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[2.2]-*para*-Cyclophane-4-carbaldehyde as building-block for chiral ligands
Part II: Epoxidation of alkenes catalyzed by the Mn(III)-complex of an atropoisomerically pure $(\alpha,\beta,\alpha,\beta)$-tetraarylporphyrin

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Abstract

The synthesis of the Mn(III)-complex of the new enantiopure, atropoisomerically pure chiral porphyrin $(\alpha,\beta,\alpha,\beta)$-**1** is described. The compound was used as the catalyst in the epoxidation of unfunctionalized olefins using aqueous NaOCl, 30%-H_2O_2 or PhIO as oxygen donors. Up to 780 overall turnovers were obtained in the presence of NaOCl and PhIO, whereas with 30%-H_2O_2 only catalase activity was observed. Contrary to expectations based on previous results [S. Banfi, A. Manfredi, F. Montanari, G. Pozzi, S. Quici, J. Mol. Catal., 113 (1996) 77], only racemic epoxides were obtained.

Keywords: Chiral catalyst; Oxidation catalyst; Manganese; Porphyrin; Epoxidation

1. Introduction

Haems are used in nature in combination with proteins to perform a wide variety of tasks, including oxygen binding and transport, energy transfer, catalysis and electron transfer [1–3]. The development of models for these enzymes and the design of new catalysts to achieve selective oxygenation are important goals in synthetic chemistry [4–6]. Particularly challenging is enantioselective epoxidation of unfunctionalized alkenes by the use of chiral catalysts [7–9]. Since high turnover numbers can be achieved by using Mn-porphyrins as epoxidation catalysts [10–13], manganese complexes of some chiral porphyrins have been synthesized and tested for this purpose [14]. The stability and catalytic activity of Mn-tetraarylporphyrins is greatly improved by the introduction of chlorine atoms at the *ortho*-positions of the *meso*-aryl groups [10–13]. This holds also for chiral complexes, as independently shown by us [15] and Vilain et al. [16,17]. They reported the synthesis of robust

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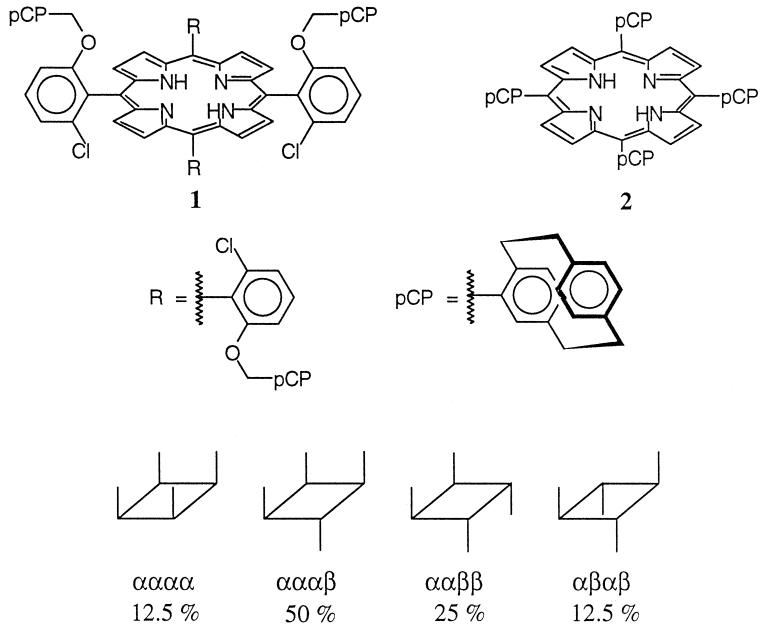


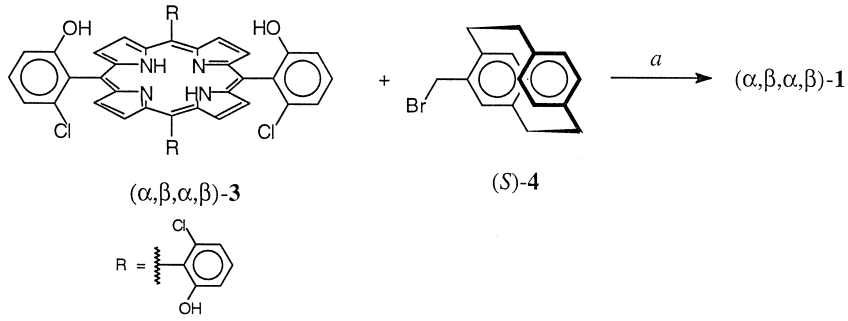
Fig. 1. Tetra-(2′-chloro-5′-(*para*-(*S*)-cyclophanemethoxyphenyl))porphyrin **1**, paracyclophane porphyrin **2** and the statistical distribution of the possible atropoisomers formed.

