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New optically active ruthenium porphyrin catalysts for asymmetric epoxidation of styrenes

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Abstract

New C_2-chiral porphyrins bearing cyclohexyl substituents at *ortho* position of the *meso*-phenyl groups have been synthesized. Their ruthenium complexes have been used as enantioselective catalysts for the epoxidation of styrene derivatives using 2,6-dichloropyridine-N-oxide as oxidant with moderate selectivity (35% e.e. with 1,2-dihydronaphtalene).

Keywords: Ruthenium porphyrins; Enantioselectivity; Epoxidation

1. Introduction

The design of chiral metalloporphyrins that catalyze the oxidation of organic substrates continues to be a very active area in asymmetric synthesis [1,2]. Several different strategies have been adopted in which optically active groups are appended to the macrocyclic ring of metalloporphyrins [3,4]. Thus, ruthenium complexes with D_4-chiral porphyrins [5–8] and with homochiral porphyrins [9–11] have been previously used. The first homochiral porphyrin was prepared by Naruta et al. using derivatives of binaphtol [12]. In some cases, these chiral metalloporphyrins catalyze the oxidation of styrene derivatives with good enantiomeric excess but with low yield [13]. The first example of epoxidation catalysis by a homochiral ruthenium porphyrin was reported in 1996 by Gross et al. [9]. A remarkable effect of the solvent on the enantioselective styrene epoxidation was detected. Utilization of benzene (e.e.: 44%) instead of dichloromethane (e.e.: 4%) gave a major improvement of the enantioselectivity. Other variables such as the nature of the oxidant and the metal (Fe, Ru and Mn) were also reported by the same group [14]. Of the three metal complexes of the same chiral porphyrin, much better results were obtained with iron and ruthenium than with manganese. It should be emphasized that stoichiometric and catalytic reactions can yield different e.e. with the same chiral porphyrin when the oxidant is 2,6-dichloropyridine-N-oxide (Cl_2pyNO). A possible double role of the oxidant: axial ligand and oxygen transfer, may explain these differences [11]. In contrast, with oxygen or iodosylbenzene as oxidants, stoichiometric and catalytic reactions yielded similar enantiomeric excess [9,11,15]. Berkessel and Frauenkron [5] and Che and co-workers also [6,16,17] described highly efficient catalytic system for the asymmetric epoxidation of unfunctionalized olefins with a different chiral porphyrin, previously reported by Halterman and Jan [18]. When

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2,6-dichloropyridine-N-oxide was used as terminal oxidant, the epoxide of 1,2-dihydronaphtalene was obtained with enantioselectivities up to 77% and with good yield (90%) [5].

Our approach to improve the efficiency has been to exploit the strong stability of ruthenium porphyrin towards oxidizing reagents. We earlier showed that relatively flexible chiral pickets can be used to induce chiral recognition during the stoichiometric oxidation of racemic phosphines [19] or racemic amino esters [20]. In this paper, we report the synthesis of two new chiral ruthenium porphyrins and their use as catalysts for asymmetric epoxidation of styrenes.

2. Experimental

2.1. Instruments and reagents

^{1}H NMR spectra were recorded in $CDCl_3$ or CD_2Cl_2 on a Bruker AV 300P spectrometer at 300.13 MHz. Mass spectra were obtained using a ZabSpec TOF micromass. Gas chromatography (GC) analysis was performed on a VARIAN CP-3380 gas chromatography (using helium as the carrier gas) equipped with a CP-1177 injector and a flame ionization detector (FID). A WCOT fused silica Chrompack capillary column coating CP-Chirasil-Dex CB (25 m × 0.25 mm i.d.; 0.25 μm film thickness) is used. The UV-Vis spectra were obtained with a UVIKON XS spectrophotometer; IR spectra were recorded on a Bruker IFS 28 spectrophotometer. Optical rotations were measured on a Perkin-Elmer model 341 polarimeter. Preparative thin layer chromatography (TLC) was carried out on silica gel plates (Merck Silica Gel 60G) and column chromatography on silica gel Geduran Si 60.

