N-Confused Porphine

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A skeleton of N-confused porphyrin (NC-porphine) has been synthesized for the first time, through a [3+1] coupling reaction. A completely planar inner 3H tautomeric form was found in the crystals, and the molecular packing shows a sandwich herringbone structure similar to that of normal porphine, whilst some of the spectroscopic properties demonstrate systematic substituent effects by the *meso*-phenyl groups on the N-confused porphyrin.

Since the discovery of porphycene[1a] by Vogel's group in 1986, a series of porphyrin isomers, such as *corrphycene*,[1b,1c] *hemiporphycene*,[1d] *isoporphycene*,[1e] and *N-confused porphyrin* (NCP),[2] differing in the numbers and positions of the pyrrole linkage carbon atoms, have been synthesized and some unique properties, different from, and in some cases superior to, those of porphyrins for application use, have been revealed.[3] For the development of novel functions by these isomers, precise comparison of the fundamental properties of each isomer to those of porphyrin is indispensable and such a study would be rationally performed by using the *standards* of $C_{20}H_{14}N_4$ frameworks, theoretically and experimentally. However, the macrocycles consisting only of the skeleton, such as porphine,[4] are not always feasible due to synthetic difficulty. With regard to NCP, various NCPs of *meso*-aryl and β-alkyl types have been reported so far, but completely unsubstituted NCP (NC-porphine, **2**) had yet to be synthesized.[5] Here we report the first synthesis of NC-porphine, together with its spectral properties and X-ray structure. Substituent effects are also described.

Initial attempts to synthesize NC-porphine by previous methods,[5] such as one-pot and stepwise reactions using pyrrole, dipyrromethane, or tripyrrane, were unsuccessful and resulted in the formation of insoluble solids. We therefore decided to introduce a bulky and lipophilic N-protecting group in a confused pyrrole ring precursor in order to ensure the stability and solubility of the intermediates in the NC-porphine synthesis. After numerous synthetic trials, NC-porphine with a *tert*-butyl group at the outer nitrogen atom (**1**) was identified as a successful precursor. Through a [3+1] coupling of N-confused *N-tert*-butyl-tripyrrane,[5d,5h,6] prepared from 1-*tert*-butyl-2,4-pyrroledicarbaldehyde, and 2,5-bis(hydroxymethyl)pyrrole,[7] *N*-protected NC-porphine **1** was obtained in 6.2% yield (Scheme 1). Subsequent removal of the *N-tert*-butyl group was carried out according to a recently reported normal porphine synthesis from β-*tert*-butylporphyrins.[8b] Treatment of **1** with H_2SO_4/H_2O at ca. 165 °C resulted in the *tert*-butyl group being readily removed to afford NC-porphine **2** in 55% yield. The solubility of **2**, similarly to that of the normal porphine, was low once it had solidified.

The structure of **2** was identified from ^{1}H NMR spectra.[9] In the upper field region, a singlet signal at δ = –6.42 ppm and a broad signal at δ = –3.70 ppm, assigned to inner CH and NH, respectively, were observed in $CDCl_3$. The NH signal appeared in the same region as that of the inner NH signal of normal porphine (δ = –3.94 ppm), and these chemical shifts are also comparable to those of *meso*-unsubstituted NCPs with β-heptaalkyl groups (δ = –6.1 to –6.3 ppm and –3.6 to –3.8 ppm for inner CH and NH, respectively).[5b,5c] Additionally, eleven peripheral protons resonated between δ = 10.3 and 9.2 ppm. The β-protons at the periphery resonated in a lower field region than those in *meso*-tetraphenyl NCP (NCTPP).[2a] Such shifts are very similar to those of normal porphyrins [*meso*-tetraphenylporphyrin (TPP): δ = 8.85 ppm vs. porphine: δ = 9.54 ppm].

