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ASYMMETRIC CYCLOPROPANATION OF ALKENES CATALYZED BY A "CHIRAL WALL" PORPHYRIN

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Key Words: Asymmetric Catalysis; Cyclopropanation; Rhodium; Porphyrin; Ethyl Diazoacetate

Abstract: The iodorhodium derivative of the "chiral wall" porphyrin is shown to be an extremely active catalyst for the asymmetric cyclopropanation of alkenes by ethyl diazoacetate. Moderate enantioselectivities are observed. The reaction is unusual in that it provides *syn* cyclopropanes as the major product.

Cyclopropanes are found in a number of interesting natural products and are versatile synthetic intermediates. Not surprisingly, the development of efficient methods for the asymmetric synthesis of these compounds has attracted considerable attention in the last few years[1,2]. Many investigators have focused on the development of catalytic asymmetric alkene cyclopropanation reactions, since this provides a potentially general and flexible route to chiral cyclopropanes[3]. The major advances in this area have been in the development of chiral metal catalysts for the decomposition of diazoesters in the presence of alkenes. While some success has been achieved with cobalt-based complexes[4], the best systems reported to date, developed by Aratani[5], Pfaltz[6], Masamune[7], and Evans[8], employ copper. The Aratani system is based on a family of chiral ligands synthesized via Schiff base formation between salicylaldehyde and various optically active 1,2 amino alcohols. By carefully optimizing ligand/substrate/diazoester combinations, e.e.'s of 40-95% can be realized with reasonable chemical efficiency. The Pfaltz system, which employs semicorrin ligands, gives higher e.e.'s with some simple olefins such as styrene and looks very promising. Masamune reports comparable enantioselectivities with the related bis-oxazoline complexes and work in Evans' group has shown outstanding e.e's can be achieved with another bis-oxazoline ligand. More recently, Doyle and co-workers have reported[9] new rhodium catalysts that also provide very good enantioselectivities. An important point is that all of these systems provide mixtures of the *syn* and *anti* cyclopropanes with the *anti* compound as the major product. There is at present no catalytic method for the asymmetric synthesis of *syn*-substituted cyclopropanes[10].

Given this gap in synthetic methodology, we were intrigued by the report of Callot and co-workers that iodorhodium porphyrins catalyze the reaction between many simple alkenes and ethyl diazoacetate quite efficiently and generally provide the *syn* isomer as the major product[11,12]. It was noted by these workers that the *syn:anti* ratio increased when bulkier porphyrins, such as tetramesitylporphyrin (TMP), were

employed. Therefore, we decided to develop an asymmetric version of this process. In this communication, we report our initial efforts towards this end.

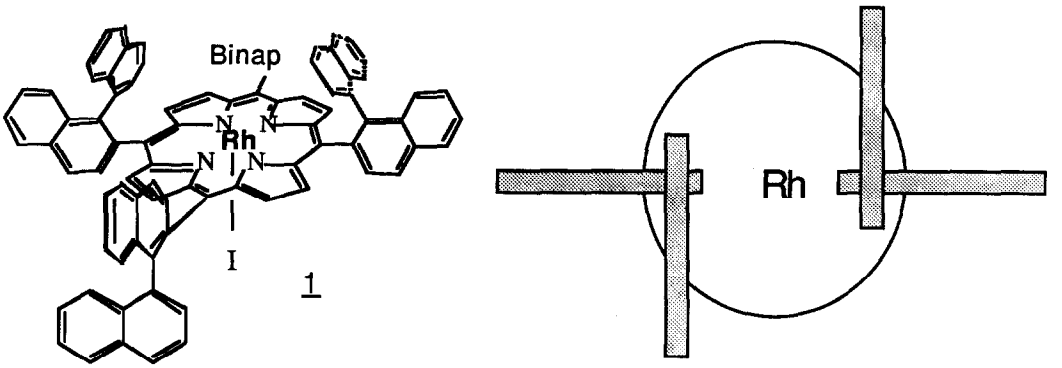
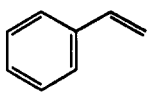
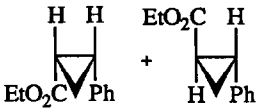
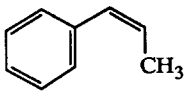
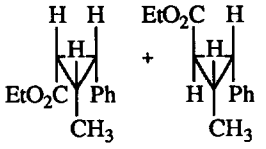
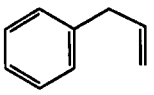
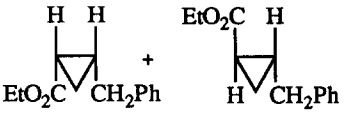


Figure 1: Structure (left) and schematic top view (right) of the iodorhodium "chiral wall" porphyrin.