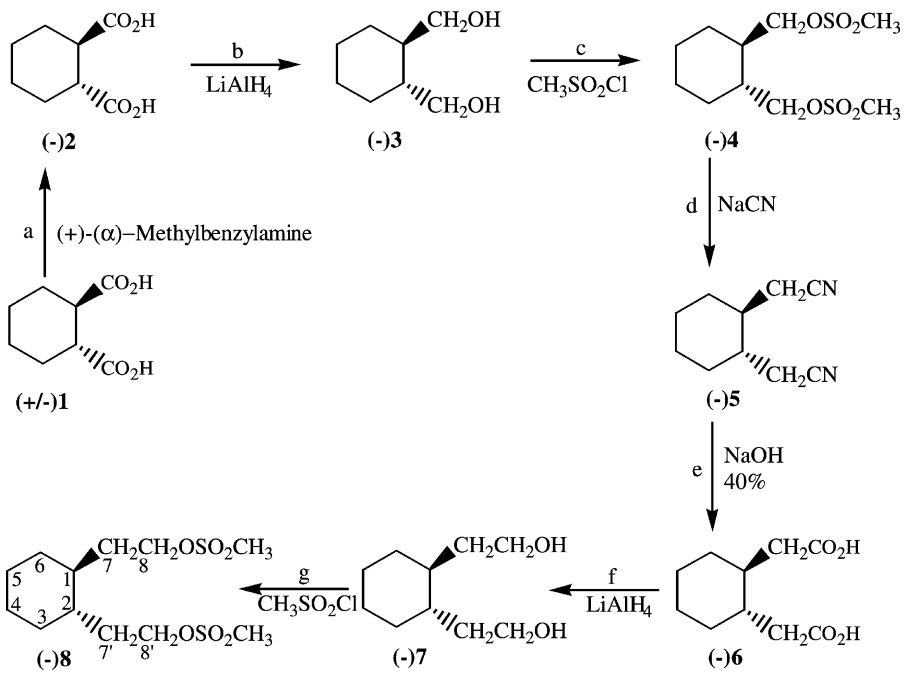
Styrene derivatives, pyrrole, 2,6-dimethoxybenzaldehyde were purchased from Aldrich, Acros and Lancaster. Before being used, chloroform, dichloromethane, benzene and dimethylsulfoxide were distilled under argon over K_2CO_3, CaH, Na/benzophenone and KOH, respectively. 2,6-Dichloropyridine-N-oxide was prepared by oxidation of 2,6-dichloropyridine with hydrogen peroxide [21]. $Ru_3(CO)_{12}$ was synthesized from $RuCl_3{\cdot}xH_2O$ (Acros) [22].

2.2. Synthesis of catalysts

2.2.1. Synthesis of optically pure cyclohexane auxiliaries

Scheme 1 shows the multistep synthesis of optically pure cyclohexane auxiliaries. Racemic *trans*-1,2-cyclohexanedicarboxylic acid (**1**) was prepared as previously reported [23]. The optical resolution of **1** was performed by the method using optically active (+)-(*R*)-α-methylbenzylamine [24]. Optically active (−)-(1*R*, 2*R*)-*trans*-1,2-cyclohexanedicarboxylic acid (**2**) $[\alpha]_D^{22}$ −20.3° (acetone) was transformed by lithium aluminum hydride reduction to the diol (**3**) $[\alpha]_D^{22}$ −19.8° (CH_2Cl_2) [23]. The bis(methanesulfonate) (**4**) $[\alpha]_D^{22}$ −25° (CH_2Cl_2) was obtained by reaction of **3** with the methanesulfonyl chloride [25]. Conversion of **4** to the dinitrile (**5**) $[\alpha]_D^{22}$ −64° (CH_2Cl_2) was realized with sodium cyanide [26]. Hydrolysis of **5** gives the diacetic acid (**6**) $[\alpha]_D^{22}$ −50° (acetone) [23,26]. The preparation of (−)-*trans*-1,2-bis(hydroxyethyl)cyclohexane (**7**) was accomplished as following a method previously reported [23]: to a solution of cold $LiAlH_4$ (3.2 g, 0.084 mol) in 75 ml dry ether under argon was added drop wise compound **6** (5.1 g, 0.025 mol) in 75 ml dry THF. The reaction mixture was heated at reflux for 3.5 h. The hydrolysis was realized by successive additions of 3.6 ml water, 3.6 ml NaOH 15% and 12 ml water. The mixture was then filtered and washed with hot THF. After evaporation, 3.2 g of compound **7** was obtained as an oily product. $[\alpha]_D^{22}$ −32° (CH_2Cl_2). ^{1}H NMR ($CDCl_3$), δ (ppm): 0.96–1.05 (m, 2H, H-4,5), 1.17–1.23 (m, 4H, H-3,4,5,6), 1.31–1.43(m, 2H, H-3,6), 1.63–1.70 (m, 2H, H-1,2), 1.73–1.88 (m, 4H, H-7,7′), 3.60–3.76 (m, 4H, H-8,8′).

