

# ChemComm

Accepted Manuscript



This is an *Accepted Manuscript*, which has been through the Royal Society of Chemistry peer review process and has been accepted for publication.

*Accepted Manuscripts* are published online shortly after acceptance, before technical editing, formatting and proof reading. Using this free service, authors can make their results available to the community, in citable form, before we publish the edited article. We will replace this *Accepted Manuscript* with the edited and formatted *Advance Article* as soon as it is available.

You can find more information about *Accepted Manuscripts* in the [Information for Authors](#).

Please note that technical editing may introduce minor changes to the text and/or graphics, which may alter content. The journal's standard [Terms & Conditions](#) and the [Ethical guidelines](#) still apply. In no event shall the Royal Society of Chemistry be held responsible for any errors or omissions in this *Accepted Manuscript* or any consequences arising from the use of any information it contains.

Cite this: DOI: 10.1039/c0xx00000x

www.rsc.org/xxxxxx

ARTICLE TYPE

# Organic Azides: “Energetic Reagents” for the *Intermolecular* Amination of C-H Bonds.

Daniela Intriери, Paolo Zardi, Alessandro Caselli and Emma Gallo\*

Received (in XXX, XXX) Xth XXXXXXXXXX 20XX, Accepted Xth XXXXXXXXXX 20XX

DOI: 10.1039/b000000x

This feature article provides an overview on the application of organic azides for the *intermolecular* amination of  $sp^3$  and  $sp^2$  C-H bonds. The catalytic activity of several metal complexes was reviewed underlining both synthetic and mechanistic aspects of the C-H amination. The majority of the aminated compounds reported in literature have been collected in this paper to provide a compendium of published procedures. In addition, the discussion of involved mechanisms has been included to assist the reader to envisage future potential of organic azides in the synthesis of aza-derivatives.

## 1. Introduction

Since the first preparation of organic azides ( $RN_3$ ) in 1864,<sup>1</sup> this class of molecules has been involved in an increasing number of applications over the last 15 years, as documented by SciFinder (Figure 1). Among all possible applications, organic azides are largely used as atom-efficient aminating agents due to the formation of eco-friendly molecular nitrogen as the only side product of the “NR” transfer reaction to an organic molecule.<sup>2,3</sup>

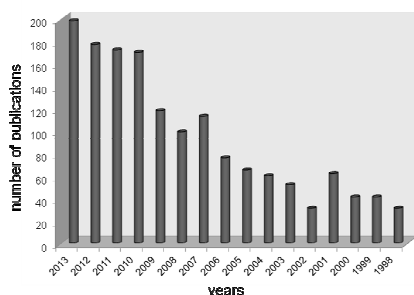


Figure 1. Manuscripts and patents on organic azides reported by SciFinder in the 1998-2013 period.

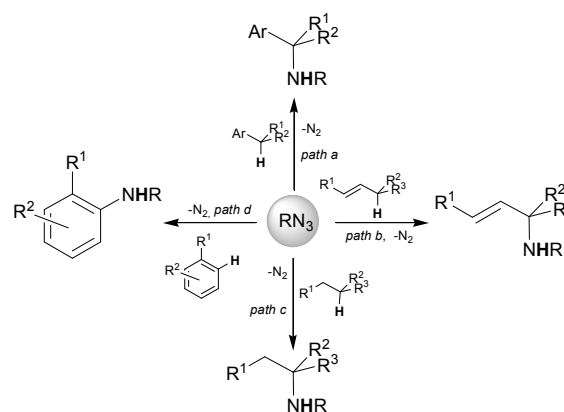
The insertion of a nitrene moiety into an organic framework is efficiently catalysed by transition metal complexes and allows the synthesis of aza-compounds which often display important biological and pharmaceutical characteristics.<sup>4</sup> As azides are active towards several classes of organic molecules, the amination reaction displays a great chemical versatility and it can be conducted using mild experimental conditions and no oxidant agent is required.

Considering the scientific interest to establish efficient

methodologies to synthesising nitrogen containing molecules, several reviews on the use of organic azides as nitrogen sources have been published<sup>5-11</sup> and great emphasis has been devoted to the amination of C-H bonds due to their ubiquity in almost all organic skeletons. Furthermore, the insertion of an aza-moiety into a hydrocarbon C-H bond allows the conversion of low cost reagents into high-added value aminated compounds.

This feature article provides an overview of the *intermolecular* C-H bond aminations by organic azides reported in Scheme 1, by underlining both synthetic and mechanistic aspects. The *intramolecular* amination was amply reviewed<sup>12-15</sup> and it is not covered in this article.

We sincerely apologise if some important contributions to this topic have been unintentionally omitted.



Scheme 1. *Intermolecular* C-H aminations by organic azides discussed in this manuscript.



Daniela Intriery was born in Italy in 1984, she obtained her master's degree in Chemistry in 2010 under the supervision of prof. Sergio Cenini at the Chemistry Department of the University of Milano (Italy). In 2014 she got her PhD in Chemical Science at the University of Milano under the supervision of prof. Emma Gallo. Her PhD thesis was on the synthesis of cobalt, ruthenium and iron porphyrins to be employed as homogeneous catalysts in C-C and C-N bond formation as well as on the study of reaction mechanisms.



Paolo Zardi was born in Italy in 1987, he received his master's degree in Chemical Sciences in 2011 with an experimental thesis concerning the heterogenisation of copper complexes to use as catalysts for asymmetric cyclopropanation under the supervision of Dr. Caselli in the Chemistry Department of the University of Milan. Currently he is a PhD Student at Milan University in prof. Emma Gallo's group and his research is focused on the synthesis of ruthenium-porphyrin complexes and their employment as catalysts in C-N bond formation reactions.



Alessandro Caselli received his PhD under the supervision of prof. Carlo Floriani at the University of Lausanne (CH) in 2000. He spent two years as post-doc at the University of Milano (Italy) under the supervision of prof. Fulvia Orsini before joining prof. Sergio Cenini's group. In 2003, he became assistant professor at the Chemistry Department of Milano University. His research has focused on: i) the employment of metal complexes with macrocyclic N-donor ligands as homogeneous catalysts; ii) the synthesis of asymmetric ligands; iii) the mechanistic aspects of catalytic reactions and iv) the heterogenisation of chiral catalysts.

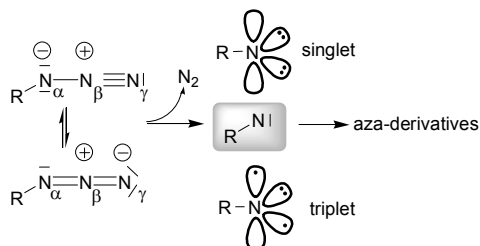


Emma Gallo received her PhD under prof. Carlo Floriani's guidance at the University of Lausanne (CH) in 1995. She spent one year in Floriani's Group as "Maitre assistant" before moving to Italy. After post-doctoral training alongside prof. Sergio Cenini at the Chemistry Department of University of Milano (Italy), she became assistant professor and then associate professor at the same university. Her research is mainly devoted to the synthesis of fine chemicals by C-C or C-N bond formation, using metal porphyrin complexes as catalysts, as well as the study of catalytic reaction mechanisms.

## 2. Amination of activated $sp^3$ C-H bonds

The insertion of a nitrene functionality into an activated C-H bond was initially studied by taking advantage of the thermal and photochemical instability of organic azides. Reactions were conducted without the assistance of a transition metal complex and consequentially drastic experimental conditions were required.<sup>16-19</sup>

Later, a transition metal was employed to promote the cleavage of the  $N_\alpha-N_\beta$  bond (scheme 2) and selectively insert the nitrene functionality into a specific position of the organic backbone.



Scheme 2. Nitrene formation by the cleavage of an azide  $N_\alpha-N_\beta$  bond.

In 1967 Kwart and Khan<sup>20</sup> reported on the catalytic activity of copper powder in the amination of cyclohexene and since then several transition metal catalysts have been developed to promote the amination of activated  $sp^3$  C-H bonds. The most representative classes of catalysts are reported in figure 2.

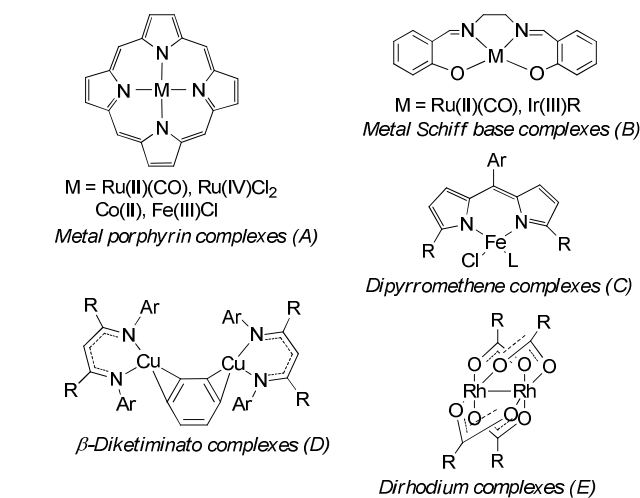


Figure 2. Catalysts for the amination of activated  $sp^3$  C-H bonds.

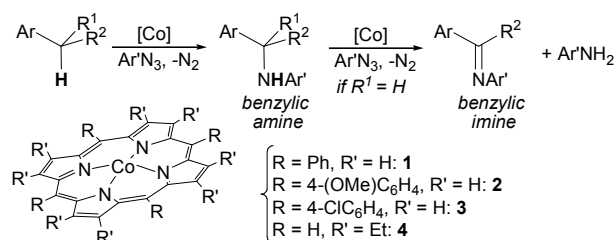
### 2.1. Amination catalysed by metal porphyrin complexes (A).

#### 2.1.1. Synthetic results.

Among all the classes of catalysts reported in figure 2, metal porphyrin complexes (A) are widely used to promote the amination of both benzylic and allylic substrates by organic azides (scheme 1, paths a and b respectively).

Cenini *et al.* reported in 2000 that cobalt(II) porphyrin complexes are active catalysts to promote the amination of both allylic and benzylic C-H bonds by using aryl azides as nitrene sources.<sup>21-24</sup> Aryl azides were chosen due to their stability/reactivity relationship that allows their use without any particular experimental cautions.<sup>25</sup> The benzylic amines were obtained together with the corresponding imines when the initially formed amine can be further oxidised by another  $ArN_3$ .

molecule. The stoichiometric by-product of this second step is the primary amine of the azide employed (scheme 3).



Scheme 3. Synthesis of benzylic amines and imines catalysed by Co(II) porphyrin complexes.

