Pergamon

*Tetrahedron Letters*, Vol. 36, No. 46, pp. 8449-8452, 1995
Elsevier Science Ltd
Printed in Great Britain
0040-4039/95 $9.50+0.00

0040-4039(95)01819-0

# Self-induced Porphyrin Dimer Formation via Unusual Atropisomerization of Tetraphenylporphyrin Derivative

**Yasuhisa Kuroda,* Ayato Kawashima, Tadashi Urai, and Hisanobu Ogoshi***

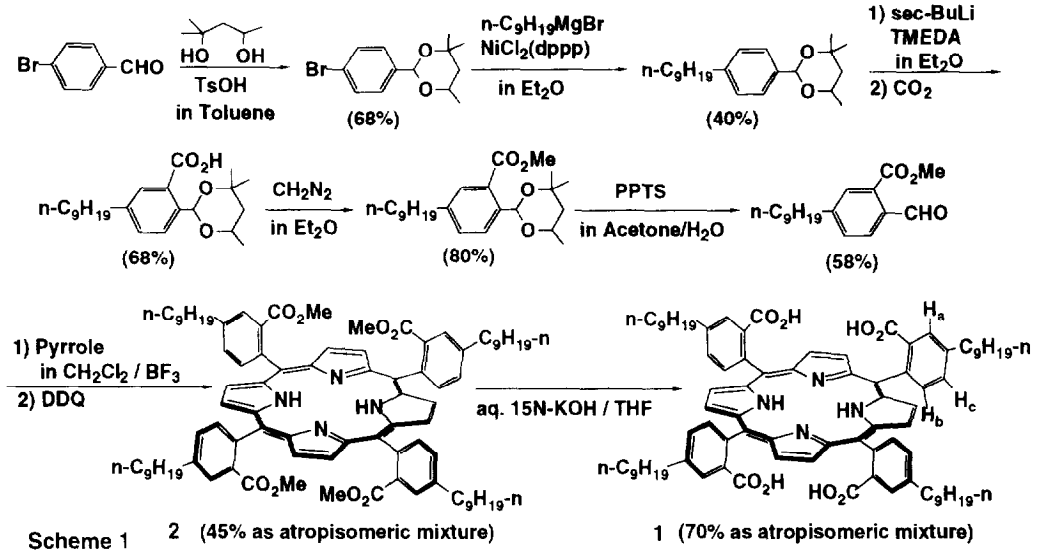
Department of Synthetic Chemistry and Biological Chemistry, Kyoto University, Sakyo-ku, Kyoto 606-01 , Japan

***Abstract*** *. Atropisomerization of meso-tetrakis(2-carboxy-4-nonylphenyl)porphyrin* **1**, *in nonpolar solvents such as* $CHCl_3$ *gives the* $\alpha\alpha\alpha\alpha$ *isomer exclusively, while the same isomerization in polar solvents such as DMSO proceeds normally. Spectroscopic investigations of* **1** *suggest that the porphyrin exists as a cofacial dimer in nonpolar solvents, where eight hydrogen bonds among four pairs of carboxylic acids in* **1** *are formed.*

Porphyrin dimers have been attracting particular attention of chemists for their characteristic chemical and physical properties relating to those of biological systems such as photosynthetic centers.[1] On the basis of such biomimetic interest, various types of synthetic methods have been developed to prepare artificial porphyrin dimers, where two porphyrin molecules were connected with covalent bonds.[2] Another interesting approach to the construction of porphyrin dimers is to utilize self-assembling functions based on molecular recognition. There have been several examples of such spontaneous dimeric porphyrin formation systems which are so designed as to use hydrogen bonds or ligand coordination as associative interactions between two porphyrin molecules.[3] These self-assembling systems usually consist of a single equilibrium process and their selectivity for dimer formation is mainly determined by spatial arrangement of interacting groups attached on the porphyrins. We report here a novel self-assembling system for porphyrin dimer formation which is accompanied by conformational change of the monomeric porphyrin. The observed self-assembling process is so highly selective for dimer formation that, even starting from mixture of undesired monomeric porphyrin isomers, the system gives the practically pure dimer of the single isomer.

