A Highly Enantiopure Biconcave Porphyrin with Effective D_4-Structure

Reinhold Schwenninger,[a, c] Yvan Ramondenc,[a, d] Klaus Wurst,[b]+ Johann Schlögl,[a] and Bernhard Kräutler*[a]

Abstract: A first representative of an effectively D_4-symmetric biconcave porphyrin (**1**) was prepared from a tetramerizing condensation of a C_2-symmetric pyrrole (**2**). The chiral pyrrole **2** was synthesized in a six-step reaction sequence starting from the C_{2h}-symmetric 2,6-di-*tert*-butylanthracene. The relevant stereochemistry was introduced in a highly diastereo-discriminating Diels–Alder reaction with fumaric acid di-(−)menthyl ester, catalyzed by aluminum chloride. X-ray analyses of two of the dimenthyl esters prepared unambiguously secured their tentatively assigned absolute configuration and that of the pyrrole **2** (as the *S*,*S* isomer). The enantiomeric purity of the pyrrole **2** was determined as 99 % *ee*, using the Co^{II} complex of the porphyrin **1** as a chiral shift reagent. The pyrrole **2** lent itself to a stereochemically nearly uniform preparation of the chiral, biconcave porphyrin **1**. Applying Horeau's principle, **1** was calculated to be present in an enantiomeric excess of about 10^9:1. The validity of the statistical considerations relevant for this estimate were verified by examination of the results from preparative tetramerization experiments in which the enantiomeric purity of the pyrrole **2** was deliberately lowered.

Keywords: asymmetric synthesis · cage compounds · chirality · porphyrinoids · structure elucidation

Introduction

Pioneered with great success with Collman's "picket-fence" porphyrins,[1] metalloporphyrins with a three-dimensionally structured skeleton have attracted considerable attention as model compounds for oxygen-binding and oxygen-activating haem proteins[1–3] and as catalysts in a range of organic transformations.[4, 5] Three-dimensionally structured, chiral porphyrins have been developed as enantioselective catalysts[4–7] and as host molecules for stereoselective recognition.[8, 9] As a rule,[10] aromatic *meso* substituents have served as the basis for the build-up of the three-dimensional architecture in these porphyrins.

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We recently opened a synthetic route to biconcave porphyrins with a rigid framework.[11] In such porphyrins well-defined and rather rigid cavities are built-up, which aid the shape-selective incorporation of guest molecules.[12] For biconcave porphyrins,[11] a construction principle complementary to the one used earlier[1–9] has been explored: it relied on pyrrolic building blocks with a rigid periphery fixed to the β,β'-positions as provided by annelated 9,10-dihydroanthracene units. The pyrrolic building blocks were prepared by a new and convenient two-step method. A Diels–Alder reaction of the potent dienophile[13a,b] acetylenedicarbonitrile and anthracene (derivatives)[13c] first gave rigidly structured maleinic dinitrile derivatives (**I**) (Scheme 1). The reduction of these cycloadducts led to the corresponding pyrroles (**II**).[11] Biconcave porphyrins **III**-$(CH_3)_{16}$ were efficiently assembled by tetramerizing condensations of the three-dimensionally structured pyrroles **II**-$(CH_3)_4$ with formaldehyde,[11] following classic procedures for the synthesis of porphyrins bearing substituents only at the β-positions of the pyrrole rings[14].

In this report, we describe the effectively D_4-symmetric biconcave porphyrin **1**, obtained in a highly enantiomerically pure form (calculated to be > 99.999999 % *ee*) from the rigidly structured, chiral pyrrole **2**, by exploiting a fourth-order Horeau amplification.[15] A diastereo-selective Diels–Alder reaction[16] was used as the key step for the synthesis of the C_2-symmetric pyrrole **2**, obtained with 99 % *ee*. The stereochemical purity of the pyrrole **2** was determined by ^{1}H NMR spectroscopy with the help of the Co^{II} complex **9** as chiral shift

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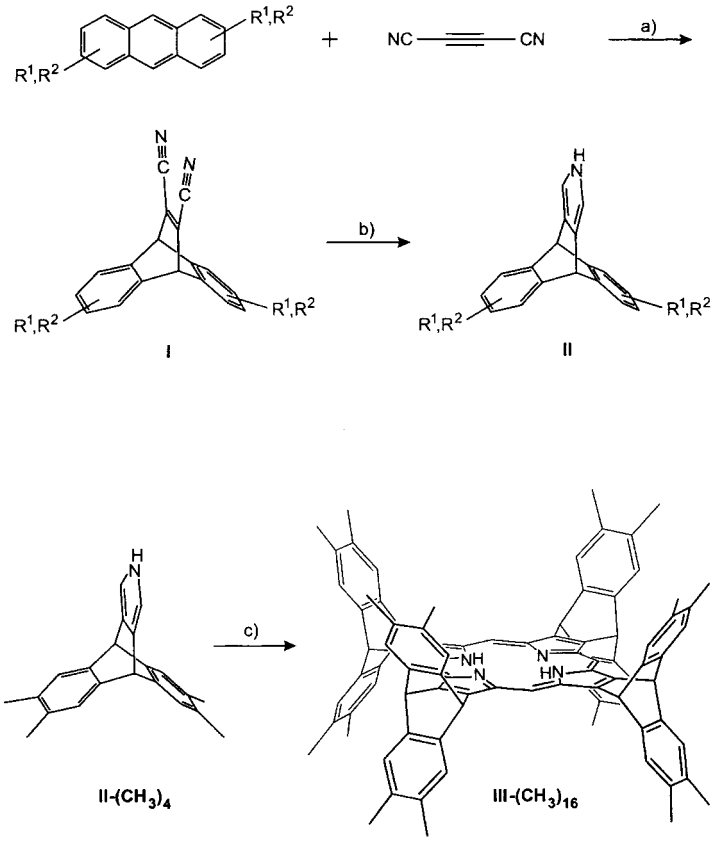

Scheme 1. General synthetic outline.

reagent. A series of further transition metal complexes of the porphyrin **1** were prepared, providing a variety of excellent and broadly functioning chiral shift reagents in ^{1}H NMR spectroscopy.[17]

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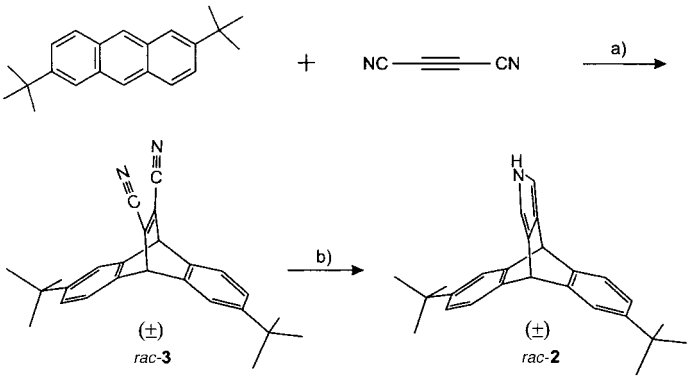
Results

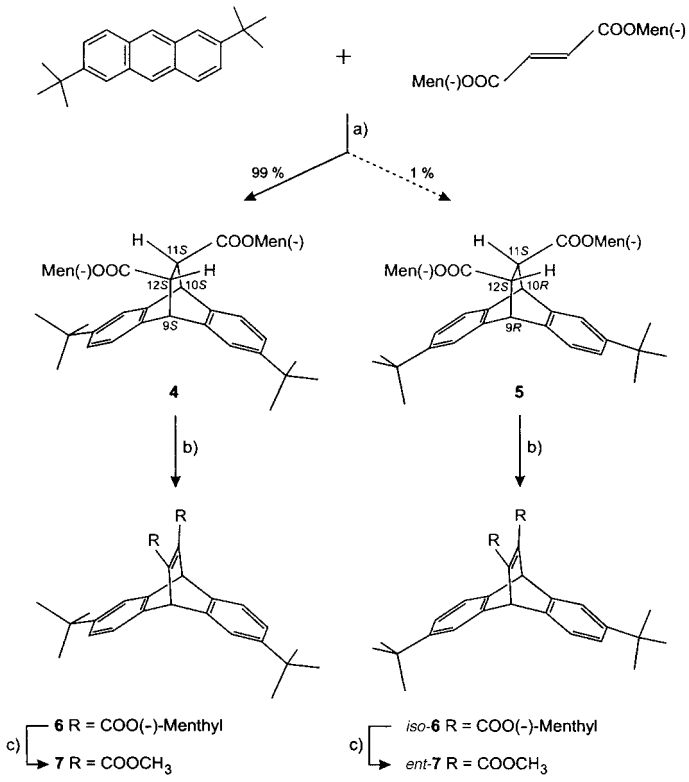
Preparation of the chiral pyrrole 2

*Preparation of the racemic form rac-**2** (Scheme 2)*: The crystalline racemic dinitrile *rac*-**3** was first obtained in 89% yield from the cycloaddition of acetylenedicarbonitrile and 2,6-di-*tert*-butylanthracene in benzene at reflux.[18] Reduction of the dinitrile *rac*-**3** with diisobutylaluminum hydride (DIBAH) at $-20\,^\circ$C gave the racemic pyrrole *rac*-**2** in 30–35% yield.



Scheme 2. Synthesis of racemic pyrrole *rac*-**2**: a) benzene, reflux, 15 h; b) DIBAH, CH_2Cl_2, $-20\,^\circ$C, 3.5 h.

