

COMMUNICATION

Stable Non-fused [22]Pentaphyrins and A Fused [24]Pentaphyrin Displaying Crystal Polymorphism between Hückel and Möbius Structures

Tomoki Yoneda*^[a], Tyuji Hoshino^[a] and Saburo Neya*^[a]

β-substituted Abstract: Partially and mesotetrakis(pentafluorophenyl)-substituted [22]pentaphyrins 11 and 12 were synthesized by acid-catalyzed condensation of a meso-C₆F₅-substituted tripyrrane dicarbinol with β -alkylated dipyrromethanes. These [22]pentaphyrins are stable, allowing their characterization by NMR and UV-vis spectroscopies, and Xray crystallography, and display strong aromaticity due to 22*π*electronic circuits. In methanol, β , β -diethoxycarbonylated pentaphyrin 12 underwent an N-fusion reaction to give N-fused pentaphyrin 13, which exhibits crystal polymorphism between Hückel and Möbius structures, depending upon the recrystallization solvent

Expanded porphyrins, porphyrinoids with more than four pyrrole units, are attracting much attention because of the optical, electrochemical, and coordination properties that arise from their large π -conjugated frameworks.^[1,2] Pentaphyrins(1.1.1.1) consisting of five pyrroles that are regularly connected through meso-carbons exhibit characteristic structural and electronic properties arising from their larger π -conjugative systems as compared with porphyrins. *β*-Alkyl-substituted pentaphyrins 1 and 2 were synthesized as the first example, showing large diatropic ring currents and thus aromaticity arising from their 22π -electronic circuits at their protonated form.^[3] Later, meso-diphenyl- and β tetraalkyl-substituted pentaphyrin 3 was synthesized to show similar aromatic characters.^[4] While the solid-state structures of these pentaphyrins have still remained unknown, it is likely that these pentaphyrins do not suffer from serious sterical distortion. In the one-pot synthesis of meso-aryl-substituted expanded meso-aryl-substituted [22]pentaphyrins porphyrins, were obtained as N-fused species, 4 and 5. The observed efficient Nfusion reaction may be ascribed to large strain of non-fused mesoaryl-substituted pentaphyrins (Scheme 2). Aromatic 22n N-fused pentaphyrins 4 and 5 can be reduced to nonaromatic 24π congeners 6 and 7.^[5] On the other hand, meso-trifluoromethylsubstituted N-fused pentaphyrin 8 is considered to be a 24π Möbius aromatic system and oxidation to its 22π counterpart did not proceed (Scheme 1). [6,7]





¹ ($R^1 = CH_2CH_2CO_2Me$, $R^2 = R^3 = Me$) **2** ($R^1 = Me$, $R^2 = Et$, $R^3 = n$ -Bu)





6 Ar = C₆F₅

7 Ar = 2,6-dichlorophenyl

 $4 \text{ Ar} = C_6 F_5$ 5 Ar = 2,6-dichlorophenyl

CF

F۹

8



Scheme 1. Reported *meso-* and β -substituted pentaphyrins.

 [a] Dr. Tomoki Yoneda, Dr. Tyuji Hoshino, Prof. Dr. Saburo Neya Department of Pharmaceutical Sciences, Chiba University 1-8-1, Inohana, Chuo-ku, Chiba, 260-8675, Japan
 E-mail: <u>yoneda@chiba-u.jp</u> sneya@faculty.chiba-u.jp

Supporting information for this article is given via a link at the end of the document.

COMMUNICATION



Scheme 2. N-fusion reaction of *meso*-aryl pentaphyrin. (DDQ = 2,3-dichloro-5,6-dichanobenzoquinone)

For the purpose of mitigating the steric constraint of pentaphyrin **4**, we prepared tetrakis(pentafluorophenyl)-substituted [22]pentaphyrin **9** bearing one unsubstituted *meso*-position and found that N-fusion reaction was actually suppressed. ^[8] Pentaphyrin **9** showed an inward-pointing free *meso*-position and modest aromaticity but underwent oxidative decomposition slowly. Chemical stability of bis(rhodium(I)) complex **10** was somewhat improved, probably through better steric protection at the free *meso*-position by the coordinated rhodium metals. The structural characteristics of these pentaphyrins were also theoretically studied by Alonso *et al.*^[9]

With these in background, we report here the synthesis of *meso*-free [22]pentaphyrins **11** and **12** (Scheme 3). It was considered that β , β -disubstituted pyrroles flanking the free *meso*-position might protect it from oxidative damage, hence enhancing the chemical stability.