The porphyrin used in this work is meso-tetrakis(2-carboxy-4-nonylphenyl)porphyrin, **1**, which was prepared according to Scheme 1. The precursor porphyrin, **2**, was easily hydrolyzed in aq. 15N NaOH/THF solution to afford **1** in 70 % yield.[4] Although the analogous porphyrin, meso-tetrakis(2-carboxyphenyl)porphyrin having no nonyl group, is known as an intermediate for functionalized porphyrin synthesis, its detailed characteristics such as an atropisomeric distribution has not been studied because of its insolubility in organic solvents.[5] In contrast, the present porphyrin **1** is highly soluble in usual organic solvents and, therefore, may be suitable for investigations of its solution properties.

The distribution of atropisomers of **2** was easily determined by using usual reverse phase HPLC column and the equilibrated solution shows the normal statistical distribution, i.e.,$\alpha\beta\alpha\beta$ : $\alpha\alpha\beta\beta$ : $\alpha\alpha\alpha\beta$ : $\alpha\alpha\alpha\alpha$ = 1 : 2 : 4 : 1.[6] Although there was no appropriate direct method to analyze an atropisomer distribution of **1**, esterification of **1** with diazomethane at room temperature showed to give **2** quantitatively without any disturbance of the original distribution. Thus, we tried to determine the atropisomer distribution of **1** in various organic solvents.




Scheme 1

Experiments of thermal equilibration in sealed tubes at 80 °C for 15 h. showed interesting behavior of **1** which was quite different from that of **2**. The most interesting point is that the atropisomerization of **1** is highly solvent-dependent and there are clear two groups of solvents which give distinct results each other; that is, one is the group of relatively polar solvents such as THF, acetone, dioxane and DMSO in which the isomerization proceeds normally to afford nearly statistical mixture of isomers, and another is that of relatively nonpolar solvents such as $CHCl_3$, $CCl_4$, $CHCl_2CHCl_2$ and benzene in which the αααα isomer is unusually enriched after thermal equilibration. The final contents of the αααα isomer in these nonpolar solvents are over 95, 99, 99 and 95 %, respectively. The typical kinetic traces of present atropisomerization are shown in Figure 1. The data clearly show monotonous increase of the αααα isomer in $CHCl_2CHCl_2$, which is in sharp contrast to monotonous decrease of the same isomer in DMSO. These results suggest that the αααα isomer was anomalously stabilized in the nonpolar solvents in spite of its thermodynamic and/or statistic disadvantage.[7] It should be also noted that the system contains no second additive, which is necessary to induce the αααα isomer in previously reported systems showing similar large deviation from statistical atropisomeric equilibration of TPP type porphyrins.[8]

In order to clarify the origin of present unusual stabilization of the αααα isomer of **1**, we investigated its spectroscopic properties in various solvents. The UV/vis, IR and NMR spectroscopic data of **1** and **2** are summarized in Table 1. It is evident that the Soret band absorption, C=O stretching vibration and $^1H$ NMR chemical shifts of **1** are strongly affected by solvent change from nonpolar to polar solvents but, in contrast, those of **2** are insensitive to change of conditions. For example, the Soret band of **1** in $CHCl_3$ shows significant blue-shift to overlap with the shoulder peak around 410 nm which is observed clearly in other conditions. Furthermore, the absorption frequency of carbonyl stretching vibration of **1** in $CH_2Cl_2$ exhibits a large shift toward lower frequencies, strongly indicating hydrogen bond formation between two carboxylic acid moieties. In the NMR spectra, signals of **1** in $CDCl_3$ alone appear differently

