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PERSPECTIVE

Making expensive dirhodium(II) catalysts cheaper: Rh(II) recycling methods

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Dirhodium(II) catalysts have been widely used as a remarkable tool in organic synthesis, ultimately resulting in a myriad of transformations and formation of a wide variety of compounds, every so often intermediaries in drug synthesis. Aiming at a more sustainable chemistry, several methods suitable for the reutilisation of expensive dirhodium complexes have been developed. Herein, we provide a combined overview of the available methods for recovering and reusing dirhodium(II) metal complexes in catalysis, covering homogeneous catalysis as well as heterogenisation methods.

1. Introduction

Over the years dirhodium(II) complexes have gained a strong foothold within the catalysts portfolio which mediate the formation of carbon–carbon and carbon–heteroatom bonds. Their unique paddlewheel structure comprises a Rh–Rh single bond, two catalytic active axial coordination sites and four bridging ligands responsible for many of the complex stereo-electronic properties (Fig. 1).[1] Appreciation for the structure, stability and catalytic activity of this family of lantern complexes led to the discovery of numerous useful applications in many different areas. They have been widely explored as: antitumor agents,[2] as sensors,[3] or as NMR shift reagents.[4] Nevertheless, most of the popularity of these paddlewheel complexes stems from their unique efficiency in mediating the formation of carbon–carbon and carbon–heteroatom bonds *via* the generation of highly reactive intermediates such as metalocarbenes.[1a–m] Despite their reactivity profile, they are not limited to this process as they successfully catalyse oxidations,[5] cycloadditions,[6] cross-couplings, C–H amination,[1h,7] among other important transformations, such as the ones in which rhodium catalysts act as Lewis acids.[8] Naturally, such a wide range of transformations results in the formation of a countless type of compounds with completely different structural frameworks. However, dirhodium complexes get their increased notoriety in asymmetric synthesis, catalysing several transformations in excellent enantioselectivities.

The methods available in the literature for the preparation of dirhodium complexes vary from the easy exchange of $Rh_2(OAc)_4$ ligands with carboxylic acids, as initially pointed by Callot,[9] to the reduction of $RhCl_3$ in the presence of the corresponding carboxylic acid.[10] Therefore it is surprising that despite the enormous synthetic value of dirhodium catalysts as proven over the years, scarce industrial applications of these complexes have been reported.[11] Rhodium supply depends mostly on South Africa (82%) and Russia (14%) and its primary use is in the catalytic converters in automobiles.[12] In addition, the fact that this metal is one of the rarest on Earth (rhodium's annual production is some 1% of gold's), makes its price performance become very volatile and extremely dependent on automobile industry demands. For instance, after a 20 fold increase from 2003 to 2008 in rhodium average price, it fell by more than 90% in 2009 as a result of the sharp decline of the global automobile industry.[13] Nowadays, rhodium is sold at 70 USD g^{-1} some 20% more than gold and 15% more than platinum, and the annual consumption is around 22 tons.[12a,14] Since dirhodium complexes are usually stable to air and moisture, the high cost of the metal allied with the difficulty in recovering and recycling it, are the major factors that limit their application in chemical industry. Furthermore, the tight legislation on metal contamination of active pharmaceutical ingredients imposes the development of efficient methods for metal removal.[15,16] Reutilisation of metal complexes can be achieved by several methods, based on heterogeneous and homogeneous strategies. Each of these methods has some intrinsic drawbacks and advantages that should be considered depending on the type of catalyst and the reaction in focus.

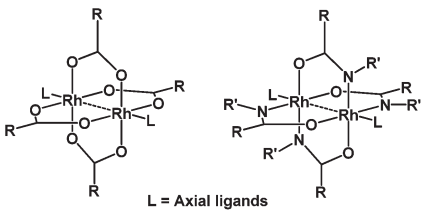

Fig. 1 General structures of two families of dirhodium(II) complexes with carboxylate and carboxamide bridging ligands.

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The heterogenisation of homogeneous catalysts can be achieved by immobilisation of the catalyst using entrapment, adsorption, ion-pairing, and covalent binding techniques, amongst other methods.[17] Organic or inorganic polymers can be used as supports for metal complexes, hence allowing the recovery of the catalyst by simple filtration or precipitation. The structural framework of dirhodium(II) complexes can be further explored by coupling to polymers through their bridging ligands or by the axial positions, in at least three distinctive coordinative ways (Fig. 2). Although such strategies allow the easy recovery of the metal catalyst, there are some problems associated with the use of heterogeneous catalysis, namely when dealing with asymmetric transformations. The immobilisation method, the properties of the polymer and the coordination site of the catalyst with the polymer will change the chiral environment around the metal atom often resulting in poorer selectivities of the product. Furthermore, the use of these methods usually leads to a lack of reproducibility in each catalytic run and it is very common that the immobilised catalyst starts losing activity and selectivity right in the second or third run. Therefore, homogeneous methods that are able to regenerate the dirhodium catalyst are complementary to the heterogeneous ones and will also be discussed in this review. Although the asymmetric dirhodium catalysis has been widely investigated, few examples about the reuse of chiral catalysts have been reported. In order to achieve the reutilisation of metal complexes using homogeneous systems, "non-conventional" solvents such as ionic liquids, fluorinated solvents, water and supercritical (sc) fluids can be employed as the reaction medium. One of the biggest disadvantages of catalyst immobilisation is the introduction of additional synthetic steps in the catalyst preparation. However, when dealing with the use of these "non-conventional" solvents, the catalyst can be easily immobilized by a simple dissolution of the complex in the solvent, whilst the reaction product can be easily extracted from the catalytic media with an immiscible solvent. Hence, no additional steps are introduced in the catalyst preparation.

In order to summarize and compare the robustness of the catalytic systems herein mentioned, three tables focusing on the recyclability of each system regarding the catalyst loading, the number of steps needed for preparation or immobilization of the dirhodium complex, the number of cycles reported, yields and selectivity of first and last run of each system is presented in the last pages of the document. The catalyst leaching is also included for all the reported cases and the reusable systems are compared with the corresponding conventional homogeneous systems. The tables are divided accordingly to the reaction type in which the catalyst was tested and only comprises catalysts or catalytic systems that were successfully reused in at least two runs (Tables 12 and 14). Due to the way such items are reported in the primary literature, it is somewhat difficult to gather all the information accurately. In any case, we hope that such tables will allow the scientific community to easily identify the best recoverable catalytic systems.

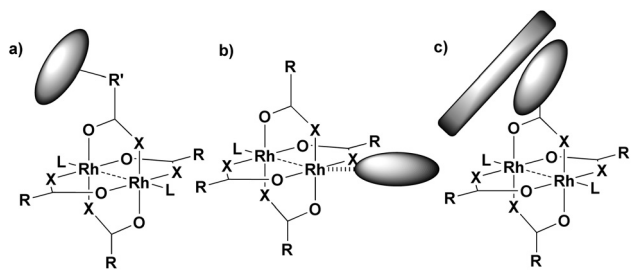


Fig. 2 Binding possibilities of dirhodium complexes for heterogenisation: (a) binding to polymer through bridging ligand exchange, (b) polymer binding by axial coordination, (c) adsorption to polymeric surface.

2. Heterogeneous systems

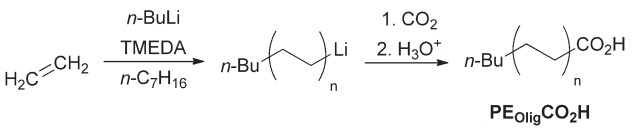
As aforementioned, dirhodium complexes can become heterogeneous by interaction with organic or inorganic polymers in several ways and involving different moieties or functional groups of the metal complex. While covalent binding or ionic pairing of a bridging ligand requires catalyst modification by exchange of one or more ligands, binding of a basic site to the axial position of the dirhodium complex is simpler to achieve. Entrapment of the dirhodium complex inside an inorganic porous material is also possible, though scarce examples can be found in the literature.[18]

2.1 Covalent binding by bridging ligand

The pioneering work of Bergbreiter[19] in the immobilisation of dirhodium complexes in polyethylene polymers validated the concept that an immobilised dirhodium complex catalyses C–H insertion and cyclopropanation. Proceeding the development of reusable catalysts based on the use of polyethylene (PE) as support medium,[20] Bergbreiter prepared an anionic polyethylene carboxylate (M_n of 1500–2000, $PE_{Olig}CO_2H$) by anionic oligomerisation of ethylene followed by carboxylation with CO_2 (Scheme 1). $Rh_2(PE_{Olig}CO_2)_4$, (**1**) was prepared and isolated after heating $PE_{Olig}CO_2H$ with $Rh_2(OAc)_4$.

The catalytic activity of the PE-immobilised dirhodium complex was clearly demonstrated by the reutilisation of the catalytic system 9 times in the cyclopropanation of 2,5-dimethyl-2,4-butadiene with ethyl diazoacetate (EDA) (Table 12, entry 29) in better *trans* : *cis* selectivity than with the homogeneous $Rh_2(OAc)_4$ catalyst. In addition to the maintained catalytic activity of the complex in the tenth cycle, the stereoselectivity of the reaction was also unchanged (from 2.3 : 1 (*trans* : *cis*) in the first cycle to the final 2.4 : 1 ratio). The prepared dirhodium catalyst was employed in the cyclopropanation of several other alkenes using an excess of alkene in toluene at 100 °C (Table 1).[19]

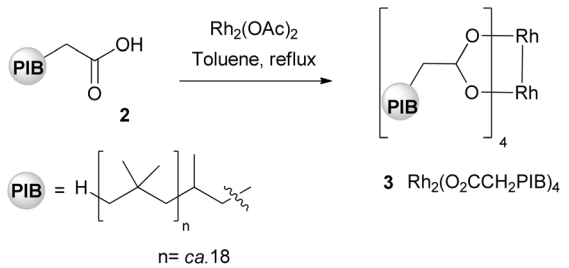
A homogeneous version of the previous catalyst was recently prepared, using polyisobutylene oligomers (PIB) as soluble supports.[21] In this case, the immobilised catalyst is recovered after extraction of the product from the non-polar reaction medium with ethyleneglycoldiacetate or acetonitrile, and evaporation of



Scheme 1 Preparation of $PE_{Olig}CO_2H$.

Table 1 Scope of $Rh_2(PE_{Olig}CO_2)_4$ in olefin cyclopropanation

Entry	Alkene	Cyclopropane yield (%)	Selectivity (*cis* : *trans* or *exo*/*endo*)
1		96	1.8
2		96	1.6
3		80	3.6
4		72	1.3
5		79	1.7



Scheme 2 Synthesis of PIB-supported dirhodium complex.

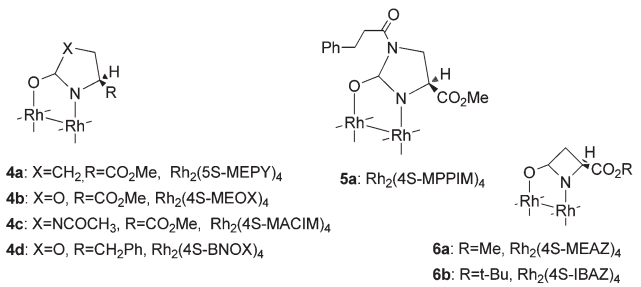
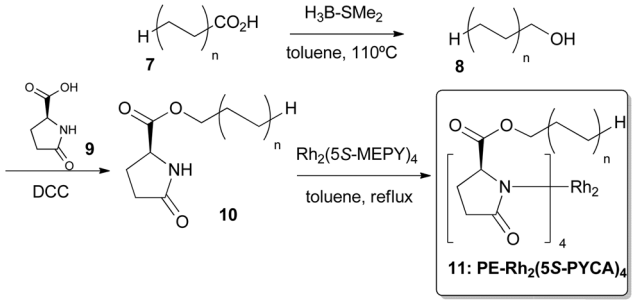


Fig. 3 Chiral dirhodium catalysts derived from carboxamidates developed by Doyle's group.

the reaction solvent. The polymer-supported dirhodium complex **3** was prepared by extensive exchange of the ligands with carboxylated polyisobutylene **2** in toluene at reflux (Scheme 2). Comparing this new version of the polymer bound dirhodium catalyst with the polyethylene bound dirhodium complex previously reported, similar selectivity and reusability were obtained in the styrene cyclopropanation with EDA in heptane.

The pioneering strategy implemented by Bergbreiter[19] was latter explored in the asymmetric intramolecular C–H insertion of 2-methoxyethyl diazoacetate and cyclopropanation of 3-methyl-2-buten-1-yl in good to excellent enantioselectivities.[22] For the preparation of the asymmetric polyethylene-immobilised dirhodium system, an analogue of $Rh_2(5S\text{-MEPY})_4$ **4a** from the group of chiral carboxamidate-derived dirhodium catalysts developed by Doyle and co-workers (Fig. 3)[23] was used as the dirhodium source.

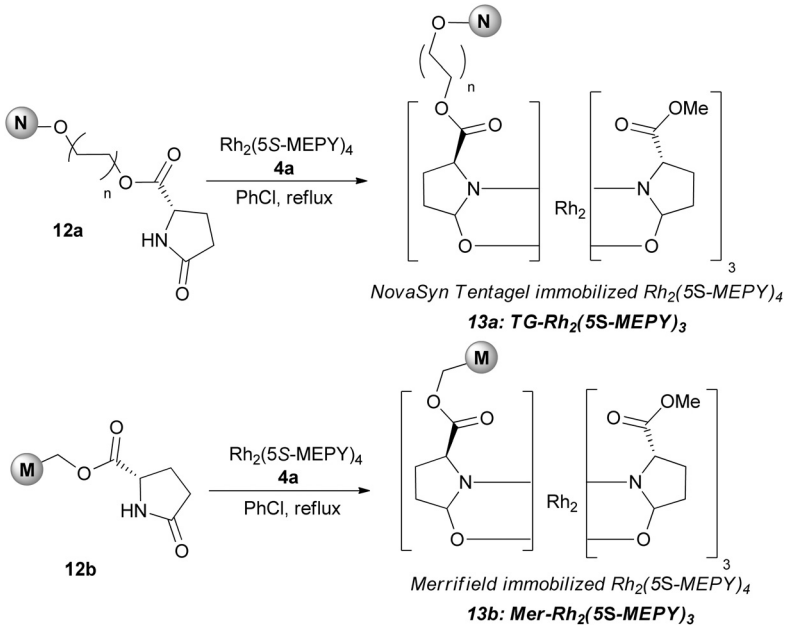
In the preparation of the chiral immobilised catalyst, the reduced oligomer was esterified with 2-pyrrolidone-5(*S*)-carboxylic acid **9** (Scheme 3). By ligand exchange of $Rh_2(5S\text{-MEPY})_4$ **4a** with the resultant oligomer **10**, the PE-$Rh_2(5S\text{-PYCA})_4$ **11** was prepared and tested in dirhodium-catalysed asymmetric transformations. The use of this immobilised catalyst in the asymmetric intramolecular C–H insertion of 2-methoxyethyl diazoacetate in refluxing benzene, resulted in lower product yields and enantioselectivities than the ones previously reported when using $Rh_2(5S\text{-MEPY})_4$ **4a** in refluxing dichloromethane. Excellent reusability was observed for PE-$Rh_2(5S\text{-PYCA})_4$ **11** after addition of a small amount of ligand (2.4–2.7 mol%), allowing the catalyst to be reused 7 times keeping the catalytic activity intact (Table 13, entries 3–4). The reutilisation of the catalyst was accomplished by a simple cold precipitation–filtration sequence.



