Pergamon

Tetrahedron Letters, Vol. 38, No. 24, pp. 4239-4242, 1997

0040-4039/97 $17.00 + 0.00

PII: S0040-4039(97)00853-8

Gadolinium(III) Porphyrin as a Novel Circular Dichroism Probe for Chirality of Amino Acids

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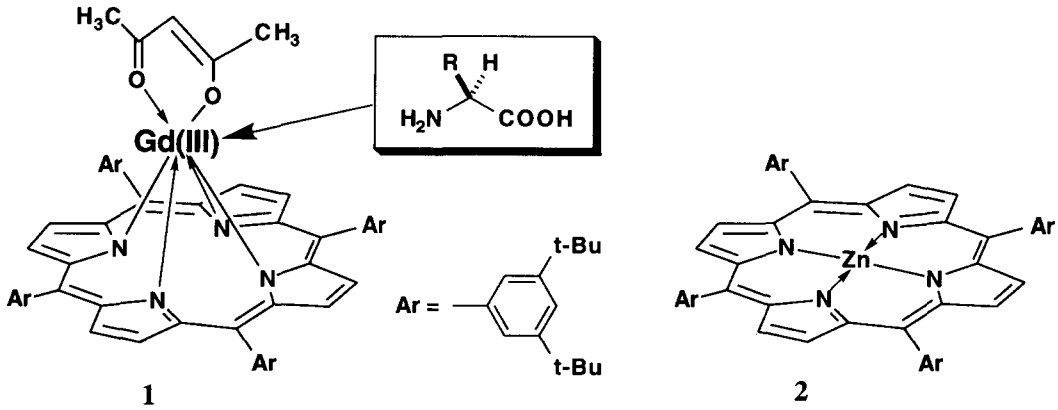
Abstract: Synthetic achiral gadolinium(III) porphyrin extracted chiral amino acids from an aqueous solution into a dichloromethane solution and the formed 1 : 1 complexes exhibited chirality-specific circular dichroism activities. © 1997 Elsevier Science Ltd.

Metalloporphyrin receptors offer interesting molecular recognition phenomena.[1] Since the porphyrin ligands can accommodate functional metal cations in the rigid and well-defined geometry, their molecular recognition functions can be finely adjusted. Although many kinds of metal cations were incorporated in the porphyrin ligands, lanthanide porphyrins were rarely characterized as receptors.[2] Here, we report unique receptor functions of easily available gadolinium porphyrin as a novel circular dichroism (CD) probe for chirality of amino acids based on supramolecular complexation.

Neutral lanthanide compounds are known to form highly coordinated complexes with several guest species, and are employed as shift reagents in NMR spectroscopy and as catalysts in organic synthesis. We recently demonstrated that lanthanide tris(β-diketonates) extracted unprotected amino acids from neutral water into dichloromethane.[3] Thus, we introduce gadolinium cation into the porphyrin ligand as the metal center and characterize the receptor functions of the resulting lanthanide porphyrin complex for amino acids. The gadolinium(III) porphyrin receptor is electrically neutralized by dianionic porphinate and monoanionic diketonate (axial) ligands and also forms highly coordinated 1 : 1 complexes with chiral amino acids (unprotected form). This receptor is achiral but exhibits chirality-specific CD activity induced by complexation with amino acid guests.[4] Although Radzki *et al.* reported that some gadolinium porphyrins bound neutral amines, phenols and nucleic bases,[2] this is the first example of lanthanide porphyrin as a supramolecular probe for unprotected amino acids of biological interest.

Gadolinium(III) porphyrin **1** was prepared from 5,10,15,20-tetrakis(3,5-di-*tert*-butylphenyl)porphyrin[5] and gadolinium(III) tris(acetylacetonate) according to the reported procedures.[2] All extraction experiments and spectroscopic measurements were done at room temperature and visible and CD absorption spectra were measured in air-saturated solvents on a Hitachi U-3500 spectrophotometer and a Jasco J-720W spectropolarimeter, respectively.



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With a dichloromethane solution of water-insoluble **1** (1.0 μmol / 80 ml, 1.3×10^{-5} M), an aqueous solution of L-phenylalanine (1.0 μmol / 3.8 ml, 2.7×10^{-4} M) was shaken for 30 min. Visible spectrum of the dichloromethane solution changed compared to that of the solution shaken with water (without the amino acid). This gave a slightly red-shifted and intense Soret band (423 nm) with a small new shoulder at longer wavelength (around 438 nm) as shown in Fig. 1A. The dichloromethane solution also gave CD peaks around the region of Soret and Q-bands (see the solid line of Fig. 1B). The reverse S-shaped band around 430 nm had much larger intensity than the positive and negative peaks at *ca.* 590 and 560 nm, respectively. When D-phenylalanine was used instead of L-isomer, the dichloromethane gave the same visible spectrum but the completely symmetrical CD spectrum: large S-shaped band at the Soret-band region with small negative/positive peaks at the Q-band region (see the broken line of Fig. 1B). Racemic D,L-phenylalanine induced no CD signals because gadolinium porphyrin **1** has no chirality. Thus, phenylalanine was extracted from the aqueous phase into the dichloromethane phase containing **1**, and the resulting supramolecular complex with achiral gadolinium porphyrin **1** and chiral phenylalanine in dichloromethane exhibited strong, chirality-specific CD bands due to the exciton coupling.

