J. Am. Chem. Soc. **2001,** *123,* 6207−6208

NH Tautomerism of N-Confused Porphyrin

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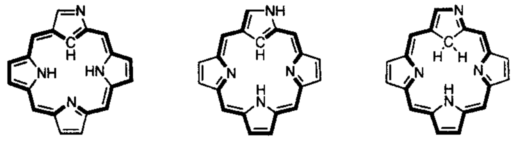
Received January 29, 2001

The proton transfer tautomerism of porphyrins and their derivatives have been widely studied because of the biological relevance and the interest of the mechanism involved.[1] Normally, the tautomerism of porphyrins occurs rapidly among the four nitrogens in the core, and each tautomer having similar stability exists in the equilibria. On the other hand, N-confused porphyrin (NCP), one of the porphyrin isomers with an inverted pyrrole ring, contains three nitrogens in the core and one at the peripheral.[2−6] As a result, the tautomers (**A**, **B**, and **C**) have different structure and stability, if they could exist (Chart 1). Previously, we and Latos-Grażyński have shown, independently, the presence of N-confused tetraphenylporphyrin (NCTPP) of type **A** form in the solid and in $CHCl_3$.[3,4] The DFT calculations on the skeleton of NCP have also supported that **A** was the most stable tautomeric form among **A**−**C**.[5] The divalent metal complexes of NCP such as Ni^{II}- and Pd^{II}-NCP, however, suggested the importance of the type **B** form bearing a hydrogen-carrying nitrogen at the peripheral.[4,6] Therefore, it is of interest to investigate whether the other NCP tautomer exists to understand the NCP chemistry. Herein, we report the definite evidence of the existence of the type **B** tautomer as well as the kinetics of the NH tautomerism in the equilibria.[7]

A hint for the other tautomer came from a dramatic color change of the NCP solution. Figure 1 shows the typical color of N-confused tetraphenylporphyrin (NCTPP) in the two solvent systems, (a) red in CH_2Cl_2 and (b) green in dimethylformamide (DMF). The absorption spectra observed in both solvents exhibited the marked difference on the Soret band and Q-bands. In DMF, the Soret band at 442 nm was broadened with a shoulder at 450 nm, and the absorption maxima was 4 nm red-shifted compared to that in CH_2Cl_2. The first Q-band at 698.5 nm was 27 nm blue-shifted and the intensity of the second Q-band around 644.5 nm was prominent, whereas the corresponding transition in CH_2Cl_2 was very small (Figure 2).

Chart 1



A **B** **C**

To clarify the species involved in the DMF solution, the ^1H NMR spectra of NCTPP were examined. The type **A** tautomer, known predominant in $CDCl_3$, showed the inner CH and two NH signals in the upfield region at −4.99 and −2.41 ppm, respectively, reflecting the ring current effect of 18 π system (Figure 3a).[3,4] On the other hand, the ^1H NMR spectrum in DMF-d_7 was completely different, showing the singlet signals at 0.76, 2.27, and 13.54 ppm, respectively (Figure 3b). The upfield signal at 0.76 ppm was inferred to the inner CH from the correlation peak with ^{13}C signal.[8] The latter two singlet signals, ascribable to the NH's, disappeared after the addition of D_2O and changed to

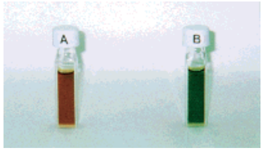


Figure 1. 1.6 × 10^{-4} M solution of NCTPP in (A) CH_2Cl_2 and (B) DMF.

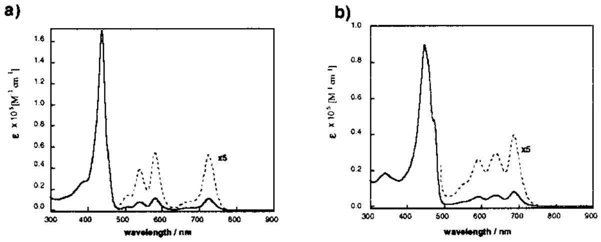


Figure 2. Absorption spectra of NCTPP in (a) CH_2Cl_2 and (b) DMF.