glycoconjugated porphyrins, in which one of the chlorine atoms is replaced by an ether linked sugar. The manganese complexes of these porphyrins catalyze the epoxidation of alkenes in the presence of H_2O_2 with enantioselectivity up to 23%. The presence of chlorine atoms is crucial, since their absence resulted in rapid decomposition of similar manganese porphyrins when H_2O_2 was used as the oxidant [16,17]. Compounds derived from [2.2]-cyclophane are thought to be very stable to the action of light, oxidation, acids, bases and relatively high temperatures [18]. We developed an efficient method for the resolution of racemic [2.2]-*para*-cyclophane-4-carbaldehyde and with the pure enantiomers in hand, chiral porphyrin **2** was synthesized (Fig. 1) [19]. Despite the inability in the separation of the atropoisomers formed, turnovers up to 700 and enantioselectivities in the range of 22–31% were obtained when Mn(III) complex of porphyrin **2** (Mn-**2**) was used in the epoxidation of unfunctionalized alkenes with aqueous NaOCl [19]. These encouraging results suggested that enantiopure [2.2]-*para*-cyclophane-4-carbaldehyde could be a good building-block for the synthesis of new chiral porphyrins. The separation of the possible atropoisomers and the catalytic activity in the presence of oxygen donors other than NaOCl, are readdressed in the present work by the synthesis of porphyrin **1** (Fig. 1). It can be envisaged that the bulky groups in the *meso*-position of this ligand might enhance separation as well as efficiency and enantioselectivity in epoxidation. Our attention was focused on the $\alpha,\beta,\alpha,\beta$ atropoisomer of porphyrin **1**, since it features two topologically identical faces characterized by the presence of two chiral cyclophanyl moieties.

2. Results and discussion

2.1. Synthesis of catalyst ($\alpha,\beta,\alpha,\beta$)-Mn-*1*

Porphyrin ($\alpha,\beta,\alpha,\beta$)-**1** was assembled from atropoisomerically pure $5\alpha,10\beta,15\alpha,20\beta$-

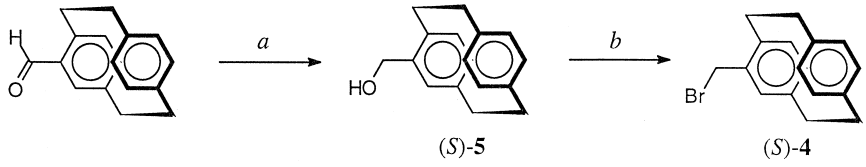


Scheme 1. Synthesis of atropoisomerically pure porphyrin $(\alpha,\beta,\alpha,\beta)$-**1**. a. K_2CO_3, DMF, RT, (100%).

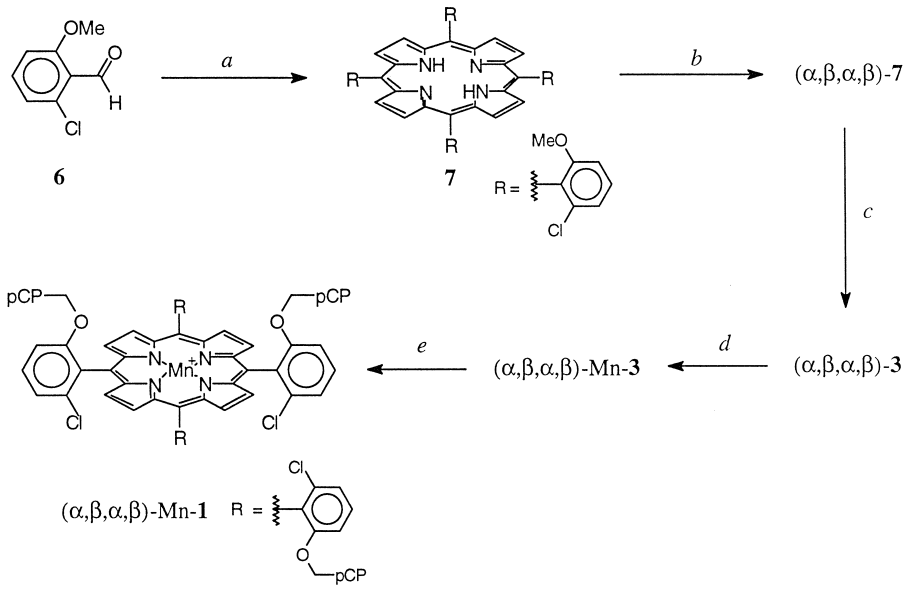
tetrakis(2-chloro-6-hydroxyphenyl)porphyrin, $(\alpha,\beta,\alpha,\beta)$-**3**, and enantiopure (*S*)-cyclophane methyl bromide (*S*)-**4** (Scheme 1).

The synthesis of bromide (*S*)-**4** started from homochiral (*S*)-[2.2]-*para*-cyclophane-4-carbaldehyde [19]. Reduction using LAH yielded alcohol (*S*)-**5** (96% yield), which was converted into the desired bromide (*S*)-**4** in 81% yield by reaction with PBr_3 (Scheme 2).