The scope of the reaction was investigated and the obtained products are reported in chart 1.<sup>22</sup>

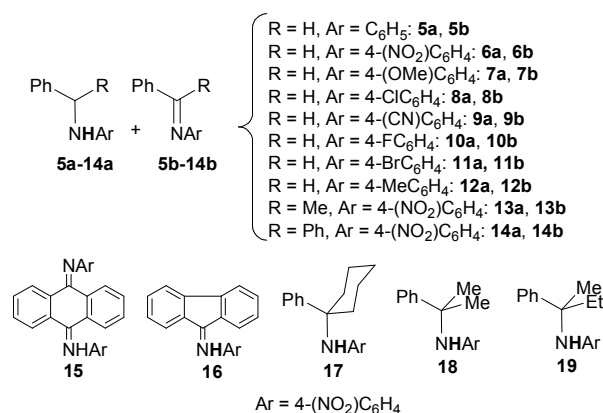


Chart 1. Amination of benzylic substrates by aryl azides catalysed by Co(II)(porphyrins) leading to benzylic amines and imines.

The reaction works well with azides bearing EWG on the aryl moiety indicating an electrophilic role of  $\text{ArN}_3$  in the catalysis.

The cobalt(II) porphyrin-catalysed amination of benzylic substrates was then performed by Zhang<sup>26</sup> by using 2,2,2-trichloroethoxycarbonyl azide ( $\text{TrocN}_3$ ) as the nitrene source. The benzylic amines reported in chart 2 were obtained without the contemporary formation of the corresponding imines.  $\text{TrocN}_3$  was demonstrated to be a better aminating agent than other azides such as sulfonyl, phosphoryl, and carbonyl azides confirming the electrophilic nature of azides in the catalytic process. It must be mentioned that the synthesis of the compound **24** which, even though it was obtained in a low yield, it represents a synthesis of an  $\alpha$ -amino ester by the direct amination of the corresponding carboxylic ester.

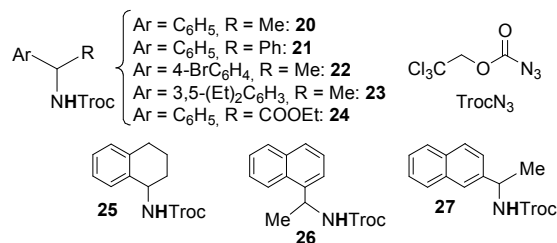
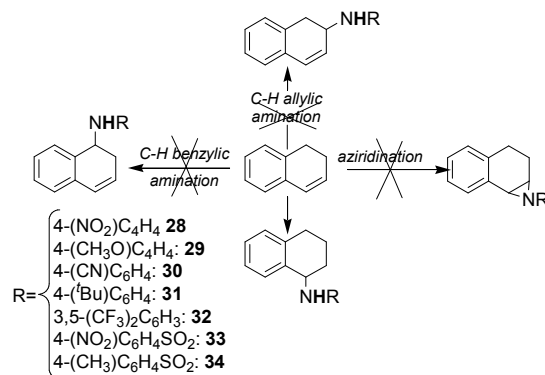


Chart 2. Amination of benzylic substrates by  $\text{TrocN}_3$  catalysed by Co(II)(porphyrin) complexes leading to benzylic amines.

Cobalt porphyrin complexes were also effective to aminate allylic C-H bonds (scheme 1, *path b*) in moderate yields. It should be noted that the double C=C bond of endocyclic olefins, such as cyclohexene, did not react with the aryl azide to give the corresponding aziridine therefore indicating a good chemoselectivity towards the allylic amine formation.<sup>24</sup>

Surprisingly, the allylic amination of dihydronaphthalene afforded the benzylic amine of tetrahydronaphthalene, instead of yielding the amine of dihydronaphthalene and neither the aziridination nor the benzylic amination of dihydronaphthalene were observed (scheme 4) (see below for a mechanistic proposal of this reaction).



Scheme 4. Reaction of dihydronaphthalene with aromatic and sulfonyl azides catalysed by cobalt(II) porphyrins.

All data discussed up to now were collected employing achiral cobalt catalysts. Until very recently, to the best of our knowledge, only the chiral complex **35** (figure 3) was reported in literature for the *intermolecular* amination of C-H bonds in spite of the potential application of chiral amines as pharmaceuticals. Although the *intermolecular* aziridination reaction of styrenic double bonds performed in the presence of **35** occurred with some enantioselectivity, the allylic amination of cyclohexene afforded the racemate product, probably due to the presence of an atropisomer mixture of the catalyst at the working temperature.<sup>23</sup>

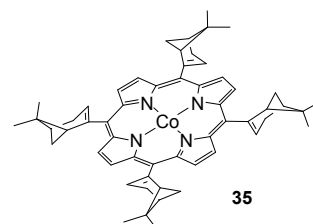


Figure 3. Structure of Co(II)(TmyrtP) (**35**) (TmyrtP = dianion of the meso-tetrakis[(1*R*)-apopin-2-yl]porphyrin).

Better synthetic results have been obtained by using ruthenium porphyrin complexes as catalytic species which are active in the amination of both benzylic and allylic C-H bonds.<sup>27-29</sup> The commercially available Ru(II)(TPP)CO (TPP = dianion of tetraphenyl porphyrin) was a good catalyst to synthesise compounds **6a**, **13a**, **14a**, **18** (chart 1), **28**, **32** (scheme 4) and those reported in chart 3. The best catalytic results were obtained by using aryl azides bearing EWG substituents on the aryl moiety and a high hydrocarbon excess.

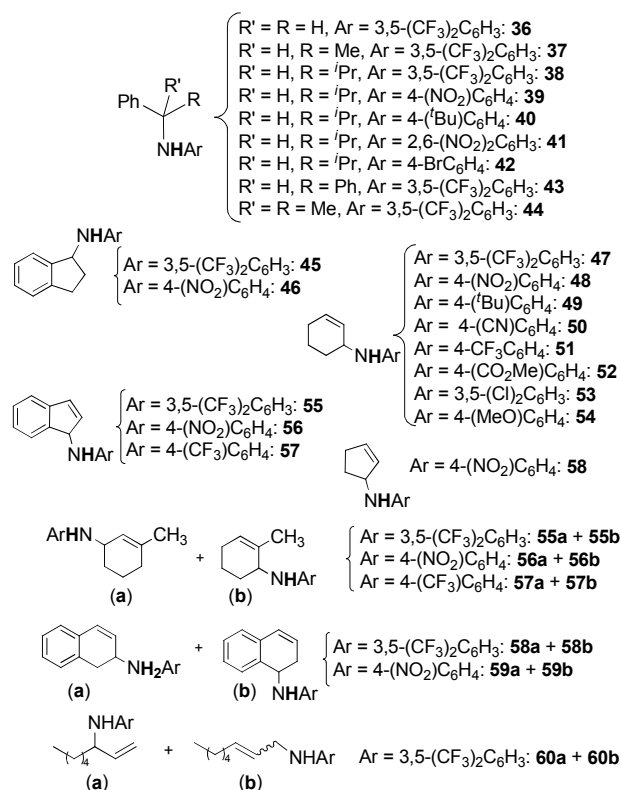
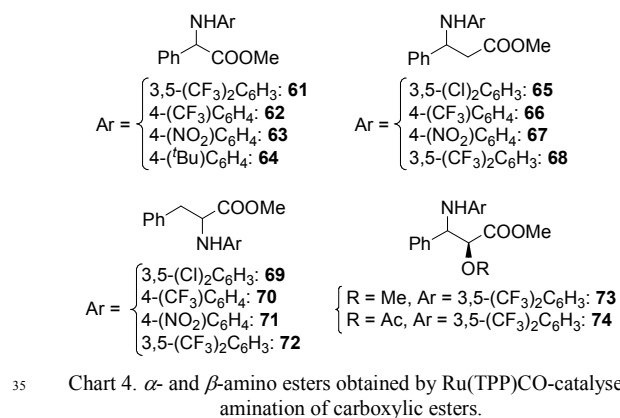


Chart 3. Benzylic and allylic amines obtained by Ru(II)(TPP)CO-catalysed amination.

While we were writing this review, Che and Lo reported the enhanced catalytic activity of *bis*(NHC)ruthenium(II) porphyrin complexes in nitrene insertion reactions into saturated C-H bonds (NHC = *N*-heterocyclic carbene ligands).<sup>30</sup> Among the [Ru(porphyrin)(NHC)<sub>2</sub>] complexes tested, [Ru(4-F-TPP)(BIME)<sub>2</sub>] (BIME = 1,3-di-methyl-2,3-dihydro-1*H*-benzimidazol-2-ylidene) showed the highest activity and allowed the smooth insertion reaction of pentafluorophenyl azide into allylic (cyclohexene) and benzylic (toluene, ethyl benzene, 4-methoxy-ethyl benzene, 1-ethyl naphthalene, 1,2,3,4-tetrahydronaphthalene, and 2,3-dihydro-1*H*-indene) sp<sup>3</sup> C-H bonds affording the corresponding amines in 88-96% isolated yields. The nitrene insertion reaction proceeded well also with the unactivated C-H bond of cyclohexane (90%). The authors proposed that the high catalytic activity is due to the strong donor strength of the axial NHC ligand in stabilising the *trans* M=NR moiety.

The use of chiral [Ru(*D*<sub>4</sub>-Por)(BIME)<sub>2</sub>] (*D*<sub>4</sub> refers to the symmetry of the ligand) as the catalyst led to the formation of the allylic amine **13a** (Ar = C<sub>6</sub>F<sub>5</sub>) in 91% yield and with 70% *ee*.<sup>30</sup>

Ru(porphyrin)CO complexes were also effective in synthesising  $\alpha$ - and  $\beta$ -amino esters by amination of benzylic C-H bonds placed in  $\alpha$  or  $\beta$  position to an ester group. This synthesis, already explored by Zhang in the presence of cobalt porphyrins,<sup>26</sup> occurred with yields up to 80% in the presence of ruthenium analogous, in spite of poor reactivity of electron deficient benzylic positions toward electrophilic metallonitrene intermediates. The catalytic procedure is also effective in synthesising the two derivatives of methyl L-3-phenyllactate **73** and **74** in order to convert them into the corresponding  $\beta$ -lactam (chart 4).<sup>31</sup>



Very recently, Che *et al.*<sup>32</sup> demonstrated that the amination of benzylic and allylic substrates (chart 4) by phosphoryl azides is also efficiently catalysed by ruthenium(IV) complexes. Among 40 tested catalysts, Ru(F<sub>20</sub>-TPP)Cl<sub>2</sub> performed the best.

