Pergamon

Tetrahedron Letters 40 (1999) 6951–6955

TETRAHEDRON LETTERS

The first chiral phosphorous porphyrins with molecular asymmetry: conformation studies on porphyrin macrocycles in solution

Katsuaki Konishi, Mizuho Suezaki and Takuzo Aida *

Department of Chemistry and Biotechnology, Graduate School of Engineering, The University of Tokyo, Hongo, Bunkyo-ku, Tokyo 113-8656, Japan

Received 15 June 1999; accepted 12 July 1999

Abstract

Enantiomers of chiral phosphorous porphyrins having two different axial groups at the *trans* positions [(EtioP)PR(=O), **1** (R=Et) and **2** (R=Ph); EtioP=etioporphyrinato I] were resolved by means of chiral HPLC. The enantiomers displayed different circular dichroism (CD) spectra in basic and acidic media due to a H^+-driven conformational change of the porphyrin ring.

Conformational characteristics of porphyrin macrocycles have attracted attention in relation to the fundamental properties of π-conjugated systems and the biological activities of heme-containing enzymes.[1,2] Chiral porphyrins and metalloporphyrins are interesting as new chiral auxiliaries and receptors for asymmetric synthesis and recognition.[3] We have designed a variety of chiral porphyrins with molecular asymmetry from enantiotopic porphyrins,[4] and have demonstrated that the chirality is useful as a probe for conformational studies on porphyrin macrocycles in solution.[5] Herein we report the first optical resolution of chiral phosphorous porphyrins with molecular asymmetry, and discuss their conformational characteristics in solution by means of circular dichroism (CD) and NMR spectroscopies.

Oxophosphorous complexes of etioporphyrin I (**1** and **2**) were synthesized by the reaction of a lithiated porphyrin with $RPCl_2$ (R=Et, Ph).[6] Since etioporphyrin I has an enantiotopic structure, the phosphorous complexes (**1** and **2**) should be chiral due to the presence of the two different axial groups at the *trans* positions. The enantiomers were obtained in optically pure forms by means of chiral HPLC. For example, **2** showed two elution peaks with comparable peak areas at 20.5 (**2**-[F1]) and 23.1 min (**2**-[F2]), when chromatographed on Sumichiral OA-4700 with hexane/dichloroethane/ethanol/diethylamine (58/40/1/1 v/v) as eluent (Fig. 1).

* Corresponding author.

0040-4039/99/$ - see front matter
PII: S0040-4039(99)01409-4

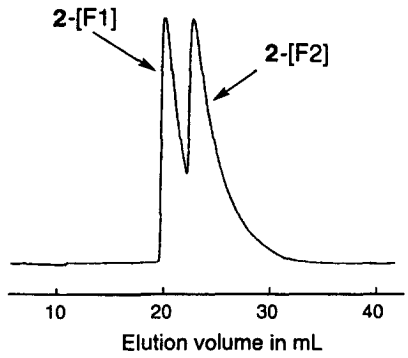
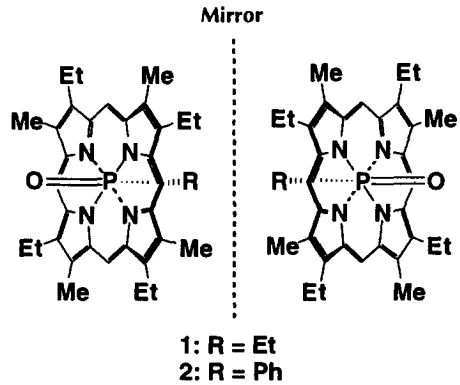
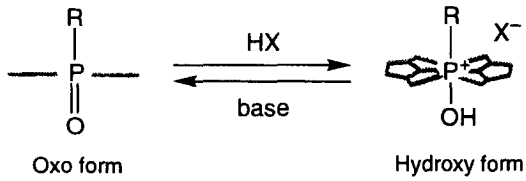


Figure 1. HPLC profile of **2** using Sumichiral OA-4700 with hexane/dichloroethane/ethanol/diethylamine (58/40/1/1 v/v) as eluent at room temperature



1: R = Et
2: R = Ph

Akiba et al. have reported that an oxophosphorous porphyrin, upon treatment with hydrochloric acid followed by recrystallization, forms single crystals of its protonated form (cationic hydroxo complex), whose porphyrin ring is ruffled and distorted from the planarity. This is in contrast with the crystal structure of the neutral oxophosphorous porphyrin, which adopts a planar conformation with respect to the porphyrin ring.[7]



Scheme 1.

