#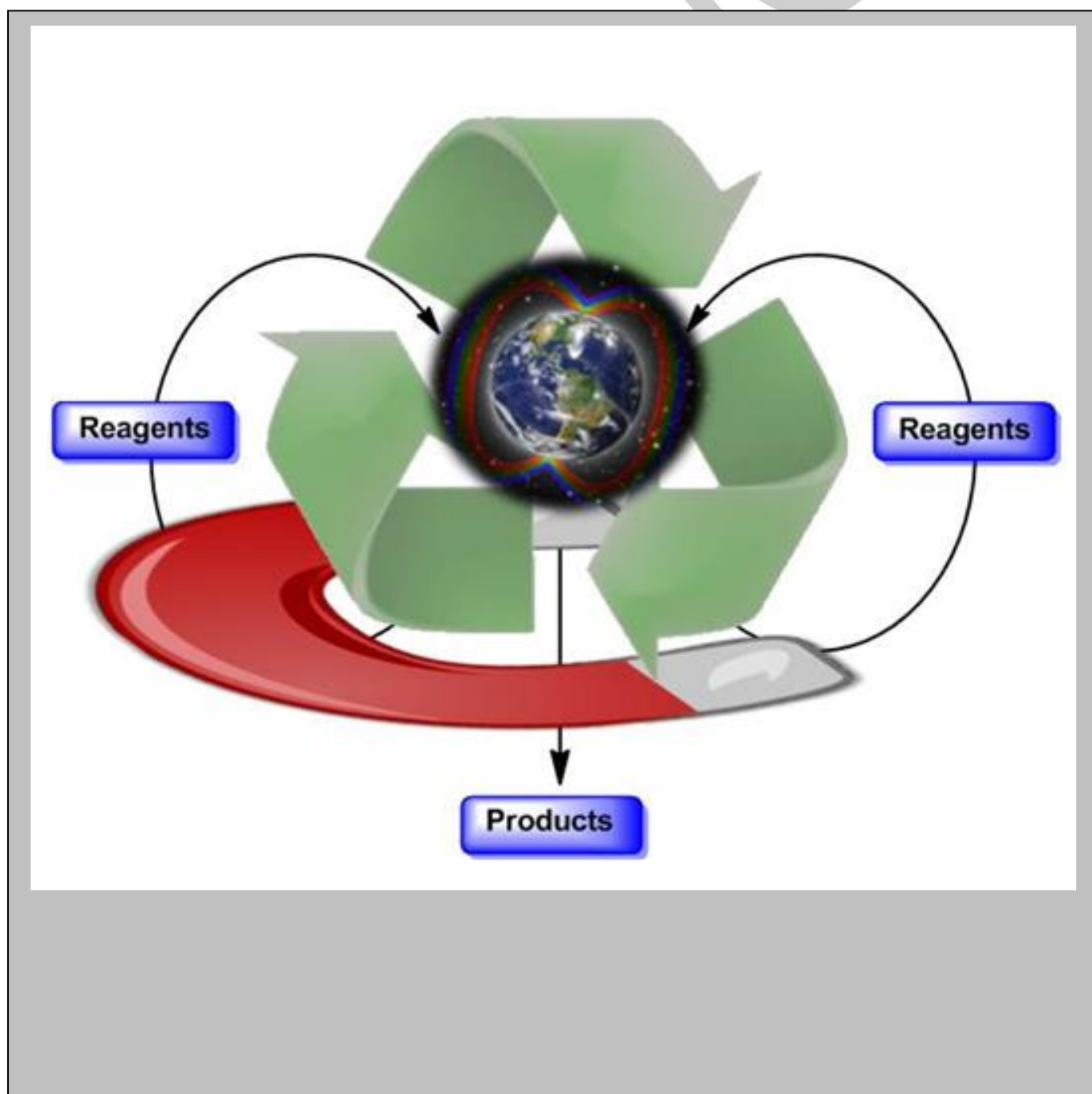 Magnetite and Metal-impregnated Magnetite Catalysts in Organic Synthesis: A Very Old Concept with New Promising Perspectives

Alejandro Baeza,*[a] Gabriela Guillena*[a] and Diego J. Ramón*[a]

Dedicated to Professor Andreas Pfaltz on the occasion of his retirement

Abstract: Magnetite is a well-known material, with the impregnation of transition metals onto its surface being a very old protocol for preparing catalysts. However, only recently, the combination of both, magnetite and impregnation protocols, have been recognized as a powerful methodology to prepare catalysts. The impregnation protocol, of nearly all transition metals in the magnetite surface, has rendered the first generation of catalysts. These simple catalysts have been used in a very broad range of organic transformations. Thus, simple imine derivative formation or unknown reactions such as the direct cross β-alkylation of primary alcohols, through dehydrogenation, oxidation, addition, hydrogen autotransfer and multicomponent reactions has been accomplished using these catalysts. In most cases, these catalysts could be just isolated by magnetic decantation and reused several times without a detrimental effect on the initial results. In some cases, the study of the surface of the catalyst by means of several surface characterization techniques has permitted to determine the real species involved in the process and their structural changes within the reaction cycles. Furthermore, the post-modification of the catalysts by reduction or oxidation of the immobilized metal, or by the addition of ligands, has enlarged the applicability of this type of catalysts.
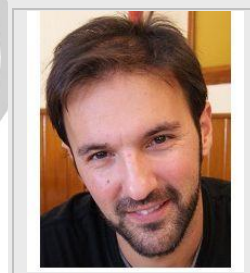
1. Introduction

Heterogeneous catalysis is an old concept profusely used by chemists. Despite this, new developments in this area are expected, since most of the chemical processes employ heterogeneous catalysis to perform the synthesis of valuable organic compounds.[1,2]

On the other hand, homogeneous catalysts have emerged as an efficient alternative, and the enormous work done in the academia has permitted the implementation of some homogeneous catalytic processes at an industrial scale.[3] Although homogenous catalysts have several advantages such as the low catalysts loadings required and the use of well defined and characterized active species compared to heterogeneous catalysts, it seems not to be enough to displace these from their central role in the industry. Probably, the main reason behind this fact is the high global cost of the homogeneous catalysts.

The social demand of low environmental impact processes, costs, energy, resources and waste reduction, according to the principles of *Green Chemistry* has made the recyclability of these catalysts compulsory from an industrial point of view.[4] In addition, the irruption of nanoscience in the last decades has led to an important progress in the solid state and surface chemistry.

Consequently, the efficiency of heterogeneous catalysts has been increased, and has given rise to numerous studies of potential organic chemistry processes prone to be implemented in industry. While in some cases the isolation processes of these catalysts, usually by filtration, is successful, in other cases, it could be difficult. However, the overall balance of the aforementioned advantages, have contributed to maintain them as the protocol of choice for the synthesis of organic compounds.

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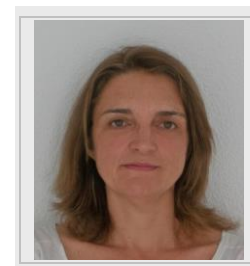
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In this review we aim to gather from all the vast amount of heterogeneous catalysts available, those which involve metal impregnated magnetite and those which are used as catalysts in synthetic organic chemistry. Although there are other supporting methods that may lead to similar catalysts to those obtained by the impregnation protocol, as will be discussed latter on, this review will be focused exclusively on impregnated catalysts. The reason behind this is their simplicity in the preparation and the particular magnetic properties of such iron oxide particles. Due to their interaction with magnetic fields, they are easily confinable, as well as isolable, in the reactor area. Moreover, these types of compounds are really attractive as catalysts; as will be discussed more extensively in the next sections.

1.1. Metal Catalyst Impregnation

From all the possible ways to immobilize or support a metal catalyst in the surface of a particle,[5] the impregnation is the most straightforward, simple and less expensive protocol.[5b,c,6] It consists either in the evaporation or in the precipitation of a solution which contains the metal or metal oxide precursors and the desired support, followed by an ulterior drying process. Although the procedure is simple, the particle distribution and morphology of the supported catalyst is governed by various factors such as the possible interactions between the support and the metal specie, the porosity of the support, the pH and the viscosity of the solution and the drying rates.

Controlling all these factors is sometimes a difficult task, and therefore some authors claim that the impregnation method is hardly reproducible, choosing other methods for the immobilization of catalysts. However, for a wide number of applications in organic synthesis, the impregnated catalyst works perfectly and their preparations are totally reproducible.

2. Magnetite as Catalyst Support

Recently, among the traditional employed solid supports (silica, alumina, ceria, titania, zirconia, carbon, etc.) magnetite is arising as an interesting alternative in order to support catalysts, due to its unique properties.

Magnetite, Fe_3O_4, is a mixed iron(II) and (III) oxide in a cubic inverse spinel structure. A wide variety of metals and molecules can be easily immobilized and supported on the surface of magnetite. Some properties of magnetite, such as the following, make this solid support a good choice; It is a non-toxic material and relatively inert. The presence of iron and oxygen atoms confers to magnetite a character of soft Lewis acid and base, respectively. Therefore, it can promote organic chemical transformations by itself, as will be described later.

Considering nanoparticles (NPs) acting as catalyst supports, the differences between the rest of metal oxides and nanomagnetite becomes more evident. Nanoparticles possess different physical and chemical properties compared to bulk oxides. They have obvious advantages in terms of their activity, especially due to the higher surface area of the active specie and the higher dispersability in common solvents. This favors

closer contact with the reactants. Therefore, they have been considered for many authors as a bridge between homogeneous and heterogeneous catalysts.[7]

At such small sizes (ranging between 1-100 nm) magnetite nanoparticles, among other iron oxides, sometimes named SPION (superparamagnetic iron oxides nanoparticles) show superparamagnetism at room temperature. Therefore, these nanoparticles do not have a permanent magnetic moment and can be only magnetized when a external magnetic field is applied. This transient magnetization of the NPs stops as soon as the external field is ceased. The superparamagnetism phenomenon is not only beneficial because it partially avoids the agglomeration but also because it can be applied for purification purposes. This fact is especially important since, generally, the purification of heterogeneous nanoparticles catalyzed processes give some problems. These are associated with the small size of the particles, which normally form a colloidal suspension, leading to a difficult and tedious recovery of the catalyst by filtration and/or centrifugation. By the contrary, superparamagnetic nanoparticles are easily separated and recovered quantitatively, by using just a magnet (magnetic purification or magnetic decantation), making the whole process even more sustainable.[8]

Additionally, magnetite nanoparticles are readily accessible by different synthetic methodologies:[9]

- *Co-precipitation*:[10] It is the simplest way to gain access to magnetite nanoparticles. It consists in the addition under an inert atmosphere of a base to an aqueous solution containing Fe(II)/Fe(III) salts. The size and the shape of the particles depends on different factors, such as pH, salt precursor, Fe(II)/Fe(III) molar ratio, temperature, etc. However, once the conditions are fixed, the synthesis is highly reproducible. Moreover, those features (especially the size) can be controlled by using organic additives as for example polyvinylalcohol (PVA), oleic acid, etc.
- *Thermal Decomposition*:[11] This methodology allows the synthesis of MNPs (magnetic nanoparticles) with a narrow size distribution and high shape control from organometallic iron precursors, with the above mentioned additives (fatty acids, polyalcohols among others). To be succesful, the control of high temperatures (ranging between 100 and 320 ºC depending on the iron precursor), as well as inert atmosphere, are the conditions required.
- *Microemulsion*:[12] It could be regarded as a co-precipitation methodology variation, which permits a better control of the size and morphology. Although notably poorer yields are achieved and a rather complicated manipulation is required.
- *Hydrothermal Synthesis*:[13] It is also a variation of thermal decomposition method, but using high pressure and temperatures. The size and shape control obtained is as high as in the microemulsion methodology. The process itself is simpler, but the yields are lower.

