

Heterometallic complexes, tandem catalysis and catalytic cooperativity

Cite this: *Chem. Sci.*, 2014, 5, 1723

José A. Mata,^a F. Ekkehardt Hahn^{*b} and Eduardo Peris^{*a}

Received 12th November 2013
Accepted 6th December 2013

DOI: 10.1039/c3sc53126k

www.rsc.org/chemicalscience

This minireview reports the most recent advances in the use of heterometallic catalysts based on single-frame N-heterocyclic carbene ligands. The article describes the synthetic strategies for the preparation of heterometallic catalysts, and their applications in the design of tandem processes by combining the catalytic properties associated with the two (or more) different metal centers. Several examples are discussed in which the use of heterometallic complexes results in a clear enhancement of the catalytic outcome compared to the results provided by mixtures of related homometallic complexes. The field constitutes a research area that is full of potential and is at its very earliest stage.

Introduction

Due to the restricted number of transition metals available, advances in the preparation of metal-based catalysts mainly rely

on the design of new ligands. Facilitating a complicated catalytic reaction with a simple and effective catalyst, or finding a way of combining several catalytic reactions into a one-pot tandem process,¹ are two of the most important challenges that encourage the design of improved catalysts. A straightforward approach for the design of sophisticated tandem processes is to combine two different metal complexes, with the aim that each of the metals facilitates mechanistically independent catalytic cycles.^{1a,c,2} In such processes, each metal center promotes an individual catalytic step, and so synergism or cooperativity is difficult to achieve. It is well accepted that catalysts containing

^aDpto. de Química Inorgánica y Orgánica, Universitat Jaume I, Avda. Sos Baynat, E-12071-Castellón, Spain. E-mail: eperis@qio.uji.es; Fax: +34 964387322; Tel: +34 964387518

^bInstitut für Anorganische und Analytische Chemie, Westfälische Wilhelms-Universität Münster, Corrensstraße 30, D-48149 Münster, Germany. E-mail: fehahn@uni-muenster.de; Fax: +49 2518333108; Tel: +49 2518333111



Jose A. Mata was born in Vila-real, Castellón, in 1974. He received a BS in chemistry from the University of Valencia (1997) and completed his PhD with honors at University Jaume I under the supervision of Prof. E. Peris in 2002 where he worked on functionalized ferrocenes with non-linear optical properties (NLO). He was a postdoctoral fellow at Yale University with Prof. Robert

Crabtree (2002–2003) working on rhodium complexes with N-heterocyclic carbene ligands. In 2004 he moved to Toulouse as a postdoctoral fellow at the Laboratoire de Chimie de Coordination (CNRS) with Prof. Rinaldo Poli and worked on atom transfer radical polymerization (ATRP). He returned to University Jaume I with the “Ramón y Cajal” program (2005–2008) and became assistant professor of chemistry in 2008. His research interests are focused on the development of new catalytic processes based on metal complexes with N-heterocyclic carbene ligands.

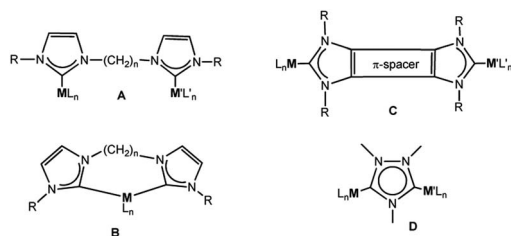


F. E. Hahn studied chemistry at the Technische Universität Berlin and the University of Oklahoma (MS 1982). He graduated with a Dr rer. nat. from the Technische Universität Berlin in 1985. After a postdoctorate with Prof. Raymond at UC Berkeley (1985–1988) he completed the Habilitation in 1990 and became Associate Professor at the Freie Universität Berlin (1992–1998) before moving in

1998 to a position as chair of Inorganic Chemistry at the University of Münster. His research is centered around the chemistry of N-heterocyclic carbenes and isocyanides ligands. He serves in the Editorial Boards of Dalton Transactions and the Journal of Organometallic Chemistry and is a member of the advisory boards of Organometallics. Since 2004 he acts as Permanent Secretary of the International Conference of Organometallic Chemistry (ICOMC).

multiple metal centers in close proximity to each other can lead to better reactivity than the equivalent mixtures of monometallic complexes, particularly when there is second order kinetic dependence on the catalyst.^{2a,3} In addition, polymetallic catalysts afford a higher nanolocal concentration of active sites, and this may also lead to better catalytic performance than the analogous monometallic catalysts, as happens in the case of some dendrimers ('dendrimer effect').⁴

The great topological versatility of N-heterocyclic carbenes (NHCs),⁵ their wide range of associated electronic properties,⁶ and their ability to form stable complexes with a large variety of metal complex fragments,⁷ have raised NHCs to a privileged position in the design of all kinds of homogeneous catalysts, including those having more than one metal.⁸ Polymetallic N-heterocyclic carbene complexes are normally supported by poly-NHCs, mostly di- or tri-NHCs.⁸ Di-NHCs, that can be bound to two different metals, may allow the preparation of NHC-based dimetallic complexes.⁹ The simplest examples of this type of ligand are those depicted in Scheme 1. Di-NHCs linked



Scheme 1



Eduardo Peris graduated in Chemistry in 1988 in Valencia. He received his PhD Degree in Chemistry (1991) in the Universidad de Valencia, under the supervision of Prof. Pascual Lahuerta. In 1994 he joined Robert Crabtree's group at Yale University, where he stayed for two years, working on a research project regarding the determination of hydrogen bonding to metal hydrides (dihydrogen

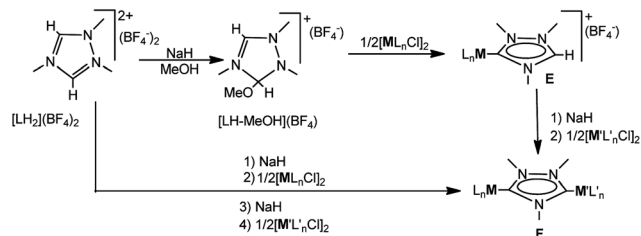
bond). In October 1995 he moved to the Universitat Jaume I (Castellón-Spain) as an Assistant Professor (1995–1997), Lecturer (1997–2007) and finally Professor of Inorganic Chemistry. At the Universitat Jaume I he started a research project related to the use of organometallic push-pull compounds with non-linear-optical properties. The current interest of his group is the design of new polytopic rigid N-heterocyclic carbene ligands (NHCs) that can be applied to the preparation of improved catalysts and advanced materials with attractive physical properties. In 2012 he's been awarded the 'Spanish Royal Society of Chemistry' award in the field of Inorganic Chemistry Research.

by aliphatic chains may lead to either the dimetallic (A) or monometallic species with a chelating di-NHC ligand (B), mostly depending upon the reaction conditions used,⁸ while Janus-type bis-NHCs ligands (C) are geometrically forced to function as bridges between two metals, therefore favouring the formation of dimetallic complexes. It is also important to take into account that ligands of type (C) tend to establish a fixed metal-to-metal separation, while the distance between the metals in complexes of type (A) may vary depending on the relative orientation of the two carbene units due to the flexibility provided by the aliphatic linker.

