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Synthesis and binding behavior of a Zn(II)-porphyrin having calix[5]arene cap

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Abstract—The synthesis and binding behavior of a Zn(II)–porphyrin having a calix[5]arene cap are presented. In order to synthesize such a bridged porphyrin, 5,15-bis(7-carboxy-1-naphthyl)-10,20-diphenylporphyrin having the *syn* arrangement of two naphthalene rings has been prepared. Amidation of the porphyrin and calix[5]arene having two amino functions and subsequent treatment of $Zn(OAc)_2$ gave a calix[5]arene capped Zn–porphyrin. Calix[5]arene–Zn–porphyrin was found to bind 4-methylpyridine much stronger than TPP·Zn.

Synthetic metalloporphyrins have received considerable attention for electron transfer, molecular transport and oxidation processes.[1] These metalloporphyrins were synthesized in order to understand the important function of the enzyme having porphyrin. A number of functionalized porphyrins carrying cyclodextrins,[2] crown ethers[3] and calixarenes[4] have been prepared. Zn(II)–porphyrin receptors for nitrogen containing guests were also reported extensively.[5] Calix[5]arene is known as a potential host molecule with binding ability towards neutral organic guest molecules, such as fullerenes, alkyl-substituted diketopiperazines and various amines.[6] It is thus interesting to design a metalloporphyrin capped with such a cavity-containing receptor to understand the cooperative role of the coordination of the axial ligand and the non-directional attractive forces such as the CH/π and van der Waals interactions between the aromatic cavity wall of the calix[5]arene cap and the axial ligand. In this paper, we report the synthesis of a calix[5]arene capped Zn–porphyrin and its ligand binding properties.

Porphyrin having a calix[5]arene cap **1** is designed as an artificial receptor (Fig. 1). It has two naphthalene moieties as the rigid linker between the calix[5]arene and porphyrin units. Because of the rigidity of naphthalene unit, a collapse of the cavity, as can be sometimes seen in a case of a capped porphyrin with flexible linker, is prevented. Thus, the ligand binding space composed of the calix[5]arene and the porphyrin units is stable in the designed host molecule. The calix[5]arene can help to grasp some small organic guest molecules with van der Waals, CH/π and π–π interactions in organic solvents.

To synthesize the bridged porphyrin, it is necessary to prepare 5,15-bis(7-carboxyl-1-naphthyl)-10,20-diphenylporphyrin **11** having the *syn* arrangement of two naphthalene rings. In order to synthesize such a *syn* arrangement regioselectively, Baldwin's strategy using bridged naphthylaldehyde **8** and 5-phenyldipyrromethane (**9**) was employed (Scheme 1).[7] Tosylation of 2-naphthol **2**, (*p*-TsCl, Et_3N in THF), followed by bromination (Br_2, Fe in AcOH) gave the corresponding bromide, whose hydrolysis (NaOH in

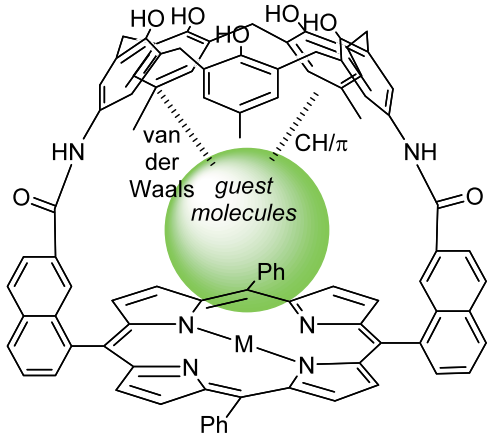

Figure 1. Compound **1** (M; metal).

Keywords: calix[5]arene; porphyrin; molecular recognition.

