Porphyrinoids

Inverted N-Confused Porphyrin Dimer

*Tomoya Ishizuka, Atsuhiro Osuka, and Hiroyuki Furuta**

Porphyrin (**1**) is a well-known tetrapyrrolic macrocycle that has four nitrogen atoms arranged inside the core that are able to co-ordinate a variety of metal ions. Normally, the porphyrin core is considered to be planar because of the resonance stabilization resulting from the 18-π electron aromatic system.[1] By contrast, porphyrin analogues display versatile structures, especially in the expanded porphyrin families where an inverted arrangement of the pyrrole rings is frequently observed.[2] The inversion of the tellurophene ring in the heteroporphyrin analogue ditelluraporphyrin (**2**) was demonstrated by Latos-Grażyński and co-workers;[3] however, such ring inversion has been rarely observed and remains unproven for the tetrapyrrolic framework (Scheme 1).

Previously, we reported the formation of the N-fused porphyrin (NFP) **4**[4] from an N-confused porphyrin (NCP) **3**,[5] which should proceed by ring inversion within the confused pyrrole and bond formation. In addition to this, we suggested the involvement of the inverted conformation of the confused pyrrole ring during the NH tautomerism of NCP.[6] Furthermore, density functional theory (DFT) calculations indicate that the energy difference between the inverted and normal conformations is much smaller than that of porphyrin.[7] The tilted angles were increased by the introduction of substituents at the inner carbon atom of the confused pyrrole. This observation led to the question of what would happen if a larger substituent, such as porphyrin, was introduced into the core. Would it induce pyrrole inversion and stabilize the inverted conformation of the confused pyrrole ring? To examine this possibility, we planned to synthesize an NCP dimer where the two NCP molecules are connected at both of the inner-carbon atoms. The synthetic strategy involved the initial preparation of an NFP dimmer followed by the nucleophilic, bond-cleavage reaction necessary to generate a covalently bonded NCP dimer. Both the structures have been elucidated by X-ray diffraction analysis. The confused pyrrole rings in the NCP dimer keep the inverted conformation and each NCP ring exhibits aromaticity, despite the highly distorted structure.

The NFP dimer was synthesized in a similar method to that used for the *meso–meso* porphyrin dimer,[8] in which a Ag(I)-promoted, oxidative-coupling reaction is employed. Briefly, N-fused tetrakis-(*p*-tolyl)porphyrin (NFTTP, **4a**) was treated with silver(I) trifluoroacetate in $CHCl_3$ at reflux for 24 hours to afford the NFP dimer **5**, in which the NFP units were covalently bonded to each other at the C2 carbon atoms of the fused rings, in a yield of 61 % (Scheme 2).

The structure of **5** was elucidated by X-ray diffraction analysis (Figure 1).[9a] The asymmetric nature of NFP and the axial chirality of dimer **5** results in the unit cell, as determined from the crystallography data, contains an enantiomeric pair of molecules of **5**. The bridging bond (1.476(9) Å) was formed between C2 and C2′. Each of the NFP units was almost planar and the mean deviations from the porphyrin plane, which consists of the core 24 atoms, were 0.072(7) and 0.083(7) Å, respectively. The NFP units were in a nearly rectangular arrangement with respect to each other and the dihedral angle between the NFP units of 75.72(5)°. The bond lengths and angles of the NFP moieties were comparable to those of **4a**.[4b] The inner NH atoms were positioned at N4 and N4′, as judged by the C_α-N-C_α angles. The three inner nitrogen atoms were located close together and form hydrogen bonds that shared

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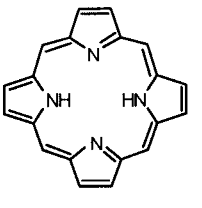
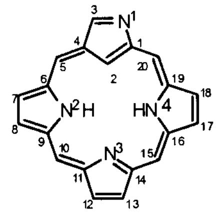
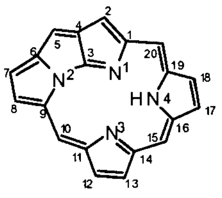


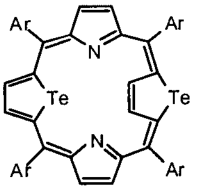
Porphyrin (**1**)



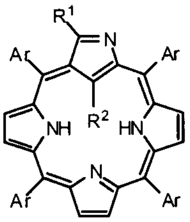
N-Confused Porphyrin (NCP)