As expected, magnetite has also some drawbacks in comparison with other commonly employed supports. On one hand, magnetite, like most of the iron oxides, is dissolved in strong acid media. This could be a limitation for the use of magnetite nanoparticles supports under those conditions.

However, in Organic Synthesis, the use of such extreme reaction media is not very common.[14] On the other hand, the main problem associated with "naked" magnetite nanoparticles, Fe_3O_4, is their tendency to slowly oxidize to the more stable maghemite (γ-Fe_2O_3) or even to the most stable iron oxide hematite (α-Fe_2O_3). This oxidation affects the properties of the support and can lead to morphologic changes, which could result in loss of magnetism and dispersability. Maghemite nanoparticles show in lower extension superparamagnetism phenomena. Therefore, many authors directly oxidized magnetite to maghemite, preventing this problem.

2.1. Approaches to Support Catalysts on Magnetite

In the actual literature, numerous approaches in order to introduce metals on a solid support surface are reported.[5] However, among those, coating, grafting, co-precipitation and impregnation are the most frequently employed to support metal catalysts on the magnetite surface (Figure 1):[9]

- *Coating*:[15] Coating of metal nanoparticles is a commonly employed procedure in material science. Silica has been chosen from all the different oxide-based coatings to support magnetite nanoparticles due mainly to economic reasons, as well as its high stability under different conditions. The procedure is based on the formation of a SiO_2 layer on the magnetite surface, which is normally generated employing the Sol-Gel strategy, and subsequent formation of a second layer containing particles of the active metal specie onto the SiO_2 coating (Fig. 1b; M_xO_y = SiO_2). This procedure has been developed in order to prevent the problems associated with the use of "naked" magnetite (mentioned previously), especially regarding the oxidation issues.

- *Grafting:* Another widespread strategy to support metals on magnetite is based on the grafting of active metal species, using tailored ligands which are able to bind effectively to the magnetite surface (Fig. 1c). In addition, when this procedure is chosen, the ligands are supposed to protect the magnetite surface against oxidation, conferring stability to the iron oxide particles.

- *Coating-Grafting*:[15] This third way is preferred by many other research groups. This procedure can be considered as a combination of the two aforementioned methods. Thus, onto a SiO_2-coated magnetite, metal species are grafted by using a ligand bearing a triethoxysilane derivative, capable to bind the silica coating (Fig. 1d). In this way, an effective protection of the magnetite is obtained, along with the introduction of specific anchoring metal points.

- *Co-precipitation and Dumbell-like composites*:[16] Although they differ in the synthesis and structure, they can be considered as a magnetite possessing a metal catalyst domain in its structure. For the co-precipitation strategy, two metal salts are precipitated together at basic pH. A spinel structure is formed after evaporation of the solvent and treatment at high temperatures. This spinel structure has different metal oxides domains normally located in a multiple region within the nanoparticles (Fig. 1e). Sometimes, all positions of Fe(II) are substituted by another transition metal

cation(II), leading to the ferrites.[17] For the dumbbell-like cases, the domain is perfectly located in a specific region, and can be conceived as a metal nanoparticle which has grown onto the magnetite surface. In fact, most of the dumbbell-like MNP are produced by precipitation of a metal salt onto the surface of a preformed magnetite nanoparticle (Fig. 1f).

- *Impregnation*:[18] As already mentioned in the previous section, the impregnation method is one the oldest ways employed to deposit metal catalyst just on the surface of inorganic materials.

Using the aforementioned coating and grafting procedures, a wide variety of transition metals have been supported on magnetite and applied in a multitude of synthetic transformations, allowing the catalyst recyclability. Most of these transformations, including catalyst preparation, have been thoroughly reviewed by other authors in the last few years.[8,9,18,19] However, little or no attention has been paid to impregnated catalysts and the uses of these in organic synthesis.
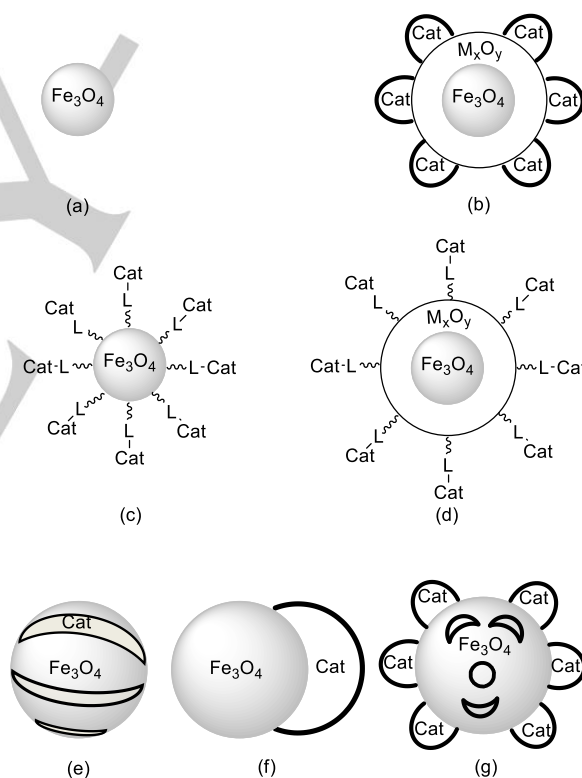

Figure 1. (a) Magnetite. (b) Coated magnetite. (c) Metal grafted magnetite. (d) Metal grafted coated magnetite. (e) Co-precipitated metal-magnetite. (f) Dumbell-like metal-magnetite. (g) Metal impregnated magnetite.

In a few cases, the final catalysts obtained either by co-precipitation, dumbbell-like or impregnation procedures are quite similar in terms of morphology, size distribution and activity. In all these strategies, the formation of magnetite could be faster than the metallic catalytic species, and the distribution onto the surface of those could be, more or less, homogenous. The

simple and straightforward impregnation protocol consists in the precipitation of the corresponding metal hydroxides and/or oxides derived from their metal halides, in an aqueous basic media onto the surfaces of preformed micro- or nanoparticles of magnetite (Figure 2). These have been sometimes admonished by some authors and therefore not used as much in synthetic organic chemistry as some of other methods. The reason behind this criticism comes from the oxidation problems, the control of the metal active species size and the metal leaching observed for some organic transformations.
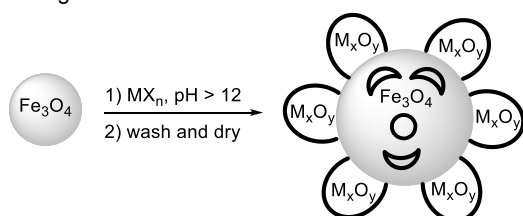

Figure 2. General procedure for magnetite wet impregnation method.

However, when impregnated magnetite was employed in organic reactions, the metal leaching and the sinterization (which can be associated to Ostwald ripening effect) observed is negligible. In addition, the impregnation method, when performed under controlled conditions, renders a good and reproducible size distribution of metal oxide nanoparticles onto the magnetite surface, which creates a high number of active sites. There are numerous examples in literature of synergistic effects, in terms of enhanced catalytic activity compared to the magnetite and the corresponding metal oxide.

3. Impregnated Magnetite in Organic Synthesis

From the purification and recyclability point of view, there are obvious advantages of supporting metal on magnetite nanoparticles. The simplicity of the impregnation methodology has encouraged the research on the synthesis of different metal, usually transition metals, impregnated nanomagnetite particles. These can be regarded as green and recyclable alternative catalysts, which can be applied in common organic transformations.

In this section a comprehensive overview of such catalysts and the organic reactions in which they have been employed are presented.[20] Subsections have been ordered by the atomic number of the metal specie impregnated onto magnetite.

3.1. Titanium

Conversely to the rest of titanium compounds, titanium oxides have not been widely applied in organic reactions. However, it has been reported their use as support for other active metal species acting as catalysts or as photocatalysts. Therefore, the impregnation of these oxides on magnetite has received little attention. Only two reports (dealing with the purification of polluted wastewater) acting as a photocatalysts of

different colorants have been published.[21] In both cases the resulting impregnated TiO_2 shows an anatase phase according to XRD analysis.

3.2. Manganese

A MnO_2-Fe_3O_4 catalyst has been prepared and tested as possible catalyst for the oxidative elimination of organic pollutants in water. The exact composition of the catalyst was confirmed by XPS and XRD analysis, having the resulting particles a grain size of 18.76 nm.[22] Recently an application in an organic transformation of catalyst has been found. Thus, the selectivity towards light olefins (C_2-C_4) of the Fischer-Tropsch synthesis was improve using catalyst containing a 6% of MnO_2 impregnated in magnetite compared to the results achieved with "naked" Fe_3O_4.[23] This improvement can be ascribed to the nonporous nature, proven by BET N_2 adsorption and desorption experiments, of the synthesized catalyst. This fact would avoid possible secondary reactions and hence favors the formation of light olefins. In addition, the MnOx impregnated turned out to be at the edge of the nanoparticle and had no effect on the crystal structure of Fe_3O_4 as confirmed by Mössbauer spectroscopy.

3.3. Iron

Iron is the most abundant transition metal on Earth. Iron compounds, and particularly iron oxides, have been traditionally used by the chemical industry as heterogeneous catalysts or as promoters of several chemical transformations of global importance due to its natural occurrence. Thus, iron oxides were involved in the Haber–Bosch process for producing ammonia,[24] the Fischer-Tropsch process for producing synthetic fuel,[25] and the water-gas shift reaction, among others.[26] However, during this century, more efficient catalysts, normally based in other transition metals have been discovered, with iron compounds being used less often. This was true until the last decade, when iron species have suffered a new renaissance. This was due to the finding of new reactivity modes,[27] and also to the use of iron oxides, such magnetite, as magnetically recoverable supports for other metal species.

