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Synthesis and Isomerization of Imino-Fused N-Confused Porphyrin

Norimasa Kashiwagi,[†] Takeshi Akeda,[†] Tatsuki Morimoto,[†] Tomoya Ishizuka,[†] and Hiroyuki Furuta*,[†,‡]

Department of Chemistry & Biochemistry, Graduate School of Engineering, Kyushu University, Fukuoka 819-0395, Japan, and PRESTO, Japan Science and Technology Agency (JST), Kawaguchi 332-0012, Japan

hfuruta@cstf.kyushu-u.ac.jp

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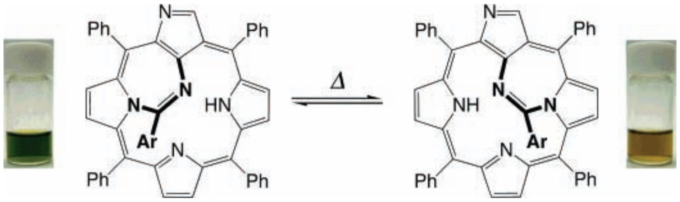
ABSTRACT



A set of mutually interconvertable inner-bridged-type porphyrinoids, imino-fused N-confused porphyrins (IF-NCPs), which possess a [5.7.5] tricyclic ring in the core, were synthesized from a condensation reaction of 21-amino-substituted NCP and an arylaldehyde, and the structures were characterized by X-ray single-crystal analysis.

Porphyrins have attracted considerable attention because of the versatile properties stemming from the characteristic π-system that can be used for a variety of applications.[1] To tune or change the properties, modification of the porphyrin framework has been attempted, and consequently, various kinds of porphyrin analogues and their derivatives have been synthesized.[2] Among such porphyrinoids, an isomeric porphyrin, N-confused porphyrin (NCP), has been shown to exhibit peculiar optical and coordination properties owing to its unique structure that possesses an NNNC core and a peripheral N atom.[3,4] Reactivity of NCP is rather high compared to that of the standard porphyrin due to the confused pyrrole ring. For example, the peripheral α-carbon (C_3) is easily oxidized,[5] and the C═N bond (C_3, N_2) serves as a dienophile for the Diels−Alder reaction.[6] The inner β-carbon (C_{21}) is readily attacked by electrophiles, such as halogen and nitronium ion.[7] By taking advantage of this high

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[†] Kyushu University.

[‡] PRESTO, JST.

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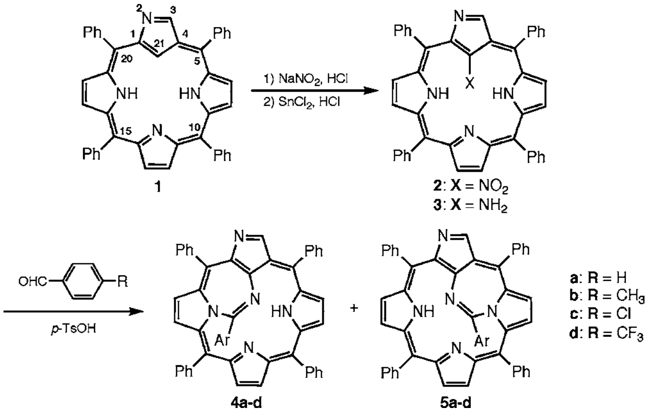
reactivity, the NCP framework can be easily modified into a novel fused porphyrinoid having a [5.5.5] tricyclic ring, N-fused porphyrin (NFP), a near-IR dye whose absorption edge reaches around 1000 nm.[7b,8] Structurally, the fused π system is of interest because it directly affects the aromatic circuit of porphyrin that is crucial for various applications such as PDT, nonlinear optics, and so on.[9] Herein, we report the synthesis of a set of new inner-bridged-type porphyrinoids, imino-fused N-confused porphyrins (IF-NCPs), which contain a [5.7.5] tricyclic ring in the core, from a condensation reaction of amino-substituted NCP and an arylaldehyde. The two isomeric IF-NCPs interconvert mutually upon heating.