*Preparation of **2** (see Schemes 3 and 4)*: A highly diastereoselective $AlCl_3$-catalyzed Diels–Alder reaction[19] of di-(−)menthylfumarate and 2,6-di-*tert*-butylanthracene at

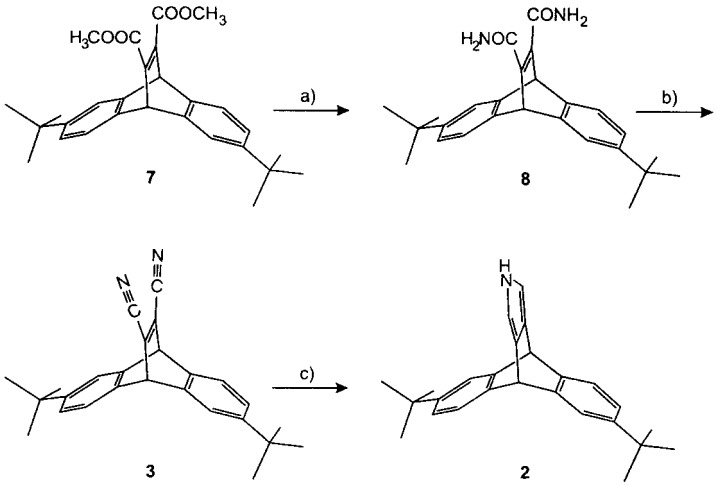


Scheme 3. Synthesis of dimethylesters **7** and *ent*-**7**: a) $AlCl_3$, toluene, $-40\,^\circ$C, 3 h, then $0\,^\circ$C, 12 h; b) 1) Ph-Se-Se-Ph, pottasium *tert*-butoxide, THF, toluene; 2) HCl, isopropyl alcohol, room temperature, 12 h; c) MeOH, methanesulfonic acid, reflux, 96 h.

$-40\,^{\circ}C$ gave the two crystalline products **4** and **5** in a ratio of about 99:1. The cycloadducts **4** and **5** were separated by column chromatography to give 94% of **4** and about 1% of **5**. Based on NOE correlations between the signals of hydrogens at the succinate bridge and of unambiguously assigned signals of aromatic protons, the structural differences between the cycloadducts **4** and **5** could be attributed to the relative positions of the ester functionalities and the *tert*-butyl groups. Accordingly, the major isomer (**4**) was indicated to have these groups in a mutual *anti* arrangement; the minor isomer (**5**) in a *syn* arrangement (Scheme 3). Following the empirical rules for C_2-symmetric chiral molecules[20] broadly applied to anthracene-9,10-cycloadducts and by correlating the sign of the optical rotation and CD spectra and the absolute configuration at the bridgehead (9,10)-positions,[21, 22] the major diastereoisomer **4** ($[\alpha]_D^{20} = -53$) was tentatively assigned as the (9*S*,10*S*,11*S*,12*S*) isomer. The minor isomer **5** ($[\alpha]_D^{20} = +4$) was correspondingly assigned as the (9*R*,10*R*,11*S*,12*S*) isomer. The identical stereochemical assignment at the 11- and 12-positions of **4** and **5** was consistent with the known high face selectivity at the dienophile dimenthylfumarate in its $AlCl_3$-catalyzed Diels–Alder reactions.[19] The relative configuration of the stereocenters in **5** was directly confirmed by X-ray structure analysis, as was its absolute configuration, based on the known structure of (−)menthol (=(1*R*)-menthol)[23] (Figure 1).

Oxidation of the major cycloadduct **4** with diphenyldiselenide and slow addition of potassium *tert*-butoxide, followed by chromatography of the reaction mixture, gave the crystalline maleic acid dimenthyl ester **6** in 92% yield ($[\alpha]_D^{20} = -91$). The structure of **6** was tentatively assigned as that of a (9*S*,10*S*)-9,10-dihydro-9,10-ethenoanthracene, which was confirmed by X-ray structure analysis (Figure 1). The chiral auxiliary groups of **6** were removed by acid-catalyzed transesterification in methanol, which gave the crystalline dimethyl ester **7** ($[\alpha]_D^{20} = -72$), whose crystal structure was also determined. Analogous transformations of the *syn* isomer **5** (oxidation with diphenyldiselenide, transesterification) resulted in *ent*-**7** (the enantiomer of **7**) with identical spectroscopic data as for **7**, except for the sign of the optical rotation ($[\alpha]_D^{20} = +73$).

Treatment of the dimethyl ester **7** with ammonia-saturated methanol at 40 °C and sodium cyanide as a catalyst provided the corresponding crystalline diamide **8** (77% yield, $[\alpha]_D^{20} = -79$; Scheme 4). Dehydration of **8** with thionyl chloride was



Scheme 4. Synthesis of chiral pyrrole **2**: a) NH_3, NaCN, MeOH, 40 °C, 5 d; b) thionyl chloride, DMF, room temperature, 48 h; c) DIBAH, CH_2Cl_2, $-20\,^{\circ}C$, 3.5 h.

performed at room temperature and gave the crystalline dinitrile **3** in 89% yield ($[\alpha]_D^{20} = -69$). The enantiomeric purity of **3** was determined by ^1H NMR spectroscopy to be 99 ± 0.2% *ee*, using the Co^{II} complex of the porphyrin **1** as chiral shift reagent (see below). Reduction of **3** with DIBAH at $-20\,^{\circ}C$[11] according to the procedure worked out earlier for *rac*-**3**, provided the chiral pyrrole **2** ($[\alpha]_D^{20} = -41$) in 39% yield (Scheme 4). Aside from the sign of the optical rotation, the spectroscopic data of the pyrrole **2** were identical to those of the racemate *rac*-**2** (^1H NMR, ^{13}C NMR, FAB-MS, FT-IR).

Preparation of the symmetric biconcave porphyrin 1 (Scheme 5): Acid-catalyzed condensation of formaldehyde and the chiral pyrrole **2** at room temperature in a degassed solution (seven days) produced a slightly reddish reaction

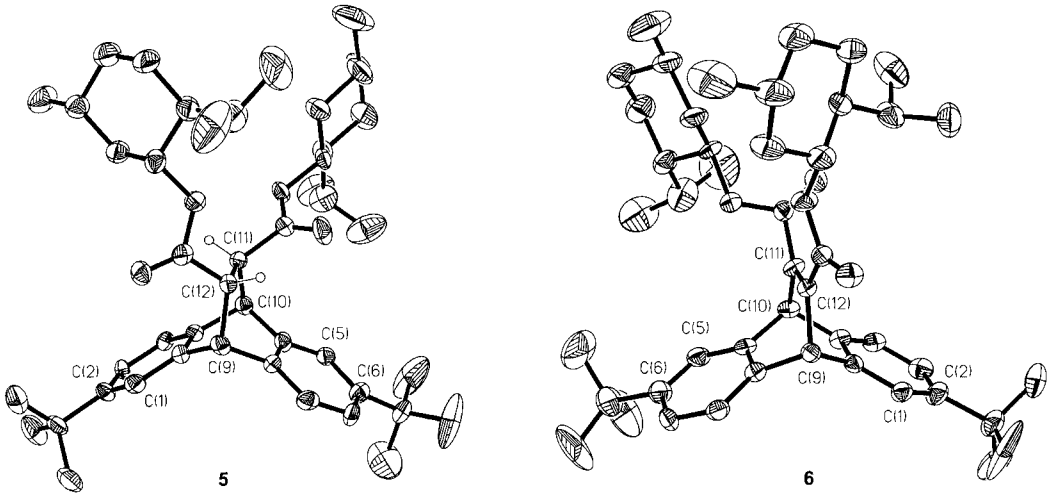


Figure 1. Structures of the *syn*-cycloadduct **5** of di-(−)menthyl fumarate and 2,6-di-*tert*-butylanthracene and of **6**, the oxidation product of the *anti*-cycloadduct **4** (ORTEP plots; thermal ellipsoids at 30% probability level are shown).

