Pergamon

Tetrahedron Letters 40 (1999) 1571–1574

TETRAHEDRON
LETTERS

Metalloporphyrin Catalyzed Asymmetric Cyclopropanation of Olefins

Zeev Gross*, Nitsa Galili, and Liliya Simkhovich

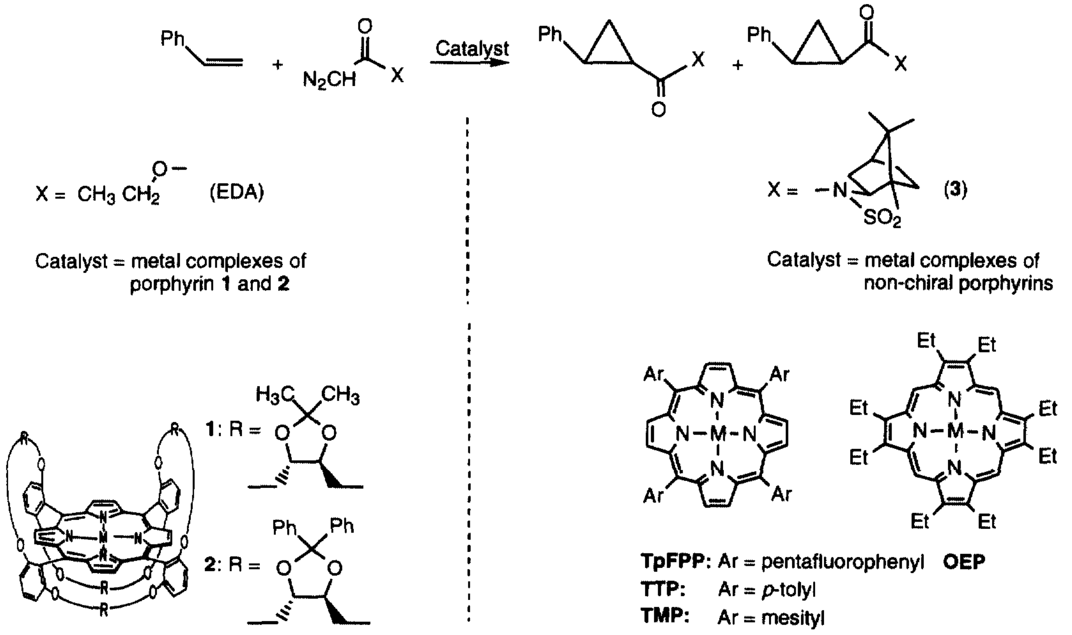
Department of Chemistry, Technion - Israel Institute of Technology, Haifa 32000, Israel

Received 9 September 1998; revised 7 December 1998; accepted 14 December 1998

Abstract: Asymmetric cyclopropanation of styrene by an enantiopure carbenoid under catalysis by simple metalloporphyrins was found to be much more efficient and selective than the alternative approach, the combination of metal complexes of enantiopure porphyrins and a non-chiral diazoester.

The main advantages of metalloporphyrins as catalysts for the cyclopropanation of olefins by diazoalkanes (carbenoids) are the relatively well defined mechanistic aspects (*vide infra*) and the exceptional *trans*/*cis* product ratio. Thus, while the reaction of styrene with ethyl diazoacetate (EDA) affords an about 2:1 mixture of the *trans*- and *cis*-cyclopropyl esters with a large range of catalysts,[1] the *trans*/*cis* product ratio with Os, Ru, Fe, and Rh porphyrins are 8.9-11.5,[2] 7.1-13.1,[3] 5.5-13,[4] and < 1,[5] respectively. With regard to asymmetric catalysis, only Rh complexes of chiral porphyrins were examined as cyclopropanation catalysts prior to 1997, with quite low enantioselection (15% ee for the *cis*-cyclopropyl ester in the reaction of styrene with EDA),[6] but chiral Ru porphyrins were more recently shown by several research groups to be much more promising.[3,7] Very large *trans*/*cis* ratios (9-23.6) were obtained, and up to 90.8% ee were achieved with the porphyrin originally introduced by Halterman.[8] Interestingly, chiral iron porphyrins—extensively utilized in oxygenation catalysis[9]—have never been tested as cyclopropanation catalysts. Also, all metalloporphyrin catalyzed cyclopropanations were performed with EDA, and the approach of using a chiral carbenoid with a non-chiral metalloporphyrin has not been examined.

Scheme 1.