Initially, we planned to synthesize an NCP bearing an arylimino group at the inner β-carbon (C_{21}) aiming to extend the π system out of the porphyrin plane. After introducing a nitro group at the C_{21} position of N-confused tetraphenylporphyrin (NCTPP, **1**),[7a] the nitro derivative (**2**) was reduced to an amino-substituted one (21-amino NCTPP, **3**) by a standard Sn(II) reduction.[10] Subsequent condensation of **3** with benzaldehyde and the usual workup with silica gel column chromatography, however, did not afford the expected 21-phenylimino-substituted NCTPP, but yielded unusual inner-bridged porphyrinoids, **4a** and **5a**, in 35% and 13%, respectively. Similar products were isolated in the reactions with arylaldehydes having other substituents, such as *p*-tolyl (**4b**, **5b**), *p*-chloro (**4c**, **5c**), and *p*-trifluoromethyl (**4d**, **5d**) groups (Scheme 1).

Scheme 1. Synthesis of IF-NCTPP (**4**, **5**)



The isomeric and aromatic fused structures of **4a** and **5a** were suggested by the MALDI-TOF-MS measurements as well as the ^{1}H NMR and UV/vis spectra. At first, the mass spectra of both products showed the same parent peak at *m/z* 715, which is smaller than that of the anticipated 21-phenylimino NCTPP by 2 Da. In the ^{1}H NMR spectra, only one NH signal was observed at -0.65 (-0.20) ppm at -50 °C for **4a** (**5a**), and the expected imino-CH proton signal was not detected. The presence of a phenyl group above the aromatic plane was demonstrated by the upfield-shifted *o*-proton signal (2H) at 3.42 (3.27) ppm for **4a** (**5a**). In the absorption spectra, both showed a similar profile with the Soret and Q-like bands at 395 (390), 458 (463), and 637 (628) nm for **4a** (**5a**) in CH_2Cl_2 (Figure 1). The above data implied that the **4a** and **5a** are isomers and possess an inner-bridged ring, which is formed by losing the hydrogen atoms from pyrrolic NH and imino-CH in the plausible intermediate, 21-phenylimino NCTPP.

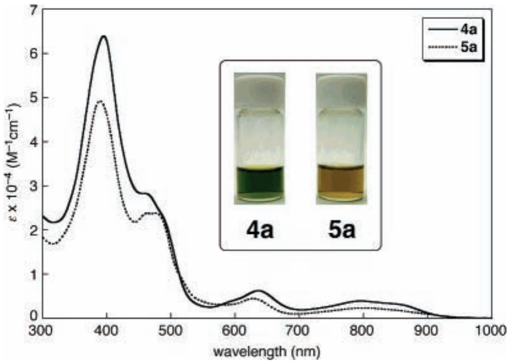


Figure 1. Absorption spectra of **4a** (solid line) and **5a** (dot line) in CH_2Cl_2 and the solution color in CH_2Cl_2 (inset).

The explicit structures of **4a** and **5a** were elucidated by the single-crystal X-ray diffraction analyses (Figure 2).[11,12] Both the structures show a [5.7.5] tricyclic ring in the core, where the fused seven-membered ring was formed by the linkage of an inner pyrrolic nitrogen atom next to the confused pyrrole and the imino-carbon atom. The difference in the two structures is only the direction of the tricyclic ring, that is, the seven-membered ring is formed on the same side of the outer nitrogen (N_2) in **4a** but on the opposite side in **5a**. Reflecting the ring fusion, the tilting angles of the confused pyrrole ring (from the mean plane consisting of 24 atoms of the NCP skeleton) in **4a** and **5a** are 24.4(4)° and 20.9(3)°, which are smaller than that of free base NCTPP (**1**), 26.9°.[3a,13] Imino-C and -N atoms of **4a** are located above

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(10) The Soret band of **3** was broadened and hypsochromic shifted by 21 nm in CH_2Cl_2 (seethe Supporting Information).