Scheme 3 Preparation of PE-$Rh_2(5S\text{-PYCA})_4$.

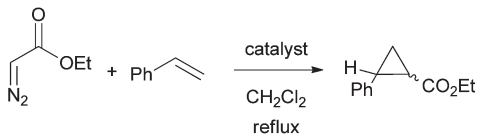
When the same catalytic system was employed in the cyclopropanation reaction of 3-methyl-2-buten-1-yl diazoacetate, the desired cyclopropane derivative was obtained in excellent enantioselectivities (Table 12, entry 37). Despite the robustness of the system, which was reused 7 times, the enantioselectivity of the transformation dropped from 98% ee in the 2nd cycle, to 83% ee in the 3rd cycle and 61% ee in the 7th cycle. In the same reaction conditions (benzene at reflux), PE-$Rh_2(5S\text{-PYCA})_4$ **11** provided the desired cyclopropane in better enantioselectivities than the homogeneous system. Unfortunately, the levels of rhodium leached after each run were not reported.

Other organic polymers were later tested as supports for dirhodium catalysts. A polymer composed of polystyrene backbone extended with poly(ethylene oxide) residues – NovaSynTentagel **12a** – and chloromethylated polystyrene – Merrifield resin **12b** – were both modified by reaction with pyroglutamic acid and further reacted with $Rh_2(5S\text{-MEPY})_4$ **4a** in the preparation of new solid-supported dirhodium materials **13a** and **13b** (Scheme 4). Ligand loading was determinant in the catalyst selectivity towards intramolecular cyclopropanation of allyl diazoacetate. The catalysts were recovered and reused in 8 to 10 cycles, maintaining the yields and stereoselectivities close to the ones reported for homogeneous $Rh_2(5S\text{-MEPY})_4$ **4a**, around 75% for Mer-$Rh_2(5S\text{-MEPY})_3$ **13b** and 10% lower for TG-$Rh_2(5S\text{-MEPY})_3$ **13a** (Table 12, entries 31–32). **13b** failed to reproduce identical results in the third run of the reaction. **13a**, on the other hand, afforded reproducible results over a wide range of catalyst amounts, and in another example tested, a slight increase in the enantioselectivity was observed, when compared with $Rh_2(5S\text{-MEPY})_4$ **4a**. Such an approach demonstrated the ability of $Rh_2(5S\text{-MEPY})_4$ **4a** to be immobilised without leading to a selectivity or yield decrease, as demonstrated in Table 2.[24]



Scheme 4 $Rh_2(5S\text{-MEPY})_4$ immobilisation in polymeric solid support.

Table 2 Catalytic cyclopropanation of styrene with EDA

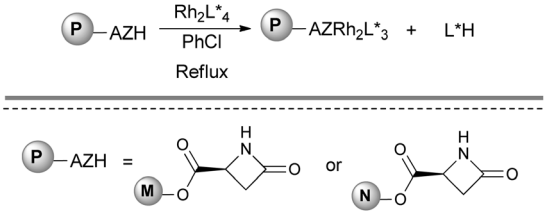


Catalyst	Catalyst loading[a]	mol %	Yield (%)	*trans* : *cis*	% ee *trans*	% ee *cis*
$Rh_2(5S\text{-MEPY})_4$**4a**		1.0	59	56 : 44	58	33
TG-$Rh_2(5S\text{-MEPY})_3$	0.054	0.8	58	66 : 34	64	43
TG-$Rh_2(5S\text{-MEPY})_3$	0.027	0.04	57	62 : 38	62	36
Mer-$Rh_2(5S\text{-MEPY})_3$	0.315	1.0	69	57 : 43	56	40
Mer-$Rh_2(5S\text{-MEPY})_3$	0.032	1.0	58	68 : 32	66	49
Mer-$Rh_2(5S\text{-MEPY})_3$	0.032	0.35	58	69 : 31	65	47

[a] Amount of dirhodium(II) catalyst in mmol per gram of resin.

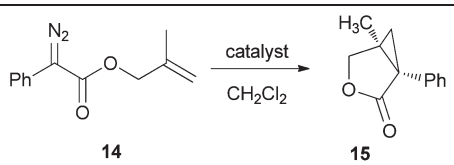
As an alternative to pyroglutamic acid, azetidinones can be used to modify Merrifield (M) and TentaGel (N) resins creating a dirhodium anchoring site (Scheme 5). This strategy was used in the replacement of one of the ligands of $Rh_2(5S\text{-MEPY})_4$, $Rh_2(4S\text{-MPPIM})_4$, $Rh_2(4S\text{-MEAZ})_4$, and $Rh_2(4S\text{-IBAZ})_4$.[25] The synthesised metal-anchored polymers were reported to be active catalysts towards cyclopropanation and intramolecular C–H insertion showing comparable yields but lower enantioselectivities to those of homogeneous catalysts (Table 3). In the intramolecular cyclopropanation of the phenyldiazo acetate derivative **14**, the polymer was recovered and reused through four cycles keeping the same yields and selectivities. A catalyst loading of 0.2 mol% was reported enough to achieve complete conversion, while water removal was determined of pivotal importance in order to achieve higher yields and reproducibility.

The influence of the immobilised catalysts in the diastereoselectivity of the intramolecular C–H insertion of cyclohexyl



Scheme 5 Preparation of dirhodium(II) immobilised Merrifield and NovasynTentagel supports.

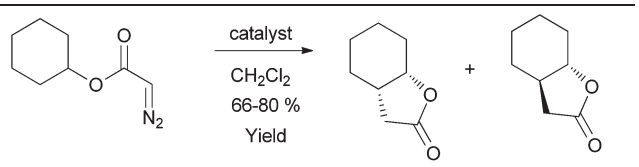
Table 3 Scope of an intramolecular cyclopropanation catalysed by Merrifield and Novasyn dirhodium immobilised polymers



14 **15**

Entry	Catalyst	Yield (%)	ee (%)
1	**Catalyst** N–$AZRh_2(4S\text{-MEAZ})_3$	83	62
2	$Rh_2(4S\text{-MEAZ})_4$	82	84
3	M–$AZRh_2(4S\text{-MEAZ})_3$	87	52
4	N–$AZRh_2(4S\text{-IBAZ})_3$	74	36
5	$Rh_2(4S\text{-IBAZ}_4)$	80	68
6	N–$AZRh_2(5S\text{-MEPY})_3$	77	22
7	$Rh_2(5S\text{-MEPY})_4$	0	—
8	M–$AZRh_2(5S\text{-MEPY})_3$	75	4
9	N–$AZRh_2(4S\text{-MPPIM})_3$	83	30
10	$Rh_2(4S\text{-MPPIM})_4$	0	—

Table 4 Intramolecular C–H insertion of cyclohexyl diazoacetate



		cis isomer		*trans* isomer	
Entry	Catalyst	%	ee (%)	%	ee (%)
1	Rh_2(4*S*-MPPIM)$_4$	100	92	0	—
2	N–AZRh_2(4*S*-MPPIM)$_3$	60	95	40	93
3	Rh_2(5*S*-MEPY)$_4$	88	>99	14	93
4	M–AZRh_2(5*S*-MEPY)$_3$	54	97	46	89

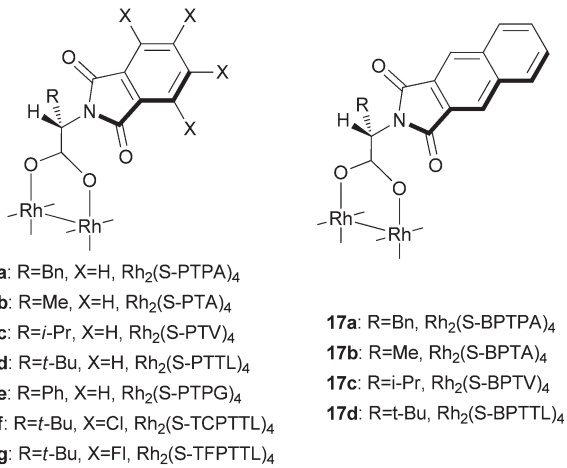


Fig. 4 Chiral dirhodium catalysts derived from protected amino acids developed by Hashimoto's group.

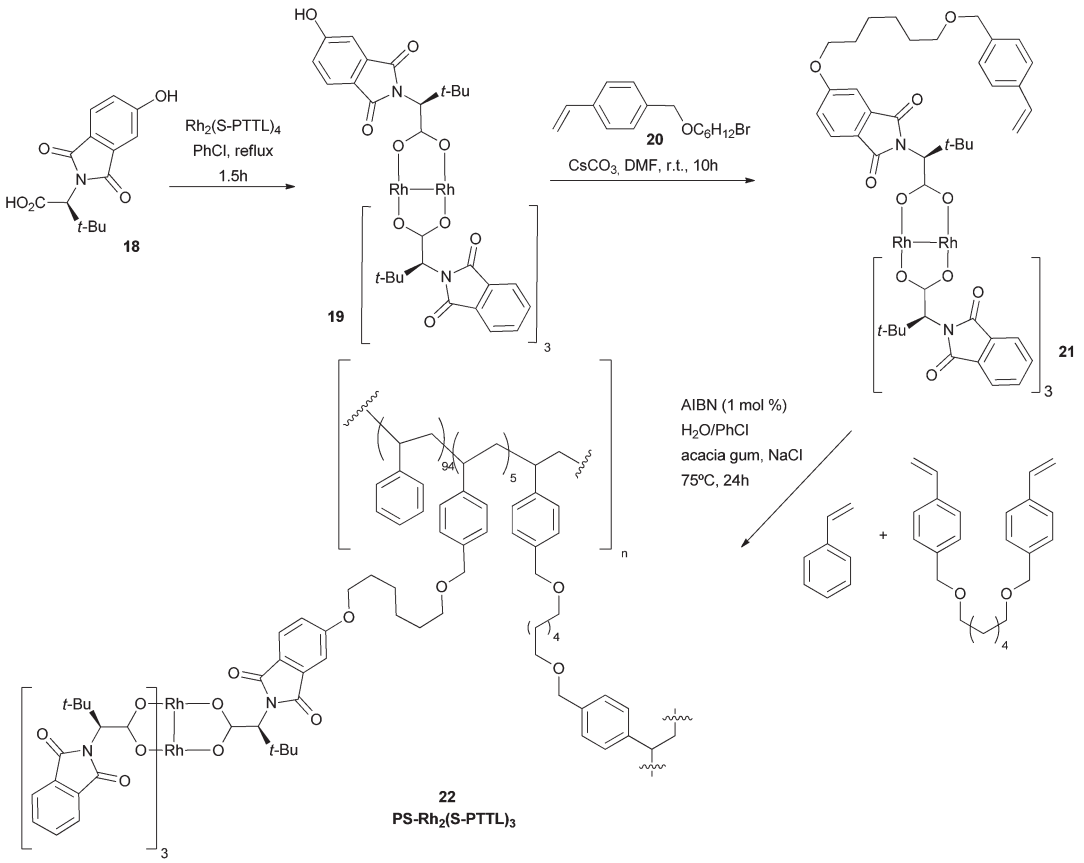
diazoacetate was also evaluated (Table 4). Despite the similar enantioselectivities reported for both types of catalysts, diastereoselective formation of the *trans* isomer was observed, and *trans* selectivity was attributed to a higher hydrocarbon content of the catalyst ester linkage.[25]

Hashimoto and co-workers developed an extremely efficient family of α-aminoacid-protected phthalimide-based catalysts (Fig. 4) for intramolecular C–H insertion reactions amongst others. These catalysts are generally extremely efficient in the mediation of metallocarbene reactivity and have been extensively explored in dirhodium(II) catalysed asymmetric transformations.[26] Recently, Rh_2(*S*-PTTL)$_4$ **16d** was immobilised in a polymer by an alternative approach. Instead of grafting the dirhodium complex into the modified polymer, Hashimoto and co-workers developed a copolymerisation strategy in which one replaced ligand Rh_2(*S*-PTTL)$_4$ was made to react with 6-(4-vinylbenzyloxy)bromohexane **20**. The obtained monomer **21** was then copolymerised with styrene and using 1,6-bis(4-vinylbenzyloxy)hexane as a cross-linker (Scheme 6).[27] With this strategy, the authors intended to develop a polymer matrix with uniform distribution of the chiral dirhodium complex that would allow unrestricted access of substrates to catalytic active sites.