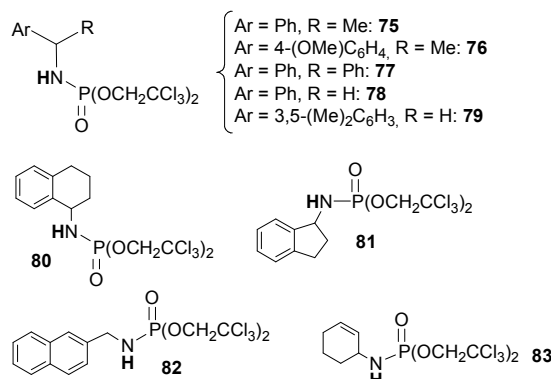


Chart 5. Benzylic and allylic amines obtained by Ru(IV)(F<sub>20</sub>-TPP)Cl<sub>2</sub>-catalysed amination.

A significant contribution to this topic was provided by Che *et al.* with the investigation of the catalytic activity of Fe(III)(F<sub>20</sub>-TPP)Cl. What makes this study important is the high sustainability of iron catalysts which are affordable, biocompatible and very reactive. Compounds **13a**, **14a**, (chart 1) **28** (scheme 4) and those reported in chart 6 were isolated in good yields.

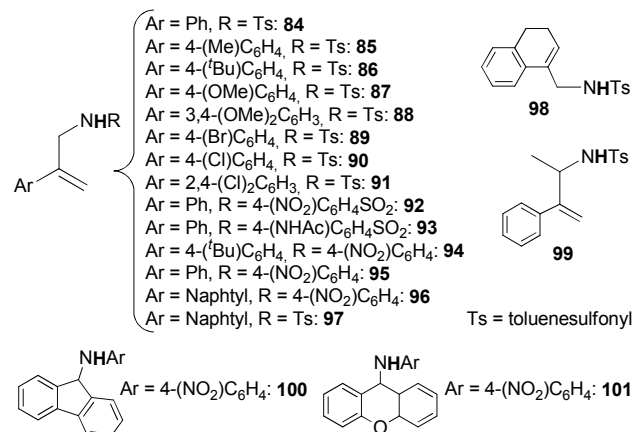


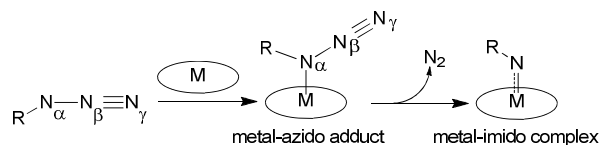
Chart 6. Benzylic and allylic amines obtained by Fe(III)(F<sub>20</sub>-TPP)Cl-catalysed amination.

The reported methodology displayed a very good chemoselectivity, in fact the allylic amination of  $\alpha$ -methyl styrene derivatives occurred without the simultaneous formation of corresponding aziridines.

### 2.1.2. Mechanistic Investigation.

Over the last decade, the development of synthetic strategies together with the investigation of reaction mechanisms have been constantly researched to fine-tune catalytic efficiencies.

It is generally assumed that the active intermediate of the metal porphyrin-catalysed nitrene transfer reaction is an imido complex which is formed after the cleavage of the  $N_\alpha$ - $N_\beta$  azide bond (scheme 5).

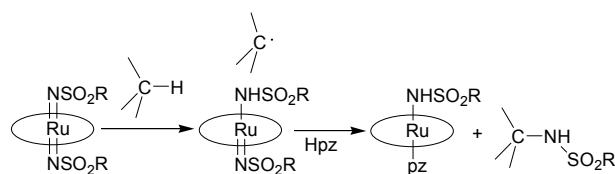


Scheme 5. Metal-imido complex formation.

The oxidation state of the metal in the imido complex depends on the oxidation state of the starting catalyst and it is crucial to define the reactivity of the imido intermediate towards the organic substrate.

When the amination reaction is catalysed by ruthenium(II) porphyrins the formation of a *bis*-imido ruthenium(VI) complex was generally proposed. Some years ago several ruthenium(VI) *bis*-imido complexes, of the general formula  $Ru(VI)(porphyrin)(NSO_2R)_2$ , were prepared by Che *et al.* by reacting ruthenium(II) precursors with imino iodine compounds ( $PhI=NSO_2R$ ). All the complexes were fully characterised and the molecular structure of  $Ru(TMP)(NMs)_2$  (**102**) ( $Ms = 4-(MeO)C_6H_4SO_2$ ;  $TMP =$  dianion of 5,10,15,20 tetramesityl porphyrin) was solved by x-ray single crystal diffraction.

$Ru(VI)(porphyrin)(NSO_2R)_2$  complexes were active in the stoichiometric nitrene transfer reaction to C-H bonds in the presence of pyrazole (Hpz) as an additional axial ligand. The suggested mechanism is depicted in scheme 6.



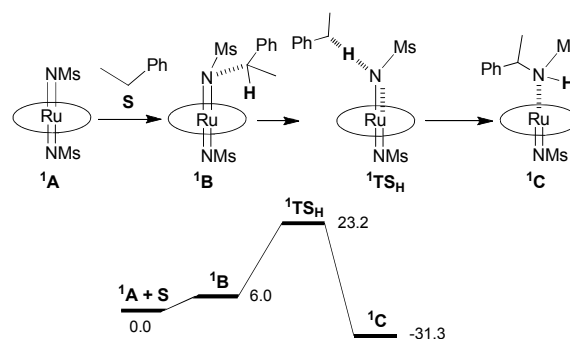
Scheme 6. Suggested mechanism for the stoichiometric transfer of a nitrene moiety from a *bis*-imido ruthenium(VI) porphyrin to a C-H bond.

The authors proposed that a C-H cleavage is involved in the rate determining step of the reaction on the basis of the large isotopic effect registered for the amination of several substrates. In fact, the formation of a carbonyl radical species by a homolytic cleavage of the C-H bond is in accord with the observed  $k_H/k_D$  values of 6.1-12. Considering that the hydrogen atom of pyrazole is necessary for releasing the amine molecule, Hpz was always used in a stoichiometric excess with respect to the hydrocarbon substrate.

The reaction mechanism illustrated in scheme 6 was also studied by Density Functional Theory (DFT) calculations.

Firstly, the molecular structure of **102** was optimised by DFT and achieved data fitted with those collected by single crystal x-ray diffraction. Then, employed functionals indicated a singlet  $d^2$  ground state electronic configuration ( $^1A$ ) for  $Ru(TMP)(NMs)_2$  (**102**) that was found at a lower energy than the analogous triplet state. The energy profile of the ethyl benzene amination by **102** indicated that the singlet pathway is the most energetically favoured.

In scheme 7 the proposed mechanism of the stoichiometric nitrene transfer from **102** to ethyl benzene is provided together with the relative potential energy surface. The last step of the mechanism illustrated in scheme 6, that corresponds to the release of the amine and pyrazole coordination, has not been supplied.



Scheme 7. Mechanism of the ethyl benzene amination and relative potential energy surface ( $\Delta G$  in  $kcal\ mol^{-1}$ ) based on DFT calculations.

Another class of *bis*-imido ruthenium(VI) complexes have been synthesised by Gallo *et al.* reacting ruthenium(II) porphyrins with an aryl azide excess. The complex  $Ru(PPP)(NAr)_2$  ( $Ar = 3,5-(CF_3)_2C_6H_3$ ) (**103**) was fully characterised and its molecular structure was determined by x-ray single crystal diffraction.

Complexes **102** and **103** (figure 4) have similar  $Ru=N$  distances (1.79(3) Å vs 1.808(4) Å) in the range of double bonds but the two imido complexes differ for the  $Ru-N-X$  ( $X = S$  for **102** and  $X = C$  for **103**) imido angles. The angle of  $162.5(3)^\circ$  of **102** indicates almost a linearity of the imido moiety whilst the values of  $139.8(3)^\circ$  and  $143.7(4)^\circ$  for  $Ru-N_1-C$  and  $Ru-N_2-C$  respectively, of **103** indicate the existence of bent imido angles.

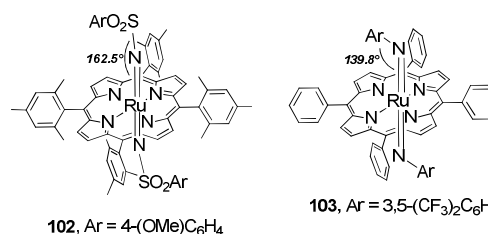
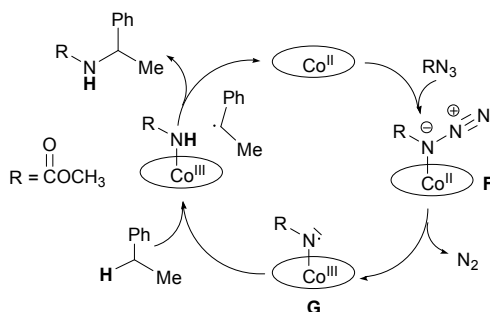


Figure 4. Structures of ruthenium (VI) imido complexes **102** and **103**.

Complex **103** displayed a good stability/reactivity relationship; it was stable for days in a solid state and decomposed when left standing in solution for a few hours. The *bis*-imido ruthenium(VI) complex **103** was active not only in stoichiometric nitrene transfer reaction from **103** to a C-H bond but was also an efficient catalyst of C-H aminations. This last feature was essential to propose **103** as a possible key intermediate of the  $Ru(PPP)CO$ -catalysed amination reactions.



azidoformate, a model of TrocN<sub>3</sub>, and ethyl benzene was then performed and it also supported the formation of **G** as the catalytic active species. The mechanistic proposal and relative energy profiles are shown in scheme 10 and figure 6.



Scheme 10. Proposed mechanism of the Co(porphyrin)-catalysed amination of ethyl benzene by methyl azidoformate.