(11) Crystal data for **4a·CH₂Cl₂**: $C_{51}H_{33}N_5{\cdot}CH_2Cl_2$, $M_w = 800.75$, monoclinic, space group $P2_1/c$ (no. 14), $a = 14.6224(7)$ Å, $b = 24.827(1)$ Å, $c = 11.4670(6)$ Å, $b = 98.278(1)°$, $V = 4119.5(4)$ Å^3, $Z = 4$, $D_{calcd} = 1.291$ g/cm^3, $T = -173$ °C, $R = 0.088$, $R_w = 0.229$, GOF = 1.038 ($I > 2\sigma(I)$). Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre with reference number CCDC 635929. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

(12) Crystal data for **5a**: $C_{51}H_{33}N_5$, $M_w = 715.82$, monoclinic, space group $P2_1/n$ (no. 14), $a = 7.7674(5)$ Å, $b = 26.8846(17)$ Å, $c = 17.8280(11)$ Å, $\beta = 99.531(2)°$, $V = 3671.5(4)$ Å^3, $Z = 4$, $D_{calcd} = 1.295$ g/cm^3, $T = -50$ °C, $R = 0.0523$, $R_w = 0.1096$, GOF = 0.951 ($I > 2\sigma(I)$). Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre with reference number CCDC 635930. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

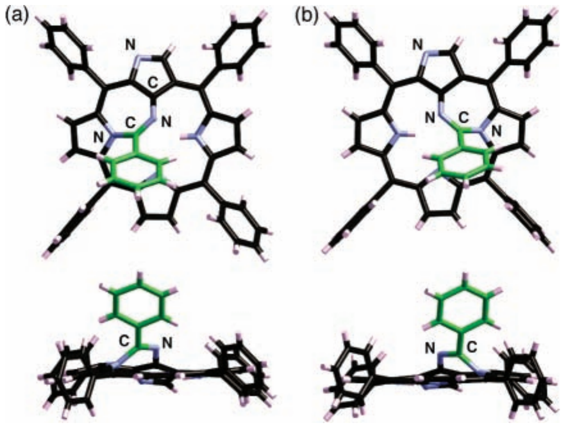
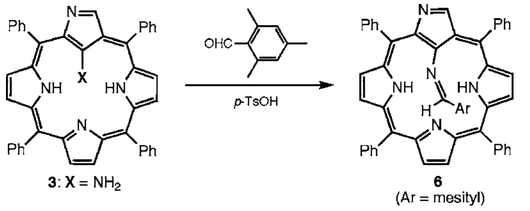


Figure 2. X-ray structures of **4a** (a) and **5a** (b). One of the enantiomers is shown in parts a and b.

the mean plane by 1.347(6) and 1.304(6) Å, respectively, whereas those of **5a** are 1.248(4) and 1.261(4) Å. These values indicate that the imino C═N bond is almost parallel to the NCP mean plane. In addition, the imino-phenyl group is tilted by 51.7(4)° and 57.4(3)° for **4a** and **5a**, respectively. Both compounds exist as racemic mixtures in the crystals, reflecting the unsymmetric structure of the NCP framework. To these inner-bridged NCPs, a trivial name of imino-fused N-confused porphyrin (IF-NCP) is given.

The plausible intermediate, 21-phenylimino NCTPP, was not obtained under the present reaction conditions, probably because of the high reactivity of the imino group. To confirm the formation of such intermediate, **3** was reacted with sterically crowded mesitaldehyde (Scheme 2).

Scheme 2. Synthesis of 21-Phenylimino NCTPP (**6**)



As expected, the formation of the seven-membered ring was completely inhibited and the imino-substituted NCP (21-phenylimino NCTPP, **6**) was obtained in 28%. The large structural difference of **4** (or **5**) from **6** was inferred from the broad absorption spectra ($\lambda_{\max}$ = 398, 432, 556, 606, and 760 nm, Figure 3). Additionally, the singlet proton signal (1H) at 4.74 ppm clearly proved the existence of the imino-CH proton.

The structure of **6** was finally confirmed by the single-crystal X-ray diffraction analysis (Figure 4).[14] Because of the steric repulsion between the methyl groups and the pyrrole rings, the successive fusing reaction of **6** could be hampered. Contrary to the case of **4a** and **5a**, the confused pyrrole ring is largely tilted (36.7(5)°) from the NCP mean plane. As a result, the imino-N and -C atoms are placed above the mean plane at a distance of 1.547(7) and 2.619(7) Å, respectively.

