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A Novel Chiral Ruthenium Porphyrin as Highly Efficient and Selective Catalyst for Asymmetric Cyclopropanations

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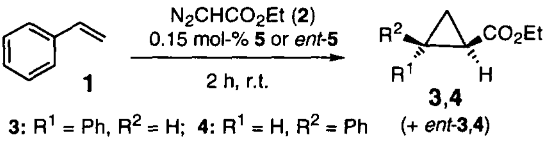
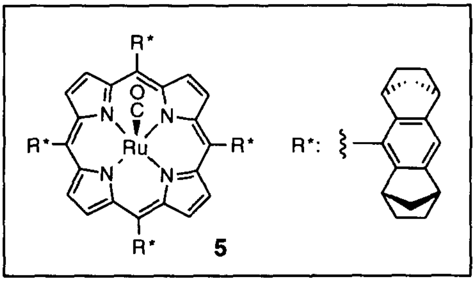
Abstract: The enantiomerically pure ruthenium carbonyl porphyrin **5** is an extremely active and selective catalyst for the asymmetric cyclopropanation of olefins with diazo compounds. At a catalyst loading of only 0.15 mol-%, quantitative yields, excellent diastereoselectivities (*trans:cis* 96:4) and high enantiomeric excesses (up to 91 %) of the product cyclopropanes were achieved in the reaction of styrene with ethyl diazoacetate. © 1997 Elsevier Science Ltd.

Within the last decade, asymmetric catalysis has evolved into one of the most powerful methods for the synthesis of enantiomerically pure compounds. In the field of transition metal-catalyzed asymmetric cyclopropanation of prochiral olefins, most of the successful catalysts[1-3] are complexes of copper, rhodium or cobalt. In contrast, only two ruthenium-based chiral catalysts have been reported so far, namely the Ru-pybox system developed by Nishiyama[4] and the chiral ruthenium porphyrin described by Simonneaux[5]. Whereas the enantiomeric excesses achieved in the latter case turned out to be moderate, the Nishiyama catalyst afforded cyclopropanes with remarkable diastereo- and enantioselectivities. For example, when styrene (**1**) was treated with ethyl diazoacetate (**2**), the corresponding cyclopropanes **3** and **4** could be obtained in 82 % yield, at a *trans:cis* (**3**:**4**) ratio of 94:6, and enantiomeric excesses up to 91 %, albeit at relatively high catalyst loadings (2 mol-%)[4b)]. We recently described the synthesis of the chiral ruthenium carbonyl porphyrin **5**, starting from the corresponding D_4-symmetric porphyrin first described by Halterman[6], and the excellent performance of **5** as a catalyst for the asymmetric epoxidation of olefins[7]. We reasoned that **5** might also catalyze the asymmetric cyclopropanation of olefins. As it turned out, **5** proved to be an extremely active and selective catalyst for this purpose.





In a typical cyclopropanation experiment, 0.4 mg (315 nmol) of the ruthenium carbonyl complex **5** and 33 mg (315 μmol) of styrene were dissolved in 2 ml of 1,2-dichloroethane at room temperature under argon. To this solution, 23.9 mg (210 μmol) of ethyl diazoacetate, dissolved in 2 ml of 1,2-dichloroethane, were added within 2 h by means of a syringe pump. The reaction proceeded smoothly, and the diazo compound was completely consumed upon completion of the addition. 1,2-Dibromobenzene (74.3 mg, 315 μmol) was added as internal standard, and the reaction mixture was subjected to GC analysis. The results are summarized in Table 1: With as little as 0.15 mol-% of catalyst (rel. to ethyl diazoacetate), the cyclopropanes were formed in quantitative yield (entries 1-3,5). When the catalyst loading was reduced by a factor of 100 (to 15 ppm), a 8 %-yield of cyclopropanes was still obtained (Table 1, entry 4). This shows that under our (non-optimized) conditions, at least ca. 5300 catalyst turnovers were achieved. The cyclopropanes were formed in an excellent *trans:cis*-ratio of 96:4.

To the best of our knowledge, this is the highest diastereoselectivity ever reported for the cyclopropanation of styrene using ethyl diazoacetate as the carbene source. When benzene was used as the solvent, the chemical yields were still quantitative, but the *trans:cis*-ratio dropped slightly to 91:9 (Table 1, entry 5). Interestingly, whereas the enantiomeric excess of the *trans*-cyclopropane remained basically unaffected [84 % ee of the (-)-enantiomer], the (+)-enantiomer of the *cis*-cyclopropane was formed predominantly in benzene (Table 1, entry 5), as opposed to the (-)-enantiomer in 1,2-dichloroethane (Table 1, entries 1,3). Running the reaction at lower temperature resulted in an increase of enantioselectivity. For example, at 0 °C, the *trans*-cyclopropane **3** was formed with an ee of 91 % (Table 1, entry 3). In all cases, not more than trace amounts of diethyl fumarate/maleate could be detected.

Table 1: Asymmetric cyclopropanation of styrene with ethyl diazoacetate, using **5** (*ent*-**5**) as catalyst.

entry	catalyst	yield[a]	*trans:cis*[b]	% ee[b] **3** (*trans*)	% ee[b] **4** (*cis*)
1	**5**	quant.	96:4	87 [1*R*,2*R* (-)]	15 [1*R*,2*S* (-)]
2	*ent*-**5**	quant.	96:4	87 [1*S*,2*S* (+)]	16 [1*S*,2*R* (+)]
3	**5**	quant.[c]	95:5	91 [1*R*,2*R* (-)]	27 [1*R*,2*S* (-)]
4	**5**	8[d]	n.d.	63 [1*R*,2*R* (-)]	n.d.
5	**5**	quant.[e]	91:9	84 [1*R*,2*R* (-)]	26 [1*S*,2*R* (+)]

a) Based on ethyl diazoacetate consumed in the course of the reaction.

b) Determined by GC using a heptakis(2,6-di-O-methyl-3-O-pentyl-β-cyclodextrin) column. The absolute configurations of the major enantiomers are based on the signs of rotation of isolated mixtures of **3**/*ent*-**3**, **4**/*ent*-**4** and ref. 8, respectively.

c) The reaction was run at 0 °C.

d) A substrate (styrene):catalyst ratio of 100.000:1 was used.

e) Benzene was used as solvent.

In summary, we herein report the first highly efficient and selective ruthenium porphyrin catalyst for asymmetric cyclopropanations. Further studies concerning e.g. the substrate spectrum of this promising new catalyst are currently under way.

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