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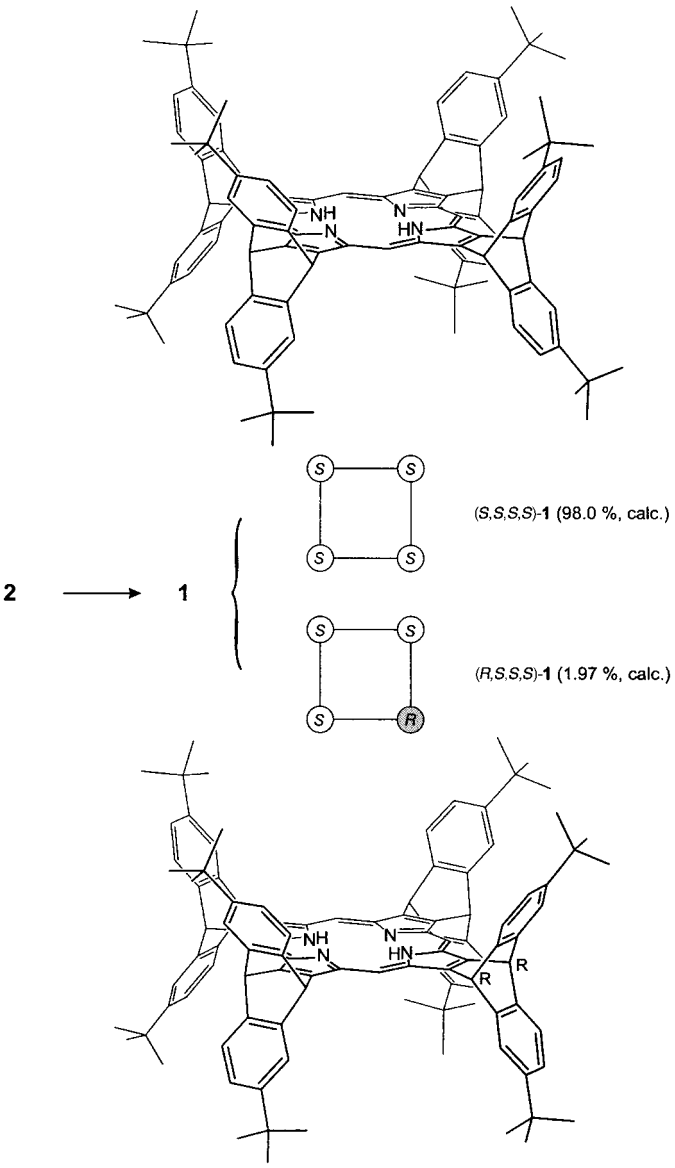


Scheme 5. Synthesis of biconcave porphyrin using **2** (99.0 % *ee*); 1) aqueous formaldehyde, HOAc, MeOH/CH_2Cl_2, room temperature, 7 d; 2) DDQ, room temperature, 2 h.

mixture that was oxidized with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) at room temperature (one hour). The crystalline chiral porphyrin **1** was isolated in 70 % yield after chromatographic separation of the reaction mixture and crystallization from acetone/water.

The constitution and the high symmetry of the porphyrin **1** was established from UV/Vis, CD, ^{1}H NMR, ^{13}C NMR, and FT IR spectra and FAB-MS data. The NMR spectra, recorded at ambient temperature (^{1}H NMR: 7 signals, ^{13}C NMR: 12 signals), indicated a highly uniform structure and were consistent with a specific effective D_4-symmetric structure of **1** in solution (Figure 2). The UV/Vis spectrum showed the characteristic bands of a metal-free porphyrin (Figure 3, bottom), while the CD spectrum revealed positive molar ellipticities for all bands at wavelengths longer than about 300 nm (Figure 3, top).

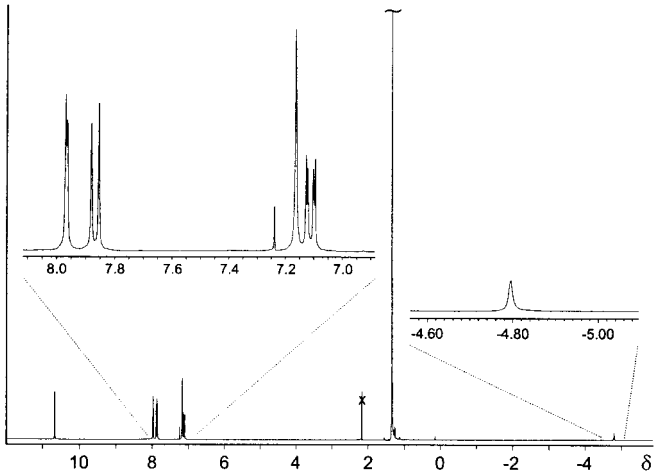


Figure 2. 300 MHz ^{1}H NMR spectrum of the porphyrin **1** (in $CDCl_3$).

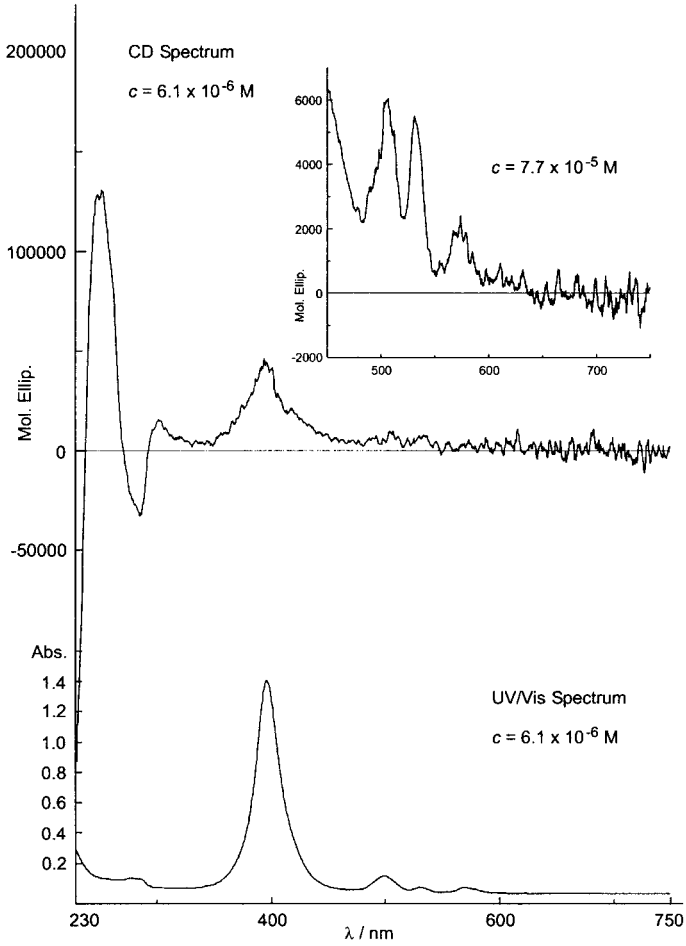
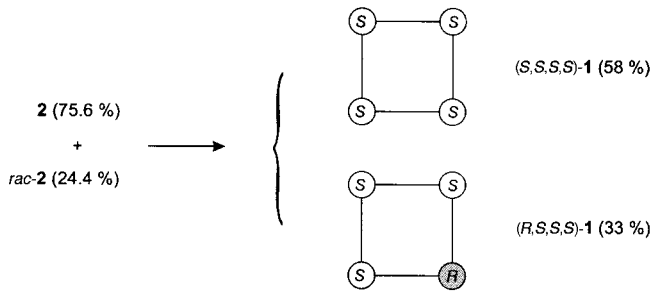


Figure 3. Top: CD spectra of porphyrin **1** (CH_2Cl_2, $c = 6.1 \times 10^{-6}$ M; inset: $c = 7.7 \times 10^{-5}$ M); bottom: UV/Vis absorbance spectrum of porphyrin **1** (CH_2Cl_2, $c = 6.1 \times 10^{-6}$ M).

Preparation of the asymmetric biconcave porphyrin ((*R*,*S*,*S*,*S*)-1, Scheme 6): In an experiment analogous to that described for the preparation of **1**, but using a mixture of the pyrroles **2** (*S* enantiomer, 99 % *ee*)[24] and of *rac*-**2** in a ratio of 75.6:24.4 (i.e. having the *S* enantiomer in an enantiomeric excess of 74.8 % *ee* only), resulted in 71 % of a raw mixture of stereoisomeric porphyrins. A ^{1}H NMR spectrum of this



Scheme 6. Synthesis of biconcave porphyrin using a mixture of **2** and *rac*-**2** (=74.8% *ee*); 1) aqueous formaldehyde, HOAc, MeOH/CH_2Cl_2, room temperature, 7 d; 2) DDQ, room temperature, 2 h.

mixture was consistent with the two main components, the symmetric porphyrin **1** (58%) and the asymmetric porphyrin (*R*,*S*,*S*,*S*)-**1** (33%). Rechromatography of part of the mixture of stereoisomeric porphyrins afforded from the second band a pure sample of the slightly more polar (*R*,*S*,*S*,*S*)-**1**, which was subjected to a ^{1}H NMR spectroscopic analysis.

Preparation of the Co^{II} porphyrinate 9: Treatment of a solution of the porphyrin **1** in THF with dry $CoBr_2$ in the presence of dry sodium acetate at room temperature[11] led to practically quantitative complexation. The red Co^{II} porphyrinate **9** was crystallized from acetone/water and isolated in 99% yield.