Scheme 3. Structure of the mono-meso-free pentaphyrins reported in this paper



Figure 1. X-Ray crystal structure of pentaphyrin 11. a) Top view and b) side view. Solvent molecules and *meso*-pentafluorophenyl groups are omitted in the side view. Thermal ellipsoids are displayed at 50% probability.

We prepared 2,3,22,23-tetramethyl-5,10,15,20first tetrakis(pentafluorophenyl)-substituted pentaphyrin 11. A solution of meso-pentafluorophenyl-substituted tripyrrane dicarbinol and 2,3,7,8-tetramethyl dipyrromethane^[10] in dichloromethane was treated with p-toluenesulfonic acid under nitrogen atomsphere. The resulting mixture was oxidized with DDQ to afford pentaphyrin 11 in 6.7% yield (SI). Contrary to 9, compound 11 was stable under ambient conditions and was isolated in a pure form by silica-gel column chromatography and recrystalization with pentane. High-resolution electrospray ionization time-of-flight mass spectroscopy (HR-ESI-TOF MS) indicated the parent ion peak of **11** at m/z = 1108.1552 (calcd for $C_{53}H_{22}N_5F_{20}$ [*M*+H]⁺ 1108.1550). The ¹H NMR spectrum of **11** displays two doublets due to the outer β protons at δ = 9.04 and 8.74 ppm and singlets due to the methyl groups at δ = 3.74 and 2.90 ppm, a singlet due to the inner NH protons at 0.55 ppm, a singlet due to the inner β protons at δ = -1.76 ppm, and a singlet due to the inner mesoproton at δ = -6.96 ppm. These ¹H NMR data indicate a strong diatropic ring current. The structure of 11 has been revealed by X-ray crystallographic analysis as a non-fused and roughly planar pentaphyrin possessing an inward-pointing meso-hydrogen atom (Figure 1).^[11] The mean plane deviation (MPD) of the pentaphyrin skeleton was calculated to be 0.264 Å. The UV-vis absorption spectrum of 11 was similar to that of 9, exhibiting a sharp Soret band at 517 nm and Q bands at 649, 681, 749, and 837 nm. These spectral features are conistent with the assignment of 11 as an aromatic expanded porphyrin (Figure 2).

Although pentaphyrin **11** was stable enough for the isolation and physical characterizations, it slowly decomposed in CH_2Cl_2 over a few weeks. Since the decomposition of *meso*-free pentaphyrins may be ascribed to oxidative damages at the free *meso*-position, we supposed that substitution of electronwithdrawing groups at the periphery would suppress its

COMMUNICATION

decomposition. Therefore, we synthesized pentaphyrin 12 having two electron-withdrawing ethoxycarbonyl groups. A solution of tripyrrane dicarbinol and 3,7-bis(ethoxycarbonyl)-2,8-dimethyl dipyrromethane^[12] in dichloromethane was treated with ptoluenesulfonic acid and subsequently oxidized with DDQ, affording pentaphyrin 12. Even being stored in CH₂Cl₂ solution under aerobic conditions, pentaphyrin 12 did not show any decomposition, showing its much improved stability. HR-ESI-TOF MS analysis indicated the parent ion peak of 11 at m/z = 1122.1495 (calcd for C₅₄H₂₄N₅F₂₀ [*M*-H]⁻: 1122.1509). The ¹H NMR spectrum of **12** displays two doublets due to the outer β protons at δ = 9.04 and 8.78 ppm, and a singlet due to the inner β protons at δ = -1.19 ppm, and a singlet due to the inner *meso*proton at δ = -5.97 ppm. These data also indicate a strong diatropic ring current. As revealed by X-ray crystallography, the structure of **12** is similar to that of **11**, showing a roughly planar non-fused pentaphyrin with MPD of 0.221 Å (Figure 3).^[13] The UVvis absorption spectrum of 12 also exhibits a strong Soret band at 523 nm and Q bands at 647, 696, and 769 nm (Figure 2).



Figure 2. UV-vis absorption spectra of 11 (black), 12 (red, dashed), and 13 (blue, dotted) in $\text{CH}_2\text{Cl}_2.$





Figure 3. X-Ray crystal structure of pentaphyrin 12. a) Top view and b) side view. Solvent molecules and *meso*-pentafluorophenyl groups are omitted in the side view. Thermal ellipsoids are shown at 50% probability.