Atropoisomerically pure $(\alpha,\beta,\alpha,\beta)$-**3** was synthesized following the pathway reported in Scheme 3. Pyrrole was condensed with 2-chloro-6-methoxybenzaldehyde **6** (see experimental part) according to modified Lindsey's procedure [20]. 5,10,15,20-Tetrakis(2-chloro-6-methoxyphenyl)porphyrin **7** was obtained in 43% yield as a mixture of four atropoisomers. Condensation of pyrrole with aromatic aldehydes bearing two different substituents in 2,6 positions is expected to produce a statistical mixture of four atropoisomeric porphyrins in the ratio shown in Fig. 1. Separation was enforced by column chromatography on silica-gel and the relative amount of the atropoisomers isolated, in the order of elution, was 6.6%, 16.5%, 66.8% and 10.1%. Depending on the batch of the porphyrin synthesis the first eluted compound might be absent. Since steric hindrance and/or electronic interaction might diminish the amount of the $\alpha,\alpha,\alpha,\alpha$ atropoisomer (see for instance the synthesis of the aforementioned glycoconjugated porphyrins [16,17]), the first eluted compound was identified as $(\alpha,\alpha,\alpha,\alpha)$-**7**. The other atropoisomers were identified by their ^{1}H-NMR spectra as well as the relative amount. According to symmetry considerations, the pattern of the β-pyrrolic protons in the different atropoisomers was expected to be: $\alpha,\alpha,\alpha,\alpha$: singlet; $\alpha,\beta,\alpha,\beta$: singlet; $\alpha,\alpha,\alpha,\beta$: four doublets and $\alpha,\alpha,\beta,\beta$: double singlet. The third eluted compound showed a double singlet for the β-pyrrolic protons in the ^{1}H-NMR. However, the methoxy protons gave three singlets with a ratio 2:1:1 as expected for the $\alpha,\alpha,\alpha,\beta$, atropoisomer, whereas for the $\alpha,\alpha,\beta,\beta$ atropoisomer a singlet was expected. Moreover, the amount formed made up for the bulk (66.8%) of the total yield. On basis of these considerations the compound was identified as the $\alpha,\alpha,\alpha,\beta$ atropoisomer (50% expected yield, see Fig. 1). Both the second and fourth eluted compounds showed singlets for the β-pyrrolic protons so



Scheme 2. Synthesis of (*S*)-**4**: a. LAH, Et_2O, (100%); b. PBr_3, Toluene, (81%).



Scheme 3. Synthesis of complex $(\alpha,\beta,\alpha,\beta)$-Mn-**1**: a. i) pyrrole, BF_3OEt_2, CH_2Cl_2, ii) DDQ, (43%), (4 atropoisomers); b. column chromatography; c. BBr_3, (90%); d. $Mn(OAc)_2 \cdot 4H_2O$, DMF, Δ, 54%; e. (*S*)-**4**, K_2CO_3, DMF, (100%).

we were not able to identify the remaining two atropisomers at this stage. The two compounds were separately subjected to demethylation using BBr_3 giving the corresponding 5,10,15,20-tetrakis(2-chloro-6-hydroxyphenyl)porphyrins **3** $(\alpha,\alpha,\beta,\beta)$-**3** and $(\alpha,\beta,\alpha,\beta)$-3 in 65–70% yield. Subsequent reaction with bromide (*S*)-**4** yielded both atropoisomeric porphyrins $(\alpha,\alpha,\beta,\beta)$-**1** and $(\alpha,\beta,\alpha,\beta)$-1 in quantitative yield. On basis of the ^{1}H-NMR spectra (double singlet for the β-pyrrolic protons) the porphyrin derived from the second eluted atropoisomer could be assigned as $(\alpha,\beta,\alpha,\beta)$-**1**, the atropoisomer with a higher symmetry degree. In fact, the other compound showed a higher number of signals in the pyrrolic region pointing to a lower symmetry degree with respect to the former atropoisomer, hence it could be identified as $(\alpha,\alpha,\beta,\beta)$-**1**.

Unfortunately introduction of manganese in $(\alpha,\beta,\alpha,\beta)$-**1** by heating under reflux manganese(II) acetate and the porphyrin overnight in DMF [21] resulted in four products as determined by thin layer chromatography (TLC). Mass spectrometry of the reaction mixture (FAB^+) indicated partial cleavage of the benzylic cyclophanyl groups. Therefore we decided to interconvert the introduction of the metal and the functionalization with the homochiral cyclophanyl moieties. The manganese complex of the hydroxy porphyrin $(\alpha,\beta,\alpha,\beta)$-**3**, obtained as described above, was thus treated with cyclophanyl bromide (*S*)-**4** affording $(\alpha,\beta,\alpha,\beta)$-Mn-**1** in quantitative yield. The nature of the reaction product (single spot by TLC) was confirmed by mass spectrometry (FAB^+).

*2.2. Catalytic activity of $(\alpha,\beta,\alpha,\beta)$-Mn-**1** in the epoxidation of alkenes*

The title compound was tested in the epoxidation of unfunctionalized olefins, in the presence of an axial ligand (4-*tert*-butylpyridine, L), using styrene, 4-bromostyrene, dihydronaphthalene and 1-methylcyclohexene as model substrates (*S*). Aqueous sodium hypochlorite (NaOCl), 30%-hydrogen peroxide (30%-H_2O_2) and iodosylbenzene (PhIO) were employed as

