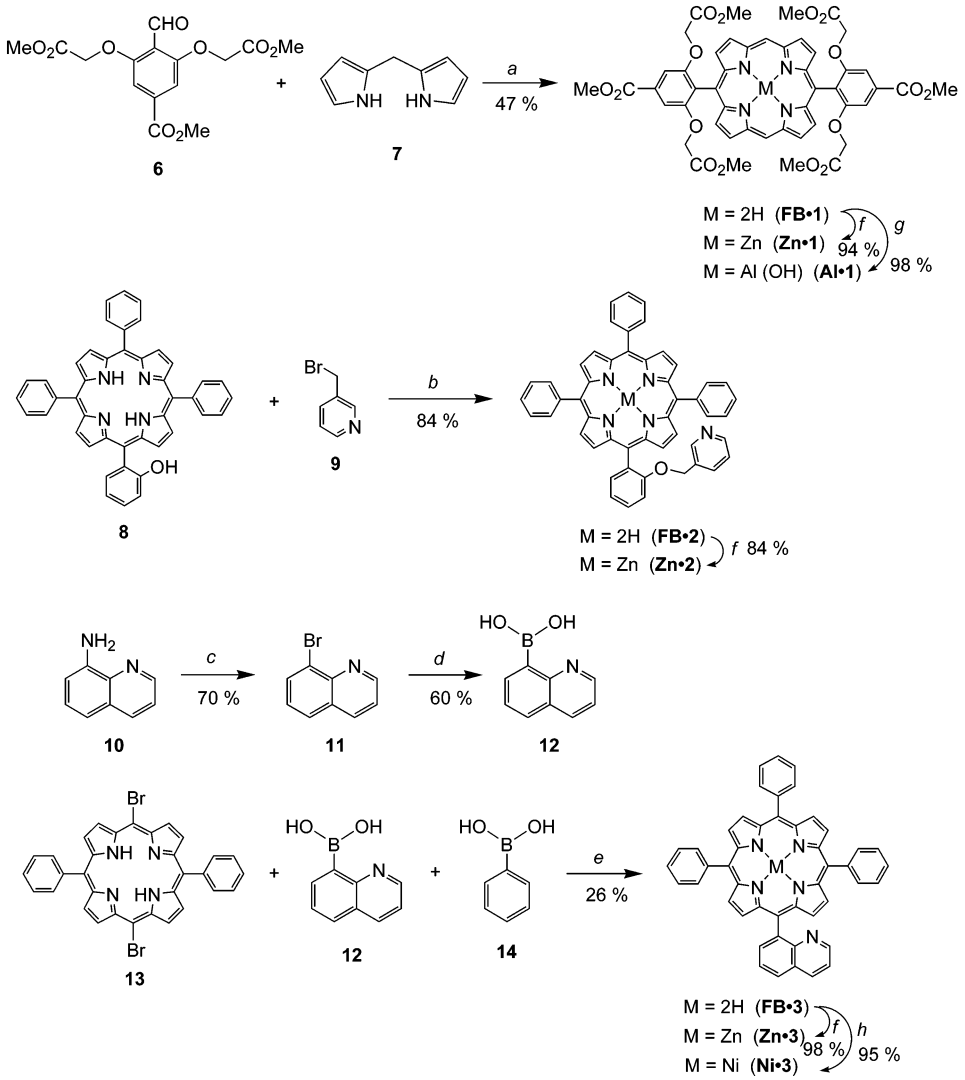


FIGURE 2. Porphyrin receptors for phenol derivatives.

SCHEME 1[a]



[a] Reagents: (a) TFA/CH_2Cl_2, then DDQ; (b) K_2CO_3/DMF; (c) *tert*-butyl nitrite, $CuBr_2/CH_3CN$; (d) *n*-BuLi/THF, $B(OMe)_3$ then H_3O^+; (e) $Pd(P(Ph)_3)_4$/2 M Na_2CO_3, EtOH, toluene; (f) $Zn(OAc)_2/CHCl_3$; (g) $AlMe_3/CH_2Cl_2$, then H_2O; (h) $Ni(OAc)_2/CHCl_3$.

These porphyrin receptors were synthesized according to Scheme 1. Porphyrin **1** was synthesized from aldehyde **6** and dipyrromethane **7** by the [2 + 2] condensation[10] using trifluoroacetic acid as acid catalyst, followed by subsequent oxidation of the porphyrinogen with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ). Hydroxo(tetraphenylporphinato)aluminum(III) **(Al·TPP)** was prepared quantitatively by the reported procedure[11] using trimethyaluminum in CH_2Cl_2, followed by reaction with water. In the synthesis of receptor **Al·1**, the reaction of **FB·1** with trimethyaluminum at room temperature caused its nucleophilic attack on the methyl ester groups. This side reaction can be avoided by adding an excess amount of trimethyaluminum at −78 °C in CH_2Cl_2. Porphyrin **2** was synthesized by a Williamson etherification of 5-(2-hydroxyphenyl)-10,15,20-triphenylporphyrin **8** with 3-bromomethylpyridine **9** under basic conditions. Porphyrin **3** was synthesized by a Suzuki cross-coupling reaction[12] of dibromoporphyrin **13**, 8-quinolylboronic acid **12,** and phenylboronic acid **14** in equimolar amounts. 8-Quinolylboronic acid **12** was synthesized from commercially available 8-aminoquinoline **10** via stepwise reactions of *tert*-butyl nitrite-anhydrous copper(II) halides

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deamination[13] and lithiation with *n*-butyllithium followed by boration with trimethyl borate.[14] Divalent metal insertion was carried out by the usual method ($Zn(OAc)_2$/$CHCl_3$ for zinc, $Ni(OAc)_2$/$CHCl_3$ for nickel). All compounds were characterized by ^1H NMR, high-resolution mass spectroscopy, and elemental analysis. Since the ^1H NMR spectrum of **Zn·2** in $CDCl_3$ shows unresolved broad peaks due to intra- and/or intermolecular coordination of the pyridyl group to the zinc atom, the ^1H NMR spectrum was recorded in deuterated DMSO.

