

# Fullerenes for Catalysis: Metallofullerenes in Hydrogen Transfer Reactions

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**[60]Fullerene hybrids have successfully been used as catalysts in hydrogen transfer reactions, namely ketones reduction and *N*-alkylation with alcohols. Due to the poor solubility in polar solvent, these hybrids behave as homogeneous/heterogeneous catalysts that can be mechanically separated and reused for several times while the final products do not need chromatographic separation.**

Hydrogenation, dehydrogenation, hydrogen storage and transfer constitute exciting and challenging topics for the replacement of a fossil fuel-based economy by clean, safe and easy accessible hydrogen-based processes. In particular, the importance of avoiding hazardous gas, such as molecular hydrogen, in organic chemistry has driven to the “golden age of the transfer hydrogenation” by means of different strategies and catalysts for hydrogenation reactions.<sup>1</sup> Since these catalysts are based on noble metal complexes, high efficiency, mild conditions, low loading and recyclability are required.

On the other hand, transition metals have been very often associated in catalysis to carbon-based structures. A classic approach relies in the use of carbon materials as support for active metals while, more recently, carbocatalysis has emerged as an effort to remove completely metals by the use of carbon nanostructures with metal-free active sites.<sup>2</sup> As heterogeneous catalysis, both strategies benefit from an easy use (mechanical separation of catalyst and products) while they suffer for the lack of a defined structure of the catalyst, sometimes reproducibility, and for the lack of a clear mechanism as it happens for molecular homogeneous catalysts.

In this regard, we wondered if fullerenes, as the sole molecular carbon allotropes, were able to gather the

properties of a homogeneous catalyst with those of carbon-based materials and, eventually, to find synergies with the chemical properties of transition metals for chemical transformations. So far, despite fullerenes have been thoroughly investigated and a wide variety of derivatives,<sup>3</sup> including chiral fullerenes,<sup>4</sup> have been synthesized, their use in catalysis has been almost neglected.

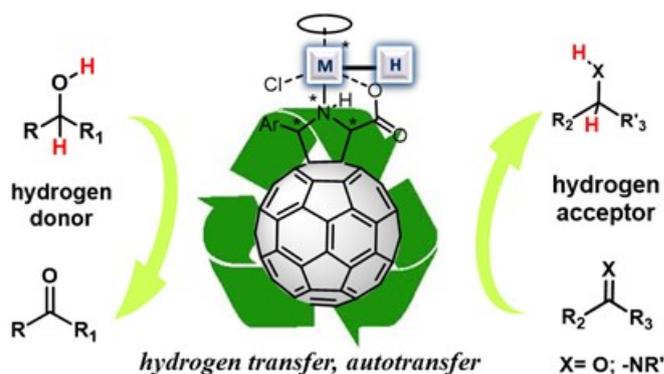


Fig 1. Transfer hydrogenation by fullerenes hybrids.

In order to address this issue, we have prepared fullerene hybrids where C<sub>60</sub> is endowed with highly active metal atoms in hydrogenation transfer reactions, such as Ir,<sup>[6]</sup> Ru,<sup>[7]</sup> or Rh,<sup>[8]</sup> and that present a metal centered chirality.<sup>5</sup> Herein, we report on the catalytic ability of these [60]fullerene hybrids in transfer hydrogenation reactions such as ketones reduction and *N*-Alkylation with alcohols by hydrogen autotransfer process (borrowing hydrogen). Remarkably, as result of the very poor solubility of fullerene cages in polar solvents, they merge the advantages of the molecular homogeneous catalyst (defined structures and stereochemical configurations) with those of heterogeneous catalysts (products are readily isolated and the catalyst recovered by mechanical means and reused). Hydrogen transfer is an alternative hydrogenation process that avoids the use of potentially explosive and difficult to handle gaseous H<sub>2</sub>. In this process, hydrogen formed from dehydrogenation of a donor molecule (typically an alcohol that

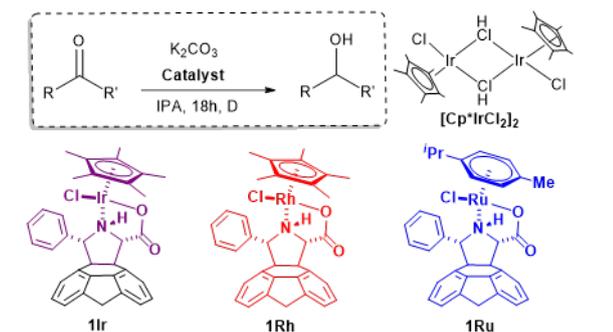
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is used as solvent or in a large excess) is added to a hydrogen acceptor molecule. In this regard, transition metal-catalyzed hydrogen transfer reactions are undergoing a growing interest since they fulfil the needs for safe, clean and atom economy processes.<sup>6</sup> Thus, we focussed our attention on the racemic metallo-pyrrolidino[60]fullerenes (metallo-fulleropyrrolidines) **1Ir**, **1Rh**, **1Ru**,<sup>5</sup> previously prepared (see also SI for their synthesis and configurational details), with the aim to evaluate their efficiency as catalysts in such a kind of chemical transformations.