Magnetite nanoparticles can be envisioned as Fe_3O_4 impregnated in a core of Fe_3O_4. They do not act simply as an inert support but on the contrary, are capable of catalyzing many transformations by themselves. Furthermore they can be easily recovered and reused in subsequent cycles without a significant loss in their activity.

One of the earliest examples, where magnetite was used as a catalyst in organic synthesis, was in the Z/E-isomerization of dimethyl maleate derivatives.[28]

Magnetite nanoparticles have been employed as catalyst in reduction reactions. Nitroarenes were efficiently transformed to the corresponding anilines employing 20 mol% of catalyst and hydrazine as hydrogen source (Scheme 1).[29] This transformation has been further expanded by implementing an *in situ* formation of magnetite nanoparticles in a continuous flow

reaction under microwave radiation. Thus, making the whole process highly attractive from the environmental point of view.[30] In this case, the magnetite particles were unambiguously identified as a single phase cubic Fe_3O_4 by means of XRD analysis, being the particle size 6 ± 2 nm according to HRTEM images.
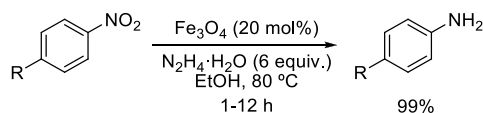

Scheme 1. Fe_3O_4 catalyzed reduction of nitroarenes.

Magnetite nanoparticles have been also employed as recoverable catalysts for different oxidations reactions,[31] as shown in Table 1. The magnetite catalyzed styrene oxidation to afford the corresponding benzaldehydes has been studied by different groups. The particle sizes of magnetite, in all the cases, ranged from 16 to 22 nm.[32] However, the reaction was not very selective. Other oxidation products, such as the corresponding epoxide, alcohol and carboxylic acid among others, were also obtained. The best result, in terms of aldehyde selectivity, is shown in the entry 1 of Table 1. Better results, in terms of both yield and selectivity, were achieved for the oxidation of aldehydes to carboxylic acids (Table 1, entry 2).[33] It should be also pointed out that the dehydrogenation of ethylbenzene derivatives to give the corresponding styrenic compounds has been reported, with little success being accomplished for this transformation. Probably, as pointed out by the authors, this was due to a blockage of the Fe_3O_4 (111) surface by adsorption of both the product and the starting material.[34]

Table 1. Oxidations reactions catalyzed by nanomagnetite

Entry	Reagents	Conditions	Products	Yield (%)
1	$PhCH=CH_2$	0.5 mol%, O_2 (4 bar), 90 ºC, 24 h	PhCHO	53-90
2	RCHO	20 mol%, air or ^tBuOOH, ethyl acetoacetate, 80 ºC, 24 h	RCO_2H	45-99

Numerous multicomponent transformations, in which the nucleophilic addition to an *in situ* formed imine represents a key step, have been published in the last years using magnetite as catalyst. One of the first examples reported was a four-component aza-Sakurai type reaction, yielding the corresponding N-protected amines in high yields. After 15th catalytic cycles (Scheme 2) similar yields were achieved. The remaining magnetite particle was almost the same that the fresh sample, as revealed by TEM, XRD and BET surface measurements.[35]
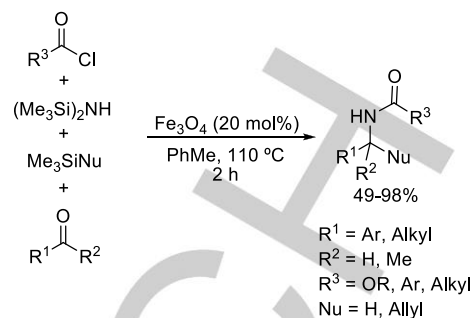

Scheme 2. Fe_3O_4 catalyzed aza-Sakurai reaction.

Different three-component reactions involving the formation of imines have been reported (Scheme 3). Some examples are the phosphite addition to imines[36] (Pudovik-type reaction), the Strecker reaction[37] and the alkyne addition to imines[38] (A^3-coupling), among others.[39] In all the cases, the catalyst was recycled several times without a substantial loss of activity.
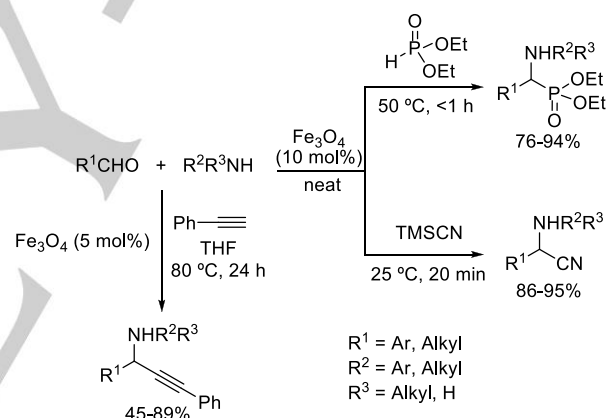
Scheme 3. Fe_3O_4 catalyzed three-component reactions.

More recently, the synthesis of β-cetoamido carbonyl compounds in a four-component reaction has been published employing magnetite as catalyst (Scheme 3).[40]
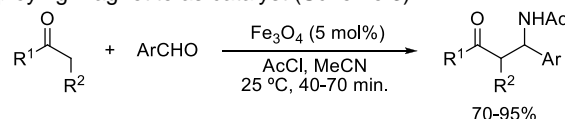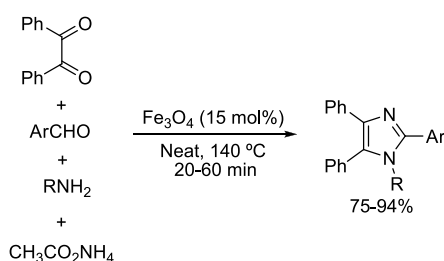

Scheme 4. Fe_3O_4 catalyzed synthesis of β-cetoamido carbonyl compounds through a four-component reaction.

The successful application of magnetite as catalyst for the synthesis of quinoxalines[41] by condensation of 1,2-dicarbonyl compounds and 1,2-diamine derivatives has been recently published. Remarkably, the highest yield was obtained when water was employed as solvent, with the catalyst being recycled

up to five times. It is also important to note that the XRD pattern confirmed the magnetite structure before and after recycling experiments, being the particle size around 20 nm.

The synthesis of imidazoles[42] (Scheme 5), as well as other heterocycles,[43] has also been described. The synthesis was accomplished in absence of solvent and the magnetite could be recycled ten times without detriment on yields. As in the previous case, the magnetite structure was confirmed by XRD, and the same size was maintained after these cycles.


Scheme 5. Fe_3O_4 catalyzed synthesis of imidazoles.

In 2009, an iron(III) hydroxide impregnated magnetite was reported to efficiently catalyze the aldol condensation, affording the corresponding α,β-unsaturated ketones in modest to excellent yields.[44] According to authors, the presence of iron(III) species seemed to be crucial for the reaction to work, since the reaction with "naked" magnetite failed completely. In addition, the catalyst was re-used up to five times with constant yields being achieved (Scheme 6). Later, the simple aldol condensation between cyclic ketones and aldehydes catalyzed by Fe_3O_4 was reported.[45]
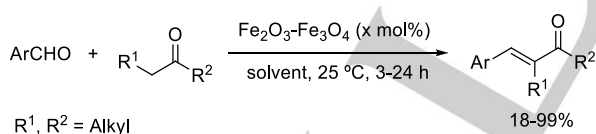
**Scheme 6.** Fe_2O_3-Fe_3O_4 catalyzed aldol condensation.

Other aldol related reactions, such as the Knoevenagel condensation, used magnetite as an efficient and recyclable catalyst. Thus, in 2011, this reaction followed by a Michael-type addition and subsequent dehydration lead to the synthesis of 4-substituted-4*H*-pyrans, in a cascade process (Scheme 7).[46] The reaction proceeded smoothly at room temperature in the presence of acetyl chloride as dehydrating agent. Although a rather high amount of catalyst was employed (65 mol%) and its recyclability was not possible, it should be pointed out that the protocol is simple and applicable to a broad range of substrates.

This protocol reduced the previously described reaction times from weeks to hours. Remarkably, similar results were obtained when Fe_2O_3 was employed as catalyst, not discarding that Fe(III) species were acting as the real catalyst of the reaction. Shortly thereafter this pioneer report, different research groups have published the synthesis of several heterocycles with a Knoevenagel condensation as starting step.[47]
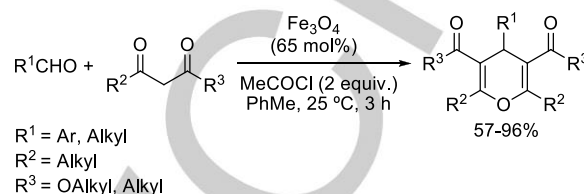

Scheme 7. Fe_3O_4 catalyzed 4*H*-pyrans synthesis.

Following the same idea, the synthesis of 1,4-dihydroquinolines was accomplished (Scheme 8).[48] The synthesis of these substrates was performed by a protocol involving a Knoevenagel condensation, an enamine Michael-type addition, and an intramolecular C-N cross coupling (Buchwald-Hartwig type reaction). This unprecedented magnetite catalyzed reaction gave rise to the corresponding products in good yields even when 2-chlorobenzadehyde derivatives were employed. In addition, the catalyst was recycled up to five times with only a slight decrease on yields being observed. In addition, the morphology of the catalyst was constant in all the reaction cycles, as shown by SEM analysis.
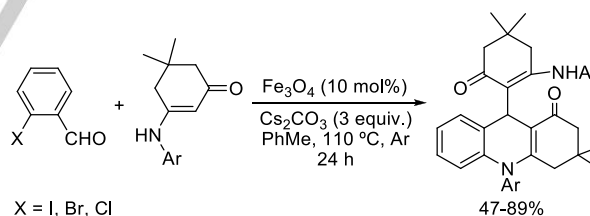

Scheme 8. Fe_3O_4 catalyzed 1,4-dihydroquinolines synthesis.