NC-porphine **2** exhibited peculiar solvatochromism, caused by NH tautomerism of NCP (Figure 1).[10] In the UV/Vis spectra, Soret bands were observed at 413 and 417 nm in CH_2Cl_2 and DMF, respectively, and the longest wavelengths of Q-bands were observed at 680 and 653 nm, respectively. Additionally, the emission spectra showed

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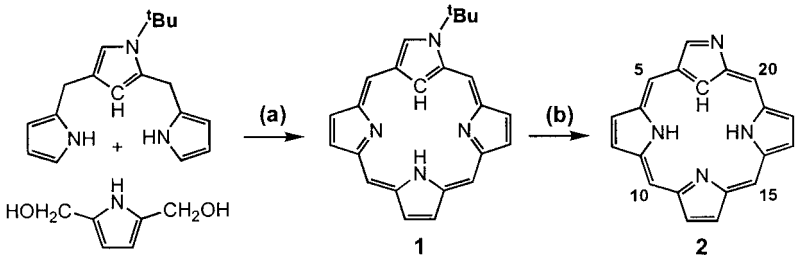

Scheme 1. Synthesis of NC-porphine **2** via *N*-protected NC-porphine **1** through a [3+1] coupling reaction. a) i) $BF_3{\cdot}OEt_2$, CH_2Cl_2, 1.5 h, ii) DDQ, 0.5 h. b) H_2SO_4/H_2O, 165 °C, 15 min. Numbering of *meso*-positions is shown in the structure of **2**.

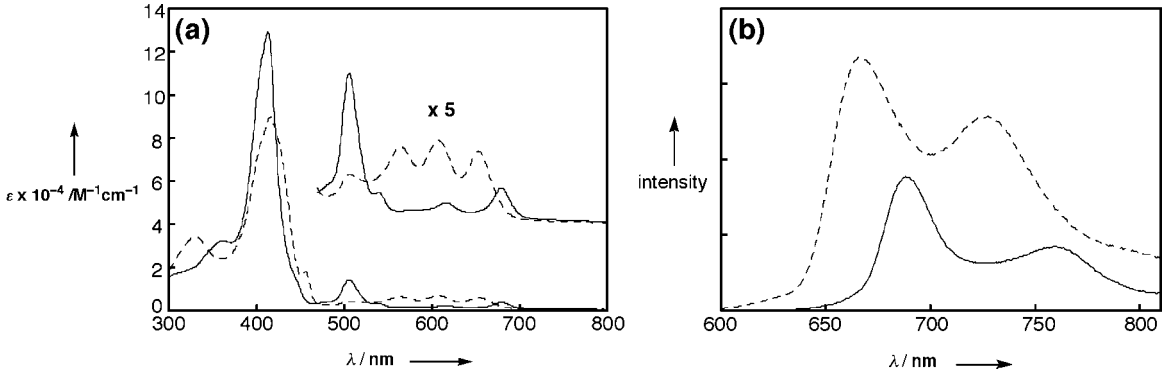

Figure 1. Electronic (a) and emission (b) spectra of NC-porphine **2** in CH_2Cl_2 (solid line) and DMF (broken line).

peaks at 689 and 760 nm in CH_2Cl_2, and at 667 and 726 nm in DMF.[11] On the other hand, the profile of the UV/Vis spectrum in CH_2Cl_2 was slightly different from that of NCTPP and, especially, the intensities of Q-bands were weaker than those of NCTPP, except for the absorption of the shortest wavelength. Such changes of intensities are also observed in the case of normal porphine and TPP.[4,7,8]

X-ray diffraction analysis confirmed the structure of **2** (Figure 2)[12] and revealed the molecule to be planar, unlike in the previously reported distorted structures of NCPs, in which the confused pyrrole is tilted by 20–30° from the mean plane.[2,5j,13] As judged by the angles around the pyrrolic nitrogen atoms, N^1 and N^3 are assignable as imine-type atoms, and N^2 and N^4 as amine-type ones: namely, the NC-porphine maintains the inner 3H tautomeric form in the solid state. In the crystals, **2** exists as a dimer separated by ca. 3.4 Å, and this pair lies above the neighboring one with a dihedral angle of ca. 64°. This packing mode is categorized as a sandwich herringbone of the four basic aromatic compound structure types.[14] In this type, two molecules stack in gliding fashion to optimize π–π interaction, while the inclined molecules interact with neighboring pairs to gain maximal CH–π interaction. Such packing may compensate for the steric repulsion between the three internal hydrogen atoms, which usually gives rise to the distorted structure. Interestingly, the molecular structure, mode of packing, and cell parameters of the NC-porphine are all very similar to those of normal porphine, in spite of the *confused* structure.[15]