We have now decided to explore the metalloporphyrin catalyzed asymmetric cyclopropanation of styrene by

0040-4039/99/$ - see front matter © 1999 Elsevier Science Ltd. All rights reserved.
PII: S0040-4039(98)02647-1

both of the above mentioned approaches (Scheme 1). The main objective was to compare the reaction of styrene with EDA in the presence of metal complexes of chiral porphyrins with the cyclopropanation by a chiral carbenoid, catalyzed by non-chiral metalloporphyrins. In both systems, several metal complexes of the same porphyrins were examined in order to obtain new mechanistic insights. As chiral ligands we took advantage of porphyrin **1** and **2** which were recently introduced by ourselves, and for which we have shown that the Fe(Cl) and Ru(CO) complexes are the most enantioselective catalysts for epoxidation of styrene.[9] The enantiopure carbenoid **3** was recently reported by Haddad and Galili, and in its $Rh_2(OAc)_4$ catalyzed reaction with styrene, a *trans/cis* product ratio of 2.1 was obtained with a diastereomeric excess (de) of 67% for the major isomer.[10]

The results for the reaction of EDA with styrene under catalysis by the various chiral metalloporphyrins are summarized in Table 1. For porphyrin **1**, the metal has several clear effects. The Rh complex is the most efficient catalyst, as reflected by the large ratio of cyclopropanation to dimerization products. However, its reaction proceeds with the lowest selectivity, as both the *trans/cis* ratio and the ee's are very low. The Ru and Fe complexes are quite similar in their efficiency and diastereoselectivities, but only with the former catalyst is a moderate ee of 58% obtained. A novel observation is that the absolute configurations of the major enantiomers in the Fe and Ru porphyrin catalyzed reactions— *trans*-(-)-(*1R,2R*) and *cis*-(-)(*1R,2S*)— are opposite to that obtained by Rh catalysis. Finally, the results obtained with the Ru complex of **2** are worse than with the corresponding complex of **1**.

Table 1. Asymmetric cyclopropanation of styrene by EDA, catalyzed by the various chiral metalloporphyrins.[a]

Entry	Porphyrin	Metal	Cyclopropanes:Olefins[b]	*trans/cis*	% ee, *trans*	%ee, *cis*
1	**1**	Ru	2.6	6.3	58 (*1R,2R*)	23 (*1R,2S*)
2	**1**	Fe	2.6	6.6	15 (*1R,2R*)	23 (*1R,2S*)
3	**1**	Rh	13.5	1.5	14 (*1S,2S*)	5 (*1S,2R*)
4	**2**	Ru	2.1	2.3	0	11 (*1S,2R*)

[a] Reaction conditions: 0.7 - 1.2 M styrene in CH_2Cl_2, styrene:EDA:catalyst = 10,0000:2000:1, addition of EDA over 6h, reaction time of 24 h at RT. [b] mostly diethyl maleate together with traces of fumarate.

The differences between the Rh and Ru porphyrin catalyzed reactions are fully consistent with previously obtained mechanistic information.[4] The key intermediates in both cases are considered to be metal-carbene complexes, but while Rh-carbene complexes are so reactive that in spite of significant efforts they have never been isolated or detected, Ru-carbene complexes are stable enough for NMR characterization during reaction. In accord with simple reactivity-selectivity considerations, catalysis by the more reactive Rh porphyrin suffers much less from the non-productive pathway— decomposition of EDA to dimerization products— but both the diastereo- and enantioselectivities are low. The opposite behaviour— quite significant amounts of byproducts together with superior selectivities— holds for the less reactive Ru porphyrin. It was further proposed that in Rh porphyrin catalysis the olefin and carbene bonds are perpendicular (due to a very early transition state), while they are almost parallel with the iron triad porphyrins (very late transition states, see also Scheme 2). The opposite enantioselectivities as a function of the metal (compare entries 1 and 2 with entry 3 of Table 1) provide significant support to this proposal, as the transition state geometries of the iron and ruthenium catalyzed reactions must be very different from that of the rhodium porphyrin. Finally, the comparison of the Ru complexes of porphyrins **1** and **2** demonstrates that the increase in the steric domain around the metal in **2**— which is highly beneficial for the enantioselective epoxidation of styrene— is disadvantageous for cyclopropanation of the same substrate. This phenomenon is most probably a reflection of the different steric demands in the reactive intermediates, the large metal-carbene moiety vs. the small metal-oxo bond. In this regard we note that the Ru complex of Halterman's porphyrin with the quite open chiral cavity is a much more selective cyclopropanation catalyst.[7a,b]

Table 2. Asymmetric cyclopropanation of styrene by **3**, catalyzed by the various non-chiral metalloporphyrins.[a]