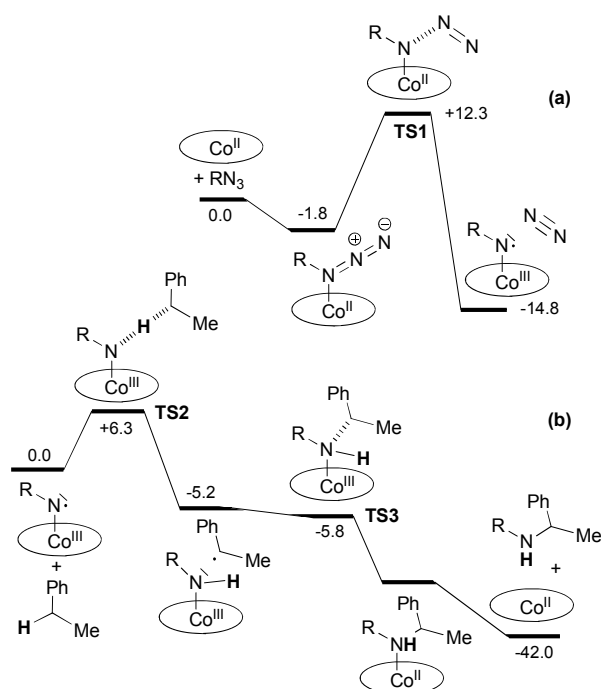
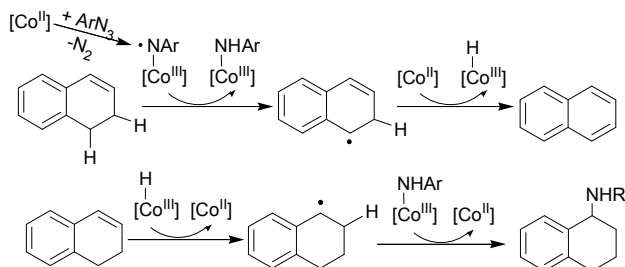


Figure 6. Reaction profile ( $\Delta H$  in kcal mol<sup>-1</sup>) for the formation of (a) the nitrene radical species and (b) the benzylic amine.

The formation of a cobalt(III) nitrene radical intermediate can also be evocated to understand the unusual formation of the amine of tetrahydronaphthalene from the reaction of dihydronaphthalene with an aryl azide (scheme 11).<sup>39</sup>

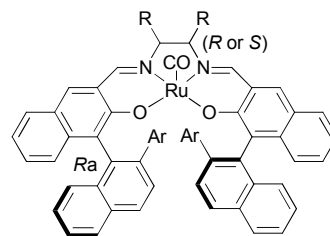


Scheme 11. Reaction between tetrahydronaphthalene and ArN<sub>3</sub>.

A mechanistic study on the iron(III) porphyrin-catalysed C-H amination has not been reported yet. It was suggested by Che *et al.* that the starting iron(III) complex can be reduced *in situ* to an iron(II) nitrene intermediate which evolves into the active iron(IV) imido derivatives.<sup>32</sup> The latter is then responsible for the nitrene transfer reaction to the organic substrate.

## 2.2. Amination catalysed by metal Schiff base complexes (B).

Schiff base complexes are very active in *intramolecular* C-H amination and aziridination of olefins by organic azides<sup>5</sup> but, to the best of our knowledge only two papers by Katsuki *et al.* were published on the *intermolecular* amination of allylic and benzylic C-H bonds. The ruthenium(II) chiral catalysts employed (figure 7) promoted the enantioselective nitrene transfer from TsN<sub>3</sub><sup>40</sup> and SESN<sub>3</sub> (SES = 2-(trimethylsilyl)ethanesulfonyl)<sup>41</sup> to several hydrocarbons.



(*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = Ph: **104**  
 (*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 3,5-(F)<sub>2</sub>-4-(Me)C<sub>6</sub>H<sub>2</sub>: **105**  
 (*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 3,5-(Cl)<sub>2</sub>-4-(TMS)C<sub>6</sub>H<sub>2</sub>: **106**  
 (*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 3,5-(Cl)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>: **107**  
 (*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 3,5-(F)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>: **108**  
 (*Ra,R*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 2,6-(F)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>: **109**  
 (*Ra,S*), R = -(CH<sub>2</sub>)<sub>4</sub>, Ar = 2,6-(F)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>: **110**  
 (*Ra,R*), R = Ph, Ar = 2,6-(F)<sub>2</sub>C<sub>6</sub>H<sub>3</sub>: **111**

Figure 7. Ruthenium(II) Schiff base catalysts employed in the *intermolecular* amination of C-H bonds.

Among all the complexes reported in figure 7, complexes **104** and **109** showed better catalytic efficiency by using TsN<sub>3</sub> and SESN<sub>3</sub> respectively. All the obtained aminated compounds are shown in chart 7.

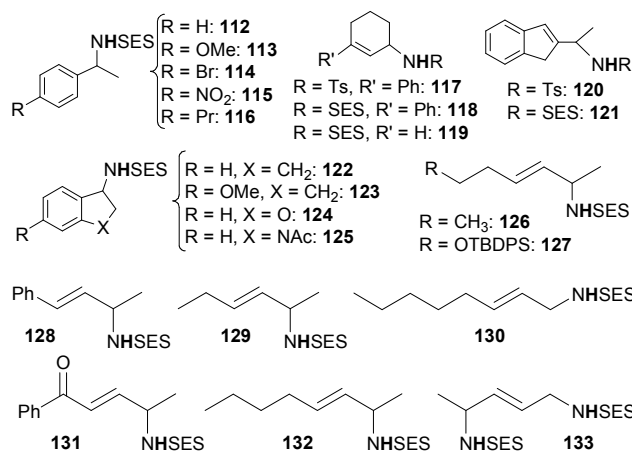


Chart 7. Benzylic and allylic amines obtained by **104** and **109**-catalysed amination (TBDDPS = *tert*-butyldiphenyl silyl).

The best catalytic results have been achieved by using SESN<sub>3</sub> as nitrene source and **109** as the catalyst. Yields and



enantioselectivities up to 99% and 99% *ee* respectively were obtained. It is worth noting that also the regioselectivity of the amination reaction was extremely high and that this data represents the best results in term of enantioselective C-H amination by organic azides.

Iridium(III) Schiff base complexes were also tested as catalysts in the amination of indane using  $\text{SESN}_3$  as the aminating agent; unfortunately the reaction occurred in low yields and modest enantioselectivities.<sup>41</sup>

### 2.3. Amination catalysed by dipyrromethene complexes (C).

#### 2.3.1. Synthetic Results

Iron(II) dipyrromethene complexes reported in figure 8 was recently synthesised and tested as C-H amination catalysts by Betler *et al.*<sup>42,43</sup> All the complexes **134-138** were fully characterised and, in some cases, the x-ray molecular structure determination was also provided. The oxidation state of iron atoms was assigned by magnetic measurements being consistent with high spin ( $S = 2$ ) Fe(II) metal centres.

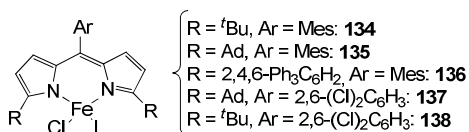


Figure 8. Iron(II) dipyrromethene catalysts employed in the intermolecular amination of C-H bonds (Mes = mesityl, Ad = adamantyl).

Initially, toluene was reacted with adamantyl azide ( $\text{AdN}_3$ ) in the presence of complex **135** as the catalyst to yield the corresponding benzylic amine.<sup>42</sup> Then, in order to enlarge the reaction scope, other substrates were aminated in the presence of iron catalysts (figure 8).<sup>43</sup> Complexes **137** and **138** showed the best catalytic efficiency to synthesize benzylic (**139-143**) and allylic (**144-148**) amines respectively (chart 8).

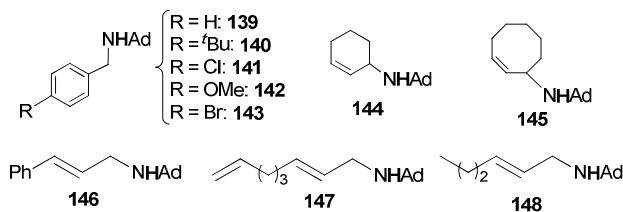
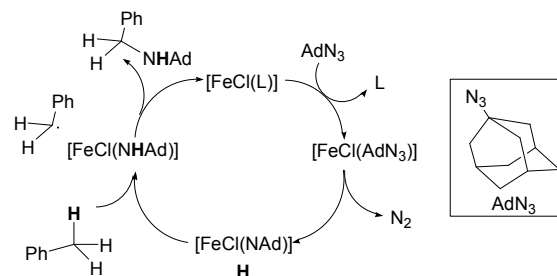


Chart 8. Benzylic and allylic amines synthesised by **137** and **138** catalysed amination.

#### 2.3.2. Mechanistic Investigation

In order to study the catalytic mechanism, the amination of toluene by adamantyl azide, as a model reaction, was investigated in the presence of **135**.

When the reaction was run in an equimolar toluene/toluene- $d_8$  mixture, an isotope effect  $k_{\text{H}}/k_{\text{D}}$  of 12.8 was observed indicating that the C-H bond cleavage was involved in the rate determining step of the cycle (scheme 12).



Scheme 12. Proposed mechanism for the **135**-catalysed toluene amination by  $\text{AdN}_3$ .

Authors suggested the formation of imido complex **H** which is responsible for a hydrogen atom abstraction from toluene substrate after which a radical rebound process finally yields the desired benzylic amine.

The formation of type **H** complex was supported by the isolation of terminal imido complex **149** from the stoichiometric reaction of  $p\text{-}^t\text{BuC}_6\text{H}_4\text{N}_3$  with **136** (figure 9).

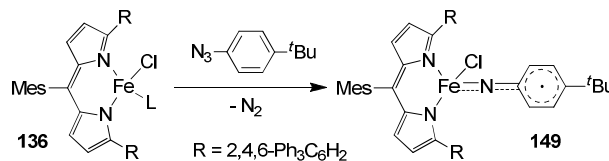


Figure 9. Synthesis of **149**.

The x-ray analysis of **149** disclosed the formation of a terminal iron-imido bond with a limited multiple-bond character.

This structural feature together with theoretical and magnetic data indicated the formation of a high-spin  $\text{Fe}^{\text{III}}$  ( $d^5$ ,  $S = 5/2$ ) centre antiferromagnetically coupled with an imido-based radical ( $S = 1/2$ ). The resulting complex can be indicated as a high-spin ( $S = 2$ ) iron(III) imido radical species.

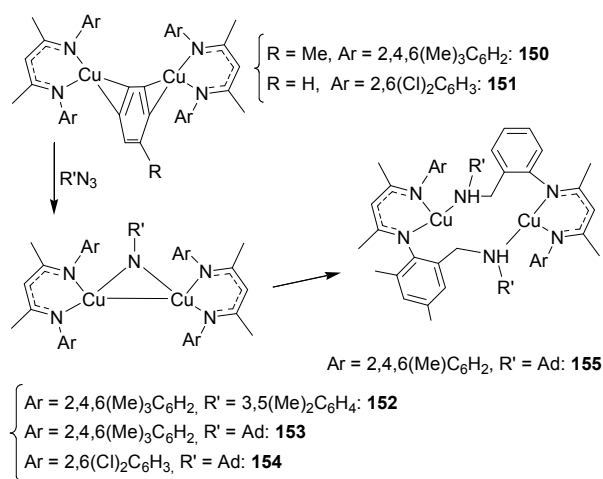
It is noteworthy that complex **149** was able to deliver the nitrene moiety to C-H bonds to support its probable involvement in the catalytic cycle.