Over the last few years, we have reported efficient methods for the preparation of homo- and heterodimetallic complexes, mostly based on a 1,2,4-triazolyl-3,5-diyliene ligand with metals of the platinum group, including gold (D).¹⁰ The preparation of such heterodimetallic complexes allowed us to study several catalytic processes in which each of the metal centers facilitated mechanistically independent cycles.¹¹ We also confirmed that the presence of the two different metals provided catalytic benefits compared to the cases in which mixtures of homodimetallic species were used,¹² in a clear illustration of the synergistic behavior between the metals present in the heterometallic complex. Several authors have also reported efficient methods for the preparation of NHC-based heterometallic complexes, such as the representative examples described by Hahn¹³ and Cowie.¹⁴ In this article we will emphasize the preparation of NHC-based heterometallic complexes and their use in homogeneous catalysis. We will focus our attention on those examples in which the ligands are purely poly-NHC ligands (mostly di-NHCs), thus we will not consider all other examples in which the heterometallic complexes are supported by NHC-containing hybrid ligands. The article will describe the preparative procedures leading to the heterometallic complexes, their singular properties in homogeneous catalysed reactions, and the perspectives and potential that this type of novel complex may bring in the near future.

Preparation of NHC-based heterometallic complexes

Most of the known NHC-based heterometallic complexes are obtained by the sequential coordination of the different metal complex fragments to a single-frame ligand; a process that often implies that the starting poly-azolium salt needs to be sequentially deprotonated. In the case of 1,2,4-trimethyl-triazolium tetrafluoroborate ([LH₂](BF₄)₂), an equimolar amount of NaH affords the methanolic adduct [LH-MeOH](BF₄).¹⁵ This adduct can react with a suitable metal source (normally a dimer of a metal-chloride complex) to afford a triazolium-ylidene-metal complex (E), which can be further deprotonated and coordinated to a second metal complex fragment of choice (Scheme 2). The reaction can also be carried out in a one-pot procedure, in which the reaction intermediates ([LH-MeOH](BF₄) and E) are used *in situ*, so that the stepwise metallation of the ligand directly provides the heterodimetallic complexes.^{10b} The one-pot process is very convenient because it simplifies the reaction workups to give the final products and also reduces the amount

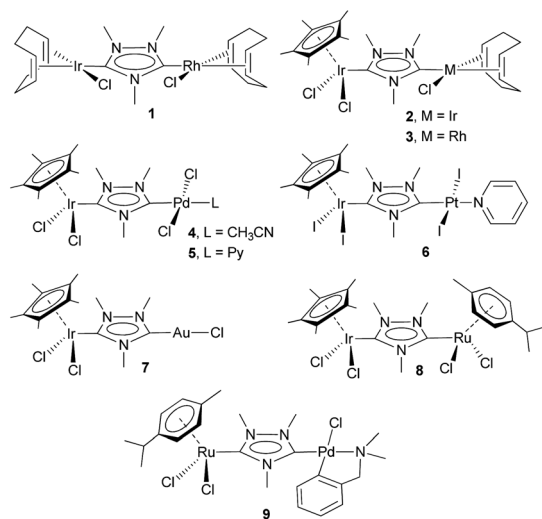


Scheme 2

of solvent used in the overall synthetic and purification processes.

By adapting this synthetic protocol to different metal sources, we were able to obtain and fully characterize the heterodimetallic complexes **1–9**,^{10b,11a,d,12,16} depicted in Scheme 3. Inspection of the X-ray molecular structures of these complexes indicates that the metal-to-metal distances are very close to 6 Å in all cases.

Analysis of the electronic properties associated with the 1,2,4-triazol-di-ylidene (*ditz*) ligand were performed using Cyclic Voltammetry (CV) and DFT studies. The CV studies performed for the diruthenium and the ruthenium–iridium (**8**) complexes,¹² revealed that the metal-to-metal electronic coupling is weak, although it is stronger than the couplings displayed by dimetallic complexes with other Janus-type di-NHC ligands.¹⁷ The separation between the oxidation bands of a *ditz*-based diruthenium complex was found to be 120 mV, which corresponds to a class II system according to the Robin and Day classification.¹⁸ The σ -donating power of *ditz* was estimated using DFT, after having proved that computational methods enable the determination of very accurate values of the Tolman-Electronic-Parameters (TEPs) of many other NHC ligands.¹⁹ Interestingly, the TEP value associated with *ditz* may be calculated by considering the ligand in various different coordination modes. If the calculation is performed considering that the di-carbene ligand is coordinated to one Ni(CO)₃ fragment while having the other end of the ligand

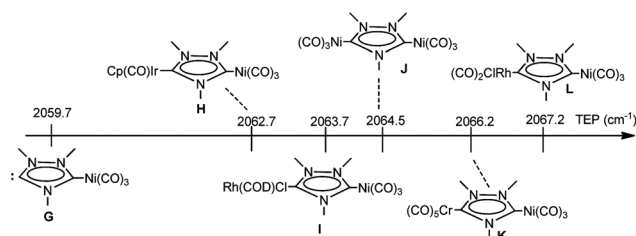


Scheme 3

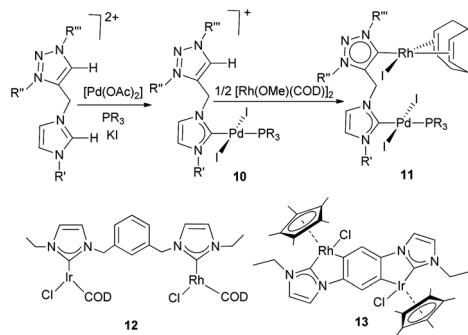
uncoordinated (**G**), Scheme 4), then the TEP value is 2059.7 cm⁻¹.²⁰ Upon coordination of the free-carbene end of the molecule to a second metal complex fragment, an overall change in the TEP is observed, the largest being observed for the dinuclear Ni–RhCl(CO)₂ complex (**L**), for which $\Delta(\text{TEP}) = 7.5 \text{ cm}^{-1}$ compared to (**G**) (Scheme 4). This study not only provided us with an interesting way of quantifying the metal-to-metal electronic interaction by measuring the variation of the TEP values, but it also illustrates how the electron-donating character of Janus-type di-NHCs may vary depending on the metal complex fragments to which they are bound.