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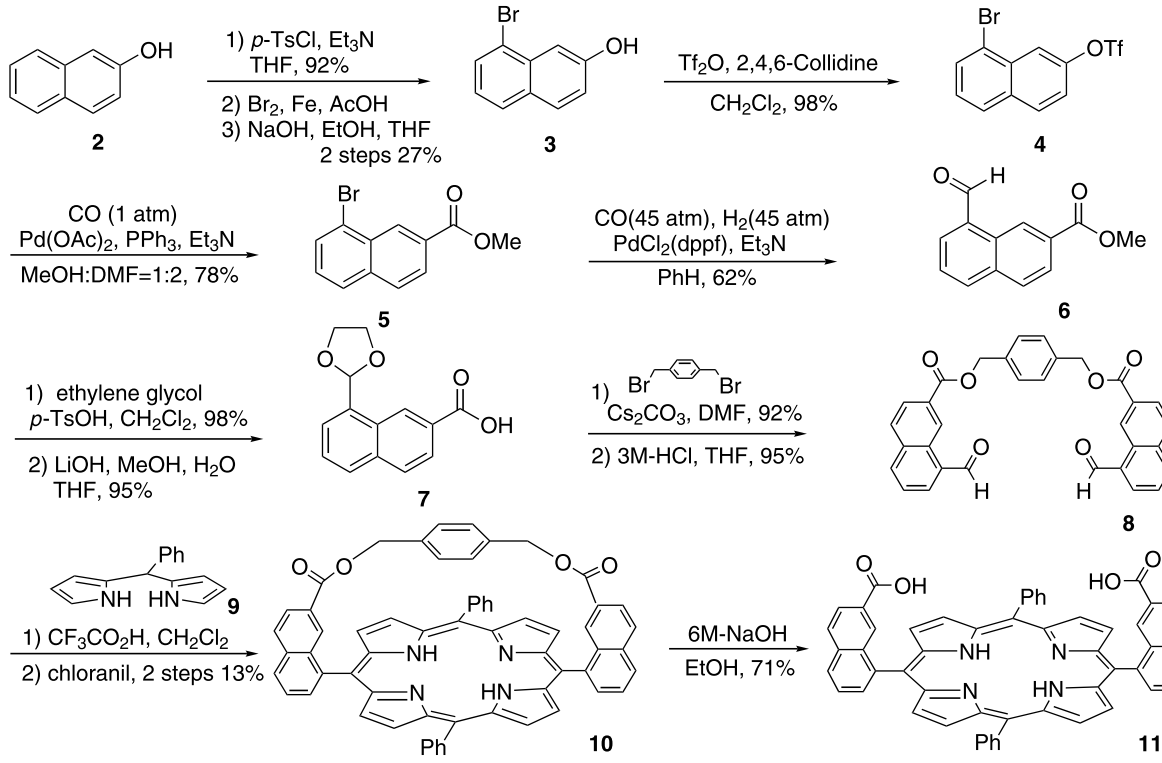


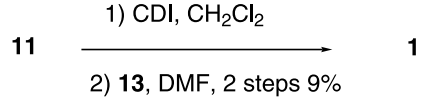
Scheme 1. Synthesis of 5,15-bis(7-carboxy-1-naphthyl)-10,20-diphenylporphyrin.

EtOH and THF) of the toluenesulfonate ester furnished 1-bromo-7-naphthol **3**. The trifluoromethanesulfonate ester **4** was prepared from **3** (Tf_2O, 2,4,6-collidine in CH_2Cl_2). Chemoselective palladium-catalyzed carbonylation of aryl triflate **4** (CO, $Pd(OAc)_2$, PPh_3, Et_3N, MeOH in DMF, 78%), and subsequent formylation (CO (45 atm), H_2 (45 atm), $PdCl_2$ (dppf), Et_3N in benzene, 62%) provided methyl 1-formyl-7-naphtoate **6**. Acetalization of **6** (ethylene glycol, *p*-TsOH in CH_2Cl_2, 98%), followed by deprotection of the methyl ester (LiOH, MeOH, H_2O, THF) gave **7**. Esterification of **7** with 1,4-bis-bromomethyl-benzene followed by hydrolysis gave **8**. Coupling of naphthylaldehyde **8** with 5-phenyldipyrromethane (**9**) in CH_2Cl_2 in the presence of a catalytic amount of trifluoroacetic acid followed by oxidation with *p*-chloranil, afforded free base porphyrin **10** in 13% overall yield from **8**. Hydrolysis of **10** (6 M NaOH in EtOH), gave 5,15-bis(7-carboxy-1-naphthyl)-10,20-diphenylporphyrin **11** in 71% yield.

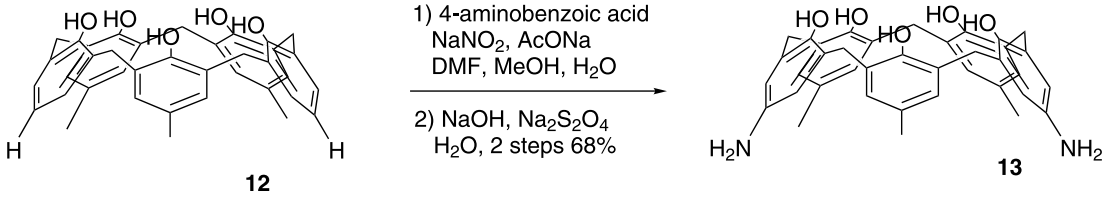
The synthesis of the calix[5]arene moiety was performed as shown in Scheme 2. Diazo coupling of **12**,[8] followed by reductive cleavage of the N=N double bond furnished diamino calix[5]arene **13** in 68% overall yield.[9]

Capping of the porphyrin with the calix[5]arene was carried out by the amide formation between **11** and **13** (Scheme 3). Treatment of **11** with carbonyl imidazole (CDI) in CH_2Cl_2 followed by coupling of diamino calix[5]arene **13** gave the porphyrin having the calix[5]arene cap **1** in 9% overall yield.[10]

In order to demonstrate the binding ability of **1**, calix[5]arene–Zn–porphyrin was prepared quantitatively from the free base porphyrin with excess $Zn(OAc)_2$ in CH_2Cl_2. Zn–porphyrins are known to bind an axial ligand resulting in a five-coordinated complex.[11] Binding studies with pyridine derivatives were performed in $CHCl_3$ using UV titration.[12] UV–vis experiments with **1**·Zn in $CHCl_3$ (1.0×10^{-5} M) showed two absorption bands at 425 and 551 nm as the Soret band and the Q-band, respectively. Bathochromic shifts of the Soret band of 8 nm and the Q-band of 12 nm



Scheme 3. Synthesis of **1**.