primary oxidants (OD), always in excess with respect to the substrate. Reactions were carried out at 0°C in the case of NaOCl and 30%-H_2O_2, and at room temperature with solid PhIO. The pH of the aqueous solutions of NaOCl and 30%-H_2O_2 was adjusted at 10.0 and 4.5 respectively, according to a procedure previously reported by us [22]. The outcome of the reactions was followed by gas chromatography and results are summarized in Table 1. As already found in the case of Mn-**2** [19], (Table 1, entries 10–12) ($\alpha,\beta,\alpha,\beta$)-Mn-**1** gave the best results when used in association with NaOCl. Epoxidation of styrene, 4-bromostyrene, dihydronaphthalene and 1-methylcyclohexene (entries 1–4) resulted in turnover numbers up to 780, with high conversion of the substrate and selectivity from moderate to good. Rather surprisingly, the best results were obtained with 1-methylcyclohexene which is the most hindered substrate. In the presence of 30%-H_2O_2 the same alkenes gave the corresponding epoxides in very low yields (entries 5–8). In all these experiments racemic epoxides were obtained, as shown by gas chromatographic analysis of the reaction mixture using a chiral column. Since the highest enantiomeric excesses reported in the literature were observed using PhIO, epoxidation of styrene with this mild oxidant was also carried out (entry 9). Although ($\alpha,\beta,\alpha,\beta$)-Mn-**1** was an effective catalyst in the presence of PhIO, even in this case no enantioselectivity ($< 5\%$) was observed.

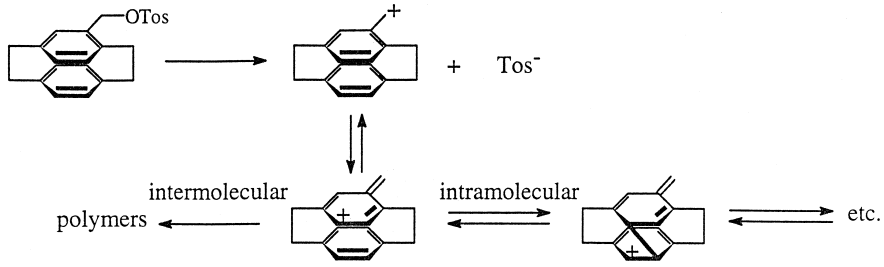
The catalytic efficiency of ($\alpha,\beta,\alpha,\beta$)-Mn-**1** was in the same range as reported for Mn-**2**. The stability of the former catalyst was lower, despite the presence of four *ortho*-chlorine atoms: in the experiment with NaOCl and dihydronaphthalene, only 20% of ($\alpha,\beta,\alpha,\beta$)-Mn-**1** remained after 1 h, as evaluated by UV–Vis. With 30%-H_2O_2 the ineffectiveness of ($\alpha,\beta,\alpha,\beta$)-Mn-**1** as epoxidation catalyst was due both to instability and to catalase activity. In a control experiment, 30%-H_2O_2 (pH = 5, 0.2 ml) was shaken with a solution of ($\alpha,\beta,\alpha,\beta$)-Mn-**1** ($5 \times 10^{-4}$ M in CH_2Cl_2, 2 ml). The evolvement of gas was evident and after 1 h iodometric titration of the aqueous layer indicated that only 50% of the initial amount of H_2O_2 was still present.

The absence of enantioselectivity in the reaction was totally unexpected. Beforehand a

Table 1
Epoxidation of unactivated olefins using complexes ($\alpha,\beta,\alpha,\beta$)-Mn-**1** and Mn-**2**[a]

Entry	Catalyst	Olefin	Oxidant	Conversion[b] (%)	Turnover[c]	Selectivity[d]	e.e. (%)
1	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	1-methylcyclohexene	NaOCl	87	780	90	< 5
2	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	styrene	NaOCl	56	360	64	< 5
3	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	4-Br-styrene	NaOCl	100	370	37	< 5
4	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	dihydronaphthalene	NaOCl	81	420	53	< 5
5	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	1-methylcyclohexene	H_2O_2	< 5	< 5	n.r.	< 5
6	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	styrene	H_2O_2	< 5	< 5	n.r.	< 5
7	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	4-Br-styrene	H_2O_2	< 5	< 5	n.r.	< 5
8	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	dihydronaphthalene	H_2O_2	< 5	< 5	n.r.	< 5
9	($\alpha,\beta,\alpha,\beta$)-Mn-**1**	styrene	PhIO[e]	54	290	52	< 5
10	Mn-**2**	dihydronaphthalene	NaOCl	95	730	77	22
11[f]	Mn-**2**	2′-methyl styrene	NaOCl	65	165	51	31
12[f]	Mn-**2**	styrene	NaOCl	95	325	68	26

[a] Molar ratios: porphyrin/substrate/ligand/oxidant = P/S/L/O = 1/1000/10/1500; $T = 0$°C.
[b] Conversion based on amount of olefin consumed.
[c] Turnover: amount of epoxide/amount of catalyst.
[d] Selectivity: amount of epoxide/amount of olefin consumed, n.r. = not relevant.
[e] $T = 25$°C.
[f] Molar ratios: P/S/L/O = 1/500/10/1500.



Scheme 4. Cation formation and subsequent polymerisation [23].

