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Short Note

Zinc(II)-5,10,15,20-tetrakis(α-pyridino-*m*-tolyl)porphyrin Tetrabromide

Yoshinobu Ishikawa [1,2,*], Takeshi Yamashita [2], Satoshi Fujii [1] and Tadayuki Uno [2,3]

[1] School of Pharmaceutical Sciences, University of Shizuoka, 52-1 Yada, Suruga-ku, Shizuoka 422-8526, Japan

[2] Graduate School of Pharmaceutical Sciences, Kumamoto University, 5-1 Oe-honmachi, Kumamoto 862-0973, Japan

[3] Graduate School of Pharmaceutical Sciences, Osaka University, 1-6 Yamadaoka, Suita, Osaka 565-0871, Japan

* Author to whom correspondence should be addressed; E-Mail: ishi206@u-shizuoka-ken.ac.jp.

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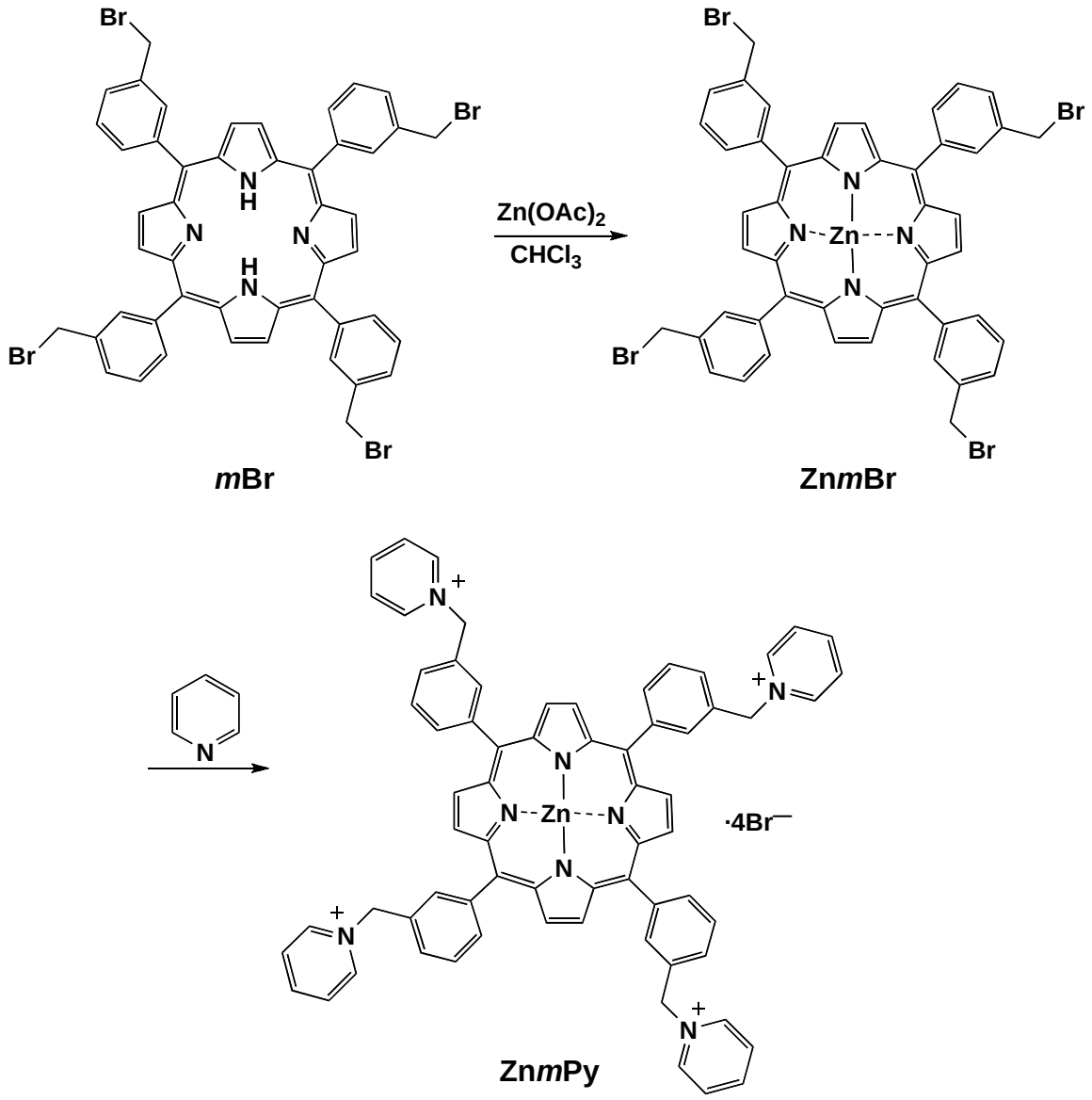
Abstract: Cationic porphyrins interact strongly with guanine quadruplex (G-quadruplex) DNA. We report the preparation of the zinc(II) complex of a porphyrin bearing cationic side arms, zinc(II)-5,10,15,20-tetrakis(α-pyridino-*m*-tolyl)porphyrin tetrabromide (**Zn*m*Py**), as a novel probe for the analysis of G-quadruplex/porphyrin interaction.

