

Remarkable selectivity in the cyclopropanation reactions catalysed by an halogenated iron *meso*-tetraphenylporphyrin

Pietro Tagliatesta*, Alessandra Pastorini

Dipartimento di Scienze e Tecnologie Chimiche, Università degli Studi di Roma-Tor Vergata,
Via della Ricerca Scientifica, 00133 Rome, Italy

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Abstract

Iron(II) *meso*-tetra(2',6'-dichlorophenyl)porphyrin, Fe^{II}(TDCPP) catalyses the cyclopropanation of styrenes by ethyldiazoacetate with high yields and remarkable *anti* selectivities. The reaction mechanism is discussed and compared with that for the rhodium catalysts. Some evidences for the presence of a radical intermediate in the iron catalysed reactions are also discussed. © 2002 Elsevier Science B.V. All rights reserved.

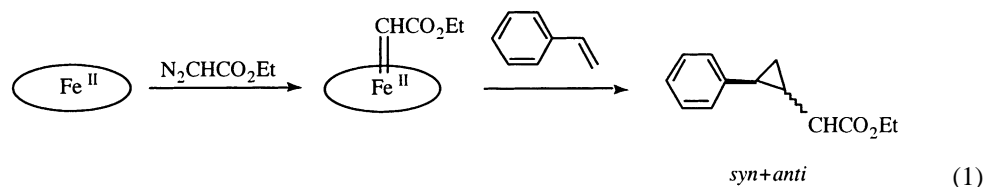
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1. Introduction

The cyclopropyl ring formation is an important reaction in organic synthesis due to the presence of such structure in a number of interesting natural products. Many methods have been developed in the past for obtaining such reaction and several copper, rhodium and osmium complexes have been reported to be efficient catalysts for the synthesis of cyclopropanes from diazocompounds [1].

Synthetic iron, rhodium and osmium porphyrins have been also reported as catalysts for the cyclopropanation reaction of simple olefins by ethyldiazoac-

tate (EDA) [2–7]. Comparing with the simple copper catalysts, like CuCl which preferentially affords the *anti* isomers, the porphyrin catalysts give interesting results in reversing the *anti/syn* ratio of the products depending on the nature of the metal. The reaction mechanism of the metalloporphyrins catalysed cyclopropanation reactions is not completely elucidated, because of the lability of the bond between the central metal and the acetate residue. The intermediate of the reaction, showed in Eq. (1), proposed, in the case of rhodium, by Callot and others [2,3] was later studied by Maxwell and Kodadek, who used the NMR spectroscopy for detecting the possible carbene species [5].



* Corresponding author. Fax: +39-6-72594754.

E-mail address: pietro.tagliatesta@uniroma2.it (P. Tagliatesta).

In a previous paper [8] we have showed the interesting results obtained on three standard olefins by us-

ing the rhodium *meso*-tetra(2',6'-dichlorophenyl)porphyrin chloride Rh(TDCPP)Cl, which affords a good improvement of the stereochemical results for styrene, cyclohexene and norbornene giving synthetically useful excesses of the *syn* isomers.

In this paper we want to report on the remarkable properties of the iron *meso*-tetra(2',6'-dichlorophenyl)porphyrin chloride, Fe(TDCPP)Cl **1**, as catalyst for the cyclopropanation of different styrenes.

2. Experimental

2.1. General

Dry chloroform (CHCl₃) was distilled over P₂O₅ under nitrogen before the use. All other reagents and solvents were of the highest analytical grade and used without further purification. Chromatographic purifications were performed on silica gel (35–70 mesh, Merck) columns. Thin-layer chromatography was carried out using Merck Kieselgel 60 F254 plates.

The free base H₂TDCPP and its iron derivative has been synthesised by literature methods [9,10]. Rh(TDCPP)Cl was synthesised as described in another paper from our laboratory [8].

All the reaction products have been previously reported in the literature [2,3] and for this work they have been synthesised by using the CuCl catalysis and separated by chromatography on silica gel column, eluting with a *n*-hexane/diethyl ether mixture.

¹H NMR spectra were recorded as CDCl₃ solutions on a Bruker AM 400 instrument using tetramethylsilane (TMS) as an internal standard. Electronic absorption spectra of the compounds were recorded on a Varian Cary 50 Scan UV-Vis spectrophotometer. FAB Mass spectra were measured on a VG-Quattro spectrometer using *m*-nitrobenzyl alcohol (NBA) as a matrix.