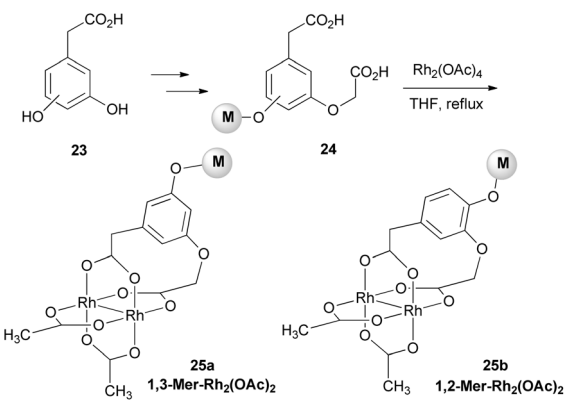
Among other properties of this newly developed polymer, it is possible to use it in carbene transformations below room temperature. Such robustness was evidenced by its consecutive use (up to 20 cycles), in the enantioselective intramolecular C–H insertion of an α-diazo ester at −78 °C, in which only the *cis* isomer of the cyclopentane derivative was obtained in yields up to 85% and excellent enantioselectivities (95% ee) (Table 13, entry 1). This polymer was applied in the enantioselective preparation of a key intermediate for the synthesis of FR115427,[28] a non-competitive NMDA receptor antagonist,[29] yielding the desired product in good to excellent yields and enantioselectivity. A remarkable use of this catalyst in 100 cycles was reported (Table 13, entry 8). The leaching level of rhodium was almost negligible as indicated by the 0.0019% of the initial rhodium amount detected in the liquid phase of the first cycle. The excellent activity of this new catalyst was attributed to a combination of good swelling properties and uniform dispersion of catalytic active sites within the polymer matrix.[27]

The use of Merrifield resin in dirhodium anchoring was previously reported by Andersen *et al.*[30] and the obtained resin-bound metal **25** was tested in the hydroformylation and hydrogenation of 1-hexene. In this case, the dirhodium complex was anchored in the customised resin by linkage of two adjacent bridging acetate moieties linked to each other. A metallocycle size of 11- or 12-membered rings was determined by computer assisted molecular modelling to cause little perturbation in the paddlewheel geometry of $Rh_2(OAc)_4$. Therefore, *meta*-disubstituted benzene derivatives containing two carboxylic acid functional groups were attached to a Merrifield resin and the dirhodium moiety was introduced by refluxing both components in THF (Scheme 7). Both polymer-bound complexes **25** were tested as catalysts in hydroformylation of 1-hexene. In addition to the good catalytic activity, leaching extent was below 0.01%, as determined by atomic absorption spectroscopy of the supernatant after the reaction (Table 14, entries 7 and 8). Regarding the transformation selectivity, contrarily to the results obtained with $Rh_2(OAc)_4$, the isomerisation to internal alkenes was suppressed at higher temperatures and the catalytic system was claimed to be as good as some catalytic systems based on Rh(I).

Chiral dirhodium *ortho*-metallated phosphine complexes ($Rh_2(O_2CR)_2(PC)_2$) **26** (Fig. 5) have been developed and successfully tested in asymmetric cyclopropanation of styrene with EDA.[31] Such catalysts were attached to polystyrene (PS) *via* two different strategies, the first relying on the reaction of $Rh_2(O_2CR)_2(PC)_2$ with the carboxyethylpolystyrene polymer by ligand exchanging reaction (**28**, Fig. 5),[32] and the other using styryl groups in the phosphine for radical copolymerisation with styrene and divinylbenzene (**29** and **30**, Fig. 5).[33] Both set of catalysts were tested in the styrene cyclopropanation with EDA. Despite the higher yields achieved, the diastereoselectivities and enantioselectivities were lower than the ones obtained with the homogeneous homologues (Table 12, entries 9–20). Comparing both types of heterogeneous catalysts, similar reactivities and selectivities were observed. Regarding the catalyst reuse, the co-polymerised catalysts with six possible anchoring sites **30** were reported to be more robust than the catalysts with three anchoring sites **29**.



Scheme 6 Preparation of polymer-supported chiral dirhodium(II) PS-Rh_2(*S*-PTTL)$_3$.



Scheme 7 Immobilisation of $Rh_2(OAc)_4$ by modification of adjacent bridging ligands (M = Merrifield resin).

2.2 Immobilisation by axial coordination

Despite the excellent results obtained for the heterogeneous systems, herein referenced so far, most of them imply the laborious modification of one of the bridging ligands, and in some cases the polymer modification in which the metal complex will be grafted to. Aiming at the development of a more practical strategy to perform the immobilisation of dirhodium complexes, Davies and co-workers envisioned a strategy based on the coordination of a Lewis base polymer with the axial position of the metal complex (Scheme 8).

Rhodium(II) prolinate catalysts **31**, firstly reported by Mckervey[34] and further studied by Davies, together with his second generation catalysts[35] **32** (Fig. 6) have been successfully applied as asymmetric inductors in several dirhodium-catalysed transformations[1m,36] such as intermolecular C–H insertion[37] and cyclopropanation reactions.[38] Additionally, they were also explored as candidates for immobilisation on a solid support.[39] In order to avoid possible interactions between the ligands of the rhodium complex and the polymer backbone, which could result in enantioselectivity decrease, a benzyl group was introduced between the tested solid support (Argopore resin) and the pyridinyl group (responsible for dirhodium chelating).[40]

The solid support used for the immobilisation of Rh_2(*S*-TBSP)$_4$ **31b** and Rh_2(*S*-biTISP)$_4$ **32b** was prepared by conversion of the hydroxyl group of Argopore–Wang resin to bromide and then reacted with sodium alkoxide of 4-pyridinylmethanol **35** for introduction of the pyridinyl group (Scheme 9). The prepared dirhodium-enriched solid supports were tested in the asymmetric cyclopropanation of styrene with methyl phenyldiazoacetate (MPDA) (Table 12, entries 21–25) and the AWP-Rh_2(*S*-biTISP)$_4$ catalytic system was reused up to 15 cycles yielding the product in excellent enantioselectivities (Table 12, entry 24). The correspondent cyclopropane rings were also obtained in good enantioselectivities when AWP-Rh_2(*S*-biTISP)$_4$ was applied to cyclopropanation of other diazoacetates (Table 5).[40] The preparation mode of the catalyst was latter demonstrated to influence the catalyst robustness. Considering the enantioselectivity and reuse of the catalyst in cyclopropanation,

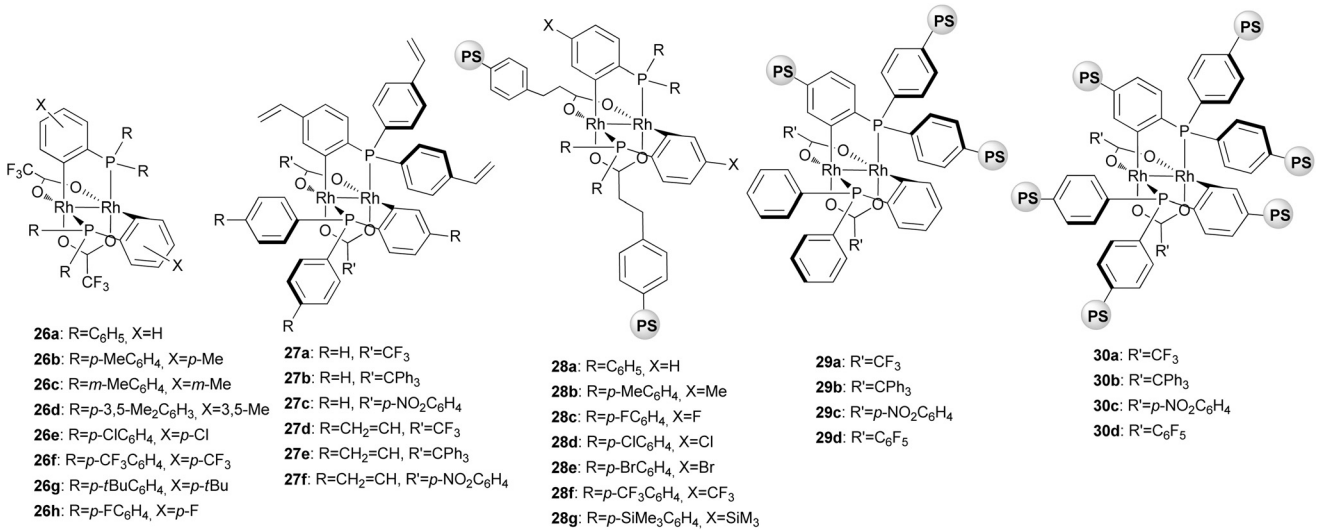
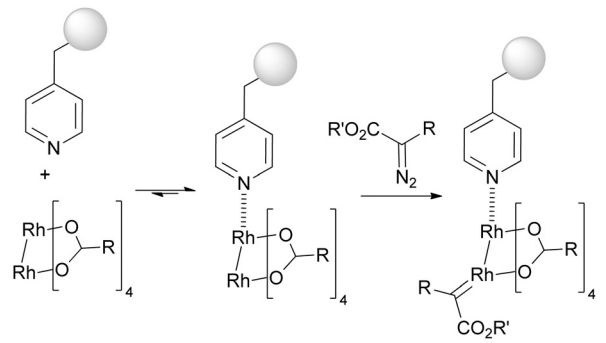
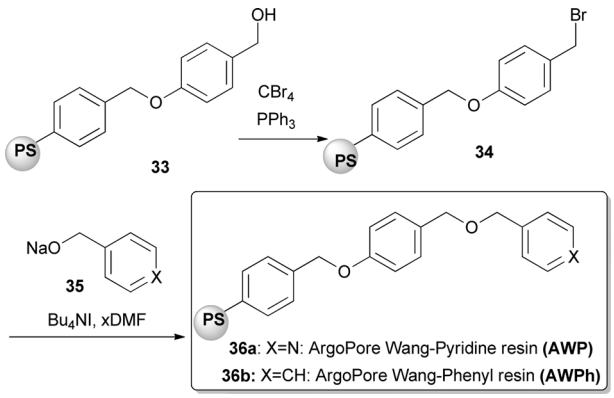


Fig. 5 Dirhodium(II) *ortho*-metallated phosphine complexes and heterogeneous derivatives.



Scheme 8 Axial coordination of solid supported pyridinyl to dirhodium complexes.



Scheme 9 Preparation of the cross-linked macroporous polystyrene resin for the immobilisation of dirhodium complexes (PS = polystyrene).

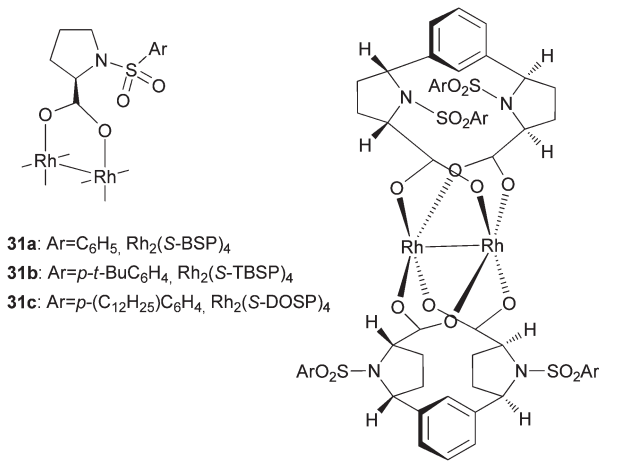
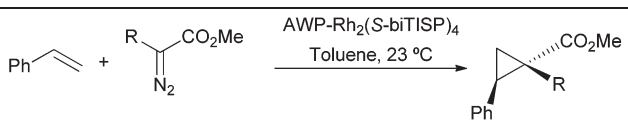


Fig. 6 Dirhodium chiral complexes derived from proline.

Table 5 Asymmetric cyclopropanation with AWP-Rh_2(*S*-biTISP)$_4$



Entry	R	Time (h)	Catalyst (mol%)	Yield (%)	ee (%)
1	Ph	3	0.04	88	88
2	2-Naphthyl	2	0.1	89	74
3	4-MeO-C_6H_4	1	0.1	90	80
4	4-Me-C_6H_4	1	0.1	89	83
5	4-Br-C_6H_4	1	0.1	87	90
6	Styryl	7	0.1	82	68

better results were achieved when the dirhodium complex was used as limiting agent in the immobilisation process and using toluene as reaction solvent.[41] Thorough investigations regarding the mode of action of these new catalysts indicated that the reactivity of the immobilised catalyst does not arise from a release-and-capture mechanism. Moreover, besides the axial coordination of the pyridinyl moiety, other factors such as microencapsulation were pointed out as being on the basis of dirhodium's immobilisation. Indeed, the use of a benzene group replacing the pyridine

terminal group (AWPh, Scheme 9) allowed the immobilisation of dirhodium complexes in a comparable extent, and this supported complex produced the desired product in similar selectivities when tested as a cyclopropanation catalyst (Table 12, entries 22 and 25).[40,41]

Using the same strategy, Rh_2(*S*-DOSP)$_4$ **31c** was also immobilised in the same resin, and the system evaluated in the asymmetric intermolecular C–H activation.[42] The reutilisation of AWP-Rh_2(*S*-DOSP)$_4$ was possible in ten cycles in the allylic C–H insertion of 1,4-cyclohexadiene without a significant drop in the enantioselectivity (Table 13, entry 21). Furthermore, good enantioselectivities were also obtained when using different aryldiazoacetates (82–87% ee). In order to demonstrate the excellent properties of this dirhodium heterogeneous method, the authors prepared several intermediaries for the synthesis of active pharmaceutical ingredients.

The same immobilisation strategy was latter applied to other dirhodium complexes such as Doyle's Rh_2(5*S*-MEPY)$_4$ **4a** and Hashimoto's Rh_2(*S*-PTTL)$_4$ **16d**. These new heterogeneous catalytic systems were applied in the asymmetric intramolecular cyclopropanation and intramolecular C–H insertion reactions in excellent selectivities. Furthermore, both catalytic systems were reused in up to three cycles (Table 12, entry 33 and Table 13, entry 9), each one without any drop in the enantioselectivity, and providing the products in similar enantioselectivities to the homogeneous catalysts.[43]

2.3 Immobilisation in inorganic supports

Inorganic supports such as mesoporous materials and zeolites can also be used as carriers in dirhodium immobilisation procedures.