The sequential deprotonation/coordination of a methylene- or ethylene-bridged di-azolium salt was used by Cowie and co-workers to prepare a series of heterodimetallic complexes with rhodium–palladium,^{14a} iridium–palladium²¹ and rhodium–iridium^{14b} metal centers. In these studies, the authors were able to prepare complexes from the related di-imidazolium, di-triazolium and mixed imidazolium–triazolium salts to afford the desired heterodimetallic complexes. Interestingly, when mixed imidazolium–triazolium salts are used, the first metallation occurs at the imidazolium part, therefore generating a imidazolylidene complex with a pendant triazolium group (**10**, Scheme 5). This is a consequence of the lower acidity of the triazolium group compared to the imidazolium group of the pre-ligand, which causes the imidazolium side to be more easily deprotonated and subsequently metallated.^{14a} Unfortunately, as stated above, the use of this type of alkylidene-linked di-azolium salt may also afford the related chelate complexes, therefore sometimes reducing the selectivity of the process. As a method to prevent the formation of di-NHC chelate complexes, Braunstein and co-workers used a di-imidazolium salt in which the twoazolium groups are bridged by a *m*-xylylene unit, which enforces the bridging coordination. By using this salt as a di-NHC precursor, the authors were able to isolate a mono-iridium complex with a pendant imidazolium group, which they used for the preparation of a heterodimetallic Ir–Rh complex (**12**).²² The same strategy was later used by Straub and co-workers for the preparation of heterometallic Pd–Au and Pd–Cu₂ complexes, using an unsymmetrical *m*-xylylene-bridged di-triazolium salt, in which one of the triazolium groups is functionalized with a thiol group.²³ A related methodology employing a rigid *p*-phenylene bridge between the imidazolium groups was recently used by Hahn and co-workers for the preparation of a heterodimetallic Ir–Rh complex (**13**).²⁴

Another interesting asymmetric poly-NHC ligand that allows the preparation of heterodimetallic complexes is our recently

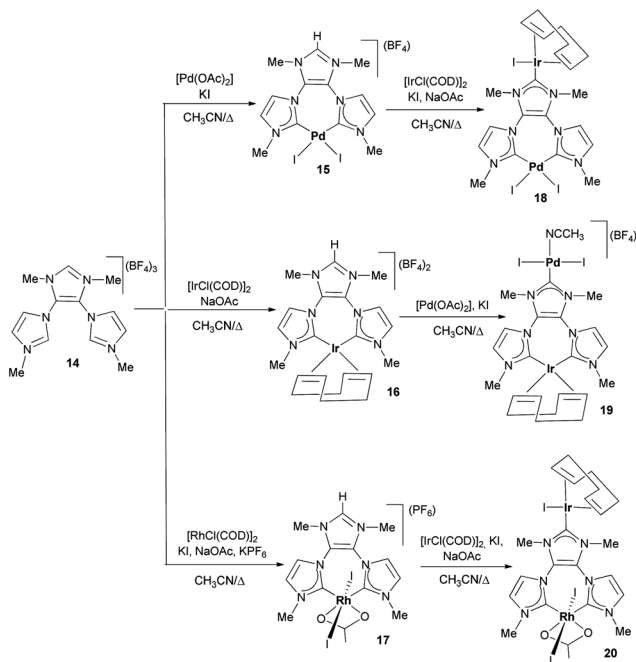


Scheme 4



Scheme 5

described Y-shaped tri-NHC, which can be obtained from the tri-imidazolium salt **14** (Scheme 6).²⁵ This ligand is capable of bridging two metals in two different coordination environments (one chelating, the other monodentate), therefore affording complexes with different reactivities at the two ends of the molecule, regardless of whether the complexes are homo- or heterometallic. Interestingly, the stepwise coordination of the ligand is selective, in the sense that the first metal will prefer to bind to the chelating part of the ligand, affording the chelate complex with a remaining imidazolium group. This observation facilitates the preparation of heterometallic complexes, as each metal can be coordinated to the desired part of the ligand just by adding the metals in the appropriate order, as in the case of the two different iridium–palladium complexes **18** and **19** (Scheme 6). A convenient aspect of the preparation of the heterometallic complexes,²⁶ is that the stepwise one-pot synthesis also affords good yields of the final complexes, providing an important simplification of the experimental procedure.



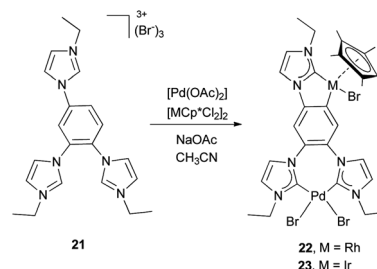
Scheme 6

Scheme 6 summarizes the general synthetic methodology for the preparation of a series of heterometallic palladium–iridium and rhodium–iridium complexes.²⁶ The analysis of the X-ray molecular structures of the complexes allowed us to determine that the metal-to-metal through-space distances fall in a narrow range (6.7–7.0 Å), illustrating the rigidity of the ligand.

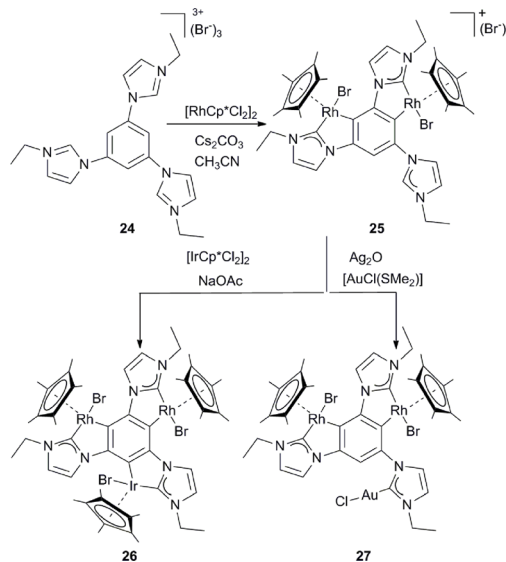
By using an unsymmetrical tri-imidazolium salt featuring a 1,2,4-substitution of a central phenyl ring (**21**), Hahn and co-workers were able to metallate simultaneously with two different complex fragments by taking advantage of the differences in their coordination chemistry.^{13b} While the Pd(II) complex fragment prefers to form a chelate di-NHC complex, the iridium (or rhodium) complex fragment tends to react with the NHC in the 4-position to form an NHC complex, which subsequently orthometalates the phenyl ring (Scheme 7). This is an elegant example of a regioselective metallation of two different metal fragments in a one-pot reaction. The related symmetrical 1,3,5-tri-imidazolium salt (**24**), allows the formation of the corresponding dirhodium complex **25**, by reacting **24** with $[\text{RhCp}^*\text{Cl}_2]_2$ in the presence of Cs_2CO_3 (Scheme 8). The formation of complex **25**, with a pendant imidazolium group, is very convenient for the preparation of the trimetallic Rh₂–Ir complex (**26**) and the Rh₂–Au complex (**27**), by reacting **25** with $[\text{IrCp}^*\text{Cl}_2]_2$ or $[\text{AuCl}(\text{SMe}_2)]$, respectively.^{13c}