Scheme 4. Non-oxidative N-fusion reaction of 12

As mentioned above, pentaphyrin **12** was quite stable in CH_2Cl_2 . However, we noticed that **12** was changed to a brown compound in methanol (Scheme 4).^[14] This transformation proceeded smoothly at room temperature, giving **13** in 86% yield after 4 h. Crystals of **13** suitable for X-ray diffraction analysis were obtained by slow diffusion of *n*-nonane into its chlorobenzene solution.^[15] The structure of **13** has been revealed to be a N-fused [24]pentaphyrin, in which the N1 atom on the pyrrole A is directly bonded to the β -position (C7) on the pyrrole B moiety (Figure 4). In this crystal, **13** exhibits a highly skewed conformation around the pyrrole E with a largest torsion angle of 62.5°. Despite the largely skewed structure, **13** has been shown to possess a Hückel topology.

COMMUNICATION



Figure 4. X-Ray crystal structure of pentaphyrin 13 formed from a chlorobenzene/nonane solution. a) Top view and b) side view. Solvent molecules and *meso*-pentafluorophenyl groups are omitted in the side view. Thermal ellipsoids are shown at 30% probability. One of two similar molecules in the asymmetric unit is illustrated.

Since the 24π skeleton of **13** is isoelectronic with the known *meso*-aryl substituted N-fused [24]pentaphyrins **6** and **7**, this reaction suggests an important insight into the mechanism of the N-fusion reactions of *meso*-aryl-substituted pentaphyrins. The N-fusion reaction of **12** to **13** is a dehydrogenation process of the β -CH and NH protons with a concurrent reduction (from 22π to 24π) of the macrocyclic π -electronic network. Therefore, the overall change is a non-redox process and this fusion reaction required no oxidant and proceeded almost spontaneously in methanol. Such a process has not been predicted in previous theoretical considerations of N-fusion reactions.^[9]





Figure 5. X-Ray crystal structure of pentaphyrin **13-Möbius** afforded from a toluene/cyclohexane solution. a) Top view and b) side view. Solvent molecules and *meso*-pentafluorophenyl groups are omitted in the side view. Thermal ellipsoids are shown at 50% probability. One of two similar molecules in the asymmetric unit is illustrated.

In the meanwhile, we found crystal polymorphism^[16] of **13**. Namely, single crystals of **13** obtained by slow diffusion of cyclohexane into its toluene solution have been shown to display a twisted Möbius structure (**13-Möbius**) with a largest torsional angle of 60.3° (Figure 5).^[17] This finding suggests that the energy barrier of the interconversion between the Hückel and Möbius conformers may be small, being influenced by packing forces induced by different solvent systems (Scheme 5). To the best of our knowledge, this is the first example of solvent-induced conformational topology switching of pentaphyrins.^[18,19] It is plausible that the omittion of one pentafluorophenyl substituent results in a reduced barrier of the topological inversion.

Nonaromatic or weakly antiaromatic character of **13** in solution has been indicated by its ¹H NMR spectrum that displays four doublets at $\delta = 6.37$, 6.20, 6.16, and 6.03 ppm due to the β -protons, two singlets at $\delta = 7.21$ and 6.79 ppm due to the *meso*-or β -protons, and three signals at $\delta = 12.8$, 6.86, and 6.62 ppm due to the NH protons. These spectral features were not significantly changed even at low temperatures (-90 °C in CH₂Cl₂), strongly suggesting that the Hückel structure is dominant in solution. The UV/vis absorption spectrum of **13** is drastically different from that of **12**, exhibiting a weak Soret band at 484 nm and a Q-like broad band at 767 nm that spreads to ~1200 nm. (Figure 2), consistent with the assignment as a nonaromatic species.

COMMUNICATION

In order to gain more information, we performed DFT calculations of 11, 12, 13, and 13-Möbius with B3LYP/6-31G(d) level.^[19] These calculations have revealed nearly degenerate HOMO/HOMO-1 and LUMO/LUMO+1 for 11 and 12 as an indication that these two pentaphyrins are both aromatic species. Namely, the HOMO-LUMO gaps for 11 and 12 have been calculated to be 2.05 and 2.01 eV, respectively. On the other hand, the HOMO-LUMO gap of 13, 1.63 eV, has been calculated to be relatively small, while that of 13-Möbius has been calculated to be 1.90 eV. These calculations have indicated that 13 is more stable than 12 by 13.1 kcal/mol, supporting the observed spontaneous N-fusion reaction of 12, and 13 is slightly more stable than 13-Möbius by 0.21 kcal/mol, in line with the observed predominant distribution of 13 over 13-Möbius. The nucleusindependent chemical shift (NICS) values^[20] at the center of the macrocycle have been calculated to be -15.54 and -15.31 ppm for 11 and 12, respectively. These results are in line with the strong aromaticity of non-fused pentaphyrins. The calculated NICS(0) value of -0.53 ppm for 13 suggests its nonaromatic character, while that of 13-Möbius is -10.07 ppm, strongly supporting its Möbius aromatic character (SI).