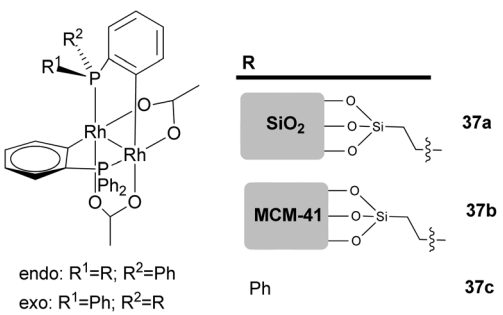
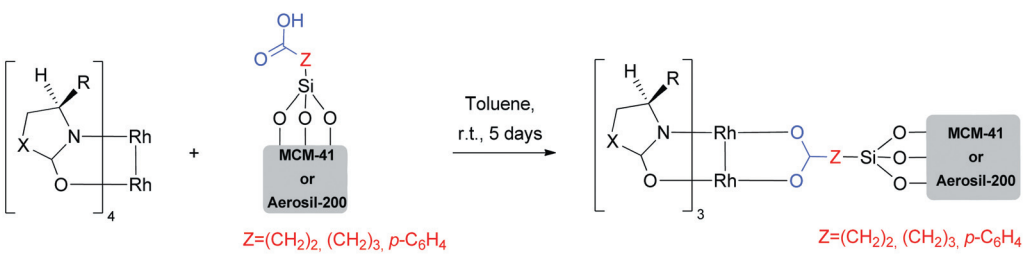


Fig. 7 Dirhodium(II) *ortho*-metallated phosphine immobilised on inorganic supports.

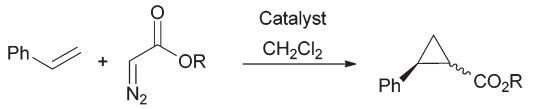
In this case, besides the stereo and electronic effects of the catalyst, the special arrangement and the grafting site of the dirhodium complex can have additional effects in the reaction's selectivity, depending on the complex grafting in the inner or outer surface of the inorganic support. Maschmeyer and coworkers have explored this concept in the preparation of heterogeneous catalysts suitable for hydroformylations,[18a,b] cyclopropanation and Si–H insertion[18c,44] reactions. Dirhodium(II) *ortho*-metallated phosphine complexes were immobilised on a modified amorphous silica support and MCM-41 (Fig. 7), and the heterogeneous catalysts **37a–b** successfully employed in the hydroformylation of styrene, leading to the exclusive formation of aldehydes. Despite the similar initial level of activity and selectivity of these catalysts in relation to their homogeneous counterparts, a drop in selectivity towards the formation of linear aldehydes was reported for the consequent catalytic runs (Table 14, entries 13–15). Regarding the catalysts' stability, contrarily to other hydroformylation catalysts, these were reported to be stable to oxygen atmosphere. Comparing both inorganic supports, a lower leaching degree was determined for the phosphine complex immobilised inside MCM-41 mesopores.[18a,b]

Doyle's Rh_2(5*S*-MEPY)$_4$ and Rh_2(4*S*-BNOX)$_4$ derivatives were also immobilised inside siliceous MCM-41 pores and Aerosil-200, after introduction of carboxylates on the carrier surface (Scheme 10). In this way, the desired complexes were prepared by ligand exchange, displacing one of the original ligands by the grafted carboxylate group. Since a complete protection of the carrier's surface was performed by introduction of carboxylate tether groups, the adsorption mechanism was discarded as being responsible for immobilisation.[18c] The prepared complexes were tested as catalysts in Si–H insertion, in which SiO_2-derived catalysts provided the desired product in good yields while MCM-41-derived catalysts failed to offer the product in more than traces (Table 6).[44] Although good yields were observed, chiral induction was somewhat low, and ee's up to 37% were reported. The recyclability of the system was also tested and a decrease in the catalytic activity was observed for Si–H insertion reaction (Table 13, entry 27), due to rhodium leaching and probably by pore clogging. Comparing the catalytic activity of the immobilised and the non-immobilised catalytic systems towards cyclopropanation, an increase of the *trans* : *cis* ratios was observed when EDA and *tert*-butyl diazoacetate (TBDA) were used as carbene precursors. The selectivity towards *trans* cyclopropane formation was attributed to the spatial confinement of the mesoporous material. Unfortunately,



Scheme 10 Immobilisation of Rh_2(5*S*-MEPY)$_4$ and Rh_2(4*S*-BNOX)$_4$ dirhodium complexes on inorganic carriers.

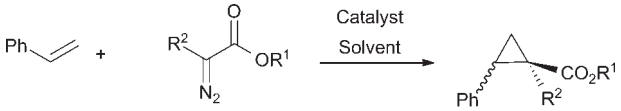
Table 6 Cyclopropanation with immobilised $Rh_2(5S\text{-MEPY})_4$ and $Rh_2(4S\text{-BNOX})_4$ on SiO_2 and MCM-41 as catalysts



EDA: R= Et
TBDA: R=*t*-Bu

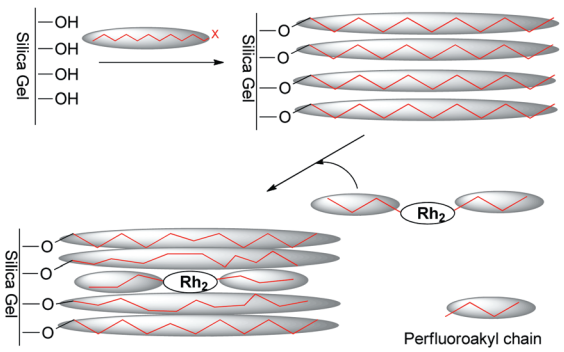
Entry	Catalyst	Diazo comp	Yield (%)	*trans* isomer %	*trans* isomer ee (%)	*cis* isomer %	*cis* isomer ee (%)
1	$Rh_2(5S\text{-MEPY})_4$	**EDA**	59	56	58	44	33
2	SiO_2-$(CH_2)_2CO_2$-$Rh_2(5S\text{-MEPY})_3$	**EDA**	73	59	35	41	29
3	MCM-41-$(CH_2)_2CO_2$-$Rh_2(5S\text{-MEPY})_3$	**EDA**	65	60	22	40	19
4	$Rh_2(5S\text{-MEPY})_4$	**TBDA**	50	60	14	40	66
5	SiO_2-$(CH_2)_2CO_2$-$Rh_2(5S\text{-MEPY})_3$	**TBDA**	62	71	27	29	30
6	MCM-41-$(CH_2)_2CO_2$-$Rh_2(5S\text{-MEPY})_3$	**TBDA**	50	74	14	26	55
7	$Rh_2(4R\text{-BNOX})_4$	**EDA**	79	46	17	54	2
8	SiO_2-$(CH_2)_2CO_2$-$Rh_2(4R\text{-BNOX})_3$	**EDA**	84	60	35	40	33
9	MCM-41-$(CH_2)_2CO_2$-$Rh_2(4R\text{-BNOX})_3$	**EDA**	51	70	36	30	29
10	$Rh_2(4R\text{-BNOX})_4$	**TBDA**	64	59	9	41	34
11	SiO_2-$(CH_2)_2CO_2$-$Rh_2(4R\text{-BNOX})_3$	**TBDA**	53	66	9	34	19
12	MCM-41-$(CH_2)_2CO_2$-$Rh_2(4R\text{-BNOX})_3$	**TBDA**	51	72	14	28	21

Table 7 Catalytic activity of dirhodium immobilised complexes inside nanoporous hosts

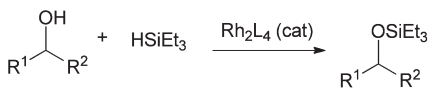


EDA: R^1= Et; R^2=H
MPDA: R^1= Me; R^2=Ph

Entry	Catalyst	Solvent	Diazo	Yield (%)	*E*/*Z*
1[46]	$Rh_2(tfa)_4$	CH_2Cl_2	**EDA**	66	44 : 56
2	SBA-15/$Rh_2(tfa)_4$	CH_2Cl_2	**EDA**	88	86 : 14
3	SBA-15/$Rh_2(tfa)_4$	CH_2Cl_2	**MPDA**	90	99 : 1
4	SBA-15/$Rh_2(tfa)_4$	Toluene	**MPDA**	86	98 : 2
5	SBA-15/$Rh_2(Opr)_4$	Toluene	**MPDA**	85	98 : 2



Scheme 11 The "bonded fluorous phase catalysis" (BFPC) approach.



Scheme 12 Dirhodium(II) catalysed silylation of alcohols with triethylsilane.

the enantioselectivity of the transformation decreased when compared with their homogeneous counterparts. The presence of polar groups in the surface was determinant in the reaction's enantioselectivity, higher ee's being achieved when unprotected carriers were used. Surprisingly, the spacer group did not show a clear relation with the selectivity levels.[44]

$Rh_2(tfa)_4$ and $Rh_2(Opr)_4$ were recently immobilised inside nanoporous hosts using an axial coordination strategy.[45] These metal complexes were embedded in the modified mesoporous silica (SBA-15) containing dangling tertiary dimethylamino groups, suitable for strong Rh–N axial coordinations. The prepared catalytic systems were tested in the styrene cyclopropanation with EDA and MPDA, and selectivity towards *E* isomer formation was observed as previously reported by Maschmeyer.[44] Better selectivity was reported for aromatic solvents, such as toluene (Table 7), and the SBA-15/$Rh_2(tfa)_4$ catalytic system could be recycled and reused 3 times maintaining the excellent diastereoselectivities in the cyclopropanation of MPDA (Table 12, entry 7).[45]

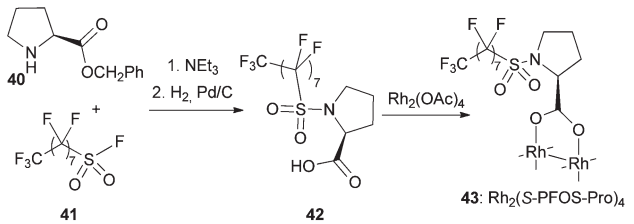
Perfluorinated dirhodium complexes derived from octanoic ($Rh_2(pfo)_4$, **39a**), decanoic ($Rh_2(pfd)_4$, **39b**), and tetradecanoic ($Rh_2(pft)_4$, **39c**) perfluorocarboxylic acids were prepared by ligand exchange reactions with $Rh_2(OAc)_4$. A strategy for the immobilisation of these complexes suitable for their use in heterogeneous conditions was developed by Biffis and coworkers.[47] A solution containing the perfluorocarboxylatedirhodium(II) complex was poured into contact with derivatised silica containing long perfluoroalkyl chains, enabling the adsorption of the complex into the solid surface (Scheme 11). Such an approach was named "bonded fluorous phase catalysis" (BFPC) and the heterogeneous supports were tested in alcohol silylation (Scheme 12). An interesting aspect of these BFP catalysts is the reversibility of the catalyst anchoring, in which the simple washing with a solvent able to bind into the complex's axial positions is enough to wash off the dirhodium metal compound.

The catalytic activity of the supported version of $Rh_2(pfo)_4$ (BFP-$Rh_2(pfo)_4$) was determined to be up to five times higher than for the homogeneous analogues in solventless conditions at room temperature (Table 8). Additionally, this approach made the catalyst reutilisation possible, with less than 3% rhodium leaching into the filtrate (Table 14, entry 1). On the other hand, BFP-$Rh_2(pft)_4$ failed to provide the silylated 1-octanol (Table 8) derivate in reasonable yield. A remarkable 0.01 mol% catalyst loading was used and reused in the silylation of several alcohols. As observed in homogeneous conditions, primary and benzyl

Table 8 Solventless triethylsilane alcoholysis using perfluorinated dirhodium complexes

Entry	Catalyst	*T* (°C)	Alcohol	Yield (%)
1	$Rh_2(pfo)_4$	50	1-Octanol	98
2	BFP-$Rh_2(pfo)_4$	50	1-Octanol	93 (63)[a]
3	$Rh_2(pft)_4$	50	1-Octanol	98
4	BFP-$Rh_2(pft)_4$	50	1-Octanol	55
5	BFP-$Rh_2(pfo)_4$	50	2-Octanol	18
6	BFP-$Rh_2(pfo)_4$	50	$PhCH_2OH$	83
7	BFP-$Rh_2(pfo)_4$	50	Cyclohexanol	77

[a] Yields of a second reaction using the recovered catalyst indicated in parenthesis.



Scheme 13 Preparation of Rh_2(*S*-PFOS-Pro)$_4$.

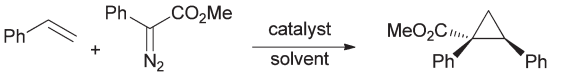
alcohols were determined to be more reactive than the secondary ones while silanes bulkier than triethylsilane were observed to afford the silylated alcohol in lower yields.[47]

A variation of dirhodium(II) prolinates complexes bearing perfluoroalkyl chains was prepared by Biffis and co-workers. The fluorous complex was obtained after preparation of the proper proline derivative and subsequent reaction with $Rh_2(OAc)_4$ in a ligand-exchange reaction (Scheme 13).[48] Using the same BFPC strategy, the fluorous Rh_2(*S*-PFOS-Pro)$_4$ **43** complex was immobilised in modified silica and tested in asymmetric cyclopropanation of styrene with MPDA (Table 9). Analogously to the previous observations on the positive effect on enantioselectivities caused by the use of alkanes as solvents on *N*-arylsulfonylprolinate catalysts, pentane was reported to be a better solvent concerning the BFP-Rh_2(*S*-PFOS-Pro)$_4$ chiral induction. On the other hand, Rh_2(*S*-PFOS-Pro)$_4$ **43** was reported to be insoluble in *n*-pentane. Comparing the activity of both complexes as catalysts in the intermolecular C–H insertion of hexane, the homogeneous catalyst demonstrated better yields and similar enantioselectivities, despite the partial solubility of Rh_2(*S*-PFOS-Pro)$_4$ **43** in cyclohexane.[48]

3. Reaction solvents as dirhodium immobilizing agents

Despite the promising breakthroughs in heterogeneous immobilisation of dirhodium metal complexes, such strategies lead in most cases to a selectivity decrease due to the carrier's presence. Ultimately, when grafting chiral metal complexes, this usually leads to a decrease in the enantioselectivity of the transformation. Contrasting to the easy reusability of heterogeneous catalytic systems, homogeneous systems have as major advantages the use of unchanged dirhodium complexes, in which the catalyst is usually recovered by extraction of the reaction products from the reaction media. Notwithstanding the homogeneous dirhodium catalytic systems developed so far, few have been employed in asymmetric transformations.[49]

Table 9 Bonded fluorous phase Rh_2(*S*-PFOS-Pro)$_4$ catalysed styrene asymmetric cyclopropanation



Entry	Catalyst	Solvent	Yield (%)	ee (%)
1[a]	Rh_2(*S*-PFOS-Pro)$_4$	CH_2Cl_2	82	48
2[a]	BFP-Rh_2(*S*-PFOS-Pro)$_4$	CH_2Cl_2	53	47
3[b]	BFP-Rh_2(*S*-PFOS-Pro)$_4$	CH_2Cl_2	47	54
4[a]	BFP-Rh_2(*S*-PFOS-Pro)$_4$	*n*-Pentane	66	60

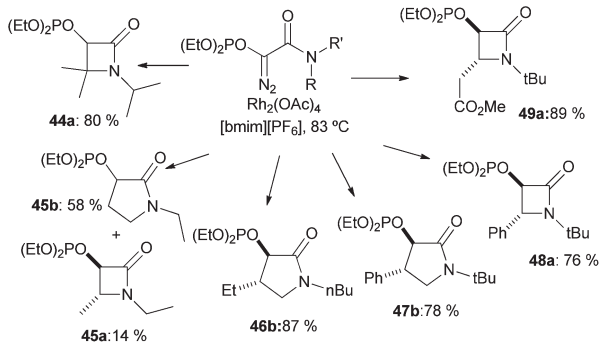
[a] MPDA addition in: MPDA addition in: 30 min or [b] 5 h.