The bis(methanesulfonate) ester **8** was prepared according to the literature [25]. Methanesulfonylchloride (8.5 g, 0.074 mol) in 20 ml of dry CH_2Cl_2 was slowly added to a cold solution at −20 °C of diol **7** (3.2 g, 0.0186 mol) and triethylamine (4.5 g, 0.044 mol) in 80 ml dry CH_2Cl_2 under argon. The reaction mixture was stirred 0.5 h. at −20 °C, then 2 h at room temperature. The solution was washed with 50 ml 1N HCl and twice with water. The solution was dried over $MgSO_4$ and the dichloromethane was removed. 4.45 g of an oily product was obtained. $[\alpha]_D^{22}$ −19° (CH_2Cl_2). ^{1}H NMR ($CDCl_3$), δ (ppm): 1.00–1.06 (m, 2H, H-4,5), 1.18–1.30 (m, 4H, H-3,4,5,6), 1.48–1.58



Scheme 1. Synthesis of optically pure cyclohexane auxiliaries.

(m, 2H H-3,6), 1.66–1.73 (m, 2H, H-1,2), 1.77–1.81 (m, 2H, H-7,7′), 1.98–2.08 (m, 2H, H-7,7′), 3.00 (s, 6H, H_{methyl}), 4.19–4.33 (m, 4H, H-8,8′).

2.2.2. Synthesis of H_2[(R)-trans-1,2-dimethoxycyclohexane)]$_4$TPP (**10**)

5,10,15,20-Tetrakis (2,6-dihydroxyphenyl)porphyrin (**9**)was prepared from 5,10,15,20-tetrakis(2,6-dimethoxyphenyl)porphyrin [27]. The demethylation was performed with pyridine hydrochloride [28]. The synthesis of the homochiral porphyrin **10** was realized as previously described in the literature with modifications [29]. To a solution of 100 mg (0.135 mmol) porphyrin **9** and 335 mg (2.42 mmol) of K_2CO_3 in 30 ml of DMSO at 110 °C under argon was added drop wise a solution of the dimethyl sulfonate **4** (243 mg, 0.81 mmol) in 30 ml of DMSO. After 15 h at 110 °C, the DMSO was removed under vacuum pump and the residue dissolved in 20 ml CH_2Cl_2. After several washes with water, the solution was dried and the CH_2Cl_2 evaporated. The porphyrin was purified by flash chromatography on silica gel eluted with ethyl acetate first, giving a fraction 1 with a Soret band at 434 nm, then with ethyl acetate:CH_2Cl_2 (50:50), giving a fraction 2 with a Soret band at 444 nm. Recrystallization of fraction 2 in CH_2Cl_2:pentane gave 15 mg of porphyrin **10** (yield: 10%). UV-Vis (CH_2Cl_2) λ (nm) ($\log \varepsilon$): 444 (5.39), 542 (4.03), 585 (4.00); $[\alpha]^{22}_{578}$ +2770° (CH_2Cl_2), $[\alpha]^{22}_{546}$ +1615° (CH_2Cl_2); FAB MS: *m/z* 1175.5908 $[M + H]^+$ for $C_{76}H_{79}N_4O_8$; ^{1}H NMR ($CDCl_3$), δ (ppm): −1.22 (s, 2H, $NH_{pyrrole}$), 0.72–1.54 (m, 40H, $H_{cyclohexane}$), 4.07–4.17 (m, 8H, H_{CH_2}), 4.37–4.40 (m, 8H, H_{CH_2}), 7.01, 7.15 (2d, 8.4 Hz, 8H, H_m), 7.58, 7.63 (2t, 8.3 Hz, 4H, H_p), 8.10, 8.25 (2d, 4.5 Hz, 8H, Hβ-pyrrole).

2.2.3. Synthesis of Ru(CO)[(R)-trans-1,2-dimethoxycyclohexane)]$_4$TPP (**11**)

Thirty-five milligrams (0.030 mmol) of chiral porphyrin **10** was dissolved in 15 ml of *o*-dichlorobenzene and argon was gently bubbled through the stirred solution. The flask was warmed in an oil bath to 185 °C. 95 mg (0.15 mmol) of $Ru_3(CO)_{12}$ was added in equal aliquots over 2 h. The solution was stirred at 185 °C an additional 5 h. Examination by visible spectroscopy and thin layer chromatography indicated that metalation was complete. The *o*-dichlorobenzene was removed under vacuum

pump. The resulting residue was dissolved in CH_2Cl_2 and flash chromatographied on a short silica gel column eluted with CH_2Cl_2:pentane:ether (50:49:1) to remove the decomposition and ruthenium metal. After purification on preparative gel plates eluted with CH_2Cl_2:pentane:ether (50:49:1), 11 mg (28%) of pure ruthenium porphyrin **11** was obtained. UV-Vis (CH_2Cl_2) λ (nm) ($\log \varepsilon$): 427 (4.88), 556 (4.02); IR (KBr) ν_{CO} (cm^{-1}): 1936.5; FAB MS: *m/z* 1302.4677 [M^+] for $C_{77}H_{76}N_4O_9Ru$; ^1H NMR ($CDCl_3$), δ (ppm): 0.50–1.62 (m, 40H, $H_{cyclohexane}$), 3.96–4.67 (3t+2m, 16H, H_{CH_2}), 6.92, 6.98 (2d, 8.4 Hz, 4H, H_m), 7.20 (dd, 4H, H_m), 7.57, 7.61 (2t, 8.4 Hz, 4H, H_p), 7.98, 8.06, 8.28, 8.50 (4d, 4.5 Hz, 8H, Hβ-pyrrole).

