Pergamon

Tetrahedron Letters, Vol. 37, No. 40, pp. 7325-7328, 1996
Copyright © 1996 Elsevier Science Ltd
Printed in Great Britain. All rights reserved
0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01599-7

First Utilization of a Homochiral Ruthenium Porphyrin as Enantioselective Epoxidation Catalyst

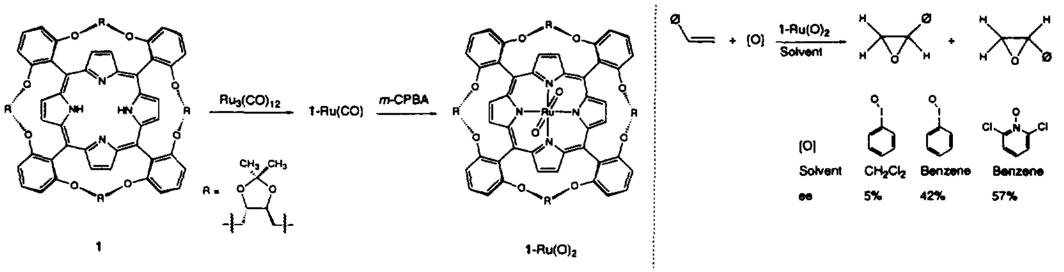
Zeev Gross,[a]* Santiago Ini,[a] Moshe Kapon,[a] and Shmuel Cohen[b]

[a] Department of Chemistry, The Technion, Israel Institute of Technology, Haifa 32000, Israel

[b] Department of Inorganic and Analytical Chemistry, The Hebrew University of Jerusalem, Jerusalem 91904, Israel

Abstract: The enantioselectivity in the first catalytic conversion of styrene to its epoxide by a homochiral ruthenium porphyrin– **1**-Ru(O)$_2$– displayed a remarkable sensitivity to the solvent and the identity of the oxidant. The latter phenomenon clearly indicates that several high valent intermediates with different selectivities participate in oxygen atom transfer from catalyst to substrate. These observations are anticipated to significantly affect research of metal complexes of other homochiral porphyrins as well. Copyright © 1996 Elsevier Science Ltd

During the last two decades synthetic metalloporphyrins were shown to be excellent catalysts for epoxidation of non activated olefins to epoxides.[1] While iron(III) and manganese(III) porphyrins are the most active catalysts, in reactions catalyzed by ruthenium porphyrins unique regioselectivities were obtained. Thus, the preference for epoxidation of *cis*- vs *trans*-olefins and the selectivity for formation of the β-oxides in cholesterol derivatives are the largest under ruthenium porphyrin catalysis.[2] The potential of homochiral metalloporphyrins as the sole chiral recognition source in catalytic epoxidation of prochiral olefins to enantiomerically enriched epoxides was first demonstrated in 1983.[3] Continuing research effort in this field concentrated on iron and manganese porphyrins, with emphasis on the superstructure of the porphyrin and on reaction conditions such as the addition of metal-coordinating ligands.[4] Although the above mentioned high regioselectivity in ruthenium porphyrin catalyzed epoxidation leads to expectations of high enantioselectivity for homochiral derivatives, the only two homochiral ruthenium porphyrin complexes reported up to date were not tested as epoxidation catalysts.[5]



Scheme 1

We have very recently reported a new homochiral porphyrin (**1** in Scheme 1),[6] which is a combination of the two most fruitful approaches in the field. It consists of the same chiral threitol units which are present in the most selective metalloporphyrin-based catalyst,[7] which are bound to both sides of the porphyrin plane in a twin coronet fashion in the present case.[8] We report now the utilization of the corresponding ruthenium complex as catalyst for enantioselective epoxidation of styrene to its epoxide, a transformation which remains a significant challenge under catalysis by chiral metal complexes.[9] The enantioselectivity of this reaction was very much dependent on the solvent and also on the primary oxidant, the oxygen atom source. The latter phenomenon clearly indicates that more than one high valent intermediate participates in oxygen atom transfer from catalyst to substrate.

