Porphyrinoids

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Synthesis of Calix[3]dipyrrins by a Modified Lindsey Protocol**

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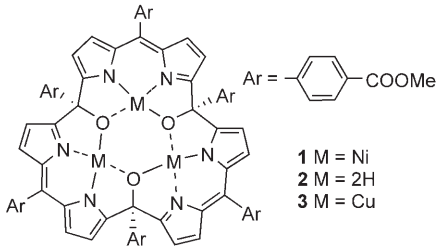
The Lindsey protocol, a one-pot two-step reaction between pyrrole and an aldehyde, has been extensively used for the synthesis of porphyrins[1] and has been revealed in recent years to provide various other pyrrolic macrocycles, such as corroles,[2] sapphyrins,[3] N-confused porphyrins,[4] and *meso*-aryl-substituted expanded porphyrins,[5] depending upon the concentrations, additives, reaction medium, stoichiometry of the pyrrole and aryl aldehyde, and structures of the substrates. The Lindsey protocol usually requires anhydrous conditions because of the dehydrative nature of the first condensation reaction between pyrrole and the aldehyde and may be influenced by the presence of water.[1] Recently, we reported that novel heptaphyrins bearing direct pyrrole–pyrrole linkages were formed from pentafluorobenzaldehyde and pyrrole by the Lindsey protocol under aqueous conditions in the presence of a sodium dodecyl sulfate micelle.[6] Herein, we report the synthesis of new hexapyrrolic macrocycles, calix[3]dipyrrins, in modest yields by a modified Lindsey protocol in the presence of a small amount of water. Whereas calix[4]pyrroles and calix[*n*]phyrins have been shown to serve as effective anion receptors,[7,8] calix[3]dipyrrins have preorganized coordination sites that can accommodate three cations in a symmetric triangular fashion.

The Ni^{II} complex of tetrakis(4-methoxycarbonylphenyl)-porphyrin was prepared by treating a solution of pyrrole and 4-methoxycarbonylbenzaldehyde in CH_2Cl_2 with trifluoroacetic acid (TFA) for 2 h. Oxidation of the mixture with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) for 1 h and subsequent metallation with $[Ni(acac)_2]$ (acac: acetylacetonate) provided the expected porphyrin product (15 %) as well as a red product that eluted slowly on a silica gel column. This side product was assigned as calix[3]dipyrrin **1** on the basis of X-ray diffraction analysis, which revealed a trimetallated calix[3]dipyrrin macrocycle consisting of three planar dipyrrin segments connected by aryl- and hydroxy-substituted methylene units (Figure 1).[9] The three Ni^{II} atoms are located at the apexes of an equilateral triangle and are bridged by three μ-alkoxo oxygen atoms to form a Ni_3O_3 hexagonal core. The Ni^{II} atoms are each coordinated by two pyrrolic N atoms with