*2.2.4. Synthesis of Ru(O)$_2$[(R)-trans-1,2-dimethoxycyclohexane)]$_4$TPP (**12**)*

Ten milligrams (7.6 μmol) of ruthenium porphyrin **11** was dissolved in 2 ml CH_2Cl_2 under argon. 3.3 mg (19.2 μmol) of *m*-chloroperoxybenzoic acid was added and the color changed from red to brown. After 5 min, the solution was flash chromatographied on a basic alumina column eluted with CH_2Cl_2. The solvent was removed and the *trans*-dioxoruthenium porphyrin **12** was isolated. UV-Vis (CH_2Cl_2) λ (nm): 449, 545. Because of the instability of the product in solution, the ^1H NMR could not be recorded.

*2.2.5. Synthesis of H$_2$[(R)-trans-1,2-diethoxycyclohexane)]$_4$TPP (**13**)*

Similar procedure to chiral porphyrin **10** was employed. From 100 mg (0.134 mol) of octahydroxyphenylporphyrin **9**, 31 mg (18%) of chiral porphyrin **13** was obtained. UV-Vis (CH_2Cl_2) λ (nm) ($\log \varepsilon$): 425 (5.74), 520 (4.38), 555 (3.97), 597 (3.89); $[\alpha]^{22}_{546}$ +711° (CH_2Cl_2); FAB MS: *m/z* 1287.7150 [$M+H$]$^+$ for $C_{84}H_{95}N_4O_8$; ^1H NMR ($CDCl_3$), δ (ppm): −2.28 (s, 2H, NH_{pyrrol}), 0.47–1.48 (m, 56H, $H_{cyclohexane}$), 3.72–4.14 (3m, 16H, H_{CH_2}), 7.02, 7.13 (2d, 8.2 Hz, 8H, H_m), 7.63, 7.66 (2t, 8.2 Hz, 4H, H_p), 8.64, 8.66 (2d, 4.8 Hz, 8H, Hβ-pyrrole).

*2.2.6. Synthesis of Ru(CO)[(R)-trans-1,2-diethoxycyclohexane)]$_4$TPP (**14**)*

Similar procedure to the ruthenium porphyrin **11** was employed. From 45 mg (0.035 mmmol) of chiral porphyrin **13**, 28 mg (50%) of pure ruthenium chiral porphyrin **14** was obtained. UV-Vis (CH_2Cl_2) λ (nm) ($\log \varepsilon$): 417 (5.16), 534 (4.17); IR (KBr) ν_{CO} (cm^{-1}): 1937.1; FAB MS: *m/z* 1414.5908 [M^+] for $C_{85}H_{92}N_4O_9$; ^1H NMR ($CDCl_3$), δ (ppm): 0.36–1.67 (m, 56H, $H_{cyclohexane}$), 3.76–4.31 (4m, 16H, H_{CH_2}), 7.06 (d, 4H, H_m), 7.17 (dd, 8.2 Hz, 4H, H_m), 7.64, 7.66 (2t, 8.1 Hz, 4H, H_p), 8.47, 8.50, 8.54, 8.56 (4d, 4.8 Hz, 8H, Hβ-pyrrole).

*2.2.7. Synthesis of Ru(O)$_2$[(R)-trans-1,2-diethoxycyclohexane)]$_4$TPP (**15**)*

The same procedure as dioxoruthenium chiral porphyrin **10** was employed. From 10 mg (0.007 mmol) of ruthenium chiral porphyrin **14,** 8 mg (80%) of dioxoruthenium chiral porphyrin **15** was obtained. UV-Vis (CH_2Cl_2) λ (nm): 428, 526; IR (KBr) $\nu_{Ru\,dioxo}$ (cm^{-1}): 820.7; ^1H NMR (CD_2Cl_2), δ (ppm): 0.40–1.61 (6m, 56H, $H_{cyclohexane}$), 3.90–4.19 (3m, 16H, H_{CH_2}), 7.19, 7.27 (2d, 8.5 Hz, 8H, H_m), 7.80, 7.82 (2t, 8.5 Hz, 4H, H_p), 8.94, 8.95, (2d, 4.5 Hz, 8H, Hβ-pyrrole).