Magnetite also has been employed as a recyclable Lewis acid able to catalyze the regioselective ring opening of epoxides with different nucleophiles (Scheme 8). Thus, heteroaromatic compounds, such as indoles and pyrroles,[49] nitrogenated compounds[50] and thiols[51] have proved to be suitable nucleophiles for this purpose, yielding the corresponding functionalized alcohols with good results. In all cases, the catalyst was reused several times keeping almost the same activity in each cycle. It is worth mentioning, that in the reaction of thiols, XRD and SEM analysis were conducted after the reusability tests, showing almost identical particle distribution in both fresh and reused catalyst.
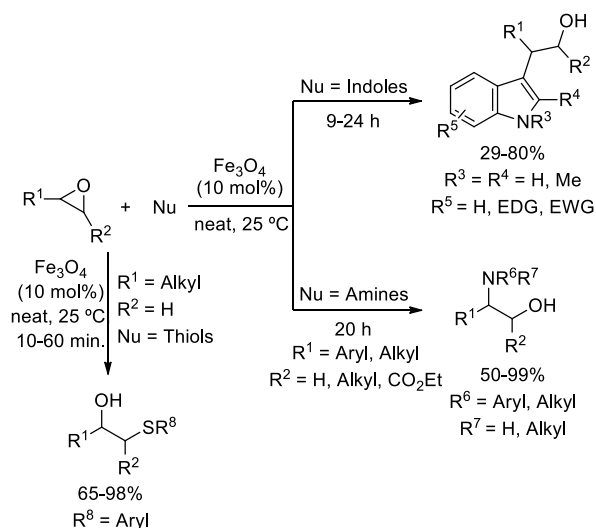
Scheme 9. Fe$_3$O$_4$ catalyzed epoxide ring-opening.

Alkyne coupling reactions can also be conducted using magnetite nanoparticles as recoverable catalyst. The C(sp^3)-C(sp^2) coupling between terminal alkynes and aryl iodides (Sonogashira-Hagihara reaction) has been described. Only 5 mol% of magnetite in ethylene glycol as solvent was required in this late-transition metal-free process. The main role of Fe$_3$O$_4$ as catalyst in this transformation was clearly demonstrated. An exhaustive study of the possible catalytic activity of the impurities (such as Pd, Cu, Ni and Co) present in commercially available magnetite was carried out. These impurities did not catalyze the mentioned coupling reaction in such small amounts (Scheme 10, eq. a).[52] More recently, the synthesis of alkynyl chalcogenides by means of the reaction between terminal acetylenes and diorganyl dichalcogenides has been also reported (Scheme 10, eq. b).[53]
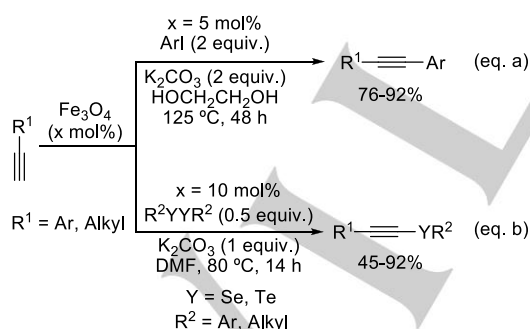
Scheme 10. Fe$_3$O$_4$ catalyzed alkyne coupling reactions.

The haloacylation of alkynes has been recently published. The magnetite catalyzed reaction between different acyl chlorides and acetylenic compounds produced in one hour, the corresponding β-chlorovinyl ketones in good yields and moderate to excellent Z-selectivity (Table 2). The reaction

products were further elaborated to the corresponding furanes in an iridium oxide impregnated magnetite (IrO$_2$-Fe$_3$O$_4$) catalyzed process. In addition, cyclopenten-2-ones and cyclopenta[a]naphtalen-1-ones can be obtained in high yields in a Nazarov-type cyclization, by choosing the appropriate acyl chloride (Table 2). Unfortunately, the catalyst could not be recycled.[54]

Table 2. Magnetite-catalyzed addition of acyl chlorides to alkynes.

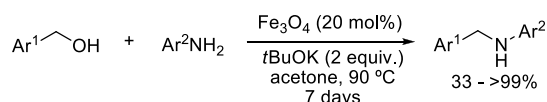| Acid chloride	Alkyne	Product/Yield
R^1 = Ar, Alkyl	R^2 = Alkyl, H, Ph R^3 = Alkyl, Ph	58-91% Z/E (2.2/1 - >20/1)
X = H, EWG, EDG	Alk—Alk	29-91%
	Ar—Alk	79-91%

[a] 13 mol% of Fe$_3$O$_4$ was used

In another reaction with alkynes in which magnetite plays the main role, the synthesis of vinyl boronates was tackled, through the borylation reaction of acetylenic compounds. The hydroboration products were obtained in high yields as a sole E-isomer using 5 mol% of catalyst. The nanomagnetite was recycled six-fold without apparent loss of activity (Scheme 11).[55]
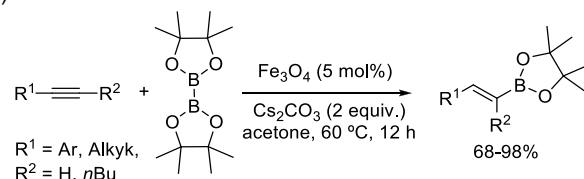
Scheme 11. Fe$_3$O$_4$ catalyzed hydroboration of alkynes.

The hydrogen autotransfer process, also called borrowing hydrogen process, is a high selective, environmentally friendly and atom-economic process for the synthesis of monoalkylated amines.[56] However, the catalysts employed are normally based on expensive transition metals, which are sometimes toxic and difficult to handle. Therefore, the whole process could be further improved by using a simple and recoverable catalyst as magnetite. Thus, the use of magnetite nanoparticles for the

monoalkylation of anilines and other poor electronic heteroaromatic amines using benzylic alcohols as electrophiles was reported (Scheme 12). The reaction turned out to be sluggish and the N-alkylation products were obtained in moderate to excellent yields. The catalyst was recycled eight times with only slight variations in yields.[57] This high recyclability could arise from the fact that no apparent sinterization occurred in the process, since no significant differences were observed between the fresh catalyst and the recycled, according to TEM images and BET area measurement experiments.

Ar^1$\diagup$OH   +   Ar^{2}NH$_2$ $\xrightarrow[\substack{t\text{BuOK (2 equiv.)}\\ \text{acetone, 90 ºC}\\ \text{7 days}}]{\text{Fe}_3\text{O}_4\ (20\ \text{mol\%})}$ Ar^1$\diagup$N(H)-Ar^2
33 - >99%

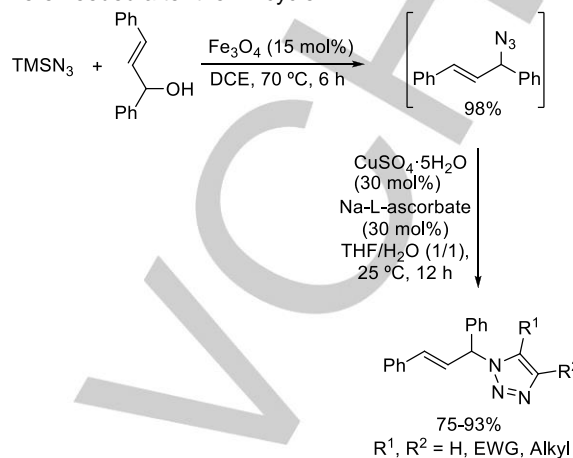**Scheme 12.** Fe$_3$O$_4$ catalyzed hydrogen autotransfer process.

The synthesis of ketones in a nanomagnetite catalyzed process has been recently described employing two different methodologies (Scheme 13). Using the first method, the cross-coupling reaction between an aromatic and an aliphatic carboxylic acid takes place releasing CO$_2$ and H$_2$O. Only 5-7 mol% of catalyst loading was necessary to promote the reaction, but harsh reaction conditions were required (250-270 ºC). Nevertheless, the corresponding ketones were obtained in good yields, in most cases.[58] Despite the harsh conditions employed, magnetite nanoparticles ranging from 17 to 28 nm, were present during the whole process, as revealed by SEM and TEM analysis conducted at different reaction stages. However, recycling experiments were not conducted. The second strategy involves a dehydrogenative coupling between aldehydes and phenols. After 24 hours of reaction, the corresponding *ortho*-hydroxybenzophenones were achieved in moderate to good yields.[59] In this case, magnetite nanoparticles were magnetically separated and reused five times with the same results.

Ar^{1}COOH   +   R^1$\diagdown$COOH (R^2) $\xrightarrow[\substack{\text{Dowtherm A}\\ \text{250-270 ºC}\\ \text{21 h}}]{\text{Fe}_3\text{O}_4\ (5\text{-}7\ \text{mol\%})}$ Ar^1-C(=O)-CH(R^1)(R^2)
27-86%
R^1 = Alkyl
R^2 = H, Alkyl

Ar^{1}CHO   +   Ar^{2}OH $\xrightarrow[\substack{\text{K}_2\text{CO}_3\ (2.2\ \text{equiv.})\\ \text{PhMe, 110 ºC}\\ \text{air, 24 h}}]{\text{Fe}_3\text{O}_4\ (20\ \text{mol\%})}$ (2-hydroxyphenyl ketone with OH)
40-67%
R = H, *t*Bu
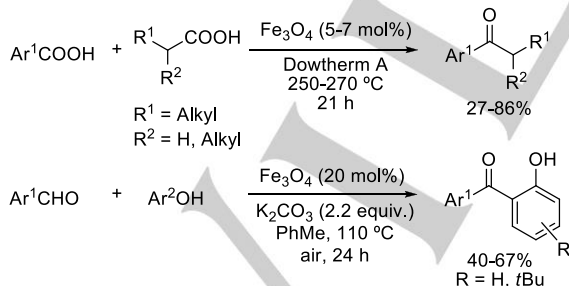
Scheme 13. Fe$_3$O$_4$ catalyzed synthesis of ketones.

The S$_N$1-type azidation of activated allylic alcohols has also been accomplished by employing nanomagnetite as catalyst. Thus, the allylic azides were obtained in high yields in only 6 hours. These azides were subsequently transformed in a

one-pot reaction into the corresponding triazoles, after removing the solvent and adding a copper(II) catalyst (Scheme 14).[60] The catalyst recycling was studied for seven azidation cycles. The yields remained above 95%, although longer reaction times were needed after the 4th cycle.