CPK-model of $(\alpha,\beta,\alpha,\beta)$-Mn-**1** indicated that the chiral cyclophanyl moieties would be located in the vicinity of the metal centre, although the $-OCH_2$- linker allows for a certain degree of conformational freedom of the chiral groups. Moreover, when an atropoisomerical mixture of catalyst Mn-**2** in combination with NaOCl as oxidant was used, enantioselectivities up to 31% were observed (entries 10–12). The source of instability in $(\alpha,\beta,\alpha,\beta)$-Mn-**1** might not be due to the presence of the cyclophanyl group only: it was tentatively ascribed to the combined presence of the $-OCH_2$- linker and the bulky and electronrich chiral cyclophane. Indeed, attempts to transform the hydroxyl group of alcohol (S)-**5** into a better leaving group by reaction with sulphonyl chlorides regularly failed. Upon evaporation during workup the solution turned deep blue, and ^{1}H-NMR indicated the formation of polymeric compounds. Apparently the cation was formed, followed by polymerization (Scheme 4) [23]. Our hypothesis was supported by a control reaction. Alcohol (S)-**5** was treated with dimethylsulphate to give the corresponding methyl ether (S)-**8** which was subsequently treated with aqueous NaOCl under the standard epoxidation conditions, using Mn-tetrakis(2,6-dichlorophenyl)porphyrin as catalyst. After 5 h at 0°C, the organic phase did not contain any trace of methyl ether (S)-**8**, and a mixture of several unknown products was detected by TLC. It should be noted that under the reaction conditions used here, metal-porphyrins only catalyze the hydroxylation of reactive hydrocarbons such as norbornene and tetrahydronaphtalene [24].

3. Conclusions

The new homochiral, atropoisomerically pure manganese complex $(\alpha,\beta,\alpha,\beta)$-Mn-**1** has been synthesized and fully characterized. It has been demonstrated that the cyclophane–methylene moiety has a reactivity that diverges from what was expected, leading to a lower stability of the porphyrin derivative. The catalytic activity of $(\alpha,\beta,\alpha,\beta)$-Mn-**1** has been established in the epoxidation of unactivated carbon–carbon double bonds using NaOCl or PhIO as oxidants. Unfortunately no significant enantioselectivity in the epoxidation was achieved. The easy decomposition of the cyclophane tethered to the porphyrin by a methyleneoxy group precludes an efficient transfer of the chiral information in the oxygen transfer from the metal to the alkene.

4. Experimental section

4.1. General remarks

^{1}H-NMR spectra were recorded on a Bruker AC-300 spectrometer at 300 MHz. $CDCl_3$ was used as a solvent unless stated otherwise. Chemical shifts are determined relative to the solvent and converted to the TMS scale. Coupling constants, J, are denoted in Hertz. ^{13}C-NMR were

recorded on a Varian XL-300 spectrometer at 75.43 MHz. Chemical shifts are determined relative to the solvent and converted to the TMS scale. MS (FAB^+) were recorded on an Analytical VG 7070 EQ spectrometer. UV–VIS spectra were recorded on a Perkin Elmer Lambda 6 spectrophotometer using CH_2Cl_2 as solvent, concentration of the solutions being 2.0×10^{-6} M. All reagents and solvents were purified, dried, and stored under nitrogen when necessary, using standard procedures. Chromatography was performed using Merck silica gel 60 (70–230 mesh). Dichloromethane for porphyrin synthesis was obtained from Baker (Baker Analyzed, stabilized with amylene, and distilled from K_2CO_3 prior to use). For epoxidation reactions, GC analyses (internal standard method) were performed on Hewlett-Packard 5890 gas chromatograph equipped with a chiral column (J&W Scientific Cyclodex-B, 30 m × 0.25 mm i.d., 0.25 μm film). The internal standards used were: PhCl (methylcyclohexene), *n*-$C_{10}H_{22}$ (styrene) and n-$C_{14}H_{30}$ (styrene, 4-Br-styrene and dihydronaphthalene). Aqueous NaOCl (about 13%) was obtained from Fluka and 30%-H_2O_2 was obtained from Aldrich. Both oxidants were analyzed by titration following literature procedures [25,26]. NaOCl was diluted with distilled H_2O before use to give 0.5 M solution. Iodosylbenzene was synthesized according to a literature procedure [27].

4.2. Synthesis of the catalyst

4.2.1. 2-chloro-6-methoxybenzaldehyde (**6**)

This compound was synthesized analogously to a literature procedure starting from 2-chloro-6-fluorobenzaldehyde [15]. The reaction was followed by TLC (silica gel; CH_2Cl_2: pet. ether) and quenched when the first traces of the di methylacetal of the aldehyde appeared. Work-up was the same as described previously. Yield: 70%; ^{1}H-NMR: δ 10.49 (s, 1H), 7.39 (t, $J = 8.2$, 1H), 7.03 (d, $J = 8.2$, 1H), 6.90 (d, $J = 8.2$, 1H), 3.90 (s, 3H); ^{13}C-NMR: δ 189.19, 151.11, 136.61, 134.59, 123.09, 122.29, 110.29, 56.24.