1 M = Ni
2 M = 2H
3 M = Cu

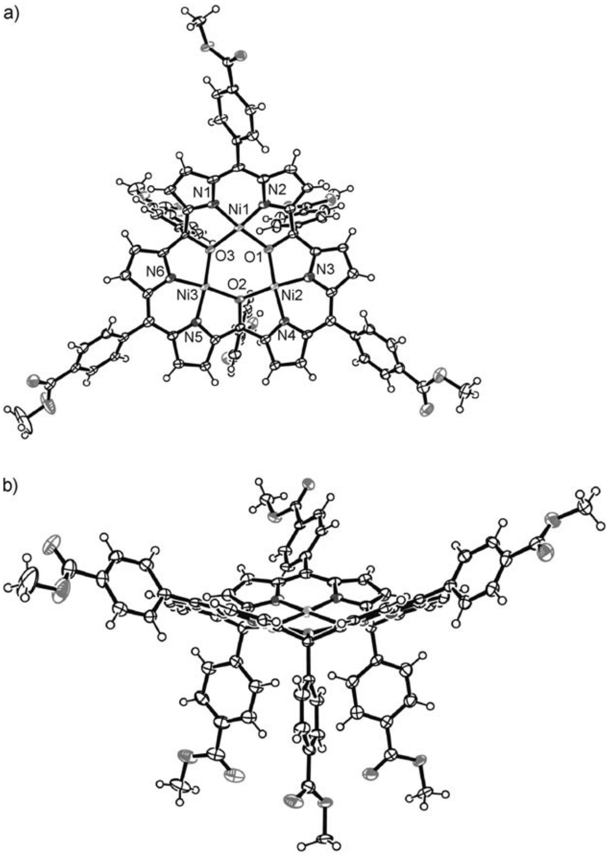


Figure 1. X-ray crystal structure of **1**: a) top view and b) side view. Solvent molecules are omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

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Ni–N distances of 1.80–1.81 Å and two bridging O atoms with Ni–O distances of 1.90–1.91 Å in a square-planar arrangement. The metallated dipyrrin segments are tilted by approximately 141° relative to one another to form a bowl-shaped macrocycle.

High-resolution electrospray ionization time-of-flight (HR ESI-TOF) mass spectrometry revealed parent ion peaks for **1** at m/z 1513.1527 (calcd for $[(C_{78}H_{54}N_6O_{15}Ni_3Na)]^+ = 1513.1583$), consistent with its structure. In the ^{1}H NMR spectra, most of the signals for **1** are consistent with the structure, but the aromatic protons of the *meso*-substituted aryl groups appeared as rather broad signals at $\delta = 8.08$, 7.54, and 7.39 ppm at 25 °C, suggesting the restricted rotation of these aryl groups. At −20 °C, these signals split into a pair of sharp doublets at $\delta = 8.11$ and 8.04 ppm ($J = 8.3$ Hz), and $\delta = 7.54$ and 7.37 ppm ($J = 8.2$ Hz). By simulating the temperature-dependent spectral profiles, a rotational energy barrier of 8.5 kcal mol^{-1} was determined (see the Supporting Information).

Importantly, [Ni(acac)$_2$] should be added after the condensation/annulation reaction; the Lindsey protocol did not afford any calix[3]dipyrrin product in the presence of the metal salt. The source of the oxygen atoms in **1** was elucidated by examining the reaction in CH_2Cl_2 in the presence of variable amounts of water or with O_2 bubbling. Almost no influence was observed when dry O_2 was bubbled through the solution, but the yield of **1** varied upon the amount of water present in CH_2Cl_2. In fact, the yield of **1** was found to be consistently more than 8 % in the presence of a small amount of water ($c(H_2O) \leq 6.7 \times 10^{-3}$ M). Even under the anhydrous conditions at the start of the reaction, the acid-catalyzed condensation of an aldehyde and pyrrole liberates a small amount of water, which seemingly promotes the formation of **1**. The yield of isolated **1** was optimal (15 %) at a concentration of 6.7×10^{-3} M of water but dropped sharply at higher concentrations (see the Supporting Information). In the presence of 3-Å molecular sieves as a dehydrating agent, the reaction provided only the porphyrin and none of the calix[3]dipyrrin **1**, which strongly suggests the importance of adventitious water for the formation of **1**. The involvement of water for the formation of **1** was confirmed by an experiment in the presence of $H_2{}^{18}O$, which gave partially ^{18}O-labeled product (Supporting Information).

Under these optimized conditions, a range of calix[3]dipyrrins were obtained in moderate to low yields from aryl aldehydes bearing electron-withdrawing groups at the 4-position (Table 1, entries 1–7) or at the 3-position (entries 8 and 9). On the other hand, no calix[3]dipyrrins were obtained either from 3,5-disubstituted (Table 1, entries 10 and 11) or 2-substituted aryl aldehydes (entries 12 and 13), probably owing to steric hindrance. Benzaldehyde and aryl aldehydes with electron-donating groups also did not furnish calix[3]dipyrrin products (Table 1, entries 14–18).

Table 1: Preparation of calix[3]dipyrrins under the modified Lindsey conditions.

