Investigation of the Enantioselectivity Observed in Epoxidation Reactions Catalysed by Bis-Strapped Chiral Porphyrins Derived from L-Proline

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The enantiomeric excesses obtained during the epoxidation reactions of *p*-chlorostyrene or 1,2-dihydronaphthalene catalysed by two different series of chiral porphyrins are reported. An attempt is made to correlate the enantioselectivity with the steric hindrance generated by the straps of these catalysts. It is shown that this steric hindrance is influenced by the nature of the strap and that it can be approximated. Additionally, the same strap is tethered in two different fashions on each side of the porphyrin, leading to either D_2- or C_2-symmetrical catalysts, for which the two sides are identically functionalised.

Introduction

Metalloporphyrins have been well known, for two decades, to be effective catalysts for unfunctionalised alkene epoxidation[1−3] or alkane hydroxylation.[4] More recently, they have also been investigated as effective catalysts for cyclopropanation[5] and aziridination[6] reactions. Indeed, when compared with metallosalens, porphyrinoid catalysts are expected to exhibit much higher turnover numbers.[7] This criterion is of course extremely important in any catalysis, but may be much more important in the case of "destructive" catalysis, such as oxidation. In the case of chiral molecules, although different encouraging results have been reported, the obtained enantioselectivities are generally lower than those described for metallosalens, and also much more difficult to rationalise. This observation can be partially explained by the fact that the complete series of these latter catalysts have been synthesised and extensively studied.[8−10] We believe that the study of a series of potential catalysts can help our understanding of how the enantioselectivity can be achieved.[11−13] Indeed, for oxidation reactions, although the use of aromatic structures such as BINAP-related straps lead to a robust catalyst, it is difficult to predict the effectiveness of the same catalyst in terms of selectivity.[7]

Recently, we have reported on the synthesis of a complete family of potential chiral catalysts for epoxidation reactions. We were able to obtain an X-ray structure of one of the catalysts metallated by zinc(II) and hence have a precise image of the chiral superstructure. Moreover, the ^{1}H NMR spectroscopic studies of the same molecule indicated that the solution structure was in agreement with the structure in the solid state.[14] In this paper, we now report on the catalytic activity of two different series of iron(III) chiral catalysts, related by the point of attachment of the chiral straps, in the asymmetric epoxidation of *p*-chlorostyrene and 1,2-dihydronaphthalene by iodosylbenzene.

Results and Discussion

In previous studies, excellent enantiomeric excesses (*ee*) and good turnover numbers have been reported on. The main goal of this study is to determine if the enantioselectivities observed for a given reaction, namely the epoxidation of an unfunctionalised olefin, can be directly correlated with the steric hindrance of the strap in a D_2-symmetrical environment, as in the first series of porphyrins **1**−**6** (Figure 1, left column). For that purpose, we needed to make use of several potential catalysts for which we have a precise representation of the catalyst in solution.

We have already published the crystal structure of the zinc counterpart of porphyrin **1**.[14] In Figure 2 we have represented two other views of the same molecule in order to describe a structural parameter that we have defined as *R*, the ratio of the steric hindrance of the chiral strap and the steric hindrance of the porphyrin core itself (R = S/P). This ratio gives an unbiased representation of the steric hindrance of the strap whilst taking into account the planarity of the porphyrin. It is graphically measured as indicated in Figure 2, with a spatial extent limited to the carbon atoms. Indeed, this ratio has been evaluated by molecular mechanics modelling for six different bis-strapped porphyrins,

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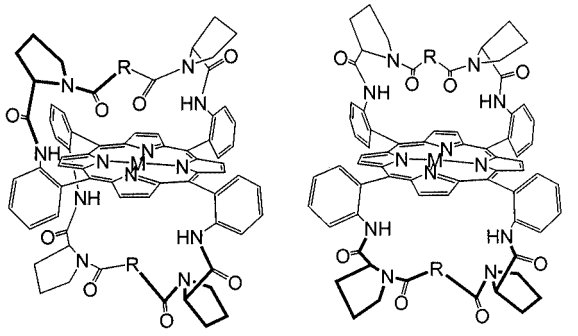

1 R = -$(CH_2)_2$- **4** R = -CH=CH- **7** R = -$(CH_2)_2$- **10** R = -*m*-phenyl-

2 R = -$(CH_2)_3$- **5** R = -*p*-phenyl- **8** R = -$(CH_2)_3$- **11** R = O*t*Bu, *t*BuO

3 R = -$(CH_2)_4$- **6** R = -*m*-phenyl- **9** R = -$(CH_2)_4$-

Figure 1. Chemical structure of the different catalysts (left column: synthesised from the αβαβ atropisomer of TAPP; right column: synthesised from the ααββ atropisomer of TAPP; M = H_2, Fe, or Zn)

and is found to range from 0.20 to 0.51 (Table 1).[15] For our study, we have assumed that the conformation observed for the zinc(II)−porphyrin is not very different from that in the iron(III) complex used in the epoxidation reaction. Furthermore, we have validated our results by modelling and comparing the *R* value calculated theoretically with the experimental value in the case of **1Zn**; the values of 0.49 and 0.51, respectively, are strikingly similar. This also proves that the intramolecular coordination of the zinc atom does not significantly influence this parameter.