Scheme 2. Synthesis of diamino calix[5]arene.

Table 1. Binding energies $-\Delta G$ (kJ/mol)[a]

Guest	**1**·Zn	**10**·Zn	TPP·Zn
Pyridine	23.5	19.4	19.5
4-Methylpyridine	25.6	20.6	19.7
4-*tert*-Butylpyridine	20.4	20.7	21.5
4-Phenylpyridine	19.0	20.4	21.0
3,5-Dimethylpyridine	19.3	19.5	20.2

[a] Measured in $CHCl_3$ at 298 K. Observed 563 nm. Standard deviation is less than 10%.

were observed upon addition of pyridine. A non-linear regression analysis[13] on the UV changes gave an association constant of $13.3\pm0.3\times10^3$ M^{-1}, and binding energies of −23.5 kJ/mol. Binding energies of the other host–guest complexes were similarly determined and are summarized in Table 1.

In the capped porphyrin case, axial pyridine ligands can bind from either side of the porphyrin. When we consider the binding energies of **1**·Zn, **10**·Zn and TPP·Zn with pyridine itself, it is clear that the ligand bound from the calix[5]arene side is **1**·Zn. It is thus evident that the attractive interaction between the axial ligand and the π-wall of calix[5]arene cavity is operative in **1**·Zn. The same is true in the case of 4-methylpyridine and **1**·Zn. On the other hand, bulky substituent(s) on pyridine ring as in the case of 4-*tert*-butylpyridine, 4-phenylpyridine and 3,5-dimethylpyridine, prevented the accommodation of the guest into the calix[5]arene cavity. Therefore, those guests bound to the Zn–porphyrin from the opposite side of the calix[5]arene cap. It is thus clear that the selectivity of the binding of pyridine derivatives depends on the size of the alkyl substituent. 4-Methyl pyridine shows the highest affinity with **1**·Zn. The methyl group should give a good complementarity to the π-basic inner surface of the calix[5]arene cavity.

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10. Compound **1**: δ 8.78 (d, $J=4.5$ Hz, 2H), 8.60 (d, $J=4.5$ Hz, 2H), 8.54 (d, $J=4.5$ Hz, 2H), 8.37 (d, $J=4.5$ Hz, 2H), 8.31 (d, $J=8.5$ Hz, 2H), 8.28 (d, $J=8.5$ Hz, 2H), 8.12 (d, $J=8.5$ Hz, 2H), 8.1 (br, 1H), 8.04 (d, $J=7.0$ Hz, 2H), 7.96 (d, $J=7.0$ Hz, 2H), 7.90 (s, 2H), 7.83 (t, $J=7.5$ Hz, 2H), 7.8 (br, 1H), 7.6 (br, 4H), 7.4 (br, 3H), 7.18 (s, 2H), 6.92 (s, 2H), 6.83 (s, 2H), 6.80 (s, 2H), 6.47 (s, 2H), 6.20 (s, 2H), 3.96 (d, $J=14.0$ Hz, 1H), 3.86 (d, $J=14.0$ Hz, 2H), 3.76 (d, $J=14.0$ Hz, 2H), 3.30 (d, $J=14.5$ Hz, 3H), 3.016 (d, $J=14.5$ Hz, 2H), 2.18 (s, 6H), 1.88 (s, 3H), -2.68 (s, 2H). IR ($CHCl_3$) cm^{-1}: 3316, 2923, 1665, 1533, 1483, 1347, 1227, 802. UV–vis ($CHCl_3$): λ_{max}, 425 nm (ε 246 000 mol^{-1} cd^3 cm^{-1}), 551 (11 400), 588 (2 100). HRMS (FAB-MS positive Mode, NBA) found 1368.5128, calcd 1368.5149 ($C_{92}H_{68}N_6O_7$).
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12. The measurements were performed by ^1H NMR titration experiments in $CDCl_3$. As host molecule **1**·Zn was added to the solution of 4-methylpyridine in $CDCl_3$, the reso-

nances of the 4-methylpyridene protons were shifted upfield, and significantly broadened. Further addition of host molecule, the resonance of guest protons were disappeared. Therefore, the NMR experiment was not carry out in detail.

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