The circular dichroism (CD) profiles of **1** and **2** are therefore quite interesting, since they are considered informative of the conformational characteristics of the porphyrin rings in solution. If the following equilibrium (Scheme 1) is also operative in solution, the CD spectra of the complexes should be different, depending on the pH of the solution. The CD spectra of the enantiomers of **1** and **2**, measured at 20°C in basic and acidic media, are shown in Fig. 2. The enantiomers of ethyl complex (**1**) in a basic medium such as C_6H_6/Et_3N (5%) showed mirror-image monosignated CD bands in the Soret region with a $|[\Theta]|$ value of approximately 5000 (Fig. 2A (a)).[8] On the other hand, in an acidic medium such as C_6H_6/CH_3CO_2H (5%), the complex showed an expected absorption spectral profile,[7] where the CD intensity was significantly enhanced to furnish a $|[\Theta]|$ value of 25000 (b). A much clearer pH dependence was observed for the CD profile of phenyl complex (**2**) (Fig. 2B): in C_6H_6/Et_3N (5%), the enantiomers

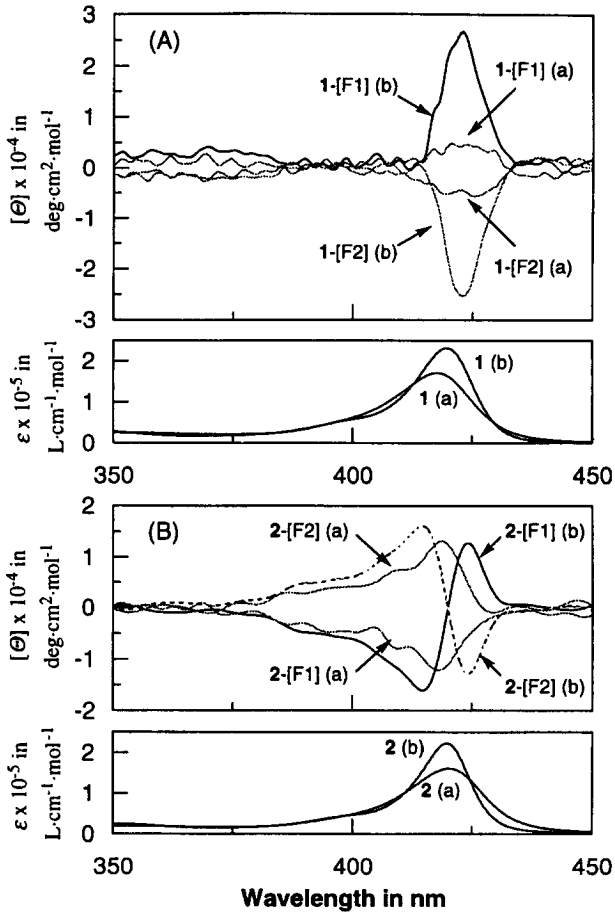


Figure 2. Circular dichroism (CD) and absorption spectra of (A) **1**-[F1]/**1**-[F2] and (B) **2**-[F1]/**2**-[F2] at 20°C; solvent: (a) C_6H_6/Et_3N (5%); (b) C_6H_6/CH_3CO_2H (5%)

2-[F1] and **2**-[F2] also showed negative and positive monosignated CD bands at 418 nm, respectively (a). On the other hand, in acidic C_6H_6/CH_3CO_2H (5%), their CD spectra showed split Cotton effects at 415 and 424 nm (b), possibly as a result of an electronic interaction between the porphyrin chromophore and the axial phenyl group of **2**.

Since NMR signals due to the *meso* protons of porphyrins are sensitive to the conformational characteristics of the porphyrin rings, we measured the ^1H NMR spectra of **1** at 20°C in acidic $C_6D_5CD_3/CD_3CO_2D$ (5%) (Fig. 3A) and neutral $C_6D_5CD_3$ (3B). However, irrespective of the pH of the medium, the complex showed a sharp singlet due to the *meso* protons. On the other hand, when the acidic solution (Fig. 3A) was cooled to −70°C, the singlet signal split into two signals characteristic of a nonplanar ruffled structure. Upon elevation of the temperature to −40°C, the paired signals coalesced, indicating a faster ring inversion than the NMR timescale. In sharp contrast, in $C_6D_5CD_3$ (Fig. 3B), no splitting of the *meso* proton signal was observed over a wide range of temperature from 20 to −90°C, indicating that the porphyrin ring adopts a planar conformation.