In summary, we have synthesized chemically stable *meso*free pentaphyrins **11** and **12**. While **12** was much more stable in CH₂Cl₂, it underwent a smooth N-fusion reaction in methanol to give N-fused pentaphyrin **13**, which displayed crystal polymorphism, taking either Hückel or Möbius conformation depending upon recrystallization solvents. Exploration of new hybrid expanded porphyrins bearing *meso*-aryl and β -alkyl substituents are now being investigated in our laboratory.

Acknowledgements

This work was supported by JSPS KAKENHI Grant Numbers 26460031 and 20249072 and the Program to Disseminate Tenure Tracking System from MEXT of Japan. We thank Dr. Takayuki Tanaka and Prof. Dr. Atsuhiro Osuka (Kyoto University) for X-ray crystallography and cyclic voltammetry measurements.

Keywords: expanded porphyrin • pentaphyrin• aromaticity • fusion reaction • crystal polymorphism

- a) J. L. Sessler, D. Seidel, Angew. Chem. Int. Ed. 2003, 42, 5134; Angew. Chem. 2003, 115, 5292; b) T. K. Chandrashekar, S. Venkatraman, Acc. Chem. Res. 2003, 36, 676; c) M. Stępień, N. Sprutta, L. Latos-Grażyński, Angew. Chem. Int. Ed. 2011, 50, 4288; Angew. Chem. 2011, 123, 4376; d) S. Saito, A. Osuka, Angew. Chem. Int. Ed. 2011, 50, 4342; Angew. Chem. 2011, 123, 4432; e) T. Tanaka, A. Osuka, Chem. Rev. 2016; DOI:10.1021/acs.chemrev.6b00371.
- [2] J.-Y. Shin, H. Furuta, K. Yoza, S. Igarashi, A. Osuka, J. Am. Chem. Soc. 2001, 123, 7190
- a) H. Rexhausen, A. Gossauer, J. Chem. Soc., Chem. Commun. 1983,
 275; b) A. K. Burrell, G. Hemmi, V. Lynch, J. L. Sessler, J. Am. Chem.
 Soc. 1991, 113, 4690.
- [4] C. Bruckner, E. D. Sternberg, R. W. Boyle, D. Dolphin, Chem. Commun. 1997, 1689.
- [5] J.-Y. Shin, H. Furuta, A. Osuka, Angew. Chem. Int. Ed. 2001, 40, 619; Angew. Chem. 2001, 113, 639.
- [6] S. Shimizu, N. Aratani, A. Osuka, *Chem. Eur. J.* **2006**, *12*, 4909.
- [7] M. Alonso, P. Geerlings, F. D. Proft, Phys. Chem. Chem. Phys. 2014, 16, 14396.
- [8] T. Yoneda, H. Mori, B. S. Lee, M.-C. Yoon, D. Kim, A. Osuka, *Chem. Commun.* 2012, 48, 6785.