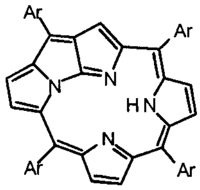
N-Fused Porphyrin (NFP)



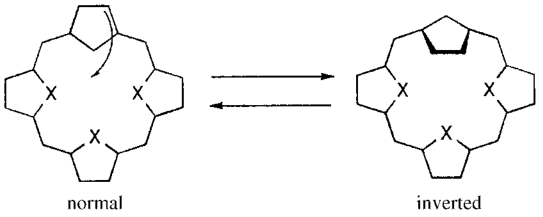
Ditelluraporphyrin (**2**)



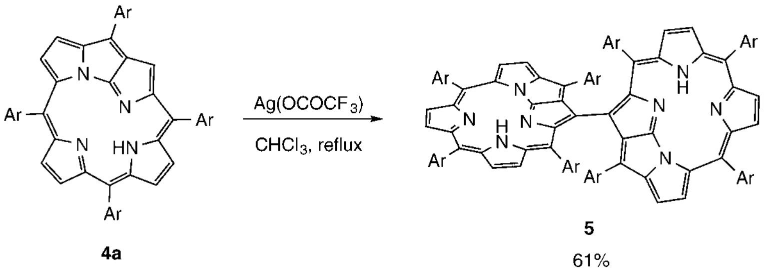
3a Ar = *p*-Tol, R^1 = H, R^2 = H
3b Ar = Ph, R^1 = H, R^2 = H
7 Ar = *p*-Tol, R^1 = H, R^2 = NO_2
8 Ar = Ph, R^1 = OMe, R^2 = H



4a Ar = *p*-Tol
4b Ar = Ph



Scheme 1. Normal and inverted conformation of porphyrinoids.



Scheme 2. Synthesis of N-fused porphyrin dimer **5**.

the inner NH hydrogen atom. Steric crowding meant that the coplanarity between the NFP core and the *meso*-aryl group at the C5 position (Ph1) found in **4**[4b] was slightly lost, as shown by with dihedral angles of 29.8(2) and 35.4(2)°, and the bond lengths of the C_{meso}–C_{ipso} bonds were relatively long (1.48(1) and 1.46(1) Å). In addition, the *meso*-aryl groups at C20 and C20′ (Ph4 and Ph4′) participate in π–π stacking with the NFP moieties that are separated by distances of 3.27(1) and 3.25(1) Å, respectively.

The ^{1}H NMR spectrum of **5** at room temperature in $CDCl_3$ shows that the proton resonance signals were relatively broad but each was distinctive and strong aromaticity was inferred from the β-proton signals of **5** appearing in the same region as those of **4a**. The four methyl signals were observed at $\delta = 2.73$, 2.58, 1.96, and 0.22 ppm, respectively, thus reflecting the symmetry of the molecule. The latter two signals are assignable to the *meso*-aryl groups (Ph1 and Ph4) that are located on the other NFP ring in the X-ray crystal structure. Similarly, the phenyl protons of Ph4 exhibited upfield shifts and four distinctive proton signals were observed at $\delta = 4.41$ and 4.72 ppm for the *ortho* protons and at $\delta = 6.17$ and 6.55 ppm for the *meta* protons, which indicates that the rotation of the benzene ring is completely disturbed by the π–π interactions with the other NFP ring, as shown in the structure determined by X-ray cyrstallography.

The aromaticity of the system is further demonstarted by the electronic absorption spectrum of dimer **5** which displays a similar profile in the 300–1000 nm region to that observed for **4a** (Figure 2a). The absorption band at the longest wavelength appeared at 977 nm, which is a bathochromic shift of 36 nm relative to **4a**.

Next, cleavage of the bridging C–N bond at the fused ring to generate the NCP ring was attempted.[4] When NFP dimer **5** was treated with sodium methoxide in THF for one hour, a diastereoiomeric mixture of covalently bonded NCP dimers **6** was produced quantitatively (Scheme 3). The signal at *m*/*z* 1400 in the mass spectrum suggested the introduction of two methoxy groups at the α-carbon atom of the confused pyrrole. The ratio of each diastereomer was determined from the ^{1}H NMR spectrum recorded in $CDCl_3$ to be 9:1.[10] The preferential formation of one of the diastereomers suggests that the second methoxide attack occurred mainly from one direction, probably because of steric hinderance in the intermediate NFP–NCP dyad. Isolation of the major diastereomer was achieved by repeated purification by column chromatography on silica gel, and, fortunately, single crystals suitable for X-ray diffraction analysis were afforded.[9b]

