Self-Assembly

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Synthesis of Chiral Porphyrins through Pd-Catalyzed [3+2] Annulation and Heterochiral Self-Assembly**

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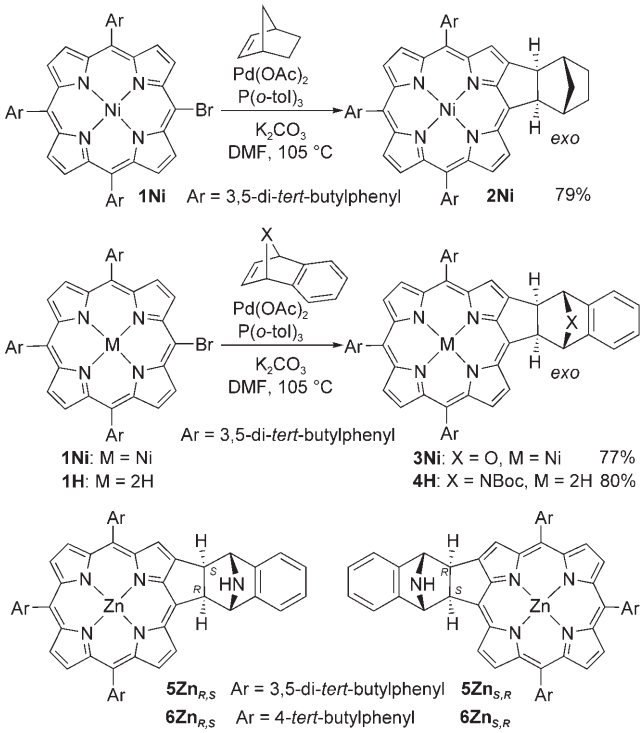
Well-ordered constructions of self-assembled porphyrins have been intriguing targets in terms of potential applications in materials science, reaction catalysis, and duplication of photosynthetic functions. The coordination interaction between the central metal atom and the peripheral ligand of a porphyrin has often been employed to construct self-sorting porphyrin architectures.[1,2] We have also reported the self-sorting assembly of pyridine-appended meso-meso-linked zinc(II) diporphyrins.[3] However, formation of a porphyrin assembly on the basis of selective heterochiral recognition is quite rare,[4] despite its wider potential in the programmed construction of molecular systems, in which several different functions are integrated by noncovalent interactions.

Chiral porphyrins have also been receiving much attention as scaffolds for precise molecular recognition, construction of supramolecular structures, and asymmetric catalysis.[5] The synthetic strategy towards chiral porphyrins often involves the introduction of chiral motifs to the porphyrin periphery. Alternatively, a restricted bond rotation at sterically encumbered positions can generate axial chirality. However, in many cases, a chiral element is connected to a porphyrin through a single bond, thus giving some flexibility to the system. In contrast, chirality that is supported rigidly by some fused structures would be advantageous to provide a defined chiral environment. Here we wish to describe the efficient palladium-catalyzed synthesis of novel fused chiral porphyrins. Owing to the unsymmetrical meso,β-fused structures, these porphyrins are chiral in a rigid situation. The formation of heterodimers of benzoazanorbornene-fused porphyrins through chiral discrimination is also reported.

To incorporate a chiral fused structure into the porphyrin periphery, we undertook a Pd-catalyzed [3+2] annulation strategy, since of meso-bromoporphyrins with alkynes provided 7,8-dehydropurpurins.[6] We anticipated that the use of reactive strained alkenes such as norbornene derivatives instead of alkynes would furnish novel fused norbornene-substituted porphyrins through the similar carbopalladation/cyclization sequence. Although there are several examples of Pd-catalyzed annulation of norbornenes,[7] its application to porphyrins has not been investigated. The reaction of 5-bromo-10,15,20-tris(3,5-di-*tert*-butylphenyl)porphyrinato nickel(II) (**1Ni**) with norbornene proceeded smoothly to afford **2Ni** in 79% yield in the presence of $Pd(OAc)_2$/ P(*o*-tol)$_3$ as the catalyst (Scheme 1). Locos and Arnold reported the Heck reaction of meso-bromoporphyrins with styrene and



Scheme 1. Pd-catalyzed [3+2] annulation of meso-bromoporphyrin with norbornene derivatives.