The results of the modelling of the six chiral porphyrins synthesised in the first αβαβ series are depicted in Figure 3. They are represented according to the same point of view as in Figure 2.[16] It is obvious that the *R* value increases as we examine the catalysts from (a) to (f). This means that if the enantioselectivity is a function of the steric hindrance during the approach of the olefin, we should obtain increasing values of *ee* as we examine the catalysts through the series **6**, **4**, **5**, **1**, **2**, and **3**. Different results emerged from the observation of the first four lines of Table 1. First of all, the different *ee* values are extremely low, as long as the straps of the catalyst are composed of a non-aromatic linker, and independent of the olefin. Indeed, with linkers such as the succinyl, fumaryl, adipyl, or glutaryl moieties, the *ee* values range from 1 to 7% in the case of a terminal olefin. Obviously, these linkers are attached just above the iron−oxo species generated by the action of iodosylbenzene on the iron(III)−porphyrin, and are likely to be easily oxidised instead of the olefin. These low *ee* values are also to be compared with those reported by Rose and Collman[17] with their "blank picket" porphyrins, for which they reported that the *ee* values vary inversely to the number of chiral pickets. It seems that our catalysts, although not at all comparable, are as poor catalysts as these picket porphyrins. On the other hand, the explanation advanced by the authors for their picket catalysts could also be valid for our

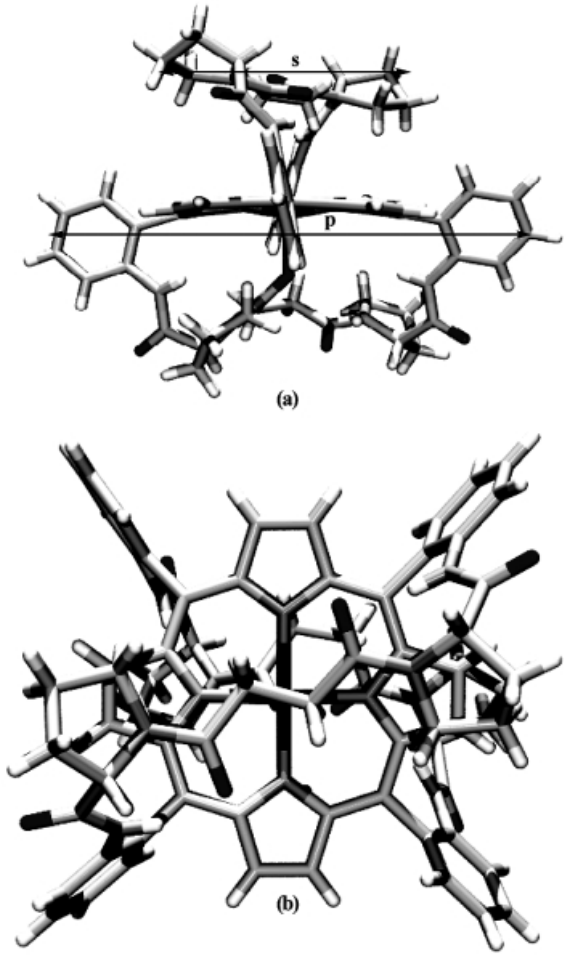

Figure 2. Stick representation (including hydrogen atoms) of the crystal structure of **1Zn**; (a) "*meso*-C_5-C_{15}" lateral view, (b) apical view

Table 1. Enantiomeric excesses obtained with the iron catalysts for two different olefins with the characteristic steric ratio *R* for catalysts **1**−**6**

Catalyst[a]	*p*-Chlorostyrene[b]	1,2-Dihydronaphthalene[b]	*R*[c]
Disucc-αβαβ (**1**)	1	0	0.49
Diglut-αβαβ (**2**)	7	4	0.50
Diadip-αβαβ (**3**)	3	1	0.54
Difum-αβαβ (**4**)	2	2	0.26
Ditere-αβαβ (**5**)	18	3	0.36
Diiso-αβαβ (**6**)	5	19	0.20
Disucc-ααββ (**7**)	26	3	−
Diglut-ααββ (**8**)	20	8	−
Diadip-ααββ (**9**)	31	26	−
Diiso-ααββ (**10**)	28	14	−

[a] Reaction conditions: catalyst (1 μmol), substrate (1000 μmol), and PhIO (100 μmol) react at room temperature in CH_2Cl_2 (2 mL).[b] Determined by GC with a Cyclodex-B chiral column. [c] In the case of **1Zn** (Figure 2), calculated equal to 0.51.

strap catalysts because the lowest *ee* value was obtained with the catalyst Disucc-αβαβ (**1**), for which the *R* value is almost the highest calculated and equal to 0.49. Now, if we

compare the side views (d) of Disucc-αβαβ (**1**) (R = 0.49) and (b) of Difum-αβαβ (**4**) (R = 0.26) (Figure 3), and if the *ee* value was to follow the lateral steric hindrance, the *ee* value should be found to be much lower in the case of Difum-αβαβ (**4**). Actually, they are almost the same. This means that either there is no relationship between this steric hindrance and the enantioselectivity or, this relation is not applicable in this case for other reasons. Indeed, the oxidative degradation of the catalyst could be consistent with this observation. The straps in catalysts such as **1**−**4** are so close to the metal centre and so sensitive to oxidation that they are oxidised immediately, and in fact, the measured *ee* value could reflect the enantioselectivity of the resulting mixture of degraded compounds. This explanation is consistent with previous results[17] for which it is believed that providing more access to the metal centre could increase the selectivity. The results obtained in the case of a (*Z*)-disubstituted olefin (1,2-dihydronaphthalene) follow the same trend and are as disappointing as in the case of the terminal olefin. Undeniably, the approach of such an encumbered olefin must be very limited and the *ee* values are even lower than for *p*-chlorostyrene.