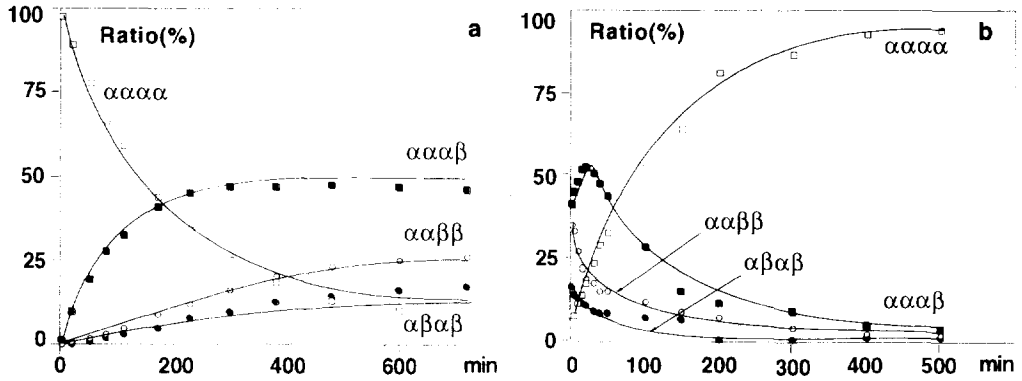



**Figure1.** Thermal isomerization of **1** in a) DMSO and b) $CHCl_2CHCl_2$ at 80 °C. Solid lines are theoretical curves obtained by curve fitting analyses using a) standard thermal TPP atropisomerization model with k=0.0014 $min^{-1}$ and b) atropisomerization model shown in Figure 2b with k = 0.017$min^{-1}$, $K_1 = 7.3x10^7M^{-1}$ and $K_2 = 4500M^{-1}$.

from the others, though chemical shifts for **1** and **2** even in THF are very similar. All of these observations strongly suggest that **1** generates some kind of molecular assembly in nonpolar solvents via hydrogen bond formation between carboxylic acid moieties. Based on these results, we measured molecular weight of **1** in $CHCl_3$ and THF by the method of vapor pressure osmometry. The results undoubtedly indicated dimer formation in $CHCl_3$ and monomeric state in THF, i.e., observed molecular weight of **1** in $CHCl_3$ and THF were 2680 ± 200 and 1260 ± 100 respectively, which are in excellent agreement with those of dimer (M.W.=2588) and monomer (M.W.=1294). Considerations of molecular models reveal the face-to-face dimer of **1** shown in Figure 2a as the most plausible structure. The equilibrium constant for dimer formation is estimated to be lager than $10^7$ $M^{-1}$ at 80 °C, which corresponds to the stabilization energy of 11 kcal/mol. The eight hydrogen bonds among four pairs of carboxylic acids in the dimer not only explain the observed stabilization energy but also give the origin of the driving force for present self-induced dimerization where phase matched atropisomerization to yield the αααα isomer is required. Theoretical curve fitting analyses reveal that the observed data in Figure 1 show excellent agreement with the kinetic model which, in addition to the standard model for the atropisomerization of TPP derivatives,[9] contains highly efficient dimerization of

**Table 1.** The UV/vis, IR and NMR spectroscopic data of **1** and **2**.[a]

| Porphyrin | UV/vis [b] | IR [c] | NMR [d] | | | | |
|---|---|---|---|---|---|---|---|
| | $\lambda_{max}$ (nm) | $\nu_{C=O}$ ($cm^{-1}$) | pyr-β-H | $H_a$ | $H_b$ | $H_c$ | NH δ (ppm) |
| **2** | 425 ($CHCl_3$) | 1727 ($CH_2Cl_2$) | 8.60 | 8.19 | 7.96 | 7.59 | -2.43 ($CDCl_3$) |
| **2** | 424 (DMSO) | 1727(THF) | 8.56 | 8.20 | 8.04 | 7.70 | -2.40 ($d_8$-THF) |
| $\Delta_{nonpolar-polar}$[e] | 1 | 0 | 0.04 | -0.01 | -0.08 | -0.11 | -0.03 |
| **1** | 420 ($CHCl_3$) | 1701($CH_2Cl_2$) | 8.22 | 8.38 | 7.26 | 7.04 | -3.24 ($CDCl_3$) |
| **1** | 427 (DMSO) | 1721(THF) | 8.56 | 8.22 | 7.96 | 7.65 | -2.43 ($d_8$-THF) |
| $\Delta_{nonpolar-polar}$[e] | -7 | -20 | -0.34 | 0.16 | -0.70 | -0.61 | -0.81 |