Typically, transformations mediated by dirhodium(II) complexes use organic solvents as the reaction media. In particular, reactions involving the generation of highly reactive metallocarbenes, usually proceed in organic solvents that cannot interfere with the reactive intermediate.[1] In this section, the use of non-common solvents that allow the reutilisation of dirhodium catalysts will be discussed.

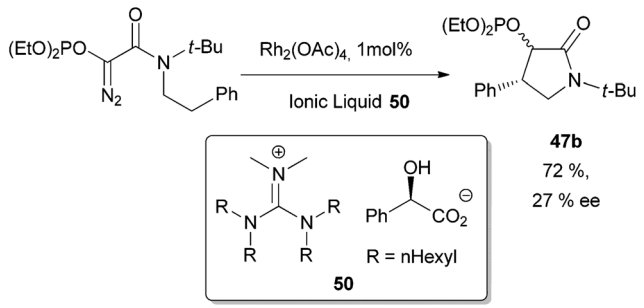
3.1 Ionic liquids

Room temperature ionic liquids (RTILs) have been recognised as an alternative to environmentally unattractive organic solvents, mainly due to their negligible vapour pressure and recyclability.[50] Their application in organic synthesis has been highlighted under several forms such as: "task-specific ionic liquids" or "designer solvents" to name a few.[50b,51] RTILs have the ability to dissolve a wide range of organic and inorganic compounds at the same time that they are also immiscible with several organic solvents as well as scCO2. These properties make them an attractive media to recycle catalysts without the complex heterogenisation and using a simple extraction approach.[50] Hence, ionic liquids have been combined with dirhodium-catalysed transformations not solely due to their role as solvent,[52] but also using the anion of the ionic liquid as ligand, forming an ionic-liquid metal-conjugate.[53]

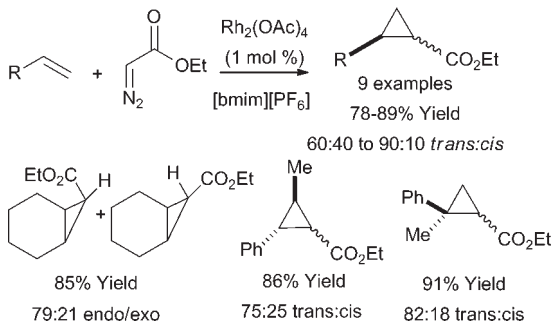
After the reported compatibility between a copper metallocarbene and ionic liquids in styrene cyclopropanation,[54] a C–H insertion reaction was carried out using [bmim][PF_6] as the reaction media.[52b] The transformation was quite successful affording the desired lactams in yields and selectivities similar to those obtained in chlorinated solvents (Scheme 14).[55] The reuse of the [bmim][PF_6]/$Rh_2(OAc)_4$ catalytic system was accomplished using *tert*-butyl-methyl-ether (TBME) as extracting solvent. This system allowed catalyst reutilisation over 6 cycles in the synthesis of γ-lactam **46b** after C–H insertion of the α-diazoacetamide precursor (Table 13, entry 13).[52b] The use of ionic liquids in the $Rh_2(OAc)_4$-catalysed intramolecular C–H insertion of α-diazo-α-phosphonoacetamides was extended to the use of chiral ionic liquids based on tetra-alkyl-dimethylguanidinium cations and natural amino acids. Possibly, due to ligand exchange between $Rh_2(OAc)_4$ and the ionic liquid anion, the



Scheme 14 C–H insertions of α-diazoacetamides using [bmim][PF_6] as the reaction media.



Scheme 15 C–H insertions of diazoacetamides using chiral ionic liquids as the reaction media.



Scheme 16 $Rh_2(OAc)_4$-catalysed cyclopropanation of alkenes in ionic liquid.

C–H insertion product **47b** was obtained with 27% enantiomeric excess (Scheme 15).[56]

Shortly after the publication of this work, Yadav *et al.* also reported the cyclopropanation reaction catalysed by $Rh_2(OAc)_4$ in [bmim][PF_6] ionic liquid. Better reaction rates, yields and diastereoselectivity towards *trans* diastereomers were observed when compared with usual organic solvents. The reaction proved to be tolerant to several olefins, such as electron rich and electron-deficient styrene derivatives, as well as α- and β-substituted styrenes (Scheme 16). The reutilisation of the catalytic system in styrene cyclopropanation was demonstrated (Table 12, entry 5), despite the slight yield drop from the first (88% yield) to the fifth run (72% yield).[52c]

Contrasting with the high stability of dirhodium paddlewheel complexes towards ionic liquids, the cationic carboxylate complex of dirhodium with oxothioethers **51** was reported to lack enough stability to allow it to be efficiently recycled in silane alcoholysis in ionic liquids. Despite the similar selectivities observed for both homogeneous systems, using dichloroethane and [bmim][PF_6], the stability of the prepared catalyst was determined to be dependent on the type of ionic liquid used.[52a] Forbes and co-workers adopted another strategy to immobilise the dirhodium(II) complex in ionic liquids which involved the synthesis of a new complex featuring imidazolium carboxylates as the bridging ligands (Fig. 8, **52**). Despite their test in the cyclopropanation of styrene having afforded the cyclopropane derivative in 62% yield, no attempt to reuse the catalyst was reported.[53]

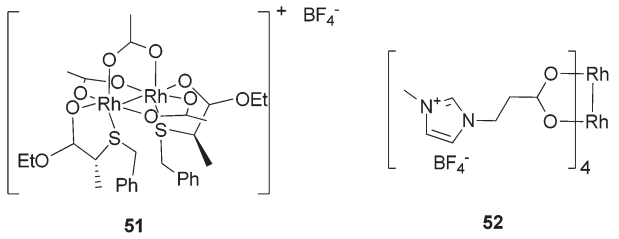
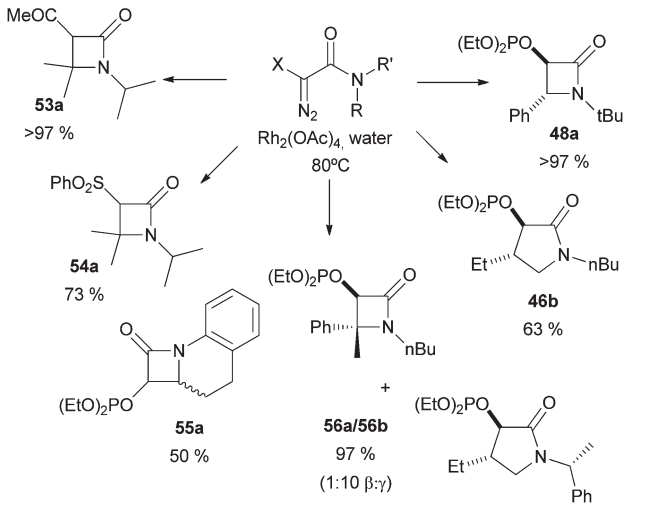


Fig. 8 Cationic carboxylate complex of dirhodium **51** and ionic liquid–metal conjugate **52**.

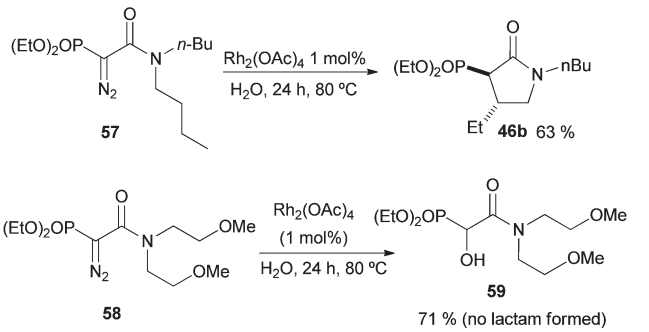
A system for the efficient hydroformylation of alkenes using a combination of $Rh_2(OAc)_4$ and phosphines as precursors of rhodium complexes in $scCO_2$ medium has been developed. After the finding that the use of ionic liquids as reaction solvent overcomes in better selectivity towards formation of linear aldehydes, [bmim][PF_6] ionic liquid was combined with [bmim][$Ph_2P(C_6H_4SO_3)$], in the hydroformylation of non-1-ene. The products could be easily removed from the reaction medium by flushing them from the reactor with $scCO_2$. Rhodium leaching started to be significant only after the 9th catalytic run, which was attributed to the ligand oxidation and formation of $scCO_2$ soluble [$RhH(CO)_4$]. The catalytic system was reused until a 12th run, although in detriment of the linear : branched ratio of the aldehydes formed (Table 14, entry 11).[57]

3.2 Water

Water is certainly one of the most desirable solvents available, because it is abundant, inexpensive and safe. Nevertheless, water notoriety does not end with this *greener relevance*, as it quite often exerts a remarkable influence over the chemical transformations performed in this media.[58] Water is not an innocent solvent as it often exerts a pivotal role in the reaction outcome. The hydrophobic effect disclosed by Breslow[59] and the acceleration effect observed by Sharpless[60] for heterogeneous reactions performed in water (the "on water effect") are testimonies of the benefits associated with the use of water as solvent. Regarding the use of dirhodium(II) complexes to perform transformations based on metallocarbenes in water, the O–H insertion process must always be considered as a likely competitive pathway.[61] Nevertheless, Charrette *et al.* reported the preferential intramolecular cyclopropanation on styrene in water and Francis *et al.* disclosed the C–H insertion on tryptophan residues of myoglobin by α-diazoacetates catalysed by diRh(II) complexes in aqueous media.[62] These two seminal works highlighted the possibility of



Scheme 17 C–H insertions of diazoacetamides using water as the reaction media – reaction scope.



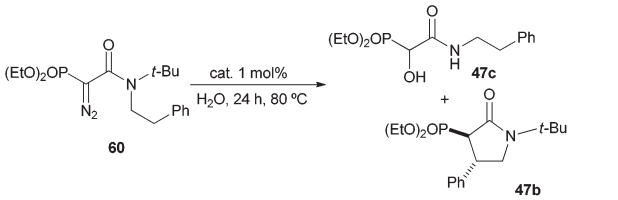
Scheme 18 C–H insertion using water as the reaction media: the effect of the diazoacetamide hydrophobic nature.

performing the cyclisation of diazoacetamides using water as solvent. The selective modification of the aromatic side chains of peptides using a dirhodium metallopeptide as catalyst is a recent example regarding the compatibility of dirhodium metallocarbenes and water.[63] The high solubility and stability of $Rh_2(OAc)_4$ in water makes the use of this solvent in the C–H insertion reaction possible. This fact accounted for the successful C–H insertion reaction of diazoacetamides using water as the reaction media (Scheme 17).[64]

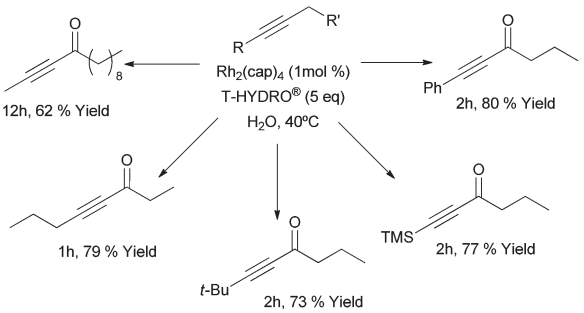
Based on competitive O–H and C–H insertion ratios, in experiments that considered the hydrophobic aspects of the ligands and acetamide substituents, it was proposed that water molecules must be extruded from the vicinity of the reactive metallocarbene in order to achieve a successful intramolecular C–H insertion reaction. This hydrophobic environment maybe created by the structure of the diazoacetamide or the dirhodium(II) catalyst.[64] As shown in Scheme 18, the symmetric diazoacetamide **57** afforded the γ-lactam **46b** in 63% while water soluble diazoacetamide **58** afforded exclusively the alcohol **59**. The catalyst's hydrophobic nature was also critical in directing the reaction of diazoacetamide **60** towards the formation of the γ-lactam **47b** (Table 10).

The high solubility of $Rh_2(OAc)_4$ in water and its low solubility in ethyl ether, allowed the reutilisation of the catalytic

Table 10 C–H insertion using water as the reaction media: the effect of the catalyst's hydrophobic nature



Entry	Catalyst	**47c** + **47b** combined yield (%)	**47c** : **47b**
1	$Rh_2(OAc)_4$	86	70 : 30
2	$Rh_2(pfb)_4$	64	9 : 91
3	$Rh_2(Ooct)_4$	76	0 : 100

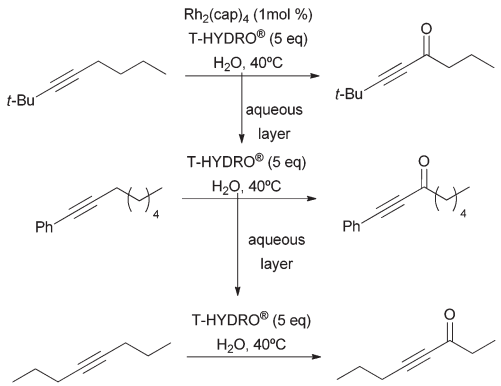


Scheme 19 $Rh_2(cap)_4$-catalysed propargylic oxidation.

system by a simple extraction of the reaction products from the reaction media with ethyl ether. This strategy proved to be quite successful as it allowed the reutilisation of the catalyst over 10 cycles (Table 13, entries 15–19).