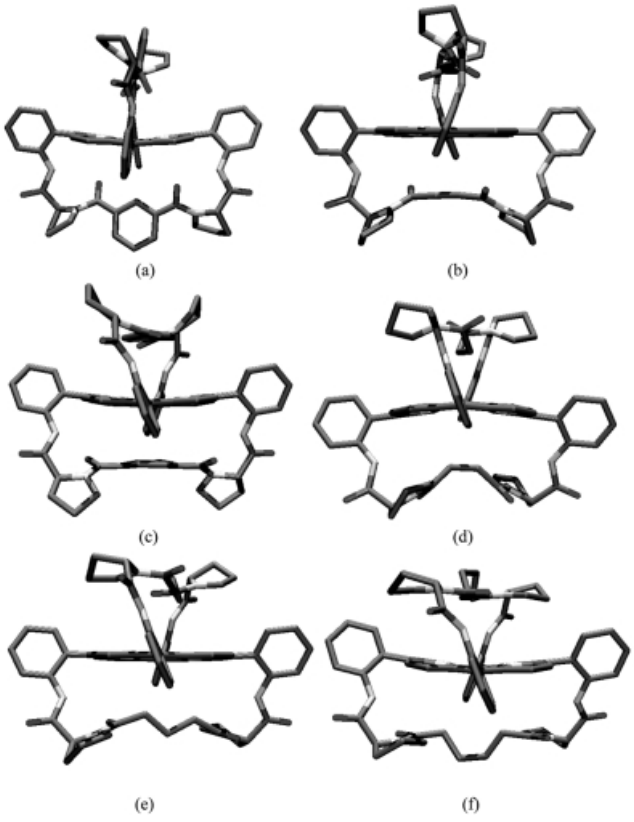

Figure 3. Stick representations of (a) **6**, (b) **4**, (c) **5**, (d) **1**, (e) **2**, and (f) **3** obtained by molecular mechanics modelling[15]

In a second study, we investigated a similar type of catalyst, but for which the linker is based on an aromatic diacyl dichloride, namely the porphyrins Ditere-αβαβ (**5**) and Diiso-αβαβ (**6**). The results of this comparison are much more informative, since the correlation between steric hindrance and enantioselectivity appears to be verified, but only for the terminal olefin. Actually, the results are contradictory when one compares the *ee* values obtained for the terminal olefin and the (*Z*)-disubstituted alkene. For porphyrin Ditere-αβαβ (**5**), which exhibits a greater R value than Diiso-αβαβ (**6**) (0.36 vs. 0.20), the observed *ee* value is 18% with *p*-chlorostyrene, but only 3% for 1,2-dihydronaphthalene. Conversely, for the catalyst Diiso-αβαβ (**6**), the *ee* value is 5% with *p*-chlorostyrene, but increases to 19% for 1,2-dihydronaphthalene. It clearly appears that with the terminal olefin, the steric hindrance is a pertinent parameter with a positive effect, whereas for a disubstituted olefin, the opposite effect is observed. This result, a priori difficult to anticipate, can be rationalised by considering two major facts. Firstly, the olefin cannot approach from the top of the catalyst,[18] but only from the side with its aromatic ring parallel to the mean plane of the porphyrin (side approach).[19] Secondly, it is striking that the aromatic rings of the straps in these two catalysts are in two extreme perpendicular positions. This observation is particularly visible in Figure 3 [views (a) and (c), bottom strap]. For catalyst Diiso-αβαβ (**6**) (a), the aromatic ring is perpendicular to the mean plane of the porphyrin whereas, for porphyrin Ditere-αβαβ (**5**) (c), it is parallel to the porphyrin plane. In the case of **5**, the enantioselectivity is much better for *p*-chlorostyrene because the olefin can introduce its double bond just above the iron−oxo species and perpendicular to the strap, with its aromatic ring avoiding the steric bulk of the L-proline ring. In the case of 1,2-dihydronaphthalene, this approach is not possible, and therefore its double bond remains parallel to the strap, resulting in no real discrimination by steric hindrance. Furthermore, in the case of **5**, the aromatic ring of the strap, parallel to the porphyrin plane, actually decreases the apparent hindrance of the five-membered ring of the L-proline. On the other hand, for catalyst **6** [Figure 3, view (a), top strap], there is a slight steric effect, mainly because the aromatic cycle remains in the plane of the strap (R = 0.20). Apparently, this subtle modification is sufficient to discriminate between the two different approaches of the disubstituted olefin, but not at all in the case of the terminal one. This explanation is in agreement with previous studies related to chiral picket porphyrins.[17] This particular comparison of two closely related catalysts with two different types of olefins is another example of how a fine difference in conformation can induce dramatic changes in the enantioselectivity, and also demonstrates that there should be a relation between the steric hindrance and the observed enantioselectivity, whether this relation is favourable or not. Furthermore, our catalyst Ditere-αβαβ (**5**), the L-prolinoyl analogue of Rose's L-alanine bis(handle) porphyrin,[20,21] must be compared with Mansuy's catalyst[22,23] that involves L-phenylalanine. In the L-phenylalanine series, an *ee* value of 50% was reported for the epoxidation of *p*-chlorostyrene, a value 2.5 times higher than the 18% *ee* obtained with **5**. This result, again, points out that a non-flexible structure such as the ring of L-proline is not a good structural feature for efficient enantioselectivity, and that L-phenylalanine, even with the possible rotation of the phenyl group around the methylene group of the lateral

chain, is a much better chiral inducer. This criterion has to be considered for further developments of chiral catalysts that involve L-proline.

In light of these instructive but relatively low enantioselectivities, we decided to extend our approach to another family of catalysts. Since 1995, we were aware of a study involving the four atropisomers of a chiral catalyst, synthesised by the condensation of a BINAP-type aldehyde with pyrrole,[24] leading to the aromatic analogues of the well-known "chiroporphyrins".[25] It was shown in this report that the iron−αααββ atropisomer was the most enantioselective catalyst among the four atropisomers for the epoxidation of styrene (59% *ee* vs. 7.5% *ee* for the αβαβ atropisomer). At a later stage this result was published,[13] and successfully generalised for a porphyrin bearing BINAP straps.[7] Thus, we have prepared the four new catalysts **7**−**10**, the analogues of **1**−**3** and **6**, respectively, with the αααββ geometry (Figure 1, right column). The lack of a crystal structure prevented us from evaluating the steric hindrance of the strap above the metal centre of the porphyrin as precisely as we did in the αβαβ series. However, we were able to estimate the steric hindrance in solution by examining the proton NMR spectra.

The ^{1}H NMR spectra of the two catalysts obtained by condensation of the glutaryl dichloride, **8** (top trace) and **2** (bottom trace) with the αααββ and αβαβ geometry, respectively, are represented in Figure 4. Clearly, in the case of **2**, the three multiplets that appear between δ = 0 and −3.5 can be assigned unambiguously to the three methylene groups of the glutaryl residues. However, an unexpected result can be seen for the chemical shifts of these three methylene groups with an αααββ geometry: their signals should be more downfield since the straps do not cross over the ring current of the porphyrin. The methylene protons with this geometry are as shielded as the methylene protons in the αβαβ geometry, and this seems to indicate that they are close to the porphyrin plane in both cases.