a) The spectra were obtained at room temperature. The solvents used were assigned in parentheses.
b) Absorption maximum of the Soret band. c) Absorption maximum of C=O stretching vibration.
d) Chemical shifts for protons in the aromatic region and pyrrole protons. For notations, see Scheme 1.
e) Differences between the polar (upper data) and nonpolar solvent (lower data).

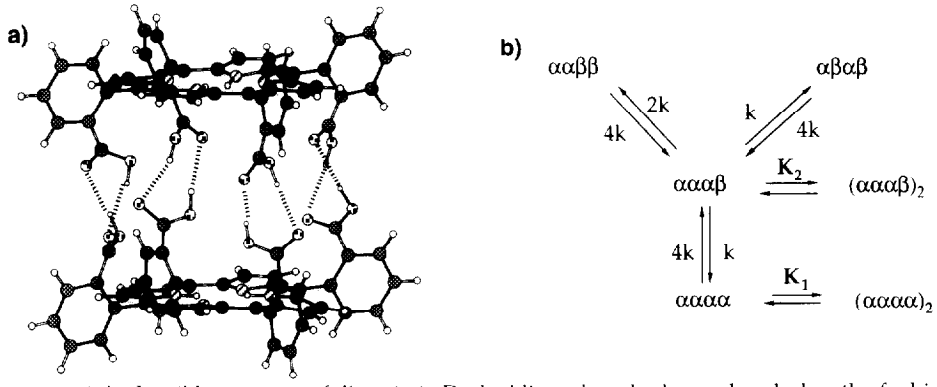



**Figure 2.** a) A plausible structure of dimeric **1**. Dashed lines show hydrogen bonds, length of which are 1.9 ± 0.1 Å. The nonyl chains were omitted. b) Plausible atropisomerization mechanism in a nonpolar solvent, where k is a rate constant of benzene rotation and $K_1$ and $K_2$ are equilibrium constants of dimer formation of αααα and αααβ isomers, respectively. The values of k, $K_1$ and $K_2$ are given in Figure 1.

the αααα isomer ($K_1 > 10^7$ $M^{-1}$) and minor one of the αααβ isomer ($K_2 \sim 4000$ $M^{-1}$) as shown in Figure 2b.[10] Further detailed investigations for this system are now underway in our laboratory.

## References and Notes


1) Deisenhofer,J;Epp,O.; Miki,K.; Huber,R; Michel, H. *J. Mol. Biol.* **1984**, 180, 385-398. Allen, J.P.; Feher,G; Yeates,T.O.; Rees,D.C.; Deisenhofer,J; Michel,H.; Huber,R *Proc.Natl.Acad. Sci. USA.* **1986**, 83, 8589-8593.

2) (a) Collman, J. P.; Elliot, C. M.; Halbert, T. R.; Tovrog, B. S. Proc. *Natl. Acad. Sci. U.S.A.* **1977**, 74, 18-22. (b) Chang, C. K. *J. Chem. Soc., Chem. Commun.*1977, 800-801. (c) Osuka, A.; Maruyama, K. ***J. Am. Chem. Soc.*** **1988**, 110, 4454-4456. (d) Sessler, J. L.; Capuano, V. L.; Harriman, A. *Ibid.* **1993**, 115, 4618-4628. (e) Overfield, R. E.; Scherz, A.; Kaufmann, K. J.; Wasielewski, M. R. *Ibid.* **1983**, 105, 4256-4260. (f) Dubowchik, G. M.; Hamilton, A. D. *J. Chem. Soc., Chem. Commun.* **1986**, 1391-1394. (g) Ogoshi, H.; Sugimoto, H.; Yoshida, Z. *Tetrahedron Lett.* **1977**, 169-172.