TMSN$_3$ +   (Ph, Ph allylic alcohol with OH) $\xrightarrow[\text{DCE, 70 ºC, 6 h}]{\text{Fe}_3\text{O}_4\ (15\ \text{mol\%})}$ [Ph-CH=CH-CH(N$_3$)-Ph]
98%

$\xrightarrow[\substack{\text{CuSO}_4\cdot 5\text{H}_2\text{O}\\ (30\ \text{mol\%})\\ \text{Na-L-ascorbate}\\ (30\ \text{mol\%})\\ \text{THF/H}_2\text{O (1/1),}\\ 25\ \text{ºC, 12 h}}]{}$

(triazole product: Ph-CH=CH-CH(Ph)-N, ring with R^1, R^2)
75-93%
R^1, R^2 = H, EWG, Alkyl

Scheme 14. Fe$_3$O$_4$ catalyzed azidation of allylic alcohols.

Magnetite has been used as catalyst for the rapid and selective trimethylsilyl protection of hydroxy groups in absence of solvent. The catalyst, used in 10 mol%, could be reused tenfold without significant loss of the catalytic performance.[61]

Finally, it is also worth mentioning that magnetite has been used in several studies as reusable initiating system for living cationic or radical polymerizations.[62]

3.4. Cobalt

The use of cobalt in organic synthesis has been traditionally linked to reactions involving carbonylations, π-bonds activation and radicals. However, recently the use of cobalt catalysts in organic transformations such as coupling reactions, C-H bond activations among others, has experimented a significant growth. This is an alternative to other noble transition metals. However, despite the multiple applications of cobalt complexes in organic synthesis and the instability of some cobalt complexes, as far as we know there are only two recent examples in literature of impregnated cobalt species onto magnetite as catalysts.

The first report deals with the use of a Co$_3$O$_4$-Fe$_3$O$_4$, obtained by wet impregnation in basic media and subsequent reduction of the corresponding oxide. This catalyst was used for the oxidation of alcohols, mainly benzylic, to the corresponding carbonyl compounds (Scheme 15). For this transformation, TBHP was the chosen oxidant, with products being obtained, at 80 ºC and after 6 hours of reaction, with 79 to 94% yields. Notably, the catalyst was recycled up to seven cycles with a slight loss of activity and negligible metal leaching.[63] The TEM image of the catalyst presented a spherical morphology of the nanoparticles with an average diameter ranging from 10 to 30

nm. The active catalytic specie was identified by XPS as Co_3O_4, excluding the existence of CoO and $Co(OH)_2$.
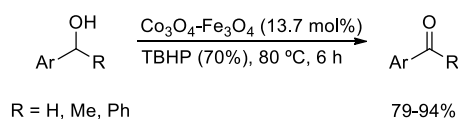
Scheme 15. Co_3O_4-Fe_3O_4 catalyzed oxidation of alcohols.

The second study describes the use of CoO impregnated on magnetite as an efficient and recyclable catalyst in the hydroacylation of azodicarboxylates. The best results were achieved for isopropyl azodicarboxylate with low catalyst loadings and under smooth reaction conditions. The corresponding hydroacylated products were generally obtained in high yields, even when aliphatic aldehydes were employed, (Scheme 16). Interestingly, the reaction with only magnetite or only cobalt oxide gave rise to products in moderate yields. In addition, the catalyst activity remained almost constant for ten cycles. After that, a partial CoO nanoparticles sinterization, as a consequence of the transformation into the corresponding hydroxide, under the reaction conditions were observed. However, apparently this change had no influence on the catalyst activity.[64]
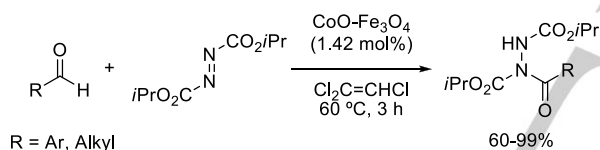
**Scheme 16.** CoO-Fe_3O_4 catalyzed hydroacylation of diazocarboxylates.

Under the reaction conditions a considerable leaching of cobalt(II) was observed. In fact, it is postulated that the reaction occurs in homogeneous phase and after reaction completion, the leached cobalt(II) species were re-adsorbed on the magnetite surface. Thus, CoO-Fe_3O_4 catalyst can be envisioned as a reservoir for Co(II) homogeneous catalyst.

3.5. Nickel

Despite the number of applications of nickel complexes in homogeneous catalysis, there are only a couple of studies where the use of impregnated nickel species onto magnetite surfaces were reported.

A NiO-Fe_3O_4 catalyst was applied for the reduction of nitroarenes and carbonyl compounds using glycerol as the hydrogen-transfer reagent. When using this NiO-Fe_3O_4 MNP (8.85 mol%) in glycerol and in basic media at 80 °C, different nitroarenes and aromatic carbonyl compounds were successfully hydrogenated. The corresponding amines and alcohols were obtained in high yields with short reaction times (Scheme 17). Remarkably, even halogen substituted arenes are hydrogenated without observing any dehalogenation process. The study of the surface composition by XPS revealed that the impregnated Ni species on the magnetite correspond to NiO, despite the authors claim to obtain Ni(0) nanoparticles by using a reducing agent after the impregnation methodology. The morphology observed by TEM images revealed spherical particles with an average size range of 15-30 nm. Finally, the catalyst has shown high performance even after eight cycles. Applying the hot filtration method a possible metal leaching was discarded.[65]
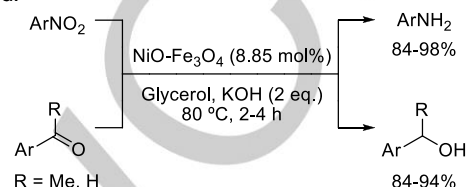
Scheme 17. Ni-Fe_3O_4 transfer hydrogenation of nitroarenes and carbonyl compounds.

Moreover, NiO-Fe_3O_4 also turned out to be an effective catalyst for hydroacylation of azodicarboxylates under the previously mentioned conditions of CoO impregnated MNP's (see Scheme 16).[64] However, in the most cases, the results achieved with CoO-Fe_3O_4 were superior.

3.5. Copper

Copper salts and complexes are one of the most employed catalysts in organic synthesis. This is due to the availability of copper compounds and their versatility. They have proven to be high efficient catalysts for a wide variety of organic transformations. Therefore, copper impregnated magnetite could be a recyclable catalyst, prone to be tested in a large variety of organic reactions.

In 2010 the first study about the use of impregnated copper on magnetite as catalysts for the three-component acetylene-Mannich reaction (A^3-coupling) to give propargylamines appeared (see Scheme 3). The reaction took place in only 3 h at 120 °C, giving the expected amines in quantitatively yields. The catalyst was recycled up to tenfold without losing its initial activity. Studies about a possible degradation of the catalyst under the reaction conditions, by means of the determination of BET surface area, concluded that no significant sinterization process occurred.[66]

The borylation of double bonds could be carried out using the same catalyst. The active copper specie, in this case, was CuO. After an exhaustive search for the optimal reaction conditions, it was observed that only 2.5 mol% of the recyclable catalysts was enough to effectively promote the addition of alkoxy diboron reagents on to both electron-rich and poor olefins (Scheme 18). As expected, the yields obtained with electron-poor olefins were higher. The performance of the catalyst remained high (ranging between 88-99%) for eight recycling experiments.[67]
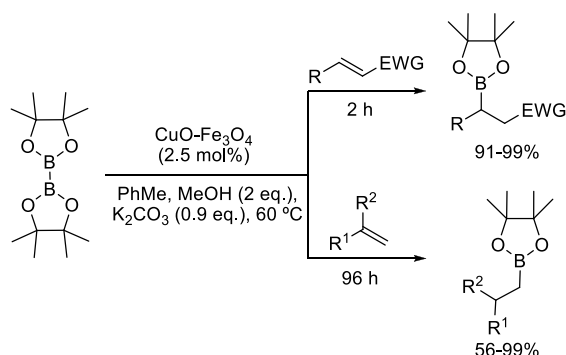
**Scheme 18.** CuO-Fe$_3$O$_4$ borylation of olefins.

The same impregnated CuO on magnetite catalyst was subsequently used for other organic transformations. The synthesis of benzofurans through a domino Sonogashira-cyclization protocol, by means of the reaction of 2-iodophenol and different alkynes was reported. The corresponding heterocycles were achieved in good to excellent yields (Scheme 19). The catalyst employed was reused up to ten times with the results remaining almost constant. In addition, the hot experiment excluded a possible metal leached catalyzed process. Importantly, neither the reaction catalyzed by Fe$_3$O$_4$, nor by CuO took place. These results can also reveal the importance of the CuO nanoparticles size, which are far more active than the bulk oxide, and a possible synergistic effect of both metal oxides.[68]
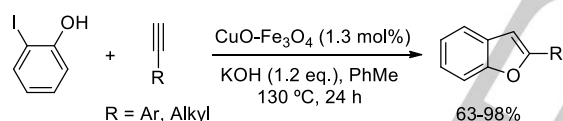
Scheme 19. CuO-Fe$_3$O$_4$ borylation of olefins.

2,5-Disubstituted furans were also successfully obtained, in a one-pot two-steps transformation, from hydration of the corresponding 1,3-dyines. Those products were synthesized in high yields by means of the homocoupling reaction of terminal alkynes employing CuO-Fe$_3$O$_4$ as catalyst.[69] The catalyst was only successfully recycled for three consecutive cycles, after which a considerable drop in yield was observed. The reasons behind this phenomenon could be the partial reduction of the Cu(II) species to Cu(0). This was observed by XPS studies. Also, the leach of Cu(II) active species towards the reaction solution was detected by ICP-MS after each cycle.

More recently, the aforementioned catalyst has been employed for the straightforward synthesis of imines through the reaction of alcohols with amines or nitroarenes using a dehydrogenation process as key reaction step. The imine formation can also be accomplished starting from the corresponding primary amines. In all examples, moderate to excellent yields were obtained using low catalyst loadings (Scheme 20).[70]
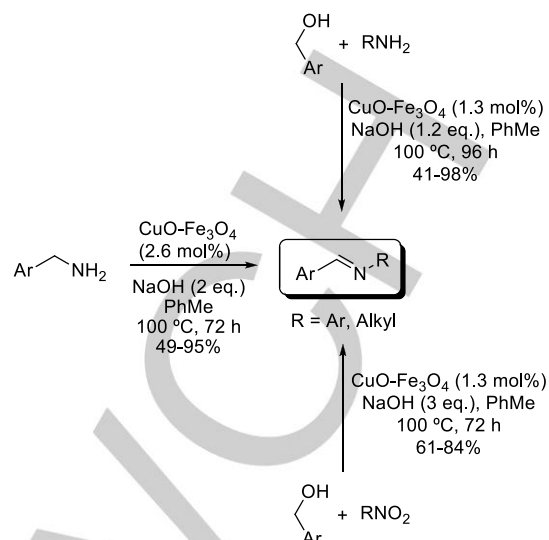
Scheme 20. CuO-Fe$_3$O$_4$ dehydrogenative imine formation.