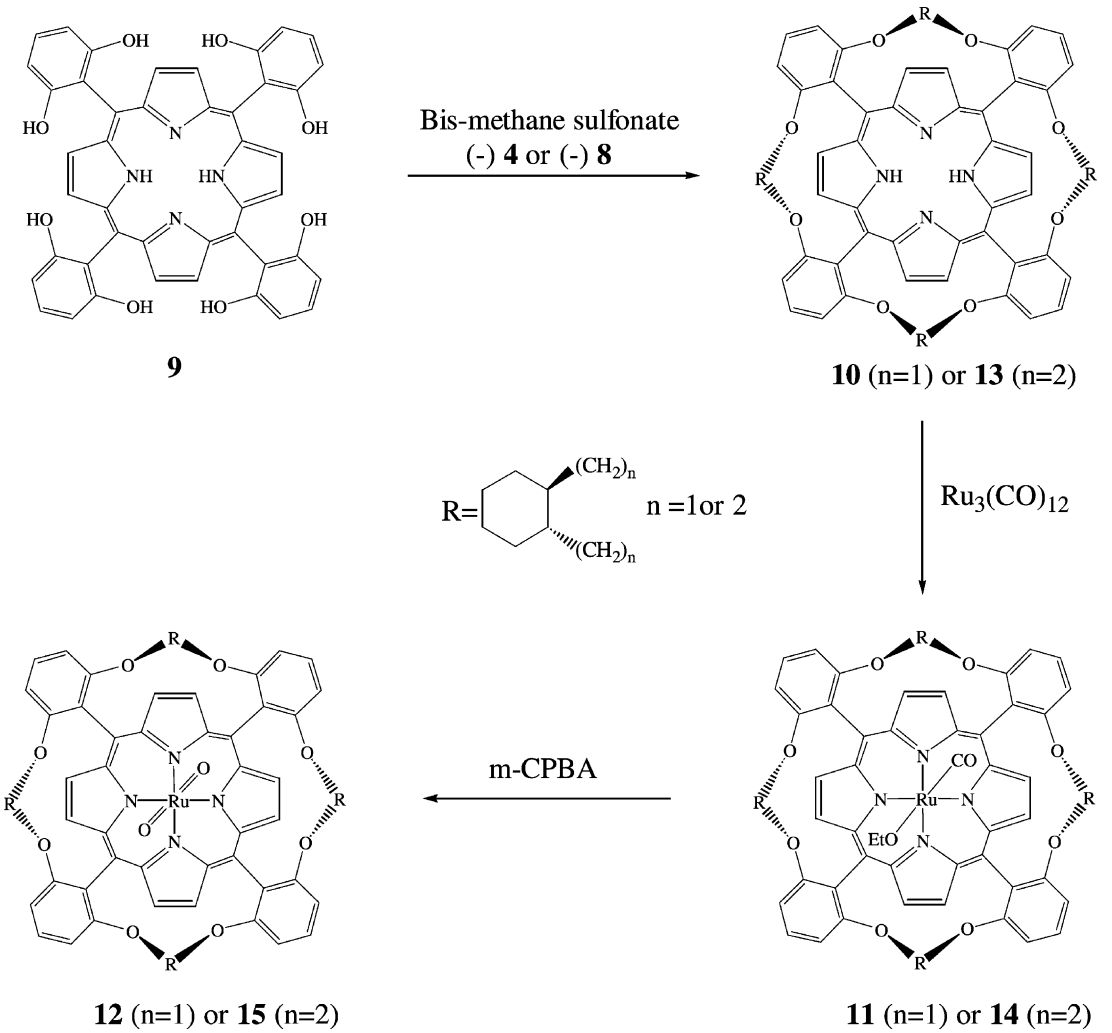
2.3. General oxidation procedure

The reactions were performed at 22 °C by adding 330 μmol of 2,6-dichloropyridine-N-oxide in one portion to a well stirred 1 ml benzene solution of 330 μmol of olefin and 1 μmol of dioxoruthenium chiral catalyst **12** or **15**. The reaction products were separated from the catalyst by chromatography on a silica gel column eluted with pentane:ether (3:1). Both chemical yield and enantiomeric excess were determined by gas chromatography using a CP-Chirasil-Dex CB capillary column.

3. Results and discussion

3.1. Syntheses

It has been proposed that a *trans*-dioxoruthenium (VI) is involved in the catalytic cycle of oxidation of double bonds using ruthenium porphyrins as catalysts [13]. Thus, the two faces of the porphyrin plane must be identical since it is necessary that the reaction should proceed inside a cavity created by the same chiral units. Such a situation was recognized in particular by Gross et al. [9], using threitol chiral units and octahydroxy porphyrins as precursors, bearing the functional OH groups in *ortho* position.