3. Reaction conditions

(a) Ethyl diazoacetate, 0.45 ml (5.1×10^{-3} mol) and styrene, 1.4 ml (1.28×10^{-2} mol), were added under stirring to 25 ml of dry CHCl₃. The solution was degassed bubbling argon for 15 min, after that 5 mg of Fe(TDCPP)Cl (5.1×10^{-6} mol)

and 9.6 mg of cobaltocene (5.1×10^{-5} mol) were added under nitrogen at room temperature. At the end of the reaction, dodecane was added as internal standard.

- (b) Ethyl diazoacetate, 0.45 ml (5.1×10^{-3} mol) and styrene, 1.4 ml (1.28×10^{-2} mol), were added under stirring to 25 ml of dry CHCl₃ containing 0.12 ml of DMSO. The solution was degassed bubbling argon for 15 min, after that 5 mg of Fe(TDCPP)Cl (5.1×10^{-6} mol) and 9.6 mg of cobaltocene (5.1×10^{-5} mol) were added under nitrogen at room temperature. At the end of the reaction, dodecane was added as internal standard.
- (c) Ethyl diazoacetate, 0.45 ml (5.1×10^{-3} mol) and styrene, 1.4 ml (1.28×10^{-2} mol), were added under stirring to 25 ml of dry CHCl₃. The solution was degassed bubbling argon for 15 min, after that 5 mg of Fe(TDCPP)Cl (5.1×10^{-6} mol) was added under nitrogen at room temperature. At the end of the reaction, dodecane was added as internal standard.
- (d) Ethyl diazoacetate, 0.45 ml (5.1×10^{-3} mol) and styrene, 1.4 ml (1.28×10^{-2} mol), were added under stirring to 25 ml of dry CHCl₃ containing 0.12 ml of DMSO. Rh(TDCPP)Cl, 3:8 mg (5.1×10^{-6} mol) was added under nitrogen and the solution was refluxed for 2 h. At the end of the reaction, dodecane was added as internal standard.
- (e) Ethyl diazoacetate, 0.45 ml (5.1×10^{-3} mol) and styrene, 1.4 ml (1.28×10^{-2} mol), were added under stirring to 25 ml of dry CHCl₃ containing mg (5.1×10^{-4} mol) of Rh(TDCPP)Cl, 3:8 mg (5.1×10^{-6} mol) was added under nitrogen and the solution was refluxed for 2 h. At the end of the reaction, dodecane was added as internal standard.

The products yields were based on ethyl diazoacetate and determined by GC analysis performed on a Carlo Erba HRGC 5160 instrument equipped with a 30 m Supelco SPB-35 capillary column and a FID detector. Chemical yields were reproducible within $\pm 2\%$ for multiple experiments.

4. Results and discussion

In Fig. 1 the structure of the catalyst used for this work is reported. The starting porphyrin free base

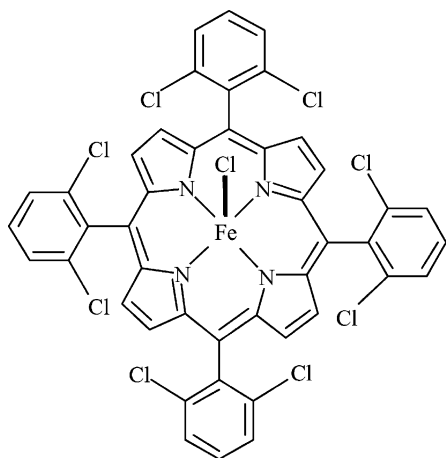


Fig. 1. Molecular structure of the catalyst.

is easily available in grams quantity from new and cheaper method of preparation [9] and the stability of its iron(III) derivative, under the reaction conditions, is excellent. Such catalyst has been recycled at least three times with no substantial change in the

observed yields and stereochemical results. The catalytic cyclopropanation reactions were carried out in neat CHCl_3 , in CHCl_3 containing 0.5% of DMSO and in CHCl_3 in the presence of cobaltocene, CoCp_2 (10 times molar ratio versus porphyrin) as cocatalyst and under strictly anaerobic conditions. The active intermediate of the reaction has been previously attributed to an iron(II) carbene intermediate [11] which, in our case, can be formed through a chemical reduction by CoCp_2 and subsequent complexation or generated in situ by the direct reaction with EDA. The observation of the ethyl diazoacetate direct reduction of the Fe(III) porphyrins has been previously reported by Kodadek and coworkers for the iron *meso*-tetra(2',3',4',5',6'-pentafluorophenyl)porphyrin chloride [11].