The results of the asymmetric epoxidation for the two olefins are interesting. The most obvious difference is represented by the *ee* values themselves. Indeed, for the epoxidation of the terminal olefin, they are much higher than for the first series. In addition, they seem to be almost the same (about 30% *ee*) for the three catalysts **7**, **9**, and **10**. Our preliminary modelling results seem to indicate that the bending of the straps over the porphyrin centre does not differ significantly when the length of the strap is varied from one methylene group to three groups. This could explain why the observed enantioselectivities are of the same order of magnitude in the case of *p*-chlorostyrene. For the disubstituted alkene, the *ee* value of one obtained for catalyst Diadip-αααββ (**9**) appears significantly different (26% *ee*) from that for the other catalysts, but is almost the same as that for the terminal olefin. This second observation can be explained by the fact that the structural feature that favours the discrimination between the two types of olefins for the catalysts in the αβαβ family, does not apply in the αααββ family. Indeed, during a side approach, the crevasse built by the bending of the straps over the porphyrin core can accommodate both types of olefins, with a slightly better selectivity for the terminal one. The two low *ee* values obtained by catalysts Disucc-αααββ (**7**) (3% *ee*) and Diglut-αααββ (**8**) (8% *ee*) for the disubstituted olefin can occur as

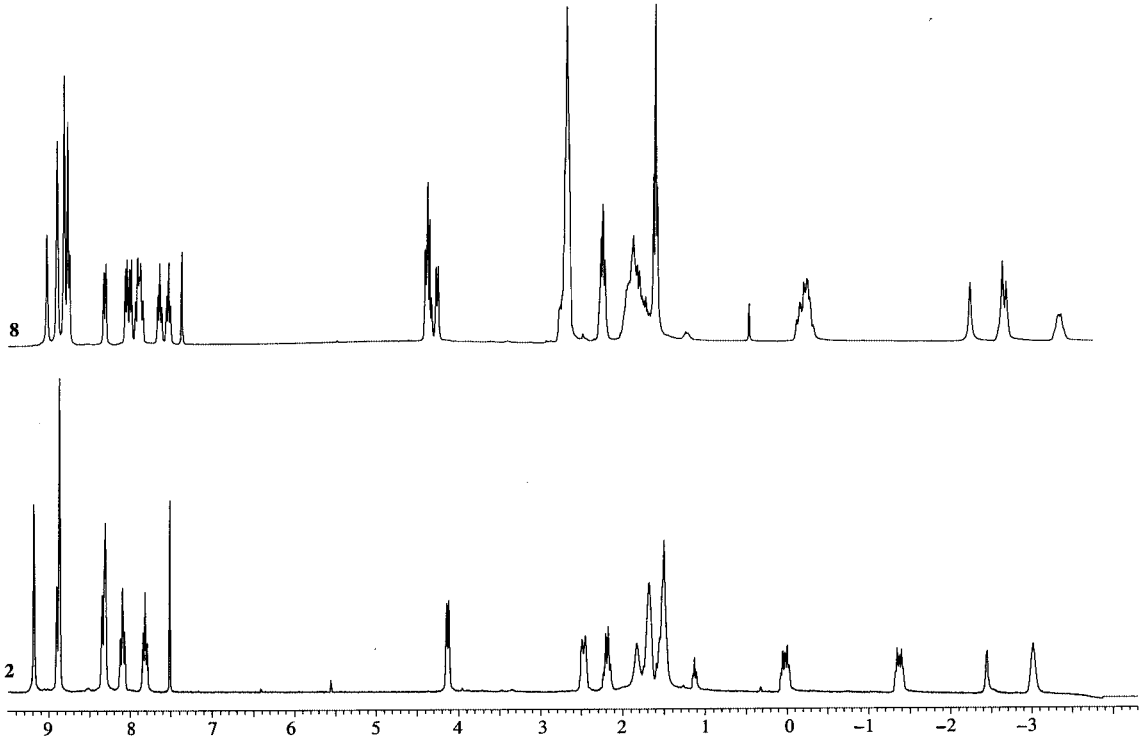

Figure 4. ^{1}H NMR spectra of porphyrins **8** and **2** ($CDCl_3$, 300 MHz, 300 K)

result of a less pronounced bending over the porphyrin, which is logical for catalysts with shorter straps than for the porphyrins Diiso-ααββ (**10**) or Diadip-ααββ (**9**). Globally, we can summarise this second part by the fact that if the linker (the diacyl dichloride employed in the last step of the synthesis) is long enough to allow the strap to bend over the metal centre, the enantioselectivity should not be decreased by switching from the αβαβ to the ααββ geometry. This phenomenon is observed only in the case of catalyst **9**, prepared with adipoyl dichloride.

Conclusion

We have reported and discussed the enantioselectivity of two closely related series of chiral bis(strapped) porphyrins, synthesised from L-prolinoyl residues. The first family, with an αβαβ geometry, with a strap crossing the porphyrin over the metal centre on each side, has been prepared to study the relationship between the steric hindrance of the strap and the observed enantiomeric excesses. For most of the catalysts under investigation, we found that congestion around the metal centre could not induce good enantioselectivities. In fact, these catalysts are poor in terms of reaction yield, and the measured enantiomeric excess does not reflect the activity of the initially designed molecule but rather of some degradation intermediates. It is important to underline that this hypothesis has already been reported for very different chiral catalysts and can now be generalised. For some well-defined catalysts, we have been able to establish that the enantioselectivity was correlated to the steric hindrance, but not always as expected. The molecules for which such a relationship exists are rather rare and deserve to be studied exhaustively. However, it must be underlined that this direct relationship between the steric hindrance and the *ee* value does not exist from a general point of view, the observed *ee* values may be influenced by many different factors. The comparison of the second series of catalysts with the first one confirms the previous explanation, namely that the enantioselectivity increases as the congestion around the metal centre decreases. Additionally, it also confirms that similar chiral inducers are more efficient with the ααββ geometry than with the αβαβ geometry. This was already known for picket structures, and is now applicable to strapped catalysts. Further studies are under investigation with these catalysts, both to evaluate them for asymmetric processes for which the catalyst is not destroyed, and to obtain a more accurate perception of their real structure in solution.