The ORTEP diagram of **6** is shown in Figure 3. The NCP units are linked by a covalent bond between C2 and C2′ with a length of 1.480(7) Å. The two methoxy groups are attached at the α-carbon atoms of the confused pyrroles and the inner NH hydrogen atoms are located at the N2 and N4 positions. Surprisingly, the confused pyrroles are still inverted, namely, the β-carbon atom points outward, whereas the N–C_α bond is directed to the inside of the ring. As a result, the NCP core planes are highly distorted and the mean deviations from the plane, which consist of 24 core atoms, are 0.338(5) and 0.365(5) Å. The dihedral angles between the least-squares plane of the four *meso*-carbon atoms and the pyrrole rings are 130.8(2) and 131.1(1)° for Py1 and Py1′,

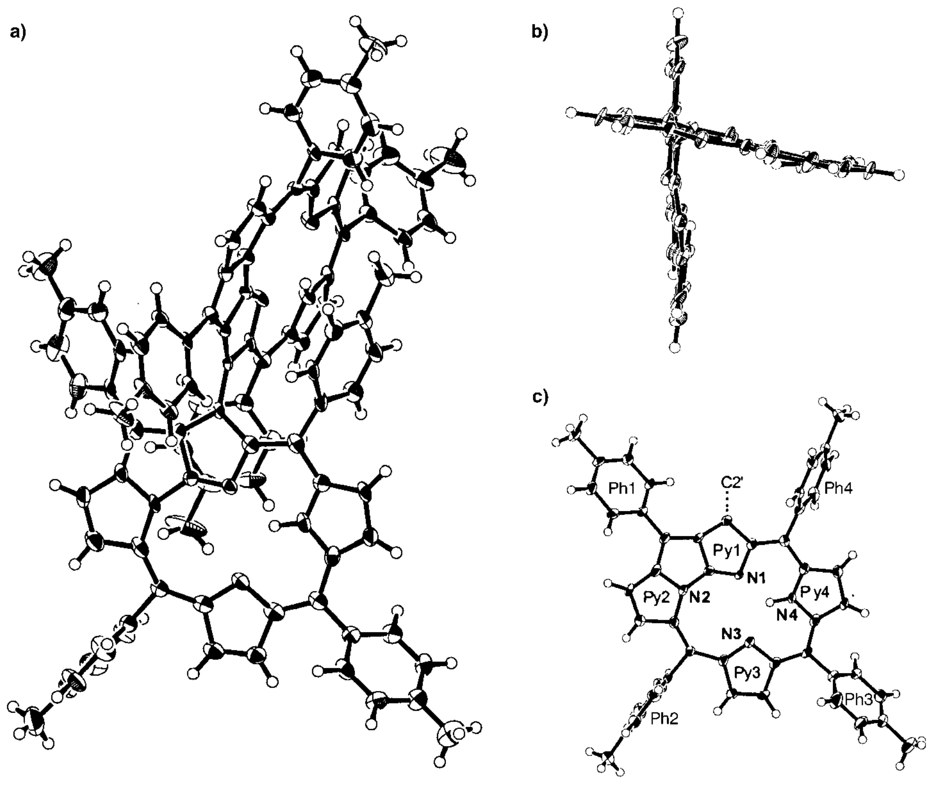
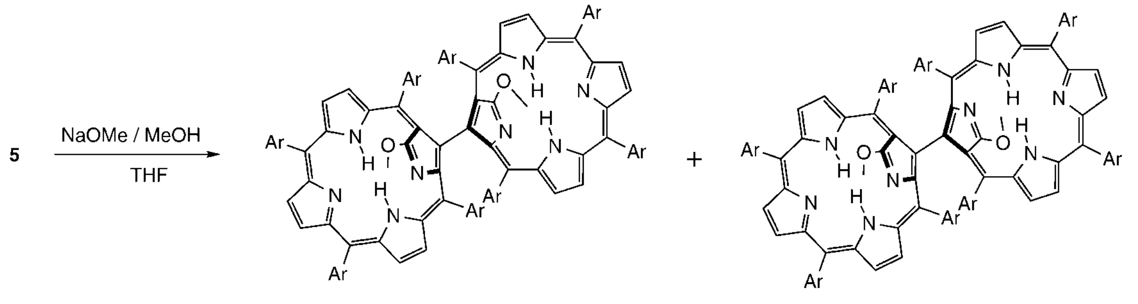


Figure 1. X-ray crystal structure of **5**. a) Top view, b) side view, and c) monomer unit. *Meso*-tolyl groups are omitted for clarity in (b).