Entry	Aryl aldehyde	Calix[3]dipyrrin	Yield [%]	
			calix[3]dipyrrinatonickel(II)[a]	porphyrinatonickel(II)[b]
1	$4\text{-}MeOOCC_6H_4CHO$	**1**	15	8
2	$4\text{-}NCC_6H_4CHO$	**4**	13	trace
3	$4\text{-}O_2NC_6H_4CHO$	**5**	11	trace
4	$4\text{-}F_3CC_6H_4CHO$	**6**	7.5	trace
5	$4\text{-}FC_6H_4CHO$	**7**	1.4	trace
6	$4\text{-}ClC_6H_4CHO$	**8**	5.5	trace
7	$4\text{-}BrC_6H_4CHO$	**9**	2.1	trace
8	$3\text{-}O_2NC_6H_4CHO$	**10**	3.9	4.1
9	$3\text{-}CF_3C_6H_4CHO$	**11**	4.0	trace
10	$3,5\text{-}(CF_3)_2C_6H_3CHO$	–	trace	trace
11	$3,5\text{-}Cl_2C_6H_3CHO$	–	0	4.9
12	$2,6\text{-}Cl_2C_6H_3CHO$	–	0	0
13	$2\text{-}O_2NC_6H_4CHO$	–	0	0
14	C_6H_5CHO	–	0	16
15	$4\text{-}MeC_6H_4CHO$	–	0	11
16	$4\text{-}MeOC_6H_4CHO$	–	0	2.4
17	$3,5\text{-}t\text{Bu}_2C_6H_3CHO$	–	0	18
18	$2,4,6\text{-}Me_3C_6H_2CHO$	–	0	0

[a] Yield of isolated calix[3]dipyrrinatonickel(II) complex. [b] Yield of isolated porphyrinatonickel(II) complex.

In contrast to the considerable robustness of Ni^{II}-porphyrins toward treatment with acid, demetallation of **1** with TFA was facile and quantitative to provide free base **2**. The structure of **2** was confirmed by X-ray diffraction analysis, which revealed that the three hydroxy groups at the sp^3-hybridized *meso* positions adopt equatorial positions, hence pointing toward the inside of the cavity with O–O distances of 4.04, 4.14, and 4.17 Å (Figure 2).[10] The dihedral angles of the dipyrrin segments (ca. 107°) in **2** are smaller than those in **1**. The macrocycle becomes more distorted upon demetallation as indicated by the larger mean plane deviation of 36 atoms of macrocycle **2** (0.622 Å) as compared to that of **1** (0.389 Å). Similar to the case of **1**, the rotational barrier of the aryl substituents at the *meso* position of the dipyrromethene was determined to be 6.2 kcal mol^{-1} (Supporting Information).

The triangular geometry of **2** appeared to offer an ideal situation for the observation of unique competing magnetic interactions, namely spin frustration, in its paramagnetic metal complexes.[12,13] This expectation led us to prepare the tris-Cu^{II} complex **3** by heating a solution of **2** in $CHCl_3$ with an excess amount of $Cu(OAc)_2$ at 50 °C (quantitative reaction). The structure of **3** was confirmed by X-ray crystallography to be essentially the same as that of **1** (Figure 3). The three Cu^{II} atoms are coordinated by two pyrrolic N atoms with Cu–N distances of 1.89–1.91 Å and two bridging alkoxo O atoms with a Cu–O distance of 1.94 Å, and a mean plane deviation of 0.393 Å.[11]

The variable-temperature magnetic susceptibility of **3** was measured over the range 2–300 K (Figure 4). At 300 K the complex **3** exhibits $\chi_M T = 1.02$ emu K mol^{-1}, which roughly corresponds to three independent Cu^{II} ions but is smaller than the expected value of 1.20 emu K mol^{-1}, which indicates some antiferromagnetic interaction. As the temperature was lowered, the $\chi_M T$ value gradually decreased and reached a value of 0.35 emu K mol^{-1} at 2 K, which was lower than the spin-only value for a single independent Cu^{II} ion of $S = 1/2$. Such temperature-dependent behavior indicates strong antiferromagnetic interactions among the three Cu^{II} ions, and the observed lower $\chi_M T$ value suggests an additional intermolec-