This fact was attributed to the presence of electron-withdrawing groups on the phenyl rings which make easier the reduction of the iron by the ethyl diazoacetate [11].

The results reported in Table 1 show that the cyclopropanes are the major products of the reaction apart from β -methylstyrene, which gives only the diethylmaleates as by-products [12].

Table 1
Catalytic cyclopropanation of olefins with ethyl diazoacetate by Fe^{II} (TDCPP) as catalyst

Entries	Olefin	Catalyst ^a	Reaction time (h) ^b	Ratio of <i>trans/cis</i> products (reaction yield) ^c	Ratio of cyclopropane/diethylmaleate products
1	Styrene	$\text{Fe}(\text{TDCPP})\text{Cl}$	2	20 (80)	82:12
2		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{CoCp}_2$	1.5	30 (97)	98:2
3		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{DMSO}$	3	35 (88)	88:12
4	<i>p</i> -Chlorostyrene	$\text{Fe}(\text{TDCPP})\text{Cl}$	0.5	13 (80)	80:20
5		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{CoCp}_2$	0.5	78 (94)	94:6
6		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{DMSO}$	2	37 (75)	74:26
7	<i>p</i> -Methoxystyrene	$\text{Fe}(\text{TDCPP})\text{Cl}$	6	8.3 (85)	^d
8		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{CoCp}_2$	2	50 (95)	^d
9		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{DMSO}$	16	4.0 (95)	96:4
10	α -Methylstyrene	$\text{Fe}(\text{TDCPP})\text{Cl}$	8	1.6 (80)	^d
11		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{CoCp}_2$	3	2.0 (95)	^d
12		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{DMSO}$	18	2.4 (70)	94:6
13	β -Methylstyrene	$\text{Fe}(\text{TDCPP})\text{Cl}$	18	–	^e
14		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{CoCp}_2$	16	–	^e
15		$\text{Fe}(\text{TDCPP})\text{Cl}/\text{DMSO}$	18	–	^e

^a 0.03–0.07% catalyst.

^b Room temperature.

^c Determined by GC analysis and based on EDA.

^d Trace diethylmaleate observed.

^e Only diethylmaleate observed.

In neat CHCl_3 , under nitrogen and at room temperature, the reaction rate for styrene, **2** and *p*-chloro styrene, **3** is very high even without CoCp_2 .

The evolution of molecular nitrogen starts after 15–30 s and in 0.5–1.5 h the reactions go to completion giving high yields (80–85% based on EDA) and remarkable selectivities. The *syn/anti* ratio for both the substrates is higher using the CoCp_2 and in the case of **2** goes from 20 to 30 (entries 1 and 2) while for **3** from 13 to 78 (entries 4 and 5). The behaviour is different for *p*-methoxystyrene, **4** and α -methylstyrene **5**, which show the lack of any visible nitrogen evolution when the reaction is performed without the cocatalyst, giving an acceptable yield in cyclopropanes after 6–8 h. For such substrates, in the presence of the cocatalyst the reaction rates increase again and the evolution of gas is clearly visible. In the case of **4**, the isomeric ratio is higher in the presence of the cocatalyst than without and reaches the value of 50 (entry 8) while for **5** is slightly affected by the presence of CoCp_2 , remaining in the range of 1.6–2.0 (entries 10 and 11).

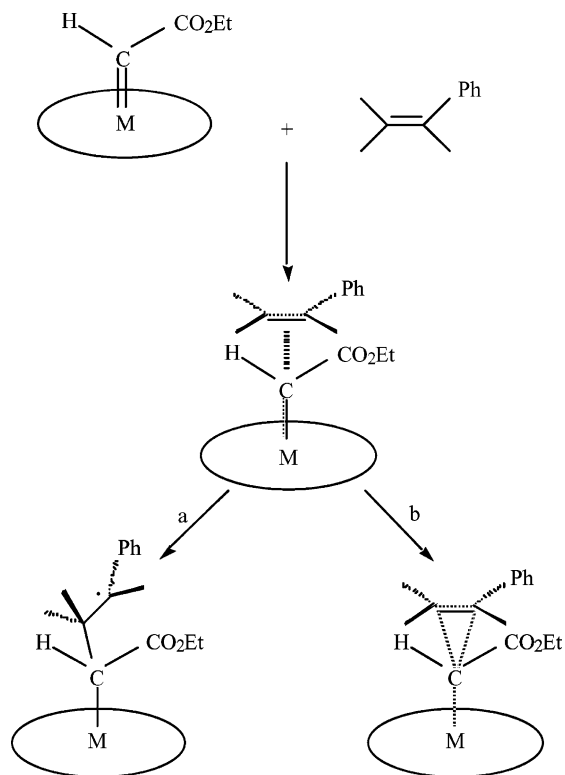
As reported by other authors [6,7,11], the effect of the cocatalyst is well known but still remains unclear. In our experiments, the amounts of the catalyst and/or the cocatalyst do not affect the isomeric ratios. To the best of our knowledge, the selectivities obtained for the first three substrates are the highest ever obtained using metalloporphyrins as catalysts and useful from the synthetic view point [11].