9.2(2) and 10.5(2)° for Py2 and Py2′, 9.2(2) and 11.3(2)° for Py3 and Py3′, and 13.9(2) and 15.8(2)° for Py4 and Py4′, respectively. The confused pyrroles (Py1 and Py1′) are, thus, highly tilted relative to **3b** (24.6(1)°)[5a] and the nitro-substituted NCP **7** (41.3(2)°).[4b] The hydrogen-bonding intraction between N1 and N4-H probably helps to retain the inverted conformation, as judged by the short atom distances between N1 (N1′) and N4 (N4′) of 2.673(6) (2.687(6)) Å, and the larger tilting angles of Py4 than those of Py2 and Py3. The two NCP molecules were crossed diagonally and the dihedral angle between them was 52.36(4)°. Furthermore, the *meso*-aryl groups at C20 and C20′ (Ph4 and Ph4′) form π–π stacking pairs with other NCP rings, with mean distances of 3.264(6) and 3.248(6) Å. The bond lengths and angles of the NCP units in **6** were very similar to **3b** except that the bond angles of the adjacent *meso*-carbon atoms of the confused pyrrole and the interior angles of the *meso*-carbon atoms were relatively narrow: 116.8(4) and 115.4(5)° for C4-C5-C6 and C4′-C5′-C6′, and 117.2(4) and 117.1(4)° for C1-C20-C19 and C1′-C20′-C19′, respectively. The similarity of the bond lengths and angles suggests that the NCP rings maintain their aromaticity despite their distorted structures.

The ^{1}H NMR spectrum of the major diastereomer of **6** in $CDCl_3$ at room temperature shows that the proton resonance signals were degenerate and reflects the molecule's twofold symmetry. The methoxy groups located on the NCP ring were observed at $\delta = -0.40$ ppm because of the diamagnetic ring current effect, which causes a $\delta = 4.4$ ppm upfield shift relative to the outer α-methoxy NCP **8**.[4b] Similar π–π stacking was observed in **6** to that seen in the NFP dimer **5**. For example, the methyl signals of the *meso*-tolyl groups at the C5 and C20 positions (Ph1 and Ph4) also exhibited upfield shifts and resonated at $\delta = 2.03$ and 0.18 ppm, respectively. The benzene protons of Ph4 produced broad signals at $\delta = 3.23$ (*o*), 4.32 (*o*), 5.35 (*m*), and 5.78 (*m*) ppm. The signals of the inner NH atoms appeared distinctively at $\delta = -3.31$ and -2.76 ppm, and the sharpness of these signals indicates that the hydrogen atoms are localized on the NMR timescale. The fact that the signals of the β protons of Py2 and Py4 were observed as double doublets because they couple with the inner NH protons supports this observation. In addition, the chemical shifts of



9 : **1**

6, ~100%

Scheme 3. Synthesis of N-confused porphyrin dimer **6**.

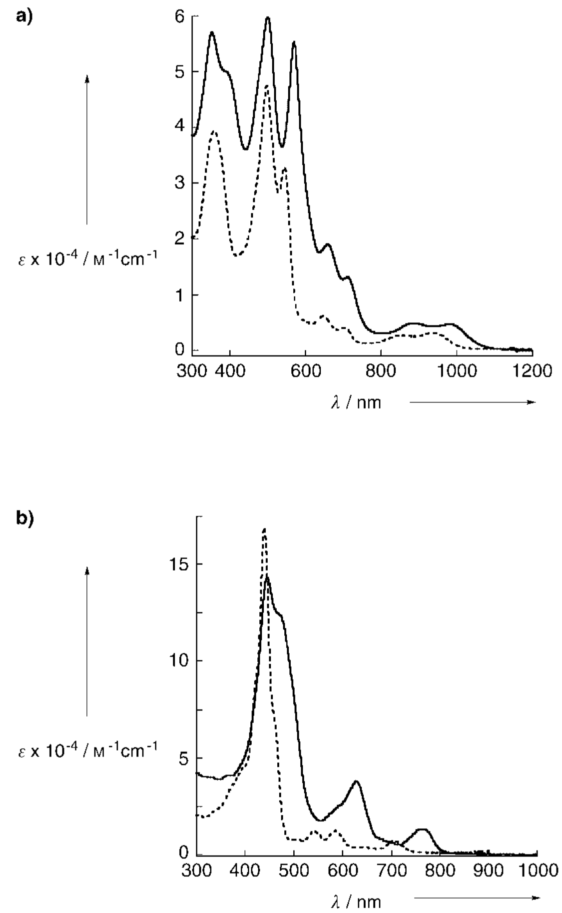


Figure 2. Optical absorption spectra of a) **4a** (•••••) and **5** (——) and b) **6** (——) and **8** (•••••) in CH_2Cl_2.