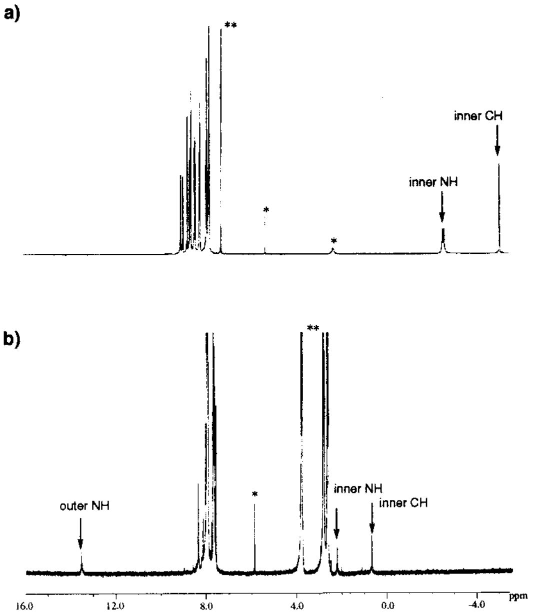


Figure 3. ^1H NMR spectra of NCTPP at −40 °C in (a) $CDCl_3$ and (b) DMF-d_7. (*) Impurities, (**) solvents.

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[⊥] Y. I. is responsible for the X-ray structure of NCTPP (Type **B**).

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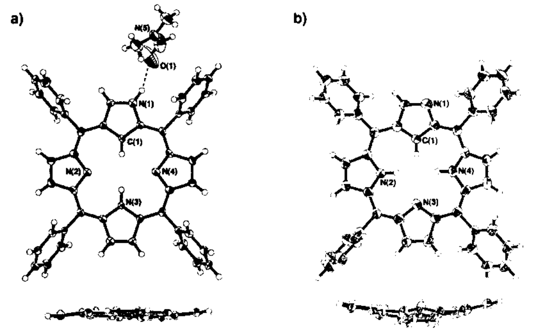

Figure 4. Molecular structures of NCTTP obtained from (a) DMF−MeOH (Type **B**) and (b) CH_2Cl_2−MeOH (Type **A** from ref 3). For clarity, *meso*-phenyl groups are omitted in the side views. The dotted line in (a) shows the hydrogen-bonding interaction. See the text.

doublet (J_{NH} = 100.0 and 95.5 Hz, respectively) when the ^{15}N-labeled NCP was used. These data suggested the advent of type **B** tautomer, which should be stabilized by the hydrogen-bonding with DMF molecule at the peripheral NH. The modest upfield shifts of the internal CH and NH signals could be explained by the weak diamagnetic ring current owing to the incomplete π-conjugated system of type **B** form.[9] Such magnetic tendency is observed with the outer *N*-methylated NCP that bears essential structural features the same as those of tautomer **B**.[10]

More direct information about the environment of the nitrogens in the type **B** species was obtained from the ^{15}N NMR measurements of ^{15}N-enriched NCP (Supporting Information Figure). In $CDCl_3$ at room temperature, four ^{15}N signals were observed at 135.64, 137.16, 238.09, and 303.58 ppm, respectively. The first two sharp signals were assigned to the inner NH's, and the third signal was attributed to the inner N.[11] The broad signal at 303.58 ppm was ascribed to the outer N where the signal could be magnetically coupled with the neighboring α-CH. In DMF-d_7, on the other hand, four ^{15}N signals resonated at 129.82, 175.72, 267.54, and 271.38 ppm. The former two signals, where the second peak was broad, were assigned to the inner and outer NH's, respectively, and the latter two signals were due to the inner N's. It is pertinent to point out here that the chemical shift difference between the outer and inner ^{15}N signals (corresponding to N(1) and N(3) in Figure 4) was smaller in type **B** compared to that in **A**. This further confirms the weaker aromaticity of type **B**.