Experimental Section

General Remarks: Unless otherwise stated, the analytical facilities were provided by the Université de Bourgogne (C.S.M.) in Dijon. ^{1}H (500.13 MHz or 300.14 MHz) and ^{13}C (125.05 MHz or 75.47 MHz) NMR spectra were recorded with Bruker Avance DRX 500 or Avance 300 spectrometers and referenced to the residual protonated solvents. Mass spectra were performed with a MS/MS ZABSpec TOF spectrometer at the Université de Rennes I (C.R.M.P.O.). UV/Vis spectra were recorded with a Varian Cary 1E spectrometer. IR spectra were recorded with a Bruker IFS 66 spectrometer. All solvents (ACS for analysis) were purchased from Carlo Erba. THF was distilled from potassium metal. CH_2Cl_2 was used as received. Triethylamine and *N*-methylpiperidine were distilled from CaH_2. The starting materials were generally used as received (Acros, Aldrich) without any further purification. All reactions were performed under argon and monitored by TLC (silica, CH_2Cl_2/CH_3OH). Column flash chromatography was performed on silica gel (Merck TLC-Kieselgel 60 H, 15 μm). Enantiomeric excesses were determined by gas chromatography with a Chirasil-Dex CB as chiral capillary column (25 m × 0.25 mm, Chrompack). Compounds **1**, **4**, **5**, **6**, and **1Zn** have already been characterised. The two following porphyrins were prepared as previously reported, by reaction of a diacyl dichloride with the known α-5,15:β-10,20-tetrakis[2-(L-prolinoylamido)phenyl]porphyrin under high-dilution conditions.[14]

α-5,15:β-10,20-Bis{2,2′-[*N,N*′-bis(1,5-dioxo-1,5-pentanediyl)-L-prolinoyldiamido]diphenyl}porphyrin (2): This compound was prepared from glutaryl dichloride and obtained in 27% (37 mg) yield. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = −3.24 (m, 4 H, glut), −2.67 (s, 2 H, NH_{pyr}), −1.60 (m, 4 H, glut), −0.21 (m, 4 H, glut), 1.29 (m, 8 H, Pro), 1.45 (m, 8 H, Pro), 1.95 (m, 4 H, Pro), 2.25 (m, 4 H, Pro), 3.90 (d, ^3J = 7.3 Hz, 4 H, Pro*), 7.58 (t, ^3J = 7.3 Hz, 4 H, aro), 7.86 (t, ^3J = 7.5 Hz, 4 H, aro), 8.09 (m, 8 H, aro + β-pyr), 8.64 (s, 4 H, NHCO), 8.66 (d, ^3J = 8.2 Hz, 4 H, aro), 8.95 (s, 4 H, β-pyr). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 15.0, 24.6, 27.3, 31.4, 46.4, 60.6, 115.4, 122.4, 123.6, 129.3, 130.3, 131.9, 134.4, 139.3, 169.6, 171.6. MS (MALDI-TOF): *m*/*z* = 1254.34 $[M]^+$. $C_{74}H_{70}N_{12}O_8{\cdot}CH_3OH{\cdot}CH_2Cl_2$ (1372.40): calcd. C 66.51, H 5.58, N 12.25; found C 66.52, H 6.05, N 11.88. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}{\cdot}cm^{-1}$]) = 421 (280.1), 516 (15.1), 549 (3.4), 588 (4.6), 643 nm (1.7). IR (KBr): ν̃ = 3477 (NH), 1691, 1631 cm^{-1} (CO).

α-5,15:β-10,20-Bis{2,2′-[*N,N*′-bis(1,6-dioxo-1,6-hexanediyl)-L-prolinoyldiamido]diphenyl}porphyrin (3): This compound was prepared from the adipoyl dichloride and obtained in 11% (15 mg) yield. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = −3.95 (m, 4 H, adip), −2.52 (m, 6 H, adip + NH_{pyr}), −1.79 (m, 4 H, adip), −0.05 (m, 4 H, adip), 1.42 (m, 4 H, Pro), 1.70 (m, 4 H, Pro), 1.88 (m, 4 H, Pro), 2.29 (m, 8 H, Pro), 2.58 (m, 4 H, Pro), 4.33 (d, ^3J = 7.3 Hz, 4 H, Pro*), 7.42 (m, 8 H, aro), 7.82 (td, 4 H, ^3J = 7.7, ^4J = 2.1 Hz, aro), 8.47 (d, 4 H, ^3J = 8.1 Hz, aro), 8.67 (s, 4 H, β-pyr), 8.85 (s, 4 H, β-pyr), 9.69 (s, 4 H, NHCO). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 19.9, 24.9, 26.4, 31.2, 46.6, 60.4, 115.8, 124.2, 124.7, 129.5, 129.9, 133.4, 134.0, 135.5, 137.7, 169.9, 172.1. HR-MS (LSI-MS); *m*/*z*($C_{76}H_{75}N_{12}O_8$ [M + H]$^+$): calcd. 1283.5831; found 1283.5848. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}{\cdot}cm^{-1}$]) = 424 (288.5), 519 (15.2), 553 (3.9), 592 (4.7), 651 nm (2.2). IR (KBr): ν̃ = 3473 (NH), 1689, 1621 cm^{-1} (CO).