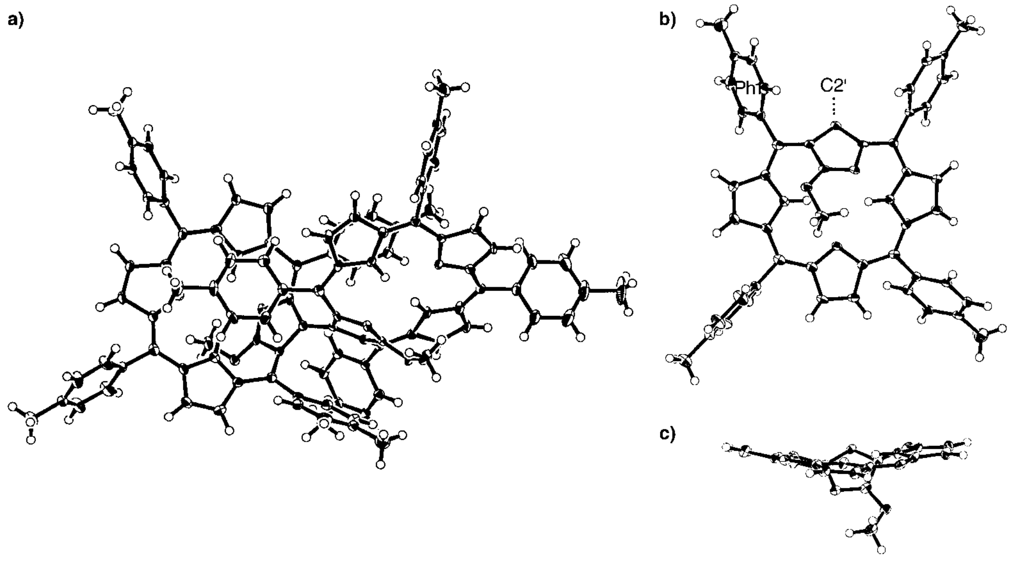


Figure 3. X-ray crystal structure of **6**. a) Top view, b) the monomer unit, and c) side view. *Meso*-tolyl groups are omitted for clarity in (c).

the inner NH protons and the β-H signals are comparable to those of **3a**[5a] and **8**,[4b] which also indicates the aromatic nature of **6**.

The UV/Vis spectrum of the major diastereomer of **6** in CH_2Cl_2 displayed a clear Soret band at 446.5 nm and two Q-bands at 629 and 765 nm, respectively (Figure 2b). The Soret band had a shoulder at 470 nm, which is possibly derived from exciton coupling between the two chromophores.[11]

In conclusion, covalently linked NFP and NCP dimers **5** and **6** were synthesized and their structures characterized by X-ray diffraction analysis. NCP dimer **6** possesses an inverted confused pyrrole ring in its macrocyclic framework and exhibits aromaticity and intense optical absorption despite its highly distorted structure. Hence, structural flexibility and pyrrole inversion are intrinsic to the nature of NCP, and the control of such properties is considered to be important to the development of NCP-based functional molecules.

Experimental Section

5: Silver trifluoroacetate (44.34 mg, 0.201 mmol) was added to a solution of **4a** (12.97 mg, 0.0194 mmol) in $CHCl_3$ (30 mL), and the reaction mixture was heated to reflux for 24 h. After removing the solvent, the residue was purified by column chromatography on silica gel with 5% $MeOH/CH_2Cl_2$. The purple fraction was collected and the product was recrystallized from CH_2Cl_2/hexane. Violet crystals of **5** (7.9 mg) were obtained in a yield of 61%. ^{1}H NMR ($CDCl_3$): $\delta =$ 9.15 (brs, 2H), 8.74 (brs, 2H), 8.39 (d, $J = 6.0$ Hz, 4H), 8.10 (brs, 4H), 7.94 (m, 6H), 7.80 (brs, 2H), 7.70 (brs, 2H), 7.54 (m, 8H), 7.35 (brs, 2H), 6.66 (d, $J = 8.4$ Hz, 4H), 6.55 (d, $J = 6.6$ Hz, 2H), 6.17 (brs, 2H), 4.72 (d, $J = 7.2$ Hz, 2H), 4.41 (brs, 2H), 2.73 (s, 6H), 2.58 (s, 6H), 1.96 (s, 6H), 0.22 ppm (s, 6H); UV/Vis (CH_2Cl_2): λ_{max} (nm) ($\log\varepsilon$ [mol^{-1}dm^{3}cm^{-1}]) = 977 (3.68), 887 (3.73), 713 (4.12), 659 (4.27), 571 (4.74), 501 (4.78), 354 (4.77); MALDI-TOF-MS: *m/z* 1335 (calcd for [M^+] 1334.6).