Efforts to recycle the catalyst were unfruitful. The reason may be ascribed to the leaching of some amount of copper (detected by ICP-MS) and the change in the particle size distribution observed by TEM images. The particle size varied from 7.0±6 nm (maximum at 3 nm) for freshly prepared catalyst to 13.0±6 nm (maximum at 15 nm) for the recycled one. According to the observations made by the authors, both effects might be facilitated by the presence of nitrogenated compounds which could chelate the copper species.

Another related process involving a dehydrogenation reaction has been very recently described using this catalyst. Thus, the CuO-Fe$_3$O$_4$ catalyzed cross-dehydrogenative coupling between tetrahydroisoquinolines and different nucleophiles has been successfully accomplished in air. The corresponding products were obtained in yields varying from moderate to excellent, depending on the nucleophile employed. The reaction was performed in a choline chloride:ethylene glycol media as a deep eutectic solvent (DES), which avoids the use of volatile organic solvent (VOC's). Results were better in DES than in organic solvent (VOC's), making the whole process even more sustainable (Scheme 21).[71]

R = 4-FC$_6$H$_4$
Nu-H = alkynes, nitrometane, indole, phosphonates, ketones
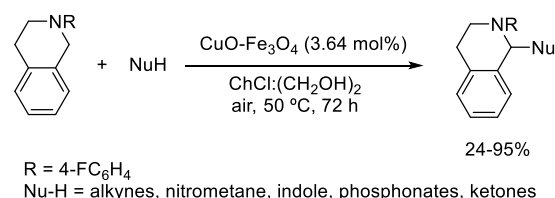
Scheme 21. CuO-Fe$_3$O$_4$ cross-dehydrogenative coupling.

The recovery of the catalyst was tackled from two perspectives. One strategy was to recycle both, the DES mixture and the catalyst, by simply extraction and decantation. In this way, the whole system was reused for 10 times without any

decrease in the yield. However, when only the catalyst was recovered by magnetic decantation, an important drop in yield was observed after the 4th cycle. This difference could be attributed to a higher leaching of copper species in the DES mixture. In fact, the DES recycled media was able to catalyze the dehydrogenative coupling after removal of CuO-Fe3O4. Thus, indicating the presence of active leached copper species. Despite the slight changes observed on the particle size, along with partial transformation of the CuO to Cu2O and Cu(OH)2 in the recycled catalyst (confirmed by XPS and AES), the catalytic activity seems not to be affected.

A similar catalyst has been successfully applied for the arylation of phenols with aryl halides. Good to high yields were achieved using bromo or iodoarenes. Meanwhile, poor yields were obtained using chloroarenes as reagents (Scheme 22). These results were maintained for 3 cycles. Although the activity of the catalyst decreased notably after the 3rd cycle, the spherical shape remained almost unaltered.[72]
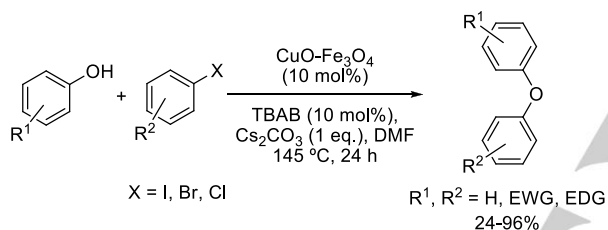

Scheme 22. CuO-Fe3O4 arylation of phenols.

This catalyst has also proven to be effective for the azide-alkyne cycloaddition reaction in water. Only 0.9 mol% of catalyst loading was enough to effectively promote the regioselective cycloaddition under mild reaction conditions (Scheme 23, eq. a). The multicomponent version was also studied and, after testing several reaction conditions, the expected product was obtained in 83% yield as the best result without solvent. Under these conditions, bimetallic catalyst NiO/Cu-Fe3O4 yielded the corresponding cycloaddition product in excellent yields (Scheme 23, eq. b). With this new catalyst, different triazoles were synthesized in moderate to excellent yields. It is remarkable that synergistic effects were observed for the bimetallic catalyst since the reaction in the presence of both impregnated magnetite as catalysts (NiO/Fe3O4 + CuO/Fe3O4) rendered the product in lower yields. In this case, the catalyst was recycled up to ten times without depreciation in its activity.[73] As expected from these results, the leaching of both metals was negligible after the recycling experiments. TEM images showed only a small change in particle size. XPS and AES revealed a change in the fresh catalyst from NiO, CuO and Cu2O species to Ni(OH)2 and Cu(OH)2 in the recycled one, which seemed not to affect the catalytic activity.
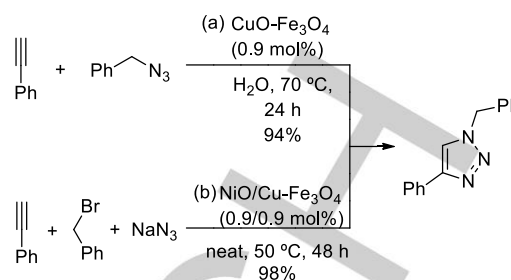
Scheme 23. CuO-Fe3O4 and NiO/Cu-Fe3O4 catalyzed synthesis of triazoles

Recently, the aforementioned catalyst was used in another synthesis of N-containing heterocycles derivatives. Different pyrazoles were obtained by Knoevenagel condensation between pyrazole-4-carbaldehyde derivatives and malononitrile and dimedona as nucleophiles. Only 0.5 mol% of catalyst was enough to efficiently promote the reaction within minutes at 140 ºC and in absence of solvent. The catalyst was reused up to 6 times without any substantial loss in its activity (Scheme 24).[74] The CuO presence was unambiguously assigned by the observed XPS pattern, being the particle size of the MNP in the range of 20-30 nm according to TEM images.
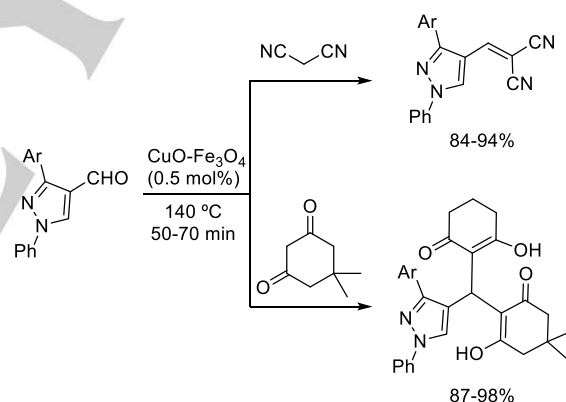

Scheme 24. CuO-Fe3O4 catalyzed Knoevenagel condensation.

3.7. Niobium

Niobium compounds, and particularly niobium oxides, have been not paid much attention in organic synthesis in comparison with neighboring periodic table elements. However, a very recent work about multicomponent Biginelli reaction has been reported employing a niobium impregnated magnetite as catalyst. The corresponding 1,4-dihydropyrimidinones were obtained in high yields, regardless of the nature and electronic properties of the coupling partners. Interestingly, the reaction only proceeded with poor yields when either Nb2O5 or magnetite was used. The catalyst was recycled up to eight cycles without any apparent loss in its activity (Scheme 25).[75] The catalytic

nanoparticle was thoroughly characterized using techniques such as XRD, ICP-OES, HRTEM and STEM.
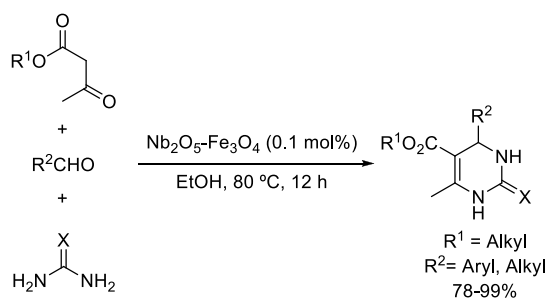
Scheme 25. Nb$_2$O$_5$-Fe$_3$O$_4$ catalyzed Biginelli reaction.

3.8. Molybdenum

Molybdenum compounds in organic synthesis are inevitably linked to carbenes and olefin metathesis as well as oxidation reactions. However, to the best of our knowledge, there is only a single report about the use of molybdenum oxide supported on magnetite using the impregnation methodology. The catalyst thus obtained, MoO$_3$-Fe$_3$O$_4$, turned out to be a highly versatile and recyclable catalyst. This catalyst was not only used for oxidation reactions but also for other transformations, such as transfer hydrogenations, hydrations and three-component acetylene Mannich reactions (Table 3).[76] The XPS analysis of the catalyst confirmed the presence of MoO$_3$ phase, being the particles sized in the 15-30 nm range as observed by TEM images. In addition, a spherical morphology in a wooly cloud-like cluster was observed.

**Table 3.** Organic transformations catalyzed by MoO$_3$-Fe$_3$O$_4$ (0.25-0.5 mol%).[a]

Entry	Reagents	Products	Yield (%)
1	PhCH$_2$OH	PhCHO	89
2	3-ClC$_6$H$_4$NO$_2$	3-ClC$_6$H$_4$NH$_2$	93
3	PhCN	PhCONH$_2$	95
4	Ph–≡ + ArCHO + piperazine	piperazine product	90-92

[a] For detailed reaction conditions, see ref. 76

3.9. Ruthenium

Despite the multiple applications of ruthenium compounds in organic synthesis, the use of impregnated ruthenium magnetite has been scarcely reported, being mainly focused on organic transformations dealing with oxidation and reduction processes. The first publication about the use of ruthenium oxide impregnated magnetite appeared in 2000, describing the use of such catalyst in the gas water shift reaction.[77] The same research group also studied its activity for the dehydrogenation of 1-butanol to give butyl butyrate.[78]

The reduction of ketones to alcohols in a Meerwein-Ponndorf-Verley type hydrogen transfer reaction was described, obtaining with high yields the corresponding products. Interestingly, the opposite process, the oxidation of alcohols in the presence of an oxygen atmosphere, was also successfully accomplished employing the same catalyst (Scheme 26). In addition, the authors also describe the oxidation of amines to the corresponding imines or nitriles. This catalyst was recovered and reused once maintaining the same activity and no leaching was observed.[79]
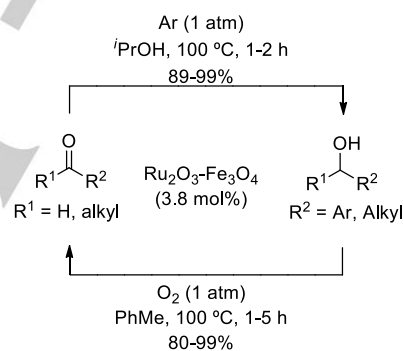
Scheme 26. Ru$_2$O$_3$-Fe$_3$O$_4$ catalyzed reduction and oxidation reaction.