Binding of Porphyrins Having Lewis Basic Sites to Phenols. To explore the strategies A and B (Figure 1), the binding constants of porphyrin receptors bearing Lewis basic groups with phenol and *p*-nitrophenol were determined by UV−visible titration in CH_2Cl_2 at 25 °C. Addition of phenol caused a red shift in the Soret band, and nonlinear least-squares curve fitting of the absorbance changes to a 1:1 association model gave satisfactory results. For all combinations of the receptors and the guests, isosbestic points were always observed, consistent with 1:1 complex formation. The results are listed in Table 1.

Receptor **Zn·1** having a recognition site composed of a Lewis acid/base combination showed weak binding to phenol ($K_a = 3\ M^{-1}$) but moderate binding to *p*-nitrophenol ($K_a = 220\ M^{-1}$). Receptor **Zn·2** did not bind to phenol but bound to *p*-nitrophenol. The binding constant of **Zn·2** is much smaller than that of **Zn·1**. This can be attributed to intramolecular or intermolecular coordination of the pyridyl group to the zinc atom or π-π stacking of the pyridyl ring to the porphyrin.[15]

Zinc receptor (**Zn·3**) showed the highest affinity among receptors used in this study; the binding constant for *p*-nitrophenol ($K_a = 540\ M^{-1}$) was two times larger than that of **Zn·1**. Phenol is expected to bind to **Zn·3** via the binding mode B (Figure 1), since the Lewis basic site is too far away to adopt the binding mode A. ^1H NMR studies also supported this binding mode (vide infra).

TABLE 1. Binding Constants, *K*, between Porphyrin Receptors and Phenol Derivatives at 25°C[a]

	$K\ (M^{-1})$		
	phenol	*p*-nitrophenol	possible interaction mode
Zn·1	3	220	Lewis acid−Lewis base
FB·1	*b*	*b*	Lewis base−π-π stacking
Zn·2	*b*	2	Lewis acid−Lewis base
FB·2	*b*	100	Lewis base−π-π stacking
Zn·3	5	540	Lewis base−π-π stacking
Ni·3	3	350	Lewis base−π-π stacking
FB·3	< 1	220	Lewis base−π-π stacking
Zn·TPP	*b*	*b*	
FB·TPP	*b*	*b*	
8-methylquinoline[c]	*e*	44	

[a] Determined by UV−vis titration experiments in CH_2Cl_2. Estimated errors of the binding constants are less than 5%. [b] Not bound. [c] determined by ^1H NMR titration experiments in CD_2Cl_2. Estimated error of the binding constant is less than 10%. [e] Not determined.

Interestingly, binding constants increase in the order **FB·3** < **Ni·3** < **Zn·3**. We speculate that the following two factors may be important to explain the affinity. First, the order appears to correspond to the electron density of the porphyrin plane. It is well-known that the porphyrin plane has high polarizability and is capable of accommodating aromatic guests.[16] Schneider et al. reported that the dispersion forces between porphyrin receptor and aromatic guests is essentially a function of the number of participating π electrons.[17] Thus, the porphyrin receptors having the central metal with larger atomic number lead to the stronger dispersion forces with the aromatic moiety of guest relative to free-base porphyrin. The binding constant of 8-methylquinoline with *p*-nitrophenol was determined to be 44 M^{-1} from ^1H NMR titration experiments in CD_2Cl_2 at 25 °C, which strongly supported that the additional dispersion force between the porphyrin and the benzene ring of the guest can stabilize the complex. Second, the order also corresponds to the reported redox potential $E_{1/2}$ (vs SCE) of the porphyrin/porphyrin cation radical couple: 1.08 V for **FB·TPP**, 1.05 V for **Ni·TPP**, and 0.78 V for **Zn·TPP**.[18] This trend implies that, although no additional charge-transfer band was found in the long-wavelength region of the UV−visible spectrum, charge-transfer interactions between the porphyrin and the aromatic moiety of the guest would provide the driving force for the complex formation.

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(15) Both **Zn·2** and **FB·2** exhibited upfield shifted pyridine proton resonances (see Experimental Section), suggesting that the pyridyl group is located near the binding site. Molecular modeling indicated the π-π stacked conformation as a major one, although a possibility of intramolecular coordination of the pyridyl group to the zinc cannot be excluded.
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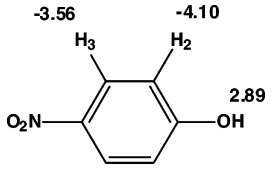

FIGURE 3. The CIS values of *p*-nitrophenol complexed with receptor **Zn·3** in CD_2Cl_2 at 25 °C.

TABLE 2. Binding Constants, *K*, between Porphyrin Receptors and Phenol Derivatives in CH_2Cl_2 at 25°C.[a]

guest	*K* (M^{-1}) FB·3	*K* (M^{-1}) Zn·3	pK_a	LUMO (eV)	HOMO (eV)
p -methylphenol	<1	16	10.26	0.33	−8.95
p-methoxyphenol	<1	9	10.25	0.22	−8.71
phenol	<1	5	9.97	0.29	−9.18
methyl 4-hydroxybenzoate	12	130	8.47	−0.42	−9.53
p -nitrophenol	220	540	7.15	−1.08	−10.17
pentafluorophenol	770	690	5.53	−1.34	−10.21

[a] Determined by UV−vis titration experiments. Estimated errors of the binding constant are less than 5%.