The constitution and the effective molecular symmetry of the Co^{II} porphyrinate **9** were established from UV/Vis, ^{1}H NMR, and FT-IR spectra and FAB MS data. The UV/Vis spectra exhibited the typically intense Soret band (402.5 nm) and two weaker bands at 514.5 and 546 nm. The ^{1}H NMR spectrum of the paramagnetic Co^{II} porphyrinate **9**, recorded at ambient temperature in benzene exhibited 6 signals, consistent with D_4-symmetry, as well as the low-field shifts ($\Delta\delta \approx 20$ for *meso*-hydrogens, $\Delta\delta \approx 7$ for bridgehead-hydrogens, but only $\Delta\delta \approx 0.2$ for the signals of the *tert*-butyl groups), characteristic of symmetric, biconcave and other Co^{II} porphyrins.[11]

Analysis of the enantiomeric purity of the dinitrile 3: The D_4-symmetric Co^{II} porphyrinate **9** was used as a chiral shift reagent for analysis of stereoisomers in ^{1}H NMR spectra. The enantiopurity of the dinitrile **3** was determined by analyzing the effect of the Co^{II} porphyrinate **9** on the signal of the bridgehead proton of **3**. In the ^{1}H NMR spectrum of a solution of **3** and *rac*-**3** in benzene, this signal was observed at $\delta = 4.78$. In the presence of **9** the corresponding signal for *rac*-**3** is split into two singlets, both shifted to a higher field. At a 11.6 mM concentration of **9** and at 30°C the two signals of the bridgehead protons of *rac*-**3** occurred at $\delta = 4.71$ ($\Delta\delta = -0.069$) and at $\delta = 4.53$ ($\Delta\delta = -0.250$). The 500 MHz ^{1}H NMR spectrum of a solution of the dinitrile **3** and of **9** in benzene (10.2 mM) showed a major signal at $\delta = 4.73$, the ^{13}C satellites at $\delta = 4.87$ and $\delta = 4.58$ and a further small signal at $\delta = 4.55$ (Figure 4). The last signal is attributed to the bridgehead protons of the minor (*R*)-stereoisomer ((*R*)-**3**)[24] of the dinitrile **3**. Based on the natural occurrence of ^{13}C isotopes (1.1%)[25] and on the integrals of the three signals, the minor

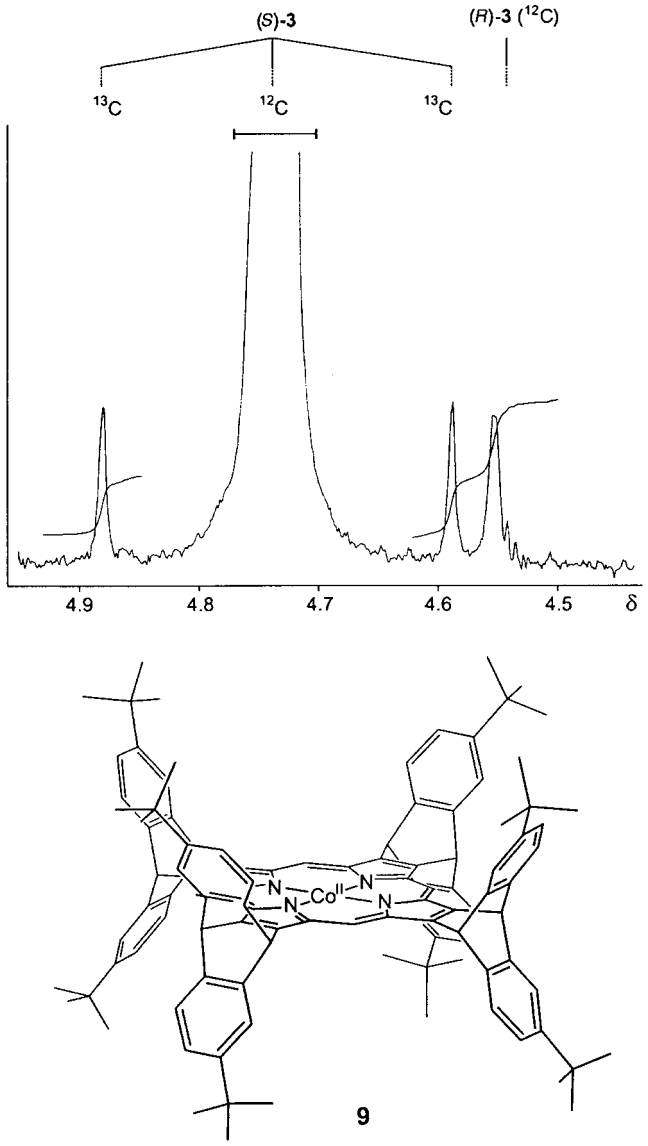


Figure 4. Section of the 500 MHz ^{1}H NMR spectrum of a solution in C_6D_6 of the dinitrile **3** and of the Co^{II} porphyrinate **9** ($c = 10.2$ mM) and structure of **9**.

isomer (*R*)-**3** was estimated to be present in our preparation of **3** at a level of 0.5 ± 0.1%. The enantiomeric purity of **3** (and of its reduction product **2**) accordingly amounts to 99 ± 0.2%.

Stereochemical analysis of the porphyrins resulting from nonracemic mixtures of the pyrroles (*S*)-2 and (*R*)-2.[24] Further experiments analogous to those described for the preparation of **1** (=98% of (*S*,*S*,*S*,*S*)-**1** and 2% of (*R*,*S*,*S*,*S*)-**1**) were carried out using varying mixtures of the pyrrole **2** (*S* enantiomer, 99% *ee*) and of *rac*-**2** (Table 1). The pyrroles **2** and *rac*-**2** were used in ratios of 75.6:24.4 (i.e. having 74.8% *ee* of the *S* enantiomer), of 84.3:15.7 (i.e. having 83.4% *ee* of the *S* isomer), and of 92.5:7.5 (i.e. having 91.6% *ee* of the *S* isomer). The crude mixtures of stereoisomeric porphyrins (64–72% yield) were analyzed by ^{1}H NMR spectroscopy to determine the relative amounts of the two main components (i.e. the symmetric porphyrin **1** and the asymmetric porphyrin (*R*,*S*,*S*,*S*)-**1**), as given in Table 1.

0947-6539/00/0607-1218 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 7

Table 1. Distribution of stereoisomeric porphyrins from tetramerizing condensation of pyrrole mixtures (*S*)-**2**/(*R*)-**2** with different enantiomeric purities. Calculated distributions were compared with corresponding values from experiments with (*S*)-**2**: 1) 91 % *ee*; 2) 83.4 % *ee*; 3) 74.8 % *ee* (see text for further details).

Porphyrin stereo isomers	Stereoisomeric composition of porphyrins from *rac*-**2** calcd[a]	(*S*)-**2**/(*R*)-**2** mixtures experiments 1)–3) calcd[a]	obs.[b]	(*S*)-**2** (99 % *ee*) calcd[a]
(*S*,*S*,*S*,*S*)-**1**	6.25	1) 84.2 2) 70.7 3) 58.4	1) 84 2) 70 3) 58	98.0
(*R*,*R*,*R*,*R*)-**1**	6.25	1) 0.0003 2) 0.0047 3) 0.025		6.2×10^{-8}
(*R*,*S*,*S*,*S*)-**1**	25.0	1) 14.8 2) 25.6 3) 33.6		1.97
(*S*,*R*,*R*,*R*)-**1**	25.0	1) 0.028 2) 0.21 3) 0.72		5.0×10^{-5}
		1) 15.8 [a] 2) 29.3 3) 41.6	1) 16 2) 30 3) 42	
(*S*,*S*,*R*,*R*)-**1**	25.0	1) 0.64 2) 2.3 3) 4.9		0.01
(*S*,*R*,*S*,*R*)-**1**	12.5	1) 0.32 2) 1.2 3) 2.4		0.005

[a] Calculated distribution of porphyrin stereoisomers based on statistical combination of stereoisomeric pyrroles (in %). [b] Yield of porphyrin diastereomers from integration of ^{1}H NMR signals (in %, ±5 %).

Discussion

In the earlier work on achiral biconcave porphyrins,[11] the required pyrroles were built-up by Diels–Alder reactions of highly symmetric anthracene derivatives. The use of C_{2h}- and less symmetric anthracenes would lead to chiral and often asymmetric pyrroles, whose tetramerization product, in general, led to a complex mixture of stereoisomeric porphyrins. The racemic C_2-symmetric pyrrole *rac*-**2** was likewise expected to give rise to a mixture of the four porphyrin diastereoisomers by statistical incorporation of each enantiomer.[26] The preparation of the C_2-symmetric pyrrole **2** in a highly enantiopure form was therefore firstly required. An asymmetric Diels–Alder reaction[19] promised to be a convenient synthetic entry to the pyrrole **2**, from which the biconcave porphyrin **1** could be assembled efficiently.

Furuta et al.[19] reported the [4+2] cycloaddition of anthracene and (−)-dimenthyl fumarate with a diastereomeric selectivity of 99 %. In this work the absolute configuration of the cycloadduct was assigned by its conversion to the corresponding diol as reference compound, for which an absolute configuration had been assigned[27] (tentatively) based on the older stereochemical correlations.[20] The Et_2AlCl-catalyzed Diels–Alder reaction of di-(+)menthyl fumarate and 2,6-*bis*-(*tert*-butyldimethylsiloxy)anthracene at 0 °C was reported by Petti et al. to yield two of the four possible diastereomers, one *anti* adduct and one *syn* adduct.[21a] The *syn*/*anti* assignment was achieved by NOE-correlated NMR spectroscopy; the diastereomeric excess of the *anti* adduct over the *syn* adduct was found to be only about 40 %, but with an apparent high facial selectivity at the dienophile.[21] The absolute configuration of the Diels–Alder cycloadducts and of the subsequent products was determined by the comparison of the sign of the optical rotation ($[\alpha]_D^{20}$) with those of related compounds,[21] as similarly and consistently done in other studies on 9,10-ethano-9,10-dihydroanthracenes.[19, 22, 27] The lack of the absolute reliability of the CD spectral analysis for the assignment of the absolute configuration of chiral 9,10-ethano-9,10-dihydroanthracenes and a specific discrepancy between the deductions of the absolute stereochemistries of some 9,10-ethano-9,10-dihydroanthracenes by CD analysis and by unambiguous X-ray crystallographic methods was pointed out by Tanaka et al., who determined the structure of (−)-1,5-diamino-9,10-ethano-9,10-dihydroanthracene by the Bijvoet method.[28] To finally put the stereochemical assignment of our products of Diels–Alder reactions (at the 9,10-positions) of a 2,6-disubstituted anthracene derivative on solid ground, therefore, we also sought unambiguous information from crystal structure analyses. The X-ray crystal structures reported here provide solid and internally consistent information on the absolute configuration of the crucial C_2-symmetric (9,10)-cycloadducts **5** and **6** of 2,6-di-*tert*-butylanthracene, based only on the known stereochemistry of (−)-menthol.[23] Our X-ray crystal structure analyses appear to provide experimental confirmation for the first time of the earlier stereochemical assignments from work[19, 21, 22, 27] based on correlations of the signs of optical rotations and of CD spectra with theoretical models.[20]

