Dalton Transactions

Accepted Manuscript

ROYAL SOCIETY OF CHEMISTRY

www.rsc.org/dalton

Journal Name

PERSPECTIVE

The Ligand Influence in Stereoselective Carbene Transfer Reactions Promoted by Chiral Metal Porphyrin Catalysts

Received 00th January 20xx,
Accepted 00th January 20xx

DOI: 10.1039/x0xx00000x

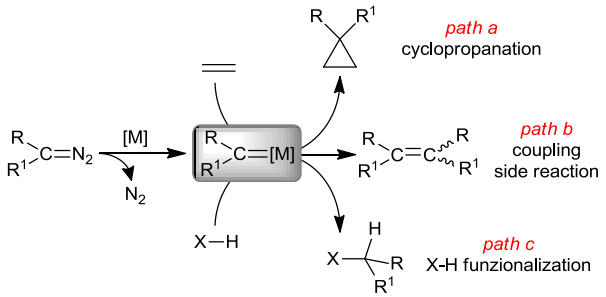
www.rsc.org/

Daniela Intrieri, Daniela Maria Carminati and Emma Gallo*

The use of diazo reagents of a general formula $N_2C(R)(R^1)$ as carbene sources to create new C-C bonds is of broad scientific interest due to the intrinsic sustainability of this class of reagents. In the presence of the opportune catalyst diazo reagents react with several organic substrates with excellent stereo-control and forming N_2 as the only by-product. In the present report the catalytic efficiency of metal porphyrins in promoting carbene transfer reactions is reviewed with emphasis on the active role of the porphyrin skeleton in stereoselectively driving the carbene moiety to the target substrate. The catalytic performance of different metal porphyrins are discussed and have been related to the structural features of the ligand with the final aim of rationalizing the strict correlation between the tridimensional structure of the porphyrin ligand and the stereoselectivity of carbene transfer reactions.

1. Introduction

Carbene transfer reactions mediated by metal transition complexes are largely employed in organic synthesis due to the high versatility of this synthetic strategy. The metal carbene intermediate, formed by the reaction of a transition metal complex with a carbene precursor, can be involved in several organic transformations and among them, the alkene cyclopropanation[1-5] (Scheme 1, *path a*) and the functionalization of X-H (X = C, Si, N, S) bonds[6-8] (Scheme 1, *path c*) represent efficient methodologies to synthesise high-added value chemicals starting from simple and cheap precursors.



Scheme 1. General formation of a metal carbene complex $(R)(R^1)C=[M]$ and its reactivity towards alkenes and X-H containing substrates.

Chemistry Department of Milan University, Via Golgi 19, 20133 Milan, Italy.
E-mail: emma.gallo@unimi.it; Fax: (+39) (0)2 50314405

Diazo derivatives of the general formula $N_2C(R)(R^1)$ are sustainable and atom-efficient starting materials of these reactions because the formation of the carbene $[(R)(R^1)C:]$ functionality occurs with the contemporary extrusion of benign molecular nitrogen as the only by-products.[9,10]
Diazo derivatives can be efficiently synthesised by introducing R/R^1 groups with different electronic behaviour (donor/donor, acceptor/donor or acceptor/acceptor) to fine-tune the reactivity of the carbene metal species with respect to the electrophilic/nucleophilic nature of the organic substrate. In addition, the steric nature of substituents onto the carbene carbon atom can affect the reaction stereoselectivity by driving the approach of the metal carbene complex to the organic substrate. The electronic and steric features of the diazo reagent can also determine the occurrence of coupling side reactions (Scheme 1, *path b*) which must be minimized to guarantee the productivity of the desired pathway. It is important to remember that the safe handling of diazo derivatives can be increased by managing them under continuous-flow technologies[11-14] which permit their synthesis and use on a large scale suitable for industrial applications.
Amongst metal complexes which are effective in activating diazo derivatives in the alkene cyclopropanation and functionalization of X-H bonds, metal porphyrins are very efficient because they couple a high catalytic activity with an excellent chemical stability.[15-22] Porphyrin ligands can be used to synthesise metal catalysts with very different electronic and steric characteristics thanks to the plethora of structural modifications which can be carried out on a porphyrin skeleton. In addition the presence of different axial ligand(s)

onto the active transition metal can further expand the chemical versatility of this class of catalysts (Figure 1).

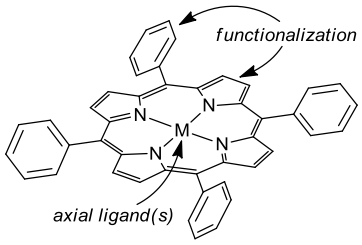


Figure 1. The parent structure of metal porphyrin complexes.

Metal porphyrin complexes can also be obtained in a pure chiral form to promote enantioselective reactions which must be applied for the synthesis of pharmaceutical and/or biological compounds. Up to now many chiral metal porphyrins[23] have been synthesised for different catalytic applications and in the present perspective we would like to survey their use in the enantioselective cyclopropanation of alkenes and functionalization of X-H bonds. The selection of chiral porphyrin structures active in stereoselective carbene transfer reactions are reported in Figure 2 and discussed below.

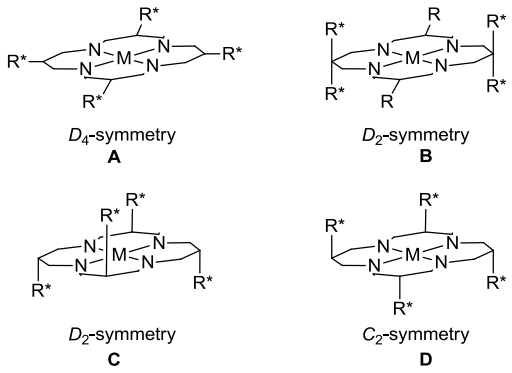


Figure 2. General structures of chiral porphyrins discussed herein.

In this report, chiral porphyrins are grouped on the basis of the porphyrin skeleton symmetry due to the importance of the ligand structure in determining the catalytic performance.
We sincerely apologise in advance if some important contributions have been unintentionally omitted.

2. D_4-Symmetric Catalysts

2.1. Chiral catalysts of Group 8

The first enantioselective cyclopropanation promoted by a chiral ruthenium(II) porphyrin was independently published in 1997 by A. Berkessel[24] and C.-M. Che.[25] Both research groups employed the D_4-symmetric chiral porphyrin (Figure 2, type **A**) reported by L. Haltermann and S. T. Jan[26] to synthesise ruthenium complexes (Halt*)Ru(CO) (**1**) and (Halt*)Ru(CO)(EtOH) (**2**) showed in Figure 3.

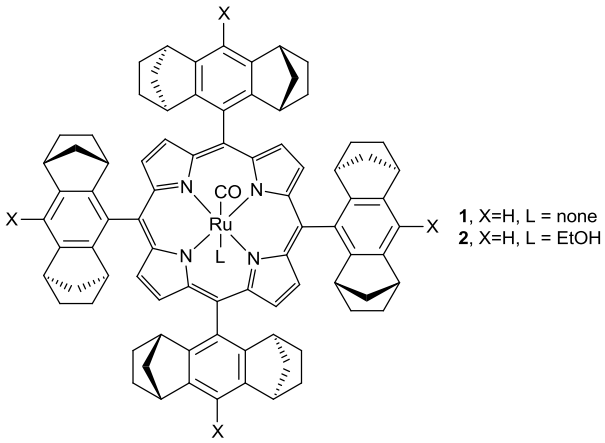
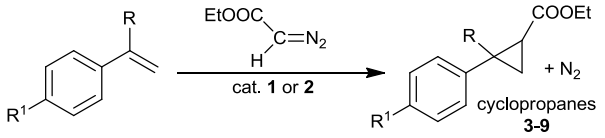


Figure 3. Structures of ruthenium complexes **1**[24] and **2**.[25]

Complex **1** was obtained as a pentacoordinated complex and it was active in the cyclopropanation of styrene by ethyl diazoacetate (EDA) at the low catalyst loading of 0.15 mol%. The cyclopropane was obtained in a quantitative yield with *trans*-diastereoselectivity ratio ($d.r._{trans}$) up to 95:5 and *trans*-enantioselectivities (ee_{trans}) up to 91%. Comparable results were obtained by C.-M. Che and co-authors by studying the cyclopropanation of styrene by EDA in the presence of **2** (0.2 mol%) which was also active in promoting the cyclopropanation of the other styrenes (Scheme 2) with differently substituted diazo reagents.[27]



3, R=R^1=H, quantitative yield, 95:5 $d.r._{trans}$, 91% ee_{trans} (cat. **1** at 0°C)
3, R=R^1=H, 63% yield, 23.6:1 $d.r._{trans}$, 91% ee_{trans} (cat. **2** at 0°C)
3, R=R^1=H, 52% yield, 36:1 $d.r._{trans}$, 98% ee_{trans} (cat. **2** at -40°C)
4, R=Me, R^1=H, 69% yield, 3:1 $d.r._{trans}$, 87% ee_{trans} (cat. **2** at RT)
5, R=H, R^1=Cl, 66% yield, 23:1 $d.r._{trans}$, 90% ee_{trans} (cat. **2** at RT)
6, R=H, R^1=F, 83% yield, 19:1 $d.r._{trans}$, 87% ee_{trans} (cat. **2** at RT)
7, R=H, R^1=Me, 78% yield, 18:1 $d.r._{trans}$, 81% ee_{trans} (cat. **2** at RT)
8, R=H, R^1=OMe, 61% yield, 15:1 $d.r._{trans}$, 85% ee_{trans} (cat. **2** at RT)
9, R=Ph, R^1=H, 76% yield, 81% *ee* (cat. **2** at RT)

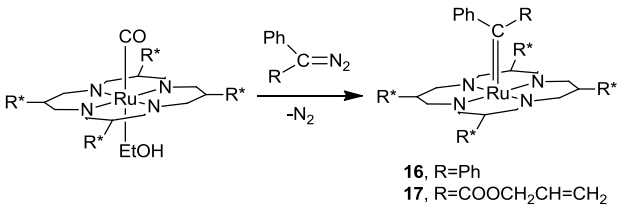
Scheme 2. Cyclopropanation of styrenes promoted by complexes **1**[24] and **2**.[25,27]

As shown in Scheme 2, the presence of the axial ligand EtOH on the ruthenium centre of **2** did not influence the catalytic efficiency and all the reactions occurred with good stereoselectivities. These first results evidenced good stereo-control exhibited by porphyrin ligands in inducing the formation of the more thermodynamically stable *trans*-diastereomer almost independently from the electronic nature of the employed alkene reagents. Thus, catalyst **2** was tested in the cyclopropanation of styrene by using diazo derivatives of the general formula $N_2CH(COOR)$ (**10**, R=Me; EDA, R=Et; **11**, R=^{t}Bu; **12**, R=*l*-menthyl; **13**, R=*d*-menthyl), which showed a different steric hindrance of the R group. Achieved

data indicated that the *trans*-diastereoselectivity enhanced by increasing the R bulk from a methyl to a *tert*-butyl group. This trend was not confirmed by using diazoderivatives **12** and **13** where the streoselectivity was worse than that observed in the reaction run with EDA as the carbene source.

Complex **2** was also active in promoting the intramolecular cyclopropanation of diazoacetate $N_2CH(COOCH_2CH=CR^1R^2)$ which formed cyclopropyl lactones in *ee* up to 85%.[27]

In order to rationalise the observed catalytic efficiency of complex **2**, C.-M. Che and co-authors investigated the reactivity of **2** towards diazo reagents. No products were isolated from the reaction of **2** with EDA while by using diazo derivatives N_2CPh_2 (**14**) or $N_2C(Ph)(COOCH_2CH=CH_2)$ (**15**) the two ruthenium carbene derivatives **16** and **17** were obtained and fully characterised including the X-ray molecular structure determination of complex **16** (Scheme 3).

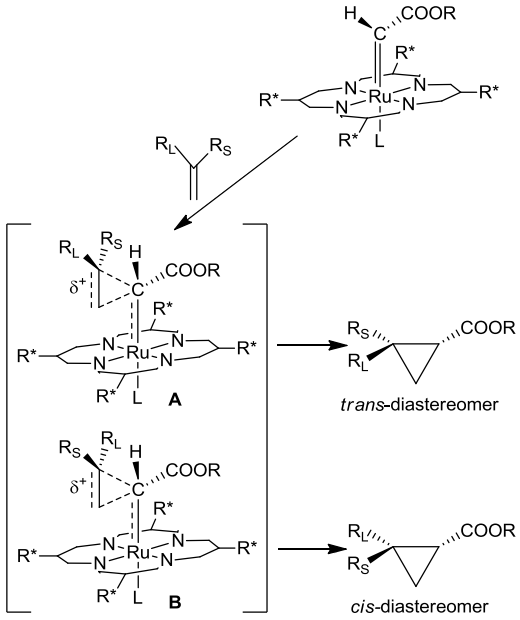


Scheme 3. Synthesis of ruthenium carbene complexes **16** and **17**.[27]

Both complexes **16** and **17** did not transfer the carbene moiety to styrene when treated with stoichiometric amounts of the alkene even at high temperatures. Conversely, complex **16** catalysed the cyclopropanation of styrenes by EDA with an efficiency comparable to that of its ruthenium precursor **2** indicating that pentacoordinated carbene complexes **16** and **17** are probably not the active intermediates of cyclopropanation reactions. In the **16**-catalysed cyclopropanation of styrene by EDA, the carbene $[Ph_2C:]$ moiety could play a role of an activating L ligand with a strong *trans* effect to promote, on the other side of the porphyrin plane, the transfer of [(COOEt)HC:] functionality deriving from EDA.

