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Metal Complexes of Chiral Möbius Aromatic [28]Hexaphyrin(1.1.1.1.1.1): Enantiomeric Separation, Absolute Stereochemistry, and Asymmetric Synthesis**

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The concept of Möbius aromaticity, first proposed by Heilbronner in 1964, predicts the aromatic characters for [4nπ]annulenes with singly twisted so-called Möbius topology.[1] Importantly, this concept complements the established Hückel aromaticity that is based on normal planar π-electronic network,[1,2] and therefore stimulates both theoretical and experimental studies. Among these studies, the first Möbius aromatic [16]annulene was reported by Herges and co-workers in 2003,[3] and was followed by an interesting example of a di-*p*-benzi-hexaphyrin that exhibited a temperature dependent structural change between Hückel and Möbius conformations.[4] In the last two years, Möbius aromatic systems have been efficiently prepared starting from meso-aryl-substituted expanded porphyrins through metal coordination,[5a,b] temperature control,[5c,d] protonation,[5e,f] and intramolecular fusion reactions.[5g,h]

Macrocycles that have a singly twisted Möbius topology are intrinsically chiral, and can be either P-twist or M-twist, as shown in Figure 1. Control of the chirality of Möbius aromatic expanded porphyrins is important to understand their magnetic properties and to apply these systems to chirality sensing and asymmetric catalysts. Although the enatiomeric separation of Möbius aromatic annulenes has been accomplished by Herges and co-workers, their absolute configurations have not been determined.[3b] In addition, only limited examples of the enantiomeric separations of twisted expanded porphyrins have been reported to date.[6]

We envisioned the enantiomeric separation of Group 10 metal complexes of [28]hexaphyrin(1.1.1.1.1.1) on the basis that hexaphyrins are considered to be rather robust, as indicated by their almost temperature-independent ^{1}H NMR spectra. Herein, we report the enantiomeric separation of these complexes by using preparative HPLC on a chiral stationary phase, as well as the asymmetric synthesis of the palladium(II) complex.

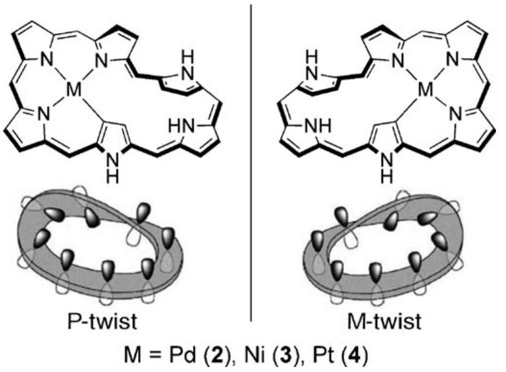

Figure 1. Two enantiomers of hexaphyrin metal complexes. C_6F_5 groups at the meso positions were omitted for simplicity.

[28]Hexaphyrin(1.1.1.1.1.1) complexes of Pd^{II} (**2**), Ni^{II} (**3**), and Pt^{II} (**4**) were prepared according to a previously reported method that entailed the addition of $PdCl_2$, $Ni(acac)_2$, and $PtCl_2$ at reflux for 12 hours, 1 hour, and 5 days, respectively (acac = acetylacetonate).[5a,7] In the case of complex **2**, we found a far more effective method that entailed treatment of [26]hexaphyrin(1.1.1.1.1.1) **1** (see Scheme 1 for structure) with $[Pd_2(dba)_3]$ in the presence of sodium acetate in a mixture of CH_2Cl_2/MeOH (dba = 1,5-diphenyl-1,4-pentadien-3-one). This method produced complex **2** in 75% yield at room temperature in 2 hours. The enantiomeric separation of complex **2** was examined by using an analytical HPLC column (SUMICHIRAL OA-3100; $\phi = 10$ mm), which, after extensive experimentation, led to a clear separation of the enantiomers with a mixture of CH_2Cl_2/*n*-hexane (v/v = 1:1) as an eluent (See the Supporting Information). Based on this finding, the preparative chiral separation of complex **2** was performed successfully on a larger HPLC column ($\phi =$ 20 mm) with a less polar eluent (CH_2Cl_2/*n*-hexane, v/v = 1:2). Under similar conditions, the enantiomeric separations of complexes **3** and **4** were also successfully accomplished.