NHC-based heterometallic complexes in catalysis

The combination of several transition-metal-catalyzed transformations in one single reaction vessel is gaining increasing attention. The strategy often involves the use of two (or more) metal catalysts for two (or more) transformations.²⁷ A rather logical application of heterometallic complexes is their use as multicatalysts in concatenated multistep processes, which allows the simple preparation of sophisticated molecules in one-pot syntheses. While multicatalysts are starting to flourish in the field of organocatalysis,²⁸ we are rather surprised that the only examples of metal-based multicatalysts (single complexes containing two different catalytically active metals) are the ones reported by us, mostly using the triazole-di-ylidene ligand (**D**) to hold two different metals together. The idea of using two different metals bound by a single-frame ligand to promote a tandem process is extremely simple and uses each metal to facilitate two (or more) mechanistically distinct (orthogonal) cycles, which may be combined to compose the overall tandem process (Scheme 9). In theory, a heterometallic catalyst may be



Scheme 7



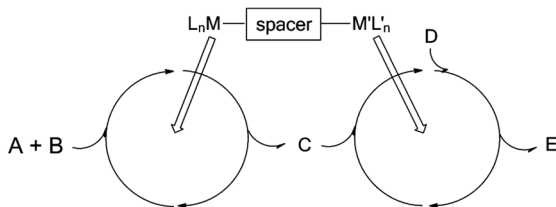
Scheme 8

appropriate for the design of many tandem processes by simply combining all of the potential individual catalytic capabilities of each metal site, thus providing a great advantage over traditional monometallic catalysts. Despite the simplicity of this idea, the practical approach to the design of efficient heterometallic complexes of multimetallic catalysis suffers from some important complications, such as: (i) the need for the two (or more) catalytic active sites to be compatible with the reaction conditions needed for each individual catalytic cycle (and with the residual materials generated in each catalytic step); (ii) the possibility of the two metals being mutually deactivated; (iii) the possibility that the single-frame ligand does not provide the stability needed to maintain the heterometallic nature of the catalyst during the whole catalytic process, which may need harsh reaction conditions, or that it may decompose to give mixtures of the related homodimetallc complexes; and (iv) the possibility that the two metals display similar reactivity patterns and therefore are able to facilitate any of the cycles comprised in the overall tandem reaction, thus making the use of the heterometallic complex obsolete.

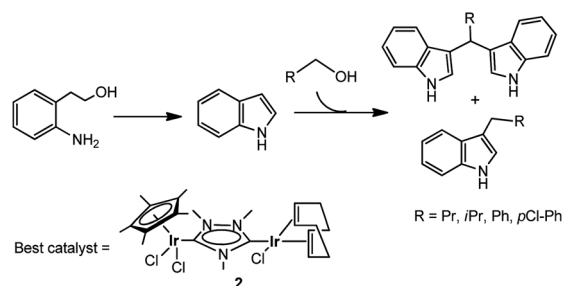
Probably due to their stability and the high yields observed in their syntheses, most of the NHC-based heterometallic complexes that have been reported to date are Ir–Rh species (see Section 2). In fact, the first *ditz*-based heterometallic complexes that we obtained were **1** and **3** (Scheme 3). In the search for a

tandem process for which these heterometallic complexes could be used, we ended up studying the consecutive oxidative cyclization of 2-aminophenyl ethyl alcohol and the alkylation of the resulting indole with a series of primary alcohols (Scheme 10).^{10b} In principle, we aimed for the first step of the reaction (the cyclization of the amino alcohol) to be catalysed by Rh(I) or Ir(I) complexes, while the second step (the alkylation of indole by the primary alcohol) should be catalysed by the Ir(III) part of the catalyst. We found that the most active catalyst for this reaction was the mixed-valence Ir^I/Ir^{III} complex **2** (Scheme 3), but also that other *ditz*-based homodimetallc complexes containing Ir^I/Ir^I and Rh^I/Rh^I were active in the reaction, although these provided lower yields and selectivities. Recently, Grigg and co-workers also demonstrated that [IrCp*Cl₂]₂ was able to promote both steps of the reaction.²⁹ Although we believe that our preliminary results were interesting because we created the basis for efficient synthesis of heterometallic complexes using the *ditz* ligand, we found it difficult to combine catalytic reactions specifically promoted by Rh^I or Ir^I and Ir^{III} due to their chemical similarities.

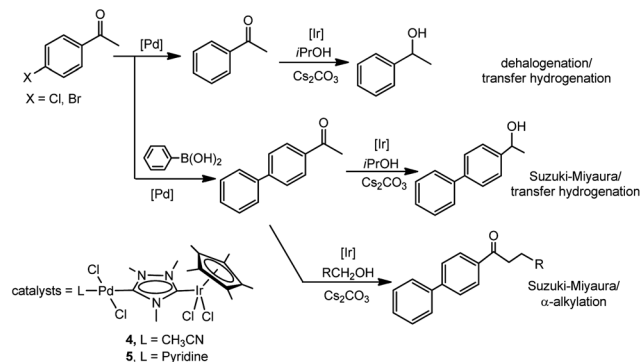
To obtain a dimetallic catalyst that is able to mediate two fundamentally different reactions, we found the combination of iridium and palladium to be a much better choice, due to the inherent differences in the catalytic behavior of these metals. Both metals are active in a large and distinct library of transformations. We thought that haloacetophenones would be very convenient substrates to start our studies with because they combine a halide–aryl bond, for which the palladium part of the catalyst should provide a large library of transformations, and a C=O bond, for which iridium may introduce a variety of modifications, most of them based on borrowing-hydrogen processes.³⁰ We started with the simplest tandem process involving the dehalogenation/transfer hydrogenation of haloacetophenone (Scheme 11), for which we obtained excellent yields in the production of 1-phenyl-ethanol.^{11a} As shown in Scheme 11, by slightly modifying the reaction conditions we were able to design two more sophisticated tandem processes, namely the Suzuki–Miyaura coupling/transfer hydrogenation (which involved the addition of phenyl boronic acid) to afford biphenylated secondary alcohols, and the Suzuki–Miyaura coupling/ α -alkylation of haloacetophenones (by adding a primary alcohol, instead of the secondary alcohol used for the transfer hydrogenation) to yield biphenylated-alkylated ketones.