^{1}H NMR Analysis on Complexation with *p*-Nitrophenol. ^{1}H NMR spectroscopic investigations of the complex between receptor **Zn·3** and *p*-nitrophenol demonstrated that *p*-nitrophenol is bound in π-π staking. The complexation-induced shifts (CIS) of the 1-OH, 2-H, 3-H resonances of *p*-nitrophenol were determined in CD_2Cl_2 in the low concentration range of receptor **Zn·3**. The observed chemical shifts were the average values of the free ligand and the complexed ligand in the limit of fast chemical exchange. Upon addition of **Zn·3**, the resonance for the 1-OH proton moved downfield and those for the 2-H, 3-H protons moved upfield. The CIS values were linearly increased as the fraction of the ligand complexed with the receptor was increased, and the CIS values for the complex are determined by extrapolation to 100% complexation: −3.56, −4.10, and 2.89 ppm for 3-H, 2-H, and 1-OH respectively (Figure 3). Similarly, the CIS values with 8-methylquinoline are determined to be −0.01 and −0.07 ppm for 3-H and 2-H, respectively. These CIS values can be explained by considering two opposing anisotropic effects: an upfield shift due to the ring current of porphyrin[19] when the ligand protons are located above the porphyrin plane and a downfield shift of the OH proton upon hydrogen bonding. The observed shifts show that the aromatic protons of *p*-nitrophenol are located close enough for π-π interaction between the aromatic systems of porphyrin and phenol.

Binding of Receptor 3 with Various Phenol Derivatives. Binding affinity of receptor **Zn·3** with various phenols exhibited an intriguing trend. Table 2 summarizes the observed binding constants, phenol derivative's pK_a,[20] and the LUMO and HOMO energy levels calculated by the PM3 semiempirical molecular orbital method. Obviously the receptor prefers the phenol having lower pK_a and lower LUMO energy, which can be associated with the stronger hydrogen bonding and stronger charge-transfer type π-π interaction. Interestingly, as pK_a and LUMO energy increase, the magnitude of the binding constants goes through a minimum at unsubstituted phenol and then slightly increases again, suggesting that dispersion forces also contribute significantly to the stabilization of the complex. This trend implies the difficulty of binding unsubstituted phenol. The natural receptor such as the estrogen receptor recognizes the ligand containing the phenol structural element by formation of a multiple hydrogen bonding network with the surrounding hydroxyl groups and a number of van der Waals contacts with the nonpolar moieties.[21] Thus tight binding for phenol may be realizable by appending a larger number of multiple interactions in receptors with a higher degree of preorganization.

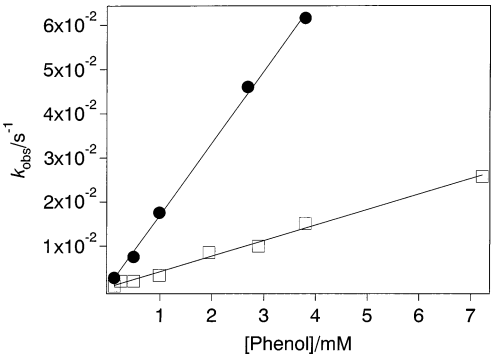

FIGURE 4. Plot of observed pseudo-first-order rate constants (k_{obs}) for **Al·1** (●, 1.7 μM) and **Al·TPP** (□, 2.5 μM) as a function of the phenol concentrations in CH_2Cl_2 at 25 °C.

Kinetics of Binding of Phenols to Aluminum Porphyrins. The association rate constants k_{on} of **Al·TPP** and **Al·1** with phenol were measured by monitoring the absorbance changes of the Soret band as a function of time in CH_2Cl_2 at 25 °C after an excess of phenol was added. The curve fitting of the saturation plot to the pseudo-first-order kinetics yields an apparent rate constant for complex formation. As shown in Figure 4, the second-order rate constant k_{on} was determined to be 3.68 and 16.6 M^{-1} s^{-1} for **Al·TPP** and **Al·1,** respectively. Half-life of complex formation was 75.5 h for **Al·TPP** and 16.7 h for **Al·1** if we assumed that equivalent reactant concentrations (1.0 μM) were used. Although the methyl ester groups of receptor **Al·1** accelerate the complex formation rate (4.5-fold increase in the association rate relative to that of receptor **Al·TPP**), we concluded that the exchange rate of the hydroxide anion to the phenoxide anion on the axial position of aluminum porphyrin is very slow, and such kinetic profile is not suited for a molecular recognition process at below a micro molar concentration. On the other hand, when one changes the guest molecules to amine, such as pyridine, the complex formation rate appears to be faster. UV−visible titration experiments showed that addition of pyridine caused an instantaneous red shift in the Soret band of the alumi-

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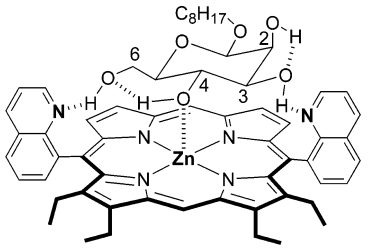