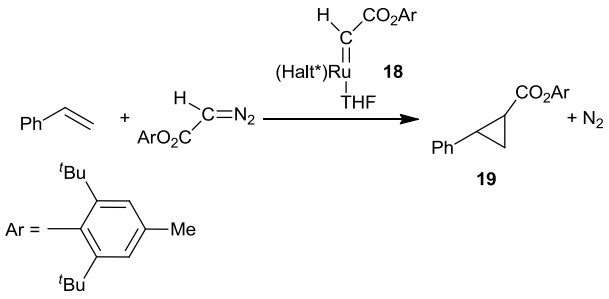
The observed diastereoselectivity was explained with the formation of the two transition states **A** and **B** described in Scheme 4 which were formed as a consequence of the *end-on* approach of the alkene to the ruthenium carbene species.

The observed *trans*-diastereoselectivity might be due to the higher stability of transition state **A** compared to **B** for the less extended steric interaction between the larger group R_L and the ester group on the carbene moiety. The parallel approach of the alkene to the ruthenium carbene bond could be the reason why terminal alkenes were more reactive substrates than non-terminal ones in complex **2**-mediated cyclopropanation reactions. The mechanism of Scheme 4 illustrated the dependence of the reaction stereoselectivity on the steric characteristics of substituents on carbene and alkene fragments.



Scheme 4. Proposed transition states **A** and **B** of the **2**-catalysed alkene cyclopropanation.[27]

The catalytic activity of pre-formed carbene complexes was also observed by G. Simonneaux and co-authors[28] by testing the reactivity of (Halt*)Ru($CHCO_2Ar$)(THF) (Ar=2,6^{t}Bu-4Me-C_6H_2) ruthenium complex **18** which was synthesised by a recrystallization of the product of the reaction of **1** with 2,6-di-*tert*-butyl-4-methylphenyl diazoacetate in the presence of THF. Complex **18** was catalytically active in the cyclopropanation of styrene by 2,6-di-*tert*-butyl-4-methylphenyl diazoacetate yielding the corresponding cyclopropane **19** in 62% yield, complete *trans*-diastereoselectivity and 60% of ee_{trans} (Scheme 5).



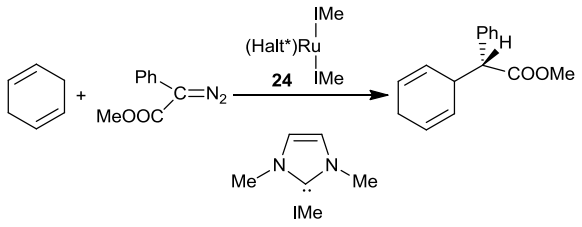
Scheme 5. Structure of ruthenium carbene complexes **18** and its catalytic activity.[28]

In order to expand the study of the catalytic capacity of Halterman-type chiral porphyrins, A. Berkessel and co-authors synthesised ruthenium porphyrins similar to **1** (Figure 3) which exhibit X = OMe (**20**), Me (**21**) and CF_3 (**22**).[29] In addition, also complex (Halt*)Ru(PF_3) (**23**) was obtained to evaluate the effect of an axial ligand on the ruthenium centre. All the complexes **20**-**23** showed a good catalytic efficiency in the cyclopropanation of styrenes and achieved data showed that the tetrakis-CF_3-substituted complex **22** was the most active

and stable catalyst of all the tested catalysts. Considering that the steric hindrance of the Halterman ruthenium porphyrin **1** is not influenced by the introduction of a CF_3 substituent on the X position (Figure 3), the improvement of the catalytic performance was only due to electronic factors which can affect the catalyst stability more than the stereo-control of the reaction. In fact, a high TON (turnover number) of 7520 was observed in the **22**-catalysed cyclopropanation of styrene by EDA.

The comparison of the catalytic activity of complexes **1** (Figure 3, X=H, L=CO) with that of complex **23** (Figure 3, X=H, L=PF_3) revealed an increase in the reaction time with a contemporary decrease in the catalytic efficiency. The authors suggested that two different catalytic intermediates were formed from the two pre-catalysts **1** and **23**. In the case of the **1**-catalysed cyclopropanation, the CO axial ligand was lost to form a five-coordinated carbene active species, whilst when complex **23** was used as the catalyst, the PF_3 axial ligand remained coordinated to the metal centre during the entire catalytic cycle and a pseudo-octahedral carbene intermediate was responsible for the cyclopropanation. It is important to note that complex **23** was active in the cyclopropanation of a non-conjugated terminal olefins such as 1-octene where the corresponding cyclopropane was obtained with 99.5:0.5 of $d.r._{trans}$ and 82% of ee_{trans}. In addition, **23** promoted the cyclopropanation of styrene and α-methylstyrene by phenyl diazomethane ($N_2CH(Ph)$) and corresponding cyclopropanes were formed with *trans*/*cis* ratio of 51:49 and 83:17 and ee_{trans} of 72% and 96% respectively.[29]

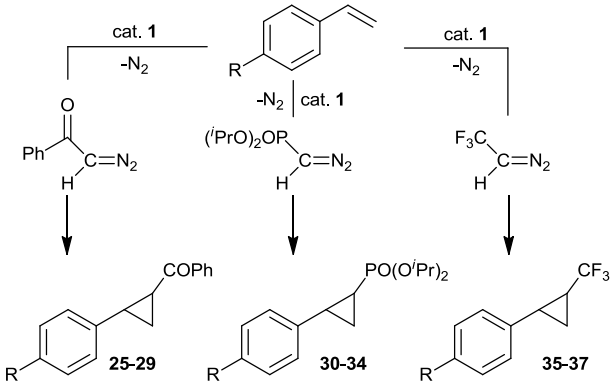
The influence of axial ligands in determining the catalytic efficiency of ruthenium porphyrin complexes was also studied by C.-M. Che and co-authors who reported the synthesis of (Halt*)Ru(IMe)$_2$ (**24**) (IMe = 1,3-dimethyl-2,3-dihydro-1*H*-imidazole) which showed two *N*-heterocyclic carbene (NHC) axial ligands on the ruthenium centre.[30] The cyclopropanation of styrene by EDA promoted by the low catalyst amount of 0.004 mol % occurred with 95% yield, 95:5 $d.r._{trans}$ and 95% ee_{trans}. Complex **24** was also active in catalysing the carbene insertion into a C-H bond of 1,4-cyclohexadiene by using methyl phenyldiazoacetate (MPDA) ($N_2C(Ph)(COOMe)$) as a carbene source.[30] The insertion of the carbene functionality into the vinyl C-H bond afforded the desired compound in 80% yield with 92% *ee* (Scheme 6).



Scheme 6. Complex **24**-catalysed insertion of a carbene functionality into a vinilyc C-H bond.[30]

As already discussed above,[27] also in this case the presence of a carbene axial ligand had a positive effect on the efficiency of the cyclopropanation reaction. A DFT study indicated that the *N*-heterocyclic carbene ligands exhibited a strong σ donor strength which stabilises the ruthenium-carbene on the *trans* position with a consequential decrease of the activation barrier for the decomposition of diazo compounds.

In order to expand the reaction scope of enantioselective cyclopropanations catalysed by ruthenium porphyrin **1** (Figure 3), G. Simonneaux et co-authors reported the use of diazo ketone $N_2CH(COPh)$, diisopropyl diazomethylphosphonate $N_2CH(OP(O^iPr)_2$ (DAMP) and 2,2,2-trifluorodiazoethane $N_2CH(CF_3)$ for the synthesis of optically active cyclopropylketones **25**-**29**,[31] *trans*-cyclopropylphosphonates **30**-**34**[32] and trifluoromethylphenyl cyclopropanes **35**-**37**,[33] respectively (Scheme 7).



25, R=H, 57% yield, 95:5 $d.r._{trans}$, 83% ee_{trans}
26, R=Me, 83% yield, 98:2 $d.r._{trans}$, 83%, ee_{trans}
27, R=OMe, 80% yield, 99:1 $d.r._{trans}$, 84%, ee_{trans}
28, R=CF_3, 46% yield, 95:5 $d.r._{trans}$, 86% ee_{trans}
29, R=Cl, 45% yield, 95:5 $d.r._{trans}$, 84% ee_{trans}
30, R=H, 97% yield, 96:4 $d.r._{trans}$, 90% ee_{trans}
31, R=Me, 93% yield, 99:1 $d.r._{trans}$, 87% ee_{trans}
32, R=OMe, 96% yield, 97:3 $d.r._{trans}$, 90% ee_{trans}
33, R=CF_3, 90% yield, 95:5 $d.r._{trans}$, 92% ee_{trans}
34, R=Cl, 92% yield, 97:3 $d.r._{trans}$, 88% ee_{trans}
35, R=H, 32% yield, 98:2 $d.r._{trans}$, 58% ee_{trans}
36, R=OMe, 35% yield, 99:1 $d.r._{trans}$, 30% ee_{trans}
37, R=Br, 24% yield, 99:1 $d.r._{trans}$, 50% ee_{trans}

Scheme 7. Complex **1**-catalysed synthesis of cyclopropylketones **25**-**29**,[31] *trans*-cyclopropylphosphonates **30**-**34**[32] and trifluoromethylphenyl cyclopropanes **35**-**37**.[33]

As reported in Scheme 7, the synthesis of compounds **25**-**29** was more productive by using electron rich alkenes than electron poor ones, while the electronic features of the unsaturated substrate did not influence the reaction stereoselectivity. *Trans*-cyclopropylphosphonates **30**-**34** were obtained in comparable yields and stereolectivities whereas the reaction efficiency of the synthesis of compounds **35**-**37** was modest.

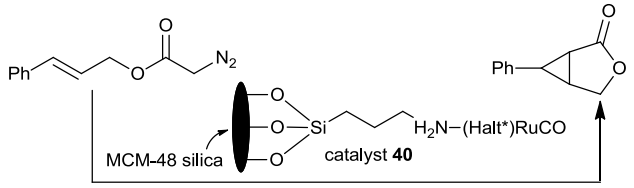
The stoichiometric reaction of DAMP with complex **1** gave a ruthenium carbene complex (Halt*)Ru=CHPO(O^{i}Pr)$_2$ (**38**) which displayed a catalytic activity in the styrene cyclopropanation by DAMP similar to that reported for complex **1**. These results support a possible involvement of **38** as a catalytic

intermediate. However, the stoichiometric transfer reaction from **38** to styrene derivatives was not reported.

Catalyst **1** was also efficient in promoting the cyclopropanation of styrene by *N*- and *O*-protected 6-diazo-5-oxo-L-norleucine (DON) which is a biological compound with antibiotic features. The corresponding cyclopropane was obtained in 75% yield, with excellent *trans*-diastereoselectivity (*trans*/*cis*=99:1) and 80% of ee_{trans}. This study was undertaken to better understand some *in vivo* processes where enzymes containing metal porphyrins could be involved.[34]

In order to mimic biological processes in where metal porphyrin complexes could play important roles, it was important to test the reactivity of porphyrin catalysts in water. In 2008 G. Simonneaux and co-authors synthesised the *para*-tetrasulfonated water soluble Halterman-type porphyrin **39** (Figure 3, X=SO_3Na, L=none).[35] The **39**-catalysed cyclopropanation of styrene occurred in 52% yield, with 96:4 of $d.r._{trans}$ and 83% ee_{trans}. The catalyst recycle was also investigated and a progressive decrease in the enantiomeric excess was observed during the second (ee_{trans}=62%) and the third (ee_{trans}=40%) cycles.

Ruthenium Halterman type porphyrins were also supported in heterogeneous systems to permit a better catalyst recyclability and reuse. The first example of the heterogenization of chiral ruthenium porphyrin catalysts on ordered molecular sieves for cyclopropanation reactions was reported in 2002 by C.-M. Che.[36] Catalyst **1** was supported on the ordered mesoporous silica MCM-48 which contains a three-dimensional porous structure to assure an efficient accessibility of reagents to catalytically active sites. Heterogeneous catalyst **40** was employed to promote the intramolecular cyclopropanation of *trans*-cinnamyl diazoacetate to yield the desired compound with high enantioselctivity of 85%. The excellent stability of heterogeneous catalyst **40** endorsed recycling for four consecutive times at the high TON of 1.5 x 10^3 (Scheme 8).