In Table 1 we also present the data obtained in the presence of 0.5% of DMSO which affect the reaction pathway, enhancing the *anti/syn* ratios in the case of **2** and **3** (entries 3, 6) when compared with the results obtained in neat CHCl_3 . In our opinion this fact could be due to the presence of two separate mechanisms involved in the cyclopropanation of the aromatic olefins. According to Kodadek, for rhodium catalysis [12], the addition of the carbene residue to the styrene double bond, involves the presence of a synchronous transfer mechanism, giving the *syn* or the *anti* isomer as preferred product, depending from the bulky substituents on the porphyrins skeleton.

The secondary kinetic isotope effect determined using styrene and d_8 -styrene in a competitive experiment was found to be 1.0 ± 0.07 suggesting a very early transition state.

For iron catalysts, an asynchronous transfer can be present and, in this case, the intermediate after rotation along the carbon–carbon bond, can give a mixture of the *syn* and *anti* isomers. This interpretation is in agreement with that reported by Kodadek [11] who found a secondary kinetic isotope effect of 0.87 ± 0.07 , suggesting a rehybridisation of the olefin in the transition state. This proposal implied the presence of a carbocation or radical species which is formed in a non-concerted insertion of the acetate residue into the olefin. In Scheme 1 we report a tentative representation of the two transition states, the first one involving, in our opinion, a radical species.

This mechanism is reminiscent of that reported for the epoxidation of *cis*-stilbene catalysed by manganese porphyrins [13], which involves two different routes, depending on the electron withdrawing substituents on the macrocycle ring. In our opinion, for the iron catalysis, the rotation can depend on the steric hindrance of the substituents on the porphyrin ring and also on the relative stability of the radical intermediates. In fact,



Scheme 1.

the substrate **5** which has a methyl in the α -position, gives no interesting stereochemical results and this fact supports the substantial absence of differences in the two transition states generated by the rotation along the carbon–carbon bond. Another observation which supports our interpretation, derives from the fact that only rhodium porphyrins give the carbene transfer for both aromatic and aliphatic substrates. In the case of iron, only styrenes undergo to the formation of cyclopropanes because the radical intermediate can be stabilised by the resonance effect.

The effect of the DMSO seems to be related to the coupling interaction of the unpaired electron of the radical with the lone pair of the sulfoxide, stabilizing the radical intermediate. This coupling could be depressed by the methoxy substituent in *p*-methoxystyrene which destabilises the radical intermediate. This is also in agreement with other observations on the reaction performed on styrene. Using Rh(TDCPP)Cl as catalyst, in neat CHCl_3 , we have been able to obtain an *anti/syn* ratio of 0.58 while with 0.5% of DMSO the result increases to 3.0. This last result is also in agreement with value of 2.8 obtained adding 1% of 3-carbamoyl tempo, a free radical, in the reaction media instead of DMSO and strongly support our interpretation of the obtained data.

5. Conclusions

We have reported that the cyclopropanation reaction catalysed by Fe^{II} (TDCPP) gives, for some olefins, the highest *anti/syn* ratios ever reported before and that the difference in the results obtained by using rhodium or iron porphyrins can be due to the presence of two different mechanisms in the carbene transfer from the metal to the double bond. In the case of rhodium the carbene transfer is concerted whilst this is not the case for iron porphyrins which show a radicaloid intermediate.

6. Synopsis

Iron(II) *meso*-tetra(2',6'-dichlorophenyl)porphyrin, affords the highest *anti/syn* ratios ever obtained for the ethyl diazoacetate cyclopropanation reactions of some olefins.

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