### 2.4. Amination catalysed by $\beta$ -diketiminato complexes (D).

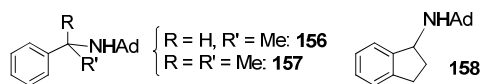
#### 2.4.1. Synthetic Results

$\beta$ -Diketiminato copper(I) complexes **150** and **151** were employed by Cundari *et al.* as precursors of imido derivatives **152-154** shown in scheme 13.<sup>44,45</sup> All these complexes were obtained by the reaction of **150** or **151** with an organic azide and also were completely characterised by x-ray diffraction analysis.

When the synthesis of **153** was conducted at room temperature for a long time, the intramolecular insertion of an adamantyl nitrene functionality into a C-H bond of one  $\beta$ -diketiminato *ortho*-methyl group of **153** was observed yielding complex **155** (scheme 13). This reaction demonstrated the capacity of this class of complexes to insert a nitrene functionality into a C-H bond.

Scheme 13. Synthesis of imido complexes **152-154**.

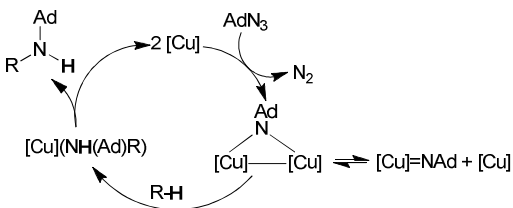
In order to avoid the *intramolecular* side reaction and to promote *intermolecular* aminations, complex **151**, that presents two chlorine atoms on the aryl *ortho* positions, was used as the starting material for the synthesis of imido complex **154**. The *intramolecular* amination of the copper complex was not observed and **151** was a competent catalyst for the *intermolecular* amination of benzylic substrates. Compound **139** (chart 8) together with compounds **156-158**, reported in chart 9, were obtained in good yields.

Chart 9. Benzylic amines synthesised by **152** catalysed amination.

#### 2.4.2. Mechanistic Investigation

Imido complexes ( $\beta$ -diketiminato)Cu(NR) were studied from a computational perspective by using several methods<sup>46</sup> providing a potentially controversial scenario. In fact, a DFT study revealed a triplet ( $S = 1$ ) ground state, but CASSCF (Complete Active Space Self-Consistent-Field) calculations indicated that also the singlet state ( $S = 0$ ) is energetically accessible and potentially active. The two species differ because the singlet copper nitrene has bent geometry, whereas triplet copper nitrene is linear.

The kinetic isotope effect  $k_H/k_D = 5.3$ , registered in the amination of ethyl benzene catalysed by **151**, suggested that nitrene C-H insertion may be rate limiting of the catalysis. The mechanism reported in scheme 14 was proposed.

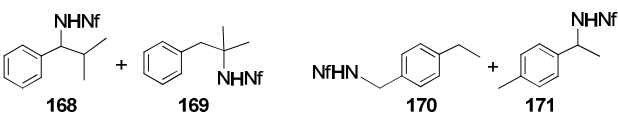
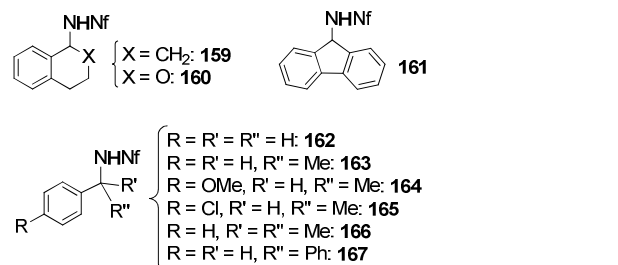
Scheme 14. Suggested mechanism for a C-H amination catalysed by  $\beta$ -diketiminato copper(I) complexes.

#### 2.5. Amination catalysed by dirhodium complexes (E)

As supported by all data discussed up to now, best synthetic results were obtained by employing azides bearing EWG

irrespective the catalyst used. The positive effect of electrophilic azides has been recently underlined by the efficiency of nonafluorobutanesulfonyl azide ( $N_3SO_2(CF_2)_3CF_3$ , NfN<sub>3</sub>) which aminated benzylic substrates in the presence of  $Rh_2(OAc)_4$ .<sup>47</sup> No amination reaction occurred in the absence of the transition metal complex.

The scope of the reaction was explored and the obtained aza-derivatives are reported in chart 10.

Chart 10. Aza-compounds obtained by  $Rh_2(OAc)_4$ -catalysed reaction.

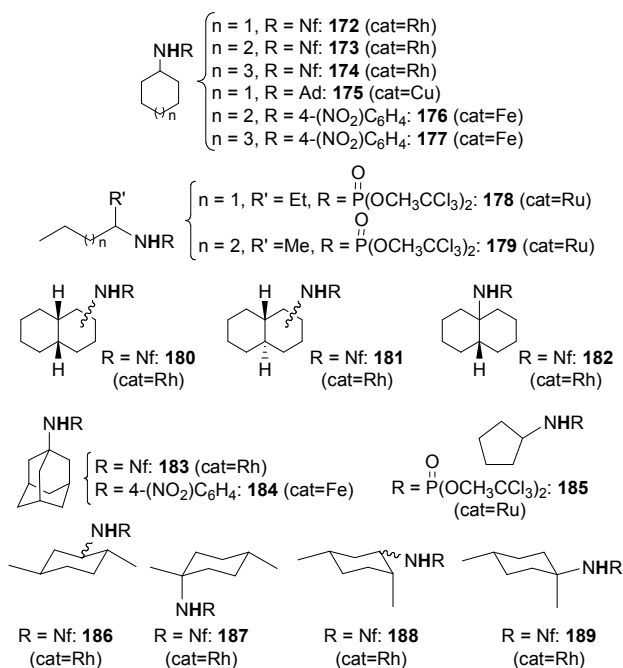
The practical importance of this reaction is also due to the chemical versatility of polyfluoroalkanesulfonamides. The reported methodology can be used for the synthesis of a variety of secondary amines by a stepwise procedure. The *N*-alkylation reaction affords *N,N*-disubstituted nonafluorobutanesulfonamides which can then be transformed into the corresponding *N*-alkylated amines.

#### 3. Amination of unactivated $sp^3$ C-H bonds

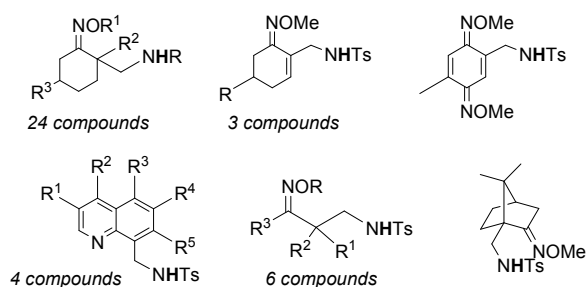
Some of the catalysts mentioned up to now were also active to promote the amination of compounds containing unactivated  $sp^3$  C-H bonds such as alkanes (scheme 1, *path c*). These reactions confirm the high reactivity of some metallo-imido complexes or metallo-azido adducts (scheme 5) in transferring the nitrene functionality into C-H bonds with high dissociation energy. Moreover, the amination of alkanes by organic azides constitutes a cost-effective strategy to obtain, in one pot, nitrogen containing molecules.

The syntheses of aza-derivatives shown in chart 11 were performed in the presence of  $Rh_2(OAc)_4$ ,<sup>47</sup> Cu(I) complex **151**,<sup>45</sup>  $Fe(III)(F_{20}-TPP)Cl_2$ <sup>32</sup> or  $Ru(IV)(F_{20}-TPP)Cl_2$ <sup>29</sup> as the catalyst.

It is difficult to compare the catalytic productivity of the different methodologies exploited for synthesising products of chart 11 due to the diversity of employed experimental conditions. Generally speaking, to insert a nitrene functionality into a strong C-H bond of alkanes it is necessary to employ an azide which displays a strong electrophilic character. However, in the presence of the copper catalyst **151** (scheme 13), also an alkyl azide such as adamantyl azide was reactive enough to aminate a cyclic alkane (chart 11, product **175**).



- Very recently, Chang *et al.* reported on the catalytic activity of  $[Ir(Cp^*Cl_2)_2]$ <sup>48</sup> in the amination of ketoxime derivatives. The catalysis occurred in the presence of silver salt  $AgX$  which is necessary to form a cationic iridium complex as the catalytically active species (see paragraph 4.1.2. for the proposed mechanism).
- The reaction productivity was enhanced by adding acetate as an additive. The catalytic system  $[Ir(Cp^*Cl_2)_2]/AgNTf_2/AgOAc$  (Tf = triflate) was active to promote the formation of the large class of compounds reported in chart 12.



- The procedure reported above was also effective for *late-stage* C–H functionalisation of natural molecules with potential biological activities.

## 4. Amination of $sp^2$ C–H bonds

### 4.1. Amination of aromatic $sp^2$ C–H bonds.

- The amination of aromatic  $sp^2$  C–H bonds has been amply studied for more than ten years<sup>49-56</sup> but only recently organic azides have been considered direct aminating agents. The latter procedure allows the amination to proceed without the formation of waste

products except for  $N_2$  (scheme 1, *path d*). The presence of a directing group (DG) is always required (scheme 15).



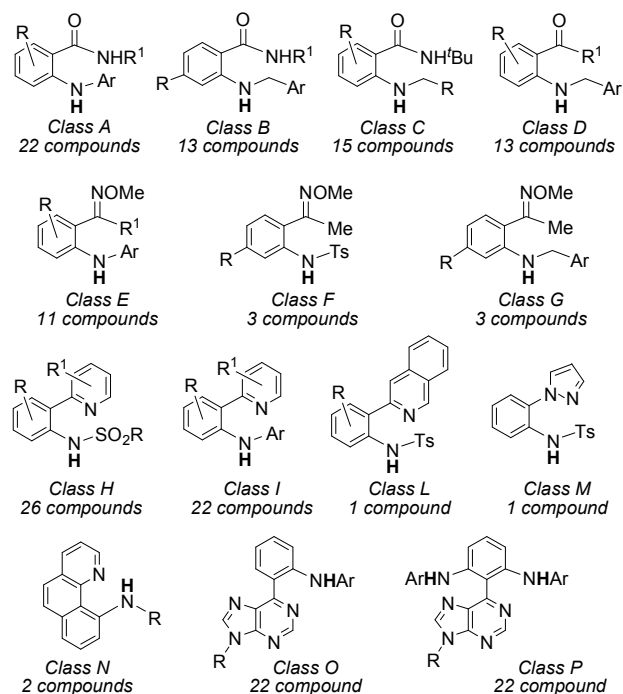
Scheme 15. General scheme for the aryl amination by  $RN_3$ .