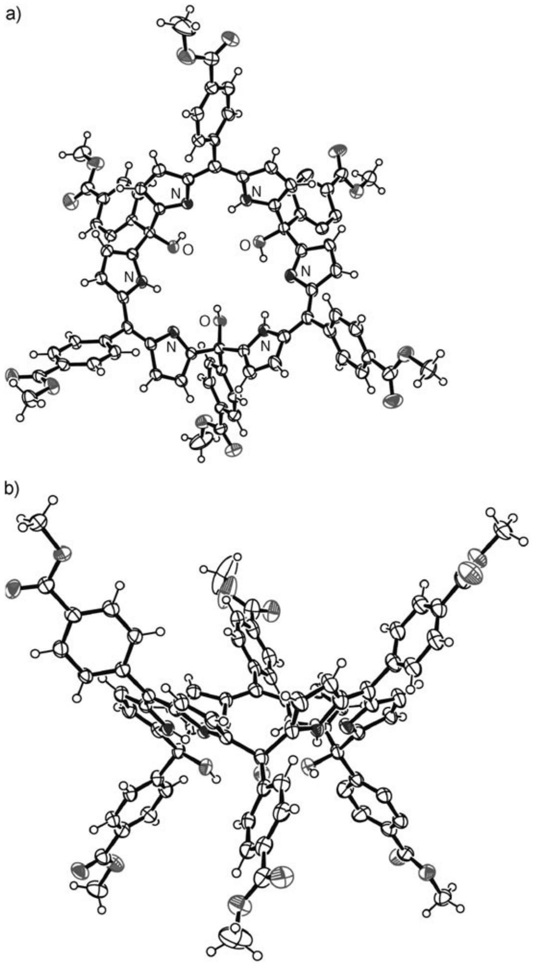

Figure 2. X-ray crystal structure of **2**: a) top view and b) side view. Solvent molecules are omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

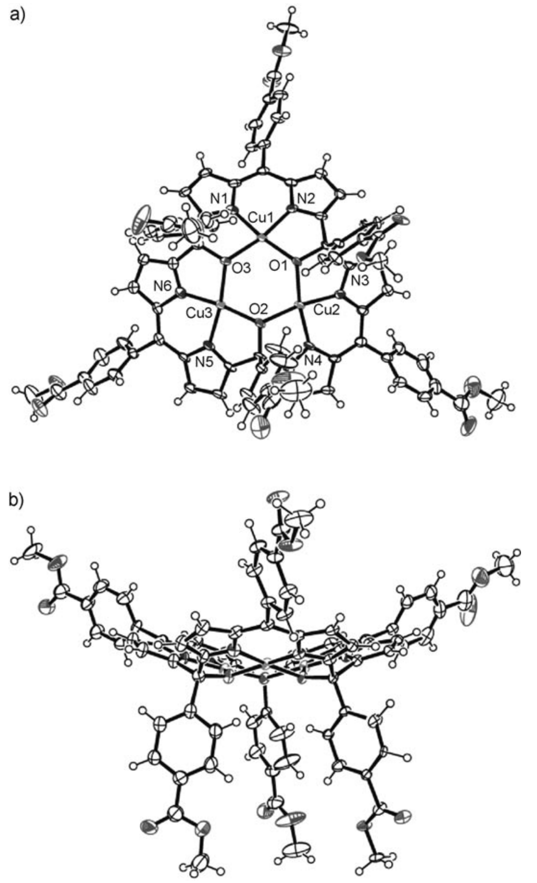

Figure 3. X-ray crystal structure of **3**: a) top view and b) side view. Solvent molecules are omitted for clarity. Thermal ellipsoids are shown at the 50% probability level.

ular antiferromagnetic interaction, as has been reported for similar triangular tris-Cu^{II} compounds.[13] The mean g value was determined to be 2.097 by ESR spectroscopy in frozen toluene at 20 K, and the ESR spectrum was consistent with a $S = 1/2$ system, which was considered the ground state of the frustration system (Supporting Information). Given that the magnetic exchange interactions among the three Cu^{II} ions is the same, the least-squares fit of the experimental data through a triangular model[12] with an intermolecular interaction θ based on the mean-field approximation gave a J value of $-44.1\ \text{cm}^{-1}$ for the intramolecular interaction and a θ value of -0.99 K ($\theta k_B = 0.69\ \text{cm}^{-1}$) for the intermolecular interaction.