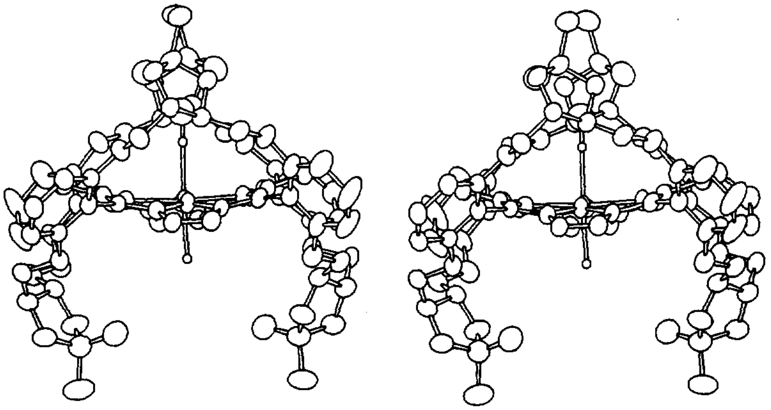


Figure 1. Ortep stereoview of the H_2O-coordinated **1**-Ru(CO) complex

The X-ray crystal structure of the ruthenium complex **1**-Ru(CO), obtained by metalation of porphyrin **1** by $Ru_3(CO)_{12}$, is presented in Figure 1.[10] It can be seen that the cavity around the metal is large enough to accommodate incoming substrates, and that the five member rings of the threitol units are arranged in a chiral fashion. The enantiomeric excess (ee) of styrene oxide (the absolute configuration of the major isomer was R(+) in all the reactions) produced in the **1**-Ru(CO) catalyzed reaction of styrene with iodosylbenzene in CH_2Cl_2 was however only 5%.[11] Utilization of the *trans*-dioxoruthenium(VI) complex **1**-$Ru(O)_2$ instead of **1**-Ru(CO) resulted in almost identical ee (4%), indicating that the active form of the catalyst is **1**-$Ru(O)_2$ in both cases.[12] A seemingly minor change of the solvent from CH_2Cl_2 to benzene resulted however in a major improvement of both the chemical yields from 11-12% to 47% and the ee's, from 4-5% to 42%. An additional increase in enantioselectivity was obtained by changing the oxygen atom source from iodosylbenzene to 2,6-dichloropyridine N-oxide, which was recently reported to be an excellent oxidant in combination with ruthenium porphyrins.[13] With **1**-Ru(CO) as catalyst, styrene oxide was produced with 58% ee and 2% conversion, and 57% ee with 16% conversion were obtained with **1**-$Ru(O)_2$. It must be emphasized that ee's of 57-58% for epoxidation of styrene are quite close to the best reported value of 69% ee by any metalloporphyrin catalyst.[7]

Presently we cannot provide any firm explanation for the remarkable positive effect of benzene, but to mention that in preliminary results obtained by utilizing the iron(III) and manganese(III) complexes of porphyrin

1 we have found a very similar effect. The ee's for the $Mn^{III}(Cl)$ and $Fe^{III}(Cl)$ complexes catalyzed epoxidation of styrene were 6% and 13%, respectively, in CH_2Cl_2, but 11% and 44% in benzene. The effect of oxidant excludes the possibility of one particular active ruthenium porphyrin intermediate in oxidation of substrate by the same catalyst. With iodosylbenzene as oxidant, the most potent intermediate has most probably the very well known *trans*-dioxoruthenium(VI) structure,[14] while different structures were suggested to be active with N-oxides as oxidants.[12] Our results provide additional support for these suggestions. In addition, assuming that in the reaction with iodosylbenzene the only pathway to products is through **1**-$Ru(O)_2$, this puts 42% ee as its limit. Accordingly, the 58% ee in the reaction with the N-oxide is either due to one different reactive form, or more probably the average of at least two forms, **1**-$Ru(O)_2$ providing the 42% ee and the other intermediate(s) being much more enantioselective. Optimization of reaction conditions in order to encourage the predominance of the more selective active form(s) of the catalyst are currently under investigation.

In summary, we report here the first utilization of a homochiral ruthenium porphyrin for enantioselective epoxidation of an olefin. We anticipate that the novel observations of this study, i.e. the remarkable solvent effect, the superior selectivity of ruthenium as compared to iron or manganese, and the effect of oxidant, will have a large impact on the research of metal complexes of other homochiral porphyrins as well.