Scheme 9



Scheme 10



Scheme 11

All of these reactions not only demonstrated a clear advance over alternative procedures to obtain the same final products, but also provided a clear illustration of the catalytic cooperativity between the two metals in the heterodimetallic unit. As can be seen in Fig. 1, mixtures of the homodimetallic complexes of iridium (**28**) and palladium (**29**) afforded significantly lower yields of the final products than the heterometallic complex **5** for reactions carried out under the same conditions after exactly identical reaction times. This result provides first evidence of catalytic cooperativity between the two different metals contained in **4** and **5**.^{11a} In a separate set of experiments, the heterometallic Ir-Pd complexes **18** and **19** (Scheme 6) were also tested in the two tandem processes that combined the dehalogenation/transfer hydrogenation, and the Suzuki-Miyaura/transfer hydrogenation.²⁶ In these two processes both catalysts showed excellent activity, and as demonstrated for **4** and **5**, the activity of the heterodimetallic complexes was higher than the activity shown by the sum of the related monometallic species.²⁶

The heterometallic Ir-Pd complex **5**, was also used for the synthesis of imines by direct reaction between nitroarenes and primary alcohols.^{11c} The reaction involves a two-step tandem

process, in which the nitroarene is reduced to an aniline by the primary alcohol, which is consequently oxidized to the aldehyde (Scheme 12). The selective coupling of the aldehyde and the amine yields the final imine. In principle, the iridium complex fragment in **5** is thought to facilitate the oxidation of the alcohol to the aldehyde with the release of hydrogen. The hydrogen may then be used by the palladium complex fragment for the reduction of the nitroarene to an aromatic amine. The stoichiometric coupling between the amine and the aldehyde affords the final imine. Control experiments were carried out to prove that the palladium-containing complexes **5** and **29** were able to reduce nitroarenes to the corresponding anilines in the presence of H₂, while the diiridium complex **28** was unable to catalyze this reaction under the same reaction conditions. This thereby suggests that the palladium side of the molecule is the one that catalyses the reduction of the nitroarene. On the other hand, the dipalladium complex **29** was unable to oxidize the primary alcohol to an aldehyde under the reaction conditions used, thus confirming the independent role of the two metals in the overall reaction.

The same reaction can be combined with the palladium-catalyzed Suzuki-Miyaura coupling if halo-nitroarenes are used, as takes place in the reaction between 4-bromonitrobenzene with benzylalcohol in the presence of phenylboronic acid (Scheme 13). This reaction affords the corresponding diarylated imine in a 77% yield, which may be considered as very high, especially if we take into account the sophisticated mechanism for this one-pot synthesis.^{11c}

Aiming to obtain a chiral version of the iridium-palladium catalysts **4** and **5**, we obtained a series of heterometallic Ir-Pd complexes with two axes of chirality related to each metal. The complexes (**30–33**, Scheme 14) were tested in a sequence of two catalytic reactions, namely the isomerization and the asymmetric hydrophosphination of 1,3-diphenylpropargyl alcohol (Scheme 14).³¹ Although the catalysts displayed high activity and regioselectivity, the enantioselectivities were very low (the maximum ee values were 17%). The work is the first (and so far the only) example, of a heterometallic complex used in an asymmetric tandem process.

Platinum is also an excellent metal to facilitate many catalytic reactions that, in addition, can be combined with iridium-catalyzed processes for the design of interesting tandem reactions. With this in mind, we used the Ir-Pt complex

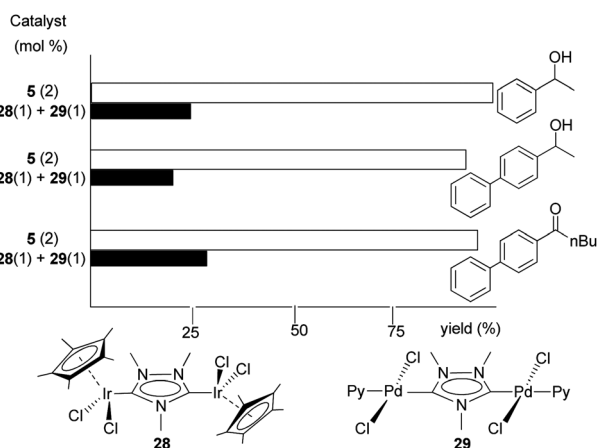
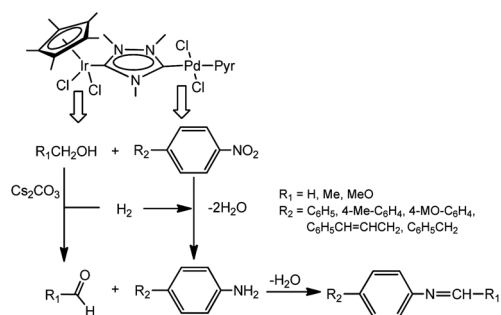
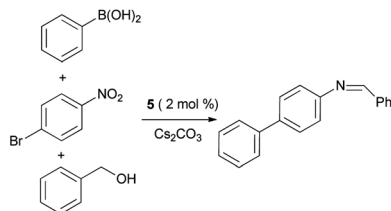


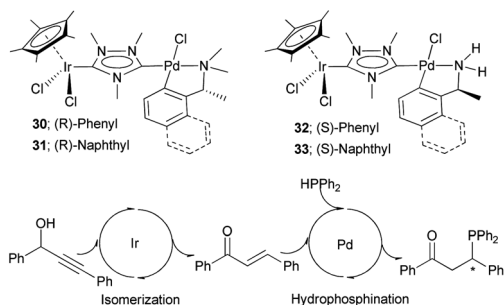
Fig. 1 Comparison between the catalytic activity of the heterodimetallic complex **5**, and the mixture of the related homodimetallic complexes of Ir (**28**) and Pd (**29**). The products were obtained according to the reactions depicted in Scheme 10.