Scheme 8. Heterogeneous intramolecular cyclopropanation of *trans*-cinnamyl diazoacetate catalysed by **40**.[36]

Then, Halterman type ruthenium porphyrins **41** and **42** (Figure 4), showing spirobifluorenyl groups on *meso* positions, were embedded in a polymeric support by an anodic oxidation in the presence of 9,9'-spirobifluorene (SBF) which provoked the coating of the electrode by a optically active film.[37] The removal of the electrode produced a chiral polymer which was tested in the enantioselective cyclopropanation of styrene by EDA that occurred with good yields but only modest enantioselectivities (up to 53% at -40°C). The good stability of catalysts poly-**41** and poly-**42** permitted their reuse for seven consecutive times without observing a considerable decrease in the catalytic efficiency in terms of both activity and enantioselectivity. The comparison of the catalytic activity of complexes **41** and poly-**41** revealed a decrease in the reaction enantioselectivity from 76% to 53% after the anodic oxidation of the monomeric complex **41**. It was envisaged that the cross-linked polymeric structure can hinder the interaction of substrates with the active sites and that a partial oxidation of ruthenium(II) to ruthenium(III) or (IV) occurred during the electropolymerization and it was responsible for a decrease of catalytically active ruthenium(II) centres.

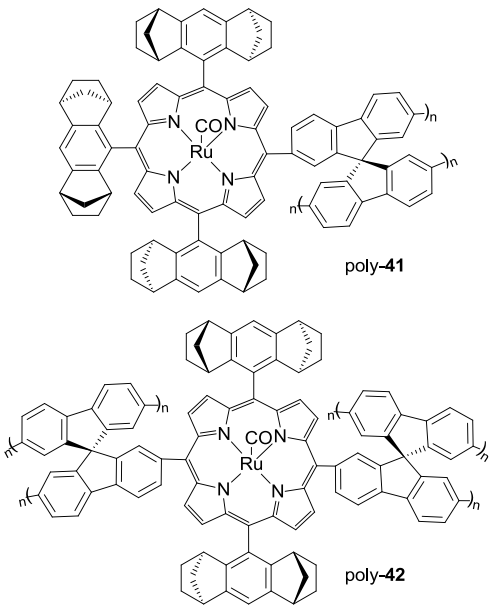
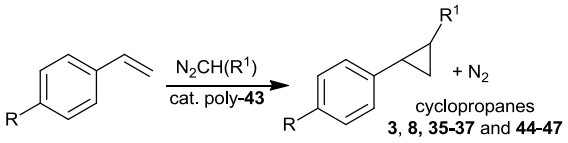


Figure 4. Structures of chiral ruthenium polymeric complexes poly-**41** and poly-**42**.[37]

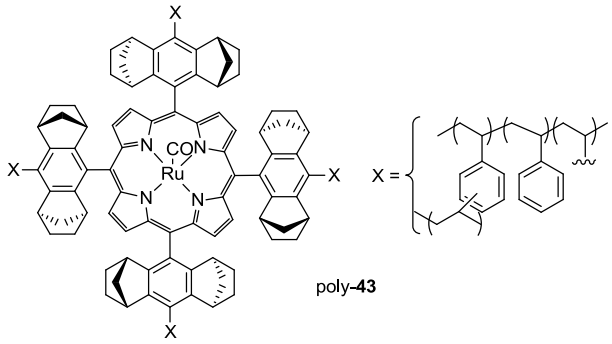
In order to improve the stereo-control accomplished by polymeric heterogeneous catalysts, G. Simonneaux and co-authors explored the polymerization of Halterman type ruthenium porphyrins functionalised with four vinyl groups.[38] Complex **43** (Figure 3, X = -CH_2=CH_2, L = none) was polymerised with styrene and divinylbenzene forming the supported poly-**43** ruthenium complex which was tested in the cyclopropanation of styrenes by EDA,[38] diazoacetonitrile[38] ($N_2CH(CN)$) and 2,2,2-trifluorodiazoethane[33] ($N_2CH(CF_3)$) (Scheme 9). Desired compounds **3**, **8** (Scheme 2) **35**-**37** (Scheme 7) and **44**-**47** (Scheme 9) were obtained with good enantiomeric excesses (up to 90%) which, in some cases, were comparable to those obtained by using homogeneous chiral ruthenium porphyrins (compare data in Schemes 2 and 6 with those of Scheme 9).

It important to point out that the asymmetric cyclopropanation with diazoacetonitrile afforded optically active *trans*-cyanocyclopropanes which are precursors of biologically active compounds. The modest diastereoselectivities observed when diazoacetonitrile was used as the carbene precursor was probably due to the small size of the CN group which disfavours the *trans*-diastereoselectivity. The authors attributed the observed low

yields of compounds **35**-**37** to the high volatility of the starting diazo 2,2,2-trifluorodiazoethane compound.

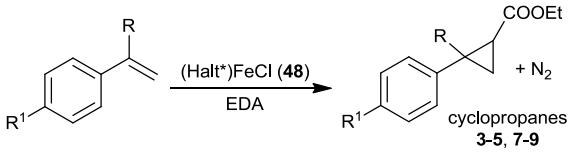


3, R=H, R^1=COOEt, 77% yield, 92:8 *d.r.*$_{trans}$, 82% *ee*$_{trans}$
8, R=OMe, R^1=COOEt, 88% yield, 92:8 *d.r.*$_{trans}$, 80% *ee*$_{trans}$
35, R=H, R^1=CF_3, 33% yield, 99:1 *d.r.*$_{trans}$, 61% *ee*$_{trans}$
36, R=OMe, R^1=CF_3, 35% yield, 94:6 *d.r.*$_{trans}$, 25% *ee*$_{trans}$
37, R=Br, R^1=CF_3, 31% yield, 96:4 *d.r.*$_{trans}$, 39% *ee*$_{trans}$
44, R=Br, R^1=COOEt, 75% yield, 93:7 *d.r.*$_{trans}$, 90% ee$_{trans}$
45, R=H, R^1=CN, 53% yield, 76:24 *d.r.*$_{trans}$, 70% *ee*$_{trans}$
46, R=OMe, R^1=CN, 55% yield, 70:30 *d.r.*$_{trans}$, 68% *ee*$_{trans}$
47, R=Br, R^1=CN, 40% yield, 75:25 *d.r.*$_{trans}$, 71% *ee*$_{trans}$



Scheme 9. Catalytic activity of poly-**43** in the cyclopropanation of styrenes by EDA,[38] diazoacetonitrile[38] or 2,2,2-trifluorodiazoethane.[33]

Chiral D_4 symmetric porphyrins are also good ligands to synthesise active iron derivatives. The interest of the scientific community in developing iron porphyrin-based catalytic protocols for carbene transfer reactions is mainly due to the sustainability of the active, low toxic and cheap iron catalytic centre.[39] C.-M. Che and co-authors reported in 2006[40] the first use of (Halt*)Fe(III)Cl complex **48** to catalyse carbene transfer reactions. The catalyst was slightly less active than the counterpart ruthenium derivative **1** or **2** (Figure 3) to promote the formation of compounds **3**-**5** and **7**-**9** (Scheme 2). These cyclopropanes were obtained with comparable *trans*-diastereoselectivities but minor enantioselectivities of the *trans* isomer (Scheme 10).



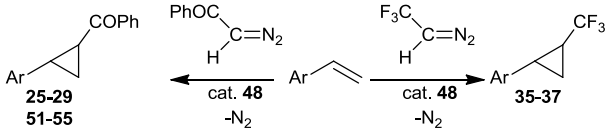
3, R=R^1=H, 60% yield, 18:1 *d.r.*$_{trans}$, 81% *ee*$_{trans}$
4, R=Me, R^1=H, 68% yield, 3:1 *d.r.*$_{trans}$, 81% *ee*$_{trans}$
5, R=H, R^1=Cl, 57% yield, 18:1 *d.r.*$_{trans}$, 75% *ee*$_{trans}$
7, R=H, R^1=Me, 56% yield,12:1 *d.r.*$_{trans}$, 79% *ee*$_{trans}$
8, R=H, R^1=OMe, 65% yield, 13:1 *d.r.*$_{trans}$, 74% *ee*$_{trans}$
9, R=Ph, R^1=H, 72% yield, 83% *ee*

Scheme 10. Iron catalyst **48**-mediated cyclopropanation of styrenes by EDA.[40]

The cyclopropanation reactions occurred without the addition of a reductive species, which is supposed to reduce the iron(III) pre-catalyst into an iron(II) species able to react with the diazo reagent to form the iron(IV) carbene active intermediate.[41] The authors proposed that EDA played a double role of the carbene source and reductive agent as already proposed for copper(II) catalysed cyclopropanations.[42] This last hypothesis was supported by the pronounced decrease of the catalytic efficiency observed when the reaction was run in air where a supposed iron(II) intermediate can be easily decomposed. The *trans*-selectivity of the reaction was enhanced by adding an axial ligand to the catalytic mixture to indicate a possible formation of an axially ligated monocarbene active intermediate. The existence of these species was supported by the electrospray mass spectrometry (ESMS) analysis of the reaction of **48** with EDA, run in the presence of pyridine (py) or 1-methylimidazole (MeIm), which detected the formation of complexes (Halt*)Fe(CHCOOEt)(py) (**49**) and (Halt*)Fe(CHCOOEt)(MeIm) (**50**), respectively. However the latter complexes were never isolated or detected in the presence of alkene substrates.

G. Simonneaux and co-authors reported that iron complex **48** was also active in the cyclopropanation of styrenes by diazoacetophenone[43] and 2,2,2-trifluorodiazoethane[33] that were efficiently promoted by ruthenium complex **1**.[31,33]

Data reported in Scheme 11 revealed that **48** was less efficient than **1** in terms of cyclopropane yields and *trans*-enantioselectivities, however similar *trans*-diastereoselectivities were observed.



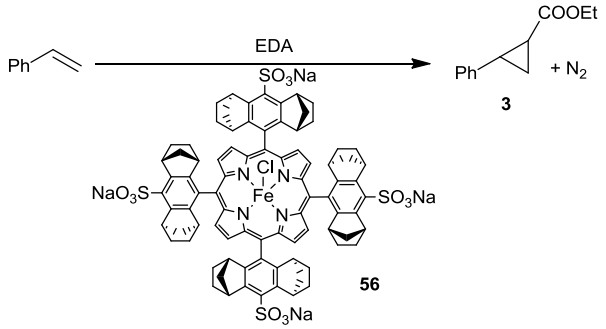
25, Ar=Ph, 67% yield, 93:7 *d.r.*$_{trans}$, 76% *ee*$_{trans}$
26, Ar=*p*-MeC_6H_4, 53% yield, 96:4 *d.r.*$_{trans}$, 76%, *ee*$_{trans}$
27, Ar=*p*-$OMeC_6H_4$, 58% yield, 93:7 *d.r.*$_{trans}$, 76%, *ee*$_{trans}$
28, Ar=*p*-$CF_3C_6H_4$, 54% yield, 93:7 *d.r.*$_{trans}$, 62% *ee*$_{trans}$
29, Ar=*p*-ClC_6H_4, 58% yield, 94:6 *d.r.*$_{trans}$, 76% *ee*$_{trans}$
51, Ar=*p*-BrC_6H_4, 58% yield, 92:8 *d.r.*$_{trans}$, 69% *ee*$_{trans}$
52, Ar=*m*-$CH_3C_6H_4$, 64% yield, 92:8 *d.r.*$_{trans}$, 68% *ee*$_{trans}$
53, Ar=*o*-$CH_3C_6H_4$, 58% yield, 92:8 *d.r.*$_{trans}$, 80% *ee*$_{trans}$
54, Ar=*m*-$CF_3C_6H_4$, 25% yield, 90:10 *d.r.*$_{trans}$, 74% *ee*$_{trans}$
55, Ar=*o*-$CF_3C_6H_4$, 24% yield, 90:10 *d.r.*$_{trans}$, 78% *ee*$_{trans}$
35, Ar=Ph, 50% yield, 99:1 *d.r.*$_{trans}$, 61% *ee*$_{trans}$
36, Ar=*p*-$OMeC_6H_4$, 42% yield, 99:1 *d.r.*$_{trans}$, 69% *ee*$_{trans}$
37, Ar=*p*-BrC_6H_4, 43% yield, 99:1 *d.r.*$_{trans}$, 67% *ee*$_{trans}$

Scheme 11. Catalytic activity of (Halt*)FeCl (**48**) in the cyclopropanation of styrenes by diazoacetophenone[43] and 2,2,2-trifluorodiazoethane[33]

G. Simonneaux and co-authors also reported a heterogeneous version of the synthesis of compounds **35**-**37** by using an iron compound which display a structure analogous to that showed in Scheme 9 for the ruthenium derivative (Ru(II)CO of poly-**43** was replaced by Fe(III)Cl in the porphyrin core to yield poly-**48**).[33] Complex poly-**48** showed a catalytic efficiency comparable to the homogeneous counterpart **48** for yields and diastereoselectivities, whereas a decrease in the

enantioselectivities was observed in all tested reactions (**35**, 52% yield, 97:3 *d.r.*$_{trans}$ and 56% *ee*$_{trans}$; **36**, 51% yield, 96:4 *d.r.*$_{trans}$ and 17% *ee*$_{trans}$; **37**, 42% yield, 97:3 *d.r.*$_{trans}$ and 37% *ee*$_{trans}$).