**Table 1.** Ketones hydrogenation with isopropanol as solvent/hydrogen source.



Entry <sup>a</sup>	Catalyst (mol% Ir)	R-, R'-	Isolated yield (%)
1	[Cp*IrCl <sub>2</sub> ] <sub>2</sub> (0.5)	Ph-, -CH <sub>3</sub>	65
2	<b>1Ir</b> (0.5)	Ph-, -CH <sub>3</sub>	>99
3	<b>1Ir</b> (0.1)	Ph-, -CH <sub>3</sub>	66 <sup>b</sup>
4	<b>1Ir</b> (1.0)	Ph-, -CH <sub>3</sub>	>99
5	<b>1Ir</b> (rc.) <sup>c</sup>	Ph-, -CH <sub>3</sub>	>99
6	<b>1Ir</b> (rc.) <sup>c</sup>	Ph-, -CH <sub>3</sub>	>99
7	<b>1Ir</b> (rc.) <sup>c</sup>	Ph-, -CH <sub>3</sub>	>99
8	<b>1Ir</b> (rc.) <sup>c</sup>	Ph-, -CH <sub>3</sub>	>99
9	<b>1Ir</b> (rc.) <sup>c</sup>	Ph-, -CH <sub>3</sub>	15 <sup>b</sup>
10	<b>1Ir</b> (0.5)	-(CH <sub>2</sub> ) <sub>5</sub> -	>99
11	<b>1Ir</b> (0.5)	Cyclohexyl-, -H	>99
12	<b>1Ir</b> (0.5)	<i>n</i> Bu-, -H	>99
13	<b>1Rh</b> (0.5)	Ph-, -CH <sub>3</sub>	76 <sup>b</sup>
14	<b>1Ru</b> (0.5)	Ph-, -CH <sub>3</sub>	17 <sup>b</sup>

[a] Reactions were carried out in refluxing isopropanol by using 40 mg of acetophenone in 2 mL of isopropanol and K<sub>2</sub>CO<sub>3</sub> in the same amount as the catalyst. [b] Conversions have been determined by NMR. [c] rc.: recycled catalyst. Iridium fulleropyrrolidine **1Ir** recovered after centrifugation from a previous reaction.

Firstly, we tested the catalytic activity of iridium-fullerene **1Ir** in the reduction of ketones by hydrogen transfer from isopropanol that is also used as solvent. Iridium dimer has been used as reference and, indeed, the presence of 0.5% iridium equivalents of this catalyst affords the acetophenone reduction with a 65% yield after 18 hours (Table 1, entry 1). For our delight, iridium-fulleropyrrolidine **1Ir** gives rise to a quantitative reduction of acetophenone after 18 hours with only 0.5% of catalyst loading (entry 2). The use of minor

amounts of catalyst led to 66% of conversion after 18 hours (entry 3). These results reveal a strong increase of the catalytic efficiency with respect to the iridium dimer, being among the most efficient iridium-based catalysts. Furthermore, it is worthy to note two other important advantages in the use of this new hybrid catalyst. Firstly, at room temperature, it is mostly insoluble in isopropanol as well as in other polar solvents and, therefore, it can be removed from the reaction medium by mechanical means, thus featuring at the same time the advantages of both homogeneous and heterogeneous catalysis. Therefore, after filtration or centrifugation, the catalyst could be removed from the solution or recovered for a further use, respectively, keeping the product pure without any further purification but solvent elimination.

Secondly, the recovered catalyst has successfully been reused for up to 5 times without observing any loss of catalytic efficiency (entries 4-8). However, exposition to oxygen and/or light has to be carefully avoided since it is the main cause of decreasing efficiency (entry 9).

In addition, catalyst **1Ir** was also able to efficiently reduce cyclohexanone, cyclohexanecarboxaldehyde and pentanal (entries 10-12).

Finally, **1Rh** and **1Ru** did not display the same efficiency and afforded 76% and 17% yield, respectively (entries 13, 14).

Based on the aforementioned results, we wondered if these hybrid catalysts could be useful in hydrogen auto-transfer processes where hydrogen donor and acceptor stem from the same source as it occurs in the *N*-alkylation of amines with alcohols (see scheme in table 2).<sup>7</sup>

We have chosen the *N*-alkylation of aniline with *p*-methoxybenzyl alcohol as reaction model to study the efficiency of the new hybrid catalyst and the effect of the fullerene cage in the process.