methyl acrylate, but such an olefinic Heck product was not detected in this reaction.[8] The parent mass ion signal of **2Ni** was observed at *m*/*z* 1045.5635 (calcd for $(C_{69}H_{80}N_4NiNa)^+$:1045.5629 $[M+Na]^+$) in the high resolution ESI-TOF mass spectrum. The ^{1}H NMR spectrum of **2Ni** in $CDCl_3$ showed six doublets and a singlet which were assigned to β protons, thus confirming the unsymmetrical meso,β-fused structure. The use of benzooxanorbornene and benzoazanorbornene as the reactive alkene partners also yielded the corresponding products **3Ni** and **4H** in good yields from **1Ni** and **1H**, respectively. Free base porphyrin **1H** underwent this annulation without metalation by palladium. The addition of the porphyrin moiety to the norbornene skeleton was

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perfectly stereoselective in each case, and X-ray diffraction analysis of **3Ni** revealed an *exo*-fused stereochemistry (see the Supporting Information).[9]

With an efficient protocol to synthesize these chiral porphyrins in hand, we then examined the self-assembly of the zinc porphyrins. Benzoazanorbornene-fused porphyrin $\mathbf{5Zn}_{rac}$, namely a racemic mixture of $\mathbf{5Zn}_{R,S}$ and $\mathbf{5Zn}_{S,R}$, was prepared by removal of the *tert*-butoxycarbonyl (Boc) group of **4H** followed by insertion of a Zn^{II} center.[10] The ^{1}H NMR spectrum of $\mathbf{5Zn}_{rac}$ in $CDCl_3$ showed substantial upfield shifts for the β protons. This is typical of face-to-face porphyrin dimers because of the shielding effect of the porphyrin ring. All the β protons appeared in the similar region as those of **1Ni** in the ^{1}H NMR spectrum of $\mathbf{5Zn}_{rac}$ in [D_5]pyridine. These facts strongly suggested that $\mathbf{5Zn}_{rac}$ forms a discrete assembly in $CDCl_3$. In addition, several minor signals were also observed (see below). Finally, X-ray diffraction analysis revealed that $\mathbf{5Zn}_{rac}$ formed a dimeric assembly mediated by the complementary coordination between the nitrogen and zinc atoms (Figure 1a,b).[9] Importantly, $\mathbf{5Zn}_{rac}$ assembles into a heterochiral dimer $(\mathbf{5Zn}_{rac})_2$, where one enantiomer of $\mathbf{5Zn}_{rac}$ favors dimerization with its antipode.

Efficient chiral separation of **4H** by HPLC was accomplished with ethyl acetate/hexane (1:2) as eluent. Each fraction was separately converted into $\mathbf{5Zn}_{R,S}$ and $\mathbf{5Zn}_{S,R}$ both in an enantiomerically pure form. Their ^{1}H NMR spectra in $CDCl_3$ were identical. All signals for the β protons were again shifted upfield, but importantly the spectrum was totally different from that of the heterochiral dimer $(\mathbf{5Zn}_{rac})_2$. This indicates that $\mathbf{5Zn}_{chi}$ ($\mathbf{5Zn}_{chi}$ represents either $\mathbf{5Zn}_{R,S}$ or $\mathbf{5Zn}_{S,R}$) also assembles into discrete, but different porphyrin oligomers. The homochiral dimeric structure of $(\mathbf{5Zn}_{R,S})_2$ was elucidated by X-ray diffraction analysis (Figure 1c,d).[9] It was also found that the minor peaks in the ^{1}H NMR spectrum of $\mathbf{5Zn}_{rac}$ correspond to those of heterochiral dimer $(\mathbf{5Zn}_{chi})_2$, with $(\mathbf{5Zn}_{rac})_2$ predominant in $CDCl_3$ (ratio of 10:1). These results reveal that heterochiral dimer $(\mathbf{5Zn}_{rac})_2$ and homochiral dimer $(\mathbf{5Zn}_{chi})_2$ coexist in a solution of $\mathbf{5Zn}_{rac}$ in $CDCl_3$ with strong preference for the heterochiral dimer. The UV/Vis absorption spectra of $\mathbf{5Zn}_{chi}$ in $CHCl_3$ showed no changes in the range from 10^{-7} to 10^{-5} M, but the fluorescence spectra were concentration-dependent in the range of 10^{-9} to 10^{-7} M (see the Supporting Information). These observations indicate that some $(\mathbf{5Zn}_{chi})_2$ dissociates into monomer $\mathbf{5Zn}_{chi}$ under dilute conditions. A good fit for the observed sigmoidal curve was obtained by assuming formation of a porphyrin dimer, which affords an association constant of $K_{homo} = 1.2 \times 10^7\,M^{-1}$ for the homochiral dimer. On the other hand, an association constant of $K_{hetero} = 1.8 \times 10^8\,M^{-1}$ was determined for the heterochiral dimer, thereby confirming the preference for this species.