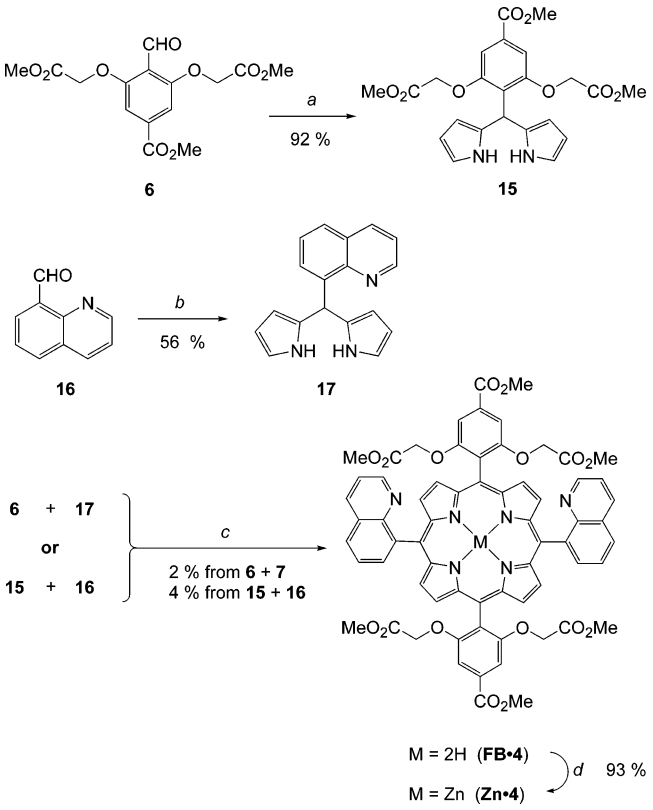
FIGURE 5. Schematic representation of hydrogen bonding networks of [*cis*-5,15-bis(8-quinolyl)octaethylporphyrinato]zinc-(II) (**Zn·5**) and *β*-octyl glucoside complex.

num porphyrin. The Soret band of a solution of **Al·TPP** in CH_2Cl_2 was shifted from 415 to 426 nm at 25 °C. The binding constants of pyridine were determined to be $K_1 = 2840\ M^{-1}$ and $K_2 = 21\ M^{-1}$ by using the 1:1 and 1:2 binding isotherm: $K_1 = [P{\cdot}G]/([P][G])$, and $K_2 = [P{\cdot}G_2]/([P{\cdot}G][G])$, where K_1 and K_2 can be ascribed to coordination of pyridine to the aluminum atom as the sixth ligand, and hydrogen bonding of another pyridine to the axial hydroxyl group, respectively. For lutidine (2,6-dimethylpyridine), the receptor and the guest form a 1:1 hydrogen-bonding complex and the binding constant was determined to be $53\ M^{-1}$. The binding constant for lutidine is similar to K_2 for pyridine, suggesting lutidine is bound to **Al·TPP** through hydrogen bonding (AlOH··· ·N), and direct coordination to the Al is hampered as a result of the steric hindrance of the 2,6-dimethyl groups.

Design and Synthesis of Carbohydrate Receptors. Our previous study[22] of the binding of carbohydrates to functionalized zinc porphyrins showed that [*cis*-5,15-bis(8-quinolyl)octaethylporphyrinato]zinc(II) (**Zn·5**) exhibited marked affinity for octyl glucoside and mannoside in $CHCl_3$ ($-\Delta G° = 4.5-6.3$ kcal mol^{-1}). Analysis of the complexation-induced shifts of the carbohydrate OH protons in the ^{1}H NMR revealed that receptor **Zn·5** bound the 4-OH group of glucoside by coordination to the zinc and the 6-OH and 3-OH groups by hydrogen bonding to the quinolyl nitrogen atoms, as shown in Figure 5. We concluded that a dominant factor of their affinity and selectivity for carbohydrates is understood in terms of the combination of Lewis acid (zinc) and Lewis bases (quinolyl nitrogens). Our strategy to employ ester and quinolyl groups as Lewis basic sites was extended to carbohydrate recognition. We prepared receptor **Zn·4** having carbomethoxymethoxy groups attached at the ortho position of the phenyl groups, which would serve as additional hydrogen bonding sites for glucoside recognition.

The retrosynthetic analysis for receptor **Zn·4** indicated that there are two synthetic routes using the [2 + 2] condensation, that is, **6** + **17** or **15** + **16** combinations. We attempted to perform both synthetic routes (Scheme 2). 5-Substituted dipyrromethanes **15**[23] and **17**[24] were prepared by Lindsey's procedures, and dipyrromethane **15** was obtained in a good yield (92%) compared with **17** (56%). For the preparation of dipyrromethane from heterocyclic aldehyde, we employed no acid catalyst

SCHEME 2[a]



[a] Reagents: (a) TFA/pyrrole; (b) pyrrole; (c) TFA/CH_2Cl_2, then DDQ; (d) $Zn(OAc)_2$/$CHCl_3$.

because it is reported that no dipyrromethane was obtained under acidic conditions.[24] The ^{1}H NMR spectrum of dipyrromethane **15** shows that the methylene resonance of the ester groups appeared as a broad signal in the upfield region in comparison with aldehyde **6**, and the pyrrolic NH appeared at 9.45 ppm, downfield shifted from that of 5-phenyldipyromethane (7.92 ppm), and suggested that an intramolecular hydrogen bond formed between pyrrolic protons and ester groups. This interaction could exert a template effect on synthesis of **15**. The [2 + 2] condensation was carried out under the optimized conditions reported by Lindsey's group.[25] Although receptor **4** has two atropisomers (*cis* and *trans* form), the rotation rate around the porphyrin-quinoline bond is slow, and the desired *cis* isomer can be readily isolated by column chromatography on silica gel. Our two synthetic routes resulted in no scrambling during the condensations, and the [**15** + **16**] combination gave a better yield (4%) than the [**6** + **17**] combination (2%).