For the five-step conversion of the cycloadduct **4** to the chiral pyrrole **2** (see Schemes 3 and 4) care was taken to avoid conditions that would allow noticeable occurrence of retro-Diels–Alder reactions. The enantiomeric purity of the dinitrile **3**, the direct precursor for the pyrrole **2**, was analyzed with the help of the D_4-symmetric Co^{II} complex **9** of the porphyrin **1** as a chiral shift reagent. The analysis was based on a comparison of the main signal of the minor enantiomer (*R*)-**3**[24] with the signals of the ^{13}C satellites of the major isomer (*S*)-**3** and indicated the dinitrile **3** to consist of 99.5 ± 0.1 % of (*S*)-**3** (i.e. to have 99.0 % *ee*, see Figure 4). As stereochemical scrambling is highly unlikely under the conditions used for the reduction of **3** (with diisobutylaluminum hydride, at −20 °C) to the pyrrole **2**, the enantiomeric purity of the dinitrile **3** was set equal to that of the chiral pyrrole **2**.

The pyrrole **2** (i.e. (*S*)-**2**[24] with 99.0 % *ee*) was subjected to an acid-catalyzed tetramerizing condensation with formaldehyde, followed by oxidation with DDQ, to give the symmetric, chiral porphyrin **1** in about 70 % yield as the only NMR-detectable stereoisomer. As previously found in the preparation of an achiral biconcave porphyrin,[11] it can be inferred that the tetrameroidization reaction produces the porphyrin precursor (porphyrinogen) gratifyingly selectively.

In **1** eight stereochemical centers of identical absolute configuration are assembled. Quantitative information on the stereochemical integrity of **1** could only be obtained indirectly. Under conditions of (practically) statistical incorporation of both enantiomeric pyrrolic building blocks (i.e. of

either (*S*)-**2** (major) or (*R*)-**2** (minor isomer present in **2**)) the stereochemical purity of the porphyrin **1** could be calculated by applying the Horeau principle.[15] Accordingly, from an nth-fold stereo-nondiscriminating oligomerization of a compound with an enantiomeric ratio q ($q = S/R$) the resulting enantiomeric ratio of the oligomer can be calculated as q^n:1. In the case of the assembly of porphyrins from pyrroles (a tetramerization, i.e. $n = 4$) that conforms to the boundary conditions relevant to Horeau's principle,[15] the homochiral tetramer is highly enantiomerically enriched compared to the monomer. Based on an enantiopurity of 99% *ee* of the pyrrole **2**, the enantiomeric ratio of (homo)chiral porphyrin **1** can be calculated to be 1.57×10^9:1 (ratio of (*S*,*S*,*S*,*S*)-**1** versus (*R*,*R*,*R*,*R*)-**1**).[24]

The basic requirement for the "nth-order Horeau amplification"[15] in the assembly of chiral *n*-mers is the absence of stereochemical discrimination in the oligomerization steps. The stereochemically statistical nature of the tetramerization steps towards the porphyrin **1** was therefore examined. For this purpose, the porphyrins resulting from enantiomerically nonuniform mixtures of pyrroles were stereochemically analyzed. By subjecting mixtures of the pyrroles (*S*)-**2** and (*R*)-**2** of known enantiomeric purity (prepared from the racemic pyrrole *rac*-**2** and **2**) to the standard conditions of the tetramerization reaction, the resulting mixtures of porphyrin isomers were investigated by NMR spectroscopy (Table 1). Within experimental errors the measured isomer distributions (Table 1, column 4) were undistinguishable from those calculated (Table 1, column 3) in the case of stereochemical nondiscrimination in the oligomerization steps. Based on these investigations, the tetramerizing condensation of the pyrrole **2** (=(*S*)-**2**, 99.0% *ee*) can be safely regarded as occurring without noticeable stereochemical discrimination in the oligomerization steps and to produce **1** with about 98% of (*S*,*S*,*S*,*S*)-**1** and less than 10^{-7}% of the enantiomer (*R*,*R*,*R*,*R*)-**1** (Table 1, column 5). The enantiomeric purity of **1** was thus calculated to amount to the extraordinary value of about 10^9:1!

There have been several reports lately on high enantiomeric enrichments during repetitive synthetic transformations that exploit Horeau's principle,[15] such as in the course of the polydihydroxylation (according to Sharpless) of squalene[29] and in the assembly of a polycyclopropane antibiotic from chiral cyclopropane building blocks.[30] Clearly, high enantiomeric purity is of a particularly decisive advantage for compounds of possible use as chiral shift reagents[17, 31] and as catalysts.[6] Nature's polymeric catalysts are the best example for the latter group.

In the chiral porphyrin **1** the concave framework provides an effectively D_4-symmetric structure (although the instantaneous position of the N-bound hydrogen atoms breaks the symmetry). The dissymmetry results from substituents bound to all of the β-positions of the four pyrrolic units. Earlier, two other effectively D_4-symmetric porphyrins were prepared, in which four chiral substituents were bound to the four *meso* positions of the porphyrin ligand.[7a,b] These chiral porphyrins served as the ligands of chiral metal complexes that were tested as catalysts for enantioselective epoxidation and cyclopropanation reactions.[7a,b] The highly enantiopure porphyrin **1** and its transition metal complexes have turned out, so far, to be very useful chiral shift reagents for a broad range of chiral organic compounds[17] and seemingly of advantage compared to most established chiral shift reagents.[31]

Conclusion

We have introduced an efficient route to the chiral biconcave porphyrin **1** with the remarkably high enantiomeric purity of about 10^9:1 and with an unambiguously assigned absolute configuration. In the metal-free porphyrin **1** an unusual and effectively highly symmetric chiral structure (D_4-symmetry) has become available. In **1**, the eight stereogenic centers are bound through β-substituents at the periphery of the pyrrole rings. In contrast to the two other cases of effectively D_4-symmetric porphyrins, in which four *meso* substituents are stereogenic, the porphyrin **1** has the same basic substituent pattern as most naturally occurring porphyrins.

Incorporation of a Co^{II} ion into **1** gave the D_4-symmetric biconcave Co^{II} porphyrinate **9**, used as chiral shift reagent. This paramagnetic cobalt–porphyrin and other (diamagnetic) biconcave metalloporphyrins based on **1** are versatile chiral NMR shift reagents.[17] In addition, the readily available biconcave porphyrin **1** may provide a basis for the development of chiral metal complexes as enantioselective catalysts.

Experimental Section

General: All reactions were carried out in oven-dried glassware under a dry argon atmosphere. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM 300 or Varian Unity 500 spectrometer. Chemical shifts are reported in δ units (ppm) using the residual ^{1}H/^{13}C signals of the deuterated solvents as a reference; $\delta(CHCl_3) = 7.24$, $\delta(CDCl_3) = 77.0$, $\delta(C_6D_5H) = 7.15$, $\delta(C_6D_6) = 128$. Infrared spectra were performed on a Mattson FTIR 3000 instrument. UV/Vis spectra were recorded on a Hitachi U 3000. CD spectra were measured on a JASCO J-715; optical rotations on a Perkin-Elmer 141 Polarimeter. A Finnigan MAT-95 instrument was used for all MS experiments. X-ray: Siemens P4 diffractometer; refinement: SHELXS-86,[32] SHELXL-93.[33] Reagents: Anthracene, diphenyldiselenide, CF_3COOH, diisobutylaluminum hydride (DIBAH, 1M in hexane), all Fluka purum; $AlCl_3$, thionyl chloride, methanesulfonic acid, all Fluka puriss.; (−)-menthol, Fluka puriss. (−):(+) ≥ 99:1 (GC); *tert*-butyl alcohol, Fluka puriss. p.a.; potassium *tert*-butoxide, Fluka pract.; $CoBr_2$, anhydrous, Johnson, Matthey & Alfa. Solvents: Acetonitrile, hexane, benzene, toluene, CH_2Cl_2, isopropyl alcohol, DMF, acetone, THF, methanol, all Fluka puriss. p.a.; dichloromethane, diethyl ether, and petroleum ether for column chromatography, all Fluka purum; TLC: Polygram SIL G/UV254 from Macherey-Nagel. Column chromatography: Silica gel 60 (0.040-0.063 mm) from Merck.

Racemic dinitrile *rac*-3 ((±)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonitrile): To a boiling suspension of 2,6-di-*tert*-butylanthracene[18] (3.00 g, 10.3 mmol) in benzene (35 mL) freshly sublimed acetylenedicarbonitrile (1.55 g, 20.4 mmol)[13c] in benzene (10 mL) was added over a period of 4 h. The reaction mixture was heated under reflux overnight under an argon atmosphere. The organic solvent was distilled off and the residue was purified by column chromatography (silica gel, petroleum ether/CH_2Cl_2 1:1) and recrystallized from acetonitrile to give *rac*-**3** (3.38 g; 89% yield); optically inactive, other spectroscopic data identical with those of the enantiopure dinitrile **3**.