The dirhodium(II) *ortho*-metallated phosphine-catalysed asymmetric cyclopropanation of styrene was also tested in water and in micellar conditions. Despite the competitive dimer and alcohol formation, cyclopropane derivatives were obtained in modest yields (up to 61%), in higher enantioselectivities (up to 91% ee) and faster than using *n*-pentane as the solvent.[65]

An oxidation system consisting of *tert*-BuOOH (TBHP) and dirhodium(II) caprolactamate ($Rh_2(cap)_4$), has been reported to be efficient in allylic,[66] benzylic,[67] amine,[68] phenol and aniline[69] oxidations. After the initial use of $Rh_2(cap)_4$ as oxidation catalyst in decane, in order to avoid hydrolysis of ligands, Doyle and coworkers found that the use of 70% aqueous TBHP (T-HYDRO) was compatible with the metal complex.[70] Hence, the organic solvent could be completely replaced by water in propargylic oxidations.[71] Using water as the solvent in 4-octyne oxidation, similar yields to the ones obtained in dichloroethane were obtained, although 10 times faster due to the heterogeneous character of the reaction mixture. The catalytic system was shown to be efficient in the oxidation of several internal alkynes (representative examples in Scheme 19), albeit lower yields were obtained for terminal triple bonds and compounds containing a primary alcohol functional group. The reaction's biphasic nature allowed the authors to reuse the catalyst by extraction of the reaction medium with ethyl ether, using the aqueous layer to catalyse other oxidations (Scheme 20).[71]



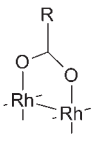
Scheme 20 Reutilisation of $Rh_2(cap)_4$ as propargylic oxidant.

3.3 Fluorinated solvents

Strategies employing the use of fluorinated solvents and fluorous compounds have also been explored as a way to reuse dirhodium catalysts. The peculiar properties of perfluorinated solvents regarding their immiscibility with organic or aqueous solvents, while keeping high affinities towards other fluorinated compounds, have been explored by Horvarth and Rábai in their seminal work on "Fluorous biphasic systems".[72] In these systems, based on fluorous liquid-phase extraction (F-LPE), a reaction mixture containing an organic solvent, fluorinated solvent, reagents, and in some cases highly fluorinated catalysts are heated to achieve homogeneous conditions. After reaction completion and upon cooling, the two layers are formed and a simple decantation of the reaction mixture provides the products and catalyst separately.[73] Such approach, applied to dirhodium catalysis, has been explored by Maas after the preparation of highly fluorinated dirhodium compounds **59** (Fig. 9) in cyclopropanation,[74] and in inter- and intramolecular C–H insertion[74*b*,75] reactions. Biffis and co-workers also explored the use of perfluorinated dirhodium complexes firstly in the silylation of alcohols[47*b*,76] and then in the asymmetric cyclopropanation of styrene with EDA.[48]

Dirhodium-catalysed silylation of alcohols was studied under fluorous biphasic conditions. As a rule of thumb, fluorine content of *ca.* 60% or higher is needed for a compound to have good solubility in perfluorinated solvents. Highly fluorinated dirhodium complexes were prepared and evaluated regarding their electronic properties, once perfluorocarboxylate-derived dirhodium complexes are known to have high electrophilicity. Two CH_2 groups were found necessary for the complete separation of the perfluoroalkyl chain from the catalyst active site.

These fluorinated complexes were tested as catalysts in the intermolecular C–H insertion of EDA with hexane, using hexane or PFMC–hexane as solvents (Table 11). The reaction's selectivity was observed to be highly dependent not only on the catalyst's electrophilicity but also on its solubility on the reaction medium, and complex **59g** was determined to be the most selective amongst all. Furthermore, the same complex could be recovered and reused in another catalytic cycle in the intramolecular C–H insertion of α-diazo-β-keto ester (Table 13, entry 11). From several fluorinated dirhodium complexes, complex **59g** was the most selective towards the formation of aromatic C–H insertion product over the aliphatic insertion product. Additionally,



59a: R=C_7F_{15} **59e:** R=C_6H_4-4-C_6F_{13}
59b: R=$CH_2C_6F_{13}$ **59f:** R=C_6H_3-3,5-di(C_6F_{13})
59c: R=$CH_2CH_2C_6F_{13}$ **59g:** R=C_6H_3-3,5-di(C_8F_{17})
59d: R=$CH_2O(CH_2)_2C_{10}F_{21}$

Fig. 9 Fluorinated dirhodium complexes developed by Maas and co-workers.

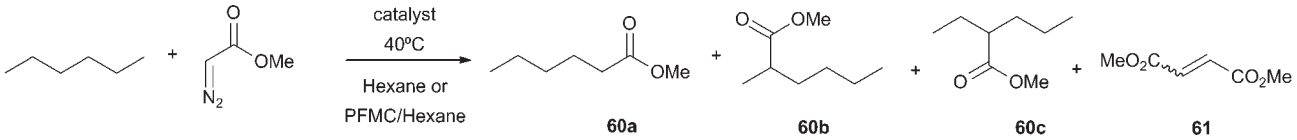
complexes **59a** and **59b** failed to catalyse the same reaction in high extent, even though harsher conditions were used. Reaction products coordination onto the axial positions of the catalysts or exchange of the bridging ligands in the harsh reaction conditions were advanced by the authors as possible causes for the catalysts deactivation, alongside their low solubility in fluorous solvents.[74*b*,75]

The catalytic activity of complexes **59e–f** was evaluated in the cyclopropanation of styrenes. Despite the good yields obtained in the formation of cyclopropane rings, the diastereoselectivities were always found to be lower than 60%. The reutilisation of the catalysts was achieved in up to five cycles, using a combination of **59e** in dichloromethane, followed by extraction of the catalyst to PFMC. Even so, the recovery rate of the catalyst after each cycle was not quantitative. For instance, after four cycles in cyclopropanation of styrene, 1-hexene, 2-methyl-2-propene and α-methylstyrene, **59e** was recovered in 56, 27, 21 and 11%, respectively.[74]

Biffis and co-workers prepared a dirhodium(II) prolinate complex bearing a perfluoroalkyl chain, which was tested in the asymmetric cyclopropanation of styrene with MPDA (Table 12, entry 26).[48] The newly synthesised fluorinated complex displayed a similar diastereoselectivity and higher chemoselectivity than the ones reported for Rh_2(*S*-TBSP)$_4$, **31b** but lower enantioselectivities.[77] From several fluorous solvents tested, PFMC was determined to own the best catalyst extraction ability, showing the best results towards the enantioselective formation of cyclopropane derivative when used as the reaction solvent. The product was quantitatively removed from the fluorous phase containing the catalyst by simple decantation. Rh_2(*S*-PFOS-Pro)$_4$ **43** was also tested in asymmetric C–H bond activation of cyclohexane with MPDA. Using cyclohexane as the solvent, the functionalised derivative was obtained in 71% yield and 61% ee, despite the catalysts' low solubility in that solvent.[48]

Perfluorinated dirhodium complexes **39a–c** were tested in the silylation of alcohols (Scheme 12) under fluorous biphasic conditions. Despite the successful reactivity of these three complexes which afforded the desired product in good yields, only Rh_2(pft)$_4$ remained confined in the fluorous phase without long extent leaching into dichloromethane. Silylation of 1-octanol with triethylsilane using Rh_2(pft)$_4$ as catalyst in a dichloromethane/Fluorinet® FC-77 biphasic mixture afforded the desired product in up to 87% yield. The catalyst was recycled by dichloromethane removal and subsequent feeding of additional equimolar amounts of triethylsilane and 1-octanol to the reactor (Table 14, entry 2). The evaluation of different alcohols as substrates demonstrated a marked preference for silylation of primary alcohols when compared to secondary ones.[76] According to the authors, the lower catalytic activity of this system can be explained by the mass-transport limitations between the two

Table 11 F-LPE intermolecular C–H insertion of EDA with hexane



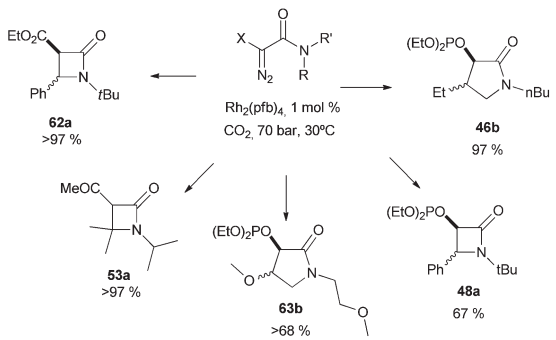
Entry	Catalyst	Yield (%) 60a	60b	60c	61
1[a]	**59a**	2.5 (0.4)	26.0 (5.7)	12.3 (2.9)	8.8 (20.6)
2	**59b**	2.6	24.9	11.9	8.7
3	**59c**	<0.2	2.2	1.0	19.9
4	**59d**	0.2	2.6	0.8	14.9
5	**59e**	0.3	7.0	2.6	17.1
6	**59g**	1.7	40.7	21.4	7.8

[a] Yields of a second reaction using the recovered catalyst indicated in parenthesis.

liquid phases, namely in comparison with the $Rh_2(pfb)_4$ homogeneous system reported by Doyle.[78] This limitation was latter overcome by using solventless conditions, in which the silylated 1-octanol derivative was obtained in 73% yield using 0.1 mol% of $Rh_2(pfo)_4$ **39a**, although encumbering the reutilisation of the perfluoro catalyst.[47b]

3.4 Supercritical fluids

According to Jessop and Leitner, supercritical fluids are: *a compound, mixture or element above its critical pressure and critical temperature but below the pressure required to condense it into a solid*.[79] Several advantages accrue from the use of supercritical (sc) fluids as solvents for homogeneous catalysis. They allow a very rapid mass transfer, they are completely miscible with gaseous reactants and they are easy to remove while allowing the catalyst–product separation. Furthermore, since solvent properties of sc fluids are pressure-dependent, the catalytic systems can be tuned keeping the chemical nature of the solvent unchanged. As a particular sc fluid, $scCO_2$ is nontoxic, non-flammable, non-halogenated, non-polluting, non-carcinogenic and does not cause other chronic problems.[79,80] Despite its low solubilising ability in some conditions, $scCO_2$ has been successfully used in many homogeneous metal catalysed reactions.[81] The major drawback in the use of sc fluids is probably the need to use expensive instrumentation such as compressors and high pressure reactors. Nevertheless, sc fluids can play a major role in the reactivity profile of the catalytic system. As an excellent example of the pressure influence of sc fluids in reaction selectivity, Jessop and co-workers observed a strong enantioselectivity dependence on styrene cyclopropanations with MPDA catalysed by Rh_2(*S*-TBSP)$_4$ in $scCHF_3$.[82] The variation in the dielectric constant of the reaction media was advanced as the responsible factor for the change in enantioselectivity. While $scCHF_3$ owns a dielectric constant analogous to liquid pentane at low pressures, the dielectric constant increases to values similar to THF or ethyl acetate with a pressure increase. Hence, the cyclopropane derivative was obtained in 40% ee for reactions performed at pressures above 100 bar and 77% ee for those at 52 bar in $scCHF_3$.[82] On the other hand, the same abrupt variation in the dielectric constant of $scCO_2$ is not verified upon pressure variation and similar enantioselectivities were observed between 79 and 110 bar (83–80% ee).[82a] Unfortunately, no reuse of the catalytic system was reported when using $scCHF_3$.



Scheme 21 $Rh_2(pfb)_4$-catalysed intramolecular C–H insertion of α-diazoacetamides CO_2.

Intramolecular C–H insertion of α-diazoacetamides was recently performed in $scCO_2$ using dirhodium(II) carboxylate derivatives as catalysts (Scheme 21).[83] Similar diastereoselectivities to the ones obtained in dichloromethane,[55] water[64a,b] or under photochemical conditions in absence of metal complex[64c] were observed. $Rh_2(pfb)_4$ was observed to catalyse the lactams' formation in good yields in a 70 bar CO_2 atmosphere at 30 °C. The same methodology was successfully applied to the enantioselective formation of β-lactam **62a** using the dirhodium catalysts derived from protected α-amino acids. Rh_2(*S*-PTPA)$_4$ and Rh_2(*S*-PTTL)$_4$ afforded the desired lactam in excellent yields (up to 97%), and moderate selectivities (52% and 65% ee, respectively), comparable to the ones obtained in water and dichloromethane. By employing the less CO_2-soluble $Rh_2(OAc)_4$, it was possible to reuse the catalytic system using the same catalyst for two runs in the formation of lactam **62a** (Table 13, entry 20).