Binding Analysis with Octyl Glucoside. Binding constants are determined in the same manner described above in amylene-containing $CHCl_3$ at 15 °C and are listed in Table 3. Although the atropisomerization from the *cis* isomer (**Zn·4**) to the *trans* isomer in a $CHCl_3$ solution occurred slowly (no isomerization was observed in the solid state), the receptor solution was prepared just before use. The binding affinities for *β*-octyl glucoside increase in the order **Zn·1** < **Zn·3** < **Zn·5** < **Zn·4**. The binding constant of receptor **Zn·3** was larger than that

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TABLE 3. Binding Constants, K/M^{-1}, between Porphyrin Receptors and β-octyl Glucoside in Amylene-Containing $CHCl_3$ at 15 °C[a]

receptor	K (M^{-1})
Zn·1	380
Zn·3	2 300
Zn·5	41 000
Zn·4	74 000

[a] Estimated errors of the binding constants are less than 5%.

of receptor **Zn·1**, which may originate from the difference in basicity between the quinolyl nitrogen and the ester oxygen. Receptor **Zn·4** showed the highest binding constant among the receptors studied in this work, suggesting additional stabilization from the ester groups. On the basis of the receptor−glucoside complex structure shown in Figure 5, we inferred that one methyl ester group would interact with acidic 4-OH of glucoside, whereas 2-OH may not interact because of steric repulsion with the bulky octyl group. The receptor **Zn·4** can be readily converted to a water-soluble receptor by alkaline hydrolysis of the methyl ester groups. Binding studies in water are currently under investigation.

Conclusions

The present study described three strategies for constructing the receptor structure having a strong oxophilic character. For recognition of phenol derivatives, we concluded that the most promising structure is porphyrin **Zn·3**, where the combination of Lewis base and π-π stacking, employing both hydrogen bonding and π-π interaction, is an effective strategy for phenol recognition in terms of affinity and selectivity. Although acidic phenols are bound with moderate affinity, unsubstituted phenol is bound only very loosely. For recognition of carbohydrates, we succeeded in improving the affinity of the previously reported bisquinolylporphyrin receptor (**Zn·5**). The more intricate Lewis acid/Lewis base combinations resulted in higher-ordered hydrogen bonding network and the coordination to the zinc atom, which led to improved binding affinity. These binding features can provide some important implications for the rational design of oxophilic artificial receptors.

Experimental Section

General Methods. ^{1}H NMR spectra (500 MHz) were recorded in deuterated solvents using solvent residuals as internal references. UV−visible spectra were recorded on a spectrophotometer with a thermostated cell compartment. High-resolution FAB mass spectra were obtained using 3-nitrobenzyl alcohol as a matrix.

Materials. Methyl 4-formyl-3,5-bis(methoxycarbonylmethoxy)benzoate (**6**),[26] dipyrromethane (**7**),[22] 5-(2-hydroxyphenyl)-10,15,20-triphenylporphyrin (**8**),[27] 5,15-dibromo-10,20-diphenylporphyrin (**13**),[10b] and 8-formylquinoline (**16**)[28] were prepared according to literature procedures. CH_2Cl_2 and CH_3CN were distilled from CaH_2, DMF was distilled from P_2O_5, and THF was distilled from sodium/benzophenone ketyl.

Titration Experiments. Titration experiments were carried out by use of UV−visible or ^{1}H NMR spectrometers. Binding constants were evaluated by a nonlinear least-squares parameter estimation based on the Damping Gauss−Newton algorithm or the Marquardt algorithm.

5,15-Bis(4-methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)porphyrin (FB·1). Aldehyde **6** (3.40 g, 10 mmol) and dipyrromethane **7** (1.46 g, 10 mmol) were dissolved in CH_2Cl_2 (1 L) under N_2, and then trifluoroacetic acid (454 μL, 5.94 mmol) was added. After the reaction mixture was stirred at room temperature for 3 h, 2,3-dichloro-5,6-dicyanobenzoquinone (3 g, 13.2 mmol) was added, and the mixture was refluxed for 2 h. The solution was then neutralized by addition of triethylamine (908 μL, 6.53 mmol) and concentrated. The mixture was separated by column chromatography (SiO_2, $CHCl_3$/AcOEt = 100/1 to 10/1), and the crude product was washed with methanol thoroughly to afford **6** as a purple solid (2.19 g, yield 47%): ^{1}H NMR ($CDCl_3$) δ −3.10 (s, 2H), 3.49 (s, 12H), 4.09 (s, 6H), 4.37 (s, 8H), 7.62 (s, 4H), 9.04 (d, J = 4.5 Hz, 4H), 9.32 (d, J = 4.5 Hz, 4H), 10.19 (s, 2H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 408 (5.78), 502 (4.47), 535 (3.96), 576 (4.00); HRMS (FAB) (M^+) calcd for $C_{48}H_{42}N_4O_{16}$ 930.2596, found 930.2593. Anal. Calcd for $C_{48}H_{42}N_4O_{16}$: C, 61.93; H, 4.55; N; 6.02. Found: C, 62.19; H, 4.60; N; 6.12.

[5,15-Bis(4-methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)porphyrinato]-zinc(II) (Zn·1). A solution of **FB·1** (600 mg, 645 μmol) and $Zn(OAc)_2$-saturated methanol (15 mL) in $CHCl_3$ (300 mL) was refluxed for 3 h. After cooling, the solution was washed successively with saturated aqueous $NaHCO_3$ (100 mL × 2) and saturated aqueous NaCl (100 mL × 2) and dried over Na_2SO_4. Evaporation of the solvent and purification by flash column chromatography (SiO_2, $CHCl_3$/AcOEt = 10/1) afforded **Zn·1** as a pink solid (600 mg, 94%): ^{1}H NMR ($CDCl_3$) δ 3.42 (s, 12H), 4.09 (s, 6H), 4.36 (s, 8H), 7.63 (s, 4H), 9.09 (d, J = 4.5 Hz, 4H), 9.37 (d, J = 4.5 Hz, 4H), 10.21 (s, 2H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 409 (5.60), 537 (4.32), 573 (4.00); HRMS (FAB) (M^+) calcd for $C_{48}H_{40}N_4O_{16}Zn$ 992.1731, found 992.1735.