In order to envisage the application of iron chiral porphyrins for the synthesis of biologically active compounds, the reactivity of pharmaceutically active diazo derivatives as well as the use of water as the medium of catalytic reactions were studied. First, catalyst **48** was active to promote the reactivity of the antibiotic species *N*- and *O*-protected 6-diazo-5-oxo-L-norleucine (DON) towards styrene yielding the corresponding cyclopropane in 95% yield, 95:5 of *trans*-diastreoselectivity ratio and 80% of *ee*$_{trans}$.[34] Then, the introduction of sulfonate groups of the porphyrin skeleton of **48** originated complex **56** which catalysed the reaction between styrene and EDA in water to yield cyclopropane **3** in 85% yield, 92:8 *d.r.*$_{trans}$ and 83% *d.r.*$_{trans}$ (Scheme 12).[35]



Scheme 12. Iron catalyst **56**-mediated cyclopropanation of styrene by EDA in water.[35]

It should be noted that the reaction of Scheme 12 occurred in the presence of cobaltocene which seems necessary to reduce the starting iron(III) pre-catalyst into an iron(II) species active towards the diazo compounds.

2.2. Chiral catalysts of Group 9

Considering that all the Halterman-type porphyrins discussed up to now do not present substantial structural dissimilarities of their ligand skeleton, the differences which were observed in the reaction stereoselectivities should be due to the nature of the catalytically active metal centre.

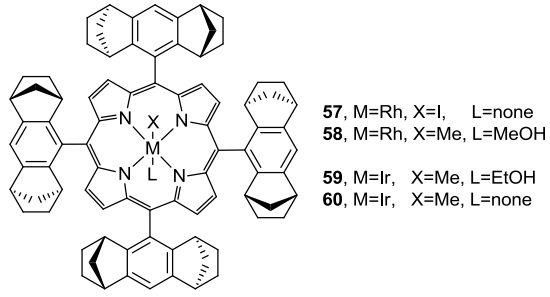
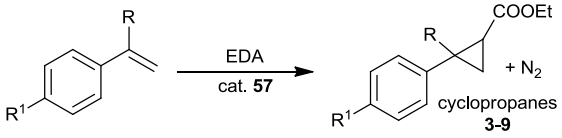


Figure 5. Structures of rhodium and iridium **57**,[44] **58**,[45] **59**[46] **60**[47] catalysts used to promote carbene transfer reactions.

Therefore the synthesis of rhodium(III)[44, 45] and iridium(III)[46, 47] complexes of Halterman chiral porphyrin (Figure 5) was of great interest in comparing their catalytic performances in carbene transfer reactions with those already reported for iron and ruthenium derivatives.

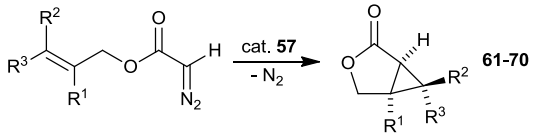
The synthesis of compounds **3**-**9** was performed in the presence of catalyst **57** and achieved data reported in Scheme 13 revealed a minor performance of the rhodium catalyst with respect to the ruthenium counterpart (compare Schemes 13 and 2).



3, R=R^1=H, 66% yield, 1.5:1 *d.r.*$_{trans}$, 61% *ee*$_{trans}$, 36% *ee*$_{cis}$
4, R=Me, R^1=H, 75% yield, 1:1 *d.r.*$_{trans}$, 46% *ee*$_{trans}$, 46% *ee*$_{cis}$
5, R=H, R^1=Cl, 81% yield, 1.2:1 *d.r.*$_{trans}$, 62% *ee*$_{trans}$, 20% *ee*$_{cis}$
6, R=H, R^1=F, 72% yield, 0.9:1 *d.r.*$_{trans}$, 62% *ee*$_{trans}$, 33% *ee*$_{cis}$
7, R=H, R^1=Me, 71% yield, 1.2:1 *d.r.*$_{trans}$, 49% *ee*$_{trans}$, 42% *ee*$_{cis}$
8, R=H, R^1=OMe, 83% yield, 1.6:1 *d.r.*$_{trans}$, 68% *ee*$_{trans}$, 44% *ee*$_{cis}$
9, R=Ph, R^1=H, 78% yield, 32% *ee*

Scheme 13. Cyclopropanation of styrenes promoted by complex **57**.[44]

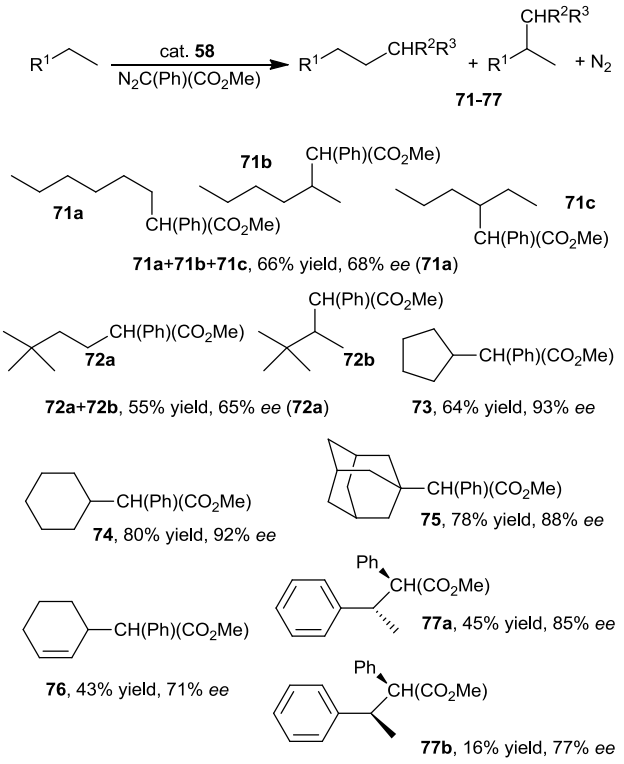
Complex **57** was also active in catalysing the intramolecular cyclopropanation of alkenes yielding corresponding lactones **61**-**70** in moderate to good yields but with modest enantioselectivities (Scheme 14).[44]



61, R^1=R^2=R^3=H, 23% yield, 20% *ee*
62, R^1=Me, R^2=R^3=H, 79% yield, 24% *ee*
63, R^1=Ph, R^2=R^3=H, 59% yield, 49% *ee*
64, R^1=R^3=H, R^2=Ph, 31% yield, 31% *ee*
65, R^1=R^2=H, R^3=Me, 33% yield, 24% *ee*
66, R^1=R^2=H, R^3=Et, 78% yield, 25% *ee*
67, R^1=R^2=H, R^3=Ph, 84% yield, 20% *ee*
68, R^1=H, R^2=R^3=Me, 81% yield, 37% *ee*
69, R^1=H, R^2=Me, R^3=  , 89% yield, 12% *ee*
70, R^1=H, R^2=  , R^3=Me, 65% yield, 48% *ee*

Scheme 14. Synthesis of lactones **61**-**70** by **57**-catalysed intramolecular cyclopropanation.[44]

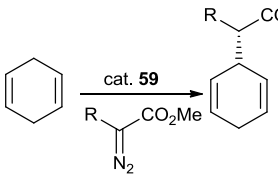
Rhodium(III) complex **58** (Figure 5) displayed a very good catalytic activity in the intermolecular carbenoid insertion into C-H bonds by using $N_2C(Ph)(COOMe)$ (MPDA) as the carbene source.[45] Compounds **71**-**77** reported in Scheme 15 were formed in up to 80% yield and up to 93% *ee*. It should be noted that the methodology was more efficient for primary than for secondary C-H bonds and **71a** and **72a** were formed in a better yield than the other isomers **71b**/**71c** and **72b**, respectively.



Scheme 15. Complex **58**-catalysed intermolecular C-H bond insertion.[45]

Complex **58** showed a very good chemical stability which allowed the catalyst to be reused for at least five consecutive times. In addition, the synthesis of compound **74** was also performed on a large scale affording 2.88 g of the desired reaction products with 73% yield and 91% *ee*.

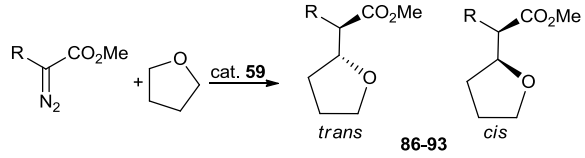
Iridium complex **59** was employed by C.-M. Che and co-authors for catalysing the stereoselective intermolecular carbene insertion into both C-H and Si-H bonds.[46] The intermolecular alkylation of 1,4-cyclohexadiene with methyl phenyl diazoacetate (MPDA) was firstly studied and then, the reaction scope was investigated by testing the reactivity of other methyl aryl diazoacetates. Obtained data indicated that substituents in positions 3 and 4 of the aryl moiety did not influence the reaction performance as well as α–thienyl and naphthyl substituents. The obtained alkylated compounds **78**-**85** are reported in Scheme 16.



78, R=C_6H_5, 90% yield, 95% *ee*
79, R=4-$MeOC_6H_4$, 94% yield, 96% *ee*
80, R=4-BrC_6H_4, 91% yield, 96% *ee*
81, R=4-ClC_6H_4, 82% yield, 98% *ee*
82, R=3-ClC_6H_4, 90% yield, 86% *ee*
83, R=2-ClC_6H_4, not detected
84, R=2-naphthyl, 85% yield, 95% *ee*
85, R=3-thienyl, 62% yield, 96% *ee*

Scheme 16. Complex **59**-catalysed synthesis of compounds **78**-**85**.[46]

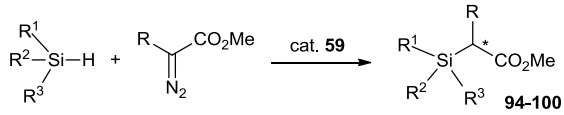
Iridium complex **59** was efficient in catalysing the reaction between tetrahydrofurane (THF) and methyl aryl diazoacetate derivatives. Carbene transfer reactions occurred in good yields, with *trans*/*cis* diastereoselectivities up to 20:1 and *trans*-enantioselectivities up to 97%. Only the synthesis of compounds **90** and **93** occurred in low yields, but with very good enantioselectivities (Scheme 17).



86, R=Ph, 82% yield, *trans*/*cis*=10:1, 90% *ee*
87,R=4-BrC_6H_4, 96% yield, *trans*/*cis*>20:1, 97% *ee*
88,R=4-ClC_6H_4, 86% yield, *trans*/*cis*=16.9:1, 97% *ee*
89,R=4-MeC_6H_4, 74% yield, *trans*/*cis*=14.6:1, 96% *ee*
90,R=4-$(MeO)C_6H_4$, 22% yield, *trans*/*cis*=2.5:1, 92% *ee*
91,R=3-ClC_6H_4, 86% yield, *trans*/*cis*=13.7:1, 81% *ee*
92,R=2-naphthyl, 76% yield, *trans*/*cis*=9.3:1, 92% *ee*
93,R=3-thienyl, 23% yield, *trans*/*cis*>20:1, 91% *ee*

Scheme 17. Complex **59**-catalysed synthesis of compounds **86**-**93**.[46]

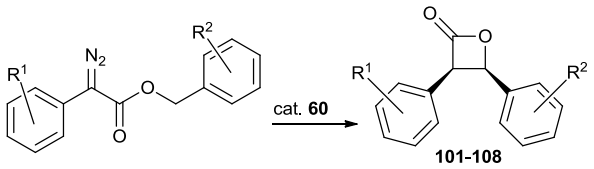
Complex **59** was also active in promoting the insertion of a carbene moiety into Si–H bonds.[46] Products **94**-**100** reported in Scheme 18 were obtained in high yields and enantioselectivities.