Scheme 2. Synthetic pathway of the chiral catalysts.

In this paper, we report the syntheses of two new homochiral porphyrins through the coupling reaction of *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin [30] and (1*R*,2*R*)-*trans*-1,2-bis(hydroxymethyl)cyclohexane or (1*R*,2*R*)-*trans*-1,2-bis(hydroxyethyl) cyclohexane, yielding, respectively, the two homochiral porphyrins **10** and **13**. The optically active precursor is (1*R*,2*R*)-*trans*-1,2-cyclohexanedicarboxylic acid in both cases [23]. Conversion to the diol by reduction with $LiAlH_4$ yields the expected (1*R*,2*R*)-*trans*-1,2-bis(hydroxymethyl)cyclohexane [23,31]. Then the dimesylate derivative was obtained from reaction of methanesulfonyl chloride with the diol [25,32]. The synthetic reactions are summarized in Scheme 1. Condensation of the dimesylate with *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin [30] gave the expected chiral porphyrin **10** with a low yield (10%) (Scheme 2). This reaction follows the procedure previously described by Gross and co-workers for threitol coupling with *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin [29]. Two topological isomers are possible, eclipsed and staggered, both of which have D_2 symmetry but with different location of their C_2 axes. The β-pyrrole hydrogens will appear as two doublets in the ^1H NMR

spectrum with the staggered isomer, whose in plane C_2 axes point toward phenyl *meso* positions. For the eclipsed isomer, the in plane C_2 axes bisect the pyrrole rings, resulting in two sets of singlets due to two different sets of pyrroles with equivalent hydrogens. Herein, due to steric interaction, only staggered **10** is obtained (vide infra).

Because the yield of **10** was low, a more flexible chiral picket was also synthesized through a nine-membered bridge between each *ortho* position. The route used to increase the size of the alkyl chain of the cyclohexyl compound has been previously reported [23] and is summarized in Scheme 1. The starting compound is (1*R*,2*R*)-*trans*-1,2-cyclohexane dimesylate. Addition of sodium cyanide in dimethylsulfoxide to the dimesylate gave the dicyanide derivative which is subsequently saponified to the expected diacid [26]. Following the previous procedure, the diacid is first reduced to the diol with $LiAlH_4$ and then reaction of methanesulfonyl chloride with the diol in presence yielded to the dimesylate derivative. Condensation of the dimesylate with *meso*-tetrakis(2,6-dihydroxyphenyl)porphyrin [30] gave the expected homochiral porphyrin **13** with 18% yield (Scheme 2). The Arndt–Eistert reaction is a possible way to homologate the acid but no attempt from **2** was undertaken.

The ruthenium complexes **11** and **14** (Scheme 2) were prepared by treatment of **10** and **13,** respectively, with $Ru_3(CO)_{12}$ in *o*-dichlorobenzene at 185 °C (7 h) as previously reported [33].

3.2. Characterization of compounds 10, 11, 12, 13, 14 and 15 by ^{1}H NMR

The structures of **10** and **13** were elucidated from their ^{1}H NMR spectrum, based on symmetry consideration since two D_2 isomers are possible, the staggered isomer with two perpendicular C_2 axes passing through the *meso* positions and the eclipsed isomer with two perpendicular C_2 axes bisecting the pyrrole rings. In the first case (staggered), the pyrrole protons appeared as two doublets whereas in the second case (eclipsed), the pyrrole protons appeared as two singlets. The β-pyrrole protons appeared as two doublets in the ^{1}H NMR spectrum of **10** and **13.** This is only consistent with a staggered configuration for **10** and **13**. However, the steric environment inside the cavity is very different in the two chiral porphyrins **10** and **13.** The geometry of **10** should become more restraint than the geometry in **13** since the lateral chains in **10** are quite short. This steric effect is easily detected in the ^{1}H NMR spectrum of **10** and **13**, regarding the chemical shifts of the internal NH protons, respectively, at −1.22 and −2.28 ppm (Table 1).

Table 1
Selected data of UV-Vis and ^{1}H NMR chiral porphyrins **10** and **13**

Porphyrins	UV-Vis Soret band	^{1}H NMR	
		NH-pyrrole	Hβ-pyrrole
10	444	−1.22	2d, 8.10, 8.25
13	425	−2.28	2d, 8.64, 8.66

Insertion of ruthenium decreases the D_2 symmetry to C_2 symmetry. Accordingly, the pyrrole protons of **11** and **14** appeared as four doublets, respectively, at 7.98, 8.06, 8.28, 8.50 ppm and 8.47, 8.50, 8.54, 8.56 ppm. The two ruthenium dioxo compounds **12** and **15** were also prepared and characterized by UV-Vis spectra but only compound **15** can be characterized by ^{1}H NMR (Fig. 1), due to the instability in solution of compound **12**. The β-pyrrole protons of **15** appeared as two doublets in the ^{1}H NMR, as expected from D_2 symmetry.