Keywords: porphyrin; zinc; pyridine; quadruplex

Guanine quadruplex (G-quadruplex) of a single-stranded overhang at the end of chromosomes is an attractive drug target for cancer therapy, because macrocyclic compounds like cationic tetra-(*N*-methyl-4-pyridyl)porphyrin (**TMPyP4**) stabilize G-quadruplex structures, and thus show anti-telomerase and anti-cancer activity [1–4]. We previously synthesized G-quadruplex-interacting porphyrins with cationic side arms at *para*- or *meta*-position of all phenyl groups of tetratolyl porphyrin [5]. These porphyrins were found to stabilize an anti-parallel G-quadruplex DNA more effectively than **TMPyP4**. On the basis of spectrophotometric and molecular modeling results, it is assumed that the chromophore of the cationic porphyrins should interact with unique sites of the anti-parallel G-quadruplex [6]. Insertion of diamagnetic zinc(II) to metal-free, cationic bis-porphyrins alters their characteristics in aqueous solution and improves the DNA-interacting and photocleaving abilities [7–10]. Thus, we herein report the preparation of the zinc(II) complex of a porphyrin bearing

cationic side arms, zinc(II)-5,10,15,20-tetrakis(α-pyridino-*m*-tolyl)porphyrin tetrabromide(**Zn*m*Py**), as a novel probe for the analysis of G-quadruplex/porphyrin interaction.

Scheme 1. Preparation of **Zn*m*Br** and **Zn*m*Py**.



The preparation of **Zn*m*Py** from ***m*Py**, 5,10,15,20-tetrakis(α-pyridino-*m*-tolyl)porphyrin, and zinc bromide failed to give the desired compound, because the purification cannot be achieved due to the highly polar character of the materials. Alternatively, the preparation of **Zn*m*Br**, zinc(II)-5,10,15,20-tetrakis(α-bromo-*m*-tolyl)porphyrin, followed by the introduction of pyridine was successful. A mixture of ***m*Br** and zinc acetate in chloroform was refluxed for 2 h, and was then passed through silica gel. After addition of heptane to the eluate, crystallization of **Zn*m*Br** was achieved by slow evaporation. **Zn*m*Py** was prepared successfully by the reaction of **Zn*m*Br** with an excess of pyridine. The ^{1}H NMR, MS and elemental analyses for **Zn*m*Br** and **Zn*m*Py** gave satisfactory results.

Experimental

^{1}H NMR spectra were recorded on a JEOL GX-400 spectrometer. Matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) mass spectrum was recorded on a Bruker REFLEX^{TM}. Electrospray-ionization time-of-flight (ESI-TOF) mass spectrum was recorded on a Micromass LCT Premier™. Elemental analysis was performed at the Analytical Center, Kumamoto University. The starting material ***m*Br** was synthesized according to the previous method [11].

Zinc(II)-5,10,15,20-tetrakis(α-bromo-m-tolyl)porphyrin (**Zn*m*Br**)

To a solution of ***m*Br** (100 mg, 0.101 mmol) in $CHCl_3$ (20 mL) was added a solution of zinc acetate (22.3 mg, 0.127 mmol) in MeOH (2 mL), and it was refluxed for 2 h with stirring. After cooling to room temperature, the mixture was passed through silica gel ($CHCl_3$). After the addition of heptane to the eluate, the solution was slowly evaporated. The purple solids were collected, dried *in vacuo* (yield: 96.5%). ^{1}H NMR ($CDCl_3$): 4.77 (s, 8H, -CH_2-), 7.72 (t, J = 7.6 Hz, 4H, H-5), 7.80 (d, J = 7.6 Hz, 4H, H-6), 8.16 (d, J = 7.6 Hz, 4H, H-4), 8.25 (s, 4H, H-2), 8.96 (s, 8H, β-pyrrolic H). MALDI-TOF MS (m/z): Calcd for $C_{48}H_{32}N_4Br_4Zn$, 1049.9 $[M]^+$. Found: 1049.7. Elemental analysis: Calcd. for $C_{48}H_{32}N_4Br_4Zn$: C, 54.92; H, 3.07; N, 5.34. Found: C, 55.10; H, 3.10; N, 5.40.

Zinc(II)-5,10,15,20-tetrakis(α-pyridino-m-tolyl)porphyrin tetrabromide (**Zn*m*Py**)

A solution of **Zn*m*Br** (50.0 mg, 0.0476 mmol) in pyridine (5 mL) was refluxed for 1.5 h with stirring. After cooling to room temperature, the purple solid was collected and dried *in vacuo* (yield: 76.1%). ^{1}H NMR (DMSO-d_6): 6.25 (dd, J = 8.0 Hz, 8H, -CH_2-), 7.90 (m, 4H, phenyl H-5), 8.03 (br d, J = 7.2 Hz, 4H, phenyl H-6), 8.23 (t, J = 6.4 Hz, 4H, phenyl H-4) 8.29 (m, 8H, pyridyl H-3 and H-5), 8.48 (m, 4H, phenyl H-2), 8.70-8.75 (m, 12H, pyridyl H-4 and β-pyrrolic H), 9.49 (m, 8H, pyridyl H-2 and H-6). ESI-TOF MS (m/z): Calcd for $C_{48}H_{32}N_4Zn$, 261.09 $[M]^{+4}$. Found: 261.07. Elemental analysis: Calcd. for $C_{68}H_{52}N_8Br_4Zn{\cdot}4H_2O$: C, 56.79; H, 4.20; N, 7.79. Found: C, 56.90; H, 3.97; N, 7.96.

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