94, R=Ph, R^1=R^2=Me, R^3=Ph, 92% yield, 72% *ee*
95, R=4-BrC_6H_4, R^1=R^2=Me, R^3=Ph, 93% yield, 91% *ee*
96, R=4-Cl-C_6H_4, R^1=R^2=Me, R^3=Ph, 75% yield, 78% *ee*
97, R=Ph, R^1=R^2=R^3=Et, 75% yield, 75% *ee*
98, R=4-BrC_6H_4, R^1=R^2=R^3=Et, 93% yield, 91% *ee*
99, R=4-ClC_6H_4, R^1=R^2=R^3=Et, 94% yield, 82% *ee*
100, R=2-naphthyl, R^1=R^2=R^3=Et, 92% yield, 75% *ee*

Scheme 18. Complex **59**-catalysed synthesis of compounds **94**-**100**.[46]

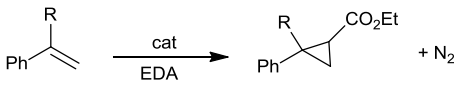
The activity of iridium complex **60** was investigated by C.-M. Che and co-authors in catalysing the intramolecular C-H carbene insertion by using several α–diazoesters as starting materials to selectively synthesise *cis*-*β*–lactones.[47] Achieved data indicated that electron-donating R^1 groups, such as a methyl group, were responsible for lower yields while the presence of an encumbered R^2 substituent had a negative effect on the reaction efficiency due to steric reasons.



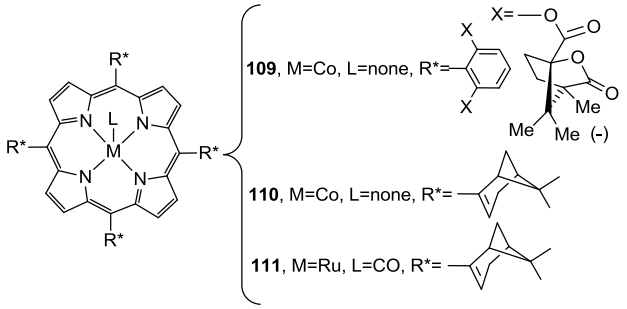
101, R^1=R^2=H, 87% yield, 76% *ee*
102, R^1=H, R^2=4-Br, 53% yield, 78% *ee*
103, R^1=H, R^2=2-Br, 50% yield, 67% *ee*
104, R^1=H, R^2=3-Cl, 53% yield, 77% *ee*
105, R^1=4-Me, R^2=H, 54% yield, 78% *ee*
106, R^1=4-F, R^2=H, 80% yield, 76% *ee*
107, R^1=3-Cl, R^2=H, 75% yield, 50% *ee*
108, R^1=3-Br, R^2=H, 72% yield, 39% *ee*

Scheme 19. Complex **60**-catalysed synthesis of enantiopure *cis*-β-lactones **101**-**108**.[47]

As described up to now, Halterman-type porphyrins have been extensively used for synthesising metal complexes active in carbene transfer reactions. The observed stereo-control, due to the chiral ligand skeleton, was only in part modified by the nature of the porphyrin core which was more responsible for the reaction chemoselectivity. In fact, when other D_4 symmetrical chiral porphyrins were used in promoting carbene transfers, worse results were achieved indicating the active role of the Halterman porphyrin skeleton in determining the stereo-control of the reaction. Metal porphyrins **109**,[48] **110**[49] and **111**[49] were tested in the cyclopropanation of styrene and α-methylstyrene by EDA affording compounds **3** and **4**, respectively (Scheme 2).



3, 73% yield, *cis*/*trans*=64:36, 77% ee_{cis}, 62% ee_{trans} (cat. **109**)
4, 26% yield, *cis*/*trans*=24:76, racemate mixture (cat. **110**)
4, 90% yield, *cis*/*trans*=26:74, 5% ee_{cis}, 10% ee_{trans} (cat. **111**)



Scheme 20. Synthesis of **3** and **4** catalysed by **109**,[48] **110**[49] and **111.**[49]

It should be noted that, even if the reaction always occurred with modest to poor stereoselectivities, (Scheme 20) cobalt(II) catalyst **109** promoted a *cis*-diastereoselectivity conversely to that which was reported for Halterman-type-catalysed cyclopropanations discussed to date.

3. D_2-Symmetric Catalysts

Considering that the stereo-control of carbene transfer reactions are strictly related to the porphyrin skeleton, many efforts have been made up to now to structurally modify the ligand to create a befitting 'active pocket' around the active metal where the catalytic reaction takes place.

In 1992 T. Kodadeck and co-authors reported the synthesis of two rhodium complexes **112** and **113** deriving from $\alpha\beta\alpha\beta$ porphyrin precursors (Figure 2, structure **C**) namely 'Chiral Wall'[50] and 'Chiral Fortress'[51], respectively (Figure 6).

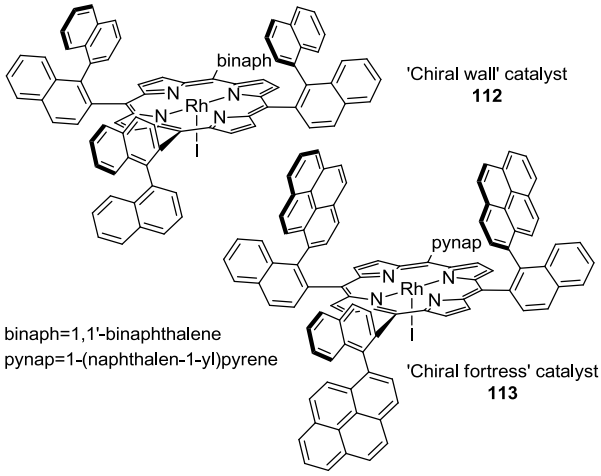


Figure 6. Structures of rhodium catalysts **112**[50] and **113**[51].

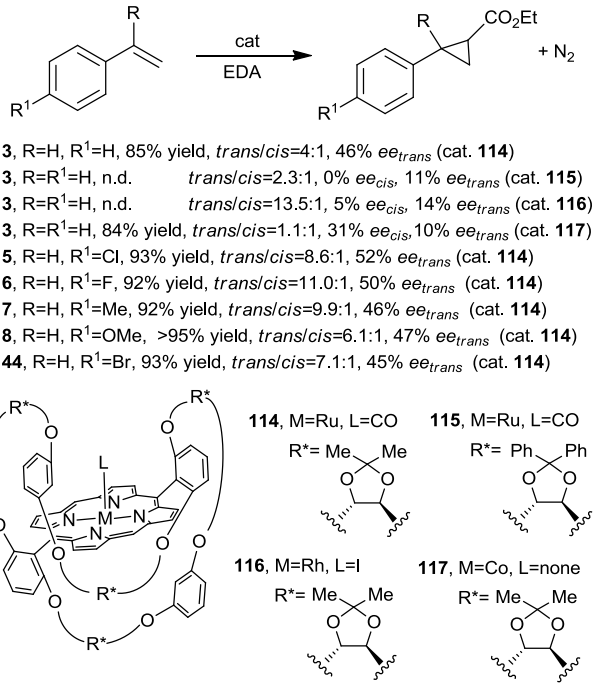
Complexes **112** and **113** were tested in the cyclopropanation of styrenes by EDA but unfortunately the stereo-control was poor with both catalysts but, in every tested case, a *cis*-diastereoselectivity (up to *cis*/*trans*=14.2:1) was observed. This result indicated a different orientation of the olefin approach with respect to Halterman-type-catalysed cyclopropanations where a *trans*-diastereoselectivity was always observed.

The authors ascribed the modest observed enantioselectivity (up to 60%) to a large number of non-equivalent orientations of the carbene moiety, which can be responsible for a lack of the stereo-control.

Better results in terms of enantioselectivity were achieved by using chiral ruthenium, rhodium and cobalt porphyrins **114**-**117**[48, 52, 53] (Figure 2, type **C**) reported in Scheme 21 together with the synthesised cyclopropanes **3**, **5**-**8** (Scheme 2) and **44** (Scheme 9).

Catalyst **114** was also used to promote the cylopropanation of styrene by DAMP, the desired compound **30** (Scheme 7) was obtained in 92% yield, 97:3 $d.r._{trans}$ and 33% ee_{trans}.[54]

Even if better stereoselectivities were observed by using catalysts **114**-**117**, it is evident that those structural modifications of the porphyrin skeleton were not effective to reach high reaction stereo-control.



Scheme 21. Synthesis of cyclopropanes **3, 5-8** and **44** catalysed by **114**,[52] **115**,[53] **116**[53] and **117**.[48]

The D_2 symmetrical dioxo-ruthenium(IV) picket-fence complex **118** (Figure 2, type **C**), bearing α-methoxy-α-(trifluoromethyl)phenylacetyl chiral groups (Figure 7) was also used to catalyse the styrene cyclopropanation by EDA. Compound **3** (Scheme 2) was formed with a *trans*/*cis* ratio of 9:1, ee_{cis} = 34% and ee_{trans} = 14%.[55]

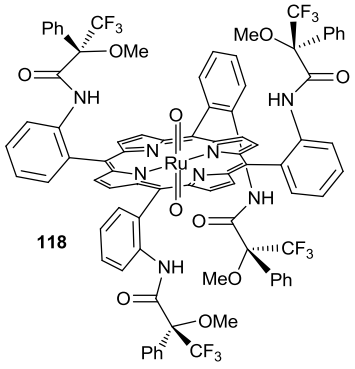


Figure 7. Structure of the D_2 symmetrical dioxo-ruthenium(IV) picket-fence complex **118**.

The authors suggested that, independently from the oxidation state of the ruthenium pre-catalyst, the active carbene intermediate of the cyclopropanation is the same that was proposed for the reaction catalysed by ruthenium(II) porphyrin complexes.

Considering the importance in driving the carbene transfer reaction into a confined chiral space to reach a high stereo-control, X. P. Zhang and co-authors developed a pool of chiral cobalt porphyrins showing a skeleton which has an active role in controlling the reaction outcome (Figure 2, type **B**).

The D_2 symmetrical structure of catalysts **119**-**131**[56-60] (Figure 8) presents, onto two of the four *meso* positions, amido functionalities which are fundamental in determining the reaction stereoselectivity by establishing hydrogen bonding interactions with the carbene functionality.

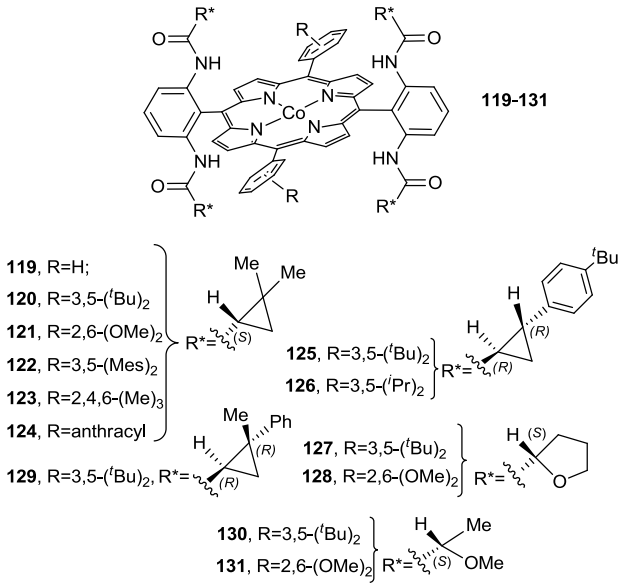


Figure 8. Structures of the D_2 symmetrical cobalt porphyrins **119**-**131**.[56-60]

Among all the catalysts reported in Figure 8, complex **120** was largely employed to catalyse the cyclopropanation of substituted alkenes by diazo reagents displaying a variety of electronic features (Chart 1).

A large number of cyclopropane derivatives were synthesised starting from aromatic alkenes,[61-65] (Chart 1, type **A**, **D**, **G** and **J**) electron deficient non-aromatic alkenes[62-66] (Chart 1, type **B**, **E** and **H**) and aliphatic alkenes[62,63,65] (Chart 1, type **C**, **F**, **I** and **L**) by using both *mono*-substituted[61,64,66] (Chart 1, type **A**-**C**) and acceptor/acceptor *bis*-substituted[62,63,65] (Chart 1, type **D**-**L**) diazo derivatives.