3.3. Catalytic epoxidation

Recently, there is a renewal of interest in reactions catalyzed by porphyrin ruthenium(II) complexes, simultaneously with the development of new chiral ruthenium porphyrins [18,29,34,35]. These reactions focus mainly on asymmetric epoxidation of olefins [5,9], although in some cases a gradual inactivation of the catalytic system is observed due to the possible formation of inactive carbonyl complexes when *trans*-dioxo(tetramesitylporphyrinato) ruthenium(VI) is used as the catalyst [36]. We now report some catalytic properties of the ruthenium complexes of the new porphyrins described above.

For all the catalytic reactions, ruthenium dioxo was first generated in situ by adding 2.5 eq. of *m*-chloroperoxybenzoic acid to the corresponding **11** and **14** complexes yielding complexes **12** and **15**, respectively. First, the reaction of styrene with

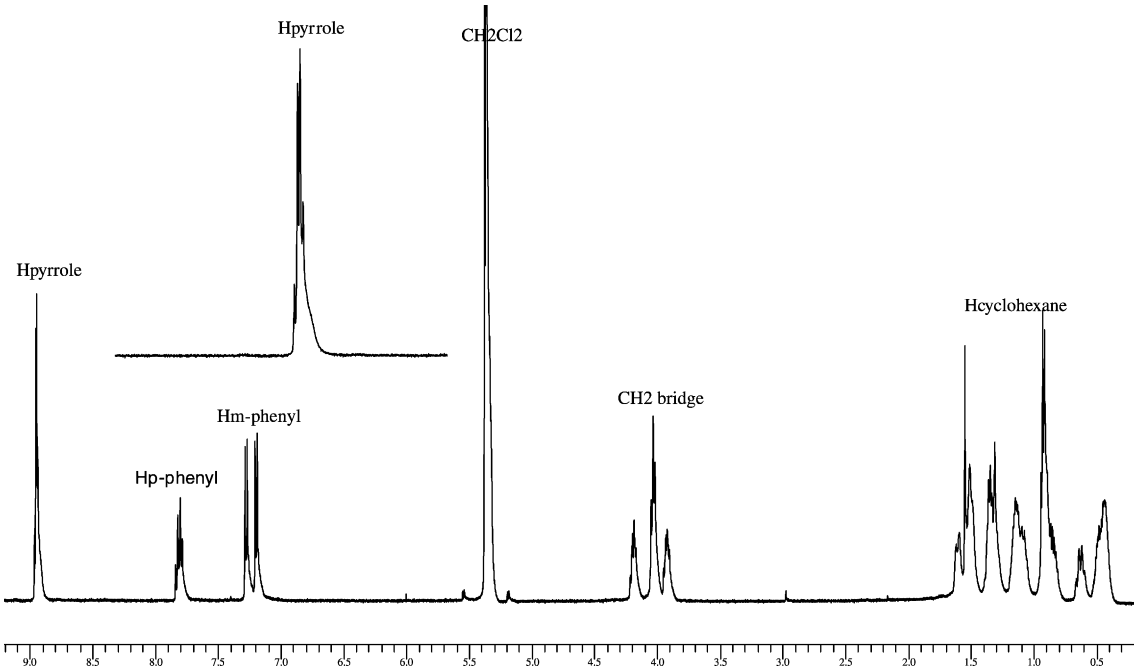


Fig. 1. ^{1}H NMR (CD_2Cl_2) spectrum of chiral dioxoruthenium porphyrin **15**.

2,6-dichloropyridine-N-oxide was examined with dioxo ruthenium porphyrin catalyst **12**. In spite of the catalytic activity, the enantioselectivity of this reaction was observed to be low (e.e.: 7.5%). Further, no significant epoxidation of 3-trifluoromethylstyrene was observed with the same oxidant, using **12** as catalyst. This feature indicates that the active site of the chiral compound **12** is not large enough to interact with the *meta*-substituted styrene. When the chiral cyclohexanes are linked by one OCH_2 group to the phenyl, very close to the center of the macrocycle, they generate steric hindrance which prevents the interaction of the dioxoruthenium group with the olefin. It should be noted that a small cavity was also suggested from the ^{1}H NMR results (vide supra). Such situation was previously observed with D_4-symmetrical tetraarylporphyrin ligands and their manganese or iron complexes [3,37,38].