We have previously synthesized a novel chiral porphyrin bearing optically pure binaphthyl groups directly appended to the macrocycle[13]. The manganese derivative of this "chiral wall" porphyrin is a robust, moderately selective asymmetric epoxidation catalyst. Therefore, we decided to investigate the activity of the iodorhodium chiral wall porphyrin, iodo(5α,10β,15α,20β,-tetrakis[(*R*)-1,1'-binaphth-2-yl]-porphyrinato)rhodium(III)[11,14] (1 in Figure 1) in the cyclopropanation reaction. Gratifyingly, porphyrin 1 proved to be an extremely active catalyst for alkene cyclopropanation in the presence of ethyldiazoacetate. With styrene as the substrate, over 3000 catalyst turnovers were observed within a few hours. The *syn* cyclopropane was the major product in all cases. The observed enantioselectivities for the few substrates tested so far are moderate to poor (Table 1). More extensive studies are underway.

Chiral wall porphyrin 1 is the first catalyst for the selective production of optically active *syn* cyclopropanes. However, although the chemical efficiency of the system is outstanding, the e.e.'s observed to date are too low to be of synthetic utility and must be improved substantially. Since the nature of the reactive intermediate and the mechanism of carbene transfer from the metal to the olefin are unknown, it is difficult to predict with certainty what sort of modifications to the skeleton of 1 will provide higher e.e.'s. However, it is reasonable to speculate that the reaction of ethyldiazoacetate with 1 provides a metallocarbene[15], at least transiently[12,16], and that the alkene approaches perpendicular to the porphyrin plane with the substituent(s) pointed away from the macrocycle[17]. In this view, the low enantioselectivities are due to insufficient hindrance of the undesired approach in the "slot" defined by the naphthyl groups. A solution based on this hypothesis would be to place a bulky group on top of the "walls" that would seal off the C_2-related quadrants of the active site from which we wish to exclude the olefin substituents. We are in the process of constructing improved catalysts based on this idea.

Table 1: Asymmetric cyclopropanation of alkenes.

Substrate	Major Products	e.e. *syn*	e.e. *anti*	*syn*/*anti* ratio
		10[a]	n.d.	2.3
		20	50	7.8
		45	60	4.3

Conditions: Porphyrin **1** (3.6 x 10^{-3} mmol), olefin (20 mmol), octane (GC standard, 5 mmol) and ethyl diazoacetate (EDA) (5 mmol) were stirred in 0.5 ml CH_2Cl_2 overnight at 0°C; the progress of cyclopropane formation was monitored by GC and additional aliquots of EDA added when the reaction slowed (to a maximum of 20 mmol EDA). The products were distilled away from the porphyrin and/or chromatographed on silica (3:1 hexane/ether eluant). In each case, the enantiomeric excess (e.e.) was determined by NMR using a chiral europium shift reagent. [a] For the styrene *syn* product, measurement of the optical rotation allowed identification of the absolute configuration of the predominant enantiomer as (+)-(1*S*,2*R*)[5]; other absolute configurations have not been assigned. n.d.=not determined

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References and Notes

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10. Of course, substrates in which the alkene and carbene center are tethered by a few carbons will provide only the *syn* product. For an example of this type of reaction, see Taber, D.F.; Amedio, J.C. and Raman, K. *J. Org. Chem.* **1988**, *53*, 2984-2990.
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14. RhTBNPI λ_{max} 435nm ($\varepsilon=1.12\times10^5$); 281nm ($\varepsilon=4.87\times10^4$); 536nm ($\varepsilon=1.72\times10^4$). M/Z ($C_{100}H_{60}N_4RhI$) 1548.
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17. This geometry is consistent with shape selectivity studies carried out by Callot's group[11] and our own (J. Maxwell, and K. Brown, unpublished results).

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