Type **A** cyclopropanes (Chart 1), in the presence of catalyst **120**, were formed with excellent *trans*-diastereoselectivities (up to 99:1) and enantioselectivities (up to 98% ee_{trans}) by using both EDA and *tert*-butyl diazoacetate (^{t}BDA) as the diazo reagent and 4-dimethylaminopyridine (DMAP) as co-catalyst.[61]

It was proposed that a coordinating ligand such as DMAP, with a relevant *trans* effect, can favour the asymmetric induction by forming a more catalytically active five-coordinated cobalt(II) intermediate from the starting four-coordinated cobalt(II) porphyrin complex.[67]

The catalytic performance was unaffected by the electronic nature of the starting alkene and the presence of several functional substituents on the alkene was well tolerated in the catalytic reaction. The reaction was also effective by using succinimidyl diazoacetate which reacted with aromatic alkenes forming cyclopropane succinimidyl esters, which are useful

synthons of the synthesis of optically active cyclopropyl carboxamides.[64]

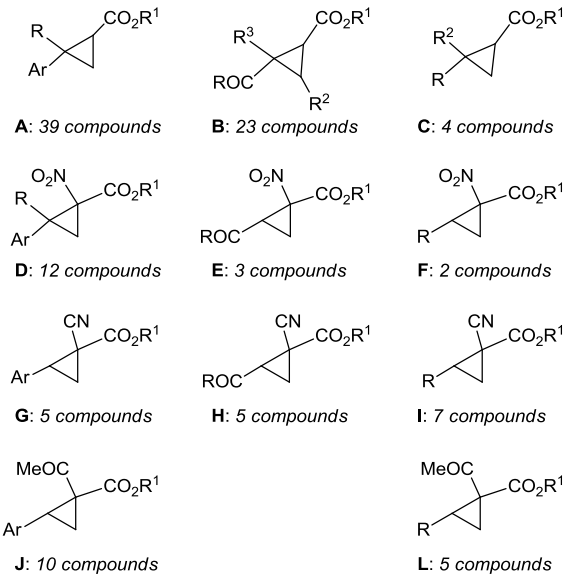
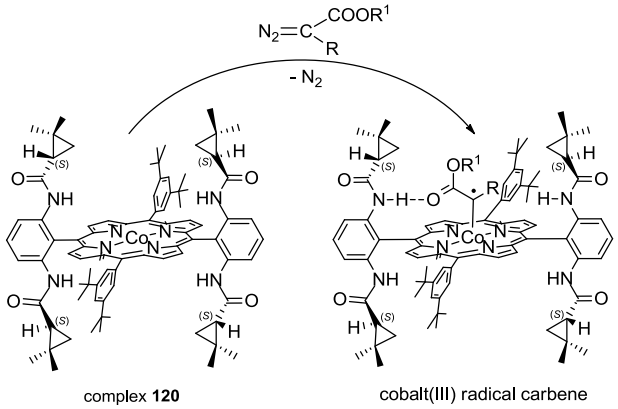


Chart 1. General structures of cyclopropanes synthesised in the presence of cobalt(II) catalyst **120**. [61-66]

Furthermore, EDA, ^{t}BDA and succinimidyl diazoacetate reacted very well in the presence of **120** with electron deficient alkenes forming electrophilic cyclopropane derivatives in high yields and high stereoselectivities (Chart 1, type **B** and **C**).[64, 66] Complex **120** catalysed the cyclopropanation of aromatic alkenes by using acceptor/acceptor *bis*-substituted diazo derivatives such as α-nitrodiazoacetate ($N_2C(NO_2)(COOEt)$)[62] (Chart 1, type **D**), α-cianodiazoacetate ($N_2C(CN)(COOEt)$)[63] (Chart 1, type **G**) and α-ketodiazoacetate ($N_2C(COMe)(COO^tBu)$)[65] (Chart 1, type **J**). Excellent results in terms of diastereo- and enantioselectivity were achieved albeit these diazo reagents usually display a low reactivity in carbene transfer reactions and perform with a poor enantioselectivity. It should be noted that the above cited acceptor/acceptor *bis*-substituted diazo derivatives also efficiently reacted with electron deficient non-aromatic alkenes (Chart 1, type **E** and **H**) and aliphatic alkenes (Chart 1, type **F**, **I** and **L**).

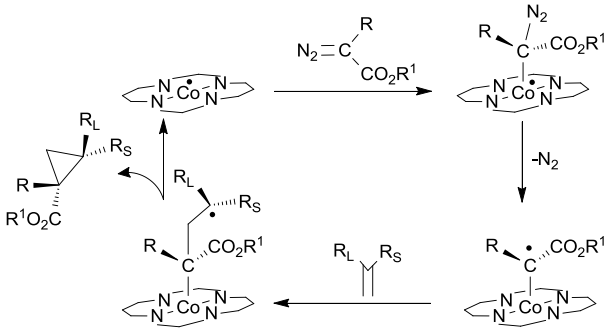
As reported above, the catalytic activity of D_2 symmetric cobalt(II) complex **120** was independent from the electronic characteristics of employed reagents. This catalytic versatility was ascribed to the formation of hydrogen-bondings between amide NH groups, located on the porphyrin ligand, and the oxygen atom of the carbonyl groups on the carbene moiety in the suggested cobalt(III) carbene radical intermediate (Scheme 22). The authors proposed that the formation of hydrogen interactions was fundamental in correctly driving the carbene addition to the alkene double bond and could be responsible for the high observed stereo-control.

Until now several studies have been performed to shed some light on the mechanism of cobalt(II) porphyrin-catalysed cyclopropanations[68-73] and over the last years X. P. Zhang, B. de Bruin and co-authors published several papers to support the radical nature of the alkene cyclopropanation and the active role of D_2 symmetrical porphyrin catalysts in influencing the reaction stereoselectivity.[74-77]



Scheme 22. Reaction of complex **120** with a diazo reagent forming cobalt(III) radical carbene.[74-77]

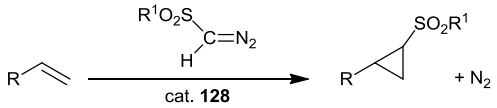
A combination of experimental EPR/ESI-MS and theoretical DFT studies of the cyclopropanation reaction was reported to support the formation of a Fisher-type radical species which interacts with the parallel alkene approaching (Scheme 23).



Scheme 23. Proposed mechanism of the D_2 symmetric cobalt porphyrin-catalysed alkene cyclopropanation.[74-77]

Considering the high influence of the porphyrin skeleton in inducing an optimised stereo-control, the catalytic activity of other cobalt D_2 symmetric chiral porphyrins was investigated by X. P. Zhang an co-authors. The use of the sterically hindered catalyst **128** (Figure 8) thus achieving a very good stereoselectivity in the cyclopropanation of several alkenes with different diazosulfones $N_2CH(SO_2Ar)$.[57,58] Better results in terms of both diastereo- and enantioselectivities were observed in the presence of **128** with respect to that observed when the reaction was performed in the presence of catalyst **120**. These results could be due to the presence of a more rigid and polar chiral environment which in turn are the results of intramolecular hydrogen bonding interactions and of the presence of cyclic structures.

Catalyst **128** was active in promoting the synthesis of compounds **132**-**143** reported in Scheme 24 with *trans*-diastereoselectivities up to 99:1 and ee_{trans} up to 97%.



132, R=Ph, R^1=*p*-MeC_6H_4, 99% yield, 99:1 *d.r.*$_{trans}$, 92% *ee*$_{trans}$
133, R=Ph, R^1=*p*-$OMeC_6H_4$, 97% yield, 97:3 *d.r.*$_{trans}$, 90% *ee*$_{trans}$
134, R=Ph, R^1=*p*-$NO_2C_6H_4$, 99% yield, 99:1 *d.r.*$_{trans}$, 90% *ee*$_{trans}$
135, R=*p*-^{t}BuC_6H_4, R^1=*p*-MeC_6H_4, 57% yield, 99:1 *d.r.*$_{trans}$, 94% *ee*$_{trans}$
136, R=*p*-$OMeC_6H_4$, R^1=*p*-MeC_6H_4, 72% yield, 99:1 *d.r.*$_{trans}$, 95% *ee*$_{trans}$
137, R=*p*-$CF_3C_6H_4$, R^1=*p*-MeC_6H_4, 88% yield, 99:1 *d.r.*$_{trans}$, 95% *ee*$_{trans}$
138, R=*m*-$NO_2C_6H_4$, R^1=*p*-MeC_6H_4, 77% yield, 99:1 *d.r.*$_{trans}$, 96% *ee*$_{trans}$
139, R=naphthyl, R^1=*p*-MeC_6H_4, 81% yield, 99:1 *d.r.*$_{trans}$, 93% *ee*$_{trans}$
140, R=CO_2Me, R^1=*p*-MeC_6H_4, 96% yield, 94:6 *d.r.*$_{trans}$, 89% *ee*$_{trans}$
141, R=CO_2Et, R^1=*p*-MeC_6H_4, 72% yield, 99:1 *d.r.*$_{trans}$, 90% *ee*$_{trans}$
142, R=COMe, R^1=*p*-MeC_6H_4, 93% yield, 99:1 *d.r.*$_{trans}$, 89% *ee*$_{trans}$
143, R=CN, R^1=*p*-MeC_6H_4, 81% yield, 79:21 *d.r.*$_{trans}$, 61% *ee*$_{trans}$

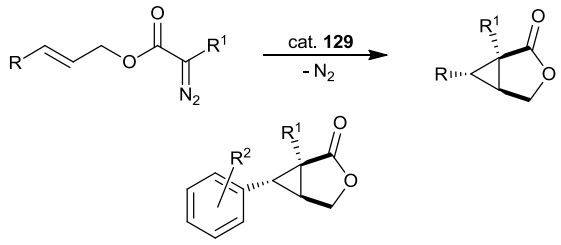
Scheme 24. Synthesis of compounds **132**-**143** catalysed by cobalt catalyst **128**.[57,58]

It should be noted that compounds reported in Scheme 24 were obtained by using alkene as the limiting agent and without requiring the slow addition of the diazo reagent, which is generally applied to limit dimerization reactions of starting diazo molecules.

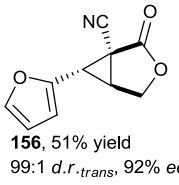
Considering the excellent results achieved in various intermolecular cyclopropanations, X. P. Zhang and co-authors tested the activity of D_2-symmetric chiral porphyrins in intramolecular cyclopropanations. Catalyst **129** (Figure 8) showed a very good catalytic efficiency in promoting the asymmetric intramolecular cyclopropanation of various allylic diazoacetates providing the differently functionalized 3-oxabicyclo[3.1.0]hexan-2-one derivatives **144**-**161** bearing three contiguous quaternary and tertiary stereocentres. It should be noted that compounds **160** and **161** were obtained starting form corresponding *cis* and *trans* starting alkenes, respectively (Scheme 25).

D_2 symmetric cobalt porphyrin **126** (Figure 8) was used to promote the stereoselective intramolecular alkylation of α-methoxycarbonyl–α–diazosulfone compounds to form *trans*–sulfolane derivatives by a C-H bond activation.[59] The synthesised compounds **162**-**173** were obtained in high yields, with *trans*-diastereoselectivities up to 97:3 and *ee*$_{trans}$ up to 94% (Scheme 26).

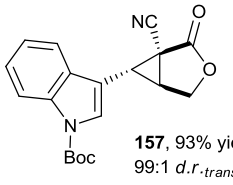
As already suggested for intermolecular reactions, the authors proposed that the very good catalytic activity could be ascribed to the formation of hydrogen bonds between the substrate and amide groups on the porphyrin skeleton. The study of the reaction scope revealed that the procedure was efficient for reacting substrates showing different electronic characteristics. The independence of the catalytic performance from the electronic nature of involved starting materials were explained by the occurrence of a metal-radical mechanism.