The X-ray crystal structure of $(\mathbf{5Zn}_{rac})_2$ shows the two porphyrin macrocycles are parallel with an interplanar distance of 4.56 Å. The plane consisting of C5, Zn1, and C15 is also parallel to the plane consisting of C5′, Zn2, and C15′. On the other hand, two macrocycles in $(\mathbf{5Zn}_{chi})_2$, are tilted at 14.08°. The plane consisting of C5, Zn1, and C15 is tilted at 11.36° to the plane consisting of C5′, Zn2, and C15′. This kinked structure of $(\mathbf{5Zn}_{chi})_2$ means that the dipole moment is not cancelled out, which leads to the preferential formation of the heterochiral dimer.

The selective assembly of the heterochiral dimer is due to chiral discrimination of one enantiomer with its antipode. This assembly allows the formation of a porphyrin heterodimer, which would be an ideal platform to incorporate two different functions into self-assembled molecules. To confirm this, porphyrin **6Zn**, having 4-*tert*-butylphenyl groups at the meso positions, was synthesized in a similar manner. ^{1}H NMR measurements of **6Zn** confirmed the same assembling behavior as **5Zn** (see the Supporting Information). The NH signals of $(\mathbf{5Zn}_{R,S})_2$ and $(\mathbf{6Zn}_{S,R})_2$ were observed at different chemical shifts in the NMR spectrum recorded in $CDCl_3$ (Figure 2a,b). After mixing $(\mathbf{5Zn}_{R,S})_2$ and $(\mathbf{6Zn}_{S,R})_2$ and heating at 40 °C, the signals due to $(\mathbf{5Zn}_{R,S})_2$ and $(\mathbf{6Zn}_{S,R})_2$ almost completely disappeared and the signals assigned to the heterodimer $\mathbf{5Zn}_{R,S}$·$\mathbf{6Zn}_{S,R}$ became predominant (Figure 2c). These results clearly indicated the formation of the heterodimer through a pseudo-heterochiral association and that $\mathbf{5Zn}_{R,S}$·$\mathbf{6Zn}_{R,S}$ is more stable than each homochiral association. In sharp contrast, the similar experiment using $(\mathbf{5Zn}_{R,S})_2$ and $(\mathbf{6Zn}_{R,S})_2$ led to the appearance of two small new NH signals corresponding to $\mathbf{5Zn}_{R,S}$·$\mathbf{6Zn}_{R,S}$. The changes in the spectra were only minor even after heating at reflux for three days in chloroform (Figure 2f). Finally, the heterodimeric