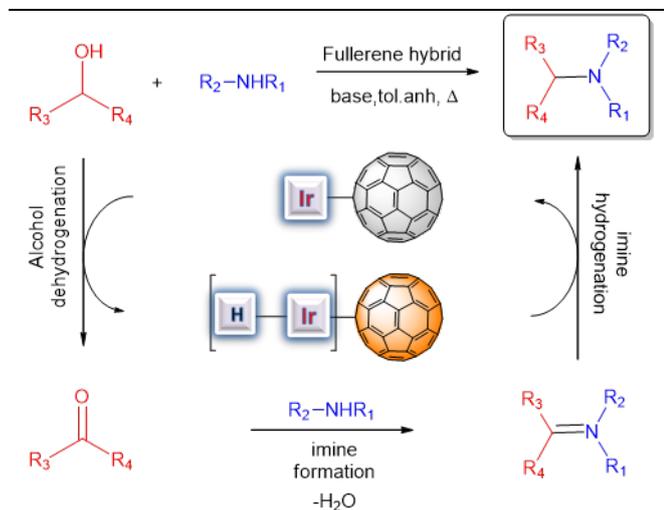
Cp\*Ir complex dimer was firstly used in 5% mol by Fujita and Yamaguchi affording the corresponding amine in 95% yield (Table 2, entry 1) and it has frequently been used as benchmark for this reaction.<sup>8</sup> While the iridium proline (**2**) was one of the more efficient complex able to afford the *N*-benzylated aniline in 93% yield in a 2% of catalytic loading, after 24 h.<sup>9</sup> Notably, the use of the iridium-fullerene hybrid **1Ir** promotes a quantitative yield with just 1.25% of catalyst (92% isolated yield, entry 3).

The scope of this catalyst has also been extended to other substrates such as aliphatic alcohols or amines and, as a general rule, the efficiency and yields obtained depend on the facility of formation of the intermediate imine.

Thus, this hybrid catalyst successfully carries out the alkylation of aniline with aliphatic alcohols such as cyclohexanol, 2-octanol or 3-hexanol in the presence of MgSO<sub>4</sub>, as dehydrating agent, with conversions that depend on the stability of the corresponding imines (99%, 91% and 40% respectively, entries 4, 5 and 6). Alkylation of *N*-methylaniline with *p*-methoxybenzyl alcohol was carried out using 4% of catalysts: Cp\*Ir dimer affords dialkylated aniline in 65% conversion (entry 7) while fullerene-iridium complex displayed a better efficiency (86%, entry 8). A similar behaviour was observed in the *N*-benzylated of piperidine that occurs with 6% yield with

Cp\*Ir dimer and in 32% yield with fullerene-iridium catalyst (entries 9, 10). Finally, benzylamine was quantitatively alkylated by cyclohexanol (entry 11). When Rh or Ru-fullerene derivatives were used, the reactions occurred with a remarkably lower yield in comparison to the related Ir derivatives.

Table 2. Amine N-alkylation by hydrogen borrowing.



Entry <sup>a</sup>	Catalyst (mol% Ir)	Product	Conversion (%)
1	[Cp*IrCl <sub>2</sub> ] <sub>2</sub> (5.0)		95
2 <sup>c</sup>	 2 (2.0)	"	93
3	1Ir (1.25)	"	99 (92) <sup>b</sup>
4	1Ir (1.25)		99
5	1Ir (1.25)		91
6	1Ir (1.25)		40
7	[Cp*IrCl <sub>2</sub> ] <sub>2</sub> (4.0)		65
8 <sup>d</sup>	1Ir (4.0)	"	86
9 <sup>d</sup>	[Cp*IrCl <sub>2</sub> ] <sub>2</sub> (2.0)		6
10 <sup>d</sup>	1Ir (2.0)	"	32
11	1Ir (1.25)		99

[a] The reactions are carried out at mmolar scale with 1 eqv. of amine, 1.2 eqv. of alcohol and the same equivalents of K<sub>2</sub>CO<sub>3</sub> as that of the catalyst. [b] Isolated yield. [c] Data reported in the literature.<sup>9</sup> [d] MgSO<sub>4</sub> was used.

In conclusion, although a lot of chemistry has been carried out onto fullerenes, to the best of our knowledge, this is the first time in which fullerene derivatives are directly involved in a catalytic process. In particular, the new C<sub>60</sub>-based catalysts showed their efficiency in fundamental hydrogen transfer reactions such as the reduction of ketones and N-alkylation of amines showing high efficiencies and some important advantages. In particular, those merged from acting as a molecular homogeneous catalyst (defined structures and stereochemical configurations) with those of heterogeneous catalysts (products are easily isolated and the catalyst recovered by mechanical means and reused), when compared to other alternative catalysts.