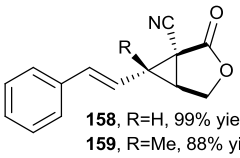
144, R^1=CN, R^2=H, 99% yield, 99:1 *d.r.*$_{trans}$, 96% *ee*$_{trans}$
145, R^1=NO_2, R^2=H, 95% yield, 99:1 *d.r.*$_{trans}$, 89% *ee*$_{trans}$
146, R^1=COMe, R^2=H, 62% yield, 99:1 *d.r.*$_{trans}$, 99% *ee*$_{trans}$
147, R^1=CO_2Et, R^2=H, 99% yield, 99:1 *d.r.*$_{trans}$, 90% *ee*$_{trans}$
148, R^1=R^2=H, 95% yield, 99:1 *d.r.*$_{trans}$, 99% *ee*$_{trans}$
150, R^1=Me, R^2=H, 82% yield, 99:1 *d.r.*$_{trans}$, 73% *ee*$_{trans}$
151, R^1=CN, R^2=*p*-^{t}Bu, 99% yield, 99:1 *d.r.*$_{trans}$, 96% *ee*$_{trans}$
152, R^1=CN, R^2=*p*-Me, 99% yield, 99:1 *d.r.*$_{trans}$, 98% *ee*$_{trans}$
153, R^1=CN, R^2=*o*-Me, 88% yield, 99:1 *d.r.*$_{trans}$, 97% *ee*$_{trans}$
154, R^1=CN, R^2=*p*-Br, 99% yield, 99:1 *d.r.*$_{trans}$, 95% *ee*$_{trans}$
155, R^1=CN, R^2=*p*-CF_3 99% yield, 99:1 *d.r.*$_{trans}$, 95% *ee*$_{trans}$



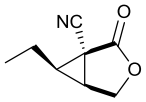
156, 51% yield
99:1 *d.r.*$_{trans}$, 92% *ee*$_{trans}$



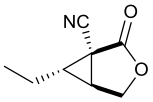
157, 93% yield
99:1 *d.r.*$_{trans}$, 91% *ee*$_{trans}$



158, R=H, 99% yield, 90:10 *d.r.*$_{trans}$, 78% *ee*$_{trans}$
159, R=Me, 88% yield, 99:1 *d.r.*$_{trans}$, 83% *ee*$_{trans}$

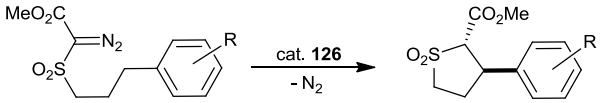


160, 99% yield
36:64 *d.r.*$_{trans}$, 69% *ee*$_{trans}$



161, 99% yield
99:1 *d.r.*$_{trans}$, 78% *ee*$_{trans}$

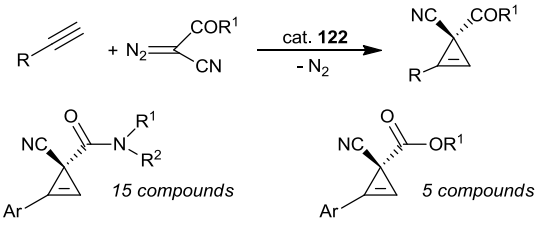
Scheme 25. Synthesis of compounds **144**-**161** catalysed by cobalt catalyst **129**.[60]



162, R=4-NO_2, 92% yield, *trans*/*cis*=96:4, 92% *ee*
163, R=4-CF_3, 91% yield, *trans*/*cis*=95:5, 84% *ee*
164, R=4-F, 98% yield, *trans*/*cis*=95:5, 91% *ee*
165, R =4-Cl, 98% yield, *trans*/*cis*=96:4, 91% *ee*
166, R=3,5-Cl_2, 89% yield, *trans*/*cis*=97:3, 84% *ee*
167, R=3-Br, 91% yield, *trans*/*cis*=95:5, 88% *ee*
168, R=H, 91% yield, *trans*/*cis*=97:3, 90% *ee*
169, R=4-Me, 96% yield, *trans*/*cis*=97:3, 92% *ee*
170, R=4-OMe, 96% yield, *trans*/*cis*=96:4, 94% *ee*
171, R=4-OH, 98% yield, *trans*/*cis*=96:4, 91% *ee*
172, R=4-NH_2, 99% yield, *trans*/*cis*=95:5, 83% *ee*
173, R=4-NHAc, 86% yield, *trans*/*cis*=96:4, 92% *ee*

Scheme 26. Synthesis of compounds **162**-**173** catalysed by cobalt catalyst **126**.[59]

D_2 Symmetric cobalt porphyrins reported in Figure 8 were also very efficient in catalysing the cyclopropenation of alkynes by using acceptor/acceptor sunbstituted diazo reagents. Complex **122** (Figure 8) showed a very good catalytic competency and compounds reported in Scheme 27 were formed with an excellent stereo-control;[78] the reactions occurred in high yields (up to 97%) and enantiomeric excesses up to 99%.



Scheme 27. Complex **122**-catalysed cyclopropenation of alkynes.[78]

4. C_2-Symmetric Catalysts

Data reported up to now on the catalytic efficiency of D_2 symmetric chiral cobalt catalysts clearly indicate that the catalytic performance in terms of stereo-control is due to a synergistic action of the active metal centre with the ligand periphery. Consequently, porphyrin ligands could be considered '*non innocent ligands*' of which the tridimensional structure could be essential to opportunely drive the carbene moiety to the target substrate.

The functionalization of $\alpha\alpha\beta\beta$ porphyrin atropoisomers with chiral moieties affords C_2 symmetric ligands (Figure 2, type **D**) which can be used for the synthesis of metal chiral catalysts.

The chiral porphyrin **174**, achieved by reacting the atropoisomer $\alpha\alpha\beta\beta$–tetrakis-(2-aminophenyl)porphyrin with diacid chlorides derived from binaphtyl, was used by E. Gallo, E. Rose and co-authors to synthesise cobalt(II) complex **175** (Figure 9) active in the cyclopropanation of styrenes.[79]

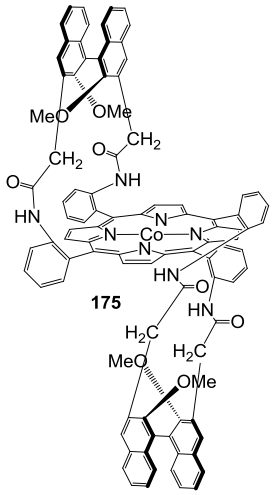
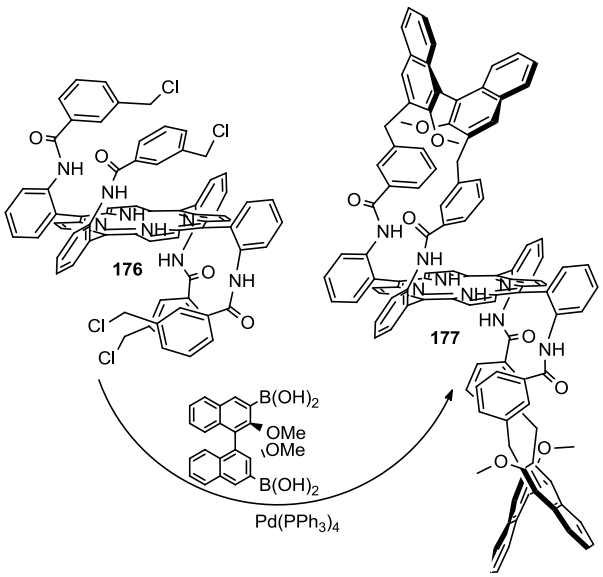


Figure 9. Structure of complex **175** used for the cyclopropanation of styrenes.[79]

Reactions occurred with modest stereo-control albeit good yields (85-99%) of desired cyclopropanes were observed. The best result was observed in the cyclopropanation of α-methylstyrene by EDA in the presence of *N*-methyl imidazole (NMI) as co-catalysts. Even if the *cis*/*trans* diastereoselectivity was only 34:66, the *cis*-diastereomer was obtained with 90% *ee* and TON of 200.

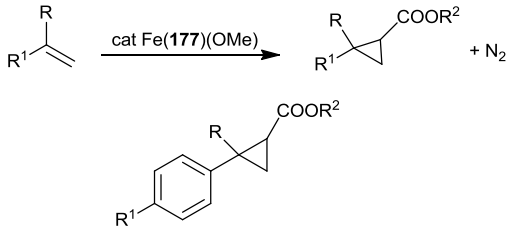
The reasons for the low degree of the stereo-control observed in cyclopropanations catalysed by complex **175** were considered from a theoretical point of view by L. Toma and co-authors, who studied the conformational properties of cobalt catalyst **175**.[80] E. Gallo, E. Rose and co-authors proposed that complex **175**-catalysed cyclopropanation occurred through the formation of an active carbene radical intermediate in which the two axial positions on the cobalt atom were occupied by NMI and $CHCO_2Et$ carbene ligands, respectively. The modelling of the supposed carbene species revealed that the cavity originated by the binaphthyl moiety surmounting the porphyrin plane was not large enough to host the carbene ethyl group. The latter, placed outside the cavity, presented a high degree of freedom which did not permit adequate chiral discrimination.

Then, to strengthen the binaphtyl arms and increase the dimension of the active space to favour the formation of the carbene intermediate into the chiral cavity, the CH_2 linker of porphyrin **174** was replaced by a benzylic moiety by reacting porphyrin **176**[81] with (*R*)-(2,2'-dimethoxy-[1,1'-binaphthal-ene]-3,3'-diyl)diboronic acid in the presence of $(Ph_3P)_4Pd$. Chiral porphyrin ligand **177** was obtained as reported in Scheme 28.[82]

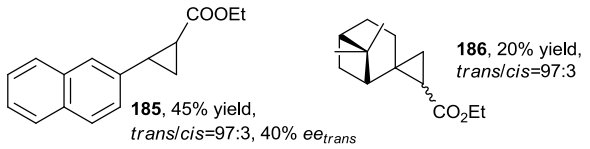


Scheme 28. Synthesis of *bis*-strapped porphyrin **177**.[82]

Porphyrin **177** was employed to synthesise the iron(III) methoxy derivative Fe(**177**)(OMe) which was able to promote the synthesis of cyclopropanes **4**, **5**, **7**-**9** (Scheme 2) and **178**-**186** listed in Scheme 29.[82,83]



4, R=Me, R^1=H, R^2=Et, 98% yield, *trans*/*cis*=98:2, 87% ee_{trans}
5, R=H, R^1=Cl, R^2=Et, 60% yield, *trans*/*cis*=98:2, 60% ee_{trans}
7, R=H, R^1=Me, R^2=Et, 72% yield, *trans*/*cis*=99:1, 68% ee_{trans}
8, R=H, R^1=OMe, R^2=Et, 72% yield, *trans*/*cis*=99:1, 60% ee_{trans}
9, R=Ph, R^1=H, R^2=Et, 25% yield, 48% ee_{trans}
178, R=Me, R^1=H, R^2=^{i}Pr, 60% yield, *trans*/*cis*=98:2, 67% ee_{trans}
179, R=Me, R^1=H, R^2=^{n}Pr, 73% yield, *trans*/*cis*=98:2, 40% ee_{trans}
180, R=Me, R^1=H, R^2=^{t}Bu, 42% yield, *trans*/*cis*=63:37, 7% ee_{trans}
181, R=Me, R^1=Cl, R^2=Et, 80% yield, *trans*/*cis*=99:1, 80% ee_{trans}
182, R=H, R^1=^{t}Bu, R^2=Et, 85% yield, *trans*/*cis*=98:2, 63% ee_{trans}
183, R=Me, R^1=F, R^2=Et, 30% yield, *trans*/*cis*=91:9, 71% ee_{trans}
184, R=H, R^1=CH_2Cl, R^2=Et, 60% yield, *trans*/*cis*=98:2, nd



Scheme 29. Complex Fe(**177**)(OMe)-catalysed synthesis of compounds **4**, **5**, **7**-**9**, **178**-**186**.[82,83]

The synthesis of compounds reported in Scheme 29 were performed by using alkene as the limiting reagent, a slight excess of the diazo compound was fundamental in achieving very good yields and stereoselectivities. In all tested reactions excellent *trans*-diastereoselectivities were observed and a general decrease of stereo-control was observed by using high sterically hindered starting compounds. The cyclopropanation of (1*S*)-*β*-pinene yielded only two of the four possible diastereomers of **186** and 1*R*,2*R*,2'*R* diastereomer was isolated as the major reaction product.

It should be noted that a catalyst loading of 0.01% (TON = 10000) was used for the synthesis of selected cyclopropanes where very short reaction times were observed resulting in excellent TOF values (up to 120000 h^{-1}). A combination of experimental and DFT studies suggested the formation of an iron carbene intermediate showing a methoxy axial ligand which plays an important role in determining the catalytic performance of the iron complex.[83] The theoretical modelling of involved carbene intermediates disclosed that the observed diasteroselectivities were due to the tridimensional arrangements of the two arms surrounding the porphyrin plane, which are able to efficiently interact with the approaching alkene. Conversely, the reaction enantiocontrol was not always satisfactory for the long distance between the chiral portion of the ligand and the incoming unsaturated substrate.

5. Conclusions

The present perspective reports an overview of the employment of chiral porphyrin metal catalysts to promote carbene transfer reactions. The influence of the porphyrin ligand structure in controlling the reaction stereoselectivity was stressed to underline the effect of the tridimensional ligand arrangement in driving the carbene towards the target molecule. The most important class of chiral porphyrin catalysts used to activate diazo compounds have been here discussed with the final aim of summarising relevant synthetic strategies yielding porphyrin skeletons capable of a high reaction stereo-control.

The analysis of published data revealed that chiral porphyrin complexes are very effective enantioselective catalysts and they generally promote the alkene cyclopropanation with a high *trans*-diasteroselectivity.

We can conclude that a very fascinating challenge for a near future could be the development of new porphyrin chiral catalysts able to couple a *cis*-diasteroselectivity with an excellent enantiocontrol.

Acknowledgements

We gratefully acknowledge the MIUR-Italy for the financial support over the years.