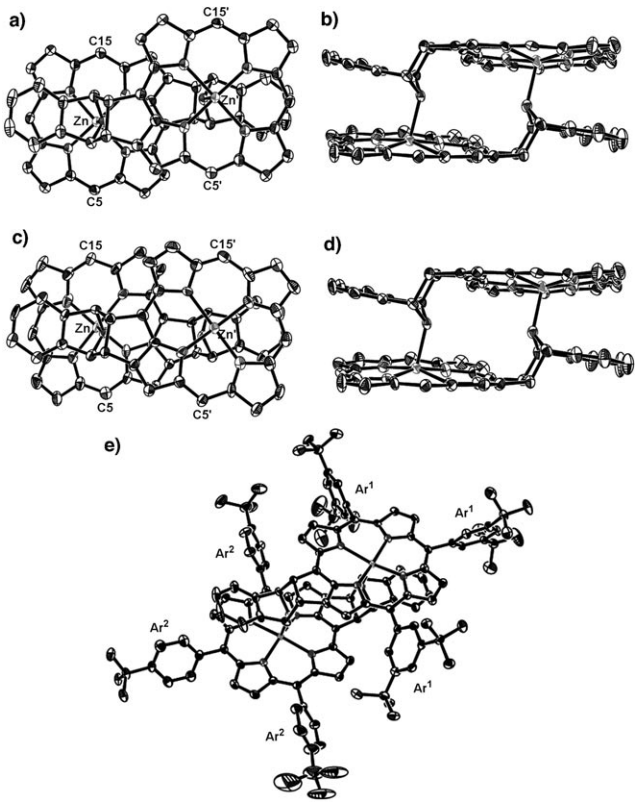

Figure 1. X-ray structures of porphyrin dimers. a) Top and b) side views of $(\mathbf{5Zn}_{rac})_2$, c) top and d) side views of $(\mathbf{5Zn}_{R,S})_2$, and e) view of heterodimer $\mathbf{5Zn}_{S,R}$·$\mathbf{6Zn}_{R,S}$. Ar^1 = 3,5-di-*tert*-butylphenyl, Ar^2 = 4-*tert*-butylphenyl. The thermal ellipsoids are at the 50% probability level. The meso-aryl substituents and hydrogen atoms are omitted for clarity except (e).

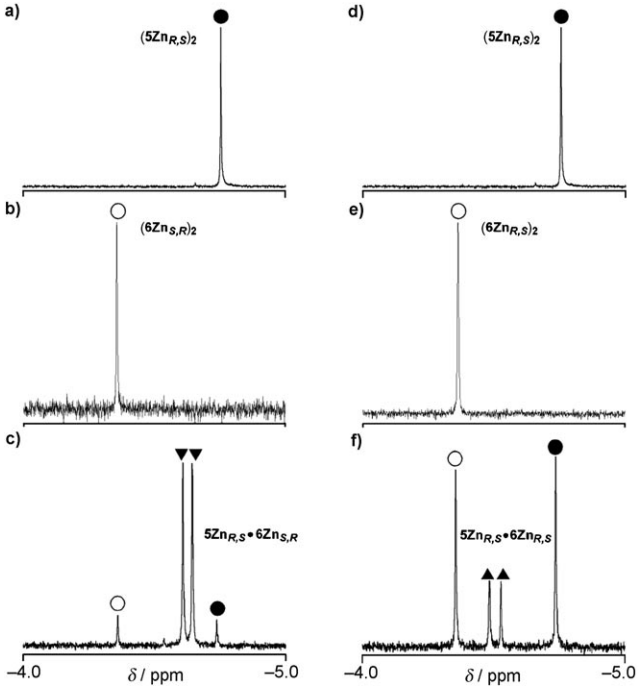

Figure 2. Change in the NH signals in the ^{1}H NMR spectra: a) $(\mathbf{5}Zn_{R,S})_2$, b) $(\mathbf{6}Zn_{S,R})_2$, and c) after heating the mixture of $(\mathbf{5}Zn_{R,S})_2$ and $(\mathbf{6}Zn_{S,R})_2$ (1.3×10^{-3} M); d) $(\mathbf{5}Zn_{R,S})_2$, e) $(\mathbf{6}Zn_{R,S})_2$, and f) after heating the mixture of $(\mathbf{5}Zn_{R,S})_2$ and $(\mathbf{6}Zn_{R,S})_2$ (1.5×10^{-3} M).

structure of $\mathbf{5}Zn_{S,R}\cdot\mathbf{6}Zn_{R,S}$ was unambiguously elucidated by X-ray diffraction analysis of a crystal grown by vapor diffusion of methanol into a solution of $(\mathbf{5}Zn_{S,R})_2$ and $(\mathbf{6}Zn_{R,S})_2$ in chloroform (Figure 1e).[9]

In summary, we have achieved the expeditious synthesis of novel chiral porphyrins with fused norbornene moieties by the use of a Pd-catalyzed [3+2] annulation strategy. The versatility of this strategy has been demonstrated in the synthesis of benzoazanorbornene-fused zinc porphyrins, which assemble to form a stable heterochiral dimer by complementary coordination in both the solid and solution states. The heterochiral assembly enables the formation of a heterodimer constructed from two components through chiral recognition. All these self-assembled porphyrin dimers were unambiguously characterized by X-ray diffraction analysis. These novel chiral porphyrins could also serve as chiral catalysts in combination with central metal ions. This issue would be a further challenging subject. Investigations on functionalized heterolytic porphyrin dimers are currently underway.