Typical Procedure for the Synthesis of Porphyrins 7−10: These porphyrins were synthesised according to the above-mentioned procedure, fully described for α-5,15:β-10,20-tetrakis[2-(L-prolinoylamido)-phenyl]porphyrin. Obviously, to obtain porphyrins **7**−**10**, the procedure was applied to the ααββ atropisomer, namely α-5,10:β-15,20-tetrakis[2-(L-prolinoylamido)phenyl]porphyrin. Thus, a solution of the former porphyrin, freshly prepared in 10 mL of THF, and a solution of the desired diacyl dichloride (0.264 mmol, 2.4 equiv.) in 10 mL of THF were added over 5 h with a syringe pump to a solution of NEt_3 (1.37 mL, 9.8 mmol, 90 equiv.) in 120 mL of THF placed under argon in an ice bath. The solution was stirred for 10 h. THF was removed under vacuum and the product was

chromatographed on silica gel. A CH_2Cl_2/CH_3OH mixture (98:2) was used for the elution.

α-5,10:β-15,20-Tetrakis[2-(*N*-*tert*-butoxycarbonyl-L-prolinoylamido)phenyl]porphyrin (11): *N*-Boc-L-proline (19.46 g, 90.4 mmol, 100 equiv.) was dissolved in dry THF (120 mL) under argon at −20 °C. *N*-Methylpiperidine (16.5 mL, 135 mmol, 150 equiv.) and then isobutyl chloroformate (11.15 mL, 85.9 mmol, 95 equiv.) were added. Immediately, a white precipitate appeared. A solution of TAPP ααββ (610 mg, 0.9 mmol) in 50 mL of THF, maintained at −20 °C, was then added. The reaction mixture was stirred for 3 h at this temperature and then warmed to room temperature. The mixture was filtered and the precipitate washed with diethyl ether. The solution was concentrated under vacuum and the residue was chromatographed on silica gel [elution with a CH_2Cl_2/CH_3OH (98:2)]. 1.18 g of pure product was obtained (89% yield). ^{1}H NMR (500 MHz, $CDCl_3$, 300 K): δ = −2.68 (s, 2 H, NH_{pyr}), −1.96 (s, 1 H, Pro), −1.63 (m, 1 H, Pro), −0.99 (m, 1 H, Pro), −0.44 (m, 2 H, Pro), −0.12 (m, 4 H, Pro), 0.63 (m, 4 H, Pro), 0.89 (m, 6 H, Pro), 1.17 (m, 36 H, Boc), 1.61 (s, 3 H, Pro), 2.66 (m, 2 H, Pro), 3.49 (m, 4 H, Pro*), 7.18 (s, 2 H), 7.64 (d, ^3J = 7.0 Hz, 2 H), 7.90 (m, 4 H), 8.00 (d, ^3J = 7.5 Hz, 4 H), 8.10 (s, 2 H), 8.16 (m, 4 H), 8.61 (d, ^3J = 6.5 Hz, 2 H), 8.71 (s, 2 H), 8.80 (s, 4 H, NHCO), 8.87 (s, 2 H). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 28.7, 28.9, 30.1, 43.9, 46.4, 59.5, 61.7, 114.5, 117.7, 120.6, 123.7, 124.6, 125.0, 127.3, 127.5, 130.2, 130.6, 131.8, 133.2, 134.0, 136.09, 139.1, 145.9, 152.9, 154.3, 170.5, 171.5. MS (FAB): *m*/*z* = 1463.0 $[M]^+$. HR-MS (LSI-MS); *m*/*z*($C_{84}H_{94}N_{12}NaO_{12}$ $[M + Na]^+$): calcd. 1485.7012; found 1485.6994. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 419 (308.2), 513 (16.8), 546 (3.9), 587 (4.9), 642 nm (1.7). IR (KBr): ṽ = 3383 (NH), 1698 cm^{-1} (CO). For the removal of the Boc group, **11** (0.16 g, 0.11 mmol) was dissolved in 10 mL of CH_2Cl_2 under argon. 1 mL of TFA was added. After 30 min, the solvent was removed under vacuum. The reaction was almost quantitative (0.11 g) and α-5,10:β-15,20-tetrakis[2-(L-prolinoylamido)phenyl]porphyrin used without any further purification.

α-5,10:β-15,20-Bis{2,2′-[*N,N*′-bis(1,4-dioxo-1,4-butanediyl)-L-prolinoyldiamido]diphenyl}porphyrin (7): This compound was prepared from succinyl dichloride and obtained in 45% (57 mg) yield. ^{1}H NMR (500 MHz, [D_5]pyridine, 383 K): δ = −1.78 (s, 2 H, NH), −1.52 (s, 2 H), −0.19 (s, 2 H), 0.12 (s, 2 H), 0.92 (s, 2 H), 1.08 (m, 8 H), 1.28 (m, 2 H), 1.43 (m, 2 H), 1.58 (m, 2 H), 1.79 (m, 2 H), 2.12 (m, 2 H), 2.46 (s, 2 H), 2.70 (m, 2 H), 2.85 (m, 2 H), 3.91 (m, 2 H, Pro*), 4.29 (m, 2 H, Pro*), 7.43 (t, ^3J = 7.5 Hz, 2 H, aro), 7.84 (m, 8 H), 8.04 (d, ^3J = 7.0 Hz, 2 H, aro), 8.34 (s, 2 H), 8.84 (d, ^3J = 4.5 Hz, 2 H, β-pyr), 8.89 (d, ^3J = 4.5 Hz, 2 H, β-pyr), 8.95 (s, 2 H), 9.04 (m, 4 H), 9.12 (s, 2 H), 9.63 (s, 2 H). ^{13}C NMR (500 MHz, $CDCl_3$, 300 K): δ = 24.2, 25.1, 25.7, 26.2, 27.6, 28.7, 45.2, 46.9, 60.1, 61.1, 114.2, 117.0, 119.7, 121.3, 122.4, 123.7, 130.1, 130.4, 131.5, 133.5, 135.1, 136.8, 138.1, 140.0, 169.7, 170.7. MS (FAB): *m*/*z* = 1227.50 $[M + H]^+$. $C_{72}H_{66}N_{12}O_8\cdot H_2O\cdot CH_2Cl_2$ (1330.32): calcd. C 65.91, H 5.30, N 12.63; found C 65.78, H 5.58, N 12.25. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 422 (265.2), 516 (14.4), 549 (3.5), 589 (4.9), 646 nm (1.2). IR (KBr): ṽ = 3449 (NH), 1681 cm^{-1} (CO).