References

1 G. Maas, *Chem. Soc. Rev.*, 2004, **33**, 183-190.
2 G. Bartoli, G. Bencivenni and R. Dalpozzo, *Synthesis*, 2014, **46**, 979-1029.
3 H. Lebel, J.-F. Marcoux, C. Molinaro and A. B. Charette, *Chem. Rev.*, 2003, **103**, 977-1050.
4 M. M. K. Boysen, in *Carbohydrates – Tools for Stereoselective Synthesis*, Wiley-VCH Verlag GmbH & Co. KGaA, 2013, pp. 313-318.
5 A. Caballero, A. Prieto, M. M. Díaz-Requejo and P. J. Pérez, *Eur. J. Inorg. Chem.*, 2009, 1137-1144.
6 M. P. Doyle, R. Duffy, M. Ratnikov and L. Zhou, *Chem. Rev.*, 2010, **110**, 704-724.
7 M. M. Díaz-Requejo and P. J. Pérez, *Chem. Rev.*, 2008, **108**, 3379-3394.
8 H. M. L. Davies and R. E. J. Beckwith, *Chem. Rev.*, 2003, **103**, 2861-2904.
9 A. Ford, H. Miel, A. Ring, C. N. Slattery, A. R. Maguire and M. A. McKervey, *Chem. Rev.*, 2015, **115**, 9981-10080.
10 N. R. Candeias, R. Paterna and P. M. P. Gois, *Chem. Rev.*, 2016, **116**, 2937-2981.
11 N. M. Roda, D. N. Tran, C. Battilocchio, R. Labes, R. J. Ingham, J. M. Hawkins and S. V. Ley, *Org. Biomol. Chem.*, 2015, **13**, 2550-2554.
12 S. T. R. Müller and T. Wirth, *ChemSusChem*, 2015, **8**, 245-250.
13 B. J. Deadman, S. G. Collins and A. R. Maguire, *Chem. Eur. J.*, 2015, **21**, 2298-2308.

14 B. Castano, E. Gallo, D. J. Cole-Hamilton, V. Dal Santo, R. Psaro and A. Caselli, *Green Chem.*, 2014, **16**, 3202-3209.
15 C.-M. Che, V. K.-Y. Lo, C.-Y. Zhou and J.-S. Huang, *Chem. Soc. Rev.*, 2011, **40**, 1950-1975.
16 D. Intrieri, A. Caselli and E. Gallo, *Eur. J. Inorg. Chem.*, 2011, 5071-5081.
17 C.-Y. Zhou, V. K.-Y. Lo and C.-M. Che, in *Handbook of Porphyrin Science*, ed. K. M. S. Edited by Kadish, Kevin M.; Guilard, Roger, World Scientific Publishing Co. Pte. Ltd., 2012, vol. 21, pp. 321-376.
18 B. J. Anding and L. K. Woo, in *Handbook of Porphyrin Science* ed. K. M. S. Edited by Kadish, Kevin M.; Guilard, Roger, World Scientific Publishing Co. Pte. Ltd., 2012, vol. 21, pp. 145-319.
19 H. Lu and X. P. Zhang, *Chem. Soc. Rev.*, 2011, **40**, 1899-1909.
20 C.-Y. Zhou, J.-S. Huang and C.-M. Che, *Synlett*, 2010, 2681-2700.
21 J. V. Ruppel, K. B. Fields, N. L. Snyder and X. P. Zhang, in *Handbook of Porphyrin Science* ed. K. M. S. Edited by Kadish, Kevin M.; Guilard, Roger, World Scientific Publishing Co. Pte. Ltd., 2010, vol. 10, pp. 1-84.
22 C.-Y. Zhou, J.-S. Huang and C.-M. Che, *Synlett*, 2010, 2681-2700.
23 G. Simonneaux and P. Le Maux, *Coord. Chem. Rev.*, 2002, **228**, 43-60.
24 M. Frauenkron and A. Berkessel, *Tetrahedron Lett.*, 1997, **38**, 7175-7176.
25 W.-C. Lo, C.-M. Che, K.-F. Cheng and T. C. W. Mak, *Chem. Commun.*, 1997, 1205-1206.
26 R. L. Halterman and S. T. Jan, *J. Org. Chem.*, 1991, **56**, 5253-5254.
27 C.-M. Che, J.-S. Huang, F.-W. Lee, Y. Li, T.-S. Lai, H.-L. Kwong, P.-F. Teng, W.-S. Lee, W.-C. Lo, S.-M. Peng and Z.-Y. Zhou, *J. Am. Chem. Soc.*, 2001, **123**, 4119-4129.
28 P. Le Maux, T. Roisnel, I. Nicolas and G. Simonneaux, *Organometallics*, 2008, **27**, 3037-3042.
29 A. Berkessel, P. Kaiser and J. Lex, *Chem. Eur. J.*, 2003, **9**, 4746-4756.
30 K.-H. Chan, X. Guan, V. K.-Y. Lo and C.-M. Che, *Angew. Chem. Int. Ed.*, 2014, **53**, 2982-2987.
31 I. Nicolas, P. L. Maux and G. Simonneaux, *Tetrahedron Lett.*, 2008, **49**, 2111-2113.
32 Y. Ferrand, P. Le Maux and G. Simonneaux, *Org. Lett.*, 2004, **6**, 3211-3214.
33 P. Le Maux, S. Juillard and G. Simonneaux, *Synthesis*, 2006, 1701-1704.
34 P. Le Maux, I. Nicolas, S. Chevance and G. Simonneaux, *Tetrahedron*, 2010, **66**, 4462-4468.
35 I. Nicolas, P. L. Maux and G. Simonneaux, *Tetrahedron Lett.*, 2008, **49**, 5793-5795.
36 J.-L. Zhang, Y.-L. Liu and C.-M. Che, *Chem. Commun.*, 2002, 2906-2907.
37 Y. Ferrand, C. Poriel, P. Le Maux, J. Rault-Berthelot and G. Simonneaux, *Tetrahedron: Asymmetry*, 2005, **16**, 1463-1472.
38 Y. Ferrand, P. Le Maux and G. Simonneaux, *Tetrahedron: Asymmetry*, 2005, **16**, 3829-3836.
39 I. Bauer and H.-J. Knolker, *Chem. Rev.*, 2015, **115**, 3170-3387.
40 T.-S. Lai, F.-Y. Chan, P.-K. So, D.-L. Ma, K.-Y. Wong and C.-M. Che, *Dalton Trans.*, 2006, 4845-4851.
41 J. R. Wolf, C. G. Hamaker, J.-P. Djukic, T. Kodadek and L. K. Woo, *J. Am. Chem. Soc.*, 1995, **117**, 9194-9199.
42 R. G. Salomon and J. K. Kochi, *J. Am. Chem. Soc.*, 1973, **95**, 3300-3310.
43 I. Nicolas, T. Roisnel, P. L. Maux and G. Simonneaux, *Tetrahedron Lett.*, 2009, **50**, 5149-5151.
44 P.-F. Teng, T.-S. Lai, H.-L. Kwong and C.-M. Che, *Tetrahedron: Asymmetry*, 2003, **14**, 837-844.
45 H.-Y. Thu, G. S.-M. Tong, J.-S. Huang, S. L.-F. Chan, Q.-H. Deng and C.-M. Che, *Angew. Chem., Int. Ed.*, 2008, **47**, 9747-9751.
46 J.-C. Wang, Z.-J. Xu, Z. Guo, Q.-H. Deng, C.-Y. Zhou, X.-L. Wan and C.-M. Che, *Chem. Commun.*, 2012, **48**, 4299-4301.
47 J.-C. Wang, Y. Zhang, Z.-J. Xu, V. K.-Y. Lo and C.-M. Che, *ACS Catal.*, 2013, **3**, 1144-1148.
48 L. Huang, Y. Chen, G.-Y. Gao and X. P. Zhang, *J. Org. Chem.*, 2003, **68**, 8179-8184.
49 A. Caselli, E. Gallo, F. Ragaini, F. Ricatto, G. Abbiati and S. Cenini, *Inorg. Chim. Acta*, 2006, **359**, 2924-2932.
50 J. L. Maxwell, S. O'Malley, K. C. Brown and T. Kodadek, *Organometallics*, 1992, **11**, 645-652.
51 S. O'Malley and T. Kodadek, *Organometallics*, 1992, **11**, 2299-2302.
52 E. Galardon, S. Roué, P. Le Maux and G. Simonneaux, *Tetrahedron Lett.*, 1998, **39**, 2333-2334.
53 Z. Gross, N. Galili and L. Simkhovich, *Tetrahedron Lett.*, 1999, **40**, 1571-1574.
54 C. Paul-Roth, F. De Montigny, G. Rethoré, G. Simonneaux, M. Gulea and S. Masson, *J. Mol. Catal. A: Chem.*, 2003, **201**, 79-91.
55 E. Galardon, P. Le Maux and G. Simonneaux, *Chem. Commun.*, 1997, 927-928.
56 Y. Chen, K. B. Fields and X. P. Zhang, *J. Am. Chem. Soc.*, 2004, **126**, 14718-14719.
57 S. Zhu, J. V. Ruppel, H. Lu, L. Wojtas and X. P. Zhang, *J. Am. Chem. Soc.*, 2008, **130**, 5042-5043.
58 S. Zhu, X. Cui and X. P. Zhang, *Eur. J. Inorg. Chem.*, 2012, **2012**, 430-434.
59 X. Cui, X. Xu, L.-M. Jin, L. Wojtas and X. P. Zhang, *Chem. Sci.*, 2015, **6**, 1219-1224.
60 X. Xu, H. Lu, J. V. Ruppel, X. Cui, S. Lopez de Mesa, L. Wojtas and X. P. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 15292-15295.
61 Y. Chen and X. P. Zhang, *J. Org. Chem.*, 2007, **72**, 5931-5934.
62 S. Zhu, J. A. Perman and X. P. Zhang, *Angew. Chem. Int. Ed.*, 2008, **47**, 8460-8463.
63 S. Zhu, X. Xu, J. A. Perman and X. P. Zhang, *J. Am. Chem. Soc.*, 2010, **132**, 12796-12799.

64 J. V. Ruppel, T. J. Gauthier, N. L. Snyder, J. A. Perman and X. P. Zhang, *Org. Lett.*, 2009, **11**, 2273-2276.
65 X. Xu, S. Zhu, X. Cui, L. Wojtas and X. P. Zhang, *Angew. Chem. Int. Ed.*, 2013, **52**, 11857-11861.
66 Y. Chen, J. V. Ruppel and X. P. Zhang, *J. Am. Chem. Soc.*, 2007, **129**, 12074-12075.
67 Y. Chen and X. P. Zhang, *Synthesis*, 2006, 1697-1700.
68 A. W. Johnson, D. Ward, P. Batten, A. L. Hamilton, G. Shelton and C. M. Elson, *J. Chem. Soc., Perkin Trans 1*, 1975, 2076-2085.
69 H. J. Callot and E. Schaeffer, *J. Organom. Chem.*, 1978, **145**, 91-99.
70 H. J. Callot and E. Schaeffer, *Nouv. J. Chim.*, 1980, **4**, 307-309.
71 P. Chattopadhyay, T. Matsuo, T. Tsuji, J. Ohbayashi and T. Hayashi, *Organometallics*, 2011, **30**, 1869-1873.
72 I. Iwakura, H. Tanaka, T. Ikeno and T. Yamada, *Chem. Lett.*, 2004, **33**, 140-141.
73 A. Penoni, R. Wanke, S. Tollari, E. Gallo, D. Musella, F. Ragaini, F. Demartin and S. Cenini, *Eur. J. Inorg. Chem.*, 2003, 1452-1460.
74 W. I. Dzik, X. Xu, X. P. Zhang, J. N. H. Reek and B. de Bruin, *J. Am. Chem. Soc.*, 2010, **132**, 10891-10902.
75 W. I. Dzik, X. P. Zhang and B. de Bruin, *Inorg. Chem.*, 2011, **50**, 9896-9903.
76 H. Lu, W. I. Dzik, X. Xu, L. Wojtas, B. de Bruin and X. P. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 8518-8521.
77 J. L. Belof, C. R. Cioce, X. Xu, X. P. Zhang, B. Space and H. L. Woodcock, *Organometallics*, 2011, **30**, 2739-2746.
78 X. Cui, X. Xu, H. Lu, S. Zhu, L. Wojtas and X. P. Zhang, *J. Am. Chem. Soc.*, 2011, **133**, 3304-3307.
79 S. Fantauzzi, E. Gallo, E. Rose, N. Raoul, A. Caselli, S. Issa, F. Ragaini and S. Cenini, *Organometallics*, 2008, **27**, 6143-6151.
80 E. Gallo, E. Rose, B. Boitrel, L. Legnani and L. Toma, *Organometallics*, 2014, **33**, 6081-6088.
81 A. Didier, L. Michaudet, D. Ricard, V. Baveux-Chambenoît, P. Richard and B. Boitrel, *Eur. J. Org. Chem.*, 2001, 1927-1926.
82 D. Intrieri, S. Le Gac, A. Caselli, E. Rose, B. Boitrel and E. Gallo, *Chem. Commun.*, 2014, **50**, 1811-1813.
83 D. M. Carminati, D. Intrieri, A. Caselli, S. Le Gac, B. Boitrel, L. Toma, L. Legnani E. Gallo, *submitted*.