Acknowledgment: This research was supported by the Israel Science Foundation, administered by the Israel Academy of Sciences and Humanities.

REFERENCES AND NOTES

1. Meunier, B. *Metalloporphyrins Catalyzed Oxidations*; Montanari, F., Casella, L. Eds.; Kluwer Academic Publishers: Dordrecht, 1994; chapter 1. Mansuy, D. *Coord. Chem. Rev.* **1993**, *125*, 129-141.
2. Groves, J. T.; Quinn, R. *J. Am. Chem. Soc.* **1985**, *107*, 5790-5792. Tavares, M.; Ramasseul, R.; Marchon, J.-C.; Bachet, B.; Brassy, C.; Mornon, J.-P. *J. Chem. Soc., Perkin Trans. 2* **1992**, 1321-9.
3. Groves, J. T.; Myers, R. S. *J. Am. Chem. Soc.* **1983**, *105*, 5791-5796.
4. Collman, J. P.; Zhang, X.; Lee, V. J.; Uffelman, E.; Brauman, J. I. *Science* **1993**, *261*, 1404-1411.
5. (a) Le Maux, P.; Bahri, H.; Simoneaux, G. *Inorg. Chem.* **1995**, *34*, 4691-4697, and references therein. (b) Mazzanti, M.; Marchon, J. C.; Tirowska-Tyrk, I.; Scheidt, W. R. *J. Inorg. Biochem.* **1995**, *59*, 504. (c) For *stoichiometric* epoxidation by a chiral non-porphyrinic ruthenium complex, see: Fung, W.-H.; Cheng, W.-C.; Yu, W.-Y.; Che, C.-M.; Mak, T. C. W. *J. Chem. Soc., Chem. Commun.* **1995**, 2007-8.
6. Ini, S.; Kapon, M.; Cohen, S.; Gross, Z. *Tetrahedron: Asymm.* **1996**, *7*, 659-662.
7. Collman, J. P.; Lee, V. J.; Kellen-Yuen, C. J.; Zhang, X.; Ibers, J. A.; Brauman, J. I. *J. Am. Chem. Soc.* **1995**, *117*, 692-703.
8. Naruta, Y.; Ishihara, N.; Tani, F.; Maruyama, K. *Bull. Chem. Soc. Jpn.* **1993**, *66, 158-166.*
9. Palucki, M.; Pospisil, P. J.; Zhang, W.; Jacobsen, E. N. *J. Am. Chem. Soc.* **1994**, *116*, 9333-4.
10. **1**-Ru(CO) was obtained in a procedure almost identical to that of Le Maux *et al* .[5] Starting with 40 mg (0.032 mmol) of **1** and 105 mg of $Ru_3(CO)_{12}$, 25 mg (55.2 %) of **1**-Ru(CO) were obtained as orange solid after recrystallization from $CHCl_3$ and heptane. Spectroscopic data for **1**-Ru(CO): $R_f = 0.8$ (alumina, CH_2Cl_2/EtOAc 1:1); UV-vis (Benzene, λ_{max}, nm): 428 (Soret), 554; IR (KBr): 1952 cm^{-1} (Ru-CO); ^1H NMR (400 MHz, $CDCl_3$): δ 8.35 (d, $J = 4.75$ Hz, 2H), 8.28 (d, $J = 4.82$ Hz, 2H), 8.24 (d, $J = 4.69$ Hz,