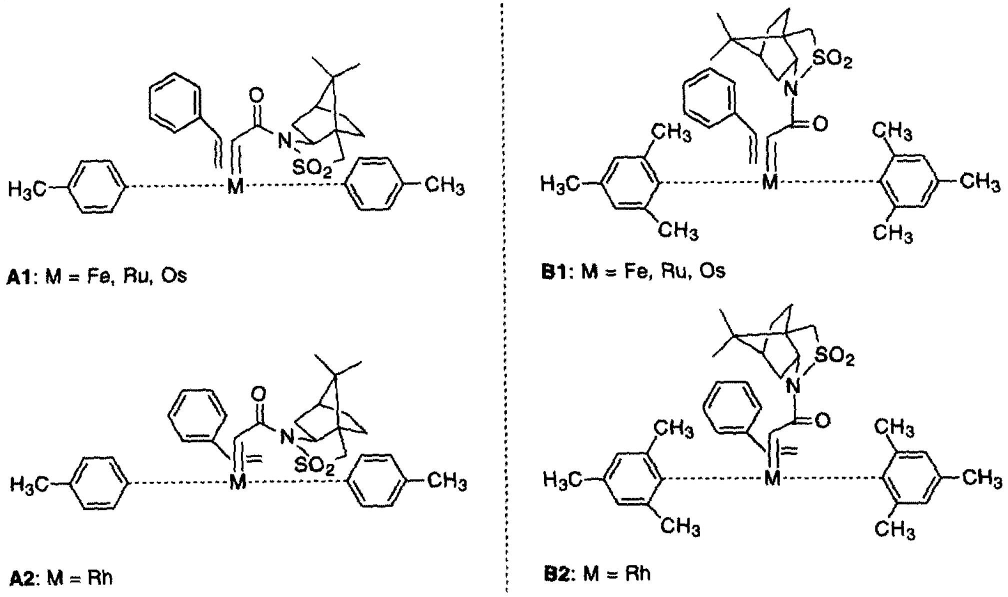
Entry	Porphyrin ligand	Metal[b]	Reaction time (h)	*trans/cis*	% de,[c] *trans*	%de,[c] *cis*	%yield[d]
1	TpFPP	Fe	24	2.7	63	65	33[e]
2	OEP	Ru	5	26.0	54	84	60[f]
3	TTP	Ru	5	14.9	57	99	60[f]
4	TMP	Ru	7 days	2.9	80*	50*	50[e]
5	OEP	Os	72	3.2	47	77	10[f]
6	TTP	Os	72	3.7	35	65	30[f]
7	TMP	Os	8 days	2.2	54*	29*	5[e]
8	TPP	Rh	72	0.7	28	74	5[e]
9	TMP	Rh	24	0.5	82*	30*	11[e]
10	$Rh_2(OAc)_4$[g]		2	2.1	67	70	67[f]

[a] Reaction conditions: 0.35 - 1.4 M styrene in CH_2Cl_2, styrene:**3**:catalyst = 2000:200:1, addition of **3** at once at RT. [b] $Fe^{III}(Cl)$ (in the presence of iron metal and 10% methanol), $Ru^{II}(CO)$, $Os^{II}(CO)$, and $Rh^{III}(I)$. [c] The absolute configurations of the major *trans*- and *cis*-isomers are (*S*,*S*) and (*S*,*R*), respectively, besides where marked by asterisks (*trans*-(*R*,*R*) and *cis*-(*R*,*S*), in entries 4, 7, and 9). [d] relative to the limiting reagent, **3**. [e] determined by GC with the aid of an internal standard. [f] isolated yield. [g] Ref. 10.

The results of the asymmetric cyclopropanation of styrene by the chiral carbenoid **3** under catalysis by non-chiral metalloporphyrins, are shown in Table 2. The comparison of entries 1 and 10 shows that the results with the simple and commercially available (TpFPP)Fe(Cl) complex are almost as good as with the most commonly used catalyst, $Rh_2(OAc)_4$. The three Ru complexes are arranged in entries 2-4 in an increasing order of steric crowding around the metal, OEP < TTP < TMP, whose effect is to slow down the reactions and to decrease the *trans/cis* product ratio from 26.0 with (OEP)Ru(CO) to only 2.9 with (TMP)Ru(CO). A clue for the unexpected decrease in the *trans/cis* ratio— with EDA an similar, but smaller effect is obtained[4]— is provided by the further details of the (TMP)Ru(CO) catalyzed reaction. The de for of the major geometric isomer is 80%, but the absolute configurations of the major diastereomers are opposite to those obtained in the reactions catalyzed by (OEP)Ru(CO) and (TTP)Ru(CO). This intriguing result repeats itself for (TMP)Os(CO) (entry 7) and (TMP)Rh(I) (entry 9), as can be seen from the comparison with entries 6 and 8, respectively.