The relative stabilities of the tautomers of **2** were estimated by ^{1}H NMR spectroscopy. Two tautomers (inner 2H and 3H types) were observed in [D_5]pyridine, as reported

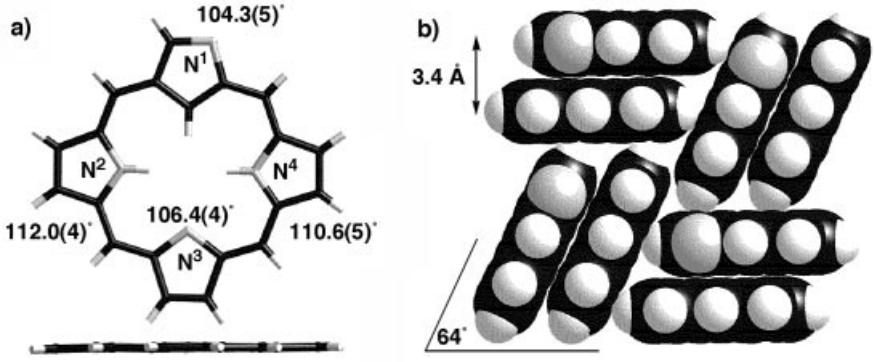

Figure 2. X-ray structure of NC-porphine **2**; a) top and side views, and b) packing diagram along the *a*-axis.

Table 1. Comparison of ^{1}H NMR, electronic spectra, and computational results for tetraphenyl-, diphenyl-, and NC-porphine **2**.

NCP	NMR [ppm][a]		NICS [ppm][b]	UV/Vis [nm][c]		LUMO [eV]	HOMO [eV]	LUMO–HOMO [eV]
meso	inner NH	inner CH		Soret band	Q-bands			
–	–3.70	–6.42	–13.8906	413	506, 680	–2.7328	–5.3861	2.6533
5,20	–3.37	–5.87	–12.9838	430	527, 566, 705	–2.7170	–5.2169	2.4999
5,10,15,20	–2.43	–5.01	–12.8016	438	540, 582, 726	–2.6950	–5.1513	2.4563

[a] In $CDCl_3$. [b] Calculated at the mean position of 24 atoms in the NCP core at the B3LYP/6-31G** level by the GIAO method (ref.[17]). [c] In CH_2Cl_2.

previously,[10] and variable-temperature NMR spectra gave the thermodynamic parameters, ΔH = +3.58 kcal·mol^{-1} and ΔS = +12.3 cal·K^{-1}·mol^{-1}, for the process from the 2H-type tautomer to the 3H-type tautomer (Supporting Information, Figure S3). This positive enthalpy term indicates that the former is more stable than the latter in pyridine, just like NCTPP, and that both values are also comparable to those for NCTPP.[10]

Systematic substituents effects on NCP in the ^{1}H NMR and absorption spectra were observed by comparison of NCTPP, diphenyl-NCP,[5j] and NC-porphine **2** (Table 1). The inner NH and CH proton signals shift upfield as the number of the substituents decreases, which is quite in contrast to the small chemical shifts seen with β-alkylation of NCP.[16] Such shifts are also observed with the inner NH signals of normal porphyrins as well [δ = –2.8, –3.3, and –3.9 ppm for TPP, 5,10-diphenylporphyrin (5,10-DPP), and porphine, respectively]. The systematic change of aromaticity was also supported by the calculated nucleus-independent chemical shifts (NICS),[17] with the NICS values decreasing with the removal of phenyl groups. In the absorption spectra, on the other hand, both the Soret and the Q-bands are hypsochromically shifted as the numbers of the substituents decrease, just like for normal porphyrins (Soret bands: 419, 405, and 394 nm for TPP, 5,10-DPP, and porphine, respectively).[18] The linear change in the HOMO–LUMO energy gap was also shown by DFT calculation at the B3LYP/6-311G**//B3LYP/6-31G** level,[19] in which the HOMO levels go up on addition of phenyl groups at the *meso*-positions, while the LUMO levels remain almost constant. This type of additivity effect indicates similar contributions of phenyl groups to the molecular orbitals regardless of the different locations of *meso*-positions due to the unsymmetrical structure of NCP. Such a relationship was also observed in the absorption spectra in DMF, as well as in the emission spectra (Table in Supporting Information).