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[1] a) T. Imamura, K. Fukushima, *Coord. Chem. Rev.* **2000**, *198*, 133; b) J. Wojaczynski, L. Latos-Grażyński, *Coord. Chem. Rev.* **2000**, *204*, 113; c) E. Iengo, E. Zangrando, E. Alessio, *Eur. J. Inorg. Chem.* **2003**, 2371; d) A. Satake, Y. Kobuke, *Tetrahedron* **2005**, *61*, 13; e) C. Maeda, T. Kamada, N. Aratani, A. Osuka, *Coord. Chem. Rev.* **2007**, *251*, 2743.

[2] a) C. A. Hunter, R. K. Hyde, *Angew. Chem.* **1996**, *108*, 2064; *Angew. Chem. Int. Ed.* **1996**, *35*, 1936; b) S. Knapp, J. Vasudevan, T. J. Emge, B. H. Arison, J. A. Potenza, H. J. Schugar, *Angew. Chem.* **1998**, *110*, 2537; *Angew. Chem. Int. Ed.* **1998**, *37*, 2368; c) G. S Wilson, H. L. Anderson, *Chem. Commun.* **1999**, 1539; d) P. N. Taylor, H. L. Anderson, *J. Am. Chem. Soc.* **1999**, *121*, 11538; e) R. A. Haycock, A. Yartsev, U. Michelsen, V. Sundström, C. A. Hunter, *Angew. Chem.* **2000**, *112*, 3762; *Angew. Chem. Int. Ed.* **2000**, *39*, 3616; f) K. Ogawa, Y. Kobuke, *Angew. Chem.* **2000**, *112*, 4236; *Angew. Chem. Int. Ed.* **2000**, *39*, 4070; g) C. Ikeda. N. Nagahara, N. Yoshioka, H. Inoue, *New J. Chem.* **2000**, *24*, 897; h) C. Ikeda, Y. Tanaka, T. Fijihara, Y. Ishii, T. Ushiyama, K. Yamamoto, N. Yoshioka, H. Inoue, *Inorg. Chem.* **2001**, *40*, 3395; i) K. Ogawa, T. Zhang, K. Yoshihara, Y. Kobuke, *J. Am. Chem. Soc.* **2002**, *124*, 22; j) R. Takahashi, Y. Kobuke, *J. Am. Chem. Soc.* **2003**, *125*, 2372; k) A. Tsuda, S. Sakamoto, K. Yamaguchi, T. Aida, *J. Am. Chem. Soc.* **2003**, *125*, 15722; l) C. Maeda, H. Shinokubo, A. Osuka, *Org. Lett.* **2007**, *9*, 2493; m) C. Maeda, H. Shinokubo, A. Osuka, *Org. Lett.* **2008**, *10*, 549.

[3] a) A. Tsuda, T. Nakamura, S. Sakamoto, K. Yamaguchi, A. Osuka, *Angew. Chem.* **2002**, *114*, 2941; *Angew. Chem. Int. Ed.* **2002**, *41*, 2817; b) I.-W. Hwang, T. Kamada, T. K. Ahn, D. M. Ko, T. Nakamura, A. Tsuda, A. Osuka, D. Kim, *J. Am. Chem. Soc.* **2004**, *126*, 16187; c) T. Kamada, N. Aratani, T. Ikeda, N. Shibata, Y. Higuchi, A. Wakamiya, S. Yamaguchi, K. S. Kim, Z. S. Yoon, D. Kim, A. Osuka, *J. Am. Chem. Soc.* **2006**, *128*, 7670.

[4] Very recently, the effect of a sulfur-centered chirality on the self-assembly of meso-sulfinylporphyrins was reported, although the level of discrimination was not high enough, see: Y. Matano, T. Shinokura, K. Matsumoto, H. Imahori, H. Nakano, *Chem. Asian J.* **2007**, *2*, 1417.

[5] a) H. Ogoshi, T. Mizutani, *Acc. Chem. Res.* **1998**, *31*, 81; b) J.-C. Marchon, R. Ramasseul in *The Porphyrin Handbook*, *Vol. 11* (Eds.: K. M. Kadish, K. M. Smith, R. Guilard), Academic Press, San Diego, **2003**, p. 75; c) G. Simonneaux, P. Le Maux, *Coord. Chem. Rev.* **2002**, *228*, 43.

[6] A. K. Sahoo, S. Mori, H. Shinokubo, A. Osuka, *Angew. Chem.* **2006**, *118*, 8140; *Angew. Chem. Int. Ed.* **2006**, *45*, 7972.