The explicit structure of the type **B** tautomer was revealed by the X-ray diffraction analysis of an NCTPP single crystal obtained from the DMF−MeOH solution (Figure 4a).[12] The molecule showed the planarity compared to the type **A** tautomer (Figure 4b); the pyrrole rings were tilted 4.7, 0.2, 2.8, and 0.9°, respectively, whereas the confused pyrrole ring of the type **A** was canted 26.9°.[3] The distance between the outer N(1) and O(1) atom of the associated DMF molecule was within the hydrogen-bonding distances, 3.101 Å. The wider interior angle around N(1) of the confused pyrrole ring, 109.2(8)°, was also consistent with the formulation of the outer NH arrangement in type **B**.[13]

The dynamic process of the NH tautomerism of NCTPP was studied by the ^1H NMR saturation transfer experiments in the pyridine-d_5 solution, where both the tautomers could exist in comparable amounts.[14] The thermodynamic parameters (ΔG^0, ΔH^0, ΔS^0, $\Delta G^\ddagger$, $\Delta H^\ddagger$, $\Delta S^\ddagger$) from tautomer **A** to **B** at 0 °C were determined to be −0.34 kcal/mol, −3.16 kcal/mol, −10.3 cal/mol·K, −14.94 kcal/mol, 1.93 kcal/mol and −47.6 cal/mol·K, respectively.[15] The association of the pyridine molecule at the peripheral NH, suggested from the downfield signal at 15.0 ppm, was effective for the stabilization of tautomer **B** as judged from the values of ΔH^0 and ΔS^0. Apart from this, the extremely negative activation entropy ($\Delta S^\ddagger$) and the small enthalpy change ($\Delta H^\ddagger$) are also characteristic in this tautomerism. Although the detail mechanism is not clear yet, one of the hypotheses that the drastic conformational change in the transition state, where the confused pyrrole ring inverts to draw the "outer" nitrogen nearer to the inner NH to receive the proton, would be worth considering. In fact, the inversion of the confused pyrrole ring was taking place in the N-fused porphyrin formation.[16]

In summary, we have shown here the NH tautomerism of NCP. The two types of tautomers, aromatic **A** and less-aromatic **B**, were found both in solutions and solids. Type **A** tautomer was predominant in $CHCl_3$ or CH_2Cl_2, while the type **B** tautomer was stabilized in DMF and pyridine with the remarkable color change. The tautomeric process in pyridine was relatively slow and controlled mainly by the entropy term. Since the optical absorption change between the tautomers is attractive, the control of the tautomerism by external stimuli, such as anions[17] or photons, would be of interest for the use in applications such as anion sensors or optical switching devices. At present, the effort to clarify the question on the third tautomer of type **C**, which was suggested to have comparable stability by calculation,[5a] is currently underway.

Supporting Information Available: ^1H and ^{15}N NMR spectra of ^{15}N-labeled NCTPP (PDF). X-ray crystallographic files (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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(8) The ^{13}C NMR measurements in DMF-d_7 were difficult due to the low solubility of NCTPP. However, by using the more soluble 2,6-dimethylphenyl NCP derivative and pyridine-d_5 as solvent, the ^{13}C signal of the inner CH of type **B** tautomer could be detected at 123.79 ppm where the correlated proton signal was observed at 2.65 ppm and the inner NH signal at 3.70 ppm.

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(12) X-ray data of NCTPP (type **B**) (23 °C): violet prismatic, $C_{50}H_{42}N_6O_2$, MW = 758.92, centric, space group $P\bar{1}$ (No. 2), a = 13.178(2) Å, b = 13.545(2) Å, c = 12.621(1) Å, α = 116.169(5)°, β = 92.716(3)°, γ = 98.691(5)°, V = 1982.2(4) Å^3, Z = 2, D_{calcd} = 1.271 g/cm^3, R = 0.068, R_w = 0.073, GOF = 0.180.

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(14) The inner CH signal of type **A** at −4.6 ppm was irradiated, and the magnetization change of the corresponding signal of type **B** at +1.6 ppm was recorded in the temperature range from 0 to −40 °C.

(15) For TPP, $\Delta G^\ddagger$, $\Delta H^\ddagger$, and $\Delta S^\ddagger$ (at 265 K) were reported to be approximately 13 kcal/mol, 9 kcal/mol, and −10 cal/mol·K, respectively. Abraham, R. J.; Hawkes, G. E.; Smith, K. M. *Tetrahedron Lett.* **1974**, *16*, 1483−1486.

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(17) Fluoride anion was found to induce the optical change of NCTPP in $CHCl_3$; see ref 3.