Scheme 12



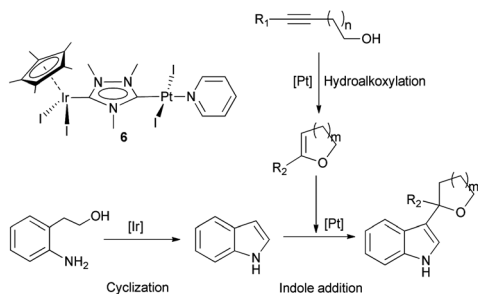
Scheme 13



Scheme 14

6 in the combination of the iridium-catalyzed oxidative cyclization of amino-alcohols to form indoles,³² and the platinum-catalyzed multistep reaction of indoles with alkyne alcohols.³³ The resulting overall tandem process combines three consecutive reactions: (i) the oxidative cyclization of an amino alcohol to form indole, (ii) the intramolecular hydroalkoxylation of an alkyne alcohol to afford a cyclic enol ether, and (iii) the addition of indole to the unsaturated bond of the enol ether (Scheme 15).^{16a} Interestingly, as previously observed for the Ir–Pd complexes **4** and **5**,^{11a} the use of **6** provides an improved catalytic outcome compared to the mixture of the analogous homodimetallic complexes (Fig. 2), thus suggesting that catalytic cooperativity should be at work between the two different metals of the heterometallic catalyst.

The combination of Ru and Pd in complex **9**, also gives access to a very promising library of catalytic reactions that may be combined to form sophisticated tandem processes. Together with the myriad of catalytic applications of the palladium complex fragment, we may think of adding the rich chemistry of ruthenium in C–C bond formation reactions through C–H



Scheme 15

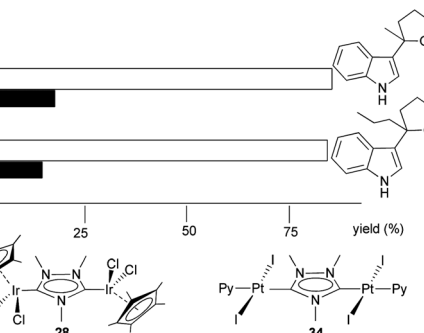
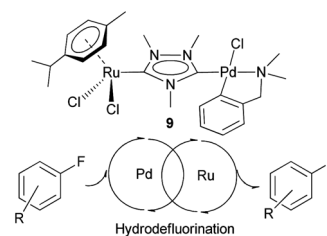


Fig. 2 Multistep functionalization of indole by the multistep reaction between an alkyne alcohol and an amino alcohol. The figure compares the activity of the Ir–Pt heterometallic complex **6** with the activity of the related homodimetallic complexes **28** and **34** (reactions carried out under the same reaction conditions).

activation.^{33,34} However, we decided to test the catalytic activity of this complex in a much simpler but equally challenging reaction: the hydrodefluorination of organic molecules (Scheme 16).³⁵ This reaction occurs in two steps: first, the C–F bond has to be broken, and then a hydrogen atom has to be introduced using a convenient hydrogen source (typically high-pressure H₂, silanes, etc.). In general, ease of the hydrodehalogenation follows the order I > Br > Cl ≫ F, which is related to the order of the C–X bond strengths (C–F bonds are typically 110 kcal mol^{−1}, thus being the strongest σ-bond to carbon). We thought that the Pd–Ru complex **9** had the potential to be a good catalyst for hydrodefluorination because the palladium complex fragment should be able to break the C–F bond, while the ruthenium part of the catalyst should facilitate the reductive step of the reaction by providing hydrogen *via* an alternative hydrogen source, namely the transfer hydrogenation using a secondary alcohol and a base.

Complex **9** (Scheme 16) proved to be a very efficient catalyst for the hydrodefluorination of a wide variety of fluoroarenes, affording quantitative yields in very short reaction times and under very mild reaction conditions (*i*PrOH, 80 °C).^{16c} More interesting is the fact that the combination of the two different metals is necessary to promote the process, as clearly shown in Fig. 3, where the independent use of the homodimetallic complexes of palladium (**35**) and ruthenium (**36**) affords negligible yields of the desired reaction product. Although a mixture of the two different homodimetallic complexes of palladium and ruthenium (**35** and **36**) seems to partially



Scheme 16

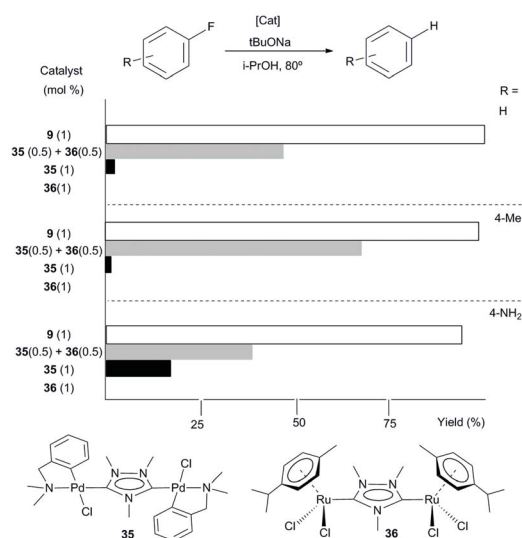
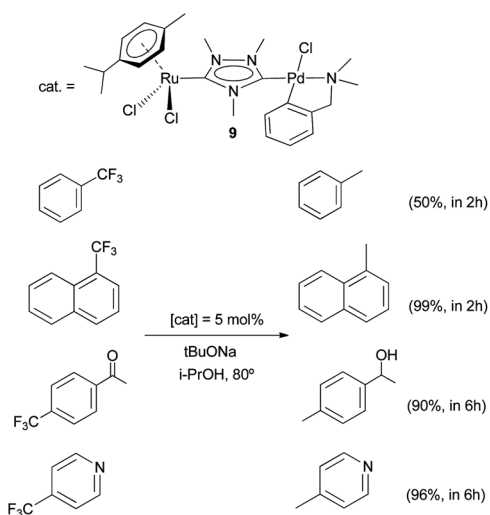


Fig. 3 Hydrodefluorination of aromatic substrates. The figure represents a comparative study on the activity of the heterodimetallic complex **9** and the homodimetallic analogues, **35** and **36**. All reactions were carried out under the same reaction conditions. Yields were taken after 1 h.

facilitate the process, the reaction clearly benefits when the two different metal fragments are linked by the single-frame ligand. This is in line with the above mentioned results that support the idea of the catalytic cooperativity between the two vicinal metals in **9**.^{16c}

Encouraged by these results, we decided to test the catalytic activity of **9** in the hydrodefluorination of the more inert aliphatic C–F bonds, for which its reaction with a series of trifluoromethyl-toluenes was tested. Some of the obtained results are listed in Scheme 17.^{16c} All of these results suggest that catalyst **9** behaves as an effective two-component catalyst, which provides clear benefits in the hydrodefluorination of a wide set of organic substrates.