4.2.2. 5,10,15,20-tetrakis(2-chloro-6-methoxyphenyl)-porphyrin (**7**)

Nitrogen was bubbled through a solution of 2-chloro-6-methoxybenzaldehyde **6** (3.41 g, 20.0 mmol) and pyrrole (1.34 g, 20.0 mmol) in CH_2Cl_2 (2000 ml) for 10 min. $BF_3.OEt_2$ (3 drops) was added. The mixture was stirred shielded from light until absence of starting aldehyde was detected by TLC (silica gel; CH_2Cl_2). Subsequently 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ, 3.42 g, 15.0 mmol) was added and the solution stirred for 1 h. Evaporation of the solvent in vacuo and column chromatography (silica gel; CH_2Cl_2 and subsequently silica gel; EtOAc:pet. ether = 1:1) yielded pure 5,10,15,20-tetrakis(2-chloro-6-methoxyphenyl)-porphyrin (**7**) (1.86 g, 43%) as a mixture of atropoisomers. Repeated column chromatography (silica gel; CH_2Cl_2:pet. ether = 3:2) yielded the pure atropoisomers.

*4.2.2.1. 5α,10α,15α,20α-tetrakis(2-chloro-6-methoxyphenyl)porphyrin [(α,α,α,α)-**7**]*. Yield: 112.9 mg (2.6%); ^{1}H-NMR: δ 8.71–8.65 (m, 8H), 7.75–7.64 (m, 4H), 7.47–7.41 (m, 4H), 7.21–7.18 (m, 4H), 3.48 (s, 12H), −2.56 (br s, 2H); ^{13}C-NMR: δ 155.69, 141.22, 132.84, 125.01, 119.57, 116.14, 108.69, 108.39, 104.05, 50.80; UV–VIS: λ_{max} (log ϵ) = 416 nm (5.39), 511 nm (4.13), 587 nm (3.72); MS (FAB^+): 869 (M^+-1), lowest-mass peak of isotope cluster.

*4.2.2.2. 5α,10β,15α,20β-tetrakis(2-chloro-6-methoxyphenyl)porphyrin [(α,β,α,β)-**7**]*. Yield: 282.6 mg (6.5%); ^{1}H-NMR: δ 8.65 (s, 8H), 7.67 (dd, $J = 8.0$, $J = 8.3$, 4H), 7.45 (d, $J = 8.0$, 4H), 7.20 (d, $J = 8.3$, 4H), 3.48 (s, 12H), −2.54 (br s, 2H); ^{13}C-NMR: δ 161.09, 138.16, 130.91, 130.29, 128.84, 121.41, 112.42, 109.39, 56.17; UV–VIS: λ_{max} (log ϵ) = 417 nm (5.53), 512 nm (4.26), 586 nm (3.79); MS (FAB^+): 869 (M^+-1), lowest-mass peak of isotope cluster.

4.2.2.3. 5α,10α,15α,20β-tetrakis(2-chloro-6-methoxyphenyl)porphyrin [(α,α,α,β)-7]. Yield: 1152 mg (26.4%); ^{1}H-NMR: δ 8.65 (s, 4H), 8.64 (s, 4H), 7.68 (dd, $J = 8.1$, $J = 8.3$, 4H), 7.46 (d, $J = 8.1$, 4H), 7.21 (d, $J = 8.3$, 4H), 3.50 (s, 6H), 3.49 (s, 3H), 3.47 (s, 3H), −2.54 (br s, 2H); ^{13}C-NMR: δ 160.20, 136.84, 130.64, 130.05, 128.61, 120.97, 112.18, 110.64, 109.55, 55.70; UV–VIS: λ_{max} (log ε) = 417 nm (5.56), 512 nm (4.28), 587 nm (3.80); MS (FAB$^+$): 869 (M$^+$-1), lowest-mass peak of isotope cluster.

4.2.2.4. 5α,10α,15β,20β-tetrakis(2-chloro-6-methoxyphenyl)porphyrin [(α,α,β,β)-7]. Yield: 173.4 mg (4.0%); ^{1}H-NMR ($CDCl_3$ plus added DMSO-*d6*): δ 8.40 (s, 8H), 7.49 (dd, $J = 8.2$, $J = 8.3$, 4H), 7.22 (d, $J = 8.2$, 4H), 7.04 (d, $J = 8.3$, 4H), 3.31 (s, 12H), −2.90 (br s, 2H); ^{13}C-NMR ($CDCl_3$ plus added DMSO-*d6*): δ 160.44, 136.67, 131.48, 130.68, 128.60, 128.39, 121.26, 112.56, 110.42, 56.20; UV–VIS: λ_{max} (log ε) = 417 nm (5.54), 512 nm (4.23), 587 nm (3.70); MS (FAB$^+$): 869 (M$^+$-1), lowest-mass peak of isotope cluster.

4.2.3. 5α,10β,15α,20β-tetrakis(2-chloro-6-hydroxyphenyl)porphyrin [(α,β,α,β)-3]

A solution of (α,β,α,β)-**7** (310 mg, 355 μmol) in CH_2Cl_2 was cooled to 0°C. To this solution was added BBr_3 (1.0 M in CH_2Cl_2, 25 ml, 25 mmol), giving an emerald green solution. The mixture was stirred for 1 h, after which the temperature was allowed to reach room temperature and subsequently stirred for 64 h. The reaction was quenched by adding ice. Aqueous $NaHCO_3$ (5%) was added until the solution turned purple. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (3 × 50 ml). The combined organic phases were dried (Na_2SO_4). Removal of the solvent gave a purple powder, that was purified by column chromatography (silica gel; CH_2Cl_2:MeOH = 95:5). Yield: 231 mg (80%); ^{1}H-NMR: δ 8.88 (s, 8H), 7.70–7.65 (m, 4H), 7.46 (d, $J = 7.9$, 4H), 7.32 (d, $J = 8.2$, 4H), 5.20 (br s, 4H), −2.67 (br s, 2H); ^{13}C-NMR: δ 151.77, 142.04, 131.92, 126.16, 125.88, 121.24, 116.17, 109.24, 105.22; UV–VIS: λ_{max} (log ε) = 416 nm (5.39), 509 nm (4.18), 584 nm (3.76); MS (FAB$^+$): 813 (M$^+$-1), lowest-mass peak of isotope cluster.