α-5,10:β-15,20-Bis{2,2′-[*N,N*′-bis(1,5-dioxo-1,5-pentanediyl)-L-prolinoyldiamido]diphenyl}porphyrin (8): This compound was prepared from the glutaryl dichloride and obtained in 24% (33 mg) yield. ^{1}H NMR (300 MHz, $CDCl_3$, 300 K): δ = −3.88 (m, 2 H, glut), −3.16 (m, 4 H, glut), −2.72 (s, 2 H, NH_{pyr}), −0.63 (m, 6 H, glut), 1.55 (m, 10 H, Pro), 1.93 (m, 4 H, Pro), 2.90 (m, 10 H, Pro), 4.16 (m, 4 H, Pro*), 7.44 (t, ^3J = 7.3 Hz, 2 H, aro), 7.56 (t, ^3J = 7.3 Hz, 2 H, aro), 7.84 (m, 4 H, aro + β-pyr), 7.92 (d, ^3J = 7.6 Hz, 2 H, aro), 7.98 (d, ^3J = 7.6 Hz, 2 H, aro), 8.25 (d, ^3J = 8.2 Hz, 2 H, aro), 8.73 (d, ^3J = 7.3 Hz, 4 H, aro), 8.79 (s, 4 H, NHCO), 8.87 (m, 4 H, β-pyr), 9.01 (s, 2 H, β-pyr). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 14.6, 15.9, 20.2, 24.6, 24.7, 26.2, 26.4, 27.3, 28.8, 31.7, 33.3, 33.6, 46.1, 47.0, 60.2, 60.5, 60.9, 115.3, 116.0, 121.6, 123.0, 124.6, 125.8, 129.8, 129.9, 131.9, 134.5, 135.6, 136.6, 138.2, 138.6, 169.6, 170.2, 171.4, 172.1, 173.4, 177.6. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 424 (301.2), 518 (15.4), 551 (4.2), 591 (5.1), 646 nm (1.8). HR-MS (LSI-MS); *m*/*z*($C_{74}H_{71}N_{12}O_8$ $[M + H]^+$): calcd. 1255.5518; found 1255.5516. IR (KBr): ṽ = 3467 (NH), 1690, 1625 cm^{-1} (CO).

α-5,10:β-15,20-Bis{2,2′-[*N,N*′-bis(1,6-dioxo-1,6-hexanediyl)-L-prolinoyldiamido]diphenyl}porphyrin (9): This compound was prepared from the adipoyl dichloride and obtained in 15% (22 mg) yield. ^{1}H NMR (500 MHz, [D_6]DMSO, 423 K): δ = −2.49 (m, 6 H, adip), −2.32 (m, 2 H, NH_{pyr}), −1.34 (m, 2 H, adip), −0.55 (m, 4 H, adip), 0.89 (m, 4 H, adip), 1.21 (m, 4 H, Pro), 1.29 (m, 6 H, Pro), 1.59 (m, 6 H, Pro), 2.18 (m, 4 H, Pro), 2.29 (m, 4 H, Pro), 3.79 (m, 2 H, Pro*), 3.92 (m, 2 H, Pro*), 7.55 (t, 2 H, ^3J = 6.8 Hz, aro), 7.63 (t, ^3J = 7.3 Hz, 2 H, aro), 7.77 (s, 4 H), 7.85 (q, ^3J = 8.2 Hz, 4 H, aro), 8.05 (d, ^3J = 6.4 Hz, 2 H, aro), 8.32 (s, 4 H), 8.61 (s, 4 H), 8.69 (s, 2 H), 8.77 (s, 4 H). ^{13}C NMR (75 MHz, $CDCl_3$, 300 K): δ = 14.6, 20.5, 24.5, 24.7, 34.3, 46.5, 60.4, 60.7, 115.6, 123.5, 124.3, 124.5, 124.9, 130.1, 130.3, 130.8, 131.8, 132.4, 133.2, 133.9, 134.8, 135.0, 135.7, 136.1, 138.6, 138.8, 149.5, 172.5, 172.7. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 423 (170.3), 517 (9.6), 551 (2.8), 591 (2.9), 647 nm (0.9). HR-MS (LSI-MS); *m*/*z* ($C_{76}H_{75}N_{12}O_8$ $[M + H]^+$): calcd.1283.5831; found 1283.5835. IR (KBr): ṽ = 3477 (NH), 1694, 1636 cm^{-1} (CO).

α-5,10:β-15,20-Bis{2,2′-[*N,N*′-bis(isophthaloyl)-L-prolinoyldiamido]diphenyl}porphyrin (10): This compound was prepared from the isophthaloyl dichloride and obtained in 29% (48 mg) yield. ^{1}H NMR (500 MHz, [D_6]DMSO, 373 K): δ = −3.30 (s, 2 H, NH_{pyr}), 0.89 (m, 2 H), 1.30 (m, 4 H), 1.42 (m, 2 H), 1.62 (m, 2 H), 1.80 (m, 6 H), 1.93 (m, 4 H), 2.51 (m, 4 H), 3.90 (m, 2 H), 4.10 (m, 4 H), 5.04 (m, 4 H), 5.70 (m, 2 H), 7.58 (m, 4 H), 7.86 (m, 8 H), 8.15 (d, ^3J = 7.1 Hz, 4 H), 8.43 (m, 2 H), 8.51 (d, ^3J = 7.7 Hz, 2 H), 8.55 (s, 2 H), 8.62 (s, 2 H), 8.67 (s, 4 H). ^{13}C NMR (125 MHz, $CDCl_3$, 300 K): δ = 22.9, 23.1, 25.5, 25.6, 25.7, 26.0, 26.6, 28.9, 29.5, 30.2, 33.5, 40.3, 40.4, 40.6, 48.1, 49.5, 49.4, 50.5, 51.2, 51.4, 61.2, 62.5, 62.8, 117.7, 119.9, 120.6, 121.3, 123.3, 123.6, 123.8, 124.4, 124.8, 125.0, 126.5, 127.0, 127.2, 127.8, 128.3, 129.9, 130.2, 130.7, 135.8, 136.5, 136.7, 136.9, 138.0. 139.0, 152.8, 154.3, 157.9, 169.1, 170.4, 171.4. HR-MS (LSI-MS); *m*/*z*($C_{80}H_{66}N_{12}NaO_8$ $[M + Na]^+$): calcd. 1345.5024; found 1345.5079. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 419 (219.7), 513 (12.5), 546 (3.3), 588 (3.8), 644 nm (1.4). IR (KBr): ṽ = 3412 (NH), 1684, 1639 cm^{-1} (CO).