Although studies implicating the importance of the electronic and steric effect on the stability and reactivity of metalloporphyrins have been published, those studies were not able to address systematic changes on the chiral position, if we except few cases [3,4]. Thus, we turned our attention to oxidation reactions catalyzed by **15**. Various substituted styrenes were investigated. The results are summarized in Table 2. At standard reaction conditions, Cl_2pyNO (330 eq. to the amount of the catalyst) was added to a benzene solution of an olefin (330 eq.) containing the dioxo ruthenium catalyst at room temperature under argon. Enantiomeric excess of the resulting epoxide was determined by chiral gas chromatography. Interestingly, the disadvantageous characteristics of the reactions with **12** are not found in the **15** catalyzed reactions of substituted styrenes with 2,6-dichloropyridine-N-oxide. Now the distance between chiral groups and active site of the catalyst is large enough to induce excellent catalytic activity and moderate enantioselectivity. Thus, introducing two OCH_2 groups in *ortho* position on the phenyl ring removes part of the steric hindrance. Since we do not have an X-ray structure determination of complexes **12** and **15**, the reason of their difference on enantioselectivity with styrene is unclear, but a slight increase of the chiral cavity above the active center during the formation of the putative high-valent ruthenium complex

Table 2
Results of aromatic alkene epoxidations[a]

Catalysts	Alkenes	Yield (%)[b]	Turnover[c]	e.e. (%)[d] (configuration[e])
$Ru(O)_2$ **12** ($n = 1$)	Styrene[f]	62	204	7.5 (*R*)
	4-Trifluoromethylstyrene	2.5	8	8 (*R*)
	3-Trifluoromethylstyrene	0	–	–
$Ru(O)_2$ **15** ($n = 2$)	Styrene	84.5	276	23 (*R*)
	2-Nitrostyrene	32.6	107	17 (*R*)
	3-Nitrostyrene	15	50	30 (*R*)
	2-Trifluoromethylstyrene	84	276	18 (*R*)
	3-Trifluoromethylstyrene	74	244	32 (*R*)
	4-Trifluoromethylstyrene	30	97	24 (*R*)
	4-Methylstyrene	43	144	27 (*R*)
	4-Bromostyrene	40	132	21 (*R*)
	Dihydronaphtalene	22	72	35 (1*S*,2*R*)
	Indene	0	–	–

[a] Reactions conditions: a mixture containing alkene (330 μmol), dichloro pyridine N-oxide (330 μmol), and catalyst (1 μmol) in degassed benzene (1 ml) was stirred at room temperature for 2.5 h.
[b] Yields are based on the amount of alkene consumed.
[c] Turnover numbers (moles of epoxides/moles of catalyst) were determined by GC.
[d] e.e.'s were determined by GC equipped with a chiral capillary column (CP-Chirasil-Dex column).
[e] Absolute configuration of styrene oxide was determined by comparison with an authentic optically pure sample. The other configurations were estimated from analogy with the chromatographic and/or spectroscopic behavior of (*R*)-styrene oxide.
[f] Phenyl acetaldehyde was also detected (2%).

[11,39] would affect the degree of the prochiral-face recognition.

These observations are very different from those obtained in the oxidation of styrenes with ruthenium complexes of similar chiral porphyrins bearing threitol units in *ortho* position instead of cyclohexane groups [29]. In the former case, when the chiral threitol units which are linked by one OCH_2 group to the phenyl, catalytic oxidation can proceed with efficiency leading to a good enantioselectivity [9].

The closely related structures of the herein dioxoruthenium complexes **12** and **15** allow a direct comparison of the catalytic results. The reactivity and the enantioselectivity are strongly dependent on the chiral cyclohexane position. The short arms in **12** induce a strong deformation of the macrocycle ring as can be seen in ^1H NMR and UV-Vis spectrum of **12** (Table 1). This gives a small chiral cavity and a weak catalytic reactivity. In contrast, when the chiral moieties are slightly moved away, they generate an environment able to induce high reactivity and moderate enantioselectivity. In this case, enantiomeric excess of 35% was obtained with dehydronaphtalene.

4. Conclusion

In conclusion, the use of cyclohexane rings as chiral entities on metalloporphyrins appears to be an attractive possibility to control both the reactivity and the enantioselectivity of olefin oxidation. The weak reactivity of the "chiral cyclohexyl short arms" gives an indication of the upper level of steric incumbrance that can be tolerated in a reactive homochiral porphyrin complex. Changing the size of the ring (cyclopentane, cyclobutane, cyclopropane) may be good alternatives, as previously reported with chiral phosphines in asymmetric hydrogenation [31,40,41].

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