Scheme 17

Conclusions and future perspectives

In the search for more efficient ways of preparing complex organic architectures, there has been increasing effort put into finding multitopic/polymetallic catalysts that may be active for a wide set of organic transformations. The combination of fundamental catalytic steps involving simple and accessible substrates can then lead to sophisticated molecules. The work that we have presented here represents a clear example of a very logical approach to the design of effective multimetallic catalysts for tandem processes. From the very simple idea of supporting two orthogonal metal fragments with a single-frame ligand, we have obtained a series of heterodimetallic catalysts that are suitable for the design of multiple tandem processes by combining the catalytic activities associated with each metal fragment. In most of the cases, combining the two metals into a single compound is beneficial, as shown by the better catalytic outcome of the bimetallic catalyst when compared to the activity provided by the mixture of the analogous homometallic complexes. Because we do not have a clear explanation for this catalytic cooperativity, we believe that further study on this effect is needed in order to establish a clear basis for the design of future heterometallic catalysts.

As stated in the first few lines of the report published for the workshop: ‘Opportunities for Catalysis in the 21st Century’, ‘The road to increased activity and selectivity is paved by a myriad of structures that will teach us by experience their connections to activity and selectivity. Thus, we need to create new types of catalyst structures and new methods for catalyst preparation to provide the data and experience to show what makes a catalyst active and selective. To date, synthesis of catalysts has often consumed more time and more effort than the testing of these catalysts. Thus, we must open the bottleneck of catalyst synthesis by learning better methods to prepare families of catalysts’.³⁶ We hope that the work described in this article will serve to open the bottleneck in catalyst synthesis by inspiring future researchers in the design of efficient multimetallic catalysts that may be used for simple access to sophisticated organic molecules.

Acknowledgements

We are thankful to all the members of the research groups, who enthusiastically contributed to the design of the heterometallic complexes described here and the study of their catalytic applications. We gratefully acknowledge financial support from MINECO of Spain (CTQ2011-24055/BQU), and the DFG (SFB 858).

Notes and references

- (a) J. M. Lee, Y. Na, H. Han and S. Chang, *Chem. Soc. Rev.*, 2004, **33**, 302–312; (b) D. E. Fogg and E. N. dos Santos, *Coord. Chem. Rev.*, 2004, **248**, 2365–2379; (c) A. Ajamian and J. L. Gleason, *Angew. Chem., Int. Ed.*, 2004, **43**, 3754–3760; (d) J. C. Wasilke, S. J. Obrey, R. T. Baker and G. C. Bazan, *Chem. Rev.*, 2005, **105**, 1001–1020.
- (a) I. Bratko and M. Gomez, *Dalton Trans.*, 2013, **42**, 10664–10681; (b) Y. Shibasaki and Y. Yamamoto, *Multimetallic*