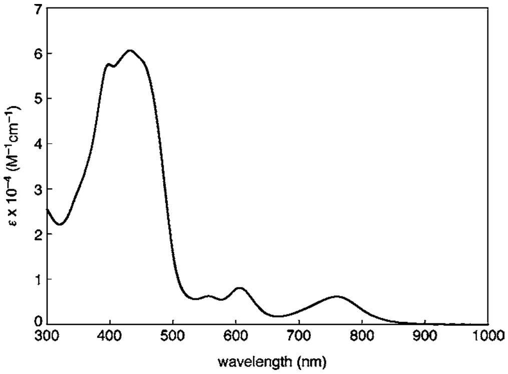


Figure 3. Absorption spectra of **6** in CH_2Cl_2.

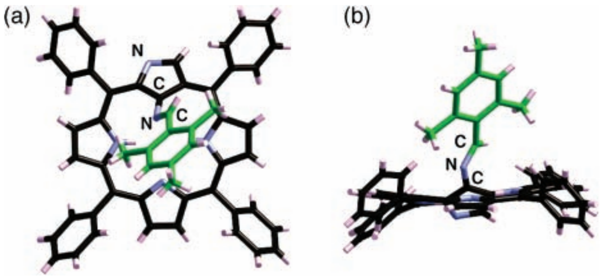


Figure 4. X-ray structure of **6**: (a) top view and (b) side view. One of the enantiomers is shown.

Interestingly, the IF-NCP (**4a**, **5a**) interconvert mutually upon heating (Figure 5). When **5a** in toluene-d_8 was heated at 381 K, **4a** was formed with following the first-order rate law. At the equilibrium, the molar ratio of **4a** and **5a** was around 4:1. Reversely, when **4a** was heated, **5a** was produced and the same equilibrium was attained. The thermodynamic parameters ($\Delta G°$, $\Delta H°$, $\Delta S°$) of the isomerization reaction from **5a** to **4a** at 298 K were determined to be −1.2 kcal/mol, −1.4 kcal/mol, and −0.65 cal/(mol·K), respectively (Supporting Information). As seen from the above data, **4a** is more stable than **5a**, which is in agreement with the results

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(13) Furuta, H.; Ishizuka, T.; Osuka, A.; Dejima, H.; Nakagawa, H.; Ishikawa, Y. *J. Am. Chem. Soc.* **2001**, *123*, 6207−6208.

(14) Crystal data for **6**: $C_{54}H_{41}N_5$, M_w = 759.92, tirclinic, space group $P\bar{1}$ (no. 2), a = 11.677(2) Å, b = 12.549(2) Å, c = 15.744(3) Å, α = 89.721(4)°, β = 70.098(5)°, γ = 71.093(4)°, V = 2037.9(7) Å^3, Z = 4, D_{calcd} = 1.238 g/cm^3, T = −50 °C, R = 0.0749, R_w = 0.1261, GOF = 0.910 ($I > 2\sigma(I)$). Crystallographic data have been deposited at the Cambridge Crystallographic Data Centre with reference number CCDC 635931. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif.

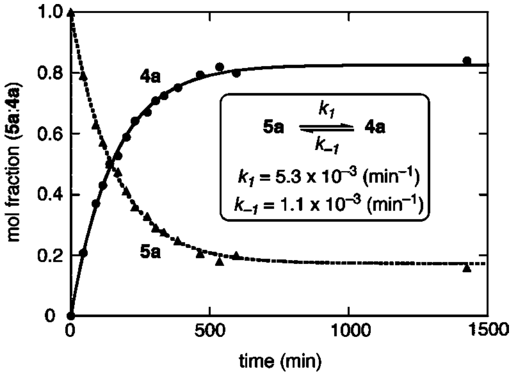

Figure 5. Time course of thermal isomerization reaction from **5a** to **4a** at 381 K in toluene-d_8.

of DFT calculations.[15] This thermal isomerization reaction was also observed in the solid state at 100 °C.