Hydroxo[5,15-bis(4-methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)porphyrinato]aluminum-(III) (Al·1). A solution of **FB·1** (122 mg, 131 μmol) in CH_2Cl_2 (30 mL) was cooled to −78 °C under N_2, and $AlMe_3$ (2.0 M in toluene, 2.0 mL, 4 mmol) was added dropwise during 30 min. After 4 h, water (20 mL) was carefully added dropwise, and then the dry ice bath was removed. The solution was washed successively with saturated aqueous NaCl (100 mL × 2) and water (50 mL), and the organic layer was dried over Na_2SO_4. Evaporation of the solvent and recrystallization from CH_2Cl_2/hexane afforded **Al·1** as a pink solid (125 mg, 98%): ^{1}H NMR ($CDCl_3$) δ 3.42 (s, 12H), 4.10 (s, 6H), 4.28 (s, 8H), 7.61 (s, 4H), 9.16 (bs, 4H), 9.43 (bs, 4H), 10.30 (s, 2H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 405 (5.54), 537 (4.12), 575 (3.63); HRMS (FAB) ((M − OH)$^+$) calcd for $C_{48}H_{40}AlN_4O_{16}$ 955.2255, found 955.2254.

5-[2-(3-Pyridylmethoxy)phenyl]-10,15,20-triphenylporphyrin (FB·2). A mixture of 5-(2-hydroxyphenyl)-10,15,20-triphenylporphyrin (**8**) (700 mg, 1.11 mmol), 3-bromomethylpyridine hydrobromide (**9**) (600 mg, 2.37 mmol), and K_2CO_3 (2.5 g) in DMF (20 mL) was stirred at 60 °C for 6 h under N_2. After AcOEt (100 mL) was added, the organic layer was washed successively with saturated aqueous NaCl (100 mL × 3) and dried over $MgSO_4$. Evaporation of the solvent and purification by flash column chromatography (SiO_2, $CHCl_3$/AcOEt = 100/1 to 10/1) afforded **FB·2** as a purple solid (670 mg, 84%): ^{1}H NMR ($CDCl_3$) δ −2.75 (s, 2H), 4.94 (s, 2H), 6.36 (m, 1H), 6.47 (d, J = 7.5 Hz, 1H), 7.35 (d, J = 7.5 Hz, 1H), 7.39 (t, J = 7.5 Hz, 1H), 7.74 (m, 10H), 8.06 (m, 3H), 8.20 (m, 6H), 8.65 (m, 8H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 418 (5.62), 515 (4.26), 548 (3.84), 592 (3.73), 648 (3.66); HRMS (FAB) (M^+) calcd for $C_{50}H_{35}N_5O$ 721.2842, found 721.2842; Anal. Calcd for $C_{50}H_{35}N_5O$: C, 83.19; H, 4.89; N; 9.70. Found: C, 82.96; H, 5.19; N; 9.59.

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5-[(2-(3-Pyridylmethoxy)phenyl)-10,15,20-triphenylporphyrinato]zinc(II) (Zn·2). This compound was prepared from **FB·2** (78 mg, 108 μmol) in a manner similar to that for **Zn·1** (71 mg, 84%): ^{1}H NMR (DMSO-d_6) δ 5.12 (s, 2H), 6.68 (dd, J = 5.0 Hz, 7.5 Hz, 1H), 6.91 (d, J = 5.0 Hz, 1H), 7.41 (t, J = 7.5 Hz, 1H), 7.56 (d, J = 7.5 Hz, 1H), 7.79 (m, 9H), 7.85 (m, 1H), 7.99 (m, 3H), 8.17 (m, 6H), 8.74 (m, 8H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 426 (5.67), 562 (4.11), 603 (3.82); HRMS (FAB) (M^+) calcd for $C_{50}H_{33}N_5OZn$ 783.1977, found 783.1995.

8-Quinolineboronic Acid (12). To a solution of anhydrous copper(II) halide (42.88 g, 192 mmol) and *tert*-butyl nitrite (35.5 mL, 320 mmol) in anhydrous CH_3CN (640 mL) was added 8-aminoquinoline **(10)** (23 g, 160 mmol) at room temperature under N_2. The reaction mixture was heated to 65 °C and then stirred for 12 h. The mixture was concentrated, and ether (600 mL) was added. The organic layer was washed with water (200 mL × 5) and dried over $MgSO_4$. Evaporation of the solvent and distillation under reduced pressure at 160−180 °C (0.4 mmHg) afforded 8-bromoquinoline (**11**) as a yellow oil (23.4 g, 70%). A solution of **11** (2.68 g, 12.8 mmol) in THF (10 mL) was cooled to −78 °C under N_2, and *n*-butyllithium (1.55 M in hexane, 10 mL, 15.5 mmol) was added dropwise during 30 min. After 1 h, trimethyl borate (3 mL) was added dropwise, and then the ice bath was removed. The mixture was stirred for 1 h at room temperature, and then 3 M HCl (30 mL) was added. The aqueous layer was washed with Et_2O and neutralized with solid $NaHCO_3$. The resulting light brown precipitate was collected, which was recrystallized from acetone/hexane to give **12** as a pale yellow solid (1.38 g, 60%): ^{1}H NMR (CD_3OD) δ 7.56 (t, J = 7.5 Hz, 1H), 7.69 (dd, J = 5.0 Hz, 7.5 Hz, 1H), 7.80 (d, J = 7.5 Hz, 1H), 8.10 (dd, J = 1.5 Hz, 7.5 Hz, 1H), 8.52 (d, J = 7.5 Hz, 1H), 8.57 (dd, J = 1.5 Hz, 5.0 Hz, 1H); HRMS (EI) (M^+) calcd for $C_9H_8BNO_2$ 173.0648, found 173.0649. Anal. Calcd for $C_9H_8BNO_2$: C, 62.49; H, 4.66; N; 8.10. Found: C, 62.41; H, 4.55; N; 8.07.