6: Sodium methoxide (25% solution in MeOH, 0.5 mL) was added to a solution of **5** (3.88 mg, 2.9 μmol) in dry THF (5 mL). The reaction mixture was poured into aqueous NH_4Cl after stirring for 1 h. The product was extracted with CH_2Cl_2 (20 mL) and the organic phase was separated and dried over Na_2SO_4. After removing the solvent, the residue was purified by column chromatography on silica gel with 2% $MeOH/CH_2Cl_2$. The green fraction was collected and the product was recrystallized from CH_2Cl_2/MeOH. Green crystals of **6** (3.96 mg) were obtained quantitatively as a mixture of diastereomeric pairs. Further purification by repeated flash column chromatography afforded the major diastereomer of **6**. Major diastereomer of **6**: ^{1}H NMR ($CDCl_3$): $\delta = 8.99$ (dd, $J = 4.8$, 2.1 Hz, 2H), 8.55 (dd, $J = 4.8$, 2.0 Hz, 2H), 8.40 (d, $J = 4.5$ Hz, 2H), 8.33 (d, $J = 5.1$ Hz, 4H), 8.19 (dd, $J = 7.7$, 1.7 Hz, 2H), 7.94 (m, 4H), 7.88 (dd, $J = 4.8$, 2.1 Hz, 2H), 7.78 (d, $J = 7.5$ Hz, 2H), 7.61 (d, $J = 7.5$ Hz, 2H), 7.54 (d, $J = 8.1$ Hz, 2H), 7.41 (m, 6H), 7.14 (d, $J = 7.8$ Hz, 4H), 5.78 (brs, 2H), 5.35 (brs, 2H), 4.32

(br s, 2H), 3.23 (br s, 2H), 2.72 (s, 6H), 2.60 (s, 6H), 2.03 (s, 6H), 0.18 (s, 6H), −0.40 (s, 6H), −2.76 (s, 2H), −3.31 ppm (s, 2H); UV/Vis (CH_2Cl_2): λ_{max} (nm) (logε [$mol^{-1} dm^3 cm^{-1}$]) 766 (4.14), 629 (4.59), 447 (5.16); MALDI-TOF-MS: m/z 1400 (calcd for [M+H^+] 1399.6).

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Keywords: aromaticity · macrocyclic ligands · N ligands · N-confused porphyrins · porphyrinoids

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[9] a) Crystal data for **5**: $C_{96}H_{70}N_8$, $M_r = 1279.64$, triclinic, space group $P\bar{1}$ (no. 2), $a = 12.328(2)$, $b = 15.263(2)$, $c = 19.177(3)$ Å, $\alpha = 92.526(3)$, $\beta = 96.507(3)$, $\chi = 103.889(3)°$, $V = 3471.0(9)$ Å^3, $T = -173.0$ °C, $Z = 2$, 53358 measured reflections, 18522 unique reflections, 5745 with $I \geq 3\sigma(I)$ used in refinement, $R = 0.081$, $R_w = 0.083$, GOF = 0.957; b) crystal data for **6**: $C_{98}H_{78}N_8O_2 \cdot CH_2Cl_2 \cdot 2H_2O$, $M_r = 1520.71$, triclinic, space group $P\bar{1}$ (no. 2), $a = 12.8732(9)$, $b = 14.891(1)$, $c = 21.011(1)$ Å, $\alpha = 87.385(2)$, $\beta = 86.629(1)$, $\chi = 76.697(1)°$, $V = 3910.7(5)$ Å^3, $T = -173.0$ °C, $Z = 2$, 24876 measured reflections, 24876 unique reflections, 13668 with $I \geq 3\sigma(I)$ used in refinement, $R = 0.099$, $R_w = 0.129$, GOF = 0.999. CCDC-233747 (**5**) and 233748 (**6**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB21EZ, UK; fax: (+44)1223-336-033; or deposit@ccdc.cam.ac.uk).

[10] See the Supporting Information.

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