- The catalysts employed to drive the reaction have a standard formula  $[M(L)Cl_2]_2$  where  $M = Rh(III)$ ,<sup>57-63</sup>  $Ru(II)$ <sup>63-65</sup> and  $Ir(III)$ .<sup>66,67</sup> These catalysts were always employed in the presence of silver salt  $AgX$  which is able to generate the catalytic active cationic species  $[M(L)]X_2$  from the neutral precursors (see below for mechanistic studies).

#### 4.1.1. Synthetic Results

- The direct aromatic amination by organic azides was disclosed by Chang *et al.* in 2012<sup>57</sup> and since then many efforts have been made by the same research group to investigate in depth the reaction scope. Initial studies were performed in the presence of rhodium(III) complexes and  $[RhCp^*Cl_2]_2$  was active in a very large pool of reactions in the presence of an excess of  $AgSbF_6$  as the silver salt. Several aryl skeletons, azides and directing groups were tested and a massive number of aza-derivatives was obtained.

- In order to give the reader an overview of the synthetic potentiality of  $[RhCp^*Cl_2]_2$ -based catalysis, several classes of aminated compounds are summarised in chart 13. The chemical nature of all the substituents is not provided due to space constraints.



- Classes A, B and C have been obtained by reacting benzamide derivatives with aryl,<sup>57</sup> benzyl<sup>60</sup> and alkyl azides.<sup>60</sup> Even if the reactivity of alkyl azides is generally modest in  $sp^3$  C–H aminations, all of these three classes of azides afforded high

yields of desired compounds. The catalytic system also works well in the amination of aromatic ketones with satisfactory yields (class D).<sup>60</sup>

In view of positive synthetic results, Chang *et al.* turned their attention to the amination of aryl ketoximes and data indicated that also the NOMe group is very active as well to correctly drive the C-H amination (classes E, F and G).<sup>57,60</sup>

A large number of aza-derivatives was synthesised by using *N*-heterocyclic compounds as directing group (DG) (classes H-N)<sup>58,59</sup> and the best results were achieved by using azides bearing electron withdrawing groups (EWG). Interestingly, when purine was present on the aryl moiety as the DG,<sup>62</sup> it was possible to isolate the mono and *bis*-aminated compounds depending on the experimental conditions employed (classes O and P).

Compounds belonging to classes A, D, H, M and F (chart 13) were also obtained by using [RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub>-based catalytic system. In 2013 two manuscripts by Chang *et al.*<sup>64</sup> and Jiao *et al.*<sup>65</sup> contemporarily appeared on this topic reporting almost identical results. The only difference between the two papers is the silver salt employed; AgNTf<sub>2</sub> (Tf = triflate) was used by Chang *et al.* while Jiao *et al.* used AgSbF<sub>6</sub>. In both reported syntheses, sulfonyl azides were employed as aminating agents.

[RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub>/AgSbF<sub>6</sub> combination in the presence of the acid additive 2-(NO<sub>2</sub>)C<sub>6</sub>H<sub>4</sub>COOH was also active in the amination of 2-phenyl pyridines by using acyl azides as a nitrene source.<sup>68</sup> Isolated compounds are reported in chart 14.

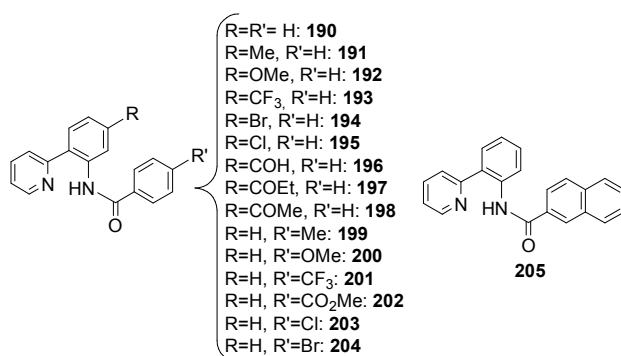
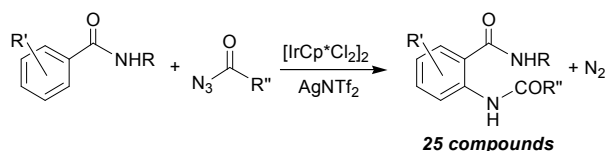


Chart 14. Aza-compounds obtained by [RuCl<sub>2</sub>(*p*-cymene)]<sub>2</sub> catalysed reactions.

The synthetic strategy illustrated above for the amination of aromatic C-H bonds was further improved by employing milder experimental conditions in terms of temperatures and times of reactions and catalyst loading. This goal was reached by running aminations in the presence of [IrCp\*Cl<sub>2</sub>]/AgNTf<sub>2</sub> catalytic systems.<sup>66,67</sup> The amination of aryl benzamides by acyl azides was effective in obtaining twenty-five aza-derivatives and their general synthesis is reported in scheme 16.<sup>66</sup>



Scheme 16. General reaction between aryl benzamides and acyl azides catalysed by [IrCp\*Cl<sub>2</sub>]/AgNTf<sub>2</sub> system.

The authors also tested the applicability of the catalytic procedure to aminate aromatic compounds containing other directing groups, finding that this methodology displayed a general applicability and that it can also be exploited to synthesising natural molecules such as peptides.

To enlarge the reaction scope, [IrCp\*Cl<sub>2</sub>]/AgNTf<sub>2</sub> catalytic system was tested in amination reactions with sulfonyl or aryl azides as aminating agents. Several compounds belonging to almost all the classes reported in chart 13 were obtained at mild experimental conditions, together with a new class of aza-derivatives achieved by aminating aryl carbamates with tosyl azide (chart 15).

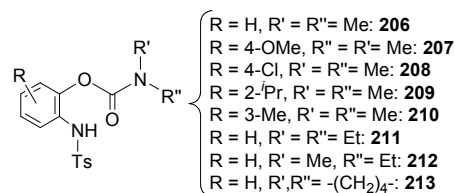
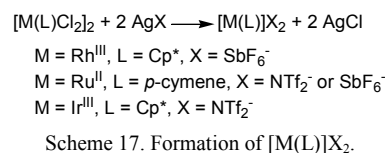


Chart 15. Aza-derivatives obtained from the reaction of aryl carbamates with tosyl azide in the presence of the [IrCp\*Cl<sub>2</sub>]/AgNTf<sub>2</sub> system.

#### 4.1.2. Mechanistic Investigation

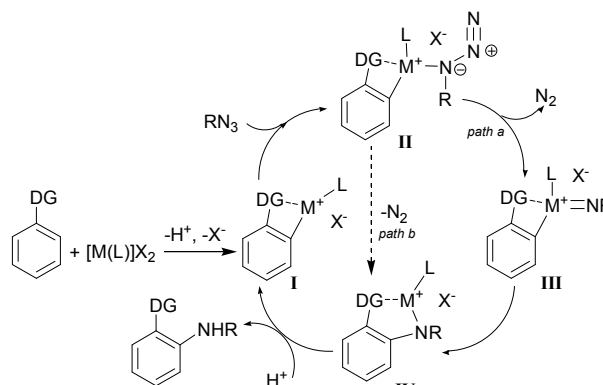
The mechanism of the aromatic amination promoted by [M(L)Cl<sub>2</sub>] was investigated in detail. In all cases the first step of the catalysis was the reaction of [M(L)Cl<sub>2</sub>] with silver salt AgX during which the chlorine atom of the pre-catalyst was replaced by a non-coordinating anion X<sup>-</sup>. The driving force of the reaction was the AgCl formation (scheme 17).



Scheme 17. Formation of [M(L)]X<sub>2</sub>.

For all catalytic systems presented in paragraph 4.1 it is possible to envisage a sequence of analogous mechanistic steps. First, the formed [M(L)]X<sub>2</sub> complex can generate, by reaction with the aromatic substrate, a cationic metallacycle active species (I), which can coordinate the azide to promote the insertion of the nitrene unit into the aromatic C-H bond.

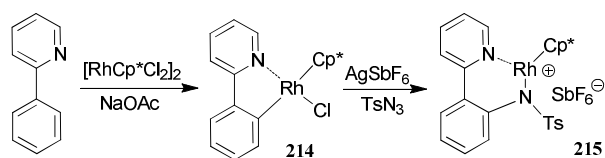
Scheme 18 provides a general mechanism which will be discussed in more depth for each catalytic system below.



Scheme 18. General mechanism for aminations catalysed by  $[M(L)Cl_2]_2/AgX$ .

As shown in scheme 18, the directing group (DG) plays a key role in the mechanism being responsible for the formation of the metallacycle **I**. The unsaturated metallacycle **I** can coordinate the organic azide yielding **IV** either by formation of the metal-imido complex **III** (*path a*) or by directly releasing molecular nitrogen (*path b*). The reaction of **IV** with a proton source reforms the catalytic active species **I** with the contemporary formation of the aromatic amine.

The mechanism of  $[RhCp^*Cl_2]_2/AgSbF_6$  catalytic system was investigated by kinetic and theoretical studies and by isolating several intermediates.<sup>61</sup> Complexes of type **I** and **IV** (scheme 18) were isolated from the reaction of 2-phenyl pyridine with *p*-toluensulfonazide (TsN<sub>3</sub>) and fully characterised also by x-ray diffraction analysis (scheme 19).



Scheme 19. Formation of complexes **214** (type **I**, scheme 18) and **215** (type **IV**, scheme 18).

The involvement of complexes **214** and **215** in the catalytic cycle was supported by the catalytic activity of **214** in the amination of 2-phenyl pyridine by TsN<sub>3</sub> and by the release of the aromatic amine from **215** when it was left reacting with a 2-phenyl pyridine excess as the proton source. This protodemetalation reaction was the last step of the cycle, being responsible for the regeneration of the catalyst **I**.

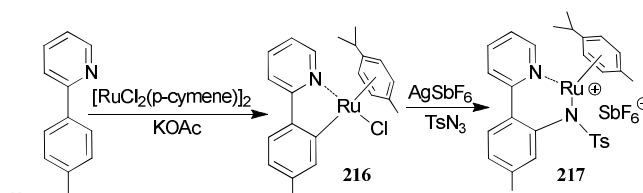
Considering that all the efforts to isolate or spectroscopically detect complexes of type **II** and **III** failed, Chang *et al.*<sup>61</sup> performed a DFT study to shed some light on the catalytic mechanism. The theoretical study indicated a rhodium(IV) imido complex formation as an energetically favourable process (*path a*, scheme 18) and ruled out the direct conversion of **I** into **IV** by a concerted mechanism (*path b*, scheme 18).