4.2.4. 5α,10α,15β,20β-tetrakis(2-chloro-6-hydroxyphenyl)porphyrin [(α,α,β,β)-3]

The reaction was performed as described for (α,β,α,β)-**3**, starting from porphyrin (α,α,β,β)-**7**. The column chromatography was performed on silica gel using CH_2Cl_2:MeOH = 9:1 as eluent. Yield: 245 mg (85%); ^{1}H-NMR: δ 8.79 (s, 8H), 7.66–7.61 (m, 4H), 7.44 (d, $J = 7.9$, 4H), 7.19 (d, $J = 8.2$, 4H), −2.81 (br s, 2H); ^{13}C-NMR: δ 159.02, 136.58, 131.76, 130.98, 128.72, 127.24, 119.62, 114.47, 112.97; UV–VIS: λ_{max} (log ε) = 416 nm (5.38), 511 nm (4.21), 585 nm (3.84); MS (FAB$^+$):813 (M$^+$-1), lowest-mass peak of isotope cluster.

4.2.5. [5α,10β,15α,20β-tetrakis(2-chloro-6-hydroxyphenyl)porphinato-N^{21},N^{22},N^{23},N^{24}] manganese chloride [(α,β,α,β)-Mn-3]

A solution of (α,β,α,β)-**3** (100 mg, 122 μmol) in DMF (25 ml) was boiled under reflux. Solid $Mn(OAc)_2 \cdot 4H_2O$ (245 mg, 1.0 mmol) was added and the resulting mixture boiled under reflux for 16 h. After removal of the solvent in vacuo the residue was redissolved in CH_2Cl_2 (25 ml) and filtered. The filtrate was washed with water (3 × 25 ml). Drying and removal of the solvent gave a brown powder, which was purified by column chromatography (silica gel; CH_2Cl_2:MeOH = 9:1). Yield: 70 mg (66%); UV–VIS: λ_{max} (log ε) = 369 nm (4.07), 478 nm (4.33), 576 nm (3.48); MS (FAB$^+$): 867 (M$^+$), lowest-mass peak of isotope cluster.

4.2.6. (S)-(tricyclo[8.2.2.2^{4,7}]hexadeca-4,6,10,12,13,15-hexaene)-methyl alcohol [(S)-5]

This compound was synthesized in quantitative yield following a procedure previously described by us, starting from (*S*)-(tricyclo-[8.2.2.2^{4,7}]hexadeca-4,6,10,12,13,15-hexaene)-

carboxaldehyde. [19] ^{1}H-NMR: δ 6.59 (dd, J = 7.8, J = 1.7, 1H), 6.56–6.45 (m, 4H), 6.40–6.37 (m, 2H), 4.53 (dd, J = 98.6, J = 12.7, 2H), 3.44–3.35 (m, 1H), 3.18–2.81 (m, 7H), 1.55 (br s, 1H); ^{13}C-NMR: δ 140.27, 139.75, 139.55, 139.27, 137.48, 135.00, 133.31, 133.25, 132.38, 132.18, 132.12, 129.07, 64.48, 35.31, 35.06, 34.42, 32.81

*4.2.7. (S)-(tricyclo[8.2.2.2^{4,7}]hexadeca-4,6,10,12,13,15-hexaene)-methyl bromide [(S)-**4**]*

To a solution of PBr_3 (50 mg, 183 mmol) in toluene (20 ml) was added pyridine (20 mg, 250 mmol). The solution was cooled to -5°C and a solution of alcohol (*S*)-**5**, 119 mg, 0.50 mmol) in toluene (10 ml) was added dropwise. The reaction mixture was stirred for 1 h, allowed to reach room temperature and stirred for 48 h. The toluene was removed in vacuo. The residue was redissolved in CH_2Cl_2, filtered and the solvent removed in vacuo. Column chromatography (silica gel; CH_2Cl_2:pet. ether = 1:1) gave pure (*S*)-**4**. Yield: 81%; ^{1}H-NMR: δ 6.60–6.53 (m, 1H), 6.53–6.46 (m, 4H), 6.42–6.33 (m, 2H), 4.36 (dd, J = 88.1, J = 10.2, 2H), 3.50–3.41 (m, 1H), 3.30–3.15 (m, 1H), 3.13–2.87 (m, 6H); ^{13}C-NMR: δ 140.40, 139.55, 139.20, 138.17, 136.35, 135.58, 134.87, 133.46, 133.22, 132.18, 129.60, 35.26, 34.87, 34.48, 33.31, 32.98.