The spectra of the isolated enantiomers displayed opposite Cotton effects (Figure 2). The CD spectrum of the enantiomer that eluted first, **2A**, shows the first Cotton effect as a negative–positive bisignate split signal around 639 nm, and the second signal as a positive Cotton effect at 397 nm (Figure 2a). The enantiomers of **3** and **4** that eluted first show practically the same CD spectra as those of **2**; the bisignate split signal and the positive signal at 639 and 387 nm for **3A** and at 619 and 383 nm for **4A**, respectively (Figure 2b,c). The large $\Delta\varepsilon$ values ($\approx 300\,\text{M}^{-1}\text{cm}^{-1}$) for these enantiomers,

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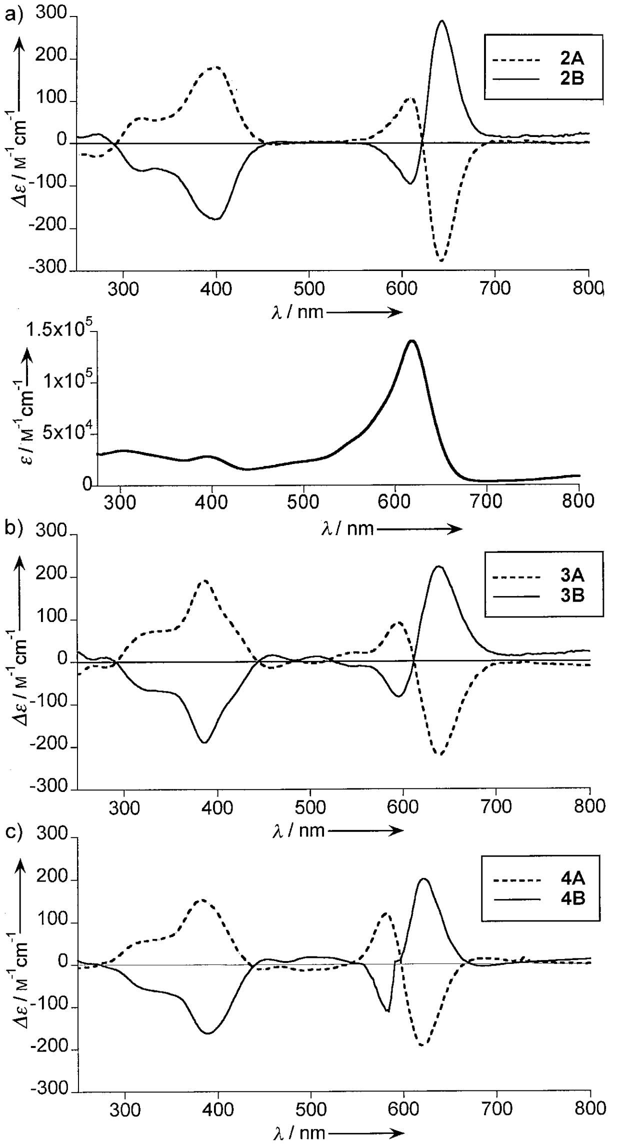


Figure 2. CD spectra of [28]hexaphyrin(1.1.1.1.1.1) metal complexes in CH_2Cl_2. a) Pd^{II} complex **2** with UV/VIS absorption spectrum directly underneath, b) Ni^{II} complex **3**, and c) Pt^{II} complex **4**; where **A** and **B** correspond to the first and second fractions collected, respectively.

attributed to the strong aromaticity, is interesting in view of their potential application as chiral sensors.

Fortunately, we obtained crystals of **2A** suitable for X-ray crystallographic analysis from an acetonitrile/H_2O solution.[8] The crystal structure is shown in Figure 3a. The asymmetric unit contains two identical molecules, both of which have the same P-twist configuration. Thus, the absolute configuration of **2A** has now been unambiguously determined. Notably, this relationship between the CD spectrum and the absolute configuration is quite analogous to the related previous examples of [36]octaphyrin(2.1.0.1.2.1.0.1) and N-fused [32]heptaphyrin(1.1.1.1.1.1.1), both of which have twisted figure-of-eight structures,[6,9] which suggest the generality of this relationship. Interestingly, this assignment was also supported by TD-DFT calculations (Figure S5 in the Supporting Information). Another interesting structural feature is a slight difference between the structures of the racemate of **2** and of **2A**; the two largest values of the dihedral angles are −41.14° and 134.13° for the former,[5a,7] and 36.55(43.28)° and 127.67 (134.55)° for the latter—the difference probably arising as a consequence of crystal packing.

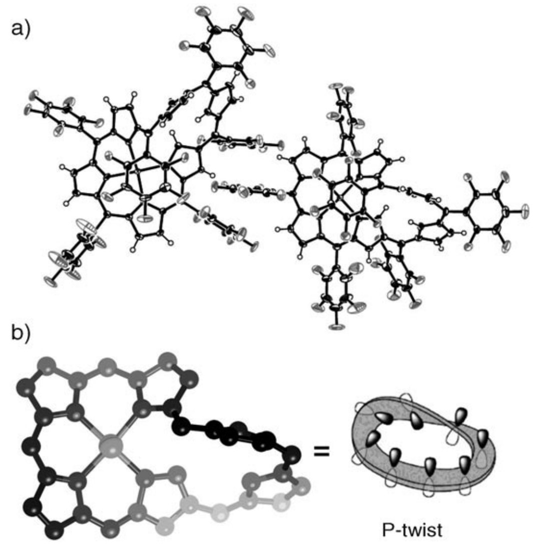
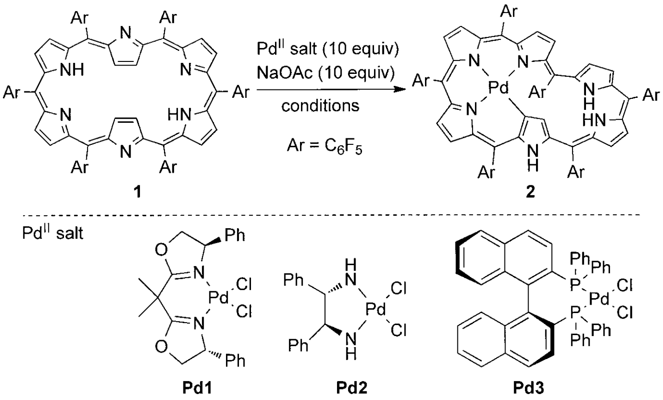