5,10,15-Triphenyl-20-(8-quinolyl)porphyrin (FB·3). A mixture of 5,15-dibromo-10,20-diphenylporphyrin **13** (240 mg, 387 μmol), 8-quinolylboronic acid **12** (67 mg, 387 μmol), phenylboronic acid **14** (47 mg, 387 μmol), and tetrakis-(triphenylphosphine)palladium (27 mg, 23 μmol) in a mixed solvent of toluene (40 mL), ethanol (4 mL), and a deoxygenated 2 M Na_2CO_3 aqueous solution (8 mL) was stirred at 80 °C for 13 h under N_2. After AcOEt (30 mL) was added, the organic layer was washed successively with 3 M HCl (40 mL), saturated aqueous Na_2CO_3 (50 mL), and saturated aqueous NaCl (100 mL × 3) and dried over Na_2SO_4. Evaporation of the solvent and purification by flash column chromatography (SiO_2, $CHCl_3$/AcOEt = 100/1 to 10/1) afforded **FB·3** as a purple solid (67 mg, 26%): ^{1}H NMR ($CDCl_3$) δ −2.59 (s, 2H), 7.37 (dd, J = 4.0 Hz, 7.5 Hz, 1H), 7.73 (m, 9H), 7.92 (dd, J = 1.5 Hz, 6.0 Hz, 1H), 8.25 (m, 6H), 8.41 (dd, J = 2.0 Hz, 7.5 Hz, 1H), 8.49 (d, J = 1.5 Hz, 1H), 8.50 (m, 1H), 8.51 (d, J = 4.5 Hz, 2H), 8.57 (dd, J = 1.5 Hz, 7.5 Hz, 1H), 8.73 (d, J = 4.5 Hz, 2H), 8.82 (m, 4H); HRMS (FAB) (M^+) calcd for $C_{47}H_{31}N_5$ 665.2579, found 665.2577; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 419 (5.63), 514 (4.21), 550 (3.72), 590 (3.63), 647 (3.28). Anal. Calcd for $C_{47}H_{31}N_5$: C, 84.79; H, 4.69; N; 10.52. Found: C, 84.94; H, 4.60; N; 10.59.

[5,10,15-Triphenyl-20-(8-quinolyl)porphyrinato]zinc-(II) (Zn·3). This compound was prepared from **FB·3** (54 mg, 81 μmol) in a manner similar to that for **Zn·1** (58 mg, 98%): ^{1}H NMR ($CDCl_3$) δ 7.37 (dd, J = 4.0 Hz, 7.5 Hz, 1H), 7.70 (m, 9H), 7.93 (t, J = 7.5 Hz, 1H), 8.16 (m, 6H), 8.27 (m, 1H), 8.35 (m, 1H), 8.44 (dd, J = 1.5 Hz, 7.5 Hz, 1H), 8.50 (m, 1H), 8.52 (d, J = 4.5 Hz, 2H), 8.77 (d, J = 4.5 Hz, 2H), 8.90 (AB quartet, J = 4.5 Hz, 4H); HRMS (FAB) (M^+) calcd for $C_{47}H_{29}N_5Zn$ 727.1714, found 727.1716; UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 420 (5.76), 509 (3.30), 548 (4.33), 588 (3.33).

[5,10,15-Triphenyl-20-(8-quinolyl)porphyrinato]nickel(II) (Ni·3). A solution of **FB·3** (26 mg, 39 μmol) and $Ni(OAc)_2$-saturated methanol (4 mL) in $CHCl_3$ (20 mL) was refluxed for 12 h. After cooling, the solution was washed successively with saturated aqueous $NaHCO_3$ (20 mL × 2) and saturated aqueous NaCl (20 mL × 2) and dried over Na_2SO_4. Evaporation of the solvent and purification by preparative thin-layer chromatography (SiO_2, $CHCl_3$/MeOH = 50/1) afforded **Ni·3** as a pink solid (27 mg, 95%): ^{1}H NMR ($CDCl_3$) δ 7.37 (dd, J = 4.0 Hz, 7.5 Hz, 1H), 7.64 (m, 9H), 7.84 (t, J = 7.5 Hz, 1H), 7.97 (m, 4H), 8.01 (m, 2H), 8.19 (d, J = 8.0 Hz, 1H), 8.27 (d, J = 7.0 Hz, 1H), 8.38 (m, 1H), 8.40 (d, J = 4.5 Hz, 2H), 8.61 (m, 1H), 8.62 (d, J = 4.5 Hz, 2H), 8.71 (AB quartet, J = 4.5 Hz, 4H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 415 (5.40), 528 (4.26); HRMS (FAB) (M^+) calcd for $C_{47}H_{29}N_5Ni$ 721.1776, found 721.1772.

5-(4-Methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)dipyrromethane (15). To a solution of aldehyde **6** (1.5 g, 4.41 mmol) in pyrrole (50 mL, 723 mmol) was added trifluoroacetic acid (100 μL, 1.31 mmol) at room temperature under N_2. After the mixture stirred for 30 min, triethylamine (417 μL, 3 mmol) was added, and the mixture was concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, $CHCl_3$) afforded **15** as a white solid (1.86 g, 92%): ^{1}H NMR ($CDCl_3$) δ 3.81 (s, 6H), 3.87 (s, 3H), 4.67 (bs, 4H), 5.96 (m, 2H), 6.05 (m, 2H), 6.37 (s, 1H), 6.67 (m, 2H), 7.20 (s, 2H), 9.45 (bs, 2H); HRMS (FAB) (M^+) calcd for $C_{23}H_{24}N_2O_8$ 456.1533, found 456.1542. Anal. Calcd for $C_{23}H_{24}N_2O_8$: C, 60.52; H, 5.30. Found: C, 60.93; H, 5.25.