Some years later, a catalyst prepared from different ruthenium precursors, was found to promote the selective reduction of the carbonyl function on α,β-unsaturated ketones. However, although the catalyst was quantitatively recovered, after three cycles the activity decreased considerably due to agglomeration of particles and a considerable ruthenium leaching. The catalyst presented an average particle size of 15 nm. The presence of Ru, confirmed by EDAX and ICP-OES analysis, decreased the saturation magnetization in comparison with the bulk magnetite.[80]

Finally, it is also remarkable the use of the aforementioned catalyst for the N-alkylation of amines, nitroarenes, sulfonamides and sulfinimides using alcohols as electrophiles through a hydrogen autotransfer process.[56] In most cases, the corresponding secondary amines (or imines) were obtained in good to excellent yields (Table 4). In the particular case of the N-alkylation of anilines with benzylic alcohol, the catalyst was recycled, using magnetic separation, ten times. The yields exceeded 90% in all the cases.[81]

Table 4. *N*-alkylation of nitrogen containing compounds with alcohols catalyzed by Ru_2O_3-Fe_3O_4.

Nitrogen source	Products	Yield (%)
ArNH$_2$[a]	R^1–CH$_2$–N(H)–Ar	71-99
ArNO$_2$	R^1–CH=N–Ar	44-99
Ar–S(O)$_2$–NH$_2$	Ar–S(O)$_2$–N(H)–R^1	86-99
^{t}Bu–S(O)–NH$_2$	^{t}Bu–S(O)–N(H)–R^1	67-76

Reaction conditions: alcohol + R^{2}NX$_2$, Ru_2O_3-Fe_2O_3 (1.3 mol%), KOH (1.3-3 eq.), PhMe, 85-130 °C, 24-72 h, product R^1–CH=N(X)–R^2

[a] In the case of using NaOH as base the corresponding imine was obtained

3.10. Rhodium.

A hollow rhodium impregnated catalyst has been used in the reduction of different nitroarenes. An excess of hydrazine was used in ethanol at 80 °C, affording the corresponding products in nearly quantitative yields. This catalyst could be reused fivefold, after magnetic decantation, without any detrimental effect on the results.[82]

3.11. Palladium.

The enormous amount of applications and organic transformations in which homogeneous palladium species are involved, together with the high cost of the palladium compounds has led to a plethora of scientific work about the synthesis and use of supported palladium nanoparticles. It is not surprising that several studies dealing with the synthesis and use of supported palladium species on magnetite nanoparticles, by means of the wet impregnation method, have been reported. The first one describes the use of a palladium(0) supported nanoparticles for the carbonylative Sonogashira coupling reaction of aryl iodides with terminal alkynes in a phosphine-free transformation. The catalyst employed, was prepared by the classical impregnation methodology (Fig. 2). A KBH$_4$ solution was used, in order to reduce the palladium(II) species to its elemental form. The process normally renders the corresponding products in high yields using only 0.2 mol% of catalyst. Its recycling was possible up to seven times with a slight loss of activity (Scheme 27).[83] The TEM images revealed iron oxide nanoparticles of 25-50 nm and entrapped palladium nanoparticles of 5 nm.
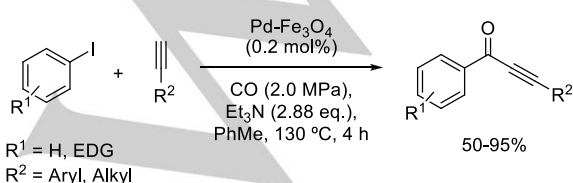
Scheme 27. Pd-Fe_3O_4 catalyzed carbonylative Sonogashira reaction.

Later on, in 2010, an important breakthrough in the use of impregnated metal species on magnetite was reported. The work describes the use of chiral-carbene decorated Pd-Fe_3O_4 catalyst for the asymmetric *α*-arylation of cyclic ketones (Scheme 28).[84] Although the yields and *ee*'s reached were moderate to good, this challenging transformation represents, to the best of our knowledge, the first and by far, the only example in which an impregnated metal specie has been employed in an enantioselective process.[85] The heterogeneous nature of the catalyst was demonstrated by several experiments such as XPS, ATR-IR, SEM-EDX and TEM. The catalyst was recycled five times without a significant decrease in both yield and enantioselectivity. In this regard, the authors claim that the carbene not only plays a role as chiral modifier but also as a stabilizer of palladium nanoparticles. Thus, preventing the possible leaching, that was not observed by ICP-OES after the recycling experiments. Curiously, the reaction performed with the same chiral carbene and Pd(AcO)$_2$ produced the desired product as a racemic mixture.
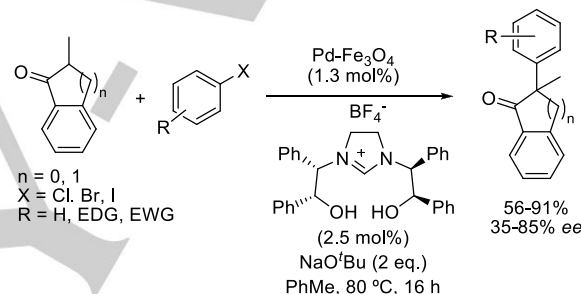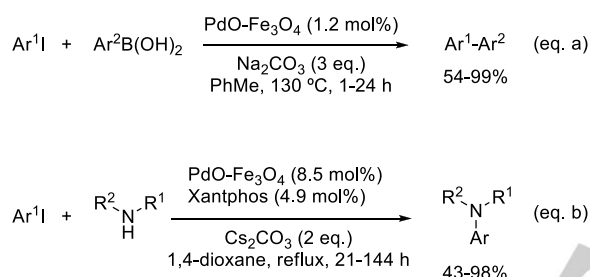

Scheme 28. Chiral NHC-Pd-Fe_3O_4 catalyzed enantioselective arylation reaction.

Shortly after, the use of PdO-Fe_3O_4 catalyst for the multicomponent reductive amination reaction was reported. Under optimized reaction conditions several secondary amines were obtained in high yields at room temperature independently of the nature of the amine employed. Nevertheless, the reaction became sluggish when poor nucleophilic amines were employed, being necessary harsh reaction conditions and longer reaction times (Scheme 29). Notably, this catalytic system also turned out to be effective in the reductive amination process when employing secondary amines. Furthermore, other reduction processes such as reduction of imines and sulfoxides were carried out using the same catalyst. However, the catalyst recycling was unsuccessful and after the third use the yield dropped dramatically. A possible explanation arises from the fact that the exposure of the catalyst to a reducing media produces a Pd(II) reduction to the less active and more prone to leach Pd(0) nanoparticles. The adsorption of silica at the surface of the MNP was also detected by XPS.[86]
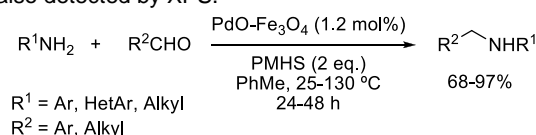
Scheme 29. PdO-Fe_3O_4 catalyzed reductive amination reaction.

In the same year, the same impregnated catalyst was also reported for the ligand-free Suzuki-Miyaura cross-coupling reaction. The reaction worked especially well for electron-rich aryl iodides and a wide variety of boronic acids (Scheme 30, eq. a). As in the previous case, the catalyst recycling was not possible, probably due to the poisoning as consequence of the different salt adsorption on the metal surface. This was visually observed. A slight leaching was also detected by ICP-MS.[87] Similar results were obtained when hollow palladium impregnated magnetite catalyst was used.[82]

In a more recent publication, this palladium impregnated system has been also able to effectively catalyze the Buchwald-Hartwig amination reaction. However, relatively high amounts of palladium and the presence of a phosphine-based ligand, such as Xantphos, were required (Scheme 30, eq. b). These small drawbacks were overcome by the fact that the catalyst could be recycled up to five times with only a slight decrease in its activity. In addition, it is important to remark that not only PdO was present in the catalyst but also Pd(0). According to the XPS spectrum the presence of Pd(OH) could not be excluded.[88]

$$Ar^1I \ + \ Ar^2B(OH)_2 \xrightarrow[\substack{Na_2CO_3 \ (3 \ eq.) \\ PhMe, \ 130 \ ^\circ C, \ 1\text{-}24 \ h}]{PdO\text{-}Fe_3O_4 \ (1.2 \ mol\%)} Ar^1\text{-}Ar^2 \quad (eq. \ a)$$
54-99%

$$Ar^1I \ + \ \underset{H}{R^2\text{-}N\text{-}R^1} \xrightarrow[\substack{Cs_2CO_3 \ (2 \ eq.) \\ 1,4\text{-}dioxane, \ reflux, \ 21\text{-}144 \ h}]{\substack{PdO\text{-}Fe_3O_4 \ (8.5 \ mol\%) \\ Xantphos \ (4.9 \ mol\%)}} \underset{Ar}{R^2\text{-}N\text{-}R^1} \quad (eq. \ b)$$
43-98%

Scheme 30. PdO-Fe$_3$O$_4$ catalyzed Suzuki-Miyaura cross-coupling and Buchwald-Hartwig amination reactions.

In addition, PdO-Fe$_3$O$_4$ or Pd-Fe$_3$O$_4$ catalysts have been also employed for other transformations such as the hydrogenation of acetylenic derivatives,[89] or nitrocompounds[90] and the selective dehalogenation of organic compounds from aqueous wastes.[91]

3.12. Cerium

Ceria (CeO$_2$) has been traditionally employed as a support for other noble metal based catalysts but not as a catalyst itself in organic synthesis. However, recently two reports about the use of impregnated ceria on magnetite as recoverable catalyst have been described.

In the first one, a mixture of CeO$_2$/Ce$_2$O$_3$ acts as a catalyst for the synthesis of 1,4-dihydropyridines in a multicomponent reaction. From the two main oxide phases of Ce present in the catalyst, CeO$_2$ turned out to be the main component on the surface as indicated by XPS analysis. The reaction proceeds rapidly and high yields were obtained for the corresponding products within minutes (Scheme 31). The catalyst was reused six times maintaining the high yields. The hot filtration experiment revealed that the leaching was negligible.[92]
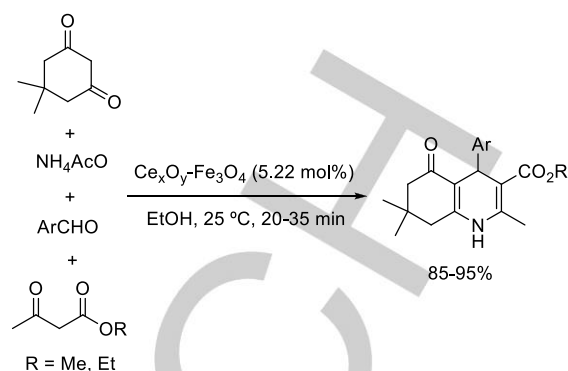
Scheme 31. Ce$_x$O$_y$-Fe$_3$O$_4$ catalyzed synthesis of dihydropyridines.