In summary, we have synthesized N-confused porphine for the first time. The basic framework of NCP shows a structure in the solid state almost similar to that of normal porphine, and exhibits intrinsic NH tautomerism in solution. In addition, the *meso*-substituent effects on NCP are also comparable to those of normal porphyrin. These tunable properties and the structural similarity may enable NCPs to take part in the various porphyrin-containing supramolecular systems and introduce unique properties derived from *confusion*.

Experimental Section

Compound 1: 2,5-Bis(hydroxymethyl)pyrrole (210.2 mg, 1.65 mmol) in MeOH (5 mL) and BF_3·OEt_2 (103 μL, 0.81 mmol) were added at room temperature under N_2 to a solution of N-confused *N*-*tert*-butyltripyrrane[9] (455.3 mg, 1.62 mmol) in CH_2Cl_2 (810 mL). After stirring for 1.5 h, the reaction mixture was passed through a silica gel column and eluted with CH_2Cl_2 (150 mL). DDQ (378.5 mg, 1.67 mmol) was added, and the resulting solution was stirred for 30 min. After concentration, the residue was purified by column chromatography on silica gel (eluent: 5% MeOH/CH_2Cl_2) to afford **1** (36.8 mg, 0.100 mmol) in 6.2% yield. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.15 (s, 1 H), 8.89 (s, 2 H), 8.45–8.42 (m, 6 H), 8.22 (d, J = 3.9 Hz, 1 H, β-H), 8.18 (d, J = 3.9 Hz, 1 H, β-H), 2.30 [s, 9 H, C(CH_3)$_3$], 1.26 (s, 1 H, inner NH), 0.44 (br., 1 H, inner CH) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 161.3, 160.9, 154.3, 151.7, 143.3, 142.9, 138.5, 137.0, 136.4, 132.3, 130.5, 130.3, 129.7, 129.6, 120.4, 117.8, 115.0, 111.9, 100.2, 99.8, 59.3, 33.1 ppm. UV/Vis (CH_2Cl_2): λ_{max} ($\varepsilon \times 10^{-4}$) = 334 (3.1), 419 (6.5), 573 (0.44), 618 (0.68), 665 (0.50) nm; (DMF): λ_{max} ($\varepsilon \times 10^{-4}$) = 334 (3.1), 419 (6.5), 572 (0.45), 616 (0.70), 661 (0.52) nm. Fluorescence (CH_2Cl_2): λ_{em} = 685, 748 nm; (DMF): λ_{em} = 678, 741 nm. MALDI-TOF-MS: m/z = 367.3 [M + H]$^+$.

Compound 2: Compound **1** (12 mg, 0.033 mmol) was treated with H_2SO_4 (1.2 mL) and H_2O (0.6 mL) at 162–165 °C for 15 min, and the solution was then neutralized with aq. $NaHCO_3$. The products were extracted with $CHCl_3$, and the solvent was evaporated. The residues were purified on a silica gel column, and recrystallization from CH_2Cl_2/hexane to afford **2** in 55% yield (5.6 mg, 0.018 mmol). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.33 (s, 1 H), 10.03 (s, 1 H), 9.92 (s, 1 H), 9.85 (s, 1 H), 9.71 (s, 1 H), 9.45 (d, J = 4.8 Hz, 1 H), 9.39 (d, J = 5.1 Hz, 1 H), 9.27 (d, J = 4.8 Hz, 1 H), 9.26 (d, J = 5.1 Hz, 1 H), 9.22 (d, J = 4.5 Hz, 1 H), 9.19 (d, J = 4.5 Hz, 1 H), –3.70 (br., 2 H, inner NH), –6.42 (s, 1 H, inner CH) ppm. UV/Vis (CH_2Cl_2): λ_{max} ($\varepsilon \times 10^{-4}$) = 362 (3.2), 413 (12.9), 506 (1.4), 680 (0.33) nm; (DMF): λ_{max} ($\varepsilon \times 10^{-4}$) = 331 (3.4), 417 (9.0), 456 (1.8), 565 (0.59), 608 (0.64), 653 (0.56). Fluorescence (CH_2Cl_2): λ_{em} = 689, 760nm; (DMF): λ_{em} = 667, 726 nm. MALDI-TOF-MS: m/z = 311.9 [M + H]$^+$.

Acknowledgments

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