As the initial concentration of phenylalanine increased in aqueous solution, the extracted amount of phenylalanine increased and saturated at the amount corresponding to 1 : 1 stoichiometry between gadolinium(III) porphyrin **1** and phenylalanine (Fig. 2A). When concentration of L-phenylalanine increased, induced CD intensity similarly increased and reached the maximum at 12 mdeg cm^{-1} ($> 4 \times 10^{-4}$ M) as shown in Fig. 2B. Thus, the induced CD signals were originated from the supramolecular 1 : 1 complexation between achiral gadolinium porphyrin **1** and chiral phenylalanine. Since no acetylacetonate ligand was observed in the aqueous phase and no pH value changed during the extraction, the phenylalanine molecule must coordinate central gadolinium metal as an additional ligand.

When zinc(II) porphyrin **2** was employed instead of gadolinium complex **1**, phenylalanine was rarely extracted from an aqueous phase into the dichloromethane phase. In order to determine the structural requirements for the guest, *N*-acetyl-L-phenylalanine and L-phenylalanine methyl ester were also examined instead of unprotected phenylalanine. Both induced weak CD signals, indicating that the guest phenylalanine might be tightly fixed on the gadolinium as a bidentate.

Among 19 natural chiral α-L-amino acids (= 20 amino acids corresponding to genetic codes – achiral glycine), 16 amino acids gave reversed S-shaped CD spectra at the Soret-band region under neutral conditions,