Typical Procedure for the Insertion of Iron Ions in Porphyrins: 50 mg of **2**−**3**, or **7**−**10** was dissolved in toluene (10 mL) inside a glove box maintained under 1 ppm of dioxygen. 2,6-Lutidine and an excess of $FeBr_2$ were added to the mixture. The solution was heated at reflux for 12 h until the reaction was complete as indicated by UV/Vis spectroscopy. The product was oxidised by air for 1 h. The solvent was removed under vacuum. The residue was dissolved in CH_2Cl_2, and washed with brine. The product was chromatographed on silica gel. A CH_2Cl_2/CH_3OH mixture (95:5) was used for the elution. The yield was almost quantitative (95%).

(α-5,15:β-10,20-Bis{2,2′-[*N,N*′-bis(1,5-dioxo-1,5-pentanediyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (2Fe): This compound was prepared from **2**. MS (MALDI-TOF): *m*/*z* = 1308.07 $[M - Cl]^+$. $C_{74}H_{68}ClFeN_{12}O_8\cdot 3CH_3OH$ (1440.83): calcd.

C 64.19, H 5.60, N 11.67; found C 64.20, H 5.31, N 10.44. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 422 (58.2), 580 nm (4.4). IR (KBr): $\tilde{\nu}$ = 3471 (NH), 1691, 1655 cm^{-1} (CO).

(α-5,15:β-10,20-Bis{2,2′-[*N,N′*-bis(1,6-dioxo-1,6-hexanediyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (3Fe): This compound was prepared from **3**. MS (MALDI-TOF): *m/z* = 1336.55 [M − Cl + H]$^+$. $C_{76}H_{72}ClFeN_{12}O_8\cdot CH_2Cl_2\cdot CHCl_3\cdot CH_3OH$ (1609.11): calcd. C 58.97, H 4.95, N 10.45; found C 58.98, H 5.53, N 10.38. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 422 (49.7), 580 nm (5.8). IR (KBr): $\tilde{\nu}$ = 3415 (NH), 1692, 1620 cm^{-1} (CO).

(α-5,10:β-15,20-Bis{2,2′-[*N,N′*-bis(1,4-dioxo-1,4-butanediyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (7Fe): This compound was prepared from **7**. MS (FAB): *m/z* = 1281.70 [M − Cl + H]$^+$. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 420 (7.6), 504 nm (1.1). IR (KBr): $\tilde{\nu}$ = 3416 (NH), 1638 cm^{-1} (CO).

(α-5,10:β-15,20-Bis{2,2′-[*N,N′*-bis(1,5-dioxo-1,5-pentanediyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (8Fe): This compound was prepared from **8**. MS (MALDI-TOF): *m/z* = 1307.54 [M − Cl]$^{+\cdot}$. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 421 (9.6), 513 nm (1.4). IR (KBr): $\tilde{\nu}$ = 3447 (NH), 1693, 1629 cm^{-1} (CO).

(α-5,10:β-15,20-Bis{2,2′-[*N,N′*-bis(1,6-dioxo-1,6-hexanediyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (9Fe): This compound was prepared from **9**. MS (MALDI-TOF): *m/z* = 1336.44 [M − Cl]$^+$. $C_{76}H_{72}ClFeN_{12}O_8\cdot CH_2Cl_2\cdot CHCl_3$ (1577.07): calcd. C 59.40, H 4.79, N 10.66; found C 59.28, H 4.95, N 10.52. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 421 (67.1), 579 nm (6.2). IR (KBr): $\tilde{\nu}$ = 3415 (NH), 1695, 1636 cm^{-1} (CO).

(α-5,10:β-15,20-Bis{2,2′-[*N,N′*-bis(isophthaloyl)-L-prolinoyldiamido]diphenyl}porphyrin)iron(III) Chloride (10Fe): This compound was prepared from **10**. MS (FAB): *m/z* = 1377.60 [M − Cl + H]$^+$. UV/Vis (CH_2Cl_2): λ (10^{-3} ε [$M^{-1}\cdot cm^{-1}$]) = 420 (36.1), 578 nm (2.6). IR (KBr): $\tilde{\nu}$ = 3394 (γNH), 1698 cm^{-1} (CO).

General Procedure for Asymmetric Olefin Epoxidation: The catalyst (1 μmol) and the olefin (1000 μmol) were dissolved in degassed CH_2Cl_2 (2 mL) in a Schlenk tube. While stirring under N_2, PhIO (100 μmol) was added in one portion. The mixture was stirred at room temperature for 30 min and then quenched with 2% PPh_3 in CH_2Cl_2. The solvent was removed under reduced pressure. Pentane was added and the mixture was filtered. Dodecane (10 μL, GC standard) was added. Enantiomeric excesses were determined by GC on a Chirasil-Dex CB capillary column. The GC conditions were as follows (epoxide, oven temperature, retention time): *p*-chlorostyrene oxide, 120 °C, 22.5 and 24.3 min; 1,2-dihydronaphthalene oxide, 130 °C, 18.9 and 20.4 min.

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