2H), 8.10 (d, J = 4.39 Hz, 2H), 7.64 (t, J = 8.52 Hz, 4H), 7.13 - 7.36 (*meta*-H, covered by solvent peak), 4.89 (d, J = 9.70 Hz, 2H), 4.83 (d, J = 10.34 Hz, 2H), 4.43 (m, 5H), 4.31 (t, J = 8.97 Hz, 2H), 4.14 (d, J = 9.77 Hz, 2H), 4.13 (d, J = 9.98 Hz, 2H), 3.79 (d, J = 8.38 Hz, 2H), 3.72 (d, J = 8.43 Hz, 3H), 2.80 (t, J = 8.54 Hz, 2H), 2.69 (t, J = 8.22 Hz, 2H), 0.90 (s, 6H), 0.82 (s, 6H), -0.28 (s, 6H), -0.45 (s, 6H). Crystals for structural determination were obtained by slow evaporation of heptane vapors into a $CHCl_3$ solution. Crystallographic data of **1**-Ru(CO): Formula unit $C_{73}H_{68}O_{18}N_4Ru\cdot 2H_2O\cdot 1.33C_2H_5OH$, crystal system hexagonal, space group $P6_2$, $a = 15.268(5)$, $c = 28.255(8)$ Å, $V = 5704.1$ Å^3, $Z = 3$, $F(000) = 2330$, $\rho_{calc} = 1.299$ gcm^{-3}, $2\theta_{max} = 140°$, radiation CuKα, $\lambda = 1.5418$ Å, $T = 293$ K, $\mu = 2.29$ mm^{-1}, LP and absorption corrections were performed, scan mode $\omega/2\theta$. Reflections collected 4109, independent reflections 3683. The Ru and part of the light atoms were found by direct methods using SHELXS86 (Sheldrick, G. M. *Acta Cryst.* **1990**, *A46*, 467). The remaining non hydrogen atoms were located by Fourier difference maps and refined against F2 using SHELXL93 (Sheldrick, G. M., SHELXL93 program for the refinement of crystal structures, University of Gottingen, Germany). The Ru and bridged porphyrin were refined anisotropically, hydrogens placed at calculated positions, whereas disordered CO, water and ethanol molecules were refined isotropically. The water and CO ligands were found statistically disordered around the Ru atom. Total number of parameters was 454, R=0.052 and wR=0.158 for 3198 Fo >4 σ (Fo). The Ru-bridged porphyrin is located on a crystallographic twofold axis. Crystallographic data for the structure reported in this paper have been submitted as supplementary material for deposition with the Cambridge Crystallographic Data Centre.

11. Reactions with iodosylbenzene were performed for 1h at 25 °C with 1 μmol catalyst, 100 μmol oxidant, and 1 mmol styrene in 2 mL of solvent. Reactions with 2,6-dichloropyridine N-oxide were performed for 3 h at 25 °C with 1 μmol catalyst, 330 μmol oxidant, and 330 μmol of styrene in 2 mL of Benzene under Ar. At the end of the reactions, the solvent, olefin, epoxide, and iodobenzene were separated from the reaction mixture by bulb to bulb vacuum transfer, leaving behind the catalyst, unreacted oxidant, and 2,6-dichloropyridine. The chemical yields and the enantiomeric excesses were determined by GC, utilizing a Cyclodex -B chiral capillary column. The absolute configuration of the major isomer in all cases was found to be R(+)-styrene oxide, by comparison to an Aldrich product. In the reactions with iodosylbenzene the reported yields are relative to the other product, iodobenzene. In the reactions with 2,6-dichloropyridine N-oxide, the conversion percentages are relative to styrene, determined by addition of a calculated amount of iodobenzene to the purified reaction mixtures.
12. **1**-Ru(O)$_2$ was prepared by *m*-CPBA oxidation of **1**-Ru(CO) in 83% yield by the procedure of Le Maux *et al*.[5] Physical data for **1**-Ru(O)$_2$: $R_f = 0.68$ (alumina, CH_2Cl_2/EtOAc 1:1); UV-vis (Benzene, λ_{max}, nm): 442 (Soret), 532; IR (KBr): disappearance of the CO stretching at 1952 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$): δ 8.65 (d, J = 4.77 Hz, 4H), 8.55 (d, J = 5.01 Hz, 4H), 7.73 (t, J = 8.52 Hz, 4H), 7.22 - 7.38 (*meta*-H covered by solvent peak), 4.89 (d, J = 10.08 Hz, 4H), 4.61 (d, J = 8.71 Hz, 4H), 4.43 (t, J = 8.88 Hz, 4H), 4.22 (d, J = 10.63 Hz, 4H), 3.75 (d, J = 8.86 Hz, 4H), 2.58 (t, J = 8.46 Hz, 4H), 0.77 (s, 12H), -0.78 (s, 12H).
13. Othake, H.; Higuchi, T.; Hirobe, M. *Heterocycles* **1995**, *40*, 867-903.
14. Groves, J. T.; Quinn, R. *Inorg. Chem.* **1984**, *23*, 3844-6.

(*Received in UK* 1 *July* 1996; *revised* 12 *August* 1996; *accepted* 15 *August* 1996)