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## Notes and references

- D. Wang and D. Astruc, *Chem. Rev.*, 2015, **115**, 6621-6686.
- (a) S. Navalon, A. Dhakshinamoorthy, M. Alvaro and H. Garcia, *Chem. Rev.*, 2014, **114**, 6179-6212; (b) D. S. Su, S. Perathoner and G. Centi, *Chem. Rev.*, 2013, **113**, 5782-5816; (c) D. R. Dreyer and C. W. Bielawski, *Chem. Sci.*, 2011, **2**, 1233.
- (a) J. L. Delgado, S. Filippone, F. Giacalone, M. Á. Herranz, B. Illescas, E. M. Pérez and N. Martín, *Top. Curr. Chem.*, 2014, **350**, 1-64; (b) A. Hirsch and M. Brettreich, *Fullerenes: Chemistry and Reactions*, Wiley VCH Weinheim, Germany, 2005; (c) M. Izquierdo, M. R. Cerón, N. Alegret, A. J. Metta-Magaña, A. Rodríguez-Forteza, J. M. Poblet and L. Echegoyen, *Angew. Chem. Int. Ed.*, 2013, **52**, 12928-12931.
- (a) E. E. Maroto, M. Izquierdo, S. Reboredo, J. Marco-Martínez, S. Filippone and N. Martín, *Acc. Chem. Res.*, 2014, **47**, 2660-2670; (b) E. E. Maroto, S. Filippone, M. Suárez, R. Martínez-Álvarez, A. De Cózar, F. P. Cossío and N. Martín, *J. Am. Chem. Soc.*, 2014, **136**, 705-712; (c) J. Marco-Martínez, S. Reboredo, M. Izquierdo, V. Marcos, J. L. López, S. Filippone and N. Martín, *J. Am. Chem. Soc.*, 2014, **136**, 2897-2904; (d) J. Marco-Martínez, V. Marcos, S. Reboredo, S. Filippone and N. Martín, *Angew. Chem. Int. Ed.*, 2013, **52**, 5115-5119; (e) E. E. Maroto, S. Filippone, A. Martín-Domenech, M. Suarez and N. Martín, *J. Am. Chem. Soc.*, 2012, **134**, 12936-12938; (f) K. Sawai, Y. Takano, M. Izquierdo, S. Filippone, N. Martín, Z. Slanina, N. Mizorogi, M. Waelchli, T. Tsuchiya, T. Akasaka and S. Nagase, *J. Am. Chem. Soc.*, 2011, **133**, 17746-17752; (g) E. E. Maroto, A. de Cózar, S. Filippone, Á. Martín-Domenech, M. Suarez, F. P. Cossío and N. Martín, *Angew. Chem. Int. Ed.*, 2011, **50**, 6060-6064; (h) S. Filippone, E. E. Maroto, A. Martín-Domenech, M. Suárez and N. Martín, *Nat. Chem.*, 2009, **1**, 578; (i) E. E. Maroto, M. Izquierdo, M. Murata, S. Filippone, K. Komatsu, Y. Murata and N. Martín, *Chem. Commun.*, 2014, **50**, 740-742.
- J. Marco-Martínez, S. Vidal, I. Fernández, S. Filippone and N. Martín, *Angew. Chem. Int. Ed.*, 2017, **56**, 2136-2139.
- (a) L. A. Oro and C. Claver, eds., *Iridium Complexes in Organic Synthesis*, Wiley-VCH, Weinheim, 2009; (b) M. Kitamura and R. Noyori, in *Ruthenium in Organic Synthesis*, Wiley-VCH Verlag GmbH & Co. KGaA, 2005, DOI: 10.1002/3527603832.ch2, pp. 3-52; (c) Y. Chi, W. Tang and X. Zhang, in *Modern Rhodium-Catalyzed Organic*

*Reactions*, ed. P. A. Evans, Wiley-VCH Verlag GmbH & Co. KGaA, 2005, DOI: 10.1002/3527604693.ch1, pp. 1-31.

7. (a) G. Guillena, D. J. Ramón and M. Yus, *Chem. Rev.*, 2010, **110**, 1611-1641; (b) G. E. Doberiner and R. H. Crabtree, *Chem. Rev.*, 2010, **110**, 681-703; (c) M. H. S. A. Hamid, P. A. Slatford and J. M. J. Williams, *Adv. Synth. Catal.*, 2007, **349**, 1555-1575.

8. K.-i. Fujita, Z. Li, N. Ozeki and R. Yamaguchi, *Tetrahedron Lett.*, 2003, **44**, 2687-2690.

9. A. Wetzel, S. Wöckel, M. Schelwies, M. K. Brinks, F. Rominger, P. Hofmann and M. Limbach, *Org. Lett.*, 2013, **15**, 266-269.