The results clearly show that the last mentioned phenomenon is not a metal, but rather a porphyrin effect. We propose that steric crowding around the metal center affects the conformation of the carbene complexes obtained from the chiral carbenoid **3** (Scheme 2). In the ruthenium complexes of OEP and TTP both the *s-trans* (**A1** and **A2**) and the *s-cis* conformations (**B1** and **B2**) are conceivable, while the *s-trans* conformation seems much less feasible for the TMP complex because of steric repulsions of its *ortho*-methyl groups with the sulfonamide function. Accordingly, conformation **A1** shows the pathways leading to the *trans*-products by OEP and TTP complexes of the iron triad, while **B1** is relevant for the TMP complexes. Formation of the *cis*-isomers requires a horizontal flip of the olefin in both cases (not shown). Since in reactions proceeding through **A1** the interaction of the olefin with the chiral group is minimal, a large *trans/cis* ratio together with a superior de for the *cis*-product may be predicted. Indeed, entries 2 and 3 of Table 2 show that the *trans/cis* ratios and the de of the *cis*-products are very large for catalysis by (OEP)Ru(CO) and (TTP)Ru(CO). Regarding conformation **B1**, the phenyl group of the olefin clashes with the bulky group of the metal-carbene in all approaches, predicting a small *trans/cis* ratio together with large de's for both geometrical isomers, as is the case for catalysis by (TMP)Ru(CO) (entry 4). For the side-on approach— relevant to catalysis by rhodium porphyrins— the predictions according to conformations **A2** for (TPP)Rh(I) and **B2** for (TMP)Rh(I) are similar. Indeed, comparing entries 8 and 9 reveals a decrease in the *trans/cis* ratio and an increase in the de of the *trans*-isomer.

Scheme 2. Proposed transition state structures for catalysis by the iron triad (**A1**, **B1**) and rhodium (**B1**, **B2**) porphyrins (only the approaches which lead to the *trans*-isomers are shown).



We conclude that the current research provides significant insight into the mechanistic aspects which determine the selectivity in the cyclopropanation of olefins by carbenoids under metalloporphyrin catalysis. The combination of an olefin with a chiral carbenoid and catalytic amounts of a moderately encumbered metalloporphyrin leads to the conversion of the olefin to the corresponding cyclopropyl sulfonamide with up to 80% de, which can be increased to > 98% de by recrystallization of the product mixture.

Acknowledgment. This research was supported by the "Technion V.P.R. fund - P. and E. Nathan Research fund, and R. and M. Rochlin Research fund".

References

1. Doyle, M. P. in *Catalytic Asymmetric Synthesis*, Ojima, I., Ed.; VCH Publishers: New York, 1993; Chapter 3.
2. Smith, D. A.; Reynolds, D. N.; Woo, L. K. *J. Am. Chem. Soc.* **1993**, *115*, 2511.
3. Galardon, E.; Le Maux, P.; Simonneaux, G. *J. Chem. Soc., Chem. Commun.* **1997**, 927.
4. Wolf, J. R.; Hamaker, C. G.; Djukic, J.-P.; Kodadek, T.; Woo, L. K. *J. Am. Chem. Soc.* **1995**, *117*, 9194.
5. Callot, H. T.; Metz, F.; Piechocki, C. *Tetrahedron* **1982**, *38*, 2365.
6. O'Malley, S.; Kodadek, T. *Tetrahedron Lett.* **1991**, *32*, 2445. O'Malley, S.; Kodadek, T. *Organometallics* **1992**, *11*, 2299.
7. a) Lo, W.-C.; Che, C.-M.; Cheng, K.-F.; Mak, T. C. W. *J. Chem. Soc., Chem. Commun.* **1997**, 1205. b) Frauenkron, M.; Berkessel, A. *Tetrahedron Lett.* **1997**, *38*, 7175. c) Galardon, E.; Roue, S.; Le Maux, P.; Simonneaux, G. *ibid.* **1998**, *39*, 2333.
8. Halterman, R. L.; Jan, S.-T. *J. Org. Chem.* **1991**, *56*, 5253.
9. Gross, Z.; Ini, S. *J. Org. Chem.* **1997**, *62*, 5514, and references therein.
10. Haddad, N.; Galili, N. *Tetrahedron: Asymmetry* **1997**, *8*, 3367.