- catalysts in organic synthesis*, Wiley-VCH, Weinheim, 2004.
- 3 (a) E. K. van den Beuken and B. L. Feringa, *Tetrahedron*, 1998, **54**, 12985–13011; (b) J. Park and S. Hong, *Chem. Soc. Rev.*, 2012, **41**, 6931–6943; (c) A. E. Allen and D. W. C. MacMillan, *Chem. Sci.*, 2012, **3**, 633–658; (d) J. I. van der Vlugt, *Eur. J. Inorg. Chem.*, 2012, 363–375.
- 4 (a) J. N. H. Reek, S. Arevalo, R. Van Heerbeek, P. C. J. Kamer and P. Van Leeuwen, in *Advances in Catalysis*, ed. B. C. Gates and H. Knozinger, 2006, vol 49, pp. 71–151; (b) B. Helms and J. M. J. Frechet, *Adv. Synth. Catal.*, 2006, **348**, 1125–1148; (c) D. Astruc, *C. R. Chim.*, 2005, **8**, 1101–1107.
- 5 (a) W. A. Herrmann and C. Köcher, *Angew. Chem., Int. Ed. Engl.*, 1997, **36**, 2163–2187; (b) D. Bourissou, O. Guerret, F. P. Gabbaï and G. Bertrand, *Chem. Rev.*, 2000, **100**, 39–91.
- 6 (a) D. L. Nelson and S. P. Nolan, *Chem. Soc. Rev.*, 2013, **42**, 6723–6753; (b) S. Diez-Gonzalez and S. P. Nolan, *Coord. Chem. Rev.*, 2007, **251**, 874–883.
- 7 (a) W. A. Herrmann, T. Weskamp and V. P. W. Bohm, *Adv. Organomet. Chem.*, 2001, **48**, 1–69; (b) F. E. Hahn and M. C. Jahnke, *Angew. Chem., Int. Ed.*, 2008, **47**, 3122–3172; (c) F. E. Hahn, *Angew. Chem., Int. Ed.*, 2006, **45**, 1348–1352; (d) P. de Fremont, N. Marion and S. P. Nolan, *Coord. Chem. Rev.*, 2009, **253**, 862–892.
- 8 M. Poyatos, J. A. Mata and E. Peris, *Chem. Rev.*, 2009, **109**, 3677–3707.
- 9 The seminal articles describing Janus-type NHCs are: (a) D. M. Khramov, A. J. Boydston and C. W. Bielawski, *Angew. Chem., Int. Ed.*, 2006, **45**, 6186–6189; (b) A. J. Boydston and C. W. Bielawski, *Dalton Trans.*, 2006, 4073–4077; (c) D. M. Khramov, A. J. Boydston and C. W. Bielawski, *Org. Lett.*, 2006, **8**, 1831–1834.
- 10 (a) E. Mas-Marza, J. A. Mata and E. Peris, *Angew. Chem., Int. Ed.*, 2007, **46**, 3729–3731; (b) A. Zanardi, R. Corberan, J. A. Mata and E. Peris, *Organometallics*, 2008, **27**, 3570–3576; (c) A. Zanardi, J. A. Mata and E. Peris, *Organometallics*, 2009, **28**, 4335–4339; (d) A. Zanardi, J. A. Mata and E. Peris, *Organometallics*, 2009, **28**, 1480–1483.
- 11 (a) A. Zanardi, J. A. Mata and E. Peris, *J. Am. Chem. Soc.*, 2009, **131**, 14531–14537; (b) A. Zanardi, J. A. Mata and E. Peris, *Chem.–Eur. J.*, 2010, **16**, 13109–13115; (c) A. Zanardi, J. A. Mata and E. Peris, *Chem.–Eur. J.*, 2010, **16**, 10502–10506; (d) S. Sabater, J. A. Mata and E. Peris, *Chem.–Eur. J.*, 2012, **18**, 6380–6385.
- 12 S. Sabater, J. A. Mata and E. Peris, *Organometallics*, 2012, **31**, 6450–6456.
- 13 (a) R. Maity, A. Rit, C. Schulte to Brinke, C. G. Daniliuc and F. E. Hahn, *Chem. Commun.*, 2013, **49**, 1011–1013; (b) R. Maity, H. Koppetz, A. Hepp and F. E. Hahn, *J. Am. Chem. Soc.*, 2013, **135**, 4966–4969; (c) R. Maity, C. Schulte to Brinke and F. E. Hahn, *Dalton Trans.*, 2013, **42**, 12857–12860.
- 14 (a) M. T. Zamora, M. J. Ferguson, R. McDonald and M. Cowie, *Organometallics*, 2012, **31**, 5463–5477; (b) M. T. Zamora, M. J. Ferguson and M. Cowie, *Organometallics*, 2012, **31**, 5384–5395.
- 15 O. Guerret, S. Sole, H. Gornitzka, G. Trinquier and G. Bertrand, *J. Organomet. Chem.*, 2000, **600**, 112–117.
- 16 (a) A. Zanardi, J. A. Mata and E. Peris, *Chem.–Eur. J.*, 2010, **16**, 13109–13115; (b) E. Mas-Marza, J. A. Mata and E. Peris, *Angew. Chem., Int. Ed.*, 2007, **46**, 3729–3731; (c) S. Sabater, J. A. Mata and E. Peris, *Nat. Commun.*, 2013, DOI: 10.1038/ncomms3553.
- 17 (a) L. Mercs, A. Neels and M. Albrecht, *Dalton Trans.*, 2008, 5570–5576; (b) A. G. Tennyson, E. L. Rosen, M. S. Collins, V. M. Lynch and C. W. Bielawski, *Inorg. Chem.*, 2009, **48**, 6924–6933; (c) O. Schuster, L. Mercs and M. Albrecht, *Chimia*, 2010, **64**, 184–187; (d) A. Prades, E. Peris and M. Alcarazo, *Organometallics*, 2012, **31**, 4623–4626.
- 18 M. B. Robin and P. Day, *Adv. Inorg. Chem. Radiochem.*, 1967, **10**, 247–422.
- 19 (a) D. G. Gusev, *Organometallics*, 2009, **28**, 763–770; (b) D. G. Gusev, *Organometallics*, 2009, **28**, 6458–6461.
- 20 D. G. Gusev and E. Peris, *Dalton Trans.*, 2013, 7359–7364.
- 21 M. T. Zamora, M. J. Ferguson, R. McDonald and M. Cowie, *Dalton Trans.*, 2009, 7269–7287.
- 22 M. Raynal, C. S. J. Cazin, C. Vallee, H. Olivier-Bourbigou and P. Braunstein, *Dalton Trans.*, 2009, 3824–3832.
- 23 S. C. Seitz, F. Rominger and B. F. Straub, *Organometallics*, 2013, **32**, 2427–2434.
- 24 R. Maity, A. Rit, C. Schulte to Brinke, J. Kösters and F. E. Hahn, *Organometallics*, 2013, **32**, 6174–6177.
- 25 S. Gonell, M. Poyatos, J. A. Mata and E. Peris, *Organometallics*, 2011, **30**, 5985–5990.
- 26 S. Gonell, M. Poyatos, J. A. Mata and E. Peris, *Organometallics*, 2012, **31**, 5606–5614.
- 27 Two interesting recent examples are: (a) M. M. Hansmann, A. S. K. Hashmi and M. Lautens, *Org. Lett.*, 2013, **15**, 3226–3229; (b) A. A. Friedman, J. Panteleev, J. Tsoung, V. Huynh and M. Lautens, *Angew. Chem., Int. Ed.*, 2013, **52**, 9755–9758.
- 28 (a) J. Zhou, *Chem.–Asian J.*, 2010, **5**, 422–434; (b) L. M. Ambrosini and T. H. Lambert, *ChemCatChem*, 2010, **2**, 1373–1380; (c) R. C. Wende and P. R. Schreiner, *Green Chem.*, 2012, **14**, 1821–1849.
- 29 S. Whitney, R. Grigg, A. Derrick and A. Keep, *Org. Lett.*, 2007, **9**, 3299–3302.
- 30 (a) M. G. Edwards, R. F. R. Jazzar, B. M. Paine, D. J. Shermer, M. K. Whittlesey, J. M. J. Williams and D. D. Edney, *Chem. Commun.*, 2004, 90–91; (b) M. Hamid, P. A. Slatford and J. M. J. Williams, *Adv. Synth. Catal.*, 2007, **349**, 1555–1575; (c) G. Guillena, D. J. Ramon and M. Yus, *Chem. Rev.*, 2010, **110**, 1611–1641; (d) G. Guillena, D. J. Ramon and M. Yus, *Angew. Chem., Int. Ed.*, 2007, **46**, 2358–2364.
- 31 S. Sabater, J. A. Mata and E. Peris, *Eur. J. Inorg. Chem.*, 2013, 4764–4769.
- 32 K. Fujita, K. Yamamoto and R. Yamaguchi, *Org. Lett.*, 2002, **4**, 2691–2694.
- 33 S. Bhuvanewari, M. Jeganmohan and C.-H. Cheng, *Chem.–Eur. J.*, 2007, **13**, 8285–8293.
- 34 (a) B. Alcaide, P. Almendros and A. Luna, *Chem. Rev.*, 2009, **109**, 3817–3858; (b) W. J. Sommer and M. Weck, *Coord. Chem. Rev.*, 2007, **251**, 860–873; (c) M. Pagliaro, S. Campestrini and R. Ciriminna, *Chem. Soc. Rev.*, 2005, **34**, 837–845; (d) B. M. Trost, F. D. Toste and

- A. B. Pinkerton, *Chem. Rev.*, 2001, **101**, 2067–2096; (e) V. Dragutan, I. Dragutan, L. Delaude and A. Demonceau, *Coord. Chem. Rev.*, 2007, **251**, 765–794; (f) V. Ritleng, C. Sirlin and M. Pfeffer, *Chem. Rev.*, 2002, **102**, 1731–1769.
- 35 (a) T. Braun and F. Wehmeier, *Eur. J. Inorg. Chem.*, 2011, 613–625; (b) K. Uneyama, *Organofluorine Chemistry* Blackwell, Oxford, 2006; (c) H. Torrens, *Coord. Chem. Rev.*, 2005, **249**, 1957–1985; (d) V. V. Grushin, *Acc. Chem. Res.*, 2010, **43**, 160–171; (e) H. Amii and K. Uneyama, *Chem. Rev.*, 2009, **109**, 2119–2183.
- 36 J. M. White and J. E. Bercaw, in *Basic Energy Sciences Advisory Committee*, ed. D. o. E. (DOE), 2002.