Racemic pyrrole *rac*-2: **((±)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-[3,4]-epipyrroloanthracene)**: Reduction of racemic dinitrile *rac*-**3** (1.50 g, 4.09 mmol) was performed with DIBAH (25 mL, 1M in hexane) as analogously described for the preparation of the enantiopure pyrrole **2**;

0947-6539/00/0607-1220 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 7

yield: 435 mg (30%) of *rac*-**2**; optically inactive, other spectroscopic data identical with those of the enantiopure pyrrole **2**.

Isomeric cycloadducts 4, **5 (di[(1*R*)-menthyl] (9*S*,10*S*,11*S*,12*S*)- and di[(1*R*)-menthyl] (9*R*,10*R*,11*S*,12*S*)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylate)**: To a solution of di-(−)menthyl fumarate (9.51 g, 24.2 mmol) in toluene (25 mL) $AlCl_3$ (6.45 g, 48.4 mmol) was added at −40 °C and the mixture was stirred for 20 min. A suspension of 2,6-di-*tert*-butylanthracene[18] (7.00 g, 24.1 mmol) in toluene (80 mL) was slowly added while the temperature was kept below −30 °C. After 3 h at −40 °C the reaction mixture was stirred overnight at 0 °C. The yellow suspension was poured into a 0.5 N HCl/ice mixture. The organic layer and two further toluene extractions of the aqueous layer were combined, washed with a saturated $NaHCO_3$ solution, and dried over Na_2SO_4. The organic solvent was distilled off and the pure product was purified by column chromatography on silica (petroleum ether/ diethyl ether 97:3, R_f(**4**) = 0.16, R_f(**5**) = 0.13). Recrystallization from methanol gave **4** (15.5 g; 94%) and *syn* isomer **5** (0.15 g; ca. 1%). The *anti* isomer **4** isolated in this way was > 99.9% isomerically pure according to HPLC (on RP-18, MeOH as eluent, detection at 215 nm). Colorless crystals of **4**: M.p. 96–98 °C; $[\alpha]_D^{20} = -53$ ($c = 0.42$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$, 23 °C): $\delta =$ 7.33 (d, $J = 1.7$ Hz, 2H), 7.10 (d, $J = 7.6$ Hz, 2H), 7.05 (dd, $J = 1.7$ Hz, $J =$ 7.6 Hz, 2H), 4.60 (s, 2H), 4.55 (td, $J = 10.6$ Hz, $J = 4.2$ Hz, 2H), 3.33 (s, 2H), 1.95–1.83 (m, 2H), 1.76–1.58 (m, 6H), 1.45–1.28 (m, 4H), 1.25 (s, 18H), 1.15–0.75 (m, 6H), 0.92 (d, $J = 7.2$ Hz, 6H), 0.82 (d, $J = 6.8$ Hz, 6H), 0.70 (d, $J = 7.2$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 172.00$, 149.14, 142.34, 137.36, 124.28, 122.62, 120.64, 74.81, 48.56, 47.03, 46.99, 40.76, 34.59, 34.26, 31.55, 31.32, 26.02, 23.16, 21.96, 20.99, 16.12; IR (KBr): $\tilde{\nu} = 1726$ cm^{-1}; MS (EI): *m*/*z* (%): 682.5 (2) [M^+], 290.2 (100), 275.2 (18). Colorless crystals of **5**: M.p. 178 °C; $[\alpha]_D^{20} = 4$ ($c = 1.71$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.24$ (d, $J = 7.8$ Hz, 2H), 7.21 (d, $J = 1.9$ Hz, 2H), 7.10 (dd, $J = 1.9$ Hz, $J =$ 7.8 Hz, 2H), 4.60 (s, 2H), 4.53 (td, $J = 10.8$ Hz, $J = 4.4$ Hz, 2H), 3.30 (s, 2H), 1.95–1.85 (m, 2H), 1.76–1.55 (m, 6H), 1.45–1.25 (m, 4H), 1.24 (s, 18H), 1.15–0.75 (m, 6H), 0.90 (d, $J = 6.8$ Hz, 6H), 0.80 (d, $J = 6.8$ Hz, 6H), 0.72 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 171.83$, 148.92, 140.14, 139.81, 122.90, 122.80, 121.75, 74.84, 48.32, 47.15, 46.72, 40.52, 34.48, 34.18, 31.53, 31.28, 26.14, 23.13, 21.95, 20.94, 16.22; IR (KBr): $\tilde{\nu} = 1736$ cm^{-1}; MS (EI): *m*/*z* (%): 682.4 (2) [M^+], 290.2 (100), 275.2 (17).

Crystallographic data of **5**: $C_{46}H_{66}O_4$, $M_r = 683.03$, crystallized from MeOH, monoclinic, space group $P2_1$ (no. 4), $a = 1331.6(4)$, $b = 1102.4(4)$, $c = 1616.5(5)$ pm, $\beta = 114.06(2)°$, $V = 2.1668(12)$ nm^3 (least-squares method for θ range $2.3 < \theta < 21.0°$), $T = 223(2)$ K, with graphite-monochromated $Mo_{K\alpha}$ radiation, $\lambda = 71.073$ pm, $\rho_{calcd} = 1.047$ Mg m^{-3}, $F(000) = 748$, colorless crystal $0.75 \times 0.25 \times 0.1$ mm, $\mu(Mo_{K\alpha}) = 0.065$ mm^{-1}, no absorption correction, ω scan, limiting indices: $-1 < h < 13$, $-1 < k < 11$, $-16 < l < 15$, 3160 reflections collected, 2716 independent reflections ($R_{int} = 0.0250$), data/parameters = 2570/452, refinement: full-matrix least-squares on F^2, GOF(F_o^2) = 1.045, $R1 = 0.0705$ and w$R2 = 0.1210$ (all data), $R1 = 0.0470$ and w$R2 = 0.1068$ $I > 2\sigma(I)$, $w = 1/[\sigma^2(F_o^2) + (0.0612P)^2 + 0.0P]$ and $P = (F_o^2 + 2F_c^2)/3$, largest difference peak and hole 164/−141 e nm^{-3}. [34]

Di-(−)menthyl ester 6: **(di[(1*R*)-menthyl] (9*S*,10*S*)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate)**: *anti* Isomer **4** (15.0 g, 22.0 mmol) and diphenyldiselenide (10.7 g, 34.2 mmol) were dissolved in toluene (260 mL). Potassium *tert*-butoxide (7.39 g, 65.9 mmol) in THF was added dropwise at room temperature. The yellow suspension was diluted with isopropyl alcohol (530 mL) and concentrated HCl (110 mL). Stirring was continued for 12 h at room temperature, then ethyl acetate (700 mL) was added and the solution was neutralized with saturated sodium bicarbonate solution. The organic layer was treated with phosphate buffer (pH 7). The solvent was removed under vacuum and the resultant crude product was purified by column chromatography (silica, petroleum ether/ deithyl ether 95:5). Recrystallization from methanol gave **6** (13.7 g; 92%; colorless crystals). M.p. 187–188 °C; $[\alpha]_D^{20} = -91$ ($c = 0.65$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (d, $J = 1.9$ Hz, 2H), 7.25 (d, $J =$ 7.8 Hz, 2H), 6.99 (dd, $J = 1.9$ Hz, $J = 7.8$ Hz, 2H), 5.30 (s, 2H), 4.75 (td, $J = 11.2$ Hz, $J = 4.4$ Hz, 2H), 2.15–2.06 (m, 2H), 1.72–1.59 (m, 4H), 2.00–1.88 (m, 2H), 1.55-1.30 (m, 4H), 1.25 (s, 18H), 1.15–0.75 (m, 6H), 0.89 (d, $J = 6.8$ Hz, 6H), 0.88 (d, $J = 6.8$ Hz, 6H), 0.79 (d, $J = 6.8$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.38$, 148.25, 146.16, 144.13, 141.30, 123.11, 121.75, 120.94, 75.67, 52.65, 46.75, 40.83, 34.54, 34.26, 31.50, 31.41, 25.88, 23.25, 22.05, 20.88, 16.22; IR (KBr): $\tilde{\nu} = 1736$ cm^{-1}; MS (EI): *m*/*z* (%): 681.4 (2), 680.4 (4) [M^+], 360.2 (24), 235.1 (18), 234.1 (100).

