Continuous Flow Cyclopropanation Reactions using Cu(I) complexes of Pc-L* ligands supported on silica as catalysts with carbon dioxide as a carrier.

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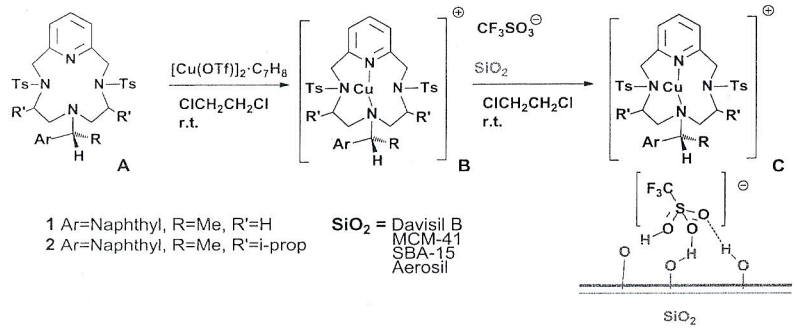
We have recently reported that copper(I) complexes of the new C_1-symmetric pyridine-based 12-membered tetraaza macrocycles, *Pyridine Containing Ligands* (**Pc-L***), are competent catalysts in the asymmetric cyclopropanation.[1,2] In order to improve our catalytic system Cu(I) complexes based on **Pc-L*** ligands were heterogeneized on mesoporous ordered and non-ordered silicas (Davisil, MCM-41, etc.) by the Supported by HydrogenBond (SHB) method.[3]



Supported catalysts **C** were tested in enantioselective cyclopropanation in batch conditions showing good catalytic activities of differently substituted olefins employing ethyl diazoacetate (EDA) as carbene precursor in n-hexane. The silica support has a strong influence on the diastereoselective outcome of the reaction, favoring the formation of the more challenging *cis* isomer. Then, catalysts **C** were tested as catalyst for the cyclopropanation reaction under flow conditions focusing our attention on the use of supercritical CO_2. As model reaction we chose the cyclopropanation of α-methyl styrene with EDA. The catalyst has been located in a reactor while the substrate (α-methyl styrene and EDA) are transported into the reactor dissolved in 1,2-DCE or in supercritical CO_2, which simultaneously acts as a transport vector for the products. Under optimised conditions, the catalyst was stable over at least 10 h of continuous flow, without drop in activity or selectivity.

References

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Catalytic asymmetric hydrogenation of naphthalenes and quinolines

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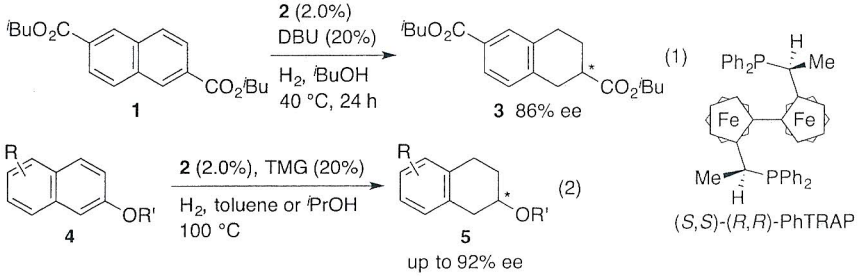
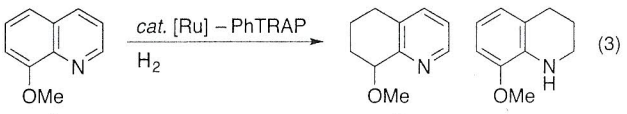
Catalytic asymmetric hydrogenation of carbocyclic arenes had been a formidable subject in organic synthesis, although various heteroarenes have been reduced through asymmetric catalysis. We have developed the highly enantioselective hydrogenations of 5-membered nitrogen-containing heteroarenes by using a chiral catalyst, PhTRAP–ruthenium.[1] In this study, we found that the chiral ruthenium catalyst is also effective for the asymmetric hydrogenation of carbocycles in naphthalenes and quinolines.
The hydrogenation of naphthalene-2,6-dicarboxylate **1** was conducted with [RuCl(*p*-cymene){(*S,S*)-(*R,R*)-PhTRAP}]Cl (**2**) and DBU under hydrogen (50 atm) in ^{t}BuOH at 40°C for 24 h. The hydrogenation product, tetralin **3**, was obtained in 98% isolated yield with 86% ee (eq. 1). The ruthenium complex **2** promote the hydrogenation of 2-alkoxynaphthalenes **4** to give the desired chiral product **5** with up to 92% ee (eq. 2).[2]



In the hydrogenation of quinolines, their nitrogen-containing rings were exclusively reduced to give 1,2,3,4-tetrahydroquinolines in general. To our surprise, the reduction preferentially occurred on the carbocycles of quinolines, when the hydrogenation was conducted in the presence of PhTRAP–ruthenium catalyst. In particular, 8-substituted quinolines were converted to chiral 5,6,7,8-tetrahydroquinolines in good stereoselectivities and high yields. In the reaction of 8-methoxyquinoline (**6**), the desired product **7** was formed with 83% ee, while no formation of 1,2,3,4-tetrahydroquinoline **8** was observed (eq. 3).



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