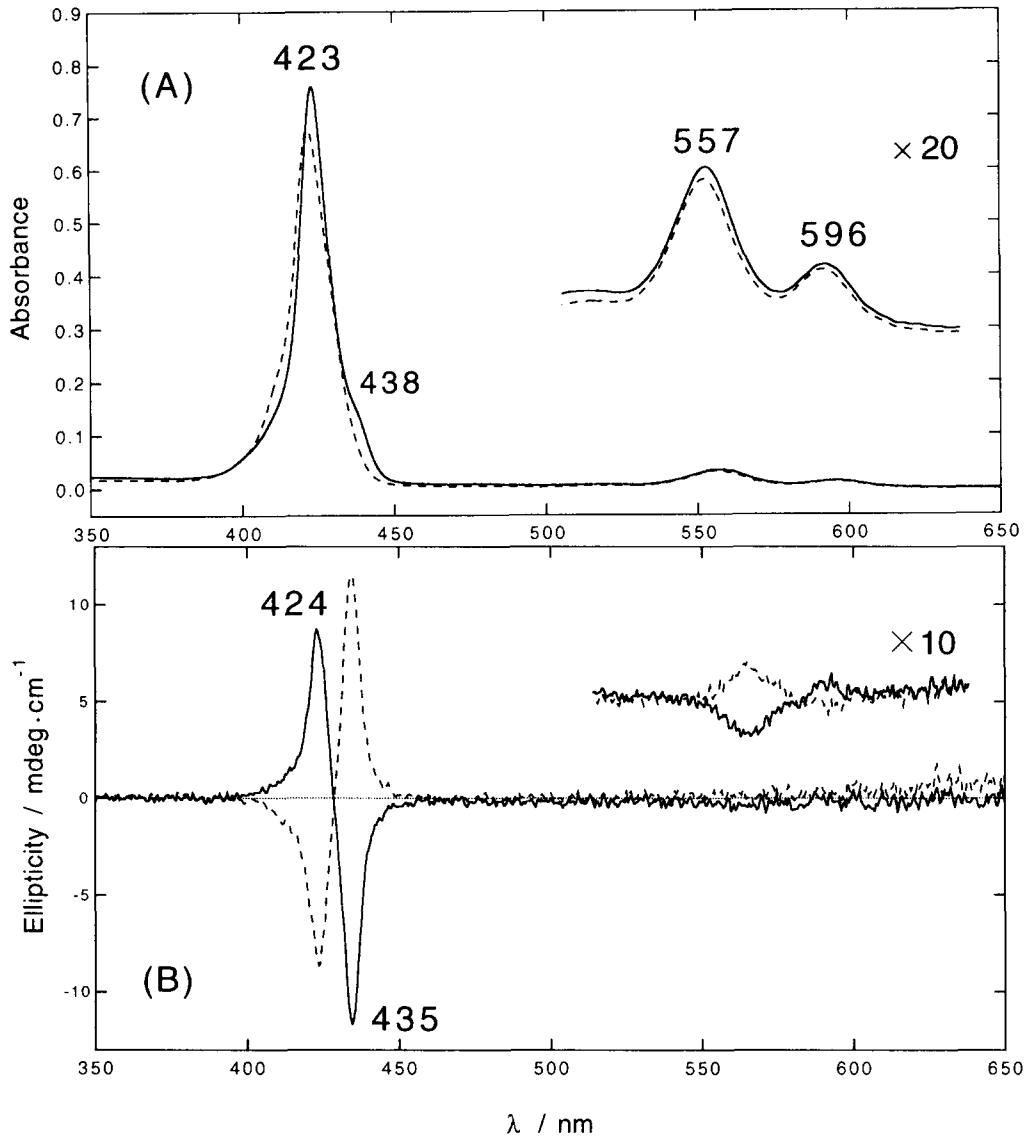

Fig. 1 (A) : Visible spectra of gadolinium(III) porphyrin **1** in dichloromethane (80 ml, 1.3×10^{-5} M) after shaking with an aqueous solution (3.8 ml) of L-phenylalanine (—, 2.7×10^{-4} M) or water (---).
(B) : CD spectra of gadolinium(III) porphyrin **1** in dichloromethane (80 ml, 1.3×10^{-5} M) after shaking with an aqueous solution (3.8 ml, 2.7×10^{-4} M) of L-phenylalanine (—) or D-phenylalanine (---).

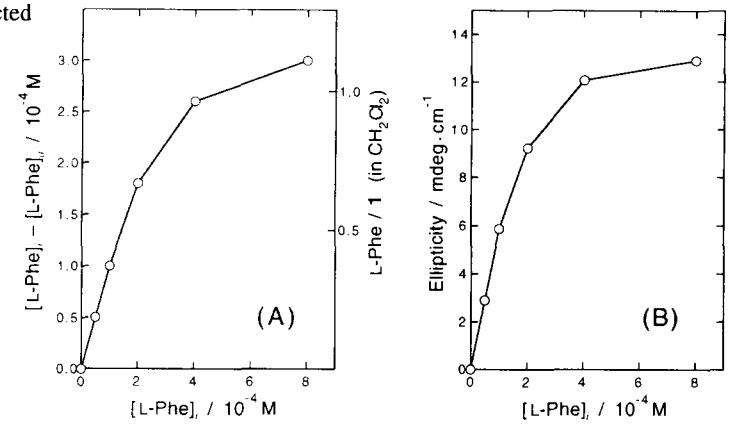

Fig. 2 (A) : Dependency of extracted L-phenylalanine (= $[L\text{-Phe}]_{initial} - [L\text{-Phe}]_{after\ shaking}$) into dichloromethane solution of **1** (1.0 μmol / 80 ml) upon the initial concentration of aqueous L-phenylalanine solution (= $[L\text{-Phe}]_i$, 3.8 ml). **(B)** : Dependency of the induced CD intensity (435-nm negative peak) of the dichloromethane solution (**1**, 1.0 μmol / 80 ml) upon $[L\text{-Phe}]_i$ (3.8 ml).

while L-aspartic acid and L-lysine gave very small CD signals and only L-histidine induced exceptional S-shaped CD signals.[6] The induced CD bands observed around the Soret band are so strong that absolute configuration of these amino acids can be sensitively determined from the sign of CD signals. For example, 1.0 μmol of L-leucine extracted by gadolinium porphyrin **1** into dichloromethane (80 ml) offered induced CD signal at 435 nm with 39 mdeg cm^{-1}, which is the same as CD signal at 199 nm of 64 μmol of L-leucine in the aqueous solution (80 ml). Thus, 64 fold amplification of the intensity (64 μmol / 1.0 μmol) and red shift of the peak from UV to visible region (199 → 435 nm) were performed in the CD spectra. The observations clearly demonstrated that the CD spectroscopic method using gadolinium(III) porphyrin **1** as a receptor probe served as a new chirality sensory system for unprotected amino acids.[7]

This work was partially supported by a Grant-in-Aid for Specific Research on Priority Areas (No. 0723026) from the Ministry of Education, Science, Sports and Culture, Japan.

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(*Received in Japan* 1 *April* 1997; *revised* 30 *April* 1997; *accepted* 2 *May* 1997)