Hydroformylation of alkenes using $Rh_2(OAc)_4$ and phosphines as precursors of rhodium catalytic species can be performed in $scCO_2$, with preferable formation of aldehyde instead of the undesired alcohol.[84] The $scCO_2$ insoluble complex

Table 12 Dirhodium based reusable catalytic systems for olefin cyclopropanation

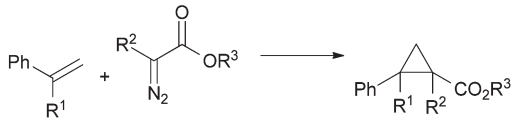
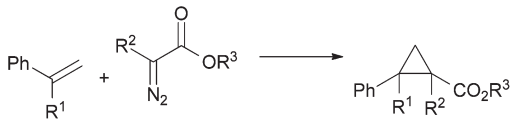
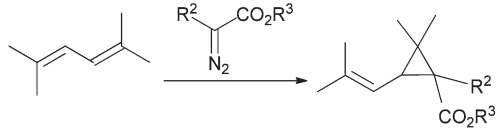
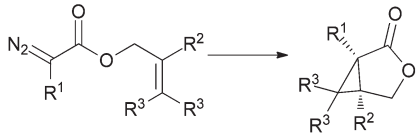
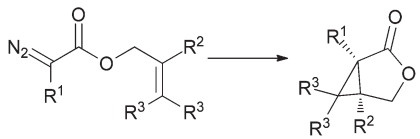
Entry	Reaction	R^1	R^2	R^3	Catalyst, Catalyst loading	Steps[a]	Reaction, Conditions	Yield (%)	Selectivity	Rhodium leaching	Runs Reported[b]	Last run, Selectivity	Ref.
1		H	H	Me	**59f**/$F_2ClCCCl_2F$, 2 mol%	0	$F_2ClCCCl_2F$ 20 °C, 12 h	70	0.99 *E*/*Z*	51% after, 5 runs	5 (67%)	67% yield, 1.04 *E*/*Z*	74*b*
2		H	H	Me	**59g**/$F_2ClCCCl_2F$, 2 mol%	0	$F_2ClCCCl_2F$ 20 °C, 12 h	76	0.88 *E*/*Z*	38% after, 5 runs	5 (75%)	0.86 *E*/*Z*	74*b*
3		Me	H	Me	**59f**/$F_2ClCCCl_2F$, 2 mol%	0	$F_2ClCCCl_2F$ 20 °C, 12 h	72	1.05 *E*/*Z*	n.d.[c]	5 (65%)	1.03 *E*/*Z*	74*b*
4		H	H	Et	$Rh_2(O_2CCH_2PIB)_4$ (**3**), 1 mol%	6	Heptane, 25 °C	44	1.4 *E*/*Z*[d]	2%	9 (75%)	—	21
5		H	H	Et	$Rh_2(OAc)_4$/[bmim][PF_6], 1 mol%	0	[bmim][PF_6], 27 °C, 6 h	88	9.0 *E*/*Z*	0.001%	5 (72%)	—	52*c*
6[i]		H	H	Et	$Rh_2(OAc)_4$, 0.5 mol%	—	CH_2Cl_2, 25 °C, 7–9 h	93	1.6 *E*/*Z*	—	—	—	85
7		H	Ph	Me	SBA-15/$Rh_2(tfa)_4$, 0.48 mmol g^{-1}	3	Toluene, r.t., 24 h	89	99 *E*/*Z*	n.d.[c]	4 (64%)	99 *E*/*Z*	45
8[i]		H	Ph	Me	$Rh_2(tfa)_4$, 1 mol%	—	CH_2Cl_2, r.t.	70	99 *E*/*Z*	—	—	—	86
9		H	H	Et	**28a**, 1 mol%	1	*n*-Pentane, Reflux, 12 h	82	1.38 *E*/*Z*, % ee: 66 (*E*); 57 (*Z*)	n.o.[e]	3 (≈75%)	≈1.50 *E*/*Z*% ee: 70 (*E*); 60 (*Z*)	32
10[i]		H	H	Et	**26a**, 1 mol%	—	*n*-Pentane, Reflux, 2 h	55	1.08 *E*/*Z*, % ee: 87 (*E*); 91 (*Z*)	—	—	—	32
11		H	H	Et	**28b**, 1 mol%	1	*n*-Pentane, Reflux, 12 h	87	1.22 *E*/*Z*, % ee: 70 (*E*); 66 (*Z*)	n.o.[e]	8 (≈55%)	≈1.22 *E*/*Z*, % ee: 72 (*E*); 66 (*Z*)	32
12[i]		H	H	Et	**26b**, 1mol%	—	*n*-Pentane, Reflux, 2 h	40	0.64 *E*/*Z*, % ee: 75 (*E*); 87 (*Z*)	—	—	—	32
13		H	H	Et	**28d**, 1 mol%	1	*n*-Pentane, Reflux, 12 h	94	1.44 *E*/*Z*, % ee: 61 (*E*); 52 (*Z*)	n.o.[e]	9 (≈62%)	≈1.56 *E*/*Z*, % ee: 61 (*E*); 45 (*Z*)	32
14[i]		H	H	Et	**26e**, 1mol%	—	*n*-Pentane, Reflux, 2 h	52	1.44 *E*/*Z*, % ee: 85 (*E*); 84 (*Z*)	—	—	—	32
15		H	H	Et	**28f**, 1 mol%	1	*n*-Pentane, Reflux, 12 h	89	1.56 *E*/*Z*, % ee: 66 (*E*); 46 (*Z*)	n.o.[e]	9 (≈50%)	≈1.22 *E*/*Z*, % ee: 45 (*E*); 25 (*Z*)	32
16[i]		H	H	Et	**26f**, 1 mol%	—	*n*-Pentane, Reflux, 2 h	56	2.13 *E*/*Z*, % ee: 88 (*E*); 84 (*Z*)	—	—	—	32
17		H	H	Et	**29b**, 1 mol%	2	*n*-Pentane, Reflux, 12 h	88	0.54 *E*/*Z*, % ee: 56 (*E*); 57 (*Z*)	n.o.[e]	8 (≈40%)	≈0.67 *E*/*Z*, % ee: 45 (*E*); 55 (*Z*)	33
18[i]		H	H	Et	**27b**, 1 mol%	—	*n*-Pentane, Reflux, 2 h	57	0.43 *E*/*Z*, % ee: 82 (*E*); 78 (*Z*)	—	—	—	33
19		H	H	Et	**30b**, 1 mol%	2	*n*-Pentane, Reflux, 12 h	86	0.52 *E*/*Z*, % ee: 59 (*E*); 60 (*Z*)	n.o.[e]	10 (≈84%)	≈0.56 *E*/*Z*, % ee: 65 (*E*); 65 (*Z*)	33

Table 12 *(Contd.)*

Entry	Reaction	R^1	R^2	R^3	Catalyst, Catalyst loading	Steps[a]	Reaction, Conditions	Yield (%)	Selectivity	Rhodium leaching	Runs Reported[b]	Last run, Selectivity	Ref.
20[i]		H	H	Et	**27e**, 1 mol%	—	*n*-Pentane, Reflux, 2 h	52	0.41 *E*/*Z*, % ee: 80 (*E*); 79 (*Z*)	—	—	—	33
21		H	Ph	Me	AWP-Rh_2(*S*-TBSP)$_4$(**36a–31b**), 0.5 mol%	3	Toluene, 23 °C, 10 min	92	99 *E*/*Z*, *E*:82% ee	n.d.[c]	4 (89%)	*E*: 70% ee	40,41
22		H	Ph	Me	AWPh-Rh_2(*S*-TBSP)$_4$(**36b–31b**), 0.5 mol%	3	Toluene, 23 °C, 21 min	92	99 *E*/*Z*, *E*:85% ee	n.d.[c]	5, (90%)	*E*: 81% ee	40,41
23[i]		H	Ph	Me	Rh_2(*S*-TBSP)$_4$(**31b**)	—	Pentane	90	99 *E*/*Z*, *E*:87% ee	—	—	—	87
24		H	Ph	Me	AWP-Rh_2(*S*-biTISP)$_2$ (**36a–32b**), 0.5 mol%	3	Toluene, 23 °C, 18 min	91	99 *E*/*Z*, *E*:85%ee	n.d.[c]	15 (89% after 92 min)	*E*: 88% ee	40,41
25		H	Ph	Me	AWPh-Rh_2(*S*-biTISP)$_2$ (**36b–32b**) 0.5 mol%	3	Toluene, 23 °C, 24 min	85	99 *E*/*Z*, *E*: 82%ee	n.d.[c]	5 (83% after 57 min)	*E*: 84% ee	40,41
26		H	Ph	Me	Rh_2(*S*-PFOS-Pro)$_4$ (**43**), 1 mol%	3	CH_2Cl_2, r.t., 3.5 h	82	99 *E*/*Z*, *E*: 48% ee	n.d.[c]	3 (86%)	*E*: 56% ee	48
27		H	Ph	Me	Rh_2(*S*-PFOS-Pro)$_4$ (**43**), 1 mol%	3	PFMC[f], r.t., 4 h	79	99 *E*/*Z*, *E*: 62% ee	0.1%	3 (65%)	*E*: 74% ee	48
28[i]		H	Ph	Me	Rh_2(*S*-TBSP)$_4$ (**31b**), 1 mol%	—	Pentane, r.t.	73	99 *E*/*Z*, *E*: 85% ee	—	—	—	77
29		—	H	Et	$Rh_2(PE_{Olig}CO_2)_4$ (**1**), 2 mol%	3	Toluene, 100 °C, 9 h	54	2.4 *E*/*Z*	<1%	10 (59%)	—	19
30[i]		—	H	Et	$Rh_2(OAc)_4$, 0.5 mol%	—	CH_2Cl_2, 25 °C, 7–9 h	81	1.8 *E*/*Z*	—	—	—	85
31		H	H	H	TG-Rh_2(5*S*-MEPY)$_3$ (**13a**), 1 mol% Rh_2	2	CH_2Cl_2, r.t., 3 h	65[g]	90% ee	n.d.[c]	8 (65%)[g]	78% ee	24
32		H	H	H	Mer-Rh_2(5*S*-MEPY)$_3$ (**13b**), 1 mol% Rh_2	2	CH_2Cl_2, r.t., 3 h	75[h]	90% ee	n.d.[c]	10 (75%)[h]	82% ee	24
33		H	H	H	AWP-Rh_2(5*S*-MEPY)$_4$ (**36a–4a**), 2 mol%	3	CH_2Cl_2, Reflux, 5 h	81	95% ee	n.d.[c]	3 (72%)	95% ee	43
34[i]		H	H	H	Rh_2(5*S*-MEPY)$_4$ (**4a**), 0.1 mol%	—	CH_2Cl_2, reflux, 12–18 h	75	95% ee	—	—	—	88
35		Ph	Me	H	AWP-Rh_2(5*S*-MEAZ)$_4$ (**36a–6a**), 2 mol%	3	CH_2Cl_2, Reflux, 5 h	80	88% ee	n.d.[c]	3 (77%)	70% ee	43
36[i]		Ph	Me	H	Rh_2(5*S*-MEAZ)$_4$ (**6a**), 1 mol%	—	CH_2Cl_2, Reflux, 2.5 h	82	84% ee	—	—	—	89
37		H	H	Me	PE-Rh_2(5*S*-PYCA)$_4$ (**11**), 1 mol%, 5*S*-MEPYH (2.7 mol%)	5	C_6H_6, Reflux	58	98% ee	n.d.[c]	7 (55%)	61% ee	22
38[i]		H	H	Me	Rh_2(5*S*-MEPY)$_4$ (**4a**), 1 mol%	—	CH_2Cl_2, Reflux, 12 h	82	99% ee	—	—	—	22,90

[a] Number of synthetic steps needed for the catalyst immobilization. [b] Number of catalytic runs reported. In parenthesis is the last run yield. [c] Not determined. [d] Averaged diastereoselectivity from 9 runs. [e] Not observed. [f] Perfluoro(methylcyclohexane). [g] Averaged yield from 8 runs. [h] Averaged yield from 10 runs. [i] Standard catalytic system.