Crystallographic data of **6**: $C_{46}H_{64}O_4$, $M_r = 681.01$, crystallized from MeOH, orthorhombic, space group $P2_12_12_1$ (no. 19), $a = 1171.3(3)$, $b = 1722.0(3)$, $c = 2179.9(8)$ pm, $V = 4.397(2)$ nm^3 (least-squares method for θ range $2.10 < \theta < 20.99°$), $T = 213(2)$ K, with graphite-monochromated $Mo_{K\alpha}$ radiation, $\lambda = 71.073$ pm, $\rho_{calcd} = 1.029$ Mg m^{-3}, $F(000) = 1488$, colorless prism $0.55 \times 0.22 \times 0.14$ mm, $\mu(Mo_{K\alpha}) = 0.064$ mm^{-1}, no absorption correction, ω scan, limiting indices: $-1 < h < 8$, $-1 < k < 17$, $-1 < l < 21$, 3152 reflections collected, 2961 independent reflections ($R_{int} = 0.0183$), data/parameters = 2746/452, refinement: full-matrix least-squares on F^2, GOF(F_0^2) = 1.064, $R1 = 0.0886$ and w$R2 = 0.1278$ (all data), $R1 = 0.0517$ and w$R2 = 0.1056$ $I > 2\sigma(I)$, $w = 1/[\sigma^2(F_o^2) + (0.0467P)^2 + 1.0002P]$ and $P = (F_o^2 + 2F_c^2)/3$, largest difference peak and hole 169/−148 e nm^{-3}.[34]

Di-(−)menthyl ester *iso*-6: **(di[(1*R*)-menthyl] (9*R*,10*R*)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-etheno-anthracene-11,12-dicarboxylate)**: *syn* Isomer **5** (29.3 mg, 0.043 mmol), diphenyldiselenide (23.1 mg, 0.074 mmol), potassium *tert*-butoxide (15 mg, 0.13 mmol). For general procedure see synthesis of **6**. Recrystallization from methanol gave *iso*-**6** (23.2 mg; 79%). M.p. 172 °C; $[\alpha]_D^{20} = -36$ ($c = 0.50$ in $CHCl_3$); ^{1}H NMR (300 MHz, $CDCl_3$): $\delta = 7.34$ (d, $J = 1.8$ Hz, 2H), 7.21 (d, $J = 7.6$ Hz, 2H), 6.98 (dd, $J = 1.8$ Hz, $J = 7.6$ Hz, 2H), 5.30 (s, 2H), 4.76 (td, $J = 10.9$ Hz, $J = 4.5$ Hz, 2H), 2.14–2.03 (m, 2H), 1.72–1.62 (m, 4H), 2.01–1.88 (m, 2H), 1.56–1.35 (m, 4H), 1.25 (s, 18H), 1.15–0.80 (m, 6H), 0.90 (d, $J = 6.8$ Hz, 6H), 0.88, 0.79 (d, $J =$ 5.6 Hz, 6H, d, $J = 6.8$ Hz, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 165.17$, 148.28, 146.70, 146.16, 141.31, 122.96, 121.74, 121.08, 75.59, 52.74, 46.90, 40.80, 34.57, 34.30, 31.53, 31.46, 26.14, 23.50, 22.03, 20.79, 16.46; IR (KBr): $\tilde{\nu} = 1734$ cm^{-1}; MS (FAB): *m*/*z* (%): 681.9 (25, [$M^+ + 1$]), 406.3 (28), 405.3 (94), 388.2 (37), 387.2 (100), 361.4 (23), 360.4 (88), 359.4 (89), 358.4 (25), 304.3 (33), 303.3 (23).

Dimethyl ester 7: **(Dimethyl (9*S*,10*S*)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate)**: A solution of **6** (12.6 g, 18.5 mmol) and methanesulfonic acid (27 mL) in methanol (500 mL) was boiled under reflux for 96 h. The solvent was evaporated and the product was extracted with ethyl acetate. The organic layer was washed with a buffer solution (pH 7). After evaporation in vacuo the residue was chromatographed (silica, petroleum ether/diethyl ether 90:10) and recrystallized from methanol to give the dimethyl ester **7** (7.5 g; 94%; colorless crystals). M.p. 168–169 °C; $[\alpha]_D^{20} = -72$ ($c = 1.1$ in $CHCl_3$); ^{1}H NMR (200 MHz, $CDCl_3$): $\delta = 7.38$ (d, $J = 1.8$ Hz, 2H), 7.28 (d, $J = 7.7$ Hz, 2H), 7.00 (dd, $J =$ 1.8 Hz, $J = 7.7$ Hz, 2H), 5.39 (s, 2H), 3.77 (s, 6H), 1.25 (s, 18H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 166.12$, 148.46, 147.32, 143.83, 140.96, 123.12, 121.91, 121.06, 52.43, 52.29, 34.58, 31.49; IR (KBr): $\tilde{\nu} = 1713$ cm^{-1}; MS (EI): *m*/*z* (%): 433.2 (27), 432.2 (100) [M^+], 417.2 (23), 404.2 (18), 374.2 (20), 373.2 (88), 372.2 (89), 357.2 (10).

Crystallographic data of **7**: $C_{28}H_{32}O_4$, $M_r = 432.56$, isothermic crystallization $CHCl_3$/hexane, monoclinic, space group $C2$ (no. 5), $a = 1920.2(5)$, $b =$ 947.0(3), $c = 1358.3(2)$ pm, $\beta = 95.47(2)°$, $V = 2.4587(11)$ nm^3 (least-squares method for θ range $3.01 < \theta < 23.01°$), $T = 213(2)$ K, with graphite-monochromated $Mo_{K\alpha}$ radiation, $\lambda = 71.073$ pm, $\rho_{calcd} = 1.168$ Mg m^{-3}, $F(000) =$ 928, colorless prism $0.6 \times 0.5 \times 0.3$ mm, $\mu(Mo_{K\alpha}) = 0.077$ mm^{-1}, no absorption correction, ω-scan, limiting indices: $-20 < h < 21$, $-1 < k < 10$, $-14 < l < 14$, 4138 reflections collected, 2492 independent reflections ($R_{int} =$ 0.0179), data/parameters = 2491/290, refinement: full-matrix least-squares on F^2, GOF(F_o^2) = 1.057, $R1 = 0.0409$ and w$R2 = 0.0947$ (all data), $R1 =$ 0.0357 and w$R2 = 0.0903$ $I > 2\sigma(I)$, $w = 1/[\sigma^2(F_o^2) + (0.0513P)^2 + 0.9359P]$ and $P = (F_o^2 + 2F_c^2)/3$, largest difference peak and hole 149/−132 e nm^{-3}.[34]

Dimethyl ester *ent*-7: **(Dimethyl (9*R*,10*R*)-2,6-di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylate)**: (9*R*,10*R*)-Cycloadduct dimenthylester *iso*-**6** (19 mg, 0.028 mmol) and methanesulfonic acid (0.44 g, 4.6 mmol) in methanol (5 mL) were used (see synthesis of **7**). Recrystallization from methanol gave *ent*-**7** (7.9 mg, 65%). M.p. 169–170 °C; $[\alpha]_D^{20} =$ +73 ($c = 0.48$ in $CHCl_3$); the other spectroscopic data were identical to **7**.

Diamide 8: **((9*S*,10*S*)-2,6-Di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarboxylic acid diamide)**: A stream of NH_3 was passed through a suspension of **7** (7.3 g, 16.9 mmol) and NaCN (35 mg) in methanol (50 mL) at room temperature. The mixture was heated for 3 d in a high-pressure vessel at 40 °C. After a second saturation of methanol with NH_3 the reaction mixture was stirred for further two days at 40 °C. The solvent was removed by distillation and the organic material was absorbed on silica gel and chromatographed (CH_2Cl_2/methanol 98:2) to give 5.22 g (77%) of the diamide **8** as colorless crystals. M.p. 253 °C (decomp);

$[\alpha]_D^{20} = -79$ ($c = 0.80$ in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.41$ (d, $J = 1.7$ Hz, 2H), 7.29 (d, $J = 7.6$ Hz, 2H), 7.00 (dd, $J = 1.7$ Hz, $J = 7.6$ Hz, 2H), 6.79 (s, b, 2H), 5.96 (s, b, 2H), 5.53 (s, 2H), 1.24 (s, 18H); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 168.48$, 148.66, 147.34, 143.93, 140.96, 123.01, 122.02, 120.96, 53.47, 34.60, 31.49; IR (KBr): $\tilde{\nu} = 1672$ cm^{-1}; MS (FAB): *m*/*z* (%): 404.3 (29), 403.3 (100) $[M^+ + 1]$, 387.2 (24), 386.2 (64), 359.4 (30), 358.4 (26), 307.2 (47).

Dinitrile 3: **((9*S*,10*S*)-2,6-Di-*tert*-butyl-9,10-dihydro-9,10-ethenoanthracene-11,12-dicarbonitrile)**: To a solution of diamide **8** (3.73 g, 9.27 mmol) in DMF (30 mL) at $-15\,^\circ$C thionyl chloride (2.43 g) in DMF (30 mL) was added dropwise. The solution was stirred for 48 h under an argon atmosphere at room temperature. The reaction mixture was poured onto crushed ice and the precipitate was filtered and washed repeatedly with water. The crude product was recrystallized from acetonitrile. The mother liquor was purified by column chromatography (silica gel, petroleum ether/CH_2Cl_2 1:1) to give the dinitrile **3** (3.03 g; 89%; colorless crystals); m.p. 252–253 °C; $[\alpha]_D^{20} = -69$ ($c = 0.70$ in $CHCl_3$); ^1H NMR (300 MHz, C_6D_6): $\delta = 7.11$ (d, $J = 1.9$ Hz, 2H), 6.85 (d, $J = 7.8$ Hz, 2H), 6.81 (dd, $J =$ 1.9 Hz, $J = 7.8$ Hz, 2H), 4.77 (s, 2H), 1.09 (s, 18H); ^{13}C NMR (50 MHz, $CDCl_3$): $\delta = 150.02$, 141.17, 138.21, 137.33, 123.83, 123.09, 121.70, 113.95 (*C*N), 54.08, 34.76, 31.37; IR (KBr): $\tilde{\nu} = 2218$ cm^{-1}; MS (FAB): *m*/*z* (%): 367.1 (60), 366.2 (100) $[M^+]$, 351.1 (32), 290.1 (9).