A kinetic isotope effect  $k_H/k_D$  (with values in the range 2-4), was observed in the amination of different substrates when they were tested in mixture with their deuterated form. These experiments indicated that the C-H bond cleavage was involved in the rate determining step of the cycle. An analogous mechanism was proposed by the same authors for the  $[Ir^{III}Cp^*Cl_2]_2$ -catalysed reactions.<sup>66</sup>

Mechanistic studies conducted on  $[Rh^{III}Cp^*Cl_2]_2$ -catalysed reactions laid the foundations to express an analogous mechanism for the aromatic amination catalysed by  $[Ru^{II}Cl_2(p\text{-cymene})]_2$ . The metallacycle **216** of type **I** (scheme 18) was isolated and structurally characterised by Chang *et al.*<sup>64</sup> from the reaction of 2-(*p*-tolyl)pyridine with  $[Ru^{II}Cl_2(p\text{-cymene})]_2$ . The treatment of **216** with sulfonyl azide gave the corresponding amido complex **217** which was detected by mass spectroscopy (scheme 20).

Also in this mechanistic investigation a kinetic isotope effect was registered indicating that the C-H cleavage is the rate limiting step of the process. The mechanistic analogies between ruthenium(II) and rhodium(III) catalysed processes allow the

authors to assume equivalent catalytic cycles for both aminations of aromatic C-H bonds (scheme 18).



Scheme 20. Synthesis of complexes **216** and **217**.

## 4.2. Amination of $sp^2$ C-H bonds of indoles and aldehydes.

The reaction of indoles with organic azides afforded different compounds depending on the nature of the catalyst employed. When  $[RhCp^*Cl_2]_2/AgSbF_6$  catalytic system was used, the insertion of the nitrene moiety from an aryl azide was observed at the C2 position of the indole skeleton.<sup>57</sup> The same position was also aminated by sulfonyl azides in the presence of  $[Cp^*Rh(MeCN)_3](SbF_6)_2$  as the catalyst.<sup>69</sup> In chart 16 the obtained C2 aminated indoles are displayed.

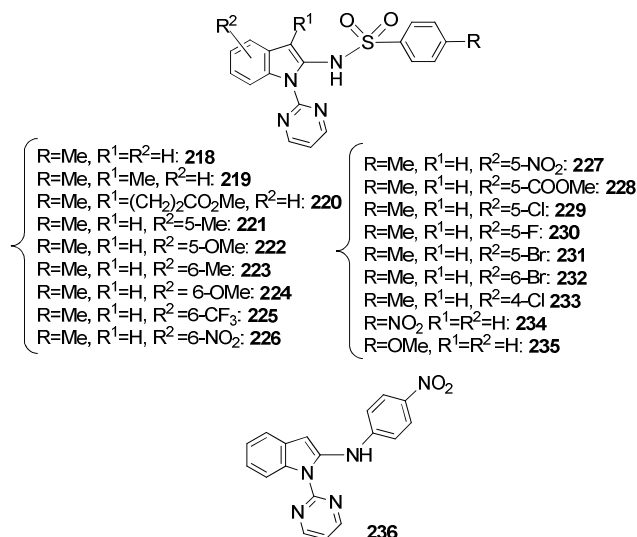


Chart 16. C2 aminated indoles.

It should be noted that the reaction of indoles with aromatic azides did not afford the corresponding aminated compounds when the catalyst  $[RhCp^*Cl_2]_2/AgSbF_6$  was replaced by  $[Cp^*Rh(MeCN)_3](SbF_6)_2$ . In both cases, the DG pyrimidyl group can easily be removed yielding a wide class of 2-amino substituted indoles.

A different reactivity of aromatic azides towards indoles was observed by Che *et al.* by performing reactions in the presence of Ru(PPP)CO as the catalyst; the diimination of indoles was achieved instead of the formation of C2 aminated compounds.<sup>70</sup> The study of the reaction scope allowed the synthesis of twenty differently substituted indoles (chart 17).

2,3-Diimination products were the only obtained aminated compounds and the monoaminated or aminated indole was neither obtained nor detected also when the reaction was performed by using an excess of indole.

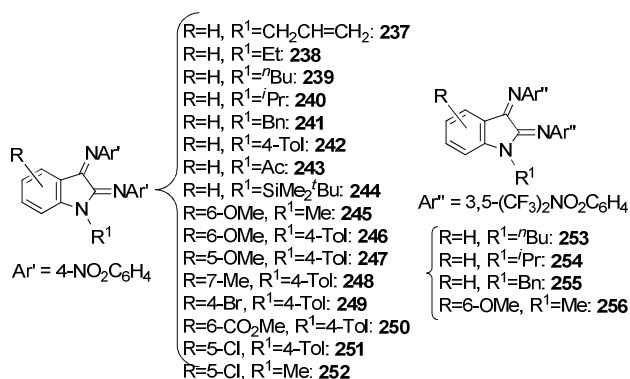
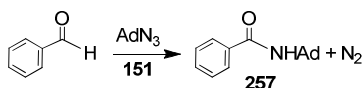


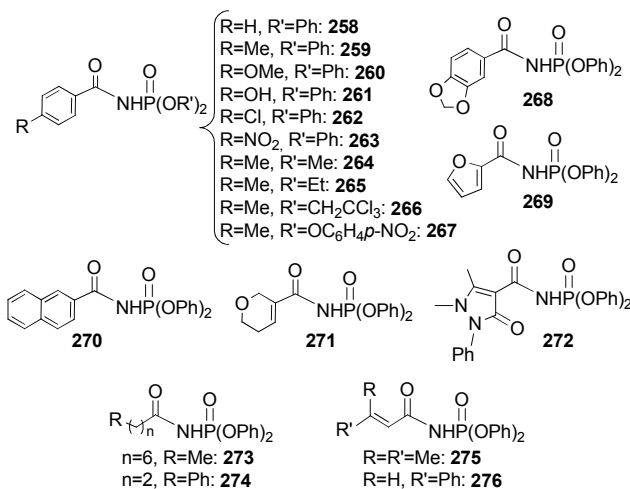
Chart 17. Ru(TTP)CO-catalysed diimination of indoles.

A preliminary mechanistic study indicated that, when 3,5-(CF<sub>3</sub>)<sub>2</sub>C<sub>6</sub>H<sub>4</sub>N<sub>3</sub> was used as the aromatic azide, the *bis*-imido ruthenium (VI) porphyrin **103**<sup>28,36</sup> can be suggested as the catalytic active intermediate.

Organic azides are also competent aminating agents of sp<sup>2</sup> C-H bonds of aldehydes. In 2008 Cundari, Warren *et al.*<sup>45</sup> reported on the catalytic activity of complex **151** in the amidation of benzaldehyde with AdN<sub>3</sub> (scheme 21).

Scheme 21. Amidation of benzaldehyde by AdN<sub>3</sub> catalysed by **152**.

Some years later, Che *et al.*<sup>71</sup> reported on the catalytic activity of Ru(IV)(TPP)Cl<sub>2</sub> complex in the same reaction by using phosphoryl azide as a nitrene source. The procedure was effective with several aldehydes and azides affording a large class of derivatives (chart 18).

Chart 18. Aza-compounds obtained by the reaction of aldehydes with phosphoryl azides in the presence of Ru(IV)(TPP)Cl<sub>2</sub>.

The deuterium kinetic isotope effect for the reaction of benzaldehyde, benzaldehyde-*d*<sub>6</sub> and N<sub>3</sub>P(O)(OCH<sub>2</sub>CCl<sub>3</sub>)<sub>2</sub> gave a *k*<sub>H</sub>/*k*<sub>D</sub> value of 4.1 indicating that the C-H bond cleavage is rate determining of the catalysis.

## 5. Conclusions

The aim of this feature article is to present the state of the art on the use of organic azides as efficient reagents for *intermolecular* aminations of C-H bonds. The incredible number of reported aza-compounds points out the great versatility of this class of aminating agents, which are currently receiving great interest from the scientific community.

Several catalysts have been tested and in some cases complementary results have been reached in the presence of different catalytic systems. Therefore, it is possible to afford structurally dissimilar aza-derivatives starting from similar starting materials. Many efforts have been made to optimise catalytic protocols and to understand mechanisms with the belief that it is always necessary to have knowledge of catalytic pathways for planning more efficient synthetic procedures. Considering the social request for eco-friendly chemical processes to synthesise fine chemicals, we strongly believe that organic azides are going to occupy a prominent role as aminating reagents in the near future. The production of benign N<sub>2</sub> as the only by-product, coupled with the high atom efficiency and selectivity of nitrene transfer reactions, is an ideal starting point to design new and more sustainable synthetic procedures.

## Notes and references

Università degli Studi di Milano - Chemistry Department, Via Golgi 19, 20136 Milano (Italy). Fax: +39 (0)2 50314405; Tel: +39 (0)2 50314374; E-mail: emma.gallo@unimi.it.