Table 13 Dirhodium based reusable catalytic systems for X–H insertion

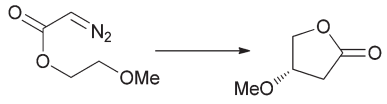
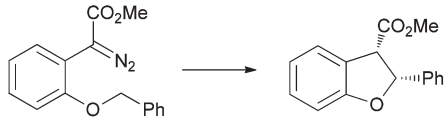
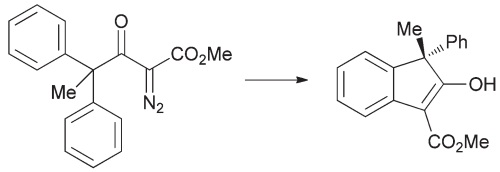
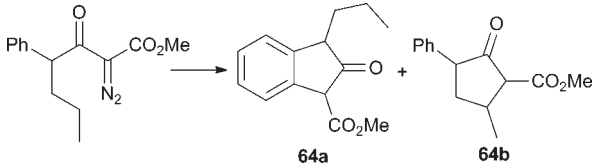
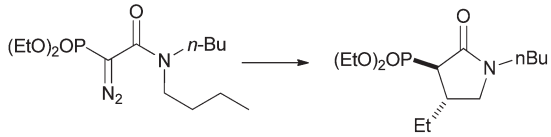
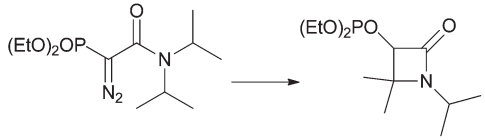
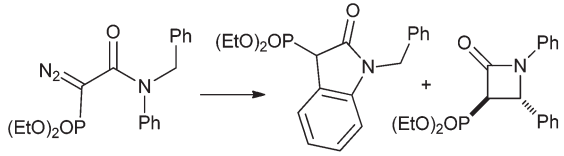
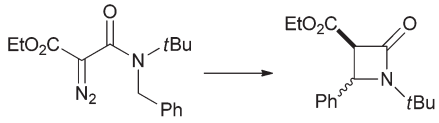
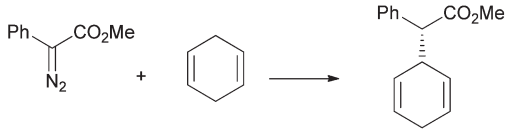
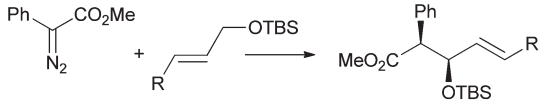
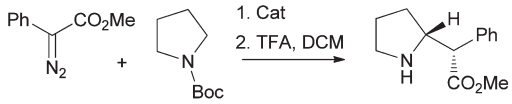
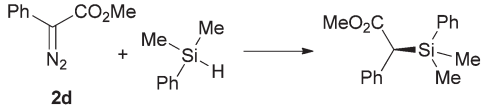
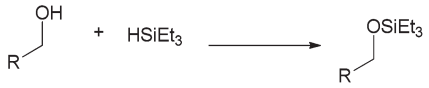
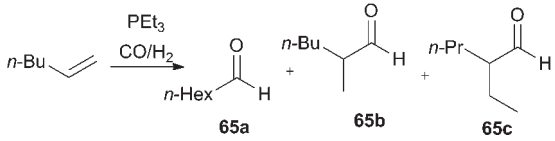
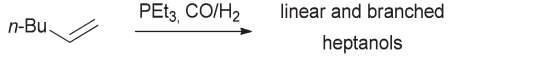
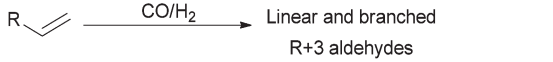
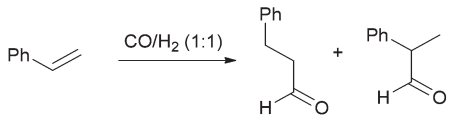
Entry	Reaction	Catalyst, Catalyst loading	Steps[a]	Reaction, Conditions	Yield (%)	Selectivity	Leaching	Runs Reported[b]	Last run, Selectivity	Ref.
1		PS-Rh_2(*S*-PTTL)$_3$ (**22**), 2 mol%	3	Toluene, −78 °C, 4 h	85	94% ee	n.d.[c]	20 (81%)	94% ee	27
2[d]		Rh_2(*S*-PTTL) (**16d**), 1 mol%	—	Toluene, −78 °C, 1.5 h	85	95% ee	—	—	—	91
3		PE-Rh_2(5*S*-PYCA)$_4$ (**11**), 1 mol%, 5*S*-MEPYH (2.5–2.8 mol%)	5	C_6H_6, Reflux	≈54	≈72% ee	n.d.[c]	8 (≈45%)	≈46% ee	22
4[d]		Rh_2(5*S*-MEPY)$_4$ (**4a**), 1 mol %	—	CH_2Cl_2, Reflux	62	91% ee	—	—	—	92
5		PS-Rh_2(*S*-PTTL)$_3$ (**23**), 2 mol%	3	Toluene, −60 °C, 2 h	83	91% ee	n.d.[c]	15 (80%)	90% ee	27
6		AWP-Rh_2(*S*-PTTL)$_4$ (**36a–16d**), 1 mol%	3	Toluene, r.t., 5 h	67	83% ee	n.d.[c]	3 (68%)	75% ee	43
7[d]		Rh_2(*S*-PTTL)$_4$ (**16d**), 1 mol %	—	Toluene, −60 °C, 0.5 h	87	90% ee	—		—	27
8		PS-Rh_2(*S*-PTTL)$_3$ (**23**), 2 mol%	3	CH_2Cl_2, 23 °C, 20 min	86	91% ee	0.0019%	100 (88%)	92% ee	27
9		AWP-Rh_2(*S*-PTTL)$_4$ (**36a–16d**), 5 mol%	3	CH_2Cl_2, r.t., overnight	80	93% ee	n.d.[c]	3 (75%)	93% ee	43
10[d]		Rh_2(*S*-PTTL)$_4$ (**16d**), 2 mol %	—	CH_2Cl_2, 23 °C, 5 min	89	91% ee	—	—	—	27
11		**59g**/$F_2ClCCCl_2F$, 1 mol%	0	$F_2ClCCCl_2F$ r.t., 13 h	70	22.3 **64a/b**	4%	2 (62%)	**64a/b** 22.3	74*b*
12[d]		$Rh_2(O_2CCF_3)_4$, 2 mol%	—	CH_2Cl_2, 0 °C, 1 h	74	3.76 **64a/b**	—	—	—	93
13		$Rh_2(OAc)_4$/[bmim][PF_6], 1 mol%	0	[bmim][PF_6], 83 °C, 4 h	77	—	n.d.[c]	6 (71%)	—	52*b*
14[d]		$Rh_2(OAc)_4$, 1 mol%	—	$C_2H_4Cl_2$, Reflux, 2 h	87	—	—	—	—	55
15		$Rh_2(OAc)_4$/H_2O, 1 mol%	0	H_2O, 80 °C, 24 h	75	—	0.4–2.3%	10 (90%)	—	64*a*
16[d]		$Rh_2(OAc)_4$, 1 mol%	—	$C_2H_4Cl_2$, Reflux, 6.5 h	88	—	—	—	—	55
17		$Rh_2(OAc)_4$/H_2O, 1 mol%	0	H_2O, 80 °C, 26 h	99	11 : 1 **γ/β**	n.d.[c]	3 (89%)	**γ/β** 16 : 1	64*b*
18[d]		$Rh_2(OAc)_4$, 1 mol%	—	$C_2H_4Cl_2$, Reflux, 24 h	50	4.8 : 1 **γ/β**	—	—	—	64*b*

Table 13 *(Contd.)*

Entry	Reaction	Catalyst, Catalyst loading	Steps[a]	Reaction, Conditions	Yield (%)	Selectivity	Leaching	Runs Reported[b]	Last run, Selectivity	Ref.
19		$Rh_2(OAc)_4/H_2O$, 1 mol%	0	H_2O, 80 °C, 24 h	93	n.d.[c]	n.d.[c]	5 (20%)	—	64*b*
20		$Rh_2(OAc)_4/scCO_2$, 1 mol%	0	$scCO_2$, 30 °C, 24 h, 70 bar	>97	0.20 *trans* : *cis*	n.d.[c]	2 (>97%)	0.10, *trans* : *cis*	83
21		AWP-Rh_2(*S*-DOSP)$_4$ (**36a–31c**), 0.5 mol%	3	Toluene, 23 °C, 20 min	79	88% ee	n.d.[c]	10 (84% after 30 min)	84% ee	42
22[d]		Rh_2(*S*-DOSP)$_4$ (**31c**), 1 mol %	—	Hexane, −50 °C, 1 h	>80	91% ee	—	—	—	94
23		AWP-Rh_2(*S*-DOSP)$_4$ (**36a–31c**), 0.6 mol%	3	Toluene, 23 °C, overnight	R = Me, 70	>94% de, 82% ee	n.d.[c]	3 (68%)	>94% de, 68% ee	42
24[d]		Rh_2(*R*-DOSP)$_4$ (**31c**), 1 mol %	—	Hexane, 23 °C, 2 h	R = H, 52	>94% de, −92% ee	—	—	—	95
25		AWP-Rh_2(*S*-DOSP)$_4$ (**36a–31c**), 0.6 mol%	3	Toluene, r.t., overnight	70	90% de, 88% ee	n.d.[c]	3 (68%)	90% de, 86% ee	42
26[d]		Rh_2(*S*-DOSP)$_4$ (**31c**), 1 mol %	—	Hexane, −50 °C, 12 h	72	92% de, 94% ee	—	—	—	96
27		SiO_2-$(CH_2)_2CO_2$-Rh_2(4*S*-BNOX)$_3$, 0.8 mol% Rh_2	3	CH_2Cl_2, Reflux, 20 h	79	33% ee	16%	3 (19%)	11% ee	18*c*,44
28[d]	**2d**	Rh_2(4*S*-BNOX)$_4$ (**4d**)	—	CH_2Cl_2, Reflux	73	2% ee	—	—	—	44

[a] Number of synthetic steps needed for the catalyst immobilization. [b] Number of catalytic runs reported. In parenthesis is the last run yield. [c] Not determined. [d] Standard catalytic system.

Table 14 Dirhodium based reusable catalytic systems for hydroformylation, silane alcoholysis and oxidations

Entry	Reaction	R	Catalyst, Catalyst loading	Steps[a]	Reaction, Conditions	Yield (%)	Selectivity	Leaching	Runs Reported[b]	Last run, Selectivity	Ref.
1		nC_7H_{15}	BFP-$Rh_2(pfo)_4$, 0.1 mol%	1	Solventless, r.t., 24 h	100	—	2.6%	3 (72%)	—	47
2		nC_7H_{15}	$Rh_2(pft)_4$/Fluorinert® FC-77 1 mol%	0	CH_2Cl_2, Fluorinert® FC-77, r.t., 6 h	68	—	n.d.[c]	3 (45%)	—	76
3[h]		nC_7H_{15}	$Rh_2(pfo)_4$ (**39a**), 0.1 mol %	—	Solventless, 50 °C, 24 h	73	—	—	—	—	47*b*
4[h]		nC_7H_{15}	$Rh_2(pfb)_4$, 1 mol%	—	CH_2Cl_2, r.t., 3 h	96	—	—	—	—	78
5		Ph	**51**/[bmim][PF_6], 0.01 mol %	0	[bmim][PF_6], 50 °C, 24 h	73	—	90% recovered	3 (20%)	—	52*a*
6[h]		Ph	**51**, 0.01 mol%	—	$C_2H_4Cl_2$, 50 °C, 24 h	90	—	—	—	—	52*a*
7		—	1,3-Mer-$Rh_2(OAc)_2$ (**25a**), 10% Rh(II)	5	Toluene, 80 °C, 10 h, 40 bar	>99	**65 a : b : c**, 54 : 35 : 11	<0.01%	2 (45%)[d]	**a:b:c** (%), 29 : 11 : 0	30
8		—	1,2-Mer-$Rh_2(OAc)_2$ (**25b**), 5% Rh(II)	5	Toluene, 80 °C, 10 h, 40 bar	>99	**65 a : b : c**, 50 : 38 : 12	<0.01%	2 (68%)[d]	**a:b:c** (%), 34 : 9:0	30
9[h]		—	$Rh_2(OAc)_4$	—	Ethanol, 120 °C, 16.5 h, 60 bar	103	2.23, *n* : *b* ratio[e]	—	—	—	97
10		*n*Bu	$P(OC_6H_4C_9H_{19})_3$ $Rh_2(OAc)_4$/$scCO_2$, 0.6 mol%	0	$scCO_2$, 100 °C, 2 h, 40 bar	84	5.6, *n* : *b* ratio[e]	<0.01%	5 (77%)	3.3, *n:b* ratio[e]	84*b*
11		C_7H_{15}	[bmim][$Ph_2P(C_6H_4SO_3)$] $Rh_2(OAc)_4$/[bmim]PF_6, 0.5 mol%	0	$scCO_2$/[bmim] PF_6, 100 °C, 1 h, 40 bar	≈78	3.7, *n* : *b* ratio[e]	<0.01% until 9th run	12 (≈64%)	2.5, *n:b* ratio[e]	57
12[h]		*n*Bu	$P(OPh)_3$ (Rh_2)$(OAc)_4$, 0.3 mol%	—	Toluene, 100 °C, 1 h, 70 bar	84	2.5, *n* : *b* ratio[e]	—	—	—	57
13		—	**37a**	2	Toluene, 60 °C, 6 h, 60 bar	>99	0.07, *n* : *b* ratio[e]	o.b.n.d.[f]	4 (6%)	0.13, *n:b* ratio[e]	18*a*
14		—	**37b**	3	Toluene, 60 °C, 6 h, 30 bar	>99	0.09, *n* : *b* ratio[e]	o.b.n.d.[f]	6 (63%)	0.29, *n:b* ratio[e]	18*a*
15[h]		—	**37c**	—	Toluene, 60 °C, 6 h, 30 bar	>99	0.09, *n* : *b* ratio[e]	—	—	—	98
16		—	$Rh_2(OAc)_4/H_2O$, 1 mol%	0	H_2O, 40 °C, 1 h	89	—	n.d.[c]	3[g]	—	71
17h		—	$Rh_2(OAc)_4$, 1 mol%	—	$C_2H_4Cl_2$, 40 °C, 10 h	86	—	—	—	—	71

[a] Number of synthetic steps needed for the catalyst immobilization. [b] Number of catalytic runs reported. In parenthesis is the last run yield. [c] Not determined. [d] Conversion values. [e] Linear:branched ratio. [f] Leaching observed but not determined quantitatively. [g] Reused in the oxidation of two other substrates. [h] Standard catalytic system.

formed *in situ* derived from $Rh_2(OAc)_4$ and $P(OC_6H_4C_9H_{19})_3$, allowed the formation of heptanal in good linear/branched selectivity over 5 runs (Table 14, entry 10). Despite the two phase system of the reaction, no rhodium leaching was detected in the oxidation of hex-1-ene.[84b]

4. Conclusions

Despite some notable breakthroughs in the immobilisation and the use of immobilised dirhodium(II) complexes in catalysis, these systems are still underexplored in transformations that do not encompass a metallocarbene formation. Despite the successful examples of such transformations (*e.g.* silylation of alcohols, hydroformylation and propargylic oxidations), other dirhodium-catalysed transformations such as C–H amination, cycloadditions, or Lewis acid-catalysed reactions have not been evaluated using dirhodium-immobilised complexes. It is quite difficult to compare the strategies to perform the reutilization of dirhodium (II) complexes because they display different catalytic properties that stem from their unique stereo-electronic profiles and also because these systems were evaluated in different reactions and conditions. In addition to this, in many studies the percentage of rhodium leaching is not presented, which limits the evaluation of the recycling efficiency. Nevertheless, some conclusions can be withdrawn from the studies presented in this review. Regarding the strategies based on heterogeneous systems, the work disclosed by Hashimoto *et al.* is worthy of a mention as up to 100 runs were performed with 0.0019% of rhodium leaching maintaining the high yields and selectivities in C–H insertion reactions.[27] Given the success of this system, it is expected that it may be further tested in other transformations such as the intermolecular C–H insertion or ylide-based reactions. Considering the reported systems in which the reaction solvent is used as the immobilization agent, the use of water as the reaction media appears as a very attractive strategy because it is less expensive then ionic liquids, fluorinated solvents or $scCO_2$ and does not require any manipulation of catalyst (10 runs with $Rh_2(OAc)_4$), nonetheless, this strategy displays important limitations in what concerts the solubility requirements of both the reactants and catalyst and the fact that no asymmetric dirhodium(II) catalyst has been developed to date to operate well in water. Based on the aforementioned, although several interesting approaches have been recently disclosed to perform the reutilization of dirhodium complexes, a large amount of work is still necessary to achieve an immobilization protocol that may serve the different families of dirhodium(II) complexes and to address the possibility to use this family of complexes on an industrial scale.

Abbreviations

AIBN	azobisisobutyronitrile
BFPC	bonded fluorous phase catalysis
bmim	1-Butyl-3-methylimidazolium
cap	caprolactamate
EDA	ethyl diazoacetate
F-LPE	fluorous liquid-phase extraction
MPDA	methyl phenyldiazoacetate
oct	octanoyl
Opr	propionate
PE	polyethylene
pfb	heptaflurobutyrate
pfd	perfluorodecanoate
PFMC	perfluoro(methylcyclohexane)
pfo	perfluorooctanoate
PFOS-Pro	(perfluorooctylsulfonyl)prolinate
pft	perfluorotetradecanoate
PIB	polyisobutylene oligomers
sc	supercritical
tfa	trifluoroacetyl
TMEDA	tetramethylethylenediamine

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