Pyrrole 2: **((9*S*,10*S*)-2,6-Di-*tert*-butyl-9,10-dihydro-9,10-[3,4]-epipyrroloanthracene)**: A 1M solution of DIBAH in hexane (26 mL) was placed in three-necked flask with an efficient mechanical stirrer under argon at $-20\,^\circ$C. The dinitrile **3** (1.65 g, 4.50 mmol) in CH_2Cl_2 (50 mL) was added slowly. The temperature had to be kept below $-15\,^\circ$C. Stirring of the yellow solution was continued for additional 2 h at $-20\,^\circ$C. The reaction mixture was diluted with CH_2Cl_2 (50 mL) and a 0.5M aqueous solution of citric acid (50 mL) was added slowly at 0 °C. The organic layer was washed with a phosphate buffer (pH 7) and dried over $MgSO_4$. Evaporation of the solvent and column chromatography (silica gel, petroleum ether/CH_2Cl_2 2.5:1) afforded the pure pyrrole (620 mg, 39%). Recrystallization from methanol gave colorless crystals of the pyrrole **2**; m.p. 273–274 °C; $[\alpha]_D^{20} = -41$ ($c =$ 0.67 in $CHCl_3$); ^1H NMR (300 MHz, $CDCl_3$): $\delta = 7.33$ (d, $J = 1.9$ Hz, 2H, $H^{1,5}$), 7.21 (d, $J = 7.8$ Hz, 2H, $H^{4,8}$), 7.17 (s, b, 1H, NH), 6.95 (dd, $J = 1.9$ Hz, $J = 7.8$ Hz, 2H, $H^{3,7}$), 6.53 (d, $J = 2.4$ Hz, 2H, α-pyrrole-H), 5.23 (s, 2H, $H^{9,10}$), 1.25 (s, 18H, CH_3); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 147.54$, 147.07, 144.36 (C^{aromat}), 131.56 ($C^{11,12}$), 122.56, 121.26, 120.64 (*C*H^{aromat}), 109.32 (*C*H^{pyrrole}), 47.17 ($C^{9,10}$), 34.48 ($C(CH_3)_3$), 31.55 (C(*C*H$_3$)$_3$); IR (KBr): $\tilde{\nu} =$ 3393 cm^{-1}; MS (FAB): *m*/*z* (%): 356.2 (52), 355.2 (100) $[M^+]$, 340.1 (31), 300.1 (18), 298.0 (31).

Porphyrin 1 (*S,S,S,S*-1): A Schlenk tube was charged with pyrrole **2** (335 mg, 0.94 mmol), aqueous formaldehyde (0.40 mL, 30%), and acetic acid (0.28 mL). The reaction mixture was dissolved in dichloromethane/methanol (5 mL, 2:3). After degassing, the solution was stirred for seven days at room temperature under an argon atmosphere. The solvents were removed by distillation and DDQ (150 mg, 0.66 mmol) in benzene (8 mL) was added to the porphyrinogen. After an hour at room temperature the dark red mixture was diluted with CH_2Cl_2 (50 mL). The organic solvent was washed with water and then dried over $MgSO_4$. Evaporation of the solvent mixture and column chromatography (silica gel, hexane/CH_2Cl_2 3:1) gave the crude porphyrin. Recrystallization from acetone/water afforded the porphyrin **1** (240 mg; 70%; red-brown needles). ^1H NMR (300 MHz, $CDCl_3$): $\delta = 10.66$ (s, 4H, H^{meso}), 7.97 (d, $J = 1.5$ Hz, 8H, $H^{1,5}$), 7.87 (d, $J =$ 8.0 Hz, 8H, $H^{4,8}$), 7.17 (s, 8H, $H^{9,10}$), 7.11 (dd, $J = 1.5$ Hz, $J = 8.0$ Hz, 8H, $H^{3,7}$), 1.34 (s, 72H, CH_3), -4.80 (s, 2H, N*H*); ^{13}C NMR (75 MHz, $CDCl_3$): $\delta = 154.01$ ($C^{pyrrole}$), 148.01, 147.94, 145.14 ($C^{aromat.}$), 138.90 (br., $C^{pyrrole}$), 123.55, 121.60, 121.40 (*C*H^{aromat}), 98.71 (C^{meso}), 50.19 ($C^{9,10}$), 34.65 ($C(CH_3)_3$), 31.57 (C(*C*H$_3$)$_3$); IR (KBr): $\tilde{\nu} = 3318$, 2959, 2905, 2868, 1479, 1462, 1412, 1364, 1262, 1233, 1208, 1074 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} (lgε) = 397 (5.36), 500.5 (4.28), 532 (3.84), 570 (3.84), 639 nm (3.29); CD (CH_2Cl_2): λ_{max} (Mol. Ellip.) = 571 nm (2200), 532 (5400), 506 (6100), 396 (44000), 302 (14000), 285 (-33000), 250 (131000); MS (FAB): *m*/*z* (%): 1464.2 (100), 1463.2 (65) $[M^+ + 1]$.

Porphyrin (*R,S,S,S*)-1: A mixture of enantiopure pyrrole **2** (23.0 mg, *ee* = 99.0%) and racemic pyrrole *rac*-**2** (7.4 mg) was used for tetramerization reaction analogous to that described for preparation of porphyrin **1** (i.e. (*S*)-**2**: 74.8% *ee*). A stereoisomeric mixture of porphyrins was obtained (22.3 mg) Analysis of this mixture by ^1H NMR spectroscopy revealed that it contained about 58% of (*S,S,S,S*)-**1** and 42% of the other stereoisomers, mainly (*R,S,S,S*)-**1**. This mixture (15 mg) was rechromatographed on silica (petroleum ether/CH_2Cl_2 9:1) to give chromatographically pure (*R,S,S,S*)-**1** (ca. 2 mg) from the second, more polar band. ^1H NMR (200 MHz, C_6D_6): $\delta = 10.82$, 10.79 (s, 4H); 7.98, 7.97, 7.90, 7.89 (8H); 7.72, 7.69, 7.62, 7.58 (8H); 7.17 (16H); 7.02, 7.01, 6.99, 6.98 (8H); 1.20, 1.19, 1.18, 1.17 (72H); -4.20 (2H).

Two further experiments analoguous to the ones described for the preparation of **1** and (*R,S,S,S*)-**1** using mixtures of isomeric pyrroles were carried out to confirm the statistical tetramerization: Mixture 1: Pyrrole **2** (40.7 mg; *S* enantiomer, 99% *ee*) and *rac*-**2** (3.3 mg; i.e. (*S*)-**2**: 91.6% *ee*); mixture 2: **2** (25.4 mg) and *rac*-**2** (4.7 mg; i.e. (*S*)-**2**: 83.4% *ee*). The obtained raw mixtures of stereoisomeric porphyrins were purified from polar compounds by column chromatography (silica, petroleum ether/CH_2Cl_2 3:1). The solvent was distilled off and the porphyrin mixtures were analyzed by ^1H NMR spectroscopy, as described. The relative amounts of the two main components ((*S,S,S,S*)-**1** and (*R,S,S,S*)-**1**) were determined by integration of their proton signals (Table 1); total yield of porphyrins: 29.2 mg (64%) for mixture 1, 22.2 mg (72%) from mixture 2.

Co^{II} porphyrinate 9: A mixture of porphyrin **1** (20.0 mg, 13.7 μmol), anhydrous sodium acetate (15 mg), and $CoBr_2$ (90 mg, anhydrous) was dissolved in dry THF (5 mL) under argon. After stirring the solution for 1 h at room temperature, it was diluted with CH_2Cl_2 (20 mL). The organic solvent was washed twice with water. Further purification of the product was performed by column chromatography on basic aluminum oxide (CH_2Cl_2/petroleum ether 1:1) and recrystallization from acetone/water to give red needles of the Co^{II} porphyrinate **9** (20.5 mg; 99%). ^1H NMR (300 MHz, C_6D_6): $\delta = 30.81$ (s, br., 4H), 14.43 (s, br., 8H), 10.74 (s, br., 8H), 10.35 (d, $J = 5.1$ Hz, 8H), 7.83 (d, $J = 5.1$ Hz, 8H), 1.46 (s, 72H); IR (KBr): $\tilde{\nu} = 2959$, 2905, 2868, 1479, 1460, 1259, 1090 cm^{-1}; UV/Vis (CH_2Cl_2): λ_{max} (lg ε) = 402.5 (5.49), 514.5 (4.19), 546 nm (4.21); MS (FAB): *m*/*z* (%): 1523.2 (33), 1522.2 (69), 1521.2 (100) $[M^+ + 1]$, 1520.2 (78).

Acknowledgements

The authors thank Prof. Robert Konrat and Dr. Walter Mühlecker for recording NMR spectra and Prof. Karl-Hans Ongania for mass spectra. We are grateful to Dr. Ludwig Call for helpful discussions on nomenclature, to Helen Gibson for linguistic improvements, and to Prof. Hugo Scheer (Botanical Institute, Ludwig Maximilian's University, Munich) for help with CD spectral measurements. This work was financially supported by the Austrian National Bank (project No. 4194).

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Received: September 23, 1999 [F2051]