The ^1H NMR spectral profiles of **1**, thus observed in Fig. 3, are compatible with the CD profiles (Fig. 2), and support the observation that protonation of oxophosphorous porphyrins gives rise to a planar-to-ruffled conformational change of the porphyrin ring in solution (Scheme 1). In relation to

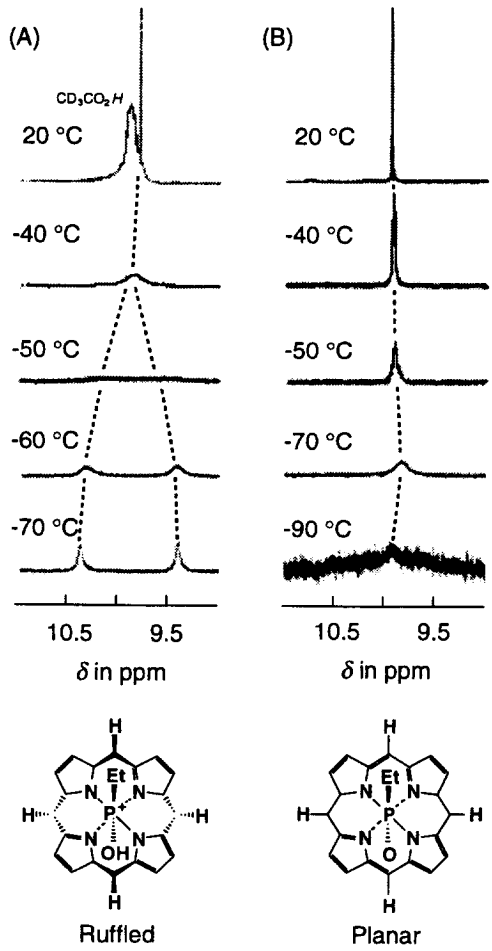


Figure 3. ^{1}H NMR spectra (*meso* proton region) of **1** in (A) $C_6D_5CD_3/CD_3CO_2D$ (5%) and (B) $C_6D_5CD_3$

this, the CD spectral changes upon protonation and deprotonation of **1** and **2** occurred in a reversible fashion. For example, when Et_3N was added to a CH_2Cl_2/CH_3CO_2H (5%) solution of an enantiomer of the protonated form of **2**, the split Cotton effects completely disappeared to give a monosignated CD band characteristic of the planar oxo complex.

In conclusion, we have succeeded in the first optical resolution of the chiral oxophosphorous porphyrins **1** and **2**. By taking advantage of the optical activity of their enantiomers as a probe, we have also demonstrated that the protonated forms of oxophosphorous porphyrins are ruffled in solution as well as in the crystalline state.[7] The results may suggest a potential utility of chiral oxophosphorous porphyrins as pH-sensors for exploring microenvironments in natural and synthetic cavities.

References

1. (a) Scheidt, W. R.; Lee, Y. *Struct. Bonding* **1987**, *64*, 1. (b) Ravikanth, M. W.; Chandrashekar, T. K. *Struct. Bonding* **1995**, *82*, 105.
2. (a) Nurco, D. J.; Medforth, C. J.; Forsyth, T. P.; Olmstead, M. M.; Smith, K. M. *J. Am. Chem. Soc.* **1996**, *118*, 10918. (b) Sparks, L. D.; Medforth, C. J.; Oark, M. S.; Chamberlain, J. R.; Ondrias, M. R.; Senge, M. O.; Smith, K. M.; Shelnutt, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 581. (c) Ochesenbein, P.; Ayougou, K.; Mandon, J. F.; Weiss, R.; Austin, R. N.; Jayaraj,

K.; Gold, A.; Terner, J.; Fajer, J. *Angew. Chem., Int. Ed. Engl.* **1994**, *33*, 348. (d) Simonis, U.; Walker, F. A.; Lee, P. L.; Hanquet, B. J.; Meyerhoff, D. J.; Scheidt, W. R. *J. Am. Chem. Soc.* **1987**, 109, 2659.