3) a) Drain, C. M.; Fischer, R.; Nolen, E. G.; Lehn, J. M. *J. Chem. Soc., Chem. Commun.* **1993**, 243-245. (b) Kobuke, Y.; Miyaji, H. *J. Am. Chem. Soc.* **1994**, 116, 4111-4112. (c) Sessler, J. L.; Wang, B.; Harriman, A. *Ibid* **1995**, 117, 704-714. (d) Aoyama, Y.; Kamohara, T., Yamagishi, A.; Toi, H.; Ogoshi, H. *Tetrahedron Lett.* **1987**, 28, 2143-2146.

4) **1**(αααα atropisomer):$^1$H-NMR (500MHz, THF) δ 8.56 (s, 8H), 8.22 (d, J=1.8Hz, 4H), 7.96 (d, j=7.5Hz, 4H), 7.65 (dd, J=7.5,1.8Hz, 4H), 2.99 (t, J=7.8Hz, 8H), 1.95 (m, 8H), 1.6-1.3 (several peaks, 48H), 0.93 (t, J=7.0Hz,12H), -2.43 (s, 2H); FAB MS 1295(M+H)$^+$;**2**(αααα atropisomer):$^1$H-NMR (500MHz, $CDCl_3$) δ 8.60 (s,8H), 8.19 (d,J=2.0Hz,4H), 7.96 (d,J=8.0Hz, 4H), 7.59 (dd, J=8.0,2.0, 4H), 2.97 (t, J=8.0Hz, 8H), 2.84 (s,12H), 1.92 (m, 8H), 1.6-1.2 (several peaks, 48H), 0.92 (t, J=7.0Hz, 12H), -2.43 (s, 2H); FAB MS 1351(M+H)$^+$

5) (a) Leondiadis, L.; Momenteau, M. *J. Org. Chem.* **1989**, 54, 6135-6138. (b) Fujimoto, T.; Umekawa, H.; Hishino, N. *Chem. Lett.* **1992**, 37-40.

6) HPLC column : YMC-Pack C4, eluent : methanol

7) Recently, interesting thermal conditions which give αβαβ or ααββ atropisomers of meso-tetrakis(o-nitrophenyl)porphyrin exclusively were reported, see (a) Rose, E.; Quelquejeu, M.; Pochet, C.; Julien, N.; Kossanyi, A.; Hamon, L. *J. Org. Chem.* **1993**, 58, 5030-5031. (b) Rose, E.; Pilotaz, A. C.; Quelquejeu, M.; Bernard, N.; Kossanyi, A. *Ibid.* **1995**, 60, 3919-3920.

8) (a) Lindsey, J. *J. Org. Chem.* **1980**, 45, 5215. (b) Elliott, C. M. *Anal. Chem.* **1980**, 52, 666-668. (c) Hayashi, T.; Asai, T.; Hokazono, H.; Ogoshi, H. *J. Am. Chem. Soc.* **1993**, 115, 12210-12211.

9) Gottwald, L. K. ; Ullman, E. F. *Tetrahedron Lett.* **1969**, 3071-3074.

10) Although equilibrium of αααβ dimer formation does not affect final atropisomeric distribution of **1** due to its small equilibrium constant compared with that for αααα dimer formation, it seriously changes the kinetic profile of the αααβ isomer.


(*Received in Japan* 7 *August* 1995; *revised* 21 *September* 1995; *accepted* 22 *September* 1995)