*4.2.8. 5α,10β,15α,20β-tetrakis(2-chloro-6-(5-((S)-tricyclo[8.2.2.2^{4,7}] hexadeca-4,6,10,12,13,15-hexaene)methoxy)phenyl)porphyrin[(α,β,α,β)-**1**]*

To a solution of ($\alpha,\beta,\alpha,\beta$)-**3** (67 mg, 82 μmol) and bromide (*S*)-**4** (248 mg, 822 μmol) in DMF (50 ml) was added K_2CO_3 (1.38 g, 10 mmol). The resulting mixture was stirred for 16 h. After removal of the solvent in vacuo the residue was redissolved in CH_2Cl_2 (25 ml) and filtered. The filtrate was washed with water (3×25 ml). Drying and removal of the solvent gave a purple powder which was purified using column chromatography (silica gel; CH_2Cl_2 until the excess of (*S*)-**4** was collected, followed by CH_2Cl_2:MeOH = 95:5). Yield: 139 mg (98%); ^{1}H-NMR: δ 8.73 (d, J = 6.1, 8H), 7.57 (dd, J = 8.3, J = 8.1, 4H). 7.41 (d, J = 8.1, 4H), 7.11 (d, J = 8.3, 4H), 6.13–6.00 (m, 16H), 5.77 (d, J = 7.9, 4H), 5.43 (s, 4H), 4.83 (d, J = 13.2, 4H), 4.74 (d, J = 7.9, 4H), 4.58 (d, J = 13.3, 4H), 2.58–2.17 (m, 24H), 1.79–1.63 (m, 8H), -2.16 (br s, 2H); ^{13}C-NMR: δ 160.93, 159.85, 139.67, 138.83, 138.34, 138.06, 137.20, 135.11. 134.56, 133.85, 133.69, 133.18 ($2\times$), 132.48, 131.78, 131.71, 130.91, 130.10, 129.54, 128.06, 121.37, 113.01, 111.19, 69.36, 34.24, 33.79, 32.39, 29.70; UV–VIS: λ_{max} (log ϵ) = 419 nm (5.64), 513 nm (4.37), 587 nm (3.93); MS (FAB$^+$): 1693 (M$^+$-1), lowest-mass peak of isotope cluster.

*4.2.9. 5α,10α,15β,20β-tetrakis(2-chloro-6-(5-((S)-tricyclo[8.2.2.2^{4,7}] hexadeca-4,6,10,12,13,15-hexaene)methoxy)phenyl)porphyrin[(α,α,β,β)-**1**]*

The reaction was performed as described for porphyrin ($\alpha,\beta,\alpha,\beta$)-**1** starting from porphyrin ($\alpha,\alpha,\beta,\beta$)-**3** and bromide (*S*)-**4**. Yield: 130 mg (94%); ^{1}H-NMR: δ 8.92–8.54 (m, 8H), 7.80–7.10 (m, 12H), 6.60–5.82 (m, 24H), 5.65–5.42 (m, 4H), 5.42–5.28 (m, 4H), 4.64–4.00 (m, 12H), 3.14–1.39 (m, 48H), -2.81 (br s, 2H); UV–VIS: λ_{max} (log ϵ) = 417 (4.98), 512 (3.77), 590 (3.20); MS (FAB$^+$): 1693 (M$^+$-1), lowest-mass peak of isotope cluster.

*4.2.10. {5α,10β,15α,20β-tetrakis(2-chloro-6-(5-((s)-tricyclo[8.2.2.2.^{4,7}] hexadeca-4,6,10,12,13,15-hexaene) methoxy) phenyl) porphinato-N^{21},N^{22},N^{23},N^{24}}Manganese chloride [(α,β,α,β)-Mn-**1**]*

Complex ($\alpha,\beta,\alpha,\beta$)-Mn **3** (25.3 mg, 28 μmol) was allowed to react with bromide (*S*)-**4** under the same conditions described for the synthesis of ($\alpha,\beta,\alpha,\beta$)-**1**. After workup 50 mg of brown powder was obtained, yield = 100%; UV–VIS: λ_{max} (log ϵ) = 374 nm (4.72), 479 nm (4.99), 581 nm (4.04); MS (FAB$^+$): 1747 (M$^+$), lowest-mass peak of isotope cluster.

4.3. Epoxidation reactions

Epoxidation reactions were carried out in a 10 ml flask equipped with a Teflon-lined screw cap and a magnetic stirrer, and the temperature maintained at 0°C with circulating ethanol. The flask was charged with: (i) 1 ml of a 1.0×10^{-3} M solution of ($\alpha,\beta,\alpha,\beta$)-Mn-**1** in CH_2Cl_2; (ii) 1 ml of a 1.0 M solution of alkene in CH_2Cl_2, containing the internal standard (0.25 M); (iii) 0.1 ml of a 0.1 M solution of *tert*-butylpyridine in CH_2Cl_2. The solution was stirred for 10 min. Subsequently the oxidant (3 ml of aqueous NaOCl 0.5 M adjusted to pH = 10.0 using 0.1 M HCl, or 0.11 ml of 30%-H_2O_2 adjusted to pH = 5.0 using sodium benzoate, or 330 mg of solid PhIO) was added and the reaction mixture was stirred for 16 h at 1300 ± 50 rpm. The layers were separated, the organic layer filtered over silica gel and analyzed by GC.

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