5-(8-Quinolyl)dipyrromethane (17). A mixture of 8-formylquinoline **16** (2.5 g, 15.9 mmol) and pyrrole (78 mL, 1127 mmol) was stirred for 12 h at 120 °C. The mixture was concentrated under reduced pressure. Purification by flash column chromatography (SiO_2, $CHCl_3$/AcOEt = 10/1) and recrystallization from CH_2Cl_2/hexane afforded **17** as an ivory-white solid (2.44 g, 56%): ^{1}H NMR ($CDCl_3$) δ 5.92 (m, 2H), 6.09 (q, J = 7.5 Hz, 2H), 6.58 (bs, 1H), 6.66 (m, 2H), 7.39 (dd, J = 7.5 Hz, 5.0 Hz, 1H), 7.48 (dd, J = 8.0 Hz, 7.5 Hz, 1H), 7.64 (dd, J = 7.5 Hz, 1.0 Hz, 1H), 7.71 (dd, J = 8.0 Hz, 1.0 Hz, 1H), 8.16 (dd, J = 8.0 Hz, 2.0 Hz, 1H), 8.78 (bs, 2H), 8.91(dd, J = 5.0 Hz, 2.0 Hz, 1H); HRMS (FAB) (M^+) calcd for $C_{18}H_{15}N_3$ 273.1266, found 273.1264. Anal. Calcd for $C_{18}H_{15}N_3$: C, 79.10; H, 5.53; N; 15.37. Found: C, 79.02; H, 5.55; N; 14.99.

***cis*-5,15-Bis(4-methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)-10,20-bis(8-quinolyl)porphyrin (FB·4).** Aldehyde **16** (504 mg, 3.2 mmol) and dipyrromethane **15** (1.46 g, 3.2 mmol) were dissolved in CH_2Cl_2 (320 mL) under N_2, and then trifluoroacetic acid (440 μL, 5.70 mmol) was added. After the reaction mixture was stirred at room temperature for 30 min, 2,3-dichloro-5,6-dicyanobenzoquinone (930 mg, 4.1 mmol) was added, and the mixture was stirred for 1 h. The solution was then neutralized by addition of triethylamine (793 μL, 5.70 mmol) and concentrated. Purification by column chromatography (SiO_2, $CHCl_3$/AcOEt = 100/1 to 10/1) and flash column chromatography (SiO_2, $CHCl_3$/AcOEt = 10/1) afforded **FB·4** as a purple solid (66 mg, yield 4%): ^{1}H NMR ($CDCl_3$) δ −2.39 (s, 2H), 3.42 (s, 6H), 3.47 (s, 6H), 4.02 (s, 6H), 4.33 (s, 4H), 4.34 (s, 4H), 7.41 (dd, J = 7.5 Hz, 4.0 Hz, 2H), 7.51 (s, 2H), 7.52 (s, 2H), 7.69 (dd, J = 5.0 Hz, 3.0 Hz, 2H), 7.88 (t, J = 3.0 Hz, 2H), 8.24 (d, J = 7.5 Hz, 2H), 8.44 (d, J = 4.5 Hz, 4H), 8.45 (dd, J = 5.0 Hz, 1.5 Hz, 2H), 8.62 (dd, J = 4.0 Hz, 1.5 Hz, 2H), 8.70 (d, J = 4.5 Hz, 4H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 420 (5.88), 514 (4.65), 548 (4.15), 588 (4.18); HRMS (FAB) (M^+) calcd for $C_{66}H_{52}N_6O_{16}$ 1184.3440, found 1184.3442. Anal. Calcd for $C_{66}H_{52}N_6O_{16}$: C, 66.89; H, 4.42; N; 7.09. Found: C, 66.97; H, 4.47; N; 7.34.

[*cis*-5,15-Bis(4-methoxycarbonyl-2,6-bis(methoxycarbonylmethoxy)phenyl)-10,20-bis(8-quinolyl)porphyrinato]zinc(II) (Zn·4). A solution of **FB·4** (20 mg, 17 μmol) and $Zn(OAc)_2$-saturated methanol (1 mL) in $CHCl_3$ (5 mL) was stirred for 3 h at room temperature. The solution was washed successively with saturated aqueous $NaHCO_3$ (10 mL × 2) and saturated aqueous NaCl (10 mL × 2) and dried over Na_2SO_4. Evaporation of the solvent and purification by preparative thin-layer chromatography (SiO_2, AcOEt) afforded **Zn·4** as a pink solid (20 mg, 93%): ^{1}H NMR ($CDCl_3$) δ 3.25 (s, 6H), 3.47 (s, 6H), 4.02 (s, 6H), 4.27 (s, 4H), 4.38 (s, 4H), 7.42 (m, 2H),

7.51 (s, 2H), 7.55 (s, 2H), 7.88 (t, J = 7.5 Hz, 2H), 8.24 (d, J = 7.5 Hz, 2H), 8.42 (m, 2H), 8.46 (m, 2H), 8.51 (d, J = 4.5 Hz, 4H), 8.60 (m, 2H), 8.77 (d, J = 4.5 Hz, 4H); UV−vis (CH_2Cl_2) λ_{max} (log ϵ) 425 (5.72), 550 (4.42); HRMS (FAB) (M^+) calcd for $C_{66}H_{50}N_6O_{16}Zn$ 1246.2575, found 1246.2573.

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