Figure 3. X-ray crystal structure of **2A**. a) ORTEP drawing of two molecules in the unit cell. Thermal ellipsoids were scaled to 50% probability levels. Solvent molecules were omitted for clarity. b) One molecule representation (C_6F_5 substituents were omitted for clarity) and schematic twisting model.

The [28]hexaphyrin(1.1.1.1.1.1) complex of Pd^{II} (**2**) is certainly structurally robust and shows practically no spectroscopic change even at 140°C, as indicated by the variable-temperature ^1H NMR measurement carried out in $[D_2]$1,1,2,2-tetrachloroethane solution, (Figure S6 in the Supporting Information). However, we found complete racemization of **2A** after heating in xylene at reflux overnight. On the basis of this finding, the racemization kinetics were examined at temperatures of 90–120°C under a nitrogen atmosphere by monitoring the decrease in intensity of the CD signal. The racemization rate constants, which obeyed first-order kinetics, were determined at different temperatures (See the Supporting Information). From these data, the following activation parameters were determined: $\Delta G^{\ddagger}_{373} = 127.2\ \mathrm{kJ\,mol^{-1}}$, $\Delta H^{\ddagger} = 124.1\ \mathrm{kJ\,mol^{-1}}$, $\Delta S^{\ddagger} = -8.3\ \mathrm{J\,mol^{-1}\,K^{-1}}$, and $\Delta E^{a} = 127.2\ \mathrm{kJ\,mol^{-1}}$. The activation barrier ΔE^{a} is higher than that of a larger figure-of-eight octaphyrin complex of Pd^{II} reported by Vogel and co-workers (96.5 $\mathrm{kJ\,mol^{-1}}$).[6b]

Next, we examined the possibility of the asymmetric synthesis of Möbius aromatic expanded porphyrins by using chiral Pd^{II} salts.[10,11] With Pd^{II} salts containing Pd−N bonds, such as **Pd1** and **Pd2**, the metalation proceeded slowly and provided complex **2** in low yields and with poor enantioselectivities (Scheme 1). However, the reaction with **Pd3** gave **2** in 33% yield and with 23% *ee* at room temperature after 3 days. To the best of our knowledge, this is the first example of effective chiral induction in the synthesis of Möbius twisted molecule. An increase of the reaction temperature to 40°C resulted in the isolation of **2** in 72% yield, although the enantioselectivity decreased to 13% *ee*. We also found the



conditions	CH_2Cl_2/MeOH RT, 3 days	DMSO 50 °C, 6 days	CH_2Cl_2/MeOH RT, 3 days	CH_2Cl_2/MeOH 40 °C, 5 days
yield [%]	59	12	33	72
ee [%][a]	−2[b]	1[b]	23[b]	13[b]

Scheme 1. Asymmetric synthesis of **2** using chiral Pd^{II} salts. [a] Determined by HPLC on a chiral stationary phase. [b] Positive *ee* value means **2A** rich (P-twist), and negative *ee* value means **2B** rich (M-twist). DMSO = dimethyl sulfoxide.

preferential precipitation of racemic crystals of **2**. Thus, simple recrystallization of **2** (+20% *ee*) gave almost racemic crystals (+2% *ee*), thus leaving the filtrate optically more enriched (+70% *ee*).[12]

In summary, [28]hexaphyrin(1.1.1.1.1.1) complexes of Pd^{II}, Ni^{II}, and Pt^{II} were all resolved into their enantiomers. The absolute configuration of an enantiomer of the Pd^{II} complex was determined by X-ray analysis, and which, as judged from the similarities in the elution behavior and in the CD spectroscopic patterns, was considered to dictate the absolute configurations for the other complexes. The activation energy for the racemization was estimated to be 127.2 kJ mol^{-1} for the Pd^{II} complex. Furthermore, the asymmetric synthesis of a Möbius aromatic expanded porphyrin was accomplished for the first time with moderate enantioselectivity. Current investigations are focused on applying these chiral Möbius aromatic hexaphyrins to sensing materials and asymmetric catalysts.

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