- [9] M. Alonso, P. Geerlings, F. D. Proft, J. Org. Chem. 2013, 78, 4419.
- [10] a) P. S. Clezy, A. W. Nichol, Aust. J. Chem. 1965, 18, 1835; b) C. K. Chang, J. Org. Chem. 1981, 46, 4610.
- [11] Crystal data for **11**, $2(C_{53}H_{21}F_{20}N_5) \cdot (\text{pentane})$ (*M*r = 2275.55), orthorhombic, space group *P*_{bcn} (No. 60), *a* = 35.84(2), *b* = 10.112(6), *c* = 27.180(17) Å, *V* = 9850(10) Å³, *Z* = 4, ρ_{calcd} = 1.535 gcm⁻³, *T* = 93(2) K, *R*₁ = 0.0769 (*I* > 2 σ (*I*)), *wR*₂ = 0.2304 (all data), GOF = 0.987. CCDC = 1519168.
- [12] J. B. Paine III, D. Dolphin, J. Org. Chem. 1988, 53, 2787.
- [13] Crystal data for **12**, $C_{57}H_{25}F_{20}N_5O_4$ (pentane) (*M*r =1295.97), monoclinic, space group P_{21}/c (No. 14), a = 19.9549(4), b = 14.3564(3), c = 20.0023(4) Å, $\beta = 104.0506(7)^{\circ}$ V = 5558.8(2) Å³, Z = 4, $\rho_{calcd} = 1.269$ gcm⁻³, T = 93(2) K, $R_1 = 0.0749$ ($l > 2\sigma(l)$), $wR_2 = 0.2360$ (all data), GOF = 1.046. CCDC = 1519169
- [14] A similar color alteration was observed in the case of 11 in methanol. However, much inseparable byproducts were also observed.
- [15] Crystal data for **13**, $2(C_{57}H_{25}F_{20}N_5O_4) \cdot 0.5(nonane) \cdot 1.5(chlorobenzene)$ (*M*r = 2670.51), triclinic, space group *P*-1 (No. 2), *a* = 14.024(4), *b* = 20.155(6), *c* = 22.672(4) Å, *a* = 64.022(19) β = 79.54(4) γ = 88.32(3) *V* = 5656(3) Å³, *Z* = 4, ρ_{calcd} = 1.568 g cm⁻³, *T* = 93(2) K, *R*₁ = 0.1162 (*I*>2 σ (*I*)), *wR*₂ = 0.3468 (all data),GOF = 1.182. CCDC = 1519170. The high *R*₁ value is derived from the weakness of diffraction spots and the disorders of solvent molecules, but the Hückel structure of **13** is unambiguously assigned.
- Polymorphism; a) J. D. Dunitz, J. Bernstein, Acc. Chem. Res. 1995, 28, 193. b) J. Bernstein, R. J. Davey, J.-O. Henck, Angew. Chem. Int. Ed. 1999, 38, 3440; Angew. Chem. 1999, 111, 3646. c) A. Nangia, Acc. Chem Res. 2008, 41, 595.
- [18] Examples of solvent-dependent Hückel-Möbius conformational changes of expanded porphyrins; a) J. Sankar, S.Mori, S. Saito, H. Rath, M. Suzuki, Y. Inokuma, H. Shinokubo, K. S. Kim, Z. S. Yoon, J.-Y. Shin, J. M. Lim, Y. Matsuzaki, O. Matsushita, A. Muranaka, N. Kobayashi, D. Kim A. Osuka, *J. Am. Chem. Soc.* 2008, *130*, 13568; b) S. Saito, J.-Y. Shin, J. M. Lim, K. S. Kim, D. Kim, A. Osuka, *Angew. Chem. Int. Ed.* 2008, *47*, 9657; *Angew. Chem.* 2008, *120*, 9803; c) M.-C. Yoon, J.-Y. Shin, J. M. Lim, S. Saito, T. Yoneda, A. Osuka, D. Kim, *Chem. Eur. J.* 2011, *17*, 6707; d) T. Yoneda, Y. M. Sung, J. M. Lim, D. Kim, A. Osuka, *Angew. Chem. Int. Ed.* 2014, *53*, 13169; *Angew. Chem.* 2014, *126*, 13385.
- [19] Topological switching of N-fused [24]pentaphyrins; a) S. Mori, J.-Y. Shin,
 S. Shimizu, F. Ishikawa, H. Furuta, A. Osuka, *Chem. Eur. J.* 2005, *11*,
 2417; b) J. K. Park, Z. S. Yoon, M.-C. Yoon, K. S. Kim, S. Mori, J.-Y. Shin,
 A. Osuka, D. Kim, *J. Am. Chem. Soc.* 2008, *130*, 1824; c) S.-i. Ishida, J.
 O. Kim, D. Kim, A. Osuka, *Chem. Eur. J.* 2016, *22*, 16554.
- [19] M. J. Frisch. et al., Gaussian09, revision A.02; Gaussian, Inc.: Wallingford, CT, 2009 (Full citation in SI).
- [20] a) P. von R. Schleyer, C. Maerker, A. Dransfeld, H. Jiao, N. J. R. v. E. Hommes, *J. Am. Chem. Soc.* **1996**, *118*, 6317; b) Z. Chen, C. S. Wannerere, C. Corminboeuf, R. T. Puchta, P. von R. Schleyer, *Chem. Rev.* **2005**, *105*, 3842.

COMMUNICATION

Entry for the Table of Contents (Please choose one layout)

reaction in methanol to give an N-fused [24]pentaphyrin, which exhibited crystal polymorphism between Hückel and Möbius structures, depending on the

COMMUNICATION

recrystallization solvents.