- P. Griess, *Proc. R. Soc. London* 1864, **13**, 375–384.
- S. Bräse, C. Gil, K. Knepper and V. Zimmermann, *Angew. Chem., Int. Ed. Engl.*, 2005, **44**, 5188–5240.
- S. Bräse and K. Banert Editors, *Organic Azides Syntheses and Applications*, John Wiley & Sons Ltd., 2010.
- J. Yamaguchi, A. D. Yamaguchi and K. Itami, *Angew. Chem., Int. Ed. Engl.*, 2012, **51**, 8960–9009.
- T. Uchida and T. Katsuki, *Chem. Rec.*, 2014, **14**, 117–129.
- S. Chiba, *Synlett*, 2012, 21–44.
- T. G. Driver, *Org. Biomol. Chem.*, 2010, **8**, 3831–3846.
- M. Minozzi, D. Nanni and P. Spagnolo, *Chem. Eur. J.*, 2009, **15**, 7830–7840.
- T. Katsuki, *Chem. Lett.*, 2005, **34**, 1304–1309.
- S. Cenini, E. Gallo, A. Caselli, F. Ragaini, S. Fantauzzi and C. Piangiolo, *Coord. Chem. Rev.*, 2006, **250**, 1234–1253.
- S. Fantauzzi, A. Caselli and E. Gallo, *Dalton Trans.*, 2009, 5434–5443.
- T. G. Driver, *Nat. Chem.*, 2013, **5**, 736–738.
- S. Chiba, *Synlett*, 2012, 21–44.
- S. Cenini, F. Ragaini, E. Gallo and A. Caselli, *Curr. Org. Chem.*, 2011, **15**, 1578–1592.
- B. J. Stokes and T. G. Driver, *Eur. J. Org. Chem.*, 2011, 4071–4088.
- G. Smolinsky, *J. Am. Chem. Soc.*, 1961, **83**, 2489–2493.
- K. R. Henery-Logan and R. A. Clark, *Tetrahedron Lett.*, 1968, 801–806.
- R. A. Abramovitch and E. P. Kyba, *J. Am. Chem. Soc.*, 1974, **96**, 480–488.
- E. F. V. Scriven and K. Turnbull, *Chem. Rev.*, 1988, **88**, 297–368.
- H. Kwart and A. A. Khan, *J. Am. Chem. Soc.*, 1967, **89**, 1951–1953.
- S. Cenini, E. Gallo, A. Penoni, F. Ragaini and S. Tollari, *Chem. Commun.*, 2000, 2265–2266.
- F. Ragaini, A. Penoni, E. Gallo, S. Tollari, C. Li Gotti, M. Lapadula, E. Mangioni and S. Cenini, *Chem. Eur. J.*, 2003, **9**, 249–259.
- A. Caselli, E. Gallo, F. Ragaini, F. Ricatto, G. Abbiati and S. Cenini, *Inorg. Chimica Acta*, 2006, **359**, 2924–2932.

24. A. Caselli, E. Gallo, S. Fantauzzi, S. Morlacchi, F. Ragaini and S. Cenini, *Eur. J. Inorg. Chem.*, 2008, 3009-3019.
25. M. Weber, G. Yilmaz and G. Wille, *Chim. Oggi*, 2011, **29**, 8-10.
26. H.-J. Lu, V. Subbarayan, J.-R. Tao and X. P. Zhang, *Organometallics*, 2010, **29**, 389-393.
27. D. Intriери, A. Caselli, F. Ragaini, S. Cenini and E. Gallo, *J. Porphyrins Phthalocyanines*, 2010, **14**, 732-740.
28. D. Intriери, A. Caselli, F. Ragaini, P. Macchi, N. Casati and E. Gallo, *Eur. J. Inorg. Chem.*, 2012, 569-580.
29. W. Xiao, J. Wei, C.-Y. Zhou and C.-M. Che, *Chem. Commun.*, 2013, **49**, 4619-4621.
30. K.-H. Chan, X. Guan, V. K.-Y. Lo and C.-M. Che, *Angew. Chem., Int. Ed. Engl.*, 2014, **53**, 2982-2987.
31. P. Zardi, A. Caselli, P. Macchi, F. Ferretti and E. Gallo, *Organometallics* in press.
32. Y. Liu and C.-M. Che, *Chem. Eur. J.*, 2010, **16**, 10494-10501.
33. S.-M. Au, J.-S. Huang, W.-Y. Yu, W.-H. Fung and C.-M. Che, *J. Am. Chem. Soc.*, 1999, **121**, 9120-9132.
34. S. K.-Y. Leung, W.-M. Tsui, J.-S. Huang, C.-M. Che, J.-L. Liang and N. Zhu, *J. Am. Chem. Soc.*, 2005, **127**, 16629-16640.
35. Z. Guo, X. Guan, J.-S. Huang, W.-M. Tsui, Z. Lin and C.-M. Che, *Chem. Eur. J.*, 2013, **19**, 11320-11331.
36. S. Fantauzzi, E. Gallo, A. Caselli, F. Ragaini, N. Casati, P. Macchi and S. Cenini, *Chem. Commun.*, 2009, 3952-3954.
37. G. Manca, E. Gallo, D. Intriери and C. Mealli, *ACS Catalysis*, 2014, **4**, 823-832.
38. V. Lyaskovskyy, A. I. O. Suarez, H. Lu, H. Jiang, X. P. Zhang and B. de Bruin, *J. Am. Chem. Soc.*, 2011, **133**, 12264-12273.
39. P. Zardi, D. Intriери, A. Caselli and E. Gallo, *J. Organomet. Chem.*, 2012, **716**, 269-274.
40. K. Omura, M. Murakami, T. Uchida, R. Irie and T. Katsuki, *Chem. Lett.*, 2003, **32**, 354-355.
41. Y. Nishioka, T. Uchida and T. Katsuki, *Angew. Chem., Int. Ed. Engl.*, 2013, **52**, 1739-1742.
42. E. R. King, E. T. Hennessy and T. A. Betley, *J. Am. Chem. Soc.*, 2011, **133**, 4917-4923.
43. E. T. Hennessy, R. Y. Liu, D. A. Iovan, R. A. Duncan and T. A. Betley, *Chem. Sci.*, 2014, **5**, 1526-1532.
44. Y. M. Badiei, A. Krishnaswamy, M. M. Melzer and T. H. Warren, *J. Am. Chem. Soc.*, 2006, **128**, 15056-15057.
45. Y. M. Badiei, A. Dinescu, X. Dai, R. M. Palomino, F. W. Heinemann, T. R. Cundari and T. H. Warren, *Angew. Chem., Int. Ed. Engl.*, 2008, **47**, 9961-9964.
46. T. R. Cundari, A. Dinescu and A. B. Kazi, *Inorg. Chem.*, 2008, **47**, 10067-10072.
47. J. R. Suarez and J. L. Chiara, *Chem. Commun.*, 2013, **49**, 9194-9196.
48. T. Kang, Y. Kim, D. Lee, Z. Wang and S. Chang, *J. Am. Chem. Soc.*, 2014, **136**, 4141-4144.
49. G. Evano, N. Blanchard and M. Toumi, *Chem. Rev.*, 2008, **108**, 3054-3131.
50. F. Paul, J. Patt and J. F. Hartwig, *J. Am. Chem. Soc.*, 1994, **116**, 5969-5970.
51. A. S. Guram and S. L. Buchwald, *J. Am. Chem. Soc.*, 1994, **116**, 7901-7902.
52. M. Kosugi, M. Kameyama and T. Migita, *Chem. Lett.*, 1983, **12**, 927-928.
53. M. Kim and S. Chang, *Org. Lett.*, 2010, **12**, 1640-1643.
54. R. T. Gephart and T. H. Warren, *Organometallics*, 2012, **31**, 7728-7752.
55. M. Zhang and A. Zhang, *Synthesis*, 2012, **44**, 1-14.
56. J. E. R. Sadig and M. C. Willis, *Synthesis*, 2011, 1-22.
57. J. Ryu, K. Shin, S. H. Park, J. Y. Kim and S. Chang, *Angew. Chem., Int. Ed. Engl.*, 2012, **51**, 9904-9908.
58. J. Y. Kim, S. H. Park, J. Ryu, S. H. Cho, S. H. Kim and S. Chang, *J. Am. Chem. Soc.*, 2012, **134**, 9110-9113.
59. C. Tang, Y. Yuan, Y. Cui and N. Jiao, *Eur. J. Org. Chem.*, 2013, 7480-7483.
60. K. Shin, Y. Baek and S. Chang, *Angew. Chem., Int. Ed. Engl.*, 2013, **52**, 8031-8036.
61. S. H. Park, J. Kwak, K. Shin, J. Ryu, Y. Park and S. Chang, *J. Am. Chem. Soc.*, 2014, **136**, 2492-2502.
62. H. J. Kim, M. J. Ajitha, Y. Lee, J. Ryu, J. Kim, Y. Lee, Y. Jung and S. Chang, *J. Am. Chem. Soc.*, 2014, **136**, 1132-1140.
63. K. Shin, J. Ryu and S. Chang, *Org. Lett.*, 2014, **16**, 2022-2025.
64. J. Kim, J. Kim and S. Chang, *Chem. Eur. J.*, 2013, **19**, 7328-7333.
65. Q.-Z. Zheng, Y.-F. Liang, C. Qin and N. Jiao, *Chem. Commun.*, 2013, **49**, 5654-5656.
66. J. Ryu, J. Kwak, K. Shin, D. Lee and S. Chang, *J. Am. Chem. Soc.*, 2013, **135**, 12861-12868.
67. D. Lee, Y. Kim and S. Chang, *J. Org. Chem.*, 2013, **78**, 11102-11109.
68. K. Shin, J. Ryu and S. Chang, *Org. Lett.*, 2014, **16**, 2022-2025.
69. J. Shi, B. Zhou, Y. Yang and Y. Li, *Org. Biomol. Chem.*, 2012, **10**, 8953-8955.
70. J. Wei, W. Xiao, C.-Y. Zhou and C.-M. Che, *Chem. Commun.*, 2014, **50**, 3373-3376.
71. W. Xiao, C.-Y. Zhou and C.-M. Che, *Chem. Commun.*, 2012, **48**, 5871-5873.

Cite this: DOI: 10.1039/coxx00000x

www.rsc.org/xxxxxx

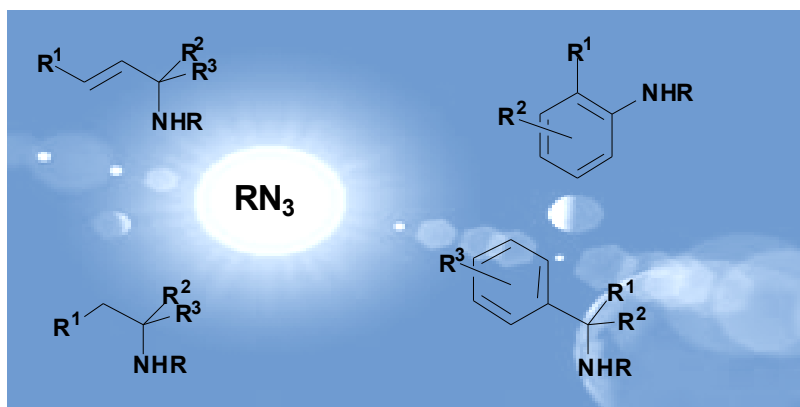
ARTICLE TYPE

## Table Of Content

**Organic Azides: “Energetic Reagents” for the *Intermolecular* Amination of C-H Bonds.**

Daniela Intriери, Paolo Zardi, Alessandro Caselli and Emma Gallo

This Feature article highlights the potentiality of organic azides ( $\text{RN}_3$ ) for the *intermolecular* amination of  $\text{sp}^3$  and  $\text{sp}^2$  C-H bonds. A compendium of employed catalytic systems, together with a discussion of involved mechanisms, is provided.



10