To elucidate the mechanism of this isomerization reaction, kinetic studies were also undertaken. From the rate constants measured at 354, 363, 373, and 381 K in toluene-d_8, the thermodynamic parameters ($\Delta G^{\ddagger}$, $\Delta H^{\ddagger}$, $\Delta S^{\ddagger}$) from **5a** to **4a** at 298 K were determined to be 29.6 kcal/mol, 30.5 kcal/mol, and 2.5 cal/(mol·K), respectively. The positive activation entropy indicates that the flexibility of the molecule could be increased in the transition state. When the *para*-position of the imino-aryl group was modified with various substituents (R = CH_3 (**5b**), Cl (**5c**), CF_3 (**5d**)), acceleration of the reaction was observed with the electron-donating group,[16] whereas the reactions were slowed down with the electron-withdrawing groups. The Hammett plots show a linear correlation between σ_p and $\ln(k_R/k_H)$ with a negative ρ value (−1.7) (Figure 6). The obtained data suggest that a cationic character is involved around the imino-aryl group in the transition state. In fact, 1.7 times acceleration was observed with the reaction of **5a** in DMSO-d_6 at 381 K. The polarized species in the transition state could be more stabilized in the polar solvent.

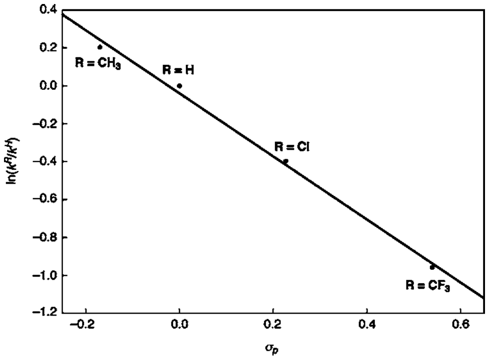

Figure 6. Hammett plots for the thermal isomerization reaction between **4a** and **5a**.

Taking into account the above results, the following energy diagrams of the isomerization reaction of IF-NCP could be drawn (Figure 7). Initially, the N−C bond between the imino-carbon and the pyrrolic nitrogen in a seven-membered ring breaks heterolytically, and succeeding rapid proton transfer and ring closure reaction could afford a paired isomer.

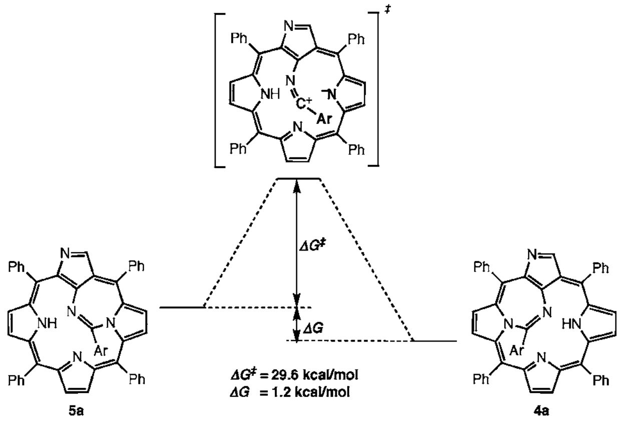

Figure 7. Potential diagram of thermal isomerization between **4a** and **5a** at 298 K.

In conclusion, the condensation of 21-amino NCTPP (**3**) and arylaldehydes gave IF-NCTPP as well as 21-imino NCTPP, depending on the bulkiness of aldehydes. IF-NCTPP isomerizes upon heating, where the intervening of a zwitterionic 21-imino NCTPP was inferred. The longer wavelength absorption band in the near-IR region and unsymmetrical structures make IF-NCP attractive for PDT agents as well as NLO materials. As shown in NFP, *the mutant NCP mutates further*. Further modification of NCP toward porphyrinoids with novel properties is currently in progress in our laboratory.

Acknowledgment. T.M. thanks the JSPS for a Research Fellowship for Young Scientists.

Supporting Information Available: Experimental procedures and spectral data of **3**−**6**, optimized geometries of the skeletons of **4a** and **5a**, van't Hoff and Arrhenius plots, and reaction time courses, as well as crystallographic data (CIF) for **4a**, **5a**, and **6**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(15) The DFT calculations on the skeletal structures at the B3LYP/6-311+G**//B3LYP/6-31G** level showed that **4a** was more stable than **5a** by 0.97 kcal/mol (see the Supporting Information).

(16) In the case of the dimethylamino group, the isomerization reaction was too fast ($t_{1/2}$ < 10 min) to determine the rate constant accurately.