[7] a) R. Grigg, P. Kennewell, A. Teasdale, V. Sridharan, *Tetrahedron Lett.* **1993**, *34*, 153; b) A. A. Pletnev, Q. Tian, R. C. Larock, *J. Org. Chem.* **2002**, *67*, 9276; c) M. Catellani, A. Del Rio, *Russ. Chem. Bull.* **1998**, *47*, 928; K. Saito, O. Katsuhiko, M. Sano, S. Kiso, T. Takeda, *Heterocycles* **2002**, *57*, 1781; d) M. Lautens, D. G. Hulcoop, *J. Org. Chem.* **2001**, *66*, 8127; e) D. G. Hulcoop, M. Lautens, *Org. Lett.* **2007**, *9*, 1761.

[8] O. B. Locos, D. P. Arnold, *Org. Biomol. Chem.* **2006**, *4*, 902.

[9] Crystal data for **3Ni**: $C_{79}H_{86}N_4NiO$, $M_r=1166.23$, triclinic, space group $P\bar{1}$ (No. 2), $a=14.234(6)$, $b=14.559(5)$, $c=16.564(5)$ Å, $\alpha=108.939(9)$, $\beta=90.923(12)$, $\gamma=95.734(12)°$, $V=3226.3(19)$ Å^3, $Z=2$, $\rho_{calcd}=1.200$ g cm^{-3}, $T=123(2)$ K, 25317 measured reflections, 11184 unique reflections, $R=0.0920$ ($I>2.0\sigma(I)$), $R_w=0.2493$ (all data), GOF = 1.017 ($I>2.0\sigma(I)$). Crystal data for $(\mathbf{5}Zn_{rac})_2$: $C_{148}H_{162}Cl_{12}N_{10}Zn_2$, $M_r=2637.06$, monoclinic, space group $P2_1/c$ (No. 14), $a=13.029(2)$, $b=25.898(5)$ $c=21.281(5)$ Å,, $\beta=108.272(7)°$, $V=6819(2)$ Å^3, $Z=4$, $\rho_{calcd}=1.284$ g cm^{-3}, $T=123(2)$ K, 62760 measured reflections, 15366 unique reflections, $R=0.0708$ ($I>2.0\sigma(I)$), $R_w=0.1977$ (all data), GOF = 1.049 ($I>2.0\sigma(I)$). Crystal data for $(\mathbf{5}Zn_{S,R})_2$: $C_{146.37}H_{160.75}Cl_{4.88}N_{10.37}O_{0.25}Zn_2$, $M_r=2373.12$, monoclinic, space group $P2_1$ (No. 4), $a=16.673(3)$, $b=18.289(3)$, $c=23.215(4)$ Å, $\beta=110.970(3)°$, $V=6610.2(2)$ Å^3, $Z=2$, $\rho_{calcd}=1.192$ g cm^{-3}, $T=90(2)$ K, 37895 measured reflections, 25705 unique reflections, $R=0.0997$ ($I>2.0\sigma(I)$), $R_w=0.2866$ (all

data), GOF = 0.994 ($I > 2.0\sigma(I)$). Crystal data for $\mathbf{5Zn_{S,R}}\cdot\mathbf{6Zn_{R,S}}$: $C_{266}H_{270}Cl_7N_{20}Zn_4$, $M_r = 4256.65$, monoclinic, space group $P2_1$ (No 4), $a = 16.665(5)$, $b = 30.973(5)$, $c = 22.024(5)$ Å, $\beta = 96.602(5)°$, $V = 11293(5)$ Å^3, $Z = 2$, $\rho_{calcd} = 1.142$ g cm^{-3}, $T = 90(2)$ K, 68724 measured reflections, 37921 unique reflections, $R = 0.0569$ ($I > 2.0\sigma(I)$), $R_w = 0.1492$ (all data), GOF = 1.023 ($I > 2.0\sigma(I)$). CCDC 680365 (**3Ni**), 679585 ($(\mathbf{5Zn}_{rac})_2$), 679586 ($(\mathbf{5Zn}_{S,R})_2$), and 679587 ($\mathbf{5Zn_{S,R}}\cdot\mathbf{6Zn_{R,S}}$) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[10] For a β,β-azanorbornene-fused zinc porphyrin, see Ref. [2b]. This porphyrin is not chiral because of its symmetric structure.