A ceria catalyst impregnated on magnetite has proven to be effective for the C-H arylation of heterocycles. In this case only CeO$_2$ was present on the MNP, as confirmed by the XRD pattern. Different benzoxazoles and benzothiazoles were selectively arylated with moderate to good yields, not only when employing aryl halides but also with arenediazonium salts. In this latter case, the reaction was carried out in water (Scheme 32). However, the reusability of the catalyst was not as good as desirable. Despite no apparent leaching was observed from ICP-MS, a decay in the yield of the product was found after each cycle.[93]
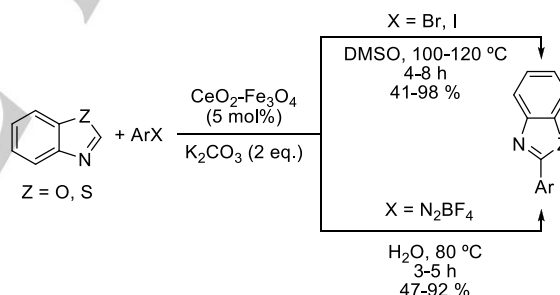
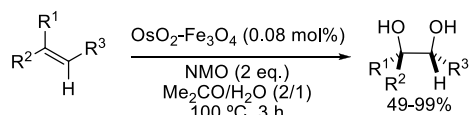**Scheme 32.** CeO$_2$-Fe$_3$O$_4$ catalyzed C-H arylation of benzoxazoles and benzothiazoles.

3.13. Tungsten

The applications of tungsten compounds in organic synthesis, beyond the chemistry of carbenes, metathesis and oxidations, are scarcely studied. Therefore, It is not surprising that the only report of a WO$_3$ supported on magnetite by impregnation method has been described as photosensitizers and photocatalysts.[94]

3.14. Osmium

Osmium is often linked to OsO$_4$ and its use as oxidizing agent. It is able to perform the oxidation of alkenes to the corresponding vicinal diols or to the corresponding carbonyl compounds, normally in combination with sodium periodate, through an olefin oxidative cleavage. However, its high toxicity

converts such compound in potentially dangerous due, in part, to its high volatility. Therefore, the heterogenization of osmium oxides, which would reduce considerably this potential danger, would be highly desirable. Among different attempts for that purpose, the wet impregnation of OsO_2 on magnetite, reported recently, is the simplest and the more straightforward way of immobilization of osmium oxides. The catalyst turned out to be extremely active for the *syn*-dihydroxylation of alkenes, giving rise to the corresponding vicinal diols in good to excellent yields. Only 0.08 mol% of catalyst loading was required to carry out the reaction depicted in Scheme 33. Unfortunately, after the magnetic separation, the catalyst could not be successfully reused again.[95] A possible explanation was the lack of $OsO_2(OH)_2$ in the recycled catalyst found by the XPS study, being present in a 1:1 ratio on the fresh sample. Os(VI) may be the active catalytic specie. Its absence observed by ICP-MS could be due to a partial leaching as well as its transformation to OsO_2 under the reaction conditions.

Scheme 33. OsO_2-Fe_3O_4 catalyzed *syn*-dihydroxylation of alkenes.

3.13. Iridium.

Iridium complexes and salts are commonly used compounds in organic synthesis, catalyzing and promoting a wide range of reactions. By the contrary, the corresponding iridium oxides are not as currently employed, and are even less used when they are impregnated on magnetite. To the best of our knowledge, there is only one example reported in which an IrO_2 impregnated on magnetite has been used in the cross-alkylation reaction of primary alcohols (Guebert reaction type) as catalyst. The catalyst resulted very efficient and 0.14 mol% loading was enough to obtain the corresponding cross-alkylation products. The reaction between different benzylic and aliphatic alcohols afforded the corresponding products in good to excellent yields (Scheme 34). In addition, the iridium-based catalyst could be re-used up to ten times maintaining its high activity nearly intact. This is in accordance with the observed TEM images, which revealed that the particle size remained almost constant suggesting no sinterization processes. Moreover, the XPS spectra were exactly the same for the fresh catalyst and the recycled catalyst. A negligible leaching was observed by ICP-MS.[96]
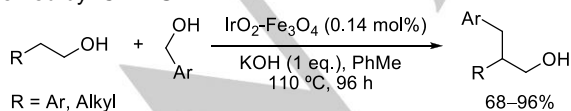
Scheme 34. IrO_2-Fe_3O_4 catalyzed cross-alkylation reaction of primary alcohols.

3.16. Platinum

Platinum species are known to be excellent activators of multiple C-C bonds, and make them prone to nucleophilic attack; hence, they are amongst the so-called π-Lewis acids. Taking advantage of this fact, multiple applications of those compounds have been developed and implemented in organic synthesis. For example, PtO_2 (Adam's catalyst) has been extensively used as heterogeneous catalyst for the hydrogenation of multiple bonds. Nevertheless, its high cost makes platinum compounds perfect candidates to be supported. As far as we know, there is only one report about supported platinum oxides on magnetite by wet impregnation. In this work an impregnated mixture of PtO/Pt_2O catalyzes the hydrosilylation of alkynes. The reaction is extremely fast and the products were obtained in high yields after 15 minutes, using low catalyst loadings (Scheme 35). In addition, this transformation showed a wide reaction scope for both reactants, alkynes and silanes. The high activity of the catalyst was kept even after ten reuses. The leached Pt amount and sinterization process were negligible according to the ICP-MS and TEM particle size measurement analysis.[97]
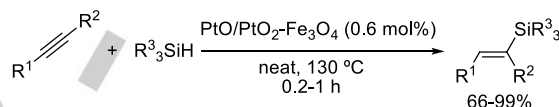
Scheme 35. PtO/PtO_2-Fe_3O_4 catalyzed hydrosilylation of alkynes.

In a recent study, platinum(0) nanoparticles were adsorbed on the surface of nanomagnetite. The resulting catalyst was successfully employed for the hydrogenation of chloronitrobenzene to chloroaniline at room temperature in a solvent-free reaction. The catalyst was reused up to four times with the same result.[98]

3.17. Gold

Although the use of homogeneous species of gold, as catalyst, has experimented a spectacular growth in recent years, this is not the case for the impregnated magnetite version. In this sense, there are only two examples in literature about the use of impregnated Au(0) nanoparticles on magnetite and their application in oxidation reactions (Scheme 36). The dehydrogenation of 1,4-butanodiol took place in the presence of hydrogen, under flow conditions (60 mL/min), reaching the expected lactone in only 60% yield. Slightly lower yields were obtained under argon or air atmosphere. This fact was explained by measuring the particle size. Thus, under oxidizing conditions (air atmosphere) the dispersed gold nanoparticle size is in the range of 12 nm due to partial oxidation. Meanwhile under reducing atmosphere (H_2), the nanoparticle size is 2.7 nm. Additionally, under air, a crystal phase transformation of the support from magnetite to the less active and more stable maghemite (γ-Fe_2O_3) was observed.[99]
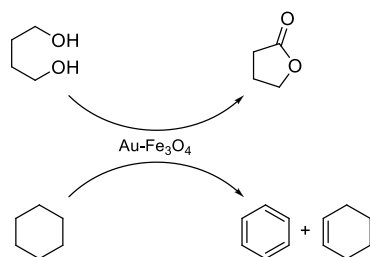
Scheme 36. Au-Fe₃O₄ catalyzed dehydrogenation reactions.

In another study, the oxidation of cyclohexane was examined in a fixed bed reaction in the presence of oxygen (4 mol% in helium). This process rendered a mixture of benzene and cyclohexene, with the highest benzene selectivity being 85% at 350 °C.[100]

4. Summary and Outlook

The social demand for environmental friendlier process has forced chemists to develop active catalysts which are easy recovered and recycled. Magnetic catalysts have the impressive property of being isolated from the reaction media by a simple and low-cost energy magnetic decantation. Although both, magnetite and the impregnation protocol were well known, it is only in the last decade when this combination has blossomed as an interesting alternative for catalyst preparation.

As introduced in this review, there are examples of nearly all transition metal impregnated on magnetite (first generation catalysts). Their use in many different reactions including; photochemistry, condensations, hydrogen autotransfer processes, additions, oxidations, hydrogenations, cross-coupling and multicomponent reactions, showed the broad scope for this type of catalysts. In many cases metal impregnated magnetite displays higher activity compared with other heterogeneous and/or homogeneous catalysts. Moreover, these types of catalysts are recyclable. It has been also described along this review the possibility of making the so-called second generation catalysts. These new type of catalysts come from the post-modification of this metal oxides supported on magnetite by reduction/oxidation processes. Thus, they are able to promote other type of unusual reactions for these metals. Also, the post-modification can be accomplished by addition of ligands, even chiral ones. This fact broadens their application in other organic transformations, including enantioselective processes. In view of all these evidences a bright future for this type of catalyst, not only in the academia but also in industry, can be envisaged.

Despite all these developments, the field is open for some important improvements. For instance, the amount of catalyst can still be reduced to allow their application in large scale synthesis. Also, the relationship between particle size, shape, morphology and other structural features with the catalytic activity must be deeply studied.

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Entry for the Table of Contents

Layout 1:

REVIEW

Old material, new catalyst: Magnetite is a well-known material but its use as support for the construction of nano-structures by an impregnation protocol is a new entry to the preparation of different catalysts. These impregnated catalysts have been used in a myriad of reactions. Their stability, recyclability, isolation, reactivity, and easy preparation anticipate a prosperous future in further transformations.
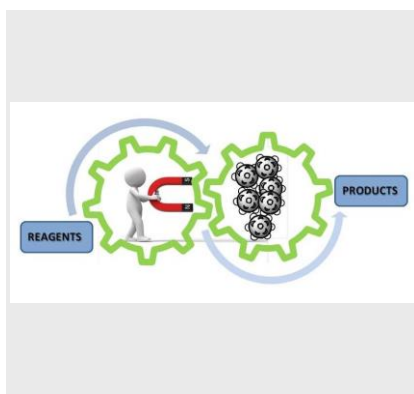
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