In summary, calix[3]dipyrrins were synthesized in moderate to low yields as novel pyrrolic macrocycles from appropriate precursors by the Lindsey protocol under non-anhydrous conditions. These calix[3]dipyrrin macrocycles accommodate three metal ions such as Ni^{II} and Cu^{II} ions in a hexagonal M_3O_3 manner. The tris-Cu^{II} complex **3** shows typical competing spin–spin interactions as revealed by temperature-dependent magnetic susceptibility measurements. Studies concerning the further use of these novel pyrrolic macrocycles are currently in progress in our laboratory.

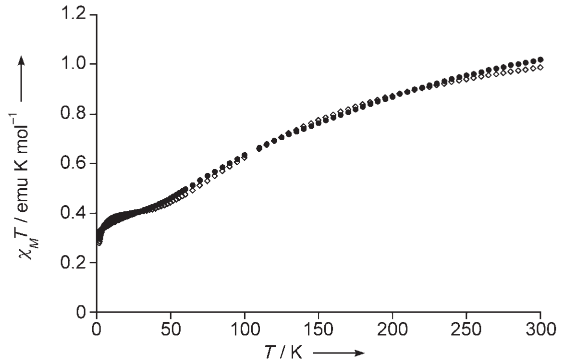

Figure 4. Temperature-dependent magnetic susceptibility of **3** (● observed; ◇ calculated).

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[9] Crystallographic data for **1**: $C_{81}H_{58}Cl_5N_6Ni_3O_{15}$, $M_w = 1708.71$, monoclinic, space group $P2_1/c$ (no. 14), $a = 11.4510(17)$, $b = 20.120(3)$, $c = 31.920(5)$ Å, $\alpha = 90$, $\beta = 98.336(3)$, $\gamma = 90°$, $V = 7276.6(19)$ Å^3, $\rho_{calcd} = 1.560\,g\,cm^{-3}$, $Z = 4$, R_1 $(I > 2.0\sigma(I)) = 0.0773$, wR_2 (all data) $= 0.2368$, GOF $= 1.079$ $(I > 2.0\sigma(I))$.

[10] Crystallographic data for **2**: $C_{80}H_{62}Cl_2N_6O_{16}$, $M_w = 1434.26$, triclinic, space group $P\bar{1}$ (no. 2), $a = 12.018(4)$, $b = 17.091(7)$, $c = 19.587(7)$ Å, $\alpha = 93.987(14)$, $\beta = 102.889(13)$, $\gamma = 95.224(13)°$, $V = 3888(3)$ Å^3, $\rho_{calcd} = 1.225\,g\,cm^{-3}$, $Z = 2$, $R_1 = 0.0985$ $(I > 2.0\sigma(I))$, wR_2 (all data) $= 0.3204$, GOF $= 1.027$ $(I > 2.0\sigma(I))$.

[11] Crystallographic data for **3**: $C_{97}H_{69}Cl_3Cu_3N_6O_{16}$, $M_w = 1871.55$, triclinic, space group $P\bar{1}$ (no. 2), $a = 11.668(7)$, $b = 19.070(12)$, $c = 19.801(12)$ Å, $\alpha = 69.599(9)$, $\beta = 87.517(10)$, $\gamma = 84.319(10)°$, $V = 4109(4)$ Å^3, $\rho_{calcd} = 1.513\,g\,cm^{-3}$, $Z = 2$, $R_1 = 0.0982$ $(I > 2.0\sigma(I))$, wR_2 (all data) $= 0.3117$, GOF $= 1.060$ $(I > 2.0\sigma(I))$. CCDC-627140 (**1**), CCDC-627141 (**2**), and CCDC-627142 (**3**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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