3. (a) Collman, J. P.; Zhang, X.; Lee, V. L.; Uffelman, E. S.; Brauman, J. I. *Science* **1993**, *261*, 1404. (b) *Comprehensive Supramolecular Chemistry*; Atwood, J. L.; Lehn, J.-M., Eds.; Pergamon Press: Oxford, 1996.
4. (a) Kubo, H.; Aida, T.; Inoue, S.; Okamoto, Y. *J. Chem. Soc., Chem. Commun.* **1988**, 1015. (b) Konishi, K.; Oda, K.; Nishida, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1992**, *114*, 1313. (c) Konishi, K.; Yahara, K.; Toshishige, H.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1994**, 116, 1337. (d) Konishi, K.; Kimata, S.; Yoshida, K.; Tanaka, M.; Aida, T. *Angew. Chem., Int. Ed. Engl.* **1996**, *23*, 2823.
5. (a) Konishi, K.; Miyazaki, K.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1990**, *112*, 5639. (b) Konishi, K.; Sugino, T.; Aida, T.; Inoue, S. *J. Am. Chem. Soc.* **1991**, *113*, 6487. (c) Konishi, K.; Takahata, Y.; Aida, T.; Inoue, S.; Kuroda, R. *J. Am. Chem. Soc.* **1993**, *115*, 1169. (d) Tashiro, K.; Konishi, K.; Aida, T. *Angew. Chem., Int. Ed. Engl.* **1997**, *24*, 856.
6. Compound **2**: To a THF solution (30 mL) of etioporphyrin I (478.7 mg, 1.0 mmol) was added a THF solution (3.0 mL) of $(Me_3Si)_2NLi$ (3.0 mmol) under dry nitrogen, and the mixture was refluxed for 1 h, giving a red solution of lithiated porphyrin. To this solution was added $PhPCl_2$ (10 mmol), and the reaction mixture was stirred for 20 h at room temperature. Then, the mixture was treated aerobically with aq. $NaHCO_3$, and subjected to column chromatography on alumina with $CHCl_3$/MeOH as eluent. The second red fraction was collected and recrystallized from CH_2Cl_2/C_6H_{12} to give a phenyl(oxo)phosphorous complex (**2**) in 35% yield. ^{1}H NMR (270 MHz, $CDCl_3$) δ 9.61 (s, 8H, *meso*), 5.23 (m, 1H, *p*-H), 4.53 (dd, 4H, *m*-H), 3.95 (m, 8H, CH_2CH_3), 3.51 (s, 12H, CH_3), 1.82 (t, 12H, CH_2CH_3), 0.12 (dd, 2H, *o*-H); HRMS calcd for $C_{38}H_{42}N_4OP$ (MH^+): *m/z* 601.3096, found: 601.3103. Compound **1** was prepared in a similar manner to the above (42% yield): ^{1}H NMR δ 10.11 (s, 8H, *meso*), 4.12 (m, 8H, porph-CH_2CH_3), 3.67 (s, 12H, CH_3), 1.93 (t, 12H, porph-CH_2CH_3), −4.95 (dt, 3H, axial-CH_2CH_3), −6.40 (m, 2H, axial-CH_2CH_3); HRMS calcd for $C_{34}H_{42}N_4OP$ (MH^+): *m/z* 553.3096, found: 553.3081.
7. Yamamoto, Y.; Nadano, R.; Itagaki, M.; Akiba, K. *J. Am. Chem. Soc.* **1995**, *117*, 8287.
8. The maximum Soret absorbance of the CD samples were adjusted to 1.5–1.8. **1**, UV–vis (C_6H_6/Et_3N (5%)): λ_{max} (ε) 350.0 (24600), 420.0 (161000), 543.5 (11800), 580.0 (11200) nm; UV–vis (C_6H_6/CH_3CO_2H (5%)): λ_{max} (ε) 355.5 (20100), 419.5 (223000), 550.0 (10900), 591.5 (14100) nm. **2**, UV–vis (C_6H_6/Et_3N (5%)): λ_{max} (ε) 347.5 (29500), 417.5 (171000), 540.0 (15800), 572.5 (13700); UV–vis (C_6H_6/CH_3CO_2H (5%)): λ_{max} (ε) 351.5 (25700), 419.5 (232000), 546.5 (12600), 589.0 (11800).